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Studies on the Reaction between Polynitrobenzene Compounds and Active Methylene Groups. X.[1] Kinetic Study on the Janovsky Reaction of Trinitrobenzene with Acetone in Methanol[2]

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The rate-determining step of the Janovsky reaction of 1,3,5-trinitrobenzene with acetone in methanol is not the deprotonating step but the attacking one of acetonate ion. Kinetic and thermodynamic parameters of the formation and the decomposition of the Janovsky complex I are determined and discussed.

The rate-determining steps of the base-catalized reactions of carbonyl compounds are, in general, the formation of their enolate ions.[4] In the Zimmermann reaction of *m*-dinitrobenzene with active methylene compound, Nambara, *et al.*[5] inferred that for simple ketones the rate-determining step is the deprotonation of the active methylene group and for fused ring systems such as oxosteroid the rate of Zimmermann color development depends not only on the relative ease of the deprotonation of α-methylene but also on the steric requirement of bulky 2,4-dinitrophenyl group to be introduced. Klyne, *et al.*[6] described that rates of the Zimmermann reactions for some of the steroid ketones can be roughly correlated with their known properties on the basis of enolization as the rate-controlling step. But these reports are semi-quantitative experiments and none of the precise kinetic study on the Zimmermann reaction has been done. The reason may be due to the fact that this reaction is very complicated accompanying the fading reaction by alkali and light. In this paper the authors deal the Janovsky reaction of 1,3,5-trinitrobenzene (TNB) with acetone in methanol, in which the color developed is so stable that the kinetics of this reaction can be analyzed without much difficulty. Since the Zimmerman reaction proceeds *via* the Janovsky type intermediate,[7] this kinetics may give valuable informations to the mechanism of the Zimmermann reaction.

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1) Part IX: M. Kimura, N. Obi and M. Kawazoi, *Chem. Pharm. Bull.* (Tokyo), **20**, 452 (1972).
2) A part of this paper was presented at the 89th Annual Meeting of the Pharmaceutical Society of Japan, Nagoya, Apr. 1969.
3) Location: *Nishi-6-chome, Kita-12-jo, Sapporo.*
4) R.P. Bell and H.C. Longuet-Higgins, *J. Chem. Soc.*, **1946**, 636; S.K. Hsü, C.K. Ingold and C.L. Wilson, *ibid.*, **1938**, 78; S.K. Hsü and C.L. Wilson, *ibid.*, **1936**, 623; P.D. Bartlett, *J. Am. Chem. Soc.*, **56**, 967 (1934).
5) M. Katō, M. Ohnishi and T. Nambara, *Chem. Pharm. Bull.* (Tokyo), **16**, 2398 (1968).
6) D.N. Kirk, W. Klyne and A. Mudd, *J. Chem. Soc.* (*C*), **1968**, 2269.
7) T. Nambara, *Japan Analyst* (Bunseki Kagaku), **13**, 184 (1964).

Experimental

The solvents and reagents were purified and standardized as previously described[1,8] and the solvents were used after reflux for several minutes in flasks equipped with soda-lime tubes. The methanolic solutions of the reagents for color development were maintained at the reaction temperature within ±0.1° in a thermostat before use. The reaction was followed by measuring the optical absorbance at 463 mμ using Hitachi EPS-3T spectrophotometer and the procedure was as follows: 1 ml of sodium methoxide in methanol was added to a mixture of 2 ml of TNB in methanol and 1 ml of acetone in methanol in the cuvette with a stopper in the thermostatted cell compartment of the spectrophotometer which was maintained at the reaction temperature within ±0.5°. In the experiment shown in Fig. 1a Hitachi RSP-2 rapid scan spectrophotometer was used employing the stopped flow method. All the procedures were taken as carefully as possible to avoid the disturbance by carbon dioxide in the air.

