

Oxidation of Carbohydrate Derivatives with Silver Carbonate on Celite. XI. Oxidation of 4,6-*O*-Alkylidene Derivatives of D-Galactose and D-Glucose

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Oxidation of 4,6-*O*-alkylidene derivatives of D-galactose and D-glucose in methanol with silver carbonate on Celite leads to 2,4-*O*-alkylidene tetroses as major products. In benzene-*N,N*-dimethylformamide, oxidation of the galactose derivatives gives mainly 3,5-*O*-alkylidene derivatives of D-lyxose; a galactonolactone derivative is also formed. Oxidation of 4,6-*O*-alkylidene-D-glucoses in benzene or benzene-*N,N*-dimethylformamide results in the formation of 4,6-*O*-alkylidene-D-glucono-1,5-lactones, degradation to arabinose derivatives is negligible.

The relative reactivities of the anomers of the 4,6-*O*-ethylidenehexoses in benzene-*N,N*-dimethylformamide are investigated, and in the light of the results obtained, the difference in the product compositions obtained from the galactose and the glucose derivatives in this solvent mixture is discussed.

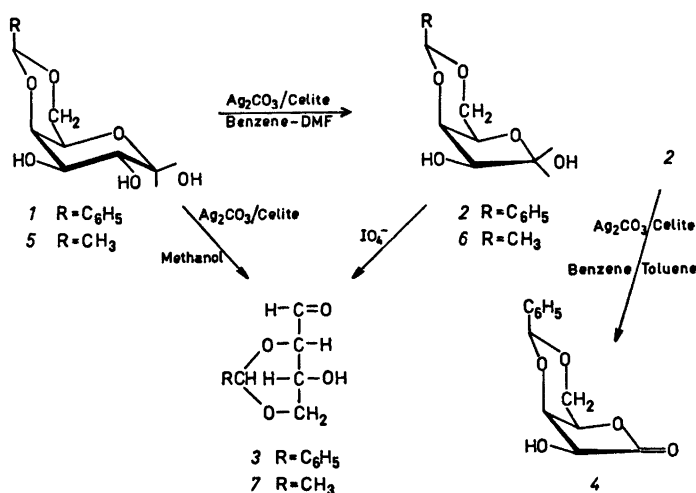
The formation of 3,5-*O*-isopropylidene-D-lyxose on oxidation of 4,6-*O*-isopropylidene-D-galactopyranose with silver carbonate on Celite in benzene, was reported in a previous paper in this series.¹ In methanol, the oxidation product was mainly 2,4-*O*-isopropylidene-D-threose. The initially formed *O*-formyl group at C-4 of the lyxose derivative, resulting from cleavage of the galactopyranose derivative between C-1 and C-2, is unstable in methanol, and the liberated hydroxyl group at C-4 may form a hemiacetal with the aldehyde group by cyclisation. The next degradation step of the sugar derivative may possibly occur in this furanose form.² Another possible way to the threose derivative is a degradation of the acyclic α -hydroxy hemiacetal formed between the lyxose derivative

and methanol. The use of benzene as a solvent in the oxidation reaction prevents both these reaction paths, and hence makes possible a one-step degradation of the galactose derivative. Five different 4,6-*O*-alkylidene derivatives of D-galactose and D-glucose have been oxidized with silver carbonate on Celite in order to obtain information about the effect of fused rings on the reactivity of aldopyranoses, and also with the purpose to investigate the possible general applicability of the method in preparation of 3,5-*O*-alkylidene pentoses. The results are reported in this paper.

RESULTS AND DISCUSSION

4,6-*O*-Benzylidene-D-galactose (1) on oxidation with silver carbonate on Celite in benzene containing a little *N,N*-dimethylformamide (DMF), followed by treatment of the product mixture with an anion exchange resin, gave 3,5-*O*-benzylidene-D-lyxose (2) in about 55 % yield. The identity was established by hydrolysis to lyxose, and by periodate oxidation which gave 2,4-*O*-benzylidene-D-threose (3). Further oxidation of 2 in benzene-toluene yielded the known³ 3,5-*O*-benzylidene-D-lyxono-1,4-lactone (4); in benzene alone this oxidation occurred very slowly. Oxidation of 4,6-*O*-benzylidene-D-galactose (1) in methanol gave mainly 2,4-*O*-benzylidene-D-threose (3).

