Selective Bridging of Calix[6]arene: Synthesis of 1,2-Calix[6]dioxocrowns

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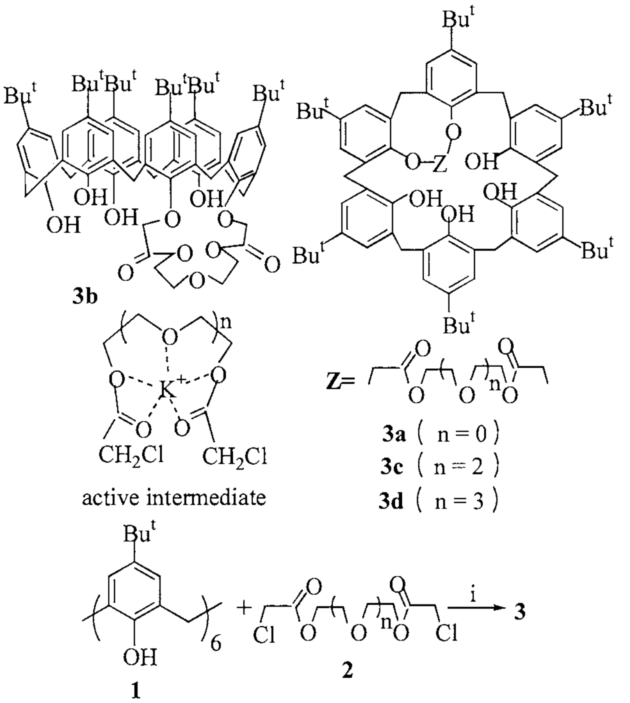
(Received January 5, 2000; CL-000013)

Treating *p-tert*-butylcalix[6]arene with oligoethylene glycol bischloroacetates, a series of ester-containing 1,2-bridged calix[6]crowns have been synthesized in reasonable yields for the first time. The longer the spacer in bischloroacetates, the higher the yield. The extraction ability towards alkali metal and ammonium cations of the obtained 1,2-calix[6]dioxocrowns are superior to that of 1,2-calix[6]crown-5.

Calixarenes are cyclic oligomers that belong to the class of $[1_n]$metacyclophanes. It was suggested that the calixarenes could be accounted as the third host molecule or the third generation of supramolecules, after crowns and cyclodextrins.[1] They are used as platforms or building blocks to construct a series of compounds with more sophisticated structures, for example, calixcrowns. By skillful use of solvents, bases, molar ratios of reactants, etc., now it can selectively synthesize all kinds of derivatives of calix[4]arenes.[1,2] However, it is not the case for calix[6]arenes. The first calix[6]crown, lower-rim 1,4-*p-tert*-butylcalix[6]crown-5 and 1,4-calix[6]crown-5, were prepared by Ungaro and co-workers in 1995.[3] Recently, we have succeeded in synthesizing a series of calix[6]crowns,[4,5] but the 1,2-calix[6]crowns-5 obtained as by-product only, and the yield is as low as 3%.[5] To the best of our knowledge, 1,2-calix[6]crown-5 is the sole 1,2-bridged calix[6]arenes with long flexible spacer up to now, although a few 1,2-bridged calix[6]arenes with short rigid spacers, such as methylene,[6] ethylene,[5] phthalyl,[7] *o*-xylyene,[8] etc. have been described. In this paper, we wish to report the synthesis of 1,2-calix[6]dioxocrowns and their extraction ability towards alkali metal and ammonium cations.

