On the Thermal Dissociation of Organic Compounds. VIII. The Effects of the Substituents on the Thermal Dissociation of Tri-substituted Ureas

By Teruaki MUKAIYAMA[1], Shoichiro OZAKI and Yasuhiro KOBAYASHI[1]

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Introduction

The kinetics of the thermal dissociation of urea and di-substituted ureas in fatty acids[2-5] and alcohols[6] have been studied and, in the present work, the kinetics of the thermal dissociation of tri-substituted ureas in fatty acids and alcohols were studied. The effects of the substituents and those of the solvents on the dissociation of these ureas compared with those of 1, 3-disubstituted ureas are discussed.

The reaction in fatty acids can be followed by measuring the rate of evolution of carbon dioxide (Eq. 3), as the reaction (1) is a rate-determining step. In the case of 1, 1-dicyclohexyl-3-*n*-propylurea in capric acid, for example, the mechanism shown by Eqs. (1)-(3) is considered.

$$(C_6H_{11})_2N-CO-NHC_3H_7 \rightleftarrows C_3H_7N=C=O+(C_6H_{11})NH \qquad (1)$$

$$C_3H_7N=C=O+C_9H_{19}COOH \rightleftarrows C_9H_{19}COOCO\cdot NH\cdot C_3H_7 \qquad (2)$$

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[1] Department of Physics and Chemistry, Gakushuin University, Mejiro, Tokyo.

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

[3] Idem, This Bulletin, **25**, 392 (1952).

[4] T. Mukaiyama and T. Matsunaga, *J. Am. Chem. Soc.*, **75**, 6209 (1954).

[5] T. Mukaiyama, S. Ozaki and T. Hoshino, This Bulletin, **27**, 578 (1954).

$$C_9H_{19}COOCO\cdot NH\cdot C_3H_7 \longrightarrow C_9H_{19}CONH\cdot C_3H_7+CO_2 \qquad (3)$$

In alcohols the dissociated isocyanate reacts with the solvent to form urethane.

$$C_3H_7N=C=O+C_6H_5CH_2OH \rightleftarrows C_3H_7NHCOOCH_2C_6H_5 \qquad (4)$$

The reaction in alcohols can be followed by measuring the amount of amine formed according to Eq. (1).

Tetra-substituted urea which has no mobile hydrogen atom did not dissociate under the same condition as that of ureas having more than one mobile hydrogen atom.

Experimental

Procedure—The procedure for measuring the rates of dissociation of ureas in fatty acids[2,3,5] and in alcohols[6] have been described previously. On plotting the logarithm of volume of carbon dioxide, ΔY, evolved at regular intervals of time, a straight line was obtained. This indicates a first order reaction rate. The rate constant is given by the gradient of such a plot, as shown in Fig. 1.

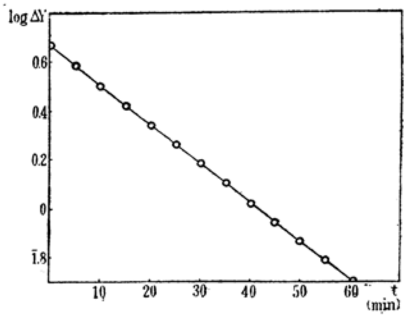

Fig. 1. Thermal dissociation of 1, 1-diisopropyl-3-phenylurea in capric acid at 139.5°C.; the plot of log ΔY against time.

Preparation of materials.—*1, 1-Dicyclohexyl-3-phenylurea*: from phenyl isocyanate and dicyclohexylamine, m. p. 174–5°C, recrystallized from ligroin. Found: N, 9.22. Calcd. for $C_{19}H_{28}ON_2$: N, 9.32 %.

1, 1-Dicyclohexyl-3-n-propylurea: from n-propyl isocyanate and dicyclohexylamine, m. p. 146°C, recrystallized from ethanol. Found: N, 10.64. Calcd. for $C_{16}H_{30}ON_2$: N, 11.84 %. This is a very hygroscopic substance.

1, 1-Diisopropyl-3-n-propylurea: from n-propyl isocyanate and diisopropylamine, m. p. 54–6°C and b. p. 129°/9mm. Found: N, 14.91. Calcd. for $C_{10}H_{22}ON_2$: N, 15.02 %.

1, 1-Diisopropyl-3-phenylurea: from phenyl isocyanate and diisopropylamine, m. p. 118°C, recrystallized from ligroin.

1, 1-Dibenzyl-3-n-propylurea: from n-propyl isocyanate and dibenzylamine, m. p. 88°C, recrystallized from ligroin.

