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Note

An improved method for the preparation of some ethyl 1-thioglycosides

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Abstract

Ethyl 1-thioglycosides were prepared in almost quantitative yield from sugar peracetates in 3:2 chloroform–ether, with boron trifluoride diethyl etherate as catalyst. D-Galactose, D-glucose, and 2-deoxy-2-phthalimido-D-glucose yielded almost exclusively β anomers, whereas L-rhamnose and D-mannose resulted predominantly in the α anomers. © 1996 Elsevier Science Ltd.

Keywords: Ethyl 1-thioglycosides; Synthesis; Boron trifluoride diethyl etherate

Ethyl 1-thioglycosides are useful compounds for oligosaccharide synthesis. There are several methods for the preparation of ethyl 1-thioglycosides from sugar peracetates and ethanethiol utilising catalysts like concentrated hydrochloric acid [1], zinc chloride [2], titanium tetrachloride [3], ferric chloride [4], boron trifluoride diethyl etherate [5,6], and zirconium chloride [7]. The most widely used method is the utilisation of ethanethiol and $BF_3 \cdot OEt_2$ in dichloromethane at 0 °C [5,6]. However, in most cases, a mixture of α- and β-thioglycosides was formed, which needed separation by chromatography. Since we have been using ethyl 1-thioglycoside donors for our work on the synthesis of oligosaccharides, we were trying to improve on the existing methods for the stereoselective synthesis of such compounds. We report here the synthesis of some thioglycoside donors (Table 1), utilising 3:2 chloroform–ether as solvent in the $BF_3 \cdot OEt_2$ catalysed procedure, in more than 95% yield. The reaction is slow, but without any side products. D-Galactose, D-glucose, and 2-deoxy-2-phthalimido-D-glucose yielded almost exclusively the 1-thio β-glycosides, whereas L-rhamnose and D-mannose resulted predomi-

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Table 1
Experimental data for ethyl 1-thioglycosides from some sugar acetates

Starting sugar acetate	Thioglycoside formed (%)	α/β Ratio	Temperature used (°C)	Time (days)	Mp and $[\alpha]_D$ of the major product
β-D-Galactose	100	1/99	7–8	7	mp 73–75 °C (ether–hexane), lit. 74–75 °C [1]; $[\alpha]_D$ −8.6° (*c* 0.60, $CHCl_3$), lit. −8° [1]
β-D-Glucose	99	2/98	7–8	6	mp 80–82 °C (EtOH), lit. 82–83 °C [7]; $[\alpha]_D$ −18° (*c* 0.83, $CHCl_3$), −24.4° [7]
2-Deoxy-2-phthalimido-β-D-glucose	99	0/100	7–8	7	mp 116–118 °C (EtOAc–hexane), lit. 118–119 °C [3]; $[\alpha]_D$ +41.5° (*c* 0.55, $CHCl_3$), lit. +44° [3]
α-L-Rhamnose	95	77/23	7–8	7	mp 66–68 °C (ether–hexane), lit. 69–70 °C [6]; $[\alpha]_D$ +86.7° (*c* 0.75, $CHCl_3$), lit. −115° [6]
α-D-Mannose	97	80/20	37	7	mp 106–108 °C (ether–hexane), lit. 107–108 °C [1]; $[\alpha]_D$ +104.0° (*c* 0.63, $CHCl_3$), lit. +104° [1]

nantly in the α anomers. It is probable that ether plays a role in the stereoselective formation of ethyl β- or α-thioglycosides. When the reactions were carried out in pure chloroform or pure dichloromethane, a mixture of α and β anomers was observed.

Experimental

A typical procedure.—To the sugar acetate (2.56 mmol) dissolved in dry $CHCl_3$ (3 mL), dry ethyl ether (2 mL) was added. The mixture was cooled in an ice-bath (5 °C). Ethanethiol (1 mL) was then added, followed by the addition of $BF_3 \cdot OEt_2$ (0.4 mL). The reaction was allowed to proceed at 7–8 °C, while monitoring with TLC (2:1 toluene-ethyl ether) every day. After 6–7 days, TLC showed full conversion to the corresponding thioglycoside. The composition of the β- and α-anomers in the product was ascertained by GLC (3% SP2340 on Gas Chrom Q at 190 °C). The reaction mixture was then washed successively with ice-cold water, satd aq $NaHCO_3$ ($\times 2$), and water ($\times 2$); dried (Na_2SO_4), and evaporated to dryness. The ethyl 1-thioglycosides (β and/or α) were purified by column chromatography (SiO_2) with 2:1 toluene–ethyl ether and crystallised. The results are given in Table 1.

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