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Synthesis of Unsymmetrical Calix[4]arene Cryptand Crown-6 in 1,3-Alternate Conformation

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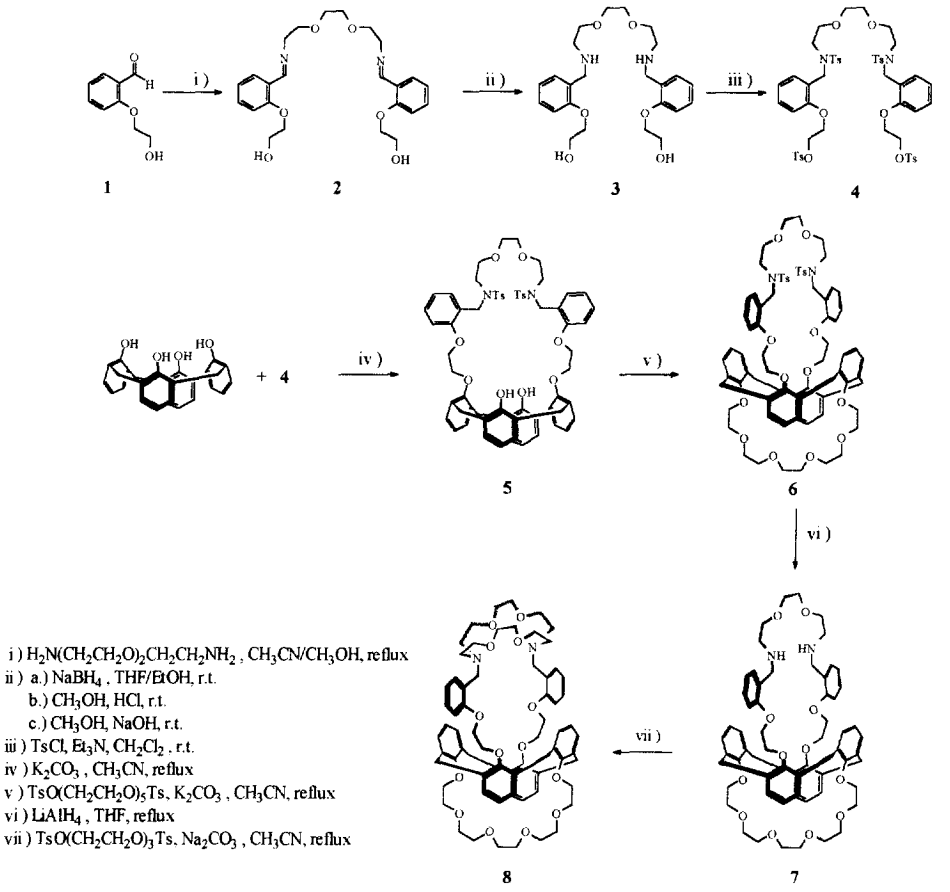
Abstract: We report the synthesis of a calix[4]arene bridged by a cryptand unit and a crown ether chain in 1,3-alternate conformation. Preliminary complexation properties with alkali metals are also described. Copyright © 1996 Elsevier Science Ltd

Calixarenes, and in particularly calix[4]arenes, are becoming an important class of compounds in supramolecular chemistry.[1,2] They are readily amenable to chemical modification at the phenolic hydroxy groups leading to molecules with selective host-guest chemistry.[1,2] In order to obtain specific properties, a number of moieties have been attached to the calixarene platform to give precise molecular architectures as manifested in their shape, size, and conformation.[3] For example, the 1,3-capping of calix[4]arene provide calix-*mono*-crowns[4,5] or calix-*bis*-crowns[6,7] which have a high selectivity towards alkali cations. Azaoxa crown ether chains have been attached to a calix[4]arene or calix[4]-crowns to provide symmetrical calix-*bis*-aza crowns[8] or unsymmetrical calix-aza crown-crowns, [9] respectively. The cryptand unit has been fixed to calix[4]arene to provide a calixcryptand[10] which was shown to complex copper(II). Similarly, a calixcryptand has been prepared by condensing the different ring-size cryptand precursor units to *syn*-1,3-diacid dichloride of *p-tert*-butyl calix[4]arene.[11]

Here, we have developed a strategy to synthesize calix[4]cryptand-crown-6 **8** by passing through calix-aza crown-crown ether intermediate and ending with the formation of the cryptand unit by the glycolic ditosylate chain. We report also a preliminary study on the complexation behavior of **8** by using proton nuclear magnetic resonance spectroscopy (^{1}H-NMR) and fast-atom bombardment mass spectroscopy (FAB (+) MS).



