Oxidation of Carbohydrate Derivatives with Silver Carbonate on Celite. V. Oxidation of Some *O*-Isopropylidene Aldoses with Unsubstituted Anomeric Hydroxyl Group

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Silver carbonate on Celite oxidizes 2,3-*O*-isopropylidene-D-ribose, 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose, and 2,3:5,6-di-*O*-isopropylidene-D-allofuranose to the corresponding aldono-1,4-lactones in boiling benzene in good to excllent yields. Under the same conditions, 3,4-*O*-isopropylidene-L-arabinopyranose gives 3,4-*O*-isopropylidene-L-arabino-1,5-lactone in fair yield; in boiling methanol 2,3-*O*-isopropylidene-L-erythrose is obtained in low yield from the same compound.

In a previous paper the oxidation of some higher methylated, 2-*O*-substituted aldoses to aldonolactones with silver carbonate on Celite was described.[1] 2,3-Di-*O*-methyl-D-glucose and 2-*O*-methyl-D-arabinose have been shown to give aldonolactones in the same way with the oxidant; the hydroxyl groups except the anomeric one, were chiefly unaffected.[2] 3-*O*-Methyl-D-glucose is, on the other hand, degraded to 2-*O*-methyl-D-arabinose by silver carbonate on Celite below 60° in methanol.[3] In the present work the investigation of silver carbonate on Celite as an oxidant is extended to some isopropylidene acetals of aldoses having their anomeric hydroxyl groups free. Aldoses with *cis*-configuration between the 2- and 3-hydroxyl groups usually give 2,3-*O*-isopropylidene acetals on acetonation, and little or no of the 1,2-*O*-isopropylidene derivatives,[4−6] as predicted by Mills.[7] Characterization of 2,3-*O*-alkylidene acetals is often performed through oxidation to the corresponding aldonolactones.[4−6,8] These lactones are in addition of value as synthetic intermediates.[9,10] The usually applied oxidants in this reaction are aqueous, alkaline permanganate [4,8,11] and dimethyl sulphoxide − acetic anhydride.[5,6,12] When the former reagent is used, the aldonic acids are obtained, and extraction from the acidified solution and lactonization is necessary. The reagent is not applicable when free primary hydroxyl groups are present. Dimethyl sulphoxide − acetic anhydride is a more convenient reagent; it is however, only usable when no other free hydroxyl groups than the anomeric

one are present. The earlier findings [1,2] that in 2-O-substituted aldoses the anomeric hydroxyl group is almost selectively oxidized by silver carbonate on Celite, in addition to the convenience of the reaction and purity of the products suggested this oxidant to be more suitable for the preparation of isopropylidene aldonolactones.

RESULTS AND DISCUSSIONS

The 2,3:5,6-di-O-isopropylidene derivatives of D-mannose (I) and D-allose (III) were oxidized quantitatively to aldonolactones (II and IV) within 30 – 40 min by the oxidant in boiling benzene. On evaporation of the solvent the products crystallized either directly, or after addition of petroleum ether,
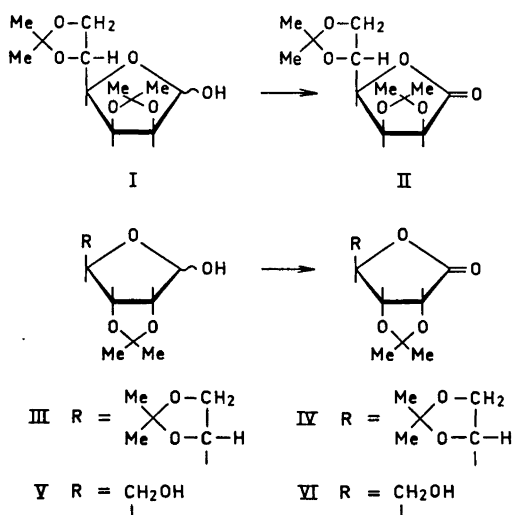
in high purity. 2,3:5,6-Di-O-isopropylidene-D-allofuranose (III) was described for the first time recently by three different groups;[4,5,13] two different melting points have, however, been reported for the corresponding aldonolactone; oxidation of the di-isopropylidene derivative (III) with alkaline permanganate,[4] as well as acetonation of D-allono-1,4-lactone,[13] has given a compound melting 30° higher than the product obtained on oxidation of the di-isopropylidene allose with dimethyl sulphoxide – acetic anhydride.[5] The lactone prepared with silver carbonate on Celite has a melting point in agreement with that of the compound obtained with dimethyl sulphoxide – acetic anhydride. Dimorphism is possibly the explanation of the difference of the melting points since the two forms show identical optical rotation.

