*Studies on the Chemical Decomposition of Simple Sugars. XIV. 3-Xylulose (a 3-Ketopentose)**

By Akira SERA

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In a previous communication, the present author has shown that so-called "glutosazone" is not an osazone of 3-ketose but is substantially glucosazone contaminated by a small amount of methylglyoxal bisphenylhydrazone and other substances. On the other hand, D-allulose[1], DL- and D-sorbose[2,3] had been obtained from D-glucose (or from D-fructose) by the action of bases. Although the production of these sugars indicates that the transformation** of carbohydrates may proceed through 2, 3- or 3, 4-enediol intermediates under suitable conditions, no 3-ketose is isolated from any transformation mixture. The absence of a 3-ketose in a mixture obtained from hexose by means of this transformation suggests that a 3-ketose or its equivalents are unstable under the conditions employed and are converted into the corresponding 2-ketoses.

Recently, attempts to prepare a 3-ketose have been carried out by many authors. Jones[4] obtained 2-*O*-methyl-L-*xylo*-3-hexulose from an L-ascorbic acid derivative. Sugihara and Yuen[5,6] oxidized 3-*O*-benzoyl-1, 2; 5, 6-di-*O*-isopropylidene-D-mannitol and 6-*O*-benzoyl-1, 2; 4, 5-di-*O*-isopropylidene-DL-galactitol with chromium trioxide and obtained 4-*O*-benzoyl-1, 2; 5, 6-di-*O*-isopropylidene-D-*arabo*-3-hexulose and 6-*O*-benzoyl-1, 2; 4, 5-di-*O*-isopropylidene-DL-*xylo*-3-hexulose respectively. After the protecting substituents had been removed, the former gave a mixture of ketoses produced via an enediol intermediate during the debenzoylation procedure. The latter, however, gave a crystalline DL-*xylo*-3-hexulose after saponification of a benzoyl group followed by hydrolysis of isopropylidene groups. Schaffer[7] prepared D-manno-3-heptulose from 3-*O*-formyl-D-*glycero*-D-*talo*heptitol. From the products formed on the oxidation of ribitol with mercuric acetate, Stoodley[8] isolated *erythro*-3-pentulose in addition to D-*threo*- and D-*erythro*-2-pentulose.

In the biological field, some 3-ketoses are produced from suitable precursors. Thus, *Acetobacter suboxydans* transforms L-fucitol into 1-deoxy-D-*xylo*-3-hexulose[9]. D-Ribose-5-phosphate, when incubated with a mouse spleen extract, gave a mixture of phosphorylated pentoses. From the dephosphorylated pentose mixture, Ashwell and Hickman[10] isolated a small amount of *erythro*-3-pentulose besides D-*threo*- and D-*erythro*-2-pentulose.

In the present paper, a new synthesis of 3-xylulose and related preliminary examinations are described. The synthesis of 3-xylulose resulted in success in the following manners.

Results and Discussion

The oxidation of a secondary hydroxyl group to a carbonyl group may be realized by using a variety of agents. However, in the presence

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** Lobry de Bruyn-Alberda van Ekenstein transformation; C. A. Lobry de Bruyn and W. Alberda van Ekenstein, *Rec. trav. chim.*, **14**, 156, 203 (1895) **15**, 92 (1896); **16**, 241, 257, 262, 274, 282 (1897); **18**, 72, 147 (1899); **19**, 1 (1900); J. C. Speck, Jr., "Advances in Carbohydrate Chemistry", **13**, 63 (1958).

1) L. Hough et al., *J. Chem. Soc.*, **1953**, 2005.

2) M. G. Blair and J. C. Sowden, *J. Am. Chem. Soc.*, **77**, 3323 (1955).

3) M. L. Wolfrom and J. N. Schumacher, ibid., **77**, 3318 (1955).

4) J. K. N. Jones, ibid., **78**, 2855 (1956).

5) J. M. Sugihara and G. U. Yuen, ibid., **79**, 5780 (1957).

