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New 1-*C*-(5-thio-D-xylopyranosyl) derivatives as potential orally active venous antithrombotics

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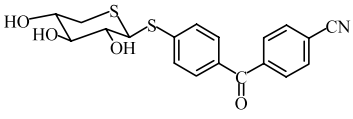
Abstract

In the search for new orally active antithrombotic drugs that are metabolically stable, we explored the synthesis of 1-*C*-(5-thio-D-xylosyl) derivatives, examining radical and nucleophilic methods. Thus synthesized were aryl, benzyl, alkylcarboxymethylenyl, arylsulfonylmethylenyl and alkylaminocarboxymethylenyl C-linked analogues of 5-thio-D-xylopyranosides.

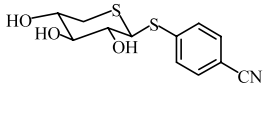
Keywords: 1-*C*-(5-Thio-D-xylopyranosyl) derivatives; Venous antithrombotics; Glycosidic linkage

1. Introduction

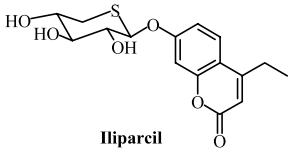
The prophylaxis of thromboembolic disorders (a major cause of morbidity and mortality in industrialized countries) is largely managed by intravenous heparin therapy (which has drawbacks associated with the mode of administration and hemorrhagic risk) or by oral warfarin therapy (which has a delayed onset of action, presents a risk of bleeding and interactions with numerous drugs). In the search for new orally active antithrombotic drugs without such serious side-effects as bleeding, we have been developing, for the past 10 years, a 'xylosides' program. This program is based on the hypothesis that β-D-xylopyranosides might be effective antithrombotic drugs[1–4] since they induce biosynthesis of glycosaminoglycans in cell cultures, as demonstrated by Okayama,[5] Schwarz[6] and others. Three representatives of this novel family have been evaluated in clinical trials (Naroparcil, Beciparcil, Iliparcil) and have demonstrated significant pharmacological properties. All three compounds proved to be good substrates for glucuronosyltransferase (EC 2.4.1.17) and were shown to undergo metabolic cleavage of the glycosidic linkage in vitro and in vivo.[7]



Naroparcil



Beciparcil



Iliparcil

In order to obtain derivatives that are more metabolically stable, we set out to synthesize 1-*C*-(5-thio-β-D-xylopyranosyl) analogues. Since little was known about the synthesis of such derivatives, we investigated various pathways to this class of sugar derivatives.

2. Results and discussion

Among known methods for synthesis of *C*-glycosyl compounds,[8–16] not all were successful. We began with

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2,3,4-tri-*O*-benzyl-5-thio-D-xylonolactone (**4**), as Lopez[17] and Boyd[18] did for 5-O-analogues. Lactone **4** could be readily synthesized from methyl 5-thio-D-xylopyranoside (**1**)[19] by standard methods[20a] via intermediates **2**[20b] and **3** (Scheme 1). Attempted transformation of lactone **4**, by methods of Lopez and Boyd's was unsuccessful. Failure to obtain the anion derived from the 7-bromomethyl-4-methyl-2*H*-1-benzopyran-2-one by metallation at C-11 with Mg was the main obstacle (magnesium–refluxing Et_2O or highly activated magnesium anthracene in THF at room temperature and under reflux according to Gallagher[21] were the two methods applied without success).

We next attempted to synthesize 2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl cyanide, which could potentially lead to either nitrogen- or oxygen-based functional groups (amide, amine, acid, alcohol).[22] The procedures used, using the acetylated glycosyl bromide[22,23] and $Hg(CN)_2$ or using the β-tetraacetate[24–29] and trimethylsilyl cyanide, failed to yield the target compound and led mainly respectively to a hemithioacetal or a 2-deacetylated product.

Attempted radical synthesis from bromide **5** and acrylonitrile, as described by Giese,[30] did not give the desired product **6**; instead while **7** was the major product (Scheme 2).

Reaction of bromide **5** with an aryl cuprate, as described by Tucker,[31] also failed to form the target product; only 2-deoxy-acetylated derivative **7** was obtained (Scheme 3), supporting previous findings.[32]

Use of Grignard reagents and bromide **5**, following Panigot and co-workers,[33] led to compounds **9** and **11** as white crystals (Scheme 2), but the yields were modest (15 and 35%, respectively). The $J_{1,2}$ coupling constants of 10.1 and 10.6 Hz supported the β anomeric configurations.

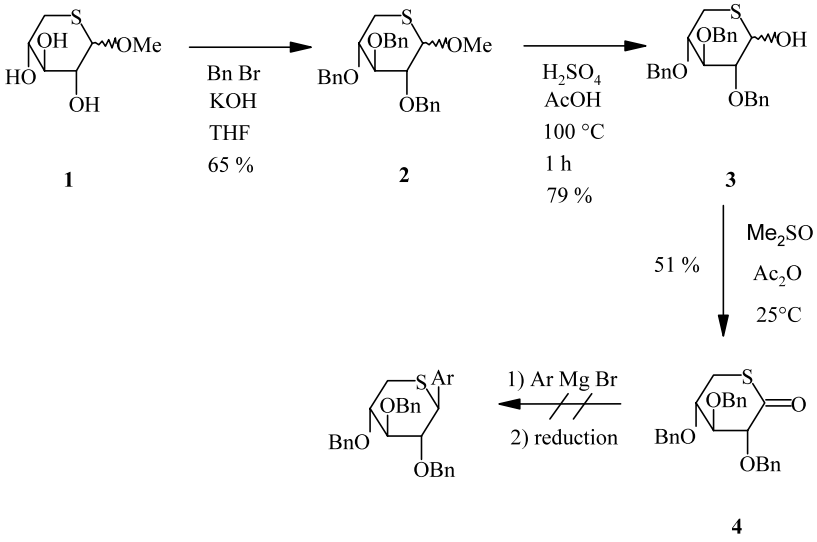
Methods utilizing silylated enol ethers, as employed by Hanessian[34] with glycosyl halides and by Schmidt[35] with sugar trichloroacetimidates (Scheme 4) gave more satisfactory results.

Table 1 summarizes the results. This strategy proved promising as it can lead to several products (such as compounds **16** and **17**), albeit in low yield. The $J_{1,2}$ coupling constants supported the β anomeric configurations (see Table 1).

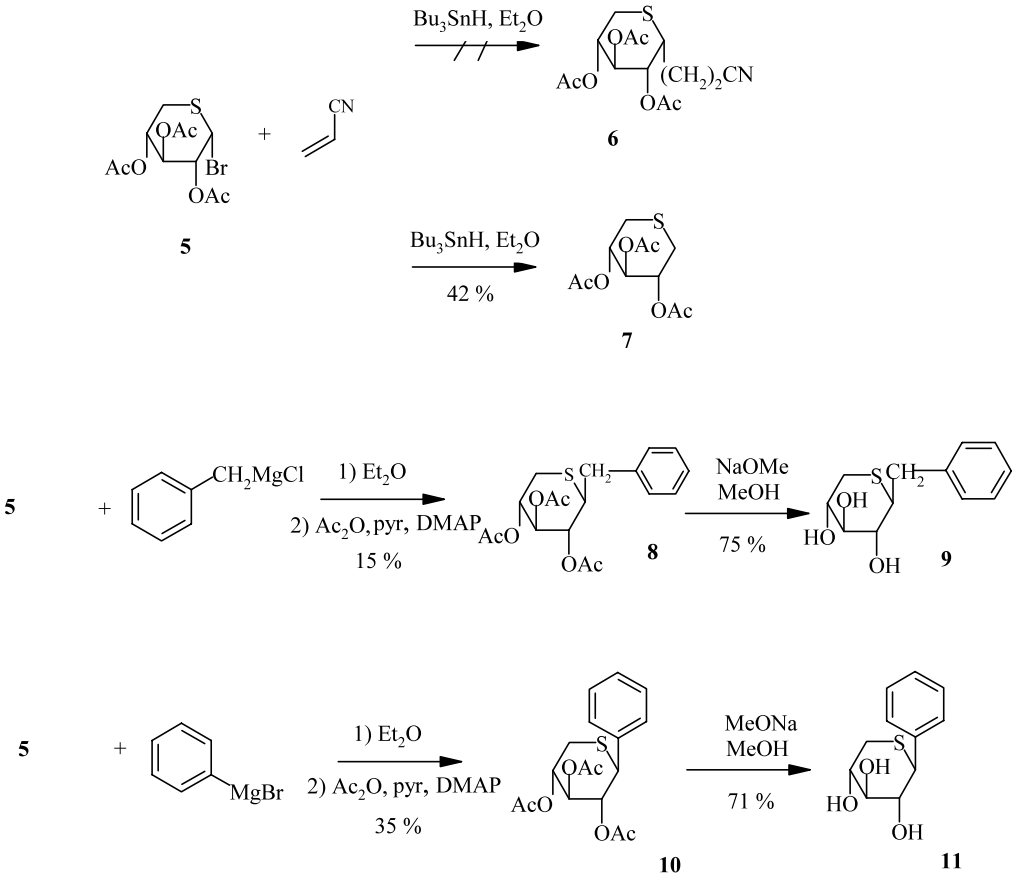
Phenylsulfonyl and phenylcarbamide derivatives are also investigated. Most methods for the synthesis of C-glycosyl compounds use protected sugar derivatives, except for that of Davidson and co-workers[36] who devised a method in which a Wittig-type reagent reacts with an unprotected sugar. Conventional methods for the synthesis of tetrahydropyran derivative using sugars, require protection of the hydroxyl groups. Davidson and co-workers reported a sodium salt of a phosphonate sulfone that reacts in a Wittig manner with unprotected sugars to yield, after treatment with base, exclusively the corresponding β tetrahydropyrans.

In this manner, thioxylosyl derivatives were synthesized from the free 5-thioxylose and the diethylaryl sulfonylmethyl phosphonate (Scheme 5).[37,38]

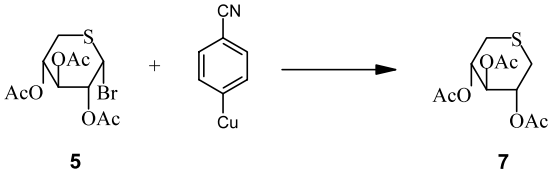
In the method described by Davidson and co-workers, the final mixture of α and β anomers was acetylated and then deacetylated to afford the β-anomer exclusively (is a retro-Michael reaction at the deacetylation step in the case of the O-sugars). This was not observed with the 5-thio sugars studied. Thus peracetylated α and β isomers had to be separated and then deacetylated to yield the desired compounds **18α** and **18β** (in 7.3 and 5.5% yields from 5-thio-D-xylopyranose) as white powders (Scheme 5). The $J_{1,2}$ coupling constants of 5 and 9.5 Hz supported the anomeric configurations.



