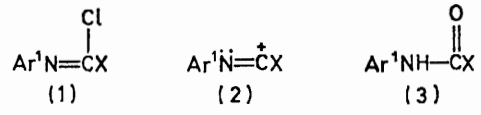
Mechanism of Hydrolysis of Imidoyl Chlorides

By **Anthony F. Hegarty,* James D. Cronin,** and **Francis L. Scott,** Chemistry Department, University College, Cork, Ireland

The rates of solvolysis of substituted imidoyl chlorides (1a), chloroimidates (1b), chlorothioimidates (1c), and chloroformamidines (1d) have been investigated in aqueous dioxan. The initial products of solvolysis are the corresponding amides (3). Studies at varying pH indicate that all solvolyse by a unimolecular mechanism over the pH range 0—14 except the chloroimidates which also show acid and base catalysed reactions. In neutral solution the stabilized carbonium ion species (2) are formed as shown by salt and common ion effects, and also by large solvent effects (m 1·0—1·4). The ease of carbonium ion formation varies as follows: (1a) > (1d) > (1c) > (1b). In all cases the N-aryl ring (Ar^1) bears a larger fraction of the charge in the transition state for formation of (2) (reflecting the importance of the ' octet-stabilized ' resonance structure) and the magnitude of ρ value for substituent variation (ρ_{Ar^1} −3·0 ± 0·15) is relatively independent of the heteroatom attached to carbon. Substituents attached to carbon in (1) [Ar, ArO, ArS, ArN(Me)] have a relatively smaller effect with $\rho \geqslant -2{\cdot}0$.

ALTHOUGH the hydrolysis of vinyl halides has been extensively studied under conditions where vinyl cations are demonstrable intermediates,[1-3] the mechanism of replacement of halide in the corresponding nitrogen system, the imidoyl halides (1a), is less well understood. Compounds such as (1a) however find wide use as synthetic intermediates, reacting rapidly both with monofunctional nucleophiles (such as amines to yield amidines) [4,5] and bifunctional reagents (such as methyl anthranilate to yield quinazolines).[6] We set out therefore to determine the conditions under which the expected unimolecular mechanism of reaction of (1a) [*i.e.* formation of (2a)] was dominant. It was also of interest to determine how the charge in the transition state for the hydrolysis of (1a) was distributed between the C- (Ar^2) and N-aryl (Ar^1) groups. By the interpolation of heteroatoms (N, O, S) between Ar^2 and carbon in (1a) (or between Ar^1 and



(1) (2) (3)

a; X = Ar^2 c; X = SAr^2

b; X = OAr^2 d; X = $N(Me)Ar^2$

nitrogen) it should then be possible to determine (a) just how the hydrolytic mechanism varies with the nature of the heteroatom, (b) the efficiency with which the heteroatom transmits charge to the aromatic nucleus, and (c) how charge in (2) is distributed when two dissimilar heteroatoms are in competition.

The available mechanistic data on the hydrolysis of imidoyl chlorides (1a) come from the work of Ugi [7] and Rappoport [8] and their co-workers. Ugi's group mainly studied imidoyl halides with aliphatic substituents on both nitrogen and carbon in acetone–water, while Rappoport's study concerned the reaction of aromatic imidoyl chlorides with amines in benzene.

Besides the imidoyl halide system (1a) we also report a mechanistic study on the related materials, chloroformimidates (1b), their thio-analogues (1c), and chloroformamidines (1d); these materials have been widely used as intermediates in synthesis but the mechanism of their reactions has not been previously studied. A dioxan–water solvent medium was used throughout, the highest aqueous content which was consistent with the reactivity of the substrates being employed.

RESULTS AND DISCUSSION

Imidoyl Chlorides.—The rates of hydrolysis of nine N-arylbenzimidoyl chlorides (1a) were studied in **9 : 1** dioxan–water (v/v) at 25° in the presence of 0·01M-$NaClO_4$ to maintain the ionic strength constant. Under these conditions the final products of solvolysis are the benzanilides (3a). The course of the hydrolyses were followed spectrophotometrically with very low substrate concentration (5×10^{-5}M) to avoid a reverse reaction found in more concentrated solution (see below). In all cases, under these conditions, the reactions closely followed first-order kinetics to >90% reaction (Table 1).

TABLE 1

Pseudo-first-order rate constants for the hydrolysis of imidoyl chlorides (1a) in 90% dioxan containing 0·01M-$NaClO_4$ at 25°

Substrate (1a)		$10^4 k_{obs}/s^{-1}$
Ar^1	Ar^2	
p-$NO_2C_6H_4$	Ph	3·5
m-$NO_2C_6H_4$	Ph	4·6
m-ClC_6H_4	Ph	31
p-ClC_6H_4	Ph	112
Ph	Ph	460
Ph	p-ClC_6H_4	126
Ph	m-ClC_6H_4	50
Ph	m-$NO_2C_6H_4$	14
Ph	p-$NO_2C_6H_4$	12
p-ClC_6H_4	Ph	4·4 [a]

[a] In the presence of 0·01M-NaCl.

