171. *Amide Hydrolysis in Very Strong Acids. Part II.*[1] *Rate Measurements in Various Media, and a Discussion of the Mechanism.*

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First-order rate constants are recorded for the hydrolysis of 11 amides at temperatures between 13·3° and 90° in mixtures of sulphuric acid with water, disulphuric acid, chlorosulphonic acid, and methanesulphonic acid; and in deuterosulphuric acid. The mechanism is discussed with regard to constitutional influences, polar and steric, on both sides of the amide group; to the effect on the rate of changes in the reaction medium; and to the temperature-dependence of the rate. It is concluded that in highly acidic media containing little free water, amide hydrolysis occurs by a rate-determining fission of the conjugate acid in its less stable form, with the proton on the amino-group: and that this step is generally-catalysed by strong acids.

It has been shown that certain amides are hydrolysed in anhydrous sulphuric acid, but that a delicate balance exists between sulphonation and hydrolysis.[1] It would be a clear advantage to continue the kinetic study in less strongly sulphonating media, for apart from avoiding this complication, measurements in different solvents should lead to further knowledge of the mechanism. The sulphonating power of sulphuric acid decreases very sharply on addition of small amounts of water.[2] Unfortunately, however, the hydrolysis can be followed cryoscopically only in 100% acid: *e.g.*, a 0·25M-solution of an amide in the presence of as little as 0·3% of water is hydrolysed according to the reaction:

$$R'\cdot C(OH^+)\cdot NHR + H_3O^+ + 2HSO_4^- \longrightarrow R'\cdot CO_2H_2^+ + R\cdot NH_3^+ + 2HSO_4^-$$

and there will be little change in the freezing point accompanying hydrolysis since the total number of solute particles remains the same.

For these reasons alternative methods have been used to measure rate constants for the hydrolysis of amides in sulphuric acid–water mixtures and in other strongly acid solutions.

Results

Table 1 gives first-order rate constants for the hydrolysis of 11 amides in sulphuric acid–water mixtures at various temperatures. The hydrolysis of isobutyramide and pivalamide was followed by estimation of the ammonia produced. The reactions of the substituted anilides were followed in each case by converting the amine, *via* the diazonium salt, into a water-soluble azo-dye whose concentration was measured spectrophotometrically. Good linear plots of log $(D_\infty - D)$ against time were obtained, D referring to optical density. The value of D_∞ chosen to give the best straight line in general agreed closely with that predicted from experiments in which the pure amine was diazotised and coupled. In the case of 2,4-dinitro-*N*-*o*-nitrobenzoylaniline, however, the values of D_∞ were rather low, and varied with the acid concentration as follows: in 100% acid, $D_\infty = 0·84$; in 95·4% acid, $D_\infty = 0·92$. This shows the presence of a side reaction, possibly sulphonation, which is more prominent in anhydrous than in aqueous sulphuric acid.

The hydrolyses of *p*-nitro-*N*-*o*- and -*N*-*p*-toluoylaniline appear from the spectrophotometric results to be free from side reactions in 98% sulphuric acid. These cases require comment since the cryoscopic results show that in 100% acid considerable sulphonation occurs.[1] From the results in Table 1, assuming that the ratio of the rate in 100% to that in 98% acid is similar to that for *N*-acetyl-3,5-dinitroaniline, we estimate the rate constant for hydrolysis in 100% acid to be 0·023 min.$^{-1}$ for the *p*-toluoyl at 50·2°, and 0·006 min.$^{-1}$ for the *o*-toluoyl compound at 20°. These values may be compared with the respective cryoscopically determined rate constants, 0·039 and 0·019 min.$^{-1}$, which will be the sum of sulphonation and hydrolysis components if both processes occur.[1] It appears from this comparison that both processes occur at comparable rates in 100% sulphuric acid. Now the rate of sulphonation in sulphuric acid–water mixtures

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[1] Part I, *J.*, 1960, 545.

