Mechanisms of Solvolytic Alkene-Forming Elimination Reactions

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1 Introduction

Solvolytic elimination is often defined as elimination that is promoted (induced) by the solvent (SOH), *i.e.*, the solvent acts as the hydron-abstracting base.[1] This review will discuss elimination in a broader sense, including all types of alkene-forming elimination reactions that accompany substitution by the solvent. Thus elimination through a carbocation intermediate as well as concerted pericyclic elimination (thermal or pyrolytic) and solvent-promoted elimination ($E2$) will be treated. It will also include heterolysis reactions in non-nucleophilic solvents in which an alkene is formed by a stepwise reaction through a carbocationic intermediate. The various types of mechanisms are summarized in Table 1. The recently published IUPAC recommendations for representation of reaction mechanisms are given in the last column of this table.[2]

Most of the review will deal with 1,2-elimination, but examples of 1,4-elimination will also be discussed. A few representative examples of reactions that follow each type of mechanism will be presented. For a more complete account of solvolytic elimination reactions, see for example a monograph of Saunders and Cockerill[3] and a review by Baciocchi.[4]

2 Extreme Kinetic Deuterium Isotope Effects as a Probe of Reaction Branching

Solvolysis reactions of secondary and tertiary substrates having at least one hydron in the β-position generally provide both a substitution product, by reaction with the solvent or added nucleophile, and an elimination product. Good nucleophilic solvents favour substitution, and elimination is often minor under such conditions. When the experimental results indicate stepwise solvolysis, the substitution and the elimination have frequently been postulated, for the sake of mechanistic simplicity, to occur *via* a common carbocation intermediate. As indicated in equation 1, the common intermediate may be an ion pair or a free, diffusionally-equilibrated carbocation that is formed by reversible or irreversible ionization. It may also be a carbocation–molecule pair (ion–dipole intermediate) formed from a substrate RX^+ with a neutral leaving group, *e.g.* an ammonium salt or a protonated ether or alcohol. As will be shown below, the magnitude of the kinetic deuterium isotope effects for the separate reactions using substrates deuteriated in the β-position may provide experimental evidence for branching through a common intermediate.

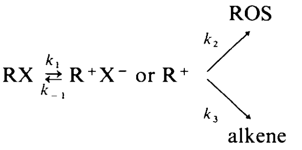
Table 1 Mechanistic classification of solvolytic elimination reactions

Dehydronation of	Base	Kinetic order	Description	Symbol	IUPAC symbol[2]
RX	B^-, SOH	2nd[a]	concerted	$E2$	$A_{xh}D_HD_N$
RX		1st	concerted pericyclic	E_i	cyclo-$D_HD_NA_n$
R^+X^-	SOH, B^- X^-	2nd[a] 1st	preequilibrium ion pair	$E2_{ip}$	$D_N^{*}A_{xh}D_H^{\ddagger}$
R^+X^-	SOH, B^-, X^-	1st	irreversible ion pair	$E1_{ip}$	$D_N^{\ddagger *}A_{xh}D_H$
R^+	SOH, B^-	1st	carbocation	$E1$	$D_N^{\ddagger +}A_{xh}D_H$

[a] Pseudo-first order if solvent is the base.

Enlarged and attenuated isotope effects have been employed extensively in this laboratory as a mechanistic probe of coupled reactions through a common intermediate.[5] The probe was first used in studies of competing elimination and proton-transfer reactions that were shown to proceed through common hydrogen-bonded carbanion intermediates. The method has also been found to be very useful in probing common intermediates in carbocation reactions.[5—10] Several of the reactions that will be discussed in this review have been studied using this probe and therefore it will be discussed in general terms in this section as an introduction.

The mechanistic model of equation 1 corresponds to the relations between the phenomenological rate constants k_S and k_E for formation of substitution and elimination product, respectively, and microscopic rate constants as described by equations 2—4.



$$\mathrm{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{R^+X^-}\ \text{or}\ \mathrm{R^+} \begin{cases} \xrightarrow{k_2} \mathrm{ROS} \\ \xrightarrow{k_3} \text{alkene} \end{cases} \qquad (1)$$

$$k_S = k_1k_2/(k_{-1} + k_2 + k_3) \qquad (2)$$

$$k_E = k_1k_3/(k_{-1} + k_2 + k_3) \qquad (3)$$

$$k_S + k_E = k_1(k_2 + k_3)/(k_{-1} + k_2 + k_3) \qquad (4)$$

The expressions for the isotope effects are:

$$\frac{k_S^H}{k_S^D} = \frac{(k_1^H/k_1^D)(k_2^H/k_2^D)(k_{-1}^D + k_2^D + k_3^D)}{(k_{-1}^H + k_2^H + k_3^H)} \qquad (5)$$

$$\frac{k_E^H}{k_E^D} = \frac{(k_1^H/k_1^D)(k_3^H/k_3^D)(k_{-1}^D + k_2^D + k_3^D)}{(k_{-1}^H + k_2^H + k_3^H)} \qquad (6)$$

$$\frac{k_S^H + k_E^H)}{(k_S^D + k_E^D)} = \frac{(k_1^H/k_1^D)[(k_2^H + k_3^H)/(k_2^D + k_3^D)]}{[(k_{-1}^H + k_2^H + k_3^H)/(k_{-1}^D + k_2^D + k_3^D)]}$$

