when ketene was passed directly into the solution of the aromatic compound, in the presence of aluminum chloride.

If the reaction was performed at 40–45°, the aluminum chloride layer gradually became fluid. In appearance it resembled the aluminum chloride layer formed in Combes' reaction,[7] which was performed in a simultaneous experiment. Combes discovered acetylacetone by hydrolyzing the product formed when a solution of acetyl chloride in chloroform was dropped upon aluminum chloride. In this reaction, hydrogen chloride was evolved vigorously. This is interesting, since the empirical formulas of ketene and of acetyl chloride differ only in the elements of hydrogen chloride. However, despite the similarity of the two products, that from ketene produced only acetic acid on hydrolysis, whereas that from acetyl chloride gave a small amount of acetylacetone, as well as acetic acid.

Summary

Ketene, in the presence of aluminum chloride, has been found to react with benzene, with anisole and with naphthalene to form rather complex mixtures from which ketones may be isolated. Scarcely any reaction occurred between ketene and acetophenone.

A reaction product of ketene and aluminum chloride has been observed which is capable of reacting with aromatic compounds, with the evolution of hydrogen chloride. Ketones are observed in the reaction mixture.

It is pointed out that ketenes might be expected to take part in the Friedel and Crafts' reaction because, in reality, ketenes are acid anhydrides. Acid anhydrides are known to enter into this reaction with success.

EVANSTON, ILLINOIS

[FROM THE LABORATORY OF BIOLOGICAL CHEMISTRY, WASHINGTON UNIVERSITY, SCHOOL OF MEDICINE]

CONDENSATION PRODUCTS OF ETHYL ACETO-ACETATE. I. A NEW COMPOUND OF GLYOXAL AND ETHYL ACETO-ACETATE, FORMYLMETHYLENE-BIS-ACETO-ACETIC ESTER

BY EDWARD S. WEST

RECEIVED JULY 6, 1925 PUBLISHED NOVEMBER 5, 1925

Shaffer[1] and Shaffer and Friedemann[2] have demonstrated that aceto-acetic acid is oxidized by hydrogen peroxide in alkaline solution if any one of several compounds be present, namely, glucose, fructose, glyceric aldehyde, glycol aldehyde, etc. The reactions by which these sugars accomplish the oxidation of aceto-acetic acid *in vitro* are considered by Shaffer to be probably similar to the reactions by which carbohydrate

[7] Combes, *Ann. chim. phys.*, [6] **12**, 207 (1887).

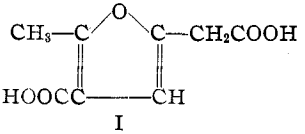
[1] Shaffer, *J. Biol. Chem.*, **47**, 433 (1921).

[2] Shaffer and Friedemann, *ibid.*, **61**, 585 (1924).

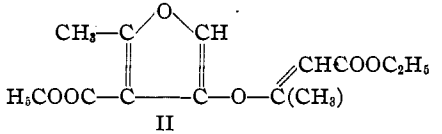
exerts its well-known antiketogenic effect in human metabolism. According to the theories of Geelmuyden,[3] Ringer,[4] Woodyatt[5] and Shaffer,[1] the antiketogenic action is due to a combination of glucose or one of its decomposition products with aceto-acetic acid or other ketogenic molecules, thereby forming a substance which is more easily oxidized in the body than the unchanged "acetone bodies." The oxidation of aceto-acetic acid *in vitro* by hydrogen peroxide in the presence of glucose or other sugars is presumably preceded by a condensation of the aceto-acetic acid with either the sugar or one of its intermediate oxidation products[1] and subsequent oxidation of the condensation product. An attempt is accordingly being made to prepare condensation products of aceto-acetic acid or its ester with various sugars[6] or their derivatives, which may possibly be concerned in the "ketolytic" reaction or with antiketogenesis in the animal body, with a view to studying the behavior of these products toward oxidation both *in vitro* and *in vivo*.

