mixture of alcohol and water brought the melting point to 94.5–95°.

*2-Acetoxy-1-phenylethyl acetylmandelate* (XIX). The remainder of the styrene oxide–acetic acid reaction mixture (see directly above) was allowed to remain at room temperature for several days and was then heated on a steam bath for 3 hr. to effect as complete rearrangement as possible to 2-acetoxy-1-phenylethanol (X). The acetic acid was distilled at atmospheric pressure, the last traces being removed under reduced pressure in a rotory evaporator, to yield 11.11 g. of glycol monoacetate. A portion was distilled at 1 mm. pressure and the following fractions were collected: (1) 1.084 g., b.p. 97–107°; (2) 3.54 g., b.p. 108–110°; (3) 0.34 g., b.p. 110–208°. Acylation of a portion (2.17 g.) of fraction 2 was carried out with 3.19 g. (14.8 mmoles) of acetylmandelyl chloride in the same manner as described in the above preparation, except that the acylation mixture was heated on a steam bath for 1 hr. The dark red oil (4.03 g.) which resulted was distilled at 1 mm. pressure. The rate of distillation was extremely slow and the thermometer was not in equilibrium with the vapor. Thus, no temperatures can be recorded. The infrared spectrum of one of the collected fractions (0.96 g.) exhibited carbonyl absorption at 1736 cm.$^{-1}$ (chloroform) and aromatic C—H bonding absorption at 757 and 689 cm.$^{-1}$ (film). This spectrum is easily distinguishable from that of the isomeric solid ester (XVIII) (see above). The residue from the distillation weighed 2.11 g. and its infrared spectrum as a film and in carbon disulfide solution indicated that it contained predominantly the isomeric ester (XVIII).

*Styrene glycol.* To a slurry of 0.368 g. (9.5 mmoles) of lithium aluminum hydride in 75 ml. of anhydrous ether, an ethereal solution of 1.70 g. (9.5 mmoles) of phenacyl acetate was added dropwise at such a rate as to maintain gentle refluxing. The reaction mixture was then heated for another hour at reflux. Water was slowly added to the cooled reaction mixture in order to decompose the excess hydride. Dilute sulfuric acid was added to dissolve the aluminum hydroxide. The ether layer was separated and the aqueous layer extracted six times with methylene chloride. The combined organic extract was dried over sodium sulfate and evaporated to yield 0.604 g. (4.4 mmoles, 46%) of crystalline material, m.p. 60–65°. Several recrystallizations from benzene–petroleum ether (b.p. 64–66°) raised the m.p. to 64.5–65.5° (lit.[28] m.p. 65–67°).

*Acknowledgment.* We wish to thank the National Science Foundation and the National Institutes of Health for their help in the purchase of the infrared and ultraviolet spectrophotometers, respectively.

PITTSBURGH 13, PA.

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[28] S. Winstein and L. L. Ingraham, *J. Am. Chem. Soc.*, **77**, 1738 (1955).

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[CONTRIBUTION FROM TOKYO INSTITUTE OF TECHNOLOGY]

# The Rate of the Reaction of Isocyanates with Alcohols. II

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In order to determine whether or not the equation proposed previously, $dx/dt = k_1(a - x)(b - x)^2 + k_2x(a - x)(b - x) + k_3(\text{cat.})(a - x)(b - x)$, is exactly applicable, the reactions of three isocyanates, *e.g.*, ethyl, propenyl, and phenyl isocyanates, with alcohols were studied in further detail. In noncatalyzed reactions, the $k_1$ value decreased a little and the $k_2$ value decreased considerably with increasing initial concentration. In the reaction carried out with a certain concentration of phenyl isocyanate and triethylamine, the $k_3$ value also decreased with increasing concentration of alcohols. The hydrogen bonding in the solutions was also investigated by infrared spectroscopy. From both results, kinetic and spectroscopic, it was concluded that in the reaction of isocyanates with alcohols the intermediate complex mechanism was operative, that hydrogen bonding among the reactants, the products, and the solvent was involved, and that the equation described above was not exactly applicable.

In previous communications,[1-3] the studies on 1-alkenyl isocyanates have been reported. The isocyanate is one of the staple compounds in organic chemistry, especially in the field of polymer chemistry, and it is also interesting to study the mechanism and kinetics of the reaction of the NCO group with another functional group. The kinetics and mechanism of the reaction with the OH group have been studied by many authors,[4-11] and it is commonly accepted that the reaction follows second-order kinetics,

$$dx/dt = k(a - x)^2 \qquad kt = x/a(a - x) \tag{1a}$$

$$dx/dt = k(a - x)(b - x) \qquad kt = \frac{2.303}{a - b}\log\frac{b(a - x)}{a(b - x)} \tag{1b}$$

However, this author proposed third-order kinetics and the following equation,[3]

$$dx/dt = k_1(a - x)(b - x)^2 + k_2x(a - x)(b - x) + k_3(\text{cat.})(a - x)(b - x) \tag{2}$$

By this mechanism the reaction of isocyanates with alcohols was explained satisfactorily, but it was not determined whether the $k_1$ and $k_2$ values in

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[1] M. Sato, *J. Org. Chem.*, **26**, 770 (1961).

