

The mixed acyl ureas from linseed oil and from China-wood oil were obtained in low yield. The former melted at 154–158° (from alcohol) and the latter at 155–162° (from alcohol). The iodine numbers were, respectively, 128 and 108.8, and the nitrogen contents 7.71 and 8.13%.

Summary

1. Monosodium urea has been prepared by the reaction of urea in liquid ammonia with one equivalent of sodium. It is a white powder insoluble in inert solvents. A mixture of disodium urea and monosodium urea was obtained from urea and two equivalents of sodium.

2. Several acyl ureas including stearyl, oleyl and benzoyl have been prepared by the reaction of monosodium urea with acid chlorides. Alkyl halides such as butyl iodide and dodecyl bromide did not react with monosodium urea.

3. Simple esters such as ethyl acetate and methyl benzoate reacted with monosodium urea in the presence of acetone to yield acyl ureas. Natural oils such as coconut, linseed and China-wood also reacted to yield high-melting mixed acyl ureas.

4. Malonic ester and its substituted derivatives reacted with monosodium urea to give barbituric acid derivatives. Barbituric acid, ethylbarbituric acid, isopropylbarbituric acid and butylbarbituric acid have been prepared in this manner.

5. Esters of higher dibasic acids, such as ethyl glutarate and ethyl pimelate, apparently yielded diureides.

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The Interconversion of Mixed Benzoin

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The reduction of 2,4,6-trimethylbenzoin (II) and 2',4',6'-trimethylbenzoin (III) to the same desoxybenzoin, phenyl 2,4,6-trimethylbenzyl ketone,¹ can be explained on the basis of an initial transformation of one of the benzoin isomers into its isomer. If this explanation is correct, the benzoin isomers should be interconvertible under mild conditions. This has proved to be the case, for when either 2,4,6- or 2',4',6'-trimethylbenzoin was warmed in alcoholic sodium acetate solution, the corresponding isomer was formed. Isolation of starting material in each case indicated the existence of an equilibrium.

Because of this ease of interconversion, an investigation was made of the reaction of the two benzoin isomers toward reagents commonly employed in testing for the hydroxyl group. The benzoin isomers, when treated with benzoyl chloride, yielded a single benzoate instead of the expected isomeric benzoates. Presumably in one case benzoylation had been preceded by conversion of the benzoin into its isomer.

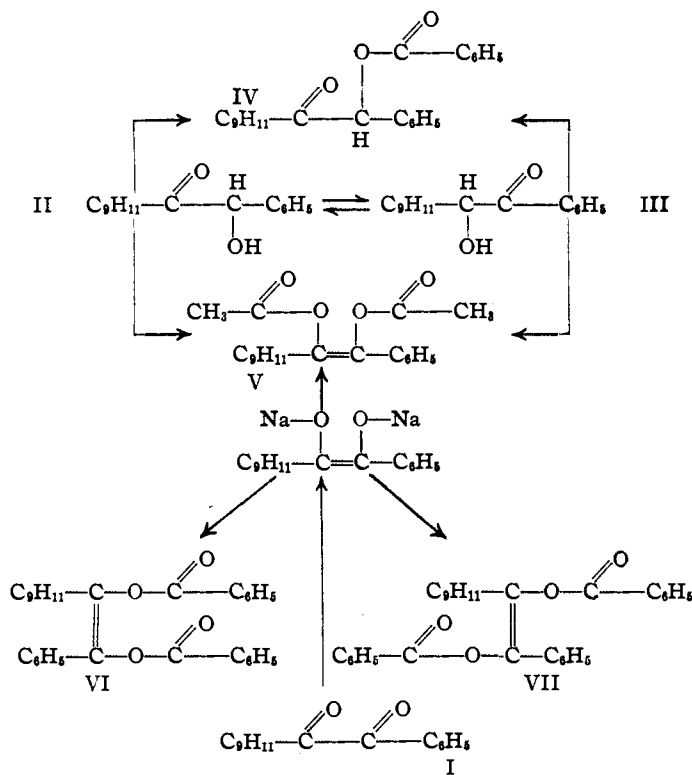
Such a conversion suggests the intermediate formation of the ene-diol. Longer treatment was, accordingly, attempted in the hope of obtaining the dibenzoate of the ene-diol. The mono-

benzoate was, however, the only product which could be isolated. The dibenzoate was made for reference by the action of benzoyl chloride on the sodium derivative of the diketone (I). Two forms (VI and VII) of the dibenzoate were isolated. The lower-melting form (139°) was converted into its isomer (170°) by heating above the melting point.

It was found possible, however, to obtain the diacetate of the ene-diol (V) by a method similar to that which was unsuccessful in the case of the corresponding dibenzoate. Subjection of either of the isomeric benzoin isomers to the action of acetic anhydride resulted in the formation of the diacetate. This structure was proved by preparing the compound by the action of acetyl chloride on the disodium salt of mesityl phenyl diketone (I). Compound III formed the diacetate more readily than did its isomer (II); when II was treated with acetic anhydride for five hours a monoacetate was formed while, under the same conditions, III formed the diacetate.

