Epimerization of Monosaccharides Under Acetolysis Conditions

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Monosaccharides with a *cis*-configuration at C-2 and -3 readily undergo inversion at C-2 in an acetolysis medium composed of acetic acid, acetic anhydride, and sulfuric acid. The acetolysis-inversion reaction has been carried out with 2,3;5,6-di-*O*-isopropylidene-D-gulofuranose, 2,3;6,7-di-*O*-isopropylidene-D-*glycero*-D-*gulo*-heptose, 2,3-*O*-isopropylidene-D-ribose, D-ribose, and D-mannose using chromatography for isolation of the deacetylated epimeric products. The reaction requires a medium with a high concentration of acetic acid (*ca.* 90%) and appears to take place only with furanose structures. Inversions observed with the unsubstituted pyranoses D-ribose and D-mannose probably occur because of tautomerization to furanose forms. The epimerization proceeds in the direction which yields a smaller number of *cis*-oriented groups at C-2, -3, and -4 of the furanose forms of monosaccharides.

Les monosaccharides avec une configuration *cis* au C-2 et -3 subissent une inversion rapide au C-2 dans un mélange acétolysant composé d'acide acétique, d'anhydride acétique et d'acide sulfurique. La réaction d'acétolyse produisant une inversion a été effectuée avec le di-*O*-isopropylidène-2,3;5,6, D-gulofuranose, le di-*O*-isopropylidène-2,3;6,7 D-*glycéro*-D-*gulo*-heptose, le *O*-isopropylidène-2,3 D-ribose, D-ribose, et le D-mannose utilisant la chromatographie pour l'isolation des composés désacétylés épimères. La réaction exige un milieu avec une grande concentration d'acide acétique (*ca.* 90%) et semble fonctionner uniquement avec des structures furanosiques. Les inversions observées avec les pyranoses non substitués tel que le D-ribose et le D-mannose sont probablement dûes à la tautomérisation vers les formes furanosiques. L'épimérisation s'oriente dans la direction qui donne un plus petit nombre de groupements orientés en position *cis* au C-2, -3, et -4 des formes furanosiques des monosaccharides.

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Introduction

Several years ago Jerkeman (1) made the unusual observation that D-glucose was formed from certain derivatives of D-mannose when they were acetolyzed. Treatment of 2,3;5,6-di-*O*-isopropylidene-D-mannofuranose, methyl β-D-mannofuranoside or 1,5,6-tri-*O*-acetyl-2,3-*O*-isopropylidene-D-mannofuranose with a mixture of acetic acid, acetic anhydride, and sulfuric acid at room temperature yielded, after deacetylation, a 4:1 mixture of D-glucose and D-mannose. No C-2 inversion was observed on acetolysis of ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranoside, methyl α-D-mannopyranoside, methyl β-D-glucopyranoside or derivatives of D-galactofuranose, D-xylofuranose, and L-arabinofuranose; phenyl β-D-glucofuranoside gave a trace of D-mannose. It was suggested that epimerization of D-mannofuranose derivatives occurs under acetolysis conditions through conversion of a *cis–trans* arrangement of three contiguous hydroxyl groups into a *trans–cis* arrangement via cyclic acetoxonium intermediates. Protonation causes the two *cis*-acyloxy groups at C-2 and -3 to join in a seven-membered ring which undergoes nucleophilic attack by an acyloxy group *trans*-situated on an adjacent carbon. The second cyclic ion which is formed then hydrolyzes to afford the epimer D-glucose. There are several related interconversions of carbohydrates which are considered to take place by similar successive neighboring acyloxy group participation. Cyclohexane polyols epimerize at elevated temperatures in 95% acetic acid – toluenesulfonic acid (2*a*), 95% acetic acid – sulfuric acid (2*b*, *c*, *d*), acetic acid – acetic anhydride – sulfuric acid (2*d*) and acetic acid – sulfuric acid (2*d*). More recently cyclopentane polyols have been isomerized in 95% acetic acid – sulfuric acid (3). Other reports describing different media include the deacylation–inversion of cyclitols (4*a*), polyhydroxytetrahydropyrans (4*b*), and aldoses (4*c*) in liquid hydrogen fluoride, and the transformations of carbohydrate acetates by antimony pentachloride (5), by zinc chloride in acetic anhydride (6), and by phosphorus pentachloride and aluminum chloride in chloroform (*cf.* 7).

