Secondary Deuterium Isotope Effects in Proton Transfers from 2-Nitropropane

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Kinetic and equilibrium secondary isotope effects have been measured for the deprotonation of 2-nitropropane by hydroxide and acetate ions. Although the Brønsted coefficients deduced lie between 0 and 1, they cannot be regarded as 'degrees of proton transfer' within the formalism of the Marcus theory. The isotope effects are interpreted in terms of two contributions, one of which does not change monotonically along the reaction coordinate. A recently reported dependence of the primary isotope effect upon isotopic solvent composition is discussed in the context of the rule of the geometric mean. A revised value of the equilibrium constant for iodination of the 2-nitropropyl anion is reported.

In proton transfer reactions between carbon acids and oxygen bases, values of the Brønsted coefficient \( \beta = \frac{\Delta G'_2}{\Delta G'_1} \) may depend upon which species is modified to bring about the change in standard free energy.\(^1,2\) We adopt a nomenclature such that \( \beta_1 \) and \( \beta_2 \) refer to substitution in the carbon and oxygen acid–base pairs respectively. Thus Bordwell et al.\(^3\) have reported \( \beta_1 = 1.61 \) for the deprotonation of a series of 1-aryl-2-nitropropanes, whereas Bell and Goodall\(^4\) found \( \beta_2 \approx 0.55 \) for the reaction of 2-nitropropane with acetate and chloroacetate bases. These values have attracted comment regarding the validity of the interpretation of Brønsted coefficients in terms of transition state symmetry.\(^4,5\) Whereas \( \beta_1 \) does not satisfy the requirement \( 0 < \beta < 1 \), the value of \( \beta_2 \) is >0.5 which is as anticipated\(^6\) from the Hammond postulate\(^7\) for a proton transfer with positive standard free energy \( (\Delta G^r > 0) \).

Secondary isotope effects may be used to define isotopic Brønsted coefficients according to equation (1)

\[
\log k'_D/k'_H = \beta^D \log K'_D/K'_H (1)
\]

where \( k'_D/k'_H \) and \( K'_D/K'_H \) are the respective secondary isotope effects on the kinetics and equilibria of proton transfer. Albery et al.\(^8,9\) have recently shown that for the protonation of 3-diazobutan-2-one by carboxylic acids, \( \beta_2 \) and \( \beta_2^D \) are equal and may be regarded as a measure of transition state symmetry within the framework of Marcus theory.\(^9,10\) To test the generality of the identity of normal and isotopic Brønsted coefficients and to examine the use of \( \beta_2^D \) (the isotopic analogue of Bordwell's value)\(^2\) as a 'degree of proton transfer' parameter, measurements of kinetic and equilibrium isotope effects are reported for reaction (2) where

\[
(\text{L}_H)_2\text{HNO}_2 + \text{B}^- \rightleftharpoons (\text{L}_D)_2\text{DNO}_2^- + \text{BH} (2)
\]

L = H or D with hydroxide \( (\Delta G^r > 0) \) and acetate \( (\Delta G^r > 0) \) bases. Isotopic Brønsted coefficients have been determined for a number of other reactions\(^11,12\) although not, as far as the author is aware, involving substitution in the carbon acid.\(^\dagger\)

The following notation is adopted for our 2-nitropropanes: \( 2\text{NP}_0 = (\text{CH}_3)_2\text{CHNO}_2 \) and \( 2\text{NP}_m = (\text{CD}_3)_2\text{CHNO}_2 \). In practice, isotope effect measurements were made on a mixture of \( 2\text{NP}_1 \) and analogues with less deuterium. The mixture is denoted as \( 2\text{NP}_m \) where \( m \) is the atom fraction of deuterium in the 1- and 3-positions. The abbreviation \( 2\text{NP} \) refers to both \( 2\text{NP}_0 \) and \( 2\text{NP}_m \).

EXPERIMENTAL

Preparation of 2-Nitropropanes.—Commercial \( 2\text{NP}_0 \) (Koch–Light) was purified by preparative g.l.c. using a Carbowax 20M column. Subsequent analytical g.l.c. indicated at least 99.95\% purity. \( 2\text{NP}_m \) was prepared by route (3) using the following method. To 7m-aqueous hydroxylamine hydrochloride \( (\text{NH}_2\text{OH}) \) and disodium hydrogen orthophosphate \( (\text{CH}_3\text{COOH}) \) solutions, the pH was adjusted with acetonitrile (30 cm\(^3\)) at 0 °C with 7m-sodium hydroxide solution (15 cm\(^3\)). Portions (1 cm\(^3\)) of \( [\text{H}_2\text{O}] \) acetone (Ryvan) and 7m-sodium hydroxide were added consecutively until 10 g of the former had been consumed. This procedure keeps the pH near 4.5 where the reaction rate is at a maximum.\(^13\) The temperature was held below 10 °C. Ether (20 cm\(^3\)) was then added to dissolve the precipitated acetoxime. After separation, the aqueous layer was extracted with ether (3 × 20 cm\(^3\)). To the combined ether samples was added light petroleum (b.p. 40–60°) (20 cm\(^3\)). After distillation of the ether, the acetoxime crystallized on cooling. A solution of peracetic acid prepared from 87% hydrogen peroxide (7.8 g), acetic anhydride (26.6 g), acetonitrile (100 cm\(^3\)), and concentrated sulphuric acid (3 drops) was added over 48 h to a rapidly stirred and gently refluxing solution of the acetoxime in acetonitrile (200 cm\(^3\)) containing urea (2 g) and disodium hydrogen orthophosphate (78 g).\(^14\) The reaction mixture was then filtered and concentrated.

**References**

water (100 cm$^3$) added. After extraction with dichloromethane (3 x 50 cm$^3$), the combined extracts were washed with saturated aqueous sodium hydrogen carbonate and dried (MgSO$_4$). Solvents were distilled off until 10 cm$^3$ of solution remained.