[2] K. Orita, M. Sato, and Y. Iwakura, *J. Chem. Soc. Japan, Ind. Chem. Sect.* (*Kogyo Kagaku Zasshi*), **64**, 1404 (1961).

[3] M. Sato, *J. Am. Chem. Soc.*, **82**, 3893 (1960).

[4] J. W. Baker and J. B. Holdsworth, *J. Chem. Soc.*, 713 (1947).

[5] J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 9 (1949).

[6] J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 19 (1949).

[7] J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 27 (1949).

[8] E. Dyer, H. A. Taylor, S. J. Mason, and J. Samson, *J. Am. Chem. Soc.*, **71**, 4106 (1949).

[9] S. Ephrain, A. E. Woodward, and R. B. Mesrobian, *J. Am. Chem. Soc.*, **80**, 1326 (1958).

[10] J. Burkus and C. F. Eckert, *J. Am. Chem. Soc.*, **80**, 5948 (1958).

[11] A. Farkas and K. G. Flynn, *J. Am. Chem. Soc.*, **82**, 642 (1960).

Equation 2 vary with reactant concentrations. In catalyzed reactions, on the other hand, the second-order rate constant varied with the concentration of the alcohol when a certain concentration of an amine was used as a catalyst. By the third-order kinetics, the $k_3$(cat.) value should not vary and the reaction should follow apparently second-order kinetics, because the relation, $k_1$(alc.)$+k_2$(urethan) $\ll k_3$ (cat.), is held when the catalyst is used in a magnitude of about one tenth the concentrations of the isocyanate and the alcohol.

Recently, the reaction of phenyl isocyanate with methanol in various solvents was studied by Ephrain *et al.*,[9] and it was found that different rate constants were obtained and that both positive and negative deviations from a second-order rate plot occurred in changing solvents. From these results, they proposed a new mechanism for the reaction of isocyanates with alcohols. It seems that the theory is novel, but it is not acceptable, since the amount of the complex, $(ROH)_2$ or (ROH solvent), increases with increasing concentration of the alcohol or the hydrogen bond-forming ability of the solvent, and therefore, the $k$ value should increase with the increase of the concentration and the ability.

It is well known from the investigation of infrared spectra that alcohols in nonpolar solvents associate intermolecularly to some extent to produce dimer, trimer, etc., and that alcohols in polar solvents associate with the solvents in addition to the former types. Badger and his coworker[12] showed that the magnitude of the shift of the OH fundamental, due to hydrogen bonding, could be used as a measure of the strength of the hydrogen bond formed, being about 35 cm.$^{-1}$/kcal. It is, therefore, considered that the reactivity of the alcohol varies with the state, because the activation energies of hydrogen bonded alcohols for urethan formation are always greater by the dissociation energy than that of the free alcohol. It was considered that the hydrogen bonding in the solution was connected with the $k$ values.

In this paper, a number of experiments were carried out in order to explain the facts mentioned above; the infrared spectra of the solutions containing methanol, methyl *N*-ethyl carbamate, methanol–methyl *N*-ethyl carbamate, and phenyl isocyanate–methyl *N*-ethyl carbamate in di-*n*-butyl ether were also measured. From both results, kinetic and spectroscopic, it was concluded that the changes in the $k_1$ and $k_3$ values are due to the hydrogen bonding of the alcohol, and that the change in the $k_2$ value is mainly due to the intermolecular association of the urethan and partly due to the hydrogen bonding of the alcohol described previously.

## EXPERIMENTAL

The materials and kinetic method were the same as described in the previous paper.[3] The infrared spectra were measured with a Perkin-Elmer Model 112 spectrophotometer using a lithium fluoride prism and a 0.1-mm. cell. The solutions containing methanol or methyl *N*-ethyl carbamate were as follows: 0.25*M*, 0.50*M*, and 1.0*M*. The solutions containing both the alcohol and the urethan were obtained by mixing the above solutions. The solution containing 0.50*M* of the urethan and 0.50*M* of phenyl isocyanate was immediately measured after it was prepared by mixing two 1.0*M* solutions.

## RESULTS

*Triethylamine-catalyzed reaction.* Temperature increase was observed in the triethylamine-catalyzed reactions of phenyl isocyanate with methanol at the same concentrations as used by Baker *et al.* Then the reaction of phenyl isocyanate with *n*-butyl alcohol was performed at low concentrations of both the reactants and the catalyst, because the $k_3$ value for *n*-butyl alcohol is smaller than that for methanol. The $k_3$(cat.) value was determined from a plot of the right-hand side of Equation 1 against $t$, because the first and second terms of Equation 2 for phenyl isocyanate may be neglected as compared with the third term. The results obtained were shown in Table I. The relationship that the $k_3$ value decreases with increasing the concentration of the alcohol is similar to those reported by other authors.