[2] (*a*) Cowdrey and Davies, *J.*, 1949, 1471; (*b*) Jacques and Leisten, unpublished work.

falls off approximately according to the square of the non-logarithmic acidity function, h_0.[2] The sulphonation rate should therefore be more than 3000 times less in 98% acid ($H_0 = -9{\cdot}36$) than in anhydrous acid ($H_0 = -11{\cdot}10$). From this we can be sure that hydrolysis alone takes place in 98% sulphuric acid, and that the only results in Table 1 that are somewhat uncertain on account of a side reaction are those for 2,4-dinitro-*N*-*o*-nitrobenzoylaniline.

TABLE 1. *Hydrolysis in sulphuric acid–water mixtures.*

Amide R·CO·NHR′ *		H_2SO_4		10^3k	H_2SO_4		10^3k
R	R′	(%)	Temp.	(min.$^{-1}$)	(%)	Temp.	(min.$^{-1}$)
Me	3,5-$(NO_2)_2C_6H_3$	100·0	48·9°	1·38	79·5	65·0°	0·90
		100·0	71·0	33·8	72·7	65·0	2·30
		100·0	65·0	13·8	70·2	65·0	4·86
		97·2	65·0	10·4	68·4	65·0	8·30
		94·9	65·0	7·55	66·1	65·0	13·2
		84·6	65·0	1·50	68·4	57·25	4·07
		(100·0% D_2SO_4	65·0	14·7)	68·4	72·2	18·3
Et	,,	68·4	65·0	14·0			
p-$NO_2{\cdot}C_6H_4$	2,4-$(NO_2)_2C_6H_3$	100·0	35·75	1·22	100·0	53·45	14·2
		100·0	42·0	2·67	94·9	53·45	6·45
		100·0	50·0	9·75	94·5	50·3	4·58
		100·0	57·9	25·8	94·5	63·4	25·1
		100·0	63·0	54·8			
o-$NO_2{\cdot}C_6H_4$	,,	100·0	13·3	20·7	95·4	13·3	6·76
		98·2	13·3	15·2	95·2	25·0	48·9
Ph	,,	100·0	13·3	22·0			
p-C_6H_4Me	*p*-$NO_2{\cdot}C_6H_4$	97·8	59·2	55·8	98·1	48·1	13·3
		97·8	37·95	3·22			
o-C_6H_4Me	,,	98·1	35·0	53·7	98·1	25·0	10·8
Ph	,,	98·1	48·1	3·91			
Me	,,	100·0	45·0	3·94	69·7	55·0	0·76
		100·0	55·0	14·8	69·7	74·7	5·48
		100·0	63·7	44·1	69·7	87·9	19·7
		92·1	55·0	1·89	63·1	55·0	4·97
		92·1	68·05	9·53	63·1	67·0	16·2
		92·1	80·9	47·2	63·1	77·0	42·8
		77·8	55·0	0·12			
Isobutyramide		97·2	90·0	0·001			
Pivalamide		97·2	90·0	0·30			

* Concn. ~0·25M.

The results in Table 1 give good Arrhenius plots, and the parameters derived from them are collected in Table 2. Also derived from these results, and the Arrhenius plots, are Table 3 and Fig. 1, which display features to be discussed below. The rate of hydrolysis of *N*-acetyl-3,5-dinitroaniline in mixtures of sulphuric acid with disulphuric acid, chlorosulphonic acid,

TABLE 2. *Arrhenius parameters.**

Amide R·CO·NHR′				
R	R′	Solvent (H_2SO_4, %)	$\log_{10} A$ (min.$^{-1}$)	E (kcal./mole)
Me	*p*-$NO_2{\cdot}C_6H_4$	100·0	16·2	27·2
		92·1	16·6	29·1
		69·7	*12·6*	*23·6*
		63·1	*11·8*	*22·6*
p-$NO_2{\cdot}C_6H_4$	2,4-$(NO_2)_2C_6H_3$	100·0	17·1	28·4
		94·5	16·8	28·4
o-$NO_2{\cdot}C_6H_4$	,,	95·2	20·6	30·0
o-C_6H_4Me	*p*-$NO_2{\cdot}C_6H_4$	97·8	16·9	27·7
o-C_6H_4Me	,,	98·1	19·4	29·3
Me	3,5-$(NO_2)_2C_6H_3$	100·0	18·7	31·8
		68·4	*12·4*	*22·5*
		{58 mole % H_2SO_4 42 mole % $Cl{\cdot}SO_3H$	17·9	30·0

