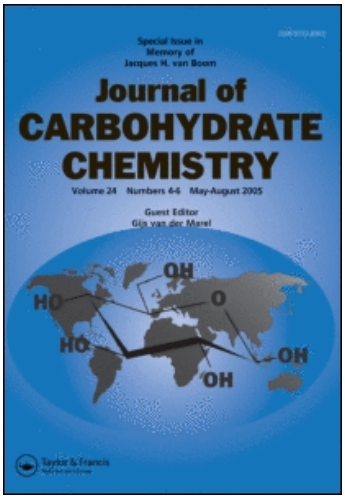

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Synthesis of 3-Substituted Xylopyrnosides from 2,3-Anhydropentosides

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SYNTHESIS OF 3-SUBSTITUTED XYLOPYRANOSIDES FROM 2,3-ANHYDROPENTOSIDES

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ABSTRACT

The facile regio- and stereoselective epoxide ring-opening of anhydropentosides described herein provides an attractive pathway to 3-substituted analogs of pentosides. Benzyl 2,3-anhydro-β-D-ribopyranoside (**2**) and benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) were obtained from benzyl β-D-arabinopyranoside (**1**) and benzyl β-L-arabinopyranoside (**3**) respectively. The anhydropentosides were converted to the corresponding new 3-amino derivatives (**8**, **9**, **10**, and **11**), alkoxy derivatives (**12**, **13**, and **14**), and deoxy sugar (**15**) in high yield. Every conversion was a one-step reaction of the anhydroglycoside with the appropriate nucleophile. Side-products due to epoxide migration were not observed.

INTRODUCTION

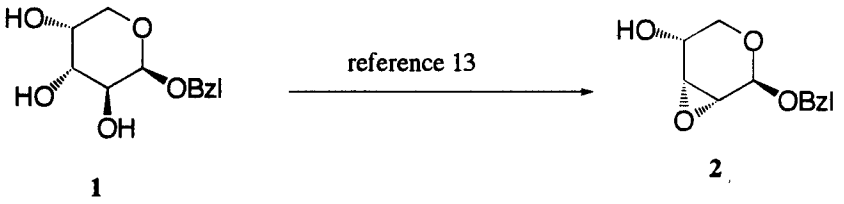
Xylopyranosides substituted selectively at the 3-position can be obtained by protecting the 2- and 4-hydroxyls using phenylboronic acid, followed by derivatizing the free 3-hydroxyl group. A limitation of boronate protection is the susceptibility of these esters to alcoholysis and hydrolysis. Boronate esters must be handled under anhydrous, alcohol-free conditions.[1] An alternative route to substituted xylopyranosides consists of epoxide ring-opening of anhydropentosides. The anhydroglycosides are versatile intermediates because they react with a wide range of nucleophiles to give substituted carbohydrates.[2-9] Furthermore, epoxide-ring opening of anhydroglycosides is a well-established reaction, and the factors leading to stereo- and regioselectivity in carbohydrate epoxide ring-opening have been extensively investigated.[10,11]

Recently, we used benzyl 3-*O*-methyl-β-D-xylopyranoside and benzyl 3-deoxy-β-D-*erythro*-pentopyranoside to determine the structural requirements for an enzyme involved in glycosaminoglycan biosynthesis.[12] Herein, we report the synthesis of 3-substituted xylopyranosides from benzyl 2,3-anhydro-β-D-ribopyranoside (**2**) and benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) by epoxide ring-opening using alkoxides, acetate, hydride, and amines. The 3-substituted xylopyranosides were obtained in high yield.

