was dried over anhydrous sodium sulfate and evaporated under diminished pressure. There was obtained a residue which, when recrystallized from hot water, separated as colorless crystals melting at 144–144.5°, with evolution of gas. The neutral equivalent was found to be 123; that calculated for 2-phenyl-3,6-dicarboxy-5,6-dihydro-1,4-pyran is 124.

When the hot alkaline reaction mixture was acidified with hydrochloric acid the product obtained was the mono-carboxylic acid (see below).

δ-Benzoyl-α-hydroxyvaleric Acid (VIII).—One gram of the cyano acid (VII) was heated under a reflux condenser with 60 cc. of a 50% solution of sulfuric acid. After fifteen minutes of boiling the cyano acid was completely dissolved. The solution darkened rapidly and at the end of an hour dark crystals began to separate. The heating was then discontinued and the reaction mixture was diluted with an equal volume of water. This solution was cooled to 0° and allowed to stand for several hours. The crystals obtained in this way were removed by filtration and recrystallized first from hot water and then from ethyl acetate. The δ-benzoyl-α-hydroxyvaleric acid thus obtained was shown to be identical with that prepared from the dicarboxylic acid as indicated in the preceding section. It melted at 120–120.5°; the yield was 88% of the theoretical.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.2; H, 6.3. Found: C, 64.3; H, 6.0.

Oxime.—The oxime was a colorless crystalline compound, melting at 144–145.5°; the yield was 63% of the theoretical.

Anal. Calcd. for $C_{12}H_{15}O_4N$: C, 60.8; H, 6.4. Found: C, 60.7; H, 6.4.

Summary

Evidence has been presented in support of a dihydro-1,4-pyran structure for the cyano ketone obtained by the cyanide ring-closure of 1,4-dibromo-1,4-dibenzoylbutane. The anilide obtained by rearrangement of the oxime of the cyano ketone has been found to hydrolyze to δ-benzoyl-α-hydroxyvaleric acid. This result furnishes convincing evidence that the cyano compound is 2-phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

PENTOSE REACTIONS. I. FURFURAL FORMATION

BY CHARLES D. HURD AND LLOYD L. ISENHOUR[1]

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It is generally known that pentoses yield furfural on distillation with mineral acids. This is the basis for the determination[2] of pentoses. Furthermore, the commercial production of furfural[3] depends on the pentosan content of oat hulls. In proportion to the general familiarity with the reaction, detailed study on it has been quite limited.

To ascertain whether or not the reaction of pentose into furfural was merely one of dehydration, xylose was heated with phosphorus pentoxide

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[1] Quaker Oats Fellow at Northwestern University, 1927–1929.

[2] Pervier and Gortner, *Ind. Eng. Chem.*, **15**, 1167, 1255 (1923).

[3] Miner and Brownlee, British Patent, 203,691, Dec. 4, 1924; *Chem. Abstracts*, **18**, 692 (1924).

and with zinc chloride (145°). Negligible yields resulted; nor did distillation of xylose with 4 molar phosphoric acid give rise to any furfural.[4] A low yield was formed, however, when xylose was distilled in the presence of a solution of zinc chloride. Distillation of xylose with several salt solutions gave immeasurable quantities of furfural. Solutions such as these were tried: saturated sodium chloride, saturated sodium sulfate, 4.1 molar calcium chloride. The use of 4 molar ammonium sulfate solution gave slight yields.

Xylose and Mineral Acids.—Pervier and Gortner[2] demonstrated that steam distillation of the mixture of pentoses and mineral acids increases the yield of furfural, but little attention has been paid to the effect caused by varying the concentration of acids. For a given acid, the important variables are the concentration, the temperature and the duration of the distillation. Almost no furfural was detectable with 3.8 *N* sulfuric acid (H_2SO_4, 16% by wt.) at 67°, and only a 2% yield was realized in one and one-half hours at 85°. This yield changed to 38%, however, when a temperature of 107° was taken.

In the technical manufacture of furfural, the yield is dependent on the high temperature which is employed. Five per cent. sulfuric acid is used[5] on the xylan of oat hulls. It is apparent that the yield of furfural at 100–102°, the distillation temperature of the acid at atmospheric pressure, would be nil. However, operating conditions are at a higher temperature (about 145–148°), since a steam pressure of 60 lb./sq. in. is maintained.

Most of the present work was performed at atmospheric pressure with varying concentrations of hydrochloric and sulfuric acids. Hydrochloric acid solutions varied between 1.3 and 5.2 normal (4.7–18.8%), and sulfuric acid concentrations between 3.8 and 12.1 normal (16–52%). Furfural yields were small at the low concentrations but they became higher as the concentration increased. The data are summarized in Tables I and II of the experimental part.

The change of xylose into furfural followed the unimolecular law. By plotting time against log $(a - x)$, the straight line functions shown in Fig. 1 result. This is in keeping with the unimolecular equation

$$k = \frac{2.3}{t} \log \frac{a}{(a - x)}$$

wherein $(a - x)$ represents the quantity of undecomposed xylose at the end of time *t*. From the curves it is evident that sulfuric and hydrochloric

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[4] Fukai, *Bul. Ferm.*, **100**, 106 (1928); *Chem. Abstracts*, **23**, 1081 (1929), states that the phosphoric acid distillate of various sugars shows only a faint test for furfurals. For further evidence of furfural formation under conditions where a simple dehydration reaction is unthinkable, see Aronovsky and Gortner, *Ind. Eng. Chem.*, **22**, 264 (1930).

