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Synthesis of new chiral 18-crown-6 ethers from D-xylose †

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Abstract

Short and efficient syntheses of chiral 18-crown-6 ethers **1**–**4** containing two ethylenoxyethyl-bridged D-xylo and D-ribofuranoside moieties starting from D-xylose are reported. Crown ethers **1**, **2** and **4** are C_2-symmetric while **3** is unsymmetrical.

1. Introduction

Amongst macrocyclic polyether ring systems, 18-crown-6 is the most extensively characterized crown ether and there is growing interest in designing and synthesizing such systems that display selectivity. Ever since chiral crown ethers were first introduced by Stoddart[1] and Cram[2–4] by incorporating chiral units into the crown ether moiety and utilized them for the discrimination of enantiomers, chiral crown ethers have gained much importance. In particular, these chiral receptors were found to behave as chiral reagents or chiral catalysts for enantioselective reactions.[5–7] Carbohydrates containing chiral crown ethers have proved to be suitable models for the study of chiral recognition reactions. Nair and co-workers[8] synthesized monosaccharide based crown ethers via 1 and 6 positions with one or more sugar moieties in the macrocyclic ring, while Miethchen and Fehring[9] made pyranosidic crown ethers locking the 1 and 2 positions. Although several crown ethers derived from carbohydrates (with C_2 symmetry) have been synthesized,[10] this class still attracts the attention of synthetic organic chemists because of the inherent maneuverability in synthesizing them with varying connectivities, symmetries and cavity sizes from different precursors. In continuation of our interest in asymmetric synthesis,[11] herein we report an efficient synthesis of furanoside based crown ethers **1**, **2**, **3** and **4** from D-xylose.

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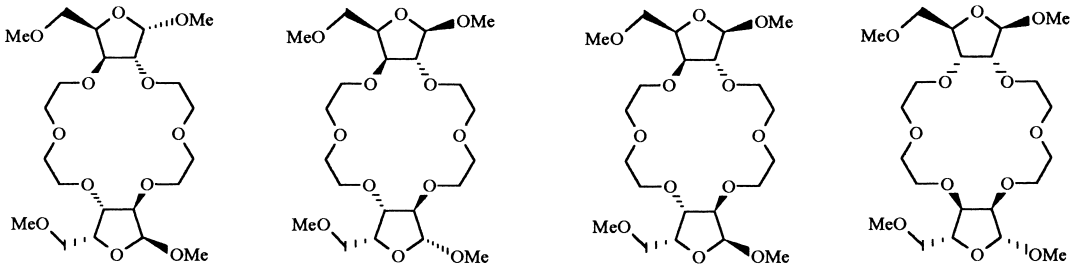
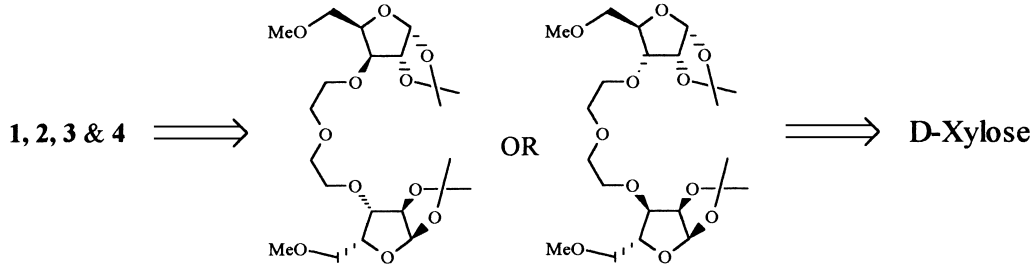


1 **2** **3** **4**

The basic strategy as depicted in Scheme 1 is to utilize the C-2 and C-3 hydroxy centers for the construction of macrocyclic ring systems of **1**, **2**, **3** and **4**. Thus, the furanosidic ethers **5** and **6**, through the C-3 hydroxy group, are the appropriate intermediates, with a C-2 hydroxy group locked in the form of acetonide. Compounds **5** and **6** in turn could be prepared from D-xylose having a free C-3 hydroxy group.



5 **6**

Scheme 1.

