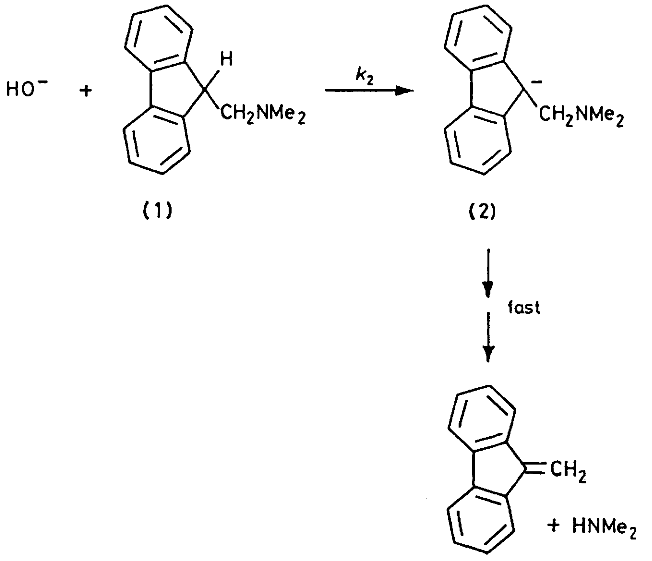
The Brønsted Relationship, Hydroxide Solvent Isotope Effects, and Isotope Exchange in *E*1cB Elimination of 9-(Dimethylaminomethyl)fluorene

By **Richard P. Kelly, Rory A. More O'Ferrall,*** and **Myles O'Brien**, Department of Chemistry, University College, Belfield, Dublin 4, Ireland

A comparison is reported between Brønsted coefficients for catalysis by amine bases (β) and from kinetic and equilibrium measurements of hydroxide solvent isotope effects, $k_{OD}/k_{OH} = (K_{OD}/K_{OH})^{\beta_i}$, for *E*1cB elimination of 9-(dimethylaminomethyl)fluorene and its conjugate acid to form dibenzofulvene. As in related reactions, agreement between values is poor (β_i 0.31 ; $\beta > 0.65$), and better agreement is sought by separating the isotope effects into contributions from the hydrogens of the hydroxy-group and its solvation shell, making use of kinetic measurements in 1 : 1 H_2O–D_2O mixtures. Following Gold, β values are defined from fractionation factors for the transition state (ϕ_1 and ϕ_2) and hydroxide ion (ϕ_a and ϕ_b) as $\phi_1 = \phi_a^{1-\beta_a}$ and $\phi_2 = \phi_b^{1-\beta_b}$ for the hydroxy and solvating hydrogens, respectively. It is found that the measured β values are very sensitive to the values of ϕ_a and ϕ_b, and since these themselves are poorly defined experimentally it appears that evaluation of a β value providing a practical measure of transition state structure is at present not possible. On the other hand, the measurements in 1 : 1 H_2O–D_2O provide a constraint on ϕ_a and ϕ_b in that solutions for the transition state fractionation factors ϕ_1 and ϕ_2 exist only outside the ranges ϕ_a 0.45—1.43 and ϕ_b 0.99—0.67. This result is sensitive to experimental error but not to the fractionation model chosen for the transition state. An attempt to compare hydroxide with methoxide solvent isotope effects in MeOH and MeOD was prevented by the occurrence of isotope exchange between solvent and substrate in MeOD. Kinetic analysis of the competing reactions of exchange and elimination in MeOD, however, offers confirmation of the mechanism of reaction and of the involvement of carbanion and zwitterion intermediates in the elimination.

SOLVENT isotope effects upon proton transfer to hydroxide and deuterioxide ions are of interest because comparison of kinetic and equilibrium effects yields an isotopic Brønsted exponent[1] which may reflect the degree of hydrogen transfer at the transition state,[1-7] and because the origin of the isotope effects can alternatively be interpreted as arising from the covalently bound hydrogen of the hydroxide ion or from its solvation shell.[1,8] A convenient reaction for measuring such isotope effects is elimination from 9-(dimethylaminomethyl)fluorene (1) (Scheme 1).[9] Reaction in aqueous hydroxide occurs with rate-determining ionisation to the fluorenyl anion (2), and precise rate constants can conveniently be obtained from spectrophotometric measurement of the increase in u.v. absorption accompanying formation of the product, dibenzofulvene. Measurements in buffer solutions allow comparison with a conventional Brønsted coefficient for general base catalysis.



SCHEME 1

In principle a comparison is also possible between the hydroxide isotope effects and solvent isotope effects for reactions with methoxide ion in MeOH and MeOD, for which contributions to the isotope effect can come only from solvating hydrogens.[1,10] In practice, measurements in MeOD were prevented by competing isotope exchange with the solvent. However, as will be seen, kinetic analysis of the isotope exchange itself provides a useful confirmation of the rather complex mechanism of the elimination reaction.

RESULTS

Brønsted Buffers.—Previous measurements of catalysis of elimination of 9-(dimethylaminomethyl)fluorene by tertiary amine buffers[9] were extended to *NN*-dimethylethanolamine and 3-dimethylaminopropiononitrile. First-order rate constants were measured from the increase in absorbance from formation of the dibenzofulvene product and are listed in Table 1 for a range of buffer ratios and concentrations. The behaviour of both buffers is consistent with base attack on protonated substrate, with buffer saturation reflecting a change in rate-determining step to leaving group loss at high buffer acid concentrations. The reaction steps are shown in equation (1), where SH, SH_2^+, and $SH^\pm$ represent the substrate, its *N*-protonated conjugate acid, and the zwitterionic *N*-protonated fluoren-9-yl carbanion, respectively, and BH^+ and B are the buffer acid and base.

$$H^+ + SH \rightleftharpoons SH_2^+ \underset{k_{-2}[BH^+]}{\overset{k_2[B]}{\rightleftharpoons}} SH^\pm \xrightarrow{k_3} \text{Olefin} \quad (1)$$

At each pH the dependence of the measured first-order rate constants ($k_{obs.}$) upon buffer acid concentration was

TABLE 1

First-order rate constants for elimination of 9-(dimethylaminomethyl)fluorene in *NN*-dimethylethanolamine and 3-dimethylaminopropiononitrile buffers at 25 °C for various buffer ratios (R) [a] and ionic strength of 0.1

$HOCH_2CH_2NMe_2$ $10^2[BH^+]$ / M	$HOCH_2CH_2NMe_2$ $10^4k_{obs.}$ / s^{-1}	$NCCH_2CH_2NMe_2$ $10^2[BH^+]$ / M	$NCCH_2CH_2NMe_2$ $10^4k_{obs.}$ / s^{-1}
(R 1/3, pH 9.87)		(R 1/9, pH 8.27)	
2.0	9.00	0.2	1.28
4.0	14.3	0.6	2.93
6.0	19.0	1.0	4.10
8.0	23.1		
10.0	26.2		
(R 1, pH 9.43)		(R 1/4, pH 7.90)	
2.0	7.23	0.2	0.66
4.0	12.2	0.4	1.08
6.0	15.8	0.8	1.88
8.0	19.0	1.2	2.29
10.0	22.9	1.6	2.72
		2.0	3.00
(R 3, pH 8.95)		(R 1, pH 7.27)	
2.0	5.50	1.0	0.59
4.0	8.86	3.0	1.07
6.0	11.5	5.0	1.29
8.0	14.5		
10.0	16.5		

[a] R = [buffer acid]/[buffer base].

fitted to equation (2), where k_0 and k_∞ are the limiting rate constants at low and high buffer concentrations and k is the

$$k_{obs.} = \frac{k_0 + k[BH^+]}{1 + (k/k_\infty)[BH^+]} \qquad (2)$$

apparent rate constant for catalysis by buffer acid. The derived rate constants at each pH are listed in Table 2.