[5] Miner, Trickey and Brownlee, *Chem. Met. Eng.*, **27**, 299, 362 (1922); Killeffer, *Ind. Eng. Chem.*, **18**, 1217 (1926).

acids give similar effects if the normality of the former is about double that of the latter. As the value of *t* increases, the furfural yield shows a tendency to fall off. This effect is the most pronounced with sulfuric acid in its higher concentrations, as Fig. 1 reveals, where the straight line functions become curved. By extending the hydrochloric acid curves, a similar falling-off would be apparent. This may be taken as evidence that some of the furfural remains in contact with the hot acid long enough to resinify. With the more concentrated acids, the rate of furfural formation may be greater than its rate of removal.

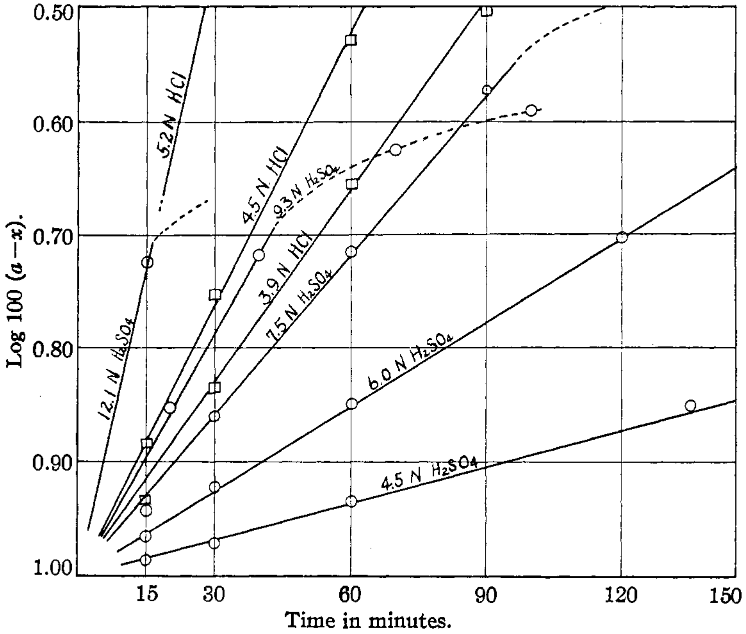

Fig. 1.—Xylose and mineral acids.

An analogous study with rhamnose substantiated this viewpoint. Methylfurfural is formed by distillation with acids, but it does not steam-distil so readily as furfural. When 0.1 g. of rhamnose was steam-distilled with 32% sulfuric acid, a fairly high yield was obtained provided that a large volume of steam was passed through the mixture. With larger quantities of rhamnose or with slower distillation conditions, humin bodies resulted and the yield of methylfurfural was low because of its reaction with the acid.

The higher the concentration of acid, the higher was its distillation temperature. A range from 101 to 107° was encountered in hydrochloric acid, and 103 to 127° with sulfuric acid. As was demonstrated above, the increased boiling temperature of the more concentrated solutions plays a part in furfural production, but two other factors enter. First, is the hydrogen-ion concentration and, second, is the nature of the acid. Nitric acid (19% concentration), for example, gave only 1.5% yield of furfural after thirty minutes of steam distillation. Trichloroacetic acid (4 molar) was no better.

Thinking that "superacid" solutions[6] might sponsor furfural production from xylose, this substance was placed in a dilute solution of sulfuric acid in butyric acid and the mixture distilled. Only a 3% yield of furfural was realized in two and one-half hours. A negligible yield came also when a mixture of xylose, acetic acid and benzenesulfonic acid was distilled.

Humins from Furfural.—The reaction of furfural with acids, according to Marcusson,[7] leads to humins and humic acid. In studying this reaction further, it was learned that refluxing furfural for two hours in hydrochloric acid of 18.8% strength destroyed three-fifths of the furfural. If such a solution was steam-distilled instead of refluxed, 99.5% recovery of the furfural was attainable.

Both alkali-soluble humic acid and alkali-insoluble humin were formed when furfural was slowly added to a refluxing solution of 14% hydrochloric acid. At the end of three hours, all but one-fourth of the furfural had entered into reaction, the reaction product being a black precipitate. The carbon content of this substance was determined by sodium peroxide fusion[8] and also by a chromic acid oxidation method.[9] A difference of 13% between the two determinations, the former giving the higher value, points to the presence of some free carbon or else to the presence of polymeric humins of such complexity that their oxidation by the chromic acid method is a matter of difficulty.

Other Pentoses and Mineral Acids.—Steam distillation of arabinose from 32% sulfuric acid gave a 45% yield of furfural. Under identical conditions, the yield from xylose was 70% of the calculated. Possibly there is a relationship between these values and the velocity coefficients of mutarotation (k) of the pentoses.[10] At least, it seems reasonable to believe that the initial effect of acid on a sugar is to convert it from the cyclic "hemi-acetal" form into the "aldehyde" form. The values of k for xylose and arabinose, respectively, are 0.021 and 0.031. The quotient of $1.5/k$ equals 74 and 45, values which are surprisingly close to the yields of furfural with the same sugars. With k for lyxose given as 0.065, then $1.5/k$ is 22. It may be predicted that the yield of furfural from lyxose (with 32%

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[6] Conant and Hall, This Journal, **49**, 3062 (1927).