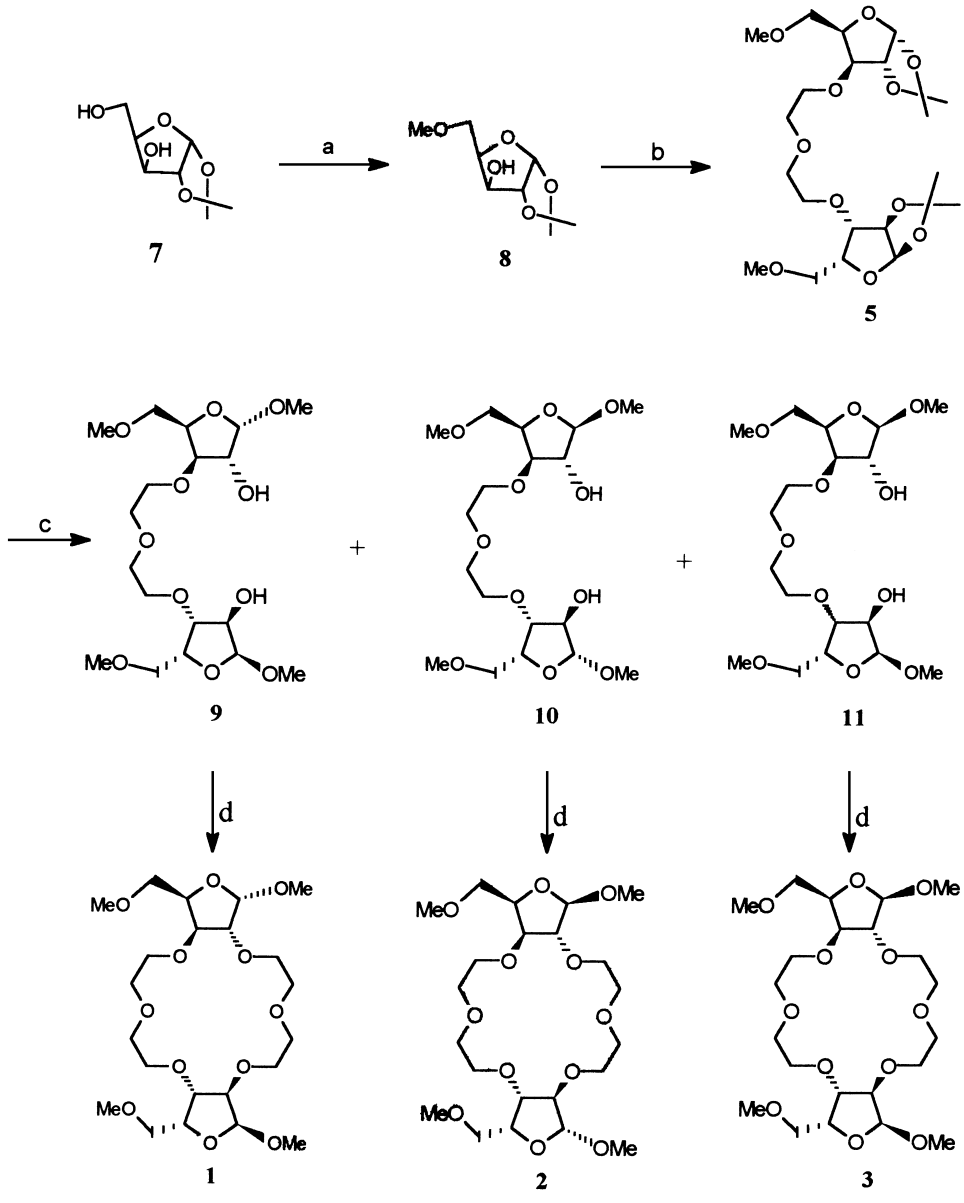
2. Results and discussion

Accordingly, D-xylose derivative **7** (Scheme 2) was subjected to regioselective alkylation[12] with Ag_2O–MeI in CH_2Cl_2 to afford the 5-*O*-methyl ether **8** in 65% yield ($[\alpha]_D$ −6.6 (*c* 1.3, $CHCl_3$)) which is a crucial building block for the synthesis of **1** to **4**.

