The properties of this compound proved to be identical with those of the hydrate VIII above. The product IX was obtained on dehydration of VIII on boiling in 50% benzene–ethyl acetate solution until water was no longer condensed. IX melted at 144° and had a neutralization equivalent of 93 ± 1 compared to the calculated value of 93. Sublimation in vacuum resulted in the loss of a mole of water and formation of VII—identified by no depression in a mixed melting point with an authentic specimen.

Anal. Calcd. for $C_8H_{10}O_5$: C, 51.6; H, 5.42. Found: C, 51.5; H, 5.44.

Preparation of Imides from Acids and Anhydrides.—One-half gram of acid or anhydride was mixed with 0.5 g. of ammonium carbonate and 1 ml. of glacial acetic acid in a small sublimator from which the condenser was removed. The mixture was heated gently and slowly brought to a boil under a good hood. When acetic acid vapors were no longer detected by moist litmus paper the condenser was replaced and the solid residue sublimed in a vacuum of approximately 10 mm. On resublimation in a high vacuum, pure products were obtained. By this procedure compounds VII, VIII and IX were converted to the reduced *exo*-imide IV, the latter being identified by mixed melting point with an authentic specimen. All attempts to convert compound V, the *trans*-dibasic acid, to an imide under the conditions described above resulted in no reaction.

Chromatographic Separation of *endo-exo* Mixtures.—The adsorbent used was activated alumina (Merck grade for chromatographic adsorption). A pressure of 55 mm. of dry (Linde Pre-purified Grade) nitrogen was used. The separation of 0.5 g. of a mixture of *endo*- and *exo*-3,6-endoxotetrahydrophthalimide (compounds I and II) in absolute ether solution is typified by the following table of results using absolute ethyl acetate–ether mixtures in 100-cc. portions for elution.

Elution fractions	Eluting solvent composition, % ethyl acetate	Melting point of product obtained on evaporation of the eluate fractions, °C.
A-C	60	131
D	70	120–139
E-F	70	162
G-I	80	162

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NEWARK, DELAWARE

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

On the Thermal Dissociation of Organic Compounds. (1) The Urea Linkage (Diphenylurea in Fatty Acids)

BY TOSHIO HOSHINO, TERUAKI MUKAIYAMA AND HIROKO HOSHINO

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On heating, a urea generally dissociates into an isocyanate and an amine. In the absence of kinetic data on this kind of reaction we have measured the rate constant and activation energy of the dissociation of *sym*-diphenylurea in fatty acids as solvents. When the dissociation is rate-determining, the reaction may be followed by noting the rate of carbon dioxide evolution that results from the reaction of phenyl isocyanate with the solvent acid. A method was devised to measure the quantity of accumulated intermediate (phenyl isocyanate) in cases where the rate of the dissociation and of the subsequent reaction were comparable. The rate of dissociation depends markedly on the nature of the solvent.

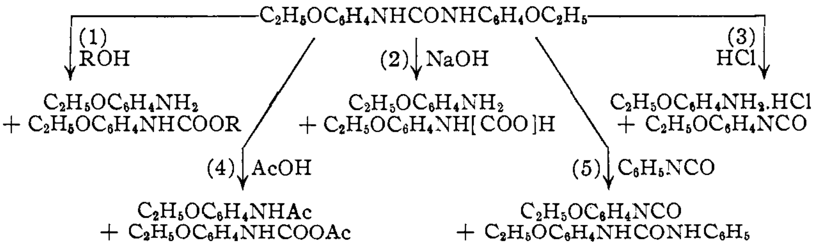
Introduction

On heating, disubstituted ureas generally dissociate to isocyanates and amines. As we shall show, this dissociation is a reversal of the formation reaction, and therefore we prefer the term "dissociation" to "decomposition," which has been used by earlier investigators.

