On the Thermal Dissociation of Organic Compounds. IX. The Urea Linkage (1, 3-Di-substituted Ureas in Alcohols)

By Teruaki MUKAIYAMA and Yasuhiro FUJITA

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Introduction

The kinetics of the thermal dissociation of substituted ureas in alcohols have been studied[1] and in the case of 1, 3-dibenzylurea in benzyl alcohol, for example, the mechanism shown by Eqs. (1) and (2) was suggested.

$$C_6H_5CH_2HNCONHCH_2C_6H_5 \rightleftarrows C_6H_5CH_2N{=}C{=}O + H_2NCH_2C_6H_5 \quad (1)$$

$$C_6H_5CH_2N{=}C{=}O + HOCH_2C_6H_5 \rightleftarrows C_6H_5CH_2HNCOOCH_2C_6H_5 \quad (2)$$

As described in the previous report, when urea is reacted in a large excess of alcohol, the equilibrium between urethane and isocyanate—alcohol in Eq. (2) is in favor of the right side of the reaction and urethane is obtained in good yields. Therefore, if the reaction (1) is the rate-determining step, one can measure the rate of dissociation of urea by determining the amount of amine formed according to Eq. (1).

In the present experiment, the rate constants of the thermal dissociation of seven 1, 3-di-substituted ureas in alcohols have been determined and the effects of the solvents and those of the substituents on the dissociation reaction are discussed.

Experimental

Materials.—*1,3-Di-n-propylurea* and *1,3-di-n-amylurea* were prepared from corresponding iscoyanate and water.

1,3-Di-n-heptylurea, *1,3-diisopropylurea*, *1,3-diisobutylurea* and *1,3-dicyclohexylurea* were prepared from corresponding amines and phosgene in aqueous potassium carbonate.

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[1] T. Mukaiyama, This Bulletin, 28, 253 (1955).

1,3-Di-t-butylurea was prepared from *t*-butyl alcohol and urea.

The melting point and the solvent used for recrystallization of these ureas are summarized in Table I.

TABLE I

Ureas	m.p. (°C)	Solvent
1,3-di-*n*-propyl-	105	ligroin
1,3-di-*n*-amyl-	84	ligroin
1,3-di-*n*-heptyl-	91	ligroin
1,3-diisopropyl-	192	ligroin
1,3-diisobutyl-	135	70% aqueous ethanol
1,3-dicyclohexyl-	227	70% aqueous ethanol
1,3-di-*t*-butyl-	248	80% aqueous ethanol

The following alcohols were used: benzyl alcohol, b.p. 114°C/38 mm.; ethylene glycol, b.p. 120°C/20 mm.; glycerol, b.p. 185°C/23 mm.:

Procedure and analysis.—The experimental procedure was essentially that used in the earlier investigation1). The amount of amine produced in any reaction system was determined by titration with 0.1N hydrochloric acid, back-titration being carried out with 0.1 N sodium hydroxide using methyl red as indicator.

The rate constants for the thermal dissociation of ureas at temperature near 175°C were determined under the following conditions:

(a) 1,3-Di-*n*-propylurea (1 mol.) in benzyl alcohol (100 mol.), given as an example of a typical run: Fig. 1. The rate constants were obtained by Guggenheim's method2).

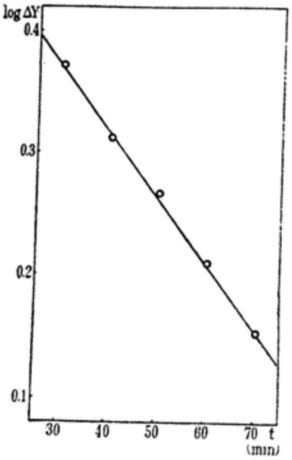

Fig. 1. Thermal dissociation of 1,3-di-*n*-propylurea in ethylene glycol at 174.8°C; the plot of log ΔY against time.

