[Contribution from the Noyes Chemical Laboratory, University of Illinois]

THE REACTION OF ARYLLITHIUM COMPOUNDS WITH HINDERED DIARYL KETONES

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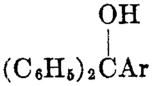
The synthesis of triarylcarbinols containing radicals such as mesityl is difficult because of the hindrance provided by such groups to the types of condensation that might serve. The only example of the class, in fact, is diphenylmesitylcarbinol, prepared by the reaction of mesitylmagnesium bromide with benzophenone (1).

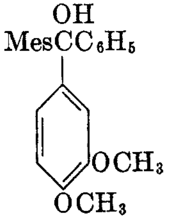
Since organolithium compounds exhibit a greater tendency than Grignard reagents to add to α,β-unsaturated carbonyl compounds in the 1,2 manner (2), it seemed probable that aryllithium compounds might produce carbinols from hindered diaryl ketones which undergo *ortho*-arylation with phenylmagnesium bromide (3).

Experiments with phenyl-, mesityl- and duryl-lithium have made possible the synthesis of a number of new carbinols containing one mesityl or duryl radical. Duryl- and mesityl-lithium combine with benzophenone to yield duryldiphenyl- (I) and mesityldiphenyl-carbinol (II), respectively.

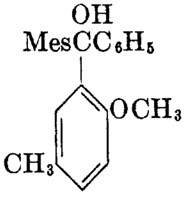


$$(C_6H_5)_2\overset{\overset{\large OH}{|}}{C}Ar$$

I Ar = (Dur)
II Ar = (Mes)



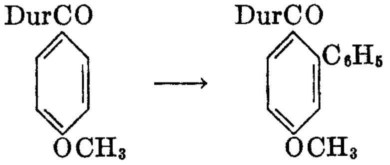
III



IV

Phenyllithium reacts with mesityl 3,4-dimethoxyphenyl ketone and mesityl 2-methoxy-5-methyl ketone to yield, respectively, 3,4-dimethoxyphenylmesitylphenylcarbinol (III) and mesityl-2-methoxy-5-methylphenylphenylcarbinol (IV). The yields of III and IV are 18% and 57%, respectively.

This type of behavior proved not to be general, however. Duryl 4-methoxyphenyl ketone (V) and mesityl 3-methoxyphenyl ketone (VII), for example, are phenylated in an *ortho*-position by phenyllithium, yielding the dihydro derivatives of VI (52.5% yield) and VIII (7.5% yield), respectively.



V VI

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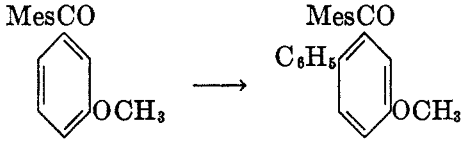
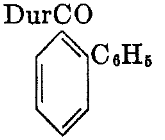
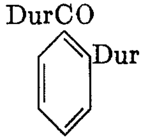


VII VIII

In a similar way duryl phenyl ketone reacted with phenyllithium to give duryl 2-phenylphenyl ketone (IX) in a 28% yield and with duryllithium to produce duryl 2-durylphenyl ketone (X) in a 40% yield.



IX



X

Reaction of mesityl- and phenyl-lithium with dimesityl ketone, which cannot undergo arylation in an *ortho*-position, had been shown by Faber and Nauta not to yield carbinols (4). It is to be noted that duryllithium, not previously reported, can be made satisfactorily by treatmentof bromodurene with lithium.

EXPERIMENTAL[2]

Arylation of p-anisyl duryl ketone with phenyllithium. To a solution of phenyllithium prepared from 23.6 g. of bromobenzene and 2.1 g. of lithium metal in 75 ml. of ether was added a solution of 10 g. of the ketone (5) in 50 ml. of benzene over a period of 30 minutes. A slight warming was observed and a brown color developed. Stirring was continued for one hour and the mixture was poured on ice. The solvent layer was washed with water three times, then with hydrochloric acid, again with water, and finally dried over sodium sulfate. Distillation of the solvents left 19 g. of red-brown, viscous material, which was dissolved in methanol. The solution deposited 6.85 g. (52.5%) of duryl 2-phenyl-4-methoxy-1,2-dihydrophenyl ketone; m.p. 137–139° (corr.). It crystallized from ethanol in white plates, m.p. 140.5–141° (corr.).