Details of purification and analysis were the same as for 2NP$_8$. The final yield of 2NP$_8$ was 23%, and $^1$H n.m.r. gave the isotopic assay as $m = 0.92 \pm 0.005$. A sample of 2NP$_8$ prepared by this method was found to have the same rate constants as the purified commercial material.

**Kinetic and Equilibrium Measurements**—All rate and equilibrium constants were determined in water at 25 °C using spectrophotometric methods. For the reaction of 2NP with hydroxide, the formation of the nitro-anions was followed at 222 nm. With acetate, the deprotonation does not run to completion. In this case, the nitro-anions were scavenged with iodine and the disappearance of $I_2^-$ was followed at 533 nm. To calculate the rate constants from the rates of iodination, it was necessary to measure $K_2$, the equilibrium constant for reaction (4).

\[
(\text{Cl}_2\text{H}_2\text{CNO}_2^- + I_2^- \rightarrow (\text{Cl}_2\text{H}_2\text{CNO}_2 + 2I^-) \quad (4)
\]

The isotope effect on the ionization equilibria of 2NP [equation (2)] is the same for all bases. This is because isotopic substitution in only the carbon acid is involved. Equilibrium constants were determined for the deprotonation of 2NP by trishydroxymethylaminomethane (Tris).

Absorbance measurements were made using a Gilford 2400S spectrophotometer. The temperature in the cell compartment was determined using a platinum resistance probe. It was found to be stable to $\pm 0.02$ °C. In the kinetic experiments absorbances were output directly onto paper tape. Measurements on 2NP$_8$ and 2NP$_m$ were carried out at the same time to reduce systematic errors. Reagents were either of AnalAr or Volumetric grade. Water was deionized and distilled.

(a) **Reaction with hydroxide**—$2 \times 10^{-4}$M-2NP was caused to react with $10^{-3}$M-sodium hydroxide. Since precise rate constants are required, it was necessary to exclude carbonate from the reaction mixture. To this end, the sodium hydroxide solutions were prepared in a nitrogen-filled glove box using water distilled under the same gas. Subsequently, samples (2-5 cm$^3$) were transferred to spectrophotometric cells which were sealed with serum caps before being exposed to the air. Reactions were initiated by injecting $2 \times 10^{-4}$M-aqueous 2NP (25 cm$^3$) and were followed for seven half-lives.

(b) **Reaction with acetate**—Buffers with $0.2M \leq [\text{CH}_3\text{CO}_2^-] \leq 0.5M$ and $[\text{CH}_3\text{CO}_2^-] : [\text{CH}_3\text{CO}_2\text{H}] = 19$ were made up from sodium acetate and hydrochloric acid solutions. Observed and predicted pH values agreed to $\pm 0.01$ units. Stock solutions of 2NP in water ($4 \times 10^3$M) were prepared with accurately known concentrations. Samples of these (1-2 cm$^3$) were weighed out into spectrophotometric cells (1 cm path length) together with the same amount of buffer. Scavenging was initiated by the injection of $10^{-3}$M-iodine (12 mm$^3$) in either 0.2M-potassium iodide. This gives an initial iodine concentration of $5 \times 10^{-3}$M and $[I]$ is $5 \times 10^{-3}$ or $10^{-3}$M. To correct for spontaneous loss of iodine in the buffer, a ‘blank’ cell was monitored during the reaction. Buffers and stock solutions were stored at 5 °C between runs. Periodically the latter were analysed for possible decomposition by diluting portions with $10^{-3}$M-sodium hydroxide and determining the anion absorbance.

(c) **Nitro-anion iodination equilibrium**—Solutions of nitro-anion at known concentration were prepared as follows: $2 \times 10^{-3}$M-2NP was dissolved in $10^{-3}$M-sodium hydroxide and after 1 h, when the reaction was complete, the solution was neutralized to pH 8 with $1M$-hydrochloric acid using a glass electrode. To hold the pH near this value, Tris buffer was added to give $[\text{TrisH}^+] = [\text{Tris}] = 10^{-3}$M. The nitro-anion concentration was then determined spectrophotometrically at 222 nm. Under these conditions the anion was found to be stable. The solutions were subsequently made up to 0-3, 0-5, or 0-7M in potassium iodide and known volumes of $10^{-3}$M-iodine in 1x-KI added. Finally, $[I_2^-]$ was determined at 333 nm. The equilibrium was found to be set up very rapidly. From the known concentrations and measured absorbances, $K_2$ may be calculated. No attempt was made to measure the isotope effect on $K_2$.

**Equilibrium with Tris**—Buffers were made up with $1 \leq [\text{TrisH}^+] : [\text{Tris}] \leq 10$ by partially neutralizing 0-55 or 0-6M-Tris with hydrochloric acid of the same concentration. Samples (0-4 cm$^3$) of freshly prepared $5 \times 10^{-3}$M stock solutions of 2NP were weighed into calibrated flasks (10 cm$^3$) and buffer, $10^{-3}$M-hydrochloric acid, or $10^{-3}$M-sodium hydroxide were added. Equilibrium in the buffer was reached within 24 or 48 h at 25 °C and within 1 h for the H$^+$ and OH$^-$ solutions. In the latter cases, the 2NP is entirely in the neutral and ionized forms respectively. We then have equation (5) for the buffers \(A\) where $A$ is the absorbance of 2NP at 222 nm in the indicated solutions.

\[
[\text{(Cl}_2\text{H}_2\text{CNO}_2^-}] = A(\text{buffer}) - A(H^+) 
\]

\[
[(\text{Cl}_2\text{H}_2\text{CNO}_2^-)] = A(\text{OH}^-) - A(\text{buffer}) \quad (5)
\]

**RESULTS**

Standard errors are used throughout. Characteristics of the u.v. spectra for the nitro-anions were found to be: $(\text{Cl}_2\text{H}_2\text{CNO}_2^-)$, $\lambda_{\max} = 222.5$ nm $(10^4$ cm$^{-1}$; $10^{-4}$ mol$^{-1}$ cm$^{-2}$); $(\text{CD}_3\text{H}_2\text{CNO}_2^-)$, $\lambda_{\max} = 221.5$ nm $(10^3$ cm$^{-1}$; $10^{-4}$ mol$^{-1}$ cm$^{-2}$).

