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ORIGINAL ARTICLE

Synthesis of novel cone-configurated *hexa-tert*-butyl-trimethoxy-calix[6]arenes bearing tris(bipyridyl) pendants and their use in recognition and ionic speciation

Har Mohindra Chawla · Rahul Shrivastava

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Abstract A series of novel cone-configurated *p-tert*-butyl-trimethoxycalix[6]arenes bearing three 2,2′-bipyridyl units at their lower rim have been synthesized. The ^{1}H NMR and ^{13}C NMR spectra of synthesized derivatives revealed that the ring inversion in calix[6]arene could be suppressed by the introduction of three 2,2′-bipyridyl moieties at the lower rim of calix[6]arene scaffold which fixes it into its cone configuration. The complexation ability of the synthesized receptors (**5a–d**) towards Fe(II) ion was investigated by UV-Visible titration to reveal that the synthesized receptors interact with Fe(II) in a 1:1 binding stoichiometry and respond to a specific oxidation state of the metal ion. The observations have significance for studies directed at the design of molecular receptors for ionic speciation through molecular recognition.

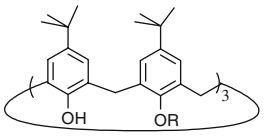
Keywords *p-tert*-Butylcalix[6]arene · 2, 2′-Bipyridine · Complexation · Speciation

Introduction

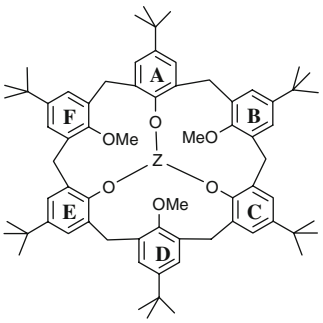
Calix[*n*]arenes (n = 4–20, where n is the number of phenyl units) are cavity-containing phenolic [1_n]-metacyclophanes that can be easily obtained by base or acid-catalyzed condensation of *p*-substituted phenols with formaldehyde or paraformaldehyde [1]. They possess easily functionalizable hydrophobic upper rim and hydrophilic lower rim to encompass a hollow cavity of varying dimensions and conformations [2]. The observed diversity of calix[*n*]arenes essentially lies in their conformational isomerism due to rotation of $ArCH_2Ar$ bonds or molecular rotation through the annulus [3]. The controlled conformational flexibility of these macrocycles is a major criterion for their ability to act as molecular receptors for ions, molecules and reaction intermediates. Unlike most studied calix [4]arenes, the calix[6]arenes have received comparatively lesser attention despite their greater potential as ionic and molecular receptors probably due to their higher degree of rotational flexibility and difficulties experienced in achieving conformational control [4]. Several attempts have been made to reduce the rotational flexibility of phenyl units in calix[6]arenes (e.g. **I** and **II**) through connectors separated by **Z** (i.e. **III–V**) or by bridging the phenyl units (**A–F**) through one bridge (**A**,**D**- and **A,C**-), two bridges (**A,C**; **D,E**) or three bridges (**A,E**; **B,D**; **C**,**F**) [5–13]. The other alternative techniques involve bridging of the upper or the lower rim with multipodal cap (**Z**) of calix[6]arenes [14, 15]. The latter technique not only represents a potential method to freeze the conformation of calix[6]arenes but also to construct interesting host molecules with unique conformations. For instance, the connectivity of six phenol groups of **I** by two triply bridging phosphate groups (**A,B,C**; **D,E,F**) could provide an example of a calix[6]-arene with immobilized conformation [16]. Other examples of conformational control through capping of their lower-rim with C_3-symmetrical tripodal caps to give **A,C,E**-bridged systems such as **III**, **IV**, **V** [17–19]. To the best of our knowledge, there seems to be no attempt to evaluate the possibility of using heteroaromatic substituents like bipyridyl moieties for such a purpose. It was envisaged that such units will not only reduce rotational flexibility of calix[6]arenes but would also provide excellent binding sites for recognition of metal ions through soft nitrogen

H. M. Chawla (✉) · R. Shrivastava
Department of Chemistry, Indian Institute of Technology, Hauz Khas, New Delhi 110016, India
e-mail: hmchawla@chemistry.iitd.ernet.in; hmchawla@gmail.com

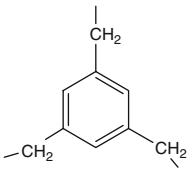
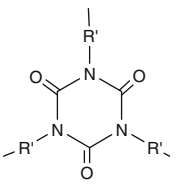
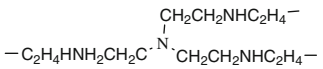
donor atoms present in these heteroaromatic units. In this paper, we present our efforts to obtain novel calix[6]arene based receptors in which the rotational freedom of calix[6]arene gets prominently suppressed by the substitution of the three 2,2′-bipyridyl moieties at their lower rim to provide a cone configurated calix[6]arene receptors (**5a**–**d**) that possess six nitrogen donor sites for exploring recognition of various transition metal ions.



I: R = H
II: R = CH_3



III-V

	III	IV	V
Z			

R' = $CH_2CH_2OCOCH_2$

Experimental

General

All the reagents used in the study were purchased from Sigma-Aldrich or Merck and were considered chemically pure. Solvents used were predried and purified by distillation as recommended in the literature. Column chromatography was performed on silica gel (60–120 mesh) obtained from Merck. Melting points were recorded on an electric melting point apparatus (Toshniwal, India) and are uncorrected. FT-IR spectra were recorded on a Nicolet Protégé 460 spectrometer using KBr discs while CHN analysis were taken on a Perkin-Elmer 240C elemental analyzer. ^{1}H NMR and ^{13}C spectrum were recorded on a 300 MHz Bruker DPX 300 instrument at room temperature using tetramethyl silane (TMS) as an internal standard.

