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CONJUGATE BIMOLECULAR REDUCTION OF HINDERED KETONES INVOLVING REPLACEMENT OF METHOXYL GROUPS

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It has been shown that when mesityl phenyl ketone is treated with the binary mixture, $Mg + MgI_2$ (1), bimolecular reduction occurs linking two phenyl rings at ortho positions (2). This reaction is analogous to nuclear alkylation of hindered ketones by Grignard reagents (3) and suggested that the presence of an ortho methoxyl group might facilitate the bimolecular coupling. Experiment bore out this idea. When an equimolar mixture of mesityl phenyl ketone and its o-methoxy derivative was subjected to the action of the binary mixture, the hydroxy ketone (I) was obtained in three times as high a yield as from the unsubstituted ketone alone.¹



The reductive coupling of an o-methoxy ketone with an unsubstituted ketone was carried out with three other pairs, shown in Table I. Pairs b and c yield products corresponding to II and IIa, respectively. The two isomers give the same hydrocarbon (III) when reduced.



¹ In this paper Mes and Dur are used to represent mesityl and duryl, respectively.

The location of the hydroxyl and carbonyl groups in these coupling products (II and IIa) was established by reduction with hydriodic acid to the isomeric ketones, IV and IVa. Ketone IV was synthesized in a manner analogous to that employed for the corresponding dimesityl ketone (2).



The identity of this sample of ketone IV with that obtained by reduction of the hydroxy ketone (II) shows that, in the reductive coupling, the carbonyl group of the methoxy ketone is the precursor of the carbinol group of the keto alcohol.

KETONES	CRYSTAL FORM (solvent)	VIELD, %	м.р., °С.	MOLECULAR FORMULA	ANALYSIS			
					Calc'd		Found	
					С	н	С	Н
(a) MesCO	Hexagonal plates (Ethyl	28	239–240	$\mathrm{C}_{32}\mathrm{H}_{32}\mathrm{O}_2$	85.68	7.19	85.71	7.17
(b) MesCO	Prisms (Ethyl acetate)	25	202–203	$C_{33}H_{34}O_2$	85.67	7.41	85.40	7.43
$\begin{array}{c} \text{DurCOC}_{\$}\text{H}_{\$} \\ \text{(c) } \text{DurCO} \overbrace{OCH_{\$}} \\ \text{MesCOC}_{\$}\text{H}_{\$} \end{array}$	Prisms (Ethyl acetate)	24	187-188	C33H34O2	85.67	7.41	85.46	7.63
(d) DurCO OCH ₃ DurCOC ₆ H ₅	Long Prisms (Tolu- ene)	23	262–263	C34H36O2	85.67	7.61	85.85	7.84

TABLE I KETO ALCOHOLS PREPARED FROM HINDERED KETONES

The facile formation of a keto alcohol by the elimination of a methoxyl group and the relationship between the methoxyl-containing ketone and the carbinol group subsequently formed, suggest a mechanism by which the reaction may take place. The coupling of two dissimilar hindered molecules involving the elimination of a methoxyl group is reminiscent of the familiar nuclear alkylation of a hindered ketone by a Grignard reagent. It has been proposed that the

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bimolecular reduction of a ketone by the binary mixture proceeds by way of a ketyl (1). It has also been shown that a free radical may be acted upon by the binary mixture to form a Grignard reagent (4). Therefore, it is possible that the initially formed ketyl which is a resonance hybrid of V and the *ortho* free radical (Va) may undergo reduction to form either of two Grignard reagents (VI and VIa).



In the formation of the hydroxy ketone, IIa, for example, it may be imagined that duryl *o*-methoxyphenyl ketone is attacked by the enolate (Grignard reagent), VIa, the coupling being accompanied by the elimination of the elements of CH₃OMgI. The enolate, VII, might be expected to behave as an alkoxide ion of which it is a vinylog. By analogy to the hydroxyl-carbonyl group equilibria (5), the hydrogen atom at the *ortho* position involved in the coupling would be transferred to the carbonyl carbon atom as a hydride ion, producing the alkoxide ion, VIII.



Actually, the isomerization would be expected to have a much greater driving force than the reactions of the usual hydroxylcarbonyl equilibria, since it involves aromatization of a benzene ring. A further example of bimolecular reduction involving the replacement of the methoxyl group is afforded by the action of the binary mixture on mesityl *o*-methoxyphenyl ketone alone. Under slightly

different conditions two products have been isolated. One product is presumably the biphenyl derivative (IX) which easily loses the elements of water to form what is believed to be the phenanthrene derivative (X). The other product has



definitely been shown to be the phenanthrene derivative (XI). This hydrocarbon was oxidized to the known 2,2'-dimesitoylbiphenyl (XII).



EXPERIMENTAL²

Reduction of the four pairs of compounds shown in Table I was carried out in a manner similar to that described for the reduction of mesityl phenyl ketone (2). An equimolar mixture of a hindered ketone and a hindered o-methoxy ketone in toluene was slowly added to the colorless magnesium-iodine binary mixture. The yield of the dimesityl keto alcohol (I) by this method was 28% as compared to a maximum yield of 10.5% obtained by reduction of the mesityl phenyl ketone alone. No other products could be isolated from the resinous material left in the mother liquor.

Mesityl o-methoxyphenyl ketone. This ketone was prepared in an 88% yield by heating a mixture of o-bromophenyl mesityl ketone (6) with a 5 N solution of sodium methoxide for 24 hours under reflux (7).

Reduction of the keto alcohols (II and IIa). A. With sodium and alcohol. The keto alcohols from pairs b and c were reduced to the same hydrocarbon (III) by the method previously mentioned (2) in yields of 45%. Crystallized from acetone or ethyl acetate, the hydrocarbon melted at 230-232°.

