ethyl β-(β'-hydroxybutyryloxy)-butyrate. This ester despite the fact that it is the ester of a secondary alcohol did not undergo alcoholysis at the temperature used for the reduction of acetoacetic ester or in a boiling alcoholic solution of sodium ethoxide. It did undergo alcoholysis at 190° in the presence of a nickel catalyst. This complex ester appears to be formed through the reduction of two molecules of acetoacetic ester with the elimination of one molecule of ethanol. This condensation product was postulated by Arndt and Nachtwey as an intermediate in the formation of dehydroacetic acid from acetoacetic acid, so that the results here reported support their hypothesis. The methyl derivative of acetoacetic ester on reduction behaved similarly to the unsubstituted ester. The α,α-dimethyl and the α-methyl-α-ethylacetoacetic ester reduced smoothly to the corresponding simple hydroxy ester either with or without a solvent since there is no possibility of the formation of a complex ester analogous to that formed from the β-ketonic esters capable of enolization.

Dehydroacetic acid appears to give heptanone-4 as the chief product in hydrogenation over nickel. The use of hydrogen pressure in excess of 300 atmospheres appears not only very greatly to accelerate the rate of hydrogenation but to favor the formation of heptanone-4 with a decrease in the products formed through the hydrolysis and alcoholysis of the dehydroacetic acid. Dehydroacetic acid has been found to undergo a smooth alcoholysis to acetoacetic ester at 190°.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

THE STRUCTURE OF PARA-DIMETHYLAMINOBENZOIN[1]

BY SANFORD S. JENKINS[2] WITH LUCIUS A. BIGELOW AND JOHANNES S. BUCK

RECEIVED JULY 30, 1930 PUBLISHED DECEMBER 18, 1930

In the preceding paper, dealing with the reduction of *p*-dimethylaminobenzil,[3] it was found that the corresponding benzoin, on treatment with tin and hydrochloric acid in alcohol solution, yielded *two* isomeric desoxy derivatives, designated as α- and β-forms, the structures of which were established. This fact made it seem possible that the benzoin itself might be a mixture of α- and β-modifications, which, at least theoretically, would be expected to exist.

Accordingly, efforts were made to separate the apparently pure benzoin (m. p. 163–164°) into isomeric components by ordinary methods. For

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[1] This paper is in part constructed from portions of a thesis presented by Sanford S. Jenkins in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Graduate School of Arts and Sciences, Duke University.

[2] Angier B. Duke Memorial Fellow, 1929–1930.

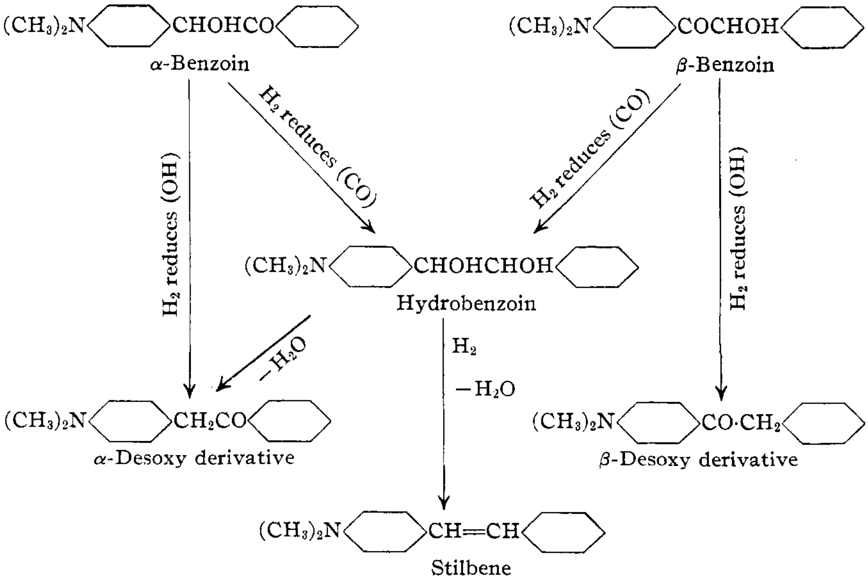
[3] Jenkins, Buck and Bigelow, THIS JOURNAL, 52, 4495 (1930).

instance, the material was repeatedly fractionally crystallized, both from glacial acetic acid and from alcohol, but, while the melting points of the different fractions varied slightly, when samples of these were mixed with the pure substance, there was no depression. Also, pure *p*-dimethylaminobenzil was reduced catalytically to the benzoin in the Adams apparatus, employing different solvents, in the hope of obtaining isomers, but in every case mixed melting points of the products with an authentic sample of the benzoin showed no depression.