Reaction branching may cause enlarged and attenuated isotope effects as will be discussed below. The isotope effect k_1^H/k_1^D is a secondary isotope effect and is expected to have a value of 1.10 ± 0.05/β-D.[11] Also k_2^H/k_2^D is a secondary isotope effect; the

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value should be close to unity The primary isotope effect k_3^H/k_3^D, on the other hand, should have a substantial value [12]

Let us assume for simplicity that internal return is negligible ($k_{-1} \ll k_2, k_3$) It can be inferred from equation 6 that the isotope effect on the elimination reaction attains a maximum value of $k_E^H/k_E^D = (k_1^H/k_1^D)(k_3^H/k_3^D)$ when elimination is much slower than substitution (k_3^H/k_2^H) The isotope effect on the substitution reaction (equation 5) attains under these conditions a maximum value of $k_S^H \ll k_S^D = k_1^H/k_1^D$ On the other hand, fast elimination, *i e* $k_3^H \gg k_2^H$, yields a minimum elimination isotope effect of $k_E^H/k_E^D = k_1^H/k_1^D$, and a minimum substitution isotope effect of $k_S^H/k_S^D = (k_1^H/k_1^D)(k_2^H/k_2^D)(k_3^D/k_3^H)$, which can be approximated to $k_S^H/k_S^D = (k_1^H/k_1^D)(k_3^D/k_3^H)$

Fast internal return ($k_{-1} \gg k_2, k_3$) yields $k_E^H/k_E^D = (k_1^H/k_1^D)(k_3^H/k_3^D)(k_{-1}^D/k_{-1}^H)$, *i e* , $k_E^H/k_E^D \approx (k_1^H/k_1^D)(k_3^H/k_3^D)$ This has the same effect on the elimination isotope effect as fast substitution Thus, the observed elimination isotope effect is enlarged owing to multiplication by a factor that is larger than unity

The above analysis shows that *competition between elimination and substitution that occurs through a common intermediate may give rise to an enlarged kinetic deuterium isotope effect for the elimination reaction, and an attenuated isotope effect for the substitution reaction The relative amounts of the elimination and substitution products, and the extent of internal return, govern how large these effects will be*

3 Concerted Solvent-Promoted Elimination

Concerted elimination with the solvent acting as the base may be considered to be the mechanistically most simple of the mechanistic types of Table 1 Despite this simplicity, the mechanism is very difficult to establish If the solvent is able to abstract a hydron, the conjugate base (SO^-) of the solvent, or another added base of higher basicity than the solvent, should be an even more efficient hydron abstractor as shown graphically in Figure 1 The experimentally obtained rate constant (k_E^0), which is measured without added base B^-, could be the pseudo-first-order reaction rate constant for a concerted solvent-promoted reaction or the first-order rate constant of a concerted pericyclic reaction It could also be the macroscopic rate constant of a multistep reaction through a carbocation or ion-pair intermediate When the lifetime of the carbocationic species is too short to be considered as an intermediate ($t_{\frac{1}{2}} < 10^{-13}$ s), the reaction is enforced to be concerted [13] This situation will be discussed below in connection with ion-pair intermediates

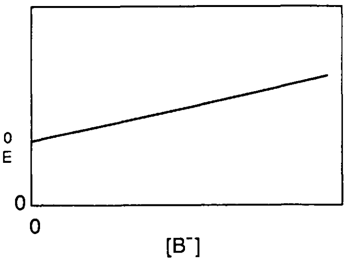
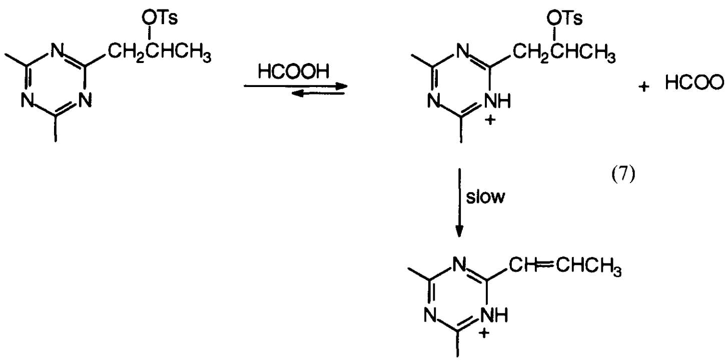


Figure 1 The expected increase in elimination rate constant as a function of added strong base (see Section 3)

The solvolysis of a sulfonate ester in formic acid has been suggested to involve a concerted solvent-promoted elimination reaction (equation 7) [14] However, there seems to be no conclusive evidence that the solvent is the active base, formate anion within an ion pair (generated in the first step) or the leaving group might be the hydron acceptor



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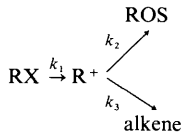
4 Stepwise Elimination *via* a 'Free', Solvent-Equilibrated Carbocation (*E*1)

The other extreme mechanism is the classical *E*1 mechanism The elimination occurs through ionization of the substrate to give the carbocation ion pair, or the ion–molecule pair if the leaving group is a neutral species The dissociation of this complex is much faster than its reaction to elimination product A parallel route to substitution product by reaction with solvent or added nucleophile has usually been assumed to occur by nucleophilic attack on the very same carbocation (equation 8)

