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Note

Formation of dicarboxylic acids from 4-*O*-methyl-D-glucuronic acid in alkaline solution in the presence and absence of oxygen

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4-O-Methyl-D-glucuronic acid is the major uronic acid constituent in xylan. During oxygen–alkali bleaching of wood pulp, some of the acid residues are split off[1] and decomposed. The reactions of 4-*O*-methylglucuronic acid in alkaline medium are therefore of interest, not only in general carbohydrate chemistry but also in pulping research.

The results of various treatments of 4-*O*-methyl-D-glucuronic acid with alkali are summarized in Table I together with g.l.c. data. The products included in Table I constituted ~90% of the compounds amenable to g.l.c. as trimethylsilyl (Me_3Si) derivatives. The starting material was completely consumed in all experiments.

As postulated by Whistler and Richards[2], the two diastereomeric 3-deoxy-2-*C*-(hydroxymethyl)pentaric acids were the preponderant products after treatment in lime water with exclusion of oxygen. These acids have previously been prepared[3] by treatment of alginates with alkali in the absence of oxygen. By analogy with the well-known formation of 3-deoxy-2-*C*-(hydroxymethyl)pentonic acids from 4-*O*-substituted hexoses, including reducing D-glucose end-groups in cellulose, it can be concluded that the acids are formed *via* intermediate **1** (Fig. 1). The first reaction-step, isomerization of 4-*O*-methyl-D-glucuronic acid to the corresponding hexulosonic acid, occurs easily in alkaline solution[4]. G.l.c.–m.s. data suggested that analogues of other C_6-saccharinic acids were formed in small proportions. The low proportion of deoxytetraric (malic) acid indicates that cleavage of the postulated intermediate is slow compared to the rate of benzilic acid rearrangement in virtually oxygen-free solution. Small proportions of 3-deoxy-*threo*-pentaric acid were produced.

In lime water in the presence of air, the formation of 3-deoxy-2-*C*-(hydroxymethyl)pentaric acids was much smaller, and in sodium hydroxide under oxygen pressure, these acids were minor products. The increased proportion of deoxytetraric acid indicates that the oxidative cleavage of the postulated dicarbonyl intermediate **1** is important. Much larger proportions of 3-deoxy-*threo*-pentaric acid were obtained in the presence of oxygen. G.l.c. indicated the presence of traces of the *erythro* isomer. The formation of deoxyaldonic acids corresponding to deoxytetraric and

TABLE I

RELATIVE AMOUNTS (MOLE %) AND RETENTION IN G.L.C. OF DICARBOXYLIC ACIDS ISOLATED AFTER VARIOUS TREATMENTS OF 4-*O*-METHYL-D-GLUCURONIC ACID

	Ca(OH)₂ *23°*		*NaOH* *97°*	*Retention of Me_3Si derivatives*[a]		
	Air excluded	*Air present*	O_2 *(0.5 MPa)*	*OV-1* *160°*	*OV-17* *160°*	*QF-1* *120°*
3-Deoxy-2-*C*-hydroxymethyl-*erythro*-pentaric	45	16	3	0.82	1.33	1.92
3-Deoxy-2-*C*-hydroxymethyl-*threo*-pentaric	48	19	4	0.73	1.19	1.49
3-Deoxy-*threo*-pentaric	2	4	11	0.31	0.60	0.79
Deoxytetraric (malic)	3	6	20	0.10	0.21	0.29
4-*O*-Methylglucaric	1	24	4	0.91	1.61	1.74
4-*O*-Methylmannaric	1	5	6	0.66	1.03	0.97
3-*O*-Methylarabinaric	0	7	19	0.35	0.75	0.86
O-Methylerythraric	0	18	27	0.13	0.30	0.37
O-Methylthrearic	0	1	6	0.14	0.36	0.49

[a]Relative to the D-glucitol derivative.

