chlorojuglone and freshly made sodium ethylate a dark purple precipitate formed immediately (in benzene solution). When this was dissolved in water and acidified with hydrochloric acid, the solution turned yellow and a yellow precipitate formed. This proved to be the hydroxychlorojuglone, m. p., 191°, described above. It showed the same color phenomena. We had hoped to find also an ethoxy derivative of dichlorojuglone.

Attempt to Prepare an Oxime.—One g. of dichlorojuglone was dissolved in 20 cc. of alcohol containing 0.3 g. of hydroxylamine hydrochloride (1 molecular equivalent), and 2 drops of strong hydrochloric acid. After the solution had boiled for 2 hours and then cooled, a product was obtained, but it contained no nitrogen and proved to be unchanged dichlorojuglone. The experiment was tried with 2 molecular equivalents of the hydroxylamine salt and boiling was continued for 8 hours, but with no better success.

Summary

1. The best method of chlorinating juglone is described.
2. A description of the sodium salt and the benzoate of dichlorojuglone is given.
3. One chlorine atom of dichlorojuglone is replaced by hydroxyl by the action of alcoholic sodium hydroxide. This hydroxyl derivative and its acetate are described.
4. Dichlorojuglone was arylated by weak bases such as aniline, *p*-chloro-aniline and *p*-toluidine but not by dichloro-aniline. In each case 1 chlorine atom is replaced.
5. Dichlorojuglone was reduced in acid solution with zinc, giving a trihydroxynaphthalene. The triacetoxy derivative was also prepared.
6. Sodium ethylate yields an hydroxy derivative of dichlorojuglone and not an ethoxy.
7. Hydroxylamine hydrochloride does not give an oxime.
8. Reasons are given for locating the chlorine atoms at Positions 2 and 3.

Chapel Hill, North Carolina

[Contribution from the Chemical Laboratory of Harvard University]

THE MECHANISM UNDERLYING THE REACTION BETWEEN ALDEHYDES OR KETONES AND TAUTOMERIC SUBSTANCES OF THE KETO-ENOL TYPE

By E. P. Kohler and B. B. Corson

Received June 9, 1923

The discovery that aldehydes and ketones can be condensed with aceto-acetic ester, cyano-acetic ester, diketones, and other substances containing active hydrogen, was a natural consequence of the use of reactions which are supposed to involve aldol condensation for the synthesis of unsaturated compounds. The reagents are not essentially different from those used in these earlier syntheses, the catalysts used to induce reaction are, for the most part, the same, and the two processes usually give the same type of unsaturated compound. Most chemists, doubtless, therefore assume that the mechanism of the two reactions is also the same, namely, aldol condensation followed by loss of water.

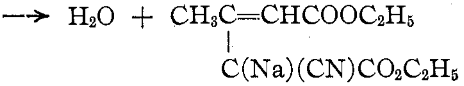
Other views have, however, also been expressed. Knoevenagel,[1] who substituted primary and secondary amines for the sodium alcoholate which had previously been used as the condensing agent, accounted for the catalytic action of the amines by the mechanism:

$$RCHO + 2R_2NH \rightleftharpoons RCH = (NR_2)_2 + H_2O \qquad (1)$$

$$RCH(NR_2)_2 + H_2C< \longrightarrow RCH = C< + 2R_2NH \qquad (2)$$

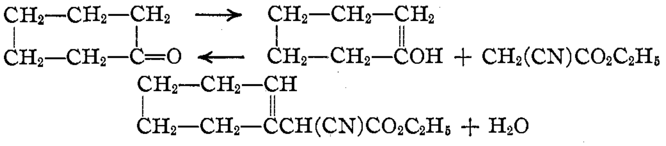
In support of this mechanism he showed that hydrobenzamide can be used in place of benzaldehyde and ammonia, and Schiff bases in place of the corresponding aldehydes and amines. It is now known,[2] however, that tertiary amines can serve as catalysts in these condensations even though they are incapable of reacting with aldehydes and ketones in the manner predicated by Knoevenagel.

