ELSEVIER

Carbohydrate Research 287 (1996) 247–253

CARBOHYDRATE RESEARCH

Note

Glycosylation reactions of 2,3,4-tri-*O*-chlorosulfonyl-β-L-fucopyranosyl chloride and 2,3,4-tri-*O*-chlorosulfonyl-β-D-xylopyranosyl chloride

Rod E. Hubbard [a], John G. Montana [b], Paul V. Murphy [a], Richard J.K. Taylor [a,*]

[a] *Department of Chemistry, University of York, York Y01 5DD, UK*
[b] *Chiroscience Ltd., Cambridge Science Park, Milton Rd., Cambridge CB4 4WE, UK*

Received 13 December 1995; accepted 6 March 1996

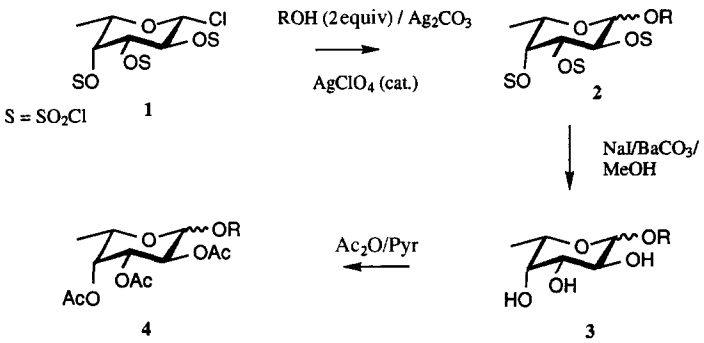
Keywords: L-Fucose; D-Xylose; Glycosylation; Chlorosulfonyl group; Glycosyl chloride

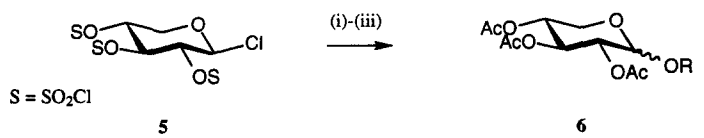
L-Fucose is an important constituent of many naturally occurring carbohydrates such as several blood-group ABH antigenic determinants [1] and the tetrasaccharide sialyl Lewis^x (siLe^x) [2]. The latter has been implicated as playing an important role in the inflammatory response because of its affinity as a ligand for E-selectin and other selectin proteins [2]. Considerable research is currently directed towards the development of simple compounds that are analogues or mimetics of siLe^x [3]. L-Fucose plays an essential role in the binding interaction to E-selectin and thus many of the compounds which are synthetic targets in this area and which have similar biological properties to the natural ligand are α-glycosides of L-fucose [3]. Thus there is much interest in methods for stereoselective synthesis of glycosides of fucose.

Some time ago it was shown that 2,3,4-tri-*O*-chlorosulfonyl-β-L-fucopyranosyl chloride (**1**) could be used as an intermediate in some glycosidation reactions of L-fucose (Scheme 1) [4–6]. The condensation of **1** with methanol in the presence of silver carbonate and silver perchlorate followed by dechlorosulfonylation using sodium iodide

* Corresponding author.

PII S0008-6215(96)00077-8





(i) ROH (2 equiv) / Ag_2CO_3 / $AgClO_4$ (cat.) (ii) NaI / $BaCO_3$/ MeOH
(iii) Ac_2O / Pyr

R = (d) C_6H_{11}, (e) Ph

Scheme 1.

