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A short synthesis of β-xylobiosides ☆

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Abstract

Benzyl 2,3,2′,3′,4′-penta-*O*-acetyl-β-xylobioside, 2-nitrophenyl β-xylobioside, 4-nitrophenyl β-xylobioside, and 2-iodobenzyl 1-thio-β-xylobioside were synthesized via a short and highly selective route. β-D-Xylopyranosides were selectively 4-*O*-triethylsilylated using dibutyltin oxide and triethylsilyl chloride and subsequently 2,3-di-*O*-acetylated. Desilylation under acidic conditions gave the 4-unprotected xylosides which then were β-D-xylosylated using 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl trichloroacetimidate.

Keywords: β-Xylobiosides; Dibutylstannylene xylopyranosides; Xylopyranosyl trichloroacetimidates; Xylosides, 4-unprotected

1. Introduction

There is an increasing interest in xylanases, both academically as well as commercially. Xylanases with no enzymic activity on cellulose are of particular interest to the pulp and paper industry since their use can diminish the need for aggressive chemicals in the bleaching process of pulp, and thus reduce the toxicity of the waste water produced [1]. Research on such enzymes requires specific substrates and inhibitors in order to assay or modulate their enzymic activity, or to be used as probes for investigations of the catalytic mechanism and the structure of the active site. Chromogenic substrates such as nitrophenyl xylo-oligosaccharides have rarely been used as substrates for these enzymes [2], despite the convenience of the assay. This is not surprising since the direct approach to making significant amounts of xylobiosides has been thwarted by the very limited accessibility of β-(1→4)-linked xylo-oligosaccharides, and thus their high price. Preparation via chemical or enzymic hydrolysis of xylan, a readily available component of hemicelluloses, is still very difficult

☆ 4-*O*-β-D-Xylopyranosyl-β-D-xylopyranosides.

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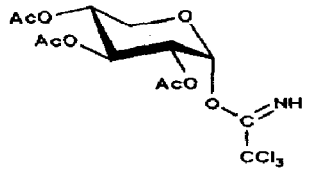
because of inhomogeneous substitutions on the main xylose chain in all natural xylans. This requires laborious additional treatments and separations of the hydrolysis mixtures [3]. The alternative approach to syntheses of xylobiosides involves their assembly from prefabricated monosaccharide building blocks. This strategy requires the efficient synthesis of a selectively protected xylosyl acceptor and a stereospecific xylosylation reaction with a suitable xylosyl donor. Similar approaches have been described by other authors previously [4]. However, the protocols described were unsatisfactory. This paper describes improved syntheses of both glycosyl donor and acceptor components, as well as an efficient coupling protocol. Examples are provided of syntheses of substrates for xylanases as well as an iodinated inhibitor of potential value in X-ray diffraction studies of xylanase structure.

2. Results and discussion

Synthesis of selectively protected β-D-xylopyranosides as xylosyl acceptors.—β-D-Xylopyranosides were chosen as readily available starting materials for the synthesis of selectively protected xylosyl acceptors. Benzyl [5] as well as 2- and 4-nitrophenyl [6] β-D-xylopyranoside are known compounds and can be prepared via Koenigs–Knorr syntheses. 2-Iodobenzyl 1-thio-β-D-xylopyranoside (**19**) was synthesized by alkylation of 2,3,4-tri-*O*-acetyl-1-thio-D-xylopyranose [7] with 2-iodobenzyl chloride according to a published procedure [7]. Regioselective acylation of β-D-xylopyranosides can be achieved by activation with one equivalent of dibutyltin oxide, followed by reaction with one equivalent of acyl halide. This reaction is reported to give acylation predominantly at O-4 of the xyloside [8]. In our hands, however, using chloroacetyl-, acetyl-, or benzoyl chloride, significant amounts of diacylated products were also formed and unprotected xyloside was left. This disadvantage, coupled with a desire for a protecting group at O-4 which can be removed under acidic conditions, allowing the use of acetate protecting groups at O-2 and O-3, led us to explore alternative routes. Triethylsilyl chloride proved to be an excellent electrophile with stannylated xylopyranosides, silylating exclusively the 4-position. In contrast to acyl chlorides, triethylsilyl chloride reacts only once, even at room temperature and even when using an excess of reagent. No disilylated products could be observed. Although 4-*O*-triethylsilyl β-D-xylopyranosides can be isolated and purified, it proved more convenient to acetylate them directly after a simple extraction of the organotin reagent with petroleum ether. The 2,3-di-*O*-acetyl-4-*O*-triethylsilyl-β-D-xylopyranosides are formed in good overall yield and are often crystalline compounds. Acidic desilylation in diethyl ether–acetic acid–water [9] gives the xylosyl acceptors, 2,3-di-*O*-acetyl-β-D-xylopyranosides in very high yields. The major advantage of this short protection–deprotection sequence is its compatibility with a large range of aglycons, thus making it a powerful building block synthesis.