A mechanism of an entirely different type was first proposed by Rogerson and Thorpe[3] when they found that sodium cyano-acetic ester can be condensed with aceto-acetic ester and with its monomethyl derivative, but not with dimethyl aceto-acetic ester. Since the possibility of condensation here appears to be related to the capacity for enolization, they assume that the metallic derivative is condensed with the enolic modification of the ketonic ester. $CH_3C(OH){=}CHCOOC_2H_5 + HC(Na)(CN)CO_2C_2H_5$



$$\longrightarrow H_2O + \underset{\displaystyle C(Na)(CN)CO_2C_2H_5}{CH_3\underset{|}{C}{=}CHCOOC_2H_5}$$

Harding, Haworth and Perkin[4] adopted this view to account for the fact that they obtained, mainly, a β,γ unsaturated ester when they condensed cyclohexanone and cyano-acetic ester in the presence of either sodium methylate or piperidine. Extending Thorpe's mechanism to ketones which at best enolize but little, and to reactions in which amines are used as condensing agents they interpret their results as follows:



Thorpe's mechanism implies that only aliphatic ketones can be condensed with cyano-acetic ester, and that β,γ unsaturated compounds are the primary products in these condensations. In its support, Haworth[5] showed, shortly afterwards, that benzophenone failed to react at all under

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[1] Knoevenagel, *Ann.*, **281,** 25 (1894).

[2] Hann and Lapworth, *J. Chem. Soc.*, **85,** 46 (1904).

[3] Rogerson and Thorpe, *ibid.*, **87,** 1685 (1905).

[4] Harding, Haworth and Perkin, *J. Chem. Soc.*, **93,** 1943 (1908).

[5] Haworth, *ibid.*, **95,** 480 (1909).

conditions in which a variety of ketones that are capable of enolization are condensed with great ease.

The latest exposition of this mechanism is contained in a lengthy discussion by Ingold[6] on the condensation of ketones and aldehydes with the sodium derivative of cyano-acetic ester. The point of view on which this discussion is based is given in the following passage:

> ". . . there can be no doubt but that it is the enolic modification of the ketone which actually enters into the reaction because ketones, such as benzophenone of which no enolic modification can exist, fail to react, while others condense with a readiness apparently proportionate to their capacity for tautomeric change."

To the reasons for holding this view which had been given by others Ingold now adds the general statement that ease of condensation is apparently related to capacity for tautomeric change. He realizes that this is inconsistent with the extraordinary ease with which aldehydes—especially aromatic aldehydes which are incapable of enolization—enter into the reaction, but disposes of the difficulty by suggesting that these may react in a tautomeric form containing bivalent carbon, as, for example, $C_6H_5—C—OH$.

The view that these condensations involve the enolization of aldehydes or ketones seemed to us improbable on a variety of grounds. We could find no reasons for assuming that the reactions with cyano-acetic ester are in any way different from those with other substances containing active hydrogen atoms. The formation of β,γ unsaturated compounds in certain special cases can be explained in other ways.[7] The relative ease with which aldehydes and the various ketones enter into the reaction seems to be adequately accounted for by the known differences in the activity of these substances in *addition reactions*. Thus the well known measurements of Stewart[8] and of Zelinskey[9] show that all aldehydes combine with other substances more rapidly than does any ketone; that acetone, aceto-acetic ester and cyclic ketones, like cyclohexanone, combine more rapidly than other ketones; and that benzophenone combines more slowly than any except the most highly substituted aliphatic ketones. The relative activity of these substances in condensation and in addition reactions is, therefore, approximately the same.

Inasmuch as there are carbonyl compounds that are incapable of enolizing and yet combine fairly readily with other substances, it ought to be possible to determine definitely whether enolization is involved in these condensations or not. The two most promising substances for this purpose are the esters of mesoxalic and benzoylformic acids. The

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[6] Ingold, *ibid.*, **119**, 329 (1921).

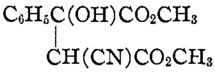
[7] Lapworth in a recent paper has adduced evidence that the ester obtained by Harding, Haworth and Perkin is probably an α,β-unsaturated compound.

[8] Stewart, *J. Chem. Soc.*, **87**, 185 (1905).

[9] Petrenko-Kritschenko, *Ann.*, **341**, 150 (1905).

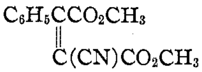
condensation of mesoxalic ester and cyano-acetic ester was studied by Schmitt.[10] In the presence of piperidine he obtained along with more complex products a substance whose structure he did not succeed in establishing, but which doubtless was the unsaturated condensation product, $(C_2H_5O_2C)_2C:C(CN)CO_2R$.

We have used methyl benzoylformate and have found that under the influence of sodium methylate, ammonia, methyl amine, aniline and piperidine, methyl cyano-acetate condenses with it in the same way and almost with the same ease that it condenses with aldehydes. The product is the unsaturated compound, II.



$$\begin{array}{l} C_6H_5C(OH)CO_2CH_3 \\ \quad | \\ \quad CH(CN)CO_2CH_3 \end{array}$$

I



$$\begin{array}{l} C_6H_5CCO_2CH_3 \\ \quad \| \\ \quad C(CN)CO_2CH_3 \end{array}$$

II

Using the same condensing agents but operating under different conditions it is possible to get as the principal product the saturated hydroxyl compound, I.

