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Syntheses of Novel Hexahomotrithiacalix[3]arenes

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Abstract

The first synthesis of the C_3-symmetrical *p-tert*-butylhexahomotrithiacalix[3]arene **7d** via one-pot procedure by the reaction of 2,6-bis(chloromethyl)-*p-tert*-butylphenol **8d** with sodium sulfide nanohydrate under high-dilution conditions is reported. Also, hexahomotrithiacalix[3]arenes **7d-f** (where **d-f** designate the type of the substituents R at the *p*-positions of the phenolic rings: **d**, R = *t*-Bu; **e**, R = CH_3; **f**, R = Cl) were synthesized via a convergent approach in good yield by the [2 + 1] cyclization reaction of 2,6-bis(chloromethyl)phenol monomers **8d-f** and bis(chloromethyl)phenol dimers **15d-f** in presence of sodium sulfide nanohydrate under high-dilution conditions. The structures of **7d-f** were determined by ^{1}H, ^{13}C NMR, MS and elemental analysis. A preliminary study of the binding properties of **7d** with alkali- and heavy metal cations using biphasic picrate extraction method showed only weak abilities to bind the cations examined.

Introduction

Calixarenes and their derivatives, **1**, have been extensively investigated for their supramolecular and molecular recognition properties during the past two decades [1]. Homooxacalixarenes are calixarene analogues in which $\mathbf{CH_2OCH_2}$ bridges partly or completely replace CH_2 bridges between the aromatic units. The most known example of these compounds is the hexahomooxacalix[3]arene **2** which has received relatively little attention despite its unique structural features, such as a cavity composed of an 18-membered ring, C_3-symmetry, a limited number of possible conformations (i.e. *cone*, *partial cone*) and the fact that the ether ring oxygens may act cooperatively with the phenolic oxygens in complexing with metal ions. Symmetrical hexahomooxacalix[3]arenes which bear the same substituents on the upper rim of the molecules have been synthesized via a single-step approach, by the cyclotrimerization of 2,6-bis(hydroxymethyl)phenols as the monomeric units [2–5].

On the other hand, hexahomooxacalix[3]arenes bearing different alkyl functionalities on their upper rim have been synthesized via multi-step procedures [5–8]. Syntheses of azacalix[3]arene analogues such as **3** have been achieved based on condensation reactions between primary amines and 2,6-bis(hydroxymethyl)-4-alkyl phenols as well as by a convergent approach [9–13].

Ito *et al* reported the synthesis of decahomotetrathiacalix[6]arenes **4a-c** and hexahomodithiacalix[3]arenes **5a-c** in high yields by coupling *p*-substituted bis(chloromethyl)phenol-formaldehyde trimers such as **6a-c** with 1,2-ethanedithiol and 1,3-propanedithiol, respectively (Scheme 2) [14–15].

In this report, we describe new thia analogues of hexahomocalix[3]arene, namely hexahomotrithiacalix[3]arenes **7d-f**, in a one-pot and a convergent procedures (Schemes 3–5). To the best of our knowledge this is the first report for the synthesis of such symmetrical hexahomotrithiacalix[3]arenes. Our interest in the synthesis of these compounds is due to: (a) their potential as suitable hosts for the binding of soft metal ions; (b) enlargement of the calix skeleton to provide larger cavities; and (c) they can be readily oxidized to the corresponding sulfoxides and sulfones and thus providing other new sulfur-bridged calixarenes.

Experimental

General: NMR spectra were recorded on a Bruker instrument at 200 MHz for ^{1}H NMR and 50.33 MHz for ^{13}C NMR. Chemical shifts are reported relative to TMS as internal standard. Mass spectra were determined by GCMS, +APCI MS or –APCI MS. Chromatographic separations were performed on silica gel columns (60–120 mesh, CDH). Thin layer chromatography (TLC) was carried out using silica gel GF_{254} (Fluka). Unless otherwise noted, all reactions were carried out under dry nitrogen.

