# **181.** *The Mechanism of Hydrolysis of Acid Chlorides. Part III.* The Effect of* p-*Substituents in* 95% *Aqueous Acetone.*

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The rate of hydrolysis of *p*-substituted benzoyl chlorides has been followed in acetone and dioxan solutions containing 5% of water by volume, and activation energies have been determined. The reactions proceed almost exclusively by the bimolecular $S_N2$ mechanism, with a rate order similar to that observed in the alcoholysis. The variable *PZ* factor and the change in rate order with increasing water content are attributed to a tendency to react by the $S_N1$ mechanism. This is particularly significant in the case of chlorides containing electron-releasing groups, and the close analogy with the tendency to ionise in sulphuric acid is discussed.

The effect of substituents on the rate of alcoholysis of benzoyl chloride has been investigated in detail by Norris *et al.* (*J. Amer. Chem. Soc.*, 1939, **61**, 141, and previous papers) and by Branch and Nixon (*ibid.*, 1936, **58**, 2499) and has been the subject of much theoretical discussion (*e. g.*, Hughes, *Trans. Faraday Soc.*, 1941, **37**, 613; Baker, *ibid.*, p. 632). Although the results are in general agreement with the bimolecular $S_N2$ mechanism (in particular, *para*-substitution, see Branch and Nixon, *loc. cit.*), close examination of the results of Norris, Fasce, and Staud (*J. Amer. Chem. Soc.*, 1935, **57**, 1420) and Norris and Young (*ibid.*, p. 1420) reveals the difficulty in interpreting the rates consistently; *e.g.*, no complete explanation of the relative rates of solvolysis of benzoyl chloride substituted in *ortho-*, *meta-*, and *para*-positions with halogens, alkyl and nitro-groups has been given. In particular, the very high reactivities of di-*o*-alkyl-substituted chlorides are difficult to explain in terms of the $S_N2$ mechanism when it is realised that in the case of the benzyl halides this same effect is taken to indicate the occurrence of the alternative $S_N1$ mechanism. Furthermore, a completely different rate order has been observed in the hydrolysis of *para*-substituted benzoyl chlorides in 50% aqueous acetone (Olivier and Berger, *Rec. Trav. chim.*, 1927, **46**, 609; 1930, **49**, 697).

For these and other reasons it has been suggested that a change in mechanism is possible in solvents of high polarity when one or more electron-releasing groups are incorporated in the benzoyl chloride molecule (Hughes, *loc. cit.*; Hudson and Wardill, *J.*, 1950, 1729). As the hydrolysis has so far been studied only in 50% aqueous acetone, it seemed desirable to ascertain whether this rate order prevails in solvents of lower water content. If there is a tendency for acid chlorides to react by the $S_N1$ mechanism under suitable conditions

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* Part II, *J.*, 1950, 3259.

(which hitherto has been considered as most unlikely owing to the strong electromeric effect of the carbonyl group, $\overset{\curvearrowright}{C=O}$), the rate order should change to that observed in the alcoholysis in a medium of sufficiently low water content. The present results show that the reversion in order is almost complete in 95% aqueous acetone (Table 1). In addition, with the exception of anisoyl chloride, the rate ratios are close to the corresponding values in 40% alcohol in ether, which is a clear indication that the reaction is proceeding by the same mechanism in the two cases. This conclusion is reinforced by an examination of the parameters of the Arrhenius equation in relation to the structural changes in the molecule.

