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The Oxidation of Glycosides

XI *. Oxidation of Methyl β-D-xylopyranoside and Methyl β-D-ribopyranoside

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Methyl β-D-xylopyranoside was oxidised with chromium trioxide in acetone and the resulting oxo-xylosides fractionated. The 2-oxo-, 3-oxo and 4-oxo-methylxylosides were isolated as amorphous materials. Platinum catalysed oxidation of methyl β-D-ribopyranoside gave methyl β-D-3-oxo-xylopyranoside (methyl β-D-3-oxo-ribopyranoside) as the principal oxidation product.

Oxidation of the anomeric methyl-6-*O*-trityl-D-glucopyranosides with chromium trioxide in acetone [1] yields mainly the 3-oxo-derivative (3—5 %) together with smaller amounts of the 2-oxo- and 4-oxo-derivatives (0.3—0.5 %). Similarly, oxidation of methyl β-D-glucopyranoside with this reagent [2] results in the aforementioned products together with a compound identified as methyl β-D-6-oxo-glucopyranoside (1.3 %). These oxidation studies have now been extended to glycosides of the pentoses and an attempt has been made to localise the oxidation by catalytic methods.

The oxidation procedure used with chromium trioxide in acetone was essentially that described by Theander [1]. The reaction mixture was shown by paper chromatography to contain at least seven products, the principal components of which were separated by chromatography on a carbon-Celite column. The 2-oxo- and 4-oxo-xylosides were eluted from the column together and in a fraction containing unreacted methyl β-D-xyloside. They were subfractionated on thick filter papers (see Experimental). As in the glucoside series [1,2] the 2-oxo- and 4-oxo-xylosides were more labile than the corresponding 3-oxo-xyloside at a pH near the neutral point and readily gave epimerisation and decomposition products. This was particularly noticeable in working up eluates from thick filter papers and in neither case was a chromatographically homogeneous product obtained. Methyl β-D-3-oxo-xylopyranoside, the principal product of the oxidation, was obtained as an amorphous powder ($[\alpha]_D$ −90°) but chromatographically and electrophoretically pure. The yield of oxo-derivatives was essentially the same as found by Theander [1] with methyl

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Table 1. Oxo-xylosides; preparation and characteristics.

	Methyl β-D-oxo-xylopyranosides			Methyl β-D-xylopyranoside
	2-oxo	3-oxo	4-oxo	
Yield [a] (%)	0.4	3.5	0.4	43
Percentage of ethanol in the eluate when substance emerged from the column[b]	7.5	12.6	7.5	8.25
Paper chromatography $R_{glucose}$ values [b]				
Irrigant A	1.62	3.48	2.01	1.81
Irrigant B	1.44	2.14	1.63	2.10
Paper electrophoresis M_V values Buffer D at room temperature[b]	1.0	1.0	1.0	0
Products of reduction and hydrolysis	xylose lyxose	xylose ribose	xylose arabinose	

a. The yields are calculated as percentage of the amount of xyloside before oxidation.
b. Data of the carbon column separation and solvents and buffer used for paper chromatoraphy and electrophoresis are given in the Experimental section.

6-*O*-trityl-β-D-glucopyranoside and are recorded in Table 1. The structure of the oxo-xylosides was shown by identifying the sugars obtained on reduction (sodium amalgam) and hydrolysis (see Table 1 for details).

The oxo-xylosides formed strong complexes in hydrogen sulphite buffer at pH 4.7 and all had an M_v value = 1 (migration relative to that of vanillin). This contrasts with the results obtained in the glucoside series [3] where the various isomers showed significant differences in their rates of migration in hydrogen sulphite buffer. The M_v values and $R_{glucose}$ values of the oxo-xylosides are recorded in Table 1. The oxo-xylosides gave strong reducing reactions with silver nitrate-sodium ethoxide reagent and a characteristic yellow colouration (absorption in UV-light) with anisidine hydrogen chloride.

