Mechanism of 1,3-Dipolar Ion Formation

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Summary Kinetic studies on hydrazidic halides in 70% dioxan at 25° show a base-catalysed process (in some cases even at pH 3·0); structural effects on this reaction, which was identified as nitrilimine formation, are reported.

DEHYDROHALOGENATION of hydrazidic halides (**1**; X = Cl or Br) under mild conditions (benzene solution with triethylamine as catalyst) provides the most convenient route to 1,3-disubstituted nitrilimines (**3**).[1] Such 1,3-dipolar ions have been shown to undergo a wide variety of cycloadditions usually *in situ* without the isolation of (**3**), but the mechanism of this process remains controversial.[2]

The hydrolysis of the bromide (**1**; R = Me_3C, Ar = $4\text{-}NO_2C_6H_4$, X = Br) has been investigated in 70:30 dioxan–water at 25° (μ = 0·10; KNO_3) as a function of pH (Figure). The product formed over the entire range was the corresponding hydrazide (**5**; R = Me_3C, Ar = $4\text{-}NO_2\text{-}C_6H_4$) (see Scheme).

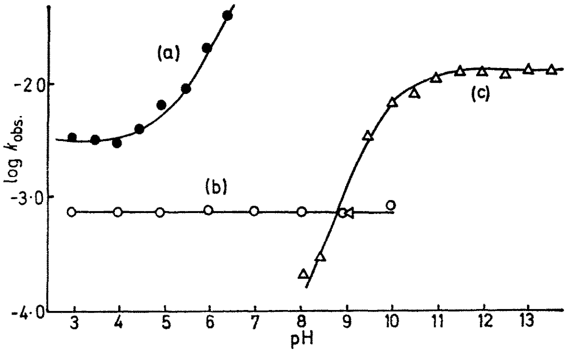
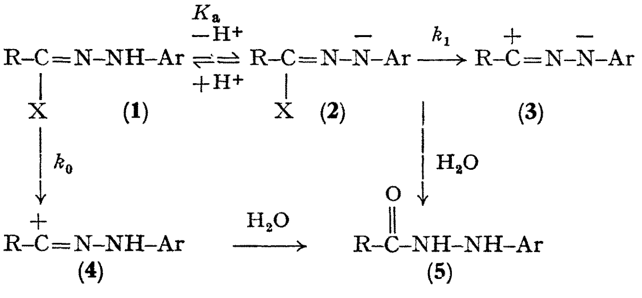


FIGURE. *Plot of the log of the observed rate constant* vs. pH *for the solvolysis (in* 70% *dioxan at* 25°) of (a) [**1**; R = Me_3C, Ar = $2,4\text{-}(NO_2)_2C_6H_3$, X = Br] (●); (b) $Me_3CC(Br){=}N\text{-}N(Me)C_6H_3\text{-}(NO_2)_2\text{-}2,4$ (○); (c) (**1**; R = Ph, Ar = $4\text{-}NO_2C_6H_4$, X = NO_2) (△).

At low pH, the observed rate of reaction is independent of [H^+], while at higher pH (> *ca.* 5) the rate increases rapidly with pH. The observed constants fit equation (1) with

$$k_{obs.} = k_0 + k_1K_a/(K_a + a_H) \qquad (1)$$

$a_H >> K_a$. The reaction in the pH-independent region (k_0) is characteristic of rate-determining ionization of the C–Br bond [*i.e.* formation of the azocarbonium ion (**4**)]. A high solvent sensitivity (m = 0·89) is shown in this region, while the presence of salts other than those containing the common ion, Br^-, enhances reactivity. The intermediate (**4**) was also trapped by nucleophiles other than water (azide ion, acetate ion), without substantial alteration of k_0.



SCHEME

The hydroxide-catalysed reaction is due to loss of bromide ion from the anion (**2**) to give the 1,3-dipolar intermediate (**3**), rather than direct attack by hydroxide ion on the hydrazidic bromide, which would be kinetically equivalent. This follows from the observation that *NN*-disubstitution of the hydrazidic bromide $Me_3CC(Br){=}N\text{-}N(Me)C_6H_3(NO_2)_2\text{-}2,4$ (see Figure) suppressed the base-catalysed reaction ($k_{obs.} = 9{\cdot}5 \times 10^{-4}\,s^{-1}$ from pH 2–10).

Representative values of k_1K_a obtained for various hydrazidic bromides are given in the Table. It was not possible to measure the pK_a values of the halides (**1**; X = Br) directly since in the pH region close to their pK_a values (*ca.* 10), loss of bromide ion from the anion is very rapid. An estimate could be made, however, using the parent hydrazone as model. For example, the pK_a of [**1**; R = Et, Ar = $2,4\text{-}(NO_2)_2C_6H_3$; X = H] was found to be 12·8 (70% dioxan; 25°). Assuming that the electron-withdrawing Br group further stabilises the anion (**2**) when X = H), k_1 for the corresponding hydrazidic bromide can be estimated as *ca.* 5×10^4—$5 \times 10^6\,s^{-1}$. Thus, loss of bromide ion from the anion (**2**) is > 10^8-fold more rapid than from the neutral hydrazidic bromide (**1**).

The substituent effects in the Table show that electron withdrawal in Ar [*e.g.* $2,4\text{-}(NO_2)_2C_6H_3$] enhances 1,3-dipolar ion formation (relative to azocarbonium ion formation) so that this is the principal pathway in some cases even when the pH of the solution is as low as 3·0. Presumably the major effect is on the acidity constant K_a, since electron withdrawal would be expected to reduce k_1.

Rate and equilibrium constants for the solvolysis of the hydrazidic bromides (**1**; X = Br) *in* 70% *dioxan at* 25° (μ = 0·10)

R	Ar	10^4k_0 (s^{-1})	k_1K_a (s^{-1})
Et	2,4-$(NO_2)_2C_6H_3$	6·3	7·5 × 10^{-7}
Me_3C	2,4-$(NO_2)_2C_6H_3$	8·0	2·1 × 10^{-7}
$BrCH_2$	2,4-$(NO_2)_2C_6H_3$	2·5	1·1 × 10^{-7}
$ClCH_2$	2,4-$(NO_2)_2C_6H_3$	2·0	1·4 × 10^{-7}
Me_3C	4-$NO_2C_6H_4$	28	2·0 × 10^{-8}
Ph	2-Br, 4-MeC_6H_3	3·55	3·8 × 10^{-11}
Ph	2-Br, 4-FC_6H_3	2·7	2·3 × 10^{-10}
Ph	2,4-$Br_2C_6H_3$	1·2	5·7 × 10^{-11}

Investigations with leaving groups other than halide also support this mechanistic interpretation. The hydrazidic ethers (**1**; R = Ar = Ph, X = OPh) and [**1**; R = Me_3C, Ar = 2,4-$(NO_2)_2C_6H_3$, X = OEt], where the leaving group was phenoxide or ethoxide ion, were relatively stable, even in basic solution. With X = NO_2 (**1**; R = Ph, Ar = 4-$NO_2C_6H_4$, X = NO_2), however, the nitrazone was of intermediate reactivity. Azocarbonium ion formation was too slow to measure in 70% dioxan at 25°, but the rate of 1,3-dipolar ion formation (k_0) was in a convenient range (Figure). The kinetic data for this compound fit equation (1) with $k_1 = 1·35 \times 10^{-2}\,s^{-1}$, $K_a = 1·0 \times 10^{-10}$) and $k_0 = 0$ (Figure). The pK_a of the nitrazone was measured independently (spectrophotometrically) and was the same (10·0) as the kinetic value.

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