Anal. Calc'd for $C_{24}H_{26}O_2$: C, 83.20; H, 7.56; Mol. wt., 346.

Found: C, 83.05; H, 7.65; Mol. wt. (ebullioscopic in benzene), 333.

The compound reacted with a solution of potassium permanganate in water and acetone within ten minutes. Dehydrogenation was accomplished by heating 1 g. of the material with 0.1 g. of a palladium-on-charcoal catalyst (10%) at 300–325° for 25 minutes and finally at 350° for five minutes. A solution of the mixture in ethanol was filtered and cooled; 0.35 g. of crystals separated; m.p. 141–143° (corr.). Duryl 2-phenyl-4-methoxyphenyl ketone separated from methanol in white crystals; m.p. 146.5–147.5° (corr.). It did not react with potassium permanganate.

Anal. Calc'd for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02.

Found: C, 83.53; H, 7.25.

3,4-Dimethoxyphenyl mesityl ketone. This ketone has been prepared previously (6) by condensing veratroyl chloride with mesitylene by the Friedel-Crafts method. It was prepared in higher yield from mesitoyl chloride and catechol dimethyl ether by the same type of reaction. A solution of 46.0 g. of the acid chloride in 100 ml. of carbon disulfide was added with mechanical stirring to a mixture of 33.4 g. of catechol dimethyl ether, 32.2 g. of alumi-

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[2] Microanalyses by Miss Rachel Kopel and Miss Emily Davis; infrared absorption data and interpretations by Miss Elizabeth Petersen and Mrs. J. L. Johnson.

num chloride, and 150 ml. of the solvent over a period of 20 minutes and stirring continued for four hours. The mixture was decomposed with cold dilute hydrochloric acid, and the solvent layer was washed with water and 10% sodium hydroxide solution. The solvent was removed by distillation; there was obtained, after recrystallization of the residue from ethanol, 56.3 g. (80%) of product; m.p. 103–104°. The pure ketone melted at 105–106°. The mixture melting point with the product obtained from veratroyl chloride and mesitylene showed no depression.

Reaction of 3,4-dimethoxyphenyl mesityl ketone and phenyllithium. A solution of 6 g. of the ketone in 25 ml. of benzene was added over a period of 15 minutes to a reagent prepared from 13.2 g. of bromobenzene and 1.2 g. of lithium in 50 ml. of ether. After being stirred for an additional hour, the purple mixture was decomposed in the usual manner. There was obtained from methanol 1.5 g. (18%) of light yellow powder; m.p. 189–192° (uncorr.). 3,4-Dimethoxyphenylmesitylphenylcarbinol crystallized from a mixture of benzene and methanol, then from ethyl acetate as white sandlike crystals; m.p. 201–202° (corr.). It did not react with a solution of potassium permanganate in acetone and water.

Treatment of the carbinol with bromine in carbon tetrachloride gave only tar. The infrared absorption spectra of this compound and that of the one obtained by the reaction of phenyllithium and mesityl 2-methoxy-5-methylphenyl ketone reveal several features of their structures. Both samples possess hydroxyl absorptions at 3550 cm.$^{-1}$ and show the absence of carbonyl absorption. The rather high hydroxyl frequency is further evidence for the carbinol structure since Coggeshall (7) has found a similar frequency for highly hindered phenols. Aromatic double-bond absorptions occur around 1500 and 1600 cm.$^{-1}$, but there is total absence of non-aromatic double-bond absorption. The presence of the mesityl, phenyl, and 1,2,4-trisubstituted phenyl groups is indicated by absorptions at 860, 706, and 810 cm.$^{-1}$, respectively.

Independent synthesis of 3,4-dimethoxyphenylmesitylphenylcarbinol. A solution of 9.0 g. of 3,4-dimethoxybenzophenone (8) in 75 ml. of ether was added over a period of 30 minutes to a reagent prepared from 28.5 g. of bromomesitylene and 2.2 g. of lithium in 75 ml. of ether. The mixture turned a slight brown and a precipitate began to form. The mixture was poured on ice, and the precipitate was washed with water. The product weighed 13.2 g. (96%), m.p. 201–202°. The pure carbinol melts at 202–203°. The mixture melting point with the product obtained above showed no depression.

