967. *The Benzoylation of Substituted Anilines. An Investigation into the Effects of Polar Substituents on the Heat of Reaction.*

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An investigation is made into the effect of ring substitution in the benzoylation of aniline on the heat of reaction, $-\Delta H$, in benzene solution:

$$2X{\cdot}C_6H_4{\cdot}NH_2 + Y{\cdot}C_6H_4{\cdot}COCl \longrightarrow X{\cdot}C_6H_4{\cdot}NH{\cdot}CO{\cdot}C_6H_4Y + X{\cdot}C_6H_4{\cdot}NH_3^+ + Cl^-$$

The reactions are exothermic and for the various substituents the rates parallel $-\Delta H$. Substituents which lower the activation energy E increase $-\Delta H$, and the equation $E = 20{\cdot}5 - 0{\cdot}3(-\Delta H)$ holds approximately. The results are discussed in terms of the Hammett equation. The effect of substituents on the rate of reaction is related to the sign of $-\Delta H$ for the rate-determining step.

MANY reactions of substituted benzene compounds follow a relation known as the Hammett equation, widely applied in the form

$$\log K_s/K_0 = \rho\sigma \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

K_s and K_0 are rate or equilibrium constants for reactions of the substituted and the unsubstituted compound respectively, σ is a constant which depends on the nature and position of the substituent, and ρ is the " reaction constant " which depends on the nature of the reaction and the conditions under which it takes place.

If the rate and the equilibrium constants for *the same series of reaction* follow relation (1) and the pre-exponential factors of the Arrhenius equation are constant for different substituents in the *para*- and *meta*-positions, it follows that [1]

$$E = B - \alpha(-\Delta H) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where E is the activation energy, $-\Delta H$ is the heat of reaction, and B and α are constants. $\alpha = \rho_r/\rho_e$, ρ_r and ρ_e being the " reaction constants " of the rate and the equilibrium respectively.

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[1] Semenov, " Some Problems of Chemical Kinetics and Reactivity," Vol. I, Pergamon Press, London, 1958.

Equation (2) is identical with the relation found by Polanyi and Evans[2] for radical reactions in the gas phase. Equation (2) may be expected to be valid for side-chain reactions of benzene compounds with *meta-* and *para-* substituents when there is no steric effect on the activation energy. The present investigation was designed to provide an experimental test.

The reaction chosen was the benzoylation of aniline in benzene solution, which had been studied kinetically by Williams and Hinshelwood[3] and by Stubbs and Hinshelwood.[4] This work had shown that the reaction takes place quantitatively according to the equations:

$$(1)\ C_6H_5{\cdot}NH_2 + C_6H_5{\cdot}COCl \longrightarrow C_6H_5{\cdot}NH{\cdot}CO{\cdot}C_6H_5 + HCl$$

$$(2)\ C_6H_5{\cdot}NH_2 + HCl \longrightarrow C_6H_5{\cdot}NH_3^+Cl^-$$

and is kinetically of the second order. The velocity constants determined for different substituted anilines cover a 50,000-fold range, the entropy of activation being approximately constant and all differences in rate arising only from changes in activation energy. These characteristics of the reaction make it very suitable for the verification of equation (2).

The only disadvantage of this reaction for the purpose of an investigation is that the products are precipitated from the solution, so that the overall heat of reaction includes the heat of the crystallisation of the product.

EXPERIMENTAL

The calorimeter was a Dewar vessel with a mechanical stirrer and it was placed in an air-thermostat. The heat of reaction was determined from the temperature change, ΔT, accompanying addition of 1 ml. of a benzene solution of benzoyl chloride to a fixed large volume of benzene containing aniline in excess.

ΔT was measured by a thermistor which had a resistance change of 3·5% for 1° at 20° c.

