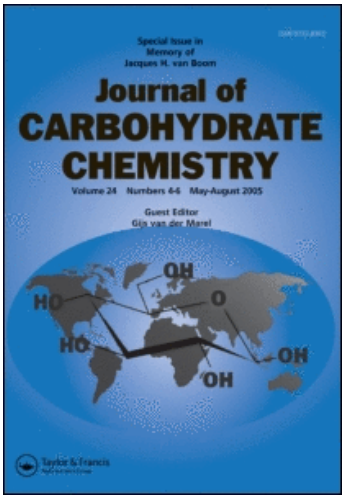

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Robert M. Giuliano[a]; John H. Buzby[a]
[a] Department of Chemistry, Villanova University, Villanova, PA

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REDUCTIONS OF METHYL 2,3-DI-O-BENZYL-4-DEOXY-β-L-THREO-HEX-4-ENODIALDOPYRANOSIDE

Robert M. Giuliano* and John H. Buzby

Department of Chemistry
Villanova University, Villanova, PA 19085

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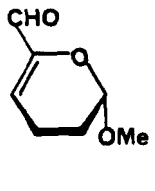
ABSTRACT

Selective reductions of the aldehyde and alkene functionalities in methyl 2,3-di-O-benzyl-4-deoxy-β-L-threo-hex-4-enodialdopyranoside (4) are described. The title compound was synthesized in six steps from methyl α-D-glucopyranoside. Catalytic reduction of the C-4 - C-5 double bond in 4 gave either methyl 2,3-di-O-benzyl-4-deoxy-α-D-xylo-hexodialdopyranoside (5) or methyl 2,3-di-O-benzyl-4-deoxy-β-L-arabino-hexodialdopyranoside (10) in high stereoselectivity depending on the reaction conditions. The α-D-xylo product is a suitable precursor to higher-carbon sugars extended at the C-6 position. Reduction of both products with sodium borohydride gave the corresponding saturated alcohols 12 and 13. The aldehyde group in the title compound was reduced with diisobutylaluminum hydride to give allylic alcohol 11 which was hydrogenated to give, unexpectedly, alcohol 12 as the only product.

INTRODUCTION

Our recent studies of the Diels-Alder reactions of dieno-pyranosides required the preparation of the α,β-unsaturated aldehydes 1-4.[1] These enodialdohexopyranosides were prepared by treatment of 4-methanesulfonate esters of suitably protected sugars with sulfur trioxide-pyridine complex in DMSO, under conditions described by Perlin[2] (vide infra). The use of 6-aldehydo sugar derivatives in the synthesis of chain-extended carbohydrates [3-5] prompted us to investigate the selective reductions of the double bond and aldehyde functionalities in the

title compound 4. In the course of this study, we have developed a convenient synthesis of methyl 2,3-di-O-benzyl-4-deoxy-α-D-xylo-hexo-



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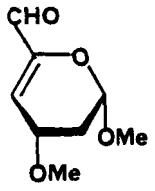

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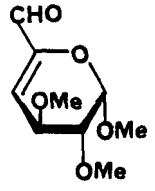

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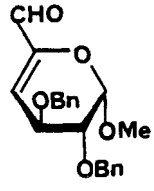
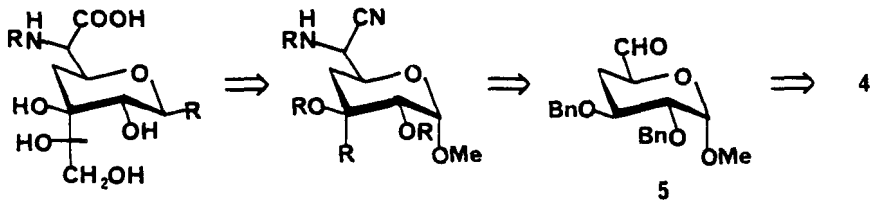


4

dialdopyranoside 5. Since 5 is deoxygenated at C-4, it may serve as a precursor to the carbohydrate component of the nucleoside antibiotic amipurimycin,[6] as suggested by retrosynthetic analysis (Scheme 1), and the recent work of Czernecki on the cyano-amination of dialdohexose derivatives.[7] The synthesis of 5 and the preparation of other reduced derivatives of 4 are described below.

RESULTS AND DISCUSSION

The synthesis of 4 from methyl 2,3-di-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside[8] 6 is shown in Scheme 2. Cleavage of the benzylidene acetal in 6 with p-toluenesulfonic acid in ethanol gave diol 7.[9] Selective protection of the primary hydroxyl group in 7 as a trityl ether and treatment of the crude product with methanesulfonyl chloride gave 8 from which the trityl group was removed with dilute acid to give crystalline mesylate 9.



