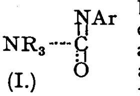
135. *The Mechanism of Aromatic Side-chain Reactions with Special Reference to the Polar Effects of Substituents. Part XIII.* Kinetic Examination of the Reaction of Aryl* iso*Cyanates with Methyl Alcohol.*

By JOHN W. BAKER and J. B. HOLDSWORTH.

The velocity of the reaction $R{\cdot}N{:}C{:}O + MeOH \longrightarrow NHR{\cdot}CO_2Me$ has been determined in di-*n*-butyl ether solution at 20° for various aryl *iso*cyanates. The reaction is shown to be a base-catalysed addition of the alcohol to the C:O group of the *iso*cyanate (see p. 716, footnote) and, in the presence of a constant concentration of a tertiary base, follows second-order kinetics. In the absence of a base catalyst the " spontaneous " reaction is autocatalysed by the weakly basic urethane product. Unlike the heterocyclic and aliphatic tertiary bases, the dialkylanilines of comparable basic strength have almost no catalytic effect. Calculation of the repulsion energies between non-bonding groups in the formation of the intermediate reaction-complex (I) between the linear $^-N{:}C{:}O$ group and the bases triethylamine, pyridine, and dimethylaniline, shows that these are much greater in the case of the dialkylaniline molecule, which is flattened by resonance, and are of such a magnitude as to confirm the suggestion that steric effects alone are sufficient to explain the lack of catalytic effect in this class of base.



$$NR_3{\cdots}\overset{\overset{\displaystyle NAr}{\|}}{\underset{\underset{\displaystyle O}{|}}{C}}$$

(I.)

The experimental velocity order $R = p\text{-}NO_2{\cdot}C_6H_4 \gg C_6H_5 > p\text{-}Me{\cdot}C_6H_4 > p\text{-}MeO{\cdot}C_6H_4 \gg$ *cyclo*C_6H_{11} is in agreement with the view that the reaction velocity is increased by increased conjugation of the unshared electron pair on the nitrogen in the *iso*cyanate group with the group R.

THE well-known reaction between aryl *iso*cyanates and alcohols is usually regarded as occurring thus :

$$Ar{\cdot}N{:}C{:}O + ROH \longrightarrow Ar{\cdot}N{:}C(OH)OR \longrightarrow Ar{\cdot}NH{\cdot}CO_2R \quad . \; . \; . \; . \; . \quad (a)$$

and a mechanism of this type was assumed in the addition of the olefin–stannic chloride acid complex to phenyl *iso*cyanate (*J.*, 1945, 724). Lack of suitable methods for the quantitative determination of either reactant or of the product probably accounts for the fact that no detailed kinetic studies of the alcohol–*iso*cyanate reaction seem to have been made. All earlier work has relied either on competition experiments, using two different alcohols in competition for a quantity of *iso*cyanate only sufficient for one of them (Davis and MacFarnum, *J. Amer. Chem. Soc.*, 1934, **56**, 883), or on the determination of yields of isolated urethane obtained under approximately standard experimental conditions after varying periods of reaction time (cf., *inter alia*, Naegali, Tyabji, Conrad, and Litwan, *Helv. Chim. Acta*, 1938, **21**, 1100, 1127; Tarbell, Mallatt, and Wilson, *J. Amer. Chem. Soc.*, 1942, **64**, 2229).

Preliminary attempts to follow the reaction between methyl alcohol and an aryl *iso*cyanate in a suitable solvent by a thermochemical method were unsatisfactory, but the chemical method for the determination of *iso*cyanate worked out by Strafford and Stagg of Imperial Chemical Industries, Ltd. (Dyestuffs Division) (*Analyst*, 1946, **71**, 557) proved to be very adaptable for the purpose and made possible a detailed study of the *iso*cyanate–alcohol reactions at 20° and in di-*n*-butyl ether as a suitable inert solvent. This paper, which is the first of a series, deals with the interesting conclusions relating to the detailed mechanism of the reaction which have been derived from a study of the reaction between a single alcohol, methyl alcohol, and various aryl *iso*cyanates under different experimental conditions.

When the necessary precautions for the rigid exclusion of moisture were taken, it was shown that (1) the *iso*cyanate does not react with the solvent, di-*n*-butyl ether, and (2) the over-all reaction (*a*) is irreversible under the experimental conditions used and is free from any side reaction, the urethane being the sole product.

Preliminary kinetic investigations on the interaction of phenyl *iso*cyanate with dry methyl alcohol, both approximately 0·25M in di-*n*-butyl ether, at 20°, gave irregular results which were not always reproducible. In general, the values of the first-order coefficient k_1 showed a marked downward drift as the reaction proceeded, whilst those of the second-order coefficient k_2 remained approximately constant, with a tendency to drift upwards in the later stages of the reaction. The observations (cf. Tarbell *et al.*, *loc. cit.*, and references there cited) that urethane formation is base-catalysed suggested that the irregularities might be due to adventitious base-catalysis, and that the upward drift of k_2 might result from weak catalysis of the reaction by the urethane product, functioning as a very weak base. Confirmation of this hypothesis was found in the demonstration of the catalytic effect of added urethane; the

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* The communication in *J.*, 1941, 796 was erroneously numbered X instead of **XI**. **Part XI** (*J.*, 1942, 191) should be renumbered XII.

results are summarised in Table I. It was shown, that, under the experimental conditions, no permanent compound formation occurs between the aryl *iso*cyanate and the urethane.

TABLE I.

Catalytic effect of added NHPh·CO$_2$Me *on the reaction between* Ph·NCO *and* MeOH, both 0·24M *in dry di-*n*-butyl ether at* 20°.

Mol. ratio [NHPh·CO$_2$Me]/[MeOH]	1	2	2·75	0 (uncatalysed)
Exptl. 10^2k_2 (g.-mol.$^{-1}$ l. min.$^{-1}$)	0·26	0·32	0·36	0·17
Calc. 10^2k_2 (g.-mol.$^{-1}$ l. min.$^{-1}$)	0·24	0·32	0·37	—

When the molecular ratio of the initial concentration of added urethane to the reactants is $\nless 2$, the relative change in concentration of the weak catalyst urethane as the reaction proceeds is too small to cause any detectable acceleration, and the experimental data accord well with the kinetics of a second-order reaction. When only one molecular proportion of urethane was added initially, the second-order reaction plot soon deviated from a straight line and gave definite indications of autocatalysis. Under such experimental conditions the reaction should be more accurately represented by the expression $dx/dt = k_0(a - x)^2 + k_b(a - x)^2(a + x)$. This is of the form of $dx/dt = (a - x)^2(K + k_bx)$, where $K = k_0 + k_ba$. Integration of this gives

$$(K + k_ba)t = \frac{x}{a(a - x)} + \frac{k_b}{k_ba + K} \cdot \ln\frac{a(K + k_bx)}{K(a - x)}$$

i.e,

$$(k_0 + 2k_ba)t = \frac{x}{a(a - x)} + \frac{k_b}{k_0 + 2k_ba} \cdot \ln\frac{a\{k_0 + k_b(a + x)\}}{(a - x)(k_0 + k_ba)}$$

Owing to the difficulty of deriving a straight-line plot from such a complex expression, its validity was tested in an experiment in which $a = 0{\cdot}24$ (k_0 being experimentally evaluated from the "spontaneous" reaction as 0·0017) by solving graphically for k_0 for each of the experimental values of t and x. These values (Table II, col. 4), although approximately constant, still show a small but pronounced upward drift in the later stages of the reaction. The same tendency is revealed when the mean value $k_b = 0{\cdot}0031$ is substituted in the above expression and the values of t are calculated for each of the experimental values of x.

TABLE II.

Autocatalysed reaction of Ph·NCO *and* MeOH, *both* 0·24M *in di-*n*-butyl ether at* 20°, *in the presence of* 0·24M*-added* NHPh·CO$_2$Me.

