## [Contribution from the Department of Chemistry, Indiana University]

# **REARRANGEMENT IN THE BENZOIN SERIES\***

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The rearrangement of benzoin to diphenylacetic acid was discovered by Lachman.<sup>1</sup> By long heating in sealed tubes in the presence of aqueous solutions of phosphoric or sulfuric acids at temperatures up to 230° he was able to convert as high as 9 per cent. of the benzoin to diphenylacetic acid. Considerable decomposition to diphenylmethane and carbon dioxide occurred, however.

 $\mathrm{C}_{6}\mathrm{H}_{5}\mathrm{CHOHCOC}_{6}\mathrm{H}_{5} \stackrel{\textstyle <}{\searrow} \frac{(\mathrm{C}_{6}\mathrm{H}_{5})_{2}\mathrm{CHCOOH}}{(\mathrm{C}_{6}\mathrm{H}_{5})_{2}\mathrm{CH}_{2} + \mathrm{CO}_{2}}$ 

This reaction is of interest from a theoretical standpoint because the alpha-hydroxy ketone benzoin is intermediate structurally between the diketone benzil and the glycols hydrobenzoin and pinacol. The benzil and glycolic rearrangements are usually almost quantitative under suitable conditions, and have attracted repeated consideration.<sup>2, 3</sup>

The benzoin rearrangement is closely related also to the rearrangement of other alpha-hydroxy ketones and alpha-hydroxy aldehydes. Danilov and Venus Danilova<sup>4</sup> found that alpha-hydroxyisobutyraldehyde could be changed to isobutyric acid in alkaline solution in the presence of hydroxides of heavy metals such as copper and lead. Heating the same aldehyde with very dilute mineral acid brought about a reaction of another type.

 $(CH_3)_2COHCHO \begin{pmatrix} (CH_3)_2CHCOOH \\ CH_3CHOHCOCH_3 \end{pmatrix}$ 

Other examples of this second type of rearrangement have been discussed recently as "interconversion of mixed benzoins"<sup>5</sup> where R'CHOHCOR"  $\rightarrow$  R"CHOHCOR'.

\* Compiled from a thesis submitted by Floyd L. James in partial fulfillment of the requirements for the degree Doctor of Philosophy.

<sup>3</sup> TIFFENEAU AND CO-WORKERS, Bull. soc. chim., 49, 1595-1851 (1931).

<sup>4</sup> DANILOV AND DANILOVA, Ber., 67, 24 (1934).

<sup>5</sup> LUIS, J. Chem. Soc., 1932, 2547.

<sup>&</sup>lt;sup>1</sup> LACHMAN, J. Am. Chem. Soc., 45, 1529 (1923).

<sup>&</sup>lt;sup>2</sup> Schönberg and Keller, Ber., 56, 1638 (1923).

The present investigation was carried out with two objects in view—(1) to find a method for obtaining more complete conversion of benzoin to diphenylacetic acid, and (2) to study the effect of substituting groups upon the rearrangement.

The more complete conversion of benzoin to diphenylacetic acid should be possible under favorable conditions, since the closely related benzil<sup>2</sup> and pinacol<sup>3</sup> rearrangements both are almost complete. However, as Lachman found<sup>1</sup>, at the high temperatures necessary to bring about the benzoin rearrangement, side reactions predominate. We tried adding several substances to aid the acid catalyst in the rearrangement. The results are summarized in Table I.

TABLE I	
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Additional Reagents in the Rearrangement of Benzoin by Acid Catalysis with 20 ml. of 60% Phosphoric Acid

SUBSTANCE ADDED	GRAMS ADDEN- DUM	GRAMS BENZOIN	темр., °С.	TIME, HOURS	DI- PHENYL- ACETIC ACID, %	GAS PRESSURE
None <sup>a</sup>		5	230	4	6	Moderate
Pumice <sup>a</sup>	2.5	5	230	4	5	Moderate
Activated charcoal	2.5	5	230	4	6	None
Activated charcoal	1.5	3	260	4	11	Moderate
Silica gel	1.5	3	240	4	18	None
Silica gel	1.0	2	270	24	54	Moderate
Activated alumina	1.5	3	250	4	27	None

 $^{\rm o}$  Twenty milliliters of 1.5 molar sulfuric acid was used instead of 20 ml. of 60% phosphoric acid.

