Formaldehyde Resins. LIII. The Acid-catalyzed Reaction of Acid Amide with Formaldehyde

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As is well known, acid amides react with formaldehyde to give methylol amides, in the presence of acid- or base-catalysts. Since urea resin is produced by this kind of reaction, many studies have been made[1-3]. Recently, Ugelstadt[4] made a kinetic study of the reactions of propylamide, monochloroacetamide and benzamide with formaldehyde, and concluded that, in acid solution, the reaction rate was represented by

$$v=\frac{-\mathrm{d}\,[\mathrm{CH_2O}]}{\mathrm{d}t}=\mathrm{const.}\,[\mathrm{R\text{-}CONH_2}]\,[\mathrm{CH_2O}] \tag{1}$$

Furthermore, the following mechanism was

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[1] A. Einhorn, *Ann.*, **343**, 207 (1905).

[2] G. A. Crowe, Jr. and C. C. Lynch, *J. Am. Chem. Soc.*, **71**, 3731 (1949); **72**, 3622 (1950).

[3] A. Iliceto, *Ann. chim. applicata*, **43**, 516 (1953).

[4] J. Ugelstadt, The reaction of formaldehyde with amides, and the alkaline hydrolysis of alkoxymethyl ureas. *Dissert. at Norges Tekniske Hogskole* (1955).

proposed for this reaction:

$$\text{i)}\quad CH_2O + HA \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \overset{+}{C}H_2OH + A^-$$

$$\text{ii)}\quad R\text{-}CONH_2 + \overset{+}{C}H_2OH \xrightarrow{k_2} [R\text{-}CONH_2CH_2OH]^+$$

$$\text{iii)}\quad [R\text{-}CONH_2CH_2OH]^+ + A^- \rightleftharpoons R\text{-}CONHCH_2OH + HA$$

in which step ii is rate determining. In order to justify this mechanism, it may be useful to examine how the reaction rate is influenced by the polar character of R in $R\text{-}CONH_2$. In the present paper, the acid-catalyzed reactions of ten acid amides with formaldehyde were studied kinetically. The results obtained were as follows: (i) An equation identical with that of Ugelstadt was obtained. (ii) The reaction rate constant (k) was estimated for each acid amide, (iii) It was confirmed that the values of k fitted Hammett's equation. (iv) The reaction mechanism was discussed.

Experimental

Materials. — The acid amides were synthesized from the corresponding carboxylic acids according to the following scheme;

$$R\text{-}COOH \xrightarrow[PCl_3]{SOCl_2\text{ or}} R\text{-}COCl \xrightarrow{NH_4OH} R\text{-}CONH_2$$

The acid amides obtained were purified by repeating recrystalizations. Thus six kinds of substituted benzamides and four kinds of aliphatic amides were prepared; *p*-methoxybenzamide (m. p., 105°C, recrystalized from water-methanol), benzamide (m. p., 128°C, from water-methanol), *p*-chlorobenzamide (m. p., 177.7°C, from water-methanol), *p*-bromobenzamide (m. p., 190°C, from water-methanol), *m*-nitrobenzamide (m. p., 142.5°C, from water-methanol), *p*-nitrobenzamide (m. p., 199°C, from water-ethanol), acetamide (m. p., 80°C from chloroform-ligroin), propylamide (m. p., 79°C, from chloroform-ligroin), *n*-butylamide (m. p., 115°C, from ethylacetate-ligroin) and isobutylamide (m. p., 128°C, from chloroform-ligroin).

The aqueous solution of formaldehyde was prepared by the following procedure; a mixture of para-formaldehyde and water was distilled after refluxing for several hours. The distillate was diluted to a concentration of 1 mol./l.

As catalyst 0.6580 N (in the case of substituted benzamide) or 1.014 N (in the case of aliphatic amide) hydrochloric acid was used.

Commercial dioxane was refluxed for 17 hr. with 10% of its volume of 1 N hydrochloric acid to remove acetaldehyde, under a current of nitrogen. To remove water, the dioxane was treated with a concentrated solution of potassium hydroxide, then allowed to stand over pellets of potassium hydroxides for 1 day and dried over sodium for several hours. It was rectified three times and the fraction above 100.5°C was used.