Experimental data.				
t, mins.	x, g.-mol./l.	$a-x$, g.-mol./l.	10^2k_b, g.-mol.$^{-1}$ l. min.$^{-1}$.	t calc. (mins.) for k_b = 0·0031.
180	0·0211	0·2188	0·21	—
410	0·0468	0·1936	0·28	402
1145	0·1002	0·1397	0·30	1140
1440	0·1146	0·1253	0·31	1436
1830	0·1317	0·1082	0·33	1883
2590	0·1547	0·0852	0·36	2746
3200	0·1669	0·0730	0·36	3413
4110	0·1809	0·0590	0·38	4500

A further check on the essential correctness of the value $k_b = 0{\cdot}0031$ is obtained by its application to the data in Table I. The expression $dx/dt = 0{\cdot}0017(a - x)^2 + 0{\cdot}0031(a - x)^2(c + x)$ (where c = concentration of added urethane) may be written as $dx/dt = (a - x)^2\{0{\cdot}0017 + 0{\cdot}0031(c + x)\}$. In the initial stages of this product-catalysed reaction (x very small) this simulates the ordinary second-order reaction expression $dx/dt = (0{\cdot}0017 + 0{\cdot}0031c)(a - x)^2$, and the calculated values of k_2 in Table I are the evaluation of $0{\cdot}0017 + 0{\cdot}0031c$ for the various values of c. The agreement with the experimental values is satisfactory.

Attention was next directed to the elucidation of the mechanism of the base catalysis, a series of tertiary bases of different basic strength being used and in varying concentrations. The powerful catalytic effect of triethylamine, already noticed qualitatively, is confirmed quantitatively by the data given in Table III.

The plot of [NEt$_3$] against 10^2k_2 gives a straight line, showing that the catalytic effect is directly proportional to the concentration of the basic catalyst. The calculated values of

10^2k_2 in Table III are derived from the more exact expression $k_2 = 0{\cdot}17 \times 10^{-2} + 7{\cdot}45[\mathrm{NEt_3}]$, where the value $0{\cdot}17 \times 10^{-2}$ is that for the slow uncatalysed reaction (determined from the initial velocity) and 7·45 is the catalytic coefficient (k_c) for triethylamine. Reproducible results giving a good second-order constant over nearly the whole course of the reaction were always obtained in the presence of added tertiary base catalyst, and all future experiments were carried out under these conditions: a base concentration of approximately 0·03M usually gave velocities convenient for measurement.

TABLE III.

Reaction between Ph·NCO *and* MeOH, *both* 0·2315M, *in the presence of different concentrations of* $\mathrm{NEt_3}$, *in di*-n-*butyl ether at* 20°.

$[\mathrm{NEt_3}]$, M.	0·2158	0·1079	0·0610	0·0306	0·0
Exptl. 10^2k_2	158	80·9	47·5	22·9	0·17
Calc. 10^2k_2	161	80·6	45·6	23·0	—

The simulated bimolecular character of the *iso*cyanate–alcohol reaction in the presence of constant base concentration is confirmed by the results in Table IV, which show the effect of varying the concentration ratio *iso*cyanate/methyl alcohol. The lower value of k_2 in the presence of a large excess of alcohol is significant, and will be discussed more fully in a further publication.

TABLE IV.

Effect of variation of the relative concentrations of Ph·NCO *and* MeOH *on the value of* 10^2k_2 *at* 20°: $[\mathrm{NEt_3}] = 0{\cdot}0305$M.

[Ph·NCO], g.-mol./l.	[MeOH], g.-mol./l.	Ratio [MeOH]/[Ph·NCO].	10^2k_2.
0·2315	0·2315	1	22·6
0·2380	0·2380	1	22·8
0·1190	0·2380	2	22·0
0·2380	0·1190	0·5	22·0
0·1241	0·4941	4	19·4

A study of the relationship between the strength of the basic catalyst and its catalytic efficiency revealed a very interesting fact. The results for a series of tertiary bases are given in Table V.

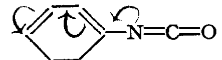
The catalytic effects of the tertiary bases in Set A run parallel with their basic strengths, and a plot of $\log_{10} K_b$ against $\log_{10} k_c$ gives a nearly straight line in accordance with the Brønsted relationship $\log k_c = x \log K_b + G$. The equally strong bases, the dialkylanilines, in Set B, however, exert almost no catalytic action, the values of 10^2k_2 in these experiments being nearly the same as that for the uncatalysed reaction. Discussion of this important anomaly is deferred until later in this paper, after the effect on the reaction velocity of substituents in the phenyl group of the aryl *iso*cyanate has first been considered.

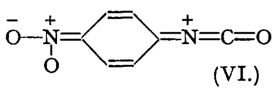
TABLE V.

Catalysis of the Ph·NCO–MeOH *reaction, both* 0·2419M *in di*-n-*butyl ether, by various tertiary bases at* 20°.

Base, and $K_b^{25°}$.	Base concn., g.-mol./l.	10^2k_2.	k_c.	Base, and $K_b^{25°}$.	Base concn., g.-mol./l.	10^2k_2.	k_c.
			Set A.				
Quinoline, $6{\cdot}3 \times 10^{-10}$	0·0306 0·0612	1·04 1·98	0·29	α-Picoline, 3×10^{-8}	0·0306 0·0612	2·00 3·99	0·61
Pyridine, $2{\cdot}3 \times 10^{-9}$	0·0306 0·0612	1·88 3·57	0·56	Triethylamine, $5{\cdot}65 \times 10^{-4}$	0·0306 0·0612	22·9 47·5	7·45
			Set B.				
Diethylaniline, $4{\cdot}5 \times 10^{-8}$	0·0306 0·0612	0·175 0·19	—	Dimethylaniline, 1×10^{-9}	0·0306	0·20	—
(Uncatalysed)	—	0·17	—				

In the later discussion of the mechanism of the reaction it is shown that urethane formation is most probably a base-catalysed addition to the carbonyl group in the *iso*cyanate * and it would therefore be anticipated that the conjugation of the unshared electron pair on the adjacent nitrogen atom, $\overset{\curvearrowleft}{^{-}\mathrm{N}}=\overset{\curvearrowleft}{\mathrm{C}}=\mathrm{O}$, would retard such addition, since it would provide an internal mechanism for satisfying the unsaturation of the carbonyl group. It would follow, therefore, that increased conjugation of this nitrogen unshared electron pair with an attached aryl group, by providing alternative locations for it as in (II), should increase the carbonyl group unsaturation and hence lead to increased velocities of urethane formation. Qualitatively, this conclusion is supported by the general experience that aryl *iso*cyanates react more readily with alcohols than do alkyl *iso*cyanates, and also by the results of Naegeli *et al.* (*loc. cit.*), but quantitative data have now been obtained by measuring the velocities of reaction of various substituted aryl *iso*cyanates with methyl alcohol under standard conditions of base catalysis. If the velocity of reaction with phenyl *iso*cyanate is taken as a reference standard, introduction of electron-repelling substituents, such as methyl and methoxyl, into the para-position, should decrease the nitrogen conjugation with the aromatic nucleus and hence should decrease the reaction velocity. Conversely, similar introduction of the strongly electron-attracting nitro-group should greatly increase reaction velocity because of the incidence of structures of the type (VI) in the resonance hybrid.


(II.)


(VI.)

Saturation of the benzene ring by reduction to *cyclo*hexyl, by removing all possibility of conjugation of the nitrogen electrons with the ring, should very greatly reduce the reaction velocity, since the sole conjugation is now with the carbonyl group. Hence, theoretical considerations predict the order

$$\mathrm{R} = cyclo\text{hexyl} \lll p\text{-MeO·C}_6\mathrm{H}_4 < p\text{-Me·C}_6\mathrm{H}_4 < \mathrm{Ph} \lll p\text{-NO}_2\text{·C}_6\mathrm{H}_4$$

for the velocities of reaction of R·NCO with methyl alcohol. The results in Table VI completely confirm this conclusion.

TABLE VI.

Reaction between R·NCO *and* MeOH, *both* 0·24M *in di-n-butyl ether, at* 20° *in the presence of* (a) 0·0306M- *and* (b) 0·0612M-*triethylamine.*

R =	*cyclo*Hexyl.	*p*-MeO·C$_6$H$_4$.	*p*-Me·C$_6$H$_4$.	C$_6$H$_5$.	*p*-NO$_2$·C$_6$H$_4$.
10^2k_2 (a)	0·021	9·9	12·3	22·6	~3000
(b)	0·04$_3$	18·8	24·0	47·5	—

The reaction with *p*-nitrophenyl *iso*cyanate is much too fast for accurate measurement; the figure given is based on one reading when 0·0305M-triethylamine was used (reaction >90% complete in 4 minutes), confirmed by extrapolation from an experiment in which only 0·0005M-catalyst was used ($10^2k_2 = 56·9$, whence for 0·0305M-catalyst, $10^2k_2 = 3482$).

