



# Synthesis of doubly bridged *p*-*tert*-butyl-calix[6]arene containing hard and soft ion binding sites

Yikun Chen and Yuanyin Chen\*

*Department of Chemistry, Wuhan University, Wuhan 430072, People's Republic of China*

Received 12 July 2000; revised 13 September 2000; accepted 20 September 2000

---

## Abstract

A conformationally preorganized,  $C_s$ -symmetrical *p*-*tert*-butyl-calix[6]-1,4-crown-4-2,6-dioxo-diaza-crown-4 with hard and soft ion binding sites at the lower rim is synthesized. The binding sites may complex alkali metal ions or transition metal ions selectively. © 2000 Elsevier Science Ltd. All rights reserved.

---

When two or more binding sites are combined together within the same architecture, a so-called polytopic system may be constructed. The binding sites may be constructed by bridging polyether chains of different lengths or different composition,<sup>1,2</sup> even of different polarity and composition segment<sup>3</sup> onto the lower rim of calix[4]arene. Once recognition of each binding subunit has been identified, the ability of multiple recognition and mutual effects of binding subunit occupation provide entries to higher forms of molecular behavior such as cooperativity, regulation etc.<sup>3</sup> However, no systematic complexation studies of these systems have been accomplished.

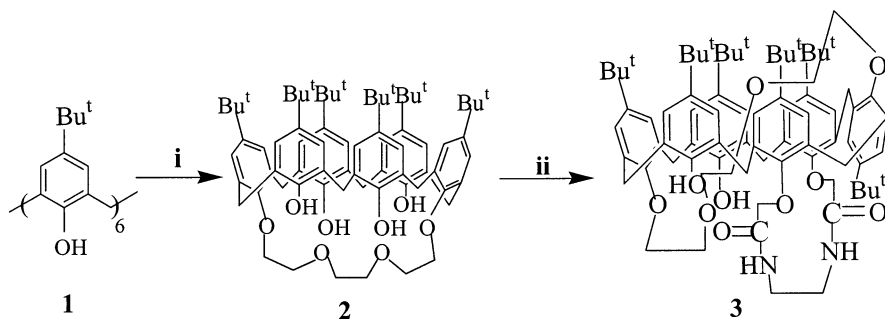
It is well known that calix[4]crowns show outstanding recognition abilities towards alkali metal cations.<sup>4,5</sup> In particular, calix[4]crown-6 hosts have been extensively investigated in the separation and removal of radioactive Cs<sup>137</sup> ion from aqueous waste mixures.<sup>6</sup> Calix[4]arenes with a diamide bridge at the lower rim exhibit high complexation ability towards some *soft* metal cations.<sup>7</sup> As for calix[6]arenes, it is well known that their higher degree of functionality (more hydroxyl groups) and greater conformational flexibility complicates their chemistry and makes isolation and characterization an often difficult task.<sup>8</sup> Intramolecular bridging chains can reduce the conformational flexibility of *p*-*tert*-butyl-calix[6]arenes, and intramolecular doubly-bridging chains can immobilize the conformation of *p*-*tert*-butylcalix[6]arenes.<sup>9,10</sup> The 1,3-4,5-double diamide-bridged *p*-*tert*-butylcalix[6]arene shows some lithium ion selectivity,<sup>9</sup> and the cone and 1,2,3-alternate stereoisomers of calix[6]-1,4-diallyloxy-2,3-5,6-bis-crown-4 show high Cs<sup>+</sup>/Na<sup>+</sup> selectivity.<sup>10</sup> No polytopic system with different ion binding sites has been constructed.

---

\* Corresponding author.

In this paper, we wish to report the synthesis of the first example of a 1,4-2,6-doubly bridged *p*-*tert*-butyl-calix[6]arene, *p*-*tert*-butyl-calix[6]-1,4-crown-4-2,6-dioxo-diaza-crown-4, which contains hard and soft ion binding sites, and also, the extraction abilities towards different metal ions by its hard and soft ion binding sites.

