THE ACETOACETIC ESTER CONDENSATION. II. THE REACTION OF ALIPHATIC ESTERS WITH SODIUM

By John M. Snell and S. M. McElvain

In a previous communication[1] from this Laboratory it was pointed out that in any study of the synthetic phase of the acetoacetic ester condensation the choice between sodium and sodium ethoxide as condensing agents was an important consideration for the reason that the metal reacts with the type of ester used in the condensation to form a distinctly different type of compound, viz., the sodium derivative of an acyloin. The acyloin and related substances may be the major if not the sole products of reaction of certain esters with sodium. The results reported at that time showed that no such complications accompany the use of sodium ethoxide as a condensing agent.

Although a number of earlier investigators had observed that certain esters react with sodium to give compounds other than the acetoacetic ester type, it was Bouveault and Locquin[2] who first formulated the reaction as being two molecules of the ester and four atoms of sodium with the formation of the sodium salt of an acyloin which was converted by hydrolysis into the acyloin

$$2RCOOR' + 4Na \longrightarrow RC(ONa) = C(ONa)R + 2NaOR'$$

$$RC(ONa) = C(ONa)R \xrightarrow{H_2O} RC(OH) = C(OH)R \longrightarrow RCHOHCOR$$
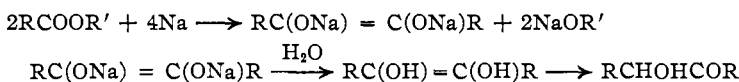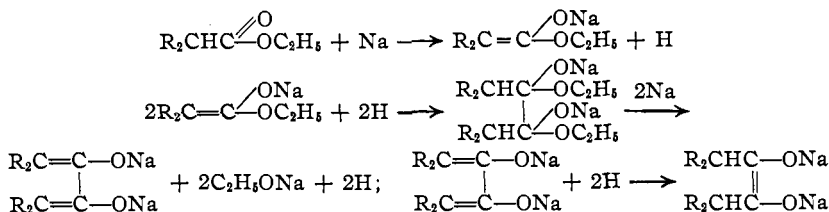
Bouveault and Locquin carried out the reaction between sodium and the ethyl esters of acetic, propionic, butyric, caproic, isobutyric and trimethylacetic acids at 0° in ether as a solvent. They obtained, after allowing the reaction to proceed for several days, quite good yields (in most cases approximately 80% of the theoretical) of the acyloins. There was generally a small amount of the diketone, RCOCOR, and some higher-boiling material obtained from the reaction. It was thought that the former compound resulted from the oxidation of the sodium derivative of the acyloin, and that the latter was produced from the acyloin during distillation. The only explanation of the mechanism of the reaction that was offered by these investigators is the one shown above. In 1920 Scheibler and Voss[3] offered an explanation for the formation of acyloins which postulated an intermediate formation of the sodium salt of the enol form of the ester. They stated that under the reaction conditions (0°) of Bouveault and Locquin the hydrogen which was given off during the formation of the enolate

[1] McElvain, THIS JOURNAL, 51, 3124 (1929).

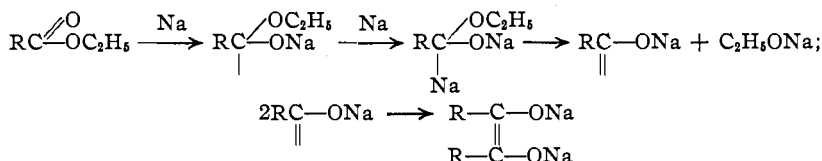[2] Bouveault and Locquin, Bull. soc. chim., [3] 35, 629 (1906).