H. Staudinger,[4] who first prepared *p*-dimethylaminobenzoin by condensing *p*-dimethylaminobenzaldehyde with benzaldehyde in the presence of potassium cyanide, states unequivocally that the product (m. p. 163–164°) can be but a single substance having the constitution expressed by the formula *p*-$(CH_3)_2NC_6H_4CHOHCOC_6H_5$, which we designate as the α-form. Certain experimental data, which form the basis for considerable speculation, are advanced in support of this assertion.

In spite of the fact that the present writers were not able to separate the benzoin into α- and β-components, they were led to doubt the validity of the conclusion reached by the earlier investigator on the basis of the following considerations.

As shown in the preceding paper, already cited, the reduction of the benzoin with tin and hydrochloric acid yields both the α- and β-desoxy derivatives, but the dehydration of the hydrobenzoin with a mixture



THE POSSIBLE REDUCTION PRODUCTS OF α- AND β-*p*-DIMETHYLAMINOBENZOIN

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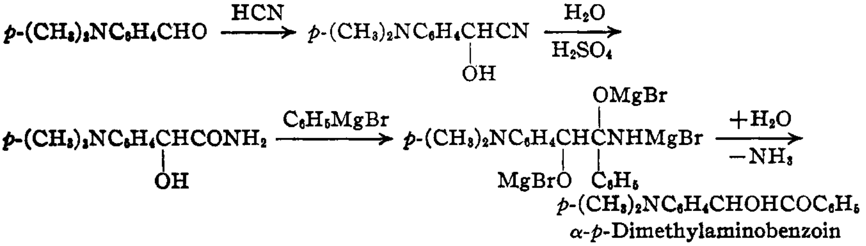
[4] Staudinger, *Ber.*, **46**, 3530, 3535 (1913).

of acetic and hydrochloric acids gives only the α-isomer. Furthermore, the action of tin and hydrochloric acid on the hydrobenzoin produces only the corresponding stilbene. From this it follows, upon theoretical considerations, that the α-form of the benzoin *cannot*, upon reduction, yield *both* desoxy compounds, whereas the β-modification, or a mixture of the two, can do so. The reasons for these statements may be made clear by reference to the diagram.

Thus, it did not seem possible that "ordinary" *p*-dimethylaminobenzoin, prepared according to Staudinger, which *does* yield two desoxy compounds upon reduction, could consist solely of the α-modification.

The writers, therefore, decided to attempt the synthesis of the α- and β-benzoins, by means of such methods as would establish definitely the structures of these substances. Accordingly, *p*-dimethylaminobenzaldehyde was treated with anhydrous hydrocyanic acid, and the resulting cyanohydrin hydrolyzed to form *p*-dimethylaminomandelamide, as described by Sachs.[5] The procedure was considerably modified, however, and is given in detail further on. The amide was then condensed with phenylmagnesium bromide according to the general method of McKenzie and Wren,[6] with the formation of the desired α-*p*-dimethylaminobenzoin of undoubted structure. The reactions may be expressed as follows:



$$p\text{-}(CH_3)_2NC_6H_4CHO \xrightarrow{HCN} p\text{-}(CH_3)_2NC_6H_4\underset{\displaystyle OH}{\underset{|}{C}}HCN \xrightarrow[H_2SO_4]{H_2O}$$

$$p\text{-}(CH_3)_2NC_6H_4\underset{\displaystyle OH}{\underset{|}{C}}HCONH_2 \xrightarrow{C_6H_5MgBr} p\text{-}(CH_3)_2NC_6H_4\underset{\displaystyle MgBrO}{\underset{|}{C}}H\overset{\displaystyle OMgBr}{\overset{|}{\underset{\displaystyle C_6H_5}{\underset{|}{C}}}}NHMgBr \xrightarrow[-NH_3]{+H_2O}$$

$$p\text{-}(CH_3)_2NC_6H_4CHOHCOC_6H_5$$

α-*p*-Dimethylaminobenzoin

The product, after crystallization from alcohol, melted at 159–160° (corr.). It gave on analysis the correct values for carbon, hydrogen and nitrogen and it had the molecular weight indicated by the formula. Upon oxidation with Fehling's solution, it formed the known benzil, and, when reduced with tin and hydrochloric acid in alcohol solution, it yielded only the α-desoxy derivative, not a trace of the β-isomer being formed. This was to be expected from the theoretical considerations already outlined.

