Synthesis and Alkaline Degradation of Methyl 4-O-Ethyl-3-O-methyl-β-D-*threo*-pentosidulose

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Specific degradation methods are needed in structural polysaccharide chemistry and methods for achieving specific polysaccharide degradations should be investigated. Various routes, *e.g.* degradation of sulphones,[1] may be used to obtain methylated polysaccharides having free hydroxyl groups whose positons are defined by the method used for their protection. On oxidation of these hydroxyl groups to carbonyl groups, followed by treatment with mild alkali, cleavage of the polysaccharide into smaller fragments may occur. Analysis of these fragments should give structural information, *e.g.* on the distribution of sugar residues or other groups removed in an earlier degradation.

This type of oxidation-degradation was investigated with methyl 2,4,6-tri-O-methyl-α- and -β-D-glucosides, as model substances for methylated polysaccharides having free hydroxyls in the 3-positions.[2,3] For both substances the glycosidic linkage was quantitatively cleaved by this treatment.

If the starting material is a methylated polysaccharide with free hydroxyls in the 2-positions, the substituent in the 4-position is expected to be eliminated during the above sequence of reactions. For a (1→4)-linked polysaccharide this would result in fragmentation. This possibility has now been investigated, using methyl 4-O-ethyl-3-O-methyl-β-D-xyloside (II) as a model substance.

Methyl 2,3-anhydro-β-D-ribopyranoside[4] was ethylated and the epoxide ring was opened by treatment with sodium methoxide,[5] yielding methyl 4-O-ethyl-3-O-methyl-β-D-xyloside (II). On oxidation of this substance with ruthenium tetraoxide[6] methyl 4-O-ethyl-3-O-methyl-β-D-*threo*-pentosidulose (III) was formed in quantitative yield.

Treatment of III with 0.05 M sodium 1-propoxide in 1-propanol-dichloromethane resulted in quantitative elimination of the 4-O-ethyl group. The same result was obtained with sodium methoxide in methanol-dichloromethane (1 : 1). For the determination, by GLC, of ethanol and any methanol formed during the reaction, the former system is preferable.

A new component was isolated from the reaction product as a syrup in 84 % yield. It showed $[\alpha]_D^{20} - 116°$ (chloroform) and carbonyl (1710 cm^{-1}) and carbon-carbon double bond (1630 cm^{-1}) absorptions in the IR. The UV spectrum, with maxima at 322 nm and 263 nm, is indicative of an α,β-unsaturated ketone. In the NMR spectrum, signals for two methoxyls were observed at τ 6.47 and 6.35. A one proton singlet at τ 5.18 was attributed to the anomeric proton. The remaining three protons appeared in the spectrum as an ABX system. A one proton quartet, τ 4.11, is attributed to the olefinic X-proton. A two proton octet, τ_A 5.33, τ_B 5.64, J_{AX} 2.5 cps, J_{BX} 4 cps, J_{AB} 19 cps, is attributed to the two protons at C-5 in the product.

The combined spectral evidence demonstrates that the substance is an R-methyl 4-deoxy-3-O-methyl-3-eno-pentosidulose formed from III by β-elimination of the ethoxyl group at C-4. The configuration at C − 1 is probably the same as in the starting material, but isomerisation during the alkaline treatment is not excluded by the present evidence.

In the mass spectrum of IV, the strongest fragments were observed at m/e 55 (100 %), 70 (32 %), 98 (38 %), and 127 (4 %). Possible routes leading to these fragments are depicted in Fig. 1. The CD spectrum of IV displayed Cotton effects at 323 nm (θ max 568°) and 285 nm (θ min 285°).

The alkaline degradation of methyl 4-O-methyl-β-D-*ribo*-hexosid-3-ulose, studied by Theander,[7] followed a similar course. The oxidation and subsequent alkaline degradation of III thus proceeded as expected, and application of the degradation to polysaccharides is under investigation.