Anal. Calc'd for $C_{24}H_{26}O_3$: C, 79.85; H, 7.23.
Found: C, 79.91; H, 7.39.

Reaction of 2-methoxy-5-methylphenyl mesityl ketone and phenyllithium. To a solution of phenyllithium, prepared from 7.1 g. of bromobenzene and 0.6 g. of lithium in 25 ml. of ether, was added over a period of 30 minutes a solution of 6 g. of the ketone (9) in 25 ml. of. ether. The mixture turned red-brown and became warm. When one-half of the ketone had been added a voluminous white precipitate began to form, the mixture becoming very viscous at the end of the addition. After being stirred for an additional 90 minutes at room temperature, the mixture was worked up as usual. Removal of the solvent left a very deep brown residue. Methanol was added and 4.4 g. (57% yield) of rust-colored crystals separated; m.p. 141–144° (corr.). Mesityl-2-methoxy-5-methylphenylphenylcarbinol separated from a mixture of benzene and methanol in light yellow plates; m.p. 149–149.5° (corr.).

Anal. Calc'd for $C_{24}H_{26}O_2$: C, 83.20; H, 7.56.
Found: C, 83.22; H, 7.61.

The infrared absorption spectrum of this compound is almost identical with that of the product from 3,4-dimethoxyphenyl mesityl ketone, discussed above.

Reaction of mesityl m-methoxyphenyl ketone and phenyllithium. A solution of 4.5 g. of the ketone (9) in 25 ml. of ether was added over a period of 20 minutes to the reagent prepared from 11.2 g. of bromobenzene and 1 g. of lithium in 50 ml. of ether. A brown color developed and the mixture refluxed gently. The usual procedures gave 8.7 g. of an amber oil which precipitated 0.45 g. (7.5%) of yellow crystals; m.p. 182–186° (corr.). The compound was recrystallized twice from high-boiling petroleum ether and again from a mixture of benzene and methanol. It formed needles melting at 189.5–191° (corr.). It did not depress the melting point of a sample of mesityl 2-phenyl-5-methoxyphenyl ketone prepared from the same ketone by the action of phenylmagnesium bromide and found to melt at 190–192° (corr.)(9).

Arylation of duryl phenyl ketone with phenyllithium. The reaction was carried out in a manner similar to that employed in the addition of phenyllithium to the previous ketones. A solution of 18.5 g. of duryl phenyl ketone in 75 ml. of benzene was added over a period of 30 minutes to a solution of phenyllithium prepared from 2.1 g. of lithium and 23.6 g. of bromobenzene in 100 ml. of ether in a nitrogen atmosphere. The mixture was stirred mechanically at room temperature during the addition and for 2 additional hours. The solution turned red initially but began to darken with stirring. The mixture was decomposed in the usual manner and the organic layer evaporated to dryness. An oil remained which failed to deposit crystals from methanol, ethanol, or benzene. The oil was distilled *in vacuo* and the fraction of b.p. 220–230°/2 mm. collected. The crude duryl 2-biphenyl ketone was recrystallized from ethanol; m.p. 130–133°; yield 7.2 g. (28%). The pure ketone melted at 134–135°.

Anal. Calc'd for $C_{23}H_{22}O$: C, 87.86; H, 7.06.
Found: C, 87.88; H, 7.14.

Independent synthesis of duryl 2-biphenyl ketone: duryl o-methoxyphenyl ketone and phenylmagnesium bromide (9). A solution of 8.5 g. of duryl *o*-methoxyphenyl ketone[3] in 40 ml. of dry ether and 15 ml. of dry benzene was added over a period of 15 minutes to the reagent prepared from 1.55 g. of magnesium and 10 g. of bromobenzene in 50 ml. of ether. A noticeable reaction occurred and the color of the solution became successively blue, green, light brown, and finally blue again. After addition of the ketone, the mixture was stirred for an additional 90 minutes and then decomposed in an ice-hydrochloric acid mixture. The organic layer was washed with water three times, once with sodium bicarbonate, and again with water. Evaporation of the solvent left the duryl 2-biphenyl ketone as an oil. It was recrystallized from methanol, m.p. 133–134°; yield 3 g. A mixture melting point with the product obtained from duryl phenyl ketone and phenyllithium melted at 133–134°.