RESULTS AND DISCUSSION

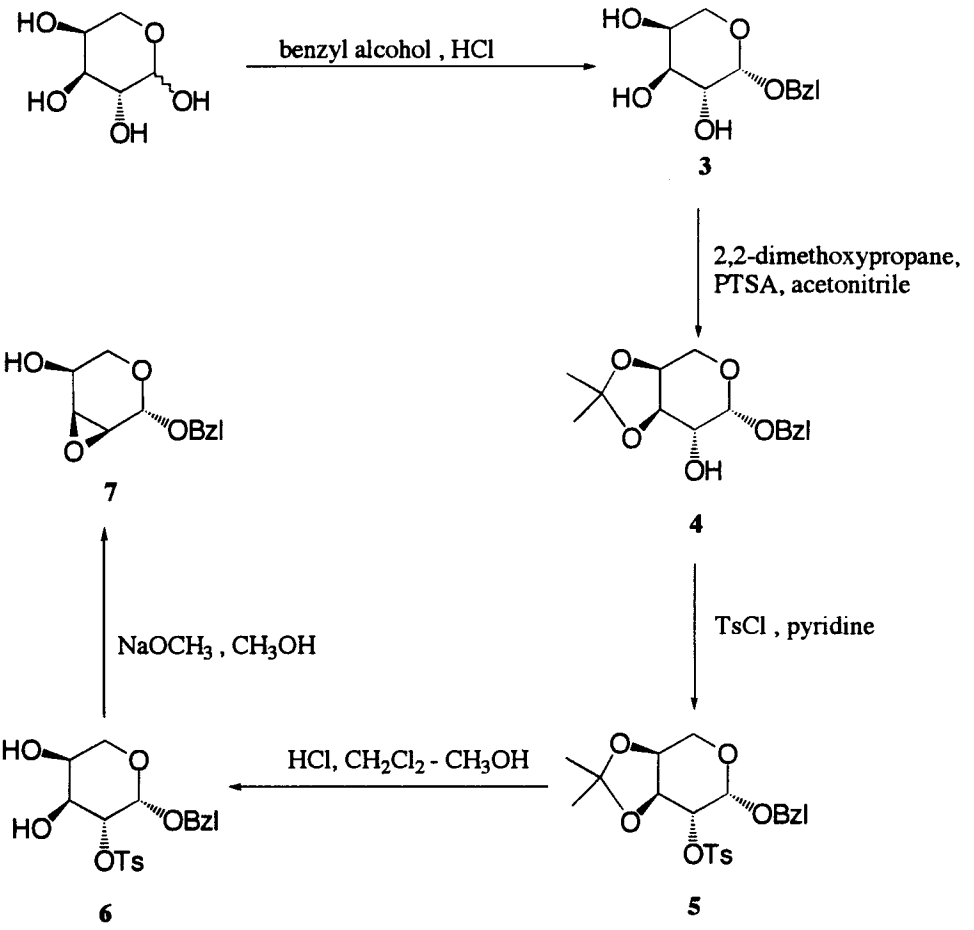
Benzyl 2,3-anhydro-β-D-ribopyranoside (**2**) was prepared from benzyl-β-D-arabinopyranoside (**1**) by following the reported method.[13] A similar method (Scheme 2), was used to synthesize benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) starting from benzyl-β-L-arabinopyranoside (**3**). Acid catalyzed condensation of L-arabinose and benzyl alcohol gave benzyl β-L-arabinopyranoside (**3**). Treatment of compound **3** with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid gave **4**. Reaction of compound **4** with *p*-toluenesulfonyl in pyridine yielded benzyl 3, 4-*O*-isopropylidine-2-tosyl-β-L-arabinopyranoside (**5**). Benzyl 2-tosyl-β-L-arabinopyranoside (**6**), was obtained by treating compound **5** with HCl in dichloromethane-methanol mixture; the anhydropentoside (**7**) was obtained by subsequent treatment with sodium methoxide.

The products of epoxide ring-opening are shown in Schemes 3 and 4. No side-products due to epoxide migrations were observed. The structures of the compounds were confirmed by ^{1}H and ^{13}C NMR (see Experimental). These 3-substituted derivatives neither consumed periodate nor reacted with lead tetraacetate, indicating the absence of vicinal *cis*-diol which would have been formed if nucleophilic attack took place at the 2-position. A quantitative yield of benzyl 3-deoxy-3-(diethylamino)-β-L-xylopyranoside (**11**) was obtained when benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) was refluxed in diethylamine in the presence of aluminum isopropoxide. Benzyl 3-deoxy-3-(diethylamino)-β-L-xylopyranoside (**11**) was previously obtained in only 45% yield by using *N*,*N*-diethyltrimethylsilylamine in the presence of anhydrous aluminum chloride.[14] The use of aluminum isopropoxide instead of aluminum chloride greatly improved the yield. When benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) was refluxed in diethylamine without aluminum isopropoxide no product was formed. The less hindered amines did not require use of a Lewis acid in order to react efficiently with the anhydropentosides. *n*-Octylamine reacted with benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) to give the corresponding 3-substituted amino analog (**10**) in high yield. *n*-Amylamine and piperidine also reacted with benzyl 2,3-anhydro-β-D-ribopyranoside (**2**) to give benzyl 3-deoxy-3-(pentylamino)-β-D-xylopyranoside (**8**) and benzyl 3-deoxy-3-(1-piperidino)-β-D-xylopyranoside (**9**)

