

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Chemical Interactions of Amino Compounds and Sugars. IV.<sup>1</sup> Significance of Furan Derivatives in Color Formation<sup>2</sup>BY M. L. WOLFROM, R. D. SCHUETZ<sup>3</sup> AND LIEBE F. CAVALIERI<sup>3</sup>

It has long been known that aqueous solutions of the reducing sugars become dark in color on heating with amino acids and that under certain conditions dark-colored, insoluble products are formed. This complex set of reactions is known as the "browning" or Maillard<sup>4</sup> reaction and is believed to play a role, at times beneficial and at times not, in the processing of foods. It is the purpose of this communication to study the possible contributions to these phenomena made by furan derivatives formed from the sugars. That furan derivatives may play a role in these reactions has been suggested by Roxas,<sup>5</sup> Beckley<sup>6</sup> and others.

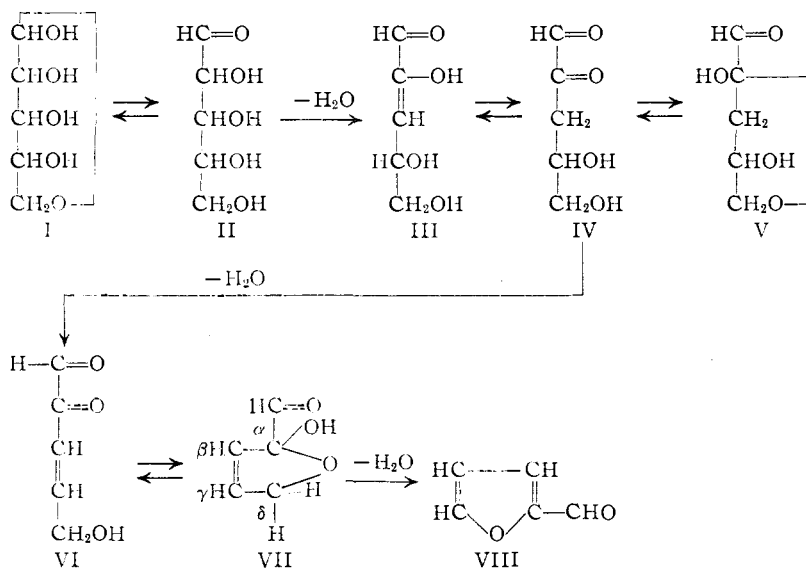


Fig. 1.—Postulated scheme for the conversion of pentoses to 2-furaldehyde.

It is well established that pentoses yield 2-furaldehyde (furfural) on heating with mineral acids. Hurd and Isenhour<sup>7</sup> have shown that this reaction

(1) Previous communication in this series: M. L. Wolfrom, R. D. Schuetz and L. F. Cavalieri, *THIS JOURNAL*, **70**, 514 (1948).

(2) The subject matter of this paper has been undertaken in cooperation with the Committee on Food Research of the Quartermaster Food and Container Institute for the Armed Forces under a contract (W-44-109Q M 1027) with The Ohio State University Research Foundation. The opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or indorsement of the War Department.

(3) Research Associate of The Ohio State University Research Foundation, Projects 278 and 238, respectively.

(4) L.-C. Maillard, *Compt. rend.*, **154**, 66 (1912); *Ann. chim.*, [9] **5**, 258 (1916).

(5) M. L. Roxas, *J. Biol. Chem.*, **27**, 71 (1916).

(6) V. A. Beckley, *J. Agr. Sci.*, **11**, 69 (1921).

(7) C. D. Hurd and L. I. Isenhour, *THIS JOURNAL*, **54**, 317 (1932); see also A. P. Dunlop, *Ind. Eng. Chem.*, **40**, 204 (1948).

is first order in its early stages if the 2-furaldehyde is removed by steam distillation as fast as formed. Mineral acidity is not required for this conversion, small amounts of 2-furaldehyde being formed when aqueous solutions of the pentoses are refluxed.<sup>8,9</sup>

We believe that the conversion of the pentoses to 2-furaldehyde follows the route outlined in Fig. 1. This scheme is analogous to that previously suggested<sup>1</sup> for the directly related conversion of hexoses to 5-(hydroxymethyl)-2-furaldehyde ("HMF") and is based upon similar evidence.

