Tetrahedron, 1965, Vol. 21, pp. 2893 to 2898. Pergamon Press Ltd. Printed in Northern Ireland

KINETICS OF THE FORMATION OF BIURET FROM UREA IN 2-METHOXYETHANOL[1]

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(*Received* 1 *May* 1965)

Abstract—The formation of biuret from urea has been studied kinetically in 2-methoxyethanol at 120° by estimating the formed biuret with visible spectrophotometry. The apparent second-order rate constant decreases with proceeding of the reaction and with increasing the initial concentration of urea and ammonia. The addition of ammonia is effective in improving the constancy of apparent second-order rate constants. The reaction is subject to the base catalysis, where imidazole is more effective than triethylamine (a stronger base) or N-methylimidazole. The kinetic data are explicable by a mechanism involving the decomposition of urea to ammonia and isocyanic acid followed by the base-catalysed addition of the latter to urea.

MELAMINE is produced in good yield by heating urea at 350–500° under 200–300 atmospheric pressure.[2] On the other hand, biuret, which is formed at early stages of melamine formation, is produced mainly by heating urea over 132°, i.e., m.p. of urea.[2–5] Although extensive studies have been done on the decomposition of urea and thiourea derivatives,[6–8] there has been little kinetic or mechanistic investigation on the biuret formation.[5,9,10]

$$2\ NH_2CONH_2 \rightarrow NH_3 + NH_2CONHCONH_2$$

In the present study, 2-methoxyethanol was chosen as a solvent for the reaction, since it could be studied kinetically in a homogeneous system at 120° which is an appropriate temperature for the kinetic measurements.

RESULTS AND DISCUSSION

The rate law. The observed rate of biuret formation neither followed the first- nor second-order rate law, although the second-order rate has been reported for an aqueous solution or a system without solvent.[9] The apparent second-order rate constants decrease as the reaction proceeds and is diminished with increasing initial concentration of urea. The initial addition of a small amount of ammonia results in

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[1] Contribution No. 71.

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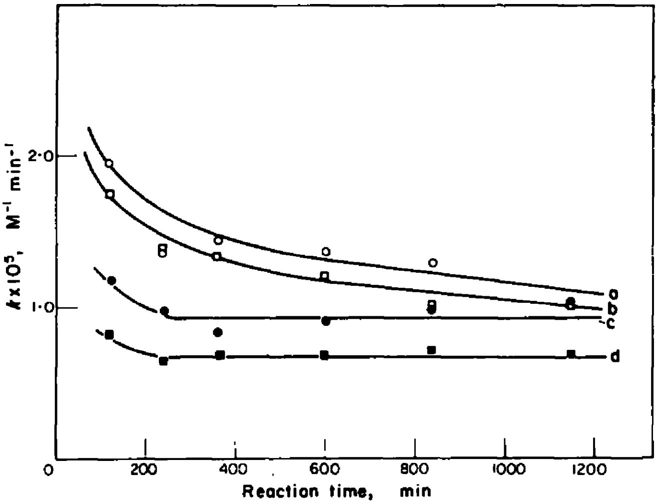

FIG. 1. Plot of the apparent second-order rate constant vs. reaction time for the biuret formation in 2-methoxyethanol at 120°.
a: $[U]_0$, 1·5M; $[NH_3]_0$, 0M
b: $[U]_0$, 3·0M; $[NH_3]_0$, 0M
c: $[U]_0$, 1·5M; $[NH_3]_0$, 0·15M
d: $[U]_0$, 3M; $[NH_3]_0$, 0·3M

a decrease in rate, and at the same time, the second-order rate constant is stabilized and becomes independent of reaction time. These results are in accordance with the following scheme involving two steps:[5]

$$NH_2CONH_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} NH_3 + HNCO \quad (1)$$

$$NH_2CONH_2 + HNCO \xrightarrow{k_2} NH_2CONHCONH_2 \quad (2)$$

A third reaction with solvent 2-methoxyethanol is possible, since urethane may be formed from isocyanate and alcohol.[11–13]

$$ROH + HNCO \xrightarrow{k_3} NH_2COOR \quad (3)$$

The application of the stationary-state method involving intermediary isocyanic acid leads to the rate of biuret formation as follows:

$$v = \frac{d[Bi]}{dt} = \frac{k_1k_2}{k_{-1}[NH_3] + k_2[U] + k_3[ROH]}[U]^2 \quad (4)$$

Here, Bi, U, and ROH represent biuret, urea and solvent, respectively. Therefore, the observed second-order rate constant is expressed as:

$$k = \frac{k_1k_2}{k_{-1}[NH_3] + k_2[U] + k_3[ROH]} \quad (5)$$

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[11] J. W. Baker and J. B. Holdsworth, *J. Chem. Soc.* 713 (1947); J. W. Baker and J. Gaunt, *Ibid.* 9, 19, 27 (1949); J. W. Baker, M. M. Davies, and J. Gaunt, *Ibid.* 2 (1949).