(b) Ureas (1 mol.) in alcohols (100 mol.)—The ureas were 1,3-di-*n*-propylurea, 1,3-di-*n*-amylurea 1,3-di-*n*-heptylurea, 1,3-diisopropylurea, 1,3-diisobutylurea, 1,3-dicyclohexylurea and 1,3-di-*t*-butylurea and the alcohols were benzyl alcohol, ethylene glycol and glycerol. The results are shown in Table II. The rates were first order with respect to ureas.

TABLE II

THE RATE CONSTANTS OF THE THERMAL DISSOCIATION OF 1,3-DISUBSTITUTED UREAS IN ALCOHOLS

$k \times 10^2$ (min.$^{-1}$) (t°C)

Alcohols / Ureas	Benzyl alcohol	Ethylene glycol	Glycerol
1,3-di-*n*-propyl-	2.10 (175.1)	1.11 (174.8)	2.30 (175.1)
1,3-di-*n*-amyl-		2.09 (174.5)	
1,3-di-*n*-heptyl-		1.79 (175.0)	
1,3-dicyclohexyl-	1.98 (175.2)	2.67 (175.9)	sparingly soluble
1,3-diisopropyl-	3.04 (175.2)	3.52 (175.6)	3.16 (175.2)
1,3-diisobutyl-	1.45 (175.2)	1.70 (175.0)	1.50 (175.2)
1,3-di-*t*-butyl-	sparingly soluble	very fast	sparingly soluble

Discussion

The amounts of disscociation of the seven 1,3-di-substituted ureas in these three alcohols increase in the following order,

benzyl alcohol<ethylene glycol<glycerol

However, the rate constants, as measured by the amount of amine produced, of dissociation in these three alcohols are nearly equal. As a typical run, the percentage of dissociated urea in the thermal dissociation of 1,3-diisobutylurea (1 mole) in benzyl alcohol, ethylene glycol and glycerol (100 moles) are shown against time listed in Table III.

TABLE III

THE PERCENTAGE OF DISSOCIATED 1,3-DIISOBUTYLUREA (1 mol.) IN ALCOHOLS (100 mol.) VS. TIME

Solvent	Temperature (°C)	Time (min.)			Rate constant
		30	60	90	
Benzyl alcohol	175.2	27	39	45	1.45
Ethylene glycol	175.0	35	53	67	1.70
Glycerol	175.2	52	75	89	1.50

A similar result was also found in the case of 1,3-dibenzylurea in these three alcohols1).

These facts suggest that the velocities of dissociation of urea in alcohols are dependent on the concentration of the hydroxylic group in the solvent alcohols. And it can be reasonably explained by assuming an intermediate complex formed by the interaction between urea and alcoholic hydroxyl groups. The mechanism of dissociation of urea in alcohols is considered1) as follows,

$$\text{urea} + \text{alcohols} \rightleftarrows (\text{urea—alcohols}) \qquad (3)$$

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

$$\text{(urea—alcohols)} \overset{k_1}{\rightleftharpoons} \text{isocyanate} + \text{amine} + \text{alcohols} \qquad (4)$$

$$\text{isocyanate} + \text{alcohol} \rightleftharpoons \text{urethane} \qquad (5)$$

$$\text{urethane} + \text{alcohols} \rightleftharpoons \text{(urethane—alcohols)} \qquad (6)$$

The rate constants of dissociation in these three alcohols are nearly equal; however, except in the case of 1,3-di-*n*-propylurea in ethylene glycol, the rates of dissociation of six 1,3-di-substituted ureas listed in Table II increase in the following order,

benzyl alcohol < glycerol < ethylene glycol

The tendency agrees with that of 1,3-dibenzylurea in alcohols described in the previous report1) and it may be concluded by the same consideration that, in the process of dissociation of 1,3-disubstituted ureas in alcohols, the solvent acts more effectively as a base to accept a proton from a urea molecule rather than it acts as an acid.

On the other hand, in a strong acid, as in fatty acids, the rates of dissociation of ureas generally increase as the acidity of the solvent acids increases3). In a strongly acidic medium, the process of protonation of urea by solvent plays an important role for the dissociation.

