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

Condensation of *t*-Butylmagnesium Chloride with α,β,β-Triphenylacrylophenone[1]

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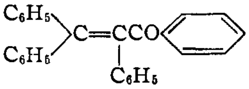
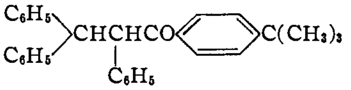
When treated with *t*-butylmagnesium chloride α,β,β-triphenylacrylophenone was found to undergo *t*-butylation in the *para* position of the benzoyl group with simultaneous hydrogenation of the side chain, the product being *p*-(*t*-butyl)-α,β,β-triphenylpropiophenone. The unhydrogenated compound, *p*-(*t*-butyl)-α,β,β-triphenylacrylophenone, was obtained however by exposing the reaction mixture to oxygen previous to decomposition. Dehydrogenation of the saturated ketone occurred, surprisingly, when it was heated with a mixture of acetic anhydride and sodium acetate in an attempt to prepare an enol acetate. The structure of the butylated acrylophenone has been established by two independent syntheses.

The ease with which *t*-butylmagnesium chloride attacks the *para* position of the phenyl ring of duryl phenyl ketone[2] and other similar ketones had led us to examine its behavior toward α,β,β-triphenylacrylophenone (I), which had been found by Kohler and Nygaard, in their classic experiment, to undergo a 1,4-addition reaction with phenylmagnesium bromide that involved the benzoyl group and left the ethylenic bond intact.[3]

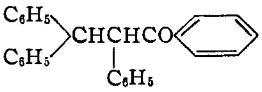
In confirmation of our expectation, the acrylophenone was found to undergo *t*-butylation at the *para* position to give the dihydro derivative of *p*-(*t*-butyl)-α,β,β-triphenylacrylophenone. It was not the dihydrobenzenoid compound that might have been expected, however, but the corresponding triphenylpropiophenone II. The butylated acrylophenone III was obtained when the reaction mixture was exposed to oxygen before it was decomposed.



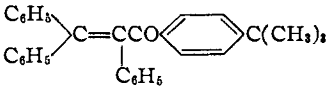
I



II



IV



III

It seemed possible that the saturation of the ethylenic bond might have been the initial step in the process. To test this idea we treated α,β,β-triphenylpropiophenone (IV) with the *t*-butyl reagent. The product proved to be the butylated acrylophenone III, the ethylenic bond having been restored. The dehydrogenation was observed even when all operations were conducted in a nitrogen atmosphere.

In an attempt to prepare an enol acetate the butylated propiophenone II was heated with a mixture of sodium acetate and acetic anhydride. Dehydrogenation occurred instead, giving the butylated acrylophenone III. This unusual reaction served to relate the two butylated products. The structure of the acrylophenone was established by independent syntheses. One of these involved the condensation of *p*-(*t*-butyl)-benzoyl chloride with the Grignard reagent made from triphenylvinyl bromide.

The second method made use of the procedure of Kohler and Nygaard with the exception that a *t*-butyl group was introduced into the benzoyl group of desoxybenzoin, which served as their primary starting material.[3]

Experimental[4]

Condensation of *t*-Butylmagnesium Chloride with α,β,β-Triphenylacrylophenone.—Three and six-tenths grams of the ketone, prepared by the method of Kohler and Nygaard,[3] was dissolved in 15 ml. of benzene, and the solution was added to a Grignard reagent made from 1.2 g. of magnesium, 7 ml. of *t*-butyl chloride and 50 ml. of ether. The reaction mixture, which had a deep orange color, was heated under reflux for 4 hours and poured into a mixture of ice and hydrochloric acid. The *p*-(*t*-butyl)-α,β,β-triphenylpropiophenone, obtained by evaporation of the ether, was a yellow-brown oil, which solidified when absolute ethanol was added, m.p. 185–188.5°. It was purified by repeated recrystallization from cyclohexane, from which it separated as colorless crystals, m.p. 189.5–190.5°, yield 2.63 g. (62%).

Anal.[5] Calcd. for $C_{31}H_{30}O$: C, 88.95; H, 7.22. Found: C, 88.92; H, 7.43.

The infrared spectrum[6] contains bands assignable to a carbonyl group (1685 cm.$^{-1}$), an aromatic system (1500, 1605 cm.$^{-1}$) and a *para* substituted phenyl radical (828 cm.$^{-1}$).

When the reaction time was limited to one hour and air was subsequently bubbled through the mixture for one hour, the product was *p*-(*t*-butyl)-α,β,β-triphenylacrylophenone. It was identified by comparison of infrared spectra and a mixed melting point determination with an authentic specimen.