* For the significance of the italicised figures see text.

methanesulphonic acid, and water, are shown graphically in Fig. 2. The spectra of 4·3 × 10^{-5}M-solutions of *p*-nitroacetanilide in ethanol, 100% sulphuric acid, and 88% sulphuric acid were

TABLE 3. *Constitutional effects on amide hydrolysis in sulphuric acid solutions.*

	Amide R·CO·NHR′				
No.	R	R′	Solvent (H_2SO_4 %)	Temp.	10^3k (min.$^{-1}$)
1	Me	3,5-$(NO_2)_2C_6H_3$	100·0	60·0°	8·56
2 *	Et	,,	100·0	60·0	22·2
3 *	CH_2Cl	,,	100·0	90·0	<0·2
4	Ph	2,4-$(NO_2)_2C_6H_3$	100·0	13·3	22·0
5	*p*-NO_2·C_6H_4	,,	100·0	13·3	0·46
6	*o*-NO_2·C_6H_4	,,	100·0	13·3	20·7
7	Ph	*p*-NO_2·C_6H_4	98·1	48·1	3·91
8	*p*-C_6H_4Me	,,	98·1	48·1	13·3
9	*o*-C_6H_4Me	,,	98·1	48·1	380

* Results obtained cryoscopically.[1]

FIG. 1. *Rates of hydrolysis of* p-*nitroacetanilide* (*A*) *and* 3,5-*dinitroacetanilide* (*B*) *in sulphuric acid–water mixtures at* 65°.

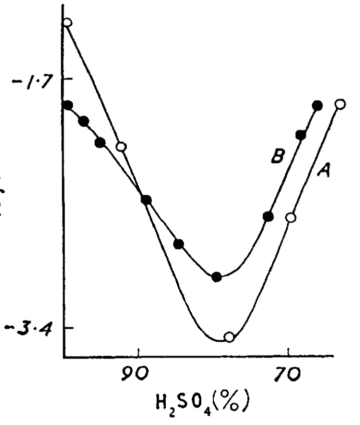
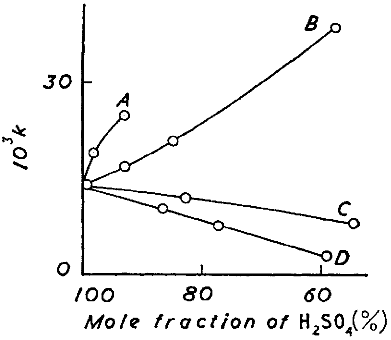


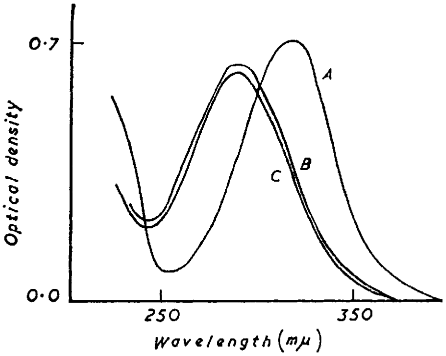
FIG. 2. *Rates of hydrolysis of* 3,5-*dinitroacetanilide in different media at* 65°.



Solvents: *A*, H_2SO_4–$H_2S_2O_7$.
B, H_2SO_4–Cl·SO_3H.
C, H_2SO_4–CH_3·SO_3H.
D, H_2SO_4–H_2O.

FIG. 3. *Absorption spectra of* p-*nitroacetanilide solutions.*

Solvents: *A*, *ethanol.*
B, 100% H_2SO_4.
C, 88% H_2SO_4.



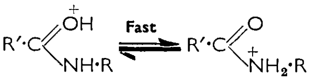
measured between 220 mμ and 400 mμ with a Beckman spectrophotometer (Fig. 3). For 3,5-dinitroacetanilide the spectra in the three solvents studied were almost indistinguishable. Peaks were observed at 237 and 274 mμ.

