## 227. On the Factors determining the Velocity of Reactions in Solution. Molecular Statistics of the Benzoylation of Amines.

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The reaction between benzoyl chloride and aniline (Grant and Hinshelwood, J., 1933, 1351) in hexane solution is rendered anomalous by a marked influence of the solid particles of product, which cause heterogeneous catalysis. In carbon tetrachloride solution the effect is much less, and the reaction is more nearly bimolecular. It now appears that in solvents where the velocity is considerably greater than in carbon tetrachloride or hexane, the homogeneous reaction quite outweighs the heterogeneous, and the anomalies disappear almost entirely. The bimolecular reaction is interesting in that it belongs to the class where the rate of change is much smaller than the possible rate of activation.

The velocity constant of such a reaction is given by the equation

$$10^3.N.k = P.Z_{AB}.e^{-E/RT} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $N$ is Avogadro's number, $E$ the energy of activation, $Z_{AB}$ the number of encounters between molecules of the two reacting substances at unit concentration of each, $k$ the velocity constant in g.-mols./l./sec., and $P$ is a factor representing the probability that some condition beyond activation is fulfilled. This condition will include correct orientation of the molecules at the moment of reaction, the possible necessity for presence of solvent molecules, and any requirements about perturbing forces to overcome quantum-mechanical restrictions (cf. J., 1933, 1357). For the benzoylation of aniline in benzene solution, $P$ is of the order $10^{-7}$.

This paper deals with two problems. The first is to determine whether the large influence of substituents in the benzene rings depends chiefly upon changes in $E$ or changes in $P$, a question which becomes specially important in a reaction where $P$ is so far removed from unity. The second is to explore further the nature of $P$ itself.

*Kinetics of the Benzoylation of Amines in Benzene Solution.*—The experimental method has already been described (Grant and Hinshelwood, *loc. cit.*). The solvent used was A.R. benzene. Since numerous specimens gave concordant results, and experiments upon the addition of small quantities of water and other substances showed that these had little effect, no special purification was undertaken. Two specimens of aniline, dried over potassium hydroxide and fractionated several times, and a number of specimens of benzoyl chloride, some fractionated at normal pressure and some in a vacuum in an all-glass still, all gave concordant results. Toluidine, chloroaniline, the nitroanilines, and nitrobenzoyl chloride were recrystallised to constant m. p. *p*-Chloro- and *p*-methyl-benzoyl chloride were specially prepared from the pure acids by the action of thionyl chloride and were fractionated in a vacuum. The chloro-compound was further purified by freezing out. It gave the same results as another specimen made by the use of phosphorus pentachloride. In general, different specimens of the various substances gave results within about 2%, *i.e.*, the limits of experimental error, so it seems clear that accidental impurities play no part. The thermostats for 25°, 40°, and 70° could be regulated to within 0·05°. For 100° a special type of constant-level boiling water-bath was used, constant to within about 0·2°. For 5° a mixture of solid and liquid benzene in a Dewar vessel, and for 15° a similar mixture of fine crystals and liquid glacial acetic acid, were used, the temperature being constant to within 0·1° in each case.

The course of the reaction is expressed by the usual bimolecular formula, as shown in Table I, where $t$ is the time in minutes, $x$ the % change, and $k$ the constant (g.-mols./l./sec.); $a$ is the initial concentration of the acid chloride, and $b$ that of the amine in g.-mols./l.; $a$ is always equal to $b/2$. Hence

$$k = \frac{1}{2 \times 60\,t}\left\{\frac{1}{(100 - x)} - \frac{1}{100}\right\} \times \frac{100}{a}$$

The three examples given in Table I are typical of all.

