bean mosaic virus have been established. Four of these coincidences can be taken as the mobility values at four different $p$H values at ionic strength 0.02. The standard error of the coincidences is approximately $0.1 \times 10^{-5}$ cm.$^2$/volt sec., and the range of mobilities covered in the study is approximately $10 \times 10^{-5}$ cm.$^2$/volt sec. The fifth coincidence can be expressed as the isoelectric point in phosphate buffer at ionic strength 0.1. This isoelectric point occurs at a $p$H of 5.10, and the standard error of the coincidence is $\pm 0.06$ $p$H unit. The previously reported study of Epstein and Lauffer[3] showed that two such quantitative coincidences can be obtained in sedimentation studies carried out in media with different densities. Thus, seven quantitative parameters of the infectious entity of Southern bean mosaic virus are indistinguishable from seven similar quantitative parameters for the characteristic particle. Since these parameters of the infectious entity are identical with those of the characteristic particle, one must conclude that the probability that the infectious entity is something different from the characteristic particle is indeed very low.

There has never been much real doubt that the characteristic particle of Southern bean mosaic virus was in effect identical with the infectious entity, and in that sense the present study contributes very little new information. However, there are many viruses and many other materials possessing biological activity for which sound information concerning the relationship or non-relationship between the biologically active entity and the characteristic particle is lacking. The real contribution of the present report is that it provides a method for investigating identity in such cases.

PITTSBURGH, PENNA.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE TOKYO INSTITUTE OF TECHNOLOGY]

# On the Thermal Dissociation of Organic Compounds. V.[5-8] The Effect of the Solvent (Fatty Acids) on the Thermal Dissociation of Urea

BY TERUAKI MUKAIYAMA AND TAKAO MATSUNAGA

RECEIVED FEBRUARY 23, 1953

On heating, a urea dissociates into an isocyanic acid and ammonia. In the absence of kinetic data on the thermal dissociation of urea in fatty acid, we have measured the rate constants of this reaction in various fatty acids by noting the rate of carbon dioxide evolution. The rate of dissociation, which is first order in urea, increases as the acidity of the solvent acid increases. In a large excess of *n*-caproic acid as solvent, the rate is accelerated by the presence of less than one mole of strong acid and is retarded by more than 1.5 moles of strong acid per mole of urea. The behavior of urea and monochloroacetic acid in cumene, tetralin or anisole was also studied.

## Introduction

It is known that, on heating, urea dissociates thermally into isocyanic acid and ammonia. Earlier investigators[1] obtained ammonium carbonate on heating urea in aqueous solution. They explained the result by assuming isocyanic acid and ammonia, formed as a result of dissociation of urea, further react with water to form ammonium carbonate.

Although a similar experiment[2] was made to clarify the behavior of urea in dilute acids and alkalies, the results were not analyzed from the viewpoint of modern reaction kinetics.

Later, Mohon[3] studied the behavior of urea in fatty acids, and, identifying the reaction products by their melting points, assumed that in the case where acetic acid was the solvent, the first step was the dissociation of urea into ammonia and isocyanic acid and subsequent steps were the reactions of these with acetic acid to form (1) ammonium acetate and (2) acetamide and carbon dioxide, respectively.

Recently Cherbuliez and Landolt[4] have reported that acid amides are prepared by treating carboxylic acids with urea at elevated temperatures.

The kinetics of the thermal dissociation of substituted ureas in fatty acids has been studied[5-7] and, in the case of *sym*-diphenylurea in acetic acid, for example, the mechanism shown by equations 1 to 3 was suggested.

$$C_6H_5NHCONHC_6H_5 \rightleftarrows C_6H_5NCO + H_2NC_6H_5 \tag{1}$$

$$C_6H_5NCO + CH_3COOH \rightleftarrows C_6H_5NHCOOCOCH_3 \tag{2}$$

$$C_6H_5NHCOOCOCH_3 \longrightarrow C_6H_5NHCOCH_3 + CO_2 \tag{3}$$

By analogy, the steps in the dissociation of urea in a fatty acid solvent are believed to proceed *via* equations 4 to 7.

$$H_2NCONH_2 \rightleftarrows HNCO + NH_3 \tag{4}$$

$$HNCO + RCOOH \rightleftarrows RCOOCONH_2 \tag{5}$$

$$RCOOCONH_2 \longrightarrow RCONH_2 + CO_2 \tag{6}$$

$$NH_3 + RCOOH \rightleftarrows RCOONH_4 \tag{7}$$

The present investigation was undertaken to gain a better understanding of the dissociation.

