Formaldehyde Resins. LXVI.[1] *The Base-catalyzed Reaction of Benzamides with Formaldehyde*

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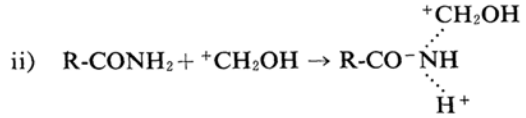
Three years ago, the present authors stated[2] that the rate of the reaction of amide with formaldehyde in the presence of hydrochloric acid was represented by the following equation:

$$R=k\,[\mathrm{HCl}]\,[\mathrm{R\text{-}CONH_2}]\,[\mathrm{CH_2O}]$$

For the reaction, an S_E2 mechanism was proposed, illustrated by the following two steps:

i) $\mathrm{CH_2O+HCl \rightarrow {}^+CH_2OH+Cl^-}$



ii) $\mathrm{R\text{-}CONH_2+{}^+CH_2OH \rightarrow R\text{-}CO^-\overset{{}^+CH_2OH}{\underset{H^+}{NH}}}$

$\mathrm{\rightarrow R\text{-}CONHCH_2OH+H^+}$

In the present paper, the base-catalyzed reaction of monosubstituted benzamides with formaldehyde will be studied kinetically. The following results have been obtained: (i) The rate of the reaction increased linearly with the concentration of formaldehyde, until the concentration reached a certain value. Above this value, the rate remained constant; i. e., the rate was independent of the concentration of formaldehyde. (ii) The reaction rate constants fit Hammett's equation. (iii) An S_E1 mechanism is proposed for the base-catalyzed reaction of benzamide with formaldehyde.

Experimental

Materials.—The preparation of six kinds of *m*- or *p*-substituted benzamides and the purification of dioxane have been described in the previous paper.[2]

As a catalyst, a 0.0428 N aqueous solution of sodium hydroxide was used.

Kinetic Procedures.—All reactions were carried out at 30°C (±0.05°C). A required amount of amide was weighed into a 50 ml. volumetric flask. The amide was dissolved in 25 ml. of dioxane. The flask was placed in a thermostat kept at 30°C for at least 30 min. The formaldehyde solution and distilled water were also kept at the same temperature. A 0.6 ml. volume of the catalyst and then a required amount of the formaldehyde solution were added to the flask. In order to avoid the effect of carbon dioxide in the atmosphere, the catalyst solution was added through a microburette in an atmosphere of air freed from carbon dioxide. The solution was then immediately diluted to 50ml. with distilled water. After a thorough mixing, the solution was brought into a reaction vessel which had been placed in the thermostat. The rate of the consumption of formaldehyde was determined by the KCN-method, as has been described in the case of an acid-catalyzed reaction.[2]

Experimental Errors Anticipated. — (1) The *N*-methylol amide produced may decompose to formaldehyde and amide in the presence of the base. However, Ugelstadt has concluded that the back reaction could be neglected until the reaction reached the consumption of ca. 10% of formaldehyde.[3]

(2) The benzamide may be hydrolyzed with the base catalyst into benzoic acid and ammonia. Ugelstadt has also concluded that this hydrolysis was negligible.

(3) As is known, formaldehyde is changed into formic acid and methanol by the Cannizzaro reaction. However, under the conditions described above, this reaction was so small as to be negligible, as Table I shows.

TABLE I. THE CONSUMPTION OF FORMALDEHYDE AT 30°C

($[\mathrm{CH_2O}]_0=0.05$ mol./l., catalyst 0.6 ml./50 ml.)

Reaction time min.	Decrease in $[\mathrm{CH_2O}]_0$ content $\times10^{-3}$ mol./l.	Decrease in $[\mathrm{CH_2O}]_{\mathrm{OCH_3}}$ content $\times10^{-3}$ mol./l.
2	0	0.5
5	0.1	1.8
25	0.1	2.6
45	0.28	6.0
60	0.28	—

In Table I, the decrease in $[\mathrm{CH_2O}]_0$ content indicates the concentration of formaldehyde consumed by the Cannizzaro reaction in the absence of amide. The decrease in $[\mathrm{CH_2O}]_{\mathrm{OCH_3}}$ content was the result of the consumption of formaldehyde by the reaction of formaldehyde with *p*-methoxybenzamide. In the present reaction, the *p*-methoxybenzamide was the most inactive amide. Even in this case, however, the $[\mathrm{CH_2O}]_0$ decrease was only a twentieth of that of $[\mathrm{CH_2O}]_{\mathrm{OCH_3}}$.