[3] Scheibler and Voss, Ber., 53, 388 (1920).

salt was utilized to reduce this salt to the acyloin, but that at the tempera-
ture (the boiling point of ether) at which they prepared the salts of the
enol forms of esters the hydrogen was evolved as such before it could
cause the reduction of the enolate.   This explanation hardly seems reason-
able, since the results reported below show that excellent yields of the acyl-
oins may be obtained at the temperature of boiling ether.   Later, in 1923,
Scheibler and Emden[4] reported a study of the formation of the acyloins
and proposed the following mechanism for the reaction

$$R_2CHC\overset{O}{\underset{OC_2H_5}{\diagup}} + Na \longrightarrow R_2C=C\overset{ONa}{\underset{OC_2H_5}{\diagup}} + H$$

$$2R_2C=C\overset{ONa}{\underset{OC_2H_5}{\diagup}} + 2H \longrightarrow \begin{matrix} R_2CHC\overset{ONa}{\underset{}{\diagup}}OC_2H_5 \\ | \\ R_2CHC\overset{ONa}{\underset{}{\diagup}}OC_2H_5 \end{matrix} 2Na \longrightarrow$$

$$\begin{matrix} R_2C=C-ONa \\ | \\ R_2C=C-ONa \end{matrix} + 2C_2H_5ONa + 2H; \qquad \begin{matrix} R_2C=C-ONa \\ | \\ R_2C=C-ONa \end{matrix} + 2H \longrightarrow \begin{matrix} R_2CHC-ONa \\ \| \\ R_2CHC-ONa \end{matrix}$$

It is seen that this mechanism also postulates the intermediate formation
of a salt of the ester enolate.   No reason was given for the necessity of
assuming alternate addition and loss of hydrogen in the process.

One grave weakness[5] in this mechanism is that it will not explain the
formation of an acyloin from such an ester as ethyl trimethylacetate which
has no hydrogen on the carbon atom adjacent to the carbethoxy group and
consequently cannot form an ester enolate.   Scheibler and Emden handle
such a case by postulating a special mechanism for this type, as follows

$$RC\overset{O}{\underset{OC_2H_5}{\diagup}} \overset{Na}{\longrightarrow} RC\overset{OC_2H_5}{\underset{ONa}{\diagup}} \overset{Na}{\longrightarrow} RC\overset{OC_2H_5}{\underset{\underset{Na}{|}}{\diagup}}ONa \longrightarrow RC-ONa + C_2H_5ONa; \\ \|$$

$$2RC-ONa \longrightarrow \begin{matrix} R-C-ONa \\ \| \\ R-C-ONa \end{matrix} \\ \|$$

Such esters must go through a different mechanism, it is pointed out, on
account of the slowness and incompleteness of the reaction.

Scheibler and Emden explained the presence of small amounts of the
diketone, RCOCOR, which often accompanies the acyloin as resulting
from the oxidation of salt of the di-enolate of the acyloin by air and pointed

[4] Scheibler and Emden, *Ann.*, 434, 265 (1923).

[5] Another may be noted. Scheibler and Emden point, in a footnote, to an ob-
servation of Bouveault and Blanc that only esters which have at least one hydrogen on
the α-carbon atom may be reduced by sodium and alcohol to the corresponding alcohol
as further substantiation of their mechanism. This "generalization" is based, ap-
parently, on the behavior of ethyl benzoate and has the common defect of such "generali-
zations," *viz.*, that it is not generally applicable. For example, Courtot [*Bull. soc.
chim.*, 35, 121 (1906)] has reported the reduction of ethyl Δ^3-2,2-dimethylbutyrate,
$CH_2=CHC(CH_3)_2COOC_2H_5$, to the corresponding alcohol and his results have been
confirmed by Folkers and Adkins in this Laboratory, who obtained a 61% yield of this
alcohol by the reduction of the above ester with sodium and alcohol.

out that the potassium salts were much more susceptible than the sodium salts to such oxidation.

Recently Corson, Benson and Goodwin[6] described a general procedure for the preparation of a number of aliphatic acyloins. They obtained yields, approximately 50% of the theoretical, of products with 25° boiling range using boiling ether as a solvent. They noted the formation of the higher-boiling products which they felt were derived in part, at least, from the acyloins during distillation and also the diketones the formation of which they ascribed, as did Scheibler and Emden, to the oxidation of the salt of the di-enolate of the acyloin.

