Note

Sugars with reactive substituents: Preparation of several epoxypropyl-derivatized sugars

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Recently we described the preparation and some reactions of 3-O-(2,3-epoxypropyl)-1,2:5,6-di-O-isopropylidene-\(\alpha\)-D-glucofuranose. Another sugar derivative having pendent oxirane groups, 1,6-anhydro-2,3,4-tri-O-(2,3-epoxypropyl)-\(\beta\)-D-glucopyranose, was patented by Carlberg and Shafizadeh. Now we have made and characterized several new sugar derivatives, which contain one, two, three, or four epoxypropyl ether groups. The multifunctional epoxide derivatives were prepared to assess their potential for use as reactive intermediates in producing crosslinked polysaccharides.

The reaction of 3-\(\alpha\)-allyl-1,2:5,6-di-O-isopropylidene-\(\alpha\)-D-glucofuranose with \(m\)-chloroperoxybenzoic acid gave 3-O-(2,3-epoxypropyl)-1,2:5,6-di-O-isopropylidene-\(\alpha\)-D-glucofuranose in quantitative yield. When 1 was treated with dilute hydrochloric acid at room temperature, 3-\(\alpha\)-allyl-1,2-O-isopropylidene-\(\alpha\)-D-glucofuranose was obtained in quantitative yield. Epoxidation of 3 with \(m\)-chloroperoxybenzoic acid or benzonitrile-50\% hydrogen peroxide resulted in 3-O-(2,3-epoxypropyl)-1,2-O-isopropylidene-\(\alpha\)-D-glucofuranose. Allylation of methyl 4,6-O-benzylidene-\(\alpha\)-D-glucopyranoside gave the corresponding 2,3-di-O-allyl derivative, which was epoxidized to yield methyl 4,6-O-benzylidene-2,3-di-O-(2,3-epoxypropyl)-\(\alpha\)-D-glucopyranoside as a solid. Treatment of 1,2-O-isopropylidene-\(\alpha\)-D-glucofuranose with sodium hydroxide-allyl bromide in \(p\)-dioxane gave the 3,5,6-tri-O-allyl derivative, which was epoxidized to 3,5,6-tri-O-(2,3-epoxypropyl)-1,2-O-isopropylidene-\(\alpha\)-D-glucopyranose. When methyl 2,3,4,6-tetra-O-allyl-\(\alpha\)-D-glucopyranoside was treated with \(m\)-chloroperoxybenzoic acid, methyl 2,3,4,6-tetra-O-(2,3-epoxypropyl)-\(\alpha\)-D-glucopyranoside was obtained as a syrup.

The epoxidation of a vinyl ether of a carbohydrate was attempted with little success. Treatment of 1,2:5,6-di-O-isopropylidene-3-O-vinyl-\(\alpha\)-D-glucofuranose with \(m\)-chloroperoxybenzoic acid gave 1,2:5,6-di-O-isopropylidene-\(\alpha\)-D-glucofuranose as the only sugar product. When benzonitrile-50\% hydrogen peroxide was used as oxidant, a minor component was detected together with 14. The \(R_F\) value of the...
minor component when compared with 13 and 14 suggested that it was the corresponding oxirane. The i.r. spectrum of the syrupy product showed two weak bands for oxirane. Based on the work of Stevens and coworkers\textsuperscript{10-13} it might be expected that epoxidation of 13 under our conditions would give the oxirane, which would decompose into 14.

Compounds 2, 4, 10, and 12 were recovered as syrups, which failed to crystallize. Compound 7 was obtained as a crystalline product. Each was homogeneous by t.l.c. and gave elemental analysis and spectral data consistent with their proposed structures. The epoxypropyl derivatives were soluble and stable in most organic solvents.

