Formation of 1,4-Anhydro-3-deoxypentitol-2-carboxylic Acids by Alkaline Degradation of Cellulose

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An anhydrosaccharinic acid obtained in large amounts by end-wise degradation of cellulose in alkaline media and in small amounts in hydrolysates of cellulose has been identified as a 1,4-anhydro-3-deoxypentitol-2-carboxylic acid (3-hydroxy-5-(hydroxymethyl)oxolane-3-carboxylic acid). Structural evidence was obtained by GC-MS studies of the compounds (as Me_3Si derivatives) obtained on degradation of the acid to 1,4-anhydro-3-deoxypentitol by reduction of the methyl ester followed by periodate oxidation and borohydride reduction.

In aqueous alkali, the acid is likely to be formed from a dicarbonyl precursor by benzilic acid rearrangement.

In aqueous alkali, cellulose is degraded from the reducing end. A main reaction pathway is isomerization of the glucose end-groups followed by β-alkoxyelimination and the formation of a new glucose end-group. The dicarbonyl intermediate formed is converted to the two diastereomeric 3-deoxy-2-C-(hydroxymethyl)-pentonic (isosaccharinic) acids by a benzilic acid rearrangement. Several carboxylic acids formed in competing fragmentation reactions have been isolated. Under certain working conditions [1] the third most abundant acid (on weight basis) in the solution is an anhydro acid, previously denoted anhydroisosaccharinic acid. In the present paper this acid is shown to be a 1,4-anhydro-3-deoxypentitol-2-carboxylic acid. The acid is formed in appreciable amounts also during alkali treatment in the presence of oxygen [2] or polysulfide.[3] Trace amounts of the diastereomer were isolated by anion exchange chromatography from the solution obtained on oxygen-alkali treatment of cellulose.[2]

Interestingly, the major diastereomer was

isolated from hydrolysates obtained by acid hydrolysis of cellulose with hydrochloric acid. Model experiments with glucose under conditions simulating those used to determine carboxylic acid groups in cellulose showed that a small amount of the acid was formed from glucose.[4] The procedure used included treatment at pH 8 at room temperature to hydrolyze ester linkages. Experiments carried out more recently in which the hydrolysate was separated directly on the acetate form of an anion exchange resin showed that the anhydro acid was formed. The amount obtained from cellulose decreased on lowering the temperature and acid concentration during hydrolysis with hydrochloric acid and was negligible after mild hydrolysis with trifluoroacetic acid.

STRUCTURE DETERMINATION

In the previous study,[1] the composition of the anhydro acid was shown to be $C_5H_7O(OH)_2COOH$. Periodate oxidation showed that no vicinal hydroxyl groups were present. Reduction of the carboxylic acid group resulted in a polyalcohol which on oxidation with periodate gave rise to formaldehyde. This demonstrates that one of the hydroxyl groups was present in the α-position. Ring opening gave rise to the two diastereomeric 3-deoxy-2-C-(hydroxymethyl)pentonic acids.

From these observations, it is concluded that the acid has the furanoid structure 1 (Fig. 1) or the corresponding pyranoid structure. To confirm this conclusion and to distinguish between the two ring forms, the acid was converted
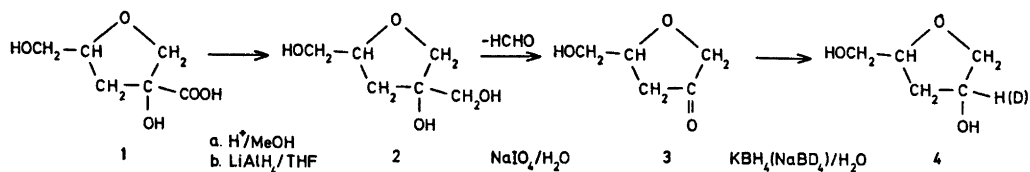
Fig. 1. Reactions of 1,4-anhydro-3-deoxypentitol-2-carboxylic acids for structure determination.