Discussion of Results.

The slow " spontaneous " reaction of an aryl *iso*cyanate with methyl alcohol in di-*n*-butyl ether is found to be catalysed by the addition of tertiary bases, and the rate of reaction is then found to follow the equation

$$\frac{d[\mathrm{Ar·NCO}]}{dt} = \frac{d[\mathrm{MeOH}]}{dt} = k_0[\mathrm{Ar·NCO}][\mathrm{MeOH}] + k_c[\mathrm{Ar·CO}][\mathrm{MeOH}][\mathrm{Base}]$$

Hence the bimolecular reaction coefficient is

$$k_{\mathrm{bi}} = \frac{1}{[\mathrm{Ar·NCO}][\mathrm{MeOH}]} \cdot \frac{d[\mathrm{Ar·NCO}]}{dt} = k_0 + k_c[\mathrm{Base}] \quad . \quad . \quad . \quad . \quad \text{(i)}$$

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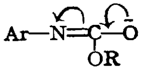
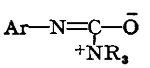
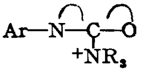
* This statement is not meant to imply that the unsaturation of the $^{-}$N⁚C group in the *iso*cyanate is ignored. From the kinetic standpoint we regard the reaction as complete when the ion (III) of the product has been formed, the subsequent co-ordination of the proton being regarded, in accordance with generally accepted views, as instantaneous. In this ion, as in that of the intermediate base


(III.)


(IV.)


(V.)

complex (IV), the true structure is, doubtless, a resonance hybrid of the general type (V). The essential feature is that the mechanism of addition of an alcohol to an *iso*cyanate is regarded as of the same type as other base-catalysed additions to carbonyl compounds, such as aldol, cyanohydrin, etc., reactions.

These reaction kinetics are consistent with the following mechanism of reaction :

$$\text{Ar·NCO} + \text{Base} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{Complex}$$

$$\text{Complex} + \text{MeOH} \xrightarrow{k_3} \text{NHAr·CO}_2\text{Me} + \text{Base}$$

$$\text{Ar·NCO} + \text{MeOH} \xrightarrow{k_0} \text{NHAr·CO}_2\text{Me}$$

Using the stationary state condition, the concentration of the complex is given by the expression

$$\text{Complex} = \frac{k_1[\text{Ar·NCO}][\text{Base}]}{k_2 + k_3[\text{MeOH}]}$$

and hence the rate of formation of the product, urethane, may be expressed as

$$\frac{\text{d}[\text{Ar·NCO}]}{\text{d}t} = k_0[\text{MeOH}][\text{Ar·NCO}] + \frac{k_1k_3[\text{Ar·NCO}][\text{MeOH}][\text{Base}]}{k_2 + k_3[\text{MeOH}]}$$

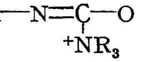
or

$$k_{\text{bi}} = k_0 + \frac{k_1k_3[\text{Base}]}{k_2 + k_3[\text{MeOH}]} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

If the value of k_2 is always very much greater than k_3[MeOH] under the conditions of experiment, then equation (ii) reduces to

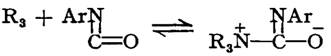
$$k_{\text{bi}} = k_0 + \frac{k_1k_3}{k_2}[\text{Base}] = k_0 + Kk_3[\text{Base}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(iii)}$$

in which $K = k_1/k_2$ is the equilibrium constant of the complex formation. Equation (iii) is identical with the experimental equation (i) if we identify $k_c = Kk_3$.

The equilibrium constant k_1/k_2. The experimental results, although pointing to the formation of a complex between the base catalyst and the *iso*cyanate,* give no information as to the nature of the complex. On generally accepted views regarding the mechanism of base-catalysed additions to the carbonyl group it seems to us that a probable structure of the complex would be  $\text{Ar—N}{=}\underset{\underset{^{+}\text{NR}_3}{|}}{\text{C}}\text{—}\bar{\text{O}}$ (cf. footnote, p. 716). If this is the case it is interesting to compare the following reactions :

$$\text{(I)}\ \ \text{NR}_3 + \text{CR}_3\text{—X} \rightleftharpoons \text{R}_3\overset{+}{\text{N}}\text{—CR}_3 + \bar{\text{X}}$$

$$\text{(II)}\ \ \text{NR}_3 + \text{H·OH} \rightleftharpoons \text{R}_3\overset{+}{\text{N}}\text{H} + \text{O}\bar{\text{H}}$$

(III) 

$$\text{(III)}\ \ \text{NR}_3 + \text{Ar}\underset{\text{C=O}}{\overset{\text{N}}{\|}} \rightleftharpoons \text{R}_3\overset{+}{\text{N}}\text{—}\overset{\overset{\text{NAr}^{-}}{\|}}{\text{C}}\text{—}\bar{\text{O}}$$

The energy changes involved in these reactions will be, respectively,

$$\text{(I)}\ + D_{\text{C—N}^+} - I'_{\text{N}} + E_{\text{X}} - D_{\text{C—X}} + S_{\text{X}'} + S_{\text{N}^+}$$

$$\text{(II)}\ + D_{\text{H—N}^+} - I''_{\text{N}} + E_{\text{OH}} - D_{\text{H—OH}} + S_{\text{OH}'} + S_{\text{N}^+}$$

$$\text{(III)}\ + D_{\text{C—N}^+} - I'''_{\text{N}} + E_0 - D_{\text{C=O}} + S$$

where $D_{\text{C—N}^+}$ is the strength of the N–C bond in the quaternary ammonium compound, I_{N} is the ionisation potential of the nitrogen in the base, E is the electron affinity of the centre which forms the negative ion, $D_{\text{C—X}}$, $D_{\text{H—OH}}$, and $D_{\text{C=O}}$ are the strengths of the bond broken in each reaction, and S is the energy of solvation.

With the same reactant and with varying bases one would expect, in the first place, that the variations of the heats of reaction would depend mainly on variations in I_{N} and, to a lesser extent, on the solvation energy of the quaternary ammonium compound. If this were true, therefore, a parallel variation in the heats of formation and the equilibrium constants of the Menschutkin reaction, the base formation, and the complex formation might be expected. Unfortunately, the only data available for this comparison are those for the basic dissociation constants and the catalytic coefficient k_3k_1/k_2 for the reaction under discussion. The data in Table V, however, reveal two striking anomalies in this comparison. Whereas there is a parallelism in the trends of log k_3k_1/k_2 (k_c) and log K_b for the Set A bases, quinoline, pyridine,

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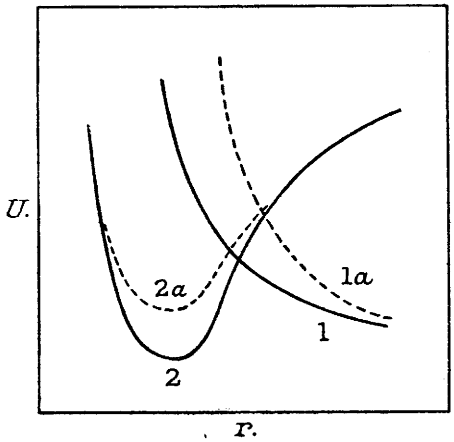
* The other possible mode of action of the base catalyst would be to increase the ionisation of the hydrogen from the alcohol by an equilibrium of the type $\text{ROH} + \text{B} \rightleftharpoons \text{R}\bar{\text{O}} + \text{B}\overset{+}{\text{H}}$. If this were the case there seems to be no valid explanation why the dialkylanilines should not show a normal catalytic activity in accordance with their basic strength, and their anomalous behaviour renders such a mechanism very improbable.

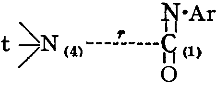
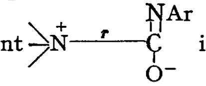
α-picoline, and triethylamine, yet the catalytic effects of the Set B bases, the dialkylanilines, are very much smaller than would be expected from their basic dissociation constants.

