

Convenient Preparation of Novel Calix[n]cryptands (n=4, 6)

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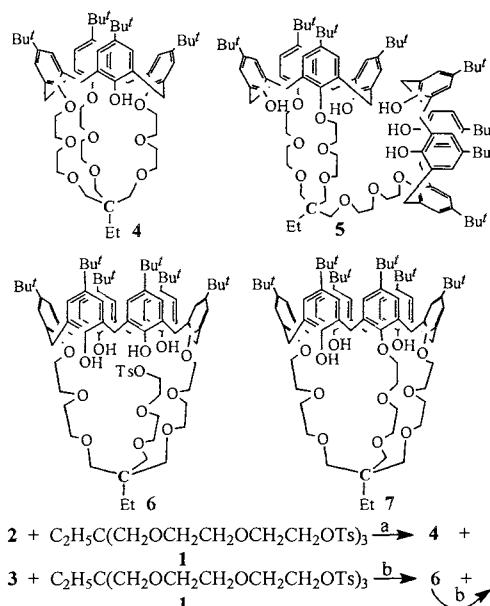
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Convenient syntheses of novel tripodal calix[4]cryptand and the first example of 1,2,4-tripodal calix[6]cryptand were reported by direct condensation of *p*-*tert*-butylcalix[4]arene or *p*-*tert*-butylcalix[6]arene with 1,1,1-tri(tosyloxyethoxyethoxy methyl)-propane. Besides, a novel type of doublecalix[4]arenes and a novel type of calix[6]crown, were co-prepared, respectively. It was suggested that the synthetic strategy described in this paper may be generally useful to explore the little-known field of calixcryptands.

In calixarene chemistry,¹ calixcryptands are just recent arrivals with cage-like structures, which are expected to be superior over calixcrown in the field of molecular recognition. Up to now, there are two types of calixcryptands described in literatures. The first one, cryptocalix[4]arene, in which the calix[4]arene subunit was incorporated into one arm of a cryptand *via* condensation of a 1,3-derived-calix[4]arene with a diazacrown.² The second one, tripodal calix[n]cryptand (n=4, 6), which is composed of a calix[n]arene subunit and a half of cryptand subunit.^{3,4} The latter one has been almost unexplored due to difficult access usually through a multi-step procedure. In 1997, Tuntulani *et al*⁵ reported the only one example of tripodal calix[4]cryptand prepared *via* a multi-step procedure with the total yield below 3% due to the rather lower yield (6%) of the key intermediate, trialdehyde calix[4]arene. In 1994, Reinhoudt *et al*⁶ reported a kind of calix[6]cryptands by covalent three-point capping a 1,3,5-trimethoxy-*p*-*tert*-butylcalix[6]arene with a cyclotrimeratrylene (CTV). Meantime, several other analogs of calix[6]cryptand, i.e. capped calix[6]arenes, were also reported.⁵⁻⁷

Just recently, we have prepared a couple of stabilized calix[6]cryptands with in- and out- stereoisomers by capping 1,3,5-trimethoxy-*p*-*tert*-butylcalix[6]arene with a key trifunctional polypode reagent, i.e. 1,1,1-tri(tosyloxyethoxyethoxy methyl)-propane (**1**).⁸ Further investigation presented in this paper reveals that directly reacting **1** with calix[n]arenes (n=4, 6) may be a convenient method with general interests to synthesize novel calixcryptands. As shown in Scheme 1, reacting **1** with *p*-*tert*-butylcalix[4]arene (**2**) or *p*-*tert*-butylcalix[6]arene (**3**), we obtained the expected calix[4]cryptand **4** and calix[6]cryptand **7**. Interestingly, the so-obtained calix[6]cryptand **7** is a 1,2,4-tripodal capped compound which represents the first example of triply-linked asymmetric calix[6]cryptand. Besides, we have co-prepared a novel type of doublecalix[4]arenes **5**, in which one subunit is a calix[4]crown and another is a calix[4]arene, and a novel type of calix[6]crown **6**, in which a side chain with terminal tosyloxy group is attached to the crown moiety.