Two different techniques were used. For comparatively fast reactions with rate constants equal to or higher than that for unsubstituted aniline with benzoyl chloride, the concentration of the reagents was chosen so that completion of the reaction occurred within 2 min. The concentration of the benzoyl chloride being kept equal for the substituted and the unsubstituted compounds, the ratio of the heats of the two corresponding reactions $(-\Delta H_s)/(-\Delta H_0)$ is equal to $\Delta T_s/\Delta T_0$. The differences in specific heat of the solutions of the different compounds at the concentrations used were negligible.

For slow reactions with rate constants equal to or lower than that of the reaction of aniline with benzoyl chloride, the course of the temperature rise was followed kinetically. It was possible to select concentrations such that $c_s > c_0$, but $V_0^0 > V_s^0$ as $k_0 > k_s$, where c, V, and k are concentration, rate, and rate constant respectively; subscripts s and o correspond to the substituted and unsubstituted compound: V^0 is the initial rate. When the reaction takes place, however, V_0 decreases faster than V_s, so that by plotting ΔT_0 and ΔT_s against time it is possible to obtain an intersection point where ΔT is the same for both reactions (Fig. 1). At any moment differences in ΔT for both reactions will not have exceeded 0·07° c, so that differences in heat losses are negligible. Therefore, if t_1 is the time at which both curves intersect, then $\Delta T_s^{t_1} = \Delta T_0^{t_1}$ and $(-\Delta H_s)m_s^{t_1} = (-\Delta H_0)m_0^{t_1}$.

Hence $$-\Delta H_s = (-\Delta H_0)m_0^{t_1}/m_s^{t_1}$$

$m_0^{t_1}$ and $m_s^{t_1}$ being the quantities of products in moles at the time t_1.

$m_0^{t_1}$ and $m_s^{t_1}$ were estimated by Volhard's method by filtering off the precipitated aniline hydrochloride and dissolving it in water as described in previous papers.[3]

The energy equivalent of the calorimeter was determined electrically. Heat was produced in a thin nichrome wire immersed in the reaction vessel containing the same amount of benzene as that used in the reaction, the electrical energy being adjusted to give a value of ΔT nearly the same as in the reaction.

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[2] Evans and Polanyi, *Trans. Faraday Soc.*, 1938, **34**, 11.

[3] Williams and Hinshelwood, *J.*, 1934, 1079.

[4] Stubbs and Hinshelwood, *J.*, 1949, 71.

The techniques used permitted the determination of differences in the heats of reaction with a precision of about 0·5 kcal./mole.

Benzoyl chloride, *p*-nitrobenzoyl chloride, and the various aniline derivatives were purified to constant m. p. or b. p. by recrystallization or fractionation. " AnalaR " benzene was used as solvent in all experiments.

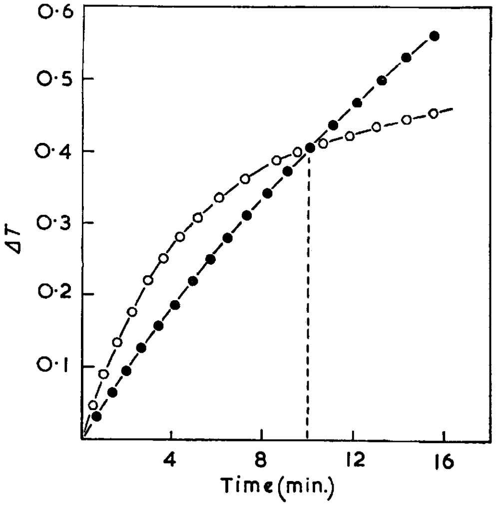

FIG. 1. *Plot of temperature change against time for the reactions* (○) $C_6H_5\cdot COCl + m\text{-}Br\cdot C_6H_4\cdot NH_2$ *and* (●) $C_6H_5\cdot COCl + C_6H_5\cdot NH_2$.