DISCUSSION

The present work was undertaken in order to establish a unimolecular mechanism of amide hydrolysis analogous to that of esters.[3] The occurrence of hydrolysis in media containing little free water suggests that such a mechanism might prevail and the results will be discussed from this standpoint. First, however, it is necessary to decide in what state the amides exist in the solutions which have been studied.

The Extent and Position of Proton Addition.—The evidence as to the extent of proton addition, although rather fragmentary, suggests that the amides are completely converted into the conjugate acids in all the solutions. First, the amides give approximately two-fold freezing-point depressions in 100% sulphuric acid.[1] Secondly, the spectrum of 3,5-dinitroacetanilide is similar in 88% to that in 100% sulphuric acid. (Comparison with the spectrum in ethanol shows that the amide and its conjugate acid are distinguishable.) Thirdly, the pK_a of acetanilide is 0·61,[4] and the value of the Hammett reaction constant, ρ, for the dissociation of substituted anilinium ions is $+2{\cdot}8$;[5] even if the same high value of ρ is assumed for the dissociation of substituted acetanilidium ions it can be shown, by using the Hammett $\sigma\rho$ relation and acidity function data,[6] that *p*-nitro- and 3,5-dinitroacetanilide are converted into conjugate acids to the extent of at least 99% in 68% sulphuric acid. Finally, solubility limits for the different amides occur in different regions of acid concentration, and appear to depend upon the basicity of the amides. Thus the most weakly basic amides studied, 2,4-dinitro-*N*-*o*- and -*p*-nitrobenzoylaniline are insoluble in 90% sulphuric acid, whereas the solubility range for *p*-nitroacetanilide extends down to about 60% sulphuric acid. The facts are better explained by assuming the amides to be insoluble, and the conjugate acids soluble, in all the solvents studied, than by general solvent effects. We shall assume accordingly that conversion into the conjugate acid is virtually complete in all cases.

The position of the added proton is also important in interpreting the kinetic results. Nuclear magnetic resonance measurements have shown that in the case of several amides the proton is attached to the oxygen atom in the stable form of the conjugate acid,[7] and this will be assumed to apply to all the compounds studied. The assumption has an important bearing on the unimolecular mechanism because a dissociation of this form of the conjugate acid cannot be seriously considered: to explain the occurrence of the reaction in highly acidic media we must assume that the heterolytic electron-shift occurs towards the added proton; in the stable form of the conjugate acid this would produce the unlikely fragments $R'{\cdot}C{\cdot}OH$ and $R{\cdot}NH^+$, and would moreover be associated with quite different polar effects from those observed. The unimolecular mechanism must therefore be written:



$$R'{\cdot}C\begin{smallmatrix}\overset{+}{O}H\\ NH{\cdot}R\end{smallmatrix} \overset{\text{Fast}}{\rightleftharpoons} R'{\cdot}C\begin{smallmatrix}O\\ \overset{+}{N}H_2{\cdot}R\end{smallmatrix} \quad \text{(1)}$$

$$R'{\cdot}CO{\cdot}NH_2R^+ \xrightarrow[\text{Slow}]{} R'{\cdot}CO^+ + R{\cdot}NH_2 \quad \text{(2)}$$

$$R{\cdot}NH_2 + H^+ \xrightarrow[\text{Fast}]{} R{\cdot}NH_3^+ \quad \text{(3)}$$

$$R'{\cdot}CO^+ + H_2O \xrightarrow[\text{Fast}]{} R'{\cdot}CO_2H_2^+ \quad \text{(4)}$$

Polar Constitutional Effects.—There is no reason to suppose that polar groups in R′ should greatly affect the position of equilibrium (1). The effect of such groups on the rate should be largely confined to the heterolysis (2). If the mechanism (1)—(4) operates we

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[3] (*a*) Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 771; (*b*) Leisten, *J.*, 1956, 1572.

[4] Heilbron, "Dictionary of Organic Compounds," Eyre and Spottiswood, 1937, Vol. I, p. 3.

