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

Displacement of Substituents in Phenyl 2,4,6-Triisopropylphenyl Ketone by the Action of Grignard Reagents[1]

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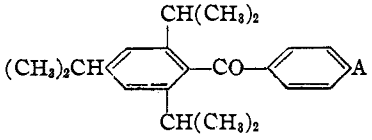
A number of derivatives of phenyl 2,4,6-triisopropylphenyl ketone have been prepared which have substituents in the *p*-position of the phenyl group. The derivatives having methoxyl, cyano and acetoxyl groups suffer displacement of these groups when treated with *t*-butylmagnesium chloride, the product in each case being *p*-*t*-butylphenyl 2,4,6-triisopropylphenyl ketone. The methoxy and cyano derivatives are converted to *p*-benzylphenyl 2,4,6-triisopropylphenyl ketone by the action of the benzyl reagent. Mesityl and duryl *p*-methoxyphenyl ketones react with the *t*-butyl reagent to give the corresponding *p*-*t*-butylphenyl ketones.

The purpose of the present investigation was to extend the study of nucleophilic displacement by Grignard reagents[2] to the 2,4,6-triisopropylphenyl ketones. The original hope, that the triisopropylphenyl group might be more favorable to this type of reaction than is mesityl or duryl, has in general not been realized. The derivatives that have been prepared are of type I in which A = CN, OCH$_3$, OH or OCOCH$_3$.



I

The cyano and methoxy compounds were made by condensing 1,3,5-triisopropylbenzene with the appropriate *p*-substituted benzoyl chlorides. When *p*-acetoxybenzoyl chloride was used, in an effort to prepare the acetoxy ketone (I, A = OCOCH$_3$), the phenolic ketone (I, A = OH), the hydrolysis product of the expected acetate, was isolated instead. This phenol could be acetylated or methylated to yield the acetoxy or methoxy ketone (I, A = OCH$_3$), respectively. Deliberate hydrolysis of the acetoxy compound or demethylation of the methyl ether regenerated the phenol.

The nitrile reacted with *t*-butyl- and benzylmagnesium chlorides to give the corresponding *t*-butyl [I, A = (CH$_3$)$_3$C] and benzyl (I, A = C$_6$H$_5$CH$_2$) derivatives, respectively. Previously displacement of the nitrile function had been effected by the action of the methyl and benzyl reagents[3] on *p*-cyanophenyl duryl ketone and by the interaction of 4-cyanoquinoline and the ethyl reagent.[4]

The acetoxy derivative, when treated with *t*-butylmagnesium chloride, gave the corresponding *t*-butyl ketone [I, A = (CH$_3$)$_3$C] in a yield of 56%.

The most noteworthy result in this series was the displacement of the methoxyl group by the action of *t*-butyl and benzylmagnesium chlorides. Attempts to displace an unflanked methoxyl group in the *p*-position had previously failed in the mesityl and duryl series.[5] These unsuccessful attempts involved the benzyl reagent, and it seemed possible that the more powerful *t*-butyl reagent might be effective. Experiment confirmed this surmise; displacement was observed in each instance.

The yields of *t*-butylation products obtained by methoxyl group displacement in the mesityl, duryl and *p*-triisopropylphenyl series were, respectively, 88, 78 and 54%.

Experimental

Mesityl *p*-Methoxyphenyl Ketone.—To a solution of 85.3 g. of anisoyl chloride and 70 g. of mesitylene in 500 ml. of carbon disulfide was added slowly (over a period of about 30 minutes) 75 g. of anhydrous aluminum chloride. After the addition was complete the mixture was stirred at room temperature until evolution of hydrogen chloride had ceased (1 to 5 hours) and poured into an iced dilute hydrochloric acid solution. After removal of the carbon disulfide, the crude product was isolated by filtration and recrystallized from methanol. The mesityl *p*-methoxyphenyl ketone melted at 77.5–79°; yield 69%. A mixture melting point with an authentic specimen showed no depression.[5]

***p*-Methoxyphenyl 2,4,6-Triisopropylphenyl Ketone.**—By the procedure described above, this ketone was produced in 72% yield, and, after recrystallization from methanol, it melted at 111–112°.

Anal.[6] Calcd. for C$_{23}$H$_{30}$O$_2$: C, 81.61; H, 8.93. Found: C, 81.68; H, 9.09.

***p*-Cyanophenyl 2,4,6-Triisopropylphenyl Ketone.**—Condensation of *p*-cyanobenzoyl chloride and 1,3,5-triisopropylbenzene by the usual method produced the crude ketone in 80% yield. After several recrystallizations from ethanol it melted at 142.5–143.5°.

