Carbohydrate Research
Elsevier Publishing Company, Amsterdam
Printed in Belgium

OXIDATION OF ALDITOLS BY MERCURY(II) ACETATE

Ľ. Stankovič, K Linek, and M Fedoroňko
Institute of Chemistry, Slovak Academy of Sciences, Bratislava (Czechoslovakia)

(Received December 11th, 1968, in revised form, February 10th, 1969)

ABSTRACT

The secondary hydroxyl groups of D-arabinitol and xylitol were shown to undergo oxidation with a boiling, methanolic solution of mercury(II) acetate to give D-*threo*-pentulose, D-*threo*-3-pentulose, D-*erythro*-pentulose, and DL-*threo*-pentulose and *erythro*-3-pentulose, respectively. The formation of dihydroxyacetone and DL-glyceraldehyde from glycerol, and mainly glycolaldehyde from ethylene glycol, indicates that primary hydroxyl groups are also oxidised These results, as well as the formation of acetone upon treatment of isopropyl alcohol with mercury(II) acetate, indicate that cyclic intermediates are not involved in these oxidations

INTRODUCTION

There is considerable interest at present in the preparation of unsubstituted ketoses 2-Ketoses are usually prepared by transformation of the appropriate aldoses in pyridine (*e g*, D-tagatose[1], D-*erythro*-pentulose[2-4], D-*threo*-pentulose[5], and D-*glycero*-tetrulose[6]), by bacterial oxidation[7] of alditols, and by the diazomethane synthesis[8 9]

The preparation of 3-ketoses is more complicated than that of 2-ketoses, and can be achieved by oxidation of partially blocked derivatives by chromium(VI) oxide, by this method, DL-*xylo*-3-hexulose[10] was prepared. 3-Pentuloses can be prepared by transformation of aldopentoses in pyridine[3].

Secondary hydroxyl groups are specifically oxidized by mercury(II) acetate, even in the presence of unsubstituted primary alcoholic groups, and *erythro*-3-pentulose and DL-*erythro*-pentulose[11] were prepared by oxidation of ribitol Similarly, D-fructose and L-sorbose were prepared[12] from D-mannitol and D-glucitol, respectively.

This paper deals with the preparation of further pentuloses by the oxidation of D-arabinitol and xylitol by mercury(II) acetate, the oxidation of glycerol, ethylene glycol, and isopropyl alcohol is also described

DISCUSSION

Oxidation of D-arabinitol, xylitol, and ribitol[11] with mercury(II) acetate gave only pentuloses, thereby proving the selective oxidation of secondary hydroxyl groups On the other hand, glycolaldehyde is formed by oxidation of ethylene glycol, and both dihydroxyacetone and DL-glyceraldehyde were obtained from glycerol These results provide evidence for the oxidation of secondary hydroxyl groups by mercury(II) acetate, and show that primary hydroxyl groups also undergo oxidation, although at a lower rate

The formation of the above products of oxidation passed through a maximum, probably because of subsequent dehydration of the resulting α-hydroxycarbonyl compounds[13] Since ketoses, which are formed to a greater extent, are dehydrated more readily than aldoses[14], it is evident that the effect of dehydration is pronounced and causes a big decrease in the yield of the α-hydroxycarbonyl compounds The structure of the dehydration products was not elucidated, but the formation of deoxypentosuloses may be presumed by analogy with the dehydration of hexuloses[13,15]

Since *erythro*-3-pentulose was not formed on oxidation of D-arabinitol, nor DL-*erythro*-pentulose and DL-*threo*-3-pentulose from xylitol, it is concluded that the initially formed pentuloses do not rearrange

Stoodley[11] assumed that the oxidation of ribitol with mercury(II) acetate proceeds through a 6-membered cyclic intermediate Such an intermediate is not possible for ethylene glycol and isopropyl alcohol, both of which are oxidised by the reagent However, the finding that the oxidations of particular, secondary hydroxyl groups do not proceed at the same rate, *e g*, in the case of D-arabinitol, indicates the operation of stereochemical effects It is worth noting that the yield of particular pentuloses need not necessarily reflect the extent of oxidation of individual secondary hydroxyl groups This can only be determined from a knowledge of the rate of dehydration of the various pentuloses Clearly, further investigation is necessary before an acceptable mechanism of oxidation of alditols can be presented

EXPERIMENTAL

Melting points were determined on a Kofler micro hotstage Solutions were evaporated under diminished pressure at 30–40°

Xylitol[16], D-*erythro*-pentulose[3], D-*threo*-pentulose[3], D-*threo*-3-pentulose[3], and *erythro*-3-pentulose[11] were prepared by literature methods All other chemicals were commercial products

Descending paper chromatography was performed on Whatman No 1 paper with (*a*) acetone–butyl alcohol–water (7 2 1) [the fraction of pentuloses ($R_P = 1$) was used as a reference for estimation of the particular spots, single pentuloses exhibited the same mobility in this solvent system]; (*b*) cyclohexanol–pyridine–water saturated with boric acid (6 5 2) and containing phenol (1 g/100 ml), the chromatography paper was soaked with 1% boric acid solution Detection was effected with aniline hydrogen phthalate[17] and potassium periodate–benzidine[18]

Preparative chromatography was performed on columns (90×4 5 cm) of Whatman cellulose or microcrystalline cellulose[19] Ion-exchange chromatography was effected on columns (200×1 cm) of Dowex-50W x8 (100–200 mesh) (Ba^{2+}) resin[20]

Polarographic determination of α-hydroxycarbonyl and α-dicarbonyl compounds was effected as previously described[21,22].