Kinetic Procedures. — All reactions were carried out at 60±0.05°C. The reaction rates were measured according to the following procedures; A required amount of acid amide was weighed into a 50 ml. measuring flask. The acid amide was dissolved in 20 ml. dioxane and then 4 ml. (in the case of substituted benzamide) or 2 ml. (in the case of aliphatic amide) of the catalyst (hydrochloric acid) was added. The flask was placed in a thermostat at 60±0.05°C for at least 30 min. The formaldehyde solution and distilled water were also kept at the same temperature. A required amount of the formaldehyde solution was added to the flask from a hole pipette. Then immediately the solution was diluted to 50 ml. with distilled water. After thorough mixing, the solution was brought into the reaction vessel which was placed in the thermostat. The time when all the reactants were mixed was taken as zero. And 8—10 aliquotes of 5 ml. were taken by a pipette at suitable time intervals. The aliquote was run into a phosphate buffer solution (pH=7.1). The time when the pipette had run empty was taken as zero. Five millilitre of 0.1 N or 0.15 N potassium cyanide was added immediately and the solution was allowed to stand for 10 min. at room temperature. Then were added 10 drops of a diphenyl carbazone solution (1% in methanol), followed by 1 N nitric acid until a light orange-yellow color appeared. The solution was then immediately titrated with 0.03 N or 0.05 N mercuric nitrate until a violet color developed. The consumed amount of CH_2O was calculated for each reaction time.

Results and Discussion

Reaction-orders of the Reactants.—To derive a rate equation of the reaction, the effects of the concentrations of each reactant on the rates were investigated. The study was carried out first on benzamide.

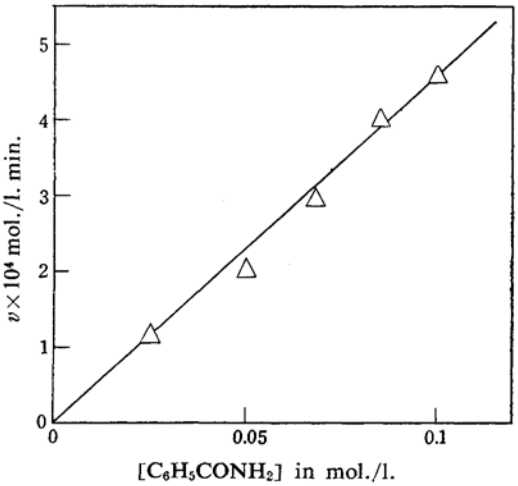

Fig. 1. The relation between the reaction rates and the concentrations of benzamide. Reaction conditions; [CH_2O]···0.05 mol./l.; [HCl]···0.05264 N; temp. 60°C.

a) *The Concentrations of Benzamide.*—Keeping the concentrations of formaldehyde and hydrochloric acid constant, the concentration of benzamide was changed from 0.025 to 0.1 mol./l. As shown in Fig. 1, the linear relationship was obtained between the reaction rates and the concentrations of benzamide. The reaction, therefore, was decided to be of first order with regard to the concentrations of benzamide.

b) *The Concentration of Formaldehyde.*—Keeping the concentrations of benzamide and hydrochloric acid constant, the concentration of formaldehyde was changed from 0.015 to 0.05 mol./l. As shown in Fig. 2, the linear relationship was obtained between the reaction rates and the concentrations of formaldehyde. So the reaction was also of first order with formaldehyde.

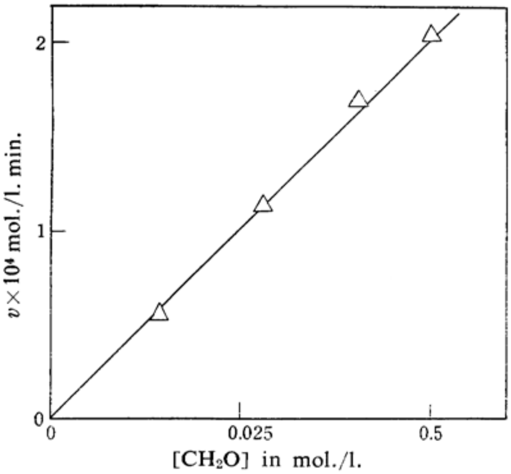

Fig. 2. The relation between the reaction rates and the concentrations of formaldehyde.
Reaction conditions ; $[C_6H_5CONH_2]$…0.05 mol./l.; [HCl]…0.05264 N ; temp. 60°C.

c) *The Concentrations of Hydrochloric Acid.*—Keeping the concentrations of $R-CONH_2$ and formaldehyde constant, the amount of the catalyst included in 50 ml. of the solution was changed from 2 ml. to 6 ml. The pH of the reaction system and the consumption rate of formaldehyde were measured. As shown in Fig. 3, a linear relationship was observed between the consumption rate of formaldehyde (v) and the concentration of hydrochloric acid. But as Fig. 4 shows, the relationship between v and pH is not linear. From the results, it was assumed that this reaction proceeded by a mechanism of general acid-catalysis and the reaction order of hydrochloric acid was unity.

