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Synthesis of cesium selective pyridyl azocalix[*n*]arenes

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Abstract—A series of pyridylazo calix[*n*]arenes ($n=4$, 6, 8) including the first examples of mixed hetroaryl azocalix(*n*)arenes have been synthesized by coupling calix[*n*]arenes with diazonium salts derived from amino pyridines. It has been observed that the coupling reaction of diazonium salt obtained from 3-aminopyridine with calix[*n*]arene gives tetrakis-, hexakis- and octakis (pyridylazo)calix[*n*]arenes ($n=4,6,8$) while those derived from 4-aminopyridine give partially substituted (4-pyridylazo)calix[*n*]arene analogs. There is no reaction of calix(*n*)arenes with diazonium salts derived from 2-aminopyridine under identical conditions of experiments. The conformational analysis of synthesized compounds have been ascertained by detailed spectral measurements and single crystal X-ray analysis of 5-(3′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene. A rational explanation for the observed partial and exhaustive coupling reaction in the synthesis of heteroaryl azocalix(*n*)arenes has been suggested. Preliminary evaluation of synthesized derivatives as molecular receptors for metal ions indicates that they have good potential to function as selective ionic filters for cesium ions.

1. Introduction

Calix[*n*]arenes ($n=4$–20, where *n* is the number of phenyl units, Fig. 1a) are phenolic [1*n*]-metacyclophanes that can be easily obtained by base or acid-catalyzed condensation of *p*-substituted phenols with formaldehyde or paraformaldehyde.[1] They are known to provide useful building blocks for hollow molecular scaffolds with easily functionalizable hydrophilic and hydrophobic lower and upper rims, respectively.[2–4] Introduction of azo groups into the calix[*n*]arene framework confer chromogenicity that can be employed for the development of molecular diagnostics and sensor materials for metal ions and organic molecules.[5–7] For example, typically substituted azocalix[*n*]arenes (Fig. 1b) have been studied by various researchers in the recent past for their use in ionic and molecular recognition.[8,9] However, despite such studies, predictive information on the usefulness of coupling reaction between calix[*n*]arenes and diazonium salts to provide regioselective azo substituted calix[*n*]arenes is very limited. For example, it has been reported that the reaction of calix[4]arene with substituted benzene diazonium flouroborate in the presence of pyridine provides tetrakis(phenylazo)calix[4]arene[10–11] in good yield but the same reaction with benzene diazonium salt derived from aniline gives a very poor yield of the related product.

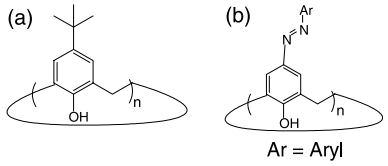

Figure 1. (a) *p-tert* Butyl calix[*n*]arene $n=4$–20, (b) *p*-substituted azo calix[*n*]arene $n=4,6,8$.

Since the base-catalyzed diazotization reaction involving diazo flouroborates usually led to the formation of tetrakis(arylazo)calix[4]arenes, Shinkai et al. ascribed this outcome to autocatalysis of the coupling reaction and suggested that deprotonation of a phenolic group by the basic solvent facilitates the reaction through hydrogen bond assistance.[12] Whether such an influence of hydrogen bonds is operative in all diazocoupling reactions is as yet a matter of speculation. During recent years, several reports have appeared in the literature[13–15] wherein the synthesis and characterization of partially substituted azo calixarenes have been utilized to elicit photoresponse to ionic or molecular recognition events. Differential observations and outcome of the coupling reaction of calix[*n*]arenes with diazonium salts derived from different aryl amine structures do not seem to have been explained. In the present work, we have attempted to understand the diazocoupling reaction of calix[*n*]arenes to rationally obtain chromogenic molecular filters that may be selective for metal ions and organic substrates. The choice of diazonium cations derived from aminopyridines[16,17] was

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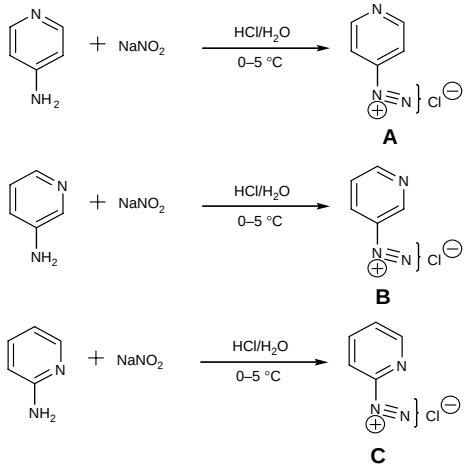
motivated by the expectation that the new azocalixarene derivatives might provide additional binding sites for the ionic and molecular guests and they may provide better visualization of the recognition process. We report herein, the results obtained on the reaction of calix[*n*]arenes with diazotized amino pyridines, a synthesis of mixed heteroaryl-azocalix[*n*]arenes and the preliminary evaluation of the synthesized derivatives for ionic recognition.

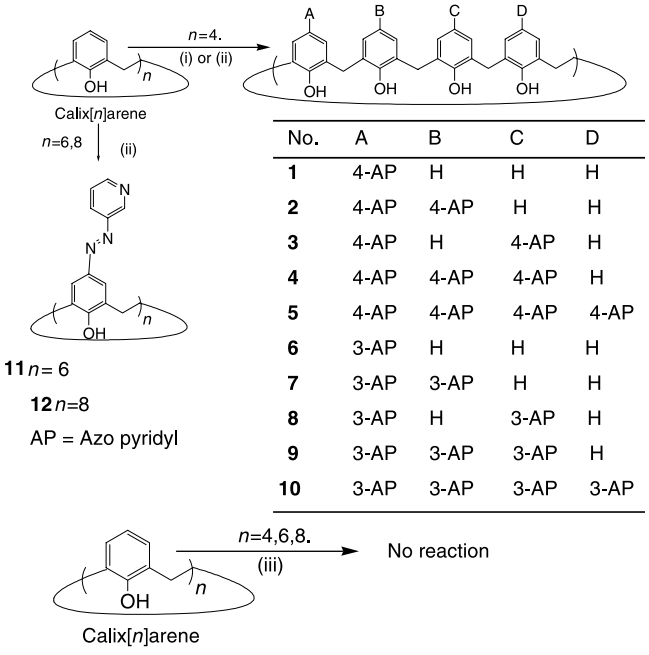
2. Results and discussion

2.1. Synthesis

The diazonium salts (**A**–**C**, Scheme 1) were prepared by treatment of corresponding amino pyridines with sodium nitrite and hydrochloric acid at low temperature (0–5 °C). (**A**), (**B**) and (**C**) were coupled with different calix[*n*]arenes as per the described experimental conditions and the products were isolated as given in Schemes 2 and 3.

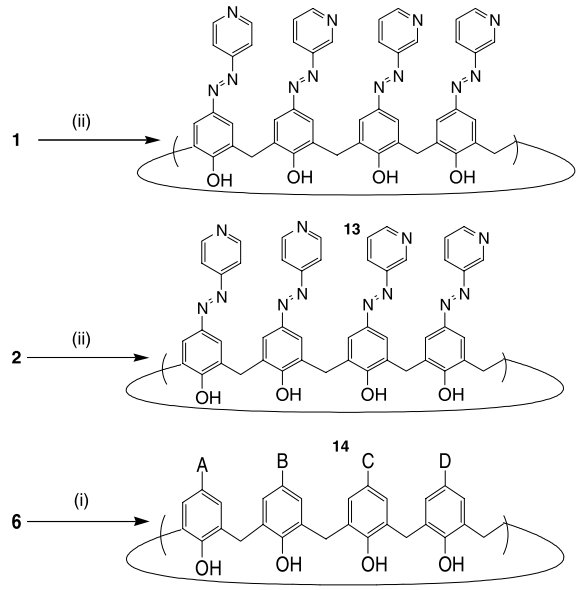


Scheme 1. Synthesis of various diazonium salts from respective amines and 2–3 equiv of $NaNO_2$ at 0–5 °C.

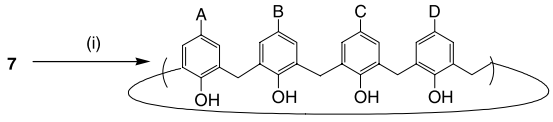


No.	A	B	C	D
1	4-AP	H	H	H
2	4-AP	4-AP	H	H
3	4-AP	H	4-AP	H
4	4-AP	4-AP	4-AP	H
5	4-AP	4-AP	4-AP	4-AP
6	3-AP	H	H	H
7	3-AP	3-AP	H	H
8	3-AP	H	3-AP	H
9	3-AP	3-AP	3-AP	H
10	3-AP	3-AP	3-AP	3-AP

Scheme 2. Synthesis of pyridyl azocalix[*n*]arenes (*n*=4, 6, 8).