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

[6] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.

[7] Berger, Loewenstein, and Meiboom, *J. Amer. Chem. Soc.*, 1959, **81**, 62; Bunton and Figgis, personal communication.

should therefore expect electron-donating groups in R′ to accelerate, and electron-attracting groups to retard, hydrolysis. Results 1—3, 4—5, and 7—8 (Table 3) show just such effects. From nos. 4—5 and 7—8, values of the Hammett reaction constant −3·4 and −3·1 can be derived which contrast sharply with the value of +1·2 found for the *A*2 hydrolysis of substituted benzamides,[8] but which are of the same sign and similar magnitude to those for $A_{\text{AC}}1$ ester hydrolysis.[3b]

Polar effects in R cannot be predicted by mechanism (1)—(4). *E.g.*, an electron-attracting group in R should increase the rate of the heterolysis (2), but it should also drive the equilibrium (1) to the left-hand side by reducing the proton-affinity of the adjacent nitrogen atom more powerfully than that of the oxygen atom: the two effects will oppose to an unknown extent. The available results are scanty, but accord with the mechanism. The rate of hydrolysis of *p*-nitroacetanilide can be greater or less than that of 3,5-dinitroacetanilide, depending upon the acid concentrations (see Fig. 1), in the region of acid concentration in which hydrolysis goes entirely by the process under consideration. (As will be seen from the discussion of the dependence of rate upon medium, this region extends from 100% to about 80% sulphuric acid.)

Steric Effects.—Results 5—7 and 8—10 (Table 3) show that *ortho*-substituents in the acyl moiety accelerate the reaction regardless of their polar nature. If polar effects of *ortho*- and *para*-substituents are taken to be equal[9] it appears from these results that an *o*-nitro-group increases the rate 45 times by a steric effect, and an *o*-methyl group 28 times. Again the results contrast with those found for amides in more aqueous acids where the *A*-2 mechanism prevails,[8] but are in the same direction as those observed for ester hydrolysis in anhydrous sulphuric acid. Comparison of the results 4 and 7 suggests that *ortho*-groups in the amine moiety also exert a large accelerative steric effect.

The Influence of the Medium.—A change in the solvent from anhydrous to aqueous sulphuric acid should have little effect on the equilibrium (1). The slow step (2) involves no change in the total electrical charge from reactant to transition state, and likewise should be rather insensitive to changes in the medium. Changes of rate with solvent composition should therefore be small and similar for different amides. The observed results (in Figs. 1 and 2, and Table 1) do not follow these conclusions: *e.g.*, in concentrated aqueous sulphuric acid the rates of hydrolysis of *p*-nitro- and 3,5-dinitro-acetanilide depend considerably, and to different extents, on the composition of the solvent (Fig. 1). This effect is shown by the results in Fig. 2 to depend on acidity. The acidity of the solvent components used in these measurements is in this order: $H_2S_2O_7 > Cl{\cdot}SO_3H > H_2SO_4 > CH_3{\cdot}SO_3H > H_2O$, and it will be observed that in all mixtures of sulphuric acid with stronger acids the rate of hydrolysis of 3,5-dinitroacetanilide is greater than that in 100% sulphuric acid, whilst in mixtures with weaker acids the rate is slower. The rates of hydrolysis of *p*-nitro- and 3,5-dinitro-acetanilide are, respectively, 13·8 and 3·8 times as fast in 100% as in 90% sulphuric acid. Over the same interval of concentration the non-logarithmic acidity function h_0 changes[6] by the factor 660. The dependence of the rate on acidity cannot therefore be reconciled with a rate-determining heterolysis of the doubly protonated amide, formed to a fractional extent in a pre-equilibrium, for such a mechanism would require the rate to increase proportionally with h_0 (or strictly h_+).[10] On the other hand the results in Fig. 2 suggest general acid-catalysis, for the reaction rate varies almost linearly with the mole fraction of the stronger acid in the solvent, particularly in cases C and D.

