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# Kinetic Studies of the Reaction of Phenyl Isocyanate with Alcohols in Various Solvents[1]

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The effect of solvent on the reaction of phenyl isocyanate with methanol at 20° has been studied. The rate varies 71-fold in the order benzene, toluene > nitrobenzene > di-*n*-butyl ether > *n*-butyl acetate > methyl ethyl ketone > dioxane > acetonitrile. The reaction rate is found to depend primarily upon the dielectric constant of the solvent and to some extent on the hydrogen bonding character of the solvent. The reaction order, however, depends only upon the hydrogen bonding character of the solvent. Studies also were made on the reaction of butanol, isopropyl alcohol, methyl cellosolve and ethylene glycol with phenyl isocyanate in selected solvents. A mechanism is proposed which postulates a reaction of phenyl isocyanate with one or more of three alcohol complexes: (i) a dimeric alcohol complex (ii) an alcohol–urethan complex, and (iii) a solvent–alcohol complex. Whereas the reaction of phenyl isocyanate with complexes (i) and (ii) predominates in non-hydrogen bonding solvents, the reaction with complexes (ii) and (iii) predominates in hydrogen bonding solvents.

The reaction of phenyl isocyanate and alcohols has been studied by several investigators.[3-6] A review of these and related investigations has recently been published.[7] The series of papers by Baker and co-workers[6] were concerned with the mechanism of the uncatalyzed and base-catalyzed reactions of phenyl isocyanate and various alcohols, principally methanol and ethanol, in two solvents, benzene and di-*n*-butyl ether. The mechanism proposed involves the initial formation of a base–isocyanate complex, the alcohol acting as a base when no additional catalyst is present, followed by reaction of the complex with the alcohol to give urethan, *via* a reaction that is between second and third order. Although this mechanism is supported by the experimental investigations, it has not received unequivocal confirmation.

In this work, the kinetics of the reaction between phenyl isocyanate and methanol in a variety of solvents have been investigated at 20°. Less extensive kinetics studies of the reaction between phenyl isocyanate and other alcohols also have been made. It will be seen that the marked influence of solvent on the reaction found in this investigation necessitates modification and extension of the earlier mechanism[6] proposed for the uncatalyzed reaction.

## Experimental

**Materials.**—All chemicals used were Fisher Certified Regents, unless stated otherwise. **Phenyl isocyanate** (Eastman) was fractionated twice under reduced pressure immediately before use (b.p. 57° (17 mm.)). **Methanol** was purified by the method of Lund and Bjerrum,[8] the first and last 25% of the total being discarded (b.p. 65° (760 mm.)). ***n*-Butyl alcohol** and **isopropyl alcohol** were purified by the method of Smith[9] (b.p., *n*-butyl alcohol, 118° (760 mm.), isopropyl alcohol 82.4° (760 mm.)). **Methyl cellosolve** and **ethylene glycol** were dried over anhydrous calcium sulfate and then fractionated; the fraction boiling at 124.5° (760 mm.) of the former and 123.1° (50 mm.) of the latter reagent were used. **Toluene** was purified by the method of Vogel,[10] stored over sodium and distilled immediately before use (b.p. 11.5° (760 mm.)). **Nitrobenzene** was shaken with 1:1 sulfuric acid, washed with distilled water and then with 10% sodium hydroxide solution, washed repeatedly with distilled water until the aqueous layer was colorless and neutral, dried over calcium chloride, and then fractionated under reduced pressure, the first and final 20% being discarded (b.p. 106° (20 mm.)). ***n*-Butyl acetate** was distilled, then refluxed with successive small portions of potassium permanganate, dried over anhydrous calcium sulfate, filtered, redistilled and then refluxed over phenyl isocyanate (b.p. 79.6° (760 mm.)). **Dioxane** (Matheson, purified) was refluxed for two days over excess metallic sodium, then fractionated (b.p. 101.5° (760 mm.)). **Acetonitrile** was refluxed for four hours over phosphorus pentoxide and then fractionated (b.p. 81° (760 mm.)). **Acetone** was refluxed with successive small quantities of potassium permanganate until the violet color persisted, then was dried over anhydrous calcium sulfate, filtered and fractionated (b.p. 56.2° (760 mm.)). **Piperidine** was dried over KOH and fractionated under reduced pressure (b.p. 35.4° (40 mm.)). A solution of this reagent was prepared by diluting 10 ml. of piperidine to 100 ml. with acetone purified as given above. The solution was discarded as soon as it began showing a yellowish tinge.