Compound **4a**

A mixture of *p*-hydroxy-benzaldehyde (0.30 g, 2.45 mmol) and anhydrous K_2CO_3 (0.70 g, 5.0 mmol) in anhydrous acetone (25 mL) was heated at reflux for 1 h. 5,5′-bis(bromomethyl)-2,2′-bipyridine (1.00 g, 2.92 mmol) was then added and the resulting mixture was refluxed for 8 h. The mixture was then filtered and solvent removed under reduced pressure. The obtained yellow solid was dissolved in CH_2Cl_2 (20 mL) and the solution washed with water (3 × 25 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The resulting crude product was purified by column chromatography using chloroform-ethylacetate (8:2) as the eluent to give pure yellow solid (0.73 g, 1.9 mmol, 66%), mp 140–143 °C, IR (KBr, pellet, cm^{-1}): 2860, 1690, ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (s, 2H, CH_2-Br), 5.23 (s, 2H, CH_2bpy), 7.09 (d, J = 8.4 Hz, 2H, ArH), 7.85 (m, 4H, H^4,$H^{4'}$bpy + ArH), 8.45 (d, J = 8.2 Hz, 1H, H^3bpy), 8.46 (d, J = 8.2 Hz, 1H, $H^{3'}$bpy), 8.69 (s, 1H, H^6bpy), 8.67 (s, 1H, $H^{6'}$bpy), 9.01 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$): 29.4, 67.6, 115.1, 121.1, 130.5, 132, 133.9, 136.2, 137.6, 148.3, 149.3, 155.4, 163.2, 190.6. FAB MS m/z: 383 (M^+ + 1). Anal. Calcd for $C_{19}H_{15}BrN_2O_2$: C, 59.55; H, 3.95; N, 7.31. Found: C, 59.63; H, 3.81; N, 7.19.

Compound **4b**

A mixture of *p*-hydroxy-acetophenone (0.30 g, 2.2 mmol) and anhydrous K_2CO_3 (0.50 g, 3.62 mmol) in anhydrous acetone (25 mL) was heated at reflux for 1 h. 5,5′-bis(bromomethyl)-2,2′-bipyridine (1.0 g, 2.92 mmol) was then added and the resulting mixture heated at reflux for 8 h, filtered and the solvent removed under reduced

pressure. The yellow solid separated was dissolved in CH_2Cl_2 (30 mL) and washed with water (3 × 25 mL). The organic layer dried (anhydrous Na_2SO_4) filtered and concentrated in vacuo to gave crude product which was purified by column chromatography using chloroform-ethylacetate (8:2) as the eluent to give pure yellow solid (0.81 g, 2.0 mmol, 70%) mp 135–138 °C, IR (KBr, pellet, cm^{-1}) 2920, 1675: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.49 (s, 3H, $COCH_3$), 4.46 (s, 2H, CH_2Br), 5.13 (s, 2H, CH_2bpy), 6.94 (d, J = 8.4 Hz, 2H, ArH), 7.80 (d, J = 8.2 Hz, 1H, H^4bpy), 7.85 (d, J = 8.2 Hz, 1H, $H^{4'}$bpy), 7.90 (d, J = 8.4 Hz, 2H, ArH), 8.30 (bs, 2H, H^3,$H^{3'}$bpy), 8.61 (s, 1H, H^6bpy), 8.66 (s, 1H, $H^{6'}$bpy); ^{13}C NMR (75 MHz, $CDCl_3$): 28.4, 29.4, 67.6, 117, 122, 130, 132.2, 133.9, 136.2, 139.6, 147.7, 148.9, 157, 165.2. FAB MS m/z: 398 ($M^+ + 1$). Anal. Calcd for $C_{20}H_{17}BrN_2O_2$: C, 60.47; H, 4.31; N, 7.05. Found: C, 60.23; H, 4.53; N, 7.11.

Compound **4c**

K_2CO_3 (0.36 g, 2.6 mmol) was added to a solution of *p*-nitro-phenol (0.20 g, 1.43 mmol) in anhydrous acetone (20 mL). The reaction mixture was refluxed for 20 min and a solution of 5,5′-bis(bromomethyl)-2,2′-bipyridine (0.59 g, 1.72 mmol) in anhydrous acetone (10 mL) was introduced. After 9 h of refluxing, the solvent was removed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed with water. Solvent evaporation led to yield a crude product which was purified by column chromatography using chloroform-ethylacetate (8.5:1.5) as the eluent to give pure yellow solid (0.47 g, 1.19 mmol, 69%), mp > 130–133 °C, ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.46 (s, 2H, CH_2Br), 5.17 (s, 2H, CH_2bpy), 6.98 (d, J = 9.1 Hz, 2H, ArH), 7.77 (d, J = 8.2 Hz, 1H, H^4bpy), 7.80 (d, J = 8.2 Hz, 1H, $H^{4'}$bpy), 8.15 (d, J = 9.1 Hz, 2H, ArH), 8.26 (d, J = 8.2 Hz, 1H, H^3bpy), 8.36 (d, J = 8.2 Hz, 1H, $H^{3'}$bpy), 8.60 (s, 1H, H^6bpy), 8,67 (s, 1H, $H^{6'}$bpy); ^{13}C NMR (75 MHz, $CDCl_3$): 29.3, 68.7, 121.1, 131, 132, 133.8, 136.6, 138.7, 148, 150.7, 156, 164. FAB MS m/z: 400 ($M^+ + 1$). Anal. Calcd for $C_{18}H_{14}BrN_3O_3$: C, 54.02; H, 3.53; N, 10.50. Found: C, 54.17; H, 3.61; N, 10.19.

