

The ketazine may also be prepared by means of the reaction of the corresponding magnesium compound with iodine.

The formation of the ketazine is a new and better method of preparing these compounds.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE COLLEGE OF LIBERAL ARTS,
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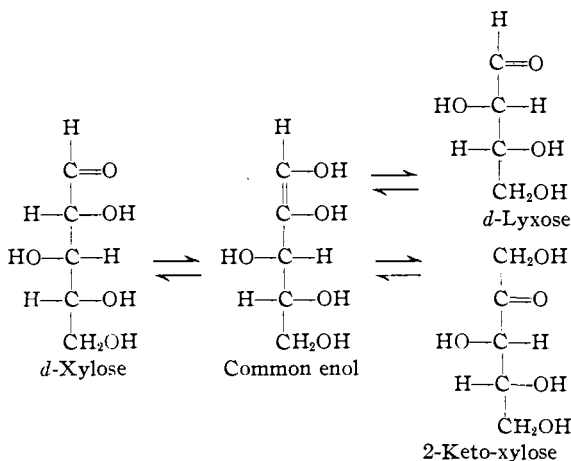
THE REACTIVITY OF THE METHYLATED SUGARS. IV. THE ACTION OF DILUTE ALKALI ON TRIMETHYLXYLOSE¹

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The theory of intermediate enol formation² which has proved so valuable in elucidating sugar reactions has nevertheless rested more upon plausibility than proof. The methylated sugars lend themselves to testing more directly the mechanism of these reactions by limiting in a predictable manner enol formation.³ This follows from the lesser lability of the methyl group as compared with the replaced hydrogen of the sugar hydroxyl. Thus the theory of selective hydration and dehydration in enol formation



¹ Abstracted from a dissertation submitted to the Graduate School of Northwestern University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

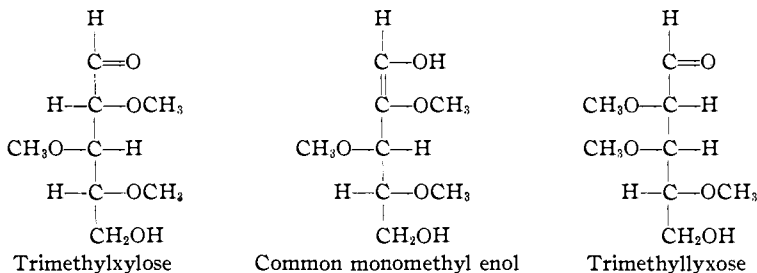
² Lobry de Bruyn and van Ekenstein, *Rec. trav. chim.*, **14**, 156 (1895); Fischer, *Ber.*, **28**, 1149 (1895); Wohl and Neuberg, *ibid.*, **38**, 3099 (1900); Nef, *Ann.*, **357**, 214 (1907); **376**, 1 (1910); **403**, 204 (1914); Evans, *Chem. Reviews*, **6**, 281 (1929); Shaffer and Friedemann, *J. Biol. Chem.*, **86**, 345 (1930); Evans and Conaway, *THIS JOURNAL*, **52**, 3680 (1930).

³ (a) Gustus with Lewis, *ibid.*, **49**, 1512 (1927); (b) Wolfrom with Lewis, *ibid.*, **50**, 837 (1928); (c) Greene with Lewis, *ibid.*, **50**, 2813 (1928).

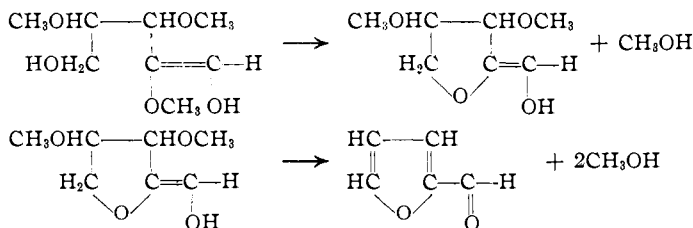
has been shown untenable, and the elimination of ketose formation in the Lobry de Bruyn reaction controlled at will.^{3b,c}

The present paper deals with an extension of this method of study to a pentose, 2,3,4-trimethylxylose. For purposes of comparison, xylose was first treated with dilute alkali using the conditions of time, temperature and concentration previously found to give a minimum of saccharinic acid formation.^{3b} Under these conditions, the system shown in the formulas just given would be expected. The major products were found to be *d*-lyxose and *d*-xylose and a condensation product of four moles of the expected 2-keto-xylose.

