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# Oxidation of Carbohydrate Derivatives with Silver Carbonate on Celite. VII. Aldopentoses

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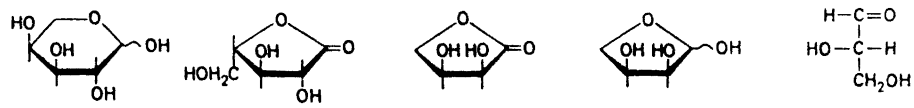
Aldopentoses are oxidized by silver carbonate on Celite in methanol to give formic esters of tetroses as major products. Pentonolactones are also formed primarily. Prolonged reaction time and higher temperatures cause extensive degradation beyond the tetrose stage, and tetronolactones as well as methyl esters of carboxylic acids with two and three carbon atoms are formed. The aldonolactones show greater resistance to the oxidant in methanol. Possible pathways for formation of most of the different products are suggested.

In a previous communication in this series the formation of tetroses as major products on oxidation of D-xylose and L-arabinose with silver carbonate on Celite in methanol and subsequent mild alkaline hydrolysis was described.[1] The yields of the tetroses were about 40 %, and spectroscopy and chromatography showed the presence also of other compounds. A more detailed investigation of the oxidation of aldopentoses with the oxidant has therefore been undertaken and is reported in the present paper.

## RESULTS AND DISCUSSIONS

As in the case of D-xylose and L-arabinose,[1] tetroses were formed initially from D-ribose and D-lyxose on oxidation in methanol and subsequent mild alkaline hydrolysis. Infrared spectra of the product mixtures after oxidation of the pentoses before hydrolysis showed a great band at 1725 $cm^{-1}$. This absorption is due to formic ester groups resulting from glycol cleavage of the aldopentoses in cyclic form between C-1 and C-2. In addition, substantial absorption was observed at 1770 – 1780 $cm^{-1}$, indicating the presence of $\gamma$-lactones. In order to isolate these compounds, the aldopentoses were subjected to prolonged oxidation which led to further degradation of the initially formed *O*-formyl tetroses; the lactones showed greater resistance to the oxidant. This facilitated their isolation by paper chromatography. From L-arabinose (I) were obtained in 20 % yield L-arabino-1,4-lactone (II) and small amounts of erythrono-1,4-lactone (III).



I II III IV V

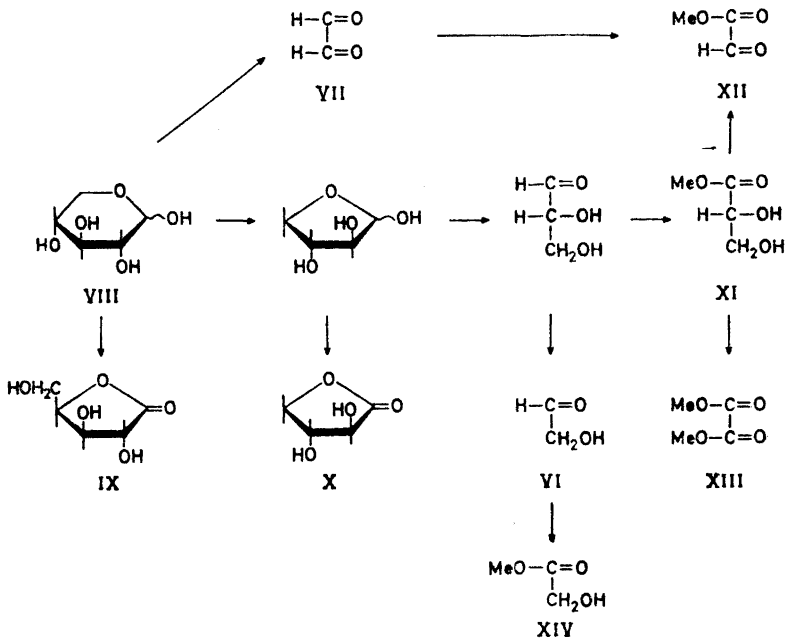
After prolonged oxidation of L-arabinose (I) at 40°C, hydrolysis and removal of acidic products, column chromatography on silica gel gave four fractions. One contained L-erythrose (IV), an other contained L-glyceraldehyde (V), both in low yields. The fastest moving fractions contained small amounts of products with chromatographic and electrophoretic behaviour corresponding to those of glycolaldehyde (VI) and glyoxal (VII), both were contaminated with at least one additional unidentified compound.

D-Ribose, D-xylose, and D-lyxose give analogous reaction mixtures on oxidation. Some of the products have been detected by chromatography and electrophoresis only (Table 1).