[7] Gortner, *J. Biol. Chem.*, **26**, 194 (1916); Marcusson, *Ber.*, **54**, 542 (1921).

[8] Parr, "The Analysis of Fuel, Gas, Water and Lubricants," McGraw-Hill Book Co., New York, 1912, p. 179.

[9] Florentine, *Bull. soc. chim.*, **31**, 1068 (1922); **35**, 228 (1924).

[10] Hudson, "Relations between Rotatory Power and Structure in the Sugar Group," Sci. Papers of the Bureau of Standards, No. 553, U. S. Printing Office, 1926, p. 271.

sulfuric acid) would be less than from arabinose. It would be interesting to learn if the yield were in the vicinity of 22%.

Experiments with rhamnose indicated it to be of the same order of activity as arabinose for furfural production, but the distillation rate for methylfurfural so differs from the rate for furfural that the results may not be strictly comparable.

It was of interest to study the behavior of ketoxylose, $CH_2OH(CHOH)_2COCH_2OH$, with acids. We are indebted to C. E. Gross[11] of this Laboratory who furnished us with a polymeric modification of this ketose. Its molecular weight indicated that it was a tetrasaccharide, $(4C_5H_{10}O_5-3H_2O)$. This ketose was distilled with 32% sulfuric acid. During the first half hour, slightly less than a 5% yield of furfural was formed, but no more came by prolonging the distillation. Figure 2 shows graphically the rate of furfural production of the various pentoses which have been considered.

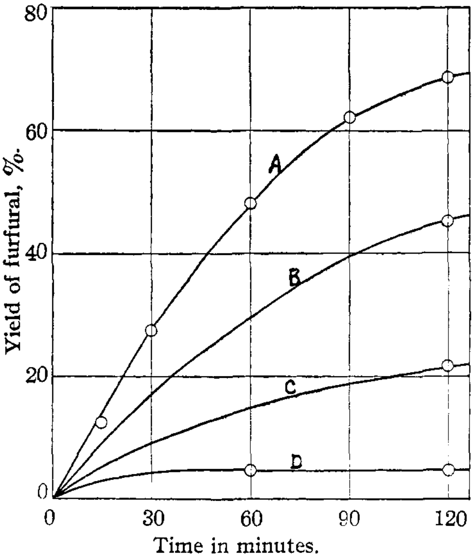
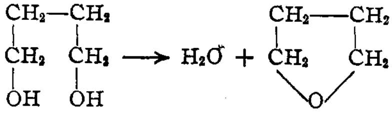


Fig. 2.—Furfural from various pentoses with 7.5 *N* sulfuric acid: A, xylose; B, arabinose; C, predicted curve for lyxose; D, ketoxylose polymer.

Tetrahydrofuran.—Tetramethylene glycol was prepared by reduction of diethyl succinate. When this glycol was refluxed with 7.5 *N* sulfuric acid (32%), a 76% yield of tetrahydrofuran was realized



$$\begin{array}{ll} CH_2-CH_2 & \\ | \qquad | & \\ CH_2 \quad CH_2 & \longrightarrow H_2O + \\ | \qquad | & \\ OH \quad OH & \end{array} \begin{array}{c} CH_2-CH_2 \\ | \qquad\quad | \\ CH_2 \qquad CH_2 \\ \diagdown \; O \; \diagup \end{array}$$

It was thought that erythritol should also give rise to a furan ring closure on heating with acids. However, no change at all was observed when mesoerythritol was refluxed for six and one-half hours with 7.5 *N* sulfuric acid. The fact that tetramethylene glycol yields tetrahydrofuran more easily than xylose yields furfural is difficult to reconcile with this non-formation of furan from natural erythritol. However, just as arabinose and xylose differ in their ease of furfural formation, so it is possible that *d*-, *l*- or *dl*-erythritol would behave differently from mesoerythritol in this respect.

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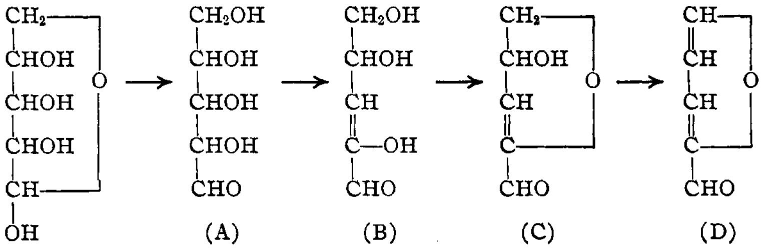
[11] Gross and Lewis, THIS JOURNAL, **53**, 2777 (1931).

Attempts to synthesize *d*-erythritol were unsatisfactory, so we have no information on this point.

The cadmium xylonate-cadmium bromide double salt was refluxed for two hours in 3.9 *N* hydrochloric acid. No furoic acid could be detected as a reaction product.