In the case of the trimethylxylose, no ketose formation would be expected due to the blocking effect of the methoxyl group on the second carbon atom. The following system should result from the treatment of 2,3,4-*d*-xylose with dilute alkali



When trimethylxylose was treated with dilute alkali under the conditions applied to *d*-xylose, evidence was obtained of a stable enol. Trimethylxylose and trimethyllyxose were proved to be present. When, however, dilute acid was added to the reaction mixture in order to de-enolize it, the total aldose fell below 100% and furfural appeared. It is suggested that the furfural results from the action of acid upon the monomethyl enediol according to the equations



This conclusion is based upon the fact that a direct relation was established experimentally between the amount of presumptive enol present and of furfural formed. Furthermore, the amount of alcohol found after de-enolization with dilute acid was roughly twice the amount found in the alkaline reaction mixture. This removal of alcohol in two portions of

roughly one-third and two-thirds supports the preceding equation. Since no ketose was found present, the methyl alcohol could not have had its source in demethylation incident to ketose formation. It is believed that no furfural results from xylose under these conditions because the intermediate enol is transient. In none of the studies of the action of dilute alkalis upon unmethylated sugars have we ever found evidence of a substance of high iodine absorbing power.⁴

The gum isolated from the de-enolized reaction mixture was shown to consist of about 70% of trimethylxylose and 26% of trimethylxylose with about 4% of partially demethylated material. The sugars were separated by fractional crystallization of the brucine salts of their acids. These were further converted into the crystalline phenylhydrazides for identification.

Experimental Part

Preparation of Trimethylxylose.—Normal 2,3,4-trimethylxylose was prepared by the methylation of four moles (600 g.) of commercial xylose with dimethyl sulfate according to the method of Carruthers and Hirst.⁵ The yield of β -methyltrimethylxyloside was 528 g. or 69% of the theoretical collected at 80° and 3 mm. pressure. Four hundred and twenty grams of purified β -methyltrimethylxyloside was hydrolyzed by heating a 7% solution containing 7% of hydrogen chloride at 80° for three hours. The solution was then neutralized, evaporated and the trimethylxylose extracted from the salty residue with chloroform. After the chloroform was removed, the residue was crystallized from ethyl ether. In the above manner, 230 g. of crystalline material was obtained, a yield of 60% of the theoretical. Upon recrystallization from absolute ether and careful drying, there was obtained 190 g. of pure material giving a final $[\alpha]_D^{20}$ of +17.8° ($\alpha = +1.0^\circ$ in a 2-dm. tube when c is 2.8116 in water). Carruthers and Hirst⁵ record a final $[\alpha]_D$ of +20° in water and +21° in methyl alcohol. Phelps and Purves⁶ found $[\alpha]_D^{20} +17.7^\circ$ in aqueous solution, for the final specific rotation of pure trimethylxylose. Hirst and Carruthers record a melting point of 87–90°; Phelps and Purves record 91–92°. In order to check the purity of the product, it was redistilled and collected at 111° and 3 mm. and at 121° and 5 mm. The liquid gave a refractive index of 1.4603 when supercooled to 20°. The entire product solidified upon cooling and was again crystallized from absolute ether. After careful drying the substance was analyzed for methoxyl.

Anal. Subs., 0.0335, 0.0911; AgI, 0.3410, 0.3353. Calcd. for $C_6H_7O_2(OCH_3)_3$: OCH_3 , 48.4. Found: OCH_3 , 48.2, 48.6.

The substance was optically homogeneous in polarized light. It gave a final specific rotation of +17.8° ($\alpha = +1.32^\circ$ in a 2-dm. tube when c is 3.70 in water). In methyl alcohol the final specific rotation was +21.3° ($\alpha = +1.11$ in a 1-dm. tube when c is 5.214°).

The Action of Dilute Alkali on *d*-Xylose.—One-half mole (75 g.) of pure *d*-xylose [specific rotation +19.2° ($\alpha = +0.94^\circ$ in a 1-dm. tube when $c = 4.895$ in water)] was made to 500 cc. with 0.04 *N* calcium hydroxide solution saturated at 35°. The final concentration of the sugar was molar in 0.035 *N* calcium hydroxide solution at 32°.

⁴ Cf., however, Montgomery and Hudson, *THIS JOURNAL*, **52**, 2103 (1930).

⁵ Carruthers and Hirst, *J. Chem. Soc.*, **121**, 2299 (1922).

⁶ Phelps and Purves, *THIS JOURNAL*, **51**, 2443–9 (1929).

The iodine oxidation method of Cajori⁷ as modified by Wolfrom and Lewis^{3b} was found to apply to the determination of xylose if the time of oxidation was thirty-five to forty-five minutes. The change in aldose content is shown in Table I and graphically in Fig. 2. The change in rotation appears in Table I and graphically in Fig. 1. The final rotation was $+11.2^\circ$ at 30° when c was molar and the aldose content 77.4%. The hydrogen-ion concentration corresponds to a P_H of 5.85 as determined by the quinhydrone electrode. The initial P_H of the lime water was 12.6, and dropped to 10.6 upon addition of the sugar.

TABLE I
EQUILIBRATION OF *d*-XYLOSE IN DILUTE ALKALI

Time, hours	$[\alpha]_D^{30^a}$	Aldose, % ^b	Aldose, % ^c	Time, hours	$[\alpha]_D^{30^a}$	Aldose, % ^b	Aldose, % ^c
0		99.6		96	12.0	81.3	
6	17.8	95.4		120	11.9		
12	16.7	94.4		122		80.6	
24	15.4	91.0	90.7	144	11.40		
36	14.8			167	11.36		
48	14.0	87.8		168.5		78.6	
71	13.2			191	11.2	77.2	76.3
72		84.3		214	11.2	77.5	

^a C = molar. ^b By iodine titration. ^c The sample is treated with 3 *N* hydrochloric acid for three hours at 20° . It is then neutralized and oxidized in the usual manner, and the excess of iodine titrated with thiosulfate.