*2.1. Synthesis of crown ethers **1**, **2** and **3***

Compound **8** (2 mol equivalents) was allowed to react with diethyleneglycol ditosylate[13] in the presence of KOH in dioxane to afford **5** (58%). The structure of **5** was confirmed by ^1H and ^{13}C NMR analysis. The spectra were highly simplified, since the protons have the same chemical shifts (half signals) due to the presence of C_2 symmetry in the molecule. H-1 and H-2 appeared as doublets at δ 5.85 and 4.55, respectively, with $J_{1,2}$=4.5 Hz.

To liberate the C-2 hydroxy group in **5** for further elaboration, it was subjected to methanolysis with H^+ resin in methanol to afford a diastereomeric mixture of glycosides **9**, **10** and **11** in 1:0.9:1.3 ratio. This mixture (αα, ββ, αβ) was resolved chromatographically into individual anomers and characterized thoroughly from the ^1H and ^{13}C NMR spectra. The ^1H and ^{13}C NMR spectra of **9** (αα) and **10** (ββ) were found to be simplified due to C_2 symmetry present in their structures. For **9**, H-1 resonated at δ 4.9 ($J_{1,2}$=4.7 Hz) as a doublet, while for **10**, H-1 appeared as a singlet at δ 4.75 and ^{13}C NMR depicted



Scheme 2. *Reagents*: (a) Ag_2O, MeI, CH_2Cl_2, rt; (b) $TsOCH_2CH_2OCH_2CH_2OTs$, KOH, dioxane, reflux; (c) MeOH, H^+, reflux, 12 h; (d) $TsOCH_2CH_2OCH_2CH_2OTs$, NaH, DMSO, 60°C

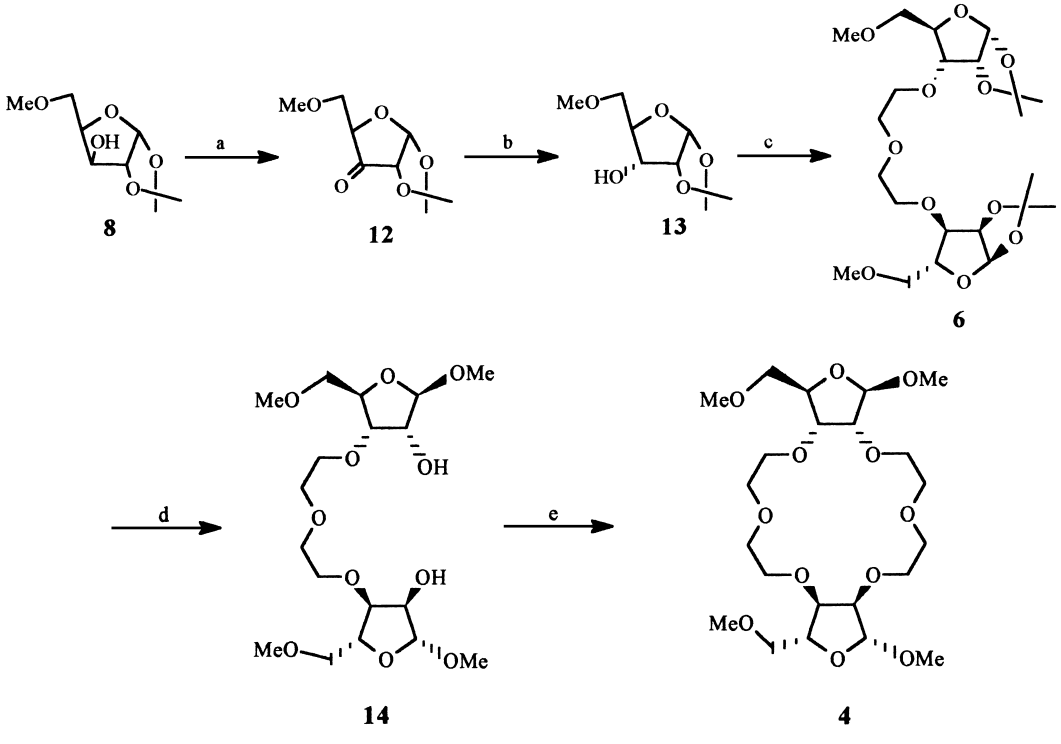
characteristic signals for the α (C-1/δ 109.0) and β (C-1/δ 102.8) glycosides. Compound **11** (αβ), since it does not contain the symmetry, ^1H and ^{13}C NMR showed two signals: H-1α at δ 4.92 (J=4.6 Hz) as a doublet/C-1 at δ 109.2, and H-1β at δ 4.8 (J=2.0 Hz) as a doublet/C-1 at δ 102.2. Thus, the structures of all the three anomeric ethers **9** to **11** were unambiguously assigned from the spectral data.