(a) **Reaction with Hydroxide**—The proton transfer follows second-order kinetics running to completion with the consumption of 2% hydroxide under the experimental conditions. In view of the precision needed, it is inadequate to take [OH$^-$]$^*$ as constant thereby treating the reaction as pseudo-first order. However, rather than use a complete second-order analysis, it proved more convenient to correct for small departures from first-order behaviour. Where $a$ and $b$ are the initial concentrations of 2NP and hydroxide respectively, application of the condition $a/b \ll 1$ to the usual integrated second-order rate equation leads to expression (7). In this equation $g_H = (a - b) + t$ and $[2NP_e] = a \exp (-b_H^\text{OH} \cdot t)$

\[a(1 - \exp [-(-a)/b_H^\text{OH}]) gb_H^\text{OH}, t is time, and $b_H^\text{OH}$ is the second-order velocity constant. The second term in $g_H$ allows for the changing [OH$^-$]$^*$.

For 2NP$_m$ there is the additional complication that we have several isotopic subspecies in significant proportions which react in parallel (m = 0-92). The Appendix treats...
this situation in the case of each subspecies reacting in a
first-order manner. Thus equation (49) with $c = [2NP]_0$
$n = 6$, $k_D = k_D^{OH}$ and $k_D^{1-}/k_D^{OH} = (k_D^{OH})/k_D^{OH}$ describes the kinetics within the approximation that
[OH$^-$] is invariant. $k_D^{OH}$ is the second-order rate constant
for the deprotonation of 2NP. It may be shown that
allowing [OH$^-$] to change by a small amount leads to
equation (8). In this equation $\tilde{g}_m = (b - a) + a(1 - \exp
\left[-(b - a)k_m^{OH}\right])k_m^{OH}$ where $k_m^{OH} = (1 - m)k_m^{OH} + mk_m^{OH}$. It can be seen that $\tilde{g}_m$ and $\tilde{g}_m$
are analogous [2NP] = $a[1 - (6 - 1)(m)] \exp - (k_m^{OH}) \tilde{g}_m + 6(1 - m) \exp - (k_D^{OH}) \tilde{g}_m/k_m^{OH}$ (8)
factors. To determine optimum values of $k_D^{OH}$ and $k_m^{OH}$,
absorbsance A were fitted to expression (9) by means of a
$A = A_w + (A_0 - A_w)[2NP]/a$ (9)
generalized least squares program. In the former case
[2NP]/a was taken from equation (7) whereas in the latter
equation (8) was used together with the known values of $k_D^{OH}$
and m. A and $A_w$ are initial and final absorbances,
respectively. Residuals were rarely greater than 0.002
units. Table 1 summarizes the results of nine determin-
ations of the secondary isotope effect. The present value
Table 1

<table>
<thead>
<tr>
<th>Kinetic isotope effect (OH$^-$)</th>
<th>1 = 25-03 °C; Ionic strength μ = 10$^{-2}$m</th>
<th>$k_D^{OH}$/1 mol$^{-1}$ s$^{-1}$</th>
<th>$k_D^{1-}$/1 mol$^{-1}$ s$^{-1}$</th>
<th>$k_D^{OH}/k_D^{1-}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.360</td>
<td>0.323</td>
<td>0.896</td>
</tr>
<tr>
<td></td>
<td></td>
<td>±0.001</td>
<td>±0.001</td>
<td>±0.002</td>
</tr>
</tbody>
</table>

of $k_D^{OH}$ is in reasonable accord with previous determinations
[Gold and Grist, 18, 0-352 (±0-003) 1 mol$^{-1}$ s$^{-1}$ at $μ = 0.1$m;
Bell and Goodall, 3 0-316 (±0-014) 1 mol$^{-1}$ s$^{-1}$ at $μ = 0.2$m].
The observed differences may be a salt effect.

(b) Reaction with Acetate.—For the iodination of 2NP in
acetate buffers, we may outline the mechanism as in
reaction (10). First-order velocity coefficients are shown.

$$(CH_3)_3CNO_2^+ + (CH_3)CO_2H \rightarrow (CH_3)_3CNO_2 + (CH_3)CO_2^-$$(10)

These are dependent upon concentrations of other species in
the system. In particular equation (11) holds and

$$k_1 = k_A[CH_3CO_2^-] + k_D[OH^-] + k^b$$

where $[I_1^-] = [I_1^-] + [I_2^-]$. The rate constants $k_A$, $k_D^{OH}$, and $k^b$ describe the deprotonation of 2NP
by acetate, hydroxide, and water respectively and $k_A$ is
the second-order rate constant for iodination of the nitro-
acan. The buffer composition and hence $k_1$ was essentially
constant for each run. It may be shown that only when
iodination is irreversible ($k_2/k_1 > 1$) and scavenging
limitingly efficient ($k_2/k_1 < 1$) will the rate of reaction be
independent of $[I_1^-]$. Under these conditions the observed
rate constant is $k_1$. However in practice, the iodination of
2NP is only approximately zero order in iodine$^3$ and
similar behaviour has been observed for nitromethane. 20
In view of this, it is necessary to treat the kinetics in some
detail.