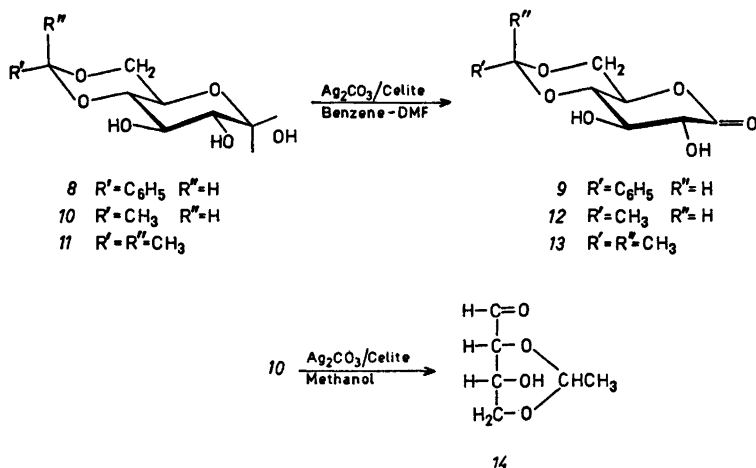
4,6-*O*-Ethylidene-D-galactose (5) in benzene-DMF reacted analogously to give 3,5-*O*-ethylidene-D-lyxose (6) as the main product, periodate oxidation of which gave 2,4-*O*-ethylidene-



D-threose (7). Small amounts of galactonolactone were detected in this case by treatment of the anion exchange resin used after oxidation of 5 with trifluoroacetic acid. 2,4-O-Ethylidene-D-threose (7) was also obtained from 5 by silver carbonate oxidation in methanol.

Oxidation of 4,6-O-alkylidene derivatives of D-glucose in benzene-DMF did not proceed in the same way as oxidation of the galactose derivatives; the main reaction was oxidation to gluconolactone derivatives. Thus, 4,6-O-benzylidene-D-glucose (8) gave crystalline 4,6-O-benzylidene-D-glucono-1,5-lactone (9) in about 50 % yield; trace amounts only of

arabinose were detected after hydrolysis of the mother liquor. 4,6-O-Ethylidene- (10) and 4,6-O-isopropylidene- (11)-D-glucopyranose were also oxidized to the corresponding aldono-lactones (12 and 13, respectively). Isolation of these compounds was difficult when the oxidation had been carried out in benzene-DMF, due to instability of the lactone ring. The use of benzene as solvent facilitated, however, the isolation of the lactones. Also in these cases, small amounts only of degradation products were detected. Since the oxidation in benzene-DMF gave 3,5-O-alkylidene-arabinoses in negligible amounts, oxidation of 4,6-O-ethylidene-D-glucopyranose (10) in methanol



was tried. Degradation beyond the pentose stage occurred, however, too rapidly to make this a suitable method for preparation of 3,5-*O*-ethylidene-D-arabinose. 2,4-*O*-Ethylidene-D-erythrose (14) was the only product after the reaction mixture had been treated with an anion exchange resin, in analogy with the results obtained on oxidation of 4,6-*O*-alkylidene derivatives of D-galactose in methanol.

A synthesis of a 3,5-*O*-benzylidene-D-lyxose has been described,⁴ in which the primary hydroxyl group of 1,3-*O*-benzylidene-D-arabinitol was selectively oxidized to give the lyxose derivative. The product was described as a syrup, and based on IR spectroscopy it was supposed to exist in *aldehyde* form. To this compound was assigned the configuration and preferred conformation 2*b*. In the 3,5-*O*-benzylidene-D-lyxose prepared here, the configuration at the benzylic carbon atom should be expected to be the same as in the starting compound 4,6-*O*-benzylidene-D-galactopyranose (1), in which the phenyl group most likely is equatorially attached to the 1,3-dioxan ring in a chair conformation.⁵ The expected configuration at the benzylic carbon atom in the produced 3,5-*O*-benzylidene-D-lyxose (*aldehyde* form 2*a*) is the opposite of that of the 3,5-*O*-benzylidene-D-lyxose 2*b*. The facts that the IR spectrum shows no carbonyl absorption, and that the compound is oxidized to a 1,4-lactone (4) in benzene-toluene, suggest that this 3,5-*O*-benzylidene-D-lyxose exists in a furanose form (2). The fact that cyclization of the benzylidenelyxose 2*b* to a furanose form

(2*c*) is not observed, may be a result of the unfavourable interactions of the hydroxyl group at C-2 in the furanose ring with the benzylic carbon atom and with C-5 in the lyxose part. These interactions are of the *syn* 1-3 diaxial type if the 1,3-dioxan ring exists in the chair conformation (2*c*) with the phenyl group equatorially attached.