The observation that aldonolactones were formed and that lower carbon sugars gradually disappeared, made an examination of the nature of the final degradation products interesting. After oxidation for 1 h at 40 – 45°C of D-xylose (VIII) with an excess of oxidant, chromatography showed the presence of several compounds detectable with hydroxylamine-ferric chloride, in addition to xylono-1,4-lactone (IX) and threono-1,4-lactone (X). Methyl glycerate (XI), methyl glyoxylate (XII), and dimethyl oxalate (XIII) have been characterized as components of the reaction mixture, and a compound with chromatographic mobility as methyl glycolate (XIV), giving an acid indistinguishable from glycolic acid on hydrolysis, was also detected.

The presence of glyceraldehyde and products assumed to be glycolaldehyde and glyoxal in the reaction mixture after oxidation of the pentoses, suggested a possible relationship between these compounds and the methyl esters of the two- and three-carbon acids which have been found to be final products in these oxidations. An investigation of the possibility of such a relationship has been performed in this laboratory, and is to be published separately.[2] This investigation has shown that α-hydroxy aldehydes are rapidly oxidized to the methyl esters of the corresponding carboxylic acids, and that glyoxal gives methyl glyoxylate with the oxidant in methanol. Methyl glycerate has been found to give a mixture of methyl glyoxylate and dimethyl oxalate at 45 – 50°C. In accordance with these results, possible routes to most of the different oxidation products from D-xylose (VIII) are shown in Scheme 1. It is, however, necessary to take into consideration the fact that several of the intermediate products exist in *O*-formylated form during parts of the reaction time, and this may alter the ease with which the reactions occur, and even the type of reaction undergone.

The rates with which the pentoses are oxidized have been compared, it has been found that L-arabinose and D-ribose are oxidized more slowly than D-xylose and D-lyxose (Fig. 1). The yields of pentonolactones from the two first mentioned pentoses are about 20 %, whereas the yield from D-xylose is only about 10 %. This fact suggests that the differences in oxidation rate are due mainly to differences in the ease with which the pentoses are degraded.




*Scheme 1.*

The instability of the formic ester group under the reaction conditions and particularly under the conditions necessary for work up makes an isolation of the primary degradation products difficult, and it has been impossible to

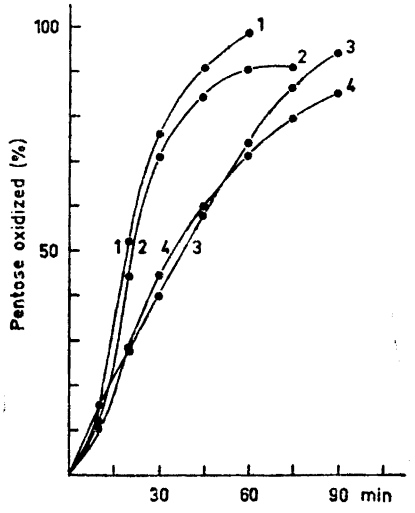



*Fig. 1.* Oxidation of aldopentoses at 30°C. Rates of disappearance of the pentoses: 1, D-xylose; 2, D-lyxose; 3, D-ribose; 4, L-arabinose.

establish in what form or forms the pentoses are degraded. Suggestions about the configurational factors to which the differences in degradation rate are to be ascribed are thus prevented.

It has previously been found that 2-*O*-methyl pentoses are stable to the oxidant in methanol at a temperature as high as 60°C.[3] The present work has shown that an unsubstituted hydroxyl group at C-2 of the aldopentoses greatly enhances the tendency to oxidation to aldonolactone; degradation is nevertheless the dominating reaction when the aldopentoses are treated with silver carbonate on Celite in methanol. It is in this connection of interest that galactono-1,4-lactone was the main product on oxidation of galactose in ethanol at 80°C, as reported recently by Fetizon and Moreau.[4]

## EXPERIMENTAL

Paper chromatography was performed on Whatman No. 1 and 3 MM papers in the following solvent systems (v/v): (A) Butanol – ethanol – water 40:11:19, (B) butanol – pyridine – water 5:3:2, and (C) butanone – acetone – formic acid – water 40:2:1:6. Thin layer chromatography (TLC) was run on Silica gel G in (D) benzene – ethanol 3:1, (E) benzene – ethanol 5:1, (F) benzene – ethanol 10:1, and (G) chloroform – methanol 50:1. Electrophoresis was performed on Whatman No. 1 paper in borate buffer, pH 10, $M_G$-values refer to the mobilities relative to glucose. As spray reagents were used diphenylamine – aniline – phosphoric acid,[5] aniline oxalate and aniline hydrogen phthalate for the sugars, hydroxyl amine – ferric chloride[6] for the esters and lactones, and sulphanilamide – β-naphthol – sodium nitrite [7] for the acids.

