the molecular structure with apparent reduction of the double bond in the 4,5 position. The natures of the final products of this change, however, have not been definitely established.

3. Yeast nucleic acid has been subjected to the action of molecular hydrogen in the presence of colloidal platinum and evidence obtained that ammonia is produced by such treatment.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

THE EQUILIBRIUM BETWEEN BENZALDEHYDE AND BENZOIN

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Introduction

When benzaldehyde is acted upon by alkali cyanides, it undergoes a condensation reaction, yielding the substance called benzoin.

$$C_6H_5CHO + C_6H_5CHO = C_6H_5CH(OH)COC_6H_5 \qquad (1)$$

Many explanations have been offered of the mechanism of this reaction. The only careful quantitative study published so far was made in 1904 by Bredig and Stern,[1] who investigated the kinetics of the condensation. Their results may be summarized as follows.

Within wide limits, the rate of condensation proceeds as the square of the benzaldehyde concentration, for a given concentration of potassium cyanide. The rate is, furthermore, directly proportional to the concentration of the catalyst, which was found to be cyano ion, CN^-. No benzoin is formed in the absence of this ion. Hydrogen cyanide forms no benzoin; and the addition of acids stops the condensation. Hydroxyl

TABLE I

REVERSAL OF BENZOIN CONDENSATION

Benzaldehyde concentration 0.28*M;* benzoin, 0.14 (initial values); potassium cyanide, 0.24 *M*. Temperature, 60°. Solvent, 66% ethyl alcohol.

Original material	Time, hours	Benzoin present Mole	Percentage of possible benzoin
Benzaldehyde	2.3	0.070	50
	3.2	.094	67
	4	.101	71
	5	.113	79
	48	.110	72
	72	.089	62
Benzoin	48	.073	51
	72	.064	45

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[1] (a) Bredig and Stern, *Z. Elektrochem.*, **10**, 582 (1904); (b) Stern, *Z. physik. Chem.*, **50**, 513 (1904). The earlier literature has been summarized by Stern: further references are given by Lachman (c), THIS JOURNAL, **45**, 1529 (1923).

ion, in the absence of cyano ion, fails to form benzoin; but the rate of the reaction is increased when the proportion of water in the solvent is augmented.

Stern further found that the reaction is reversible. A recalculation of some of his data shows the preceding results.

It will be seen that the formation of benzoin shows a maximum in 5 hours, then very slowly falls off.

A short time before the work of Bredig and Stern, an important observation was made by Lapworth,[2] who found that the addition of hydrogen cyanide to aldehydes is chiefly an addition of cyano ion. He was able to convert benzaldehyde into a considerable proportion of mandelonitrile, within two minutes, by shaking it with a cold, aqueous solution of potassium cyanide.

Lapworth's work was confirmed by Stern, and extended to some conductivity measurements which strongly indicate the formation of a mandelonitrile ion at temperatures below 25°. At 60°, Stern's usual working temperature, there was little evidence of such an ion.[3]

This somewhat detailed account of Bredig and Stern's data is given here, in view of a recent article by Anderson and Jacobson,[4] which tends to confuse the facts already established. Anderson and Jacobson assume as a new fact a simple reversible equilibrium between benzaldehyde and benzoin. Without any reference to the above material, they give two tables, one starting from benzaldehyde, the other from benzoin, which indicate indeed a fair constancy of the ratio A^2/B, where A is the concentration of benzaldehyde, B that of benzoin.

The experimental work of Anderson and Jacobson, however, is open to a number of serious criticisms. Their temperature control was imperfect. The period of heating was one hour when benzaldehyde was the original material, and 1.5 hours when benzoin was taken. These periods were designated as the "correct times." Benzoin was measured by direct weighing, after diluting the reaction mixture to a definite percentage of alcohol; and benzaldehyde was measured by difference, the total loss in weight suffered by benzoin being taken as the weight of benzaldehyde present. As benzaldehyde enters into the calculation of the constant as the square, errors in estimating its amount are greatly magnified.

The inadequacy of the heating period is evident from Table I. A further source of error is due to failure of Anderson and Jacobson to vary the concentration of the catalyst; it is clear, from Lapworth's work, that in the reversible reaction

$$C_6H_5CHO + KCN + H_2O \rightleftharpoons C_6H_5CH(OH)CN + KOH \qquad (2)$$

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[2] Lapworth, *J. Chem. Soc.*, **83**, 995 (1903).

[3] Mandelonitrile cannot be distilled, even at as low a pressure as 5 mm. (temperature of vapors, 65–70°) without complete dissociation.

[4] Anderson and Jacobson, THIS JOURNAL, **45**, 836 (1923).

the concentration of potassium cyanide must affect that of benzaldehyde, and therefore any equilibrium between benzaldehyde and benzoin.

As will be shown here, the actual relationship between benzoin and benzaldehyde is much more complicated than Anderson and Jacobson infer from their limited observations.

The Equilibrium between Benzaldehyde and Benzoin in the Absence of Solvents

When benzoin is heated to about 300°, benzaldehyde is formed. There has been some uncertainty as to the amount produced; earlier investigators reported considerable quantities, but some later studies report very small yields. Thus, Engler and Grimm[5] who heated benzoin under pressure noted only "a very small fraction" from 20 g.; and Knoevenagel and Tomasczewski,[6] using palladium as a catalyst at atmospheric pressure obtained 0.2 g. of benzaldehyde from 10 g. of benzoin. It seems likely that the heat decomposition of benzoin is greatly influenced, both qualitatively and quantitatively, by impurities acting as catalysts.[7]

When a highly purified benzoin was heated to about 300°, practically identical results were noted at atmospheric pressure and in sealed tubes. No gases were formed; formation of benzaldehyde amounted to 10–13%. The other reaction products were benzil, desoxybenzoin, toluylene hydrate and benzoic acid. At temperatures below 250°, purified benzoin decomposes so slowly that there was little change even after 48 hours.

