3. *The Mechanism of the Reaction of Aryl* iso*Cyanates with Alcohols and Amines. Part II.* The Base-catalysed Reaction of Phenyl* iso*Cyanate with Alcohols.*

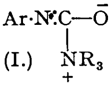
By John W. Baker and J. Gaunt.

A detailed kinetic study of the effects of concentration and temperature on the base-catalysed reaction between phenyl *iso*cyanate and various alcohols in di-*n*-butyl ether as solvent has been carried out in order to test the validity of the mechanism previously suggested (Part I, *J.*, 1947, 713), *viz.*, (i). The value of k_{bi} decreases in the series ROH = MeOH > EtOH ~ PhOH > Pr$^{\beta}$OH ≫ Bu$^{\gamma}$OH.

The application of stationary-state conditions requires that the second-order velocity coefficient k_{bi} (determined, for any particular base concentration, from the relationship $k_{bi} = k_{exp} - k_0$, where k_0 is the second-order velocity coefficient for the "spontaneous" reaction) is given by the expression

$$k_{bi} = k_1k_3[\mathrm{NR_3}]/(k_2 + k_3[\mathrm{ROH}]),\ \text{whence}\ [\mathrm{NR_3}]/k_{bi} = 1/k_c = k_2/k_1k_3 + (1/k_1)[\mathrm{ROH}].$$

This straight-line relationship has been confirmed experimentally for the whole series of alcohols over the concentration range 0·24—2·4M, and for several basic catalysts at varying concentrations at 20° and 30°, and has thus made possible the evaluation of k_1 and k_2/k_3 at the two temperatures. These data have shown that k_1 and E_1 are dependent on the *nature* but not on the *concentration* of the alcohol, ROH. Two tentative explanations consistent with all the experimental data are advanced : (*a*) That the alcohol and the base rapidly form a hydrogen-bonded complex of the general type $\mathrm{NR_3 + ROH \rightleftharpoons NR_3 \ldots H{\cdot}OR}$, and that *both* the free base, $\mathrm{NR_3}$, *and* its alcohol complex react with the *iso*cyanate to form the *same* reaction transition complex (I), a hypothesis which is supported by a study of the infra-red absorption spectra (cf. Part IV, this vol., p. 24). (*b*) That alcohol solvation of the highly polar complex $\mathrm{Ph{\cdot}N{:}C(\overset{+}{N}R_3){-}\bar{O}}$ plays an important part in the facilitation of its formation. Since the energy of such solvation would be expected to diminish in the order MeOH > EtOH > Pr$^{\beta}$OH, the values of k_1 should also decrease in this order; experimental values agree with this deduction.



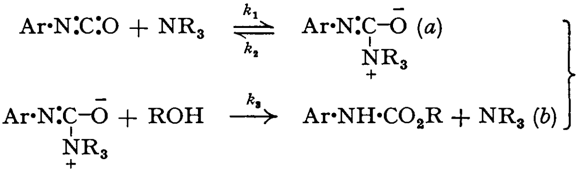
(I.)

$$\mathrm{Ar{\cdot}N{:}\underset{\underset{+}{\overset{|}{N}}R_3}{C}{-}\bar{O}}$$

The combined operation of both polar and steric factors in the alcohol ROH on the velocity of the reaction are discussed and are shown to be qualitatively in agreement with the experimental data.

In Part I * (*loc. cit.*) it was shown that the reaction between aryl *iso*cyanates and methyl alcohol, in di-*n*-butyl ether as solvent, comprises a "spontaneous" reaction (autocatalysed by the product urethane) and a base-catalysed reaction the velocity of which is, *ceteris paribus*, directly proportional to the concentration of the base : *i.e.*, $k_{exp} = k_0 + k_c[\mathrm{B}]$, where $k_c = k_{bi}/[\mathrm{B}]$. The present paper describes a more detailed kinetic study of this base-catalysed reaction.

It was suggested (Part I, *loc. cit.*) that the reaction kinetics agree with a mechanism of the type



$$\left.\begin{array}{l} \mathrm{Ar{\cdot}N{:}C{:}O + NR_3} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{Ar{\cdot}N{:}\underset{\underset{+}{\overset{|}{N}}R_3}{C}{-}\bar{O}}\ (a) \\ \mathrm{Ar{\cdot}N{:}\underset{\underset{+}{\overset{|}{N}}R_3}{C}{-}\bar{O} + ROH} \xrightarrow{k_3} \mathrm{Ar{\cdot}NH{\cdot}CO_2R + NR_3}\ (b) \end{array}\right\} \quad . \quad . \quad . \quad . \quad \text{(i)}$$

on the basis of which, from the stationary-state condition,

$$k_{bi} = \frac{k_1k_3[\mathrm{NR_3}]}{k_2 + k_3[\mathrm{ROH}]} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

If k_3[ROH] is very small compared with k_2, or if [ROH] does not vary greatly, this relationship approximates to second-order kinetics, $k_{bi} = K[\mathrm{NR_3}]$, and one or other of these conditions

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* The communication, *J.*, 1947, 713, is regarded as Part I of this new series.

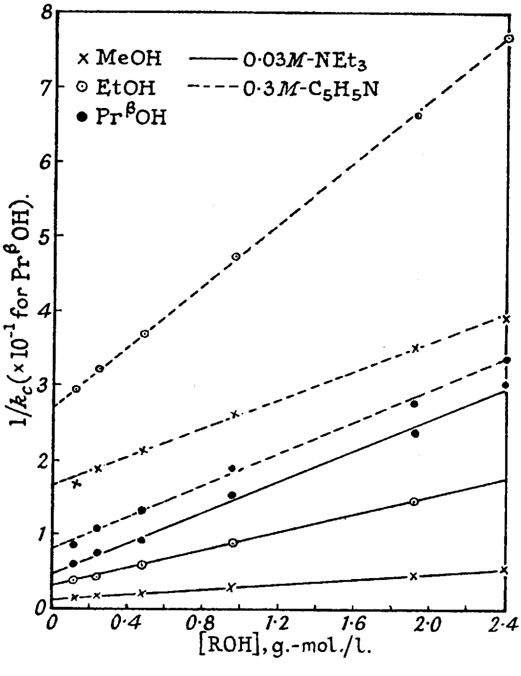
would seem to be fulfilled over the course of any one reaction between the *iso*cyanate and alcohol since the second-order plot of the individual experimental observations always gives a good straight line. Considerable deviations from true second-order kinetics might, however, be expected when the initial concentration of alcohol is varied over a fairly wide range, and a pointer that such is the case was obtained in the earlier work (*loc. cit.*, Table IV, p. 715).