TABLE 2

Rate constants [a] for elimination of 9-(dimethylaminomethyl)fluorene in hydroxy- and cyano-ethyldimethylamine buffers at 25 °C and ionic strength 0.1

Buffer	$[BH^+]/[B]$	pH	10^4k_0 / s^{-1}	10^4k_∞ / s^{-1}	$10^4k_{BH^+}/s^{-1}$ A [c]	$10^4k_{BH^+}/s^{-1}$ B [c]	k/k_∞ [b] A [c]	k/k_∞ [b] B [c]
$NCCH_2CH_2NMe_2$	1.0	7.27	0.03	1.86	5 380	3 390	59	37
	0.25	7.90	0.04	5.31	4 050			
	0.111	8.27	0.17	10.9	4 050			
$HOCH_2CH_2NMe_2$	3.0	8.95	1.8	60.1	430	351	4.2	4.2
	1.0	9.43	2.4	86.1	445			
	0.333	9.87	2.4	72.2	325			

[a] Based on unweighted least-squares analysis. [b] $k/k_\infty = k_{-2}/k_3$ in reaction (1). [c] *Cf.* methods A and B in ref. 8 and the Experimental section: pK_a of substrate 8.68.

From Table 2 it can be seen that the constants depend upon pH and this dependence is consistent with protonation of the dimethylamino-group of the substrate with pK_a (p$K_{SH_2^+}$) previously determined as 8.54.[9] Also included in Table 2 are rate constants for buffer acid catalysis, $k_{BH^+} = k(1 + [H^+]/K_{SH_2^+})$ (corrected for substrate protonation using a revised value of p$K_{SH_2^+}$ of 8.68), and values of k/k_∞ [$= k_{-2}/k_3$ in reaction (1)], which are independent of pH. Rate constants for base attack on protonated substrate used in the Brønsted plot were obtained as $k_2 = k_{BH^+}K_{SH_2^+}/K_a$ where K_a is the ionisation constant of the buffer acid. The headings A and B for the right hand columns of Table 2 refer to different methods of data analysis noted in the Experimental section and described in ref. 9.

Hydroxide Isotope Effects.—First-order rate constants for elimination in H_2O, D_2O, and 1 : 1 H_2O–D_2O mixtures at different hydroxide concentration ($k_{obs.}$) are shown in Table 3. Plotted against hydroxide concentration the rate constants yield a slope k_1 and intercept k_0 corresponding to rate-determining hydroxide attack upon neutral (Scheme 1) and protonated [equation (1)] substrate, respectively. The derived values of $k_1^{H_2O} = 1.67 \pm 0.04$ and $k_1^{D_2O} = 2.17 \pm 0.03$ yield the isotope effect $k_1^{D_2O}/k_1^{H_2O} = 1.30 \pm 0.026$. Measurements in 1 : 1 H_2O–D_2O were less extensive than in H_2O or D_2O and the corresponding isotope effect $k_1^{HDO}/k_1^{H_2O} = 1.08 \pm 0.01$ was evaluated from equation (3), where $k_{obs.}^{H_2O}$ and $k_{obs.}^{HDO}$ are rate constants at the same

$$\frac{k_1^{HDO}}{k_1^{H_2O}} = \frac{k_{obs.}^{HDO} - k_0^{HDO}}{k_{obs.}^{H_2O} - k_0^{H_2O}} \qquad (3)$$

base concentration in H_2O and 1 : 1 H_2O–D_2O and k_0^{HDO} (the value of k_0 in 1 : 1 H_2O–D_2O) was taken as the mean of the nearly equal values of $k_0^{H_2O}$ and $k_0^{D_2O}$ (1.35 and 1.30 × 10^{-4} s^{-1}) rather than from extrapolation of measurements at relatively high base concentrations. Solutions of 1 : 1 H_2O–D_2O were prepared from stocks used for measurements in H_2O and D_2O; the value of $k_1^{D_2O}/k_1^{H_2O} = 1.31$ based on these measurements alone is close to that from the full data given above. Probably little significance should be attached to the isotope effect on k_0 as it is based on measurements with unbuffered solutions. In the discussion $k_1^{D_2O}/k_1^{H_2O}$ is written as the less unwieldy abbreviation k_{OD}/k_{OH}.

Previous kinetic measurements suggested that at high concentrations of sodium hydroxide elimination of 9-dimethylaminofluorene underwent a change in kinetic order from first to zero in hydroxide ion,[9] reflecting a change in rate-determining step from ionisation to a carbanion to loss of leaving group from the carbanion, a change which in D_2O should lead to isotope exchange at the 9-position of the substrate in competition with elimination.[11,12] To ensure that the measured isotope effects did indeed refer to the ionisation step therefore the measurements in D_2O were inspected for characteristic departures from first-order kinetics indicating isotope exchange. No evidence of exchange was found either in the concentration range of the isotope measurements (0.002—0.02M) or at higher concentrations, although above 0.2M-hydroxide high reaction rates and salting out of the substrate hindered investigations. The point is considered further below.

Elimination in MeOH *and* MeOD.—First-order rate constants for elimination in NaOMe–MeOH are shown in Table 4. As in NaOH–H_2O [9] the reaction is substantially

TABLE 3

First-order rate constants for hydroxide-catalysed elimination of 9-(dimethylaminomethyl)fluorene in H_2O, D_2O, and 1 : 1 D_2O–H_2O at 25 °C

$10^2[OH^-]$ or $[OD^-]$/M	$10^4k/s^{-1}$ (H_2O)	$10^4k/s^{-1}$ (D_2O)	$10^4k/s^{-1}$ (D_2O–H_2O)
0.200	1.68	1.78	
0.400	2.01	2.17	
0.727	2.51	2.83	
1.000	3.11	3.44	
1.330	3.60	4.21	3.75
1.670	4.08	4.87	4.21
1.820	4.31	5.35	4.59
2.000	4.76	5.61	4.97

first order in base but approaches limiting base-independent rates at high and low base concentrations. In contrast to aqueous media, however, elimination in deuteriated solvent reveals marked competition from isotope exchange. For reaction of isotopically normal substrate in MeOD, elimination rates measured from the increase in absorption due to the product showed an initially rapid reaction followed by a slower limiting rate, consistent with replacement of the fluoren-9-yl hydrogen by the less reactive deuterium isotope as elimination proceeds.[11-14]

TABLE 4

First-order rate constants for elimination of 9-(dimethylaminomethyl)fluorene in NaOMe–MeOH

$10[MeO^-]$/M	$10^4k/s^{-1}$	$10[MeO^-]$/M	$10^4k/s^{-1}$	$10[MeO^-]$/M	$10^4k/s^{-1}$
0.0069	0.106	0.206	1.27	0.686	3.15
0.0137	0.298	0.208	1.285	1.37	5.67
0.0274	0.342	0.308	1.82	1.37	5.75
0.0525	0.437	0.343	1.96	2.06	7.77
0.0686	0.612	0.385	2.20	3.43	10.08
0.103	0.745	0.500	2.56	5.49	12.86
0.105	0.761	0.549	3.07	6.86	14.19