The reaction temperature can be greatly lowered if solid potassium cyanide is added to benzoin. At 150–160° over half the weight of benzoin taken may be distilled in a vacuum as benzaldehyde, within a short time. In sealed tubes, much less benzaldehyde is formed at this same temperature, indicating a condition of equilibrium; a series of measurements was therefore made, starting from benzoin, with increasing amounts of added benzaldehyde (compare Table II of the experimental section). The results, however, were unsatisfactory from the quantitative side.

A large lot of benzoin (100 g.) was then heated for several hours in an evacuated, sealed flask with 10% of solid potassium cyanide. The products were 75 g. of unchanged benzoin, 12 g. of benzaldehyde, 5 g. of benzyl alcohol, 6 g. of benzoic acid, and 2 g. of benzyl benzoate.

The production of benzyl benzoate is a matter of some interest; Claisen, a number of years ago, attempted to convert benzyl benzoate into benzoin,

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[5] Engler and Grimm, *Ber.*, **30**, 2921 (1897).

[6] Knoevenagel and Tomasczewski, *Ber.*, **36**, 2829 (1903).

[7] Engler and Grimm observed diphenylmethane among their reaction products; I have not been able to do so, working with pure benzoin alone. On the other hand, I found recently that when benzoin is heated with acids, diphenylacetic acid is formed, which by loss of carbon dioxide is converted into diphenylmethane (compare Ref. 1c, p. 1531).

and *vice versa,* without success.[8] Benzoyl cyanide, $C_6H_5CO(CN)$, is the probable intermediate here; for if ethyl alcohol is used to work up the reaction mixture, ethyl benzoate is formed.

The "side reaction" in the benzoin-benzaldehyde equilibrium, namely, formation of benzyl benzoate (and its hydrolysis products) is seen to equal the main reaction in extent. However, if benzaldehyde is removed from the system by distillation, as fast as it is formed, it is almost the only reaction product; a small amount of benzoic acid, etc., can be isolated, but the main products are benzaldehyde and unchanged benzoin. The benzaldehyde formation is evidently faster than that of benzoyl cyanide, etc.; it is, however, reversible, while the production of benzoyl cyanide is irreversible. The amount of the latter substance produced from a given weight of benzoin must therefore increase with time, if escape of benzaldehyde is prevented.

The action of solid potassium cyanide on benzoin is very rapid; but the reverse reaction, that of solid cyanide with benzaldehyde, will hardly take place in the absence of water. Smith[9] has reported good yields when benzaldehyde was stirred with powdered cyanide at 150° for 45 minutes, a condition favoring absorption of water; but when the experiment was repeated using dry benzaldehyde and crystallized reagent potassium cyanide and with protection from atmospheric moisture, no trace of benzoin could be found with Fehling's solution. When a small amount of water is added, reaction is prompt and yields are good.

Benzoin is able to take the place of water under the conditions just described. When benzaldehyde, benzoin and solid cyanide are heated to 150°, an increase in the amount of benzoin takes place. Benzoin cannot, however, replace potassium cyanide; a mixture of benzaldehyde and benzoin, with or without addition of water, is not changed by heating to the same temperature (compare Table III).

It is apparent that benzoin has something like a definite vapor tension of benzaldehyde in the presence of solid potassium cyanide. Furthermore, benzoin yields benzaldehyde when sufficiently heated in the absence of this catalyst. What of the reversed process; will benzaldehyde, heated without a catalyst, form benzoin?

Benzaldehyde is very resistant to heat; prolonged heating at temperatures up to 250° gave back unaltered material, except for a small amount of residue in which neither benzoin nor benzil could be detected. At 300°, however, a change occurred, *but exclusively in the direction of Cannizzaro's reaction;* there was a conversion of 30% in 2 hours, of 80% when heating was continued overnight. Neither benzoin nor benzil was present, within the limits of the very sensitive tests for these substances.

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[8] Claisen, *Ber.*, **20,** 646 (1887).

[9] Smith, *Am. Chem. J.*, **22,** 255 (1899).

This result was entirely unexpected; it may account, in part, for some of the products observed when benzoin is heated, such as benzoic acid and toluylene hydrate. This latter substance, as shown by Knoevenagel and Arndts,[10] is readily formed from benzyl alcohol liberated from benzoin. The benzaldehyde used as described above contained 0.2–0.6% of free benzoic acid, and probably traces of water.

Equilibrium Conditions in the Presence of Solvents

The fairly constant value calculated by Anderson and Jacobson for the equilibrium between benzaldehyde and benzoin in alcohol solution, must be regarded as accidental. When their work was repeated at the same temperature, figures approaching theirs were noted when time and catalyst concentration were in approximate agreement; but when the time was increased, or the catalyst concentration reduced, widely divergent data were obtained. Anderson and Jacobson report a "constant" ranging from 0.20 to 0.28. In Tables IV, V, VI, in the experimental section, values vary from 0.01 to 4.45. This extreme variation might readily have been predicted from the data of Bredig and Stern.

How far the assumption made by Anderson and Jacobson, that all benzoin lost during reaction goes over into benzaldehyde, departs from the facts, is indicated by the following experiment. In an atmosphere of nitrogen, 100 g. of benzoin was heated in alcoholic solution for two hours with an excess of sodium cyanide. Benzoin weighing 43 g. was recovered; the other reaction products were 18 g. of benzoic acid, 17 g. of benzaldehyde,[11] 11 g. of benzyl alcohol, 3 g. of ethyl benzoate, 6 g. of toluylene hydrate. Similar results were obtained when starting from benzaldehyde.

The production of ethyl benzoate points to the intermediate formation of benzoyl cyanide from benzoin, and it is likely that most of the benzoic acid found owes its origin to hydrolysis of this ester; but even if the entire amount of acid is due to Cannizzaro's reaction occurring with benzaldehyde first formed from benzoin, the equilibrium between these two substances is disturbed to a large, and at present incalculable, extent.