Equation (ii) may be transposed into the form

$$[NR_3]/k_{bi} = 1/k_c = k_2/k_1k_3 + [ROH]/k_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (iii)$$

Hence, if the suggested mechanism is correct, a plot of the various values of $1/k_c$ obtained with varying initial alcohol–*iso*cyanate concentration ratios against the initial alcohol concentration, should give a straight line, the slope of which is $1/k_1$ and the intercept $= k_2/k_1k_3$. The results discussed in Part III (following paper) show that the value of k_0, for the " spontaneous " reaction, is also dependent on the initial molecular ratio [Ar·NCO]/[ROH]; hence, in the determination of the true value of k_{bi} for any particular concentration of alcohol (and of base catalyst) from the relationship $k_{bi} = k_{exp} - k_0$, it is essential to use the appropriate value of k_0 obtained for the *same* [Ar·NCO]/[ROH] ratio. *All values of* k_{bi} *in this paper are thus obtained, the units being g.-mol.*$^{-1}$ *l. min.*$^{-1}$.

Base-catalysed reaction between Ph·NCO *and* ROH *in di*-n-*butyl ether at* 20°.



The data obtained in the experimental test of the relationship (iii) for methyl, ethyl, and *iso*propyl alcohols are given in Table I, and the agreement with the anticipated straight-line relationships is clearly shown in the figure.

The relationship is equally valid when 0·304M-pyridine replaces 0·031M-triethylamine as a catalyst and is thus not dependent on the particular base catalyst employed. The validity is also unaffected by alteration, over a fairly wide range,* in the concentration of the base catalyst; this is proved by the agreement between the values of $1/k_c$, given in Table II, when both alcohol and triethylamine concentrations are varied.

Experimental verification of the relationship (iii) on the basis of kinetic form is thus very satisfactory, but certain difficulties arise when a further test is applied. Equation (iii) requires that the value of k_1, the velocity coefficient for the formation of the base–*iso*cyanate complex, should be independent of the nature of the reacting alcohol. The values of k_1 and the ratio

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* A *large* increase in the [Base]/[ROH] ratio has a small effect on k_c as is shown by a comparison of the corresponding values in Table I (b) (0·304M) with those in Table VI (a) (1·2M-pyridine).

TABLE I.

Effect of varying concentrations of ROH *on the velocity of the base-catalysed reaction between* Ph·NCO(0·24M) and ROH *in di-*n*-butyl ether at 20° in the presence of* (a) 0·031M-NEt_3 *and* (b) 0·304M-*pyridine.*

[ROH], = g.-mol./l.	MeOH.			EtOH.			Pr$^\beta$OH.		
	10^2k_{exp}.	10^2k_{bi}.	$1/k_c$.	10^2k_{exp}.	10^2k_{bi}.	$1/k_c$.	10^2k_{exp}.	10^2k_{bi}.	$1/k_c$.
(*a*) 2·4	6·32	5·45	0·57	3·17	1·73	$1{\cdot}76_5$	0·51	0·10	30·30
1·92	7·41	6·65	0·46	3·19	2·07	1·47	0·52	0·13	23·81
0·96	11·35	10·89	0·28	4·26	3·42	0·89	0·54	0·21	15·15
0·48	16·43	16·17	0·19	5·96	5·40	0·56	0·55	0·33	9·17
0·24	20·46	20·29	0·15	7·64	7·35	0·41	0·57	0·42	7·30
0·12	23·64	23·58	0·13	8·63	8·54	0·36	0·60	0·525	5·81
(*b*) 2·4	8·63	7·76	3·94	5·11	3·94	7·69	1·31	0·90	33·8
1·92	9·47	8·71	3·51	5·70	4·58	6·64	1·49	1·10	27·8
0·96	12·17	11·71	2·61	7·28	6·44	4·72	1·95	1·62	18·7
0·48	14·75	14·49	2·11	8·82	8·26	3·68	2·54	2·33	13·0
0·24	16·58	16·41	1·87	9·79	9·50	3·20	3·05	2·91	10·5
0·12	18·58	18·52	1·65	10·48	10·39	2·93	3·70	3·63	8·4

TABLE II.

Effect of varying the concentrations of both MeOH *and* NEt_3 *on the velocity of the base-catalysed reaction with* Ph·NCO (0·24M) *in di-*n*-butyl ether at* 20°.

[MeOH], g.-mol./l.	[NEt_3], g.-mol./l.									Mean value, $1/k_c$.
	0·0307.			0·0460.			0·0613.			
	10^2k_{exp}.	10^2k_{bi}.	$1/k_c$.	10^2k_{exp}.	10^2k_{bi}.	$1/k_c$.	10^2k_{exp}.	10^2k_{bi}.	$1/k_c$.	
2·4	6·32	5·45	*0·57*	—	—	—	12·6	11·73	*0·52*	$0{\cdot}54_5$
1·92	7·41	6·65	*0·46*	—	—	—	14·4	13·64	*0·45*	$0{\cdot}45_5$
0·96	11·35	10·89	*0·28*	—	—	—	22·2	21·74	*0·28*	0·28
0·48	16·43	16·17	*0·19*	26·0	25·74	*0·18*	34·7	34·44	*0·18*	0·18
0·24	20·46	20·29	*0·15*	31·4	31·23	*0·15*	38·3	38·13	*0·16*	0·15
0·12	23·64	23·58	*0·13*	33·3	33·24	*0·14*	44·2	44·14	*0·14*	0·14

TABLE III.

Values of k_1 *and* k_3/k_2 *for the base-catalysed reaction of* ROH *with* 0·24M-Ph·NCO *in di-*n*-butyl ether.*

ROH =	MeOH.			EtOH.			Pr$^\beta$OH.	
	a.	*b.*	*c.*	*a.*	*b.*	*c.*	*a.*	*b.*
$k_1^{20°}$	5·45	1·02	1·20	1·60	0·48	$0{\cdot}48_5$	0·096	0·095
$k_1^{30°}$	12·05	—	1·87	3·45	—	1·19	0·282	—
$k_3/k_2^{20°}$	1·71	0·60	0·54	2·27	0·79	0·79	2·26	1·32
$k_3/k_2^{30°}$	1·01	—	0·59	1·41	—	0·49	1·37	—

(*a*) = 0·0307M-NEt_3; (*b*) = 0·304M-C_5H_5N; (*c*) = 1·2M-C_5H_5N (cf. p. 15).

k_3/k_2 at 20° and 30°, determined from the straight-line plots of $1/k_c$ against [ROH] (as in the figure) are given in Table III.

