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The Oxidation of Glycosides

XIII *. The Oxidation of Methyl β-D-Glucopyranoside with Fenton's Reagent

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Methyl β-D-glucopyranoside has been oxidised by Fenton's reagent. The four carbonyl compounds resulting from oxidation at C-2, C-3, C-4, and C-6 were isolated together with D-arabinose, D-glucose, D-erythronolactone, D-arabinolactone and some unidentified products.

The degradation of cellulose on exposure to light [1,2] and during the ageing of alkalicellulose in the presence of oxygen [3] are both due to oxidation by radical mechanisms. The modification and degradation of cellulose and other carbohydrates by ionising radiation [4] are initiated by hydroxyl radicals, formed from water present in the system. Fenton's reagent is a convenient source for hydroxyl radicals and the products formed by the action of this reagent and of ionising radiation are often remarkably similar [5].

Fenton and Jackson [6] obtained a 40 % yield of mannose on the oxidation of mannitol with hydrogen peroxide-ferrous sulphate. The products from the reaction of Fenton's reagent with glucose have been investigated by Küchlin [7] and by Bourne and coworkers [8]. Demethylation of sugar derivatives by this reagent was demonstrated by Jones and coworkers [9].

The oxidation of methyl β-D-glucopyranoside with several oxidising agents has been studied in this Department, with the aim of isolating and characterising the primary oxidation products. The results of these studies have been reviewed by Theander [10]. We now report similar studies, using Fenton's reagent as the oxidant.

Methyl β-D-glucopyranoside was oxidised at room temperature with Fenton's reagent, using 1.5 moles of hydrogen peroxide per mole of glucoside. After deionisation the neutral fraction was separated by a combination of carbon column and cellulose column chromatography.

The yields of the main products are given in Table 1. All these products have been isolated after the oxidation with other agents[10], but in different rela-

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Table 1. Reducing carbohydrates isolated after oxidation of methyl β-D-glucopyranoside (30 g) with Fenton's reagent.

Substance	Yield (g) Expt. I	Yield (g) Expt. II
D-Arabinose	0.08	—
D-Glucose	1.27	—
Methyl β-D-*arabino*-hexopyranosidulose	0.08	0.11
Methyl β-D-*ribo*-hexopyranosid-3-ulose	0.34	0.26
Methyl β-D-*xylo*-hexopyranosid-4-ulose	0.06	0.09
Methyl β-D-*gluco*-hexodialdo-1,5-pyranoside	0.26	0.21

tive proportions. The oxidative demethylation seems to be higher with Fenton's reagent. It must be remembered, however, that the yield of a product depends not only upon the ease with which it is formed but also upon its stability to further oxidation. In addition to the products in Table 1 a trace quantity of erythrose was observed. The acid fraction was not investigated but the neutral fraction contained several lactones, two of which, D-erythrono-γ-lactone and D-arabino-γ-lactone were identified.

Oxidative demethylation and oxidation of the primary and secondary alcohol groups in methyl β-D-glucopyranoside seem to be the first reactions on oxidation by hydroxyl radicals. The other products are probably formed by further oxidation of the glucose and the carbonyl glucosides. It seems reasonable to assume that other radical initiated oxidations of carbohydrates follow a similar course. In the ageing of alkali cellulose, and other oxidations in alkaline media, the initially formed carbonyl glycoside residues will become rapidly degraded to acidic products.

EXPERIMENTAL

Concentrations were performed under reduced pressure and at a bath temperature < 40°.

Chromatographic solvent systems: A Butan-1-ol — ethanol — water, 10:3:5.
B Ethyl acetate — acetic acid — water, 3:1:1.
C Methyl ethyl ketone, saturated with water.
D Ethyl acetate — pyridine — water, 8:2:1.
Buffers for paper electrophoreses: E 0.1 M Hydrogen sulphite, pH 4.7 (at 50°)
F 0.1 M Borate, pH 10.

Oxidation of methyl β-D-glucopyranoside. Methyl β-D-glucopyranoside (30 g), which was free from D-glucose, and ferrous sulphate heptahydrate (3 g) were dissolved in water (150 ml) and 6 % aqueous hydrogen peroxide (135 ml) was added in 20 ml portions over 2 h. During the addition the solution was externally cooled with tap water and then kept at room temperature for a further 2 h. The solution was deionised (Dowex 50(H^+) and Dowex 3 (free base)), concentrated to 50 ml and then freeze-dried. The residue was taken up in hot ethanol, from which unchanged methyl β-D-glucoside crystallised. The residue was concentrated to a syrup (15 g) and was added to a carbon-Celite column (6.5 × 52 cm) which was then irrigated with aqueous ethanol (10 l, 0→15 %, then 4 l, 15→20 % and finally 4 l, 50%). Analogous separations have been described in previous communications [11]. Most fractions contained two or several components and were further fractionated, either on cellulose columns or thick filter paper. The substances listed in Table 1 (Expt. I) were thus obtained chromatographically and electrophoretically pure and indistinguishable from the authentic substances on paper chromatograms in A, B, C, and D and paper

electrophoreses in E and F. D-Arabinose (m.p. 157–159°), D-glucose (m.p. 149–150°) and methyl β-D-*ribo*-hexopyranosid-3-ulose (m.p. 129–130°) were also obtained crystalline, identical with the authentic substances. In addition to the compounds in Table 1 D-erythrono-γ-lactone (traces) and D-arabino-γ-lactone (40 mg) were isolated. The former was identified by paper chromatography only. The latter on borohydride reduction yielded a mixture of D-arabinose and D-arabinitol, (chromatographical evidence) and was further characterised as the crystalline 2-(D-*arabino*-1,2,3,4-tetrahydroxybutyl)benzimidazole, m.p. 236–238°, $[\alpha]_D^{25}$ −40° (5 % aqueous citric acid, *c* 2); Lit.-values [12] m.p. 240–241°, $[\alpha]_D^{20}$ −49.5°. The methyl β-D-glucoside recovered amounted to 13.7 g.

A second oxidation experiment, starting from 30 g methyl β-D-glucoside was performed as described above. The deionised solution, adjusted to pH 6.5 with ammonia, was added to a Dowex 2–X 8 column (50 × 4 cm) in the hydrogen sulphite form,[13] which had previously been washed with water of pH 6.5. Elution with water of pH 6.5 removed all the methyl β-D-glucoside, part of the arabinose and glucose but only traces of the carbonyl glucosides. The latter, and the rest of the arabinose and glucose, were eluted with aqueous acetic acid; a small part with 1 % acid, most of the material with 10 % acid and the last traces with 25 % acid. The carbonyl glucoside fraction was fractionated as described above. This fractionation, which was simplified by the absence of methyl β-D-glucoside, yielded the four carbonyl glycosides in approximately the same amounts (Table 1, Expt II) as were obtained in the first experiment.

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