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

A New Synthesis of Benzoins. 2',4',6'-Trimethylbenzoin

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The great reactivity of the aldehyde group in α-ketoaldehydes suggested that, in the presence of aluminum chloride, these compounds might condense with aromatic hydrocarbons to give benzoins, according to the equation

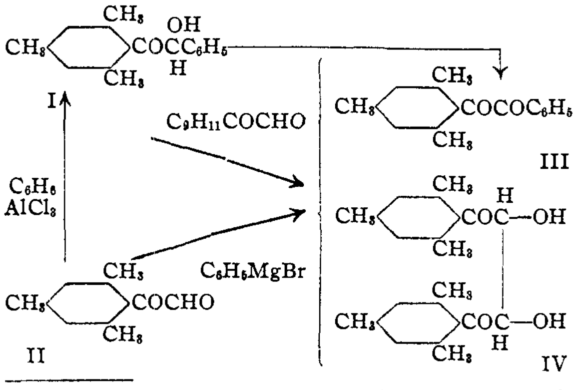
$$\mathrm{RCOCHO + ArH \xrightarrow{AlCl_3} RCOCH(OH)Ar}$$

We have been able to show that this is a general method for the synthesis of benzoins of the type indicated. In view of the fact that the selenium dioxide oxidation method[1] has made α-keto aldehydes readily available, it is felt that the new method of preparing benzoins will prove in many instances to be superior to older methods. A detailed report of the work on this method will be published separately. The work presently reported makes use of the new synthesis in a study of the benzoin, 2',4',6'-trimethylbenzoin (I).

2',4',6'-Trimethylbenzoin (I) was not obtained when mesitylglyoxal (II) was condensed with phenylmagnesium bromide; instead, there resulted a mixture of mesityl phenyl diketone (III) and 1,2-di-(2,4,6-trimethylbenzoyl)-ethylene glycol (IV).[2] To account for this result it was suggested that the bromomagnesium alkoxide may have been oxidized to the diketone by the keto aldehyde, the latter being reduced to the bromomagnesium derivative of the glycol.

$$\mathrm{C_9H_{11}COCH(OMgBr)C_6H_5 + 2C_9H_{11}COCHO \longrightarrow}$$
$$\mathrm{C_9H_{11}COCOC_6H_5 + C_9H_{11}COCH(OMgBr)\underset{COC_9H_{11}}{CH(OH)}}$$

The present work has been carried out in an effort to test this hypothesis.



The benzoin is easily prepared by condensing mesitylglyoxal with benzene in the presence of aluminum chloride. It is very readily converted to the diketone by the action of oxidizing agents. In particular, it is rapidly oxidized in solution by the oxygen of the air. This ease of oxidation seems to offer a satisfactory explanation for the fact that in many attempts to synthesize the benzoin the product was the oxidation product.

Of especial interest, of course, was the action of mesitylglyoxal on the benzoin. It was found that when the benzoin is treated with mesitylglyoxal in benzene solution, reaction occurs and the diketone and the glycol are formed. This result provides an explanation of the fact that the benzoin could not be obtained from mesitylglyoxal and phenylmagnesium bromide.

Another method which was tried in the early attempts to prepare the benzoin was the action of alkali on mesityl phenyl triketone (V). De Neufville and von Pechmann[3] had found that diphenyl triketone was decomposed by alkali to give benzoin, together with benzoic acid, mandelic acid and carbon dioxide. Since we happened to have some mesityl phenyl triketone, it occurred to us that it might react with alkali to give the desired benzoin. As a matter of fact, the products which were isloated were the diketone (VI), 2,4,6-trimethylbenzoic acid (VII) and carbon dioxide.

$$\underset{\mathrm{V}}{\mathrm{C_9H_{11}COCOCOC_6H_5}} \xrightarrow{\mathrm{NaOH}}$$
$$\underset{\mathrm{VI}}{\mathrm{C_9H_{11}COCOC_6H_5}} + \mathrm{CO_2} + \underset{\mathrm{VII}}{\mathrm{C_9H_{11}COOH}}$$

Experimental

Phenyl Mesityl Triketone.—The triketone was made by oxidation of 2,4,6-trimethyldibenzoylmethane, which was prepared by the method of Kohler and Barnes.[4] Ten grams of the diketone was dissolved in 200 cc. of commercial dioxane, and 8.2 g. of selenium dioxide was added. After eight hours of refluxing, the mixture was allowed to cool to room temperature. Hydrogen sulfide was bubbled through the reaction mixture for three hours, and then it was allowed to stand for two hours. The precipitated selenium and sulfur were removed by filtration, and a clear orange-colored solution was obtained. The dioxane was

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[1] Riley, Morley and Friend, *J. Chem. Soc.*, 1875 (1932); "Organic Syntheses," John Wiley and Sons, Inc., 440 Fourth Ave., New York City, 1935, Vol. XV, p. 67.

[2] Gray and Fuson, THIS JOURNAL, **56**, 739 (1934).

[3] De Neufville and von Pechmann, *Ber.*, **23**, 3375 (1890).

[4] Kohler and Barnes, THIS JOURNAL, **55**, 690 (1933).

removed by distillation under diminished pressure; the red oil which remained underwent partial crystallization when treated with a small amount of ligroin. Fractional crystallization (from ligroin) of this material gave 2.6 g. of mesityl phenyl triketone, which is a yellow solid, melting at 90–91°.

