The 2-isomer was prepared similarly from 2-acetylpyridine. However, this isomer was very difficult to crystallize when poured into the ice and water mixture. When crystalline, it was necessary to filter while cold, and to recrystallize the whole yield from absolute ethanol at once. A crystallized yield of 63% of the theoretical amount was obtained, m. p. 65–67°. A picrate melted with slight decomposition at 178–180°.

The Pyridylacetic Acids.—Forty-four and four-tenths grams (0.2 mole) of 4-pyridylthioacetmorpholide, 12 g. of potassium hydroxide and 200 ml. of 95% ethanol were placed in a 500-ml. flask equipped with a reflux condenser. The mixture was refluxed gently on a steam-bath for seventy-two hours. At the end of that time, the mixture was poured into two volumes of water. The resulting solution was distilled at reduced pressure to approximately one-third volume, and another volume of water was added. The mixture was distilled again under reduced pressure, this time nearly to dryness. The residue was acidified with hydrochloric acid and evaporated to dryness under reduced pressure. The residue was extracted with three 200-ml. portions of absolute ethanol. The alcohol mixture was decolorized with carbon, filtered, evaporated to one-half volume, filtered, cooled and added to an excess of ether. The yield of white 4-pyridylacetic acid hydrochloride, m. p. 130–131°, was 30 g., or 86% of the theoretical amount. It formed a picrate which melted at 114–116°.

Anal. Calcd. for $C_7H_8NO_2Cl$: C, 48.43; H, 4.65; N, 8.07; Cl, 20.43. Found: C, 48.34; H, 4.75; N, 8.33; Cl, 20.34.

3-Pyridylacetic acid was prepared in the same manner. It was isolated both as the hydrochloride, m. p. 153–155°, and as the free acid, m. p. 144–146°, the latter in 74% yield. It formed a picrate which melted at 99–101°.

2-Pyridylacetic acid was synthesized similarly, but in very small yield. It was identified as the picrate, m. p. 140–142°.

The Ethyl Pyridylacetates.—The 3- and 4-pyridylacetic acids were esterified by the method of LaForge.[15] Ethyl 3-pyridylacetate, b. p. 121–122° at 10 mm., was obtained in 60% yield. This boiling point corresponds to that obtained by Hartman and Bosshard.[9] The ester forms a picrate which melts at a temperature of 110–112°.

Ethyl 4-pyridylacetate, b. p. 107–108° at 3 mm., was obtained in 49% yield. A picrate melted at a temperature of 121–123°.

Anal. Calcd. for $C_9H_{11}O_2N$: C, 65.43; H, 6.71; N, 8.48. Found: C, 65.41; H, 6.75; N, 8.40.

The Piperidylethanols.—The ethyl pyridylacetates were reduced by the procedure of Sandborn and Marvel[18] for ethyl nicotinate. The 3-piperidylethanol was obtained in 25% yield as a thick oil, b. p. 121–123° at 6 mm., $n^{25}D$ 1.4920. This boiling point is the same as that obtained by Merchant and Marvel,[19] however, they obtained an index of refraction of $n^{25}D$ 1.4888.

The 4-piperidylethanol[20] was obtained as a thick oil in 10% yield, b. p. 138–140° at 12 mm., $n^{25}D$ 1.5082. This boiling point corresponds to that obtained by Meisenheimer.[4]

Acknowledgment.—The authors are indebted to Dr. W. Albert Noyes, Jr., for the use by R. L. M. of laboratory space and equipment at the University of Rochester during part of this investigation.

Summary

The pyridylthioacetmorpholides were synthesized and then hydrolyzed to the corresponding pyridylacetic acids. The ethyl esters of 3- and 4-pyridylacetic acids were reduced to the corresponding piperidylethanols.

(18) Sandborn and Marvel, THIS JOURNAL, **50**, 563 (1928).

(19) Merchant and Marvel, *ibid.*, **50**, 1197 (1928).

(20) Much of the work of this investigation had been completed when Reilly Tar and Chemical Corporation announced the commercial availability of 4-pyridylethanol of 95% purity. A redistilled sample of their material gave the same compound as above when reduced with sodium and alcohol.