It is seen that substituents attached to nitrogen or carbon have broadly the same effect, *i.e.* electron-withdrawing substituents slow and electron-donating substituents speed up the rate of hydrolysis. Plotting the log of the observed rate constants *versus* the ' normal '

[1] C. A. Grob and G. Cseh, *Helv. Chim. Acta*, 1964, **47**, 194.
[2] P. J. Stang, *Progr. Phys. Org. Chem.*, 1973, **10**, 205.
[3] Z. Rappoport and A. Gal, *J. Amer. Chem. Soc.*, 1969, **91**, 5246.
[4] H. Ulrich, ' The Chemistry of Imidoyl Halides,' Plenum Press, New York, 1968.
[5] R. Bonnet in ' The Chemistry of the Carbon-Nitrogen Double Bond,' ed. S. Patai, Interscience, New York, 1970, p. 597.
[6] Ref. 5, p. 643.
[7] I. Ugi, F. Beck, and U. Fetzer, *Chem. Ber.*, 1962, **95**, 126.
[8] Z. Rappoport and R. Ta-Shma, *Tetrahedron Letters*, 1972, 5281.

σ values of McDaniel and Brown [9] for Ar^1 gave a Hammett ρ of −2·75 (*r* 0·998). The ρ value calculated for variation of substituents adjacent to the C–Cl bond (Ar^2) is −2·03 (*r* 0·992). In both cases, the correlations obtained were satisfactory and were not improved (in fact there was a significant deterioration in some cases) when alternative scales of σ were used. However the reaction centre could conceivably interact with a substituent (in Ar^2 at least) capable of electron donation by resonance (*e.g.* *p*-MeO or *p*-Me): no such substituents were included in the correlation because of this complication.

The sign and magnitude of the ρ values obtained for substituents in Ar^2 and Ar^1 provide support for a mechanism involving the formation of an azocarbonium ion intermediate. Substituents attached to nitrogen have a greater effect on the rate of hydrolysis than similar substituents attached to carbon indicating the importance of resonance form (4b). Further evidence for a mechanism involving (4) as an intermediate is the *ca.* 25-fold decrease in the rate of hydrolysis in the presence of 0·01M-NaCl (Table 1).

$$Ar^1\dot{N}{=}\overset{\curvearrowright}{C}Ar^2 \longleftrightarrow Ar^1\overset{+}{N}{\equiv}CAr^2$$

(4a) (4b)

The difficulties reported by Ugi *et al.*[7] in obtaining reliable rate measurements for the hydrolysis of the imidoyl chlorides (1a) can be understood in terms of this unusually large common ion effect. We have found that the rate of hydrolysis of (1a; $Ar^1 = Ar^2 = Ph$) is highly sensitive to initial substrate concentration, even at 5×10^{-4}M (where k_{obs} is *ca.* $3{\cdot}0 \times 10^{-2}$ s^{-1} compared with $4{\cdot}66 \times 10^{-2}$ s^{-1} at 5×10^{-5}M in 9 : 1 dioxan–water at 25 °C containing 0·01M-$NaClO_4$). Apparently the chloride ion released, even at this low concentration is sufficient to slow the reaction appreciably (by a common ion effect). A similar effect has been noticed recently in

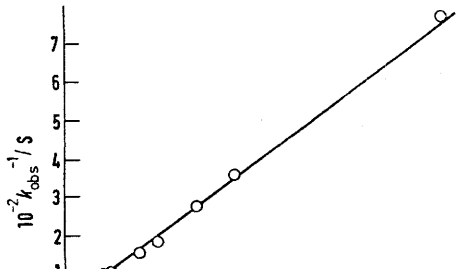


FIGURE 1 Plot of $1/k_{obs}$ against chloride ion concentration for the hydrolysis of *N*-phenylbenzimidoyl chloride (1a; $Ar^1 = Ar^2 = Ph$) in 9 : 1 dioxan–water at 25° (μ = 0·01; $NaClO_4$)

the solvolysis of vinyl chlorides.[10] The pseudo-first-order rate constants continued to increase until [substrate] $< 1 \times 10^{-4}$M.

[9] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.

[10] S. Rappoport and A. Gal, *Tetrahedron Letters*, 1970, 1845.

To examine in more detail the common ion effect the rate of hydrolysis of *N*-phenylbenzimidoyl chloride was studied in the presence of various amounts of added NaCl; the results are summarised in terms of a linear $1/k_{obs}$ against $[Cl^-]$ plot in Figure 1. From these data an

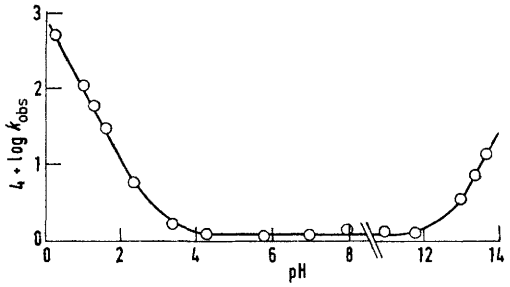


FIGURE 2 Plots of log k_{obs} against pH for the hydrolysis of phenyl *N*-phenylchloroformimidate (1b; $Ar^1 = Ar^2 = Ph$) in 1 : 1 dioxan–water at 50° (μ = 0·50; $NaClO_4$)