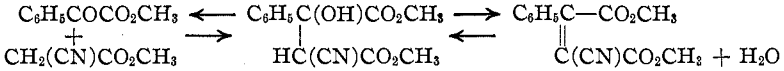
With these facts established there remains no reason for assuming that either the reaction between aldehydes or ketones and substances which have active hydrogen, or aldol condensation involves the enolization of aldehydes or ketones.

The addition product (I) is a stable substance. When it is perfectly pure it neither readily loses water nor reverts to its components. Thus, when it is dissolved in pure boiling methyl alcohol or acetone it causes an elevation corresponding to its molecular weight and the solutions can be boiled for hours without further change in the boiling point. When it is heated under very low pressures it partly distils, partly dissociates into its components. Efficient dehydrating agents, however, eliminate water. Thus when it is heated with phosphorus pentachloride in phosphorus oxychloride or digested with glacial acetic acid it passes smoothly into the unsaturated ester (II). Since none of this unsaturated ester is obtained when a mixture of equivalent quantities of the two components is treated in the same way, it must here be formed by loss of water from the hydroxy ester.

The addition product is exceedingly sensitive to bases, disappearing more or less rapidly in the presence of any of the condensing agents used in its synthesis. Thus, when it is added to boiling methyl alcohol or acetone containing relatively very small quantities of any of these bases the boiling point steadily rises and when it finally becomes constant, the elevation corresponds to a molecular weight that is much too small. The solution now contains dimethyl malonate, and methyl benzoylformate aswell as addition product; no unsaturated compound could be isolated from it. When solutions of the addition product, containing a larger quantity of these

[10] Schmitt, *Ann. chim.*, [8] **12**, 408 (1907).

bases are boiled or, better, when the solid addition product is suspended in a little of these solvents containing a small quantity of base, and the mixture is kept at the ordinary temperature it gradually passes into the unsaturated compound. These relations are most plausibly expressed by the following scheme:



$$\begin{array}{ccccc} C_6H_5COCO_2CH_3 & \longleftarrow & C_6H_5C(OH)CO_2CH_3 & \longrightarrow & C_6H_5C{-}CO_2CH_3 \\ + & \longrightarrow & | & \longleftarrow & \| \\ CH_2(CN)CO_2CH_3 & & HC(CN)CO_2CH_3 & & C(CN)CO_2CH_3 + H_2O \\ & & \text{I} & & \text{II} \end{array}$$

If this scheme correctly represents the mechanism by which the unsaturated ester is formed, then the basic condensing agents that are constantly employed in the synthesis of α,β unsaturated compounds fulfil a 2-fold function; they bring about condensation, and they cause elimination of water. There is, however, at present, no proof that the hydroxy ester is an intermediate product in the formation of the unsaturated compound, just as there is no satisfactory evidence that the analogous reactions which are used in the synthesis of unsaturated aldehydes and ketones really involve aldol condensation. Inasmuch as the addition product in the presence of bases reverts to an equilibrium with its components, it is impossible, in the absence of all accurate knowledge of the kinetics of the reaction, to determine whether the unsaturated ester is formed by loss of water from the addition product or directly from the components by some other path. This phase of the matter is still under investigation and will be considered in a later paper.

There is nothing peculiar in the condensations with cyano-acetic esters. Dimethyl malonate behaves in precisely the same way. The addition product is less soluble, and therefore a little more easily got; the residual hydrogen in the malonic ester residue is less active than that in the cyano ester, hence the addition product loses water less readily, and as the resulting unsaturated compound is a liquid it is more difficult to get it as a direct product of condensation. These are only such minor differences as are to be expected. The course of the reaction is the same: probably addition—equivalent to aldol condensation—followed by loss of water. It is safe to assume, therefore, that all condensations between aldehydes or ketones and substances containing active hydrogen occur in this manner.

Experimental Part

I. Preparation of Materials

Benzoylformic Acid.—The acid was made by the oxidation of acetophenone as directed by Claus[11] as well as by the oxidation of mandelic acid by the method of Acree.[12] We prefer the latter; it is more convenient,

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[11] Claus and Neukranz, *J. prakt. Chem.*, [2] **44,** 77 (1891). Kailan, *Monatsh.*, **28,** 1187 (1907).