**EXPERIMENTAL**

Optical rotations were determined with a Model 80 Rudolph* Polarimeter in 1-dm tubes. Melting points were recorded on a Fisher–Johns melting-point apparatus. I.r. spectra were recorded on a Perkin–Elmer 137 Infracord spectrophotometer. For column chromatography, Silica Gel Adsorbosil (Applied Science Laboratories, Inc., P.O. Box 140, State College, Pennsylvania), 60–100 mesh, neutralized to pH 7.0 with ammonium hydroxide, was used with a graded hexane–chloroform eluant. T.l.c. was conducted on 20 × 20-cm plates of Silica Gel G (Brinkmann Instruments, Inc., Cantiague Road, Westbury, New York) with a 2:1 hexane–acetone irrigant\textsuperscript{1}, 2, 14. The plates were developed by spraying with a solution of 20% sulfuric acid in ethanol and

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heating then for 20 min at 140°. Colored solutions were decolorized with Darco G-60 carbon.

3-O-(2,3-Epoxypropyl)-1,2-O-isopropylidene-α-D-glucofuranose (4). — 3-O-Allyl-1,2-O-isopropylidene-α-D-glucofuranose (3) (1.5 g, \( R_f \) 0.16) was dissolved in benzene (50 ml) and \( m \)-chloroperoxybenzoic acid (1.02 g, 85% pure) was added. After the reaction mixture had been stirred for 6 h at room temperature, t.l.c. showed approximately 60% conversion of 3 to 4. An additional 1.0 g of \( m \)-chloroperoxybenzoic acid was added and after a total of 24 h the reaction was complete. The mixture was evaporated to 10 ml under diminished pressure at room temperature and then placed on a silicic acid column to remove the acid. The product was eluted from the column with acetone and yielded 4 as a pure syrup (1.59 g, 100%).

Compound 4 was also formed by treating 3 (1.5 g, \( R_f \) 0.16) with benzonitrile (0.80 ml), 50% hydrogen peroxide (0.51 ml), and potassium hydrogen carbonate (0.15 g) in absolute methanol (5 ml). After 24 h, t.l.c. showed a 95% conversion of 3 to 4. The addition of more reagents failed to increase the yield. Evaporation of the reaction mixture under diminished pressure at room temperature, followed by the addition of benzene (10 ml) and separation by column chromatography as described above, yielded 4 as a pure syrup (1.41 g, 89%).

Analysis of 4. The i.r. spectrum showed absorption at 3550 cm\(^{-1}\) (OH) and at 840, 915, and 1250 cm\(^{-1}\) (oxirane). \([\alpha]_{D}^{20} -32^\circ (c 1, \text{CHCl}_3), R_f 0.06.

Anal. Calc. for \( \text{C}_{12}\)\( \text{H}_{22}\)\( \text{O}_7 \): C, 52.17; H, 7.24. Found: C, 52.31; H, 7.42.

Methyl 4,6-O-benzylidene-2,3-di-O-(2,3-epoxypropyl)-α-D-glucopyranoside (7). — Methyl 2,3-di-O-allyl-4,6-O-benzylidene-α-D-glucopyranoside (6) (7.7 g, \( R_f \) 0.61) was dissolved in benzene (200 ml) and \( m \)-chloroperoxybenzoic acid (9.0 g, 85% pure) was added. After the reaction mixture had been stirred for 24 h at room temperature, t.l.c. showed about a 90% conversion of 6 to 7. An additional 2.0 g of \( m \)-chloroperoxybenzoic acid was added, and after a total of 48 h the reaction was complete. The reaction mixture was filtered and the filtrate was washed with several 200-ml portions of a saturated sodium hydrogen carbonate solution. The benzene solution was dried with sodium sulfate and evaporated under diminished pressure. The remaining traces of the acid were removed by column chromatography to yield 7. The syrup was crystallized and recrystallized from hexane to afford 7 (8.0 g, 95%).

Analysis of 7. The i.r. spectrum of 7 showed no absorption at either 3500 cm\(^{-1}\) (OH) or at 1650 cm\(^{-1}\) (C=C), but several absorptions for oxirane were present at 825, 858, 910, and 1250 cm\(^{-1}\). M.p. 91–92°, \([\alpha]_{D}^{20} +57^\circ (c 1, \text{CHCl}_3), R_f 0.26.

Anal. Calc. for \( \text{C}_{20}\)\( \text{H}_{26}\)\( \text{O}_8 \): C, 60.91; H, 6.60. Found: C, 61.16; H, 6.60.