The saccharinic acid content was calculated as 3.4% by direct titration after removal of calcium ions. No furfural was present according to the aniline acetate test.

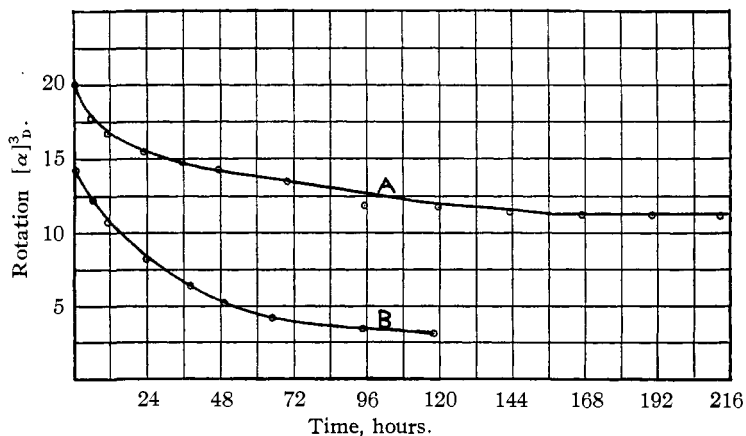


Fig. 1.—Change in rotation of *d*-xylose and trimethylxylose in dilute alkali: A, xylose; B, trimethylxylose.

Separation of Aldoses and Ketoses.—By the oxidation of 350 cc. (corresponding to 50.03 g. of xylose) of the final equilibrated solution using Hudson and Isbell's⁸ neutral bromine method, the aldoses were converted to aldonic acids and the ketoses presumably unattacked. The final solution (corresponding to 49.0 g. of xylose due to

⁷ Cajori, *J. Biol. Chem.*, **54**, 617 (1928).

⁸ Hudson and Isbell, *THIS JOURNAL*, **51**, 2225 (1929).

sampling) freed of benzoate, bromide and silver ions, after concentration to 150 cc. was treated with an excess of cadmium carbonate. The excess cadmium carbonate was removed by filtration and the cadmium salts precipitated by the addition of 500 cc. of ethyl and 500 cc. of methyl alcohols with rapid stirring. The cadmium salt dried over sulfuric acid *in vacuo* weighed 58.0 g.

The filtrate from the precipitation of cadmium salt was evaporated to dryness and then taken up in absolute methyl alcohol and added with vigorous stirring to absolute ether. A very fine white precipitate formed which on standing became distinctly granular. The total yield of this ketosic material was 4.82 g.

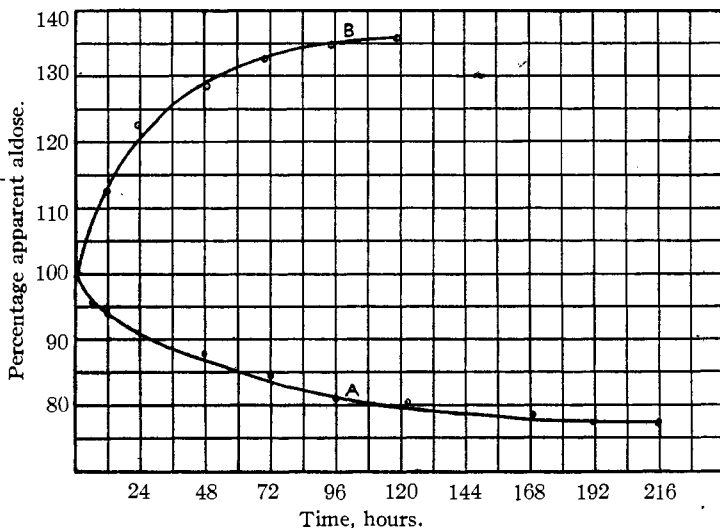


Fig. 2.—Change in apparent aldose content calculated from the iodine titration: A, xylose; B, trimethylxylose.

Separation of the Cadmium Salts.—Fifty-seven grams of cadmium salt was dissolved in water and the amount of cadmium bromide sufficient to convert all cadmium salts to cadmium bromide, cadmium xylonate double salt was added. Sixty-six and one-tenth grams of the double salt was obtained after concentrating and allowing the solution to stand. It gave a specific rotation of $+8.4^\circ$ ($\alpha = 0.20^\circ$ in a 2-dm. tube when c is 1.182 in water). It contained 21.23% of bromine. Nef⁹ recorded a specific rotation of $+7.4^\circ$, while Hudson and Isbell⁸ found a rotation of $+8.8^\circ$.

Anal. Subs., 0.0912; AgBr, 0.0455. Calcd. for $\text{CdBr}_2 \cdot \text{Cd}(\text{C}_5\text{H}_9\text{O}_6)_2 \cdot 2\text{H}_2\text{O}$: Br, 21.31. Found: Br, 21.23.