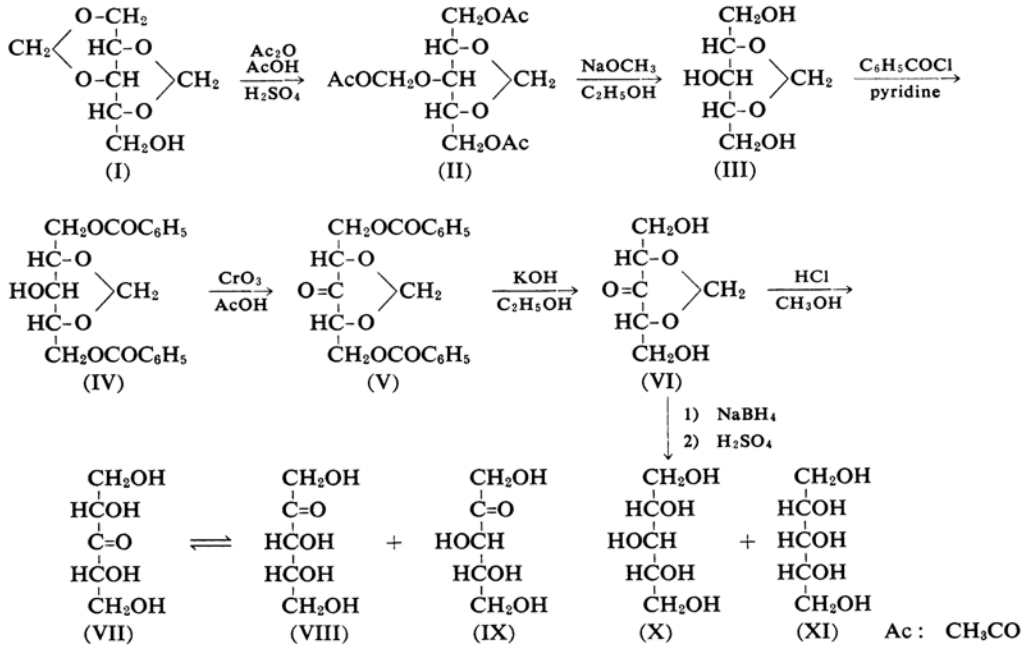
6) G. U. Yuen and J. M. Sugihara, *J. Org. Chem.*, **26**, 1598 (1961).

7) R. Schaffer, *J. Am. Chem. Soc.*, **81**, 2838 (1959).

8) R. J. Stoodley, *Can. J. Chem.*, **39**, 2593 (1961).

9) The first recorded 3-ketose. L. E. Stewart et al., *J. Am. Chem. Soc.*, **72**, 4934 (1950).

10) G. Ashwell and J. Hickman, ibid., **77**, 1062 (1955).



of acid- and base-sensitive groups in the starting material, chromium trioxide in pyridine or acetic acid is the most suitable oxidant. For preparing 3-ketose from polyol, the hydroxyl groups attached at other carbons than carbon 3 in polyol must be protected by suitable substituents (i. e., isopropylidene, benzylidene, methylene, and/or ester groupings); then the remaining free hydroxyl group on carbon 3 may be oxidized with chromium trioxide. After the protecting groups have been removed, the oxidized polyol may give an unsubstituted 3-ketose. α-Ketol, however, when dissolved in an alkaline solution in the presence of oxygen, gives acidic products produced by autoxidation[11] and carbon chain fission. In the case of the synthesis of 3-ketoses, the products are easily transformed through an enediol intermediate (Lobry de Bruyn—Alberda van Ekenstein transformation) into a mixture of ketoses through the action of alkalis.

The behavior of some acetoxyketones as model compounds in a dilute alkaline solution are shown in Fig. 1. As is shown α-ketols were autoxidized easily, even in a dilute solution (such as 0.05 N) in the presence of oxygen. Furthermore, α, α'-diacetoxyketones gave the corresponding dicarbonyl derivatives in an alkaline solution in accordance with the β-hydroxy-carbonyl elimination mechanism[12,13].

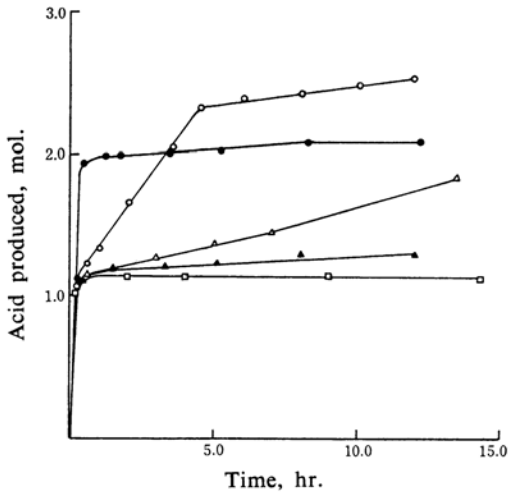


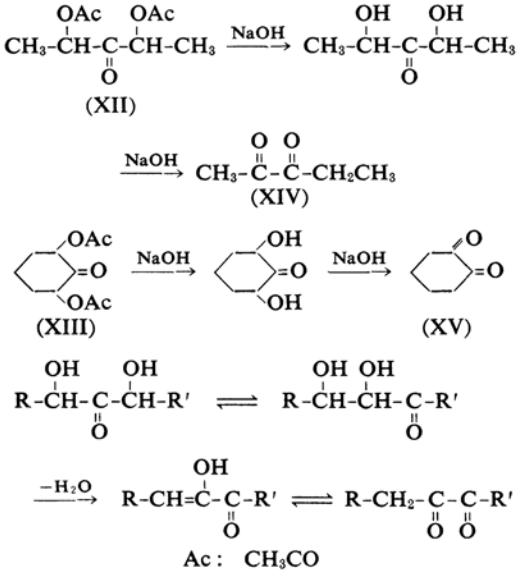
Fig. 1. Production of acid from acetoxyketones.
- ○ 2-Acetoxycyclohexanone in 0.5 N NaOH under aeration
- ● 2,6-Diacetoxycyclohexanone in 0.046 N NaOH under N_2 atmosphere
- △ 2-Acetoxycyclohexanone in 0.045 N NaOH
- ▲ 2-Acetoxypentan-3-one in 0.051 N NaOH under N_2 atmosphere
- □ 2-Acetoxycyclohexanone in 0.045 N NaOH under N_2 atmosphere