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This equation explains the effect of the initial concentration of urea and ammonia on the rate. If no ammonia is added initially, the concentration of ammonia in the system increases gradually according to the stoichiometry, i.e., the apparent second-order rate constant (k) should, as observed, decrease as the reaction proceeds.

The effect of urea and ammonia on the rate implies that $k_{-1}[\mathrm{NH_3}]$ is comparable to $k_2[\mathrm{U}]$ in order. Since the concentration of urea (ca. 3M) is much higher than that of ammonia (<0·3M),

$$k_{-1} > k_2$$

The contribution of the third term ($k_3[\mathrm{ROH}]$) in the denominator in Eq. 5 to rate is comparatively small, because the reaction in dimethylformamide, which cannot react with isocyanic acid, gives nearly the same rate constant as in 2-methoxyethanol.[14]

Eq. 5 may lead to:

$$\frac{1}{k} = \frac{k_{-1}}{k_1 k_2}[\mathrm{NH_3}] + \left(\frac{1}{k_1}[\mathrm{U}] + \frac{k_3}{k_1 k_2}[\mathrm{ROH}]\right) \qquad (6)$$

Here, both the second and third terms on the right may hold approximate constancy in the early stage of reaction (within 10% conversion) and hence Eq. 6 may be expressed as a linear equation:

$$\frac{1}{k} = a[\mathrm{NH_3}] + b \qquad (7)$$

Here, a (min) and b (M min) are constants in the early stage. The plot of the reverse of an average rate constant at a given time ($1/k_t$) vs. the concentration of ammonia estimated by the concentration of biuret formed at that time ($[\mathrm{NH_3}]_t$) gives a straight line (Fig. 2) as expected from Eq. 7.

TABLE 1. BASE CATALYSIS WITH TERTIARY AMINES FOR THE BIURET FORMATION IN 2-METHOXYETHANOL AT 118° (Initial conc. of urea: 3M)

Base	pK_B of base	Conc. of base M	$10^5 k$ $M^{-1}\,min^{-1}$	$10^5 k'^{a}$ $M^{-1}\,min^{-1}$
Triethylamine	3·25	0·58	2·01	1·45
Dimethylaniline	8·95	0·64	1·10	0·56
Pyridine	8·63	0·72	0·68	0·41
Quinoline	9·22	0·54	1·09	0·36
—	—	—	0·94	0·46
Ammonia	4·76	—	—	—
Urea	13·82	—	—	—

[a] Addition of ammonia with initial concentration of 0·3M.

Base catalysis. The effect of tertiary amines on the rate of biuret formation has been studied (Table 1). The stronger base, triethylamine, is a good catalyst for the reaction. Little catalysis was observed with other bases, dimethylaniline, pyridine, and quinoline, probably because of their low basicities. Ammonia, a stronger base, which is present in the reaction system may also catalyse the reaction and the catalysis

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[14] Here, the solvent effect may be neglected. The observed rate constant in 2-methoxyethanol ($1·3 \times 10^{-5}\ M^{-1}\,min^{-1}$ at 120°) appears to be substantially equal to that in aqueous solution ($1·1 \times 10^{-6}\ M^{-1}\,min^{-1}$ at 100°) and without solvent ($2·8 \times 10^{-5}\ M^{-1}\,min^{-1}$ at 140°) at higher initial concentrations of urea.[9]

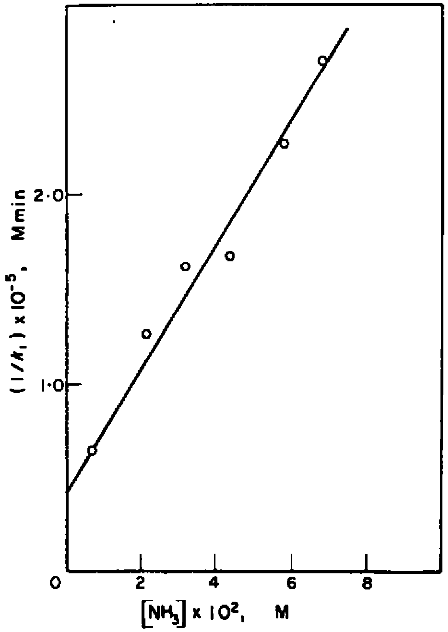


FIG. 2. Illustration of a linear relationship between the reverse of second-order rate constant ($1/k_t$) and the concentration of ammonia ($[NH_3]_t$) in the reaction system (eq. 7) for the biuret formation in 2-methoxyethanol at 120°.

