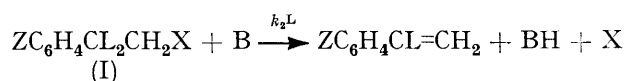


Solvent Dependence of the Primary Deuterium Kinetic Isotope Effect in the Sodium Hydroxide-catalysed *E2* Elimination of Hydrogen Bromide from *p*-Acetyl- and *p*-Nitro-phenethyl Bromide

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Rate constants have been determined from the NaOH-catalysed 1,2-elimination of HBr from *p*-acetyl- and *p*-nitro-phenethyl bromide over a range of dimethyl sulphoxide concentrations. The calculated k_2^H/k_2^D ratios show no dependence on the *para*-substituent or the dimethyl sulphoxide concentration except for *p*-nitrophenethyl bromide at 59.7 and 69.7 mole %. The change in the isotope effect for the *p*-nitro-compound cannot be satisfactorily explained in terms of a change in transition-state symmetry. The previously reported substituent-induced maximum in the isotope effect for phenethyl bromides is shown to be due to a specific solvent effect rather than indicative of a 'Westheimer' maximum. The implication of the overall lack of variation is briefly discussed.

WE have been interested in the substituent effect on the magnitude of the primary deuterium kinetic isotope effect and recently reported^{1,2} on the results obtained for the base-catalysed *E2* elimination from phenethyl compounds (I) where Z = a *meta*- or *para*-substituent,



L = H or D, and X = $\overset{\oplus}{\text{S}}\text{Me}_2$ or Br. For the three systems studied, the ratio k_2^H/k_2^D increased with the electron-withdrawing power of Z, for both the charged and neutral substrates, although for X = Br in the KOBu^t-Bu^tOH system the variation could be accounted for by experimental error, with the exception of Z = *p*-MeO. For the 1,2-elimination of ArCH₂CH₂Br in 50.2 mole % Me₂SO-H₂O¹ a maximum in the isotope effect which could not be accounted for by the estimated errors was observed, the maximum value occurring at Z = *p*-Ac. Whether this data constitutes a maximum in the Westheimer sense³ is uncertain, as the Bronsted β values⁴ for Z = H and *p*-NO₂ are inconsistent with such an interpretation¹ based on an 'E1cB-like' *E2* transition state for the elimination⁵⁻⁷ and currently accepted theoretical views of the substituent effect on such transition states.^{8,9} The general increase in k_2^H/k_2^D observed in these reactions has also been noted in several other cases,^{10,11} while a decrease¹² and invariant ratios¹³ are known but so far no other substituent-induced maxima have been reported.

Attempts have been made to produce a maximum in k_2^H/k_2^D by the addition of Me₂SO to the reaction

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² L. F. Blackwell, P. D. Buckley, K. W. Jolley, and A. K. H. MacGibbon, *J.C.S. Perkin II*, 1973, 169.

³ F. H. Westheimer, *Chem. Rev.* 1961, **61**, 265.

⁴ R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1964, 5.

⁵ L. J. Steffa and E. R. Thornton, *J. Amer. Chem. Soc.*, 1967, **89**, 6149.

⁶ A. F. Cockerill, 'Elimination Reactions,' in 'Comprehensive Chemical Kinetics,' eds. C. H. Bamford and C. H. F. Tipper, Elsevier, Amsterdam, 1973, vol. 9, ch. 3, and references therein.

⁷ A. Fry, *Quart. Rev.*, 1972, 163.

⁸ E. R. Thornton, *J. Amer. Chem. Soc.*, 1967, **89**, 2915.

⁹ R. A. More O'Ferrall, *J. Chem. Soc. (B)*, 1970, 274.

mixtures. Additions of Me₂SO to solutions of NaOH in water bring about marked increases in the thermodynamic basicity of the solutions along with very large rate enhancements.^{10,14-18} Such effects would be expected on theoretical grounds to lead to significant changes in the isotope effect,^{3,19} however, in general, isotope effects for neutral substrates exhibit no dependence on the Me₂SO concentration. It has been claimed¹⁴ that PhCH₂CH₂ $\overset{\oplus}{\text{S}}\text{Me}_2$ does exhibit a maximum at 50.2 mole % Me₂SO, but this maximum depends on the accuracy of rate constants measured at the limits of conventional kinetic techniques. The lack of any such solvent effect for *p*-AcC₆H₄CH₂CH₂ $\overset{\oplus}{\text{S}}\text{Me}_2$ ¹⁸ throws further doubt on the validity of this maximum.