TABLE 1. *The effect of solvent changes on the relative rates of solvolysis of* p-*substituted benzoyl chlorides.*

| Medium | Dielectric const. | Relative velocity constants : | | | | |
|---|---|---|---|---|---|---|
| | | $NO_2$ | Br | Cl | $CH_3$ | $CH_3O$ |
| 40% EtOH + 60% $Et_2O$ ......... | 12·8 | 32 | 2·5 | 2·1 | 0·47 | 0·25 |
| EtOH ................................ | 25·7 | 21·6 | 2·1 | 1·9 | 0·70 | 0·81 |
| 5% $H_2O$ + 95% $COMe_2$ ......... | 22·2 | 35 | 3·2 | — | 0·55 | 0·60 |
| 50% $H_2O$ + 50% $COMe_2$ ......... | 51·5 | 11·5 | 0·92 | 0·85 | 2·9 | ~30 |

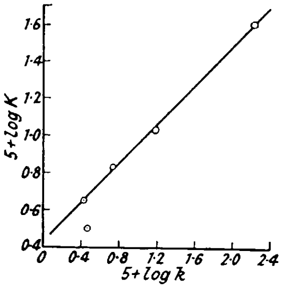


FIG. 1. *Relation between velocity constant and dissociation constant of the corresponding benzoic acid.*

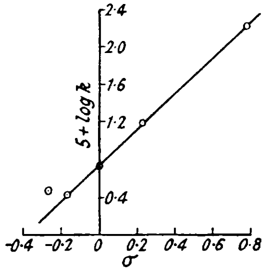


FIG. 2. *Relation between the velocity constant and the Hammett parameter for substituted benzoyl chlorides.*

The results given in Table 3 show that the velocity constants are governed primarily by the activation energy, which decreases regularly as the velocity constant increases. It is seen, however, that the temperature-independent factor *PZ* increases considerably with the activation energy, as in the alcoholysis, which is characteristic of many reactions of this type (Fairclough and Hinshelwood, *J.*, 1937, 538, 1573). Before this relationship is discussed further, the change in velocity constant with changes in significant physical properties will be investigated.

The generalised treatment of the variation in the velocity constant $k$ with a continuous change in a parameter related directly to the changing structure of the molecule (see Glasstone, Laidler, and Eyring, " Theory of Rate Processes," New York, 1941, 464) is based on the general equation of the absolute rate theory $k = (\boldsymbol{k}T/\boldsymbol{h})e^{-\Delta G/\boldsymbol{R}T}$, whence

$$\log_e k = \log_e \frac{\boldsymbol{k}T}{\boldsymbol{h}} - \frac{1}{\boldsymbol{R}T}\left[\frac{\delta\Delta G}{\delta\chi}\right] d\chi$$

This leads to the empirical equations of Brønsted and Hammett (" Physical Organic Chemistry," New York, 1940, 186), if $\delta\Delta G/\delta\chi$ is assumed to be constant. In the present case it is found that both equations are obeyed satisfactorily. Fig. 1 shows the relation between the velocity constants $k$ and the dissociation constant $K$ of the related benzoic acid, in accordance with the Brønsted relation, $\log k = \text{const.} + \text{const.} \times \log K$. The Hammett relation is usually written in the form $\log k_s = \rho\sigma + \log k_u$, where the subscript $s$ refers to the substituted, and $u$ to the unsubstituted molecule. The substitution parameter $\sigma (\equiv d\chi)$ is a constant for a given substituent, irrespective of the molecule in which it is introduced or the nature of the reaction. Fig. 2 shows that $\log k$ is linear with $\sigma$, with the exception of the value for anisoyl chloride. Hammett has explained his equation in terms of potential-energy changes alone, and has shown that its derivation involves the assumption that $\Delta S$ does not change with the substituent. The values of log $PZ$ given in Table 3, however, show that in the case now considered, this is by no means true. This relation may be applied to a wide series of reactions with considerable success, where in many cases the entropy of activation changes considerably with substitution.

This apparently fortuitous agreement may be examined further, on the principles laid down by Hinshelwood, Laidler, and Timm (*J.*, 1938, 848). These workers showed that in substitution reactions where electrostatic forces exert a controlling influence, a substituent affects the rate by affecting the density of charge at the seat of the reaction, which is reflected primarily in the activation energy. The parameter $\chi$ represents an intensity factor which in this instance may be associated with the electric field strength at the reaction centre. Hence, according to the treatment of Hinshelwood *et al.*, a change in $\chi$ should cause a proportional change in $E$. This relationship is demonstrated by the approximately linear relation between activation energy and moment of the substituted group (Fig. 3), which is related directly to the change in charge density at the central carbon atom.