It is immediately apparent that, with either triethylamine or pyridine as catalyst, the value of k_1 is, contrary to the requirements of equation (iii), very dependent on the *nature* of the alcohol participating in the reaction. None of the many mechanisms which have been considered, in which the alcohol concentration is directly concerned in the formation of the intermediate base–*iso*cyanate complex as, for example, the establishment of an equilibrium of the type $NEt_3 + ROH \rightleftharpoons NEt_3,ROH$ complex, this complex *alone* being the effective catalyst, will fit the kinetic data or give the straight-line relationship (iii) in which only the first power of the [ROH] enters. Any base–alcohol interaction of the type $NEt_3 + ROH \rightleftharpoons \overset{+}{N}HEt_3\}\overset{-}{O}R$, followed by attack by the alkoxide ion on the *iso*cyanate, is a catalytic mechanism already excluded (Part I, *loc. cit.*) by the observation that the dialkylanilines exhibit no catalytic activity. The direct proportionality of k_{bi} with base concentration (for any given initial alcohol and *iso*cyanate concentrations) is another difficulty in the acceptance of such mechanisms. In non-hydroxylic solvents the medium effect of the addition of an alcohol cannot be overlooked, but it is considered unlikely that the concentrations of alcohol used (maximum 2·4M) would cause such large deviations by a purely *differential* medium effect when, say, methyl alcohol is replaced by ethyl alcohol. The data thus compel the conclusion that the velocity of interaction between the base and the *iso*cyanate must be dependent on the *nature* of the reacting alcohol, without the concentration of the alcohol entering directly into the kinetics of stage (i, *a*) of the reaction mechanism. Further evidence that the alcohol is, in some way, concerned in stage (i, *a*) is provided by results derived from the effect of temperature on the reaction. The results given in Table IV show that the ratio $k_{bi}^{30°}/k_{bi}^{20°}$ (and hence the Arrhenius critical activation energy, E_{bi}, derived from it) increases with increasing concentration of the alcohol.

TABLE IV.

Values of k_{bi} *at* 20° *and* 30° *for the reaction between* Ph•NCO (0·24M) with varying *concentrations of* ROH *in di*-n-*butyl ether, catalysed by* 0·031M-NEt$_3$.

[ROH], = g.-mol./l.	MeOH.				EtOH.			
	$10^2k_{bi}^{20°}$.	$10^2k_{bi}^{30°}$.	$k_{bi}^{30°}/k_{bi}^{20°}$.	E_{bi}, kcals.	$10^2k_{bi}^{20°}$.	$10^2k_{bi}^{30°}$.	$k_{bi}^{30°}/k_{bi}^{20°}$.	E_{bi}, kcals.
2·4	5·45	10·7	1·96	11·9	1·73	3·42	1·98	12·1
1·92	6·65	12·7	1·91	11·4	2·07	3·95	1·91	11·4
0·96	10·9	19·7	1·81	10·5	3·42	5·59	1·63	8·6
0·48	16·2	25·0	1·54	7·6	5·40	8·66	1·60	8·3
0·24	20·29	27·6	1·36	5·4	7·35	11·48	1·56	7·8
0·12	23·6	—	—	—	8·54	13·56	1·59	8·2

[ROH], g.-mol./l.	Pr$^\beta$OH.			
	$10^2k_{bi}^{20°}$.	$10^2k_{bi}^{30°}$.	$k_{bi}^{30°}/k_{bi}^{20°}$.	E_{bi}, kcals.
2·4	0·10	0·26	2·60	16·7
1·92	0·13	0·32	2·49	16·1
0·96	0·21	0·51	2·42	15·6
0·48	0·33	0·68	2·05	12·6
0·24	0·42	0·88	2·08	12·9
0·12	$0·52_5$	1·22	2·33	14·9

With a given, constant, concentration of base catalyst, the second-order velocity coefficient $k_{bi} = k_1k_3/(k_2 + k_3[\text{ROH}])$, whence

$$\begin{aligned} E_{bi} &= \frac{\boldsymbol{R}T_2T_1}{T_2 - T_1} \cdot \ln k_{bi}^{30°}/k_{bi}^{20°} \\ &= \frac{\boldsymbol{R}T_2T_1}{T_2 - T_1} \ln \left\{ \frac{k_1^{30°}k_3^{30°}}{k_2^{30°} + k_3^{30°}[\text{ROH}]} \times \frac{k_2^{20°} + k_3^{20°}[\text{ROH}]}{k_1^{20°}k_3^{20°}} \right\} \\ &= E_1 + E_3 + \frac{\boldsymbol{R}T_2T_1}{T_2 - T_1} \cdot \ln \frac{k_2^{20°} + k_3^{20°}[\text{ROH}]}{k_2^{30°} + k_3^{30°}[\text{ROH}]} \end{aligned}$$

From the values of k_3/k_2 at 20° and 30°, given in Table III, the value of k_3 can be determined in terms of k_2. Substitution of these values in the above expression enables it to be reduced to the form

$$E_{bi} = E_1 + E_3 - E_2 + \frac{\boldsymbol{R}T_2T_1}{T_2 - T_1} \cdot \ln \left\{ \frac{1 + a[\text{ROH}]}{1 + b[\text{ROH}]} \right\}$$

where E_1, E_2, E_3 are the activation energies associated with k_1, k_2, and k_3 in the mechanism (i) (p. 9) and $k_3^{20°} = ak_2^{20°}$ and $k_3^{30°} = bk_2^{30°}$. The data in Table III show that the values of a and b for the three alcohols are as follows.

ROH =	MeOH.	EtOH.	Pr$^\beta$OH.
a =	1·71	2·27	2·26
b =	1·01	1·41	1·37

Thus the suggested mechanism (i) requires that the value of E_{bi} *should* be dependent on the alcohol concentration, the magnitude of this dependence being determined by the value of the term $\frac{\boldsymbol{R}T_2T_1}{T_2 - T_1} \ln \left\{ \frac{1 + a[\text{ROH}]}{1 + b[\text{ROH}]} \right\} = \varepsilon$. The values of this term for the various concentrations of the three alcohols studied are given in Table V.

