CHIRAL COMPLEXING AGENTS AND PHASE-TRANSFER AGENTS. COMMUNICATION 2. SYNTHESIS OF DISUBSTITUTED 18-CROWN-6 ETHERS WITH C_2 SYMMETRY STARTING FROM D-SORBITOL

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In a previous communication [1], we described the synthesis of a disubstituted 15-crown-5 ether with C_2 symmetry starting from mannitol, while mannitol and also L-iditol had already been used earlier in the synthesis of crown ethers with this symmetry [2]. The most readily available hexitol — D-sorbitol — has until now not been used in the synthesis of homotopic chiral crown ethers, although it is known [2] that insertion of two identical asymmetric (C_1 symmetry) chiral fragments into the macrocycle leads to the formation of two positional isomers with C_2 symmetry, one of which will be homotopic. In this communication we examine a simple two-stage synthesis of disubstituted crown ethers with functionalized substituents starting from the readily available 3,5:4,6-di-O-ethylidene-D-sorbitol (I) [3] and 3,5:4,6-di-O-benzylidene-D-sorbitol (II) [4].

Chiral 18-crown-6 ethers with two substituents that are bicyclic diacetal fragments of glycols (I) and (II) are obtained by direct condensation of these glycols with diethylene glycol ditosylate (III) in a 'superbasic medium' (fused alkali—DMSO) under conditions of medium dilution. In the case of derivative (I), a mixture of (2R,12R)-disubstituted 18-crown-6 ether (IV) and (2R)-disubstituted 9-crown-3 ether (V) was obtained, the yields of which after chromatographic treatment were 26 and 19%, respectively. The analogous reaction of derivative (II) with ditosylate (III) under the same conditions after twofold chromatographic purification gave 18-crown-6 ether (VI) and its 'monomer' (VII) with yields of 14.5 and 11.2%. In order to increase the probability of forming the required regioisomer, addition of tosylate (III) to the reaction medium was carried out in two batches (0.5 equivalents each, interval 5-10 h, 50°C).

Under these conditions formation of the heterotopic regioisomers (VIII) and (IX) does not occur, which is demonstrated by TLC in several chromatographic systems and by comparison of the IR, ^1H and ^{13}C NMR spectra of ethers (IV) and (VI) with the spectra of those compounds obtained by unequivocal counter-synthesis as described below. The monomeric ethers (V) and (VII) are virtually indistinguishable from (IV) and (VI) according to their ^1H and ^{13}C NMR spectra and also according to their chemical ionization mass spectra (since cluster ions of composition $M + C_3H_7^+$ are formed) and we mistook them for regioisomers (VIII) and (IX). Their structure was concluded to be that of 9-crown-3 ethers on the basis of their inability to form stable complexes with 1-phenylethylammonium salts while 18-crown-6 ethers (IV) and (VI) are capable of this.

The structure of crown ethers (IV) and (VI) has been established by their countersynthesis from diols (I) and (II) by a four-stage scheme leading unequivocally to (2R,12R)-disubstituted 18-crown-6 compounds. Di-O-ethylidene-D-sorbitol (I) was converted with 69% yield to the 1-O-trityl derivative (X), which was condensed with ditosylate (III) in the presence of excess NaH in THF and the ditritylate derivative (XII) was isolated after chromatographic treatment. Detritylation of (XII) was carried out by the action of Li/NH_3 in THF according to [5], and after treatment with KU-2-8 cation exchange resin (H^+ form) diol (XIII) was obtained in 35% yield. Condensation of diol (XIII) with ditosylate (III) in superbasic medium under conditions of medium dilution gave after twofold chromatographic purification only crown ether (IV) in 51.7% yield, which was identical to the sample of (IV) obtained by the two-stage synthesis. The overall yield by this scheme was 9% with respect to diol (I) or 3.4% with respect to D-sorbitol.

