

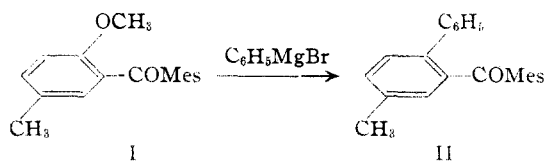
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

***ortho* Alkylation and Arylation of Mesityl Aryl Ketones**

BY REYNOLD C. FUSON AND S. B. SPECK

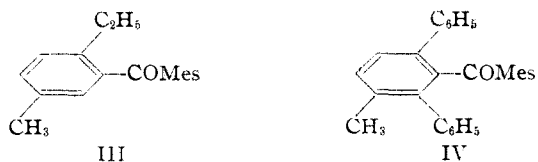
The action of aryl Grignard reagents on mesityl aryl ketones<sup>1</sup> and aryl mesitoates<sup>2</sup> has been shown to bring about *ortho* arylation. The change evidently involves 1,4 addition followed by oxidation of the addition product, although the manner in which the latter transformation occurs has not been determined. It amounts to the elimination of a molecule of hydrogen from the dihydrobenzenoid compound or its enol form.

A method has now been discovered whereby the arylation can be effected smoothly and in high yields. It consists simply in the use of mesityl *o*-methoxyaryl ketones. An example is the conversion of 2-methoxy-5-methylbenzoylmesitylene (I) to 2-phenyl-5-methylbenzoylmesitylene (II) by the action of phenylmagnesium bromide.



The reaction proceeded readily and in good yield at room temperature.

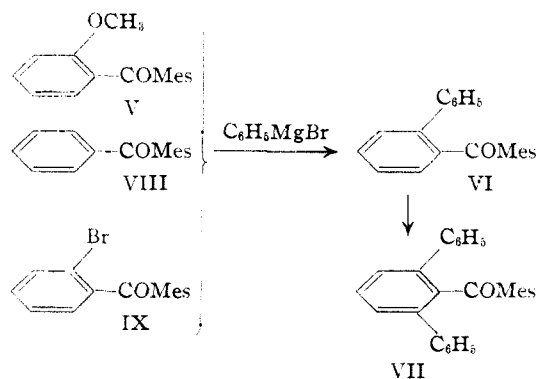
*ortho*-Alkylation could be effected also. When ethylmagnesium bromide was used the product was 2-ethyl-5-methylbenzoylmesitylene (III).



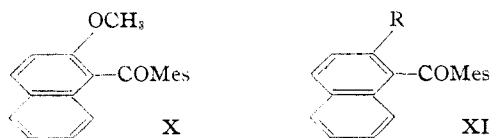
As was to be expected, phenylmagnesium bromide at higher temperatures brought about diphenylation to produce 2,6-diphenyl-3-methylbenzoylmesitylene (IV).

Similar results were obtained with 2-methoxybenzoylmesitylene (V). One or two phenyl groups could be introduced, the products being VI and VII, respectively. The monophenyl derivative (VI) had been obtained, though in lower yield, by the action of phenylmagnesium bromide on benzoylmesitylene (VIII).<sup>1</sup> It is significant that the 2-bromo derivative (IX) yielded the diphenylated ketone, VII. Presumably, this transforma-

tion involves the monophenyl ketone (VI) as an intermediate.

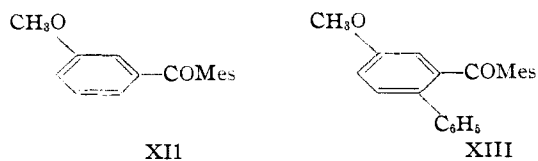


The conversion of the methoxyl compound (V) to the monophenyl ketone takes place much more readily than the introduction of the second phenyl group, *i. e.*, the transformation of VI to VII. The two processes are evidently dissimilar in nature. In order to simplify the study of the replacement of methoxyl groups, the investigation was extended to 1-mesityl-2-methoxynaphthalene (X) which has no second *ortho* position. This ketone reacted smoothly with phenylmagnesium bromide to yield 1-mesityl-2-phenylnaphthalene (XI). R = C<sub>6</sub>H<sub>5</sub>.



In a similar manner methyl, ethyl, *n*-butyl and  $\alpha$ -naphthyl groups were introduced by use of the appropriate Grignard reagents. The yields varied from 56 to 80%.

An attempt to replace a methoxyl group in a meta position was unsuccessful. 3-Methoxybenzoylmesitylene (XII) reacted with phenylmagnesium bromide to yield a methoxy compound, which probably has the structure represented by XIII.

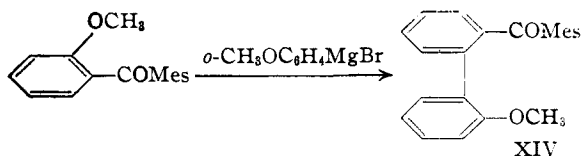


(1) Fuson, Armstrong and Speck, *J. Org. Chem.*, **7**, 297 (1942).

(2) Fuson, Bottorff and Speck, *THIS JOURNAL*, **64**, 1430 (1942).

