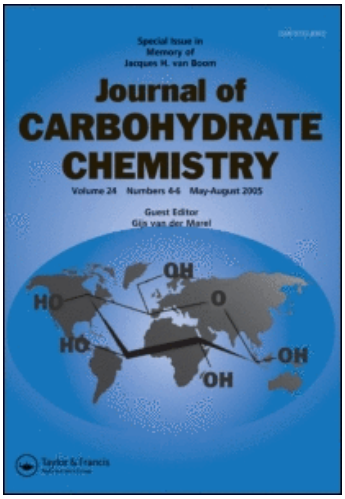

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Syntheses of 4, 5-Di-O-bexzyl-2-deoxy-2-C-methyl L-lyxose and Methyl 4, 5-Di-O-bexzyl-2-deoxy-2-C-methyl-3-O-metkyl-L-lyxonate

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SYNTHESES OF 4,5-DI-O-BENZYL-2-DEOXY-2-C-METHYL L-LYXOSE AND METHYL 4,5-DI-O-BENZYL-2-DEOXY-2-C-METHYL-3-O-METHYL-L-LYXONATE

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ABSTRACT

The title compounds, which possess C-methyl groups at the α-position of carbonyl groups and vicinal hydroxyl groups with *syn* (*threo*) relationship, were synthesized efficiently from known 3-deoxy-1,2-O-isopropylidene-3-C-methyl-α-D-allofuranose. The synthetic routes involve: 1) inversion of C-5 configuration of the starting sugar, 2) suitable protection of the 5,6-diol, and 3) glycol cleavage of the 1,2-diol to an aldehyde or direct oxidation of the diol to carboxylic acid.

INTRODUCTION

Extensive progress has been made in stereospecific and stereoselective introduction of 1,2- and 1,3-diol systems by means of aldol condensation-like reactions.[1] The use of carbohydrates as chiral pools is a promising approach to obtaining the desired diol systems in optically pure forms.[2]

Introduction of a methyl group on a carbon skeleton is often a challenging problem in natural product synthesis. In addition, carbonyl groups (aldehyde or carboxylic ester) on a

