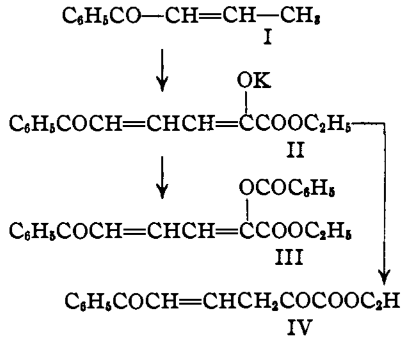
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Condensation of Propenyl Ketones with Ethyl Oxalate

BY REYNOLD C. FUSON, R. E. CHRIST[1] AND G. M. WHITMAN

Propenyl ketones and their higher vinylogs[2] might be expected to exhibit the properties characteristic of methyl ketones. Thus condensation with ethyl oxalate would lead to the synthesis of substances of the type $\mathrm{RCO(CHCH{=})_{\mathit{n}}{-}CH_2COCOOC_2H_5}$ analogous to the unsaturated keto esters of the type $\mathrm{RO_2C(CH{=}CH)_{\mathit{n}}CH_2{-}COCOOR}$ derived from crotonic ester and its vinylogs.[3] The realization of this expectation would open the way to the preparation of keto acids of the type $\mathrm{RCO(CH{=}CH)_{\mathit{n}}COOH}$.

As a first step in this process we have studied the action of ethyl oxalate on two propenyl ketones—phenyl propenyl ketone (I) and mesityl propenyl ketone (V). Phenyl propenyl ketone was treated with ethyl oxalate in ether solution, potassium ethoxide being employed as a catalyst. The reaction led to the formation of the potassium salt (II); this demonstrates that the methyl group of I possesses the activity which was to be predicted.



$$\mathrm{C_6H_5CO{-}CH{=}CH{-}CH_3}\quad \text{I}$$

$$\mathrm{C_6H_5COCH{=}CHCH{=}\overset{OK}{\overset{|}{C}}COOC_2H_5}\quad \text{II}$$

$$\mathrm{C_6H_5COCH{=}CHCH{=}\overset{OCOC_6H_5}{\overset{|}{C}}COOC_2H_5}\quad \text{III}$$

$$\mathrm{C_6H_5COCH{=}CHCH_2COCOOC_2H_5}\quad \text{IV}$$

When treated with benzoyl chloride, the salt was converted into the benzoate (III). The free keto ester (IV) was produced by dissolving the potassium salt in water and acidifying with acetic acid. This is a somewhat unstable substance. As first obtained, it is a light yellow crystalline compound. Upon exposure to air, it assumes a brilliant orange color and finally changes to a reddish oil. Its alcoholic solution is colored a light brown by ferric chloride, showing that it exists to some extent, at least, in its enolic form. It is readily soluble in alkali.

Phenyl propenyl ketone was found to give a positive iodoform test; however, the production of iodoform is slow. Undoubtedly, the alkali employed in this reaction is capable of splitting the ketone into acetophenone and acetaldehyde, both of which would give the iodoform reaction. At any rate, the hydrolytic cleavage of the double bond conjugated with the carbonyl group was accomplished by refluxing the ketone with potassium carbonate solution. The acetophenone was actually isolated and characterized, but the aldehyde underwent condensation in the presence of the carbonate solution. This is in accord with the results of Meyer[4] on the hydrolytic cleavage of similar unsaturated ketones.

Mesityl propenyl ketone (V), a new compound, was prepared from crotonyl chloride and mesitylene, employing the Friedel–Crafts synthesis.

$$\mathrm{(CH_3)_3C_6H_2{-}CO{-}CH{=}CH{-}CH_3}$$
V

$$\mathrm{(CH_3)_3C_6H_2{-}CO{-}CH{=}CH{-}CH_2{-}CO{-}COOC_2H_5}$$
VI

$$\mathrm{(CH_3)_3C_6H_2COOH}$$
VII

This ketone was condensed with ethyl oxalate in an alcoholic solution, using potassium ethoxide as a catalyst. The product isolated was the expected keto ester (VI). It is a light yellow crystalline substance, which, unlike the corresponding phenyl compound, is quite stable in air. It is readily soluble in alkali, showing that it exists in its enolic form. Oxidation with hydrogen peroxide leads to the formation of β-isodurylic acid (VII).

