

with the cooling bath at  $-25^{\circ}$ . Furan (13.6 g., 0.2 mole) was added dropwise at  $-25^{\circ}$  and stirring was continued for 4 hr. at  $-15^{\circ}$ . The halide (0.2 mole), diluted with an equal volume of tetrahydrofuran, was added. Stirring was continued for 1 hr. at  $-15^{\circ}$  and then the cooling bath was removed. The mixture was allowed to stand overnight. It was poured over crushed ice and the two layers were

separated. The aqueous layer was extracted with ether, and the ether extract was added to the tetrahydrofuran layer. The combined organic layers were dried and fractionated. In this way 19.2 g. (77.4%) of 2-*n*-butylfuran, b.p.  $137^{\circ}$  at 759 mm., was obtained.

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

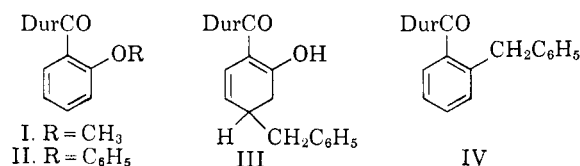
## *p*-Benylation of Duryl *o*-Methoxyphenyl Ketone with the Grignard Reagent<sup>1</sup>

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Duryl *o*-methoxyphenyl ketone and duryl *o*-phenoxyphenyl ketone were found to react with benzylmagnesium chloride to give duryl 2-hydroxy-4-benzyl-3,4-dihydrophenyl ketone. Aromatization of this ketone gave duryl 2-hydroxy-4-benzylphenyl ketone, the structure of which was established by its conversion into duryl 2-phenyl-4-benzylphenyl ketone, which was synthesized by an independent method.

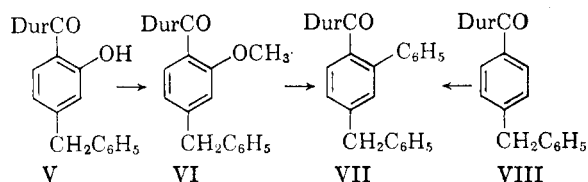
*p*-Alkylation of hindered ketones takes place with a number of Grignard reagents including the *t*-butyl and benzyl reagents.<sup>2,3</sup> In particular, *t*-butylmagnesium chloride has been found to convert duryl *o*-methoxyphenyl ketone (I) into duryl 2-methoxy-4-*t*-butylphenyl ketone.<sup>3</sup> In the present work, the action of benzylmagnesium chloride has been studied; with the methoxy ketone I, however, it gave an unexpected product which proved to be duryl 2-hydroxy-4-benzyl-3,4-dihydrophenyl ketone (III). The same product III was obtained by treatment of duryl *o*-phenoxyphenyl ketone (II) with benzylmagnesium chloride. In either case, ether group displacement occurred to a small extent to give *o*-benzylphenyl duryl ketone (IV).



The dihydro compound III underwent dehydrogenation when heated with a palladium-on-charcoal catalyst to give duryl 2-hydroxy-4-benzylphenyl ketone (V). The infrared spectra of hydroxy ketones III and V both have an absorption band at 1630  $\text{cm}^{-1}$  assignable to a conjugated, hindered, hydrogen-bonded ketone. Methylation of compound V gave duryl 2-methoxy-4-benzylphenyl ketone (VI) in which the carbonyl group absorption band is

raised to 1670  $\text{cm}^{-1}$ , assignable to a conjugated and hindered, but not hydrogen-bonded, ketone.

The structure of the ketone V was established by treating the methylation product VI with phenylmagnesium bromide, which gave duryl 2-phenyl-4-benzylphenyl ketone (VII). This ketone was prepared by an independent synthesis which consisted in conjugate addition of phenyllithium to the known<sup>2</sup> *p*-benzylphenyl duryl ketone (VIII).