1, 1-Dibenzyl-3-phenylurea: from phenyl isocyanate and dibenzylamine, m. p. 124°C, recrystallized from ligroin.

1, 1, 3, 3-Tetra-n-butylurea (I): Phosgene was passed through a solution of 12 g. (1/10 mole) of di-n-butylamine and 26 g. (1/5 mole) of potassium carbonate for three hours. Then the precipitated potassium chloride was filtered and the solution was extracted with benzene. After drying over anhydrous sodium sulfate, benzene was evaporated and 4 g. of colorless liquid (I) was obtained by distillation boiling at 177–8°C/19 mm. Found: C, 71.30; H, 12.35. Calcd. for $C_{17}H_{36}ON_2$: C, 71.77; H, 12.76 %.

Solvent.—Solvents were purified by the same method as described[5,6] previously. The boiling points for fatty acids and alcohols are as follows: n-Capric acid b. p. 121-3°/3.2–3.5 mm.; n-caproic acid b. p. 104–6°/16.5–17 mm.; phenylacetic acid b. p. 117°/4.5 mm.; benzoic acid m. p. 122°; glycerol 185°/23 mm.; benzyl alcohol b. p. 114°/38 mm.; ethylene glycol b. p. 120°/20 mm.

The ratio of ureas to solvents were 1 mole: 100 moles. The rate constants of the thermal dissociation of these ureas in fatty acids and alcohols are summarized in Table I. The rates were first order with respect to ureas.

Discussion

As to the effects of the subtituents on the dissociation, it is shown by the present experiment that the rates of dissociation of six ureas decrease in the order,

1, 1-dicyclohexyl-3-phenylurea >
1, 1-dicyclohexyl-3-n-propylurea,
1, 1-diisopropyl-3-phenylurea >
1, 1-diisopropyl-3-n-propylurea ≫
1, 1-dibenzyl-3-phenylurea >
1, 1-dibenzyl-3-n-propylurea

As shown in the above order, as to the 1, 1-substituents, the rates of dissociation decrease in the series,

1, 1-dicyclohexyl > 1, 1-diisopropyl >
1, 1-dibenzyl

and as to the 3-substituents, the rates decrease in the series,

3-phenyl > 3-n-propyl

These results can be explained by the proposed mechanism[5], in which ureas dissociate by the double transfer of their proton. Accordingly, the basicity of one nitrogen atom and the acidity of the other nitrogen atom in ureas are dominant factors for the dissociation. As described in the previous report[5], the relative basicity of the nitrogen atom in ureas is represented by the basicity of the corresponding amines. Benzylamine is a weaker base than cyclohexyl and isopropyl amines and, in these six ureas studied, 1, 1-dibenzylureas are less likely to take up

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[6] T. Mukaiyama, ibid, 28, 253 (1955).

proton from solvent than the other four ureas.

Also, the steric strain considered in four ureas other than 1, 1-dibenzylureas will be favorable for the dissociation which forms less strained component compounds.

These two effects will explain the slower rates in 1, 1-dibenzyl ureas.

Tri-substituted ureas, except in the case of 1, 1-dibenzylureas, dissociate much faster than 1, 3-di-substituted ureas as shown in Tables I and II. In tri-substituted ureas, the basicity of one nitrogen atom corresponds to a secondary amine and the ureas have a stronger tendency to take up a proton from a solvent molecule than 1, 3-di-substituted ureas having a nitrogen atom which corresponds to a primary amine.

As mentioned in the previous reports, the ability of ureas to donate a proton to solvent is also an important factor. In these six ureas, three ureas have a phenyl group on the 3-nitrogen atom and the rest have an *n*-propyl group on the 3-nitrogen atom. The acidity of the former ureas are stronger than the latter because of the +E effect of the phenyl group. Therefore, 3-phenyl substituted ureas are easier to donate a proton to solvent than 3-*n*-propyl ureas. The slower rate in 3-*n*-propylureas than in 3-phenylureas are shown in the experiment.