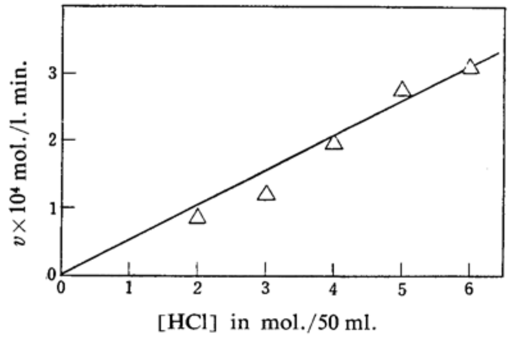

Fig. 3. Plot of the reaction rates against the concentrations of the hydrochloric acid.
Reaction conditions ; $[C_6H_5CONH_2]$…0.05 mol./l.; $[CH_2O]$…0.05 mol./l.; temp. 60°C.

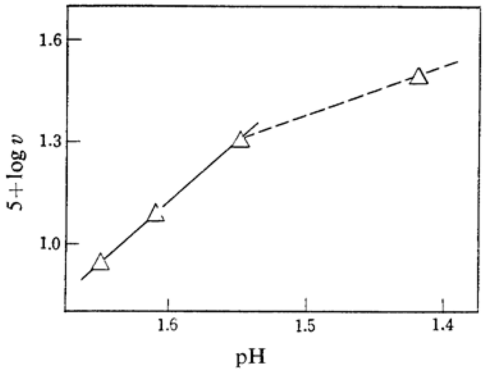

Fig. 4. Plot of the reaction rates against pH.

d) *Rate Equation.*—From the results obtained above, the experimental rate equation is represented as follows ;

$$v=\frac{-\mathrm{d}[CH_2O]}{\mathrm{d}t}=k'[HCl]\,[R-CONH_2]\,[CH_2O] \tag{2}$$

Since [HCl] was assumed to be constant during the reaction, Eq. 2 was simplified to

$$v=k\,[R-CONH_2]\,[CH_2O] \tag{3}$$

To examine whether the Eq. 3 obtained for benzamide is also applicable to the other amides or not, this equation was tested for acetamide. When the initial concentrations of formaldehyde and acetamide were both a mol./l. and the consumption of formaldehyde was x mol./l., Eq. 4 may be adopted in order to confirm the correctness of Eq. 3.

$$\frac{x}{a(a-x)}=kt \tag{4}$$

A linear relationship was obtained between $\frac{x}{a(a-x)}$ and t, at the initial stage of the reaction. (see Fig. 5) Accordingly, Eq. 3 was well supported. The deviation from the linearity at longer reaction time was attributed to the reversed reaction. For the other nine amides, the values of k were estimated by the

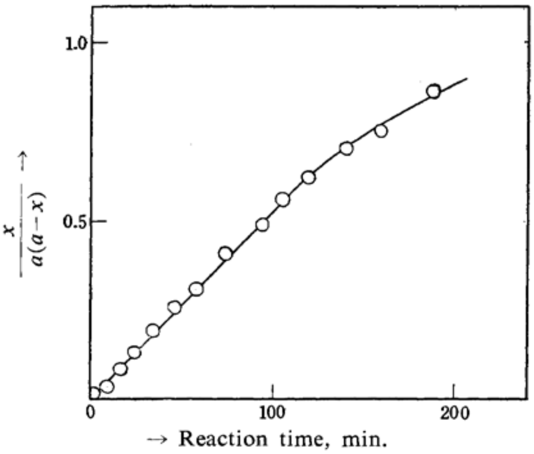

Fig. 5. Plot of $\frac{x}{a(a-x)}$ vs. reaction time.
Reaction conditions; $[CH_3CONH_2]$…0.1 mol./l.; [HCl]…0.02028 N; $[CH_2O]$…0.1 mol./l.; solvent…water; temp. 60°C.

TABLE I. RATE CONSTANTS FOR SUBSTITUTED BENZAMIDES

Acid amide	$k† \times 10^3$
p-Methoxybenzamide	19.4
Benzamide	8.16
p-Chlorobenzamide	4.95
p-Bromobenzamide	4.56
m-Nitrobenzamide	1.36
p-Nitrobenzamide	1.25

† $[R\text{-}CONH_2]$ 0.05 mol./l., $[CH_2O]$ 0.05 mol./l., [HCl] 0.05364 mol./l., temp. 60°C.