Xylosylation of the selectively protected xylosides.—Typical approaches to xylosylation reactions have involved the use of a protected α-D-xylopyranosyl bromide as donor coupled with mercury salts as promotors [10]. These conditions, however, have several disadvantages: the instability of the xylosyl bromide, the toxicity of mercury salts, and their lack of stereospecificity in Koenigs–Knorr reactions. Mixtures of α- and β-xylosides are generally formed. Glycopyranosyl trichloroacetimidates have previously been used as glycosyl donors



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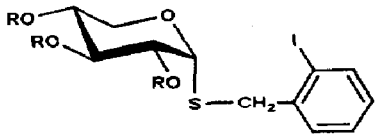
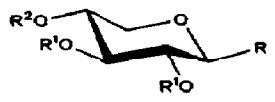


2 R = Ac
3 R = H



	R	R^1	R^2
4	*O*-Bzl	H	H
5	*O*-Bzl	Ac	$SiEt_3$
6	*O*-Bzl	Ac	H
7	*O*-Bzl	Ac	2,3,4-tri-*O*-acetyl-*β*-D-xylopyranosyl
8	*O*-4-nitrophenyl	H	H
9	*O*-4-nitrophenyl	Ac	$SiEt_3$
10	*O*-4-nitrophenyl	Ac	H
11	*O*-4-nitrophenyl	Ac	2,3,4-tri-*O*-acetyl-*β*-D-xylopyranosyl
12	*O*-4-nitrophenyl	H	*β*-D-xylopyranosyl
13	*O*-2-nitrophenyl	H	H
14	*O*-2-nitrophenyl	Ac	$SiEt_3$
15	*O*-2-nitrophenyl	Ac	H
16	*O*-2-nitrophenyl	Ac	2,3,4-tri-*O*-acetyl-*β*-D-xylopyranosyl
17	*O*-2-nitrophenyl	H	*β*-D-xylopyranosyl
18	*S*-2-iodobenzyl	Ac	Ac
19	*S*-2-iodobenzyl	H	H
20	*S*-2-iodobenzyl	Ac	$SiEt_3$
21	*S*-2-iodobenzyl	Ac	H
22	*S*-2-iodobenzyl	Ac	2,3,4-tri-*O*-acetyl-*β*-D-xylopyranosyl
23	*S*-2-iodobenzyl	H	*β*-D-xylopyranosyl

in oligosaccharide synthesis [11], combining mild and acidic reaction conditions with high yields and excellent β-stereoselectivity. The anomeric mixture of the xylosyl trichloroacetimidates was prepared via a general protocol [12], and the anomers separated by column chromatography. Only the α anomer (**1**) was used in the xylosylation reactions described in the Experimental section. However, use of the β anomer also gave exclusively β-linked xylobiosides (data not shown). Xylosylations of xylosyl acceptors using compound **1**, with boron trifluoride etherate as a catalyst in dichloromethane at low temperatures, were extremely fast and proceeded in good yields. No α-linked disaccharides could be detected.

In this way, two good xylanase substrates, the 4-nitrophenyl and 2-nitrophenyl β-xylobiosides, along with a useful inhibitor, 2-iodobenzyl-1-thio-β-xylobioside were prepared.

The latter is proving particularly useful in X-ray diffraction studies on xylanase structure. These syntheses of alkyl and aryl xylobiosides and thioxylobiosides indicate the general applicability of this synthetic strategy.

3. Experimental

General methods.—Melting points were determined with a Mel-Temp II apparatus (Laboratory devices, Holliston, Ma, USA) and are not corrected. Reactions were monitored by TLC on DC-Alufolien Kieselgel 60 F_{254} 0.2 mm (E. Merck). ^{1}H NMR spectra were recorded with a Bruker AC 200 (200 MHz) or a Bruker WH 400 (400 MHz) NMR spectrometer in the solvents indicated and are referenced to the solvent peak. Decoupling experiments were performed to obtain proton assignments. The petroleum ether used had a boiling range of 30–50°C.

*Benzyl 2,3-di-*O*-acetyl-4-*O*-triethylsilyl-β-*D*-xylopyranoside* (**5**).—Benzyl β-D-xylopyranoside (**4**) [5] (2.97 g, 12.4 mmol) and dibutyltin oxide (3.7 g, 14.9 mmol) in 1:3 benzene–toluene (150 mL) were refluxed overnight on a Dean–Stark trap. The resulting clear solution was cooled in an ice bath under N_2 and triethylsilyl chloride (3 mL, 17.8 mmol) was added dropwise with stirring. The solution was kept at room temperature for 2 days, concentrated, and the residue dissolved in 1:1 MeCN–petroleum ether (300 mL). The petroleum ether layer was removed. The MeCN layer was washed with fresh petroleum ether (2×100 mL), concentrated, and the residue acetylated with 3:2 pyridine–Ac_2O (30 mL) overnight. The product was transferred into water (400 mL) and extracted with CH_2Cl_2 (4×50 mL). The combined extracts were neutralized with 5% $NaHCO_3$ (200 mL), washed with water (200 mL), dried ($MgSO_4$), and concentrated. The crude product was purified by column chromatography (1:7 EtOAc–hexanes), and crystallized from EtOH to give **5** (3.57 g, 66%); mp 99–101°C; R_f 0.46 (1:5 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 4.45 (d, 1 H, $J_{1,2}$ 7.2 Hz, H-1), 4.88 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 4.97 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 3.83 (dt, 1 H, $J_{4,5a}$ 9.5, $J_{4,5b}$ 5.4 Hz, H-4), 3.25 (m, 1 H, H-5a), 3.90 (dd, 1 H, $J_{5a,5b}$ 10.5 Hz, H-5b), 7.20–7.35 (m, 5 H, Ar), 4.57 and 4.86 (2 d, 2 H, *J* 12.2 Hz, Bzl), 0.91 (t, 9 H, *J* 7.6 Hz, CH_3), 0.55 (q, 6 H, CH_2), 1.98 and 2.02 (2 s, 6 H, Ac). Anal. Calcd for $C_{22}H_{34}O_7Si$: C, 60.24; H, 7.81. Found: C, 59.94; H, 7.89.

