The Competing Mechanisms of Substitution, Hydrolysis, and Cyclization of 1-Chloro- and 1,4-Dichloro-2,3-diazabuta-1,3-dienes

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In aqueous dioxan 1-chloro- and 1,4-dichloro-1,4-diaryl-2,3-diazabuta-1,3-dienes (2) and (3) are smoothly converted to arylidenearenecarbohydrazides (5) and 2,5-diaryl-1,3,4-oxadiazoles (6) respectively. Substituent effects in Ar^1 ($\rho = -2{\cdot}3$) and Ar^2 ($\rho = -1{\cdot}2$) on the rates of hydrolysis have been measured for both series of compounds and indicate a similar slow step in both reactions, *viz.* unimolecular C–Cl bond cleavage to form a stabilized azocarbonium ion in which there is efficient delocalization of charge towards the remote aryl ring. This is in agreement with the observed variation of rate with solvent ($m = 0{\cdot}97$) and the large common ion effect. In acidic solution azomethine bond hydrolysis (with formation of arenecarbaldehyde and substituted benzohydrazide) competes with C–Cl bond cleavage for the monochlorides (2). The dichlorides (3) do not undergo C=N bond cleavage under these conditions but an intermediate in the cyclization of (3) to (6) (*N*-benzoylbenzohydrazonyl chloride) is sufficiently long lived to permit its spectrophotometric detection in acid. In basic solution both series of compounds (2) and (3) undergo S_N2 attack by HO^- but only if electron-withdrawing substituents are present; otherwise the rate is depressed at high $[HO^-]$. This change-over in mechanism results in markedly non-linear free energy relationships for hydrolysis in this region.

BOTH 1-chloro- (2) and 1,4-dichloro-diazabutadienes (3) have long been known as the products of halogenation of diazabutadienes (aldazines) (1) under certain conditions.[1-4] A related series of materials, dichloroazoalkanes (4) have more recently been obtained as the products of chlorine addition to ketazines.[5-8] The ketazine adducts (4) display two general kinds of reactivity, namely fragmentation of the molecule on heating (which has led to their being used as free radical initiators [9]), and replacement of chloride ion by external nucleophiles. The dichlorodiazabutadienes (3) similarly exhibit a duality of mechanism with various nucleophiles, the alternative reactions in this case being either simple replacement of halide by external nucleophile or cyclization (possibly preceded by nucleophilic attack) to form, for example, oxadiazoles (6).

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[1] R. Stolle, *J. prakt. Chem.*, 1912, **85**, 386.

[2] R. Stolle and F. Helwerth, *Ber.*, 1914, **47**, 1132.

[3] R. Stolle and K. Thoma, *J. prakt. Chem.*, 1906, **73**, 288; R. Stolle, *ibid.*, p. 277.

[4] W. T. Flowers, D. R. Taylor, A. E. Tipping, and C. N. Wright, *J. Chem. Soc. (C)*, 1971, 1986, 3097.

[5] S. Goldschmidt and B. Acksteiner, *Chem. Ber.*, 1958, **91**, 502; *Annalen*, 1958, **618**, 173.

[6] E. Benzing, *Annalen*, 1960, **631**, 1, 23.

[7] D. S. Malament and J. M. McBride, *J. Amer. Chem. Soc.*, 1970, **92**, 4586.

[8] D. S. Malament and J. M. McBride, *J. Amer. Chem. Soc.*, 1970, **92**, 4593.

[9] F. M. Lewis and M. S. Matheson, *J. Amer. Chem. Soc.*, 1949, **71**, 747; G. G. Overberger and B. S. Marks, *ibid.*, 1955, **77**, 4097.

Previous studies on the mechanism of halide displacement have been limited to the solvolytic behaviour of the dichloroazoalkanes (4). Benzing[6] has shown that in aqueous acetone the rate-determining step for the hydrolysis of compounds (4) involves unimolecular C–Cl bond fission; subsequent steps under these conditions led to rapid fragmentation of the azoalkanes. Both the halogenation of ketazines [formation of (4)] and solvolysis of (4) have been studied by Malament and McBride.[7,8] Evidence is presented that both reactions involve the same azocarbonium ion (7); in this C–N–N bond rotation is restricted, with the result that the halogenated product (4) is formed stereospecifically.

$Ar^1CH{=}N{-}N{=}CHAr^2$

(1)

$Ar^1CCl{=}N{-}N{=}CHAr^2$

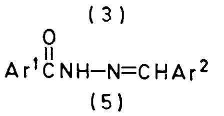
(2)

$Ar^1CCl{=}N{-}N{=}CClAr^2$

(3)

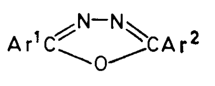
$R^1R^2CCl{-}N{=}N{-}CClR^1R^2$

(4)

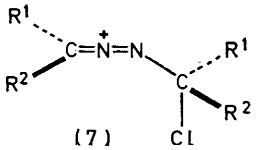


$Ar^1\overset{\overset{O}{\|}}{C}NH{-}N{=}CHAr^2$

(5)



(6)



(7)

The mono- and dichloro-diazabutadienes (2) and (3) may possibly undergo unimolecular C–Cl bond fission and/or direct nucleophilic attack, a duality of mechanism shown by the oxygen analogous, aroyl halides.[10,11] In addition, hydrolysis of the azomethine (–CH=N–) bond may also occur in this case. This work presents a study of the mechanisms of these various reactions and defines conditions where either hydrolysis, cyclization, or direct nucleophilic attack might be maximized.[12]

RESULTS AND DISCUSSION

The original method used by Stolle[1-3] for the preparation of mono- and dichloro-diazabutadienes (2 and 3; $Ar^1 = Ar^2 = Ph$) involves direct chlorination of the azine (1) in carbon tetrachloride. The monochloro-material (2) is formed at 0° while dichlorination occurs under more vigorous conditions. This method is of limited utility for the synthesis of unsymmetrically substituted monochloro-compounds (2; $Ar^1 \neq Ar^2$) and, as has been found by us and others,[13] the disubstituted materials (3) are obtained in poor yield when aryl rings carry substituents other than hydrogen. The monochloro-materials (2) were synthesised by the reaction of aroylarylidenehydrazines (5) and thionyl chloride and were formed in good yield.* The dichlorides (3) were best prepared by direct chlorination of the corresponding aldazine (1) in anhydrous acetic acid. This method obviates any separation of unchanged starting material or monochlorinated material, the required products (3) precipitating directly from the reaction solution. An attempt was also made to form the bromo-analogues of (3) using this method but the products formed were azine perhalide adducts.[14] Stepwise chlorination with thionyl chloride [(5) $\longrightarrow$ (2)] and chlorine in acetic acid [(2) $\longrightarrow$ (3)] was also successful and was found to be the best method of synthesising dichlorodiazabutadienes (3) in which the aryl substituents are dissimilar. Attempts to form compounds of this type starting with unsymmetrical azines (1; $Ar^1 \neq Ar^2$) are complicated by the ready disproportionation to symmetrical aldazines.[4] An attempt was also made to synthesise 1-chloro-1,4-diphenyl-4-methyl-2,3-diazabuta-1,3-diene by treating α-methylbenzylidenebenzohydrazide with thionyl chloride; a vigorous reaction took place in the cold and the only product isolated was 4-phenyl-1,2,3-thiadiazole.

pH–*Rate Profiles for the Hydrolysis of* (2) *and* (3).—The rates of hydrolysis of 1-chloro-1,4-diaryl-2,3-diazabuta-1,3-dienes and 1,4-dichloro-1,4-diaryl-2,3-diazabuta-1,3-dienes were studied in 3 : 1 (v/v) water–dioxan at 25 and at 50° and in 3 : 2 water–dioxan at 50° as a function of the pH of the solvent. The solutions were buffered where appropriate, but in all cases a constant ionic strength (usually $\mu = 1{\cdot}0$ using sodium perchlorate) was maintained. Under these conditions the final products of solvolysis of the dichlorides (3) are the oxadiazoles (6) and (except at extremes of high and low pH) the hydrazides (5) are formed from the monochlorides (2). The products of hydrolysis were isolated by carrying out the reactions on a larger scale (see Experimental section); t.l.c. was also used to confirm the presence of the same products under the conditions used to study the kinetics. The courses of the hydrolyses were followed spectrophotometrically and also in some instances using a pH-stat; in all cases the reactions followed first-order kinetics closely to $\geqslant 98\%$ reaction, and the final spectra were identical with those of authentic samples of the indicated products measured under the same conditions. The results obtained have been summarised in Tables 1—3.

The main feature of these pH–rate profiles is the large pH independent ' plateau ' where the rate of hydrolysis does not vary as the pH of the medium is changed (Figure 1). The extent of the plateau varies with the substituents present but usually occurs over 10 pH units [from pH 3 to 13 in the case of (2; $Ar^1 = Ar^2 = Ph$)].

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* A similar method for the preparation of (2) from (5) also involving thionyl chloride was developed independently by Flowers *et al.*[4]

[10] S. L. Johnson, *Adv. Phys. Org. Chem.*, 1967, **5**, 237.

[11] M. L. Bender and M. C. Chen, *J. Amer. Chem. Soc.*, 1963, **85**, 30, 37.

[12] Some of the results have already been presented in communication form, P. A. Cashell, A. F. Hegarty, and F. L. Scott, *Tetrahedron Letters*, 1971, 4767.