to its methyl ester and reduced with lithium aluminium hydride. The polyalcohol 2 was oxidized with periodate and the resulting ketose 3 reduced with borohydride to obtain the alcohol(s) 4. A reaction scheme valid for the furanoid form is given in Fig. 1. All species were analysed by GC-MS after preparation of the trimethylsilyl (Me$_3$Si) derivatives under conditions previously used.[5] The GC results indicated almost quantitative yield in each of the reaction steps. The mass spectra of 1 and 2 (Fig. 2) are in full agreement with the structural features mentioned above but could not be used to unequivocally distinguish between the furanoid and the pyranoid structures. In contrast to the pyranoid derivative of 4, the furanoid derivative can be predicted to give an abundant m/e 159 ion by loss (α-cleavage) of the
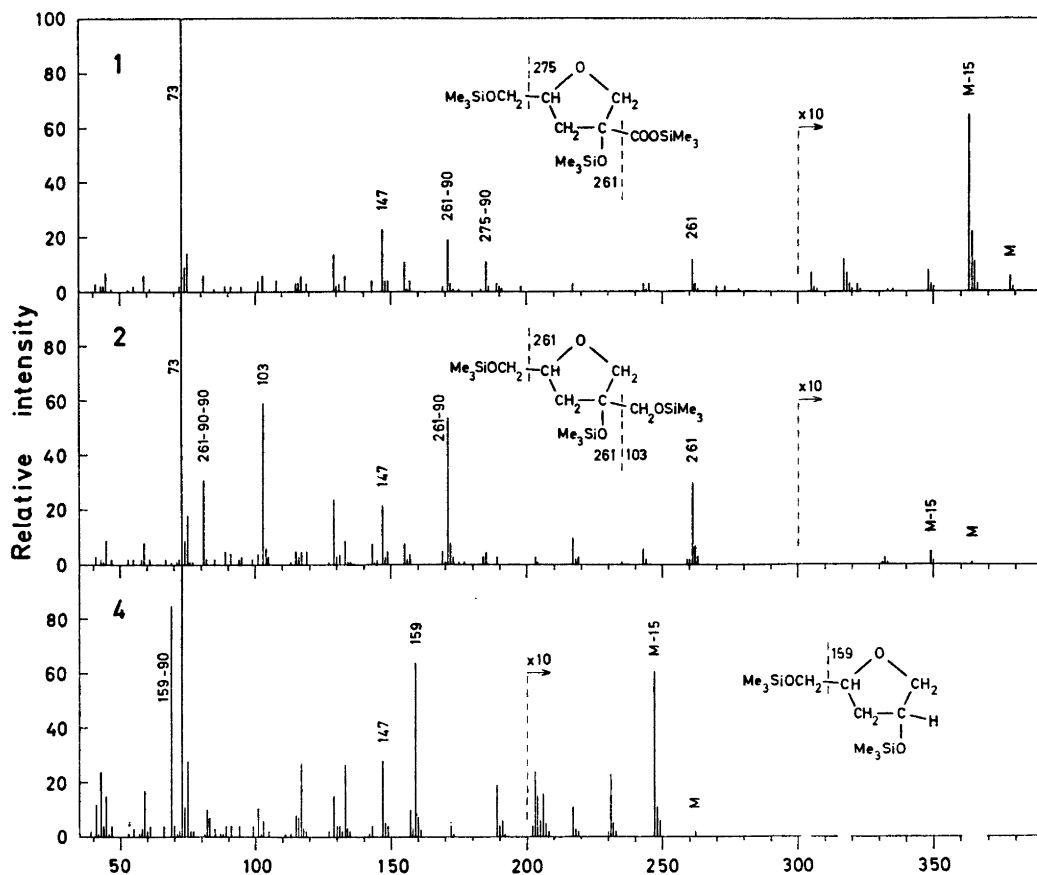
Fig. 2. Mass spectra at 70 eV of the Me$_3$Si derivatives of 1,4-anhydro-3-deoxypentitol-2-carboxylic acid (1), 1,4-anhydro-3-deoxy-2-C-(hydroxymethyl)pentitol (2) and 1,4-anhydro-3-deoxypentitol (4).

CH$_2$OSiMe$_3$ branch. Charge delocalization over the ring oxygen should promote such fragmentation. A corresponding prominent peak present in the spectrum (Fig. 2) demonstrates a furanoid structure. This structure was confirmed by an almost complete shift to m/e 160 when the last reduction step was made with borodeuteride. For the pyranoid derivative, an m/e 159 ion might be formed by a rearrangement involving the loss of a CH$_2$OSiMe$_3$ group, although this fragmentation reaction appears unlikely. The pyranoid derivative would, however, contain two symmetrically located CHOSiMe$_3$ groups, and in the deuterated derivative only one of these would contain deuterium. Hence, approximately 50 % of the m/e 159 ions would not be shifted to m/e 160 for the deuterated form. A spectrum of the pyranoid derivative would also be expected to differ from the observed spectrum in several other respects. The main fragmentation features are indicated in Fig. 2 and include the formation of the M $-$ 15, m/e 73 and m/e 147 ions which are characteristic of Me$_3$Si derivatives. The remaining ions, marked by their mass, are the specific α-cleavage ions and the ions produced by further elimination of Me$_3$SiOH (90 mass units). The mass spectra of the Me$_3$Si derivatives of 3 and the syn and $anti$ isomers of its oxime were also recorded and were compatible with the anticipated structures.

The configuration at the two chiral carbon atoms were not determined. Lactone formation might be possible for the diastereomer with the carboxyl and the primary hydroxyl groups on the same side of the ring. Efforts to prepare a lactone by evaporation with 1 M acetic acid or 6 N hydrochloric acid at 50 °C failed and resulted in the production of intermolecular esters. Previous indications for the formation of a lactone [1] should, therefore, be disregarded.