Experimental

Crotonyl Chloride.—This substance was prepared by a slight modification of the method of Kohler.[5] Crotonic acid and thionyl chloride were used instead of sodium crotonate and phosphorus oxychloride.

One mole (86 g.) of crotonic acid was heated under reflux with 300 cc. of thionyl chloride in a 1-liter, three-necked flask, equipped with a stirrer and reflux condenser, until the evolution of hydrogen chloride ceased. The mixture was then fractionally distilled from a modified Claisen flask. The excess thionyl chloride distilled at 75–80°. The temperature then rose rapidly to 124°, where the crotonyl chloride began to distill. The yield was 90 g., b. p. 124–126°, or 86% of the theoretical amount.

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(1) Du Pont Post-doctorate Fellow, 1935–1936.

(2) Fuson, *Chem. Rev.*, **16**, 1 (1935).

(3) Kuhn and Grundmann, *Ber.*, **69**, 1757 (1936).

(4) Meyer, *Helv. Chim. Acta*, **18**, 461 (1935).

(5) Kohler, *Am. Chem. J.*, **42**, 395 (1909).

Phenyl Propenyl Ketone.—The directions of Kohler[5] were used to prepare this ketone with the modification that benzene was substituted for carbon disulfide as solvent.

Two hundred grams of aluminum chloride was placed in a 1-liter, three-necked flask with 600 cc. of benzene. The mixture was cooled to 0° and exposed to the rays of a mercury vapor lamp. With vigorous stirring, 146 g. of crotonyl chloride was run in over a period of thirty minutes. There was brisk evolution of hydrogen chloride and the deposition of a colorless aluminum chloride complex. After fifteen minutes, the contents was poured into an ice-hydrochloric acid mixture, extracted with ether, washed with 10% sodium hydroxide solution, dried and distilled under reduced pressure. The fraction having a boiling point of 90–95° (2 mm.) was collected as the desired ketone. The total weight was 124 g., representing a 61% yield; n^{26}_{D} 1.5475.

The residue in the flask solidified upon cooling. Recrystallization from alcohol gave 65 g. of a product having a melting point of 74°. This was the product ($C_6H_5CH(CH_3)CH_2COC_6H_5$) obtained by Kohler by the condensation of two molecules of benzene with one of crotonyl chloride.

Hydrolytic Cleavage of Phenyl Propenyl Ketone.—In an all-glass refluxing apparatus were placed 4.0 g. of phenyl propenyl ketone, 10 g. of potassium carbonate and 50 cc. of water. To the top of the reflux condenser was attached a tube leading into a solution of 4 g. of semicarbazide hydrochloride and 4 g. of sodium acetate dissolved in 50 cc. of water. The object of this was to collect any acetaldehyde which might be formed from the hydrolysis. The solution was refluxed for a period of twenty-one hours. Twice during this time, the water was removed from the condenser to allow a small amount of vapor to pass over into the semicarbazide solution. It was hoped that in this way any acetaldehyde would be detected. However, the semicarbazone isolated proved to be that of acetophenone; m. p. 201°.

The solution remaining in the flask was extracted twice with ether, washed and then dried over calcium chloride. Upon distillation, 2.11 g. of product was obtained, having a boiling point of 196–203°. About 0.5 g. of higher boiling material remained in the flask. The semicarbazone of the 196–203° fraction was prepared, and was found to have a melting point of 200°. A mixed melting point with an authentic sample of acetophenone semicarbazone (m. p. 202°) was found to be 201°. This proved that acetophenone was formed by the hydrolytic cleavage of the phenyl propenyl ketone. The other product, which would have to be acetaldehyde, was not isolated. It probably underwent condensation in the presence of alkali, accounting for the residue remaining in the distilling flask.

Iodoform Reaction with Phenyl Propenyl Ketone.—In this test the reagent of Fuson and Tullock[6] was used. A small amount of iodoform was obtained.