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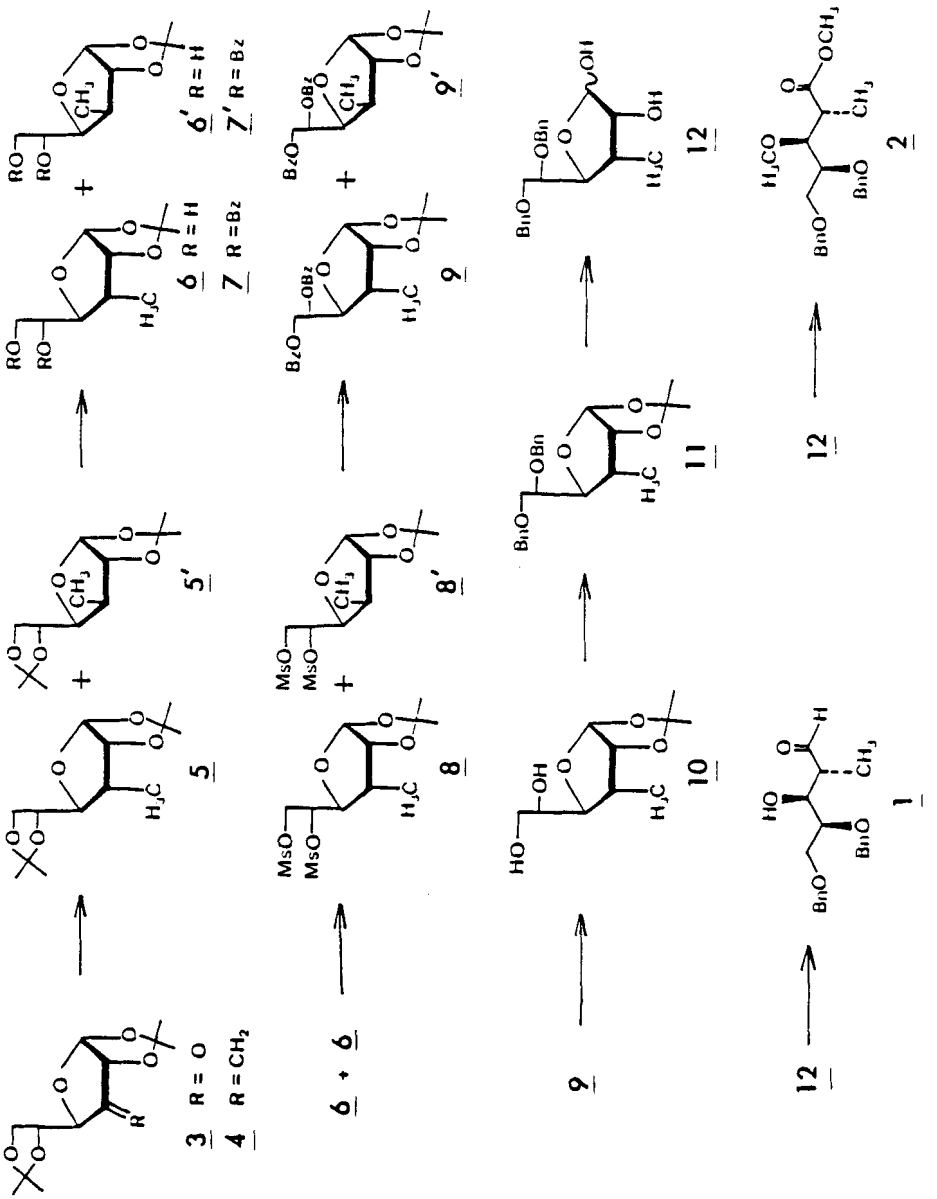
carbon skeleton are utilizable for a variety of carbon-carbon bond formation reactions, aldol-condensations, Grignard reactions, Wittig reactions, and so on. From this point of view, we have synthesized 4,5-di-O-benzyl-2-deoxy-2-C-methyl-L-lyxose (1) and methyl 4,5-di-O-benzyl-2-deoxy-2-C-methyl-3-O-methyl-L-lyxonate (2), from the readily available D-glucose derived compound (4), as chiral synthons for natural product synthesis. Both compounds 1 and 2 possess a diol system on C-3 and 4 with a *syn* relationship and a C-methyl group at α-position to the carbonyl group. Compounds 1 and 2 may be useful intermediates for the synthesis of natural products such as macrolide or ionophore antibiotics.

RESULTS AND DISCUSSION

The synthesis of 1 and 2 were started from known 3-deoxy-1,2:5,6-di-O-isopropylidene-3-C-methylene-α-D-*ribo*-hexofuranose 4. The preparation of 4 was reported by Rosenthal and Spinzl[3] and by Szarek and coworkers[4] by Wittig olefination of 1,2:5,6-di-O-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (3). We improved the yield of 4 using crystalline 3 which was obtained by pyridinium chlorochromate (PCC) oxidation[5] of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose. Hydrogenation of compound 4 to 3-deoxy-1,2:5,6-di-O-isopropylidene-3-C-methyl-α-D-allofuranose (5) using the reported procedure,[3] was not effective in our case. We examined the hydrogenation of 4 in the presence of Raney nickel in a slightly acidic (acetic acid) methanol solution for completion of the reaction. Consequently, an approximately 10 to 1 mixture of compound 5 and the D-gluco derivative (5') was obtained in 92% yield. In spite of the contamination with 5', the yield of 5 was improved. The D-gluco derivative could be easily separated at a later stage.

The mixture of 5 and 5' was selectively hydrolyzed with 60% aqueous acetic acid to afford a 5,6-diol derivative (a mixture



of 6 and 6') in 81% yield. Mesylation of the mixture with mesyl chloride in pyridine gave the 5,6-di-O-mesyl derivative (a mixture of 8 and 8') in 89% yield. Nucleophilic displacement of the mesyloxy groups in 8 and 8' by benzoate anions with inversion of the C-5 configurations was accomplished by refluxing the mixture in DMF with sodium benzoate. The reaction gave the L-talo derivative (9) from 8 and the L-ido derivative (9') from 8', which were easily separated by silica gel column chromatography in 73% and 7% yield, respectively. The ^{1}H NMR spectrum of 9 was clearly distinguishable from the mixture of compounds (7) and (7') (10%) prepared by benzoylation of the mixture of 6 and 6'. The proton on C-5 of 7 appeared at δ 5.35-5.59 as a multiplet. The proton on C-5 of 9 appeared at δ 5.60 as a doublet of triplets (J=2 and 7 Hz). This spectral change indicates a change of configuration at C-5 of 7 to the L-talo configuration of 9.

