

THERMAL DEHYDRATION OF SUGARS

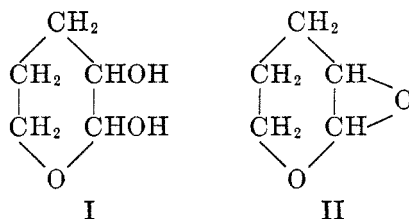
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Pictet and Castan (1) reported that α -D-glucose readily lost one mole of water at 150° under 15 mm. pressure to yield a crystalline product which was named α -glucosan. These workers, and later Cramer and Cox (2) working in the same laboratory, brought forth evidence supporting a 1,2-anhydroglucose structure for this material.

Examination of this evidence, however, shows it to be in conflict with established facts. From their α -glucosan, on treatment with sodium methoxide in methanol, they obtained a substance which was considered to be 2-methyl-D-glucose, since it reduced Fehling's solution but gave no phenylosazone (1). Actually, however, 2-methyl-D-glucose has since been shown (3) to give D-arabohexose phenylosazone when treated with phenylhydrazine and acetic acid at room temperature. Their trimethyl- α -glucosan (2), which was synthesized by treatment of an aqueous solution of α -glucosan at 35–40° with methyl sulfate and sodium hydroxide solution, was hydrolyzed on boiling with water into trimethyl-D-glucose. The phenylosazone of the latter melted at 163–164°, differing from either of the two forms (m.p. 80–82° and 137–138°) of the phenylosazone of 3,4,6-trimethyl-D-glucose (4) or of the phenylosazone (m.p. 70–72°) of 3,5,6-trimethyl-D-glucose (5). Unless another crystalline modification of one of these osazones exists, the trimethyl ether reported by Cramer and Cox is not of the structure assigned.

When α -glucosan was heated with methyl iodide and methanol in a sealed tube at 130°, and the resulting methyl iododesoxyglucoside reduced with sodium amalgam, a sirupy product was formed which was regarded as methyl 2-deoxy-D-glucoside, since on acetylation with acetic anhydride in pyridine it yielded a crystalline triacetate of m.p. 96–97°, the same melting point as that previously found (6a) for methyl triacetyl-2-deoxy-D-glucoside. This supports the structure of α -glucosan as 1,2-anhydro-D-glucopyranose. It so happens, however, that 1,2-anhydro-3,4,6-triacetyl-D-glucose has been prepared otherwise by Brigl (6b) by treatment of 3,4,6-triacetyl-D-glucosyl chloride in benzene with ammonia. Both Brigl's compound and 1,2-anhydro-D-mannose (7) have been shown to be very sensitive toward water or methanol. This is in marked contrast to the reported stability of α -glucosan and its tribenzoate. Several groups of workers have reported unsuccessful attempts to prepare crystalline α -glucosan (8).

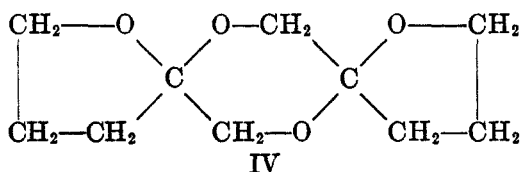


Racemic 3,4-dideoxyaldopentose (I), prepared by hydroxylation of dihydropyran (9), seemed to offer possibilities for the elucidation of this general problem. If any tendency exists for the formation of a 3-membered ring on heating glucose, it follows that the dideoxyaldopentose should show a similar tendency with the resultant formation of II. Accordingly, I was pyrolyzed under conditions comparable to those used with glucose. Like glucose, this model compound also lost water on heating to 150° under reduced pressure, or when xylene was distilled from it. Nothing resembling II was found, however. Instead, certain distillable products were obtained, namely, tetrahydrofurfural and two crystalline isomers (m.p. 103° and 190°) of formula C₁₀H₁₆O₄. There was a non-volatile water-soluble residue of mean molecular weight near 300, representing over half of the starting material.

The weight of the 103°-compound was about one-fifth that of the original (I). It was indifferent toward acetic anhydride in pyridine or toward Benedict's solution; hence it contained no free hydroxyl group or aldehyde group. It was stable to alkali but was hydrolyzed rapidly by dilute mineral acid to a reducing substance which gave both a 2,4-dinitrophenylhydrazone and a 2,4-dinitrophenylosazone. The 2,4-dinitrophenylhydrazone was isomeric with the corresponding derivative obtained from I, whereas the osazones were identical. This suggests that the hydrolysis product was 3,4-dideoxyketopentose (III), and that its crystalline precursor which melted at 103° was IV. Two names for IV are 2,5-bis(trimethyleneoxy)-1,4-dioxane and 1,6,12,13-tetraoxadispiro-[4·2·4·2]tetradecane.¹ The identical ring system occurs in the "Difructose Anhydride I," of Jackson and Goergen (10). In contrast to the ease of hydrolysis of our compound, however, theirs showed marked resistance to acid hydrolysis.



