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Synthesis of Cylindrical Large Ring Crown Hosts

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Synopsis. New cylindrical crown hosts, tridecalino-27-crown-9, tridecalino-21-crown-7, didecalino-cyclohexano-21-crown-7, and didecalinio-21-crown-7 have been synthesized.

In resemblance to naturally occurring cyclic antibiotics, increasing interests are being shown in the large ring crown hosts such as 27-crown-9 and 21-crown-7.[1] As part of the study of a new type of cylindrical crown host (Fig. 1), we have previously revealed that didecalino-18-crown-6† exhibits an excellent complexing ability and conspicuous stoichioselectivity toward alkali metal ions due to the remarkable embedding effect of decalin moieties.[2,3] In this connection, we report herein the synthesis of novel cylindrical large ring crown hosts, *i.e.*, tridecalino-27-crown-9 (**8**), tridecalino-21-crown-7 (**9**), didecalino-cyclohexano-21-crown-7† (**10**), and didecalino-21-crown-7 (**11**), which would be expected to form complexes with organic guest cations.

Cylindrical crown host tridecalino-27-crown-9 (**8**) was synthesized as outlined in Scheme 1. Reaction of *cis*-4*a*,8*a*-decalindiol (**1**) with diethylene glycol ditosylate gave didecalinodiol **2** in 27% yield. Williamson synthesis of **2** with chloroacetic acid followed by esterification and hydride reduction produced "two-arm" alcohol **4** in 36% overall yield. Similarly, "two-arm" tosylate **7** was synthesized from **1** in 57% overall yield. According to similar synthetic routes, **9**, **10**, and **11** were also synthesized from **2** with appropriate "two-arm" tosylates (**9**: 6.5%, semisolid; **10**: 2.0%, oily; **11**: 4.9%, oily). Thus we could synthesize cylindrical crown hosts in spite of difficulties which were easily expected for the etherification of the tertiary alcohol. Moreover, it was proved that the synthetic method using chloroacetic acid was very useful for the synthesis of cylindrical crown hosts.

Studies on the complexing abilities of these cylindrical large ring crown hosts with various organic cations, such as guanidinium cation,[4] are in progress.[5]

Experimental

IR spectra were recorded using a Hitachi 260-10 spectrometer. ^{1}H and ^{13}C NMR spectra were obtained on a JEOL JNM-PS-100 and JEOL JNM-FX-60 spectrometer respectively, using Me_4Si as an internal standard and $CDCl_3$ as a solvent unless otherwise stated. Mass spectra were measured with a Hitachi RMU-6E spectrometer.

1,2:10,11-Didecalino-3,6,9-trioxaundecane-1,11-diol (2). A mixture of 10.0 g (59 mmol) of **1**,[2] 1.68 g (70 mmol) of NaH, and 80 ml of *N*,*N*-dimethylformamide (DMF) was stirred for 1 h at room temperature. To this mixture a solution of 12.0 g (29 mmol) of diethylene glycol ditosylate[6] in 80 ml of DMF was added dropwise and the mixture was stirred for 57 h. After addition of small amount of water, the reaction mixture was filtered through Celite. The filtrate was evaporated, and the residue was extracted with chloroform. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. 5.80 g (58%) of **1** was recovered by vacuum distillation (155 °C/1.5 Torr (1 Torr=133.322 Pa)) and the residue (>160 °C/1.5 Torr) was chromatographed over silica gel to give additional 0.47 g (5%) of **1** (ether/petroleum ether=3/7) and 3.3 g (27%) of **5** (ether/petroleum ether=5/5) as a colorless oil: IR (neat) 3550, 1080 cm^{-1}; ^{1}H NMR δ=1.00—2.16 (m, 32H), 2.42 (br s, 2H), 3.48—3.88 (m, 8H); MS *m/z* 392 (M^+-H_2O). Found: C, 70.27; H, 10.61%. Calcd for $C_{24}H_{42}O_5$: C, 70.20; H, 10.31%.