To identify the xylic acid further, 6.0 g. of the double salt was converted to the brucine salt after removal of the cadmium and bromine ions. There was obtained 3.5 g. of once recrystallized brucine xylonate which melted at $172\text{--}173^\circ$ and gave a specific rotation of -19.1° ($\alpha = -0.544^\circ$ in a 1-dm. tube when c is 2.842 in water). Nef¹⁰ records a melting point of $172\text{--}174^\circ$ and a specific rotation of -18.7° .

The residual liquor from the precipitation of cadmium bromide cadmium xylonate double salt was freed of cadmium and bromide ions and then converted to the brucine

⁹ Nef, *Ann.*, **403**, 253 (1914).

¹⁰ Nef, Ref. 9, p. 254.

salt. This yielded 16.9 g. which was very sparingly soluble in alcohol. From the alcohol-soluble portion 0.5 g. of brucine xylonate and 0.8 g. of brucine lyxonate were separated by fractional crystallization. The total of 17.7 g. of brucine lyxonate had a specific rotation of -26.4° ($\alpha = -0.92^\circ$ in 1-dm. tube when c is 3.483 in water). Ten grams was then converted to the phenylhydrazide, which gave 4.0 g. of anhydrous phenylhydrazide. This melted at $162-164^\circ$ and gave a specific rotation of -11.0° ($\alpha = -0.18^\circ$ in a 2-dm. tube when c is 0.818 in water). Wohl and List¹¹ recorded a melting point of $162-164^\circ$ and a specific rotation of -11.2° for the anhydrous phenylhydrazide. The brucine xylonate was identified by melting unchanged with known brucine xylonate.

Nature and Constants of the Ketose.—The ketose isolated reduced Fehling's solution only upon heating and did not reduce neutral permanganate solution. The ketose expected would be a "gamma" sugar and yet the material isolated exhibited none of the properties of a "gamma" sugar. The isolated solid material would not condense with methyl alcoholic hydrogen chloride even after three hours' refluxing. The final rotation in water was $+3.0^\circ$ ($\alpha = +0.09$ in a 2-dm. tube when c is 1.474 in water). In methyl alcohol the final rotation was $+6.4^\circ$ ($\alpha = +0.133^\circ$ in a 1-dm. tube when c is 2.068 in methyl alcohol). A determination of the molecular weight by rise in boiling point of methyl alcohol gave 524 and 540. If four moles of keto-xylose condensed with the elimination of three moles of water, the resulting compound would have a molecular weight of 546.

Summary of Products Isolated from Equilibrated Solution of Xylose.—From 100 g. of xylose equilibrated there were isolated the following products calculated to equivalent xylose: first, 52.9 g. of xylose as xylonic acid derivatives (this represents the amount of xylose unchanged after equilibration); second, 8.3 g. of xylose as lyxonic acid derivatives; third, 9.8 g. of xylose as the crystalline condensed ketose; fourth, 3.4 g. of xylose as the presumptive saccharinic acid.

Action of Dilute Alkali on Trimethylxylose.—It was determined in preliminary experiments that the iodine oxidation method for aldose, as used on xylose, was applicable to trimethylxylose if the time of oxidation was at least ten minutes. The changes in rotation and in aldose content when trimethylxylose was treated with saturated lime water at 35° are recorded in Table II and graphically in Figs. 1 and 2. The solutions gave a final specific rotation of $+3.0^\circ$ and were but very slightly alkaline. No furfural was present in the alkaline equilibrated solution. Calculations based on the known rotations of the two epimers, trimethylxylose and

TABLE II
EQUILIBRATION OF TRIMETHYLXYLOSE IN DILUTE ALKALI

Time, hours	$[\alpha]_D^{30^a}$	Apparent aldose, % ^b	Time, hours	$[\alpha]_D^{30^a}$	Apparent aldose, % ^b
0.5		100.3	33.5	6.5	
1.25	14.6		49.0	5.2	128.5
7.0	12.0		58.0	4.5	
11.75	10.9		71.0		132.9
12.0		112.4	95.0	3.1	134.5
24.0	8.1	122.4	119.0	3.0	135.6

^a C equals molar. ^b Calculated from the iodine titration.

¹¹ Wohl and List, *Ber.*, 30, 3105 (1897).

trimethylxylose, and the final rotation indicated the presence of 37.2% of trimethylxylose. Direct titration after removal of the calcium ion indicates 2.5% of acidic substances calculated as saccharinic acid.

The high apparent aldose indicates the presence of an "enolic" substance encountered by Wolfrom and Lewis^{3b} and Greene and Lewis^{3c} in treating methylated sugars with dilute alkali. The latter authors showed that, in the case of tetramethylglucose and tetramethylmannose, no ketose or methyl alcohol was present in the reaction mixture. In the present work no direct evidence has been obtained for the absence of ketose, but the materials isolated were entirely aldonic in character since no reducing sugar was left after neutral bromine oxidation.