TABLE I

$k_3$ VALUES FOR TRIETHYLAMINE-CATALYZED REACTION OF PHENYL ISOCYANATE WITH *n*-BUTYL ALCOHOL AT 25°

| *n*-Butyl Alcohol, Mole/L. | $k_3$ (Cat.), Mole$^{-2}$L.$^2$ Min.$^{-1}$ | $k_3$, Mole$^{-2}$L.$^2$ Min.$^{-1}$ |
|---|---|---|
| PHENYL ISOCYANATE, 0.25*M*, TRIETHYLAMINE, 0.025*M* | | |
| 0.125 | $1.00 \times 10^{-1}$ | 4.0 |
| 0.25 | 0.77 | 3.1 |
| 0.50 | 0.65 | 2.6 |
| PHENYL ISOCYANATE, 0.125*M*, TRIETHYLAMINE, 0.0125*M* | | |
| 0.0625 | 0.51 | 4.1 |
| 0.125 | 0.46 | 3.7 |
| 0.25 | 0.43 | 3.4 |

*Spontaneous reaction.* The reactions of the typical isocyanates with methanol were studied, and the $k_1$ value was determined by extrapolating the $k$ value of Equation 1 to zero reaction time, because the $k_1a$ or $k_1b$ value at $t = 0$ is equal to the value of Equation 1. The $k_2$ value for the reaction of ethyl or propenyl isocyanate was determined from the following equations by the method described previously,[3]

$$k_2t = \frac{2.303}{a^2}\log\frac{x}{(a-x)} + \frac{1}{a(a-x)} + K \qquad (3a)$$

$$k_2t = \frac{2.303}{ab}\log x + \frac{2.303}{a(a-b)}\log(a-x) - \frac{2.303}{b(a-b)}\log(b-x) + K \qquad (3b)$$

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[12] R. M. Badger and S. H. Bauer, *J. Chem. Phys.*, 5, 839 (1937).

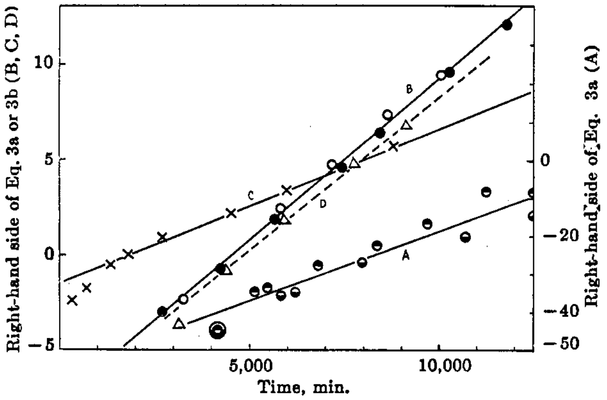

Fig. 1. Relation between right-hand side of Equation 3 and reaction time for ethyl isocyanate; solvent, di-*n*-butyl ether; reaction temp., 25 ± 0.05°. ◓◒, a = b = 0.25*M*; ○●, a = b = 0.50*M*; ×, a = b = 1.00*M*; △, a = 0.25*M*, b = 0.75*M*

*Phenyl isocyanate.* In the reaction of phenyl isocyanate with methanol, a plot of the right-hand side of Equation 1 against $t$ gave a straight line as obtained by other authors, but the $k$ value calculated from Equation 1 varied with reaction time agreeing with Ephraim's results. At high concentrations of both the reactants, the value decreased quite rapidly with reaction time and in other cases the decrease was not great. Therefore, the $k_1$ value was determined by extrapolating the $k$ value calculated from Equation 1 zero reaction time. The results obtained are shown in Table II. Excepting the last run, the $k_1$ values were nearly constant, but in this case the value was considerably greater than the others.

TABLE II

$k_1$ VALUE FOR SPONTANEOUS REACTION OF PHENYL ISOCYANATE WITH METHANOL AT 25°

| Phenyl Isocyanate, Mole/L. | Methanol, Mole/L. | $k_1a$ or $k_1b$, $\text{Mole}^{-2}\text{L.}^2$ $\text{Min.}^{-1}$ | $k_1$, $\text{Mole}^{-2}\text{L.}^2$ $\text{Min.}^{-1}$ |
|---|---|---|---|
| 0.186 | 0.186 | $0.18 \times 10^{-2}$ | $0.99 \times 10^{-2}$ |
| 0.25 | 0.25 | 0.24 | 0.96 |
| 0.50 | 0.50 | 0.53 | 1.06 |
| 0.75 | 0.75 | 0.71 | 0.95 |
| 0.25 | 0.75 | 0.65 | 0.87 |
| 0.75 | 0.25 | 0.38 | 1.50 |

*Ethyl isocyanate.* The rate of the reaction of ethyl isocyanate with methanol increased in all runs with reaction time. The $k_1$ value decreased a little. The straight line relationship of a plot of the right-hand side Equation 3 against $t$ was always obtained (see Fig. 1), but the $k_2$ value decreased considerably with increasing concentration. The results obtained are shown in Table III.