Davis and Blanchard[1] obtained *sym*-phenylethyl urea and *sym*-diphenylurea on heating *sym*-diethylurea with aniline, a result attributed to the existence of four equilibria involving both of the possible isocyanates and both of the corresponding amines. Taüfel, Wagner and Dünwald[2] hence assumed that decomposition, in aqueous solution, of *p*-phenetylcarbamide leads mainly to phenetyl isocyanate and ammonia, and, in minor amount, to phenetidine and isocyanic acid; they also measured the velocity constant for the over-all decomposition.

$$C_2H_5OC_6H_4NHCONH_2 \begin{cases} \rightarrow C_2H_5OC_6H_4NCO + NH_3 \\ \rightarrow C_2H_5OC_6H_4NH_2 + HNCO \end{cases}$$

As shown by Iwakura and Nagakubo[3] of this Laboratory, *sym*-di-*p*-phenetylurea yields on heating phenetidine and phenetyl isocyanate. This conclusion is based on the following results: (1) In *n*-butanol phenetidine and *n*-butylphenetylurethan are produced. (2) Alkali in butanol, isoamyl alcohol, anisole, tetralin or decalin causes quantitative conversion to phenetidine. (3) Under the influence of dry hydrogen chloride in anisole, phenetyl isocyanate along with phenetidine hydrochloride is obtained. (4) In acetic acid or anhydride, phenacetine is formed. (5) With phenyl isocyanate in anisole, phenetyl isocyanate and *sym*-phenetylphenylurea are formed.



The thermal dissociation of diphenylurea in acetic acid involves the reactions

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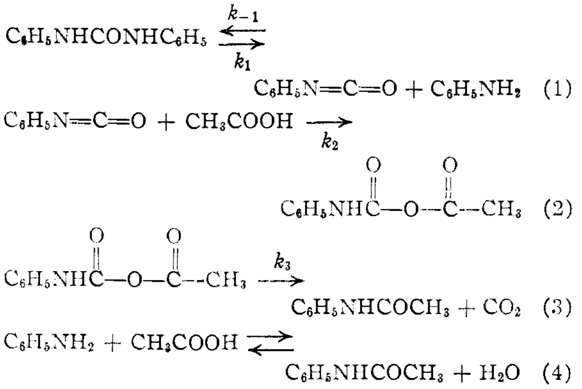
[1] T. L. Davis and K. C. Blanchard, THIS JOURNAL, **45**, 1816 (1923).

[2] K. Täufel, C. Wagner and H. Dünwald, *Z. Elektrochem.*, **34**, 115 (1928).

[3] Y. Iwakura and K. Nagakubo, *Bull. Tokyo Inst. Technol.*, **13**, 25 (1948).



$$C_6H_5NHCONHC_6H_5 \underset{k_1}{\overset{k_{-1}}{\rightleftarrows}} C_6H_5N{=}C{=}O + C_6H_5NH_2 \quad (1)$$

$$C_6H_5N{=}C{=}O + CH_3COOH \xrightarrow[k_2]{} C_6H_5NH\overset{O}{\overset{\|}{C}}{-}O{-}\overset{O}{\overset{\|}{C}}{-}CH_3 \quad (2)$$

$$C_6H_5NH\overset{O}{\overset{\|}{C}}{-}O{-}\overset{O}{\overset{\|}{C}}{-}CH_3 \xrightarrow{k_3} C_6H_5NHCOCH_3 + CO_2 \quad (3)$$

$$C_6H_5NH_2 + CH_3COOH \rightleftarrows C_6H_5NHCOCH_3 + H_2O \quad (4)$$

In treating the dissociation reaction, the phenylisocyanate dissociated during the reaction was caught, and in the separate experiment, the reaction of isocyanate (1 mole) with acetic acid (150 moles) satisfied the requirement for first order kinetics with respect to the isocyanate. Thus we assume that the reaction of isocyanate with acetic acid to form anilide and carbon dioxide (process (2) and (3)) is limited by the process (2). Under the conditions used, k_{-1} can be neglected.