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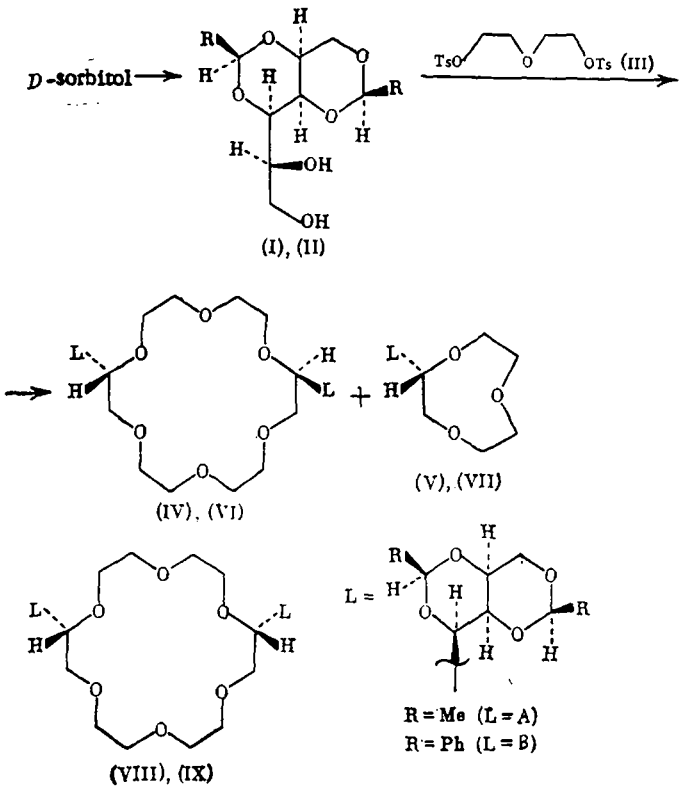
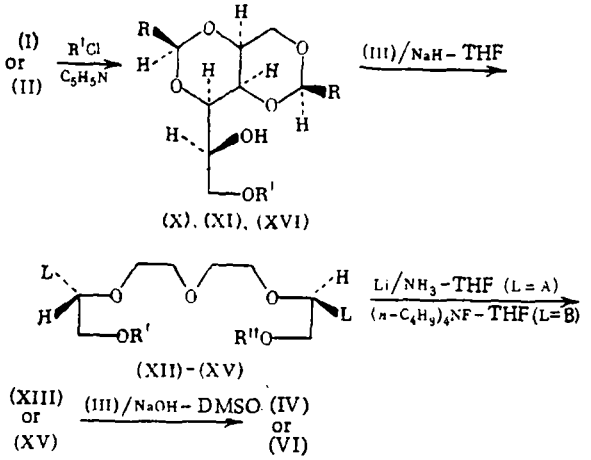


R = CH_3(I), C_6H_5(II); L = A (IV), (V), (VIII); L = B (VI), (VII), (IX).

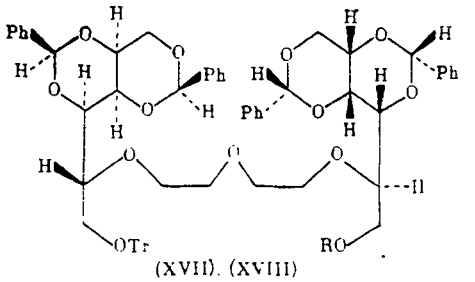
Counter-synthesis of the analogous crown ether (VI) was carried out using a similar method only with the distinction that protection of the primary OH group in derivative (II) was achieved using phenyldimethylchlorosilane and the corresponding silyl derivative (XI) was obtained. Removal of the protecting group from condensation product (XIV) using tetra(n-butyl)-ammonium fluoride [6] gave the corresponding diol (XV) in good yield, from which after condensation with tosylate (III) crown ether (VI) was obtained. The overall yield of (VI) from (II) in four stages was 7.5%.