When the equilibrated solutions (200 cc.) were distilled at low pressure and in a 35°-bath using all precautions to prevent the loss of vapor from multiple receivers at -20°, a distillate one-third the volume of the equilibrated solution distilled was collected. Upon repeated refractionation at atmospheric pressure, a final distillate was obtained upon which methyl alcohol was determined by means of the specific gravity and refractive index. Two separate equilibrations gave, respectively, 0.359 and 0.342 mole of methyl alcohol per mole of trimethylxylose equilibrated. A trace of furfural was also found in the distillate amounting to 0.0006 and 0.0005 mole per mole of trimethylxylose, respectively.

The Action of Dilute Acid upon the Equilibrated Solutions.—It was found that very low concentrations of acid produced furfural from the equilibrated solutions of trimethylxylose. This is in decided contrast to the behavior of dilute acid upon either equilibrated solutions of xylose or tetramethylglucose. In the case of tetramethylglucose, the effect of acid is primarily that of de-enolization. In the case of trimethylxylose, the action is primarily that of furfural production and, perhaps, of de-enolization as well. The rate of de-enolization is shown in Table III and graphically in Fig. 3.

TABLE III
DE-ENOLIZATION OF EQUILIBRATED TRIMETHYLXYLOSE SOLUTION (0.0667 *M*) BY DILUTE ACID (0.667 *N*)

Time, hours	Apparent aldose, % ^a	Time, hours	Apparent aldose, % ^a
0	136.6	6.67	98.6
0.5	109.0	9.5	96.4
1.0	107.8	17.67	93.2
1.33	104.9	28.0	90.7
3.67	101.9	44.0	90.0

^a By iodine titration.

It was found that the action of the same concentration of acid upon untreated trimethylxylose, the condensed keto-xylose isolated and equilibrated solutions of xylose, produced no furfural. The production of

furfural by the action of acid upon equilibrated solutions of trimethylxylose was attributed to the decomposition of the 1,2-monomethylene-diol.¹²

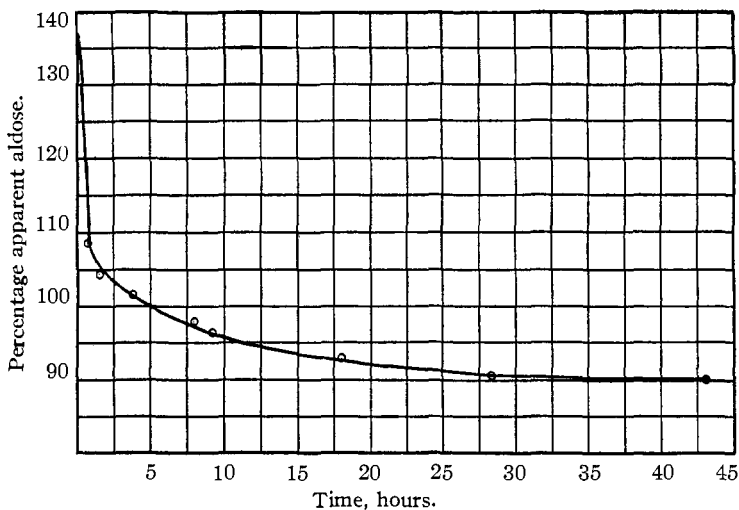


Fig. 3.—Rate of de-enolization of trimethylxylose solutions in dilute acid.

In Table IV and Fig. 4 are shown the relative amounts of furfural produced by the action of the same acid concentrations for the same time upon equilibrated solutions having various apparent aldose values (enol content).

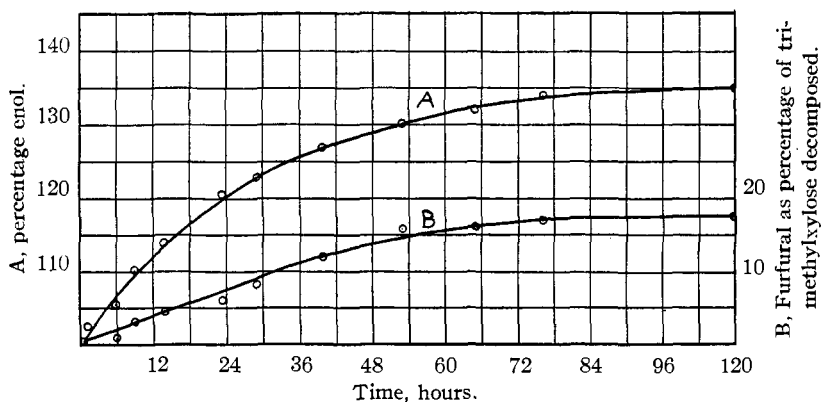


Fig. 4.—Relationship of presumptive enol to furfural formation.