Silica gels prepared from sodium silicate and (1) acetic acid, (2) hydrochloric acid, (3) carbon dioxide, (4) ferric chloride, and (5) sulfur dioxide, and activated at temperatures from 150 to 450° we found to be of about equal effectiveness in this rearrangement.

Heating benzoin with zinc chloride or with cobalt chloride in an open test-tube for 4 hours at 230° gave no diphenylacetic acid.

The effect of variations in time and temperature is shown in Tables II and III.

In an attempt to accomplish the benzoin rearrangement by less drastic treatment, we tried the method which Gomberg and Bachmann<sup>6</sup> found to be effective in the pinacol rearrangement. The pinacol rearrangement, like the benzoin rearrangement, is ordinarily brought about by heating with mineral acid in sealed tubes. We found that their process of refluxing in glacial acetic acid with a little iodine was totally ineffective in bringing

<sup>&</sup>lt;sup>6</sup> GOMBERG AND BACHMANN, J. Am. Chem. Soc., 49, 246 (1927).

about the benzoin rearrangement. When 5 g. benzoin was thus treated we recovered 4.6 g. unchanged benzoin, along with 0.26 gm. benzil.

The following substituted benzoins were prepared and their rearrangement attempted: furoin, 4-methoxybenzoin<sup>\*</sup>, 4-dimethylaminobenzoin, 4,4'-dimethoxybenzoin (anisoin), 4-methoxy-2'-chlorobenzoin, 4,4'-dimethylbenzoin (toluoin), 4,4'-diisopropylbenzoin (cuminoin), and alphaphenyl benzoin  $[(C_6H_5)_2COHCOC_6H_5]$ .

TABLE 1	II
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REARRANGEMENT OF BENZOIN IN THE PRESENCE OF SILICA GEL AND 60% PHOSPHORIC Acid in 24 Hours

TEMP., <sup>°</sup> C.	DIPHENYL- ACETIC ACID, %	DIPHENTL- CETIC ACID, %	
240	38.3	No pressure	
250	46.1	Slight pressure	
260	50.3	No pressure	
270	53.9	Slight pressure	
280	50.5	Slight pressure, some darkening	
<b>2</b> 90	15.3	Much pressure, contents almost black	

### TABLE III

Rearrangement of Benzoin in the Presence of Silica Gel and 60% Phosphoric Acid at  $250^\circ$ 

TIME, HOURS	DIPHENTL- ACETIC ACID, %	COMMENTS
4	37	No pressure
<b>24</b>	46.1	Slight pressure
48	52.2	Slight pressure, some darkening
72	50.6	No pressure, contents almost black

When the substituted benzoins furoin, 4-methoxybenzoin, 4-dimethylaminobenzoin, 4,4'-dimethoxybenzoin, and 4-methoxy-2'-chlorobenzoin were heated with phosphoric acid and silica gel or alumina, in every case severe charring occurred and in most cases pressure was developed. None of the expected substituted diphenylacetic acids were obtained. Using acid of lower concentration did not reduce decomposition appreciably.

With the alkyl-substituted benzoins better results were obtained. With

\* In accordance with the usage of *Chemical Abstracts* since 1927, in naming mixed benzoins, primes are given to the numbered constituents on the benzene ring next to the CHOH group. Buck and Ide [J. Am. Chem. Soc., 54, 3304 (1932)] suggest and use a system exactly opposite—giving primes to the numbered constituents on the benzene ring next to the CO group. These conflicting usages make the literature rather confusing, since some authors do not specify which system they use.

4,4'-dimethylbenzoin and 4,4'-diisopropylbenzoin, decomposition did not occur, but the extent of rearrangement was less than with benzoin; with 4,4'-dimethylbenzoin about 25 per cent. of ditolylacetic acid was produced, while with 4,4'-diisopropylbenzoin only 5 per cent. was converted to organic acids. This was shown not to be pure dicuminylacetic acid, so the amount of actual rearrangement was less than 5 per cent.

A chain-substituted benzoin was prepared to find out whether the conversion of the secondary hydroxyl of benzoin to a tertiary hydroxyl would encourage rearrangement. Alpha-phenylbenzoin  $[(C_6H_6)_2COHCOC_6H_5]$  remained unchanged when heated with phosphoric acid and silica gel or alumina.

#### EXPERIMENTAL

The variables involved in the rearrangement of benzoin are temperature, time, kind of acid, acid strength, and the presence of additional catalysts. Lachman<sup>1</sup> found that sulfuric and phosphoric acids were about equally effective, and that variation in acid strength did not affect the reaction greatly. After a few preliminary experiments we selected 60% phosphoric acid as a suitable catalyst.

