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A Comparison of the Reactions of Mesityl Cyclopropyl Ketone and Mesityl Propenyl Ketone

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Ethyl 1,1-cyclopropanedicarboxylate has been shown to react with ethyl malonate in the presence of sodium ethoxide in a manner analogous to α,β-unsaturated carbonyl compounds.[1] Halogen acids also react in a conjugate manner with cyclopropane carbonyl compounds, including cyclopropyl ketones.[2,3]

The ability of α,β-unsaturated ketones to condense with the Grignard reagent[4-7] and with aromatic hydrocarbons,[8-10] in addition to active methylene compounds and halogen acids, suggested that a hindered cyclopropyl ketone might also combine with these reagents. Such reactions would lend additional support to the theory that the three-membered ring can react in a manner analogous to a carbon–carbon double bond when conjugated with a carbonyl group. In order to decrease the possibility of reaction by the carbonyl group alone and to favor possible reactions of the conjugated system, mesityl cyclopropyl ketone was chosen for study. The carbonyl group in this ketone is masked by the adjacent methyl groups to such a degree that it is unaffected by ordinary carbonyl reagents. A parallel investigation of mesityl propenyl ketone was necessary for purposes of comparison.

In the present research it has been found that two aromatic hydrocarbons, benzene and mesitylene, react with mesitylcyclopropyl ketone in the presence of aluminum chloride to produce the *gamma* substituted butyromesitylenes. The ketone combines with hydrobromic acid in a like manner. Reaction with active methylene compounds or the Grignard reagent was not observed.

Mesityl cyclopropyl ketone was prepared by acylation of mesitylene in the Friedel–Crafts manner. With carbon disulfide as the solvent, cyclopropanecarboxylic acid chloride reacted with mesitylene in the presence of anhydrous aluminum chloride to produce the cyclopropyl ketone. The action of mesitylmagnesium bromide on cyclopropyl cyanide and on cyclopropanecarboxylic acid chloride also was found to yield the ketone, although in poor yields.

The ketone did not decolorize cold alkaline permanganate, indicating the absence of ordinary unsaturation. Since the possibility existed that the cyclopropane ring had opened during the course of the synthesis to form the isomeric propenyl ketone, reactions characteristic of active methyl compounds were attempted. The ketone failed to condense with *p*-chlorobenzaldehyde as would be expected if the three-membered ring were intact. The propenyl ketone, on the other hand, condensed with *p*-chlorobenzaldehyde rapidly in the cold to give *p*-chlorocinnamalacetomesitylene.

The infrared spectra[11] of mesityl cyclopropyl ketone and mesityl propenyl ketone showed marked differences. The cyclopropyl derivative exhibits a conjugated carbonyl stretching frequency at 1679 cm.$^{-1}$, while the carbonyl absorption of the propenyl derivative is at a lower frequency, 1651 cm.$^{-1}$, a position characteristic of doubly conjugated ketones. Furthermore, the propenyl ketone has strong absorption bands at 1280 and 1171 cm.$^{-1}$ while the cyclopropyl ketone does not. Both ketones show the characteristic carbon–carbon stretching frequencies of the mesityl ring at 1575 and 1612 cm.$^{-1}$.

In the preparation of the cyclopropyl ketone by the Friedel–Crafts method, a small amount of γ-mesitylbutyromesitylene was isolated. This compound was formed by the conjugate addition of mesitylene to mesityl cyclopropyl ketone. When mesitylene and the cyclopropyl ketone were heated with anhydrous aluminum chloride in the absence of carbon disulfide, the yield of γ-mesitylbutyromesitylene was substantially increased. This ability to undergo condensation with aromatic hydrocarbons was further exemplified by the conjugate addition of benzene to the ketone, producing γ-phenylbutyromesitylene. That the γ- and not the β-substituted product had been obtained was proven by the preparation of the trinitro derivatives of β-phenylbutyromesitylene and of γ-phenylbutyromesitylene. The β-isomer, prepared by the addition of benzene to mesityl propenyl ketone, was formed also by the action of phenylmagnesium bromide on the unsaturated ketone.

Since only the γ-isomers were obtained, it is very unlikely that γ-chlorobutyromesitylene is an intermediate in the condensation of the cyclopropyl ketone with benzene or mesitylene. If this compound were formed initially, followed by alkylation of the hydrocarbon in the normal fashion, *both* the β and γ-derivatives might have been expected. It is more likely that the active inter-

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(1) Bone and Perkin, *J. Chem. Soc.*, **67**, 108 (1895).

(2) Kishner, *J. Russ. Phys.-Chem. Soc.*, **43**, 1163 (1911).

