[Contribution from the Chemical Laboratory of Harvard University]

SOME ADDITION REACTIONS OF PHENYL BENZOYL ACETYLENE

By E. P. Kohler and G. R. Barrett

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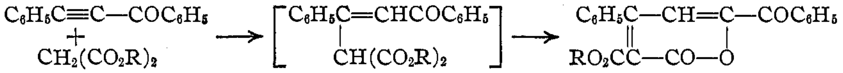
The work of a number of investigators, especially that of Thorpe and his collaborators, has shown that in glutaconic ester and its homologs the unsaturated system, $—CO—CH{=}CH—CH_2CO—$, has exceedingly interesting properties. For the further study of the peculiar reactions of this system it would be advantageous to use substances in which the two groups joined to its ends are different. The following investigation was originally undertaken with the object of ascertaining whether substances of this type can be obtained by adding suitable esters to phenyl benzoyl acetylene.

As was shown in an earlier paper[1] malonic esters combine very readily with phenyl benzoyl acetylene in the presence of sodium alcoholates. Unfortunately the reaction does not stop with addition; the product immediately undergoes condensation to a pyrone derivative.

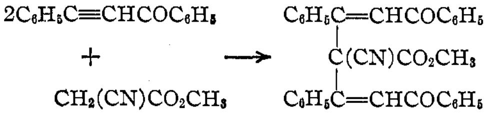


I

By de-carboxylating this pyrone ester, however, and subsequently opening the pyrone ring, it was possible to get an acid of the desired type: $C_6H_5COCH_2C(C_6H_5){=}CHCO_2H$. We examined the solid methyl ester of this acid but found it useless for our purpose, because in every attempt at addition or alkylation, the ester was converted almost quantitatively into pyrone.

We tried a similar condensation, using diethyl ethylmalonate in the expectation that the reaction would end with the addition because the product would lack the hydrogen necessary for the formation of a pyrone derivative. Addition readily takes place, doubtless, to form the unsaturated ester; but the product is an undistillable oil and, therefore, not adapted to the work in hand.

Since the malonic esters did not serve our purpose we turned to α-cyano esters. Methyl cyano-acetate combines with great ease but the result is a trimolecular addition product:



$$\begin{matrix} 2C_6H_5C{\equiv}CHCOC_6H_5 & & C_6H_5C{=}CHCOC_6H_5 \\ + & \longrightarrow & | \\ & & C(CN)CO_2CH_3 \\ & & | \\ CH_2(CN)CO_2CH_3 & & C_6H_5C{=}CHCOC_6H_5 \end{matrix}$$

I

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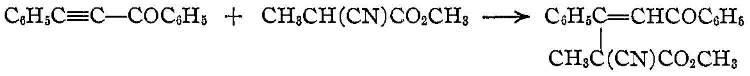
[1] Kohler, This Journal, **44,** 379 (1922).

Such trimolecular condensation products are generally encountered in addition reactions to unsaturated ketones, but not as sole reaction products; very often by proper control of conditions trimolecular condensation may be rendered negligible. All efforts to achieve this in this case were fruitless.

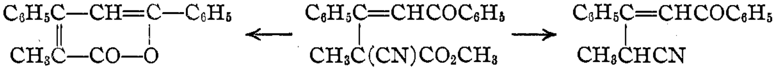
Methyl α-cyanopropionate also combines fairly readily with phenyl benzoyl acetylene. The result depends upon the amount of sodium methylate used. In the presence of a small quantity of this condensing agent the reaction stops with addition and the product is an unsaturated open-chained cyano ester.



$$\mathrm{C_6H_5C{\equiv}C{-}COC_6H_5} + \mathrm{CH_3CH(CN)CO_2CH_3} \longrightarrow \begin{array}{l}\mathrm{C_6H_5C{=}CHCOC_6H_5} \\ \quad | \\ \mathrm{CH_3C(CN)CO_2CH_3}\end{array}$$

II

When larger quantities of the methylate are used the result is a mixture of secondary products, a pyrone derivative (III) and a small quantity of an open-chained unsaturated nitrile (IV).



$$\begin{array}{l}\mathrm{C_6H_5C{-}CH{=}C{-}C_6H_5} \\ \quad\;\, \| \qquad\qquad\; | \\ \mathrm{CH_3C{-}CO{-}O}\end{array} \longleftarrow \begin{array}{l}\mathrm{C_6H_5C{=}CHCOC_6H_5} \\ \quad | \\ \mathrm{CH_3C(CN)CO_2CH_3}\end{array} \longrightarrow \begin{array}{l}\mathrm{C_6H_5C{=}CHCOC_6H_5} \\ \quad | \\ \mathrm{CH_3CHCN}\end{array}$$

