CHAPTER 2

SYNTHESIS AND CHARACTERIZATION OF

POLYMER SUPPORTED CALIX[4/6]ARENES
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2.1 SYNTHESIS OF CALIXARENES

Calixarenes are synthesized by the following two methods:

(i) Base prompted one step synthesis
(ii) Acid catalyzed one step synthesis

2.1.1 Base Prompted One Step Synthesis

Base induced condensation of p-substituted phenols and formaldehyde results in a mixture of linear and cyclic oligomers (Method 1)\(^{[6]}\).

\[
\begin{align*}
\text{C(CH}_3\text{)}_3 \text{OH} & \xrightarrow[\text{OH}^-/\Delta]{\text{HCHO}} \text{C(CH}_3\text{)}_3 \text{OH} \\
\text{Method 1}
\end{align*}
\]

\[\begin{align*}
(1) \ n = 4 \\
(2) \ n = 6 \\
(3) \ n = 8
\end{align*}\]

p-tert-butylcalix[4]arene (1) is synthesized in 49 % yield by heating a mixture of p-tert-butylphenol, 37 % formaldehyde and 0.045 equivalent NaOH with respect to phenol. The use of 0.34 equivalent of KOH instead of NaOH in refluxing xylene instead of diphenyl ether produces p-tert-butylcalix[6]arene (2), yield 88 %. p-tert-butylcalix[8]arene (3) can be prepared from p-tert-butylphenol, paraformaldehyde and 0.03 equivalent of NaOH in refluxing xylene, yield 65 %. Ninagawa and Matsuda isolated p-tert-butylcalix[5]arene in 6 % yield employing potassium butoxide as a base in tetralin at 150\(^\circ\) C\(^{[7]}\) and the yield was further improved to 15 % by Gutsche et al\(^{[8]}\). Employing dioxane as solvent, 2 equivalents of KOH as a base, and a 30 hours heating period, Nakamoto and Ishita obtained a mixture of cyclic oligomers, from which they isolated 6 % of p-tert-butylcalix[7]arene\(^{[9]}\). The yield of heptamer was
than scaled up to 20 % by increasing the amount of base. In 1999, Gutsche et al have reported isolation, characterization and conformational properties of p-tert-butylcalix[9-20]arenes.

The effect of the reaction conditions on the synthesis of p-tert-butylcalixarenes can be summarized as follows:

(i) Higher amount of base and the use of KOH and RbOH are required for the preferential formation of p-tert-butylcalix[6]arene;
(iii) The cyclic octamer and hexamer are converted, at higher temperatures under basic conditions, to the cyclic tetramer.

The limits of base induced one step synthesis of phenol derived calixarenes can be summarized as follows:

(i) Only bulky p-alkyl or p-phenylphenols can be employed;
(ii) Generally complex mixtures of cyclic products, with the even numbered calixarenes as the main components, are produced;
(iii) As yet the guidelines to find the correct reaction conditions are very few, so the selection of the experimental procedures for the synthesis of each calix[n]arene is not easy.

2.1.2 Acid Catalyzed One Step Synthesis

Calixarenes have not been isolated from acid catalyzed reactions of p-substituted phenols with formaldehyde or higher aldehydes. Acid catalyzed reactions of resorcinol with formaldehyde give polymers, higher aldehydes lead to cyclic tetrarers (Method 2).
2.2 FUNCTIONALIZATION AT THE METHYLENE BRIDGE

Very few examples of calixarenes bearing substituent on the methylene bridges have been reported. Bohmer and Sartori described the synthesis of calix[4]arenes bearing aryl groups on this position starting from triphenylmethanes \[^{[15,16]}\]. CrO\(_3\) oxidation of methylene bridges of calixarene derivatives affords the corresponding ketones \[^{[17]}\].

2.3 FUNCTIONALIZATION AT THE PHENOLIC HYDROXYL GROUPS (LOWER RIM)

2.3.1 Complete Functionalization

The complete functionalization at the lower rim of calixarenes has been performed using a variety of alkylating or acylating agents and in different reaction conditions to yield different products (Figure 1) \[^{[1,2,18]}\].

\[
R^1 = \text{H, alkyl; } R^2 = \text{alkyl, allyl, benzyl, CH}_2\text{CH}_2\text{OR}^3, \text{CH}_2\text{COOR}^3, \text{CH}_2\text{CONR}^3, \text{CH}_2\text{COOH, CH}_2\text{CONHOH, COR, COAr etc.}
\]

(Figure 1)
2.3.2 Selective Functionalization

The direct selective alkylation of calixarenes at the lower rim exploits the difference in acidity of the phenolic –OH groups to give different products \(^{[18,19-32]}\). It is difficult to obtain accurate pK\(_a\) data for calix[n]arenes in aprotic media where most of the alkylation reactions are usually performed. However from the few data available on calix[4]arenes and by extrapolating the results obtained for water soluble calixarenes it is possible to conclude that the first phenolic –OH group is much more acidic than the others, probably because its conjugate anion can be stabilized by two intramolecular hydrogen bonds, and that the second dissociation occurs at the distal position.

Synthetic methodologies similar to those used for selective functionalization of calix[4]arenes have also been used for calix[6]arenes, although in this case the regiochemical control is less pronounced, due to the higher number of apparently equivalent phenolic –OH groups present in these macrocycles \(^{[33-42]}\).

2.3.3 Replacement of Phenolic –OH Groups

One of the approaches to modify the lower rim of calixarenes involve the replacement of phenolic –OH groups or their substitution with other groups such as amino or thiol leading to various derivatives (Figure 2) \(^{[43-48]}\).
2.4 FUNCTIONALIZATION AT THE AROMATIC NUCLEI

(UPPER RIM)

tert-butyl groups can be easily removed from p-tert-butylcalix[n]arenes by transalkylation using AlCl₃ and an acceptor solvent such as toluene\textsuperscript{[49,50]}. Subsequent reactions on these substrates allow the introduction of a variety of functional groups on the upper rim of calixarenes. Ipso substitution of tert-butyl groups is another possible route to obtain upper rim functionalized calixarenes\textsuperscript{511} (Method 3).