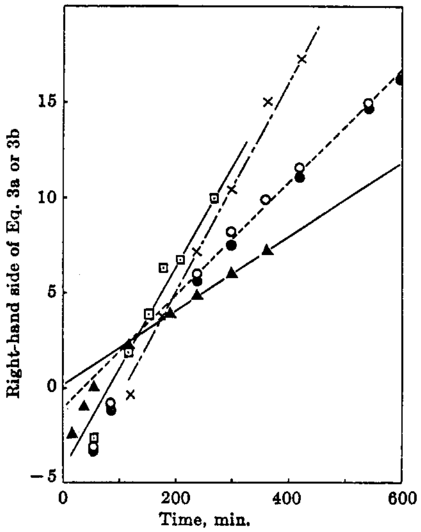

Fig. 2. Relation between right-hand side of Equation 3 and reaction time for propenyl isocyanate; solvent, di-*n*-butyl ether; reaction temp., 25 ± 0.05°. ○●, a = b = 0.50*M*; ▲, a = b = 0.75*M*; ×, a = 0.75*M*, b = 0.25*M*; ⊡, a = 0.25*M*, b = 0.75*M*

TABLE III

$k_1$ AND $k_2$ VALUES FOR SPONTANEOUS REACTION OF ETHYL ISOCYANATE WITH METHANOL AT 25°

| Ethyl Isocyanate, Mole/L. | Methanol, Mole/L. | $k_1a$ or $k_1b$, $\text{Mole}^{-2}\text{L.}^2$ $\text{Min.}^{-1}$ | $k_1$, $\text{Mole}^{-2}\text{L.}^2$ $\text{Min.}^{-1}$ | $k_2$, $\text{Mole}^{-2}\text{L.}^2$ $\text{Min.}^{-1}$ |
|---|---|---|---|---|
| 0.186 | 0.186 | $0.32 \times 10^{-4}$ | $0.17 \times 10^{-3}$ | $0.66 \times 10^{-2}$ |
| 0.25 | 0.25 | 0.35 | 0.14 | 0.43 |
| 0.50 | 0.50 | 0.55 | 0.11 | 0.18 |
| 1.00 | 1.00 | 1.00 | 0.10 | 0.08 |
| 0.25 | 0.75 | 0.75 | 0.10 | 0.16 |

*Propenyl isocyanate.* The $k$ value calculated from Equation 1 increased with reaction time excepting the reaction of 0.25*M* of propenyl isocyanate with 0.75*M* of methanol in which the value was kept approximately constant over the course investigated. The $k_1$ value decreased a little with increasing concentration as did the $k_1$ value for ethyl isocyanate. The straight line relationship of Equation 3 was also obtained in all cases (see Fig. 2). The $k_2$ value obtained decreased considerably with increasing concentration as it did with ethyl isocyanate. The values in the last two runs are equal to each other, and it is, consequently, clear that the concentration of the urethan mainly affects the $k_2$ value. The results are shown in Table IV.

*Urethan-catalyzed reaction.* When the urethan is initially added, the reaction should follow the following equation,

$$dx/dt = \{k_1a + (k_2 - k_1)x + k_2c\}(a - x)^2 \quad (4a)$$

$$dx/dt = \{k_1b + (k_2 - k_1)x + k_2c\}(a - x)(b - x) \quad (4b)$$

where $c$ is the concentration of the urethan added. In extrapolating the $k$ value calculated from Equation 1 to zero reaction time, the value is equal to $k_1a+k_2c$ or $k_1b+k_2c$. By determining the $k_1a$ or

TABLE IV

$k_1$ AND $k_2$ VALUES FOR SPONTANEOUS REACTION OF PROPENYL ISOCYANATE WITH METHANOL AT 25°

| Propenyl Isocyanate, Mole/L. | Methanol, Mole/L. | $k_1a$ or $k_1b$, Mole$^{-2}$L.$^2$ Min.$^{-1}$ | $k_1$, Mole$^{-2}$L.$^2$ Min.$^{-1}$ | $k_2$, Mole$^{-2}$L.$^2$ Min.$^{-1}$ |
|---|---|---|---|---|
| 0.186 | 0.186 | $0.24 \times 10^{-2}$ | $0.13 \times 10^{-1}$ | $0.63 \times 10^{-1}$ |
| 0.25 | 0.25 | 0.24 | 0.096 | 0.57 |
| 0.50 | 0.50 | 0.41 | 0.082 | 0.29 |
| 0.75 | 0.75 | 0.52 | 0.070 | 0.19 |
| 0.75 | 0.25 | 0.21 | 0.084 | 0.55 |
| 0.25 | 0.75 | 0.63 | 0.084 | 0.53 |

$k_1b$ value from the spontaneous reaction, the $k_2$ value should be obtained. In this paper, the reaction of ethyl isocyanate with methanol was primarily investigated and the reaction of phenyl isocyanate was also studied, but the reaction of propenyl isocyanate could not be studied, since methyl $N$-propenyl carbamate was partly insoluble in di-$n$-butyl ether during recrystallization.

