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

REACTIONS OF BROMOMAGNESIUM ENOLATES OF MESITYL KETONES. I

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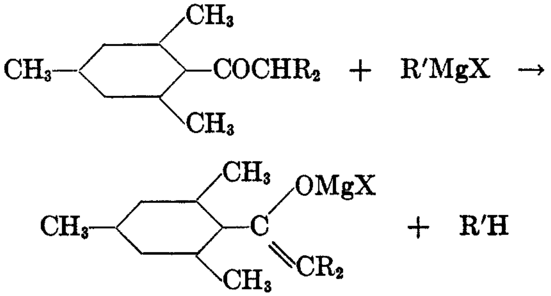
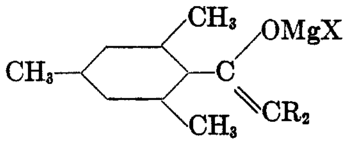
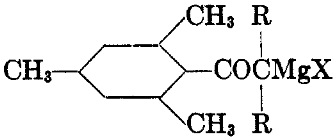
Mesityl ketones which have one or more *alpha* hydrogen atoms react with the Grignard reagent in an abnormal fashion. Since addition to the carbonyl group is inhibited by the steric hindrance offered by the two *ortho* methyl groups, enolization occurs with the resulting formation of the corresponding halomagnesium enolates:[1]



These enolates are of great interest because they give products which would suggest either of the following structures:





The evidence for this is that they react with acid chlorides to give enol esters (I) or 1,3-diketones (II), *i.e.*, they undergo *O*-acylation or *C*-acylation, respectively.[2a]

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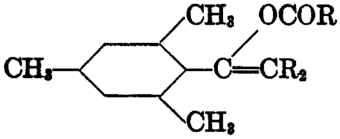
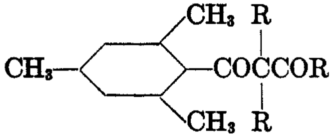
[1] (*a*) Klages, *Ber.*, **35**, 2635 (1903); (*b*) Kohler and Baltzly, *J. Am. Chem. Soc.*, **54**, 4015 (1932).

[2] (*a*) Kohler, Tischler, and Potter, *ibid.*, **57**, 2517 (1935); (*b*) Kohler and Potter, *ibid.*, **58**, 2166 (1936).



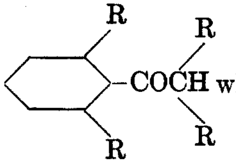
I

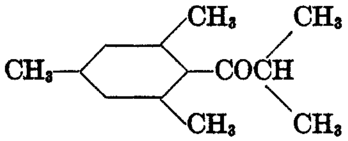


II

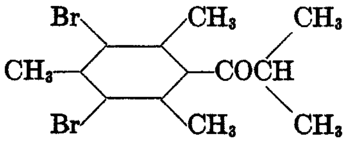
Similar results have been obtained with alkylating agents. In polar solvents tosylacetomesitylene[2b] and cyanoacetomesitylene[3] yield *O*-alkylation products exclusively.

The tendency of carbonyl compounds to undergo *O*-acylation and *O*-alkylation is usually associated with the readiness with which they enolize. Thus phenols and permanent enols generally give *O*-alkyl and *O*-acyl derivatives. In harmony with this point of view is the observation that mesityl ketones show a pronounced tendency to enolize.

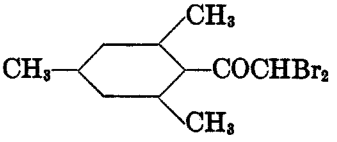
There is evidence also that this tendency is not limited to mesityl ketones but may be general for ketones whose addition reactions are highly restricted by the radicals surrounding the functional group, *i.e.*, it is in part, at least, a manifestation of steric hindrance.[4] In view of this the effect should be extreme in a ketone of the type  whose hindrance to addition reactions of the carbonyl group is prohibitive. The present paper deals principally with compounds of this general type. Isobutyromesitylene (III), 3,5-dibromoisobutyromesitylene (IV) and α,α-dibromoacetomesitylene (V) were examined in some detail with regard to their tendency to undergo acylation.