To explain these results as well as those which are accounted for satisfactorily by mechanism (1)—(4) we propose the following modification of that mechanism: that step (3) occurs synchronously with the heterolysis (2), *i.e.*, that proton addition to the nitrogen atom commences before the transition state of the heterolysis is fully formed. This

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[8] Leisten, *J.*, 1959, 765.

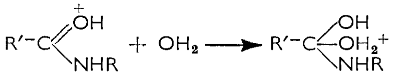
[9] Taft, *J. Amer. Chem. Soc.*, 1952, **74**, 3120.

[10] Long and Paul, *Chem. Rev.*, 1957, **57**, 935.

modification accounts for general acid-catalysis. It also explains why the rate of hydrolysis of *p*-nitroacetanilide is more sharply dependent upon acidity than that of 3,5-dinitroacetanilide: it is because the extent of catalysis depends, not only upon the strength of the acid, but also upon the basic strength of the amine which is formed, and *p*-nitroaniline is a stronger base than 3,5-dinitroaniline.

The faster rate in deuterosulphuric acid than in sulphuric acid is perhaps surprising: it should be remembered, however, that the two protons originally on the nitrogen atom will be replaced by deuterons in this solvent and the rate may be subject to secondary isotope effects.

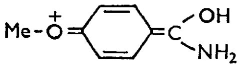
The A2 Mechanism.—Below 78% sulphuric acid the rate of hydrolysis rises with decreasing acid concentration. This is a normal property of the *A*-2 mechanism, the rate increase being attributed to the increasing concentration of free water;[11] for under the present conditions, where the amide is entirely converted into its conjugate acid, the rate by this mechanism is determined solely by the attack of water, (5):



$$R'\text{-}C(\overset{+}{O}H)(NHR) + OH_2 \longrightarrow R'\text{-}C(OH)(OH_2^+)(NHR) \quad . \; . \; . \; . \; . \; . \; . \quad (5)$$

The curves for *p*-nitro- and 3,5-dinitro-acetanilide in Fig. 1 are parallel in this region, showing that the rate variation is associated with the solvent and not with the particular amide. This is expected for the process (5) and has been previously demonstrated in the case of aqueous perchloric acid.[8] It is also expected for this process that electron-attracting substituents should have an accelerating effect, whether in R′ or R. Polar effects in R have not been previously studied, but the present results suggest that this is the case, for in the *A*2 region 3,5-dinitroacetanilide is hydrolysed about 2·5 times faster than *p*-nitroacetanilide in solutions of the same acid concentrations.

Contrary to what might be deduced from polar and steric effects on reaction (5), the hydrolysis of 3,5-dinitro-*N*-propionylaniline is faster than that of 3,5-dinitroacetanilide: the rates in 68·4% sulphuric acid at 65° are 0·014 and 0·0083 min.$^{-1}$ respectively. This apparent anomaly is not confined to the present work, because propionamide has been found to be hydrolysed faster than acetamide over a wide range of acid concentration.[12] A likely explanation is that the conjugate acid of the amide is stabilised by conjugation, or hyperconjugation, with R′. No such stabilisation can occur of the addition complex, and increased conjugation therefore increases the potential energy barrier and slows reaction (5). Propionamides have one less hydrogen atom capable of hyperconjugation than acetamides. The same explanation could be applied to the anomalously slow hydrolysis in perchloric acid solutions of anisamide, the results for which fail to obey an otherwise excellent σρ relation.[8] In this case the conjugate acid is probably stabilised, relatively to the transition complex, by the important structure (A).



(A)

Temperature Dependence.—The values of the Arrhenius parameters in Table 2 accord with the conclusions which have been reached in two respects. First, the values for all those hydrolyses which are held to proceed by the modified mechanism (1)—(4) fall in rather narrow ranges. (E = 27·2—31·8 kcal./mole, and $\log_{10} A$ = 16·2—18·7, except that for compounds with an *ortho*-group in the acyl moiety higher values of A are found.) These values are well separated from those for *A*-2 hydrolysis, which are italicised in Table 2 (E = 22·5—23·6, $\log_{10} A$ = 11·8—12·6). The latter values are in the ranges previously observed for *A*-2 amide hydrolysis: *e.g.*, the figures in Table 2 are almost identical with those for the hydrolysis of benzamide in 1—10M-hydrochloric acid.[12] Secondly, the results for hydrolysis by the modified (1)—(4) mechanism give a linear

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[11] Ref. 3(*a*), p. 788.