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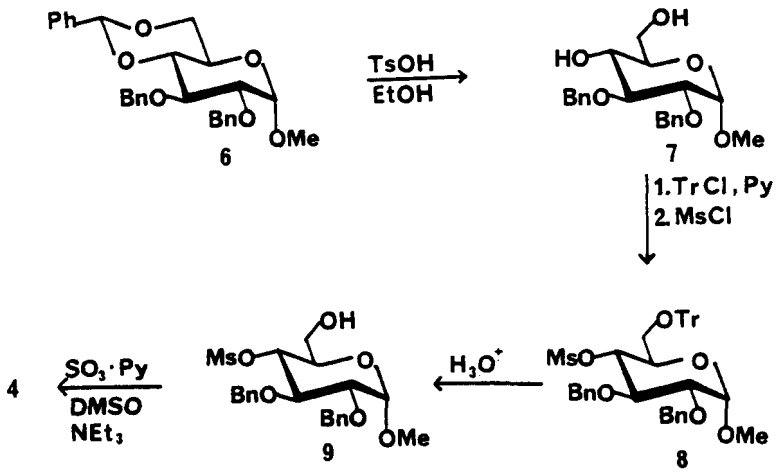
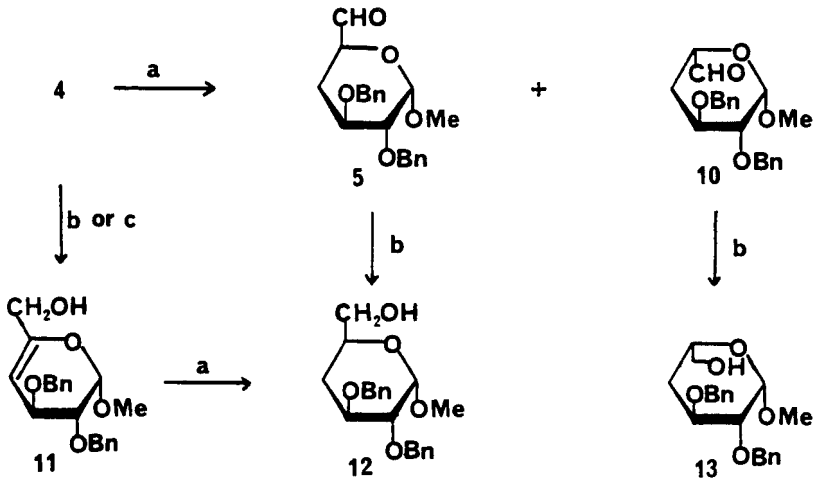
SCHEME 1



SCHEME 2

Oxidation of 9 with sulfur trioxide-pyridine complex was accompanied by elimination of the 4-methanesulfonate group to give α,β-unsaturated aldehyde 4 in 83% yield (27% overall from 7). The sequence leading from 7 to 4 is general and was used to prepare compounds 1-3 with only slight modifications.

Catalytic hydrogenation of 4 was attempted under 1 atm (balloon) of hydrogen in the presence of various catalysts and solvents. With 10% palladium on carbon as the catalyst, a complex mixture which contained products resulting from reduction of the double bond and debenzylation was obtained. Selective hydrogenation of the C4-C5 double bond was achieved using 5% palladium on barium carbonate as the catalyst and ethyl acetate as the solvent (Scheme 3). Two diastereomeric aldehydes, resulting from the addition of hydrogen to either the α or β-face of 4, were formed in the reaction; however, either product could be obtained selectively depending on the conditions. Aldehyde 10, having the β-L configuration, was isolated in 82% yield after a reaction time of 40 minutes, along with only traces of diastereomeric aldehyde 5. When the reaction was conducted for 3 days in the presence of sodium carbonate, a mixture of aldehydes consisting of a 16.5:1 ratio of 5 to 10 was isolated in 77% yield. These results suggest that reduc-



a: H_2, 5% Pd/$BaCO_3$, EtOAc b: $NaBH_4$ c: DIBAL

SCHEME 3

tion of 4 occurs from the less hindered β-face to give 10 as the kinetic product, and that epimerization of 10 takes place at longer reaction times to give the more stable isomer 5. The diastereomeric aldehydes 5 and 10 are readily distinguished by ^{1}H-NMR spectroscopy at 200 MHz. The spectrum of 5 exhibits a signal for the H-4 axial proton at δ1.47 that is coupled trans diaxially to both H-5 and H-3 with J values of 11.1 and 12.7, respectively. A third large coupling constant is observed for $J_{2,3}$ in 5. Smaller values are observed for these couplings in the spectrum of 10 as well as different chemical shifts for nearly all protons. Aldehydes 5 and 10 were reduced to the corresponding D-xylo and L-arabino alcohols, (12) and (13), with sodium borohydride in methanol.