III

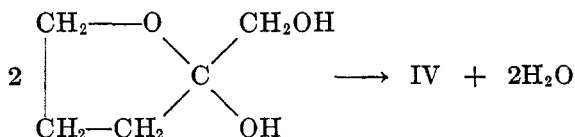


IV

To explain the formation of IV from I, it is believed that the acyclic form of I first undergoes enolization to HOCH₂CH₂CH₂C=CHOH, then changes to III.

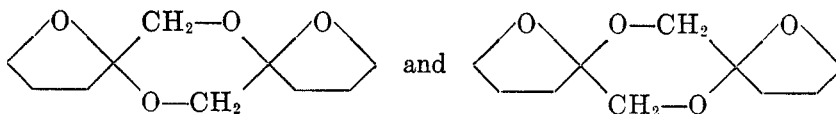


Bimolecular dehydration of III would yield IV:

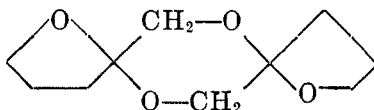


¹ In the course of our work we learned that Samuel Swadesh and A. P. Dunlop were working on the same substance, obtained from a different source (*J. Org. Chem.*, following article).

It is possible for IV to exist as a racemic pair,¹

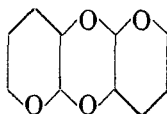


or a *meso* form,



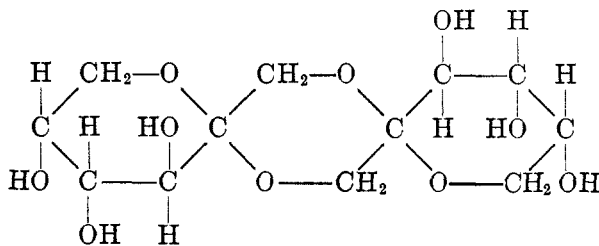
Which of these is the substance under discussion cannot be stated.

The second crystalline compound, m.p. 190.5°, was also nonreducing and stable to alkali. It was hydrolyzed very slowly by hot mineral acid to a substance which gave the 2,4-dinitrophenylosazone of I. It also may have been of structure IV (either the racemic pair or the *meso* compound), but since the new 2,4-dinitrophenylhydrazone was not obtained it also may be a dimeric anhydride of I, such as

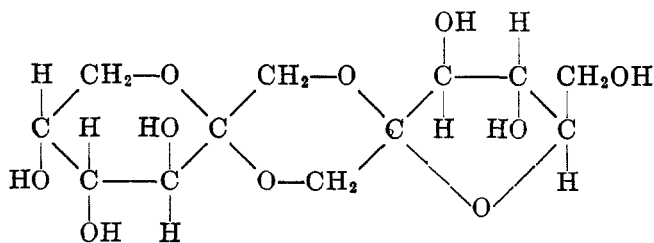


Unfortunately, the osazone is not a critical derivative and conditions were not found for the preparation of a hydrazone.

Related to these observations is the known fact that on heating concentrated solutions of D-fructose, it is possible to effect a similar kind of anhydridization. Two crystalline products have been obtained (11), one of which possesses structure V. Structure VI has been proposed for the other.



V



VI

Attempts to distill the higher molecular weight pyrolysis products from the 3,4-dideoxyaldopentose resulted in the production of considerable quantities of tetrahydrofurfural; it is, therefore, possible that all the tetrahydrofurfural

TABLE I
MELTING POINTS OF DERIVATIVES, °C.

PARENT COMPOUND	A	B	C	D	E
I.....	174.5-175.5 ^b	132-133	242 ^b	128.5-129.5 ^a	246-247 ^a
III.....	154-157	164-165	242	—	—
Tetrahydrofurfural.....	—	133-134	242	146-147	—

^a Unpublished results obtained in work with Miss Patricia Craig.

^b Ref. 9.

A. Bis-3,5-dinitrobenzoate.

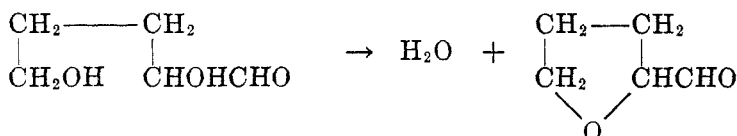
B. 2,4-Dinitrophenylhydrazone.

C. 2,4-Dinitrophenylosazone.

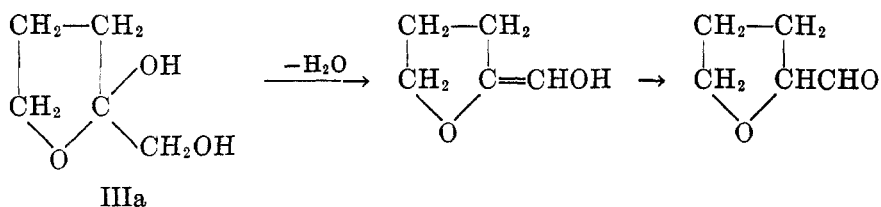
D. *p*-Nitrophenylhydrazone.

