

Deuterium Kinetic Isotope Effect in Elimination from Phenethyl Bromides in t-Butyl Alcohol

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Deuterium kinetic isotope effects (k_2^H/k_2^D) have been measured for the elimination of HBr from a series of substituted phenethyl bromides. No variation in the magnitude of the isotope effect was observed. The k_2^H values have been correlated by the Hammett equation to give $\rho = 2.85$. Some evidence for proton tunnelling has been obtained.

PRIMARY kinetic isotope effects have been used extensively as probes of transition-state structure in proton-

transfer reactions. According to theoretical predictions¹⁻⁹ the size of the deuterium isotope effect can be

¹ R. P. Bell, W. H. Sachs, and R. L. Tranter, *Trans. Faraday Soc.*, 1970, **66**, 1995.

² R. P. Bell, *Discuss. Faraday Soc.*, 1965, **39**, 16.

³ W. J. Albery, *Trans. Faraday Soc.*, 1967, **63**, 200.

⁴ F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265.

⁵ J. Bigeleisen, *Pure Appl. Chem.*, 1964, **8**, 217.

⁶ A. V. Willi, *Trans. Faraday Soc.*, 1964, **60**, 2097.

⁷ R. A. More O'Ferrall and J. Kouba, *J. Chem. Soc. (B)*, 1967, 985.

⁸ R. A. More O'Ferrall, *J. Chem. Soc. (B)*, 1970, 785.

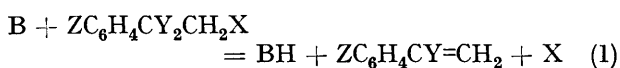
⁹ A. M. Katz and W. H. Saunders, jun., *J. Amer. Chem. Soc.*, 1969, **91**, 4467.

used as a qualitative measure of the extent of proton transfer, maximum values being associated with symmetrical transition states and smaller values being associated with asymmetrical transition states. Most of the calculations have been based on a three-centre model and some recent studies¹⁰⁻¹² provide experimental support for the existence of a maximum in the isotope effect for such reactions.

Little work has appeared on multicentre reactions but a recent calculation based on the *E2* mechanism of 1,2-elimination⁹ predicts a similar maximum in the isotope effect when the proton is half-transferred. However, the maximum value to be expected in these reactions is considerably less than that predicted by the three-centre model and depends on the degree of coupling with the motions of other nuclei. Cockerill¹³ has shown the existence of such a maximum in the isotope effect for the hydroxide ion-catalysed 1,2-elimination of phenethylsulphonium bromides in aqueous dimethyl sulphoxide solutions. The transition-state symmetry is presumably changing as a result of the large increase in the basic strength of the hydroxide ion with increasing mole fraction of Me₂SO,¹⁴ but interpretation of these isotope effects in terms of the transition-state structure is complicated by concurrent changes in the solvation of the leaving group.

There is general agreement that a spectrum of transition states is available for base-catalysed *E2* eliminations, ranging from the paenecarbanion extreme with C-H bond breaking more advanced than C-X bond breaking, through 'central' where both bond-breaking processes have made approximately equal progress, to the paenecarbonium extreme in which C-X bond breaking is more advanced than C-H.

For 1,2-eliminations (1) from phenethyl compounds,



where Z = a *meta*- or a *para*-substituent, Y = H or D, and X represents the leaving group, the experimental data support a transition state with considerable carbanion character at the 2-carbon. A recent theory¹⁵ predicts that the degree of carbanion character in these reactions will increase as (i) the leaving group becomes more basic, (ii) the base strength increases, and (iii) the acidity of the 2-hydrogen increases. Introduction of 2-phenyl substituents should alter the acidity of the 2-hydrogens and cause a shift in the transition-state geometry. Such a shift should be reflected in the magnitude of the deuterium isotope effect.

We therefore decided to study the deuterium isotope effect in the elimination of hydrogen bromide from the neutral substrate phenethyl bromide catalysed by

¹⁰ R. P. Bell and B. G. Cox, *J. Chem. Soc. (B)*, 1971, 783.

¹¹ J. L. Longridge and F. A. Long, *J. Amer. Chem. Soc.*, 1967, **89**, 1292.

¹² A. J. Kresge and Y. Chiang, *J. Amer. Chem. Soc.*, 1969, **91**, 1025.

¹³ A. F. Cockerill, *J. Chem. Soc. (B)*, 1967, 964.

¹⁴ K. Bowden, *Chem. Rev.*, 1966, **66**, 119.