The present communication reports the preparation of condensation products of aceto-acetic ester with glyoxal, the intermediate oxidation product of glycol aldehyde.

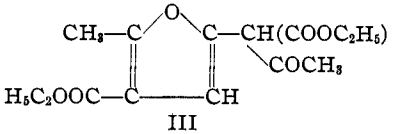
The condensation of aldehydes and ketones with 1,3-diketones and ketonic esters was first studied by Claisen[7] who effected the condensation with dry hydrogen chloride. A systematic study of this type of reaction was carried out by Knoevenagel[8] and co-workers in which it was shown that various amines may be used as condensing agents, diethylamine and piperidine being the most efficient.



I
Crystalline solid
(m. p., 207°)



II
Crystalline solid
(m. p., 139°)



III
Heavy yellow oil
(b. p., 290–300°)

[3] Geelmuyden, *Z. physiol. Chem.*, **41**, 136 (1904).

[4] Ringer, *J. Biol. Chem.*, **17**, 107 (1914).

[5] Woodyatt, *J. Am. Med. Assoc.*, **55**, 2109 (1910).

[6] Condensation products of glucose and aceto-acetic ester have been prepared. Attempts are being made to extend the reaction to other sugars and 1,3-diketones. A preliminary report will appear in the near future.

[7] Claisen, *Ann.*, **218**, 121, 170 (1883).

[8] Knoevenagel, (a) *Ann.*, **281**, 25 (1894); (b) *Ber.*, **37**, 4461 (1904) (bibliography).

The aldol condensations of the dialdehyde, glyoxal, have been little studied. Polonowski[9] condensed ethyl aceto-acetate with glyoxal using zinc chloride as the condensing agent, and obtained the preceding products.

Several years ago Professor Shaffer[10] noted that when a mixture of glyoxal and ethyl aceto-acetate is made slightly alkaline, or treated with piperidine, reaction takes place with the evolution of heat and the separation of a heavy brown oil. In the fall of 1923 the writer began a study of this reaction to determine the optimum conditions for condensation and the identity and properties of the compounds formed. A very complex mixture, containing a considerable amount of resinous products, is obtained when glyoxal and ethyl aceto-acetate react in even weakly alkaline solution. The compounds, however, react smoothly with practically no resinification when brought together in approximately neutral solution. A crystalline compound separates in the form of orthorhombic needles accompanied by a heavy yellowish oil. The crystalline compound has the empirical formula $C_{14}H_{20}O_7$, and contains two ethoxyl groups per molecule. Molecular-weight determinations give values close to 300. With hydroxylamine hydrochloride in alcoholic solution an oxime is formed which has lost a molecule of water. Dilute alkali causes resinification and loss of a molecule of carbon dioxide. The compound reduces Tollen, Benedict and Fehling reagents.

The formation of the compound may be represented by the equation,

$$2CH_3COCH_2COOC_2H_5 + HOCCOH \longrightarrow \underset{(IV)}{HOC.CH[CH(COOC_2H_5)COCH_3]_2} \quad (3)$$

according to which it is formylmethylene-*bis*-aceto-acetic ester.

It is possible that glyoxal may react with ethyl aceto-acetate forming the unsaturated aldol, aceto-acetic-ester-hydroxymethyl-methylene-aceto-acetic ester,

$$2CH_3COCH_2COOC_2H_5 + HOCCOH \longrightarrow \underset{(V)}{H—O—CH[CH(COOC_2H_5)COCH_3]CH:C(COOC_2H_5)COCH_3} \quad (4)$$

which also has the formula $C_{14}H_{20}O_7$ and contains two ethoxyl groups but no aldehyde group. Another possibility is the formation of the double aldol, *sym.*-diaceto-acetic-ester-glycol,

$$2CH_3COCH_2COOC_2H_5 + HOCCOH \longrightarrow \underset{(VI)}{[HOCHCH(COOC_2H_5)COCH_3]_2} \quad (5)$$

which might lose a molecule of water in several different ways, both with and without ring closure, to form a compound, $C_{14}H_{20}O_7$, containing two ethoxyl groups and no aldehyde group.

