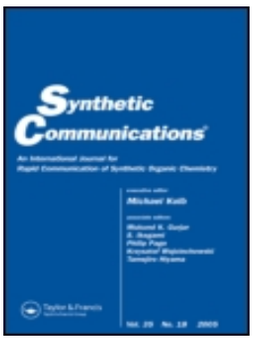

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NOVEL CALIX[4]ARENE AZACROWN ETHER

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ABSTRACT: 1,3-diproyloxycalix[4]arene azacrown ether was successfully synthesized in the fixed 1,3-alternate conformation which was confirmed by a solid state structure.

Calix[4]arenes have long been considered as an important class in supramolecular chemistry.[1] Several groups have succeeded in demonstrating that calix[4]arenes serve as an excellent receptor for the specific binding of guest atoms and molecules.[2,3] Reinhoudt et al. have reported the synthesis of 1,3-dialkoxycalix[4]arene-crown-6 derivatives and their excellent complexation with cesium ion.[4] Apart from the cavity geometry, the nature of donor sites plays the most important role in complexation selectivity.[5] In this point, azacrown ether has quite long been studied. The azacrown ether in which nitrogen atoms are

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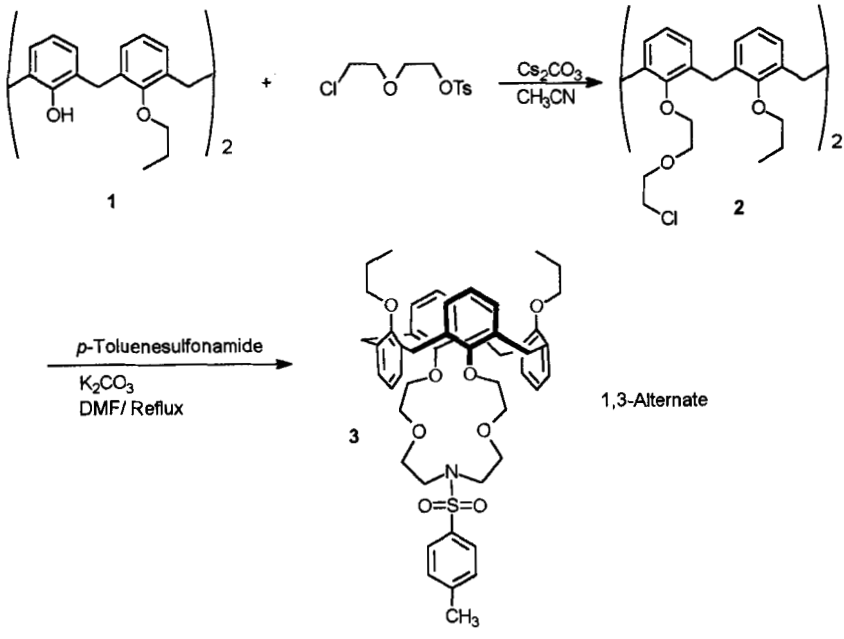
incorporated was found to be one of the most excellent ligating agents for transition metal ion such as Ag^{+}.[6] However, little attention has been paid to calix[4]arene azacrown ether in which the azacrown ether moiety is incorporated into the calix[4]arene framework. Now we report the facile synthetic method for *N*-tosyl 1,3-dipropyloxycalix[4]arene azacrown ether which can be appropriately functionalized by dealing with nitrogen atom after detosylation.

Scheme 1.



Synthetic route for the preparation of calix[4]arene azacrown ether (**3**) is described in Scheme 1. Reaction of 25,27-bis(1-propyloxy)calix[4]arene with tosylate of 2-(2-chloroethoxy)ethanol in the presence of cesium carbonate as a

base gave the tetraalkylated calix[4]arene (**2**) in fairly good yield. Splitting pattern of the proton NMR is so complicate that the conformation of **2** could not be determined. Cyclization is a key role in these reactions. Number of attempts for cyclization including varied solvent, reaction temperature, and base were conducted. The use of THF or acetonitrile as a reaction solvent with reflux for even 7 days gave less than 10 % yield. Cyclization with DMF and at condition of reflux temperature provided the best yield (72 %) with one spot of TLC (0.7 R_f value) in ethyl acetate and hexanes (1:10) as co-solvents. In addition, it is noteworthy that the two reactants (**2** and *p*-toluenesulfonamide) in DMF, respectively, should be added simultaneously (see experimental section), or the product is obtained with much lower yield.

It was presumed that the difference in chemical shifts for the two hydrogens in the methylene group between benzenes by geminal coupling, $\Delta\nu_{AB}$, might be used as a qualitative measure of the relative rates of conformational inversion of compound **3**.[7] In addition, it was reported that when calix[4]arene crown ether takes an 1,3-alternate conformation, due to magnetically equivalent on NMR time scale, singlet peak (8 hydrogens of methylene bridge) around 3.8 ppm is shown in ^{1}H NMR.[4] However, **3** exhibits an small AB splitting pattern (J=15.8 Hz, $\triangle\nu$= 9.5 Hz, chemical shift difference value) at δ 3.78. ^{13}C NMR spectra of **3** revealing one signal around 38 ppm implies 1,3-alternate conformation. Fortunately, we could obtain the ORTEP structure of compound **3** which can be one of the most promising evidences for this conformation as shown in Figure 1.

Therefore, since H_{exo} and H_{endo} of **3** are not equivalent on the NMR time scale, compound **3** might be conformationally less flexible than normal 1,3-alternate calixarene crown ether. Complexation studies upon the ion transport of transition metal ions through bulk liquid membrane and supported liquid membrane using **3** and detosylated corresponding azacrown ether are now in progress and will be reported soon.