The desired 1 and 2 were synthesized from 9 as follows. O-Debenzoylation of 9 with methanolic sodium methoxide gave (10) in 82% yield. O-Benzylation of 10 with benzyl bromide in the presence of sodium hydride furnished the 5,6-di-O-benzyl derivative (11) in 76% yield. O-Deisopropylidenation of 11 with 2 M HCl gave 5,6-di-O-benzyl-3-deoxy-3-C-methyl-L-talofuranose (12) as an anomeric mixture in 88% yield. Treatment of 12 with sodium borohydride followed by periodate oxidation afforded 1 in 81% yield. Bubbling oxygen into an aqueous $Ba(OH)_2$ solution[6] of 12 followed by treatment with methyl iodide gave 2 in 72% yield.

EXPERIMENTAL

General Procedures. Melting points were determined with a Mitamura Riken micro apparatus and are uncorrected. Solutions were concentrated under diminished pressure at a bath temperature below 40 °C. Specific rotations were measured in a 1-dm tube

with a JEOL DIP-4 polarimeter. Column chromatography was performed with Wakogel C-300 (Wako Pure Chemicals), and TLC was carried out on glass plates coated with Wakogel B-5F, compounds being detected with UV light and by spraying with sulfuric acid followed by heating. Preparative TLC (PTLC) was performed on glass plates (20 x 20 cm) coated with Merck Kieselgel 60 PF_{254} and compounds were extracted with chloroform. IR spectra were recorded with a Hitachi Model-225 spectrometer (KBr) and with a JEOL Model A-202 spectrometer ($CHCl_3$). ^1H NMR spectra were recorded with a Varian EM-390 spectrometer, and chemical shifts for a $CDCl_3$ solution are recorded in δ values from internal tetramethylsilane. High resolution mass spectra were taken on a Hitachi M-80 mass spectrometer. Elemental analyses were performed by Mr. Saburo Nakada to whom our thanks are due.

3-Deoxy-1,2:5,6-di-O-isopropylidene-3-C-methylene-α-D-*ribo*-hexofuranose (4). To a stirred solution of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (29.7 g, 0.12 mol) in dry dichloromethane (290 mL) were added PCC (99.2 g, 0.46 mol) and molecular sieves 3A (powder, 115 g). After stirring for 2 h, the mixture was applied on SiO_2 column (300 g, packed with ether) and eluted with ether. Fractions corresponding to R_f 0.52 on TLC (ethanol:toluene=1:5) were concentrated to afford the 3-ulose (3) (28.4 g, 95%) as white crystals. For the Wittig reaction, 3 was dried at 50 °C *in vacuo* for 1 h. Sodium hydride (50% emulsion in mineral oil, 15.0 g, 0.32 mol) was washed with petroleum ether (15 mL x 3), and suspended in dry DMSO (650 mL). The mixture was stirred at 75 °C for 1 h under nitrogen flow, then cooled to room temperature. To this was added methyltriphenylphosphonium bromide (134 g, 0.38 mol), and the mixture was stirred for 30 min. Then a solution of 3 (27.0 g, 0.105 mol) in dry DMSO (600 mL) was added to the mixture. After stirring for 1 h under nitrogen flow, the solution was poured into ice cold water (800 mL). The aqueous solution was extracted with ether (300 mL x 5), and the extracts were washed with water (300 mL x 2). The aqueous washing were extracted with ether (200 mL x 2),