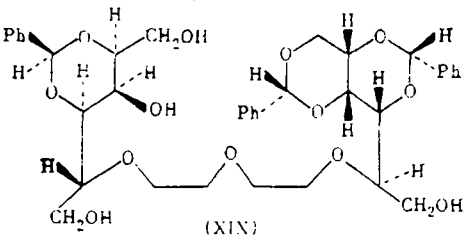
R = Me, R′ = Tr(X); R = Ph, R′ = $SiMe_2Ph$(XI); R = Ph, R′ = Tr(XVI); L = A, R′ = R″ = Tr(XII); L = A, R′ = R″ = H(XIII); L = B, R′ = R″ = $SiMe_2Ph$(XIV); L = B, R′ = R″ = H(XV).

An attempt to obtain (VI) via the 1-O-trityl derivative of di-O-benzylidene-D-sorbitol (XVI) proved unsuccessful. Condensation of (XVI) with (III) in the system NaH/THF gave the cross-linked product (XVII) in good yield, but both methods for detritylation using mild conditions [7, 8] tried by us led to partial cleavage of the benzylidene acetal bonds in molecule (XVII). When (XVII) was brought into contact with silica gel in benzene according to the method in [7], instead of the required diol (XVI) monotrityl derivative (XVIII) was ob-

tained together with a product which corresponded to the removal of two trityl and one benzylidene group with a structure probably that of (XIX) according to the data of its ^1H NMR and IR spectra. The formation of (XIX) and other products derived by partial deacetalization when (XVII) is brought into contact with SiO_2 in benzene is possibly due to chemisorption of the monodetritylation product (XVIII) on silica gel through the OH group, as a result of which the neighboring benzylidene acetal group is exposed to the acidic centers of the adsorbent.



(XVII), (XVIII)



(XIX)

R = Tr(XVII), H(XVIII).

The complex-forming properties of the compounds obtained will be discussed in a separate communication.

EXPERIMENTAL

Preparative chromatography was carried out on neutral Al_2O_3 (Brockmann activity II) or on silica gel L, Florisil, or Silpearl on glass columns. Preparative TLC was carried out on the same adsorbents on 22 × 32 cm plates with layer thickness of 1.5 mm. The purity of the compounds was monitored by TLC on Silufol plates or on plates with a mobile layer of Al_2O_3, SiO_2, Florisil, Silpearl in several solvent systems. Dehydration of THF was carried out over 'blue' benzophenone sodium ketyl. Chloroform containing no traces of HCl was obtained by twofold distillation over $CaCO_3$. DMSO was purified by twofold distillation over powdery NaOH. Removal of petrolatum oil from NaH was carried out using pentane (not less than 5 times) and the NaH was dried under vacuum in an atmosphere of Ar to constant weight. For the experiments conducted in a superbasic medium, NaOH and KOH were melted immediately before reaction and on cooling were ground to a powder. All reactions were carried out under argon.

IR spectra were recorded on a UR-10 instrument (in $CHCl_3$), ^1H and ^{13}C NMR spectra were recorded on a Bruker WM instrument (250 MHz, in $CDCl_3$), and mass spectra were recorded on a Varian MAT-44 instrument using electron impact for compound (V) (L = A) and chemical ionization (working gas isobutane) for compound (IV) (L = A), (VII) (L = B), and by PMR spectroscopy for compound (VI) (L = B).

Diethylene glycol ditosylate (III) was obtained according to [9] in 70% yield, mp 86-87°C. 3,5:4,6-Di-O-ethylidene-D-sorbitol (I) was obtained according to [3] in 37% yield, mp 210-212°C (from C_2H_5OH), $[\alpha]_D^{20}$ + 13.5° (C 4.1; H_2O) (lit. 211-213°C, $[\alpha]_D^{20}$ + 12.15° (C 1.7; H_2O). PMR spectrum (τ, ppm) 1.27 m (6H, CH_3), 3.25 m (2H, OH), 3.5-4.0 m (8H, CH_2, CH), 4.67-4.78 m (2H, O—CH—O). ^{13}C NMR spectrum (δ, ppm): 20.88, 20.94 (CH_3), 64.0, 69.7 (CH_2OH, CH—OH), 70.5 (CH_2), 69.2, 71.4, 78.8 (CH), 99.71, 99.67 (O—CH—O). 3,5: 4,6-Di-O-benzylidene-D-sorbitol (II) was obtained according to [4] in 40.5% yield, mp 200-203°C (from C_2H_5OH), $[\alpha]_D^{20}$ + 23.1° (C 3.7; DMSO) (lit. 219-221°C, $[\alpha]_D^{20}$ +21.6° (C 1.04; pyridine) [10]). ^1H NMR spectrum (δ, ppm, DMSO as external standard): 3.77-4.53 m (10H, CH_2, CH, OH), 6.02 s (2H, O—CH—O), 7.08 m (C_6H_5). Found: C 67.04; H 6.19%.