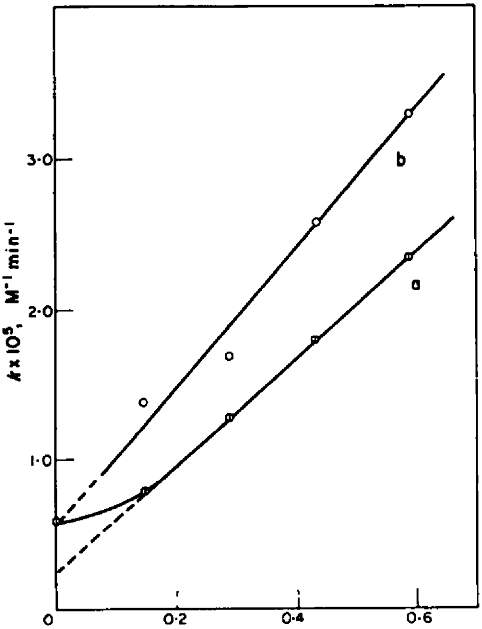


FIG. 3. Relationship between the observed second-order rate constant and the concentration of triethylamine for the biuret formation at 120°.

a: $[U]_0$, 3M, in 2-methoxyethanol

b: $[U]_0$, 2M, in dimethylformamide

may be more significant than with dimethylaniline, pyridine, and quinoline, and may obscure their catalytic effects. The initial addition of ammonia (0·3M) decreases the rate by 0·5 M^{-1} min^{-1} (k in Table I), but the addition does not affect the order for the rate of base catalysis with various amines.

As shown in Fig. 3, the rate constants both in 2-methoxyethanol and in dimethylformamide are expressed as the following equation in 0·15M or higher concentration of triethylamine.

$$k = k_0 + k[\mathrm{N\varepsilon t_3}] \tag{8}$$

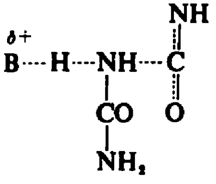
The catalytic constant k_0 for ammonia, urea, and the solvent is negligible in the presence of triethylamine.

Since the decomposition of urea (Eq. 1) is not subject to base catalysis,[6–8] the catalysis may be operative in step 2, as reported in the formation of urethane.[11–13]

Nucleophilic catalysis. The catalytic action of triethylamine and imidazoles were compared (Table 2). Base catalysis with imidazole (pK_b, 7·05) is somewhat stronger than that with the stronger base, triethylamine (pK_b, 3·25), and much stronger than that with N-methylimidazole (pK_b, 6·95). These results suggest that this base catalysis is different from the ordinary base catalysis, i.e., withdrawal of a proton, and is the so-called nucleophilic catalysis which means the activation by the formation of an addition complex as reported for the hydrolysis of esters[15,16] and the formation of urethane.[11,13] If the ordinary base catalysis operated, then the catalysis should be more effective with stronger base, triethylamine, than with imidazole, and imidazole should be comparable with N-methylimidazole in catalylic effect but this is not the case.

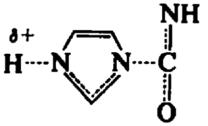
TABLE 2. COMPARISON OF THE SECOND-ORDER RATE CONSTANTS WITH TRIETHYLAMINE, IMIDAZOLE, AND N-METHYLIMIDAZOLE FOR THE BASE-CATALYSED BIURET FORMATION IN 2-METHOXYETHANOL AT 118°
(Initial conc.: urea, 3M; ammonia, 0·3M)

	Second-order rate constant, $10^5\,k$, M^{-1} min^{-1}			
Added base	None	Triethylamine	Imidazole	N-Methylimidazole
M				
0·095	0·55	0·76	0·96	—
0·12	—	—	1·01	—
0·25	—	1·02	1·15	—
0·12	0·50	—	0·68	0·48



I

Ordinary base catalysis



II

Nucleophilic base catalysis

The reaction mechanism. The data obtained suggests a mechanism involving a preliminary reversible dissociation of urea to ammonia and isocyanic acid (11) followed