It is obvious, from Lapworth's work (compare Equation 2), that Cannizzaro's reaction may be expected to occur along with the benzoin condensation. But as the ordinary methods of preparing benzoin give yields of

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[10] (a) Knoevenagel and Arndts, *Ber.*, **35**, 1982 (1902). The formation of toluylene hydrate is given by the equation, $2C_6H_5CH_2OH = C_6H_5CH_2CH(OH)C_6H_5 + H_2O$, and involves a coupling of carbon bonds similar to that in the case of benzoin. Benzyl alcohol may also lose water, on simple heating, to form dibenzyl ether, $C_6H_5CH_2$-O-$CH_2C_6H_5$, with oxygen linking in place of carbon bonds [Lachman, (b) This Journal, **45**, 2356 (1923)]. There is a striking similarity to the behavior of benzaldehyde, which gives benzoin (C-bonds) or benzyl benzoate (O-bonds), according to conditions.

[11] Benzaldehyde appears as mandelonitrile, which, however, is completely dissociated during distillation.

85–90%, it appears that Cannizzaro's reaction is subordinated or possibly even suppressed. This raises the question whether the function of cyano ion, during the benzoin synthesis, may not be to "poison" hydroxyl ion.

The action of potassium cyanide on benzaldehyde in the presence of excess of potassium hydroxide was therefore studied. It was found that both reactions proceed simultaneously, although the rate of benzoin formation increases as the concentration of cyanide is increased.[12] (Compare Table VII.)

Hydrolysis of the cyano ion plays but little part in the synthesis of benzoin or in its reversal.[14] It seemed desirable, however, to study the process in a solvent in which hydrolysis could not take place. Such a solvent is pyridine, which mixes with benzaldehyde, and which dissolves 17 g. of benzoin per 100 cc. at room temperature. Potassium and sodium cyanides are practically insoluble in pyridine (less than 0.1 g. per liter).

It was found that the reactions previously described take place when benzoin is boiled with solid sodium cyanide in pyridine suspension, only more slowly. When, however, a cold saturated solution of benzoin is shaken with the same catalyst, in a finely divided condition, a gel is slowly formed. This gel may be filtered, washed with pyridine, and dried in a vacuum; it then contains benzoin and sodium cyanide in varying proportions, according to the extent of separating undissolved particles of cyanide from the gel before filtration. A molecular combination of benzoin and sodium cyanide should contain 81% of benzoin; the values found varied from 23 to 43%. The addition product is readily hydrolyzed by water and by alcohol; when the latter solvent is used, an odor of ethyl benzoate may be noted. It has not been possible to prepare a similar complex from potassium cyanide.

Can Benzoin be Formed by Other Catalysts?

Stern found that sodium hydroxide, carbonate and borate did not produce benzoin. During the present work numerous other substances were tested with benzaldehyde. The following gave negative results: sodium or potassium fluoride, hypophosphite, acetate, nitrite, hydrosulfide, and phenolate; also, pyridine, benzonitrile and phenyl isocyanide.

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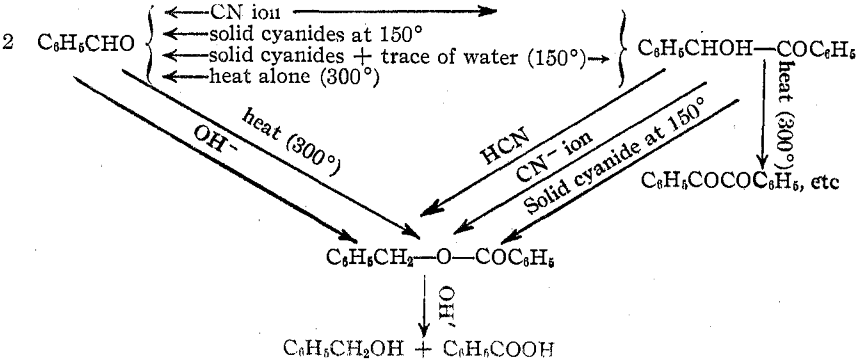
[12] The quantitative interpretation of the results obtained is made difficult by the formation of large amounts of ethyl dibenzil. This substance, which is also known as ethyl dibenzoin, is of uncertain composition and unknown structure. It is closely related to benzilic acid; cold sulfuric acid dissolves it giving a deep yellow solution, which on heating changes in color to the characteristic intense vermilion due to benzilic acid. It is impossible to give any significance, at present, to its appearance here.[13]

[13] For literature references, compare Lachman, This Journal, 45, 1510 (1923).

[14] Stern obtained a loss of about 2% of cyano ion in 2 hours, in 66% alcohol, at 60°.

Discussion

The relations between benzaldehyde and benzoin, as determined experimentally, may be graphically shown thus:



It was shown in an earlier paper that hydrocyanic acid, in alcoholic solution, slowly acts on benzoin to form ethyl benzoate and benzyl alcohol,[15] in a manner quite analogous to the behavior of benzil. Benzil is ruptured, rapidly by cyano ion, more slowly by alcoholic hydrocyanic acid, into ethyl benzoate and benzaldehyde.

$$C_6H_5COCOC_6H_5 + ROH \; (+ \; KCN \text{ or } HCN) = C_6H_5COOR + C_6H_5CHO \quad (3)$$

$$C_6H_5CH_2OHCOC_6H_5 + ROH = C_6H_5COOR + C_6H_5CH_2OH \quad (4)$$

and it was shown that benzoyl cyanide, C_6H_5COCN, must be regarded as intermediate in the case of benzil. The data in the present study also point strongly to the same mechanism when benzoin is ruptured.

Stern[16] has given a discussion of the theory of the benzoin condensation, and found that two suggestions are in accord with his own data. The theory that has enjoyed the widest circulation is that of Chalanay and Knoevenagel,[17] which is based on the following equations.

$$C_6H_5CHO + KCN = HCN + C_6H_5(CO)K \quad (5)$$

$$HCN + C_6H_5CHO = C_6H_5CHOH(CN) \quad (6)$$

$$C_6H_5(CO)K + C_6H_5CHOH(CN) = C_6H_5COCHOHC_6H_5 + KCN \quad (7)$$

The second theory which Stern finds adequate, is the one offered by Lapworth.[18] It is founded on the tendency of cyano ion to form complex ions; first, the mandelonitrile ion

$$C_6H_5CHO + CN^- = C_6H_5CH(CN)(O^-) \quad (8)$$

which adds to a second molecule of benzaldehyde, forming cyano-benzoin ion.

$$C_6H_5CH(CN)(O^-) + C_6H_5CHO = C_6H_5(CN)(O^-)—CHOHC_6H_5 \quad (9)$$

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[15] Ref. 13, p. 1522.

