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

REACTIONS OF BROMOMAGNESIUM ENOLATES OF MESITYL KETONES. III. CONDENSATION WITH BENZALDEHYDE

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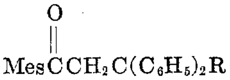
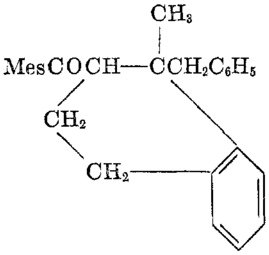
Substituents in the alkyl group of a bromomagnesium enolate of an alkyl mesityl ketone may hinder or inhibit its reaction as an organometallic compound. For example, compounds of type I in which R is methyl, ethyl, or phenyl were found by Kohler and Barnes (1) to be exceedingly unreactive. In connection with other work we have found that the enolates of mesityl 1-benzyl-1-methyl-1,2,3,4-tetrahydro-2-naphthyl ketone (II) (2) and β-benzyl-β-phenylbutyromesitylene (III) are similarly unreactive.

These difficulties led us to investigate the behavior of some simpler ketones. For this purpose we have examined the enolates of valeromesitylene, capromesitylene, γ-phenylbutyromesitylene, and δ-phenylvaleromesitylene with special reference to their reactions with benzaldehyde.

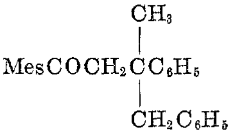


$MesC(=O)CH_2C(C_6H_5)_2R$

I

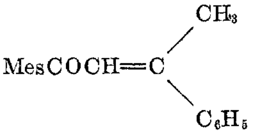


II



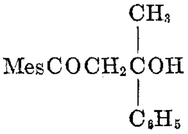
$MesCOCH_2C(CH_3)(CH_2C_6H_5)C_6H_5$

III



$MesCOCH{=}C(CH_3)C_6H_5$

IV



$MesCOCH_2C(CH_3)(OH)C_6H_5$

V

$MesCOCH{=}CH_2$

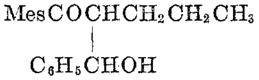
VI

$MesCOCH_2CH_2CH_2C_6H_5$

VII

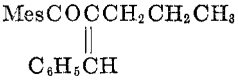
$MesCOCH_2CH_2CH_2OCH_2CH_3$

VIII



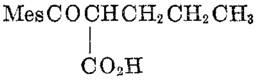
$MesCOCH(CH(OH)C_6H_5)CH_2CH_2CH_3$

IX



$MesCOC(=CHC_6H_5)CH_2CH_2CH_3$

X



$MesCOCH(CO_2H)CH_2CH_2CH_3$

XI

In each case the reaction proceeded satisfactorily; the expected intermediate hydroxy ketones were isolated and dehydrated by heating with concentrated hydrochloric acid. For example, the enolate of valeromesitylene gave α-*n*-propyl-β-hydroxy-β-phenylpropiomesitylene (IX) and its dehydration product, believed to be the conjugated unsaturated ketone, α-*n*-propylbenzalacetomesitylene (X). With carbon dioxide this enolate gave α-mesitoylvaleric acid (XI).

β-Methylbenzalacetomesitylene (IV) was prepared by treatment of the bromomagnesium enolate of acetomesitylene with acetophenone (2). It was found, however, that about one-third of the product was in the form of the intermediate alcohol (V), an observation not previously reported. The alcohol was dehydrated with ease to the α,β-unsaturated ketone by concentrated hydrochloric acid. In succeeding preparations, the crude mixture of products was dehydrated with concentrated hydrochloric acid before isolation of the β-methylbenzalacetomesitylene. Addition of benzylmagnesium chloride to β-methylbenzalacetomesitylene (IV) produced β-benzyl-β-phenylbutyromesitylene (III) in 78% yield.

The preparation of mesityl vinyl ketone (VI) was carried out by acylation of mesitylene with β-chloropropionyl chloride (3). As observed earlier (3) substantial amounts of β-mesitylpropiomesitylene were obtained in some preparations. The addition of benzylmagnesium chloride to mesityl vinyl ketone (VI) gave γ-phenylbutyromesitylene (VII) in 58% yield. When phenethylmagnesium bromide was employed the product was δ-phenylvaleromesitylene.

