Note

Aldehyde participation in carbohydrates*. The reaction of 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-L-rhamnose with sodium ethanethioxide

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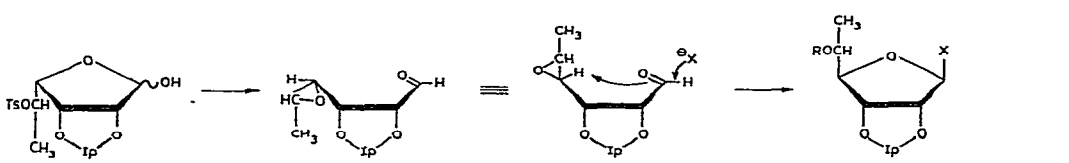
The reaction of 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-L-rhamnose (**1**) with methanolic sodium methoxide to give methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-allofuranoside (**3**) was discovered by Levene and Compton[1]. The rearrangement, involving configurational inversion at C-4 and C-5, is one of the first examples of neighboring-group participation by an aldehyde[2] group in carbohydrate chemistry. In recent years, a number of additional examples of this rearrangement have been reported[3–7]. These examples have been initiated either by alcoholic sodium alkoxide, resulting in the formation of the new sugar as a glycoside, or by water to give the free aldose.

It was of interest to examine the effect of nucleophiles containing a reactive center other than oxygen, in order to prepare other types of glycosides. The use of sodium ethanethioxide in this reaction to prepare an ethyl 1-thioglycoside is described in this paper.

N,*N*-Dimethylformamide has been used with outstanding success, as a solvent in nucleophilic-displacement and neighboring-group participation reactions in the field of carbohydrate chemistry. However treatment of **1** with sodium ethanethioxide in *N*,*N*-dimethylformamide gave a syrup that consisted of a complex mixture (t.l.c.), and no discrete products could be isolated. However, substitution of methanol for *N*,*N*-dimethylformamide as the solvent led to a crystalline product in 51% yield whose analysis indicated it to be the ethyl 1-thioglycoside **4**. Mechanistically, the



1 **2**

3, X = OMe, R = H
4, X = SEt, R = H
5, X = SEt, R = *p*-$NO_2C_6H_4CO$

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product could have been a 4- or 5-ethylthio derivative, resulting from an SN2 displacement by the thioxide ion on the *p*-toluenesulfonate **1** or epoxide **2**. The product isolated however, was nonreducing and its n.m.r. spectrum was compatible with that expected for the ethyl 1-thio-β-glycoside **4**. A comparison between the n.m.r. spectra of the methyl glycoside **3** and the ethyl 1-thioglycoside **4** is given in Table I, and illustrates the similarity between the two spectra—further confirmation that **4** is, indeed, a 1-thio-β-glycoside.

TABLE I

N.M.R. SPECTRA OF GLYCOSIDES OF 6-DEOXY-2,3-*O*-ISOPROPYLIDENE-β-D-ALLOSE

Glycoside	*Chemical shifts*[a] (τ)				
	H-1	*H-2*	*H-3*	*H-4*	*H-5*
Methyl (3)	5.00 ($J_{1,2}$ 0)	5.40 ($J_{2,3}$ 6)	5.10 ($J_{3,4}$ 0)	5.90 ($J_{4,5}$ 4)	6.20 ($J_{5,6}$ 6)
Ethyl 1-thio (4)	5.65 ($J_{1,2}$ 2)	5.40 ($J_{2,3}$ 6)	5.10 ($J_{3,4}$ 1)	6.0	6.0

[a]Coupling constants are given in Hz.

Although neither of the 4- or 5-ethylthio derivatives were isolated from the reaction in methanol, it is possible that formation of such products is responsible for the non-quantitative yield of **4**, and may account for the complexity of the reaction in *N*,*N*-dimethylformamide.

