

Molecular Design of Calixarene 5. Syntheses and Cation Selectivities of Novel Schiff's Base *p*-*tert*-Butylcalix[4]arenes

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Five novel Schiff's bases *p*-*tert*-butylcalix[4]arenes have been synthesized in high yields by the reaction of 1,3-distally disubstituted *p*-*tert*-butylcalix[4]arene amine (1) with the corresponding aromatic aldehydes, and their cation binding abilities and selectivities with alkali and heavy metal ions have been evaluated by solvent extraction of aqueous metal picrates to show the highest Ag⁺ extractability for Schiff's base *p*-*tert*-butylcalix[4]arene (6) and the best Na⁺/Li⁺ and Ag⁺/Tl⁺ selectivities for Schiff's base *p*-*tert*-butylcalix[4]arene (4 and 2) over any other calix[4]arene derivatives, respectively.

Keywords Calix[4]arene derivatives, syntheses, cation selectivity, solvent extraction

Introduction

Calixarenes have enjoyed widespread use in various areas of science and technology ever since the pioneering work about two decades ago by Gutsche *et al.*¹ and have recently received much attention in supramolecular chemistry. To improve or enhance the original ion/molecule binding abilities and selectivities of calixarenes, a wide variety of novel calixarene derivatives with donating or nondonating side-arms attached to the lower rim have been designed and synthesized in recent years.²⁻⁵ Meanwhile, the recent investigations have revealed that the binding abilities and selectivities of cations and molecules by calixarene depend not only on the ring size of the calixarene skeleton, conformation and conformation mobility, lipophilicity, but also on the nature and spatial arrangement of the binding functional

groups, and the degree of preorganization of the calixarenes.⁶ As we know, the involvement of ether, ester, ketone, carboxylic acid, amide, and thioamide binding sites to the lower rim of calix[4]arenes has produced a series of new lipophilic cation receptors in a fixed cone conformation with remarkable complexing properties towards a variety of cations.⁵ Unfortunately, only a few papers reported the synthesis and complexation studies relating to calixarenes containing Schiff's base side-arms appending to lower rim.^{7,8} In the present study, we now wish to report the synthesis of five Schiff's base *p*-*tert*-butylcalix[4]arenes 2-6 (Chart 1) in order to investigate effects of different functional side-arms upon their cation binding abilities and selectivities with some alkali and heavy metal ions.

Experimental

Apparatus

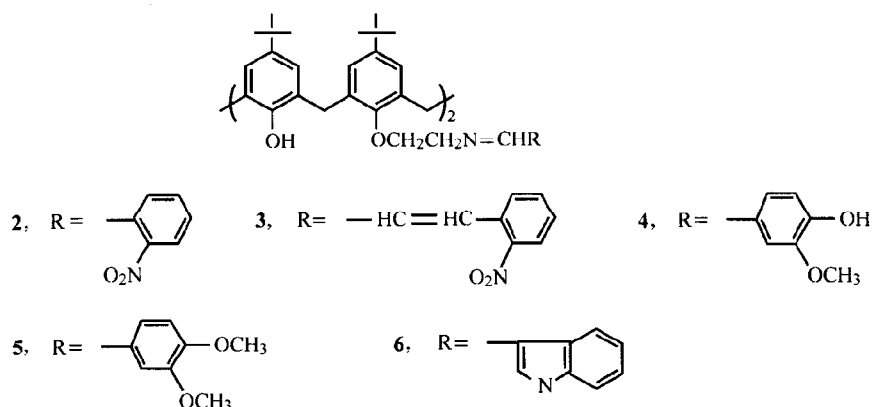
Melting points measured by an XT-4 apparatus are uncorrected. ¹H NMR spectra were recorded at 200 MHz in CDCl₃ solution, using tetramethylsilane as an internal reference. Infrared and ultraviolet spectra were recorded on Shimadzu Bio-Rad FTS 135 and Shimadzu UV-2401/PC instruments, respectively. Elemental analyses were performed on a Perkin-Elmer 2400C instrument. Mass spectra were measured by using a VG ZAB-HS instrument.

