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Note

Synthesis of glycosyl xanthates from reducing sugar derivatives under phase-transfer conditions

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Thio sugars are widely used in synthetic carbohydrate chemistry[1] and xanthates have attracted attention for the preparation of 1-thio sugars[2].

The stereoselective formation of glycosyl xanthates is generally achieved by nucleophilic displacement, usually of halogen, from the anomeric centre, using an alkyl dithiocarbonate in hot ethanol[3]. The reaction of acylated glycosyl halides and potassium xanthates has been used widely for the synthesis of glycosyl xanthates[4], *e.g.*, the ethyl xanthates of D-glucose[5], D-arabinose[6], D-glucuronic acid[7], 2-amino-2-deoxy-D-glucose[8], D-mannose[9], and D-ribose[9]. Benzylated ethyl 1-xanthates have been prepared from sugar benzyl ethers *via* the acetate and 1-halide[10,11].

A good leaving-group can be generated from a hydroxyl group by treatment with a sulfonyl chloride under phase-transfer conditions[12]. Using these conditions, diols can be converted into oxirane derivatives[13]. We now report application of the phase-transfer method for the synthesis of glycosyl dithiocarbonates.

Treatment of the monosaccharide with tosyl chloride and potassium *O*-ethyl or *O*-isobutyl dithiocarbonate under phase-transfer conditions gave almost quantitative yields of *O*-alkyl *S*-glycosyl dithiocarbonates. The stereoselectivity of the reaction was dependent on the substrate used. 2,3,4,6-Tetra-*O*-benzyl-D-gluco- (**1**), and -D-galacto-pyranose (**2**) formed only β products ($J_{1,2}$ values of 9.6 and 10.0 Hz, respectively). This result is similar to that observed by Anderson *et al.*[14]. 2,3,4,6-Tetra-*O*-benzyl-D-mannopyranose (**3**), 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**4**), and 2,3,4-tri-*O*-benzyl-D-xylopyranose (**5**) each gave an $\alpha\beta$-mixture of dithiocarbonates in which, for **3** and **4**, the α isomer preponderated. For **5**, the β anomer was the major product. The formation of disaccharides was not detected

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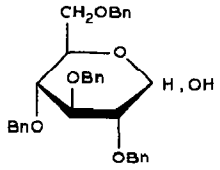
and side reactions (hydrolysis, degradation) were unimportant under the conditions used.

The method described involves a simple one-pot procedure which gives high yields of products and can be used with sugar derivatives containing acid-labile protecting groups.



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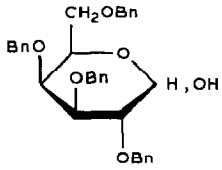

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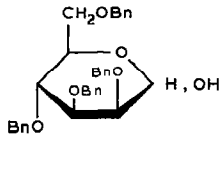

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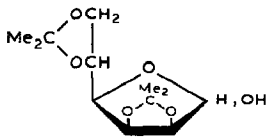

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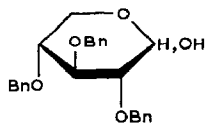

5

EXPERIMENTAL

General. — Melting points are not corrected. Optical rotations were measured with a Polamat A automatic polarimeter (Zeiss–Jena) for solutions in chloroform. T.l.c. was carried out on Silica Gel G (Merck) with benzene–ethyl acetate (2:1) or benzene–ethyl acetate (8:1) and detection by charring with sulfuric acid. Column chromatography was performed on Silica Gel 60 (Merck 0.063–0.2 mm) with benzene–ethyl ether (25:1). ^{1}H-N.m.r. spectra were recorded with Tesla (60 MHz) and Bruker (100 MHz) spectrometers for solutions in $CDCl_3$ (internal Me_4Si or Me_6Si_2O). U.v. spectra were recorded with a UV-VIS spectrometer (Zeiss–Jena) for solutions in methanol. All organic solutions were concentrated under reduced pressure at 40°.

2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose[15], -D-galactopyranose[15], and -D-mannopyranose[15], 2,3,4-tri-*O*-benzyl-D-xylopyranose[16], 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose[17], and *O*-alkyl potassium dithiocarbonates[18] were prepared as described in the literature.

