[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE STATE COLLEGE OF WASHINGTON]

Crossed Cannizzaro Reactions—Benzaldehyde and Furfural[1]

BY STEWART E. HAZLET AND ROBERT B. CALLISON

It is known that furfural undergoes the Cannizzaro reaction, forming furoic acid and furfuryl alcohol.[2a] This change is similar to the original observation[2b] of Cannizzaro in which benzaldehyde was the aldehyde employed.

Within recent years a number of crossed Cannizzaro reactions have been studied. In 1936, Bailar reported results on the behaviors of a number of mixtures of aromatic aldehydes.[3] Among the studies on the type of reaction under consideration, the one by Davidson and Bogert,[4] in which a mixture of an aromatic aldehyde and formaldehyde, the latter in large excess, was used with the result that the aromatic aldehyde was reduced almost quantitatively to the corresponding alcohol and the formaldehyde was oxidized to formic acid, has probably resulted in the most applications. The study of Rodionov and Fedorova[5] using mixtures of formaldehyde and furfural which resulted in a good yield of furfuryl alcohol is somewhat analogous to that of Davidson and Bogert.

The purpose of this investigation was to determine the disproportionation which would occur when mixtures of furfural and benzaldehyde react under the conditions which bring about the Cannizzaro reaction in the case of furfural alone. Therefore, the procedure followed in this work was essentially that described in "Organic Syntheses"[2a] with such modifications as are indicated in the Experimental Part.

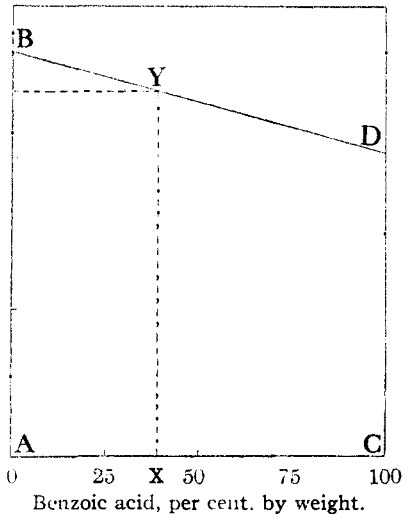

Fig. 1.

In order to determine the amount of each product formed in the reaction

$$\begin{array}{c}\text{Furfural} + \\ \text{Benzaldehyde}\end{array} \xrightarrow{\text{NaOH}} \begin{array}{c}\text{Furoic acid} \\ \text{and} \\ \text{benzoic acid}\end{array} + \begin{array}{c}\text{Furfuryl alcohol} \\ \text{and} \\ \text{benzyl alcohol}\end{array}$$

it was necessary to develop methods for analyzing benzoic acid–furoic acid and benzyl alcohol–furfuryl alcohol mixtures. Several procedures were tried. The following were adopted, after they had been shown to give satisfactory results consistently with mixtures of known compositions:

(1) For the mixtures of benzyl and furfuryl alcohols—determination of the refractive index of the two component system after distillation at reduced pressure.

(2) For the mixtures of benzoic and furoic acids—(a) determination of the *total acidity* of a sample of the mixed acids, (b) oxidation by alkaline permanganate (under controlled conditions) of the furoic acid and determination of the amount of residual benzoic acid, and (c) calculation of the amount of furoic acid by the difference: (a) − (b).

In preliminary experiments attempts were made to separate the alcohol mixtures by fractional distillation at reduced pressures. From these experiments it appeared that the molar ratio of benzyl alcohol to furfuryl alcohol was about 2:1. This method was not sufficiently accurate for the present work and it was abandoned.

For the analysis of the acid mixtures, methods which were tried but discarded for the more satisfactory one indicated above included the following: (a) Mixtures of benzoic and furoic acids were treated with methanol and dry hydrogen chloride and refluxed for different periods of time. The excess methanol was removed and after the usual purification steps the refractive indices of the mixtures were determined. (Experimental determination of the refractive index curve for the system methyl benzoate–methyl furoate showed that it deviated only slightly from linearity.) Because yields were not quantitative and results were not in agreement with calculated values, a more suitable method was sought. (b) Another method, similar to a procedure used by Cornog[6] for analyzing iodine–chlorine mixtures, was investigated. A graph was constructed so that in Fig. 1 AB corresponds to the number of milliliters of 0.1 N alkali solution which would neutralize exactly one gram of furoic acid, and CD corresponds to the number of milliliters of 0.1 N alkali

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(1) Presented before the Organic Division, American Chemical Society, Detroit Meeting, September, 1940.