The kinetic dependence of the absorbance change in MeOD was fitted by equation (4), which was previously applied to elimination in MeOD or D_2O of 9-(methoxymethyl)- and 9-(hydroxymethyl)-fluorenes.[11,12,14] In this equation OD_0, OD, and OD_∞ are measured optical densities

$$\left\{\frac{OD_\infty - OD}{OD_\infty - OD_0}\right\} = (1 - Q)e^{-k_x^H[MeO^-]t} + Qe^{-k_E^D[MeO^-]t} \quad (4)$$

at times $t = 0$, $t = t$, and $t = \infty$, k_x^H and k_E^D are second-order rate constants for isotope exchange of protiated substrate and elimination of deuteriated substrate, respectively, and $Q = (k_x^H - k_E^H)/(k_x^H - k_E^D)$, where k_E^H is the rate constant for elimination of protiated substrate.[13] Values of k_x^H, k_E^H, and k_E^D were obtained by iteratively optimising the fit of observed to calculated optical densities and are shown together with the isotope effects k_E^H/k_E^D in Table 5. Strictly speaking equation (4) applies only to isotopically pure solvents, and in Table 5 the rate constants have been corrected for the presence of 4.6% MeOH in the MeOD as described previously.[13,14]

The measured rate constants of Table 5 may be interpreted in terms of the molecular rate constants of Scheme 2, which is an elaboration of Scheme 1 to include isotope exchange *via* the carbanion intermediate and details of leaving group loss. SH and SD denote 9-protiated and 9-deuteriated substrates, S^-, $SD^\pm$, and P denote the fluoren-9-yl carbanion, *N*-protonated zwitterion, and product respectively, k_1 and k_{-1} are rate constants for formation and reprotonation of the carbanion, K_2 is the basic dissociation constant of the zwitterion, and k_3 is the rate constant for expulsion of dimethylamine from the carbanion; all rate and equilibrium constants refer to MeOD as solvent, with the isotope at the 9-position of the substrate indicated by a superscript. The relationship between observed and molecular rate constants is given by equations (5)—(7), in which α, the fraction of carbanion formed undergoing elimination, is as defined in equation (8).

$$\begin{tikzcd}
\text{S–H} \arrow[r, "k_1^H[MeO^-]"] & S^- \arrow[r, shift left, "K_2/[MeO^-]"] \arrow[d, shift left, "k_1^D[MeO^-]"] & SD^\pm \arrow[l, shift left] \arrow[r, "k_3"] & P \\
& SD \arrow[u, shift left, "k_{-1}^D"] & &
\end{tikzcd}$$

SCHEME 2

$$k_x^H = k_1^H \quad (5)$$

$$k_E^H = \alpha k_1^H \quad (6)$$

$$k_E^D = \alpha k_1^D \quad (7)$$

$$\alpha = \frac{k_3K_2}{k_3K_2 + k_{-1}^D[MeO^-]} \quad (8)$$

From Table 5 it can be seen that the exchange rate constant k_x^H increasingly exceeds the elimination rate constant k_E^H as the concentration of methoxide increases and approaches it as the concentration falls. As expected, within experimental error (which is greater than for simple first-order kinetics), k_x^H is independent of the concentration of base while k_E^H and k_E^D are base dependent; the isotope effect k_E^H/k_E^D (= k_1^H/k_1^D) is also independent of base concentration.

TABLE 5

Rate constants (l mol^{-1} s^{-1}) and isotope effects for methoxide-catalysed elimination and exchange of 9-(dimethylaminomethyl)fluorene in MeOD at 25 °C

$[MeO^-]$/M	$10^3k_x^H$	$10^3k_E^H$	$10^3k_E^D$	k_E^H/k_E^D
0.1	28.9	18.2	2.95	6.2
0.3	29.3	14.7	2.13	6.9
0.5	31.9	13.7	2.21	6.2
0.75	26.2	8.71	1.97	4.4
1.0	29.6	6.60	1.30	5.1
1.5	43.7	5.55	0.98	5.7

DISCUSSION

Brønsted Relationship.—Figure 1 shows the Brønsted plot for ionisation of the 9-hydrogen of *N*-protonated 9-(dimethylaminomethyl)fluorene (3) by tertiary amine bases. The ionisation is the rate-determining step at moderate pH values and buffer concentrations for elimination to dibenzofulvene *via* the zwitterion intermediate (4) shown in Scheme 3.[9] Knowledge of the

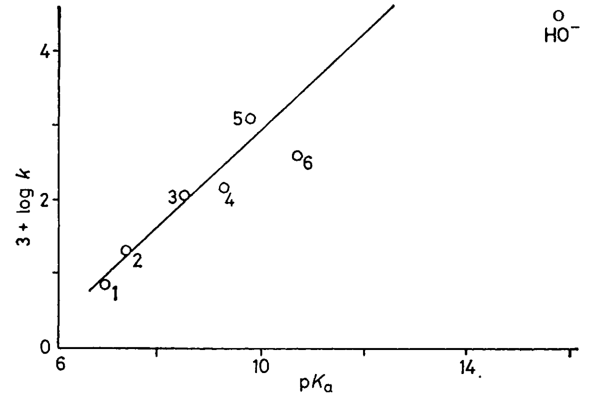
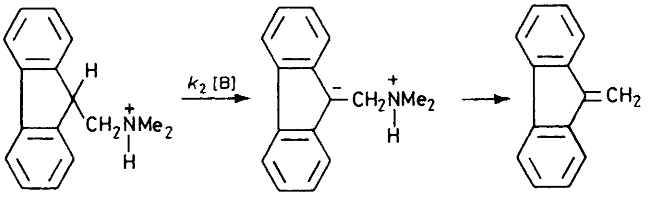


FIGURE 1 Brønsted plot for ionisation of *N*-protonated 9-(dimethylaminomethyl)fluorene by hydroxide ion and tertiary amine bases: 1, dimethylaminopropiononitrile; 2, *N*-methylmorpholine; 3, *N*-methyldiethanolamine: 4, *NN*-dimethylaminoethanol amine; 5, trimethylamine; 6, triethylamine

pK_a for protonation of the substrate (8.68) allows the ionisation rate constant k_2 to be derived from the experimental rate measurements, and values of k_2 are listed together with the pK_a values of the amine bases in Table 6.



(3) (4)

SCHEME 3

The choice of bases in the Brønsted plot is restricted by the tendency of secondary amines to add to the dibenzofulvene product, and Figure 1 shows the considerable scatter of the tertiary amines used in the study and the normally large deviation of hydroxide ion. The slope of the correlation line drawn is based on a plot of log k_2 against log k for reaction of the corresponding bases in the elimination of 9-(chloromethyl)fluorene studied by Spencer *et al.*[15] As shown in ref. 9 this plot shows a good straight line of slope 1.3 including the hydroxide ion. Since for 9-(chloromethyl)fluorene enough bases were used (17) to give a reliable Brønsted exponent of 0.5, it follows that β for 9-(dimethylaminomethyl)fluorene is 0.65. Figure 1 shows that this value of β yields an acceptable correlation of the amines of Figure 1 with expected negative deviations of hydroxide ion and triethylamine (point 6).