If the observed variations in the values of E_{bi} are completely accounted for by the concentration-dependent term ε, the values of $E_{bi} - \varepsilon = E_1 + E_3 - E_2$ should be constant and independent of the initial alcohol concentration. Caution is necessary in the application of this test to the experimental data. The experimental technique employed was found to be unsatisfactory at temperatures >30°; hence the values of E_{bi} are derived from velocity determinations at only two temperatures. Moreover, with *iso*propyl alcohol further errors arise because, in the determination of k_{bi} from the relationship $k_{bi} = k_{exp} - k_0$, the velocities are small and $k_0 \gg k_{bi}$ when the initial concentration of alcohol is large. The E_{bi} values are thus probably liable to an error of ~1 kcal. and their accuracy is probably greatest with methyl alcohol and least with *iso*propyl alcohol. Table V shows that, for methyl alcohol, the values of $E_{bi} - \varepsilon$ for [MeOH] = 0·48—2·4M are approximately constant, the mean deviation from the mean value of 4·75 kcals. being only 0·4 kcal. The value for [MeOH] = 0·24M shows a wider divergence (1·5 kcals.). If this figure is included, the mean value of $E_{bi} - \varepsilon$ over the whole concentration range studied is 4·5±0·6 kcals. The mean deviations in the cases of ethyl and *iso*propyl alcohols are progressively larger. It is evident that the *main* cause of the variation of E_{bi} with alcohol concentration is the term ε, which arises directly from the postulated reaction mechanism (i) (p. 9), and the fact that the reaction is not a true second-order one as is assumed in the calculation of the individual values of k_{bi}. On the other hand, the variation of k_1 and E_1 (derived from the value of the ratio $k_1^{30°}/k_1^{20°}$) with the different alcohols indicates that the alcohol must play some part in stage (i, *a*) of the reaction mechanism, whilst the irregularities in the separate values of $E_{bi} - \varepsilon$ for any one alcohol *may* indicate a possible small concentration-dependence of E_2 and/or E_3.

TABLE V.

Value of ε, E_{bi}, E_1 (kcals./mol.) *and* $(PZ)_1$ (*units in min.*$^{-1}$) *in the reaction of varying concentrations of* ROH *with* Ph•NCO (0·24M) *with* 0·031M-NEt$_3$ *as catalyst in di*-n-*butyl ether.*

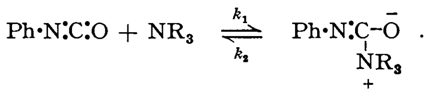
[ROH], = g.-mol./l.	MeOH.			EtOH.			Pr$^{\beta}$OH.		
	E_{bi}.	ε.	$E_{bi}-\varepsilon= E_1+E_3-E_2$.	E_{bi}.	ε.	$E_{bi}-\varepsilon= (E_1+E_3-E_2)$.	E_{bi}.	ε.	$E_{bi}-\varepsilon= (E_1+E_3-E_2)$.
2·4	11·9	7·0	4·9	12·1	6·9	5·2	16·7	7·1	9·6
1·92	11·4	6·6	4·8	11·4	6·5	4·9	16·1	6·8	9·3
0·96	10·5	5·2	5·3	8·6	5·3	3·3	15·6	5·6	10·0
0·48	7·6	3·6	4·0	8·3	3·9	4·4	12·6	4·0	8·6
0·24	5·4	2·2	3·2	7·8	2·5	5·3	12·9	2·6	10·3
0·12	—	1·3	—	8·2	1·5	6·7	14·9	1·5	13·4
		Mean 4·5±0·6			Mean 5·0±0·8			Mean 10·1±1·05	
E_1		14·0		13·7			19·0	(From temp. coeffs. of k_1 and k_3/k_2, respectively.)	
$E_3 - E_2$		−9·4		−8·5			−8·7		
$(PZ)_1$		$1·45 \times 10^{11}$		$1·6 \times 10^{10}$			$1·5 \times 10^{13}$		

Examination of the infra-red absorption of methyl and ethyl alcohols in di-*n*-butyl ether and the effect of added triethylamine, described in Part IV (this vol., p. 24), shows that there is no detectable unassociated OH band at 2·76 μ in this medium even at considerable dilution, but that association of the alcohol molecules with the solvent, possibly with themselves, *and with the added base*, occurs. Any explanation of the above anomalies based on alcohol–alcohol or alcohol–solvent association alone would, on the basis of mechanism (i), fail to explain the variation of k_1 and E_1 with different alcohols, and it seems probable that any alcohol dependence must be associated with the formation and dissociation of the base–*iso*cyanate complex.

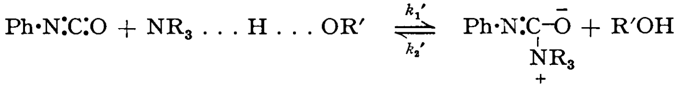
Two possible explanations (not necessarily mutually exclusive) of this observation have been explored. Neither is completely satisfactory since they both involve postulates which are not susceptible to direct experimental verification. The first hypothesis, which finds some support from the infra-red absorption data (*loc. cit.*), is that the amine catalyst and the alcohol rapidly form a complex (most probably by hydrogen-bonding) in accordance with the general scheme :

$$NR_3 + HOR' \rightleftharpoons NR_3 \ldots H \ldots OR' \quad . \quad . \quad . \quad . \quad . \quad \text{(iv)}$$

and *both* the free amine molecules *and* the base–alcohol complex can function as catalysts for the reaction, the *same iso*cyanate–base complex resulting from attack by either catalytic entity. On this view, stage (i, *a*) in the mechanism on p. 9 is really a composite of the following closely similar equilibria :



$$Ph{\cdot}N{:}C{:}O + NR_3 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Ph{\cdot}N{:}\underset{\underset{+}{NR_3}}{\overset{|}{C}}{-}\bar{O} \quad . \quad . \quad . \quad . \quad . \quad (i, a)$$



$$Ph{\cdot}N{:}C{:}O + NR_3 \ldots H \ldots OR' \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} Ph{\cdot}N{:}\underset{\underset{+}{NR_3}}{\overset{|}{C}}{-}\bar{O} + R'OH \quad . \quad . \quad (i, a')$$

With such a composite mechanism the straight-line relationship (iii) (p. 10) would not apply strictly. The true relationship would be of the type $[\mathrm{B}]/k_{\mathrm{bi}} - K[\mathrm{B}] = k_2/k_1k_3 + [\mathrm{ROH}]/k_1$, where K is a composite constant composed of the velocity coefficients involved in the various reaction stages. It would depend on the (unknown) magnitude of the term $K[\mathrm{B}]$ whether the resulting correction to the value of $1/k_0$ were sufficiently large to cause a detectable deviation from the straight-line relationship.