The anomalous influence of dilution found with hexane has almost disappeared in benzene. Table II gives the variation of $k$ with dilution. Dilution I represents $a = 0{\cdot}01$, $b = 0{\cdot}02$,

TABLE I.

| Aniline and benzoyl chloride at 25·0°. | | | Aniline and $p$-chlorobenzoyl chloride at 25·0°. | | | $p$-Nitroaniline and $p$-nitrobenzoyl chloride at 70·0°. | | |
|---|---|---|---|---|---|---|---|---|
| $a$ = 0·005, $b$ = 0·01. | | | $a$ = 0·0025, $b$ = 0·005. | | | $a$ = 0·005, $b$ = 0·01. | | |
| $x$. | $t$. | 100$k$. | $x$. | $t$. | 100$k$. | $x$. | $t$. | $k \times 10^4$. |
| 10 | 2·5 | 7·41 | 20 | 7·8 | 10·7 | 10 | 210 | 8·81 |
| 20 | 5·6 | 7·44 | 30 | 13·3 | 10·7 | 20 | 474 | 8·79 |
| 30 | 9·6 | 7·45 | 40 | 21·1 | 10·5 | 30 | 792 | 9·01 |
| 40 | 14·6 | 7·61 | 50 | 32·3 | 10·3 | 40 | 1242 | 8·96 |
| 50 | 21·5 | 7·75 | 60 | 49·7 | 10·1 | 50 | 1920 | 8·68 |
| 60 | 32·5 | 7·72 | 70 | 76·0 | 10·2 | 60 | 2952 | 8·47 |
| 70 | 52·2 | 7·46 | | | | 70 | 4680 | 8·32 |

dilutions II and III representing one-half and one-quarter of these concentrations respectively. The constants are mean values of series such as those given in Table I.

TABLE II.

k × $10^2$ *at 25° for various reactants at different dilutions.*

| | Dilution I. | Dilution II. | Dilution III. |
|---|---|---|---|
| Aniline, benzoyl chloride | 7·73 | 7·55 | 6·88 |
| $p$-Chloroaniline, benzoyl chloride | 1·73 | 1·63 | 1·50 |
| Aniline, $p$-nitrobenzoyl chloride | — | 60·7 | 58·1 |
| $p$-Toluidine, benzoyl chloride | — | 33·4 | 29·8 |
| $m$-Nitroaniline, benzoyl chloride | 0·0468 | 0·0444 | 0·0441 |

To allow for such small trend as the constant shows, all results, which for practical convenience had to be determined at different dilutions, are corrected to corresponding dilutions by the aid of this table before being compared with one another.

The influence of temperature is given in Table III, the substituents denoting those in the aniline and in the benzoyl chloride; the constants recorded are corrected for the small expansion of benzene with temperature. The values of $E$ are found by plotting log $k$ against $1/T$ in the usual way.

TABLE III.

*Mean values of* k × $10^2$ *for various temperatures.*

| Substituent. | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Amine. | Acid chloride. | Dilution. | 5·0°. | 15·0°. | 25·0°. | 40·0°. | 70·0°. | 100·0°. |
| H | $p$-NO$_2$ | III | 28·6 | 36·5 | 58·1 | 87·1 | — | — |
| $p$-CH$_3$ | H | III | 13·4 | 20·7 | 29·8 | 55·2 | — | — |
| H | $p$-Cl | III | 4·65 | — | 10·4 | 17·8 | 54·6 | — |
| H | H | II | 3·08 | — | 7·55 | 12·2 | 41·7 | — |
| H | $p$-CH$_3$ | III | 1·64 | — | 3·91 | 7·46 | 23·9 | — |
| $p$-Cl | H | II | 0·68 | — | 1·63 | 2·98 | 9·5 | — |
| $p$-NO$_2$ | $p$-NO$_2$ | II | — | — | 0·0097 | 0·0214 | 0·093 | 0·409 |
| $p$-NO$_2$ | H | I | — | — | 0·00421 | 0·0110 | 0·062 | 0·253 |

*Influence of Substituents on the Factors determining the Reaction Velocity.*—Table IV gives the values of the energy of activation and the values of $k$, for dilution III, at 25° for all the pairs of compounds investigated.

TABLE IV.