EXPERIMENTAL

General. — Melting points are corrected. Thin-layer chromatograms were run on Silica gel GF (E. Merck A.G., Darmstadt). Spots were detected by iodine vapor. Organic solutions were dried using anhydrous magnesium sulfate. N.m.r. spectra were recorded by using a Varian T-60 spectrometer for solutions in chloroform-*d*, with tetramethylsilane (*c* 1.00) as the internal standard.

Ethyl 6-deoxy-2,3-O-isopropylidene-1-thio-β-D-allofuranoside (*4*). — To a solution of 0.875 g (16.5 mmoles) of sodium methoxide in 25 ml of methanol was added 5 ml (67.5 mmoles) of ethanethiol and then 2.0 g (5.5 mmoles) of 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-L-rhamnose[1] (**1**). The mixture was stirred for 2 days at 30° and then neutralized with Amberlite IRC-50, filtered, and the filtrate evaporated to dryness *in vacuo*. The residue was partitioned between 75 ml each of chloroform and water. The chloroform layer was dried and then evaporated to dryness *in vacuo*, to give 1.15 g of crude product as a brown oil. Chromatography on silica gel (55 g) with 1:1 (v/v) chloroform–ethyl acetate gave 0.70 g (51%) of solid product; λ_{max}^{film} 2.90 (OH), 7.30 (methyl), 8.60 μm (gem dimethyl).

Anal. Calc. for $C_{11}H_{20}O_4S$: C, 53.2; H, 8.12; S, 12.9. Found: C, 53.4; H, 8.10; S, 12.5.

Ethyl 6-deoxy-2,3-O-isopropylidene-5-O-p-nitrobenzoyl-1-thio-β-D-allofuranoside (5). — To a solution of 300 mg (1.2 mmole) of ethyl 6-deoxy-2,3-*O*-isopropylidene β-D-allofuranoside (4) in 2 ml of pyridine that had been cooled to 0° was added 244 mg (1.32 mmole) of *p*-nitrobenzoyl chloride in 1 ml of chloroform. The solution was stirred for 15 min at 0° and then was stored for 18 h at room temperature. The reaction was quenched by pouring the product into 1 ml of ice-cold, saturated, aqueous sodium hydrogen carbonate. The layers were separated and the aqueous phase was extracted with 3 ml of chloroform. The chloroform extracts were washed twice with saturated aqueous sodium hydrogen carbonate and twice with water, and were then dried and evaporated to dryness *in vacuo*.

The solid residue (530 mg) was recrystallized from methanol to give white crystals, m.p. 64–67°, $[\alpha]_D^{23}$ −158° (0.5, chloroform); *c* λ_{max}^{nujol} 5.73 (C=O), 6.55 (NO_2), 8.6 μm (gem dimethyl).

Anal. Calc. for $C_{18}H_{23}NO_7S$: C, 54.4; H, 5.85; N, 3.54; S, 8.07. Found: C, 54.6; H, 5.67; N, 3.46; S, 7.85.

REFERENCES

1 P. A. LEVENE AND J. COMPTON, *J. Biol. Chem.*, 116 (1936) 169.
2 E. J. REIST, L. GOODMAN, R. R. SPENCER, AND B. R. BAKER, *J. Amer. Chem. Soc.*, 80 (1958) 3962.
3 T. IWASHIGE AND H. SAEKI, *Chem. Pharm. Bull.*, 15 (1967) 132.
5 J. S. BRIMACOMBE AND L. C. N. TUCKER, *Carbohyd. Res.*, 5 (1967) 36.
5 J. S. BRIMACOMBE, F. HUNEDY, AND L. C. N. TUCKER, *J. Chem. Soc.*, (1968) 1381.
6 N. M. K. NG YING KIN, J. M. WILLIAMS, AND A. HORSINGTON, *Chem. Commun.*, (1969) 971.
7 N. A. HUGHES AND P. R. H. SPEAKMAN, *J. Chem. Soc.*, (1967) 1186.