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Note

Stereoselective syntheses of acetylated *o*-tolyl 1-thioglycosides

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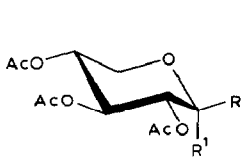
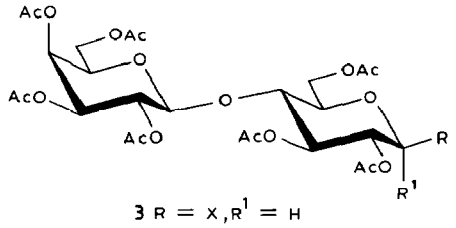
Many 1-thioglycosides and their derivatives are biologically active and some can inhibit the growth and metabolism of cancer cells[1]. Hence, there has been much interest in the synthesis and properties of these compounds[2].

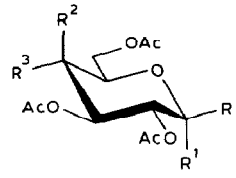
There are several methods for the synthesis of 1-thio-β-D-glycosides[3]. Apparu *et al.*[4] synthesised 1-thio-α-D-glucopyranosides and 1-thio-α-D-galactopyranosides from the corresponding β-D-glycopyranosyl chlorides in hexamethylphosphoric triamide followed by column chromatography. We now report on the synthesis of the acetylated *o*-tolyl 1-thio-D-glycosides **1**–**7** by the condensation of *o*-toluenethiol with the acetylated α-D-glycosyl bromide or β-D-glycosyl chloride according to the procedure of Purves[5];



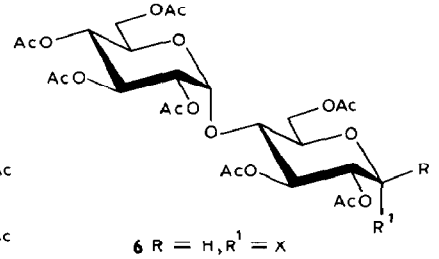
1 R = X, R^1 = H
2 R = H, R^1 = X
D-xylopyranoside



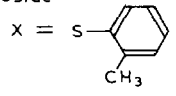
3 R = X, R^1 = H
4 R = H, R^1 = X
D-lactoside



5 R = X, R^1 = R^2 = H, R^3 = OAc
D-glucopyranoside
7 R = X, R^1 = R^3 = H, R^2 = OAc
D-galactopyranoside



6 R = H, R^1 = X
D-maltoside



X = S–C_6H_4–CH_3

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TABLE I

Data on the acetylated *o*-tolyl 1-thioglycopyranosides **1–7**

Compound	*Yield* (%)	*M.p.* (*degrees*)	$[\alpha]_D^{20}$ (*degrees*)	*Formula*	*Elemental analysis* (%)			
					Calc.		*Found*	
					C	*H*	*C*	*H*
1 (β-D-xylo)[a]	75	66	−44 (*c* 1.06)	$C_{18}H_{22}O_7S$	56.55	5.76	56.40	5.77
2 (α-D-xylo)	36	104	117 (*c* 1.14)	$C_{18}H_{22}O_7S$	56.55	5.76	56.37	5.73
3 (β-D-lacto)	61.5	97.5	−18 (*c* 1.17)	$C_{33}H_{42}O_{17}S$	53.37	5.66	52.98	5.62
4 (α-D-lacto)	53	149	129 (*c* 1.31)	$C_{33}H_{42}O_{17}S$	53.37	5.66	53.11	5.64
5 (β-D-gluco)[b]	81	102	−14 (*c* 1.35)	$C_{21}H_{26}O_9S$	55.51	5.73	55.64	5.78
6 (α-D-malto)	68	158	203 (*c* 0.98)	$C_{33}H_{42}O_{17}S$	53.37	5.66	53.21	5.64
7 (β-D-galacto)[c]	73	97	−0.2 (*c* 1.0)	$C_{21}H_{26}O_9S$	55.51	5.73	55.64	5.78

[a] Ref. 10; m.p. 65–68°, $[\alpha]_D^{20}$ −44.2° (chloroform). [b] Ref. 6; m.p. 104–106°, $[\alpha]_D^{20}$ −16.4° (chloroform). [c] Ref. 7; m.p. 98–99°, $[\alpha]_D^{20}$ ~0° (chloroform).

however, the reactions were carried out in chloroform and the products were crystallised directly. The data on **1**–**7** are shown in Table I.

The β anomers **1**, **5**, and **7** have been described[6,7], but no spectral data were reported.

The ^{13}C-n.m.r. data for **1**–**7** are recorded in Table II. The chemical shifts of the C-1 resonances for the α-D-glycosides accord with those reported by Apparu *et al.*[4].

For the pairs of anomers **1**/**2** and **3**/**4**, the chemical shifts of the C-1β resonances were larger than those of the C-1α resonances (1.53 and 1.49 p.p.m., respectively). The chemical shifts of the C-1β resonances of **5** and **7** were similar to those of C-1β for **1** and **3**, and that of C-1α of **6** was similar to those of C-1α of **2** and **4**, in agreement with data for acetylated aryl glycosides[8], but the $\Delta\delta$ value for the 1-thio-D-glycopyranosides was smaller, reflecting the deshielding by the sulfur atom.

