350. *The Mechanism of Hydrolysis of Acid Chlorides. Part I. The Effect of Hydroxyl Ions, Temperature, and Substituents on the Rate of Hydrolysis of Benzoyl Chloride.*

By R. F. Hudson and J. E. Wardill.

The velocity of hydrolysis of benzoyl chloride has been measured electrically using 50% aqueous acetone as solvent. Hydrogen-ion catalysis was not detected, in agreement with previous observations. It was found that the ratio of the bimolecular velocity constant for the reaction with hydroxyl ions to the velocity constant of the pseudo-unimolecular reaction for the neutral hydrolysis is of the same order as for the hydrolysis of benzyl chloride. In addition, the activation energies for the neutral hydrolysis of benzoyl chloride and several *p*-substituted benzoyl chlorides varied little with the nature of the substituent. This contrasts with the alcoholysis in a solvent of lower ionising power. These results have been interpreted in terms of a dual mechanism involving bimolecular substitution and unimolecular ionisation, a conclusion which is supported fully by alcoholysis studies.

Benzyl chloride is usually considered to be hydrolysed after preliminary ionisation, which is rate-determining. In support of this mechanism, it is found that substituents which increase the electron density at the reactive carbon atom increase the rate of reaction (Olivier and Berger, *Rec. Trav. chim.*, 1926, **45**, 452; 1930, **49**, 697). The effect of introducing an oxygen atom at the reactive carbon atom is to withdraw electrons from the seat of reaction, and hence to promote a bimolecular mechanism (Hughes, *Trans. Faraday Soc.*, 1941, **37**, 613). The effect of substituents on the rate of a bimolecular reaction is less definite than for a unimolecular mechanism, owing to the relative complexity of a bimolecular transition state (see Hinshelwood, Laidler, and Timm, *J.*, 1938, 848). It is not surprising therefore that difficulty has been experienced in interpreting the experimental data in terms of this mechanism.

The hydrolyses of benzyl and benzoyl halides are similar in the following ways : (1) The rate is unaffected by the hydrogen-ion concentration, but is increased by addition of hydroxyl ions (Olivier and Berger, *Rec. Trav. chim.*, 1927, **46**, 609; Beste and Hammett, *J. Amer. Chem. Soc.*, 1940, **62**, 2481). (2) The effect of solvent in both cases is such that the rate of hydrolysis increases considerably with increasing ionising power of the solvent. (3) Benzyl halides show positive salt effects (Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979). The benzoyl halides exhibit salt effects of a comparable magnitude (Peeling, Ph.D. Thesis, London, 1946).

On the other hand, the effect of substituents on the rate of hydrolysis of benzyl chloride is the reverse of the effect on the rate of the alcoholysis of benzoyl chloride. This is usually quoted as evidence of the bimolecular nature of the latter reaction. The effect of substituents on the rate of hydrolysis of benzoyl chloride differs greatly from the effect on the rate of the alcoholysis—and the former reaction cannot be interpreted simply in terms of any one mechanism.

Previous methods of following the rate of hydrolysis of benzoyl chloride were not of a high degree of accuracy, owing to the use of titration methods in relatively rapid reactions. An E.M.F. method similar to that developed by Ross and Swain (*J. Amer. Chem. Soc.*, 1946, **68**, 658) was used in the present work, and enabled activation energies to be determined and the effect of hydroxyl ions to be investigated. In addition, the original conclusion of Olivier and Berger that hydrogen ions have no effect on the rate was confirmed.

It is observed that hydroxyl ions increase the rate of hydrolysis by a bimolecular reaction superimposed on the pseudo-unimolecular solvolysis, as in the case of benzyl chloride (Beste and Hammett, *loc. cit.*). Thus the overall rate of reaction is give by the expression,

$$dx/dt = k_1(a - x) + k_2(a - x)(b - x)$$

where $(a - x)$ is the concentration of benzoyl chloride, and $(b - x)$ that of hydroxide ions at time t, k_1 the pseudo-unimolecular constant for the neutral hydrolysis, and k_2 the bimolecular constant for the reaction with hydroxyl ions.

Evaluation of k_2 for the hydrolysis of benzoyl and benzyl chlorides shows that the bimolecular reaction with hydroxyl ions affects the overall rate to approximately the same extent in the two cases, as shown by the following values :

Hydrolysis.	Medium.	D, 20°.	k_2/k_1.
(*a*) $C_6H_5{\cdot}COCl$	Water 50%, acetone 50%	51	20
(*b*) $C_6H_5{\cdot}CH_2Cl$	Water 40%, dioxan 60%	34	150

(*a*) Present work. (*b*) Beste and Hammett.