2,3-O-Isopropylidene-D-ribose (V) was oxidized to the corresponding lactone (VI) in good yield, and as for the above mentioned compounds, it was obtained in high purity without recrystallization.
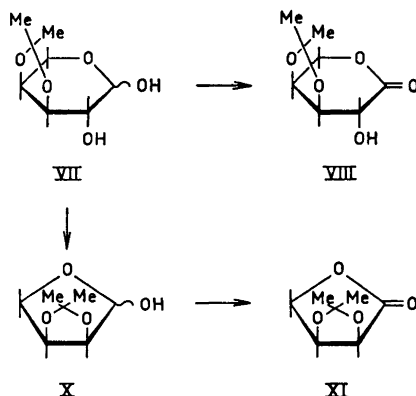
The oxidation pattern of 3,4-O-isopropylidene-L-arabinose (VII) was also investigated. In view of the results obtained on oxidation of 3-O-methyl-D-glucose,[3] it was expected to be degraded to a derivative of L-erythrose. However, this compound showed great resistance to degradation in benzene solution, and 3,4-O-isopropylidene-L-arabino-1,5-lactone (VIII) was isolated in almost 50 % yield after reflux in benzene solution for 1 h with the oxidant. Substantial amounts of unchanged starting material were still present. The identification of the lactone (VIII) was based on infrared and nuclear magnetic resonance spectroscopy, and on removal of the isopropylidene group and conversion of the product to the characteristically high melting L-arabinonic acid phenylhydrazide (IX). After treatment of 3,4-O-isopropylidene-L-arabinose (VII) with the oxidant in methanol at reflux temperature for 40 min, conditions which are sufficient to degrade 3-O-methyl-D-glucose completely,[3] more than 50 % of the starting material was recovered. The reaction product was found to be 2,3-O-isopropylidene-L-erythrose (X), contaminated with small amounts of a compound assumed to be its 4-O-formyl derivative. After hydrolysis in weakly alkaline solution, further oxidation with silver carbonate on Celite in benzene solution afforded 2,3-O-isopropylidene-L-erythronolactone (XI).

The mechanism of the degradation of aldoses by silver carbonate on Celite is not known, and, hence, a satisfactory explanation of the resistance of 3,4-O-isopropylidene-L-arabinose (VII) to oxidation is impossible. It has, however, been found earlier[3] that 3-O-methyl-D-glucose is oxidized at least partially in cyclic forms, and if its oxidation occurs most rapidly in furanose form, this will explain why the arabinose derivative (VII), which cannot exist in furanose form, is oxidized more slowly. In this connection it is worth to remind that lead tetra-acetate oxidation of reducing aldose derivatives proceeds in their furanose forms,[14] whereas sodium periodate oxidized these compounds in their pyranose forms.[15] The fact that 2,3-O-isopropylidene-L-erythrose (X) is the principal product after the oxidation of 3,4-O-isopropylidene-L-arabinose (VII) in methanol solution does not exclude the possibility that the oxidation occurs in cyclic forms, as the formyl ester, which then would be the primary product, is unstable under the reaction conditions.[3] An alternative explanation of the low oxidation rate of the iso-

propylidene arabinose (VII) might be an unfavorable conformation for the oxidative degradation, forced upon the arabinopyranose ring by the condensed five-membered ring.

It is hoped that light will be thrown on this problem through investigation of the effect of silver carbonate on Celite on differently substituted aldose derivatives.