Reaction (3) is considered to be irreversible under the experimental conditions used.[4] Reaction (4) is not of immediate interest to the present study; although reaction (1) is strongly influenced by the presence or absence of water, the amount of water produced *via* process (4) is too small to have any effect.

If reaction (1) is rate-determining, the rate of dissociation becomes measurable if one determines the amount of carbon dioxide evolved according to (3); if (1) and (2) proceed at comparable rates, an indirect determination is possible, which will be described below.

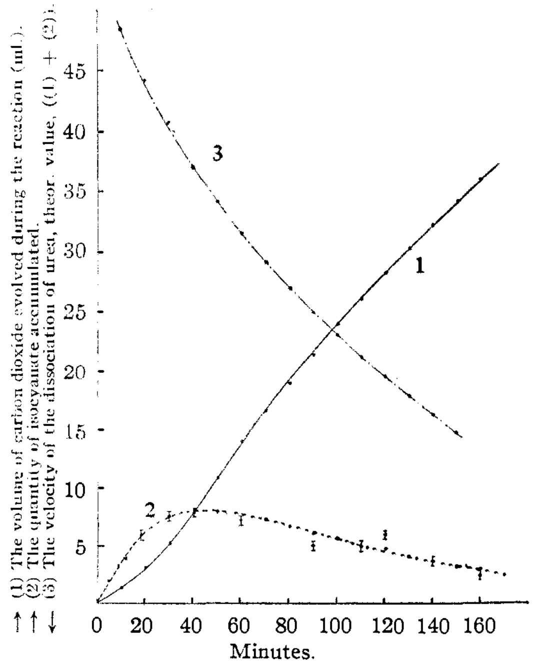


Fig. 1.—Thermal dissociation of *sym*-diphenylurea in acetic acid at 99.8°.

Experimental

A 35-ml. long-necked, round-bottomed flask was connected to a gas buret by means of a capillary tube. Halfway along the extent of the capillary tube, a 10-ml. bulb was inserted, which was maintained at 0° to condense reaction products less volatile than carbon dioxide. The reaction vessel was maintained at a desired, constant temperature by immersion into the vapors above a suitable boiling liquid contained in a three-necked flask equipped with condenser and thermometer; the reaction vessel was inserted in the center neck of the flask. Vapors of the following liquids were used as heating agents: water, toluene–acetic acid (72:28 by weight), toluene, isoamyl alcohol, di-*n*-butyl

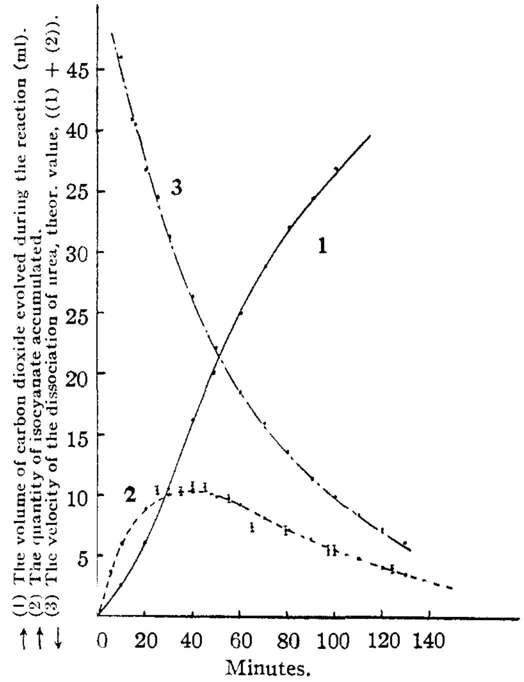


Fig. 2.—Thermal dissociation of *sym*-diphenylurea in acetic acid at 105.0°.