in methanol in the presence of barium carbonate and *O*-acetylation has been shown to have a 9:1 preference for the α anomer (**4a**) [4]. The stereoselectivity of the reaction in the absence of silver perchlorate was essentially unaffected [5]. It was also shown that when **1** was treated with methanol in the presence of sodium iodide and barium carbonate followed by *O*-acetylation a 6:1 mixture of anomers (**4a**) enriched in α was obtained [5]. The condensation of **1** with 4-nitrobenzyl alcohol in the presence of silver carbonate with subsequent deprotection has also been reported to give only the α-L-fucopyranoside **3b**, in a crystallised yield of 35% [4]. Similar selectivity was observed with 2,3,4-tri-*O*-chlorosulfonyl-β-D-xylopyranosyl chloride (**5**) [7]. Methanolysis of **5** using silver carbonate followed by dechlorosulfonylation and acetylation has been reported to give only methyl 2,3,4-tri-*O*-acetyl-α-D-xylopyranoside [7]. Also the condensation of **5** with 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose using silver carbonate and silver perchlorate followed by dechlorosulfonylation and deacetylation has been shown to give a mixture of disaccharides, 6-*O*-α- and -β-D-xylopyranosyl-D-mannopyranose, in a ratio of 19:1 [7]. These results have been rationalised by suggesting that the 2-*O*-chlorosulfonyl group does not participate in the glycosylation [4,7].

The literature precedence summarised above indicated to us that **1**, prepared in only one step from L-fucose, could be used as an intermediate in highly stereoselective, even stereospecific syntheses of a range of simple α-glycosides of fucose. Thus we were interested in utilising the obvious potential of **1** as a valuable intermediate in the

Table 1
Ratios and yields of products obtained from Ag_2CO_3 / $AgClO_4$-promoted glycosidation reactions of **1** and **5**

No.	Product	R	Yield (α:β) [c] (%)	
			A [a]	B [b]
Fucose series				
i	**2a**	Me	57 (9:1) [d] [4]	87 (9:1) [e] [5]
ii	**4b**	4-NO_2-$C_6H_4CH_2$	41 (1:1.3) [f]	27 (1:1.3)
iii	**4c**	$C_6H_{11}CH_2$	61 (1:6)	10 (1:4)
iv	**4d**	C_6H_{11}	71 (1:6)	38 (1:4)
v	**4e**	Ph	39 (1:4)	Complex mixture
Xylose series				
vi	**6d**	C_6H_{11}	80 (1:0)	–
vii	**6e**	Ph	46 (2:1)	–

[a] A, *Method A*: catalytic $AgClO_4$, excess Ag_2CO_3, 2 equiv alcohol, 24 h.
[b] B, *Method B*: no $AgClO_4$, excess Ag_2CO_3, 10 equiv alcohol, 8–10 days.
[c] The ratios were determined for the per-*O*-acetylated derivatives **4** and **6** by ^{1}H NMR unless otherwise stated.
[d] Yield reported for isolation of **2a**(α); the anomeric ratio was determined by ^{1}H NMR.
[e] The yield is given for methyl (α + β)-L-fucopyranoside (**3a**) and the ratio was determined by GLC analysis of the trimethylsilyl ethers.
[f] In the literature [4] the yield of **3b**(α) is reported as 35%, but the β anomer was apparently not observed.

synthesis of novel siLe^x analogues. In view of the current interest in synthesis of analogues of siLe^x, we now report the results of our model studies with **1** which show that the selectivity reported in the literature for **1** is not general and that the reaction of **1** with a range of representative alcohols promoted by silver salts favours formation of the β anomer in all the cases we have studied.

We first repeated some of the reactions reported in the literature and examined the selectivity of both fucose and xylose donors **1** and **5** with a range of alcohols previously unreported. The results of our study are collected in Table 1.

Dealing with fucose first, we observed similar α-selectivity to that described above for the condensation of **1** with methanol under the same conditions (Table 1, i, conditions A). When glycosylation of 4-nitrobenzyl alcohol was repeated we observed approximately equal amounts of α and β anomers (Table 1, ii) which were characterised as the per-*O*-acetylated derivatives (**4b**) [in the published procedure [4] the presence of the β anomer was not described and the α anomer was characterised as 4-nitrobenzyl α-L-fucopyranoside (**3b**)]. We observed that the glycosylation reactions of **1** with cyclohexylmethanol, cyclohexanol, and phenol, using silver carbonate in the presence of catalytic silver perchlorate as promoter, unexpectedly gave the β anomer as the major product (**4c–e**) after dechlorosulfonylation and acetylation of the reaction residue (Table 1, iii–v). The effect of silver perchlorate on the anomeric ratio was investigated by carrying out these reactions in its absence; slower reactions were observed but with no substantial change in the product ratio. In fact, to observe any reaction in the absence of a catalyst a large excess of alcohol (10 equiv) and reaction times of between 8–10 days were required (Table 1, conditions B).