Anal. Calcd. for C$_{23}$H$_{27}$ON: C, 82.85; H, 8.15; N, 4.19. Found: C, 82.75; H, 8.15; N, 4.23.

***p*-Hydroxyphenyl 2,4,6-Triisopropylphenyl Ketone.**—*p*-Acetoxybenzoyl chloride was condensed with 1,3,5-triisopropylbenzene by the Friedel–Crafts procedure; *p*-hydroxyphenyl 2,4,6-triisopropylphenyl ketone was produced in 44% yield.

The hydroxy ketone was made also by heating the methoxy ketone for 18 hours under reflux with a slight excess of 55% hydriodic acid in a large excess of glacial acetic acid. The product, isolated by the usual procedures, was obtained in 95% yield and, after recrystallization from a mixture of 60% methanol and 40% ethanol, melted at 224–225.5° dec.

***p*-Acetoxyphenyl 2,4,6-Triisopropylphenyl Ketone.**—Heating the *p*-hydroxy ketone with acetic anhydride for 30 minutes produced the *p*-acetoxy ketone in a 61% yield. After recrystallization from ethanol it melted at 87.5–88.5°. The infrared spectrum[7] shows absorption peaks at 1662 and 1737 cm.$^{-1}$, which are usually assignable to hindered carbonyl and ester groups, respectively. Hydrolysis of the *p*-acetoxy ketone in base produced the original *p*-hydroxy ketone.

General Procedure for the Treatment of *p*-Substituted Hindered Diaryl Ketones with Grignard Reagents.—An ethereal solution, containing five moles of Grignard reagent,

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(1) Supported in part by the Office of Ordnance Research under Contract No. DA-11-022-ORD-874, Project Designation TB2-0001 (567).

(2) For the preceding paper in this series see R. C. Fuson and W. D. Emmons, THIS JOURNAL, **73**, 5175 (1951).

(3) R. C. Fuson, W. D. Emmons and R. Tull. *J. Org. Chem.*, **16**, 648 (1951).

(4) P. Rabe and R. Pasternack, *Ber.*, **46**, 1026 (1913).

(5) R. C. Fuson and R. Gaertner, *J. Org. Chem.*, **13**, 496 (1948).

(6) The microanalyses were performed by Mr. Joseph Nemeth, Mrs. Katherine Pih, Mrs. Esther Fett and Mrs. Lucy Chang.

(7) Determined and interpreted by Miss Helen Miklas.

TABLE I

Hindered ketone	Grignard reagent	Product	Melting point, °C.	Yield, %	Analyses, % Calcd. C	H	Found C	H
p-Tip$\overset{O}{C}$–C_6H_4–CN[a]	t-C_4H_9MgCl	p-Tip$\overset{O}{C}$–C_6H_4–$C(CH_3)_3$	115.5–116.8	45	85.65	9.95	85.60	9.88
p-Tip$\overset{O}{C}$–C_6H_4–CN	C_6H_5–CH_2MgCl	p-Tip$\overset{O}{C}$–C_6H_4–$CH_2C_6H_5$	119.5–120.5	35	87.39	8.60	87.15	8.54
p-Tip$\overset{O}{C}$–C_6H_4–OCH_3	t-C_4H_9MgCl	p-Tip$\overset{O}{C}$–C_6H_4–$C(CH_3)_3$[b]	114.5–115.5	54				
p-Tip$\overset{O}{C}$–C_6H_4–OCH_3	C_6H_5–CH_2MgCl	p-Tip$\overset{O}{C}$–C_6H_4–$CH_2C_6H_5$[b]	118–120	9				
p-Dur$\overset{O}{C}$–C_6H_4–OCH_3	t-C_4H_9MgCl	p-Dur$\overset{O}{C}$–C_6H_4–$C(CH_3)_3$[b]	125.5–126.5	78				
p-Mes$\overset{O}{C}$–C_6H_4–OCH_3	t-C_4H_9MgCl	p-Mes$\overset{O}{C}$–C_6H_4–$C(CH_3)_3$[c]		88	85.67	8.63	85.40	8.68
p-Tip$\overset{O}{C}$–C_6H_4–$O\overset{O}{C}CH_3$	t-C_4H_9MgCl	p-Tip$\overset{O}{C}$–C_6H_4–$C(CH_3)_3$[b]	115.5–116.8	56				
p-Tip$\overset{O}{C}$–C_6H_4–$O\overset{O}{C}CH_3$	C_6H_5–CH_2MgCl	No displacement prod.						