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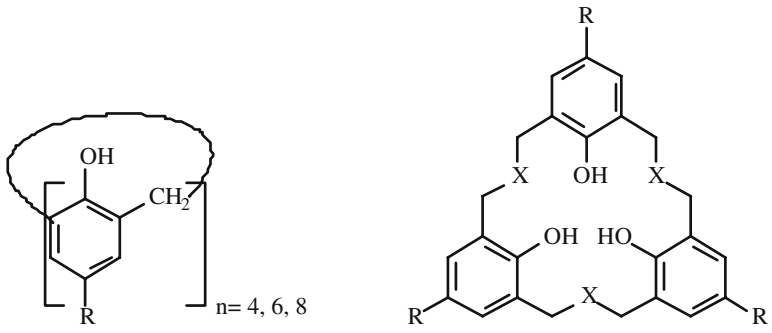
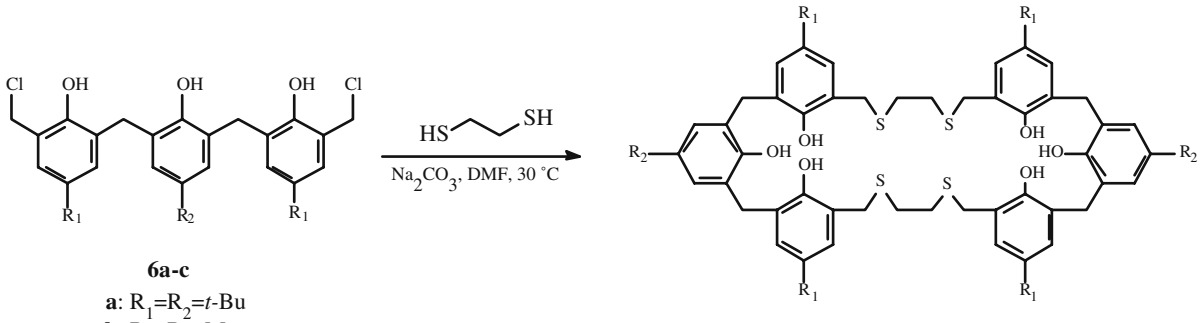


1R = alkyl

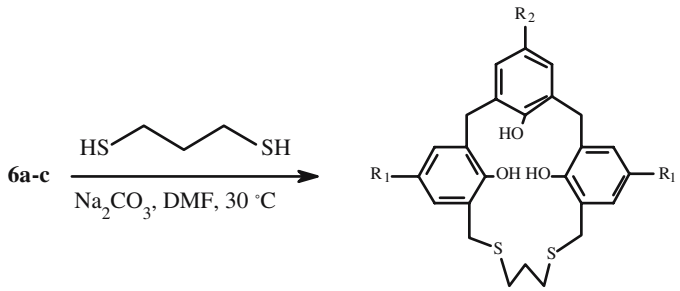
2R = alkyl, X = O
3R = alkyl, X = NR

Scheme 1.



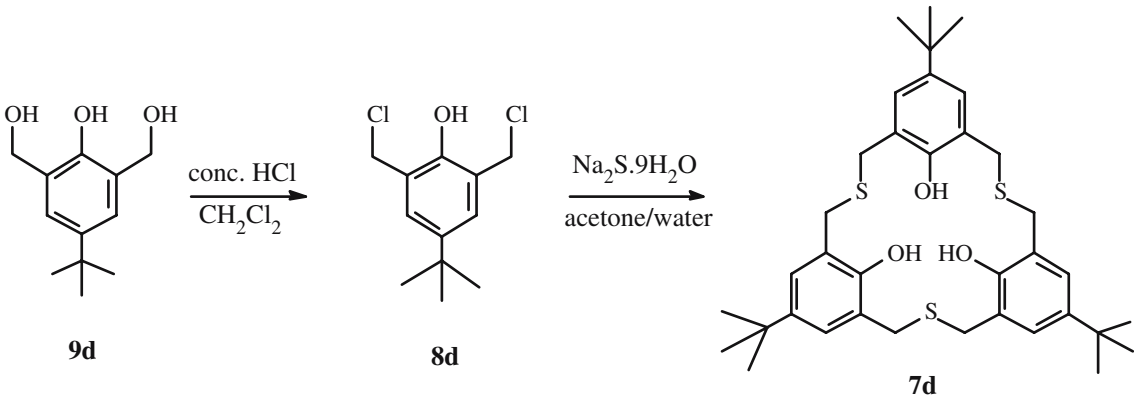
6a-c
a: R_1=R_2=*t*-Bu
b: R_1=R_2=Me
c: R_1=Me, R_2=*t*-Bu