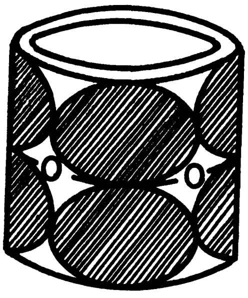

Fig. 1.

4,5:13,14-Didecalino-3,6,9,12,15-pentaoxaheptadecanedioic Acid Diethyl Ester (3). A mixture of 6.36 g (16 mmol) of **2** and 2.23 g (93 mmol) of NaH in 150 ml of tetrahydrofuran (THF) was refluxed for 1.5 h under N_2. To this suspension was added dropwise a solution of 3.66 g (39 mmol) of chloroacetic acid in 50 ml of THF. The mixture was stirred under reflux for 15 h. After addition of water (2 ml), the solvent was evaporated and 50 ml of water was added to the residue. The aqueous solution was acidified with concentrated aqueous HCl and extracted with chloroform. The organic phase was dried ($MgSO_4$) and evaporated to afford 10.1 g of oil. This crude oil was dissolved in 90 ml of 1:1 mixture of absolute ethanol and benzene, and 0.13 g of *p*-toluenesulfonic acid was added. The mixture was refluxed for 10 h, with continuous circulation of condensed vapor through anhydrous Na_2SO_4. After removal of the solvent, the residue was dissolved in dichloromethane, washed with aqueous $NaHCO_3$ and brine, and dried ($MgSO_4$). The solvent was evaporated to afford 9.27 g of oil. The crude product was chromatographed over silica gel to give 3.78 g (42%) of **3** and 1.51 g (24%) of unreacted diol **2** (ether/petroleum ether=3/7): IR (neat) 1750, 1720 cm^{-1}; ^{1}H NMR δ=1.00—2.60 (m, t at 1.28, 38H), 3.32—3.88 (m, 8H), 4.18 (q, 4H), 4.32 (d, 4H); MS *m/z* 582 (M^+). Found: C, 66.04; H, 9.64%. Calcd for $C_{32}H_{54}O_9$: C, 65.95; H, 9.34%.

4,5:13,14-Didecalino-3,6,9,12,15-pentaoxaheptadecane-1,17-diol (4). Ester **3** (3.65 g, 6.27 mmol) was reduced with 0.63 g (17 mmol) of lithium aluminum hydride (LAH) in 30 ml of boiling THF. Usual workup gave 2.63 g (84%) of **4** as a colorless oil: IR (neat) 3400, 1090 cm^{-1}; ^{1}H NMR δ=1.00—2.20 (m, 32H), 3.00—4.00 (m, 18H); MS *m/z* 498 (M^+). Found: C, 67.25; H, 10.29%. Calcd for $C_{28}H_{50}O_7$: C, 67.43; H, 10.11%.

4,5-Decalino-3,6-dioxaoctane-1,8-diol (6). Ester **5** was prepared from **1** according to the similar procedure described for **3** in 70% yield as an oil: bp 131—132 °C/0.3 Torr; IR (neat) 1750, 1730 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.00—2.20 (m, t at 1.24, 22H), 3.92—4.24 (m, 8H); MS *m/z* 342 (M^+).