*Procedure.*—The specified materials were placed in combustion tubes, which were then sealed. An electric resistance furnace of the Carius type provided the high temperatures. After the tube was cool, the end was broken off and an ether extraction was made directly from the combustion tube. To the ether extract was added 40 ml. of 5% aqueous sodium carbonate solution. After shaking and letting stand, the aqueous layer was run off and acidified with concentrated hydrochloric acid. This brought down a heavy white precipitate which, after collection on a weighed filter paper, washing with distilled water, and drying at 110° was weighed. This crude diphenylacetic acid melts at 143 to 145° and may be recrystallized readily from hot water in long white needles of the pure acid melting at 148°. A second and very much smaller portion may be obtained by extracting the mother liquor and wash waters with ether, shaking with 10 ml. of 5% sodium carbonate solution, and separating and acidifying the aqueous layer.

Preparation of materials.—The benzoin was prepared by the usual cyanide condensation and was recrystallized several times from hot ethyl alcohol until it was almost white and had a melting point of 135 to 136°.

Furoin<sup>7</sup>, m.p. 135°; 4-dimethylaminobenzoin<sup>8</sup>, m.p. 163°; 4-methoxy-2'-chlorobenzoin<sup>9</sup>, m.p. 82°; 4-methoxybenzoin<sup>10</sup>, m.p. 102 to 103°; 4,4'-dimethoxybenzoin<sup>11</sup>, m.p. 113; 4,4'-dimethylbenzoin<sup>12</sup>, m.p. 88 to 89°; and 4,4'-diisopropylbenzoin<sup>13</sup>, m.p. 101 to 102°, were all prepared by cyanide condensations of the respective aldehydes in essentially the manner described in the references, and purified by recrystallization from ethyl alcohol.

- <sup>8</sup> STAUDINGER, Ber., 46, 3535 (1913).
- <sup>9</sup> BUCK AND IDE, J. Am. Chem. Soc., 52, 4107 (1930).
- <sup>10</sup> KINNEY, *ibid.*, **51**, 1595 (1929).
- <sup>11</sup> Bösler, Ber., 14, 327 (1881).
- <sup>12</sup> STIERLIN, *ibid.*, **22**, 380 (1889).
- <sup>13</sup> WIDMAN, *ibid.*, **14**, 609 (1881).

<sup>&</sup>lt;sup>7</sup> FISCHER, Ann., 211, 218 (1881).

Alpha-phenylbenzoin, m.p. 88°, was prepared by the method of Acree<sup>14</sup>, in which phenylmagnesium bromide reacts with benzil.

Rearrangement of 4,4'-dimethylbenzoin.—When 2 g. of 4,4'-dimethylbenzoin was heated with 1 g. silica gel and 20 ml. of 60% phosphoric acid for 11 hours at 250°, the procedure outlined above for separation of organic acids gave 0.491 g. (24.6%) of white ditolylacetic acid melting after recrystallization at 143.5 to 144° and giving on titration an equivalent weight of 242.2 (calc'd, 240.1).

Rearrangement of 4,4'-diisopropylbenzoin.—Samples of 4,4'-diisopropylbenzoin were treated as follows: (1) 1.5 g. with silica gel and 60% phosphoric acid 24 hours at 250°; (2) 1 g. with silica gel and 60% phosphoric acid 24 hours at 270°; (3) 1.5 g. with alumina and 50% phosphoric acid 24 hours at 250°.

The acidic material obtained from these three experiments was so scanty that the three portions were combined, giving a total of only 0.21 g. before purification, or 5% of the starting material. Titration after recrystallization gave a value of 353 for the equivalent weight instead of the 296 calculated for  $[(CH_3)_2CHC_6H_4]_2CHCOOH$ . The acidified titration solution was ether-extracted, and the ether was allowed to evaporate. The white residue did not completely dissolve in aqueous 5% sodium carbonate solution, indicating the presence of some non-acidic material which gave too high a value for the equivalent weight.