The observed differences between 4,6-*O*-alkylidene derivatives of glucose on one hand and those of galactose on the other, in the oxidation with silver carbonate on Celite in benzene-DMF could arise from steric differences in the pyranose rings caused by the *trans*-fused 1,3-dioxan ring in the glucose derivatives, resulting in a very rigid, *trans*-decalin type conformational situation,⁶ whereas the dioxan ring is *cis*-fused in the galactose derivatives, and hence leads to a much more flexible, *cis*-decalin type situation. The explanation could, however, also be found simply in differences in the anomeric ratio of the reacting hexose derivatives, and a product composition dependent on this ratio. It was therefore of interest to determine the relative reactivity of the anomers of 4,6-*O*-alkylidenehexoses. Samples withdrawn from the reaction mixtures during the oxidation of the ethylidene derivatives (5 and 10), were therefore trimethylsilylated and analysed by GLC (Table 1). A rapid decrease in the amounts of the β -anomeric forms was observed, and the α -anomer of 4,6-*O*-ethylidene-D-galactopyranose was also relatively rapidly oxidized, whereas the α -anomer of the glucose derivative disappeared

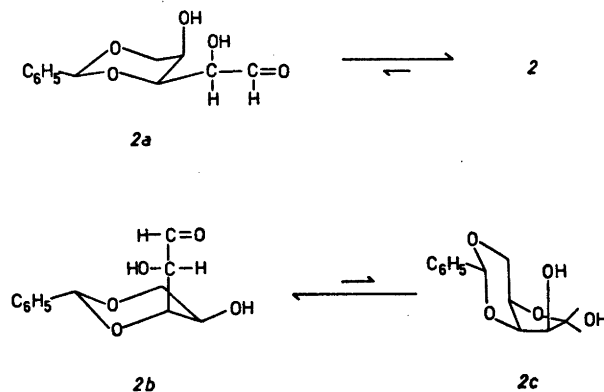


Table 1. GLC of the anomers of 4,6-*O*-ethylidenehexoses and their oxidation products as *O*-trimethylsilyl derivatives. For conditions see experimental part.

Compound	Relative retention time
4,6- <i>O</i> -Ethylidene- α -D-glucopyranose	1.00
4,6- <i>O</i> -Ethylidene- β -D-glucopyranose	1.20
4,6- <i>O</i> -Ethylidene-D-glucono-1,5-lactone	1.79
4,6- <i>O</i> -Ethylidene- α -D-galactopyranose	1.24
4,6- <i>O</i> -Ethylidene- β -D-galactopyranose	1.53
Major product ^a	1.44
Minor product ^b	3.09

^a Presumably 4-*O*-formyl-3,5-*O*-ethylidene-*aldehydo*-D-lyxose. ^b Presumably 4,6-*O*-ethylidene-D-galactono-1,5-lactone.

slowly. The minor oxidation product from the galactose derivative, presumably 4,6-*O*-ethylidene-D-galactono-1,5-lactone, was found to be formed rapidly in the initial phase of the reaction, the rate being comparable to that with which the β -anomeric form of the 4,6-*O*-ethylidenehexoses disappeared. From the glucose derivative (10), almost exclusively one product, indistinguishable from 4,6-*O*-ethylidene-D-glucono-1,5-lactone (12), was observed.

The results obtained indicate that the β -anomeric forms of the 4,6-*O*-ethylidenehexoses are oxidized to the corresponding lactones. The α -anomer of the galactose derivative is cleaved between C-1 and C-2 more rapidly than it is anomerized, the reactivity of the α -anomer of the glucose derivative, on the other hand, seems to be very low, and anomerization to the β -form, followed by oxidation of this anomer to the lactone, occurs more rapidly than degradation.

