Stereospecific Bimolecular Displacement at a Carbon–Nitrogen Double Bond leading to Open Chain Imidoyl Azides

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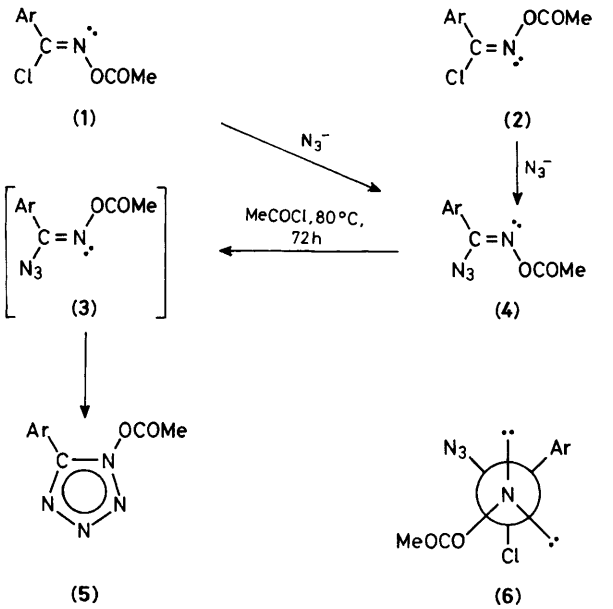
Use of the 'azide trap' for a *cis* lone pair on nitrogen shows that the *Z*-halides (**1**) undergo retention and the *E*-halides (**2**) inversion of configuration on reaction with azide ion.

Acyclic imidoyl azides spontaneously cyclize to the tetrazole unless the acyclic form is stabilized by special structural features.[1] Chief among these is the presence of a substituent attached to the imidoyl nitrogen which is capable of slowing the rate of spontaneous inversion of this nitrogen. It has been shown that only when the lone pair and the azido group are *cis* does cyclization take place,[2] a finding which is in line with theoretical studies.[3] We have used this novel structural probe to investigate the stereochemistry of addition–elimination at the carbon–nitrogen double bond.

Acylation of *Z*-benzohydroximoyl chloride with acetyl chloride in benzene leads to a single *O*-acyl isomer (as shown by n.m.r. and t.l.c.); this also has the *Z*-configuration (**1**) as shown by the facile hydrolytic removal of the acetyl group to regenerate the hydroximoyl chloride. Photoisomerisation of (**1**) leads to a mixture of (**1**) and (**2**) which can be separated by preparative t.l.c.

Treatment of (**1**) (Ar = Ph) with sodium azide in acetone–water (1 : 1) at 25 °C leads to the quantitative formation of the *Z*-azide (**4**). No trace of the corresponding *E*-isomer (**3**), or of the acylated hydroxy tetrazole (**5**), [to which (**3**) should spontaneously cyclize], or of the hydroxy tetrazole [from deacylation of (**5**)] was detected. Kinetic studies† in water at 25 °C show that this is a bimolecular reaction, first order in [(**1**)] and in [N_3^-] giving a second-order rate constant of 4.5×10^{-3} mol^{-1} dm^3 s^{-1} at 25 °C. Electron-withdrawing substituents in Ar aid reaction [a Hammett ρ value calculated from three compounds (**1**) with Ar = XC_6H_4: X = *p*-NO_2, *p*-Cl, H is +1.24] consistent with nucleophilic attack by N_3^- in the slow step. Thus bimolecular displacement of Cl by N_3 in (**1**) proceeds stereospecifically with retention of configuration about the C=N bond.



Displacement of Cl^- by N_3^- was also investigated in the *E*-isomer (**2**). This was also shown to be bimolecular (with a Hammett ρ value of +0.66) but (**2**) (Ar = Ph) reacted *ca.* 10-fold slower than (**1**) (Ar = Ph). Interestingly, however, the product obtained was the open-chain azido compound (**4**) [with no trace of the tetrazole (**5**)] so that reaction in this case was also stereospecific but with *inversion* of configuration at the C=N bond.

Cyclization of the azide (**4**) to the tetrazole (**5**) could be achieved under more vigorous conditions by refluxing with an excess of acetyl chloride in benzene for 72 h.[4] In this case acetyl chloride presumably acts as a Lewis acid, involving reversible *N*-acylation of (**4**), allowing C=N bond rotation (equivalent to a nitrogen inversion) followed by cyclization to (**5**).

The results can be rationalised in terms of stereoelectronically controlled attack by N_3^- on (**1**) to give (**6**); (**6**), which has a lone pair antiperiplanar to Cl, can undergo rapid loss of Cl^- without further stereomutation (nitrogen inversion or C–N bond rotation). However, the adduct formed from (**2**) cannot undergo direct Cl^- loss and therefore reverts rapidly to (**2**) consistent with the slow overall reaction of (**2**). Stereomutation *via* C–N bond rotation to the least hindered adduct (Ar and OCOMe *trans*) must occur before Cl^- loss to give the observed product (**4**). This is consistent both with the lower rate of reaction and observed substitutent effect (in Ar) for (**2**) relative to (**1**).

Although addition–elimination reactions at the C=N bond occur widely in chemical and biological systems, few studies of the stereochemistry of these reactions have been made.[5] The substrates reported here, (**1**) and (**2**), both have an excellent leaving group (Cl^-) so that the elimination occurs rapidly; this and stereoelectronic control of the addition and elimination account for the clear stereospecificity of these reactions.

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† The kinetics were studied spectrophotometrically at 25 and 55 °C in acetone–water (1 : 1); the solutions were buffered at an apparent pH of 5.8 using phosphate and ionic strength maintained at 1.0 (sodium perchlorate). The second order rate constants were calculated from linear $k_{obs.}$ *vs.* [N_3^-] plots which had zero intercept at [N_3^-] = 0. The azides (**2**) and acylated tetrazoles (**5**) had physical characteristics (microanalysis, n.m.r., i.r.) consistent with the proposed structures.

References

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3 L. A. Burke, J. Elguero, G. Leroy, and M. Sana, *J. Am. Chem. Soc.*, 1976, **98**, 1685; L. A. Burke, G. Leroy, M. T. Nguyen, and M. Sana, *ibid.*, 1978, **100**, 3668.
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5 See for example, J. E. Johnson, E. A. Nalley, C. Weidig, and M. Arfan, *J. Org. Chem.*, 1981, **46**, 3623 and references therein; P. Deslongchamps, 'Stereoelectronic Effects in Organic Chemistry,' Pergamon Press, Oxford, 1983, ch. 6.