There are two possible causes of this anomalous behaviour. One is that in the case of the dialkylanilines the formation of the complex might be accompanied by a large negative entropy change. In this connection it is important to remember that the abnormal slowness of the Menschutkin reaction (I, p. 717) is due to the large negative entropy change accompanying the formation of the transition-state complex. In the present case, however, there is little difference in the moments of inertia between molecules such as quinoline and α-picoline, which show normal behaviour, and the dialkylanilines, which are abnormal, and it is not possible that such small changes in moments of inertia should cause large variations in the entropy change accompanying association.

In the above discussion the argument for a parallel behaviour between bases and complex formation rested on the assumption that the value of D_{C-N^+} remained sensibly constant from one base to another. There is now evidence that, with heavily substituted centres, the energy of bond formation may be profoundly modified by the energy of repulsion between the substituent groups which are not directly involved in the bond. For example, Polanyi and Evans have shown (*Nature*, 1943, **152**, 738) that the heat of polymerisation of *iso*butene is reduced by 10 k.-cals. per mole by the repulsion energy between the substituent methyl groups, and recently Dostrovsky, Hughes, and Ingold (*J.*, 1946, 173) have calculated that the activation energy of bimolecular bromine exchange in the *neo*pentyl halides is increased by a value of 11·7 k.-cals. per mole by steric repulsion. At the time when we had formed the opinion that steric factors might explain the anomalous catalytic behaviour of the dialkylanilines in the *iso*cyanate–alcohol reaction, Dostrovsky, Hughes, and Ingold had just completed their quantitative assessment of this factor in certain cases of the bimolecular halogen replacement reaction in alkyl halides. We are greatly indebted to Professor Ingold for allowing us to see the manuscript of their (then unpublished) paper and for the suggestion that it might be worth while to attempt a similar quantitative treatment of steric effects in the formation of the base–*iso*cyanate complex. We also wish to express our deep appreciation to Professor M. G. Evans, of the Department of Physical and Inorganic Chemistry, for much invaluable advice and continual assistance in the development of such a treatment.

FIG. 1.



In the case of the *iso*cyanate–base complex steric effects between the substituent groups may have one of two effects : (*a*) the repulsion energy may have the effect of increasing the activation energy of complex formation, and so reducing the magnitude of k_1 to such a value that the reaction scheme set out on p. 717 is no longer applicable and stationary state conditions for the concentration of the complex cannot be applied ; * (*b*) the repulsion energy between the substituent groups in the final complex may be so large as to reduce the heat of formation of the complex and hence the value of k_1/k_2. These two possibilities are shown diagrammatically in Fig. 1. Curve 1 represents the change in potential energy as a function of the distance r for the bond assignment  $>N_{(4)}\overset{r}{\cdots\cdots}\overset{\overset{N\cdot Ar}{\|}}{\underset{\underset{O}{\|}}{C}}_{(1)}$ and in the absence of repulsion energy between the substituent groups on centre $N_{(4)}$ and $C_{(1)}$. Curve 1*a* represents the same system when the size and configuration of substituent groups are such that there is a large repulsion energy between them. Curve 2 represents the change in potential energy as a function of the distance r for the bond assignment  $>\overset{+}{N}\overset{r}{——}\overset{\overset{NAr}{\|}}{\underset{\underset{O^-}{|}}{C}}$ in the absence of repulsion energy between

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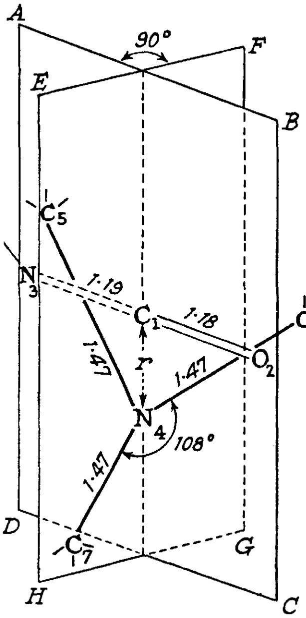
* Preliminary experimental evidence suggests that, in the *absence* of base catalysis, the alcohol–*iso*cyanate reaction may, in fact, proceed by a different mechanism.

substituent groups, and curve 2*a* the same system where repulsion energy comes into play. It is important to note that, for the corresponding values of *r*, the value of the repulsion energy will not be the same for curve 2 and curve 1 because of the change in the bond character of the substituent groups. These will have a different configuration in the two cases.

The influence of repulsion energy on curve 1. In the case under consideration information as to configurations, polarisabilities, and ionisation potentials of the centres involved is much less certain than it is in the case dealt with by Dostrovsky, Hughes, and Ingold (*loc. cit.*) or in other cases previously examined, and hence any discussion of the repulsion energy must be considered as only semi-quantitative.

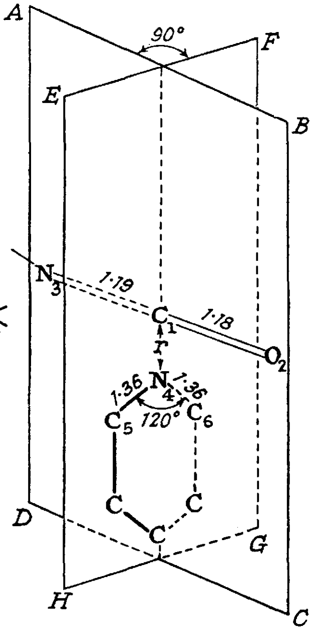
Such treatment has been attempted in three typical cases, *viz.*, for triethylamine, pyridine, and dimethylaniline. The structure of the -N:C:O group of the aryl *iso*cyanate has been taken as a linear configuration with the distances $r_{\text{NC}} = 1{\cdot}19$ A. and $r_{\text{CO}} = 1{\cdot}18$ A. given by Cowley and Partington (*J.*, 1935, 46), based on dipole moment measurements. The dialkylaniline molecule has been assumed to be flat with the alkyl groups in the plane of the benzene ring. The basis of this assumption is that this molecule has an appreciable resonance energy arising from such canonical structures as

FIG. 2.



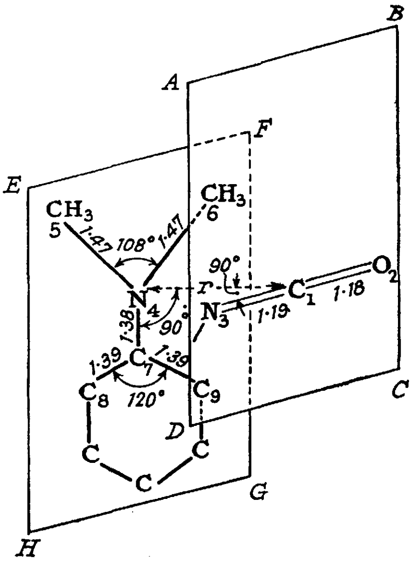
Configuration of groups in N(CH$_3$)$_3$-Ar·NCO *approach.*

FIG. 3.

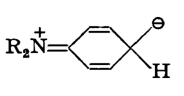


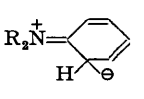
Configuration of groups in C$_5$H$_5$N-Ar·NCO *approach.*

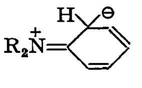
FIG. 4.



Configuration of groups in NPhMe$_2$-Ar·NCO *approach.*







which will tend to flatten the whole structure. The normal structures and bond distances have been taken for triethylamine and pyridine.

In each of the three cases the most favourable orientation of approach of the base catalyst to the *iso*cyanate group has been chosen, *viz.*, that in which there is minimum interference between the various pairs of atoms or groups involved so that compression would be a minimum. Such orientations are represented in Figs. 2, 3, and 4 for triethylamine, pyridine, and dimethylaniline, respectively. In Fig. 2 the linear group N:C:O is in the plane *ABCD* and the atoms C$_1$–N$_4$–C$_7$ (Me) are in the plane *EFGH* at 90° with *ABCD*, the atoms C$_1$–N$_4$ being in the line of intersection of the planes at a distance *r* A. apart. The various bond lengths and angles used are the experimentally determined values recorded in the literature. In Fig. 3 the group N:C:O is in the plane *ABCD* and the plane of the pyridine ring is in the plane *EFGH* at right angles, atoms C_1–N_4 again being in the line of intersection of the planes at a distance r A. apart. Examination of scale models showed that the optimum method of approach of the dimethylaniline molecule to the *iso*cyanate is that depicted in Fig. 4. The N⁚C⁚O group is in the plane *ABCD* parallel to the plane, *EFGH*, of the planar dimethylaniline molecule. The angle C_7–N_4–C_1 is 90°, C_1 being vertically over N_4.