E. *p*-Nitrophenylosazone.

arises in this fashion. It is equally possible, however, that some of the tetrahydrofurfural is formed directly from the 3,4-dideoxyaldopentose as follows:



or indirectly *via* the rearrangement product (IIIa).



In connection with this study, tetrahydrofurfural *p*-nitrophenylhydrazone was prepared. Synthesis of the benzylphenylhydrazone was repeated, and its melting point was found to be higher than that reported in the literature. It was also demonstrated that on heating in acid solution with 2,4-dinitrophenylhydrazine, tetrahydrofurfural gives the same 2,4-dinitrophenylosazone as I and III. Thus the tetrahydrofuran ring is subject to ready hydrolytic cleavage. In Table I the constants of these and other derivatives are collected.

Epoxy compounds may be synthesized by the action of peroxybenzoic acid on olefins. Conceivably, therefore, 2,3-epoxytetrahydropyran (II) would be formed in this manner from dihydropyran. In studying this synthesis, we found that the bulk of the reaction product was a thick, non-volatile oil, which was insoluble in water. There was produced, however, a poor yield of an unstable,

volatile, sparingly-soluble liquid which seemed to be the desired epoxy compound. The properties of these products differ from the substances described above which were isolated following the pyrolysis of I.

In view of the above considerations, the pyrolysis of glucose was reinvestigated. It was proposed to heat the sugar under diminished pressure until a definite quantity of water was detached, then to propionylate the mixture. If the change was merely one of intramolecular dehydration as proposed by Pictet and co-workers, the propionic derivative should be completely distillable at about 200° (0.001 mm.). Monosaccharide propionates are known (12) to distil in this range. These observations were made in the present study.

(a) The loss of water from α -D-glucose under a given pressure increases steadily with time even beyond one mole. In our experiments the rate was considerably slower than that reported by Pictet. Crushed soft glass or Pyrex glass accelerates the loss of water as does diminished pressure.

(b) If an anhydroglucose is present in the lower molecular weight material the bulk of it is stable to methanol (authentic 1,2-anhydroaldoses give methyl aldoses at room temperature with dry methanol), but is converted to glucose by dilute acid and to glucose esters by acid anhydride in pyridine.

(c) Contrary to Pictet and Castan's report, β -D-glucose dehydrates as readily as α -D-glucose.

(d) Higher molecular weight materials are formed in this process, although when one mole of water has been removed, one-fourth of the product is still monosaccharide, but crystalline glucose as such was not recovered if more than two-thirds of a mole of water had been removed. These condensed materials have mean molecular weights in the di- and tri-saccharide ranges, this molecular weight increasing with the loss of water. Even the methanol-soluble product is partly polymeric, the higher molecular weight portion being resistant to hydrolysis by acid. The propionates of the higher molecular weight material could not be distilled in a molecular still, so probably contained little anhydrodisaccharide hexapropionate. Thus, although there is no direct evidence that glucose changes into a spiro compound in the way that I changes into IV, it must be remembered that the major product from I was not IV, but a material of greater complexity.

(e) An interesting aspect of the present study was the isolation of an anhydrous complex, *sodium chloride diglucose* of m.p. 168°, $(C_6H_{12}O_6)_2 \cdot NaCl$, by direct crystallization from methanol. A hydrated form of this complex has been known for over a century. Röhmann (13) obtained such a hydrate and from it by desiccation at 110° secured the anhydrous complex which may have been the same as our material. He reported no melting point, however.

Recent work on the pyrolysis of D-glucose at 170–210° has been reported by Puddington (14). He also found that dehydration continues after one mole of water is detached but that the first half mole is lost at a faster rate than otherwise. Carbon dioxide and carbon monoxide were produced. The reaction product was an amber-colored glass and no evidence was found for a crystalline C_6 α -glucosan. In view of the rapid dehydration involving 0.5 mole of water,

Puddington suggests that the first step in this reaction is a condensation dimerization: $2C_6H_{12}O_6 \rightarrow C_{12}H_{22}O_{11} + H_2O$. Our observation that dextrose was still present in most of our runs, and that monosaccharide remained even after the loss of one mole of water, is difficult to reconcile with this suggestion. His data however, are not incompatible with our suggestion that still higher condensations ensue.