III II IV

In order to make the unsaturated ester (II) available for the purpose of the investigation it was necessary to hydrolyze it, and then to get rid of one of the carboxyl groups. Here a new difficulty presented itself; the cyanogen group, as is frequently the case with tertiary nitriles, stubbornly resisted hydrolysis with acids, and all attempts to hydrolyze the substance with bases gave either the mixture of pyrone (III) and nitrile (IV) or else oils resulting from deeper seated decompositions.

After concluding these experiments, which convinced us that phenyl benzoyl acetylene would not serve for the preparation of the type of substances we desired, we examined a few other addition reactions of the ketone that promised to yield useful types of unsaturated compounds. The nitroparaffins combine in the presence of sodium alcoholate, but the reaction takes place so slowly that most of the ketone is lost as dibenzoylmethane. Toluenesulfinic acid, on the other hand, combines with the substance even more easily than it does with ethylenic ketones, and forms two isomeric unsaturated sulfone ketones.

Experimental Part

The phenyl acetylene used in the preparation of the acetylenic ketone was obtained by the method recommended by Hessler.[2] The yield was excellent, 345 g. from 1 kg. of cinnamic acid. The acetylenic ketone itself was made in accordance with the directions given by Dufraisse.[3] In a

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[2] Hessler, THIS JOURNAL, **44,** 425 (1922).

[3] Dufraisse, *Thesis,* Paris, **1921.** Lucas, *Ann. chim.,* [8] **17,** 138 (1909).

typical experiment 72 g. of phenyl acetylene gave 66 g. of crude ketone, most of which was collected at 180° (5 mm.) and which solidified almost completely; 25 g. of pure phenyl acetylene was recovered and 29 g. of tarry residue remained in the distilling apparatus.

I. Experiments with Gamma-Benzoyl-Beta-Phenyl-Crotonic Acid

The method of preparing this acid which was described in an earlier paper[4] was improved as follows.

The pyrone ester (I) is suspended in 4–5 times its weight of hot alcohol and an excess of concd. aqueous sodium hydroxide added. The solution at once turns to a deep red color, but the color disappears in a minute or two and the mixture becomes almost solid with precipitated pyrone. When this is shaken for a few minutes it redissolves, forming a yellow solution which sometimes contains a small quantity of suspended sodium carbonate or sodium salt. The solution is diluted and shaken with ether which extracts a small quantity of pyrone. The aqueous layer, on acidification, precipitates impure phenyl-benzoyl-crotonic acid. Repeated recrystallization from a mixture of ethyl acetate and petroleum ether gives the pure acid, melting with decomposition at 138°.

Methyl-γ-benzoyl-β-phenyl-crotonate, $C_6H_5COCH_2C(C_6H_5):CHCO_2CH_3$.—The ester cannot be prepared by treating the acid with methyl alcohol and hydrochloric or sulfuric acid because this mixture rapidly transforms the acid into the pyrone derivative. The ester is readily obtained, however, by the action of methyl iodide on the silver salt of the acid. When the silver salt is made from pure acid, the ester crystallizes well both from methyl alcohol and from a mixture of ether and petroleum ether, separating in needles that melt at 83°. Silver salt made from impure acid gave oils from which it was difficult to isolate any solid products. The ester melting at 36°, which was reported in the earlier paper, was not found in any of our products.

Analyses. Calc. for $C_{18}H_{16}O_3$: C, 77.1; H, 5.8. Found: C, 77.0; H, 5.7.

Owing to the ease with which the ester is transformed into diphenyl pyrone it was impossible to alkylate it. A little acid or a trace of alkali in alcohol sufficed to convert it into pyrone in a few seconds, and powdered sodium and methyl iodide in ether had the same effect. Attempts to methylate the pyrone by allowing it to remain in contact with methyl iodide and sodium methylate for 36 hours at the ordinary temperature, or by boiling the same mixture for 8 hours gave neither methylated pyrone nor methylated benzoyl phenyl crotonic acid but only unchanged pyrone.

II. Condensation with Alpha-Cyano Esters

α-Cyano-acetic Ester.—When sodium methylate is added to a solution of phenyl benzoyl acetylene and methyl cyano-acetate in methyl alcohol an intense red color is produced at once.