Treatment of 2-duroylphenol with *t*-butylmagnesium chloride is known to give duryl 2-hydroxy-4-*t*-butyldihydrophenyl ketone, presumably the 3,4-dihydro derivative.<sup>4</sup> The assigned positions of the double bonds in the dihydro compound III also have not been unequivocally established but are consistent with the nuclear magnetic resonance spectrum of this ketone. A doublet appears at 4.44  $\tau$  assignable to the vinyl proton at the 6-position, the absorption line of which would be expected to be split into a doublet by the vinyl proton at the 5-position. A doublet appears in the region of 4.63  $\tau$  assignable to a vinyl proton at the 5-position, the absorption line of which would be expected to be split by the vinyl proton at the 6-position. Each half of this doublet is split further; this effect would be expected to be caused by the tertiary proton at the 4-position.

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

(2) R. C. Fuson and B. C. McKusick, *J. Am. Chem. Soc.*, **65**, 60 (1943).

(3) R. C. Fuson and B. Vittimberga, *J. Am. Chem. Soc.*, **79**, 6030 (1957).

(4) R. C. Fuson and F. T. Fang, *J. Am. Chem. Soc.*, **77**, 3781 (1955).

EXPERIMENTAL<sup>5</sup>

*Treatment of duryl o-methoxyphenyl ketone with benzylmagnesium chloride.* The Grignard reagent prepared from 2.5 g. (0.02 mole) of benzyl chloride, 0.5 g. (0.02 g.-atom) of magnesium turnings, and 25 ml. of anhydrous ether was added dropwise with stirring to a solution of 4.0 g. (0.015 mole) of duryl *o*-methoxyphenyl ketone<sup>6</sup> in 45 ml. of anhydrous ether and 10 ml. of benzene under a nitrogen atmosphere. The bright red reaction mixture was stirred for 2 hr. and treated with dilute hydrochloric acid solution. The product was taken up in ether, and the solution was washed successively with water, dilute sodium bicarbonate solution, and water. Concentration of the extract and fractional crystallization of the residue from 95% ethanol gave 1.5 g. (29% yield) of duryl 2-hydroxy-4-benzyl-3,4-dihydroxyphenyl ketone, m.p. 112–113.5°. An analytical sample prepared by sublimation melted at 113–114°.

*Anal.* Calcd. for  $C_{24}H_{26}O_2$ : C, 83.20; H, 7.56. Found: C, 83.44; H, 7.77.

A solution of the ketone in acetone rapidly decolorized aqueous potassium permanganate solution and gave a dark blue coloration with aqueous ferric chloride solution. The infrared spectrum (10%,  $CS_2$ ) has bands assignable to a conjugated, hindered, hydrogen-bonded ketone (1630  $cm^{-1}$ ), a monosubstituted phenyl derivative (690, 735  $cm^{-1}$ ), a conjugated ethylenic bond (1610  $cm^{-1}$ ), and a duryl group (870  $cm^{-1}$ ).

The nuclear magnetic resonance spectrum<sup>7</sup> (20%,  $CS_2$ ) has absorption lines assignable to an aromatic proton on a duryl group (3.16  $\tau$ , singlet), a vinyl proton (4.44  $\tau$ , doublet), another vinyl proton (4.63  $\tau$ , doublet with each half split), benzylic and allylic protons (7.36 to 7.50  $\tau$ ), six protons on the two methyl groups at the 2- and 6-positions of the duryl group (7.85  $\tau$ , singlet), and six protons on the two methyl groups at the 3- and 5-positions of the duryl group (8.01  $\tau$ , singlet).

A second fraction crystallized from 95% ethanol to give 0.25 g. (5.1% yield) of *o*-benzylphenyl duryl ketone, m.p. 117.5–119.5°; the melting point of a mixture of this product with an authentic sample<sup>2</sup> was not depressed. The infrared spectra of the two samples are superimposable.

A similar procedure with duryl *o*-phenoxyphenyl ketone<sup>8</sup> in place of the methoxy derivative gave duryl 2-hydroxy-4-benzyl-3,4-dihydroxyphenyl ketone in 68.4% yield and *o*-benzylphenyl duryl ketone in 7.0% yield.