*Oxidation of aldopentoses. A. Identification of lower carbon sugars.* Pentose (500 mg) in methanol (100 ml) was stirred with silver carbonate on Celite [8] (12 g) at 40°C for 10 – 25 min. The solution was filtered, and sodium bicarbonate (0.5 g) in water (50 ml) was added. After 1 h, the solution was treated with Dowex 50W ($H^+$) and subsequently with Dowex 1 ($HCO_3^-$) ion exchangers, and the solvents were removed. The composition of the residue was examined by paper chromatography (solvent B), TLC (solvent D), and electrophoresis. Treatment of the residue with acetone sulphuric acid and isolation of the resulting *O*-isopropylidene tetrose was performed as described previously;[1] the results are shown in Table 1.

*B. Identification of aldonolactones.* Pentose (500 mg) in methanol (100 ml) was treated with silver carbonate on Celite (12 g) for 40 min at 40°C. After filtration of the solution and evaporation of the solvent, the residue was subjected to preparative paper chromatography (solvent A). Two main fractions were obtained, the fraction with the lowest mobility, which contained pentonolactone, was eluted with water. Aldonic acid phenylhydrazides were prepared from the lactones with phenylhydrazine (100 mg to 100 mg of the lactones) in ethanol (1 ml) at 80°C for 3 h. The products were recrystallized from ethanol – ethylacetate. The results are shown in Table 2.

The fastest moving fraction obtained after the preparative paper chromatography contained as one component products with chromatographic mobilities (paper chromatography solvents A and B, TLC solvent D) corresponding to those of the tetronolactones (Table 2).

*Identification of erythrono-1,4-lactone after oxidation of* L-*arabinose.* The tetronolactone-containing fraction obtained from L-arabinose was treated with acetone-sulphuric acid. Neutralization of most of the sulphuric acid with solid sodium bicarbonate, filtration and evaporation yielded after purification by preparative TLC (solvent F) and crystallization from petroleum ether (b.p. 40 – 65°C), 2 mg of a product with chromatographic mobility (TLC, solvents F and G) corresponding to that of 2,3-*O*-isopropylidene-L-erythrono-1,4-lactone, m.p. 66 – 68°C, (lit.[1] 66.5 – 68°C).

*Prolonged oxidation of* L-*arabinose.* L-Arabinose (500 mg) in methanol (500 ml) was stirred with silver carbonate on Celite (15 g) for 40 min at 40°C. The solution was filtered and the solvent evaporated. The residue was hydrolyzed in 0.1 M sulphuric acid for 48 h at room temperature, the solution was neutralized and the acidic products were

*Table 1.* Oxidation of aldopentoses at 40°C for 10–25 min; lower-carbon sugars obtained.

| Pentose | Tetrose | Isopropylidene derivatives | | | Glyceraldehyde |
|---|---|---|---|---|---|
| | | Yield (%) | $[\alpha]_D$ | M.p. | |
| L-Arabinose | L-Erythrose | 41 | +75° (*c* 1, MeOH), lit.[11] +72° | – | [b] |
| D-Ribose | D-Erythrose | 19 | −60° (*c* 1, water), lit.[12] −66° | – | [b] |
| D-Xylose | D-Threose | 38 [a] | −13° (*c* 2, acetone), lit.[13] −15° | 81–83°C, lit.[13] 84°C | [b] |
| D-Lyxose | Threose [b] | – | – | – | [b] |

[a] Oxidation at room temperature. [b] Detected by TLC and electrophoresis.

*Table 2.* Aldolactones formed on oxidation of aldopentoses at 40°C for 40 min.

| Pentose | Pentonolactones | | | Tetronolactones |
|---|---|---|---|---|
| | Yield (%) | $[\alpha]_D$ (equil.) | M.p. of phenylhydrazides | |
| L-Arabinose | 20 | −33° (*c* 1, water), lit.[14] −36.1° | 212–214°C, lit.[15] 215° | Erythrono- |
| D-Ribose | 21 | +7° (*c* 2, water), lit.[16] +8.4° | 159–161°C, lit.[16] 162° | Erythrono-[a] |
| D-Xylose | <12 | not pure | – | Threono-[a] |
| D-Lyxose | [a] | – | – | Threono-[a] |

[a] Detected chromatographically.

removed with Dowex 1 ($HCO_3^-$) ion exchanger. The residue after removal of the water under reduced pressure was chromatographed on a Silica gel column with benzene–ethanol 3:1 (v/v), benzene–ethanol 5:2, and finally benzene–ethanol 2:1. Four fractions were obtained.