Acetolysis has many valuable applications in carbohydrate chemistry (8). The general desirability of avoiding inadvertant production of artefacts made further examination of the acetolysis-inversion reaction of interest. It was highly unlikely that such epimerization was unique to D-mannofuranose derivatives. It was also of

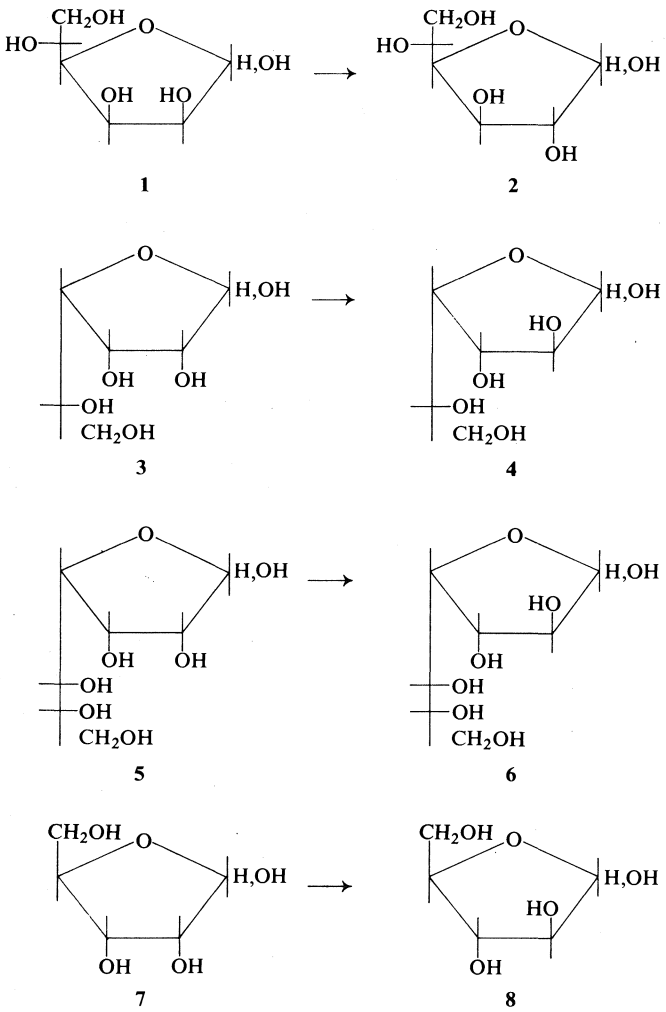
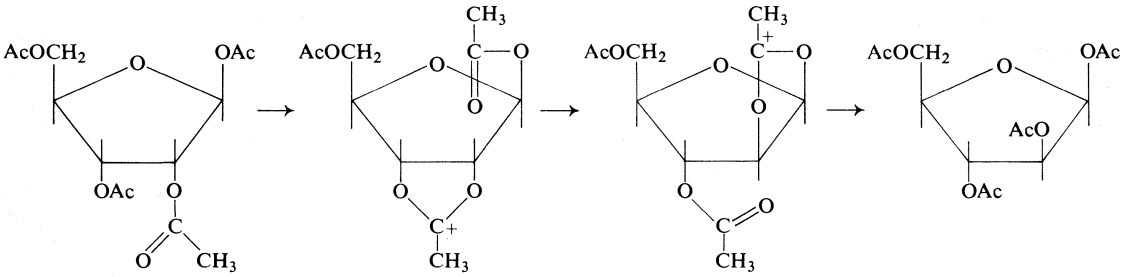


FIG. 1. Furanose structures of D-mannose (**1**), D-glucose (**2**), D-gulose (**3**), D-idose (**4**), D-*glycero*-D-*gulo*-heptose (**5**), D-*glycero*-D-*ido*-heptose (**6**), D-ribose (**7**), and D-arabinose (**8**).

interest to investigate the acetolysis-inversion reaction since, unlike the inversions mentioned above, it appeared to be confined to furanose sugars. In addition, the reaction appeared to have some value in synthesis for carrying out C-2 hydroxyl inversion without resort to the Lobry de Bruyn – Alberda van Ekenstein transformation (9) which normally requires an alkaline medium.

