On the Thermal Dissociation of Organic Compounds. VI. The Effect of the Substituent and That of the Solvent on the Thermal Dissociation of Ureas

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Introduction

It is known that, on heating, ureas dissociate thermally into isocyanates and amines.

$$RHN-CO-NHR \rightleftarrows R-N=C=O+H_2N-R$$

The kinetics of the thermal dissociation of urea and some substituted ureas in fatty acid solvents have been studied[2-4] and, in the case of urea in *n*-butyric acid, for example, the mechanism shown by Equations (1)-(4) was suggested.

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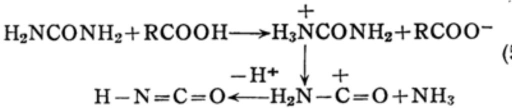
[2] T. Hoshino, T. Mukaiyama and H. Hoshino, *J. Am. Chem. Soc.*, **74**, 3097 (1952).

[3] T. Hoshino, T. Mukaiyama and H. Hoshino, This Bulletin, **25**, 392 (1952).

[4] T. Mukaiyama and T. Matsunaga, *J. Am. Chem. Soc.*, **75**, 6209 (1953).

$$H_2N-CO-NH_2 \rightleftarrows H-N=C=O+NH_3 \quad (1)$$
$$H-N=C=O+C_3H_7COOH \rightleftarrows C_3H_7CO-O-CONH_2 \quad (2)$$
$$C_3H_7CO-O-CONH_2 \longrightarrow C_3H_7CO-NH_2+CO_2 \quad (3)$$
$$NH_3+C_3H_7COOH \rightleftarrows C_3H_7COONH_4 \quad (4)$$

The dissociation of urea in fatty acid was considered as a general acid catalyzed reaction, which is shown by the following process.



$$\begin{array}{c} H_2NCONH_2+RCOOH \longrightarrow H_3\overset{+}{N}CONH_2+RCOO^- \\ \downarrow \\ H-N=C=O \xleftarrow{-H^+} H_2N-\overset{+}{C}=O+NH_3 \end{array} \quad (5)$$

As shown in the previous reports, the rates of dissociation of ureas are deeply dependent on the nature of solvents and the kind of substituents. In the present work, the dissociation of eight substituted ureas in five fatty acids were studied and the relation between the nature of acids and the kind of substituents were discussed.

The reaction can be followed by measuring the rate of evolution of carbon dioxide (Eq. 3), provided it is evolved as soon as formed. Since the reaction temperature was near 155° it is reasonable to believe that this is true, and also that the reverse reaction is negligible under the conditions of the experiments. If reaction (1) is the rate-determining step, then the rate of dissociation is measurable.

On plotting the logarithm of volume of carbon dioxide, ΔY, 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,[5] as shown in Fig. 1.

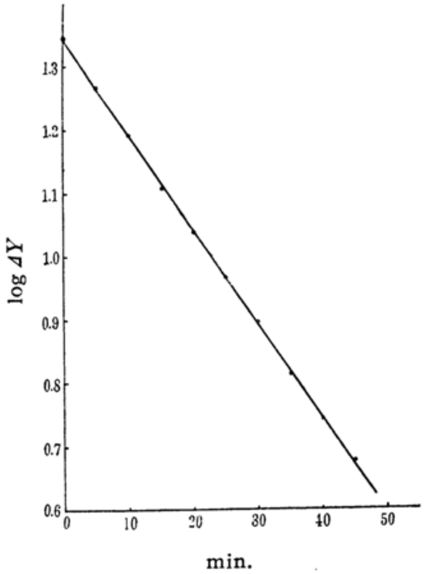


Fig. 1. The plot of t against log ΔY. 1, 1, 3-Triethylurea in n-capric acid at 155.1°C.

Experimental

The apparatus employed was the same as that described in previous reports.[2,3] In this experiment, the reaction vessel was maintained at desired, constant temperature by immersion into the thermostat containing rape-seed oil. In order to prevent the heat loss at this high temperature, the thermostat was surrounded by asbestos and placed in a cabinet thickly filled with glasswool. The temperature control of the reaction thermostat was accurate to ±0.03 within the temperature range 140—160° using a tetraline-mercury regulator.