Condensation of Ethyl Oxalate with Phenyl Propenyl Ketone.—Twenty-six grams of finely cut potassium was placed in a flask with 170 cc. of dry ether and cooled to 0°; 116 cc. of absolute alcohol was added, with shaking.

To the ether solution of potassium ethoxide was then added 48.8 g. of ethyl oxalate dissolved in 20 cc. of ether. Fifteen minutes later, 48.8 g. of phenyl propenyl ketone dissolved in 20 cc. of ether was added, with continued shaking. The color of the solution began to darken after a period of time. The mixture was allowed to stand in an ice box for twenty-four hours; a heavy layer of brilliant orange crystals of the potassium salt (II) settled out.

The mixture was filtered rapidly, and the potassium salt was then washed several times with dry ether. Afterward it was dried in a desiccator for twelve hours under reduced pressure. The weight of the final product was 77 g.; yield 81.3%.

Reaction of the Potassium Salt (II) with Benzoyl Chloride.—Ten grams of the salt was mixed with 5.3 g. of benzoyl chloride dissolved in 75 cc. of ether and allowed to stand for a period of twelve hours at room temperature.

The solution was practically colorless by this time, and a precipitate of potassium chloride crystals was on the bottom of the flask. After addition of water, the insoluble ether layer was separated and washed several times. The solvent was then evaporated, leaving a yellow crystalline mass of the benzoyl derivative. This was collected on a filter, washed with 10% sodium hydroxide to remove any benzoyl chloride or benzoic acid present and then recrystallized three times from alcohol.

The final product was a light yellow crystalline substance having a melting point of 123°. The total weight was 5.28 g., representing a 43% yield.

Anal. (semi-micro) Calcd. for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 71.75; H, 5.30.

Preparation of the Keto Ester (IV) from the Potassium Salt.—Ten grams of the salt was dissolved in 100 cc. of water. The addition of an excess of 2 *N* acetic acid caused a yellow semicrystalline mass to be thrown out of solution. The weight of crude material, obtained by filtering and drying by suction, amounted to 7.8 g.

The keto ester is somewhat unstable. Even during the crystallization a change appears to take place. The best solvent was found to be alcohol to which a few drops of acetic acid had been added. The crystals, as first obtained, have a faintly yellow color and melt at 106°, with decomposition. Upon exposure to air, they assume a brilliant orange color, and finally melt to form a reddish oil. When the compound is stored in a desiccator at reduced pressure, no change occurs. The compound dissolves in alkali, giving a light yellow coloration.

Anal. (semi-micro) Calcd. for $C_{14}H_{14}O_4$: C, 68.26; H, 5.73. Found: C, 68.14; H, 5.79.

Preparation of Mesityl Propenyl Ketone.—This is a new compound. It was prepared from crotonyl chloride and mesitylene by use of the Friedel–Crafts synthesis.

Two hundred eighty grams of aluminum chloride was placed in a 2-liter, three-necked flask with 800 cc. of carbon disulfide. The mixture was cooled to 0° and exposed to the rays of a mercury vapor lamp. With vigorous stirring, 209 g. of crotonyl chloride and 240.2 g. of mesitylene dissolved in 200 cc. of carbon disulfide were run in slowly over a period of two hours. There was a vigorous evolution of hydrogen chloride. The solution was stirred for an additional two hours at room temperature. The contents were then poured into iced hydrochloric acid solution, extracted with ether, washed with alkali, dried over calcium chloride and distilled under reduced pressure. A total of

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(6) Fuson and Tullock, THIS JOURNAL, **56**, 1638 (1934).

284 g. of the desired ketone was obtained; b. p. 128° (5 mm.); n^{20}_D 1.5330; d^{20}_4 0.9819. This represents a yield of 75%.

Anal. (semi-micro) Calcd. for $C_{13}H_{16}O$: C, 82.92; H, 8.57. Found: C, 82.61; H, 8.46.

Condensation of Mesityl Propenyl Ketone with Ethyl Oxalate.—A total of 6.5 g. of finely cut potassium was placed in a flask with 45 cc. of dry ether. Absolute alcohol (29 cc.) was added, with shaking, to convert the potassium to potassium ethoxide.