Result and Discussion

Sodium methoxide was added to TNB and acetone in methanol and the absorption spectrum was measured along the time-course. The absorption maxima due to the Janovsky complex I, were found at 463 and 556 mμ. Immediately after the start of the reaction, however, the other maxima due to the complex II were detected at 425 and 495 mμ by using the rapid scan type spectrophotometer (Fig. 1). The order of the addition of the reagents did not influence the color development in contrast to the Janovsky reaction of 2,4,6-trinitroanisole in acetone.[8] This fact shows that diacetone alcohol is not formed. It is very interesting that diacetone alcohol is not formed in methanol and the formation of II can be detected by using only the rapid scan spectrophotometer.[9]

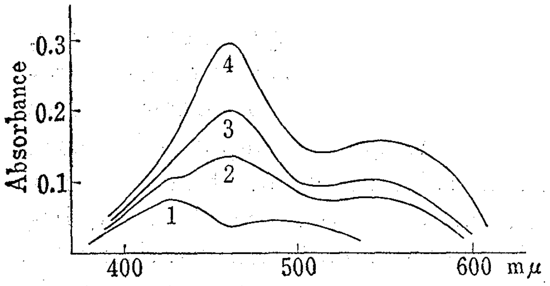

Fig. 1. Absorption Spectra of Janovsky Reaction of TNB with Acetone in Methanol

condition: $[\mathrm{TNB}]_{st}=3\times10^{-5}\mathrm{M}$, $[\mathrm{CH_3COCH_3}]_{st}=5\times10^{-1}\mathrm{M}$, $[\mathrm{MeO^-}]_{st}=3\times10^{-3}\mathrm{M}$
time after the start of the reaction: 1) 5 sec, 2) 30 sec, 3) 1 min, 4) 2 min

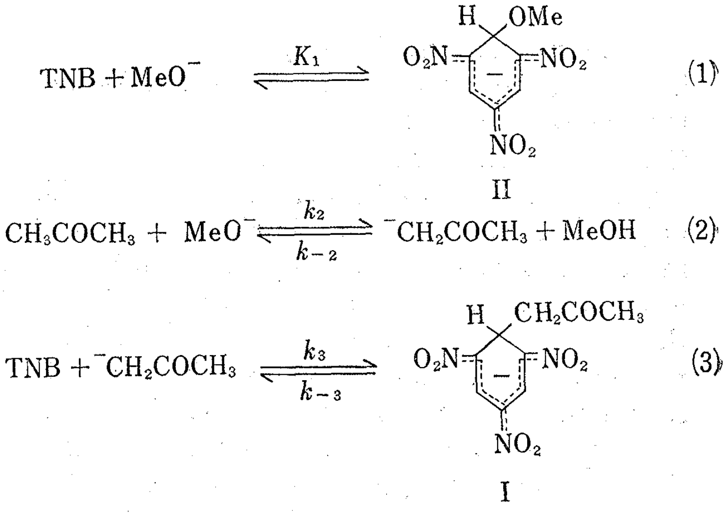

Chart 1

Consequently, the reactions in Chart 1 may be considered. Since reaction (1) is rapid in methanol,[11] kinetic interest is whether the rate-determining step is the forward reaction in reaction (2) or not. The rate of the formation of I is given by equation (4).

$$d[\mathrm{I}]/dt = k_3[^-\mathrm{CH_2COCH_3}][\mathrm{TNB}] - k_{-3}[\mathrm{I}] \qquad (4)$$

The rate of acetonate ion formation is as follows.

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[8] M. Kimura, N. Obi and M. Kawazoi, *Chem. Pharm. Bull.* (Tokyo), **17**, 531 (1969).
[9] The reason may be as follows: since the anion of diacetone alcohol and II are large polarizable anions, they must be far less stable in methanol than in acetone.[10]
[10] A.J. Parker, *Quart. Rev.* (London), **16**, 163 (1962).
[11] V. Gold and C.H. Rochester, *J. Chem. Soc.*, **1964**, 1692.

$$d[^{-}\mathrm{CH_2COCH_3}]/dt = k_2[\mathrm{CH_3COCH_3}][\mathrm{MeO^-}] - k_{-2}[^{-}\mathrm{CH_2COCH_3}] - k_3[\mathrm{TNB}][^{-}\mathrm{CH_2COCH_3}] + k_{-3}[\mathrm{I}] \qquad (5)$$

From the steady state treatment of equation (5) the concentration of acetonate ion is shown as follows.

$$[^{-}\mathrm{CH_2COCH_3}] = \frac{k_2[\mathrm{CH_3COCH_3}][\mathrm{MeO^-}]+k_{-3}[\mathrm{I}]}{k_{-2}+k_3[\mathrm{TNB}]} \qquad (6)$$