γ-Ethoxypropyl chloride, prepared according to the directions of Smith and Sprung (4), formed a Grignard reagent which reacted with mesitoyl chloride to produce γ-ethoxybutyromesitylene (VIII) in 42% yield. Valeromesitylene and capromesitylene were made from mesitylene and the appropriate acid chloride by the method of Friedel and Crafts. β-Methoxypropiomesitylene was synthesized by treatment of mesityl vinyl ketone with methanol and a trace of hydrochloric acid (3).

EXPERIMENTAL

β-Methylbenzalacetomesitylene (IV). This ketone was prepared in 52% yield by the procedure of Fuson, Fugate, and Fisher (5). When the residue remaining after distillation of the acetophenone and acetomesitylene was not treated with concentrated hydrochloric acid as described in their procedure, it could be separated, by fractional crystallization from ethanol, into two compounds. Approximately two-thirds of the mixture was β-methylbenzalacetomesitylene and one-third was β-phenyl-β-hydroxybutyromesitylene (V), a colorless compound melting at 77–78°.

Anal.[1] Calc'd for $C_{19}H_{22}O_2$: C, 80.81; H, 7.86.
Found: C, 81.06; H, 8.10.

The hydroxy compound was converted to β-methylbenzalacetomesitylene by treatment with concentrated hydrochloric acid.

β-Benzyl-β-phenylbutyromesitylene (III). To a solution of benzylmagnesium chloride, prepared from 208.5 g. of benzyl chloride, 200 g. of magnesium, and 1100 ml. of dry ether, was added, with stirring, over a period of 30 minutes, 90 g. of β-methylbenzalacetomesitylene in 500 ml. of dry ether. The mixture was stirred and heated at reflux for an additional 15 minutes and decomposed by pouring into a mixture of ice and concentrated hydrochloric acid. The ether layer was washed with water and dried over magnesium sulfate. The ether and toluene were removed and the residual β-benzyl-β-phenylbutyromesitylene was crystal-

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[1] The microanalyses were performed by Miss Emily Davis, Miss Rachel Kopel, Mrs. Jean Fortney, Mrs. Katherine Pih and Mrs. Esther Fett.

lized from *n*-butyl ether and then recrystallized from ethanol; m.p. 78.5–80°; yield 81 g. (68%).

Anal. Calc'd for $C_{26}H_{22}O$: C, 87.60; H, 7.92.
Found: C, 87.78; H, 8.12.

γ-Phenylbutyromesitylene (VII). A solution of 25 g. of mesityl vinyl ketone, prepared in 66% yield by the method of Fuson and McKeever (3), in 125 ml. of ether was added over a period of 12 hours, with stirring, to a solution of benzylmagnesium chloride, prepared from 26.5 g. of benzyl chloride, 7 g. of magnesium, and 250 ml. of dry ether. The mixture was stirred and heated at reflux for an additional 9 hours and decomposed with ice and hydrochloric acid. The ether layer was washed with water and dried over magnesium sulfate. The ether was removed, and the γ-phenylbutyromesitylene was distilled *in vacuo*; b.p. 160–175° (1 mm.); yield 70%. Redistillation through a Vigreux column gave a light yellow oil; b.p. 147–150° (0.2 mm.); n_D^{20} 1.5529.

Anal. Calc'd for $C_{19}H_{22}O$: C, 85.67; H, 8.33.
Found: C, 85.85; H, 8.54.

One gram of this ketone was nitrated according to the procedure of Fuson and Baumgartner (6). The product, a trinitro derivative, was crystallized from a mixture of ethanol and benzene; m.p. 171–171.5°. The melting point reported earlier is 168–169°.

Anal. Calc'd for $C_{19}H_{19}N_3O_7$: C, 56.86; H, 4.77; N, 10.47.
Found: C, 57.05; H, 5.00; N, 10.57.