¹⁵ J. F. Bunnett, *Surveys Progr. Chem.*, 1969, **5**, 53.

potassium *t*-butoxide in *t*-butyl alcohol, in the expectation of providing some reliable kinetic isotope effect data. *t*-Butyl alcohol is a poorly solvating solvent and hence the data should be uncomplicated by solvation effects. This reaction has been shown to be cleanly *E2*, providing essentially complete conversion into the corresponding styrenes.

EXPERIMENTAL

Preparation of Solvent and Base.—All reagents for kinetic studies were stored and handled in a dry-box which was continually flushed with dry nitrogen. *t*-Butyl alcohol was purified and potassium *t*-butoxide solutions were prepared essentially as described by Cockerill *et al.*¹⁶ The solutions were standardised immediately before use against 0.1M-hydrochloric acid with bromocresol green-methyl red indicator. Fresh base solutions were prepared every week as the absorbance at 260 nm increased with time, thus reducing the precision of the measurements.

Substituted Phenethyl Bromides.—These were mostly prepared from the corresponding phenethyl alcohols by treatment with phosphorus tribromide by a procedure similar to that described by Rupe.¹⁷ The compounds with Z = *p*-Ac and Z = *p*-NO₂ were prepared by direct acetylation¹⁸ and direct nitration¹⁹ respectively of the parent phenethyl bromide. The compound with Z = *m*-NO₂ was prepared from *m*-nitrophenylacetic acid by reduction of the acid with sodium borohydride and aluminium chloride²⁰ followed by reaction with phosphorus tribromide.¹⁷ The n.m.r. and mass spectra were consistent with the assigned structure. The compounds deuteriated in the 2-position were prepared from the corresponding deuteriated phenylacetic acids. These acids were deuteriated by repeatedly refluxing the sodium salts in deuterium oxide until mass spectral analysis showed an acceptable level of deuteriation. All the compounds thus prepared were pure by g.l.c. The physical parameters are in Table 1.

Kinetic Studies.—The rate constants for base-catalysed elimination from phenethyl bromides in dry *t*-butyl alcohol are markedly sensitive to the presence of traces of water.¹⁶ We experienced difficulty in reproducing the absolute values of the rate constants to better than $\pm 20\%$ during a period of time, despite claims in the literature of reproducibility in the range $\pm 1-2\%$. Also, the deuteriation procedure employed gave a maximum of 1.91 atoms D per molecule and, unless a correction is applied for the amount of protium in the sample, errors in the measured isotope effect arise. Since even small variations in the rate constants obtained from individual runs on the deuteriated and non-deuteriated compounds can lead to substantial differences in the isotope effect, we followed the mixed kinetic method described by Jones²¹ for determining isotope effects on partially deuteriated samples. This procedure eliminates any solvent errors since the isotope-effect ratio is determined directly and is therefore not subject to the

¹⁶ A. F. Cockerill, S. Rottschaefter, and W. H. Saunders, jun., *J. Amer. Chem. Soc.*, 1967, **89**, 901.

¹⁷ H. Rupe, *Annalen*, 1912, **395**, 114.

¹⁸ L. H. Amundsen and L. S. Nelson, *J. Amer. Chem. Soc.*, 1951, **73**, 242.

¹⁹ E. L. Foreman and S. M. McElvain, *J. Amer. Chem. Soc.*, 1940, **62**, 1435.

²⁰ W. Foerst, 'Newer Methods of Preparative Organic Chemistry,' vol. IV, Academic Press, New York, p. 271.

²¹ J. R. Jones, *J. Chem. Educ.*, 1967, **44**, 31.

variations in the absolute value of the second-order rate constants.

A stock solution containing a 1:2 mixture of the deuteriated and non-deuteriated compounds (total substrate concentration 10^{-2}M) in dry *t*-butyl alcohol was prepared. Two cuvettes were filled with the potassium *t*-butoxide solution (2 cm^3) and placed in the thermostatted cell compartment of an SP 500 Unicam spectrophotometer. After thermal equilibrium had been achieved (5–10 min), 20 mm^3 of the substrate stock solution was added to one of the cuvettes, the other being used as a blank. The reaction

The data used in these calculations were collected over at least three half lives and good fits were obtained providing a stable infinity value could be obtained.