18 V. Gold and S. Grist, J. C.S. Perkin II, 1972, 89.
Medd., 1932, 1, 1.

The validity of the condition $k_1/k_2 > 1$ was tested in the following way. A solution of $2 \times 10^{-4}$ m-nitro-anion at pH 8
was prepared as described in the Experimental section (c).
To a sample in a spectrophotometric cell was added enough
iodine in potassium iodide solution to give $[I_1^-] = 2 \times 10^{-6}$
in the absence of reaction but however rapid the mixing,
it was impossible to measure the decay of $I_1^-$. Thus we can
write $2 \times 10^{-4}k_2 > 1$ s$^{-1}$ or $k_2 > 5 \times 10^2$ mol$^{-1}$ s$^{-1}$. To estimate $k_1$, it is necessary to consider the equilibrium
(12) and we have equation (13). The dissociation constants

$$(CH_3)_3CNO_2 + CH_3CO_2^- \rightarrow k_3$$

$$k_3[CH_3CO_2^-] + CH_3CO_2H$$

$$(12)$$

$$k_1/k_3 = K_{I_1^-}[I_1^-]$$

$$(13)$$

of 2NP$^{18,22}$ and acetic acid$^{23}$ give the equilibrium constant
$K_1 = 1 \times 10^{-3}$. From experiment, $k_1 \leq 6 \times 10^2$ s$^{-1}$
(Table 2) and we know the buffer ratio under the reaction
conditions. Using these values in equation (13) gives
$k_1 < 3 \times 10^9$ s$^{-1}$. Combining the limits on $k_1$ and $k_2$ yields relation (14) and the condition $k_1/k_2 > 1$ is
satisfied to high accuracy down to at least $[I_1^-] = 5 \times 10^{-6}$.

$$k_1/k_2 > k_1[I_1^-]/[I_1^-] > 2 \times 10^6[I_1^-]$$

Having demonstrated the efficiency of scavenging, we
ascribe the dependence of the observed rate on $[I_1^-]$ to
the reversibility of the second step in equation (10). Further,
the inequalities $k_2 > k_1$ and $k_2 > k_1$ may be combined to
give the relation $k_1 + k_2 > k_1 + k_2$. This condition
requires that the second equilibrium is set up much more
rapidly than the first and hence the nitro-anions and the
iodo-derivatives are present in equilibrium proportions
during the reaction. Thus from equation (4) we may
write (15) and we also have equation (16). Using the

$$\frac{[I_1^-]}{[I_1^-]} = \frac{K_1[I_1^-]}{K_1[I_1^-]}$$

$$K_1 = [I_1^-][I_1^-]$$

stochiometric relationships (17) and (18) together with

$$[2NP]_0 = [2NP] + [I_1^-][I_1^-] + [I_1^-][I_1^-]$$

$$[I_1^-] = [I_1^-] + [I_1^-]$$

equations (15) and (16) we can relate the change in [2NP] to
the observed change in $[I_1^-]$ by expression (19). Under
$$[2NP]_0 - [2NP] = \frac{[I_1^-] - [I_1^-]}{1 + \frac{1}{[I_1^-]} + \frac{[I_1^-]}{[I_1^-]}}$$

the experimental conditions $[I_1^-]$ is effectively constant.
Values of $K_1$ are discussed below and $K_2 = 713$ l mol$^{-1}$.$^{24}$
Equation (19) relates [2NP] and $[I_1^-]$ rather than a simple
linear expression because all the 2NP which ionizes is not
iodinated.

By combining equations (13), (15), and (17) with the rate
law (20) it may be shown that for all but the last 10% of

$$-d[2NP]/dt = k_1[2NP] - k_1[CH_3]CNO_2^-$$

23 G. Kortum, W. Vogel, and K. Andrusow, ' Dissociation
Constants of Organic Acids in Aqueous Solution,' Butterworths,
the iodination, [2NP] follows a first-order course which is characterized by $k_1$ to within 0-1%.

Consequently, after subtracting a small contribution for spontaneous loss of iodine in the 'blank' cell (<2% of the rate), absorbances for 90% reaction were fitted to equation (21) where

$$A = A_0 - F[2NP]_0(1 - \exp - k_1t)$$  \hspace{1cm} (21)

equation (22) applies and $\varepsilon$ is the extinction coefficient of $F = (1 + [K_+/I^-])(1 + [I^-]^2/[K_A])$ \varepsilon  \hspace{1cm} (22)

$I_2^-$. Residuals were invariably less than 0-003 units. The correction term, $([I^-]^2/K_A)$, reaches a maximum value of 0.01. The same kinetic treatment was used for both 2NP$^-_m$ and 2NP$^-_o$. This is because, in contrast to the hydroxide reaction, only 0.25% of 2NP$^-_m$ is deprotonated and hence the isotopic composition is constant throughout the iodination. The observed isotope effect is corrected by using equation (50) (see Appendix).

To obtain $k_A$, the other contributions to $k_1$ are required [equation (11)]. The known values, $K_{H^{37}} = 0.361 \pm 10^3$ s$^{-1}$ and $[OH^-] = 1.1 \times 10^{-8}$ M together with the estimate, $h_0 = 4 \times 10^9$ s$^{-1}$ [give $h_A = 4.0(8.9 - 8 \times 10^9)/[CH_3CO_2^-]$]. Since the correction to $k_1$ is never larger than 3% and the dependence of the secondary isotope effect on the base is small, a value of $h_0/\varepsilon$ for each experiment was evaluated directly from equation (25). Subscripts $H$, $M$, and $D$ show

$$h_0/\varepsilon = h_0/[CH_3CO_2^-]_H/[H_2O][CH_3CO_2^-]_D$$  \hspace{1cm} (23)

the isotopic composition to which the rate constants or concentrations refer. Table 2 summarizes the kinetic data for acetate. The mean value of $10^6 k_A$, 2.64 (±0.03) M$^{-1}$ s$^{-1}$, is lower than 3.02 (±0.14) M$^{-1}$ s$^{-1}$ as found by Bell and Goodall. Independent measurements carried out in this laboratory using 2NP$^-_o$ prepared by spinning band distillation give $10^6 k_A = 2.71 (±0.1)$ M$^{-1}$ s$^{-1}$. The mean isotope effect $h_A/h_A$ is 0.907 ± 0.007. Uncertainties in the composition of the stock solutions are included in the standard error.