The bromomagnesium enolate of γ-phenylbutyromesitylene (10 g.) reacted with benzaldehyde (4.56 g.) to form a light yellow, viscous oil, which could not be induced to crystallize. This liquid, presumed to be the expected hydroxy ketone, was heated on a steam-cone for 30 minutes, with stirring, with 60 ml. of concentrated hydrochloric acid. The mixture was cooled, diluted with water, and extracted with ether. The product, believed to be α-benzal-γ-phenylbutyromesitylene, was a yellow oil; b.p. 200–204° (0.12 mm.); n_D^{20} 1.6062; yield 8.25 g. (68.5%).

Anal. Calc'd for $C_{26}H_{26}O$: C, 88.09; H, 7.39.
Found: C, 87.81; H, 7.33.

The infrared spectrum[2] shows the absorption peaks generally associated with hindered and conjugated carbonyl (1647 cm.$^{-1}$), mesityl (1615 cm.$^{-1}$), and monosubstituted benzene (698 and 746 cm.$^{-1}$) groups.

α-Benzhydryl-γ-phenylbutyromesitylene. α-Benzal-γ-phenylbutyromesitylene (3.6 g.) was treated with an excess of phenylmagnesium bromide, the mixture being heated under reflux for 18 hours. From the product, which appeared to be a mixture, the benzhydryl compound was isolated by crystallization from petroleum ether and then from a mixture of methanol and ethanol; m.p. 115–116°.

Anal. Calc'd for $C_{32}H_{32}O$: C, 88.84; H, 7.46.
Found: C, 89.09; H, 7.71.

The infrared spectrum has peaks at 1680, 850, and 710 cm.$^{-1}$ which are assignable, respectively, to hindered carbonyl, mesityl, and monosubstituted benzene groups.

δ-Phenylvaleromesitylene. This ketone was made from mesityl vinyl ketone (34.8 g.) and an excess of phenethylmagnesium bromide by a procedure similar to that outlined for γ-phenylbutyromesitylene. The product was purified by distillation *in vacuo*; b.p. 162–163° (0.2 mm.); n_D^{20} 1.5485; yield 39%.

Anal. Calc'd for $C_{20}H_{24}O$: C, 85.67; H, 8.62.
Found: C, 85.64; H, 8.88.

Nitration by the usual procedure gave a *tetranitro derivative*, which was recrystallized from an ethanol-benzene mixture; m.p. 138.5–139.5°.

Anal. Calc'd for $C_{20}H_{20}N_4O_7$: C, 52.17; H, 4.38; N, 12.17.
Found: C, 52.46; H, 4.63; N, 11.98.

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[2] The infrared spectra mentioned in this paper were observed and interpreted by Miss Elizabeth Petersen and Miss Helen Miklas.

α-Hydroxybenzyl-δ-phenylvaleromesitylene. Benzaldehyde (4.25 g.) condensed with the enolate made from 10 g. of δ-phenylvaleromesitylene to give 11.4 g. of a white solid, which after recrystallization from a 1:1 mixture of low-boiling petroleum ether and high-boiling petroleum ether, melted at 80.5–82°.

Anal. Calc'd for $C_{27}H_{30}O_2$: C, 83.90; H, 7.82.
Found: C, 83.74; H, 7.55.

The infrared spectrum has bands generally assigned to hydroxyl (3495 cm.$^{-1}$), hindered carbonyl (1682 cm.$^{-1}$), and monosubstituted benzene (701 cm.$^{-1}$) groups.

α-Benzal-δ-phenylvaleromesitylene. The hydroxy compound (1.72 g.) was dehydrated by heating with concentrated hydrochloric acid. The product was purified by recrystallization from methanol; m.p. 84–85°.

Anal. Calc'd for $C_{27}H_{28}O$: C, 88.00; H, 7.66.
Found: C, 87.91; H, 7.60.

Infrared analysis revealed significant absorption bands at 1644, 1615, and 700 cm.$^{-1}$ which may be assigned, respectively, to conjugated and hindered carbonyl, mesityl, and monosubstituted benzene functions.