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CONTRIBUTION FROM THE BIOCHEMISTRY LABORATORY, DIVISION OF FOOD SCIENCE AND TECHNOLOGY, NEW YORK STATE AGRICULTURAL EXPERIMENT STATION, CORNELL UNIVERSITY]

Color Formation in Furfural Systems[1]

BY R. G. RICE, Z. I. KERTESZ AND E. H. STOTZ[2]

Introduction

Furfural has been suspected for some time to be an important intermediate involved in the "browning" of sugar solutions and various food products.[3] Since the literature contains no specific information concerning the factors involved in the coloration of originally colorless furfural solutions, a study of this reaction was undertaken. Dunlop, *et al.*,[4] studied the decomposition of furfural and concluded that color and acid formation in furfural at room temperature were due to autoxidation. Schenck[5] proposed a somewhat similar mechanism for the oxidative decomposition of furan and 2,5-dimethylfuran. These investigators did not deal with water solutions of the compounds in question.

Materials and Methods

Eastman Kodak Co. technical furfural served as the source of furfural for most of these experiments. This material was fractionated using an all-glass apparatus. The fraction used was nearly colorless and had a boiling point of 160–161° (cor.).

The amino acids obtained for this work were: Pfanstiehl C. P. glycine, ammonia free: Amend Drug and Chemical Company *d*-arginine monohydrochloride, C. P.; and Eimer and Amend *dl*-aspartic acid, C. P., m. p. 280° (dec.).

Samples of biacetyl, crotonaldehyde and purified

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(2) The subject matter of this communication has been undertaken in coöperation with the Committee on Food Research of the Quartermaster Food and Container Institute for the Armed Forces under a contract (W-11-009-Q.M.-70188) with the New York State Agricultural Experiment Station. 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 the indorsement of the War Department.

(3) H. Schiff, *Ann.*, **239**, 332 (1887).

(4) A. P. Dunlop, P. R. Stout and S. Swadesh, *Ind. Eng. Chem.*, **38**, 705 (1946).

(5) G. O. Schenck, *Ber.*, **77**, 661 (1945).

sodium pyruvate were kindly contributed by Dr. R. F. Witter of this Laboratory.

All other reagents were of commercial C. P. grade.

Doubly-distilled water was used in preparing all solutions.

No attempt was made to exclude air in any of the experiments reported.

Measurement of Color Formation.—The optical density was measured at 4300 Å. with the Lumetron photoelectric colorimeter.

Varying the *p*H from 3.1 to 6.6 had no effect on the optical density of the colored solutions as measured at 4300 Å. Diluting portions of the colored samples demonstrated that Beer's law was followed for solutions whose optical densities were less than 82% absorption. The Beckman *p*H-meter was used to measure all hydrogen ion activities.

Dialysis Experiments and Brown Precipitate Characterization.—Viscose dialyzing tubing was used in dialysis studies. Fractionating of the brown precipitates formed in furfural solutions for spectrophotometric analysis was carried out as follows. Solutions of the desired concentration of furfural and amino acid were adjusted to *p*H 4.0. These samples were heated under reflux for ninety-two hours by which time a quantity of dark brown insoluble material had formed. The dark brown precipitates were recovered by centrifuging, washed twice with distilled water, and extracted with two 10-ml. portions of 0.1 *M* sodium hydroxide. The extracts were combined and acidified by adding 1 *M* hydrochloric acid drop by drop with rapid stirring until a fluffy brown precipitate formed, and then a slight excess of the acid was added. This material was collected by centrifuging and the washing repeated. The resulting precipitate was extracted again with two portions of 0.1 *M* sodium hydroxide, total volume 15 ml., and the acid precipitation and one washing with water repeated. The product was completely soluble in 0.1 *M* sodium hydroxide forming a deep brown solution in each case. These solutions were diluted with 0.1 *M* sodium hydroxide to similar concentrations (as indicated by optical density) for analysis.

Effect of *p*H on the Relative Rate of Color Formation.—Treatment of dilute furfural solutions with mineral acid, alkali or by heat produced colored material, similar fractions of which were insoluble in dilute mineral acid and soluble in dilute alkali, showed a high degree of unsaturation, and the same absorption spectra. The color reaction was particularly enhanced by alkalies.

In studying the effect of hydrogen ion activity upon the relative rate of color formation in 1% furfural heated at 80°, a series of samples covering the range *p*H 3.3 to 6.8 were prepared by adjusting to the given *p*H with 0.1 *M* hydrochloric acid or 0.01 *M* sodium hydroxide.[6] This range was chosen so as to fall within the normal range of foodstuffs. The temperature decided on was based upon the fact that lower temperatures prolonged the reaction and that higher controlled temperatures were difficult to maintain for long periods.

Hydrogen ion activity had little effect upon the rate of color development over the range studied.