![Functionalization Diagram]

\textbf{Method 3}

\textbf{2.4.1 Complete Functionalization}

The complete functionalization of calix[n]arenes was initially performed with the aim of introducing new hydrophilic groups on the aromatic nuclei viz. SO₃Na⁺, CH₂NMe₃⁺, CH₂PO(O)Na₂, etc. Method 4 shows the main products obtained by the upper rim functionalization of calix[n]arenes.

\begin{align*}
(a) & \quad X₁ = X₂ = X₃ = X₄ = H \\
(b) & \quad X₁ = X₃ = H; X₂ = X₄ = OH \\
(c) & \quad X₁ = X₄ = H; X₂ = X₃ = OH \\
(d) & \quad X₁ = H; X₃ = NH₂; X₂ = X₄ = OH \\
(e) & \quad X₁ = X₃ = NH₂; X₂ = X₄ = OH \\
(f) & \quad X₁ = X₃ = SH; X₂ = X₄ = OCH₃ \\
(g) & \quad X₁ = X₃ = SH; X₂ = X₄ = H \\
(h) & \quad X₁ = X₂ = X₃ = X₄ = SH
\end{align*}
The synthetic routes leading to calixarene derivatives completely functionalized at the upper rim are:

(i) nitration\textsuperscript{51,52}, (ii) sulfonation\textsuperscript{53}, (iii) bromination\textsuperscript{54-57}, (iv) iodination\textsuperscript{58,59}, (v) acylation\textsuperscript{60,61}, (vi) chloromethylation\textsuperscript{62-66}, (vii) formylation\textsuperscript{67-69}, (viii) diazo coupling\textsuperscript{70-73}, (ix) oxidation to calixquinones\textsuperscript{72,74}.

2.4.2 Selective Functionalization

By exploiting the results of the selective functionalization of the lower rim of calix[4]arenes, regiocontrolled introduction of substituents at the upper rim of calix[4]arenes has been accomplished\textsuperscript{18}. In this way it has been possible to introduce selectively a variety of substituents on the phenol rings by electrophilic aromatic and ipso substitution\textsuperscript{22,51,59,67,75-79}. There are very few reports on the selective functionalization of p-tert-butylcalix[6]arene at the upper rim\textsuperscript{80}.

\begin{center}
\begin{tabular}{llll}
Entry & $R^1$ & Y & Z \\
\hline
a & alkyl & Br & Li, COOH, CN, Ar etc. \\
b & H & SO$_2$H & NO$_2$ \\
c & H & NO$_2$ & NH$_2$ \\
d & alkyl & COR$_2$ & COOH \\
e & H & CH$_2$NR$^2$ & CH$_2$NR$^2$:CH$_3^+$, CH$_2$CN, CH$_2$OCH$_3$ \\
f & H & CH$_2$CH=CH$_2$ & CH$_2$CHO, CH$_2$CH$_2$Y, CH=CHCH$_3$ \\
g & H/alkyl & CH$_2$Cl & CH$_3$, C$_2$H$_5$, CH$_2$Ar, CH$_2$PO(OR)$_2$ \\
h & alkyl & CHO & CH$_2$OH, CH$_2$X, COOH etc. \\
i & alkyl & I & Ar, COOR$_2$, NH$_2$ etc \\
j & H & N=N-Ar & NH$_2$ \\
\end{tabular}
\end{center}

(Method 4)
2.5 EXPERIMENTAL

2.5.1 Apparatus

Precoated silica gel plates (Merck 60 F254) were used for TLC. FT IR spectra were recorded on a Jasco infrared spectrophotometer as KBr pellets. Elemental analysis was done on Heraeus Carlo Erba 1108 elemental analyzer. The $^1$H NMR spectra were recorded on Bruker operating at 100 MHz for proton in DMSO–d6 with tetramethyl silane as the internal standard.

2.5.2 Reagents

All chemicals used in this work were of analytical grade of E. Merck or Lancaster. The solvents were purified by the method of Weissberger et al.[81]. Commercially available Merrifield peptide resin [chloromethylated polystyrene divinylbenzene co-polymer or CMPDB] (1 % cross linked, 1.5 mmol equivalent of Cl / g of resin, 200-400 mesh) was procured from Aldrich. The glassware used were soaked in 10 % HNO$_3$ overnight before use and cleaned repeatedly with double distilled deionized water.

2.6 SCHEME 1: (pp. 80-82)

2.6.1 Synthesis and Characterization of Resin (A):

[i]: Synthesis of 1 pentacyclo[19.3.1.1$^3$.7.1$^9$.13.1$^{15}$.1$^{19}$]octacosa-l(25),3,5,7(28),
9,11,13(27),15,17,19(26),21,23-dodecaene-25,26,27,28-tetrol-5,11,17,23-
tetrakis(1,1-dimethylethyl)

or

Preparation of precursor:

A mixture of 10 g (66.6 mmol) of p-tert-butylphenol (PTBP), 6.2 ml 37 % formaldehyde solution (83 mmol HCHO) and 0.12 g (3 mmol) NaOH (corresponding to 0.045 equivalent with respect to PTBP) in 0.3 ml water was placed in a 250 ml, three-necked, flask equipped with a mechanical stirrer. The contents of the open flask were allowed to stir for 15 minutes at room temperature and then heated for 2 hours at 120° C by means of a heating mantle. The reaction mixture, which was clear and colourless at the beginning, became light yellow after 30 minutes, a somewhat deeper yellow after 2 hours and eventually changed to thick slurry as the water evaporated and finally turned to a deep yellow or brown yellow viscous mass. During this period there was considerable frothing and the reaction mixture filled most of the flask before shrinking back to the original volume. Stirring was discontinued, the reaction vessel was removed from the heating mantle and the reaction mixture was allowed to cool to room temperature. 100 ml warm diphenyl ether was added to the flask to dissolve the residue and the contents were stirred. The process required about 1 hour.

Pyrolysis of the precursor:
The 250 ml, three-necked flask was fitted with a N₂ gas inlet. The contents of the flask were stirred and heated at 120° C with a heating mantle and a stream of N₂ gas was blown rapidly into the reaction mixture to facilitate the removal of the water as soon as it was formed. During this period the colour of the solution changed from yellow to a grey or a light brown. When the evolution of water subsided and a solid started to form, the flask was fitted with a condenser and the contents of the flask were stirred and heated to 160° C for a few minutes and then refluxed for 4 hours under a flow of N₂ gas. During this phase of the reaction the solid dissolved and a clear dark brown to greyish black solution was formed. The reaction mixture was cooled to room temperature and the product was precipitated by the addition of 150 ml ethyl acetate. The resulting mixture was stirred for 30 minutes and allowed to stand for 30 minutes. Filtration yielded the material that was washed twice with 10 ml portions of ethyl acetate, once with 20 ml acetic acid, twice with 10 ml portions of water and twice with 5 ml portions of acetone to yield 6.6 g (61 %) of crude product which was pure enough to be used in subsequent reactions without recrystallization.