4a-c



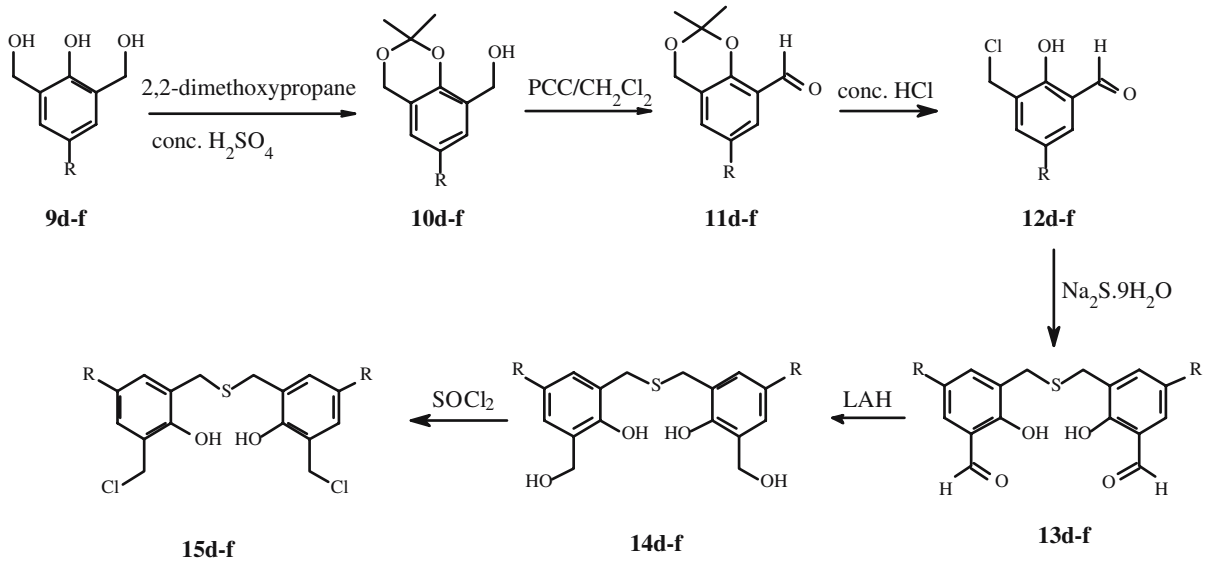
5a-c

Scheme 2.



9d **8d** **7d**

Scheme 3.



Scheme 4.

Lithium, sodium, potassium, robidium, cesium and silver picrates were prepared according to the literature procedure [16a]. Pb(II) [16b], Cd(II), Ni(II), Cu(II), Zn(II), Mn(II), Co(II) [16c] and Hg(II) [16d] picrates were prepared in a similar manner as the literature procedures. The compounds **8d-f**, **9d-f**, **10d-e**, **11e** and **12e** were prepared according to general literature conditions [4,6,13].

*General procedures for the synthesis of hexahomotrithiacalix[3]arenes (**7d-f**): A- One-pot procedure*

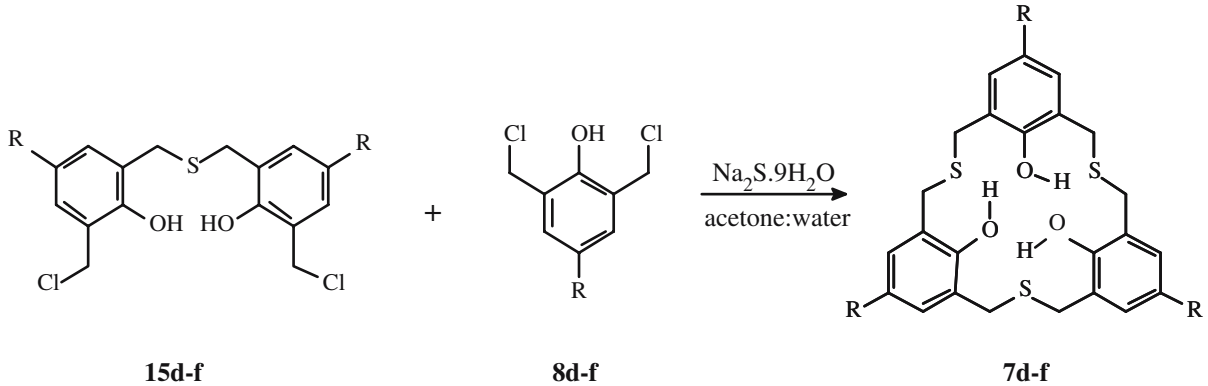
*Synthesis of p-Tert-butylhexahomotrithiacalix[3]arene (**7d**)*

To acetone (200 ml) in a 500-ml three-necked R.B flask was added simultaneously over a period of 12 h, a solution of 2,6-bis(chloromethyl)-*p-tert-butyl*phenol **8d** (2.03 mmol) in acetone (130 ml), and a solution of $Na_2S.9H_2O$ (2.03 mmol) in a mixture of acetone/water (10:1, 130 ml). The reaction mixture was stirred at room temperature overnight. The solid which formed was filtered off and washed with aqueous 5% HCl, followed with distilled water until the aqueous washes become neutral to pH paper. After drying in air, the solid was washed with diethyl ether and then with dichloromethane to give **7d** as pale brown solid, 51% yield, m.p 159–160 °C, ^{1}H NMR ($CDCl_3$) δ_H 1.24 (s, 27H, *t*-Bu), 3.75 (s, 12H, $ArCH_2S$), 6.87 (br, 3H, OH), 7.08 (s, 6H, Ar-H); ^{13}C NMR (DMSO-d_6) δ_C 31.4, 32.0, 34.4, 125.6, 126.2, 141.5, 151.0 (C-OH); + APCI MS (m/z): calcd for $C_{36}H_{48}S_3O_3$ $(M+1)^+$ 625.94, found 625.3 (100%); Anal. calcd for $C_{36}H_{48}S_3O_3$: C, 69.91; H, 7.74; S, 15.39, found: C, 70.22; H, 7.58; S, 15.22.