The reaction can be followed by measuring the rate of evolution of carbon dioxide (eq. 6), provided it is evolved as soon as formed. Since the reaction temperatures were near 140° it is reasonable to believe that this is true, and also that the reverse reaction is negligible under the conditions of the

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[1] C. E. Fawsitt, *Z. physik. Chem.*, **41**, 601 (1902).

[2] E. A. Werner, *J. Chem. Soc.*, **113**, 84 (1918).

[3] J. Mohon, *J. Indian Chem. Soc.*, **10**, 117 (1933).

[4] E. Cherbuliez and F. Landolt, *Helv. Chim. Acta*, **29**, 1438 (1946).

[5] T. Hoshino, T. Mukaiyama and H. Hoshino, THIS JOURNAL, **74**, 3097 (1952).

[6] T. Hoshino, T. Mukaiyama and H. Hoshino, *Bull. Chem. Soc. Japan*, **25**, 392 (1952).

[7] T. Hoshino, T. Mukaiyama and H. Hoshino, *ibid.*, **25**, 396 (1952).

experiments. If reaction 4 is the rate-determining step, then the rate of dissociation is measurable.

On plotting the volume of carbon dioxide, $\Delta Y$, evolved at regular intervals of time we have obtained a straight line. This indicates a first-order reaction rate. The rate constant is given by the gradient of such a plot,[8] as shown in Fig. 1.

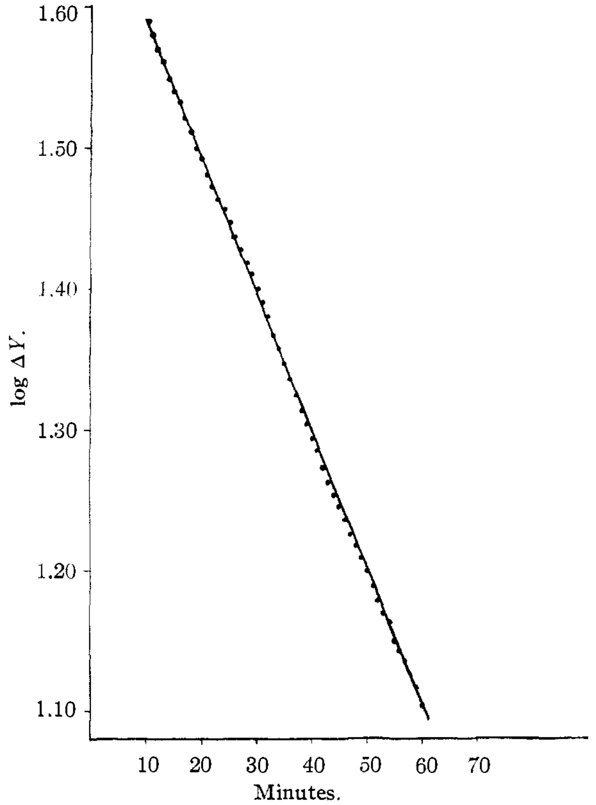

Fig. 1.—Thermal dissociation of urea in α-chloroisocaproic acid at 138.5°; the plot of log $\Delta Y$ against $t$.

## Experimental

The apparatus employed was the same as that described in previous reports.[5,9] The materials employed in this experiment were purified by the following methods. Urea was twice recrystallized from 85% aqueous alcohol. The purified urea, m.p. 132°, was ground in the agate mortar, and stored in a vacuum desiccator over calcium chloride. Propionic, *n*-butyric, *n*-caproic, *n*-caprylic, myristinic and thioglycolic acids were carefully purified by vacuum distillation. The boiling points of these acids under reduced pressures were the same as those described in the literature. α-Chloroisocaproic acid, furnished by Ajinomoto Co., Inc., was purified by vacuum distillation employing a 50-cm. fractionating column; b.p. 93–95° at 5.5 mm. This did not accord with that previously described.[10] Phenylacetic acid, furnished by Nihon Kihatsuyu Co., Ltd., was recrystallized from hot water, m.p. 77°. Chloroacetic acid was distilled thrice, m.p. 62°. Tetralin, anisole and cumene were distilled twice and tetralin was used within one week.

The rate constants for the thermal dissociation of urea at temperatures near 140° (except 152.5° in Fig. 3), were determined under different conditions, as follows: (a) **urea (1 mole) in α-chloroisocaproic acid (100 moles)**, given as an example of a typical run; Fig. 1.