α value (the mass law constant [11]) of *ca.* 3400 can be calculated. The ability of the carbonium ion (4) to discriminate between chloride ion and water as nucleophiles is thus approximately an order of magnitude better than triphenylmethylcarbonium ion.[12]

Chloroformimidates.—The rates of hydrolysis of chloroformimidates (1b) were studied in 1 : 1 dioxan–water (v/v) at 50° as a function of the pH of the solvent (Figure 2). The solutions were buffered where appropriate, but in all cases a constant ionic strength (μ 0·5 using sodium perchlorate) was maintained. Under these conditions the final product of hydrolysis of (1b) was the corresponding carbamate (5) at pH < 8, but in the basic region (5) was itself hydrolysed to *N*-phenylcarbamic acid (6) and phenoxide ion. The ultimate products then on

$$Ar^1NH{-}\underset{\underset{O}{\|}}{C}{-}OAr^2 \xrightarrow{OH^-} Ar^1N{=}C{=}O + Ar^2O^-$$

(5)

$$Ar^1NH_2 + CO_2 \longleftarrow Ar^1NHCO_2^-$$

(6)

acidification were the corresponding aniline and phenol. In the pH region 8—11·7 the rate of hydrolysis of (1b; $Ar^1 = Ar^2 = Ph$) could not be measured accurately because the rates of formation and hydrolysis of (5; $Ar^1 = Ar^2 = Ph$) were of the same order of magnitude. This was verified by an examination of the rate of hydrolysis of the carbamate (5; $Ar^1 = Ar^2 = Ph$) which was synthesized independently. This was not a serious limitation since the rate of hydrolysis of (1b) did not appear to vary in the pH range 8—11·7.

In Figure 2, log k_{obs} is plotted against pH; there are three different regions in this profile, each representing a different mechanism of hydrolysis.

(a) *Neutral hydrolysis.* Hydrolysis of (1b) in the

[11] L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold, and N. A. Taher, *J. Chem. Soc.*, 1940, 979.

[12] C. G. Swain, C. B. Scott, and K. H. Lohmann, *J. Amer. Chem. Soc.*, 1953, **75**, 136.

neutral region (pH 5·8) led to the carbamates (5) for all the compounds studied. To probe the charge distribution in the transition state the rates of hydrolysis of a series of compounds, in which the substituents in Ar^1 and Ar^2 were varied, were studied and the results are presented in Table 2.

TABLE 2

Pseudo-first-order rate constants for the hydrolysis of (1b) in 2 : 3 dioxan–water at neutral pH (5·8) at 50° (μ 0·5; $NaClO_4$)

Substrate (1b)		
Ar^1	Ar^2	$10^4k_{obs}/s^{-1}$
Ph	p-MeC_6H_4	4·7
Ph	Ph	3·7
Ph	p-ClC_6H_4	0·87
p-ClC_6H_4	Ph	0·71

The data for varying the substituent in Ar^1 are limited but yield a Hammett ρ value of −3·15. The data for Ar^2 do not correlate very well, but the average ρ value calculable is −1·75. Further evidence for an azocarbonium ion intermediate (2b) for the neutral hydrolysis was provided when the solvolysis of phenyl *N*-phenylchloroformimidate was studied in 1 : 1, 2 : 3, and 3 : 7 dioxan–water at 50° and pH 5·8 (μ 0·5; $NaClO_4$). Plotting log k_{obs} against the corresponding Y values of Fainberg and Winstein[13] gave an m value of 0·98 (±0·08); m values of this order have been interpreted in terms of a carbonium ion mechanism.[14]

The rate of hydrolysis of phenyl *N*-phenylchloroformimidate in 7 : 3 water–dioxan is increased by a factor of 1·74 in the presence of 0·5M-$NaClO_4$, consistent with charge formation in the intermediate. The presence of a similar concentration of sodium chloride decreases the rate by a factor of two and when allowance is made for the rate enhancement due to ionic strength, the overall rate decrease due to common ion is only *ca.* three-fold, in contrast to the large effect observed for imidoyl chlorides.

(b) *Basic hydrolysis.* Above pH 13 the log of the rates of hydrolysis of phenyl *N*-phenylchloroformimidates are directly proportional to pH. This implies an overall bimolecular mechanism; to examine this further the rates of hydrolysis of a series of chloroformimidates (1b) were studied in 1 : 1 dioxan–water containing 0·5M-NaOH at 50° and the results are presented in Table 3.