B- Convergent procedure

*Synthesis of hexahomotrithiacalix[3]arenes (**7d-f**)*

To acetone (150 ml) in a 500-ml three-necked R.B flask was added simultaneously over a period of 8–12 h, a solution consisting an appropriate 2,6-bis(chloromethyl)phenol monomer **8d-f** (0.68 mmol) and bis(chloromethyl)phenol dimer **15d-f** (0.68 mmol) in acetone (50 ml + 1 ml of DMF), and a solution of $Na_2S.9H_2O$ (1.36 mmol) in a mixture of acetone/water (10:1, 50 ml). The reaction mixture was stirred



Scheme 5.

at room temperature overnight. The solvent was evaporated under vacuum and the solids which formed were filtered off and washed with aqueous 5% HCl, followed with distilled water until the aqueous washes become neutral to pH paper. After drying in air, the solids were washed with diethyl ether and then with dichloromethane. Each of the respective products had the following physical and spectroscopic properties:

7d: 93% yield. Its m.p and spectroscopic properties were identical to those of the product which obtained via one-pot procedure.

7e: pale brown solid, 60% yield, m.p 102–104 °C, ^{1}H NMR (DMSO-d_6) δ_H 2.15 (s, 9H, CH_3), 3.68 (s, 12H, $ArCH_2S$), 6.79 (s, 6H, Ar-H), 8.38 (s, 3H, OH); ^{13}C NMR (DMSO-d_6) δ_C 20.1, 30.0, 125.5, 128.0, 130.2, 151.0 (C-OH); -APCI MS (m/z): calcd for $C_{27}H_{30}S_3O_3$ $(M\text{-}1)^+$ 497.72, found 497.19 (100%); Anal. calcd for $C_{27}H_{30}O_3S_3$: C, 65.13; H, 6.06; S 19.29 found: C, 65.09; H, 6.09; S, 19.21.

7f: pale brown solid, 43% yield, m.p 180–185 °C, ^{1}H NMR (DMSO-d_6) δ_H 3.65 (s, 12H, $ArCH_2S$), 7.11 (s, 6H, Ar-H), 8.92 (s, 3H); ^{13}C NMR (DMSO-d_6) δ_C 31.0, 123.2, 128.6, 129.1, 152.0 (C-OH); MS (m/z): 558.9 (M^+, 5), 524.9, 493.0, 372.6, 340.6, 306.6, 185.3, 155.4, 125.3, 91.2; Anal. calcd for $C_{24}H_{21}Cl_3O_3S_3$: C, 51.48; H, 3.78; Cl 18.99; S 17.18, found: C, 51.42; H, 3.69; Cl, 18.91; S, 17.12.

*Synthesis of 2,2-dimethyl-8-(hydroxymethyl)benzo-1,3-dioxin (**10f**)*

It was prepared according to general literature conditions [6, 13] as **10d** and **10e** to give after column chromatographic purification using ethyl acetate:hexane (1:4) a colorless solid in 84% yield, m.p 83–84 °C, ^{1}H-NMR ($CDCl_3$) δ_H 1.57 (s, 6H, CH_3), 4.61 (s, 2H, $ArCH_2OH$), 4.82 (s, 2H, $ArCH_2O$), 6.92 (s, 1H, Ar-H), 7.18 (s, 1H, Ar-H); ^{13}C NMR ($CDCl_3$) δ_c 24.9, 25.0, 60.2, 101.0, 120.5, 123.4, 125.2, 126.9, 130.6, 147.4; GCMS: 228 (M^+, 25), 171 (28), 170 (85), 141 (48), 107 (100), 79 (42), 77 (44), 51 (32).

*Synthesis of 2,2-dimethyl-6-substituted-8-formylbenzo-1,3-dioxin (**11d** and **11f**)*

They were prepared according to general literature conditions [13] as **11e** to give:

11d: yellow oil, 100% yield, ^{1}H-NMR ($CDCl_3$) δ_H 1.29 (s, 9H, *t*-Bu), 1.56 (s, 6H, CH_3), 4.92 (s, 2H, $ArCH_2O$), 7.20 (s, 1H, Ar-H), 7.75 (s, 1H, Ar-H), 10.45 (s, 1H, -C*H*O); GCMS: 248 (M^+, 13), 190 (31), 175 (100), 162 (39), 147 (39), 91 (26), 77 (19).

11f: pale yellow solid, 87% yield, m.p 104–106 °C, ^{1}H-NMR ($CDCl_3$) δ_H 1.60 (s, 6H, CH_3), 4.88 (s, 2H, $ArCH_2O$), 7.24 (s, 1H, Ar-H), 7.72 (s, 1H, Ar-H), 10.36 (s, 1H, -C*H*O); ^{13}C NMR ($CDCl_3$) δ_c 24.5, 60.0, 101.0, 122.1, 124.9, 126.0, 130.1, 152.5, 187.6 (-*C*HO); GCMS: 226 (M^+, 13), 168 (37), 140 (100), 112 (23), 77 (47).