Anal. Calc'd for C33H36: C, 91.61: H, 8.39.

Found: C, 91.58; H, 8.62.

A mixture melting point of the samples of the hydrocarbon from the two different keto alcohols showed no depression.

B. With hydriodic acid. By use of the previously reported method (2) the keto alcohols (II and IIa) were reduced to the corresponding isomeric ketones (IV and IVa) with hydriodic acid in acidic acid. The keto alcohol (IIa) from pair c gave a ketone which crystallized from ethyl acetate as clusters of needles; m.p. 221-222°.

Anal. Calc'd for C22H34O: C, 88.76; H, 7.68.

Found: C, 88.46; H, 7.74.

The ketone (IV) obtained from pair b was shown by the method of mixture melting points to be identical with the product described in the following section.

Alternate synthesis of the ketone (IV). In a manner entirely analogous to the previously described preparation (2), the Grignard reagent from 14.5 g. of o-bromophenylmesityl-

² The microanalyses were performed by Miss Emily Davis and Miss Rachel Kopel.

methane was condensed with 10.0 g. of duryl *o*-methoxyphenyl ketone. The resulting ketone, crystallized from ethyl acetate, was obtained in a yield of 8.2 g., or 49%; m.p. 209-210°.

Anal. Calc'd for C33H34O: C, 88.76; H, 7.68.

Found: C, 88.64; H, 7.81.

Bimolecular reduction of mesityl o-methoxyphenyl ketone. By means of the previously described method (2), 36 g. of mesityl o-methoxyphenyl ketone was treated with the binary mixture prepared from 20 g. of magnesium powder and 40 g. of iodine in the toluene-butyl ether solvent. After the red solution had been heated under reflux for eight hours, it was decanted free from the unchanged magnesium and decomposed by pouring into a mixture of 2 l. of ether, 2 l. of crushed ice, and 200 ml. of concentrated hydrochloric acid. After the organic layer had been washed with water, sodium thiosulfate solution, and sodium bicarbonate solution, evaporation of the solvent *in vacuo* left a red oil which was induced to crystallize by the addition of alcohol. The yield of crude 9, 10-dimesitylphenathrene was 6.28 g. or 10.5%. Recrystallization from toluene raised the melting point to $245-246^{\circ}$ ($249-250^{\circ}$ corr.).

Anal. Calc'd for C32H30: C, 92.70; H, 7.28.

Found: C, 93.03; H, 7.09.

The structure of this hydrocarbon was established by treatment of 0.51 g. with 1.5 g. of chromium trioxide in 5 ml. of glacial acetic acid at 90° for one-half hour. The reaction mixture was poured into water and the product extracted with ether. The ether layer was washed with water and dilute sodium bicarbonate solution. Evaporation of the solvent left 0.15 g. (27% yield) of 2,2'-dimesitoylbiphenyl; m.p. 225-227°.

Anal. Calc'd for C₃₂H₃₀O₂: C, 86.06; H, 6.77.

Found: C, 85.83; H, 7.05.

A mixture melting point with an authentic sample (8) showed no depression.

From several runs of the reduction of mesityl o-methoxyphenyl ketone an alcohol was isolated. This product, which had been isolated by Speck (9), was obtained in yields as high as 22%. Recrystallization from methanol or high-boiling petroleum ether gave a pure material, m.p. 195.0-196.5°.

Anal. Calc'd for C33H34O2: C, 85.67; H, 7.41.

Found: C, 85.78; H, 7.34.

Infrared analysis³ indicated the presence of a hydroxyl group. The ultraviolet spectrum was characteristic of a biphenyl system. When an attempt was made to form the acetyl derivative by the acetic anhydride-pyridine method the alcohol lost the elements of water readily and almost quantitatively. A similar change occurred when an attempt was made to sublime the alcohol at 230° at 0.3 mm. The dehydrated product melted at 233-234° after recrystallization from methanol.

Anal. Calc'd for C33H32O: C, 89.15; H, 7.26.

Found: C, 89.62; H, 7.46.

Since the ultraviolet spectrum indicated a phenanthrene ring system, the product is believed to be 9,10-dimesityl-1-methoxyphenanthrene.

From three reduction runs no bimolecular product could be isolated. Steam-distillation of the reaction mixture led to the isolation of o-hydroxyphenyl mesityl ketone (m.p. $81-82^\circ$).

Anal. Calc'd for C₁₆H₁₆O: C, 80.00; H, 6.85.

Found: C, 79.87; H, 6.79.

The infrared analysis showed a highly chelated carbonyl group at 1623 cm^{-1} . The product was shown by a mixture melting point to be the same as the hydroxy ketone obtained from mesityl *o*-methoxyphenyl ketone by cleavage with hydriodic acid.

SUMMARY

When an equimolar mixture of mesityl phenyl ketone and mesityl *o*-methoxyphenyl ketone is treated with the binary mixture, $Mg + MgI_2$, the hydroxy

³ The authors are indebted to Miss Elizabeth Petersen for the measurement and interpretation of the infrared spectra mentioned in this paper. ketone, I, is obtained in much higher yields than when mesityl phenyl ketone alone is used.

Reduction of an equimolar mixture of benzoylmesitylene and *o*-methoxybenzoyldurene produces the keto alcohol, IIa. Other pairs of ketones behave similarly. The precursor of the carbinol group in the duryl mesityl keto alcohols has been shown to be the carbonyl group of the methoxy ketone.

The action of the binary mixture on mesityl *o*-methoxyphenyl ketone gives rise to two products one of which has been shown to be 9,10-dimesitylphenan-threne.

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