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Note

A convenient synthesis of carbohydrate oxiranes *via* sulfonates*

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Carbohydrate oxiranes are useful in synthesis[1]. The standard method for their formation involves treatment of a suitable tosylate or mesylate with base[2]. As a result of attack of the alkoxide ion on the anhydro sugar, in some reactions unwanted opening of the newly-formed epoxide ring occurs[3,4]. Hydroxide ion-initiated reactions under conditions of phase-transfer (p.t.) catalysis can greatly facilitate nucleophilic substitution reactions[5] and allow a simple one-pot method for preparation of epoxides from carbohydrate diols *via* the monosylates[6]. The application of this method to carbohydrate vicinal ditosylates is now reported.

The reaction involves S_N2 cleavage of the sulfur–oxygen bond and the rate depends on the basicity of the reagent used[7]. Under p.t. conditions at high concentrations of NaOH or KOH, the basicity of the hydroxide ion in the organic phase is increased dramatically[8]. When methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-α-D-glucopyranoside (**1**) was stirred with aqueous 40% sodium hydroxide under p.t. conditions using tetrabutylammonium hydrogensulfate, or the more lipophilic tetra-octylammonium chloride[9], only 15% reaction occurred due to the association of the quaternary ammonium ion with tosylate anion and "catalyst poisioning"[10]. However, when a small amount of an alcohol was added to transfer some of the base into benzene, probably due to the solvation of hydroxide ion[11], the α-*allo*-epoxide **2** was obtained in good yield. The effect of various alcohols (Table I) is roughly parallel to their ability to transfer the base.

Application of the method to methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-β-D-glucopyranoside (**3**), which resists detosylation[4], gave the β-*allo*-epoxide **4**. Likewise, methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-α-D-galactopyranoside (**5**) was converted into a mixture of the *gulo*-epoxide **6** (64%) and *talo*-epoxide **7** (25%), and the β-

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TABLE I

SYNTHESIS OF THE *allo*-EPOXIDE **2** FROM METHYL 4,6-*O*-BENZYLIDENE-2,3-DI-*O*-TOSYL-α-D-GLUCOPYRANOSIDE (**1**) UNDER P.T. CONDITIONS[a]

Catalyst	*Alcohol*	*Base*[b] *(mmol)*	*Yield of* **2** *(%)*
	None		15
	$CH_3CH_2CH_2CH_2OH$	0.15	85
Bu_4NHSO_4	$CH_3CHOHCH_2CH_3$	0.12	75
	$(CH_3)_3COH$	0.10	71
	$CH_3OCH_2CH_2OH$	0.18	90

[a]A mixture of **1** in benzene (10 mL) and alcohol (1 mmol) was stirred with saturated aqueous sodium hydroxide (5 mL) for 30 min at 20°. [b]A solution of Bu_4NHSO_4 (0.2 mmol) and alcohol (1 mmol) in benzene (10 mL) was stirred with saturated aqueous sodium hydroxide (5 mL) containing sodium tosylate (1 mmol). The basicity of the organic phase was determined potentiometrically.

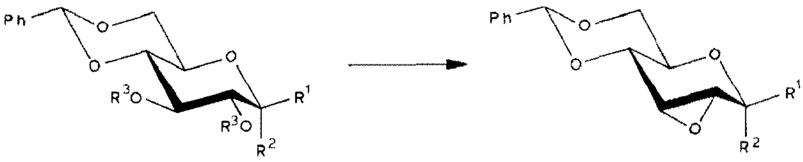
anomer (**8**) of **5** gave 79% of the *talo*-epoxide **9**. The ditosylates **5** and **8**, when treated with sodium ethoxide[12], gave epoxides in poor yield[13,14]. Similarly, 1,6-anhydro-2,3,4-tri-*O*-tosyl-β-D-glucopyranose (**10**) afforded 85% of 1,6:3,4-dianhydro-2-*O*-tosyl-β-D-galactopyranose (**11**) within a few minutes at room temperature.

Attemps to prepare the *allo*-epoxide **2** directly from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**12**) were only partly successful. Thus, treatment of **12** with 2 mol of tosyl chloride under p.t. conditions afforded the *allo*-epoxide **2** (76%) and the *manno* isomer (12%). In the absence of the quanternary ammonium salt, the ditosylation of **12** can be performed in good yield in the presence of powdered potassium hydroxide or sodium hydroxide–potassium carbonate. Thus, a one-pot synthesis of **2** from **12** involves tosylation followed by the addition of tetrabutylammonium salt and alcohol. Likewise, methyl 4,6-*O*-benzylidene-β-D-gluco- (**13**) and -galactopyranoside (**14**) yielded the *allo*-epoxide **4** (69%) and the *talo*-epoxide **9** (69%), respectively. In the reaction of 1,6-anhydro-β-D-glucopyranose with 3 mol of tosyl chloride under p.t. conditions that allowed extensive hydroxide transfer, **11** was the only product.

The rapid tosylation of sugars in a two-phase system followed by the addition of a p.t. catalyst and an alcohol is a one-pot synthesis of epoxides which is more convenient than the previously reported two-step procedures[1,2].