(2) (a) Gilman, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1932, Col. Vol. 1, p. 270. (b) Cannizzaro, *Ann.*, **88**, 129 (1853).

(3) Bailar, Barney and Miller, THIS JOURNAL, **58**, 2110 (1936).

(4) Davidson and Bogert, *ibid.*, **57**, 905 (1935).

(5) Rodionov and Fedorova, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 947 (1937).

(6) Jacob Cornog, private communication.

solution which would neutralize exactly one gram of benzoic acid; then, one gram of a sample of a mixture of benzoic and furoic acids which would exactly react with a volume of 0.1 N alkali corresponding to XY would have a composition of AX per cent. benzoic acid and CX per cent. furoic acid. With mixtures of pure benzoic and furoic acids this method gave very satisfactory results; also, the linearity of the curve (BD) had been established experimentally. However, the acid mixtures from the crossed Cannizzaro reactions contained small amounts of impurities (apparently 2 to 3%), and this together with the slight slope of BD (due to small differences in the molecular weights of benzoic and furoic acids) did not permit of sufficiently accurate analysis of the reaction mixtures by this method.

Experimental Part

Purification of Materials

Furfural.—Technical furfural was fractionally distilled under reduced pressure in an atmosphere of nitrogen; b. p. 62° (17 mm.) and $n^{20}\mathrm{D}$ 1.5246.[7]

Benzaldehyde.—This compound (Eastman Kodak Company's practical grade) was purified in the same manner as the furfural; b. p. 69° (17 mm.) and $n^{20}\mathrm{D}$ 1.5456.[8]

Benzyl Alcohol.—This alcohol (Eastman Kodak Company's product of highest purity) was treated with calcium oxide, and the mixture warmed on a steam-bath for two hours. It was then filtered through glass wool. Three volumes of absolute ether was added to the filtrate, the ethereal solution was dried successively with anhydrous sodium sulfate and anhydrous copper sulfate, and the ether was removed by distillation. The alcohol was then fractionally distilled under reduced pressure, and that portion was retained which boiled at 97° (12 mm.). This fraction was redistilled; b. p. 94° (10 mm.) and $n^{20}\mathrm{D}$ 1.5404.[9]

Furfuryl Alcohol.—Technical furfuryl alcohol was purified by the same method as that described above in the case of benzyl alcohol; b. p. 70° (10 mm.) and $n^{20}\mathrm{D}$ 1.4873.[10]

Benzoic Acid.—This compound was recrystallized from water three times; m. p. 122.1–122.2 (cor.)[11] (the melting point was determined from a freezing point curve; the thermometer which was used had been standardized against one calibrated by the United States Bureau of Standards). The total acidity (calculated as benzoic acid) was found to be 100.03%.

Furoic Acid.—Technical furoic acid was crystallized four times from water; m. p. 130.8–131.0° (cor.)[12] (this m. p. was determined in the same manner as that of the benzoic acid). Titration of this product gave the total acidity (calculated as furoic acid) as 99.89%.

Crossed Cannizzaro Reactions

After distillation of the aldehydes in an atmosphere of nitrogen at reduced pressure as described under Purification of Materials, they were transferred under nitrogen pressure into long-neck reaction bottles which had been flushed out thoroughly with nitrogen. One-half gram molecule of each aldehyde (53 g. of benzaldehyde and 48 g. of furfural) was employed in each reaction. While the reaction vessels containing the mixtures of aldehydes were cooled in ice water, 22.5 g. of sodium hydroxide in 45 ml. of water was added and necks of the bottles were sealed off. The reaction vessels were placed in a mechanical shaking device for two hours; after that they were allowed to stand at room temperature for from twenty-four to forty-eight hours. The vessels were opened, sufficient water was added to dissolve the solids which were present, and extractions were carried out in a specially constructed apparatus (Fig. 2) as described below.

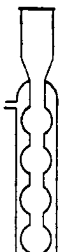

Fig. 2.—Extractor.