The dehydrogenation of polyols by treatment with oxygen in the presence of platinum catalysts has recently been reviewed by Heyns and Paulsen [4]. In the cyclitol series it has been found that axial hydroxyl groups are preferentially dehydrogenated. *myo*-Inositol has, for example, been selectively dehydrogenated to *myo*-inosose-2. These reactions are generally reversible as axial hydroxyl groups are preferentially formed by platinum catalysed hydrogenation of the corresponding ketones. Theander [5] has shown that platinum catalysed reduction of an oxo-glucoside results in a mixture of glycosides in which the epimer with the axial hydroxyl group predominates. Methyl β-D-ribopyranoside on treatment with oxygen over reduced Adams' catalyst gave a mixture of products, the main component of which was chromatographically indistinguishable from methyl β-D-3-oxo-xylopyranoside (methyl β-D-3-

oxo-ribopyranoside). Carbon column chromatography gave four main fractions (see Experimental) one of which contained relatively pure methyl β-D-3-oxo-xylopyranoside. Reduction of this fraction with sodium amalgam and subsequent hydrolysis gave two sugars indistinguishable from ribose and xylose in irrigants A—C. Another fraction, containing some 3-oxo-derivative together with much unreacted methyl β-D-ribopyranoside, was effectively separated by chromatography on a carbon-Celite column using sodium hydrogen sulphite elution [2]. The yield of methyl β-D-3-oxo-xylopyranoside (*ca.* 6 %) is limited by secondary oxidation and degradation reactions which occur on prolonged oxidation.

In the sterically favoured C-1 conformation of methyl β-D-ribopyranoside only the hydroxyl at $C_{(3)}$ is axially disposed and it seems, as in the cyclitol series, that preferential dehydrogenation occurs at this position. Other experiments, for example with methyl α-L-arabinopyranoside ($C_{(4)}$ hydroxyl group axial), indicated that dehydrogenation occurs at the axial hydroxyl group. This reaction is complicated by the ease of epimerisation and degradation of the initially form oxo-compounds at a pH near the neutral point. Methyl β-D-xylopyranoside (all hydroxyl groups equatorial) was largely unaffected under identical conditions but some slight oxidation was observed. This suggests that either some dehydrogenation occurs at the equatorial hydroxyl groups or that the molecule can react in a sterically unfavourable conformation.

EXPERIMENTAL

Melting points are corrected. All distillations were carried out under reduced pressure (bath temperature < 35°) or by freeze-drying. Whatman 1 filter papers were used for paper chromatography and electrophoresis except for preparative separations which were made on Whatman 3 MM filter papers previously washed thoroughly with water.

Irrigants and buffer used:

A. Ethyl acetate-acetic acid-water, 3:1:3 (upper phase)
B. Butanol-ethanol-water, 10:3:5
C. Ethyl acetate-pyridine-water, 2:1:2
D. Hydrogen sulphite buffer [3] pH 4.7, 0.1 M.

Oxidation of methyl β-D-xylopyranoside with chromium trioxide

The oxidation and fractionation procedures were essentially as described by Theander [1] and an abbreviated description only is given.

Methyl β-D-xylopyranoside (20.0 g) in acetone (1.2 l) was oxidised by treatment under reflux with chromium trioxide (18.3 g) in acetone (1.2 l) for 30 min. The brown chromium oxides were filtered from the oxidation mixture and boiled with acetone (4 × 400 ml) for 10 min with intermediate filtrations. The combined filtrates were evaporated to a dark brown clear solution, adjusted to 500 ml with acetone and treated with 0.5 N alcoholic hydrogen chloride (60 ml) at 25° for 30 min to reduce the chromium in solution to Cr^{3+}. The solution was adjusted (Ag_2CO_3) with agitation and cooling to pH 5. The silver precipitate was filtered, washed with acetone and water and the combined filtrate and washings evaporated to a small volume and deionised [Dowex 50(H^+) and Dowex 3(free base)]. The solution, which had a pH of 5, was evaporated to a semi-crystalline mass (13.6 g) which was fractionated on a carbon-Celite column (70 × 8 cm) using linear gradient elution technique (ethanol: 0—20 %, 16 l). The following main fractions were collected in 50 ml portions.