Results and Discussion

The close similarity between the furanose structures of D-mannose (**1**) and D-gulose (**3**) (Fig. 1) suggested that carbohydrate derivatives with the *gulo* configuration might be convertible to the *ido* by acetolysis. 2,3;5,6-Di-*O*-isopropylidene-D-gulose (10) and 2,3;6,7-di-*O*-isopropylidene-D-*glycero*-D-*gulo*-heptose (11) were each treated with the mixture of acetic acid, acetic anhydride, and sulfuric acid described by Jerkeman (1). Experiments followed by t.l.c. indicated that the maximum yield of epimers from both *gulo* sugars occurred at about 30 h. This time is one-half that reported for the conversion of D-mannose to D-glucose (1). After treatment of the reaction mixtures with triethylamine for deacetylation, the products were isolated chromatographically and weighed. From 2,3;5,6-di-*O*-isopropylidene-D-gulose, D-idose and D-gulose were obtained in a ratio of approximately 3 to 1.



The ratio ranged between 2.5 to 1 and 3.4 to 1, possibly because of decomposition of sugars during acetolysis and variability in chromatographic recovery which in turn may have been related to the scale of the experiment. The yield of D-idose varied between 36 and 51%. The 2,3;6,7-di-*O*-isopropylidene-D-*glycero*-D-*gulo*-heptose on acetolysis gave D-*glycero*-D-*ido*-heptose and D-*glycero*-D-*gulo*-heptose in a ratio of 2 to 1; the yield of D-*glycero*-D-*ido*-heptose was 47%. The use of triethylamine for deacetylation is a procedure communicated to Jerkeman by Whelan (1). The possibility of epimerization under deacetylation conditions was investigated by deacetylation of D-*glycero*-D-*gulo*-heptose hexaacetate and examination of the product by t.l.c. No D-*glycero*-D-*ido*-heptose was detected.

Jerkeman, after finding that derivatives of D-galactose, D-xylose, and L-arabinose did not rearrange on acetolysis, suggested that C-2 inversion would be observed with the furanosidic acetates of their epimers (1). The prediction has now been confirmed for ribose. 2,3-*O*-Isopropylidene-D-ribofuranose (12) was acetolyzed at room temperature for 90 h, not necessarily the optimum time, and worked-up in the usual manner. D-Arabinose and D-ribose were isolated chromatographically in the ratio of 0.8 to 1.

An observation relating to furanoses is that acetolysis of the 1,2-*O*-isopropylidene derivatives of D-glucofuranose triacetate and D-xylofuranose diacetate leaves the sugars in the furanose form with little or no conversion to pyranose acetate taking place (1, 13). A recent synthesis of 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose from methyl D-ribofuranoside takes advantage of the stability of the acetylated furanose structure in an acetolysis medium (14). It appeared possible that if free sugars were dissolved in an acetolyzing medium, tautomerization might occur with the formation of relatively large amounts of furanoses. The acetolysis-inversion data accumulated thus far show that derivatives of certain sugars epimerize only in the furanose form. Therefore a pyranose to furanose conversion of the free sugars should be indicated by the appearance of epimers. This expectation was borne out by results of experiments with D-ribose and D-mannose. Crystalline D-ribose, which has a pyranose structure (15), and α-D-mannopyranose were each acetolyzed for 24 h in the usual manner. From the reaction with D-ribose, D-arabinose and D-ribose were isolated in the ratio of 0.85 to 1, while D-mannose yielded a mixture of D-glucose and D-mannose in 0.3 to 1 ratio. The epimerizations are indirect evidence for the existence of furanose modifications of the two monosaccharides in the acetolysis medium which was employed.

In the original work on C-2 inversion of D-mannofuranose (1), the formation of a seven-membered cyclic acetoxonium ion as the first species was favored in conformity with a mechanism postulated for transformations of cyclitol acetates in hydrogen fluoride (4*a*). An alternative mechanism with five-membered cyclic acetoxonium ions was preferred to explain the epimerization of cyclitols in acetic acid – sulfuric acid (2*d*). More recently direct evidence for a five-membered cyclic structure has been provided from n.m.r. studies of *cis* and *trans* isomers of 1,2-diacetoxycyclohexane in hydrogen fluoride (16). The *trans* isomer was unreactive while the *cis* was quantitatively converted to a 2-methyl-1,3-dioxolenium ion and acetic acid. The cyclic ion was isolated as the crystalline tetrafluoroborate. In the case of furanoses in an acetolysis medium, inversion at the central carbon of a *cis–trans* sequence of substituents probably proceeds through a transient tricyclic system of five-membered rings in which little change in position is required for the atoms directly involved.