[13] K. Issleib and A. Balszuweit, *Chem. Ber.*, 1966, **99**, 1316.

[14] F. L. Scott and P. A. Cashell, *J. Chem. Soc.* (*C*), 1970, 2674.

TABLE 1

Pseudo-first-order rate constants (s^{-1}) for the hydrolysis of 1,4-diaryl-1-chloro-2,3-diazabuta-1,3-dienes (2) in 3 : 1 water–dioxan at 25° (μ = 1·0)

	Substrate		
	(2; $Ar^1 = Ar^2$ = Ph)	(2; Ar^1 = Ph, Ar^2 = *m*-ClC_6H_4)	(2; Ar^1 = Ph, Ar^2 = *p*-ClC_6H_4)
pH [a]	10^4k_{obs}	10^4k_{obs}	10^4k_{obs}
14·0	77	84	75·5
13·7	122	65	104
13·4	153	64	118
13·1	165	61	115
12·8	169		
12·5	178		
12·2	180	63	
11·9	178		
11·6	167		
11·0	167	64	
9·0			
6·5	169	64	115
4·0			
3·0	190		
2·6	220		
2·3	294		
2·0	450		
1·6	790		
1·3	1150		

[a] The acid concentrations are expressed as pH = $-\log [H^+]$, where $[H^+]$ is the actual hydrogen ion concentration used to prepare the solution. In purely aqueous solution this would correspond to the measured pH of the solution. In 3 : 1 dioxan–water the measured 'pH' values were *ca.* 0·3 unit higher in the basic region and 0·5 unit lower in acid range than those quoted in the Tables (the glass electrode having been standardized in aqueous buffers).

TABLE 2

Pseudo-first-order rate constants (s^{-1}) for the hydrolysis of 1,4-diaryl-1-chloro-2,3-diazabuta-1,3-dienes (2) in 3 : 2 water–dioxan at 50° (μ = 1·0)

	Substrate			
	(2; $Ar^1 = Ar^2$ = Ph)	(2; Ar^1 = Ph, Ar^2 = *p*-$NO_2C_6H_4$)	(2; Ar^1 = p-$NO_2C_6H_4$, Ar_2 = Ph)	(2; Ar^1 = *m*-$NO_2C_6H_4$, Ar^2 = Ph)
pH	10^4k_{obs}	10^4k_{obs}	10^4k_{obs}	10^4k_{obs}
14	63·1	685	411	197
13·7	290	523	342	184
13·4	436	300	208	101
13·1	548	228	116	55
12·8		160	68·5	33·8
12·5		141	44·5	
12·2		120	34·0	
11·9		91	29·5	
11·6		62	18·5	
6·5	654			

In acidic solution there is a rate increase (most pronounced for compounds with electron-donating substituents) while in basic solution the rate of hydrolysis changes, generally increasing but decreasing markedly in some cases (Table 2). In spite of the different products formed [(5) and (6)], the two series of compounds (2) and (3) have in general a similar hydrolytic behaviour and can be considered together. The three pH regions (neutral, acidic, and basic) in which different mechanisms and products of hydrolysis are involved will be dealt with in turn.

Hydrolysis of (2) *and* (3) *in Neutral Solution.—Substituent effects.* In this region (3 < pH < 10), repetitive scans of the u.v. spectra and comparison with authentic samples showed that the sole products of hydrolysis were the hydrazide (5) from the monochloride (2) and the oxadiazole (6) from the dichloride (3). Neither was there an appreciable build-up of intermediates during reaction as shown by tight isosbestic points (two at a minimum) for each compound. The rate of cyclization of (3) was very sensitive to the nature of the aryl substituents present but was 42-fold slower than hydrolysis of (2) when, in both cases, $Ar^1 = Ar^2$ = Ph (3 : 2 water–dioxan; 50°).

TABLE 3

Pseudo-first-order rate constants (s^{-1}) for the hydrolysis of 1,4-diaryl-1,4-dichloro-2,3-diazabuta-1,3-dienes (3) at 50° (μ = 1·0) in 3 : 1 and 3 : 2 water–dioxan

	Substrate			
	(3; $Ar^1 = Ar^2$ = Ph)		(3; $Ar^1 = Ar^2$ = *p*-ClC_6H_4)	(3; Ar^1 = *p*-ClC_6H_4; Ar^2 = Ph)
pH	10^4k_{obs} *	10^4k_{obs} †	10^4k_{obs} †	10^4k_{obs} †
14	19	5·3	22	9·3
13·7	30	9·5	18	
13·4	40		11	
13·1	51			
12·8			4·0	
12·5			3·5	
12·2	56			
11·9	52		2·3	
11·0	53		2·7	
6·5	53	15	2·3	7·4

* Solvent: 3 : 1 water–dioxan. † Solvent: 3 : 2 water–dioxan.

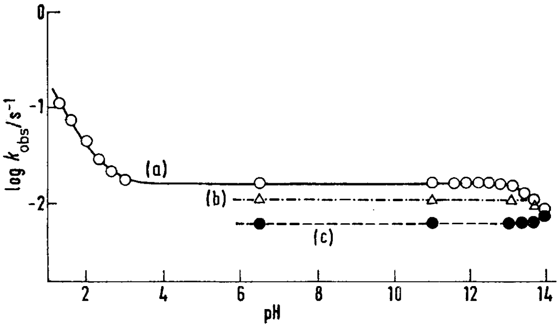

FIGURE 1 Plot of log of the observed rate constants *vs.* pH for the hydrolysis of (a) 1-chloro-1,4-diphenyl-2,3-diazabuta-1,3-diene (○); (b) 1-chloro-1-*p*-chlorophenyl-4-phenyl-2,3-diazabuta-1,3-diene (△); (c) 1-chloro-1-*m*-chlorophenyl-4-phenyl-2,3-diazabuta-1,3-diene (●) at 25° in 3 : 1 dioxan–water (μ = 1·0). In the case of (a) the curve drawn is theoretical (see text)

To probe the charge distribution in the transition state of the hydrolysis of (2), the rates of hydrolysis of two series of compounds were studied in which the substituents in Ar^1 and Ar^2 were systematically varied (Table 4). Plotting the log of the observed rate constants *vs* the σ values [15] for Ar^1 (the ring adjacent to the C–Cl bond undergoing cleavage) gave a Hammett ρ value of $-2·3$ (*r* 0·998) in 3 : 2 water–dioxan at 50°. The ρ value calculated from data for variation of sub-

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

stituents in the remote ring ($\mathrm{Ar^2}$) is −1·2 (r 0·990) in 3 : 2 water–dioxan at 40° and also in 3 : 1 water–dioxan at 25° (r 0·998).

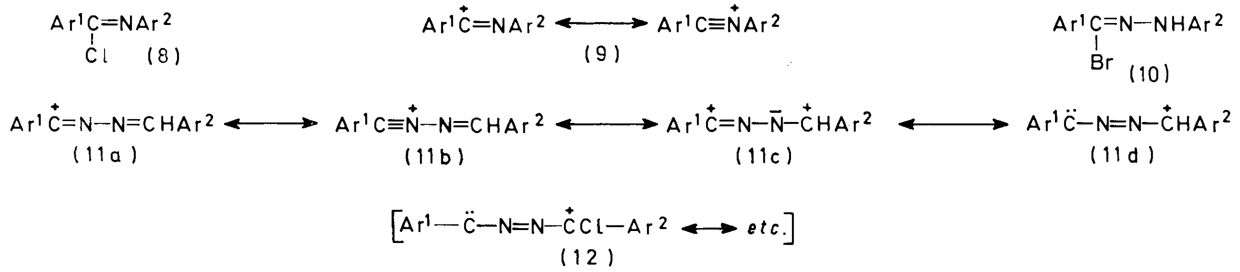
TABLE 4

Pseudo-first-order rate constants for the hydrolysis of 1,4-diaryl-1-chloro-2,3-diazabuta-1,3-dienes (2) in water–dioxan at neutral pH (*ca.* 6·5) with μ = 1·0 ($\mathrm{NaClO_4}$)

Substrate (2)		$10^4k/\mathrm{s^{-1}}$		
$\mathrm{Ar^1}$	$\mathrm{Ar^2}$	3 : 1 Water–dioxan, 25°	3 : 2 Water–dioxan, 40°	3 : 2 Water–dioxan, 50°
Ph	Ph	169	253	654
Ph	p-$\mathrm{MeC_6H_4}$	316	392	
Ph	p-$\mathrm{ClC_6H_4}$	115	156	
Ph	m-$\mathrm{ClC_6H_4}$	65	84	
Ph	p-$\mathrm{NO_2C_6H_4}$	[a]	28	
p-$\mathrm{MeC_6H_4}$	Ph			1250
p-$\mathrm{ClC_6H_4}$	Ph			197
p-$\mathrm{NO_2C_6H_4}$	Ph			11
m-$\mathrm{NO_2C_6H_4}$	Ph			12

[a] Insoluble.

The sign and magnitude of the ρ value obtained for substituents in the $\mathrm{Ar^1}$ group provide support for a mechanism involving the formation of an azocarbonium ion intermediate in this pH region. The value is numerically smaller than typical values obtained in solvolyses in which the carbonium ion formed is located largely on the carbon atom adjacent to the aryl ring.[16] More closely related is the work of Ugi *et al.*[17] on the hydrolysis of imidoyl chlorides (8) in aqueous acetone. Ion pair formation, involving the stabilized azocarbonium ion (9) was postulated; the values calculated from the available data are −2·4 for $\mathrm{Ar^1}$ and −1·7 for $\mathrm{Ar^2}$, consistent with the values reported here for solvolysis of (2).