*Ethyl isocyanate.* The same concentration with respect to the urethan and two reactants was used in order to determine the $k_2$ value at 50% conversion for the spontaneous reaction, because the straight line relationship of Equation 3 was generally obtained above 30% conversion. The $k$ value calculated from Equation 1 increased with reaction time excepting the last run in Table V. In this case, the value should increase with reaction time for $(k_2-k_1)x>0$, but the value decreased. The $k_2$ value was calculated by neglecting $k_1a$ or $k_1b$ as compared with $k_2c$, but the value decreased with increasing the concentration of the reactants as shown in Table V. There is a discrepancy between the $k_2$ value determined from the spontaneous reaction (Table III) and that determined from the urethan-catalyzed reaction (Table V).

TABLE V

$k_2$ VALUE FOR METHYL $N$-ETHYL CARBAMATE-CATALYZED REACTION OF ETHYL ISOCYANATE WITH METHANOL AT 25°

| Initial Concentration | | | $k_1a + k_2c$ or $k_1b + k_2c$, Mole$^{-2}$L.$^2$ Min.$^{-1}$ | $k_2$, Mole$^{-2}$L.$^2$ Min.$^{-1}$ |
|---|---|---|---|---|
| Ethyl isocyanate, mole/l. | Methanol, mole/l. | Urethan, mole/l. | | |
| 0.125 | 0.125 | 0.125 | $0.24 \times 10^{-3}$ | $0.19 \times 10^{-2}$ |
| 0.25 | 0.25 | 0.25 | 0.31 | 0.11 |
| 0.50 | 0.50 | 0.50 | 0.33 | 0.066 |
| 0.25 | 0.75 | 0.25 | 0.23 | 0.092 |

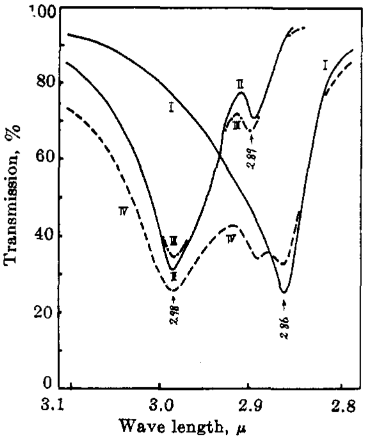

Fig. 3. Infrared spectra in di-$n$-butyl ether with lithium fluoride prism (0.1-mm. cell thickness). I—0.50$M$ of methanol, II—0.50$M$ of methyl $N$-ethyl carbamate, III—0.50$M$ of phenyl isocyanate and methyl $N$-ethyl carbamate, IV—0.50$M$ of methanol and methyl $N$-ethyl carbamate

*Phenyl isocyanate.* In the previous paper,[3] the $k_2$ value for the reaction of propenyl isocyanate with methanol was determined from the reaction which was carried out at 0.25$M$ with respect to phenyl isocyanate, methanol, and methyl $N$-phenyl carbamate, and the value was $0.55 \times 10^{-2}$ mole$^{-2}$l.$^2$ min.$^{-1}$ The same reaction was again carried out at 0.50$M$ for both the isocyanate and methanol and 0.25$M$ for the urethan; the $k_1a + k_2c$ value was $0.54 \times 10^{-2}$ mole$^{-2}$ l.$^2$ min.$^{-1}$ (Table II) and then the $k_2$ value was $0.04 \times 10^{-2}$ mole$^{-2}$l.$^2$ min.$^{-1}$ This fact may be related to the fact that the $k_2$ values for ethyl and propenyl isocyanates decreased with increasing concentration.

*Infrared spectra.* The $k_1$, $k_2$, and $k_3$ values varied as described and this fact was considered to be due to hydrogen bonding. Among three types of urethans, methyl $N$-ethyl carbamate has the greatest basicity, and so it should possess the greatest hydrogen bond-forming ability. Therefore, the infrared spectra of the solutions containing methanol, methyl $N$-ethyl carbamate, and both of these compounds in di-$n$-butyl ether, were measured. The results obtained were shown in Fig. 3. The methanol solution (Curve I) has a band at 2.86 μ concerned with the solvent-bonded OH group, because the free OH group and the self-associated OH group arise at 2.73 μ and near 2.95 μ in nonpolar solvents.[13] The methyl $N$-ethyl carbamate solution(Curve II) had a strong band at 2.98 μ and a weak band at 2.89 μ. It is probable that the former band is concerned with the intermolecular hydrogen bond of the urethan and the latter band is caused from the intermolecular hydrogen bond between the urethan and the solvent. The solution containing 0.50$M$ concentrations of both the urethan and methanol had three bands, 2.86 μ, 2.89 μ, and 2.98 μ (Curve IV). The intensity was more decreased at the first band and more increased at the third band than that of the corresponding band of the solution containing methanol or the urethan only. This fact shows that the amount of the solvent-bonded OH group in a 0.50$M$ methanol solution changes whether or not the ure-

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[13] J. W. Baker, M. M. Davis, and J. Gaunt, *J. Chem. Soc.*, 24 (1949).

than is present. Solutions of the following concentrations were also measured: Both were $0.125M$, $0.25M$, and methanol was $0.75M$ and the urethan was $0.25M$. From these results, Lambert-Beer's law on the band at 2.86 $\mu$ was not exactly applicable, but the discrepancy was not large.