**Procedures.**—The reaction between phenyl isocyanate and the various alcohols with time at 20 ± 0.02° was followed by analyzing for residual isocyanate, using a method which is a modification of that originally developed by Stagg.[11] An all-glass apparatus open to the outside atmosphere through a tube filled with dehydrated silica was used. The apparatus consisted principally of a reaction flask fitted with a semi-microburet from which a given amount of reaction solution could be collected at any time interval. The reaction sample (10 ml.) was measured into a previously chilled 125-ml. glass-stoppered flask containing 10 ml. of solvent and 5 ml. of standard piperidine solution in acetone. After chilling the flask 15 additional minutes, 15 ml. of absolute methanol and two drops of brom phenol blue were added and the contents titrated with standard hydrochloric acid in methanol solution. A blank determination on the solvent only also was run and a correction made.

The method was checked for each solvent by titration of a known amount of phenyl isocyanate. Since isocyanates are very reactive with water, special care was taken in drying the various solvents, as described above. Moreover, solvents were used only after they had been found to show no significant reaction with phenyl isocyanate over a 48-hour period at room temperature.

## Experimental Results

The experimental data for the methanol–phenyl isocyanate reaction in toluene at three initial react-

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ant concentration ratios are given in Table I. The concentration of phenyl isocyanate remaining at time $t$, $[C_6H_5NCO]_t$, as determined by titration, is given in the second column of the table. Assuming that the amount of alcohol reacted equals the amount of isocyanate reacted, the alcohol concentration at time $t$, $[ROH]_t$, was found as given in column 3. A second-order rate constant calculated for each time interval is given in the fourth column. It is apparent than an increase in the initial methanol to phenyl isocyanate concentration results in an increase in the apparent rate constant as noted previously.[6c] From the usual analysis of this data it is found that the reaction is first order with respect to the phenyl isocyanate concentration and is between first and second order with respect to the methanol concentration.

TABLE I

THE REACTION OF PHENYL ISOCYANATE AND METHANOL IN TOLUENE AT 20°

| Time, min. | $[C_6H_5NOC]t$, mole/l. | $[ROH]t$, mole/l. | $k \times 10^4$, l./moles/min. |
|---|---|---|---|
| 0 | 0.250 | 0.250 | .. |
| 5 | .2455 | .2455 | 140 |
| 30 | .234 | .234 | 90 |
| 60 | .219 | .219 | 71 |
| 90 | .2075 | .2075 | 91 |
| 150 | .196 | .196 | 73 |
| 360 | .153 | .153 | 71 |
| 540 | .131 | .131 | 67 |
| 700 | .118 | .118 | 64 |
| 1200 | .0895 | .0895 | 60 |
| 1650 | .0776 | .0776 | 54 |
| 2880 | .0587 | .0587 | 45 |
| 5700 | .0419 | .0419 | 35 |
| 0 | .250 | .125 | .. |
| 15 | .248 | .123 | 43 |
| 60 | .243 | .118 | 39 |
| 150 | .233 | .108 | 41 |
| 250 | .225 | .0997 | 38 |
| 550 | .205 | .0796 | 37 |
| 1350 | .170 | .0447 | 38 |
| 2800 | .145 | .0115 | 36 |
| 0 | .125 | .250 | .. |
| 20 | .118 | .243 | 117 |
| 90 | .0994 | .2245 | 107 |
| 150 | .0890 | .214 | 100 |
| 270 | .0673 | .1923 | 106 |
| 450 | .0497 | .1747 | 100 |
| 1330 | .0156 | .1406 | 91 |
| 1580 | .0095 | .1345 | 99 |

The results obtained for the reaction of phenyl isocyanate with methanol in six solvents at 20° are plotted in Fig. 1 in terms of a second-order reaction. The dotted lines represent a true second-order dependence in a given solvent as based upon the initial reaction rate. The starting alcohol and phenyl isocyanate concentrations were the same and equal to 0.25 mole/l. in the runs carried out in toluene, methyl ethyl ketone (MEK), acetonitrile and nitrobenzene. Therefore for these runs a plot of $1/c$ *vs.* $t$ was made, where $c$ is the concentration of both reactants at time $t$. For the runs in dioxane and $n$-butyl acetate the starting methanol concentrations were 0.25 and 0.31 mole/l., respectively, while the isocyanate to methanol ratios were 0.83 and 0.91, respectively, necessitating a plot of $1/(b - a) \log (a - x)/(b - x)$ where $b$ is the initial isocyanate concentration and $a$ the initial alcohol concentration and $x$ is the amount of each reactant at time $t$. It is readily apparent from Fig. 1 that two effects occur upon changing the solvent, one being deviations from a second-order rate plot, both positive and negative deviations occurring, and the other being changes in the reaction rate. The plots for the reactions in MEK and acetonitrile are found to indicate a second-order reaction over the complete range investigated. For the reactions in toluene and nitrobenzene downward curvature in the plots is apparent; for the runs in $n$-butyl acetate and dioxane the plots show upward curvature. The apparent second-order rate constants obtained from the initial slope of the second-order plots for the various solvent are found to decrease in the following series: benzene, toluene > nitrobenzene > di-$n$-butyl ether > $n$-butyl acetate > MEK > dioxane > acetonitrile. The apparent second-order rate constants derived from the data given in Fig. 1 are recorded in Table II; in this table apparent second-order rate constants are also given for the reaction between phenyl isocyanate and $n$-butyl alcohol, isopropyl alcohol, methyl cellosolve and ethylene glycol in one or more solvents. In toluene the apparent rate constant at the same initial reactant concentrations was found to be about 15% greater when $n$-butyl alcohol was used in place of methanol. The reaction of $n$-butyl alcohol in MEK, however, is the same as for methanol. A different order for the rate constant values is found when ethylene glycol is substituted for methanol in acetonitrile and dioxane, however.