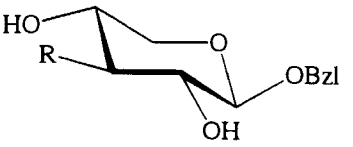


1 2

Scheme 1

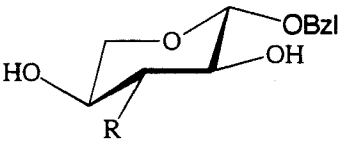


Scheme 2



8 R = -NH(CH_2)$_4CH_3$ **9** R = -N

Scheme 3



10 R = - NH(CH_2)$_7CH_3$ **12** R = -OCOCH$_3$ **14** R = -OCH_2CH_2OH

11 R = -N **13** R = -OCH_3 **15** R = -H

Scheme 4

respectively. Epoxide ring-opening of benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) with sodium ethylene glycol alkoxide was also achieved and produced benzyl 3-deoxy-3-*O*-(2-hydroxyethyl)-β-L-xylopyranoside (**14**) in good yield. The product was separated from the high-boiling ethylene glycol by column chromatography on reversed phase silica gel.[15] Reaction of benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) with sodium methoxide under gentle reflux gave benzyl 3-*O*-methyl-β-L-xylopyranoside (**13**), which was purified by recystallization form isopropyl alcohol. The ^{1}H-^{1}H COSY NMR of (**13**) indicated the appropriate regiochemistry.[16]

Attempted synthesis of benzyl 3-*O*-acetyl-β-L-xylopyranoside (**12**) using aluminum oxide and acetic acid in ether[17] was not successful. The target compound was obtained only when benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) and an equimolar amount of sodium

acetate were refluxed in acetic acid. Benzyl 3-*O*-acetyl-β-L-xylopyranoside (**12**) was separated from the unreacted starting material and the unidentified side-products by column chromatography. Treatment of benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) with lithium aluminum hydride afforded benzyl 3-deoxy-β-L-*erythro*-pentopyranoside (**15**).

These examples indicate that the regio- and stereoselective epoxide ring-opening of benzyl 2,3-anhydro-β-D-ribopyranoside (**2**) and benzyl 2,3-anhydro-β-L-ribopyranoside (**7**) provides an efficient route to 3-substituted xylopyranosides. Reaction of the anhdydroglycosides is especially facile with amines. Several 3-substituted amino xylopyranosides were synthesized by refluxing different amines with the anhydroglycosides. Other nucleophiles also opened the epoxide in a predictable manner to furnish different 3-substituted xylopyranosides.

One of the interesting findings of this study is that ethylene glycol alkoxide will react with benzyl 2,3-anhydro-β-L-ribopyranoside to produce benzyl 3-deoxy-3-*O*-(2-hydroxyethyl)-β-L-xylopyranoside. The primary hydroxyl group of this product may be manipulated to obtain other branched xylopyranosides. These glycosides will be used in further studies of carbohydrate-metabolizing enzymes and to study the processes in which these enzymes are involved.

EXPERIMENTAL

General methods. Melting points were determined with Fisher-Johns melting point apparatus and are not corrected. Optical rotations were measured with a Rudolf Polarimeter model 80 at 25 °C, with concentrations in g/mL. NMR spectra were recorded at 298K in Me_2SO using a Varian-Gemini 200 spectrometer (200 MHz for ^1H and 50.1 MHz for ^{13}C). Chemical shifts are expressed in parts per million downfield from TMS. The composition of reaction mixtures was monitored by TLC using alumina sheets precoated with silica gel $60F_{254}$ (0.2 mm thickness, E. Merck, Darmstadt, Germany); detection was effected by observation under short wavelength UV light (254 nm), then spraying with 5% H_2SO_4 in methanol and charring with heat. Column chromatography was performed using silica gel 60Å (0.063-200 mm, E. Merck). Elemental analyses were performed by the Robertson Microlit Laboratories, Inc., (Madison, NJ, USA).