The low reactivity of 4,6-*O*-alkylidene- α -D-glucopyranoses in degradation to pentose derivatives in benzene-DMF could be due to a pronounced difference in energy between the preferred chair conformation and a conformation with the C-1-O-1 and C-2-O-2 bonds in

the pyranose ring co-planar, caused by the *trans*-fused 1,3-dioxan ring. A related phenomenon is the relatively great deviation from planarity of the same bonds in 1,2:4,6-di-*O*-alkylidene- α -D-glucopyranoses.⁷ On the other hand, in the 4,6-*O*-alkylidene- α -D-galactopyranoses the *cis*-fused 1,3-dioxan ring results in a high conformational flexibility in the pyranose ring and presumably in a much lower energy difference between the preferred conformation of the pyranose ring and the transition state conformation. Previous results support the proposal that co-planarity of the groups involved in degradation by silver carbonate on Celite is favourable, since a preference for oxidative degradation of sugars in furanose forms has been observed,^{2,8} in which co-planarity of these groups is readily attained by the anomer with *cis*-configuration at C-1, C-2 or for ketoses C-2, C-3.

The resistance against flattening of the pyranose ring in the 4,6-*O*-alkylidenehexoses might, however, also be expected to lead to a decreased reactivity in oxidation to lactones, since introduction of a lactone group in a six-membered ring causes a change towards planarity of the carbon and oxygen atoms involved in order to allow resonance stabilization.⁹ As no difference in reactivity was observed between the β -anomers of the 4,6-*O*-ethylidenehexoses, the effect of such a resistance must be considerably less important than it is in the degradation of the α -anomers. The observed instability of the lactone rings of 4,6-*O*-alkylidene-D-glucono-1,5-lactones is, on the other hand, presumably a result of the tendency to release the strain in the lactone ring in the compounds.

That the oxidation of 4,6-*O*-ethylidene-D-glucopyranose (10) in methanol, contrary to what is observed in benzene-DMF, leads to degradation may possibly be explained by the possibility of hemiacetal formation between the sugar and the solvent and degradation of the resulting α -hydroxy hemiacetal, which is present in equilibrium with the pyranose forms.

The proposed need for co-planarity of the reacting C-O bonds in degradation with silver carbonate on Celite, may also explain why 3,5-*O*-benzylidene-D-lyxose (2) is oxidized to the corresponding lactone (4) in benzene-toluene, and not degraded to 2,4-*O*-benzylidene-

D-threose (3). The β -anomer, which has the needed *cis*-configuration at C-1, C-2 for degradation, is unlikely to be present in substantial amounts since four substituents on the same side of a furanose ring are energetically unfavourable. An additional explanation could be that for the β -anomer, the approach to the oxidant surface of the reacting hydroxyl groups is hindered by the 3,5-*O*-benzylidene group.

The results obtained in the present work show the importance of conformational effects on the product composition obtained from sugar derivatives with silver carbonate on Celite in benzene or benzene-DMF.

From the 4,6-*O*-alkylidenegalactoses, where the *cis*-fused 1,3-dioxan ring leads to a conformationally flexible pyranose ring, the product ratio seems to be determined mainly by the ratio of the anomers present. The 4,6-*O*-alkylidene-glucoses, on the other hand, seem to be oxidized almost exclusively in the β -form, presumably due to resistance against degradation of the α -form caused by the puckering effect of the *trans*-fused 1,3-dioxan ring.

The importance of the choice of solvent is also clearly demonstrated. The earlier finding^{1,10} that oxidation in methanol gives the most extensive degradation, presumably due to the possibility of this solvent to form hemiacetals with the α -hydroxyaldehydes and hence allowing degradation in acyclic form to occur, is supported by the present results.

EXPERIMENTAL

Paper chromatography was performed on Whatman No. 1 paper with butanol-pyridine-water 5:3:1 (v/v), and electrophoresis in borate buffer at pH 10. TLC was carried out on Silica gel G plates in A, benzene-ethanol 3:1; B, benzene-ethanol 5:1; and C, chloroform-methanol 10:1. The compounds were detected with aniline oxalate (PC), diphenylamine-aniline-phosphoric acid¹¹ (electrophoreses and TLC), and hydroxylamine-iron(III) chloride¹² (TLC). GLC was performed on a Perkin-Elmer F 11 gas chromatograph, equipped with a flame-ionization detector, using a glass column (180 \times 0.15 cm) with 3% XE 60 on Chromosorb G AW-DMCS (80-100 mesh). The operating temperatures were 120 $^{\circ}$ C for 5 min, and then programmed at 2 $^{\circ}$ C/min for *O*-isopropylidene derivatives, prepared for identification of degradation products, and 140-215 $^{\circ}$ C programmed at 3 $^{\circ}$ C/min for *O*-trimethylsilyl derivatives. The nitrogen flow-

rate was 20 ml/min. Mass spectrometry was carried out with an AEI MS-902 and a Micro-mass 12 F mass spectrometer.

