Regioselective Bridging of Calixarenes − Syntheses, Structural Elucidation and Extraction Studies of 1,2-Calix[*n*]dioxocrowns ($n = 6, 8$)

Fafu Yang[a] and Yuanyin Chen*[a]

Keywords: Calixarenes / Crown compounds / Alkali metals / Cations / Supramolecular chemistry

A series of ester-containing 1,2-bridged calix[*n*]crowns (n = 6,8) have been synthesized in reasonable yields by treating *p-tert*-butylcalixarenes with oligoethylene glycol bischloroacetates in the presence of K_2CO_3. It was found that K_2CO_3 not only acts as a weak base, but also plays the role of template. The template effect is based on the formation of a real active species derived from the bischloroacetates and K^+. The longer spacer in bischloroacetates shows the stronger template effect and gives the higher yield. The extraction ability towards alkali metals and ammonium cations of the obtained 1,2-calix[6]dioxocrowns are superior to that of 1,2-calix[6]crown-5. The complexation abilities of calix[8]crowns are studied for the first time.

Introduction

Calixarenes are cyclic oligomers that belong to the class of $[1_n]$metacyclophanes. In recent years, they have been used as versatile building blocks for artificial receptors in supramolecular chemistry enabling the design and construction of more elaborate molecules and assemblies.[1] In order to prepare the calixarenes with well-defined structures suitable for complexation, intramolecular bridging, with crown segments[2] is deemed to be the most promising approach for the large oligomers of this class, i.e. hexamers and octamers. Thus, many kinds of calix[6]crowns have been prepared by skillful use of solvents, bases, molar ratios of reactants, etc.[3−5] Although in most cases the reactions of calix[8]arene are more complex than that of calix[6]arene, a few calix[8]crowns have been described by Neri and coworkers.[6−8] Among the calix[6,8]crowns, the synthesis of 1,2-calix[6,8]crowns was the most difficult task. 1,2-*p-tert*-Butylcalix[8]crown-4 was reported previously,[6] and was obtained as a by-product in a yield as low as 5%. Although the 1,2-bridged calix[6]arenes with short rigid spacers, such as ethylene,[5] phthalyl,[9] *o*-xylyene,[10] etc. have been described, the first 1,2-calix[6]crown formed only in the reaction of *p-tert*-butylcalix[6]arene with the ditosylates possessing the longest spacer, tetraethylene glycol ditosylate, as a by-product in a yield as low as 3%.[5] Recently, we were interested in finding out what happens when *p-tert*-butylcalix[6]arene is treated with another type of long flexible crown segment, oligoethylene glycol bischloroacetates: we found that 1,2-calix[6]dioxocrowns were obtained as the only isolated products in reasonable yields ,and a new type of template effect based on the formation of a real active species composed of the dichloroacetates and potassium cations could be postulated.[11] Further investigations revealed that this kind of cation template reaction can be further developed to prepare 1,2-bridged calix[8]crowns. In this paper, we wish to report the possible nature of this type of template effect, the preparation of 1,2-bridged calix[*n*]dioxocrowns (n = 6, 8) and their extraction ability towards alkali metal and ammonium cations.

Results and Discussion

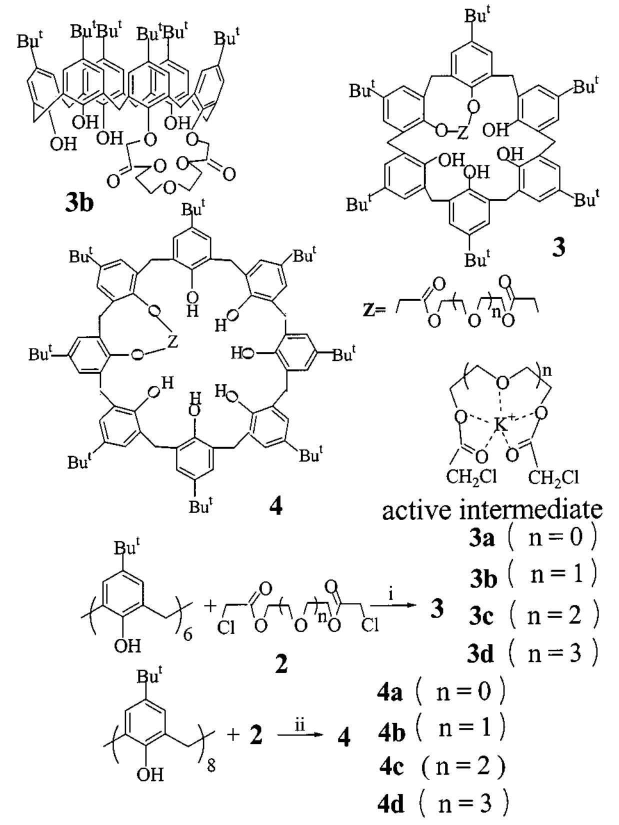
Synthesis of *p-tert*-Butylcalix[*n*]-1,2-dioxocrowns (n = 6,8)