To the ether solution was then added 12.2 g. of ethyl oxalate dissolved in 15 cc. of ether. Fifteen minutes later, 15.7 g. of mesityl propenyl ketone dissolved in 15 cc. of ether was added, with continued shaking. The color of the solution soon changed to a dark red. The mixture was allowed to stand for a period of twenty hours in an ice box.

The solution was then treated with water and neutralized with acetic acid. The ether layer was separated and dried. Evaporation of the solvent left a crystalline mass. Crystallization from alcohol gave 22 g. of beautiful light yellow crystals which melted, with decomposition, at 156°; yield 90%.

Anal. (micro) Calcd. for $C_{17}H_{20}O_4$: C, 70.78; H, 6.99. Found: C, 70.74; H, 6.96.

Oxidation with Hydrogen Peroxide.—One gram of the ester was placed in a flask with 20 cc. of 10% sodium hydroxide solution and 100 cc. of 3% hydrogen peroxide solution. The mixture was allowed to stand for a period of twelve hours at room temperature.

The solution was then acidified with acetic acid. The precipitate which formed was collected on a filter and redissolved in alkali. It was then thrown out of solution again by the addition of more acetic acid. Recrystallization from a mixture of benzene and low-boiling petroleum ether gave 0.34 g. of beautiful colorless crystals of β-isodurylic acid; m. p. 152°.

Summary

Phenyl propenyl ketone (I) has been prepared from crotonyl chloride and benzene by use of Friedel–Crafts synthesis. The ketone was condensed with ethyl oxalate in ether solution, potassium ethoxide being employed as a catalyst.

The potassium salt (II) was converted into the benzoate (III) by treatment with benzoyl chloride. When the salt was acidified with acetic acid, the free keto ester (IV) was produced.

Mesityl propenyl ketone (V) has been prepared in an analogous manner. It was, likewise, condensed with ethyl oxalate, producing a keto ester (VI).

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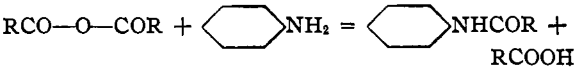
[CONTRIBUTION FROM THE AMMONIA DEPARTMENT OF E. I. DU PONT DE NEMOURS & COMPANY]

Quantitative Determination of Anhydrides of Carboxylic Acids

BY DONALD MILTON SMITH AND W. M. D. BRYANT

Organic acid anhydrides ordinarily are estimated analytically either by hydrolysis followed by titration of both acidic groups, or by the use of a reaction which converts one acidic residue into a neutral substance leaving only one carboxyl as a measure of the anhydride present. While both analytical schemes are bases of accepted methods, it is apparent that neither alone is sufficient to differentiate sharply between anhydrides and free acids. However, by using the two principles in combination, it becomes possible to determine the -CO-O-CO- content of a mixture, even though the exact nature and composition of the mixture is unknown. Radcliffe and Medofski[1] have made a careful investigation of the above-mentioned procedures as applied to acetic anhydride. The majority of these procedures make use of the fact that an anhydride reacts with aniline to form a mole each of anilide and acid, respectively[2]



The action of alcoholates of the alkali metals upon anhydrides is analogous to that of aniline, a mole of ester and a mole of alkali salt resulting from the reaction carried out as a titration.[3]

Except for the closely related work of Holde[4] on the titration of higher fatty acid anhydrides with alcoholic sodium hydroxide, little use has been made of the above reaction in an analytical way.

In the present investigation a standard solution of sodium methylate was used in place of aniline,

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(1) Radcliffe and Medofski, *J. Soc. Chem. Ind.*, **36**, 628 (1917).

(2) Menschutkin and Vasiliev, *J. Russ. Phys.-Chem. Soc.*, **21**, 190 (1889).

(3) Caudri, *Rec. trav. chim.*, **48**, 778 (1929).

(4) Holde and Smelkus, *Ber.*, **53**, 1889 (1920); Holde and Tacke, *ibid.*, **53**, 1898 (1920).