*Synthesis of 2-hydroxy-3-chloromethyl-5-substitutedbenzaldehyde (**12d** and **12f**)*

They were prepared according to general literature conditions [13] as **12e** to give:

12d: red oil, 100% yield, ^{1}H-NMR ($CDCl_3$) δ_H 1.35 (s, 9H, *t*-Bu), 4.70 (s, 2H, CH_2Cl), 7.51 (s, 1H, Ar-H), 7.65 (s, 1H, Ar-H), 9.90 (s, 1H, OH), 11.30 (s, 1H, -C*H*O); GCMS: 226 (M^+, 25), 213 (33), 211 (100), 191 (23), 175 (70), 147 (20), 119 (18), 91 (52), 77 (52).

12f: brown solid, 95% yield, m.p 90–91 °C, ^{1}H-NMR ($CDCl_3$) δ_H 4.64 (s, 2H, CH_2Cl), 7.55 (s, 1H, Ar-H), 7.64 (s, 1H, Ar-H), 9.86 (s, 1H, OH), 11.36 (s, 1H, -C*H*O); ^{13}C NMR ($CDCl_3$) δ_c 39.0, 120.8, 124.2, 127.8, 130.3, 137.1, 157.6, 195.1 (-*C*HO); GCMS: 188 (M^+-OH, 13), 186 (40), 169 (M^+-Cl), 168 (55), 142 (32), 140 (100), 112 (32), 77 (72), 51 (33).

*Synthesis of dialdehyde dimers (**13d-f**)*

To a solution of $Na_2S.9H_2O$ (0.53 g, 2.21 mmol in 3 ml of H_2O and 17 ml of acetone) was added a solution of aldehyde (4.42 mmol in 20 ml acetone) dropwise at room temperature. The reaction was stirred at room temperature for 3 h. Work-up was conducted by adding 40 ml of dichloromethane and 5 ml of aqueous 5% HCl. The organic layer was separated, dried over anhydrous $MgSO_4$ and evaporated to give dark yellow crude product which was purified by column chromatography using ethyl acetate:hexane (1:4) as eluent to give:

13d: pale yellow solid, 83% yield, m.p 62–63 °C, ^{1}H-NMR ($CDCl_3$) δ_H 1.33 (s, 18H, *t*-Bu), 3.80 (s, 4H, $ArCH_2S$), 7.45 (d, $J = 2.4$ Hz, 2H, Ar-H), 7.66 (d, $J = 2.4$ Hz, 2H, Ar-H), 9.90 (s, 2H, OH), 11.25 (s, 2H, -C*H*O); ^{13}C NMR ($CDCl_3$) δ_c 29.2, 31.2, 34.1, 119.9, 126.5, 129.3, 135.3, 142.5, 157.4, 196.9 (-*C*HO); +APCI MS (m/z): calcd for $C_{24}H_{30}SO_4$ $(M+1)^+$ 415.56, found 415.23 (100%).

13e: yellow solid, 58% yield, m.p 126–127 °C, ^{1}H-NMR ($CDCl_3$) δ_H 2.31 (s, 6H, CH_3), 3.76 (s, 4H, $ArCH_2S$), 7.20 (d, $J = 2.4$ Hz, 2H, Ar-H), 7.38 (d, $J = 2.4$ Hz, 2H, Ar-H), 9.82 (s, 2H, OH), 11.24 (s, 2H, (-C*H*O)); ^{13}C NMR ($CDCl_3$) δ_c 20.5, 29.5, 120.0, 127.1, 128.8, 132.6, 138.6, 157.5, 197.0 (-*C*HO); -APCI MS (m/z): calcd for $C_{18}H_{18}SO_4$ $(M\text{-}1)^+$ 329.40, found 329.18 (100%).

13f: pale yellow solid, 65% yield, m.p 150–152 °C, ^{1}H-NMR ($CDCl_3$) 3.76 (s, 4H, $ArCH_2S$), 7.42 (d, $J = 2.6$ Hz, 2H, Ar-H), 7.51 (d, $J = 2.6$ Hz, 2H, Ar-H), 9.85 (s, 2H, OH), 11.35 (s, 2H, -C*H*O); ^{13}C NMR ($CDCl_3$) δ_c 29.0, 30.0, 121.0, 124.4, 128.9, 131.2, 157.6, 195.5 (-*C*HO); -APCI MS (m/z): calcd for $C_{16}H_{12}SO_4Cl_2$ $(M\text{-}1)^+$ 370.24, found 370.18 (20%).