*Dehydrogenation of duryl 2-hydroxy-4-benzyl-3,4-dihydroxyphenyl ketone.* A mixture of 1.5 g. (0.0043 mole) of duryl 2-hydroxy-4-benzyl-3,4-dihydroxyphenyl ketone and 0.15 g. of 10% palladium-on-charcoal was heated at 220–230° for 1 hr. under a slow stream of nitrogen, allowed to cool, and extracted with acetone. The solution was filtered and concentrated. Crystallization of the residue from 95% ethanol gave 0.93 g. (63% yield) of duryl 2-hydroxy-4-benzylphenyl ketone, m.p. 111–112°. An analytical sample was prepared by sublimation.

*Anal.* Calcd. for  $C_{24}H_{24}O_2$ : C, 83.69; H, 7.02. Found: C, 83.79; H, 7.04.

A solution of the product in acetone did not decolorize aqueous potassium permanganate solution and gave a ma-

roon coloration with aqueous ferric chloride solution. The infrared spectrum (10%,  $CS_2$ ) has bands assignable to a conjugated, hindered, hydrogen-bonded ketone (1630  $cm^{-1}$ ), a monosubstituted phenyl derivative (695, 725  $cm^{-1}$ ), a 1,2,4-trisubstituted phenyl derivative (975  $cm^{-1}$ ), and a duryl group (870  $cm^{-1}$ ).

*Methylation of duryl 2-hydroxy-4-benzylphenyl ketone.* Preliminary attempts to methylate this ketone by dissolution in methanolic sodium hydroxide followed by the addition of methyl iodide gave starting material. Success was achieved, however, by the Purdie method. A mixture of 0.668 g. (0.00194 mole) of duryl 2-hydroxy-4-benzylphenyl ketone, 1.1 g. of dry silver oxide, and 100 g. of methyl iodide was heated under reflux for 12 hr. The reaction mixture was allowed to cool, and filtered. Concentration of the filtrate and crystallization of the residue from methanol gave 0.669 g. (96.5% yield) of duryl 2-methoxy-4-benzylphenyl ketone, m.p. 105–107°. The infrared spectrum (10%,  $CS_2$ ) has bands assignable to a conjugated hindered ketone (1670  $cm^{-1}$ ), a monosubstituted phenyl derivative (705, 750  $cm^{-1}$ ), and a duryl group (875  $cm^{-1}$ ).

*Duryl 2-phenyl-4-benzylphenyl ketone from duryl 2-methoxy-4-benzylphenyl ketone.* The Grignard reagent prepared from 3.92 g. (0.025 mole) of bromobenzene, 0.61 g. (0.025 g.-atom) of magnesium turnings, and 50 ml. of anhydrous ether was placed in a dropping funnel; 15 ml. of the reagent was added dropwise with stirring to a solution of 0.395 g. (0.0011 mole) of duryl 2-methoxy-4-benzylphenyl ketone in 10 ml. of benzene under a nitrogen atmosphere. The reaction mixture was heated under reflux with continued stirring for 1 hr., and then hydrolyzed with dilute hydrochloric acid solution; the product was taken up in ether, and the solution was washed with water and concentrated. The residue was chromatographed over 20 g. of alumina. Elution with 15 to 20% ether in cyclohexane gave an oil that crystallized from methanol to give 0.206 g. (46% yield) of duryl 2-phenyl-4-benzylphenyl ketone, m.p. 117–118°; the melting point of a mixture of this product with that obtained from conjugate addition of phenyllithium to *p*-benzylphenyl duryl ketone was not depressed. An analytical sample was prepared by recrystallization from ethanol.

*Anal.* Calcd. for  $C_{30}H_{28}O$ : C, 89.07; H, 6.98. Found: C, 89.18; H, 7.13.

The infrared spectrum (10%,  $CS_2$ ) has bands assignable to a conjugated hindered ketone (1675  $cm^{-1}$ ), a monosubstituted phenyl derivative (705, 765  $cm^{-1}$ ), and a duryl group (875  $cm^{-1}$ ).