No.	A	B	C	D
15	3-AP	4-AP	H	H
16	3-AP	H	4-AP	H
17	3-AP	4-AP	4-AP	H
18	3-AP	4-AP	H	4-AP
19	3-AP	4-AP	4-AP	4-AP



No.	A	B	C	D
20	3-AP	3-AP	4-AP	H
14	3-AP	3-AP	4-AP	4-AP

Scheme 3. Synthesis of mixed pyridyl azocalix[4]arenes at 0–5 °C. Reagents: (i) diazonium salt (A), DMF/MeOH, CH_3COONa; (ii) diazonium salt (B), DMF/MeOH, CH_3COONa; (iii) diazonium salt (C), DMF/MeOH, CH_3COONa.

2.2. Results

The coupling reaction of 8 equiv diazonium salt (**A**) and calix[4]arene for 4 h, provided a mixture of products (Table 1), which contained mono(4-pyridylazo)calix[4]-arene **1** as the major product (yield 30%) along with small amounts of bis(4-pyridylazo)calix[4]arenes **2** and **3** (yield 12 and 3%, respectively). A major portion of calix[4]arene was found to remain unchanged in this reaction and tris- and tetrakis(4-pyridylazo)calix[4]arene products could not be obtained at all. However, when four successive portions of 5 equiv of A were added in the coupling reaction after every 6 h and the reaction was continued for 30 h, the tris- and tetrakis (4-pyridylazo)calix[4]arenes **4** and **5** could be obtained in 12 and 4% yield (Table 1).

A similar coupling reaction of the diazonium salt (**A**) with calix[6]arene or calix[8]arene under identical experimental conditions, always resulted in a mixture of products, which was difficult to separate. Fully substituted

Table 1. Effect of reaction parameters on product distribution of coupling of calix[4]arene with diazonium salts (**A**), (**B**) and (**C**)

S. no.	Reactant (AP)[a]	Molar ratio[b]	Reaction time (h)	Product distribution (mmol %)					Proximal product:distal product ratio
				Mono-	Bis-(distal)	Bis-(proximal)	Tris-	Tetrakis-	
1	4-AP	1:1	1	3	—	—	—	—	—
2	4-AP	1:4	1	8	—	—	—	—	—
3	4-AP	1:4	4	16	—	4	—	—	—
4	4-AP	1:8	4	30	3	12	—	—	4
5	4-AP	1:16	4	35	6	20	—	—	3.3
6	4-AP	1:30[c]	24	25	7	22	12	4	3.1
7	3-AP	1:1	3	20	6	21	3	4	3.5
8	3-AP	1:2	3	30	10	35	5	15	3.5
9	3-AP	1:4.5	3	—	—	—	—	94	—
10	2-AP	1:16	24			No reaction			—

[a] Aminopyridine.
[b] Molar ratio of aminopyridine: calix[4]arene.
[c] Addition was effected in small portions.

(4-pyridylazo)calix[*n*]arenes (*n*=6, 8) were never obtained as major products in these reactions.

On the other hand the coupling reaction of a diazonium salt (**C**) and calix[*n*]arene (*n*=4,6,8) did not yield any diazo-coupled product even after 24 h of the reaction under identical conditions of experiments and respective starting materials could be recovered from the reaction broth (Scheme 2).

When the coupling reaction was attempted with a diazonium salt (**B**) with calix[4]arene, it exhibited significantly different results (Scheme 2). The use of 1 equiv of a diazonium salt gave a mixture of products (**6–10**). When the quantity of the diazonium salt was increased to 4.5 equiv, the tetra substituted compound **10** was obtained in 95% yield. Though the isolated yield of **10** was found to change with varying molar equivalents of the diazonium salt, the formation of the tetra substituted product was always observed in the reaction. Similarly, hexasubstituted compound **11** and octasubstituted compound **12** could be obtained in more than 90% yield through the coupling reaction of diazonium salt (**B**) with calix[6]arene and calix[8]arene, respectively (Scheme 2).

2.3. Characterization of products of the reaction

The IR spectra of synthesized pyridyl azocalixarenes (**1–20**) showed absorptions for OH as a broad band at a considerable higher frequency (3450–3200 cm^{-1}) than parent calix[4]-arenes[18] (~3120 cm^{-1}) indicating that hydrogen bonds are comparatively weaker in pyridyl azocalix[*n*]arenes. An asymmetric stretching vibration for the –N=N– group appeared in the 1600–1550 cm^{-1} range.[19]

The synthesized pyridyl azocalix[4]arenes (**1–20**) could be characterized by analysis of their ^1H and ^{13}C NMR spectra. The position of NMR signals for methylene carbons in the δ 29–34 range for synthesized compounds allowed us to conclude that these derivatives were present in their cone conformation. This conclusion is in accordance with results reported in the literature.[20] The chemical shift values and splitting pattern of synthesized bis(pyridylazo)calix[4]-arenes are listed in Table 2.

The identification of distal and proximal isomers of bis(pyridylazo)calix[4]arenes could be achieved by analysis of their ^1H and ^{13}C NMR spectra. For instance, four protons

Table 2. ^1H NMR spectral analysis of synthesized bis(pyridylazo)calix[4]arenes and ^{13}C NMR data for methylene carbons (δ, 300 MHz, 25 °C)

Compound no.	^1H NMR values and splitting patterns (δ, 300 MHz, 25 °C)			^{13}C NMR values for methylene carbons
	Pyridine core protons	Calixarene core protons	Methylene bridge protons	
2	8.75 (br s, 4H), 7.62 (d, *J*=5.1 Hz, 4H)	7.83 (s, 2H), 7.76 (s, 2H), 7.17 (d, *J*=8.1 Hz, 2H), 7.11 (d, *J*=7.2 Hz, 2H), 6.80 (t, *J*=7.5 Hz, 2H)	4.33 (br s, 4H), 3.73 (br s, 4H)	33.98, 32.72, 32.33
3	8.57 (br s, 4H), 7.56 (d, *J*=5.4 Hz, 4H)	7.70 (s, 4H), 6.99 (m, 4H,), 6.47 (m, 2H)	3.87 (br s, 4H)[a]	31.68
7	9.01 (s, 2H), 8.56 (br s, 2H), 7.99 (d, *J*=7.2 Hz, 2H), 7.37 (br s, 2H)	7.74 (s, 2H), 7.67 (s, 2H), 7.11 (d, *J*=7.2 Hz, 2H), 7.04 (d, *J*=7.2 Hz, 2H), 6.72 (t, *J*=7.2 Hz, 2H)	3.99 (br s, 6H)[a]	32.34, 31.38, 31.02
8	9.02 (s, 2H), 8.56 (br s, 2H), 7.96 (d, *J*=7.2 Hz, 2H), 7.35 (dd, *J*=4.2 Hz, 2H)	7.65 (s, 4H), 7.14 (d, *J*=7.5 Hz, 4H), 6.77 (t, *J*=7.5 Hz, 2H)	4.25 (br s, 4H), 3.65 (br s, 4H)	31.23
15	9.11 (s, 1H), 8.74 (d, *J*=3.6 Hz, 2H), 8.65–8.63 (m, 1H), 8.05 (d, *J*=8.1 Hz, 1H), 7.62 (d, *J*=6.3 Hz, 2H), 7.41 (dd, *J*=4.5, 4.5 Hz, 1H)	7.84–7.72 (m, 4H), 7.17 (dd, *J*=3.6 Hz, *J*=2.7 Hz, 2H), 7.10 (d, *J*=7.5 Hz, 2H), 6.79 (t, *J*=7.5 Hz, 2H)	4.33 (br s, 4H), 3.73 (br s, 4H)	31.82, 31.70, 31.58
16	9.02 (s, 1H), 8.68 (br s, 2H), 8.57 (br s, 1H), 7.99 (d, *J*=7.5 Hz, 1H), 7.58 (br s, 2H), 7.36 (dd, *J*=4.5, 4.5 Hz, 1H)	7.75–7.53 (m, 4H), 7.12 (d, *J*=7.8 Hz, 4H), 6.78 (t, *J*=7.8 Hz, 2H)	4.25 (br s, 4H), 3.65 (br s, 4H)	31.69

[a] The signals due to contaminant H_2O and solvents disturb this region.

of substituted calixarene core of **7** exhibited two singlets at δ 7.74 and 7.67 in its ^{1}H NMR spectrum while **8** gave a singlet at δ 7.65 for these protons. Methylene bridge carbons in **7** appeared as three peaks at δ 32.34, 31.38 and 31.03 in the ^{13}C NMR spectrum while only one resonance at δ 31.23 was observed for the methylene carbon in the NMR spectrum of **8**. These data indicate that **7** was proximal isomer while **8** was a distal isomer. Similarly, other proximal (**2**, **15**) and distal (**3**, **16**) isomers (Fig. 2) were characterized.

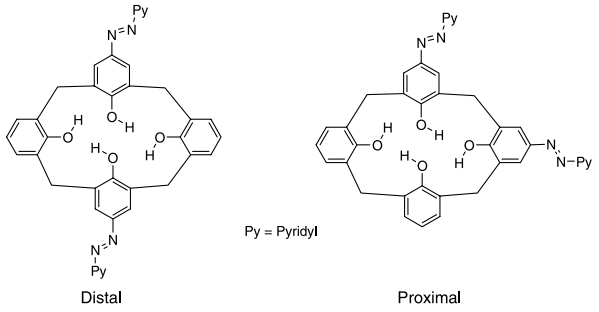


Figure 2. The distal and proximal isomers of bis(pyridylazo)calix[4]arene.