Attempted rearrangement of alpha-phenylbenzoin.—Two grams of alpha-phenylbenzoin, 1 g. of silica gel, and 20 ml. of 60% phosphoric acid were heated for 8 hours at 245°. There was no increase in pressure, but the contents changed in color from almost white to almost black. After ether extraction the ether was shaken with 10% aqueous sodium carbonate solution. Acidification of the aqueous layer with hydrochloric acid gave no precipitate of triphenylacetic acid. Evaporation of the ether layer gave balls of white alpha-phenylbenzoin melting at 87.5° alone or mixed with alpha-phenylbenzoin.

A second attempt was made to rearrange alpha-phenylbenzoin by heating 2 g. with 1 g. of silica gel and 20 ml. of 50% phosphoric acid at  $260^\circ$  for 10 hours. The blackened contents of the reaction tube were extracted with benzene, and the extract was shaken with 10% aqueous sodium hydroxide solution, since triphenyl acetic acid is referred to as a very weak acid. On acidification of the aqueous layer with hydrochloric acid, however, there was no precipitate of triphenylacetic acid. Evaporation of the acidified solution to dryness left a white residue which was almost completely insoluble in boiling benzene, while triphenylacetic acid is soluble in this solvent. So once again, no triphenylacetic acid had been produced.

#### DISCUSSION

Inspection of Tables I, II, and III shows that the rearrangement of benzoin will proceed to the extent of about 50 per cent. on heating for 24 hours with 60 per cent. phosphoric acid and silica gel or alumina at 250 to 260°. This method of producing diphenylacetic acid is more direct than the ordinary preparation from benzoin through benzil and benzilic acid, but it has the disadvantages of lower yields and of requiring the use of sealed tubes.

Lachman<sup>1</sup> had found that a great deal of carbon dioxide pressure developed even at 230° when benzoin was heated with 6-molar phosphoric acid. He believed the formation of at least part of this carbon dioxide to be due

<sup>14</sup> ACREE, *ibid.*, **37**, 2758 (1904).

to decarboxylation of diphenylacetic acid at 230°. We heated diphenylacetic acid with 60 per cent. (8.6-molar) phosphoric acid at 240° for 4 hours and found no carbon dioxide. This shows that the carbon dioxide is produced by a side reaction during the rearrangement rather than from diphenylacetic acid after rearrangement. The presence of silica gel or alumina retards the side reaction, permitting the use of higher temperatures where rearrangement is more complete.

The benzil and pinacol rearrangements have been studied extensively, the benzoin and hydrobenzoin less so, with two chief theoretical considerations in view: (1) devising a satisfactory mechanism to explain these and related rearrangements, and (2) determining the relative migratory aptitudes of various radicals.

Among the most acceptable mechanisms of rearrangement are those of Lachman<sup>15</sup> and Whitmore<sup>16</sup>. Lachman assumes that a hydroxyl radical migrates to an adjacent carbon, creating an unstable structure which is readjusted by a shift of the phenyl group to give diphenylacetic acid.

 $C_6H_5$ -CHOH-CO- $C_6H_5 \rightarrow C_6H_5$ -CH  $\div$  COOH- $C_6H_5 \rightarrow (C_6H_5)_2$  CH-COOH The division sign indicates the unstable structure.

Whitmore suggests that the formation of an "open electron sextet" by loss of a negative group, such as hydroxyl, with its two electrons may cause a group such as phenyl to move in to complete the octet, but at the same time leaving another atom with an open sextet. The negative hydroxyl radical then returns to the structure to complete an octet, giving the rearranged product.

The principal difference between these two mechanisms seems to be in the timing of the various steps. Lachman's theory calls for (1) detachment of hydroxyl, (2) reattachment, and (3) rearrangement by transfer of phenyl. Whitmore's specifies (1) detachment of hydroxyl, (2) transfer of phenyl, and (3) reattachment of hydroxyl. We see no reason why migration of the phenyl group with its pair of electrons and reattachment of hydroxyl with its pair could not take place simultaneously, making the two mechanisms identical.

Comparison of migratory aptitudes of radicals by the extent of rearrangement has been made chiefly in the symmetrical pinacol series, where only the relative migratory aptitudes of the radicals is the determining factor in deciding which product will appear in greater amount.

$$\begin{array}{c|cccc} OH OH & R^1 & O & R^2 & O \\ | & | & \\ R^2 - C - C - R^2 \rightarrow H_2 O + R^2 - C - C - R^2 & \text{or } R^2 - C - C \\ | & | & \\ R^1 & R^1 & R^1 & R^1 & R^1 \end{array}$$

<sup>15</sup> LACHMAN, J. Am. Chem. Soc., 44, 330 (1922); 45, 1509 (1923).
<sup>16</sup> WHITMORE, *ibid.*, 54, 3274 (1932).