In the work which is now reported a study has been made of the reaction between sodium and the following esters: ethyl acetate, ethyl propionate, ethyl butyrate, ethyl isobutyrate and ethyl trimethylacetate. Ether, benzene and an excess of the ester were used as solvents. The temperature of each reaction was determined by the boiling point of the particular solvent used. In the cases when the two inert solvents were used one mole of the ester was allowed to react with two atoms of sodium. A number of different procedures for the decomposition of the sodium salts in the reaction mixture were tried, and it was soon discovered that considerable attention had to be given to this point if consistent and comparable results were to be obtained. The procedure finally adopted used the calculated amount of 35% sulfuric acid for the decomposition of these salts. This amount and concentration of sulfuric acid, besides destroying the alkalinity of the reaction mixture rapidly, converted all of the sodium which had been used into the solid $Na_2SO_4 \cdot 10H_2O$ from which the supernatant liquid could be directly decanted. The products of each reaction were separated into an acidic and neutral fraction by extraction of the former with a sodium carbonate solution. These two portions were then dried and subjected to fractional distillation.

Experimental Part

Materials Used.—The esters, ethyl acetate, ethyl propionate, ethyl butyrate, ethyl isobutyrate and ethyl trimethylacetate were carefully purified and dried by the procedure previously described (Ref. 1) in the first paper of this series. The ether and benzene (thiophene free) were distilled from phosphorus pentoxide before use.

General Procedure.—Two gram atoms of sodium was powdered by heating and vigorous stirring under xylene in a 3-liter flask fitted with a stirrer, reflux condenser and a dropping funnel. The xylene was then cooled and decanted from the sodium. The sodium was washed several times with dry ether to remove the xylene and finally covered with 600–800 cc. of ether. To this ether suspension of sodium 1 mole of the ester was added and the mixture stirred and refluxed until the reaction appeared to be complete.

There was a very noticeable difference in the reactivity of the various esters with powdered sodium in ether. In the case of ethyl acetate twenty-four hours of refluxing was required to complete the reaction. Ethyl propionate reacted quite completely

⁶ Corson, Benson and Goodwin, THIS JOURNAL, **52**, 3988 (1930).

after about two hours of refluxing. In the case of ethyl butyrate, ethyl isobutyrate and ethyl trimethylacetate, the reaction was so vigorous that it could not be controlled if the ester were added in a single portion. For this reason the ester was added gradually from a dropping funnel at such a rate as to keep the ether boiling vigorously. The reaction of each of these three higher esters appeared to be complete in one to one and one-half hours. The reaction converted the sodium into a voluminous, amorphous, yellow, insoluble solid. A very noticeable feature of the reaction of ethyl trimethylacetate was that considerable sodium remained unreacted even after two hours of refluxing, while with each of the other esters practically all of the sodium was used up. The reaction, however, was complete so far as the ester was concerned for practically no unchanged ethyl trimethylacetate was recovered from the reaction mixture.

After the reaction was finished the calculated quantity of 35% sulfuric acid for neutralization of the sodium that had been used was added from the dropping funnel. During this addition the flask was cooled with ice and the contents vigorously stirred. It required about five or ten minutes to complete this neutralization. The sodium sulfate with its water of crystallization readily separated and solidified in the bottom of the reaction flask. The supernatant liquid was decanted, the precipitate washed with 200 cc. of ether and the combined ether solutions extracted with a 20% solution of sodium carbonate. The carbonate extract was then acidified with sulfuric acid and extracted several times with ether. After drying, the ether extract of the acidic products and the original ether solution of the reaction products were fractionated.

A procedure similar to that outlined above was followed with benzene as the solvent instead of ether. Under these conditions of reaction the esters showed the same variation in reactivity that they did in the ether solution. Ethyl acetate was not used with benzene as the solvent on account of the rather uncertain results which it gave in ether solution. A considerable amount of unreacted sodium remained after the reaction of ethyl trimethylacetate in benzene as was the case in the ether solution.

