

[CONTRIBUTION FROM THE EXPERIMENTAL RESEARCH LABORATORIES, BURROUGHS
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MIXED BENZOINS. V. REVERSIBILITY OF THE BENZOIN CONDENSATION AND THE PREPARATION OF MIXED FROM SIMPLE BENZOINS

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Much work has been done on the benzoin condensation and various suggestions have been advanced as to its mechanism, but it can scarcely be said that the reversibility of the reaction has been demonstrated in an unexceptionable manner. Much of the work is irrelevant as it was carried out under conditions far different from those ordinarily used. For example, the heating of the dry reagents to high temperatures can scarcely be called a benzoin reaction. In most cases where the conditions were comparable, benzaldehyde was estimated by difference, or detected by the odor, a risky procedure where many side-products may be formed. Another factor apparently not recognized by earlier workers is what may be called the eccentricity of the reaction, that is, the occasional rapid and unusually favorable progress of the reaction. An instance is remarked by Adams¹ and the present authors have frequently encountered similar cases. No explanation for this phenomenon can be offered at present.

The best yields recorded for benzoin itself are about 90%, the other 10% being accounted for as unchanged benzaldehyde and side-products such as mandelic acid, benzoic acid, benzyl alcohol, toluylene hydrate, amarine, etc. In the equation $2C_6H_5CHO \longleftrightarrow C_6H_5CHOHCOC_6H_5$ it is evident that the equilibrium lies well over to the right. A means of removing benzaldehyde as generated would enable the right-to-left reaction to be demonstrated clearly. Such a means was found by adding a second aldehyde to the solution of benzoin² in aqueous alcoholic potassium cyanide, whereby a mixed benzoin was formed. In a number of cases this mixed benzoin could be isolated and identified.² The equation is



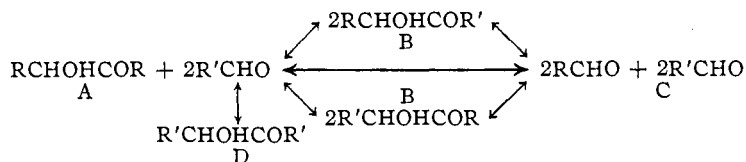
Specifically, benzoin and *p*-dimethylaminobenzaldehyde, refluxed in aqueous-alcoholic solution, in the presence of potassium cyanide, gave an excellent yield of *p*-dimethylaminobenzoin, proving beyond doubt that the benzoin had broken up into benzaldehyde. Piperoin and fuoin were found to behave similarly. In the case of anisoin, no mixed benzoin was

¹ Adams, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1921, Vol. I, p. 34.

² Hörbye, "Dissertation," Dresden, 1917, seems to have had a similar idea in mind. He heated benzoin with anisaldehyde and anisoin with benzaldehyde (no cyanide was used) and obtained only negative results.

obtained, but a portion of the anisoïn was recovered, even after ample refluxing.

Having proved that a benzoin may give rise to the corresponding aldehyde, the scheme shown for the formation and equilibrium of a mixed benzoin follows logically



In previous work, the authors have obtained the mixed benzoin B by going from C to B. In the present work, the benzoin B is obtained by the route A to B. It would be of interest to compare these two routes from a strictly quantitative point of view, but the practical difficulties in the way are formidable.

The above scheme carries several interesting implications. A mixed benzoin, in the presence of aqueous-alcoholic potassium cyanide, should give rise to a mixture containing the two corresponding simple benzoin. In the presence of added aldehydes, further mixed benzoin would be formed. Similarly, a mixture of two simple benzoin should be capable of giving rise to mixed benzoin. There is also a possibility that a given mixed benzoin, in aqueous-alcoholic potassium cyanide solution, might change into its isomer, but this would only be expected in the sense of the less stable isomer changing into the more stable isomer. Work is in progress on some of these possibilities, but it is not to be expected that more than a few instances of each type will be found, on account of experimental difficulties. It is evident that unless one particular product is uncommonly favored by conditions such as yield, solubility, crystallizing tendency, etc., its isolation from a complex reaction mixture would be impossible—at least, provided that it contained no special groups such as $-\text{NMe}_2$. The same considerations make it evident why comparatively few mixed benzoin are isolable from the usual condensation mixtures.

Ideally, the same point should be reached (using appropriate molecular proportions) by starting with (a) two aldehydes X and Y, (b) aldehyde X with the benzoin from Y, (c) aldehyde Y with the benzoin from X, (d) the benzoin from X with the benzoin from Y, (e) either of the isomeric mixed benzoin from X and Y. It is improbable that this can be demonstrated for several reasons, such as the formation of side products, the instability of certain aldehydes (*e. g.*, furfural), the inability of an aldehyde to form a simple benzoin (*e. g.*, *p*-dimethylaminobenzaldehyde) or the impossibility of isolating the simple benzoin (*e. g.*, veratrin), and the difference in stability of any two isomeric mixed benzoin.

The method under discussion (the preparation of a mixed from a simple benzoin) does not appear to offer any marked advantages over the older method, starting with two aldehydes. It is also limited by the non-existence of many simple benzoin.

The authors have refrained from discussing the various hypotheses of benzoin formation given in the literature. Lachman³ gives a review of this field.