Wallach[14] has reported that the corresponding α-dicarbonyl compounds were obtained either when α, β-dibromoketones were treated with potassium hydroxide or when α, β-unsaturated

11) C. Walling, "Free Radicals in Solution," John Wiley & Sons, Inc., New York (1957), p. 461.
12) J. C. Sowden, "Advances in Carbohydrate Chemistry", 12, 36 (1957).
13) R. L. Whistler and J. N. BeMiller, ibid., 13, 289 (1958).
14) O. Wallach, *Ann.*, 437, 148 (1924).

ketones were oxidized with potassium permanganate. The α,β-dihydroxyketones produced through above-mentioned treatments seemed smoothly to eliminate their β-hydroxy groups under alkaline conditions in both cases.

When 2, 4-diacetoxypentan-3-one (XII) and 2, 6-diacetoxycyclohexanone (XIII) were treated with an ethanolic sodium hydroxide solution under a nitrogen atmosphere, pentan-2, 3-dione (XIV) and cyclohexan-1, 2-dione (XV) were produced respectively. In these reactions it is considered that the α,α'-dihydroxyketone produced by means of the saponification rearranges itself to an α,β-dihydroxyketone* which easily eliminates its β-hydroxyl group and gives rise to an enolic form of dicarbonyl compounds.



Sugihara and Yuen[5,6] failed to obtain crystalline products from 4-*O*-benzoyl-1, 2; 5, 6-di-*O*-isopropylidene-D-*arabo*-3-hexulose after debenzoylation and deacetonation. They mentioned that the enediol produced by saponification of benzoyl group would provide a mixture of four isomeric ketoses. Consequently, in the final stage during the synthetic route of unsubstituted 3-ketose, alkaline treatment must be avoided, if possible.

In attempting to synthesize 3-xylulose, 1, 3; 2, 4-di-*O*-methylene-xylitol (I) was used as a starting substance. The preparation of this compound was carried out by a modification of the procedure of Hann, Ness and Hudson[15]. The acetolysis of 1, 3; 2, 4-di-*O*-methylene-xylitol gave crystalline 3-*O*-acetoxymethyl-1, 5-di-*O*-acetyl-2, 4-*O*-methylene-xylitol (II) in a good yield (96%). All attempts to obtain 1, 5-di-*O*-acetyl-2, 4-*O*-methylene-xylitol by the limited hydrolysis of the *O*-acetyl group on carbon 3 failed. The saponification of all ester linkages in 3-*O*-acetoxymethyl-1, 5-di-*O*-acetyl-2, 4-*O*-methylene-xylitol, followed by the benzoylation of the resulting 2, 4-*O*-methylene-xylitol (III) with two molar equivalents of benzoyl chloride, gave 1, 5-di-*O*-benzoyl-2, 4-*O*-methylene-xylitol (IV) in a 79% yield. The infrared spectrum of IV shows the presence of benzoyl groups (conjugated carbonyl absorptions at 1685 and 1715 cm^{-1}, and phenyl group absorptions at 1580 and 1595 cm^{-1} respectively). The 1 and 5 positions for the benzoyl groups were assigned because of the well-known preferential benzoylation of primary hydroxyl groups under the conditions employed.

After being oxidized with chromium trioxide in anhydrous pyridine, 1, 5-di-*O*-benzoyl-2, 4-*O*-methylene-xylitol was recovered unchanged, but when pyridine was replaced with glacial acetic acid, the oxidation afforded crystalline 1, 5-di-*O*-benzoyl-2, 4-*O*-methylene-3-xylulose (V) in a 30% yield. In the infrared spectrum, V shows an absorption peak at 1725 cm^{-1}, indicating the presence of a carbonyl group. No absorption, however, is observed near 3420 cm^{-1}, where the parent compound IV had an absorption because of its free hydroxyl group.