This implies that in the benzoylation III rather than II isomerizes. It is for this reason that the monobenzoate (IV), the structure of which is conjectural, is represented as a derivative of II rather than of III.

(1) Weinstock and Fuson, *THIS JOURNAL*, **58**, 1233 (1936).



That both II and III readily rearrange to the ene-diol form was confirmed by treatment of the two benzoin isomers with methylmagnesium iodide, according to the method of Kohler, Stone and Fuson.² Considerably more than one mole of gas was formed by each of the isomers and, as would be expected, II, which contains the sterically hindered carbonyl group, and thus would have a longer period of time to enolize before addition took place, gives the greater amount of methane.

The action of iodine upon the isomeric benzoin isomers produced an unexpected result. In the presence of small amounts of iodine, both II and III were found to undergo disproportionation to yield mesityl phenyl diketone (I), and phenyl 2,4,6-trimethylbenzoyl ketone.³

The reaction took place in hot, glacial acetic acid or at high temperatures in the absence of solvent. Disproportionation could not be made to take place in the absence of a trace of iodine. One explanation would be that the iodine oxidized one molecule of the benzoin to I with the formation

(2) Kohler, Stone and Fuson, *THIS JOURNAL*, **49**, 3181 (1927).

(3) Matsumura [*ibid.*, **57**, 955 (1935)] by treating β -*p*-dimethylaminobenzoin with alcoholic hydrochloric acid, obtained *p*-dimethylaminobenzoin, and α -*p*-dimethylaminodesoxybenzoin. Compound II would not undergo disproportionation under the same conditions. It is interesting to note that the desoxybenzoin formed by disproportionation of both benzoin isomers is the same one which is formed exclusively in the reduction of I, II and III.¹

of hydrogen iodide, which then reduced another molecule of the benzoin to phenyl 2,4,6-trimethylbenzoyl ketone, regenerating the iodine.

Experimental

Because of the ease of oxidation of 2,4,6- and 2',4',6'-trimethylbenzoin in solution, all reactions were carried out in an atmosphere of nitrogen.

Interconversion of the Benzoin isomers.—Two grams of 2,4,6-trimethylbenzoin (II),⁴ 0.75 g. of sodium acetate, 30 cc. of ethyl alcohol and 1 cc. of water were heated under reflux for twenty hours. The solution was diluted with water and cooled. From 1.2 g. of colorless material which separated, there was obtained on fractional crystallization, 0.1 g. of substance which melted at 93–94°. A mixed melting point with a known sample of 2',4',6'-trimethylbenzoin (III) showed no depression.

From 1 g. of III⁵ 0.1 g. of II was obtained by the same method. In both cases the equilibrium mixture was difficult to separate, and the yield of converted isomer was probably higher than given above.

A simple *monobenzoate* (IV) was obtained from both II and III by the following procedure. One gram of the benzoin was added to 1 cc. of benzoyl chloride in 5 cc. of pyridine. The reaction was maintained at a temperature of 80° for thirty minutes, and poured into 10 cc. of sodium carbonate solution. The emulsion was extracted with ether, the ether layer dried over calcium chloride, and the ether removed by evaporation. The residual oil was taken up in alcohol. When allowed to stand, the solution deposited a colorless, granular substance, melting at 127–127.5°, which was only slightly soluble in alcohol. The benzoates obtained from II and III were shown to be identical by the method of mixed melting points.

Anal. Calcd. for C₂₄H₂₂O₂: C, 80.44; H, 6.14. Found: C, 80.55; H, 6.29.

Allowing the reaction to proceed for a longer period of time did not yield the dibenzoate. Two grams of II, 15 cc. of pyridine and 2.5 cc. of benzoyl chloride were boiled under reflux for ten hours. There was obtained 1.5 g. of substance, melting at 115°, which, on purification, proved to be the monobenzoate. Hydrolysis of the monobenzoate with alcoholic potassium hydroxide solution gave I, m. p. 134–135°. A mixed melting point with mesityl phenyl diketone showed no depression. It seems probable that the monobenzoate has the structure represented by formula IV.

The isomeric dibenzoates of 2,4,6-trimethyl- α , α' -stilbenediol (VI and VII) were prepared by the action of benzoyl chloride on the disodium derivative of mesityl phenyl diketone. In a typical experiment, 3.5 g. of one dibenzoate was obtained from 8 g. of I. No method was evolved by which one could predict the isomer which would be

(4) Fuson, Weinstock and Ulliot, *ibid.*, **57**, 1803 (1935).

(5) Arnold and Fuson, *ibid.*, **58**, 1295 (1936).

formed. The isomers were both colorless compounds and melted at 138.5–139° and 169.5–170°. They were recrystallized from ethyl alcohol, in which they were difficultly soluble.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 80.52; H, 5.63. Found: (139°) C, 80.58; H, 5.79; (170°) C, 80.35; H, 5.68.