The appearance of only one resonance at δ 31.69 for the methylene carbon in the ^{13}C NMR spectrum of the tetrakis(3-pyridylazo)calix[4]arene **10** could also be attributed to its symmetric nature. This could be further confirmed by its DQF-COSY spectrum, which exhibited correlating cross peaks for only two types of methylene protons as given in Figure 3b. The detailed spectral analysis also led to the assignment of signals at δ 9.08, 8.71, 8.25 and 7.70 to the pyridine protons and the signals centered at δ 7.87 to the calixarene core protons in the ^{1}H NMR spectrum of **10**. Their correlations are represented in Figure 3a.

Mixed azo calix[4]arenes substituted by differently mixed azo calix[4]arenes substituted by differently positioned pyridyl groups could also be characterized by ^{1}H and ^{13}C NMR spectra. For example, signals at δ 8.96, 8.59, 8.04 and 7.50 for the 3-azopyridyl protons, signals at δ 8.67 and 7.61 for the 4-azopyridyl protons and a broad signal at δ 7.80 for the calix[4]arene core aromatic protons could be discovered in the ^{1}H NMR spectrum of **13**. ^{13}C NMR spectrum of **13** gave two signals at δ 31.73 and 31.89, which could be attributed to the methylene bridge carbons.

2.4. X-ray crystallographic analysis

Some of the synthesized azocalix[*n*]arenes were subjected to crystallization in different solvents to obtain single crystal X-ray diffraction for structural elucidation. For example, **6** could be crystallized from chloroform–diethyl ether (10/1) to provide crystals suitable for analysis by X-ray diffraction. An ORTEP diagram[21] and content of the unit cell for **6** are shown in Figure 4a and b. It appears that **6** crystallizes with chloroform embedded in the calixarene cavity with torsion angles ϕ and χ around Ar-CH_2-Ar bonds about C7, C14, C21 and C28 as −97.7(1), 86.4(1), −88.0(1), 92.2(1), −95.3(1), 84.6(1), −86.1(1) and 86.0(1), respectively. This is consistent with the cone conformation[22,23] found in parent *p-tert*-butylcalix[4]arene[24] and calix[4]arene.[25] All the four aromatic rings A(C1–C6), B(C8–C13), C(C15–C20) and D(C22–C27) seem to be almost planar with angles C6–C7–C8 = 112.86(85), C12–C14–C15 = 113.47(90), C19–C21–C22 = 113.51(93) and C26–C28–C2 = 114.36(96). The dihedral angle between the azo pyridyl group plane (C29–C33) is −10.5(17), which corroborate the alignment of heterocyclic ring with the cone conformation of calixarene skeleton. The corresponding hydroxyl substituents O1, O2, O3 and O4 are directed inwards the cavity of the calixarene architecture. The chloroform molecule shows prominent C–H–π interactions with an average H···π distance of 3.4 Å that holds the solvent molecule within the cavity. Hydroxyl groups corresponding to plane A and D do not seem to take part in intramolecular hydrogen bonding, while a significant intramolecular hydrogen bonding is observed amongst hydroxyl groups attached to plane B and C (O3–H3O–O4 = 1.877(8), O2–H2–O3 = 1.864(8) (Fig. 4c). There is prominent C–H–π interaction (with H–π distance 3.56 Å) that brings the substituted azo pyridyl group much closer to the plane A of adjacent ring with inversion center lying between the two calixarene molecules (Fig. 4c). Intermolecular C–H···N hydrogen bonds between N2 and H11 are observed at a distance of 2.75(2) Å. A prominent intermolecular C–H–π interaction exists between pyridyl hydrogen (C31–H31) and ring A (with H–π distance 3.37 Å) resulting in columnar packing (Fig. 4d) with two parallel up and down columns running along the axis *b*.

2.5. Discussion

The foregoing results reveal that exhaustively coupled (3-pyridylazo)calix[*n*]arenes are obtained in the case of

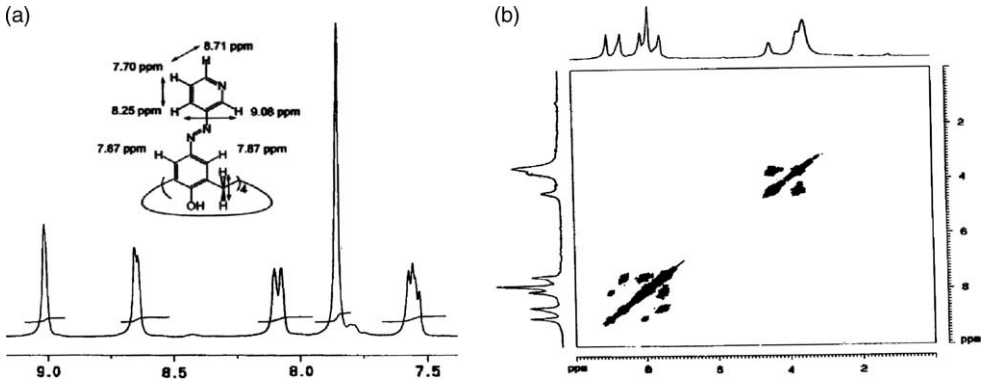


Figure 3. (a) Aromatic region of the ^{1}H NMR spectrum of **10** and DQF-COSY correlations given by arrows in the structure, (b) correlation of methylene and aromatic protons in DQF-COSY spectrum of **10** in d_6-DMSO at 25 °C and 300 MHz.

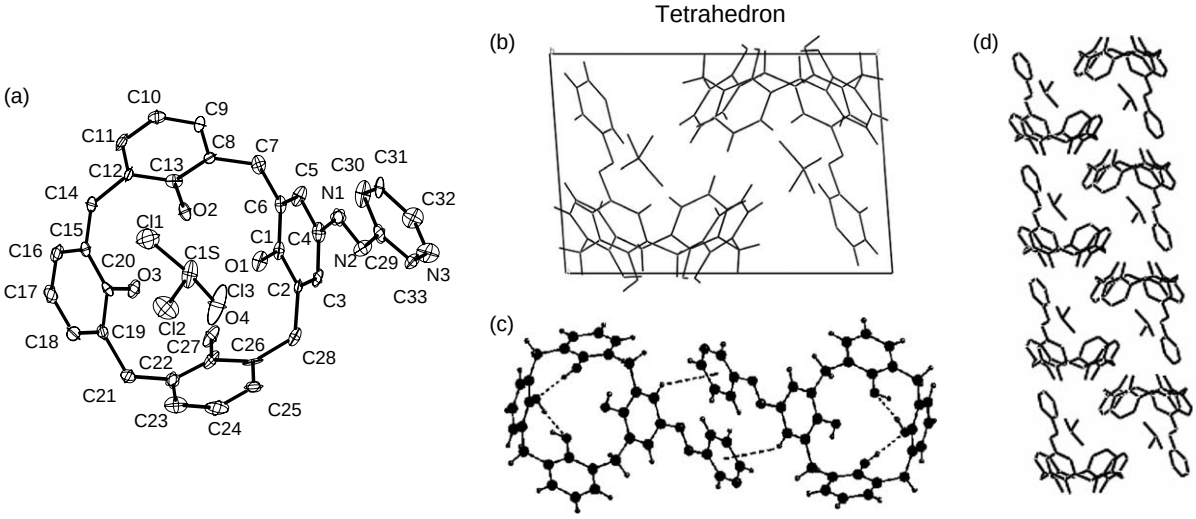


Figure 4. (a) ORTEP diagram showing labeling of atoms in **6** containing encapsulated chloroform. Hydrogens have been omitted for clarity, (b) contents of the unit cell, (c) intramolecular hydrogen bonds and CH–π interactions in **6**, (d) view of the molecular packing along the axis *b*.

diazotized 3-aminopyridine, while partially coupled (4-pyridylazo)calix[*n*]arenes are obtained in the case of 4-aminopyridines. These observations can be explained on the basis of differential electron attraction in (**A**) and (**B**) with appropriate position of ring nitrogen. Since the formation of tetrakis(phenylazo)calix[4]arenes have been earlier ascribed to hydrogen bond assistance,[12] one can reasonably believe that hydrogen bond assistance is inhibited in the coupling reaction of (**A**) and (**C**). Since calixarene skeleton and experimental conditions remain the same in all the reactions, it can *inter alia* be concluded that the earlier proposed autocatalysis of diazonium coupling due to hydrogen bond assistance is operative only in the case of coupling reaction of (**B**) and calixarene, but only partially in the case of coupling reactions of (**A**) with the same substrate. There does not seem to be any assistance in the case of diazo coupling reaction of (**C**) under identical reaction conditions and one needs to develop a different strategy for the desired (2-pyridylazo)calix[*n*]arenes.