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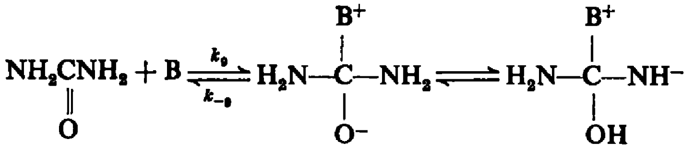
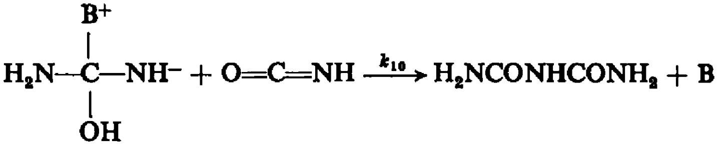
by the base-catalysed addition of isocyanic acid with urea to form biuret (2). The base may act as an activator of urea which acts as a nucleophile on isocyanic acid.

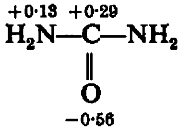


$$\underset{\underset{\displaystyle O}{\|}}{NH_2CNH_2} + B \underset{k_{-9}}{\overset{k_9}{\rightleftharpoons}} H_2N{-}\overset{\overset{\displaystyle B^+}{|}}{\underset{\underset{\displaystyle O^-}{|}}{C}}{-}NH_2 \rightleftharpoons H_2N{-}\overset{\overset{\displaystyle B^+}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}{-}NH^- \qquad (9)$$



$$H_2N{-}\overset{\overset{\displaystyle B^+}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}{-}NH^- + O{=}C{=}NH \xrightarrow{k_{10}} H_2NCONHCONH_2 + B \qquad (10)$$

The following electronic density pattern is in accordance with the addition of base to the carbonyl carbon of urea.[17] The data also satisfy another mechanism in which



$$\overset{+0{\cdot}13}{H_2N}{-}\overset{+0{\cdot}29}{\underset{\underset{\underset{\displaystyle -0{\cdot}56}{\displaystyle O}}{\|}}{C}}{-}NH_2$$

the base activities isocyanic acid to attack a nitrogen atom of urea, but this seems less probable, since the addition of base to isocyanic acid should reduce the electrophilicity of the carbonyl carbon in isocyanic acid and further it is known that the reaction of isocyanic acid with amines in water is not subject to base catalysis with triethylamine.[18] The observed catalytic effect with added amines is relatively small, since the amines convert free isocyanic acid into its conjugate base which is unreactive as an electrophile.

EXPERIMENTAL

Materials. Commercial urea was recrystallized from MeOH, m.p. 131·5–132°. Commercial 2-methoxyethanol was purified by rectification, b.p. 122°–123°. Authentic biuret, m.p. 197°, was prepared from urea.[19] N,N-Dimethylaniline b.p. 189–191°, was purified by the treatment with acetic anhydride.[20] Quinoline, b.p. 85–86° (5·5 mm), and pyridine, b.p. 114°, were purified by rectifications, and imidazole, m.p. 88–89°, was purified by recrystallization from benzene. Triethylamine was of guaranteed reagent grade. N-methylimidazole, b.p. 72–74° (8 mm), was prepared from imidazole and MeI.[21]

Quantitative determination of biuret. Biuret was estimated by the modified biuret reaction—4N NaOH aq (4·0 ml), 0·2M $CuSO_4$ aq (2·0 ml) and a solution of biuret in 2-methoxyethanol (2·0 ml) were mixed and the solution diluted with pure water to 10 ml in a volumetric flask cooled in an ice bath. After standing for 1 hr below 10°, the precipitate was removed by centrifuge and the absorption of the clear solution (at 560 mμ) determined by a Shimadzu spectrophotometer SV 50A. The plot of the absorbances at 560 mμ (E_{560}) vs. the conc. (0·002–0·024M) gave a straight line.

Kinetic procedure. Urea (4·5 g) was dissolved in 2-methoxyethanol and diluted to 25 ml with the same solvent (if necessary, NH_4OH aq was added); the 3M urea solution obtained was transferred to a glass-stoppered flask in a polyethylene glycol bath (thermostat; 120 ± 0·5°). Aliquots were pipetted out at regular intervals of time and the conc. of the biuret formed was determined by means of the above biuret reaction. The rate was followed up to 10% conversion.

Acknowledgment—The authors are grateful to Toho Rayon Co. for their gift of materials.

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