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Note

Synthesis of bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl and -galactopyranosyl) sulfide using phase-transfer catalysis

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Thiodisaccharides are an important class of compounds[1]. 1-Thio-β-D-galactopyranosyl-β-D-galactopyranoside[2] (**1**) inhibits the growth of *Escherícha coli,* and competitive inhibitors of this type attached to a suitable matrix have been used for the purification of enzymes by affinity chromatography[3]. Thiodisaccharides have been used extensively in investigations of the mechanism of enzymic processes[4].

The synthesis of model compounds for a study of the modes of binding by lactose carrier protein required considerable quantitities of **1**. Thiodisaccharides can be obtained by the reaction of glycosyl halide and a thio sugar[5], but our attempts to prepare **1** from 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**3**) and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactose afforded only modest yields (~50%, after crystallisation) of the desired products. This procedure also requires the synthesis of a 1-thio sugar. Landini and Rolla[6] have reported the preparation of dialkyl sulfides from sodium sulfide and alkyl halides using phase-transfer catalysis.

Treatment of a benzene solution of **3** with aqueous sodium sulfide in the presence of tetrabutylammonium bromide resulted in slow reaction and also hydrolysis. The limiting condition for this phase-transfer catalysed reaction is the lower ability of the tetra-alkylammonium ion to transfer sulfide, in comparison with bromide ion, from the aqueous into the organic phase. Consequently, as the reaction proceeds[7], the concentration of S^{2-} anion in the organic phase becomes lower and the displacement is inhibited.

Since a singly charged ion is extracted more easily than a doubly charged ion[8], hydrogen sulfides should be more advantageous for the preparation of thiodisaccharides. Good results were obtained. Thus, by using an aqueous solution of sodium sulfide and sodium hydrogensulfate, the hydrogen sulfide anion should be transferred easily into the organic phase with the aid of an organic cation and react with the glycosyl bromide to give the thio sugar. Sulfur nucleophiles have a high probability[9] of reacting with glycosyl halides by an S_N2 process and we have observed (t.l.c.) that, under phase-transfer catalysed conditions, inversion of con-

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figuration occurred at the anomeric center and the 1-thio-β-sugar was formed which reacted readily with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl or -galactopyranosyl bromide to give bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl and -galactopyranosyl) sulfide, respectively, in good yields.

The preparative procedure is relatively short, simple, and inexpensive.

EXPERIMENTAL

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl[10] and -D-galactopyranosyl bromide[11] were prepared as described in the literature. Melting points are not corrected. Optical rotations were measured with a Zeiss–Jena Polamat A automatic polarimeter for solutions in chloroform. T.l.c. was carried out on silica gel G (Merck), using benzene–ethyl acetate (2:1) or benzene–ethyl acetate (8:1) and detection with Bromocresol Green (for glycosyl halides) or charring with sulfuric acid.

Preparation of acetylated thiodisaccharides. — A solution of acetohalogeno sugar (1 mmol) in benzene (10 mL) was added to a solution of $Na_2S \cdot 9\,H_2O$ (5 mmol), $NaHSO_4$ (5 mmol), and tetrabutylammonium bromide (0.5 mmol) in water (2.5 mL), and the mixture was boiled under reflux for 15 min, then cooled, and diluted with benzene (10 mL). The organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated to give the crude product (almost theoretical yield) which was recrystallised from methanol.

Bis(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl) sulfide (87%) had m.p. 196–197°, $[\alpha]_D^{18}$ $-14°$ (*c* 0.65, chloroform): lit.[12] m.p. 199–202°, $[\alpha]_D^{20}$ $-14°$ (chloroform).

Bis(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) sulfide (93%) had m.p. 171–172°, $[\alpha]_D^{20}$ $-43°$ (*c* 0.6, chloroform): lit.[12] m.p. 176–178°, $[\alpha]_D^{20}$ $-41.9° \pm 2°$ (chloroform).

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