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Resolution of the non-steady-state kinetics of the elimination of HBr from 2-(*p*-nitrophenyl)ethyl bromide in alcohol/alkoxide media

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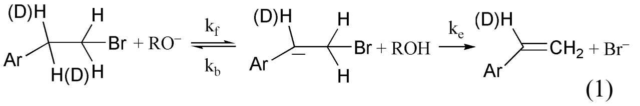
Non-steady-state kinetic studies reveal that the elimination of HBr from 2-(*p*-nitrophenyl)ethyl bromide in alcohol/alkoxide media, the classical concerted E2 reaction, actually takes place by a two-step mechanism involving the intermediate formation of the carbanion.

Introduction

We find that kinetic data for the elimination of HBr from 2-(*p*-nitrophenyl)ethyl bromide (NPEB) in ethanol or methanol containing the corresponding alkoxide ions are inconsistent with the concerted E2 mechanism. Extent of reaction–time profiles for these reactions deviate significantly from the expected response for the E2 mechanism and extent-of-reaction-dependent apparent deuterium kinetic isotope effects (KIE_{app}) were observed. The kinetic data are consistent with the reversible consecutive second-order mechanism, eqn. (1). The formation of the carbanion is rate determining by virtue of the fact that loss of bromide ion (k_e) is rapid compared to protonation of the carbanion (k_b). The latter precludes D/H exchange during the elimination reactions of NPEB-2-d_2.



(1)

The elimination reactions of NPEB in ethanol containing ethoxide ions is a classic example[1–3] of a reaction believed to take place by a concerted E2 mechanism. Recent studies published by the Thibblin group[4–15] and others[16–19] continue to provide significant new mechanistic detail. These studies have been concerned with the factors influencing elimination reactions in the border-line region between the E1CB and E2 mechanisms. The effect of structure on reactivity, kinetic isotope effects, and Brønsted parameters has been heavily relied upon in these discussions.

Our recent non-steady-state kinetic studies[20–26] have revealed that many organic reactions previously believed to follow simple second-order kinetics follow the reversible consecutive second-order mechanism and do not reach a steady state before late in the first half-life. These include proton transfer reactions of methylarene radical cations,[19,20,22] proton transfer between a nitroalkane and hydroxide ion,[21] hydride transfer of an NADH model compound,[25] and the S_N2 reaction between the *p*-nitrophenoxide ion and methyl iodide in aqueous acetonitrile.[26] We anticipated that our non-steady-state kinetic method would be applicable to the E2–E1CB manifold of reactions.

Results and discussion

Table 1 Pseudo-first-order initial and apparent rate constants for the elimination reactions of 2-(*p*-nitrophenyl)ethyl bromide in alcohols containing alkoxide ions at 293 K

Substrate[a]	Solvent	$[RO^-]$/mM	k_{init}/k_{pfo} [b c]	$t_{0.50}/t_{0.05}$ [b c]
NPEB	EtOH	300	0.810	11.12
		150	0.763	10.52
NPEB-d_2	EtOH	300	0.881	12.03
		150	0.929	12.61
NPEB	MeOH	300	0.840	11.58
		150	0.783	11.08
NPEB-d_2	MeOH	300	0.714	8.72
		150	0.750	9.04

[a] NPEB = 2-(*p*-nitrophenyl)ethyl bromide [b] As defined in the text. [c] Each value was derived from 40–60 extent of reaction–time profiles processed from digitally smoothed absorbance (335 nm)–time data (2000 points) generated with either a Hi-Tech model SF-61 or a SF-62 stopped flow instrument. Extent of reaction defined as $[NS]/[NPEB]_0$ where NS is the product, *p*-nitrostyrene.

The analysis of extent of reaction–time profiles is an effective means for distinguishing between the irreversible second-order mechanism (2) and the reversible consecutive second-order mechanism (3) providing that kinetic data in the *pre-steady-state* time period can be accessed.[24] Once steady-state is reached, the two mechanisms

$$A + B \xrightarrow{k_{irrev}} C \qquad (2)$$

$$A + B \underset{k_b}{\overset{k_f}{\rightleftharpoons}} I \xrightarrow{k_p} C \qquad (3)$$