Since diazonium salts in the present study were produced in situ, the results could also be ascribed to differential basic nature of aminopyridines, which might ionize calixarene hydroxyls to different extents [pK_a values at 20 °C = 5.98 (3-aminopyridine), 6.86 (2-aminopyridine), 9.17 (4-aminopyridine).[26] This conjecture, however, seems less likely to be true because diazonium salts from aminopyridines were obtained in situ when the solution was made acidic. This acidic solution was added to a calix[4]arene solution in DMF and methanol. The adopted reaction conditions were chosen in such a way that formation of self-coupled products from aminopyridines was avoided.

The above observations were further examined by carrying out the coupling reaction of calix[*n*]arenes with a mixture of diazonium salts to obtain mixed pyridyl azocalixarenes. For example, calix[4]arene on reaction with an equimolar mixture of (A) and (B) (5 equiv each) yielded **13** as the major product. Since 13 has more substituents derived from (**B**) than those from A, it indicates a better reactivity of (**B**) in comparison to that of (**A**) in the coupling reaction of calix[4]arenes with diazotized aminopyridines. Likewise when **1** was reacted with (**B**), it gave **13** (with three *para* positions substituted by 3-azopyridyl groups and one position substituted by 4-azopyridyl group), while when **2** was reacted with the same reaction mixture under identical conditions of experiments, it gave **14** as the only product, that is, completely substituted azocalix[4]arene derivative was formed. On the other hand, when partially substituted (3-pyridylazo)calix[4]arene was reacted with comparatively less reactive diazonium salt (**A**), it again resulted in a partially substituted (4-pyridylazo)calix-[*n*]arene. For example, when **6** was reacted with (**A**) it resulted in a mixture of compounds, which included **15** as the major product. Likewise, when reacted with (**A**), **7** gave **20** as the major product.

The above observations on the diazo coupling reaction of calix[*n*]arenes indicate that the earlier suggestion[12] to explain exhaustive coupling reaction in calix[*n*]arenes in terms of hydrogen bond assistance is not enough.

It was also observed that the diazo coupling reaction led to the formation of both the proximal and the distal isomers in the case of bis(pyridylazo) calix[4]arenes. Though the reason for the higher yield of the proximal isomers [**2**, **7**, **15**] as compared to that of the distal [**3**, **8**, **16**] isomers (about 3–4 times as much) can be ascribed to higher statistical probability of substitution due to deprotonation of one hydroxyl leading to further reaction to yield proximal compounds in the diazocoupling reaction. Since the ratio of proximal: distal compounds (as given in Table 1) has been found to be almost constant in all the reactions carried out; for example, reaction of calix[4]arene with (**A**) or (**B**) or that of **6** with (**A**), the initial reaction seems to be hydrogen bond assisted to lead to disubstituted derivatives. The reaction may then proceed further to form a tetra substituted compound only if it is favoured by electronic factors, for example, in the case of 3-aminopyridine.

It can therefore be concluded that the major product of the diazocoupling reaction of calix[*n*]arenes is decided by a subtle interplay of stereoelectronic factors and hydrogen bond assistance.

Table 3. Optical response of pyridyl azocalix[*n*]arenes (**1**, **2**, **4**, **6**, **7**, **9**, **10**, **11**, **12**, **13** and **14**) on addition of various metal ion salts

No.		**1**[a]	**2**[a]	**4**	**6**	**7**	**9**	**10**	**11**	**12**	**13**	**14**
λ_{max} (nm)		433	392	381	422	382	380	368	370	360	369	375
Salts		Metal-induced wavelength changes ($\Delta\lambda_{max}$ (nm))[b]										
Li^+		0	—	0	0	0	0	−6	+10	+3	+4	−1
Na^+		0	0	+8	0	0	0	−4	+6	+4	+3	+4
K^+		0	+3	+14	0	0	0	+2	+10	+11	+12	+21
Rb^+		—	—	+22	0	0	0	+11	+20	+10	+15	+33
Cs^+[c]	i	0	+35	+44	0	0	0	+40	+32	0	+28	+50
	ii	0	+108	+131	0	0	0	+122	+123	+16	+134	+118
Mg^{++}		0	0	0	0	0	0	0	0	−4	+3	0
Ca^{++}		0	0	0	0	0	0	0	0	+1	+3	0
Ba^{++}		0	0	+30	−46	−11	−8	−1	0	+3	+11	+30
Ti^{+++}		—	—	+31	—	−17	−13	—	—	—	—	+29
Cr^{+++}		−16	—	+30	−82	−27	−25	−12	−8	0	−9	+31
Co^{++}		+1	—	+30	−48	−13	−9	−1	0	+9	+12	+27
Ni^{++}		0	—	0	−8	+1	+2	0	+8	+7	+4	0
Cu^{++}		+16	—	+9	−11	−3	0	0	0	+1	+2	0
Hg^{++}		0	−3	+43	−51	−11	−4	+4	0	+1	+13	+23
Cd^{++}		0	+3	0	−63	0	0	0	0	—	+2	—
Ag^+		—	—	+28	−66	−30	−14	—	0	+10	+2	+28
Pb^{++}		—	—	+29	−46	−11	−10	−2	0	+7	+11	+6

Addition of a few drops of $CHCl_3$ were used for better solubility.
[a] Excess of metal salts were added in place of 100 equiv.
[b] (+) and (−) in wavelength changes denote red and blue shifts, respectively. Samples were prepared by mixing equal volumes of stock solutions of **1**, **2**, **4**, **6**, **7**, **9**, **10**, **11**, **12**, **13** and **14** and the metal salts.
[c] In addition to the red shift of the main band (i) a new peak (ii) also observed.

2.6. Preliminary investigation of synthesized pyridyl azocalix[*n*]arenes for ionic recognition

We were curious to determine if the azopyridyl unit in the compounds in this series could play a role in encapsulating metal ions to elicit changes in the absorption maxima in the UV/vis spectrum. All the synthesized compounds except **6**, **7** and **9** were found to exhibit a red shift of about 50 nm on addition of excess of cesium metal ion with the appearance of a new absorption band near 500 nm accompanied by a profound color change. Other ions did not interfere in such an interaction with cesium. Since till date, no azo calixarene without crown loop has been reported to be used as a selective filter for the radioactive wastes[27] containing cesium,[28,29] these compounds were examined as selective ionic filters for it. The changes in λ_{max} of the pyridyl azocalix[*n*]arenes (**1**, **2**, **4**, **6**, **7**, **9**, **10**, **11**, **12**, **13** and **14**) on addition of different ions, are given in Table 3. One representative example of changes in the UV/vis spectra of **14** on addition of alkali metal salts in methanol are depicted in Figure 5. Two isobestic points at 311 and 393 nm were

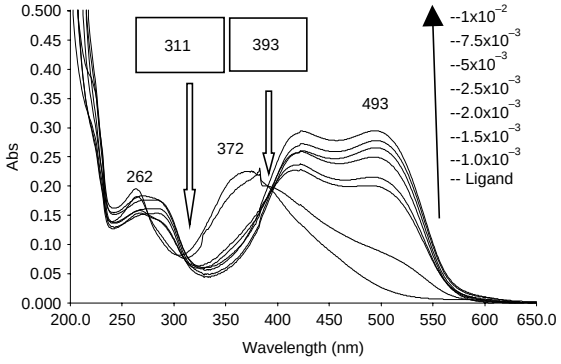


Figure 5. Change in the UV/vis spectrum of **14** when titrated by Cs_2CO_3 showing isobestic points at 311 and 393 nm.

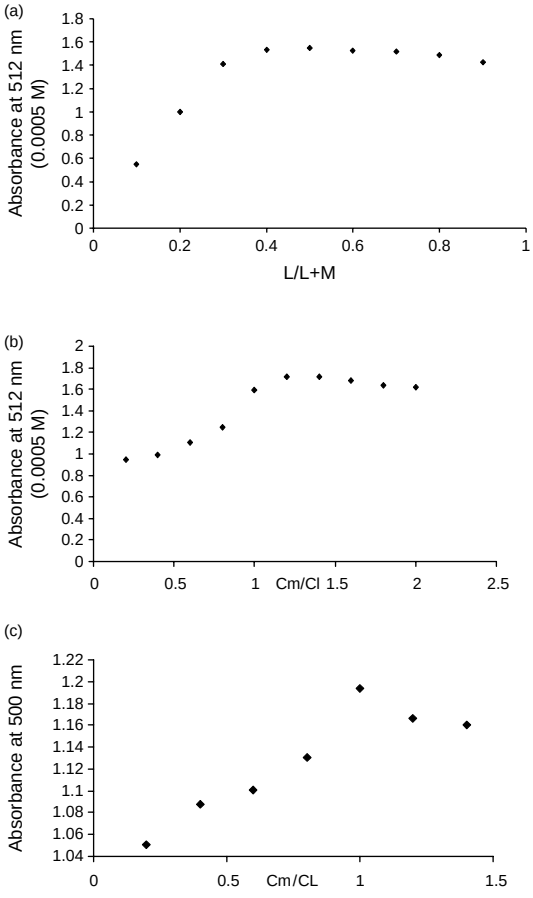


Figure 6. (a) Job's plot for complexation of **4** with Cs^+ ion revealing 1:1 stoichiometry, (b) mole ratio plot for complexation of **4** with Cs^+ ion confirming 1:1 stoichiometry and (c) mole ratio plot for complexation of **13** with Cs^+ ion revealing 1:1 stoichiometry.

identified in the case of **14** when it was titrated with Cs_2CO_3 solution in methanol.