(3) Allen and Boyer, *Can. J. Research*, **9**, 159 (1933).

(4) Kohler, *Am. Chem. J.*, **31**, 642 (1904).

(5) Kohler, *ibid.*, **38**, 511 (1907).

(6) Kohler and Burneley, *ibid.*, **43**, 412 (1910).

(7) Kohler, Tishler and Potter, THIS JOURNAL, **57**, 1316, 2517 (1935).

(8) Kohler, *Am. Chem. J.*, **44**, 60 (1910).

(9) Vorländer and Friedberg, *Ber.*, **56**, 1144 (1923).

(10) Eaton, Black and Fuson, THIS JOURNAL, **56**, 687 (1934).

(11) The authors are indebted to Dr. F. A. Miller and Mrs. J. L. Johnson for the measurement and interpretation of the infrared spectra.

mediate is a polarized aluminum chloride complex molecule. Addition of the hydrocarbon to the complex molecule and rupture of the cyclopropane ring occur simultaneously so that there is no possibility for isomerization to occur. Thus only the γ derivatives are obtained.

Mesityl cyclopropyl ketone and hydrobromic acid react in the presence of glacial acetic acid in the expected manner to produce γ-bromobutyromesitylene. The reaction does not occur in the absence of glacial acetic acid, attesting to the stabilizing influence of the mesitoyl group.

Attempts to condense ethyl malonate with mesityl cyclopropyl ketone failed. The three-membered ring appears to be quite stable in basic media, even at elevated temperatures and pressures. The Grignard reagent likewise was not observed to condense with the cyclopropyl ketone in a conjugate manner. The propenyl ketone, on the other hand, reacted in the cold with ethyl malonate as well as the Grignard reagent.

Experimental

Mesityl Cyclopropyl Ketone.—Cyclopropanecarboxylic acid, prepared by the directions of McCloskey and Coleman,[12] boiled at 89–91° (24 mm.); yield, 72%. The acid chloride, prepared from cyclopropanecarboxylic acid and phosphorus trichloride according to the directions of Lipp,[13] boiled at 114–119°; yield, 85%.

A mixture of 46.5 g. of anhydrous aluminum chloride and 100 ml. of dry carbon disulfide was cooled to 0° by means of an ice–salt-bath. A solution of 40 g. (0.33 mole) of mesitylene, 34.5 g. of freshly distilled cyclopropanecarboxylic acid chloride, and 30 ml. of dry carbon disulfide was added slowly to the cold mixture over a period of forty-five minutes. The mixture was allowed to stand at room temperature with stirring for an additional two hours. It was decomposed with a cracked ice and hydrochloric acid mixture, and the carbon disulfide layer removed. The aqueous layer was washed with ether, and the ether washings were added to the carbon disulfide solution. The combined extracts were washed successively with a sodium carbonate solution and water, and dried over Drierite. Distillation *in vacuo* yielded 40.5 g. (65%) of mesityl cyclopropyl ketone; b. p. 117–118° (2.6 mm.); $n^{20}{}_D$ 1.5312; $d^{20}{}_4$ 1.010.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 83.19; H, 8.61.

A solution of the distillation residue in hot alcohol was boiled with Norite and filtered. White leaflets separated as the solution cooled. After recrystallization from ethanol, the substance melted at 103–104° and had the composition of γ-mesitylbutyromesitylene.

Anal. Calcd. for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.56; H, 8.80.

Mesityl cyclopropyl ketone was also prepared by the action of the Grignard reagent on cyclopropyl cyanide and cyclopropanecarboxylic acid chloride.

Mesityl Propenyl Ketone.—This compound was synthesized from crotonyl chloride and mesitylene according to the directions of Fuson, Christ and Whitman.[14] Crotonyl chloride was prepared in 75% yield from crotonic acid and phosphorus trichloride following the general procedure of Lipp.[14]

γ-Bromobutyromesitylene.—Fuming hydrobromic acid was added dropwise to 4 g. of mesityl cyclopropyl ketone in 20 ml. of glacial acetic acid until the solution became cloudy. Sufficient glacial acetic acid was added to clarify the solution. After standing at room temperature for eighteen hours, the mixture became cloudy; addition of water caused the formation of two layers. The oily layer was collected in 50 ml. of ether and washed with a sodium carbonate solution. The ether was removed and the bromoketone distilled *in vacuo;* b. p. 135–137° (0.4 mm.); yield 5 g. or 87% of the theoretical amount.

Anal. Calcd. for $C_{13}H_{17}OBr$: C, 58.00; H, 6.37; Br, 29.69. Found: C, 58.12; H, 6.53; Br, 29.32.