An aqueous solution of D-xylose was refluxed. After ninety minutes of refluxing, a distinct band

with a maximum at 227  $m\mu$  (Fig. 3, curve 1) was evident. After three and one-half hours of heating (curve 2) a second band was developing in the region of 277  $m\mu$ . At the end of eight hours (curve 3) the maximum at 227  $m\mu$  had increased and that at 277  $m\mu$  was increasing at an even greater rate. On continued heating for twelve and one-half hours (curve 4) the ratio of the substance producing the band at 277  $m\mu$  to the other (producing the band at 227  $m\mu$ ) became about equal. Further heating for periods of sixteen hours (curve 5) and nineteen hours (curve 6), respectively, greatly increased the ratio of the substance causing absorption at 277  $m\mu$  to that producing absorption at 227  $m\mu$ .

Finally, after a period of heating of twenty-two hours (curve 7), the typical absorption spectrum of 2-furaldehyde (Fig. 4) was developing. The absorption characteristics of 2-furaldehyde as shown in Fig. 4 are in agreement with previously reported<sup>10</sup> data.

It is to be noted first that after one and one-half hours there is absorption only at 227  $m\mu$ . That

(8) C. D. Hurd, C. D. Kelso and (Mrs.) E. Roadestvedt (Report to the Quartermaster Food and Container Institute for the Armed Forces, July to September, 1945) have isolated 2-furaldehyde, identified as the semicarbazone, in 2% yield, by steam-distilling aqueous solutions of D-xylose in the presence of glycine.

(9) R. G. Rice, Abstracts of Papers, 112th Meeting American Chemical Society, New York, N. Y., p. 3A, September, 1947, has identified 2-furaldehyde in the steam-distillate from aqueous solutions of D-xylose and L-arabinose in the presence and absence of glycine.

(10) I. Marchlewski and J. Mayer, *Bull. intern. acad. polon. sci. Classe sci. math. nat.*, 1929A, No. 3, 169.

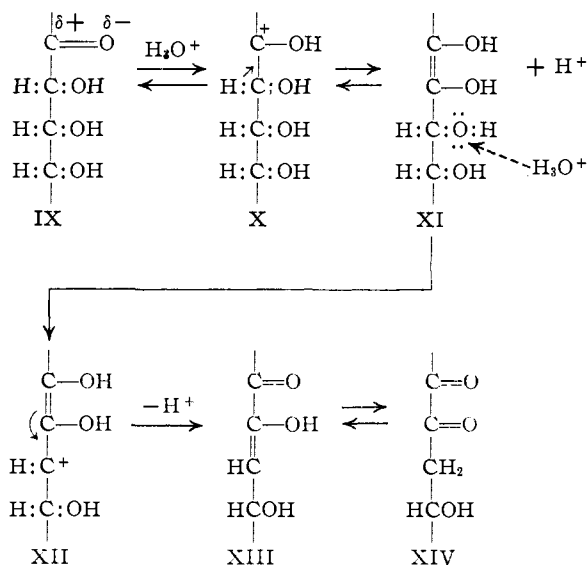


Fig. 2.—Possible mechanism of dehydration.

the substance producing this band is not 2-furaldehyde is evident from the fact that the major peak at 277  $m\mu$  is missing. The absorption band at 227  $m\mu$  is such as would be given by a conjugated acyclic diene or enal.<sup>1</sup>

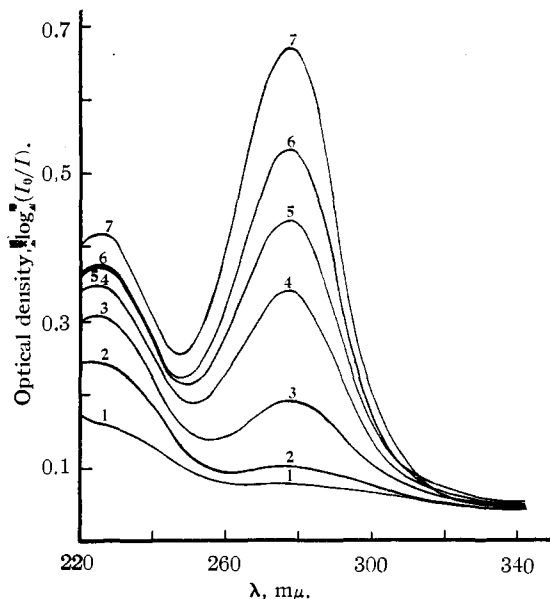


Fig. 3.—Absorption spectra of a 0.0033 molar aqueous D-xylose solution, initial pH 6.5, after refluxing for various time intervals. Curve 1, after one and one-half hours; curve 2, after three and one-half hours; curve 3, after eight hours; curve 4, after twelve and one-half hours; curve 5, after sixteen hours; curve 6, after nineteen hours; curve 7, after twenty-two hours. Beckman spectrophotometer (Model DU), 1-cm. cell, slit width 0.19–0.61 mm., optical densities 0.025–1.743.