[16] Ref. 1 b, p. 554.

[17] Chalanay and Knoevenagel, *Ber.*, **25**, 293 (1892).

[18] Ref. 2, p. 1004.

which, however, is unstable, loses CN^- ion, yields benzoin, and furnishes thus a fresh supply of the catalyst.[19]

The chief objection to Lapworth's mechanism lies in the assumption of the formation of an *unstable* complex cyanide ion. He cites as analogous the production of ferrocyanide ion, etc.; but such ions are more stable than their components. Another obstacle is found in the absence of any reaction between two molecules of benzaldehyde with hydrocyanic acid alone. This acid is but slightly dissociated; but sufficiently so for it to add to benzaldehyde, and for it to react, in alcoholic solution, with benzoin and with benzil.[20] Stern, however, found that no trace of benzoin is formed by the action of hydrocyanic acid on benzaldehyde; if cyano ion is the *only* necessary catalyst, there should be at least a slow production of benzoin.

The theory of Chalanay and Knoevenagel, which assumes that benzaldehyde, even in dilute solutions containing water, goes over into a salt of the structure, $C_6H_5\text{-}CK(C{=}O)$, is highly improbable in that form; and the data in the present paper show that the reaction postulated in Equation 5 does not take place at all, and that the presence of water is required for benzoin to make its appearance.

The need of a few drops of water to initiate, and to carry through to a rapid state of (at least temporary) equilibrium, the condensation of benzaldehyde into benzoin in the presence of cyanides, points to a somewhat modified Knoevenagel mechanism. The first action of the three necessary components on one another is undoubtedly

$$2C_6H_5CHO + KCN + H_2O = C_6H_5CHOH(CN) + C_6H_5CHOH(OK) \quad (10)$$

Lapworth has shown that the formation of mandelonitrile is very rapid; and the tendency of benzaldehyde to add sodium hydroxide (or alkoxide or their ions) is but the common behavior of carbonyl groups. These products, by their interaction, yield benzoin either as the alkali cyanide, or alkali hydroxide, addition product.

$$C_6H_5CHOHCN + C_6H_5CHOH(OK) = C_6H_5C(OK)(CN)CHOHC_6H_5 + H_2O \quad (11)$$
$$C_6H_5CHOHCN + C_6H_5CHOH(OK) = C_6H_5C(OK)(OH)CHOHC_6H_5 + HCN \quad (12)$$

Both types of benzoin addition are known; the cyanide is described in the present paper, the hydroxide in a recent one.[21] Equation 11 accounts better for the phenomena of reversal as they have been described above.

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[19] Mention may be made of a more recent theory offered by Staudinger [*Ber.*, **46**, 3535 (1913)]. He assumes that one molecule of the aldehyde has a reactive H atom, the other a reactive CO group. But he gives no criteria for the conditions that make these atoms reactive, and assigns no function to the catalyst, which makes his theory too indefinite to be useful.

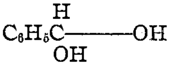
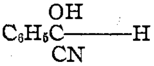
[20] Ultée, *Rec. trav. chim.*, **28**, 1 (1909), finds that mandelonitrile is dissociated into its components to the extent of 4% at 25°. Stern found a high degree of dissociation at 60°, under the conditions of the benzoin condensation.

[21] Ref. 1c, p. 1534.

The simultaneous progress of the benzoin and the Cannizzaro condensations, as shown in Table VII, is also cleared up by Equation 11. When potassium benzaldehyde hydroxide reacts with mandelonitrile, benzoin is formed; when it reacts with a molecule of benzaldehyde, the result is benzyl benzoate.[10b] Which of these concurrent reactions shall predominate is merely a question of relative rates, and of mass relations; the actual rates probably do not differ greatly, and the mass effect is therefore decisive.

Conclusion

The benzoin and the Cannizzaro condensations can be accounted for by a single pair of assumptions: (a) benzaldehyde adds M—OH (or —OR), and in this addition product —OH is the more labile group; and (b) benzaldehyde adds hydrocyanic acid, in which H is more labile:

A 
$C_6H_5\overset{H}{\underset{OH}{C}}\text{———}OH$
and B 
$C_6H_5\overset{OH}{\underset{CN}{C}}\text{———}H$

A reacts with benzaldehyde by transfer of hydroxyl to yield benzyl benzoate as previously shown; it reacts with B according to Equation 11; if both benzaldehyde and B are present, it reacts with both; if A is absent, as in acidified solutions, benzoin fails to form.

Moreover, we can account for the abnormalities noted by Stern during his investigations of the rate of benzoin formation. When a large proportion of potassium cyanide acts on benzaldehyde, the rate is depressed. This is because under these conditions we have more B, but much less A, present, as shown by Lapworth. Stern found that variation of hydroxyl-ion concentration had but little effect on the rate. Such an addition will increase A, but it will reduce B, the net effect being negligible. The proportionality between rate and cyano-ion concentration, up to the limit just discussed, is due to the dependence of B on the concentration of this ion, as shown by Lapworth and the more accurate measurements of Ultée.

The mysterious function of cyano ion as the *only* catalyst that will convert benzaldehyde into benzoin[22] also becomes clearer. Benzaldehyde forms addition products of the general type $C_6H_5CH(OH)$ (X) with sodium bisulfite, hydrochloric acid, and hydrocyanic acid;[23] but of these three, only the last is capable of existence under the conditions necessary for the presence of A, namely, alkaline solution. The comparative stability of mandelonitrile is probably due to the carbon-carbon bond.