Preparation of Materials.—*1, 1-Dimethylurea*: the commercial product, m.p. 181°, was used. *1, 3-Diethylurea*: from ethyl isocianate[6] and water, m.p. 110°, recrystallized from petroleum ether. *1, 1, 3-Triethylurea*[7]: from ethyl isocyanate and diethylamine, m.p. 65°, recrystallized from petroleum ether. *1, 3-Diisopropylurea*: from isopropyl isocyanate[8] and water, m.p. 190°, recrystallized from 70% aqueous ethanol. *1, 3-Dihexylurea*: from hexyl isocyanate and water, m.p. 75°, recrystallized from petroleum ether. Found N, 12.79%. Calcd for $C_{13}H_{28}N_2O$: N, 12.28%. *Hexyl isocyanate* was prepared from heptoic acid hydrazide *via* heptoic acidazide by heating in anhydrous benzene, b.p. 71—72°/31 mm. *1, 3-Dibenzylurea*: from benzyl isocyanate[9] and water, m.p. 167°, recrystallized from ethanol. *1, 1-Diethyl-3-isopropylurea*: from isopropyl isocyanate and diethylamine, m.p. 66°, recrystallized from petroleum ether. *1, 3-Di-t-butylurea*: from urea and *t*-butyl alcohol by the method described in Organic Syntheses,[10] m.p. 243° (in sealed tube), recrystallized from 80% aqueous ethanol.

Solvent: *n*-Butyric and *n*-caproic acids were distilled after boiling with phosphorous pentoxide and re-distilled employing a fractionating column, b.p. 159–160° and 104–106°/16.5–17mm, respectively. *n*-Capric acid was twice distilled in vacuo b.p. 121–123°/3.2–3.5 mm. Phenylacetic acid was recrystallized from water and then distilled in vacuo b.p. 117°/4.5 mm. Benzoic acid was used without further purification, m.p. 122°.

The rate constants for the thermal dissociation of ureas were determined under the following conditions: 1, 1, 3-triethylurea (1 mole) in *n*-capric acid (50 moles), given as an example of a typical run: Fig. 1. Ureas (1 mol.) in a carboxylic acids (50 mol.). The ureas were 1, 1-dimethyl, 1, 3-diethyl, 1, 1, 3-triethyl, 1, 3-diisopropyl, 1, 3-dihexyl, 1, 3-dibenzyl, 1, 1-diethyl-3-isopropyl and 1, 3-di-*t*-butyl. The acids were *n*-butyric, *n*-caproic, *n*-capric, phenylacetic and benzoic.

The results are summarized in Table I. The rates were first order with respect to ureas.

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[5] E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).
[6] T. Curtius and H. Hille, *J. prakt. Chem.*, **64** 401 (1901).
[7] Wurtz, Beilstein, IV, 120.
[8] O. Hambsch, *J. prakt. Chem.*, **125**, 182 (1930).
[9] T. Curtius and E. Boetzlen, *J. prakt. Chem.*, **64**, 316 (1901).
[10] "Organic Syntheses," **29**, 18.

TABLE I

THE RATE CONSTANTS OF THE THERMAL DISSOCIATION OF UREAS IN FATTY ACIDS

$k \times 10^2$ (min.$^{-1}$) (at t°C)

acids ureas	*n*-butyric acid	*n*-caproic acid	*n*-capric acid	phenylacetic acid	benzoic acid
1, 1-dimethylurea	1.11 (139.5°)	2.97 (155.2°)	1.2 (155.1°)	3.02 (155.0°)	0.545 (155.0°)
1, 3-diethylurea		2.65 (155.2°)	2.66 (155.1°)	2.86 (155.0°)	1.07 (155.0°)
1, 1, 3-triethylurea	4.09 (139.5°)	3.42 (155.0°)	3.39 (155.1°)	10.9 (155.0°)	2.09 (155.0°)
1, 3-diisopropylurea	1.79 (139.6°)	2.61 (155.0°)	3.08 (155.0°)	4.86 (155.0°)	0.967 (154.95°)
1, 3-dihexylurea	1.24 (139.6°)	3.65 (155.0°)	3.26 (155.0°)	2.10 (154.9°)	0.659 (155.0°)
1, 3-dibenzylurea	1.27 (139.6°)	2.68 (155.0°)	2.70 (155.0°)	3.85 (154.9°)	0.418 (155.0°)
1, 1-diethyl-3-isopropylurea	3.15 (139.45°)	6.2 (155.0°)	3.19 (155.0°)	very fast (154.9°)	1.60 (155.1°)
1, 3-di-*t*-butylurea	3.87 (139.4°)	3.93 (155.0°)	6.8 (155.0°)	fast (155.0°)	0.900 (154.95°)

Discussion

According to the results of experiments summarized in Table I, the effects of solvents on the rate of dissociation of ureas are in the following order:

phenylacetic acid, *n*-butyric acid$>$*n*-caproic acid, *n*-capric acid$>$benzoic acid.