Fraction 1 (15 mg) contained a compound indistinguishable by chromatography (TLC, solvent E) and electrophoresis ($M_G$ 1.17) from glyoxal; the colours obtained with the spray reagents were identical with those obtained from glyoxal. This fraction in addition contained an other, unidentified component.

Fraction 2 (11 mg) contained a compound indistinguishable by TLC (solvent E) and electrophoresis ($M_G$ 0.65) from glycolaldehyde. This fraction also contained an unidentified component, presumably the same as the unidentified compound in fraction 1.

Fraction 3 contained L-glyceraldehyde (12 mg), $[\alpha]_D$ −8° (*c* 1, water) [lit.[9] −8.7°], mobilities by TLC (solvent D) and electrophoresis ($M_G$ 0.78) and colours obtained with the spray reagents corresponded to those of authentic D-glyceraldehyde.

Fraction 4 contained erythrose (41 mg), indistinguishable by chromatography (paper, solvent B; TLC, solvent D) and electrophoresis from authentic erythrose.

*Oxidation of* D-*xylose; identification of the methyl esters of oxalic and glyoxylic acid.* D-Xylose (250 mg) in methanol (50 ml) was stirred at 45°C with silver carbonate on Celite (15 mg) for 1 h. The solution was then filtered, the solvent evaporated and the residue dissolved in chloroform (30 ml). The chloroform solution was extracted with water (6 × 5 ml), the water extracts 3 to 6 were combined and the solvent was removed. The resulting oily residue (14 mg) was chromatographically homogeneous and indistinguishable (TLC, solvent E) from authentic methyl glyoxylate, and the infrared spectrum ($CHCl_3$, strong absorption at 1740 $cm^{-1}$) was identical with that of the authentic sample. The methyl ester was hydrolyzed in 0.5 M trifluoroacetic acid at 60°C overnight, and water and trifluoroacetic acid were removed under reduced pressure. The product was indistinguishable from authentic glyoxylic acid by paper chromatography (solvent C), both samples gave somewhat elongated spots.

The chloroform solution was dried with anhydrous sodium sulphate, the solution was filtered and the solvent evaporated. The residual syrup (19 mg) was chromatographically (TLC, solvent F) homogeneous and indistinguishable from authentic dimethyl oxalate. The infrared spectrum ($CHCl_3$, strong absorptions at 1740 and 1765 $cm^{-1}$) was identical with that of the authentic dimethyl oxalate. Hydrolysis in 0.5 M trifluoroacetic acid as described for methyl glyoxylate, gave a compound indistinguishable from oxalic acid by paper chromatography (solvent C).

*Oxidation of* D-*xylose. B. Identification of methyl glycerate.* D-Xylose (500 mg) in methanol (100 ml) was oxidized with silver carbonate on Celite (12 g) at 40°C for 40 min, the solution was filtered and the solvent evaporated. The residue was shown by TLC (solvent E) to contain at least five components detectable with hydroxylamine–ferric chloride. Two of the products had mobilities corresponding to those of glyceric acid methyl ester and glycolic acid methyl ester (traces). The product mixture was hydrolyzed in 0.5 M trifluoroacetic acid overnight at 60°C. After removal of the solvent and trifluoroacetic acid under reduced pressure, the residue was subjected to preparative paper chromatography (solvent B). Two zones with high mobility and two with very low mobility were obtained. The zones with low mobility were eluted with water and rechromatographed on paper (solvent C). Three fractions were obtained, the one with highest mobility contained a compound with chromatographic mobility as glycolic acid (4 mg), the next fraction (5 mg) contained a product with mobility corresponding to that of authentic D-glyceric acid, the third fraction was a mixture of the acid from the second fraction and an acid with mobility as glyoxylic acid. The acid from fraction 2 was stirred with Dowex 50W ($H^+$) ion exchanger in methanol for 24 h. Filtration of the solution and evaporation of the solvent yielded a syrup, chromatographically (TLC, solvent E) indistinguishable from methyl D-glycerate. The infrared spectrum ($CHCl_3$, strong absorption at 1735 $cm^{-1}$) was identical with that of the authentic sample.

*Measurements of the rate of oxidation.* The pentoses (50 mg) in methanol (10 ml) were stirred with silver carbonate on Celite (1.2 g) at 30°C. Aliquots (25 µl) were withdrawn at intervals, and the amount of unoxidized pentose determined by the paper chromatographic–colorimetric method described by Wilson.[10] The results are shown in Fig. 1.

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