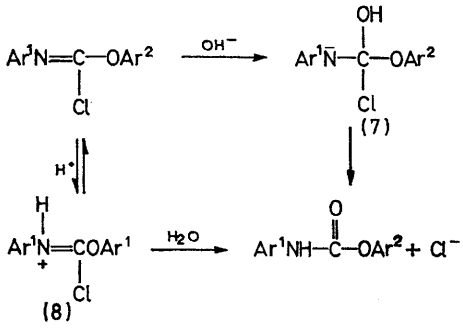
TABLE 3

Pseudo-first-order rate constants for the hydrolysis of (1b) in 1 : 1 dioxan–water containing 0·5M-NaOH at 50° (μ 0·5)

Ar^1	Ar^2	$10^4k_{obs}/s^{-1}$
Ph	p-MeC_6H_4	8·8
Ph	Ph	14
Ph	p-ClC_6H_4	33
p-ClC_6H_4	Ph	49

Plotting log k_{obs} against the corresponding σ values of McDaniel and Brown[9] yielded a Hammett ρ value of +2·39 for Ar^1 and +1·41 (±0·22) for Ar^2. These values are in direct contrast to the negative ρ values obtained in the neutral region. This indicates that the hydrolysis in both regions occurs by different mechanisms. Positive ρ values indicate the development of negative charge in the transition state and this is consistent with direct attack of hydroxide ion on the neutral substrate (Scheme). Again the ρ value for Ar^1 is larger than that for Ar^2; this is explicable in terms of the formation of a tetrahedral intermediate (or transition state) such as (7) in which the negative charge can be effectively delocalised on nitrogen.

(c) *Acidic hydrolysis.* At low pH, the rate of hydrolysis of (1b) is inversely proportional to the pH of the medium (Figure 2). Since on changing the 'salt' from 0·5M-$NaClO_4$ to 0·5M-$HClO_4$ the rate is increased *ca.* 500-fold, it is unlikely that this is due to a specific salt effect. Since chloroformimidates (1b) have a free electron pair on nitrogen they have some basic character which can be utilized for salt formation. The incursion of the acid



SCHEME

catalysed pathway therefore is probably due to water attack on the protonated species (8).

The bimolecular pathways for the hydrolysis of (1b), by HO^- attack in basic solution and by protonaton followed by H_2O attack in acid, become operative in the present instance only because of the relatively slow rate of the pH-independent hydrolysis. In none of the other cases studied does this occur.

Chlorothioformimidates.—The rates of hydrolysis of a series of *N*-aryl 1-chlorobenzothioformimidates (1c) were studied in 7 : 3 dioxan–water containing 0·025M-$NaClO_4$ at 25° (Table 4). In acidic solution the hydrolytic

TABLE 4

Pseudo-first-order rate constants for the hydrolysis of (1c) in 7 : 3 dioxan–water containing 0·025M-$NaClO_4$ at 25°

Ar^1	Ar^2	$10^4k_{obs}/s^{-1}$
p-$NO_2C_6H_4$	Ph	1·8
p-ClC_6H_4	Ph	84
Ph	Ph	46
Ph	p-ClC_6H_4	158

products were the corresponding aryl *N*-arylthiocarbamates (3c). However, in most cases above pH 5, (3c) is itself hydrolysed further to give ultimately the aniline and benzenethiol. Since the rates of hydrolysis were independent of pH over a wide region (see Table 5)

[13] A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, 1956, **78**, 2770.

[14] J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions,' Wiley, New York, 1963, p. 297.

the rates were measured at pH 4 or 10 in order to eliminate inaccuracies due to the incursion of subsequent reactions of the products. Correlating the results in Table 4 with the Hammett equation yielded a ρ value of −3·1 for variation of substituents in Ar^1 and −2·06 for variation of substituents in Ar^2.

TABLE 5

Relative rates of hydrolysis of (1c; $Ar^1 = p\text{-}ClC_6H_4$; Ar^2 = Ph) at 25° in the presence of various added salts in 17 : 3 dioxan–water and of (1c; $Ar^1 = p\text{-}NO_2C_6H_4$; Ar^2 = Ph) at 25° in the presence of added salts in 7 : 3 dioxan–water

(1c; $Ar^1 = p\text{-}ClC_6H_4$; Ar^2 = Ph)		(1c; $Ar^1 = p\text{-}NO_2C_6H_4$; Ar^2 = Ph)	
[Salt]	k_{rel}	[Salt]	k_{rel}
0	1 *	0	1 †
0·025M-$NaClO_4$	22	0·1M-$NaClO_4$	8
0·05M-$NaClO_4$	38	0·1M-NaOH	5·6
0·05M-$HClO_4$	57	0·1M-$HClO_4$	7·0
0·05M-$NaNO_3$	44	0·1M-NaCl	0·29
0·05M-NaOAc	23		
0·05M-NaCl	0·82		
0·01M-$NaClO_4$	10·8		
0·01M-NaOH	9·0		

* $k_{obs} = 3{\cdot}83 \times 10^{-4}$ s^{-1}. † $k_{obs} = 12{\cdot}2 \times 10^{-4}$ s^{-1}.

Further evidence that (2c) is an intermediate is given by the solvent effects which yield an *m* value of +1·41. This is an extremely large value and can only be interpreted in terms of a carbonium ion intermediate, whose stability is highly sensitive to the ionizing power of the solvent.