TABLE 6

Rate constants for reaction of *N*-protonated 9-(dimethylaminomethyl)fluorene with various bases at 25 °C [a]

Base	pK_a	10^2k_2	k_{-2}/k_3
$Me_2NCH_2CH_2CN$	7.0	0.710	37
N-Methylmorpholine	7.41	2.09	41.2
$(HOCH_2CH_2)_2NMe$	8.52	11.1	
$HOCH_2CH_2NMe_2$	9.31	15.0	4.2
Me_3N	9.76	127	14.0
Et_3N	10.72	40	
HO^-	15.76	3 090	0.021

[a] From present work or ref. 9. Rate constants of ref. 9 are re-evaluated using pK_a 8.68 for *N*-protonated 9-(dimethylaminomethyl)fluorene.

The value of the Brønsted exponent is of interest as a criterion of transition state structure, both in relation to the extensive studies of the ionisation of fluorene derivatives [9,11,13-16] and for comparison with β_i from the measurements of hydroxide solvent isotope effects discussed below. It should be noted, however, that elimination of 9-(dimethylaminomethyl)fluorene can occur by alternative reaction paths depending on whether protonation of the dimethylamino-group precedes or follows ionisation of the fluoren-9-yl hydrogen (compare Schemes 1 and 3), and while the Brønsted plot of Figure 1 refers to ionisation of protonated substrate, the isotope measurements are for reaction of the neutral substrate. The lower reactivity of neutral compared with protonated substrate (by a factor of 3 000 for hydroxide ion [9]) can be expected to lead to an enhanced Brønsted exponent. The value of 0.65 obtained here therefore may be regarded as a lower limit for comparison with the isotopic measurements.

Hydroxide Solvent Isotope Effects.—An isotopic Brønsted exponent β_i for proton transfer to OH^- and DO^- ions [(9) and (10)] is most simply defined by the relationship between kinetic and equilibrium isotope effects, k_{OD}/k_{OH} and K_{OD}/K_{OH}, of equation (11).[1] A precise value of K_{OD}/K_{OH} is available from measurement [17] of the equilibrium constant $K_L = 5.10$ for the isotope exchange (12).[18] On the assumption that free energies of transfer of the substrate SH and its conjugate base S^- between H_2O and D_2O cancel (a reasonable assumption for a weakly solvated organic base such as a fluorenyl anion), $K_{OD}/K_{OH} = K_L^{1/2}$. From the measurement of $k_{OD}/k_{OH} = 1.30$ for ionisation of 9-(dimethylaminomethyl)fluorene to its fluoren-9-yl anion ($\equiv k_1^{D_2O}/k_1^{H_2O}$ of Scheme 1) one then obtains β_i 0.31.

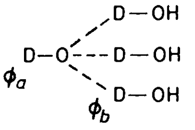
$$HO^- + SH \longrightarrow [HO\text{--}H\text{--}S]^\ddagger \longrightarrow H_2O + S^- \qquad (9)$$

$$DO^- + SH \longrightarrow [DO\text{--}H\text{--}S]^\ddagger \longrightarrow HDO + S^- \qquad (10)$$

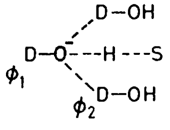
$$k_{OD}/k_{OH} = (K_{OD}/K_{OH})^{\beta_i} \qquad (11)$$

$$2DO^- + H_2O \xrightleftharpoons{K_L} 2HO^- + D_2O \qquad (12)$$

The isotopic Brønsted exponent is of interest as a possible measure of transition state structure. This it plausibly is for proton transfer to hydroxide ion if kinetic and equilibrium isotope effects are controlled by the hydrogen of the hydroxy-group. It then seems reasonable that the zero-point energy of OH^- in the transition state should be intermediate between that of OH^- in the reactants and the OH of H_2O in the products. However, Gold and Grist have pointed out that the isotope effects may also be interpreted as arising primarily from the solvation shell of the hydroxide ion.[1] If so (5) and (6), in which hydrogens contributing to the isotope effect are denoted D, provide the simplest models for the solvated ion and proton-transfer transition state, respectively. In (5) the OH^- ion is solvated by three water molecules, and in (6) one of these is replaced by the substrate. Now different numbers of hydrogens contribute to k_{OD}/k_{OH} in the reactants and transition state and it seems unlikely that β_i from the simple equation (11) could properly measure the structure of the transition state.



(5)



(6)

Comparison of β_i 0.31 with β 0.65 obtained above as the minimum value of the Brønsted coefficient for catalysis by amine bases indeed appears to confirm that β_i from equation (11) fails to provide a simple measure of transition state structure, and this conclusion is consistent with other measurements of hydroxide isotope effects.[1,4] As an alternative to equation (11) therefore we have examined the possibility that values of β_i based on contributions to the net isotope effects from the individual hydrogens of structure (5) and (6) might provide such a measure.

Dissection of isotope effects into contributions from individual hydrogens is conveniently expressed in terms of fractionation factors. For a hydrogen X–H the fractionation factor[5,6] ϕ_X is defined by the equilibrium constant for isotope exchange with solvent water shown in equation (13). Denoting fractionation factors for the

$$X\text{-}H + \tfrac{1}{2}D_2O \xrightleftharpoons{\phi_X} X\text{-}D + \tfrac{1}{2}H_2O \qquad (13)$$

covalently bound and hydrogen-bonded hydrogens of the hydroxide ion respectively ϕ_a and ϕ_b in the solvated ion and ϕ_1 and ϕ_2 in the transition state, the equilibrium and kinetic isotope effects and isotopic Brønsted relationships for covalently bound and solvating hydrogens may be written as equations (14)—(17), remembering that the fractionation factor for water itself is 1.0.

$$K_{OD}/K_{OH} = 1/\phi_a\phi_b^3 \qquad (14)$$

$$k_{OD}/k_{OH} = \frac{\phi_1\phi_2^2}{\phi_a\phi_b^3} \qquad (15)$$

$$\phi_1/\phi_a = (1/\phi_a)^{\beta_i} \qquad (16)$$

$$\phi_2/\phi_b = (1/\phi_b)^{\beta_i} \qquad (17)$$

The Brønsted relationships (16) and (17) now involve four unknown fractionation factors, and for their solution, in addition to kinetic and equilibrium measurements in pure H_2O and D_2O [equations (14) and (15)], measurements in H_2O–D_2O mixtures are required. In H_2O–D_2O mixtures solvent isotope effects are also expressible in terms of fractionation factors, with a contribution $(1 - x + x\phi)$ from each exchangeable hydrogen at an isotopic solvent composition of deuterium atom fraction x. Conveniently, measurements are made in 1 : 1 H_2O–D_2O mixtures ($x = 0.5$), for which the kinetic isotope effect for reaction of hydroxide ion (denoted $k_{\frac{1}{2}}/k_{OH}$) is given by equation (18). Equations (18) and

$$\frac{k_{\frac{1}{2}}}{k_{OH}} = \frac{2(1 + \phi_1)(1 + \phi_2)^2}{(1 + \phi_a)(1 + \phi_b)^3} \qquad (18)$$

(15) may be solved for ϕ_1 and ϕ_2 if ϕ_a and ϕ_b are known.