*Benzyl 2,3-di-*O*-acetyl-β-*D*-xylopyranoside* (**6**).—Water (15 mL) was added to a solution of **5** (1.86 g, 4.24 mmol) in 1:2 diethyl ether–AcOH (45 mL) and the solution left at room temperature for 3 h. The mixture was then diluted with water (400 mL) and extracted with CH_2Cl_2 (5×25 mL). The combined extracts were neutralized with 5% $NaHCO_3$ (2×50 mL), washed with water (100 mL), dried ($MgSO_4$), and concentrated. The crude product was purified by column chromatography (1:1 EtOAc–hexanes) yielding **6** as a colourless syrup (1.32 g, 96%); R_f 0.33 (1:1 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 4.52 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.87 (t, 1 H, $J_{2,3}$ 7.5 Hz, H-2), 4.96 (dd, 1 H, $J_{3,4}$ 6.5 Hz, H-3), 3.82 (dt, 1 H, $J_{4,5a}$ 8.5, $J_{4,5b}$ 4.8 Hz, H-4), 3.36 (dd, 1 H, $J_{5a,5b}$ 11.8 Hz, H-5a), 4.10 (dd, 1 H, H-5b), 7.25–7.40 (m, 5 H, Ar), 4.57 and 4.85 (2 d, 2 H, *J* 12.5 Hz, Bzl), 2.02 and 2.08 (2 s, 6 H, Ac).

*Benzyl 2,3,2′,3′,4′-penta-*O*-acetyl-β-xylobioside* (**7**).—A solution of **6** (1.0 g, 3.08 mmol) and **1** (2.0 g, 4.75 mmol) in anhyd CH_2Cl_2 (50 mL) was stirred at −25 to −20°C

over 3A molecular sieves under N_2 for 15 min. A solution of boron trifluoride etherate (77 mg, 0.54 mmol) in anhyd CH_2Cl_2 (5 mL) was slowly added and the mixture stirred for another 30 min. The catalyst was then quenched by addition of Et_3N (0.5 mL), the mixture warmed to room temperature, and filtered. The filtrate was concentrated and the residue purified by column chromatography (2:3 EtOAc–hexanes). The product crystallized from EtOH to give **7** (1.36 g, 76%); mp 118–119°C; $[\alpha]^{20}$ −86.2° (*c* 0.9, EtOAc); lit. [13] 126–127°C; $[\alpha]_D^{22}$ −104.7 (*c* 1.28, $CHCl_3$); R_f 0.40 (1:1 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 4.47 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1), 4.90 (dd, 1 H, $J_{2,3}$ 9.1 Hz, H-2), 5.08 (t, 1 H, $J_{3,4}$ 9.1 Hz, H-3), 3.84 (dt, 1 H, $J_{4,5a}$ 9.3, $J_{4,5b}$ 5.2 Hz, H-4), 3.29 (dd, 1 H, $J_{5a,5b}$ 11.5 Hz, H-5a), 4.00 (dd, 1 H, H-5b), 4.55 (d, 1 H, $J_{1',2'}$ 6.0 Hz, H-1′), 4.78 (dd, 1 H, $J_{2',3'}$ 7.7 Hz, H-2′), 5.07 (t, 1 H, $J_{3',4'}$ 7.7 Hz, H-3′), 4.86 (dt, 1 H, $J_{4',5'a}$ 7.7, $J_{4',5'b}$ 4.6 Hz, H-4′), 3.38 (dd, 1 H, $J_{5'a,5'b}$ 12.2 Hz, H-5′a), 4.08 (dd, 1 H, H-5′b), 7.22–7.38 (m, 5 H, Ar), 4.57 and 4.83 (2 d, 2 H, *J* 12.0 Hz, Bzl), 1.99, 2.01, 2.02, 2.04, and 2.05 (5 s, 15 H, Ac).

*4′-Nitrophenyl 2,3-di-*O*-acetyl-4-*O*-triethylsilyl-β-*D*-xylopyranoside* (**9**).—4-Nitrophenyl β-D-xylopyranoside (**8**) [6] (2.2 g, 8.11 mmol) was selectively protected using dibutyltin oxide (2.1 g, 8.44 mmol) and triethylsilyl chloride (1.5 mL, 8.94 mmol), and then acetylated, as described for **5**. The residue was purified by column chromatography (1:4 EtOAc–hexanes) and crystallized from EtOAc–hexanes to give **9** (2.5 g, 66%); mp 124–125°C; R_f 0.67 (1:2 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 5.05–5.20 (m, 3 H, H-1, 2, and 3), 3.90 (dt, 1 H, $J_{4,5a}$ 9.0, $J_{4,5b}$ 5.2 Hz, H-4), 3.46 (dd, 1 H, $J_{5a,5b}$ 11.0 Hz, H-5a), 3.98 (dd, 1 H, H-5b), 6.99–8.23 (m, 4 H, Ar), 0.93 (t, 3 H, *J* 7.7 Hz, CH_2CH_3), 0.58 (q, 2 H, CH_2CH_3), 2.03 and 2.07 (2 s, 6 H, Ac). Anal. Calcd for $C_{21}H_{31}NO_9Si$: C, 53.72; H, 6.65; N, 2.98. Found: C, 53.78; H, 6.70; N, 3.00.