In a few minutes lemon-yellow needles begin to separate even from a hot solution. An experiment in which the reactants were heated for an hour in the presence of a trace of sodium methylate gave a 70% yield of this product. The substance is very sparingly soluble in alcohol but may be recrystallized from hot benzene or acetone in which it is moderately soluble. It crystallizes in yellow needles and melts at 209°.

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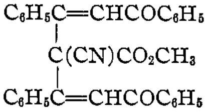
[4] Ref. 1, p. 382.

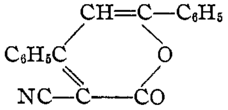
Analyses. Calc. for $C_{34}H_{26}O_4N$: C, 79.8, H, 4.9. Found: C, 79.7; H, 4.9.

The substance readily reduced permanganate in acetone and gave benzoic acid as the sole organic oxidation product. This shows that it is the trimolecular condensation product (A) and not the pyrone derivative (B) which does not greatly differ from it in composition.



$$\begin{array}{l} C_6H_5C{=}CHCOC_6H_5 \\ \quad | \\ \quad C(CN)CO_2CH_3 \\ \quad | \\ C_6H_5C{=}CHCOC_6H_5 \end{array}$$

A



B

Various attempts to get the simpler dimolecular addition product were unsuccessful. A reaction that was allowed to continue for only a few minutes and then stopped by addition of acid gave only the trimolecular compound and unchanged components, and even when the cyano ester was used in sufficient excess to serve as solvent the trimolecular compound was still the only addition product formed.

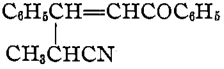
α-Cyanopropionic Ester.—As cyanopropionic ester invariably combines less readily with unsaturated compounds than cyano-acetic ester, the condensation was first tried with one equivalent of condensing agent. A solution of 10 g. of the unsaturated ketone, 7.5 g. of the ester and about one equivalent of sodium methylate in 25 cc. of dry methyl alcohol was refluxed for 20 minutes and set aside. After remaining at the ordinary temperature for 15 hours the liquid was acidified and extracted with ether. This extract yielded about 1 g. of a colorless solid.

Most of the product was retained by the aqueous alcoholic layer. This gradually deposited a yellow solid during the extraction with ether but most of this substance was obtained when the alcohol and water were removed completely by warming under diminished pressure. The total yield of yellow solid was 9 g.

α-Cyano-α-methyl-β-phenyl-butenyl-phenyl Ketone (III).—The colorless solid was purified by recrystallization from methyl alcohol from which it separated in prisms which melted at 129°.

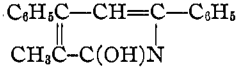
Analyses. Calc. for $C_{18}H_{15}ON$: C, 82.7; H, 5.8. Found: C, 82.7; H, 5.9.

The substance might be either an unsaturated δ-ketonic nitrile (III) or an isomeric hydroxy pyridine.



$$\begin{array}{l} C_6H_5CH{=}CHCOC_6H_5 \\ \quad | \\ CH_3CHCN \end{array}$$

III



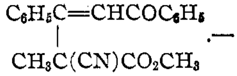
V

That the open-chained formula is correct is shown by the melting point which is considerably too low for the hydroxypyridine, by the fact that the substance reduces permanganate in the cold, and that it gives an intensely yellow sodium compound when treated with sodium alcoholate.

3-Methyl-4,6-diphenyl Pyrone (III).—The colored product of the reaction separated in greenish-yellow needles which turned red at about 260° and melted completely at 264°. This substance dissolved with some difficulty in boiling methyl alcohol but none of it was recovered from the solution. Instead, the solution on evaporation deposited sodium chloride and a new yellow compound, which on recrystallization from hot methyl alcohol separated in stout yellow needles and melted at 113°. As this substance contains no nitrogen and no active hydrogen, and does not reduce permanganate it must be the pyrone (IV).

Analyses. Calc. for $C_{18}H_{14}O_2$: C, 82.4; H, 5.3. Found: C, 82.2; H, 5.5.

β-(α-Cyano-α-carbomethoxy Ethyl)-benzal Acetophenone,



$$\begin{array}{l} C_6H_5C{=}CHCOC_6H_5 \\ \quad | \\ CH_3C(CN)CO_2CH_3 \end{array}$$

.—Since the condensation of methyl cyanopropionate and phenyl benzoyl acetylene gave only secondary products when one equivalent of sodium methylate was used, the experiment was repeated with a small quantity of condensing agent. Four g. of the ketone and 3 g. of the ester were dissolved in hot dry methyl alcohol, and to this solution sufficient sodium methylate was added to produce a permanent red color. The solution was boiled for 10 minutes, then allowed to stand at the ordinary temperature overnight. The mixture was poured into cold dil. hydrochloric acid and this mixture extracted with ether. The washed and dried ethereal solution, on evaporation, left an oil that solidified when rubbed with methyl alcohol. The solid was purified by recrystallization from methyl alcohol from which it separated in colorless needles that melted at 70°.