*Influence of substituents on* E *and on the reaction rate.*

| Substituent. | | | | Substituent. | | | |
|---|---|---|---|---|---|---|---|
| Amine. | Acid chloride. | 100$k_{25°}$ | $E$. | Amine. | Acid chloride. | 100$k_{25°}$. | $E$. |
| H | $p$-NO$_2$ | 58·1 | 5900 | $p$-Cl | H | 1·50 | 7,600 |
| $p$-CH$_3$ | H | 29·8 | 6800 | $m$-NO$_2$ | H | 0·044 | 10,500 |
| H | $p$-Cl | 10·4 | 7000 | $p$-NO$_2$ | $p$-NO$_2$ | 0·0097 | 10,400 |
| H | H | 6·88 | 7350 | $p$-NO$_2$ | H | 0·0042 | 11,800 |
| H | $p$-CH$_3$ | 3·91 | 7800 | | | | |

Qualitatively, the influence of the substituents is what might be predicted from Robinson's theory of the reactivity of organic compounds. The present problem is to decide which of the factors in equation (1) is chiefly responsible for the changes in velocity. If the substituent influences $E$ principally, leaving $P$ more or less constant throughout the series, then

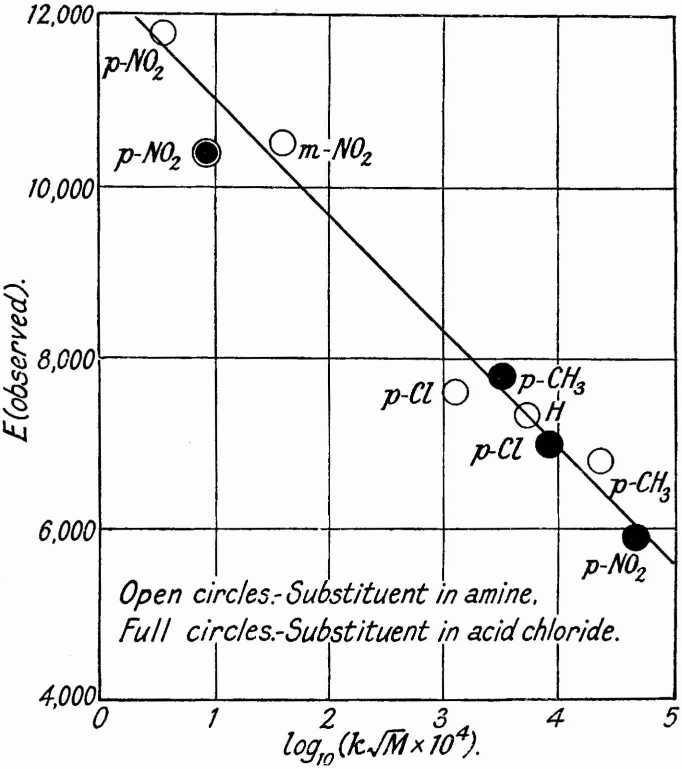
$$\ln(k/Z_{AB}) = \text{constant} - E/RT \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$Z_{AB} = N^2 . \sigma^2_{AB} (8\pi RT/M)^{\frac{1}{2}}$, where $1/M = 1/m_A + 1/m_B$, $\sigma_{AB}$ being the mean diameter, and $m_A$ and $m_B$ the respective molecular weights. For the series of compounds, $\sigma_{AB}$ will be taken as nearly constant. For comparative purposes at a given temperature, relation (2) reduces to

$$2{\cdot}303 \log k.M^{\frac{1}{2}} = \text{constant} - E/RT$$

In Fig. 1 the value of log ($k.M^{\frac{1}{2}} \times 10^4$) is plotted against the observed value of $E$. It is important to note that the line is made to pass through the point representing the two unsubstituted compounds, and has the theoretical slope 2·303 $RT$ required by the formula.

Fig. 1.