3,5-*O*-Benzylidene-D-lyxose (2). 4,6-*O*-Benzylidene-D-galactopyranose⁵ (1, 100 mg) in DMF (40 ml) and benzene (200 ml) was refluxed and stirred with silver carbonate on Celite (2 g) for 90 min. The solution was filtered and the solvents removed under reduced pressure. The residue was treated with Dowex 1 (HCO_3^-) ion exchange resin in water (10 ml) and methanol (10 ml) for 30 min. Filtration and evaporation of the solvents gave a chromatographically homogeneous (TLC, solvents B and C) residue which crystallized on standing. Yield 49 mg (55%), after recrystallization from acetone the product had m.p. 148-150 $^{\circ}$ C, $[\alpha]_D^{20} + 18^{\circ}$ (c 1, acetone). Found: C 59.70; H 5.88. Calc. for $\text{C}_{13}\text{H}_{14}\text{O}_5$: C 60.50; H 5.88. IR (KBr): No carbonyl absorption.

Hydrolysis of a few mg of the product in 0.5 M sulfuric acid at 90 $^{\circ}$ C for 1 h, neutralization with Dowex 1 (HCO_3^-) ion exchange resin and subsequent paper chromatographic and electrophoretic investigation of the solution showed a single component, indistinguishable from lyxose.

Periodate oxidation of 3,5-*O*-benzylidene-D-lyxose (2). 3,5-*O*-Benzylidene-D-lyxose (2, 40 mg) in water (5 ml) was treated with sodium periodate (50 mg) for 1 h, the solution being maintained at pH 7 by addition of small amounts of sodium hydrogen carbonate. Barium acetate (0.5 M) was added until precipitation was complete, and after centrifugation of the solution and evaporation of the solvent, the residue was extracted with chloroform. Removal of the chloroform gave solid 2,4-*O*-benzylidene-D-threose (3), m.p. 110-115 $^{\circ}$ C (reported¹³ for the L-enantiomer 119-120 $^{\circ}$ C), $[\alpha]_D^{20} + 66^{\circ}$ (c 0.3, pyridine) (lit.¹⁴ +77.6 $^{\circ}$). The product was indistinguishable (TLC) from a sample of 2,4-*O*-benzylidene-D-threose (m.p. 110-113 $^{\circ}$ C) prepared from 4,6-*O*-benzylidene-D-galactose (1) by periodate oxidation. From both preparations two components were seen, each giving a yellow colour when visualized with diphenylamine-aniline-phosphoric acid (R_F 0.63 and 0.69 in solvent B, R_F 0.77 and 0.85 in solvent C), presumably corresponding to a monomeric and a dimeric form of 2,4-*O*-benzylidene-D-threose.

Treatment of the product with acetone containing 1% sulfuric acid for 2 h, neutralization with solid sodium hydrogen carbonate, filtration and evaporation of the acetone, gave 1,2-*O*-isopropylidene- β -D-threo-furanose, m.p. 81-84 $^{\circ}$ C (lit.¹⁵ 84 $^{\circ}$ C), $[\alpha]_D^{20} - 11^{\circ}$ (c 1, acetone) (lit.¹⁵ -15.3 $^{\circ}$). The product was indistinguishable from an authentic sample¹⁶ (TLC, solvent C).

Oxidation of 3,5-*O*-benzylidene-D-lyxose (2) with silver carbonate on Celite in benzene-toluene. 3,5-*O*-Benzylidene-D-lyxose (2, 10 mg) in benzene (40 ml) and toluene (10 ml) was

stirred with silver carbonate on Celite at reflux temperature until TLC (solvent B) showed complete conversion of the starting material. The solution was filtered and the solvents were evaporated to give crystalline 3,5-*O*-benzylidene-D-lyxono-1,4-lactone (4), m.p. 205–207 °C, (lit.³ 203.5–206 °C). The product was detectable on the TLC-plate with the ester detecting reagent only. IR (chloroform): 1780 cm⁻¹ (s) (C = O, 1,4-lactone).