Benzyl 2,3-Anhydro-β-D-ribopyranoside (2) was obtained by following the reported method.[13]

Benzyl 3-Deoxy-3-(pentamino)-β-D-xylopyranoside (8). Benzyl 2,3-anhydro-β-D-ribopyranoside **2** (0.90 g, 4 mmol) and *n*-amylamine (5 mL) was refluxed for 4 h. Ethanol (10 mL) was added and the mixture concentrated. The solid was recrystallized from a mixture of ethyl acetate and hexane to give a pure **8** (1.1 g, 87%): mp

148-149 °C; $[\alpha]_D$ -106° (*c* 0.01, Me_2SO). ^1H NMR δ 0.9 (t, 3H, CH_3), 1.35 (bm, 6H, CH_2 pentyl), 2.3 (m, 1H), 2.7 (m, 1H), 3.1 (m, 1H), 3.75 (dd, J = 4.68, 11.00 Hz, 1H, H-5e), 4.30 (d, J = 7.24 Hz, 1H, H-1), 4.60 (d, J = 12.29 Hz, 1H, OCH_2Ar), 4.80 (d, J = 12.33 Hz, 1H, OCH_2Ar), 4.95 (s, 1H, OH), 5.20 (s, 1H, OH), 7.35 (m, 5H, Ar). ^{13}C NMR δ 14.27, 22.38, 29.29, 29.98, 48.45, 65.16, 66.79, 69.07, 69.80, 71.90, 103.30 C1, 127.65, 127.83, 128.42, 138.29.

Anal. Calcd for $C_{17}H_{27}NO_4$ (309): C, 66.02; H, 8.73; N, 4.53. Found: C, 66.09; H, 8.69; N, 4.49.

Benzyl 3-Deoxy-3-(1-piperidino)-β-D-xylopyranoside (9). A mixture of benzyl 2,3-anhydro-β-D-ribopyranoside **2** (0.45 g, 2 mmol) and piperidine (5 mL) was refluxed. After 4 h, the mixture was cooled, and ethanol (10 mL) added. The solid obtained after concentration was recrystallized from disopropyl ether to give pure **9** (0.54 g, 90%): mp 137-139 °C; $[\alpha]_D$ -71° (*c* 0.01, CH_2Cl_2). ^1H NMR δ 1.50 (bm, 6H, CH_2 piperidinyl), 2.20 (t, J = 10.09, 9.93 Hz, 1H, H_3), 2.80 (m, 4H, CH_2, piperidinyl), 3.10 (t, J = 10.18, 9.99 Hz, 1H, H-2), 3.30 (m, 1H), 3.50 (dd, J = 10.97, 3.95 Hz, 1H, H-5a), 3.80 (dd, J = 10.97, 5.09 Hz, 1H, H-5e), 4.25 (d, J= 9.44 Hz, 1H, H-1), 4.45 (d, J = 3.83, 1H, OH), 4.60 (m, 2H), 4.80 (d, J = 12.29 Hz, 1H, OCH_2Ar), 7.45 (bm, 5H, Ar). ^{13}C NMR δ 25.00, 26.90, 50.93, 65.09, 67.42, 68.89, 69.83, 72.27, 104.22 C1, 127.61,127.74, 128.40, 138.37.

Anal. Calcd for $C_{17}H_{25}NO_4$ (307): C, 66.45; H, 8.14, N, 4.50. Found: C, 66.40; H, 8.00; N, 4.63.

Benzyl β-L-Arabinopyranoside (3). A mixture of 100 g of L-arabinose in 400 mL of benzyl alcohol was saturated with hydrochloric acid gas and shaken overnight. Cold ethanol (1 L) was added and the mixture cooled at 4° for 3 h. The crystals were collected by filtration, dried and recrystallized from absolute ethanol to give 65 g of pure **3** Concentration of the mother liquor yielded another 10 g, mp 174-175 °C; $[\alpha]_D$ +154° (*c* 0.01, Me_2SO). ^1H NMR δ 3.45 (m, 1H), 3.70 (m, 4H), 4.45 (d, J = 12.37 Hz, 1H, OCH_2Ar), 4.60 (d, J = 4.52Hz, 1H, OH), 4.6 (d, J = 3.55 Hz, 1H, H-1), 3.70 (d, J = 12.41 Hz, 1H, OCH_2Ar), 3.75 (d, J = 3.17 Hz, 1H, OH), 3.85 (d, J = 2.40 Hz, 1H, OH), 7.35 (m, 5H, Ph). ^{13}C NMR δ 63.57, 68.57, 68.67, 68.90, 69.33, 99.19, 127.58, 127.71, 128.44, 138.47.