Application of Job's continuous variation method[30] to probe a possible complexation ratio between **4**, **13** and Cs^+ ion revealed that the complex concentration approaches its maximum when the mole fraction of [L]/[L]+[Cs^+] was about 0.5 (Fig. 6a), where L represents the synthesized azocalixarenes examined in this study. The results obtained indicate the formation of a 1:1 complex in general. Similar results were obtained in the mole ratio experiments[30] (Fig. 6b and c). Further work to determine the specific nature of the interaction is in progress.

3. Experimental

All the reagents used in the study were purchased from Sigma–Aldrich or Merck and were chemically pure. The solvents used were distilled and used further without drying. Column chromatography was performed on silica gel (60–120 mesh) obtained from Merck. ^{1}H, ^{13}C NMR, DEPT-135 and DQF-COSY spectra were recorded on a 300 MHz Bruker DPX 300 instrument at room temperature using tetramethylsilane (TMS) at 0.00 as an internal standard. IR spectra were recorded on a Nicolet Protégé 460 spectrometer in KBr disks while X-ray data was recorded using a Bruker SMART CCD single crystal diffractometer. UV/vis spectra were obtained on a Perkin Elmer (Lambda-3B) recording spectrophotometer. The FAB mass spectra were recorded on a JEOL SX102/DA-6000 Mass spectrometer/Data System using Argon/Xenon (6 kV, 10 mA) as the FAB gas. Melting points were determined on an electrothermal toshniwal melting point apparatus and were uncorrected.

3.1. General procedure for the synthesis of pyridyl azocalix[*n*]arene

The pyridyl diazonium chloride solutions were prepared by the addition of an aqueous solution of sodium nitrite (1.5 equiv of amine) into solution of aminopyridine (2-, 3- or 4-substituted) in concd HCl (10–20 equiv) and distilled water (5–10 ml) at 0–5 °C. The diazotized solution was slowly added (in standardized molar ratio with respect to calix[*n*]arenes) into an ice-cold (0–5 °C) solution of calix[*n*]arenes (n=4, 6, 8) in DMF–methanol (8/5), sodium acetate (pH 7–9) with constant stirring to give yellow to dark red suspension. Reaction mixture was stirred for 2–24 h (variable for different compounds) at 0–5 °C and then for 30 min at room temperature. The suspension was poured into water, acidified with concd HCl to give a yellow to dark red precipitate, which was filtered to give a product or a mixture of products. The mixture was then separated by column chromatography (silica gel) to give substituted azocalix[*n*]arene derivatives.

p-tert-Butylcalix[4]arene, *p-tert*-butylcalix[6]arene, *p-tert*-butylcalix[8]arene, calix[4]arene, calix[6]arene and calix[8]arene were synthesized by the method described by Gutsche.[31,32]

3.1.1. 5-(4′-Pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 1. A solution of 4-aminopyridine (0.71 g, 7.5 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and 1.04 g (15.1 mmol) of chilled $NaNO_2$ solution in H_2O (2 ml) was added to it to produce a diazonium salt solution. After 15 min stirring, this diazonium salt solution was added dropwise to calix[4]arene (0.20 g, 0.47 mmol) at 0–5 °C in a mixture of DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol). The reaction mixture was stirred at the same temperature for 3 h. 2 N HCl was added to precipitate a deep red suspension, which was filtered off and washed with water. Further separation by column chromatography using chloroform–methanol (9.9/0.1) as the eluent afforded 0.087 g of **1** as dark red solid. Yield: 35%, mp>230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3606, 3092, 1631, 1592, 1449. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.70 (d, J=5.7 Hz, 2H), 7.90 (d, J=6.3 Hz, 2H), 7.85 (s, 4H), 7.90 (d, J=6.3 Hz, 2H), 7.15–7.03 (m, 6H), 6.64–6.56 (m, 3H), 4.20 (br s, 8H); ^{13}C NMR (300 MHz, DMSO-d_6): 174.5, 160.5, 151.9, 151, 144.7, 143.1, 133.1, 130.7, 128.4, 128.2, 127.8, 127.3, 120.3, 119.9, 116, 32.1, 30.7. DEPT-135 NMR (300 MHz, DMSO-d_6): 144.6, 128.4, 128.2, 127.8, 127.3, 120.3, 119.9, 116.0 (CH), 32.1, 30.7 (CH_2). ES MS m/z: 530.0 (M^+). Anal. Calcd for $C_{33}H_{27}N_3O_4$: C, 74.84; H, 5.14; N, 7.93. Found: C, 74.74; H, 5.14; N, 7.94. UV (λ_{max}, MeOH): 280, 434 nm.

3.1.2. 5,11-Bis(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 2. By the procedure described for **1**, **2** was synthesized and purified by column chromatography using chloroform–methanol (9.8/0.2) as the eluent to afford 0.075 g of **2** as dark red solid. Yield: 20%, mp>230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3422, 1634, 1593, 1457. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.19 (br s, 4H, D_2O exchangeable), 8.75 (br s, 4H), 7.83 (s, 2H), 7.76 (s, 2H), 7.62 (d, J=5.1 Hz, 4H), 7.17 (d, J=8.1 Hz, 2H), 7.11 (d, J=7.2 Hz, 2H), 6.80 (t, J=7.5 Hz, 2H), 4.33 (br s, 4H), 3.73 (br s, 4H); ^{13}C NMR (300 MHz, $CDCl_3$): 152.5, 151.1, 148.4, 147.3, 129.3, 129.2, 128.2, 127.2, 125.5, 124.7, 124.2, 122.6, 116, 31.7, 31.6, 29.6. DEPT-135 NMR (300 MHz, DMSO-d_6): 150.9, 129.2, 129.0, 125.3, 124.0, 122.4, 115.8 (CH), 31.7, 31.6, 29.6 (CH_2). ES MS m/z: 635.5 (M^++1). Anal. Calcd for $C_{38}H_{30}N_6O_4$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.61; H, 4.77; N, 13.20. UV (λ_{max}, MeOH): 271, 392 nm.

3.1.3. 5,17-Bis(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 3. By the procedure described for **1**, **3** was synthesized and purified by column chromatography using chloroform–methanol (9.85/0.15) as the eluent to afford 0.018 g of **3** as dark red solid. Yield: 6%, mp>230 °C (decomp.). ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.29 (br s, 4H, D_2O exchangeable), 8.67 (br s, 4H), 7.75 (s, 4H), 7.62 (d, J=5.4 Hz, 4H), 7.07 (t, J=7.5 Hz, 4H), 6.56 (t, J=7.5 Hz, 2H), 4.39 (d, J=12.6 Hz, 4H), 4.17 (d, J=12.9 Hz, 2H), 3.67 (d, J=13.2 Hz, 2H). ES MS m/z: 635.5 (M^++1). Anal. Calcd for $C_{38}H_{30}N_6O_4$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.84; H, 4.78; N, 13.30. UV (λ_{max}, MeOH): 273, 390 nm.

3.1.4. 5,11,17-Tris(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 4. A solution of 4-aminopyridine (0.22 g, 2.35 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.32 g, 4.7 mmol) solution in H_2O (2 ml) was added to it to yield a solution of the diazonium

salt. After about 15 min stirring, this diazonium salt solution was added dropwise at 0–5 °C to calix[4]arene (0.20 g, 0.47 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution. The reaction mixture was stirred at the same temperature for 6 h. Three successive portions of same amount of 4-aminopyridyl diazonium salt solution were freshly prepared and added to debutylated calix[4]arene after every 6 h while maintaining the temperature at 0–5 °C. The reaction was continued for 6 h at 0–5 °C and 2 N HCl was added to precipitate a deep red suspension, which was filtered off and washed with water. Further purification by column chromatography using chloroform–methanol (9.6/0.4) as the eluent afforded 0.042 g of **3** as dark red solid. Yield: 12%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3432, 1635, 1591, 1384. ^1H NMR (300 MHz, DMSO-d_6): δ 8.67 (br s, 6H), 7.83 (s, 2H), 7.78 (s, 2H), 7.76 (s, 2H), 7.61 (br s, 6H), 7.09 (d, J= 7.2 Hz, 2H), 6.59 (t, J=7.2 Hz, 1H), 4.40 (br s, 4H), 3.58 (br s, 4H). ES MS *m/z*: 740.1 (M^+). Anal. Calcd for $C_{43}H_{33}N_9O_4$: C, 69.81; H, 4.50; N, 17.04. Found: C, 69.70; H, 4.50; N, 16.98. UV (λ_{max}, MeOH): 262, 381 nm.