(b) **Urea (1 Mole) in a Carboxylic Acid (100 Moles).**—The acids were propionic, *n*-butyric, *n*-caproic, *n*-caprylic, myristinic, thioglycolic, α-chloroisocaproic, phenylacetic and chloroacetic. The results are shown in Table I. The rates were first order with respect to urea.

TABLE I

THE RATE CONSTANT OF THE THERMAL DISSOCIATION OF UREA IN FATTY ACID

| Solvent, acid | $t$ (°C.) | $k \times 10^{-3}$ min.$^{-1}$ | Solvent, acid | $t$(°C.) | $k \times 10^{-3}$ min.$^{-1}$ |
|---|---|---|---|---|---|
| Propionic | 130.6 | 6.65 | Monochloroacetic | 138.3 | 49.0 |
| *n*-Butyric | 142.8 | 6.10 | α-Chloroisocaproic | 138.5 | 22.4 |
| *n*-Caproic | 138.5 | 3.45 | Thioglycolic | 138.4 | 48.8 |
| *n*-Caprylic | 138.6 | 3.36 | Dichloroacetic | 138.4 | 43.3 |
| Myristinic | 138.5 | 2.70 | Phenylacetic | 137.9 | 12.5 |

(c) **Urea (1 Mole) and Monochloroacetic Acid (2–20 Moles) in a Solvent (35 Moles).**—The solvents were tetralin, cumene and anisole. Urea (1 mole) and monochloroacetic acid (2 moles) in anisole (35 moles), given as an example of a typical run; Fig. 2. In Table II are the results in different solvents. The rates were first order with respect to urea. The rate of dissociation increases as the concentration of monochloroacetic acid increases.

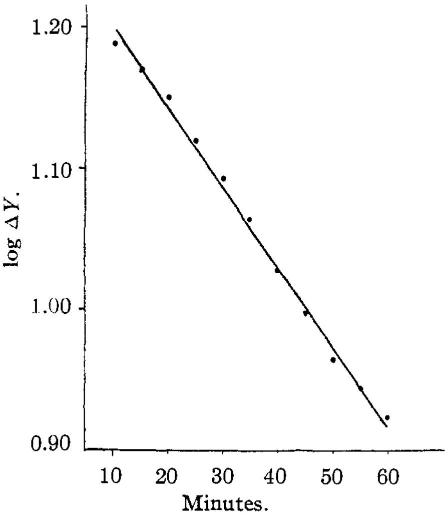

Fig. 2.—Urea (1 mole) and monochloroacetic acid (2 moles) in anisole (35 moles) at 139.2°: the plot of log $\Delta Y$ against $t$.

As shown in Table II, the amount of carbon dioxide evolved was only about half of the theoretical in experiment 3 and it increases as the molar ratio of monochloroacetic acid to urea increases in experiments 4–7. The reason for these phenomena can be explained as follows: In the presence of a large excess of monochloroacetic acid, the isocyanic acid formed reacts with the chloroacetic acid and evolves carbon dioxide *via* equation 6. However, in the presence of only a small excess of chloroacetic acid in anisole, the iso-

TABLE II

THE RATE CONSTANT OF THE THERMAL DISSOCIATION OF UREA IN SOLVENT IN THE PRESENCE OF CHLOROACETIC ACID

| Expt. | Solvent | Urea, mole | Monochloroacetic acid, moles | $t$, °C. | $k \times 10^{-3}$, min.$^{-1}$ | $CO_2$, ml. Evolved | Theor. |
|---|---|---|---|---|---|---|---|
| 1 | Cumene | 1 | 2 | 143.1 | 23.9 | *ca.* 35 | 72 |
| 2 | Tetraline | 1 | 2 | 139.0 | 15.9 | *ca.* 35 | 72 |
| 3 | Anisole | 1 | 2 | 139.2 | 7.41 | *ca.* 30 | 72 |
| 4 | Anisole | 1 | 4 | 139.4 | 13.35 | *ca.* 45 | 72 |
| 5 | Anisole | 1 | 6 | 139.3 | 14.48 | *ca.* 50 | 72 |
| 6 | Anisole | 1 | 10 | 139.2 | 22.9 | *ca.* 65 | 72 |
| 7 | Anisole | 1 | 20 | 138.8 | 39.8 | *ca.* 70 | 72 |

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[8] E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).