Scheme 1.



Scheme 2.



Scheme 3.

The Wittig–Horner reaction conditions used by Davidson and co-workers[36] were modified to yield a mixture of anomers (α/β: 70/30 as shown in Scheme 5). The acetylation separation sequence yielded the isomeric compounds **21β** and **21α**, which were deacetylated to form products **20β** and **20α** under mild reaction conditions that avoid anomerization (by the retro-Michael reaction because of the acidic α-hydrogen of the arylsulfonyl group). Compounds **20α** and **20β** were obtained as white powders in 9 and 3% yields from 5-thio-D-xylopyranose. The $J_{1,2}$ coupling constants of 5 and 9.5 Hz supported the anomeric configurations.

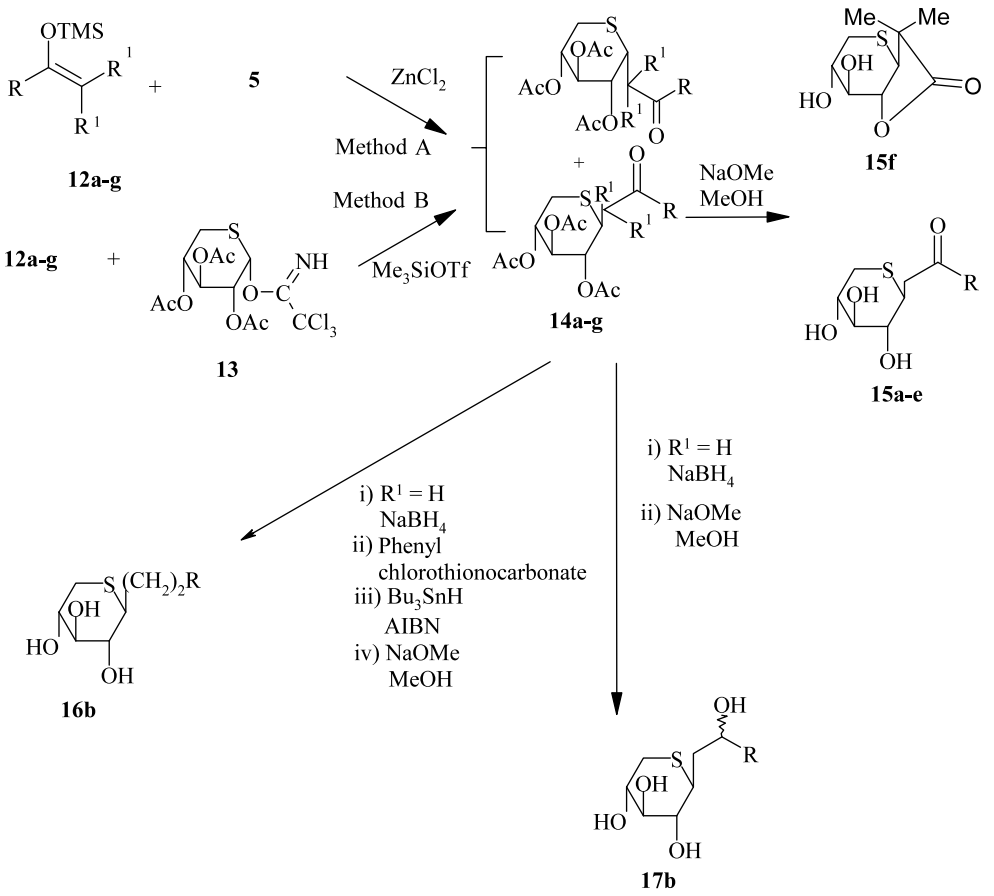
We were also interested in preparing another type of C-thioxylose analogue of Beciparcil, which was obtained by using a Wittig reaction (Scheme 6). The reaction conditions described by Fraser-Reid and co-workers[39] did not give the expected compounds; use of pyridine as solvent afforded the Wittig adduct, which immediately cyclized to yield **22**. In the case of the corresponding O-xyloside, the α,β-unsaturated ester obtained by the Wittig reaction did not cyclize immediately but required a cyclization step in basic media.[40] Aminolysis of the ester using 4-aminobenzonitrile led to the desired product (Scheme 6). Derivative **23β** was obtained in 9% yield from 5-thio-D-xylopyranose. The $J_{1,2}$ coupling constant of 9.5 Hz supported the anomeric configuration.

All products were studied in Wessler's rat model for venous thrombosis.[41] In these experiments, factor Xa is the thrombogenic agent, with thrombosis being studied 4 h after oral administration of the product. Only **15b**, **16b**, and **17b** demonstrated activities similar to that of Beciparcil. Surprisingly, compound **16b** was extensively metabolized in in vitro studies with human microsomes[8] and so could not be evaluated in clinical trials.

3. Experimental

3.1. General methods

TLC was performed on precoated plates of Silica gel 60-254-F; components were detected by UV light and by spraying the plates with 10% H_2SO_4 and subsequent



a : R = Ph R^1 = H
b : R = 4-CNC_6H_4 R^1 = H
c : R = HC = CH-Ph R^1 = H
d : R = $(CH_2)_2$Ph R^1 = H
e : R = $(CH_2)_2$-4-CNC_6H_4 R^1 = H
f : R = OMe R^1 = Me
g : R =Me R^1 = H

Scheme 4.

heating. Melting points were determined with Kofler apparatus and are uncorrected. Specific rotations were recorded with a Perkin–Elmer 241 polarimeter. ^{1}H NMR spectra were recorded with a Bruker ACP-300 spectrometer and chemical shifts refer to an internal standard of Me_4Si ($\delta = 0.00$). Elemental analyses were performed with a Perkin–Elmer CHN 2400 instrument.

3.2. 2,3,4-Tri-*O*-benzyl-5-thio-D-xylonolactone (4)

Potassium hydroxide (52 g, 0.93 mol) and benzyl bromide (79.6 g, 0.46 mol) were added slowly to a solution of methyl 5-thio-D-xylopyranoside[19] (**1**, 8.39 g, 46.6 mmol) in tetrahydrofuran (100 mL). The solution was refluxed for 4 h, cooled and then poured into 1 M aq HCl. This mixture was extracted with Et_2O. The organic layer was washed twice with water, dried ($MgSO_4$), and concentrated under diminished pressure. The residue was purified by flash chromatography on silica gel with 9:1 toluene–EtOAc to give methyl 2,3,4-tri-*O*-benzyl-5-thio-D-xylopyranoside[20b] (**2**, 16.75 g, 79%) as white crystals, mp 66 °C; $[\alpha]_D^{28}$ +11° (*c* 0.67, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.44 (m, 1 H, H-5), 2.76 (m, 1 H, H-5), 3.41 (s, 1.41 H, $CH_3\alpha$), 3.55 (s, 1.59 H, $CH_3\beta$), 3.73 (m, 3 H, H-2,3,4), 4.32 (d, 0.47 H, $J_{1,2}$ 1.2 Hz, H-1α), 4.40 (d, 0.53 H, $J_{1,2}$ 8.6 Hz, H-1β), 4.75 (m, 6 H, CH_2Ph), 7.32 (m, 15 H, Ph).

A solution of **2**[20b] (1 g, 2.2 mmol) and 1 M H_2SO_4 in AcOH (30 mL) was heated at 100 °C with stirring. One hour later, the mixture was poured into ice. The solution was extracted with CH_2Cl_2, the organic layer washed with brine, dried ($MgSO_4$), and concentrated under diminished pressure. The residue was purified by flash chromatography on silica gel with 12:1 toluene–EtOAc

Table 1
Results of the silylated enol ethers strategy (A, **5**+Zn Cl_2; B, **13**+Me_3SiOTf)

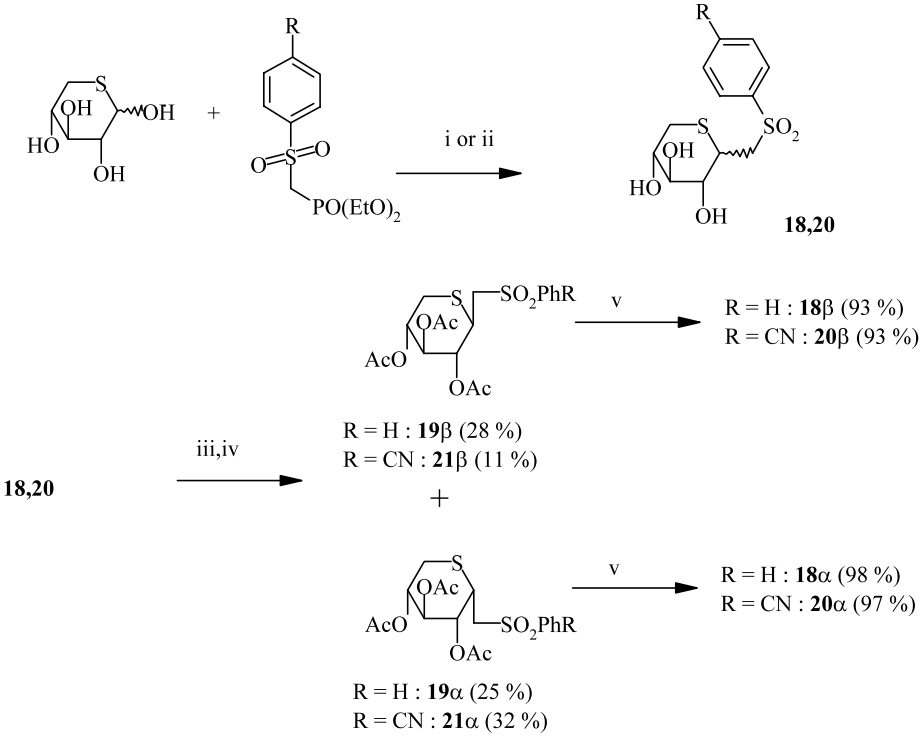
Product	R	R^1	Strategy	Yield (product 14)	$J_{1,2}$ (Hz)
12 a	Ph	H	A	51%	10.1
12 b[41a]	4-CNC_6H_4	H	B	33%	10.3
12 c[41b]	CH=CH-Ph	H	B	29%	10.2
12 d[41c]	$(CH_2)_2Ph$	H	B	13%	9.6
12 e	$(CH_2)_2$-4-CNC_6H_4	H	B	11%	9.6
12 f	OCH_3	CH_3	A	54%	10.7
12g	CH_3	H	A	41%	10.2

to give 2,3,4-tri-*O*-benzyl-5-thio-D-xylopyranose (**3**, 760 mg, 79%) as white crystals; mp 68 °C; $[\alpha]_D^{28}$ +1° (*c* 1.4, MeOH); ^1H NMR (300 MHz, Me_2SO): δ 2.79 (m, 2 H, H-5), 3.6 (m, 3 H, H-2,3,4), 4.77 (m, 6 H, CH_2 Ph), 4.9 (d, 0.15 H, $J_{1,2}$ 11 Hz, H-1β), 5.08 (s, 0.85 H, H-1α), 7.31 (m, 15 H, Ph). Anal. Calcd for $C_{25}H_{27}O_4S$: C, 70.89; H, 6.43. Found: C, 70.91; H, 6.47.

