

Isobornylane is stable toward the treatment with aqueous magnesium chloride at 425°.

When isocamphane is heated at 400° with aqueous magnesium chloride it retains the dicyclic

ring structure; part of the isocamphane undergoes dehydrogenation.

EVANSTON, ILLINOIS  
RIVERSIDE, ILLINOIS

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## Formation of 5-Hydroxymethylfurfural from D-Glucose in Aqueous Solution<sup>1</sup>

BY BARRETT L. SCALLET WITH JOHN H. GARDNER<sup>2</sup>

The literature pertaining to the decomposition of D-glucose during heating in aqueous solution reveals that, in each case studied, some other substance besides glucose and water was present. Decomposition in the presence of amino acids with the production of colored compounds has been extensively studied,<sup>3,4,5</sup> and the action of oxygen on hot aqueous glucose solutions has been noted in the presence and absence of amino acids.<sup>6</sup> In these cases, extent of reaction was judged by amount of color formation or oxygen consumption. Alkaline reagents such as 5% sodium phosphate,<sup>7</sup> dilute potassium hydroxide,<sup>8</sup> and dilute sodium carbonate<sup>9</sup> lead to formation of small quantities of methylglyoxal from glucose, while dilute acids yield 5-hydroxymethylfurfural.<sup>10</sup>

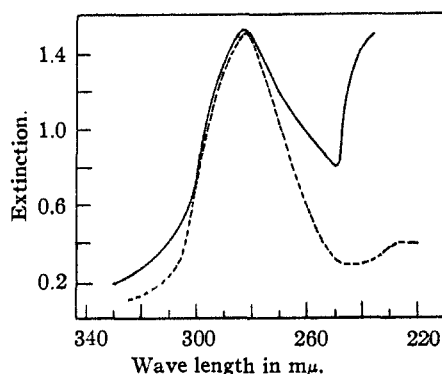


Fig. 1.—Ultraviolet absorption curves: full line, 16.7% glucose solution heated seven hours, diluted 1:4; broken line, benzene extract of a heated glucose solution.

However, no one has attempted to follow the decomposition of glucose in pure aqueous solution. It has now been found that heating such a solution leads to formation of 5-hydroxymethyl-

furfural in small quantity. The reaction can be followed by measuring the ultraviolet absorption of the solution (Fig. 1, full curve), since 5-hydroxymethylfurfural shows a characteristic, intense absorption band in the ultraviolet (Fig. 2). This permits its determination in very low concentrations such as are present when glucose is decomposed under relatively mild conditions. A glucose solution (16.7%), heated for one hour in boiling water, yielded 6 parts of 5-hydroxymethylfurfural per million parts of glucose and showed no color. Solutions heated two and one-half and seven hours contained 15 and 170 p. p. m., respectively, and the latter was highly colored.

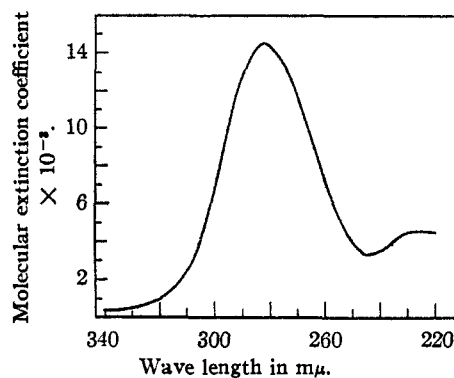


Fig. 2.—Ultraviolet absorption curve for 5-hydroxymethylfurfural.

The presence of the reactive aldehyde and hydroxyl groups in 5-hydroxymethylfurfural suggests that this compound may easily polymerize to give long-chain molecules. Joslyn<sup>11</sup> has indicated that this reaction does take place, yielding brown pigments. Undoubtedly some of the color produced during heating of glucose solutions is due to this reaction. When a heated glucose solution is extracted with benzene the color decreases markedly, but the extracted material, which is nearly pure 5-hydroxymethylfurfural (Fig. 1, broken curve), is almost colorless. In one run, a glucose solution heated overnight in boiling water had a pronounced color. During subsequent extraction with benzene the color decreased about 25%. On evaporation of the benzene, 5-hydroxymethylfurfural, colored a pale

(1) Part of a dissertation presented to the Board of Graduate Studies of Washington University by Barrett L. Scallet in partial fulfillment of the requirements for the degree of Master of Science, 1943.

(2) Present address, J. T. Baker Chemical Co., Phillipsburg, N. J.

(3) Maillard, *Compt. rend.*, **153**, 1078 (1911).

(4) Ruckdeschel, *Z. ges. Brauw.*, **37**, 430 (1914).

(5) Ambler, *Ind. Eng. Chem.*, **21**, 47 (1929).

(6) Lieben and Bauminger, *Biochem. Z.*, **202**, 371 (1937).

(7) Dakin and Dudley, *J. Biol. Chem.*, **15**, 127 (1913).

(8) Evans, Edgar and Hoff, *THIS JOURNAL*, **48**, 2665 (1926).

(9) Fischler and Lindner, *Z. physiol. Chem.*, **175**, 237 (1928).

(10) Alberda van Ekenstein and Blankisma, *Chem. Weekblad*, **6**, 217 (1909); *Ber.*, **43**, 2355 (1910).