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Chart 1



Materials

Starting materials were commercially available unless otherwise noted. 2-Nitrobenzaldehyde and indole-3-carboxaldehyde were purchased from Fluka (Buchs, Switzerland). 5, 11, 17, 23-Tetra-*tert*-butyl-25, 27-bis(2-aminoethoxy)-26, 28-dihydroxy-calix[4]arene (**1**), and 2-nitrocinnamic aldehyde were synthesized respectively according to the procedure reported.^{8,9}

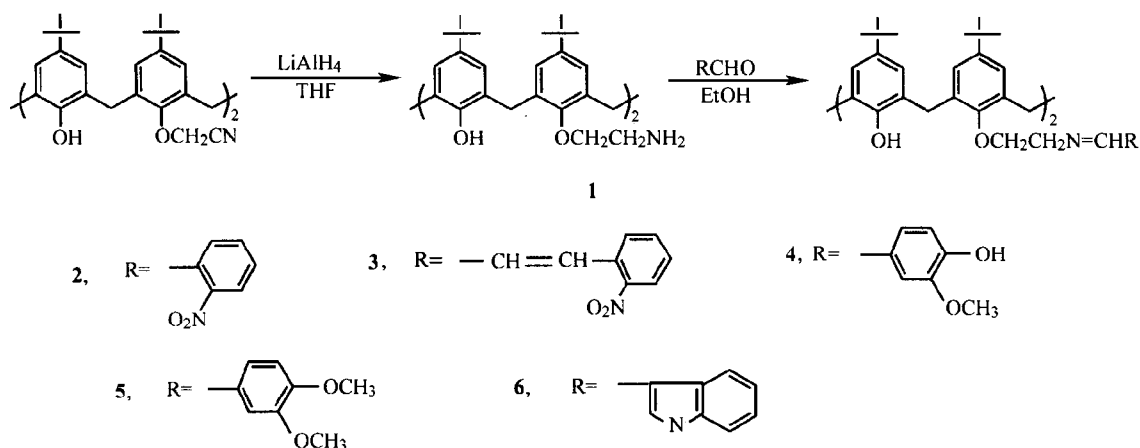
Synthesis of Schiff's base *p*-*tert*-butylcalix[4]arenes

(2–6)

General procedure

A sample of 5, 11, 17, 23-tetra-*tert*-butyl-25, 27-bis(2-aminoethoxy)-26, 28-dihydroxy-calix[4]arene (**1**) (0.27 mmol) was added to the corresponding aldehyde (0.54 mmol) in absolute ethanol (5 mL) with stirring for an hour on a steam bath. After cooling, the precipitate obtained was filtrated and recrystallized from ethanol to obtain pure Schiff's base *p*-*tert*-butylcalix[4]arene in high yield (Scheme 1).

Scheme 1



5, 11, 17, 23-Tetra-*tert*-butyl-25, 27-bis [2-[*N*-(2-nitrobenzylidene) amino] ethoxy]-26, 28-dihydroxy-calix[4]arene (**2**) Yield 96%. mp 222–224°C. ν_{\max} (KBr): 3481.3, 3407.9, 3037.4, 2958.5, 2906.2, 2868.8, 1637.6 (C = N), 1572.9, 1523.6,

1484.6, 1461.1, 1347.1, 1302.6, 1197.9, 1124.6, 1097.4, 1046.7, 872.1, 782.6, 738.4 cm^{-1} . δ_{H} : 10.39(s, 2H, OH), 8.89(s, 2H, CH = N), 8.09(d, $J = 8.6$ Hz, 2H, ArH), 7.94(d, $J = 8.6$ Hz, 2H, ArH), 7.68–7.46(m, 4H, ArH), 6.96(s, 4H,

ArH), 6.69(s, 4H, ArH), 4.25(d, $J = 13.2$ Hz, 4H, ArCH₂Ar), 4.18(t, $J = 4.8$ Hz, 4H, OCH₂), 4.10(t, $J = 4.8$ Hz, 4H, NCH₂), 3.29(d, $J = 13.2$ Hz, 4H, ArCH₂Ar), 1.26(s, 18H, C(CH₃)₃), 0.87(s, 18H, C(CH₃)₃). FAB-MS m/z : 1001.5(M⁺). Anal. C₆₂H₇₂N₄O₈. Calcd: C, 74.37; H, 7.25; N, 5.60. Found: C, 74.19; H, 7.09; N, 5.69.