Benzyl 3,4-*O*-Isopropylidine-β-L-arabinopyranoside (4). Benzyl β-L-arabinopyranoside **3** (60 g, 0.25 mol), was suspended in acetonitrile (400 mL) and 2,2-dimethoxypropane (36 g, 42mL, 0.35 mol) in acetonitrile (100 mL) was added followed by *p*-toluenesulfonic acid monohydrate (1 g). The reaction mixture was stirred at room temperature. After 16 h, triethylamine was added to the light brown mixture to neutralize it. The solution was concentrated and the solid was recrystallized from a mixture of hexane

and diethyl ether, (61g, 86%): mp 58-59 °C; $[\alpha]_D$ +179° (*c* 0.08, CH_2Cl_2). ^1H NMR δ 1.30 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 3.55 (m, 1H), 3.85 (m, 2H), 4.05 (m, 1H), 4.25 (d, J = 5.62 Hz, 1H), 4.50 (d, J = 12.17 Hz, 1H, OCH_2Ar), 4.70 (d, J = 12.36 Hz, 1H, OCH_2Ar), 4.75 (d, J = 3.30 Hz, 1H, H-1), 5.20 (d, J = 6.63Hz, 1H, OH), 7.40 (m, 5H, Ph). ^{13}C NMR δ 26.55, 28.48, 58.80, 68.81, 70.09, 73.02, 75.88, 98.38, 107.92, 127.75, 127.81, 128.49, 138.02.

Anal. Calcd for $C_{15}H_{20}O_5$ (280): C, 64.28; H, 7.14. Found: C, 64.50; H, 7.40.

Benzyl 3,4-*O*-Isopropylidine-2-tosyl-β-L-arabinopyranoside (5). Benzyl 3,4-*O*-isopropylidine-β-L-arabinopyranoside **4** (56 g, 0.2 mol) was dissolved in pyridine (400 mL). *p*-Toluenesulfonyl chloride (57 g, 0.30 mol)) was added and the mixture stirred at room temperature. After 16 h, ice-water (150 mL) was added and the mixture extracted with dichloromethane (3x300mL). The organic layer was washed with 5% sodium bicarbonate (50 mL) and concentrated. Ethanol (3 x 60 mL) was added and the mixture concentrated again. The solid (73 g, 90%), was recrystallized from a mixture of ethyl acetate and hexane to give pure **5** (70 g, 86%): mp 92-93 °C; $[\alpha]_D$ +160° (*c* 0.25, CH_2Cl_2). ^1H NMR δ 1.10 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 2.5 (3H, CH_3), 3.92 (m, 2H), 4.20 (m, 2H), 4.40 (d, J = 12.08 Hz, 1H, OCH_2Ar), 4.70 (d, J = 12.09 Hz, 1H, OCH_2Ar), 4.90 (d, J = 2.12 Hz, 1H, H-1), 7.35 (bm, 5H, Ar), 7.50 (d, J = 8.14 Hz, 2H, OSO_2ArCH_3), 7.80 (d, J = 8.06 Hz, 2H, OSO_2ArCH_3). ^{13}C NMR δ 21.39, 26.28, 27.53, 58.23, 69.33, 72.04, 73.67, 79.55, 95.39 (C1), 108.69, 127.93, 128.09, 128.18, 128.62, 130.36, 131.55, 137.07, 145.49.

Anal. Calcd for $C_{22}H_{26}O_7S$ (434): C, 60.81; H, 6.03; S, 7.38. Found: C, 61.02; H, 6.01; S, 7.40.

Benzyl 2-Tosyl-β-L-arabinopyranoside (6). Benzyl 3,4-*O*-isopropylidine-2-tosyl-β-L-arabinopyranoside **5** (43 g, 0.1 mol) was dissolved in 400 mL of methanol/dichloromethane (1:1 v/v) mixture. Concentrated HCl (7.7 mL) was added and the mixture stirred at room temperature for 24 h. Triethylamine was added to neutralize the solution and the mixture concentrated. The solid was recrystallized from a mixture of ethyl acetate and hexane, (38 g, 92%): mp 123-124 °C; $[\alpha]_D$ +140° (*c* 0.2, CH_2Cl_2). ^1H NMR δ 2.40 (s, 3H, CH3), 3.45 (dd, 1H), 3.80 (m, 3H), 4.25 (d, J = 11.12 Hz, OCH_2Ar, 4.50 (m, 1H), 4.60 (d, J = 11.52 Hz, OCH_2Ar), 4.80 (d, J = 3.30 Hz, 1H, OH), 5.00 (d, J = 3.22 Hz, 1H, OH), 5.15 (d, J = 6.15 Hz, 1H), 7.35 (m, 5H, Ar), 7.50 (d, J = 7.98Hz, 2H, Ar), 7.75 (d, J = 8.26Hz, 2H, Ar). ^{13}C NMR δ 21.40, 63.53, 66.13, 69.08, 69.26, 79.02, 96.34, 127.79,127.89, 128.53, 130.19, 133.708, 137.59, 144.98.