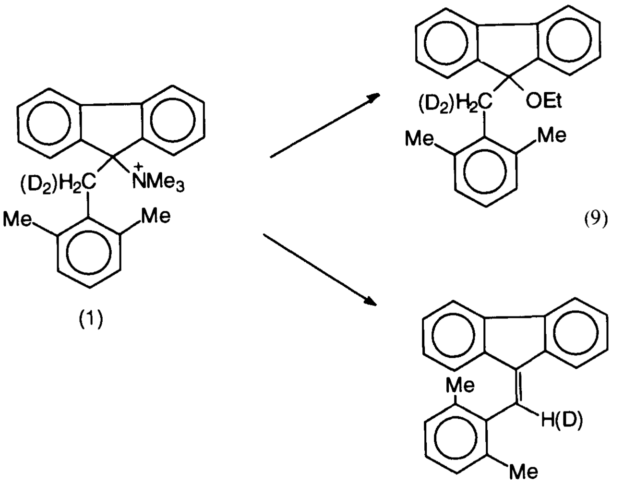


$$RX \xrightarrow{k_1} R^+ \begin{cases} \xrightarrow{k_2} ROS \\ \xrightarrow{k_3} \text{alkene} \end{cases} \quad (8)$$

Pure *E*1 reactions as defined above are probably not common for solvolytic reactions of substrates with leaving groups that are negatively charged or are neutral but efficient bases There seems to be no evidence that solvolytic elimination from such substrates occurs mainly or exclusively from the 'free', diffusionally equilibrated carbocation

The leaving group of an ion pair is often very efficient in promoting elimination by abstraction of a β-hydron, *even in highly aqueous media* It has been reported that 1,1-diphenylethyl derivatives, Ph_2CMeX, react to elimination product through the ion pair [15] The leaving groups AcO^- and *p*-nitrobenzoate give rise to three times as much elimination as the leaving groups MeOH and HOAc in 20 vol% Me_2SO in water However, dissociation of the ion pair has been concluded to be faster than elimination since the measured nucleophilic selectivities are very similar with different leaving groups Despite the relatively high stability of the free carbocation and the highly aqueous solvent, most of the elimination arises from the ion pairs The free carbocation obviously yields less elimination than the ion pairs

The solvolysis of (1) in ethanol at 57 3 °C has been found to provide 28% of alkene and 72% of ether (equation 9) [16] The



(1)

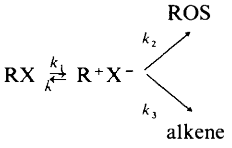
(9)

corresponding compound with only one *ortho* substituent reacts slower but gives a greater yield of alkene product. The formation of the free carbocation was concluded to be rate limiting since a low concentration of triethylamine (3.5 mM) or sodium ethoxide (3.1 mM) does not significantly change product composition or overall rate. The $E1$ mechanism (equation 8) was proposed. A Hammett ρ of -2.5 was calculated from rate data of (1) combined with rate data for the substrate having a bromo-substituent on the 9-fluorenyl ring.

The kinetic deuterium isotope effect for the disappearance of the substrate (1) deuteriated in the β-position was measured as $k^{\mathrm{H}}_{\mathrm{obs}}/k^{\mathrm{D2}}_{\mathrm{obs}} = 1.62$ at 57.3 °C and was concluded to be in accord with a secondary isotope effect. However, the maximum secondary β-deuterium isotope effect for this type of process has been estimated to be $k^{\mathrm{H}}/k^{\mathrm{D2}} = 1.32$ at 25°C, *i.e.* 1.15/β-D.[11] This discrepancy is probably due to significant internal return from an ion–molecule pair $\mathrm{R^+NMe_3}$. It is very likely that the basic leaving group $\mathrm{NMe_3}$ promotes elimination by abstracting one of the benzylic hydrons and that substitution by the solvent occurs *via* the solvent-separated ion–molecule pair or the free carbocation. Such a mechanism has been proposed for the solvolysis of a substrate with pyridine as leaving group (see Section 5). The result of an analysis of the kinetic deuterium isotope effects for the separate steps [which can be derived from the reported product ratios and the overall rate constant of (1)] is consistent with a branched mechanism (equation 10) through the ion-molecular pair.

5 Irreversible Ion Pair (or Ion–Molecule Pair) ($E1_{\mathrm{ip}}$)

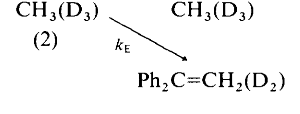
Rate-limiting formation of the ion pair followed by fast dehydronation characterizes the $E1_{\mathrm{ip}}$ mechanism (equation 10, $k_{-1} \ll k_2 + k_3$). The substitution product does not necessarily come directly from the ion pair. It is presumably more common with a multistep process involving nucleophilic attack on the solvent-separated ion pair or the free carbocation. Consistently, an increase in the ionizing power of the solvent generally decreases the fraction of elimination at the expense of substitution. The solvent-separated ion pair has been excluded from the reaction scheme of equation 10 for simplicity. It is not needed for the following discussion.



$$\mathrm{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{R^+X^-} \begin{cases} \xrightarrow{k_2} \mathrm{ROS} \\ \xrightarrow{k_3} \text{alkene} \end{cases} \qquad (10)$$

where $k_3 = k'_3 + k''_3[\mathrm{B}\ \ ]$

The solvolysis of the very reactive 1,1-diphenyl-1-chloroethane [(2), equation 11] in mixtures of acetonitrile with methanol has been concluded to go through an almost irreversibly formed ion–pair intermediate.[10] Analysis of the kinetic deuterium isotope effects for the elimination and substitution processes strongly indicates that these competing reactions have a common intermediate. Very significant base catalysis from the leaving group indicates that this intermediate is the contact ion pair.