The saponification of the substituted 3-xylulose (V) with an alcoholic potassium hydroxide solution gave crystalline 2, 4-*O*-methylene-3-xylulose (VI) in a 64% yield. The sodium borohydride reduction of the product VI, followed by the hydrolysis of the methylene group with sulfuric acid, gave an excepted mixture containing xylitol (X) and ribitol (XI) (paper chromatographic separation), confirming that the parent compound VI is of a 3-ketose structure. 2, 4-*O*-Methylene-3-xylulose (VI) has an absorption at 3317 cm^{-1} (hydroxyl groupings), but it has no peaks at 1580~1600 cm^{-1} (phenyl groupings), indicating the completeness of saponification. However, no absorption at 1700~1735 cm^{-1} is observed because of its carbonyl grouping. Hence, in 2, 4-*O*-methylene-3-xylulose, the carbonyl group must be masked, presumably by a dimer formation, in which the carbonyl group of the ketose may be combined with the free hydroxyl groups of the other to form acetal linkage. Späth and his co-workers[16] established that β-hydroxy-aldehyde, in general, took a dimeric form containing a 1, 3-dioxane ring structure. Schaffer and

* According to the acyloin rearrangement or to the Lobry de Bruyn-Alberda van Ekenstein transformation, in the sense of carbohydrate chemistry.

15) R. M. Hann, A. T. Ness and C. S. Hudson, *J. Am. Chem. Soc.*, **66**, 670 (1944).

16) E. Späth et al., *Ber.*, **74**, 859 (1941); **76**, 57, 949, 1196 (1943).

Isbell[17] found that 5-aldo-1, 2-*O*-isopropylidene-D-*xylo*-pentofuranose existed in the form of a dimer, as has been mentioned above.

The demethylenation of 2, 4-*O*-methylene-3-xylulose (VI) with methanolic hydrogen chloride gave a syrup which did not crystallize. The acid hydrolysis of the syrup gave a viscous syrup which also did not give a crystalline product. Paper chromatographic investigations of this syrup showed that it was composed of 3-xylulose (VII), *erythro*-2-pentulose (VIII*), and of *threo*-2-pentulose (IX)* (R_f values: 0.369, 0.359 and 0.347 respectively). The R_f value of 3-xylulose (0.369) corresponds to 1.26 in R_{rib}** value. Stoodley[8] has recorded the R_{rib} of 1.23 for 3-xylulose obtained from ribitol. The observation that the syrup obtained by removing the methylene group was a mixture of 3-ketose and corresponding 2-ketoses suggests that isomerization plays a leading role during acid treatment. It is suggested also that the unsubstituted 3-ketose does, in general, not exist in a stable form but is transformed into its isomers according to the Lobry de Bruyn—Alberda van Ekenstein transformation.

Further investigations related to those described in this communication are in progress.

Experimental

All melting points and boiling points are corrected. All concentrations were carried out under reduced pressure at 30~40°C (bath temp.) unless otherwise stated. Paper chromatographic analyses were carried out on Toyo Roshi No. 50 filter paper by the descending method at 30°C, using a *n*-butanol—ethanol—acetic acid—water mixture (40 : 10 : 5 : 15, vol./vol.) as a developer. Spots were located on chromatograms by the following color reagents: a) silver nitrate in ammonium hydroxide, b) lead tetraacetate in anhydrous benzene, c) naphthoresorcinol in hydrochloric acid and d) aniline hydrogenphthalate in *n*-butanol saturated with water. Multiple developments were employed for the complete separation of spots, if necessary. Infrared spectra were determined by using an infrared recording spectrophotometer (Model D. S. 301, Nippon Bunko Co., Ltd.).

Acetoxyketones.—Acetoxyketones were prepared by the method of Cavill and Solomon[18]. The samples obtained were as follows: 2-acetoxycyclohexanone, b. p., 103~104°C/6 mmHg, n_D 1.4598 (Cavill and Solomon reported a b. p. of 123~126°C/16 mmHg); 2,6-diacetoxycyclohexanone***, b. p., 140~142°C/1 mmHg, m. p., 147~148°C (leaflets, recrystallized from ethanol—petroleum ether) (Cavill and Solomon reported a b. p. of 158~160°C/10 mmHg and m. p. 145~146°C); 2-acetoxypentan-3-one, b. p., 58~60°C/3 mmHg, n_D 1.4181; and 2,4-diacetoxypentan-3-one, b. p., 81~82°C/2 mmHg (Cavill and Solomon reported a b. p. of 80°C/1 mmHg).