Mechanism of Furfural Formation.—Whether or not an aldopentose is considered to possess the cyclic hemi-acetal formula or the open-chain aldehyde formula, it seems obvious that the latter is an essential intermediate between the former and furfural. Acetals, quite generally, are hydrolyzed by acids. Following Fittig's suggestion,[12] it has often been assumed that dehydration into a heterocyclic ring is the first step. In our opinion, this is the second step, the first one being a dehydration to an α,β-unsaturated aldehyde as follows



These facts support such a picture. (1) β-Hydroxyaldehydes, such as aldol, lose water very readily in the manner of (A) to (B). (2) Secondary alcohols which are not β-hydroxyaldehydes also lose water in the manner of (A) to (B), but much less readily. Just as isopropyl alcohol is more difficult to dehydrate to an unsaturated compound than aldol (compare [$CH_3CHOH—CH_2$]H and [$CH_3CHOH—CH_2$]CHO), so erythritol should be more difficult to dehydrate to an unsaturated compound than an aldopentose (compare [R—CHOH—CHOH]H and [R—CHOH—CHOH]-CHO, wherein R is the radical $CH_2OH—CHOH—$). Actually, furan could not be formed from erythritol. This suggests that step (C) cannot be realized in the case of erythritol, because the change from (A) to (B) is blocked. (3) The formation of tetrahydrofuran from tetramethylene glycol demonstrates how readily a furan ring closure may be effected when no interfering hydroxyl groups are present. Several other cases of furan ring closure from the action of acids on gamma glycols are listed in the literature. The fact that butanetriol-1,2,4 may be converted into hydroxytetrahydrofuran

$$\underset{OH}{CH_2}—CHOH—CH_2—\underset{OH}{CH_2} \longrightarrow \underbrace{CH_2—CHOH—CH_2—CH_2}_{O}$$

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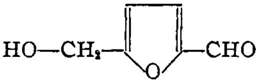
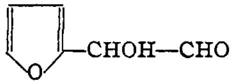
[12] Fittig, *Ann.*, **303**, 169 (1898).

on boiling with water[13] shows that the presence of one hydroxyl group on the chain does not exert steric hindrance to prevent ring closure. (4) Unless step (B) precedes step (C), it is difficult to explain why the cause which blocks erythritol does not also block xylose. (5) Applied to the hexoses, this mechanism leads logically to the production of hydroxymethylfurfural. If the first step were regarded as that of heterocyclic ring formation, both this compound and its isomer furylgylcolic aldehyde should result for ring closure of this type should occur equally readily in a hexose between carbon atoms 2,5, or 3,6. Only the former evidently occurs.



Hydroxymethylfurfural



Furylglycolic aldehyde

Experimental Part

Xylose was synthesized from corn cobs[14] hy hydrolysis with dilute sulfuric acid (7%) following the usual method. From 1 kg. of cobs, 100 g. of pure xylose was obtained. For some of the concluding experiments in this work, xylose was generously donated by the Bureau of Standards.

Xylose from Oat Hulls.—Except for a preliminary soaking in ammonium hydroxide and for somewhat milder conditions of acid hydrolysis, oat hulls were hydrolyzed to xylose using a method which was similar to that used with corn cobs. Xylose was definitely identified but difficulties in the purification procedure limited the yield to about one-third that from corn cobs.

A mixture of 4 liters of water, 400 cc. of concd. ammonium hydroxide and 500 g. of oat hulls was left at room temperature for fifty-two hours. Then the hulls were filtered off and washed with 4 liters of water. The hulls were placed in 3 liters of water which contained 350 cc. of concd. sulfuric acid. After twenty-three hours, 3 liters of water was added and the mixture was left for seventy-two hours more, following which it was refluxed for one hour. After filtration, the filtrate was almost neutralized with calcium hydroxide and the neutralization completed with calcium carbonate. The calcium sulfate was collected on a filter and washed with 2 liters of water. The filtrate was made acid with 5 cc. of 85% phosphoric acid, 30 g. of decolorizing carbon added, air bubbled through the warm suspension for half an hour and finally filtered. The filtrate was concentrated under diminished pressure to a volume of 400 cc. No darkening occurred. A liter of alcohol was added and the precipitate of calcium sulfate removed. The filtrate from this operation was concentrated to a thick sirup (about 100 cc.) under reduced pressure, cooled and diluted with an equal volume of absolute alcohol. After seeding with a small crystal of xylose, the mixture was left for two weeks in a desiccator over sulfuric acid. The mass was then placed on a suction filter overnight after it had been thinned with about 25 cc. of 90% alcohol. About 40 g. of a mixture of xylose and gum was obtained. This was dissolved in 75 cc. of hot 90% alcohol. The solution was evaporated to a thick sirup on the steam-bath, seeded with a crystal of xylose and crystallized in a desiccator. The crystals which resulted were filtered and washed thoroughly with four 20-cc. portions of 80% alcohol and finally with a little absolute alcohol. The yield of dry crystals was 14 g., or 2.8%.

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[13] Pariselle, *Ann. chim. phys.*, **24**, 315 (1911).

[14] Hudson and Harding, THIS JOURNAL, **40**, 1601 (1918); Harding, *Sugar*, **25**, 124 (1923).

Identification.—Two grams of the crystalline product was dissolved in 20 cc. of water and the volume made up to 25 cc. The optical rotation was then determined, using a one-decimeter tube. This gave a constant rotation of +1.5°, from which the specific rotation is +18.75°. Hudson's value[15] is 19°. This rotation did not change when the solution was left for two months.

For further identification of the pentose from the oat hulls, the crystals were converted to xylosazone[16] which melted at 156° (corr.) and to the double salt of cadmium bromide and cadmium xylonate. The latter is especially characteristic of xylose.