The synthetic procedure is shown in Scheme 1. Treating *p-tert*-butylcalix[6]arene **(1)** with oligoethylene glycol bischloroacetates **(2)** [$ClCH_2COOCH_2(CH_2OOCH_2)_nCH_2OCOCH_2Cl$ (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, gave the corresponding calix[6]dioxocrowns, **3b**, **3c** and **3d** in yields of 15%, 22% and 30%, respectively. These results show that the longer spacer gives the higher yield of calix[6]dioxocrown, and also that no calix[6]dioxocrown-4 could be obtained. Thus, we postulate in this reaction that the real active species is the coordinated compound consisting of the oligoethylene glycol bischloroacetate **2** and the potassium cation, and that **2** plays the role of pseudo crown with the oxygen atoms of the ether bonds and the carbonyl group incorporated into the coordination shell, as shown in Scheme 1. In other words, a new kind of template effect is occurring.[11] The oxygen atoms of **2a** are not enough to form the pseudo crown and therefore no **3a** is formed. This explanation is also in agreement with the observation that 1,2-calix[6]crown-5 is the only 1,2-bridged calix[6]arene obtained from the reaction 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 the pseudo crown.[5] With other solvents such as acetonitrile, DMF or tetrahydrofuran instead of benzene, the reaction is speeded up but only very complicated products are obtained; the separation of these mixtures was unsuccessful. This phenomenon can be explained by the competing complexation of the solvent

---

[a] Department of Chemistry, Wuhan University,
Wuhan 430072, P. R. China

1434−193X/01/0102−0365 $ 17.50+.50/0



Scheme 1. Reagents and conditions: i. K_2CO_3, KI/dry benzene, reflux, 3 days; ii. K_2CO_3, KI/acetone, reflux, 2 days

and phenolic hydroxyl to restrain the formation of the cation template active species shown in Scheme 1.

The 1,2-*p*-*tert*-butylcalix[8]dioxocrowns were synthesized by an analogous procedure, but with acetone instead of benzene as the solvent. The 1,2-*p*-*tert*-butylcalix[8]dioxocrowns **4b, 4c,** and **4d** were isolated in yields of 12%, 21%, and 26%, respectively. Due to the lower activities of hydroxyl in *p*-*tert*-butyl calix[8]arene relative to that in *p*-*tert*-butylcalix[6]arene, and poor solubility in benzene, the reaction should be carried out in acetone instead of benzene and it is obvious that the active species shown in Scheme 1 can also be formed in this solvent. With benzene, toluene or acetonitrile as solvent, most of the calix[8]arene did not react, even after prolonging the reaction time to three days.