**Preparation of ligands.** The synthetic procedure for the preparation of *p*-*tert*-butyl-calix[6]-1,4-crown-4-2,6-dioxo-diaza-crown-4 **3** is illustrated in Scheme 1. Reacting *p*-*tert*-butylcalix[6]arene with 1.2 equiv. of triethylene glycol ditosylate in the presence of 6 equiv. of  $K_2CO_3$  in refluxing toluene for 24 h, gave *p*-*tert*-butyl-calix[6]-1,4-crown-4 **2** in 38% yield. Further treatment of **2** with 1 equiv. of *N,N'*-bis(chloroacetyl)ethylenediamine in refluxing  $CH_3CN$  in the presence of 4 equiv.  $Cs_2CO_3$  and 4 equiv. KI under nitrogen atmosphere for 8 h, followed by distilling off the solvent and purification by column chromatography [ $CH_2Cl_2/CH_3OH=100/1$  (v/v),  $R_f=0.3$ ], gave the title compound, *p*-*tert*-butylcalix[6]-1,4-crown-4-2,6-dioxo-diaza-crown-4 **3** as a yellow solid in 32% yield.



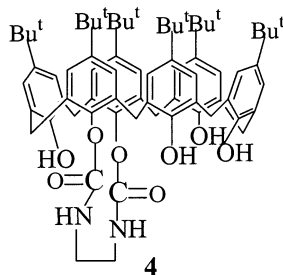
Scheme 1. Reagents and conditions. (i)  $K_2CO_3$ , toluene,  $TsO(CH_2CH_2O)_3Ts$ , reflux, 24 h; (ii)  $Cs_2CO_3/KI$ ,  $CH_3CN$ ,  $(CH_2)_2(NHCOCH_2Cl)_2$ , reflux, 8 h

The structures of compounds **2** and **3** were characterized by FAB-MS spectra, elemental analyses and  $^1H$  NMR spectra.<sup>11</sup> The  $^1H$  NMR spectrum of **2** shows two singlets (ratio 1:2) for the *tert*-butyl groups as well as for the aromatic protons, and one singlet for the hydroxyl proton, indicating the calix[6]arene moiety is 1,4-substituted. Two pairs of **AB** doublets in a 2:1 ratio for the methylene protons in calixarene skeleton suggest that **2** adopts a cone conformation at ambient temperature.

After the structure of **2** was confirmed, **3** may be one of 1,4-2,3, 1,4-2,5 and 1,4-2,6 substituted products. The 1,4-2,3- and 1,4-2,5-isomers should give three singlets for the *tert*-butyl groups in a 1:1:1 ratio, and the 1,4-2,6 isomer should give four singlets for the *tert*-butyl groups in 1:2:2:1 ratio.<sup>12</sup> The  $^1H$  NMR spectrum of **3** shows four singlets in a 1:2:2:1 ratio for the *tert*-butyl groups as well as for the aromatic protons, indicating the calixarene moiety of **3** is  $C_3$ -symmetrical, and the diamide spacer connects the 2 and 6 positions, and the other isomers can be ruled out. Thus, **3** is a 1,4-2,6-doubly bridged *p*-*tert*-butyl-calix[6]arene. The signal pattern of the  $ArCH_2Ar$  region is the criterion to judge the conformation of compound **3**. There is a rule that the hydrogen atoms of a methylene group connecting two neighboring aryl groups of a calix[6]arene appear as pairs of **AB** doublets in the  $^1H$  NMR spectrum, if the aryl groups are *syn* to one another, resulting in the different environment of each of the methylene hydrogen atoms. On the other hand, a singlet for the methylene hydrogen atoms indicates that the aryl groups are *anti* to one another, and the two methylene hydrogen atoms are in a similar environment.<sup>13</sup> In the  $^1H$  NMR spectrum of **3**, two pairs of doublets and one singlet in a 1:1:1 ratio for the

methylene protons in calixarene skeleton support that **3** adopts a (u,u,u,d,u,u) conformation at ambient temperature. Furthermore, the resonance signals of the  $\text{OCH}_2\text{CH}_2\text{O}$  group at  $\delta$  4.02–4.24 in compound **2** shift to  $\delta$  2.82–3.24 in compound **3**, indicating that **3** is a kind of self-anchored rotaxane,<sup>14</sup> in which the polyether chain crosses through the cyclic cavity of the calix[6]arene and the amide chain is over the cavity as shown in Scheme 1. The conformation of calix[6]arene **3** is rigidified by the two different bridging units.