In principle ϕ_a and ϕ_b are available from equation (14) for $\phi_a\phi_b^3$ and equilibrium measurements of aqueous hydroxide isotope exchange in 1 : 1 H_2O–D_2O, through equation (19). In practice, although measurements of

$$\frac{K_{\frac{1}{2}}}{K_{D_2O}} = \frac{(1 + \phi_a)(1 + \phi_b)^3}{16} \qquad (19)$$

autoprotolysis constants of H_2O–D_2O mixtures by Gold and Lowe[19] and of isotope fractionation between aqueous hydroxide solutions and water vapour by Heinzinger and Weston[20] provide suitable data for their determination, the individual values of ϕ_a and ϕ_b obtained arise as small differences between larger quantities and are much less precisely defined than their product $\phi_a\phi_b^3$. Moreover, there are alternative solutions of ϕ_a and ϕ_b corresponding to the possibilities noted above that the isotope effects are principally controlled respectively by the hydrogen of the hydroxy-group (ϕ_b *ca.* 1.0) or the hydrogens of its solvation shell (ϕ_a *ca.* 1.0).[1] The two principal sets of measurements[19,20] which illustrate these points are shown in Table 7 and are discussed in more detail in refs. 1 and 18.

In practice, because of the uncertainty of ϕ_a and ϕ_b, rather than try to evaluate ϕ_1, ϕ_2, and β_i from the values of Table 7, it proved more useful to use our relatively precise kinetic measurements to better define ϕ_a and ϕ_b themselves. Thus, if we assume that the kinetic and equilibrium fractionation factors fit a Brønsted relationship and take β_i as the coefficient measured from general base catalysis we can formally evaluate our four fractionation factors from relationships (16) and (17). Or, more sensibly and more generally, we may test the consistency of values of ϕ_a and ϕ_b with the Brønsted assumption for a range of values of β_i.

TABLE 7

Different measurements and solutions of fractionation factors for the hydroxide ion

	Solution 1		Solution 2	
Method of measurement	ϕ_a	ϕ_b	ϕ_a	ϕ_b
Liquid–vapour [a] isotope fractionation	0.39	1.04	1.54	0.66
Autoprotolysis constants of H_2O–D_2O mixtures [b]	0.55	0.92	1.15	0.72

[a] Ref. 20. [b] Ref. 19.

In carrying out this analysis, it was convenient to follow Albery and Davies's procedure and separate out contributions to the solvent isotope effects from the transition state fractionation factors ϕ_1 and ϕ_2, denoting them y_x, where x signifies the atom fraction of D in the solvent.[21] For pure D_2O ($x = 1$) and 1 : 1 H_2O–D_2O ($x = 0.5$) we obtain for y_1 and $y_{\frac{1}{2}}$ equations (20)—(23). Then with $\phi_a\phi_b^3$ 0.434 and k_{OD}/k_{OH} 1.30, equations (20)

$$y_1 = \phi_1\phi_2^2 \quad (20)$$

$$= \phi_a\phi_b^3k_{OD}/k_{OH} \quad (21)$$

$$y_{\frac{1}{2}} = \frac{(1+\phi_1)(1+\phi_2)^2}{8} \quad (22)$$

$$= \frac{(1+\phi_a)(1+\phi_b)^3}{16}\,k_{\frac{1}{2}}/k_{OH} \quad (23)$$

and (21) give $\phi_1\phi_2^2$ 0.564, and it is possible to plot a range of values of $y_{\frac{1}{2}}$ as a function of either ϕ_1, using equation (22), or ϕ_a, using equation (23). Both plots are shown as full lines in Figure 2, where they form inverted bells, and it is apparent that a horizontal line representing a particular value of $y_{\frac{1}{2}}$ intersects the two curves to yield complementary solutions of ϕ_1 and ϕ_a (and thus also of ϕ_2 and ϕ_b). For each value of $y_{\frac{1}{2}}$ two pairs of solutions of ϕ_1 and ϕ_a are obtained, consistent with the two solutions of ϕ_a from the equilibrium measurements.

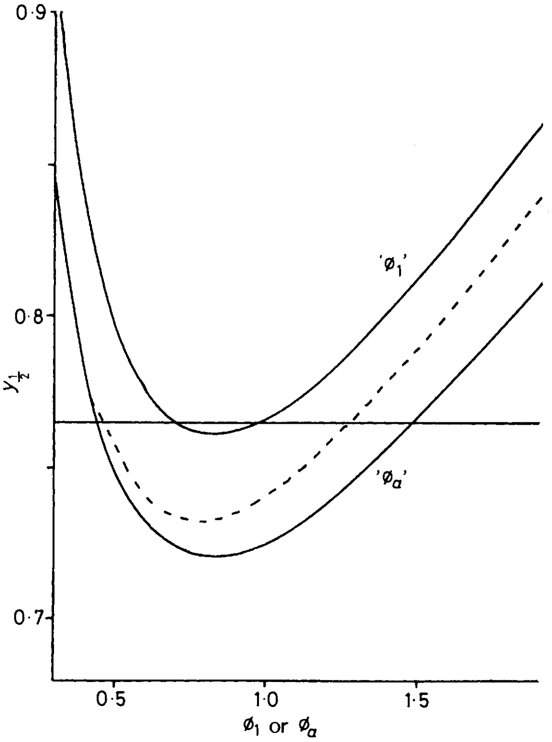


FIGURE 2 Plots of $y_{\frac{1}{2}}$ against ϕ: upper full line, $y_{\frac{1}{2}}$ from equation (22) *versus* ϕ_1; lower full line, $y_{\frac{1}{2}}$ from equation (23) *versus* ϕ_a; dashed line, $y_{\frac{1}{2}}$ from equation (25) *versus* ϕ_a with a medium effect $\Phi_S = 1.3$

The values of ϕ_1 and ϕ_a may be used to calculate β_i and the particular solution of ϕ_1 and ϕ_a shown corresponds to $\beta_i = 0.65$, the value of the Brønsted exponent obtained from base catalysis. The solution is for the small value of ϕ_a and gives ϕ_a 0.44.

Before considering specific values of ϕ_a and ϕ_b compatible with particular values of β_i, however, it should be noted that Figure 2 implies a more general limitation on the range of ϕ_a and ϕ_b. For the plot of $y_{\frac{1}{2}}$ against ϕ_1 forming the upper curve of the figure it is evident that if ϕ_a lies between 0.45 and 1.43 no solutions for ϕ_1 (or ϕ_2) exist. This bears on the discrepancy between alternative values of ϕ_a obtained from direct measurements shown in Table 7; the values of 0.39 and 1.54 from liquid–vapour isotope fractionation[20] fall within this limitation but the values of 0.55 and 1.15 from the autoprotolysis constants of H_2O–D_2O mixtures[19] fall well outside it.