Structural Elucidation of *p*-*tert*-Butylcalix[*n*]-1,2-dioxocrown ($n = 6,8$)

All new compounds were characterized by FAB-MS spectra, elemental analysis and ^{1}H NMR spectroscopy. The ^{1}H NMR spectra 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, indicating that the calix[6]arene moieties in **3** are intramolecularly bridged at the 1,2-positions.[5] Furthermore, in the ^{1}H NMR spectrum of **3b**, four pairs of doublets(2:2:1:1, one is overlapped with the signal of the thylene protons) can be assigned for methylene bridge protons, indicating that **3b** is in the cone conformation. However, the conformation of **3c** and **3d** cannot deduced in a similar manner due to the complicated and overlapped signals for the methylene protons. As regards the calix[8]dioxocrowns, the ^{1}H NMR spectrum of **4b** and **4c** show three singlets (1:2:1) for the *tert*-butyl groups and three singlets (1:1:1) for the hydroxyl groups, indicating that the calix[8]arene moieties in **4b** and **4c** are intramolecularly bridged at the 1,2-positions, in accordance with previous studies.[6] The ^{1}H NMR spectrum of **4d** shows four singlets (1:1:1:1) for the *tert*-butyl groups and three singlets (1:1:1) for the hydroxyl groups, indicating two possible bridging patterns: 1,2- or 1,4-bridging. However, Neri et al. have previously pointed out that the chemical shift values for the three 2H hydroxyl groups can be used as a sensitive structural probe to distinguish the 1,2- and 1,4-isomers.[6,12] In the ^{1}H NMR spectrum of **4d**, the resonances appear at $\delta = 8.24, 8.72, 8.81$, and can thus be attributed to an OH single-H-bonded in a semicircular array and two double-H-bonded hydroxyl groups, respectively. Thus, **4d** is also a 1,2-bridged isomer.

Extraction Studies

Examination of the CPK molecular models reveals that compounds **3** and **4** are well preorganized for binding cations. The percentage extraction of **3** and **4** as well as *p*-*tert*-butylcalix[6]-1,2-crown-5[5] (**5**, as reference compound) towards several picrate salts from water into $CHCl_3$ at 20 °C are summarized in Table 1. It can be seen that **3** exhibits a very high extraction ability towards alkali metals and ammonium cations (except K^+) relative to **5**. Considering the analogous structures of **3b** and **5**, this can be attributed to the beneficial influence of the ester groups on complexation, as described previously.[13] Moreover, it is worthy to note the difference in the sequence of extraction ability among alkali metal cations. The highest extraction percentage among the alkali metals tested is for Na^+ with **3** as compared to K^+ with **5**. Compound **4** also exhibits a high extraction ability towards alkali metal and ammonium cations (except K^+), although it is lower than that of **3**. These results may be explained by the more flexible conformations of *p*-*tert*-butylcalix[8]dioxocrowns than those of *p*-*tert*-butylcalix-[6]dioxocrowns — this flexibility of conformation is not favorable for binding cations. Furthermore, the extraction selectivity towards alkali metal cations is also different. It is interesting to note that **4c** and **4d** exhibit higher extraction percentages towards Li^+. This may be attributed to the appropriate size of the newly created cavity composed of the *p*-*tert*-butylcalix[8]arene moiety and crown segment.

Conclusions

A series of 1,2-bridged *p*-*tert*-butylcalix[*n*]dioxocrowns ($n = 6, 8$) was selectively synthesized by the reaction of *p*-*tert*-butylcalixarene with oligoethylene glycol bischloroacetates, based on the formation of a postulated active species composed of potassium cation and oligoethylene glycol bischloroacetates, in reasonable yields. This type of template effect was not been reported before in the field of ca-

Table 1. Percentage extraction (%E) of picrate salts from water into $CHCl_3$ at 20 °C (1.00 mL of a 0.005 M receptor solution in $CHCl_3$ was shaken (20 min) with 1.00 mL of a 0.005 M picrate salt solution in triply distilled H_2O and the percentage extraction was measured from the resulting absorbance at 380 nm; control experiments showed that no picrate extraction occurred in the absence of the calixarene derivative); arithmetic mean of several experiments, standard deviation on the mean: $\sigma_{N-1} \leq 1$.

