Water and hydrogen atom elimination from ionised *n*-propanol: extraordinarily large kinetic isotope effects

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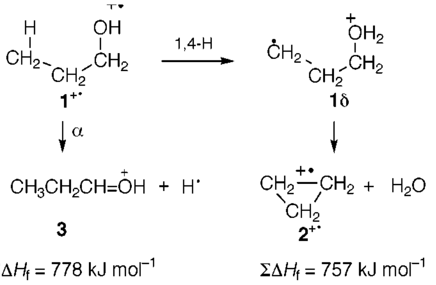
Hydrogen atom loss from ionised *n*-propanol occurs specifically from the α-carbon atom and is subject to a kinetic isotope effect of approximately 500 : 1; somewhat smaller, though still very large, isotope effects are manifested in water loss, which is initiated by an essentially site-specific 1,4-hydrogen transfer.

The properties and reactions of ions in the absence of solvent may be conveniently studied by mass spectrometry. Low-energy (metastable) ions almost always dissociate from the ground electronic state with internal energies in the transition states that are comparable to those found in classical solution experiments.[1,2] Perhaps the most compelling evidence indicating the importance of relative critical energies[3] in influencing the relative rates of competing reactions of metastable ions is the frequent intervention of kinetic isotope effects, some of which are large, especially for small species.[4,5]

Direct bond cleavages, which are probably the simplest of all elementary chemical reactions, are ubiquitous in the dissociation of radical cations.[6] Isotope effects often contain information on bond cleavages and several detailed studies have shown that alkyl radical elimination by seemingly simple cleavages may be more complicated than expected.[7–11] The related process of hydrogen atom loss occurs less frequently,[6] and may involve some unique features.

Metastable ionised *n*-propanol $\mathbf{1}^{+\cdot}$, dissociates by two routes, each of which has been shown to proceed with extremely high site selectivity.[12] The dominant reaction, loss of water, takes place after a unidirectional 1,4-hydrogen transfer from the γ-carbon atom to the oxygen atom to give the distonic[13] ion,[14] $\cdot CH_2CH_2CH_2OH_2^+$, **1δ**, which then expels water to form ionised cyclopropane, $\mathbf{2}^{+\cdot}$. About 2% of $\mathbf{1}^{+\cdot}$ dissociates by eliminating a hydrogen atom to give protonated propionaldehyde **3** (Scheme 1). Labelling evidence[12] provides indirect evidence that one of the α-hydrogen atoms is specifically lost, but expulsion of deuterium ($D^{\cdot}$) rather than protium ($H^{\cdot}$) has not yet been detected. Thus, it has been shown that both $CH_3CH_2CH_2OH^{+\cdot}$ and $CH_3CD_2CH_2OH^{+\cdot}$ eliminate predominantly H_2O and a minor proportion of $H^{\cdot}$. On the other hand, $CD_3CH_2CH_2OH^{+\cdot}$ loses HOD and $H^{\cdot}$ in comparable quantities. Moreover, $CH_3CH_2CD_2OH^{+\cdot}$ expels essentially only H_2O (but no $H^{\cdot}$ or $D^{\cdot}$), whereas $CH_3CH_2CHDOH^{+\cdot}$ loses mainly H_2O, a little $H^{\cdot}$, but no $D^{\cdot}$.



Scheme 1

These data indicate that both the 1,4-hydrogen transfer which initiates water loss and cleavage of the carbon–hydrogen bond resulting in hydrogen atom elimination are influenced by very large isotope effects. Although a lower limit of 30 : 1 for the isotope effect for hydrogen atom loss was set,[12] an accurate value could not be determined because $CH_3CH_2CHDOH^{+\cdot}$ does not lose $D^{\cdot}$ at a measurable rate. However, the overall isotope effect on water loss was estimated to be *ca.* 44 : 1 from the difference in the ratios of hydrogen atom and water lost from $CH_3CH_2CH_2OH^{+\cdot}$ and $CD_3CH_2CH_2OH^{+\cdot}$. The total enthalpy of formation (778 kJ mol^{-1}) of the products of hydrogen atom loss, which appears to involve little or no reverse critical energy[15] even though it entails a large isotope effect, is only slightly higher than that (757 kJ mol^{-1}) of the products of water expulsion.[12] Moreover, the energy of the transition state for the 1,4-hydrogen transfer must lie above 757 kJ mol^{-1} because this step is rate-limiting and subject to an isotope effect. Consequently, the competition between water and hydrogen atom loss is strongly influenced by relatively small differences in the energetics of these reactions.