and the combined extracts were washed with water (300 mL). The extracts were dried (Na_2SO_4) and concentrated. The residue was dissolved in petroleum ether (600 mL) and stored in a refrigerator overnight. Precipitated triphenylphosphine oxide was removed by filtration, and the filtrate was concentrated. The residue was purified on SiO_2 (100 g, ethyl acetate:toluene=1:5), fractions corresponding to R_f 0.37 on TLC (ethyl acetate:toluene=1:5) were concentrated to afford 4 (19.4 g, 72%) as a syrup, $[\alpha]_D^{25}$+98.9° (*c* 1.82, $CHCl_3$), [lit.[3] $[\alpha]_D^{22}$+104° (*c* 2, $CHCl_3$)]; IR $\nu_{max}^{CHCl_3}$ 2990, 2940, 2880 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (6H, s, $C(CH_3)_2$), 1.49, 1.57 (each 3H, each s, $C(CH_3)_2$), 3.90-4.18 (3H, m, H-5,6,6'), 4.57-4.77 (1H, m, H-4), 4.83-4.93 (1H, m, H-2), 5.39-5.51 (2H, m, $=CH_2$), 5.81 (1H, d, J=4 Hz, H-1).

Mixture of 3-deoxy-1,2-O-isopropylidene-5,6-di-O-benzoyl-3-C-methyl-α-D-allofuranose and the D-gluco isomer (7 and 7'). A solution of 4 (704 mg, 2.75 mmol) in methanol (21 mL) containing two drops of acetic acid (pH 4) was hydrogenated in the presence of Raney nickel T-4 (5 g) in a Parr apparatus for 17 h. The catalyst was removed by filtration and the filtrate was concentrated. The residue was purified on SiO_2 (50 g, ethyl acetate:toluene=1:5), fractions corresponding to R_f 0.59 on TLC (ethyl acetate:toluene=1:5) were concentrated to afford a mixture of 5 and 5' (651 mg, 92% yield) as a syrup, ^1H NMR ($CDCl_3$) δ 0.95 (d, J=7 Hz, CH_3-3), 1.18 (d, J=8 Hz, CH_3-3), 4.28 (d, $J_{1,2}$=4 Hz, H-2), 4.49 (t, $J_{1,2}=J_{2,3}$=4 Hz, H-2). The signals at δ 0.95 and 4.28 were of 5' and the signals at δ 1.18 and 4.49 were of 5. [lit.[3] ^1H NMR ($CDCl_3$) of pure 5, δ 4.50 (1H, t, $J_{1,2}=J_{2,3}$=3.7 Hz, H-2).

A solution of the mixture of 5 and 5' (3.04 g, 11.8 mmol) in 60% aqueous acetic acid (20 mL) was stirred at room temperature for 15 h. The solution was concentrated, and the residue was purified on SiO_2 (90 g, ethyl acetate:toluene=1:6). Fractions corresponding to R_f 0.42 on TLC (ethanol:toluene=1:5) were concentrated to afford a mixture of 6 and 6' (2.07 g, 81%) as a syrup, ^1H NMR ($CDCl_3$) δ 0.94 (d, J=7 Hz, CH_3-3 for 6'), 1.09 (d,

J=8 Hz, CH_3-3 for 6), 4.24 (d, $J_{1,2}$=4 Hz, H-2 for 6'), 4.43 (t, $J_{1,2}=J_{2,3}$=4 Hz, H-2 for 6), 5.64 (d, $J_{1,2}$=4 Hz, H-1 for 6 and 6').

To a stirred solution of the mixture of 6 and 6' (47 mg, 0.22 mmol) in pyridine (1 mL) was added benzoyl chloride (0.08 mL, 0.65 mmol) at 0 °C. After stirring for 2.5 h, the mixture was concentrated. The residue was partitioned between chloroform (10 mL) and water (10 mL), and the aqueous layer was extratced with chloroform (10 mL x 2). The extracts were dried (Na_2SO_4) and concentrated. The residue was purified on SiO_2 (10 g, ethyl acetate:toluene=1:5), and fractions corresponding to R_f 0.52 on TLC (ethyl acetate:toluene=1:5) were concentrated to afford the mixture of 7 and 7' (78 mg, 85%) as a syrup, IR $\nu_{max}^{CHCl_3}$ 1720, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (3H, d, J=8 Hz, CH_3-3), 1.32, 1.50 (each 3H, each s, $C(CH_3)_2$), 1.92-2.40 (1H, m, H-3), 4.02 (1H, dd, J=5 Hz, J=10 Hz, H-4), 4.31-4.80 (3H, m, H-2,6,6'), 5.35-5.59 (1H, m, H-5), 5.70 (1H, d, J=4 Hz, H-1), 6.90-8.14 (10H, m, 2 x $OCOC_6H_5$).