Experimental. GLC separation of the alcohols was performed at 130° on a Perkin-Elmer model 990 instrument using a glass column packed with 5 % UCON on Poropac Q (100−120 mesh). Peak areas were measured with a Hewlett-Packard 3370 electronic integrator. For GLC−MS, the alcohol mixtures were injected into a Perkin-Elmer 270 gas chromatograph−mass spectrometer fitted with the
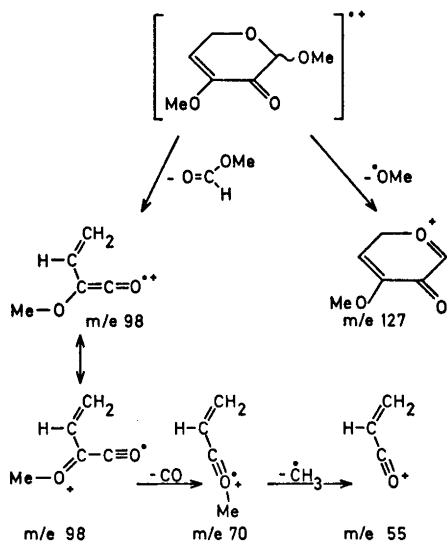
Fig. 1. Fragmentation routes for *R*-methyl 4-deoxy-3-*O*-methyl-3-eno-pentosidulose.

appropriate column. The mass spectra were recorded at a manifold temperature of 200°, ionisation potential of 70 eV, ionisation current of 80μA and an ion source temperature of 120°. The CD spectra were determined on a Cary 60 apparatus equipped for CD.

Methyl 4-O-ethyl-2,3-anhydro-β-D-riboside (I). Silver oxide (10.0 g) was added to a solution of methyl 2,3-anhydro-β-D-ribo-pyranoside[4] (5.0 g) in ethyl iodide (50 ml). The resulting mixture was refluxed with stirring for 12 h, after which time no starting material remained. The reaction mixture was filtered and the silver salts were washed with acetone. The combined filtrates were concentrated to dryness yielding crude I (6.2 g). Sublimation gave white needles, m.p. 41−43°, $[\alpha]_D^{22} - 3.3°$ (*c* 1.01, chloroform). (Found: C 54.9; H 7.90. $C_8H_{14}O_4$ requires: C 55.1; H 8.12.) NMR demonstrated, *inter alia*, the presence of one ethoxyl and one methoxyl group. The anomeric proton appeared as a singlet at τ 5.10.

Methyl 4-O-ethyl-3-O-methyl-β-D-xyloside (II). A solution of I (3.5 g) in 2 M sodium methoxide in methanol (125 ml) was refluxed overnight. Water (100 ml) was added, the methanol was distilled off, and the organic phase was taken up in chloroform. The chloroform extracts were washed until neutral with water and concentrated to dryness. The

resulting syrup (2.9 g) crystallised on standing. Recrystallisation from light petroleum—ethanol (20 : 1, v/v) yielded pure II, m.p. 75−77°, $[\alpha]_D^{22} - 83°$ (*c* 1.02, chloroform). (Found: C 52.3; H 8.84. $C_9H_{18}O_5$ requires: C 52.4; H 8.81.) NMR showed, *inter alia*, one ethoxyl and two methoxyl groups. The anomeric proton gave a doublet (τ 5.75), with a coupling constant of 6 Hz.

Methyl 4-O-ethyl-3-O-methyl-β-D-threo-pentosidulose (III). Excess ruthenium tetraoxide (0.05 M in carbon tetrachloride) was added portionwise to a stirred solution of II (300 mg) during 1 h at 22°. The excess ruthenium tetraoxide was destroyed by the addition of isopropanol (1 ml). The resulting suspension was filtered and concentrated to dryness. The yield of IV was 300 mg. Sublimation yielded the pure compound, m.p. 66−68°, $[\alpha]_D^{22} - 81°$ (*c* 0.6, chloroform). (Found: C 52.7; H 7.94. $C_9H_{16}O_5$ requires: C 52.9; H 7.91.) A singlet at τ 5.30 in the NMR spectrum was attributed to the anomeric proton. The infrared spectrum had a single absorption in the carbonyl region at 1760 cm^{-1}. The CD spectrum gave a maximum at 320 nm with the amplitude $(\theta) = 3370°$.

