# The Kinetic Isotope Effect on Proton Transfer from p-Nitrophenol to Imidazole

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The kinetic isotope effect on direct proton transfer from p-nitrophenol to imidazole in aqueous solution at 25 °C was found to be $k_H/k_D = 2.8 \pm 0.3$, in good agreement with maximum isotope effects measured previously for proton transfer between normal acid–base centres in more complex systems.

Proton transfer between normal[1] acid–base centres is generally very fast, and this reaction is therefore commonly regarded as being a diffusion-controlled process, i.e. one in which encounter of reactants, equation (1), or separation of products, equation (3), rather than proton transfer itself, equation (2), is rate-determining. The recent discovery of primary kinetic isotope effects on this process,[2] however,

$$B + HA \rightleftharpoons B \cdot HA \qquad (1)$$

$$B \cdot HA \rightleftharpoons BH \cdot A \qquad (2)$$

$$BH \cdot A \rightleftharpoons BH + A \qquad (3)$$

showed that the proton transfer step can in fact be at least partly rate-determining when the acid and base strengths of the proton donor and proton acceptor are closely matched in the region near $\Delta pK = 0$ [$\Delta pK = pK_a$ (donor) $- pK_a$ (acceptor)]. These isotope effects were found in complex systems where proton transfer follows a strongly endoergonic pre-equilibrium; consequently their interpretation, though not in doubt, is nevertheless not straightforward. We report that we have now observed an isotope effect on direct proton transfer between a simple normal acid–base pair which is in remarkably good agreement with these earlier results.

We made the present measurements by the temperature-jump method with p-nitrophenol, $pK_a = 7.16$,[3] as the proton donor, HA, and imidazole, conjugate acid $pK_a = 6.99$,[4] as the proton acceptor, B. This gave us an acid-base pair with

$\Delta pK$ ca. zero† and also enabled us to work at pH = 7 where contributions to observed relaxation times, $\tau$, from proton transfer through protolysis and hydrolysis reaction pathways are at a minimum.[5] Under these conditions, $\tau$ is a simple function of forward and reverse rate constants, $k_f$ and $k_r$, plus reactant concentrations, equation (5), which, since $k_f/k_r = K$ and $K$ is known, can be recast in terms of just one rate constant and a function of concentrations $f(c)$.

$$HA + B \underset{k_r}{\overset{k_f}{\rightleftharpoons}} A^- + HB^+ \qquad (4)$$
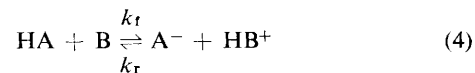
$$\tau^{-1} = k_f([HA] + [B]) + k_r([A^-] + [HB^+])$$
$$= k_f([HA] + [B]) + ([A^-] + [HB^+])/K = k_f f(c) \qquad (5)$$

We monitored the reaction spectrophotometrically, using the absorption maximum of the p-nitrophenolate ion at 395 nm, and measured $\tau$ for series of solutions with approximately constant concentrations of p-nitrophenol, p-nitrophenolate, and hydrogen ion but varying imidazole and imidazolium ion concentrations. The results, displayed in Figure 1, show that $\tau^{-1}$ is the expected linear function of $f(c)$; least squares analysis gave $k_f(H_2O) = (2.71 \pm 0.29) \times 10^8$ dm$^3$ mol$^{-1}$ s$^{-1}$ and $k_f(D_2O) = (0.98 \pm 0.04) \times 10^8$

† This is true in $D_2O$ as well as in $H_2O$ and the equilibrium isotope effect on the overall reaction [equation (4)] is only $K(H_2O)/K(D_2O) = 1.23$; the kinetic isotope effect measured can therefore have little (if any) equilibrium component.
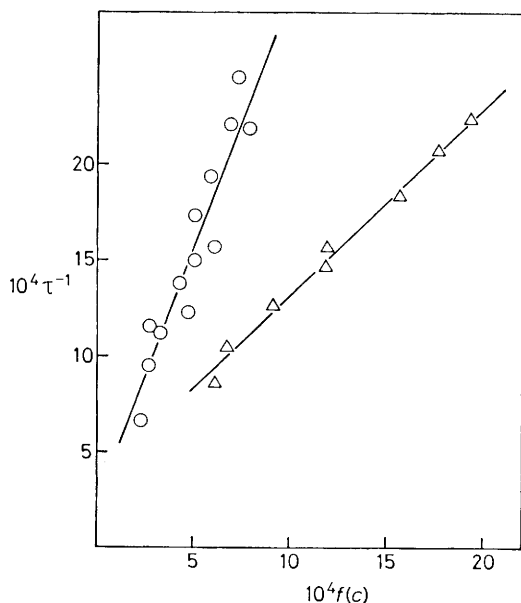
**Figure 1.** Dependence of $\tau$ upon $f(c)$ for the reaction of $p$-nitro-phenol with imidazole in aqueous solution at 25 °C and ionic strength $= 0.10$ mol dm$^{-3}$; circles: $H_2O$, triangles: $D_2O$.

dm$^3$ mol$^{-1}$ s$^{-1}$. These determinations were made with our laser T-jump apparatus operating in the slow mode.[6] We also carried out some measurements with the apparatus in the fast mode[6] using a single more concentrated solution ($H_2O$) for which $f(c) = 97 \times 10^{-4}$ mol dm$^{-3}$; this gave $\tau = 3.7 \times 10^{-7}$ s, in excellent agreement with $\tau = 3.6 \times 10^{-7}$ s obtained by extrapolating the results of the measurements at lower concentrations.

These data give the isotope effect $k_H/k_D = 2.8 \pm 0.3$. This agrees very well with $k_H/k_D = 2.8$, the maximum isotope effect observed at $\Delta pK = 0$ for proton transfer between normal acid–base centres following a pre-equilibrium step in the reaction of methoxyamine with $p$-methoxybenzaldehyde,[2a] and it is also nicely consistent with the maximum isotope effect, $k_H/k_D = 2.5$, found for a similar situation in the hydroxy-aminolysis of benzhydrylidenedimethylammonium ion.[2c] In both of these reactions, proton transfer occurs by the encounter, transfer, and separation sequence of equations (1)—(3). On the other hand, in the only other pre-equilibrium system examined so far, the methoxyaminolysis of phenyl acetate, a preassociation mechanism operates and the maximum isotope effect is somewhat greater, $k_H/k_D = 3.8$.[2b]

## References

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