Finally, the macrocyclic ring formation on anomers **9** to **11** was carried out independently[14] with diethyleneglycol ditosylate in the presence of NaH in DMSO leading to three new 18-crown-6 ethers: **1** (37%), **2** (42%) and **3** (38%). The structures of all the three new crown ethers were unambiguously assigned based on the spectral analysis. Thus, due to the C_2 symmetry element, ^1H and ^{13}C NMR of **1** and **2** were simplified and showed half signals. In the ^1H NMR of **1**, H-1 appeared at δ 4.89 as a

doublet, while for **2**, H-1 appeared at δ 4.8 as a singlet/C-1 at δ 101.5. In contrast, the unsymmetrical crown ether **3** exhibited H-1 of the two furanosides at δ 4.9 (doublet) and 4.8 (singlet) for α and β anomeric centers, respectively. Mass and HRMS analysis also indicated the expected molecular weight and molecular formulae for all the new crown ethers.

*2.2. Synthesis of crown ether **4***

The new crown ether **4** (Scheme 3) was also prepared from monomethyl ether **8**. Accordingly, **8** on oxidation with PDC–Ac_2O in CH_2Cl_2 gave ketone **12**, which, on reduction with $NaBH_4$, afforded the ribo derivative **13**. H-3 for **13** in the ^1H NMR was indicated at δ 4.45 as a triplet characteristic of D-ribo configuration. Treatment of **13** with diethyleneglycol ditosylate gave the C_2-symmetric ether **6** (68%). A simplified (half signals) ^1H NMR spectrum was indicated for **6**, where H-1 resonated at δ 5.7 as a doublet ($J_{1,2}$=4.2 Hz). Methanolysis (MeOH, H^+) of **6** gave the β-glycoside (72%) as a major product which was clearly indicated from the H-1 chemical shift at δ 4.82 as a singlet. Cyclization of **14** with diethyleneglycol ditosylate in the presence of NaH in DMSO gave **4** in 57% yield. The structure of **4** was proved beyond doubt, from the simplified ^1H and ^{13}C NMR spectra, where H-1 resonated at δ 4.8 as a singlet and C-1 at δ 106.2. Mass and HRMS analysis further confirmed the proposed structure for **4**.



Scheme 3. *Reagents*: (a) PDC, Ac_2O, CH_2Cl_2, reflux; (b) $NaBH_4$, MeOH, rt; (c) $TsOCH_2CH_2OCH_2CH_2OTs$, KOH, dioxane, reflux; (d) MeOH, H^+, reflux, 12 h; (e) $TsOCH_2CH_2OCH_2CH_2OTs$, NaH, DMSO, 60°C

Since chiral crown ethers are finding extensive use in asymmetric transformations, such as asymmetric Michael reaction, the short and efficient synthetic protocol reported here for the preparation of chiral 18-crown-6 ethers **1** to **4** would find immense use in organic synthesis.

3. Experimental

Solvents were dried over standard drying agents and freshly distilled prior to use. ^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were measured with a Varian Gemini spectrometer, with tetramethylsilane as internal standard for solutions in deuteriochloroform. *J* values are given in hertz. Optical rotations were measured with a JASCO DIP-370 instrument, and $[\alpha]_D$ values are in units of 10^{-1} deg cm^2 g^{-1}. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 40°C in vacuo.