Substitution of the above equation in equation (4) yields the following equation.

$$d[\mathrm{I}]/dt = \frac{k_2k_3[\mathrm{CH_3COCH_3}][\mathrm{MeO^-}][\mathrm{TNB}]-k_{-2}k_{-3}[\mathrm{I}]}{k_{-2}+k_3[\mathrm{TNB}]} \qquad (7)$$

If $k_{-2} \ll k_3[\mathrm{TNB}]$, equation (7) is as follows.

$$d[\mathrm{I}]/dt = k_2[\mathrm{CH_3COCH_3}][\mathrm{MeO^-}] - k_{-2}k_{-3}[\mathrm{I}]/k_3[\mathrm{TNB}] \qquad (8)$$

If $k_{-2} \gg k_3[\mathrm{TNB}]$, equation (7) is as follows.

$$\begin{aligned} d[\mathrm{I}]/dt &= k_2k_3[\mathrm{CH_3COCH_3}][\mathrm{MeO^-}][\mathrm{TNB}]/k_{-2}-k_{-3}[\mathrm{I}] \\ &= K_2k_3[\mathrm{CH_3COCH_3}][\mathrm{MeO^-}][\mathrm{TNB}] - k_{-3}[\mathrm{I}] \end{aligned} \qquad (9)$$

The initial rate of the formation of I is the zero order with respect to the concentration of TNB in the case of equation (8) and the first order in equation (9). In the experiment shown in Fig. 2 the initial rate of the color development depends upon the concentration of TNB. So the rate of the formation of I seems to depend on equation (9). This suggests that the rate determining step of the Zimmermann reaction may not be the deprotonation of acetone. The kinetic study was, therefore, practiced depending on equation (9).

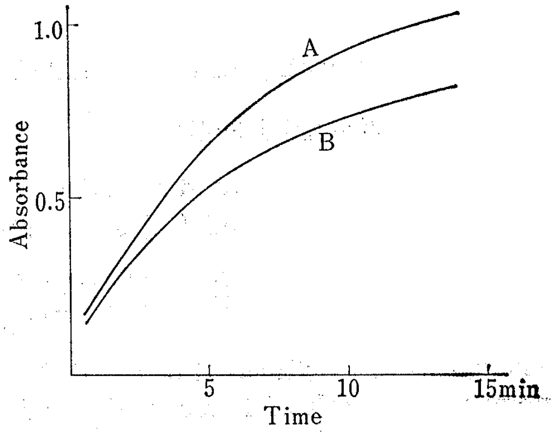


Fig. 2. Rate of Color Development

condition: 463 mμ; at 15°; $[\mathrm{MeO^-}]_{st}$ 4.71×10^{-3}M; $[\mathrm{CH_3COCH_3}]_{st}$ 5.00×10^{-1}M; $[\mathrm{TNB}]_{st}$ 4.00×10^{-5}M—A, 3.00×10^{-5}M—B

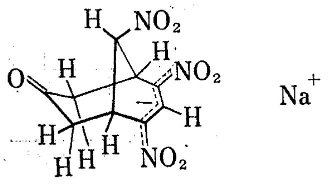
The stoichiometric concentrations of acetone, alkali and TNB are expressed as follows.

$$[\mathrm{CH_3COCH_3}]_{st} = [\mathrm{CH_3COCH_3}] + [^{-}\mathrm{CH_2COCH_3}] + [\mathrm{I}] \qquad (10)$$

$$[\mathrm{MeO^-}]_{st} = [\mathrm{MeO^-}] + [^{-}\mathrm{CH_2COCH_3}] + [\mathrm{II}] + [\mathrm{I}] \qquad (11)$$

$$[\mathrm{TNB}]_{st} = [\mathrm{TNB}] + [\mathrm{II}] + [\mathrm{I}] \qquad (12)$$

Under the condition where the stoichiometric concentrations of acetone, alkali and TNB are approximately 10^{-1}, 10^{-3} and 10^{-5}M, respectively, no reaction other than equations (1), (2) and (3) occurs[12] and equations (10) and (11) can be simplified as equations (13) and (14), respectively.



III

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[12] In this experiment none of the concentrations of three reagents, TNB, MeO$^-$ and acetone is able to use large excess compared with the other two reagents enough to apply the isolation method. Because in the large excess, TNB may react with I forming the Zimmermann complex and MeO$^-$ may react with I forming III[13] and acetone may extremely change the property of solvent.