FIG. 3. *Relation between the activation energy and dipole moment of the substituted group (data of Maxwell and Partington, J., 1936, 1175).*

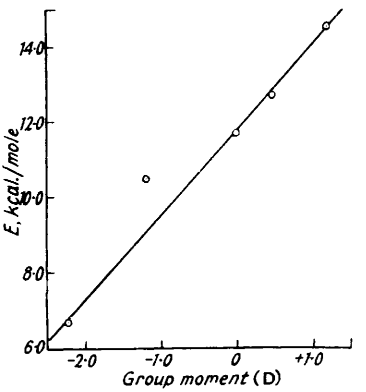
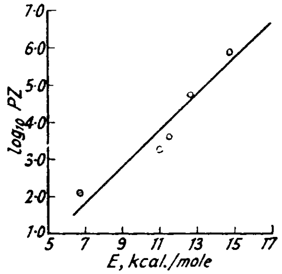


FIG. 4. *Relation between activation energy and collision frequency for the hydrolysis of substituted benzoyl chlorides.*



If therefore a regular change in the intensity parameter $\chi$ with substitution causes a proportional change in activation energy, the quantity $\delta\Delta G/\delta\chi$ is constant if (*a*) $\Delta S$ is constant or zero or (*b*) $\Delta S$ is a linear function of $E$, as in the present case (Fig. 4). Hammett's treatment (*op. cit.*) deals fully with the first condition, and the second will now be examined briefly.

A functional relation between the $PZ$ factor and activation energy has been observed in various rate processes, and in particular in several reactions involving pseudo-ionic transition states (Fairclough and Hinshelwood, *loc. cit.*; Timm and Hinshelwood, *J.*, 1938, 862). In other reactions of this type, however, the $PZ$ factor in a given solvent is insensitive to structural changes, although the value of $P$ may be either extremely low ($\sim 10^{-8}$) or of the order of unity. The first class include typical $S_N2$ reactions, *e.g.*, the benzoylation of amines (Williams and Hinshelwood, *J.*, 1934, 1079) and the reaction between substituted anilines and methyl iodide (Laidler, *J.*, 1938, 1786). On the other hand, reactions proceeding by the $S_N1$ mechanism are usually associated with high $P$ factors, as shown by the values calculated from the collected data of Grunwald and Winstein (*J. Amer. Chem. Soc.*, 1948, **70**, 846) given in Table 2. Only the values for solvents with a polarity comparable to that of those used in the present investigation have been considered. In addition, Nixon and Branch (*ibid.*, 1936, **58**, 492) have observed that the $PZ$ factors are almost independent of the nature of the substituted group in the alcoholysis of triarylmethyl chlorides, the values again being high ($\sim 10^{8}$). It is noteworthy that the velocity changes in the hydrolysis of ethyl halides are due to changes in the *PZ* factor (Hughes and Shapiro, *J.*, 1937, 1177).

TABLE 2. *Parameters of the Arrhenius equation for hydrolyses proceeding by the* $S_N1$ *mechanism.*

| Halide | Temp. | Solvent | $10^6k$, sec.$^{-1}$ | $E$ | $\log_{10} PZ$ |
|---|---|---|---|---|---|
| BuCl ........................ | 25° | 80% COMe$_2$ | 1·9 | 22·6 | 10·67 |
| BuBr ........................ | ,, | 95% ,, | 2·1 | 22·7 | 10·77 |
| CHPhMe·Cl ................ | — | 80% ,, | 1·44 | 21·8 | 9·96 |
| CHPh$_2$Cl ...................... | — | 90% ,, | 4·6 | 19·6 | 8·6 |