EXPERIMENTAL

3,4-Didesoxyaldopentose. The reaction between hydrogen peroxide and 200 g. of dihydropyran in *tert*-butyl alcohol was carried out in a manner identical to that of Hurd and Kelso (9). After removal of the *tert*-butyl alcohol under reduced pressure, the product was warmed on the steam-bath for one hour with 400 cc. of 1 *N* hydrochloric acid, then left overnight at room temperature. After neutralization, the solution was concentrated to a thick oil at 90° under 15 mm. pressure. The organic matter was extracted into acetone, the solution dried, and the solvent distilled. The 169 g. of oil was acetylated with acetic anhydride in pyridine and the resulting acetate distilled under 1 mm. pressure. Refractionation of the distillate gave 125 g. (26% over-all yield) of ester, b.p. 96–100° under 1 mm. and having n_D^{27} 1.443 to 1.444. In addition to higher- and lower-boiling cuts, there was 60 g. of much higher-boiling residue. The 60 g. was deacetylated, hydrolyzed at 90° for two hours with 1 *N* hydrochloric acid and the product recovered and acetylated as above. One-third of the acetate boiled at 95–125° (2 mm.), n_D^{28} 1.4420 to 1.4458. The remainder was still of higher molecular weight.

To a solution of 61.8 g. of the 3,4-didesoxyaldopentose diacetate in 250 cc. of absolute methanol at 3° was added 0.2 g. of sodium. The solution stood for six hours at 0°, then was neutralized by the dropwise addition of concentrated hydrochloric acid. The product was freed of methanol and methyl acetate and was again put through the deacetylation procedure. The resulting oil was dissolved in dry acetone, the salts separated, and the solvent removed. The didesoxypentose was extracted into dry ether, leaving a syrupy residue. The soluble material was a nearly colorless oil (30 g., 84% yield), n_D^{28} 1.480.

2,5-Dihydroxypentanal 2,4-dinitrophenylhydrazone. A hot concentrated methanol solution of 2,4-dinitrophenylhydrazine hydrochloride was added slowly to an agitated ice-cold solution of 1.34 g. of 3,4-didesoxyaldopentose in 10 cc. of water. The addition was continued, with intermediate concentration below room temperature in an air stream and filtration, until no more derivative could be obtained. The 3.5 g. of product melted up to 72°. Recrystallization of this from methanol removed 0.4 g. of 2,4-dinitrophenylhydrazine, and after two more recrystallizations the tiny light-yellow plates melted at 132–133° when immersed at 110°.

Anal. Calc'd for $C_{11}H_{14}N_4O_6$: C, 44.29; H, 4.74; N, 18.78.

Found: C, 44.21; H, 4.82; N, 18.96.

When heated with methanol containing a trace of hydrochloric acid, or with 2,4-dinitrophenylhydrazine in methanol, it gave the *2,4-dinitrophenylosazone* reported by Hurd and Kelso (9), m.p. 242°.

Pyrolysis of 3,4-didesoxyaldopentose. The sugar (22.3 g.) was placed in a 50-ml. Claisen flask fitted with a capillary connected to a nitrogen source and set up for vacuum distillation. When the system was evacuated to 17 mm. pressure, and the oil-bath was heated to 145°, distillation commenced. The bath temperature was raised during one hour to 155° and during the next two hours to 180°. In this time 2.8 g. of distillate collected (cut 1), and the cold-trap (–78°) in the system collected 2.2 g. of liquid. Further heating was carried out under 1 mm. pressure. In the bath temperature range 130–170° (vapor 75–80°), 3.7 g. of distillate was obtained (cut 2) and when the temperature was raised to 185°, a further 0.9 g. (cut 3) distilled. A further 0.6 g. collected in the cold-trap. The residue in the flask weighed 12 g.

A sample of cut 1 when reacted with 2,4-dinitrophenylhydrazine hydrochloride in methanol at room temperature gave the corresponding osazone of 2,5-dihydroxypentanal and the 2,4-dinitrophenylhydrazone of tetrahydrofurfural. The latter had the form of fine yellow needles when recrystallized from methanol, m.p. 133-134° when immersed at 115°.

Anal. Calc'd for $C_{11}H_{12}N_4O_6$: C, 47.13; H, 4.32; N, 19.99.

Found: C, 47.29; H, 4.18; N, 20.70.

This derivative has been reported (16) as melting at 131° and 136°.

A concentrated solution of cut 2 in ether when chilled deposited 2.5 g. of a compound of m.p. 103°, and about 0.2 g. of a compound sparingly soluble in ether, m.p. 190.5°. Cut 3 yielded 0.2 g. each of the 103° compound and the 190.5° compound. The liquids from the mother liquors gave the 2,4-dinitrophenylosazone of the starting material and the 2,4-dinitrophenylhydrazone of 3,4-didesoxyketopentose (see below). When these liquids were distilled under 1 mm. pressure, approximately 1.5 g. of the 103° compound was obtained from the distillate, and more high-boiling residue was formed. In all, 4.1 g. of the 103° compound was isolated.