In order to obtain a better estimate of the ^2H isotope effect on hydrogen atom loss and to determine whether this process also shows a ^{13}C isotope effect, a wider range of labelled analogues of $\mathbf{1}^{+\cdot}$ has been investigated (Table 1). In general, where these data overlap with those previously reported,[12] the agreement is good, although there are some minor variations that may be attributed to instrumental parameters. Hydrogen atom loss competes slightly more effectively with water loss and the kinetic energy releases are marginally larger in the new data. Three significant deductions may be made from the new data.

Table 1 Reactions of metastable ionised *n*-propanol and labelled analogues

	Neutral species lost							
	H_2O		HOD[a]		$H^{\cdot}$		$D^{\cdot}$	
Initial structure	*R*[b]	*T*[c]	*R*[b]	*T*[c]	*R*[b]	*T*[c]	*R*[a]	*T*[c]
$CH_3CH_2CH_2OH^{+\cdot}$	97.4	1.4			2.6	8.3		
$CH_3CH_2CHDOH^{+\cdot}$	93.6	1.6			6.4	10.0	< 0.05	
$CH_3CH_2CD_2OH^{+\cdot}$	100	1.7					< 0.01	
$CH_3CD_2CH_2OH^{+\cdot}$	89.9	1.2	*d*		10.1	10.3		
$CD_3CH_2CH_2OH^{+\cdot}$	*d*		41.0	1.9	59.0	12.4		
$CH_2DCH_2CH_2OH^{+\cdot}$	77.8	2.0	7.5	2.2	2.8	12.3		
$CD_3CH_2CHDOH^{+\cdot}$	*d*		49.4	1.7	30.5	8.8	0.1	*e*
$CH_3CH_2{}^{13}CH_2OH^{+\cdot}$	92.4	1.5			7.6	4.3		
$CD_3CH_2{}^{13}CH_2OH^{+\cdot}$			42.4	1.6	57.6	7.7		

[a] None of these metastable ionised labelled propanols loses D_2O. [b] *R* = Relative abundances normalised to a total of 100 units and measured by metastable peak heights on the VG Analytical ZAB-R mass spectrometer (ref. 20). [c] *T* = Kinetic energy release (in kJ mol^{-1}), estimated from the width at half-height of the appropriate metastable peak with no correction for the width of the main beam. Values are quoted to one decimal place to aviod introducing rounding errors. [d] Extremely weak peaks were detected, but these signals are attributable to water loss from the ^{13}C satellite signal of the $[M–H]^+$ peak. [e] Peak too weak to permit accurate measurements.

First, the value of *ca.* 54 : 1 obtained for the overall isotope effect on water loss is quite similar to that (*ca.* 44 : 1) reported previously[12] from considering the suppression of HOD loss relative to $H^{\cdot}$ elimination from $CD_3CH_2CH_2OH^{+\cdot}$ compared to the behaviour of $CH_3CH_2CH_2OH^{+\cdot}$. However, the loss of H_2O and HOD in the ratio of *ca.* 10 : 1 from $CH_2DCH_2CH_2OH^{+\cdot}$ corresponds to a much smaller primary isotope effect of only *ca.* 5 : 1 for the initial hydrogen transfer step. This value is a lower limit and would be approximately doubled if account were taken of the overlapping loss of H_2O and HOD in similar quantities from the ^{13}C satellite signal of the oxonium ion, $CH_2DCH_2CH{=}OH^+$, formed by hydrogen atom loss from $CH_2DCH_2CH_2OH^{+\cdot}$. The discrepancy between the extremely large overall isotope effect and the much less pronounced, although still substantial, primary isotope effect probably indicates that a significant secondary isotope effect operates in this system. Thus, the rate of D transfer from the CD_3 group of $CD_3CH_2CH_2OH^{+\cdot}$ is reduced by both a primary isotope effect (because a C–D bond is being broken) and a secondary isotope effect (because a CD_2 group in which the hybridisation at carbon changes from sp^3 to sp^2 is left at the migration origin). In contrast, the rate of D transfer from the CH_2D group of $CH_2DCH_2CH_2OH^{+\cdot}$ is reduced by the same primary isotope effect (because a C–D bond is being broken), but the secondary isotope effect does not operate (because a CH_2 group is at the migration origin). Although secondary isotope effects usually are smaller than primary isotope effects, there are clear examples of systems in which secondary effects are comparable in magnitude to primary effects.[16] Water loss from $\mathbf{1}^{+\cdot}$ appears to be another example of this behaviour.