5, 11, 17, 23-Tetra-*tert*-butyl-25, 27-bis [2-[*N*-(2-nitrocinnamioaldehydelidene)-amino] ethoxy]-26, 28-dihydroxycalix[4]arene (3) Yield 93%. mp 197—199°C. ν_{\max} (KBr): 3486.4, 3041.3, 2959.3, 2906.2, 2868.8, 1635.4(C = N), 1570.0, 1522.4, 1484.3, 1460.2, 1345.5, 1310.4, 1197.0, 1163.7, 1122.9, 1098.5, 1048.0, 976.0, 960.3, 872.2, 862.1, 782.7, 740.2 cm⁻¹. δ_{H} : 9.78(d, $J = 8.2$ Hz, 2H, CH = N), 8.40(d, $J = 8.2$ Hz, 2H, ArCH), 8.04—7.90(m, 2H, CH = CH), 7.55—7.41(m, 8H, ArH), 7.01(s, 2H, OH), 6.95(s, 4H, ArH), 6.67(s, 4H, ArH), 4.25(d, $J = 13.2$ Hz, 4H, ArCH₂Ar), 4.21(t, $J = 4.8$ Hz, 4H, OCH₂), 4.19(t, $J = 4.8$ Hz, 4H, NCH₂), 3.23(d, $J = 13.2$ Hz, 4H, ArCH₂Ar), 1.24(s, 18H, C(CH₃)₃), 0.85(s, 18H, C(CH₃)₃). FAB-MS m/z : 1053.2(M⁺). Anal. C₆₆H₇₆N₄O₈ · 2H₂O. Calcd: C, 72.77; H, 7.40; N, 5.14. Found: C, 72.86; H, 7.13; N, 5.08.

5, 11, 17, 23-Tetra-*tert*-butyl-25, 27-bis [2-[*N*-(4-hydroxy-3-methoxy-benzylidene)-amino] ethoxy]-26, 28-dihydroxycalix[4]arene (4) Yield 92%. mp 207—208°C. ν_{\max} (KBr): 3424.7, 2962.0, 2906.2, 2870.0, 1645.8(C = N), 1603.8, 1514.2, 1485.0, 1464.0, 1431.9, 1363.7, 1286.9, 1243.2, 1205.7, 1124.3, 1034.9, 872.9, 818.2 cm⁻¹. δ_{H} : 9.81(s, 2H, OH), 8.69(s, 2H, CH = N), 7.55—7.40(m, 6H, ArH), 7.10(s, 2H, ArOH), 7.00(s, 4H, ArH), 6.64(s, 4H, ArH), 4.24(d, $J = 12.8$ Hz, 4H, ArCH₂Ar), 4.07(t, $J = 5.2$ Hz, 4H, OCH₂), 3.92(s, 6H, OCH₃), 3.67(t, $J = 5.2$ Hz, 4H, NCH₂), 3.24(d, $J = 12.8$ Hz, 4H, ArCH₂Ar), 1.23(s, 18H, C(CH₃)₃), 0.87(s, 18H, C(CH₃)₃). FAB-MS m/z : 1003.3(M⁺). Anal. C₆₄H₇₈N₂O₈ · H₂O. Calcd: C, 75.26; H, 7.90; N, 2.74. Found: C, 75.50; H, 7.85; N, 2.85.