Preparation of glycosyl xanthates. — A solution of sugar (1 mmol), tetrabutylammonium chloride (70 mg, 0.25 mmol), and *p*-tolylsulfonyl chloride (285 mg, 1.5 mmol) in benzene (15 mL) was stirred with potassium *O*-ethyl dithiocarbonate or *O*-isobutyl dithiocarbonate (1 mmol) and aqueous 50% sodium hydroxide (10 mL) at room temperature for 1–3 h (see Table I). The organic layer was separated,

washed with water, dried (Na_2SO_4), and concentrated, and the product was subjected to column chromatography. The following compounds were prepared by the above procedure.

O-Ethyl *S*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl) dithiocarbonate, m.p. 78–80°, $[\alpha]_D^{23}$ +45° (*c* 1.7), {(lit.[14] m.p. 83°, $[\alpha]_D^{25}$ +27.1° (*c* 1.6)}; λ_{max} 276 (ε 7150). ^{1}H-N.m.r. data: δ 7.29–7.19 (m, 20 H, 4 Ph), 5.35 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1β), 4.88–3.57 (m, 16 H, H-2,3,4,5,6, $PhCH_2$, and CH_3CH_2), 1.38 (t, 3 H, *J* 7 Hz, CH_3CH_2).

Anal. Calc. for $C_{37}H_{40}O_6S_2$: C, 68.95; H, 6.20; S, 9.95. Found: C, 68.99; H, 6.27; S, 10.06.

TABLE I

PREPARATION OF *O*-ALKYL *S*-GLYCOSYL DITHIOCARBONATES (Gl-S-C-OR, ‖ S)

Substrate	*R*	*Reaction time (h)*[a]	*Yield (%)*[b]	*Proportion of isomers*[c] α:β
1	Et	2	98	0:1.0
	^{i}Bu	2	97	0:1.0
2	^{i}Bu	2	89	0:1.0
3	Et	2	85	0.7:0.3
	^{i}Bu	2	95	0.7:0.3
4	Et	1.5	96	0.7:0.3
	^{i}Bu	1	95	0.7:0.3
5	Et	3	89	0.4:0.6

[a] Evaluated by t.l.c. [b] After chromatography. [c] Estimated from ^{1}H-n.m.r. spectra.

O-Isobutyl *S*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl) dithiocarbonate, syrup, $[\alpha]_D^{20}$ +44° (*c* 1.3); λ_{max} 276 (ε 11,100). ^{1}H-n.m.r. data: δ 7.30–7.19 (m, 20 H, 4 Ph), 5.36 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1β), 4.97–3.50 (m, 16 H, H-2,3,4,5,6, PhC*H*$_2$, and Me_2CHCH_2), 2.25–1.60 (m, 1 H, Me_2CHCH_2), 0.98 (d, 6 H, *J* 7 Hz, Me_2CHCH_2).

Anal. Calc. for $C_{39}H_{44}O_6S_2$: C, 69.65; H, 6.54; S, 9.54. Found: C, 69.70; H, 6.56; S, 9.48.

O-Isobutyl *S*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl) dithiocarbonate, syrup, $[\alpha]_D^{21}$ +36° (*c* 1.5); λ_{max} 276 (ε 6000). ^{1}H-N.m.r. data: δ 7.30–7.10 (m, 20 H, 4 Ph), 5.30 (d, 1 H, $J_{1,2}$ 10.0 Hz, H-1β), 5.10–3.45 (m, 16 H, H-2,3,4,5,6, PhC*H*$_2$, and Me_2CHCH_2), 2.30–1.20 (m, 1 H, Me_2CHCH_2), 0.87 (d, 6 H, *J* 7 Hz, Me_2CHCH_2).

Anal. Calc. for $C_{39}H_{44}O_6S_2$: C, 69.65; H, 6.54; S, 9.54. Found: C, 69.76; H, 6.48; S, 9.72.