A solution of **3** (500 mg, 1.15 mmol) and Ac_2O (1.5 mL) in Me_2SO (5 mL) was stirred[20] for 48 h. The mixture was then extracted with Et_2O. The organic layer was diluted with CCl_3CH_3, washed with water, dried ($MgSO_4$) and concentrated under diminished pressure. The product **4** was obtained by precipitation with ether as white crystals; mp 120 °C; $[\alpha]_D^{28}$ −1° (*c* 0.3, 1:1 MeOH–Me_2SO); ^1H NMR (300 MHz, $CDCl_3$): δ 3.21 (dd, 1 H, $J_{5,5'}$ 12 Hz, $J_{4,5}$ 3.8 Hz, H-5eq), 3.86 (m, 1 H, H-3), 4.0 (m, 1 H, H-4), 4.12 (d, 1 H, $J_{2,3}$ 6 Hz, H-2), 4.41 (m, 1 H, H-5ax), 4.53 (m, 5 H, CH_2Ph), 4.85 (d, 1 H, *J* 11.7 Hz, CH_2Ph), 7.31 (m, 15 H, Ph). Anal. Calcd for $C_{26}H_{26}O_4S$: C, 71.86; H, 6.03. Found: C, 71.19; H, 5.70.

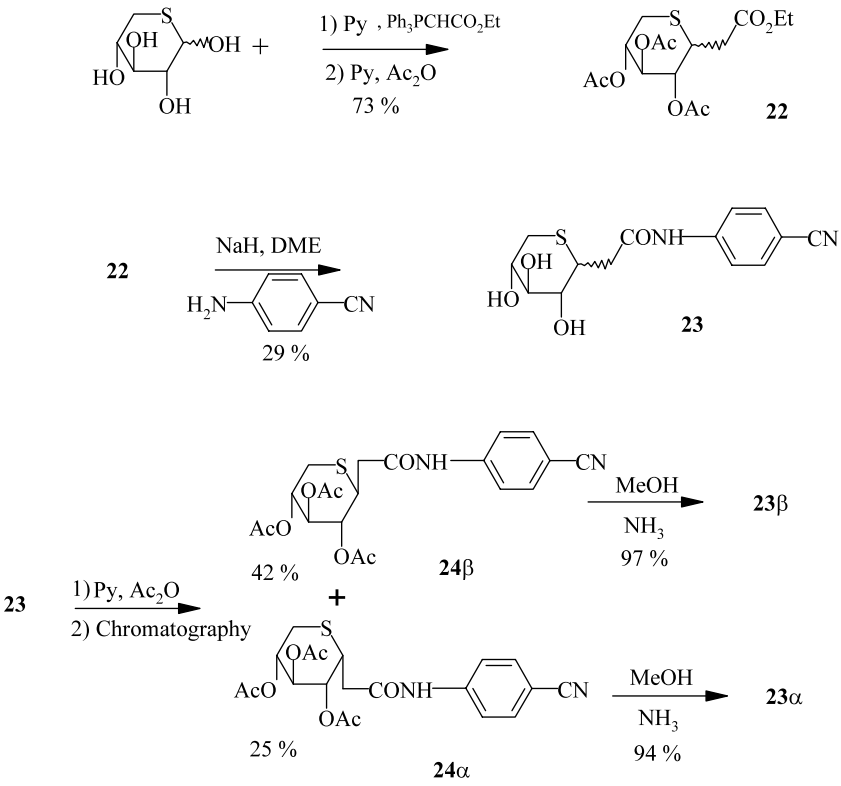
3.3. 1,5-Anhydro-2,3,4-tri-*O*-acetyl-5-thio-D-xylitol (7)

Acrylonitrile (987 μL, 15 mmol) and then tributyltin hydride (960 mg, 3.3 mmol) were added dropwise to a suspension of bromide **5** (1.065 g, 3 mmol) in ether (6 mL). After 24 h of irradiation with a sun lamp (750 W), the mixture was concentrated under diminished pressure. The residue was purified by flash chromatography on silica gel with 5:1 toluene–EtOAc to give **7** as white solid (345 mg, 42%); mp 129 °C; $[\alpha]_D^{23}$ 0° (*c* 1, $CDCl_3$); ^1H NMR (300 MHz, Me_2SO): δ 1.98 (s, 9 H, OAc), 2.7 (m,



i) R = H / NaHMDS, pyr, 100°C, 15 min, 30 %, **18**, a/b = 50/50; ii) R = CN / NaH, pyr, 10 h, 5°C, 31 %, 20, a/b = 70/30; iii) Ac_2O, pyr; iv) Chromatography; v) NaOMe, MeOH

Scheme 5. (i) R = H/NaHMDS, pyr, 100 °C, 15 min, 30%, **18**, a/b = 50/50; (ii) R = CN/NaH, pyr, 10 h, 5 °C, 31%, **20**, a/b = 70/30; (iii) Ac_2O, pyr; (iv) chromatography; (v) NaOMe, MeOH.



Scheme 6.

4 H, CH_2), 4.8 (m, 2 H, H-2, H-4), 5.05 (t, 1 H, *J* 9.6 Hz, H-3). Anal. Calcd for $C_{11}H_{16}O_6S$: C, 47.82; H, 5.84. Found: C, 47.77; H, 5.88.

3.4. α-(5-Thio-β-D-xylopyranosyl)-toluene (9)

Benzyl chloride (20 mL, 0.174 mol) in ether (100 mL) was added dropwise to a suspension of magnesium turnings (5 g, 0.205 mol) in ether (50 mL) for 30 min at room temperature (rt). After refluxing for 2 h, a solution of bromide **5** (4.26 g, 12 mmol) in ether (100 mL) was added dropwise during 30 min to the Grignard reagent. The mixture was boiled under reflux for 3 h and then poured into iced water and AcOH. After stirring, the organic layer was concentrated and the residue was treated with Ac_2O (50 mL), pyridine (50 mL) and small amounts of 4-dimethylaminopyridine. The mixture was stirred overnight, poured into iced 1 M HCl (800 mL) and extracted with ether. The dried extract was evaporated and the residue purified by flash chromatography on silica gel with 8:1 toluene–EtOAc to give α-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)toluene (**8**), mp 164 °C; $[\alpha]_D^{28}$ +4° (*c* 0.3, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 1.96 (s, 9 H, OAc), 2.4 (m, 1 H, CH_2), 2.67 (m, 1 H, H-5eq), 2.81 (m, 1 H, H-5ax), 3.0 (m, 1 H, CH_2), 3.45 (m, 1 H, H-1), 4.82 (m, 1 H, H-4), 4.94 (t, 1 H, *J* 10.1 Hz, H-2), 5.08 (t, 1 H, *J* 9.5 Hz, H-3), 7.26 (m, 5 H, Ph); ^{13}C NMR (60 MHz, $CDCl_3$): δ 20.6 (CH_3CO_2), 30.0 (CH_2S), 36.8 (CH_2Ph), 46.6 (C-2), 72.9 (C-5), 74.4 (C-3), 75.6 (C-4), 126–137 (Ph), 169 (CO). Anal. Calcd for $C_{18}H_{22}O_6S$: C, 59.00; H, 6.05. Found: C, 59.52; H, 5.80.

Sodium methoxide (8.8 mg, 0.16 mmol) was added to a suspension of compound **8** (600 mg, 1.63 mmol) in MeOH (25 mL) and the mixture stirred for 1.5 h at rt. The mixture was then neutralized with Amberlite® IR-120 (H^+). Filtration and lyophilisation of the solution gave compound **9** (295 mg, 75%); mp 103 °C; $[\alpha]_D^{24}$ +17° (*c* 0.2, Me_2SO); ^{1}H NMR (300 MHz, Me_2SO): δ 2.76 (m, 1 H, H-4), 2.85 (m, 3 H), 2.91 (m, 1 H, H-2), 3.1 (m, 1 H, H-3), 3.34 (s, 2 H), 4.89 (d, 1 H, *J* 4.2 Hz, OH), 5.01 (d, 1 H, *J* 4.5 Hz, OH), 5.11 (d, 1 H, *J* 5.2 Hz, OH), 7.20 (m, 5 H, Ph). Anal. Calcd for $C_{12}H_{16}O_3S$; 0.39 H_2O: C, 58.27; H, 6.84. Found: C, 58.16; H, 6.64.

3.5. (5-Thio-β-D-xylopyranosyl)benzene (11)

A solution of 7 g (19.7 mmol) of the bromide **5** in ether (200 mL) was added dropwise during 30 min to phenylmagnesium bromide (43 g, 0.24 mol) in ether (180 mL). The mixture was refluxed for 3 h and then poured into iced water and AcOH. After stirring, the organic layer was concentrated and the residue was treated with Ac_2O (50 mL), pyridine (60 mL) and small amounts of 4-dimethylaminopyridine. The mixture was stirred overnight, poured into iced 1 M HCl and extracted with ether. After concentrating under decreased pressure, the residue was purified by flash

chromatography on silica gel using 9:1 toluene–EtOAc as eluent to give compound **10** as white crystals (2.4 g, 35%); mp 191 °C; $[\alpha]_D^{22}$ +2° (*c* 0.46, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 1.63–2.5 (m, 9 H, OAc), 2.84 (m, 1 H, H-5eq), 3.07 (m, 1 H, H-5ax), 4.35 (d, 1 H, $J_{1,2}$ 10.6 Hz, H-1), 5.03 (m, 1 H, H-4), 5.18 (t, 1 H, H-3), 5.36 (t, 1 H, H-2), 7.3 (m, 5 H, Ph). Anal. Calcd for $C_{17}H_{20}O_6S$: C, 57.94; H, 5.72. Found: C, 58.06; H, 5.63.

To a suspension of compound **10** (1 g, 2.86 mmol) in MeOH (25 mL) was added NaOMe (30.8 mg, 0.57 mmol). After stirring during 2 h the mixture was neutralized with Amberlite® IR-120 (H^+). Filtration followed by flash chromatography on silica gel with 10:1 CH_2Cl_2–MeOH gave compound **11** as white crystals (459 mg, 71%); mp 195 °C; $[\alpha]_D^{21}$ +47° (*c* 0.5, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 2.59 (m, 2 H, H-5), 3.03 (m, 1 H, H-2), 3.5 (m, 1 H, H-4), 3.65 (m, 2 H, H-3,1), 4.76 (d, 1 H, *J* 4 Hz, OH), 4.96 (d, 1 H, *J* 5 Hz, OH), 5.12 (d, 1 H, *J* 5 Hz, OH), 7.29 (m, 5 H, Ph). Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.38; H, 6.23. Found: C, 58.09; H, 6.23.