For comparative purposes we prepared 2,3,4-tri-*O*-chlorosulfonyl-β-D-xylopyranosyl chloride (**5**) [7] and observed totally stereoselective α-glycosylation with cyclohexanol

and a predominance of the α anomer with phenol in accordance with literature expectations (Table 1, vi, vii) [7].

In summary, we have shown that although the silver carbonate/silver perchlorate-promoted glycosylation reaction of **1** is useful for the synthesis of the methyl α-glycoside it is not a general reaction for the stereoselective synthesis of α-glycosides of L-fucose. This contrasts with the xylose donor **5**, which favours formation of the α anomer under the same conditions in the two cases examined.

1. Experimental

The ^1H and ^{13}C NMR spectra were recorded with a JEOL JNM-GX 270 spectrometer for solutions in $CDCl_3$. Measurement of $[\alpha]_D$ values was effected with a JASCO DIP-370 digital polarimeter, using a sodium lamp ($\lambda = 589$ nm), at 20 °C. Petroleum ether is the fraction bp 40–60 °C. Column chromatography was performed on silica gel (Matrex® Silica 60, 70–200 μm) using an acetone–petroleum ether gradient from concentration 1:20 to 1:5. Analytical TLC was performed on Merck aluminium-backed silica gel sheets (Silica Gel 60 F_{254}) and 1:5 acetone–petroleum ether as eluting solvent. Elemental composition was determined by microanalysis and/or high-resolution mass spectrometry.

2,3,4-Tri-O-chlorosulfonyl-β-L-fucopyranosyl chloride (**1**) *[4,5].*—This compound was prepared by the reaction of L-fucose (5 g, 0.03 mol) and sulfuryl chloride at low temperature as previously described [4,5], giving a white solid (4.7 g, 37%) on crystallisation of the reaction residue from $CHCl_3$–petroleum ether; mp 111.5–112.5 °C; $[\alpha]_D$ −28° (*c* 1.0, $CHCl_3$); lit. mp 112.5 °C; $[\alpha]_D$ −31° (*c* 1.0, $CHCl_3$) [5]; lit. mp 128 °C; $[\alpha]_D$ −30° (*c* 1.0, $CHCl_3$) [4]. The ^1H NMR spectral data of **1** were in excellent agreement with those previously reported [5].

2,3,4-Tri-O-chlorosulfonyl-β-D-xylopyranosyl chloride (**5**) *[7].*—This compound was prepared by the reaction of D-xylose (4.2 g, 0.029 mol) and sulfuryl chloride at low temperature as previously described [7], giving a white solid (9.2 g, 68%); mp 83.3–84.2 °C ($CHCl_3$–petroleum ether); $[\alpha]_D$ −87° (*c* 1.0, $CHCl_3$); lit. mp 84 °C; $[\alpha]_D$ −91° (*c* 1.06, $CHCl_3$) [7]. The ^1H NMR spectral data were consistent with the structure of **5**.

General procedure for the reaction of **1** *and* **5** *with alcohols.—Method A.* Chlorosulfonyl compound **1** or **5** (0.4–3.0 mmol) was stirred in $CHCl_3$ (5–30 mL) in the presence of Ag_2CO_3 (1.5–8.0 g, excess), $AgClO_4$ (0.03–0.22 g, 0.15–1.0 mmol), alcohol (2 equiv), and Drierite (1–4 g) for 24 h at room temperature. The mixture was filtered through Celite (washing thoroughly with $CHCl_3$) and the solvent removed (for reactions with phenol the residue was dissolved in ether and the solution washed with aq 5% NaOH, dried, and evaporated to dryness before the next stage). The residue was taken up in MeOH (~ 10–20 mL) and $BaCO_3$ (~ 1–2 g) was added followed by a few crystals of NaI. The mixture was stirred for 1 h, or until further addition of NaI did not liberate I_2, then filtered, the solvent removed, and the resulting residue dried under vacuum. Excess of 1:1 Ac_2O–Pyr (1–5 mL) was added to the residue which was left to stand for 48 h at room temperature. Water was added and the product extracted with EtOAc. The organic layer was washed successively with aq 10% $KHSO_4$ and water, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed to give a mixture