[12] Acree, *Am. Chem. J.*, **50,** 389 (1913). Evans, *ibid.*, **35,** 115 (1906).

less expensive and more easily conducted on a large scale. Probably the best method for getting pure acid from residues which, owing to the presence of water or small quantities of benzoic acid, are reluctant to crystallize, is distillation under diminished pressure. In a good vacuum the pure acid distils practically without decomposition—the boiling point being about 148° at 4–6 mm. The oily residues distilled at 145–149° at 4–6 mm.; the distillate was colorless and solidified promptly. When the quantity distilled was not too great there was no evidence of decomposition until near the very end of the distillation.

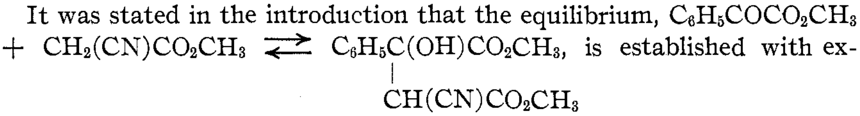
Methyl Benzoylformate.—Claisen[13] states that the esters of benzoylformic acid are readily made by saturating alcoholic solutions of the acid with hydrogen chloride, but he usually made them from benzoyl cyanide. He gives 246–248° as the boiling point of the methyl ester. Our first preparation made from the acid and methyl alcohol, boiled at 257°—nearly 10° above the point given by Claisen. As it proved to be unexpectedly resistant to condensation, it was analyzed and found to be the acetal, $C_6H_5C(OCH_3)_2CO_2CH_3$.

Analyses. Calc. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.7. Found: C, 63.1, 62.5; H, 6.7, 6.2.

Other preparations by the same method gave products composed largely of the ketonic ester, but in order to avoid all possible complications nearly all condensations were first carried out with ester that was made through the silver salt.

II. Condensation of Methyl Benzoylformate and Methyl Cyano-acetate

It was stated in the introduction that the equilibrium,



$$C_6H_5COCO_2CH_3 + CH_2(CN)CO_2CH_3 \rightleftharpoons \begin{array}{l} C_6H_5C(OH)CO_2CH_3 \\ \quad\;| \\ \quad CH(CN)CO_2CH_3 \end{array}$$

is established with extraordinary rapidity. The evidence for this statement is as follows. When a few drops of a saturated solution of sodium methylate in methyl alcohol is added to a mixture of equivalent quantities of the two esters which is kept at 0°, the liquid rapidly thickens, a solid addition product begins to separate, and in 5 to 10 minutes the entire mixture solidifies. It now contains 75 to 80% addition product, and as this does not increase when the mixture is allowed to stand for several hours it evidently represents the amount in equilibrium under these conditions. A small quantity of ammonia, methyl amine, or piperidine may be substituted for the sodium methylate without altering the result. Diluting the mixture with a solvent both diminishes the rate and shifts the equilibrium towards the left, as would be expected, but the latter effect can be counteracted by operating at a lower temperature; in an equal volume of methyl alcohol at —20° the amount of addition product is still 72–75%.

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[13] Claisen, *Ber.*, **12,** 629 (1879).

At 0° in the presence of these small quantities of base, the reaction does not go beyond the formation of the addition product, or more probably it does not go further at a rate that is significant. In a mixture that was kept at this temperature for 4 hours no unsaturated compound could be detected by the delicate test with permanganate. The isolation of the pure addition product, therefore, involves only its separation from the unchanged esters and the base used as catalyst. This is, however, not at all easy to accomplish. The equilibrium is so mobile that the substance partially reverts to its components when it is dissolved in any solvent in the presence of even the small quantity of base that is occluded by the crystals. In the presence of acids, on the other hand, it slowly loses water and passes into the unsaturated compound. After comparing a number of methods for handling the material we adopted the following procedure.

Four or five drops of a saturated solution of sodium methylate in methyl alcohol is added to a mixture of 16.4 g. of methyl benzoylformate and 13 g. of methyl cyanoacetate. The mixture is shaken in ice water until it has completely solidified (10–15 minutes), then placed in a freezing mixture in which it is allowed to remain for an equal length of time. It is then thoroughly mixed with about 10 cc. of acetyl chloride, care being taken to break up any small lumps that may form in the process, filtered, washed—first with cooled acetyl chloride diluted with ether, and finally very thoroughly with water—and dried. This leaves about 20 g. of a very finely divided solid that melts at 140–145°, and usually can be recrystallized without further trouble, but occasionally contains traces of occluded base. It is best, therefore, to digest it with 10 cc. of acetyl chloride for several hours, during which the fine powder is changed into small lustrous crystals. The substance is now analytically pure, but still melts poorly at 140–145°. It probably contains a small quantity of a stereoisomer because, while the melting point improves somewhat on repeated recrystallization from ether or chloroform, it becomes sharp at 155° after recrystallization from chloroform that contains a small quantity of phosphorus pentachloride.