Our kinetic measurements thus favour extreme values of ϕ_a well removed from 1.0. This is of interest in connection with discussion of the magnitude of these values and of their significance for the structure of the solvated hydroxide ion.[1,18] This discussion need not be pursued here but it should be noted that the conclusion drawn is not sensitively dependent on the structural models chosen for the hydroxide ion or the transition state. The analysis of Figure 2 is well adapted to assessing the effect of structural variations, as may be illustrated for the most extreme modification of the fractionation factor model, namely the inclusion of a medium effect potentially arising from accumulations of small fractionation effects, notably in association with solvation.[5,6] For the hydroxide reactants a medium effect Φ_S may be included in equations (14) and (23) as (24) and (25), respectively. The dashed line in Figure 2 corresponds to Φ_S 1.3 and the range of excluded values of ϕ_a is

$$K_{OD}/K_{OH} = 1/\phi_a\phi_b^3\Phi_S \quad (24)$$

$$y_{\frac{1}{2}} = (1+\phi_a)(1+\phi_b)^3\,\Phi_S^{\frac{1}{2}}k_{\frac{1}{2}}/16k_{OH} \quad (25)$$

moderated to 0.5—1.2. A medium effect of Φ_S 0.7 in the transition state would have the same result.

In practice there seems to be little scope for appreciable medium effects in the reaction studied. More seriously, the dashed line in Figure 2 also represents the effect of an accumulated error of only 2% between $k_{\frac{1}{2}}/k_{OH}$ and k_{OD}/k_{OH}. The experimental measurements were made with care but the customary sensitivity to error of interpretations of results from H_2O–D_2O mixtures casts its shadow. For comparison, the similar measurements of Gold and Grist[1] for the ionisation of 2-nitropropane, with k_{OD}/k_{OH} 1.35 and $k_{\frac{1}{2}}/k_{OH}$ 1.12, lead to an excluded range of ϕ_a of 0.54—1.21. (Here the contribution of a medium effect from the incipient nitronate anion[22] is perhaps more likely than in the case of our fluorenyl anion.)

Returning to the structural significance of β_i, Table 8 lists values of β_i derived from $\phi_1 = \phi_a^{1-\beta_a}$ and $\phi_2 = \phi_b^{1-\beta_b}$ as functions of ϕ_a and ϕ_b where β_a and β_b distinguish β_i values based on ϕ_a and ϕ_b, respectively. As may be seen the β_i values are quite sensitive to the magnitudes of ϕ_a and ϕ_b, especially in the range that β_i might be regarded as being structurally significant, *i.e.* not too far removed from β 0.65, the Brønsted exponent for base catalysis. Only for β_i based on ϕ_a, incidentally, does the possibility of β_i being a measure of transition state structure even arise. For the solution with $\phi_a < 1.0$ both ϕ_2 and ϕ_b are too close to 1.0, and with $\phi_a > 1.0$ β_b is consistently too small.

TABLE 8

Dependence of values of β_i for ionisation of 9-(dimethylaminomethyl)fluorene upon hydroxide fractions factors ϕ_a and ϕ_b

Solution 1 [a]		Solution 2 [a]		
ϕ_a	β_a [b]	ϕ_a	β_a [b]	β_b [b]
0.3	0.24	1.8	0.43	0.05
0.4	0.35	1.7	0.54	0.10
0.42	0.51	1.6	0.68	0.17
0.44	0.60	1.55	0.80	0.22
0.45	0.87	1.50	0.95	0.29
0.46		1.45	1.30	0.42

[a] Alternative solutions of ϕ_a (and ϕ_b): (1) $\phi_a < 1.0$, (2) $\phi_a > 1.0$. [b] β_a and β_b are defined by $\phi_1 = \phi_a^{(1-\beta_a)}$ and $\phi_2 = \phi_b^{(1-\beta_b)}$, respectively.

Unfortunately even for β_i based on ϕ_a (β_a) the conclusion to be drawn from Table 8 is that the marked sensitivity of β_i to values of ϕ_a and ϕ_b for the hydroxide ion, coupled with the uncertainty of ϕ_a and ϕ_b themselves, means that there is no possibility at present of deriving a value of β_i from hydroxide solvent isotope effects providing a rational measure of transition state structure. This is not to say that for a series of substrates a progression in measured hydroxide isotope effects cannot be interpreted, as Winey and Thornton have interpreted them,[2] as reflecting a systematic variation in transition state structure, but the detailed treatment we have carried out adds nothing to this more limited analysis and indeed underlines its limitations.

On the other hand, as we have seen, the sensitivity of β_i to the magnitudes of ϕ_a and ϕ_b seen in Table 8 makes the kinetic results useful in defining limits to the magnitudes of ϕ_a and ϕ_b of interest in trying to understand the structure of the aqueous hydroxide ion.[8]

Isotope Effects and Isotope Exchange in MeOD.—Rates of elimination of 9-(dimethylaminomethyl)fluorene were measured in MeOH and MeOD with the intention of providing a comparison of hydroxide with methoxide solvent isotope effects. The reaction in methanol is similar to that in water. It is first-order in base at moderate concentrations of methoxide ion but becomes zero-order at low and high concentrations, as shown by the plot of observed rate constants against [MeO$^-$] in Figure 3 (open circles). As in aqueous solution, the base dependence is described by equation (26) in which k_0 and $k_{max.}$ are the limiting rate constants at low and high base concentrations, respectively, and k_1 refers to

$$k_{obs.} = k_0 + \frac{k_1[\mathrm{MeO^-}]}{1 + (k_1/k_{max.})[\mathrm{MeO^-}]} \qquad (26)$$

the first-order dependence on [MeO$^-$]. The line through the points in Figure 3 represents a best fit of the equation to the experimental rate constants up to 0.5M (the range shown and above which deviations occur, probably as a result of encroaching acidity function dependence), and the values of k_0/k_1 and $k_{max.}$ used are compared with those from aqueous solution in Table 9. The similarity of the aqueous and methanolic rate constants suggests a similarity of reaction mechanisms, namely predominantly base attack upon neutral substrate (k_1), with a change in rate-determining step to loss of leaving group (k_3) at high base concentrations [equation (27)], and a change in reaction path to base attack on protonated substrate at low base concentrations (Scheme 3).

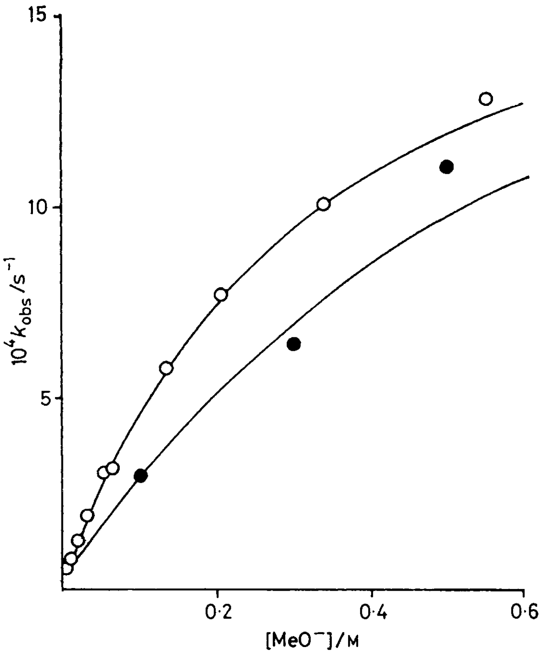


FIGURE 3 Plots of observed first-order rate constants against [MeO$^-$] to 0.6M for elimination of 9-(dimethylaminomethyl)-fluorene in MeOH (○) and MeOD (●, ^{2}H substrate). Lines are calculated from the best fits to equation (26)