Compound **5a**

A solution of trimethoxy calixarene (0.1 g, 0.098 mmol) in anhydrous THF (15 mL), NaH (0.1 g, 4.42 mmol) was added and the reaction mixture stirred for 10 min at room temperature. A solution of compound **4a** (0.188 g, 0.49 mmol) in 5.0 mL anhydrous THF was added and after 2 h of stirring at room temperature the reaction mixture heated for additional 30 h in nitrogen atmosphere at 80 °C. The solution was evaporated under vacuum and residue was recrystallized from methanol to yield a white precipitate which was further purified by column chromatography using chloroform-ethylacetate (3:7) as the eluent to give pure white solid (0.157 g, 8.0×10^{-2} mmol, 83%), mp > 210–215 °C, IR (KBr, pellet, cm^{-1}): 2865, 1692, ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.75 (s, 27H, t-butyl), 1.30 (s, 27H, t-butyl), 2.21 (s, 9H, OCH_3), 3.31 (d, J = 15.3 Hz, 6H, $ArCH_2Ar$), 4.50 (d, J = 15.3 Hz, 6H, $ArCH_2Ar$), 4.98 (s, 6H, CH_2bpy), 5.15 (s, 6H, bpyCH_2), 6.63 (s, 6H, ArH_{calix}), 7.02 (d, J = 8.3 Hz, 6H, ArH), 7.20 (s, 6H, ArH_{calix}), 7.77 (m, 9H, H^4bpy + ArH), 7.94 (d, 3H, J = 8.2 Hz, $H^{4'}$bpy), 8.30 (d, 3H, J = 8.2 Hz, H^3bpy), 8.40 (d, 3H, J = 8.2 Hz, $H^{3'}$bpy), 8.67 (s, 3H, H^6bpy), 8.72 (s, 3H, $H^{6'}$bpy), 8.98 (s, 3H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$): 29.9, 31.1, 31.6, 60.2, 67.8, 72.0, 115, 121, 123.78, 128, 131, 132.4, 132.9, 133.6, 136.2, 136.8, 145, 148.3, 148.8, 151, 155, 156.2, 190.7. FAB MS m/z: 1922 ($M^+ + 1$). Anal. Calcd for $C_{126}H_{132}N_6O_{12}$: C, 78.72; H, 6.92; N, 4.37. Found: C, 78.61; H, 6.55; N, 4.79.

Compound **5b**

A solution of trimethoxy calixarene (0.1 g, 0.098 mmol) in anhydrous THF (15 mL), NaH (0.1 g, 4.42 mmol) was added and the reaction mixture stirred for 10 min at room temperature. A solution of compound **4b** (0.176 g, 0.44 mmol) in anhydrous THF (5.0 mL) was added and stirred for 2 h at room temperature after which it was heated for additional 30 h in nitrogen atmosphere at 80 °C. The solution was evaporated under vacuum and the resulting residue recrystallized from methanol to give a white precipitate which was further purified by column chromatography using chloroform-ethylacetate (3:7) as the eluent to give pure white solid (0.176 g, 8.9×10^{-2} mmol, 88%), mp > 210–218 °C, IR (KBr, pellet, cm^{-1}): 2958, 1676, ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (s, 27H, t-butyl), 1.37 (s, 27H, t-butyl), 2.29 (s, 9H, OCH_3), 2.55 (s, 9H, $COCH_3$), 3.38 (d, J = 14.3 Hz, 6H, $ArCH_2Ar$), 4.56 (d, J = 14.3 Hz, 6H, $ArCH_2Ar$), 5.06 (s, 6H, CH_2bpy), 5.20 (s, 6H, bpyCH_2), 6.70 (s, 6H, ArH_{calix}), 7.02 (d, J = 7.1 Hz, 6H, ArH), 7.26 (s, 6H, ArH_{calix}), 7.94 (m, 12H, H^4,$H^{4'}$bpy + ArH), 8.4 (bs, 6H, H^3,$H^{3'}$bpy), 8.73 (s, 3H, H^6bpy), 8.79 (s, 3H, $H^{6'}$bpy); DEPT-135 (75 MHz, $CDCl_3$): 26.3, 30.2, 31.0, 31.5, 60.1, 67.5, 72, 114, 121, 123.7, 128, 130.6, 136.2, 148.2, 148.7. FAB MS m/z: 1964 ($M^+ + 1$). Anal. Calcd for $C_{129}H_{138}N_6O_{12}$: C, 78.87; H, 7.08; N, 4.28. Found: C, 78.71; H, 6.93; N, 4.33.

Compound **5c**

A solution of trimethoxy calixarene (0.1 g, 0.098 mmol) in anhydrous THF (15 mL), NaH (0.1 g, 4.16 mmol) was added and the reaction mixture stirred for 10 min at

room temperature. A solution of compound **4c** (0.1 g, 0.25 mmol) in anhydrous THF (5.0 mL) was added and mixture stirred for 2 h at room temperature after which it was heated for additional 30 h in nitrogen atmosphere at 80 °C. The solution was evaporated under vacuum and the resulting residue was recrystallized from methanol to yield a white precipitate which was further purified by column chromatography using chloroform-ethylacetate (4:6) as the eluent to give pure white solid (0.170 g, 8.61×10^{-2} mmol, 91%), mp > 218–222 °C, IR (KBr, pellet, cm^{-1}): 2958, 1594; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (s, 27H, t-butyl), 1.37 (s, 27H, t-butyl), 2.28 (s, 9H, OCH_3), 3.38 (d, J = 14.3 Hz, 6H, $ArCH_2Ar$), 4.57 (d, J = 14.3 Hz, 6H, $ArCH_2Ar$), 5.05 (s, 6H, CH_2bpy), 5.24 (s, 6H, bpyCH_2), 6.71 (s, 6H, ArH_{calix}), 7.08 (d, J = 9.17 Hz, 6H, ArH), 7.27 (s, 6H, ArH_{calix}), 7.90 (d, J = 8.2 Hz, 3H, H^4bpy), 8.04 (d, J = 8.2 Hz, 3H, $H^{4'}$bpy), 8.24 (d, J = 9.1 Hz, 6H, ArH), 8.45 (bs, 6H, H^3,$H^{3'}$bpy), 8.45 (s, 3H, H^6bpy), 8.74 (s, 3H, $H^{6'}$bpy); ^{13}C NMR (75 MHz, $CDCl_3$): 29.1, 31.5, 32.3, 61.3, 68.2, 72.3, 114, 123, 124.78, 128.3, 131.4, 132.4, 133.2, 134.2, 135.2, 136.8, 147, 147.3, 148.8, 152, 156, 157.2. FAB MS m/z: 1974 ($M^+ + 1$). Anal. Calcd for $C_{123}H_{129}N_9O_{15}$: C, 74.86; H, 6.59; N, 6.39. Found: C, 74.61; H, 6.55; N, 6.79.

