J Incl Phenom Macrocycl Chem (2010) 68:369–379
DOI 10.1007/s10847-010-9796-2

ORIGINAL ARTICLE

Synthesis and metal extraction behavior of pyridine and 1,2,4-triazole substituted calix[4]arenes

Ashok Kumar · Pratibha Sharma · Bhagwan Lal Kalal · Lal Kumar Chandel

Received: 18 February 2010 / Accepted: 28 April 2010 / Published online: 16 May 2010

Abstract Three series of heterocycle substituted calixarenes, derivatized at lower and upper rim, were synthesized and successfully evaluated for metal extraction towards alkali, alkaline, transition and heavy metal ions. The presence and placement of sulfur, heterocycle functionality at upper/lower rim played a crucial role toward the extractability and selectivity of metal ions. The lower rim substituted calixarenes have shown high extractability and poor selectivity. In contrast to this, upper rim substituted calixarenes exhibited good selectivity. Moreover, sulfur functionalized calixarenes have shown better selectivity for heavy metal ions than alkali and alkaline metal ions. Among upper rim substituted calixarenes, **17** and **18** were found to be suitable for Na^+, K^+ and Ag^+, **19,13** for heavy metal ions i.e., Pb^{2+}, Hg^+, Hg^{2+} and Ag^+, and **11,12** for Pb^{2+} and Ag^+ only.

Keywords Calixarenes · Heterocycles · Solvent extraction · Metal extraction

Introduction

Calix[n]arenes play an increasingly important role in host–guest chemistry largely because they provide a well organized platform for the attachment of pendant groups [1, 2]. Numerous ionophores have been synthesized by using this approach i.e., attachment of various ligating functionalities to calixarenes skeleton. These ionophores have unique complexation properties and selectivity [3]. Lower rim substituted calixarene derivative e.g. ester, amide and carbonyl in their cone conformation are selective ligands for Na^+ cations [4], and are used in various sensors. Similarly, 1,3-calix crown ethers in 1,3-alternate conformation are highly selective for K^+ ions [5], while calixcrown-6 shows exceptionally high Cs^+ ion selectivity [6] and used for the extraction of cesium ion from high-salinity nuclear waste [7]. The literature clearly revealed that binding at lower rim via oxygen or nitrogen provides selective extraction of group I and II metal ions. On the other hand, little has been published on the extractive ability of upper rim substituted calixarenes, which comparatively possesses large cavity size and could be effective extractant towards transition and heavy metal ions. Moreover, the type of substituent on calixarene moiety also plays a crucial role towards the metal extraction, in particular, N and S containing heterocycles are well known for metal ligation in coordination chemistry. Bonnamour et al. have reported the extraction properties of derivatized azocalix[4]arenes bearing ester [8], amide [9], bipyridyl [10], and bithiazoyl [11] functionalities. They have shown that the amide derivatives of calixarene are able to complex alkali metal cations, whereas bipyridyl analogue are able to complex soft cations such as zinc. In this perspective, pyridine and triazole heterocycles are quiet known for their basicity and ligation [12–18] with metal ions. Hence, it is possible that when sulfur, ester/amide, heterocyclic functionalities are suitably placed on calixarene skeleton, they would provide a well preorganized coordination sphere for metal binding and hence, enhanced extractability may be attained. Keeping this in mind and in continuation of our research devoted to heterocycles [19, 20] and calixarenes [21–23], we have synthesized upper and lower rim substituted calixarenes by incorporating heterocycles/sulfur/amide functionalities, and explored their potential as metal extractant.

A. Kumar (✉) · P. Sharma · B. L. Kalal · L. K. Chandel
School of Chemical Sciences, Devi Ahilya University, Takshashila Campus, Indore 452 001, India
e-mail: drashoksharma2001@yahoo.com

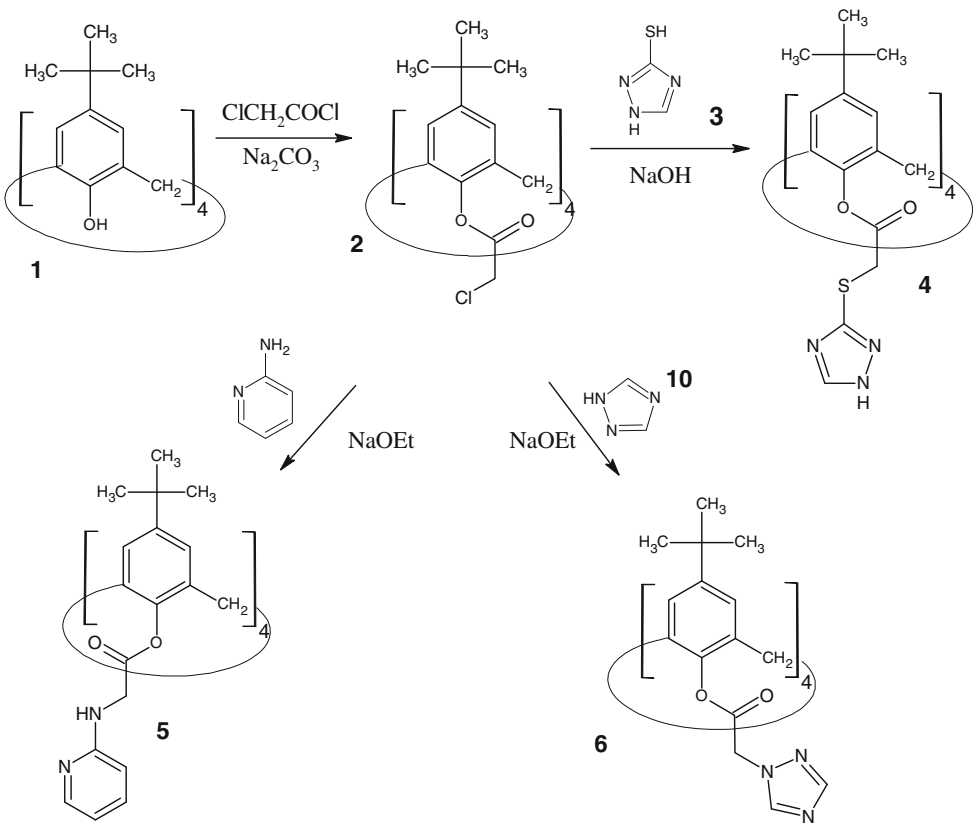
Synthesis

Synthesis of desired calixarenes was accomplished as depicted in Schemes 1, 2 and 3. The calixarene **1** was synthesized by established literature procedure reported by Gutsche et al. [24]. Synthesis of lower rim substituted calixarenes **4,5**,**6** was initiated by the acylation of **1** with chloroacetyl chloride and sodium carbonate (Scheme 1). The conformation of product **2** was confirmed by characteristic pair of doublet at 4.88 and 3.94 ppm for bridged methylene. Reaction of **2** with 2-aminopyridine and 1,2,4-triazole (**10**) in presence of sodium ethoxide yielded **5** and **6,** respectively. Synthesis of **4** was achieved by reaction of **2** with 1,2,4-triazole-3-thiol **(3)**, in presence of NaOH, to maximize the yield of **4** and to limit the synthesis of other products. The accomplishment of these reactions was ascertained by preparative TLC by taking out the reaction mixture time to time. The conformation of **4,5,6** was ascertained cone, as the reactant **2** has cone conformation and the alkyl subsituent i.e., chloroacetyl group at lower rim is large enough to restrict conformation inversion through lower rim. The substitution of chloride at lower rim by heterocycle was ascertained by complete disappearance of peak at 3.67 ppm for CH_2Cl in ^1H NMR spectra.

