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A STUDY OF THE BENZOIN CONDENSATION[1]

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Introduction

In the condensation of benzaldehyde to benzoin under the influence of an alkali cyanide, the specific action of the catalyst has been ascribed, in general, to its ion or to its hydrolysis product. There is a large amount of experimental work which supports this but nearly all has been done in an ionizing solvent which contains water. No systematic attempt has ever been made to observe the reaction under conditions where no ionization nor hydrolysis can occur. In this paper we shall report experiments which show that the reaction will take place in anhydrous petroleum ether, and that an addition compound consisting of one molecule of benzaldehyde and one of sodium cyanide can be obtained, which in the dry state, slowly changes to benzoin. These facts cannot be explained by the common mechanisms. We have, therefore, suggested two possible ways in which the catalyst may function. The results also raise the question as to whether the mechanism in ionizing solvents has been correctly represented in the past.

Experiments

The general experimental method was as follows. Two grams of benzaldehyde (Eastman Kodak Co. technical grade) and one gram of potassium cyanide were put into an 8-inch test-tube with a given amount of the solvent. The test-tube was tightly stoppered and shaken overnight. The contents were then poured into an Erlenmeyer flask, dilute acetic acid added to stop the reaction and the mixture boiled for a short time to volatilize the organic solvent. Any high boiling amines used with the solvent were soluble in the acid solution. The insoluble benzoin was filtered, dried and weighed. A number of these test-tube runs were made at one time. A blank experiment, identical in all respects except that the solvent was 95% alcohol alone, was made with each series. The results are referred to this blank on a basis of 100. Values recorded as (s) slight and (vs) very slight indicate yields of benzoin too small to be measured by our method.

Effect of Solvent

Series 1.—The solvent was 12 cc. of 95% alcohol with 12 cc. of another liquid. The yield in the blank was 1.44 g. of benzoin. Comparative yields were in alcohol with carbon disulfide vs, ethyl bromide vs, ether vs, acetone s, carbon tetrachloride 14, chlorobenzene 31, petroleum ether 120. These results show the marked effect of petroleum ether as compared with carbon disulfide, ether, acetone and certain chlorides.

Series 2.—Twenty-five cc. of a single solvent was used. No effort was made to dry the solvent; in fact, at this stage of the work a trace of moisture was supposed to be favorable in order to hydrolyze the cyanide. Comparative yields were in acetic acid 0,

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[1] From the thesis of Joseph R. Stevens presented in partial fulfilment of the requirements for the degree of Bachelor of Science, 1929.

iso-amyl alcohol vs, tertiary butyl alcohol 6, benzene 47,[2] toluene 52, xylene 55, water 83, methyl alcohol 95.

Series 3.—The comparative yield in a solvent consisting of 20 cc. of 95% alcohol with one gram of phenol was 0, with phthalic anyhdride vs, formaldehyde vs, ethyl acetate vs, isopropyl alcohol 2, aniline 2, hexamethylene tetramine 46, triethylamine hydrochloride 62, benzyl chloride 67, benzal chloride 68, diphenylamine 68, dimethyl aniline 89, hydroquinone 95, pyridine 94, urea 101, acetamide 102, butyl isocyanide 106. The series shows the inhibitory effect of many carbonyl and amine compounds.

The Inhibitory Effect of Ethyl Acetate.—These experiments were made to study the effect of one of the compounds in Series 3 when used in several different concentrations. The solvent was 10 cc. of petroleum ether with 2 cc. of 95% alcohol, this ratio having been found to be very suitable in a number of preliminary tests. Table I gives the results.

TABLE I

RESULTS

KCN, moles	0.02	0.02	0.02	0.03	0.04
Ethyl acetate, moles	.00	.01	.02	.01	.02
Yield of benzoin, g.	.810	.375	.228	.400	.195

Comparison of Sodium Cyanide with Potassium Cyanide. Yield vs. Time.—The solvent was 5 cc. of petroleum ether with 1 cc. of 95% alcohol. An excess of the cyanide (2 g.) was added, which was sufficient to keep the solution saturated at all times with the catalyst and to combine with the product.