Arylation of duryl phenyl ketone with duryllithium. The reaction was carried out in accordance with the directions for the preparation of duryl 2-biphenyl ketone. To 20 g. of bromodurene dissolved in 200 ml. of ether was added, with stirring, 1.42 g. of lithium. Stirring was continued for 2 hours, after which much of the lithium remained unchanged. To the mixture was added 10 g. of duryl phenyl ketone over a period of 1 hour. A red-brown color resulted, and stirring was continued for 2 additional hours. After recrystallization from ethanol the product, duryl 2-durylphenyl ketone, melted at 191–192°. The yield was 6.8 g. (43%).

Anal. Calc'd for $C_{27}H_{30}O$: C, 87.52; H, 8.16.
Found: C, 87.85; H, 8.27.

Preparation of biphenylmesitylcarbinol. A solution of 10 g. of benzophenone in 75 ml. of ether was added to an ether solution of mesityllithium prepared from 2.8 g. of lithium and 40 g. of bromomesitylene. The formation of mesityllithium took place very slowly and the reaction was not complete when the ketone was added. The complex was decomposed without washing with dilute hydrochloric acid. The crude carbinol was recrystallized from ethanol; m.p. 88–90°; yield 11.2 g. (68%). The pure compound melted at 90–91°.

Anal. Calc'd for $C_{22}H_{22}O$: C, 87.38; H, 7.34.
Found: C, 87.33; H, 7.41.

Preparation of biphenyldurylcarbinol. A solution of 15 g. of benzophenone was added to a solution of duryllithium prepared from 1.42 g. of lithium and 20 g. of bromodurene dissolved in 200 ml. of absolute ether. The mixture was stirred for 3 hours and poured on ice. The product was washed three times with water, the organic layer dried over sodium sulfate,

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[3] This ketone was prepared in an 89% yield from *o*-bromophenyl duryl ketone by refluxing for 14 hours in a 5 *N* solution of sodium methoxide in methanol (10).

the solvent removed, and the crude alcohol recrystallized from ethanol; m.p. 139–140°; yield 16 g. (62%).

Anal. Calc'd for $C_{22}H_{24}O$: C, 87.30; H, 7.64.
Found: C, 87.01; H, 7.72.

Reaction of 2,6-dimethoxyphenyl mesityl ketone with phenyllithium. Treatment of 2.5 g. of the ketone (11) with phenyllithium as described above yielded 3 g. of a light brown oil. It could not be induced to crystallize from the usual solvents.

Reaction of 2,2′,4,4′-tetramethylbenzophenone and mesityllithium. Addition of a solution of 10 g. of the ketone (12) to mesityllithium prepared from 1.95 g. of lithium and 28 g. of bromomesitylene caused the solution to develop a brown color, which gradually changed to blue. The solution was stirred for an additional 90 minutes after the ketone was added. The reaction mixture was decomposed with ice. Usual procedures yielded 4.4 g. (30%) of white crystals which were recrystallized from methanol; m.p. 148° with development of a blue color.

Anal. Calc'd for $C_{26}H_{30}O$: C, 87.10; H, 8.43.
Found: C, 86.84; H, 8.28.

An attempt to prepare the methyl ether of the above carbinol failed. A deep blue solution resulted when pyridine was added to extract the hydrochloric acid. This behavior was found to be characteristic of this compound. The white carbinol turns red in hydrochloric acid and very dark red in sulfuric acid. When the solution is made basic with dilute sodium hydroxide a blue solution results. A blue compound (m.p. 172–173°) was isolated which had the same composition as the white carbinol.

Anal. Calc'd for $C_{26}H_{30}O$: C, 87.10; H, 8.43.
Found: C, 87.05; H, 8.59.

The white carbinol, 2,2′,4,4′-tetramethylbiphenylmesitylcarbinol, was stable in pyridine and dilute sodium hydroxide. However, if a drop of hydrochloric acid was added to the carbinol in basic solution, a blue color resulted. When the solution was made acid a red color was obtained. This compound appears to behave as a true indicator and in acid or base has the characteristics of a dye.

SUMMARY

The action of phenyl-, mesityl-, and duryl-lithium with various diaryl ketones has been studied. Five triarylcarbinols were prepared in which one of the aryl groups is mesityl or duryl. Two hindered ketones containing methoxy groups were found to yield carbinols, whereas two others underwent arylation at an *ortho*-position.

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