Behavior of Acetoxyketones in a Dilute Alkaline Solution.—*In the Presence of Oxygen.*—In a 0.05 N sodium hydroxide solution (70% aqueous ethanol*), each acetoxyketone was dissolved and allowed to stand at room temperature. When the solution was aerated with a stream of gas, a dry ice—acetone condenser was fitted to the reaction flask to prevent the evaporation loss of the solvent. At suitable intervals, an aliquot of the reaction mixture was pipetted out and titrated with 0.05 N hydrochloric acid, using phenolphthalein as an indicator.

b) In the Absence of Oxygen. — The above-mentioned procedure was carried out using an oxygen-free alkaline solution. Nitrogen gas was passed through the mixture during the reaction period. The results obtained (a) and b)) are shown in Fig. 1.

c) Cyclohexan-1,2-dione (XV) from 2,6-Diacetoxycyclohexanone (XIII).— 2,6-Diacetoxycyclohexanone was dissolved in a 0.28 N sodium hydroxide solution (70% aqueous ethanol) under nitrogen gas bubbling for 3 hr. at room temperature. After the solution had been neutralized with dilute hydrochloric acid to a slightly alkaline state, phenylhydrazine hydrochloride and sodium acetate were added and the mixture was allowed to stand overnight. The precipitate was then filtered and recrystallized from ethanol. Cyclohexane-1,2-dione bisphenylhydrazone was obtained as golden yellow needles; m. p. 150.5~151.0°C.

Found: N, 19.08. Calcd. for $C_{18}H_{20}N_4$: N, 19.16%.

d) Pentan-2,3-dione (XIV) from 2,4-Diacetoxypentan-3-one (XII). — After the treatment of 2,4-diacetoxypentan-3-one in a 0.048 N sodium hydroxide solution (70% aqueous ethanol), as mentioned above, bisphenylhydrazone of pentane-2,3-dione was obtained in the form of yellow needles (recrystallized from benzene—ethanol); m. p., 170~171°C.

Found: N, 20.30. Calcd. for $C_{17}H_{20}N_4$: N, 19.99%.

e) Analysis of the Reaction Mixture.— From the reaction mixture (2-acetoxycyclohexanone in 0.5 N sodium hydroxide, under aeration), an aliquot was pipetted ont at suitable intervals, neutralized with dilute acetic acid, and deionized by Amberlite IR-120*. The resulting aqueous solution** was concentrated under reduced pressure. To the distillate, which was collected in a cold trap, a 2 N hydrochloric acid solution of 2,4-dinitrophenylhydrazine was added. After the whole solution had been allowed to stand overnight, cyclohexane-1,2-dione bisphenylhydrazone was obtained (m. p., 225~226.5°C), after recrystallization from ethyl acetate—ethanol. From the distillation residue, adipic

17) R. Schaffer and H. S. Isbell, *J. Am. Chem. Soc.*, **79**, 3864 (1957).

* Both the sugars showed R_f values similar to that of the authentic specimens prepared by the pyridine epimerization of D-xylose and of D-ribose respectively.

** The rate of movement relative to that of D-ribose.

*** Two moles of lead tetraacetate were employed for one mole of ketone.

18) G. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.*, 1955, 4426.

* Aldehyde free, freshly distilled.

** Rohm and Haas Co., Philadelphia, Pa., U. S. A.

*** Periodate oxidation of this aqueous solution gave only a trace of adipic acid semialdehyde, indicating the absence of 2-hydroxycyclohexanone in the solution.

TABLE I. RESULTS OF THE ALKALI TREATMENT OF 2-ACETOXYCYCLOHEXANONE

Time hr.	Yield of products from 1 g. of ketone: Cyclohexane-1,2-dione mg.	Adipic acid mg.
6	660	85
10	210	125
15	140	325

acid was isolated, by recrystallizing from ethanol, in the form of crystals (m. p. and mixed m. p. 150~151°C). The results obtained are shown in Table I.

1,5-Di-*O*-acetyl-3-*O*-acetoxymethyl-2,4-*O*-methylene-xylitol (II).—Twenty grams of finely powdered 1,3; 2,4-di-*O*-methylene-xylitol (I) was added into an ice-cold acetylating mixture containing 140 ml. of acetic anhydride, 60 ml. of glacial acetic acid, and 4 ml. of sulfuric acid. The diacetal dissolved slowly, and, after standing 15 min. at 5°C, the reaction mixture was poured into 500 ml. of ice and water. The precipitate was filtered by suction and washed with a small amount of cold water (first crop). The filtrate and the washings were combined, and the whole solution was neutralized with aqueous sodium carbonate to a slightly alkaline state; then the produced precipitate was collected by filteration (second crop). The filtrate was extracted with chloroform (150 ml. ×3), and the chloroform layer was washed with water and dried over magnesium sulfate. After removal of the solvent, a yellow solid was obtained (third crop). After recrystallizing from water, the combined product (34.8 g., 95.6%) gave crystalline 1,5-di-*O*-acetyl-3-*O*-acetoxymethyl-2,4-*O*-methylene-xylitol (II); yield, 31.5 g., m. p., 136~137.5°C. After two recrystallizations from water, an analytical sample was obtained, m. p., 139.5~140.0°C.

Found: CH_3CO, 39.0. Calcd. for $C_{13}H_{20}O_9$: CH_3CO, 40.3%.