are kinetically indistinguishable. In our non-steady-state kinetic studies we determine two parameters, k_{init}/k_{pfo} and $t_{0.50}/t_{0.05}$, which serve as mechanism probes. The first is defined as the ratio of the initial rate constant (k_{init}) during the extent of reaction ranging from 0 to 0.05 divided by the apparent pseudo first-order rate constant (k_{pfo}) in the range from 0.05 to 0.50. The second is the time ratio, which corresponds to time at extent of reaction 0.50 ($t_{0.50}$) divided by that at extent of reaction equal to 0.05 ($t_{0.05}$). For mechanism (2) k_{init}/k_{pfo} is equal to 1.00 and $t_{0.50}/t_{0.05}$ is equal to 13.51 under pseudo-first-order conditions with reactant B in large excess. In the early states of a reaction following mechanism (3), increase in [C] lags behind the decrease in [A]. When the increase in [C] is monitored under these conditions, k_{init} will be diminished and $t_{0.05}$ will be increased giving rise to k_{init}/k_{pfo} less than unity and $t_{0.50}/t_{0.05}$ less than 13.51. Just how large these deviations will be will depend upon the relative magnitudes of the rate constants k_f, k_b and k_p and in the limit both values approach those for mechanism (2). For elimination reactions, eqn. (2) corresponds to the concerted E2 mechanism and eqn. (3) to the E1CB mechanism in which I is the carbanion.

The data in Table 1 summarizes the mechanism probe parameters observed for the elimination of HBr from NPEB and NPEB-2-d_2 in EtOH and in MeOH containing the corresponding alkoxide ions at 293 K. The last 2 columns in Table 1 show that both k_{init}/k_{pfo} and $t_{0.50}/t_{0.05}$ deviate drastically from the theoretical values for mechanism (2), 1.00 and 13.51, respectively. The extent of reaction–time profiles for the reactions of NPEB and NPEB-d_2 in ethanol are illustrated in Figs. 1 and 2, respectively. The experimental data are shown as solid squares and the solid lines represent the expected response for mechanism (2). The data in Table 1 and Figs. 1 and 2 force the

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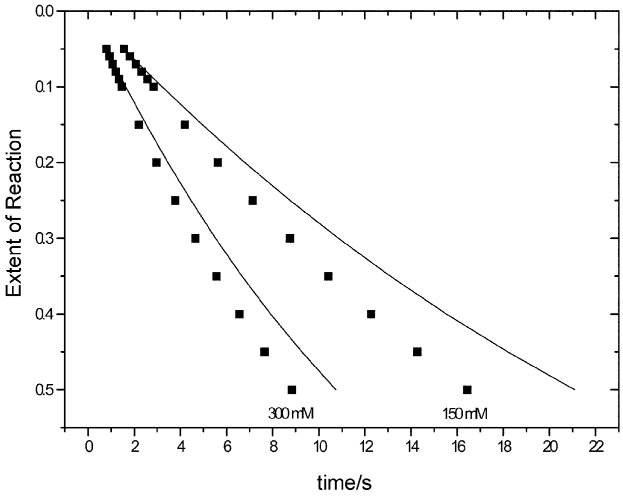

Fig. 1 Extent of reaction–time profiles for the reaction of 2-(*p*-nitrophenyl)ethyl bromide in ethanol containing ethoxide at 293.2 K. Experimental data (solid squares) and theoretical data for the E2 mechanism (solid lines). [EtO$^-$] indicated on the figure.

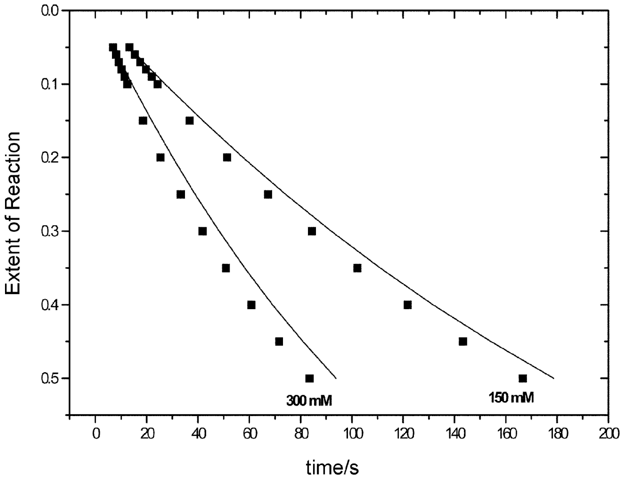

Fig. 2 Extent of reaction–time profiles for the reaction of 2-(*p*-nitrophenyl)ethyl bromide-d$_2$ in ethanol containing ethoxide at 293.2 K. Experimental data (solid squares) and theoretical data for the E2 mechanism (solid lines). [EtO$^-$] indicated on the figure.

conclusion that the elimination of HBr from NPEB in alcohols containing alkoxide ions does not follow the concerted E2 mechanism.