Table 2

<table>
<thead>
<tr>
<th>$[\text{CH}_3\text{CO}_2^-]_M$</th>
<th>$\mu$</th>
<th>$N$</th>
<th>$10^6 k_A$</th>
<th>$10^6 h_A$</th>
<th>$h_A/h_A$</th>
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<tbody>
<tr>
<td>0.0037</td>
<td>0.1</td>
<td>3</td>
<td>2.57</td>
<td>2.86</td>
<td>0.917</td>
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<tr>
<td>0.0407</td>
<td>0.15</td>
<td>4</td>
<td>±0.03</td>
<td>±0.03</td>
<td>±0.005</td>
</tr>
<tr>
<td>0.1802</td>
<td>0.2</td>
<td>2</td>
<td>±0.04</td>
<td>±0.02</td>
<td>±0.004</td>
</tr>
<tr>
<td>0.2317</td>
<td>0.25</td>
<td>4</td>
<td>±0.04</td>
<td>±0.02</td>
<td>±0.004</td>
</tr>
</tbody>
</table>

Equation (21): $K_2 = 2.6 \times 10^6$ mol$^{-1}$; $K_3 = 713$ mol$^{-1}$; $\varepsilon = 2.55 \times 10^4$ m$^{-1}$ mol$^{-1}$ (from ref. 24).

Table 3

<table>
<thead>
<tr>
<th>Values of $K_2$</th>
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<tr>
<td>$t = 25^\circ C$</td>
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<tr>
<td>$[I^-]/[M]$</td>
</tr>
<tr>
<td>$10^6 k_A/M$</td>
</tr>
</tbody>
</table>

(c) Nitro-anion Iodination Equilibrium.—Table 3 gives values of $K_2$. Each is the mean of three determinations.

We may compare the final value, $K_2 = 2.6 \times 10^6$ mol$^{-1}$, with the potentiometric measurements of Bell and Gelles. They determined the equilibrium constant for reaction (24)

$$(\text{CH}_3)_2\text{CHNO}_2 + I_2 \rightleftharpoons (\text{CH}_3)_2\text{CHNO}_2 + I^- + \text{H}^+$$  \hspace{1cm} (24)

which gives $K_2 = 3 \times 10^6$ mol$^{-1}$ when combined with $K_3$ and the acid dissociation constant for 2NP$^-$. We attempted to study equilibrium (24) by the spectrophotometric determination of I$^-$. The result was rendered impractical by the oxidation of I$^-$ to I$_2$ by 2NP. Use of the value $K_2 = 3 \times 10^6$ mol$^{-1}$ in equation (21) gave a significantly lower value to the kinetic data. It is also notable that Bell and Gelles obtained more precise results for the iodination of ketones than for the nitroalkanes. In the direct determination of $K_2$, no slow proton transfer step is involved so the equilibrium is set up very rapidly and problems of oxidation do not arise.

(d) Equilibrium with Tris.—Equilibrium constants were calculated from equation (25) where the activity coefficient

$$K' = \frac{[\text{CL}_4]^2\text{CHNO}_2^-][\text{Tris}^+]}{[\text{CL}_3]^2\text{CHNO}_2^-][\text{Tris}]}$$  \hspace{1cm} (25)

product $\Gamma$ was evaluated using expression (26). Small

$$\log \Gamma = -1.02 (1 + \mu)$$  \hspace{1cm} (26)

corrections were applied to the Tris buffer ratio to allow for the ionization of 2NP. Values of $K'_{H}$ showed no systematic pH dependence. Results are summarized in Table 4. Combining the mean value of $K'_{H}$ with the

Table 4

<table>
<thead>
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<th>Equilibrium isotope effect</th>
</tr>
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<tr>
<td>$t = 25-0^\circ C$; $C' = [\text{Tris}] + [\text{Tris}^+]$</td>
</tr>
<tr>
<td>$CT/H$</td>
</tr>
<tr>
<td>0.12</td>
</tr>
<tr>
<td>0.24</td>
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</table>

dissociation constant $^{27}$ for Tris$^+$ ($pK_4 = 8.07$) gives p$pK_4 = 7.72 (±0.02)$ for 2NP. This is in excellent agreement with the values 7-68 (±0.03) and 7-7-7 obtained potentiometrically. $^{23}$ The mean value of $K_{H}/K_{H}$ is corrected by the equilibrium analogue of equation (50) (see Appendix) to give the result $K_{H}/K_{H} = 0.77 (±0.01)$.

DISCUSSION

Table 5 summarizes the secondary isotope effect data. $\beta_0^p$ is obtained by using equation (1) and $\Delta pK_a = 7-72 - pK_a(BH)$ $^{22}$ [equation (2)]

Table 5

<table>
<thead>
<tr>
<th>Collected results</th>
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<tbody>
<tr>
<td>$h_0/\beta_0^p$</td>
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<tr>
<td>B$^-$</td>
</tr>
<tr>
<td>OH$^-$</td>
</tr>
<tr>
<td>CH$_3$CO$_2^-$</td>
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</tbody>
</table>

(a) Isotropic and Normal Brønsted Coefficients.—Our value of $\beta_0^p = 0.43$ for OH$^-$ differs from the result $\beta_0 = 1.61$ obtained by Bordwell et al. for the deprotonation of 1-aryl-2-nitropropanes by OH$^-$-OMe$^-$. It is thus not true that in general isotopic and normal Brønsted coefficients are the same for carbon acids. This contrasts with an increasing body of evidence in
the case of oxygen acids.\textsuperscript{4,5,8} Further, $\beta_\text{p}^\text{D}$ for acetate is significantly different from the value $\beta_\text{p} = 0.55$ ($\pm 0.02$) obtained by Bell and Goodall \textsuperscript{3} for the reaction of 2NP\textsubscript{o} with acetate and chloroacetate.