The substance melting at 139° was quantitatively converted into its isomer by heating above the melting point for five minutes. The high-melting isomer was hydrolyzed with alcoholic potassium hydroxide to give a mixture from which I (m. p. 133–135°) and II (m. p. 100–101°) were isolated. These substances were identified by mixed melting point determinations. The spatial configuration of the dibenzoates was not determined.

The monoacetate of 2,4,6-trimethylbenzoin was obtained by heating a solution of 2 g. of II and 1 g. of sodium acetate in 20 cc. of acetic anhydride under reflux for five hours. The solution was cautiously treated with water and extracted with ether. The ether layer was dried over calcium chloride, and the ether removed by evaporation. The residual yellow oil was taken up in alcohol and allowed to stand at room temperature; 1.5 g. of a colorless, granular substance separated. On recrystallization from dilute ethyl alcohol, the compound melted at 73–73.5°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.03; H, 6.76. Found: C, 77.10; H, 6.75.

Diacetate of 2,4,6-Trimethyl- α,α' -stilbenediol (V).—A. Treatment of II by the above procedure, except that heating was carried out for twenty-four hours, gave 0.8 g. of a colorless product; m. p. 92–98°. The pure compound melted (from alcohol) at 104–104.5°.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.56; H, 6.51. Found: C, 74.61; H, 6.49.

B. Treatment of III by the same procedure, except that the reaction mixture was heated for five hours, resulted in the formation of the diacetate; m. p. 104–104.5°. A mixed melting point with the product prepared from II showed no depression.

C. The diacetate was prepared by the action of acetyl chloride on the sodium derivative of mesityl phenyl diketone, according to the usual procedure. From 2 g. of I, 0.4 g. of sodium and 6 cc. of acetyl chloride was obtained 0.6 g. of product, m. p. 95–100°. The melting point was 103–104° after recrystallization. A mixed melting point with the diacetate prepared from II and III showed no depression.

Reaction with the Grignard Reagent.⁶—The benzoin (II and III) were treated with methylmagnesium iodide, in an apparatus of the type described by Kohler and Richtmyer.⁷ Approximately 0.0005 mole of substance was used in each run. The solution of the benzoin in the excess Grignard reagent was held at a temperature of 90° for thirty minutes before decomposition to allow the reaction to go to completion. The results showed that II gave 1.78 moles of gas, and 0.29 mole of the reagent was added.

(6) The Grignard analyses were made by Mr. J. W. Robinson, Jr.

(7) Kohler and Richtmyer, *THIS JOURNAL*, **52**, 3736 (1930).

Compound III likewise used two moles of reagent, but in this case 1.30 moles of gas was evolved and 0.75 mole of reagent was added.

Reaction with Iodine.—A. A solution of 1 g. of II and 0.1 g. of iodine in 50 cc. of glacial acetic acid was heated under reflux for three hours. The solution was poured, while hot, into 25 cc. of 2% sodium bisulfite solution. The hot solution was filtered and allowed to cool. A solid formed which, by a process of slow crystallization and decantation from alcohol, was separated into two sets of crystals: (a) 0.40 g. of large, yellow needles which melted at 135–136°—a mixed melting point with mesityl phenyl diketone showed no depression; (b) 0.37 g. of colorless fibrous clusters; m. p. 161–162°. After recrystallization from alcohol, the crystals melted at 164–165°. This substance was shown to be identical with phenyl 2,4,6-trimethylbenzyl ketone by means of a mixed melting point determination.

In another experiment, 2 g. of II and a small crystal of iodine were placed in a small Pyrex flask and held at a temperature of 200° for five minutes. The water which was formed in the reaction collected as a vapor on the upper surface of the flask. The product was taken up in alcohol after cooling. There was obtained 0.60 g. of mesityl phenyl diketone (m. p. 135.5–136.5°) and 0.55 g. of phenyl 2,4,6-trimethylbenzyl ketone (m. p. 162–163°).

Only starting material was recovered when II was heated to 220° or boiled under reflux in glacial acetic acid for three hours, no iodine being used in either case. Treatment of II with alcoholic hydrochloric acid and copper sulfate caused no disproportionation.

B. One and four-tenths grams of III was heated at 220° in the presence of a crystal of iodine. There was obtained 0.60 g. of phenyl 2,4,6-trimethylbenzyl ketone (m. p. 158–161°) and 0.55 g. of mesityl phenyl diketone (m. p. 133.5–135°). Mixed melting points of the purified substances with authentic samples showed no depression.

Summary

2,4,6-Trimethylbenzoin (II) and its isomer, 2',4',6'-trimethylbenzoin (III), underwent interconversion when heated in the presence of sodium acetate. It is postulated that the ene-diol is an intermediate in these transformations. Evidence in support of this is that with benzoyl chloride the two benzoin yield the same monobenzoate, and with acetic anhydride they give the same diacetate.

With methylmagnesium bromide, II and III react in the ene-diol form to the extent of 78 and 30%, respectively.

When heated in the presence of a crystal of iodine, II and III underwent disproportionation to the diketone and phenyl 2,4,6-trimethylbenzyl ketone.

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