Molar solutions of trimethylxylose made as usual with saturated lime water were heated at 35° until the aldose values were as indicated. They were made 0.0667 *M* in sugar and 0.667 *N* in hydrochloric acid and heated

¹² Cf., however, Carruthers and Hirst, Ref. 5, who report furfural formation during the acid hydrolysis of trimethyl- β -methylxyloside.

for twelve hours at 35°. The furfural was then determined colorimetrically¹³ on the distillate from the acid solution after neutralization. The distillation was continued until a negative test was obtained on 1 cc. of distillate. It was found repeatedly using known furfural mixtures that with the above method a recovery of 88% could be made consistently. In Table IV the furfural is calculated as trimethylxylose decomposed and corrected for an 88% recovery.

TABLE IV
RELATION OF IODINE TITRATION EXPRESSED AS APPARENT PER CENT. ALDOSE TO FURFURAL PRODUCTION BY ACID

Time, hours	Apparent % of aldose	Furfural as % trimethylxylose decomp.	Time, hours	Apparent % of aldose	Furfural as % trimethylxylose decomp.
0	100.0	..	29.0	123.0	8.17
1.0	102.5	0.25	40.0	127.0	11.82
6.0	105.2	.80	53.0	130.0	15.90
9.5	110.0	3.22	65.0	132.0	15.80
14.0	114.0	4.70	76.5	134.0	16.60
23.5	120.5	6.36	120.0	135.0	17.75

Amount of Methyl Alcohol after De-enolization.—In a manner similar to the determination of methyl alcohol present in the equilibrated solution, the amount of methyl alcohol formed during de-enolization was determined. This amounted to 0.790 mole per mole of trimethylxylose equilibrated. Thus, the total methyl alcohol found after de-enolization was 0.350 and 0.790 or 1.140 moles, an amount corresponding to 38.1% of trimethylxylose decomposed to furfural, assuming that all methyl groups are lost from each molecule of trimethylxylose decomposing. It was shown in preliminary experiments that furfural itself is decomposed by the mild acid used; so the difference of 17.75% of furfural found and the 38.1% indicated by methyl alcohol found may be explained on the basis that some furfural was decomposed by the acid before it was determined.

A significant fact appears to be the relationship of the amounts of methyl alcohol in the alkaline equilibrated solution and that formed by the action of acids upon the equilibrated solution after removal of the free methyl alcohol. The relationship is roughly 1 to 2, suggesting that one mole of methyl alcohol is split off in alkaline solution and two additional moles in the acid solution from each mole of trimethylxylose decomposing. This would be in conformity with the equations given on page 2773.

Preliminary Separation of the Equilibrated Solution.—The presence of trimethylxylose was indicated by the levo rotation of the sirup isolated after acid distillment of the equilibrated solution. An impure *d*-trimethoxyglutaric dimethyl ester was formed by the method of Hirst and Purves¹⁴

¹³ Leach, "Food Inspection and Analysis," 3d ed., 1913, p. 746.

¹⁴ Hirst and Purves, *J. Chem. Soc.*, 123, 1352 (1923).

from the trimethylpentose gum isolated. A pure *l*-trimethoxyglutaramide was separated after conversion to the amides. A pure *i*-trimethoxyglutaramide could not be obtained.

A bromine oxidation and subsequent formation of brucine salts gave derivatives which could be separated due to differences in their solubilities in acetone.

Quantitative Study of the Equilibration of Trimethylxylose.—Two-tenths of a mole (38.4 g.) of trimethylxylose was made up to a volume of 200 cc. with lime water saturated at 35°. The initial aldose content by the iodine oxidation method was 100.5% and after heating at 35° for one hundred and twenty hours, it was 138%. The final specific rotation was +3.0° and the solution was alkaline to phenol red indicator. No furfural was present according to the aniline acetate test.

The above equilibrated solution was de-enolized by heating a solution 0.1 *M* in trimethylxylose and 1 *M* in respect to hydrochloric acid for one hour at 35°. The solution was then neutralized with sodium carbonate.

The solution was then concentrated under diminished pressure, precautions being taken as usual to prevent loss of methyl alcohol from the distillate. Upon continued refractionation of the neutral distillate after polymerizing the furfural by the use of sodium hydroxide and determining the content of methyl alcohol by means of the specific gravity and refractive index of the final distillate, it was found that 7.74 g. of methyl alcohol boiling at 65° was recovered from 37.4 g. of trimethylxylose. The methyl 3,5-dinitrobenzoate formed from it melted at 107°¹⁶ and melted unchanged on mixing with the known compound. The total amount of methyl alcohol found (7.74 g. from 37.4 g. of trimethylxylose) corresponds to 1.24 moles per mole of trimethylxylose equilibrated. Calculated as trimethylxylose decomposed, it represents a complete decomposition of 41.3%.

After concentration of the de-enolized solution to 100 cc., this volume was extracted with five 200 cc. portions of chloroform. The aqueous portion was then evaporated to dryness and the salt residue crushed and extracted with two 500 cc. portions of boiling chloroform. The combined chloroform extracts were dried and evaporated. The gum was then dried by heating at 80° and 10 mm. for several hours. The gum weighed 20.8 g., which is a recovery of 55.7% of the theoretical of trimethylpentose. This gum gave 100.3% presumptive trimethylpentose by the iodine oxidation method. It gave a specific rotation of -13.2° (*c* = 5 in water) and contained 44.6% of methoxyl (calcd. 48.4%). The above constants indicate a mixture largely of trimethylxylose with some trimethylxylose and probably some partially demethylated pentose.