The white to beige coloured crude product was dissolved in 180 ml boiling toluene that was concentrated to 90 ml. On cooling, 6.1 g (49 %) product 1 was obtained as glistening white rhombic crystals, mp 342° C. The product of crystallization from toluene was a 1:1 complex of 1 and toluene, from which toluene was removed by drying under 1 mm vacuum and 140° C for 24 hours. IR (KBr): 3160 cm⁻¹ (O-H str.).

\(^1\)H NMR (CDCl₃) (δ in ppm): 10.2 (s,4,ArOH); 7.0 (s,8,ArH); 3.9 (s,8,ArCH₂Ar); 1.3 (s,36,C(CH₃)₃). Anal. calculated for C₄₄H₅₆O₄: C, 81.43; H, 8.70. Found: C, 81.17; H, 8.51.

[ii]: Synthesis of 2 pentacyclo[19.3.1.1\(^3\).1\(^9\).1\(^{13}\).1\(^{15}\).1\(^{19}\)]octacosa-1(25),3,5,7(28),36,38-diepoxide.
250 ml, three-necked flask was equipped with a mechanical stirrer, N₂ gas inlet and a water condenser with a CaCl₂ guard tube. 10 g 1 (13.5 mmol), 1.75 g phenol (18.6 mmol) and 100 ml toluene were taken in the flask and stirred for 10 minutes. In the colourless heterogeneous mixture, 10 g AlCl₃ (75 mmol) was added with vigorous stirring and the mixture was stirred. Within 30 minutes a viscous deep red sticky phase separated on the walls of the flask. It was stirred at room temperature for 3 hours while the progress of the reaction was monitored by TLC [solvent system; hexane:ethyl acetate::4:1]. After completion of the reaction the reaction mixture was poured into a beaker containing 200 g crushed ice. The reaction vessel was rinsed with 100 ml dichloromethane and 100 g crushed ice and this washing was added to the beaker content. The contents of the beaker were stirred with a glass rod. It was then transferred to a separating funnel and 400 ml dichloromethane was added to it. The contents of the funnel were shaken and the organic phase was separated. The organic phase was washed thrice with 100 ml portions of 1 N HCl and then twice with 100 ml water. The organic phase was separated and dried over anhydrous Na₂SO₄. The filtrate was collected in a 500 ml round bottomed flask and the solvent was distilled under reduced pressure using a rotary evaporator. 50 ml diethyl ether was added to the oily orange residue for the precipitation of 2. The heterogeneous mixture was allowed to stand at -15° C for 1 hour. The solid was collected by suction filtration on a Buchner funnel. The pale yellow solid was poured into a beaker and triturated with 100 ml diethyl ether. It was allowed to stand at -15° C for 1 hour and filtered on
a Buchner funnel. The resulting white powder was product 2. Recrystalization in methanol / chloroform afforded 6.9 g (80 %) of colourless crystals of 2, mp 315° C. IR (KBr): 3130 cm\(^{-1}\) (O-H str.). \(^1\)H NMR (CDCl\(_3\)) (δ in ppm): 10.1 (s,4,ArOH); 7.2 (s,12,ArH); 3.8 (s,8,ArCH\(_2\)Ar). Anal. calculated for C\(_{28}\)H\(_{24}\)O\(_4\): C, 79.21; H, 5.70. Found: C, 78.94; H, 5.43.

[iii]: Synthesis of 3 26,28-dimethoxypentacyclo[19.3.1.1\(^3\)\(^7\).1\(^9\)\(^{13}\).1\(^{15}\)\(^{19}\)]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-25,27-diol

or


A suspension of 30 g 2 (70.7 mmol), 10.7 g anhydrous K\(_2\)CO\(_3\) (77.4 mmol) and 26.3 g methyl tosylate (141.4 mmol) was refluxed in 500 ml acetonitrile for 24 hours in a 1000 ml round bottomed flask. After distillation of the solvent the mixture was taken in 500 ml dichloromethane and washed twice with 50 ml 1 N HCl and 50 ml water. The organic layer was dried with MgSO\(_4\) and the solvent was distilled under reduced pressure using a rotary evaporator to afford the product 3 as a pure white solid; yield 30.8 g (97 %); mp>300° C (decompose). IR (KBr): 3135 cm\(^{-1}\) (O-H str.); 1246 cm\(^{-1}\) (C-O str.). \(^1\)H NMR (CDCl\(_3\)) (δ in ppm): 8.0 (s,2,ArOH); 6.5-7.1 (m,12,ArH); 3.4 (br d,8,ArCH\(_2\)Ar); 4.0 (s,6,CH\(_3\)). Anal. calculated for C\(_{30}\)H\(_{28}\)O\(_4\): C, 79.62; H, 6.24. Found: C, 79.69; H, 6.35.

[iv]: Synthesis of 4 26,28-dimethoxy-11,23-dinitropentacyclo[19.3.1.1\(^3\)\(^7\).1\(^9\)\(^{13}\).]

1\(^{15}\)\(^{19}\)octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-25,27-diol

or

A mixture of 10 g 3 (22.1 mmol), 10 ml acetic acid and 65 % 3.5 ml HNO3 (48 mmol) in 1000 ml dichloromethane was stirred vigorously for 12 hours at room temperature in a 2000 ml two-necked flat bottomed flask on a magnetic stirrer. The contents were then transferred in a 5000 ml beaker. After addition of 1500 ml dichloromethane to dissolve the precipitate formed, the solution was washed twice with 500 ml saturated NaHCO3 solution. The organic layer was dried with MgSO4 and distilled under reduced pressure using a rotary evaporator to afford a yellow solid, which was further purified by flash chromatography (SiO2; dichloromethane:petroleum ether::4:1) to give a white solid 4: yield 6.8 g (57 %); mp>300° C. IR (KBr): 3140 cm⁻¹ (O-H str.); 1240 cm⁻¹ (C-O str.). ¹H NMR (CDCl3) (δ in ppm): 9.0 (s,2,ArOH); 8.0 (s,4,ArH); 6.6-7.0 (m,6,ArH); 3.5 (br d,8,ArCH2Ar); 3.9 (s,6,OCH3). Anal. calculated for C₃₀H₂₆O₈N₂: C, 66.40; H, 4.83; N, 5.17. Found: C, 66.15; H, 4.51; N, 4.94.


or


A suspension of 5 g 4 (9.2 mmol), 10 ml hydrazine hydrate and a catalytic amount of Raney nickel in 100 ml methanol was refluxed for 6 hours in a 250 ml round bottomed flask. The reaction mixture was allowed to cool to room temperature, filtered and the solvent was distilled under reduced pressure using a rotary evaporator. The residue was taken up in 60 ml dichloromethane, washed thrice with 30 ml water and dried over MgSO4 After filtration, the solvent was distilled under reduced
pressure using a rotary evaporator to give pure 5 in 3 g (68 %) yield; mp>300° C. IR (KBr): 3180 cm\(^{-1}\) (O-H stretching); 1252 cm\(^{-1}\) (C-O stretching); 3435 cm\(^{-1}\) (N-H stretching). \(^1\)H NMR (DMSO-d\(_6\)) (δ in ppm): 9.7 (s,2,ArOH); 7.2 (s,10,ArH); 3.4 (br d,8,ArCH\(_2\)Ar); 3.7 (s,6,OCH\(_3\)); 5.5 (s,4,ArNH\(_2\)). Anal. calculated for C\(_{30}\)H\(_{30}\)O\(_4\)N\(_2\): C, 74.65; H, 6.27; N, 5.81. Found: C, 74.39; H, 6.08; N, 5.61.