$\mathrm{Ar^1}\underset{\substack{|\\ \mathrm{Cl}}}{\mathrm{C}}\mathrm{{=}NAr^2}$ (8)

$\mathrm{Ar^1\overset{+}{C}{=}NAr^2} \longleftrightarrow \mathrm{Ar^1C{\equiv}\overset{+}{N}Ar^2}$ (9)

$\mathrm{Ar^1}\underset{\substack{|\\ \mathrm{Br}}}{\mathrm{C}}\mathrm{{=}N{-}NHAr^2}$ (10)

$\underset{(11a)}{\mathrm{Ar^1\overset{+}{C}{=}N{-}N{=}CHAr^2}} \longleftrightarrow \underset{(11b)}{\mathrm{Ar^1C{\equiv}\overset{+}{N}{-}N{=}CHAr^2}} \longleftrightarrow \underset{(11c)}{\mathrm{Ar^1\overset{+}{C}{=}N{-}\overset{-}{N}{-}\overset{+}{C}HAr^2}} \longleftrightarrow \underset{(11d)}{\mathrm{Ar^1\ddot{C}{-}N{=}N{-}\overset{+}{C}HAr^2}}$

$\left[\mathrm{Ar^1{-}\ddot{C}{-}N{=}N{-}\overset{+}{C}Cl{-}Ar^2} \longleftrightarrow etc.\right]$ (12)

The ρ value of −1·2 obtained for the variation of substituents in $\mathrm{Ar^2}$ in (2) is remarkably high considering its remoteness from the site of C–Cl bond fission. For example, in the hydrolysis of the related hydrazonyl bromides (10) a ρ value of −0·63 was obtained [18] for $\mathrm{Ar^2}$. Based on the greater distance of $\mathrm{Ar^2}$ from the carbon–halogen bond in (2) we would therefore expect the ρ value for $\mathrm{Ar^2}$ to be less in the case of (2). The relatively high sensitivity to substituent effects in $\mathrm{Ar^2}$ is however explicable in terms of the formation of a stabilized azocarbonium ion intermediate (11). Resonance structures can be drawn for (11) [(11c, d), *etc.*] in which a formal positive charge is placed on the remote =CH– group (and thus adjacent to $\mathrm{Ar^2}$). The fact that the rate of formation of (11) is so dependent on the nature of $\mathrm{Ar^2}$ is good evidence that a relatively large fraction of the charge in the transition state is delocalised towards $\mathrm{Ar^2}$ by means of structures such as (11d). It is interesting that (11) can be written as a 1,3-dipolar ion ($\mathrm{-\overset{+}{C}{=}N{-}\overset{-}{N}-}$) with a carbonium ion substituent attached to nitrogen. When the =CH– group carries the positive charge therefore the various stabilizing structures appropriate for 1,3-dipolar ions can be written for the rest of the molecule. It is not possible to achieve such extensive delocalization of the azocarbonium ion formed from the hydrazonyl halide (10), consistent with the low ρ value for $\mathrm{Ar^2}$ in this case.

The rates of cyclization of a series of dichlorides (3) were also measured in 3 : 2 water–dioxan at 50° at *ca.* neutral pH (Table 5). The dichlorides are hydrolysed considerably more slowly than similarly substituted monochlorides (2). This is entirely consistent with rate-determining formation of the azocarbonium ion species (12) also in this case. The electron-withdrawing chloro-group, now attached directly to the carbon carrying a considerable fraction of the charge, destabilizes (12) relative to (11). Note that the chloro-group in this position has about the same depressive effect on the rate as does a p-nitro-group in $\mathrm{Ar^1}$.

TABLE 5

Pseudo-first-order rate constants for the hydrolysis of 1,4-diaryl-1,4-dichloro-2,3-diazabuta-1,3-dienes (3) in 3 : 2 water–dioxan (μ = 1·0, $\mathrm{NaClO_4}$) at 50°

Substrate (3)		$10^4k/\mathrm{s^{-1}}$
$\mathrm{Ar^1}$	$\mathrm{Ar^2}$	
Ph	Ph	15·3
p-$\mathrm{MeC_6H_4}$	p-$\mathrm{MeC_6H_4}$	74
p-$\mathrm{ClC_6H_4}$	p-$\mathrm{ClC_6H_4}$	2·25
p-$\mathrm{ClC_6H_4}$	Ph	7·4

Correlation of the data in Table 5 for those dichlorides (3) which are symmetrically disubstituted ($\mathrm{Ar^1 = Ar^2}$) gave a Hammett ρ value of −3·81 (r 0·999). This value compares favourably with that calculated for a symmetrically disubstituted monochloride (2) where the total ρ value for the simultaneous variation of $\mathrm{Ar^1}$ and

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[16] J. Hine, ‘Physical Organic Chemistry,’ McGraw-Hill, New York, 1962.

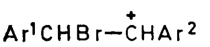
[17] I. Ugi, F. Beck, and U. Fetzer, *Chem. Ber.*, 1962, **95**, 126.

[18] F. L. Scott, M. Cashman, and A. F. Hegarty, *J. Chem. Soc.* (*B*), 1971, 1607.

Ar^2 is —3·5 (the sum of the ρ values for Ar^1 and Ar^2, see above). It is interesting to note that when Ar^1 and Ar^2 are different, then the dichlorides (3) can undergo initial C–Cl bond fission at a site adjacent to either Ar^1 or Ar^2. By comparing data for (3; $Ar^2 = p\text{-}ClC_6H_4$, $Ar^1 = Ph$) with the unsubstituted material (3; $Ar^1 = Ar^2 = Ph$), then a ρ value of —1·4 can be calculated for Ar^2. Clearly ionization occurs in this case to form the more stable azocarbonium ion species (11), *i.e.* the charge is preferentially orientated so that it is largely stabilized by the phenyl, rather than the *p*-chlorophenyl, ring. Introduction of a second *p*-chloro-group into the other ring (Ar^1) now causes a far larger rate depression [ρ —2·3, calculated from data for (3; $Ar^1 = Ar^2 = p\text{-}ClC_6H_4$ and $Ar^1 = Ph$, $Ar^2 = p\text{-}ClC_6H_4$)]; in this case it is not possible to orient carbonium ion formation away from the *p*-chlorophenyl substituent. This has the interesting implication that if one of the substituents (say Ar^1) was varied in (3) while the other (Ar^2) remained constant then the rate of solvolysis would vary non-linearly with Hammett σ values, since ρ would vary from *ca.* —2·4 (when Ar^1 contained a more electron-donating substituent than Ar^2) to *ca.* —1·4 (when the reverse was true). A similar markedly non-linear free-energy relationship has recently been noted[19] in the bromination of substituted stilbenes (13); in this case the carbonium ion intermediate (14) is oriented so that maximum stabilization is gained from the more electron-donating group Ar^2. Some of the ρ values reported for compounds, related to (2) and (3) together with reaction conditions are summarised in Table 6. Clearly in these reactions (which have all been interpreted in terms of rate-determining azocarbonium ion formation[20]) the ρ value for Ar^1 lies within the range —1·3 to —2·6, but is more generally ⩾—2·0. Interpolation of an –NH– or –S– between the reaction site and Ar^1 causes a marked decrease in sensitivity (ρ decreases from *ca.* —2·4 to —1·0, see Table 6).

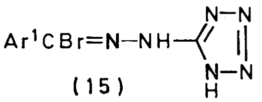
$Ar^1CH{=}CHAr^2$

(13)



$Ar^1CHBr{-}\overset{+}{C}HAr^2$

(14)



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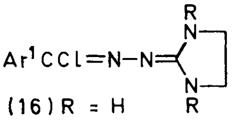
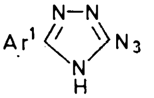


(16) R = H
(17) R = Me

$Ar^1SCBr{=}N{-}N{=}CHAr^2$

(18)



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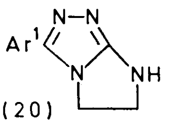

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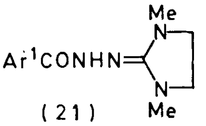
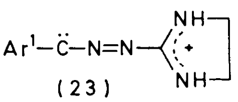


(21)

$Ar^1SCONHN{=}CHAr^2$

(22)



(23)

TABLE 6

Summary of substituent effects for azocarbonium ion formation from hydrazonyl, imidoyl, and related halides

Substrate	Product	Conditions	ρ Values	Ref.
(8)	$Ar^1CONHAr^2$	1 : 2 Acetone–water	—2·4 (Ar^1) —1·7 (Ar^2)	17
(9)	$Ar^1CONHNHAr^2$	1 : 3 Dioxan–water	—2·6 (Ar^1)	*a*
		4 : 1 Dioxan–water	—0·63 (Ar^2)	18
(15)	(19)	95% Ethanol	—1·8 (Ar^1)	*b*
(16)	(20)	4 : 1 Dioxan–water	—1·7 (Ar^1)	*c*
(17)	(21)	4 : 1 Dioxan–water	—1·3 (Ar^1)	*c*
(18)	(22)	2 : 3 Dioxan–water	—1·0 (Ar^1)	23
(2)	(5)	2 : 3 Dioxan–water	—2·3 (Ar^1) —1·2 (Ar^2)	
(3)	(6)	2 : 3 Dioxan–water	—2·4 (Ar^1) —1·4 (Ar^2)	

[a] A. F. Hegarty, M. P. Cashman, J. B. Aylward, and F. L. Scott, *J. Chem. Soc.* (*B*), 1971, 1879. [b] F. L. Scott, D. A. Cronin, and J. K. O'Halloran, *J. Chem. Soc.* (*C*), 1971, 2769. [c] A. F. Hegarty, J. O'Driscoll, J. K. O'Halloran, and F. L. Scott, *J.C.S. Perkin II*, 1972, 1887.

