

The Chlorine Oxidation of Glycosides

II.* Oxidation of Methyl Glycosides of Galactose, Mannose and Xylose

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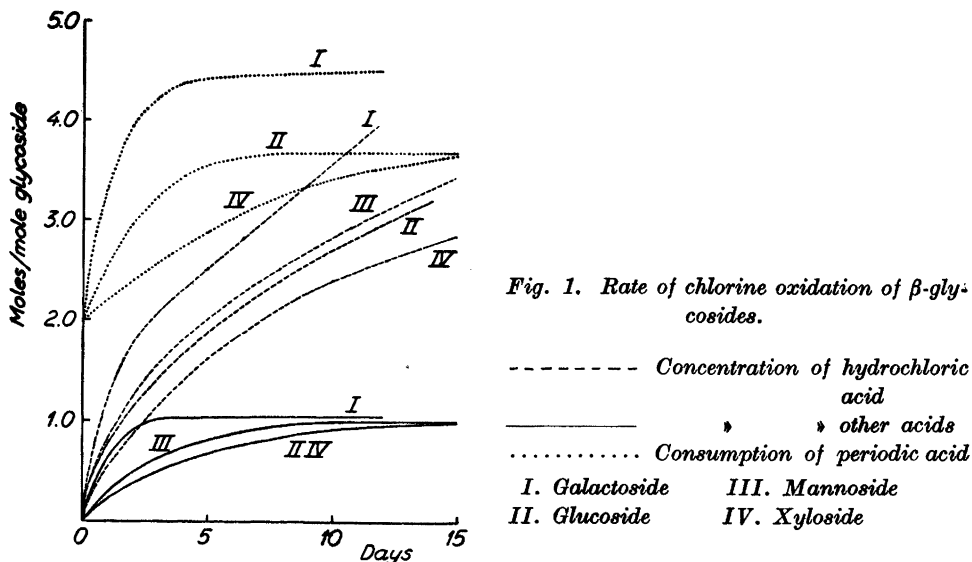
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This paper describes the continuation of work aimed at elucidating the mechanism of the oxidative degradation of cellulose by chlorine, a problem which is of considerable interest to the wood pulp and cellulose industry. Part I dealt with an investigation of the action of chlorine water on a simple model substance for cellulose, methyl β -glucoside; it was shown that this leads to the formation of D-gluconic acid, which in turn is further oxidised to 5-keto-gluconic acid. It was also shown that methyl α -glucoside undergoes a similar reaction, but at a very much slower rate than the β -isomeride.

This work has now been extended to include glycosides of two other hexoses, namely galactose and mannose, and of a pentose, namely xylose. The latter is of interest owing to the presence of xylans in the hemicellulose constituents of wood. Both the α - and β -isomerides of each glycoside have been studied. The oxidations were carried out by treating an approximately 0.5 *M* aqueous solution of the glycoside with a slow stream of chlorine gas at room temperature in the absence of light. The reactions were followed by measurement of the optical rotation, estimation of the hydrochloric acid and other acids formed, and determination of the consumption of periodic acid by the solution. At suitable time intervals portions of the reaction mixture were withdrawn for qualitative examination. This involved first analysis of the solution on the paper chromatogram by the standard methods, using in general ammoniacal silver nitrate or alkaline potassium permanganate to detect aldonic acids and their

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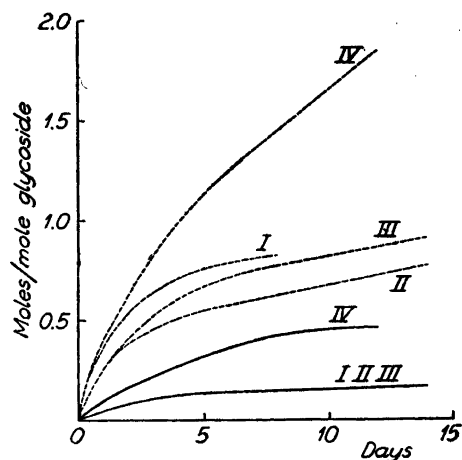
lactones, and resorcinol in alcoholic hydrogen chloride for keto-acids. This analysis was followed whenever possible by isolation of the reaction products so indicated in the form of suitable derivatives.