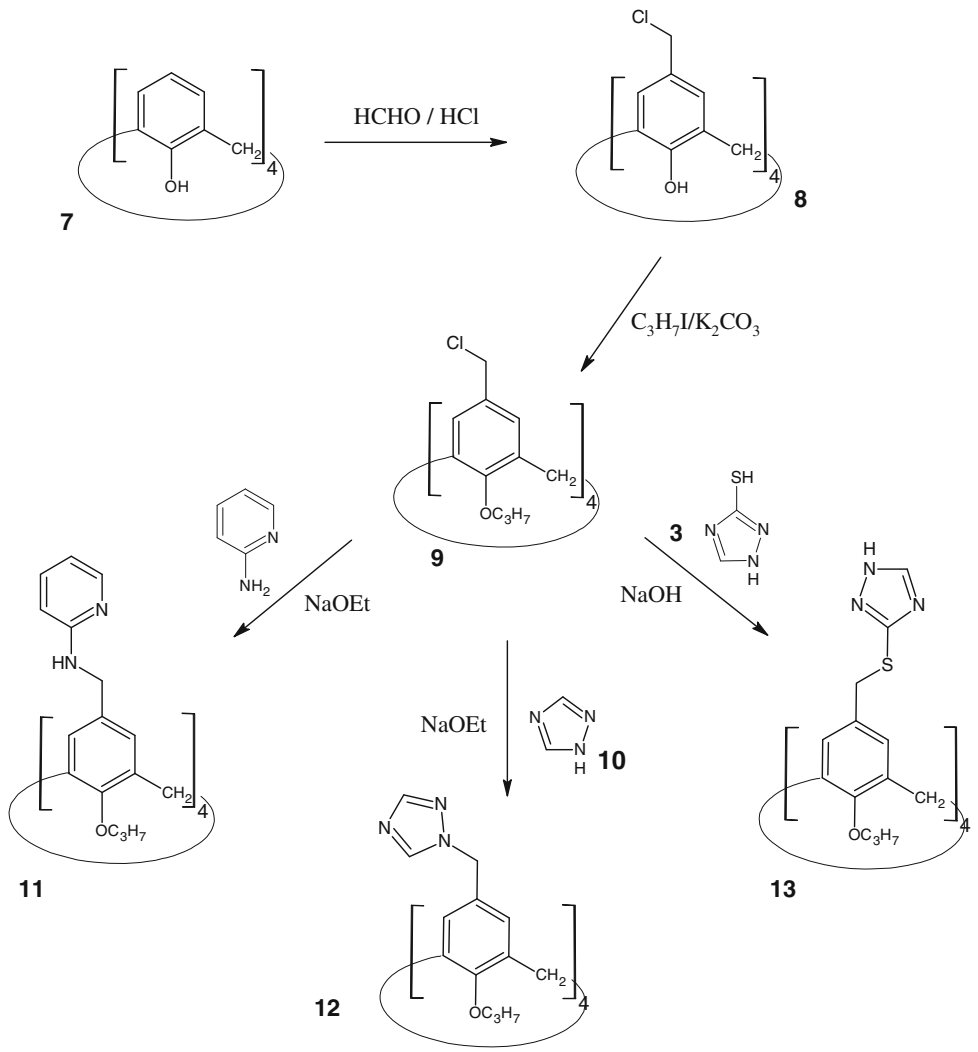
Rest of the calixarene derivatives (**11**,**12**,**13**,**17**,**18**,**19**) are upper rim derivatized and their syntheses were initiated by dealkylating **1** with phenol and $AlCl_3$ to afford **7** as starting material (Scheme 2). Complete debutylation was confirmed by the absence of peak at 0.98 ppm in its ^1H NMR spectrum. The compound **7** was chloromethylated at para position by HCHO and HCl in presence of glacial acetic acid and H_3PO_4 to yield **8**. In IR spectrum of **8**, a strong band at 684 cm^{-1} for C–Cl stretching, while in ^1H NMR spectrum a singlet at 3.67 ppm with area correspond to 8H has confirmed the tetra substitution. Calixarene **8** was subjected to tetra alkylation at lower rim by K_2CO_3 and propyl iodide to afford **9**. From this, calixarenes **11**, **12** were synthesized by nucleophilic substitution of chloride with 2-aminopyridine and 1,2,4-triazole **(10)** using sodium ethoxide as base, while **13** was synthesized by 1,2,4-triazole-3-thiol **(3)** and NaOH (Scheme 2).

Synthesis of upper rim substituted calixarenes **17**,**18**, and **19** was initiated by lower rim alkylation of **7** with propyl iodide and sodium hydride to obtain **14** (Scheme 3). It was subjected to Friedel Craft acylation at para position by acetylchloride and aluminum chloride in dichloromethane. The acetyl group of **15** was oxidized to carboxylic group by bromine and sodium hydroxide in DMF. Resultant **16** was treated with equivalent amount of thionyl chloride followed by 2-aminopyridine, 1,2,4-triazole (**10**) and 1,2,4-triazole-3-thiol (**3**) to yield **17, 18,** and **19**, respectively. To maximize the yield and to force the

Scheme 1 An overview of synthetic strategy for lower rim substituted calix[4]arenes **4,5,6**



Scheme 2 An overview of synthetic strategy for upper rim substituted calix[4]arenes **11,12,13**



reaction in forward direction, the reaction was performed in the presence of sodium hydroxide. Tetra substitution was confirmed by molecular ion peak in FAB mass spectra. The conformation of **17,18,** and **19** was assigned cone by characteristic peak for methylene bridge.

Solvent extraction

A chloroform solution (10 mL) of ligand (1×10^{-3} M) and an aqueous solution (10 mL) containing 2×10^{-5} M picric acid and 1×10^{-2} M metal salts (chloride, nitrate, hydroxide, carbonate) were stirred at 298 K for 10 min contact time. An aliquot of the aqueous solution was withdrawn, and the UV spectrum was recorded. A similar extraction was performed in the absence of ligand. The extractability of the metal cations was calculated by taking into account the valency of metal ion, using following equation:

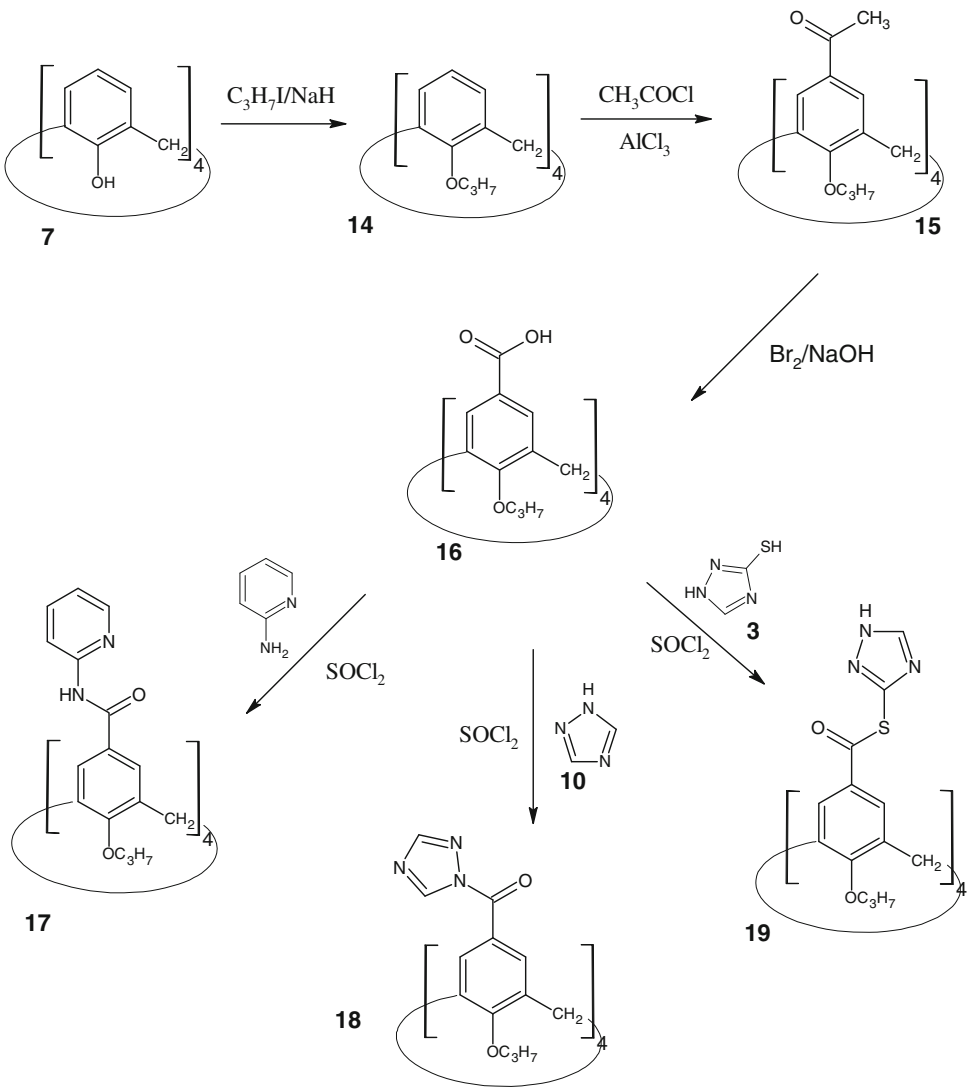
$$\text{Extractability}(\%) = 100(A_0 - A)/A_0$$