Experimental

The experimental conditions were chosen so that the reactions took place under conditions approximating those of the usual benzoin condensation. One mole of the benzoin and two moles of the aldehyde were dissolved hot in the given volume of alcohol and the potassium cyanide added in saturated aqueous solution. The mixture was then boiled under a reflux condenser on the steam-bath, 5 cc. of water being added as soon as boiling commenced. After the elapse of the stated time, the flask was removed and cooled, alcohol or water added as required, and the mixture kept in a cold place. With manipulation and attention, the product crystallizes out in time. A second or third crop may sometimes be obtained by diluting the liquors or by adding further potassium cyanide and again refluxing. The yields are given for unrecrystallized but washed material of good grade. For identification, this was recrystallized and compared with an authentic specimen. Mixed melting point determinations also were made. Experiments carried out with anisoin and different aldehydes resulted in the recovery of part of the anisoin. Mixed benzoin, which were doubtless formed, were not isolated. A peculiar product was obtained from anisoin and piperoin. This appears to be a double compound of anisoin and piperoin, since it can be obtained by simply crystallizing anisoin with piperoin from alcohol. Analysis so far has not given concordant results, but the crystalline form, melting point, etc., of the product are distinct from those of the components.

p-Dimethylaminobenzpiperoin, not previously described, may be obtained as given in the table, or, more conveniently, by refluxing for two hours, 6.00 g. of piperonal and 5.96 g. of *p*-dimethylaminobenzaldehyde, dissolved together in 30 cc. alcohol, with 4.0 g. of potassium cyanide (added in saturated aqueous solution). The crystalline mass which separates is filtered off after three days and recrystallized from alcohol. The compound forms a dull-white mass of tiny fern-like crystals. It is moderately soluble in alcohol, soluble in cold acetic acid, cold dilute (1:1) hydrochloric acid, cold acetone and cold chloroform; readily soluble in warm benzene, and soluble in cold concd. sulfuric acid to an intense blackish-crimson solution. The benzoin melts at 132° to a turbid liquid, clear at 136°.

Anal. Calcd. for C₁₇H₁₇O₄N: C, 68.19; H, 5.73; N, 4.68. Found: C, 68.47; H, 5.92; N, 4.77.

³ Lachman, THIS JOURNAL, 46, 708 (1924).

TABLE I
 PREPARATIONAL DATA

	Taken, g.	Aldehyde	Taken, g.	Product	Yield, g.	KCN, g.	Hours heating	Cc. of alcohol
Benzoin	4.24	Dimethylam- inobenz-	5.96	Dimethylam- inobenzoin ⁴	9.18	3.0	3.0	20
Benzoin	4.24	Anis-	5.44	Benzanisoin ⁵	7.36	4.0	2.0	20
Benzoin	4.24	Furfural	3.84	Benzfuroin ⁵	3.98	3.0	1.5	20
Benzoin	4.24	Piperonal	6.00	Benzpiperoin ²	2.16	2.0	0.5	30
Piperoin	3.00	Dimethylam- inobenz-	2.98	Dimethylamino- benzpiperoin	2.12	2.0	3.0	15
Piperoin	3.00	<i>o</i> -Chloro- benz-	2.82	<i>o</i> -Chlorobenz- piperoin ⁶	2.05	2.0	3.0	15
Piperoin	6.00	Benz-	4.24	Benzpiperoin ²	1.29	4.0	2.0	30
Furoin	3.84	Dimethylam- inobenz-	5.96	Dimethylamino- benzfuroin ⁵	5.77	3.0	1.5	20
Furoin	3.84	Benz-	4.24	Benzfuroin ⁵	4.06	2.0	0.16	20

⁴ Staudinger, *Ber.*, **46**, 3535 (1913).

⁵ Fischer, *Ann.*, **211**, 214 (1882).

⁶ Buck and Ide, *THIS JOURNAL*, **52**, 220 (1930).

Summary

A general method for demonstrating the reversibility of the benzoin condensation is described, involving the preparation of mixed benzoin from simple benzoin. Some of the consequences of the reversibility are discussed. A new mixed benzoin is described.

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

STEREOCHEMISTRY OF N,N'-DIPYRRYLS. RESOLUTION OF N,N',2,5,2',5'-TETRAMETHYL-3,3'-DICARBOXYDIPYRRYL. XVI¹

BY CHIN CHANG² AND ROGER ADAMS

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The resolution of N,2-carboxyphenyl-2,5-dimethyl-3-carboxypyrrole^{1b} (I) demonstrated that optical isomerism which was possible in properly substituted diphenyls, due presumably to restricted rotation of the rings, may also occur in substituted N-phenylpyrroles. This indicates the probability of optical isomerism in other dicyclic compounds such as in properly substituted dipyrlyls. The more important general types of this class of compounds which from analogy to the diphenyls might exhibit isomerism may be represented by the Formulas II, III, IV.

The investigation described in this communication has involved the

¹ For the previous papers in this series see (a) Shildneck and Adams, *THIS JOURNAL*, **53**, 343 (1931); (b) Bock and Adams, *ibid.*, **53**, 374 (1931).

² This communication is an abstract of a portion of a thesis submitted by Chin Chang in partial fulfillment of the requirements for the degree of Doctor of Philosophy in chemistry.