(2R,12R)-Di((1'S,2'R,4'S,6'S,9'R)-2'-(4',9'-dimethyl-3',5',8',10'-tetraoxabicyclo[4.4.0]-decyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (IV) (L = A) and (2R)-((1'S,2'R,4'S,6'S,9'R)-2'-

(4',9'-dimethyl-3',5',8',10'-tetraoxabicyclo[4.4.0]decyl)-1,4,7-trioxacyclononane (V) (L = A). To a solution of 2.34 g (10 mmoles) of diol (I) in 60 ml of DMSO was added 3.36 g (60 mmoles) of freshly fused KOH which was ground to a powder, and the mixture was agitated for 2 h at 50°C, then over 10 h 2.48 g (6 mmoles) of (III) in 20 ml of DMSO was added, the mixture was agitated for 6 h at 65°C, and a further 2.48 g (6 mmoles) of (III) in 20 ml of DMSO was added slowly and the mixture agitated for 6 h at 80°C. Most of the DMSO was distilled off under vacuum and the residue was treated with 50 ml of a $CHCl_3$:H_2O (1:1) mixture. The chloroform layer was separated and the aqueous layer extracted with chloroform (7 × 25 ml). The combined chloroform solution was evaporated down and the residual DMSO distilled off under vacuum; the residue (3.66 g) was fractionated by means of preparative TLC on four Silpearl silica gel plates in the system $CHCl_3$: CH_3OH (15:1) and three zones were separated. Elution of the upper zone (R_f 0.85) with $CHCl_3$ gave 1.5 g of (III). Elution of the second zone (R_f 0.59) gave 0.58 g of crystalline (V) (L = A), with mp 190°C, $[\alpha]_D^{20}$ +3.5° (C 2.5; $CHCl_3$), yield 19%. PMR spectrum (δ, ppm): 1.38 m (6H, CH_3), 3.5-4.0 m (16H, CH_2–O and CH–O), 4.7-4.8 m (2H, O–CH–O). ^{13}C NMR spectrum (δ, ppm): 20.8, 21.1 (CH_3), 68.2 (CH), 69.6 (CH_2), 70.1 (CH), 72.7, 72.8, 73.5, 73.8 (CH_2), 76.8, 78.3 (CH), 98.7 (O–CH–O). IR spectrum (ν, cm^{-1}): 3025, 1450, 1420, 1310, 1150, 1120, 942. Mass spectrum, m/z: 343 [$M^+ + C_3H_3$], 647 [$2M^+ + C_3H_3$], 651 [$2M^+ + C_3H_7$]. Calculated: $C_{12}H_{18}O_7$, M^+ 304.

Elution of the third zone (R_f 0.34) gave 0.74 g of pure (IV) (L = A) in the form of a colorless oil, $[\alpha]_D^{20}$ −9.4° (C 3.7; $CHCl_3$), yield 26%. PMR spectrum (δ, ppm) 1.38 m (12H, CH_3), 3.5-4.2 m (32H, CH_2O and CH–O), 4.7-4.8 (4H, O–CH–O). ^{13}C NMR spectrum (δ, ppm): 20.9, 21.1 (CH_3), 68.4 (CH), 69.6 (CH_2), 70.1 (CH), 70.6, 70.9, 71.3 (CH_2), 75.9, 76.5 (CH), 98.6 (O–CH–O). IR spectrum (ν, cm^{-1}) 3020, 1450, 1410, 1335, 1150, 1120, 945. Mass spectrum, m/z: 651 [$M^+ + C_3H_7$], 647 [$M^+ + C_3H_3$]. Calculated $C_{24}H_{36}O_{14}$, M^+ 608.