(b) Application of Marcus Theory.—A prima facie interpretation of the $\beta_\text{p}^\text{D}$ versus $\Delta pK_a$ data in Table 5 might be that the ‘degree of proton transfer’ is 0.41 for $-8 < \Delta pK_a < 3$ and the increasing product-like character of the transition state predicted from the Hammond postulate \textsuperscript{7} as $\Delta pK_a$ becomes more positive is small compared with experimental error. This view is inconsistent with the Marcus treatment of proton transfer reactions \textsuperscript{5,9,10} as we now show. For the equilibria (27) Marcus gives equations (28) and (29).

$$\text{AH} + \text{B}^- \xrightleftharpoons{W_p} (\text{AHB}^-) \xrightarrow{\Delta G^\circ} (\text{A}^-\text{HB}) \xrightarrow{\Delta G^\circ} \text{A}^- + \text{BH}$$

$$\Delta G^\circ = W_R + \lambda(1 + \Delta G_K^\circ)/\lambda/4$$

$$\Delta G^\circ = W_R + \Delta G_K^\circ + W_P$$

We follow the nomenclature of Albery et al.\textsuperscript{4} who describe the theory in more detail. The species in parentheses in equilibria (27) are collision complexes with standard free energies of formation, $W_R$ and $-W_P$. $\lambda/4$ is the standard free energy of activation for their interconversion, $\Delta G^\circ$, is zero. To express a second-order rate constant $k^\text{H}$ in terms of $\Delta G^\circ$ it is necessary to choose a standard state. Unit mole fraction seems most appropriate if for no other reason than because in expression (30) the pre-exponential factor is ca. 10\textsuperscript{14} 1 mol\textsuperscript{-1} s\textsuperscript{-1} as required by

$$k^\text{H} = \frac{(RT/\lambda[H_2O]) \exp -\Delta G^\circ/RT}{RT\lambda[H_2O]}$$

Marcus.\textsuperscript{9} We also need statistical factors. Where there are $q$ equivalent basic sites on $\text{B}^-$ and $p$ equivalent acidic sites on $\text{BH}$ (equation (2)) standard free energies are given by equations (31) and (32). The symbols

$$\Delta G^\circ = -RT\lambda(\ln k^\text{H}/\lambda) - \ln \left\{\frac{RT/\lambda[H_2O]}{RT\lambda[H_2O]}\right\}$$

$$\Delta G^\circ = -RT\lambda(\ln \lambda - 2\lambda pK_a)$$

$R$, $\lambda$, $h$, and $T$ have their usual significance and [H\textsubscript{2}O] = 55.6 M.

When $W_R$, $W_P$, and $\lambda$ are invariant to changes in $\Delta G^\circ$, Marcus, by appealing to model proton transfers, interprets the Bronsted coefficient as a transition state symmetry parameter. Under the same conditions he gives equation (33) and the theory may then be regarded as an algebraic form of the Hammond postulate combined with Leffler’s interpretation of Bronsted coefficients. Since equation (28) is only valid for $-\lambda < \Delta G^\circ \leq \lambda$, the restriction, $0 < \beta < 1$ is imposed on equation (33). The value, $\beta_\text{p} = 1.61$,\textsuperscript{8} being outside this range, has been discussed variously in terms of changing $\lambda$ or changing $W_R$ and $W_P$.\textsuperscript{4}

We proceed to examine whether $\beta_\text{p}^\text{D}$ satisfies equation (33). If this is the case, we have from equation (28), equation

$\Delta G^\circ = W_R + \lambda(1 - \beta_\text{p}^\text{D})^2$ (34)

for the reverse reaction equation (35). For

$\Delta G^\circ - \Delta G^\circ = -W_P + \lambda(1 - \beta_\text{p}^\text{D})^2$ (35)

$\text{OH}^-$, $W_P$ vanishes since HB [equation (27)] is simply a solvating water molecule and $\lambda$ may be evaluated using equations (31), (32), and (35). We take $q = 1$ and $p = 2$. Values of $k^\text{H}$ and $\Delta pK_a$ for 2NP\textsubscript{o} were selected although use of the corresponding quantities for 2NP\textsubscript{i}, or indeed different statistical factors does not change the result of the analysis. Knowing $\lambda$, we may use equation (35) with estimates of $W_P$ to predict values of $\beta_\text{p}^\text{D}$ for other bases with known rate and equilibrium constants. Carrying through this procedure we obtain $\beta_\text{p}^\text{D} = 0.53$ ($\pm 0.02$) for acetate ($q = 2$, $p = 1$) when $W_P$ is zero. Larger values of $-W_P$ only serve to increase $\beta_\text{p}^\text{D}$ and it is unlikely that $-W_P < 0$. Hence observed $[k^\text{H}$ (Table 5)] and predicted (0.53) values of $\beta_\text{p}^\text{D}$ for acetate do not agree and thus equation (33) does not hold for this parameter. Since the validity of (33) and the interpretation of $\beta$ in terms of transition state symmetry have the same basis (constant $W_R$, $W_P$, and $\lambda$) the ‘degree of proton transfer’ is not simply related to $\beta_\text{p}^\text{D}$. This result is unchanged by using a standard state of unit molarity for $\Delta G^\circ$. Thus like $\beta_\text{p}$, $\beta_\text{p}^\text{D}$ does not give us transition state symmetry despite the fact that $0 < \beta_\text{p}^\text{D} \leq 1$.

Although there are insufficient data to carry out a complete Marcus analysis for changes in $B^-$ [equation (2)], it is interesting to adopt a simplified approach by neglecting $W_P$ and $W_R$ [equations (28) and (29)]. Thus $\lambda$ calculated from $k^\text{H}$ and $\Delta pK_a$ for acetate can be used to predict $\beta$ [equation (33)] and $k^\text{H}$ [equation (28)] for any base of known $pK_a$. Results of this approach are given in Table 6. We anticipate that for hydroxide the transition state will be somewhat nearer to the reference.

