822. *The Benzoylation of Substituted Anilines in Different Solvents.*

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The bimolecular rate constants (k) and activation energies (E) have been measured for the benzoylation of various mono- and di-substituted anilines in nitrobenzene and some other polar solvents. Changes in rate with substitution are mainly due to changes in E. In nitrobenzene the activation energy is uniformly lower than in benzene, the effect being partially compensated by a lower value of the pre-exponential factor of the Arrhenius equation.

There is a linear relation between log k and log K (K = basic dissociation constant in water). The slope of the line is the same for the reactions in nitrobenzene and in benzene, showing that a highly polar solvent does not affect the transmission of the electronic influence of the substituent to the nitrogen atom.

In most examples the changes in activation energy caused by two substituents are nearly additive.

The kinetics of the benzoylation of substituted anilines in benzene were systematically studied by Stubbs and Hinshelwood.[1] For this reaction (*a*) the entropy of activation

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[1] Stubbs and Hinshelwood, *J.*, 1949, S71.

remains very nearly constant, (*b*) the resultant effect on the activation energy of two substituents in the same benzene nucleus of the amine is approximately the sum of their individual effects, and (*c*) there is a functional relationship between the reactivity of the mono-derivatives and the polarity of the substituent or the dissociation constant of the amine.

We now extend the work to polar solvents. The kinetics of benzoylation of eighteen substituted anilines in nitrobenzene were studied to find out (*a*) whether the entropy of activation in this solvent also is constant, (*b*) whether the plot of $\log_{10}k$ (in the solvent) against the logarithm of the dissociation constant of the amine (in water) is a line of the same slope as for benzene or whether the highly polar solvents affect the transmission of the influence of the substituent, (*c*) how the energy of activation and the frequency factor of the reaction are affected when the solvent is changed, and (*d*) whether the additive effect of the substituents still holds as it does in benzene.

The kinetics of benzoylation of eight substituted anilines in chlorobenzene, bromobenzene, toluene, and phenyl cyanide were also studied to see how the rate depends on the dipole moment of the solvent.

EXPERIMENTAL

Aniline is benzoylated quantitatively according to the equations $\mathrm{Ph{\cdot}COCl + Ph{\cdot}NH_2 = Ph{\cdot}NH{\cdot}COPh + HCl}$ (slow); $\mathrm{Ph{\cdot}NH_2 + HCl = Ph{\cdot}NH_2,HCl}$ (rapid). The aniline hydrochloride was filtered off and dissolved in water, the chloride being estimated by Volhard's method. This procedure proved satisfactory for the reaction in toluene, chlorobenzene, and bromobenzene but with phenyl cyanide and nitrobenzene, in which the hydrochloride is slightly soluble, the reaction mixture was cooled to −20° and excess of benzene was added; the complete precipitation of the hydrochloride in these conditions was confirmed by the fact that the method gave the theoretical end point for the reaction.

In most of the experiments the concentrations of the reaction mixture were 0·01M-aniline and 0·005M-benzoyl chloride (dilution I). For some of the substituted anilines in nitrobenzene dilution I was unsuitable since the hydrochloride was not precipitated completely even after cooling and addition of benzene, so the concentrations used were 0·02M-aniline and 0·01M-benzoyl chloride (dilution II). For certain compounds for which the reactions were too fast to be measured accurately at dilutions I and II, the concentrations used were 0·005M-aniline and 0·0025M-benzoyl chloride. Stubbs [2] showed that the velocity constant does not change appreciably with the dilution.

For the determination of the activation energy, E, velocity constants, k, in nitrobenzene and phenyl cyanide were measured at four or five different temperatures from 6° to 30°. For chlorobenzene, toluene, and bromobenzene velocity constants were determined at four different temperatures between 20° and 50°. Thermostats could be regulated to ±0·02° between 20° and 50°, and below 20° to ±0·05°.

All materials were purified to constant m. p. or b. p. by recrystallisation or fractionation. " AnalaR " nitrobenzene was used as solvent.

