Tetrahedron Letters No. 40, pp 4143 - 4146, 1972. Pergamon Press. Printed in Great Britain.

OXIDATION OF CARBOHYDRATES WITH THE FERRATE(VI) ION

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(Received in USA 23 June 1972; received in UK for publication 5 September 1972)

Audette *et al.*[1] have reported on the use of potassium ferrate(VI) as a selective agent for the oxidation of primary alcohols and amines to aldehydes and secondary alcohols to ketones. BeMiller and Darling,[2] using potassium ferrate for the oxidation of carbohydrates, found greater specificity. In these compounds, only the primary hydroxymethyl group(s) were oxidized to an aldehyde group(s), for sodium borohydride reduction of the oxidation product yielded only the starting material. They found no evidence for the presence of diastereoisomers that would have resulted from the oxidation and subsequent reduction of secondary hydroxyl groups. More details of this work are given here.

Potassium ferrate was prepared as described by Wood,[3] substituting a 2-propanol wash for the ethanol wash so as not to reduce the activity of the preparation through oxidation of ethanol. Normally, potassium ferrate preparations retained enough base to give sufficient alkalinity to the reaction solution for stability of the ferrate. To insure stability, all oxidations were effected in 0.1M sodium carbonate or sodium phosphate.[4] Presumably, oxidation of methyl α-D-hexopyranosides with potassium ferrate formed methyl α-D-hexodialdo-1,5-pyranosides which were not isolated. Their further oxidation or reduction proved the identity of the product.

Methyl α-D-galactopyranoside (1.0 g) was dissolved in 50 ml of 0.1M sodium carbonate solution at 50°. Potassium ferrate (3-5.0 g) was added to this solution in small portions. The amount of potassium ferrate used depended upon the activity (purity)[4] of the preparation. After reaction was complete as determined by paper chromatography in 6:4:3 v/v 1-butanol-pyridine-water and spraying with silver nitrate and sodium hydroxide, the solution was centrifuged; and the filtrate was neutralized by treatment with Amberlite IR-120(H^+) cation-exchange resin and evaporated under diminished pressure at low temperature (∿40°). The product was separated from remaining ferric hydroxide by extraction with methanol or ethanol. It had a strong absorbance at 209 nm, indicating the presence of an aldehyde group, but was contaminated with some unreacted starting compound. The oxidation product could be reduced to the starting material with sodium borohydride in aqueous solution at room temperature.[5]

The preparation, presumably containing mainly methyl α-D-*galacto*-hexodialdo-1,5-pyranoside, was oxidized with sodium hypoiodite[6] or sodium chlorite[7] to sodium methyl α-D-galactopyranosiduronate and then passed through a column of Amberlite IR-120(H^+) cation-exchange resin. The pH of the eluate was adjusted to 7.5-8.0 with barium hydroxide solution, concentrated to about 100 ml and filtered; 2-3 volumes of ethanol were added to precipitate barium methyl α-D-galactopyranosiduronate which was washed well with 75% ethanol. It was then redissolved in hot water, and the precipitation and washing were repeated. It did not melt at temperatures up to 220-225° but turned light brown about 200°; $[\alpha]_D^{30}$ +93° (*c* 0.3, water); lit.[8] $[\alpha]_D$ +99° (*c* 1.03, water), stable as high as 215°, turning light brown at about 200°. Finally, the precipitate was dissolved in hot water, and the solution was treated with Amberlite IR-120(H^+) cation-exchange resin or sulfuric acid to remove barium ions. Removal of the solvent gave a colorless syrup which crystallized after cooling; yield 0.4 g (40%) of methyl α-D-galactopyranosiduronic acid, $[\alpha]_D^{30}$ +140° (*c* 2.0, water), mp 105-106°; lit.[9] $[\alpha]_D^{25}$ +128° (*c* 2.0, water), mp 107-108°.

Methyl α-D-mannopyranoside was oxidized to methyl α-D-mannopyranosiduronic acid using the above procedure; $[\alpha]_D^{30}$ +50° (*c* 0.14, water), mp 120-123°; lit.[10] $[\alpha]_D$ +57° (*c* 1.4, water), mp 114-115°.

Methyl α-D-glucopyranoside was also oxidized using the same procedure. The resulting pale yellow syrup contained two components separated by preparative thin-layer chromatography on Silica Gel H with 7:2:1 v/v ethyl acetate-acetic acid-methanol. The slower moving compound, believed to be methyl α-D-glucopyranosiduronic acid, had $[\alpha]_D^{30}$ +75° (*c* 0.16, water). Preparation of the calcium salt ($[\alpha]_D^{25}$ +24°), followed by conversion to the free acid with Amberlite IR-120(H^+) ($[\alpha]_D^{25}$ +39°), evaporation, drying and redissolution, gave products with $[\alpha]_D^{25}$ +16-+26°. The faster moving component was assumed to be a lactone(s).

Barker *et al.*[10] prepared the sodium salt of methyl α-D-glucopyranosiduronic acid. Easty[11] made the barium salt. Neither reported any physical constants. Timell *et al.*[16] reported the acid to be a syrup that was probably a mixture of the free acid and lactones; $[\alpha]_D$ +129° (*c* 1.0, water).

In most ferrate oxidations, the main product, after long reaction times, was a compound that could not be reduced with sodium borohydride nor oxidized with sodium hypoiodite, was not an acid, and from which no 2,4-dinitrophenylhydrazone could be formed. These coumpounds had lower R_f values and are, perhaps, 3,6-hemiacetals or, more likely, a dimer or higher polymerization product. That they arise from ketones has not been ruled out.

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