When the new benzoin was mixed with the corresponding substance, prepared according to Staudinger, the melting point was depressed 15–18°, indicating clearly that the two compounds are different. These facts appear to prove with certainty that *p*-dimethylaminobenzoin prepared by the potassium cyanide condensation method is not the α-isomer.

It remained to be ascertained, however, whether the so-called "ordi-

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[5] Sachs and Lewin, *Ber.*, **35**, 3571 (1902).

[6] McKenzie and Wren, *J. Chem. Soc.*, **93**, 311 (1908).

nary" benzoin was the pure β-isomer, or a mixture of the two forms which was uncommonly difficult to separate. Either possibility accorded with the known facts at this time. Having had success with the method outlined above in the synthesis of the α-derivative, the writers decided to prepare the β-benzoin by an analogous procedure. Mandelamide was therefore synthesized, as described by McKenzie and Wren, in their paper already cited, and condensed with *p*-dimethylaminophenylmagnesium bromide. The Grignard reagent was prepared by refluxing *p*-bromodimethylaniline with magnesium, activated with a little ethyl bromide. The reaction was sluggish, however, and the yield not very favorable. The condensation took place in a manner similar to that already illustrated, and must lead to the β-benzoin.

The product, after crystallization from alcohol, melted at 163–164°. It also gave, on analysis, the correct values for carbon, hydrogen and nitrogen. On oxidation, it formed the benzil, and on reduction with tin and hydrochloric acid in alcohol solution it yielded *both* the α- and β-desoxy derivatives. When it was mixed with the α-benzoin, the melting point was sharply depressed, but when the corresponding substance, prepared according to Staudinger, was added, no change in the melting point was observed.

It therefore seems certain that *p*-dimethylaminobenzoin prepared by the potassium cyanide condensation method is a single substance, consisting of the β- and not the α-isomer, and having the structure *p*-$(CH_3)_2NC_6H_4COCHOHC_6H_5$.

It appears to the writers that the only conclusion which it is possible to draw from the facts here reported is that in this instance the assertion of the earlier investigator cannot be sustained.

Experimental

***p*-Dimethylaminobenzaldehyde Cyanohydrin.**—The method finally adopted for the preparation of this substance was a modification of that described by Sachs and already cited. It was not found possible, however, to obtain results, using liquid hydrogen cyanide synthesized according to Wade and Panting[7] until it was noticed that a trace of calcium chloride, which was carried into the apparatus by chance, catalyzed the reaction. This fact, together with the observations that hydrocyanic acid of German manufacture containing calcium chloride as a drying reagent, produced results, while purified calcium chloride did not, made it evident that the actual catalyst was calcium oxide, contained in the commercial chloride. In the presence of a trace of the oxide, the reaction took place without the slightest difficulty. The detailed procedure consisted in placing 10 g. of *p*-dimethylaminobenzaldehyde and about 0.2 g. of calcium oxide in a thick-walled bottle of 400-cc. capacity, cooled in a freezing mixture. Ten cc. of anhydrous hydrogen cyanide was then distilled into the bottle, which was tightly corked and heated to 40–45° in a water-bath until the reaction mixture had solidified, requiring about thirty-five minutes. The excess hydrogen cyanide was removed by

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[7] Wade and Panting, *J. Chem. Soc.*, 73, 256 (1898).

suction and the solid residue dissolved in 50 cc. of warm chloroform. Finally, ligroin (b. p. 60–70°) was added until precipitation appeared to be complete. The white solid cyanohydrin was filtered off and dried. It weighed 7 g., which is 59% of the theoretical, melted at 110–113° and was sufficiently pure for use in the subsequent work.

***p*-Dimethylaminomandelamide.**—This compound was also prepared by Sachs, but the details given are rather meager. The writers proceeded as follows. Four grams of the cyanohydrin was dissolved in approximately 10 cc. of sulfuric acid (sp. gr. 1.84) and the mixture allowed to stand for about fifteen minutes. After this it was poured slowly, with constant shaking, into a slush of ice and water. Then the solution was carefully neutralized with ammonia (sp. gr. 0.90). During these operations care was taken that the temperature at no time rose above 15°. Just before the neutral point was reached a brown amorphous precipitate was formed, which was filtered off and discarded. The resulting neutral mixture was allowed to stand in the ice box overnight, when the amide crystallized out. A further quantity was obtained on evaporating the mother liquor. The product weighed 2 g. (45% of the theoretical), and after two crystallizations from water melted at 184–186° (uncorr.). The yields obtained in different runs varied considerably.