The data collected in the present work and that of Jerkeman (1) indicate that only monosaccharides with a *cis*-2,3 configuration epimerize in an acetolysis medium. The inversion can be related to the nonbonded repulsive interactions in the furanose forms of such monosaccharides. The initial configuration of the anomeric group is unimportant since it can be assumed to readily take up a configuration *trans* to its neighbor. It is apparent then that the C-2 inversion of monosaccharides in an acetolyzing medium proceeds in the direction which yields a smaller number of *cis*-groups at C-2, -3, and -4 of the furanose form. The conversions which have been observed and the number of groups in a *cis*-orientation are as follows: D-mannose (**1**) to D-glucose (**2**) (3 and 2), D-gulose (**3**) to D-idose (**4**) (3 and 2), D-*glycero*-D-*gulo*-heptose (**5**) to D-*glycero*-D-*ido*-heptose (**6**) (3 and 2) and D-ribose (**7**) to D-arabinose (**8**) (2 and 0). The case of furanoses with all *cis* substituents at C-2, -3, and -4 (mannose and gulose configurations) is interesting. They have comparatively high free energies and n.m.r. spectra of aqueous equilibrium solutions of D-mannose and D-lyxose show no furanose while that of D-*glycero*-D-*gulo*-heptose shows very little (17). In water the interactions between *cis* substituents on adjacent carbon atoms are relieved by a ring expansion to the pyranose form which accommodates bulky groups in equatorial positions. In an acetolysis medium of a suitable composition, an alternative device consisting of a furanose (*cis*) to furanose (*trans*) transformation by way of acetoxonium ions becomes feasible. The mild conditions under which the inversion takes place with furanoses are in remarkable contrast to similar inversions reported with other five-membered cyclic structures, the cyclopentanepolyols (3). The latter require heating in 95% acetic acid – sulfuric acid for many hours.

The easy C-2 inversion of D-ribose in an acetolyzing medium appeared to be inconsistent with the results of Reist *et al.* who acetolyzed 4-*S*-benzoyl-4-thioribopyranose derivatives to 4-thio-ribofuranose compounds without epimerization of the latter (18). When their experimental conditions were used with D-ribose, the starting material was recovered accompanied by only a trace of D-arabinose detectable by paper chromatography. The experiment was repeated maintaining the 1:1 ratio of acetic acid:acetic anhydride but in one case increasing the concentration of sulfuric acid and in another raising the temperature from 0° to room temperature. These modifications had no effect on the extent of epimerization and again only a trace of D-arabinose was detectable. Under the more vigorous reaction conditions an unidentified compound with a chromatographic mobility greater than that of D-ribose was formed. It was not examined further. Epimerization in an acetolysis medium is thus related to the concentration of acetic acid since inversion occurs in a medium of 10:1 but not 1:1, acetic acid:acetic anhydride.

The importance of acetic acid concentration explains why C-2 inversion has not been observed more often during the long history of acetolysis. Epimerization takes place in a medium of 10:1 acetic acid:acetic anhydride in the presence of sulfuric acid. In contrast the classic "isomerizing mixture" first used by Hudson and associates in 1934 (ref. 19 and refs. in 20) for anomerization and for acetolysis of glycosides, acetals, and anhydrosugars was a 3:7 or 1:2 mixture of acetic acid and acetic anhydride plus sulfuric acid. On one occasion, D-*glycero*-D-*gulo*-heptose was treated for 48 h at 20° with a 1:2 mixture of acetic acid and acetic anhydride, with 2.5% by volume of sulfuric acid (21). An 80% yield of α- and β-hexaacetates of D-*glycero*-D-*gulo*-heptose was obtained. On the other hand in the present work with an "epimerizing mixture", acetolysis of the isopropylidene derivative of the same heptose yielded the *ido* isomer as the major product. A preparation of 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose by acetolysis of a methyl ribofuranoside mixture has been described (14). In one variation the ratio of acetic acid to acetic anhydride was 1.5 to 2 while in the other it was 30 to 7. In the latter case an unidentified component was detected by t.l.c. It is possible that this is the acetate of D-arabinose. Studies of anomerization mechanisms have not been inconvenienced by C-2 inversions since they have been conducted usually, but not always, with low acetic acid:acetic anhydride ratios of 1:1 (22) and 3:10 (23) and confined to acetylated pyranoses. For the acetolysis of polysaccharides, a valuable technique in structural investigations (8), it is customary to use mixtures containing from 0 to 50% acetic acid. It appears that, fortuitously, undesirable C-2 inversions have been avoided. The present work suggests that particular care should be taken if acetolyses are carried out for