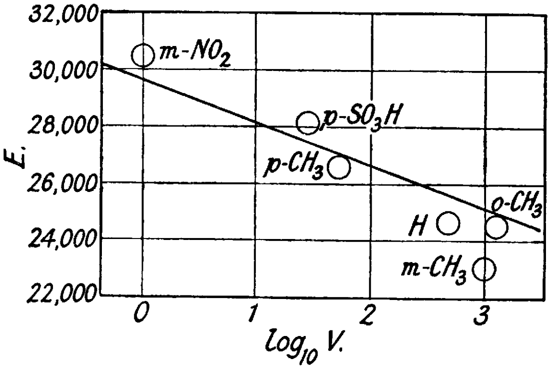
*Correlation between variations in velocity and changes in the activation energy.*

It is evident that the variations in velocity are in the main accounted for by the changes in the energy of activation. This result is specially interesting in the present example where $P$ is so far removed from unity that very wide variations in it might have been expected. Whatever the nature of $P$, we may conclude that it remains of the same order of magnitude in any given solvent, and that the very marked internal electronic displacements in the benzene ring, caused by the substituents, may change $E$ considerably, while having far less effect on $P$. Such variations in $P$ as do occur are not surprising : it is only remarkable that they are not greater.

A similar test can be made for a reaction of quite a different type, *viz.*, one depending upon interaction of solvent and solute, with the results of Cain and Nicoll (J., 1902, **81**, 1434) on the decomposition of various diazo-compounds in aqueous solution. Unfortunately, some of the measurements were made over too limited a range of temperature to allow calculation of accurate $E$ values. All that has been done, therefore, is to plot $E$ against the logarithm of the relative speed of decomposition at 60°, as shown in Fig. 2. The line has the theoretical slope of 2·3 × 1·98 × 333. It can be seen that, if changes in $E$ are not the whole effect of the substituents, they are at least the most important factor. Correction of the $E$ values for variation of the viscosity of water with temperature (see Moelwyn-Hughes, " Kinetics of Reactions in Solution," Oxford, 1933, p. 20) would change the slope slightly, but the data are not accurate enough for elaborate treatment.

*Relation between* E *and the Polarity of Substituents.*—Nathan and Watson (J., 1933, 890, 1248) have shown that for certain reactions of aromatic compounds containing a variable substituent X, $\log(k/Z_{AB})$ shows a functional relation with the dipole moment, $\mu$, of $C_6H_5X$. Changes in $\log(k/Z_{AB})$ were assumed to measure changes in $E$, *i.e.*, $P$ was assumed constant. Since the reactions dealt with were of the type for which $P$ is usually of the order unity (Grant and Hinshelwood, J., 1933, 258; Moelwyn-Hughes, *op. cit.*), this procedure was reasonable. Nevertheless, it is not without interest to plot directly observed values of $E$ against $\mu$ in the same way. This has been done, in Fig. 3, for the two series of reactions, $C_6H_5\cdot NH_2$ with $p$-$X\cdot C_6H_4\cdot COCl$ and $p$-$X\cdot C_6H_4\cdot NH_2$ with $C_6H_5\cdot COCl$, all in benzene solution.

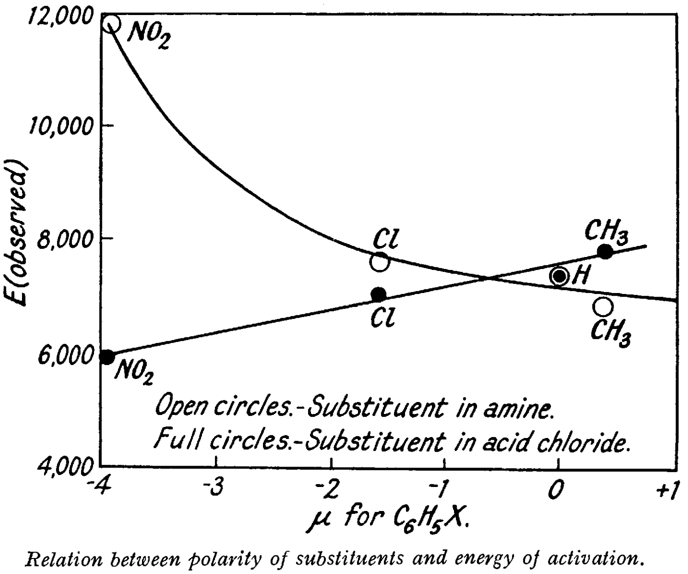
Fig. 2.