This is in contrast to the action of phenylmagnesium bromide on V, the ortho isomer of XII, to produce *o*-phenylbenzoylmesitylene (VI).

The new reaction served to establish the structure of 2-(2-methoxyphenyl)-benzoylmesitylene (XIV) reported previously.<sup>2</sup> It was found possible to obtain it by condensing 2-methoxybenzoylmesitylene with *o*-methoxyphenylmagnesium bromide.



The new method for introducing alkyl and aryl radicals into an aromatic ring appears to depend on 1,4 addition of the Grignard reagent followed by the elimination of the elements of methanol. The ether is a vinylog of methyl mesitoate and would, therefore, be expected to react with the Grignard reagent in an analogous manner. This suggests also the alternate possibility that the replacement of the methoxyl group might be the result of simple metathesis.

### Experimental<sup>3</sup>

**1-Mesityl-2-methoxynaphthalene (X).**—A solution of 76 g. of mesitoyl chloride in 90 cc. of carbon disulfide was added slowly to a mixture of 75 g. of  $\beta$ -naphthyl methyl ether, 63 g. of aluminum chloride and 150 cc. of carbon disulfide. The mixture was stirred at room temperature for about twelve hours and then treated with an ice-hydrochloric acid mixture. The organic layer was separated and washed with dilute sodium hydroxide solution and water. The solvent was removed by evaporation, and the solid product, 1-mesityl-2-methoxynaphthalene, was recrystallized from ethanol. The yield of 1-mesityl-2-methoxynaphthalene was 65 g. The ketone crystallized from alcohol in yellow plates; m. p. 109–110°.

*Anal.* Calcd. for C<sub>27</sub>H<sub>20</sub>O<sub>2</sub>: C, 82.57; H, 6.95. Found: C, 82.97; H, 6.49.

**2-Methoxy-5-methylbenzoylmesitylene (I).**—This compound was prepared by the Friedel-Crafts method in a manner similar to the foregoing. From 36.6 g. of 4-methylanisole and 54.6 g. of mesitoyl chloride was obtained 54 g. of the methoxy ketone. It crystallized from ethanol as light green needles; m. p. 103°.

*Anal.* Calcd. for C<sub>18</sub>H<sub>20</sub>O<sub>2</sub>: C, 80.55; H, 7.52. Found: C, 80.63; H, 7.44.

***m*-Methoxybenzoylmesitylene.**—This ketone was prepared from *m*-methoxybenzoyl chloride and mesitylene by the Friedel-Crafts method. The yield was 58% of the theoretical. The compound separated from ethanol as colorless crystals; m. p. 76°.

(3) Micronalyses by Miss Margaret McCarthy and Miss Theta Spoor.

*Anal.* Calcd. for C<sub>17</sub>H<sub>18</sub>O<sub>2</sub>: C, 80.29; H, 7.10. Found: C, 80.15; H, 7.36.

***o*-Methoxybenzoylmesitylene (V).**—The Grignard reagent prepared from 14 g. of magnesium and 85 g. of *o*-bromoanisole in 250 cc. of dry ether was added slowly, with stirring, to a solution of 72 g. of mesitoyl chloride in 200 cc. of dry ether. Heat was generated and a white precipitate formed. The mixture became semi-solid when all the reagent had been added. It was decomposed with dilute acid and washed with successive portions of water, dilute sodium hydroxide, and more water. The solvent was removed by evaporation and the residue crystallized from alcohol. The yield was 30 g. of *o*-methoxybenzoylmesitylene, which separated from ethanol in light yellow-green crystals; m. p. 112–113°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>18</sub>O<sub>2</sub>: C, 80.29; H, 7.10. Found: C, 80.15; H, 7.23.

**Action of Grignard Reagents on Mesityl *o*-Methoxyaryl Ketones.**—The experimental procedures for the reactions are very similar and can be indicated by a detailed description of two representative procedures.

**2-Methoxy-5-methylbenzoylmesitylene and Phenylmagnesium Bromide.**—A solution of 13.4 g. of 2-methoxy-5-methylbenzoylmesitylene in 60 cc. of dry benzene was added slowly to the reagent prepared from 3 g. of magnesium and 16.0 g. of bromobenzene in 30 cc. of dry ether and the mixture was heated under reflux for eight hours. The temperature remained at about 60°. The color of the solution changed successively to green, deep blue and, finally, dark red. The reaction mixture was treated with cold dilute hydrochloric acid. The organic layer was washed with dilute acid and water and the solvent removed by evaporation. The viscous red oil was distilled under reduced pressure. About 3.5 g. of a solid was isolated from a fraction of the distillate. This substance crystallized from alcohol in colorless needles. It had the composition of 2,6-diphenyl-3-methylbenzoylmesitylene (IV).

Table I lists this and five other condensations that were carried out in a similar manner with 2-methoxybenzoylmesitylene and 2-methoxy-5-methylbenzoylmesitylene. Yields, melting points and analytical data are given for the products.