[13] M.J. Strauss and H. Schran, *J. Am. Chem. Soc.*, **91**, 3974 (1969); K. Kohashi, Y. Ohkura and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **18**, 2151 (1970).

$$[\mathrm{CH_3COCH_3}]_{\mathrm{st}} = [\mathrm{CH_3COCH_3}] \tag{13}$$

$$[\mathrm{MeO^-}]_{\mathrm{st}} = [\mathrm{MeO^-}] \tag{14}$$

The equilibrium constant of equation (1) is written as follows.

$$K_1 = \frac{[\mathrm{II}]}{[\mathrm{TNB}][\mathrm{MeO^-}]} = \frac{[\mathrm{II}]}{[\mathrm{TNB}][\mathrm{MeO^-}]_{\mathrm{st}}} \tag{15}$$

By combining equation (12) with (15), the concentration of TNB is expressed as follows.

$$[\mathrm{TNB}] = \frac{[\mathrm{TNB}]_{\mathrm{st}} - [\mathrm{I}]}{1 + K_1[\mathrm{MeO^-}]_{\mathrm{st}}} \tag{16}$$

When equations (13), (14) and (16) are substituted in equation (9), the following equation is obtained.

$$d[\mathrm{I}]/dt = \frac{K_2k_3[\mathrm{MeO^-}]_{\mathrm{st}}[\mathrm{CH_3COCH_3}]_{\mathrm{st}}}{1 + K_1[\mathrm{MeO^-}]_{\mathrm{st}}}([\mathrm{TNB}]_{\mathrm{st}} - [\mathrm{I}]) - k_{-3}[\mathrm{I}] \tag{17}$$

Integration of the above equation gives equation (18).

$$\begin{aligned} &\log\{[\mathrm{TNB}]_{\mathrm{st}} - (1 + k_{-3}/mK_2k_3)[\mathrm{I}]\} \\ &\qquad = -0.4343(mK_2k_3 + k_{-3})t + \log[\mathrm{TNB}]_{\mathrm{st}} \end{aligned} \tag{18}$$

where m is as follows.

$$m = \frac{[\mathrm{MeO^-}]_{\mathrm{st}}[\mathrm{CH_3COCH_3}]_{\mathrm{st}}}{1 + K_1[\mathrm{MeO^-}]_{\mathrm{st}}} \tag{19}$$

The concentration of I is calculated from equation (20).

$$E = \varepsilon_{\mathrm{II}}[\mathrm{II}] + \varepsilon_{\mathrm{I}}[\mathrm{I}] \tag{20}$$

where E is absorbance, and $\varepsilon_{\mathrm{II}}$ and ε_{I} are the extinction coefficients of II and I, respectively. When equations (15) and (16) are combined with equation (20), equation (21) is obtained.

$$[\mathrm{I}] = \frac{E(1 + K_1[\mathrm{MeO^-}]_{\mathrm{st}}) - \varepsilon_{\mathrm{II}}K_1[\mathrm{MeO^-}]_{\mathrm{st}}[\mathrm{TNB}]_{\mathrm{st}}}{\varepsilon_{\mathrm{I}} + K_1[\mathrm{MeO^-}]_{\mathrm{st}}(\varepsilon_{\mathrm{I}} - \varepsilon_{\mathrm{II}})} \tag{21}$$

Though wave length could be selected arbitrarily in visible region, 463 mμ that is the maximum wave length of I was used to minimize the experimental error. ε_{I} was estimated as $2.90 \times 10^4 \mathrm{M^{-1}cm^{-1}}$ at that wave length by the method reported previously.[8] $\varepsilon_{\mathrm{II}}$ was reported as $3.12 \times 10^4 \mathrm{M^{-1}cm^{-1}}$ at 425 mμ—the maximum wave length of II in methanol.[11] From the absorption curve of sodium salt of II $\varepsilon_{\mathrm{II}}$ at 463 mμ was estimated as $1.98 \times 10^4 \mathrm{M^{-1}cm^{-1}}$. Though the values of ε_{I} and $\varepsilon_{\mathrm{II}}$ were obtained at room temperature and the former is the value in methanol containing $5 \times 10^{-1}\mathrm{M}$ of acetone, they are used in this paper at other conditions, for the experimental conditions were similar to the condition at which ε_{I} and $\varepsilon_{\mathrm{II}}$ were obtained.