EXPERIMENTAL

Oxidation of 2,3:5,6-di-O-isopropylidene-D-mannofuranose (I). 2,3:5,6-Di-O-isopropylidene-D-mannofuranose (I) [16] (40 mg) in benzene (50 ml) was refluxed with silver carbonate on Celite [17] (2 g) for 35 min. The solid material was filtered off and washed three times with hot benzene. On evaporation of the collected benzene solutions, 2,3:5,6-di-O-isopropylidene-D-mannono-1,4-lactone (II) crystallized (39 mg, 98 % of theoretical), m.p. 125° (lit.[12] 126°), [α]$_D$ + 50° (c 1, chloroform) {lit.[12] + 50°}.

Oxidation of 2,3:5,6-di-O-isopropylidene-D-allofuranose (III). 2,3:5,6-Di-O-isopropylidene-D-allofuranose (III) [5] (80 mg) in benzene (60 ml) gave with silver carbonate on Celite (2 g) after reflux for 40 min, filtration and washing of the solid three times with hot benzene, followed by evaporation of the benzene solutions, 2,3:5,6-di-O-isopropylidene-D-allono-1,4-lactone (IV) (71 mg, 92 % of theoretical) as a chromatographically (thin layer chromatography, benzene − ethanol 10 : 1, silica gel) homogeneous syrup, which crystallized from petroleum ether; m.p. 41 − 42° (lit.[5] 38 − 39°, and [13] 72 − 74°). [α]$_D$ − 76° (c 1, chloroform) {lit.[5,13] − 78.7, − 77.8}. Infrared absorption (in chloroform) was observed at 1790 cm^{-1}, which is characteristic of γ-lactones.

Oxidation of 2,3-O-isopropylidene-D-ribose (V). By the above procedure 2,3-O-isopropylidene-D-ribose (V) [18] (50 mg) gave 2,3-O-isopropylidene-D-ribono-1,4-lactone (VI) (40 mg, 80 % of theoretical), which crystallized directly, m.p. 137 − 138° (lit.[19] 138 − 139°), [α]$_D$ − 65° (c 1, pyridine) {lit.[19] − 65.7°}.

Oxidation of 3,4-O-isopropylidene-L-arabinopyranose (VII). A. In benzene. 3,4-O-Isopropylidene-L-arabinopyranose (VII),[20] prepared as described for the D-enantiomeric compound,[21] (100 mg) in benzene (100 ml) was refluxed for 1 h with silver carbonate on Celite (4 g), filtration and washing three times with hot benzene of the solid material, followed by evaporation of the combined benzene solutions, gave a syrupy residue. The residue was extracted with petroleum ether at 35° (50 ml), evaporation of the petroleum ether gave a crystalline residue (VIII) (48 mg, 48 % of theoretical) which after recrystallization from petroleum ether had m.p. 95 − 97°, [α]$_D$ − 1° (c 3, chloroform). Infrared absorption was observed at 1755 cm^{-1} (chloroform), which is characteristic of δ-aldonolactones. NMR signals were located at δ 4.45 (multiplet), 3.25 (broad), 1.52 (singlet) and 1.40 (singlet) with relative intensities 5 : 1 : 3 : 3, in chloroform-d_3 solution. (Found: C 51.02; H 6.36. Calc. for $C_8H_{12}O_5$: C 51.06; H 6.43.)

L-Arabinonic acid phenylhydrazide (IX). 3,4-O-Isopropylidene-L-arabino-1,5-lactone (VIII) (20 mg) was treated with 0.2 M trifluoroacetic acid (5 ml) at 40° for 20 h. The solution was evaporated to a syrup, which was treated with phenylhydrazine (14 mg) in ethanol (2 ml) on a water bath for 1 h. The solution was kept at 3° for 1 h, and the crystallized L-arabinonic acid phenylhydrazide (IX) (9 mg) was filtered off. After recrystallization from ethanol, it had m.p. 209 − 210° (lit.[22] 215°).