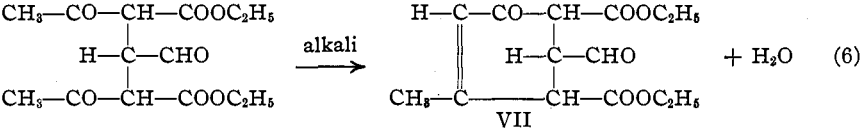
The fact that the compound easily resinifies when treated with alkali and reduces Tollen reagent quickly in the cold suggests the presence of an aldehyde group. There are many compounds, however, which are

[9] Polonowski, *Ann.*, **246**, 27 (1888).

[10] Unpublished observations.

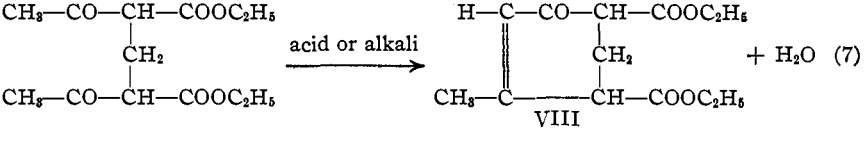
not aldehydes, that resinify when treated with alkali, and methylene-*bis*-aceto-acetic ester and ethylidene-*bis*-aceto-acetic ester, which contain no aldehyde group, reduce Tollen reagent instantly.[11] A quantitative determination of unsaturation showed that the compound had not added bromine in carbon tetrachloride solution after 24 hours. A compound of Formula V should add bromine if the double bond is active under the conditions of the experiment. Neutral permanganate is decolorized quickly in the cold by the compound. Either formula would account for this fact. Attempts to prepare acetyl and benzoyl derivatives failed. The oxime of the compound does not reduce Tollen, Benedict or Fehling solution and is not resinified by alkali, while the compound itself gives a positive reaction in each case. These facts indicate that probably an aldehyde group has been converted into an oximino group.

The action which takes place when the compound is treated with dilute alkali is probably first a loss of water and ring closure



VII

with the production of 4,6-dicarboxyethyl-5-formyl-3-methyl-Δ^2-cyclohexenone, which then loses one carboxyl group (which one is unknown) by decarboxylation. This is in accord with the work of Knoevenagel,[8a] who has shown that *bis*-alkylidene condensation products of 1,3-diketones and ketonic esters, which contain alkyl groups, readily lose water and form cyclohexenone derivatives when treated with acid or alkali. Thus methylene-*bis*-aceto-acetic ester undergoes the change with great ease,



VIII

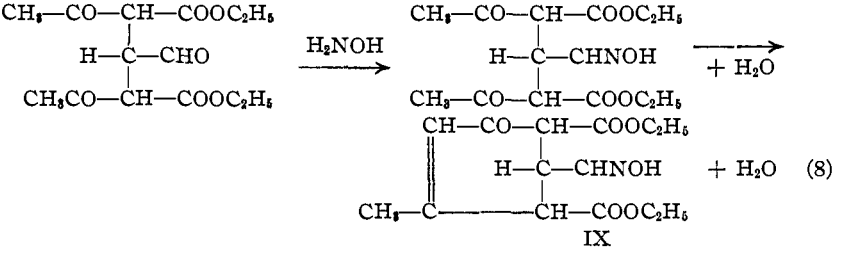
the product of the action being 4,6-dicarboxyethyl-3-methyl-Δ^2-cyclohexenone. Continued action causes the loss of both carboxyl groups and the formation of 3-methyl-Δ^2-cyclohexenone.

A solution of the compound in very dilute alkali plus a small amount of any of the following, carbazol, dimethylglyoxime, α- or β-naphthol, β-naphthylamine, followed by a layer of concd. sulfuric acid, gives a characteristic color reaction. When, however, preliminary treatment with alkali is omitted, no coloration develops. The alkali possibly effects ring closure into the compound of Formula VII or its decarboxylation product which condenses with the reagent to form a colored product.