Examination of the CPK molecular model reveals that the compound **3** is preorganized for binding cations. Percentage extractions of **2**, **3**, as well as the *p*-*tert*-butylcalix[6]-1,3-dioxodiazacrown-4<sup>9</sup> **4** (see Scheme 2) towards picrate salts from water into  $\text{CHCl}_3$  at 25°C are summarized in Table 1. It is valuable to note that the compound **3** shows a very high extraction ability and selectivity towards cesium ions when compared with the *p*-*tert*-butylcalix[6]-1,4-crown-4 **2**. Among the alkali metal ions used, the larger the ion radii, the higher the extractive percentage, especially for compound **3**. Thus, it can be concluded that the alkali metal ion was included into the cavity composed of the polyoxyethylene spacer, and some cooperativity of the polyoxyethylene bridge and the diamide bridge occurs, i.e. the diamide segment strengthens the extraction ability and selectivity of the hard ion binding site towards cesium ion. As for host **4**, the inverse sequence is observed, i.e. the smaller the ion radii of the alkali metal ion, the higher the extraction percentage. Thus, the highest complexation ability towards the smallest nickel ion among the transition metal tested should be attributed to the contribution of the soft ion binding site composed of diamide spacer subunit in **3**.



Scheme 2. Compound **4**: 1,3-dioxodiazacrown-4<sup>9</sup>

Table 1  
Percentage extraction (%*E*) of picrate salts from water into  $\text{CHCl}_3$  at 25°C<sup>a</sup>

Host	% <i>E</i>							
	$\text{Li}^+$	$\text{Na}^+$	$\text{K}^+$	$\text{Cs}^+$	$\text{Cu}^{2+}$	$\text{Ni}^{2+}$	$\text{Hg}^{2+}$	$\text{Pd}^{2+}$
<b>2</b>	2.6	6.5	4.5	10.2	1.2	1.6	0.2	0.4
<b>3</b>	0.2	0.4	2.5	20.8	5.8	26.8	0.8	0.3
<b>4</b> <sup>b</sup>	5.3	1.2	0.9					
Ion radii (Å)	0.68	0.97	1.33	1.67	0.72	0.69	1.10	0.80

<sup>a</sup> [Host]=[guest]=0.005 mol dm<sup>-3</sup>. The percentage extraction (%*E*) was measured from the decrease in the aqueous phase (absorbance at 354 nm) and reconfirmed by the increase in the chloroform layer (absorbance at 380 nm).

<sup>b</sup> These data are quoted from Ref. 9.

## Acknowledgements

Financial support from the National Natural Science Foundation of China is gratefully acknowledged.