Baker *et al.*[13] investigated the infrared spectra of the solutions containing both triethylamine and methanol in benzene or di-*n*-butyl ether. It was found that the OH band shifts toward the longer wave-length region when the triethylamine was mixed, but they could not confirm the formation of the catalyst-isocyanate complex. In order to determine whether the complex is formed from phenyl isocyanate and methyl *N*-ethyl carbamate, the solution containing $0.50M$ concentrations of both the urethan and phenyl isocyanate was also measured. In this spectrum, the intensity was more decreased at 2.98 $\mu$ and more increased at 2.89 $\mu$ than that of the solution containing the urethan only.

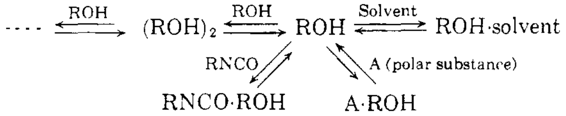
## DISCUSSION

It seems that Baker *et al.* and others overlooked the following two points: (1) It was disregarded that the urethan produced catalyzed the reaction. (2) The concentration of alcohols was not so large as compared with that of isocyanates that it could not be considered that the concentration was constant throughout the course of reaction, and then the equation,

$$\frac{dx}{dt} = \frac{k_1'k_3'(\mathrm{ROH})}{k_2' + k_3'(\mathrm{ROH})}(\mathrm{ROH})(\mathrm{RNCO}) + \frac{k_1''k_3''x}{k_2'' + k_3''(\mathrm{ROH})}(\mathrm{ROH})(\mathrm{RNCO})$$

should be integrated according to the intermediate complex mechanism. Recently, the complex was confirmed by Pestemer and his co-worker.[14] They measured the infrared spectrum of the mixture of phenyl isocyanate and tertiary amine or triethylaluminum in paraffin oil, and found that the spectrum had no NCO band near 4.44 $\mu$ and had a CO band near 6.06 $\mu$. In this paper, the infrared spectrum of the solution of phenyl isocyanate and methyl *N*-ethyl carbamate was also measured, and it was found that the intensity decreased at 2.98 $\mu$ and increased at 2.89 $\mu$ more than in a solution containing the urethan only. This fact seems to show that the complex is produced by the interaction between the urethan and the isocyanate. From two facts above, it is shown that the reaction proceeds through the isocyanate-alcohol and catalyst complexes, contrary to Ephraim's mechanism in which the alcohol produces complexes with the alcohol, the solvent and the urethan, and then the complexes react with the isocyanate to give the urethan. Accordingly, Equation 2 should be applicable. Nevertheless, the $k_1$ values for three isocyanates and the $k_3$ value for phenyl isocyanate decreased a little, and the $k_2$ values for ethyl and propenyl isocyanates decreased considerably with increasing concentration.

From infrared and other physical investigations, it is well known that alcohols in nonpolar solvents are present as a mixture of various states, *e.g.*, monomer, dimer, trimer, etc., and in polar solvents a greater part of the alcohols bond with the solvents even at low concentrations. The amount of self-associated alcohols in various states increases with increasing concentration and with decreasing the hydrogen bond-forming ability of the alcohols. If the solution contains other polar substances, the alcohols associate with the substances to some extent in addition to the above hydrogen bonding. Therefore, alcohols in reaction are present in the following equilibrium:



$$\begin{tikzcd}
\cdots \arrow[r, shift left, "\mathrm{ROH}"] & (\mathrm{ROH})_2 \arrow[l, shift left] \arrow[r, shift left, "\mathrm{ROH}"] & \mathrm{ROH} \arrow[l, shift left] \arrow[r, shift left, "\mathrm{Solvent}"] \arrow[dl, shift left, "\mathrm{RNCO}"'] \arrow[dr, shift left, "\mathrm{A\ (polar\ substance)}"] & \mathrm{ROH{\cdot}solvent} \arrow[l, shift left] \\
 & \mathrm{RNCO{\cdot}ROH} \arrow[ur, shift left] & & \mathrm{A{\cdot}ROH} \arrow[ul, shift left]
\end{tikzcd}$$

It is also clear that the amount of unbonded alcohol or solvent-bonded alcohol is not directly proportional to the concentration of alcohol, and the ratio of the unbonded alcohol or the solvent-bonded alcohol to the self-associated alcohol decreases with concentration. It is considered that the bonded alcohol has a lower reactivity for dissociation than the unbonded alcohol; then each of the $k$ values obtained decreases with increasing concentration. It was shown by Ephraim *et al.* that the $k$ value for the reaction of phenyl isocyanate with methanol in various solvents is approximately connected with the hydrogen bond-forming ability of solvents.