From the geometry of these orientations the values of the distances d between the various pairs of atoms or groups have been calculated in terms of r, the distance between the base nitrogen atom N_4 and the carbon atom C_1 of the *iso*cyanate group. The values of d (in A.), for all pairs which might show significant compression, are recorded in Table VII. For simplicity the case of NMe_3 has been used instead of NEt_3 in Fig. 1, since the β-carbon atoms of the ethyl groups are too far away to exert any appreciable effects.

Casual inspection of Table VII immediately reveals that, apart from the distances N_4–O_2 and N_4–N_3, which are common to all three cases, the most important compression is likely to occur between the methyl groups C_5 and C_6 and the atoms N_3 and O_2, respectively, and that such compression is likely to be very much greater in the dialkylaniline case. The evidence becomes much clearer and more convincing when these distances are translated into terms of repulsion energy.

TABLE VII.

Distances d (*in* A.) *between various pairs of atoms in the base–*iso*cyanate complex formation in in terms of* r.

NMe_3 (Fig. 2).		C_5H_5N (Fig. 3).		$NPhMe_2$ (Fig. 4).	
Atom pair.	*d.*	Atom pair.	*d.*	Atom pair.	*d.*
N_4–O_2 * N_4–N_3	$\sqrt{r^2 + 1{\cdot}393}$	N_4–O_2 N_4–N_3	$\sqrt{r^2 + 1{\cdot}393}$	N_4–O_2 N_4–N_3	$\sqrt{r^2 + 1{\cdot}393}$
C_1–C_7	$\sqrt{r^2 + 1{\cdot}051r + 2{\cdot}161}$	C_5–O_2 C_6–O_2 C_5–N_3 C_6–N_3	$\sqrt{r^2 + 1{\cdot}36r + 3{\cdot}248}$	C_6–O_2 C_5–N_3	$\sqrt{r^2 + 0{\cdot}706}$
C_6–O_2 C_5–N_3	$\sqrt{r^2 + 1{\cdot}045r + 0{\cdot}746}$			O_2–C_9 N_3–C_8	$\sqrt{r^2 + 4{\cdot}312}$
C_7–O_2 C_7–N_3	$\sqrt{r^2 + 1{\cdot}045r + 3{\cdot}554}$			C_7–O_2 C_7–N_3	$\sqrt{r^2 + 3{\cdot}31}$

* The recorded difference (0·01 A.) between the bond distances N=C and C=O in the –N⁚C⁚O group is almost certainly within the error of measurement and has been ignored. The extra symmetry resulting from the assumption that C_1 is midway between N_3 and O_2 greatly simplifies the calculations, and causes no significant error in the values of d.

An estimate of the repulsion energy for the non-bonding forces between each of the group pairs in Table VII has been determined for various values of d by using the expression (London, *Z. physikal. Chem.*, 1930, *B*, **11**, 222).

$$U = -\left\{\frac{3}{2}\frac{\alpha_1\alpha_2}{d^6} + \frac{b}{d^9}\right\}\frac{I_1I_2}{I_1 + I_2}$$

For the ionisation potential I_1 and I_2 it was considered sufficiently accurate for the approximate nature of the calculation involved to assume an average value of 12 e.v. When $d = d_0$, the van der Waals " touching " distance between the respective groups, $\delta U/\delta d = 0$, whence b is calculated as $d_0{}^3\alpha_1\alpha_2$. The values of the polarisabilities α_1, α_2, were determined from the expression $\alpha = 3[R_D]/4\pi\boldsymbol{N}$, where $[R_D]$ is the appropriate atomic refraction constant, and $\boldsymbol{N}$ is Avogadro's number $6{\cdot}02 \times 10^{23}$. The values used are given in Table VIII and are taken from Landolt–Börnstein " Tabellen " except where otherwise stated.

By plotting the values of U so obtained against d for each of the interacting pairs of atoms or groups in Table VII the various compression energies for any value of d (and hence, from the data on Table VII, for any value of r) could be evaluated. Summation of these energies for all the interacting groups then gave ΣU, the total energy increment due to compression for any required value of r. This ΣU represents a *maximum* value for the energy due to compression, to be added to the corresponding repulsion energies for the approach of N_4 to C_1 (similarly calculated by means of the equation above). Thus data for the plotting of both Curve 1 and Curve 1*a* in Fig. 1 were obtained. The actual energy increments for values of r between 1·0 and 2·6 A. are given in Tables IX for the catalysts triethylamine, pyridine, and dimethylaniline.

TABLE VIII.

Atom.	$[R_D]$, c.c.	$10^{24}\alpha$.	
NEt_3 case (as NMe_3).			
N_4	N in NR_3, 2·92	1·15	
N_3	N in C—N—C, 4·10	1·62	
O_2	O in C=O, 2·287	0·92	
CH_3	—	2·2	(Evans and Warhust, *Trans. Faraday Soc.*, 1939, **35,** 596.)
C_1	{ C, 2·41 + double bond, 1·7 } 4·11	1·62	
C_5H_5N case.			
N_4	N in C—N—C, 4·10	1·62	
C_5, C_6	C + H = 2·41 + 1·09 = 3·5	1·38	
$NPhMe_2$ case.			
N_4	N in $NArR_2$, 4·363	1·72	

van der Waals radii: CH_3, 2·0; C, 1·6; N, 1·5; O, 1·4; CH = C + $\frac{1}{3}\{2·0 - 1·6\}$ = 1·73 A. (Pauling " The Nature of the Chemical Bond," 1945, p. 189).

TABLE IX.

Correlation of various non-bonding distances (d) *with* r *and corresponding values of* U (*in electron volts*).

(*a*) Triethylamine as catalyst.

	N_4–N_3.		N_4–O_2.	C_1–C_7.		O_2–C_6.		N_3–C_5.	O_2–C_7.		N_3–C_7.	
r, A.	*U.*	*d.*	*U.*	*d.*	*U.*	*U.*	*d.*	*U.*	*U.*	*d.*	*U.*	Σ*U.*
1	4·634	*1·55*	2·314	*2·05*	0·834	3·888	*1·67*	7·602	0·097	*2·37*	0·216	19·585
1·2	2·010	*1·68*	0·858	*2·21*	0·312	1·380	*1·86*	2·736	0·050	*2·50*	0·109	7·455
1·4	0·864	*1·83*	0·438	*2·36*	0·156	0·840	*2·04*	1·260	0·022	*2·64*	0·053	3·633
1·6	0·360	*1·99*	0·204	*2·53*	0·063	0·210	*2·23*	0·420	0·006	*2·79*	0·019	1·282
1·8	0·138	*2·15*	0·060	*2·70*	0·032	0·074	*2·42*	0·162	—	*2·95*	0·006	0·472
2·0	0·048	*2·32*	0·018	*2·87*	0·011	0·025	*2·61*	0·058	—	*3·11*	—	0·160
2·1	0·026	*2·41*	0·009	*2·96*	0·006	0·015	*2·71*	0·040	—	*3·19*	—	0·094
2·2	0·008	*2·50*	0·002	*3·05*	0·002	0·006	*2·81*	0·018	—	*3·27*	—	0·036
2·4	—	*2·68*	—	*3·32*	—	—	*3·00*	—	—	*3·44*	—	—
2·6	—	*2·86*	—	*3·42*	—	—	*3·20*	—	—	*3·61*	—	—

(*b*) Pyridine as catalyst.