Two of the substrates (16) and (17) quoted in Table 6 are structurally similar to (2) but the ρ values for the variation of Ar^1 are markedly lower. This is best explained in terms of very efficient delocalization of charge away from Ar^1 and onto the neighbouring guanidino-group [see (23)] so that the substituents in Ar^1 interact with a markedly reduced charge (an apparent saturation of π electron resonance stabilization[21a]). The greater stability of (23) relative to (11) is also reflected in the higher reactivity of (16) ($k_{obs} = 1{\cdot}5 \times 10^{-1}\,s^{-1}$ at 25° in 4 : 1 dioxan–water when $Ar^1 = p\text{-}ClC_6H_4$); in more aqueous solvent (2 : 3 dioxan–water) and at higher temperature (50°) (2; $Ar^1 = p\text{-}ClC_6H_4$, $Ar^2 = Ph$) reacts more slowly ($k_{obs} = 2 \times 10^{-2}\,s^{-1}$).

Solvent effects. The effect of systematic variation of the binary solvent system dioxan–water on the rates of solvolysis of (2 and 3; $Ar^1 = Ar^2 = Ph$) is summarised in Table 7. A plot of log *k vs.* the corresponding *Y* values of Fainberg and Winstein[21b] gave a slope (the substrate *m* value) of +0·97 (*r* 0·999) for the monochloride (2).

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[19] M. F. Ruasse and J. E. Dubois, *J. Org. Chem.*, 1972, **37**, 1770.

[20] A. F. Hegarty, M. P. Cashman, and F. L. Scott, *J.C.S. Perkin II*, 1972, 44.

[21] (*a*) A. F. Hegarty, J. S. Lomas, W. V. Wright, E. D. Bergmann, and J. E. Dubois, *J. Org. Chem.*, 1972, **37**, 2222; (*b*) A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, 1956, **78**, 2770.

This high solvent sensitivity is good evidence for an S_N1 type dissociative process, since reactions for which an S_N1 mechanism is otherwise well-established hydrolyse with *m* values in the range *ca.* 0·85 — 1·2.[22a]

TABLE 7

Observed pseudo-first-order rate constants for the conversion of (2; $Ar^1 = Ar^2 = Ph$) to (5; $Ar^1 = Ar^2 = Ph$) in aqueous dioxan mixtures at neutral pH

	Solvent composition (water–dioxan)				
	1 : 4	2 : 3	1 : 1	3 : 2	4 : 1
$10^4k_{obs}/s^{-1}$ [a]	0·56	13·6	101	173	
$10^4k_{obs}/s^{-1}$ [b]		1·34	5·8	21·8	151

[a] At 50° in the presence of 0·1M-sodium acetate–acetic acid. [b] At 25° in the presence of 0·1M-sodium perchlorate.

Salt effects. The rates of solvolysis of (2) and (3) are also dependent on the nature of added salts (Table 8).

TABLE 8

Relative rates of solvolysis of (2; $Ar^1 = Ar^2 = Ph$) at 25° and of (3; $Ar^1 = Ar^2 = Ph$) at 50° in the presence of 1·0M-added salts (solvent 3 : 1 water–dioxan)

		Salt				
Substrate		$NaClO_3$	$NaNO_3$	NaOAc	NaOH	NaCl
(2)	1·0	1·6	1·23	0·66	0·73	0·007
(3)	1·0	2·17				0·047

Except in the case of added chloride ion, small rate enhancements or depressions (relative to the rate in the absence of added salt were observed. The large common ion effect [140-fold for (2; $Ar^1 = Ar^2 = Ph$)] is consistent with the other evidence presented above for the existence of an intermediate of the type (11) of sufficient stability to distinguish between the various nucleophiles present and react preferentially with Cl^-, reforming (2).[22b]

In view of this, the small rate changes observed in the presence of other salts are surprising; however, the aqueous content of the solvent is already high (75%), reducing the possible role of the salt in enhancing its ionizing power. In particular it is difficult to visualise why there is a rate depression in the presence of the nucleophilic anions acetate and hydroxide (at 1·0M concentration). The rate depression is even more marked (up to 10-fold) when the aqueous content of the solvent is reduced (see Table 2) and is shown by all compounds studied [(2), (3), and (17) [23]] in which Ar^1 and Ar^2 do not carry electron-withdrawing groups. The rate depression in the presence of hydroxide ion (or enhancement in the presence of perchlorate ion) is proportional to the mole fraction of salt present (see Figure 2). In any event the slower rate of halide ion displacements in these compounds in the presence of nucleophilic anions rules out the intervention of significant direct S_N2 halide ion displacement for these compounds.

There is thus evidence available that the solvolysis of (2) and (3) in the neutral pH region involves the formation of a stabilized azocarbonium ion intermediate (24) (Scheme 1). The hydrolysis product from (2) is the hydrazide (25; X = H); however when X = Cl, (25) can react further *via* the conjugate anion (26) to give the 1,5-dipolar ion (27). 1,5-Dipolar ring closure then gives the observed oxadiazole products (6). Since the latter reactions are rapid at high pH (and further evidence presented below supports this), the ionization step (k_1) is rate determining in both cases.

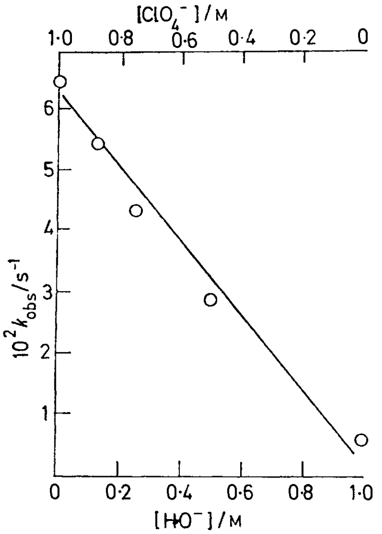
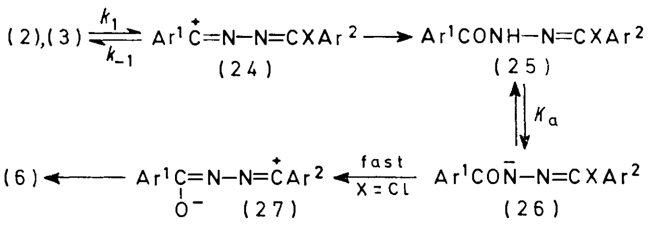


FIGURE 2 Plot of the observed rate constants for the hydrolysis of 1-chloro-1,4-diphenyl-2,3-diazabuta-1,3-diene (2; $Ar^1 = Ar^2 = Ph$) in 3 : 2 water–dioxan at 50° as a function of hydroxide ion concentration (in all cases [NaOH] + [NaClO$_4$] = 1·0M)



SCHEME 1

Hydrolysis of (2) *and* (3) *in Acidic Solution.*—(a) *The monochlorides* (2). In acidic solution (pH <3) the ultimate products of hydrolysis of the monochloride (2; $Ar^1 = Ar^2 = Ph$) are benzaldehyde and benzohydrazide (28; $Ar^1 = Ph$). Since the hydrazide (5) is also hydrolysed to these products under these conditions, the possibility arises that these are formed either directly and/or *via* prior formation of (5); it is apparent from the following data that both pathways are operative.

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[22] (*a*) J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions,' Wiley, New York, 1963, p. 297; (*b*) L. C. Bateman, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 1940, 960.

[23] J. Donovan, J. Cronin, F. L. Scott, and A. F. Hegarty, *J.C.S. Perkin II*, 1972, 1050.

At 350 nm none of the products of hydrolysis absorb, so that it was possible to measure the overall rate of disappearance of the substrate (2; $\mathrm{Ar}^1 = \mathrm{Ar}^2 = \mathrm{Ph}$) at this wavelength at low pH. From the data obtained (Table 1) it is clear that in this region the observed rate increases as the hydrogen ion concentration is increased (the solid line in Figure 1 has been drawn assuming that $k_{\mathrm{obs}} \propto [\mathrm{H}^+]$ at low pH). Since the hydrazide is hydrolysed more slowly (*ca.* 50-fold), it was possible to determine the quantity of (5) formed at each pH (see Figure 3). This was done by measuring the absorption at 305 nm as a function of time. There was an initial rapid decrease [due to hydrolysis of (2)] followed by a slower change in absorption as (5) itself was hydrolysed. Extrapolation back to zero time gave (on comparison with standard solutions) the quantity of hydrazide (5) formed from (2). From the data (Figure 3) it is clear that the percentage of hydrazide formed is *ca.* 100 in neutral solution but this decreases as the acid concentration is increased below pH 3. The sigmoid curve in Figure 3 has been drawn assuming that 50% of the hydrazide is formed from (2) at pH 2·0 (this value best fits the data); the solid line at low pH in Figure 1 was similarly drawn assuming that at pH 2·0, 50% of the observed rate was due to hydrazide formation (*via* the normal azocarbonium ion pathway) and 50% due to acid catalysed hydrolysis of (2) resulting in the formation of benzohydrazide and benzaldehyde directly. The increase in rate in acidic solution is thus exactly paralleled by the formation of benzohydrazide and benzaldehyde directly from (2).