Host					% E		
	Li^+	Na^+	K^+	NH_4^+	$Me_2NH_2^+$	$Et_2NH_2^+$	$nPrNH_4^+$
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
4b	20.5	26.7	11.8	13.6	15.4	13.5	17.6
4c	25.1	19.3	10.3	18.6	16.8	21.9	12.3
4d	19.7	12.4	10.5	15.7	17.3	19.8	13.7
5[a]	1.6	6.8	18.0	3.4	4.6	5.2	2.8

[a] These data quoted from ref.[5]

lixarene chemistry.[11] The active intermediate in the reaction of calix[6]arene with oligoethylene glycol bischloroacetates is easily formed in weakly polar solvents such as benzene. As for *p-tert*-butylcalix[8]arene, due to the lower activity of the hydroxyl group and poor solubility the reaction was preferably carried out in acetone. Moreover, the longer spacer in bischloroacetates shows a stronger template effect and gives higher yields. Extraction experiments indicated that these ester-containing calixcrowns exhibit more promising complexation abilities towards alkali metal and ammonium cations than those of normal calixcrowns. Furthermore, the complexation abilities of *p-tert*-butylcalix[8]dioxocrowns, studied for the first time here, are weaker than those of *p-tert*-butylcalix[6]dioxocrowns due to the larger conformational flexibility, and even though the size of the cavity in calix[8]arene is so large, its appropriate derivative can still complex the smallest alkali metal cation, Li^+, effectively.

Experimental Section

Melting points are uncorrected. Benzene and acetone were freshly distilled before use. All other solvents were used directly as received. K_2CO_3 was heated at 450 °C for 4 h. ^1H NMR spectra were recorded on Bruker-ARX 300 instruments at ambient temperature. TMS was used as an internal standard. FAB-MS spectra were obtained on a Kratos MS80RF mass spectrometer. UV/Vis measurements were recorded on a Shimadzu-240 Uv-Vis spectrophotometer equipped with two thermostat cell compartments. Elemental analyses were performed by the analytical laboratory of the department of chemistry.

General Procedure for the Syntheses of *p-tert*-Butylcalix[6]-1,2-dioxocrowns: A mixture of *p-tert*-butylcalix[6]arene (1.0 mmol), oligoethylene glycol dichloroacetate (1.1 mmol), K_2CO_3 (5.0 mmol) and KI (2.2 mmol), was stirred in refluxing benzene (100 mL) for three days under N_2. After distilling off the solvent, the residue was treated with HCl (10%, w/v) and extracted with $CHCl_3$. The organic layer was separated, dried ($MgSO_4$), filtered, and the filtrate concentrated under vacuum. Compounds **3b, 3c, 3d** were obtained in yields of 15%, 22%, 30%, respectively, by column chromatography on silica gel (90% CH_2Cl_2, 10% Et_2O).

3b: M.p. 235−238 °C. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.11 [s, 18 H, $C(CH_3)_3$], 1.26 [s, 18 H, $C(CH_3)_3$], 1.27 [s, 18 H, $C(CH_3)_3$], 3.49 (d, *J* = 15.3 Hz, 2 H, $ArCH_2Ar$), 3.56−3.70 (m, 6 H, OCH_2CH_2 and $ArCH_2Ar$), 3.85 (br. s, 4 H, OCH_2CH_2), 4.20−4.39 (m, 6 H, OCH_2CO and $ArCH_2Ar$), 4.47 (d, *J* = 15.6 Hz, 1 H, $ArCH_2Ar$), 4.62 (d, *J* = 15.3 Hz, 2 H, $ArCH_2Ar$), 4.72 (d, *J* = 14.7 Hz, 1 H, $ArCH_2Ar$), 4.87 (d, *J* = 14.7 Hz, 1 H, $ArCH_2Ar$), 5.03 (d, *J* = 15.6 Hz, 1 H, $ArCH_2Ar$), 6.96, 7.04, 7.07, 7.09, 7.11, 7.13 (s each, 2 H each, ArH), 8.27 (br. s, 2 H, ArOH), 9.08 (br. s, 2 H, ArOH). − MS (FAB): *m*/*z* (%) = 1159 (40) [MH^+], 1198 (10) [MHK^+]. − $C_{74}H_{94}O_{11}$ (1159.6): calcd. C 76.65, H 8.17; found C 76.68, H 8.19.