The amounts and types of reaction products obtained from the reaction of these esters with sodium in the inert solvents, ether and benzene, are summarized in Table I. A ferric chloride test applied to a portion of the ether or benzene solution of reaction products before distillation indicated that small amounts of β-ketonic esters, resulting from an acetoacetic ester condensation, had been formed from ethyl acetate and ethyl propionate, but after distillation there was no evidences of such products in any of the fractions. Presumably the distillation had destroyed their identity so far as the ferric chloride test could determine and converted them into higher-boiling materials through condensation with other products of the reaction. The acidic products shown in the last two columns were obtained from the sodium carbonate extraction of the ether or benzene solution of the reaction products after the sodium salts of the reaction mixture had been decomposed and the $Na_2SO_4 \cdot 10H_2O$ filtered off. The calculations of the percentage yield of the diketone and acyloin are based on the amount of ester which was put into the reaction.

A very noticeable difference in reactivity of these esters with sodium was noted when an excess of the ester was used as the solvent. In these cases four to five moles of the ester was reacted with 23 g. (1 atom) of powdered sodium. The sodium could be covered directly with ethyl ace-

TABLE I

THE PRODUCTS OF REACTION BETWEEN SODIUM AND CERTAIN ALIPHATIC ESTERS IN ETHER AND BENZENE SOLUTION

Ester, ethyl	Amount used, g.	Solvent	Yield of RCOCOR[a] g.	%	Yield of RCHOHCOR[b] g.	%	Yield of higher boiling products,[c] g.	Yield of higher RCOOH, g.	Yield of higher acids, g.
Acetate	88	Ether	3	7	10	23	10	2	7
Propionate	102	Ether	5	9	30	52	14	...	...
Butyrate	116	Ether	5	7	52	72	7	3	...
Isobutyrate	116	Ether	3	4	54	75	2	4	4
Trimethylacetate	100	Ether	21	32	41	62	..	...	...
Propionate	102	Benzene	4	7	17.5	30	19	1	3
Butyrate	116	Benzene	5	7	44	61	13	3	2
Isobutyrate	116	Benzene	6	8	48.5	68	3	4	9
Trimethylacetate	50	Benzene	5	15	20	63	..	3	...

[a] This fraction was composed of material boiling higher than the ester and lower than the acyloin and represented approximately a 40° range. The major portion of this fraction in the case of ditrimethylacetyl boiled over a 10° range. It had the deep yellow color characteristic of the 1,2-diketones.

[b] This fraction had a boiling range of 5–10°. The highest boiling acyloin boiled under 100° (15 mm.).

[c] This fraction represents the material boiling higher than the acyloin and which had not reacted with sodium carbonate. It boiled as high as 200° (15 mm.). A small amount of undistillable residue was obtained from the ethyl acetate and ethyl propionate reactions.

tate or ethyl propionate and very little reaction appeared to take place until heat was applied. The reaction in either case was in no sense vigorous and it was necessary to reflux the ester for about two hours before the sodium had disappeared. The reaction mixture appeared quite homogeneous. With the three higher esters it was necessary to add the sodium in small portions to the ester. This was done by dipping the powdered sodium which was kept covered with dry ether with a dipper having a perforated bottom (constructed from a Gooch crucible) and allowing most of the ether to drain off before the addition of the sodium to the ester. The heat of reaction was sufficient to sustain refluxing until all of the sodium had reacted. The reaction mixture appeared as a thick pasty mass. The reaction products were isolated as described above and are summarized in Table II. The calculations of the yields of the various products were based on the amount of sodium (23 g. in each case) that was put into the reaction.

Some Properties of the Diketones and Acyloins. The Diketones.— With the exception of ditrimethylacetyl, the diketones were obtained in quite small yields from the above reactions. They are characterized by their deep yellow color. They generally boil about 20–25° lower than the acyloin and about the same amount higher than the esters from which they are derived.

TABLE II

THE PRODUCTS OF REACTION OF SODIUM WITH AN EXCESS OF CERTAIN ALIPHATIC
ESTERS

Ester, ethyl	Yield of RCOCOR[a] g.	%	Yield of RCHOHCOR[b] g.	%	Yield of β-keto ester[c] g.	%	Yield of higher boiling products, g.	Yield of RCOOH[d] g.	%	Yield of higher acids, g.
Acetate	...	...	..	..	46[e]	35	6[e]	14	23	3
Propionate	...	...	..	..	51[e]	32	15[e]	14	19	3
Butyrate	6[f]	8	2.5[f]	7	..	..	23	48	55	20
Isobutyrate	5	.7	20	56	..	..	13.5	51	58	5
Trimethyl acetate	...	...	42	98	..	..	6	46	45	..