[vi]: Synthesis of 6 11,23-bis(chlorodiazengyl)-26,28-dimethoxypentacyclo[19.3.1.1\(^9\).1\(^{15}\).1\(^{19}\)]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-25,27-diol

or

\(11,23\text{-bis(chlorodiazengyl)-26,28-dimethoxy-calix[4]arene-25,27-diol:}\)

10 g amine 5 (20.7 mmol) was diazotized in 35 ml HCl (20 %) at 0°C in ice-bath with constant stirring for 30 minutes using 10 g NaNO\(_2\) (145 mmol) in 100 ml water:ethanol::1:1 media to yield 6, which was then reacted further in situ.

[vii]: Synthesis of 7 5-{(Z)-[17-{(Z)-(3-{(E)-(aminocarbonyl)hydrazono}methyl)-4-hydroxy-5-methoxyphenyl)diazenyl]-26,28-dimethoxy-25,27-dihydroxy pentacyclo[19.3.1.1\(^9\).1\(^{15}\).1\(^{19}\)]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaen-5-yl]diazenyl}-2-hydroxy-3-methoxy benzaldehyde semicarbazone

or

\(11,23\text{-bis(o-vanillinsemicarbazone)-26,28-dimethoxy-calix[4]arene-25,27-diol:}\)

The solution containing 6 was taken as such in the ice-bath in a beaker with an addition funnel supported over it containing 10 g o-VSC (47.8 mmol) [Note 1] in 40 ml NaOH (15 g, 375 mmol) in water. Addition was completed in 1 hour at 0°C with constant stirring. The brownish-red coloured product 7 was solidified by evaporation
of solvent. Purification was done by crystallization in iso-amyl acetate. Yield: 15 g (79 %), mp>300° C (decompose). IR (KBr): 3469 cm\(^{-1}\) & 3276 cm\(^{-1}\) (O-H str.); 1593 cm\(^{-1}\) (CH=N str.); 1681 cm\(^{-1}\) (C=O str.). \(^1\)H NMR (DMSO-d\(_6\)) (δ in ppm): 3.3 (s,8,ArCH\(_2\)Ar); 3.5-3.9 (s,12,OCH\(_3\)); 7.1-8.3 (s,14,ArH); 10.2 (s,4,ArOH). Anal. calculated for C\(_{48}\)H\(_{46}\)O\(_{10}\)N\(_{10}\): C, 62.45; H, 5.03; N, 15.18. Found: C, 62.31; H, 4.95; N, 14.98.

[Note 1: Synthesis of 2-hydroxy-3-methoxybenzaldehyde semicarbazone (o-VSC)

5 g o-vanillin (33 mmol) was refluxed with 3.7 g semicarbazide hydrochloride (33 mmol) in 80 ml, 95 % ethanol at 78° C with constant stirring for 4 hours. 0.5 g sodium acetate was added to maintain pH > 7. The reaction mixture was then cooled and filtered. The crude product was washed thrice with ethanol and water. The yield of pure o-VSC was 7.8 g, mp 197° C.]

[viii]: Synthesis of Resin (A) by loading of 7 on CMPDB

A mixture containing 10 g 7 (10.8 mmol), 10 g K\(_2\)CO\(_3\) (72 mmol) and 10 g of CMPDB in 150 ml of dimethylformamide:tetrahydrofuran::2:1 was heated at 75° C temperature for 8 hours under N\(_2\) gas atmosphere. Thereafter the polymeric beads of Resin (A) were separated through porous filter at pump. Repeated washing with the solvents dimethylformamide and tetrahydrofuran followed by water were carried out to ensure complete removal of unreacted 7 and the weight of the dried Resin (A) was found to be 12.2 g. The amount of 7 loaded on CMPDB was evaluated by difference of mass taken before and after coupling for the dried resin and was found to be 22 %.

\[
\text{Percentage of 7 hooked on CMPDB} = \frac{W_2-W_1}{W_1} \times 100 \%
\]
Where, Weight of dried CMPDB: \( W_1 \)
Weight of dried Resin (A): \( W_2 \)

The elemental analysis of nitrogen in Resin (A) was found to be 2.73%, which further confirmed the amount of loading to be 22-23%. This result shows that only 0.4 mmol i.e. 26% of the total available Cl (1.5 mmol / g of CMPDB) reacted with 0.195 mmol of ligand 7.

2.6.2 Synthesis and Characterization of Resin (B):

Products 1, 2, 3, 4, 5 and 6 were prepared as per the methods described in the section 2.6.1.

[vii]: Synthesis of 7 5-\{(Z)-[17-\{(Z)-(3-\{(E)-[(aminocarbothioyl)hydrazono]methyl\}-4-hydroxy-5-methoxyphenyl)diazeny]-26,28-dimethoxy-25,27-dihydroxypentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaen-5-yl]diazeny]-2-hydroxy-3-methoxy benzaldehyde thiosemicarbazone

or


The solution containing 6 was taken as such in the ice-bath in a beaker with an addition funnel supported over it containing 10 g o-VTSC (44.4 mmol) [Note 2] in 40 ml NaOH (15 g, 375 mmol) in water. Addition was completed in 1 hour at 0°C with constant stirring. The brownish-red coloured product 7 was solidified by evaporation of solvent. Purification was done by crystallization in iso-amyl acetate. Yield: 16 g (81%), mp > 300°C (decompose). FT IR (KBr): 3464 cm\(^{-1}\) & 3227 cm\(^{-1}\) (O-H str.); 1591 cm\(^{-1}\) (CH=N str.). \(^1\)H NMR (DMSO-\(d_6\)) (\(\delta\) in ppm): 3.3 (s,8,ArCH\(_2\)Ar); 3.6-3.8
(s,12,OCH₃); 7.1-8.1 (s,14,ArH); 10.1 (s,4,ArOH). Anal. calculated for C₄₈H₄₆O₈N,oS₂: C, 60.34; H, 4.86; N, 14.67; S, 6.72. Found: C, 59.96; H, 4.65; N, 14.76; S, 6.45.