In the kinetic run of the Janovsky reaction, the extrapolation of the absorbance at 463 mμ to time zero gives some absorbance corresponding to the concentration of II in equilibrium condition established by reaction 1. Thus, K_1 is able to be calculated by employing equation (15):

$$\begin{aligned} K_1 &= \frac{[\mathrm{II}]}{[\mathrm{TNB}][\mathrm{MeO^-}]_{\mathrm{st}}} = \frac{[\mathrm{II}]}{([\mathrm{TNB}]_{\mathrm{st}} - [\mathrm{II}])[\mathrm{MeO^-}]_{\mathrm{st}}} \\ &= \frac{E_0/\varepsilon_{\mathrm{II}}}{([\mathrm{TNB}]_{\mathrm{st}} - E_0/\varepsilon_{\mathrm{II}})[\mathrm{MeO^-}]_{\mathrm{st}}} \end{aligned} \tag{22}$$

where E_0 is the absorbance at time zero. The results calculated are shown in Fig. 3. K_1 in methanol is in fairly good agreement with the Gold's datum ($15.4\mathrm{M^{-1}}$ at 28°[11]) though slightly differs from the Bernasconi's one (23.1M^{-1} at 25°[14]). The ΔH value of reaction 1 in methanol was calculated as 3.1 kcal mol^{-1} which agrees roughly with the Bernasconi's datum (1.0±1.5 kcal mol^{-1} [14]). K_1 increases with the rise of temperature and with the increase of the concentration of acetone. This phenomenon may be due to the solvation of acetone to II. Although acetone is not typical dipolar aprotic solvent as dimethylsulfoxide, it may solvate to large polarizable anion in fairly high degree.[10]

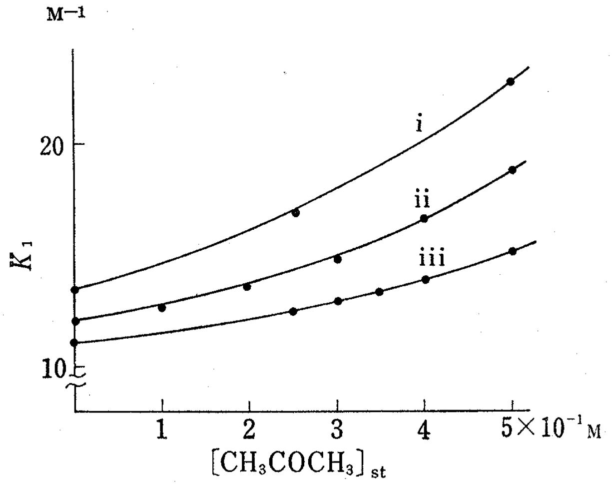

Fig. 3. Formation Constant of II

temperature: i) 20°, ii) 15°, iii) 10°

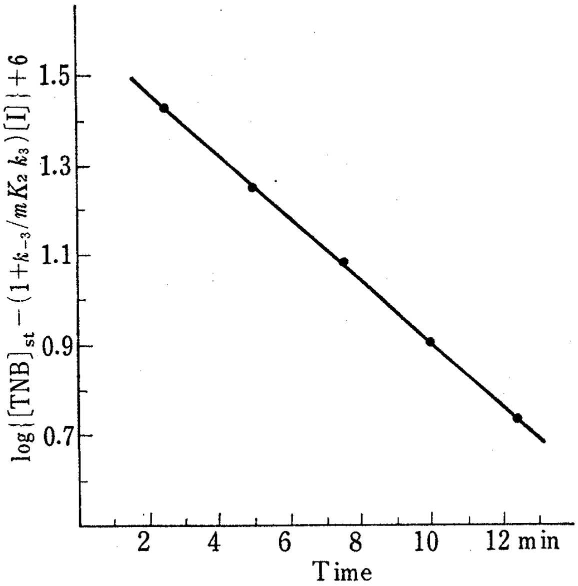

Fig. 4. Plots of log $\{[\text{TNB}]_{\text{st}}-(1+k_{-3}/mK_2k_3)[\text{I}]\}$ against t