The *pKa* values for these five acids are shown in Table II.

TABLE II

THE *pKa* VALUES FOR FATTY ACIDS[11]

acid	*pKa*
n-butyric acid	4.82
n-caproic acid	4.85
n-capric acid	4.90
phenylacetic acid	4.31
benzoic acid	4.17

As known from their *pKa* values, if the dissociation of urea proceeds according to a general acid catalyzed reaction (5), the effects of solvents on the rate of dissociation should fall in the order,

Benzoic acid$>$phenylacetic acid$>$*n*-butyric acid$>$*n*-caproic acid$>$*n*-capric acid.

Benzoic acid, as shown in the above order, should accelerate the rates of dissociation of ureas more than the other four acids. However, the rates of dissociation of ureas in benzoic acid are very slow in comparison with that in other acids and this shows that the previously proposed mechanism (5) is an unsatisfactory one to explain the dissociation reaction.

As to the effects of substituents, it is shown by the present experiment that the rate of dissociation increases in the series,

urea$<$1, 1-dimethylurea$\leq$1, 3-dibenzylurea $<$1, 3-dihexylurea$\leq$1, 3-diethylurea, 1, 3-diisopropylurea$<$1, 3-di-*t*-butylurea$\leqslant$1, 1, 3-triethylurea, 1, 1-diethyl-3-isopropylurea.

In the process of dissociation of urea, the one nitrogen atom of urea accepts a proton to form an amine and the other nitrogen atom donates a proton to form an isocyanate. Thus, there are two factors which can be considered to dominate the dissociation of ureas.

(a) Ability of one nitrogen atom in urea as a proton-acceptor, namely basicity.

(b) Ability of one nitrogen atom in urea as a proton-donor, namely acidity.

When one compares the relative strength of basities of ureas, those of corresponding amines may be used. A urea nitrogen atom having two substituents is bonded to three carbon atoms and therefore might be expected to behave as a tertiary one. However, by comparing the rate of dissociation of 1, 1, 3-triethylurea with that of 1, 3-diethylurea, the former urea dissociates more easily than the latter. The one nitrogen atom of these two ureas has the same substituent group and therefore the difference in reactivity is due to the difference in the ability of the other nitrogen atom as a protonacceptor. The fact shows that 1, 1, 3-triethylurea has a stronger tendency to accept a proton than 1, 3-diethylurea, namely, the former urea might be more basic. This conclusion does not agree with the consideration that the relative basity of a urea nitrogen atom having two substituents corresponds to that of a tertiary amine. In considering the structure of 1, 1, 3-triethylurea, one of three carbon atoms bonded to a urea nitrogen is that of carbonyl and, be-

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[11] L. F. Fieser and M. Fieser "Text-book of Organic Chemistry" p. 157 (1952).

cause of the planar configuration of carbonyl group, the B-strain[12] considered to exist in an ordinary tertiary amine is reduced in the urea. Accordingly, it may be reasonable to assume that the relative strength of a urea nitrogen atom having two substituents corresponds to the basity of secondary amine and that of a urea nitrogen having one substituent corresponds to that of primary amine.

The pKb[13] values for the corresponding amines are shown in Table III.