Scheme 1. Synthetic pathway to unsymmetrical calix[4]cryptand crown-6 **8**

The synthesis of **8**, shown in Scheme 1, began by the condensation of aldehyde **1**[12] with 0.5 equiv. of 1,8-diamino-2,6-dioxa octane in a mixture of 1:1 acetonitrile : methanol with reflux for 24 h., leading to a quantitative yield of Schiff base **2.** Compound **2** was directly reduced by 8 equivs. of $NaBH_4$ in 1:1 THF : ethanol at rt for 4 h. After treatment with hydrochloric acid and NaOH in methanol respectively, diaza dioxa **3** was extracted from CH_2Cl_2/H_2O in quantitative yields. Compound **3** was reacted with 4 equivs. of tosylchloride in the presence of 5 equivs. of Et_3N in CH_2Cl_2 for 24 h. at rt. The residue was purified on silicagel column by using 85:15 CH_2Cl_2:acetone as eluent to give the tetra(N,O)tosylate **4** as a transparent oil in 65% yield. By the conventional method[8], the 1,3-capping of calix[4]arene was carried out by reaction of 1 equiv. of **4** in refluxing acetonitrile in the presence of K_2CO_3 for 2 weeks. After purification by silicagel chromatography using 97:3 CH_2Cl_2:acetone as eluent, the calix[4]-diaza dioxa **5** was obtained in 48% yield. Compound **5** was deduced to be in cone conformation by the appearance of an AB system at 4.29 and 3.27 ppm (J = 12.7 Hz) for the protons of methylene bridges. As described in our former

works[8,9,12], compound **5** was bridged with 1 equiv. of pentaethylene glycol ditosylate in the presence of K_2CO_3 in acetonitrile under reflux for 24 h. The desired product **6**[14] was eluted on a silicagel column with 85:15 CH_2Cl_2:acetone as eluent and was shown to be in 1,3-alternate conformation due to the presence of a singlet at 3.83 ppm for the protons of methylene bridges. The detosylation of **6** was achieved by treatment of **6** with 25 equivs. of $LiAlH_4$ in freshly distilled THF under reflux for 48 h. as described in literature[13] to give calix[4]-diaza dioxa-crown-6 **7**[15] in 38 % yield after purification on silicagel by using 70:30 CH_2Cl_2:methanol as eluent. N-cyclocondensation to cryptand unit was performed by reacting **7** with 1 equiv. of triethylene glycol ditosylate in the presence of 10 equivs. of Na_2CO_3 in acetonitrile under reflux for 1 week.[16] The residue was purified by silicagel chromatography using 90:10 CH_2Cl_2:methanol as eluent to provide calix[4]-cryptand-crown-6 **8**[17] in 8% yield.

Preliminary complexation studies of calix[4]cryptand crown-6 **8** with potassium picrate (K^+Pic^-) and cesium picrate (Cs^+Pic^-) were realized by means of proton nuclear magnetic resonance spectroscopy (^{1}H-NMR) and fast-atom bombardment mass spectroscopy (FAB (+) MS). After a period of 7 days reaction between solid potassium picrate and a chloroform solution of **8** the ratio of metal to ligand in solution, as estimated by integration of the picrate proton resonance versus those for the glycolic chains, was 1:1. This ratio was also evidenced by the FAB (+) MS data presenting M^+ = 1191.6 (70%) for the 1:1 complex and $M^+ - K^+$ = 1153.6 (100%) corresponding to the free ligand. For the 1:1 complex of potassium picrate, we observed the shifts of the aromatic protons from 7.47 ppm (d, J = 7.3 Hz) to 7.40 ppm (d, J = 7.1 Hz) and of NCH_2CH_2 signal from 3.09 ppm (t, J = 6.2 Hz) to 2.70 ppm ((br)s) which implied the potassium to be located in the cryptand cavity. Such an upfield shift has already been described for potassium [2.2.2] cryptate[18]. Similarly, we isolated the 1:1 complex of **8** with cesium picrate. FAB (+) MS data showed the only presence of M^+ = 1258.4 (100%) indicating the cesium complex to be stronger than the potassium one. For the 1:1 cesium complex, no shift was observed for the NCH_2CH_2 triplet. So the cesium was located in the crown-6 chain. The location of the cesium cation in the glycolic chain may also be assumed due to evidence of highly selective complexation of cesium by calix[4]crowns-6[19]. After the formation of 1:1 complexes, we tried to form the 1:1:1 hetero-bimetallic-complexes by adding the picrate salts alternatively. We reacted potassium picrate with the 1:1 complex of cesium picrate and the cesium picrate with the 1:1 complex of potassium picrate. After 6 days, 1:2 complexes were detected by ^{1}H-NMR which gave the same spectra. From the shift of the NCH_2CH_2 triplet in a very similar manner to that of the 1:1 complex with potassium, we deduced the ligand **8** to complex potassium in the cryptand unit and the cesium in the glycolic chain. By FAB (+) MS of the 1:1:1 complex we could not detect the $\mathbf{8}.K^+.Cs^+$ signal but we observed the mass signal corresponding to the 1:1:1 complexes ($\mathbf{8}.Na^+.Cs^+$) probably due to the presence of sodium in the matrix.