	N_3–N_4.		O_2–N_4.		O_2–C_5.	O_2–C_6.	N_3–C_5.	N_3–C_6.	
r, A.	*U.*	*d.*	*U.*	*d.* {	*U.*	*U.*	*U.*	*U.*	Σ*U.*
1	6·534	*1·55*	3·257	*2·37*	0·035	0·035	0·078	0·078	10·017
1·2	2·808	*1·68*	1·398	*1·51*	0·013	0·013	0·033	0·033	4·298
1·4	1·218	*1·83*	0·594	*2·67*	0·003	0·003	0·012	0·012	1·842
1·6	0·510	*1·99*	0·252	*2·83*	—	—	—	—	0·762
1·8	0·186	*2·15*	0·072	*2·99*	—	—	—	—	0·258
2·0	0·072	*2·32*	0·030	*3·16*	—	—	—	—	0·102
2·1	0·036	*2·41*	0·012	*3·24*	—	—	—	—	0·048
2·2	0·012	*2·50*	0·002	*3·33*	—	—	—	—	0·014
2·4	—	*2·68*	—	*3·50*	—	—	—	—	—
2·6	—	*2·86*	—	*3·68*	—	—	—	—	—

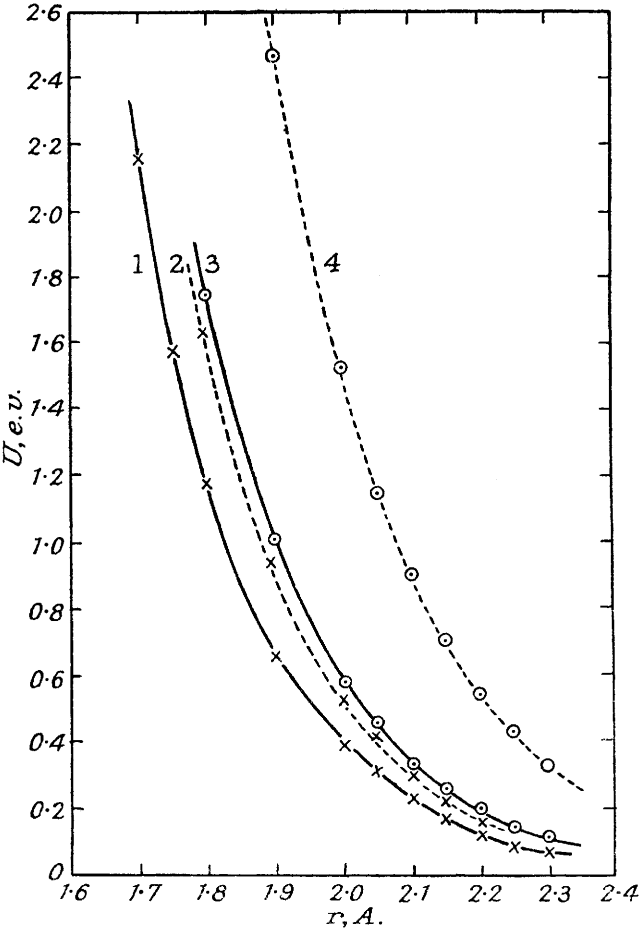
(*c*) Dimethylaniline as catalyst.

	N_3–N_4.		O_2–N_4.	C_6–O_2.		C_5–N_3.	O_2–C_9.		N_3–C_8.	O_2–C_7.		N_3–C_7.	
r, A.	*U.*	*d.*	*U.*	*U.*	*d.*	*U.*	*U.*	*d.*	*U.*	*U.*	*d.*	*U.*	Σ*U.*
1	6·930	*1·55*	3·463	39·000	*1·31*	75·600	0·051	*2·30*	0·102	0·096	*2·08*	0·207	122·449
1·2	2·988	*1·68*	1·500	14·340	*1·47*	26·700	0·029	*2·40*	0·063	0·055	*2·18*	0·120	45·795
1·4	1·302	*1·83*	0·624	5·100	*1·63*	9·600	0·014	*2·51*	0·035	0·024	*2·29*	0·057	16·756
1·6	0·528	*1·99*	0·264	1·800	*1·81*	3·450	0·006	*2·62*	0·014	0·012	*2·42*	0·024	6·098
1·8	0·192	*2·15*	0·072	0·702	*1·99*	1·380	—	*2·75*	—	0·006	*2·56*	0·012	2·364
2·0	0·072	*2·32*	0·030	0·285	*2·17*	0·540	—	*2·88*	—	—	*2·70*	—	0·957
2·1	0·036	*2·41*	0·012	0·174	*2·26*	0·348	—	*2·95*	—	—	*2·78*	—	0·570
2·2	0·012	*2·50*	0·002	0·128	*2·36*	0·225	—	*3·03*	—	—	*2·85*	—	0·367
2·4	—	*2·68*	—	0·037	*2·54*	0·090	—	*3·17*	—	—	*3·01*	—	0·127
2·6	—	*2·86*	—	0·012	*2·73*	0·030	—	*3·33*	—	—	*3·17*	—	0·042

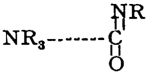
It is shown later that a probable value of *r* in the transition complex is ~1·8 A. Inspection of the Σ*U* values for *r* = 1·8 A. in Table IX, (*a*) and (*b*), shows that the energy increase arising from compression is greater with triethylamine (0·472 e.v.) than with pyridine (0·258 e.v.).

Notwithstanding this adverse factor, the catalytic coefficient of triethylamine (7·45) is much greater than is that (0·56) for pyridine. This must mean that the greater catalytic efficiency of triethylamine is due to its greater basic strength and, in the case of these two catalysts, compression factors probably play only a very minor rôle, so that the pyridine case need not be further considered. With dimethylaniline, however [Table IX (*c*)], the corresponding value of ΣU (2·364 e.v.) is very much greater. The data so far obtained permit the plotting of the repulsion energy curves (1 and 1*a* in Fig. 1) for the cases of triethylamine and dimethylaniline when energy due to compression is taken into account. The relevant data are given in Table X, and the corresponding curves are depicted in Fig. 5.

FIG. 5.



Repulsion energy in the formation of the complex NR$_3$-------



$$\mathrm{NR_3}\text{-------}\overset{\overset{\mathrm{NR_3}}{\|}}{\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}}$$

1. NEt$_3$ *without replusion energy.* 3. NPhMe$_2$ *without repulsion energy.*
2. „ *with* „ „ 4. „ *with* „ „

The differentiation between the values of k_1 for triethylamine and dimethylaniline clearly depends upon the value of r at which the transition state is formed in the two cases. This value cannot be determined without calculating Curve 2 in Fig. 1, which it is not possible to do with the data at present available. The range of values of r in which the transition state value r_T will lie can, however, be defined. This range will extend from $r = 1·28$ A. to $r = 2·3$ A. The first value is the sum of the covalent radii of carbon (0·77 A.) and N$^+$ (0·51 A.),*

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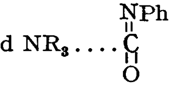
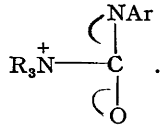
* This radius of N$^+$ was obtained by reducing the value for N (0·70 A.) by an amount 0·19 A., which is the contraction in atomic radius for the loss of one electron.

TABLE X.

$$\text{Repulsion energy } U = a_1 a_2 \left\{ -\frac{1{\cdot}5}{r^6} + \frac{r_0{}^3}{r^9} \right\} \frac{I_1 I_2}{I_1 + I_2} \quad \ldots \text{ e.v. for } C_1\text{–}N_4.$$

	NEt_3 as catalyst.			$NPhMe_2$ as catalyst.		
r, A.	*U* (without compression).	Σ*U* (from Table IX, *a*).	Total *U*.	*U* (without compression).	Σ*U* (from Table IX, *c*).	Total *U*.
1·8	1·185	0·472	1·657	1·773	2·364	4·137
1·9	0·675	0·272	0·947	1·010	1·46	2·470
2·0	0·39	0·160	0·550	0·581	0·957	1·538
2·05	0·30	0·120	0·420	0·441	0·715	1·156
2·10	0·224	0·094	0·318	0·335	0·570	0·905
2·15	0·170	0·056	0·226	0·254	0·453	0·707
2·20	0·128	0·036	0·164	0·191	0·367	0·558
2·25	0·099	—	—	0·148	0·288	0·436
2·30	0·072	—	—	0·107	0·220	0·327

and the second is the value of *r* at which the activation energy would reach a value of 2 k.-cals. and which is certainly a lower limit. Within this range of *r* the potential-energy curve 1*a*, for dimethylaniline, lies very much higher than that for triethylamine, and hence the value of k_1 for the former catalyst will be considerably smaller than for the latter; *e.g.*, at the mean value $r_T = 1{\cdot}8$ A., the maximum difference in the compression energy in the formation of the bond  $NR_3 \ldots\ldots \overset{\overset{\displaystyle NPh}{\|}}{\underset{\underset{\displaystyle O}{\|}}{C}}$ when NR_3 is dimethylaniline and triethylamine, respectively, is $2{\cdot}364 - 0{\cdot}472 = 1{\cdot}892$ e.v. = 44 k.-cals. per mol.