of acetylated glycosides which were separated by chromatography and characterised. The stereochemical ratio was determined by ^{1}H NMR analysis of the crude per-*O*-acetylated product.

Method B. The procedure was identical to that in Method A, but no $AgClO_4$ was added, the reaction time was increased to 8–10 days, and the concentration of alcohol was increased (10 equiv). For cyclohexylmethanol the glycosylation reaction in the absence of $AgClO_4$ was incomplete as evidenced by formation of methyl 2,3,4-tri-*O*-acetyl-α-L-fucopyranoside and methyl 2,3,4-tri-*O*-acetyl-β-L-fucopyranoside from unreacted **1** during the subsequent dechlorosulfonylation and acetylation of the reaction residue [5].

*4-Nitrobenzyl 2,3,4-tri-*O*-acetyl-α- and -β-L-fucopyranoside* (**4b**).—Treatment of **1** (0.5 g, 1.0 mmol) with 4-nitrobenzyl alcohol as described in Method A gave an oil (0.35 g). Chromatography gave, in order of elution, the α anomer (R_f 0.09) as a heavy syrup (0.08 g, 18%); $[\alpha]_D$ −139° (*c* 1.6, $CHCl_3$); and the β anomer (R_f 0.06) as a white crystalline solid (0.10 g, 23%); mp 115.2–115.8 °C (EtOAc–petroleum ether); $[\alpha]_D$ +35° (*c* 2.1, $CHCl_3$). NMR data for **4b**(α): ^{1}H, δ 1.14 (d, 3 H, $J_{6,5}$ 6.5 Hz, H-6), 2.00, 2.08, 2.18 (3 s, each 3 H, OAc), 4.18 (q, 1 H, H-5), 4.65 and 4.83 (AB doublets, each 1 H, *J* 13.5 Hz, OCH_2Ar), 5.16–5.20 (m, 2 H, H-1 and H-3), 5.33 (d, 1 H, $J_{4,3}$ 3.0 Hz, H-4), 5.42 (dd, 1 H, $J_{2,1}$ 3.8, $J_{2,3}$ 10.5 Hz, H-2), 7.52 and 8.22 (AB doublets, each 2 H, *J* 9.6 Hz, Ar–H); ^{13}C, δ 15.8 (C-6), 20.6, 20.7, 20.8 (*Me*CO), 64.9, 67.9, 68.0, 70.2 (C-2–5), 68.5 (OCH_2), 96.1 (C-1), 123.7, 127.7 (Ar–CH), 144.7, 147.5 (Ar–C), 170.0, 170.1, 170.3 (C=O). Mass spectrum (CI): found *m/z* 443.1668, required 443.1666 [M + NH_4]. NMR data for **4b**(β): ^{1}H, δ 1.26 (d, 3 H, $J_{6,5}$ 6.3 Hz, H-6), 2.00, 2.07, 2.20 (3 s, each 3 H, OAc), 3.87 (q, 1 H, H-5), 4.59 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.72 and 5.04 (AB doublets, each 1 H, *J* 13.5 Hz, OCH_2Ar), 5.06 (dd, 1 H, $J_{3,4}$ 3.6, $J_{3,2}$ 10.4 Hz, H-3), 5.31 (dd, 1 H, H-2), 5.27 (d, 1 H, H-4), 7.48 and 8.20 (AB doublets, each 2 H, *J* 9.6 Hz, Ar–H); ^{13}C, δ 16.0 (C-6), 20.6, 20.7, 20.8 (*Me*CO), 68.9, 69.3, 69.4, 70.2 (C-2–5), 69.1 (OCH_2), 100.4 (C-1), 123.6, 127.5 (Ar–CH), 144.8, 147.4 (Ar–C), 169.5, 170.2, 170.7 (C=O). Mass spectrum (CI): found *m/z* 443.1666, required 443.1666 [M + NH_4]. Anal. **4b**(β) Calcd for $C_{19}H_{23}NO_{10}$: C, 53.7; H, 5.4; N, 3.3. Found: C, 53.7; H, 5.3; N, 3.2.