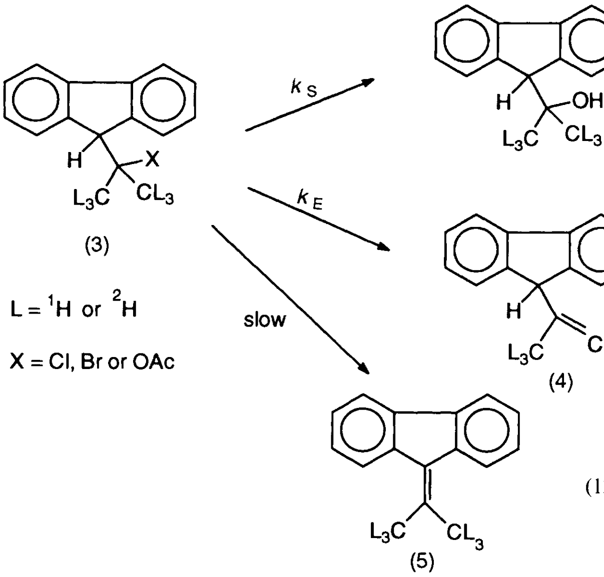
$$\underset{(2)}{\mathrm{Ph_2C(Cl)CH_3(D_3)}} \begin{cases} \xrightarrow{k_S} \mathrm{Ph_2C(OMe)CH_3(D_3)} \\ \xrightarrow{k_E} \mathrm{Ph_2C{=}CH_2(D_2)} \end{cases} \qquad (11)$$

Let us look at some of the experimental data. The changes in the measured kinetic deuterium isotope effects are in accordance with the analysis of the isotope effects for competing elimination and substitution given above (see Section 2). The elimination isotope effect $k^{\mathrm{H}}_{\mathrm{E}}/k^{\mathrm{D3}}_{\mathrm{E}}$ increases from 1.73 to 3.20 at 25 °C when the fraction of substitution increases from 0 to 44%. The substitution isotope effect $k^{\mathrm{H}}_{\mathrm{S}}/k^{\mathrm{D3}}_{\mathrm{S}}$ increases with increasing methanol content from 0.84 to 0.96 corresponding to 13 and 44% substitution, respectively. It does not seem possible to accommodate these isotope-effect values and trends in isotope-effect values in a reaction scheme with two competing parallel reactions that do not have an intermediate in common. However, branching through a common intermediate as shown in equation 10 may account for the results. The intermediate undergoes some internal return at low methanol fraction of the solvent as indicated by the isotope effect value $k^{\mathrm{H}}/k^{\mathrm{D3}} = 1.73$ at 0% methanol.

Addition of a strong base increases the fraction of olefin product, the fraction is larger for solvolysis in 2M sodium methoxide than in methanol. Catalysis from added base has been found in some other solvolysis reactions *via* carbocationic intermediates.[5—10,17]

The ion pair was estimated to eliminate > 3000 times faster than the free carbocation in 0.4 vol% water in acetonitrile. The acid-catalysed $E1$ elimination of water from the corresponding alcohol in 25 vol% acetonitrile in water which involves rate-limiting hydron-transfer from the free carbocation (or possibly from the ion–molecule pair) is very sensitive to isotopic substitution, $k^{\mathrm{H}}_{\mathrm{E}}/k^{\mathrm{D3}}_{\mathrm{E}} = 6.5$.[10] The substitution reaction with water, which gives back starting material, is a much faster reaction than elimination, *i.e.* $k_2 \gg k_3$ (equation 10), which in accord with equation 6 results in an enlarged elimination isotope effect.

Other examples of reactions following the $E1_{\mathrm{ip}}$ mechanism are the hydrolyses of (3) in water–acetonitrile mixtures (equation 12).[7] The chloride was found to yield about 64% of olefin (4) and 36% of alcohol, and only a trace of the thermodynamically more stable olefin (5) was formed in 25 vol% acetonitrile in water at 25 °C. The addition of the common ion $\mathrm{Cl^-}$ does not depress the disappearance of the substrate (k_{obs}) substantially but catalyses the formation of alkene (4). This indicates rate-limiting ionization. Also weak bases as well as the leaving group catalyse elimination from the ion pair. The catalysis from substituted acetate anions was found to be small, $\beta = 0.05$. As shown in Figure 2, the catalysis from halide anions is described fairly well by the same Brønsted line. The presence of strong base, on the other hand, opens up a parallel bimolecular concerted elimination route ($E2$).[7,18] This route provides exclusively the more stable olefin (5) and exhibits a large kinetic isotope effect of $k^{\mathrm{H}}/k^{\mathrm{D}} = 8.1$ (substrate deuteriated at the 9-position of the fluorene moiety). The intermediate showed very small discrimination between the nucleophiles azide anion, methanol, and water. Thus, an azide anion is about five times more reactive