III



IV



V

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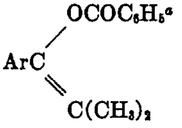
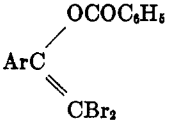
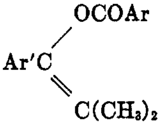
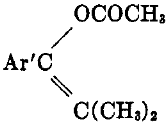
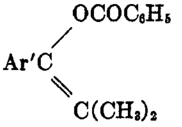
[3] Fuson, Ullyot, and Gehrt, *ibid.*, **60**, 1199 (1938).

[4] Smith and Guss, *ibid.*, **59**, 804 (1937); Ross and Fuson, *ibid.*, **59**, 1508 (1937).

The desired bromomagnesium derivatives were obtained from the mesityl ketones by use of ethylmagnesium bromide. They were then treated with reagents designed to explore their capacities for behaving as enolates, on the one hand, and as Grignard reagents on the other.

TABLE

Enol Esters Obtained by Treatment of the Bromomagnesium Enolates with Acid Chlorides

FORMULA OF ENOL ESTER	M.P., °C.	ANALYSES %					
		Calculated			Found		
		C	H	Br	C	H	Br
 $\mathrm{ArC(OCOC_6H_5)=C(CH_3)_2}$ [a]	87–88	81.63[b]	7.48		81.2 82.04 81.18	7.6 7.55 7.31	
 $\mathrm{ArC(OCOC_6H_5)=CBr_2}$	73–74.5	50.94	3.77	37.7	51.20	3.64	37.5
 $\mathrm{Ar'C(OCOAr)=C(CH_3)_2}$	113–114	55.87	5.24	32.4	55.88	5.13	32.6 32.2
 $\mathrm{Ar'C(OCOCH_3)=C(CH_3)_2}$	77–78	46.15	4.61	41.0	46.08	4.71	41.
 $\mathrm{Ar'C(OCOC_6H_5)=C(CH_3)_2}$	109–109.5	53.09	4.42	35.4	53.08	4.82	35.6

[a] Ar = mesityl; Ar′ = 3,5-dibromomesityl.

[b] All of the analytical data reported in this paper were obtained by microanalysis. The analyses were performed by Mr. Charles W. Beazley.

O-ACYLATION

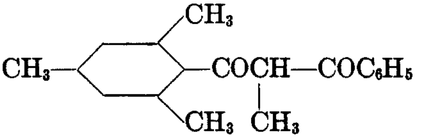
The former objective was fully realized by the use of acid chlorides. In every instance enol esters were formed and in no case could any trace of diketone be isolated. Evidently acid chlorides gave only *O*-derivatives. These are shown in the table of the experimental part.

The structures of the enol esters were deduced from the fact that these compounds were readily cleaved by bromine or alkalies. Confirmation of the structures was obtained by comparing the enol benzoate of isobutyromesitylene with the corresponding diketone (VII). The ester was found to be different from the diketone.

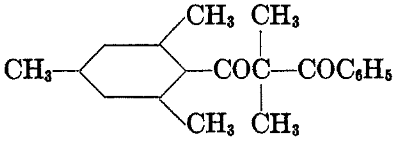
CONDENSATION REACTIONS

The synthesis of the diketones, α-benzoylpropiomesitylene (VI) and α-benzoylisobutyromesitylene (VII), serves to illustrate the capacity of the bromomagnesium enolates to act as true Grignard reagents.[2a] The reaction proceeds as though the bromomagnesium compound had the structure $RCOC(R)_2MgBr$.

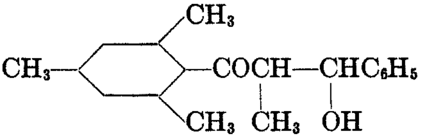
Thus the bromomagnesium derivative of propiomesitylene reacts with benzaldehyde to give the carbinol, VIII, in excellent yields. Similarly the bromomagnesium derivative of isobutyromesitylene with benzaldehyde yields the carbinol, IX. Oxidation of carbinols VIII and IX gave the corresponding mono- and dimethyl diketones. The monomethyl diketone (VI) prepared in this way was identical with that obtained from α-methyl-β-methoxy-β-mesitylacrylonitrile (X) by the action of phenylmagnesium bromide.[5] Long treatment with alkali converted the diketone (VI) into benzoic acid and propiomesitylene. The latter was identified by condensation with benzaldehyde. Benzalpropiomesitylene was formed; it gave a dibromide when treated with bromine.