DISCUSSION

Anhydroisosaccharinic acid, now denoted 1,4-anhydro-3-deoxypentitol-2-carboxylic acid, is obtained in high yield from hydrocellulose at a temperature so low that attack along the cellulose chain is excluded. This demonstrates that the acid is formed by rearrangement and elimination of the terminal reducing glucose moiety. A new reducing glucose end-group is
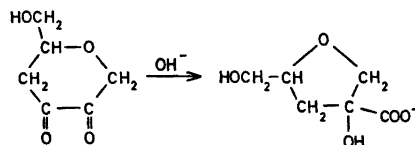
Fig. 3. Formation of 1,4-anhydro-3-deoxypentitol-2-carboxylic acids from 1,5-anhydro-4-deoxy-2,3-hexodiulose.

formed in this reaction. The observation that the anhydro acid like 3-deoxy-2-C-(hydroxymethyl)pentonic acids contains a methylene group at C-3 which in these species corresponds to C-4 in the reducing glucose moiety strongly suggests that the reaction which gives rise to the methylene group is a β-alkoxyelimination. Accordingly, the acid was formed also by alkali treatment of cellobiose but not from laminarin. Separate experiments have shown that no detectable amount of the anhydro acid was formed when the 3-deoxy-2-C-(hydroxymethyl)pentonic acids were heated in alkaline solution at 100 °C for several hours.

Since dicarbonyl compounds formed as intermediates after β-alkoxyelimination undergo benzilic acid rearrangement on treatment with alkali, it can be concluded that 1,5-anhydro-4-deoxy-2,3-hexodiulose is a precursor of the 1,4-anhydro-3-deoxypentitol-2-carboxylic acids (Fig. 3). Formation of these acids from cellobial by this route has been postulated by Corbett and Kidd.[6] Paper chromatographic evidence was presented for the formation of one of the acids. Benzilic acid rearrangements of other pyranoid dicarbonyl compounds have been demonstrated.[7] In the present case the predominance of one of the diastereomers demonstrates a high stereospecificity for the rearrangement.

EXPERIMENTAL

Degradation of 1,4-anhydro-3-deoxypentitol-2-carboxylic acid. Each of the reaction steps shown in Fig. 1 was first carried out on an analytical scale starting with approximately 10 mg of the substances. The products were studied by GC and the reaction conditions modified to maximize the yield. Subsequently, the compounds were prepared in the 100 mg range by scaling up the experiments.

The methyl ester was prepared by treating the acid (15 mg/ml) with methanolic hydrochloric acid (1.5 M) for 1 h at ambient temperature. The ester (10 mg/ml) was reduced in

tetrahydrofuran with 2 mg LiAlH$_4$/mg ester. The solvent was prepurified by passing it through a column of aluminium oxide. The hydride was added carefully and the reaction mixture kept at 40 °C overnight with ultrasonic treatment. Excess hydride was destroyed and cations removed by the addition of wet cation exchanger (H+) until the solution became clear. The product was isolated by transfer of the slurry to a column, rinsing with water and evaporation to dryness.

The periodate oxidation was achieved by mixing equal volumes of aqueous solutions of the polyalcohol and sodium periodate in a dark flask. The concentrations were chosen to give a two-fold molar excess and a 0.05 M final concentration of periodate. The reaction mixture was kept overnight at 30 °C. The solution was then passed through columns packed with an anion exchanger (Ac⁻) and a cation exchanger (H+). The product was isolated from the effluent by evaporation.

For the final reduction, aqueous solutions of KBH$_4$ or NaBD$_4$ (5 mg/ml) and of the product from the previous step (10 mg/ml) were prepared, cooled to 0 °C and mixed to give an approximately two-fold molar excess of the hydrides. The mixture was kept in a refrigerator overnight, after which a cation exchanger (H+) was added in excess of the amount needed for hydrogen formation to cease. The resin was washed with water and boric acid was removed by twice evaporating with methanol to give the pure 1,4-anhydro-3-deoxypentitol(s).

Gas chromatographic data. Relative retentions of the Me$_3$Si derivatives, directly comparable with previously published data for related compounds,[5] were determined with the derivative of glucitol as reference. The same equipment and instrumental settings as in the previous study were used. The relative retention of the 1,4-anhydro-3-deoxypentitol-2-carboxylic acid (*1*) was 0.206 on OV-1 (160 °C), 0.436 on OV-17 (160 °C), 0.456 on QF-1 (120 °C) and 0.530 on XE-60 (120 °C). The value for the methyl ester on QF-1 (120 °C) was 0.361. The corresponding data for the other compounds were 0.298 for the 1,4-anhydro-3-deoxy-2-*C*-(hydroxymethyl)pentitol (*2*), 0.099 for the 1,4-anhydro-3-deoxy-2-pentulose (*3*), 0.088 for the 1,4-anhydro-3-deoxypentitol(s) (*4*) and 0.101 and 0.117 for the two isomers of the 1,4-anhydro-3-deoxy-2-pentulose oxime.

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