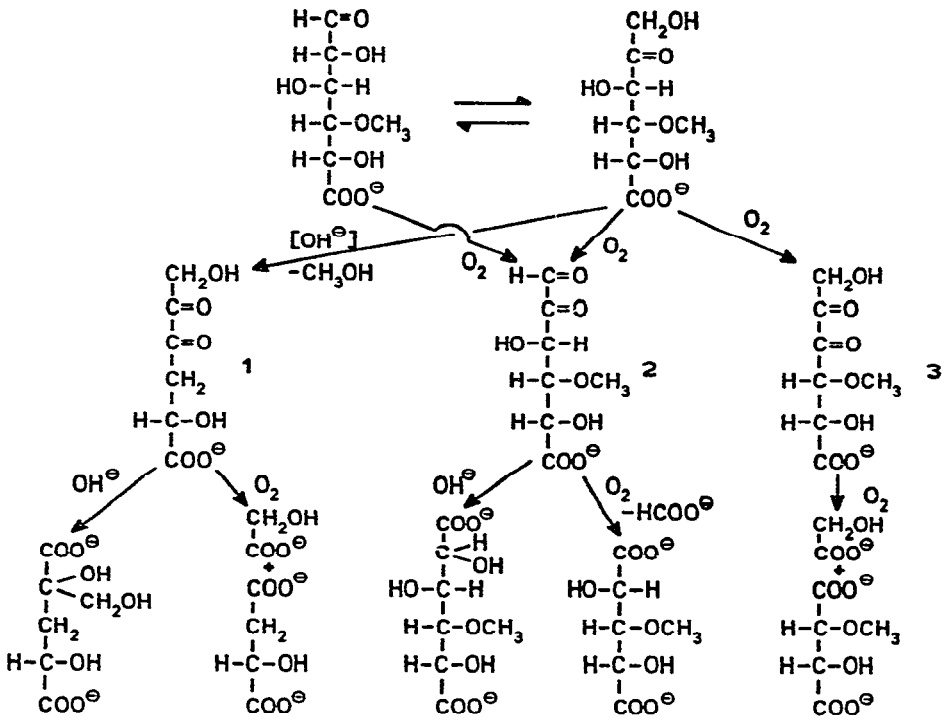

Fig. 1. Schematic representation of the main degradation routes of 4-*O*-methyl-D-glucuronic acid during oxygen–alkali treatment.

3-deoxypentaric acids has been observed after oxygen–alkali treatment of cellulose[5].

In the presence of oxygen, another plausible reaction-pathway parallelling the reactions of cellulose is oxidation to intermediate **2** (Fig. 1) followed by a benzilic acid rearrangement to 4-*O*-methylhexaric acids. For the sake of clarity, these acids are termed 4-*O*-methylhexaric rather than 3-*O*-methylhexaric. Large proportions of 4-*O*-methyl-D-glucaric and moderate proportions of 4-*O*-methyl-D-mannaric acids were obtained in lime water when air was present. After oxygen–sodium hydroxide treatment, the proportion of 4-*O*-methyl-D-glucaric acid was much lower. The reactions correspond to the formation of D-gluconic and D-mannonic acid end-groups in cellulose after oxygen–alkali treatment. The increased proportion of 3-*O*-methylpentaric acid indicates that these conditions favour cleavage of intermediate **2**. This reaction pathway corresponds to the formation of D-arabinonic acid end-groups in cellulose, and the acid identified as a 3-*O*-methylpentaric acid by m.s. was assumed, by analogy, to be 3-*O*-methyl-D-arabinaric acid.

The two diastereomeric *O*-methyltetraric acids were formed in the presence of oxygen. Oxidative cleavage of the dicarbonyl intermediate **3** offers an explanation for their formation. The analogous reaction of cellulose is the formation of tetronic acid end-groups. The reaction pathway *via* intermediate **3** is consistent with the formation

of glycolic acid, which constituted 70% of the monocarboxylic acid fraction from the oxygen–sodium hydroxide treatment. Minor proportions of 2-hydroxypropanoic, 2-deoxytetronic, and glyceric acids were also recorded. In addition, g.l.c. indicated the formation of small proportions of oxalic and tartronic acids by other fragmentation reactions.

The results given above show that the reactions of 4-*O*-methyl-D-glucuronic acid in alkaline solution are very similar to those of the reducing D-glucose residue in cellulose[5]. The unsubstituted acids formed correspond to soluble acids produced by an endwise attack, whereas the *O*-methylated acids correspond to carboxylic acid end-groups formed in the presence of oxygen. By analogy, 4-*O*-methylglucuronic acid can be regarded as a model for (1→4)-linked hexuronic acids in polysaccharides, with respect to degradation from the reducing end. A test was made with a pectic substance expected to contain mainly (1→4)-linked galacturonic acid residues. The sample (1 g) was treated with M sodium hydroxide (50 ml) at 95° for 4 h without special precautions to exclude air. The *threo* (18% yield) and *erythro* (7%) forms of 3-deoxy-2-*C*-(hydroxymethyl)pentaric acid and deoxytetraric acid (5%) were obtained, in good agreement with the results for 4-*O*-methyl-D-glucuronic acid [*cf.* Ref. 3].