TABLE III

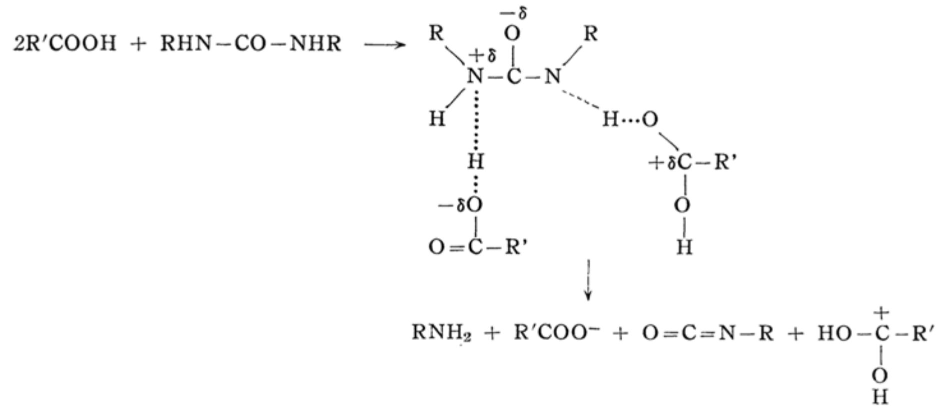
THE pKb VALUES FOR AMINES[13]

amine	pKb
dimethylamine	3.22
trimethylamine	4.13
ethylamine	3.28
diethylamine	2.90
triethylamine	3.36
isopropylamine	3.28
t-butylamine	3.47
benzylamine	4.62
ammonia	4.75

The effect of factor (a) on the dissociation reaction is shown in the results that 1, 1-diethyl substituted ureas dissociate faster than other 1-monosubstituted ureas and that urea itself dissociates slower than other substituted ureas. However, the results that the rate of dissociation of 1, 3-dibenzylurea is nearly equal to that of 1, 3-dihexylurea and that 1, 3-di-*t*-butylurea dissociates more readily than 1, 3-diethylurea can not be explained by the factor (a) alone. And factor (b), i.e. the ability of one nitrogen atom in urea as a proton-donor comes into consideration.

Just as the protonation of urea molecule by the solvent acid is an important factor on the dissociation, the deprotonation of urea molecule by the solvent acid is also an important one. In 1, 3-dibenzylurea, one nitrogen atom is a weak base which facilitates the deproponation and hence the reaction.

The effects of solvents and those of substituents mentioned above are explained by considering the following mechanism.



(I)

Under the condition of the experiments, the molar ratio of fatty acid to urea is 50 : 1, therefore the transition state (I) which contains two fatty acid molecules and one urea molecule might be considered as a reasonable one. One acid in the state (I) acts as an acid to donate a proton and the other acts as a base to accept a proton.

Contrary to the expectation that the stronger the acidity of solvent acid the faster the dissociation, the rates of dissociation of ureas in benzoic acid are slower than in the other acids. This slow rate may come from the fact that the weak basicity of benzoic acid makes the deprotonation of urea in state (I) more difficult. That the rates of dissociation of ureas in *n*-butyric acid are faster than those in *n*-caproic and *n*-capric acids will be explained by considering the difficulty of forming a state (I) in the latter acids because of their spatial requirement. As described in the previous report,[2,4] the rates of dissociation of ureas in acetic, propionic and *n*-butyric acids fall in the following order:

acetic acid>propionic acid>*n*-butyric acid.

This order agrees with the above consideration that the smaller the molecular size the greater the frequency to attack urea molecule.

The effects of substituents controlled by two factors (a) and (b) on the thermal dissociation of ureas can also be explained by considering the state (I), in which two acids

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[12] In general, secondary amine is a stronger base than a tertiary one. This phenomenon does not agree with the tendency anticipated from the palar effect, and this was explained by the so-called B-strain proposed by H. C. Brown. L. N. Ferguson, "Electron Structures of Organic Molecules" p. 114, (1952).

[13] Calculated from the dissociation constants. I. Heilbron et al., "Dictionary of Organic Compounds," Eyre & Spottiswoode Pub. Ltd. London (1946).

act as a proton-acceptor and as a proton-donor to one urea molecule at the same time.

It can be concluded that the thermal dissociation of ureas in fatty acids is more favorable when solvent acids and substituents tend to donate or accept a proton.

Summary

The rate constants of the thermal dissociation of 1, 1-dimethyl, 1, 3-diethyl, 1, 3-diisopropyl, 1, 1, 3-triethyl, 1, 3-dihexyl, 1, 3-dibenzyl, 1, 1-diethyl-3-isopropyl and 1, 3-di-*t*-butyl ureas in *n*-butyric, *n*-caproic, *n*-capric, phenylacetic and benzoic acids were determined. The effects of substituents and those of solvents on the reaction rate were discussed. The transition state of the dissociation containing two fatty acids and one urea molecule was considered and the experimental results were reasonably explained by the proposed mechanism.

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