*4′-Nitrophenyl 2,3-di-*O*-acetyl-β-*D*-xylopyranoside* (**10**).—Compound **9** (1.79 g, 3.81 mmol) was desilylated as described for **6**. The crude product was purified by column chromatography (1:1 EtOAc–hexanes) and crystallized from EtOAc–hexanes to give **10** (1.23 g, 91%); mp 158–159°C; R_f 0.29 (1:1 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 5.27 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1), 5.17 (dd, 1 H, $J_{2,3}$ 8.6 Hz, H-2), 5.00 (t, 1 H, $J_{3,4}$ 8.3 Hz, H-3), 3.88 (dt, 1 H, $J_{4,5a}$ 8.3, $J_{4,5b}$ 6.4 Hz, H-4), 3.57 (dd, 1 H, $J_{5a,5b}$ 13.5 Hz, H-5a), 4.16 (dd, 1 H, H-5b), 7.02–8.23 (m, 4 H, Ar), 2.70 (s, 1 H, OH), 2.08 and 2.13 (2 s, 6 H, Ac). Anal. Calcd for $C_{15}H_{17}NO_9$: C, 50.71; H, 4.82; N, 3.94. Found: C, 50.40; H, 5.06; N, 3.68.

*4″-Nitrophenyl 2,3,2′,3′,4′-penta-*O*-acetyl-β-xylobioside* (**11**).—Compound **10** (356 mg, 1.0 mmol) was xylosylated with **1** (800 mg, 1.9 mmol) in CH_2Cl_2 (20 mL), using a solution of boron trifluoride etherate (50 mg, 0.40 mmol) in CH_2Cl_2 (2 mL), as described for **7**. The product was purified by column chromatography (1:1 EtOAc–hexanes) and crystallized from the same solvents to give **11** (431 mg, 70%); mp 182–184°C; R_f 0.38; ^{1}H NMR ($CDCl_3$): δ 5.22 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1), 5.10 (t, 1 H, $J_{2,3}$ 6.4 Hz, H-2), 5.20 (t, 1 H, $J_{3,4}$ 7.0 Hz, H-3), 3.90 (ddd, 1 H, $J_{4,5a}$ 8.0, $J_{4,5b}$ 4.2 Hz, H-4), 3.52 (dd, 1 H, $J_{5a,5b}$ 11.8 Hz, H-5a), 4.04 (dd, 1 H, H-5b), 4.58 (d, 1 H, $J_{1',2'}$ 6.2 Hz, H-1′), 4.82 (dd, 1 H, $J_{2',3'}$ 8.0 Hz, H-2′), 5.10 (t, 1 H, $J_{3',4'}$ 8.0 Hz, H-3′), 4.87 (dt, 1 H, $J_{4',5'a}$ 8.0, $J_{4',5'b}$ 4.8 Hz, H-4′), 3.39 (dd, 1 H, $J_{5'a,5'b}$ 12.0 Hz, H-5′a), 4.09 (dd, 1 H, H-5′b), 7.01 and 8.03 (2 m, 4 H, Ar), 2.01, 2.03, 2.04, 2.05, and 2.07 (5 s, 15 H, Ac). Anal. Calcd for $C_{26}H_{31}NO_{16}$: C, 50.90; H, 5.09; N, 2.28. Found: C, 51.10; H, 5.08; N, 2.23.

4-Nitrophenyl β-xylobioside (**12**).—Solid NaOMe was added to a suspension of **11** (350 mg, 0.57 mmol) in anhyd MeOH (30 mL) until the mixture remained basic. The solid

dissolved during the reaction, and the solution was passed through a short silica gel column (2×5 cm, MeOH). The filtrate was concentrated and the residue purified by column chromatography (17:2:1 EtOAc–MeOH–H_2O). Attempts to crystallize the product failed. It was freeze-dried to give **12** (218 mg, 91%) as a colourless foam; $[\alpha]_D^{20}$ −88.8° (*c* 1, MeOH); R_f 0.32 (17:2:1 EtOAc–MeOH–H_2O); ^{1}H NMR (D_2O): δ 5.30 (d, 1 H, $J_{1,2}$ 7.2 Hz, H-1), 3.45 (dd, 1 H, $J_{2,3}$ 9.0 Hz, H-2), 3.53 (t, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 3.68 (dt, 1 H, $J_{4,5a}$ 8.0, $J_{4,5b}$ 4.4 Hz, H-4), 3.41 (dd, 1 H, $J_{5a,5b}$ 11.5 Hz, H-5a), 3.99 (dd, 1 H, H-5b), 4.30 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′), 3.10 (dd, 1 H, $J_{2',3'}$ 9.0 Hz, H-2′), 3.26 (t, 1 H, $J_{3',4'}$ 9.0 Hz, H-3′), 3.47 (ddd, 1 H, $J_{4',5'a}$ 11.5, $J_{4',5'b}$ 5.5 Hz, H-4′), 3.14 (t, 1 H, $J_{5'a,5'b}$ 11.5 Hz, H-5′a), 3.81 (dd, 1 H, H-5′b), 7.01 and 8.03 (2 d, 4 H, *J* 9.2 Hz, Ar). Anal. Calcd for $C_{16}H_{21}NO_{11}\cdot H_2O$: C, 45.61; H, 5.50; N, 3.32. Found: C, 45.62; H, 5.47; N, 3.28.