The hydrolytic rates are very dependent on both the quantity and the nature of the added salt (Table 5). For the *p*-chloro-substrate (1c; $Ar^2 = p\text{-}ClC_6H_4$), the rate increases on the addition of an inert salt, but shows no significant rate enhancement in acidic or basic solution. When allowance is made for the salt effect, this substrate also shows a large common ion effect due to added chloride ion.

Chloroformamidines (1d).—The rates of hydrolysis of three chloroformamidines were measured in 9 : 1 dioxan–water containing 0·01M-$NaClO_4$ at 25°. The results are presented in Table 6. The products of hydrolysis in all cases were the corresponding stable ureas (3d).

TABLE 6

Pseudo-first-order rate constants for the hydrolysis of chloroformamidines ($Ar^1N{=}CCl{-}NR^2R^1$) in 9 : 1 dioxan–water containing 0·01M-$NaClO_4$ at 25°

Ar^1	R^1	R^2	10^4k_{obs}/s^{-1}
Ph	Ph	Me	335
$p\text{-}ClC_6H_4$	Ph	Me	74
$p\text{-}ClC_6H_4$	$(CH_2)_2{-}O{-}(CH_2)_2$		240

Electron-withdrawing substituents in Ar^1 decrease the rate of hydrolysis and the ρ value is −2·9. When a morpholino-group is introduced instead of Ar^2 and CH_3 the rate of hydrolysis is increased *ca.* three-fold. The effects of added salts on the rates of hydrolysis of chloroformamidines are summarised in Table 7. The rate is reasonably insensitive to the nature of the salt present (whether acidic, basic, or nucleophilic) and this, in itself, is good evidence that nucleophilic attack is not rate determining in the solvolysis reaction of chloroformamidines. Also, there is overall an 18-fold decrease in the rate of hydrolysis in the presence of 0·01M-NaCl. A solvent *m* value of +1·2 was calculated for this compound.

Thus, *in summary*, only when the ionization pathway is slowed by attachment of an electron-withdrawing aryloxy-substituent to carbon [as in the chloroformimidates (1b)] does the competing S_N2 pathway become dominant. Even in the one case where S_N2 attack was demonstrated, high concentrations of the strong nucleophile HO^- (*ca.* 0·1M) were required. Thus direct nucleophilic attack on the chlorides (1) by weaker nucleophiles such as amines does not occur to any significant extent in aqueous solvent mixtures. This was also demonstrated by measuring the rates of reaction of the chlorides in the presence and absence of 0·1M-morpholine at pH *ca.* 8·5. Morpholine has a pK_a in this region and the solution was therefore self-buffered. In each case the presence of the amine (at constant ionic strength) caused no significant rate enhancement. However, the products formed were

TABLE 7

Relative rates of hydrolysis of *N*-methyl-*N*-phenyl-*N'*-(*p*-chlorophenyl)chloroformamidine in 17 : 3 dioxan–water at 25° in the presence of added salts

[Salt]	0	0·01M-$NaClO_4$	0·01M-$NaNO_3$	0·01M-NaOAc
k_{rel}	1 *	16	18	15
[Salt]	0	0·01M-NaOH	0·01M-$HClO_4$	0·01M-NaCl
k_{rel}	1 *	19·5	21·5	0·87

* $k_{obs} = 18 \times 10^{-4}$ s^{-1}.

TABLE 8

Relative rates of azocarbonium ion formation from imidoyl and related chlorides (1)

Substrate	k_{rel} [a]	Sensitivity to Added Cl^-	Sensitivity to Added salt	ρ_{Ar^1}	ρ_{Ar^2}
(1a)	$3{\cdot}5 \times 10^7$	High	High	−2·75	−2·03
(1d)	$2{\cdot}8 \times 10^7$	High	High	−2·90	
(1c)	$2{\cdot}8 \times 10^6$	High	High	−3·10	−2·06
(1b)	1 [b]	Low	Low	−3·15	−1·75

[a] Under standard conditions 9 : 1 dioxan–water; 25°; 0·01M-$NaClO_4$. [b] Calculated by extrapolation from data at higher temperature and using solvents of higher aqueous content.

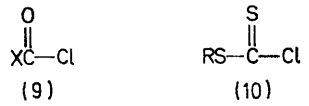
the corresponding amidines together with small quantities of the amides (3). This is readily explicible in terms of demonstrated high selectivity of the carbonium ion species (2) formed in the rate-determining step; the intermediate reacts preferentially with the stronger nucleophile, the amine. It appears likely therefore that the synthetic utility of substrates (1) arises from the rapid ionization to form a highly selective azocarbonium ion intermediate.

