

Synthesis of a New Calix[4]crown-5-azacrown-5 Dimeric Nano-tube

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Calix[4]arenes as cation receptors have received much attention because of their easy functionalization and special geometries when functional groups are incorporated into either or both the lower or the upper rim of the calixarenes.¹ It was reported that calix[4]arenes were shown to be useful as 3-D molecular building blocks for the synthesis of receptors with specific properties.¹ They can exist in four different conformations: cone, partial cone, 1,2-alternate, and 1,3-alternate.¹ In order to enhance the extractability and the selectivity for specific metal ions, so far a number of calixarene derivatives have been synthesized and characterized.

In particular, calix[4]crowns with various ring sizes have exhibited high extractability and selectivity for specific metal ions and may be useful in treatment of radioactive wastes.² Organic chemists have reported calixtubes consisting of two or more calixarene units in the 1,3-alternate conformation because of the special geometry of the calix[4]arene in the 1,3-alternate conformation allowing metal cation tunneling through the π -basic tube of the calix framework.²

It was also reported that the reaction of *p*-tert-butyl-calix[4]arene with an excess of tetraethylene glycol ditosylate and K₂CO₃ leads to the formation of a double calix[4]biscrown-5 in which the two calix[4]crown-5 moieties were crowned, thus constraining the calixarenic units into the 1,3-alternate conformation.³ Selectivity of complexation was observed for K⁺ and Rb⁺, which were found to lie in the central cavity of the tritopic receptor.³ More recently, we have reported that a dimeric structure was obtained by reacting 1,3-dipropyl calix[4]arene with *N*-tosyl tetraethylene glycol dimesylate under basic conditions.⁴ Nano-tubes consisting of two⁵⁻⁷ or three⁵ calix[4]arene units in the 1,3-alternate conformation were also constructed by linkages at the *para* position instead of at the phenolic oxygen atoms. We also reported the syntheses of crown ether-capped multimeric calix[4]tubes composed of two, three, four and five 1,3-alternate calix subunits which are linked to each other by diethylene glycol spacers and their binding properties toward metal ions.^{8,9}

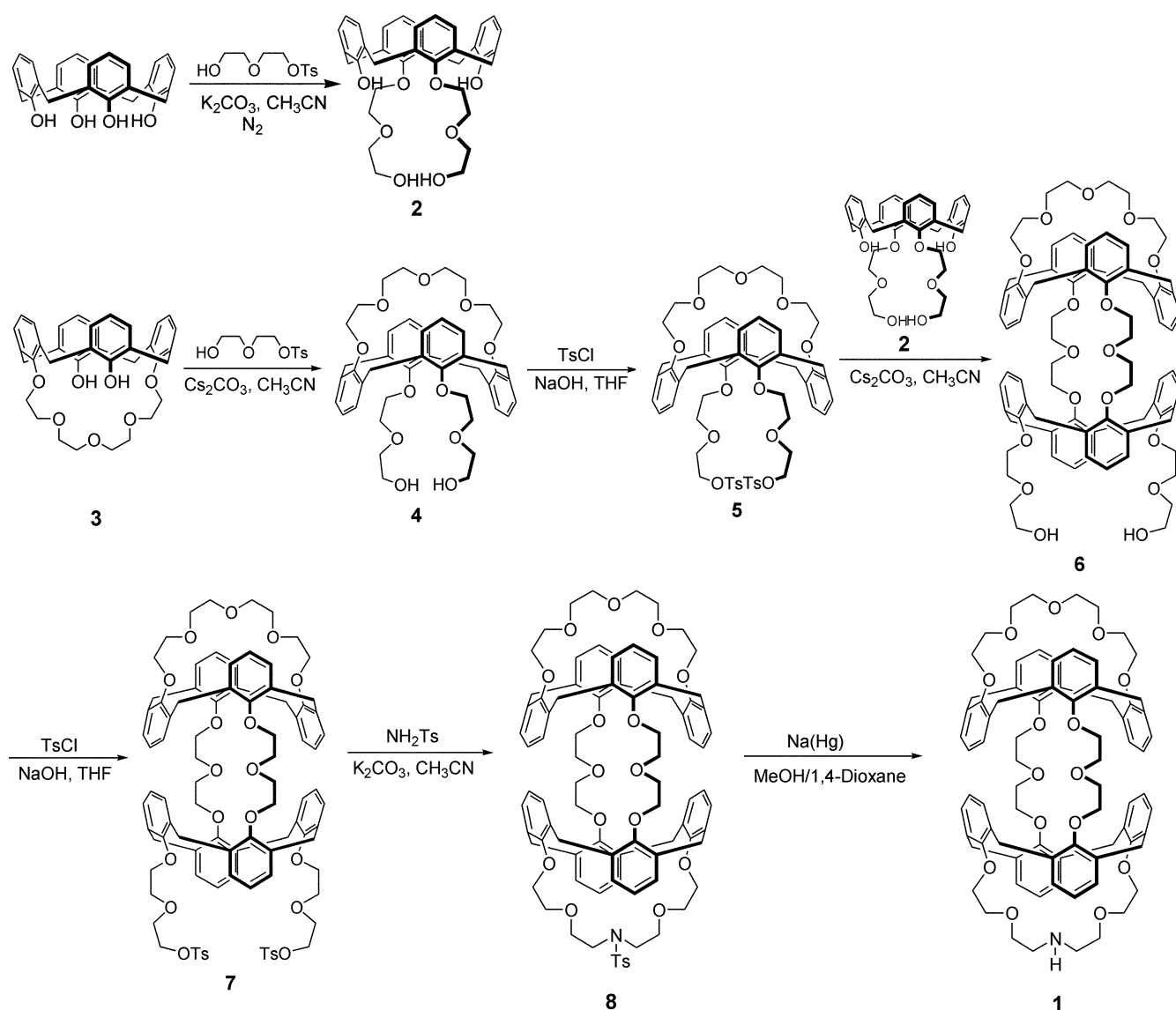
In a continuation of the synthesis of dimeric calix[4]crowns, we hereby report a multi-step synthesis of a novel 1,3-alternate calix[4]crown nano-tube capped with a crown-5 ring at one end and with an azacrown-5 ring at the other