Anal. Calcd for $C_{22}H_{22}O_7S$ (394): C, 57.86; H, 5.62; S, 8.13. Found: C, 57.90; H, 5.59 ; S, 7.99.

Benzyl 2,3-Anhydro-β-L-ribopyranoside (7). Benzyl 2-tosyl-β-L-arabinopyranoside **6** (20 g, 0.05 mol) was dissolved in 0.5 M sodium methoxide (450 mL) and stirred overnight at room temperature. The solution was neutralized with glacial acetic acid (1.1 mole equivalent) and concentrated. The solid (11 g, 90%) was recrystallized from isopropyl ether to give pure **7** (10 g, 81%): mp 73-74 °C; $[\alpha]_D$ +148° (*c* 0.2, CH_2Cl_2). ^1H NMR δ 3.25 (m, 3H), 3.40 (t, J = 4.42, 3.95 Hz, 1H, H3), 3.65 (dd, J = 4.85, 6.96 Hz, 1H H-5e), 3.95 (m, 1H, H-4), 4.60 (d, J = 11.72 Hz, 1H, OCH_2Ph), 4.75 (d, J = 11.77 Hz, OCH_2Ar), 4.95 (s, 1H, H-1). 5.20 (d J = 6.31 Hz, 1H, OH), 7.40 (m, 5H, Ar). ^{13}C NMR δ 52.52, 53.076, 61.58, 62.200, 69.72, 94.77, C_1, 127.93, 128.09, 128.58, 137.83.

Anal. Calcd for $C_{12}H_{14}O_4$ (222): C, 64.85; H, 6.35. Found: C, 64.69; H, 6.20; S, 6.90.

Benzyl 3-Deoxy-3-(octylamino)-β-L-xylopyranoside (10). Benzyl 2,3-anhydro-β-L-ribopyranoside **7** (220 mg, 2 mmol) and 5 mL of *n*-octylamine were gently heated under reflux for 2 h. The brown mixture was cooled and ethanol (10 mL) added. Concentration under high vacuum at room temperature yielded benzyl 3-octylamine-3-deoxy-β-L-xylopyranoside **10** as a yellowish solid. Recrystallization from ethyl acetate and hexane mixture gave white flakes ((370 mg, 99%): mp 129-130 °C; $[\alpha]_D$ +75.5° (*c* 0.2, Me_2SO). ^1H NMR δ 0.90 (t, 3H CH_3), 1.35 (bm, 6H octyl CH_2s), 1.65 (s, 1H), 2.30 (t, J = 8.69, 8.79, 1H), 2.70 (bs, 2H), 3.15 (m, 2H), 330 (m, 1H), 3.75 (dd, J = 4.39, 10.99 Hz, H-5e), 4.25 (d, J = 7.32 Hz, 1H, H-1), 4.55 (d, J = 12.09 Hz, 1H, OCH_2Ph), 4.75 (d, J = 12.09 Hz, 1H, OCH_2Ph), 4.90 (d, J = 5.29 Hz, 1H, OH), 5.15 (d, J = 5.25 Hz, 1H, OH), 7.35 (m, 5H, Ph). ^{13}C NMR δ 14.26, 22.39, 27.13, 29.03, 29.32, 30.56, 31.57, 48.66, 65.27, 66.80, 69.27, 69.77, 72.06, 103. 32 C1, 127.64, 127.82, 128.41, 138.32. 10

Anal. Calcd for $C_{20}H_{33}NO_4$ (351): C, 68.38; H, 9.40; N, 3.99. Found: C, 68.43; H, 9.44; N, 4.14.