Selective reduction of the aldehyde functionality in 4 proved difficult owing to the instability of the product. Allylic alcohol 11 was obtained in yields of 20-30% by treatment of 5 with either sodium borohydride in methanol or diisobutylaluminum hydride in toluene. Catalytic hydrogenation of 11, carried out as described above for the reduc-

tion of 4 to 10, gave a single product whose ^{1}H-NMR spectrum was identical with that of 12. This result was surprising, since the stereoselectivity of the reduction of 11 was expected to be similar to that of 4; namely, that which results from the addition of hydrogen to the β-face. The complete absence of 13 from the reaction product suggests that 11 exhibits a large preference for the addition of hydrogen to the opposite, α-face. In view of the anticipated steric hindrance of the axial methoxyl group toward addition to the α-face of 11, it is difficult to rationalize the exclusive formation of 12 in the reduction.

In conclusion, enodialdopyranoside 4, synthesized in six steps from methyl α-D-glucopyranoside, underwent selective 1,2 and 1,4-reductions of the enal functionality. Aldehyde 5, obtained by catalytic hydrogenation of 4 under basic conditions, is a well-developed precursor to higher-carbon sugars deoxygenated at C-4.

EXPERIMENTAL

General Procedures. Melting points were determined on a Thomas-Hoover melting point apparatus and are reported uncorrected. Infrared spectra were recorded on a Perkin-Elmer 299 infrared spectrophotometer or an Analect FX-6130 infrared spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian XL-200 spectrometer at 200.05 MHz. ^{13}C-NMR spectra were recorded on a Varian XL-200 at 50.3 MHz with complete proton decoupling. Coupling data for ^{13}C-NMR spectra were recorded using the gated decoupling 2-pulse sequence with an acquisition time of 0.5 sec and a delay of 0.75 sec. Chemical shifts for ^{1}H resonances were recorded relative to tetramethylsilane (0.0), deuteriochloroform (7.27), or deuteriobenzene (7.27). Chemical shifts for ^{13}C-NMR were recorded relative to tetramethylsilane (0.0), deuteriochloroform (76.91), or deuteriobenzene (128.5). Mass spectra were recorded on a Hewlett-Packard 5982-A spectrometer. High resolution mass spectra were recorded on a VG-7070H spectrometer at the Mass Spectrometry Center, University of Pennsylvania. Optical rotations were determined with a Perkin-Elmer 241 polarimeter at room temperature. Liquid chromatography was performed using a system which consisted of a Beckman 163 variable wavelength detector set at 254nm, a Beckman 110-B solvent delivery module, and a Kipp and Zonen recorder. Analytical columns (4.6 mm x 25 cm) were reverse phase and

contained Beckman Ultrasphere ODS as the stationary phase. The progress of reactions was monitored by thin-layer chromatography using aluminum supported plates of silica gel 60 (0.2 mm, F-254, E. Merck). Solvent systems consisted of ethyl acetate and petroleum ether in volume:volume ratios as indicated following the R_f value. Components were detected by observation under short wavelength ultraviolet light, spraying with concentrated sulfuric acid, and charring with a heat gun. Flash chromatography was performed on silica 60 (230-400 mesh) or florisil (60-100 mesh). Chloroform and dichloromethane were dried by passing through a column of basic alumina (Woelm, activity 1). Tetrahydrofuran was distilled from calcium hydride; methanol was dried by distillation from magnesium; pyridine was dried by distillation from barium oxide; benzene was dried by distillation from sodium benzophenone; dimethylsulfoxide was dried by vacuum distillation from calcium hydride; and triethylamine was dried by distillation from barium oxide.

Methyl 2,3-di-O-benzyl-α-D-glucopyranoside 7. A mixture of 6 (7.15 g, 15.5mmol), ethanol (120mL), and p-toluenesulfonic acid monohydrate (0.04 g, 0.2 mmol) was stirred under reflux for 18 h (oil bath, 85-90°C). The reaction was cooled and transferred to a 500mL separatory funnel with chloroform (200 mL). The organic layer was washed with saturated sodium hydrogen carbonate solution (150 mL), water (150 mL), dried with anhydrous sodium sulfate, and concentrated under reduced pressure to afford a crude syrup contaminated with benzaldehyde. The crude product was taken up in a small amount of ethyl acetate and crystallized by adding low boiling pet. ether; yield, 4.36 g (75%). R_f: 0.29 (1:1) mp: 78-79°C, lit.[9] 79-80°C. $[\alpha]_D$: +16.5° (c 0.279, $CHCl_3$). IR (cm^{-1}, film): 3440 (OH). ^{1}H-NMR ($CDCl_3$): δ 2.00-2.80 (br s, 2H, OH), 3.08 (s, 3H, OCH_3), 3.47 (dd, 1H, $J_{2,3}$ = 9.5, $J_{2,1}$ = 3.4, H2), 3.67 (m, 1H, H4), 3.69 (br s, 1H, H5), 3.82 (br s, 2H, H6), 4.01 (dd, 1H, $J_{3,4}$ = 9.0, H3), 4.48 (ABq, 2H, OCH_2Ph), 4.59 (d, 1H, H1), 4.87 (ABq, 2H, OCH_2Ph), 7.00 - 7.30 (m, 6H, Ph), 7.30-7.40 (m, 4H, Ph). ^{1}H-coupled ^{13}C-NMR ($CDCl_3$): δ 55.2 (q, OCH_3), 62.4 (t, C6), 70.4 (d, C4/C5), 70.7 (d, C4/C5), 73.1 (t, OCH_2Ph), 75.4 (t, OCH_2Ph), 79.8 (d, C2/C3), 81.3 (d, C2/C3), 98.2 (d, C1), 128.0 (Ph), 128.1 (Ph), 128.5 (Ph), 128.6 (Ph), 138.0 (Ph), 138.7 (Ph). Anal. Calcd for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.52; H, 6.91.