Table 2 shows the observed variation in the isotope effect for $Z = m\text{-NO}_2$ obtained from a number of mixed kinetic runs for which stable infinity values were obtained. Although the absolute values of the measured second-order rate constants vary by up to $\pm 20\%$, it can be seen that the isotope effects which are measured directly by the mixed kinetic method show an overall variation of only $\pm 3\%$. This behaviour was typical of all the compounds studied and

TABLE 1
Physical properties for $\text{ZC}_6\text{H}_4\text{CY}_2\cdot\text{CH}_2\text{Br}$ compounds

Z	Y	B.p. $\left(\frac{P}{\text{mmHg}}\right)$ °C	B.p. $\left(\frac{P}{\text{mmHg}}\right)$ (lit.) °C	n_D ($t/^\circ\text{C}$)	n_D ($t/^\circ\text{C}$) (lit.)	Atoms D/mol	Ref.
H	H	100—102(18)	66(2)	1.5545(26)	1.5542(26)	—	<i>b</i>
H	D	100—102(18)	94(15)	1.5537(23)	—	1.90	24
<i>p</i> -MeO	H	146—148(15)	63(0.5)	1.5584(24)	1.5595(21)	—	<i>b</i>
<i>p</i> -MeO	D	144—146(18)	—	1.5585(24)	—	1.62	—
<i>p</i> -Cl	H	132—134(18)	86.5(1.6)	1.5686(22)	1.5697(25)	—	<i>b</i>
<i>p</i> -Cl	D	132—134(18)	—	1.5661(23)	—	1.86	—
<i>m</i> -Br	H	77—88(0.1)	98—100(1)	1.5920(22)	—	—	<i>c</i>
<i>m</i> -Br	D	136—138(0.5)	—	1.5906(25)	—	1.88	—
<i>m</i> -NO ₂ ^a	H	136—138(0.5)	—	1.5852(22)	—	—	—
<i>m</i> -NO ₂	D	118—126(0.1)	—	—	—	1.88	—
<i>p</i> -NO ₂	H	M.p. 68—69	M.p. 69—70	—	—	—	19
<i>p</i> -NO ₂	D	M.p. 68—69	—	—	—	1.91	—
<i>p</i> -Ac	H	136—140(0.4)	117—118(0.1)	1.5760(25)	1.5724(25)	—	19

^a $\lambda_{\text{max.}} = 242\text{ nm}$; $\epsilon = 15,500$ in solvent Bu^tOH . ^b W. H. Saunders and R. A. Williams, *J. Amer. Chem. Soc.*, 1957, **79**, 3714.
^c C. H. DePuy and D. H. Froemsdorf, *J. Amer. Chem. Soc.*, 1957, **79**, 3710.

cell was thoroughly shaken and the percentage transmission (T_t) monitored as a function of time. The base concentrations was kept in large excess so that pseudo-first-order kinetics were observed and tests showed that the derived second-order rate constants were independent of the base concentration. In most cases measurements were made

forms the basis of our assignments of experimental error to the other substituted compounds. The value obtained for $Z = p\text{-NO}_2$ must be considered the least reliable, since the reactivity of these compounds was such that a considerable portion of the non-deuteriated compound decomposed during mixing.

The values of the second-order rate constants used in the construction of the Hammett plot (Table 3) are the maximum values obtained for each individual compound, on the assumption that these will be the best approximation to the true second-order rate constants. The values obtained in this way show reasonable agreement with the literature values.¹⁶

TABLE 2

Isotope effects determined from the mixed kinetic runs for $X = m\text{-NO}_2$ at 30.0°C

Base concn./M	0.013	0.013	0.004	0.004	0.006
$10^2 k_2^{\text{H}}/1\text{ mol}^{-1}\text{ s}^{-1}$	70.1	61.6	78.1	70.9	58.6
$k_2^{\text{H}}/k_2^{\text{D}}$	8.65	8.85	8.39	8.63	8.91
Average	8.69 ± 0.3				

at 260 nm but the appearance of the *m*- and *p*-nitrostyrenes was followed at 242 and 300 nm respectively. The infinity transmission was obtained by reading the percentage transmission after at least ten times the measured half life for the deuteriated species.