[11] The second paper of this series, to be published shortly in the *J. Biol. Chem.*, will present a theory in explanation of the ease of oxidation of condensation products of aldehydes and aceto-acetic ester.

A fact which constitutes evidence that the compound is the formyl substitution product of methylene-*bis*-aceto-acetic ester is that both it and methylene-*bis*-aceto-acetic ester, when dissolved in dilute alkali and the solutions treated with phloroglucinol, give strikingly similar pink or red colorations. If the color reaction in each case is dependent upon the preliminary formation of a cyclohexenone derivative by the alkali, as suggested above, an inspection of the formulas of these derivatives, VII and VIII, suggests the plausibility of similar color reactions with phloroglucinol. The ketone group probably enters into the condensation because Formula VIII contains no aldehyde group.

The reaction of the compound with hydroxylamine probably proceeds as follows.



(8)

IX

The product is the aldoxime of 4,6-dicarboxyethyl-5-formyl-3-methyl-Δ^2-cyclohexenone. In the formation of the oxime, both the alcohol present and the acid set free (from the hydroxylamine hydrochloride) should lead to the loss of water and ring closure quite analogous to the action represented in Reactions 6 and 7.

Apparently the only property of the compound not in accord with Formula IV, which represents it as formyl-methylene-*bis*-aceto-acetic ester, is that it does not color Schiff's aldehyde reagent. The failure to do so may be due to its pronounced insolubility in water. However, certain aldehydes are known to give negative reactions with this reagent, among which are *p*-homosalicylic aldehyde, *p*-nitrophthalic aldehyde, and glyoxal.[12] It may well be that the inability of glyoxal to react with Schiff's reagent is retained by the free aldehyde group after condensation of glyoxal with aceto-acetic ester.

The facts, as now known, are most in accord with the structure (Formula IV) which represents the compound as formylmethylene-*bis*-aceto-acetic-ester.

The oily product formed simultaneously with the crystalline compound in the reaction of glyoxal and aceto-acetic ester was separated and purified. After it had stood for some time a crystalline solid separated that was found to have the formula $C_{14}H_{18}O_6$. It contains two ethoxyl groups; m. p., 138–139.5°. The composition, melting point and properties of the

[12] Bitto, *Z. anal. Chem.*, **36**, 375 (1897).

compound indicate that it is identical with the crystalline substance $C_{14}H_{18}O_6$, m. p. 139°, obtained by Polonowski (see Formula II).

The oil, after purification, was found to boil at 290–300° (760 mm.) and to have the composition $C_{14}H_{18}O_6$. It is thus an isomer of the crystalline compound $C_{14}H_{18}O_6$, m. p. 139°, which was separated from it. The oil has properties identical with those of the oil, b. p. 290–300°, which the writer prepared according to the procedure of Polonowski.

Experimental Part

Reagents.—Glyoxal was prepared according to a modified procedure of Ljubawin.[13] The ethyl aceto-acetate used was from the Eastman Kodak Company.