structural analysis of polysaccharides containing furanose sugars with *cis*-2,3 configurations. The existence of such polysaccharides has been reported recently following the discovery of D-ribofuranose in antigenic lipopolysaccharides of *Salmonella* (24).

Experimental

General

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Optical rotations were obtained with a Carl Zeiss photoelectric polarimeter Model 0.005° using a sodium spectral light source. Visualization reagents for paper chromatography and t.l.c. were *p*-anisidine hydrochloride (25) and silver nitrate – sodium hydroxide (26). Dibenzyl dithioacetals were prepared by treatment of the sugar with toluenethiol in the presence of trifluoroacetic acid (27) for 2 h at room temperature, followed by evaporation of the mixture to dryness.

*Acetolysis of 2,3;5,6-Di-O-isopropylidene-*D*-gulofuranose*

2,3;5,6-Di-*O*-isopropylidene-D-gulofuranose was prepared by sodium borohydride reduction of 2,3;5,6-di-*O*-isopropylidene-D-gulonolactone in ether containing acetic acid (10). Yields up to 93% were obtained by using powdered borohydride from a freshly-opened bottle and by prolonging the reaction time to *ca.* 3 days. Acetolysis was carried out as described by Jerkeman (1). Preliminary experiments followed by paper chromatography indicated that the highest ratio of D-idose to D-gulose occurred at around 30 h. The following procedure was then used. To a stirred and cooled solution of 2,3;5,6-di-*O*-isopropylidene-D-gulofuranose (200 mg) in acetic acid (6 ml) and acetic anhydride (0.8 ml) was added sulfuric acid (0.3 ml). The reaction mixture was left at room temperature for 30 h and then poured into ice-water. The aqueous solution was extracted with chloroform and the extract washed with saturated sodium bicarbonate solution followed by water. The chloroform solution was evaporated to a syrup which was deacetylated overnight by a mixture of methanol (16 ml), water (2 ml), and triethylamine (2 ml). The resulting mixture was evaporated to a syrup (80 mg) which was separated on Whatman No. 4 paper in ethyl acetate – pyridine–water (5:2:5 *v*/*v*, top layer). Appropriate zones were extracted with water to yield D-idose (50 mg, 36% yield based on di-*O*-isopropylidene-D-gulose) and D-gulose (20 mg). The ratio of D-idose to D-gulose and the yield were not constant as the scale was varied. For example, in acetolysis on a 12 g scale the ratio of D-idose to D-gulose was 3.4 to 1 after chromatography on 10 sheets (46 × 57 cm) of Whatman 3MM paper; the yield of D-idose from di-*O*-isopropylidene-D-gulose was 51%.

The syrupy D-idose, $[\alpha]_D^{22}$ +16.2° (*c* 2.5 in water), was acetylated in pyridine – acetic anhydride but the resulting acetate did not crystallize. The syrupy acetate (100 mg) was then treated with a mixture of acetic anhydride (1 ml), acetic acid (0.5 ml), and sulfuric acid (0.02 ml) for 43 h. After work-up in the usual manner there was obtained 1,2,3,4,6-penta-*O*-acetyl-α-D-idopyranose, m.p. 92–94° and $[\alpha]_D^{22}$ +54.7° (*c* 2 in chloroform). Literature values are m.p. 91–92° and $[\alpha]_D^{21}$ +54° (*c* 1.6 in chloroform) (28).