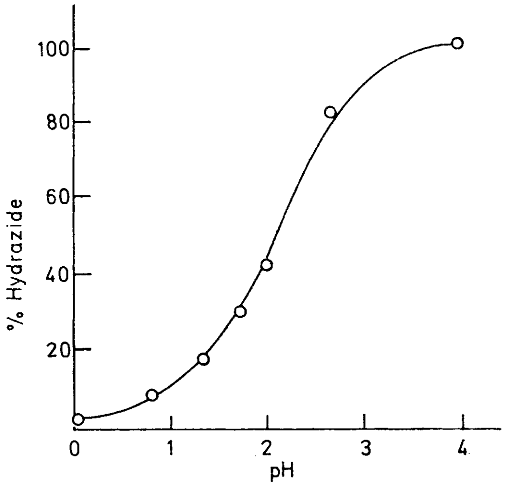
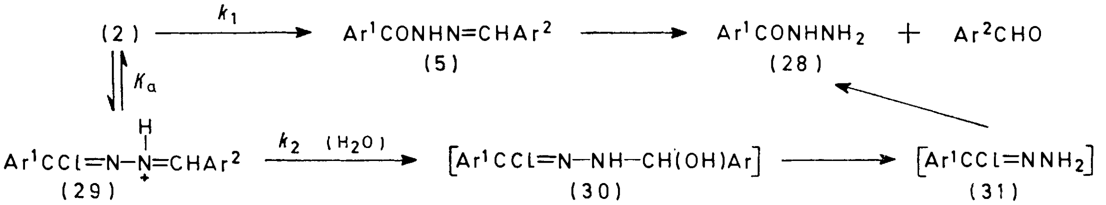


Figure 3 Plot of the observed percentage of hydrazide (5; $\mathrm{Ar}^1 = \mathrm{Ar}^2 = \mathrm{Ph}$) formed on hydrolysis of (2; $\mathrm{Ar}^1 = \mathrm{Ar}^2 = \mathrm{Ph}$) in 3 : 1 water–dioxan at 25° ($\mu = 1{\cdot}0$) as a function of the pH of the medium. The line is a theroetical sigmoid curve (% hydrazide = $100K/(K + [\mathrm{H}^+])$ assuming 50% hydrazide formation at pH 2 (*i.e.* $K = 10^{-2}$)

A mechanism consistent with this is outlined in Scheme 2. The normal S_N1 hydrolysis of (2) to (5) occurs but its role becomes less important as the acidity of the medium is increased. In high acid medium the azomethine bond adjacent to Ar^2 undergoes hydration [by water attack on the conjugate acid (29)] to give the carbinolamine (30). The formation and dehydration of carbinolamines have been well documented;[24] in the acidic hydrolysis of imines the step involving breakdown to amine and aldehyde is rate determining for the overall process.[25] Rapid hydrolysis of the benzohydrazonyl chloride (31) formed from (30) then gives the observed benzohydrazide (28). Hydrolysis of (5) is slower (50-fold at pH 2), presumably because the electron-withdrawing $\mathrm{Ar}^1\mathrm{CONH}$ group decreased the basicity of the adjacent –C=N– bond. Similarly the dichlorides (3) do not show an acid catalysed reaction. 1,4-Diphenyl-2,3-diazabuta-1,3-diene (1; $\mathrm{Ar}^1 = \mathrm{Ar}^2 = \mathrm{Ph}$), on the other hand, is hydrolysed almost as rapidly as is (2) in acidic solution, the products in this case being benzaldehyde (2 equiv.) and hydrazine. These results are consistent with cleavage occurring in (2) at the C=N bond adjacent to Ar^2 rather than that adjacent to Ar^1. Introduction of electron-withdrawing groups into Ar^1 and Ar^2 also decreases the overall rate of acid-catalysed hydrolysis of (2). Presumably the faster rate of water attack on the conjugate acid (29) is not sufficient to compensate for the lower basicity of chloride (2).



Scheme 2

(b) *The dichlorides* (3). In acidic solution the ultimate products of hydrolysis of (3) are (as in neutral solution) the oxadiazoles (6). However, below pH 3 an intermediate is formed as shown by repetitive scans of the u.v. region (Figure 4). The characteristics of this intermediate [*e.g.* the u.v. spectrum is almost identical with that of (5)] are consistent with its being the hydrazonyl chloride (25; X = Cl). The rates of formation and disappearance of the intermediate could be measured at appropriate wavelengths at pH <2 (Table 9). The first step [(13) $\longrightarrow$ (25), see Scheme 1] is relatively

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[24] W. P. Jencks, ' Catalysis in Chemistry and Enzymology,' McGraw-Hill, New York, 1969, ch. 10.

[25] E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, 1962, **84**, 4319.

insensitive to the acidity of the medium; even in 1·0M-perchloric acid the hydrolytic rate is <3-fold greater than in 1·0M-sodium perchlorate. The cyclization of (25; X = Cl) was more difficult to measure but from the available data (Table 9) it is clear that at very low pH cyclization is relatively pH independent; above pH 2 this reaction increases very rapidly so that at pH 4 (25; X = Cl) can no longer be observed spectrophotometrically and tight isosbestic points are obtained for the conversion of (3) ⟶ (6). This behaviour is typical of hydrazonyl halides which may react either by an azo-carbonium ion pathway (which is pH independent) or *via* base-catalysed 1,3-dipolar ion formation.[20] The base-catalysed pathway, however, intervenes at very low pH in this case, emphasising the importance of electron-withdrawing groups attached to nitrogen in facilitating 1,3-dipolar ion formation from hydrazonyl halides.[20]

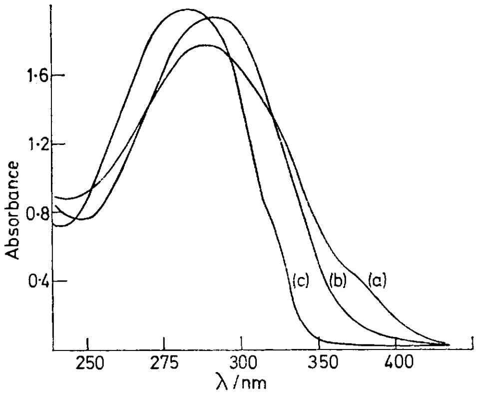

FIGURE 4 Repetitive u.v. spectra for the hydrolysis of (3; $Ar^1 = Ar^2 = Ph$) at 50° in 3 : 1 water–dioxan in the presence of 0·5M-perchloric acid: (a) recorded immediately (still largely unchanged starting dichloride; (b) after 5 min the intermediate (25; $Ar^1 = Ar^2 = Ph$, X = Cl) is the major species present; (c) after 3 h the spectrum is identical with that of the oxadiazole (6; $Ar^1 = Ar^2 = Ph$)

TABLE 9

Observed pseudo-first-order rate constants (s^{-1}) for the conversion of (3; $Ar^1 = Ar^2 = Ph$) to (25; $Ar^1 = Ar^2 = Ph$, X = Cl) and for cyclization of (25; $Ar^1 = Ar^2 = Ph$, X = Cl) in 3 : 1 water–dioxan at 50° (μ = 1·0, $NaClO_4$)

pH	10^4k_{obs} (3) ⟶ (25)	10^4k_{obs} (25) ⟶ (6)
0·0	147	6·6
1·0	70	4·8
2·0	53	9·0
3·0	55 [a]	Rapid

[a] See also Table 3.

Although *N*-arylhydrazonyl halides are well known, several attempts have previously been made to isolate (or detect) hydrazonyl bromides in which a carbonyl function is attached directly to nitrogen (25; X = Cl or Br, Ar^1 = Ph, NH_2, or NMe_2). In most cases halogenation of hydrazones of type (5) gives only cyclic products[26] or halogen complexes[27] with (5). Presumably the carbonyl group increases the acidity (K_a, Scheme 1) of the neighbouring nitrogen, facilitating 1,3-dipolar ion formation, and consequently cyclization. Compounds of type (25; X = halogen) which have been isolated have usually had special structural features which suppressed rapid dehydrohalogenation.[28,29]

We have made several attempts to form the hydrazonyl chloride (25; $Ar^1 = Ar^2 = Ph$, X = Cl) by the chlorination of benzylidenebenzohydrazide (5; $Ar^1 = Ar^2 = Ph$) in anhydrous acetic acid. The only product isolated (50% yield) was the corresponding oxadiazole (6; $Ar^1 = Ar^2 = Ph$). Stolle[1] has previously reported that (6) could be obtained by chlorination of (5) in carbon tetrachloride in the cold. An attempt to prepare (25; X = Cl) by the reaction of *NN'*-dibenzoylhydrazine with thionyl chloride was also unsuccessful, the only product formed being the oxadiazole (6). These results are consistent with the ready cyclization of the chloride (25; X = Cl), which is a likely intermediate in each case, to the oxadiazole (6).