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.1; H, 5.71. Found: C, 76.73, 77.04; H, 5.7, 5.96.

In addition to the triketone and a large amount of the red oil (which did not solidify and which could not be distilled) there was obtained 1 g. of an orange-yellow solid, melting at 169–170°. It contained selenium. *Anal.* Found: C, 70.84, 70.87; H, 5.39, 5.77. This compound has not yet been identified.

The Action of Alkali on Mesityl Phenyl Triketone.—Two grams of the triketone was added to 10 cc. of a 10% solution of sodium hydroxide; a reaction occurred and the solution became opaque. The triketone disintegrated, and a new solid formed which melted at 134.5–135.5°, and proved to be mesityl phenyl diketone. The alkaline filtrate was allowed to stand overnight; during this time additional small amounts of the diketone separated. These were removed by filtration, and the solution was acidified by hydrochloric acid. Carbon dioxide was identified by passing the evolved gas into a solution of calcium hydroxide. The acidification of the solution caused the precipitation of an acid which melted at 151–152°, and proved to be 2,4,6-trimethylbenzoic acid.

2 - Phenyl - 3 - (2,4,6 - trimethylbenzoyl) - quinazoline.—Five-tenths of a gram of mesityl phenyl triketone and 0.21 g. of *o*-phenylenediamine were dissolved in 4.5 cc. of hot alcohol. The orange color of the solution faded to a pale yellow, and a colorless crystalline compound separated. The product, after recrystallization from alcohol, was light yellow in color, and melted at 134–134.5°.

Anal. Calcd. for $C_{24}H_{20}ON_2$: N, 7.95. Found: N, 8.07.

2′,4′,6′-Trimethylbenzoin.—To a mixture of 26.6 g. of anhydrous aluminum chloride and 100 cc. of dry benzene contained in a 500-cc., three-necked flask immersed in water at a temperature of 10° was added 17.6 g. of mesitylglyoxal[5] dissolved in 100 cc. of dry benzene. The addition was carried out, with stirring, over a period of two hours. Stirring was continued an additional five hours at room temperature. The mixture was poured slowly into ice and concentrated hydrochloric acid. The benzene layer, containing the benzoin, was removed. The aqueous layer was extracted once with a small amount of benzene. The benzene solution was added to the main portion of the solution. The benzene was removed at 50° by evaporation at diminished pressure. Because of the ease of oxidation of the benzoin, nitrogen instead of air was admitted through the ebulliator tube. The residual yellow liquid was crystallized from 100 cc. of ethyl alcohol. There was obtained 16.1 g. of a colorless substance, melting at 97–99°. The pure compound melted sharply at 102°.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.3; H, 7.08. Found: C, 79.9; H, 7.10.

Urethan Derivative.—One cubic centimeter of phenyl isocyanate was added to 0.5 g. of 2′,4′,6′-trimethylbenzoin dissolved in 20 cc. of high-boiling petroleum ether. The solution was refluxed for four hours, cooled, and filtered. There was obtained a good yield of a white crystalline substance, which, after recrystallization from petroleum ether, melted at 158.5–159°.

Anal. Calcd. for $C_{24}H_{23}O_3N$: C, 77.62; H, 6.20. Found: C, 77.33; H, 6.20.

Oxidation.—One gram of 2′,4′,6′-trimethylbenzoin was added to 40 cc. of glacial acetic acid. Dry air was bubbled through the solution for eight hours at a temperature of 50°. The solution was reduced by evaporation under diminished pressure to a volume of 5 cc., cooled, and the bright yellow solid which crystallized was collected on a filter. The yield of mesityl phenyl diketone (m. p. 133–134.5°) was 0.72 g. A mixed melting point with a known sample of mesityl phenyl diketone showed no depression.

The Action of 2′,4′,6′-Trimethylbenzoin on Mesitylglyoxal.—Five grams of 2′,4′,6′-trimethylbenzoin and 5.6 g. of mesitylglyoxal in 150 cc. of dry benzene were refluxed for four hours. The benzene was removed at 50° under diminished pressure, no ebulliator tube being used. The yellow oil remaining was dissolved in 50 cc. of ethyl alcohol, cooled, and filtered. The crude product melted at 122–127°. Treatment of this with hot, high-boiling petroleum ether left 0.35 g. of a white, insoluble substance, melting at 155–157°. Cooling of the petroleum ether solution yielded 3.6 g. of a bright yellow substance (m. p. 129–132°) which, on purification, was shown (by the mixed melting point method) to be mesityl phenyl diketone. By the same method, the white solid was found to be identical with 1,2-di-(2,4,6-trimethylbenzoyl)-ethylene glycol.

Summary

2′,4′,6′-Trimethylbenzoin was prepared by condensing mesitylglyoxal with benzene in the presence of aluminum chloride. This is a general method for making benzoins.

Attempts to prepare the benzoin by condensing mesitylglyoxal with phenylmagnesium bromide, and by decomposition of mesityl phenyl triketone with alkali, failed; in each case the product was mesityl phenyl diketone.

2′,4′,6′-Trimethylbenzoin is readily converted to the diketone by oxidizing agents.

Mesitylglyoxal oxidizes the benzoin to the benzil, being itself reduced to the pinacol.

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[5] The mesitylglyoxal was prepared by the method of Gray and Fuson [THIS JOURNAL, **56**, 739 (1934)], who report it to be a liquid boiling at 118–119° at 12 mm. It has now been found to have a melting point of 45°.