***α-p*-Dimethylaminobenzoin.**—A mixture of 30 g. of bromobenzene, 5.5 g. of magnesium turnings and 50 cc. of anhydrous ether was refluxed until most of the metal had dissolved. Then 2.5 g. of finely powdered *p*-dimethylaminomandelamide was added, in small portions, over a period of fifteen minutes. After each addition of the amide, a vigorous reaction occurred, which was allowed to subside before the next portion was added. After heating on the water-bath for twelve hours the solution was poured into 200 g. of crushed ice containing 30 g. of concd. sulfuric acid. The ether was removed, and the aqueous layer extracted with two 100-cc. portions of ether. The extracts were discarded. The acid solution was then neutralized with ammonia and the yellow precipitate which formed was separated, dissolved in 50 cc. of alcohol and filtered hot. On cooling, a mass of yellow needles separated which weighed 1.5 g. (45%) and melted at 152–153°. After three recrystallizations from alcohol, the product melted at 159–160° (corr.). When this was mixed with a sample of the benzoin prepared according to Staudinger, the melting point was depressed 12–18°.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.29; H, 6.67; N, 5.49; mol. wt. 255. Found: C, 75.19; H, 7.02; N (Kjeldahl), 5.58, 5.29; mol. wt. (in benzene), 258.

Oxidation of *α-p*-Dimethylaminobenzoin.—About 0.10 g. of the benzoin dissolved in 10 cc. of alcohol was heated on the water-bath with concentrated Fehling's solution for one hour, after which the cuprous oxide was filtered off and the mixture diluted with 50 cc. of water. On standing a yellow crystalline precipitate formed, which was removed by filtration and recrystallized from 60% alcohol. The product melted at 115–116° and a mixed melting point taken with known *p*-dimethylaminobenzil showed no depression.

Reduction of *α-p*-Dimethylaminobenzoin.—The reduction was carried out by treating 1.0 g. of the benzoin with 1.0 g. of mossy tin, 5 cc. of hydrochloric acid (sp. gr. 1.19), 0.10 g. of copper sulfate pentahydrate and 20 cc. of alcohol. The solution was refluxed for five hours, filtered hot and diluted with 30 cc. of water. After standing overnight, no precipitate whatever had formed, indicating the absence of the *β*-desoxy derivative, which is relatively insoluble in dilute acid mixtures. The solution was then made alkaline with ammonia and filtered, after which the yellow precipitate was extracted with 100 cc. of boiling alcohol. The extract was evaporated to a volume of about 25 cc. and allowed to stand.

The product which separated consisted of long white prisms which weighed 0.70 g. (74%) and melted at 127–128°. When it was mixed with known *α-p*-dimethylaminodesoxybenzoin, no depression in the melting point was observed.

An exactly parallel reduction of *p*-dimethylaminobenzoin prepared according to Staudinger, yielded 0.30 g. of the α-desoxy compound and 0.47 g. of the β-desoxy derivative. In this case the total yield was 0.77 g., which is 82% of the theoretical quantity.

β-*p*-Dimethylaminobenzoin.—A mixture of 30 g. of *p*-bromodimethylaniline, 3.1 g. of magnesium turnings and 75 cc. of absolute ether was refluxed for forty-eight hours. To start the reaction, about 12 drops of ethyl bromide was added in two portions. After the heating, 1.5 g. of finely powdered mandelamide, prepared according to McKenzie and Wren,[8] was added in small portions, over a period of ten minutes. A vigorous reaction ensued after each addition. The solution was then refluxed for fifteen hours more, and poured into 200 g. of crushed ice which contained 20 g. of sulfuric acid (sp. gr. 1.84). The clear yellow aqueous layer was extracted six times with 50-cc. portions of ether and, in this case, the aqueous layer was discarded. The ether was removed by distillation and the solid residue, after one crystallization from a small amount of alcohol, weighed 0.7 g. (25%) and melted at 159–161°. After two further recrystallizations from alcohol the product formed stout yellow needles melting at 161–162° (corr.). When a sample of this was mixed with the benzoin prepared according to Staudinger, the melting point was not depressed.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.29; H, 6.67; N, 5.49. Found: C, 75.43; H, 7.04; N (Kjeldahl), 5.28, 5.39.