Hydrolysis of (2) *and* (3) *in Basic Solution.*—The mono- and dichloro-compounds (2) and (3) hydrolyse smoothly in basic solution. When the hydrolyses were studied spectrophotometrically it was apparent that both series of compounds went cleanly to products as both were characterised by tight isosbestic points in the u.v. At all pH values the dichlorides (3) gave the corresponding oxadiazoles (6) but the monochlorides (2), as well as varying amounts of the hydrazide (5), gave additional products in basic solution. The hydrazide (5; $Ar^1 = Ar^2 = Ph$) was formed in *ca.* 40% yield in 1·0M-HO^-; less hydrazide was formed on hydrolysis of those monochlorides (2) with electron-withdrawing substituents so that when Ar^1 or Ar^2 was *p*-$NO_2C_6H_4$ no hydrazide was formed in 1·0M-HO^-.

In contrast to the behaviour observed in neutral solution, those dichlorides (3) with strongly electron-withdrawing substituents cyclized fastest in base (see Table 3 for an example). This was a consequence of two factors: (a) those dichlorides with electron-donating substituents in Ar^1 and Ar^2 reacted more slowly in 1·0M-NaOH than in 1·0M-$NaClO_4$ and (b) the rate of hydrolysis of dichlorides with electron-withdrawing substituents increased with increasing [HO^-]. Both these effects have also been observed for the monochlorides (2) (see Tables 1 and 2). In the case of (2; $Ar^1 = Ar^2 = Ph$) the rate depression on going from 1·0M-$NaClO_4$ to 1·0M-NaOH is most dramatic in 3 : 2 water–dioxan (see Figure 2). The decrease in the rate of carbonium ion formation in the presence of hydroxide

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[26] A. F. Hegarty, P. J. Moroney, A. Moynihan, and F. L. Scott, *J.C.S. Perkin II*, 1972, 1892, and references therein.

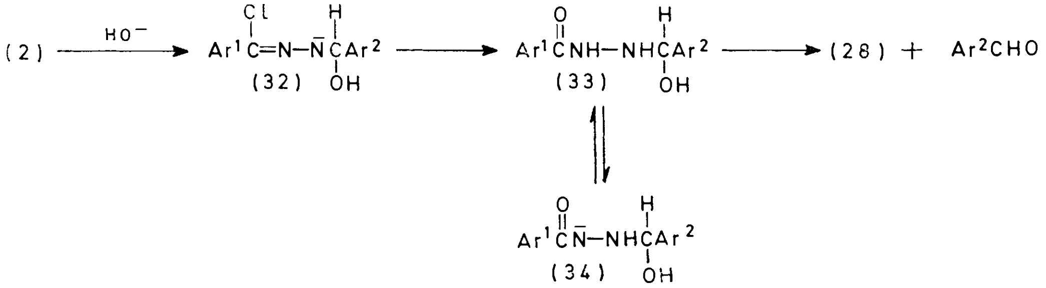
[27] M. S. Gibson, *Tetrahedron*, 1963, **19**, 1584; F. L. Scott, T. M. Lambe, and R. N. Butler, *Tetrahedron Letters*, 1971, 1729.

[28] T. Bacchetti, *Gazzetta*, 1961, **91**, 866.

[29] G. Werber, F. Buccheri, and M. L. Marino, *Ann. Chim.* (*Italy*), 1972, **62**, 11; G. Werber, F. Buccheri, and F. Maggio, *ibid.*, 1967, **56**, 1210.

ion in this case is probably even greater than the 10-fold depression noted since up to 40% of a new product is formed, most likely by direct S_N2 attack by HO^-; the actual depression in the rate of reaction *via* the carbonium ion pathway is therefore *ca.* 20-fold on changing the salt from perchlorate to hydroxide.

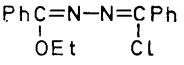
Because of the symmetry of the dichlorides (3) hydroxide ion attack at either of the C=N sites can lead to the intermediate hydrazide (25; X = Cl). Cyclization of the latter to the oxadiazole (6) would then be very rapid at high pH. Thus both the pH independent and hydroxide-catalysed pathways give the same product (*viz.* the oxadiazole). On the other hand the monochlorides (2) have two different sites for reaction with HO^-. If HO^- attacks at the carbon adjacent to Ar^1 then the hydrazide (5) is the expected product since Cl^- (a very good leaving group) would be preferentially expelled. However the hydrazides (5) are both stable and spectrally dissimilar from the products formed in 1·0M-HO^- under the conditions used to study the kinetics. The other hydrolysis products observed from (2) at high pH therefore most likely arise from HO^- attack at the azomethine –C(H)=N–. Moreover electron-withdrawing substituents in Ar^2 (which is adjacent to this bond) have a larger effect on the reactivity of (2) towards HO^- than do substituents in Ar^1 (Table 2). A possible mechanism of hydrolysis is outlined in Scheme 3.



Scheme 3

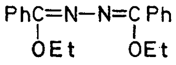
Hydroxide ion attack on (2) at the azomethine bond gives a hydrazonyl chloride, which at the high pH of the reaction solution would undergo rapid halide ion loss from the anion (32). Addition of water to the 1,3-dipolar ion formed gives the hydrazide derivative (33) which as a carbinolamine may undergo acid-catalysed hydrolysis to form benzohydrazide (28) and arenecarbaldehyde. A possible stabilizing feature of the hydrazide (33) in basic solution is the conversion to the anion (34); this occurs at high $[HO^-]$ even for the benzohydrazides (28; $Ar^1 = p$- or m-$NO_2C_6H_4$). Several attempts were made to isolate all the products formed from the monochlorides (2) at high pH; however at least one was water soluble and acidification caused irreversible change. T.l.c. of the reaction solution showed the presence of the aldehyde (Ar^2CHO), the substituted benzohydrazide (28), and varying amounts of the hydrazide (5). The hydrolysis of the related benzylideneanilines[30] is known to occur by a base-catalysed mechanism at high pH, where the rate of hydrolysis is proportional to the hydroxide ion concentration. This is due to direct hydroxide ion attack on the neutral imine followed by breakdown of the intermediate carbinolamine to give the carbonyl compound and aniline. The rate-determining step is the initial attack of hydroxide ion.

When the dichloride (3; $Ar^1 = Ar^2 = Ph$) was refluxed in ethanolic NaOH, the oxadiazole (6; $Ar^1 = Ar^2 = Ph$) was formed as the major product but, in addition, 1,4-diethoxy-1,4-diphenyl-2,3-diazabuta-1,3-diene (36) was formed in 29% yield. The formation of these two products can be rationalised in terms of the competition of hydroxide and ethoxide ion for (3). The intermediate formed by HO^- attack [(25; X = Cl)] cyclises rapidly, whereas a similar reaction is not possible in the intermediate (35) formed on halide displacement by ethoxide. The diethoxy-material (36) is then formed by displacement with a second mole of ethoxide.



$PhC(OEt)=N-N=C(Cl)Ph$

(35)



$PhC(OEt)=N-N=C(OEt)Ph$

(36)

Because of the fact that the mechanism of hydrolysis of compounds (2) in basic solution varies from unimolecular C–Cl bond fission (when Ar^1 and Ar^2 are electron donating) to S_N2 attack by HO^- (when Ar^1 and Ar^2 are electron withdrawing), the rates of hydrolysis vary in a non-linear fashion with the σ value of the substituent present. An example of this is shown in Table 10. There is a rate minimum when Ar^1 is phenyl, both electron-withdrawing and -donating substituents increasing the hydrolytic rate (by different mechanisms).

TABLE 10

Observed pseudo-first-order rate constants for the hydrolysis of monochlorides (2; Ar^2 = Ph) at 50° in 3 : 2 dioxan–water in the presence of 0·1M-NaOH

Ar^1	p-$NO_2C_6H_4$	m-BrC_6H_4	p-ClC_6H_4	Ph	p-MeC_6H_4
$10^3k_{obs}/s^{-1}$	4·91	3·11	2·10	1·99	2·88

Because the balance between the two mechanisms

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[30] A. Bruylants and E. Feytmants-de Medicis, 'The Chemistry of the Carbon-Nitrogen Double Bond,' ed. S. Patai, Interscience, New York, 1970, ch. 10.

varies with pH (tending towards S_N2 at high [HO$^-$]) the shapes of Hammett ρσ plots are also different (but always concave upwards) in this region. Curves of this type have also been obtained for the neutral hydrolysis of benzoyl chlorides.[10] The mechanism of benzoyl chloride hydrolysis is also dependent on solvent polarity. Thus, whereas in 2 : 3 ethanol–ether a displacement pathway operates as shown by the ρ value of +1·9 obtained,[31] a duality of mechanism becomes apparent in ethanol[32] and in 95% acetone,[33] as indicated by the slight upward turn in the log *k vs.* σ plots for these solvents for electron-releasing substituents. When the more polar solvent 50% acetone was used a V shaped plot was obtained,[34] indicating that a duality of mechanism was operating, one pathway facilitated by electron withdrawal, the other by electron release. In the highly polar solvent 99% formic acid the S_N1 (acylium ion) mechanism solely occurs[35] with ρ = −4·4.