3.6. Use of enoxysilanes: C-glycosyl bond formation

3.6.1. Procedure A. To a solution of bromide **5** and 2.2 equiv of $ZnCl_2$ in CH_2Cl_2 was added dropwise enol ether **12**[43] (2 equiv). One hour later, the mixture was poured into iced water and extracted with CH_2Cl_2. The organic layer was washed (HCl 1 M, brine) and dried ($MgSO_4$). The residue was purified by flash chromatography on silica gel. To a suspension of the triacetate **14** in MeOH was added 0.1 equiv of NaOMe and 1 h later the solution was made neutral with Amberlite® IR-120 (H^+). Filtration and evaporation of the filtrate gave the product **15**.

3.6.1.1. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)propan-2-one (14g). Flash chromatography (3:2 EtOAc–petroleum ether) gave **14g** as white crystals; mp 79 °C; $[\alpha]_D^{21}$ −15° (*c* 0.5, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.1 (t, 1 H, $J_{3,4}$ 9.4 Hz, H-3), 5.02 (m, 1 H, $J_{4,5e}$ 5.2 Hz, H-4), 4.95 (dd, 1 H, $J_{2,3}$ 9.4 Hz, H-2), 3.55 (ddd, 1 H, $J_{1,2}$ 10.2 Hz, H-1), 2.94 (dd, 1 H, $J_{4,5a}$ 10.3 Hz, H-5a), 2.8 (dd, 1 H, $J_{5a,5e}$ 13.3 Hz, H-5e), 2.76 (dd, 1 H, *J* 4.8 and 17 Hz, CH_2), 2.44 (dd, 1 H, *J* 8.4 Hz, CH_2), 2.13 (s, 3 H, CH_3), 1.97 (s, 3 H, OAc), 1.96 (s, 6 H, OAc). Anal. Calcd for $C_{14}H_{20}O_7S$: C, 50.59; H, 6.07. Found: C, 50.6; H, 6.16.

3.6.1.2. 2′-(5-Thio-β-D-xylopyranosyl)acetophenone (15a). Flash chromatography with 2:3 EtOAc–petroleum ether gave 2′-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)acetophenone **14a** in 51% yield; mp 128 °C; $[\alpha]_D^{21}$ −31° (*c* 0. 3, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.93 (d, 2 H, *J* 7 Hz, Ar), 7.6 (t, 1 H, *J* 7 Hz, Ar), 7.48 (t, 2 H, *J* 7 Hz, Ar), 5.17 (t, 1 H, $J_{2,3}$ 9.7 Hz, $J_{3,4}$ 9.7 Hz, H-3), 5.22–5.06 (m, 2 H, H-2,4), 3.67 (ddd, 1 H, $J_{1,2}$ 10.1 Hz, H-1), 3.18 (dd, 1 H, *J* 5 and 17 Hz, CH_2), 3.01 (dd, 1 H, *J* 7.7 Hz, CH_2), 2.91–2.7 (m, 2 H, H-5), 2.03 (s, 3 H, OAc), 2.01 (s, 3 H, OAc), 1.89 (s, 3 H, OAc). Anal. Calcd for $C_{19}H_{22}O_7S$: C, 57.86; H, 5.62. Found: C, 57.84; H, 5.65.

Compound **15a** formed as white crystals (99% yield); mp 174 °C; $[\alpha]_D^{21}$ +30° (*c* 0.6, pyridine); ^{1}H NMR (300 MHz, C_5D_5N): δ 8.17 (d, 2 H, *J* 7 Hz, Ar), 7.47 (t, 1 H, *J* 7 Hz, Ar), 7.4 (t, 2 H, *J* 7 Hz, Ar), 4.31 (m, 1 H, $J_{4,5e}$ 5.9 Hz, $J_{4,5a}$ 8.9 Hz, H-4), 4.23 (dd, 1 H, *J* 3.9 and 16.5 Hz, CH_2), 4.1 (dd, 1 H, $J_{2,3}$ 8.3 Hz, H-2), 3.97 (ddd, 1 H, $J_{1,2}$ 10 Hz, H-1), 3.86 (t, 1 H, H-3), 3.3 (dd, 1 H, *J* 8.5 Hz, CH_2), 3.1–2.92 (m, 2 H, H-5). Anal. Calcd for $C_{13}H_{16}O_4S$: C, 58.19; H, 6.01. Found: C, 57.94; H, 5.99.

3.6.1.3. 3,7-Anhydro-2,2-dimethyl-4-thio-L-*gluco*-heptonic acid, γ-lactone (15f). Flash chromatography with 5:1 toluene–EtOAc produced 2-methyl-2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)propanoic acid methyl ester **14f** in 54% yield; mp 119 °C; $[\alpha]_D^{25}$ −29° (*c* 0.43, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13, 1.32 (2s, 6 H, CH_3), 1.92, 1.93, 2.0 (3s, 9 H, OAc), 2.65 (m, 1 H, H-5ax), 2.91 (m, 1 H, H-5eq), 3.53 (d, 1 H, $J_{1,-2}$ 10.7 Hz, H-1), 3.7 (s, 3 H, OCH_3), 5.0 (m, 2 H, H-2, H-4), 5.23 (t, 1 H, H-3). Anal. Calcd for $C_{16}H_{24}O_8S$: C, 51.05; H, 6.43. Found: C, 50.96; H, 6.67.

Compound **15f** was obtained: white crystals; quantitative yield; mp 200 °C; $[\alpha]_D^{25}$ +71° (*c* 0.43, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 1.04, 1.18 (2s, 6 H, CH_3), 2.6 (m, 1 H, H-5ax), 2.73 (m, 1 H, H-5eq), 3.33 (m, 1 H, H-3), 3.43 (m, 1 H, H-4), 4.05 (t, 1 H, *J* 9.5 Hz, H-2), 5.46, 5.59 (2d, 2 H, OH); ^{13}C NMR (60 MHz, Me_2SO): δ 18.0 (CH_3), 22.0, (CH_3), 33.8 (CH_2S), 42.8 (C-1), 52.1 ($C(CH_3)_2$), 74, 75.7 (C-4, C-3), 83 (C-2), 179.4 (C=O). Anal. Calcd for $C_9H_{14}O_4S$: C, 49.52; H, 6.46. Found: C, 49.45; H, 6.40.

3.6.2. Procedure B. To a solution of the trichloroacetimidate **13**[44] and 1 equiv of enol ether **12** in CH_2Cl_2 was added dropwise 0.1 equiv of trimethylsilyltriflate. One hour later diisopropylethylamine was added to the mixture, which was poured into iced water and then extracted with EtOAc. The organic layer was dried ($MgSO_4$) and concentrated under diminished pressure. The residue was purified by flash chromatography on silica gel and the compound **14** was then deacetylated as in Procedure A to give **15**.

3.6.2.1. 4-Cyano-2′-(5-thio-β-D-xylopyranosyl)acetophenone (15b). Flash chromatography using 9:1 toluene–EtOAc gave 4-Cyano-2′-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)acetophenone (**14b**) in 33% yield; mp 182 °C; $[\alpha]_D^{24}$ −38° (*c* 0.64, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93 (s, 3 H, OAc), 2.02 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), 2.76 (m, 1

H, H-5ax), 2.86 (m, 1 H, H-5eq), 3.08 (m, 2 H, CH_2CO), 3.63 (m, 1 H, H-1), 5.11 (t, 1 H, H-3), 4.96 (t, 1 H, $J_{1,2}$ 10.3 Hz, H-2), 4.88 (m, 1 H, H-4), 7.78 (d, 2 H, J 8.4 Hz, Ph), 8 (d, 2 H, J 8.4 Hz, Ph); ^{13}C NMR (60 MHz, $CDCl_3$): δ 20.1, 20.5, 20.8 (CH_3CO), 30.3 (C-5), 39.5, 39.8 (C-1, CH_2CO), 72.6, 74, 75.1 (C-2, C-3, C-4), 116.8 (Ph), 117.7 (CN), 128.6 (Ph), 132.7 (Ph), 139 (Ph), 169.7 (CO_2), 194.7 (CO). Anal. Calcd for $C_{20}H_{21}NO_7S$: C, 57.27; H, 5.05; N, 3.34. Found: C, 57.04; H, 3.90; N, 3.16.Compound **15b** was obtained by flash chromatography using 10:1 CH_2Cl_2–MeOH then crystallization with 2-propanol; 66% yield; mp 118 °C; $[\alpha]_D^{22}$ +10° (*c* 0.5, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 2.5 (m, 2 H, H-5, H-5′), 2.94 (m, 2 H, CH_2CO), 3.08 (m, 1 H), 3.16 (m, 1 H), 3.39 (m, 1 H), 3.60 (dd, 1 H, J 16.3 Hz, J 3.9 Hz, CH_2CO), 4.90 (d, 1 H, J 4 Hz, OH), 5.08 (d, 1 H, J 4.6 Hz, OH), 5.19 (d, 1 H, J 4.6 Hz, OH), 8,04 (m, 4 H, Ph). Anal. Calcd for $C_{14}H_{15}NO_4S$: C, 57.32; H, 5.15; N, 4.77. Found: C, 56.77; H, 5.21; N, 4.67.

3.6.2.2. 4-Phenyl-1-(5-thio-β-D-xylopyranosyl)-(*E*)-3-buten-2-one (15c). Flash chromatography using 9:1 toluene–EtOAc yielded 4-phenyl-1-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-(*E*)-3-buten-2-one (**14c**) (29%); mp 156 °C; $[\alpha]_D^{23}$ +19° (*c* 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93, 1.95, 1.98 (3s, 9 H, OAc), 2.73, (m, 2 H, H-5eq, CH_2CO), 2.96 (m, 1 H, CH_2CO), 2.98 (m, 1 H, H-5ax), 3.71 (m, 1 H, H-1), 4.86 (m, 1 H, H-3), 4.92 (t, 1 H, J 10.2 Hz, H-2), 5.1 (t, 1 H, J 9.5 Hz, H-3), 6.94 (d, 1 H, J 15 Hz, CH=CHPh), 7.3 (m, 5 H, Ph), 7.60 (d, 1 H, CH=CH Ph). HRMS: Calcd for $C_{21}H_{24}O_7NaS$ [M+Na], 443.1140; Found: 443.1140.

Compound **15c** was obtained by flash chromatography using 9:1 CH_2Cl_2–MeOH; 80% yield; mp 117 °C; $[\alpha]_D^{19.50}$ +27° (*c* 0.6, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 2.45 (m, 2 H), 2.57 (m, 1 H), 2.95 (m, 1 H), 3.06 (2 H), 3.12 (m, 1 H), 3.40 (m, 1 H), 4.95 (broad s, 1 H, OH), 5.08 (broad s,1 H, OH), 5.17 (broad s, 1 H, OH), 6.92 (d, 1 H, J 16.2 Hz), 7.43 (m, 3 H), 7.60 (d, 1 H, J 16.2 Hz), 7.73 (m, 2 H, Ph). Anal. Calcd for $C_{15}H_{18}O_4S$; 0.16 H_2O: C, 60.612; H, 6.21. Found: C, 60.39; H, 6.20.