The synthesis procedures were shown in Scheme 1. Treating calix[6]arene **1** with oligoethylene glycol bischloroacetates **2** ($ClCH_2COOCH_2(CH_2CH_2O)_nCH_2OCOCH_2Cl$, n=0, 1, 2, 3, corresponding to **2a**, **2b**, **2c** and **2d**) in the presence of K_2CO_3 as the base and KI as the catalyst in benzene, the corresponding calix[6]dioxocrowns **3a**, **3b**, **3c** and **3d** were isolated in yields of 0%, 15%, 22% and 30%, respectively. Using other solvents such as toluene, acetonitrile or tetrahydrofuran etc. instead of benzene, only very complicated products were obtained, and the separations of such products were unsuccessful. Furthermore, the reaction was not sensitive to the amount of base and the molar ratio of **1** to **2**. These results show that the longer the spacer, the higher the yield of calix[6]dioxocrown, and also, no calix[6]dioxocrown-4 could be obtained. A plausible explanation is that the real active specie is the coordinated compound composed of oligoethylene glycol bischloroacetates **2** and the cation of the base, **2** plays a role as pseudo crown and the oxygen atoms of the carbonyl is incorporated into the coordinated shell as shown in Scheme 1. The oxygen atoms of **2a** are not enough to form the pseudo crown resulting in no **3a** formed. This explanation is also in agreement with the 1,2-calix[6]crown-5 being the only obtained 1,2-bridged calix[6]arene in the reactions of a series of polyethylene glycol ditosylates and *p-tert*-butylcalix[6]arene because the oxygen atoms of the tetraethylene glycol ditosylate are just enough to form pseudo crown.

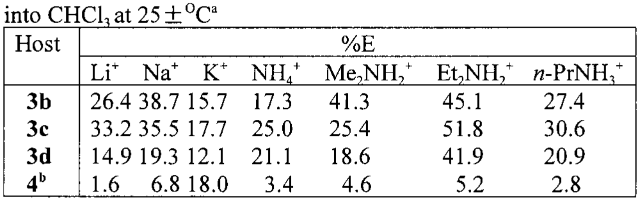


Scheme 1. Reagents and conditions: i. K_2CO_3, KI / dry benzene, reflux, 3 days.

The structures of **3b**, **3c** and **3d** were characterized by FAB-MS spectra, elemental analyses, ^1H NMR spectra.[10] The ^1H NMR spectrum of **3b**, **3c** and **3d** showed three singlets (1:1:1) for the *tert*-butyl groups, six singlets for the aromatic protons and two singlets (1:1) for the hydroxyl protons, which certainly indicate that the calix[6]arene moieties in **3** are intramolecularly bridged at 1,2-positions.[5] Furthermore, in the ^1H NMR spectrum of **3b**, four pairs of doublets (2:2:1:1, one was overlapped with ethylene protons) can be assigned for methylene bridge protons, which indicated that **3b** is in cone conformation. However, no defined conformation of **3c** and **3d** can be deduced similarly due to the complicated and overlapped signals for the methylene protons.

Examination of the CPK molecular models reveals that compound **3** are highly preorganized for binding cations. The percentage extraction of **3b**, **3c**, **3d** as well as *p-tert*-butylcalix[6]-1,2-crown-5[5] (**4**, as reference compound) towards several picrate salts from water into $CHCl_3$ at 25 °C are summarized in Table 1. It is worthy to note that they exhibited very high extraction ability towards alkali metal and ammonium cations (except K^+) as comparing with **4**. Considering the analogous structures of **3b** and **4**, this can be attributed to the beneficial influence of ester groups on complexation as described before.[9]

Table1. Percentage extraction (%E) of picrate salts from water into $CHCl_3$ at $25 \pm {}^{O}C$[a]



Host	%E						
	Li^+	Na^+	K^+	NH_4^+	$Me_2NH_2^+$	$Et_2NH_2^+$	n-$PrNH_3^+$
3b	26.4	38.7	15.7	17.3	41.3	45.1	27.4
3c	33.2	35.5	17.7	25.0	25.4	51.8	30.6
3d	14.9	19.3	12.1	21.1	18.6	41.9	20.9
4[b]	1.6	6.8	18.0	3.4	4.6	5.2	2.8

[a][Host]=[Guest]=0.005 mol dm^{-3}. [b]These data were quoted from Ref. 5.

In conclusion, this work not only describes a convenient method for preparation of 1,2-bridged calix[6]arene with long flexible spacer, but also provides an interesting idea to design and synthesize other 1,2-bridged calixarenes.