In agreement with experiment, the value of the (composite) k_1 would then be dependent on the *nature* of the alcohol and, since the sum of the concentrations of the two postulated catalytic entities would always be proportional to the total concentration of added base catalyst, the direct proportionality observed between k_{bi} and catalyst concentration is also accounted for. An explanation of the variations in E_1 with different alcohols is also possible. The formation of the *iso*cyanate–base complex with the free amine is, in terms of Lewis's acid–base theory, merely the neutralisation of a secondary acid (carbonyl group) with a primary base ($\mathrm{NR_3}$), but the formation of the same reaction complex with the alcohol–amine entity would also involve the rupture of the hydrogen bond of the association complex, the nature of which differs from alcohol to alcohol. Also, it might be expected that the formation of the base–*iso*cyanate complex would occur less readily by scheme (i, *a′*) than by scheme (i, *a*). This might be due to an effect on either E_1 or $(PZ)_1$ in the Arrhenius equation. Displacement of the equilibrium (iv) to the right could increase the relative proportion of reaction which occurs by scheme (i, *a′*) instead of by (i, *a*), and would therefore increase the overall activation energy for the formation of the base–*iso*cyanate complex.

In an attempt to apply an experimental test to this hypothesis, a series of experiments was carried out in which, unlike the conditions previously employed, the concentration of the base catalyst was never smaller than, and was usually very much greater than, that of the reacting alcohol. Under such conditions there is the possibility that reaction *via* the free amine itself as the catalytic entity might greatly predominate, with the consequences that (*a*) the activation energy $E_{\mathrm{bi}} - \varepsilon$ would remain sensibly constant for varying initial alcohol concentrations, and (*b*) k_1 and E_1 might be much less dependent on the nature of the alcohol. Because of the very great velocities involved with high concentrations of basic catalyst, the experimental technique of such a test was not easy, and investigation has only been possible by using the much weaker base pyridine in 1·2M-concentration as the catalyst with an alcohol concentration varying from 0·12 to 1·2M. The results are given in Table VI.

With both alcohols prediction (*a*) is fulfilled since, over the whole range of $[\mathrm{ROH}] = 0{\cdot}12 - 1{\cdot}2\mathrm{M}$, the mean deviation from the mean value of $E_{\mathrm{bi}} - \varepsilon$ is, for methyl alcohol, $9{\cdot}6 \pm 0{\cdot}5$, and, for ethyl alcohol, $7{\cdot}3 \pm 0{\cdot}3$ kcals. The values of k_1 for the two alcohols still differ, but less widely (especially at 30°) than do those obtained when $[\mathrm{ROH}] \gg [\mathrm{Base}]$ [cf. Table III (a) and (c)] but a large variation in E_1 for the two alcohols is still shown, the difference in this case being between methyl and ethyl alcohols for which the values were nearly identical with triethylamine catalysis.

The alternative hypothesis, which is preferred by the authors, is also based essentially on the rôle solvation plays in the reaction. In Part I (*loc. cit.*, p. 717) it was noted that the energy changes involved in the formation of the base–*iso*cyanate complex are $+ D_{\mathrm{O-N}} - I_{\mathrm{N}} + E_{\mathrm{O}} - D_{\mathrm{C:O}} + S$, where S is the energy of solvation; S is really a composite term which includes the solvation energies of the amine, the *iso*cyanate, and the base–*iso*cyanate complex, *i.e.*, $S = - S_{\mathrm{NR_3}} - S_{\mathrm{Ph{\cdot}NCO}} + S_{\mathrm{complex}}$. Nothing is known regarding the solvation of the *iso*cyanate, but the infra-red data show that the solvation of the amine by the alcohol is significant. Owing to the more polar nature of the postulated, intermediate complex, $\mathrm{Ph{\cdot}N{:}C(\overset{+}{N}R_3){-}\overset{-}{O}}$, however, it would be expected that the solvation of this entity would be more important and hence that the term S_{complex} would make a major contribution towards the total solvation energy S. The greater the degree of solvation of the complex, the more facile should be the forward reaction (i, *a*), and hence the greater the value of k_1. On both polar and steric grounds such solvation would be expected to decrease in the order MeOH > EtOH > $\mathrm{Pr^{\beta}OH}$, in agreement with the experimentally observed decrease in the value of k_1 in the same sequence (Table III), with both triethylamine and pyridine catalysis.

As the velocity coefficient k_1 falls, the values of both E_1 and $\ln (PZ)_1$ increase, and this increase is more marked the weaker is the catalyst base. Although a detailed discussion of this change is not yet possible, the authors believe that it indicates very clearly the rôle that the solvation is playing in the reaction. Such compensating changes in E and $\ln PZ$ are usually associated with reactions in which solvation energy and entropy are important. Incidentally, it will be noticed that, on this second hypothesis, the persistent variation of k_1 with different

TABLE VI.

(a) *Effect of varying* [ROH] *on the velocity of the reaction between* Ph•NCO (0·24M) *and* ROH *with an excess of the base catalyst, pyridine* (1·2M) *in di-*n*-butyl ether at* 20° *and* 30°.

[MeOH], g.-mol./l.	20°.			30°.				
	10^2k_{bi}.	k_c.	$1/k_c$.	10^2k_{bi}.	k_c.	$1/k_c$.	$k_{bi}^{30°}/k_{bi}^{20°}$.	E_{bi}, kcals.
1·20	46·65	0·39	2·57	79·2	0·66	1·51	1·70	9·3$_5$
0·96	51·81	0·43	2·32	84·2	0·70	1·43	1·63	8·6
0·48	62·39	0·52	1·92$_5$	102·4	0·85	1·17	1·64	8·7
0·24	64·25	0·57	1·76$_5$	114·9	0·96	1·04	1·79	10·3
0·12	74·15	0·62	1·62	123·2	1·03	0·97	1·66	8·9
						Mean	1·68	9·1

[EtOH], g.-mol./l.	20°.			30°.				
	10^2k_{bi}.	k_c.	$1/k_c$.	10^2k_{bi}.	k_c.	$1/k_c$.	$k_{bi}^{30°}/k_{bi}^{20°}$.	E_{bi}, kcals.
1·20	23·55	0·20	5·10	44·44	0·37	2·70	1·89	11·4
0·96	26·25	0·22	4·57	46·54	0·39	2·58	1·77	10·2
0·48	34·24	0·28$_5$	3·51	56·91	0·47	2·11	1·67	9·0
0·24	38·04	0·32	3·15	62·00	0·52	1·93	1·63	8·7
0·12	47·91	0·40	2·51	73·00	0·61	1·64$_5$	1·53	7·6