where A_0 and A are the absorbance in the absence and presence of ligand.

Results and discussion

The heterocyclic compounds are very well known for complexation of metal ions, especially, pyridine/triazole are quite good ligand for the metal complexation. Hence, with a view to observe the effects of heterocycles, sulfur, ester, and carbonyl functionality on metal extraction behavior, various lower and upper rim substituted calixarene derivatives **4-19** (Schemes 1, 2 and 3) were synthesized. In this perspective, a range of metal ions; alkali, alkaline, transition and heavy metal ions were taken into consideration and their extractability towards all the calixarenes have been evaluated by mean of solvent extraction of their metal picrates from aqueous to organic phase. Calix **4, 5, 6** are lower rim heterocyclic substituted

Scheme 3 An overview of synthetic strategy for upper rim substituted calix[4]arenes **17,18,19**



derivatives, whereas rest are upper rim substituted. All the synthesized calixarenes have multiple interacting sites viz., sulfur, ester, amide, carbonyl, and heterocycles, with different cavity size at their interacting sites. Among synthesized calixarenes, calix **4** has shown extractability towards all metal ions (Table 1), except Mg^{2+}, As^{3+}, Pb^{2+}, and Hg^{+}. These metal ions are either too small or too large to fit into the calixarene cavity and hence not extracted by calix **4**. In accordance, calix **4** has shown low extraction for K^{+} ions owing to big size of latter to fit lower rim of former. Surprisingly, though the Hg^{+} and Ag^{+} metal ions have similar size but they differ a lot in extractability ($Hg^{+} = 0$, $Ag^{+} = 60\%$). It can be explained by the fact that at lower rim, as we move from rim to ester, sulfur and towards the end of substituent, the cavity size become smaller, successively and at sulfur functionality, where Hg^{+} ion interact, cavity size is small to fit Hg^{+} ions. On the other hand, Ag^{+} ions interact with ester functionality where the cavity size of calixarene is large enough to fit it. The extractive ability of **5** is similar as **4**, but it shows zero extractability for heavy metal ions due to the absence of sulfur functionality, which could have responsible for interaction of calix **5** with heavy metal ions. The extractability of **5** for Na^{+} and Ca^{2+} is slightly higher than **4**, due to the presence of suitably placed NH group, which provide well preorganized cavity through hydrogen bonding for interaction of metal ions with carbonyl group of ester functionality. The extractability of **5** for transition metal ions is lower than **4** and **6**, which suggests that triazole is better complexing functionality than pyridine. The extractability trend of **6** is similar to **5**, but it shows low extractability for Na^{+} and Ca^{2+}, attributable to the absence of hydrogen bonding to provide well preorganized cavity for proper fit at lower rim. The calixarene **17** and **18** are quite selective towards the extraction of Na^{+}, K^{+}, Ca^{2+} and Ag^{+} metal ions. The low extractability for these metal ions in comparison to **4, 5,** and **6** is a result of expansion of cavity size at upper rim. On the other hand, **17** and **18** have shown

Table 1 Percentage extraction of alkali, alkaline earth, transition and heavy metal picrates into $CHCl_3$ at 25 °C

Metal	Calixarenes								
	4	5	6	17	18	19	11	12	13
Na^+	98.0	99.9	92.1	43.2	16.2	1.3	2.2	1.6	2.2
K^+	5.1	0.5	1.1	86.5	65.3	2.1	2.9	1.4	2.3
Mg^{++}	0.3	0.3	0.6	1.1	0.4	1.6	3.1	1.9	1.8
Ca^{++}	79.9	89.2	79.2	37.8	12.1	3.3	1.5	1.1	1.4
As^{+++}	1.1	0.6	0.7	1.2	1.2	2.5	2.6	1.7	2.9
Fe^{++}	12.1	0.4	0.1	0.9	0.4	1.2	1.5	1.3	2.4
Co^{++}	73.3	61.4	59.8	3.1	1.6	1.6	1.9	1.4	2.1
Ni^{++}	64.2	51.9	55.2	1.5	1.8	3.4	2.2	2.5	3.1
Cu^{++}	81.0	72.1	74.8	0.5	2.1	2.9	1.7	1.6	2.2
Zn^{++}	86.8	81.0	84.2	2.1	2.5	1.2	1.9	2.1	2.8
Pb^{++}	0.2	0.3	1.1	1.4	1.2	80.8	52.1	57.5	78.0
Hg^{++}	67.2	0.1	1.8	0.8	3.1	54.1	1.4	1.7	68.9
Cd^{++}	69.2	1.5	0.6	3.5	1.2	0.6	1.2	1.3	1.7
Pd^{++}	75.3	1.1	2.1	2.5	1.8	0.3	1.8	1.6	1.0
Hg^+	0.1	0.2	1.6	1.4	0.9	96.1	1.4	1.9	86.8
Ag^+	60.1	0.8	2.1	51.0	37.2	74.9	36.1	40.3	52.1

no extractability for heavy metal ions due to the absence of sulfur functionality in their structure. These derivatives have shown good extractability for K^+, Na^+, Ag^+ and Ca^{2+}, in comparison to transition metal ions. The quite promising reason for this, K^+, Ca^{2+}, Na^+ and Ag^+ interact at carbonyl functionality of amide (Fig. 4), where the cavity size is appropriate for complexation. On the other hand, transition metal ions interact primarily with heterocyclic functionality, at the end of pendant group, where cavity expansion is maximum (Fig. 4) and hence, calixarene could not provide a proper fit for metal complexation. Due to the presence of sulfur and large cavity size at upper rim, calixarenes **19** and **13** have shown extractability for heavy metal ions (Pb^{2+}, Hg^{2+}, Hg^+, Ag^+). In contrast to this, they have exhibited no extractability for alkali/alkaline metal ions, attributable to the absence of ester/amide functionality on calixarene skeleton. A different trend of extractability has been observed for compound **11** and **12**. These derivatives are quite selective toward Pb^{2+} and Ag^+ ions. Large cavity size and absence of sulfur, ester and amide functionality in **11** and **12** allows selective extraction of Pb^{2+} and Ag^+ ions only. A comparative view of metal extractive ability and interaction of various substituted calixarenes towards metal ions is depicted in Figs. 1, 2, 3 and 4.