(11) Joslyn, *Ind. Eng. Chem.*, **33**, 308 (1941).

yellowish-green, was obtained. An aqueous solution of this material was colorless, indicating that removal of 5-hydroxymethylfurfural from the glucose solution may have reversed the polymerization reaction, thus decreasing the color.

### Experimental

**Anhydrous D-glucose** (Merck) was used in all experiments. The preparation was of exceptional purity. A 20% solution showed no color in a 5-inch tube, and the nitrogen content was only 0.0003%. When a solution of this material was heated side by side with a similar solution of U. S. Bureau of Standards dextrose, the absorption spectra were identical in the visible and ultraviolet regions.

Glucose solutions ranging in concentration from 15 to 35% were heated under reflux in a boiling water-bath. Time of heating varied from one-half to twenty-four hours. The pH values were originally about 6.5, but dropped somewhat during heating.

**Ultraviolet Absorption Spectra.**—These were photographed in a Hilger Model E spectrograph<sup>12</sup> with sector-photometer, illuminated by a hydrogen discharge tube. The cell length was 2 cm., and the sector settings used corresponded to extinction values of 0 to 1.8 in steps of 0.1. Plates were read visually, after enlarging to 15 × 20 inches, with a probable error of ±0.02 extinction unit. The wave length scale of the instrument was standardized against the absorption bands of thiophene-free redistilled benzene.

**Separation of 5-Hydroxymethylfurfural from the Glucose Solution.**—Vacuum distillation of a heated glucose solution removed only about one-sixth of the 5-hydroxymethylfurfural. Direct extraction of the solution in an all-glass continuous liquid-liquid extraction apparatus (500 ml. capacity) removed about half of the product in sixteen hours. Evaporation of benzene from the extract at atmospheric pressure volatilized about one-fifth of the 5-hydroxymethylfurfural.

Color was measured in a split-field comparator by matching the color of combinations of Lovibond slides (series 510 yellow, series 200 red) against the color of a 5-inch column of the solution. A 35% glucose solution (450 ml.), heated seventeen hours under reflux in boiling water, had a color of 4.3 yellow and 1.4 red. After extraction with benzene for seventy-two hours the color was 3.2 yellow and 1.1 red. Evaporation of the benzene left about 0.1 ml. of pale yellowish-green 5-hydroxymethylfurfural, which was colorless when dissolved in water.

Ether extracts, however, contained some highly colored material along with the 5-hydroxymethylfurfural.

(12) Kindly loaned by Anheuser-Busch, Inc.

**Characterization of the Extract.**—The benzene-extracted material gave the same absorption curve (Fig. 1, broken line) as did 5-hydroxymethylfurfural prepared by the method of Middendorp.<sup>13</sup> Schiff reagent gave a transitory purple color with the extract, characteristic of 5-hydroxymethylfurfural.<sup>14</sup> The extract, dissolved in about 5 ml. of water, gave an instantaneous precipitate at room temperature with 20 ml. of 2,4-dinitrophenylhydrazine reagent (1.67% solution in 2 N hydrochloric acid). After one hour, this material was filtered off, washed, recrystallized once from dilute alcohol and once from 95% alcohol. The melting point was 197–199° (cor.), and there was no depression of the melting point when the material was mixed with 5-hydroxymethylfurfural 2,4-dinitrophenylhydrazine, which melted at 198–200°.<sup>15</sup>

The 2,4-dinitrophenylhydrazine, dried at 110°, was analyzed for nitrogen by the semi-micro Kjeldahl procedure as modified by Elek and Sobotka.<sup>16</sup>

*Anal.* Calcd. for C<sub>12</sub>H<sub>10</sub>O<sub>6</sub>N<sub>4</sub>: N, 18.30. Found: N, 18.11.

Known 5-hydroxymethylfurfural 2,4-dinitrophenylhydrazine gave 18.32% nitrogen by this method.

**Quantitative Determination of 5-Hydroxymethylfurfural.**—Crystalline 5-hydroxymethylfurfural was dissolved in water and a series of dilutions was prepared ranging in concentration from 1 to 10 γ per ml. The extinction readings at 283 mμ (the absorption maximum), plotted against concentration, gave a straight line; an extinction value of 1.00 corresponds to 4.4 γ per ml. (2-cm. cell).

### Summary

Heating pure aqueous solutions of glucose leads to formation of small amounts of 5-hydroxymethylfurfural, a precursor of some of the brown color formed during heating.

5-Hydroxymethylfurfural has been determined by means of its ultraviolet absorption, and a quantitative absorption curve for this substance is given.

ST. LOUIS, MISSOURI

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(13) Middendorp, *Rec. trav. chim.*, **38**, 1 (1910).

(14) Feulgen and Imhäuser, *Z. physiol. Chem.*, **148**, 1 (1925).

(15) Blanksma and Wackers, *Rec. trav. chim.*, **35**, 655 (1936), give for 5-hydroxymethylfurfural 2,4-dinitrophenylhydrazine, m. p. 184°. Bredereck, *Ber.*, **65**, 1333 (1932), has shown that a number of similar compounds derived from members of the furfural series show evidence of *syn*- and *anti*-isomerism, which may account for the discrepancy in melting points noticed here.

(16) Elek and Sobotka, *This Journal*, **48**, 501 (1926).