

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Friedel-Crafts Reaction with Cinnamic, Crotonic, and β -Chlorocrotonic Acids

BY C. F. KOELSCH, HARRY HOCHMANN AND C. D. LE CLAIRE

Benzene reacts with crotonic acid in the presence of aluminum chloride to form β -phenylbutyric acid, and with cinnamic acid to form β,β -diphenylpropionic acid.¹ It has now been found that if three equivalents of aluminum chloride are used to carry out the reactions, they proceed further and lead to 3-methyl- and 3-phenylhydrindones, respectively. The methyl derivative may be isolated in a yield of 81–83%, furnishing a most convenient method for preparing this interesting ketone. The yield of the phenyl derivative is only 35–40%, and for this reason 3-phenylhydrindone is best prepared by isolating β,β -diphenylpropionic acid, converting the acid to its chloride, and cyclizing this.²

The behavior of β -chlorocrotonic acid in the Friedel-Crafts reaction has not been studied previously. With benzene and aluminum chloride this substance gives β,β -diphenylbutyric acid in a yield of 35–38%. The method is shorter and less troublesome than the one previously used³ for preparing β,β -diphenylbutyric acid.

β,β -Diphenylbutyryl chloride has been cyclized to 3-methyl-3-phenylhydrindone.⁴ The preparation is shortened and the yield is improved if the chloride is not isolated, but simply prepared in benzene and treated there with aluminum chloride. This preparation and the conversion of the product into 3-methyl-3-phenylindandione are described in the experimental part of the present paper.

Experimental

3-Phenylhydrindone.—A solution of cinnamic acid (85 g.) in benzene (375 ml.) was added to aluminum chloride (250 g.), and the mixture was boiled for five hours. Worked up in the usual way, the products were β,β -diphenylpropionic acid (33 g., 25%) and 3-phenylhydrindone (47 g., 39%).

3-Methylhydrindone.—A solution of crotonic acid (68 g.) in benzene (500 ml.) was added to aluminum chloride (318 g., 3 eq.) and the mixture was boiled for five hours. There were obtained β -phenylbutyric acid (5 g., 4%) and 3-methylhydrindone (94 g., 81.5%). The latter boiled at 132–137° at 15 mm. (reported,⁵ 118–119° at 11 mm.).

(1) Eijkman, *Chem. Weekblad*, **5**, 655; *Chem. Abs.*, **3**, 779 (1909).(2) Kohler, *Am. Chem. J.*, **31**, 649 (1904).(3) Bergmann, Taubadel and Weiss, *Ber.*, **64**, 1500 (1931).(4) Blum-Bergmann, *ibid.*, **65**, 119 (1932).(5) v. Braun and Kirshbaum, *ibid.*, **46**, 3044 (1913).

Non-distillable tarry material formed the remainder of the product.

The use of more than three equivalents of aluminum chloride gave similar results, but with only two equivalents of the condensing agent there were obtained 29–32% of β -phenylbutyric acid and 50–56% of 3-methylhydrindone.

β,β -Diphenylbutyric Acid.—A mixture of β -chlorocrotonic acid (48 g.), benzene (530 ml.) and aluminum chloride (175 g.) was boiled for fifteen minutes. The complex was decomposed with iced hydrochloric acid, the benzene was steam distilled, and the product was isolated by boiling with sodium carbonate solution. It distilled at 225° at 20 mm, and then weighed 35 g. (36.5%) and had a neutral equivalent of 239 (calcd. 240). The same properties were observed for a sample prepared in a yield of 58% by the addition of benzene to β -methylcinnamic acid (reported³ yield, 40%).

3-Methyl-3-phenylhydrindone.—A solution of β,β -diphenylbutyric acid (50 g.) in benzene (140 ml.) was added to phosphorus pentachloride (60 g.) under 200 ml. of benzene. The mixture was boiled for thirty minutes, then cooled and treated with aluminum chloride (60 g.). The mixture was stirred for one hour, then poured into iced hydrochloric acid. The oil was washed with sodium carbonate solution and distilled, giving 35 g. (78%) of a product which boiled at 194–196° at 15 mm. (reported,⁴ 197–199° at 16 mm.). In one experiment where the mixture was boiled for thirty minutes after the addition of the aluminum chloride, the yield dropped to 58%.

The oxime of 3-methyl-3-phenylhydrindone formed colorless crystals that melted at 167–168°.

Anal. Calcd. for $C_{16}H_{15}NO$: C, 81.0; H, 6.3. Found: C, 81.1; H, 6.5.

Nitrosation of 3-Methyl-3-phenylhydrindone.—A solution of the hydrindone (38 g.) in butyl nitrite (20 g.) and ethanol (75 ml.) was treated with 5 ml. of concd. hydrochloric acid. The temperature of the mixture was allowed to rise to 40–45°, and when heat was no longer evolved, the whole was allowed to remain at room temperature for twelve hours. The product, removed by filtration and crystallized from dilute alcohol, formed faintly yellow crystals (27 g., 63%) that melted at 168–168.5°. A mixture with the oxime described in the preceding paragraph was completely melted at 129°. 2-Isonitroso-3-methyl-3-phenylhydrindone was insoluble in dilute sodium carbonate, but gave a yellow-red solution in dilute sodium hydroxide.