TABLE II. RATE CONSTANTS FOR ALIPHATIC AMIDES

Acid amide	$k† \times 10^3$	σ^-	E_s
Acetamide	3.37	0.00	0.00
Propylamide	5.19	−0.10	−0.07
n-Butylamide	3.29	−0.115	−0.36
Isobutylamide	2.55	−0.190	−0.47
Benzamide	3.12	+0.610	+1.24

† Reaction conditions are; $[R\text{-}CONH_2]$ 0.1 mol./l., $[CH_2O]$ 0.1 mol./l., [HCl] 0.02028 N, temp. 60°C.

Eq. 3. The results are given in Tables I and II.

The Effects of the Polar Character on Reaction Rates.—These values of k were correlated with Hammett's[5] and Taft-Ingold's[6] equations. The linear relationships were obtained as Figs. 6 and 7.

The two equations were as follows;

$$\log \frac{k}{k_0} = -1.10\,\sigma$$

for the substituted benzamides.

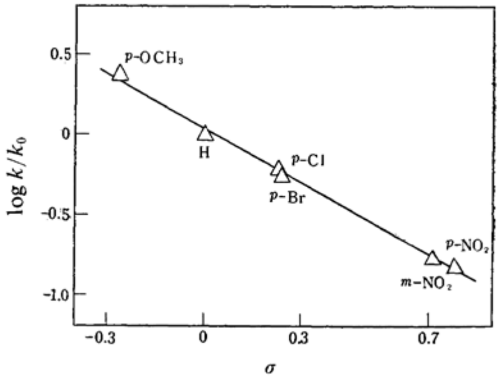

Fig. 6. Hammett equation plot
$\log k/k_0$ vs. σ for substituted benzamides.
$\log k/k_0 = -1.10\,\sigma$

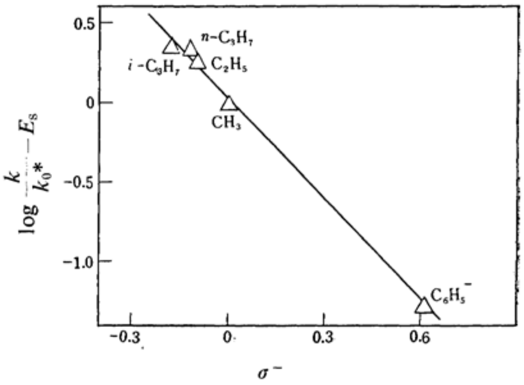

Fig. 7. Taft-Ingold equation plot
$\log \frac{k}{k_0{}^*} - E_s$ vs. σ^- for aliphatic amides.
$\log \frac{k}{k_0{}^*} - E_s = -2.16\,\sigma^-$

$$\log \frac{k}{k_0{}^*} - E_s = -2.16\,\sigma^-$$

for the aliphatic acid amides. The rate constants for benzamide and acetamide were denoted by k_0 and $k_0{}^*$ respectively.

The negative values of ρ indicate that introducing of the electron releasing groups increases the reaction rate.

The Effect of the Polar Character on the Activation Energy and the Activation Entropy.—For *p*-methoxybenzamide, benzamide and *p*-nitrobenzamide, the activation energies were calculated according to Arrhenius equation. (see Table III and Fig. 8). Using the values of the activation energy $\Delta E^{\ddagger}$ thus obtained, the activation entropies $\Delta S^{\ddagger}$ were calculated according to the following equation,

$$k = \kappa \cdot \frac{kT}{h} \cdot e^{-\Delta E^{\ddagger}/RT} \cdot e^{\Delta S^{\ddagger}/R}$$

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[5] L. P. Hammett, "Physical Organic Chemistry", McGraw-Hill Book Co., New York (1940), p. 184.

[6] M. S. Newman, "Steric Effects in Organic Chemistry", John Willy & Sons Inc., New York (1956), p. 586.

where transmission coefficient denoted by κ was assumed to be unity. The results are given in the third column of Table III.

It seems reasonable to consider that the higher value of k for the amide having a more electron-releasing group is due mainly to the lower activation energy. The compensation rule is likely to exist for each amide.