Oxidation of 4,6-*O*-benzylidene-D-galactopyranose (1) in methanol. 4,6-*O*-Benzylidene-D-galactopyranose (1, 300 mg) was stirred with silver carbonate on Celite (6 g) in methanol (60 ml) at 55 °C. After 1 h, TLC (solvent B) showed almost complete oxidation of the starting material, and after 3 h also the initially formed *O*-benzylidenelyxose was oxidized. The solution was filtered, and after addition of water (30 ml), it was stirred with Dowex 1 (HCO₃⁻) ion exchange resin for 30 min. Filtration of the solution and evaporation of the solvents gave 2,4-*O*-benzylidene-D-threose (3), yield 138 mg (59 %). TLC (solvents B and C) showed also in this case the presence of two components, indistinguishable from those obtained on periodate oxidation of 4,6-*O*-benzylidene-D-galactopyranose. The product was extracted with ethanol, and evaporation of the solvent gave a solid residue, m.p. 110–113 °C, [α]_D²⁰ +70° (c 0.3, pyridine).

Treatment of a part of the product with acetone containing 1 % sulfuric acid as described above, gave a compound indistinguishable from 1,2-*O*-isopropylidene-β-D-threofuranose (m.p. and TLC, solvent C).

3,5-*O*-Ethylidene-D-lyxose (6). 4,6-*O*-Ethylidene-D-galactopyranose (5, 500 mg) in DMF (5 ml) was poured into a stirred, boiling suspension of silver carbonate on Celite (5 g) in benzene (150 ml). After 4 h of continued boiling, the solution was filtered and the solvents were evaporated under reduced pressure. The residue was stirred with Dowex 1 (HCO₃⁻) ion exchange resin in methanol (10 ml) and water (10 ml) for 30 min, the solution was filtered and the solvents were evaporated to give syrupy 3,5-*O*-ethylidene-D-lyxose (6). Yield 330 mg (77 %), [α]_D²⁰ +12° (c 3, methanol). MS [IP 70 eV; *m/e* (% rel inst.)]: 175 (1.5), 161 (1.5), 159 (2), 149 (5), 117 (24), 102 (24), 73 (56), 45 (100), 43 (67). Mol. wt. M–H obs. 175.0617, calc. for C₇H₁₁O₆ 175.0606.

Hydrolysis as described for 3,5-*O*-benzylidene-D-lyxose (2) gave a product indistinguishable (paper chromatography and electrophoresis) from lyxose.

Identification of D-galactonic acid. The ion exchange resin from the previous experiment was treated with 1 M trifluoroacetic acid, the water and acid were evaporated under reduced pressure and the residue was treated with acetic acid (30 %) at 90 °C for 18 h. Evaporation of the solvents gave a syrup (80 mg), indistinguishable from D-galactono-1,4-lactone by TLC

(solvent A), [α]_D²⁰ –42° (c 2, water, final) (lit.¹⁸ –48.2°), m.p. of the derived phenylhydrazide 198–200 °C (lit.¹⁹ 200–205 °C).

Periodate oxidation of 3,5-*O*-ethylidene-D-lyxose (6). 3,5-*O*-Ethylidene-D-lyxose (6, 40 mg) was oxidized as described for 3,5-*O*-benzylidene-D-lyxose (2) to give a crystalline product. Initially the m.p. was 107–125 °C, but a slow increase of the melting point was observed with time. After recrystallization from ethanol–light petroleum it was 165–166 °C (reported²⁰ for the dimeric form of 2,4-*O*-ethylidene-D-threose 163–165 °C), [α]_D²⁰ –5° (c 2, chloroform) (lit.²⁰ –5.2°).

The obtained 2,4-*O*-ethylidene-D-threose (7) was treated with acetone–sulfuric acid as described for 2,4-*O*-benzylidene-D-threose (3), to give 1,2-*O*-isopropylidene-β-D-threofuranose, indistinguishable from the authentic sample (TLC, solvent C, and m.p.).