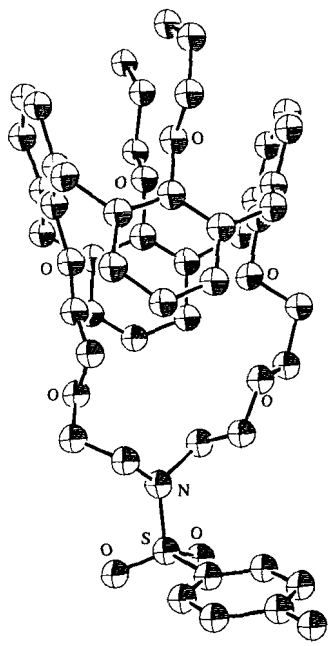


Figure 1. X-ray crystal structure of compound **3**.

Experimental

Melting points were taken by the use of a Mel-Temp of Fisher-Johns melting point apparatus without any correction. IR spectra were obtained with a

Perkin-Elmer 1600 Series FT-IR on potassium bromide pellet and on deposited KBr window in the case of soild product and oil, respectively, are recorded in reciprocal centimeters. ^{1}H NMR spectrum was recorded with a 400 MHz (Bruker ARX-400) spectrometer, the chemical shifts (δ) reported downfield from the internal standard, tetramethylsilane. Elemental analysis was performed by Vario EL of Elemental Analyzer in Korea Basic Science Institute in Seoul, Korea. FAB^+ mass spectra was obtained from JEOL-JMS-HX 110A/110A High Resolution Tendem Mass Spectrometry in Korea Basic Science Institute in Taejon, Korea. Unless specified otherwise, reagent grade reactants and solvents were obtained from chemical suppliers and used as received. Acetonitrile was pre-dried from molecular seives (3Å) and distilled over diphosphorous pentaoxide. Compounds **1** was prepared as described in the literatures.[8]

25,27-Bis(5-chloro-3-oxapentyloxy)-26,28-bis(1-propyloxy)calix[4]arene (2). Under nitrogen a mixture of 25,27-bis(1-propyloxy)calix[4]arene (0.92 g, 1.81 mmol), tosylate of 2-(2-chloroethoxy)ethanol (1.84 g, 3.62 mmol), and cesium carbonate (1.2 g, 3.62 mmol) in 50 mL of dried acetonitrile refluxed for 24 hours. After the solvent was removed *in vacuo*, 50 mL of 10 % HCl solution and 50 mL of methylene chloride were added. The organic layer was separated, washed with 10 % HCl solution (2 × 50 mL), and dried over anhydrous $MgSO_4$ to give a brown oil. Column chromatography from ethyl acetate and hexanes (1:10) on silica gel provided 0.78 g (60 %) of desire product as a white solid. Mp 149-151 ℃. IR (KBr pellet, cm^{-1}): 2926, 1451, 1251, 1189, 1127, 1050, 764. ^{1}H NMR ($CDCl_3$) δ 7.07-6.99 (m, 8 H),

6.79-6.67 (m, 4 H), 3.77-3.52 (m, 28 H), 1.65-1.53 (m, 4 H), 0.91 (t, 6 H). ^{13}C NMR ($CDCl_3$) 157.2, 156.4, 134.32, 134.33, 130.5, 130.4, 122.6, 122.3, 74.3, 72.0, 71.1, 70.8, 43.5, 36.9, 24.1, 11.1 ppm. FAB MS *m/z* (M^+) calcd 721.77, found 722.60. Anal. Calcd for $C_{42}H_{50}Cl_2O_6$: C, 69.83; H, 6.93. Found: C, 69.71; H, 6.96.

25,27-Bis(1-propyloxy)calix[4]arene azacrown ether (3). Under nitrogen, potassium carbonate (0.96 g, 6.95 mmol) with 30 mL of dry DMF was placed in three neck round bottom flask. Compound **2** (1.00 g, 1.38 mmol) in 10 mL of dry DMF was poured into dropping funnel. *p*-Toluenesulfonamide (0.23 g, 1.38 mmol) in 10 mL of DMF was prepared with another dropping funnel. To potassium carbonate solution were simultaneously added dropwise **2** and *p*-toluenesulfonamide during a period of 2 hours at 60 ℃. Upon complete addition, the reaction mixture refluxed for 24 hours. Removal of DMF by simple distillation gave a brown oil. $NaHCO_3$ (100 mL) and methylene chloride (100 mL) were added and the organic layer was separated, washed with water and dried over anhydrous $MgSO_4$ provided yellowish oil. Column chromatography from ethyl acetate and hexanes (1:10) on silica gel provided 0.90 g (72 %) of desire product as a white solid. Mp 168-171 ℃. IR (KBr pellet, cm^{-1}): 2919, 1458, 1397, 1340, 1248, 1210, 1160, 1092, 1056, 1009, 965, 762. ^1H NMR ($CDCl_3$) δ 7.76-6.60 (m, 7.07-6.99 (m, 16 H), 6.79-6.67 (m, 4 H), 3.80 (dd, J=15.8 Hz, $\triangle\nu$= 9.5 Hz, 8H), 3.53-3.24 (m, 20 H), 2.46 (s, 3 H), 1.30-1.22 (m, 4 H), 0.72 (t, 6 H). ^{13}C NMR ($CDCl_3$) 157.9, 157.4, 143.9, 137.3, 134.7, 134.2, 130.6, 130.3, 127.8, 122.8, 122.6, 72.6,

71.7, 71.3, 70.8, 49.3, 38.7, 23.2, 10.7 ppm. FAB MS *m/z* (M^+) calcd 819.2, found 820.3. Anal. Calcd for $C_{49}H_{57}NO_8S$: C, 71.79; H, 6.96. Found: C, 71.52; H, 6.94.

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