<table>
<thead>
<tr>
<th>B⁻</th>
<th>$\Delta pK_a$</th>
<th>$\beta$</th>
<th>$k^\text{H}$</th>
<th>$k^\text{H}$</th>
<th>$h_\text{H}/k_D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>B⁻</td>
<td>$\Delta pK_a$</td>
<td>$\beta$</td>
<td>$k^\text{H}$</td>
<td>$k^\text{H}$</td>
<td>$h_\text{H}/k_D$</td>
</tr>
<tr>
<td>OH⁻</td>
<td>-8.03</td>
<td>0.43</td>
<td>4.9 x 10⁻¹</td>
<td>3.6 x 10⁻¹</td>
<td>7.4</td>
</tr>
<tr>
<td>CH₃COO⁻</td>
<td>-2.97</td>
<td>0.53</td>
<td>2.6 x 10⁻⁶</td>
<td>2.6 x 10⁻⁶</td>
<td>7.6</td>
</tr>
</tbody>
</table>

* Predicted. † Observed. ‡ Primary isotope effects determined by Bell and Goodall.\textsuperscript{3}

 actants, whereas for acetate the ‘degree of proton transfer’ is somewhat >0.5. This conclusion is not inconsistent with the primary isotope effects which suggest that both transition states are not far from symmetrical. Predicted and observed values of $h_\text{H}^\text{D}$ are in remarkable agreement considering both the simplicity of the treatment and the extrapolation over 11 $pK_a$ units. Further, the predicted $\beta$ for acetate is close to the experimental value, $\beta_\text{p} = 0.55$ ($\pm 0.02$). In the case of hydroxide, the equality of $\beta_\text{p}$ (Table 5)
with the value of $\beta$ anticipated by the Marcus theory can only be fortuitous since as we have already shown $\beta^P$ does not obey equation (33).

(c) Interpretation of Secondary Isotope Effects.—We now consider the secondary isotope effects in the light of a model needed to describe the influence of normal substituent changes in the nitroalkanes. To set up the model, three items of evidence are invoked. (1) $pK_a$ values for the series CH$_3$HNO$_2$, CH$_2$CH$_2$NO$_2$, and (CH$_3$)$_2$CHNO$_2$. (2) Relative rate constants for the nitroalkanes in item (I) as a function of the $pK_a$ of the deprotonating base. (3) Bordwell’s Bronsted coefficient for the 1-aryl-2-nitroalkanes.$^5,30$

The $pK_a$ values in item (I) are not in accord with the CH$_3$ group acting as an electron donor in the inductive mode (Table 7). However, as has previously been pointed out,$^8$ the order may be correlated with the familiar lowering of standard free energy$^{31}$ which occurs in processes involving the formation of a $\pi$ bond when CH$_3$ replaces hydrogen on an $\alpha$-carbon atom. (This effect may arise from hyperconjugation.) We deduce that in the nitro-anions, structure (II) is dominant over structures of type (I). Table 7 collects together relative rate constants for the deprotonation of nitromethane, nitroethane, and 2NP. Values for each base are taken from a common source where possible. Here, in contrast to the equilibrium case, the $\alpha$-methyl groups behave inductively although this effect tends to become less pronounced for weaker bases. Thus, it is necessary to invoke a transition state model in which resonance structures of type (III) are dominant. (For simplicity, we have omitted the base and show only one of the two possible resonance forms involving the nitro-group.) Structures (IV) are however becoming relatively more important for bases of low $pK_a$ and since (II) is dominant in the product, this is in accordance with the Hammond postulate. Evidently proton transfer runs ahead of the delocalization of charge into the nitro-group. If this were not the case, structures (III) and (IV) would have the same relative weights as (I) and (II) at every point along the reaction co-ordinate.

### Table 7

<table>
<thead>
<tr>
<th>Nitroalkane</th>
<th>$pK_a$</th>
<th>2NP</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$HNO$_2$</td>
<td>5.20</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>CH$_2$CH$_2$NO$_2$</td>
<td>9.25</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>(CH$_3$)$_2$CHNO$_2$</td>
<td>15.75</td>
<td>1</td>
<td>37</td>
</tr>
</tbody>
</table>

* Estimate. All values refer to 25 °C in water.

A similar conclusion has been reached by Bordwell et al.$^2$ and we may use their findings for the deprotonation of 1-aryl-2-nitropropanes by OH$^-$–MeO$^-$ to elaborate on our model. In these compounds, the reaction centre is insulated by a methylene link from the direct resonance effects of substituents in the phenyl group. Consequently, only inductive changes modify the rate and equilibrium constants. The value $\beta_1 = 1.61$ therefore implies that there is a greater charge on the $\alpha$-carbon atom in the transition state than in the product. This is entirely feasible since the transition state is closer to (III) than (IV) whereas the product is nearer to (II).

It is helpful to express the model in diagrammatic form. The Figure shows the charge on the $\alpha$-carbon atom ($Q$) and the order of $\pi$ bonding ($N$) as schematic functions of the extent of proton transfer ($R$). Thus the

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values of $Q$ and $N$ at $R = 1$ are determined by the relative weights of structures (I) and (II) respectively. Values of $R$ for hydroxide and acetate transition states are taken as $\beta$ in Table 6. For both these bases, and indeed for all bases in Table 7, $Q > N$ because (III) dominates (IV). Further, $Q$ in the region of the hydroxide transition state is drawn greater than $Q$ at $R = 1$ as required by $\beta_1$. Finally, we have imposed the constraint, $R = Q + N$.

It is often helpful to discuss secondary isotope effects in the same terminology as is employed for normal substituent effects and we adopt this approach here. Thus in proton transfer equilibria, deuterium remote from the reaction centre usually behaves as an electron donor.\textsuperscript{38-41} Our result, $K_D/K_H = 0.77$, fulfills this expectation. This value is close to the isotope effect, $K_D/K_H = 0.76$, found for the dissociation (36) of the dimethylammonium ion,\textsuperscript{41} but here the charge in

$$\text{(Cl$_2$)$_2$NH$_2^+$} \rightleftharpoons \text{(Cl$_2$)$_2$NH} + \text{H}^+ \quad (36)$$

charge at the reaction centre is much greater than for 2NP. Thus the value $K_D/K_H = 0.77$ is too low to be ascribed to an inductive effect only and it appears that hyperconjugation (or some other effect arising from the presence of the $\pi$ bond) is involved. We may therefore consider that the secondary isotope effect has two contributions, one depending on $Q$ and the second upon $N$. The Figure shows how these quantities change along the reaction co-ordinate. The inductive component is larger in the kinetic isotope effect than in the equilibrium effect. Therefore we may ascribe the failure of $\beta_1^D$ as a transition state symmetry parameter to the non-monotonic behaviour of $Q$ with respect to proton transfer.