An Estimation of the Initial Rate of Reaction. —Figure 1 shows a typical example of the reaction course. The ordinate, -[F], showed the concentration of consumed formaldehyde. Extrapolating the

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[1] LXV: M. Imoto, N. Kotani and T. Toda, *J. Chem. Soc. Japan, Ind Chem. Soc.* (*Kogyo Kagaku Zasshi*), in press.

[2] Part LIII of this series: M. Imoto and M. Kobayashi, This Bulletin, 33, 1651 (1960).

[3] J. Ugelstadt, Dissertation, Leiden University (1955).

remaining concentration of formaldehyde, [F], to time zero, the initial concentration of formaldehyde, $[F]_0$, was estimated. The inclination of the curve of -[F] vs. time at time zero gave the rate of the reaction, $-d[F]/dt$.

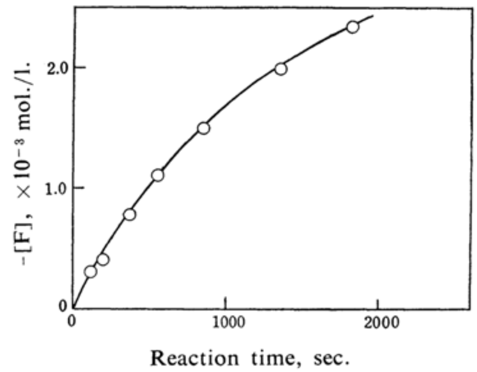

Fig. 1. The consumption of formaldehyde vs. the reaction time.
($[F]_0=0.0955$ mol./l., $[C_6H_5CONH_2]_0$ $=0.05$ mol./l., at 30°C)

Results and Discussion

Reaction-orders of the Reactants.—Ugelstadt[3] has previously given the following rate equation for the base-catalyzed reaction of benzamide with formaldehyde:

$$R = -d[F]/dt$$
$$= k[C_6H_5CONH_2][CH_2O][OH^-] \qquad (1)$$

To confirm Ugelstadt's formula, the rate of the consumption of formaldehyde, R, was investigated at various concentrations of benzamide and formaldehyde.

The Reaction-order of Benzamide.—While the concentrations of formaldehyde and of the catalyst were kept at 0.05 mol./l. and 0.60 ml./50 ml. respectively, the rate was measured in various concentrations of benzamide over the range from 0.0125 to 0.05 mol./l. As Fig. 2 shows, a linear relationship was obtained.

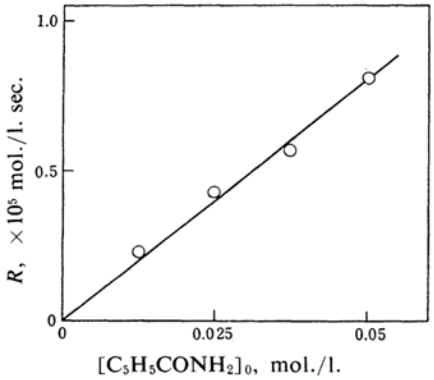

Fig. 2. The relationship between R and $[C_6H_5CONH_2]_0$.

The reaction, therefore, was of the first order with benzamide.

The Reaction-order of Formaldehyde.—While the concentration of benzamide was kept at 0.05 mol./l., the concentration of formaldehyde was changed from 0.013 to 0.200 mol./l. The result obtained was peculiar, as is shown in Fig. 3. Such a relationship between $[F]_0$ and R was found for the first time.