Dimethyl α-Phenyl-α-cyano-β-hydroxysuccinate. I.—The addition product is sparingly soluble in ether and acetyl chloride, moderately soluble in chloroform and in carbon tetrachloride, readily soluble in acetone and in methyl alcohol. It crystallizes from chloroform in 6-sided plates, from ether in hard lustrous tables. It does not lose water when heated by itself but even the purest specimens partially dissociate into methyl benzoylformate and methyl cyano-acetate when heated to a high temperature in glass.

Analysis. Calc. for $C_{13}H_{13}O_5N$: C, 59.3; H, 4.9; N, 5.3. Found: C, 58.9; H, 5.1; N, 5.2.

Dimethyl α-Phenyl-β-cyano-ethylene Dicarboxylate. II.—The unsaturated condensation product is much easier to get and to handle than the addition product. When the mixtures that give the saturated compound at low temperatures are allowed to stand at the ordinary temperature or when the amount of catalyst is increased the principal product is the unsaturated compound. The reaction is reversible but the process is slow and the equilibrium favorable. The most effective condensing agent is sodium methylate, but when this is used as the catalyst there are complications due to the water which is one of the products of the reaction. This not only destroys the methylate but also leads to by-products, because both benzoylformic and cyano-acetic esters are hydrolyzed with uncommon ease. The following experiments illustrate the formation of the substance by direct condensation.

I. A small quantity of a solution of sodium methylate was added to a solution of 5 g. (1 molecular equivalent) of methyl benzoylformate and 4 g. (1.3 molecular equivalents) of methyl cyano-acetate in 10 cc. of dry methyl alcohol. The mixture was boiled for an hour during which alkalinity was maintained by successive additions of small quantities of the alcoholate—in all about 0.2 molecular equivalent. The clear, pale yellow solution was then kept at the ordinary temperature for several days during which it gradually deposited a mass of colorless crystals. These were washed with cold methyl alcohol and recrystallized either from ether or methyl alcohol. The average yield in 5 condensations by this method was 72%.

II. A mixture of 5 g. of the ketonic ester and 4 g. of the cyano ester was diluted with 1 cc. of methyl alcohol and then treated with 0.2 g. of methylamine hydrochloride and 0.2 g. of dry sodium carbonate. After standing at room temperature for 3 days this mixture began to deposit crystals of the unsaturated compound. After 3 weeks the yield of pure unsaturated ester was about 70%.

The ester is also easily obtained by the action of bases or of acids on the hydroxy ester. Thus, when a drop of concd. sodium methylate solution was added to 5 g. of the finely powdered ester suspended in 5 cc. of dry methyl alcohol, the liquid became pale yellow, the hydroxy ester gradually disappeared, and large crystals of the unsaturated compound took their place. After 5 days, during which alkalinity was maintained by occasional additions of methylate, the yield was 75%.

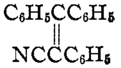
The most satisfactory method for transforming the hydroxy into the unsaturated ester consists in heating its solution in glacial acetic acid. For this purpose a suspension of the ester in 4 times its weight of glacial acetic acid is digested on a steam-bath for 3 hours. It is then free from hydroxy ester. The unsaturated ester may be isolated either by diluting the solution with just enough water to produce a faint milkiness or by pouring it into sodium carbonate solution and extracting with ether. The only by-product in either case is a trace of acid.

Analysis. Calc. for $C_{13}H_{11}O_4N$: C, 63.7; H, 4.5. Found: C, 63.8; H, 4.5.

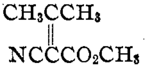
The ester melts at 79–80°. It is moderately soluble in ether and in cold methyl alcohol, sparingly soluble in benzene, and insoluble in petroleum ether. When allowed to crystallize slowly from methyl alcohol it separates in large, transparent prisms. Its solution in acetone reduces permanganate with great ease.