After being treated with boiling 70% acetic acid for 2 hr., or after being stirred with Amberlite IR-45 for 2 hr., II was recovered unchanged.

2,4-*O*-Methylene-xylitol (III).—In 25 ml. of chloroform (dried over phosphorous pentoxide), 5.9 g. of 1,5-di-*O*-acetyl-3-*O*-acetoxymethyl-2,4-*O*-methylene-xylitol (II) was dissolved and the solution was cooled with an ice-bath. Into the cold solution, 20 ml. of absolute ethanol and 20 ml. of 0.1 N sodium methoxide in methanol were added. The ice-bath was removed after 1 hr., and the solution was allowed to stand overnight at room temperature. The solvent was distilled off under reduced pressure, the residue obtained was dissolved in 5 ml. of water, and the solution was decolorized with active carbon. The resulting pale yellow solution was evaporated under reduced pressure to dryness. After being recrystallized from 5 ml. of ethanol, the residue gave a crystalline solid (2.1 g.). An additional 0.5 g. of the product was obtained from the mother liquor after it had been left standing for a few days. Yield, 2.6 g. (86.1%). After several recrystallizations from ethanol, 2,4-*O*-methylene-xylitol (III) was obtained as needles which melted at 110~110.5°C. The infrared spectrum is shown in Fig. 2.

1,5-Di-*O*-benzoyl-2,4-*O*-methylene-xylitol (IV).—Ten grams of 2,4-*O*-methylene-xylitol (III) was dissolved in 100 ml. of ice-cooled anhydrous pyridine (dried over barium oxide and stored over calcium hydride); 14 ml. (2 mol. equiv.) of benzoyl chloride was then added with agitation into the solution. The reaction mixture, which after being stirred for 2.5 hr. at room temperature became slushy, was poured into 700 ml. of ice and water. The amorphous precipitate was filtered by suction, washed with cold water, and dried. Yield, 18.0 g. (79.3%); recrystallizations from absolute ethanol gave pure 1,5-di-*O*-benzoyl-2,4-*O*-methylene-xylitol (IV) in the form of long needles (m. p., 140.5~141.0°C).

Found: C, 64.64; H, 5.59; C_6H_5CO, 55.9. Calcd. for $C_{20}H_{20}O_7$: C, 64.51; H, 5.41; C_6H_5CO, 56.4%.

The infrared spectrum is shown in Fig. 3.

A solution of 1,5-di-*O*-benzoyl-2,4-*O*-methylene-xylitol (1.0 g.) in 3 ml. of glacial acetic acid and 7 ml. of acetic anhydride was treated with the above-mentioned acetylating mixture (10 ml.) for 1 hr. at room temperature, and the resulting slushy mixture was poured into 250 ml. of ice and water. The resulting precipitate, after filtration, washing with water, and drying, weighed 850 mg. Two recrystallizations from absolute ethanol gave 1,5-di-*O*-benzoyl-3-*O*-acetyl-2,4-*O*-methylene-xylitol in the form of long needles (m. p., 174.5~175.0°C).

Found: C, 63.96; H, 5.49; acyl groups, 60.3.

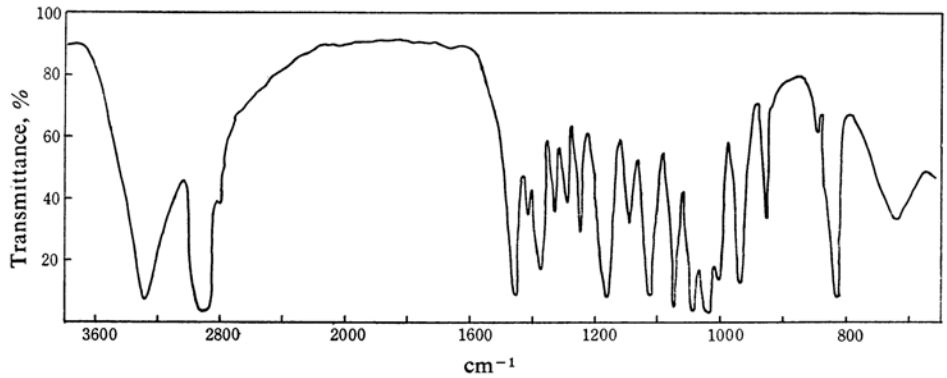


Fig. 2. Infrared spectrum of 2,4-*O*-methylene-xylitol (III), in Nujol.