These facts suggest that, in a given solvent, the greater the *PZ* factor the greater is the tendency for the halide to react by the $S_N1$ mechanism. It is becoming widely recognised that there is no sharp boundary between $S_N1$ and $S_N2$ processes, but rather that a gradual change from one extreme to the other obtains. This interpretation is explicit in Hinshelwood, Laidler, and Timm's treatment (*loc. cit.*), and has recently been supported by Winstein *et al.* (*J. Amer. Chem. Soc.*, 1950, **73**, 2700) and by Swain and Langsdorf (*ibid.*, *p.* 2813). Hence if bond-making influences predominate over the bond-breaking process, the reaction will exhibit $S_N2$ characteristics from the point of view of the effect of substituents. If the other process predominates, the reaction will exhibit $S_N1$ characteristics, although it may still be sensitive to alkali unless the bond-making process makes an insignificant contribution to the activation energy.

The results given in Table 3 show that the *PZ* factor increases considerably from the *p*-nitro- to the *p*-methoxy-compound, which value approaches the lower values given in Table 2, for $S_N1$ processes. On the above interpretation, therefore, this change is due to a considerable change in the structure of the transition state leading to a more highly ionised form in the case of anisoyl chloride. This conclusion is supported by the change in rate order with water content. This is due to the considerable differences in the effect of solvent on the rate of hydrolysis of the various chlorides. Thus as the polarity of the solvent increases, the rate of solvolysis of the chlorides containing electron-releasing groups is affected to a much greater extent than the rates of the other chlorides. An increase in the water content of the acetone solution from 5 to 50% by volume causes a 12·7-fold increase in the

TABLE 3.

| R | $10^5k_0$, sec.$^{-1}$ | $10^5k_{15}$, sec.$^{-1}$ | $10^5k_{25}$, sec.$^{-1}$ | $10^5k_{35}$, sec.$^{-1}$ | $E$, kcal./mole | $\log_{10} PZ$ |
|---|---|---|---|---|---|---|
| Experiments in aqueous acetone. | | | | | | |
| CH$_3$O ........... | — | — | 3·00 | 6·39 | 14·7 | 5·89 |
| | — | — | 2·88 | 6·67 | — | — |
| | -- | — | 2·88 | 6·57 | — | — |
| CH$_3$ ........... | — | — | 2·65 | 5·58 | 12·7 | 4·75 |
| | — | — | 2·71 | 5·43 | — | — |
| | — | — | 2·70 | 5·31 | — | — |
| H .............. | — | 2·65 | 5·44 | — | 11·3 | 3·61 |
| | — | 2·63 | 5·39 | — | 11·7 | — |
| | — | 2·61 | 5·37 | — | — | — |
| Br .............. | 3·11 | 8·7 | 15·5 | 30·7 | 11·0 | 3·27 |
| | 3·14 | 8·8 | 14·4 | 30·5 | — | — |
| | 3·08 | 8·9 | 16·4 | 30·4 | — | — |
| | — | — | 15·5 | — | — | — |
| NO$_2$ ........... | 58·8 | 134 | 169 | — | 6·67 | 2·12 |
| | 58·3 | 122 | — | — | — | — |
| | 58·6 | 114 | — | — | — | — |

Experiments in aqueous dioxan : values of $10^5k_{25}$, sec.$^{-1}$.

R = CH$_3$O ........... 2·57, 2·71, 2·64 R = CH$_3$ ........... 3·44, 3·56, 3·56, 3·29

TABLE 4. *The effect on the rate order of replacing acetone by dioxan.*

| Solvent | Dielectric const. | $10^5k_{25}$, sec.$^{-1}$ | | |
|---|---|---|---|---|
| | | *p*-CH$_3$O | *p*-CH$_3$ | H |
| 95% Acetone ........................ | 22·2 | 2·92 | 2·69 | 5·45 |
| 95% Dioxan ........................ | 3·8 | 2·64 | 3·46 | 7·30 |

rate of hydrolysis of the *p*-nitro-compound, whereas the rate of the reaction with anisoyl chloride increases *ca.* 2000 fold.