TABLE 9

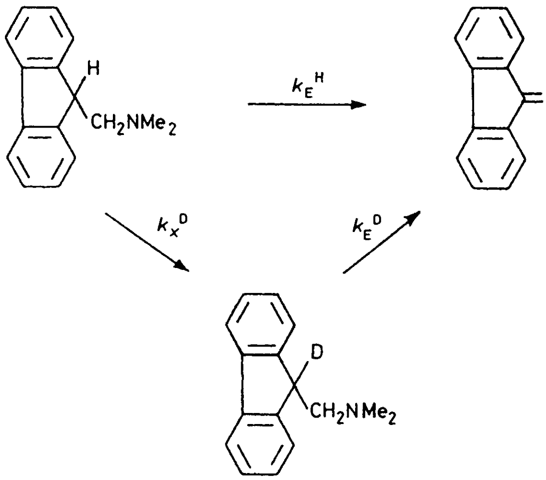
Rate constants [a] and solvent isotope effects for ionisation of 9-(dimethylaminomethyl)fluorene in aqueous sodium hydroxide and methanolic sodium methoxide at 25 °C

	10^3k_0	10^3k_1	$10^3k_{max.}$	k_1^{ROD}/k_1^{ROH} [b]	$k^{ROH}_{max.}/k^{ROD}_{max.}$
H_2O	0.152	16.0	10.3	1.30	
MeOH	*c*	6.41	1.85	4.6	1.3

[a] Rate constants refer to equation (22). Values are taken from ref. 9 and differ slightly from new measurements of Table 4. [b] For 9-protio-substrate. [c] Value of k_0 8.8×10^{-6} unconfirmed by buffer measurements (likewise values in D_2O and MeOD).

$$\mathrm{SH} \underset{k_{-1}}{\overset{k_1[\mathrm{MeO^-}]}{\rightleftharpoons}} \mathrm{S^-} \underset{K/[\mathrm{MeO^-}]}{\overset{\mathrm{Fast}}{\rightleftharpoons}} \mathrm{SH^{\pm}} \xrightarrow{k_3} \mathrm{P} \qquad (27)$$

Unlike the reaction in aqueous solution, however, the kinetics of elimination of 9-(dimethylaminomethyl)fluorene in deuteriated solvent, MeOD, are not clearly first-order, but show a rapid initial reaction characteristic of competing β-hydrogen isotope exchange, reflecting comparable rates of reprotonation (deuteriation) and leaving group loss from a carbanion intermediate. A kinetic analysis yields the rate constants $k_E{}^H$ and $k_E{}^D$ for elimination of protio- and deuterio-substrates and $k_x{}^H$ for exchange of protio-substrate shown in Scheme 4.



Scheme 4

Values of $k_x{}^H$, $k_E{}^H$, and $k_E{}^D$ at various methoxide concentrations are shown in Table 5: $k_x{}^H$ refers to ionisation of protio-substrate ($k_1{}^H$) and $k_E{}^D$ to elimination of isotopically exchanged substrate. It is evident that $k_E{}^D$ is less than $k_x{}^H$ and decreases with increasing base concentration whereas $k_x{}^H$ remains constant; this behaviour reflects the increasing ratio of exchange to elimination rates and the change in rate-determining step of elimination from base-dependent ionisation to base-independent loss of the leaving group as the base concentration increases. The ratio $k_E{}^H/k_E{}^D$ is independent of base concentration and corresponds to the isotope effect on the ionisation step, $k_1{}^H/k_1{}^D$. The average value of the isotope effect of 6.0 is close to that for proton abstraction by methoxide ion from other 9-substituted fluorenes, *e.g.* 6.3 and 6.4 for 9-hydroxymethyl-[14] and 9-methoxymethyl-fluorene.[13]

The dependence of 'observed' rate constants for elimination of deuteriated substrate ($k_{obs.} = k_E{}^D[MeO^-]$) upon methoxide concentration is also described by equation (26) with k_1 and $k_{max.}$ now the values in deuterio-solvent. Figure 3 compares experimental values (closed circles) with values calculated from equation (26) with $k_1{}^D$ evaluated from $k_1{}^H$ ($k_x{}^H$) and $k_1{}^H/k_1{}^D$ (6.0), $k_0 = 0$ (approximately), and $k_{max.}(MeOH)/k_{max.}(MeOD) = 1.3$ adjusted to give reasonable agreement of observed with calculated values. The greater scatter of the plot than that for the protio-solvent reflects the greater uncertainty of these rate constants than values derived from simple first-order kinetics.

The solvent isotope effect on the ionisation step is obtained from the rate constants of Tables 5 and 9 as $k_1{}^H(MeOD)/k_1{}^H(MeOH) = 4.6$. As in similar comparisons the effect is much larger than for the corresponding hydroxide reaction, notwithstanding the similarity of the respective equilibrium solvent isotope effects. As Gold and Grist note,[1,23] this suggests a fundamental difference between the hydroxide and methoxide effects. Unfortunately the change in rate-determining step and isotopic exchange affecting the methoxide reaction in our case make the measurements too imprecise to justify the more detailed analysis that would be possible had accurate measurements in MeOD and MeOH–MeOD mixtures been available. The single previous comparison of this type is Gold and Grist's measurements with 2-nitropropane.[1,23]

On the other hand the observation of isotope exchange nicely confirms the evidence of a change in rate-determining step and involvement of a carbanion intermediate, indicated by the non-linear dependence of elimination rates upon hydroxide and methoxide concentrations. Failure to observe exchange with DO^-–D_2O is not difficult to understand. The relative importance of exchange and elimination reflects the ratio of rates of reprotonation of and leaving group expulsion from the carbanion, *i.e.* $k_{-1}[OH^-]/k_3K$ in (27), or in terms of the observed rate constants for ionisation and the limiting rate of elimination when exchange is rapid, $k_1[OH^-]/k_{max.}$. Thus the observation of exchange depends on the concentration of base and the magnitude of $k_1/k_{max.}$. From Table 9 $k_1/k_{max.}$ in MeOH is twice that in H_2O, and in deuteriated solvents where the main difference should stem from the greater solvent isotope effect of MeOD than D_2O a further factor of 2 can be expected [the measured value $k_1{}^D(MeOD)/k_1{}^H(MeOH) = 4.6$ is probably too large to be free of error]. Since exchange is observable at 0.1M-NaOMe in MeOD it should be seen at 0.4—0.5M in NaOD–D_2O. However, measurements at this concentration of NaOD are hindered by salting out effects and the significantly higher rates in D_2O than in MeOD, which especially affect observation of the rapid preliminary exchange reaction.

Is exchange in H_2O and D_2O nonetheless sufficient to affect the error-sensitive hydroxide solvent isotope effects? At the highest concentration of hydroxide of 0.02M in Table 3 $k_1[OH^-]/k_{max.} = 0.033$ indicating 3% exchange and a corresponding underestimation of the ionisation rate. In D_2O the amount of exchange is reduced because of a primary isotope effect of 6—7 on k_1 (or k_{-1}) and k_{D_2O}/k_{H_2O} is thus overestimated. The value of $k_{\frac{1}{2}}/k_{H_2O}$ is also overestimated but by a smaller factor because in 1 : 1 H_2O–D_2O the rate of carbanion reprotonation is more than half that in pure H_2O. While the main conclusion is that the effects of exchange are small, with respect to the earlier discussion it may be noted that they accumulate between the measurements so as to moderate the range of hydroxide fractionation factors ϕ_a and ϕ_b excluded by the solvent isotope measurements.