*Acetolysis of 2,3;6,7-Di-O-isopropylidene-*D*-glycero-*D*-gulo-heptose*

2,3;6,7-Di-*O*-isopropylidene-D-*glycero*-D-*gulo*-heptose, m.p. 93–95°, and $[\alpha]_D^{21}$ −29.8° (*c* 1.2 in chloroform), was prepared by condensation of acetone with D-*glycero*-D-*gulo*-heptose as described by Brimacombe and Tucker (11) except that the sulfuric acid catalyst was replaced by zinc chloride – phosphoric acid (29) and in column chromatography ether was used in place of acetone–toluene. With zinc chloride – phosphoric acid instead of sulfuric acid as acetalation catalyst, the heptose appeared to dissolve and react more readily with less formation of acetone condensation by-products.

Small scale experiments followed chromatographically were carried out to determine the duration of acetolysis for maximum formation of the *ido* epimer of the heptose. The following procedure was then used. To a cooled and stirred mixture of 2,3;6,7-di-*O*-isopropylidene-D-*glycero*-D-*gulo*-heptose (500 mg), acetic acid (15 ml), and acetic anhydride (2 ml) was added concentrated sulfuric acid (0.75 ml). After 24 h at room temperature, the reaction was worked-up and the product deacetylated as described above for the hexose. A portion (140 mg) of the syrupy mixture (320 mg) was separated by preparative t.l.c. on two plates (20 × 20 cm) of cellulose using ethyl acetate – pyridine–water (10:4:3 *v*/*v*) as developing solvent. D-*glycero*-D-*ido*-Heptose (76 mg, 49% yield based on di-*O*-isopropylidene-D-*glycero*-D-*gulo*-heptose) and D-*glycero*-D-*gulo*-heptose (36 mg) were isolated. The D-*glycero*-D-*ido*-heptose was characterized as its dibenzyl dithioacetal, m.p. 129–130° and $[\alpha]_D^{21}$ +70° (*c* 1 in pyridine). Literature values are m.p. 130–131° and $[\alpha]_D^{20}$ +71.4° (*c* 2.6 in pyridine) (30).

To test whether any epimerization occurred in the deacetylation step, a crude crystalline mixture of α- and β-D-*glycero*-D-*gulo*-heptose hexaacetates, m.p. 122–124°, was prepared from D-*glycero*-D-*gulo*-heptose and acetic anhydride using boron trifluoride etherate as catalyst. The heptose acetate was treated with trimethylamine in the same way as the acetolysis product. Only the starting sugar, D-*glycero*-D-*gulo*-heptose, was detectable by t.l.c.

*Acetolysis of 2,3-O-Isopropylidene-*D*-ribose*

2,3-*O*-Isopropylidene-D-ribose (12) (1.0 g, b.p.$_{0.1}$ 122–124°) was acetolyzed for 90 h at room temperature in a mixture of acetic acid (30 ml), acetic anhydride (4 ml), and sulfuric acid (1.5 ml). The reaction mixture was worked-up and a portion (300 mg) of the deacetylated product was separated by t.l.c. on four plates of cellulose (20 × 20 cm) developed twice in ethyl acetate – pyridine–water (8:2:1 *v*/*v*). D-Arabinose (95 mg) and D-ribose (118 mg) were isolated. The D-arabinose, on crystallization from aqueous ethanol had m.p. 158–159° and $[\alpha]_D^{22}$ −107° (*c* 2.3 in water). Literature values are m.p. 158.5–160° and $[\alpha]_D^{25}$ −105 ± 3° (equilibrium; *c* 2 in water) (31*a*). The syrupy D-arabinose also yielded *N*-(4-nitrophenyl)-D-arabinosylamine, m.p. 204°, on reaction with *p*-nitroaniline. The literature m.p. is 206° (31*a*). The recovered D-ribose crystallized with m.p. 87–89° and $[\alpha]_D^{22}$ −18.3° (*c* 2.8 in water). Literature values are m.p. 87° and $[\alpha]_D^{25}$ −19° (equilibrium; water) (31*b*).

Epimerization of D-*Ribose in an Acetolysis Mixture*

Crystalline D-ribose (1.0 g) was treated with a mixture of acetic acid (30 ml), acetic anhydride (4 ml), and sulfuric acid (1.5 ml) at room temperature for 24 h. The reaction mixture was worked-up and a portion (200 mg) of the deacetylated product (0.84 g) was separated by chromatography on a sheet of Whatman 3MM paper developed in butanol–pyridine–water (6:4:3 *v/v*). D-Arabinose (70 mg) and D-ribose (82 mg) were isolated. The D-arabinose, $[\alpha]_D^{22}$ −107° (*c* 1.8 in water), was characterized as the dibenzyl dithioacetal, m.p. 148–149° and $[\alpha]_D^{22}$ +17.8° (*c* 1.2 in pyridine). Literature values for the thioacetal are m.p. 149° and $[\alpha]_D$ +18.6° (*c* 3.88 in pyridine) (32).