The velocity constants were calculated from the equation

$$k = \frac{1}{120t}\left(\frac{1}{100 - x} - \frac{1}{100}\right) \times \frac{100}{a}$$

where k is the velocity constant in l. mole^{-1} sec.$^{-1}$, t the time in minutes, a the initial concentration of benzoyl chloride and x the percentage change. The experimental error in the velocity constants was about ±2·5%.

The results are summarised in Tables 1—4.

DISCUSSION

From the results given in Table 1, $\log_{10} k_{25}$ has been plotted against the energy of activation E (Fig. 1). Out of eighteen compounds studied the results for more than half

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[2] Stubbs, D.Phil. Thesis, Oxford University, 1948.

TABLE 1. *Parameters for the benzoylation of substituted anilines in nitrobenzene.*

Aniline	$100k_{25}$	$\log_{10} A$	E (cal./mole)	Diln.	Aniline	$100k_{25}$	$\log_{10} A$	E (cal./mole)	Diln.
m-Chloro-	12·9	3·34	5700	I	4-Chloro-2-methyl-	23·1	3·57	5700	I
p-Chloro-	40·4	3·29	5000	I	2 : 4-Dichloro-	0·287	3·70	8400	I
o-Chloro-	1·163	4·22	8400	I	2 : 5-Dichloro-	0·075	3·82	9400	I
m-Nitro-	1·685	3·54	7200	I	5-Bromo-2-methoxy-	8·20	3·60	6400	I
p-Nitro-	0·0766	3·56	9100	II	2-Methoxy-5-nitro-	1·755	4·31	8200	I
m-Bromo-	21·1	3·78	6000	I	2-Methyl-5-nitro-	0·551	4·56	9100	I
5-Chloro-2-methoxy-	11·04	3·53	6100	II	4-Chloro-3-nitro-	0·966	4·78	9200	I
5-Chloro-2-methyl-	7·14	4·09	7200	II	2-Methoxy-4-nitro-	0·598	3·02	8500	II
3-Chloro-2-methyl-	7·30	3·72	6600	I	2-Methyl-4-nitro-	0·0294	3·17	9100	II

TABLE 2. *Substituent effects calculated from the theoretical value of the activation energy of aniline in the solvent nitrobenzene.*

Substituent group	*m*-Chloro-	*p*-Chloro-	*o*-Chloro-	*m*-Nitro-	*p*-Nitro-	*m*-Bromo-	*o*-Methyl- *
ΔE (cal. mole^{-1}) ...	+1700	+1000	+4400	+3200	+5100	+2000	+500

* Calculated from the theoretical value of *o*-methylaniline.

TABLE 3. *Theoretical values for the activation energies of disubstituted anilines calculated additively.*

Aniline	E (calc.)	E (obs.)	Difference	Aniline	E (calc.)	E (obs.)	Difference
2 : 4-Dichloro-	9400	8400	+1000	3-Chloro-2-methyl-	6200	6600	−400
2 : 5-Dichloro-	12,800	9400	+3400	2-Methyl-4-nitro-	9600	9100	+500
4-Chloro-3-nitro- ...	8200	9200	−1000	4-Chloro-2-methyl-	5500	5700	−200
5-Chloro-2-methyl-	8900	7200	+1700				

TABLE 4. *Velocity constants at 25° ($100k_{25}$) in phenyl cyanide, chlorobenzene, bromobenzene, and toluene (dilution I).*

Aniline	Toluene	Chloro-benzene	Bromo-benzene	Phenyl cyanide	Aniline	Toluene	Chloro-benzene	Bromo-benzene	Phenyl cyanide
m-Chloro- ...	0·554	0·512	0·805	16·40	*m*-Nitro-	0·150	0·1116	0·1424	4·85
m-Methyl- ...	8·78	10·45	11·22	—	*p*-Chloro- ...	1·457	1·360	1·451	40·6
o-Methyl- ...	1·44	1·098	1·29	—	Aniline	5·55	5·99	7·22	—
p-Methyl- ...	20·75	23·60	31·65	—					

fall on or very near the line of slope $-2{\cdot}303\boldsymbol{R}T$. Six compounds, namely 2-methoxy-5-nitro-, 4-chloro-3-nitro-, 2-methyl-5-nitro-, 5-chloro-2-methyl-, 2-methoxy-4-nitro-, and *o*-chloro-aniline, which are mainly substituted nitro-compounds, are further from the line than experimental error would account for. With them, not only the energy of activation but also the frequency factor varies.