Conclusion

In summary, we have synthesized new heterocycle substituted calixarene derivatives and performed solvent extraction studies with alkali, alkaline earth, transition, and heavy metal ions. The effect of S, N, ester, and heterocyclic functionality in calixarene has been carefully envisaged for extraction purpose. Lower rim substituted calixarenes found to be effective extractant towards alkali, alkaline and transition metal ions, but have lack of selectivity. In contrast to this, upper rim substituted calixarenes exhibited good selectivity. Among these, **17** and **18** were found to be suitable for Na^+, K^+ and Ag^+, **19,13** for heavy metal ions i.e., Pb^{2+}, Hg^+, Hg^{2+} and Ag^+, and **11,12** for Pb^{2+} and Ag^+ ions, only. This study would be useful for multiple applications in laboratory, environmental, pharmaceutical, and industrial processes for the determination and extraction of various metal ions using two-phase solvent extraction.

Experimental

Reagents and apparatus

All the chemicals used were of AR grade purity. IR spectra were recorded on Perkin Elmer model 377 spectrophotometer in KBr pellets. ^{1}HNMR spectra were recorded on a

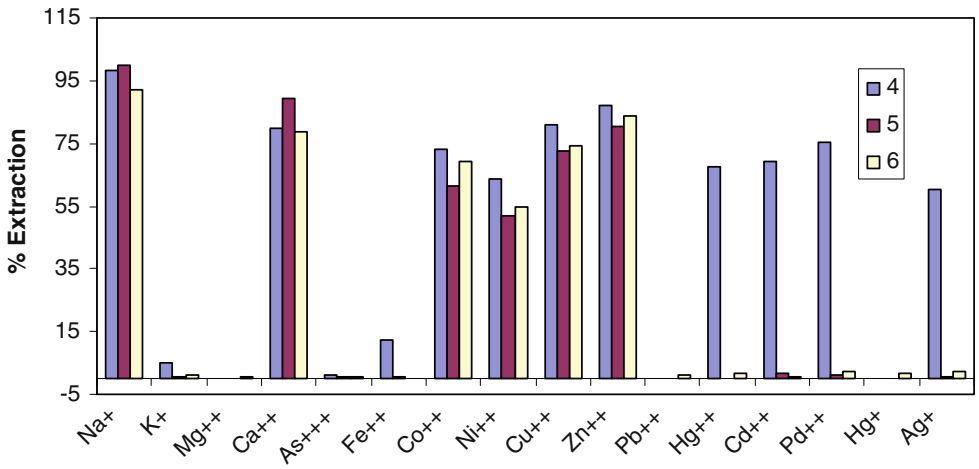


Fig. 1 A comparative overview of metal extracting ability of **4**,**5**,**6** towards metal ions

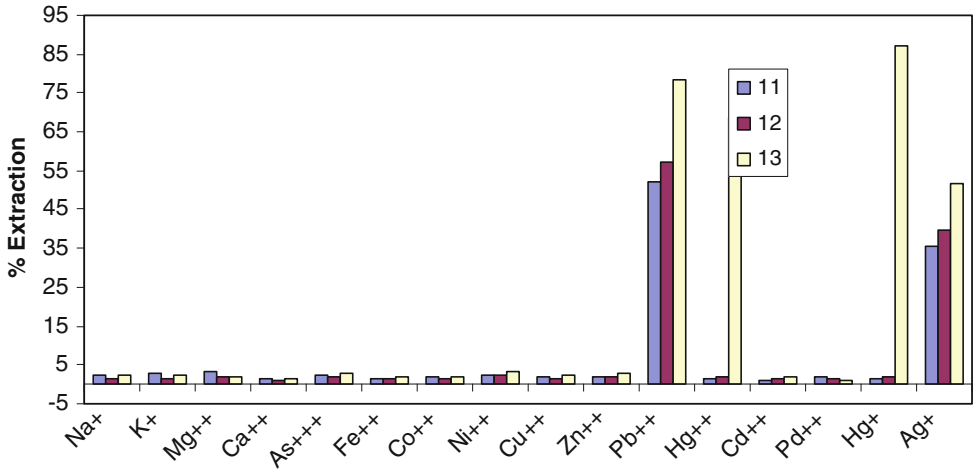


Fig. 2 A comparative overview of metal extracting ability of **11**,**12**,**13** towards metal ions

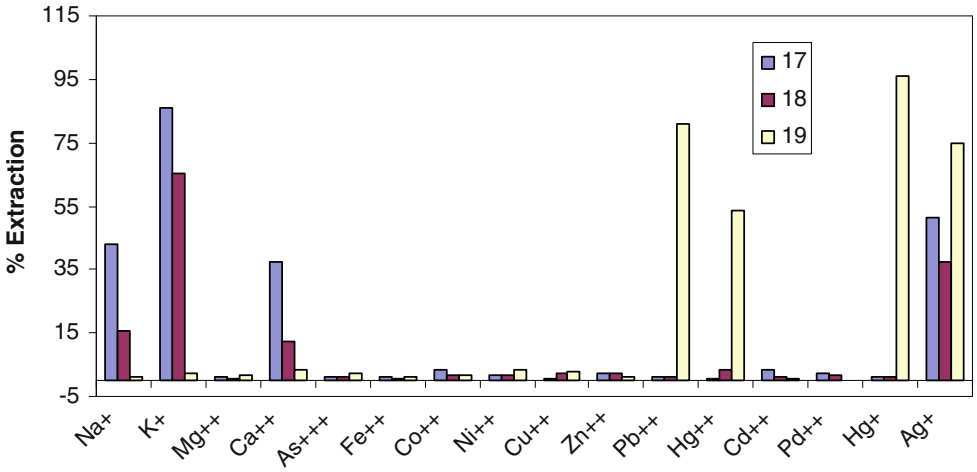


Fig. 3 A comparative overview of metal extracting ability of **17**,**18**,**19** towards metal ions

Bruker DRX300 MHz instrument. The FAB mass spectra were recorded on a JEOLSX102/DA-6000 Mass Spectrometer using Argon/Xenon (6 kV, 10 mA) as the FAB gas. Analytical thin layer chromatography was performed using E. Merck silica gel G, 0.50 mm plates (Merck No. 5700). The melting points were determined on an electric melting point apparatus in open capillaries.

25,26,27,28-Tetrahydroxy-*p*-*tert*-butylcalix[4]arene **(1)**

It was synthesized by literature procedure [24]. m.p. 338 °C. IR $\left[\nu_{max}^{KBr}(cm^{-1})\right]$: 3172 (-OH); ^{1}HNMR [$CDCl_3$ (δ ppm)] : 0.98(s, 36H, $-C(CH_3)_3$), 3.86 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.49 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.12 (m, 8H, Ar–H), 10.25 (s, 4H, ArOH); FAB MS, *m/z*: 648 (M^+); Anal calc.(%) for $C_{44}H_{56}O_4$: C, 81.44; H, 8.70; Found C, 81.12; H, 8.62.

25,26,27,28-Tetra[(chloroacetyl)oxy]-*p*-*tert*-butylcalix[4]arene **(2)**

1 (14.8 g, 20 mmol) was dispersed in 200 mL dry tetrahydrofuran and treated with sodium carbonate (6.35 g, 60 mmol) followed by 4.8 mL (60 mmol) of chloroacetyl chloride. The reaction was carried out at room temperature for 1 h. After the completion of reaction, the mixture was distributed between chloroform and 1 N HCl (100/50 mL). The chloroform extract was washed with water (about 100 mL) and dried over $MgSO_4$. The chloroform evaporation afforded a crude product, which was recrystallized by ethanol to yield a pure product **2**. Yield 15.0 g (79%), m.p. 222 °C.