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 76.5; H, 5.2. Found: C, 76.5; H, 5.3.

3-Methyl-3-phenylindandione-1,2.—A mixture of the isonitroso compound (1 g.), acetic acid (10 ml.), water (8 ml.), concd. hydrochloric acid (2 ml.) and pyruvic acid (2 g.) was boiled for thirty minutes. Water was then added to cloudiness, and the mixture was allowed to cool. The diketone crystallized in almost the theoretical amount. Formaldehyde was found to be inferior to pyruvic acid in

carrying out the hydrolysis; the best procedure when it was used consisted in passing hydrogen chloride into a suspension of the isonitroso compound in formalin.

The diketone separated from alcohol in the form of orange plates that melted at 115–116°. The absorption spectrum has been reported.⁵

Anal. Calcd. for C₁₈H₁₈O₂: C, 81.3; H, 5.1. Found: C, 81.4; H, 5.1.

With *o*-phenylenediamine in alcohol, the diketone gave 11-methyl-11-phenylindeno[1,2-*b*]quinoxaline (Ring Index 2517), colorless crystals that melted at 129–130°.

Anal. Calcd. for C₂₂H₁₈N₂: C, 85.7; H, 5.2. Found: C, 85.5; H, 5.2

Suspended in dilute sodium hydroxide and treated with an excess of hydrogen peroxide, the diketone gave α -

(6) Koelsch and Hochmann, *J. Org. Chem.*, **3**, 503 (1938).

methyl- α -phenylhomophthalic acid, which melted at 170–172° after crystallization from ether-ligroin.

Anal. Calcd. for C₁₆H₁₄O₄: C, 71.1; H, 5.2. Found: C, 71.1; H, 5.4.

Summary

In the presence of three equivalents of aluminum chloride, crotonic acid and benzene interact to form 3-methylhydrindone; and cinnamic acid and benzene form 3-phenylhydrindone.

The reaction of benzene with β -chlorocrotonic acid affords a convenient preparation of β,β -diphenylbutyric acid. This acid has been converted into 3-methyl-3-phenylhydrindone and thence into 3-methyl-3-phenylindandione.

MINNEAPOLIS, MINNESOTA RECEIVED NOVEMBER 3, 1942

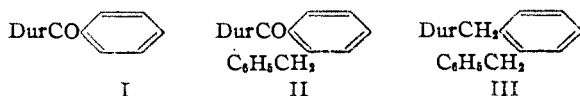
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

para-Alkylation of Benzoyldurene by the Grignard Reagent

BY REYNOLD C. FUSON AND B. C. MCKUSICK¹

The action of phenylmagnesium bromide on certain mesityl ketones has been shown to effect the introduction of a phenyl group into an *ortho* position, presumably by 1,4 addition of the reagent² to the conjugated system formed by the carbonyl group and a double bond of the benzene ring. In an attempt to realize this type of condensation with other hindered ketones it was found that benzylmagnesium chloride could be added to benzoyldurene (I) in a similar manner.

Investigation showed, however, that the product was not the *o*-benzyl derivative (II) which would arise from 1,4 addition of the Grignard reagent. When the new ketone was reduced with sodium and alcohol it yielded not 2'-benzyl-2,3,5,6-tetramethyldiphenylmethane (III) but an isomer of it. This was established by comparison

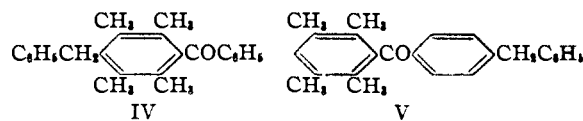


of the ketone and its reduction product with authentic specimens of II and III, respectively.

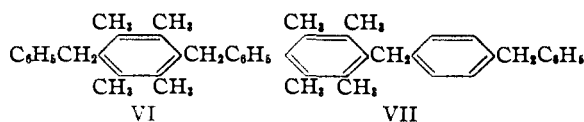
The elimination of the *o*-benzyl ketone (II) as a possibility made it appear probable that the benzyl group had entered one of the *para* positions, yielding 4-benzyl-2,3,5,6-tetramethylbenzophenone (IV) or 4'-benzyl-2,3,5,6-tetramethylbenzophenone (V).

(1) Röhms and Haas Research Assistant.

(2) Fuson, Armstrong and Speck, *J. Org. Chem.*, **7**, 297 (1942).



The first of these possibilities was excluded when it was found that an authentic specimen of dibenzoyldurene (VI) was different from the hydrocarbon obtained by reduction of the original benzylated ketone.



There remained structure V, which proved to be the correct one. This structure was established by synthesis of the ketone from durene and *p*-benzylbenzoyl chloride by the Friedel-Crafts method. It was confirmed by the discovery that the ketone could be cleaved, by heating with sirupy phosphoric acid, to yield durene and *p*-benzylbenzoic acid. It follows that the reduction product is 4'-benzyl-2,3,5,6-tetramethyldiphenylmethane (VII).

The addition of *t*-butylmagnesium chloride was found to take place in a similar manner, yielding 4'-*t*-butyl-2,3,5,6-tetramethylbenzophenone (VIII). This compound was synthesized from