The substituent effects and relative rates for the hydrolysis of the chlorides (1) *via* the unimolecular pathway are summarised in Table 8. It is seen that the amount of charge delocalized onto nitrogen (as measured by ρ_{Ar^1}) is remarkably constant throughout the series in spite of the large differences in reactivity observed. Also those substrates which show a high reactivity are

highly sensitive to the presence of added Cl^- and to the presence of ' inert ' salts, reflecting the selective nature of the more stable carbonium ion intermediates. The fraction of charge transmitted through an oxygen or sulphur attached directly to the carbonium ion centre is surprisingly large. Thus substituents in the *S*-aryl ring (and to a lesser extent the *O*-aryl ring) can change the reaction rate by almost the same amount as substituents in the C-aryl ring of imidoyl chlorides (see Table 8). The relatively high sensitivity shown by substituents in the Ar^1 ring of the formimidates is surprising in view of the low reactivity of these materials which has been ascribed in part to the inability of the oxygen to stabilize the carbonium ion centre by electron donation by resonance. A possible compensating factor in this case is that the transition state for the formation of the less stable carbonium ion (2b) formed in the hydrolysis of (1b) occurs later in the reaction co-ordinate than for the other chlorides. More charge may therefore be concentrated in the transition state for hydrolysis of (1b) so that the reaction becomes relatively more sensitive to the substituents (Ar^1 and Ar^2) present.

The large difference in S_N1 reactivity shown between, on one hand the imidoyl chlorides (1a), the thioimidates (1c), and the formimidates (1d), and the imidates (1b) on the other is most striking. This can be attributed to initial state stabilization by resonance [of (1b and c) relative to (1a)] and more effective mesomeric stabilization by electron donation involving sulphur (relative to oxygen) in the azocarbonium ion intermediate. Both sulphur and oxygen withdraw charge inductively from the positive centre; there is evidence however that sulphur does so less powerfully.[15] Both effects combine to make (2c) more stable than (2b).

It has been well established that alkylchloroformates



(9) (10)

(9; X = RO^-) undergo solvolytic reactions much more slowly than other acid chlorides [such as (9; X = Ar)]. In a detailed study of the mechanism of hydrolysis of chloroformates (9; X = RO^-), thiochloroformates (9; X = RS), and thionoformates (10), Queen [16-18] has demonstrated that the thio-analogues show both largely S_N1 type reactivity and hydrolyse much more rapidly than the chloroformates (9; X = RO), which hydrolyse by both S_N1 and S_N2 pathways. The results for both systems (1) and (9) are therefore parallel.

EXPERIMENTAL

Materials.—All inorganic chemicals were AnalaR grade and were dried at 120° for 3 h before use. AnalaR dioxan (B.D.H.) was used directly as supplied and deionized water was twice distilled from alkaline potassium permanganate. The aqueous dioxan solutions (v/v) were made up at 20°.

The arylcarbonimidoyl dichlorides were prepared by the following general method.

p-Chlorophenylcarbonimidoyl dichloride.—In a three-necked flask (250 ml) fitted with a stirrer, a thermometer, a reflux condenser, and a gas outlet, sulphuryl chloride (16·2 ml, 0·2 mol) was dissolved in thionyl chloride (60 ml). *N*-(*p*-chlorophenyl)formamide (31 g, 0·2 mol) was added in portions at 15—20° and stirring was continued for 5 h at room temperature. The solution was then slowly heated to 80°, hydrogen chloride and sulphur dioxide being liberated. The excess of thionyl chloride was recovered by distillation, and vacuum distillation of the residue yielded *p*-chlorophenylcarbonimidoyl dichloride (33 g, 80%), b.p. 73° at 4 mmHg (lit.,[19] 110—113° at 10 mmHg).

p-Nitrophenylcarbonimidoyl dichloride was prepared similarly and had b.p. 132° at 0·9 mmHg and m.p. 78—80° (lit.,[19] b.p. 127° at 0·35 Hg, m.p. 78—82°). *N*-Phenylcarbonimidoyl dichloride (Aldrich) was commercially available and was distilled once before use.

Substrates.—Phenyl N-phenylchloroformimidate. N-Phenylformimidoyl dichloride (4·35 g, 3·39 ml, 25 mmol) was dissolved in dry ether and an equal quantity of absolute alcohol added. The mixture was cooled with ice–water, and to it was slowly added a solution made by dissolving sodium (0·575 g, 0·025 g-atom) in absolute alcohol and adding phenol (2·35 g, 25 mmol). An immediate precipitate of sodium chloride was noticeable. The mixture was kept cold with ice for 5 min and left in a dish of cold water for 3 h. It was then poured into an excess of cold water and the oil taken up with ether. The ethereal solution was washed with sodium hydroxide solution to remove any excess of phenol and then repeatedly washed with water. After drying ($CaCl_2$) the ether was distilled off and the residue distilled at reduced pressure to yield phenyl *N*-phenylchloroformimidate (70%), m.p. 41—43° (lit.,[20] 43°).

Similarly prepared were: p-*tolyl N-phenylchloroformimidate*, m.p. 50° (Found: C, 68·4; H, 4·9; N, 5·7. $C_{14}H_{12}ClNO$ requires C, 68·9; H, 5·3; N, 5·7); *phenyl* N-(p-*chlorophenyl*)*chloroformimidate*, m.p. 50—52° (Found: C, 58·8; H, 3·7; N, 5·4. $C_{13}H_9Cl_2NO$ requires C, 58·7; H, 3·4; N, 5·2); p-*chlorophenyl N-phenylchloroformimidate*, b.p. 163—165° at 1·5 mmHg, m.p. 31—33° (Found: C, 58·7; H, 3·4; N, 5·1. $C_{13}H_9Cl_2NO$ requires C, 58·7; H, 3·4; N, 5·2). The chloroformimidates decomposed slowly to the corresponding carbamates on storing. They were best stored as amorphous solids *in vacuo*.