IR $\left[\nu_{max}^{KBr}(cm^{-1})\right]$: 1750 (C=O); ^{1}HNMR [$CDCl_3$ (δ ppm)] : 0.94 (s, 36H, $-C(CH_3)_3$), 3.67 (s, 8H, CO–CH_2–Cl), 3.94 (d, 4H, Ar–CH_2–Ar, J = 12.6 Hz), 4.88 (d, 4H, Ar–CH_2–Ar, J = 12.6 Hz), 7.19 (m, 8H, Ar–H); FAB MS, *m/z*: 954 (M^+); Anal calc.(%) for $C_{52}H_{60}O_8Cl_4$: C, 65.41; H, 6.33; Found C, 65.01; H, 6.27

1H-1,2,4-Triazole-3-thiol **(3)**

It was synthesized as per the literature procedure [25]. Yield 2.8 g (70%), m.p. 220 °C.

IR $\left[\nu_{max}^{KBr}(cm^{-1})\right]$: 2700–2900 (N–H); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 7.1 (S, H, SH), 8.32 (s, H, –NH–C<u>H</u>=N), 13.5 (s, H,

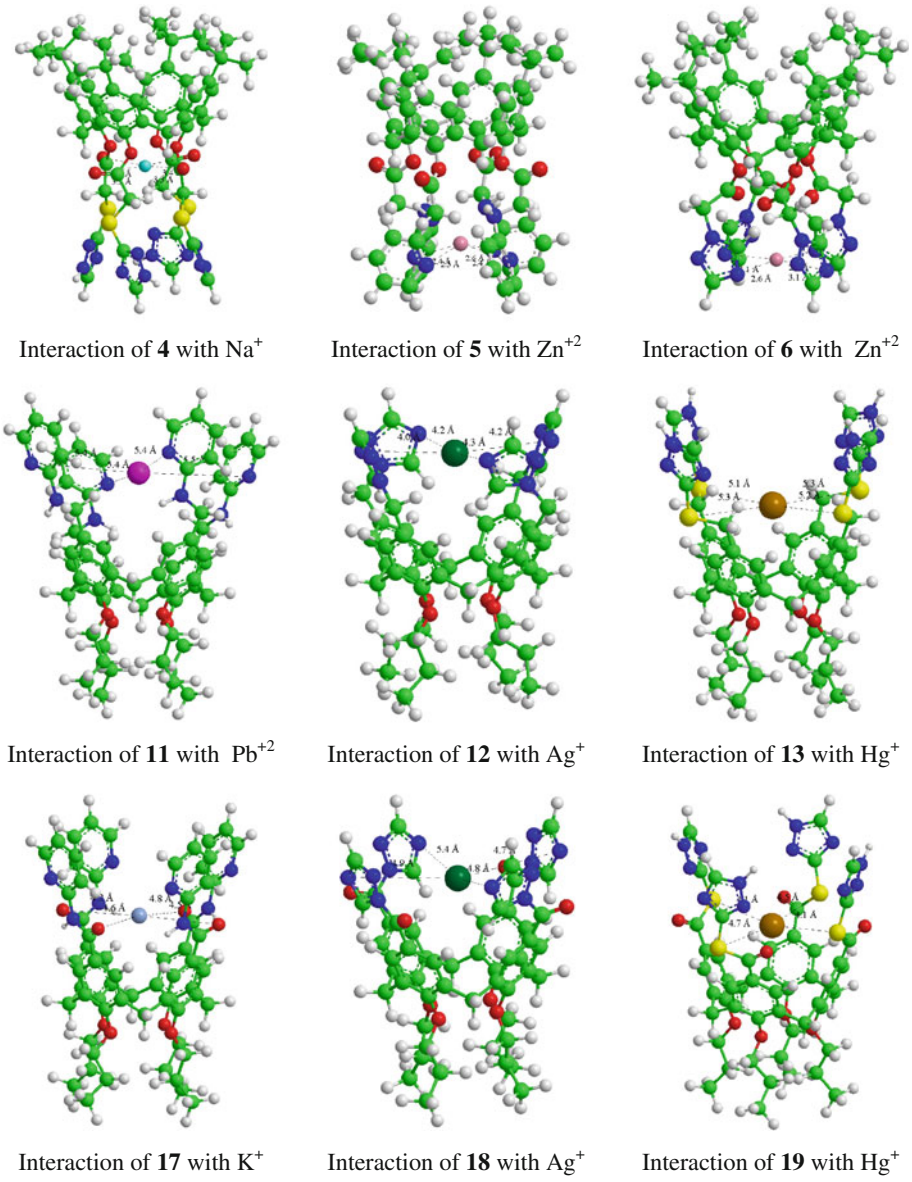


Fig. 4 Interaction of various calixarene derivatives with best fit metal ion

N–NH–CH); FAB MS, *m/z*: 101 (M^+); Anal calc.(%) for $C_2H_2N_3S$: C, 23.75; H, 5.65; S, 31.71; Found C, 23.66; H, 5.61; S, 31.61.

25,26,27,28-Tetra{[(1*H*-1,2,4-triazol-3-ylsulfanyl)acetyl]oxy}-*p*-*tert*-butylcalix[4]arene **(4)**

Thiol **3** (2.02 g, 20 mmol) was dispersed in 100 mL of dry tetrahydrofuran and treated with NaOH (0.8 g, 20 mmol) followed by 0.95 g (1 mmol) of **2** was added. The reaction was carried out at reflux temperature for 12 h. Reaction was monitored by preparative TLC (ethylacetate/xylene, 1:20). After the completion of reaction, the reaction mixture was distributed to the chloroform/diluted aqueous HCl (25/50 mL) mixture. The chloroform extract was washed with water (about 50 mL) and dried over $MgSO_4$. The solvent evaporation afforded a crude mass, which was purified by column chromatography (Alumina column; neutral); gradient of chloroform/acetone (20/1 to 3/1). Yield 0.97 g (68%), m.p. 214 °C.

IR $\left[\nu_{max}^{KBr}(cm^{-1})\right]$: 2700–2900 (N–H), 1746 (CO–O–Ar); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 1.05 (s, 36H, –$C(CH_3)_3$), 2.50 (s, 8H, CO–CH_2–S), 3.88 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.36 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.25 (m, 8H, Ar–H), 8.29 (s, 4H, –NH–CH=N), 13.02 (s, 4H, N–NH–CH); FAB MS, *m/z*: 1213 (M^+); Anal calc.(%) for $C_{60}H_{68}N_{12}O_8S_4$: C, 59.38; H, 5.65; N, 13.85; S, 10.57; Found C, 59.15; H, 5.61; N, 13.78; S, 10.51.

25,26,27,28-Tetra{[(pyridin-2-ylamino)acetyl]oxy}-*p*-*tert*-butylcalix[4]arene **(5)**

2-amino pyridine (1.86 g, 20 mmol) was dissolved in 100 mL of dry tetrahydrofuran and treated with freshly prepared sodium ethoxide (1.36 g, 20 mmol) followed by 0.95 g (1 mmol) of **2** was added. The reaction was carried out at reflux temperature for 16 h. Reaction was monitored by preparative TLC (ethylacetate/xylene, 1:20). After the completion of reaction, excess of sodium ethoxide was quenched with water (about 20 mL) and reaction mixture distributed to the chloroform/diluted aqueous 1 N HCl (50/25 mL). The chloroform extract was washed with water (about 50 mL) and dried over $MgSO_4$. The solvent evaporation afforded a crude mass, which was purified by column chromatography (Alumina column; neutral); gradient of chloroform/acetone (20/1 to 3/1). Yield 0.64 g (55%), m.p. 189 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 1742 (CO–O–Ar), 3254 (N–H); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 0.96 (s, 36H, –$C(CH_3)_3$), 2.89 (s, 8H, CO–C<u>H</u>$_2$–NH), 3.91 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.14 (s, 4H, Ar–N<u>H</u>–CH_2), 4.36 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 6.59 (m, 4H, N=CH–C<u>H</u>), 6.75 (dd, 4H, N–C(NH)=C<u>H</u>), 7.06 (m, 8H, Ar–H), 7.36 (m, 4H, N–C(NH)=CH–C<u>H</u>), 8.11 (m, 4H, N=C<u>H</u>–CH); FAB MS, *m/z*: 1185 (M^+); Anal calc.(%) for $C_{72}H_{80}N_8O_8$: C, 72.95; H, 6.80; N, 9.45; Found C, 72.55; H, 6.71; N, 9.39.