3.1.5. 5,11,17,23-Tetrakis(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 5. Reported by our group in Ref. 17. By the procedure described for **4**, **5** was synthesized and purified by column chromatography using chloroform–methanol (9.4/0.6) as the eluent to afford 0.016 g of **5** as dark red solid. Yield: 4%, mp > 230 °C (decomp.). ^1H NMR (300 MHz, DMSO-d_6): δ 8.66 (br s, 8H), 7.71 (s, 8H), 7.60 (br s, 8H), 4.38–372 (m, 8H). FAB MS *m/z*: 845 (M^+). Anal. Calcd for $C_{48}H_{36}N_{12}O_4$: C, 68.24; H, 4.29; N, 19.89. Found: C, 68.30; H, 4.26; N, 19.88. UV (λ_{max}, MeOH): 274, 392 nm.

3.1.6. 5-(3′-Pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 6. A solution of 3-aminopyridine (0.09 g, 0.95 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.13 g, 1.91 mmol) solution in H_2O (2 ml) was added to it to yield a solution of the diazonium salt. After about 15 min stirring, this diazonium salt solution was added dropwise at 0–5 °C to calix[4]arene (0.20 g, 0.47 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution. The reaction mixture was stirred for 3 h and 2 N HCl was added to precipitate an orange suspension, which was filtered off and washed with water. Further purification by column chromatography using chloroform–methanol (9.95/0.05) as the eluent afforded 0.050 g of **6** as a yellow solid. Yield: 30%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3199, 1591, 1455. ^1H NMR (300 MHz, $CDCl_3$): δ 9.08 (s, 1H), 8.64 (d, J=4.5 Hz, 1H), 8.06 (d, J=7.8 Hz, 1H), 7.73 (s, 2H), 7.44 (dd, J=9.0, 4.8 Hz, 1H), 7.17–7.06 (m, 6H), 6.79–6.70 (m, 3H), 3.99 (br s, 4H), 2.94 (br s, 4H); ^{13}C NMR (300 MHz, $CDCl_3$): 152.3, 150.87, 148.3, 147, 146.6, 129, 128.9, 128.8, 128.1, 127.8, 127.3, 126.5, 124, 123.6, 122.2, 31.4, 31.3. FAB MS *m/z*: 530 (M^+). Anal. Calcd for $C_{33}H_{27}N_3O_4$: C, 74.84; H, 5.14; N, 7.93. Found: C, 74.98; H, 5.13; N, 7.90. UV (λ_{max}, MeOH): 277, 422 nm.

3.1.7. 5,11-Bis(3′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 7. By the procedure described for **6**, **7** was synthesized and purified by column chromatography using chloroform–methanol (9.85/0.15) as the eluent afforded 0.105 g of **7** as orange solid. Yield: 35%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3394, 3219, 1688, 1584, 1457. ^1H NMR (300 MHz, DMSO-d_6): δ 9.01 (s, 2H,), 8.56 (br s, 2H), 7.99 (d, J=7.2 Hz, 2H), 7.74 (s, 2H), 7.67 (s, 2H), 7.37 (br s, 2H), 7.11 ((d, J=7.2 Hz, 2H), 7.04 (d, J= 7.2 Hz, 2H), 6.72 (t, J=7.2 Hz, 2H), 3.99 (br s, 8H); ^{13}C NMR (300 MHz, DMSO-d_6): 161.8, 151.3, 148.3, 147.5, 144, 142.9, 131.2, 130.8, 129.8, 129.4, 128.2, 125.4, 124.6, 124.1, 120.2, 32.3, 31.3, 31.0. FAB MS *m/z*: 635 (M^+). Anal. Calcd for $C_{38}H_{30}N_6O_4$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.78; H, 4.71; N, 13.26. UV (λ_{max}, MeOH): 271, 382 nm.

3.1.8. 5,17-Bis(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 8. By the procedure described for **6**, **8** was synthesized and purified by column chromatography using chloroform–methanol (9.85/0.15) as the eluent afforded 0.030 g of **8** as orange solid. Yield: 10% mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3457, 3428, 1615, 1454. ^1H NMR (300 MHz, $CDCl_3$): δ 10.1 (br s, 4H, D_2O exchangeable), 9.02 (s, 2H), 8.56 (br s, 2H), 7.96 (d, J= 7.2 Hz, 2H), 7.65 (s, 4H), 7.35 (dd, J=4.2 Hz, 2H), 7.14 (d, J=7.5 Hz, 4H), 6.77 (t, J=7.2 Hz, 2H), 4.25 (br s, 4H), 3.65 (br s, 4H); ^{13}C NMR (300 MHz, DMSO-d_6): 160.4, 151.3, 147.8, 147.5, 144.2, 142.1, 131.0, 129.6, 128.2, 124.6, 124.3, 119.2, 31.23. FAB MS *m/z*: 635 (M^+). Anal. Calcd for $C_{38}H_{30}N_6O_4$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.77; H, 4.70; N, 13.24. UV (λ_{max}, MeOH): 266, 376 nm.

3.1.9. 5,11,17-Tris(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 9. By the procedure described for **6**, **9** was synthesized and purified by column chromatography using chloroform–methanol (9.4/0.6) as the eluent afforded 0.017 g of **9** as orange solid. Yield: 5%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3435, 1594, 1472. ^1H NMR (300 MHz, DMSO-d_6): δ 12.7 (br s, 4H, D_2O exchangeable), 8.96 (s, 3H), 8.59 (br s, 3H), 8.05 (d, J= 8.1 Hz, 3H), 7.79 (s, 2H), 7.75 (s, 2H), 7.73 (s, 2H), 7.53 (dd, J=4.5, 6 Hz, 3H), 7.08 (d, J=7.5 Hz, 2H), 6.59 (t, J= 7.5 Hz, 2H), 4.45 (d, J=11.7 Hz, 2H), 4.33 (d, J=12 Hz, 2H), 3.63 (d, J=11.7 Hz, 2H), 3.46 (d, J=12.6 Hz, 2H); ^{13}C NMR (300 MHz, DMSO-d_6): 160.1, 150.4, 147.7, 145.5, 144.5, 131.6, 130.1, 128.1, 126.5, 124.3, 123.2, 120, 32.3, 31.44. ES MS *m/z*: 740.3 ($M^+ + 1$). Anal. Calcd for $C_{43}H_{33}N_9O_4$: C, 69.81; H, 4.50; N, 17.04. Found: C, 69.84; H, 4.52; N, 17.01. UV (λ_{max}, MeOH): 268, 380 nm.

3.1.10. 5,11,17,23-Tetrakis(3′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 10. A solution of 3-aminopyridine (0.22 g, 2.35 mmol) in 2 N HCl (5 ml) was chilled in an ice bath. A chilled $NaNO_2$ (0.32 g, 4.70 mmol) solution in H_2O (2 ml) was added to it to yield a solution of the diazonium salt of 3-aminopyridine. After about 15 min stirring, this diazonium salt solution was added dropwise at 0–5 °C to calix[4]arene (0.20 g, 0.47 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution. The reaction mixture was stirred for 3 h at 0–5 °C and 2 N HCl was added to precipitate an orange suspension, which was filtered off and washed with water, chloroform and methanol to afford 0.374 g of **10** as yellow solid. Yield: 94%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3484, 1592, 1471. ^1H NMR (300 MHz,

DMSO-d_6): δ 13.05 (br s, 4H, D_2O exchangeable), 9.01 (s, 4H), 8.65 (d, $J=3.9$ Hz, 4H), 8.09 (d, $J=7.8$ Hz, 4H), 7.85 (s, 8H), 7.57 (dd, $J=4.8$, 6 Hz, 4H), 4.45 (br s, 4H), 3.71 (br s, 4H); ^{13}C NMR (300 MHz, DMSO-d_6): 160.3, 148.6, 148.1, 144.6, 143.8, 130.6, 128.6, 125, 124.2, 31.6; DEPT-135 NMR (300 MHz, DMSO-d_6): 149.5, 144.7, 129.4, 125.9, 125.0 (CH), 31.6 (CH_2). ES MS *m/z*: 845.6 ($M^+ + 1$). Anal. Calcd for $C_{48}H_{36}N_{12}O_4$: C, 68.24; H, 4.29; N, 19.89. Found: C, 68.24; H, 4.24; N, 19.87. UV (λ_{max}, MeOH): 262, 367 nm.