Comparison of the Frequency Factor and the Energy of Activation in Benzene and Nitrobenzene.—When the medium is changed from benzene to nitrobenzene there is a general tendency for both the frequency factor and the activation energy to be decreased together, these effects influencing the rate in opposite senses. The net effect, however, is that the rate is several times greater in nitrobenzene. 2-Methyl-5-nitroaniline and 4-chloro-3-nitroaniline are exceptional in that the frequency factors are slightly higher than in benzene, but the energies of activation are lower as in all the other cases.

The frequency factor in the Arrhenius equation, for reactions in the liquid phase, can be considered in terms of the probability factor P and the number of collisions Z, or in terms of the factor $\alpha_A\alpha_B/\alpha^*$ where α_A and α_B are the activity coefficients of the two reactants A and B respectively and α^* is that of the so-called " activated complex."

According to the collision theory, Z decreases with the molecular weight of a reactant and increases with its diameter. In benzene solutions the molecular weight of benzoyl chloride is constant and the other factors do not vary much from compound to compound, so that Z is nearly constant. But for reactions in polar nitrobenzene it is not certain whether the simple molecular weight of the reactants can be taken since molecules of the reactants may be more or less permanently loaded with molecules of the solvent which would increase the molecular weight from the point of view of collisions and hence effectively decrease Z. This factor might contribute to the lowering of the frequency factor but the influence is unpredictable and probably small.

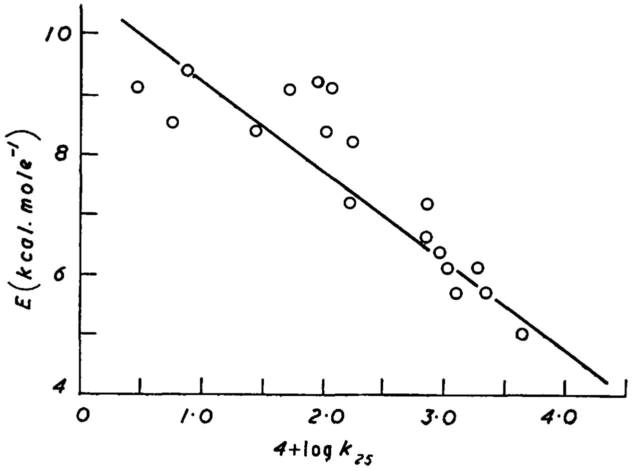

FIG. 1. *Plot of experimentally-measured activation energy against* log k_{25}.

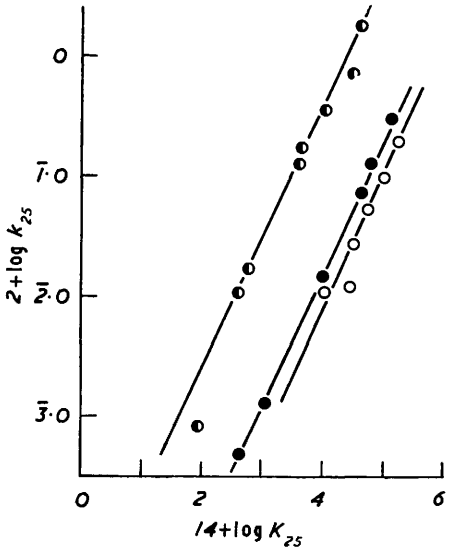

FIG. 2. *Plot of* log k_{25} *against logarithm of dissociation constant.*

◐ Nitrobenzene.
● Benzene.
○ Chlorobenzene.