O-Ethyl *S*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-mannopyranosyl) dithiocarbonate, syrup, $[\alpha]_D^{21}$ +11° (*c* 1.5); λ_{max} 276 (ε 7200). ^{1}H-N.m.r. data: δ 7.30–7.10 (m, 20 H, 4 Ph), 5.45 (s, 1 H, H-1β), 5.00 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1α), 4.93–3.70 (m, 16 H, H-2,3,4,5,6, PhC*H*$_2$, and CH_3CH_2), 1.25 (t, 3 H, *J* 7 Hz, CH_3CH_2).

Anal. Calc. for $C_{37}H_{40}O_6S_2$: C, 68.95; H, 6.20; S, 9.95. Found: C, 68.99; H, 6.27; S, 9.76.

O-Isobutyl *S*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-mannopyranosyl) dithiocarbonate, syrup, $[\alpha]_D^{21}$ −1.25° (*c* 1.6); λ_{max} 276 (ε 8800). ^{1}H-N.m.r. data: δ 7.30–7.10 (m, 20 H, 4 Ph), 5.45 (s, 1 H, H-1β), 5.07 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1α), 4.96–3.70 (m, 16 H, H-2,3,4,5,6, PhC*H*$_2$, and Me_2CHCH_2), 2.40–2.00 (m, 1 H, Me_2CHCH_2), 0.90 (d, 6 H, *J* 7 Hz, Me_2CHCH_2).

Anal. Calc. for $C_{39}H_{44}O_6S_2$: C, 69.65; H, 6.54; S, 9.54. Found: C, 69.72; H, 6.58; S, 9.78.

O-Ethyl *S*-(2,3:5,6-di-*O*-isopropylidene-α,β-D-mannofuranosyl) dithiocarbonate, syrup, $[\alpha]_D^{19}$ −13° (*c* 1.5); λ_{max} 276 (ε 11,650). ^{1}H-N.m.r. data: δ 6.13 (s, 1 H, H-1β), 5.72 (d, 1 H, $J_{1,2}$ 3 Hz, H-1α), 5.08–3.50 (m, 8 H, H-2,3,4,5,6 and CH_3CH_2), 1.55, 1.50, 1.48, 1.39 (4 s, 12 H, 2 Me_2C), 1.20 (t, 3 H, *J* 7 Hz, CH_3CH_2).

Anal. Calc. for $C_{15}H_{24}O_6S_2$: C, 49.46; H, 6.59; S, 17.61. Found: C, 49.56; H, 6.52; S, 17.50.

O-Isobutyl *S*-(2,3:5,6-di-*O*-isopropylidene-α,β-D-mannofuranosyl) dithiocarbonate, syrup, $[\alpha]_D^{20}$ −4° (*c* 0.5); λ_{max} 276 (ε 16,500). ^{1}H-N.m.r. data: δ 6.13 (s, 1 H, H-1β), 5.72 (d, 1 H, $J_{1,2}$ 3 Hz, H-1α), 5.10–3.50 (m, 8 H, H-2,3,4,5,6 and Me_2CHCH_2), 2.60–2.07 (m, 1 H, Me_2CHCH_2), 1.55, 1.50, 1.48, 1.39 (4 s, 12 H, 2 Me_2C), 1.03 (d, 6 H, *J* 7 Hz, Me_2CHCH_2).

Anal. Calc. for $C_{17}H_{28}O_6S_2$: C, 52.05; H, 7.14; S, 16.35. Found: C, 52.17; H, 7.15; S, 16.42.

O-Ethyl *S*-(2,3,4-tri-*O*-benzyl-α,β-D-xylopyranosyl) dithiocarbonate, syrup, $[\alpha]_D^{19}$ +62° (*c* 1.1); λ_{max} 276 (ε 5000). ^{1}H-N.m.r. data: δ 7.40–7.14 (m, 15 H, 3 Ph), 6.29 (d, 1 H, $J_{1,2}$ 5 Hz, H-1α), 5.44 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1β), 4.84–3.30 (m, 13 H, H-2,3,4,5,5, PhC*H*$_2$, and CH_3CH_2), 1.40 (t, 3 H, *J* 7 Hz, CH_3CH_2).

Anal. Calc. for $C_{29}H_{32}O_5S_2$: C, 66.42; H, 6.10; S, 12.23. Found: C, 66.49; H, 6.14; S, 12.09.

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