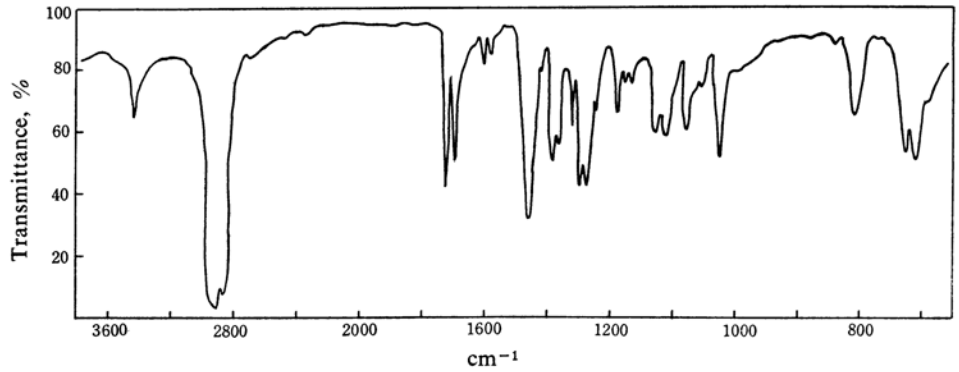


Fig. 3. Infrared spectrum of 1,5-di-*O*-benzoyl-2,4-*O*-methylene-xylitol (IV), in Nujol.

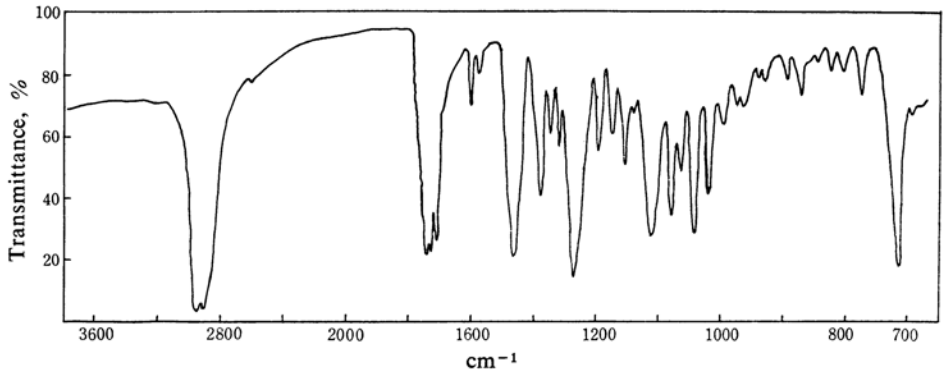


Fig. 4. Infrared spectrum of 1,5-di-*O*-benzoyl-2,4-*O*-methylene-3-xylulose (V), in Nujol.

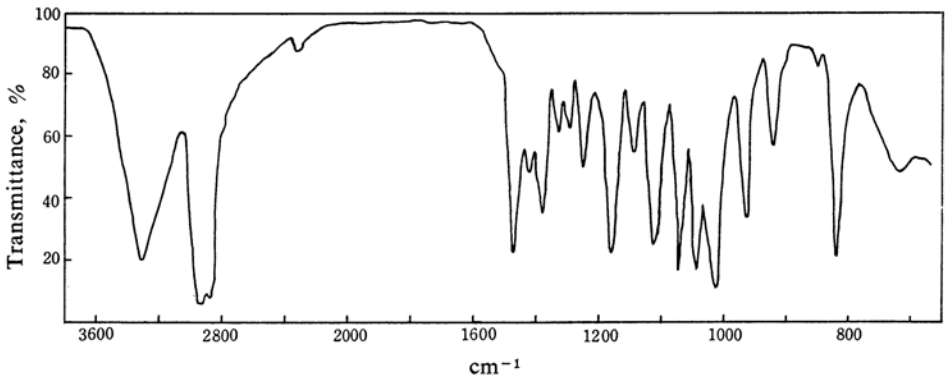


Fig. 5. Infrared spectrum of 2,4-*O*-methylene-3-xylulose (VI), in Nujol.

Calcd. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35; acyl groups, 61.1%.

1, 5-Di-*O*-benzoyl-2,4-*O*-methylene-3-xylulose (V). — A portion (4.4 g.) of 1,5-di-*O*-benzoyl-2,4-*O*-methylene-xylitol (IV) was dissolved in 200 ml. of glacial acetic acid (treated with chromium trioxide and distilled). To the resulting solution maintained at 15°C, 5.0 g. of chromium trioxide in 300 ml. of acetic acid was added with agitation. After this addition, the mixture was stirred for 1 hr. and then allowed to stand overnight at room temperature. The excess of the oxidant was decomposed by adding methanol, and the mixture was evaporated under reduced pressure to a black residue. The residue was extracted three times with warm diisopropyl ether (100 ml. portions). The combined ethereal solution was washed successively with water, 5% aqueous sodium bicarbonate, and again with water, and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure, and the resulting thick syrup was dissolved in 30 ml. of warm ethanol and decolorized with active carbon. When the solvent was evaporated under reduced pressure, a crystalline mass

TABLE II. PAPER CHROMATOGRAPHIC SEPARATION OF THE SYRUP

Spot No.	R_f	Color with Reagent a)	Color with Reagent b)	Coloration with reagent a)	Remarks
1	0.12~0.14	Black	—	Strong	Unknown
2	0.25~0.27	Black	Pink	Weak	Aldose (?)
3	0.347	Black	Light brown	Strong	*threo*-2-Pentulose
4	0.357	Black	Light brown	Strong	*erythro*-2-Pentulose
5	0.369	Black	Brown	Strong	3-Xylulose
6	0.54~0.56	Black	Faint	Variable	Unchanged substance

Spot 2 gave a blue color with reagent c).