Oxidation of 3,4-O-isopropylidene-L-arabinopyranose (VII). B. In methanol. 3,4-O-Isopropylidene-L-arabinopyranose (VII) (85 mg) in methanol (60 ml) was refluxed with silver carbonate on Celite (2 g) for 40 min, the solid material was filtered off and washed with hot methanol. The methanol solutions were combined and evaporated to give a partially crystalline residue. The residue was extracted with petroleum ether (50 ml) at 40°, and after 1 h at room temperature crystallized starting material was filtered of from the petroleum ether solution. The solvent was evaporated, and the obtained residue reextracted with petroleum ether (40 ml) at 35°. Evaporation of this solution afforded a syrupy residue; thin layer chromatography (benzene − ethanol 5 : 1) showed the presence of one principal product, contaminated with small amounts of starting material and a trace of a third component. The syrup was dissolved in methanol (8 ml), and sodium carbonate (200 mg) in water (2 ml) was added. After 1 h, the solution was neutralized

with Dowex 50 W ion exchange resin, filtered and evaporated to a syrupy residue of 2,3-O-isopropylidene-L-erythrose (X) (21 mg, 29 % of theoretical), $[\alpha]_D$ + 75° (c 1, methanol) {lit.[23] + 72°}.

   2,3-O-Isopropylidene-L-erythrono-1,4-lactone (XI). 2,3-O-Isopropylidene-L-erythrose (X) (20 mg) in benzene (40 ml) was refluxed with silver carbonate on Celite (500 mg) for 35 min, the solid material was filtered off and washed with hot benzene. Evaporation of the combined benzene solutions gave a crystalline residue of 2,3-O-isopropylidene-L-erythrono-1,4-lactone (XI), (14 mg, 70 % of theoretical) which after recrystallization from petroleum ether had m.p. 66 − 67° (reported for the D-enantiomeric compound [24] 65 − 67.5°) and $[\alpha]_D$ + 112° (c 0.3, water) {reported for the D-enantiomer [24] − 116°}. Infrared absorption was observed at 1780 cm^{-1}, characteristic of γ-lactones.

REFERENCES

1. Morgenlie, S. *Acta Chem. Scand.* **25** (1971) 1154.
2. Morgenlie, S. *Unpublished results*.
3. Morgenlie, S. *Acta Chem. Scand.* **25** (1971) 2773.
4. Ballard, J. M. and Stacey, B. E. *Carbohyd. Res.* **12** (1970) 37.
5. Haga, M., Takano, M. and Tejima, S. *Carbohyd. Res.* **14** (1970) 37.
6. Brimacombe, J. S. and Gent, P. A. *Carbohyd. Res.* **9** (1969) 231.
7. Mills, J. A. *Advan. Carbohyd. Chem.* **10** (1955) 1.
8. Besshard, W. *Helv. Chim. Acta* **18** (1935) 482.
9. Hanessian, S. and Haskell, T. H. *J. Heterocyclic Chem.* **1** (1964) 57.
10. Zhdanov, Y. A., Alexeev, Y. E. and Khourdanov, C. A. *Carbohyd. Res.* **14** (1970) 422.
11. Ohle, H. and Berend, G. *Ber.* **58** (1925) 2590.
12. Horton, D. and Jewell, J. S. *Carbohyd. Res.* **2** (1966) 251.
13. Kohn, B. D., Kohn, P. and Dublin, A. *Carbohyd. Res.* **18** (1971) 349.
14. Perlin, A. S. *Advan. Carbohyd. Chem.* **14** (1959) 9.
15. Schöpf, C. and Wild, H. *Chem. Ber.* **87** (1954) 1571.
16. Schmidt, O. T. *Methods Carbohyd. Chem.* **2** (1963) 319.
17. Balogh, V., Fetizon, M. and Golfier, M. *Angew. Chem.* **81** (1969) 423.
18. Barker, G. R. and Spoors, J. W. *J. Chem. Soc.* **1956** 1192.
19. Hough, L., Jones, J. K. N. and Michell, D. L. *Can. J. Chem.* **36** (1958) 1720.
20. Ohle, H. and Berend, G. *Ber.* **60** (1927) 810.
21. Jones, J. K. N., Kent, P. W. and Stacey, M. *J. Chem. Soc.* **1947** 1341.
22. Fischer, E. *Ber.* **23** (1890) 2625.
23. Baxter, J. N. and Perlin, A. S. *Can. J. Chem.* **38** (1960) 2217.
24. Schaffer, R. *J. Res. Natl. Bur. Std.* **A 65** (1961) 507.