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Bachmann<sup>17</sup> found that except for the ortho-substituted radicals the relative migratory aptitudes follow the order of electronegativity as determined by Kharasch and Reinmuth<sup>18</sup>. In unsymmetrical pinacol, benzil, and benzoin rearrangements the factors influencing rearrangement become more complex and the relation between the migratory aptitude and the electronegativity of a radical is less exact.

We succeeded in rearranging, besides unsubstituted benzoin, the 4,4'dimethyl and the 4,4'-diisopropyl derivatives. Bachmann<sup>17</sup> gives the relative migratory aptitudes of phenyl, 4-isopropylphenyl, and 4-methylphenyl respectively as 1 (arbitrarily assigned), 9, and 15.7. If this alone were the determining factor in the benzoin rearrangement, it should proceed most readily with 4,4'-dimethyl, next most readily with 4,4'-diisopropyl, and least readily with unsubstituted benzoin. But we found unsubstituted benzoin to rearrange most completely, 4,4'-dimethylbenzoin next, and 4,4'-diisopropyl hardly at all under the conditions tried.

To find out whether the ease of losing a hydroxyl determines the extent of rearrangement, as Lachman's and Whitmore's mechanisms might suggest, we prepared alpha-phenylbenzoin  $[(C_6H_5)_2COHCOC_6H_5]$ , and attempted its arrangement. Here the secondary hydroxyl of benzoin is replaced by tertiary to give a more negative carbon. Koopal,<sup>19</sup> in a generalization from rearrangements in the glycol series (pinacol, hydrobenzoin, etc.), showed that in such rearrangements a tertiary hydroxyl is invariably more mobile than a secondary or primary hydroxyl. So one might hope for the rearrangement of alpha-phenylbenzoin to triphenylacetic acid to take place more readily than that of benzoin to diphenylacetic acid. We found that this was not the case. Upon subjecting alphaphenylbenzoin to the conditions of the benzoin rearrangement, unchanged alpha-phenylbenzoin but no triphenylacetic acid was recovered. This failure was not entirely unexpected, since Weissberger<sup>20, 21</sup> showed that the speed of oxidation of benzoins to arylacetic acids with air in alkaline solution increased with increasing dissociation constants of the acids formed, and that the same relationship holds true in the Cannizzaro oxidation-reduction of aromatic aldehydes. Since the benzoin rearrangement is essentially an intramolecular oxidation-reduction, and since triphenylacetic acid is known to be an extremely weak acid<sup>22</sup>, on the basis of Weissberger's findings we would not expect this acid to be produced readily by rearrangement.

<sup>&</sup>lt;sup>17</sup> BACHMANN AND CO-WORKERS, *ibid.*, 56, 2081 (1934), and earlier papers.

<sup>&</sup>lt;sup>18</sup> KHARASCH AND REINMUTH, J. Chem. Educ., 8, 1713 (1931).

<sup>&</sup>lt;sup>19</sup> KOOPAL, Rec. trav. chim., 34, 115 (1915).

<sup>&</sup>lt;sup>20</sup> WEISSBERGER, Ber., 65, 1815 (1932).

<sup>&</sup>lt;sup>21</sup> WEISSBERGER AND HAASE, J. Chem. Soc., 1934, 535.

<sup>&</sup>lt;sup>22</sup> SCHMIDLIN AND HODGSON, Ber., 41, 441 (1908).

## SUMMARY

1. The presence of alumina or silica gel in the rearrangement of benzoin to diphenylacetic acid by acid catalysis allowed the use of high temperatures without decomposition.

2. Approximately 50 per cent. rearrangement was attained in 24 hours with 60 per cent. phosphoric acid and silica gel or alumina at 250 to  $260^{\circ}$ .

3. Treatment of furoin, 4-methoxybenzoin, 4-dimethylaminobenzoin, 4,4'-dimethoxybenzoin, and 4-methoxy-2'-chlorobenzoin in the same manner resulted only in their decomposition.

4. The alkyl-substituted benzoins 4,4'-dimethylbenzoin and 4,4'-diisopropylbenzoin rearranged under the conditions stated in (2), but not so completely as benzoin.

5. Alpha-phenylbenzoin  $[(C_6H_5)_2COHCOC_6H_5]$  was found to remain unchanged under the conditions stated in (2).