Oxidation of 4,6-*O*-ethylidene-D-galactopyranose (5) in methanol. 4,6-*O*-Ethylidene-D-galactopyranose (5, 300 mg) in methanol (60 ml) was stirred at reflux temperature with silver carbonate on Celite (6 g) for 2 h. The solution was filtered and water (30 ml) was added and the solution was treated with ion exchange resin as described above. Work-up in the usual way gave crystalline 2,4-*O*-ethylidene-D-threose (7). Yield 138 mg (65 %), m.p. 122–127 °C, after recrystallization from ethanol–light petroleum, crystals were obtained with m.p. 163–164 °C, [α]_D²⁰ –6° (c 2, chloroform). The product was indistinguishable from the product obtained by periodate oxidation of 3,5-*O*-ethylidene-D-lyxose (6) by TLC (solvents B and C).

Oxidation of 4,6-*O*-benzylidene-D-gluco-pyranose (8) in benzene–DMF. 4,6-*O*-Benzylidene-D-gluco-pyranose (8, 250 mg) in DMF (2.5 ml) was added to stirred silver carbonate on Celite (2.5 g) in boiling benzene (75 ml). Stirring was continued for 3.5 h at reflux temperature, the solution was then filtered and somewhat concentrated. From the solution 4,6-*O*-benzylidene-D-glucono-1,5-lactone (9) crystallized. Yield 123 mg (49 %), m.p. 190 °C (after recrystallization from ethyl acetate), [α]_D²⁰ +33° (c 1, acetone). Anal. C₁₅H₁₆O₆: C, H, IR (KBr): 1740 cm⁻¹ (s), (C = O, 1,5-lactone), the product was detectable (TLC) with hydroxylamine–iron(III) chloride only.

Hydrolysis of the product in 50 % aqueous acetic acid at 90 °C for 3 h, gave a product indistinguishable from glucono-1,4-lactone by TLC (solvent A, R_F 0.33), small amounts of a component with mobility corresponding to that of the 1,5-lactone (R_F 0.27) were also present.

The mother liquor from the crystallization of 4,6-*O*-benzylidene-D-glucono-1,5-lactone (9) was evaporated under diminished pressure and the residue was hydrolyzed in aqueous acetic acid as above. Paper chromatography of the product showed, as the only reducing sugars,

a compound indistinguishable from glucose and traces of a component with a mobility corresponding to that of arabinose.

Oxidation of 4,6-O-ethylidene-D-glucopyranose (10) in benzene. 4,6-O-Ethylidene-D-glucopyranose (10, 100 mg) in boiling benzene (250 ml) was stirred with silver carbonate on Celite (3 g) for 3 h. Filtration and concentration of the solution gave a crystalline product; after addition of small amounts of light petroleum (b.p. 60–80 °C), the product was filtered off. Recrystallization from chloroform gave pure 4,6-O-ethylidene-D-glucono-1,5-lactone (12). Yield 70 mg (71 %), m.p. 136–141 °C, $[\alpha]_{\text{D}}^{20} + 19^{\circ}$ (c 0.5, chloroform). Anal. $\text{C}_8\text{H}_{12}\text{O}_6$: C, H. IR (chloroform): 1750 cm^{-1} (s) (C=O, 1,5-lactone), detectable (TLC) with hydroxylamine-iron(III) chloride only.

Hydrolysis of a part of the product in 50 % aqueous acetic acid for 3 h at 90 °C and evaporation of the solvents gave a syrup, containing a mixture of the D-glucono-1,4- and -1,5-lactones, indistinguishable by TLC (solvent A) from authentic samples, $[\alpha]_{\text{D}}^{20} + 6^{\circ}$ (c 2, water, 48 h) (reported²¹ for the 1,5-lactone $+ 9^{\circ}$ after 24 h), m.p. of the derived phenylhydrazide 196–198 °C (lit.¹⁹ 195–200 °C).