3.6.2.3. 4-Phenyl-1-(5-thio-β-D-xylopyranosyl)-2-butanone (15d). Flash chromatography using 4:1 methylcyclohexane–EtOAc yielded 4-phenyl-1-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-2-butanone **14d** (13%); mp 124 °C; $[\alpha]_D^{25}$ +21° (*c* 0.5, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 1.92, 1.94, 1.97 (3s, 9 H, OAc), 2.43 (m, 1 H, CH_2CO), 2.67 (m, 1 H, CH_2CO), 2.76 (s, 4 H, CH_2–CH_2), 2.77 (m, 1 H, H-5eq), 2.95 (m, 1 H, H-5ax), 3.6 (m, 1 H, H-1), 4.82 (t, 1 H, J 9.6 Hz, H-2), 4.86 (m, 1 H, H-4), 5.07 (t, 1 H, J 9.6 Hz, H-3), 7.22 (m, 5 H, Ph). HRMS: Calcd for $C_{21}H_{26}O_7NaS$ [M+Na], 445.1297; Found: 445.1289.

4-Phenyl-1-(5-thio-β-D-xylopyranosyl)-2-butanone **15d**: flash chromatography using 24:1 CH_2Cl_2–MeOH; 72% yield; mp 115 °C; $[\alpha]_D^{23}$ +19° (*c* 0.5, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 2.25 (m, 1 H), 2.49 (m, 2 H), 2.72 (m, 4 H), 2.97 (m, 4 H), 3.38 (m, 1 H), 4.9 (d, 1 H, J 3.8 Hz, OH), 5.06 (d, 1 H, J 5 Hz, OH), 5.12 (d, 1 H, J 5 Hz, OH), 7.28 (m, 1 H, Ph). Anal. Calcd for $C_{15}H_{20}O_4S$: C, 60.78; H, 6.80. Found: C, 60.35; H, 6.87.

3.6.2.4. 4-[[4-(5-Thio-β-D-xylopyranosyl)-3-oxo]butyl]-benzonitrile (15e). To a solution of 4-(3-oxobutyl)benzonitrile[42] (2.77 g, 16 mmol) in THF (20 mL) at −40 °C under Ar atmosphere, was added 1.1 equiv of lithium diisopropylamide followed by dropwise addition of trimethylsilyl triflate (14.22 g, 64 mmol) during a period of 10 min. The reaction was quenched with diisopropylethylamine (10 mL) and poured into $NaHCO_3$ solution (50 mL) with ice. The mixture was extracted with pentane and the organic layer was concentrated under diminished pressure. The residue was purified by flash chromatography on silica gel with 5:1:0.01 pentane–ether–triethylamine and the product, a colorless liquid (yield 34%) was used immediately for the synthesis of **14e**.

Starting from 4-[3-[(trimethylsilyl)oxy]-3-butenyl]benzonitrile, flash chromatography using 5:2 cyclohexane–EtOAc yielded 4-[[4-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-3-oxo]butyl]benzonitrile **14e** (11%); mp 170 °C; $[\alpha]_D^{29}$ −12° (*c* 0.15, $CHCl_3$); ^{1}H NMR (300 MHz, Me_2SO): δ 1.93, 1.94, 1.98 (3s, 9 H, OAc), 2.46 (m, 1 H, CH_2CO), 2.72 (m, 2 H, H-5eq, CH_2CO), 2.83 (s, 4 H, CH_2–CH_2), 2.95 (m, 1 H, H-5ax), 3.60 (m, 1 H, H-1), 4.82 (t, 1 H, $J_{1,2}$ 9.6 Hz, H-2), 4.88 (m, 1 H, H-4), 5.07 (t, 1 H, J 9.6 Hz, H-3), 7.42 (d, 2 H, J 8.4 Hz, Ar), 7.73 (d, 2 H, J 8.4 Hz, Ar). Anal. Calcd for $C_{22}H_{25}NO_7S$: C, 59.05; H, 5.63. Found: C, 59.15; H, 5.70.

4-[[4-(5-Thio-β-D-xylopyranosyl)-3-oxo]butyl]benzonitrile **15e**: Flash chromatography using 6:4:0.01 MeCN–water–trifluoroacetic acid; yield 77%; mp 153 °C; $[\alpha]_D^{24}$ +12° (*c* 0.22, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 2.26 (m, 1 H), 2.49 (m, 1 H), 2.90 (m, 8 H), 3.37 (m, 1 H), 4.90 (d, 1 H, J 4.2 Hz, OH), 5.07 (d, 1 H, J 4.9 Hz, OH), 5.14 (d, 1 H, J 4.9 Hz, OH), 7.42 (d, 2 H, J 8.4 Hz, Ar), 7.73 (d, 2 H, J 8.4 Hz, Ar). Anal. Calcd for $C_{16}H_{19}NO_4S$; 0.37 H_2O: C, 58.58; H, 6.06; N, 4.27. Found: C, 58.46; H, 5.92; N, 4.18.

3.6.2.5. 2-[5-Thio-β-D-xylopyranosyl)-1-hydroxy-ethyl]benzonitrile (17b). To a solution of compound **14b** (510 mg, 1.22 mmol) in CH_2Cl_2 (25 mL) and MeOH (5 mL) was added $NaBH_4$ (100 mg, 2.6 mmol) under an inert atmosphere. The mixture was hydrolyzed 30 min later on iced water and extracted with CH_2Cl_2. The organic layer was washed with water, dried and evaporated under diminished pressure. The residue

gave [2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-1-hydroxyethyl]benzonitrile (500 mg, 97.5%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.01, (s, 9 H, OAc), 2.03, (m, 2.5 H), 2.33 (d, 0.5 H, *J* 4.5 Hz OH), 2.6 (m, 1.5 H) 2.9 (m, 1 H), 3.26 (m, 0.5 H), 5.04 (m, 4 H), 7.47 (m, 2 H, Ph), 7.65 (m, 2 H, Ph). To this product (380 mg, 0.9 mmol) in MeOH (20 mL) was added a NaMeO solution (55 μL, 18% in MeOH). After stirring this mixture one for 1 h, the mixture was neutralized with Amberlite® IR-120 (H^+ resin). After filtration, the residue was concentrated under diminished pressure and purified by flash chromatography on silica gel with 9:1 CH_2Cl_2–MeOH and by lyophilisation to give **17b** (260 mg; 97%); mp 80 °C; $[\alpha]_D^{22}$ −9.2° (*c* 0.24, Me_2SO); ^{1}H NMR (300 MHz, Me_2SO): δ 1.28 (m, 0.5 H, C*H*$_2$Ph), 1.60 (m, 0.5 H, C*H*$_2$CPh), 2.40 (m, 3.5 H, H-1, C*H*$_2$CPh, H-5), 2.85 (m, 1.5 H, H-3,2), 3.12 (m, 1 H, H-2), 3.40 (m, 1 H, H-4), 4.86 (m, 1 H, OH), 5.07 (m, 2 H, OH), 5.12 (m, 2 H, OH, C*H*Ph), 5.55 (d, 0.5 H, *J* 4.5 Hz, OH), 5.62 (d, 0.5 H, *J* 4.5 Hz OH), 7.54 (m, 2 H, Ph), 7.82 (m, 2 H, Ph). Anal. Calcd for $C_{14}H_{17}NO_7S$: C, 55.61; H, 5.93; N, 4.63. Found: C, 55.27; H, 5.85; N, 4.56.

3.6.2.6. [2-(5-Thio-β-D-xylopyranosyl)ethyl]benzonitrile (16b). A solution of [2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-1-hydroxyethyl]benzonitrile (2 g, 4.75 mmol), dimethylaminopyridine (6.08 g, 50 mmol), phenyl chlorothionocarbonate (2 mL, 15 mmol) in MeCN (60 mL) was stirred under inert atmosphere for 2 h. The mixture was then neutralized ($NaHCO_3$ 5%) and concentrated under diminished pressure. The residue was dissolved in CH_2Cl_2, washed with water, dried and evaporated. [2-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-1-(phenylthiocarbonate)oxoethyl)benzonitrile was obtained (2.38 g, 90%) by flash chromatography on silicagel with 3:2 methylcyclohexane–EtOAc. A solution of [2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-1-(phenylthiocarbonate)oxoethyl]benzonitrile (2.3 g, 4.12 mmol), azobisisobutyronitrile (138 mg, 0.84 mmol), tributyltin hydride (1.7 mL, 6.43 mmol) in toluene (60 mL) was boiled at 110 °C for 45 min. The mixture was evaporated and subjected to flash chromatography on silica gel with 6:1 toluene–EtOAc. [2-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)ethyl]benzonitrile was obtained (1.37 g, 82%); ^{1}H NMR (300 MHz, Me_2SO): δ 1.51 (m, 1 H, C*H*$_2$CH$_2$Ph), 1.91 (m, 1 H, C*H*$_2$CH$_2$Ph), 1.95, 1.97, 2.0 (3s, 9 H, OAc), 2.65 (m, 1 H, CH$_2$Ph), 2.83 (m, 3 H, C*H*$_2$Ph, H-5), 3.14 (m, 1 H, H-1), 4.90 (m, 2 H, H-2,4), 5.05 (t, 1 H, H-3), 7.40 (d, 2 H, Ph), 7.75 (d, 2 H, Ph). To a suspension of this product (1.53 g, 3.78 mmol) in MeOH (60 mL) was added 18% MeOH solution of NaOMe (180 μL). One hour later the mixture was neutralized with Amberlite® IR-120 (H^+) resin, filtered and evaporated. The residue was crystallized in MeOH–ether to give **16b** (0.5 g, 50%); mp 144 °C; $[\alpha]_D^{23}$ −24° (*c* 0.41, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 1.53 (m, 1 H, CH$_2$C*H*$_2$Ph), 2.26 (m, 1 H, C*H*$_2$CH$_2$Ph), 2.45 (m, 1 H, H-5ax), 2.56 (m, 1 H, H-5eq), 2.67 (m, 1 H, C*H*$_2$Ph), 2.85 (m, 2 H, C*H*$_2$Ph, H-2), 3.12 (m, 2 H, H-3,4), 3.38 (m, 1 H, H-1), 4.86 (d, 1 H, *J* 4.2 Hz, OH), 5.04 (m, 2 H, OH), 7.41 (d, 2 H, *J* 8.2 Hz, Ph) 7.74 (d, 2 H, *J* 8.2 Hz, Ph). Anal. Calcd for $C_{14}H_{17}NO_3S$: C, 60.19; H, 6.13; N, 5.01. Found: C, 59.88; H, 6.14; N, 4.81.