Phenyl N-phenylchlorothioformimidate. To a solution of *N*-phenylformimidoyl dichloride (3·39 ml, 25 mmol) in dry benzene (100 ml) was added triethylamine (3·44 ml, 25 mmol) followed, dropwise, by benzenethiol (2·75 g, 25 mmol) in dry benzene (25 ml). The solution was stirred for 3 h at room temperature and the triethylamine hydrochloride (3·1 g, 90% of theoretical) which separated was filtered off. Benzene was evaporated from the filtrate and the residue vacuum distilled to yield phenyl *N*-phenylchlorothioformimidate (4·03 g, 65%), m.p. 55—57° (lit.,[19] 56—58°).

Similarly prepared were: *phenyl* N-(p-*nitrophenyl*)*chlorothioformimidate*, m.p. 50—52° (from pentane) (Found: C,

[15] J. Donovan, J. Cronin, F. L. Scott, and A. F. Hegarty, *J.C.S. Perkin II*, 1972, 1050.
[16] A. Queen, *Canad. J. Chem.*, 1967, **45**, 1619.
[17] A. Queen, T. A. Nour, M. N. Paddon-Row, and K. Preston, *Canad. J. Chem.*, 1970, **48**, 522.
[18] D. M. McKinnon and A. Queen, *Canad. J. Chem.*, 1972, **50**, 1401.
[19] E. Kuhle, B. Anders, and G. Zumack, *Angew. Chem. Internat. Edn.*, 1967, **6**, 649.
[20] O. Mumm, *Ber.*, 1910, **43**, 886; O. Mumm, H. Volquartz, and H. Hesse, *ibid.*, 1914, **47**, 751.

52·8; H, 3·3; N, 9·8. $C_{13}H_9ClN_2O_2S$ requires C, 53·3; H, 3·1; N, 9·6%); *phenyl* N-(p-*chlorophenyl*)*chlorothioformimidate*, m.p. 66—68° (Found: C, 55·1; H, 3·3; N, 5·2. $C_{13}H_9ClNS$ requires C, 55·3; H, 3·2; N, 5·0%); p-*chlorophenyl* N-*phenylchlorothioformimidate*, m.p. 43—45° (Found: C, 55·2; H, 3·3; N, 5·0. $C_{13}H_9Cl_2NS$ requires C, 55·3; H, 3·2; N, 5·0%).

N-*Methyl*-N-*phenyl*-N′-(p-*chlorophenyl*)*chloroformamidine*. In a round bottomed flask (100 ml) fitted with a reflux condenser and a gas outlet phosphorus pentachloride (4·17 g, 20 mmol) was added to *N*-methyl-*N*-phenyl-*N*′-(*p*-chlorophenyl)urea (5·2 g, 20 mmol). Dry benzene (20 ml) was then added and the mixture was heated slowly to reflux temperature with occasional swirling. Hydrogen chloride was evolved and the mixture gradually became a homogeneous solution. The reaction was complete when no further hydrogen chloride was evolved. Benzene and phosphorous oxychloride were removed under reduced pressure and the residue vacuum distilled to yield N-*methyl*-N-*phenyl*-N′-(p-*chlorophenyl*)*chloroformamidine* (4·4 g, 79%), b.p. 192—194° at 0·8 mmHg, m.p. 68—70° (Found: C, 59·9; H, 4·4; N, 10·2. $C_{14}H_{12}Cl_2N_2$ requires C, 60·2; H, 4·3; N, 10·0%).

NN′-*Diphenyl*-N-*methylchloroformamidine*. This was prepared similarly from *NN*′-diphenyl-*N*-methylurea and phosphorus pentachloride and had b.p. 162—164° at 0·5 mmHg, m.p. 38—40° (Found: C, 68·7; H, 5·4; N, 11·8. $C_{14}H_{13}ClN_2$ requires C, 68·7; H, 5·4; N, 11·5%).

N-(p-*Chlorophenyl*)-N′-*morpholinochloroformamidine*. To a solution of *N*-*p*-chlorophenylformimidoyl dichloride (1·95 g, 10 mmol) in dry benzene (20 ml) at 0°, was added dropwise, a solution of morpholine (1·74 g, 20 mmol) in dry benzene (10 ml). Morpholine hydrochloride (1·11 g, 90% of theoretical), which separated immediately on addition, was removed by filtration. The benzene was removed under reduced pressure and the residue distilled under vacuum to yield *N*-(*p*-chlorophenyl)-*N*′-morpholinochloroformamidine, m.p. 83—85° (lit.,[20] m.p. 85°).

N-*Phenylbenzimidoyl chloride*. This was prepared by the method of Ugi and had m.p. 39—41° (lit.,[7] m.p. 40—41°).