There is clearly a need for further systematic investigation into the effect of Z and Me₂SO on k_2^H/k_2^D , since only an unambiguous observation of a 'true' Westheimer maximum would constitute proof of the validity of using isotope effects as probes for subtle changes in transition-state structure. With this aim in view we have now investigated the solvent dependence of the k_2^H/k_2^D ratios for compounds (I; Z = *p*-Ac and *p*-NO₂, L = H) in NaOH-H₂O-Me₂SO mixtures.

EXPERIMENTAL

Materials.—The preparations of (I; Z = *p*-Ac and *p*-NO₂, L = H) and their deuteriated analogues (L = D) have been described previously.^{1,2} The levels of deuteriation were 1.90 and 1.91 atoms D per molecule respectively as determined by mass spectrometry. Solvents were

¹⁰ P. J. Smith and A. N. Bourns, *Canad. J. Chem.*, 1974, **52**, 749.

¹¹ P. J. Smith and S. K. Tui, *Tetrahedron Letters*, 1973, 61.

¹² P. J. Smith and S. K. Tui, *J. Amer. Chem. Soc.*, 1973, **95**, 4760.

¹³ D. J. McLennan and R. Wong, *J.C.S. Perkin II*, 1974, 526.

¹⁴ A. F. Cockerill, *J. Chem. Soc. (B)*, 1967, 964.

¹⁵ A. F. Cockerill, S. Rottschaefel, and W. H. Saunders, jun., *J. Amer. Chem. Soc.*, 1967, **89**, 901.

¹⁶ A. F. Cockerill and W. H. Saunders, jun., *J. Amer. Chem. Soc.*, 1967, **89**, 4985.

¹⁷ C. A. Pollock and P. J. Smith, *Canad. J. Chem.*, 1971, **49**, 3856.

¹⁸ L. F. Blackwell, unpublished results.

¹⁹ R. A. More O'Ferrall and J. Kouba, *J. Chem. Soc. (B)*, 1967, 985.

prepared as previously¹ and the Me₂SO-H₂O solutions were made up by weight at the temperature of the measurements (30°). Solutions were not adjusted to constant ionic strength but the same base solution was used for each pair of substrates at each Me₂SO concentration.

Kinetics.—The rates were followed at the wavelength maximum of the corresponding styrene, either on a Unicam SP500 u.v. spectrophotometer or on a Durrum-Gibson D110 stopped flow spectrophotometer. Generally reactions with half-lives of < 1 min gave unreliable values for the rate constants when measured on the conventional spectrophotometer. All reactions were carried out under pseudo-first-order conditions with [NaOH] ≥ 10 [substrate].

Kinetic runs for k_2^H were carried out in groups of three and were repeated until a *minimum* of three runs agreed to within 2%. Points were taken for at least two half-lives. As (I; Z = *p*-Ac and *p*-NO₂, L = D) both contained some protium, it was necessary to wait $8t_{1/2}^H$ ($\approx t_{1/2}^D$) before collecting data for the determination of k_2^D . As discussed in a previous paper¹ it was necessary to follow the reaction into the third half-life to obtain consistent values for k_2^D . Again runs were repeated until at least three values agreed to within 3%. Because of the scatter in the third half-life it was necessary to set larger error limits. It was not possible to measure a meaningful value of k_2^H/k_2^D for (I; Z = *p*-Ac) in 6 mole % Me₂SO since the rate of the deuterated reaction was too slow even for 0.3M-NaOH, which is close to the solubility limit.

Stopped-flow runs gave better kinetic plots but the agreement between the runs was sometimes no better than ±5%. Sufficient runs (*ca.* 10) were recorded at each Me₂SO concentration in order to allow deviant runs to be identified and discarded. All runs were hand-plotted before computer fitting and all calculations were as previously described. The errors listed in Table 2 were calculated from the standard deviation from the mean of the individual rate constants.

