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Syntheses of Lower-Rim-1,3-Crowned Calix[6]Arenes and their Complexation Abilities Toward Cations

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SYNTHESES OF LOWER-RIM-1,3-CROWNED CALIX[6]ARENES AND THEIR COMPLEXATION ABILITIES TOWARD CATIONS

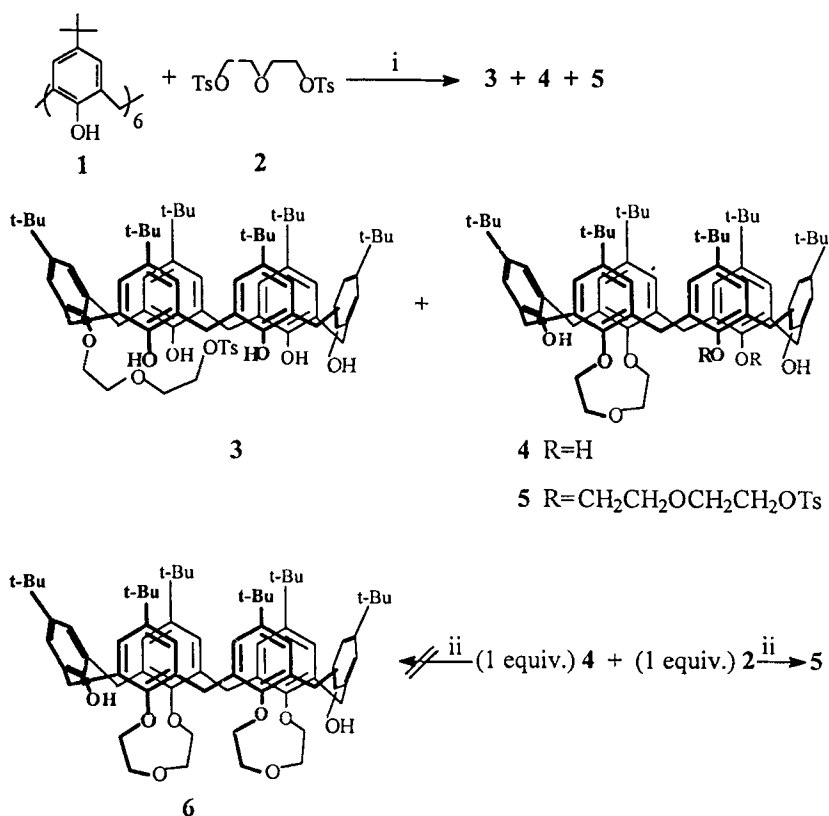
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ABSTRACT : An approach to lower-rim-1,3-crowned calix[6]arene and its derivatives in one-pot process has been accomplished. In the presence of very excess Na_2CO_3 (27-150 equivalent per mole *p*-*tert*-butylcalix[6]arene **1**) in acetonitrile, the lower-rim-1,3-bridged calix[6]crown-3 (**4**), the bistosylethoxy-ethyl derivative of **4** (**5**), as well as the intermediate of **4**, monotosylethoxyethyl *p*-*tert*-butylcalix[6]arene **3**, were obtained in rational yields, the distribution of the three compounds varied with the amount of the base used and other selected experimental conditions. **4** exhibits high selectivity towards Li^+ . **3** may be the first example of ionophore with high Et_2NH_2^+ selectivity.