Benzyl 3-Deoxy-3-(diethylamino)-β-L-xylopyranoside (11). Benzyl 2,3-anhydro-β-L-ribopyranoside **7** (0.5 g, 2.5 mmol) was refluxed in dimethylamine (8 mL) containing aluminum isopropoxide (100 mg). After 16 h, the mixture was concentrated and partitioned between ethyl acetate and water. The organic layer was concentrated and the syrup was purified on a short silica gel column to give benzyl 3-deoxy-3-(diethylamino)-β-L-xylopyranoside (0.7 g, 95%). ^1H NMR δ 1.00 (t, 6H, CH_3), 2.45 (q, J = 9.97, 10.17 Hz, 1H, H-3), 2.75 (q, 4H, CH_2), 3.20 (m, 2H), 3.50 (m, 1H), 3.85 (dd, J = 4.76, 11.35 Hz, 1H, H-5e), 4.35 (d, J = 7.32, 1H, H-1), 4.40 (d, J = 3.30 Hz, 1H, OH), 4.50 (d, J = 2.56 Hz, 1H, OH), 4.60 (d, J = 12.07 Hz, IH, OCH_2Ar), 4.80

(d, J = 12.07 Hz, 1H, OCH_2Ar), 7.35 (m, 5H, Ar). ^{13}C NMR δ 15.21, 44.43, 65.57, 67.44, 67.56, 69. 37, 69.90, 104.28, 127.63, 127.78, 128.41, 138.36.

Benzyl 3-*O*-Acetyl-β-L-xylopyranoside (12). A mixture of benzyl 2,3-anhydro-β-L-ribopyranoside **7** (0.44 g, 2 mmol) and sodium acetate (164 mg, 2 mmol) were gently refluxed in acetic acid (8 mL). After 1 h,[18] the reaction mixture was cooled and ethanol (25 mL) was added. The pure material was obtained after column chromatography using hexane-ethyl acetate mixture (250mg, 45%): mp 64-65 °C. ^1H NMR δ 2.05 (s, 3H, OAc), 3.20 (m, 2H), 3.50 (m, 1H), 3.80 (dd, J = 3.58,13.39Hz, 1H, H-5e), 4.35 (d, J = 7.73 Hz, 1H, H-1), 4.55 (d, J = 12.17 Hz, 1H, OCH_2Ar), 4.75 (t, J = 9.20, 8.13 Hz, 1H, H_3), 4.80 (d, J = 12.37 Hz, 1H, OCH_2Ar), 5.20 (d, J = 5.49 Hz, 1H, OH), 5.45 (d, J = 5.50 Hz, 1H, OH), 7.35 (m, 5H, Ar). ^{13}C NMR δ 21.38, 65.76, 67.80, 70.15, 71.31, 71.45, 77.84, 103.07, 127.71, 127.86, 128.43, 138.13, 170.00, C=O.

Anal. Calcd for $C_{14}H_{18}O_6$ (282): C, 59.57; H, 6.38. Found: C, 59.49; H, 6.30.

Benzyl 3-*O*-Methyl-β-L-xylopyranoside (13). Benzyl 2,3-anhydro-β-L-ribopyranoside **7** (450 mg, 2 mmol) and 1 M sodium methoxide in methanol (10 mL) were gently refluxed. After 6 hours, the mixture was cooled and neutralized with glacial acetic acid. The syrup obtained after concentration was partitioned between dichloromethane and water. The organic layer was dried (Na_2SO_4) and concentrated. The solid was recrystallized from isopropyl ether (406 mg, 80%): mp 122-123 °C; $[\alpha]_D$ 120° (*c* 0.01, CH_2Cl_2). ^1H NMR δ 2.90 (t, J = 8.84, 8.80 Hz, 1H, H-3), 3.10 (m, 2H), 3.45 (m, 1H), 3.70 (dd, J = 5.42, 11.07Hz, 1H, H-5), 4.25 (d, J = 7.51Hz, 1H, H-1), 4.55 (d, J = 12.33 Hz, 1H, OCH_2Ar), 4.80 (d, J = 12.21 Hz, 1H, OCH_2Ar), 5.15 (d, J = 6.41 Hz, 1H, OH), 5.85 (d, J = 6.46 Hz, 1H, OH), 7.35 (m, 5H, Ar). ^{13}C NMR δ 60.22, 65.90, 69.35, 70.00, 73.04, 86.67, 103.24 C_1, 127.67, 127.85, 128.42, 138.24.

Anal. Calcd for $C_{13}H_{18}O_5$ (254): C, 61.42; H, 7.09. Found: C, 61.12; H, 7.21.