The quantities of benzoin formed with potassium cyanide as a catalyst were so very small that only one point could be determined. The results are plotted in Fig. 1. The fact that the values fall on a straight line suggests that the main factor in this solvent is that of the solubility of the catalyst. The solubilities were determined by shaking an excess of the cyanide with the solvent for one hour at room temperature, filtering, evaporating to dryness, and heating in a vacuum oven at 110° to constant weight. The solubility of sodium cyanide was found to be 0.067 mole; that of potassium cyanide 0.0063 mole per liter of solution. The sodium cyanide is therefore 10.6 times more soluble than the potassium cyanide; its reaction velocity is only 6.8 times greater. Since only one point was obtained with potassium cyanide, we are unable to say that this difference is beyond the error of the experiment.

The product from potassium cyanide was white; that from sodium cyanide was yellow. Franzen[3] has prepared the addition compound between calcium cyanide and benzaldehyde and found it to be bright orange-yellow in color. When our sodium cyanide was recrystallized the yellow color largely disappeared. Since sodium cyanide is made from the calcium salt, it is very probable that the orange-yellow color is due to some calcium cyanide present.

Comparison of the Reaction in Alcohol and in Petroleum Ether-Alcohol.—In this series each test-tube contained 6 cc. of 95% alcohol, 2 cc. of benzaldehyde and 2 g. of sodium cyanide. The procedure was identical with that of the experiment just above and the results are plotted in the same figure.

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[2] Conclusions from these series must not be too hastily drawn. The solubility of the cyanide is of very great importance and, as will be shown later, the sodium is much more soluble than the potassium salt. Had sodium cyanide been used in this series instead of potassium cyanide the results for benzene, toluene and xylene might have been very good. The experiments were made to locate any pronounced effect of a solvent and not to assign an absolute value to each.

[3] Franzen, *Ber.*, **42**, 3293 (1909).

A constant calculated for this reaction (see Table II) shows that for the first five hours at least the formation of benzoin is in agreement with that expected from the equation for a bimolecular irreversible reaction in which the initial concentration of benzaldehyde is taken as 2 g. The sodium cyanide concentration is assumed to be constant and does not enter into the equation.

TABLE II

RESULTS OF EXPERIMENTS

Time, hours	1.5	2.5	3.5	4.5	5.5
Benzoin, g.	0.52	0.81	0.95	1.05	1.13
K	.12	.14	.13	0.12	0.12

The solubility of sodium cyanide in 95% alcohol was determined in the same manner as in the petroleum ether–alcohol mixture and found to be 0.405 mole per liter. This is six times the solubility of sodium cyanide in the 5:1 mixture. The values as plotted in Fig. 1 show, however, that at no time did the amount of benzoin formed in alcohol even at the very start of the reaction exceed by three times that in the mixed solvent. Per sodium cyanide dissolved, therefore, the reaction is faster in the solvent containing petroleum ether[4] than in alcohol alone. The type of velocity curve is also different with the two solvents. In alcohol the sodium cyanide is so soluble that the formation of benzoin can proceed according to the mass action principle and the customary curves will be obtained; in the petroleum ether–alcohol mixture the sodium cyanide is so slightly soluble and is so continually removed by the precipitation of the addition compound that the rate is governed almost entirely by the rate of solution of the sodium cyanide.