[a] Percentage yield calculated on the basis of 2Na producing 1RCOCOR. [b] Percentage yield calculated on the basis of 4Na producing 1RCHOHCOR. [c] Percentage yield calculated on the basis of 1Na producing 1RCOCHR'COOC₂H₅. When, however, the alcohol was distilled out of the reaction of ethyl acetate and sodium a 72% yield of acetoacetic ester was obtained. [d] Percentage yield calculated on the basis of 1Na producing 1RCOOH. [e] Colorless, water-white liquids. [f] Deep yellow-colored liquids.

They are readily polymerized and rearranged by sodium ethoxide, as is shown by the following experiment. A solution of 9 g. of dibutyryl in 50 cc. of benzene was heated for two hours on a water-bath with 5 g. of sodium ethoxide. The reaction mixture was then acidified with sulfuric acid and separated into a neutral and acidic portion by extraction with sodium carbonate. The former portion yielded on fractionation 1 g. of unchanged dibutyryl and 4 g. of higher-boiling material. The acidic portion was separated by fractionation into 2 g. of butyric acid and 1 g. of di-*n*-propylglycolic acid,[7] m. p. 76°, neutral equivalent 166. Di-isobutyryl showed a similar behavior except that about 2 g. (18% of the calcd.) of di-isopropylglycolic acid,[8] m. p. 108–110°, neutral equivalent 163, was obtained. A similar experiment using 10 g. of ditrimethylacetyl yielded 7.5 g. of unchanged diketone, 1 g. of trimethylacetic acid and 1 g. of an undistillable tar.

The Acyloins.—The acyloins which are reported in Tables I and II were collected over a 5–10° boiling range. Acetoin boiled at 140–150°, propionoin at 160–170°, butyroin at 85–95° (12 mm.), isobutyroin at 175–180°, pivaloin (hexamethylacetoin) 80–90° (15 mm). The latter compound solidified on cooling and melted at 80–81°. All of the acyloins as obtained from the reaction show a yellow coloration which is much less intense than that characteristic of the diketones. This color is no doubt due to the presence of small quantities of the diketone.

In contrast to the diketones the acyloins are hardly affected by sodium

[7] *Cf.* Crichton, *J. Chem. Soc.*, **89**, 933 (1906).

[8] *Cf.* Barylowitsch, *Ber.*, **28**, 2465 (1895); Claisen, *Ann.*, **297**, 96 (1897); Scheibler, *ibid.*, **434**, 284 (1923).

ethoxide; for example, 8 g. of isobutyroin was recovered unchanged when 10 g. of this acyloin was refluxed with 5 g. of sodium ethoxide in benzene solution. These reaction conditions, it was pointed out above, readily polymerized and rearranged the diketones with the exception of ditrimethylacetyl.

Bouveault and Locquin[2] thought that the higher-boiling products of the reaction were derived from the acyloin by polymerization during distillation. However, samples of propionoin, butyroin and isobutyroin after one and one-half hours of boiling under a reflux condenser were found to distil completely over the temperature range at which they had originally boiled. It would seem quite certain from this fact that the higher-boiling products owe their origin to some other source.

The Higher-Boiling Products.—Very little investigation was made on the nature of these products. With the exception of those obtained from ethyl acetate and ethyl propionate when an excess of the ester was used as the solvent (Table II), these products all possessed the yellow color suggestive of the diketone structure. The product from ethyl propionate (Table I) did not show any appreciable reduction with hydrogen in the presence of either catalytic platinum or nickel (propionoin was reduced quantitatively with the latter catalyst at 50° and under 150 atmospheres of hydrogen[9] to the 3,4-hexanediol). The product from ethyl propionate reacted with acetic anhydride in the ratio of 307 g. of the former to one mole of the anhydride. With the similar product from ethyl butyrate the ratio was 500 g. to one mole of the anhydride. They showed no reaction with semicarbazide but with phenylhydrazine a red viscous liquid was formed.