The syntheses of **4** and **5** were accomplished by the improved method described for the preparation of *p*-*tert*-butyl calix[4]crown-5.⁹ Treatment of **2** with **1** gave **4** and **5** in isolated yields of 7% and 35%, respectively. Using polar solvents such as MeCN, THF, DMF or Me₂CO instead of benzene and strong bases such as NaH or *t*-BuOK instead of K₂CO₃ gave rather complex crude products which are difficult to be separated. The syntheses of **6** and **7** were achieved by refluxing a mixture of **3** and **1** in THF in the presence of K₂CO₃. The products **6** and **7** were obtained in isolated yields of 43% and 5%, respectively. In fact, we have tried several other solvents such as benzene, MeCN or Me₂CO instead of THF, and bases such as NaH or *t*-BuOK instead of K₂CO₃, but in each case the conversion of *p*-*tert*-butylcalix[6]arene (**3**) is less than 50% and the reaction products are very complex.



Scheme 1. Reagents and Conditions: (a) K₂CO₃ / dry benzene, reflux, 3 days; (b) K₂CO₃ / THF, reflux, two days.

The structures of **4**, **5**, **6** and **7** were characterized by FAB-MS spectra, elemental analyses, ¹H NMR spectra and ¹³C NMR spectra. The ¹H NMR spectrum of **4** shows three singlets (ratio 1:1:2) for the *tert*-butyl groups as well as for the aromatic protons, one singlet for the hydroxyl proton, two pairs of doublets for the protons in the calixarene methylene skeleton indicating the calix[4]arene moiety adopted a cone conformation. In the ¹H NMR spectrum of **5**, two singlets at δ 10.30 (1 OH) and 9.40 (2 OH) obviously indicate that one of the two

calix[4]arenes is mono-substituted.¹⁰ Two singlets in a 1:1 ratio for the aromatic protons in the crowned calix[4]arene moiety indicates the crowned moiety is 1,3-bridged.¹¹ A pair of doublets for the protons in the calix[4]arene methylene skeleton may reveal that the crowned calix[4]arene moiety adopted a cone conformation. The ¹H NMR spectrum of **6** shows one singlet at δ 2.45 and a pair of doublets at δ 7.37 and 7.80 for the tosyloxy group. The presence of two singlets in a 2:1 ratio for the *tert*-butyl groups seems to indicate that the calix[6]arene moiety is 1,4-substituted. However, no defined conformation of **6** at ambient temperature can be presented due to the overlapping signals in the region of δ 3.33-4.15. The ¹H NMR spectrum of **7** shows the structure of **7** is asymmetrical. Three singlets in a 1:2:3 ratio for the *tert*-butyl groups as well as for the aromatic protons and two singlets in a 1:2 ratio for the hydroxyl protons reveal that the calixarene moiety of **7** may be 1,2,4-substituted. Three pairs of doublets (ratio 3:2:1) for the methylene protons in calixarene skeleton (one of which is disturbed by superposition with the spacers) may support that **7** adopts a cone (or *syn*-) conformation at ambient temperature.¹²

Refluxing **6** in THF in the presence of excess K_2CO_3 gave a small amount of compound **7**, which can be considered as an indirect evidence for the structure of **7**.

Table 1. Percentage extraction (%E) of picrate salts from water into $CHCl_3$ at 25 ± 1 °C^a

Host	%E						
	Li^+	Na^+	K^+	NH_4^+	$n-PrNH_3^+$	$Me_2NH_2^+$	$Et_2NH_2^+$
4	49.2	46.3	44.5	32.7	30.8	16.4	36.8
5	14.5	15.7	50.4	48.6	37.2	28.5	31.1
7	16.0	14.2	11.5	5.4	3.6	1.1	14.7
8^b	0.08	0.3	11.8	1.5			

^a[Host]=[Guest]=0.005 mol dm⁻³. ^bThese data were quoted from Ref. 13.

Examination of the CPK molecular models reveals that compounds **4**, **5** and **7** are highly preorganized for binding cations. The *p*-*tert*-butylcalix[4]crown-5 (**8**)¹³ is used as a reference compound for extraction experiments. Percentage extraction of hosts **4**, **5** and **7** towards several picrate salts from water into $CHCl_3$ at 25 °C are summarized in Table 1. It can be seen from Table 1, the average extraction abilities of hosts **4**, **5** and **7** are high or very high though showing no much selectivity.

Comparing with *p*-*tert*-butylcalix[4]crown-5 (**8**), the extraction level of calix[4]cryptand (**4**) is dramatically high, which reveals that, as expected, the contribution of the cryptand subunit in **4** to cation extractions is much more than that of the crown subunit in **8**.

In conclusion, we think our strategy for the molecular design of calixcryptands is potentially useful for the development of novel types of tripodal calixcryptands with special ion and molecular recognition abilities. Further modifying the structure of the above ones, for example, varying the length of the spacers and introduction of functional groups such as esters and amides, may produce new ligands showing high selectivities toward cations.

References and Notes

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