(b) *Values of* E_{bi}, ε, E_1 (*kcals./mol.*) *and* (PZ) (*units in min.*$^{-1}$) *in the reactions of varying concentrations of* ROH *with* Ph•NCO (0·24M) *with* 1·2M-*pyridine as catalyst in di-*n*-butyl ether.*

[ROH], g.-mol./l.	MeOH.			EtOH.		
	E_{bi}.	ε.	$E_{bi}-\varepsilon$ $(=E_1+E_3-E_2)$.	E_{ib}.	ε.	$E_{bi}-\varepsilon$ $(=E_1+E_3-E_2)$.
1·2	9·4	−0·7	10·1	11·4	3·6	7·8
0·96	8·6	−0·6	9·2	10·2	3·2	7·0
0·48	8·7	−0·3	9·0	9·0	2·0	7·0
0·24	10·3	−0·2	10·5	8·7	1·1	7·6
0·12	8·9	−0·1	9·0	7·6	0·6	7·0
			Mean 9·6±0·5			Mean 7·3±0·3
	E_1		7·8	15·8	(From temp. coeffs. of k_1 and k_3/k_2, respectively.)	
	$E_3 - E_2$		1·4	−8·5		
	$(PZ)_1$		$7{\cdot}2 \times 10^5$	$2{\cdot}4 \times 10^{11}$		

alcohols in the experiments in which $[C_5H_5N] > [ROH]$ is understandable, since the [ROH] (0·12—1·2M) was, with one exception, >[Ph·NCO] (0·24M) and hence also >[complex].

If either of the modified views of the mechanism of the reaction is correct, the earlier hope that, by a study of the effect of varying alcohol concentrations at different temperatures, it would be possible to evaluate the activation energy for the co-ordination of any base with the *iso*cyanate molecule, cannot be realised. For the same reasons, since k_2 is also composite, quantitative interpretation of the values of $E_3 - E_2$ would be of doubtful value. Certain qualitative deductions may, however, be made. When the catalyst is the strong base, triethylamine, the ratio k_3/k_2 is always >1 and the value of $E_3 - E_2$ is negative, *i.e.*, $k_3 > k_2$ and $E_2 > E_3$, which means that there is a greater tendency for the *iso*cyanate–base complex to react with alcohol to form the urethane than to dissociate into its original components. With the weaker base, pyridine, in 0·3M-concentration, the converse would seem to be true ($k_2 > k_3$), since $k_3/k_2 < 1$ for methyl and ethyl alcohols, but not for the very slow reaction with *iso*propyl alcohol for which $k_3 > k_2$.

The Catalytic Coefficient of the Base.—The observation that the value of k_c is dependent not only on the nature of the alcohol taking part in the reaction but also, for any one alcohol, on the initial concentration of this reactant, raises the question as to the real meaning and significance of this entity. If either of the mechanisms of catalysis suggested on the basis of the results described in this communication is correct, the determination of any absolute value for the catalytic coefficient of the base itself would seem to be impossible. For the purposes of comparison of the relative values of k_c for different bases, the best measure would seem to be the extrapolated value derived from equation (iii) (p. 10) when the concentration of the alcohol is zero : k_c then becomes k_1k_3/k_2 or Kk_3 with which it was identified in Part I (*loc. cit.*, p. 717), but it must be remembered that k_1 and k_2 are probably themselves dependent of the nature of the alcohol so that any comparison between the catalytic effects of different bases must be made using the values for reaction with the same alcohol in every case. On this basis the values obtained for triethylamine and pyridine are given in Table VII. The relative value of k_c for triethylamine and pyridine so obtained (15·2) for the reaction with methyl alcohol does not differ greatly from that (7·45/0·56 = 13·3) previously obtained under the standard reaction conditions of Part I.

TABLE VII.

Values of $k_c = Kk_3$ *when* [ROH] = 0 *for* (a) NEt_3, (b) C_5H_5N.

	MeOH.	EtOH.	Pr$^\beta$OH.		MeOH.	EtOH.	Pr$^\beta$OH.
(*a*) $k_c^{20°}$	9·3	3·6	0·22	(*b*)	0·61	0·38	0·12$_5$
$k_c^{30°}$	19·3	5·0	0·38$_5$		—	—	—
k_c^a/k_c^b at 20° ...	15·2	9·5	1·75		—	—	—

Effect of varying the Reacting Alcohol—The experiments so far described on the effect of varying alcohol concentration on the velocity and activation energy of the reaction with phenyl *iso*cyanate have been restricted to the three alcohols, methyl, ethyl, and *iso*propyl, since, with *tert.*-butyl alcohol, the reaction velocity is too slow and, in consequence, the numerical values too susceptible to error to justify such an extended investigation. Reactions with both *tert.*-butyl alcohol and phenol have, however, been studied under the standard conditions of equimolecular concentration (0·24M). The comparative data for the whole series are given in Table VIII.

TABLE VIII.

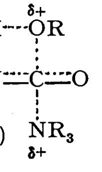
Reaction of ROH *with* Ph·NCO (*both* 0·24M) *in di*-n-*butyl ether with* 0·0306M-NEt_3 *at* 20° *and* 30°:

R =		Me.	Et.	Pr$^\beta$.	Bu$^\gamma$.	Ph.
10^2k_{exp}	20°	20·46	7·64	0·57	0·009	7·20
	30°	27·92	11·99	1·12	0·016	10·0 *
10^2k_{bi}	20°	20·29	7·35	0·42	0·003$_5$	7·19
	30°	27·62	11·48	0·88	0·0073	10·0
E_{bi}, *k*cals.		5	7·85	13	13	5·8

* Extrapolated from the value obtained when using 0·0312M-NEt_3 as catalyst.

The large velocity decrease in the series Me > Et > Pr$^\beta$ > Bu$^\gamma$ is only partly accounted for by a corresponding increase in the activation energy, which suggests that steric factors are also important. It is very unlikely that fission of the alcohol occurs thus R ¦ $^-$OH, and such a possibility is excluded by the observation that both the spontaneous and the base-catalysed reaction of phenyl *iso*cyanate with (—)-borneol give the optically active urethane. If the reaction involved the formation of $\overset{+}{R}$ at any stage, considerable racemisation would be expected, hence it seems almost certain that the fission of the alcohol occurs between the hydrogen and the oxygen, as, indeed, would be expected.