The Acidic Reaction Products.—The origin of that portion of the acidic reaction products representing the acid, the ester of which was used in the reaction, is discussed below. From the higher-boiling acidic products there were obtained, in the cases of ethyl butyrate and ethyl isobutyrate, small yields of di-n-propylglycolic acid and di-isopropylglycolic acid. These acids were obtained by recrystallization of fractions which boiled at 140–170° (15 mm.). After this fraction was removed the bulk of the higher acidic portion remained as an undistillable residue. This residue was no longer soluble in alkali. The dialkylglycolic acids are formed, as shown above, from the rearrangement of the diketones with sodium ethoxide and this reaction is, no doubt, responsible for their presence in the reaction mixtures obtained from ethyl butyrate and ethyl isobutyrate. The undistillable residue after the removal of the dialkylglycolic acid, since it was insoluble in alkali, was quite probably a lactide resulting from the heating of the α-hydroxy acids.
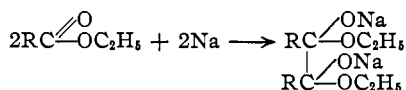
Discussion of the Experimental Results and the Mechanism of the Reaction between the Esters and Sodium

An inspection of the data presented above shows that there is no perceptible difference in the rate at which the three esters, ethyl butyrate, ethyl isobutyrate and ethyl trimethylacetate react with sodium nor is there any great difference in the completeness with which they react in the inert solvents to form diketones and acyloins. The need, therefore, of a special mechanism to account for the slowness and incompleteness of reaction of those esters which cannot enolize does not exist, for ethyl trimethylacetate reacts somewhat more completely and just as rapidly as the other two. Corson, Benson and Goodwin[6] made a somewhat similar observation on the behavior of ethyl dimethylethylacetate. Since the only group capable of reaction that these three esters have in common is the carbethoxy group it is logical to conclude that the reaction of sodium with such esters involves only this particular group. The postulate of Scheibler and Emden that the reaction proceeds, when possible, through the salt of the enol form of the ester, or, when this is not possible, through an entirely different mechanism, has no experimental support and would seem to be quite unnecessary, if not erroneous.
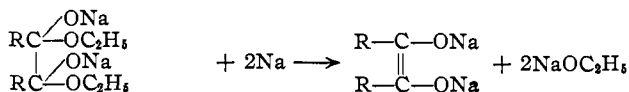
It is also evident from the experimental data presented in Table I that the diketone is an intermediate product in the formation of the acyloin rather than the result of an oxidation of the acyloin as previous investigators of the reaction have thought. Egorova[10] arrived at a similar conclusion in his study of the action of sodium on the chloride of trimethylacetic acid. It would be difficult to explain the relatively high yields of the diketone in the case of ethyl trimethylacetate in Table I on the basis of atmospheric oxidation when the reaction conditions were practically identical to the conditions used with the other esters and *unreacted sodium remained* in the reaction mixture. The fact that dibutyryl and di-isobutyryl are readily polymerized and rearranged by sodium ethoxide while the ditrimethylacetyl is quite stable to this reagent is not without significance and indicates that the low yield of the former two is due to their partial destruction by the sodium ethoxide produced in the reaction.

It would seem, therefore, logical and consistent with the experimental facts to represent the reaction between sodium and such aliphatic esters as taking place in two steps. First, the formation of a diketone–sodium ethoxide addition product by the reaction of two molecules of the ester with two atoms of sodium

$$2RC\diagup^{O}_{OC_2H_5} + 2Na \longrightarrow \begin{array}{c} RC\diagup^{ONa}_{OC_2H_5} \\ | \diagup^{ONa} \\ RC\diagdown_{OC_2H_5} \end{array}$$

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[10] Egorova, *J. Russ. Phys.-Chem. Soc.*, **60**, 1199 (1928); *Chem. Abstracts*, **23**, 2935 (1929).