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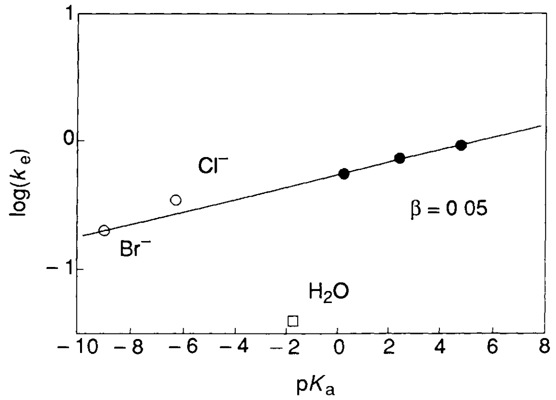


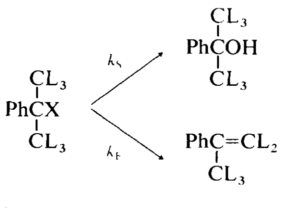
Figure 2 Brønsted plot for the dehydronation of the ion-pair intermediate formed from (3) (X = Cl) with substituted acetate anions (●) in 25 vol% acetonitrile in water, ionic strength 0 75 M maintained with sodium perchlorate The pK_a values refer to water

than a solvent molecule towards the carbocation intermediate, *i e* , $k_{N_3}/k_{H\ O} \sim 5$ The selectivity is so small that it may represent reaction within a pool of solvent molecules that are present at the time of ionization to the ion pair [13] The rate constant for the reaction of the intermediate with water to form the alcohol was estimated at $\sim 4 \times 10^{10}$ s ^{1} based upon a diffusion-controlled reaction with azide anion with $k_d = 5 \times 10^9$ M ^{1}s ^{1} [7,17,19] Accordingly, the rate constant for deprotonation of the intermediate by solvent water is $\sim 7 \times 10^{10}$ s ^{1} These rate constants are larger than, or at least comparable to, the estimated rate of diffusional separation of the ion pair Thus, it was concluded that the dehydronation of the intermediate and the nucleophilic substitution are processes that occur mainly at the ion-pair stage before the ion pair undergoes diffusional separation The elimination reaction promoted by addition of acetate anion should occur by a stepwise preassociation mechanism in which the base comes into reaction position for hydron abstraction before the ionization to the ion pair

The measured kinetic isotope effects support the equation 10 mechanism with $k_{-1} \ll k_2 + k_3$ The isotope effect on the disappearance of the substrate having the methyl groups fully deuteriated was measured as $k^{H}/k^{D6} = 2\ 2$ at 25 °C This large secondary kinetic β-deuterium isotope effect, which corresponds to a value of 1 14 per deuterium, shows that the bonds to the hydrons are weakened considerably in the ionization step The kinetic isotope effect on substitution and elimination for the solvolysis of the chloride were measured as $k^{H}_{S}/k^{D6}_{S} = 1\ 4$ and $k^{H}_{E}/k^{D6}_{E} = 3\ 7$ These isotope effects are in accord with a mechanism in which a rate-limiting ionization step is followed by branching The competing paths show differences in sensitivity to isotopic substitution Owing to this competition, the isotope effects on k_S and k_E are attenuated and enlarged, respectively, compared with the isotope effects on the rate-limiting ionization of the substrate The experimental data for the chloride in 25 vol% acetonitrile in water and the mechanistic model are consistent with $k^{H}_{2}/k^{D6}_{2} = 1\ 0$ and $k^{H}_{3}/k^{D6}_{3} = 2\ 8$ (equation 10)

The consistency of the measured isotope effects with equations 4—6 both at low and high water concentration indicates that internal return from the ion pairs is not significant The large ionization isotope effect, $k^{H}/k^{D6} = 2\ 2$, suggests that the ionization is accompanied by considerable reorganization of the carbocation structure and the solvent These processes slow down the collapse of the ion pair back to covalent material [20]

There are rather many examples in the literature on elimination promoted by the leaving group from carbocation intermediates [21] Usually, the alkene is formed in minor amount, the substitution product being dominant in nucleophilic solvents An example is cumyl derivatives, *i e* 2-X-2-phenylpropane, which solvolyse in 25 vol% acetonitrile in water mainly to alcohol accompanied by 2-phenylpropene (equation 13) [9] The kinetic results with hexadeuteriated substrates suggest a branched mechanism in which the elimination and the substitution go through the same ion-pair intermediate Internal return is probably slow, but there is no conclusive evidence for this The nucleophilic substitution occurs *via* the solvent-separated or the free carbocation but the elimination was concluded to be promoted by hydron-abstraction by the leaving group The elimination is also catalysed by added general bases The Brønsted parameter value of $\beta = 0\ 13$ for cumyl chloride indicates an early transition state It is consistent with the relatively small kinetic isotope effect $k^{H}_{3}/k^{D6}_{3} = 3\ 5 \pm 0\ 2$ that was measured with acetate anion at 25 °C



$$\mathrm{Ph\overset{CL_3}{\underset{CL_3}{C}}X} \xrightarrow{k_S} \mathrm{Ph\overset{CL_3}{\underset{CL_3}{C}}OH} \qquad \mathrm{Ph\overset{CL_3}{\underset{CL_3}{C}}X} \xrightarrow{k_E} \mathrm{Ph\underset{CL_3}{C}{=}CL_2} \tag{13}$$