Methyl 2,3-di-O-benzyl-4-O-methanesulfonyl-6-O-triphenylmethyl-α-D-glucopyranoside 8. To a solution of 8 (1.1 g, 2.9 mmol) in dry pyridine (50 mL) was added triphenylmethyl chloride (0.90 g, 3.3 mmol), and the mixture was stirred at room temperature for three days. The reaction mixture was poured into cold water (50 mL) in a separatory funnel and was extracted with ether (300 mL). The organic layer was washed with 2.5% hydrochloric acid solution (1 x 200 mL), saturated sodium hydrogen carbonate solution (1 x 200 mL), and water (2 x 100 mL), dried with anhydrous sodium sulfate, and concentrated under reduced pressure. Traces of water and pyridine were removed by azeotroping with benzene. The crude product was dried under vacuum and purified by flash chromatography to give methyl 2,3-di-O-benzyl-6-O-triphenylmethyl-α-D-glucopyranoside as a viscous syrup (1.72 g, 98%). R_f: 0.73 (1:3). $[\alpha]_D$: + 4.66° (c 0.3, $CHCl_3$) lit.[10] +14.5° (c, 3, $CHCl_3$). IR (cm^{-1}, film): 3500 (OH). ^{1}H-NMR ($CDCl_3$): δ 3.20 - 3.40 (m, 2H, H6), 3.42 (s, 3H, $-OCH_3$), 3.48 - 3.60 (m, 2H, H2/H4) 3.60 - 4.00 (m, 2H, H3/H4), 4.67 (d, $J_{1,2}$ = 3.5, H1), 4.72 (ABq, 2H, OCH_2Ph), 4.86 (ABq, 2H, OCH_2Ph), 7.20 - 7.40 (m, 25H, Ph). ^{1}H-coupled ^{13}C-NMR ($CDCl_3$): δ 55.1 (q, OCH_3), 63.9 (t, C6), 69.9 (d, C4/C5), 71.6 (d, C4/C5), 73.1 (t, OCH_2Ph), 75.6 (t, OCH_2Ph), 79.7 (d, C2/C3), 81.6 (d, C2/C3), 86.8 (s, $OCPh_3$), 98.0 (d, C1), 127.0 ($OCPh_3$), 127.8 ($OCPh_3$), 128.0 (OCH_2Ph), 128.5 (OCH_2Ph), 128.7 ($OCPh_3$), 138.2 (OCH_2Ph), 138.8 (OCH_2Ph), 143.8 (CPh_3). Anal. Calcd for $C_{39}H_{40}O_6$: C, 77.46; H, 6.67. Found: C, 77.62; H, 6.78.

To a stirred solution of the 6-O-tritylether (7.02 g, 11.4 mmol) in pyridine (100 mL) at 0°C was added methanesulfonyl chloride (3 mL, 39 mmol) in chloroform (25 mL) over a 20-minute period. The reaction was stirred overnight at room temperature, poured into water (200 mL), and extracted with ether. The organic layer was washed with 5% hydrochloric acid solution (1 x 200 mL), saturated sodium hydrogen carbonate solution (1 x 200 mL), and water (2 x 150 mL), dried with anhydrous sodium sulfate, and concentrated under reduced pressure. Column chromatography on silica gel afforded 9 was a white amorphous solid (4.08 g, 52%). R_f: 0.82 (1:3). mp: 143-144°C. $[\alpha]_D$: +20.0° (c 0.195, $CHCl_3$). IR (cm^{-1}, film): 1360/1180 ($-S(=O)_2$). ^{1}H-NMR ($CDCl_3$): δ 2.52 (s, 3H, OSO_2CH_3), 3.26 (dd, 1H, $J_{6,6'}$ = 10.5, $J_{5,6}$ = 6.7, H6), 3.43 (dd, 1H, $J_{5,6'}$ = 1.9, H6'), 3.51 (s, 3H, OCH_3), 3.61 (dd, 1H, $J_{1,2}$ = 3.6, $J_{2,3}$ = 9.6, H2), 3.80 - 4.05 (m, 2H, H3,H5), 4.43 (dd, 1H, $J_{3,4}$ = 9.3, $J_{4,5}$ = 10.1, H4),