Reaction of Glyoxal and Ethyl Aceto-acetate under Different Conditions

Many experiments were carried out with variations in conditions of time, temperature, Sörensen value (P_H), molecular proportions and added condensation catalysts. The most satisfactory procedure from the standpoint of yield of crystalline material and freedom from resinification was found to be as follows. Forty cc. of *M* glyoxal solution containing approximately 2 g. of glyoxal (1 molecular equivalent) is carefully neutralized to litmus with sodium hydroxide and to this is added 10 g. of ethyl aceto-acetate (2 + molecular equivalents). The mixture is diluted with water to approximately 100 cc. and allowed to stand, preferably at a temperature not far from 20°. Very soon reaction slowly takes place and the solution becomes slightly yellow. After about 12 hours a heavy, yellowish oil begins to separate, followed in a day or two by long, needle-shaped crystals. The crystals often have the appearance of growing or crystallizing from the oil. The reaction comes to a standstill after five to six days, when the flask contains a large amount of loose crystals saturated with a heavy yellow oil. When the crystals are removed by suction on a filter, a second crop separates from the mixture. This can be repeated two or three times. Dilution of the reaction mixture to approximately 100 cc. is desirable. The crystalline material does not separate well from a more concentrated solution and a large amount of oily products is obtained. Greater dilution decreases the rate of reaction. At higher temperatures there is a smaller yield of crystalline material and resinification occurs, which becomes extensive at 50–60°. With increasing Sörensen values above 7, the reaction rate is markedly increased, but resinification sets in sharply and very complex, reddish, oily products are obtained. A buffer of sodium bicarbonate—carbon dioxide does not prevent profound resinification. As the Sörensen value decreases below 7 the rate of reaction progressively decreases, though some action slowly takes place at P_H 4–5. The product should be worked up as soon as the reaction is complete. Longer standing leads to resinification unless the temperature is considerably lowered. The reaction takes place readily when piperidine is added as in the Knoevenagel aldol condensation.[14] Its use has no advantage and causes resinification when too much is added.

Formylmethylene-bis-aceto-acetic Ester

The crystalline reaction product was separated as thoroughly as possible from the oily material by suction on a filter. It was then placed in a beaker with a little ether-petroleum ether (1:1) and thoroughly stirred; the crystals were separated, and the process was repeated. The compound was purified by solution in an excess of warm ether and addition of 2–3 volumes of petroleum ether. Soon short blunt, prismatic

[13] *J. Biol. Chem.*, **61**, 599 (1924).

[14] Ref. 8 a, p. 29.

needles separated. After one or two recrystallizations the compound melts at 109–110° (uncorr.). It is also easily purified by solution in warm ether followed by partial evaporation of the solvent; yield, 15–20%.

The compound is soluble in alcohol and chloroform, moderately soluble in benzene and ether, practically insoluble in petroleum ether and insoluble in water. Aqueous alkali dissolves it to give a red-brown solution with resinification. The compound reduces Tollen reagent quickly in the cold, and Fehling and Benedict solutions when heated. Boiling it in alkaline solution tends to destroy its reducing properties. The Fehling test is best conducted by adding the solid or an alcoholic solution to the hot reagent. The compound quickly decolorizes neutral permanganate in the cold, and absorbs bromine from a carbon tetrachloride solution with copious evolution of hydrogen bromide. It does not form an addition product with sodium bisulfite. Hydrazines act to form smeary products which soon become black and tarry. The compound does not restore the color to Schiff's reagent.

Anal. Subs., 0.3770, 0.2598: CO_2, 0.7736, 0.5319; H_2O, 0.2252, 0.1556. Calcd. for $C_{14}H_{20}O_7$: C, 55.98; H, 6.71. Found: C, 55.98, 55.85; H, 6.68, 6.70.

Subs., 0.3949, 0.3767: 26.69, 25.56 cc. of 0.1 *N* I soln.; ethoxyl, 0.11988, 0.1150. Calcd. for two ethoxyl groups: 30.00. Found: 30.35, 30.53.

Ethoxyl[15] was determined by a modified Zeisel method. The precipitate of silver iodide was fused with alkali carbonates, the mass dissolved in water, filtered and acidified with sulfuric acid; ferric sulfate was added and the iodine distilled into cold potassium iodide and titrated. One cc. of 0.1 *N* iodine equals 0.0045 g. of ethoxyl.

Mol. wt. (Ebullioscopic method; solvent, ethyl acetate). Subs., 0.1897, 0.1761: solvent, 17.54, 17.49; Δt, 0.093, 0.084. Calcd.: mol. wt. 300.23. Found: 303.56, 312.87.