If the apparent concentration of alcohols due to hydrogen bonding decreases to 90%, by a third-order mechanism the $k$ value becomes 0.81 compared with the value obtained when the alcohols dissociate entirely, and decreasing to 80%, the value becomes 0.64. The decrease in the $k_1$ value for ethyl and propenyl isocyanates with increasing concentration of alcohol is explained by such hydrogen bonding. The $k_1$ value for phenyl isocyanate did not vary with the concentration of alcohols except in the reaction of excess isocyanate which gave a greater $k_1$ value than others. This fact seems to arise from the greater hydrogen bond-forming ability of phenyl isocyanate which has more conjugations than the former with one conjugation or not against the NCO group. Therefore, in this case, the following equilibrium proceeds toward the right-hand side,

$$(\mathrm{ROH})_x \rightleftarrows \mathrm{ROH{\cdot}solvent\ (or\ ROH)} \rightleftarrows \mathrm{ROH{\cdot}RNCO}$$

and $(\mathrm{ROH})_x$ becomes smaller and $(\mathrm{ROH{\cdot}RNCO})$ becomes greater than the others. Consequently,

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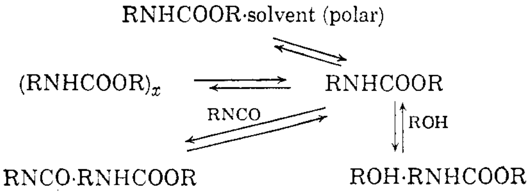
[14] M. Pestemer and D. Lauerer, *Angew. Chem.*, **72**, 612 (1960).

the $k_1$ value does not vary with concentration of alcohol and the value for excess isocyanate becomes apparently great, but in the same concentration of the isocyanate, the value for 0.25$M$ methanol is greater than that for 0.75$M$ methanol. The $k_3$ value for the triethylamine-catalyzed reaction decreased a little with increasing the concentration of $n$-butyl alcohol. It is well known that the molecules of triethylamine do not associate with each other and form hydrogen bond with alcohols to some extent. It is therefore, probable that the decrease of the $k_3$ value is mainly due to the hydrogen bonding of alcohols similarly to the $k_1$ values.

If a urethan is contained, the urethan associates with alcohols and also intermolecularly with urethan molecules. Therefore, the urethan is in the following equilibrium,



The amount of unassociated urethan is not directly proportional to the concentration of the urethan, and the discrepancy increases with increasing the concentration and with the basicity and the configuration of the urethan molecule. Therefore, the amount of RNHCOOR·RNCO does not increase in direct proportion to the concentration of the urethan. It is, in the extreme case, considered that the amount of the unassociated urethan is unchangeable regardless of the urethan concentration and then, the intermediate complex which is in equilibrium to it becomes constant. On the other hand, the urethan associates with alcohols and then the apparent concentration of the alcohols decreases. Therefore, it is probable that the $k_2$ value for spontaneous reactions should vary. Indeed, the $k_2$ values for ethyl and propenyl isocyanates decreased considerably and the decreasing magnitude was greater for ethyl isocyanate than for propenyl isocyanate. The $k_2$ value for propenyl isocyanate did not vary greatly with the concentration of methanol and the isocyanate. These facts show that the urethan concentration mainly affects the $k_2$ value. In increasing the initial methanol concentration for the reaction of 0.25$M$ ethyl isocyanate, the $k_2$ value decreased considerably (see Table III). This fact shows that the alcohol concentration partially affects the $k_2$ value.

In the 0.25$M$ urethan-catalyzed reaction of phenyl isocyanate, two different $k_2$ values were obtained: $0.55 \times 10^{-2}$ mole$^{-2}$ l.$^2$ min.$^{-1}$ at 0.25$M$ for both reactants, and $0.04 \times 10^{-2}$ mole$^{-2}$ l.$^2$ min.$^{-1}$ at 0.50$M$ for both reactants. Since the urethan concentration was the same, it is considered to be caused mainly by a decrease in the reactivity due to the state of the alcohols as shown in Fig. 3, *i.e.*, the increase of the rate due to the $k_2$-(urethan) term is cancelled by the decrease of the rate due to the state of the alcohol. When the concentration of all the reactants was doubled in the urethan-catalyzed reaction of ethyl isocyanate, the $k_2$ value was reduced by about half as in the spontaneous reaction of ethyl isocyanate. There was a difference between the $k_2$ values for the spontaneous and urethan-catalyzed reaction. The reason may be explained as follows: (1) The $k_2$ value for urethan-catalyzed reactions is determined at zero reaction time, corresponding to 50% conversion for spontaneous reactions, which is not so in the latter cases. (2) The isocyanate reacts in spontaneous reactions with the moisture contained in the solvent or present during the operation and with the urethan to produce a small amount of the corresponding urea and $N$-carboethoxydiethylurea, and these compounds catalyze the reaction to give a greater $k_2$ value for spontaneous reactions than that for the urethan-catalyzed reactions. By considering the $k_1$ and $k_2$ values in various solvents, both positive and negative deviations from the second-order rate plot obtained by Ephraim *et al.* are explained well.