3c: M.p. 217−219 °C. − ^1H NMR: δ = 1.10 [s, 18 H, $C(CH_3)_3$], 1.27 [s, 18 H, $C(CH_3)_3$], 1.28 [s, 18 H, $C(CH_3)_3$], 3.43 (d, *J* = 15.3 Hz, 2 H, $ArCH_2Ar$), 3.45−3.80 (m, 8 H, OCH_2CH_2), 3.83 (t, *J* = 7.5 Hz, 4 H, OCH_2CH_2), 3.99 (d, *J* = 15.0 Hz, 2 H, $ArCH_2Ar$), 4.33−4.60 (m, 6 H, OCH_2CO and $ArCH_2Ar$), 4.72 (d, *J* = 15.0 Hz, 2 H, $ArCH_2Ar$), 4.80 (br. s, 4 H, $ArCH_2Ar$), 6.91, 7.02, 7.09, 7.11, 7.17, 7.19 (s each, 2 H each, ArH). 8.58 (br. s, 2 H, ArOH), 9.07 (br. s, 2 H, ArOH). − MS (FAB): *m*/*z* (%) = 1203 (30) [MH^+], 1243 (20) [MHK^+]. − $C_{76}H_{98}O_{12}$ (1203.6): calcd. C 75.82, H 8.20; found C 76.80, H 8.18.

3d: M.p. 209−213 °C. − ^1H NMR: δ = 1.08 [s, 18 H, $C(CH_3)_3$], 1.24 [s, 18 H, $C(CH_3)_3$], 1.27 [s, 18 H, $C(CH_3)_3$], 3.44 (d, *J* = 15.0 Hz, 2 H, $ArCH_2Ar$), 3.48−3.68 (m, 14 H, OCH_2CH_2 and $ArCH_2Ar$), 3.84 (br. s, 4H, OCH_2CH_2), 4.18 (d, *J* = 15.0 Hz, 2 H, $ArCH_2Ar$), 4.27 (d, *J* = 15.6 Hz,2 H, $ArCH_2Ar$), 4.49 (br. s, 4 H, OCH_2CO), 4.56 (d, *J* = 15.3 Hz, 1 H, $ArCH_2Ar$), 4.53 (d, *J* = 15.3 Hz, 1 H, $ArCH_2Ar$), 4.85 (d, *J* = 15.6 Hz, 2 H, $ArCH_2Ar$), 6.86, 7.06, 7.09, 7.10, 7.13. 7.14 (s each, 2 H each, ArH). 8.48 (br. s, 2 H, ArOH), 9.23 (br. s, 2H, ArOH). − MS(FAB): *m*/*z* (%) = 1247 (20) [MH^+], 1285 (15) [MHK^+]. − $C_{78}H_{102}O_{13}$ (1247.7): calcd. C 75.07, H 8.24; found C 75.11, H 8.23.

General Procedure for the Syntheses of *p-tert*-Butylcalix[8]-1,2-dioxocrown: A mixture of *p-tert*-butylcalix[8]arene (1.0 mmol), oligoethylene glycol dichloroacetate (1.1 mmol), K_2CO_3 (3.0 mmol) and KI (2.2 mmol) was stirred in refluxing acetone (100 mL) for 48 h under N_2. After distilling off the solvent, the residue was treated with HCl (10%, w/v) and extracted with $CHCl_3$. The organic layer was separated, dried ($MgSO_4$), filtered, and the filtrate concentrated under vacuum. Compounds **4b**, **4c**, **4d** were obtained in yields of 12%, 21%, 26%, respectively, by column chromatography on silica gel (95% CH_2Cl_2, 5% Et_2O).

4b: M.p. 248−251 °C. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.19, 1.24, 1.27 [s, $C(CH_3)_3$, 18 H, 36 H, 18 H], 3.70−4.58 (overlapped, OCH_2CH_2 and $ArCH_2Ar$, 28 H), 7.00−7.32 (overlapped, ArH, 16 H), 8.01, 8.85, 8.96 (s, ArOH, 2 H each). − MS (FAB): *m*/*z* (%) = 1483 (30) [MH^+]. − $C_{96}H_{122}O_{13}$ (1484.0): calcd. C 77.70, H 8.29; found C 77.74, H 8.25.