*3.1. 1,2-*O*-Isopropylidene-5-*O*-methyl-α-*D*-xylofuranose **8***

To a stirred suspension of 1,2-*O*-isopropylidene-α-D-xylofuranose **7** (16 g, 84.2 mmol) and Ag_2O (23.4 g, 101.0 mmol) in CH_2Cl_2 (120 mL) was added MeI (6.57 mL, 92.6 mmol) then stirred at room temperature for 6 h. The reaction mixture was filtered through Celite, washed with CH_2Cl_2 (2×100 mL), evaporated and the residue purified by column chromatography (Si-gel, 9% EtOAc in hexane) to afford **8** (11.1 g) in 65% yield as a syrup. $[\alpha]_D$ −6.6 (*c* 1.3, $CHCl_3$); ^{1}H NMR: δ 1.4, 1.55 (2s, 6H, CH_3), 2.3 (br d, 1H, -OH), 3.42 (s, 3H, OCH_3), 3.55, 3.7 (2dd, 2H, *J*=4.2, 12.0 Hz, H-3, 4), 3.8–3.95 (m, 2H, H-5), 4.52 (d, 1H, *J*=4.5 Hz, H-2), 5.8 (d, 1H, *J*=4.5 Hz, H-1).

*3.2. 1,2-*O*-Isopropylidene-3-*O*-(1,2-*O*-isopropylidene-3-*O*-ethylenoxyethyl-5-*O*-methyl-α-*D*-xylofuranose)-5-*O*-methyl-α-*D*-xylofuranose **5***

To a solution of **8** (5.6 g, 27.45 mmol) in dioxane (80 mL), KOH (4.6 g, 82.35 mmol) was added and heated at reflux. After 1 h, diethyleneglycol ditosylate (5.68 g, 13.72 mmol) in dioxane (25 mL) was added dropwise and then stirred for 12 h at the same temperature. The reaction mixture was cooled to room temperature and dioxane was removed in vacuo. The residue was dissolved in saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 (3×150 mL), washed with saturated aqueous NaCl solution, dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography (Si-gel, 20% EtOAc in hexane) affording **5** (7.45 g) in 57% yield as a syrup. $[\alpha]_D$ −19.0 (*c* 1.35, $CHCl_3$); ^{1}H NMR: δ 1.32, 1.5 (2s, 6H, CH_3), 3.4 (s, 3H, OCH_3), 3.55–3.75 (m, 6H, H-5, -OCH_2CH_2O-), 3.9 (d, 1H, *J*=4.0 Hz, H-3), 4.25–4.35 (m, 1H, H-4), 4.55 (d, 1H, *J*=4.5 Hz, H-2), 5.85 (d, 1H, *J*=4.5 Hz, H-1); ^{13}C NMR: δ 26.0, 26.5, 58.8, 68.2, 69.65, 70.36, 78.7, 82.2, 82.7, 104.7, 111.2; FABMS: 463 (M−15); HRMS: calcd for $C_{22}H_{38}O_{11}$: 478.241413. Observed: 478.239823.

*3.3. Methanolysis of **5***

A solution of **5** (4 g, 8.36 mmol) in MeOH (30 mL) containing H^+ resin (0.4 g) was stirred at reflux for 12 h, cooled to room temperature, filtered and evaporated. The residue containing a mixture of three isomers was separated chromatographically (200 mesh Si-gel, 2% MeOH in $CHCl_3$) in 1:0.9:1.3 ratio, overall in 62% yield. Eluted firstly was methyl 3-*O*-(methyl-3-*O*-ethylenoxyethyl-5-*O*-methyl-α-D-xylofuranoside)-5-*O*-methyl-α-D-xylofuranoside **9**, $[\alpha]_D$ +77.5 (*c* 3.3, $CHCl_3$); ^{1}H NMR: δ 3.37, 3.45 (2s, 6H, -OCH_3), 3.46–3.6 (m, 4H, -OCH_2CH_2O-), 3.65–3.72 (m, 2H, H-5), 3.90 (t, 1H, *J*=4.9, 12.5 Hz, H-2), 4.12 (d, 1H, *J*=3.2 Hz, H-3), 4.25–4.32 (m, 1H, H-4), 4.9 (d, 1H, *J*=4.7 Hz, H-1); ^{13}C NMR: δ 54.7, 61.2, 69.0, 69.5, 70.2, 74.3, 79.7, 81.3, 109.0; FABMS: 449 (M+Na); HRMS: calcd for $C_{18}H_{34}O_{11}Na$: 449.199882. Observed: 449.201409.