**1-Mesityl-2-methoxynaphthalene and Ethylmagnesium Bromide.**—A solution of 7.6 g. of 1-mesityl-2-methoxynaphthalene in 25 cc. of dry ether was added over a period of ten minutes to the reagent prepared from 1.2 g. of magnesium and 4.2 g. of ethyl bromide in 30 cc. of dry ether and 20 cc. of dry benzene. The stirring was continued for an additional fifteen minutes. The color of the reaction mixture became pale green and later changed to orange-red. A large amount of a white precipitate formed. The mixture was treated with an ice-hydrochloric acid mixture and the organic layer washed with water. The solvent was removed by evaporation and the solid residue taken up with alcohol and allowed to crystallize. A yield of 6 g. of 1-mesityl-2-ethylnaphthalene was obtained. This substance separated from aqueous alcohol in colorless crystals.

This and four other condensations are shown in Table II. Melting points, yields and analytical data are given for the products.

TABLE I

Reactants		Temp. of reaction, °C.	Product <sup>a</sup>		M. p., °C.	Yield, %	Analyses, %			
R in formula	Grignard reagent		Substituted benzoylmesitylene				Calcd.	Found	Calcd.	Found
H	C <sub>6</sub> H <sub>5</sub> MgBr	30	2-Phenyl <sup>1</sup>		89	35	...	...	...	...
H	C <sub>6</sub> H <sub>5</sub> MgBr	60	2,6-Diphenyl <sup>b</sup>		162	20	89.32	6.43	89.74	6.44
H	<i>o</i> -CH <sub>2</sub> OC <sub>6</sub> H <sub>4</sub> MgBr	60	2-(2-Methoxyphenyl) <sup>2</sup>		94	47	...	...	...	...
CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> MgBr	30	2-Phenyl-5-methyl-		73	18	87.84	7.07	87.82	7.20
CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> MgBr	60	2,6-Diphenyl-5-methyl-		131	20	89.18	6.71	89.50	6.87
CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub> MgBr	30	2-Ethyl-5-methyl-		58	28	85.65	8.34	85.77	7.93

<sup>a</sup> The products were purified by recrystallization from ethanol. <sup>b</sup> This compound was obtained in 2.5% yield by the action of phenylmagnesium bromide on *o*-bromobenzoylmesitylene. It was also formed in traces by the condensation of phenylmagnesium bromide with 2-phenylbenzoylmesitylene.

TABLE II

## REACTIONS OF 1-MESITOYL-2-METHOXYNAPHTHALENE

Grignard reagent	Temp. of the reaction, °C.	Product		Analyses, %					
		Substituted 1-mesitylnaphthalene	M. p., °C.	Yield, %	Calcd.	Found	Calcd.	Found	
C <sub>6</sub> H <sub>5</sub> MgBr	60	2-Phenyl <sup>a</sup>	136	59	89.09	6.34	88.64	6.35	
$\alpha$ -C <sub>10</sub> H <sub>7</sub> MgBr	30	2- $\alpha$ -Naphthyl <sup>2,b</sup>	181	76					
CH <sub>3</sub> MgI	30	2-Methyl <sup>a,c</sup>	67	56	87.47	7.01	87.56	7.17	
C <sub>2</sub> H <sub>5</sub> MgBr	30	2-Ethyl <sup>a</sup>	90	80	87.36	7.34	87.47	7.21	
<i>n</i> -C <sub>4</sub> H <sub>9</sub> MgBr	30	2- <i>n</i> -Butyl <sup>a</sup>	73	55	87.22	7.93	86.96	7.79	

<sup>a</sup> Recrystallized from ethanol. <sup>b</sup> Recrystallized from a mixture of benzene and ethanol. <sup>c</sup> 1-Mesityl-2-methylnaphthalene was prepared also from 2-methyl-1-naphthoyl chloride and mesitylene by the Friedel-Crafts method and by the condensation of 2-methyl-1-naphthoyl chloride with mesitylmagnesium bromide. These syntheses were carried out by Mr. B. C. McKusick.

**Action of Phenylmagnesium Bromide on *m*-Methoxybenzoylmesitylene.**—A solution of 6.4 g. of *m*-methoxybenzoylmesitylene in 50 cc. of dry benzene was added to a solution of Grignard reagent prepared from 1.5 g. of magnesium, 8.0 g. of bromobenzene and 25 cc. of dry ether. The mixture was heated for eight hours under reflux, during which time it developed a red-brown color. Decomposition in the usual manner and distillation of the product yielded 0.5 g. of a solid that, after recrystallization from petroleum ether (b. p. 60–120°), melted at 194–195° (cor.). It was probably 2-phenyl-5-methoxybenzoylmesitylene.

*Anal.* Calcd. for C<sub>23</sub>H<sub>22</sub>O<sub>2</sub>: C, 83.59; H, 6.72. Found: C, 83.59; H, 7.02.

## Summary

It has been found that when 2-methoxyaryl mesityl ketones are treated with a Grignard reagent the methoxyl group is smoothly replaced by the hydrocarbon radical of the Grignard reagent. The reaction occurs with either alkyl or aryl Grignard reagents.

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