4c: M.p. 237−241 °C. − ^1H NMR (300 MHz, $CDCl_3$): δ=1.23, 1.27, 1.30 [s, $C(CH_3)_3$, 18 H, 36 H, 18 H], 3.65−4.52 (overlapped, OCH_2CH_2 and $ArCH_2Ar$, 32 H), 7.02−7.33 (overlapped, ArH, 16 H), 8.32, 8.88, 9.18 (s, ArOH, 2 H each). − MS (FAB): *m*/*z* (%) = 1527 (20) [MH^+]. − $C_{98}H_{126}O_{14}$ (1528.1): calcd. C 77.03, H 8.31; found C 77.08, H 8.27.

4d: M.p. 240−243 °C. − ^1H NMR (300 MHz, $CDCl_3$): δ=1.12, 1.20, 1.24, 1.25 [s, $ArC(CH_3)_3$, 18 H each], 3.65−4.63 (overlapped, OCH_2CH_2 and $ArCH_2Ar$, 36 H), 6.84−7.26 (overlapped, ArH, 16 H), 8.24, 8.72, 8.88 (s, ArOH, 2 H each). − MS (FAB): *m*/*z* (%) = 1571 (15) [MH^+]. − $C_{100}H_{130}O_{15}$ (1572.1): calcd. C 76.40, H 8.34; found C 76.43, H 8.29.

Acknowledgments

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

---

[1] For example: [1a] V. Böhmer, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713−745. − [1b] A. Ikeda, S. Shinkai, *Chem. Rev.* **1997**, *97*, 1713−1734.

[2] Z. Asfafi, S. Wenger, J. Vicens, *J. Incl Phenom.* **1994**, *19*, 137−148.

[3] A. Casnati, P. Jacopezzi, A. Opochini, F. Ugozzoli, R. Cacciapaglia, L. Mandolini, R. Ungaro. *Tetrahedron* **1995**, *51*, 591−598.

[4] Y. Y. Chen, J. S. Li, J. Xi, Z. L. Zhong, S. L. Gong, and X. R. Lu, *Synth. Commun*. **1999**, *29*, 705−711.

[5] J. S. Li, Y. Y. Chen, X.R. Lu, *Tetrahedron.* **1999**, *55*, 10365−10374.

[6] C. Geraci, M. Piattelli, P. Neri, *Tetrahedron Lett*. **1996**, *37*, 3899−3902.

[7] C. Geraci, G. Chessari, M. Piattelli, P. Neri, *Chem. Commun.* **1997**, 921−922.

[8] C. Geraci, M. Piattelli, P. Neri, *Tetrahedron Lett*. **1995**, *36*, 5429−5432.

[9] D. Kraft, V. Bohmer, W. Vogt, G. Ferguson, and J. F. Gallagher, *J. Chem. Soc., Perkin Trans. 1* **1994**, 1221−1230.

[10] H. Otsuka, K. Araki, and S. Shinkai, *J. Org. Chem.* **1994**,*59*, 1542−1547.

[11] A few papers concerning the template effect for calixarene have appeared. For example:[11a] T. Yamato, F. Zhang, T. Sato, S. Ide. *J. Chem. Res.* **2000,** 10−12. − [11b] Y. Tokunaga, D. M. Rudkevich, J. Santanmaria, G. Hilmersson, J. Rebek, Jr. *Chem. Eur. J.* **1998**, *4*, 1449−1457. − [11c] T. Yamato, Y. Saruwatari, M. Yasumatsu, S. Ide. *Eur. J. Org. Chem.* **1998**, 309−316.

[12] F. Cunsolo, G. M. L. Consoli, M. Piattelli, P. Neri, *J. Org. Chem.* **1998**, *63*, 6852−6858.

[13] F. Arnaud-Neu, E. M. Collins, M. Deasy, G. Ferguson, S. J. Harris, B. Kaitner, E. Marques, M. J. Schwing-Weill and E. M. Seward, *J. Am. Chem. Soc.* **1989**, *111*, 8681−8691.

Received July 17, 2000
[O00363]