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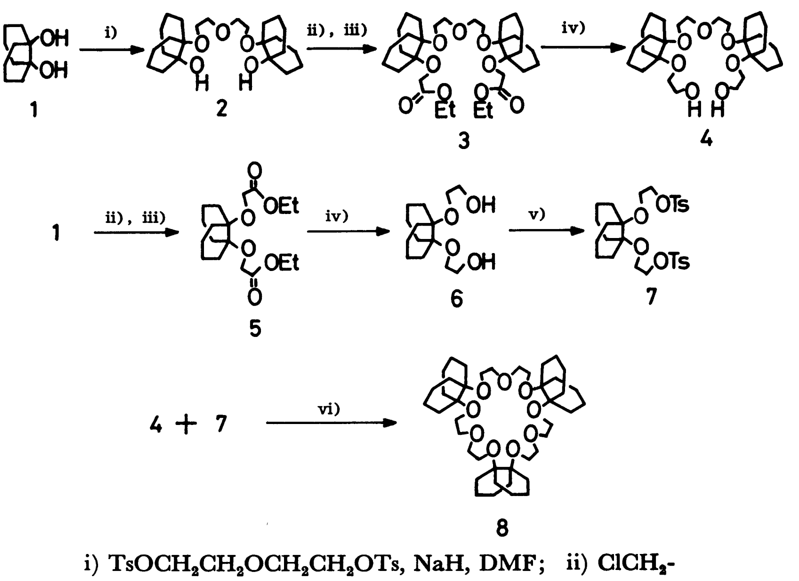
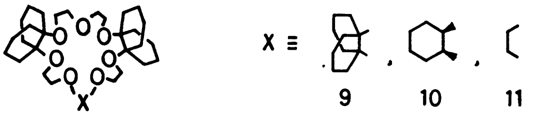
† Ortho-fused cyclic compounds are tentatively named "decalino" and "cyclohexano" for decahydronaphtho[4*a*,8*a*] and perhydrobenzo respectively.



i) $TsOCH_2CH_2OCH_2CH_2OTs$, NaH, DMF; ii) $ClCH_2$-COOH, NaH, THF; iii) EtOH, TsOH, C_6H_6; iv) $LiAlH_4$, THF; v) TsCl, C_5H_5N; vi) NaH, THF.

Scheme 1.



Found: C, 63.42; H, 8.93%. Calcd for $C_{18}H_{30}O_6$: C, 63.13; H, 8.83%. LAH reduction of **5** gave **6** in 85% yield after recrystallization from ligroin: mp 83—85 °C; IR (KBr) 3400, 3310, 1095, 1060 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.00—2.40 (m, 16H), 3.00—4.12 (m, 10H); MS m/z 258 (M^+). Found: C, 64.96; H, 10.17%. Calcd for $C_{14}H_{26}O_4$: C, 65.08; H, 10.14%.

4,5-Decalino-3,6-dioxaoctane-1,8-diol Ditosylate (7). **7** was prepared from **6** by the method similar to that of Dale and Kristiansen⁶⁾ in 96% yield after recrystallization from ethanol: mp 97—99 °C; IR (KBr) 3050, 1595, 1350, 1170 cm^{-1}; ^{1}H NMR δ=1.00—2.00 (m, 16H), 2.40 (s, 6H), 3.20—3.80 (m, 4H), 3.92—4.12 (2d, 4H), 7.42 (AB q, 8H). Found: C, 59.05; H, 6.80; S, 11.25%. Calcd for $C_{28}H_{38}O_8S_2$: C, 59.34; H, 6.76; S, 11.31%.

Tridecalino-27-crown-9 (8). To a refluxing mixture of 1.99 g (4.0 mmol) of diol **4** and 0.48 g (20 mmol) of NaH in 100 ml of THF was added dropwise over 10 h a solution of 2.26 g (4.0 mmol) of **7** in 50 ml of THF. The mixture was refluxed for 36 h, and then another 2.26 g (4.0 mmol) of **7** in 50 ml of THF was added over 10 h. The mixture was refluxed for 36 h and cooled. Water (2 ml) was added and the solvent was evaporated. The residue was extracted with dichloromethane and dried ($MgSO_4$), and the solvent was removed to give 4.69 g of oil. This oil was chromatographed over silica gel (ether/petroleum ether=5/5) to afford 1.01 g (35%) of **8**, which was recrystallized from ether: mp 90—91 °C; IR (KBr) 1080 cm^{-1}; ^{1}H NMR δ=1.00—2.00 (m, 48H), 3.20—3.92 (m, 24H); ^{13}C NMR (57 °C) δ=22.0 (t, 12C), 30.3 (t, 12C), 60.7 (t, 6C), 71.2 (t, 6C), 77.9 (s, 6C); MS m/z 614 ($M^+-C_4H_{10}O_3$ (diethylene glycol)). Found: C, 69.95; H, 10.07%. Calcd for $C_{42}H_{72}O_9$: C, 69.96; H, 10.07%.