Oxidation of β-*p*-Dimethylaminobenzoin.—The reaction was performed by heating 0.12 g. of the benzoin, dissolved in 15 cc. of alcohol, with Fehling's solution. The mixture was heated on the water-bath for three-fourths of an hour and the reagent added in small portions until no further action occurred. The cuprous oxide was filtered off, the solution diluted with 50 cc. of water and the precipitate which formed on standing filtered and recrystallized from 15 cc. of 60% alcohol. The product formed yellow prisms melting at 116–117°, and weighing 0.072 g., which is 60% of the theoretical. When it was mixed with a sample of known *p*-dimethylaminobenzil, the melting point was not depressed.

Reduction of β-*p*-Dimethylaminobenzoin.—The reduction was carried out in a manner similar to that described for the case of the α-isomer. After the reaction was complete, the mixture was allowed to stand in the cold and the β-desoxy derivative separated. It weighed 0.20 g. and on crystallization from alcohol formed plates melting at 163–164°. The mother liquors from the reduction mixture were worked up as already described, and yielded 0.50 g. of the α-desoxybenzoin. After this had been purified in the usual way, it melted at 127–128°. The combined yields of the α- and β-isomers amounted to 0.70 g., which is 74% of the theoretical amount. When samples of these were mixed with known α- and β-*p*-dimethylaminodesoxybenzoin, respectively, the melting points were not depressed.

Reduction of *p*-Dimethylaminohydrobenzoin.—In order to show that no β-desoxybenzoin results from the reduction of the hydro derivative even with tin and hydrochloric acid in alcohol solution, the following experiment was carried out: 2.55 g. of "ordinary" *p*-dimethylaminobenzoin was dissolved in 50 cc. of absolute alcohol and reduced to the hydro compound in the Adams apparatus, in the presence of 0.1 g. of platinum oxide. The method is essentially identical with those described in the preceding paper, already cited. The catalyst was filtered off, and, without isolating the product, 3 g. of tin, 10 cc. of hydrochloric acid (sp. gr. 1.19) and a crystal of copper sulfate pentahydrate were added to the solution, which was refluxed for six hours. The unchanged tin was filtered off, and 90 cc. of water added. On standing, no precipitate appeared, so the mixture was neutralized with sodium carbonate, and the resulting product filtered, washed and extracted with alcohol. On cooling, the extract deposited colorless scales weighing 1.9 g. and melting at 147–148°. When these were mixed with known *p*-dimethylamino-

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[8] McKenzie and Wren, *J. Chem. Soc.*, **93**, 311 (1908).

stilbene, the melting point was not depressed, thus determining the identity of the product. The yield was 85%.

Summary

1. α- and β-*p*-Dimethylaminobenzoin have been synthesized by the Grignard method, leaving no reasonable doubt as to their structures.

2. The reduction products of these isomers have been studied and correlated with the corresponding substances produced by reducing *p*-dimethylaminobenzoin as prepared by condensing the corresponding aldehydes in the presence of potassium cyanide.

3. *p*-Dimethylaminobenzoin, as prepared by the condensation method, is shown to be the β-isomer, and not the α-derivative, as was hitherto supposed. It has the structure *p*-$(CH_3)_2NC_6H_4COCHOHC_6H_5$.

DURHAM, NORTH CAROLINA

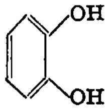
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

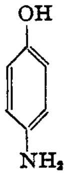
AN INDIRECT METHOD OF STUDYING THE OXIDATION-REDUCTION POTENTIALS OF UNSTABLE SYSTEMS, INCLUDING THOSE FROM THE PHENOLS AND AMINES

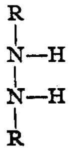
BY LOUIS F. FIESER

RECEIVED AUGUST 2, 1930 PUBLISHED DECEMBER 18, 1930

With certain unstable oxidation-reduction systems it has been found possible to measure the potentials with a reasonable degree of accuracy even though decomposition of the oxidant occurs so rapidly that the half-life period is less than one minute.[1] A limit was reached, however, in the application of the method in its present form. Such substances as amphi-naphthoquinone and *o*-quinone-di-imine decompose so very rapidly that no adequate measurements could be made. The number of such failures of the direct method, to be sure, is comparatively small. In over two hundred cases the simultaneous removal by oxidation of two hydrogen atoms from hydroxyl or amino groups which are ortho or para or adjacent to one another, or which bear some similar relationship, gives rise to a fairly stable oxidant and the system formed by the two components is electromotively active and its potential can be determined by one means or another which involves the direct observation of that potential. The following substances thus belong to what may be termed the "hydroquinone type."



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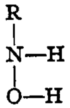
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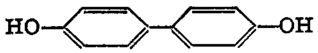

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[1] Fieser, THIS JOURNAL, **52**, 4915 (1930).