III. Proof of the Structure of the Condensation Products

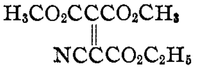
Our formula for the addition product is based on the method by which it is obtained and on its relation to the unsaturated ester which is formed from it by the elimination of water. But few substances are known which are constituted like this unsaturated compound. These are



$\begin{array}{c}C_6H_5CC_6H_5\\ \| \\ NCCC_6H_5\end{array}$

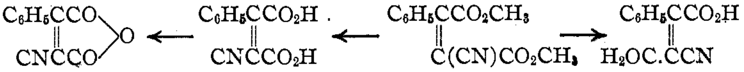


$\begin{array}{c}CH_3CCH_3\\ \| \\ NCCCO_2CH_3\end{array}$



$\begin{array}{c}H_3CO_2CCCO_2CH_3\\ \| \\ NCCCO_2C_2H_5\end{array}$

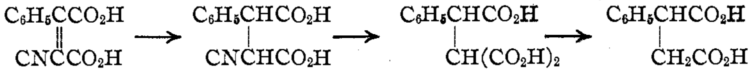
The characteristic property of all of these substances is their extreme resistance to hydrolysis. Our unsaturated compound shows the same peculiarity, but we succeeded in transforming it into two stereoisomeric acids that still contained the cyanogen group. We undertook, therefore, to relate it to phenylfumaric acid but were balked by the behavior of these dibasic acids, when they were heated. One of them readily lost water and formed an anhydride; the other sublimed without decomposition.



$$\begin{array}{c}C_6H_5CCO\\ \| \quad\; \rangle O\\ CNCCO\end{array} \longleftarrow \begin{array}{c}C_6H_5CCO_2H\\ \| \\ CNCCO_2H\end{array} \longleftarrow \begin{array}{c}C_6H_5CCO_2CH_3\\ \| \\ C(CN)CO_2CH_3\end{array} \longrightarrow \begin{array}{c}C_6H_5CCO_2H\\ \| \\ H_2OC.CCN\end{array}$$

IV III II V

The problem was finally solved by the addition of hydrogen to the unsaturated ester as well as to one of the dibasic acids and by transforming the hydrogenated compounds into phenyl succinic acid.



$$\begin{array}{c}C_6H_5CCO_2H\\ \| \\ CNCCO_2H\end{array} \longrightarrow \begin{array}{c}C_6H_5CHCO_2H\\ | \\ CNCHCO_2H\end{array} \longrightarrow \begin{array}{c}C_6H_5CHCO_2H\\ | \\ CH(CO_2H)_2\end{array} \longrightarrow \begin{array}{c}C_6H_5CHCO_2H\\ | \\ CH_2CO_2H\end{array}$$

III VI VII VIII

Hydrolysis of the Unsaturated Ester with Bases.—Fourteen and four-tenths g. of the ester was added to 100 cc. of a cold saturated solution of potassium hydroxide in methyl alcohol. The ester dissolved at once and a crystalline solid soon began to separate from the solution. After the mixture had been kept at the ordinary temperature for 36 hours, the solid was removed, and thoroughly washed, first with dry methyl alcohol, finally with dry ether. It was completely soluble in water. From its water solution concd. acids precipitated an unsaturated dibasic acid, while dil. acids precipitated the corresponding acid potassium salt.

α-Cyano-β-phenylmaleic Acid, III.—The acid is precipitated from solutions of its salts in fine very pale yellow needles. It is moderately soluble in warm water; readily soluble in acetone, in alcohol, and in ether; almost insoluble in chloroform, in carbon disulfide, and in petroleum ether. As it does not crystallize well from any of these solvents, it was dried in a vacuum and analyzed without further purification.

Analysis. Calc. for $C_{11}H_7O_4N$: C, 60.8; H, 3.2. Found: C, 60.7; H, 3.3.

The acid potassium salt, precipitated by adding dil. acid to aqueous solutions of the dipotassium salt, is moderately soluble in water or methyl alcohol. It was recrystallized from the latter, and thus obtained in colorless needles that melted at 193–195°.

Analyses. Calc. for $C_{11}H_6O_4NK$: K, 15.3. Found: 15.5, 15.3.

α-Cyano-β-phenylmaleic Anhydride, IV.—When the unsaturated dibasic acid is heated rapidly it melts with effervescence at about 142°. The effervescence is due to loss of water, which begins at a much lower temperature, and the melting point is that of the anhydride. The ease with which the acid loses water accounts for the difficulties met in recrystallizing it; solutions in boiling water deposit the anhydride in place of the acid. The substance was recrystallized from ether, from which it separated in fine yellow needles that melted at 145–146°.

Analysis. Calc. for $C_{11}H_5O_3N$: C, 66.3; H, 2.5. Found: C, 66.3; H, 2.6.

All attempts to hydrolyze either the condensation product or the unsaturated dibasic acid to the corresponding tribasic acid were unsuccessful. Cold alcoholic potassium hydroxide produced no further effect. Concd. aqueous alkalies attacked the cyano ester only on heating; ammonia was given off freely but the alkali evidently reversed the condensation reaction, because the principal product was benzoyl-formic acid.