end.

Scheme 1 shows the synthetic route for the dimeric calix[4]crown-5-azacrown-5 (**1**). Calix[4]arene was reacted with 2 equiv. of diethylene glycol monotosylate in the presence of 1 equiv. of K₂CO₃ in refluxing acetonitrile for 24 h to give diglycolic calix **2** (44% yield) in the cone conformation. Calix[4]monocrown-5 (**3**)¹⁰ was prepared from the reaction of calix[4]arene and tetraethylene glycol ditosylate in the presence of 1 equiv. of K₂CO₃. Attachment of *bis*-diethylene glycol units onto the calix[4]monocrown-5 (**3**) using 3 equiv. of diethylene glycol monotosylate gave **4** in 90% yield. Tosylation of **4** using *para*-toluenesulfonyl chloride gave **5** in 80% yield.⁶ Reaction of compound **2** with compound **4** in the presence of 3 equiv. of Cs₂CO₃ in refluxing acetonitrile provided double calix (**6**) (35%) in which both calix subunits are in the 1,3-alternate conformation which was confirmed by ¹H-NMR spectra. Referring to the ¹H-NMR spectra using tetramethylsilane (TMS) as a standard, a singlet at 3.93 ppm from the bridged methylene of the ArCH₂Ar indicates the 1,3-alternate conformation. Subsequently, tosylation of the hydroxyl groups was carried out with 3 equiv. of tosyl chloride in THF in the presence of 10 equiv. of aqueous NaOH. Column chromatography on silica-gel using a mixture of ethyl acetate/hexane (3 : 1) as eluent gave double calix ditosylate **7** (78% yield) in which the 1,3-alternate conformation retains. Cyclization of the dimeric calix ditosylate **7** was conducted with 1 equiv. of *para*-toluenesulfonamide by refluxing acetonitrile in the presence of 3 equiv. K₂CO₃ for 24 h. Purification by column chromatography on silica-gel provided *N*-tosyl calix[4]crown-5-azacrown-5 dimer (**8**) in 58% yield. Removal of the protecting tosyl group from the nitrogen atom was achieved by refluxing **8** with 6% Na(Hg) amalgam and Na₂HPO₄ in the mixture of methanol:dioxane (1 : 5) for 2 days to produce the target molecule of calix[4]crown-5-azacrown-5 dimer (**1**) in 58% yield. Two singlet peaks at 3.98 and 3.93 ppm in the ¹H-NMR spectrum and one peak at 38.8 ppm in the ¹³C-NMR spectrum proved double calix **1** to be composed of two 1,3-alternate calix subunits.

Introduction of chromogenic and fluorogenic pendants into the nitrogen atom of the azacrown ring as well as metal ion shuttling studies with alkali and alkaline earth metal ions are now in progress and their color change upon metal ion complexation will be reported soon.

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Scheme 1. Synthetic route for dimeric calix[4]crown-5-azacrown-5 (1).

Experimental Section

Reagent and instruments. Melting points were taken on a Mel-Temp of Fisher-Johns melting point apparatus without any correction. IR spectra were obtained with a Perkin-Elmer 1600 Series FT-IR spectrometer in the form of potassium bromide pellets and by deposition on KBr window in the case of solid product and oil, respectively. ^1H and ^{13}C NMR spectra were recorded with a 400 MHz (Bruker ARX-400) and an 100 MHz spectrometer, respectively. The chemical shifts (δ) reported downfield from the internal standard, tetramethylsilane. Elemental analysis was performed by a Vario EL Elemental Analyzer in Korea Basic Science Institute in Seoul, Korea. FAB⁺ mass spectra were recorded on a JEOL-JMS-HX 110A/110A high resolution tandem mass spectrometer at the Korea Basic Science Institute in Taejeon, Korea.

