

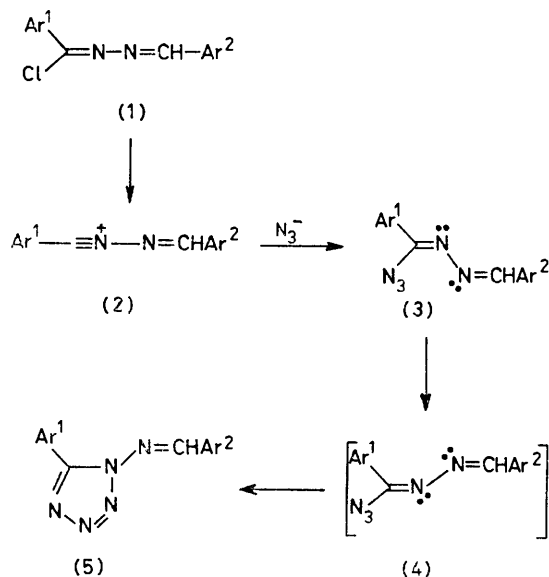
Inverse Substituent Effect in an Imidoyl Azide to Tetrazole Cyclization Limited by Nitrogen Inversion

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Summary The azides (**3**) are stabilised in the open-chain form by a slow *Z-E* isomerisation about the C=N bond; electron-withdrawing substituents in Ar² can either lower

(by the operation of a mesomeric effect) or raise (by the inductive effect) this inversion barrier.

THE mechanism of *E-Z* isomerisation about the carbon-nitrogen double bond has recently been the subject of controversy and limiting mechanisms of nitrogen inversion (by a lateral shift of the substituent attached to nitrogen) and rotation (involving an unpairing of the π -electrons in the double bond) have been proposed.¹⁻³ Most studies have concluded in favour of a transition state which is close to the lateral shift extreme, except in those cases where strongly electron-withdrawing substituents polarise the double bond.⁴ One of the more intriguing aspects of the lateral shift mechanism is the prediction, from theoretical studies,^{1,3,5} that electron-withdrawing substituents will aid inversion by a mesomeric effect while slowing inversion by the inductive effect of the substituent. We report confirmation of this proposal in two related systems, where the same substituent is shown to aid and hinder reaction, respectively.



We have found that the imidoyl azides (3) can be cyclized to the tetrazoles (5) on heating in an inert solvent. The azides (3) are themselves formed on reaction of 1,4-diaryl-1-chloro-2,3-diazabuta-1,3-dienes (1) with azide ion, which involves trapping of an intermediate nitrilium ion (2). The cyclization of (3) to (5) is insensitive to the addition of moderate quantities of acid or base [although 0.1M acid or base, as expected, causes direct hydrolysis of the azide (3)], and could therefore be studied over a wide solvent range. Substituents in the remote Ar^2 ring have the largest effect on reactivity, with electron-withdrawal increasing the rate of cyclization; a Hammett plot (Figure) gives a ρ value of +1.45. Substituents in Ar^1 have a small effect ($\text{Ar}^1 = m\text{-NO}_2\text{C}_6\text{H}_4$ reacts *ca.* 30% slower than $\text{Ar}^1 = \text{Ph}$) on the rate of cyclization. These substituent effects rule out the cyclization of the azide as the rate determining step, since this step should be retarded by electron-withdrawal (as can be inferred from azide-tetrazole equilibria in bicyclic systems⁶ and from theoretical studies⁷). Moreover the rate of conversion of (3) \rightarrow (5) is solvent independent.⁸ We therefore conclude that *Z-E* isomerisation [(3) \rightarrow (4)] is