*Cyclohexylmethyl 2,3,4 tri-*O*-acetyl-α- and -β-L-fucopyranoside* (**4c**).—Treatment of **1** (1.5 g, 3.1 mmol) with cyclohexylmethanol as described in Method A gave an oil (1.2 g). Chromatography gave, in order of elution, the α anomer (R_f 0.20) as a heavy syrup (0.10 g, 8%); $[\alpha]_D$ −121° (*c* 0.5, $CHCl_3$); and the β anomer (R_f 0.16) also as a heavy syrup (0.61 g, 53%); $[\alpha]_D$ +6° (*c* 1.0 $CHCl_3$). NMR data for **4c**(α): ^{1}H, δ 0.80–0.95 (m, 2 H, cyclohexyl-CH_2), 1.09 (d, 3 H, $J_{6,5}$ 6.3 Hz, H-6), 1.08–1.19 (m, 4 H, cyclohexyl-CH_2), 1.25–1.75 (m, 5 H, cyclohexyl-CH_2 and -CH), 1.94, 2.01, 2.11 (3 s, each 3 H, OAc), 3.13 [dd, 1 H, $J_{a,b}$ 11.5, J_{vic} 6.5 Hz, OCH(H)C_6H_{11}], 3.43 [dd, 1 H, $J_{a,b}$ 11.5, J_{vic} 6.5 Hz, OCH(H)C_6H_{11}], 4.10 (q, 1 H, H-5), 4.98 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.04 (dd, 1 H, $J_{3,4}$ 3.5, $J_{3,2}$ 10.0 Hz, H-3), 5.35 (d, 1 H, H-4), 5.40 (dd, 1 H, H-2); ^{13}C, δ 15.8 (C-6), 20.5, 20.6, 20.7 (*Me*CO), 25.4, 25.7, 26.4, 29.7, 29.8 (CH_2), 37.6 (cyclohexyl-CH), 64.0, 68.1, 68.3, 71.1 (C-2–5), 76.5 (OCH_2), 96.1 (C-1), 170.0, 170.4, 170.5 (C=O). Mass spectrum (CI): found *m/z* 404.2283, required 404.2284 [M + NH_4]. NMR data for **4c**(β): ^{1}H, δ 0.90–1.03 (m, 2 H, cyclohexyl-CH_2), 1.30 (d,

3 H, $J_{6,5}$ 6.4 Hz, H-6), 1.26–1.31 (m, 4 H, cyclohexyl-CH_2), 1.58–1.81 (m, 5 H, cyclohexyl-CH_2 and -CH), 1.80, 2.12, 2.25 (3 s, each 3 H, OAc), 3.29 [dd, 1 H, $J_{a,b}$ 9.7, J_{vic} 7.3 Hz, OC*H*(H)C_6H_{11}], 3.82–3.90 [m, 2 H, H-5 and OCH(*H*)C_6H_{11}], 4.48 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 5.09 (dd, 1 H, $J_{3,4}$ 3.4, $J_{3,2}$ 10.5 Hz, H-3), 5.27 (dd, 1 H, H-2), 5.31 (d, 1 H, H-4); ^{13}C, δ 16.0 (C-6), 20.5, 20.6, 20.7 (*Me*CO), 25.5, 25.6, 25.7, 29.5, 29.7 (CH_2), 37.7 (cyclohexyl-CH), 69.0, 69.1, 70.3, 71.3 (C-2–5), 75.7 (OCH_2), 101.4 (C-1) 169.5, 170.2, 170.7 (C=O). Mass spectrum (CI): found *m/z* 404.2280, required 404.2284 [M + NH_4]. Anal. **4c**(β) Calcd for $C_{19}H_{30}O_8$: C, 59.1; H, 7.8. Found: C, 58.7; H, 7.7.

