Kinetics and Isotope Effects in the Reaction of 4-Nitrophenylnitromethane with Amidines in Toluene

By OTTO ROGNE

(*Norwegian Defence Research Establishment, Division for Toxicology*, N-2007 *Kjeller, Norway*)

Summary The reactions of the deuteriated analogue of 4-nitrophenylnitromethane with alkylamidines in toluene show complex kinetics compared to the corresponding proton transfer reaction due to H–D exchange, making it difficult to obtain reliable isotope effects unless the deuteriated analogue of the base is also used

THE reaction (1) of 4-nitrophenylnitromethane (4-NPNM) with imine bases $NH{=}CR^1R^2$, such as tetramethylguanidine, $NH{=}C(NMe_2)_2$, and *NN*-diethylbenzamidine, $NH{=}CPh{-}NEt_2$, has recently been used for studies of the tunnel effect.[1,2] In solvents of low polarity large kinetic deuterium isotope effects have been observed and attributed to tunnelling.[1,3] As an extension of this work we studied the

reactions of 4-NPNM and [$^2H_2$]-4-NPNM with n-alkylamidines [NH=C(NEt$_2$)R] in toluene using a Canterbury SF-3A stopped-flow spectrophotometer and a transient recorder (Intertechnique Didac 800). Runs were analysed and rate constants calculated by fitting the digitized signal to the first-order rate equation by the LSKIN programme of DeTar.[4] The proton-transfer reaction behaves kinetically according to (1), being first-order in acid and base.[5] In contrast, the deuteron-transfer is kinetically complex, showing systematic deviations from first-order kinetics in runs with the base in excess. The calculated first-order rate constant depends systematically on the proportion of the reaction-time curve analysed, decreasing progressively as more and more of the initial reaction is excluded. These complications made it impossible to obtain accurate values for the deuteron transfer rate constants and hence for the isotope effects.

$$O_2NC_6H_4CH_2NO_2 + NH{=}CR^1R^2 \underset{k_b}{\overset{k_f}{\rightleftharpoons}} O_2NC_6H_4\bar{C}HNO_2\,\overset{+}{N}H_2{=}CR^1R^2 \quad (1)$$

$$O_2NC_6H_4CD_2NO_2 + HN{=}C< \underset{k_2}{\overset{k_1}{\rightleftharpoons}} O_2NC_6H_4\bar{C}DNO_2\,\overset{+}{H}DN{=}C<$$

$$\downarrow k_3$$

$$O_2NC_6H_4CHDNO_2 + DN{=}C<$$

$$O_2NC_6H_4CHDNO_2 + HN{=}C< \underset{k_5}{\overset{k_4}{\rightleftharpoons}} O_2NC_6H_4\bar{C}DNO_2\,\overset{+}{H}_2N{=}C<$$

$$k_6\downarrow \quad \uparrow k_7$$

$$O_2NC_6H_4\bar{C}HNO_2\,\overset{+}{H}DN{=}C< \xrightarrow{k_8} O_2NC_6H_4CH_2NO_2 + DN{=}C<$$

$$O_2NC_6H_4CH_2NO_2 + HN{=}C< \underset{k_{10}}{\overset{k_9}{\rightleftharpoons}} O_2NC_6H_4\bar{C}HNO_2\,\overset{+}{H}_2N{=}C<$$

SCHEME

The complex kinetics of the deuteron-transfer reaction can be accounted for by the H–D exchange mechanism shown in the Scheme. Theoretical runs calculated on the basis of the Scheme by the REMECH programme of De Tar[6] reproduce the experimentally observed deviations from first-order kinetics, and fit the experimental data quantitatively if we assume isotopic rate ratios of *ca.* 10—15. The values of the rate constants in the Scheme, used for calculating theoretical runs, were obtained as follows. Since the proton transfer reaction is free from complications, the forward, k_f^H, and backward, k_b^H, rate constants are known. This gives values of $k_9 = k_f^H$ and $k_5 = k_{10} = k_b^H$. By assuming a value for the isotope effect, equal for the forward and backward reaction (*i.e.* equilibrium isotope effect = 1), values for the forward, k_f^D, and backward, k_b^D, deuterium transfer reaction can be calculated. This gives a value for $k_1 = k_f^D$. In the half-deuteriated species a statistical factor of 2 is assumed such that $k_2 = k_7 = \frac{1}{2}k_b^D$, $k_3 = k_8 = \frac{1}{2}k_b^H$, $k_4 = \frac{1}{2}k_f^H$, and $k_6 = \frac{1}{2}k_f^D$.

The exchange shown in the Scheme cannot occur if the deuteriated analogue of the base is used (ND=C< in place of NH=C<). In agreement with this, runs with excess of deuteriated base showed satisfactory first-order kinetics and gave kinetic isotope effects of 13 ± 1 and 8 ± 0·5 at 25 °C for diethyl-n-butylamidine and diethyl-n-nonylamidine, respectively. Further, the reaction in toluene of 4-NPNM with the base 1,5-diazabicyclo[5.4.0]undec-5-ene, which contains no exchangeable proton, showed the same simple kinetics for both the proton and deuteron transfer reaction and gave an isotope effect of 13 ± 1 at 25 °C.

The magnitude of the effects due to the exchange for a given system will evidently depend on the rate and equilibrium constants concerned, but in principle they might alter the value of the isotopic rate ratios for other bases of the general formula NH=CR^{1}R^2, including tetramethylguanidine for which a high isotopic rate ratio (k_H/k_D = 37·8 ± 1·4 at 30 °C) has been reported in its reaction with 4-nitrophenylnitromethane.[1]

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[1] E. F. Caldin and S. Mateo, *J.C.S. Faraday I*, 1975, **71**, 1876.
[2] C. D. Hubbard and D. Hooper, unpublished work.
[3] E. F. Caldin and C. J. Wilson, *Discuss. Faraday Soc.*, No. 10, 1975, 121.
[4] D. F. DeTar in 'Computer Programs for Chemistry,' Vol. I, ed. D. F. DeTar, Benjamin, New York, 1968.
[5] O. Rogne, unpublished work.
[6] Ref. 4, Vol. II.