RESULTS AND DISCUSSION

The measured rate constants are listed in Table 1. The most notable feature of the Table is the large rate

TABLE 1

Rate constants for NaOH-catalysed elimination of HBr from ZC₆H₄CL₂CH₂Br in Me₂SO-H₂O mixtures at 30°^a

[Me ₂ SO] ^b	L	$k_2/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	
		Z = <i>p</i> -Ac	Z = <i>p</i> -NO ₂
6.0	H		0.0152
22.2	H	0.053	0.402
32.6	H	0.354	3.08
50.7	H	7.51	82.5
59.7	H		268
69.7	H	129.3	1 265
		$10k_2^D$	$10k_2^D$
6.0	D		0.0162
22.2	D	0.058	0.436
32.6	D	0.384	3.22
50.7	D	7.81	93.4
59.7	D		348
69.7	D	143	1 990

^a Temperature maintained to within ±0.1°. ^b Mole fraction of Me₂SO × 100.

enhancement (*ca.* 9×10^4) with added Me₂SO. This seems large for the reaction between an ion and a

neutral molecule when compared with the value of *ca.* 4.5×10^2 reported by Bell and Cox²⁰ for the base catalysed inversion of (–)-menthone over a similar range of Me₂SO concentrations. The enhancement is similar to that observed for the reaction of hydroxide ion with the charged substrates ArCH₂CH₂S⁺Me₂ (for Z = H and *p*-Ac) which presumably indicates that it is the increase in solvent basicity which is the dominant factor in determining the rates. This is evidenced by the increase in the H_- function^{21,22} and the parallel between $\log k_2^L$ and the function $H_- + \log C_{H_2O}$ as shown in the Figure.

Solvent Effect on the k_2^H/k_2^D Ratios.—The isotope effects for (I; Z = *p*-Ac and *p*-NO₂, L = H) are given in Table 2. The values are high as noted previously,¹

TABLE 2

Isotope effects for reaction of ZC₆H₄CH₂CH₂Br with NaOH in Me₂SO-H₂O mixtures at 30°

[Me ₂ SO] ^a	[NaOH] ^b	Z = <i>p</i> -Ac	Z = <i>p</i> -NO ₂
6.0	0.3		9.4 ± 0.3
22.2	0.04	9.1 ± 0.3	9.3 ± 0.2
32.6	0.005	9.2 ± 0.5	9.6 ± 0.3
50.7	0.05	9.6 ± 0.4	8.8 ± 0.5
59.7	0.024		7.7 ± 0.4
69.7	0.01	9.0 ± 0.4	6.5 ± 0.4

^a Mole fraction of Me₂SO × 100. ^b mol dm⁻³.

and probably include a small secondary isotope effect. We made no attempt to determine Arrhenius parameters (in order to detect tunnelling contributions) since the differences are smaller than the errors. For (I; Z = *p*-Ac) there is clearly no trend toward a maximum whatsoever despite the large increase in the absolute rate; in fact k_2^H/k_2^D remains constant within experimental error. The average value (9.2 ± 0.3) compares favourably with the value of 9.7 ± 0.3 listed previously¹ in 50.2 mole % Me₂SO at 20°. The difference $d(k_2^H/k_2^D)/dT = 0.5$ is about what is expected for a 10° temperature change in this system.¹ The situation for (I; Z = *p*-NO₂) is interesting and in the light of the results obtained for (I; Z = *p*-Ac), is unexpected. Between 6 and 50.7 mole % Me₂SO there is again no variation in the isotope effect at all which can be considered significant in relation to the experimental error and the values are identical with those obtained for (I; Z = *p*-Ac). This confirms the general insensitivity of the isotope effects^{11,15,17} to changes in Me₂SO concentration and suggests that the decrease in k_2^H/k_2^D from Z = *p*-Ac to *p*-NO₂ noted previously¹ does not imply a Westheimer maximum.³

Above 50.7 mole % however there is a fairly dramatic decrease in the value of k_2^H/k_2^D [for (I; Z = *p*-NO₂)] and the change is one of the largest ever recorded (from 9.6 to 6.4) for a relatively limited change in the system. We are unable to provide a satisfactory explanation of this decrease on the basis of the available data, but

²⁰ R. P. Bell and B. G. Cox, *J. Chem. Soc. (B)*, 1970, 194.

²¹ K. Bowden, *Chem. Rev.*, 1966, **66**, 119.

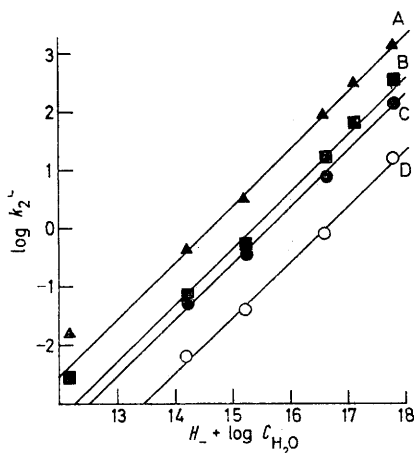
²² K. Bowden and A. F. Cockerill, *J. Chem. Soc. (B)*, 1970, 173.

when the results for (I; $Z = p\text{-Ac}$ and $p\text{-NO}_2$) are considered together, it seems clear that they cannot be accounted for by a consideration of changes in transition state symmetry.