Oxidation of D-*arabinitol.* — A solution of D-arabinitol (10 g, 0.065 mole) and mercury(II) acetate (42 g, 0.13 mole) in absolute methanol (250 ml) was refluxed for 12 h. The insoluble mercury(I) acetate was filtered off, and washed with methanol. Mercury salts, precipitated from the filtrate by hydrogen sulphide, were filtered off and washed with methanol. The combined filtrates were evaporated, and the residual syrup was treated with absolute ethanol (75 ml). Unreacted D-arabinitol (4 g), which crystallized from this solution at 0°, was filtered off, and the filtrate was evaporated anew. According to paper chromatography [system (*a*)], the syrupy residue consisted of unreacted D-arabinitol (R_F 0.60), pentuloses, and three dehydration products (R_F 1.32, 1.52, and 1.76). This mixture was separated by cellulose column chromatography [solvent (*a*)] to give the dehydration products (1.05 g, 10.5%), pentuloses (1.71 g, 17.1%), and D-arabinitol. The mixture of pentuloses was fractionated by ion-exchange chromatography, with water as eluent, to give D-*threo*-pentulose (1.10 g, 11%), D-*threo*-3-pentulose (0.25 g, 2.5%), and D-*erythro*-pentulose (0.12 g, 1.2%).

When the reaction time of oxidation was extended to 24 h, 11% of oxidation products and 19.3% of dehydration products were isolated. When the molecular ratio of oxidation agent to D-arabinitol was changed to 4:1 for a reaction time of 12 h, 9.4% of oxidation products and 21.0% of dehydration products were obtained.

Oxidation of xylitol. — A solution of xylitol (10 g, 0.065 mole) and mercury(II) acetate (42 g, 0.13 mole) in absolute methanol (250 ml) was refluxed for 8 h and worked up as in the previous case, except that the unreacted xylitol did not crystallize. Paper chromatography [solvent (*a*)] showed that the reaction mixture contained unreacted xylitol (R_F 0.60), pentuloses, and two dehydration products (R_F 1.32 and 1.52).

The reaction mixture was first separated by means of ion-exchange chromatography, with water as eluent, to give DL-*threo*-pentulose and *erythro*-3-pentulose; both fractions were contaminated with dehydration products, as well as with unreacted xylitol. Each of these fractions was further separated by cellulose column chromatography [solvent (*a*)] to give dehydration products (1.78 g, 17.8%), DL-*threo*-pentulose (1.20 g, 12.0%), and *erythro*-3-pentulose (0.16 g, 1.6%).

Characterisation of pentuloses. — Pentuloses were identified by optical rotation and by the sign of their Cotton effect[23], by conversion into their crystalline hydrazones, and by paper chromatography [solvent (*b*)] of the pentitols resulting from reduction with sodium borohydride.

D-*threo*-Pentulose[5], syrup, $[\alpha]_D^{20}$ $-32°$ (*c* 1.0, water), positive Cotton effect; 2,4-dinitrophenylhydrazone[3], m.p. 175–176° (chloroform) (Found: C, 39.87; H, 4.25; N, 17.05. $C_{11}H_{14}N_4O_8$ (330.3) calc.: C, 40.00; H, 4.27; N, 16.96%). D-Arabinitol and xylitol were identified as reduction products.

D-*threo*-3-Pentulose, syrup, $[\alpha]_D^{20}$ $-118°$ (*c* 1.0, water), was obtained in purer form than previously reported[23]; negative Cotton effect; 2,5-dichlorophenylhydrazone[3], m p 146–147° (chloroform) (Found. C, 42.46, H, 4.48; N, 9.00% $C_{11}H_{14}Cl_2N_2O_4$ (309.1) calc · C, 42.74; H, 4.57; N, 9.06%) D-Arabinitol was formed by the reduction

D-*erythro*-Pentulose, syrup, *o*-nitrophenylhydrazone[3], m.p 165–166° (ethanol); $[\alpha]_D^{20}$ −50° (*c* 0.2, methanol) (Found C, 46.52, H, 5.46, N, 14.95 $C_{11}H_{15}N_3O_6$ (285.3) calc. C, 46.32, H, 5.30, N, 14.73%) Ribitol and D-arabinitol were identified as reduction products

DL-*threo*-Pentulose, syrup, phenylosazone[24], m.p 205–207° (ethanol) (Found C, 62.37, H, 6.35; N, 17.05% $C_{17}H_{20}N_4O_3$ calc.: C, 62.15, H, 6.14, N, 17.06%) DL-Arabinitol and xylitol were identified as reduction products

erythro-3-Pentulose, syrup, 2,5-dichlorophenylhydrazone[11], m p 126–127° (chloroform) (Found· C, 42.49, H, 4.43, N, 9.01%. $C_{11}H_{14}Cl_2N_2O_4$ (309.1) calc C, 42.74, H, 4.57, N, 9.06%) Ribitol and xylitol were found to be the reduction products.