3.6.2.7. Phenyl (5-thio-α,β-D-xylopyranosyl)methyl sulfone (18). To a stirred solution of diethyl phenylsulfonylmethyl phosphonate (14 g, 47.9 mmol) in THF (10 mL) under N_2 cooled at 0 °C was added dropwise a solution of sodium bis(trimethylsilyl)amide (96 mL, 96 mmol, 1 M in THF). The solution was stirred for 30 min, and then concentrated under vacuum. A solution of 5-thio-D-xylopyranose (4 g, 24.07 mmol) in dry pyridine (50 mL) was added to the white crystals. The solution was then stirred under N_2 at 80 °C for 25 min and then concentrated in vacuo. Flash chromatographic purification (9:1 CH_2Cl_2–CH_3OH) on silica gel yielded 2.2 g (30%) of **18** as a yellow oil (1:1 mixture of α and β anomers). ^{1}H NMR (300 MHz, Me_2SO): δ 2.39–2.48 (m, 2 H, H-5), 2.82–2.94 (m, 1 H, H-1β,3β), 3.01–3.09 (m, 1 H, H-2β,3α), 3.12–3.18 (m, 0.5 H, H-1α), 3.32–3.40 (m, 1.5 H, H-4, CH_2SO_2β), 3.52–3.58 (m, 1 H, H-2α, CH_2SO_2α), 3.68 (dd, 0.5 H, *J* 9.0 and 15.0 Hz, CH_2SO_2α), 3.82 (dd, 0.5 H, *J* 2.0 and 15.0 Hz, CH_2SO_2β), 4.89 (d, 0.5 H, *J* 4.5 Hz, OH), 4.95 (d, 0.5 H, *J* 4.5 Hz, OHα), 5.01 (d, 0.5 H, *J* 4.5 Hz, OHβ), 5.10 (d, 0.5 H, *J* 4.5 Hz, OHα) 5.31 (d, 0.5 H, *J* 5.5 Hz, OHβ), 5.33 (d, O.5 H, *J* 5.5 Hz, OHα), 7.61–7.67 (m, 2 H, Ar meta), 7.71–7.75 (m, 1 H, Ar para), 7.89–7.92 (m, 2 H, Ar ortho).

3.6.2.8. Phenyl (5-thio-α-D-xylopyranosyl)methyl sulfone (18α). (2,3,4-Tri-*O*-acetyl-5-thio-α-D-xylopyranosyl)methylphenyl sulfone **19**α (0.4 g, 0.93 mmol) was deacetylated using the procedure described for [2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)ethyl]benzonitrile with sodium methoxide. The compound was obtained as a white powder (0.277 g, 98% yield); mp 50 °C; $[\alpha]_D^{27}$ + 95° (*c* 0.40, CH_3OH); ^{1}H NMR (300 MHz, Me_2SO): δ 2.43 (m, 2 H, H-5), 3.05 (m, 1 H, H-3), 3.16 (m, 1 H, H-1), 3.36 (m, 1 H, H-4), 3.52–3.59 (m, 2 H, H-2, CH_2SO_2), 3.68 (dd, 1 H, *J* 9.0 and 15.0 Hz, CH_2SO_2), 4.95 (d, 1 H, *J* 4.5 Hz, OH), 5.10 (d, 1 H, *J* 5.5 Hz, OH), 5.31(d, 1 H, *J* 5 Hz, OH), 7.64 (t, 2 H, *J* 7 Hz, Ar meta), 7.70–7.76 (m, 1 H, Ar para), 7.91 (d, 2 H, *J* 7 Hz, Ar ortho). Anal. Calcd For $C_{12}H_{16}O_5S_2$; 0.39 H_2O: C, 46.28; H, 5.43, Found: C, 45.86; H, 5.17.

3.6.2.9. Phenyl (5-thio-β-D-xylopyranosyl)methyl sulfone (18β). (2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)methyl phenyl sulfone (**19β**, 0.43 g, 1 mmol) was deacetylated with NaOMe using the procedure de-

scribed for [2-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)ethyl]benzonitrile. The compound was obtained as a white powder (0.26 g, 65% yield); mp 163 °C; $[\alpha]_D^{28}$ +4° (*c* 0.42, CH_3OH); ^1H NMR (300 MHz, Me_2SO): δ 2.37 (dd, 1 H, *J* 10.5 and 13.0 Hz, H-5), 2.82–2.94 (m, 2 H, H-1,3), 3.05 (m, 1 H, H-2), 3.34–3.37 (m, 2 H, H-4, CH_2SO_2), 3.82 (dd, 1 H, *J* 2.0 and 15.0 Hz, CH_2SO_2), 4.89 (d, 1 H, *J* 4.5 Hz, OH), 5.01 (d, 1 H, *J* 4.5 Hz, OH), 5.31 (d, 1 H, *J* 5.5 Hz, OH), 7.62 (t, 2 H, *J* 7.0 Hz, Ar meta), 7.75 (t, 1 H, *J* 7.0 Hz, Ar para), 7.91 (d, 2 H, *J* 7.0 Hz, Ar ortho). Anal. Calcd For $C_{12}H_{16}O_5S_2$: C, 47.35; H, 5.30. Found: C, 46.94; H, 5.14.

3.6.2.10. (2,3,4-Tri-*O*-acetyl-5-thio-α- and β-D-xylopyranosyl)methyl phenyl sulfone (19α and 19β). Phenyl (5-thio-D-xylopyranosyl)methyl sulfone (**18**, 1.44 g, 4.73 mmol) was acetylated conventionally and after flash chromatographic purification on silica gel (6:4 toluene–ether), afforded 0.415 g of compound **19β** as white powder (28% yield); mp 50 °C; $[\alpha]_D^{28}$ −5° (*c* 0.42, $CHCl_3$); ^1H NMR (300 MHz, Me_2SO): δ 1.93 (s, 3 H, Ac), 1.94 (s, 3 H, Ac), 1.96 (s, 3 H, Ac), 2.69 (dd, 1 H, *J* 4.5 and 13.0 Hz, H-5), 2.95 (dd, 1 H, *J* 11 and 13.5 Hz, H-5′), 3.34 (m, 1 H, H-1), 3.40–3.60 (m, 2 H, CH_2SO_2), 4.77–4.84 (m, 1 H, H-4), 4.82 (t, 1 H, *J* 9.5 Hz, H-2), 5.10 (t, 1 H, *J* 9.5 Hz, H-3), 7.64 (t, 2 H, *J* 7.0 Hz, Ar meta), 7.77 (m, 1 H, Ar para), 7.95 (d, 2 H, *J* 7.0 Hz, Ar ortho); HRMS: Calcd for $C_{18}H_{22}O_8NaS_2$ [M+Na], 453.0654; Found: 453.0642, and 0.376 g of **19α** isomer as white powder (25% yield); mp 145 °C; $[\alpha]_D^{27}$ +92° (*c* 0.38, $CHCl_3$); ^1H NMR (300 MHz, Me_2SO): δ 1.90 (s, 3 H, Ac), 1.96, (s, 3 H, Ac), 1.97 (s, 3 H, Ac), 2.63 (dd, 1 H, *J* 4.5 and 13.5 Hz, H-5), 2.96 (dd, 1 H, *J* 11 and 13.5 Hz, H-5′), 3.32 (m, 1 H, H-1), 3.50 (dd, 1 H, *J* 2.0 and 15.0 Hz, CH_2SO_2), 4.23 (dd, 1 H, *J* 9.0 and 15.0 Hz, CH_2SO_2), 4.83 (ddd, 1 H, *J* 4.5, 10.0 and 11.0 Hz, H-4), 4.85 (dd, 1 H, *J* 5.0 and 10.0 Hz, H-2), 5.03 (t, 1 H, *J* 10.0 Hz, H-3), 7.66 (t, 2 H, *J* 7.5 Hz, Ar meta), 7.76 (t, 1 H, *J* 7.5 Hz, Ar para), 7.93 (d, 2 H, *J* 7.5 Hz, Ar ortho). HRMS: Calcd for $C_{18}H_{22}O_8NaS_2$ [M+Na], 453.0654; Found: 453.0642.

3.6.2.11. 4-((5-Thio-D-xylopyranosyl)methyl sulfonyl)benzonitrile (20). To a stirred solution of diethyl methyl-(4-cyanophenyl)sulfonyl phosphonate (23.9 g, 78 mmol) in anhydrous pyridine (50 mL) under N_2 and cooled at 5 °C was added NaH (3 g, 125 mmol). The mixture, which became pale yellow, was stirred for 20 min and then 5-thio-D-xylopyranose (2.5 g, 15 mmol) was added. The mixture was stirred at rt under N_2 at 80 °C for 2 h and then concentrated under vacuum.

The crude product was purified by flash chromatography (9:1 CH_2Cl_2–CH_3OH) to yield 1.55 g (31%) of yellow powder as a 7:3 mixture of α and β anomers. ^1H NMR (300 MHz, Me_2SO): δ 2.38–2.44, (m, 2 H, H-5), 3.01–3.16 (m, 3 H, H-1,2,3), 3.30–3.64 (m, 2 H, CH_2SO_2, H-4), 3.88–3.96 (m, 1 H, CH_2SO_2), 4.95 (d, 1 H, *J* 5 Hz, OH), 5.12 (d, 1 H, *J* 5 Hz, OH), 5.37 (d, 1 H, *J* 5 Hz, OH), 8.14 (s, 4 H, Ar).

3.6.2.12. 4-([5-Thio-α-D-xylopyranosyl)methyl sulfonyl]benzonitrile (20α). 4-[(2,3,4-Tri-*O*-acetyl-5-thio-α-D-xylopyranosyl)methyl sulfonyl]benzonitrile (**21α**, 0.80 g, 1.76 mmol) was deacetylated using the usual procedure with MeOH–NH_3 for 2 h. The product was obtained as a white powder (0.56 g, 97% yield); mp 170 °C; $[\alpha]_D^{23}$ +124° (*c* 0.26, CH_3OH); ^1H NMR (300 MHz, Me_2SO): δ 2.32–2.45 (m, 2 H, H-5), 3.02 (td, 1 H, *J* 8.5 and 4.5 Hz, H-3), 3.12–3.16 (m, 1 H, H-1), 3.34–3.38 (m, 1 H, H-2), 3.53 (ddd, 1 H, *J* 8.5 and 4.5 and 5.5 Hz, H-4), 3.60 (dd, 1 H, *J* 15.0 and 2.5 Hz, CH_2SO_2), 3.93 (dd, 1 H, *J* 15.0 and 10.0 Hz, CH_2SO_2), 4.96 (d, 1 H, *J* 4.5 Hz, OH); 5.12 (d, 1 H, *J* 4.5 Hz, OH); 5.39 (d, 1 H, *J* 5.5 Hz, OH); 8.14 (s, 4 H, Ar). Anal. Calcd For $C_{13}H_{15}NO_5S_2$; 0.5 H_2O: C, 46.09; H, 4.72; N, 4.13. Found: C, 45.73; H, 4.70; N, 3.98.