Eluted secondly was methyl 3-*O*-(methyl-3-*O*-ethylenoxyethyl-5-*O*-methyl-β-D-xylofuranoside)-5-*O*-methyl-β-D-xylofuranoside **10**, $[\alpha]_D$ −27.8 (*c* 1.96, $CHCl_3$); ^{1}H NMR: δ 3.4, 3.41 (2s, 6H, -OCH_3), 3.5–3.8 (m, 6H, H-5, -OCH_2CH_2O-), 3.92 (dd, 1H, *J*=2.2, 5.8 Hz, H-2), 4.15 (d, 1H, *J*=2.5 Hz, H-3), 4.35 (q, 1H, *J*=7.1, 11.6 Hz, H-4), 4.75 (s, 1H, H-1); ^{13}C NMR: δ 54.7, 59.0, 69.1, 69.9, 72.9, 74.3, 79.7, 80.6, 102.8; FABMS: 449 (M+Na), 427 (M+1); HRMS: calcd for $C_{18}H_{35}O_{11}$: 427.217937. Observed: 427.219954.

Eluted thirdly was methyl 3-*O*-(methyl-3-*O*-ethylenoxyethyl-5-*O*-methyl-α-D-xylofuranoside)-5-*O*-methyl-β-D-xylofuranoside **11**, $[\alpha]_D$ +29.5 (*c* 1.5, $CHCl_3$); ^{1}H NMR: δ 3.4 (s, 6H, -OCH_3), 3.42, 3.49 (2s, 6H, -OCH_3), 3.5–3.85 (m, 12H, H-5, 5′, -OCH_2CH_2O-), 3.92–4.06 (m, 2H, H-2, 2′), 4.18 (2d, 2H, H-3, 3′), 4.29–4.43 (m, 2H, H-4, 4′), 4.8 (d, 1H, *J*=2.0 Hz, H-1), 4.92 (d, 1H, *J*=4.6 Hz, H-1); ^{13}C NMR: δ 55.3, 54.4, 58.8, 58.9, 70.1, 70.5, 70.9, 71.3, 72.0, 76.2, 76.4, 78.4, 79.4 (2C), 84.3, 85.3, 102.2, 109.2; FABMS: 449 (M+Na); HRMS: calcd for $C_{18}H_{34}O_{11}$: 426.210112. Observed: 426.210750.

*3.4. 18-Crown-6 ether **1***

To a stirred solution of **9** (0.13 g, 0.3 mmol) in DMSO (10 mL), NaH (22 mg, 0.91 mmol) was added in portions at 0°C, then stirred for 1 h at 60°C. Diethyleneglycol ditosylate (126 mg, 0.3 mmol) in DMSO (3 mL) was added to the reaction mixture and stirred for 40 h at 60°C. The reaction mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc (3×35 mL). The organic layer was washed with water and brine, dried (Na_2SO_4) and the residue was purified by column chromatography (200 mesh Si-gel, $CHCl_3$) to afford **1** (56 mg) in 37% yield as a colorless syrup. $[\alpha]_D$ +62.4 (*c* 1.5, $CHCl_3$); ^{1}H NMR: δ 3.34, 3.36 (2s, 6H, -OCH_3), 3.5–3.8 (m, 10H, H-5, -OCH_2CH_2O-), 3.8 (d, 1H, *J*=3.5 Hz, H-3), 4.12 (d, 1H, *J*=3.7 Hz, H-2), 4.20–4.32 (m, 1H, H-4), 4.89 (d, 1H, *J*=4.1 Hz, H-1); FABMS: 519 (M+Na); HRMS: calcd for $C_{22}H_{40}O_{12}Na$: 519.241747. Observed: 519.243389.