*Values derived from Cain and Nicoll's measurements on decomposition of diazo-compounds.*

*Further Investigation of the Nature of the Factor* P.—The rate of reaction is much smaller than that of activating collisions between the reactant molecules. Since, *e.g.*, in nitrobenzene the rate is about 100 times as great as in carbon tetrachloride, it is obvious that the solvent plays a fundamental part in determining the interaction. The question arises whether the ratio of the number of molecules reacting to the number of activating collisions is simply measured by the probability that the appropriate solvent molecules should be present during the encounter. Light can be thrown on this question by studying the effect on the reaction in a relatively inert solvent of increasing amounts of a much more active solvent. With benzene as a solvent, the addition of nitrobenzene causes a *linear*

Fig. 3.



*Relation between polarity of substituents and energy of activation.*

increase in the velocity of reaction, both for the benzoylation of aniline and for that of *m*-nitroaniline. As shown by the results in Table V, the rate can be expressed in the former case by the formula

$$-d[\mathrm{Ph{\cdot}COCl}]/dt = k_0[\mathrm{Ph{\cdot}COCl}][\mathrm{Ph{\cdot}NH_2}] + k_1[\mathrm{Ph{\cdot}NO_2}][\mathrm{Ph{\cdot}COCl}][\mathrm{Ph{\cdot}NH_2}]$$

where $k_0$ and $k_1$ at 25° are 0·0755 and 0·0828 respectively.

For *m*-nitroaniline and benzoyl chloride a similar formula holds and $k_1$ is $11{\cdot}6 \times 10^{-4}$. The form of the equation suggests that the constant $k_0$ is of the form $k'[C_6H_6]$. If we give a kinetic interpretation to the action of the solvent, the linear relationship shows that we are dealing with ternary collisions, and not with collisions of still higher order.

### TABLE V.

*Additions of nitrobenzene to the benzene solution.*

Aniline and benzoyl chloride at 25·0°, dilution II.

| Normality of $\mathrm{Ph{\cdot}NO_2}$, $n$ ...... | 0 | 0·2 | 0·5 | 0·7 | 1·0 | 1·2 | 1·5 | 1·7 | 2·0 |
|---|---|---|---|---|---|---|---|---|---|
| 100 $(k_0 + k_1n)$, obs. ............ | 7·55 | 9·31 | 11·86 | 13·51 | 15·57 | 17·43 | 20·14 | 21·8 | 24·66 |
| ,, calc. ............ | 7·55 | 9·21 | 11·69 | 13·34 | 15·83 | 17·48 | 19·96 | 21·62 | 24·1 |

Repetition of the experiments at 5° and at 40° gave a value of 6,500 calories for the $E$ corresponding to $k_1$.

*m*-Nitroaniline and benzoyl chloride at 40·0°.

| Normality of $\mathrm{Ph{\cdot}NO_2}$, $n$ ........................ | 0·5 | 1·0 | 1·5 | 2·0 |
|---|---|---|---|---|
| $k_1 \times 10^4 = (k_{\mathrm{total}} - k_0)/n$ ........................ | 10·2 | 10·5 | 11·3 | 11·6 |