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[22] This is not literally true; metallic sodium yields benzoin among the products of reaction with benzaldehyde. But the conditions are such that no comparison can be made with the ordinary benzoin synthesis. This reaction is being investigated.

[23] Ammonia does not form the normal addition product with benzaldehyde, giving instead hydrobenzamide. The addition product of hydrochloric acid is very unstable; compare Schiff, *Ann.*, **154**, 346 (1870), and also the experimental section below.

The mechanism of the oxidation-reduction process which leads to benzoin is of the type commonly called condensation—loss of hydroxyl (reduction) and of hydrogen (oxidation)—as distinguished from metakliny (intramolecular oxidation and reduction), observed with benzyl benzoate, benzilic acid, etc. Benzoin, however, is not the end state of the oxidation-reduction process, as shown above. It is relatively stable to weak cyanide- and hydroxide-ion concentrations, however, and thus forms a "hump" in the downward slope of energy change that leads from benzaldehyde to benzyl benzoate and to benzyl alcohol and benzoic acid.[24]

Experimental Section

Preparation of Benzoin.—To 100 g. of benzaldehyde add 1 g. of water and 10 g. of finely divided potassium cyanide (or an equivalent weight of sodium cyanide). Boil under a reflux condenser for one hour; then cool slightly, and through the condenser add 100 cc. of glacial acetic acid (*Caution:* hydrocyanic acid fumes are evolved). Heat until all is dissolved, and allow to cool. Filter, wash with a little water, drain as dry as possible, and redissolve in 100 cc. of hot glacial acetic acid; yield, about 85–90 g. Benzoin is but slightly soluble in cold acetic acid; at the boiling point, 1 g. of acetic acid dissolves more than 1.5 g. of benzoin.

Behavior of Benzoin when Heated.—Twenty g. of benzoin was heated in a sealed tube to 220–230° for 48 hours. The contents of the tube were yellow; they were extracted, when cold, with 100 cc. of dry ether, in which benzoin is very slightly soluble. The undissolved portion weighed 19.1 g., was pure white, and melted at 134°.

Forty g. of benzoin was heated, in a sealed tube, in a preheated oven for 2 hours at 300–303°. When cooled, the contents consisted of a yellow liquid in which water was suspended; there was a slight gas pressure. On direct distillation at atmospheric pressure, 1 g. of water and 4 g. of benzaldehyde were obtained up to 195°; the benzaldehyde promptly solidified with sodium bisulfite solution, the mixture being practically free from any material soluble in ether. Distillation was then continued in a vacuum; a few drops of benzaldehyde passed over; the remainder distilled between 160° and 165° (5 mm.), partly solidifying; the distillate weighed 34 g. Extraction with sodium carbonate solution gave 2 g. of benzoic acid, m. p., 121° before recrystallization. It was entirely free from diphenylacetic acid. The neutral, yellow, low-melting distillate was dissolved in hot alcohol; as the solution cooled, 13 g. of benzil, melting at 90°, separated; when recrystallized from alcohol it melted at 94°. The alcoholic filtrate was evaporated, and the residue extracted twice with warm, low-boiling ligroin. The ligroin solution was evaporated and the residue dissolved in ether; the ether solution was cooled to about —20°, and gave 3 g. of toluylene hydrate; m. p., 56°; when recrystallized from very dilute alcohol, needles were obtained melting at 61–62°. It gave no precipitate with phenylhydrazine hydrochloride. The ether mother liquor was added to the fraction insoluble in ligroin; from this, by recrystallization from a small amount of warm alcohol, 14 g. of desoxybenzoin (m. p., 40; after recrystallization, m. p., 56°) was obtained. It gave a yellow precipitate with phenylhydrazine salt, in dilute alcoholic solution.

Eighty-five g. of benzoin was heated in a distilling flask over the direct flame, at atmospheric pressure, with the thermometer inserted in the melt; 30 minutes'

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[24] The heats of combustion are: 2 benzaldehyde, 1684 Cal; benzoin, 1673 Cal; benzyl benzoate, 1668 Cal; benzyl alcohol + benzoic acid, 1668 Cal.

heating at 230–235° had no effect; after 30 minutes' further heating to 280°, a slight refluxing was visible on the sides of the flask, but no distillate appeared, and no gases were given off. The temperature was then raised to 300–305°, and held there for one hour, during which 11 g. of benzaldehyde and 1.5 g. of water distilled. Finally, the heat was increased to 325° for 15 minutes; 1 g. of benzaldehyde distilled. Distillation in a vacuum at 5 mm. then gave 70 g. of a yellow oil between 160° and 165°, which was handled as described above. The products isolated were 27 g. of benzil, 28 g. of desoxybenzoin, 6 g. of toluylene hydrate, 5 g. of benzoic acid. In both cases, no benzoin remained unchanged; the residues from the original distillation gave no test with Fehling's solution.

Heating Benzoin with Solid Cyanides.—A mixture of 50 g. of benzoin and 12 g. of crystallized potassium cyanide was heated in a flask evacuated to 5 mm., heat being applied through a paraffin bath, At 148–150° (bath temperature) distillation began; the temperature was slowly raised to 160°. Owing to the increasing sublimation of benzoin, heating was discontinued after 40 minutes. The distillate weighed 29 g.; on redistillation at atmospheric pressure, 28 g. boiling constantly at 178–179° was obtained, with a small residue of benzoin.

The original distillation residue was extracted with cold water, and cyano ion estimated in the filtrate by titration with standard silver solution; there was a loss equivalent to 7% of potassium cyanide. The water-insoluble residue was then dissolved in hot alcohol, and allowed to crystallize; 14 g. of benzoin was obtained. The alcoholic mother liquor was concentrated by careful distillation; hydrocyanic acid passed over with the alcohol vapors. The residue from the alcohol, which had a strong odor of ethyl benzoate, was dissolved in a little ether, the ether evaporated, and the dark brown oil obtained distilled with steam. A colorless oil, weighing 1.6 g., boiling at 208–210°, was obtained.[25] From the aqueous potassium cyanide extract 1.1 g. of benzoic acid was recovered.