The fit of experimental data to theoretical data for mechanism (3), carried out using procedures recently described,[24] for the elimination reactions of NPEB and NPEB-d$_2$ in ethanol are illustrated in Figs. 3 and 4. Once again the experimental data are shown as solid squares and the solid lines are theoretical data for mechanism (3). In all cases, reasonably close correspondence between experimental and theoretical data are observed. The fitting procedure which involved systematically changing the rate constants and minimizing the difference between experimental and theoretical data until a best fit was obtained invariably resulted in k_f very nearly equal to k_{app}, defined by eqn. (4). Since k_f can only equal k_{app} when k_b is zero, the fitting results require that k_b is very small.

$$k_{app} = k_f k_p/(k_p + k_b) \qquad (4)$$

It is likely that the k_b are non-zero but not large enough to influence the fitting of experimental to theoretical data. It should be pointed out that an additional constraint was applied during the fitting for the reactions of NPEB-d$_2$ (Fig. 4) that consisted of assuming the value for k_p to be equal to that derived during the fitting of data for NPEB (Fig. 3).

Table 2 Rate constants for the elimination reactions of NPEB and NPEB-d$_2$ in alcohols containing alkoxide ions at 293 K

Substrate	Solvent	k_{app}/M^{-1} s$^{-1\,a}$	k_f/M^{-1} s$^{-1\,b}$	k_p/s$^{-1\,c}$
NPEB	EtOH	0.228	0.228	18.1
NPEB-d$_2$	EtOH	0.0288	0.0288	18.1^d
NPEB	MeOH	0.0150	0.0150	1.53
NPEB-d$_2$	MeOH	0.00218	0.00218	1.53^d

^{a} Experimental value evaluated from $t_{0.50}$ and refined in the fitting procedure. ^{b} Best fit value obtained during the fitting procedure. ^{c} Best fit value obtained during the fitting procedure. ^{d} Constraint placed on the fitting that k_p for NPEB-d$_2$ be equal to that for NPEB.

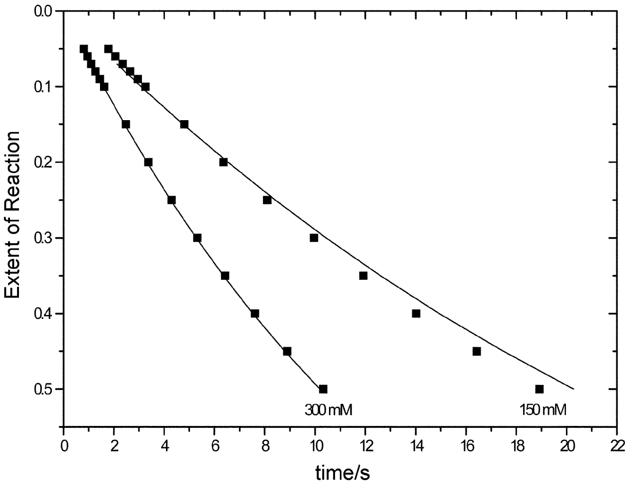

Fig. 3 Extent of reaction–time profiles for the reaction of 2-(*p*-nitrophenyl)ethyl bromide in ethanol containing ethoxide at 293.2 K. Experimental data (solid squares) and best-fit theoretical data for the reversible consecutive second-order mechanism (solid lines). [EtO$^-$] indicated on the figure.

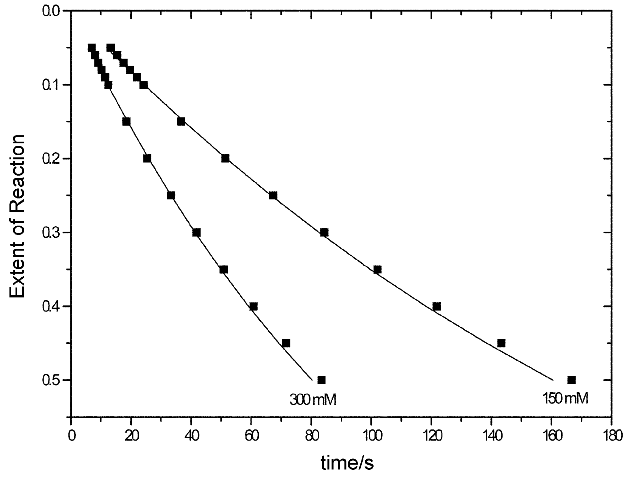

Fig. 4 Extent of reaction–time profiles for the reaction of 2-(*p*-nitrophenyl)ethyl bromide-d$_2$ in ethanol containing ethoxide at 293.2 K. Experimental data (solid squares) and best-fit theoretical data for the reversible consecutive second-order mechanism (solid lines). [EtO$^-$] indicated on the figure.