Influence of repulsion energy on the equilibrium constant k_1/k_2. The other possibility to be envisaged is that the mechanism set out on p. 717 holds even when the catalytic constant $k_3 k_1/k_2$ is exceedingly small. In this case the anomalous behaviour of the dialkylanilines must be sought in the value of k_1/k_2 and not of k_1 alone. This necessitates an evaluation of the repulsion energy terms in the final state of the complex structure  $\overset{+}{R_3N}\text{——}\overset{\overset{\displaystyle NAr}{|}}{\underset{\underset{\displaystyle O}{|}}{C}}$. This structure will probably have a different configuration from that of the transition complex because of the change in bond character. Although it has not been possible to carry out detailed calculations in this case, it can be assumed that the large substituent groups on the N^+ and the carbon will have a similar effect to that described in the discussion of the value of k_1, and it is felt that the semi-quantitative treatment which has been possible with the available data do support the view that the very small catalytic effect of the dialkylanilines in the alcohol–*iso*cyanate reaction could be accounted for entirely by steric factors. It should be noted that repulsion terms will not be important in the basic dissociation constants which show no abnormality since, in this case, the hydrogen atom, because of its small size, will not exert any appreciable steric influence.

Further investigations regarding the mechanism of the interaction of the alcohol with the transition complex and of the uncatalysed reaction are in progress.

EXPERIMENTAL.

Materials.—Specimens of liquid *iso*cyanates were either purchased or prepared by the usual method (base hydrochloride and carbonyl chloride in dioxan solution) and were purified by repeated fractional distillation, over phorphoric oxide in the later stages. All specimens were redistilled over phosphoric oxide under reduced pressure immediately before use. The specimens used had the following b. ps.: phenyl 54·0°/16 mm., *p*-tolyl 79·5°/20 mm., *p*-methoxyphenyl 105·9°/16·5 mm., *cyclo*hexyl 59·0°/16·5 mm. The purchased specimen of *p*-nitrophenyl *iso*cyanate was very impure. It was extracted in an all-glass Soxhlet extractor with boiling sodium-dried ligroin (b. p. 40—60°) with rigid exclusion of moisture, until the ligroin solution just began to develop a slight yellow tinge. The ligroin solution was then immediately concentrated to about 200 c.c., filtered hot, and the colourless filtrate allowed to crystallise in a desiccator over phosphoric oxide. The clean, colourless needles were washed by decantation with dry ligroin, dried in a vacuum over phosphoric oxide, and stored in a weighing bottle over phosphoric oxide for use. The product had m. p. 58°.

Methyl phenylcarbamate, prepared by the action of an excess of pure methyl alcohol on pure dry phenyl*iso*cyanate, was purified by repeated crystallisation from ligroin (b. p. 40—60°) and dried over phosphoric oxide in a vacuum; m. p. 48°.

Absolute methyl alcohol (500 c.c.) was refluxed for 10 hours with magnesium turnings (2·5 g.) and mercuric chloride (0·5 g.) and fractionated through a Widmer column; b. p. 64·7°/766 mm.

Tertiary bases, used as catalysts, were usually specimens specially purified for previous kinetic work, dried over potassium hydroxide, and refractioned: triethylamine b. p. 89°, pyridine b. p. 116°, α-picoline b. p. 42·2—42·3°/28 mm., quinoline b. p. 114°/19 mm., diethylaniline b. p. 96·2—96·4°/15·5 mm., piperidine b. p. 35—36°/40 mm. In order to ensure complete absence of primary and secondary bases, dimethylaniline (80 g., " AnalaR ") was refluxed with 0·8 g. of " AnalaR " acetic acid for 8 hours and steam-distilled, and the oily layer in the distillate was separated, dried first over anhydrous potassium carbonate and then over potassium hydroxide, and repeatedly fractionated; b. p. 85·5°/20 mm. The base gave a picrate, m. p. 164°, without further purification.

Di-*n*-butyl ether was freed from peroxides by Williamson's method [cf. *Ind. Eng. Chem.* (News Edition), 1939, **17**, 209]. It was then washed (four times) with concentrated hydrochloric acid to ensure freedom from basic compounds, then with water (5 times), and dried, first over calcium chloride and then over sodium. The product was refluxed, under reduced pressure, over clean sodium, fractionated through a Widmer column, and the processes repeated until no action occurred with fresh sodium. The fraction, b. p. 47·4—47·5°/24 mm., was stored in dark bottles for use.

Determination of the Aryl iso*Cyanate*.—The following modification of the method of Strafford and Stagg (*loc. cit.*) was employed.

Solutions used. Hydrochloric acid in constant-boiling alcohol, 0·526(2)N; aqueous sodium hydroxide, 0·525(7)N; indicator, 5 parts of a 0·2% solution of methyl red + 1 part of a 0·5% solution of methylene-blue; piperidine solution, 10 ml. of pure dry piperidine dissolved in pure dry acetone and the solution made up to 100 ml.—this gives an almost exactly molar solution. This solution was stored in the apparatus used by Baker and Hemming (*J.*, 1942, 197; Fig. 2) for sampling the cyanohydrin reaction mixture, the 5-ml. portions of the solution being forced into the ground-in 5-c.c. pipette by slight pressure of dry nitrogen. All other solutions were introduced into the pipettes by slight suction from a filter-pump through flexible rubber leads protected from back diffusion of water vapour by phosphoric oxide drying tubes.

Determination of the calibration curve for phenyl iso*cyanate*. Dry di-*n*-butyl ether (10 ml.) was pipetted into each of six 100-ml. glass-stoppered conical flasks, the flasks cooled in ice, and 5 ml. of the piperidine solution added to each, and washed down into the reaction medium by a few ml. of dry acetone. Various quantities of pure phenyl *iso*cyanate, freshly distilled over phosphoric oxide directly into a weight pipette, were then weighed directly into each of the flasks in turn, which were then left stoppered in ice for 15 minutes. Constant-boiling alcohol (15 ml.) was then added from a burette, followed by 10 ml. of the standard hydrochloric acid and four drops of the indicator, and the mixture was titrated to a *bright* green (sharp end-point) with the standard sodium hydroxide solution. A blank determination was carried out in an identical manner but with omission of the *iso*cyanate. A typical result is as follows:

Blank = 0·380, 0·370, 0·370 ml.; mean = 0·370 ml. of NaOH.

Wt. of Ph·NCO, g.	0·0404	0·0695	0·1147	0·1569	0·1936	0·2324
Vol. of NaOH required, ml.	1·000	1·485	2·200	2·875	3·430	4·055
Less blank, ml.	0·630	1·115	1·830	2·505	3·060	3·685

A plot of weight of Ph·NCO added against the corrected volume of alkali solution required gave a good straight line which was used as a calibration curve for the determination of the weight of phenyl *iso*cyanate present in reaction samples. The weight of phenyl *iso*cyanate calculated from this curve corresponded to 99·1% of the actual weight added in the calibration. A fresh blank was determined for each new batch of piperidine solution (which was discarded as soon as it acquired a faint yellow tinge) and calibration curves for each of the *iso*cyanates used were constructed in a similar manner. It was shown that the addition of the product urethane had no effect on the blank titration.

Preliminary investigations. These were undertaken to prove (*a*) that the *iso*cyanate does not react under the conditions of experiment with (1) the solvent, di-*n*-butyl ether, or (2) the product, methyl phenylcarbamate, and (*b*) that the reaction is essentially irreversible under the conditions of experiment.

(*a*, 1) Pure dry phenyl *iso*cyanate (1·7207 g.) was weighed from a weight pipette into di-*n*-butyl ether, and the solution made up to 50 ml. at 20° in the thermostat. At intervals, 10-ml. samples were taken and the concentration of the solution was determined by the method described above.

Time, mins.	0	570	1390
Ph·NCO, g.-mol./l.	0·2888	0·2888	0·2861

(*a*, 2) Similar experiments were carried out with 50 ml. of a solution containing phenyl *iso*cyanate, 0·2315M, in the solvent also containing methyl phenylcarbamate, 0·2314 g.-mol./l.

Time, mins.	0	20	118	297	1358	5640
Ph·NCO, g.-mol./l.	0·2315	0·2310	0·2306	0·2294	0·2200	0·2067

Hence, any reaction with the product is negligible over the normal period of experiments.