Alkaline degradation of III. Sodium methoxide in methanol (0.1 M, 1 ml) was added to a solution of III (100 mg) in methylene chloride (1 ml). After 15 min at room temperature no starting material remained and the mixture was neutralised with glacial acetic acid and concentrated to dryness. TLC (silica gel, ethyl acetate−light petroleum, 2 : 1, v/v) showed only one major spot. The main component was purified by preparative TLC; yield 67 mg of a syrup $[\alpha]_D^{22} - 106°$ (*c* 0.8, chloroform).

To study, quantitatively, the elimination of the ethoxyl group a solution of III (20.0 mg) in dichloromethane (0.15 ml) was treated with 0.1 M sodium 1-propoxide in 1-propanol (0.15 ml). Samples were withdrawn from the reaction mixture, neutralised with glacial acetic acid and analysed for ethanol and methanol. After 20 min 0.97 mol of ethanol, and 0.13 mol of methanol had been formed. The identity of the alcohols was demonstrated by mass spectrometry.

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Oxidation of Carbohydrate Derivatives with Silver Carbonate on Celite. IV. Oxidation of L-Sorbose, an Alternative Synthesis of L-Threose

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Three of the four aldotetroses are readily prepared from different aldohexoses and pentoses by common degradation reactions. An analogous synthesis of the fourth aldotetrose, L-threose, is forbidden by the lack of a readily available precursor with a correct configuration. The most convenient existing method for the preparation of L-threose seems to be periodate oxidation of 1,3-O-benzylidene-L-arabinitol,[1] which involves preparation of the starting material. It has been found in this laboratory that silver carbonate on Celite, reported in previous papers in this series to shorten the carbon chain of aldoses [2] and derivatives,[3,4] is a convenient degradation reagent also for ketoses. The present communication reports its application in preparation of L-threose from the commercially available, and inexpensive L-sorbose. A more detailed report on the oxidation of ketoses will be published elsewhere.
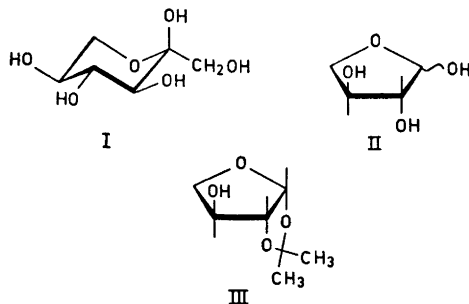
L-Sorbose (I) is completely oxidized in methanol at 40° within 40 min. The product exhibits strong infrared absorption at 1735 cm^{-1} and the major component of the product mixture is detectable on a thin-layer plate by spray reagents for reducing sugars as well as for esters. This compound gives L-threose (II) on acid hydrolysis and subsequent treatment of the hydrolysate with anion exchanger. The initially formed product is in light of these facts assumed to be a glycolic ester of L-threose, resulting from glycol-cleavage between C-2 and C-3 of L-sorbose in a cyclic form.

The threose formed in this reaction is contaminated with small amounts of a compound which is assumed on chromatographic evidence to be glyceraldehyde. The tetrose is, however, pure enough to allow direct preparation of crystalline 1,2-O-isopropylidene-β-L-threofuranose (III), by treatment with acetone – sulphuric acid. The yield of this compound was about 40 % based on L-sorbose. If a chromatographically pure threose is desired, this is readily obtained by hydrolysis of the 1,2-O-isopropylidene derivative (III) with aqueous acetic acid.

Experimental. Thin-layer chromatography was performed on silica gel in the solvent systems (V/V): (A) benzene – ethanol 5 : 2 and (B) chloroform – methanol 30 : 1, paper chromatograms were run on Whatman No. 1 paper in (C) butanol – pyridine – water 5 : 3 : 2. As spray reagents were used diphenylamine – aniline – phosphoric acid [5] and hydroxylamine ferric chloride.[6]

Oxidation of L-sorbose (I). L-Sorbose (I) (1 g) in methanol (200 ml) was stirred at 40° for 40 min with silver carbonate on Celite [7] (22 g), solid material was filtered off and the solvent evaporated under reduced pressure. The resulting syrupy residue showed strong