Action of Hydroxylamine on Formylmethylene-*bis*-aceto-acetic Ester. Preparation of the Aldoxime of 4,6-Dicarboxy-ethyl-5-formyl-3-methyl-Δ^2-cyclohexenone.—Formylmethylene-*bis*-aceto-acetic ester (3 g.) was dissolved in 50 cc. of alcohol, powdered hydroxylamine hydrochloride (3 g.) added, and the mixture allowed to stand for 24 hours at 35–40°, or about two days at room temperature. The solution gradually became brown. Too long action should be avoided, else there is troublesome resinification. The alcoholic solution was gradually poured into 10 volumes of water during constant stirring. The oxime separated as bulky, very fine, silky needles; yield, 60–70% of crude material. The compound was purified by solution in alcohol and precipitation with water, repeated several times and was air-dried on a porous plate. When heated slowly it began to brown at 90–92° and melted with decomposition at 94–95° to form a black, tarry liquid. When dried in a vacuum desiccator for 18 hours over sulfuric acid the compound lost weight (water and ammonia (?)) and passed into a substance that began to turn brown at 126° and melted at 140° with decomposition. Water and ammonia were given off when it was heated to 100° under a pressure of 20–30 mm. The compound is soluble in dilute, aqueous alkali and insoluble in hydrochloric acid. It does not resinify when treated with alkali, nor does it reduce Tollen, Benedict, or Fehling solution.

Anal.[16] (Nitrogen was determined by the modified Kjeldahl method using salicylic-sulfuric acid, preliminary reduction with zinc dust, and sugar.) Calcd. for $C_{14}H_{19}NO_8$: 4.72. Found: 4.69, 4.67, 4.78, 4.81.

Action of Dilute Alkali on Formylmethylene-*bis*-aceto-acetic Ester.—Dilute

[15] The use of acetic anhydride gave low results.

[16] Successful combustion of the compound is exceedingly difficult. Attempts were made using both copper oxide and lead chromate but with unsatisfactory results.

alkali eliminates one molecule of carbon dioxide from the compound. The results of some experiments are as follows: wt. of compound, 0.500 g.; millimoles of compound taken, 0.500/0.300, 1.66; cc. of 976 *N* NaOH, 25.00; approximate temp., 33°; time, 5 days; cc. of *N* NaOH neutralized by CO_2, 3.58; cc. of *N* NaOH neutralized by 1 mm. of comp., 2.15; moles of CO_2 lost per mole of compound, 1.075.

When heated with 2 *N* sodium hydroxide solution for two hours in a boiling water-bath the compound lost 0.94 mole of carbon dioxide per molecule.

Carbon dioxide was determined by aeration into standard alkali, addition of barium chloride and titration. Blank determinations were run.

Color Reactions of Formylmethylene-*bis*-aceto-acetic Ester.—A summary of color reactions of the compound is given in Table I.

TABLE I

COLOR REACTIONS

No.	Solution	Reagent	Results
1	Alcoholic	Ferric chloride	Purplish brown
2	Dil. alkali	Phloroglucinol	Pink to red. Very sensitive
3	Alc. alkali	Phloroglucinol	Beautiful violet
4	Dil. alkali	Sodium nitroprusside	Red-brown. Violet and acetic acid
5	Dil. alkali	Carbazol and layer of concd. H_2SO_4	Red ring test.
6	Dil. alkali	Dimethylglyoxime and concd. H_2SO_4	Pink ring, very sensitive
7	Dil. alkali	Diphenylamine and concd. H_2SO_4	Pink ring
8	Dil. alkali	*p*-Toluidine and concd. H_2SO_4	Red ring
9	Dil. alkali	α-Naphthylamine and concd. H_2SO_4	Pink; green-yellow border next to H_2SO_4
10	Dil. alkali	β-Naphthylamine and concd. H_2SO_4	Pink ring
11	Dil. alkali	α-Naphthol and concd. H_2SO_4	Yellow ring
12	Dil. alkali	β-Naphthol and concd. H_2SO_4	Pink aqueous layer; green-yellow ring

Catechol becomes brown when placed in alkaline solution and exposed to the air. The addition of a very small amount of formylmethylene-*bis*-aceto-acetic ester greatly accelerates the formation of the brown color.

Control reactions were carried out in all cases.