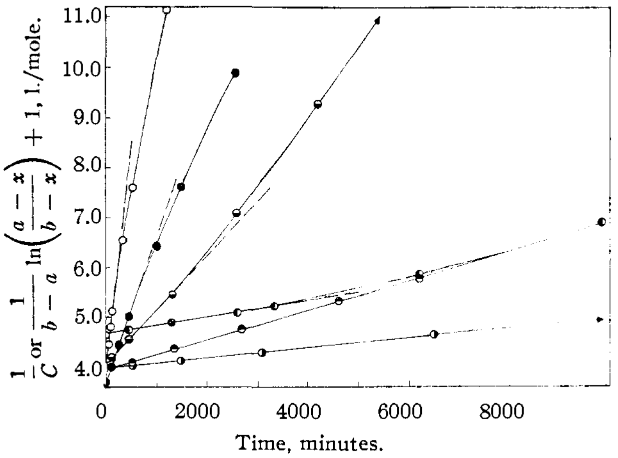

Fig. 1.—The reaction of phenyl isocyanate with methanol as a function of time at 20° in various solvents: toluene (○) nitrobenzene (●); $n$-butyl acetate (◒); MEK (◓); dioxane (◐); acetonitrile (◑).

## Discussion

The reaction of methanol with phenyl isocyanate is known[6] to be base catalyzed as well as subject to autocatalysis due to the weakly basic character of the reaction product, methyl phenyl urethan. As a consequence of autocatalysis, the upward drift of the second-order plot (see Fig. 1) for the methanol–phenyl isocyanate reaction in $n$-butyl acetate

TABLE II

INITIAL SECOND-ORDER RATE CONSTANTS FOR THE REACTION BETWEEN PHENYL ISOCYANATE AND SOME ALCOHOLS AT 20°

| Alcohol | Solvent | $[\mathrm{ROH}]$, $[\mathrm{C_6H_5\text{-}CO}]$ moles/mole | $[\mathrm{ROH}]$, mole/l. | $k_2 \times 10^4$, l. mole$^{-1}$-min.$^{-1}$ |
|---|---|---|---|---|
| Methanol | Benzene$^a$ | 1 | 0.24 | 71 |
| | Toluene | 0.5 | .125 | 41 |
| | | 1 | .25 | 70 |
| | | 2 | .25 | 105 |
| | Nitrobenzene | 1 | .25 | 27 |
| | Di-*n*-butyl ether$^a$ | 1 | .24 | 17 |
| | *n*-Butyl acetate | 0.91 | .31 | 11 |
| | MEK | 1 | .25 | 3.1 |
| | Dioxane | 0.5 | .25 | 1.7 |
| | | 0.83 | .25 | 1.7 |
| | Acetonitrile | 1 | .25 | 1 |
| Butanol | Toluene | 1 | .25 | 82 |
| | Methyl ethyl ketone | 1 | .25 | 3.0 |
| Isopropyl alc. | Toluene | 1 | .25 | 37 |
| Methyl cellosolve | Toluene | 1 | .25 | 8.4 |
| Ethylene glycol | Acetonitrile | 0.5 | .125 | 1 |
| | Dioxane | 0.5 | .125 | 0.5 |

Values taken from reference 6c.

and dioxane solvents is expected if the reaction in these solvents is truly second order. The straight line plot for the reaction in MEK and acetonitrile and downward curvature found for the runs in toluene and nitrobenzene at longer times is indicative of an order greater than two with respect to the initial reactants. It is found that the apparent deviations from a second-order reaction toward a higher order, in the sequence toluene > nitrobenzene > acetonitrile > MEK > *n*-butyl acetate > dioxane, increase with an increase in the hydrogen-bonding capacity of the solvent as deduced from infrared measurements.[12-14]

The differences in the initial rate of the phenyl isocyanate–methanol reaction, however, appear to be only slightly related to the hydrogen-bonding capacity of the solvent. With the exception of nitrobenzene and dioxane, the log of the apparent second-order rate constant is found to decrease linearly with an increase in the quantity[15] $(D - 1)/(2D + 1)$, where $D$ is the dielectric constant of the solvent. It is expected that the deviations exhibited by the rate of the reaction in dioxane would be somewhat lessened if the "local" molecular dielectric constant was considered.