*2′-Nitrophenyl 2,3-di-*O*-acetyl-4-*O*-triethylsilyl-β-*D*-xylopyranoside* (**14**).—2-Nitrophenyl β-D-xylopyranoside (**13**) [6] (1.22 g, 4.5 mmol) was selectively protected using dibutyltin oxide (1.38 g, 5.54 mmol), triethylsilyl chloride (0.95 mL, 5.66 mmol), and pyridine–Ac_2O (15 mL) as described for **5**. The product was crystallized from EtOAc–hexanes to give **14** (1.8 g, 85%); mp 124–125°C; R_f 0.60 (1:2 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 4.99–5.18 (m, 3 H, H-1, 2, and 3), 3.83–3.98 (m, 1 H, $J_{4,5a}$ 8.0, $J_{4,5b}$ 5.2 Hz, H-4), 3.44 (dd, 1 H, $J_{5a,5b}$ 11.0 Hz, H-5a), 4.02 (dd, 1 H, H-5b), 7.76 (dd, 1 H, $J_{3',4'}$ 8.3, $J_{3',5'}$ 1.7 Hz, H-3′), 7.14 (ddd, 1 H, $J_{4',5'}$ 7.4, $J_{4',6'}$ 1.3 Hz, H-4′), 7.50 (ddd, 1 H, $J_{5',6'}$ 8.0 Hz, H-5′), 7.29 (dd, 1 H, H-6′), 0.59 (q, 6 H, *J* 7.5 Hz, CH_2), 0.93 (t, 9 H, CH_3), 2.08 and 2.09 (2 s, 6 H, Ac). Anal. Calcd for $C_{21}H_{31}NO_9Si$: C, 53.72; H, 6.65; N, 2.98. Found: C, 53.78; H, 6.33; N, 2.95.

*2′-Nitrophenyl 2,3-di-*O*-acetyl-β-*D*-xylopyranoside* (**15**).—Compound **14** (1.22 g, 2.6 mmol) was desilylated in 1:2:1 diethyl ether–AcOH–H_2O (60 mL) as described for **6**. The product was purified by column chromatography (2:1 EtOAc–hexanes) and crystallized from EtOAc–hexanes to give **15** (0.887 g, 96%); mp 104–105°C; R_f 0.16 (EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 5.33 (d, 1 H, $J_{1,2}$ 4.3 Hz, H-1), 5.14 (dd, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 4.96 (t, 1 H, $J_{3,4}$ 6.0 Hz, H-3), 3.84 (q, 1 H, $J_{4,5a}$ 5.3, $J_{4,5b}$ 3.3 Hz, H-4), 3.60 (dd, 1 H, $J_{5a,5b}$ 12.0 Hz, H-5a), 4.23 (dd, 1 H, H-5b), 7.78 (dd, 1 H, $J_{3',4'}$ 8.1, $J_{3',5'}$ 1.6 Hz, H-3′), 7.14 (dt, 1 H, $J_{4',5'}$ 7.5, $J_{4',6'}$ 1.2 Hz, H-4′), 7.52 (ddd, 1 H, $J_{5',6'}$ 8.2 Hz, H-5′), 7.31 (dd, 1 H, H-6′), 2.14 and 2.16 (2 s, 6 H, Ac). Anal. Calcd for $C_{15}H_{17}NO_9$: C, 50.71; H, 4.82; N, 3.94. Found: C, 50.77; H, 4.79; N, 3.97.

*2″-Nitrophenyl 2,3,2′,3′,4′-penta-*O*-acetyl-β-xylobioside* (**16**).—Compound **15** (871 mg, 2.45 mmol) was glycosylated in CH_2Cl_2 (30 mL) using **1** (2.0 g, 4.75 mmol) and a solution of boron trifluoride etherate (75 mg, 0.53 mmol) in CH_2Cl_2 (3 mL), as described for **7**. The product was purified by column chromatography (2:3 EtOAc–hexanes) and crystallized from EtOAc–hexanes to give **16** (1.14 g, 76%), mp 188°C; R_f 0.48 (1:1 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 5.26 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 5.05 (dd, 1 H, $J_{2,3}$ 6.5 Hz, H-2), 5.17 (t, 1 H, $J_{3,4}$ 6.5 Hz, H-3), 3.86 (dt, 1 H, $J_{4,5a}$ 6.6, $J_{4,5b}$ 3.2 Hz, H-4), 3.54 (dd, 1 H, $J_{5a,5b}$ 12.2 Hz, H-5a), 4.11 (dd, 1 H, H-5b), 4.59 (d, 1 H, $J_{1',2'}$ 6.2 Hz, H-1′), 4.84 (dd, 1 H, $J_{2',3'}$ 7.9 Hz, H-2′), 5.11 (t, 1 H, $J_{3',4'}$ 7.9 Hz, H-3′), 4.90 (dt, 1 H, $J_{4',5'a}$ 8.1, $J_{4',5'b}$ 4.0 Hz, H-4′), 3.38 (dd, 1 H, $J_{5'a,5'b}$ 11.9 Hz, H-5′a), 4.09 (dd, 1 H, H-5′b), 7.76 (dd, 1 H, $J_{3'',4''}$ 8.0, $J_{3'',5''}$ 1.8 Hz, H-3″), 7.13 (dt, 1 H, $J_{4'',5''}$ 8.0, $J_{4'',6''}$ 1.0 Hz, H-4″), 7.50 (dt, 1 H, $J_{5'',6''}$ 7.9 Hz, H-5″), 7.26 (dd, 1 H, H-6″), 2.01, 2.03, and 2.10 (3 s, 15 H, Ac). Anal. Calcd for $C_{26}H_{31}NO_{16}$: C, 50.90; H, 5.09; N, 2.28. Found: C, 50.87; H, 5.08; N, 2.26.