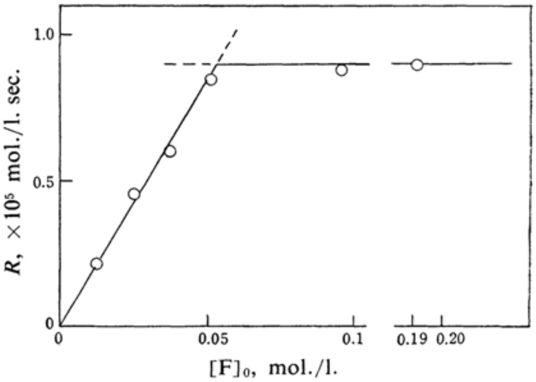

Fig. 3. The relationship between R and $[F]_0$. 0.6 ml. of the catalyst was added.

When the concentration of formaldehyde was less than ca. 0.05 mol./l., the reaction was of the first order with formaldehyde. However, in a higher concentration of formaldehyde than this characteristic concentration, the reaction order of formaldehyde became zero. A similar bending point in the curve of R vs. $[F]_0$ was also observed in the reaction of every substituted benzamide, as Fig. 4 shows.

The Reaction-order of Sodium Hydroxide.—According to the paper by Ugelstadt, it may be assumed that the reaction-order of $[OH^-]$ was first under the conditions described above. This will also be confirmed by us in a later paper.[4]

From the results obtained, the experimental rate equation can be represented as follows: In the case of a lower concentration of formaldehyde than usual:

$$R_2 = \frac{-d[F]}{dt}$$
$$= k_2[C_6H_5CONH_2][CH_2O][OH^-] \qquad (2)$$

By a higher concentration of formaldehyde than usual;

$$R_1 = \frac{-d[F]}{dt} = k_1[C_6H_5CONH_2][OH^-] \qquad (3)$$

The Effect of the Polar Character on the Reaction Rate. — The electron-releasing or attracting group substituted in the benzene

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[4] Part LXVII of this series: M. Imoto and A. Ninagawa, This Bulletin, 36, 1508 (1963).

nucleus of benzamide was expected to have a strong effect on the rate of the reaction. While the concentration of the substituted benzamide was kept constant (0.05 mol./l.), the relationship between R and $[F]_0$ was measured. The results obtained are illustrated by Fig. 4.

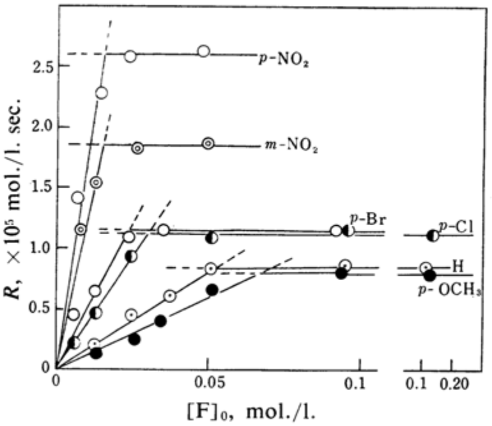

Fig. 4. The relationship between the initial concentration of formaldehyde and R. $[X\text{-}C_6H_4CONH_2]=0.05$ mol./l. Catalyst $=0.6$ mi./50 ml.

From the results of the experiments illustrated in Fig. 4, the reaction constants, $k_1[OH^-]$ and $k_2[OH^-]$, were calculated. (Table II).

These values of $k[OH^-]$ were correlated with Hammett's equation. The linear relationship shown in Fig. 5 was obtained.

TABLE II. RATE CONSTANTS FOR SUBSTITUTED BENZAMIDE

Benzamide	$k_1[OH^-]$	$k_2[OH^-]$	σ
p-OCH$_3$	1.60	1.92	-0.268
H	1.80	3.51	0.0
p-Cl	2.32	6.91	$+0.227$
p-Br	2.40	9.61	$+0.232$
m-NO$_2$	3.72	38.5	$+0.710$
p-NO$_2$	5.28	41.8	$+0.778$

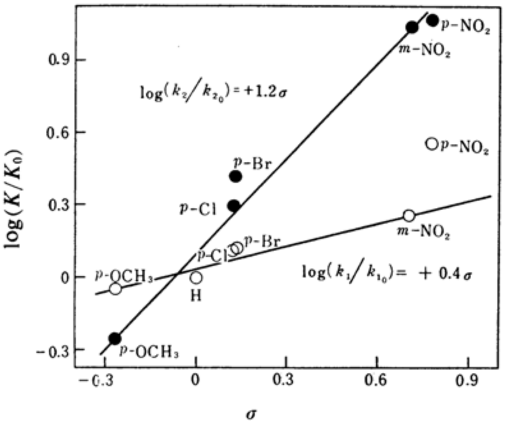

Fig. 5. Plots for Hammett's equation.