As k_1 increases greatly with increase in the dielectric constant D, it follows that the hydroxyl-ion effect is almost identical for the two substances. In some cases where the reaction is thought to be bimolecular, *e.g.*, the hydrolysis of acetic anhydride (Gold, *Trans. Faraday Soc.*, 1948, **44**, 506), the ratio is much greater, *ca.* 10^4. These results indicate that benzoyl chloride may be hydrolysed by a S_N1 mechanism in highly aqueous solvents, a possibility which is supported by the following experimental results.

Table I records the activation energies for the neutral hydrolyses of benzoyl chloride and *p*-substituted benzoyl chlorides. These values, when compared with corresponding values for the alcoholysis of triphenylmethyl and benzoyl chlorides, show that substituents in the *p*-position have little effect on E, although the rate is affected considerably (see below).

TABLE I.

	Activation energy (cals.)			
	alcoholysis			hydrolysis
p-Substituent.	triphenylmethyl chlorides.	benzoyl chlorides.		
NO_2	16,710 [a]	11,100 [a]	— [b]	15,600 [c]
Br	—	13,400	—	16,700
Cl	13,480	13,850	14,120	—
H	13,420	14,400	15,530	16,100
CH_3	12,450	15,900	14,900	15,800

[a] Alcoholysis in 40 : 60 ethyl alcohol–ether; Nixon and Branch, *J. Amer. Chem. Soc.*, 1936, **58**, 492, 2499. [b] Alcoholysis in pure ethyl alcohol; Norris and Young, *ibid.*, 1935, **57**, 1420. [c] Present work.

The effect of substituents on activation energy has been discussed fully by Hinshelwood, Laidler, and Timm (*loc. cit.*) in terms of electron accession at the seat of reaction. It has been observed that E increases as the strength of the C–Cl bond increases in certain reactions which are thought to be governed by preliminary ionisation. In the alcoholysis of the benzoyl chlorides in alcohol–ether mixtures, however (Nixon and Branch, *J. Amer. Chem. Soc.*, 1936, **58**, 2499), the effect of substituents on E shows it to be governed mainly by the repulsion energy. In this bimolecular reaction, substituents increase the energy of activation in the order, $NO_2 < Br < Cl < H < CH_3 < CH_3O$, as these groups increase the electron density at the seat of reaction in the same order. The present work dealing with the hydrolysis has shown that E remains almost constant with substitution, but is somewhat less for the *p*-CH_3 *and p*-NO_2-compounds than for the unsubstituted chloride. This indicates that in the hydrolysis of unsubstituted benzoyl chloride the C–Cl bond strength and the repulsion energy contribute equally to the activation energy.

In a highly aqueous medium, therefore, reaction may proceed either by unimolecular solvolysis or by bimolecular substitution. Thus methyl substitution increases the rate and decreases E, as reaction proceeds mainly by the ionisation mechanism, whereas the nitro-group increases the rate by promoting the bimolecular reaction. The possibility of this change in mechanism has been discussed briefly by Hughes (*Trans. Faraday Soc.*, 1941, **37**, 601), to explain the effect of substitution on the rate of solvolysis in pure alcohols.

The results for alcoholysis will now be reviewed in greater detail. It is seen from Table II that increasing the ionising power of the solvent changes the order of the activation energies.

TABLE II.

Order of *E*.	Solvent.	*D*, 20°.
$CH_3 > H > Cl$	Alcohol 40%, ether 60%	12·8
$H > CH_3 > Cl$	Alcohol 100%	25·7
$Br > H > CH_3$	Water 50%, acetone 50%	51·2

In a solution of low alcohol content, the methyl-substituted chloride is apparently hydrolysed according to a bimolecular mechanism, as also is the unsubstituted chloride, but in pure alcohol the unimolecular mechanism preponderates.