After the above determination had been made, 20.0 g. of gum remained which was oxidized with bromine according to the method of Hudson.⁸ After fifty-six hours the

TABLE V
PARTIAL SEPARATION OF BRUCINE SALTS

Fraction	Weight, g.	Rotation, degrees
I	42.0	-18.9
II	5.5	-23.1
III	2.7	-22.7
IV	5.2	-33.0
Total	55.4	

¹⁶ Kamm, "Qualitative Organic Analysis," John Wiley and Sons, Inc., New York, 1923, p. 151.

solution no longer reduced boiling Fehling's solution. It was then treated in the usual manner for the removal of the objectionable ions and the free acids converted to brucine salts. After removal of the water, the brucine salts were dissolved in a minimum of hot water and fractionated as shown in Table V.

The theoretical yield of brucine salt of trimethylpentonic acid would be 60.6 g. The yield was then 91.4% of the theoretical. By a tedious process of fractional crystallization from acetone, the above fractions were resolved into the least soluble brucine trimethylxylonate and the more soluble brucine trimethyllyxonate, with a small residue of extremely soluble partially de-methylated pentonic acids.

TABLE VI
SEPARATION OF BRUCINE SALTS

Compound	Weight, g.	Specific rotation, degrees	M. p., °C.	Methoxyl, %
Trimethylxylonate	12.63	- 6.6	114-115	26.45
Trimethyllyxonate	33.59	-23.0	99-100	26.68
Partially methylated pentonates	2.0	-30.2	145-150	19.0
	48.22	Calcd. methoxyl,		25.8

The brucine salts separated (48.22 g.) amounted to a recovery of 89.0% of the theoretical (55.4 g.). The amount separated (48.22 g.) corresponds to a yield of 79.6% from the trimethylpentose gum oxidized (20.0 g.).

Known brucine trimethylxylonate gave a specific rotation of -6.2° ($\alpha = -0.221$ in a 1-dm. tube when c is 3.57 in water) and melted at $114.5-115^\circ$. The methoxyl content was 26.42%.

Anal. Subs., 0.1107: AgI, 0.2215. Calcd. for $C_{26}H_{27}N_2O_6(OCH_3)_3$: OCH_3 , 25.8. Found: OCH_3 , 26.42.

The presumptive brucine trimethylxylonate (12.63 g.) gave a specific rotation of -6.6° ($\alpha = -0.187$ in a 2-dm. tube when c is 1.42 in water) and melted at $114-115^\circ$. It contained 26.45% methoxyl.

Anal. Subs., 0.1013: AgI, 0.2032. Calcd. for $C_{26}H_{27}N_2O_6(OCH_3)_3$: OCH_3 , 25.8. Found: OCH_3 , 26.45.

To identify still further the presumptive brucine trimethylxylonate, 9.0 g. was converted to the phenylhydrazide according to the method of Hirst.¹⁶ The hydrazide once recrystallized from benzene weighed 3.18 g., which is 68.8% of the calcd. It melted at $134-135^\circ$ and when again recrystallized melted at $136-137^\circ$. The rotation is $+31.1^\circ$ ($\alpha = +0.335$ in a 1-dm. tube when c is 1.079 in methyl alcohol). It contains 30.8% of methoxyl. Hirst¹⁶ records a melting point of $137-138.5^\circ$.

Anal. Subs., 0.0908: AgI, 0.2120. Calcd. for $C_{11}H_{13}N_2O_2(OCH_3)_3$: OCH_3 , 31.2. Found: OCH_3 , 30.8.

The presumptive brucine trimethyllyxonate (33.59 g.) melted at $99-100^\circ$ and gave a specific rotation of -23.0° ($\alpha = -0.554$ in a 1-dm. tube when c is 2.41 in water). The methoxyl content was 26.68%.

Anal. Subs., 0.1066: AgI, 0.2155. Calcd. for $C_{26}H_{27}N_2O_6(OCH_3)_3$: OCH_3 , 25.8. Found: OCH_3 , 26.68.

Ten grams of the presumptive brucine trimethyllyxonate was converted to the phenylhydrazide according to the method of Hirst¹⁶ after removal of the brucine. There was obtained 3.82 g. once recrystallized from benzene, which amounts to a yield of 74.6%.

¹⁶ Hirst, *J. Chem. Soc.*, 3147 (1928).

It melted at 179–180° and after a second recrystallization melted at 179.5–180°. The specific rotation was -30.1° ($\alpha = -0.465^\circ$ in a 1-dm. tube when c is 1.548 in methyl alcohol). It had a methoxyl content of 30.78%.

Anal. Subs., 0.1144; AgI, 0.2663. Calcd. for $C_{11}H_{13}N_2O_2(OCH_3)_3$: OCH_3 , 31.2. Found: OCH_3 , 30.78.