Compound **5d**

A solution of trimethoxy calixarene (0.1 g, 0.098 mmol) in anhydrous THF (20 mL), NaH (0.1 g, 4.16 mmol) was added and the reaction mixture stirred for 10 min at room temperature and a solution of 5-(bromomethyl)-5′methyl-2,2′-bipyridine (**3a**) (0.071 g, 0.27 mmol) in anhydrous THF (8.0 mL) was introduced. After 2 h stirring, the reaction mixture was heated for additional 30 h in nitrogen atmosphere at 80 °C. The solution was evaporated under vacuum and resulting residue recrystallized from methanol to give a white precipitate which was further purified by column chromatography using chloroform-ethylacetate (4:6) as the eluent to give pure white solid (0.135 g, 8.67×10^{-2} mmol, 88%), mp > 220 °C (decompose), ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81 (s, 27H, t-butyl), 1.25 (s, 27H, t-butyl), 2.27 (s, 9H, OCH_3), 2.39 (s, 9H, CH_3bpy), 3.36 (d, J = 11.5 Hz, 6H, $ArCH_2Ar$), 4.56 (d, J = 11.5 Hz, 6H, $ArCH_2Ar$), 5.04 (s, 6H, -CH_2bpy), 6.69 (s, 6H, ArH_{calix}), 7.26 (s, 6H, ArH_{calix}), 7.60 (d, J = 8.2 Hz, 3H, H^4bpy), 7.86 (d, J = 8.2 Hz, 3H, $H^{4'}$bpy), 8.27 (d, J = 8.2 Hz, 3H, H^3bpy), 8.33 (d, J = 8.2 Hz, 3H, $H^{3'}$bpy), 8.49 (s, 3H, H^6bpy), 8.66 (s, 3H, $H^{6'}$bpy); ^{13}C NMR (300 MHz, $CDCl_3$): 12.3, 29.4, 31.4, 62.4, 71.8, 113.8, 121, 125.38, 127.3, 131.3, 132.5, 133.1, 133.7, 134.8, 135.2, 144.6, 147.3, 148.3, 151.3, 157, 159.3. FAB MS m/z: 1561 ($M^+ + 1$). Anal. Calcd for $C_{105}H_{120}N_6O_6$: C, 80.73; H, 7.74; N, 5.38. Found: C, 80.29; H, 7.65 N, 5.47.

Analytical procedure

Procedure for UV-visible experiments

All the UV-visible experiments were carried out in methanol unless otherwise specified. Any shift in the UV-visible spectra of the bipyridyl-calix[6]arenes was recorded on addition of metal salt (100 equiv) solutions in chloroform:methanol (1:9 v/v).

Job's plot experiment: Stock solutions of compound **5a** (2×10^{-5} M) and $FeSO_4 \cdot 7H_2O$ (2×10^{-5} M) in chloroform and methanol (1:9) were prepared and the concentrations of each solution was varied with their total volume fixed to 5.0 mL. The mixture was shaken for 2 min and the UV-visible absorbance at 549 nm was recorded in each case. Assuming that only one complex (ML_n) was formed at equilibrium; the value of 'n' could be calculated from the plot of χ_{max} [mole fraction of the ligand (χ_L) at maximum absorption] by the following relationship, $n = \chi_{max}/1 - \chi_{max}$. The value of χ_{max} was noted from the plot of absorbance versus χ_L.

Determination of the association constants: The association constant (K_s) of **5a**/Fe^{+2} complex was determined from the following Benesi–Hildebrand equation [26]:

$$\frac{1}{A - A_0} = \frac{a}{a - b} \times \left[\frac{1}{K_s[M]} + 1\right]$$

Where K_s = Association constant, A_0 = The observed absorption in the absence of cation, A = The observed absorption after cation addition, [M] = The concentration of the cation-added, a and b are constants, the association constant value K_s was evaluated graphically by plotting 1/ΔA against 1/[M].

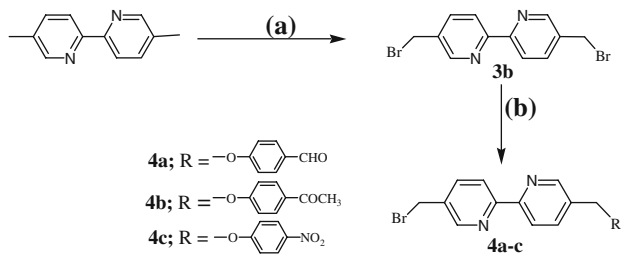
Mole ratio experiments: Solutions of compounds **5a** (2×10^{-5} M) in chloroform and methanol (1:9) and ferrous ion (1×10^{-3} M) in methanol were prepared as stock solutions. The concentration of **5a** in different solutions was held constant while that of the metal ion solution was varied. After shaking for 5 min, the UV/visible absorbance at 549 nm was recorded. A plot of absorbance versus mole ratio of the reactants was then prepared to calculate the mole ratio of **5a** and metal ion to understand the nature of interaction.