Mixture of 3-deoxy-1,2-O-isopropylidene-5,6-di-O-mesyl-3-C-methyl-α-D-allofuranose and the D-gluco isomer (8 and 8'). To a stirred solution of the mixture of 6 and 6' (772 mg, 3.5 mmol) in pyridine (15 mL) was added mesyl chloride (0.82 mL, 10.6 mmol). After stirring for 3 h at room temperature, the mixture was concentrated. The residue was partitioned between chloroform (70 mL) and water (70 mL), and the aqueous layer was extracted with chloroform (70 mL x 2). The extracts were dried (Na_2SO_4) and concentrated to afford the mixture of 8 and 8' as an amorphous powder. Resolidification of the powder from several solvents could not change the ratio of 8 and 8', mp 157-159 °C; IR ν_{max}^{KBr} 1185, 1175 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (3H, d, J=8 Hz, CH_3-3), 1.32, 1.50 (each 3H, each s, $C(CH_3)_2$), 1.70-2.38 (1H, m, H-3), 3.02 (3H, s, OSO_2CH_3), 3.08 (3H, s, OSO_2CH_3), 3.90 (1H, q, H-4), 4.10 (3H, m, H-5,6,6'), 5.64 (1H, d, $J_{1,2}$=4 Hz, H-1).

Anal. calcd for $C_{12}H_{22}O_9S_2$: C, 38.49; H, 5.92; S, 17.12. Found: C, 38.73; H, 5.74; S, 16.80.

5,6-Di-O-benzoyl-3-deoxy-1,2-O-isopropylidene-3-C-methyl-β-L-talo- (9) and β-L-idofuranose (9'). A solution of the mixture of 8 and 8' (1.18 g, 3.2 mmol) in dry DMF (20 mL) with sodium benzoate (dried *in vacuo* for 1 d, 1.14 g, 7.9 mmol) was gently refluxed with vigorous stirring for 4 h. The mixture was concentrated with butanol, and the residue was diluted with water (70 mL). The aqueous solution was extracted with ethyl acetate (70 mL x 3). The extracts were dried (Na_2SO_4) and concentrated. The residue was purified on SiO_2 (100 g, ethyl acetate:toluene=1:10), and fractions corresponding to R_f 0.57 on TLC (ethyl acetate:toluene=1:10) were concentrated to afford 9 (977 mg, 73%) as a syrup. Fractions corresponding to R_f 0.49 were concentrated to afford 9' (89 mg, 7%) as white crystals.

9: $[\alpha]_D^{22}$ -16.8° (*c* 0.75, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 1720, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (3H, d, J=8 Hz, CH_3-3), 1.33, 1.51 (each 3H, each s, $C(CH_3)_2$), 1.66-2.25 (1H, m, H-3), 4.00 (1H, dd, $J_{3,4}$= 10 Hz, $J_{4,5}$=2 Hz, H-4), 4.42 (1H, t, $J_{1,2}=J_{2,3}$=4 Hz, H-2), 4.60 (2H, d, $J_{5,6}=J_{5,6'}$=7 Hz, H-6,6'), 5.60 (1H, d of t, $J_{4,5}$=2 Hz, $J_{5,6}$=7 Hz, H-5), 5.71 (1H, d, $J_{1,2}$=4 Hz, H-1), 7.02-8.09 (10H, m, 2 x $OCOC_6H_5$).

Anal. calcd for $C_{24}H_{26}O_7$: C, 67.59; H, 6.15. Found: C, 67.33; H, 6.13.

9': mp 62-64 °C; $[\alpha]_D^{21}$ -21.0° (*c* 0.63, $CHCl_3$); IR ν_{max}^{KBr} 1720, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (3H, d, J=8 Hz, CH_3-3), 1.31, 1.52 (each 3H, each s, $C(CH_3)_2$), 2.23-2.60 (1H, m, H-3), 4.26-4.73 (4H, m, H-4,5,6,6'), 5.60 (1H, dd, J=7 Hz and 13 Hz, H-5), 5.80 (1H, d, $J_{1,2}$=4 Hz, H-1), 6.82-8.10 (10H, m, 2 x $OCOC_6H_5$).