Analyses. Calc. for $C_{20}H_{17}O_3N$: C, 75.2; H, 5.4. Found: C, 74.8; H, 5.5.

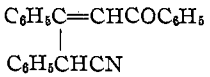
The yield of ester was small—2 g.—less than 33%. Attempts to hydrolyze it were unsuccessful, the only products being the open-chained nitrile and the pyrone.

Benzyl Cyanide.—When an alcoholic solution of phenyl benzoyl acetylene and benzyl cyanide is treated with sodium methylate it immediately turns to a deep red. This production of color, which was observed in all previous condensations, indicates the formation of the sodium derivative of a condensation product. When the mixture obtained with benzyl cyanide was treated in the usual way, however, no condensation product could be isolated. The principal product was dibenzoyl methane, evidently formed by addition of water to the ketone. As this indicated that the reaction with benzyl cyanide was reversible, benzene was substituted for alcohol as solvent.

A suspension of the sodium derivative of benzyl cyanide in benzene was prepared either by shaking a benzene solution with sodium methylate which had been dried in a vacuum at 130°, or by boiling a similar solution of the nitrile with freshly powdered sodamide. When a benzene solution of the unsaturated ketone was added to this solution, the crimson sodium derivative of the condensation product separated at once with considerable evolution of heat. To complete the reaction the mixture was heated for 10 minutes and constantly shaken. The yield was probably a little better with the suspension made from sodamide than with that made from sodium methylate, but did not exceed 50%. The red sodium compound was filtered off, the cake pressed as dry as possible, washed with benzene, and then shaken with dil. hydrochloric acid until all the color had disappeared. The colorless solid that was left was recrystallized from acetone and water.

Analyses. Calc. for $C_{23}H_{17}ON$: C, 85.4; H, 5.3. Found: C, 85.2; H, 5.5.

α-Cyano-α-phenyl-β-phenyl-butenyl-phenyl Ketone,



$$\begin{array}{l} C_6H_5C{=}CHCOC_6H_5 \\ \quad | \\ C_6H_5CHCN \end{array}$$

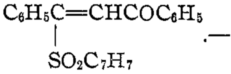
.—α-Cyano-α-phenyl-β-phenyl-butenyl-phenyl ketone crystallizes in colorless needles, and melts at 137°. It reduces permanganate in acetone, readily forms a phenylhydrazone, and regenerates the crimson sodium compound when treated with sodium methylate. All attempts to hydrolyze or esterify the cyanogen group were unsuccessful. Alkalies reversed the addition reaction, while hydrogen chloride in methyl alcohol, and strong sulfuric acid, resulted in the formation of a high-melting, greenish-yellow substance which was evidently a very complex product and, therefore, not investigated.

PHENYLHYDRAZONE.—The phenylhydrazone was made by adding 1 g. of phenylhydrazine to a hot solution of 0.7 g. of the substance in glacial acetic acid, allowing the mixture to stand for half an hour and then pouring it into ice water. The finely divided precipitate was recrystallized from alcohol. It separated in heavy, pale yellow needles, melting with decomposition at 150–151°.

Analyses. Calc. for $C_{29}H_{23}N_3$: C, 84.3; H, 5.6. Found: C, 84.4; H, 5.65.

III. Addition of Para-Toluene Sulfinic Acid

p-Toluene sulfinic acid combines with phenyl benzoyl acetylene, as it does with the corresponding ethylenic ketones in the absence of any condensing agent. The process stops, as would be expected, with the addition of one equivalent of the acid.

β-Tolylsulfonyl Benzal Acetophenone,  $C_6H_5\underset{\underset{SO_2C_7H_7}{|}}{C}=CHCOC_6H_5$.—A solution of 5 g. of the ketone and 3.8 g. of the acid in 50 cc. of alcohol was heated for a few minutes on a steam-bath, then set aside. As no solid separated after the solution had been kept for several days, a few drops were evaporated, and the remainder inoculated with the residue. It deposited an abundant crop of white crystals, more of which separated on longer standing, the total yield being 8 g. The product is moderately soluble in hot alcohol from which it crystallizes in colorless six-sided plates melting at 141°. The substance is extraordinarily hard to burn; complete combustion for analytical purposes could be obtained only by using a metal boat and adding copper oxide to the sample.