*Synthesis of diol dimers (**14d-f**)*

To a suspension of LAH (0.15 g, 3.8 mmol) in dry THF (20 ml) was added a solution of dimers **13d-f** (1.93 mmol) in dry THF (10 ml) dropwise at room temperature under nitrogen and stirred for 15 min. The reaction mixture was poured into cooled wet diethyl ether (50 ml). The reaction mixture was neutralized with

aqueous 10% HCl. Drying and evaporating the solvents give:

14d: colorless oil, 88% yield, ^{1}H-NMR ($CDCl_3$) δ_H 1.27 (s, 18H, *t*-Bu), 3.71 (br, 2H, CH_2OH), 3.78 (s, 4H, $ArCH_2S$), 4.74 (s, 4H, CH_2OH), 7.12 (d, $J = 2.4$ Hz, 2H, Ar-H), 7.24 (d, $J = 2.4$ Hz, 2H, Ar-H), 7.78 (br, 2H, Ar-OH); ^{13}C NMR ($CDCl_3$) δ_c 31.5, 31.7, 34.0, 64.1, 123.6, 124.4, 125.4, 127.4, 142.6, 152.2; +APCI MS (m/z): calcd for $C_{24}H_{34}SO_4$ 418.59, found 418.37 (18%).

14e: colorless solid, 98% yield, m.p 82–83 °C, ^{1}H-NMR ($CDCl_3$) δ_H 2.23 (s, 6H, CH_3), 3.77 (s, 4H, $ArCH_2S$), 4.76 (s, 4H, CH_2OH), 6.85 (s, 2H, Ar-H), 6.88 (s, 2H, Ar-H), 7.46 (s, 2H, Ar-OH); ^{13}C NMR ($CDCl_3$) δ_c 20.5, 31.6, 64.1, 120.4, 126.1, 128.1, 129.0, 130.2, 152.0; -APCI MS (m/z): calcd for $C_{18}H_{22}SO_4$ $(M-1)^+$ 333.42, found 333.28 (100%).

14f: colorless solid, 85% yield, m.p 123–124 °C, ^{1}H-NMR (acetone-d_6) 3.76 (s, 4H, $ArCH_2S$), 4.82 (s, 4H, CH_2OH), 5.20 (br, 2H, CH_2OH), 7.06 (d, $J = 2.6$ Hz, 2H, Ar-H), 7.19 (d, $J = 2.6$ Hz, 2H, Ar-H), 8.56 (br, 2H, Ar-OH); ^{13}C NMR (acetone-d_6) δ_c 31.3, 62.0, 123.4, 125.6, 127.8, 128.5, 152.9; -APCI MS (m/z): calcd for $C_{16}H_{16}SO_4Cl_2$ 374.27, found 374.95 (6%).

*Synthesis of chloromethyl dimers (**15d-f**)*

To a solution of diol dimers **14d-f** (0.36 mmol) in dry benzene (50 ml) and dry DMF (0.2 ml) was added freshly distilled thionyl chloride (0.1 ml, 1.44 mmol) at room temperature under nitrogen. The reaction stirred for 0.5–1 h. Cold water (5 ml) was added and the organic layer was washed with water (10x3 ml). Drying and evaporating the solvent under vacuum give:

15d: pale yellow solid, 81% yield, m.p 75–76 °C ^{1}H-NMR ($CDCl_3$) δ_H 1.31 (s, 18H, *t*-Bu), 3.70 (s, 4H, $ArCH_2S$), 4.71 (s, 4H, CH_2Cl), 7.05 (s, 2H, Ar-H), 7.11 (s, 2H, Ar-H); ^{13}C NMR ($CDCl_3$) δ_c 31.5, 32.0, 34.0, 43.1, 122.6, 124.2,125.3, 126.9, 128.1, 150.2; +APCI MS (m/z): calc. for $C_{24}H_{32}SO_2Cl_2$ $(M+1)^+$ 456.49 found 456.40 (8%).

15e: colorless solid, 95% yield, m.p 76–77 °C, ^{1}H-NMR ($CDCl_3$) δ_H 2.20 (s, 6H, CH_3), 3.68 (s, 4H, $ArCH_2S$), 4.66 (s, 4H, CH_2Cl), 7.10 (s, 2H, Ar-H), 7.35 (s, 2H, Ar-H); ^{13}C NMR ($CDCl_3$) δ_c 20.0, 31.2, 42.0, 119.0, 128.5, 130.5, 131.6, 132.1, 136.5; -APCI MS (m/z): calc. for $C_{18}H_{20}SO_2Cl_2$ (M^+) 371.32 found 371.11 (6%).

15f: pale brown solid, 85% yield, m.p 67–68 °C, ^{1}H-NMR (acetone-d_6) 3.89 (s, 4H, $ArCH_2S$), 4.82 (s, 4H, CH_2Cl), 7.37 (s, 2H, Ar-H), 7.46 (s, 2H, Ar-H); ^{13}C NMR (acetone-d_6) δ_c 31.6, 42.1, 128.2, 130.0, 131.1, 131.9, 153.9; MS (m/z): 224.5 ($C_8H_7SOCl^{35.5}Cl^{37.5}$, 4), 332.7 (8), 299.6 (6), 253.7 (9), 165.4 (46), 133.4 (100).