Another interesting fact is that, tri-substituted ureas dissociate faster in alcohols than in fatty acids in contrast with 1,3-di-substituted ureas. In tri-substituted ureas having more basic nitrogen atoms than in 1, 3-di-substituted ureas, deprotonation by solvent may be a more dominant factor than protonation in the process of dissociation. This would be a reason for the faster rates

TABLE I

THE RATE CONSTANTS OF THE THERMAL DISSOCIATION OF TRISUBSTITUTED UREAS IN FATTY ACIDS AND ALCOHOLS

$k\times10^3$ (min.$^{-1}$) (at t°C)

Solvents / Ureas	Fatty acids				Alcohols		
	n-Capric	*n*-Caproic	Phenyl-acetic	Benzoic	Ethylene glycol	Benzyl alcohol	Glycerol
1, 1-Dicyclohexyl-3-phenylurea	106±4.0 (139.5)	106 (139.5)	126 (139.5)	28.6 (139.5)	very fast (100)	23.7 (100)	sparingly soluble (100)
1, 1-Dicyclohexyl-3-*n*-propylurea	96.7±0.3	100	115	29.4	fast	18.8	sparingly soluble
1, 1-Diisopropyl-3-phenylurea	36.8	86.3	81	29.3	very fast	19.8	sparingly soluble
1, 1-Diisopropyl-3-*n*-propylurea	93.5±2.7	37.6	34.5	25.0	20.3	17.8	sparingly soluble
1, 1-Dibenzyl-3-phenylurea	4.58±0.08	4.33	24.5	8.0	21.6 (150)	10.4 (150)	18.4 (150)
1, 1-Dibenzyl-3-*n*-propylurea	3.06±0.46	9.9	23.3	7.9	29.9 (150)	0.54 (150)	17.0 (150)

TABLE II

THE RATE CONSTANTS OF THE THERMAL DISSOCIATION OF 1, 3-DI-SUBSTITUTED UREAS IN FATTY ACIDS5) AND ALCOHOLS6)

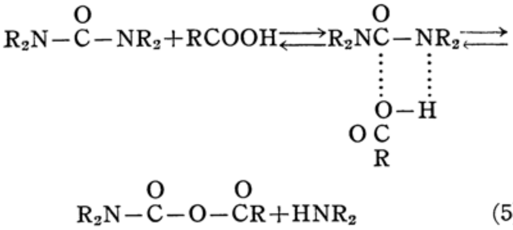
$k\times10^3$ (min.$^{-1}$) (at t°C)

Solvents / Ureas	Fatty acids				Alcohols		
	n-Capric	*n*-Caproic	Phenyl acetic	Benzoic	Ethylene glycol	Benzyl alcohol	Glycerol
1, 3-Diethylurea	26.5 (155)	26.5 (155)	28.6 (155)	10.7 (155)			
1, 3-Di-*n*-propylurea					11.1 (174.8)	21.0 (175.1)	23.0 (175.1)
1, 3-Diisopropylurea	30.8	26.1	48.6	9.67	35.2 (175.6)	30.4 (175.2)	31.6 (175.2)
1, 3-Di-*n*-hexylurea	32.6	36.5	21.0	6.59			
1, 3-Dicyclohexylurea					26.7 (175.9)	19.8 (175.2)	sparingly soluble

for dissociation of tri-substituted ureas in alcohols than in acids which are very weak bases. However, less basic tri-substituted ureas, as in 1, 1-dibenzylureas, dissociate faster in fatty acids than in alcohols as in 1, 3-di-substituted ureas.

Tetra-substituted ureas, such as 1, 1, 3, 3-tetra-*n*-butylurea, which do not have a mobile hydrogen atom can not be formed by the addition reaction. These ureas do not react under the same condition as that of urea and mono-, di- and tri-substituted ureas which are formed by the addition of two component compounds.

By the result, the bimolecular mechanism of the direct attack of solvent on ureas as shown in Eq. (5) is denied.



$$R_2N-\overset{O}{C}-NR_2+RCOOH\rightleftharpoons \underset{\substack{\vdots\qquad\vdots\\ O-H\\ O\,C\\ R}}{R_2N\overset{O}{C}-NR_2}\rightleftharpoons R_2N-\overset{O}{C}-O-\overset{O}{C}R+HNR_2 \qquad (5)$$

And it can be emphasized that the dissociation of ureas proceeds by the proposed mechanism in which the double transfer of their protons is involved.

Summary

The rate constants of the thermal dissociation of tri-substituted ureas in fatty acids and alcohols were determined. It was shown that tri-substituted ureas dissociate faster than 1, 3-di-substituted ureas. In tri-substituted ureas, the rates in alcohols are faster than in fatty acids in contrast with 1, 3-di-substituted ureas.

Tetra-substituted ureas which are not formed by the addition reaction do not react under the same condition with tri-substituted ureas.

The bimolecular mechanism for the dissociation of ureas involving the direct attack of one solvent molecule on urea was denied.

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Laboratory of Organic Chemistry,
Tokyo Institute of Technology,
Tokyo