A mixture of 100 g. of benzoin and 10 g. of potassium cyanide was heated for four hours in a sealed, evacuated flask in an air-bath at 160–165°. The flask contents when cool were repeatedly extracted with cold, sodium-dried ether (800 cc. in all). The ether contained 11.5 g. of benzaldehyde (55°, constant at 6 mm.) and 4 g. of benzoin (140–145° at 6 mm.). No benzyl alcohol nor benzyl benzoate appeared here. The flask contents remaining after ether extraction were next dissolved in pyridine[26] (400 cc. in four portions). The residue of potassium cyanide, etc., insoluble in pyridine, was dissolved in water, and gave 3 g. of benzoic acid.

The pyridine solution was concentrated, and gave 68 g. of benzoin, after it had been washed with a little alcohol. The remaining pyridine solution (plus the alcohol wash liquid) was diluted with water, and gave an oily precipitate. A small amount of dil. sodium hydroxide solution was added, and the oil extracted with a little ether. The alkaline portion gave 3 g. of benzoic acid. The ether extract was fractionated at 5 mm.; it gave 1 g. of benzaldehyde (50–55°), 5 g. of benzyl alcohol (80–85°), and 5 g. of a mixture of benzyl benzoate and benzoin (150–160°), which on separation with a little cold ether and redistillation gave 2 g. of benzyl benzoate. This latter was hydrolyzed with cold alcoholic alkali, and gave 55.2% of benzoic acid (calcd., 57.6). The products

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[25] The oil was not pure enough for analysis; it promptly saponified with alkali, but gave only 72% of benzoic acid (cald., 81.5). Benzyl alcohol is probably also formed, but if formed would go into the aqueous potassium cyanide extract, and be lost during concentration.

[26] The pyridine had been redistilled, boiling at 116–117°, but was not dehydrated, and must have contained a small amount of water.

obtained were, therefore, benzoin 75 g., benzaldehyde 12 g., benzoic acid 6 g., benzyl alcohol 5 g., benzyl benzoate 2 g.[27]

Attempt to Measure Benzaldehyde-Benzoin Equilibrium without Solvents.—Mixtures of benzaldehyde and benzoin, totaling 5.0 g., were heated to 165° in sealed, evacuated tubes with 0.5 g. of potassium cyanide for three hours. At the end of the heating period the tubes were cooled by immersion in cold water. The contents were then digested with 40 cc. of pyridine and the mixtures poured into 300 cc. of water. The precipitated benzoin was filtered off, washed with a few drops of ether to remove colored substances, and dried (m. p., 131–132° for all).

TABLE II

BENZALDEHYDE BENZOIN EQUILIBRIUM IN THE ABSENCE OF SOLVENTS

Materials taken		Materials found	
Benzoin	Benzaldehyde	Benzoin	Benzaldehyde by diff.
1.00	4.00	1.70	3.30
2.00	3.00	1.99	3.01
3.00	2.00	2.04	2.96
4.00	1.00	2.63	2.47
5.00	....	2.82	2.18

Benzoin as a Catalyst for the Benzoin Condensation.—Various mixtures of benzaldehyde, benzoin, water and potassium cyanide, as shown below, were heated to 150° for one hour in sealed, evacuated tubes. The mixtures free from cyanide were then directly distilled, at 5 mm., and the benzoin remaining was weighed; mixtures containing cyanide were first extracted with pyridine.

TABLE III

BENZOIN AS CATALYST

Materials taken				
Benzaldehyde	Benzoin	KCN	Water	Benzoin found
25	2.5	...	....	2.5
25	2.5	2.5	....	3.5
25	2.5	...	0.25	2.5
25	...	2.5	....	none
25	...	2.5	0.25	12.0

It will be seen that benzaldehyde does not condense to form benzoin, with solid cyanide, unless either water or benzoin itself is present.

This was confirmed when a mixture of 200 g. of benzaldehyde and 20 g. of potassium cyanide (reagent, crystallized, 95%) was boiled for one hour, under a reflux condenser. It was then cooled; a 10cc. sample gave no trace of benzoin with Fehling's solution. Thereupon 2 cc. of water was added to the remainder, and boiling resumed for one hour longer. The mixture solidified almost as soon as the flame was removed and 165 g. of benzoin (recrystallized) was isolated.

Behavior of Benzaldehyde when Heated without Added Catalysts.—Lots of 25 g. each of freshly redistilled benzaldehyde (0.2–0.6% of benzoic acid) were heated, in

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[27] The products total 99 g.; the hydrolysis of 11 g. of benzyl benzoate takes up 2 g. of water, so that 102 g. is the calculated weight of the products. It will be noted that benzyl benzoate is present in the original reaction mixture in an ether-insoluble form, similar to the addition product with sodium hydroxide described by Kohn and Trantom [*J. Chem. Soc.*, 75, 1155 (1899)]. However, an attempt to make benzyl benzoate combine with solid potassium cyanide was not successful.

sealed tubes, and then fractionated. After 24 hours at 140°, 24+ g. was recovered; after 40 hours at 200°, 23+ g. was recovered; after 18 hours at 255°, 23+ g. was unchanged. The residues gave no test for benzoin or benzil.[28]

Fifty g. of benzaldehyde (benzoic acid content, 0.6%) was heated as described above for two hours to 300–305° (oven preheated). There was slight pressure in the tube when cool. On distillation, 2 g. of toluene and 35 g. of benzaldehyde were obtained; the next distillate solidified in the condenser. This solid distillate and the flask residue were dissolved in cold, very dilute sodium hydroxide solution, from which 4 g. of benzoic acid was precipitated. An oily residue, weighing 8 g., was insoluble in the alkali. Of this, 7 g. distilled between 130 and 160° (5 mm.). This fraction was hydrolyzed with alcoholic sodium hydroxide and gave 1.5 g. of benzoic acid, and 5 g. of an oil, which when distilled at 5 mm. gave 1 g. at 80–90° (benzyl alcohol) and 3 g. boiling constantly at 135–137° (dibenzyl ether).[29]

Twenty-five g. of benzaldehyde (benzoic acid content, 0.6%) was heated to 300–320° for 15 hours. There was much pressure in the tube; the contents were black and solid. Tarry substances caused some difficulty in working up the mixture; there was an undetermined amount of toluene, and 11 g. of benzoic acid (calcd. for complete Cannizzaro reaction, 14 g.); no other substances could be identified.