On the basis of either of the hypotheses discussed above, it would be anticipated that the *differential* influence of both steric and polar factors on the formation of the base–alcohol complex would be relatively unimportant, a view which finds support in the close similarity between the infra-red absorption curves for methyl and ethyl alcohols in the presence of triethylamine (Part IV, *loc. cit.*). The important stages would be, most probably, the formation of the *iso*cyanate–base complex and the further reaction of this with the alcohol. Solvation of the amine by a bulky alcohol molecule would prevent its close approach to the *iso*cyanate molecule, and it has already been noticed that solvation of the base–*iso*cyanate complex would be expected to diminish as the alcohol series is ascended. Thus both factors would tend to favour a velocity order Me > Et > Pr$^\beta$ > Bu$^\gamma$ for the first stage of the reaction. The large increase (*ca.* 5 kcals.) in the value of E_1 (p. 13) when reaction with the secondary, *iso*propyl alcohol replaces that with ethyl alcohol confirms this conclusion. The formation of the product urethane by the attack of an alcohol molecule on the base–*iso*cyanate complex must involve a transition complex of the general type (II). The ready formation of such a complex, and the completion of the reaction to give the urethane, would be favoured by (1) the necessary close approach of the alcohol molecule to the base–*iso*cyanate complex, which would be hindered if the alcohol were of the bulky character of *tert.*-butyl, and (2) the ease of breaking of the H–O bond in the alcohol.* Thus, in this stage also, both polar and steric factors in the alcohol favour


(II.)

$$\begin{array}{c} \overset{\delta+}{H\cdots OR} \\ \vdots \\ PhN \overset{\cdots}{=} C \overset{\cdots}{=} O \\ \vdots \\ \underset{\delta+}{NR_3} \end{array}$$

---

* The acid strength sequence MeOH > EtOH > Pr$^\beta$OH > Bu$^\gamma$OH, derived from the general inductive effects (+*I*) of alkyl groups, is confirmed if use is made of the heats of combustion, in the gas phase, of the various alcohols to calculate the energy of the molecule, and hence, using the accepted values of the C-H, C-C, and C-O bond energies, to estimate the bond energies of the O-H bond in the four alcohols. The values so obtained are: MeO-H, 89·4; EtO-H, 94·0; Pr$^\beta$O-H, 100·0; Bu$^\gamma$O-H, 101·1 kcals./mol.

a reaction velocity order Me > Et > Pr^{β} > Bu^{γ}. This order is thus anticipated as the result of the operation of both polar and steric factors on all the significant stages in the proposed reaction mechanism and is in harmony with the experimental data.

The case of the much more strongly acidic phenol is interesting. The very slow " spontaneous " reaction of this alcohol with phenyl *iso*cyanate is discussed in the following paper, but in the base-catalysed reaction its velocity is closely similar to that of the much more weakly acidic ethyl alcohol. Although the more strongly acidic character of phenol will facilitate the fission of the PhO–H bond in the final formation of the urethane, it would also be expected to favour the formation of a relatively stable amine–phenol complex so that, in this reaction, the more important catalytic entity may be the complex NEt_3 . . . H . . . OPh, containing a much stronger hydrogen bond which has to be broken in the formation of the base–*iso*cyanate complex. This factor, possibly augmented by a steric effect due to the size of the phenol group and the resonance-stabilised planar configuration of the molecule, could explain the observation that phenol reacts more slowly with phenyl *iso*cyanate than does the much more weakly acidic methyl alcohol.

Thus the modifications of the original mechanism tentatively advanced on pp. 13 and 14 and for which there is some support from the study of the infra-red absorption, do permit plausible explanations for *all* the experimental data, which no other mechanism yet suggested is able to do, and may be regarded as at least a close approximation to the real nature of the *iso*cyanate–alcohol reaction. It is hoped that some information on the effect of association and solvation of the alcohol on the reaction may accrue from studies in a hydrocarbon solvent which are at present in hand (cf. Part V, this vol., p. 27).

EXPERIMENTAL.

Materials.—*Di*-n-*butyl ether.* The original sample, purified as described below, was reclaimed from the residues obtained in earlier kinetic experiments, in the following manner. The collected residues were shaken with 1·5 times their own volume of water, and basic substances were removed from the separated ethereal layer by five extractions with concentrated hydrochloric acid followed by five washings with water. After drying ($CaCl_2$), the ether was kept in the dark for 14 days over 1% of solid potassium hydroxide and 1% of powdered potassium permanganate to remove peroxides. After filtration, the ether was again washed repeatedly with water, dried ($CaCl_2$), and distilled under reduced pressure. Drying was then completed by refluxing the ether over fresh sodium until no further action occurred, and the sample was carefully fractionated through a Widmer column. The fraction, b. p. 45·4°/23 mm., was stored over clean sodium wire in a glass-stoppered flask in the dark and the requisite quantities were redistilled just before use.

Methyl alcohol. Absolute methyl alcohol (500 ml.) was refluxed for 10 hours with 2·5 g. of magnesium turnings and 0·5 g. of mercuric chloride and fractionated through a Widmer column in an apparatus from which atmospheric moisture was excluded by phosphoric oxide drying tubes; b. p. 64·0°. All alcohols were stored in sealed, dry tubes, previously ignited and cooled in a vacuum desiccator to remove moisture occluded in the glass.

Ethyl alcohol. This was purified and dried by the method of Lund and Bjerrum (*Ber.*, 1931, **64**, 210) and fractionated through a Widmer column; b. p. 77·8°.

iso*Propyl alcohol.* The original specimen was found to contain a considerable quantity of water, which was removed by refluxing (twice) over freshly ignited calcium oxide. Drying was completed on the distilled sample either by (1) refluxing for 6 hours with solid aluminium *iso*propoxide or (2) refluxing with aluminium amalgam (Vogel, *J.*, 1927, 597). Fractionation through a Widmer column gave a specimen, b. p. 81·5°.

tert.-*Butyl alcohol.* The solid alcohol was partly melted until about 25% had liquefied, and the liquid was decanted. The residual solid alcohol was refluxed for 6 hours with freshly ignited calcium oxide, distilled, refluxed with 2% of its weight of sodium, and finally fractionated through a Widmer column; b. p. 81·0°.

Phenol. " AnalaR " Phenol (50 g.) was refluxed with 1 g. of pure phenyl *iso*cyanate under reduced pressure for 24 hours and then fractionated through a Widmer column, the sample, b. p. 86·5°/23 mm., being collected.