2'-Nitrophenyl β-xylobioside (**17**).—Compound **16** (1.0 g, 1.63 mmol) was deacetylated as described for **12**. The product was purified by column chromatography (27:2:1 EtOAc–MeOH–H_2O) and crystallized from acetonitrile to give **17** (528 mg, 80.3%); mp 113–115°C; $[\alpha]_D^{20}$ −81.3° (*c* 0.9, MeOH); R_f 0.32 (17:2:1 EtOAc–MeOH–H_2O); ^{1}H NMR (D_2O): δ 5.04–5.10 (m, 1 H, H-1), 3.40–3.59 (m, 2 H, H-2 and 3), 3.72 (dt, 1 H, $J_{4,5a}$ 9.5, $J_{4,5b}$ 5.0 Hz, H-4), 3.40 (dd, 1 H, $J_{5a,5b}$ 12.0 Hz, H-5a), 3.99 (dd, 1 H, H-5b), 4.31 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 3.10 (dd, 1 H, $J_{2',3'}$ 9.0 Hz, H-2'), 3.26 (t, 1 H, $J_{3',4'}$ 9.0 Hz, H-3'), 3.48 (ddd, 1 H, $J_{4',5'a}$ 11.5, $J_{4',5'b}$ 5.3 Hz, H-4'), 3.14 (t, 1 H, $J_{5'a,5'b}$ 11.5 Hz, H-5'a), 3.81 (dd, 1 H, H-5'b), 7.77 (dd, 1 H, $J_{3'',4''}$ 8.0, $J_{3'',5''}$ 1.5 Hz, H-3''), 7.09 (dt, 1 H, $J_{4'',5''}$ 7.6, $J_{4'',6''}$ 1.0 Hz, H-4''), 7.51 (dt, 1 H, $J_{5'',6''}$ 7.5 Hz, H-5''), 7.25 (dd, 1 H, H-6''). Anal. Calcd for $C_{16}H_{21}NO_{11}$: C, 47.65; H, 5.25; N, 3.47. Found: C, 47.98; H, 5.47; N, 3.19.

2'-Iodobenzyl 2,3,4-tri-O-acetyl-1-thio-α- and -β-D-xylopyranoside (**2** *and* **18**).—A solution of the anomeric mixture of 2,3,4-tri-*O*-acetyl-1-thio-D-xylopyranose [7] (3.0 g, 10.2 mmol) and 2-iodobenzyl chloride (2.8 g, 11.1 mmol) in acetone (10 mL) was combined with a solution of K_2CO_3 (1.4 g, 10.1 mmol) in water (10 mL), and vigorously stirred at room temperature for 1.5 h. The mixture was then diluted with water (300 mL) and extracted with CH_2Cl_2 (4×25 mL). The combined extracts were washed with water (200 mL), dried ($MgSO_4$), and concentrated. The anomers formed were separated by column chromatography (1:4 → 1:2 EtOAc–hexanes). Compound **2** was the first eluted, and was obtained as a colourless syrup (1.35 g, 26%); R_f 0.45 (1:2 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 5.46 (d, 1 H, $J_{1,2}$ 5.4 Hz, H-1), 4.90 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-2), 5.30 (t, 1 H, $J_{3,4}$ 9.3 Hz, H-3), 4.89 (ddd, 1 H, $J_{4,5a}$ 5.7, $J_{4,5b}$ 10.0 Hz, H-4), 3.76 (dd, 1 H, $J_{5a,5b}$ 11.5 Hz, H-5a), 3.99 (dd, 1 H, H-5b), 6.84–7.84 (3 m, 4 H, Ar), 3.78 and 3.83 (2 d, 2 H, *J* 13.0 Hz, Bzl), 1.99, 2.00, and 2.02 (3 s, 9 H, Ac).

Compound **18** was eluted second and was crystallized from MeOH (3.35 g, 65%); mp 85–86°C; R_f 0.38 (1:2 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 4.45 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 4.94 (t, 1 H, $J_{2,3}$ 8.1 Hz, H-2), 5.10 (t, 1 H, $J_{3,4}$ 8.1 Hz, H-3), 4.93 (dt, 1 H, $J_{4,5a}$ 8.7, $J_{4,5b}$ 5.0 Hz, H-4), 3.35 (dd, 1 H, $J_{5a,5b}$ 11.7 Hz, H-5a), 4.23 (dd, 1 H, H-5b), 6.89–7.36 (3 m, 4 H, Ar), 3.89 and 4.02 (2 d, 2 H, *J* 13.0 Hz, Bzl), 2.01, 2.02, and 2.03 (3 s, 9 H, Ac). Anal. Calcd for $C_{18}H_{21}IO_7S$: C, 42.53; H, 4.16. Found: C, 42.68; H, 4.13.