1-O-Trityl-3,5:4,6-di-O-ethylidene-D-sorbitol (X). This was obtained according to the method in [10], mp 92°C (MeOH), $[\alpha]_D^{20}$ −5.4° (C 4.42; $CHCl_3$), yield 69.2%.

(2R,10R)-Di((1'S,2'R,4'S,6'S,9'R)-2'-(4',9'-dimethyl-3',5',8',10'-tetraoxabicyclo[4.4.0]-decyl)-1,11-dihydroxy-3,6,9-trioxaundecane (XIII), (L = A). To a suspension of 0.58 g (24.2 mmoles) of NaH and 7.11 g (15 mmole) of (X) in 100 ml of THF was added a solution of 3.29 g (8 mmoles) of (III) in 50 ml of THF and the mixture was boiled with agitation for 48 h; 2 ml of MeOH was added and the mixture filtered and evaporated under vacuum. Crude (XII) (L = A) was obtained (12 g) in the form of a heavy brown oil. TLC on Silpearl silica gel plates in the system C_5H_{12}: ethyl acetate led to the isolation of a pure sample of (XII) (L = A) (R_f 0.66). PMR spectrum (δ, ppm) 1.38 m (12H, CH_3), 3.56-4.2 m (24H, CH_2, CH), 4.65 m (4H, O–CH–O), 7.1-7.5 m (30H, C_6H_5). IR spectrum (ν, cm^{-1}) 3020, 2875, 1600, 1500, 1450, 1400, 1270, 1250, 1100, 940.

To a solution of 1.86 g (1.8 mmoles) of crude (XII) (L = A) in 160 ml of THF was added 100 ml of liquid NH_3 (cooled with a mixture of acetone and solid CO_2) and 0.63 g (90.7 mmoles) of Li in several doses. The mixture was agitated for 3 h, 3 ml of MeOH were added, the NH_3 was removed by keeping the mixture at 20°C, and the residue was neutralized with solid CO_2. The mixture was treated with water (30 ml), the THF was evaporated under vacuum, to the residue was added MeOH (30 ml), and the aqueous methanol solution was shaken with 10 g of KU-2-8 ion-exchange resin (H^+ form). The resin was filtered off and then washed with a mixture of $CHCl_3$:MeOH (1:1) (3 × 50 ml) and water (2 × 20 ml). The combined solutions were evaporated, the residue was dissolved in THF, the insoluble sediment was filtered off, and the filtrate was evaporated. After chromatographic purification of crude product on a Silpearl silica gel plate in the system $CHCl_3$:MeOH (100:3), 0.22 g of pure (XIII) (L = A) was isolated in the form of a colorless oil, yield 35%. PMR spectrum (δ, ppm): 1.30 m (12H, CH_3), 3.32-3.95 m (24H, CH_2, CH, OH), 4.74 m (4H, O–CH–O). IR spectrum (ν, cm^{-1}): 3600, 3020, 1450, 1440, 1275, 1225, 1100, 942.

(2R,12R)-18-Crown-6 (IV) (L = A). To a solution of 0.24 g (0.45 mmole) of diol (XIII) (L = A) in 30 ml of DMSO was added 0.1 g (2.6 mmoles) of freshly fused NaOH that had been ground to a powder; the mixture was agitated for 30 min at 50°C, then over 1 h solution of 0.23 g (0.55 mmole) of (III) in 20 ml of DMSO was added, and the mixture was agitated for 48 h at 75°C. After standard treatment 0.1 g of (2R,12R)-disubstituted 18-crown-6 ether (IV) (L = A) was isolated, having all constants and spectra identical to those reported above.