4.69 (d, 1H, H1), 4.72 (ABq, 2H, J = 12.0 OCH_2Ph), 4.85 (ABq, 2H, OCH_2 Ph), 7.20 - 7.60 (m, 25H, Ph). ^{1}H-coupled ^{13}C-NMR ($CDCl_3$): δ 38.5 (q, OSO_2CH_3) 55.3 (q, OCH_3), 62.8 (t, C6), 68.8 (d, C5), 73.5 (t, OCH_2Ph), 75.7 (t, OCH_2Ph), 78.1 (d, C4), 79.0 (d, C2/C3), 80.2 (d, C2/C3), 86.8 (s, $OCPh_3$), 97.4 (d, C1), 127.1 ($OCPh_3$), 127.8 ($OCPh_3$), 128.1 (OCH_2Ph), 128.4 (OCH_2Ph), 128.5 (OCH_2Ph), 128.8 ($OCPh_3$), 137.8 (OCH_2Ph), 137.9 (OCH_2Ph), 143.6 ($OCPh_3$). Anal. Calcd for $C_{41}H_{42}O_8S$: C, 70.87; H, 6.09. Found: C, 70.78; H, 6.01.

Methyl 2,3-di-O-benzyl-4-O-methanesulfonyl-α-D-glucopyranoside 9. A solution of 10 (4.04 g, 5.9 mmol) and p-toluenesulfonic acid (40 mg) in ethanol (120 mL) was stirred under reflux overnight. The reaction was transferred to a 500 mL separatory funnel and diluted with chloroform (200 mL). The mixture was washed with saturated sodium hydrogen carbonate (2 x 100 mL), dried with anhydrous sodium sulfate, and concentrated under reduced pressure. Column chromatography on silica gel (1:1 ethyl acetate: petroleum ether) gave a residue which was crystallized from petroleum ether (bp 30-60°C); yield, 1.62 g (63%). R_f: 0.3 (1:1). mp: 83-84°C. $[\alpha]_D$: +40.9° (c 0.235, $CHCl_3$). IR (cm^{-1}, film): 3540 (OH), 1353/1178 ($-S(=O)_2$). ^{1}H-NMR ($CDCl_3$): δ 2.80 (s, 3H, OSO_2CH_3), 3.34 (s, 3H, OCH_3), 3.60 (dd, 1H, $J_{2,3}$ = 9.6, $J_{2,1}$ = 3.5, H2), 3.68 - 3.97 (m, 3H, H5,H6), 4.05 (dd, 1H, $J_{4,3}$ = 9.7, H4), 4.63 (d, 1H, H1), 4.71 (ABq, 2H, J = 12.0, OCH_2Ph), 4.88 (ABq, 2H, J = 11.1, OCH_2Ph), 7.33 (br s, 10H, Ph). ^{1}H-coupled ^{13}C-NMR ($CDCl_3$): δ 38.3 (q, OSO_2CH_3), 55.5 (q, OCH_3), 60.4 (t, C6), 69.6 (d, C5), 73.3 (t, OCH_2Ph), 75.7 (t, OCH_2Ph), 77.6 (d, C4), 78.5 (d, C2/C3), 80.2 (d, C2/C3), 97.7 (d, C1), 127.8 (Ph), 127.9 (Ph), 128.2 (Ph), 128.5 (Ph), 128.6 (Ph), 137.5 (s, Ph), 137.9 (Ph). Anal. Calcd for $C_{22}H_{28}O_8S$: C, 58.39; H, 6.24. Found: C, 58.32; H, 6.23.

Methyl 2,3-di-O-benzyl-4-deoxy-β-L-threo-hex-4-enodialdopyranoside 4. To a solution of 10 (2.50, 5.5 mmol) in dry dimethylsulfoxide (25 mL) and dry triethylamine (11 mL, 77 mmol), stirred for 20 min, was added sulfur trioxide pyridine complex (2.60 g, 16.4 mmol) in dry dimethylsulfoxide (25 mL). The reaction was stirred 30 min and then poured into cold water (25 mL) in a separatory funnel and extracted with chloroform. The organic extracts were washed with saturated tartaric acid solution (1 x 50 mL), saturated sodium hydrogen carbonate (1 x 50 mL), water (1 x 50 mL), dried with anhydrous sodium sulfate, and concentrated to a resi-