To confirm spots 3 and 4 as *threo*- and *erythro*-2-pentulose, authentic specimens prepared by the pyridine epimerization of the corresponding aldoses, were dotted on the side of the paper and then developed.

Spot 6 was negative against reagent b).

was obtained (1.3 g. (29.3%); m. p., 111~112°C). After repeated recrystallizations from diisopropyl ether, an analytical sample of 1,5-di-*O*-benzoyl-2,4-*O*-methylene-3-xylulose (V) was obtained as long needles (m. p., 115.5~116.5°C).

Found: C, 64.44; H, 4.96; C_6H_5CO, 56.9. Calcd. for $C_{20}H_{18}O_7$: C, 64.86; H, 4.90; C_6H_5CO, 56.8%.

The infrared spectrum is shown in Fig. 4.

2,4-*O*-Methylene-3-xylulose (VI). — In 20 ml. of ethanol, 480 mg. of 1,5-di-*O*-benzoyl-2,4-*O*-methylene-xylulose (V) was dissolved, and to this solution, 30 ml. of 95% ethanol containing 0.5 g. of potassium hydroxide was then added. The solution was allowed to stand overnight, after which the solvent was evaporated by a jet of dry air. The residual syrup was dissolved in 10 ml. of water and deionized by passing it through a column containing ion exchange resins (5 ml. of Amberlite IR-45 and of IR-120). The effluent and the washings were decolorized with active carbon, concentrated under reduced pressure to dryness. After recrystallization from ethanol—diisopropyl ether (1 : 1, vol./vol.), the resulting white solid gave 2,4-*O*-methylene-3-xylulose (VI) as fine needles (80 mg.; m. p., 90~92°C). After further recrystallizations from the same solvent, an analytical sample was obtained (m. p., 95.5~97.5°C).

Found: C, 43.97; H, 6.10. Calcd. for $C_6H_{10}O_5$: C, 44.44; H, 6.22%.

The infrared spectrum is shown in Fig. 5.

Reduction of 2,4-*O*-Methylene-3-xylulose (VI). —In 5 ml. of water, 120 mg. of 2,4-*O*-methylene-3-xylulose was dissolved; this solution was then cooled and maintained at 5°C. Ten milliliters of a 1.5% sodium borohydride aqueous solution was added drop by drop under agitation. After being allowed to stand for 1.5 hr., the reaction mixture was acidified by dilute acetic acid to a slightly acid state and concentrated under reduced pressure to 5 ml. To the resulting solution, 0.5 ml. of concentrated sulfuric acid was added, and the solution was heated on a water bath for 4 hr. The hydrolysate was neutralized with barium carbonate and filtered through a layer of Celite*, and the filtrate and the washings were deionized by passing it through a column (Amberlite IR-45 and IR-120), decolorizing it by active carbon, and dried under reduced pressure to a thick syrup. Paper chromatographic separation of the syrup, using reagent a) and b) as detectors, showed the presence of xylitol (X) and ribitol (XI) (R_f 0.243 and 0.281 respectively).

Hydrolysis of 2,4-*O*-Methylene-3-xylulose (VI) into 3-Xylulose (VII). — In 10 ml. of a 9.3% methanolic hydrogen chloride solution was dissolved 620 mg. of 2,4-*O*-methylene-3-xylulose (VI); the solution was then allowed to stand for 48 hr. at room temperature (about 15°C). The resultant mixture was evaporated under reduced pressure to a thick syrup, which was then dissolved in 5 ml. of water, followed by deionizing (Amberlite IR-45) and by decolorizing by a small amount of active carbon. The clear solution obtained was concentrated under reduced pressure to a thick syrup which did not crystallize. When the methanolysis was carried out for 10, 24, and 72 hr., the resulting syrups also failed to yield a crystalline product. The syrup obtained was hydrolyzed in 0.1 N hydrochloric acid for 24 hr. at room temperature. After the removal of acid with Amberlite IR-45, the solution was concentrated under reduced pressure to a thick syrup, which reduced a warm Fehling's solution. Paper chromatographic investigations of this syrup gave the results shown in Table II.

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Institute of Chemistry
Faculty of Science
Kyoto University
Sakyo-ku, Kyoto

* A filter-aid; Johns-Manville Co., New York, N. Y., U. S. A.