[9] T. Mukaiyama, S. Motogi and Y. Hamada, *Bull. Chem. Soc. Japan*, **26**, 49 (1953).

[10] P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **83**, 591 (1929), give the boiling point of *l*-2-chloroisocaproic acid as 80–95° at 1 mm.

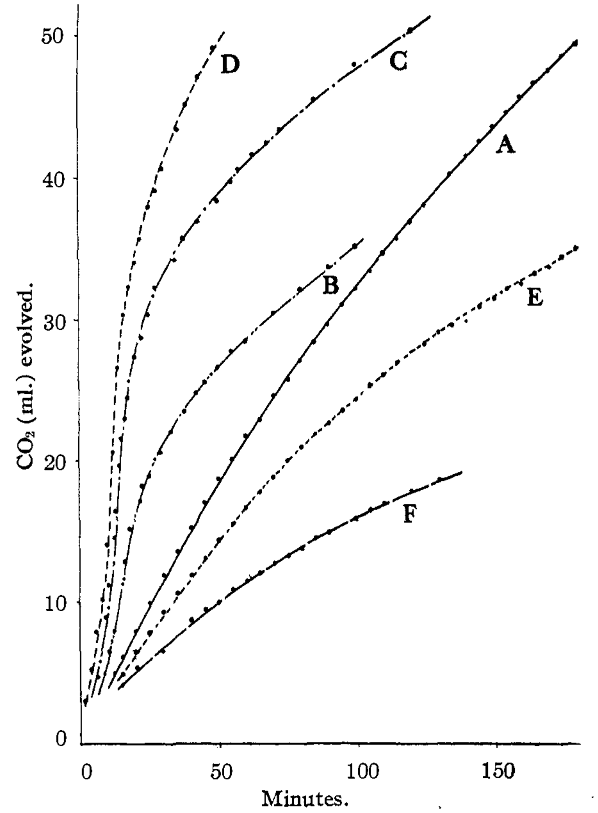

Fig. 3.—Thermal dissociation of urea in caproic acid with additional sulfuric acid:

| Expt. | Urea, mole | Caproic acid, mole | $H_2SO_4$, mole | *t*., °C. |
|---|---|---|---|---|
| 8 (A) | 1 | 100 | | 138.5 |
| 9 (B) | 1 | 100 | $^1/_4$ | 138.6 |
| 10 (C) | 1 | 100 | $^1/_2$ | 138.9 |
| 11 (D) | 1 | 100 | 1 | 138.0 |
| 12 (E) | 1 | 100 | 1.5 | 139.5 |
| 13 (F) | 1 | 100 | 3.5 | 138.8 |

cyanic acid reacts preferentially with urea, to form biuret (eq. 8).

$$NH_2CONH_2 + HNCO \rightleftarrows NH_2CONHCONH_2 \quad (8)$$

Biuret was shown to be formed, along with ammonia, when urea (1 mole) was heated in anisole (35 moles) at 140° for 150 min. Also, the formation of ammonia in expt. 3 is shown by the separation of ammonium chloroacetate during the heating and by the isolation of chloroacetamide from the solution, confirmed by mixed melting points with an authentic sample. Biuret was confirmed by the biuret reaction.

The rate of dissociation of biuret (1 mole) in anisole (35 moles) in the presence of chloroacetic acid (20 moles) was approximately first order with respect to biuret. The rate constant, *k*, was found to be $3.84 \times 10^{-3}$ min.$^{-1}$ at 138.9°. The theoretical amount of carbon dioxide was evolved and ammonium chloroacetate separated from solution. These results show that biuret dissociates in the presence of chloroacetic acid, but at a slower rate than urea. Thus equation 8 is reversible, and the decomposition of biuret probably proceeds *via* equations 4, 5, 6 and 8, according to equation 9.

$$NH_2CONHCONH_2 + 3RCOOH \longrightarrow 2RCONH_2 + RCOONH_4 + 2CO_2 \quad (9)$$

Evidence in favor of this view is obtained from the reaction of biuret (1 mole) and chloroacetic acid (2 moles) in anisole (35 moles) at 138.5°. The reaction proceeds very slowly, and the rate is not first order in biuret. Thus the formation of biuret explains the fact that less than the theoretical amount of carbon dioxide is evolved at low concentrations of acid.