β-Phenylbutyromesitylene. 1. From Phenylmagnesium Bromide.—A solution of 12 g. (0.06 mole) of mesityl propenyl ketone and 100 ml. of anhydrous ethyl ether was added slowly to 0.08 mole of phenylmagnesium bromide in 250 ml. of ethyl ether. After the reaction was complete, the mixture was stirred for an additional one-half hour and decomposed with an ammonium chloride solution. The ether layer was separated, dried over anhydrous calcium chloride, and distilled *in vacuo*. The β-phenylbutyromesitylene boiled at 162–165° (0.6 mm.); $n^{20}{}_4$ 1.5539; yield, 5.2 g. or 65%.

Anal. Calcd. for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.86; H, 8.40.

Mesityl cyclopropyl ketone did not condense with phenylmagnesium bromide.

2. From Benzene in the Presence of Anhydrous Aluminum Chloride.—Dry hydrogen chloride was passed into a solution of 15 g. of mesityl propenyl ketone and 100 ml. of dry benzene for thirty minutes. The generator was disconnected and 13 g. of anhydrous aluminum chloride was introduced. After the evolution of hydrogen chloride had ceased and the mixture had been allowed to stand at room temperature for fourteen hours, the initial yellow color had changed to a dark red. The mixture was poured over 100 g. of cracked ice and 50 ml. of concentrated hydrochloric acid, and subjected to steam distillation until all the volatile material had been removed. The non-volatile material was collected in ether and separated from the aqueous layer. The ether layer was washed with a sodium carbonate solution and dried over Drierite. Distillation *in vacuo* yielded 19 g. (89%) of a light yellow oil boiling at 162–165° (0.5 mm.). Infrared analysis showed that the oil was identical with the sample of β-phenylbutyromesitylene prepared in the previous experiment.

3,5-Dinitromesityl β-Nitrophenylpropyl Ketone.—One gram of β-phenylbutyromesitylene was added dropwise to an ice-cold mixture of 12 ml. of concentrated sulfuric acid and 12 ml. of concentrated nitric acid at such a rate that the temperature did not rise above 10°. The solution was kept cold for twenty minutes and poured on cracked ice. The trinitro derivative crystallized from methanol in pale yellow needles melting at 171–172°.

Anal. Calcd. for $C_{19}H_{19}N_3O_7$: C, 56.88; H, 4.77; N, 10.44. Found: C, 56.92; H, 4.89; N, 10.51.

γ-Phenylbutyromesitylene.—To a solution of 6 g. of mesityl cyclopropyl ketone and 40 ml. of dry benzene was added 9.3 g. of anhydrous aluminum chloride. The mixture was heated under reflux for three hours and allowed to stand overnight at room temperature. The mixture, now dark brown, was poured into a mixture of cracked ice and hydrochloric acid and subjected to steam distillation. The non-volatile residue was collected in ether, washed with a sodium carbonate solution, and dried. The γ-phenylbutyromesitylene distilled *in vacuo* at 155–160° (0.3 mm.); yield, 2 g. or 23%.

Anal. Calcd. for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.40; H, 8.56.

3,5-Dinitromesityl γ-Nitrophenylpropyl Ketone.—One gram of γ-phenylbutyromesitylene was added dropwise to an ice-cold mixture of 10 ml. of concentrated sulfuric acid and 10 ml. of concentrated nitric acid. It was necessary to cool and stir the mixture continuously to keep the temperature below 10°. The solution was allowed to stand in the cold for twenty minutes and poured on cracked ice. The trinitro derivative was crystallized from a benzene–ethanol mixture; m. p. 168–169°.

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[12] McCloskey and Coleman, "Organic Syntheses," **24**, 36 (1944).

[13] Lipp, Buchkremer and Seeles, *Ann.*, **499**, 13 (1932).

[14] Fuson, Christ and Whitman, THIS JOURNAL, **58**, 2450 (1936).

Anal. Calcd. for $C_{19}H_{19}N_3O_7$: C, 56.88; H, 4.77; N, 10.44. Found: C, 56.53; H, 4.94; N, 10.36.

A mixture with the trinitro derivative of β-phenylbutyromesitylene melted at 145–155°.

β-Mesitylbutyromesitylene.—This compound was prepared from mesityl propenyl ketone and mesitylmagnesium bromide according to the directions of Fuson and Meek.[15] The β-mesitylbutyromesitylene melted at 43–44°. Attempts to prepare this compound by conjugate addition of mesitylene to mesityl propenyl ketone in the presence of anhydrous aluminum chloride were unsuccessful.