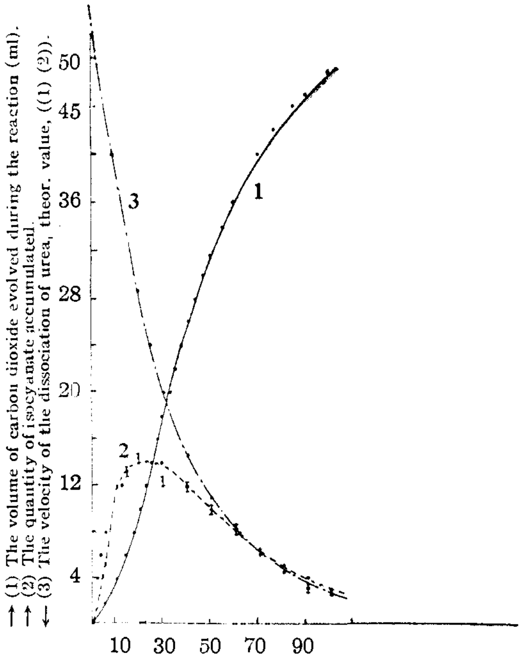


Fig. 3.—Thermal dissociation of *sym*-diphenylurea in acetic acid at 109.9°.

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(4) W. Diekmann and F. Breest, *Ber.*, **39**, 3052 (1906).

ether and anisole. The liquids were distilled prior to each run; during the course of an experiment (one to two hours) the temperature remained satisfactorily constant, as long as the atmospheric pressure did not fluctuate.

Diphenylurea was made from urea and aniline, and purified from acetic acid; m.p. 293.0°. Acetic acid was distilled after prolonged boiling with acetic anhydride. Propionic, butyric and caproic acids were purified by careful vacuum distillation.

The ratio of diphenylurea to acetic acid was 1 mole:150 moles; with the higher fatty acids a ratio of 1 mole:100 moles was employed. First-order kinetics with respect to diphenylurea was observed.

As the reaction products, in acetic acid with and without added water and in higher fatty acids, corresponding acid amides were obtained.

(a) **Diphenylurea in Anhydrous Acetic Acid.**—Under these conditions, the rate of process (1) is comparable to that of (2), and isocyanate accumulates. However, in the presence of 5% (by volume) of water, acetic acid reacts about fifty times faster with isocyanate, than does anhydrous acetic acid, and at the same time small amounts of water markedly retard process (1). Based on the two experimental facts above mentioned, we were able to measure the amount of isocyanate accumulated by including in the system a sealed ampoule containing 1.0 cc. of water (23 moles to 1 mole of urea); at the end of a specified period the ampoule was broken and the carbon dioxide which was evolved was collected (see Figs. 1, 2, 3).

By a separate experiment we determined that under the reaction conditions the reverse reaction in process (1) does not take place: when 1 mole of aniline was treated with 1 mole of urea the reverse reaction could not be detected, and consequently may be neglected in cases where very small amounts of aniline are present in the acetic acid medium. The kinetic results are represented graphically in Figs. 1, 2, 3 and 4. Rate constants and activation energies are listed in Table I.

TABLE I

Solvent	Reactants	T (absolute)	k, min.$^{-1}$	E_{act}, $k_{cal.}$
Acetic acid	Diphenylurea	372.8	0.0083	36.2
	+ acetic	378.0	.0164	
	acid	382.9	.0300	
Acetic acid	Diphenylurea	371.8	.0021	
+ more than	acetic acid			
5% water				

The rate constant of reaction of isocyanate dissociated during the reaction with acetic acid could be calculated. The method of calculation is described in the later section. Rate constants are listed in Table II.

TABLE II

Acetic acid	Isocyanate and	372.8	0.0410[a]
	acetic acid	378.0	.0442
		382.9	.0548
		372.5	.0363[b]
		380.0	.0644

[a] Calculated. [b] Measured.

These values approximately coincide with corresponding rate constants measured experimentally by using another synthetic sample of phenyl isocyanate with acetic acid. Those values were obtained by measuring the volume of carbon dioxide evolved during the reaction when isocyanate and acetic acid reacted. The experiment was carried out as follows: the phenyl isocyanate (1 mole) was sealed in an ampoule and placed in the reaction vessel which contained the anhydrous acetic acid (150 moles). Maintaining the acetic acid at required temperature, the ampoule was broken for the reaction. First-order kinetics with respect to phenyl isocyanate was observed. Rate constants are listed in Table II.