This reaction may involve the intermediate formation of a free radical, $RC(OC_2H_5)ONa$, such as Blicke[11] noted in the reaction of benzaldehyde, phenyl benzoate and ethyl benzoate and sodium. This diketone–sodium ethoxide addition product is then converted by two more atoms of sodium into the sodium salt of the acyloin and sodium ethoxide

$$\begin{matrix} RC\overset{ONa}{\underset{OC_2H_5}{<}} \\ \overset{ONa}{\underset{OC_2H_5}{|}} \\ RC\overset{}{\underset{}{<}} \end{matrix} + 2Na \longrightarrow \begin{matrix} R-C-ONa \\ \| \\ R-C-ONa \end{matrix} + 2NaOC_2H_5$$

Whether or not the addition product reacts directly with the sodium or first loses sodium ethoxide to allow the free diketone to react with the sodium cannot be decided from any experimental data now available. Egorova[10] has shown that the latter reaction (between the diketone and sodium) does take place with ditrimethylacetyl.

The mechanism of Scheibler and Emden, it might be pointed out, allows for the intermediate formation of diketone–sodium ethoxide addition product in those cases in which the ester involved may enolize. Their mechanism, however, for the reaction of such esters as ethyl trimethylacetate, from which the intermediate formation of the diketone is so apparent in Table I, does not involve this intermediate, and is obviously inadequate.
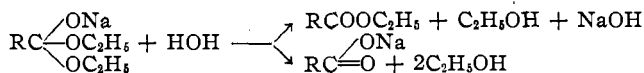
Table II shows that with an excess of ester as the solvent the acetoacetic ester condensation takes place with ethyl acetate and ethyl propionate. Judging from the color of the reaction products, no products of the diketone or acyloin type were formed. With ethyl butyrate very little of the diketone and acyloin, but considerable higher-boiling material with the characteristic yellow color of the diketones is produced. With ethyl isobutyrate the combined yield of di-isobutyryl and isobutyroin is only about 13% lower than those obtained when benzene was used as the solvent but it is seen that the amount of higher-boiling material is correspondingly higher. The very high yield of the acyloin and the absence of any diketone in the case of ethyl trimethylacetate must be due to the favorable conditions for the reaction when the ester is used as the solvent.

The source of the higher-boiling materials is a matter of speculation. It is the opinion of the authors that they are not derived from the acyloin during distillation for the reason, mentioned above, that the acyloin appears to remain practically unchanged after a period of boiling. The fact that the diketones are readily polymerized and rearranged by sodium ethoxide indicates that they are responsible, to some extent at least, for the presence of the higher-boiling materials in the reaction mixture. It is significant that very little or no higher-boiling products are obtained from ethyl trimethylacetate, the diketone of which is quite stable to sodium ethoxide. Added to this probability is the possibility of Claisen condensa-

[11] Blicke, THIS JOURNAL, 47, 229 (1925).

tions between an ester molecule and the diketone or acyloin induced by the sodium ethoxide formed in the reaction in the cases of those esters possessing a structure (two hydrogens on the α-carbon atom) capable of undergoing such a condensation. The fact that ethyl butyrate in Table II shows higher-boiling products almost to the exclusion of the acyloin while ethyl isobutyrate and ethyl trimethylacetate produce quite high yields of the acyloin type would seem to lend support to this latter suggestion.

The high yields of the acids, RCOOH in Table II, are striking. Previous investigators have noted the formation of such acids. Egorova[10] thought that the trimethylacetic acid which he obtained from the action of sodium on trimethylacetyl chloride resulted from the decomposition of the intermediate diketone, ditrimethylacetyl, by alkali. The data in Table II, particularly for ethyl trimethylacetate, show that such an explanation is insufficient for it is seen that practically all (98%) of the sodium put into the reaction was used in the formation of the acyloin and that no diketone could have been present. Still a 45% yield of the acid was obtained. Scheibler and Marhenkel[12] suggested that the acid resulted from one type of hydrolysis of the salt of the ortho ester thus

$$RC\begin{smallmatrix}/ONa\\-OC_2H_5\\\backslash OC_2H_5\end{smallmatrix} + HOH \longrightarrow \begin{smallmatrix}\nearrow RCOOC_2H_5 + C_2H_5OH + NaOH\\ \begin{smallmatrix}/ONa\end{smallmatrix}\\ \searrow RC\!\!=\!\!O + 2C_2H_5OH\end{smallmatrix}$$