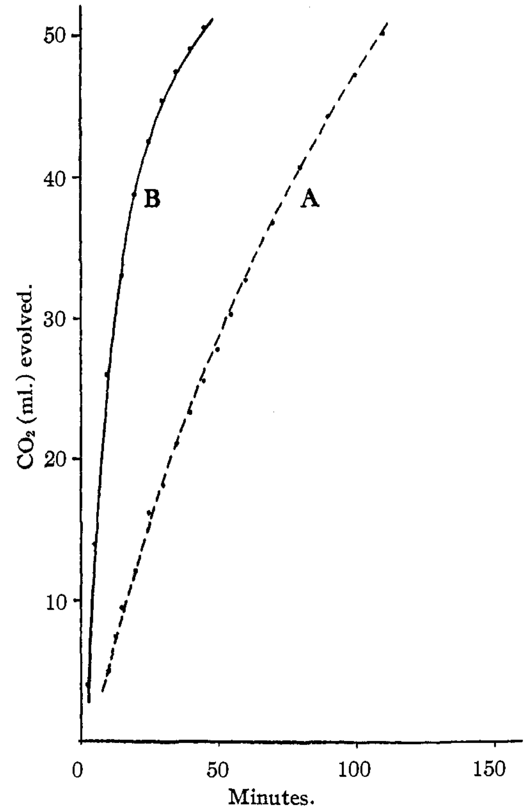

Fig. 4.—Thermal dissociation of urea in caproic acid with additional *p*-toluenesulfonic acid:

| | Urea, mole | Caproic acid, moles | *p*-Toluenesulfonic acid, mole | *t*., °C. |
|---|---|---|---|---|
| (A) | 1 | 100 | | 152.5 |
| (B) | 1 | 100 | 1 | 152.4 |

(d) **Urea (1 mole) in *n*-caproic acid (100 moles) plus added sulfuric acid**, Fig. 3, or ***p*-toluenesulfonic acid**, Fig. 4.—In the experiments 10–13, when urea is mixed with the solution of *n*-caproic acid and sulfuric acid an oily substance precipitates, which changes into ammonium sulfate as the reaction proceeds. The oily substance crystallizes in a hygroscopic pale pink colored crystal at room temperature. Sulfate contents in this compound were gravimetrically determined by using barium chloride, and the result shows that the molar ratio of urea and sulfuric acid is 1:1.

## Discussion

The catalytic effect of acids is due to the formation of the conjugate acid of urea, and the decelerating effect of excess strong acid is due to a further protonation of urea.

$$H_2NCONH_2 \underset{-H^+}{\overset{+H^+}{\rightleftarrows}} H_2NCO\overset{+}{N}H_3 \underset{-H^+}{\overset{+H^+}{\rightleftarrows}} H_3\overset{+}{N}CO\overset{+}{N}H_3$$

The retarding effect of a solvent is due in part to the equilibria shown above and to the side reaction of forming biuret, owing to the lower concentration of monochloroacetic acid, and in part, especially in the case of anisole, to the basic nature of the solvent.

On the above basis, the dissociation of urea probably proceeds through the conjugate acid, $H_2NCO\overset{+}{N}H_3$.

$$H_2NCO\overset{+}{N}H_3 \xrightarrow{-NH_3} H_2\overset{+}{N}CO \xrightarrow{-H^+} HNCO$$

As shown in expt. 1–7, isocyanic acid may react with urea to form biuret, but in the presence of much carboxylic acid it reacts to form carbon dioxide and the amide of the acid, probably through an intermediate anhydride.

**Acknowledgment.**—The authors wish to express their sincere thanks to Professor T. Hoshino for his many helpful suggestions throughout the course of this work, to the referee for his helpful discussion on the mechanisms of the acid-catalyzed dissociation reaction in this and previous reports, and also for his help in preparing this manuscript, and to the Nippon Soda Co., Ltd., Hodogaya Chemical Manufacturing Co., Ltd., Nihon Kihatsuyu Co., Ltd., and Ajinomoto Co., Inc., for furnishing propionic, *n*-caproic, phenylacetic and $\alpha$-chloroisocaproic acids.