RESULTS AND DISCUSSION

Isotope Effects.—The isotope effects measured by the mixed kinetic method are given in Table 4 and are listed in order of the increasing electron-withdrawing power of the 2-phenyl substituents. They are larger than the

TABLE 3
Rate constants for reaction of phenethyl bromides in anhydrous *t*-butyl alcohol

Substituent $10^2 k_2^{\text{H}}/1\text{ mol}^{-1}$	<i>p</i> -MeO	H	<i>p</i> -Cl	<i>m</i> -Br	<i>m</i> -NO ₂	<i>p</i> -Ac	<i>p</i> -NO ₂
	0.219	0.716	2.76	4.95	78.1	63.8	1046.9

A value of k_2^{D} was obtained by performing a least-squares fit on the plot of $\log \log (T_t/T_\infty)$ against time when the elimination from the non-deuteriated compound was essentially complete. A similar least-squares fit was then carried out on the \log (difference) plot²¹ for the early part of the run to obtain k_2^{H} . The isotope-effect ratio so obtained is free from any solvent effects. Computations were carried out on an IBM 1130 computer.

theoretical estimates⁹ and are significantly larger than the value of 3.81 recorded for the pyridine-catalysed elimination of *t*-butyl chloride²² and the values of 3.2—6.7 recorded for the *anti*-elimination of some trimethylammonium ions.²³

²² D. N. Kevill and J. C. Dorsey, *J. Org. Chem.*, 1969, **34**, 1985.
²³ W. H. Saunders, jun., and T. A. Ashe, *J. Amer. Chem. Soc.*, 1969, **91**, 4473.

No correction has been applied for the possibility of a secondary isotope effect arising from the presence of the second deuterium atom, the effect of which would be to decrease the size of the observed value. However, there is some evidence that the effect, if it exists, is very small²⁴ and another explanation must be sought. A more likely

TABLE 4

Isotope effects and Arrhenius parameters for reaction of phenethyl bromide with potassium t-butoxide in t-butyl alcohol

	$t/^\circ\text{C}^a$	$k_2^{\text{H}}/k_2^{\text{D}^b}$	$(E_a^{\text{D}} - E_a^{\text{H}})/$ kJ mol^{-1}	$A_{\text{H}}/A_{\text{D}}$
<i>p</i> -MeO	30	7.00 ± 0.1		
	41.7	6.27 ± 0.3	9.6 ± 0.8	0.16
	50.0	5.57 ± 0.2		
H	30.0	8.12 ± 0.1	7.1 ± 4.2^c	0.46^c
<i>p</i> -Cl	30.0	8.40 ± 0.2		
<i>m</i> -Br	30.0	8.25 ± 0.1		
<i>m</i> -NO ₂	30.0	8.68 ± 0.3		
	40.8	7.90 ± 0.1	7.5 ± 0.8	0.46
	49.6	7.38 ± 0.1		
<i>p</i> -NO ₂	30.0	9.14 ± 0.4		

^a Temperatures were maintained to $\pm 0.1^\circ\text{C}$ of the stated value. ^b Measured by mixed kinetic method (ref. 21). ^c Ref. 16.

possibility is the presence of a quantum-mechanical tunnelling effect,²⁵ since there is evidence for such an effect in the closely related elimination of 1-bromo-2-phenylpropane with sodium ethoxide in ethanol.²⁶ This prompted us to examine the temperature-dependence of the isotope effect for $Z = p\text{-MeO}$ and $Z = m\text{-NO}_2$ and the results are in Table 4.

The Arrhenius parameters were obtained by plotting $\log(k_2^{\text{H}}/k_2^{\text{D}})$ against T^{-1} since the slope of this plot yields directly the difference in the activation energies ($E_a^{\text{D}} - E_a^{\text{H}}$) and the intercept, $\log(A_{\text{H}}/A_{\text{D}})$. The differences in the activation energies so obtained are both significantly greater than the theoretical maximum value of 5.1–5.5 kJ mol⁻¹²⁵ calculated on the basis of loss of the stretching vibration of a C–H and C–D bond respectively. The value of $A_{\text{H}}/A_{\text{D}}$ for $Z = p\text{-MeO}$ is significantly less than the value expected in the absence of tunnelling,²⁵ although the value for $Z = m\text{-NO}_2$ is close to the theoretical limit. These results suggest that tunnelling is an important factor in this reaction, at least for the $Z = p\text{-MeO}$ compound, and could account for the size of the isotope effects.