The Reaction Mechanism of Benzamide with Formaldehyde in the Presence of a Base Catalyst.—Ugelstadt has concluded that the reaction of benzamide proceeded via three steps:

i) $R\text{-}CONH_2+B \rightarrow R\text{-}CONH^- + BH^+$

ii) $R\text{-}CONH^- + CH_2O \rightarrow RCONH\text{-}CH_2O^-$

iii) $RCONHCH_2O^- + BH^+$
$\rightarrow RCONHCH_2OH + B$

Of these three steps, it is clear that iii is not the rate-determining step. Ugelstadt considered step ii to be rate-determining and kinetically derived Eq. 1. However, this conception can not completely interpret the present results.

Step i may be concluded to be the slowest step from the consideration that, when an electron-attracting group is introduced into the phenyl nucleus, the release of protons from the NH$_2$ group of benzamide by the attack of hydroxyl ions becomes easier. This conception may be experimentally demonstrated, as in Fig. 5. In the range of the lower, and also of the higher, concentrations of formaldehyde, the signs of ρ were positive. The values of ρ were estimated to be $+1.2$ and $+0.4$ respectively.

The mechanism presented above may be classified as S$_E$1, namely, a unimolecular electrophilic substitution. The existence of Eq. 2 in the range of the lower concentration of formaldehyde was, apparently, consistent with the theory of S$_E$2. However, a new conception was applicable as follows: By step ii $X\text{-}C_6H_4CONH^-$ reacts immediately with formaldehyde, which exists in the solvated cage. Accordingly, until formaldehyde reaches the saturating concentration in the solvated cage, the rate of the consumption of formaldehyde is dependent on the added amounts of formaldehyde. In case the concentration of formaldehyde is higher than the saturated concentration in the solvated cage, the rate of the consumption of formaldehyde is independent of the amounts of formaldehyde.

It can be accepted that the bending points in the curves in Fig. 5 may be indicative of the saturated concentration of formaldehyde in the solvated cage. These points were obtained by extending the upward and lying lines to the crossing points. The concentrations of formaldehyde at this point were denoted as $[F]_c$.

In the ion of $X\text{-}C_6H_4CONH^-$, if X is an electron-attracting group, the electron-density about the nitrogen atom becomes smaller than when an electron-releasing group such as X is present. It is to be anticipated that the smaller

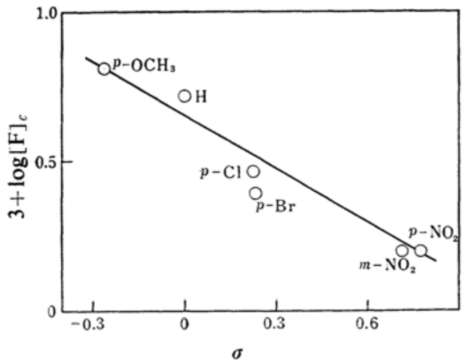

Fig. 6. The relation of the saturating concentration of formaldehyde in solvated cage with Hammett's constants.

the electron-density about the nitrogen atom, the smaller the solvating ability of the ion of $X\text{-}C_6H_4CONH^-$. The values of $[F]_c$ were estimated as follows: *p*-OCH_3 0.065 mol./l., H 0.052, *p*-Cl 0.0305, *p*-Br 0.024, *m*-NO_2 0.015, and *p*-NO_2 0.015. The results obtained here were applied to Hammett's equation, as Fig. 6 shows. These results strongly supported the conception of S_E1.

Summary

The mechanism of the reaction of the substituted benzamides with formaldehye in dioxane-water (1 : 1) in the presence of sodium hydroxide has been studied kinetically. Equations 2 and 3 have been obtained. An electron-attracting group increased the rate of the reaction, while an electron-releasing group decreased it. The reaction rates fit Hammett's equation. It was concluded that the S_E1-mechanism is suitable for interpreting the results obtained.

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