## References

- Asfari, Z.; Nicolle, X.; Vicens, J.; Dozol, J. F.; Duhart, A.; Harrowfield, J. M.; Skelton, B. W.; White, A. *J. Incl. Phenom.* **1999**, *33*, 251.
- Asfari, Z.; Thuéry, P.; Nierlich, M.; Vicens, J. *Tetrahedron Lett.* **1999**, *40*, 499.
- Aeungmaitrepirom, W.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **1997**, *38*, 1907.
- Takeshita, M.; Shinkai, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1088.
- (a) Yamamoto, H.; Shinkai, S. *Chem. Lett.* **1994**, 1115. (b) Asfari, Z.; Wenger, S.; Vicens, J. *Pure & Appl. Chem.* **1995**, *67*, 1037. (c) Lamare, V.; Dozol, J. F.; Fuangswasdi, S.; Arnaud Neu, F.; Thuéry, P.; Nierlich, M.; Asfari, Z.; Vicens, J. *J. Chem. Soc., Perkin Trans 2* **1999**, 271. (d) Nicod, L.; Rostaing, S.; Chitry, F.; Lemaire, M. *Tetrahedron Lett.* **1998**, *39*, 9443.
- Asfari, Z.; Pulpoka, B.; Saadioui, M.; Wenger, S.; Nierlich, M.; Thuéry, P.; Reynier, N.; Dozol, J. F.; Vicens, J. *J. Mol. Recognit. Inclusion, Proc. 9th Int. Symp.* **1998**, 173.
- (a) Ostaszewski, R.; Stevens, T. W.; Verboom, W.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1991**, *10*, 294. (b) Asfari, Z.; Wenger, S.; Vicens, J. *Pure & Appl. Chem.* **1995**, *67*, 1037.
- Rogers, J. S.; Gutsche, C. D. *J. Org. Chem.* **1992**, *57*, 3152.
- Chen, Y. K.; Chen, Y. Y. *Organic Lett.* **2000**, *2*, 743.
- Blanda, M. T.; Farmer, D. B.; Brpdbelt, J. S.; Goolsby, B. J. *J. Am. Chem. Soc.* **2000**, *122*, 1486.
- Microanalytical and spectral data were obtained for compounds **2** and **3**.  
Compound **2**: mp 258°C (dec.); MS(FAB):  $m/z = 1086$  [M]<sup>+</sup>. Anal. calcd for C<sub>72</sub>H<sub>94</sub>O<sub>8</sub>: C, 79.52; H, 8.71; Found: C, 79.67; H, 8.67; <sup>1</sup>H NMR(300 MHz, CDCl<sub>3</sub>): 1.14 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.30 (s, 36 H, C(CH<sub>3</sub>)<sub>3</sub>), 3.38 (d, 2 H, ArCH<sub>2</sub>Ar,  $J = 12.6$  Hz), 3.49 (d, 4H, ArCH<sub>2</sub>Ar,  $J = 12.9$  Hz), 3.93 (d, 2H, ArCH<sub>2</sub>Ar,  $J = 12.6$  Hz), 4.04 (t, 4H, OCH<sub>2</sub>CH<sub>2</sub>O,  $J = 7.2$  Hz), 4.14 (t, 4H, OCH<sub>2</sub>CH<sub>2</sub>O,  $J = 7.2$  Hz), 4.21 (s, 4H, OCH<sub>2</sub>CH<sub>2</sub>O), 4.41 (d, 4 H, ArCH<sub>2</sub>Ar,  $J = 12.9$  Hz), 6.97 (s, 4 H, ArH), 7.11 (d, 4H, ArH,  $J = 2.1$  Hz), 7.14 (d, 4H, ArH,  $J = 2.1$  Hz), 7.85 (s, 4 H, ArOH). Compound **3**: mp 235°C (dec.), MS(FAB):  $m/z = 1228$ [M+2H]<sup>+</sup>. Anal. calcd for C<sub>78</sub>H<sub>102</sub>O<sub>10</sub>N<sub>2</sub>: C, 76.35; H, 8.32; Found: C, 76.11; H, 8.28; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): 1.15 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 1.24 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.27 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.34 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 2.80 (t, 4H, OCH<sub>2</sub>CH<sub>2</sub>O,  $J = 7.2$  Hz), 3.20–3.45 [m, 12 H, OCH<sub>2</sub>CH<sub>2</sub>O(8 H) and NCH<sub>2</sub>CH<sub>2</sub>N(4H)], 3.75 (s, 4H, ArCH<sub>2</sub>Ar), 3.84 (d, 2H, ArCH<sub>2</sub>Ar,  $J = 15.0$  Hz), 3.95 (d, 2H, ArCH<sub>2</sub>Ar,  $J = 15.6$  Hz), 4.07 (d, 2H, OCH<sub>2</sub>CO,  $J = 9.6$  Hz), 4.22 (d, 2H, ArCH<sub>2</sub>Ar,  $J = 15.0$  Hz), 4.32 (d, 2H, ArCH<sub>2</sub>Ar,  $J = 15.6$  Hz), 4.37 (d, 2H, OCH<sub>2</sub>CO,  $J = 9.6$  Hz), 6.80 (s, 2H, ArH), 7.01 (s, 4H, ArH), 7.12 (s, 4H, ArH), 7.15 (s, 2H, ArH), 7.60 (s, 2H, ArOH), 7.70 (bs, 2H, NH).
- Otsuka, H.; Araki, K.; Shinka, S. *Tetrahedron* **1995**, *51*, 8757.
- Ross, H.; Lüning, U. *Liebigs Ann.* **1996**, 1367.
- Casnati, A.; Jacopozi, P.; Pochini, A.; Ugozzoli, F.; Cacciapaglia, R.; Mandolini, L.; Ungaro, R. *Tetrahedron* **1995**, *51*, 591.