3.6.2.13. 4-[(5-Thio-β-D-xylopyranosyl)methyl sulfonyl]benzonitrile (20β). 4-[(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)methyl sulfonyl]benzonitrile (**21β**, 0.15 g, 0.33 mmol) was deacetylated with MeOH–NH_3 for 2 h. The product was obtained as a white powder (0.1 g, 93% yield); mp 180 °C; $[\alpha]_D^{23}$ +15° (*c* 0.43, CH_3OH); ^1H NMR (300 MHz, Me_2SO): δ 2.41–2.49 (m, 2 H, H-5), 2.83–2.94 (m, 2 H, H-1,3), 3.05 (td, 1 H, *J* 9.5 and 5.5 Hz, H-2), 2.29–3.35 (m, 1 H, H-4), 3.52 (dd, 1 H, *J* 9.5 and 15.0 Hz, CH_2SO_2), 3.86 (dd, 1 H, *J* 2.0 and 15.0 Hz, CH_2SO_2), 4.95 (d, 1 H, *J* 5.5 Hz, OH), 5.05 (d, 1 H, *J* 5.5 Hz, OH), 5.37 (d, 1 H, *J* 5.5 Hz, OH), 8.14(s, 4 H, Ar). Anal. Calcd For $C_{13}H_{15}NO_5S_2$; 0.5 H_2O: C, 46.09; H, 4.72; N, 4.13. Found: C, 45.70; H, 4.79; N, 4.07.

3.6.2.14. 4-([2,3,4-Tri-*O*-acetyl-5-thio-α- and β-D-xylopyranosyl)methyl sulfonyl]benzonitrile (21α and 21β). 4-([5-Thio-D-xylopyranosyl)methyl sulfony]benzonitrile (**20**) (4.08, 12.4 mmol) was for acetylated and, conventionally after flash chromatographic separation on silica gel (6:4 toluene–ether), afforded 1.28 g of the **21α** anomer as a white powder (32% yield); mp 117 °C; $[\alpha]_D^{23}$ +122° (*c* 0.40, CH_3OH); ^1H NMR (300 MHz, Me_2SO): δ 1.96 (s, 3 H, Ac), 1.97 (s, 3 H, Ac), 1.98 (s, 3 H, Ac), 2.59 (dd, 1 H, *J* 4.5 and 13.5 Hz, H-5), 2.86 (dd, 1 H, *J* 11.0 and 13.5 Hz, H-5), 3.37–3.41 (m, 1 H, H-1), 3.63 (dd, 1 H, J 2.5 and 15.5 Hz, CH_2SO_2), 4.45 (dd, 1 H, *J* 10.0 and 15.5 Hz, CH_2SO_2), 4.83 (ddd, 1 H, *J* 10.0, 11.0 and 4.5 Hz, H-4), 4.94 (dd, 1 H, *J* 5.0 and 10.0 Hz, H-2), 5.06 (t, 1 H, *J* 10.0 Hz, H-3), 8.16 (s, 4 H, Ar). Anal. Calcd For $C_{19}H_{21}NO_8S_2$: C, 50.10; H, 4.65; N, 3.07. Found: C, 49.77; H, 4.63; N, 3.20. The anomer **21β** was obtained as a white powder (0.41 g, 11% yield); mp 153 °C; $[\alpha]_D^{23}$ −1° (*c* 0.60, $CHCl_3$); ^1H NMR (300 MHz,

Me_2SO): δ 1.98 (s, 3 H, Ac), 1.99 (s, 3 H, Ac), 2.01 (s, 3 H, Ac), 2.68 (dd, 1 H, *J* 4.5 and 13.0 Hz, H-5), 2.92 (dd, 1 H, *J* 11.0 and 13.0 Hz, H-5), 3.52–3.69 (m, 3 H, H-1, CH_2SO_2), 4.77–4.85 (m, 2 H, H-2,4), 5.10 (t, 1 H, *J* 9.5 Hz, H-3), 8.16 (s, 4 H, Ar). Anal. Calcd For $C_{19}H_{21}NO_8S_2$: C, 50.10; H, 4.65; N, 3.07. Found: C, 50.02; H, 4.68; N, 2.96.

3.6.2.15. Ethyl (2,3,4-tri-*O*-acetyl-D-thioxylopyranosyl)acetate (22). 5-Thio-D-xylopyranose (9.1 g, 54.76 mmol) and (ethoxycarbamylmethylene) triphenyl phosphorane (30.5 g, 87.55 mmol) were dissolved in pyridine (60 mL). The reaction mixture was then stirred at 90 °C for 10 h. The solvent was then removed under vacuum and the crude mixture purified by flash chromatography (95:5 CH_2Cl_2–CH_3OH) to yield ethyl (5-thio-D-xylopyranosyl)acetate as a brown oil (4.64 g, 36%). Recrystallization in ether gave a yellow powder (2.74 g, 21%); mp 75 °C; ^{1}H NMR (300 MHz, Me_2SO): δ 1.18 (m, 3 H, CH_3), 2.10 (dd, 0.5 H, *J* 9 and 15 Hz, CH_2CO), 2.43 (dd, 0.5 H, *J* 11 and 15 Hz, CH_2CO), 2.49 (s, 1 H, CH_2CO), 2.90 (m, 2 H, H-5), 3.13 (m, 2 H, H-3,4), 3.39 (m, 1 H, H-1), 3.57 (m, 1 H, H-2), 4.08 (m, 2 H, OCH_2), 4.84 (d, 1 H, *J* 3 Hz, OH), 5.02 (d, 1 H, *J* 5 Hz, OH,), 5.11 (d, 0.5 H, *J* 5.5 Hz, OH), 5.15 (d, 0.5 H, *J* 5 Hz, OH). Ethyl (5-thio-D-xylopyranosyl)acetate (10.5 g, 44.44 mmol) was dissolved in pyridine–CH_2Cl_2 (60 mL, 2:1) and cooled in an ice bath, and then Ac_2O (30 mL) was added dropwise. The mixture was stirred overnight at rt, cooled in an ice bath, quenched with 1 M aq HCl (100 mL), and extracted with ether (500 mL). The organic layer was washed with 1 M HCl (100 mL), saturated $NaHCO_3$ (2×100 mL), water (100 mL) and dried ($MgSO_4$). The solvent was removed under diminished pressure to yield 15.4 g of α and β anomers (1:1) as a yellow oil (96% yield). ^{1}H NMR (300 MHz, Me_2SO): δ 1.18 (2t, 3 H, *J* 7.0 Hz, CH_3), 1.95–1.99 (6s, 9 H, $COCH_3$), 2.22 (s, 2 H, CH_2CO_2Et), 2.58–3.04 (2m, 2 H, H-5), 3.35 (m, 0.5 H, H-2), 3.53 (m, 0.5 H, H-1β), 4.10 (m, 2 H, OCH_2CH_3), 4.83–4.91 (m, 2.5 H, H-2β,4), 5.03 (dd, 0.5 H, *J* 5.0 and 10.0 Hz, H-2α), 5.11 (t, 0.5 H, *J* 10.0 Hz, H-3β), 5.14 (t, 0.5 H, *J* 10.0 Hz, H-3α). Anal. Calcd For $C_{15}H_{22}O_8S$: C, 49.71; H, 6.12. Found: C, 49.86; H, 6.22.

3.6.2.16. 4-[(5-Thio-D-xylopyranosyl)acetamido]-benzonitrile (23). 4 Aminobenzonitrile (14.5 g, 122.74 mmol) was dissolved in dimethoxyethane (DME, 50 mL) and molecular sieves 13 × was added. Then NaH (7.4 g, 308.33 mmol) was added slowly. To the reaction mixture which became yellow then green and then brown in 15 min, DME (50 mL) was added. After 30 min of stirring at rt compound **22** (8.90 g, 24.56 mmol) in DME (10 mL) was added. The reaction was complete in 10 min. The reaction mixture was poured on ice (200 mL) extracted with EtOAc (3×300 mL), dried ($MgSO_4$) and the solvent removed under diminished pressure. Purification by flash chromatography 9:1 CH_2Cl_2–CH_3OH yielded 2.22 g (29%) of brown powder as a 1:1 mixture of α and β anomers. ^{1}H NMR (300 MHz, Me_2SO): δ 2.18 (t, 0.5 H, *J* 15.0 Hz, H-5β), 2.38–2.66 (m, 3 H, CH_2, H-5), 2.86 (dd, 0.5 H, *J* 3.5 and 15.0 Hz, H-5α), 2.96–3.10 (m, 1.5 H, H-2β,3β,4β), 3.14 (m, 0.5 H, H-3α), 3.25 (m, 0.5 H, H-4α), 3.25–3.47 (m, 1 H, H-1), 3.62 (m, 0.5 H, H-2α), 4.92 (d, 0.5 H, *J* 4 Hz, OH), 4.94 (d, 0.5 H, *J* 3.5 Hz, OH), 5.08 (d, 0.5 H, *J* 4.5 Hz, OH), 5.20 (d, 0.5 H, *J* 5 Hz, OH), 5.21 (d, 0.5 H, *J* 4.5 Hz, OH), 5.25 (d, 0.5 H, *J* 5 Hz, OH), 7.77 (s, 4 H, Ar), 10.41 (s, 0.5 H, NHCO), 10.50 (s, 0.5 H, NHCO).

3.6.2.17. 4-[(5-Thio-α-D-xylopyranosyl)acetamido]-benzonitrile (23α). The same procedure as those used for **23β** yielded 0.3 g of **23α** (93.5% yield); mp 90 °C; $[\alpha]_D^{25}$ + 221° (*c* 0.43, CH_3OH); ^{1}H NMR (300 MHz, Me_2SO): δ 2.53–2.66 (m, 3 H, CH_2, H-5), 2.86 (dd, 1 H, *J* 3.5 and 15.0 Hz, H-5′), 3.14 (m, 1 H, H-3), 3.25 (m, 1 H, H-4), 3.43 (m, 1 H, H-1), 3.62 (m, 1 H, H-2), 4.92 (d, 1 H, *J* 4.0 Hz, OH), 5.21 (d, 1 H, *J* 4.5 Hz, OH), 5.25 (d, 1 H, *J* 5.0 Hz, OH), 7.77 (s, 4 H, Ar), 10.5 (s, 1 H, NHCO). Anal. Calcd For $C_{14}H_{16}N_2O_4S$; 0.44 H_2O: C, 53.16; H, 5.38; N, 8.86. Found: C, 53.22;H, 5.35; N, 8.69.