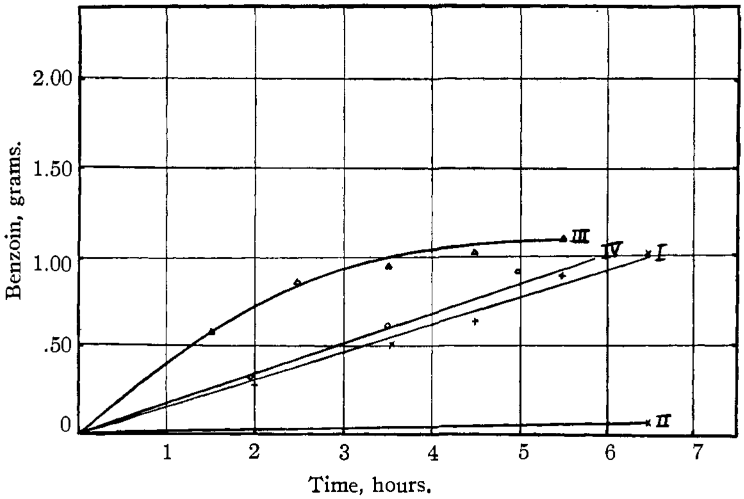

Fig. 1.—I, NaCN in 5:1 mixture of petroleum ether and ethyl alcohol; II, KCN in 5:1 mixture of petroleum ether and ethyl alcohol; III, NaCN in ethyl alcohol; IV, same as I but with purified benzaldehyde.

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[4] The reason for this may be the chemical inertness of petroleum ether. The polar groups present in other solvents would form complexes with the sodium cyanide, thus competing with the benzaldehyde.

Comparison of Technical with Purified Benzaldehyde.—Benzaldehyde was purified by shaking the technical grade with a dilute solution of sodium carbonate, drying over anhydrous potassium carbonate, filtering and distilling. The first 25 cc. out of the 100 cc. was rejected and 2 cc. from the next fraction collected and used at once. This run was made to compare with the results given in Fig. 1, Curve I, for sodium cyanide and the experimental conditions were, therefore, identical in all respects except in regard to the purity of the benzaldehyde. The results are plotted in Fig. 1, Curve IV. The agreement is within 8%, which is as close a check as the experimental conditions would allow.

Isolation of the Addition Compound.—In all of the reactions run in a solvent containing petroleum ether, an addition compound was precipitated. This compound was isolated and analyzed as follows. In a 250-cc. Erlenmeyer flask 3 to 5 g. of sodium cyanide lumps about the size of small peas were placed. A solution of 5 cc. of benzaldehyde in about 30 cc. of the 5:1 petroleum ether–alcohol mixture was added. The mixture was allowed to stand for one-half hour, after which it was shaken and 20 cc. of benzaldehyde added. A large precipitate formed; 100 cc. of petroleum ether was then added and the solution filtered. The large particles of sodium cyanide either settled out before filtration or were mechanically separated from the dried flocculent compound on the paper. The addition product was washed with petroleum ether to free it from benzaldehyde and dried in a vacuum desiccator. Two analyses gave 14.8 and 13.9% of sodium; the calculated value for a product consisting of one molecule of benzaldehyde to one of sodium cyanide is 14.8%. When decomposed with water immediately after removing from the filter paper and drying, benzaldehyde and sodium cyanide were recovered. When allowed to stand in the desiccator over calcium chloride it very slowly changed to benzoin.

Reaction in Anhydrous Medium

Experiment A.—A dry glass tube was sealed off at one end and in it was placed 4–5 g. of sodium cyanide which had been dried in a vacuum oven at 110° for two hours. From 100 cc. of technical benzaldehyde from a freshly opened bottle the first 40 cc. was distilled in a current of dry hydrogen and rejected; 5 cc. of the middle fraction was then distilled directly into the tube and sealed in an atmosphere of hydrogen. No solvent was used. After two days a precipitate was formed which steadily increased in amount. When decomposed with water this proved to be benzoin.