*Cyclohexyl 2,3,4-tri-*O*-acetyl-α- and -β-*L*-fucopyranoside* (**4d**).—Treatment of **1** (1.0 g, 2.1 mmol) with cyclohexanol as described in Method A gave an oil (0.65 g). Chromatography gave, in order of elution, the α anomer (R_f 0.22) as a heavy syrup (0.08 g, 10%); $[\alpha]_D$ −105° (*c* 1.5, $CHCl_3$); and the β anomer (R_f 0.16) also as a heavy syrup (0.45 g, 61%); $[\alpha]_D$ +6° (*c* 2.5, $CHCl_3$). NMR data for **4d**(α): ^{1}H, δ 1.12 (d, 3 H, $J_{6,5}$ 6.6 Hz, C-6), 1.20–1.81 (m, 10 H, cyclohexyl-CH_2), 1.98, 2.06, 2.16 (3 s, each 3 H, OAc), 3.52 (m, 1 H, cyclohexyl-CH), 4.24 (q, 1 H, H-5), 5.04 (dd, 1 H, $J_{3,4}$ 3.9, $J_{3,2}$ 10.0 Hz, H-3), 5.19 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 5.29 (d, 1 H, H-4), 5.35 (dd, 1 H, H-2); ^{13}C, δ 15.9 (C-6), 20.6 (3 signals, *Me*CO), 23.6, 23.9, 25.5, 31.4, 33.2 (CH_2), 64.2, 68.2, 68.4, 71.1 (C-2–5), 76.1 (OCH), 94.3 (C-1), 170.1 (2 signals, C=O), 170.5 (C=O). Mass spectrum (CI): found *m/z* 390.2119, required 390.2128 [M + NH_4]. NMR data for **4d**(β) [8]: ^{1}H, δ 1.17 (d, 3 H, $J_{6,5}$ 6.5 Hz, H-6), 1.18–1.65 (m, 10 H, CH_2), 1.94, 2.00, 2.12 (3 s, each 3 H, OAc), 3.58 (m, 1 H, cyclohexyl-CH), 3.75 (q, 1 H, H-5), 4.47 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.97 (dd, 1 H, $J_{3,4}$ 3.4, $J_{3,2}$ 10.4 Hz, H-3), 5.11 (dd, H-2), 5.18 (d, 1 H, H-4); ^{13}C, δ 16.0 (C-6), 20.5, 20.6, 20.7 (*Me*CO), 23.5, 23.6, 25.4, 31.5, 33.2 (CH_2), 68.9, 69.1, 70.2, 71.3 (C-2–5), 77.4 (OCH), 99.5 (C-1), 169.4, 170.2, 170.7 (C=O). The NMR data for **4d**(β) are in excellent agreement with those previously reported [8]. Mass spectrum (CI): found *m/z* 390.2122, required 390.2128 [M + NH_4].