*Duryl 2-phenyl-4-benzylphenyl ketone from p-benzylphenyl duryl ketone.* A solution of 4.97 g. (0.0151 mole) of *p*-benzylphenyl duryl ketone<sup>2</sup> in 25 ml. of benzene was added dropwise with stirring over a period of 45 min. to a solution of phenyllithium prepared in a nitrogen atmosphere from 9.6 g. (0.061 mole) of bromobenzene, 0.84 g. (0.122 g.-atom) of lithium wire, and 30 ml. of anhydrous ether. The reaction mixture was stirred for an additional hour and poured into a mixture of ice and hydrochloric acid. The products were taken up in ether, and the solution was washed with water and concentrated. The residue was chromatographed over 250 g. of alumina. Elution with 30% ether in cyclohexane gave a mixture that, when fractionally crystallized from ethanol, gave 0.32 g. (5.2% yield) of duryl 2-phenyl-4-benzylphenyl ketone, m.p. 115–117°. The infrared spectrum of this product is superimposable on that of the product obtained by treatment of duryl 2-methoxy-4-benzylphenyl ketone with phenylmagnesium bromide. The same chromatographic fraction gave 1.1 g. of an unidentified solid, m.p. 195–200°. The infrared spectrum (5%,  $CS_2$ ) has bands assignable to a conjugated hindered ketone (1690  $cm^{-1}$ ), a monosubstituted phenyl derivative (695, 750  $cm^{-1}$ ), and a duryl group (875  $cm^{-1}$ ). Elution with 50% ether in cyclohexane gave 1.62 g. of another unidentified solid, m.p. 190–193°. The melting point of a mixture of this product with the material melting at 195–200° was depressed to 170°. The infrared spectrum (5%,  $CS_2$ ) has bands assignable to a conjugated hindered

(5) All melting points are uncorrected. The microanalyses were performed by Miss Mary Ann Weatherford and Mr. Gary D. Callahan. The infrared spectra were determined with a Perkin-Elmer Model 21 B spectrophotometer by Mr. Paul E. McMahan, Mr. William Dalton, Mr. Keith J. Sims, and Miss Dorothy Wood.

(6) R. C. Fuson and R. O. Kerr, *J. Org. Chem.*, **19**, 373 (1954).

(7) The nuclear magnetic resonance spectrum was determined by Mr. Oliver W. Norton with a Varian high resolution spectrometer (Model V-4300 B with superstabilizer) at 60 mc. with tetramethylsilane as an internal standard.

(8) R. C. Fuson and W. S. Friedlander, *J. Am. Chem. Soc.*, **76**, 4989 (1954).

ketone (1667  $\text{cm}^{-1}$ ), a monosubstituted phenyl derivative (692, 755  $\text{cm}^{-1}$ ), and a duryl group (870  $\text{cm}^{-1}$ ).

*Conversion of duryl 2-hydroxy-4-benzyl-3,4-dihydrophenyl ketone into 2,4-dibenzylphenyl duryl ketone.* The Grignard reagent prepared from 3.52 g. (0.028 mole) of benzyl chloride, 0.68 g. (0.028 g.-atom) of magnesium turnings, and 50 ml. of anhydrous ether was placed in a dropping funnel; 20 ml. of the reagent was added dropwise with stirring to a solution of 1.0 g. (0.0029 mole) of duryl 2-hydroxy-4-benzyl-3,4-dihydrophenyl ketone in 20 ml. of anhydrous ether under a nitrogen atmosphere. The reaction mixture was heated under reflux for 1 hr., and stirring was continued for 12.5 hr. After hydrolysis with dilute hydrochloric acid solution, the product was taken up in ether, and the solution washed with water and concentrated; 1.0 g. (79% yield) of a  $\text{C}_{21}\text{H}_{24}\text{O}_2$  compound precipitated as colorless crystals, m.p. 206.5–208°, dec. An analytical sample melted at 210–210.5°.

*Anal.* Calcd. for  $\text{C}_{21}\text{H}_{24}\text{O}_2$ : C, 84.89; H, 7.81. Found: C, 84.75; H, 7.74.