[Note 2: Synthesis of 2-hydroxy-3-methoxybenzaldehyde thiosemicarbazone (o-VTSC)]

5 g o-vanillin (33 mmol) was refluxed with 3 g thiosemicarbazide (33 mmol) in 80 ml, 95% ethanol at 75° C with constant stirring for 4 hours. 0.5 g sodium acetate was added to maintain pH > 7. The reaction mixture was then cooled and filtered. The crude product was washed thrice with ethanol and water. The yield of pure o-VTSC was 7 g, mp 207° C.

[viii]: Synthesis of Resin (B) by loading of 7 on CMPDB:

A mixture containing 10 g 7 (10.5 mmol), 10 g K₂CO₃ (72 mmol), and 10 g of CMPDB in 150 ml of dimethylformamide:tetrahydrofuran::2:1 was heated at 75° C temperature for 8 hours under N₂ gas atmosphere. Thereafter the polymeric beads of Resin (B) were separated through a porous filter at pump. Repeated washing with the solvents dimethylformamide and tetrahydrofuran followed by water were carried out to complete remove unreacted 7 and the weight of the dried Resin (B) was found to be 12.34 g. The amount of 7 loaded on CMPDB was evaluated by difference of mass taken before and after coupling for the dried resin and was found to be 23.4 %.

The elemental analysis of nitrogen and sulphur in Resin (B) were found to be 2.78 % and 1.26 % respectively, which further confirmed the amount of loading to be 23-24 %. This result shows that only 0.4 mmol i.e. 26.5 % of the total available Cl (1.5 mmol / g of CMPDB) reacted with 0.2 mmol 7.
Scheme 1:
Step-1:

(PTBP)

37% HCHO
NaOH

H2C
\(-\)
CH3
\(-\)
CH3
OH

(1)

C2H5OH
AlCl3

H2C
\(-\)
CH3
\(-\)
CH3
OH

(2)

Methyl tosylate
K2CO3

NO2
\(-\)
OH
OCH3

65% HNO3
CH3COOH

(3)

Raney Ni
NH2NH2 H2O

NH2
\(-\)
OH
OCH3

(4)

20% HCl
NaNO2

N2Cl'

(5)

(6)
Step-I:

\[
\text{NH}_2 + \text{H}_2\text{N}-\text{CN}-\text{X} + \text{NH}_2 - \text{CH}_3\text{COONa} \rightarrow \text{NH}_2 - \text{CH}_3\text{COONa} + \text{NH}_3 + \text{X} \rightarrow \text{NH}_2 - \text{CH}_3\text{COONa} + \text{NH}_3 + \text{X}
\]

(o-V) (SC / TSC) (o-VSC / o-VTSC)

Step-II:

\[
\begin{array}{c}
\text{OCH}_3 \\
\text{CHO} \\
\text{OCH}_3 \\
\text{OH} \\
\end{array}
\quad \text{+} \quad \begin{array}{c}
\text{NH}_2 - \text{CH}_3\text{COONa} \\
\text{OCH}_3 \\
\text{CHO} \\
\text{OCH}_3 \\
\end{array}
\rightarrow \begin{array}{c}
\text{OCH}_3 \\
\text{CHO} \\
\text{OCH}_3 \\
\text{OH} \\
\end{array}
\quad \text{CH}_3\text{COONa} \rightarrow \begin{array}{c}
\text{OCH}_3 \\
\text{CHO} \\
\text{OCH}_3 \\
\text{OH} \\
\end{array}
\]

(o-VSC / o-VTSC)

Step-III:

\[
\begin{array}{c}
\text{N} + \text{Cl} \\
\text{NH}_2 - \text{CH}_3\text{COONa} \\
\text{OCH}_3 \\
\text{CHO} \\
\text{OCH}_3 \\
\end{array}
\quad \text{NaOH} \rightarrow \begin{array}{c}
\text{OCH}_3 \\
\text{CHO} \\
\text{OCH}_3 \\
\text{OH} \\
\end{array}
\]

(o-VSC / o-VTSC)

(6)

(7)
**Step IV:**

Resin (A): CMPDB supported calix[4]arene-o-vanillinsemicarbazone

Resin (B): CMPDB supported calix[4]arene-o-vanillinthiosemicarbazone
2.7 SCHEME 2: (pp. 91-93)

2.7.1 Synthesis and Characterization of Resin (C):

[i]: Synthesis of 1 heptacyclo[31.3.1.1^{3,7}.1^{9,13}.1^{15,19}.1^{21,25}.1^{27,31}]octaconta-
1(37),3,5,7(42),9,11,13(41),15,17,19(40),21,23,25(39),27,29,31(38),33,35-
octadecaene-37,38,39,40,41,42-hexol-5,11,17,23,29,35-hexakis(1,1-
dimethylethyl)

or


A round-bottomed flask equipped with a N₂ gas inlet, mechanical stirrer and a
Dean-Stark trap and condenser was placed in a heating mantle. 10 g (66.5 mmol)
PTBP, 13.5 ml 37 % formaldehyde solution (180 mmol of HCHO) and 1.5 g (22.7
mmol) KOH pellets (corresponding to 0.34 equivalent of PTBP) were added to the
flask. Heating and stirring were begun and after 15 minutes N₂ gas was blown across
the reaction mixture. The reaction mixture was heated and stirred for 2 hours. During
this period some frothing occurred and the reaction mixture expanded somewhat before shrinking to the original volume. 100 ml xylene was added to the flask to dissolve the semisolid mass and give a yellow solution that was brought quickly to reflux by increasing the temperature of the heating mantle. After 30 minutes precipitates were formed and the colour of the reaction mixture changed from yellow to orange. Refluxing was continued for 3 hours, the heating mantle was removed and the mixture was allowed to cool to room temperature. The mixture was filtered and the precipitates were washed with 20 ml xylene and dried on a Buchner funnel to yield 11 g crude, almost colourless product. This material was powdered, dissolved in 250 ml chloroform and treated with 80 ml 1 N HCl. After 15 minutes the stirred solution turned yellow to light orange. Stirring was continued for an additional 10 minutes and the mixture was transferred to a separatory funnel. The chloroform layer was drawn off, the aqueous layer was extracted with additional 25 ml chloroform and the combined chloroform extracts were washed once with water and dried over MgSO₄. The chloroform solution was concentrated to 100 ml by the distillation under reduced pressure using a rotary evaporator and 100 ml hot acetone was added to the boiling chloroform solution. The mixture was allowed to cool and filtered to give 9.5 g (88 %) product 1 as a white powder, mp 372° C. IR (KBr): 3400 cm⁻¹ (shoulder, O-H str.); 3150 cm⁻¹ (O-H str.). ¹H NMR (CDCl₃) (δ in ppm): 10.4 (s,6,ArOH); 7.1 (s,12,ArH); 3.8 (s,12,ArCH₂Ar); 1.3 (s,54,C(CH₃)₃). Anal. calculated C₆₆H₈₄O₆: C, 81.43; H, 8.70. Found: C, 81.23; H, 8.44.