On considering the effect of the position of the substituent, it is noted that in the hydrolysis and alcoholysis (Norris and Young, *loc. cit.*; Olivier *et al.*, *loc. cit.*) the rates for the methyl and nitro-compounds change in reverse orders: $o\text{-} \gg m\text{-} \sim p\text{-CH}_3$; $o\text{-} \ll m\text{-} \ll p\text{-NO}_2$. Although *ortho*-groups often introduce anomalies in rate (Hughes, *Quart. Reviews*, 1948, **2**, 107), these sequences indicate that the effect of the *o*-methyl group in releasing electrons is much greater than the effect produced by the *m*- or *p*-group, and consequently the unimolecular mechanism is promoted to a greater extent. In the second case, the *m*- and the *p*-nitro-group greatly increase the rate of the bimolecular reaction by removing electrons from the reactive carbon atom. For the *ortho*-compound, however, the rate is decreased considerably owing to the steric hindrance offered by the large nitro-group to an approaching water dipole. It is significant that the activation energy for the alcoholysis, with pure ethyl alcohol, of the *o*-nitro-compound (12·9 kcals.) is much less than that of the *o*-methyl compound (16·5 kcals.), although the rate of alcoholysis of the latter compound is greater than that of the former (Norris and Young, *loc. cit.*).

Finally the peculiar di-*ortho*-effects in the alcoholyses provide strong support for the theory that the benzoyl chlorides may be hydrolysed by alternative mechanisms. Norris and Ware (*J. Amer. Chem. Soc.*, 1939, **61**, 1418) found that 2 : 6- and 2 : 4 : 6-substituents affect the rate in two distinct ways. Positive groups (*i.e.*, electron-repelling with respect to hydrogen), *e.g.*, methyl, methoxy-, and ethoxy-, reacted so fast in the pure alcohol that the actual rate could not be measured. On the other hand negative groups, *e.g.*, nitro-, bromo-, and chloro-, decrease the rate considerably. Here we are concerned with very large differences in rate—much greater than the changes caused by monosubstitution. Steric hindrance has been suggested to explain the large reductions in rate, a similar reduction being observed in the hydrolysis of 2 : 6-dibromobenzoyl chloride (Olivier, *Rec. Trav. chim.*, 1929, **48**, 227).

That steric hindrance is not exhibited by the di- and tri-methyl, -methoxy-, and -ethoxy-compounds shows that these are hydrolysed by a different mechanism, which does not involve the close approach of an attacking molecule. These positive groups in the *ortho*-positions would promote unimolecular solvolysis, the rate of which is unaffected by steric hindrance. In support of this mechanism, Hughes (*loc. cit.*) has observed that hydroxyl ions have very little catalytic effect on the rate of alcoholysis of 2 : 4 : 6-trimethylbenzoyl chloride.

EXPERIMENTAL.

Purification of Materials.—Commercial benzoyl chloride was distilled under reduced pressure several times, and a final fraction (b. p. 196°) obtained by distillation under atmospheric pressure. This was introduced into a conical flask provided with a ground-glass joint and attached to a microburette. The whole of the apparatus was carefully dried before benzoyl chloride was admitted, and all openings to the air were connected to tubes containing calcium chloride and phosphoric oxide.

p-Toluoyl chloride, prepared from *p*-toluic acid by phosphorus pentachloride and purified by distillation at reduced pressure, had b. p. 102°/15 mm.

p-Nitrobenzoyl chloride, prepared from *p*-nitrobenzoic acid in the usual way and purified by repeated recrystallisation from light petroleum (b. p. 60—80°), had m. p. 73°.

p-Bromotoluene and potassium permanganate at 130° (for a day) gave *p*-bromobenzoic acid, m. p. 249°. The acid was refluxed with the calculated quantity of phosphorus pentachloride, and when reaction ceased, extracted with light petroleum (b. p. 60—80°). The crude bromide was recrystallised from light petroleum several times to give a pure product, m. p. 42°.

Large quantities of acetone were purified as follows. 2—3 L. were shaken for 1/2 hour with 100 ml. of 2% potassium permanganate solution containing 20 ml. of concentrated sulphuric acid, and then set aside for several hours; the acetone was distilled off through a 5 ft. Vigreux column. The distillate was treated with 50 ml. of concentrated silver nitrate solution and 20 ml. of 2N-sodium hydroxide. After the mixture had been occasionally shaken during several hours, calcium chloride was added and the mixture set aside overnight. The acetone was subsequently decanted into a distillation flask, treated with 20 g. of calcium chloride, and distilled again. The collected fraction, b. p. 56—57°, was allowed to remain overnight in contact with calcium chloride, and fractionated as before, the first 50 ml. being rejected. The final distillate was collected in a bottle fitted with a calcium chloride guard-tube.