Tetrahydrofurfural. The liquid in the cold-trap consisted of water and a water-soluble, ether-soluble liquid. The latter gave a positive Schiff test and had an odor similar to acetaldehyde. It gave the 2,4-dinitrophenylosazone, m.p. 242°, and in addition to the 2,4-dinitrophenylhydrazone of tetrahydrofurfural, the following derivatives of that aldehyde were prepared.

Benzylphenylhydrazone. Faintly colored needles from methanol, m.p. 74-75°.

Anal. Calc'd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.97.

Found: C, 77.17; H, 7.27; N, 10.09.

Tetrahydrofurfural benzylphenylhydrazone is reported (17) to melt at 67°.

p-Nitrophenylhydrazone. Yellow needles from methanol, m.p. 146-147° when immersed at 130°.

Anal. Calc'd for $C_{11}H_{13}N_3O_5$: C, 56.15; H, 5.57; N, 17.86.

Found: C, 56.19; H, 5.67; N, 17.99.

When 0.15 g. of tetrahydrofurfural 2,4-dinitrophenylhydrazone was heated for one and one-half hours with a methanol solution of 2,4-dinitrophenylhydrazine hydrochloride, 0.13 g. of fine needles was obtained. After one recrystallization from nitromethane, these melted at 242° and showed no mixed m.p. depression when mixed with the 2,4-dinitrophenylosazone of 3,4-didesoxyketopentose.

2,5-Bis(trimethyleneoxy)-1,4-dioxane. The compound melting at 103° had the form of thick, nearly rectangular plates.

Anal. Calc'd for $C_{16}H_{16}O_4$: C, 59.99; H, 8.06; Mol. wt. 200.

Found: C, 60.08; H, 8.05; Mol. wt. (cryoscopically in benzene), 191.

It could be readily recrystallized from ether, was very soluble in methanol and sparingly soluble in water. It reduced hot neutral permanganate, and after a short induction period, it rapidly decolorized a solution of bromine in chloroform with hydrogen bromide evolution. It was inert to hot Benedict's reagent and was unchanged after standing for sixteen hours with acetic anhydride in pyridine. Dilute mineral acid readily hydrolyzed the compound to 3,4-didesoxyketopentose.

3,4-Didesoxyketopentose 2,4-dinitrophenylhydrazone. A 0.25-g. sample of the 103°-compound was heated with 2 cc. of water containing one drop of concentrated hydrochloric acid until it had completely dissolved (one minute). The solution was cooled in ice, and a hot saturated solution of 0.5 g. of 2,4-dinitrophenylhydrazine in methanol containing hydrochloric acid was added slowly while the mixture was agitated. The 0.65 g. of product when recrystallized from methanol separated as fine yellow needles, m.p. 164-165° when immersed at 140°.

Anal. Calc'd for $C_{11}H_{14}N_4O_6$: C, 44.29; H, 4.74; N, 18.78.

Found: C, 44.33; H, 4.83; N, 18.5.

When 0.1 g. of the above derivative was heated with a methanol solution of 0.1 g. of 2,4-dinitrophenylhydrazine as its hydrochloride, a slow precipitation of the 2,4-dinitro-

phenylosazone started. A total of 0.1 g. was obtained melting at 240°. It did not depress the melting point of an authentic sample prepared from 3,4-didesoxyaldopentose.

3,4-Didesoxyketopentose bis-3,5-dinitrobenzoate. A 0.3-g. sample of the 103° compound was hydrolyzed as described above, the acid neutralized, and the bulk of the water removed under reduced pressure. By use of ether there was extracted 0.33 g. of oil from the residue. This was dissolved in 2 cc. of pyridine, 1.5 g. of 3,5-dinitrobenzoyl chloride was added, and the solution was left overnight. The mixture was then dissolved in chloroform, washed free of pyridine, acid, and acid chloride, dried, and the chloroform distilled away. The product was a glass weighing 0.85 g. This readily crystallized from acetone, from which it was obtained microcrystalline. After repeated recrystallization, it melted at 154–157° when immersed at 135°.

Anal. Calc'd for $C_{19}H_{14}N_4O_{13}$: C, 45.06; H, 2.79; N, 11.06.

Found: C, 45.38; H, 2.89; N, 11.04.

3,4-Didesoxyketopentose dibenzoate. The oil from the hydrolysis of 0.3 g. of the 103°-compound when left overnight with 0.9 g. of benzoyl chloride and 3 cc. of pyridine gave 0.6 g. of ester. After long standing, this crystallized in part. The product after two recrystallizations from a mixture of ether and petroleum ether had the form of long needles, m.p. 67°.

Anal. Calc'd for $C_{19}H_{16}O_6$: C, 69.93; H, 5.56.

Found: C, 70.05; H, 5.56.

The high-melting compound. After recrystallization from methanol, this melted at 189.5–190.5° when immersed at 165°.

Anal. Calc'd for $C_{10}H_{16}O_4$: C, 59.99; H, 8.06; Mol. wt., 200.

Found: C, 59.88; H, 8.22; Mol. wt., 188.