Tridecalino-21-crown-7 (9). A solution of 0.33 g (0.58 mmol) of **7** and 0.24 g (0.58 mmol) of **2** in 20 ml of DMF was added to a suspension of 0.28 g (12 mmol) of NaH in 50 ml of DMF over 3 h under N_2 at room temperature and the mixture was stirred for 7 d. Workup as described above gave 24 mg (6.5%) of **9** as a semisolid and 155 mg of recovered diol **2** (65%): IR (neat) 1080 cm^{-1}; ^{1}H NMR δ=1.00—2.40 (m, 48H), 3.28—4.00 (m, 16H); MS m/z 632 (M^+). Found: C, 72.33; H, 10.30%. Calcd for $C_{38}H_{64}O_7$: C, 72.11; H, 10.19%.

Didecalino-cyclohexano-21-crown-7 (10). Reaction of 3.86 g (9.4 mmol) of **2**, 4.82 g (9.4 mmol) of 4,5-cyclohexano-3,6-dioxaoctane-1,8-diol ditosylate prepared from *cis*-cyclohexane-1,2-diol according to the similar method described for **7**, and 4.5 g of NaH in 300 ml of DMF for 7 d gave 3.5 g (93%) of unreacted diol **2** and 11 mg (2.0%) of **10** as an oil: IR (neat) 1080 cm^{-1}, ^{1}H NMR δ=1.00—2.20 (m, 40H), 3.20—4.00 (m, 18H); MS m/z 578 (M^+). Found: C, 70.31; H, 10.21%. Calcd for $C_{34}H_{58}O_7$: C, 70.55; H, 10.10%.

Didecalino-21-crown-7 (11). Reaction of 11.4 g (27.8 mmol) of **2**, 57.6 g (126 mmol) of triethylene glycol ditosylate,⁶⁾ and 12.6 g (525 mmol) of NaH in 550 ml of DMF for 7 d gave 7.5 g (66%) of unreacted diol **2** and 72 mg (4.9%) of **11** as an oil: IR (neat) 1080 cm^{-1}; ^{1}H NMR δ=1.12—2.10 (m, 32H), 3.24—4.00 (m, 20H); MS m/z 419 ($M^+-C_4H_9O_3$ (diethylene glycol-H)). Found: C, 68.54; H, 9.95%. Calcd for $C_{30}H_{52}O_7$: C, 68.67; H, 9.99%.

References

1) B. Son, B. P. Czech, D. A. Babb, and R. A. Bartsh, *Tetrahedron Lett.*, **25**, 1647 (1984), and references cited therein.

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3) K. Kobiro, K. Kakiuchi, Y. Tobe, and Y. Odaira, *Chem. Lett.*, **1984**, 487.

4) J. A. A. de Boer, J. W. H. M. Uiterwijk, J. Geevers, S. Harkema, and D. N. Reinhoudt, *J. Org. Chem.*, **48**, 4821 (1983).

5) Preliminary experiments have revealed that the large ring crown host **8** gave 1:1 crystalline complex with an organic salt, guanidinium perchlorate, in good yield (mp 165—167 °C, 55%), though, as compared with dicyclohexano-21-crown-7, none of the crown hosts **9**—**11** showed notable alkali metal cation selectivities upon solvent extraction of aqueous alkali metal picrates.

6) J. Dale and P. O. Kristiansen, *Acta. Chem. Scand.*, **26**, 1471 (1972).