[ii]: Synthesis of 2 heptacyclo[31.3.1.1⁷.1⁹.1³⁰.15.1⁹.1₂¹.2₅.1²₇.3₁]octetraconta-
(37),3,5,7(42),9,11,13(41),15,17,19(40),21,23,25(39),27,29,31(38),33,35-
octadecaene-37,38,39,40,41,42-hexol

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or

**calix[6]arene-37,38,39,40,41,42-hexol**: [82]

Slurry of 10.5 g 1 (11 mmol), 6.2 g (66 mmol) phenol, and 11.75 g (88 mmol) AlCl₃ in 125 ml toluene was stirred for 1 hour in N₂ gas atmosphere at room temperature in a 500 ml three-necked round bottomed flask. The reaction was quenched by the addition of 100 ml ice water and the organic phase was separated. The toluene was removed by distillation under reduced pressure using a rotary evaporator and the residue was triturated with 70 ml CH₃OH to leave 6.81 g crude, colourless product 2. It was recrystallized from CH₃OH-CHCl₃ to afford 6.1 g (89 %) white powder. mp 417° C. IR (KBr): 3200 cm⁻¹ (O-H str.). ¹H NMR (CD₂Cl₂) (δ in ppm): 10.4 (s,6,ArOH); 7.4 (s,18,ArH); 4.0 (s,12,ArCH₂Ar). Anal. calculated for C₄₂H₃₆O₆: C, 79.21; H, 5.70. Found: C, 78.94; H, 5.48.

[iii]: Synthesis of 3 38,39,41,42-tetramethoxyheptacyclo[31.3.1.1³⁺⁷.1⁹⁺¹³.1⁵⁺¹⁷.1⁹⁺²¹.2₃]octaconta-1(37),3,5,7(42),9,11,13(41),15,17,19(40),21,23,25(39),27,29,31(38),33,35-octadecaene-37,40-diol

or


A 250 ml, three-necked flat bottomed flask equipped with a magnetic stirrer, N₂ gas inlet and water condenser was placed on a hot plate. 3.9 g sodium hydride (98 mmol), 80 ml dimethylformamide solvent, 5 g 2 (8 mmol) and 11.4 ml methyl iodide (80 mmol) were added carefully in the given order. The contents were stirred for 12 hours with a slow purging of N₂ gas. After 12 hours 150 ml 2 N HCl was slowly added. The precipitates were filtered on a Buchner funnel and washed twice with 100 ml water. This solid was transferred into a 100 ml flat bottomed flask on a hot plate.
30 ml methanol was added and gently heated at 60°C. The flask was then placed in a refrigerator and after 3 hours the resulting solid was filtered on a Buchner funnel to afford the product 3 as a pure white powder with 5 g yield (92%); mp>300°C decompose. IR (KBr): 3305 cm⁻¹ (O-H str.); 1256 cm⁻¹ (C-O str.). ¹H NMR (CDCl₃) (δ in ppm): 9.8 (s,2,ArOH); 6.6-7.0 (m,18,ArH); 4.2 (br d,12,ArCH₂Ar); 3.8 (s,12,OCH₃). Anal. calculated for C₄₆H₄₄O₆: C, 79.73; H, 6.41. Found: C, 79.42; H, 6.13.


or

38,39,41,42-tetramethoxy-17,35-dinitro-calix[6]arene-37,40-diol:

A mixture of 10 g compound 3 (14.4 mmol), 10 ml acetic acid and 65 % 3.5 ml HNO₃ (48 mmol) in 1000 ml CH₂Cl₂ was stirred vigorously for 12 hours at room temperature in a 2000 ml flat bottomed flask on a magnetic stirrer. The contents were then transferred in a 5000 ml beaker. After addition of 1500 ml CH₂Cl₂ to dissolve the precipitates formed, the solution was washed twice with 500 ml concentrated NaHCO₃ solution. The organic layer was dried with MgSO₄ and distilled under reduced pressure using a rotary evaporator to afford a yellow solid, which was further purified by flash chromatography (SiO₂; CH₂Cl₂:petroleum ether::4:1) to give a white solid 4: yield 7 g (65%); mp>300°C. IR (KBr): 3310 cm⁻¹ (O-H str.); 1261 cm⁻¹ (C-O str.). ¹H NMR (CDCl₃) (δ in ppm): 10.0 (s,2,ArOH); 7.2-7.7 (s,16,ArH); 4.1 (br d,12,ArCH₂Ar); 3.7 (s,12,OCH₃). Anal. calculated for C₄₆H₄₂O₁₀N₂: C, 70.56; H, 5.41; N, 3.58. Found: C, 70.30; H, 5.14; N, 3.35.
[v]: Synthesis of 5 17,35-diamino-38,39,41,42-tetramethoxyheptacyclo[31.3.1.1.3.1.9.13.115.19.121.25.127.31]octetraconta-1(37),3,5,7(42),9,11,13(41),15,17,19(40),21,23,25(39),27,29,31(38),33,35-octadecaene-37,40-diol

or

17,35-diamino-38,39,41,42-tetramethoxy-calix[6]arene-37,40-diol:

A suspension of 5 g 4 (6 mmol), 15 ml hydrazine hydrate and a catalytic amount of Raney nickel in 100 ml CH₂OH was refluxed for 6 hours in a 250 ml round bottomed flask on a heating mantle. The reaction mixture was allowed to cool to room temperature, filtered and the solvent was distilled under reduced pressure using a rotary evaporator. The residue was taken up in 50 ml CH₂Cl₂, washed thrice with 40 ml water and dried over MgSO₄. After filtration, the solvent was distilled under reduced pressure using a rotary evaporator to give pure 5 in 3 g yield (74 %); mp>300° C. IR (KBr): 3315 cm⁻¹ (O-H str.); 1260 cm⁻¹ (C-O str.); 1590 cm⁻¹ (N-H bending). ^1H NMR (CDCl₃) (δ in ppm): 10.0 (s,2,ArOH); 7.1 (s,16,ArH); 4.1 (br d,12,ArCH₂Ar); 3.6 (s,12,OC₂H₃); 5.3 (s,4,ArNH₂). Anal. calculated for C₄₆H₄₆O₆N₂: C, 76.42; H, 6.42; N, 3.88. Found: C, 76.39; H, 6.11; N, 3.51.