Beautifully formed crystals of the xylose were obtained by crystallization from 90% alcohol in a desiccator. When examined under a polarizing microscope, the crystals were found to be of the negative biaxial type. The alpha index of refraction was 1.515 and the beta index 1.540. These values agree with the published values of Wherry,[17] namely, 1.517 and 1.544.

Furfural Analysis.—The colorimetric method of Youngberg and Pucher[18] using aniline acetate in an excess of acetic acid was employed. For careful work, about forty-five minutes was required from one analysis to the next, but approximate results could be obtained in fifteen minutes. Youngberg and Pucher recommended the use of standard comparison solutions of 0.02 and 0.05 mg. furfural per cc. In the present work, a 0.05-mg. standard has served all purposes. Its use allows the concentration of the unknown to vary from 0.01 to 0.09 mg. per cc. Where the furfural content of the unknown was as low as 0.01 mg. per cc., 4 cc. was matched against 1 cc. of the standard, thus making the ratio of the total furfural contents as 4 to 5. This permitted accurate analysis.

A colorimetric method using benzidine[19] was studied. It cannot be recommended, for the color faded rapidly. In addition, the color was much harder to match than that obtained by the aniline acetate method.

A reagent which was useful in determining the end-point of a furfural steam-distillation was a mixture of 1 cc. of glacial acetic acid and 0.5 cc. of aniline. When 2 to 3 cc. of distillate gave no coloration with this reagent in one minute, furfural was considered to be absent. This was somewhat more satisfactory than the aniline hydrochloride paper which was recommended by Pervier and Gortner.

Production of Furfural from Xylose

Phosphorus Pentoxide.—When 0.5 g. of xylose and 2 g. of phosphoric anhydride were heated in a distilling flask at 107° and 80 mm. for five hours, there was no evidence of a distillate which contained furfural. The aniline acetate test was negative, whereas minute quantities of furfural give a red coloration with aniline in acetic acid.

Zinc Chloride. (a) Without Water.—Xylose (0.5 g.) and zinc chloride in excess were heated for twenty-five minutes at 145° and 80 mm. A slight charring occurred and a trace of distillate was collected. It contained about 1.5 mg. of furfural; yield, less than 0.1%.

(b) With Water. Very Concentrated Solution.—In a 25-cc. distilling flask were placed 0.36 g. of xylose, 0.25 cc. of water and 1.0 g. of zinc chloride. It was connected to an ice-cooled receiver and the pressure lowered to 45 mm. Heating in a bath at 180° caused vigorous bubbling for ten minutes, after which a charred, porous mass remained. The distillate was diluted to a volume of 350 cc. and analyzed. The furfural content showed a 15.3% yield.

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[15] Hudson, Ref. 10, p. 269.

[16] Heuser and Brunner, *J. prakt. Chem.*, **104,** 279 (1922).

[17] Wherry, THIS JOURNAL, **40,** 1852 (1918).

[18] Youngberg and Pucher, *J. Biol. Chem.*, **61,** 741 (1924).

[19] McCance, *Biochem. J.*, **20,** 1111 (1926).

The data of this analysis will be listed, but not in subsequent analyses. From the 350 cc. of unknown solution, 1 cc. was matched colorimetrically against 2 cc. of a standard which contained 0.10 mg. (0.05 mg. per cc.) of furfural. In most of the analyses, 1 cc. of the unknown was matched against 1 cc. of the standard. The depth of the standard solution was 31 mm., whereas the unknown solution matched it at 30.8 mm. Thus, the 1 cc. of unknown solution contained (31/30.8) (0.10 mg.) or 0.10064 mg. of furfural. From this, the 350 cc. contained 35.225 mg., as opposed to a theoretical yield of 229.5 mg.; percentage yield, 15.3.

Four Molar Zinc Chloride (**4.4** *M*).—A solution of 0.1 g. of xylose, 120 g. of zinc chloride and water was made up to 200 cc. The solution was steam distilled during two hours. The distillate was collected in four periods, at the end of fifteen, thirty, sixty and one hundred and twenty minutes from the start. Furfural analyses on each gave 2.47, 9.7, 15.9 and 13.11% yields, respectively, or a total yield of 41.2%. The temperature of the reaction mixture rose from 108 to 109.5° during the first thirty minutes. The subsequent temperature was 109.5–110°.

Other Salts.—Distillation of xylose from saturated sodium chloride solution, saturated sodium sulfate solution or from a 4.1 molar calcium chloride solution gave nearly immeasurable quantities of furfural. Traces were formed, but only slightly more (due to increased temperature) than would have been formed by distilling xylose from a pure water solution.

Distillation of Xylose with Acids

Phosphoric Acid.—Steam distillation of xylose (0.1 g.) with 4 molar phosphoric acid solution (200 cc. contained 64 g. of HPO_3) gave no appreciable quantity of furfural.

Oxalic Acid.—A solution of xylose in 200 cc. of 4 molar oxalic acid distilled at a temperature of 103°. In forty-five minutes, less than 3% of the xylose had been converted into furfural.

Trichloroacetic acid, in 4 molar solution, gave a quantity of furfural which was insufficient to analyze.

Nitric Acid.—One-tenth gram of xylose and 150 cc. of a 19.5% solution of nitric acid (3.4 normal) were steam distilled for seven hours. The distillation temperature was 104°. Colorimetric analyses showed that 11.85 mg. of furfural had distilled over in the 435 cc. of distillate, which represented an 18.5% yield. The yield was about 3% at the end of the first hour, which is indicative of a uniform reaction rate.