Rate Measurement.—The principle of the concentration cell was employed in following the rate of hydrolysis. A silver/silver chloride electrode, immersed in the hydrolysing solution, set up an E.M.F.

which was just opposed by a similar electrode in a solution of hydrochloric acid of known concentration. The electrodes were connected through a galvanometer which was used as a null-point instrument, hydrochloric acid being titrated into the calibration cell. The apparatus is shown diagrammatically in Fig. 1.

A small constant-speed electric motor was connected through a small fibre gear-wheel to two large equivalent gears fitted to vertical stainless steel axles. A small steel cup was screwed to the top of each axle, the lower ends of which were fitted to two identical glass stirrers. Equal lengths of chloridised silver wire, of *ca.* 1-mm. diameter, were wound spirally round the stirrers and the upper ends fixed to screw terminals in the steel axles. A thick steel wire was supported in the centre of each steel cup and made electrical contact with a small quantity of mercury placed in each cup. The two steel wires were connected *via* a tapping key to a mirror galvanometer with a sensitivity of the order of 50 mm./m./microamp. The stirrers were allowed to rotate in the centre of two 100-ml. beakers which were connected by means of an agar–salt bridge. One beaker contained the reacting solution, the other being used as the titration cell, and both were fixed in a small thermostatically controlled bath.

FIG. 1.

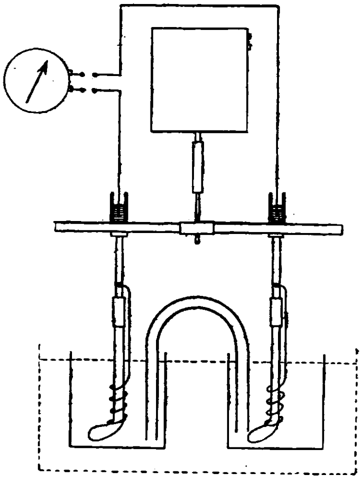
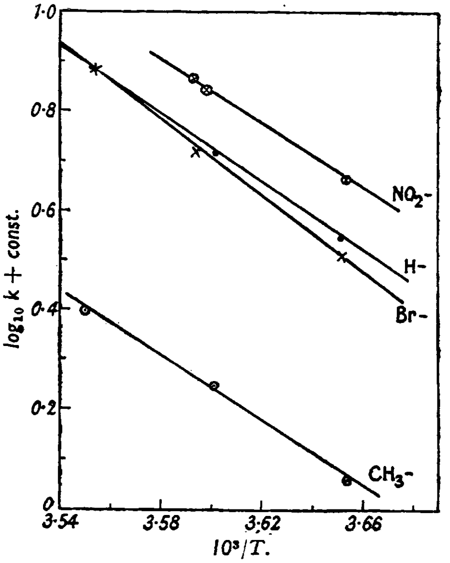


FIG. 2.



In a typical experiment, 25 ml. of 0·45N-potassium nitrate were pipetted into each beaker and stirred slowly until the liquids reached the temperature of the bath. In the meantime two 25-ml. portions of purified acetone, in separate dry boiling tubes, were cooled for ½ hour in an alcohol–carbon dioxide bath at −41·5°. Several drops of benzoyl chloride were added from the storage microburette to one of these samples, so that the approximate concentration was known. The acetone was then quickly added to the nitrate solution in the titration cell, followed by a known volume (1 drop) of standard hydrochloric acid. The reaction was then started by rapid addition of the cooled solution of benzoyl chloride in acetone to the other beaker. A stop watch was started immediately after the addition, which took approx. 1 second, and the time observed when the galvanometer was not deflected. A further drop of hydrochloric acid was added from the microburette to the calibration cell and a second balance time obtained, this procedure being continued until the sensitivity of the system became too low for accurate measurements.

At the end of the experiment, the hydrolysing solution was transferred to a 400-ml. beaker and analysed gravimetrically as silver chloride. The reactions were performed in the presence of potassium nitrate to eliminate solution junction potentials as far as possible.

Similar procedures were adopted in the experiments using substituted benzoyl chlorides. In the case of the two solid derivatives, the samples were weighed directly into the cooled acetone solutions.

The chief difficulty encountered in these experiments was the temperature control, owing to the large heat of mixing of acetone and water. Thus the acetone had to be pre-cooled to −41·5° to obtain a final temperature of *ca.* 0°, so that in no two cases could the temperature be exactly reproduced. In the following results the rate constants are corrected in some cases to obtain 0° values where comparisons are required, utilising the experimentally determined temperature coefficient.