There is no reliable indicator of transition-state symmetry for a concerted $E2$ elimination, but the electron-withdrawing power of the 2-phenyl substituent should serve as an indication of the ΔpK parameter employed by Bell *et al.*²⁷ There appears to be an increase in the value of the isotope effect from $Z = p\text{-MeO}$ to $Z = \text{H}$ but the values for the other phenethyl bromides are the same within experimental error. There is therefore no evidence for a maximum in the isotope effect as the electron-withdrawing power of the substituent in-

creases. These results therefore indicate that either ΔpK , and hence the transition-state geometry, is not changing or, that even if it is, such changes are not being reflected in the magnitude of the isotope effect²⁸ over the range of compounds studied. Interpretation of our results is further complicated by the proton-tunnelling contributions to the isotope effects. As there is no general agreement about the shape of the maximum when tunnelling is important,^{1,6,7} it is impossible to interpret the observed isotope effects in terms of transition-state geometry in a meaningful way. It has recently been suggested¹ that the isotope effect is primarily determined by the tunnel correction, the position of the proton remaining unchanged over a wide range of ΔpK .

In a related study of the potassium t-butoxide-catalysed 1,2-elimination of phenethyl bromide in the presence of increasing dimethyl sulphoxide concentrations, Cockerill *et al.*¹⁶ found that the isotope effect remained constant. They were not able to demonstrate conclusively the presence of proton tunnelling, but their $A_{\text{H}}/A_{\text{D}}$ value is close to the theoretical limit. However, in another paper, Cockerill¹³ was able to demonstrate significant variations in the isotope effect for the 1,2-elimination of phenethylsulphonium bromide (in which $X = +\text{SMe}_2$, a poor leaving group) catalysed by hydroxide ion, in varying concentrations of dimethyl sulphoxide. No attempt was made to demonstrate the presence of proton tunnelling.

The lack of variation in the isotope effect observed for the phenethyl bromide systems therefore appears to be related either to the potassium t-butoxide base, which may be subject to steric hinderance,^{1,29} or to the presence of the good leaving group ($X = \text{Br}$).

The Hammett Plot.—There have been two previous analyses of the effect of substituents on the reactivity of this system. Cockerill *et al.*¹⁶ report a value of 2.53 ± 0.09 for $Z = p\text{-MeO}$, $p\text{-Me}$, H, and $p\text{-Br}$, whereas DePuy and Bishop³⁰ report a value of 2.08 ± 0.02 for $Z = p\text{-MeO}$, H, $p\text{-Cl}$, and $m\text{-Br}$. Both sets of workers based their reaction constants on a limited range of substituents and have plotted their data against Hammett σ values rather than σ^0 .

We have repeated the work of DePuy and Bishop but have extended the range of substituents by a factor of two by including the value for $Z = m\text{-NO}_2$. The plot of $\log k_2^{\text{H}}$ against σ^0 gives a reasonable straight line with a ρ value of 2.85 ± 0.22 ($r = 0.992$) which is appreciably higher than that reported previously. Nevertheless we feel that our value must be considered more reliable in view of the range of substituents covered. The higher value of ρ confirms the carbanionic nature of this elimination with C–H bond breaking in the transition state considerably more advanced than C–Br bond breaking. The points for both $Z = p\text{-Ac}$ and $Z = p\text{-NO}_2$ lie off the

²⁸ F. G. Bordwell and W. J. Boyle, jun., *J. Amer. Chem. Soc.*, 1971, **93**, 512.

²⁹ E. S. Lewis and L. H. Funderburk, *J. Amer. Chem. Soc.*, 1967, **89**, 2322.

³⁰ C. H. DePuy and C. A. Bishop, *J. Amer. Chem. Soc.*, 1960, **82**, 2532.

²⁴ W. H. Saunders, jun., and D. H. Edison, *J. Amer. Chem. Soc.*, 1960, **82**, 138.

²⁵ E. F. Caldin, *Chem. Rev.*, 1969, **69**, 138.

²⁶ V. L. Shiner and M. L. Smith, *J. Amer. Chem. Soc.*, 1961, **83**, 593.

²⁷ R. P. Bell and D. J. Barnes, *Proc. Roy. Soc.*, 1970, **A**, **318**, 421.

regression line in the direction of σ^- with derived σ values of +0.73 and +1.15 respectively. These enhanced values for the strong *p*-(*-M*) groups are consistent with the development of a considerable degree of negative charge in the transition states for these two compounds.

Conclusion.—It was expected that changes in the phenyl ring substituents would alter the transition-state symmetry and perhaps allow the observation of a

maximum in the isotope effect. However, the isotope effect remained constant and the possibility of proton tunnelling in this system has not allowed any interpretation of the results in terms of the transition-state structure. Hence no information can be obtained about the extent of C-H bond breaking throughout the reaction series.

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