A mixture of 0.35 g. (0.0008 mole) of the product ( $\text{C}_{21}\text{H}_{24}\text{O}_2$ ) and 0.06 g. of 10% palladium-on-charcoal was heated at 250–275° for 1 hr. under a slow stream of nitrogen, allowed to cool, and extracted with acetone. The solution was filtered and concentrated. Crystallization of the residue from methanol and water solution gave 0.054 g. (16% yield) of 2,4-dibenzylphenyl duryl ketone, m.p. 93–95°. The melting point of a mixture of this ketone with an authentic sample<sup>9</sup> was not depressed. The intermediate compound (m.p. 210–210.5°) undergoes not only dehydrogenation when heated with palladium-on-charcoal but loses the elements of water as well; in it the hydroxyl group and one of the benzyl groups are *ortho* to the ketone group. Whether they are attached to the same carbon atom or not has not been established.

URBANA, ILL.

(9) R. C. Fuson, J. P. Freeman, and J. J. Looker, *J. Org. Chem.*, **26**, 4217 (1961).

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

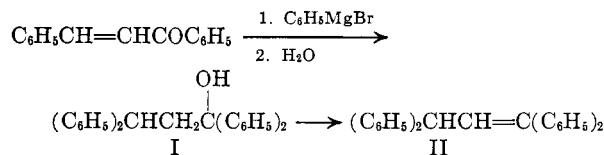
## Condensation of Benzalacetophenone with Phenylmagnesium Bromide. 2-Benzhydryl-2-hydroxy-3,3-diphenylpropionic Acid<sup>1</sup>

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1,1,3,3-Tetraphenyl-1-propanol (I) was formed by treating benzalacetophenone with a large amount of phenylmagnesium bromide and decomposing the reaction mixture with water. When the reaction mixture was poured on solid carbon dioxide, 2-benzhydryl-3-hydroxy-3,3-diphenylpropionic acid (IV) was produced.

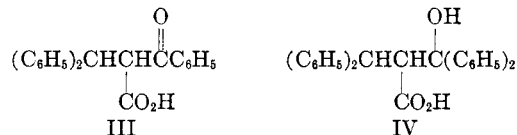
When the reaction mixture obtained by the treatment of benzalacetophenone with large amounts of phenylmagnesium bromide was hydrolyzed, 1,1,3,3-tetraphenyl-1-propanol (I), a *di-addition* product, was obtained accompanied by the 1,4-addition product,  $\beta,\beta$ -diphenylpropiophenone. Dehydration of the propanol by the use of acetic anhydride or a glacial acetic acid–hydrochloric acid mixture afforded 1,1,3,3-tetraphenylpropene (II). This propene had been made also by Vorländer and Siebert.<sup>3</sup>



*p*-Chlorobenzalacetophenone was found to undergo a similar condensation when treated with large amounts of phenylmagnesium bromide. Dehydration of the resulting carbinol gave 1,1,3,3-triphenyl-3-*p*-chlorophenylpropene. The structure of this propene was proved by synthesis. The olefin was made by adding phenylmagnesium bromide to

$\beta$ -*p*-chlorophenyl- $\beta$ -phenylpropiophenone and dehydrating the carbinol that was produced.

Treatment of benzalacetophenone with large amounts of the phenyl reagent followed by pouring the reaction mixture on solid carbon dioxide gave, in addition to  $\alpha$ -benzhydrylbenzoylacetic acid (III), an acid (in low yield) that corresponds to the addition of two moles of the Grignard reagent to the unsaturated ketone followed by carbonation. The acid has now been identified as 2-benzhydryl-3-hydroxy-3,3-diphenylpropionic acid (IV).



When a solution of the acid IV in ethanol was treated with hydrochloric acid, dehydration took place accompanied by decarboxylation, and 1,1,3,3-tetraphenylpropene (II) was isolated as the product. The formation of this hydrocarbon indicated that the acid IV probably was a  $\beta$ -hydroxy acid; such acids are known to undergo this type of reaction.<sup>4</sup> The methyl ester, prepared with the aid of diazomethane, was stable to long heating in acetic anhydride.

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

(2) State Scholar of the Government of the Union of Burma, 1954–1957.

(3) D. Vorländer and C. Siebert, *Ber.*, **39**, 1024 (1906).

(4) D. S. Noyce, P. A. King, and G. L. Woo, *J. Org. Chem.*, **26**, 632 (1961).