(*b*) A solution containing 0·2425 g.-mol./l. of pure methyl alcohol and 0·2397 g.-mol./l. of methyl phenylcarbamate in di-*n*-butyl ether was kept in a thermostat at 20° and any phenyl *iso*cyanate formed was determined, at intervals, on 10-ml. samples.

Time, mins.	5	495	795	2370
0·526N-NaOH required, ml.	0·370	0·345	0·350	0·345
Normal blank, ml.*	0·375	0·360	0·360	0·355

* The slight variation in the " blank " figures is due to the use of freshly prepared piperidine solutions at intervals throughout the experiment.

Velocity Determinations.—Examination of the residual reaction mixture after completion of a run showed the presence of only methyl phenylcarbamate as the reaction product, contaminated with only a trace of carbanilide. The introduction of slight traces of water vapour is almost unavoidable during the taking of samples, but the standard technique described below reduced the amount of carbanilide formed to negligible proportions.

The reaction vessel consisted of a long-necked flask fitted with a ground-in stopper half-way down the neck. The stopper was attached to a long glass handle closed at the top by a rubber cork fitting into the neck of the flask. The reaction vessel could thus be immersed to the level of the stopper in the thermostat so that the whole vessel was at constant temperature. All graduated flasks and reaction vessels were well dried, first at 110° in an electric oven and then in a vacuum desiccator over phosphoric oxide. Long tubular desiccators, containing calcium chloride and large enough to contain the graduated flasks, were immersed in the thermostat so that the flasks and solutions were kept in a dry atmosphere whilst they were attaining temperature equilibrium in the thermostat. Solutions of pure methyl alcohol of appropriate concentration, with or without the addition of a tertiary base catalyst, in di-*n*-butyl ether were made up in graduated flasks by using a weight pipette, and adjusted to the mark in the thermostat after temperature equilibrium was attained. A similar solution of the aryl *iso*cyanate (freshly distilled over phosphoric oxide directly into the dry weight pipette) was also prepared. The methyl-alcoholic solution (25 ml.) and solvent (50 ml.) were pipetted into the reaction vessel in the thermostat and, after attainment of temperature equilibrium, 25 ml. of the *iso*cyanate solution were added to start the reaction. All pipetting was carried out by use of suction through drying tubes from a water pump. At intervals, a 10-ml. sample was run directly into a mixture of 10 ml. of di-*n*-butyl ether and 5 ml. of the freshly-prepared standard piperidine solution, previously cooled to 0°, and the flask stoppered and kept at 0° for 15 mins. Constant-boiling alcohol (15 ml.) was added, followed by 10 ml. of 0·526N-hydrochloric acid in constant-boiling alcohol, four drops of the indicator added, and the excess acid was back-titrated with 0·526N-sodium hydroxide solution by a semi-microburette, to the first appearance of *bright* green colour. A blank determination was carried out each time fresh piperidine solution was used. All volumetric apparatus was calibrated to N.P.L. standard. All determinations are at 20°.

Uncatalysed reactions. The value of the velocity coefficient for the uncatalysed reaction was determined from the slope of the straight line obtained by plotting $\log_{10} b(a - x)/a(b - x)$ or (for equal initial concentrations) $x/(a - x)$ against time for the early stages of the reaction before any catalysis by the product formed caused deviation from the straight-line relationship. The results are tabulated below. In all cases the number of observations used in plotting the reaction-velocity curves are given in parentheses after each value of k_2.

[MeOH], g.-mol./l.	0·2350	0·2350	0·2399	
[Ph·NCO], g.-mol./l.	0·2774	0·2774	0·2399	
$10^2k_2^{20°}$, g.-mol.$^{-1}$ l.min.$^{-1}$	0·173(6)	0·168(6)	0·172(6)	Mean : 0·170

Catalytic effect of added methyl phenylcarbamate. The experiments were repeated with the addition of varying initial concentrations of methyl phenylcarbamate. With approximately equimolecular proportions of added product the plot for a second-order reaction rapidly became convex to the time axis, since the total concentration of urethane rapidly increased as the reaction proceeded. The recorded values of 10^2k_2 were those obtained for the initial stages of the reaction. With larger initial concentrations of added urethane the second-order plot remained a straight line over a large portion of the reaction, since the urethane formed during the reaction had only a small effect on the total urethane concentration present. The results are tabulated below :

[MeOH], g.-mol./l.	0·240	0·2386	0·2386
[Ph·NCO], g.-mol./l.	0·240	0·2386	0·2386
[NHPh·CO_2Me], g.-mol./l.	0·240	0·4772	0·6561
$10^2k_2^{20°}$, g.-mol.$^{-1}$l. min.$^{-1}$	0·263(4)	0·317(8)	0·355(7)

The correlation of these results with the expression for an autocatalysed reaction has already been noted (p. 714).

Reactions catalysed by tertiary bases. (*a*) Triethylamine. In the presence of varying concentrations of this tertiary base the procedure was the same except that 15 ml. of hydrochloric acid were used in the determination of the *iso*cyanate and a new blank was determined in the presence of the same concentration of triethylamine as was used in the experiment. The results obtained with varying concentrations of triethylamine are summarised below.

[MeOH], g.-mol./l.	0·2315	0·2315	0·2320	0·2320
[Ph·NCO], g.-mol./l.	0·2316	0·2316	0·2404	0·2360
[NEt_3], g.-mol./l.	0·2158	0·1079	0·0610	0·0306
$10^2k_2^{20°}$, g.-mol.$^{-1}$l. min.$^{-1}$	157(2)	80·9(6)	47·5(9)	22·9(9)

Effect of varying the molecular ratio MeOH/Ph·NCO *with catalysis by* 0·0305M-*triethylamine.*

[MeOH], g.-mol./l.	[Ph·NCO], g.-mol./l.	Ratio [MeOH]/[Ph·NCO].	$10^2k_2^{20°}$.
0·2380	0·2380	1	22·9(8)
0·2380	0·1190	2	22·1(7)
0·1190	0·2380	0·5	22·1(8)
0·4941	0·1241	4	19·0(6)

In the presence of a constant concentration of triethylamine the reaction thus stimulates a second-order one.

(*b*) Pyridine, α-picoline, quinoline, and diethylaniline, etc. With the weaker tertiary bases the base catalyst had no effect on the acid–alkali titre in the determination of the *iso*cyanate, and the standard technique was used.

	Pyridine.		α-Picoline.		Quinoline.		Diethylaniline.			
[MeOH], g.-mol./l.	0·2419	0·2419	0·2424	0·2424	0·2420	0·2420	0·2433	0·2422	0·2433	0·2426
[Ph·NCO], g.-mol./l.	0·2420	0·2410	0·2424	0·2424	0·2420	0·2420	0·2434	0·2422	0·2434	0·2426
[Base, g.-mol./l. ...	0·0306	0·0612	0·0306	0·0612	0·0306	0·0612	0·0306	0·0306	0·0612	0·0306 *
$10^2k_2^{20°}$, g.-mol.$^{-1}$/l. min.$^{-1}$	1·88(9)	3·57(9)	2·00(8)	3·99(8)	1·04(9)	1·98(9)	0·17(8)	0·175(7)	0·19(7)	0·20(9)

* With dimethylaniline.

Reactions with substituted aryl iso*cyanates* (ArNCO). The applicability of the method for the determination of the aryl *iso*cyanate was tested with each derivative and a straight-line calibration curve was plotted for each. In all cases the determination gave 99—100% of the actual weight of pure *iso*cyanate added. The experimental data are summarised in the following table.

	Initial concentrations, g.-mol./l.				
Ar.	Ar·NCO.	MeOH.	NEt$_3$.	10^2k_2 (mean), g-.mol.$^{-1}$ l.min.$^{-1}$.	No. of observtns.
p-Me·C_6H_4	0·2392	0·2394	0·0306	12·25	8
,,	,,	,,	0·0612	24·1	7
p-MeO·C_6H_4	0·2398	0·2399	0·0306	9·86	7
,,	,,	,,	0·0612	18·8	8
p-NO_2·C_6H_4 *	0·1602	0·1838	0·0291	2320	1
,,	0·1802	0·1980	0·0005	56·9	6
cyclo-C_6H_{11}	0·2424	0·2424	0·0306	0·021	5
,,	,,	,,	0·0612	0·043	4

* Determination difficult owing to great speed of reaction and very sparing solubility of urethane product.

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