The compound had a slight solubility in hot water, and could be recovered unchanged from solution in hot Benedict's reagent. After 100 mg. of this compound had been heated for three hours on the steam-bath with 3 cc. of methanol, 2 cc. of water, and two drops of concentrated hydrochloric acid, 75 mg. was recovered unchanged. The aqueous solution of the hydrolysis products, when warmed on the steam-bath with 2,4-dinitrophenylhydrazine hydrochloride gave 0.1 g. of *3,4-didesoxy-pentose 2,4-dinitrophenylosazone*, m.p. 242°. The compound could be recovered unchanged from solution in chloroform containing bromine.

Run 2. The bulk of the *o*-xylene was distilled from a mixture of 18.5 g. of 3,4-dideoxyaldopentose and 125 cc. of *o*-xylene over a period of two and one-half hours. Approximately 0.8 cc. of water distilled with the *o*-xylene. After removal of the last of the *o*-xylene under reduced pressure, an attempt was made to distill the products under 11 mm. pressure at bath temperatures up to 145°, without success. The cold-trap (–78°) collected 0.4 cc. of water. Another 75 cc. of the hydrocarbon was then distilled from the residue. It carried with it 0.2 cc. of water, making a total of 1.4 g. (50 mole per cent) of water collected. The water and the *o*-xylene contained a reducing substance which gave the *2,4-dinitrophenylosazone* of *3,4-dideoxy-pentose*.

The residue was distilled under reduced pressure.

(A) 6.6 g. b.p. 135° at 11 mm. n_D^{20} 1.4751

(B) 0.6 g. b.p. 90° at 1 mm. n_D^{20} 1.4763

(C) 1.0 g. b.p. 90–100° at 1 mm.

The cold-trap (–78°) in the system collected 0.4 g. of water containing a reducing substance, and some *o*-xylene.

When an attempt was made to redistill (A) the distillate crystallized in the condenser. A concentrated ether solution of the cut yielded 2.6 g. of 2,5-bis(trimethyleneoxy)-1,4-dioxane. When the oil from the mother liquors was redistilled under 1 mm. pressure, the distillate yielded approximately 1 g. of the same compound.

Less volatile pyrolysis products. Twenty-five grams of residues from the distillation of pyrolysis products from several runs were submitted to distillation under 1 mm. pressure in a modified Claisen flask with a very low side arm. A stream of nitrogen was introduced

through a capillary. As the bath temperature was slowly raised to 205°, a total of 5.4 g. of distillate collected. The last cut had the molecular weight 163 ± 10 . Less than 0.1 g. of the 103°-compound was obtained from the first cut, the remaining distillate being an oil. The 16.5 g. of residue was a viscous reddish-brown oil of mol. wt. 275 ± 15 , insoluble in ether but soluble in water. The cold-trap (-78°) collected 2.5 g. of a mobile liquid. This contained water, and gave tetrahydrofurfural derivatives equivalent to 1 g. of the aldehyde.

Action of hydrogen chloride on 3,4-didesoxyaldopentose. Dry hydrogen chloride was bubbled for one minute into 2.3 g. of the sugar. A red color developed quickly. The mixture thickened during five hours and crystallized in part. The product was then extracted with chloroform which dissolved the crystals and part of the oil. The chloroform solution was washed with aqueous sodium carbonate, dried, and the solvent distilled away. The resulting oil deposited crystals which were separated by dissolving the oil in ether. After one recrystallization from methanol, the 0.13 g. of crystals melted at 189° and proved identical with the compound melting at 190.5° obtained by pyrolysis.

2,3-Epoxytetrahydropyran. A solution of 52 g. (0.38 mole) of peroxybenzoic acid in 610 cc. of chloroform was prepared (18). Dihydropyran (29 g., 0.35 mole) was added during forty-five minutes to the above solution while the temperature of the mixture was kept below 5°. The reaction was exothermic. The solution was left at -6° for sixteen hours, at the end of which time the peroxybenzoic acid was almost completely gone. The chloroform solution was washed thoroughly with sodium carbonate solution, dried, filtered, and distilled. When the residual volume reached 150 cc., acid appeared in the distillate. The solution was washed thoroughly with sodium bicarbonate solution to remove benzoic acid. After drying and filtering, the solvent was distilled. The residual liquid was distilled under 9 mm. pressure:

Cut 1, b.p. 75-79°, 8.2 g. of nearly water-white liquid which turned yellowish-brown overnight. The residue was a brown oil which contained acid. It was dissolved in chloroform, washed with sodium carbonate solution, freed from solvent, and then distilled under 10 mm. pressure.

Cut 2, b.p. up to 125°, 5.8 g. of light yellow oil which became reddish-brown overnight. The residue was 12.3 g. of viscous oil.