Experiment B.—A 16-mm. glass tube was heated nearly to its softening point in a current of dry air until no cloud of moisture appeared on the surface of the glass when it was allowed to cool and then reheated. Ten cc. of petroleum ether dried for twenty-four hours over sodium wire, and 3–4 g. of sodium cyanide prepared from commercial sodium cyanide by recrystallizing once from water and drying in a vacuum oven at 110° for four hours, were put into this tube. Ten cc. of benzaldehyde, treated as in Experiment A (except that nitrogen purified by passing through pyrogallol solution and drying with concentrated sulfuric acid was used instead of hydrogen) was distilled directly into the reaction vessel. The tube was then filled with dried nitrogen, sealed off and allowed to stand. A white addition compound formed on the surface of the cyanide; in four days the appearance of benzoin in fair quantity was observed and in ten days a large precipitate had formed.

These experiments do not exclude the possibility of catalysis by an extremely minute quantity of water, but they do show that when the reactants are dried in a manner fully equivalent to that used in reactions where water must be excluded, such as the preparation of the Grignard reagent, the benzoin condensation will still occur. It is necessary only to dissolve the catalyst and to exclude oxygen which would form benzoic acid with the benzaldehyde.

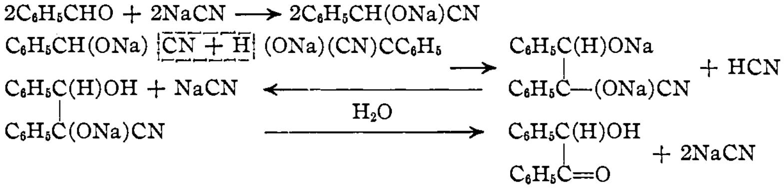
Other Addition Compounds.—Cinnamic aldehyde does not undergo the benzoin condensation. Hence when finely powdered sodium cyanide was added to a solution of an excess of the aldehyde in alcohol, the addition compound was precipitated from the solution and later recrystallized from alcohol. This compound has already been observed but not analyzed by Zincke and v. Hagen.[5] We found 11.1 and 13.0% of sodium as compared with a calculated value of 12.7 for the addition compound, $NaCN{\cdot}C_9H_8O$.

Other addition compounds which were observed but not analyzed were those of sodium cyanide with ethyl benzoate and benzoyl cyanide. Ethyl acetate and benzamide apparently formed no solid addition compound under the conditions of the experiment.

Reaction at Higher Temperature.—Cinnamyl aldehyde[6] will not undergo the benzoin condensation nor will ethyl benzoate condense with benzaldehyde. Since addition compounds are formed in these cases which by their stability might hinder the reaction, higher temperatures were tried. When heated to 150° no condensation occurred in either case. Benzamide and benzaldehyde melted together with sodium cyanide gave off ammonia but nothing was isolated except benzoic acid.

Catalysts Other than Potassium or Sodium Cyanide.—The effect of other compounds as catalysts in this reaction was tried in 10 cc. of the 5:1 petroleum ether–alcohol mixture. About 5 cc. of benzaldehyde and 1 g. of the cyanide compound were used in each experiment. No effect was observed with mercuric, cuprous, thallous, triphenylmethyl, and tertiary butyl cyanides. Barium cyanide had a slight effect. Because sodium cyanide is more soluble[7] than potassium cyanide, it was thought that lithium cyanide would be even more soluble in an organic solvent and therefore a better catalyst. The single attempt to prepare lithium cyanide failed.

Mechanism of the Reaction.—Since the reaction goes in an anhydrous non-ionizing medium it is absolutely impossible to apply the ordinary interpretation to our experiments. It is necessary to consider instead the role of the non-ionized portion. This may be done in two ways. (1) Sodium cyanide may add across the double bond of the carbonyl group. The equations for this would be



$$2C_6H_5CHO + 2NaCN \longrightarrow 2C_6H_5CH(ONa)CN$$

$$C_6H_5CH(ONa)\,\boxed{CN + H}\,(ONa)(CN)CC_6H_5 \longrightarrow \begin{array}{l} C_6H_5C(H)ONa \\ \quad\ | \\ C_6H_5C{-}(ONa)CN \end{array} + HCN$$

$$\begin{array}{l} C_6H_5C(H)OH + NaCN \\ \quad\ | \\ C_6H_5C(ONa)CN \end{array} \begin{array}{c} \longleftarrow\!\!\!-\!\!\!-\!\!\!-\!\!\!-\!\!\!- \\ \xrightarrow{\quad H_2O \quad} \end{array} \begin{array}{l} C_6H_5C(H)OH \\ \quad\ | \\ C_6H_5C{=}O \end{array} + 2NaCN$$