γ-Ethoxybutyromesitylene (VIII). To a solution of γ-ethoxypropylmagnesium chloride, prepared from 84.7 g. of γ-ethoxypropyl chloride (4), 16.7 g. of magnesium, and 200 ml. of dry ether, was added dropwise, with stirring, 125 g. of mesitoyl chloride in 100 ml. of dry ether. The mixture was then heated at reflux for an hour, with stirring, and decomposed with ice and hydrochloric acid. The ether layer was washed with 5% sodium carbonate solution and with water and dried over sodium sulfate. When the sodium carbonate solution was acidified, 55 g. of mesitoic acid was obtained. The ether was removed and the γ-ethoxybutyromesitylene was distilled *in vacuo*; b.p. 126–130° (0.6 mm.); n_D^{20} 1.5017; d_{20}^{20} 0.9781; yield 34 g. (21%).

Anal. Calc'd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46; MR., 69.54.
Found: C, 77.04; H, 9.58; MR., 70.67.

Valeromesitylene. To a mixture of 72 g. of mesitylene, 60 g. of aluminum chloride, and 150 ml. of carbon disulfide—cooled to 10°—was added in the course of 45 minutes 48 g. of valeryl chloride, the temperature being kept below 10°. The reaction mixture was stirred during the mixing and for an additional hour in the cold and during a similar period while the temperature was allowed to rise to 25°. Hydrochloric acid (10%) was added slowly until the precipitate had formed a compact mass. After the precipitate had been dissolved by the addition of 360 ml. of hydrochloric acid (25%) and the carbon disulfide had been distilled, the aqueous solution was extracted with ether. The ketone, isolated by usual procedures, was a light yellow oil; b.p. 118–122° (3 mm.); yield 59.3 g. (73%). Redistillation gave a colorless liquid; b.p. 91–92° (0.5 mm.); n_D^{20} 1.5046.

Anal. Calc'd for $C_{14}H_{20}O$: C, 82.31; H, 9.79.
Found: C, 82.56; H, 9.92.

3,5-Dinitrovaleromesitylene. This ketone, prepared in high yield by the method of Fuson, Ross, and McKeever (7), was recrystallized from methanol in colorless needles; m.p. 125.5–126.5°.

Anal. Calc'd for $C_{14}H_{18}N_2O_5$: C, 57.13; H, 6.16; N, 9.52.
Found: C, 57.24; H, 5.97; N, 9.64.

α-Bromovaleromesitylene. This ketone was made by adding bromine to the bromomagnesium enolate of valeromesitylene in the usual way. The yield of crude product [b.p. 140–147° (3.4 mm.)] was 4.42 g. (64%). The bromo ketone was purified by distillation; b.p. 121° (0.75 mm.); n_D^{20} 1.5383.

Anal. Calc'd for $C_{14}H_{19}BrO$: C, 59.37; H, 6.77.
Found: C, 59.72; H, 6.71.

α-Bromo-3,5-dinitrovaleromesitylene. The nitration product was recrystallized from methanol; m.p. 130.5–131.5°.

Anal. Calc'd for $C_{14}H_{27}N_2O_5$: C, 45.05; H, 4.59; N, 7.51.
Found: C, 45.16; H, 4.37; N, 7.35.

Reaction of the enolate of valeromesitylene with benzaldehyde. Condensation of the enolate of valeromesitylene with benzaldehyde gave a solid and a liquid. The solid, after recrystallization from methanol and then from ethanol, was colorless, m.p. 95–96.5°.

Anal. Calc'd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44.
Found: C, 81.49; H, 8.64.

The infrared spectrum shows a peak at 3370 cm.$^{-1}$ attributable to hydroxyl. The compound was identified as *α-n-propyl-β-hydroxy-β-phenylpropiomesitylene.*

The liquid product, obtained in 23% yield, was purified by distillation; b.p. 148–149° (1.8 mm.); n_D^{20} 1.5820.

Anal. Calc'd for $C_{21}H_{24}O$: C, 86.25; H, 8.27.
Found: C, 86.50; H, 8.32.

The infrared spectrum shows a peak at 1650 cm.$^{-1}$ assignable to the α,β-unsaturated ketone function. The compound, on this basis would be *α-n-propylbenzalacetomesitylene.*

Anal. Calc'd for $C_{21}H_{26}O$: C, 85.66; H, 8.90.
Found: C, 85.70; H, 9.13.