In toluene solution under the same conditions as employed with methanol, butanol is found to give essentially a second-order reaction with phenyl isocyanate, exhibiting a rate somewhat faster than that for methanol. This behavior probably is due to a slightly more basic character of the oxygen in butanol as the result of an inductive effect. The slower rate for isopropyl alcohol under the same conditions may be attributed to steric factors. The presence of the ether linkage in methyl cellosolve facilitating intermolecular hydrogen bonding and consequently reducing the availability of free hydroxyl groups may account for the even slower reaction rate for this alcohol and phenyl isocyanate in toluene.

With regard to the mechanism of this reaction it has been postulated[6c] that the initial step involves complex formation between the alcohol and phenyl isocyanate, followed by reaction of the complex with methanol to yield products. However, no evidence for such complex formation has been published in support of this contention. Methanol has been shown to complex with itself to a small extent at high concentrations in benzene[6d]; in a solvent of high dielectric constant, such as di-*n*-butyl ether, it complexes both with itself and with the solvent.[6d]

In contrast to the mechanism of Baker and coworkers[6] the results of this study suggest the following mechanism for the reaction between methyl alcohol (ROH) and phenyl isocyanate (RNCO) to give methylphenylurethan

$$\begin{aligned}
&2\mathrm{ROH} \underset{}{\overset{K_{1a}}{\rightleftharpoons}} \text{complex 1} && \text{(1a)}\\
&\mathrm{ROH} + \text{solvent} \overset{K_{1b}}{\rightleftharpoons} \text{complex 2} && \text{(1b)}\\
&\mathrm{ROH} + \text{urethan} \overset{K_{1c}}{\rightleftharpoons} \text{complex 3} && \text{(1c)} \quad \text{(A)}\\
&\text{complex 1} + \mathrm{RNCO} \xrightarrow{k_{2a}} \text{urethan} + \mathrm{ROH} && \text{(2a)}\\
&\text{complex 2} + \mathrm{RNCO} \xrightarrow{k_{2b}} \text{urethan} + \text{solvent} && \text{(2b)}\\
&\text{complex 3} + \mathrm{RNCO} \xrightarrow{k_{2c}} 2\ \text{urethan} && \text{(2c)}
\end{aligned}$$

where $K_{1a}$, $K_{1b}$, $K_{1c}$, are the equilibrium constants and $k_{2a}$, $k_{2b}$ and $k_{2c}$ are the rate constants for the reactions shown. The rate of isocyanate disappearance is found from mechanism A to be given by the expression

$$\frac{-\mathrm{d}[\mathrm{RNCO}]}{\mathrm{d}t} = k_{2a}[\text{Complex 1}][\mathrm{RNCO}] + k_{2b}[\text{Complex 2}][\mathrm{RNCO}] + k_{2c}[\text{Complex 3}][\mathrm{RNCO}]$$

If it is assumed that steps 2a, 2b and 2c are rate determining and therefore slow, resulting in $k_{2a}[\mathrm{RNCO}] << k_{-1a}$, $k_{2b}[\mathrm{RNCO}] << k_{-1b}$, $k_{2c}[\mathrm{RNCO}] << k_{-1c}$, where $k_{-1a}$, $k_{-1b}$, $k_{-1c}$ are the rate constants for the reverse reactions in equations 1a, 1b and 1c, respectively, equation 3 can be written as

$$\frac{-\mathrm{d}[\mathrm{RNCO}]}{\mathrm{d}t} = \frac{k_{2a}}{K_{1a}}[\mathrm{ROH}]^2[\mathrm{RNCO}] + \frac{k_{2b}}{K'_{1b}}[\mathrm{ROH}][\mathrm{RNCO}] + \frac{k_{2c}}{K_{1c}}[\mathrm{ROH}][\text{urethan}][\mathrm{RNCO}] \quad (4)$$

where $K'_{1b} = K_{1b}/[\text{solvent}]$. It is evident that the order of the initial reaction rate constant will lie between two and three depending upon the relative importance of the first two terms on the right-hand side of equation 4. In solvents which form hydrogen bonds with the alcohol substrate the second term would predominate and at low extent of reaction and low alcohol concentrations a second-order reaction would be found. In either case, beyond the initial stage, the reaction rate is increased by autocatalysis due to the last term in equation 4.

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