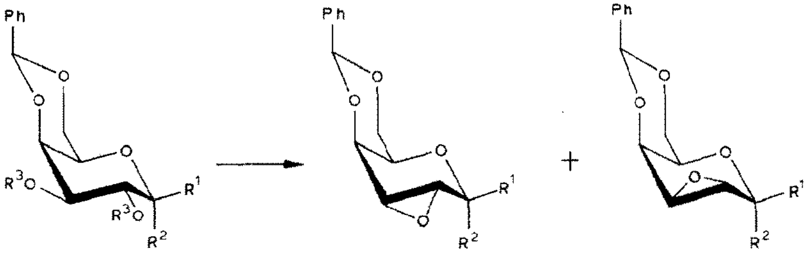
EXPERIMENTAL

General. — Optical rotations were determined for solutions in chloroform (*c* 1) at 20°. T.l.c. was performed on Kieselgel G (Merck), using 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 μm), using benzene–ether (20:1). Organic solutions were dried with $MgSO_4$ and concentrated under diminished pressure. ^{1}H-N.m.r. spectra were recorded with a Tesla spectrometer (60 MHz) for



	R^1	R^2	R^3
1	H	OMe	Ts
3	OMe	H	Ts
12	H	OMe	H
13	OMe	H	H

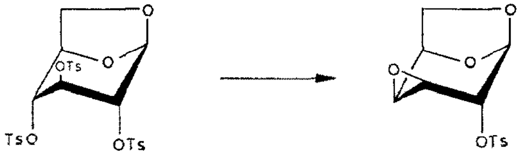
2 $R^1 = H, R^2 = OMe$
4 $R^1 = OMe, R^2 = H$



	R^1	R^2	R^3
5	H	OMe	Ts
8	OMe	H	Ts
14	OMe	H	H

6 $R^1 = H, R^2 = OMe$

7 $R^1 = H, R^2 = OMe$
9 $R^1 = OMe, R^2 = H$



10 **11**

solutions in $CDCl_3$ (internal Me_4Si). P.t. catalysts were commercial products.

Preparation of epoxides. — (a) From ditosylates. A solution of methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-D-glycopyranoside (0.59 g, 1 mmol) in benzene (10 mL), methyl sulfoxide (0.5 mL), and 2-methoxyethanol (0.2 mL) was stirred with tetrabutylammonium hydrogensulfate (0.08 g) and powdered sodium hydroxide-potassium carbonate (1:3, 2 g), or aqueous 50% sodium hydroxide (3 mL). The progress of reaction was monitored by t.l.c. and, when complete, benzene (30 mL) and water (20 mL) were added. The organic layer was washed with water (3 x 10 mL), dried, and concentrated. The residue was subjected to column chromatography. The following compounds were prepared by the above procedure.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (**2**; 0.24 g, 91%), from **1**, had m.p. 199–200°, $[\alpha]_D$ +138°; lit.[2] m.p. 199–200°, $[\alpha]_D$ +140°.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-allopyranoside (**4**; 0.22 g, 84%), from **3**, had m.p. 136–137°, $[\alpha]_D$ −17°; lit.[15] m.p. 138°, $[\alpha]_D$ − 15.6°.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-gulopyranoside (**6**; 0.17 g, 64%), from **5**, had m.p. 177–178°, $[\alpha]_D$ −8°; lit.[12] m.p. 178–179°, $[\alpha]_D$ −7.4°.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-talopyranoside (**7**; 0.07 g, 25%), from **5**, had m.p. 241°, $[\alpha]_D$ −41°; lit.[12] m.p. 242°, $[\alpha]_D$ −40°.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-talopyranoside (**9**; 0.21 g, 79%), from **8**, had m.p. 246–248°, $[\alpha]_D$ −140° (pyridine); lit.[12] m.p. 248–249°, $[\alpha]_D$ −142.5° (pyridine).

*(b) From methyl 4,6-*O*-benzylidene-D-glycopyranosides.* A solution of the glycoside (0.28 g, 1 mmol) in benzene (5 mL) and methyl sulfoxide (0.5 mL) was stirred with powdered sodium hydroxide–potassium carbonate (1:3, 2 g). A solution of tosyl chloride (0.4 g, 2.1 mmol) in benzene (5 mL) was added and stirring was continued for 30 min. 2-Methoxyethanol (0.5 mL) and tetrabutylammonium hydrogensulfate (0.08 g) were added and the progress of the reaction was monitored by t.l.c.; when complete, the mixture was worked-up as in (*a*). The following compounds were prepared by the above procedure.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (**2**; 0.2 g, 76%), from **12**, had m.p. 199–200°.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-allopyranoside (**4**; 0.18 g, 69%), from **13**, had m.p. 135–137°.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-talopyranoside (**9**; 0.18 g, 69%), from **14**, had m.p. 246–248°.

*1,6:3,4-Dianhydro-2-*O*-tosyl-β-D-galactopyranose* (**11**). — (*a*) A solution of 1,6-anhydro-2,3,4-tri-*O*-tosyl-β-D-glucopyranose (**10**; 0.53 g, 1 mmol) in benzene (20 mL) and 2-methoxyethanol (0.5 mL) was stirred with saturated aqueous sodium hydroxide (5 mL) and tetrabutylammonium hydrogensulfate (0.08 g) for 10 min. Benzene (10 mL) was then added, and the organic layer was separated, washed with water (3 x 10 mL), dried, and concentrated. The solid residue was recrystallised from alcohol to yield **11** (0.25 g, 85%), m.p. 148–150°, $[\alpha]_D$ −41°; lit.[16] m.p. 148–150°, $[\alpha]_D$ −40°.

(*b*) To a solution of 1,6-anhydro-β-D-glucopyranose (0.16 g, 1 mmol) in methyl sulfoxide (1 mL) was added benzene (10 mL), and the solution was stirred with powdered sodium hydroxide–potassium carbonate (1:3, 2 g). A solution of tosyl chloride (0.63 g, 3.3 mmol) in benzene (10 mL) was added, and stirring was continued for 10 min. 2-Methoxyethanol (0.5 mL) and tetrabutylammonium hydrogensulfate (0.08 g) were added and stirring was continued for 20 min. The mixture was worked-up as in (*a*) to give **11** (0.20 g, 67%), m.p. 148–150°.

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