Phenyl iso*cyanate, triethylamine, pyridine, and piperidine.* These were purified and dried as described in earlier work (Baker and Holdsworth, *J.*, 1947, 713). Samples were redistilled from the appropriate drying agent immediately before use : the b. p.s were : phenyl *iso*cyanate, 64·5°/23 mm.; triethylamine, 89°; pyridine, 115·5°; piperidine, 105°. The acetone, b. p. 56°, constant b. p. alcohol, b. p. 77·0°, and the screened methyl-red indicator were prepared as previously described (*loc. cit.*).

Determination of Phenyl iso*Cyanate.*—The method used was essentially that described in Part I (*loc. cit.*) but, in view of the very large number of kinetic experiments involved in the investigation, it was adapted to the micro-scale. All pipettes and graduated flasks used were weight-calibrated with the actual solvent, di-*n*-butyl ether, both absolutely and against each other; the density values for the ether were those given by the International Bureau of Standards (*Chem. Abs.*, 1931, **25**, 2038), *viz.*, $d^{0°}$ 0·78563, $d^{15°}$ 0·77254, $d^{30°}$ 0·75976. The total volume of reaction solution was 20 ml., and 2 ml. samples were taken for each determination, the quantities of the various other materials being correspondingly reduced, *viz.*, piperidine solution (0·5M instead of 1·0M) 2 ml.; 0·563N-alcoholic hydrogen chloride, 2 ml.; constant b. p. alcohol, 3 ml. The final titration with 0·568N-sodium hydroxide solution was carried out using an N.P.L. standard 2 ml. microburette, 3 drops of the indicator being used for each titration. A calibration curve for the determination of the phenyl *iso*cyanate was constructed from the following data, obtained with various weights of the *iso*cyanate delivered from a weight pipette :

Blank = 0·203, 0·205, 0·204; mean = 0·204 ml. of NaOH solution.

Ph·NCO (mg.)	96·9	70·9	57·0	42·1	29·4	11·2	5·6
Vol. of NaOH required (ml.)	1·575	1·218	1·009	0·800	0·624	0·372	0·294
Less blank (ml.)	1·371	1·014	0·805	0·596	0·420	0·168	0·090

A plot of the weight of phenyl *iso*cyanate against the corrected volume of sodium hydroxide solution gave a good straight line, showing direct proportionality over the whole concentration range studied.

Application of this method to a study of the reaction between 0·2449M-phenyl *iso*cyanate and 0·2414M-methyl alcohol, catalysed by 0·0309M-triethylamine, gave values of 10^2k_2 slightly lower than those (22·9) obtained previously by the original technique, but the reproducibility of the values (20·5, 20·6) confirmed the reliability of the micro-technique, the small difference probably being due to even more effective exclusion of moisture resultant on the general improvement in technique consequent on longer experience with the method.

Velocity Determinations.—These were carried out in a manner exactly similar to that previously described (Part I, *loc. cit.*) except that the reaction vessels, of the same pattern as those previously used, had a capacity of *ca.* 30 ml. and the total initial volume of the reaction solution was only 20 ml. : 2-ml. samples were taken and the phenyl *iso*cyanate was determined by the micro-technique, the appropriate calibration curve being used. The very large number of separate velocity determinations makes it impracticable to record details of individual runs. In general 6—9 separate determinations at suitable time intervals were taken and the value of the second-order velocity coefficient was determined from the slope of the best straight-line plot of either $x/(a - x)$ or $\log_{10} b(a - x)/a(b - x)$ against time (in minutes). In every case all the individual experimental points fell closely on such a straight line. The values of k_{exp} thus determined under varying reaction conditions have already been given. The values of the second-order coefficients for the "spontaneous" reaction were similarly determined for identical *iso*cyanate–alcohol concentrations and these values (recorded in Part III, following paper) were used to determine the true values of k_{bi}, the second-order velocity coefficient for the base-catalysed reaction which are given in this communication. The reproducibility of the results was frequently checked by duplicate determinations, always with satisfactory agreement.

The following results are not recorded elsewhere in this paper.

Proof of the Non-reversibility of Urethane Formation in the Presence of a Base Catalyst.—A 0·24M-solution of pure *iso*propyl phenylcarbamate, m. p. 89·0°, in di-*n*-butyl ether, which was also 0·03M with respect to triethylamine, was kept at 20° and any phenyl *iso*cyanate formed was estimated at intervals by the usual technique. The following results were obtained, the blank value being the final sodium hydroxide titre in the presence of the piperidine and 2 ml. of 0·03M-triethylamine alone.

Time (mins.)	0	1530	2850	8730
Vol. of NaOH for blank (ml.)	0·082	0·107	0·105	0·109
,, ,, required (ml.)	0·082	0·106	0·105	0·109

Hence, no phenyl *iso*cyanate had been formed in the reaction mixture after about 13 days.

Direct Proportionality between k_{bi} *and* [NEt_3] *when the Catalyst Concentration exceeds the Original* [ROH].—The velocity of the reaction of *iso*propyl alcohol with phenyl *iso*cyanate, both 0·24M, in the presence of [NEt_3] of 0·03—1·20M at 20° gave the following data, the figures in parentheses being the number of experimental observations upon which the recorded mean of k_{exp} was based :

[NEt_3], g.-mols./l.	0·03	0·06	0·09	0·12	0·24	0·48	0·96	1·20	
10^2k_{exp}	0·56(7)	0·97(8)	1·35(8)	2·04(6)	3·90(6)	6·60(6)	11·90(7)	16·21(7)	
10^2k_{bi}	0·42	0·83	1·21	1·90	3·76	6·46	11·76	16·07	
10^2k_{bi}/[NEt_3]	14·0	13·8	13·4	15·8	15·7	13·4	12·3	13·4	(Mean 13·9)

Retention of Optical Activity in ROH *during Reaction with Phenyl* iso*Cyanate.*—(−)-Borneol was purified by sublimation, and 1 g. of the pure alcohol, m. p. 204°, was sealed with 2 g. of phenyl *iso*cyanate and kept for 24 hours. The solid mass was dissolved in acetone, poured into a large volume of water to decompose the excess of phenyl *iso*cyanate, and the dried crystalline deposit was extracted (Soxhlet) with ligroin (b. p. 60—80°). The urethane which crystallised from the ligroin solution had m. p. 141° (lit., m. p. 138°) and $[\alpha]_D - 35°$. The same result was obtained when the experiment was repeated in the presence of triethylamine. Thus optical activity is retained in both the uncatalysed and the catalysed reaction.

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