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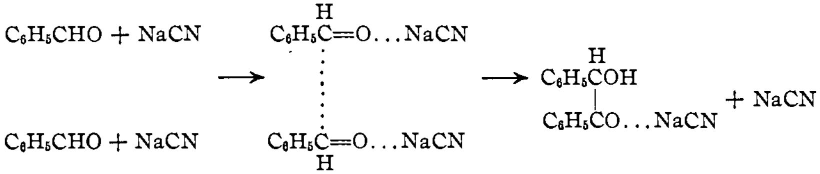
[5] Zincke and v. Hagen, *Ber.*, **17**, 1814 (1884).

[6] Cinnamic aldehyde, ethyl acetate, ethyl benzoate and benzamide may not undergo the benzoin condensation because they contain other polar groups in the molecule which combine with the cyanide salt and therefore hinder the reaction in the same manner that ethers, chlorides, alcohols or esters used as solvents block the catalytic influence of the condensing agent. One exception to this is here noted. Smith, *Proc. Chem. Soc.*, **29**, 266 (1913), has reported that benzoyl chloride condenses with *o*-nitrobenzaldehyde in the same manner that benzaldehyde condenses with itself. The product is benzoyl-*o*-nitromandelonitrile, the chlorine atom being replaced by the cyano group.

[7] Tripropylamine cyanide should be a very good catalyst since its organic nature would make it soluble in petroleum ether and Lapworth, *J. Chem. Soc.*, **83**, 1004 (1903), has shown that tripropylamine, mandelonitrile and benzaldehyde form benzoin when allowed to stand together.

This is the nearest approach possible to the common interpretation of the reaction. Its weakness lies in the fact that free hydrogen cyanide instead of a salt must split out to cause the condensation. (2) A molecular addition compound may form which then adds to another molecule of the same kind. The reaction is completed by the wandering of a hydrogen atom in the complex. In the formation of the first intermediate compound the sodium cyanide absorbs some of the valence energy of the oxygen atom in the benzaldehyde. This will cause a certain amount of energy to become available on the carbon atom of the benzaldehyde, *i. e.*, it will possess a certain amount of unsaturation. When two of these addition compounds come close to each other, a valence is realized between the unsaturated carbon atoms with the simultaneous wandering of a hydrogen atom. The steps are graphically represented in the equations



$$\begin{array}{l} C_6H_5CHO + NaCN \\ \\ \\ C_6H_5CHO + NaCN \end{array} \longrightarrow \begin{array}{c} C_6H_5\overset{H}{C}{=}O\ldots NaCN \\ \vdots \\ C_6H_5\underset{H}{C}{=}O\ldots NaCN \end{array} \longrightarrow \begin{array}{l} C_6H_5\overset{H}{C}OH \\ \qquad | \\ C_6H_5CO\ldots NaCN \end{array} + NaCN$$

This formulation[8] of the role of an addition compound as an intermediate has been developed by Pfeiffer,[9] who states that the catalytic action of metal salts and acids, which in many cases is dependent upon the formation of addition compounds,[10] can be ascribed to the formation of a single unsaturated active carbon atom. He gives as examples of this the catalytic saponification of esters by hydrochloric acid, the formation of ketones in the Friedel–Crafts reaction, and the polymerization of unsaturated compounds by means of sulfuric acid. This picture gives us a very simple explanation for the occurrence of a side reaction, namely, the formation of benzyl benzoate. If instead of the reaction above pictured the single unsaturated carbon atom in the molecular addition compound should unite with the oxygen of another molecule of benzaldehyde, the product upon the wandering of a hydrogen atom will be benzyl benzoate. The possibilities in the reaction of benzaldehyde with itself in the presence