Methyl β -galactoside was found to be oxidised by chlorine in a similar manner to the corresponding glucoside, but at a considerably greater rate than the latter (see Fig. 1). After the reaction had proceeded for only 3 days the amount of acids formed other than hydrochloric acid reached a value of 1 mole per mole of galactoside, and thereafter increased only very slightly. The amount of hydrochloric acid present in the solution at this stage was about 2 moles per mole, and the periodic acid consumption approximately 4 moles per mole of galactoside. These facts all indicated the formation of a monobasic organic acid, and by analogy with the results of the oxidation of methyl β -glucoside this was expected to be D-galactonic acid. Chromatographic analysis of the reaction mixture did in fact show the presence of galactonic acid and its lactone, and confirmation of this was obtained by isolation of the acid as the phenylhydrazide. After the chlorine oxidation had proceeded for 8 days, a white precipitate began to form in the solution and steadily increased in amount as the reaction was prolonged further. This substance was identified as the dicarboxylic acid mucic acid. The fact that titration still showed the solution to contain not appreciably more than 1 equivalent of other acids even at this stage can be ascribed to the low solubility of mucic acid, which was probably further diminished by the presence of hydrochloric

Fig. 2. Rate of chlorine oxidation of α -glycosides.

----- Concentration of hydrochloric acid
 _____ » » other acids

I. Galactoside	III. Mannoside
II. Glucoside	IV. Xyloside



acid. It is of interest to note that the isomeric acid, saccharic acid, could not be detected as a product of the oxidation of methyl β -glucoside. No evidence of the formation of keto-acids on prolonged oxidation of methyl β -galactoside could be obtained.

An experiment was carried out to determine the stability of methyl β -galactoside to acid hydrolysis; after treatment with 2 *N* hydrochloric acid at room temperature for 21 days a 66% recovery of the unchanged galactoside was obtained.

The action of chlorine water on methyl α -galactoside was found to be extremely slow, the reaction curves being closely similar to those for methyl α -glucoside (see Fig. 2). After treatment for 12 days, only 0.16 equivalent of other acids was formed and it was possible to recover the unchanged galactoside in 88% yield.

Methyl β -mannoside showed a closely similar behaviour to the corresponding glucoside when treated with chlorine, the reaction rates for the two compounds differing only very slightly (Fig. 1). The results of the determination of periodic acid consumption in this case were extremely erratic, however, and of no interpretative value; no explanation of this fact is apparent. Chromatographic analysis of the reaction mixture after a period of 10 days showed the presence of mannonic acid and its lactone, which was confirmed by preparation of the phenylhydrazide. No evidence of keto-acids was obtained at this stage, but after the oxidation had continued for a total of 29 days the solution gave a faint positive reaction with the resorcinol reagent.

Methyl α -mannoside also behaved very similarly to the corresponding glucoside; after treatment with chlorine water for 14 days only 0.16 equivalent

of other acids was formed (Fig. 2) and it was possible to recover 72 % of the starting material unchanged.

Rather unexpectedly, the oxidation of methyl β -xyloside closely paralleled that of the β -glucoside (Fig. 1). After the reaction had proceeded for 10 days, chromatographic analysis of the solution indicated the presence of xylonic acid and its lactone. Isolation of the acid as the phenylhydrazide was not satisfactory owing to the difficulty of purifying the derivative, but good results were obtained by preparation of the benzimidazole according to the method of Moore and Link¹. Only a small amount of keto-acids was detected in the reaction mixture, and this did not increase appreciably when the oxidation was prolonged for a total of 20 days.

With methyl α -xyloside, a profound difference was observed from the other α -glycosides investigated, since it reacted with chlorine water at an appreciable rate roughly intermediate between that for the other α -forms and that for the β -xyloside (Fig. 2). After a reaction time of 12 days, chromatography of the solution showed the presence of small amounts of xylonic acid and its lactone and also of keto-compounds. No reaction products were isolated in this case.

To summarise the results of these experiments and those of the preceding paper, it is clear that the oxidation of methyl glycosides by chlorine to form the corresponding aldonic acids may be regarded as a general reaction for the series. It may furthermore be said that in each pair of anomeric glycosides one form, in the examples studied the β -form, reacts comparatively rapidly while the other is only slowly oxidised. The corresponding anomeric forms of the free sugars show analogous differences in the rate at which they are oxidised by bromine². The reason for these differences is at present obscure. It may, however, be noted that under conditions where a reversible transformation between α - and β -glycosides can take place, *e.g.* in solution in methanolic hydrogen chloride, the equilibrium mixture always contains a predominating proportion of one of the anomerides and a comparatively small proportion of the other. In the case of the sugars concerned in this investigation it is the α -glycoside which predominates. It is highly probable that the same configurational relationships which determine this difference in stability also cause the α -glycoside to be more stable than the β -isomeride towards chlorine oxidation.

EXPERIMENTAL

General procedure

The detailed procedure adopted in the oxidation experiments was the same as that described in Part I. The chromatographic analyses were also carried out in the same manner as in the earlier investigations.

