Note

The preparation of 2,3-epoxypropyl β-D-glucopyranoside

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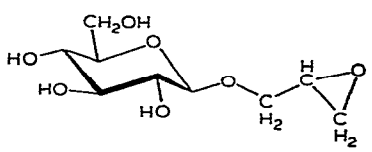
The use of substrate-directed, irreversible inhibitors to form a covalent bond with the active site of enzymes has become widespread[1]. Recently, lysozyme has been shown to be inactivated by 2,3-epoxypropyl glycosides of *N*-acetylated chitobiose and chitotriose[2]. We previously attempted to inactivate the carrier for transport of active intestinal sugar in hamsters by using methyl 2,3-anhydro-α-D-allopyranoside and methyl 3,4-anhydro-α-D-galactopyranoside, but these sugars did not bind to the active site of the carrier[3]. The specificity requirements for transport of active sugar in the hamster intestine are sterically very strict[3,4], and C-1 is the only position of the D-glucose molecule into which substitution of large groups still allows binding with the carrier. We have therefore synthesized 2,3-epoxypropyl β-D-glucopyranoside, in which the epoxide group, which can potentially react with protein, is in this sterically allowed position. Since the substance may be of general interest as a potential inhibitor of enzymes that utilize D-glucose or a D-glucopyranoside, we report here the method of synthesis. 3-*O*-(2,3-epoxypropyl)-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose has recently been synthesized[5] and its stability towards ring cleavage investigated[6].

Allyl β-D-glucopyranoside tetra-acetate[7] was treated with 3-chloroperoxybenzoic acid to give a high yield of 2,3-epoxypropyl β-D-glucopyranoside tetra-acetate (**1**). No attempt was made to determine the stereochemistry at C-2 of the epoxypropyl residue. Catalytic deacetylation of **1** with sodium methoxide gave syrupy 2,3-epoxypropyl β-D-glucopyranoside (**2**). The infrared and p.m.r. analyses were consistent with the structure proposed, and acetylation of **2** regenerated **1**.



2

Transport studies have shown that 2,3-epoxypropyl β-D-glucopyranoside is actively accumulated by a preparation[3] of hamster intestinal slices, giving, with an initial mM concentration, a tissue–medium ratio after 30 min of 3.5 compared with

5.6 for methyl α-D-glucopyranoside. D-Mannitol, which is not actively transported, gave a ratio of 0.2. A ratio greater than 1 implies active transport. The epoxide (10 mM) also inhibited D-galactose (1–5 mM) accumulation. However, when the epoxide (10 mM) was pre-incubated with the tissue rings for times varying between 0 and 60 min before they were washed and tested for D-galactose accumulation, there was no significant reduction in D-galactose transport compared with that in controls pre-incubated with methyl α-D-glucopyranoside. It must therefore be concluded that, although the epoxide binds to the sugar carrier and is transported by it, there are no groups on the carrier which can react at a significant rate with 2,3-epoxypropyl β-D-glucopyranoside.

EXPERIMENTAL

General methods. — Infrared and p.m.r. spectra were obtained with Unicam SP-200 and Varian HA-100 instruments, respectively. Optical rotations were measured on a Perkin–Elmer 141 polarimeter. Thin-layer chromatography (t.l.c.) was performed on Silica Gel F_{254} with ethyl acetate–light petroleum (b.p. 40–60°) (3:2), and 5% sulphuric acid in ethanol for detection.

2,3-Epoxypropyl β-D-glucopyranoside tetra-acetate. — Allyl β-D-glucopyranoside tetra-acetate[7] (6 g, m.p. 80–82°) was dissolved in chloroform (20 ml) and 3-chloroperoxybenzoic acid (6 g) in chloroform (70 ml) was added during 30 min. The solution was left at room temperature overnight when a precipitate formed. More chloroform (100 ml) was added, and the chloroform layer was washed with aqueous solutions of sodium sulphite, sodium hydrogen carbonate, sodium thiosulphate, and sodium carbonate, and with water. The chloroform layer was dried over calcium chloride and evaporated to dryness *in vacuo* to give 2,3-epoxypropyl β-D-glucopyranoside tetra-acetate (**1**), which was recrystallized from ethanol. Yield, 4.8 g; m.p. 115–117°, $[\alpha]_D$ −18.9° (*c* 0.04, chloroform) (Found: C, 50.6; H, 6.0. $C_{17}H_{25}O_{11}$ calc.: C, 50.4; H, 6.2%). The compound had R_F 0.29 on t.l.c. (*cf.* allyl β-D-glucopyranoside, 0.45).

2,3-Epoxypropyl β-D-glucopyranoside. — The tetra-acetate **1** (300 mg) was suspended in dry methanol (5 ml) and M methanolic sodium methoxide (0.2 ml) was added. The suspension was shaken until the solid dissolved and left for a further 15 min. Solid carbon dioxide was added, the solution was evaporated to dryness *in vacuo*, and the residue was chromatographed on Whatman No 3MM paper (loading of 2 mg/cm) with butyl alcohol–ethanol–water (4:1:5, upper layer). The major band of 2,3-epoxypropyl β-D-glucopyranoside (R_{Glc} 1.6) was detected on marker strips by using alkaline silver nitrate. Excision, elution and freeze-drying gave material (120 mg), $[\alpha]_D$ −35.8° (*c* 0.18, methanol), which failed to crystallise.

Treatment of the product (80 mg) with acetic anhydride–pyridine, in the usual manner, gave the tetra-acetate **1**, m.p. and m.m.p. 112–113°. The infrared spectrum of the acetate was indistinguishable from that of the authentic **1**.

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