γ-Mesitylbutyromesitylene.—Nine grams of anhydrous aluminum chloride was added slowly to a solution of 6 g. of mesityl cyclopropyl ketone and 60 g. of mesitylene. The mixture was heated at 80° for three hours and allowed to stand overnight at room temperature. The reaction mixture, which had developed a dark brown color, was poured on cracked ice and hydrochloric acid and subjected to steam distillation. The non-volatile residue was a dark oil which solidified upon cooling. A solution of the solid in hot ethanol was boiled for ten minutes with charcoal and filtered. After crystallization from ethanol, the white leaflets melted at 103–104°. The product was identical with the by-product from the preparation of mesityl cyclopropyl ketone. γ-Mesitylbutyromesitylene prepared by Lutz and Wood[16] by reduction of γ-chloro-γ-mesitylbutyromesitylene melts at 105–105.5°.

Anal. Calcd. for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.46; H, 9.35.

Ethyl α-Carbethoxy-β-methyl-γ-mesitoylbutyrate.—The general procedure of Kohler[17] was followed in the preparation of this compound. To a solution of 0.25 g. of metallic sodium dissolved in 10 ml. of absolute ethanol was added a solution of 15 g. of mesityl propenyl ketone, 13 g. of ethyl malonate, and 50 ml. of absolute ethanol. The mixture was allowed to stand at room temperature for twenty-four hours with occasional shaking. It was diluted with water, made acid to litmus with acetic acid, and extracted several times with ether. The ether extracts were combined and dried over anhydrous magnesium sulfate. Distillation *in vacuo* yielded 20 g. of ethyl α-carbethoxy-β-methyl-γ-mesitoylbutyrate; b. p. 165–169° (0.2 mm.).

Anal. Calcd. for $C_{20}H_{28}O_5$: C, 68.94; H, 8.09. Found: C, 68.77; H, 7.82.

Attempts to condense ethyl malonate with mesityl cyclopropyl ketone were unsuccessful even at elevated temperatures and pressures.

β-Methyl-γ-mesityoylbutyric Acid.—To a solution of 3.5 g. of potassium hydroxide and 50 ml. of water was added 5 g. of ethyl α-carbethoxy-β-methyl-γ-mesitoylbutyrate. The mixture was heated under reflux until all of the insoluble ester had disappeared. After cooling, the solution was acidified with hydrochloric acid. The oil which separated was removed and heated under reflux for four hours with an excess of 50% hydrochloric acid. The oily layer was removed from the aqueous layer, dissolved in ten per cent. sodium hydroxide, and filtered. Acidification with dilute acid caused the separation of an oil which solidified on standing. The product was crystallized from dilute ethanol; m. p. 81–82°.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12; neut. eq., 251.8. Found: C, 72.39; H, 8.25; neut. equiv., 248.3.

***p*-Chlorocinnamalacetomesitylene.**—Three grams of mesityl propenyl ketone and 2 g. of *p*-chlorobenzaldehyde were dissolved in 20 ml. of 95% ethanol. Ten per cent. sodium hydroxide solution was added dropwise until the reaction mixture became cloudy. Sufficient alcohol was added to clarify the solution, which was then allowed to stand at room temperature for ten minutes. During this period, crystals formed slowly. The *p*-chlorocinnamacetomesitylene crystallized from ethanol in bright yellow needles melting at 104–105°; yield 2 g., or 45%.

Anal. Calcd. for $C_{20}H_{19}OCl$: C, 77.28; H, 6.16; Cl, 11.41. Found: C, 77.10; H, 6.30; Cl, 11.42.

Summary

Mesityl cyclopropyl ketone has been prepared from cyclopropanecarboxylic acid chloride and mesitylene in the presence of anhydrous aluminum chloride. Its structure has been characterized by means of its infrared spectrum.

This cyclopropyl ketone reacts in a conjugate manner with benzene and with mesitylene in the presence of anhydrous aluminum chloride to form γ-phenyl- and γ-mesitylbutyromesitylene. The position of the substituent on the side chain was determined by comparison with β-phenyl- and β-mesitylbutyromesitylene prepared from mesityl propenyl ketone. Hydrobromic acid cleaves the cyclopropane ring to form γ-bromobutyromesitylene.

Attempts to condense the Grignard reagent and ethyl malonate with the cyclopropyl ketone were unsuccessful. The propenyl ketone gave the expected conjugate addition products with these reagents.

Mesityl propenyl ketone readily condenses in the aldol manner with *p*-chlorobenzaldehyde to produce *p*-chlorocinnamalacetomesitylene.

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[15] Fuson and Meek, *J. Org. Chem.*, **10**, 551 (1945).

[16] Lutz and Wood, THIS JOURNAL, **60**, 713 (1938).

[17] Kohler, *Am. Chem. J.*, **37**, 385 (1907).