Neither benzoin nor benzil was found in this, or the previous experiment.

The So-called Equilibrium of Anderson and Jacobson.—In the following tables are given the results of a repetition of the data of Anderson and Jacobson, with variation of time and of catalyst concentration. In each case, 5 g. of benzoin, or of benzaldehyde, was heated almost to boiling with 75 cc. of ordinary alcohol; then the given quantity

TABLE IV

EFFECT OF VARIATION OF TIME

Potassium cyanide, 0.46 *M*; original material, benzoin, 5.0 g. = 0.24 *M*. Three g. of potassium cyanide was used in each experiment

Time, hours	1	2	4	8
Benzoin, g.	3.06	2.55	1.54	1.39
K	0.23	0.44	1.46	1.79

TABLE V

EFFECT OF VARIATION OF CATALYST, WITH CONSTANT TIME, STARTING WITH BENZOIN

Benzoin, 5.0 g. = 0.24*M*. Time, 1.5 hours

KCN, g.	1.5 (0.23*M*)	0.75 (0.12*M*)	0.40 (0.06*M*)	0.20 (0.03*M*)
	3.58	4.20	4.38	4.50
K	0.11	0.03	0.02	0.01

TABLE VI

EFFECT OF VARIATION OF CATALYST, WITH CONSTANT TIME, STARTING WITH BENZALDEHYDE

Benzaldehyde, 5.0 g. = 0.47 *M*. Time, 1.5 hours

KCN, g.	3.0	1.5	0.75	0.40	0.20
Benzoin, g.	2.67	2.70	2.43	1.65	0.77
K	0.38	0.37	0.51	1.28	4.45

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[28] Minute quantities of benzil or benzoin can be detected by boiling for a few minutes with a few drops of sodium hydroxide, allowing access of air. This converts either substance into benzilic acid, which gives a very delicate color test.

[29] Benzyl alcohol, when superheated, gives dibenzyl ether; the latter gives toluene and benzaldehyde. For further details, compare Ref. 10b, *p.* 2358.

of potassium cyanide, dissolved in 25 cc. of water, was added, and the flask quickly stoppered and placed in a bath at 79° ±1°. After the heating period, the contents of each flask were acidified with a slight excess of acetic acid, previously diluted to 50 cc. The precipitates were cooled for one hour at 20°, filtered off, washed twice with a little 50% alcohol, and dried at 70° to constant weight; an allowance was made for the amount of dissolved benzoin, using the value given by Anderson and Jacobson. In the tables, K is the observed equilibrium constant (the volume of mixture being assumed to be 100 cc. with sufficient accuracy), and the benzaldehyde is measured by difference.

Products Formed by the Action of an Excess of Cyanide on Benzoin.—A mixture of 100 g. of benzoin, 45 g. of sodium cyanide, and 1000 cc. of ordinary alcohol was vigorously boiled under a reflux condenser for two hours in an atmosphere of nitrogen. A small portion of sodium cyanide did not dissolve. As the mixture cooled, benzoin separated; in all, including further recoveries as solvent was removed, 43 g. was isolated. All benzoin crops were washed with water to remove cyanide, benzoate, etc. These washes, when acidified, gave 18 g. of benzoic acid. Alcohol was evaporated from the benzoin filtrate in a stream of nitrogen, at reduced pressure (35°) with a long column. After the volume had been reduced to about 100 cc., 600 cc. of ether was added to precipitate salts, benzoin, etc. The ethereal solution was then concentrated, and distilled in a vacuum; the distillates were redistilled at atmospheric pressure. The products obtained were 17 g. of benzaldehyde (177–185°), 6 g. of toluylene hydrate, and 15 g. of mixed ethyl benzoate and benzyl alcohol (200–215°). The last fraction was washed with sodium bisulfite solution to remove benzaldehyde, and hydrolyzed. It gave 2.6 g. of benzoic acid (equivalent to 3.2 g. of ethyl benzoate) and 11 g. of benzyl alcohol (200–205°).

Products Formed by the Action of an Excess of Cyanide on Benzaldehyde.—The experiment just described was repeated, except that 100 g. of benzaldehyde was substituted for benzoin. The products isolated were benzoin 41 g., benzoic acid 21 g.,[30] benzyl alcohol 16 g., benzaldehyde 2 g.;[31] ethyl benzoate was present, by olfactory evidence, but no direct estimation of its amount could be made.

Competition between Cyanide and Hydroxide Condensation of Benzaldehyde.—The given weights of potassium cyanide were placed in small flasks; there were then added 50 cc. of water, 15 cc. of sodium hydroxide (10 N = 0.15 mole), 100 cc. of ordinary alcohol, and finally 25 cc. of benzaldehyde (26.5 g. = 0.25 mole). All gave clear solutions in the cold. The flasks were then sealed, and heated to 79° for two hours. After they had cooled in ice water, 35 cc. of water was added to reduce the alcoholic strength to approximately 50%, and the benzoin was filtered off and dried; the melting points

TABLE VII

ACTION OF A MIXTURE OF HYDROXYL ION AND CYANO ION ON BENZALDEHYDE

Benzaldehyde, 0.25 mole; hydroxyl ion, 0.15 mole. Temp., 79°. Time, two hours.

KCN G.	Mole	Benzoin G.	Ethyl dibenzil G.	Benzoic acid G.	Cannizzaro reaction %
....	....	....	...	10.2	67
1	0.016	3.3	6.4	5.2	34
2	0.31	8.4	4.7	4.8	31
4	0.63	10.1	4.4	4.0	26
8.1	0.125	10.9	4.8	3.7	24
16.2	0.25	16.6	1.9	1.6	10

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[30] Benzoic acid was free from ethyl dibenzil.