Correlation of $\log k_2^L$ with $H_- + \log C_{H_2O}$.—Linear correlations of $\log k_2^L$ against H_- are not common for $E2$ reactions²³ but it has been shown that¹⁴ relationship (1) derived by Anbar *et al.*²⁴ does correlate the rates

$$\log k_2^L = \log H_- + \log C_{H_2O} + \text{a constant term} \quad (1)$$

of elimination for $\text{ArCH}_2\text{CH}_2\text{SMe}_2$ in $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ mixtures. We have similarly plotted $\log k_2^L$ against $H_- + \log C_{H_2O}$ for all four substrates and have obtained good linear correlations as shown in the Figure. (The



Plot of $\log k_2^L$ against $H_- + \log C_{H_2O}$ at 30°: A, $Z = p\text{-NO}_2$, $L = H$; B, $Z = p\text{-NO}_2$, $L = D$; C, $Z = p\text{-Ac}$, $L = H$; D, $Z = p\text{-Ac}$, $L = D$. H_- Values are taken from ref. 21 and $\log C_{H_2O}$ was calculated according to ref. 14

points for 6% Me_2SO lie well off the plots and probably reflect the fact that the H_- against $[\text{Me}_2\text{SO}]$ plots are curved in this highly aqueous region.) The slopes of the plots are unity within experimental error as expected and this could be taken to confirm a common mechanism ($E2$) for (I; $Z = p\text{-Ac}$ and $p\text{-NO}_2$). However it can also be argued that a linear correlation of this type merely confirms a proton transfer, either rate determining or pre-equilibrium²⁴ which would be consistent with the $E2$ and both the reversible and irreversible carbanion mechanisms and thus is not a sensitive probe for changes in mechanism. It is noticeable for (I; $Z = p\text{-NO}_2$)

however that the k_2^D values at 59.7 and 69.7% Me_2SO tend towards the k_2^H values (see also Table 1) which shows up as a slight deviation from the $\log k_2^D - H_-$ plot (line B in the Figure). This is the reason that the isotope effect decreases in size. If this deviation from the $\log k_2^D - H_-$ plot for (I; $Z = p\text{-NO}_2$, $L = D$) is regarded as significant, it must indicate some solvent dependent change which is only apparent for this substrate. It is hard to envisage any difference either between the two isotopically substituted compounds (I; $Z = p\text{-NO}_2$, $Z = H$ or D) or between (I; $Z = p\text{-Ac}$ or $p\text{-NO}_2$) which could cause a deviation from the $\log k_2^L - H_-$ plot in one case but not for the other three. It is possible that the effect is a consequence of our method of measurement, since we only monitor *total* [olefin] in our experiments and hence a factor such as deuterium exchange, which could account for the deviation, would not be observed for the non-deuteriated substrate. A satisfactory explanation of this behaviour however must await further work.

Conclusions.—Despite the fact that large rate accelerations are observed when Me_2SO is added to this system, up to 69.7 mole % it appears that the k_2^H/k_2^D ratios remain constant, except for (I; $Z = p\text{-NO}_2$) at 59.7 and 69.7% Me_2SO . We are thus forced to the conclusion that our previously reported¹ maximum in the isotope effect for $\text{ArCH}_2\text{CH}_2\text{Br}$ in 50.2 mole % $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ at 20° as Z is varied is the result of some other solvent-dependent factor. It is instructive to note that we would not have observed any change between these two substituents had we carried out our measurements at 40 mole % Me_2SO instead of at 50 mole %. There does not appear therefore to be any convincing experimental evidence available to suggest that a maximum in the isotope effect has in fact ever been achieved in an elimination reaction for either neutral or charged substrates. Thus interpretations of *changes* in k_2^H/k_2^D ratios in terms of subtle changes in transition-state geometry must be treated with reserve for reactions in which C-H bond breaking is coupled with other bond changes, both from experimental and theoretical considerations.^{25,26}

We thank the University Grants Committee for funds to purchase the stopped-flow spectrophotometer.

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²⁶ R. P. Bell, W. H. Sachs and R. L. Tranter, *Trans. Faraday Soc.*, 1970, **66**, 1995.