EXPERIMENTAL

Lime-water treatment. — In an experiment designed to exclude air, 105 mg of calcium hydroxide were suspended in 15 ml of water, and the suspension was boiled for 5 min and then covered with a layer of paraffin oil. A solution of 70 mg of 4-*O*-methyl-D-glucuronic acid in 3.5 ml of boiled water was injected into the cooled suspension, and the flask was kept at 23° for 13 days. A parallel experiment was made without any precautions to exclude air. At the end of these treatments, calcium was removed by stirring with a cation exchanger (Dowex, 50-x8, H^+). After filtration, neutralization with sodium hydroxide, and evaporation, the acids were converted into Me_3Si derivatives, and analysed by g.l.c. and g.l.c.–m.s.[6]. The quantitative determinations were based on the assumption that the g.l.c. peak-areas were proportional to the weights of the derivatives.

Hot oxygen–sodium hydroxide treatment. — An aqueous solution (10 ml) of 70 mg of 4-*O*-methyl-D-glucuronic acid was injected into a Teflon reactor[7] which contained 89 g of preheated 0.13M sodium hydroxide. The solution was kept at 97° for 10 min at an oxygen pressure of 0.5 MPa and was then cooled, brought to pH 10 by the addition of a cation-exchange resin (H^+), and passed through a filter and through an anion-exchange column (Dowex, 1-x8, acetate form). After rinsing with water, monocarboxylic (12 mg) and dicarboxylic (47 mg) acid fractions were eluted with 2M acetic acid and 0.3M magnesium acetate, respectively[5], and the acids were analysed.

Identifications. — The g.l.c.–m.s. identification of the acids lacking *O*-methyl groups (*cf.* Table I) was made as described previously[8]. To determine the configuration, one of the 3-deoxy-2-*C*-(hydroxymethyl)pentaric acids was isolated by anion-

exchange chromatography (Dowex, 1-x8), using 0.3M sodium acetate in 2M acetic acid (30°) as eluent[5]. The volume distribution coefficient (D_v) was 9.5, and that of the isomer 7.7. A sample of the acid was dissolved in 3M hydrochloric acid, the solution was evaporated, and the resulting ester–lactone mixture was reduced with potassium borohydride. The products were analysed by g.l.c.–m.s. as acyclic Me_3Si derivatives. 3-Deoxy-2-*C*-hydroxymethyl-*threo*-pentonic acid was obtained in ~30% yield. The g.l.c.–m.s. data for the two other major products, obtained in similar yields, were fully compatible with the anticipated species, 3-deoxy-4-*C*-(hydroxymethyl)pentonic acid and 3-deoxy-2-*C*-(hydroxymethyl)pentitol. The results show that the isolated acid was the *threo* isomer and establish the configuration of the two 3-deoxy-2-*C*-(hydroxymethyl)pentaric acids.

The structures (except for configuration) of the *O*-methylated acids (Table I) were deduced from the mass spectra of their Me_3Si derivatives. The structural assignments were based on the fragmentation analogies between Me and Me_3Si derivatives, and on the known fragmentation characteristics of Me_3Si derivatives of aldaric acids[8]. The configurations of the *O*-methyltetraric acids were deduced from the g.l.c. retention-times. By analogy with the tetraric acids, the *threo* form should have the longer retention time. Authentic samples of 4-*O*-methyl-D-glucaric and 4-*O*-methyl-D-mannaric acids were prepared by hypoiodite oxidation[9] of the corresponding uronic acids. The products were isolated according to Schaffer and Isbell[10]. Species having the same g.l.c.–m.s. behaviour as the two acids from alkaline treatments were obtained. The oxidation of 4-*O*-methyl-D-glucuronic acid was quantitative, whereas the yield from 4-*O*-methyl-D-mannuronic acid was only 50%. This is in agreement with the observation that mannose is oxidized more slowly than glucose[9].

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