The presumptive brucine partially demethylated pentonates (2.0 g.) melted at 145–150° and when mixed with either brucine trimethyllyxonate or xylonate melted over a range 20° lower. The specific rotation was -30.2° ($\alpha = -0.37^\circ$ in a 1-dm. tube when c is 1.231 in water). It contained 19.2 and 18.8% of methoxyl.

Anal. Subs., 0.1047, 0.1295; AgI, 0.1521, 0.1842. Calcd. for $C_{26}H_{28}N_2O_6(OCH_3)_4$: OCH_3 , 21.1; for $C_{26}H_{28}N_2O_7(OCH_3)_3$: OCH_3 , 16.2. Found: OCH_3 , 19.2, 18.8.

Therefore the gum consisted of about 70% trimethylxylose, 26% trimethyllyxose and 4% of partially methylated materials. Considering the methyl alcohol isolated as indicating the complete decomposition of trimethylxylose to furfural and methyl alcohol, then 41.3% was decomposed. The gum isolated accounts for 55.7% and therefore a calculated total of 97% of the equilibrated xylose is accounted for as isolated. The furfural found is only a portion of that formed since acid causes its decomposition. The gum isolated was separated into its components in 79.6% yield after conversion to aldonic acid and separation of the brucine salts from acetone. Trimethylxyloic and trimethyllyxononic acids were identified as the known crystalline phenylhydrazides.

Conclusion

From the equilibration of 38.4 g. of trimethylxylose (less 1 g. for samples) there was isolated 20.8 g. of trimethylpentose gum or 55.7%. There was also isolated 7.74 g. of methyl alcohol, which indicates the decomposition of 41.3% of the trimethylxylose used, assuming loss of three moles of methyl alcohol from each mole of trimethylxylose decomposed. The total trimethylxylose accounted for in this manner is, therefore, 97.0%.

The remainder of the trimethylpentose gum (20.0 g.) was oxidized to trimethylpentonic acids and converted to brucine salts. A total of 55.4 g. of brucine salt was isolated or a yield of 91.4%. The 55.4 g. of brucine salt was separated by fractional crystallization from acetone into brucine trimethyllyxonate 33.59 g., brucine trimethylxyloate 12.63 g. and brucine mono- and di-methoxypentonic acids 2.00 g. The separation was effected with a recovery of 89.0%. The brucine salts separated amounted to 79.6%.

If the amount of trimethylxylose and trimethyllyxose were relatively the same in the original equilibrated solution as in the gum isolated, then the equilibrated solution would have had 38.8% of trimethyllyxose and data for rotations indicated 37.0%. The composition of the isolated gum was trimethyllyxose, 69.6%, trimethylxylose, 26.2% and partially demethylated pentose, 4.2%.

Summary

1. When xylose was treated with lime water at 35°, there were identified 52.9% of xylose, 8.3% of lyxose, 9.8% of a crystalline condensed ketose and 3.4% of presumptive saccharinic acid, expressed as percentage of pentose.

2. The equilibrated solution gave no evidence of a stable enol and treatment with acid did not produce furfural.

3. When trimethylxylose was treated with dilute alkali under the same conditions, it was transformed in part into the epimeric trimethyllyxose, a high iodine absorbing compound believed to be the monomethylenediol and saccharinic acid, the latter in small amount.

4. Methyl alcohol was found in the alkaline solution of trimethylxylose approximately in the proportion of one mole to each mole of methylated sugar decomposed. On treatment with dilute acids, two further moles of methyl alcohol was liberated per mole of sugar decomposed and furfural was formed. A mechanism is proposed for this reaction.

5. The gum formed consisted of trimethylxylose, trimethyllyxose and partially demethylated products in the proportion of 26 to 70 to 4 parts, respectively. Indirect evidence is advanced for the absence of ketose.

6. The conversion of normal trimethylxylose into normal trimethyllyxose confirms the identity of their ring structures.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE EXPERIMENTAL RESEARCH LABORATORIES, BURROUGHS
WELLCOME AND COMPANY]

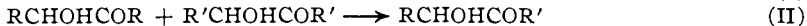
MIXED BENZOINS. VI. FURTHER EXAMPLES OF REVERSIBILITY. THE FORMATION OF ADDITION COMPOUNDS

BY JOHANNES S. BUCK AND WALTER S. IDE

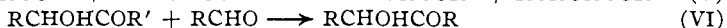
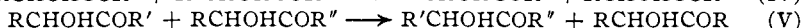
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In Part V¹ the reversibility of the benzoin condensation was demonstrated by means of the reaction $RCHOHCOR + R'CHO \rightarrow RCHOHCOR'$. This change took place under conditions comparable to those of the usual benzoin reaction. A scheme was formulated for the equilibrium conditions of a benzoin reaction mixture of any type. As noted in part V the scheme implied that a number of other transformations were possible, and most of these implications have now been investigated. Positive results were obtained in two of the possible reactions, namely



The results are tabulated. The remaining possibilities



were examined, but only negative results were obtained. The inability to isolate the expected product means either that it was formed in amounts

¹ Buck and Ide, *THIS JOURNAL*, 53, 2350 (1931).