It is interesting to note that in the ring tests using concd. sulfuric acid (5–12), no characteristic coloration was produced when the compound was simply suspended in water. Preliminary treatment with alkali is necessary. The presence of alkali is also necessary in the phloroglucinol reactions (2–3).

The Ether of Ethyl β'-Hydroxy-α-Methyl-β-furan-carboxylate and Ethyl β-Hydroxycrotonate

The oily material, after removal of formylmethylene-*bis*-aceto-acetic ester, was separated from water as much as possible (drying in vacuum desiccator over sulfuric acid is a good procedure), taken up in an excess of ether, two volumes of petroleum ether being added, and allowed to stand in the icebox for several weeks. This treatment brings about the separation of some formylmethylene-*bis*-aceto-acetic ester. The ether solution was separated from the crystals, repeatedly washed with saturated sodium bicarbonate solution until the washings were practically colorless, then with water, decolorized by treatment with Norite, dried with powdered calcium chloride and evaporated in a vacuum. The oil was dissolved in alcohol and boiled with Norite, the solution filtered, cooled and 1–2 volumes of ether were added. The alcoholic ether solution was

washed with concd. sodium chloride solution, saturated sodium bicarbonate solution, water, and the remaining ether solution dried with calcium chloride and evaporated. The residual heavy brown oil was dried in a vacuum over phosphorus pentoxide at 95° for four days. After this had stood for two weeks in a desiccator, crystals had formed throughout the oil. The crystals were separated by treatment with cold 70–80% alcohol in which the oil is soluble. (The alcohol mixture should stand several days in the cold for the more complete separation of crystals.) The crystals were purified by recrystallization from hot 70–80% alcohol. The compound separated as short, prismatic needles; m. p., 138–139.5°. The yield is small. It is soluble in benzene and chloroform, moderately soluble in ether, very slightly soluble in cold alcohol but soluble in hot, and insoluble in dilute or concentrated aqueous alkalies. It is soluble in cold concd. sulfuric acid from which it is precipitated by dilution. The compound reduces Fehling and Benedict solutions (not vigorously) when added to the boiling reagent in alcoholic solution. It does not reduce Tollen reagent. It gives no color reactions with ferric chloride or sodium nitroprusside.

Anal. Subs., 0.2608, 0.2415: CO_2, 0.5662, 0.5248; H_2O, 0.1453, 0.1383. Calcd. for $C_{14}H_{18}O_6$: C, 59.55; H, 6.43. Found: C, 59.05, 59.11; H, 6.19, 6.36.

Subs., 0.3200, 0.3047: 22.06, 20.45 cc. of 0.1 *N* iodine; ethoxyl, 0.09927, 0.09202. Calcd. for two ethoxyl groups: 31.91. Found: 31.02, 30.20.

Ethyl α'-Aceto-acetic-ester-α-methyl-β-furan-carboxylate

The alcoholic solution of the oil, after separation of the crystals melting at 138–139.5°, was evaporated in a vacuum, and the residual oil purified by fractional distillation in a vacuum; yield, about 10–15%. The compound distils with slight decomposition, as a heavy, pale yellow oil possessing an ethereal odor, at 130–140° under a pressure of 0.5–0.8 mm. It distils at 290–300° under atmospheric pressure; d_{24}^{24}, 1.1488. It is very soluble in all of the common organic solvents, quite insoluble in water and very little soluble in dilute aqueous alkali. It is resinified by concd. hydrochloric acid. An alcoholic solution gives a beautiful port wine color with ferric chloride. Sodium nitroprusside added to the compound in aqueous alkali gives a red color which instantly fades to yellow. Upon acidification with acetic acid the solution gradually becomes blue. The compound reduces Tollen reagent instantly in the cold, and Benedict and Fehling solutions when heated. Phenylhydrazine reacts to produce smeary, brown to black, resinous substances.

Anal. Subs., 0.1956, 0.1388: CO_2, 0.4280, 0.3043; H_2O, 0.1137, 0.0830. Calcd. for $C_{14}H_{18}O_6$: C, 59.55; H, 6.43. Found: C, 59.66, 59.78; H, 6.45, 6.64.