[vi]: Synthesis of 6 17,35-bis(chlorodiazeny1)-38,39,41,42-tetramethoxyhepta cyclo[31.3.1.1.3.7.9.13.11.15.19.121.25.127.31]octetraconta-1(37),3,5,7(42),9,11,13(41),15,17,19(40),21,23,25(39),27,29,31(38),33,35-octadecaene-37,40-diol

or

17,35-bis(chlorodiazeny1)-38,39,41,42-tetramethoxy-calix[6]arene-37,40-diol:

10 g amine 5 (14 mmol) was diazotized in 40 ml HCl (20 %) at 0° C in ice-bath with constant stirring for 30 minutes using 10 g NaNO₂ (145 mmol) in 100 ml...
water-ethanol (1:1) media to yield intermediate 6, which was then reacted further in situ.

[vii]: Synthesis of 7 5-\{(Z)-[23-[(Z)-(3-\{E\)-(aminocarbonyl)hydrazono)methyl]-4-hydroxy-5-methoxyphenyl]diazenyl]-37,40-dihydroxy-38,39,41,42-tetra-methoxyheptacyclo[31.3.1.1^37,1^9,13,1^15,19,1^21,25,1^27,31]octetraconta-1(37),3,5,7(42),9,11,13(41),15,17,19(40),21,23,25(39),27,29,31(38),33,35-octa-decaen-5-yl]diazenyl]-2-hydroxy-3-methoxybenzaldehyde semicarbazone or

\[17,35\text{-bis(}o\text{-vanillinsemicarbazone})-38,39,41,42\text{-tetramethoxy-calix[6]arene}-37,40\text{-diol}\]:

The solution containing 6 was taken as such in the ice-bath in a beaker with an addition funnel supported over it containing 10 g o-VSC (47.8 mmol) in 40 ml NaOH (15 g, 375 mmol) in water. Addition was completed in 1 hour at 0°C with constant stirring. The brownish-red coloured product 7 was solidified by evaporation of solvent. Purification was done by crystallization in iso-amyl acetate. Yield: 12.5 g (80%); mp>300°C. IR (KBr): 3450 cm\(^{-1}\) & 3256 cm\(^{-1}\) (O-H str.); 3440 cm\(^{-1}\) (N-H str.); 1592 cm\(^{-1}\) (CH=N str.); 1681 cm\(^{-1}\) (C=O str.). \(^1\)H NMR (DMSO-\text{d}_6) (δ in ppm): 3.5 (s,12,ArCH\textsubscript{2}Ar); 3.9 (s,18,OCH\textsubscript{3}); 6.8-7.4 (s,20,ArH); 10.0 (s,4,ArOH). Anal. calculated for C\textsubscript{64}H\textsubscript{62}O\textsubscript{12}N\textsubscript{10}: C, 66.06; H, 5.38; N, 12.05. Found: C, 65.67; H, 4.99; N, 11.76.

[viii]: Synthesis of Resin (C) by loading of 7 on CMPDB:

A mixture containing 10 g 7 (8.5 mmol), 10 g K\textsubscript{2}CO\textsubscript{3} (72 mmol) and 10 g CMPDB in 150 ml of dimethylformamide::tetrahydrofuran::2:1 was heated at 75°C temperature for 8 hours under N\textsubscript{2} gas atmosphere. Thereafter the polymeric beads of
**Resin** (C) were separated through porous filter at pump. Repeated washing with the solvents dimethylformamide and tetrahydrofuran followed by water was done to ensure complete removal of unreacted 7 and the weight of the dried **Resin** (C) was found to be 12.4 g. The amount of 7 loaded on CMPDB was evaluated by difference of mass taken before and after coupling for the dried resin and was found to be 24 %.

The elemental analysis of nitrogen in **Resin** (C) was found to be 2.33 %, which further confirmed the amount of loading to be 24 %. This result shows that only 0.33 mmol i.e. 22.2 % of the total available Cl (1.5 mmol / g of CMPDB) reacted with 0.166 mmol of ligand 7.

### 2.7.2 Synthesis and Characterization of Resin (D):

Products 1, 2, 3, 4, 5 and 6 were prepared as per the methods described in the section 2.7.1.

[vii]: Synthesis of 7 5-{(Z)-[(Z)-{(E)-(aminocarbothioyl)hydrazono]methyl}-4-hydroxy-5-methoxyphenyl}diazenyl}-37,40-dihydroxy-38,39,41,42-tetramethoxyheptacyclo[31.3.1.13,7.19,11.15,19.11,25,27,31]octetraconta-1(37),3,5,7(42),9,11,13(41),15,17,19(40),21,23,25(39),27,29,31(38),33,35-octadecaen-5-yl}diazenyl]-2-hydroxy-3-methoxybenzaldehyde thiosemicarbazone

or

17,35-bis(o-vanillinthiosemicarbazone)-38,39,41,42-tetramethoxy-calix[6]arene-37,40-diol:

The solution containing 6 was taken as such in the ice-bath in a beaker with an addition funnel supported over it containing 10 g o-VTSC (44.4 mmol) in 40 ml NaOH (15 g, 375 mmol) in water. Addition was completed in 1 hour at 0° C with
constant stirring. The brownish-red coloured product 7 was solidified by evaporation of solvent. Purification was done by crystallization in iso-amyl acetate. Yield: 13 g (81 %); mp>300° C. IR (KBr): 3444 cm⁻¹ & 3207 cm⁻¹ (O-H str.); 3400 cm⁻¹ (N-H str.); 1581 cm⁻¹ (CH=N str.). ¹H NMR (DMSO-d₆) (δ in ppm): 3.5 (s,12,ArCH₂Ar); 3.8 (s,18,OCH₃); 7.0-7.5 (s,20,ArH); 10.1 (s,4,ArOH). Anal. calculated for C₆₄H₆₂O₁₀N₁₀S₂: C, 64.29; H, 5.23; N, 11.72; S, 5.37. Found: C, 63.87; H, 4.92; N, 11.56; S, 5.45.