*3.5. 18-Crown-6 ether **2***

To a stirred solution of **10** (156 mg, 0.36 mmol) in DMSO (10 mL), NaH (26 mg, 1.0 mmol) was added in portions at 0°C, then stirred for 1 h at 60°C. Diethyleneglycol ditosylate (151 mg, 0.36 mmol) in DMSO (4 mL) was added to the above suspension and stirred for 30 h at 60°C. The reaction mixture was worked up as described for **1** and purified by column chromatography (200 mesh Si-gel, $CHCl_3$) affording **2** (76 mg) in 42% yield as a colorless syrup. $[\alpha]_D$ −17.9 (*c* 1.6, $CHCl_3$); ^{1}H NMR: δ 3.8 (1s, 6H, -OCH_3), 3.5–3.7 (m, 10H, H-5, -OCH_2CH_2O-), 3.85 (d, 1H, *J*=2.5 Hz, H-3), 3.95 (s, 1H, H-2), 4.35 (q, 1H, *J*=7.18, 11.6 Hz, H-4), 4.8 (s, 1H, H-1); ^{13}C NMR: δ 55.0, 59.1, 69.8 (2C), 70.0, 70.3, 74.2, 79.6, 80.0, 80.8, 101.5; FABMS: 519 (M+Na); HRMS: calcd for $C_{22}H_{40}O_{12}Na$: 519.241747. Observed: 519.243145.

*3.6. 18-Crown-6 ether **3***

Compound **11** (160 mg, 0.375 mmol) in DMSO (10 mL) was treated with NaH (34 mg, 0.75 mmol) in portions at 0°C, then stirred for 1 h at 60°C. Diethyleneglycol ditosylate (155 mg, 0.375 mmol) in DMSO (2 mL) was added to the above suspension and after 40 h at 60°C it was worked up as described for **1** and purified by column chromatography (200 mesh Si-gel, $CHCl_3$) to afford **3** (70 mg) in 38% yield as a colorless syrup. $[\alpha]_D$ +38.3 (*c* 0.96, $CHCl_3$); ^{1}H NMR: δ 3.42, 3.45 (2s, 12H, OCH_3), 3.5–3.7 (m, 22H, H-5, 5′, 2, 2′, -OCH_2CH_2O-), 4.1 (m, 2H, H-3, 3′), 4.32 (m, 2H, H-4, 4′), 4.8 (s, 1H, H-1), 4.9 (d,

1H, *J*=4.5 Hz, H-1′); ^{13}C NMR ($CDCl_3$): δ 54.9, 55.5, 58.9, 59.0, 69.3, 69.7, 69.8, 69.9, 70.1, 70.3 (2C), 71.4, 71.5, 72.1, 75.5, 79.5, 82.1, 83.0, 85.3, 87.7, 100.2, 107.8; FABMS: 519 (M+Na); HRMS: calcd for $C_{22}H_{40}O_{12}Na$: 519.241747. Observed: 519.242201.

3.7. 1,2-O-Isopropylidene-5-O-methyl-α-D-ribofuranose ***13***

To a stirred solution of **8** (5.0 g, 24.5 mmol) in CH_2Cl_2 (45 mL) were added sequentially PDC (9.2 g, 24.5 mmol, freshly prepared) and Ac_2O (2.7 mL, 24.5 mmol) at 0°C, then heated at reflux for 5 h. The reaction mixture was cooled to room temperature, CH_2Cl_2 was evaporated, the residue was treated with ether (3×100 mL) and filtered through silica gel. The ethereal layer was washed with sat. $NaHCO_3$ solution, dried (Na_2SO_4) and evaporated to afford **12** (3.2 g) in 65% yield.

The above crude product **12** (3 g, 14.85 mmol) was treated with $NaBH_4$ (0.82 g, 22.2 mmol) in MeOH (20 mL). After 2 h MeOH was removed, the residue was dissolved in water and extracted with ether (2×100 mL). The organic layer was washed with sat. NaCl solution, dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography (Si-gel, 15% EtOAc in hexane) to afford **13** (2.33 g) in 77% yield as a colorless syrup. $[\alpha]_D$ +40.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR: δ 1.4, 1.55 (2s, 6H, CH_3), 2.3 (br d, 1H, OH), 3.42 (s, 3H, OCH_3), 3.55, 3.7 (2dd, 2H, *J*=4.2, 12.0 Hz, H-3, 4), 3.8–3.95 (m, 2H, H-5), 4.52 (t, 1H, *J*=4.1, 9.2 Hz, H-2), 5.8 (d, 1H, *J*=4.5 Hz, H-1).