Calixcrowns have attracted much more attention due to the combination of calixarenes and crown ethers with preorganized structures and special ion, molecular recognition abilities by co-operation effects.^[1,2] It is well-known that some of the calix[4]crowns exhibit outstanding recognition abilities towards cations. For example, the selectivities of diethylcalix[4]crown-4, diethylcalix[4]crown-5 (both in 1,3-alternate conformation) are $\text{Na}^+/\text{K}^+=10^{5.3}$ and $\text{K}^+/\text{Na}^+=10^{4.07}$, respectively.^[3] A variety of calix[4]crowns bridged at 1,3-lower-

rim and 1,2-lower-rim positions, etc. have been prepared, and the synthetic methods have been investigated in details.^[2,4] However, in contrast to the research extension of calix[4]crowns, only a few papers concerned calix[6]crowns,^[5] even their related compounds^[6-8]. In 1995, Ungaro *et al.* reported the synthesis of lower-rim-1,4-bridged calix[6]crown-5 in the presence of *t*-BuOK in benzene, and found that its derivative can bind tetramethylammonium cation in the polar region at the lower rim showing an association constant $K_a = 750 \text{ M}^{-1}$ in CDCl_3 .^[5] To the best of our knowledge, no paper concerning the synthesis of lower-rim-1,3-crowned calix[6]arenes has been reported so far.



Scheme 1. Reagents and Conditions : (i) Na_2CO_3 , acetonitrile, reflux; (ii) NaOH (50%), PEG-400, toluene, reflux.

In this paper, we wish to report the syntheses of the first lower-rim-1,3-crowned calix[6]arene, *p*-*tert*-butylcalix[6]-1,3-crown-3 (**4**), as well as its bistosylethoxyethyl derivative **5**, its intermediate, monotosylethoxyethyl *p*-*tert*-butylcalix[6]arene **3** by reacting *p*-*tert*-butylcalix[6]arene **1** with diethylene glycol ditosylate **2**, together with their selective complexation abilities towards Li⁺ and Et₂NH₂⁺ ions. The synthetic routine is shown in Scheme 1.

Reacting *p*-*tert*-butylcalix[6]arene **1** with diethylene glycol ditosylate in the presence of very excess Na₂CO₃ in acetonitrile^[9], **4**, **5** and **3**^[10] can be selectively obtained and easily isolated in fair to good yields according to the selected experimental conditions (Table 1).

As can be seen from Table 1, compound **4** and **3** were selectively obtained, respectively. Compound **5** was obtained as a main by-product in experiment No. 5 or 6. The choice of Na₂CO₃ and acetonitrile is a predominant successful factor. In fact, we have tried several other kinds of reaction systems, such as K₂CO₃/acetone, K₂CO₃/THF, NaH/DMF, NaH/THF, NaH/acetone, *t*-BuOK/benzene, etc., only

Table 1. Reaction of *p*-*tert*-butylcalix[6]arene **1** and diethylene glycol ditosylate **2** in various experimental conditions and distribution of products.^a

No.	Reaction Conditions			Distribution of Products / %		
	1 mol · dm ⁻³	2 mol · dm ⁻³	Na ₂ CO ₃ ^b equiv. · dm ⁻³	3	4	5
1	0.012	0.024	15	20 ^c	0 ^d	0 ^d
2	0.012	0.024	27	50 ^c	8 ^c	0 ^d
3	0.012	0.026	45	1 ^d	37 ^c	1 ^d
4	0.015	0.025	50	0 ^d	41 ^c	2 ^c
5	0.022	0.033	100	0 ^d	30 ^c	5.3 ^c
6	0.022	0.033	150	0 ^d	25 ^c	8.2 ^c

^aThe reaction was carried out under refluxing temperature for two days, and the conversion of **1** was 100% except in experiment No. 1 and 2, which were 50% and 86%, respectively. ^bThe equivalent of Na₂CO₃ is calculated for compound **1**.

^cIsolated yield. ^dTLC yield.

very complex products being difficultly separable were obtained, and the conversion of **1** was incomplete. Finally, we found that in the presence of very excess Na_2CO_3 in acetonitrile, the conversion of *p*-*tert*-butylcalix[6]arene in most cases was complete after refluxing for two days, which resulted in relative easy separation of the desired products in the next step.