due under reduced pressure. Column chromatography on silica gel (1:3 ethyl acetate:petroleum ether) afforded the product as a viscous syrup (1.63 g, 83%). R_f: 0.83 (1:1). $[\alpha]_D$: +147.7°(c 0.627, $CHCl_3$). IR (cm^{-1}, film): 2730 (CHO), 1700 (C = O), 1640 (C = C). ^{1}H-NMR ($CDCl_3$): δ 3.45 (s, 3H, OCH_3), 3.80 (dd, 1H, $J_{2,1}$ = 2.57, $J_{2,3}$ = 8.09, H2), 4.48 (dd, $J_{3,4}$ = 2.74, H3), 4.73 (ABq, 2H, OCH_2Ph), 4.76 (ABq, 2H, OCH_2Ph), 4.94 (d, 1H, H1), 5.87 (d, 1H, H4), 7.35 (br s, 10H, Ph), 9.17 (s, 1H, CHO). ^{1}H-coupled ^{13}C-NMR ($CDCl_3$): δ 57.0 (q, OCH_3), 72.6 (t, OCH_2Ph), 73.2 (d, C2/C3), 73.5 (t, OCH_2Ph), 76.3 (d, C2/C3), 99.8 (d, C1), 120.6 (dd, C4), 127.8 (Ph), 128.0 (Ph), 128.0 (Ph), 128.1 (Ph), 128.6 (Ph), 137.6 (Ph), 137.8 (Ph), 148.3 (s, C5), 186.1 (s, C6). CI - MS, m/z (relative intensity): 355 (1, M + H), 337 (2, M + H-H_2O), 323 (3, M + H-MeOH), 295 (30, M + H-OMe-CHO), 248 (17, M + H-OCH_2Ph), 247 (100, M + H-$PhCH_2OH$), 215 (19, M + H-MeOH-$PhCH_2OH$), 187 (M + H-OMe-CHO-$PhCH_2$), 91 (17, C_7H_7); exact mass calcd for $C_{21}H_{22}O_5$: 354.1467, found, 354.1454.

Methyl 2,3-di-O-benzyl-4-deoxy-β-L-arabino-hexodialdopyranoside 10. A mixture of 4 (0.44 g, 1.2 mmol), methanol (50 mL), and 5% palladium on barium carbonate (0.88 g) was stirred under hydrogen (balloon) in a 10 mL flask for 40 min. The reaction mixture was filtered through celite in a scintered glass funnel and concentrated under reduced pressure to afford a mixture of 5, 4, and 11. Column chromatography on silica gel gave pure 11 as a clear colorless liquid (0.36 g, 82%). R_f: 0.81 (1:1). $[\alpha]_D$: +13.9°(c 1.84, $CHCl_3$). IR (cm^{-1}, film); 1728 (C = O). ^{1}H-NMR ($CDCl_3$): δ 1.76 (ddd, 1H, $J_{4,4'}$ = 13.5, $J_{4,3}$ = 7.90, $J_{4,5}$ = 5.39, H4), 2.43 (ddd, 1H, $J_{4',5}$ = 5.51, $J_{4',3}$ = 4.30, H4'), 3.48 (dd, 1H, $J_{1,2}$ = 2.60, $J_{2,3}$ = 7.36, H2), 3.54 (s, 3H, OCH_3), 3.78 (ddd, 1H, H3), 4.16 (t, 1H, $J_{5,4}$ = 5.29, H5), 4.61 (s, 2H, OCH_2Ph), 4.72 (d, 1H, H1), 4.75 (ABq, 2H, OCH_2Ph), 7.33 (br s, 10H, -Ph), 9.70 (s, 1H, CHO). ^{1}H-coupled ^{13}C-NMR ($CDCl_3$): δ 28.0 (t, C4), 57.4 (q, $-OCH_3$), 72.0 (d, C2/C3/C5), 72.7 (d, C2/C3/C5), 73.5 (d, C2/C3/C5), 76.4 (t, OCH_2Ph), 77.3 (t, OCH_2Ph), 101.1 (d, C1), 127.5 (Ph), 127.6 (Ph), 127.7 (Ph), 127.8 (Ph), 138.1 (Ph), 138.2 (Ph), 201.4 (d, C6). CI-MS, m/z (relative intensity): 374 (33, M + NH_4), 324 (10, M-MeOH), 295 (18, M-MeOH-CHO), 265 (100, M + NH_4-$PhCH_2OH$), 240 (35), 217 (54, M-MeOH-OCH_2Ph), 181, 159 (60, M + NH_4-OCH_2Ph-$PhCH_2OH$), 121 (99); exact mass calcd for $C_{21}H_{28}O_5N$: 374.1967, found, 374.1992.