Epimerization of D-*Mannose in an Acetolysis Mixture*

Crystalline D-mannose (1.0 g) was treated for 24 h at room temperature with a mixture of acetic acid (30 ml), acetic anhydride (4 ml), and sulfuric acid (1.5 ml). The reaction mixture, after work-up and deacetylation in the usual manner, yielded a syrupy product (0.8 g). A portion (300 mg) of the mixture was separated by chromatography on Whatman 3MM paper in ethyl acetate – pyridine–water (8:2:1 *v/v*). D-Glucose (53 mg), $[\alpha]_D^{23}$ +50.1° (*c* 0.78 in water) and D-mannose (189 mg), $[\alpha]_D^{23}$ +14.6° (*c* 1.1 in water), were isolated as syrups. The D-glucose was converted to its dibenzyl dithioacetal, m.p. 136–138° and $[\alpha]_D^{22}$ −97.6° (*c* 0.8 in pyridine). Literature values are m.p. 139° and $[\alpha]_D^{15}$ −98.4° (pyridine) (33). The D-mannose was characterized as its phenylhydrazone, m.p. 200–201°. The literature value is m.p. 199–200° (34).

Non-epimerization of D-*Ribose in an Acetolysis Mixture*

The acetolysis conditions used by Reist *et al.* (18) for converting 4-*S*-benzoyl-4-thio-ribopyranosides to 4-thio-ribofuranose derivatives without observable C-2 epimerization were applied to D-ribose. To an ice-cold solution of acetic acid (38 ml), acetic anhydride (38 ml), and sulfuric acid (2.3 ml) was added 0.9 g (0.06 mol) of D-ribose. The reaction mixture was kept at 0° for 48 h and then decomposed by the addition of anhydrous sodium acetate (8.5 g). The resulting mixture was evaporated to dryness *in vacuo* with the bath temperature below 30°. The residue was partitioned between water (50 ml) and chloroform (20 ml). The aqueous layer was extracted with chloroform (3 × 10 ml) and the combined chloroform extracts were dried (anhydrous sodium sulfate) and evaporated to dryness. The residue was evaporated with methanol several times and then redissolved in chloroform (20 ml). The chloroform solution was washed with saturated sodium bicarbonate solution (3 × 10 ml), dried (anhydrous sodium sulfate), and evaporated to dryness. The resulting syrup (1.27 g) was deacetylated overnight in a solution of methanol (20 ml), water (2.5 ml), and triethylamine (2.5 ml). Evaporation of the mixture yielded a syrup (0.78 g) which was examined by paper chromatography in butanol–pyridine–water (10:3:3 *v/v*). It was composed of ribose with only a trace of arabinose. The syrupy D-ribose crystallized with m.p. 85–86°, mixed m.p. 85–87°, and $[\alpha]_D^{23}$ −18.5° (*c* 1.3 in water)

The above experiment was repeated using the same conditions (0° for 48 h) except that the concentration of sulfuric acid was increased from 2.3 to 3.3 ml. The reaction mixture was worked-up and examined chromatographically. Again, the syrupy product contained mainly D-ribose with only a trace of D-arabinose, barely detectable with the *p*-anisidine and silver nitrate reagents. The mixture contained *ca.* 10% of an unidentified component giving a positive reaction with both spray reagents and having a mobility relative to D-ribose (R_{ribose}) of 1.9.

In another variation, the procedure was repeated as before (D-ribose 0.9 g, acetic acid 38 ml, acetic anhydride 38 ml, sulfuric acid 2.3 ml, time 48 h) but the temperature was room temperature (23°) instead of 0°. The product, after work-up, was examined chromatographically. D-Ribose was the major component with a trace of D-arabinose, *ca.* 30–40% of the component with R_{ribose} 1.9 and a small amount of a second unidentified component with R_{ribose} 2.2.

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