According to the theory of reaction rates developed by Wynne-Jones and Eyring[3] and Stearn and Eyring[4]

$$A = (\boldsymbol{k}T/\boldsymbol{h})(f_V^5/f_R^3f_T^3)$$

where f_V, f_T, and f_R are partition functions for the vibrational, translational, and rotational degrees of freedom. The power indicates a product of that number of factors of the same type not necessarily equal. In benzoylation the product, and hence probably the activated complex, is more polar than the reactants. Solvation by the highly polar

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[3] Wynne-Jones and Eyring, *J. Chem. Phys.*, 1953, **21**, 166.
[4] Stearn and Eyring, *J. Chem. Phys.*, 1937, **5**, 113.

nitrobenzene will therefore lower the activation energy from its value in a less polar solvent such as benzene. K will be governed by the equation

$$\text{Complex} + n \text{ solvent molecules} \rightleftharpoons \text{solvated complex}$$

The equilibrium constant will contain a term:

$$(\text{Partition function of complex})/(\text{Partition fuction of free solvent molecules})^n$$

The denominator will contain products of the form $(f_R{}^3 f_T{}^3)^n$ which will have been replaced in the numerator by f_V terms in corresponding numbers. Since $f_V \ll f_R$ or f_T, the result is a marked lowering of the frequency factor.

Thus the release of the energy of solvation, which lowers E, and the lowered frequency factor tend to compensate one another as the experimental findings show.

Relation between Velocity Constants and Dissociation Constants of the Amines.—If log k for the benzoylation of different substituted anilines in various solvents is plotted against the logarithm of the corresponding dissociation constant (in water), K, parallel straight lines are obtained (Fig. 2). The correlation can be explained on the basis of the dependence of both the basic strength and the rate of benzoylation on the availability of the unshared pair of electrons on the nitrogen atom.

It is noteworthy that the slopes of the lines are the same for two solvents of such widely different polarities as benzene and nitrobenzene. This shows that the solvent dipole does not interact with that due to the substituent in such a way as to alter the effect which the substituent can transmit to the reaction centre.

Additive Effects of the Substituents.—The energy of activation for the benzoylation of aniline in nitrobenzene could not be determined experimentally, since the reaction is too fast. It was therefore estimated by the following method. Since the plot of $\log_{10} k_{25}$ against $\log_{10} K$ is straight, and since the experimental point for aniline falls on the line in the case of benzene and chlorobenzene solutions, it is assumed that in the corresponding plot for nitrobenzene the point relating to aniline would again fall on the line. In this way the value of $\log_{10} k_{25}$ in nitrobenzene was estimated. The corresponding value of the energy of activation in nitrobenzene can be obtained from the plot of E against $\log_{10} k_{25}$. The estimated value of E is 4000 cal. mole^{-1}.

Table 2 contains the value of ΔE, the difference between E for the compound and E for aniline, in nitrobenzene. There is very little difference between the ΔE values for different groups in nitrobenzene and benzene, which again confirms the conclusion that for monosubstituted anilines the solvent does not alter the transmission of the electronic effects to the nitrogen atom.

Theoretical values for the activation energies of disubstituted anilines have been calculated by the addition of the values of ΔE for the two substituted groups to the value of E for aniline. Results in Table 3 show that for 3-chloro-2-methyl-, 4-chloro-2-methyl-, and 2-methyl-4-nitro-aniline the predicted and the experimental value of E agree well. For the rest of the compounds the difference is between 10% and 25%.

Other Solvent Effects.—The velocity constants k_{25} for the reaction in toluene, chlorobenzene, and bromobenzene (Table 4) are not very different from those for benzene and are much lower than the values for nitrobenzene and phenyl cyanide. This is qualitatively related to the last two solvents' having the highest dielectric constants, which results in solvation and lowered energy of activation. No relationship, however, could be obtained between the dipole moment of the various solvents and the velocity constants.

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