Methyl 2,3-di-O-benzyl-4-deoxy-α-D-xylo-hexodialdopyranoside 5. A mixture of 4(1.60 g, 4,5 mmol), methanol (50 mL), and 5% palladium on

barium carbonate (1.76 g) was stirred under hydrogen (balloon) for 18 h. Sodium carbonate (0.78 g, 7.4 mmol) was added, and the reaction was stirred an additional 46 h. Solids were removed by filtration through celite, and the filtrate was concentrated under reduced pressure to a volume of 60 mL and diluted with dichloromethane (100 mL). The solution was extracted with water, dried with anhydrous sodium sulfate, and concentrated under reduced pressure to afford 5 as a clear viscous syrup (1.24 g, 77%) which was contaminated with traces of β-L-isomer. Separation was effected by flash chromatography (silica gel) to give an isolated α to β ratio of 16.5:1. R_f: 0.52 (1:1). $[\alpha]_D$: +23.2°(c 2.95, $CHCl_3$). IR (cm^{-1}, film): 1725 (C = O). ^{1}H-NMR ($CDCl_3$): δ 1.47 (ddd, 1H, $J_{4,4'}$ = 12.7, $J_{4,5}$ = 11.1, $J_{4,3}$ = 12.7, H4), 2.35 (ddd, 1H, $J_{4',5}$ = 5.0, $J_{4',3}$ = 2.9, H4'), 3.41 (s, 3H, OCH_3), 3.46 (dd, 1H, $J_{2,1}$ = 5.6, $J_{2,3}$ = 9.6, H2), 3.97 (ddd, 1H, H3), 4.16 (dd, 1H, H5), 4.72 (ABq, 2H, OCH_2Ph), 4.75 (d, 1H, H1), 4.75 (ABq, 2H, OCH_2Ph), 7.35 (br s, 10H, Ph), 9.61 (s, 1H, CHO). ^{13}C-NMR ($CDCl_3$): δ 31.6 (C4), 55.7 (OCH_3), 72.2, 72.4, 73.5, 74.5, 79.7 (OCH_2Ph), 99.3 (C1), 127.5, 127.8, 127.9, 127.9, 128.0, 127.3, 128.3, 138.1 (Ph), 138.3 (Ph), 199.6 (CHO).

Methyl 2,3-di-O-benzyl-4-deoxy-β-L-threo-hex-4-enopyranoside 11.

To a stirred solution of 4 (1.50 g, 4.2 mmol) in dry toluene (50 mL) at 0°C was added diisobutylaluminum hydride (4.3 mL, 1M in hexane, 4.3 mmol) by syringe. Aliquots (1.0 mL) of DIBAL again were added after 25 min and 75 min while the reaction temperature was allowed to rise to 15°C over a 90 min period. After 90 min, the reaction was transferred to a 250 mL beaker which contained ice water (100 mL). After brief stirring (5 min), the gelatinous mixture was filtered with a Buchner funnel into a 500 mL separatory funnel. The mixture was extracted with dichloromethane (1 x 150 mL), dried with anhydrous sodium sulfate and concentrated under reduced pressure at 50°C to afford the crude product and traces of starting material. Column chromatography on Florisil (1:9 ethyl acetate:petroleum ether) afforded the acid sensitive product as a colorless syrup (0.31 g, 21%). R_f: 0.50 (40%). $[\alpha]_D$: +155.2°(c 0.42, C_6H_6). IR (cm^{-1}, film): 3380 (-OH), 1670 (C = C). ^{1}H-NMR (C_6D_6): δ 2.85 (t, 1H, $J_{6,OH}$ = 6.3, OH), 3.27 (s, 3H, OCH_3), 3.86 (dd, 1H, $J_{2,3}$ = 6.3, $J_{2,1}$ = 2.2, H2), 4.02 (d, 2H, H6), 4.36 (dddd, 1H, $J_{3,4}$ = 3.1, $J_{3,1}$ = 1.5, $J_{3,6}$ = 1.5, H3), 4.52 (ABq, 2H, OCH_2Ph), 4.66 (s, 2H, OCH_2Ph), 4.88 (d, 1H, H1), 5.17

(ddd, 1H, $J_{4,6}$ = 1.0, H4), 7.10 - 7.50 (m, 10H, $OCH_2\underline{Ph}$). ^{1}H-coupled ^{13}C-NMR (C_6D_6): δ 56.4 (qd, OCH_3), 61.9 (td, C6), 71.0 ($O\underline{CH}_2Ph$) 73.1 ($O\underline{CH}_2Ph$), 73.8 (d, C2/C3), 77.2 (d, C2/C3), 97.0 (d, C4), 100.0 (dd, C1), 127.7, 127.8, 128.0, 128.1, 128.6, 139.2 (Ph), 139.4 (Ph), 152.7 (dd, C5). Cl-MS, m/z (relative intensity): 374 (M + NH_4), 357 (M + H), 339 (M + H-H_2O), 325 (M + H-MeOH), 307 (M + H-H_2O-MeOH), 283 (M + H-C_7H_7), 265 (M + NH_4-C_7H_7-H_2O), 250 (M + H-OCH_2Ph), 231 (M + H-MeOH-$PhCH_2OH$), 159 (M + NH_4-C_7H_7-H_2O-$PhCH_2Ph$), 144 (M + H-OCH_2Ph-$PhCH_2OH$), 127 (M + H-MeOH-$PhCH_2$-OH-C_7H_7 + H); exact mass calcd for $C_{21}H_{25}O_5$: 357.1702, found, 357.1706.