The acrylophenone was obtained also in an attempt to prepare an enol acetate by heating a mixture of 1.5 g. of anhydrous sodium acetate and 25 ml. of acetic anhydride. The heating, carried out under reflux, was continued for 52 hours and the mixture was poured into 25 ml. of ice-water. The product, a brown solid, was purified by treatment with Norit in boiling alcohol and repeated recrystallization from cyclohexane, m.p. 216°; the yield was low. The infrared spectrum was identical to that of an authentic sample of acrylophenone and a mixed melting point determination with the two samples was not depressed.

A third route to the acrylophenone involved treatment of α,β,β-triphenylpropiophenone with the *t*-butyl reagent. A mixture of 3.62 g. of the ketone, made by the method of Kohler and Mydans,[7] and 20 ml. of ether was added to a Grignard reagent, made from 1.2 g. of magnesium, 7 ml. of *t*-butyl chloride and 50 ml. of ether, and the resulting mixture was heated under reflux for 2 hours. During the second hour air was passed through the reaction flask. The product, isolated in the usual way, was *p*-(*t*-butyl)-α,β,β-triphenylacrylophenone, m.p. 213–214°, yield 1 g. (24%). A mixed melting point with an authentic specimen was not depressed. Also, the two samples had identical infrared spectra. Even when the experiment was carried out in an atmosphere of nitrogen, the product was the acrylophenone.

Synthesis of *p*-(*t*-Butyl)-α,β,β-triphenylacrylophenone from Triphenylvinyl Bromide.—The procedure was similar

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[1] This investigation was supported in part by a grant from the Office of Ordnance Research (Contract No. DA-11-022-ORD-874).

[2] R. C. Fuson and R. Tull, THIS JOURNAL, **71**, 2543 (1949).

[3] E. P. Kohler and E. M. Nygaard, *ibid.*, **52**, 4128 (1930).

[4] All melting points are corrected.

[5] The microanalyses were carried out by Mrs. Lucy Chang, Mrs. Esther Fett and Mr. Joseph Nemeth.

[6] The infrared spectra were recorded and interpreted by Miss Helen Miklas and Mr. James Brader.

[7] E. P. Kohler and W. E. Mydans, THIS JOURNAL, **54**, 4667 (1932).

to that devised by Koelsch.[8] A mixture of 10 g. of triphenylvinyl bromide, 0.8 g. of magnesium and a small crystal of iodine was covered with 100 ml. of ether, and 0.05 ml. of ethyl bromide was added. The mixture, when heated under reflux to start the reaction, assumed a light green color. At the end of 10 minutes 5 ml. of *p*-(*t*-butyl)-benzoyl chloride, prepared from *p*-(*t*-butyl)-benzoic acid[9] by treatment with thionyl chloride,[10] was added. The mixture, which assumed a red color, was heated for 2 hours, and decomposed in the usual manner. Evaporation of the ether from the ether solution left a yellow oil, which crystallized when absolute ethanol was added, m.p. 193–199°. By repeated recrystallization from cyclohexane, the ketone was obtained as a colorless, micro-crystalline solid, m.p. 215.5°, yield 2.0 g. (16%).

Anal. Calcd. for $C_{31}H_{28}O$: C, 89.30; H, 6.78. Found: C, 89.06; H, 7.10.

The infrared absorption spectrum contains bands assignable to a conjugated carbonyl group (1670 cm.$^{-1}$), an aromatic system (1500, 1610 cm.$^{-1}$), a *para*-substituted phenyl radical (821 cm.$^{-1}$) and a *t*-butyl group (847 cm.$^{-1}$).

Alternate Synthesis of *p*-(*t*-(Butyl)-triphenylacrylophenone. 1. Benzyl *p*-(*t*-Butyl)-phenyl Ketone.—The method was similar to that employed for desoxybenzoin.[11] To a mixture of 67 g. of *t*-butylbenzene, prepared by the method of Huston, Fox and Binder,[12] 77.5 g. of phenylacetyl chloride and 400 ml. of carbon disulfide was added, with continuous stirring, 75 g. of anhydrous aluminum chloride. At the end of 20 hours the reaction mixture was poured into an ice–hydrochloric acid mixture. The ketone was isolated as a brown oil, which solidified when treated with methanol, m.p. 43–44°, yield 90 g. (71.3%).

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.66; H, 7.99. Found: C, 85.93; H, 8.08.

2. **α,β-Diphenyl-β-chloro-*p*-(*t*-butyl)-propiophenone.**—From this point the synthesis was patterned after that of Kohler and Nygaard.[3] A solution of 51 g. of benzyl *p*-(*t*-butyl)-phenyl ketone in 23.3 g. of benzaldehyde was cooled in a freezing mixture and hydrogen chloride was passed into it for 7 hours. The solid cake that formed when the mixture was allowed to stand overnight was broken up under ethanol and recrystallized from this solvent, m.p. 196–197°, yield 48.8 g. (65%).

Anal. Calcd. for $C_{25}H_{25}OCl$: C, 79.67; H, 6.69. Found: C, 79.84; H, 6.79.