3.8. 1,2-O-Isopropylidene-3-O-(1,2-O-isopropylidene-3-O-ethylenoxyethyl-5-O-methyl-α-D-ribofuranose)-5-O-methyl-α-D-ribofuranose ***6***

To a solution of **13** (2.07 g, 10.1 mmol) in dioxane (15 mL), KOH (1.7 g, 30.0 mmol) was added and heated at reflux for 1 h and diethyleneglycol ditosylate (2.1 g, 5.0 mmol) in dioxane (5 mL) was added dropwise. After 12 h, the reaction mixture was worked up as described for **5** and the residue was purified by column chromatography (Si-gel, 20% EtOAc in hexane) to afford **6** (3.33 g) in 68% yield. $[\alpha]_D$ +86.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR: δ 1.25, 1.5 (2s, 6H, CH_3), 3.3 (s, 3H, OCH_3), 3.45 (dd, 1H, *J*=4.0, 9.3 Hz, H-3), 3.54–3.62 (m, 4H, -OCH_2CH_2O-), 3.7–3.8 (m, 2H, H-5), 3.9–4.0 (m, 1H, H-4), 4.5 (t, 1H, *J*=4.1, 9.2 Hz, H-2), 5.7 (d, 1H, *J*=4.2 Hz, H-1); ^{13}C NMR: δ 26.0, 26.5, 58.5, 69.5, 69.6, 70.3, 78.7, 82.2, 82.7, 104.0, 111.2; FABMS: 463 (M−15); HRMS: calcd for $C_{22}H_{38}O_{11}$: 478.241413. Observed: 478.241728.

3.9. Methanolysis of ***6***

A solution of **6** (3.0 g, 6.27 mmol) in MeOH (20 mL) containing H^+ resin (0.3 g) was stirred at reflux for 12 h. It was worked up as described for **9** and the crude product was purified by column chromatography (200 mesh Si-gel, 2% MeOH–$CHCl_3$) to afford methyl 3-*O*-(methyl-3-*O*-ethylenoxyethyl-5-*O*-methyl-β-D-ribofuranoside)-5-*O*-methyl-β-D-ribofuranoside **14** (1.73 g) in 72% yield as a colorless syrup. $[\alpha]_D$ +42.1 (*c* 1.2, $CHCl_3$); ^{1}H NMR: δ 3.32, 3.4 (2s, 6H, OCH_3), 3.5–3.85 (m, 6H, H-5, -OCH_2CH_2O-), 3.9 (dd, 1H, *J*=4.4, 7.2 Hz, H-3), 4.05–4.15 (m, 2H, H-2, 4), 4.82 (s, 1H, H-1); ^{13}C NMR: δ 54.7, 59.0, 69.1, 69.9, 72.9, 74.3, 79.7, 80.6, 108.1; FABMS: 449 (M+Na), 427 (M+1); HRMS: calcd for $C_{18}H_{35}O_{11}Na$: 449.199882. Observed: 449.200214.

3.10. 18-Crown-6 ether ***4***

A solution of **14** (230 mg, 0.53 mmol) in DMSO (12 mL) was treated with NaH (49 mg, 1.07 mmol) in portions at 0°C, then stirred for 1 h at 60°C. Diethyleneglycol ditosylate (227 mg, 0.53 mmol) in DMSO

(2 mL) was added to the reaction mixture and stirred for 40 h at 60°C. It was worked up as described for **1** and the residue was purified by column chromatography (200 mesh Si-gel, $CHCl_3$) to afford **4** (152 mg) in 57% yield as a colorless syrup. $[\alpha]_D$ +14.7 (*c* 1.06, $CHCl_3$); ^1H NMR: δ 3.32–3.39 (2s, 6H, OCH_3), 3.5–3.9 (m, 12H, H-2, 3, 5, -OCH_2CH_2O-), 4.1–4.2 (m, 1H, H-4), 4.82 (s, 1H, H-1); ^{13}C NMR: δ 55.0, 59.1, 69.8 (2C), 70.1, 70.3, 74.1, 79.4, 80.0, 80.8, 106.2; FABMS: 519 (M+Na); HRMS: calcd for $C_{22}H_{40}O_{12}Na$: 519.241747. Observed: 519.241150.

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