$[\text{TNB}]_{\text{st}}=4.00\times10^{-5}\text{M}$, $[\text{MeO}^-]_{\text{st}}=4.71\times10^{-3}\text{M}$, $[\text{CH}_3\text{COCH}_3]_{\text{st}}=5.00\times10^{-1}\text{M}$ temperature: 15° $k_{-3}/mK_2k_3=1.4\times10^{-2}$

Using ε_{I}, ε_{II} and the value of K_1 the concentration of I was calculated from the absorbance by employing equation (21). Using this value the term k_{-3}/mK_2k_3 in equation (18) was determined by trial-and-error method so as to give the best straight line in plotting the value of the left hand side of equation (18) against time t. From the slope of the plots and k_{-3}/mK_2k_3, K_2k_3 and k_{-3} could be determined. In the case of A in Fig. 2, if the term k_{-3}/mK_2k_3 is determined as 1.4×10^{-2}, the best straight line is obtained as shown in Fig. 4. K_2k_3 and k_{-3} are calculated as $7.32\times10\text{M}^{-2}\text{min}^{-1}$ and $2.2\times10^{-3}\ \text{min}^{-1}$, respectively. K_2 is unknown but it was reported as 10^{-20}M^{-1} in water.[15] So k_3 may be very large.

Table I. K_2k_3 and k_{-3} ($[\text{CH}_3\text{COCH}_3]_{\text{st}}=5\times10^{-1}\text{M}$, 15°)

$[\text{TNB}]_{\text{st}}\times10^5$ (M)	$[\text{MeO}^-]_{\text{st}}\times10^3$ (M)	$K_2k_3\times10^{-1}$ ($\text{M}^{-2}\ \text{min}^{-1}$)	$k_{-3}\times10^3$ (min^{-1})
3.00	3.52	7.65	1.8
3.00	4.71	7.98	2.4
3.00	4.71	6.86	5.4
3.50	3.52	8.31	1.1
4.00	3.52	6.96	1.7
4.00	4.71	7.60	3.1
4.00	4.71	7.32	2.2
	mean	7.52±0.41[a]	2.5±1.0[a]

[a] ±shows the average deviation

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[14] C.F. Bernasconi, *J. Am. Chem. Soc.*, 92, 4682 (1970).

[15] R.P. Bell, *Trans. Faraday Soc.*, 39, 253 (1943).

K_2 and k_{-3} are independent of the concentration of acetone in equation (18). Nevertheless they are influenced by its concentration as K_1 is. First, in the condition in which the concentration of acetone was fixed at 5×10^{-1}M, the Janovsky reaction was performed in various concentrations of TNB and sodium methoxide at 15° and the absorbance was measured at 463 mμ along the time-course. Then K_2k_3 and k_{-3} were calculated as mentioned above. The results are given in Table I. The values at 10° and 20° are shown in Table II together with the results at 15°. The activation energies of the formation and decomposition of the Janovsky complex I obtained from the Arrhenius plots (Fig. 5) are 12.6 and 38.3 kcal mol^{-1}, respectively. The entropies of activation of these reactions are −8 and +61 cal deg^{-1}, respectively. The small activation energy of the formation reaction shows the effective solvation at the transition state and the large activation energy of the decomposition reaction shows the large stability of I.

TABLE II. K_2k_3 and k_{-3} at 10, 15 and 20° ($[CH_3COCH_3]_{st} = 5.00 \times 10^{-1}$M)

Temperature (°C)	No. of Runs	$K_2k_3 \times 10^{-1}$ (M^{-2} min^{-1})	$k_{-3} \times 10^3$ (min^{-1})	$K_2K_3 \times 10^{-4}$ (M^{-2})
10	2	4.96±0.12[a)]	0.79±0.16[a)]	6.3
15	7	7.52±0.41	2.5 ±1.0	3.0
20	4	10.57±0.03	7.9 ±1.8	1.3