(2R,12R)-Di((1'S,2'R,4'S,6'S,9'R)-2'-(4',9'-diphenyl-3',5',8',10'-tetraoxabicyclo[4.4.0]-decyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (VI) (L = B) and (2R)-(1'S,2'R,4'S,6'S,9'R)-2'-(4',9'-Diphenyl-3',5',8',10'-tetraoxabicyclo[4.4.0]decyl)-1,4,7-trioxacyclononane (VII) (L = B). These were obtained under conditions similar to those for the synthesis of compounds (IV)

and (V) (L = A). From 3.58 g (10 mmoles) of (II), 4.97 g (12 mmoles) of (III), and 3.36 g (60 mmoles) of KOH in 100 ml of DMSO was obtained 8.45 g of a mixture, which when separated by means of TLC on Silpearl silica gel in the system $CHCl_3$:MeOH (15:1) and with elution of the R_f 0.55 zone with $CHCl_3$ gave crystalline (VII) (L = B), with mp 185°C, $[\alpha]_D^{20}$ +13.01° (C 11.7 $CHCl_3$). Yield 0.48 g (11.2%). ^1H NMR spectrum (δ, ppm): 3.45-4.40 m (16H, CH, CH_2), 5.5-5.7 m (2H, O—CH—O), 7.25-7.60 m (10H, C_6H_5). ^{13}C NMR spectrum (δ, ppm): 68.72, 70.12, 70.61 (CH), 72.61, 72.79, 73.03, 73.5, 73.82 (CH_2), 77.28, 78.62 (CH), 100.66, 100.78 (C—CH—O), 126.34, 126.52, 128.22, 129.01, 137.94, 138.24 (C_6H_5). IR spectrum (ν, cm^{-1}): 3025, 1650, 1530, 1460, 1400, 1150, 1110, 925. Mass spectrum, m/z: 471 [$M^+ + C_3H_7$], 467 [$M^+ + C_3H_3$]. Calculated: M^+ 428.

Elution of the zone with R_f 0.34 gave crystalline (VI) (L = B), with mp 218°C, $[\alpha]_D^{20}$ +8.49° (C 11.3; $CHCl_3$). Yield 0.62 g (14.5%). PMR spectrum (δ, ppm): 3.50-4.50 m (32H, CH, CH_2), 5.45-5.70 m (4H, O—CH—O), 7.40-7.60 m (20H, C_6H_5). ^{13}C NMR spectrum (δ, ppm): 68.91, 69.15, 69.88, 70.18 (CH), 70.61, 71.33, 75.52, 76.62 (CH_2), 100.35, 100.64 (O—CH—O), 126.40, 128.22, 128.83, 138.30, 138.54 (C_6H_5). IR spectrum (ν, cm^{-1}): 3020, 1675, 1525, 1460, 1400, 1335, 1175, 1115, 925. Mass spectrum, m/z: 879 [$M^+ + Na^+$]. Calculated: M^+ 856.

(2R,10R)-Di((1'S,2'R,4'S,6'S,9'R)-2'-(4',9'-diphenyl-3',5',8',10'-tetraoxabicyclo[4.4.0]-decyl)-1,11-di(dimethylphenylsilyloxy)-3,6,9-trioxaundecane (XIV) and (2R,10R)-Di((1'S,2'R,4'-S,6'S,9'R)-2'-(4',9'-diphenyl-3',5',8',10'-tetraoxabicyclo[4.4.0]decyl)-1-dimethylphenylsilyl-oxy-11-hydroxy,3,6,9-trioxaundecane (XIV) (R' = H, R'' = $Si(CH_3)_2C_6H_5$). In accordance with the method in [6], 3.58 g (10 mmoles) of (II), 1.88 g (11 mmoles) of $C_6H_5(CH_3)_2SiCl$, and 0.87 g (11 mmoles) of pyridine gave 4.25 g of crude 1-dimethylphenylsilyloxy-3,5:4,6-O-dibenzylidene-D-sorbitol (XI) in the form of a heavy oil, R_f 0.75 Silufol, $CHCl_3$:MeOH (30:1). PMR spectrum (δ, ppm): 3.36-4.10 m (9H, CH_2, CHOH), 5.20-5.56 m (2H, O—CH—O), 7.0-7.10 m (15H, C_6H_5) (calculated from the $SiCH_3$ signal). IR spectrum (ν, cm^{-1}): 3660, 3555, 3054, 2875, 1590, 1450, 1400, 1260, 1100, 825.