Results and discussion

Synthesis and characterization

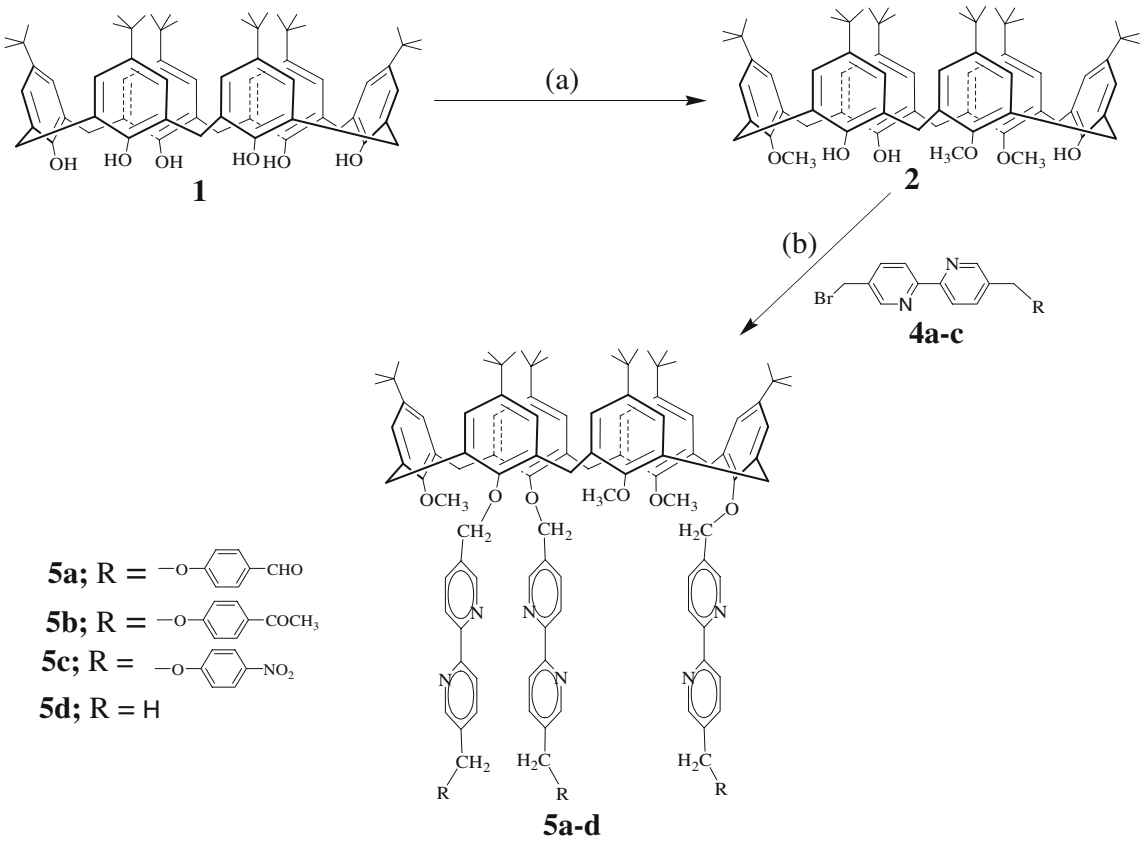
The required starting *p-tert*-butyl-calix[6]arene **1** was obtained by adopting the method described by Gutsche et al. [20]. It was reacted with methyl iodide in the presence of K_2CO_3 in anhydrous acetone at 70 °C at 80 psi pressure

to yield symmetrical 5,11,17,23,29,35-hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-trihydroxycalix[6]arene (**2**) in 72% yield [21]. The other precursor compounds, i.e. 5-(bromomethyl)-5′-methyl-2,2′-bipyridine (**3a**) and 5,5′-Bis(bromomethyl)-2,2′-bipyridine (**3b**) were obtained in more than 90% yields by radical bromination of 5,5′-dimethyl-2,2′-bipyridine with *N*-bromosuccinimide (1 equiv or 2 equiv respectively) by using 2,2′-azobisisobutyronitrile as a radical initiator and CCl_4 as a solvent through a modification of the reported method for related derivatives [22]. The 5,5′-bis(bromomethyl)-2, 2′-bipyridine (**3b**) was then reacted with *p*-hydroxy benzaldehyde, *p*-hydroxy-acetophenone and *p*-nitro-phenol in anhydrous acetone using K_2CO_3 as a base to provide **4a–c** in good yields (**4a**, 66%, **4b**, 70%, **4c**, 69% respectively) as depicted in Scheme 1. Treatment of 5,11,17,23,29,35-hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-trihydroxycalix[6]arene with **3a** and **4a–c** in anhydrous THF using NaH as a base at 80 °C for 24 h in nitrogen atmosphere provided **5a–d** in excellent yields (>80%) (Scheme 2).



Scheme 1 Reagents and reaction conditions: (a) NBS, AIBN, CCl_4, refluxing, 22 min; (b) *p*-hydroxybenzaldehyde/*p*-hydroxyacetophenone/*p*-nitrophenol, K_2CO_3, anhydrous acetone, reflux, 8–9 h

All the synthesized compounds were characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, Mass, UV-visible spectroscopy and elemental analysis. For instance, the ^{1}H NMR spectrum of **5a** exhibited two distinct singlets at δ 0.75 and 1.30 for *tert*-butyl protons and two singlets at δ 6.63 and 7.20 for the aromatic protons of calix[6]arene. A typical AB pattern represented by a pair of doublet at δ 3.31 and 4.50 for Ar-CH_2-Ar protons of calix[6]arene indicated that **5a** existed in a symmetrical cone conformation (Fig. 1b). The appearance of a resonance signal at δ 29.9 for the methylene carbon in its ^{13}C NMR spectrum could also be attributed to its symmetric nature. This could be further confirmed by recording its two dimensional HSQC (^{1}H-DEPT-135) spectrum, which exhibited cross peaks **1** and **2** at δ 29.9/3.31 and δ 29.9/4.50 that could be assigned for coupling of two types of methylene protons with single