***p*-(*t*-Butyl)-α,β-diphenylacrylophenone.**—A mixture of 37.65 g. of α,β-diphenyl-β-chloro-*p*-(*t*-butyl)-propiophenone, 26.4 g. of fused potassium acetate, 8.48 g. of sodium carbonate and 300 ml. of methanol was boiled, with constant, vigorous stirring, for 3 hours, cooled and filtered. The solid was washed with sufficient water to remove inorganic salts completely and recrystallized repeatedly from ethanol; m.p. 98.5–100°, yield 24.5 g. (72.3%).

Anal. Calcd. for $C_{25}H_{24}O$: C, 88.19; H, 7.11. Found: C, 88.10; H, 6.97.

***p*-(*t*-Butyl)-α,β,β-triphenylacrylophenone.**—Seventeen grams of *p*-(*t*-butyl)-α,β-diphenylacrylophenone was added to a Grignard reagent made from 13 ml. of bromobenzene, 2.83 g. of magnesium and 50 ml. of ether. The solution was heated for 30 minutes and cooled in a freezing mixture while 17 g. of bromine was added, dropwise and with constant stirring. It was then poured into a mixture of ice and hydrochloric acid and the resulting mixture was shaken until solid began to separate. The ether layer was diluted with petroleum ether and the solid product was washed with water, with a mixture of ether and petroleum ether and finally with petroleum ether alone; m.p. 207–209°, yield 14 g. (56.5%).

The *p*-(*t*-butyl)-α-bromo-α,β,β-triphenylpropiophenone obtained in this way was difficult to purify, apparently because it loses hydrogen bromide readily. It was mixed with an equal weight (12 g.) of fused potassium acetate and 300 ml. of absolute ethanol, and the mixture was boiled for 2 hours with stirring sufficiently rapid to prevent bumping. When the reaction mixture was cooled, a mixture of the unsaturated ketone and potassium chloride separated. Additional amounts of product were obtained by concentration of the mother liquor. After being washed and dried, the compound was recrystallized from cyclohexane, m.p. 215–216°. The yield was very low.

A mixed melting point determination with the sample made by the method of Koelsch showed no depression. Also, the infrared spectra of the two samples were identical.

A slurry of 1.3 g. of the unsaturated ketone in 75 ml. of ether was added to a Grignard reagent made from 1.2 g. of magnesium, 7 ml. of *t*-butyl chloride and 50 ml. of ether and the mixture was stirred for 16 hours. Only starting material was isolated.

URBANA, ILLINOIS

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[8] C. F. Koelsch, THIS JOURNAL, **54**, 2045 (1932).

[9] This acid was kindly supplied by the Shell Chemical Corporation.

[10] R. C. Fuson and R. Tull, THIS JOURNAL, **71**, 2543 (1949).

[11] C. F. H. Allen and W. E. Barker, "Organic Syntheses," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 156.

[12] R. C. Huston, W. B. Fox and M. N. Binder, *J. Org. Chem.*, **3**, 251 (1938).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Diamines and Bicyclic Amines Derived from *cis*-2,5-Bis-(hydroxymethyl)-tetrahydrofuran

BY ARTHUR C. COPE AND BURTON C. ANDERSON

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Bicyclic tertiary amines (VII and VIII) are formed as the major products in the reaction of *cis*-2,5-bis-(hydroxymethyl)-tetrahydrofuran ditosylate (I) with dimethylamine and diethylamine, with elimination of an alkyl group attached to nitrogen in the secondary amines. The expected diamines (VI and IX) also are formed but in smaller amounts. The reactions leading to the bicyclic amines are interpreted as proceeding by an intramolecular alkylation forming a bicyclic quaternary salt XII, a course that is favored as a six-membered ring closure leading to the 8-oxa-3-azabicyclo[3.2.1]octane ring system. The Gabriel phthalimide synthesis proceeded normally in this series, leading from I to 2,5-bis-(aminomethyl)-tetrahydrofuran (V).

The reaction of *cis*-2,5-bis-(hydroxymethyl)-tetrahydrofuran ditosylate (I) with ammonia[1,2] or primary amines[3] results in closure of a six-membered heterocyclic ring by two displacement reactions on the same nitrogen atom, forming 8-oxa-3-azabicyclo[3.2.1]octane (II) or its N-alkyl derivatives (III). The bicyclic ring system of II and III formed so readily that diamines which might be obtained by reaction of the ditosylate I with two equivalents of ammonia or primary amines were not found as by-products, and must have been formed in small amount if at all.

In continuing the study of amines derived from *cis*-2,5-bis-(hydroxymethyl)-tetrahydrofuran, the ditosylate I was treated with potassium phthalimide

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[1] F. H. Newth and L. F. Wiggins, *J. Chem. Soc.*, 155 (1948).

[2] D. J. C. Wood and L. F. Wiggins, *Nature*, **164**, 402 (1949).

[3] A. C. Cope and W. N. Baxter, THIS JOURNAL, **77**, 393 (1955).