Unless specified otherwise, reagent grade reactants and solvents were purchased from chemical suppliers and used

as received. Dry solvents were prepared as follows: tetrahydrofuran was freshly distilled from sodium metal ribbon or chunks; dichloromethane was freshly distilled from lithium aluminum hydride. Acetonitrile was pre-dried from molecular sieves (3 Å) and distilled over diphosphorous pentoxide.

Synthesis. Compounds **2-7** were prepared following procedures reported in literature.⁸⁻¹¹

N-Tosyl calix[4]crown-5-azacrown-5 dimer (8). Under nitrogen, to a three-neck round bottom flask K_2CO_3 (0.51 g, 3.68 mmol), 100 mL of dry acetonitrile, **7** (2.00 g, 1.23 mmol), and *p*-toluenesulfonamide (0.23 g, 1.35 mmol) were added and the mixture was refluxed for 24 h. After cooling down the reaction mixture to room temperature, acetonitrile was completely removed *in vacuo*. 100 mL of 10% aqueous NaHCO_3 solution and 100 mL of CH_2Cl_2 were added. The organic layer was separated and washed with water (50 mL \times 2), dried over MgSO_4 , and then filtered. Evaporation of CH_2Cl_2 *in vacuo* gave a yellowish oil which was purified by

column chromatography using ethyl acetate : hexane (1 : 3) to provide 1.04 g (58%) of **8** as a white solid. Mp 138 °C. IR (KBr pellet, cm^{-1}): 2909, 2250, 1725, 1449, 1328, 1241, 1129, 1028, 904, 723. ^1H NMR (400 MHz, CDCl_3): δ 7.73-7.71 (d, 2H, Ar-*H*-tosyl), 7.34-7.32 (d, 2H, Ar-*H*-tosyl), 7.19-7.17 (d, 8H, Ar-*H*_m), 7.10-7.08 (d, 4H, Ar-*H*_m), 7.04-7.01 (t, 4H, Ar-*H*_m; 4H, Ar-*H*_p), 6.92-6.89 (t, 2H, Ar-*H*_p), 6.85-6.81 (t, 2H, Ar-*H*_p), 3.91-3.89 (d, 16H, Ar- CH_2 -Ar), 3.55-2.57 (m, 44H, $-\text{OCH}_2\text{CH}_2\text{O}-$; 4H, $-\text{OCH}_2\text{CH}_2\text{N}-$), 2.44 (s, 3H, Ar- CH_3 -tosyl). ^{13}C NMR (100 MHz, CDCl_3): 157.7, 156.7, 143.8, 134.6, 130.4, 129.9, 129.6, 129.4, 127.9, 127.1, 71.3, 70.5, 69.6, 68.8, 67.0, 66.7, 38.8, 38.7, 38.5, 22.3, 22.1 ppm. Anal. Calcd. for $\text{C}_{87}\text{H}_{95}\text{NO}_{17}\text{S}$: C, 71.65; H, 6.52. Found: C, 71.63; H, 6.49.

Calix[4]crown-5-azacrown-5 dimer (1). Under nitrogen, to a solution of 30 mL of 1,4-dioxane and 6 mL of methanol 1.00 g (0.69 mmol) of *N*-tosyl calix[4]crown-5-azacrown-5 dimer (**8**), 0.21 g (1.51 mmol) of Na_2HPO_4 and 6.0 g of 6% Na(Hg) were added. The reaction mixture was refluxed for 2 days at 80 °C. After cooling to room temperature, the solvent was evaporated *in vacuo*. 50 mL of CH_2Cl_2 and 50 mL of water were added, and the organic layer was separated. The CH_2Cl_2 layer was washed twice with 10% aqueous Na_2HPO_4 solution and then dried over MgSO_4 . After filtration of magnesium sulfate, the solvent was removed *in vacuo* to give a white solid. Upon recrystallization from 30 mL of diethyl ether, 0.58 g (66%) of **1** was obtained as a crystalline solid. Mp 280 °C (dec.). IR (KBr pellet, cm^{-1}): 3125, 2419, 1454, 1359, 1251, 1204, 1127, 1096, 926, 826, 772. ^1H NMR (400 MHz, CDCl_3): δ 7.24-6.92 (m, 24H, Ar-*H*), 3.98-3.93 (d, 16H, Ar- CH_2 -Ar), 3.63-2.61 (m, 44H, $-\text{OCH}_2\text{CH}_2\text{O}-$; 4H, $-\text{OCH}_2\text{CH}_2\text{N}-$), ^{13}C NMR (100 MHz, CDCl_3): 157.3, 156.5, 135.1, 134.8, 134.6, 130.4, 129.5, 129.3, 123.8, 71.4, 70.5, 69.8, 66.7, 38.8 ppm. FAB MS m/z (M^+): calcd 1304.6, found 1304.7. Anal. Calcd. for $\text{C}_{80}\text{H}_{89}\text{NO}_{15}$: C, 73.67; H, 6.83. Found: C, 73.69; H, 6.80.

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