25,26,27,28-Tetra[(1*H*-1,2,4-triazol-1-ylacetyl)oxy]-*p*-*tert*-butylcalix[4]arene **(6)**

It was synthesized by treating 1,2,4-triazole and **2**, as per the procedure for **5**. Yield 0.66 g (61%), m.p. 206 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 1741 (CO–O–Ar); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 0.88 (s, 36H, –$C(CH_3)_3$), 2.89 (s, 8H, CO–CH_2–N), 3.67 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.36 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.25 (m, 8H, Ar–H), 8.15 (s, 8H, N–C<u>H</u>=N); FAB MS, *m/z*: 1085 (M^+); Anal calc.(%) for $C_{60}H_{68}N_{12}O_8$: C, 66.40; H, 6.32; N, 15.49; Found C, 66.13; H, 6.26; N, 15.39.

25,26,27,28-Tetrahydroxycalix[4]arene **(7)**

It was synthesized as per the literature procedure [26]. Yield 68%, m.p. 298 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 3168 (–OH); ^{1}HNMR [$CDCl_3$ (δ ppm)] : 3.86 (d, 4H, Ar–CH_2–Ar, J = 12.7 Hz), 4.58 (d, 4H, Ar–CH_2–Ar, J = 12.7 Hz), 7.22 (m, 8H, Ar–H), 10.39 (s, 4 H, ArOH); FAB MS, *m/z*: 424 (M^+); Anal calc.(%) for $C_{28}H_{24}O_4$: C, 79.22; H, 5.70; Found C, 78.88; H, 5.65.

25,26,27,28-Tetrahydroxy-*p*-chloromethylcalix[4]arene **(8)**

A solution of calix[4]arene **7** (3.54 g, 8.35 mmol), paraformaldehyde (5.30 g, 175 mmol), glacial acetic acid (56 mL), conc. H_3PO_4 (60 mL), and conc. HCl (63 mL) in dioxane (200 mL) was stirred at 80 °C for 12 h. The mixture was concentrated to 100 mL, poured into an ice/water mixture (200 mL) and extracted with $CHCl_3$ (3 × 40 mL). The combined organic layer was washed with H_2O, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give **8**. Yield 4.38 g (85%), m.p. 215 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 3172 (–OH), 684 (C–Cl); ^{1}HNMR [$CDCl_3$ (δ ppm)] : 3.67 (s, 8H, Ar–CH_2–Cl), 3.86 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.49 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.1 (m, 8H, Ar–H), 10.25 (s, 4H, ArOH); FAB MS, *m/z*: 618 (M^+); Anal calc.(%) for $C_{32}H_{28}Cl_4O_4$: C, 62.15; H, 4.56; Found C, 61.89; H, 4.51.

25,26,27,28-Tetrapropoxy -*p*-chloromethylcalix[4] arene **(9)**

A total of 6.18 g (10.0 mmol) of **8** was dissolved in anhydrous acetone followed by 21 g (200 mmol) of K_2CO_3 and 34 g (200 mmol) of 1-iodopropane were added. The reaction mixture was heated for 24 h at reflux temperature followed by cooled at room temperature and filtered. The filtrate was diluted with water and extracted with chloroform. The organic layer was dried over $MgSO_4$ and concentrated to dryness. The residual solid was subjected to column chromatography [silica gel, $CHCl_3$/acetone (15/1 to 2/1)]. Yield 6.7 g (85%), mp 189–190 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 675 (C–Cl); ^{1}HNMR [$CDCl_3$ (δ ppm)] : 0.81(t, 8H, CH_2–CH_2–<u>CH_3</u>), 1.18 (m, 8H, CH_2–<u>CH_2</u>–CH_3), 3.52 (t, 8H, O–<u>CH_2</u>–CH_2), 3.71 (s, 8H, Ar–CH_2–Cl), 3.81 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.44 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.09 (m, 8H, Ar–H); FAB MS, *m/z*: 786 (M^+); Anal calc.(%) for $C_{44}H_{52}Cl_4O_4$: C, 67.18; H, 6.66; Found $C_{44}H_{52}Cl_4O_4$: C, 66.87; H, 6.59.

1*H*-1,2,4-Triazole **(10)**

It was synthesized as per the literature procedure [25]. Yield 2.76 g (55%), m.p. 120 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 2700-2900 (N–H); ^{1}HNMR [$CDCl_3$ (δ ppm)] : 8.32 (s, 2H, –NH–C<u>H</u>=N), 13.42 (s, H, N–N<u>H</u>–CH); FAB MS, *m/z*: 69 (M^+); Anal calc.(%) for $C_2H_3N_3$: C, 34.78; H, 4.38; N, 60.84; Found C, 29.63; H, 4.34; N, 60.62.

25,26,27,28-Tetrapropoxy-*p*-(pyridn-2-ylamino)methylcalix[4]arene **(11)**

It was synthesized by reacting **9** with 2-amino pyridine, as per the procedure for **5**. Yield (60%), m.p. 222 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 3280 (N–H); ^{1}HNMR [$CDCl_3$ (δ ppm)] : 0.85 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.25 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 3.15 (s, 8H, Ar–CH_2–NH), 3.67 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.91 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.14 (s, 4H, Ar–$\underline{NH}$–CH_2), 4.35 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 6.59 (m, 4H, N = CH–$\underline{CH}$), 6.75 (dd, 4H, N–C(NH)=$\underline{CH}$), 7.06 (m, 8H, Ar–H), 7.36 (m, 4H, N–C(NH)=CH–$\underline{CH}$), 8.02 (m, 4H, N=$\underline{CH}$–CH); FAB MS, *m/z*: 1017 (M^+); Anal calc.(%) for $C_{64}H_{72}N_8O_4$: C, 75.56; H, 7.13; N, 11.01; Found C, 75.24; H, 7.01; N, 10.92.

25,26,27,28-Tetrapropoxy-*p*-(1*H*-1,2,4-triazol-1-yl)methylcalix[4]arene **(12)**

It was synthesized by reacting **9** with 1,2,4-triazole, as per the procedure for **5**. Yield (58%), m.p. 219 °C.

^{1}HNMR [$CDCl_3$ (δ ppm)] : 0.88 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.21 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 2.89 (s, 8H, Ar–CH_2–N), 3.57 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.83 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.36 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.17 (m, 8H, Ar–H), 8.14 (s, 8H, N–$\underline{CH}$=N); FAB MS, *m/z*: 917 (M^+); Anal calc.(%) for $C_{52}H_{60}N_{12}O_4$: C, 68.10; H, 6.59; N, 18.33; Found C, 67.81; H, 6.51; N, 18.22.

25,26,27,28-Tetrapropoxy-*p*-(1*H*-1,2,4-triazol-1-ylsulfanyl)methylcalix[4] arene **(13)**

It was synthesized by reacting **9** with 1,2,4-triazole-3-thiol, as per the procedure for **4**. Yield 54% m.p. 235 °C.

^{1}HNMR [$CDCl_3$ (δ ppm)] : 0.84 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.15 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 2.38 (s, 8H, Ar–CH_2–S), 3.60 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.91 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.33 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.11 (m, 8H, Ar–H), 8.38 (s, 4H, –NH–$\underline{CH}$=N), 13.02 (s, 4H, N–$\underline{NH}$–CH); FAB MS, *m/z*: 1045 (M^+); Anal calc.(%) for $C_{52}H_{60}N_{12}O_4S_4$: C, 59.74; H, 5.79; N, 16.08; S, 12.27; Found C, 59.49; H, 5.72; N, 15.89; S, 12.16.