To explain these absorption curves it is postu-

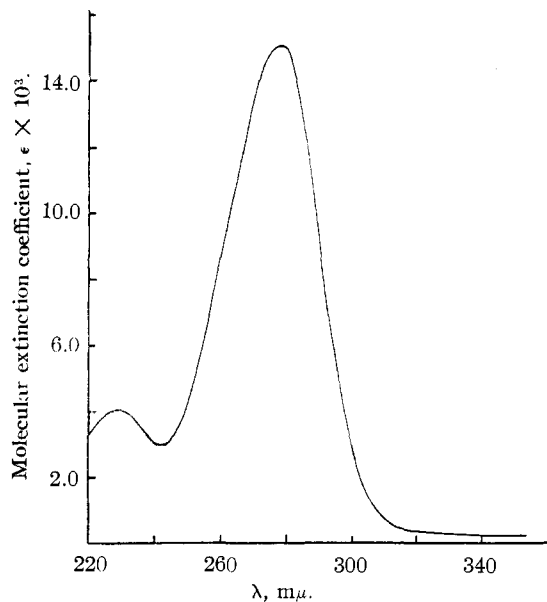


Fig. 4.—Absorption spectrum of pure 2-furaldehyde in water: concentration,  $1.155 \times 10^{-4}$  mole per liter;  $\epsilon = 1/c \log (100/T)$  wherein  $c$  is the molar concentration and  $T$  is the percentage transmission;  $\epsilon = 15,100$ , max. 277  $m\mu$  (major peak);  $\epsilon = 4060$ , max. 227  $m\mu$  (minor peak); slit width 0.19–0.61 mm., optical densities 0.025–1.743; Beckman spectrophotometer (Model DU).

lated that D-xylose, represented by I (Fig. 1) is transformed first into II or its aldehydol.<sup>11</sup>

Substance II is a  $\beta$ -hydroxy carbonyl compound and undergoes dehydration to yield the conjugated enal III. The keto tautomer IV again loses water by dehydration from a  $\beta$ -hydroxy carbonyl system and produces VI. Both IV and VI can be in equilibrium with their ring structures V and VII, respectively. A final dehydration with bond adjustment then yields 2-furaldehyde (VIII). Such a bond adjustment may possibly involve a proton shift from the  $\delta$  carbon of VII subsequent to a dehydration between its  $\alpha$  and  $\beta$  carbons. Support for this reaction sequence is found in the work of Wolfrom, Wallace and Metcalf.<sup>12</sup> These workers isolated, in the form of its phenylsazone, the analog of VI as an intermediate in the action of mineral acid upon a hexose derivative. Isbell<sup>13</sup> assumes the same intermediates as involved in a series of successive electron displacements, the driving force for which is the combination of hydroxyl groups with hydrogen ions to form water.

The ease of acid dehydration of  $\beta$ -hydroxy carbonyl compounds may be interpreted electronically in the following fashion (Fig. 2). The polarization (IX) of the carbonyl group as enhanced by acid catalysis (X) allows the release of a proton

(1) See R. Bieber and G. Trümpler, *Helv. Chim. Acta*, **30**, 1860 (1947).

(12) M. L. Wolfrom, E. G. Wallace and E. A. Metcalf, *This Journal*, **64**, 265 (1942).

(13) H. S. Isbell, *J. Research Natl. Bur. Standards*, **32**, 45 (1944); **33**, 45 (1944).

to form the enediol XI. These reactions are reversible and all of the hydroxyls present are under attack by the hydronium ions present in the solution. That hydroxyl will be released which is the most basic. Of the hydroxyl groups present, the several secondary hydroxyls are more basic than either the enolic hydroxyls or the terminal primary hydroxyl. The secondary hydroxyl which is removed, however, is that one adjacent to the enolic hydroxyl, the extra impetus for its release being provided by the electron pair of the endiolic function tending to produce the resonating system of conjugated double bonds shown in XIII (its tautomer is XIV). The essentially irreversible change from XI to XIII is represented as passing through the intermediate XII which is stabilized by the ejection of a proton and the shift of the electron pair down the carbon chain.