Secondly, a better estimate for the isotope effect on hydrogen atom loss may be obtained by considering the behaviour of $CD_3CH_2CHDOH^{+\cdot}$ because the dominant water loss reaction is slowed by the isotope effects influencing the initial D transfer, thus permitting $H^{\cdot}$ (and, to a very limited extent, $D^{\cdot}$) loss to compete. Even so, the signal for $D^{\cdot}$ loss is barely detectable and is only *ca.* 0.2% of that for $H^{\cdot}$ elimination. This enormous isotope effect of *ca.* 500 : 1 is probably the largest so far detected in the dissociation of any ion containing four heavy atoms. This estimate is a lower limit for the primary isotope effect since any secondary isotope effect would favour $D^{\cdot}$ loss.

Thirdly, the small but reproducible increase in the ratio of HOD to $H^{\cdot}$ loss from $CD_3CH_2CH_2OH^{+\cdot}$ (0.70 : 1) and $CD_3CH_2{}^{13}CH_2OH^{+\cdot}$ (0.74 : 1) gives a value of *ca.* 1.06 : 1 for the overall ^{13}C isotope effect on hydrogen atom loss. This value is increased to *ca.* 1.2 if peak areas rather than heights are used to estimate the relative abundances of the competing processes. Although ^{13}C isotope effects are by their nature much smaller than ^2H isotope effects and this particular ^{13}C isotope effect is quite large, it is surprisingly small in view of the enormous ^2H isotope effect of *ca.* 500 : 1. Furthermore, the behaviour of $CH_3CH_2{}^{13}CH_2OH^{+\cdot}$, for which the ratio of H_2O loss relative to $H^{\cdot}$ elimination (12 : 1) is reduced compared to that (37 : 1) for $CH_3CH_2CH_2OH^{+\cdot}$, seems to suggest that water loss is somehow affected by a ^{13}C isotope effect (*ca.* 3.1 : 1 from peak heights or *ca.* 2.1 : 1 from peak areas). Any such ^{13}C isotope effect on water loss would offset that on hydrogen atom elimination and give values of *ca.* 3.2 : 1 (peak heights) or 2.6 : 1 (peak areas) for the true ^{13}C isotope effect on hydrogen atom loss. This value is exceptionally large and is in keeping with the enormous ^2H isotope effect of *ca.* 500 : 1.

The unanticipated conclusion that water loss is affected by a ^{13}C isotope effect is supported by a similar reduction in the ratio of $H^{\cdot}$ loss relative to H_2O elimination (15 : 1) for $CH_3CH_2CHDOH^{+\cdot}$, compared to that found for $CH_3CH_2CH_2OH^{+\cdot}$, thus suggesting that a secondary ^2H isotope effect of *ca.* 2.6 : (peak heights) or *ca.* 2.5 : 1 (peak areas) also discriminates against water loss. Recent high-level molecular orbital calculations on ionised ethanol reveal that the C–C bond is unusually long.[17] Geometry optimisations at the MP2(FC)6-311G** level[18] of theory using the GAUSSIAN 94 suite of programs[19] indicate that the C(1)–C(2) bond is similarly elongated (to 1.738 Å) in the lowest energy structure of $\mathbf{1}^{+\cdot}$. In contrast, the corresponding bond in **1δ** is not appreciably elongated (1.515 Å) and is very similar in length to the C(2)–C(3) bond (1.501 Å). The peculiar geometry of the minimum energy form of $\mathbf{1}^{+\cdot}$ may provide a key to explain the unusual features of water and hydrogen atom loss. This structure is inappropriate for water elimination (the methyl and hydroxy groups are held well apart, thus preventing the initial hydrogen transfer) and hydrogen atom elimination (the wrong bond is stretched and further elongation would lead to ethyl radical loss by α-cleavage). In order to facilitate either water or hydrogen atom elimination, quite considerable changes to the C(1)–C(2) bond length would be necessary, thus accounting for the large isotope effects on both reactions.

Regardless of their precise origin, the sheer magnitude of these isotope effects, particularly that for hydrogen atom loss, reveals that α-cleavage and hydrogen transfers are sometimes complex processes worthy of further investigation.

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