Methyl 2,3-di-O-benzyl-4-deoxy-α-D-xylo-hexopyranoside 12.

a. From 5. Sodium borohydride (24 mg, 0.63 mmol) was added to a solution of 5 (0.215 g, 0.60 mmol) in dry methanol at room temperature with stirring. After 5 min, excess borohydride was decomposed with 2.5% hydrochloric acid solution (1 mL), the solution was filtered through layers of sodium sulfate and florisil with ethyl acetate, and evaporated under reduced pressure to give syrupy 13 (0.201 g, 93%). R_f: 0.34 (1:1). $[\alpha]_D$: +75.4°(c 1.425, CH_2Cl_2). IR (cm^{-1}, film): 3410 (OH). ^{1}H-NMR (C_6D_6): δ 1.42 (ddd, 1H, $J_{4,3}$ = 12.1, $J_{4,5}$ = 12.1, $J_{4,4'}$ = 12, H4), 1.68 (ddd, 1H, $J_{4',3}$ = 5.26, $J_{4',5}$ = 2.50, H4'), 3.12 (s, 3H, OCH_3), 3.35 (d, 1H, $J_{6,5}$ = 3.29, H6), 3.37 (d, 1H, $J_{6',5}$ = 1.37, H6'), 3.44 (dd, 1H, $J_{2,3}$ = 9.38, $J_{1,2}$ = 3.51, H2), 3.50 - 3.60 (m, 1H, H5), 4.00 (ddd, 1H, H3), 4.57 (s, 2H, OCH_2Ph), 4.63 (ABq, 2H, OCH_2Ph), 4.67 (d, 1H, H1), 7.17 (br s, 6H, Ph-H), 7.30 - 7.40 (br m, 4H, Ph-H). ^{13}C-NMR (C_6D_6): δ 33.6 (C4), 54.9 (OCH_3), 65.5, 68.5, 72.3, 73.1, 75.2, 81.7, 99.4 (C1), 139.6 (Ph), 139.9 (Ph). Exact mass calcd for $C_{21}H_{30}NO_5$ (M + NH_4), 376.2124. Found: 376.2120.

b. From 12. Catalytic hydrogenation of 12 was conducted at 1 atm (balloon) using 5% $Pd/BaCO_3$ as the catalyst in ethyl acetate as described for the reduction of 4 to 11. The ^{1}H-NMR spectrum of the product was identical with that shown above for 12 synthesized by sodium borohydride reduction of 5.

Methyl 2,3-di-O-benzyl-4-deoxy-β-L-arabino-hexopyranoside 13. The reduction of 11 was carried as described above for 5. From (0.36 g, 1.0 mmol) 11 there was obtained 0.22 g (61%) of syrupy 13 which displayed the following properties. R_f: 0.27 (1:1). $[\alpha]_D$: +56.8°(c 2.46, $CHCl_3$). IR (cm^{-1}, film): 3400 (-OH). ^{1}H-NMR ($CDCl_3$): δ 1.56 (ddd, 1H, $J_{4,4}$ =

14.0, $J_{4eq,5}$ = 2.64, $J_{4eq,3}$ = 2.64, H4eq), 1.85 (ddd, 1H, $J_{4ax,5}$ = 11.3, $J_{4ax,3}$ = 3.0, H4ax), 3.00 (br s, 1H, OH), 3.53 (d, 1H, $J_{6,5}$ = 2.1, H6), 3.54 (s, 3H, OCH_3), 3.57 (m, 1H, H2), 3.64 (d, 1H, $J_{6,6}$ = 1.8, H6'), 3.74 (ddd, 1H, $J_{3,2}$ = 3.5, H3), 3.94 (m, 1H, H5), 4.44 (s, 2H, $O\underline{CH}_2Ph$), 4.71 (d, 1H, $J_{1,2}$ = 1.4, H1), 4.72 (ABq, 2H, J = 12.5, $O\underline{CH}_2Ph$), 7.20 - 7.45 (m, 10H, Ph-H). ^{1}H-coupled ^{13}C-NMR ($CDCl_3$): δ 27.1 (t, C4), 56.7 (q, $-OCH_3$), 65.4 (t, C6), 70.8 (t, $O\underline{CH}_2Ph$), 71.5 (d, C2/C3/C5), 73.4 (t, $O\underline{CH}_2Ph$), 73.5 (d, C2/C3/C5), 100.5 (d, C1), 127.2 (Ph), 127.4 (Ph), 127.5 (Ph), 127.7 (Ph), 128.1 (Ph), 128.2 (Ph), 137.9 (Ph), 138.3 (Ph).

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