Anal. calcd for $C_{24}H_{26}O_7$: C, 67.59; H, 6.15. Found: C, 67.46; H, 6.03.

3-Deoxy-1,2-O-isopropylidene-3-C-methyl-β-L-talofuranose (10). To a solution of 9 (597 mg, 1.30 mmol) in dichloromethane (10 mL) was added sodium methoxide in methanol (1 M, 3.9 mL, 3.9 mmol). After 2 h stirring at 5 °C, the mixture was concentrated. The residue was purified on SiO_2 (50 g, ethanol:toluene=1:5), and fractions corresponding to R_f 0.36 on TLC (ethanol:toluene=

1:5) were concentrated to afford 10 (250 mg, 82%) as a syrup, $[\alpha]_D^{21}$+42.5° (*c* 0.79, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ 3550, 2980 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (3H, d, J=8 Hz, CH_3-3), 1.32, 1.50 (each 3H, each s, $C(CH_3)_2$), 1.95-2.50 (1H, m, H-3), 2.74 (2H, s, 2 x OH), 3.45-3.80 (4H, m, H-4,5,6,6'), 4.45 (1H, t, $J_{1,2}=J_{2,3}=4$ Hz, H-2), 5.68 (1H, $J_{1,2}=4$ Hz, H-1).

Anal. calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 54.73; H, 8.10.

5,6-Di-O-benzyl-3-deoxy-1,2-O-isopropylidene-3-C-methyl-β-L-talofuranose (11). Sodium hydride (50% emulsion in mineral oil, 108 mg, 2.25 mmol) was washed with petroleum ether (2 mL x 3) and suspended in DMF (2 mL). A solution of 10 (196 mg, 0.9 mmol) in DMF (8 mL) was added to the suspension, and the mixture was stirred for 25 min. Then, benzyl bromide (0.43 mL, 3.6 mmol) was added. After 20 h stirring, ethanol (6 mL) was added. The mixture was poured into water (50 mL) and extracted with ethyl acetate (50 mL x 3). The extracts were dried (Na_2SO_4) and concentrated. The residue was purified on SiO_2 (50 g, ethyl acetate:toluene=1:10), and fractions corresponding to R_f 0.50 on TLC (ethyl acetate:toluene=1:5) were concentrated to afford 11 (271 mg, 76%) as a syrup, $[\alpha]_D^{19}$+57.2° (*c* 1.08, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.80 (3H, d, J=8 Hz, CH_3-3), 1.30, 1.45 (each 3H, each s, $C(CH_3)_2$), 1.90-2.30 (1H, m, H-3), 3.47-3.90 (4H, m, H-2,4,6,6'), 4.28-4.49 (1H, m, H-5), 4.38-4.81 (2H, m, $OCH_2C_6H_5$), 4.43 (2H, s, $OCH_2C_6H_5$), 5.65 (1H, d, $J_{1,2}=4$ Hz, H-1), 7.25 (10H, s, 2 x $OCH_2C_6H_5$).

Anal. calcd for $C_{24}H_{30}O_5$: C, 72.34; H, 7.59. Found: C, 72.27; H, 7.55.

5,6-Di-O-benzyl-3-deoxy-3-C-methyl-α,β-L-talofuranose (12). A solution of 11 (481 mg, 1.2 mmol) in a mixture of dioxane (3 mL) and 2 M HCl (3 mL) was heated at 60 °C for 4 h. The solution was neutralized with 2 M NaOH, diluted with water (40 mL) and extracted with chloroform (40 mL x 3). The extracts were dried (Na_2SO_4) and concentrated. The residue was crystallized from ethyl acetate-hexane to afford 12 (240 mg).

The mother liquor was purified on PTLC (ethanol:toluene=1:10, R_f 0.35) to afford another crop of 12 (112 mg, total 88%), mp 86-88 °C; IR ν_{max}^{KBr} 3360, 3300, 2930, 2880 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (3H, d, J=7 Hz, CH_3-3), 1.62-1.89 (1H, br s, OH), 2.02-2.46 (1H, m, H-3), 3.30-4.00 (5H, m, H-2,4,5,6,6'), 4.42-4.88 (2H, m, $OCH_2C_6H_5$), 4.44 (2H, s, $OCH_2C_6H_5$), 4.88-5.39 (1H, m, H-1), 7.32 (10H, s, 2 x $OCH_2C_6H_5$).