Compound **5** can be conveniently synthesized by refluxing **4** with equal equivalent of **2** in toluene using NaOH as a base and PEG-400 as a phase transfer catalyst. The yield was 71% (based on **2**). It is interesting that no expected bis-calix[6]crown **6** was detected by TLC method in such experimental condition.

Examination of the CPK molecular models reveals that **3**, **4** and **5** are well-preorganized to complex cations. Percentage extraction of **3**, **4** and **5** towards picrate salts from water into CHCl_3 at 25°C are summarized in Table 2. It is noteworthy that compound **4** shows high Li^+ selectivity and compound **3** shows high Et_2NH_2^+ selectivity. The high Li^+ selectivity is rarely observed in calixarene chemistry.^[11,12] To the best of our knowledge, **3** may be the first example of ionophore with high Et_2NH_2^+ selectivity in calixarene chemistry.

Table 2 Percentage extraction (%E) of picrate salts from water into CHCl_3 at 25°C .^a Arithmetic mean of several experiments-standard deviation on the mean: $\sigma_{N-1} \leq 1$.

Host	%E						
	Li^+	Na^+	K^+	NH_4^+	n-PrNH_3^+	Me_2NH_2^+	Et_2NH_2^+
3	4.5	5.2	4.1	3.3	1.0	0.8	11.8
4	6.6	3.4	3.3	3.2	3.3	4.0	5.9
5	6.9	4.6	3.2	5.4	7.5	4.6	12.5

^a1.00 ml of $0.005 \text{ mol dm}^{-3}$ receptor solution in CHCl_3 was shaken (10min) with 1.00 ml of $0.005 \text{ mol dm}^{-3}$ picrate salt solution in H_2O and the percentage extraction was measured from the resulting absorbance at 380nm.

ACKNOWLEDGMENT

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9. A typical procedure for the preparation of the desired products: A mixture of *p*-tert-butylcalix[6]arene **1** and diethylene glycol ditosylate **2** (molar ratio see

Table 1) was stirred and refluxed in the presence of Na_2CO_3 (the amount was listed in Table 1) in acetonitrile under nitrogen for two days. The mixture was allowed to cool down to room temperature and filtered. The solvent was evaporated. The residue was saturated with petroleum ether (b.p. 60–90°C) and hot filtered. The solvent was evaporated again. The residue was recrystallized from cyclohexane (3), or petroleum ether (b.p. 60–90°C) (4), or purified by column chromatography on silica gel (4 and 5) to afford pure products.