Benzyl 3-deoxy-3-*O*-(2-hydroxyethyl)-β-L-xylopyranoside (14). Sodium (0.5 g) was reacted with previously dried ethylene glycol (8 mL). When the reaction was complete, benzyl 2,3-anhydro-β-L-ribopyranoside **7** (0.45g, 2 mmol) and 3Å molecular sieves (3 g) were added to the alkoxide . The mixture was gently heated under reflux. After 4 h thin-layer chromatography indicated completion of the reaction. Ethanol (15 mL) and acetic acid (10 mL) were added and the mixture filtered through a pad of Celite. After removal of ethanol and acetic acid under high vacuum, the product was purified using C-18 reversed phase Sep-pak cartridges.[18] An amorphous solid (0.42 g, 75%) was obtained. ^1H NMR δ 3.15 (m, 3H), 3.45, m, 4H), 3.75 (m, 3H), 4.30 (d, J = 7.28 Hz, 1H, H-1), 4.60 (d, J = 12.25 Hz, 1H, OCH_2Ar), 4.75 (d, J = 12.21 Hz, 1H,

OCH_2Ar), 5.5 (bs, 2H, OH), 7.35 (m, 5H, Ar). ^{13}C NMR δ 61.064, 65.82, 69.49, 70.00, 73.18, 74.17, 85.93, 103.16, 127.69, 127.85, 28.43, 138.22.

Anal. Calcd for $C_{14}H_{20}O_6$ (284): C, 59.15; H, 7.04. Found: C, 59.24; H, 7.26.

Benzyl 3-Deoxy-β-L-*erythro*-pentopyranoside (15). To benzyl 2,3-anhydro-β-L-ribopyranoside **7** (0.5g, 2.5 mmol) in anhydrous ether (10 mL) was added lithium aluminum hydride (3 mmol of 1.0 M solution in ether). The mixture was refluxed for 1 h and cooled. Ethyl acetate (20 mL) was added and the mixture filtered through a pad of Celite. The residue was washed with more ethyl acetate (20 mL). The filtrate was concentrated and partitioned between dichloromethane (50 mL) and saturated sodium chloride solution (5 mL). The organic layer was dried (Na_2SO_4) and concentrated to obtain a pure syrup (0.45g, 95%). ^1H NMR δ 1.45 (m, 1H, H-3a), 2.05 (m, 1H, H-3e), 3.20 (dd, J = 7.61, 11.00 Hz, 1H, H-5a), 3.40 (m, 1H, H-2), 3.65 (m, 1H, H-4), 3.80 (m, 1H), 4.30 (d, J = 5.75 Hz, 1H, H-1), 4.55 (d, J = 12.17 Hz, 1H, OCH_2Ar), 4.80 (d, J = 12.17 Hz, 1H, OCH_2Ar), 5.0 (d, J = 5.38 Hz, OH), 5.10 (d, J = 5.78 Hz, OH), 7.35 (m, 5H, Ar). ^{13}C NMR δ 37.63 C3, 64.32, 67.02, 68.17, 69.34, 102.94, 127.69, 127.89, 128.46, 138.31.

Anal. Calcd for $C_{12}H_{16}O_4$ (224): C,64.29; H, 7.14. Found: C, 64.23; H, 7.05.

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15. The Waters Sep-Pak Vac 35cc C18-10g was washed with 100 mL of methanol followed by 100 mL water to equilibrate it. Water (100 mL) was added to the reaction mixture. The solution was loaded on the cartridge, and the cartridge

washed sequentially with (100 mL) of each of the following solutions: 100% water and increasing amounts of methanol (5%, 10%, 50% and 100%). The majority of the product eluted with the 50% methanol in water.

16. ^{1}H-^{1}H COSY NMR spectra of benzyl 3-*O*-methyl-β-L-xylopyranoside **13** in DMSO and DMSO-D_2O were ran as an example to prove the regiochemistry. Analysis of the spectra showed that H-1 at δ 4.25 (d, J = 7.51 Hz) was coupled to H-2 at δ 3.15 (ddd, J = 8.80 Hz, 7.51 Hz, 6.41 Hz) which was in turn coupled to H-3 at δ 2.90 (t, J = 8.80 Hz, 8.84 Hz) and 2-OH at δ 5.15 (d, J = 6.41 Hz) indicating that -OCH_3 is at postion 3.
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18. Prolonged refluxing produced a dark mixture from which isolation of the desired product was difficult.