5, 11, 17, 23-Tetra-*tert*-butyl-25, 27-bis [2-[*N*-(3-methoxy-4-methoxy-benzylidene)-amino] ethoxy]-26, 28-dihydroxycalix[4]arene (5) Yield 92%.

mp 233—234°C. ν_{\max} (KBr): 3425.5, 2959.0, 2906.2, 2869.4, 1642.9(C = N), 1600.4, 1587.3, 1514.5, 1484.7, 1463.7, 1420.9, 1362.9, 1268.5, 1239.9, 1199.0, 1162.4, 1027.7, 873.4, 815.7 cm⁻¹. δ_{H} : 9.83(s, 2H, OH), 8.56(s, 2H, CH = N), 7.39—6.86(m, 6H, ArH), 7.01(s, 4H, ArH), 6.67(s, 4H, ArH), 4.24(d, $J = 12.8$ Hz, 4H, ArCH₂Ar), 4.07(t, $J = 5.2$ Hz, 4H, OCH₂), 3.95(s, 6H, OCH₃), 3.85(s, 6H, OCH₃), 3.67(t, $J = 5.2$ Hz, 4H, NCH₂), 3.31(d, $J = 12.8$ Hz, 4H, ArCH₂Ar), 1.26(s, 18H, C(CH₃)₃), 0.85(s, 18H, C(CH₃)₃). FAB-MS m/z : 1031.8(M⁺). Anal. C₆₆H₈₂N₂O₈. Calcd: C, 76.86; H, 8.01; N, 2.72. Found: C, 76.70; H, 8.07; N, 2.73.

5, 11, 17, 23-Tetra-*tert*-butyl-25, 27-bis [2-[*N*-(indole-3-carboxaldehydelidene)-amino] ethoxy]-26, 28-dihydroxycalix[4]arene (6) Yield 86%. mp > 280°C. ν_{\max} (KBr): 3398.9, 3051.2, 2958.8, 2906.2, 2868.9, 1637.8(C = N), 1534.5, 1483.8, 1458.3, 1391.8, 1362.3, 1340.5, 1298.7, 1197.1, 1121.9, 1040.1, 920.3, 872.7, 744.6 cm⁻¹. δ_{H} : 9.82(s, 2H, OH), 8.68(s, 2H, CH = N), 8.20(s, 2H, NH), 7.68—7.12(m, 10H, Indolyl), 7.01(s, 4H, ArH), 6.63(s, 4H, ArH), 4.24(d, $J = 12.8$ Hz, 4H, ArCH₂Ar), 4.12(t, $J = 5.0$ Hz, 4H, OCH₂), 3.62(t, $J = 5.0$ Hz, 4H, NCH₂), 3.23(d, $J = 12.8$ Hz, 4H, ArCH₂Ar), 1.25(s, 18H, C(CH₃)₃), 0.88(s, 18H, C(CH₃)₃). FAB-MS m/z : 989.1(M⁺). Anal. C₆₆H₇₆N₄O₄ · C₂H₅OH. C, 78.88; H, 7.98; N, 5.41. Found: C, 78.92; H, 8.21; N, 5.44.

Solvent extraction

A sample of 5 mL of chloroform solution of calixarene (1.0×10^{-4} M) and 5 mL of aqueous solution containing a metallic picrate (1.0×10^{-4} M) were placed in a flask. The mixture was shaken for 5 min and stored for 2 h at 20°C. The extractability was not affected by further shaking, indicating that the equilibrium has been attained within 2 h. The aqueous phase was separated and subjected to the analysis by UV absorption spectrometry in near 357 nm.¹⁰ The extractability (Ex. %) was determined from the decrease in the picrate concentration in the aqueous phase: $\text{Ex. \%} = \{([\text{Pic}]_{\text{blank}} - [\text{Pic}]_{\text{water}}) / [\text{Pic}]_{\text{blank}}\} \times 100$, where $[\text{Pic}]_{\text{blank}}$ and

$[\text{Pic}]_{\text{water}}$ denote the picrate concentrations in the aqueous phase after extraction with pure chloroform and with the chloroform solution containing calixarenes **2–6** as extractants, respectively.

Results and discussion

Synthesis of Schiff's base *p*-*tert*-butylcalix[4]arenes (**2–6**)

It is convenient to synthesize Schiff's base *p*-*tert*-butylcalix[4]arenes in absolute ethanol by the reaction of 1,3-distally disubstituted *p*-*tert*-butylcalix[4]arene amine (**1**) with the corresponding aromatic aldehydes. The constitutions of **2–6** were proved by ^1H NMR,

FAB-MS spectra and elemental analysis, and also confirmed by the presence of imine group absorption in FT-IR spectra. All of **2–6** had the cone conformation, which was determined by ^1H NMR spectra showing singlets for *tert*-butyl groups and AB quartets for bridging methylenes of the calixarene skeleton.¹¹

Solvent extraction of alkali and heavy metal picrates from aqueous solutions into chloroform by ligands **2–6**

A preliminary evaluation of the binding efficiencies of **2–6** was carried out by solvent extraction of Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , Ag^+ , and Tl^+ from aqueous solution into chloroform under neutral conditions. The extractabilities (Ex. %) and selectivities obtained are summarized in Table 1.