Scheme 2 Reagents and reaction conditions: (a) CH_3I, K_2CO_3, CH_3CN, 24 h, 80 psi, 70 °C; (b) **4a–c**, **3a**, NaH, THF, 80 °C, 24 h

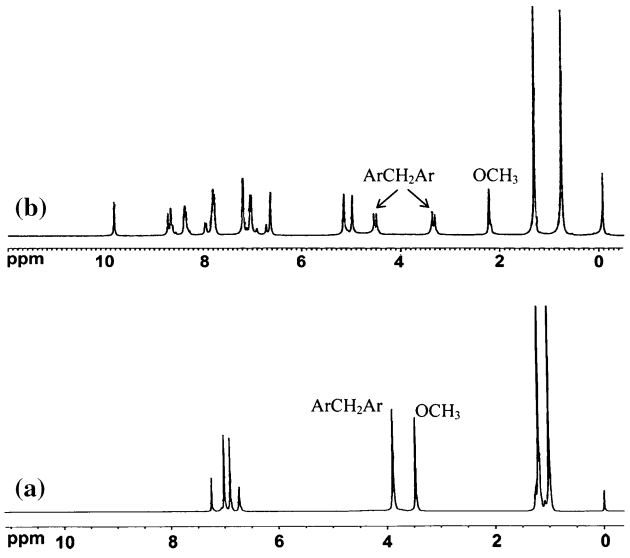


Fig. 1 ^{1}H NMR spectrum of compound (**a**) **2** and (**b**) **5a** in $CDCl_3$ at 298 K

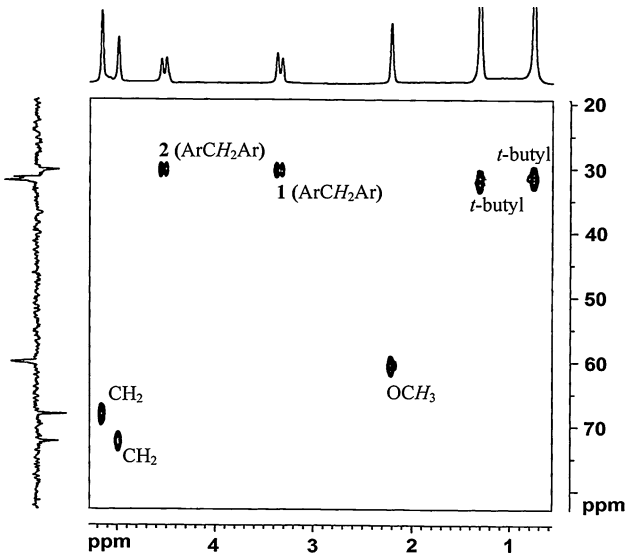


Fig. 2 Partial HSQC (^{1}H-DEPT-135) spectrum of **5a** in $CDCl_3$ at 298 K

methylene carbon (Fig. 2). Three singlets at δ 5.15, 4.98 and 2.21 could be assigned to the bpyCH_2, OCH_2bpy and OCH_3 protons while the aromatic protons of bipyridine unit appeared as three doublets at δ 7.94, 8.30 and 8.40 and two singlets at δ 8.67 and 8.72. A multiplet at δ 7.77 was determined to include aromatic protons of bipyridine and benzaldehyde units while a doublet at δ 7.02 could be assigned to the remaining aromatic protons of benzaldehyde unit. A singlet at δ 8.98 could be assigned to the CHO proton (Fig. 1b). These observations are consistent with a C_3-symmetrical cone conformation of the calix[6]arene scaffold. Salient features of ^{1}H NMR spectrum of different calix[6]arene-bipyridyl derivatives are given in Table 1.

The ^{1}H NMR spectrum of **5a** at 25 °C revealed that the methoxy protons appeared at a higher magnetic field (δ 2.21) than usual (δ 3.89). This is in consonance with previously reported results on triply capped calix[6]arenes (**IV** and **V**) which revealed that the methoxy protons of **5a** are flattened into the cavity of calix[6]arene in contrast to the other triply bridged calixarenes (**III**) where methoxy protons appeared at relatively low magnetic field (δ 3.85) in the ^{1}H NMR spectra at 25 °C. This is also in conformity with the molecular mechanics calculations which suggest that in its energy-minimized conformation, the methyl groups are flattened into the cavity of the molecule [17, 23, 24]. On the other hand the chemical shift values (δ_H) for the *tert*-butyl protons of bipyridyl substituted phenyl units and anisole units appeared at δ 0.75 and 1.30 respectively thereby confirming that the anisole units are indeed flattened into the cavity while bipyridyl substituted phenyl units are standing up in **5a**.

The ^{1}H NMR spectrum of receptor **5a** when recorded at different temperatures varying between −60 and 60 °C in deuterated chloroform (Fig. 3), revealed that the position of the pair of doublets for methylene bridge protons appeared consistently over the studied temperature range (−60 to 60 °C). This indicated that the ring inversion in calix[6]arene scaffold did not occur on the NMR time-scale and **5a** firmly maintained a cone conformation. The methoxy signal of calix[6]arene was found to shift at δ 2.05 on lowering of temperature to −60 °C while increase in the temperature up to 60 °C, this signal shifted to δ 2.38 (Fig. 3). These observations indicated that at low temperatures, methyl group of the anisole ring preferred a position situated deep inside the calixarene cavity but at higher temperatures the same methyl group was not deeply embedded inside the calixarene cavity.