Effect of Amino Acids on the Relative Rate of Coloration.—Since amino acids play an important role in the "browning" reaction of sugar solutions and foods,[7] it was desirable to study their effect upon color formation in furfural solutions. One per cent. solutions of furfural containing the desired concentration of amino acid and adjusted to the desired *p*H were placed in glass-stoppered Pyrex flasks. The samples were then placed in a water-bath at 80°.

Table I shows the results of such an experiment using glycine. These data demonstrate that glycine has a very pronounced effect upon the relative rate of color formation in dilute furfural solutions. Furthermore, color formation in this system is very sensitive to the hydrogen ion activity in the range studied. Color formation was found to be induced at room temperature in this system at *p*H 6.8 by increasing the concentration of glycine sufficiently.

TABLE I

EFFECT OF GLYCINE ON THE RELATIVE RATE OF COLOR[a] FORMATION IN 1% FURFURAL (0.12 *M*)

Sample + glycine / glycine concn., *M*	*p*H	Acceleration of color formation[b]
0.01	3.3	3.3
.05	3.3	3.3
.01	3.9	4.7
.05	3.9	10.0
.01	5.2	8.0
.05	5.0	27.0
.01	6.3	14.0
.05	5.8	35.0
.01	6.9	26.0
.05	6.6	46.5

[a] Optical densities were measured after heating samples four hours at 80°. [b] Values for the acceleration of color formation represent the ratios of optical densities with glycine to samples without glycine.

In view of the effect of acids and bases on furfural solutions, the dicarboxylic amino acids and the diamino acids were of special interest. Experiments were performed similar to those with glycine, substituting aspartic acid or arginine. The general behavior of these amino acids was similar to that for glycine. However, mole for mole arginine was more effective than glycine over the entire *p*H range. Aspartic acid was more effective than glycine only below *p*H 5. Above *p*H 5, there was little difference between them.

Varying the furfural concentration disclosed that a two-fold increase in the concentration over the range 1 to 4% approximately doubled the relative rate of color formation.

Effect of Some Other Compounds on the Relative Rate of Coloration.—The effect of a series of available compounds on the relative rate of color formation in furfural solutions was measured. Ammonium chloride and pyruvate were tried because of their possible formation in a system furfural-alanine.[8] Biacetyl was studied because of its relationship to pyruvate and its occurrence in food products. Crotonaldehyde and formaldehyde were reactive aldehydes of interest to us. Hydrogen peroxide[9] and sodium bisulfite[7] were of interest because they have been reported as inhibitors in "browning" reactions. Morpholine, a secondary amine, was also studied.

One per cent. solutions of furfural (0.12 *M*) containing the desired concentration of these substances were prepared and treated as described earlier.

Table II outlines the data thus obtained. Among the compounds tested, ammonium chloride, pyruvate, biacetyl, hydrogen peroxide and morpholine accelerated the color reaction in furfural solutions over the concentration ranges studied. Sodium bisulfite and formaldehyde slowed the reaction considerably. Crotonaldehyde had relatively little effect on the color reaction during the period studied.

Since the color reaction is produced by both acids and bases, the Lowry mechanism[10] might well explain the effect of most of the added compounds.

Dialysis and Characterization of Fractions of Colored Material.—Dialysis studies of the colored furfural solutions were made in order to obtain information on the particle size of the colored material formed. Portions of heated 1% furfural solutions were placed in Viscose dialyzing tubing with a few glass beads for stirring. The

(6) Solutions containing only furfural were adjusted to higher *p*H's (1% furfural solutions have a *p*H of about 4) using 0.01 *N* sodium hydroxide since the rate of addition of base affected the final *p*H of the solution.

(7) M. A. Joslyn, *Ind. Eng. Chem.*, **33**, 310 (1941).

(8) S. Akabori, *J. Chem. Soc. Japan*, **52**, 893 (1931).

(9) J. Seaver and Z. I. Kertesz, unpublished data.

(10) T. M. Lowry, *J. Chem. Soc.*, **127**, 1371 (1925); T. M. Lowry and E. M. Richards, *ibid.*, 1385 (1925).