The experimental (k_{app}) and best-fit (k_f and k_p) rate constants derived from extent of reaction–time profiles in both solvent systems are summarized in Table 2. The features of most interest are (a) that the relatively small k_p values are about two orders of magnitude greater than the corresponding k_f values and (b) k_f are about 15 times as great in ethanol as compared to methanol. Another feature of interest of the experimental data is that the apparent deuterium kinetic isotope effects (KIE$_{app}$) are extent-of-reaction dependent. This is illustrated by the plots in Fig. 5a (EtOH) and 5b (MeOH).

Table 3 The effect of the k_p/k_f ratio on the non-steady-state mechanism probes for the E2–E1CB mechanism manifold[a]

k_p/s^{-1}	k_{init}/s^{-1}	k_{pfo}/s^{-1}	$t_{0.50}/t_{0.05}$
1	0.144	0.478	4.72
2	0.230	0.650	4.85
4	0.280	0.814	5.28
8	0.380	0.930	6.12
16	0.502	0.983	7.41
32	0.638	0.997	9.01
64	0.768	1.000	10.01
128	0.867	1.000	11.85
256	0.929	1.000	12.63
512	0.963	1.000	13.06
1000	0.981	1.000	13.28
10000	0.998	1.000	13.49

[a] Mechanism (3), $[A]_0 = 0.001$ M, $[B]_0 = 1$ M, $k_f = 1$ M^{-1} s^{-1}, $k_b = 0$.

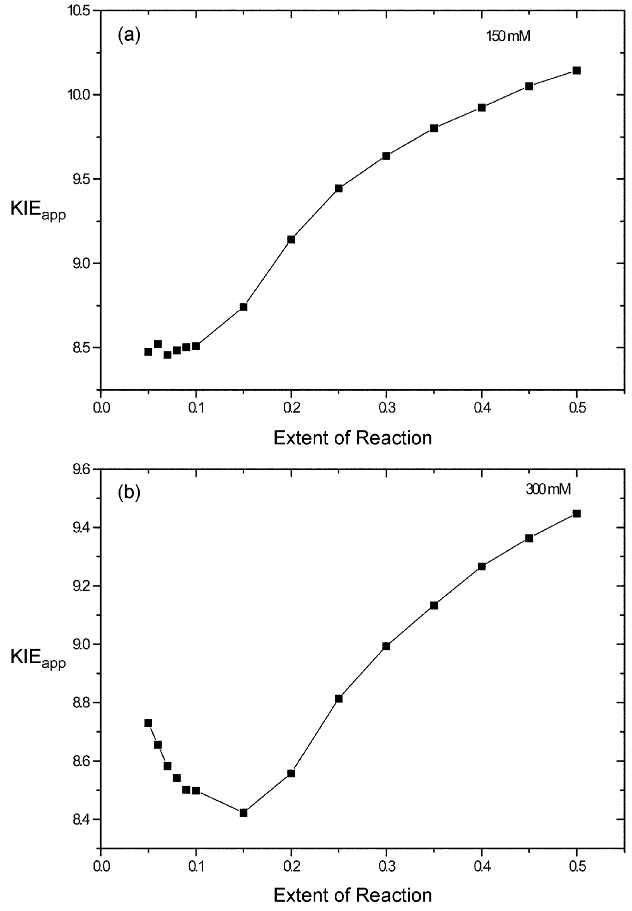

Fig. 5 Apparent deuterium kinetic isotope effects as a function of extent of reaction ($[EtO^-]$ = 150 mM (a) and 300 mM (b)) for the elimination of HBr from 2-(*p*-nitrophenyl)ethyl bromide.

In order to provide further insight into how the relative values of k_f and k_p influence the magnitudes of the mechanistic probes, (k_{init}/k_{pfo} and $t_{0.50}/t_{0.05}$), theoretical data were calculated for the hypothetical case where $k_{app} = k_f$ (1 M^{-1}s^{-1}), $k_b = 0$, and k_p was varied over a wide range. These results are summarized in Table 3. The most interesting feature of these data is that k_{pfo} approaches k_f when k_p/k_f is about 32 while k_{init} does not approach the k_f value until the ratio is nearly 10,000. This provides a very wide range of k_p values where $t_{0.50}/t_{0.05}$ deviates significantly from the limiting value of 13.51.