[12] Rabinowitch and Winkler, *Canad. J. Res.*, 1942, **20**, *B*, 73.

enthalpy–entropy relation from which the *ortho*-substituted benzanilides depart in accordance with the size of the *ortho*-group. Reactions which proceed by the same mechanism often give this type of relation: it is known to fail where substituents have a steric influence on the rate.[13]

EXPERIMENTAL

Materials.—To prepare 2,4-dinitroacetanilide, 2,4-dinitroaniline (10 g.), acetic anhydride (5 ml.), and acetic acid (5 ml.) were refluxed for ¾ hr., and the cooled mixture poured into water. The precipitate, recrystallised from ethanol, had m. p. 120°. *N*-Benzoyl-*p*-nitroaniline was prepared by heating *p*-nitroaniline (13·8 g.) and benzoyl chloride (11·5 ml.) at 220° for ¾ hr. The product, recrystallised from ethanol, had m. p. 198°. Pivalic acid was converted into pivaloyl chloride,[14] and hence into pivalamide [15] which had m. p. 151° (from ethanol). Chlorosulphonic acid was purified by distillation (b. p. 153°), and methanesulphonic acid was distilled under reduced pressure. Deuterosulphuric acid was prepared from pure sulphur trioxide and deuterium oxide: [16] it had f. p. 14·33°.

Kinetic Measurements.—Hydrolysis of the substituted anilides was followed by estimation of the substituted anilines formed. The estimation was based on a method of Ridd and Larkworthy.[17] In the case of 3,5-dinitroacetanilide 1 ml. samples of the reaction mixture (initially 0·25M in anilide) were pipetted on to ice. In each case the solution was diluted to 10 ml. and its temperature adjusted to 25—27°. 25 drops of 6% sodium nitrite solution were added and the solution was stirred and diluted to exactly 20 ml. with water. A 0·2% aqueous solution (5 ml.) of sodium β-naphthol-3,6-disulphonate and 6% borax solution (10 ml.) were placed in a 50 ml. volumetric flask, and 2 ml. of the diazotised solution were added. The solution was made up to 50 ml. with 6% borax solution, and 10 ml. were further diluted 5 times with borax. The optical density at 474 mμ was then determined by means of a Beckman spectrophotometer. It was shown that Beer's law was obeyed and that the colour was stable for several days. A typical set of results is given below, for initially 0·22M-3,5-dinitroacetanilide reacting in 68·4% sulphuric acid at 72·2°. A value of 1·420 was chosen for D_∞, and the graphically determined rate constant was 18·3 × 10^{-3} min.$^{-1}$.

Time (min.)	0	16·5	24·5	37·5	57	89·5
D (λ 476 mμ)	0·012	0·389	0·530	0·708	0·928	1·146
10^3k (min.$^{-1}$)	—	18·9	18·7	18·2	18·4	18·3

2,4-Dinitro- and *p*-nitro-acetanilide were treated in a similar way, but in both these cases the spectrophotometric measurements were made at 490 mμ on solutions of half the concentraction used for 3,5-dinitroacetanilide. The hydrolyses of pivalamide and isobutyramide were followed by estimation of the ammonia produced.[18]

We thank the Department of Scientific and Industrial Research for a maintenance grant (to J. A. D.).

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[*Received, July* 31*st*, 1959.]

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[13] Leffler, *J. Org. Chem.*, 1955, **20**, 1202.
[14] Brown, *J. Amer. Chem. Soc.*, 1938, **60**, 1325.
[15] Aschan, *Ber.*, 1898, **31**, 2344.
[16] Flowers, Gillespie, Oubridge, and Solomons, *J.*, 1958, 667.
[17] Dr. J. H. Ridd, personal communication.
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