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[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

# Addition of Formic Acid to Olefinic Compounds. I. Monoölefinic Compounds[2]

BY H. B. KNIGHT, R. E. KOOS AND DANIEL SWERN

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Formic acid at its boiling point at atmospheric pressure adds readily to the double bonds of oleic, elaidic and 10-hendecenoic (undecylenic) acids, methyl oleate, oleyl alcohol, cyclohexene, 1-hexene and the unreacted olefinic material separated from the hydrolyzed reaction product of oleic acid with formic acid, to yield the corresponding formate esters which are readily hydrolyzed. Oleic and elaidic acids and methyl oleate are readily converted in good yields to monohydroxystearic acids; oleyl alcohol yields dihydroxyoctadecanes; 1-hexene yields a mixture of 2-hexanol ($^2/_3$) and 3-hexanol ($^1/_3$); and 10-hendecenoic acid yields monohydroxyhendecanoic acids (isolated as methyl esters). Castor oil, methyl ricinoleate and crotyl alcohol do not add formic acid to the double bond. In the absence of catalysts, approximately 24 hours are required for 80% addition of anhydrous formic acid; perchloric acid in small amounts (0.5–2% by weight of olefinic compound) reduces the reaction time to 5 to 15 minutes. Sulfuric acid is a slightly less efficient catalyst when anhydrous formic acid is used but the efficiency of these catalysts is reversed with 90% formic acid. Boron fluoride–acetic acid complex (1:2) is also an efficient catalyst. Acetic acid, catalyzed by perchloric acid, also adds to the double bond but at a lower rate and less completely than formic acid.

This paper describes the uncatalyzed and catalyzed addition of 90–100% formic acid to certain monoölefinic compounds, namely, oleic, elaidic and 10-hendecenoic (undecylenic) acids, methyl oleate, oleyl alcohol, cyclohexene, 1-hexene, and the unreacted olefinic material (approximately 20%) separated from the hydrolyzed reaction product of oleic acid with formic acid. The attempted addition of formic acid to methyl ricinoleate (methyl 12-hydroxy-*cis*-9-octadecenoate), castor oil (which consists predominantly of glycerides of ricinoleic acid) and crotyl alcohol is also reported.

The addition of formic acid to olefinic compounds is, generally, a homogeneous and easily controlled reaction, excess formic acid is readily recovered by vacuum distillation, and hydrolysis of the intermediate formate esters is not difficult. Furthermore, in the hydration of oleic acid, the melting point of the once crystallized monohydroxystearic acid is relatively high and sharp (*ca.* 75°), suggesting that a complicated mixture of isomeric hydroxy acids is not obtained and that the 9- and 10-isomers predominate. Pure 10-hydroxystearic acid, m.p. 81°, readily can be isolated from the crude monohydroxystearic acids obtained from oleic acid by formic acid addition and hydrolysis, whereas its isolation from the monohydroxystearic acid mixture obtained from oleic acid by sulfation and hydrolysis is tedious and poor yields are obtained.

In most of the work reported in this paper, the 99–100% grade of formic acid was employed because the reaction mixtures were usually homogeneous and the reactions were complete almost instantaneously regardless of the size of the experiment. As shown in the experimental part under the hydration of oleic acid, however, the readily available and inexpensive 90% commercial grade of formic acid worked almost as well, with minor modifications in the reaction procedure. In this case the reaction mixture was heterogeneous throughout the entire reaction period and in reactions about ten times the size reported, reaction times had to be increased significantly. It is noteworthy that even when the anhydrous grade of formic acid was employed in the addition reactions, the acid recovered was about 90% presumably because of the accumulation of water during the decomposition of formic acid to carbon monoxide and water.[3,4] The rate of decomposition of formic acid at its boiling point in the presence or absence of strong acids is high when its water content is 3% or less, but its decomposition is negligible at an initial water content of about 10% during the relatively short reaction periods required.

The addition of acetic acid to the double bond of oleic acid in the absence of catalysts is negligible at its boiling point. With perchloric acid as catalyst, maximum addition to the double bond is only about 40% in a reaction time of 15 min. or one hour, whereas with formic acid 80% addition is usually obtained. Maximum yields of once crystallized monohydroxystearic acids from the hydrolyzed acetic acid–oleic acid product are only 30%. When sulfuric acid is employed as the catalyst instead of perchloric acid, only poor yields of monohydroxystearic acids can be obtained after hydrolysis even though the crude reaction products have low iodine numbers. Undesirable side re-

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[1] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Service, United States Department of Agriculture.

[2] Presented at the Fall Meeting of the American Chemical Society, Atlantic City, New Jersey, September 16, 1952.

[3] H. N. Barham and L. W. Clark, THIS JOURNAL, **73**, 4638 (1951).

[4] E. R. Schierz, *ibid.*, **45**, 447 (1923).