3.1.11. 5,11,17,23,29,35-Hexakis(3′-pyridylazo)-37,38,39,40,41,42-hexahydroxycalix[4]arene, 11. A solution of 3-aminopyridine (0.21 g, 2.23 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.31 g, 4.46 mmol) solution in H_2O (2 ml) was added to it to produce a diazonium salt solution. After stirring for 15 min, the diazonium salt solution was added dropwise at 0–5 °C to calix[6]arene (0.20 g, 0.31 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution and the reaction mixture was stirred for 3 h at 0–5 °C. 2 N HCl was added to precipitate an orange suspension, which was filtered off and washing with water and chloroform to provide 0.358 g of **11** as yellow solid. Yield: 90%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3405, 1568, 1410. ^{1}H NMR (300 MHz, DMSO-d_6): δ 14.18 (br s, 6H, D_2O exchangeable), 9.0 (s, 6H), 8.6 (br s, 6H), 8.1 (d, $J=8.1$ Hz, 6H), 7.96 (s, 4H), 7.87 (s, 4H), 7.57 (br s, 6H), 7.37 (s, 4H), 4.28 (d, $J=11.7$ Hz, 4H), 3.96 (s, 4H), 3.77 (d, $J=11.7$ Hz, 4H); ^{13}C NMR (300 MHz, DMSO-d_6): 168, 160.2, 150.9, 149.9, 149.4, 148.6, 148.1, 145.8, 145.4, 145, 143, 142.4, 130.4, 129.6, 128.6, 127.4, 125, 124.4, 123.9, 119.7, 33.62, 32.63. FAB MS *m/z*: 1268 (M^+). Anal. Calcd for $C_{72}H_{54}N_{18}O_6$: C, 68.24; H, 4.29; N, 19.89. Found: C, 68.09; H, 4.26; N, 19.85. UV (λ_{max}, MeOH): 264, 379 nm.

3.1.12. 5,11,17,23,29,35,41,47-Octakis(3′-pyridylazo)-49,50,51,52,53,54,55,56-octahydroxycalix[4]arene, 12. A solution of 3-aminopyridine (0.20 g, 2.12 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.29 g, 4.25 mmol) solution in H_2O (2 ml) was added to it to give a solution of diazonium salt. After 15 min stirring, this diazonium salt solution was added dropwise at 0–5 °C to calix[8]arene (0.20 g, 0.23 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution and the reaction mixture was stirred for 3 h at 0–5 °C. 2 N HCl was added to precipitate an orange suspension, which was filtered off and washed with water and chloroform to afford 0.366 g of **12** as yellow solid. Yield: 92%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3429, 1635, 1592, 1466. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.0 (s, 8H), 8.62 (br s, 8H), 8.09 (d, $J=6.3$ Hz, 8H), 7.78 (s, 16H), 7.52 (br s, 8H), 4.07 (br s, 16H); ^{13}C NMR (300 MHz, DMSO-d_6): 160.5, 150.5, 147.7, 145.6, 144.3, 129.3, 127.9, 126.6, 124.4, 32.2; DEPT-135 NMR (300 MHz, DMSO-d_6): 151.3, 147.6, 129.5, 127.5, 125.2 (CH), 32.2 (CH_2). FAB MS *m/z*: 1690 (M^+). Anal. Calcd for $C_{96}H_{72}N_{24}O_8$: C, 68.24; H, 4.29; N, 19.89. Found: C, 68.37; H, 4.31; N, 19.87. UV (λ_{max}, MeOH): 280, 352 nm.

3.1.13. 5,11,17-Tris(3′-pyridylazo)-23-(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 13. A solution of 3-aminopyridine (0.12 g, 1.32 mmol) in of 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.18 g, 2.64 mmol) solution in H_2O (2 ml) was added to it to produce a solution of the diazonium salt. After 15 min stirring, this diazonium salt solution was added dropwise at 0–5 °C to **1** (0.20 g, 0.38 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution. The reaction mixture was stirred for 3 h at 0–5 °C followed by addition of 2 N HCl was added to precipitate a deep red suspension, which was filtered off. It was washed with water to give 0.290 g of **13** as dark red solid. Yield: 91%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3484, 1633, 1592, 1473. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.96 (s, 3H), 8.67 (br s, 2H), 8.59 (br s, 3H), 8.04 (d, 3H), 7.85 (s, 8H), 7.61 (br s, 2H), 7.50 (br s, 3H), 4.40 (br s, 4H); ^{13}C NMR (300 MHz, DMSO-d_6): 159.7, 151.1, 150.6, 147.7, 145.6, 144.7, 130.7, 126.6, 124.3, 123.9, 115.7, 31.8, 31.7; DEPT-135 NMR (300 MHz, DMSO-d_6): 151.1, 150.6, 146.6, 126.6, 124.6, 124.3, 124.0, 115.7 (CH), 31.8, 31.7 (CH_2). FAB MS *m/z*: 845 (M^+). Anal. Calcd for $C_{48}H_{36}N_{12}O_{44}$: C, 68.24; H, 4.29; N, 19.89. Found: C, 68.19; H, 4.29; N, 19.79. UV (λ_{max}, MeOH): 263, 368 nm.

3.1.14. 5,11-Bis(3′-pyridylazo)-17,23-bis(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 14. A solution of 3-aminopyridine (0.06 g, 0.63 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.09 g, 1.27 mmol) solution in H_2O (2 ml) was added to it to produce a diazonium salt solution. After stirring for 15 min, the diazonium salt solution was added dropwise at 0–5 °C to **2** (0.20 g, 0.31 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution. The reaction mixture was stirred for 3 h at 0–5 °C followed by addition of 2 N HCl was added to precipitate a red suspension, which was filtered off and washed with water to give 0.224 g of **14** as dark orange solid. Yield: 84%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3383, 1597, 1457. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.02 (s, 2H), 8.74 (br s, 4H), 8.67 (br s, 2H), 8.10 (d, $J=7.2$ Hz, 2H), 7.90 (m, 8H), 7.67 (br s, 4H), 7.58 (dd, $J=4.2$ Hz, 2H), 4.45 (br s, 4H), 3.74 (br s, 4H); ^{13}C NMR (300 MHz, DMSO-d_6): 161.4, 159.3, 157.1, 151.1, 150.7, 147.8, 145.5, 144.8, 144.4, 139.4, 130.7, 126.7, 124.52, 124, 115.8, 108.7, 31.9, 31.7, 31.4; DEPT-135 NMR (300 MHz, DMSO-d_6): 146.0, 145.6, 140.4, 121.5, 119.5, 118.9, 110.7, 103.6 (CH), 31.9, 31.7, 31.4 (CH_2). FAB MS *m/z*: 845 (M^+). Anal. Calcd for $C_{48}H_{36}N_{12}O_4$: C, 68.24; H, 4.29; N, 19.89. Found: C, 68.08; H, 4.28; N, 19.86. UV (λ_{max}, MeOH): 262, 374 nm.

3.1.15. 5-(3′-Pyridylazo)-11-(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 15. A solution of 4-aminopyridine (0.21 g, 2.26 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.31 g, 4.53 mmol) solution in H_2O (2 ml) was added to it to produce a diazonium salt solution. After stirring for 15 min, the diazonium salt solution was added dropwise at 0–5 °C to **6** (0.20 g, 0.38 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution. The reaction mixture was stirred for 3 h at 0–5 °C. 2 N HCl was added to precipitate a deep red suspension, which was filtered off and washing with water afforded 0.072 g of **15** as dark red solid. Yield: 30%, mp > 230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3383, 1630, 1598, 1457. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.10 (br s, 4H, D_2O exchangeable), 9.11 (s, 1H),

8.74 (d, J=3.6 Hz, 2H), 8.65–8.63 (m, 1H), 8.05 (d, J=8.1 Hz, 1H), 7.84–7.72 (m, 4H), 7.62 (d, J=6.3 Hz, 2H), 7.41 (dd, J=4.5, 4.5 Hz, 1H), 7.25–7.07 (m, 4H), 6.79 (t, J=7.5 Hz, 2H), 4.31 (br s, 4H), 3.72 (br s, 4H); ^{13}C NMR (300 MHz, $CDCl_3$): 152.3, 151.1, 151.0, 148.5, 147.9, 147.4, 146.9, 129.3, 129.2, 128.5, 128.2, 127.3, 126.78, 125.5, 125.1, 124.7, 124.3, 123.9, 123.8, 122.5, 116.0, 31.8, 31.7, 31.5. FAB MS m/z: 635 (M^+). Anal. Calcd for $C_{38}H_{30}N_6O_4$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.76; H, 4.75; N, 13.20. UV (λ_{max}, MeOH): 264, 378 nm.

3.1.16. 5-(3′-Pyridylazo)-17-(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 16. By the procedure described for **15**, **16** was synthesized and purified by column chromatography using $CHCl_3$–methanol (9.8/0.2) as the eluent to afford 0.019 g of **16** as a dark red solid. Yield: 8%, mp>230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3429, 1635, 1592, 1466. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.16 (br s, 4H, D_2O exchangeable), 9.02 (s, 1H), 8.68 (br s, 1H), 8.57 (br s, 2H), 7.99 (d, J=7.5 Hz, 1H), 7.75–7.64 (m, 4H), 7.58 (br s, 2H), 7.36 (dd, J=4.5, 4.5 Hz, 1H), 7.12 (d, J=7.5 Hz, 4H), 6.78 (t, J=7.5 Hz, 2H), 4.25 (br s, 4H), 3.48 (br s, 4H); ^{13}C NMR (300 MHz, $CDCl_3$): 152.3, 151.0, 148.5, 146.9, 129.3, 128.2, 127.3, 126.7, 125.5, 125.1, 124.7, 123.8, 122.5, 116.0, 31.6. FAB MS m/z: 635 (M^+). Anal. Calcd for $C_{38}H_{30}N_6O_4$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.68; H, 4.75; N, 13.21. UV (λ_{max}, MeOH): 265, 379 nm.