A dilute solution (0.05 *M*) of D-xylose was refluxed for one thousand minutes in the presence and absence of significant amounts of glycine. At the end of this period the amount of 2-furaldehyde formed was determined spectroscopically in the solution. The data are recorded in Table I and it is seen that the total conversion to furan bodies is small and is enhanced by the presence of glycine. Similar conclusions were expressed by Rice<sup>9</sup> on employing somewhat different experimental conditions. It is believed that the main aldehydic substance determined spectroscopically is 2-furaldehyde but it is not excluded that other carbonyl-containing compounds might have been present and caused absorption in the same band. The dilute solutions were adopted in order to yield sharp spectroscopic data. The presence of

2-furaldehyde in these solutions is established by its isolation in this Laboratory and in others.<sup>8,9</sup>

We next sought to determine whether this small amount of 2-furaldehyde, produced on heating aqueous solutions of pentoses, could be a factor in the "browning" of such solutions on heating with glycine. To this end equimolar (0.25 *M*) solutions of the pertinent substances were refluxed and the degree of coloration at various time intervals was measured at a selected wave length (490  $m\mu$ ). Highly purified materials were employed and the results were reproducible to within approximately 5%. Curve F of Fig. 5 shows that 2-furaldehyde and glycine "brown" at a high rate of speed in accordance with the findings of Kertesz and co-workers.<sup>14</sup> No initial induction period was present. The upturn of the curve at the end, indicating a decreased rate of color formation, may be due at least in part to the formation of a colloidal solution containing suspended particles removed from the reaction sphere; particles actually separated at the last point measured. Thus 2-furaldehyde seems to be a real and powerful color precursor for glycine solutions. D-Xylose and pure 2-furaldehyde, alone or in admixture (curves A, B and C), do not produce significant colorations in the time intervals measured; with longer time these incipient colorations would become significant. The inverted S or sigmoid curve E is that of an admixed equimolar D-xylose and glycine solution. The slow rate of initial color development gives indication of an initial induction period. It is reasonable that this may be due to the time required for the formation of color precursors. The nature of the colored bodies formed is presently unknown but it is believed that they are formed by polymerization reactions in which glycine plays a part. It is possible that the furan ring may be an integral constituent of these polymers. It is not excluded that there may be an initial carbonyl-amino reaction followed by dehydrations to furan or other derivatives.

Since D-galacturonic acid is a constituent of pectins and is an established 2-furaldehyde precursor, its behavior under our selected "browning" conditions was of interest; curve D (0.25 *M* in D-galacturonic acid and glycine) of Fig. 5 is the result. A longer induction period was present. Seaver and Kertesz<sup>15</sup> have shown that D-galacturonic acid is a potent color producer with amino acids and it has been demonstrated<sup>16</sup> that furan intermediates are involved in the browning of dried apricots.

While the pentoses are convertible to 2-furaldehyde, the hexoses are convertible to 5-(hydroxymethyl)-2-furaldehyde and finally to levulinic acid. This reaction is enhanced by acidity but

TABLE I

Conversion of 0.0500 *M* Aqueous Solutions of D-Glucose and D-Xylose to Furan Bodies on Heating under Reflux (101°) for 1000 Minutes in the Presence and Absence of Glycine

Sugar	Glycine, <i>M</i>	$\text{pH}$		$T_p^a$ %	Conversion to furan bodies, <sup>b</sup> %
		Initial	Final		
D-Glucose	0.0	6.5	4.8	9.5	0.124
	.0	6.5	4.8	6.6	.144
	.0300	6.4	5.1	5.4	.154
	.0500	6.4	5.2	49.6 <sup>c</sup>	.185
	.0500	6.4	5.2	50.6 <sup>c</sup>	.179
	.0751	6.3	5.0	43.1 <sup>c</sup>	.222
	.1000	6.2	5.0	28.2 <sup>c</sup>	.333
D-Xylose	.1000	6.2	5.0	27.6 <sup>c</sup>	.339
	0.0	6.7	4.4	14.7 <sup>c</sup>	0.556
	.0	6.7	4.4	14.3 <sup>c</sup>	.564
	.0300	6.6	5.1	11.2 <sup>c</sup>	.633
	.0500	6.5	5.1	5.3 <sup>c</sup>	.850

<sup>a</sup> Per cent. transmission at 285  $m\mu$  ( $\epsilon_{\text{max.}} = 1/[\text{HMF}] \log 100/T = 16,500$ ) for D-glucose and at 277  $m\mu$  ( $\epsilon_{\text{max.}} = 1/[\text{F}] \log 100/T = 15,000$ ) for D-xylose; 1 cm. cell; Beckman spectrophotometer, Model DU; all solutions made from triply distilled water. <sup>b</sup> Conversion to 5-(hydroxymethyl)-2-furaldehyde (HMF) for D-glucose and 2-furaldehyde (F) for D-xylose. <sup>c</sup> Diluted five times for absorption measurements.

(14) R. G. Rice, Z. I. Kertesz and E. A. Stotz, *THIS JOURNAL*, **69**, 1798 (1947).