L = ^{1}H or ^{2}H

Cleavage of carbon–carbon bonds in heterolysis of cumyl derivatives has been reported Thus, the reaction of $\mathrm{PhCMe_2C(CN)_3}$ in $\mathrm{Me_2SO}$ yields 2-phenylpropene in almost quantitative yield,[22] presumably through the ion pair The reaction is five times slower than the total rate of solvolysis in methanol The heterolysis of t-BuC(CN)$_2$NO$_2$ to 2-propene in $\mathrm{Me_2SO}$ was found to be eleven times faster than the heterolysis of t-BuCl [23] It is not clear if internal return is fast in these reactions

It has also been suggested that the elimination from the cumyl derivative with pyridine as leaving group is promoted by the departing pyridine, methanol as leaving group gives eight times less of olefin [21a] Thus, the results indicate that the elimination occurs through the ion–molecule pair

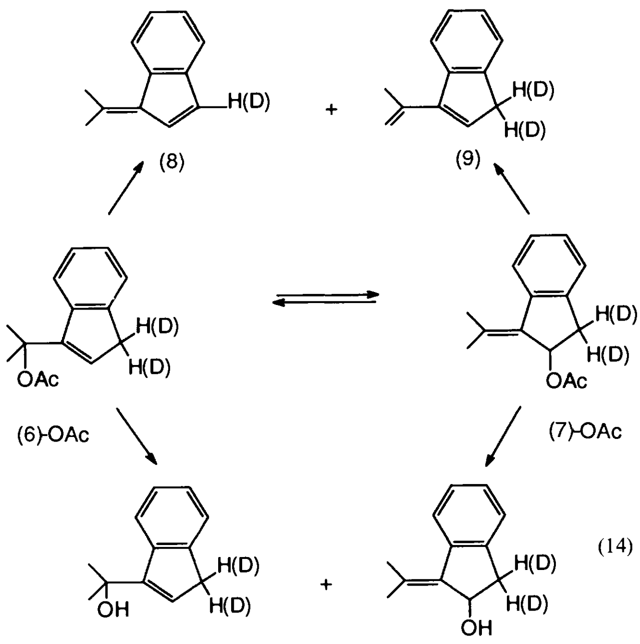
Both 1,2- and 1,4-elimination have been reported for the solvolysis of the allylic isomers (6)-OAc and (7)-OAc (equation 14) [6] The elimination reactions are catalysed by the leaving group as well as by adding general bases Brønsted parameters for the deprotonation of the carbocation intermediates by acetate anions were measured as $\beta = 0\ 16$ and $\beta = 0\ 14$ for formation of alkene (8) and (9), respectively The kinetic and product data are consistent with the mechanism shown in equation 15 Two discrete ion-pair intermediates must be involved since product compositions are quite different for the two isomeric acetates

The ionization of these acetates is not completely irreversible and some internal return accompanies the elimination and dissociation The measured kinetic deuterium isotope effects for the acetates (deuteriated in the benzylic position as shown in equation 14) supports this mechanistic interpretation The 1,4-elimination of HOAc from (6)-OAc and (7)-OAc are not 'true' 1,4-eliminations but occur through intramolecular allylic rearrangement of the ion pairs followed by 1,2-elimination promoted by the leaving acetate anion Both acetates undergo 1,2-elimination faster than 1,4-elimination

6 Pre-Equilibrium Ion Pair (or Ion–Molecular Pair) ($E2_{ip}$)

Elimination reactions that follow this type of mechanism involve rate-limiting hydron transfer directly from the ion pair The mechanism is otherwise quite similar to the $E1_{ip}$ mechanism and is shown in equation 10 ($k_{\ 1} \gg k_2 + k_3$) The reaction to alkene with added base B is kinetically of second order and the mechanism is accordingly difficult to distinguish from $E2$ [24]

A large fraction of elimination product for this type of reaction seems to require a preassociation mechanism in which the dilute reactant B gets into reaction position before the bond to the leaving group is ruptured [13,25] A much more dominant



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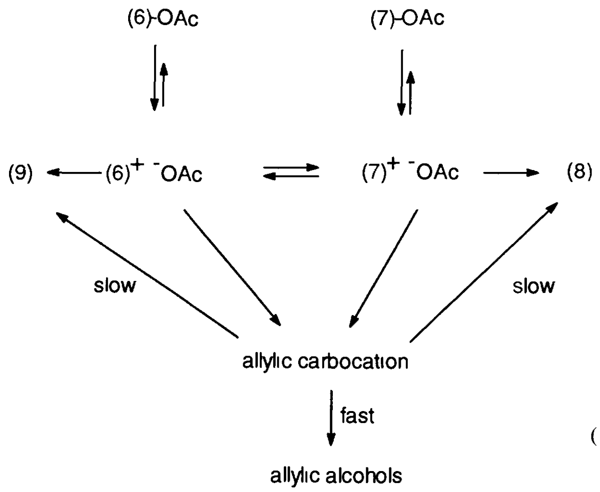

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route to alkene is presumably with the solvent or the leaving group acting as the base