The mother liquor after the crystallization of 4,6-O-ethylidene-D-glucono-1,5-lactone (12) was evaporated, and the residue was hydrolyzed in 0.5 M sulfuric acid at 90 °C for 1 h. The solution was neutralized with Dowex 1 (HCO_3^-) ion exchange resin and the solvent evaporated; the resulting syrup contained glucose as the major component, together with traces of arabinose, indistinguishable from authentic samples by paper chromatography and by GLC after conversion to O-isopropylidene derivatives.²²

Oxidation of 4,6-O-ethylidene-D-glucopyranose (10) in methanol. 4,6-O-Ethylidene-D-glucopyranose (10, 300 mg) was oxidized at 55 °C in methanol (60 ml) with silver carbonate on Celite (6 g) for 1 h. Work-up as described for 2,4-O-ethylidene-D-threose (7) gave chromatographically homogeneous (TLC) amorphous 2,4-O-ethylidene-D-erythrose (14), the yield was 131 mg (61 %). $[\alpha]_{\text{D}}^{20} - 36^{\circ}$ (c 1, water) (lit.²³ $- 36.8^{\circ}$). The product was indistinguishable (TLC, solvents B and C) from an authentic sample.²³ Treatment of a part of the product with acetone-sulfuric acid as described above for the 2,4-O-alkylidene-threoses (3 and 7), and subsequent oxidation of the product with silver carbonate on Celite in benzene gave 2,3-O-isopropylidene-D-erythro-1,4-lactone, m.p. 64–67 °C (lit.²⁴ 65–67.5 °C), $[\alpha]_{\text{D}}^{20} - 85^{\circ}$ (c 1, acetone) (lit.²⁴ $- 116^{\circ}$, c 0.3, water), indistinguishable from an authentic sample⁸ by TLC (solvent C).

Oxidation of 4,6-O-isopropylidene-D-glucopyranose (11) in benzene. 4,6-O-Isopropylidene-D-glucopyranose²⁵ (11, 100 mg) was stirred with silver carbonate on Celite (3 g) in boiling benzene (250 ml) for 3 h. Filtration and concentration of the solution and addition of light

petroleum (b.p. 60–80 °C) gave amorphous 4,6-O-isopropylidene-D-glucono-1,5-lactone (13), chromatographically (TLC, solvents B and C) homogeneous, detectable with hydroxylamine-iron(III) chloride only. Yield 71 mg (72 %), $[\alpha]_{\text{D}}^{20} + 23^{\circ}$ (c 2, chloroform). Anal. $\text{C}_9\text{H}_{14}\text{O}_6$: C, H. MS [IP 70 eV; m/e (% rel. int.)]: 203 (34), 160 (3), 143 (22), 131 (5), 125 (5), 115 (6), 101 (5), 97 (9), 85 (7), 73 (34), 59 (74), 43 (100). IR (chloroform): 1750 cm^{-1} (s), (C=O, 1,5-lactone).

Hydrolysis of a part of the product as described for 4,6-O-ethylidene-D-glucono-1,5-lactone (12) gave the D-glucono-1,4- and -1,5-lactones, indistinguishable from the authentic specimens by TLC (solvent A), $[\alpha]_{\text{D}}^{20} + 10^{\circ}$ (c 2, water, 48 h), m.p. of the derived phenylhydrazide 195–199 °C.

The concentrated solution obtained from separation of 4,6-O-isopropylidene-D-glucono-1,5-lactone (13) was taken to dryness under reduced pressure, the residue after hydrolysis contained glucose and small amounts of arabinose, as detected by GLC of their O-isopropylidene derivatives.

Comparison of the reactivities of the anomers of the 4,6-O-ethylidenehexoses (5 and 10). The 4,6-O-ethylidenehexose to be investigated (10 mg) was dissolved in DMF (2 ml), the solution was heated at 80 °C for 15 min. Benzene (20 ml) was added and the solution heated at reflux temperature for 20 min. To 20 ml of the solution was added silver carbonate on Celite (400 mg) and the mixture was stirred under reflux. Aliquots (50 μl) were withdrawn at intervals, immediately trimethylsilylated (trimethylchlorosilane-hexamethyldisilazane-pyridine 0.05:0.1:0.5 ml) and subjected to GLC. From the remaining part (2 ml) of the solution, which was kept at reflux temperature without oxidant, samples were also withdrawn, trimethylsilylated and investigated by GLC to ensure that no significant change in the anomeric ratio occurred in the absence of oxidant. Assignment of configuration to the anomers in the gas chromatogram was achieved by trimethylsilylation followed by GLC of the crystalline α -anomers of the 4,6-O-ethylidenehexoses, almost exclusively a single peak was observed in both cases.

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