The distillates were combined and fractionated under 9 mm. pressure using a 12-cm. Vigreux column. The cuts boiling up to 76° (3.8 g.) contained considerable methyl benzoate (carried over from the preparation of the peroxy acid). The remaining volatile material came over between 77° and 87° (3.0 g.) at bath temperatures up to 175°. It had n_D^{25} 1.455. All the cuts were sparingly water-soluble. The distillation residue was 5 g. of viscous reddish-brown oil.

The distillates could be hydrolyzed by heating with 1 *N* hydrochloric acid to a reducing, water-soluble oil which when heated with a solution of 2,4-dinitrophenylhydrazine hydrochloride gave the *2,4-dinitrophenylosazone* of *3,4-didesoxyaldopentose*, m.p. 242°.

The two distillation residues were hydrolyzed by fifteen minutes' heating on the steam-bath with 1 *N* hydrochloric acid, the solution neutralized and the water distilled under reduced pressure. The product was 12.9 g. of an ether-soluble oil. This gave the *2,4-dinitrophenylosazone* of *3,4-didesoxypentose* under the usual conditions. When it was acetylated using acetic anhydride and pyridine and the product distilled, 9.5 g. of acetate (b.p. 70-78° under less than 1 mm. pressure; n_D^{25} 1.444) was obtained. This corresponds in properties with the *diacetate* of *3,4-didesoxyaldopentose* and was hydrolyzed to a reducing substance which gave the *2,4-dinitrophenylosazone* of the aldose.

Pyrolysis of glucose. These are general directions for the several experiments. The glucose sample (alone or mixed with crushed glass) was placed in a 200-cc. round-bottom flask and weighed. The air in the flask was replaced by nitrogen, the flask evacuated and then immersed in a bath at the desired temperature. At the end of the heating period, the flask and its contents were cooled and dry air introduced. The loss in weight was determined. If the resulting glassy product was to be extracted with dry methanol, it was broken up as well as possible under that solvent.

For the dioxane extractions the product was heated to near the boiling point of dioxane

in the presence of the dry solvent. The glassy product was soft at that temperature and therefore could be worked mechanically to aid contact with the solvent. The dioxane solution was decanted, cooled, and the bulk of the solvent removed under reduced pressure. The semisolid which separated was filtered in a stream of dry air.

Propionylation and acetylation were carried out by dissolving the material in up to ten times its weight of dry pyridine, adding ten times its weight of acid anhydride with cooling to keep the temperature near 30°, then allowing the mixture to stand at room temperature for fifteen to twenty hours.

Deacetylations were effected by treatment of the esters with a little sodium methoxide in a large excess of dry methanol at 0°. After a period of four hours the base was neutralized with acetic acid and then the methanol and methyl ester removed under diminished pressure.

Selected runs are collected in Table II.

Distillation of propionates. The propionate of the methanol-soluble fractions (29 g.) from runs 1, 2, and 4 in Table I was distilled at 10^{-5} to 10^{-3} mm. (A) Bath temperature 185–190°; 3.4 g.; $[\alpha]_D +23.9^\circ$ (*c*, 1.05 in methanol); Mol. wt., 410; propionyl content 59.5%. (B) Bath temperature 210–225°; 6.6 g.; $[\alpha]_D +32^\circ$ (*c*, 1.48 in methanol); Mol. wt., 412; propionyl content 61.3%. (C) Bath temperature up to 265°; 1.7 g.; $[\alpha]_D +31^\circ$ (*c*, 1.27 in methanol); Mol. wt., 430; propionyl content 60.0%. (D) Bath temperature 265°; 3.0 g.; $[\alpha]_D +43.5^\circ$ (*c*, 1.30 in methanol); Mol. wt., 540; propionyl content 55.5%.

The molecular weights were determined cryoscopically in benzene. From values for knowns it is probable that the above values are 5–10% low.

The propionyl determinations were made by the method of Kunz and Hudson (15). The above values are corrected for a consistent error of +1% found with glucose penta-propionate when the ester stood for three hours at -10° in the presence of the base.

An attempt was made to distill the residue from this distillation in a simple molecular still. In four hours at 200° under 10^{-5} mm. a negligible quantity distilled. When cuts 1, 2, and 3 were depropionylated, the products consisted of glucose and amorphous residues which gave considerable glucose acetates on acetylation. Cut 4 gave no crystalline sugar or acetate.