TABLE III. ACTIVATION ENERGIES AND ACTIVATION ENTROPIES FOR SUBSTITUTED BENZAMIDE

Acid amide	$\Delta E^{\ddagger}$ kcal./mol.	$\Delta S^{\ddagger}$ cal./deg.
p-Methoxybenzamide	17.1	−23.86
Benzamide	20.2	−16.30
p-Nitrobenzamide	23.5	−10.16

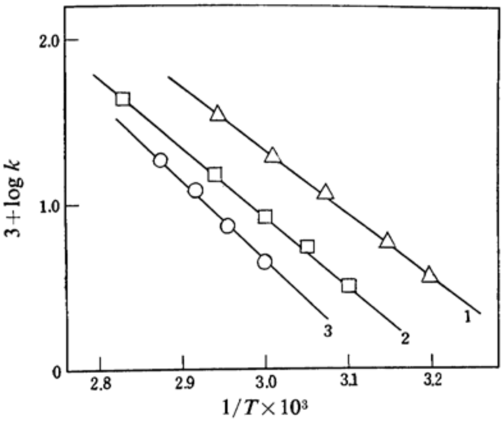


Fig. 8. Temperature dependence of the rate constants.
Upper curve; *p*-methoxybenzamide
Middle curve; benzamide
Lower curve; *p*-nitrobenzamide

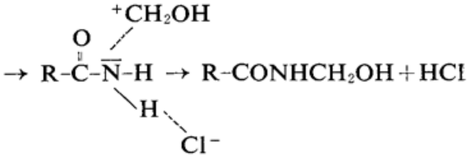
Reaction Mechanism of Benzamide with Formaldehyde.—From the reaction mechanism having been introduced by Ugelstadt, it follows that

$$v=\frac{-\mathrm{d}[\mathrm{CH_2O}]}{\mathrm{d}t}$$
$$=\frac{k_1}{k_{-1}}k_2[\mathrm{HCl}]\,[\mathrm{R\text{-}CONH_2}]\,[\mathrm{CH_2O}]$$
$$=k\,[\mathrm{CONH_2}]\,[\mathrm{CH_2O}]$$

Taking into account of his hypothesis that the step of attacking of $^{+}CH_2OH$ on the lone-pair of the nitrogen atom in $-CONH_2$ is rate determining, we could expect that the larger rate constant was observed for the amide having higher electron density at the nitrogen atom. Therefore our results can be well explained with this mechanism. But on the other hand, another mechanism, a S_E2 mechanism, may be also possible, as follows:

i) $CH_2\dot{O}+HCl \rightleftharpoons {}^{+}CH_2OH+Cl^-$

ii) $R\text{-}CONH_2+{}^{+}CH_2OH+Cl^-$



In this mechanism, the step ii is rate determining.

Which mechanism is more correct remains undetermined.

On the Existence of $\mathbf{RCONH_3^+}$.—Notwithstanding a weak basicity of nitrogen atom of acid amides, it was proved from a spectroscopic study that the addition of a cation to the nitrogen atom was probable.

The infrared spectrum of hydrochloric acid salt of *p*-methoxybenzamide (1 : 1) at solid state (nujol) was compared with that of *p*-methoxybenzamide (see Fig. 9).

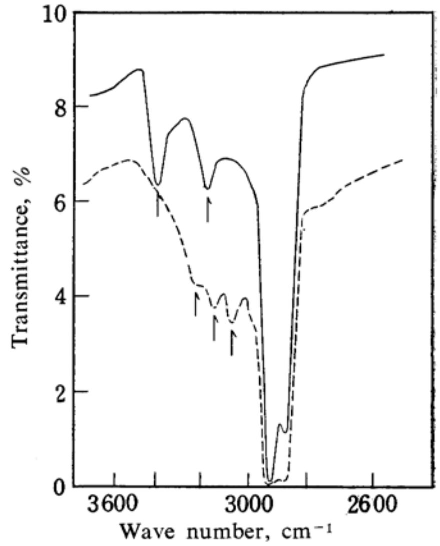


Fig. 9. The infrared spectra of *p*-methoxybenzamide and its hydrochloric acid salt.
Solid line ··· *p*-methoxybenzamide
Dotted line ··· hydrochloric acid salt

The absorption bands at 3382 and 3170 cm^{-1} of the amide may be assigned to the stretching vibrations of the NH_2 group under the influence of hydrogen bonding. Comparing with Hopkin's result about urea nitrate(7), the 3237, 3150 and 3068 cm^{-1} bands may be decided as due to the stretching vibrations of NH_3^+. The disappearance of the 3382 cm^{-1} band in the salt shows an absence of free NH_2 group in the molecule.

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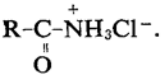
7) M. Davies and L. Hopkins, *Trans. Faraday Soc.*, **53**, 1563 (1957).

From the facts cited above, we may reasonably assume the structure of the salt as



$\mathrm{R-\underset{\overset{\parallel}{O}}{C}-\overset{+}{N}H_3Cl^-}$.

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