3.6.2.18. 4-[(5-Thio-β-D-xylopyranosyl)acetamido]benzonitrile (23β). 4-[(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)acetamido]benzonitrile (**24β**, 0.77 g, 1.77 mmol) was dissolved in MeOH (30 mL) and a saturated solution of NH_3 in MeOH (6 mL) was added. The mixture was then stirred at rt for 3 h, the solvent removed under diminished pressure, and the crude product lyophilised from water to yield 0.6 g of **25**β (97%); mp 162 °C; $[\alpha]_D^{22}$ +20° (*c* 1.02, CH_3OH); ^{1}H NMR (300 MHz, Me_2SO): δ 2.18 (t, 1 H, *J* 15.0 Hz, H-5), 2.38–2.50 (m, 3 H, CH_2, H-5′), 2.96–3.11 (m, 3 H, H-2,3,4), 3.38 (m, 1 H, H-1), 4.94 (d, 1 H, *J* 3.5 Hz, OH), 5.08 (d, 1 H, *J* 4.5 Hz, OH), 5.20 (d, 1 H, *J* 5.0 Hz, OH), 7.77 (s, 4 H, Ar), 10.41 (s, 1 H, NHCO). Anal. Calcd For $C_{14}H_{16}N_2O_4$ S; 0.48 H_2O: C, 53.04; H, 5.39; N, 8.84. Found: C, 53.31; H, 5.29; N, 8.76.

3.6.2.19. 4-[(2,3,4-Tri-*O*-acetyl-5-thio-α- and β-D-xylopyranosyl)acetamido]benzonitrile (24α and 24β). 4-[(5-Thio-D-xylopyranosyl)acetamido]benzonitrile **23** (2 g, 6.49 mmol) was dissolved in pyridine–Ac_2O (60/20 mL) at 0 °C and then stirred overnight at rt. After conventional workup (see compound **22**) the crude product was flash chromatographed using 1:1 toluene–ether as solvent to yield 1.18 g of the β anomer (42% yield); mp 201 °C; $[\alpha]_D^{25}$ +9° (*c* 0.51, MeOH); ^{1}H NMR (300 MHz, Me_2SO): δ 1.91 (s, 3 H, Ac), 1.95 (s, 3 H, Ac), 1.98 (s, 3 H, Ac), 2.33 (dd, 1 H, *J* 15 and 19 Hz, CH_2), 2.70 (dd, 1 H, *J* 15 and 5 Hz, CH_2), 2.75 (dd, 1 H, *J* 13 and 4.5 Hz, H-5), 2.99 (dd, 1 H, *J* 13 and 11 Hz, H-

5′), 2.61 (sextet, 1 H, *J* 9.5, 9 and 5 Hz, H-1), 4.90 (m, 1 H, H-4), 4.91 (t, 1 H, *J* 9.5 Hz, H-2), 5.12 (t, 1 H, *J* 9.5 Hz, H-3), 7.77 (s, 4 H, Ar), 10.41 (s, 1 H, NHCO). Anal. Calcd for $C_{20}H_{22}N_2O_7S \cdot 0.11\ H_2O$: C, 54.85; H, 5.15; N, 6.40. Found: C, 54.73; H, 5.01; N, 6.24. The α anomer (0.57 g, 25% yield) had mp 195 °C; $[\alpha]_D^{22}$ +150° (*c* 0.31, CH_3OH); ^1H NMR (300 MHz, Me_2SO): δ 1.95 (s, 3 H, Ac), 2.00 (s, 3 H, Ac), 2.01 (s, 3 H, Ac), 2.80 (dd, 1 H, *J* 5.0 and 11.5 Hz, H-5), 2.93–3.02 (m, 3 H, CH_2, H-5′), 3.50 (m, 1 H, H-1), 4.92 (m, 1 H, H-4), 5.09 (dd, 1 H, *J* 4.5 and 10.0 Hz, H-2), 5.16 (t, 1 H, *J* 10.0 Hz, H-3), 7.77 (m, 4 H, Ar,), 10.5 (s, 1 H, NHCO). Anal. Calcd For $C_{20}H_{22}N_2O_7S$: C, 55.29; H, 5.10; N, 6.45. Found: C, 55.27; H, 5.18; N, 6.19.

References

1. Bellamy, F.; Horton, D.; Millet, J.; Picart, F.; Samreth, S.; Chazan, J. B. *J. Med. Chem.* **1993**, *36*, 898–903.
2. Samreth, S.; Barberousse, V.; Bellamy, F.; Horton, D.; Masson, P.; Millet, J.; Renaut, P.; Sepulchre, C.; Theveniaux, J. *Trends Recept. Res.* **1993**, *20*, 41–59.
3. Bellamy, F.; Barberousse, V.; Martin, N.; Masson, P.; Millet, J.; Samreth, S.; Sepulchre, C.; Theveniaux, J.; Horton, D. *Euro. J. Med. Chem.* **1995**, *30*, 101s–115s.
4. Samreth, S.; Barberousse, V.; Bellamy, F.; Horton, D.; Masson, P.; Millet, J.; Renaut, P.; Sepulchre, C.; Theveniaux, J. *Actual. Chim. Ther.* **1994**, *21*, 23–33.
5. Okayama, M.; Kimata, K.; Suzuki, S. *J. Biochem. (Tokyo)* **1973**, *74*, 1069–1073.
6. Schwartz, N. B. *J. Biol. Chem.* **1977**, *252*, 6316–6321.
7. Guichard, J.P.; Guillou, F. Unpublished results.
8. Postema, M. H. D. *Tetrahedron* **1992**, *48*, 8545–8599.
9. (a) Levy, D. E.; Tang, C. *The Chemistry of C-glycosides*; Pergamon Elsevier Science Ltd: Oxford, 1995;
   (b) Postema, M. H. D. *C-Glycoside Synthesis*; CRC Press: Boca Raton, FL, 1995.
10. Belosludtsev, Y. Y.; Bhatt, R. K.; Falck, J. R. *Tetrahedron Lett.* **1995**, *36*, 5881–5882.
11. Wang, X.; Gross, P. H. *J. Org. Chem.* **1995**, *60*, 1201–1206.
12. Mazeas, D.; Skrydstrup, T.; Beau, J. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 909–912.
13. Mata, F. Z.; Martinez, M. B.; Perez, J. A. G. *Carbohydr. Res.* **1992**, *225*, 159–161.
14. Toshima, K.; Matsuo, G.; Tatsuta, K. *Tetrahedron Lett.* **1992**, *33*, 2175–2178.
15. Jaramillo, C.; Knapp, S. *Synthesis* **1994**, 1–20.
16. Dheilly, L.; Frechou, C.; Beaupere, D.; Uzan, R.; Demailly, G. *Carbohydr. Res.* **1992**, *224*, 301–306.
17. Lopez, R.; Fernandez-Mayoralas, A. *J. Org. Chem.* **1994**, *59*, 737–745.
18. Boyd, V. A.; Drake, B. E.; Sulikowski, G. A. *J. Org. Chem.* **1993**, *58*, 3191–3193.
19. Whistler, R. L.; Van Es, T. *J. Org. Chem.* **1963**, *28*, 2303–2304.
20. (a) Yuasa, H.; Tamura, J. I.; Hashimoto, H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2763–2769;
   (b) McAllister, G. D.; Taylor, R. J. K. *Tetrahedron Lett.* **2001**, 1197–1200.
21. Gallagher, M. J.; Harvey, S.; Raston, C. L.; Sue, R. E. *J. Chem. Soc., Chem. Commun.* **1988**, 289–290.
22. BeMiller, J. N.; Yadav, M. P.; Kalabokis, V. N.; Myers, R. W. *Carbohydr. Res.* **1990**, *200*, 111–126.
23. Coxon, B.; Fletcher, H. G., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 922–925.
24. Allevi, P.; Anastasia, M.; Ciuffreda, P.; Frecchi, A.; Scala, A. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1275–1280.
25. Kobayashi, M.; Shimadate, T. *Chem. Pharm. Bull.* **1986**, *34*, 4069–4074.
26. Cai, M. S.; Qiu, D. X. *Carbohydr. Res.* **1989**, *191*, 125–126.
27. Allevi, P.; Anastasia, M.; Ciuffreda, P.; Scala, A. *J. Carbohydr. Chem.* **1993**, *12*, 209–222.
28. Garcia Lopez, M. T.; De las Heras, F. G.; San Felix, A. *J. Carbohydr. Chem.* **1987**, *6*, 273–279.
29. Drew, K. N.; Gross, P. H. *J. Org. Chem.* **1991**, *56*, 509–513.
30. Giese, B.; Dupuis, J.; Leising, M.; Nix, M.; Lindner, H. J. *Carbohydr. Res.* **1987**, *171*, 329–341.
31. Tucker, C. E.; Magid, T. N.; Knochel, P. *J. Am. Chem. Soc.* **1992**, *114*, 3983–3985.
32. Bihovsky, R.; Selick, C.; Giusti, J. *J. Org. Chem.* **1988**, *53*, 4026–4031.
33. (a) Panigot, M. J.; Curley, R. W., Jr. *J. Carbohydr. Chem.* **1994**, *13*, 293–302;
   (b) Panigot, M. J.; Humphries, K. A.; Curley, R. W., Jr. *J. Carbohydr. Chem.* **1994**, *13*, 303–321.
34. Ogawa, T.; Pernet, A. G.; Hanessian, S. *Tetrahedron Lett.* **1973**, *37*, 3543–3546.
35. Hoffmann, M. G.; Schmidt, R. R. *Liebigs Ann. Chem.* **1985**, 2403–2419.
36. Davidson, A. H.; Hughes, L. R.; Qureshi, S. S.; Wright, B. *Tetrahedron Lett.* **1988**, *29*, 693–696.
37. Green, M. *J. Chem. Soc.* **1963**, 1324–1327.
38. Mbongo, A.; Frechou, C.; Beaupère, D.; Uzan, R.; Demailly, G. *Carbohydr. Res.* **1993**, *246*, 361–370.
39. Dawe, R. D.; Fraser-Reid, B. *J. Org. Chem.* **1984**, *49*, 522–528.
40. Horton, D.; Koh, D. *Carbohydr. Res.* **1993**, *250*, 231–247.
41. Theveniaux, J.; Millet, J. Unpublished results.
42. Condon, S.; Dupre, D.; Fargayrac, G.; Nedelec, J.-Y. *Eur. J. Org. Chem.* **2002**, *1*, 105–111.
43. (a) Bajic, M.; Kumar, A.; Boykin, D. W. *Heterocyclic Commun.* **1996**, *2*, 135–140;
   (b) Yokokawa, F.; Asano, T.; Shioiri, T. *Tetrahedron* **2001**, *57*, 6311–6327;
   (c) Aggarwal, V. K.; Sheldon, C. G.; MacDonald, G. J.; Martin, W. P. *J. Am. Chem. Soc.* **2002**, *124*, 10300–10301.
44. Samreth, S.; Millet, J.; Bellamy, F.; Bajgrowicz, J.; Barberousse, V. EP-365 397; *Chem. Abstr*. **1991**, *114*, 858.