a) ±shows the average deviation

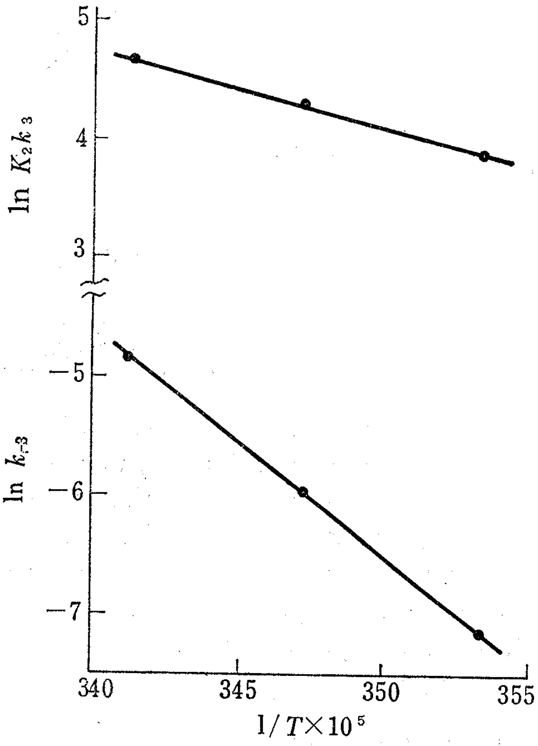

Fig. 5. Arrhenius Plots of K_2k_3 and k_3

Second, the experiment in which the concentration of acetone was changed was done. These results are given in Table III, Fig. 6 and 7. As the concentration of acetone increases, K_2k_3 increases gently at first and steeply later. The behavior of k_{-3} is in contrast to K_2k_3. This shows that the solvating feature of transition state is affected by fairly high concentration of acetone but I is effectively solvated by only small content of acetone.

TABLE III. K_2k_3 and k_{-3} at 15° in Various Concentration of Acetone

$[CH_3COCH_3]_{st} \times 10$ (M)	No. of runs	$K_2k_3 \times 10^{-1}$ (M^{-2} min^{-1})	$k_{-3} \times 10^3$ (min^{-1})	$K_2K_3 \times 10^{-4}$ (M^{-2})
1	3	6.03±0.16[a)]	6.0±1.4[a)]	1.0
2	4	6.01±0.13	4.0±0.7	1.5
4	3	6.53±0.39	2.3±0.8	2.8
5	7	7.52±0.41	2.5±1.0	3.0

a) ±shows the average deviation

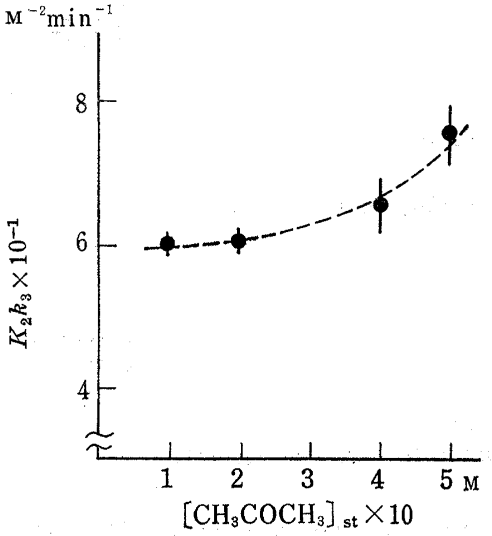

Fig. 6. Plots of K_2k_3 against the Concentration of Acetone

-●-: shows the average deviation

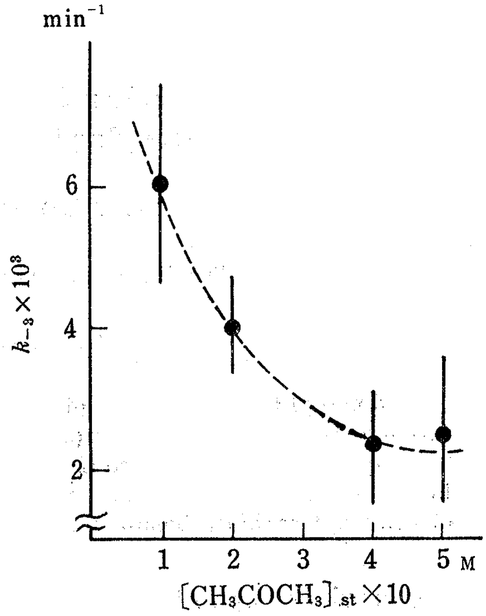

Fig. 7. Plots of k_{-3} against the Concentration of Acetone

-●-: shows the average deviation

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