3.1.17. 5-(3′-Pyridylazo)-11,17-bis(4′-pyridylazo)-25,26,27,28-hydroxycalix[4]arene, 17. By the procedure described for **15**, **17** was synthesized and purified by column chromatography using $CHCl_3$–methanol (9.5/0.5) as the eluent to afford 0.028 g of **17** as a dark red solid. Yield: 10%, mp>230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3378, 1601, 1456. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.75 (s, 1H), 8.52–8.47 (m, 4H), 8.41 (br s, 1H), 7.84 (d, J=8.7 Hz, 1H), 7.69–7.42 (m, 10H), 7.33 (dd, J=4.5, 4.8 Hz, 1H), 6.90 (t, J=7.5 Hz, 2H), 6.40–6.35 (m, 1H), 4.05 (br s, 8H); ^{13}C NMR (300 MHz, DMSO-d_6): 158.7, 153.0, 152.6, 152.3, 152.0, 151.8, 149.5, 149.2, 148.3, 147.8, 131.6, 131.0, 130.1, 129.6, 129.3, 128.9, 128.3, 126.8, 125.9, 125.0, 124.5, 123.3, 120.2, 116.3, 115.9, 32.0, 31.7, 31.1, 29.0. ES MS m/z: 740.3 (M^+). Anal. Calcd for $C_{43}H_{33}N_9O_4$: C, 69.81; H, 4.50; N, 17.04. Found: C, 69.71; H, 4.52; N, 17.01. UV (λ_{max}, MeOH): 268, 380 nm.

3.1.18. 5-(3′-Pyridylazo)-11,23-bis(4′-pyridylazo)-25,26,27,28-hydroxycalix[4]arene, 18. By the procedure described for **15**, **18** was synthesized and purified by column chromatography using $CHCl_3$–methanol (9.5/0.5) as the eluent to afford 0.011 g of **18** as a dark red solid. Yield: 4%, mp>230 °C (decomp.), ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.03 (s, 1H), 8.66 (br s, 4H), 8.57 (br s, 1H), 7.96 (d, J=8.7 Hz, 1H), 7.76 (s, 4H), 7.69 (s, 2H), 7.53 (s, 4H), 7.31 (dd, J=4.5, 4.8 Hz, 1H), 7.18 (d, J=7.5 Hz, 2H), 6.75 (t, J=7.5 Hz, 1H), 4.28 (br s, 4H), 3.68 (br s, 4H); ^{13}C NMR (300 MHz, $CDCl_3$): 157.3, 152.2, 151.1, 147.0, 129.5, 126.7, 125.69, 125.1, 124.2, 123.8, 122.8, 116.0, 114.0, 31.7, 29.7. ES MS m/z: 740.3 (M^+). Anal. Calcd for $C_{43}H_{33}N_9O_4$: C, 69.81; H, 4.50; N, 17.04. Found: C, 69.86; H, 4.51; N, 17.04. UV (λ_{max}, MeOH): 268, 380 nm.

3.1.19. 5-(3′-Pyridylazo)-11,17,23-tris(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 19. A solution of 4-aminopyridine (0.32 g, 3.39 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.47 g, 6.79 mmol) solution in H_2O (2 ml) was added to it to yield a solution of diazonium salt. After stirring for 15 min, the diazonium salt solution was added dropwise at 0–5 °C to **6** (0.20 g, 0.38 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution. The reaction mixture was stirred for 3 h at 0–5 °C. 2 N HCl was then added to precipitate a deep red suspension, which was filtered off and washed with water. Further purification by column chromatography using $CHCl_3$–methanol (8.5/1.5) as the eluent afforded 0.080 g of **19** as a dark red solid. Yield: 20%, mp>230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3394, 1631, 1592, 1386. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.83 (s, 1H), 8.54 (br s, 7H), 7.87 (d, J=4.5 Hz, 1H), 7.75–7.67 (m, 8H), 7.53 (br s, 6H), 7.33 (br s, 1H), 4.21 (br s, 4H), 3.74 (br s, 4H). ES MS m/z: 845.6 (M^++1). Anal. Calcd for $C_{48}H_{36}N_{12}O_4$: C, 68.24; H, 4.29; N, 19.89. Found: C, 68.13; H, 4.31; N, 19.91. UV (λ_{max}, MeOH): 262, 367 nm.

3.1.20. 5,11-Bis(3′-pyridylazo)-17-(4′-pyridylazo)-25,26,27,28-tetrahydroxycalix[4]arene, 20. A solution of 4-aminopyridine (0.12 g, 1.27 mmol) in 2 N HCl (5 ml) was chilled in an ice bath and chilled $NaNO_2$ (0.18 g, 2.55 mmol) solution in H_2O (2 ml) was added to it to produce a diazonium salt solution, which was added dropwise to **7** (0.20 g, 0.31 mmol) in DMF (16 ml), MeOH (10 ml) and sodium acetate trihydrate (5 g, 36.7 mmol) solution at 0–5 °C. The reaction mixture was stirred for 3 h at 0–5 °C. 2 N HCl was added to precipitate a deep red suspension, which was filtered off and washed with water. Further separation by column chromatography using $CHCl_3$–MeOH (9.4/0.6) as the eluent provided 0.093 g of **20** as a dark red solid. Yield: 58%, mp>230 °C (decomp.), IR (KBr pellet, cm^{-1}): 3448, 1633, 1592, 1457. ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.66 (br s, 4H, D_2O exchangeable), 8.88 (s, 2H), 8.58 (br s, 2H), 8.51 (br s, 2H), 7.95 (br s, 2H), 7.69–7.42 (m, 10H), 6.90 (br s, 2H), 6.40–6.35 (br s, 1H), 4.33 (br s, 8H). ES MS m/z: 740.3 (M^+). Anal. Calcd for $C_{43}H_{33}N_9O_4$: C, 69.81; H, 4.50; N, 17.04. Found: C, 69.71; H, 4.52; N, 17.05. UV (λ_{max}, MeOH): 268, 380 nm.

3.2. UV/vis experiments

3.2.1. General procedures for UV/vis experiments. All the UV/vis experiments were carried out in methanol unless otherwise specified. Any shift in the UV/vis spectra of the pyridyl azocalixarenes were recorded on addition of metal salt (100 equiv) solutions.

3.2.2. Job's plot experiments. A stock solution of pyridyl azocalixarenes and Cs_2CO_3 were prepared in methanol. The Cs_2CO_3 and pyridyl azocalix[n]arene solutions with identical concentrations were mixed in different ratios in such a way that the total volume of the reactants in each mixture remains fixed at 5.0 ml but the mole ratio of the reactants varied systematically. After shaking for 5 min, the UV/vis absorbance at 500 nm was recorded. Assuming that only one complex was formed (ML_n) at equilibrium, the value of n could be calculated from the plot of χ_{max} [mole fraction of the ligand (χL) at maximum absorption] by

the following relationship —$n=\chi_{max}/[1-\chi_{max}]$ from the plot of absorbance versus χL, the value of χ_{max} was noted.

3.2.3. Mole ratio experiments. Solutions of pyridyl azocalixarenes in methanol and Cs_2CO_3 in methanol were prepared as stock solutions. The concentration of calixarene dye solution was held constant while that of the metal ion solution was varied. After shaking for 5 min, the UV/vis absorbance at 500 nm was recorded. A plot of absorbance versus mole ratio of the reactants was then prepared to calculate the mole ratio of calixarene and metal ion forming a potential complex.

3.3. X-ray structure determination of 6

Crystal data: $C_{37}H_{27}N_3O_4\cdot CHCl_3$, $M=648.94$, triclinic, $a=9.496(8)$ Å, $b=11.183(9)$ Å, $c=14.841(12)$ Å, $\alpha=76.317(14)^\circ$, $\beta=83.586(13)^\circ$, $\gamma=80.741(14)^\circ$, $V=1507(2)$ Å^3, $Z=2$, $D_c=1.430$ g cm^{-3}, $\mu=0.349$ mm^{-1} space group=P-1. Intensity data were collected up to $\theta=42^\circ$ by using 2θ scanning mode with graphite filtered Mo Kα radiation ($\lambda=0.71073$) on a $0.231\times0.098\times0.045$ mm^3 crystal at 298 K. A total of 7252 reflections were measured, 3234 were independent and of, which 1324 [$I>2$ (I)] were considered observed. The structure was solved by direct methods and refined by full matrix least-square techniques on F^2 using SHELXTL. All the nonhydrogen atoms were refined anisotropically. C–H hydrogen atoms were placed in geometrically calculated positions by using a riding model. SADABS was applied for absorption correction. Final R indices [$I>2\sigma$ (I)] $R1=0.2090$, $wR2=0.2160$, and R indices (all data) $R1=0.0897$, $wR2=0.1689$ was found for 3234 observed reflections, 0 restraints and 404 parameters. Torsion angles and H-bonding were calculated by using PARST. Crystal data have been deposited with the Cambridge Crystallographic Data Center, under reference CCDC 268185.

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