The aqueous alkaline reaction mixture was placed in the extractor, and water was added to bring the level to within about 1 cm. of the lower siphon tube; an appropriate volume of ether was placed in the flask attached to the side arm, and extraction was carried out for from eight to twelve hours.

Then the stopcock on the lower siphon tube was closed and a slight excess of sulfuric acid (1:1) was added, the flask on the side arm was changed, and the acidic mixture was extracted with a fresh supply of ether for from eight to twelve hours.

The ethereal extract from the alkaline mixture was shaken with strong sodium bisulfite solution and then returned to the extractor; in turn, extraction was carried out for four hours. The ether extract was then dried with anhydrous magnesium sulfate and filtered. The ether was removed by distillation, and the mixture of alcohols was distilled in an atmosphere of nitrogen under reduced pressure. This distillate was analyzed as described in a later section of this report.

The ether extract from the acidic mixture was washed with two 10-ml. portions of water, and the ether was removed by distillation. The sample of mixed acids was stored in a vacuum desiccator over calcium chloride. The "cake" which formed was broken up, the product was pulverized, and it was returned to the desiccator and stored until it attained constant weight. The mixture of acids was then analyzed as described in a subsequent paragraph.

Alcohol Mixtures.—Mixtures of benzyl and furfuryl alcohols with known compositions were prepared in weighing bottles, and the refractive indices were determined in the same manner and with the same apparatus as other data reported from this Laboratory by Schutz.[13] When these values were plotted against composition (wt. %), the resulting curve deviated only slightly from linearity, thus: deviation in $n^{20}\mathrm{D}$ (wt. % furfuryl alcohol) 0.0000 (2.95%); +0.0003 (10.64%); +0.0007 (24.81%): +0.0009 (38.37%); +0.0007 (50.62%); +0.0005 (69.18%): +0.0005 (78.95%): +0.0004 (84.99%); +0.0003 (96.72%).

By determining the refractive index of the alcohol distillate from the crossed Cannizzaro reactions containing furfuryl and benzyl alcohols, the composition was obtained by inspection of the graph.

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(7) Bruhl, *Ann.*, **7**, 235 (1886), reported $n^{20}\mathrm{D}$ 1.52608.

(8) Reported values: (a) Auwers and Eisenlohr, *J. prakt. Chem.*, **82**, 119 (1910), $n^{17.6}\mathrm{D}$ 1.54629; (b) Landriew, Baylocq and Johnson, *Bull. soc. chim.*, **45**, 36 (1929) (*Chem. Abst.*, **23**, 2967 (1929)), $n^{20}\mathrm{D}$ 1.5450.

(9) The recorded value is $n^{20}\mathrm{D}$ 1.5403.[8b]

(10) The recorded value is $n^{20}\mathrm{D}$ 1.4876.[8b]

(11) The m. p. reported by Timmermans and Burriel, *Chimie & industrie*, Special No. 196–7, March, 1931 (*Chem. Abstr.*, **25**, 3324 (1931)) was 122.45°.

(12) The m. p. recorded by Kellog and Kellog, *Ind. Eng. Chem., Anal. Ed.*, **6**, 251 (1934), was 131°.

(13) Schutz, THIS JOURNAL, **61**, 2691 (1939).

To test the applicability of this method of analysis, determinations were made with mixtures of known compositions with the following results: samples as prepared, weights and compositions (in terms of wt. % furfuryl alcohol)—25.0 g. of 20%, 30.0 g. of 30.0% and 17.3 g. of 65.3%; after distillation—22.5 g. of 19.5%, 28.3 g. of 31.7% and 16.2 g. of 64.8%, respectively. The recovery of product was satisfactory and the composition was in good agreement with the mixture as prepared in each case.

Acid Mixtures.—(a) The total acidity of a sample, approximately 1 g., of the mixture of acids obtained from the crossed Cannizzaro reaction was determined by titration with standard alkali (phenolphthalein as indicator).