EXPERIMENTAL AND DATA ANALYSIS

9-(Dimethylaminomethyl)fluorene was prepared as before[9] save that reduction of the corresponding dimethylamide was effected with lithium aluminium hydride rather than diborane. No method of reduction tried gave other than a poor yield. The amine product was purified by dissolving in a minimum quantity of chloroform, adding excess of light petroleum (b.p. 40—60 °C), evaporating to a small volume, and allowing to crystallise.

The amine buffers were purified as the amine hydrochlorides, which were prepared by precipitation from a solution of the amine in ether using dry HCl. The hydrochlorides were recrystallised from recommended solvents.[24] Deuteriomethanol was purchased from the Merck Chemical Co. or prepared by Streitwieser's method.[25]

Kinetic measurements were made as described previously by following the increase in absorbance at 255 nm due to the dibenzofulvene product. Rate constants were obtained from first-order kinetic data for buffer solutions by two methods, A and B, described previously.[9] Method A was the more suitable for obtaining data for pH-rate profiles and method B for obtaining accurate molecular rate and equilibrium constants. Application of method B to *NN*-dimethylethanolamine buffers gave a best fit with a pK_a of 8.68 for *N*-protonation of the substrate and a rate constant $k_{\max.}$ of 9.0×10^{-3} s^{-1} for the buffer-independent expulsion of leaving group from the conjugate acid of the substrate. With this pK_a for the substrate the dimethylaminopropiononitrile buffer measurements gave the same value of $k_{\max.}$. The values obtained are in satisfactory agreement with the pK_a of 8.54 and $k_{\max.} = 7.3 \times 10^{-3}$ s^{-1} derived earlier from trimethylamine and *N*-methylmorpholine buffer measurements.[9] The present results are preferred for determining the pK_a of the substrate because, of the suitable buffers, *NN*-dimethylethanolamine has the closest pK_a (9.31). The value obtained for $k_{\max.}$ is also closer to the independently determined value of 10.2×10^{-3} s^{-1} from elimination promoted by hydroxide ion.[9] The rate constants k_2 for reaction of buffer bases with protonated substrate listed in Table 6 and used in the Brønsted plot therefore are based on the pK_a of 8.68 for the substrate and differ slightly from the values of ref. 9 based on the pK_a of 8.54.

Kinetic and pH measurements in buffer solutions were made at an ionic strength of 0.1, maintained with sodium chloride, and measured pH values differ by up to 0.3 units from values calculated from the thermodynamic pK_a values of the buffer acids. The substrate pK_a was measured relative to a substituted dimethylamine buffer and the recorded value is presumed to be the thermodynamic value.

We thank the National Board for Science and Technology, Ireland for financial support.

[1/839 *Received, 27th May*, 1981]

REFERENCES

[1] V. Gold and S. Grist, *J. Chem. Soc., Perkin Trans. 2*, 1972, 89.

[2] D. A. Winey and E. R. Thornton, *J. Am. Chem. Soc.*, 1975, **97**, 3102.

[3] F. G. Bordwell and W. J. Boyle, jun., *J. Am. Chem. Soc.*, 1975, **97**, 3447.

[4] A. J. Kresge and A. C. Lin, *J. Am. Chem. Soc.*, 1975, **97**, 6257.

[5] W. J. Albery in 'Proton Transfer Reactions,' eds. E. F. Caldin and V. Gold, Chapman and Hall, London, 1975.

[6] V. Gold, *Adv. Phys. Org. Chem.*, 1969, **7**, 259.

[7] A. J. Kresge in 'Proton Transfer Reactions,' eds. E. F. Caldin and V. Gold, Chapman and Hall, London, 1975; R. L. Schowen, *Prog. Phys. Org. Chem.*, 1972, **9**, 275; M. M. Kreevoy in 'Isotope Effects in Organic Reactions,' eds. E. Buncel and C. C. Lee, Elsevier, Amsterdam, 1978, vol. III; C. E. Taylor and C. Thomlinson, *J. Chem. Soc., Faraday Trans. 1*, 1974, 1132.

[8] A. J. Kresge and R. A. More O'Ferrall, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1840.

[9] R. P. Kelly and R. A. More O'Ferrall, *J. Chem. Soc., Perkin Trans. 2*, 1979, 681.

[10] V. Gold and S. Grist, *J. Chem. Soc. B*, 1971, 1665; J. M. A. Al-Rawi, J. P. Bloxsidge, J. A. Elvidge, J. R. Jones, and R. A. More O'Ferrall, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1593.

[11] R. A. More O'Ferrall and S. Slae, *J. Chem. Soc. B*, 1970, 260.

[12] D. J. Hupe, M. C. R. Kendall, G. T. Sinner, and T. A. Spencer, *J. Am. Chem. Soc.*, 1973, **95**, 2260; M. B. Davy, K. T. Douglas, J. S. Loran, A. Steltner, and A. Williams, *ibid.*, 1977, **99**, 1196; A. J. Kirby and G. J. Lloyd, *J. Chem. Soc., Perkin Trans. 2*, 1976, 1762; D. Bethell and R. J. E. Talbot, *J. Chem. Soc. B*, 1968, 638.

[13] R. A. More O'Ferrall and P. J. Warren, *Proc. R. Ir. Acad. Sect. B*, 1977, **77**, 713.

[14] R. A. More O'Ferrall, *J. Chem. Soc. B*, 1970, 268.

[15] T. A. Spencer, M. C. R. Kendall, and I. D. Reingold, *J. Am. Chem. Soc.*, 1972, **94**, 1250.

[16] F. G. Bordwell, G. E. Drucker, and G. J. McCollum, *J. Org. Chem.*, 1976, **41**, 2786; A. Streitwieser, jun., W. B. Hollyhead, A. H. Pudjaatmaka, P. H. Owens, T. L. Kruger, M. L. Brookaw, W. K. C. Chu, and H. M. Niemeyer, *J. Am. Chem. Soc.*, 1971, **93**, 5088.

[17] R. Gary, R. G. Bates, and R. A. Robinson, *J. Phys. Chem.*, 1964, **68**, 1186; M. Goldblatt and W. M. Jones, *J. Chem. Phys.*, 1969, **51**, 1881.

[18] Y. Chiang, A. J. Kresge, and R. A. More O'Ferrall, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1832.

[19] V. Gold and B. M. Lowe, *Proc. Chem. Soc.*, 1963, 140; *J. Chem. Soc. A*, 1967, 936.

[20] K. Heinzinger and R. E. Weston, jun., *J. Phys. Chem.*, 1964, **68**, 2179.

[21] W. J. Albery and M. H. Davies, *Trans. Faraday Soc.*, 1969, **65**, 1059.

[22] D. M. Goodall and F. A. Long, *J. Am. Chem. Soc.*, 1968, **90**, 238.

[23] V. Gold and S. Grist, *J. Chem. Soc. B*, 1971, 2282.

[24] D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, 'Purification of Laboratory Chemicals,' Pergamon, London, 1980, 2nd edn.

[25] A. Streitwieser, jun., L. Verbit, and P. Stang, *J. Org. Chem.*, 1964, **29**, 3706.