Metal picrate binding studies

Extractions of metal picrates from deionized water into chloroform (spectrograde) were performed according to the following typical procedure [17]: 5.0 ml of an aqueous 1.0×10^{-4} M solution of the metal picrate and 5.0 ml of a 1.0×10^{-4} M solution of hexahomotrithiacalix[3]arene **7d** in chloroform was mechanically shaken in a 10.0 ml E. flask for 24 h at 25 °C. After the two phases were allowed to settle for 1 h, the absorbance of the metal picrate remaining in the aqueous phase was determined spectrophotometrically at 354 nm. Percentage extraction (%E) is calculated from the expression $\%E = 100(A_o\text{-}A)/A_o$, where A_o is the absorbance of the aqueous solution of the metal picrate without the ligand. The results are summarized in Figure 2.

Results and Discussion

This study shows that there are two possible synthetic routes to form the symmetrically hexahomotrithiacalix[3]arene macrocycles **7d-f** involve either (1) one-pot approach by the cyclization of the dichloro-monomers **8a-c** in presence of sodium sulfide nanohydrate (Scheme 3) or (2) a convergent approach by the condensation of dichloro-dimers **15d-f** with dichloro-monomers **8d-f** in presence of sodium sulfide nanohydrate (Scheme 5).

Applying one-pot approach (Scheme 3), sodium sulfide nanohydrate was reacted with an equimolar amount of, for example, 2,6-bis(chloromethyl)phenol **8d** which is in turn derived from the corresponding bis(hydroxymethyl)phenol **9d** in aqueous acetone at room temperature, under high dilution conditions. *Tert*-butylhexahomothiacalix[3]arene **7d** was formed as pale brown solid in 51% yield and was sufficiently pure as determined by its spectral properties. The structure of macrocycle **7d** was characterized by NMR, MS and elemental analysis. In ^{1}H NMR ($CDCl_3$) spectrum (Figure 1): the *tert*-butyl group protons appear at δ 1.24 ppm as singlet signal, a singlet signal due to the methylene bridge protons appears at δ 3.75 ppm, the singlet signal due to the aromatic protons is at δ 7.08 ppm, and one singlet signal due to the hydroxyl groups protons appears at δ 6.87 ppm. Although the ^{1}H NMR chemical shift for the OH groups of **7d** in $CDCl_3$ suggested the formation of intramolecular hydrogen bonding, this bonding appears to be weaker than that in *p-tert*-butylhexahomotrioxacalix[3]arene which shows up at δ 8.35 ppm [4]. This might be attributed to the enlarged skeleton of hexahomotrithiacalix[3]arene ring which results in the OH groups being spread further apart from one another. On the other hand, ^{1}H NMR chemical shift for the OH groups signal in DMSO-d_6 shows up at 8.42 ppm. This might be ascribed to the intermolecular hydrogen bonding between the hydroxyl group protons and the solvent. In the variable temperature dependent ^{1}H NMR spectra of **7d**, the signal of the methylene protons of the $ArCH_2\text{-}S\text{-}CH_2Ar$ moiety was observed as singlet at ambient temperature, and did not split at –60 °C in $CDCl_3$, indicating high conformational flexibility. Although higher members of homothiacalix[*n*]arenes could be formed also by the condensation of 2,6-bis(chloromethyl)phenol **8d** with Na_2S, however **7d** was the only isolable cyclic compound; as evidenced

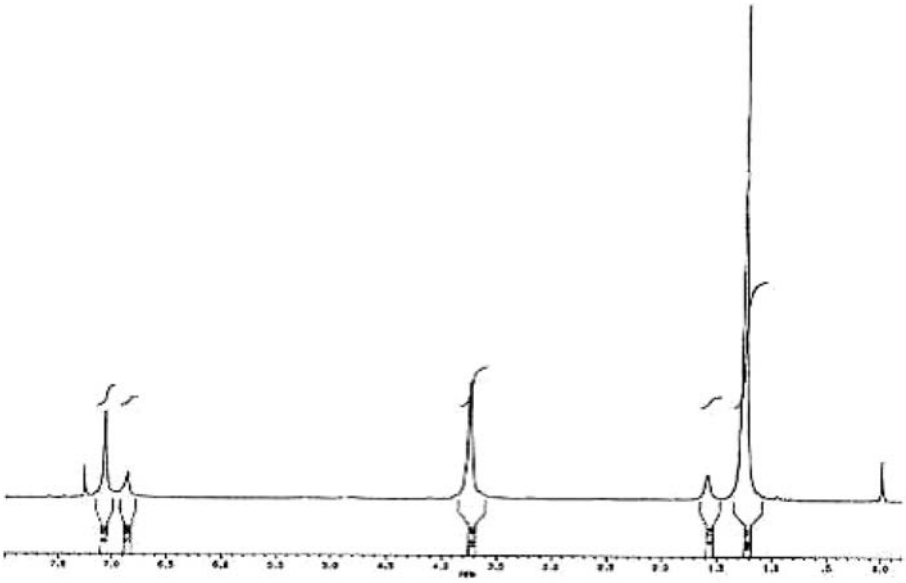


Figure 1. ^{1}H NMR spectrum of 7d in $CDCl_3$.

from its APCI mass spectra showing the molecular ion peak at $m/z = 625.3$ (100%).