Table 1 Solvent extraction of aqueous metal picrates with Schiff's base *p*-*tert*-butylcalix[4]arenes **2–6**^a

Ligand	Ex. (%) ^b							Selectivity ^c	
	Li^+	Na^+	K^+	Rb^+	Cs^+	Ag^+	Tl^+	Na^+/Li^+	Ag^+/Tl^+
2	1.78	3.27	1.93	3.00	1.20	8.05	0.97	1.84	8.30
3	9.40	20.69	19.24	24.32	15.23	34.68	4.86	2.20	7.14
4	0.76	11.56	6.80	8.86	6.00	16.74	3.44	15.20	4.87
5	7.60	14.87	8.94	14.24	15.58	24.93	6.50	1.96	3.84
6	25.03	32.40	31.76	32.56	35.70	66.60	21.23	1.29	3.14

^a Temperature $25.0 \pm 0.1^\circ\text{C}$; aqueous phase (5 mL); $[\text{picrate}] = 1.0 \times 10^{-4}$ M; organic phase (CHCl_3 , 5 mL); $[\text{calixarene}] = 1.0 \times 10^{-4}$ M. ^b Defined as percent picrate extracted into the organic phase. Average of twice independent runs; error < 3% of the reported value. ^c Relative cation selectivity determined by the distribution ratio of metal ion between the organic and aqueous phases.

As readily recognized from Table 1, calixarene derivatives **2–6** possessing the similar cavity size exhibit higher extractabilities for Na^+ over Li^+ and K^+ , and the highest for Ag^+ over any other cations, which may be accounted for that the size-fit concept between host calixarenes and guest cations plays an important role. However, host compounds **2–6** exhibit entirely different extractabilities and cation selectivities for Na^+ and Ag^+ , which mainly resulted from the introduce of different functional side-arms to the lower rim of calixarene. It is significantly noted that ligand **6** extracted all metal ions used more than other four kinds of ligands, which was probably attributed to that the bulky indolyl substituents tethered in amino moieties of calix[4]arene serve a suitable binding geometry of the pseudo-cavity to capture metal cations. On the contrary, ligand **2** showed the poorest cation binding ability among five ligands, which may be ascribed to the steric barrier of nitro groups on the double arm calixarene. As compared with

2, ligand **3** exhibited higher extractability for all cations used, which obviously revealed that the relative longer Schiff's base chains attached on the lower rim of calix[4]arene platform not only decreased the steric hindrance of nitro group, but also increased the donicity and flexibility of the binding chains. Ligand **4**, which is capable of forming intramolecular hydrogen bonding to restrain the complexation with cations, showed lower extractability than ligand **5**. Meanwhile, **2–6** exhibited the highest extractability for Ag^+ over any other six ions. A plausible explanation is that the interaction of ligands containing nitrogen atoms and aromatic rings with soft silver ion is much stronger than with other heavy and alkali metal cations.¹²

It is also interestingly noted that the higher extractability by calixarene derivatives does not immediately mean the higher cation selectivities. As shown in Table 1, ligand **6** showing the highest extractability, however, gives the poorest selectivities for Na^+/Li^+ and Ag^+/Tl^+

Tl⁺. On the contrary, ligands **2** and **4** possessing the poorest extractability give the highest selectivity for Ag⁺/Tl⁺ and Na⁺/Li⁺, respectively.

In conclusion, we have demonstrated that the functional Schiff's base side-arms appended to lower rim of calix[4]arene can fine-adjust the size and shape of the induced pseudo cavity upon complexation with metal ions, which not only alters the cation binding ability but also significantly enhances the cation selectivity for the specific cation.

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