Hydrochloric Acid.—For all studies of the rate of formation of furfural from xylose, the following apparatus was used. A 300-cc. long-necked, round-bottomed flask was fitted with a steam inlet, a thermometer and a vertical 46-cm. delivery tube leading to a condenser. The long delivery tube served as a fractionating column. In this way it was possible to have a large volume of steam coming out of the reaction mixture without the necessity of having an unduly large amount of distillate. Thus, a more efficient removal of the furfural from the reaction mixture was realized without the disadvantage of having a solution too dilute for analysis after the vapor was condensed.

Hydrochloric acid was studied in four concentrations. The results are collected in Table I. The weight of xylose taken for each distillation was 0.1 g. and the original volume of acid solution for each was 200 cc. In the acids of higher concentration, the distillate was collected in five fractions, each of which was analyzed individually.

Sulfuric Acid.—Xylose (0.1 g.) was distilled from sulfuric acid solutions of several different concentrations. Two hundred cc. of the acid was always taken, except with the 6.0 *N* acid, when 150 cc. was used. The results are tabulated in Table II. These results, and also the results obtained with hydrochloric acid, are plotted on Fig. 1. With 7.5 *N* acid, or higher, the reaction mixture darkened somewhat as distillation progressed.

TABLE I

XYLOSE AND HYDROCHLORIC ACID

Acid concn.		Distn. temp., °C.	Distn. period, minutes	Vol. of distillate, cc.	Furfural yield		100 $(a - x)$	$k_{\text{min.}}$
% by wt.	Normality				mg.	%		
4.70	1.3	101	30	103	0.39	0.62	9.938	0.00021
9.45	2.6	102.5	510	2250	56.61	88.4[a]	1.16	.0042
14.15	3.9	104	15	250	8.62	13.5	8.65	.010
			15	100	11.54	18.0	6.85	.013
			30	100	14.71	23.0	4.55	.013
			30	100	8.77	13.7	3.18	.013
			30	100	4.92	7.7	2.41	.012
		Totals	120			75.9		
16.5	4.5	106	15	250	15.24	23.81	7.619	.018
			15	100	13.15	20.55	5.564	.018
			30	250	13.95	21.80	3.384	.018
			60	180	10.92	17.05	1.679	.015
			70	260	0.65	1.00	1.579	.010
		Totals	190			84.21		
18.8	5.2	107	30	250	46.05	72.0	2.80	.042
			30	250	9.12	15.5	1.25	.035
			30	114	2.38	4.1	0.84	.028
			30	106	0.62	1.0	.74	.022
			30	100	nil	...		
		Totals	150			92.6		

[a] Furfural was still being formed at the end of eight and one-half hours.

TABLE II

XYLOSE AND SULFURIC ACID

Acid concn.		Distn. temp., °C.	Distn. period, minutes	Vol. of distillate, cc.	Furfural yield		100 $(a - x)$	$k_{\text{min.}}$
% by wt.	Normality				mg.	%		
19.2	4.5	103	15	50	1.59	2.5	9.75	0.0017
			15	50	2.43	3.8	9.37	.0022
			30	100	4.73	7.4	8.63	.0024
			75	325	10.16	15.9	7.03	.0026
		Totals	135			29.6		
25.6	6.0	106	15	100	4.98	7.8	9.22	.0054
			15	100	5.66	8.84	8.34	.0061
			30	150	8.26	12.9	7.05	.0059
			60	170	12.8	20.0	5.05	.0057
		Totals	120			49.5		
25.6	6.0[a]	106	15	150	10.05	8.2	9.18	.0058
			15	150	12.1	9.4	8.24	.0065
			30	200	20.14	15.7	6.67	.0067
			60	200	27.0	21.1	4.56	.0066
		Totals	120			54.4		

TABLE II (*Concluded*)

Acid concn. % by wt.	Acid concn. Normality	Distn. temp., °C.	Distn. period, minutes	Vol. of distillate, cc.	Furfural yield mg.	Furfural yield %	100 $(a - x)$	$k_{\text{min.}}$
32	7.5	108.7	15	250	7.91	12.36	8.76	0.009
			15	100	9.74	15.22	7.24	.011
			30	100	13.16	20.56	5.19	.011
			30	100	8.99	14.05	3.78	.011
			30	50	4.29	6.7	3.11	.010
		Totals	120			68.9		
40	9.3	112–113	20	250	18.85	29.4	7.06	.017
			20	250	12.44	19.4	5.12	.017
			30	250	5.68	8.9	4.23	.012
			30	50	0.83	1.3	4.10	.009
		Totals	100			59.0		
52	12.1	127	15	250	30.12	47.1	5.29	.042
			15[b]	250	0.9	1.4	5.15	...
		Totals	30			48.5		
16	3.8	67[c]	..	100	nil	...		
		85[c]	90			1.5–2	9.83	.0002
		90[c]	15	22	0.36	0.56	9.94	.0005
			15	19.5	0.48	0.74	9.87	.0004
			30	46	1.19	1.85	9.68	.0005
			30	50	1.92	3.0	9.38	.0007
		Totals	90			6.15		
16	3.8	107[d]	15	75	3.84	6.0	9.40	.0042
			15	50	4.6	7.2	8.68	.0047
			30	100	6.91	10.8	7.60	.0046
			30	100	8.82	13.8	6.22	.0053
		Totals	90			37.8		

[a] A duplicate run, wherein 0.2 g. of xylose was taken rather than 0.1 g. [b] Continued distillation gave too little furfural to analyze. [c] Reduced pressure in the distilling system. [d] Increased pressure in the distilling system.