By hydrogenation in absolute ethanol in the presence of Raney nickel at 1800 p.s.i. it was converted to *α-n-propyl-β-phenylpropiomesitylene*; b.p. 148–149° (0.3 mm.); n_D^{20} 1.5475.

Anal. Calc'd for $C_{22}H_{28}O$: C, 85.66; H, 9.15.
Found: C, 85.70; H, 9.13.

α-Mesitoylvaleric acid. Treatment of the enolate of valeromesitylene with a slurry of solid carbon dioxide and ether gave the corresponding acid in a yield of 11.5%. It crystallized from a mixture of ether and low-boiling petroleum ether in beautiful transparent square plates; m.p. 132–134°, with decomposition.

Anal. Calc'd for $C_{15}H_{20}O_2$: C, 72.55; H, 8.12.
Found: C, 72.58; H, 8.12.

Capromesitylene. This ketone was made from 54 g. of caproyl chloride and 72 g. of mesitylene by a procedure very similar to that described for valeromesitylene. It was collected as a light yellow oil; b.p. 99–103 (0.5 mm.); yield 60.3 g. (69.5%). The analytical sample was colorless; b.p. 105–107° (0.8 mm.); n_D^{20} 1.5042.

Anal. Calc'd for $C_{15}H_{22}O$: C, 82.59; H, 10.13.
Found: C, 82.83; H, 10.46.

The dinitro derivative, prepared by the method indicated for nitrating valeromesitylene, was obtained in high yield. It crystallized from methanol in long colorless needles; m.p. 122.5–123°.

Anal. Calc'd for $C_{15}H_{20}N_2O_5$: C, 58.43; H, 6.53; N, 9.08.
Found: C, 58.67; H, 6.43; N, 9.37.

α-Bromocapromesitylene. The bromination was effected as with valeromesitylene and the product, purified by distillation, was a colorless oil; b.p. 128–129° (0.5 mm.); n_D^{20} 1.5342.

Anal. Calc'd for $C_{15}H_{21}BrO$: C, 60.61; H, 7.12.
Found: C, 60.98; H, 7.17.

α-Bromo-3,5-dinitrocapromesitylene. This compound, prepared in the usual way, crystallized from methanol as colorless needles; m.p. 123–124°.

Anal. Calc'd for $C_{15}H_{19}N_2O_5$: C, 46.52; H, 4.95; N, 7.25.
Found: C, 46.56; H, 4.83; N, 7.06.

Reaction of the enolate of capromesitylene with benzaldehyde. The results were similar to those reported for valeromesitylene. The *α-n-butyl-β-hydroxy-β-phenylpropiomesitylene* separated from low-boiling petroleum ether in thick colorless, crystals; m.p. 77.5–79°.

Anal. Calc'd for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70.
Found: C, 81.58; H, 8.73.

The dehydration product, believed to be *α-n-butylbenzalacetomesitylene*, is a very viscous liquid; b.p. 163–165° (0.5 mm.); n_D^{20} 1.5758. The yield was 55%. The infrared spectrum has an absorption band at 1651 cm.$^{-1}$ attributable to the conjugated unsaturated ketone function.

Anal. Calc'd for $C_{22}H_{26}O$: C, 86.22; H, 8.55.

Found: C, 85.92; H, 8.45.

Hydrogenation converted the unsaturated ketone to *α-n-butyl-β-phenylpropiomesitylene*; b.p. 154° (0.12 mm.); n_D^{20} 1.5410.

Anal. Calc'd for $C_{22}H_{28}O$: C, 85.66; H, 9.14.

Found: C, 85.48; H, 9.31.

Nitration of the saturated ketone produced a tetranitro derivative, which crystallized from ethanol in light yellow platelets; m.p. 110–111°.

Anal. Calc'd for $C_{22}H_{24}N_4O_2$: C, 54.09; H, 4.95; N, 11.47.

Found: C, 54.20; H, 5.02; N, 11.52.

URBANA, ILLINOIS

SUMMARY

The bromomagnesium enolates of valeromesitylene, capromesitylene, γ-phenylbutyromesitylene, and δ-phenylvaleromesitylene have been found to condense with benzaldehyde to give the corresponding hydroxy ketones. Dehydration of the hydroxy compounds gave the expected unsaturated ketones.

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