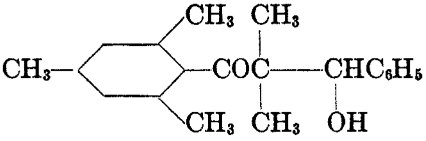
VI



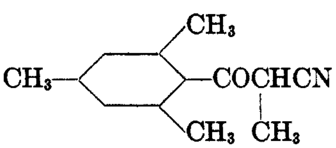
VII



VIII



IX



X

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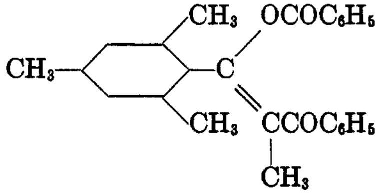
[5] Fuson, Ullyot, Stedman, and Tawney, *ibid.*, **60**, 1447 (1938).

Propiomesitylene, in contrast to the more highly substituted acetomesitylenes, appears to undergo C-acylation. The action of benzoyl chloride on its bromomagnesium derivative failed to give a monobenzoyl derivative, however; instead the product was the enol benzoate of α-benzoylpropiomesitylene (XI).



XI

The compound was identified by hydrolysis with dilute alkali to give benzoic acid and α-benzoylpropiomesitylene (VI). This latter product was identified by comparison with the compound obtained by oxidation of the keto alcohol (VIII). Presumably *C*-benzoylation first occurs yielding the diketone (VI) which then undergoes *O*-benzoylation to give the benzoate (XI). Kohler and Baltzly[1b] found that acetomesitylene also gave a dibenzoyl derivative; their compound, however, was a triketone. This must mean that the methyl group in the intermediate diketone (VI) favors *O*-benzoylation. This result accords well with the foregoing, since the diketone (VI), like the dimethyl (III, IV) and dibromo (V) compounds, has only one *alpha* hydrogen atom.

Summarizing, it would appear that only *O*-acylation occurs with mesityl ketones which are of the type $(CH_3)_3C_6H_2COCHA_2$ where A may be a methyl group, a bromine atom or a ketone group. It seems probable that this will prove to be general for mesityl ketones which have only one *alpha* hydrogen atom.

EXPERIMENTAL

The preparation of the enol esters.—These compounds were made by the interaction of a bromomagnesium enolate with an acid chloride. The following description of the preparation of the enol benzoate of 3,5-dibromoisobutyrylmesitylene is typical.

A solution of 18.8 g. of dibromoisobutyrylmesitylene in 125 cc. of ether was added from a separatory funnel during thirty minutes to 42 cc. (0.082 mole) of ethylmagnesium bromide. The white precipitate was treated with 23 g. of benzoyl chloride and the mixture was stirred for two hours. Decomposition with water gave a 72% yield of the enol benzoate. The enol ester was purified by recrystallization from 95% alcohol. Similar results were obtained when α,3,5-tribromoisobutyromesitylene was used in place of 3,5-dibromoisobutyromesitylene.

The enol benzoate of α-benzoylpropiomesitylene (XI).—A solution of 17.6 g. (0.1 mole) of propiomesitylene in 40 cc. of ether was added slowly to 100 cc. of a solution containing 0.107 mole of ethylmagnesium bromide. The mixture was refluxed for thirty minutes, cooled in an ice bath and treated with 21 g. (0.15 mole) of benzoyl chloride. The mixture was refluxed for four hours, decomposed with iced hydrochloric acid and extracted with ether. Extraction with sodium carbonate solution removed 9 g. of benzoic acid. The ether was evaporated, and the residue was treated with ligroïn and cooled. Ten grams of colorless crystals was obtained. After recrystallization from methanol they melted at 95.5–96°.

Anal. Calc'd for $C_{26}H_{24}O_3$: C, 81.21; H, 6.3.

Found: C, 81.47, 81.22, 81.10; H, 6.56, 6.51, 6.23.

Three grams of propiomesitylene was recovered from the ligroïn filtrate.