As shown in Table IV, the rates of dissociation of 1,3-disubstituted ureas in fatty acids4) are faster than those in alcohols and it can be concluded that, in these two kinds of solvents, the acidity of the solvent, namely the ability to donate a proton to a urea molecule is an important factor for the dissociation.

TABLE IV

THE RATE CONSTANTS OF THE THERMAL DISSOCIATION OF 1,3-DI-SUBSTITUTED UREAS IN FATTY ACIDS

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

Acids	*n*-Butyric	*n*-Caproic	*n*-Capric	Phenyl acetic
1,3-Diisopropylurea	1.79 (139.6)	2.61 (155.0)	3.08 (155.0)	4.86 (155.0)
1,3-Di-*n*-hexylurea	1.24 (139.6)	3.65 (155.0)	3.26 (155.0)	2.10 (154.9)
1,3-Di-*t*-butylurea	3.87 (139.4)	3.93 (155.0)	6.8 (155.0)	fast (155.0)

As to the effects of the substituents, the rates of dissociation of the seven 1,3-di-substituted ureas studied in this experiment increase in the series,

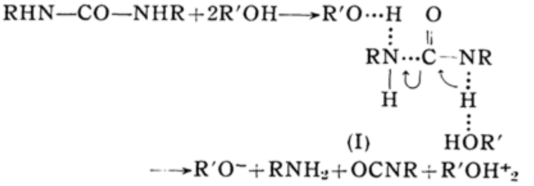
1,3-di-*n*-propylurea, 1,3-di-*n*-amylurea, 1,3-di-*n*-heptylurea, 1,3-diisobutylurea, 1,3-dicyclohexylurea < 1,3-diisopropylurea ⩽ 1,3-di-*t*-butylurea

1,3-Di-*t*-butylurea dissociates most readily and 1,3-diisopropylurea dissociates more easily than the other ureas with *n*-alkyl or cyclohexyl groups.

Generally, the rates of dissociation of 1,3-di-substituted ureas are not so markedly affected by the substituents, but ureas with tertiary and secondary alkyl groups in which the internal strain is considered to be important dissociate more readily. In these two ureas, especially in 1,3-di-*t*-butylurea, the strained structure due to the two bulky substiutents are considered. And, when the urea is heated in alcohol, by the interaction of the solvent alcohol which facilitates the proton transfer, it dissociates very readily into less strained isocyanate and amine.

In addition to the electronic effects, namely the abilities of the two nitrogen atoms in ureas to accept or to donate a proton, mentioned in the previous reports1,3), the structural effects are also important in determining the reactivity of ureas.

As mentioned above, the dissociation of ureas in alcohols are considered to proceed via the intermediate complex which is formed by one urea and two alcohol molecules.



$$\text{RHN—CO—NHR} + 2\text{R'OH} \longrightarrow \text{(I)} \longrightarrow \text{R'O}^- + \text{RNH}_2 + \text{OCNR} + \text{R'OH}_2^+$$

(I)

In the state(I), the one alcohol acts as a base to accept a proton and the other acts as an acid to donate a proton at the same time. By the shift of an electron pair, the state (I) dissociates to isocyanate and amine.

As shown in the above mechanism, the dissociation proceeds by the double transfer of the proton. Therefore, ureas act to solvent molecules as a base and acid at the state (I). And the effects of the substituents on the rates of the thermal dissociation of 1,3-di-substituted ureas having the same substituents in 1- and 3-nitrogen atoms are small.

Summary

The rate constants of the thermal dissociation of 1,3-di-*n*-propylurea, 1,3-di-*n*-amylurea, 1,3-di-*n*-heptylurea, 1,3-diisopropylurea, 1,3-diisobutylurea, 1,3-dicyclohexylurea and 1,3-di-*t*-butylurea in benzyl alcohol, ethylene glycol and glycerol were determined.

The effects of the substituents on the thermal dissociation of 1,3-di-substituted

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

4) T. Mukaiyama, S. Ozaki and T. Hoshino, This Bulletin, 27, 478 (1954).

ureas was discussed and the effects of the solvents on the reaction was also discussed in comparison with those in fatty acids.

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Department of Physics and Chemistry,
Gakushuin University, Tokyo