[31] Benzaldehyde was probably present as hydrobenzamide, as ammonia was given off at this stage of the recovery.

ranged from 126° to 129°. From the filtrate, after careful evaporation of the alcohol, benzyl alcohol and traces of benzoin were obtained, but no benzaldehyde could be detected, showing that the reaction had gone to completion.[32] The residual alkaline liquor, after it had been boiled to remove ether and alcohol, was precipitated with hydrochloric acid, giving a colorless mixture of benzoic acid and ethyl dibenzil. These were separated by boiling water, from which perfectly pure benzoic acid precipitated; 1.169 g. required 9.65 cc. of *N* alkali (calcd. 9.60 cc.); it was free from benzilic acid as indicated by the color test.

Addition Product of Benzoin and Sodium Cyanide.—Two g. of finely crystallized sodium cyanide was added to a cold solution of 10 g. of benzoin in 60 cc. of pyridine dried over sodium. The mixture was frequently shaken; a gel slowly formed, which after standing overnight did not dissolve when slightly warmed (35–40°). The volume of gel did not seem to increase after two days; on the third day, the mixture was filtered off, washed with dry pyridine, and dried in a vacuum over sulfuric acid; weight, 4 g. For analysis, 1.779 g. was shaken with excess of cold water, filtered off and the precipitate dried to constant weight; m. p., 133°; 0.765 g. or 43% was recovered, while the calculated value for equal moles of benzoin and sodium cyanide is 81%.[33]

When the addition product is moistened with alcohol, an odor of ethyl benzoate is evolved, but this ester has not been actually isolated; 42 g. of benzoin was boiled for two hours with 10 g. of sodium cyanide in 100 cc. of pyridine. After the mass was cooled it was filtered and the cake washed with a little pyridine; the filtrate and wash liquor were distilled, and 7 g. of benzaldehyde was recovered. Distillation residue and filter cake were extracted with 100 cc. of cold ether, but no positive evidence of the presence of benzyl benzoate, etc., was secured. The ether-insoluble mixture of benzoin, sodium cyanide, etc., was then digested with 25 cc. of cold alcohol. The alcohol was filtered, poured into water, and distilled with steam; 0.5 g. of white oil was obtained having a strong odor of ethyl benzoate, but the amount was too small for purification. The cake remaining after extraction with ether and alcohol was washed with water, and gave 31 g. of benzoin; the water extract contained 1.1 g. of benzoic acid.

When a mixture of benzaldehyde (40 g.), pyridine (140 cc.), and sodium cyanide

TABLE VIII

CATALYSTS WHICH DO NOT FORM BENZOIN

Reagent	Amount taken G.	Benzaldehyde G.	Volume of solvent Cc.	Time, hours
Na hypophosphite	15	50	50	6
Na nitrite	10	60	150	24
Na sulfhydrate	5	40	30	3
Na bisulfite	10	40	100	7
Na fluoride	15	50	100	5
Na phenolate	12	65	50	48
K acetate	10	20	50	24
Pyridine	10	50	50	6
Phenyl cyanide	10	50	75	3
Phenyl isonitrile	10	75	150	3

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[32] Except in the case of the first flask, which contained hydroxide, but no cyanide.

[33] The experiment was repeated several times, with widely divergent values for the benzoin content of the addition product; the highest figure was that given above; the lowest was 23%. The gel seems to grow from the particles of sodium cyanide, which is itself almost insoluble in pyridine; separation of gel from these particles is difficult.

(3 g.) was boiled for an hour, the color changed to dark red; but after the mixture was filtered and the pyridine and benzaldehyde were distilled at 5 mm. pressure, a mere trace of residue was obtained, which gave a faint reduction with Fehling's solution.

Attempts to Prepare Benzoin with Other Catalysts.—In Table VIII are given the substances which, when boiled with diluted alcohol and benzaldehyde, failed to form benzoin. After the reaction mixture had been heated for the stated time, the solvent was evaporated and the bulk of the remaining benzaldehyde distilled with steam. The residual oil was then tested for benzoin with Fehling's solution, the test being negative in each case.

Action of Hydrochloric Acid on Benzaldehyde.—Benzaldehyde readily absorbs dry hydrogen chloride, with the development of much heat. The liquid assumes a dark red color, and fumes in the air. A mixture of 90 g. of benzaldehyde and 3 g. of hydrochloric acid was allowed to stand for three weeks, but no benzoin was formed. A mixture of 200 g. of benzaldehyde and 12 g. of hydrochloric acid after three weeks was shaken with water, then washed with a very little sodium bicarbonate solution, and distilled; 195 g. of constant-boiling benzaldehyde was recovered. The slight distillation residue gave no test for benzoin.

Summary

1. The condensation of benzaldehyde (2 moles) into benzoin (1 mole) requires the combined action of hydroxyl and of cyano ions.

2. These catalysts also reverse the condensation; but at the same time, they convert benzoin into benzyl benzoate, and then into benzyl alcohol and benzoic acid. This step is not reversible.

3. Heating to 300° converts benzoin partially into benzaldehyde; but heating benzaldehyde yields no benzoin; instead, benzyl benzoate, etc., are formed.

4. A consistent explanation is given for the benzoin and Cannizzaro condensations.

5. A simplified method of preparing benzoin without the use of alcohol is described.

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THE MULTIPLE NATURE OF BIOS[1]

By Ellis I. Fulmer, W. W. Duecker and V. E. Nelson

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Wildiers came to the conclusion that the yeast dietary must contain, aside from mineral salts and sugar, organic material of biological origin. To this constituent of the medium supposed to be necessary for the growth of yeast he gave the name "bios."[2]

The necessity of bios for the growth of yeast was first seriously questioned by Fulmer and Nelson and co-workers and by MacDonald and McCollum.

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[1] Reported before the meeting of the American Chemical Society at Milwaukee, Wisconsin, September, 1923.

[2] Wildiers, *La Cellule*, 18, 313 (1901).