Isomerisation about the C–N and C=N Bonds of *E*- and *Z*-Amidines

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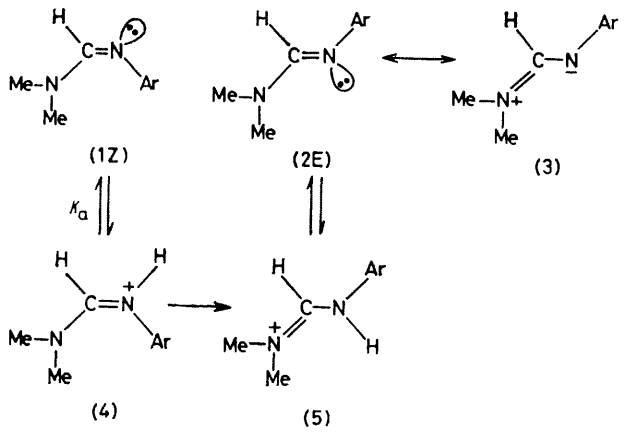
Summary The unstable *Z*-formamidines are 'frozen' in the perpendicular configuration (**6**), ready isomerisation [*via* the conjugate acid (**4**)] occurs to the *E*-form (**2**)

We have recently reported[1] that 1 1-addition of secondary amines to isocyanides at low temperature in the presence of silver chloride leads stereospecifically to isolable *Z*-formamidines, such as (**1Z**) These *Z*-formamidines are thermo-

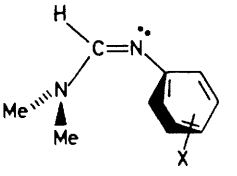
dynamically unstable and isomerise completely on heating in an inert solvent or on treatment with acid at room temperature to the corresponding *E*-isomers (**2**). The isolation of these unstable materials presents us with a unique opportunity to comment on the underlying reasons for the instability of the *Z*-isomers, the mechanism of the (**1Z**) → (**2E**) interconversion (which is an apparent nitrogen inversion), and restricted rotation about the N–C bond in both isomers.



Previously reported studies[2] on restricted rotation about the N–C bond in amidines have been carried out on what we now know to be the more stable *E*-isomers. Restricted N–C bond rotation is observed for (**2**; Ar = 3-ClC_6H_4); n.m.r. spectroscopy shows that the NMe_2 groups are equivalent at 34 °C but on cooling to −30 °C (in $CDCl_3$) separate signals of equal intensity are obtained (the coalescence temperature is −5 °C). The coalescence temperature (and thus the energy barrier for C–N bond rotation) is raised when Ar contains an electron-withdrawing group or when measurements are carried out in an aromatic solvent (*e.g.* C_6D_6). Restricted rotation clearly arises from the contribution of structures such as (**3**), the importance of which would be enhanced by electron withdrawal in Ar.

The *Z*-isomer (**1**) presents quite a different picture since the signal for the $-NMe_2$ groups remains as a singlet over the temperature range 34 → −80 °C. This equivalence could arise owing to either (a) rapid rotation about the C–N bond at all temperatures or (b) the possibility that the *Z* isomer is 'frozen' even at 34 °C in a conformation where the methyl groups are in equivalent positions. Explanation (a) would imply that N–C bond rotation is freer in the *Z*-isomer (which is more highly congested) than in the *E*-isomer. We, however, suggest that the *Z*-amidine has the structure (**6**) where both the N-aryl and amino functions are orthogonal to the N–C=N plane. Rapid N-aryl group rotation might still be occurring; however, when the aryl group contains an *ortho*-substituent (**6**, X = *o*-Cl or *o*-NO_2) the two Me groups become non-equivalent,† clearly pointing to a fixed configuration about the N–C and N-aryl bonds. A *meta*-substituent (*e.g.* X = *m*-Cl) does not bring about non-equivalence of the –Me groups either because rotation about the N-aryl group is rapid or (more likely) the Cl substituent is too remote to cause an appreciably different environment for the two –Me groups.

The formamidines are basic (pK_a's are in the range 6—9) and are readily protonated by DOAc in $CDCl_3$ or in CF_3CO_2D. On protonation the *E*-isomer (**2**; Ar = *m*-ClC_6H_4) shows restricted rotation (the –Me groups give signals at δ 3·22 and 3·05) about the C–NMe_2 bond even at 34 °C, consistent with increasing double bond character (see **5**). On the other hand the N–Me_2 signals of the *Z* isomer do not change from a singlet on protonation to give (**4**), consistent with our conclusion above that rotation about this bond is already restricted in the free base (**1Z**).



(6)

As mentioned above, protonation of (**1**) also causes *Z* → *E* isomerisation. In fact when the rate of conversion of (**1**) → (**2**) (Ar = Ph) was measured‡ in aqueous solution at 25 °C, it was clear that the protonated form (**4**) is the *only* form undergoing reaction. Thus the rate of *Z* → *E* isomerisation is pH-independent ($k_{obs} = 2{\cdot}50 \times 10^{-3}\ s^{-1}$) from pH 0 to 8 and then decreases [corresponding to the presence of the free base (**1**)]. We have found no evidence for the isomerisation of the free base by direct nitrogen inversion under these conditions (although reaction at pH 9 could not be studied because hydrolysis of the amidine was faster than *Z*–*E* isomerisation). This result contrasts with the slow rates of rotation for simple iminium salts (protonated imines)[3] although acid catalysis does occur in the isomerisation of related imidates[4] and amidoximes.[5]

There is thus clear evidence of highly restricted rotation in the *Z*-form of these amidines. This arises from severe steric crowding which is relieved on isomerisation to the *E*-form. Other properties of these unique *Z*- and *E*-amidines, such as their ability to act as bifunctional catalysts, are at present under investigation.

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† The n.m.r. signals are at δ 2·40 and 2·46 for (**6**: X = *o*-NO_2) and 2·15 and 2·21 for (**6**; X = *o*-Cl) in $CDCl_3$ at 34 °C and do not change on varying the temperature (34 → −80 °C).

‡ Followed by u.v. spectroscopy at 305 nm where the *Z*-isomer is more strongly absorbing than the *E*-isomer.

[1] A. F. Hegarty and A. Chandler, *Tetrahedron Letters*, in the press.
[2] G. Schwenker and H. Rosswag, *Tetrahedron Letters*, 1968, 2691; Z. Rappoport and R. Ta-Shma, *ibid.*, 1972, 5281; J. S. McKennis and P. A. Smith, *J. Org. Chem.*, 1972, **37**, 4173; D. J. Bertelli and J. T. Gerig, *Tetrahedron Letters*, 1967, **26**, 2481.
[3] W. B. Jennings, S. Al-Showiman, M. S. Tolley, and D. R. Boyd, *J.C.S. Perkin II*, 1975, 1535.
[4] A. C. Satterthwait and W. P. Jencks, *J. Amer. Chem. Soc.*, 1974, **96**, 7018, 7031.
[5] K. J. Dignam, A. F. Hegarty, and P. L. Quain, *J.C.S. Perkin II*, 1977, 1457.