Rapid Uncatalysed and Acid Catalysed *ZE*-Isomerisation of Amidoximes

By Kieran J. Dignam and Anthony F. Hegarty*
(*Chemistry Department, University College, Cork, Ireland*)

Summary *NN*-Disubstituted amidoximes, prepared under mild conditions as pure (*Z*) isomers, undergo rapid and complete isomerisation about the carbon–nitrogen double bond in aqueous solution.

Oximes and oxime ethers have a unique place in the chemistry of azomethines because of their apparent resistance to uncatalysed isomerisation.[1] As a consequence of this configurational stability, oxime isomerisation is normally achieved either photochemically or in the presence of strong acids;[2] thus data for the thermal isomerisation and relative stability of the isomers are not generally available. We now report the first isolation, characterisation, and interconversion of (*Z*) and (*E*) isomers (**3** and **4**; $R^1 = H$ or $PhCH_2$) of the related amidoximes.

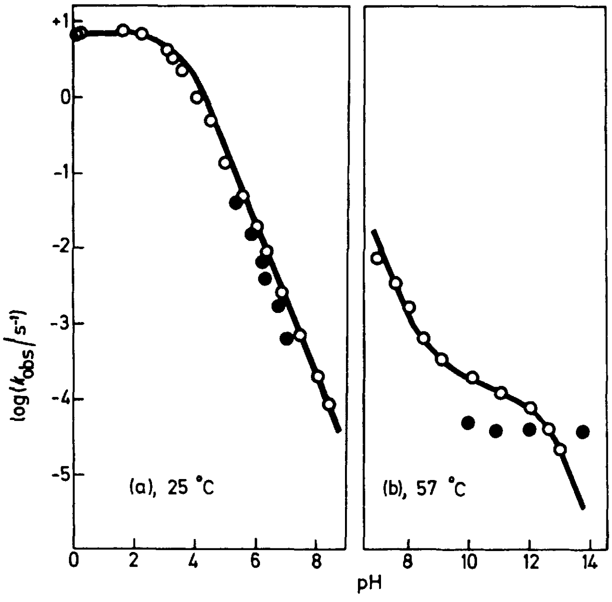
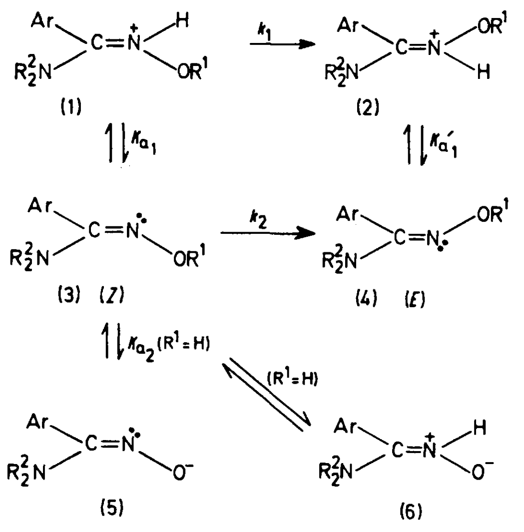


Figure. Plot of the log of the observed rate constants for the isomerisation of (**3**) to (**4**) ($Ar = p\text{-}NO_2C_6H_4$, $R^1 = H$, $R^2{}_2 = -[CH_2]_2O[CH_2]_2-$) in water ($\mu = 1{\cdot}0$, $NaClO_4$) (a) at low pH at 25 °C and (b) at high pH at 57 °C. The closed circles refer to data for (**3**; $R^1 = CH_2Ph$). The lines are theoretical with (a) $k_1 = 6{\cdot}8\ s^{-1}$, $K_{a_1} = 3{\cdot}98 \times 10^{-4}$ and (b) $k_1/K_{a_1} = 1{\cdot}25 \times 10^5\ s^{-1}$, $k_2 = 1{\cdot}32 \times 10^{-4}\ s^{-1}$ and $K_{a_2} = 6{\cdot}6 \times 10^{-13}$.