This explanation involves the reaction of the sodium ethoxide produced in the reaction with a portion of the ester which is in excess of that required for the primary reaction and is supported by the fact that high yields of the acid, RCOOH, were obtained in each case when an excess of the ester was used as the solvent. In order to check this possibility, 68 g. of sodium ethoxide was refluxed with 380 g. of ethyl butyrate for thirty minutes. The reaction mixture after cooling was treated with the calculated amount of 35% sulfuric acid as was done in each of the above experiments. A yield of 49 g. (56% based on the sodium ethoxide) of butyric acid was obtained from the sodium carbonate extract.

It is apparent from the data presented above that sodium produces two distinct types of reaction with aliphatic esters, the acetoacetic ester condensation and the acyloin type of condensation. Whether or not the metal is directly responsible for the former type of reaction cannot be definitely decided from any experimental facts now known. There is no doubt, however, that the metal is the direct cause of the acyloin condensation and the simultaneous production of sodium ethoxide. It is quite probable that it is this latter compound that is responsible for any acetoacetic ester type of condensation which may take place. Obviously the alcohol produced in this latter condensation would react with the metal to produce more of the active condensing agent. Such a functioning of the sodium has been

[12] Scheibler and Marhenkel, *Ann.*, **458,** 8 (1927).

previously suggested by Higley.[13] Some significance, therefore, may be attached to the fact that those esters, ethyl acetate and ethyl propionate, which are the most sluggish in their reaction with sodium in the inert solvents, react through the acetoacetic ester condensation when an excess of the ester is the solvent.

Summary

1. The reaction of ethyl acetate, propionate, butyrate, isobutyrate and trimethylacetate with sodium has been studied under various conditions.

2. The mechanisms which have been proposed for the formation of acyloins are discussed on the basis of the experimental results obtained.

MADISON, WISCONSIN

A HEAT COAGULABLE PROTEIN FROM GELATIN

BY S. E. SHEPPARD, J. H. HUDSON AND R. C. HOUCK

In a report on the specification of a standard gelatin[1] attention was called to the desirability of specifying the permissible amount of heat coagulable protein in a standard gelatin. The presence of albuminous substances in gelatin has been frequently indicated, especially in articles dealing with its manufacture and purification.[2]

The following is an account of some preliminary work on the estimation, separation, and analysis of the heat coagulable protein from a number of different gelatins.

The results are insufficient to decide whether the substance is a single homogeneous protein or a mixture. They do, however, definitely establish its nature, in gelatin, as a foreign impurity of different constitution and composition.

Experimental

In separating the coagulable protein from gelatin it is found necessary first to adjust the P_H of the gelatin, with acetic acid, to near the isoelectric point of gelatin. Fifty grams of a gelatin with a P_H range of 5.9 to 6 dissolved in 800 cc. of water will require about 5 cc. of glacial acetic acid to bring the P_H to 4.7. Heating overnight on a steam-bath at a temperature of 80 to 100° is sufficient to hydrolyze the gelatin and allow the protein to

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[13] Higley, *Am. Chem. J.*, **37**, 302 (1907).

[1] Hudson and Sheppard, *Ind. Eng. Chem.*, **21**, 263 (1929), "A Contribution to the Preparation of Standard Gelatin," Communication 364. Davis, Sheppard and Briefer, *ibid.*, *Anal. Ed.*, **1**, 56 (1929), "Specifications for Gelatin Standards."

[2] Bogue, "Chemistry and Technology of Gelatin and Glue," McGraw-Hill Book Co., Inc., New York, 1922, 1st ed.; Sheppard, "Gelatin in Photography," Monograph No. 1 from Kodak Research Laboratories, Rochester, New York. 1923, p. 131.