Furfural and Hydrochloric Acid

Recovery from 5.2 Normal Acid.—A solution of 100 mg. of furfural in 150 cc. of 5.2 N hydrochloric acid was steam-distilled for four and three-fourths hours. The 800 cc. of distillate was diluted to two liters and analyzed for furfural. The quantity present was 99.5 mg., or only 0.5% non-recovery. Under the conditions of this experiment, xylose was shown to yield 90–93% of furfural.

Refluxing.—A solution of 5.2 N hydrochloric acid which contained 0.4 mg. of furfural per cc. was prepared and refluxed for two hours. The furfural content was then checked colorimetrically against a similar portion which had not been heated. The furfural contents were in the ratio of 4 to 10, showing that 60% of the furfural had been destroyed.

Humin Formation.—Twenty-five grams of furfural was added slowly to a refluxing solution of 3.9 N hydrochloric acid. After three hours the mixture was cooled and filtered. A heavy black precipitate had formed during that time. Upon being washed with water and dried, it weighed 15 g. Analysis of the filtrate from the precipitate showed that 6.6 g. of the furfural had not been destroyed. The 15 g. of precipitate, or humin, had been formed from 18.4 g. of furfural. No gaseous or liquid products could be isolated.

Only traces of the humin could be dissolved in organic solvents. The portion known as humic acid could be dissolved in aqueous alkali. The solution was cherry-red in color. Addition of mineral acids precipitated the humic acid from its solution in alkali. This precipitate was flocculent and brown in color. The humic acid was converted into the insoluble humin by refluxing for six to eight hours with mineral acid or by heating alone. The humin was analyzed for carbon by two different methods, by Parr's sodium peroxide fusion method and by Florentine's[9] chromic acid oxidation method. The latter consisted in refluxing the sample with 10 g. of chromic acid, 10 cc. of water, 1 g. of mercuric sulfate and 25 cc. of concd. sulfuric acid. In both, the liberated carbon dioxide was determined volumetrically.

Anal. (Sodium peroxide fusion). Found: C, 79.1, 82.0; (chromic acid), 67.6, 67.5.

Sulfuric Acid with Other Carbohydrates.—In Table III are summarized the data showing the action of 7.5 *N* sulfuric acid on arabinose, rhamnose and ketoxylose. With rhamnose, which yielded methylfurfural instead of furfural, a colorimetric method was developed similar to the one which was employed for furfural. Pure methylfurfural (2.5 g.) was dissolved in 500 cc. of toluene-saturated water. Three cc. of this solution was made up to 10 cc., and 1 cc. of it (which contained 1.5 mg. of methylfurfural) was compared with 4 cc. of the unknown. To both colorimetric tubes were added 4 cc. of glacial acetic acid, 0.5 cc. of aniline and water to 10 cc. In the rhamnose distillation experiments some tarring occurred. This indicated that not all of the methylfurfural was being removed.

TABLE III

SULFURIC ACID ON OTHER CARBOHYDRATES

Substance taken	Weight, g.	Vol. of acid, cc.	Distn. period, min.	Vol. of distillate, cc.	Furfural content, mg.	Furfural yield, %
Arabinose	0.1338	150	120	310	38.75	45.0
Arabinose	.1590	150	120	550	46.58	45.7
Rhamnose	.2603	150	120	310	80.3	51.0
Rhamnose	.2847	150	120	250	66.6	38.7
Ketoxylose polymer[b]	.1149	75	30[a]	61	7.2	4.99

[a] In a second 30-min. distillation period, 50 cc. was collected which contained no furfural. [b] Gross and Lewis, THIS JOURNAL, 53, 2777 (1931).

Tetramethylene Glycol and Tetrahydrofuran.—This glycol was prepared from diethyl succinate by reduction with sodium and alcohol. The method was essentially that described by Müller.[20]

A solution of 2.79 g. of tetramethylene glycol in 150 cc. of 7.5 *N* sulfuric acid was refluxed during two hours. The reflux condenser was heated with water at 65–70°. The vapors passing over were condensed in a U-tube which was immersed in a freezing mixture. Two cc. of a liquid was collected which, after fractionation, yielded 1.7 g. of tetrahydrofuran. Due to its volatility, some was probably lost in manipulation, but even so the yield was 76%. Its boiling point was 64–65°, and its index of refraction, n^{21}_{D} was 1.4043.

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[20] Müller, *Monatsh.*, 49, 27 (1928).

Glycerol and Hydrochloric Acid.—Ten grams of glycerol was refluxed for two hours with 100 cc. of 3.9 *N* hydrochloric acid. On cooling, the solution was neutralized. It gave no test for unsaturation with potassium permanganate solution, and it was without effect on hot Fehling's solution.

Erythritol and Sulfuric Acid.—Five grams of meso erythritol was refluxed with 100 cc. of 7.5 *N* sulfuric acid during six and one-half hours. The temperature of the reflux condenser was 35–50°. It was connected to a cold condenser and then to a U-tube which was immersed in a freezing mixture. No distillate of furan was collected.