(15) Joan L. Seaver and Z. I. Kertesz, *ibid.*, **68**, 2178 (1946).

(16) Victoria A. Haas, E. R. Stadtman, F. H. Stadtman and G. MacKinney, *ibid.*, **70**, 3576 (1948); A. Wahhab, 3580; F. H. Stadtman, 3583; G. MacKinney and Odette Temmer, 3586

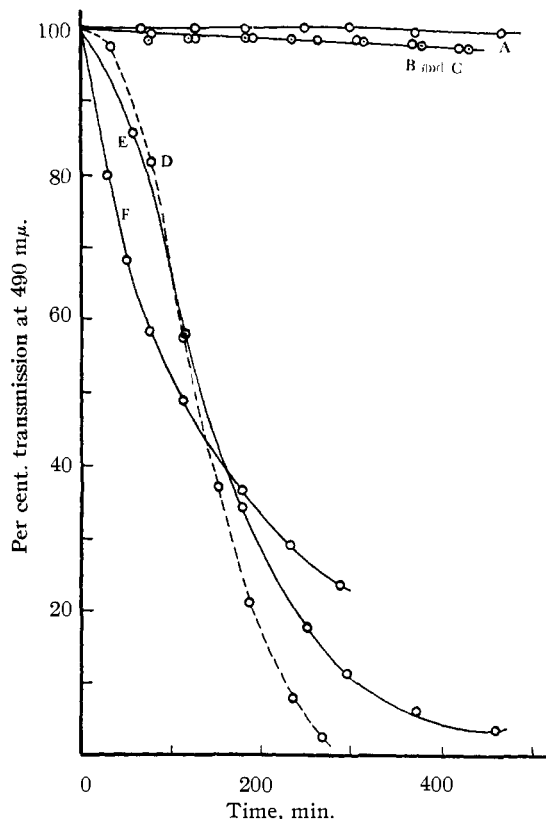


Fig. 5.—Rate of change in the percentage transmission at 490 mμ of D-xylose, D-galacturonic acid and 2-furaldehyde in the presence and absence of glycine; 0.2500 molar (in each constituent) aqueous solutions at reflux temperature (102°): Curve A, D-xylose alone; B, O, 2-furaldehyde alone; C, O, D-xylose and 2-furaldehyde; D, D-galacturonic acid and glycine; E, D-xylose and glycine; F, 2-furaldehyde and glycine; Lumetron (Mod. 402E) photoelectric colorimeter.

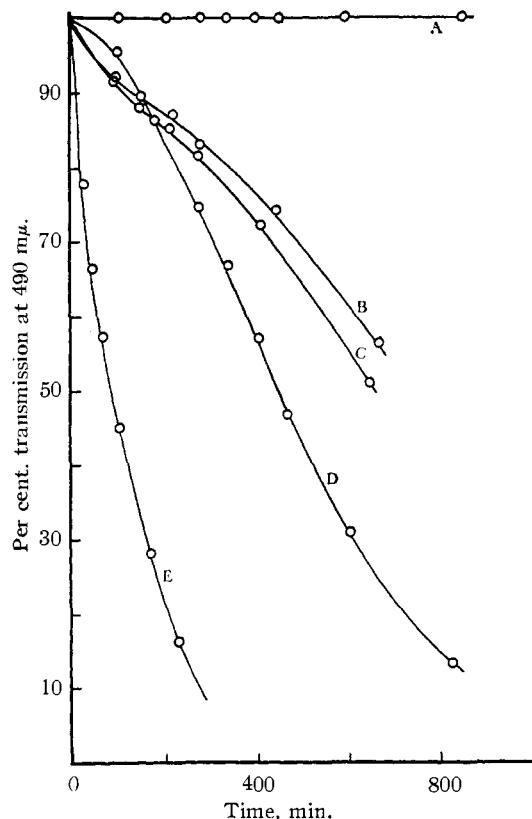
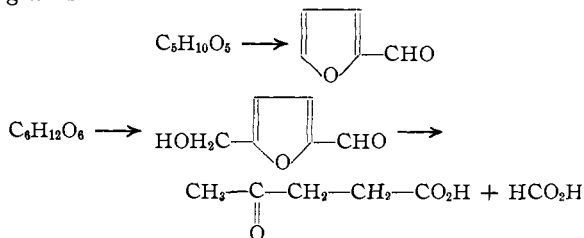