Acid hydrolysis. A solution of 2.5 g. of the methanol-soluble product from runs 1, 2, and 4 in 8 cc. of 0.3 N hydrochloric acid was heated on the steam-bath for forty minutes, the final volume being 4 cc. After the addition of 15 cc. of ethanol and neutralization of the acid with sodium carbonate, the solution was filtered from precipitated salt and colored gum. After removal of 0.3 g. of the complex of glucose and sodium chloride which slowly crystallized, the solvent was removed from the solution under reduced pressure. The residue was acetylated with acetic anhydride in pyridine. A small quantity of β -D-glucose pentaacetate was obtained from a methanol solution of the 3.1 g. of product. The remaining 2.8 g., after removal of the methanol, was dissolved in benzene and put through a 2.5 × 29.5-cm. column of 5:1 Magnesol-Celite mixture previously wet with benzene. The chromatogram was developed using benzene-ethanol solutions changing in ethanol content from a 100-1 to a 1-1 ratio. The eluate contained no ester. The column was sectioned and found to contain the bulk of the material between the 18 and 26 cm. depths, half of it in a 2.5-cm. range. The *acetate* ranged in molecular weight from 530 at the top to 440 at the bottom of the absorbed material (Calc'd for monosaccharide pentaacetate, 390; an anhydro-disaccharide hexaacetate, 576). None of the acetates from the various segments could be crystallized.

Action of methanol and hydrochloric acid. Methanol-soluble material from runs 1, 2, and 4 (0.58 g.) was dissolved in 15 cc. of dry methanol and hydrogen chloride was bubbled through the solution for two minutes. The solution was heated on the steam-bath for fifteen minutes, neutralized with solid sodium carbonate, treated with activated charcoal, and filtered. After concentration to a volume of 3 cc. and seeding, 0.2 g. of methyl α -D-glucoside crystallized. Fifty mg. of methyl β -D-glucoside crystallized slowly from the mother liquor. The remaining material could not be crystallized.

Sodium chloride diglucose. The 0.3 g. of crystals mentioned above was crystallized

TABLE II
 PYROLYSIS OF D-GLUCOSE

α -D-GLUCOSE G.	PRES- SURE MM.	TEMP., °C.	TIME MIN.	LOSS OF WATER		REMARKS
				g.	mole %	
20.0	22	157-163	230	1.8	90	Product 60% soluble in dry methanol. Benzoate of soluble material could not be crystallized.
10.0	15	150-155	330	1.0	100	Product 80% soluble in methanol. No crystalline solid obtained.
20.0	1	151-155	150	0.7	35	Recovered 7% of the glucose unchanged. Less than 1 g. extracted by 60 cc. of boiling dry dioxane. Amorphous, and gave glucose acetates.
25.2	1	165	165	1.3	55	Propionate 50% distilled. Distillate Mol wt., 430. Residue Mol wt., 820.
11	1	150-160	285	1.5	140	Product 30% soluble in dry methanol.
12	1	148-154	150	0.8	66	Crushed soft glass added. Product completely soluble in dry methanol; 20% of the glucose recovered.
26.0	1	153-157	150	2.1	80	Crushed soft glass. Propionate 40% distillable. Distillate Mol wt., 430. Residue Mol wt., 930.
21.0	1	160	150	2.4	110	Crushed soft glass. Two 50-cc. portions of hot dry dioxane dissolved 2 g. of amorphous solid. This gave glucose esters.
20.0	3	163-167	135	1.3	65	Crushed soft glass. Propionate 50% distillable. Distillate Mol. wt., 440. Residue Mol. wt., 890.
21.2	1	163-167	150	2.2	100	Crushed pyrex glass. Propionate 25% distillable. Distillate Mol. wt., 425. Residue Mol. wt., 1020.
β -D-GLUCOSE, g. 14	1	160	150	1.0	70	Amorphous product. Only a trace of dioxane-soluble material. No glucose recoverable.

thrice from dry methanol. When immersed in a bath at 140° and heated, the crystals softened at 164° and melted at 168°. The compound gave an ash when burned, reacted instantly with aqueous silver nitrate to form silver chloride, and gave a mixture of glucose

pentaacetates when treated with acetic anhydride and pyridine. Specific rotation, $[\alpha]_D^{25}$ (c, 1.534 in water) changed from 77.6° to 46.2°.

Anal. Calc'd for $C_{12}H_{24}ClNaO_{12}$: C, 34.4; H, 5.74.

Found: C, 34.49; H, 5.68.

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SUMMARY

The literature on crystalline α -glucosan has been critically reviewed. The thermal dehydration of α - and β -D-glucose under reduced pressure has been found to give predominantly materials of higher molecular weight. No evidence for the formation of α -glucosan was found.

The anhydrous crystalline complex of glucose and sodium chloride, $(C_6H_{12}O_6)_2 \cdot NaCl$, was described.

Pyrolysis of 3,4-dideoxyaldopentose has been shown to yield tetrahydrofurfural, 2,5-bis(trimethyleneoxy)-1,4-dioxane, a crystalline isomer of the latter, and water-soluble materials of higher molecular weight. Mechanisms were suggested for the formation of the products.

Derivatives of 3,4-dideoxyketopentose were described. New derivatives of tetrahydrofurfural were included also.

The action of peroxybenzoic acid on dihydropyran was shown to give crude 2,3-epoxytetrahydropyran and higher molecular weight products which could be hydrolyzed in part to tetrahydropyran-2,3-diol.

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