25,26,27,28-Tetrapropoxycalix[4]arene **(14)**

To a suspension of 4 g of NaH (100 mmol; washed with 3 × 90 mL of hexane) in 250 mL of anhydrous THF, 4.24 g of **7** (10 mmol) was added. The reaction mixture was stirred for 10 min at reflux temperature, followed by 1-iodopropane (17 g, 100 mmol) was added. The reaction mixture was stirred for an additional 1 h at reflux temperature, cooled to room temperature, and then quenched by the dropwise addition of 7 mL of methanol. After the removal of solvent under reduced pressure, 300 mL of water was added followed by stirred additional 5 min. The solid organic product was separated, washed with methanol (3 × 100 mL) and recrystallized from acetone. Yield 4.68 g (79%), m.p. 165 °C.

^{1}HNMR [$CDCl_3$ (δ ppm)]: 0.86 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.18 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 3.52 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.79 (d, 4H, Ar–CH_2–Ar, J = 12.7 Hz), 4.52 (d, 4H, Ar–CH_2–Ar, J = 12.7 Hz), 6.92 (m, 12H, Ar–H); FAB MS, *m/z*: 592 (M^+); Anal calc.(%) for $C_{40}H_{48}O_4$: C, 81.04; H, 8.16; Found C, 80.64; H, 8.11.

25,26,27,28-Tetrapropoxy-*p*-acetylcalix[4]arene **(15)**

In a 250 mL round bottomed flask, aluminum chloride (5.13 g, 38.4 mmol) was added to 100 mL of CH_2C1_2, followed by acetyl chloride (24.95 g, 108 mmol). To this, 4.15 g (7 mmol) of **14,** dissolved in 70 mL CH_2C1_2, was added dropwise with stirring and then the reaction mixture stirred for 5 h at room temperature. After that, 30 mL of water followed by 34.65 mL of 1 N HC1 was added and product was extracted with 150 mL of CH_2C1_2. The CH_2C1_2 layer was separated, evaporated and obtained solid was purified with column chromatography (300 g silica gel, gradient of $CHCl_3$/acetone (20/1 to 3/1). Yield 2.4 g (45%), m.p.195 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 1710 (C=O); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 0.79 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.16 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 2.22 (m, 12H, CO–CH_3), 3.57 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.86 (d, 4H, Ar–CH_2–Ar, J = 13.5 Hz), 4.49 (d, 4H, Ar–CH_2–Ar, J = 13.5 Hz), 7.14 (m, 8H, Ar–H); FAB MS, *m/z*: 760 (M^+); Anal calc.(%) for $C_{48}H_{56}O_8$: C, 75.76; H, 7.42; Found C, 75.51; H, 7.35.

25,26,27,28-Tetrapropoxy-*p*-carboxycalix[4]arene **(16)**

A fresh sodium hypobromite solution, prepared by adding 30.46 mg (191 mmol) of Br_2 to 77 mL of aqueous NaOH solution (23%), was cooled to 0 °C. To this, 2.28 g (3 mmol) of **15** (dissolved in 350 mL of DMF) was added slowly within 30 min. By adding subsequent 200 mL of DMF, it was heated for 18 h at 80 °C. It was then cooled to room temperature and quenched with 517 mL of 1 M HC1. A solvent extraction was performed with 3 × 500 mL of $CHCl_3$. The chloroform layer was collected and evaporated under reduced pressure by heating. The obtained residue was washed by 3 × 200 mL of water and purified by column chromatography; (300 g silica gel, $CHC1_3$/MeOH/H_2O (65/25/4). Colorless solid of **16** was obtained. Yield 1.3 g (33%), m.p. 205 °C.

IR $[\nu_{max}^{KBr}(cm^{-1})]$: 2700 (COOH); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 0.80 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.18 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 3.53 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.86 (d, 4H, Ar–CH_2–Ar, J = 12.9 Hz), 4.57 (d, 4H, Ar–CH_2–Ar,

J = 12.9 Hz), 7.48 (m, 8H, Ar–H), 12.05 (m, 4H, COOH); FAB MS, *m/z*: 842 (M^+); Anal calc.(%) for $C_{44}H_{44}Cl_4O_8$: C, 62.72; H, 5.26; Found C, 62.32; H, 5.22.

25,26,27,28-Tetrapropoxy-*p*-(pyridn-2-yl)carbonylcalix[4]arene **(17)**

In a 250 cc round bottomed flask, 0.84 g (1 mmol) of **16** was taken followed by 0.6 mL (5 mmol) of $SOCl_2$ was added. The reaction mixture was stirred for 15 min at room temperature. Now, the reaction mixture was suspended into 100 mL THF followed by 0.8 g (20 mmol) of NaOH and 1.88 g (20 mmol) of 2-aminopyridine was added. The reaction mixture was refluxed for 20 h and reaction was monitored by TLC (ethylacetate/xylene, 1:10). After the completion of reaction, the remaining THF was removed under reduced pressure by heating. The residue was distributed between chloroform/diluted aqueous 1 N HCl (100/50 mL). The chloroform layer was separated and evaporated to dryness. Obtained residue was purified by column chromatography (Alumina column; neutral); gradient of $CHCl_3$/acetone (20/1 to 3/1). Yield 0.73 g (58%), m.p. 192 °C.

IR $\left[\nu_{max}^{KBr}(cm^{-1})\right]$: 3280 (N–H), 1738 (CONH); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 0.87 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.19 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 3.67 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.94 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.16 (s, 4H, Ar–N$\underline{H}$–CO), 4.36 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 6.59 (m, 4H, N=CH–C$\underline{H}$), 6.75 (dd, 4H, N–C(NH)=C$\underline{H}$), 7.14 (m, 8H, Ar–H), 7.44 (m, 4H, N–C(NH)=CH–$\underline{CH}$), 8.08 (m, 4H, N=C$\underline{H}$–CH); FAB MS, *m/z*: 1331 (M^+); Anal calc.(%) for $C_{78}H_{78}N_{10}O_{11}$: C, 70.36; H, 5.90; N, 10.52; Found C, 70.11; H, 5.86; N, 10.47.

25,26,27,28-Tetrapropoxy-*p*-(*1H*-1,2,4-triazol-1-yl)carbonylcalix[4]arene **(18)**

It was synthesized by reacting **16** with thionyl chloride followed by 1,2,4-triazole, as per the procedure for **17**. Yield (65%), m.p. 232 °C.

IR $\left[\nu_{max}^{KBr}(cm^{-1})\right]$: 1738 (CONH); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 0.84 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.21 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 3.35 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.67 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.33 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.22 (m, 8H, Ar–H), 8.20 (s, 8H, N–C$\underline{H}$=N); FAB MS, *m/z*: 973 (M^+); Anal calc.(%) for $C_{52}H_{52}N_{12}O_8$: C, 64.19; H, 5.39; N, 17.27; Found C, 63.85; H, 5.52; N, 17.18.

25,26,27,28-Tetrapropoxy-*p*-(1*H*-1,2,4-triazol-3-ylsulfanyl)carbonylcalix [4]arene **(19)**

It was synthesized by reacting **16** with thionyl chloride followed by 1,2,4-triazole-3-thiol, as per the procedure for **17**. Yield (60%), m.p. 212 °C.

IR $\left[\nu_{max}^{KBr}(cm^{-1})\right]$: 1738 (COS); ^{1}HNMR [$CDCl_3$ (δ ppm)]: 0.88 (t, 12H, CH_2–CH_2–$\underline{CH_3}$), 1.25 (m, 8H, CH_2–$\underline{CH_2}$–CH_3), 3.34 (t, 8H, O–$\underline{CH_2}$–CH_2), 3.91 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 4.34 (d, 4H, Ar–CH_2–Ar, J = 12.4 Hz), 7.06 (m, 8H, Ar–H), 8.38 (s, 4H, –NH–C$\underline{H}$=N), 13.02 (s, 4H, N–N$\underline{H}$–CH); FAB MS, *m/z*: 1101 (M^+); Anal calc.(%) for $C_{52}H_{52}N_{12}O_8S_4$: C, 56.71; H, 4.76; N, 15.26; S, 11.65; Found C, 56.42; H, 4.72; N, 15.16; S, 11.57.