[a] Tip = 2,4,6-triisopropylphenyl radical; Dur = 2,3,5,6-tetramethylphenyl radical; Mes = 2,4,6-trimethylphenyl radical. [b] A mixed melting point with an authentic sample showed no depression. [c] B.p. 143–150° (0.25 mm.); $n^{20}D$ 1.5638. The infrared spectrum of this material was identical with that of an authentic sample obtained by treating mesitylene with p-t-butylbenzoyl chloride. A trinitro derivative made by adding the ketone, dissolved in petroleum ether, to fuming nitric acid at 0° melted at 200–201.5° dec. *Anal.* Calcd. for $C_{20}H_{21}N_3O_7$: C, 57.83; H, 5.10; N, 10.12. Found: C, 57.86; H, 5.30; N, 10.13.

to each mole of ketone to be employed, was filtered through a glass wool plug into refluxing ether. Then the p-substituted hindered diaryl ketone, dissolved in benzene, was added during 5 to 10 minutes. The mixture generally developed a dark red-brown color, which gradually faded to a light tan in 30 minutes to 5 hours, indicating the reaction had gone to completion. Decomposition was accomplished by pouring the reaction mixtures into iced dilute hydrochloric acid. After the organic layer had been dried, the solvent was removed by evaporation. The resulting light yellow viscous oils could be induced to crystallize from methanol, and the products were then recrystallized from ethanol. The results are shown in Table I.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Friedel–Crafts Alkylation of Aromatic Compounds with Vinyl Sulfones[1]

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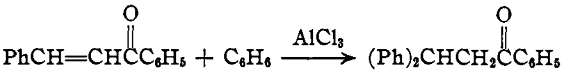
Methyl ω-styryl sulfone in the presence of 97% sulfuric acid alkylates benzene and toluene to give β,β-diphenylethyl methyl sulfone and β-phenyl-β,p-tolylethyl methyl sulfone, respectively. Under the same conditions ω-styryl p-tolyl sulfone alkylates toluene to give β-phenyl-β,p-tolylethyl p-tolyl sulfone. Methyl vinyl sulfone does not alkylate toluene, benzene, m-xylene or mesitylene under the conditions studied.

Vinyl ketones have been used to alkylate aromatic compounds under Friedel–Crafts conditions.[2] However, similar reactions with vinyl sulfones



$$PhCH{=}CH\overset{\overset{O}{\|}}{C}C_6H_5 + C_6H_6 \xrightarrow{AlCl_3} (Ph)_2CHCH_2\overset{\overset{O}{\|}}{C}C_6H_5$$

do not appear to have been reported previously. During a study of the conversion of ω-styrenesulfonyl chloride (I) to α,β-unsaturated sulfones, equations 1 and 2

$$C_6H_5CH{=}CHSO_2Cl + C_6H_6 \xrightarrow{AlCl_3} C_6H_5CH{=}CHSO_2C_6H_5 \quad (1)$$

$$C_6H_5CH{=}CHSO_2Cl + C_7H_8 \xrightarrow{AlCl_3} C_6H_5CH{=}CHSO_2C_6H_4CH_3\text{-}p \quad (2)$$

the formation of β-phenyl-β,p-tolylethyl p-tolyl sulfone (III) was observed in the aluminum chloride-catalyzed reaction of the sulfonyl chloride I with toluene at reflux temperature. The structure of product III was established by the following independent synthesis.

$$p\text{-}CH_3C_6H_4(C_6H_5)C{=}CH_2 + p\text{-}C_7H_7SH \xrightarrow{(C_6H_5CO)_2O_2} p\text{-}CH_3C_6H_4(C_6H_5)CHCH_2SC_7H_7\text{-}p \xrightarrow{H_2O_2} \underset{III}{p\text{-}CH_3C_6H_4(C_6H_5)CHCH_2SO_2C_7H_7\text{-}p}$$

Product III may have been formed by the condensation of toluene with the sulfone II which is prepared in good yield when I is treated with toluene at room temperature.[3] This hypothesis is supported by the observation that when II[4] is treated with toluene in the presence of 97% sulfuric acid, III is obtained in good yield.

The aluminum chloride-catalyzed condensation of methyl ω-styryl sulfone, prepared from sodium ω-styrenesulfinate, with toluene at room temperature for 59 hours or with benzene at reflux tempera-

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[1] Taken from Mr. Simms's and Mr. Hill's M.S. Theses.

[2] "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 236–237.

[3] The reaction of ω-styrenesulfonyl chloride with toluene to give the *trans*-sulfone also was reported recently by A. P. Terent'ev, R. A. Gracheva and Z. F. Shcherbatova, *Doklady Akad. Nauk S.S.S.R.*, **84**, 975 (1952); *C. A.*, **47**, 3262 (1953).

[4] E. P. Kohler and H. A. Potter, THIS JOURNAL, **57**, 1316 (1935).