Results.—(a) *The effect of hydrogen ions.* Small quantities of nitric acid were added to the reaction mixture and also to the titration cell, and the rate of hydrolysis was determined. Control experiments in the absence of nitric acid, but with small known quantities of added water, were performed to determine the accelerating influence of the water in the added nitric acid solution. Table III shows that there is no difference in rate in the presence of hydrogen ions, in agreement with previous observations of Olivier and Berger (*loc. cit.*).

TABLE III.

Temp., °c.	Normality of $C_6H_5{\cdot}COCl$.	Normality of HNO_3.	Vol. of H_2O (ml.).	k_1, min.$^{-1}$.	k_1 (corr.), min.$^{-1}$.
0·7	0·00833	0·0073	0·323	0·0346	0·0322
0·9	0·00860	0·0137	0·596	0·0367	0·0336
0·6	0·0147	0·0137	0·596	0·033	0·0310
0·8	0·0109	0·027	1·179	0·0361	0·0333
0·7	0·0093	—	0·323	0·0340	0·0316
0·7	0·0124	—	0·596	0·0355	0·0330
0·7	0·00985	—	1·178	0·0365	0·0340

Thus in contrast to several other similar compounds containing a highly labile chlorine atom (cf. Böhme, *Ber.*, 1941, **74**, 248; Leimu and Salomaa, *Acta Chem. Scand.*, 1947, **1**, 353) there is no evidence of hydrogen-ion catalysis in the acid hydrolysis of benzoyl chloride. From the results in the above table, and from many other experiments, it was found that the rate of reaction is almost independent of benzoyl chloride concentration in the range 0·004—0·03N.

(b) *The effect of hydroxyl ions.* See Table IV.

TABLE IV.

Temp., °c.	$C_6H_5{\cdot}COCl$ (a).	NaOH (b).	$t_{\frac{1}{2}}$ (mins.).	Initial rate.*	k_2, l./g.-mol./min.
0·8	0·0058	0·0062	17—50	0·0401	0·82
0·8	0·0075	0·0062	18—0	0·0392	0·70
0·9	0·0129	0·0224	11—10	0·0541	0·85
0·7	0 0224	0 0224	15—0	0·0497	0·67
0·8	—	—	—	—	—

* Fractional decomposition of $C_6H_5{\cdot}COCl$ (x/a), per min.

$k_1 = 0{\cdot}035$ min.$^{-1}$. Mean value of $k_2 = 0{\cdot}76$ l./g.-mol./min.

The bimolecular constant was computed from the limiting rate at zero time, obtained graphically thus:

$$\frac{1}{a}\left(\frac{dx}{dt}\right)_{t=0} = k_1 + k_2 b$$

This approximate method was used because integration of the fundamental equation

$$dx/dt = k_1(a - x) + k_2(a - x)(b - x)$$

leads to the following complex solution which cannot be used directly to determine k_2:

$$t = \frac{1}{k_1 + k_2(b - a)} \ln \frac{a}{a - x} - \ln \frac{k_1 + k_2 b}{k_1 + k_2(b - x)}$$

It is seen that for 50% aqueous-acetone mixtures, the ratio $k_2/k_1 = 20$, the significance of which has been discussed above.

(c) *Temperature and substituents.*

TABLE V.

	Temp., °c.	k_1, min.$^{-1}$.	E (±300 cals.).	$\log_{10} B$.
Benzoyl chloride	0·7	0·0350	16,100	9·5
	4·4	0·0525		
	8·3	0·0770		
p-Bromobenzoyl chloride	0·7	0·0320	16,700	9·9
	5·0	0·0518		
	9·0	0·0770		
p-Nitrobenzoyl chloride	0·5	0·460	15,600	10·3
	4·7	0·692		
	5·0	0·750		
p-Toluoyl chloride	0·5	0·115	15,800	9·8
	4·5	0·177		
	8·5	0·250		

Detailed results of velocity constants at three temperatures are given in Table V, and the graphs of $\log_{10} k_1$ against $1/T$ in Fig. 2. Table V also includes values of the activation energy E and frequency factor B, determined graphically by application of the simple Arrhenius equation, $\ln k_1 = (-E/\mathbf{R}T) + \ln B$. The significance of these activation energies has already been discussed.

We thank Prof. J. R. Partington for his interest and advice, Dr. R. F. Garwood with whom several helpful discussions were held, and the Central Research Fund for financial assistance.

QUEEN MARY COLLEGE, MILE END ROAD, LONDON, E.1. [*Received, March* 18*th*, 1950.]