Conclusions

Our primary conclusion from this preliminary study of the kinetics of elimination reactions is that the classic example of a concerted E2 mechanism, the elimination of HBr from NPEB, takes place by the E1CB mechanism accompanied by the formation of the carbanion which undergoes loss of bromide ion at a moderate rate. Our secondary conclusion, which is equally important, is that the non-steady-state mechanism probes are highly effective in the analysis of elimination reactions. Our recently developed data fitting procedure facilitates the resolution of the kinetics of the 2-step mechanism into the microscopic rate constants of the individual steps.

Acknowledgements

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References

1 R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1964, 5–15.
2 L. F. Blackwell, P. D. Buckley, J. W. Jolley and A. K. H. MacGibbon, *J. Chem. Soc., Perkin Trans. 2*, 1973, 169–173.
3 J. R. Gandler and W. P. Jencks, *J. Am. Chem. Soc.*, 1982, **104**, 1937–1951.
4 X. Zeng and A. Thibblin, *J. Chem. Soc., Perkin Trans. 2*, 2002, 1352–1358.
5 Z. S. Jia, J. Rudzinski, P. Paneth and A. Thibblin, *J. Org. Chem.*, 2002, **67**, 177–181.
6 Q. Meng and A. Thibblin, *J. Chem. Soc., Perkin Trans. 2*, 1999, 1397–1404.
7 Q. Meng, B. Du and A. Thibblin, *J. Phys. Org. Chem.*, 1999, **12**, 116–122.
8 Q. Meng and A. Thibblin, *J. Chem. Soc., Perkin Trans. 2*, 1998, 583–590.
9 Q. Meng and A. Thibblin, *J. Am. Chem. Soc.*, 1997, **119**, 1224–1229.
10 Q. Meng, A. Gogoll and A. Thibblin, *J. Am. Chem. Soc.*, 1997, **119**, 1217–1223.
11 A. Thibblin and Y. Saeki, *J. Org. Chem.*, 1997, **62**, 1079–1082.
12 Q. Meng and A. Thibblin, *J. Chem. Soc., Chem. Commun.*, 1996, 345–346.
13 Q. Meng and A. Thibblin, *J. Am. Chem. Soc.*, 1995, **117**, 9399–9407.
14 Q. Meng and A. Thibblin, *J. Am. Chem. Soc.*, 1995, **117**, 1839–1840.
15 A. Thibblin, *Organic Reaction Mechanisms*, 1992, 327–343; A. Thibblin, *Organic Reaction Mechanisms*, 1991, 335–346.
16 P. Ryberg and O. Matsson, *J. Am. Chem. Soc.*, 2001, **123**, 2712–2718.
17 F. G. Larkin, R. A. More O'Ferrall and D. G. Murphy, *Coll. Czech. Chem. Commun.*, 1999, **64**, 1833–1848.
18 B. R. Cho, H. S. Chung and S. Y. Pyun, *J. Org. Chem.*, 1999, **64**, 8375–8378.
19 W. H. Saunders, Jr., *J. Org. Chem.*, 1999, **64**, 861–865.
20 V. D. Parker, Y. Zhao, Y. Lu and G. Zheng, *J. Am. Chem. Soc.*, 1998, **120**, 12720–12727.
21 Y. Zhao, Y. Lu and V. D. Parker, *J. Am. Chem. Soc.*, 2001, **123**, 1579–1586.
22 Y. Lu, Y. Zhao and V. D. Parker, *J. Am. Chem. Soc.*, 2001, **123**, 5900–5907.
23 Y. Zhao, Y. Lu and V. D. Parker, *J. Chem. Soc., Perkin Trans. 2*, 2001, 1481–1487.
24 V. D. Parker and Y. Zhao, *J. Phys. Org. Chem.*, 2001, **14**, 604–611.
25 Y. Lu, Y. Zhao, K. L. Handoo and V. D. Parker, *Org. Biomol. Chem.*, 2003, **1 (DOI: 10.1039/b208186e).**
26 Y. Lu, K. L. Handoo and V. D. Parker, *Org. Biomol. Chem.*, 2003, **1 (DOI: 10.1039/b208635b).**