Hydrolysis of the Unsaturated Ester with Acids.—The cyanogen group in the condensation product is just as resistant to the action of acids as it is to that of bases. The ester was recovered almost completely from a solution in dry methyl alcohol which had been saturated with hydrogen chloride and kept at the ordinary temperature for 3 days; and the result was the same when a similar solution was heated for 27 hours in a steam-jacketed autoclave. A partial hydrolysis of the ester was obtained as follows.

A mixture composed of 10 g. of ester, 10 g. of glacial acetic acid, and 20 cc. of concd. sulfuric acid was heated first on a steam-bath for 3 hours, and finally at the boiling point for 5 minutes. It was then cooled and diluted with water whereupon it very slowly deposited 3 g. of pale yellow crystals.

α-Cyano-β-phenylfumaric Acid, V.—The acid crystallizes from boiling water in colorless plates containing 2 molecules of water of crystallization which is given off below 100°. The anhydrous acid melts without decomposition at 158–160°, and in a vacuum sublimes without change. It is readily soluble in acetone, moderately soluble in methyl alcohol and in boiling water, sparingly soluble in chloroform and in ether.

Analyses. Calc. for $C_{11}H_7O_4.2H_2O$: H_2O, 14.2; C, 52.2; H, 4.4. Found: H_2O, 14.5; C, 52.3; H, 4.4.

This method of hydrolysis was very unsatisfactory; it never gave more than 30% of the possible amount of dibasic acid, in many cases it gave much less or none, and it was always difficult to get a pure product.

Reduction.—The unsaturated dibasic acid was reduced with sodium amalgam, and the ester catalytically in the presence of platinum. In each case a part of the material was reduced further than to the corresponding saturated compound, the reduction involving also the cyanogen group. The product obtained by catalytic reduction was ultimately transformed into phenylsuccinic acid, but as the reduction with sodium amalgam proved to be more satisfactory only this will be described.

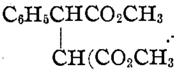
Thirty per cent. more than the calculated amount of 2% sodium amalgam was added in the course of 3 hours to an aqueous solution of the dipotassium salt, the alkalinity being reduced from time to time by the addition of acid. The solution was then made feebly acid and shaken with ether. This extracted an acid which after crystallization melted at 168–169°. This substance was also isolated from the mixture by boiling the product from catalytic reduction with alkali.

Analysis. Calc. for $C_{11}H_{13}O_4N$: C, 59.2; H, 5.8. Found: C, 59.2; H, 6.1.

The substance contains nitrogen, and the composition corresponds to that of the amino acid which would be obtained by complete reduction: $C_6H_5CH_2(CO_2H)CH(CH_2NH_2)CO_2H$.

The filtrate from the amino acid was evaporated to complete dryness, the residue first extracted with acetone to remove the last of the amino acid, then dissolved in water and acidified with concd. hydrochloric acid. This precipitated an acid which melted at 162–164°, and gave a methyl ester that melted at 56–57°. It was completely identified by comparison with a specimen of phenylsuccinic acid prepared according to Bredt and Kallen.[14]

Trimethyl-phenylethane Tricarboxylate,



$\begin{array}{l} C_6H_5CHCO_2CH_3 \\ | \\ CH(CO_2CH_3)_2 \end{array}$

.—Some of the dipotassium salt of the unsaturated ester was reduced with sodium amalgam, which was added rapidly at a low temperature. After half an hour the alkaline solution was decanted from the mercury, acidified with excess of strong hydrochloric acid, and extracted with ether. The ether, on evaporation, left an oil. This was esterified with methyl alcohol and hydrogen chloride. The resulting ester was purified by recrystallization from a mixture of ether and ligroin. It crystallizes in needles and melts at 107–108°.

Analysis. Calc. for $C_{14}H_{16}O_6$: C, 60.0; H, 5.7. Found: C, 59.7; H, 5.6.

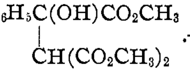
IV. Addition of Dimethyl Malonate to Methyl Benzoylformate

The addition was brought about in exactly the same way as that of methyl cyano-acetate. It apparently took place with the same rapidity and resulted in an equilibrium not very different from that formed in the case of the cyano ester, the yield of solid addition product being about 80%. The solid was digested with acetyl chloride and then recrystallized from ether.

Analysis. Calc. for $C_{14}H_{16}O_7$: C, 56.8; H, 5.4. Found: (I) C, 56.5; H, 5.5. (II) C, 56.8; H, 5.4.

MOLECULAR WEIGHT: Calc. for $C_{14}H_{16}O_7$: mol. wt., 296. Found, in freezing glacial acetic acid: 304.