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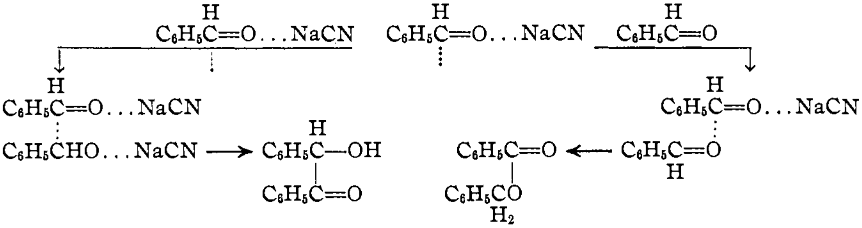
[8] The sodium cyanide might be attached through its unsaturated carbon atom to the benzaldehyde. On this point we have no evidence. We have preferred the formula as above written because metallic sodium alone will cause the condensation and because certain analogies might be drawn with alkaline condensing agents in general and with pinacone formation.

[9] Pfeiffer, *Ann.*, **383**, 93 (1911).

[10] *Sammlung Chemischer und chemisch-technischer Vorträge*, **30**, 136 (1928). Muller expresses Pfeiffer's views by saying that the positive metal ion strongly pulls the electron of the carbon atom. The bonding electrons between the carbon and oxygen atoms then move far toward the oxygen side. The carbon atom which now possesses only a small part of the binding electron will then possess a secondary valence.

of a catalyst such as sodium cyanide are illustrated in the following diagram.



Lachman[11] has shown that benzyl benzoate is formed to some extent in the synthesis of benzoin. In the case of alkali hydroxide or alcoholate addition compounds the formation of benzyl benzoate may be assumed to predominate to the entire exclusion of the formation of benzoin.

This conception[12] also eliminates the peculiar role of the cyanide salts as the only catalysts which can bring about the reaction. Lachman[13] mentions that benzoin is sometimes formed by metallic sodium and Blicke[14] in the same year published a study of the action of sodium on benzaldehyde in which he discovered benzoin among the products.

Summary

A preliminary study of the effect of various solvents upon the benzoin condensation has been made. The reaction has been found to proceed in the absence of water and in a non-ionizing medium.

An addition compound has been isolated which consists of one molecule of benzaldehyde and of sodium cyanide. This solid addition compound changes to benzoin upon standing.

Previous mechanisms which involve ionized or hydrolyzed sodium cyanide are not applicable to our work. Two mechanisms have been suggested which accord with the facts observed. One of these mechanisms is based upon Pfeiffer's view of the role of addition compounds as catalysts.

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[11] Lachman, THIS JOURNAL, **46**, 712 (1924).

[12] A similar mechanism might possibly apply to other reactions catalyzed by sodium cyanide. Thus Chalanay and Knoevenagel [*Ber.*, **25**, 291 (1892)] found that the benzoin condensation took place in the case of certain chlorides and nitriles. Smith [*Ber.*, **26**, 60 (1893)] condensed benzaldehyde with acetophenone, benzoin with acetophenone, and benzoin with mesityl oxide in the presence of potassium cyanide. Strain has shown that benzylidene-aniline and benzylidene-*p*-toluidine [THIS JOURNAL, **50**, 2219 (1928)] undergo the benzoin condensation. In case the mechanism is applicable in ionizing solvents, it might be possible to interpret the action of alkalies in certain condensations such as the Schotten–Baumann reaction on this same basis.

[13] Ref. 10, p. 716.

[14] Blicke, THIS JOURNAL, **46**, 2560 (1924).