The results are summarized in Table 1. Activation energies for all compounds except *p*-phenylenediamine are taken from the previous papers.[3,4] That for *p*-phenylenediamine was estimated by plotting E against σ for various substituents and extrapolating the straight line at $\sigma = -0{\cdot}660$ for the *p*-amino-group.[5]

DISCUSSION

The results in Table 1 demonstrate a very strong dependence of the heat of reaction on the polar effect. The range covered is from 35·5 kcal./mole for *m*-nitroaniline and benzoyl chloride to 54 kcal./mole for aniline and *p*-nitrobenzoyl chloride, the corresponding range of activation energies being from 10·64 to 5·9 kcal./mole.

TABLE 1. *Benzoylation of substituted anilines in benzene solution.*

Amine	Activation energy E (kcal. mole^{-1})	Heat of reaction $-\Delta H$ (kcal. mole^{-1})	Amine	Activation energy E (kcal. mole^{-1})	Heat of reaction $-\Delta H$ (kcal. mole^{-1})
p-Phenylenediamine	4·70 *	51·70	*o*-Toluidine............	8·18	44·15
3,4-Dimethylaniline	6·43	46·55	*p*-Chloroaniline	8·53	39·50
p-Toluidine	6·75	46·15	*m*-Chloroaniline ...	9·27	36·20
m-Toluidine	7·24	43·15	*m*-Bromoaniline ...	9·34	37·10
2,4-Dimethylaniline	7·35	49·10	*o*-Chloroaniline	10·58	33·45
o-Anisidine	7·49	43·35	*m*-Nitroaniline	10·64	33·30
Aniline	7·60	41·70	(Aniline †	5·90	54·15)

* Calculated value. † With *p*-nitrobenzoyl chloride.

Fig. 2 shows a plot of activation energy against the heat of reaction. Almost all the points lie approximately on the straight line $E = 20{\cdot}5 - 0{\cdot}30(-\Delta H)$, in agreement with the equation (2), α having nearly the same value as for gas-phase radical reactions.

It should be noted that *para-*, *meta-*, and some of the *ortho*-derivatives lie on the same line, showing that the *ortho*-effect in the activation energy corresponds to an *ortho*-effect in the heat of reaction. For *o*-toluidine and 2,4-dimethylaniline the activation energy is somewhat higher than that according to the equation. This may be due to some kind of

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[5] Jaffee, *Chem. Rev.*, 1953, **53**, 191.

steric effect. The point corresponding to the reaction of *p*-nitrobenzoyl chloride also lies above the straight line.

In the reaction of *p*-nitrobenzoyl chloride with aniline, the precipitate is still aniline hydrochloride as in the reaction of aniline with unsubstituted benzoyl chloride, but the former reaction is 12 kcal. more exothermic than the latter. This means that the difference in heat between these two reactions lies in bond energy and not in heat of crystallisation.

From equation (2) it follows that when $\Delta(\Delta H) \longrightarrow 0$, ΔE approaches zero, that is, there is no change in activation energy when a polar substituent does not change the heat of reaction [$\Delta(\Delta H) = -\Delta H_s - (-\Delta H_0)$ and $\Delta E = E_s - E_0$].

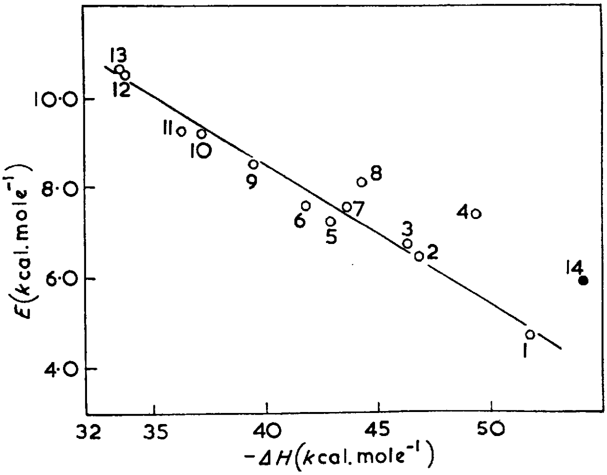

FIG. 2. *Relation of energy of activation to heat of reaction. Substituents in the amine*: 1, *p*-NH_2; 2, 3,4-Me_2; 3, *p*-Me; 4, 2,4-Me_2; 5, *m*-Me; 6, H; 7, *o*-OMe; 8, *o*-Me; 9, *p*-Cl; 10, *m*-Br; 11, *m*-Cl; 12, *o*-Cl; 13, *m*-NO_2. *Substituent in acid chloride*: 14, *o*-NO_2.