(b) **Diphenylurea Containing More than 5% of Water.**—When more than 5% (by volume) of water is present, isocyanate does not accumulate, and the rate of dissociation is followed by noting the continuous carbon dioxide evolution. The rate constant is recorded in Table I.

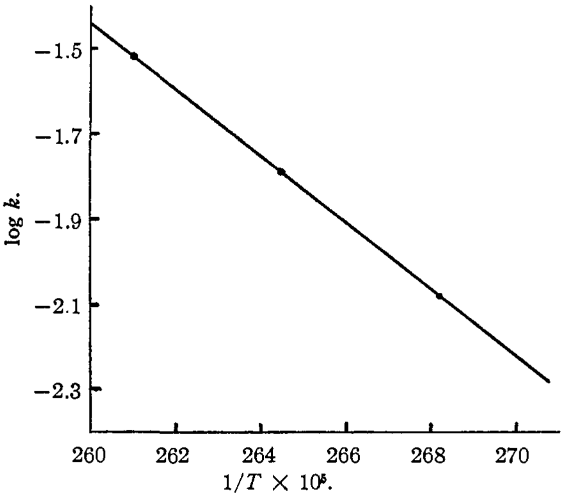


Fig. 4.—Thermal dissociation of *sym*-diphenylurea in acetic acid: the plot of log k against $1/T$.

(c) **Diphenylurea in Propionic, Butyric and Caproic Acids.**—No isocyanate accumulates when these solvents are used; the rates were determined by measuring the volume of gas evolved, and the results appear in Table III.

TABLE III

Solvent	T (absolute)	k, min.$^{-1}$	E_{act}, $k_{cal.}$
Propionic acid	387.5	0.0029	27.9
	391.6	.0047	
	401.5	.0088	
	406.0	.0164	
Butyric acid	402.4	.0021	28.0
	410.0	.0040	
	413.0	.0049	
	421.5	.0096	
Caproic acid	402.3	.0031	28.3
	405.5	.0043	
	412.6	.0075	
	421.0	.0148	

Calculation

To compute the rate of the reaction of isocyanate with acetic acid in our dissociation mixtures, we have used the following treatment, where [A] denotes the concentration of diphenylurea, [B] that of phenyl isocyanate and [C] that of acetanilide or carbon dioxide. Then

$$-\mathrm{d}[\mathrm{A}]/\mathrm{d}t = k_1[\mathrm{A}] \qquad (1)$$

$$-\mathrm{d}[\mathrm{B}]/\mathrm{d}t = k_2'[\mathrm{B}] - k_1[\mathrm{A}] \qquad (2)$$

$$\mathrm{d}[\mathrm{C}]/\mathrm{d}t = k_2'[\mathrm{B}] \qquad (3)$$

where k_2' denotes the rate constants of reaction of isocyanate with acetic acid to form acetanilide and carbon dioxide. Now

$$k_2' = \frac{[\mathrm{C}(t+h)] - [\mathrm{C}(t)]}{\int_t^{t+h}[\mathrm{B}(t)]\mathrm{d}t} = \frac{[\mathrm{C}(t+h)] - [\mathrm{C}(t)]}{\beta(t)}$$

where h and t have the meaning shown in Fig. 5, and where $\beta(t)$ denotes the shaded area in Fig. 5. Values for $[\mathrm{C}(t+h)] - [\mathrm{C}(t)]$ may be taken from curve 1 in Fig. 5 which shows the evolution of carbon dioxide during the reaction; for a given h,