Using a more concentrated sulfuric acid solution (50%, rather than 32%), Henninger[21] obtained a substance which he named erythran. Nothing of this type was found in the present study. After neutralizing the acid solution with barium carbonate and filtering off the barium sulfate, only unused erythritol was found. Three grams was recovered, and it is reasonable to assume that the remainder was lost in manipulation.

No furan was formed when erythritol and hydrochloric acid of varying concentrations to concentrated acid were refluxed together for several hours.

Xylose, Sulfuric Acid and Salts

Sodium Sulfate.—A 7.7 *N* sulfuric acid solution was made by dissolving 45 cc. of 92% sulfuric acid in water which contained 75 g. of sodium sulfate. This solution, made up to 200 cc., boiled at 112°. One-tenth gram of xylose was added to it and three 250-cc. portions of distillate were collected in fifteen, fifteen and sixty minute periods. The furfural yields in these were 16.6, 15.6 and 33.1%, or a cumulative yield of 65.3%.

Magnesium Sulfate.—Seventeen cc. of 92% sulfuric acid was added to 135 cc. of a saturated aqueous solution of magnesium sulfate. It was, therefore, 3.9 *N* in acid. It boiled at 109.8–110°. Distillation of 0.1 g. of xylose from it in four periods of fifteen, fifteen, thirty and sixty minutes (distillation volumes of 150, 75, 200 and 200 cc.) yielded furfural, respectively, 5.3, 6.4, 13.8 and 20.7%; total yield, 46.2%.

When the effect of this 3.9 *N* acid solution (with magnesium sulfate) is compared with that of the 4.5 *N* acid (without magnesium sulfate, and therefore 7° lower boiling), it is seen that the furfural yield with the former is about double that with the latter. However, with 7.5 *N* acid (containing no magnesium sulfate), which boiled at 108.7°, the yield of furfural was considerably greater than with the aforesaid 3.9 *N* acid of b. p. 110°. These results illustrate the effect of temperature and of acid concentration.

Xylose and a Butyric Acid Solution of Sulfuric Acid.—Three cc. of concd. sulfuric acid was added to 150 cc. of butyric acid, thereby making a 0.67 *N* sulfuric acid solution with a boiling point of 162°. To it, 0.2836 g. of xylose was added and the mixture distilled from a 250-cc. flask. Butyric acid was added from a dropping funnel at about the same rate as it distilled away. The distillate was neutralized as it came over. In two and one-half hours, 205 cc. of distillate was collected. Only 3% of furfural was formed.

Acetic Acid Solution of Benzenesulfonic Acid.—Twenty grams of benzenesulfonic acid, 170 g. of glacial acetic acid and 0.1 g. of xylose in 5 cc. of water were distilled (118.5–121°) for half an hour. Acetic acid was constantly supplied as it distilled away. Only 1.1% yield of furfural resulted.

Summary

A study has been made of the change of xylose into furfural. Dehydrating agents such as phosphorus pentoxide or anhydrous zinc chloride failed to promote this change. Solutions of phosphoric, trichloroacetic or nitric acid gave either no furfural or else gave very small yields of it. Both

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[21] Henninger, *Ann. chim. phys.*, [6] **7**, 211 (1886).

hydrochloric and sulfuric acid solutions promoted furfural formation at distillation temperatures, the yield being dependent on the acid concentration, the temperature and on the duration of the distillation. This is a first order reaction.

The behavior of mineral acids at distillation temperatures on furfural, arabinose, rhamnose, tetramethylene glycol, ketoxylose, xylonic acid, glycerol and erythritol was investigated. In the last four cases there was little or no reaction. The significance of these results on the mechanism of the pentose-to-furfural reaction has been discussed.

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[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

SOME OBSERVATIONS ON THE FRIES REACTION[1]

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We became interested in the Fries reaction[2] because it seemed possible that this reaction might play a role in the formation of hydroxydiarylphthalides such as phenolphthalein. Furthermore, we wished to determine whether or not diphenyl phthalate, as well as phenyl 2-(*p*-hydroxybenzoyl)-benzoate, under the influence of aluminum chloride, would yield 2-(4″-hydroxybenzoyl)-4′-hydroxybenzophenone.[3]

It has been stated by Rosenmund and Schnurr[4] that phenyl benzoate, when heated with aluminum chloride, is converted quantitatively into 4-hydroxybenzophenone. Similar results were obtained by us. We found that the benzoate of 4-hydroxydiphenyl behaves in an analogous manner to yield a compound which was, undoubtedly, 4-(*p*-hydroxyphenyl)-benzophenone since the material obtained by the action of aluminum chloride on the ester, after methylation, was identical with the substance prepared by condensation of benzoyl chloride with the methyl ether of 4-hydroxydiphenyl.

Csanyi[5] reported that diphenyl phthalate and aluminum chloride yield phenolphthalein but the amount of the latter which is produced and the experimental conditions which govern its formation were not recorded.

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[1] This investigation was made possible by the establishment of the Michigan State Pharmaceutical Association Research Fund. We wish to express our appreciation for the aid which has been given us.

[2] A recent study of this reaction has been reported by Cox, THIS JOURNAL, **52**, 352 (1930).

[3] This substance is isomeric with phenolphthalein and is easily obtained from it. The preparation of this compound is described by the authors in an article which will be published in an early issue of THIS JOURNAL.

[4] Rosenmund and Schnurr, *Ann.*, **460**, 89 (1928).

[5] Csanyi, *Ber.*, **52**, 1792 (1919).