Subs., 0.2593: 17.06 cc. of 0.1 *N* iodine; ethoxyl, 0.07677. Calcd. for two ethoxyl groups: 31.91. Found: 29.61.

The writer wishes to express his appreciation to Professor Shaffer for his kindly aid and criticism during the course of this investigation.

Summary

1. Glyoxal and ethyl aceto-acetate have been shown to react in approximately neutral solution.

2. Formylmethylene-*bis*-aceto-acetic ester, a new compound, has been isolated from the reaction product.

3. Ethyl α'-aceto-acetic-ester-α-methyl-β-furan-carboxylate and the ether of ethyl β'-hydroxy-α-methyl-β-furan-carboxylate and ethyl β-hydroxycrotonate were also found among the products of the reaction.

These compounds are apparently identical with the isomers obtained by Polonowski in the condensation of glyoxal and ethyl aceto-acetate with zinc chloride.

4. All of these condensation products are easily oxidized.

ST. LOUIS, MISSOURI

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

THE ACETONE–ISO-ACETONE EQUILIBRIUM

BY WILLIAM LLOYD EVANS AND WILLIAM DICKSON NICOLL

RECEIVED JULY 8, 1925 PUBLISHED NOVEMBER 5, 1925

Acetone is oxidized in either neutral or acid solutions of potassium permanganate to acetic acid and carbon dioxide. When the oxidation takes place in the presence of alkalies, the reaction products are acetic and oxalic acids, carbon dioxide and, under carefully controlled conditions, pyruvic acid.[1]

It has been shown by Sefton and one of us[2] that the yield of oxalic acid and carbon dioxide obtained through the oxidation of acetone at a given temperature with alkaline potassium permanganate increases with the concentration of the alkali used, while that of acetic acid diminishes. The reaction mechanism involved in the oxidation of acetone in alkaline solutions is best understood when one considers with Denis[3] and Witzemann[4] that one of the functions of the alkali in these reactions is that of forming the salt of iso-acetone as is shown by Reactions 1 and 2.

$$CH_3.CO.CH_3 \rightleftharpoons CH_3.C(OH)=CH_2 \quad (1)$$

$$CH_3.C(OH)=CH_2 + KOH \longrightarrow CH_3.C(OK)=CH_2 + H_2O \quad (2)$$

That these compounds of acetone do exist has been pointed out by Freer[5] who succeeded in preparing sodium acetone in non-aqueous solvents. He also regenerated the acetone in large amounts when the sodium iso-acetone was treated with acids.

It is evident, therefore, that the next step in the oxidation of acetone in alkaline potassium permanganate solutions must be the conversion of a portion of the iso-acetone molecules to acetol, a compound which is then converted into carbon dioxide, acetic and oxalic acids.[6] When acetol is oxidized under conditions similar to those used for acetone, the same general results are obtained when one considers the influence exerted

[1] Dumas and Stas, *Ann.*, **35**, 160 (1840). Gottlieb, *Ann.*, **52**, 130 (1844). Herz *Ann.*, **186**, 258 (1877). Cochenhausen, *J. prakt. Chem.*, [2] **58**, 454 (1898). Fournier. *Bull. soc. chim.*, [4] **3**, 259 (1908).

[2] Evans and Sefton, THIS JOURNAL, **44**, 2276 (1922).

[3] Denis, *Am. Chem. J.*, **38**, 567 (1907).

[4] Witzemann, THIS JOURNAL, **39**, 2657 (1917); compare Ref. 2, p. 2281.

[5] Freer, *Am. Chem. J.*, **12**, 355 (1890); **13**, 320 (1891). Compare Bacon and Freer, *Philippine J. Sci.*, **2A**, 68 (1907). Denis, *Am. Chem. J.*, **38**, 367 (1907).

[6] Evans and Hoover, THIS JOURNAL, **44**, 1730 (1922).