The result suggests that the reaction proceeds in one elementary stage with no steric hindrance from the substituent. This is the case for isotopic exchange, *e.g.*, $X{\cdot}C_6H_4{\cdot}CH_2I + KI^* \longrightarrow X{\cdot}C_6H_4{\cdot}CH_2I^* + KI$. Here for all the substituents $-\Delta H = 0$ and $\Delta(\Delta H) = 0$. In Table 2, results for this reaction are given, taken from the papers of Kahn *et al.*[6] It can be seen that the polar effect in this series is very small. *p*-NO_2 changes the rate only by a factor 1·7 in methyl alcohol at 20°, whereas the corresponding substitution in aniline decreases the rate by a factor of 1800. However, the effect of a polar substituent is too large to be accounted for by experimental error and is not entirely unexpected. Though the polar substituent does not affect the overall heat of the reaction, it does affect the potential energy curve involved in the definition of the transition state. The substituent NO_2 decreases the repulsion of the I^-ion approaching the carbon atom. Such effects should be smaller than those predicted by equation (2), and probably they do not follow the Hammett equation quantitatively.

TABLE 2. $X{\cdot}C_6H_5{\cdot}CH_2I + I^{*-} \longrightarrow X{\cdot}C_6H_5{\cdot}CH_2I^* + I^-$.

X	H	*p*-NO_2	*p*-Br	*p*-I
k_{20}	0·47	0·81	0·70	0·73
E (cal. mole^{-1})	16,200	15,570	16,656	16,600

According to equation (2), in reversible systems, there must be opposite effects of polar substituents on the direct and the opposed reaction, since

$$\Delta E = -\alpha\Delta(\Delta H) \text{ for forward reactions}$$
$$\Delta E = (1 - \alpha)\ .\ \Delta(\Delta H) \text{ for reverse reactions}$$

In terms of the Hammett equation this means that ρ_1 for the direct reaction has the

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[6] Kahn *et al.*, *J. Amer. Chem. Soc.*, 1953, **75**, 3579; 1954, **76**, 3796; U.S. Atomic Energy Commission, 1954, 1873 UNM; L.A., 1956, 2017 UNM.

opposite sign from ρ_2 for the opposed reaction, the absolute value of ρ_e for the equilibrium being therefore higher than either ρ_1 or ρ_2.

There are few examples of reactions where all the three values of ρ are known under the same conditions. One of these is the reaction [5]

$$\mathrm{H{\cdot}CO_2H} + \mathrm{C_6H_5{\cdot}NH_2} \underset{2}{\overset{1}{\rightleftharpoons}} \mathrm{C_6H_5{\cdot}NH{\cdot}CHO} + \mathrm{H_2O} \text{ at } 100^\circ$$

$$\rho_1 = -1{\cdot}224, \qquad \rho_2 = 0{\cdot}318, \qquad \rho_e = -1{\cdot}429$$

On this basis it is possible to explain the opposite effect of a polar substituent on reactions of identical mechanism. Such an effect can be expected when the heat change for the rate-determining step of the reactions is of opposite sign. Substituents which increase the heat of reaction will increase the rate of an exothermic reaction and have the reverse effect on the rate of an endothermic one.

These conclusions are not always open to direct experimental verification. They are valid for elementary reactions only. Interpretation is more difficult for reactions in which the overall process involves several stages, which are affected by a polar substituent.

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