Fig. 6.—Rate of change in the percentage transmission at 490 mμ of D-glucose and 5-(hydroxymethyl)-2-furaldehyde in the presence and absence of glycine; 0.2500 molar (in each constituent) aqueous solutions at reflux temperature (102°): Curve A, D-glucose alone; B, D-glucose and 5-(hydroxymethyl)-2-furaldehyde; C, 5-(hydroxymethyl)-2-furaldehyde alone; D, D-glucose and glycine; E, 5-(hydroxymethyl)-2-furaldehyde and glycine; Lumetron (Mod. 402E) photoelectric colorimeter.

takes place in a refluxing aqueous solution of D-glucose.<sup>17</sup>



The data of Table I show the conversion of D-glucose to 5-(hydroxymethyl)-2-furaldehyde as measured spectroscopically directly in the heated (refluxed for one thousand minutes) solution. It is believed that the main component of the analyzing band is 5-(hydroxymethyl)-2-furaldehyde but the presence of other contributing carbonyl compounds is not excluded. It is noted that the presence of significant amounts of glycine has a

(17) B. J. Scallet with I. H. Gardner, *THIS JOURNAL*, **67**, 1934 (1945)

promoting effect upon the furan bodies formed. The conversion of the hexose to furan bodies is apparently lower than with the pentose D-xylose but this may be more apparent than real since the 5-(hydroxymethyl)-2-furaldehyde produced is subject to further conversion to levulinic acid. The pH of both the hexose and pentose solutions (Table I) drifts downward with time. That 5-(hydroxymethyl)-2-furaldehyde is formed from D-glucose in the presence of glycine was established by isolation from such a mixture.

The degree of conversion of hexoses and pentoses to furan bodies (Table I) is small but the measured figure represents only the amount of substance actually exhibiting the absorption at the wave length employed. This is undoubtedly an intermediate value and the total quantity of hexose or pentose passing through this stage may be much greater.

Singh, Dean and Cantor<sup>18</sup> have shown that the 5-(hydroxymethyl)-2-furaldehyde formed in acid

(18) B. Singh, G. R. Dean and S. M. Cantor, *ibid.*, **70**, 517 (1948)

solutions of D-glucose is the prime cause of color development in them. We are then presently concerned with attempting to determine whether this same intermediate is a probable factor in the "browning" of aqueous solutions of D-glucose by glycine. To this end we employed the same color-forming conditions as we used for the pentoses. The results are diagrammed in Fig. 6. D-Glucose alone (Fig. 6, curve A) did not form colored substances as readily as did our sample of D-xylose (Fig. 5, curve A). 5-(Hydroxymethyl)-2-furaldehyde alone is a good source of color (curve C), much more than is 2-furaldehyde. Admixture with D-glucose (curve B) has little effect upon this property. Refluxing of 5-(hydroxymethyl)-2-furaldehyde with glycine (curve E) produces a very rapid color formation. The curve (D) of D-glucose and glycine is similar in general characteristics to that of D-xylose and glycine (curve E of Fig. 5); it exhibits even a more pronounced initial induction period. Thus the behavior of D-glucose is similar to that of D-xylose.

On heating in dilute aqueous solution an equimolar mixture of D-glucose and glycine ethyl ester, the pH falls gradually (curve A of Fig. 7).

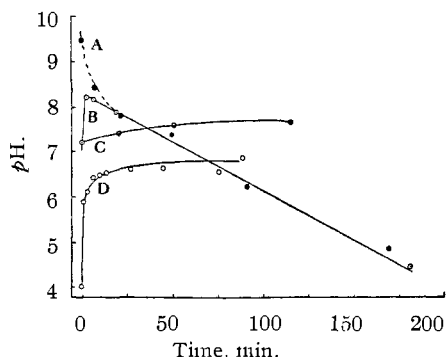


Fig. 7.—Change in pH of a 0.001 molar solution of N-D-glucosylglycine ethyl ester: at room temperature (20–25°), curve C; at 90–92°, curve B; in 0.02 N hydrochloric acid at room temperature (20–25°), curve D. Change in pH of a mixture of D-glucose and glycine ethyl ester at an equivalent concentration, 90–92°, curve A. Measurements of pH on the heated solutions were made by rapidly cooling an aliquot to room temperature.

When an equivalent amount of crystalline N-D-glucosylglycine ethyl ester is heated under the same conditions (curve B, Fig. 7), a very rapid initial increase in pH occurs followed by a slower drop in pH which merges into the pH-time curve of the D-glucose-glycine ester system. These data are those predictable should the N-D-glucosylglycine ethyl ester have hydrolyzed largely to D-glucose and glycine ethyl ester with the latter substance then undergoing a slower hydrolysis to glycine. N-D-Glucosylglycine ethyl ester undergoes hydrolysis at room temperature (curve C, Fig. 7) and its instability toward water is shown also by the rapid and essentially quantitative release of

the amino group (ninhydrin colorimetric assay) on heating in aqueous solution for only a few minutes. Toward mineral acid, the substance is very unstable at room temperature (curve D, Fig. 7). This hydrolytic behavior shows that only a small amount of N-D-glucosylglycine could possibly be formed by the interaction of D-glucose and glycine in aqueous solution. It is not excluded, however, that this small amount may be a significant factor in a complex equilibrium.