To a suspension of 0.19 g (8 mmoles) of NaH in 50 ml of THF was added a solution of 2.98 g of crude (XI) in 20 ml of THF at 20°C, then over 2 h was added a solution of 1.66 g (4 mmoles) of (III) in 25 ml of THF, and the mixture was agitated for 48 h at 65°C. The mixture was supplemented with 2 ml of MeOH and the solution was filtered and evaporated. The residue was chromatographed on Silpearl silica gel plates in the system $CHCl_3$:MeOH (30:1). Elution with ether and $CHCl_3$ gave (XIV) in the form of a colorless oil (R_f 0.43). PMR spectrum (δ, ppm): 3.62-4.63 m (24H, CH_2, CH), 5.60 m (4H, O—CH—O), 7.22-7.48 (30H, C_6H_5). IR spectrum (ν, cm^{-1}): 3054, 3020, 2875, 1590, 1450, 1400, 1275, 1225, 1100, 825. Yield 0.49 g (9.3%). Elution of the next zone gave monosilyl derivative (XIV) (R' = H, R'' = $Si(CH_3)_2C_6H_5$) in the form of a colorless oil (R_f 0.29). PMR spectrum (δ, ppm): 3.63-4.55 m (25H, CH_2CH, OH), 5.58 (4H, O—CH—O), 7.26-7.40 (30H, C_6H_5). IR spectrum (ν, cm^{-1}): 3675, 3050, 3020, 2075, 1600, 1450, 1400, 1275, 1225, 1100, 830. Yield 0.48 g (12.2%). Elution of the third zone (R_f 0.11) gave 1.07 g of a product not containing silyl groups.

(2R,10R)-Di((1'S,2'R,4'S,6'S,9'R)-2'-(3',9'-diphenyl-3',5',8',10'-tetraoxabicyclo[4.4.0]-decyl)-1,11-dihydroxy-3,6,8-trioxaundecane (XV). This was obtained according to the method in [6]. To a solution of 0.4 g (0.36 mmole) of disilyl ether (XIV) in 10 ml of THF at 0°C was added 0.6 g (2.3 mmoles) of n-Bu_4NF in 5 ml of THF and the mixture was agitated for 45 min; the solution was evaporated under vacuum and the residue (an oil) was chromatographed on a Silpearl silica gel plate in the system $CHCl_3$:MeOH (100:3). Pure (XV) was obtained in the form of an oil (R_f 0.27). PMR spectrum (δ, ppm): 3.32-4.60 m (24H, CH_2, CH, OH), 5.47-5.62 m (4H, O—CH—O), 7.28-7.55 m (20H, C_6H_5). IR spectrum (ν, cm^{-1}), 3600, 3050, 3020, 2870, 1450, 1400, 1275, 1225, 1100, 840. Yield 0.19 g (65%).

18-Crown-6 (VI) (L = B). To a suspension of 0.12 g (3 mmoles) of NaOH in 25 ml of DMSO at 50°C was added over 10 h a solution of 0.2 g (0.25 mmole) of diol (XV) and 0.14 g (0.35 mmole) of (III) in 25 ml of DMSO and the mixture was agitated for 72 h at 75°C. The DMSO was distilled off under vacuum, and the residue was dissolved in water and extracted with $CHCl_3$ (5 × 20 ml). The extract was dried with $MgSO_4$. The solution was evaporated under vacuum, the residue (0.38 g) was chromatographed on Silpearl silica gel in the system $CHCl_3$:MeOH (15:1), and a product was isolated with R_f 0.34, mp 218°C, $[\alpha]_D^{20}$; +8.49°; all of its spectral characteristics were identical to those of crown ether (VI) (L = B) described earlier. Yield 0.085 g (39%).