2'-Iodobenzyl 1-thio-α-D-xylopyranoside (**3**).—Compound **2** (1.8 g, 3.54 mmol) was deacetylated as described for **12**. The crude product crystallized spontaneously and was recrystallized from EtOH to give **3** (1.26 g, 93%); mp 145–148°C; R_f 0.53 (17:2:1 EtOAc–MeOH–H_2O); ^{1}H NMR (CD_3OD): δ 5.18 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 3.64 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 3.40–3.68 (m, 3 H, H-3, 4, and 5a), 3.88 (dd, 1 H, $J_{4,5b}$ 9.5, $J_{5a,5b}$ 11.0 Hz, H-5b), 7.84 (dd, 1 H, $J_{3',4'}$ 8.2, $J_{3',5'}$ 1.2 Hz, H-3'), 6.94 (ddd, 1 H, $J_{4',5'}$ 7.5, $J_{4',6'}$ 2.0 Hz, H-4'), 7.30 (dt, 1 H, $J_{5',6'}$ 7.5 Hz, H-5'), 7.40 (dd, 1 H, H-6'), 3.80 and 3.90 (2 d, 2 H, *J* 13.0 Hz, Bzl). Anal. Calcd for $C_{12}H_{15}IO_4S$: C, 37.71; H, 3.96. Found: C, 37.90; H, 3.92.

2'-Iodobenzyl 1-thio-β-D-xylopyranoside (**19**).—Compound **18** (2.9 g, 5.70 mmol) was deacetylated as described for **12**. The product crystallized spontaneously and was recrystallised from EtOH to give **19** (1.62 g, 74%); mp 183–184°C; R_f 0.52 (17:2:1 EtOAc–MeOH–H_2O); ^{1}H NMR (CD_3OD): δ 4.17–4.28 (m, 1 H, H-1), 3.14–3.27 (m, 2 H, H-2 and 3), 3.50 (ddd, 1 H, $J_{3,4}$ 9.0, $J_{4,5a}$ 10.0, $J_{4,5b}$ 5.2 Hz, H-4), 3.18 (dd, 1 H, $J_{5a,5b}$ 11.2 Hz, H-5a), 3.94 (dd, 1 H, H-5b), 7.84 (dd, 1 H, $J_{3',4'}$ 8.0, $J_{3',5'}$ 1.2 Hz, H-3'), 6.95 (ddd, 1 H, $J_{4',5'}$ 7.3, $J_{4',6'}$ 2.0 Hz, H-4'), 7.32 (dt, 1 H, $J_{5',6'}$ 7.3 Hz, H-5'), 7.40 (dd, 1 H, H-6'), 3.90

and 4.08 (2 d, 2 H, *J* 13.2 Hz, Bzl). Anal. Calcd for $C_{12}H_{15}IO_4S$: C, 37.71; H, 3.96. Found: C, 37.87; H, 3.93.

*2′-Iodobenzyl 2,3-di-*O*-acetyl-4-*O*-triethylsilyl-1-thio-β-*D*-xylopyranoside* (**20**).—Compound **19** (2.0 g, 5.23 mmol) was selectively silylated using dibutyltin oxide (1.46 g, 5.86 mmol) and triethylsilyl chloride (1.4 mL, 8.34 mmol), and then acetylated as described for **5**. The crude product was purified by column chromatography (1:7 EtOAc–hexanes) to give **20** (2.25 g, 74%) as a colourless syrup; R_f 0.42 (1:5 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 4.33 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.87 (t, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 4.96 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 3.82 (ddd, 1 H, $J_{4,5a}$ 10.1, $J_{4,5b}$ 5.4 Hz, H-4), 3.26 (dd, 1 H, $J_{5a,5b}$ 11.3 Hz, H-5a), 3.97 (dd, 1 H, H-5b), 7.82 (dd, 1 H, $J_{3',4'}$ 8.0, $J_{3',5'}$ 1.0 Hz, H-3′), 6.94 (ddd, 1 H, $J_{4',5'}$ 6.5, $J_{4',6'}$ 2.3 Hz, H-4′), 7.29 (dt, 1 H, $J_{5',6'}$ 6.5 Hz, H-5′), 7.31 (dd, 1 H, H-6′), 3.89 and 4.04 (2 d, 2 H, *J* 13.2 Hz, Bzl), 0.92 (t, 3 H, *J* 7.9 Hz, CH_2CH_3), and 0.56 (q, 2 H, CH_2CH_3), 1.99 and 2.02 (2 s, 6 H, Ac). Anal. Calcd for $C_{22}H_{33}IO_6SSi$: C, 45.52; H, 5.73. Found: C, 45.89; H, 5.69.

*2′-Iodobenzyl 2,3-di-*O*-acetyl-1-thio-β-*D*-xylopyranoside* (**21**).—Compound **20** (2.0 g, 3.45 mmol) was desilylated in 1:2:1 diethyl ether–AcOH–H_2O (60 mL) as described for **6**. The product was purified by column chromatography (1:1 EtOAc–hexanes) and crystallized from EtOAc–hexanes to give **21** (1.49 g, 92%); mp 107°C; R_f 0.25 (1:1 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 4.45 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.85 (t, 1 H, $J_{2,3}$ 8.0 Hz, H-2), 4.93 (t, 1 H, $J_{3,4}$ 8.0 Hz, H-3), 3.79 (dt, 1 H, $J_{4,5a}$ 8.5, $J_{4,5b}$ 4.8 Hz, H-4), 3.35 (dd, 1 H, $J_{5a,5b}$ 11.8 Hz, H-5a), 4.20 (dd, 1 H, H-5b), 7.83 (dd, 1 H, $J_{3',4'}$ 8.0, $J_{3',5'}$ 0.8 Hz, H-3′), 6.89–7.09 (m, 1 H, H-4′), 7.26–7.34 (m, 2 H, H-5′,6′), 3.89 and 4.02 (2 d, 2 H, *J* 13.0 Hz, Bzl), 2.52 (s, 1 H, O*H*), 2.02 and 2.08 (2 s, 6 H, Ac). Anal. Calcd for $C_{16}H_{19}IO_6S$: C, 41.21; H, 4.11. Found: C, 41.35; H, 4.11.