Finally we may state that our findings stand contrary to the statement of Enders<sup>11</sup> that these furan derivatives do not brown with sufficient rapidity to be of significance in the Maillard reaction. When present in sufficient concentration, both 2-furaldehyde and 5-(hydroxymethyl)-2-furaldehyde form deeply colored products with glycine and do so at a high rate of speed.

### Experimental

**Materials.**—The colorless 2-furaldehyde required in this investigation was obtained from a commercial sample that had been freshly triply distilled under reduced pressure. 5-(Hydroxymethyl)-2-furaldehyde was prepared according to the procedure of Middendorp<sup>20</sup> with some modification. An amount of 180 g. (0.527 mole) of sucrose was dissolved in 600 ml. of water. To this was added 0.180 g. (0.00143 mole) of oxalic acid. The resulting solution was refluxed for twenty hours, after which it was cooled to room temperature and the black, insoluble material was removed by filtration. The filtrate was neutralized with 11.0 g. (0.110 mole) of calcium carbonate with mild heating. To the neutralized filtrate was added 2 g. of basic lead acetate and after standing for ninety minutes the solution was again filtered. The 5-(hydroxymethyl)-2-furaldehyde was extracted with a 100-ml. portion of ethyl acetate and then with four 50-ml. quantities. The solvent was removed under reduced pressure from the dried extract and the 5-(hydroxymethyl)-2-furaldehyde was purified by molecular distillation at  $2 \times 10^{-3}$  mm.; m. p. 33.3–33.5° (cor.).

The glycine and the carbohydrates employed were highly purified materials recrystallized in our own laboratories. The D-galacturonic acid used was the  $\alpha$ -monohydrate. All aqueous solutions were made with triply distilled water.

**Isolation and Characterization of 2-Furaldehyde from the Decomposition of D-Xylose in the Presence of Glycine.**—An aqueous solution (100 ml.) of D-xylose and glycine (2.5 molar in each constituent) was refluxed for two hours. It was then steam-distilled, the distillate being led directly into a heated solution of 2 N hydrochloric acid saturated with 2,4-dinitrophenylhydrazine. The resulting 2,4-dinitrophenylhydrazone was filtered and recrystallized from pyridine; m. p. 229° (dec., Fisher-Johns apparatus), accepted value 229° (dec., cor.).<sup>21</sup> In an identical manner, a 2,4-dinitrophenylhydrazone of like melting point was isolated from a 2.5 M solution of D-xylose alone after refluxing for sixteen hours. Mixed melting points of these two products with an authentic reference compound were unchanged.

**Isolation and Characterization of 5-(Hydroxymethyl)-2-furaldehyde from the Decomposition of D-Glucose in the Presence of Glycine.**—An aqueous solution (400 ml.) of D-glucose and glycine (2.5 molar in each constituent) was refluxed for twenty hours and then extracted with ethyl acetate for eight to ten hours in a continuous extractor. Crude 5-(hydroxymethyl)-2-furaldehyde was obtained as a light brown oil on solvent removal under diminished

(19) C. Enders, *Biochem. Z.*, **312**, 339 (1912).

(20) J. A. Middendorp, *Rec. trav. chim.*, **38**, 1 (1919).

(21) A. Wahhab, ref. 16.

pressure; yield 1-2 g. Identification was effected by ultraviolet absorption<sup>1,18</sup> and by the preparation of two crystalline derivatives: the 2,4-dinitrophenylhydrazone of m. p. 198-200° (dec., Fisher-Johns apparatus) (after recrystallization from 95% ethanol; in agreement with accepted value<sup>21</sup>) and the condensation product with  $\beta$ -naphthylamine of m. p. 130-131° (after recrystallization from benzene; accepted value<sup>22</sup> 131-132°). These two derivatives showed no depression in melting point on admixture with authentic samples of like melting point.