## CONCLUSION

It is probable that the reaction of isocyanates with alcohols proceeds through the intermediate complexes which are formed from isocyanates and alcohols, isocyanates and urethans, and isocyanates and catalysts, so that Equation 2 should be theoretically applicable. However, there is association in the reaction medium. Therefore, the $k_1$, $k_2$, and $k_3$ values are not entirely constant, but the reaction apparently follows Equation 2. The $k_1$ and $k_3$ values decrease a little with increasing the concentration of alcohols, and the $k_2$ value changes considerably with the concentration of reactants, *i.e.*, the value is greatly determined by the concentration of urethans and also determined by the concentration of alcohols. The magnitude varies also with the ratio of urethans to alcohols, the kind of isocyanates, alcohols, solvents, etc. By this mechanism, all the phenomena in the reaction of isocyanates with alcohols are explained. Comparing the $k_1$ value for various isocyanates with each other, the value should be determined from the reaction using excess alcohol (the reaction of 0.25$M$ isocyanates with 0.75$M$ alcohol), since the $k_1b + (k_2 - k_1)x$ value does not increase rapidly. Comparing the $k_2$ values with each other, the value should be determined from the reaction using the same moles of both the reactants (0.15$M$ to 0.25-$M$), since such concentrations are generally used and the ratio of unassociated urethans to self-associated urethans will not be great.

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# Electrophilic Displacement Reactions. XIV. Two Novel Reactions Involving Areneboronic Acids and Halogens[1-3]

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*meta*-Methoxybenzeneboronic acid has been found to react with one, two, and three moles of bromine to yield, respectively, 2-bromo-5-methoxybenzeneboronic acid, 2,4-dibromo-5-methoxybenzeneboronic acid, and 2,4,5-tribromoanisole. Chlorination yields 2-chloro-5-methoxybenzeneboronic acid and, probably, 3-methoxy-4-chlorobenzeneboronic acid. Reaction with iodine chloride yields 2-iodo-5-methoxybenzeneboronic acid along with the chloro acids.

Benzeneboronic acid reacts with hypochlorite and hypobromite to give phenol, which then reacts to form halophenols.

*Halogenation of m-methoxybenzeneboronic acid.* It has been known for some time that areneboronic acids suffer replacement of the boronic acid group on treatment with a number of reagents such as halogens,[4] hydrogen peroxide,[5] mercuric,[5] and thallium salts.[6] Hydrolysis occurs in water at 150° to yield benzene and boric acid; it is catalyzed by strong acid,[5] strong base,[5] and salts of cadmium,[5] zinc,[5] and silver.[7,8] Because of this ease of replacement of the boronic acid group the acids have proved to be valuable in the study of aromatic electrophilic displacement reactions. A singular advantage lies in the fact that the seat of attack by the electrophilic reagent is generally known and difficulties attending the analysis of mixtures of isomers are eliminated. Exceptions to the rule that the boronic acid group is replaced in preference to hydrogen include the nitration of benzeneboronic acid[5,9] to *o*- or *m*-nitrobenzeneboronic acid and the reaction of *m*-hydroxybenzeneboronic acid and *m*-diethylaminobenzeneboronic acids with diazonium salts.[10] Coupling occurs *para* to the hydroxyl and diethylamino groups.

Another exception to the general rule has now been found in the reaction of *m*-methoxybenzeneboronic acid with halogens. When bromine was added to a solution of the boronic acid in 20% acetic acid, the color disappeared in a few seconds. On the basis of the effects of other substituents on the rate of the brominolysis reaction[11] it had been expected that the reaction would take days to go to completion. When this reaction was carried out on a synthetic scale with one molar equivalent of bromine, a new monobromoboronic acid was isolated in analytically pure state in 90% yield. It was hydrolyzed with aqueous zinc chloride to *p*-bromoanisole (92%). Thus the bromination product was 2-bromo-5-methoxybenzeneboronic acid, B—Br (Chart I).

The bromination was carried out with two moles of bromine per mole of *m*-methoxybenzeneboronic acid, yielding up to 90% of a dibromobenzeneboronic acid. This was characterized by oxidation with hydrogen peroxide to 2,4-dibromo-5-methoxyphenol, H—Br, as 2,4-dibromo-5-methoxybenzeneboronic acid, F—Br.

Three moles of bromine reacted with *m*-methoxybenzeneboronic acid to yield 2,4,5-tribromoanisole, G—Br, isolated in 57% yield.

Thus, groups with high capacities for conjugative electron release activate the *ortho* and *para* positions toward electrophilic attack to such an extent that the hydrogens in these positions are replaced preferentially. The fact that attack occurs in the position *para* to the methoxy group indicates that neither the steric effect nor the electron-withdraw-

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(1) Preceding paper in this series: H. G. Kuivila and T. C. Muller, *J. Am. Chem. Soc.*, **84**, 377 (1962).

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