Preliminary investigation of synthesized bipyridyl pendant calix[6]arenes for ionic recognition

The synthesized tris-bipyridyl receptors **5a–d** were examined for their interaction with transition metal ions (Co^{2+}, Ni^{2+}, Cd^{2+}, Ag^{+}, Cu^{2+}, Pd^{2+}, Pt^{2+}, Cs^{2+}, Hg^{2+}, Hg^{+}, Pb^{2+}) by UV-visible spectroscopy in $CHCl_3$:CH_3OH (1:9 v/v). The UV-visible spectrum of **5a–d** showed absorption peaks at 290 nm with a shoulder that could correspondingly be attributed to the collective absorption maxima (λ_{max}) for the bipyridyl [25] unit and calixarene [1–3] moiety present in the receptor molecules. For instance, when 2×10^{-5} M solution of **5a** was treated with different concentration of Fe(II) ions (2×10^{-3} to 2×10^{-4}), the absorption peak at 290 nm was found to split into two absorption peaks at 270 and 302 nm with the appearance of a new absorption peak at 549 nm in its UV-visible (Fig. 4) which was accompanied by a prominent 'naked-eye' color

Table 1 ^{1}H NMR splitting (300 MHz, 25 °C), ^{13}C NMR (75 MHz, 25 °C) and the UV-visible data of **5a–d**

Comp. No	^{1}H NMR values (δ) and splitting patterns (300 MHz, 25 °C)				^{13}C NMR signals for $ArCH_2Ar$ (δ, 25 °C, 75 MHz)	UV (λ_{max}) (nm)
	$-OCH_3$	CH_2-bpy	bpy-CH_2	Methylene bridge protons (8H) Ar-CH_2-Ar		
5a	2.21 (s, 9H)	4.98 (s, 6H)	5.15 (s, 6H)	3.31 (d, 6H, J = 15.3 Hz) 4.50 (d, 6H, J = 15.3 Hz)	29.9	290
5b	2.29 (s, 9H)	5.06 (s, 6H)	5.20 (s, 6H)	3.38 (d, 6H, J = 14.3 Hz) 4.56 (d, 6H, J = 14.3 Hz)	30.2	289
5c	2.28 (s, 9H)	5.05 (s, 6H)	5.24 (s, 6H)	3.38 (d, 6H, J = 14.3 Hz) 4.57 (d, 6H, J = 14.3 Hz)	29.1	288
5d	2.27 (s)	5.04 (s, 6H)	2.39 (s, 9H)	3.36 (d, 6H, J = 11.5 Hz) 4.56 (d, 6H, J = 11.5 Hz)	29.4	290

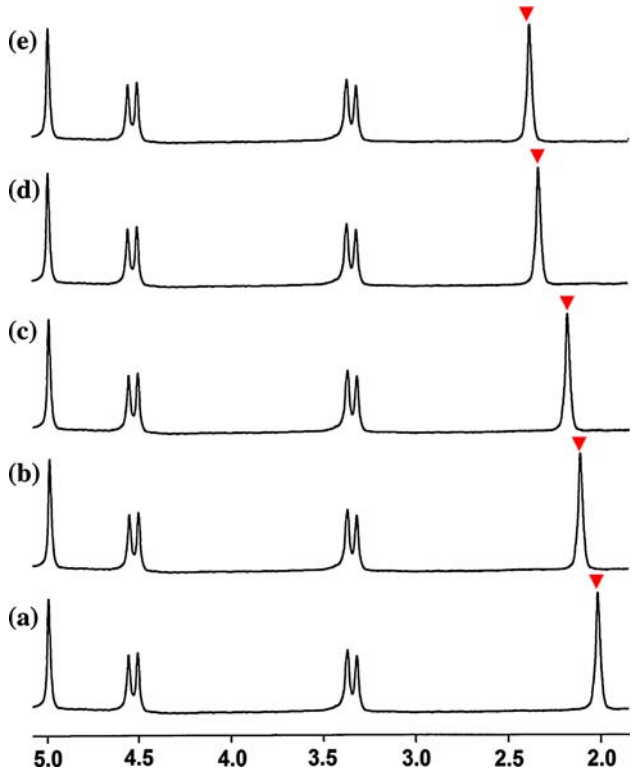


Fig. 3 Partial ^{1}H NMR spectra of **5a**: **a** −60 °C, **b** −30 °C, **c** 0 °C, **d** 25 °C, **e** 60 °C (▼ = OCH_3) in $CDCl_3$

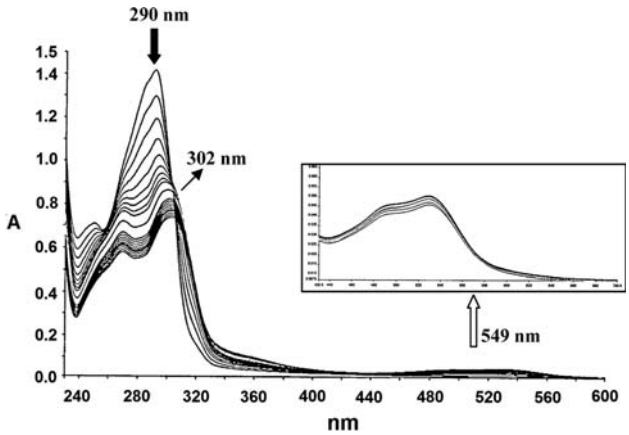


Fig. 4 Changes in the UV-visible spectra of **5a** (2×10^{-5}) upon titration by $FeSO_4 \cdot 7H_2O$ in a chloroform:methanol (1:9) as a solvent where the concentration of $FeSO_4 \cdot 7H_2O$ (1) 2×10^{-4}, (2) 4×10^{-4}, (3) 6×10^{-4}, (4) 8×10^{-4}, (5) 1.0×10^{-3}, (6) 1.2×10^{-3}, (7) 1.4×10^{-3}, (8) 1.6×10^{-3}, (9) 1.8×10^{-3}, (10) 2.0×10^{-3} showing a new band at 549 nm

change from light yellow to red. The observed bathochromic shift and splitting of the 290 nm absorption peaks of **5a** on interaction with ferrous ion could possibly be ascribed to the interaction of ferrous ion with bipyridyl units that could result in the bathochromic shift of an absorption peak at 290 to 302 nm. This interaction with bipyridyl was also confirmed by the appearance of a new peak at 549 nm with color change from light yellow to red possibly due to the metal-to-ligand charge transfer process.