Fraction I (0.123 g), 120—130, contained a mixture of methyl 2- and 4-oxo-xylosides and was subfractionated on thick filter papers using irrigant A. As the oxo-compounds

were quite labile and further transformed to other products even at pH 4—7, eluates from the thick filter papers were evaporated by freeze-drying in silicone treated flasks.

Fraction II (9.45 g), 132—195, consisted mainly of methyl β-D-xyloside and traces of methyl 2- and 4-oxo-xylosides. The mother-liquors were fractionated on thick filter papers to give further small quantities of 2- and 4-oxo-xylosides after removal of the methyl β-D-xyloside by crystallisation. Fraction III (0.7 g) 202—242 contained methyl β-D-3-oxo-xyloside which was obtained as an amorphous powder $[\alpha]_D^{21.5}$ −90° (*c*, 1.0 in water) after removal of the solvent.

Characterisation of methyl β-oxo-xylosides

Methyl β-D-3-oxo-xylopyranoside (0.2 g) in water (5 ml) was treated over 2 h with 2.5 % sodium amalgam and pH 6 maintained by gradual addition of glacial acetic acid. After deionisation [Dowex 50(H^+) and Dowex 3(free base)] and concentration, the solution was hydrolysed with 0.5 N sulphuric acid for 16 h at 100°. The neutral (Dowex 3) solution was concentrated and the sugars formed were separated on thick filter papers using irrigant A. After elution and evaporation, ribose was obtained as a syrup which failed to crystallise but gave a crystalline 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 162—163°.

Methyl β-D-2-oxo-xylopyranoside (20 mg) gave on similar treatment two sugars chromatographically indistinguishable from xylose and lyxose in irrigants A—C.

Methyl β-D-4-oxo-xylopyranoside (20 mg) gave on reduction and hydrolysis two sugars chromatographically indistinguishable from xylose and arabinose in irrigants A—C.

Platinum catalysed oxidation of methyl β-D-ribopyranoside

A stream of hydrogen was passed through a suspension of platinum dioxide (2 g) in water (200 ml) in a 500 ml Kluyver flask until reduction was complete. Excess hydrogen was removed in a stream of nitrogen and oxygen then passed in a rapid stream until the metal was finely suspended; β-methyl-D-ribopyranoside (4 g) was added and oxidised at atmospheric pressure for 5 h at 20°. On paper chromatograms, run in irrigant A, the oxidised solution gave a strong spot with $R_{glucose}$ value 3.48, which showed a characteristic colour reaction with anisidine hydrogen chloride spray and was chromatographically indistinguishable from methyl β-D-3-oxo-xylopyranoside. The oxidised solution was shaken with Dowex 3(free base) to remove any acids produced, filtered and the filtrate concentrated under reduced pressure. The combined yield of two such treatments was chromatographed on a carbon-Celite column (70 × 8 cm) using the linear gradient elution technique (ethanol: 0—20 %, 16 l). The following fractions were collected in 50 ml portions.

Fraction I (0.3 g), 128—160, contained three components, the main component having $R_{glucose}$ value 1.58. This fraction was not further investigated.

Fraction II (0.38 g), 178—187, contained relatively pure methyl β-D-3-oxo-xylopyranoside. It was chromatographically indistinguishable from the methyl β-D-3-oxo-xylopyranoside obtained by chromium trioxide oxidation. Ribose and xylose were the only sugars formed on reduction and hydrolysis.

Fraction III (4.8 g), 188—244, contained a small amount of methyl β-D-3-oxo-xylopyranoside together with unreacted starting material. Separation of 2.3 g of this fraction on a carbon-Celite column (35 × 3 cm) using 0.1 N sodium hydrogen sulphite elution [2] gave a further quantity (42 mg) of the 3-oxo-derivative.

Fraction IV (1.8 g), 246—280, contained mainly methyl β-D-ribopyranoside which crystallised on removal of the solvent.

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