The complexity of both isotope and normal substituent effects in the nitroalkanes arises ultimately from the extensive electronic redistribution which accompanies proton abstraction. This contrasts with the simpler nature of changes occurring in the base. Thus for acetate, it seems likely that the charge on the carboxylic carbon atom changes monotonically along the reaction co-ordinate. It is therefore understandable that $\beta_1^D$ agrees with the prediction of transition state symmetry from the (simplified) Marcus theory.

\textbf{(d) Solvent Isotope Dependence of the Primary Isotope Effect.—Gold and Grist}\textsuperscript{18} have recently reported that the primary kinetic isotope effect for 2NP is dependent upon the isotopic composition of the solvent. We point out that the phenomenon may be interpreted as a manifestation of the breakdown of the "rule of the geometric mean."\textsuperscript{43,43} In the case of reaction with hydroxide we may also argue that the effect is consistent with an approximately symmetrical transition state.

The usual treatment of solvent isotope effects\textsuperscript{44,45} assumes that the fractionation factor $\phi$ for a given site does not depend upon whether other sites in the system are occupied by $H$ or $D$. In other words, isotope effects on $\phi$ are neglected. Abandoning this assumption, we may define two different fractionation factors for exchange in the solvent [equation (37)]. Thus allowing

$$\text{H}_2\text{O} \rightleftharpoons \text{HOD} \rightleftharpoons \text{D}_2\text{O} \quad (37)$$

for statistical factors, processes (38) and (39) have

$$\text{H}_2\text{O} + \frac{1}{2}\text{D}_2\text{O} \rightleftharpoons \text{HOD} + \frac{1}{2}\text{H}_2\text{O} \quad (38)$$

$$\text{HOD} + \frac{1}{2}\text{D}_2\text{O} \rightleftharpoons \text{D}_2\text{O} + \frac{1}{2}\text{H}_2\text{O} \quad (39)$$

equilibrium constants $2\phi_H$ and $\phi_D/2$ respectively. We then have equations (40) and (41) where $K$ is the equilibrium constant for $\text{H}_2\text{O} + \frac{1}{2}\text{D}_2\text{O} \rightleftharpoons 2\text{HOD}$ and has the value 3.76\textsuperscript{46} at 25 °C. Consequently, $\phi_H = 0.97$ and $\phi_D = 1.03$. (The usual approximation puts $\phi_H = \phi_D = 1$.)

For the reaction of (CH$_3$)$_2$CNO$_2$ with $\text{OH}^-$, we consider the simplest model (42) and show the primary fractionation factors in the case of $\text{H}_2\text{O}$ as solvent.

$$\phi_{\text{HH}} \frac{\phi_{\text{HD}}}{\phi_{\text{DP}}} = 1 \quad (40)$$

$$\phi_{\text{HH}} = \frac{1}{2}K^{1/2} \quad (41)$$

Thus allowing from the data of Gold and Grist,\textsuperscript{18} we have equation (44).

$$\frac{K_D}{K_H} \frac{K_D}{K_H} \frac{K_D}{K_H} = 1.04 \pm 0.01 \quad (44)$$

Thus the solvent isotope dependence of the primary kinetic isotope effect lies about halfway between unity.


\textsuperscript{47} A. J. Kresse, Pure Appl. Chem., 1964, 8, 243.

and the corresponding equilibrium value. This is satisfactory for a process with a near symmetrical transition state. Finally, we note that the solvent isotope effects for \((\text{CH}_2)_2\text{CHNO}_2\) and \((\text{CH}_2)_2\text{CDNO}_2\) will be slightly different.

**APPENDIX**

**Kinetics for the Reactions of Statistical Isotopic Mixtures.**

The species, \(\text{XL}_n\) has \(n\) equivalent non-exchanging sites which can be occupied by H or D. The constituent isotopic subspecies, \(\text{XD}_n\text{H}_{n-r}\), undergo a first-order reaction in which all sites remain equivalent.

**Symbols.** Symbols used are \(c = \lbrack \text{XL}_n\rbrack\), \(k_r = \) first-order rate constant for \(\text{XD}_n\text{H}_{n-r}\), \(k_H = k_r\), and \(k_D = k_r\). The following assignments apply at time \(t = 0\): \(m = \) atom fraction of D in \(\text{XL}_n\), \(c_m = \) observed first-order velocity coefficient, \(a = c\), and \(a_r = \lbrack \text{XD}_n\text{H}_{n-r}\rbrack\).

The system is characterized by equation (45) and the assumption of a statistical distribution of isotopes at \(t = 0\) leads to expression (46). If every deuteriation

\[
\frac{a_r}{a} = \frac{\pi 10^n(1-m)^{n-r}}{r!(n-r)!}
\]

(46) gives rise to the same isotope effect (constant \(k_r\)), equation (47) follows. Combination of equations (45)—(47)

\[
k_r = k_H^{1/n}k_D^{(1-r/n)}
\]

(47) yields (48) and when \(m\) is close to unity this simplifies to

\[
c = a \sum_{r=0}^{n} \frac{\pi 10^n(1-m)^{n-r}}{r!(n-r)!} \exp \left( k_H^{1/n}k_D^{(1-r/n)}t \right)
\]

(48)

First-order velocity coefficients may be found by

\[
c = a \left( [1 - n(1 - m)] \exp \left( k_D t \right) + n(1 - m) \exp \left( k_D^{1/n}k_H^{1/n} t \right) \right)
\]

(49) evaluating \(-d\ln c/dt\) from equation (48) and in particular \(k_m\) is given by equation (50). The similarity of equation

\[
k_m = k_H \left[ 1 - m + m \left( \frac{k_D}{k_H} \right)^{1/n} \right]
\]

(50) to the expressions of fractionation factor theory \(44,45\) arises from the use of analogous assumptions.

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