Kinetic Deuterium Isotope Effect in Aromatic Substitution

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THE presence of an addition intermediate during nucleophilic aromatic substitution has been confirmed by recent reactions of protic amines.[1] However, little is known about the kinetic deuterium isotope effect of these reactions and this limits our knowledge of the mechanism.

After the discovery of the first genuine kinetic deuterium isotope effect[2] in the reactions of piperidine or [1-^{2}H]piperidine with 2,4-dinitrophenyl phenyl ether in benzene, which was tentatively interpreted as a primary isotope effect,[2] another one was reported by Brieux and his co-workers for reactions of the above amines with 4-chloro-3-nitrobenzotrifluoride in benzene.[3] This isotope effect was definitely interpreted as a primary one, and it was suggested that failure to observe such isotope effects in other similar reactions resulted from the use of too narrow a range of amine concentrations.

Our results throw doubt on this suggestion.[3]

The reactions of piperidine (Pip) or [1-^{2}H]piperidine with chloro-4,7-dinitronaphthalene in benzene at 25° give quantitative yields of *N*-4,7-dinitronaphthylpiperidine. The rate data agree with the equation

$$\text{Rate}/[\text{ArCl}][\text{Pip}] = k_0 + k_{\text{Pip}}[\text{Pip}]$$

in the range 0·046—1·85 M amine. Linear regression analysis gives $k_0 = 1{\cdot}09 \times 10^{-5}$ mole^{-1} l. sec.$^{-1}$ and $k_{\text{Pip}} = 1{\cdot}84 \times 10^{-4}$ mole^{-2} l.^{2}sec.$^{-1}$, which gives $k_{\text{Pip}}/k_0 = 16{\cdot}9$ mole^{-1} l. Moreover, substitution of [1-^{2}H]piperidine (90% deuteriated) for piperidine does not alter the kinetics in the whole concentration range within the 4% experimental error.

As our reaction is no less susceptible to amine acceleration, as measured by the ratio k_{Pip}/k_0 at low amine concentration, and the nucleophile concentration range investigated here is broader than in Brieux' work[3] (0·05—0·63 M), direct comparison can be made. Failure to find an isotope effect in our system makes it clear that the presence of a primary deuterium isotope effect is by no means normal for these reactions, and contrary to Brieux' suggestion, they cannot be considered to proceed by rate-limiting ammonium proton transfer from the addition-intermediate to a base.

While unable to confirm Brieux' predictions, we have found, in agreement with our report,[2] that the displacement of a very poor leaving group like cyclohexyloxy involves a kinetic deuterium isotope effect. These are preliminary results for the reactions of piperidine or [1-^{2}H]piperidine with cyclohexyl 2,4-dinitrophenyl ether in benzene at 100°. Here, in the range 1·0—2·0 M amine concentration, neither elimination nor substitution at the cyclohexyl moiety compete effectively with aromatic substitution and the reaction is wholly amine-catalysed. Moreover, at the highest amine concentration the reaction becomes 1½ times slower on substitution of *N*-deuteriated amine.

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† m.p. 48—49°. Satisfactory elemental analysis, ^{1}H n.m.r. and i.r. spectra support the assigned structures.

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