Treatment of *p*-nitrobenzohydroxamoyl chloride with morpholine at 0 °C gave (**3**; $Ar = p\text{-}NO_2C_6H_4$, $R^2_2 = -[CH_2]O[CH_2]_2-$), m.p. 158—160 °C; δ 3·67 (4H) and 3·28 (4H); λ_{max} 267 nm ($\log \epsilon$ 3·93) and 340 nm (3·30). This single isomer could be recrystallised (from $CHCl_3$–pentane, < 25 °C) but on heating (60 °C, inert solvent) or addition of acid, rapid and complete isomerisation to (**4**) occurred [δ 3·64 (4H) and 2·91 (4H); λ_{max} 264 nm ($\log \epsilon$ 4·10) and 340 nm (3·08)]. Similar pairs of isomers were isolated when other secondary amines (pyrrolidine, *N*-methylaniline) were used and with other hydroxamoyl chlorides ($Ar = p\text{-}ClC_6H_4$ or $2,4,6\text{-}Me_3C_6H_2$).

The effect of pH on the rate of isomerisation of (**3**; $Ar = p\text{-}NO_2C_6H_4$, $R^1 = H$, $R^2_2 = -[CH_2]_2O[CH_2]_2-$) measured using u.v. spectrometry at 25 and 57 °C in water is shown in the Figure. Clearly isomerisation is acid catalysed and rapid ($t_{\frac{1}{2}}$ 0·1 s at pH < 2). In two pH regions (pH < 2 and *ca.* 10), the rate of isomerisation becomes pH-independent. The major reactions in these regions can be attributed to isomerisation of the protonated (**1**) and neutral forms of the oxime (**3**) respectively (see Scheme); (**1**) isomerises to (**2**) > 10^5-fold more rapidly than does (**3**) to (**4**). Consistent with this scheme, the more stable isomer (**4**) has a pK_{a_1}' of



Scheme

2·6, while pK_{a2} is 11·2 (measured spectrophotometrically at 25 °C).

At high pH the rate of isomerisation is inversely proportional to [HO$^-$], showing that isomerisation of the oximate anion (**5**) does not occur to an appreciable extent under these conditions.

It is unlikely that the relatively rapid uncatalysed isomerisation observed for (**3**) occurs *via* the isomeric nitrone (**6**) when R=H, although simple aldo- and keto-nitrones are known to undergo *EZ* isomerisation.[4] This was shown by the similarity in kinetic behaviour of the *O*-benzylamidoxime (**3**, $R^1 = CH_2Ph$) (see Figure, closed circles), which cannot tautomerise to (**6**); at high pH the rate of isomerisation of (**3**, $R^1 = CH_2C_6H_4$) is pH independent since it (unlike **3**, $R^1 = H$) is not converted into (**5**).

Hindered rotation about the carbon–nitrogen single bond (which is expected to have considerable double bond character, as in amidines) is also a potential source of isomerism in amidoximes.[5] However such isomerism is not observed in the present instance, since several of the amidoximes examined are symmetrical (with both R^2 groups identical).

Addition of acid or complexation of the lone pair on nitrogen has been shown to inhibit *EZ* isomerisation of imines which react by a lateral shift mechanism.[6] The acid catalysis observed in the present instance for amidoximes is consistent with a rotation mechanism for isomerisation of (**1**); the electron withdrawing *N*-hydroxy and donating $R^2{}_2N$-groups both serve to reduce the carbon–nitrogen double bond character.

(*Received*, **9*th August*** **1976**; *Com.* **924**.)

---

[1] D. Y. Curtin, E. J. Grubbs, and C. G. McCarty, *J. Amer. Chem. Soc.*, 1966, **88**, 2775; C. G. McCarty in 'The Chemistry of the Carbon Nitrogen Double Bond,' ed. S. Patai, Wiley–Interscience, New York, 1970, p. 383.

[2] J. E. Johnson, E. A. Nalley, Y. E. Kunz, and J. R. Springfield, *J. Org. Chem.*, 1976, **41**, 252; A. Padwa and F. A. Albrecht, *ibid.*, 1974, **39**, 2361.

[3] The configurational assignments are consistent with dipole moment measurements and agree with those reported previously (H. Gozlan, R. Michelot, and R. Rips, *Tetrahedron Letters*, 1975, 859) for the thermodynamically more stable isomer (**4**, $R^1 = H$, $R^2 = Me$).

[4] W. B. Jennings, D. R. Boyd, and L. C. Waring, *J.C.S. Perkin II*, 1976, 610.

[5] A. Dondoni, L. Lunazzi, P. Giorgianni, and D. Macciantelli, *J. Org. Chem.*, 1975, **40**, 2979; O. Exner, V. Jehlička, A. Dondoni, and A. C. Boiceili, *J.C.S. Perkin II*, 1974, 567.

[6] E. A. Jeffrey, A. Meisters, and T. Mole, *Tetrahedron*, 1969, **25**, 741.