In summary, the hydrolysis of (2) and the cyclization of (3) to (6) proceed by parallel mechanisms. The major pathway is *via* uncatalysed rate-determining C–Cl bond cleavage, followed by internal or external nucleophilic attack. In acidic solution substrates (2) also undergo acid-catalysed azomethine bond cleavage; in basic solution the azomethine bond of compounds (2) which have electron-withdrawing substituents is rapidly cleaved, while cyclization of (3) to (6) is accelerated.

EXPERIMENTAL

Materials.—AnalaR dioxan (BDH) was used directly as supplied. Deionized water was triply distilled from alkaline potassium permanganate. The solvent mixtures, *e.g* 3 : 2 (v/v) water–dioxan, were made up at 20°. The salts employed, sodium acetate, sodium and potassium nitrate, sodium perchlorate, were AnalaR grade and were finely ground and dried at 120° for 2 h before use. The aqueous sodium hydroxide and hydrochloric acid solutions were made up from Volucon (M and B) standard ampoules.

Substrates.— 1,4-*Diaryl*-1-*chloro*-2,3-*diazabuta*-1,3-*dienes*. The following is a typical procedure. *m*-Bromobenzoic acid (10·05 g, 0·05 mol) was converted to its ethyl ester by refluxing in ethanol (35 ml) in the presence of concentrated sulphuric acid (3 ml) for 3 h. The ester was isolated by extraction with ether, and was dissolved in n-butanol (10 ml). To this was added hydrazine hydrate (2·3 ml, 0·05 mol) and the mixture was refluxed for 10 h. On cooling, *m*-bromobenzohydrazide (8·4 g, 0·039 mol, 78%) precipitated. To this, dissolved in ethanol (50 ml), was added benzaldehyde (3·99 ml, 0·039 mol) in ethanol (40 ml). The mixture was refluxed (1 h) and on cooling *benzylidene*-m-*bromobenzohydrazide* separated (56%); on recrystallization (twice) from aqueous ethanol it had m.p. 158—159° (Found: C, 55·2; H, 3·7; N, 9·15. $C_{14}H_{11}BrN_2O$ requires C, 55·5; H, 3·6; N, 9·25%).

Benzylidene-*m*-bromobenzohydrazide (4·0 g, 0·013 mol) was refluxed for 10 h with thionyl chloride (3·0 ml, 0·04 mol) at *ca.* 120—125°. On cooling 1-m-*bromophenyl*-1-*chloro*-4-*phenyl*-2,3-*diazabuta*-1,3-*diene* (68%) separated and was dried (over P_2O_5). On recrystallisation from absolute ethanol it had m.p. 167—169° (Found: C, 52·4; H, 3·1; N, 8·6. $C_{14}H_{10}BrClN_2$ requires C, 52·3; H, 3·1; N, 8·7%). The 1-chlorodiazabutadienes could be stored *in vacuo* over P_2O_5 without significant decomposition.

The same general method was used in the preparation of most of the other benzylidene substituted benzohydrazides. Benzylidene-*p*-methyl and -*p*-chlorobenzohydrazides were synthesized by reaction of benzaldehyde hydrazone with the appropriate acid chloride. The benzylidene(substituted benzohydrazides) had the following m.p. and analytical data: substituent *p*-NO_2, m.p. 254—256°, 88% yield (Found: C, 74·7; H, 5·6; N, 12·3. $C_{14}H_{12}N_2O$ requires C, 75·0; H, 5·4; N, 12·5%); *m*-NO_2, 204—206°, 40% (Found: C, 62·3; H, 4·1; N, 15·4. $C_{14}H_{11}N_2O$ requires C, 62·5; H, 4·1; N, 15·6%); *p*-MeO, 195—197°, 11% (Found: C, 70·6; H, 5·6; N, 10·8. $C_{15}H_{14}N_2O$ requires C, 70·9; H, 5·6; N, 11·0%); *p*-Cl, 231—233°, 58% (Found: C, 64·7; H, 4·2; N, 10·7. $C_{14}H_{11}ClN_2O$ requires C, 65·0; H, 4·3; N, 10·8%); *p*-Me, 234—235°, 64% (Found: C, 75·4; H, 5·8; N, 11·6. $C_{15}H_{14}N_2O$ requires C, 75·6; H, 5·9; N, 11·8%). The (substituted benzylidene)benzohydrazides were prepared in an analogous manner: substituent: *p*-NO_2, m.p. 241—242° (Found: C, 62·6; H, 4·3; N, 15·6. $C_{14}H_{11}N_2O$ requires C, 62·5; H, 4·1; N, 15·6%); *m*-Cl, 188—189° (Found: C, 65·1; H, 4·5; N, 11·3. $C_{14}H_{11}ClN_2O$ requires C, 65·0; H, 4·3; N, 10·8%); *p*-Me, 159—160° (Found: C, 75·9; H, 6·1; N, 11·6. $C_{15}H_{14}N_2O$ requires C, 75·6; H, 5·9; N, 11·8%).

In the case of one of the 1-chlorodiazabutadienes (1-chloro-1,4-diphenyl-2,3-diazabuta-1,3-diene) the method of Stolle[1] (direct chlorination of the diazabutadiene in carbon tetrachloride at 0°) was employed. Otherwise the thionyl chloride method (detailed above) was used for the synthesis of 1-chloro-4-phenyl-1-(substituted phenyl)-2,3-diazabuta-1,3-dienes: substituent: H, m.p. 57° (lit.,[1] 57°); *p*-NO_2, 137—139° (lit.,[4] 135°); *m*-NO_2, 79—80° (Found: C, 58·6; H, 3·8; N, 15·1. $C_{14}H_{10}ClN_2O$ requires C, 58·4; H, 3·5; N, 14·6%); *m*-Br, 167—168° (Found: C, 52·4; H, 3·1; N, 8·6. $C_{14}H_{10}BrClN_2$ requires C, 52·3; H, 3·1; N, 8·7%); *p*-Cl, 128—129° (Found: C, 60·2; H, 3·5; N, 9·9. $C_{14}H_{10}Cl_2N_2$ requires C, 60·7; H, 3·6; N, 10·1%); *p*-Me, 71—72° (Found: C, 70·1; H, 5·1; N, 10·9. $C_{15}H_{13}ClN_2$ requires C, 70·2; H, 5·1; N, 10·9%). 1-Chloro-1-phenyl-4-(substituted phenyl)-2,3-diazabuta-1,3-dienes: substituent, *p*-NO_2, m.p. 158—159° (lit.,[4] 159°); *m*-Cl, 51—52° (Found: C, 60·6; H, 3·8; N, 10·6. $C_{14}H_{10}Cl_2N_2$ requires C, 60·7; H, 3·6; N, 10·1%); *p*-Cl, 98° (Found: C, 60·6; H, 3·6; N, 9·8. $C_{14}H_{10}Cl_2N_2$ requires C, 60·7; H, 3·6; N, 10·2%); *p*-Me, 89—90° Found: C, 70·4; H, 5·2; N, 11·4. $C_{15}H_{13}ClN_2$ requires C, 70·2; H, 5·1; N, 10·9%).

1,4-*Diaryl*-1,4-*dichloro*-2,3-*diazabuta*-1,3-*dienes*. The 1,4-diaryl-2,3-diazabutadiene (which was prepared by the reaction of two moles of the appropriate substituted benzaldehyde with one mole of hydrazine hydrate in ethanol) was dissolved in the minimum quantity of anhydrous acetic acid at 40°. The solution was cooled to *ca.* 20° and a stream of dry chlorine gas was passed through the solution until it was saturated. On standing the dichloride normally precipitated; in some cases partial evaporation of the solvent (at room temperature) was necessary to induce

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crystallization. The 1,4-dichloro-1,4-bis(substituted phenyl)-2,3-diazabuta-1,3-dienes were recrystallised (usually twice), from anhydrous acetic acid: substituent: *p*-Cl, m.p. 120—122°; 78% yield (Found: C, 49·0; H, 2·4; N, 8·4. $C_{14}H_8Cl_4N_2$ requires C, 48·6; H, 2·3; N, 8·1%); H, 120—122° (lit.,[13] m.p. 121—122°), 68%; *p*-F, 130—132°, 83% (Found: C, 53·55; H, 2·63; N, 9·05. $C_{14}H_8Cl_2F_2N_2$ requires C, 53·7; H, 2·57; N, 8·95%); *m*-Cl, 148—151°, 61% (Found: C, 49·0; H, 2·6; N, 8·1. $C_{14}H_8Cl_4N_2$ requires C, 48·6; H, 2·3; N, 8·1%); *p*-Me, 142—144°, 77% (Found: C, 62·9; H, 4·7; N, 9·4. $C_{16}H_{14}Cl_2N_2$ requires C, 63·0; H, 4·6; N, 9·2%); *p*-Me_2CH, 92—94·5°, 89% (Found: C, 66·2; H, 6·1; N, 7·8. $C_{20}H_{22}Cl_2N_2$ requires C, 66·5; H, 6·1; N, 7·75%). 1,4-Dichloro-1,4-diphenyl-2,3-diazabuta-1,3-diene was also prepared by the method of Stolle[3] (using carbon tetrachloride as solvent), but the yield of product was low (<10%). *1,4-Dichloro-1-(*p*-chlorophenyl)-4-phenyl-2,3-diazabuta-1,3-diene* was prepared by the chlorination (in anhydrous acetic acid) of 1-chloro-1-(*p*-chlorophenyl)-4-phenyl-2,3-diazabuta-1,3-diene and had m.p. 87—88° (Found: C, 53·9; H, 2·9; N, 8·9. $C_{14}H_9Cl_3N_2$ requires C, 53·9; H, 2·9; N, 9·0%).