We may now make an estimate of the probability of such collisions. The number of ternary collisions (see *e.g.*, Steiner, *Z. physikal. Chem.*, 1932, *B*, **15**, 249) between molecules A, B, and M per c.c. per sec. is given by the formula

$$Z_{\mathrm{ABM}} = N^3\tau\sigma^2_{\mathrm{AB}}\sigma^2_{\mathrm{ABM}}8\pi RT\sqrt{\frac{1}{m_{\mathrm{A}}} + \frac{1}{m_{\mathrm{B}}}}\sqrt{\frac{1}{m_{\mathrm{AB}}} + \frac{1}{m_{\mathrm{M}}}}\,C_{\mathrm{A}}C_{\mathrm{B}}C_{\mathrm{M}}$$

where $N$ is Avogadro's number, $C_{\mathrm{A}}$, $C_{\mathrm{B}}$, and $C_{\mathrm{M}}$ are the concentrations in g.-mols./c.c., $m_{\mathrm{A}}$, $m_{\mathrm{B}}$, and $m_{\mathrm{M}}$ are the molecular weights of A, B, and M, and $m_{\mathrm{AB}}$ is that of A and B taken together; $\sigma_{\mathrm{AB}}$ is $(\sigma_{\mathrm{A}} + \sigma_{\mathrm{B}})/2$ and $\sigma_{\mathrm{ABM}}$ is $(\sigma_{\mathrm{A}} + \sigma_{\mathrm{B}} + \sigma_{\mathrm{M}})/2$, where $\sigma_{\mathrm{A}}$, $\sigma_{\mathrm{B}}$, and $\sigma_{\mathrm{M}}$ are the collision diameters of A, B, and M. $\tau$ is the least definite of the quantities involved, being the duration of a binary collision between A and B. In order not to make arbitrary assumptions about it, a convenient plan will be to calculate the value which it would have to be given for every activated ternary collision to be effective, *i.e.*, in order that $P$ of equation (1) should simply be the probability of the presence of the solvent molecule.

For the reaction represented by the second term of equation (2), we have: no. of g.-mols./l./sec. reacting when all three concentrations are 1 g.-mol./l. $= k_1 = 0{\cdot}0828$. Therefore the actual number of molecules reacting per c.c. per sec. is $0{\cdot}0828N \,.\, 10^{-3}$. This can be equated to $Z_{\mathrm{ABM}} \,.\, e^{-E/RT}$. In calculating $Z_{\mathrm{ABM}}$, $c_{\mathrm{A}} = c_{\mathrm{B}} = c_{\mathrm{M}} = 10^{-3}$. The collision diameters will all be taken as $6 \times 10^{-8}$ cm.; $E$ is 6500 cals. On this basis, the value of $\tau$ is $5 \times 10^{-20}$ sec. The time during which a pair of colliding molecules are within a molecular distance of one another is $10^{-11}$—$10^{-13}$ sec., unless association occurs, in which case the time will be greater. The value found for $\tau$, therefore, shows that our original assumption is impossible. To give a physically intelligible value to $\tau$, we must assume that a small fraction only, even of the ternary collisions, are effective. Thus the existence of the probability factor, $P$, independent of activation, cannot, in this example, be explained away as a purely kinetic factor, depending on the necessity for collisions with solvent molecules.

## SUMMARY.

The rate of a bimolecular reaction in solution is given by the formula: number of molecules reacting $= P \,.\, Z \,.\, e^{-E/RT}$, where $P$ is a factor independent of the activation rate. In the benzoylation of amines, $P$ is extremely small. In spite of this, it has been found that the influence of substituents on the velocity of benzoylation of aromatic amines in

benzene solution depends principally on changes in the activation energy. Changes in *P* are of much smaller importance as long as the medium is unchanged.

There are indications from other work that changes in *E* are the important factors determining the variation with substitution of the rate of reaction of aromatic compounds generally.

A functional relation between the energy of activation and the polarity of the substituent groups exists in the benzoylation reaction, as well as in other cases, where *P* approaches unity.

Experiments in mixed solvents indicate that the factor, *P*, cannot be explained away as a purely kinetic factor depending on ternary collisions with solvent molecules, although such collisions appear to be an essential part of the reaction mechanism.

We are indebted to the Royal Society and to Imperial Chemical Industries Ltd. for grants.

[*Received, May* 10*th*, 1934.]