*2″-Iodobenzyl 2,3,2′,3′,4′-penta-*O*-acetyl-1-thio-β-xylobioside* (**22**).—Compound **21** (1.13 g, 2.42 mmol) was xylosylated with **1** (1.7 g, 4.04 mmol) in anhyd CH_2Cl_2 (40 mL) using a solution of boron trifluoride etherate (68 mg, 0.48 mmol) in CH_2Cl_2 (3 mL), as described for **7**. The crude product was purified by column chromatography (2:3 EtOAc–hexanes) and **22** (1.33 g, 76%) was obtained as a colourless foam; R_f 0.41 (1:1 EtOAc–hexanes); ^{1}H NMR ($CDCl_3$): δ 4.35 (d, 1 H, $J_{1,2}$ 9.0 Hz, H-1), 4.86 (t, 1 H, $J_{2,3}$ 9.0 Hz, H-2), 5.04 (t, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 3.81 (dt, 1 H, $J_{4,5a}$ 9.5, $J_{4,5b}$ 4.5 Hz, H-4), 3.27 (dd, 1 H, $J_{5a,5b}$ 11.5 Hz, H-5a), 4.06 (dd, 2 H, H-5b and 5′b), 4.53 (d, 1 H, $J_{1',2'}$ 5.7 Hz, H-1′), 4.75 (dd, 1 H, $J_{2',3'}$ 7.2 Hz, H-2′), 5.05 (t, 1 H, $J_{3',4'}$ 7.2 Hz, H-3′), 4.83 (dt, 1 H, $J_{4',5'a}$ 7.5, $J_{4',5'b}$ 4.5 Hz, H-4′), 3.37 (dd, 1 H, $J_{5'a,5'b}$ 12.0 Hz, H-5′a), 7.81 (d, 1 H, $J_{3'',4''}$ 8.0 Hz, H-3″), 6.93 (dt, 1 H, $J_{4'',5''}$ 4.5, $J_{4'',6''}$ 4.5 Hz, H-4″), 7.28 (d, 2 H, H-5″ and 6″), 3.86 and 4.00 (2 d, 2 H, *J* 13.0 Hz, Bzl), 1.98, 2.00, 2.01, and 2.03 (4 s, 15 H, Ac).

2″-Iodobenzyl 1-thio-β-xylobioside (**23**).—Compound **22** (1.23 g, 1.69 mmol) was deacetylated as described for **12**. The product was crystallized from EtOH, the mother liquor purified by column chromatography (17:2:1 EtOAc–MeOH–H_2O), and recrystallized with the first crop to give **23** (829 mg, 95%); mp 197–198°C; $[\alpha]_D^{20}$ −156.8° (*c* 0.7, MeOH); R_f 0.26 (17:2:1 EtOAc–MeOH–H_2O); ^{1}H NMR (CD_3OD): δ 4.26 (d, 1 H, $J_{1,2}$ 9.1 Hz, H-1), 3.26 (t, 1 H, $J_{2,3}$ 9.1 Hz, H-2), 3.30 (t, 1 H, $J_{3,4}$ 9.1 Hz, H-3), 3.49 (ddd, 1 H, $J_{4,5a}$ 10.4, $J_{4,5b}$ 5.5 Hz, H-4), 3.22 (t, 1 H, $J_{5a,5b}$ 11.4 Hz, H-5a), 3.88 (dd, 1 H, H-5b), 4.32 (d, 1 H, $J_{1',2'}$ 7.6 Hz, H-1′), 3.20 (dd, 1 H, $J_{2',3'}$ 9.0 Hz, H-2′), 3.39 (t, 1 H, $J_{3',4'}$ 9.0 Hz, H-3′), 3.66 (ddd, 1 H, $J_{4',5'a}$ 10.2, $J_{4',5'b}$ 5.2 Hz, H-4′), 3.29 (dd, 1 H, $J_{5'a,5'b}$ 11.6 Hz, H-5′a),

4.10 (dd, 1 H, H-5′b), 7.84 (dd, 1 H, $J_{3'',4''}$ 7.9, $J_{3'',5''}$ 1.0 Hz, H-3″), 6.95 (dt, 1 H, $J_{4'',5''}$ 7.7, $J_{4'',6''}$ 1.7 Hz, H-4″), 7.32 (dt, 1 H, $J_{5'',6''}$ 7.7 Hz, H-5″), 7.40 (dd, 1 H, H-6″), 3.90 and 4.07 (2 d, 2 H, J 13.3 Hz, Bzl). Anal. Calcd for $C_{17}H_{23}IO_8S$: C, 39.7; H, 4.51. Found: C, 39.77; H, 4.51.

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