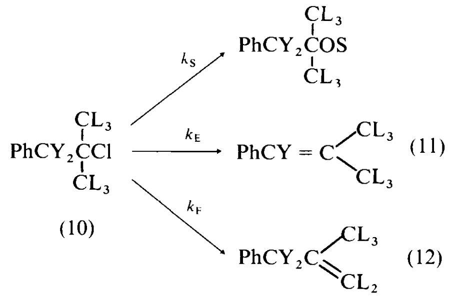
The following scheme (equation 16) shows various ways of alkene formation directly from the substrate or through the ion pair, k_e represents elimination promoted by the leaving group and/or by the solvent The reaction route *via* the preassociation complex (B^- RX) followed by dehydronation (k_c) is the ordinary base-promoted *E*2 mechanism The stepwise preassociation mechanism [13,15] involves formation of the complex followed by ionization (k'_1) and base-promoted elimination from the ion pair (k'_e) This mechanism is preferred for the stepwise base-promoted elimination when collapse of (B^- R^+ X^-) to (B^- RX) is faster than B^- can diffuse away, *i e* , $k'_{-1} > k_{-d}$ This may be the case when X is a potent nucleophile and when *only minor reorganization of carbocation structure and solvent is needed for the collapse to occur*

It is conceivable that some elimination reactions that have been classified as *E*2 with carbocationic transition states consist, in fact, of a mixture of concerted elimination and elimination through a reversibly formed ion-pair intermediate This hypothesis is in accord with Bordwell's suggestion that, in systems that undergo ionization,[26] lyate ions promote elimination from ion pairs rather from the substrate itself The reason for this is that ion pairs are far superior to covalent substrate as hydron donors

$$\begin{tikzcd}
 & & \text{alkene} & \\
RX \arrow[rr, shift left, "k_1"] \arrow[d, shift right, "K_{as}"'] & & R^+X^- \arrow[ll, shift left, "k_{-1}"] \arrow[u, "k_c"'] \arrow[r] \arrow[d, shift right, "k_d[B\ ]"'] & ROS \\
B\ \ RX \arrow[u, shift right, "\pm B"'] \arrow[rr, shift left, "k_1"] \arrow[dr, "k_c"'] & & B\ \ R^+X \arrow[ll, shift left, "k_{-1}"] \arrow[u, shift right, "k_{\ d}"'] \arrow[dl, "k"] & \\
 & \text{alkene} & &
\end{tikzcd} \tag{16}$$

Accordingly, elimination occurs *via* hydron abstraction from the $B^-R^+X^-$ complex (k'_e, equation 16) rather than by concerted elimination (k_c, equation 16) from the preassociation complex When the base–ion-pair complex is too unstable to exist as an intermediate, *i e* , $t_{\frac{1}{2}} < 10^{-13}$ s, the reaction is forced to be concerted [13,27]

Recently it was concluded that $PhCH_2CMe_2Cl$ [(10) equation 17] reacts by an *E*2 mechanism with methoxide anion in methanol to give alkene (11) [8] This elimination product is also formed by a stepwise route *via* a reversibly formed ion pair by dehydronation with solvent and added bases, and probably also by the leaving group The other alkene (12) is only formed by the carbocationic route through reaction of the ion pair (equation 17) Solvolysis without any base present provides all three products Let us look briefly at the experimental results on which these mechanistic assignments are based



(17)

(a) Y = ¹H and L = ¹H
(b) Y = ²H and L = ¹H
(c) Y = ¹H and L = ²H

There are several indications for reversible ionization in methanol as well as in highly aqueous solvent Thus, the solvolysis in 25 vol% acetonitrile in water is somewhat faster in the presence of azide anion or bromide anion than perchlorate anion which suggest nucleophilic attack on a reversibly formed ion-pair intermediate giving rise to a bimolecular contribution to the observed rate The isotope effect on the total reaction rate also suggests reversible ionization since $k^{\mathrm{H}}_{\mathrm{obs}}/k^{\mathrm{D2}}_{\mathrm{obs}}$ = 1.41 and 1.42 for reaction at 25 °C in the aqueous medium and methanol, respectively, corresponding to an isotope effect of 1.19 per deuterium that is too large for a secondary β-deuterium isotope effect Values of 1.10 ± 0.05/β-D have been reported for secondary isotope effects [11]

The following expressions for the isotope effects can be derived from equations 17 and 18, reaction through the ion pair (*cf* Section 2)

$$k^{\mathrm{H}}_{\mathrm{S}}/k^{\mathrm{D}}_{\mathrm{S}} = (K^{\mathrm{H}}_{\mathrm{eq}}/K^{\mathrm{D}}_{\mathrm{eq}})(k^{\mathrm{H}}_2/k^{\mathrm{D}}_2)$$

$$k^{\mathrm{H}}_{\mathrm{E}}/k^{\mathrm{D}}_{\mathrm{E}} = (K^{\mathrm{H}}_{\mathrm{eq}}/K^{\mathrm{D}}_{\mathrm{eq}})(k^{\mathrm{H}}_3/k^{\mathrm{D}}_3)$$

$$k^{\mathrm{H}}_{\mathrm{E}}/k^{\mathrm{D}}_{\mathrm{E}} = (K^{\mathrm{H}}_{\mathrm{eq}}/K^{\mathrm{D}}_{\mathrm{eq}})(k^{\mathrm{H}}_4/k^{\mathrm{D}}_4)$$

$$k^{\mathrm{H}}_{\mathrm{obs}}/k^{\mathrm{D}}_{\mathrm{obs}} = (K^{\mathrm{H}}_{\mathrm{eq}}/K^{\mathrm{D}}_{\mathrm{eq}})[(k^{\mathrm{H}}_2 + k^{\mathrm{H}}_3 + k^{\mathrm{H}}_4)/(k^{\mathrm{D}}_2 + k^{\mathrm{D}}_3 + k^{\mathrm{D}}_4)]$$

where $k_{\mathrm{obs}} = k_{\mathrm{S}} + k_{\mathrm{E}} + k_{\mathrm{E}}$ and $(K^{\mathrm{H}}_{\mathrm{eq}}/K^{\mathrm{D}}_{\mathrm{eq}}) = (k^{\mathrm{H}}_1/k^{\mathrm{D}}_1)(k^{\mathrm{H}}{}_{1}/k^{\mathrm{D}}{}_{1})$