1-O-Trityl-3,5:4,6-di-O-benzylidene-D-sorbitol (XVI). This was obtained according to the method in [10], with a yield of 69.2%, mp 178°C, $[\alpha]_D^{20}$ +21° (C 4.7 $CHCl_3$). PMR spectrum (δ,

ppm): 3.56-4.60 m (9H, CH_2, CH, OH), 5.64-6.0 m (2H, O—CH—O), 7.28-7.50 (10H, C_6H_5). IR spectrum (ν, cm^{-1}): 3520, 3380, 3060, 2875, 1600, 1450, 1400, 1110.

(2R,10R)-Di((1'S,2'R,4'S,6'S,9'R)-2'-(4',9'-diphenyl-3',5',8',10'-tetraoxabicyclo[4.4.0]-decyl)-1,11-dityryl-3,6,8-trioxaundecane (XVII). To a suspension of 0.5 g (20.8 mmoles) of NaH in 50 ml of THF was added 4.18 g (6.97 mmoles) of (XVI) and the mixture was agitated for 1 h at 50°C. A solution of 1.43 g (3.48 mmoles) of (III) in 20 ml of THF was added over 3 h and the mixture was agitated for 20 h at 65°C. The solution was filtered and evaporated under vacuum, the residue (6.16 g) was treated with ether, and the ether solution was filtered and evaporated. White crystals of (XVII) were obtained, with mp 185°C (from EtOH). PMR spectrum (δ, ppm): 3.25-4.20 m (24H, CH_2CH), 5.37-5.58 m (4H, O—CH—O), 7.03-7.36 m (50H, C_5H_6). IR spectrum (ν, cm^{-1}): 3020, 2870, 1750, 1600, 1500, 1450, 1400, 1270, 1250, 1100, 940.

Attempt to Hydrolyze Dityryl Ether (XVII). a) Method of [7]. A solution of 2 g (0.79 mmole) of (XVII) in 8 ml of absolute C_6H_6 was applied to a column with 100 g of SiO_2, 170 ml of absolute C_6H_6 was added, and the column was covered and left overnight. Elution with benzene gave 0.7 g (70%) of initial (XVII), 0.096 g (7%) of monodetritylation product (XVIII), and 0.17 g (18.7%) of product (XIX). PMR spectrum of product (XVIII) (δ, ppm): 3.56-4.39 m (25H, CH and CH_2OH), 5.48-5.63 m (4H, CH), 7.16-7.38 m (35H, C_6H_5). IR spectrum (ν, cm^{-1}): 3020, 3000, 1450, 1375, 1225, 1100, 1025. PMR spectrum of product (XIX) (δ, ppm): 3.58-4.52 m (24H, CH and CH_2 + 4H from OH), 6.0 br.s (3H, CH), 7.56-7.74 (15H, C_6H_5). IR spectrum (ν, cm^{-1}) 3590, 3015, 1400, 1375, 1220, 1115, 1030. b) A mixture of 0.46 g of (XVII) and 13.8 g of SiO_2 in 35 ml of C_6H_6 was boiled for 12 h, filtered, the precipitate was washed with $CHCl_3$, the filtrate was evaporated, and the residue was chromatographed on an Al_2O_3 plate in the system $CHCl_3$:MeOH (60:1). After elution with $CHCl_3$ 0.078 g (21%) of (XVIII) and 0.25 g (54%) of initial (XVII) were isolated. c) Method of [8]. A mixture of 1.2 g of (XVII) and 1.5 g of anhydrous $CuSO_4$ in 20 ml of C_6H_6 was boiled for 72 h. Monitoring by means of TLC on Silufol showed that hydrolysis had not occurred.

CONCLUSIONS

(2R,12R)-Disubstituted 18-crown-6 ethers with C_2 symmetry containing bulky bicyclic chiral substituents have been obtained from D-sorbitol.

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