TABLE II

EFFECT OF SOME COMPOUNDS ON THE RELATIVE RATE OF[a] COLOR FORMATION IN 1% FURFURAL

Sample + cpd.	*p*H	Acceleration of color formation[b]
0.05 *M* NH_4Cl	6.7	4.0
.01 *M* sodium pyruvate	6.8	7.5
.01 *M* biacetyl[c]	6.6	25.0
.01 *M* crotonaldehyde	6.8	1.0
.005 *M* CH_2O	6.8	0
.1 *M* H_2O_2[d]	3.9	8.0
.2 *M* $NaHSO_3$	6.1	0
.2 *M* $NaHSO_3$ + 0.05 *M* glycine	6.1	0.5
.05 *M* morpholine[e]	6.7	43.0

[a] Optical densities were measured after heating samples four hours at 80° except in the case of crotonaldehyde where measurement was after twenty-four hours. [b] Values for the acceleration of color formation represent the ratios of optical densities with the compound to samples without it. [c] The optical density was corrected for the initial slight color of the solution due to the biacetyl itself. [d] In the case of hydrogen peroxide, the relative rate of color formation varies inversely with *p*H. [e] The sample turned yellow on mixing the two colorless components of the solution.

samples were dialyzed against 0.01 *M* sodium chloride until no more colored material could be removed from the solution. The results indicated that the yellow colored material formed in the early stages of the color reaction was freely dialyzable. However, when dark brown solutions were dialyzed, a light orange colored material remained in the dialyzate and small amounts of brown material precipitated from the solution. This indicates that the formation of the brown colored material involves a polymerization reaction. Spectrophotometric analyses of heated furfural solutions disclosed the fact that only a negligible amount of furfural is involved in forming the colored material in the system.

The colored material from several furfural-amino acid systems prepared by the method previously described was characterized. The samples were indistinguishable by spectrophotometric means, all showing the typical end-absorption curves found for products obtained from "browning" reactions. They were all relatively insoluble in water, glacial acetic acid, 95% ethanol and ether. Alkaline solutions of the products tended to disintegrate as shown by the decreased amount of material precipitable by acid with increased age of the solution. The material precipitated by acid from aged alkaline solutions is soluble in 95% ethanol.

Bromine decolorized the brown precipitates.

Summary

1. The effect of *p*H on the relative rate of color formation in 1% furfural at 80° is slight over the range *p*H 3.3 to 6.8.

2. Glycine, aspartic acid and arginine are excellent accelerators for the color reaction in furfural solutions. Their effect increases markedly with *p*H over the range 3.3 to 6.8.

3. In the range 1 to 4%, doubling the furfural concentration increases the relative rate of color formation in the system at 80° roughly two-fold.

4. Under the conditions examined, ammonium chloride, pyruvate, biacetyl, hydrogen peroxide and morpholine also accelerate the formation of color. Sodium bisulfite and formaldehyde decrease the relative rate of the reaction.

5. The color reaction in the studies reported involves changes of a very small magnitude with reference to the amount of furfural. Fractions of colored material isolated from several furfural systems were indistinguishable by the methods used.

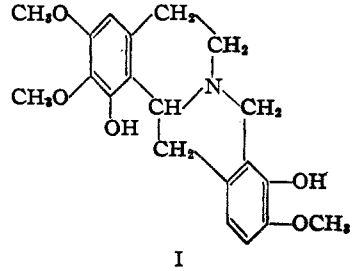
GENEVA, N. Y. RECEIVED DECEMBER 9, 1946

[CONTRIBUTION FROM THE RESEARCH LABORATORY, DOMINION RUBBER CO. LTD.]

The Alkaloids of Fumariaceous Plants. XLI. The Constitution of Capaurimine

BY RICHARD H. F. MANSKE[1]

Capaurimine is an alkaloid isolated by the author from *Corydalis pallida* Pers.[2] and from *C. Montana* (Engelm.) Britton.[3] It contains three methoxyl and two phenolic hydroxyl groups and when methylated with diazomethane, it yields capaurine O-methyl ether. Since the constitution of capaurine is already known[4] there remains only the location of the hydroxyl groups on the protoberberine skeleton. For this purpose the alkaloid was ethylated and the resulting non-phenolic base oxidized with permanganate. The expected fragments, namely, a 3,4-dialkoxyphthalic acid and a 3,4,5-trialkoxyphthalic acid, were isolated as their respective N-ethylimides. The former proved to be identical with the imide of 3-ethoxy-4-methoxyphthalic acid, a product already obtained by the author from the O-ethyl ether of scoulerine[5] and the latter was identical with the imide of 3-ethoxy-4,5-dimethoxy-phthalic acid obtained from the O-ethyl ether of capaurine.[4] The structural formula of capaurimine is therefore unambiguously represented by (I).



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(1) Director of Research.
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(3) Manske, *ibid.*, **20B**, 49–52 (1942).
(4) Manske and Holmes, THIS JOURNAL, **67**, 95 (1945).
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