Hydrolysis of the enol benzoate of α-benzoylpropiomesitylene (*XI*).—A mixture of 3.85 g. of the enol benzoate, 0.6 g. of sodium hydroxide and 150 cc. of ethyl alcohol was refluxed for one and one-half hours. After distillation of the solvent the residue was shaken with a mixture of dilute sodium hydroxide solution and ether. Acidification of the alkaline layer gave 0.78 g. of benzoic acid. Treatment of the ether layer with a solution of copper acetate gave 0.8 g. of the copper derivative of α-benzoylpropiomesitylene. It was transformed into the diketone; n_D^{20} 1.5888. The diketone gave an intense color with ferric chloride.

2-Methyl-2-(2,4,6-trimethylbenzoyl)-1-phenyl-1-propanol (*IX*).—Twenty grams of isobutyromesitylene was converted into a bromomagnesium derivative with one equivalent of ethylmagnesium bromide. Eleven and nineteen-hundredths grams of freshly distilled benzaldehyde was added to the new Grignard reagent over a period of one and one-half hours and the mixture was refluxed one-half hour. It was then decomposed with ice and hydrochloric acid and the product when isolated from the ether layer crystallized from high-boiling ligroïn to give a colorless solid; yield, 13 g.; m.p. 85–85.5°.

Anal. Calc'd for $C_{20}H_{24}O_2$: C, 81.02; H, 8.16.

Found: C, 81.28; H, 8.07.

α-Benzoylisobutyromesitylene (*VII*).—One cubic centimeter of a solution of 1.12 g. of chromic oxide in 10 cc. of glacial acetic acid and 3 cc. of water was added to a solution of 5 g. of the carbinol (IX) in 40 cc. of glacial acetic acid. The mixture was heated nearly to boiling. After reaction set in, as indicated by the development of a green color, the rest of the chromic oxide solution was added in three portions. The mixture was boiled ten minutes and poured into a beaker of ice. The precipitated solid was collected and crystallized from alcohol. The yield was 4 g.; m.p. 100–100.2°.

Anal. Calc'd for $C_{20}H_{22}O_2$: C, 81.58; H, 7.53; OCH_3, 0.0.

Found: C, 81.26, 81.29; H, 7.62; OCH_3, 0.69.

The *semicarbazone* was crystallized by dissolving it in hot carbon tetrachloride and adding low-boiling ligroïn; m.p. 151–152.5°.

Anal. Calc'd for $C_{21}H_{25}O_2N_2$: C, 71.75; H, 7.17; N, 11.96.

Found: C, 71.6; H, 7.05; N, 11.94.

Synthesis of 2-(2,4,6-trimethylbenzoyl)-1-phenyl-1-propanol (*VIII*).—One hundred nineteen grams of propiomesitylene was converted into a Grignard reagent with ethylmagnesium bromide. The new Grignard reagent was caused to react with 72 g. of benzaldehyde as in the preparation of VIII. Seventy-eight grams of product was obtained by crystallization first from high-boiling ligroïn and then from slightly diluted alcohol; m.p. 94.5–96°.

Anal. Calc'd for $C_{19}H_{21}O_2$: C, 80.89; H, 7.52.

Found: C, 80.79, 80.69; H, 8.06, 7.78.

The first filtrate was evaporated and the residue was distilled *in vacuo*. Thirty-eight grams of propiomesitylene was recovered. A second fraction consisting of 23.3 g. of a pale-yellow liquid boiling at 178–180°/3 mm. was obtained. Redistillation gave a product boiling at 172–174°/2 mm.; n_D^{20} 1.5991. This was identified as benzalpropiomesitylene by conversion into the corresponding dibromide.

A sulfuric acid solution of the hydroxy ketone (VIII) was heated on a steam bath and the resulting deep-red solution was poured into water; 2,4,6-trimethylbenzoic acid was formed.

α-Benzoylpropiomesitylene (VI) and its copper derivative.—A hot solution of 10 g. of the keto alcohol (VIII) in 50 cc. of glacial acetic acid was mixed slowly, with shaking, with a hot solution of 2.3 g. of chromic oxide, in 20 cc. of glacial acetic acid and 10 cc. of water. The mixture was heated on a steam cone for twenty minutes and then boiled for three minutes. The resulting dark green solution was poured into a beaker of ice, diluted with water and extracted several times with ether. The ether solution was treated with solid sodium carbonate, washed with a solution of sodium carbonate and then with water. The resulting ether solution was shaken intermittently over a period of one-half hour with a saturated aqueous solution of cupric acetate. The deep green ether solution was separated and evaporated; alcohol was added to the residue and the green copper derivative was collected on a filter. The yield was 1.8 g. The copper derivative was crystallized by dissolving it in a minimum of hot benzene and adding ligroïn.