These values may be compared with the values given by Hughes and Ingold for the solvent effect on $S_N1$ and $S_N2$ reactions (*J.*, 1936, 225; 1940, 925): for a change in solvent from 80% to 60% of ethyl alcohol in water, the rate of hydrolysis of methyl and ethyl bromides is approximately doubled, showing that the rate is approximately proportional to the water content. The more extensive data of Bird, Hughes, and Ingold (*J.*, 1943, 255) for the hydrolysis of *n*-butyl bromide in methyl alcohol–water mixtures are in agreement with these figures, and show that the rate increase is of the order of 8—10 times on changing the solvent from 95 to 50% of alcohol by volume.

Although the effect of solvent on reaction velocity is by no means clearly understood, these observations substantiate the view that the polarity of the transition state increases considerably from the *p*-nitro- to the *p*-methoxy-compound, owing to an increase in charge separation in the C–Cl bond. This view is also supported by the observation that the replacement of acetone by dioxan causes an increase in the rate of hydrolysis of *p*-toluoyl chloride and the unsubstituted chloride, but a decrease in the rate of hydrolysis of anisoyl chloride, following the decrease in dielectric constant (Table 4).

The order of reactivities in 50% aqueous acetone, with the exception of the value for the nitro-compound, is identical with that of the benzyl chlorides in the same solvent (Bennett and Jones, *J.*, 1935, 1515). Although the hydrolysis of benzyl chloride is known to proceed mainly by the $S_N2$ mechanism in this solvent, it is usually considered to react by the $S_N1$ mechanism in more aqueous solvents. The above considerations suggest, therefore, that the tendency for the benzoyl chlorides to react by the $S_N1$ mechanism is at least as pronounced as with the benzyl chlorides, in agreement with the hydroxyl-ion effect recorded previously (Hudson and Wardill, *loc. cit.*). This conclusion is in agreement with recent work on the production of benzoyl ions in concentrated sulphuric acid, which shows that the stability of the acyl ion is very sensitive to structural changes; *e.g.*, the existence of the stable 2 : 4 : 6-trimethylbenzoyl cation has been realised for some time (Treffers and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 1708), but later work (Kuhn and Corwin, *ibid.*, 1948, **70**, 3370) suggested that the free *p*-methoxybenzoyl ion may also be formed, but subsequently react with sulphuric acid to give the acyl sulphonate, and Gillespie (*J.*, 1950, 2997) has shown that benzoic and acetic anhydrides readily give rise to the corresponding ions. On the other hand, electron-attracting groups inhibit this ionisation, and consequently there is a complete parallel between these ionisations and the tendency for $S_N1$ hydrolysis discussed above.

## EXPERIMENTAL

The solvent and substituted chlorides were prepared and purified as described previously (*J.*, 1950, 1729). Owing to the relatively slow rates of reaction in 5% aqueous solution, the rates can be followed conveniently by titration with alkali. The reaction mixture was prepared in each case by pipetting 50 ml. of water into a graduated flask and adding purified solvent up to 1 l.; in each experiment 100 ml. of solvent were contained either in stoppered bottles or in a specially constructed flask with a fitted pipette for the faster runs. The chloride was either weighed directly into the reaction mixture or delivered from a small pipette fitted with a ground-glass joint to fit into a vessel containing the sample of pure chloride, to give a 0·02N-solution.

5-Ml. samples were withdrawn at convenient intervals and run into 50 ml. of pure acetone to stop the reaction. These solutions were titrated against standard 0·02N-sodium hydroxide, lacmoid being used as indicator. When the hydrolysis of *p*-nitrobenzoyl chloride was followed, each 5-ml. sample was delivered into 50 ml. of acetone cooled to −30° to −40°. The results are summarised in Table 3, R being the substituent.

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