The interaction of **5a** and ferrous ions was further examined by Job's continuations variation plot at 25 °C which revealed a maximum absorbance at 0.5 mole fraction of **5a** (Fig. 5a) indicating the binding interaction to be 1:1. The mole ratio plot of **5a** and ferrous ion was further confirmed this conclusion (Fig. 5b).

Several modes of interaction of the synthesized molecular receptors and the metal ions can be envisaged under such conditions. These modes are being probed through extensive theoretical and experimental studies and will be reported in due course. In the present case, the stability constants (K_s) of the plausible complexes formed with different bipyridyl pendanted calix[6]arene derivatives (**5a–d**) and ferrous ions were calculated at 25 °C by using the Benesi–Hildebrand plots (Table 2) [26].

It was also observed that the **5a** did not exhibit any shift in their absorption maxima at 290 nm on interaction with Fe(III) ions under identical conditions of experiments. This was further investigated by oxidation of Fe(II) in the Fe(II)-bipyridyl complex into Fe(III) by the treatment of

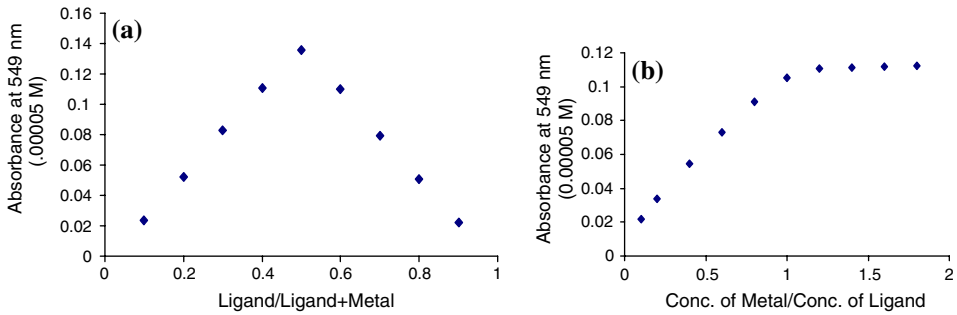


Fig. 5 **a** Jobs plot for complexation of **5a** with Fe^{2+} ion revealing 1:1 stoichiometry, **b** mole ratio plot for complexation of **5a** with Fe^{2+} ion confirming 1:1 stoichiometry

Table 2 The UV-Vis properties of the receptors **5a–d** in chloroform:methanol (1:9 v/v) upon addition of Fe(II) solutions at 25 °C

Compound	λ_{max}/nm	K_s (M^{-1})
5a	549	8.43×10^3
5b	542	8.13×10^3
5c	543	8.29×10^3
5d	538	8.35×10^3

the purple coloured 1:1 stoichiometric Fe(II)-bipyridyl complex with excess of ammonium persulphate for a few minutes at 70 °C which led to the reappearance of absorption peak of 290 nm for **5a** and the absorption peak at 549 nm. The purple colour of the Fe(II)-bipyridyl complex disappeared concomitantly to yield a colourless solution. When the colourless solution was reduced by ascorbic acid, it led to the formation of the purple colour and splitting of the 290 nm peak with reappearance of absorption peak at 549 nm. This indicated that **5a** is capable of interacting only with Fe(II) ion and not with Fe(III) ion despite the presence of six lower-rim methyl ether oxygen atoms of calix[6]arene which plausibly could act as a crown ether macrocycle type hard binding cavity [27]. These results are consistent with observations in the case of an earlier reported receptor in which three bipyridine units analogously bridged onto a 1,3,5-substituted benzene ring. The latter ligand also showed a strong tendency to form a complex with Fe(II) with similar UV-visible spectrum [28].

Likewise, receptor **5a** exhibited a significant interaction with cuprous ion but no such interaction was observed for the cupric ion. The UV studies of **5a** with Cu(I) ion when carried out in chloroform:methanol (1:9 v/v) exhibited a bathochromic shift from 290 to 311 nm for receptor **5a** (Fig. 6) with a simultaneous color change from light yellow to light green. Surprisingly no metal-to-ligand charge transfer band (450–460 nm) was observed for the **5a**-Cu(I) complex as generally observed in Cu(I)-bipyridyl complexes. This suggested that the nature of interaction of metal ion and **5a** was indeed non-covalent [29].

In conclusion, we have synthesized novel calix[6]arene based receptors in which the rotational freedom of

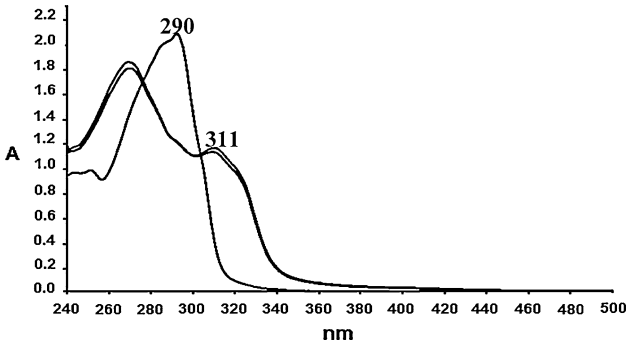


Fig. 6 Changes in the UV-visible spectra of **5a** (5×10^{-5}) upon the addition of excess of Cu (I) metal ion in a chloroform as a solvent

calix[6]arene gets suppressed by the substitution of the three 2,2′-bipyridyl moieties at their lower rim to provide a cone configurated calix[6]arene receptors (**5a–d**) which exhibited selective recognition of Fe(II) ions though 1:1 stoichiometry with high binding stability. It is significant to note that the synthesized tis(bipyridyl) pendanted calix[6]arene derivatives can differentiate different common oxidation state of iron and copper and therefore constitute examples of metal ion speciation through molecular recognition by using synthesized calix[6]arene derivatives. Further investigations are required to understand the exact binding of molecular receptors with ferrous and cuprous ions.

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