10. Compound 3: m.p. 227°C(dec.). ^1H NMR (CDCl_3 , 500MHz): δ 1.15 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.22 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.26 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.28 (s, 18H, $\text{C}(\text{CH}_3)_3$), 2.08 (s, 3H, ArCH_3), 3.46 (d, 2H, $J=14.0\text{Hz}$, ArCH_2Ar), 3.52 (d, 2H, $J=13.9\text{Hz}$, ArCH_2Ar), 3.56 (d, 2H, $J=14.5\text{Hz}$, ArCH_2Ar), 3.92 (d, 2H, $J=13.9\text{Hz}$, ArCH_2Ar), 4.00 (d, 2H, $J=14.0\text{Hz}$, ArCH_2Ar), 4.03 (bs, 4H, OCH_2CH_2), 4.21 (bs, 4H, OCH_2CH_2), 4.33 (d, 2H, $J=14.5\text{Hz}$, ArCH_2Ar), 6.93 (d, 2H, $J=8.0\text{Hz}$, ArH), 7.01 (s, 2H, ArH), 7.07 (s, 4H, ArH), 7.08 (s, 2H, ArOH), 7.11 (s, 2H, ArOH), 7.12 (s, 4H, ArH), 7.14 (s, 2H, ArH), 7.26 (s, 1H, ArOH), 7.64 (d, 2H, $J=8.0\text{Hz}$, ArH). MS(FAB): $m/z=1215(\text{MH}^+)$. Anal. Calcd for $\text{C}_{77}\text{H}_{98}\text{SO}_{10}$, C: 76.08, H: 8.03, S: 2.64. Found, C: 76.19, H: 8.06, S: 2.59. The ^1H NMR spectrum of 3 shows three pairs of doublets for the methylene protons in calixarene skeleton indicating that 3 adopts a cone conformation. The methyl protons of the tosyl group has the appearance of one singlet with upfield shift at δ 2.08 indicating that the tosyl group may be "self-inclusioned" in the calix[6]arene annulus. Compound 4: m.p. 172–173 °C. ^1H NMR(CDCl_3 , 500MHz): δ 1.10 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.15(s, 9H, $\text{C}(\text{CH}_3)_3$), 1.25 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.27(s, 18H, $\text{C}(\text{CH}_3)_3$), 3.44 (d, 2H, $J=15.1\text{Hz}$, ArCH_2Ar), 3.51 (d, 2H, $J=14.3\text{Hz}$, ArCH_2Ar), 3.52 (d, 2H, $J=15.1\text{Hz}$, ArCH_2Ar), 3.97 (bs, 4H, OCH_2CH_2), 4.17 (d, 2H, $J=14.3\text{Hz}$, ArCH_2Ar), 4.27 (d, 2H, $J=15.1\text{Hz}$, ArCH_2Ar), 4.60 (bs, 4H, OCH_2CH_2), 5.21 (d, 2H, $J=15.1\text{Hz}$, ArCH_2Ar), 6.92 (bs, 1H, ArOH), 7.07 (s, 2H, ArH), 7.08 (s, 4H,

ArH), 7.09 (s, 2H, ArOH), 7.12 (s, 2H, ArH), 7.14 (s, 4H, ArH), 8.17 (bs, 1H, ArOH). MS(FAB): $m/z=1042(M^+)$. Anal. Calcd for $C_{70}H_{90}O_7$, C: 80.57, H: 8.69. Found, C: 80.78, H: 8.64. The 1H NMR spectrum of **4** shows four singlets (ratio 1:1:2:2) for the *tert*-butyl groups as well as for the aromatic protons, which identifies **4** as 1,3-lower-rim-bridged. Three pairs of doublets for the methylene protons in calixarene skeleton may reveal that **4** adopts a cone conformation. Compound **5**: m.p. 255 °C (dec.) 1H NMR($CDCl_3$, 500MHz) : δ 0.88 (s, 18H, $C(CH_3)_3$), 0.91 (s, 18H, $C(CH_3)_3$), 1.19 (s, 9H, $C(CH_3)_3$), 1.24 (s, 9H, $C(CH_3)_3$), 2.11 (s, 6H, $ArCH_3$), 3.25 (bs, 4H, OCH_2CH_2), 3.51 (bs, 4H, $ArCH_2Ar$), 3.60~3.75 (m, 12H, OCH_2CH_2), 4.10~4.25 (m, 16H, OCH_2CH_2 and $ArCH_2Ar$), 6.73 (bs, 4H, ArH), 6.98 (bs, 10H, ArH and ArOH), 7.07 (s, 4H, ArH), 7.19 (bs, 4H, ArH). MS(FAB): $m/z=1527(MH^+)$. Anal. Calcd for $C_{92}H_{118}S_2O_{15}$, C: 72.31, H: 7.78, S: 4.20. Found, C: 72.25, H: 7.78, S: 4.18. The 1H NMR spectrum of **5** shows four singlets (ratio 2:2:1:1) for the *tert*-butyl groups as well as for the calixarene aromatic protons, which reveals that **5** may be 1,3-4,6-substituted. One singlet with upfield shift at δ 2.11 for the methyl protons of the two tosyl groups may reveal that they are "self-inclusioned" in the calix[6]arene annulus. However, in the region of δ 3.60~3.75 and 4.10~4.25, only many complex signals were observed, which is hard to be explained.

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