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14. Analytical data of compound **6** : (Mp 94 - 95 °C) ^{1}H-NMR (200 MHz, $CDCl_3$) : δ (ppm) 7.70 (d, *J* = 8.0 Hz, Ar*H*,4 H), 7.36 (d, *J* = 7.0 Hz, Ar*H*, 2 H), 7.28 (d, *J* = 8.0 Hz ,Ar*H*, 4 H), 7.13 (d, *J* = 7.0 Hz, Ar*H*, 4 H), 7.04 - 6.98 (m, Ar*H*, 6 H), 6.90 (t, *J* = 7.0 Hz, Ar*H*, 2 H), 6.89 (t, *J* = 7.0 Hz, Ar*H*, 2 H), 6.71 (t, *J* = 7.0 Hz, Ar*H*, 2 H), 6.59 (d, *J* = 8.0 Hz, Ar*H*, 2 H), 4.37 (s, ArCH_2N, 4 H), 3.83 (s, ArCH_2Ar, 8H), 3.71 (s, OCH_2 , 4 H), 3.68 - 3.41 (m, OCH_2 , 20 H), 3.34 - 3.21 (,m, OCH_2 and NCH_2CH$_2$, 12 H), 3.04 (s, OCH_2, 4 H), 2.38 (s, ArCH_3 , 6 H). *Anal. Found* C, 67.65; H, 6.20. *Calc.* For $C_{74}H_{86}N_2S_2O_{16}$: C, 67.73; H, 6.44.
15. Analytical data of compound **7** : (Mp 68 - 69 °C) ^{1}H-NMR (200 MHz, $CDCl_3$) : δ (ppm) 7.26 (d, *J* = 4.0 Hz, Ar*H*, 2 H), 7.15 - 7.08 (m, Ar*H*, 10 H), 6.93 - 6.83 (m, Ar*H*, 6 H), 6.70 (d, *J* = 8.0 Hz, Ar*H*, 2 H), 3.84 (s, ArCH_2Ar, 8 H), 3.81 (s, ArCH_2N, 4 H), 3.71- 3.48 (m, OCH_2, 32 H), 3.36 (t, *J* = 6.0 Hz, NCH$_2$CH_2, 4 H), 2.71 (t, *J* = 5.0 Hz, NCH_2CH$_2$, 4 H). *Anal. Found* C, 60.65; H, 7.73. *Calc.* For $C_{62}H_{74}N_2O_{12}.10H_2O$. CH_3OH: C, 60.45; H, 7.90.
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17. Analytical data of compound **8** : ^{1}H-NMR (200 MHz, $CDCl_3$) : δ 7.47 (d, *J* = 7.0 Hz, Ar*H*, 4 H), 7.18 - 7.07 (m, Ar*H*, 10 H), 6.94 (t, *J* = 7.5 Hz, Ar*H*, 2 H), 6.87 - 6.77 (m, Ar*H*, 6 H), 3.94 ((br)s, ArCH_2N, 4 H), 3.74 (s, ArCH_2Ar, 8 H), 3.70- 3.50 (m, OCH_2, 44 H), 3.09 (t, *J* = 6.0 Hz, NCH_2CH$_2$, 8 H); FAB (+) MS, m/z 1153.6 (M^+)
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