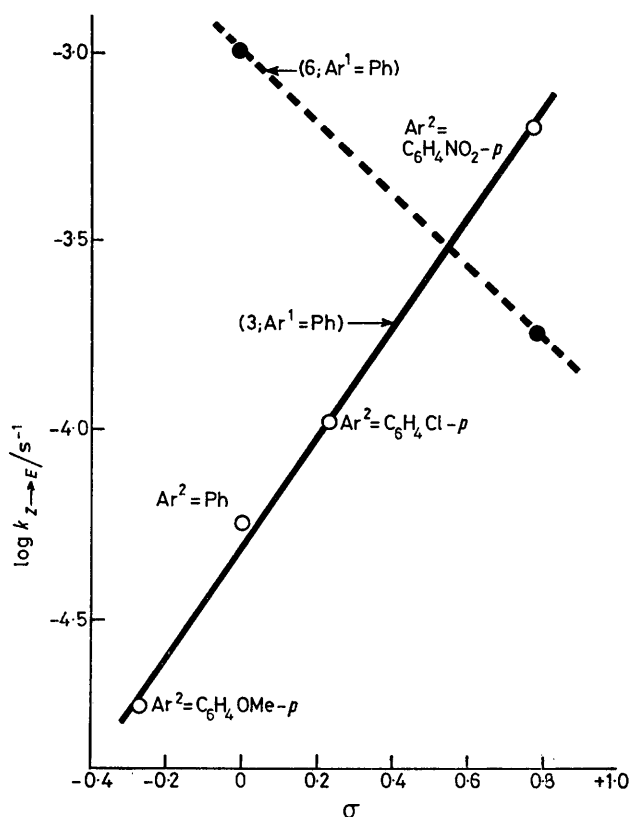
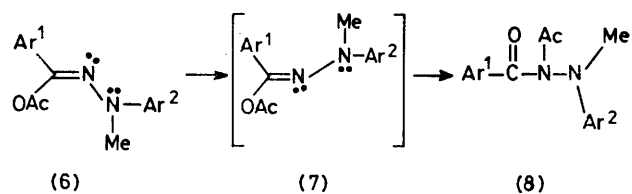


FIGURE. Hammett plots of the log of the observed rate constants (k_{obs} in s^{-1}) against σ values for the conversion of (3) into (4) and (6) into (7). The slopes (or Hammett ρ values) are +1.45 and -1.0, respectively.

rate determining in the overall reaction scheme and that the unusual stability of the azide is attributable to this. Consistent with this is the likelihood that the azide will be formed initially in the *Z*-configuration (*i.e.*, (3) due to stereoelectronic control of the reaction of azide ion with the nitrilium ion (2).⁹



In contrast to this, electron withdrawing substituents in Ar^2 actually slow the rate of *Z* \rightarrow *E* isomerisation ($\rho = -1.0$ for substituents in Ar^2 , see Figure) of the related *Z*-imidoyl acetate (6) to the *E*-isomer (7) [which is then trapped by a rapid $\text{O} \rightarrow \text{N}$ acyl group transfer⁹ to give (8)]. It is unlikely that there is a change in the mechanism of *Z-E* isomerisation between the two systems [(3) and (6)] since substituents in the *C*-aryl ring (Ar^1) have just about the same small effect (23% reduction in rate of conversion of (6) into (7) when $\text{Ar}^1 = p\text{-NO}_2\text{C}_6\text{H}_4$ relative to $\text{Ar}^1 = \text{Ph}$) in 1:1 dioxan-water at 55 °C.

Thus the same substituent in Ar² which markedly aids the conversion of (3) → (4) reduces the rate of (6) → (7). The most obvious difference between the two systems is the potential modes of transmission of substituent effects, with possible direct mesomeric effects from substituents in Ar² [(p-p) π conjugation] acting on the forming vacant p-type orbital on the imino-nitrogen in the transition state for (3) → (4). Direct conjugative interaction between the p-orbital and the aryl ring is blocked by the intervening

amino-group in (6) so that substituents can only act on the nitrogen undergoing inversion according to their inductive effect; in this case, in agreement with prediction,^{1,3,5} electron withdrawal slows inversion by reducing the energy release on rehybridization of nitrogen (sp² to sp) in the transition state.

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