Action of chlorine on the β -glycosides

Methyl β -galactoside. A 0.5 M solution of the galactoside was treated with chlorine for 3 days; a portion (10 ml) was then withdrawn, neutralised with silver carbonate, filtered, the filtrate saturated with H_2S , filtered again and the solution aerated until free of H_2S . A spot of this solution on filter paper reduced the alkaline $KMnO_4$ reagent but did not react with the resorcinol reagent. A paper chromatogram of the solution (suitably diluted) together with a reference solution of authentic galactonic acid, showed two pairs of spots with identical R_F values after development with alkaline $KMnO_4$, one pair corresponding to the free acid and the other (lower) pair to a lactone.

Galactonic acid was isolated as the phenylhydrazide as follows. The neutral reaction solution was heated with phenylhydrazine (1 ml) and glacial acetic acid (1.5 ml) on the boiling water-bath for 1 hour. After cooling, the crystalline phenylhydrazide was collected, washed with water and ether, and recrystallised from hot water. It had m.p. 194.5–195° * (decomp.), undepressed on admixture with authentic material. Yield, 0.14 g.

After the oxidation had proceeded for about 8 days a white precipitate began to separate from the solution, and when a further 4 days had elapsed this was collected and washed with alcohol. Yield, 0.11 g. After recrystallisation from hot water it had m.p. 212° (decomp.), undepressed on admixture with an authentic specimen of mucic acid.

Methyl β -mannoside. The starting material was prepared as a syrup by Zemplén deacetylation of the tetraacetate, and the exact concentration of the prepared aqueous solution determined by measurement of its optical rotation. After the chlorine oxidation had proceeded for 11 days, the solution contained approximately 3 equivalents of hydrochloric acid and 1 equivalent of other acids. A portion of the mixture was withdrawn at this stage, freed from hydrochloric acid in the usual way and analysed chromatographically. Mannonic acid was isolated from the neutral solution (10 ml) as the phenylhydrazide by the usual method; the crude derivative (0.45 g) was recrystallised from water, after which it had m.p. 212°, undepressed on admixture with authentic material.

Methyl β -xyloside. After oxidation of a 0.5 M solution of methyl β -xyloside for 9 days a small portion was removed, freed from hydrochloric acid and analysed on the chromatogram. The reaction was then allowed to proceed for a total of 20 days; the solution then contained 3.3 equivalents of hydrochloric acid, 1 equivalent of other acids, and the periodate consumption was 3.7 moles per mole of xyloside. From a portion (10 ml) of this solution xylonic acid was isolated as the benzimidazole derivative (0.06 g) by the method of Moore and Link¹; the product had m.p. 225–226°, undepressed on admixture with an authentic specimen.

Action of chlorine on the α -glycosides

Methyl α -galactoside. After treatment with chlorine for 12 days, the observed optical rotation of a 0.5 M solution of methyl α -galactoside changed only from + 17.4° to + 16.5°. The solution (18.4 ml) was then aerated until free from chlorine and treated with Amberlite IR-4B ion exchange resin until neutral. Evaporation of the solution under reduced pressure gave a crystalline residue of unchanged starting material; yield, 1.57 g (88 % recovery). The substance contained a small amount of impurities which depressed the

* All melting-points uncorrected.

melting-point considerably and could not be removed by repeated recrystallisations. Acetylation of the product with acetic anhydride — pyridine, however, gave after one recrystallisation from alcohol pure tetraacetyl methyl α -galactoside, m.p. 85.5–87°.

Methyl α -mannoside. Treatment of a 0.5 *M* solution of methyl α -mannoside with chlorine for 14 days caused the optical rotation to change only from + 15.39° to + 14.91°. The solution (50 ml) was aerated and then freed from acids present by treatment with Amberlite IR-4B resin; evaporation under reduced pressure yielded a crystalline residue (4.4 g) which was recrystallised from alcohol. Unchanged methyl α -mannoside, m.p. 190–192°, was obtained; yield, 3.5 g (72 % recovery).

Methyl α -xyloside. The free glycoside was prepared by deacetylation of the triacetate, and the concentration of an aqueous solution of the product determined by measurement of the optical rotation. After oxidation for 12 days the solution was analysed chromatographically. No reaction products were isolated.

Action of hydrochloric acid on methyl β -galactoside

A 0.5 *M* solution of methyl β -galactoside in 2 *N* hydrochloric acid was kept at room temperature and the optical rotation periodically determined. After 21 days the α_D value, originally + 0.06°, had changed only to + 0.64°. The solution (7.5 ml) was neutralised with silver carbonate, filtered and evaporated to dryness under reduced pressure. The crystalline residue was recrystallised from alcohol, giving unchanged starting material, m.p. 174–176°; yield, 0.48 g (66 % recovery).

SUMMARY

The investigation of the action of chlorine water on the methyl glucosides has been extended to include the galactosides, mannosides and xylosides. A general reaction appears to exist whereby one of the anomeric forms of each glycoside, in the examples studied the β -form, is comparatively readily oxidised to the corresponding aldonic acid, while the other undergoes a similar oxidation at a very much slower rate.

REFERENCES

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