2,5-Diaryl-1,3,4-oxadiazoles.—The 1,4-diaryl-1,4-chloro-2,3-diazabuta-1,3-diene (0·02 mol) was refluxed for 5 h in 3 : 2 dioxan–water (50 ml) containing 0·2M-sodium hydroxide. On cooling (ice–salt freezing mixture) the oxadiazoles separated as white solids. Addition of water precipitated further oxadiazole. The 2,5-bis(substituted phenyl)-1,3,4-oxadiazoles were recrystallised to constant m.p. (from ethanol): substituent: H, m.p. 137—138°, 86% yield (lit.,[3] m.p. 138°); *p*-Cl, 246—248°, 67% (lit.,[36] m.p. 243°); *p*-F, 203—204°, 94% (lit.,[36] m.p. 202°); *m*-Cl, 275—277°, 75% (Found: C, 57·9; H, 2·9; N, 9·4. $C_{14}H_8Cl_2N_2O$ requires C, 57·8; H, 2·8; N, 9·6%); *p*-Me, 178—180°, 88% (lit.,[37] m.p. 175°); *p*-Me_2CH, 82—84°, 81% (Found: C, 78·5; H, 7·2; N, 9·1. $C_{20}H_{22}N_2O$ requires C, 78·4; H, 7·2; N, 9·15%).

Reaction of 1,4-Dichloro-1,4-diphenyl-2,3-diazabuta-1,3-diene in Alkaline Ethanol.—1,4-Dichloro-1,4-diphenyl-2,3-diazabuta-1,3-diene (2·04 g, 0·007 mol) was refluxed for 5 h in ethanol (200 ml), to which sodium hydroxide (2·0 g) was added, thus giving a solution 0·25M in base. The mixture was allowed to stand overnight at room temperature and then cooled (ice–salt freezing mixture). The precipitated material was recrystallised (twice) from 95% ethanol and had m.p. 80—82° (0·64 g, 29%). Analysis, molecular weight, and spectral data for this material were consistent with its being *1,4-diethoxy-1,4-diphenyl-2,3-diazabuta-1,3-diene* [Found: C, 72·9; H, 6·8; N, 9·6; O, 11·1%; mol. wt. 291 (vapour pressure method). $C_{18}H_{20}N_2O_2$ requires C, 73·0; H, 6·8; N, 9·45; O, 10·8%; mol. wt. 296]; the ^1H n.m.r. spectrum ($CDCl_3$) showed a quartet centred at τ 5·90, (CH_2), a triplet at 8·73 (CH_3), and a complex aromatic multiplet at 2·2—2·8; the i.r. spectrum showed strong absorptions at 1613 (C=N) and 1124 cm^{-1} (C–O).

Water (200 ml) was added to the filtrate from the reaction mixture and ether extraction gave a further quantity of solid. On recrystallization from absolute ethanol (twice) this had m.p. 136—138° (0·85 g, 52%) and was shown to be 2,5-diphenyl-1,3,4-oxadiazole.

Chlorination of Benzylidenebenzohydrazide.—Benzylidenebenzohydrazide (3·45 g, 0·015 mol) was dissolved in anhydrous acetic acid (150 ml, containing 0·5% acetic anhydride) and dry chlorine was passed through the solution until it was saturated. The white solid which precipitated on standing at room temperature was 2,5-diphenyl-1,3,4-oxadiazole, m.p. 137—138° (1·60 g, 47%). On partial evaporation of the solvent (at room temperature), the starting hydrazide (1·41 g, 41%) precipitated from solution.

Products of Hydrolysis of Monochlorides (2).—In neutral and mildly basic solution the products of hydrolysis of the monochlorides (2) were the corresponding hydrazides (5). Because of solubility difficulties, higher relative dioxan concentrations had to be used when product analysis was carried out on a macroscale. The monochloride (2) (0·4—1·7 mmol) was refluxed for 2 h in 3 : 2 dioxan–water (50 ml) containing 0·1M-sodium acetate. On cooling the solution was ether extracted and the dried extract evaporated to give the hydrazides (5) which were identical with authentic samples [yields: 76% ($Ar^1 = Ar^2 =$ Ph); 82% ($Ar^1 = Ar^2 = p$-$NO_2C_6H_4$); 69% ($Ar^1 = Ar^2 = m$-$NO_2C_6H_4$); 91% ($Ar^1 = Ar^2 = m$-BrC_6H_4); 74% ($Ar^1 = Ar^2 = p$-ClC_6H_4); 73% ($Ar^1 = Ar^2 = p$-MeC_6H_4)]. The u.v. spectra of the products formed on hydrolysis of the chlorides (2) were identical with and varied with pH in the same way as the hydrazides (5); this was in agreement with t.l.c. [on silica gel, using hexane–diethyl ether (1 : 1) as eluant] analysis of the reaction solutions.

Reaction of NN′-Dibenzoylhydrazine with Thionyl Chloride.—Dibenzoylhydrazine (6·2 g, 0·026 mol), prepared from benzohydrazide and benzoyl chloride, was added to thionyl chloride (5·0 ml) and heated at 120° for 4 h. The clear solution was allowed to cool and was left at room temperature for 24 h. On cooling to 0°, the solid which precipitated had m.p. 137—138° (from ethanol) and was identified as 2,5-diphenyl-1,3,4-oxadiazole (3·2 g, 55%). A similar result has been reported by other workers using phosphorus oxychloride.[38]

Reaction of α-Methylbenzylidenebenzohydrazide with Thionyl Chloride.—To benzoylhydrazine (27·2 g, 0·2 mol) in ethanol (200 ml) was added acetophenone (23·3 ml, 0·2 mol) in ethanol (40 ml). The mixture was refluxed for 5 h, cooled, and the precipitated *hydrazide* was recrystallised from ethanol, m.p. 154° (Found: C, 75·3; H, 5·9; N, 11·7. $C_{15}H_{14}N_2O$ requires C, 75·6; H, 5·9; N, 11·8%). α-Methylbenzylidenebenzohydrazide (3·9 g, 0·016 mol) was added to thionyl chloride (2·0 ml); unlike the other benzohydrazides, vigorous effervescence occurred on addition. The mixture was heated at 120° for 4 h, cooled to room temperature, and left for three days. The precipitated material was recrystallised from ethanol and had m.p. 74—76°. The product which did not contain oxygen or chlorine gave C, 57·4; H, 3·7; N, 17·5; S, 18·9%; mol. wt. (vapour pressure) 171 ($C_8H_6N_2S$ requires C, 59·2; H, 3·7; N, 17·3; S, 19·75%; mol. wt. = 164.) The i.r. spectrum (KBr disc) showed the absence of oxadiazole absorption [at *ca.* 1620 cm^{-1} (C=N)]. Its n.m.r. spectrum, in addition to aromatic multiplet (τ 2·1—2·8) showed a sharp singlet (one proton) at τ 1·52, comparable with the value of τ 1·47 reported for the proton at the 5-position of 3,4-diphenyl-

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1,2-thiazole.[39] These data are consistent with the product being 4-phenyl-1,2,3-thiadiazole (lit.,[40] m.p. 77—78°).

Kinetic Methods.—The kinetics of hydrolysis were followed spectrophotometrically at appropriate wavelengths in the u.v. using methods previously described in detail.[20] Either a Unicam model SP 800 or SP 1800 spectrometer was used, both fitted with thermostatted cell blocks and external recorders. In all cases the hydrolyses were studied under pseudo-first-order conditions with the substrate concentration *ca.* 10^{-4}M. Good pseudo-first-order rate constants were obtained from data covering several half-lives and using experimental infinity values. The rate constants were computed graphically or using a special least squares programme written for the Olivetti–Underwood Programma 101.

The dioxan–water solutions used for the kinetic experiments were made up by mixing appropriate volumes of solutions containing 1·0M-sodium perchlorate solution with 1·0M-sodium hydroxide or 1·0M-perchloric acid made up in the same solvent. The acid and base used were from standardized concentrated Volucon solutions. These solutions thus were of constant ionic strength (1·0M) and had known concentrations of acid or hydroxide ion. The ' pH ' values quoted in the text refer for convenience to the pH of the corresponding 100% aqueous solutions containing the same quantity of acid or base. The indicated pH values of the dioxan–water solutions were also measured using a Radiometer model PHM 26 pH meter with a Metrohm EA 125U glass combination electrode, having first standardized the electrode in aqueous buffers (Radiometer) and then allowed it to steep in the dioxan–water for *ca.* 30 min before making a measurement. The indicated ' pH ' values thus obtained are not quoted (except for values *ca.* pH 7) but were within 0·5 pH unit of the values given in the Tables. The measurements with the electrode were used to verify that no pH drift occurred during a kinetic run.

A pH-stat assembly (Radiometer pH meter PHM 26, Titrator, type TTTIB, Titrigraph type SBR2, and Autoburette type ABU 12) was also used to measure the rate of hydrolysis of (2; $Ar^1 = Ar^2 = Ph$) near neutral pH. Although of necessity a high concentration of substrate (10^{-3}M) was used, the results obtained agreed with the spectrophotometric measurements.

[3/434 *Received, 26th February,* 1973]

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