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An Efficient Synthesis of Benzothiazole Derivatives of Thiosugars under Phase-Transfer Conditions

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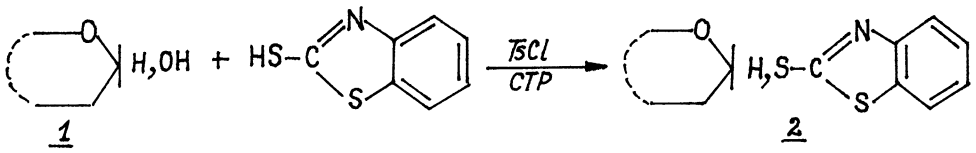
2-Benzothiazole derivatives of thiosugars can be conveniently prepared by treatment of reducing monosaccharides with tosyl chloride and 2-mercaptobenzothiazole under phase-transfer conditions.

The most intricate problem of the glycosidation reaction is that its stereospecificity, which until the present has not been resolved on general ground. There have been a number of the investigations devoted to the study of the new methods of the activation of anomeric position in sugar molecules.[1] It was observed that the anomeric thiogroup in sugars opens up possibilities for selective activation by the action of thiophilic reagents.[2-4] Mukaiyama et al. reported[5] an efficient method for the preparation of α-D-glucosides from benzothiazolyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-glucopyranoside in the presence of cupric triflate, which was used to promote the reaction and to scavenage 2-mercaptobenzothiazole formed in the course of the reaction. Benzothiazolylthio activation was also employed successfully in the synthesis of erythromycin.[6]

The benzothiazole derivative of thioglycosides (2a) had been prepared by the glycosidation of 2-mercaptobenzothiazole with 2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl chloride in the presence of 1,8-bis-(dimethylamino)naphthalene.[5] This method requires activation of the anomeric center by introduction of a halogen and is not suitable for sugar derivatives containing acid labile protecting groups.

We have found that a good leaving group can be generated from a hydroxy group by treatment with a sulfonyl halide under phase-transfer conditions.[7] This method has been successfully applied for the synthesis of S-glycosyl-O-alkyldithiocarbonates[8] and S-glycosyl-N,N-diethyldithiocarbamates.[9] In the present communication we report application of this proposition for the preparation of 2-benzothiazole derivatives of thiosugars, directly from reducing sugar derivatives (1). The 2-benzothiazolyl derivatives of 2,3,4,6-tetra-O-benzyl-D-glucopyranose (2a), 2,3:5,6-di-O-isopropylidene-D-mannofuranose (2b) and 2,3,4-tri-O-benzyl-D-xylopyranose (2c) have been prepared by the following procedure: A mixture of the reducing sugar derivative 1 (0.5 mmol) in benzene (15 mL), tetrabutylammonium chloride (35 mg, 0.125 mmol), tosyl chloride (133 mg, 0.7 mmol), and 2-mercaptobenzothiazole (84 mg, 0.5 mmol) was stirred with aqueous 50% NaOH (5 mL) at room temperature for 1-3 h (Table 1). The organic layer was separated, washed with H_2O, dried (Na_2SO_4), and concentrated. The syrupy product was purified by column chromatography on silica gel (eluent: benzene/Et_2O 25:1 v/v).



1 2

Table 1. 2-Benzothiazole derivatives of thiosugars 2 from reducing monosaccharides 1

Product	Reaction time h	Yield %	$[\alpha]_{546}^{20}$ ($CHCl_3$) a) (c: g/100 mL)	Mp °C	Ratio of isomers b) α:β	^{1}H-NMR ($CDCl_3$/TMS) c) δ, J/Hz
2a	3	95	+40.0 (0.2)	67-70	25:75	7.97-7.08 (m, 24H, $C_6\underline{H}_5CH_2$, $C_6\underline{H}_4$); 6.28 (d, 1H, H-1α, J=5); 5.21 (d, 1H, H-1β, J=8)
2b	2	92	+125.0 (0.5)	114-115	25:75	7.90-7.20 (m, 4H, $C_6\underline{H}_4$); 6.20 (s, 1H, H-1α); 5.90 (d, 1H, H-1β, J=3); 1.60, 1.50, 1.45, 1.41 (4s, 12H, $C(C\underline{H}_3)_2$)
2c	1.5	81	+52.0 (0.9)	syrup	45:55	8.10-7.10 (m, 19H, $C_6\underline{H}_5CH_2$, $C_6\underline{H}_4$); 6.35 (d, 1H, H-1α, J=4); 5.32 (d, 1H, H-1β, J=8)

a) Measured using a Polamat A automatic polarimeter (Zeiss-Jena).
b) Estimated from ^{1}H-NMR spectra.
c) Obtained on a Brucker (100 MHz) spectrometer.

Due to its simplicity and the good yields, the present method is an attractive one-pot procedure for the preparation of benzothiazole derivatives of thiosugars. It is noteworthy that sugar derivatives containing acid-labile acetal protective groups can also be used as substrate.

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