Acknowledgements We thank Council of Scientific and Industrial Research (CSIR), India for the financial support of this work through project No. 01(1991)/05/EMR-II. We are also thankful to Central Drug Research Institute, Lucknow for providing spectroanalytical facilities.

References

1. Böhmer, V.: Calixarenes: macrocycles with (almost) unlimited possibilities. Angew. Chem. Int. Ed. **34**, 713–745 (1995)
2. Gutsche C.D.: Calixarenes revisited. In: Stoddart J.F. (ed) RSC monographs in supramolecular chemistry. Royal Society of Chemistry, Cambridge, UK (1998)
3. McKervey M.A., Schwing-Weill M.J., Arnaud-Neu F. In: Gokel GW (ed.) Comprehensive Supramolecular Chemistry, vol. 1, pp 537–603. Pergamon, Oxford, UK (1996)
4. Schwing-Weill, M.J., Arnaud-Neu, F., McKervey, M.A.: Modulation of the cation complexing properties in the lower rim of chemically modified calixarene series. J. Phys. Org. Chem. **5**, 496–501 (1992)
5. Casnati, A., Pochini, A., Ungaro, R., Bocchi, C., Ugozzoli, F., Egberink, R.J.M., Struijk, H., Lugtenberg, R., De Jong, F., Reinhoudt, D.N.: 1,3-Alternate calix[4]arenecrown-5 conformers: new synthetic ionophores with better K^+/Na^+ selectivity than valinomycin. Chem. Eur. J. **2**, 436–445 (1996)
6. Ungaro, R., Casnati, A., Ugozzoli, F., Pochini, A., Dozol, J.F., Hill, C., Rouquette, H.: Dialkoxycalix[4]arenecrowns-6 in 1,3-alternate conformation: cesium selective ligand that exploit cation–arene interactions. Angew. Chem. Int. Ed. **33**, 1506–1509 (1994)
7. Dozol, J.F., Simon, N., Lamare, V., Rouquette, H., Eymard, S., Tournois, B., De Marc, D., Macias, R.M.: A solution for cesium removal from high-salinity acidic or alkaline liquid waste: the crown calix[4]arenes. Sep. Sci. Technol. **34**, 877–909 (1999)
8. Halouani, H., Dumazet-Bonnamour, I., Lamartine, R.: Synthesis of novel chromogenic bi- and tri-functionalized calix[4]arenes. Tetrahedron Lett. **43**, 3785–3788 (2002)
9. Halouani H., Dumazet-Bonnamour I., Duchamp C., Bavoux C., Ehlinger N., Perrin M., Lamartine R.: Synthesis, conformations and extraction properties of new chromogenic calix[4]arene amide derivatives. Eur. J. Org. Chem. **24**, 4202–4210 (2002)
10. Oueslati, F., Dumazet-Bonnamour, I., Lamartine, R.: New chromogenic azocalix[4]arene podands incorporating 2,2-bipyridyl subunits. New J. Chem. **27**, 644–647 (2003)
11. Oueslati, F., Dumazet-Bonnamour, I., Lamartine, R.: Synthesis of new chromogenic 2,2′-bithiazoylcalix[4]arenes. Tetrahedron Lett. **42**, 8177–8180 (2001)
12. Goodgame, D.M.L., Grachvogel, D.A., White, A.J.P., Williams, D.J.: Diverse polymeric metal complexes formed by the ambidentate ligand 1-(4′-pyridyl)pyridin-4-one. Inorg. Chim. Acta **348**, 187–193 (2003)

13. Osz, K., Varnagy, K., Sovago, I., Lennert, L., Vargha, H.S., Sanna, D., Micera, G.: Equilibrium and structural studies on transition metal complexes of amino acid derivatives containing the bis(pyridin-2-yl)methyl residue. New J. Chem. **25**, 700–706 (2001)
14. Schweinfurth D., Pattacini R., Strobel S., Sarkar B.: New 1,2,3-triazole ligands through click reactions and their palladium and platinum complexes. Dalton Trans. 9291–9297 (2009)
15. Mukai, H., Sohrin, Y.: 4,5-Bis(diphenylphosphinoyl)-1,2,3-triazole ligand: studies on metal complex formations in liquid–liquid distribution systems. Inorg. Chim. Acta **362**, 4526–4533 (2009)
16. Meng Z. S., Yun L., Zhang W. X., Hong C. G., Herchel R., Ou Y. C., Leng J. D., Peng M. X., Lina Z. J., Tong M. L. (2009) Reactivity of 4-amino-3,5-bis(pyridin-2-yl)-1,2,4-triazole, structures and magnetic properties of polynuclear and polymeric Mn(II), Cu(II) and Cd(II) complexes. Dalton Trans. 10284–10295
17. Drabent, K., Ciunik, Z.: Copper(I) complexes with N4-functionalized-1,2,4-triazole and bidentate spacer ligands: from one- to three-dimensional architecture. Cryst. Growth Des. **9**, 3367–3375 (2009)
18. Chen, D., Wang, D.Z., Zhang, J.B., Cao, L.H.: Synthesis, structures of novel zinc and copper compounds based on pyridazino[3,2-c]1,2,4-triazole derivatives. J. Mol. Struct. **920**, 342–349 (2009)
19. Sharma, P., Kumar, A., Rane, N.: An expedient synthesis of novel, fused pyrimido[4,5-d]pyrimidine and pyrimido[5,4-e][1,2,4]triazolo[4,3-c]pyrimidine analogues from 4-amino-2,6-dichloropyrimidine. Heteroat. Chem. **17**, 245–253 (2006)
20. Sharma, P., Kumar, A., Rane, N., Gurram, V.: Hetero Diels–Alder reaction: a novel strategy to regioselective synthesis of pyrimido[4,5-d]pyrimidine analogues from Biginelli derivative. Tetrahedron **61**, 4237–4248 (2005)
21. Kumar, A., Sharma, P., Mandloi, A.: Synthesis of 25,26,27-tris(ethoxycarbonylmethoxy)-28-(substitutedoxycarbonylmethoxy)calixarene: first example of calix-imidazole/benzimidazole analogue. Synth. Commun. **33**, 373–380 (2003)
22. Kumar, A., Sharma, P., Chandel, L.K., Kalal, B.L.: Synergistic extraction and spectrophotometric determination of palladium(II), iron(III), and tellurium(IV) at trace level by newly synthesized p-[4-(3,5-dimethylisoxazolyl)azophenylazo]calix(4)arene. J. Inclusion Phenom. Macrocycl. Chem. **61**, 335–342 (2008)
23. Kumar, A., Sharma, P., Chandel, L.K., Kalal, B.L., Mate, S.K.: Synergistic solvent extraction of copper, cobalt, rhodium and iridium into 1,2-dichloroethane at trace level by newly synthesized 25,26,27,28-tetrahydroxy-5,11,17,23-tetra-[4-(*N*-hydroxyl-3-phenylprop-2-enimidamido)phenylazo]calix[4]arene. J. Inclusion Phenom. Macrocycl. Chem. **62**, 285–292 (2008)
24. Gutsche, C.D., Iqbal, M., Stewart, D.: Synthesis procedures for *p-tert*-butylcalix[4]arene. J. Org. Chem. **51**, 742–745 (1986)
25. Ainsworthl C.: Org Synth **40**, 99–102 (1960)
26. Gutsche, C.D., Levine, J.A., Sujeeth, P.K.: Functionalized calixarenes: the Claisen rearrangement route. J. Org. Chem. **50**, 5802–5806 (1985)