Analyses. Calc. for $C_{22}H_{18}O_3S$: C, 72.9; H, 5.0. Found: C, 73.5; H, 5.1.

In addition to the colorless sulfone which constitutes the main product, there is usually formed a small quantity of a yellow substance that crystallizes in needles. This is a stereoisomeric sulfone, which can be obtained quantitatively by treating the colorless isomer with a trace of alkali. Thus, 12 g. of the finely ground colorless isomer was suspended in 50 cc. of alcohol containing a trace of sodium alcoholate. The suspended particles turned yellow immediately. The suspension was allowed to stand with occasional stirring for several hours, then filtered, and the solid recrystallized from boiling alcohol in which it is sparingly soluble. It separated in slender, lemon-yellow needles melting at 157°. The sample was mixed with copper oxide for analysis.

Analyses. Calc. for $C_{22}H_{18}O_3S$: C, 72.9; H, 5.0. Found: C, 73.2; H, 5.3.

The structure of the two sulfones was established by reduction. One g. of each was dissolved in hot glacial acetic acid containing a little water. After the addition of an excess of zinc dust the two solutions were heated for half an hour, then filtered to remove the unused zinc, and diluted with water. This precipitated solids that on recrystallization from alcohol in each case were found to be composed of two substances. One of these crystallized in very fine needles and melted at 249°; this was, doubtless, a dimolecular reduction product. The other crystallized in coarser needles and melted at about 185°; this was identified as β-*p*-tolyl-sulfonyl-β-phenyl propiophenone,[5] $C_6H_6SO_2CH(C_6H_5)CH_2COC_6H_5$, by comparison with a sample made by adding *p*-toluene sulfinic acid to benzalacetophenone. The two substances are, therefore, stereoisomers.

Summary

1. In the presence of a little sodium methylate, phenyl benzoyl acetylene combines more or less readily with cyano-acetic esters, cyanopropi-

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[5] Kohler and Reimer, *Am. Chem. J.*, **31**, 182 (1904).

onic ester, and benzyl cyanide. It also combines readily with *p*-toluenesulfinic acid.

2. With cyano-acetic ester no substance composed of one molecule of each of the components could be obtained, the sole product being a trimolecular substance containing one molecule of the ester to two of the ketone. Cyanopropionic ester and benzyl cyanide gave the normal addition products that were to be expected; but these proved to be ill adapted for studying the unsaturated system that is responsible for the peculiarities of the glutaconic acids.

3. *p*-Toluene sulfinic acid gives two isomeric unsaturated sulfones.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

THE PREPARATION OF ALKYL CHLORIDES

BY JAMES F. NORRIS AND HAZEL B. TAYLOR

RECEIVED DECEMBER 3, 1923

The conversion of alcohols into alkyl halides by means of aqueous solutions of hydrochloric, hydrobromic and hydriodic acids has been described in papers previously published from this Laboratory.[1]

All the alcohols studied were converted into bromides and iodides when they were heated in an open vessel with an aqueous solution of the corresponding hydrogen halide. The yields of the halides obtained were excellent when the constant-boiling solutions of the acids were used; and the products obtained were free from impurities. This method of preparing alkyl bromides and iodides has, consequently, come into general use.

Only a few of the large number of alcohols studied were converted into chlorides when they were boiled with aqueous hydrochloric acid. The method could not be applied to the saturated primary alcohols. Tertiary alcohols, some secondary alcohols, and certain primary compounds in which the hydroxyl group was activated by the presence of a neighboring negative radical did, however, furnish satisfactory yields of chlorides.

We have recently returned to the study of the reaction in the hope of discovering the conditions necessary to prepare alkyl chlorides from the primary saturated alcohols. As the result of the investigation of certain condensations through the aid of zinc chloride, it seemed probable that the latter reagent does not act, as has been supposed in the past, as a dehydrating agent when it is used in the preparation of alkyl chlorides from alcohols and hydrogen chloride. Zinc chloride markedly activates the carbon-oxygen bond in ethers, esters and anhydrides, and makes it possible to bring about reactions between these substances and other compounds.

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[1] *Am. Chem. J.*, **38**, 627 (1907); THIS JOURNAL, **38**, 1071 (1916); **42**, 2093 (1920).