3,5,6-Tri-O-(2,3-epoxypropyl)-1,2-O-isopropylidene-α-D-glucofuranose (10). — 3,5,6-Tri-O-allyl-1,2-O-isopropylidene-α-D-glucofuranose (9) (1.8 g, \( R_f \) 0.75) was dissolved in benzene (200 ml) and \( m \)-chloroperoxybenzoic acid (6.0 g, 85% pure) was added. After the reaction mixture had been stirred for 24 h at room temperature, t.l.c. showed complete conversion of 9 to 10. Workup was completed as described in the preceding section to yield 10 as a pure syrup (2.09 g, 100%).

Analysis of 10. The i.r. spectrum of 10 showed no absorption at either 3550 cm\(^{-1}\)
(OH) or at 1650 cm\(^{-1}\) (C=C), but several absorptions for oxirane were present at 805, 855, 910, and 1250 cm\(^{-1}\). \([\text{x}]_D^{20} -16^\circ \) (c 1, CHCl\(_3\)), \(R_F\) 0.23.

\textit{Anal.} Calc. for C\(_{18}\) H\(_{38}\) O\(_9\) : C, 55.67; H, 7.22. Found: C, 55.62; H, 7.54.

\textit{Methyl 2,3,4,6 tetra-O-(2,3-epoxypropyl)\(\alpha\)-D-glucopyranoside (12).} — Methyl 2,3,4,6-tetra-O-allyl-\(\alpha\)-D-glucopyranoside\(^6\) (11) (2.3 g, \(R_F\) 0.75) was dissolved in benzene (200 ml) and \(m\)-chloroperoxybenzoic acid (7.5 g, 85% pure) was added. After the reaction mixture had been stirred for 24 h at room temperature, t.l.c. showed about a 60% conversion of 11 to 12. Several 2.0-g portions of \(m\)-chloroperoxybenzoic acid were added on subsequent days, but only an 80% conversion could be obtained. Workup was completed as previously described to yield 12 as a pure syrup (2.18 g, 80%).

Analysis of 12. The i.r. spectrum of 12 showed no absorption at either 3550 cm\(^{-1}\) (OH) or at 1650 cm\(^{-1}\) (C=C), but several absorptions for oxirane were present at 810, 860, 910, and 1255 cm\(^{-1}\). \([\text{x}]_D^{20} +84^\circ \) (c 1, CHCl\(_3\)), \(R_F\) 0.09.

\textit{Anal.} Calc. for C\(_{19}\) H\(_{30}\) O\(_{10}\) : C, 54.54; H, 7.18. Found: C, 54.43; H, 7.30.

\textit{Epoxidation of 1,2:5,6-di-O-isopropylidene-3-O-vinyl-\(\alpha\)-D-glucofuranose\(^9\) (13).} — Compound 13 (1.6 g, \(R_F\) 0.70) was dissolved in benzene (100 ml) and \(m\)-chloroperoxybenzoic acid (1.1 g, 85% pure) was added. After the reaction mixture had been stirred overnight at room temperature, t.l.c. showed complete reaction. Workup was completed as previously described to yield a solid; m.p. and mixed m.p. with 14 108–109\(^\circ\); \(R_F\) 0.41.

The experiment was repeated with a different oxidant. Compound 13 (0.48 g, \(R_F\) 0.70) was dissolved in methanol (3 ml) and potassium hydrogen carbonate (0.1 g), benzonitrile (0.5 ml), and 50% hydrogen peroxide (0.34 ml) were added. After the reaction mixture had been stirred overnight at room temperature, t.l.c. showed complete reaction. Workup was completed as previously described for 4 to yield a syrup. T.l.c. analysis showed 14 (80%, \(R_F\) 0.41) and another component (20%, \(R_F\) 0.37) which was assumed to be the oxirane. The i.r. spectrum showed no absorption at 1655 and 1645 cm\(^{-1}\) (vinyl), but weak absorption for oxirane was present at 925 and 795 cm\(^{-1}\).

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\textbf{REFERENCES}