*Phenyl 2,3,4-tri-*O*-acetyl-α- and -β-*L*-fucopyranoside* (**4e**).—Treatment of **1** (1.0 g, 2.1 mmol) with phenol as described in Method A gave an oil (0.31 g). Chromatography gave, in order of elution, the α anomer (R_f 0.16) as a heavy syrup (0.06 g, 8%); $[\alpha]_D$ −165° (*c* 1.6, $CHCl_3$); and the β anomer (R_f 0.11) also as a heavy syrup (0.23 g, 31%); $[\alpha]_D$ −18° (*c* 1.3, $CHCl_3$). NMR data for **4e**(α): ^{1}H, δ 1.13 (d, 3 H, $J_{6,5}$ 6.6 Hz, H-6), 2.04, 2.07, 2.20 (3 s, each 3 H, OAc), 4.29 (q, 1 H, H-5), 5.28 (dd, 1 H, $J_{3,4}$ 3.3, $J_{3,2}$ 10.8 Hz, H-3), 5.37 (d, 1 H, H-4), 5.60 (dd, 1 H, $J_{2,1}$ 3.7 Hz, H-2), 5.74 (d, 1 H, H-1); ^{13}C, δ 16.0 (C-6), 20.8 (3 signals, *Me*CO), 65.1, 67.7, 67.9, 70.9 (C-2–5), 94.3 (C-1), 116.3, 122.4, 129.8 (Ar–CH), 156.0 (Ar–C), 169.3, 170.2, 170.3 (C=O). Mass spectrum (CI): found *m/z* 384.1656, required 384.1658 [M + NH_4]. NMR data for **4e**(β): ^{1}H, δ 1.26 (d, 3 H, $J_{6,5}$ 6.5 Hz, H-6), 2.00, 2.04, 2.18 (3 s, each 3 H, OAc), 3.95 (q, 1 H, H-5), 5.04 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 5.10 (dd, 1 H, $J_{3,4}$ 3.6, $J_{3,2}$ 10.5 Hz, H-3), 5.30 (d, 1H, H-4), 5.45 (dd, 1 H, H-2); ^{13}C, δ 16.0 (C-6), 20.6 (3 signals, *Me*CO), 68.7, 69.0, 70.0, 71.1 (C-2–5), 99.4 (C-1), 116.7, 123.0, 129.5 (Ar–CH), 157.0 (Ar–C), 169.4, 170.1, 170.6 (C=O). Mass spectrum (CI): found *m/z* 384.1652, required 384.1658 [M + NH_4]. Anal. **4e**(β) Calcd for $C_{18}H_{22}O_8$: C, 59.0; H, 6.0. Found: C, 58.7; H, 5.9.

Cyclohexyl 2,3,4-tri-O-acetyl-α-D-xylopyranoside (**6d**).—Treatment of **5** (1.0 g, 2.1 mmol) with cyclohexanol as described in Method A gave the α anomer (R_f 0.23) as a solid (0.60 g, 80%); mp 116.2–116.9 °C (EtOAc–petroleum ether); $[\alpha]_D$ +119.5° (*c* 1.0, $CHCl_3$). NMR data for **6d**(α): ^{1}H, δ 1.32–1.89 (10 H, m, CH_2), 2.12, 2.13, 2.15 (3 s, each 3 H, OAc), 3.58 (m, 1 H, cyclohexyl-CH), 3.80–3.85 (m, 2 H, H-5ax, H-5eq), 4.83 (dd, 1 H, $J_{2,1}$ 3.9, $J_{2,3}$ 10.0 Hz, H-2), 5.03 (m, 1 H, H-4), 5.25 (d, 1 H, H-1), 5.59 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-3); ^{13}C, δ 20.7 (2 signals, *Me*CO), 20.8 (*Me*CO), 23.5, 23.9, 25.5, 31.2, 33.2 (CH_2), 58.2 (C-5), 69.6, 69.7, 71.3 (C-2–4), 76.5 (cyclohexyl-CH), 93.7 (C-1), 170.0, 170.1, 170.3 (C=O). Mass spectrum (CI): found *m/z* 376.1969, required 376.1971 [M + NH_4]. Anal. Calcd for $C_{17}H_{26}O_8$: C, 57.0; H, 7.3. Found: C, 56.9; H, 7.4.