Anal. calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.59; H, 7.27.

4,5-Di-O-benzyl-2-deoxy-2-C-methyl-L-lyxose (1). To a stirred solution of 12 (171 mg, 0.48 mmol) in ethanol (1 mL) was added an ethanolic solution of sodium borohydride (36 mg, 0.96 mmol). After 50 min stirring, the solution was neutralized with 1 M HCl. To the solution was added an aqueous (1 mL) solution of sodium periodate (102 mg, 0.48 mmol). After 1 h stirring, the solution was diluted with water (6 mL). The solution was extracted with ethyl acetate (10 ml x 3). The extracts were dried (Na_2SO_4) and concentrated. The residue was purified on PTLC (ethanol:toluene=1:12) to afford 1 (127 mg, 81%) as a syrup, R_f 0.84 on TLC (ethanol:toluene=1:14); $[\alpha]_D^{21}$+8.2° (*c* 1.19, MeOH); IR $\nu_{max}^{CHCl_3}$ 3450, 2860, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (3H, d, J=7 Hz, CH_3-3), 2.40-2.63 (1H, m, H-2), 3.43-3.86 (4H, m, H-3,4,5,5'), 4.29-4.74 (2H, m, $OCH_2C_6H_5$), 4.40 (2H, s, $OCH_2C_6H_5$), 7.28 (10H, s, 2 x $OCH_2C_6H_5$), 9.68 (1H, d, J=3 Hz, H-1).

Anal. calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 72.87; H, 7.51.

Methyl 4,5-di-O-benzyl-2-deoxy-2-C-methyl-3-O-methyl-L-lyxonate (2). To a suspension of barium hydroxide (octa hydrate, 291 mg, 0.92 mmol) in a mixture of dioxane (2.5 mL) and water (0.5 mL) was bubbled oxygen for 30 min. To the suspension was added a solution of 12 (301 mg, 0.84 mmol) in water:dioxane (1:5, 3 mL), and oxygen was bubbled into the mixture at 60 °C for 4.5 h. The mixture was diluted with water (25 mL) and CO_2 gas was passed for 30 min. The mixture was

acidified with 1 M HCl (pH 3) and extracted with chloroform (30 mL x 3). The extracts were dried (Na_2SO_4) and concentrated. The residue was used in the next step without purification. Sodium hydride (50% emulsion in mineral oil, 101 mg, 2.1 mmol) was washed with petroleum ether (1 mL x 2) and suspended in DMF (0.5 mL). To the suspension was added a solution of the above residue in DMF (2.5 mL), and stirred for 30 min. Then, iodomethane (0.26 mL, 4.2 mmol) was added. After 16 h stirring, ethanol (3 mL) was added to the mixture. The solution was diluted with water (30 mL) and extracted with chloroform (30 mL x 3). The extracts were washed with 30% $Na_2S_2O_3$ solution (30 mL) and water (30 mL x 2). The extracts were dried (Na_2SO_4) and concentrated. The residue was purified by PTLC (ethyl acetate:toluene=1:8) to afford 2 (226 mg, 72%) as a syrup, R_f 0.43 on TLC (ethyl acetate:toluene=1:8); $[\alpha]_D^{21}$ -3.6° (*c* 0.50, MeOH); IR $\nu_{max}^{CHCl_3}$ 2940, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (3H, d, J=8 Hz, CH_3-3), 2.70-3.08 (1H, m, H-2), 3.24-3.94 (4H, m, H-3,4,5,5'), 3.45 (3H, s, OCH_3), 3.74 (3H, s, $COOCH_3$), 4.53-4.98 (2H, m, $OCH_2C_6H_5$), 4.65 (2H, s, $OCH_2C_6H_5$), 7.52 (5H, s, $OCH_2C_6H_5$), 7.54 (5H, s, $OCH_2C_6H_5$). High resolution mass spectrum, calcd for $C_{22}H_{28}O_5$: *m/z* 372.1935, found: M, 372.1944.

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