Oxidation of ethylene glycol — Ethylene glycol (2 g, 0.032 mole) was oxidized with mercury(II) acetate (20 g, 0.063 mole) in absolute methanol (100 ml) for 7 h Glycolaldehyde thus prepared was estimated polarographically[21], mercury salts being first precipitated by hydrogen sulphide, after 2 h, 2.4%; 4 h, 2.0%, 7 h, 1.4%.

Oxidation of glycerol — Glycerol (2 g, 0.022 mole) was oxidized with mercury(II) acetate (14 g, 0.044 mole) in absolute methanol (100 ml) for 7 h The oxidation products (dihydroxyacetone and DL-glyceraldehyde), as well as pyruvaldehyde formed by dehydration, were estimated polarographically[22], the soluble mercury salts being first removed by hydrogen sulphide It was ascertained that the yield of dihydroxyacetone and DL-glyceraldehyde increased with time of oxidation up to *ca* 5 h (maximum, *ca.* 1.5% of each triose) The yield then decreased, with an accompanying increase of the dehydration product, *i e*, pyruvaldehyde

Oxidation of isopropyl alcohol. — Isopropyl alcohol (25 g, 0.42 mole) was subjected to oxidation with mercury(II) acetate (60 g, 0.19 mole) in absolute methanol (300 ml) for 32 h Acetone (3.5%) thus formed was determined gravimetrically as the 2,4-dinitrophenylhydrazone

Dehydration of pentuloses — Chromatographically pure pentuloses were refluxed in N methanolic acetic acid Two substances (R_P 1.32 and 1.52) were obtained by dehydration of D-*erythro*-pentulose. Two substances of similar R_P values were obtained from D-*threo*-pentulose, and one substance (R_P 1.76), in small proportion, from D-*threo*-3-pentulose. *erythro*-3-Pentulose underwent no detectable dehydration All of the above-mentioned substances were detected with potassium periodate–benzidine and by aniline hydrogen phthalate; an intense red coloration was formed, as with the dehydration products of pentitols formed by reaction with mercury(II) acetate.

ACKNOWLEDGMENTS

We express our thanks to Dr. S Bauer, Head of this Institute, for his deep interest in the present work, and to Mrs A Pufflerova for elemental analysis

REFERENCES

1 E L Totton and H A Lardy, *Methods Carbohyd Chem*, 1 (1962) 155
2 C Glatthaar and T Reichstein, *Helv Chim Acta*, 18 (1935) 80
3 M Fedoroňko and K Linek, *Collection Czech Chem Commun*, 32 (1967) 2177.
4 K Linek and M Fedoroňko, Czechoslovak Patent No 127,270
5 O T Schmidt and R Treiber, *Ber*, 66 (1933) 1765
6 K Linek, M Fedoroňko, and Š Bauer, Patent pending 6229/67
7 V Moses and R. J. Ferrier, *Biochem J*, 83 (1962) 8
8 M L Wolfrom and R B Bennett, *J. Org Chem*, 30 (1965) 458
9 M L. Wolfrom, S M Olin, and E F Evans, *J Amer Chem Soc*, 66 (1964) 204
10 G U Yuen and J. M Sugihara, *J Org Chem*, 26 (1961) 1598
11 R J Stoodley, *Can J Chem*, 39 (1961) 2593
12 G N Dorofenko, *Ukr. Khim Zh*, 27 (1961) 114
13 E F. L. J Anet, *Advan. Carbohyd Chem*, 19 (1964) 181
14 M Fedoroňko and K Linek, *Chem Zvesti*, 19 (1965) 550
15 E F L J Anet, *Australian J Chem*, 18 (1965) 240
16 M Abdel-Akher, J K Hamilton, and F Smith, *J Amer Chem Soc*, 73 (1951) 4691.
17 S M Partridge, *Nature*, 164 (1949) 443
18 J A Cifonelli and F Smith, *Anal Chem*, 26 (1954) 1132.
19 K Linek, Ľ Kuniak, and B Alinče, *Chem Zvesti*, 21 (1967) 99
20 J K N Jones and R. A Wall, *Can J Chem*, 38 (1960) 2290
21 T. Wasa and S Musha, *Bull Chem Soc Japan*, 40 (1967) 1624
22 M Fedoroňko, J Konigstein, and K Linek, *J Electroanal Chem*, 14 (1967) 357
23 T Sticzay, C Peciar, K Babor, M Fedoroňko, and K Linek, *Carbohyd Res*, 6 (1968) 418.
24 L Hough and J K N Jones, *J Chem Soc*, (1952) 4047