N-*Phenyl*-m-*chlorobenzimidoyl chloride*. In a round bottomed flask (100 ml) fitted with a reflux condenser and a gas outlet phosphorus pentachloride (4·17 g, 20 mmol) was added to *m*-chlorobenzanilide (4·63 g, 20 mmol). Dry benzene (20 ml) was then added and the mixture was heated slowly to reflux temperature with occasional swirling. Hydrogen chloride was evolved and the mixture gradually became an homogeneous solution. After completion of the reaction, which was indicated by the cessation of hydrogen chloride evolution, benzene and phosphoryl chloride were removed under reduced pressure and the residue vacuum distilled to yield N-*phenyl* m-*chlorobenzimidoyl chloride* (4·0 g, 80%), b.p. 160° at 0·6 mmHg, m.p. 73—75° (Found: C, 61·9; H, 3·6; N, 5·7. $C_{13}H_9Cl_2N$ requires C, 62·4; H, 3·6; N, 5·6%).

The other imidoyl chlorides were prepared by this general method and their physical and analytical data are presented in Table 9. In all cases the spectral properties, for both the imidoyl chlorides and substrates (1) were consistent with the proposed structures and with those previously reported.

Product Analysis.—Reaction of imidoyl chlorides with water. The products of hydrolysis of imidoyl chlorides, under our conditions, were in all cases the corresponding benzanilides. This was determined by comparing the u.v. spectrum obtained at the completion of a kinetic experiment with the spectrum of an authentic sample of the product measured under the same conditions and also by repeating the experiment on a preparative scale.

Reaction of chloroformimidates with water. In the neutral and acidic region the products are the corresponding carbamates as determined spectrophotometrically and confirmed preparatively. Phenyl *N*-(*p*-chlorophenyl)chloroformimidate (1·33 g, 5 mmol) was dissolved in dioxan–water (100 ml; 3 : 1) containing 0·1M-perchloric acid and the solution was refluxed for 3 h. On cooling, ice-cold water was added and the separated precipitate was collected by filtration. The resultant solid (1·08 g, 87%) was dried *in vacuo* over phosphorus pentoxide and had m.p. 148—150°. A mixed m.p. with an authentic sample of phenyl *N*-(*p*-chlorophenyl)carbamate was not depressed. Above pH 9, the carbamate formed as initial product was itself hydrolysed so that at pH 13 it could not be detected spectrophotometrically as an intermediate. The above preparative procedure was then repeated in the presence of 0·1M-NaOH and t.l.c. confirmed that the products present were phenol and *p*-chlorophenylcarbamic acid (which is hydrolysed to *p*-chloroaniline on acidification). Similar results were obtained for the 1-chlorothioformamidines.

Kinetic Method.—The kinetics of hydrolysis were followed spectrophotometrically at appropriate wavelengths in the u.v. using methods previously described.[21] Either a Unicam model SP 800 or 1800 or a Perkin-Elmer 124 spectrometer was used, each fitted with thermostatted cell blocks and external recorders. In all cases the hydrolyses were studied under pseudo-first-order conditions with substrate concentration *ca.* 2×10^{-4}M. In most cases (see text), good pseudo-first-order rate constants were obtained covering

TABLE 9

Physical and analytical data for the imidoyl chlorides (1a)

Substituent			Found (%)				Required (%)		
Ar^1	Ar^2	M.p. (°C)	C	H	N	Formula	C	H	N
p-$NO_2C_6H_4$	Ph	118—120	60·3	3·7	10·4	$C_{13}H_9ClN_2O_2$	59·9	3·5	10·7
m-$NO_2C_6H_4$	Ph	80—81	59·8	3·7	10·7	$C_{13}H_9ClN_2O_2$	59·9	3·5	10·7
p-ClC_6H_4	Ph	62—63	62·7	3·6	5·8	$C_{13}H_9Cl_2N$	62·4	3·6	5·6
m-ClC_6H_4	Ph	37—39	61·9	3·6	5·7	$C_{13}H_9Cl_2N$	62·4	3·6	5·6
Ph	Ph	39—41	72·1	4·7	6·6	$C_{13}H_{10}ClN$	72·4	4·7	6·5
Ph	*m*-ClC_6H_4	73—75	62·7	3·4	5·5	$C_{13}H_9Cl_2N$	62·4	3·6	5·6
Ph	*p*-ClC_6H_4	65—67	62·6	3·2	5·9	$C_{13}H_9Cl_2N$	62·4	3·6	5·6
Ph	*m*-$NO_2C_6H_4$	68—69	59·6	3·4	10·9	$C_{13}H_9ClN_2O_2$	59·9	3·5	10·7
Ph	*p*-$NO_2C_6H_4$	134—136	59·7	3·9	10·9	$C_{13}H_9ClN_2O_2$	59·9	3·5	10·7

[21] A. F. Hegarty and L. N. Frost, *J.C.S. Perkin II*, 1973, 1719.

several half-lives and using experimental infinity values. When the rates deviated from first order with progression of the reaction, because of inhibition by chloride ion, the substrate concentration was diluted to 5×10^{-5}M and the rates were measured using the maximum pen expansion on the spectrometers and/or recorders. The rate constants were determined from the kinetic data graphically and regression lines confirmed by the method of least squares.

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