Trimethyl β-Phenyl-β-hydroxy-ethane-α,α,β-tricarboxylate,



$\begin{array}{l} C_6H_5C(OH)CO_2CH_3 \\ | \\ CH(CO_2CH_3)_2 \end{array}$

.—The addition product is sparingly soluble in ether, moderately soluble in benzene, chloroform and carbon tetrachloride, readily soluble in acetone and glacial acetic acid. It crystallizes from ether in lustrous prisms and melts at 109–111°. The pure substance is stable, but like the analogous product obtained with cyano-acetic ester it is extremely sensitive to alkalies. This is illustrated by our first attempt to determine its molecular weight by the boiling-point method. The solvent was methyl alcohol which had been distilled from lime and then slowly redistilled twice with the aid of an efficient still head. The substance (2.7547 g.) was added to the boiling solvent (23.43 g.) in pellets. It dissolved at once but the boiling point continued to rise steadily for half an hour. When it finally became constant the elevation (0.48°) corresponded to a molecular weight of 215 instead of 296 calculated. Similar results were obtained in carefully purified acetone. In these cases methyl benzoylformate could be detected by the odor and its presence was definitely established by pouring the solutions into water, extracting with ether and shaking the ethereal solution with bisulfite.

That this reversal of the addition reaction is due to the presence of a trace of base was established as follows. The substance was recrystallized from ether which had been washed with 1:1 sulfuric acid and distilled. The acetone was refluxed with tartaric acid, distilled and fractioned with the aid of a Glinsky still head. Using these materials the

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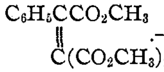
[14] Bredt and Kallen, *Ann.*, **293,** 342 (1896).

boiling point became constant in 4 minutes and did not change materially in 3 hours; 2.0713 g. of substance in 23.1 g. of acetone produced an elevation of 0.556° corresponding to a molecular weight of 274 instead of 296 calculated.

Dimethyl β-Phenyl-ethylene-α,α,β-tricarboxylate,



$C_6H_5CCO_2CH_3 = C(CO_2CH_3)_2$.—As the unsaturated ester was obtained only as a liquid it was not easy to determine the effect of dehydrating agents on the hydroxy ester. We used, therefore, the means that had been found most effective in the case of the corresponding cyano compound. A solution of the ester in phosphorus oxychloride containing a little more than one equivalent of phosphorus pentachloride was sealed up in a tube and heated in a steam-jacketed autoclave for several hours. The chlorides of phosphorus were then removed with ice water, the oil dissolved in ether, the ethereal solution washed with sodium carbonate, dried and distilled. Under a pressure of 10 mm. most of the product distilled at 180–190°. Thus far the oil has shown no tendency to crystallize.

Analysis. Calc. for $C_{14}H_{16}O_6$: C, 60.4; H, 5.0. Found: C, 59.8; H, 5.1.

Hydrolysis and Reduction.—A small quantity of the oil was added to cold concd. alcoholic potassium hydroxide. It dissolved at once and a solid potassium salt soon began to separate. This was washed with methyl alcohol and ether, then redissolved in water and acidified. As the resulting acid was a liquid it was neutralized and reduced at 40° with excess of sodium amalgam. The result was a solid acid that melted at 190°. Spiegel[15] gives 191°, Alexander[16] 170–171° as the melting point of phenylethane tricarboxylic acid. On esterification with methyl alcohol it gave a methyl ester that melted at 108° and when it was heated it lost carbon dioxide, forming phenylsuccinic acid which was identified by its melting point and that of a mixture with a sample of this acid.

Summary

1. At low temperatures, in concentrated solutions, and in the presence of sodium methylate, ammonia, methyl amine and piperidine, methyl benzoylformate and methyl cyano-acetate react and very quickly form the equilibrium, $C_6H_5COCO_2CH_3 + CH_2(CN)CO_2CH_3 \rightleftharpoons C_6H_5\text{-}\underset{\displaystyle CH(CN)CO_2CH_3}{\underset{|}{C(OH)CO_2CH_3}}$.

2. At higher temperatures, the product of the reaction is an unsaturated ester which can also be formed by eliminating water from the addition product.

3. The reaction between methyl benzoylformate and dimethyl malonate is in every respect like that with the cyano-acetate.

4. The question whether the unsaturated compounds which are obtained in reactions like these are formed by addition and loss of water from the resulting aldol or ketol, or by some other path, remains to be answered; but it is certain that neither aldol condensation nor the reaction between aldehydes or ketones and substances containing active hydrogen involves the enolization of aldehydes or ketones.

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[15] Spiegel, *Ann.*, **219**, 31 (1883).

[16] Alexander, *ibid.*, **258**, 76 (1890).