Phenyl 2,3,4-tri-O-acetyl-α- and -β-D-xylopyranoside (**6e**).—Treatment of **1** (1.0 g, 2.1 mmol) with phenol as described in Method A gave an oil (0.35 g). Chromatography gave, in order of elution, the α anomer (R_f 0.17) as a heavy syrup (0.11 g, 14%); $[\alpha]_D$ +71° (*c* 4.5, $CHCl_3$); and the β anomer (R_f 0.13) as a solid (0.25 g, 32%); mp 134.5–135.0 °C (EtOAc–petroleum ether); $[\alpha]_D$ −61° (*c* 2.7, $CHCl_3$). NMR data for **6e**(α): ^{1}H, δ 2.21, 2.23, 2.25 (3 s, each 3 H, OAc), 3.90 (t, 1 H, $J_{5ax,4}$ 11.0, $J_{5ax,5eq}$ 11.0 Hz, H-5ax), 4.03 (dd, 1 H, $J_{5eq,4}$ 3.6 Hz, H-5eq), 5.16 (dd, 1 H, $J_{2,1}$ 3.6, $J_{2,3}$ 10.2 Hz, H-2), 5.26 (m, 1 H, H-4), 5.89 (1 H, t, $J_{3,4}$ 10.2 Hz, H-3), 5.87 (d, 1 H, H-1), 7.20–7.54 (ms, 5 H, Ar–H); ^{13}C, δ 20.6 (3 signals, *Me*CO), 58.8 (C-5), 69.1, 69.4, 70.5 (C-2–4), 94.1 (C-1), 116.5, 122.7, 129.5 (Ar–CH), 156.1 (Ar–C), 169.4, 170.0, 170.1 (C=O). Mass spectrum (CI): found *m/z* 370.1492, required 370.1502 [M + NH_4]. NMR data for **6e**(β): ^{1}H, δ 2.24, 2.25, 2.30 (3 s, each 3 H, OAc), 3.66 (dd, 1 H, $J_{5ax,4}$ 10.4 Hz, $J_{5ax,5eq}$ 12.2 Hz, H-5ax), 4.38 (dd, 1 H, $J_{5eq,4}$ 4.3 Hz, H-5eq), 5.17 (m, 1 H, H-4), 5.39–5.42 (ms, 3 H, H-1–3), 7.14–7.49 (ms, 5 H, Ar–H); ^{13}C, δ 20.7 (3 signals, *Me*CO), 61.8 (C-5), 68.5, 70.1, 70.7 (C-2–4), 98.5 (C-1), 116.8, 123.1 129.5 (Ar–CH), 156.6 (Ar–C), 169.4, 169.8, 169.9 (C=O). Mass spectrum (CI): found *m/z* 370.1502, required 370.1502 [M + NH_4]. Anal. **6e**(α) Calcd for $C_{17}H_{20}O_8$: C, 58.0; H, 5.7. Found: C, 57.6; H, 5.4.

References

[1] H.M. Flowers, *Adv. Carbohydr. Chem. Biochem.*, 39 (1981) 279–345.
[2] Y. Ichikawa, R.L. Halcomb, and C.H. Wong, *Chem. Br.*, (1994) 117–121.
[3] For some recent advances, see T. Unchigama, V.P. Vassileu, T. Kagimoto, W. Wong, H. Huang, C.C. Liu, and C.H. Wong, *J. Am. Chem. Soc.*, 117 (1995) 5395–5396; H. Huang and C.H. Wong, *J. Org. Chem.*, 60 (1995) 3100–3106; J.C. Prodger, M.J. Bamford, P.M. Gore, D, M Holmes, V. Saez, and P. Ward, *Tetrahedron Lett.*, 36 (1995) 2339–2342; F. Dasgupta and B.N.N. Rao, *Exp. Opin. Invest. Drugs*, 3 (1994) 709–724; P.J. Sanfilippo, *Exp. Opin. Ther. Patents*, 5 (1995) 35–40; C.R. Bertozzi, *Chem. Biol.*, 2 (1995) 703–708.
[4] M.E. Rafestin, D. Delay, and M. Monsigny, *Can. J. Chem.*, 52 (1974) 210–212.
[5] J.-R. Pougny, P. Sinaÿ, and G. Hajduković, *Carbohydr. Res.*, 34 (1974) 351–360.
[6] J.-R. Pougny and P Sinaÿ, *Carbohydr. Res.*, 47 (1976) 69–79.
[7] H.J. Jennings, *Can. J. Chem.*, 46 (1968) 2799–2805.
[8] H. Kondo, S. Aoki, Y. Ichikawa, R.L. Halcomb, H. Ritzer, and C.H. Wong, *J. Org. Chem.*, 59 (1994) 864–877.