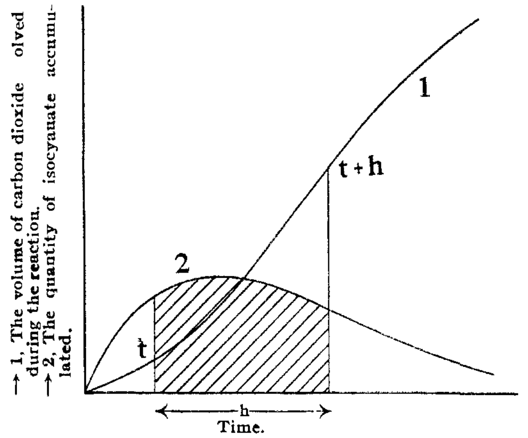


Fig. 5

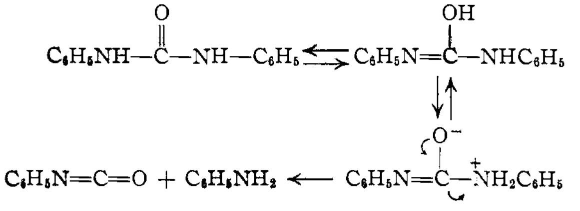
Fig. 5 may be evaluated graphically to give values for $\beta(t)$, and then k_2 can be computed. For example, the experiment outlined in Fig. 3 gave the following results, calculated with the value of h = 50 min.

TABLE IV

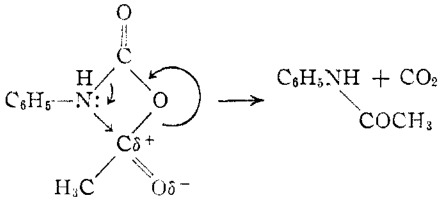
Time	CO_2 evolved, cc.	$[C(t + 50)] - [C(t)]$	$\beta(t)$	k_2, min.$^{-1}$
10	3.6	32.4	585	0.0554
60	36.0			
20	10.0	30.0	529	.0566
70	40.0			
30	17.7	25.4	447	.0567
80	43.1			
40	25.8	19.5	367	.0534
90	45.3			
50	31.5	15.4	294	.0523
100	46.9			
			Ave.	.0548

Discussion

The dissociation of diphenylurea may be rationalized as preceded by a tautomerization



In the presence of a large excess of acetic acid recombination of the cleavage products does not take place, as shown above. The isocyanate reacts with the acetic acid to give a mixed anhydride of phenylcarbaminic and acetic acids; this decomposes to give carbon dioxide and acetanilide, conceivably by way of an internal nucleophilic displacement as sketched below. The use of isotopic carbon should be serviceable to demonstrate that the carbon dioxide evolved originated from the urea molecule.



Solvent effects were noted as follows: (1) The rate of dissociation is lowered to about one-fourth as one goes from anhydrous to water-containing acetic acid. (2) The rate of dissociation in acetic acid is higher than in butyric acid. (3) The rate in propionic acid is about four times that observed in butyric acid. (4) The rates in butyric and caproic acids are nearly equal.

These differences may be due to either dielectricity or acidity function[5] effects, or to both. A qualitative relation is known to exist[6] between log k and D, where D is the dielectric constant, and a general acid catalysis for the reaction may be visualized as

$$RCOOH + C_6H_5NHCONHC_6H_5 \longrightarrow RCOO^- +$$
$$C_6H_5NH_2 + C_6H_5NHC^+ = O \xrightarrow{-H^+} C_6H_5N{=}C{=}O$$

A comparison of the dielectric constants (acetic 6.4 (20°), propionic 3.2 (17°), butyric 2.8 (20°), caproic 3.2 (18°)) shows that the increased rate in acetic acid may well be due to the greater value of D for acetic acid. Addition of water is expected to decrease the acidity function[5] of the medium, but this inhibitory effect is, no doubt, more than compensated for by the increase in dielectric constant. However, since the reaction can proceed in anisole, an acidic medium appears not to be required, or the reaction may proceed by means of intramolecular proton transfers; these questions may be answered by rate studies using anisole or alcohols as the solvent.

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(5) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 267.

(6) S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 420.