I.r. data for **1**–**7** are shown in Table III. Varma *et al.*[9] noted for acetylated phenyl 1-thio-D-gluco- and -galacto-pyranosides that the α anomers had i.r. bands at 848 cm^{-1} and the β anomers at 895–900 cm^{-1}. For **1**–**7**, the β anomers had i.r. bands near 823 cm^{-1}, and the α anomers near 775 and 560 cm^{-1}. These bands can be used to distinguish

TABLE II

^{13}C-N.m.r. data[a] for **1**–**7**

Atom	**1**(β)	**2**(α)	**3**(β)	**4**(α)	**5**(β)	**6**(α)	**7**(β)
C-1	86.81	85.28	86.28	84.79	86.57	84.66	87.27
C-1′			101.02	101.14		95.96	
C-2	70.20	69.86	70.20	70.20	70.47	69.49	67.67
C-2′			69.29	69.37		70.05	
C-3	72.22	71.08	74.01	69.59	74.08	73.71	72.14
C-3′			70.88	70.94		72.44	
C-4	68.64	69.19	76.75	76.72	68.66	74.81	67.44
C-4′			66.83	66.89		71.14	
C-5	65.24	60.19	76.34	71.18	75.65	68.67	74.58
C-5′			71.06	71.18		71.14	
C-6			62.41	62.30	62.43	62.97	61.75
C-6′			61.01	61.03		61.67	

[a] In $CDCl_3$ (internal Me_4Si).

TABLE III

Selected i.r. bands (cm^{-1}) for **1**–**7**

1(β)	**2**(α)	**3**(β)	**4**(α)	**5**(β)	**6**(α)	**7**(β)
823.4		828.9		821.4		823.8
	772.2		775.1		785.2	
	551.1		565.6		563.7	
905.4	902.1	912.9	905.1	908.8	901.9	914.2

1-thio-α- and -β-D-glycopyranosides. Both the α and β anomers had i.r. bands in the range of 900–910 cm^{-1}, with those of the α anomers at lower frequency (*cf.* ref. 10).

The e.i.-mass spectra of **1**–**7** at 70 eV had the base peak at *m/z* 43 (Ac^+). However, at 20 eV, the base peak was at *m/z* 259 for the pentopyranosides **1** and **2** (corresponding to $C_{11}H_{15}O_7^+$), at *m/z* 169 (for $C_8H_9O_4^+$) for the hexopyranosides **5** and **7**, and at *m/z* 331 (for $C_{14}H_{19}O_9^+$) for the disaccharide derivatives **3**, **4**, and **6**. The fragmentation patterns for the pairs **1**/**2** and **3**/**4** were similar. The intensities of the high-mass peaks were larger for the α anomers. At 70 eV, only the α anomers gave peaks for M^+.

For the disaccharide derivatives, the configurations at C-1 and C-1′ were β,β for **3**, α,β for **4**, and α,α for **6**. In the 70-eV mass spectra, the peaks at *m/z* 331 (cleavage at C-1′) were stronger for **3** and **4** than for **6**. Thus, α-cleavage occurs more readily for C-1′β than for C-1′α, in accord with the findings of Kadentsev *et al.*[11] for methyl glycosides.

EXPERIMENTAL

General methods. — Melting points were determined with a Mettler FP 5 apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 MC polarimeter. Elemental analyses were determined with a Yanaco MT-3 instrument. F.t.-i.r. spectra (KBr discs) were recorded with a Nicolet 170 spectrometer. ^{13}C-N.m.r. spectra were recorded with a Varian FT-80 spectrometer for solutions in $CDCl_3$ (internal Me_4Si). Mass spectra were obtained with a VG 7070 mass spectrometer, using in-beam electron impact. Solvents were evaporated at $<35°$.

The potassium salt of *o*-toluenethiol was obtained by dissolving potassium hydroxide in a solution of *o*-toluenethiol in MeOH. Acetylated α-D-glycopyranosyl bromides and β-D-glycopyranosyl chlorides were obtained as reported[12].

Acetylated o-*tolyl 1-thio-*α-D-*glycopyranosides* (**2**, **4**, *and* **6**). — The following method is typical. A methanolic solution of *o*-toluenethiol potassium salt (0.010 mol) was added dropwise to a solution of acetylated β-D-xylopyranosyl chloride (0.005 mol, 1.5 g) in $CHCl_3$ (5 mL). The mixture was then stirred for 38 h at room temperature, diluted with $CHCl_3$ (10 mL), and washed with water. The water layer was extracted twice with $CHCl_3$, the combined $CHCl_3$ solutions were dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. Treatment of the residue with MeOH at $\sim 5°$ gave **2** (0.68 g). Data on **2**, **4**, and **6** are given in Tables I–III.

Acetylated o-*tolyl 1-thio-*β-D-*glycopyranosides* (**1**, **3**, **5**, *and* **7**). — The following procedure is typical. A methanolic solution of *o*-toluenethiol potassium salt (0.010 mol) was added dropwise to a solution of acetylated α-D-xylopyranosyl bromide (0.005 mol, 1.7 g) in $CHCl_3$ (5 mL). The mixture was stirred for 48 h at room temperature, then treated as described above to give **1** (1.4 g). Data on **1**, **3**, **5**, and **7** are given in Tables I–III.

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