(b) A sample, usually about 1 g., of the mixture of acids was dissolved in 10 ml. of 10% sodium hydroxide solution, an equal volume of water was added, and the solution was heated almost to boiling where it was maintained during the next step. Saturated potassium permanganate solution was added until a pink color persisted for one minute. The excess permanganate was destroyed by the addition of sodium bisulfite solution. After the mixture had cooled, 15 ml. of sulfuric acid (1:1) and then sufficient sodium bisulfite to dissolve the manganese dioxide, which had precipitated, were added. The mixture was boiled gently under a reflux condenser for one hour. The solution was cooled, the condenser was washed down with a small quantity of ether, and the mixture was transferred to the extractor. After extraction had proceeded for from six to eight hours, the ethereal solution was washed with two 10-ml. portions of water and transferred to a titration flask. All but the last 5 or 10 ml. of ether was distilled off through a 60-cm. Vigreux column; the last portion of solvent was allowed to evaporate at room temperature. The amount of residual benzoic acid was determined by titration.

(c) From the difference between total acidity and benzoic acid, the amount of furoic acid was calculated.

That the method described above gives results of sufficient accuracy for the problem at hand is shown by the following data obtained with mixtures of furoic and benzoic acids of known compositions: mixtures as prepared—34.16, 31.74, 29.78 and 43.24% benzoic acid; found by analysis—34.36, 31.77, 29.96 and 43.14% benzoic acid, respectively.

Results

For mixtures of furfural and benzaldehyde treated as outlined for the crossed Cannizzaro reaction and the reaction mixtures analyzed by the methods described above, the condensed and summarized results shown in Table I were obtained.

TABLE I

DISPROPORTIONATION IN THE CROSSED CANNIZZARO REACTION WITH FURFURAL AND BENZALDEHYDE

Reaction no.	Alcohols recov., wt. in g.	Molar ratio, furfuryl alcohol: benzyl alcohol	Acids recov., wt. in g.	Molar ratio, benzoic acid: furoic acid
1	42.6	0.42:1	49.2	0.44:1
2	51.6	0.47:1	55.4	0.65:1
3	32.1	0.60:1	57.2	0.65:1
4	34.0	0.64:1	55.9	0.72:1
5	38.2	0.67:1	47.7	0.47:1
6			55.5	0.68:1
7			56.6	0.69:1
8			54.6	0.71:1
Ave.	39.7	0.56:1	54.0	0.63:1

The furfural, furfuryl alcohol and furoic acid used in this work were generously furnished by the Quaker Oats Company, Chicago.

Summary

Mixtures of furfural and benzaldehyde were subjected to the conditions under which the Cannizzaro reaction usually occurs.

Satisfactory methods were found for the analysis of mixtures of reaction products.

In the reaction studied, the furfural was oxidized to a greater extent than the benzaldehyde: the ratio was approximately 5:3.

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The Photochemical Inactivation of Trypsin and Papain Solutions in the Ultraviolet Region

BY F. L. KAUFFMAN AND W. M. URBAIN

It has been demonstrated that ultraviolet light will cause the inactivation of many enzymes,[1] but relatively few experiments have been conducted under conditions which allowed quantitative calculations to be made. Quantum yields (molecules inactivated per quantum absorbed) have been calculated for the photochemical inactivation of urease,[2] and can be calculated from the data of Gates[3] for pepsin. The quantum yields for the inactivation of trypsin[4] have been calculated also at certain wave lengths of ultraviolet light.

Bersin[5] has reported that he found ultraviolet rays to have an initial activating effect upon papain solutions. However, further exposure to ultraviolet light caused the papain solutions to become inactive.

The purpose of this investigation was to determine the general qualitative characteristics and the quantitative relationships of the ultraviolet light required for the inactivation of trypsin and papain solutions by using commercially available mercury arc ultraviolet light sources.

Materials and Methods

Solutions containing 0.10% papain were prepared from crude, powdered Ceylon papain obtained from Parke, Davis and Company. The solutions were prepared fresh for each test, adjusted to a *p*H of 6.4, and chemically

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(1) C. Ellis, A. A. Wells and F. F. Heyroth, "The Chemical Action of Ultraviolet Rays," Reinhold Publ. Corp., New York, N. Y., 1941, p. 680.

(2) E. W. Landen, THIS JOURNAL, **62**, 2465 (1940).

(3) F. L. Gates, *J. Gen. Physiol.*, **18**, 265 (1934).

(4) F. M. Uber and A. D. McLaren, *J. Biol. Chem.*, **141**, 231 (1941).

(5) T. Bersin, *Z. physiol. Chem.*, **222**, 177 (1933).