**Preparation of N-D-Glucosylglycine Ethyl Ester.**—This compound was first recorded by Euler and Zeile.<sup>23</sup> The following is an improved method of preparation which makes this substance readily available. An amount (66 g.) of freshly prepared glycine ethyl ester was added to a suspension of 115 g. of anhydrous D-glucose in 200 ml. of absolute ethanol and the mixture was mechanically stirred and heated under reflux on a water-bath while protected from moisture by a guard tube. The heating was continued until all of the D-glucose had dissolved, about seventy-five minutes of heating time generally being required. The resultant solution was tea-colored. Approximately 125 ml. of ethanol was then removed under diminished pressure and ca. 150 ml. of acetone added to the residual sirup. The resultant solution was nucleated and allowed to stand at room temperature until crystallization was complete (overnight). The crude product was removed by filtration and washed with absolute ethanol; yield 110 g. (64%), m. p. 80°. Quite pure material was obtained on three recrystallizations from equal parts of hot absolute ethanol; yield 50 g. (30%), m. p. 108°,  $[\alpha]_D^{25} -5^\circ$  (c 3, absolute ethanol). A significant purification could be obtained by making a slurry of the crude product with absolute ethanol, filtering and washing with a small amount of ethanol. The filtrate was discarded and the filtered material was crystallized from hot absolute ethanol.

**Hydrolytic Breakdown of N-D-Glucosylglycine Ethyl Ester in Water; Ninhydrin Reaction.**—An amount (0.26 g.) of D-glucosylglycine ethyl ester was heated on a water-bath in 10 ml. of water containing ninhydrin. The charac-

teristic color developed in a few minutes and heating was continued for a total of thirty minutes. Comparison of this solution (cooled rapidly to room temperature) with a solution containing an equivalent amount of glycine by means of a photoelectric colorimeter revealed that both solutions absorbed to the same extent.

**Acknowledgment.**—The assistance of Mrs. Clare B. Spitler is gratefully acknowledged. We are also pleased to acknowledge the counsel of Dr. T. L. Tan and of Professors W. R. Brode, M. S. Newman and F. H. Verhoek of this department.

### Summary

1. Aqueous solutions of D-xylose form small amounts of 2-furaldehyde on being heated. The presence of a relatively large amount of glycine promotes this conversion as it does the analogous conversion of hexoses to 5-(hydroxymethyl)-2-furaldehyde.

2. The course of the formation of 2-furaldehyde from D-xylose has been followed spectroscopically and on this basis structures are postulated for several intermediates.

3. It is demonstrated that 5-(hydroxymethyl)-2-furaldehyde, in the case of D-glucose, and 2-furaldehyde, in the case of the pentoses and D-galacturonic acid, are important precursors in the formation of the brown colors developed when aqueous solutions of these substances are heated with glycine.

4. Evidence is presented which shows that the carbonyl-amino reaction could occur to only a slight extent if at all in dilute aqueous solutions of D-glucose and glycine.

COLUMBUS, OHIO

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(22) W. F. Cooper and W. H. Nuttall, *J. Chem. Soc.*, **101**, 1080 (1912).

(23) H. v. Euler and K. Zeile, *Ann.*, **487**, 163 (1931).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF RUTGERS UNIVERSITY AND THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

## A Synthesis for 4-Bromo-7-methoxyhydrindene

BY RODERICK A. BARNES, ELISE R. KRAFT<sup>1</sup> AND LOUIS GORDON<sup>2</sup>

In a previous paper<sup>3</sup> the use of 4-substituted hydrindenes as starting materials for preparation of cyclopentanophenanthrene derivatives has been illustrated. The present work was undertaken in order to extend the scope of this method by making available a new 4-substituted hydrindene (IV).

The method which finally proved successful for the synthesis of IV and which was most readily applicable to large-scale preparation was based on the hydrindone synthesis of von Auwers.<sup>4</sup> Although halogen substituted hydrindones have not

previously been prepared by this procedure, we have found that it can be used to synthesize 4-bromo-7-hydroxy-1-hydrindone (II) in 40-50% yield. The Clemmensen reduction (80% yield) to 4-bromo-7-hydroxyhydrindene (III) and methylation of III with diazomethane complete the synthesis.

The von Auwers preparation of hydrindones takes place in two steps, first a Fries rearrangement of the phenol ester of an  $\alpha$ - or  $\beta$ -halopropionic acid, and second a cyclization of the intermediate haloketone. In harmony with this conception of the reaction we have found that the best yields of II were obtained when I was heated with aluminum chloride at 95-100° for five to six hours to complete the Fries rearrangement and then at 170° for one hour to cause cyclization. Extended heating at the higher temperature results in de-

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(2) A portion of this work was taken from a thesis presented by Louis Gordon in partial fulfillment of the requirements for the Ph.D. degree, Columbia University, June 1948.

(3) Barnes and Gordon, *THIS JOURNAL*, **71**, 2644 (1949).

(4) von Auwers, *Ann.*, **489**, 132 (1924).