Anal. Calc'd for $(C_{19}H_{19}O_2)_2Cu$: C, 73.34; H, 6.16; Cu, 10.2.
Found: C, 73.66, 73.64; H, 6.43, 6.19; Cu, 9.68, 9.83.

The copper was determined by weighing the copper oxide remaining after the combustion determination.

The copper derivative was decomposed by shaking it with ether and dilute hydrochloric acid in a separatory funnel. It was washed with water, dried with calcium chloride and evaporated. The residual diketone (VI) was distilled *in vacuo*. A heavy, viscous oil, slightly yellow in color was obtained. It did not crystallize; b.p. 183–184.5°/3 mm.; n_D^{20} 1.5880. It gives an intense purple color with ferric chloride.

Anal. Calc'd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19.
Found: C, 81.14, 81.12, 81.27; H, 7.48, 7.53, 7.32.

Alkaline hydrolysis of α-benzoylpropiomesitylene (VI).—One gram of α-benzoylpropiomesitylene was refluxed overnight with a mixture of 80 cc. of 15% aqueous potassium hydroxide and 5 cc. of methyl alcohol. The reaction mixture was cooled and extracted with ether. The ether extract was dried over calcium chloride and evaporated. Three-tenths of a gram of oil was obtained; it was cooled in an ice bath, and a mixture of 5 cc. of concentrated nitric acid and 5 cc. of concentrated sulfuric acid, cooled to 0°, was added. The mixture was kept in an ice bath fifteen minutes, or until a precipitate formed, and was then poured into a beaker of ice. The precipitate was collected, dried and crystallized from benzene and a little ligroïn. Fine, colorless needles, melting at 230–233°, were obtained. The substance was alkali-soluble, and was shown by a mixture melting point determination to be 3,5-dinitro-2,4,6-trimethylbenzoic acid. The same product was obtained from 0.3 g. of propiomesitylene under exactly the same conditions. From the aqueous filtrate 0.3 g. of pure benzoic acid was obtained.

Benzalpropiomesitylene.—Twenty grams of propiomesitylene and 12 g. of benzaldehyde were added to a solution of 4.5 g. of sodium hydroxide in 30 cc. of alcohol and 60 cc. of water. The mixture was stirred at room temperature for eight hours and then for two hours at 70–80°. It was allowed to stand for two days; an oily layer settled to the bottom of the flask. The mixture was diluted with water and extracted with ether. The ether solution was washed with water, with a bisulfite solution, then water again. The solution was dried over calcium chloride and the solvent evaporated. The remaining oil was distilled *in vacuo*. Twenty grams of product was obtained; b.p. 178–180°/3 mm.; n_D^{20} 1.5996.

Anal. Calc'd for $C_{19}H_{20}O$: C, 86.46; H, 7.64.
Found: C, 86.01; H, 7.4.

Dibromobenzalpropiomesitylene.—A small amount of benzalpropiomesitylene was dissolved in carbon tetrachloride, and the solution was placed in an ice bath. Bromine, dissolved in chloroform, was added in portions to the cooled solution, the color being allowed to disappear from the reaction mixture after each addition of bromine. After sufficient bromine had been added so that the reaction mixture remained colored, ligroïn was added to hasten crystallization which had already commenced. The colorless solid was collected and crystallized by dissolving it in hot carbon tetrachloride, adding ligroïn and cooling. The melting point varied between 134 and 139°. Decomposition accompanied melting, and red bromine vapors were evolved.

Anal. Calc'd for $C_{19}H_{20}Br_2$: C, 53.77; H, 4.75.
Found: C, 53.69; H, 5.10.

It was necessary to add the bromine in the cold in order to inhibit substitution reactions.

SUMMARY

The bromomagnesium enolates of isobutyromesitylene (III), 3,5-dibromoisobutyromesitylene (IV) and α,α-dibromoacetomesitylene (V) have been shown to react with acid chlorides to give only enol esters.

The bromomagnesium enolates of propiomesitylene and isobutyromesitylene have been condensed with benzaldehyde to give keto alcohols. These yielded diketones when oxidized.