[viii]: Synthesis of Resin (D) by loading of 7 on CMPDB:

A mixture containing 10 g 7 (8.4 mmol), 10 g K₂CO₃ (72 mmol), and 10 g of CMPDB in 150 ml of dimethylformamide:tetrahydrofuran::2:1 was heated at 75° C temperature for 8 hours under N₂ gas atmosphere. Thereafter the polymeric beads of Resin (D) were separated through porous filter at pump. Repeated washing with the solvents dimethylformamide and tetrahydrofuran followed by water was done to completely remove unreacted 7 and the weight of the dried Resin (D) was found to be 12.35 g. The amount of 7 loaded on CMPDB was evaluated by difference of mass taken before and after coupling for the dried resin and was found to be 23.5 %.

The elemental analysis of nitrogen and sulphur in Resin (D) were found to be 2.23 % and 1.02 % respectively, which further confirmed the amount of loading to be 23-24 %. This result shows that only 0.318 mmol i.e. 21.2 % of the total available Cl (1.5 mmol / g of CMPDB) reacted with 0.159 mmol 7.
Scheme 2:
Step-1:

1. 20% HCI, NaNO₃, H₂O

2. C₆H₅OH, AlCl₃

(PTBP) → (1) → (2)

3. NaH, CH₃I

(4) → (3)

4. 65% HNO₃, CH₃COOH

(3) → (4)

5. Raney Ni, NH₂NH₂·H₂O

(3) → (5)

6. 20% HCl, NaNO₂

(5) → (6)
Step II:

\[
\begin{align*}
\text{OCH}_3 \quad \text{(o-V)} \\
\text{CHO} \\
\text{OH} \\
\end{align*}
\]

+ \[
\begin{align*}
\text{H}_2\text{N} - \text{C}-\text{X} & \quad \text{(SC / TSC)} \\
\text{H}_2\text{NH} & \quad \text{NH}_2
\end{align*}
\]

\[
\rightarrow \text{CH}_3\text{COONa} \
\rightarrow \begin{align*}
\text{OCH}_3 \\
\text{CHO} \\
\text{OH} \\
\text{CH} = \text{N} - \text{C}-\text{X} & \quad \text{(o-VSC / o-VTSC)} \\
\text{NH} & \quad \text{NH}_2
\end{align*}
\]

Step III:

\[
\begin{align*}
\text{N}_2\text{Cl}^- \\
\text{(6)} \\
\rightarrow \text{NaOH} \\
\rightarrow \begin{align*}
\text{OCH}_3 \\
\text{CHO} \\
\text{OH} \\
\text{CH} = \text{N} - \text{C}-\text{X} & \quad \text{(o-VSC / o-VTSC)} \\
\text{NH} & \quad \text{NH}_2
\end{align*}
\]

\[
\begin{align*}
\text{N} = \text{N} \\
\text{OCH}_3 \\
\text{CHO} \\
\text{OH} \\
\text{CH} = \text{N} - \text{C}-\text{X} & \quad \text{(7)} \\
\text{NH} & \quad \text{NH}_2
\end{align*}
\]
Step IV:

R = -CH₃
X = O  Resin (C): CMPDB supported calix[6]arene-o-vanillinsemicarbazone
X = S  Resin (D): CMPDB supported calix[6]arene-o-vanillinthiosemicarbazone

R' = -N≡N-

X = O  Resin (C): CMPDB supported calix[6]arene-o-vanillinsemicarbazone
X = S  Resin (D): CMPDB supported calix[6]arene-o-vanillinthiosemicarbazone
2.8 LIGANDS FOR METAL IONS IN MACROCYCLIC SYSTEMS

- HSAB (Hard Soft Acid Base) Principle

Metal ions (Lewis acid, electron acceptor) are divided into two classes:

(i) **Hard acids**: (high positive charge, low polarizability, small size)

eg. Al(III), Ti(IV), Cu(II), Mn(III), Fe(III), Co(III), Cr(VI) etc.

(ii) **Soft acids**: (low positive charge, high polarizability, large size)

eg. Cu(I), Ag(I), Au(I), Pd(II), Pt(II) etc.

The ligands (Lewis base, electron donor) are divided into two classes:

(i) **Hard bases**: (high electronegativity, difficult to oxidize, low polarizability)

(ii) **Soft bases**: (low electronegativity, easily oxidized, high polarizability, high negative charge)

The HSAB principle states that hard acids prefer to coordinate to hard bases and soft acids prefer soft bases.

- The size of the ligand cavity should be large enough (nearly matching) to accommodate the size of the metal cation, taking into account kinetic restrictions in case of very rigid molecules and self-complexation in case of very flexible molecules. During complexation, the hydration shell should be removed from the metal ion and substituted by the donor atoms of the ligand.

Calix[4]arene based **Resins (A) and (B)**, as seen from their performance, have a compatible cavity size for the metal ions under purview.

- **Resins (A) and (B)** have a more centrosymmetric and compact geometrical structure than **Resins (C) and (D)**.

- There are sufficient numbers of donor atoms in the ligand in order to match the coordination number of the metal ion.
• The molecular conformation significantly contributes to selectivity through steric and electronic reasons. Thus the donor atoms are held by the calixarene backbone with limited flexibility in positions suitable to match the shape of the coordination sphere.

• There is a possibility to attach chelating moieties onto calixarenes, thus combining chelate and the macrocyclic effect. However, the chelating groups increase the flexibility of the ligand and may reduce the overall selectivity.

The resin which gave best results among the four synthesized Resins A - D with the given set of metal ions has been described in the thesis. After exhaustive study of all the resins with all the metal ions cited above, it was found that Resin (A) was most suitable for separation and preconcentration of U(VI), Th(IV), La(III) and Ce(III) while Resin (B) was ideal for separation, preconcentration and trace determination of Cu(II), Cd(II), Pb(II) and Cr(VI), As(III), Tl(I).

2.9 PROPOSED ANALYTICAL APPLICATIONS OF SYNTHESIZED RESINS

The synthesized Resins A - D have been used for the separation, preconcentration and determination of certain biologically, toxicologically and strategically important metal ions viz. copper, cadmium, lead, uranium, thorium, lanthanum, cerium, chromium, arsenic and thallium in a variety of standard and natural water and geological samples. The various parameters determined or optimized for the analytical applications of these resins, in the next three chapters, are as follows.

1. pH Range
2. Flow Rate
3. Concentration of Eluting Agent
4. Total Sorption Capacity
5. Distribution Coefficient (K_d)
6. Exchange Kinetics (t_{1/2})
7. Breakthrough Capacity
8. Preconcentration Factor
9. Stability of the Resin
10. Tolerance Limits of Electrolytes and Cations
11. Average Recovery
12. Relative Standard Deviation (%)
13. Limit of Detection (LOD)
14. Limit of Quantification (LOQ)
REFERENCES