Reaction of **8e** or **8f** under similar conditions used for the synthesis of **7d** in attempts to produce **7e** or **7f** were unsuccessful and produced only resinous products. This may indicate that the presence of the bulky *tert*-butyl group at the *para* position is essential in some way, or favouring the cyclization step. Therefore, for further confirming the structure of compound **7d** obtained by one-pot approach and to synthesize the other compounds **7e** and **7f**, a convergent approach was applied as shown in Schemes 4 and 5. This route involves [2 + 1] condensation of dimers **15d-f** and the monomers **8d-f** in presence of sodium sulfide nanohydrate to yield the cyclic trimers **7d-f**. According to Scheme 4, the dimers **15d-f** were synthesized from *p*-substituted 2,6-bis(hydroxymethyl)phenols **9d-f**. Treatment of 2,6-bis(hydroxymethyl)phenols with 2,2-dimethoxypropane in presence of a catalytic amount of concentrated H_2SO_4 afforded the acetonide **10d-f** which were oxidized with PPC to yield the protected aldehydes **11d-f** in nearly quantitative yield. A one-pot reaction for deprotection and chlorination of **11d-f** with concentrated HCl resulted the formation of chloromethyl aldehydes **12d-f** in high yield. Coupling of two equivelants of each chloromethylaldehyde monomer with one equivalent of sodium sulfide nanohydrate afforded the aldehyde dimers **13d-f** in good yield after column chromatographic purification. Reduction of the dimers **13d-f** with $LiAlH_4$ in dry THF followed by chlorination with freshly distilled thionylchloride in dry benzene to produce the bis-chloromethyl dimers **15d-f** in excellent yield.

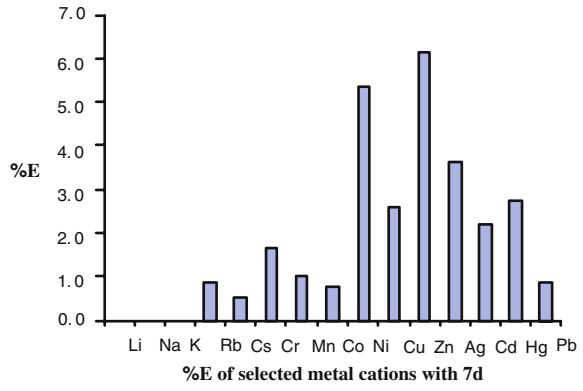


Figure 2. %E of selected metal cations with 7d.

Symmetrical hexahomotrithiacalix[3]arenes **7d-f** *were obtained as follows:*

A solution of equimolars of bis(chloromethyl)dimer **15d-f** and bis(chloromethyl)monomer **8d-f** in DMF-acetone (1:50) and a solution of two equivalents of sodium sulfide nanohydrate in H_2O-acetone (1:10) were added simultaneously to acetone over a period of 8–12 h with stirring at room temperature under nitrogen and then the mixture was further stirred overnight affording **7d-f** in 93, 60 and 43% yield, respectively. The physical and spectral properties of **7d** obtained by this a convergent procedure were identical to those of the product that obtained from the cyclization of **8d** by one-pot procedure. The structures of **7e** and **7f** were established on the bases of their NMR, MS and elemental analyses. The signals of the $ArCH_2$-S-CH_2Ar methylene proton in DMSO-d_6 were observed at 3.62 and 3.66 ppm respectively, while the hydroxyl group protons signals appear at 8.41 and 8.92 ppm respectively. It is worth noting that the chemical shift of the OH protons of **7f** is higher than both the chemical shifts of the OH protons of **7d** and **7e**. This indicated that the OH protons of **7f** are more

deshielded than the OH protons of **7d** and **7e** due to the inductive effect of chlorine atoms.

To evaluate the ability of **7d** to bind different metal ions and to compare its recognition selectivity, its extraction behavior towards Li^+, Na^+, K^+, Rb^+, Cs^+, Ag^+, Cu^{2+}, Pb^{2+}, Hg^{2+}, Zn^{2+}, Cr^{2+}, Ni^{2+}, Cd^{2+}, Co^{2+} and Mn^{2+} was determined using a picrate-$CHCl_3$ extraction experiments were performed. It was found that **7d** showed only insignificant ability to bind the cations investigated (Figure 2). Overall, the percent extraction (%E) values are small, but suggest that the most efficiently extracted metal ions are Zn^{2+} and Ni^{2+}.

In order to prevent its rapid interconversion between its conformers, and to enhance its complexation ability, synthesis of different derivatives of **7d** is currently underway. A study of their complexation properties with metal cations in additional solvents under basic conditions and their inclusion abilities of neutral organic guests such as fullerenes will be reported in due course.

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