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

Reference and Notes

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10 **3b:** ^1H NMR (300 MHz, $CDCl_3$): 1.11(s, 18H, $ArC(CH_3)_3$), 1.26(s, 18H, $ArC(CH_3)_3$), 1.27(s, 18H, $ArC(CH_3)_3$), 3.49(d, 2H, J = 15.3 Hz, $ArCH_2Ar$), 3.56-3.70(m, 6H, OCH_2CH_2 and $ArCH_2Ar$), 3.85(bs, 4H, OCH_2CH_2), 4.20-4.39(m, 6H, OCH_2CO and $ArCH_2Ar$), 4.47(d, 1H, J = 15.6 Hz, $ArCH_2Ar$), 4.62(d, 2H, J = 15.3 Hz, $ArCH_2Ar$), 4.72(d, 1H, J = 14.7 Hz, $ArCH_2Ar$), 4.87(d, 1H, J = 14.7 Hz, $ArCH_2Ar$), 5.03(d, 1H, J = 15.6 Hz, $ArCH_2Ar$), 6.96, 7.04, 7.07, 7.09, 7.11, 7.13 (s each, 2H each, ArH), 8.27(bs, 2H, ArOH), 9.08(bs, 2H, ArOH). MS(FAB): m/z 1,159(MH^+, 40%), 1198(MHK^+,10%), Anal. calcd for $C_{74}H_{94}O_{11}$: C, 76.65; H, 8.17%. Found: C, 76.68; H, 8.19%.

3c: ^1H NMR (300 MHz, $CDCl_3$): 1.10(s, 18H, $ArC(CH_3)_3$), 1.27(s, 18H, $ArC(CH_3)_3$), 1.28(s, 18H, $ArC(CH_3)_3$), 3.43(d, 2H, J = 15.8 Hz, $ArCH_2Ar$), 3.45-3.80(m, 8H, OCH_2CH_2), 3.83(t, 4H, J = 7.4 Hz, OCH_2CH_2), 3.99(d, 2H, J = 15.0 Hz, $ArCH_2Ar$), 4.33-4.60(m, 6H, OCH_2CO and $ArCH_2Ar$), 4.72(d, 2H, J = 15.0 Hz, $ArCH_2Ar$), 4.80(bs, 4H, $ArCH_2Ar$), 6.91, 7.02, 7.09, 7.11, 7.17, 7.19(s each, 2H each, ArH). 8.58(bs, 2H, ArOH), 9.07(bs, 2H, ArOH). MS(FAB): m/z 1,203(MH^+, 30%), m/z 1,243(MHK^+, 20%), Anal. calcd for $C_{76}H_{98}O_{12}$: C, 75.82; H, 8.20%; Found: C, 76.80; H, 8.18%.

3d: ^1H NMR (300 MHz, $CDCl_3$): 1.08(s, 18H, $ArC(CH_3)_3$), 1.24(s, 18H, $ArC(CH_3)_3$), 1.27(s, 18H, $ArC(CH_3)_3$), 3.44(d, 2H, J = 15.0 Hz, $ArCH_2Ar$), 3.48-3.68(m, 14H, OCH_2CH_2 and $ArCH_2Ar$), 3.84(bs, 4H, OCH_2CH_2), 4.18(d, 2H, J= 15.0 Hz, $ArCH_2Ar$), 4.27(d, 2H, J = 15.6 Hz, $ArCH_2Ar$), 4.49(bs, 4H, OCH_2CO), 4.56(d, 1H, J = 15.1 Hz, $ArCH_2Ar$), 4.53(d, 1H, J = 15.1 Hz, $ArCH_2Ar$), 4.85(d, 2H, J = 15.6 Hz, $ArCH_2Ar$), 6.86, 7.06, 7.09, 7.10, 7.13. 7.14(s each, 2H each, ArH). 8.48(bs, 2H, ArOH), 9.23(bs, 2H, ArOH). MS(FAB): m/z 1,247(MH^+, 20%), m/z 1285(MHK^+,15%), Anal. Calcd for $C_{78}H_{102}O_{13}$: C, 75.07; H, 8.24%; Found: C, 75.11; H, 8.23%.