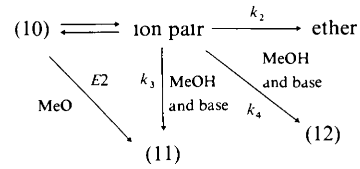
The isotope effects for the separate steps were calculated for solvolysis in methanol and without base addition with the help of these equations $K^{H}_{eq}/K^{D2}_{eq} = 1.15$ $k^{H}_{2}/k^{D2}_{2} = 1.16$, $k^{H}_{3}/k^{D2}_{3} = 2.2$, $K^{H}_{eq}/K^{D6}_{eq} = 1.50$, $k^{H}_{2}/k^{D6}_{2} = 1.13$, $k^{H}_{4}/k^{D6}_{4} = 2.3$.

The addition of methoxide anion to methanol increases the overall rate of disappearance of the substrate. This increase in total rate is caused by a large increase of elimination to give (11) but also by an increase in the rate of formation of (12) (equation 17). However, the rate of formation of the ether decreases. There is also a large increase in k^{H}_{obs}/k^{D6}_{obs} and k^{H}_{E}/k^{D2}_{E} but k^{H}_{E}/k^{D2}_{E} and k^{H}_{E}/k^{D6}_{E} are not changed (Table 2). These results strongly indicate a parallel, competing methoxide-promoted concerted *E*2 reaction (equation 18). Further indications are the observed decreases in k^{H}_{obs}/k^{D6}_{obs} and k^{H}_{E}/k^{D6}_{E}.

Table 2 Isotope effects for the reactions of (10) in methanol[a] at 25.00 ± 0.03 °C

Base	k^{H}_{obs}/k^{i}_{obs}	k^{H}_{S}/k^{i}_{S}	k^{H}_{E}/k^{i}_{E}	k^{H}_{E}/k^{i}_{E}
		i = D2		
none	1.42	1.33	2.53	1.15
NaOAc[b]	1.46	1.36	2.56	1.18
NaOMe[c]	2.39	1.46	3.89	1.15
		i = D6		
none	1.81	1.70	1.50	3.4
NaOAc[b]	1.81	1.72	1.47	3.4
NaOMe[c]	1.35	1.47	1.16	3.4

3.74 vol% water [b] 0.98 M 2.00 M



(18)

The results do not indicate a parallel *E*2 reaction for formation of the other alkene (12) but are completely in accord with base-promoted and solvent-promoted elimination *via* the reversibly formed ion pair.

The experimentally measured isotope effect $k^{H}_{E}/k^{D2}_{E} = 3.89$ (Table 2) is the isotope effect for formation of alkene (11) both through the *E*2 route and the carbocationic path. The assumption that the rate constant ratio k_3/k_4 (equation 18, pseudo-first order rate constants for reaction with solvent and base) is approximately the same with and without added base makes it possible to calculate the isotope effect for the *E*2 reaction with MeO^-, $k^{H}/k^{D2} = 4.9$. The isotope effect for the carbocationic route to (11) is 2.5 and 1.5 for the di-deuteriated and the hexa-deuteriated substrates, respectively. The values are similar to those obtained without base.

6.1 Mechanistic Borderline

How are the borders between the different stepwise mechanisms of Table 1 defined? The relative rates of the different microscopic processes determine which reaction path is the dominant one. Jencks' definition,[13] which has been generally accepted,[27,28] of a reaction intermediate as a molecular entity with a lifetime appreciably longer than a molecular vibration, which is about 10^{-13} s, implies a rather sharp border between one-step and multi-step reactions.

A presumably rather common type of change of mechanism for a reaction involves two concurrent mechanisms having different transition-state structures.[7,8,18] A change in experimental conditions or structure of the reactants lowers the energy of one of the transition states relative to the energy of the other, which may induce a shift in the major reaction path. Accordingly, the reaction product may, in principle, be formed simultaneously by two parallel reactions, 'reaction channels'.[29] At the borderline, both transition states are of equal energy. Owing to a large difference in energy between the transition states, one of the mechanisms frequently dominates and is the only mechanism observed.

The mechanistic change for reaction of (10) to (11) is concluded to be of this type. Accordingly, in pure methanol the *E*2 transition state (with methanol as hydron acceptor) is much higher in energy than the transition state of the stepwise reaction through the ion pair. Thus the elimination reaction exclusively employs the carbocationic path. With methoxide, the *E*2 transition state is much lower in energy and can compete successfully with the dehydronation of the ion pair with methanol as well as with methoxide anion. The *E*2 reaction should be about four times faster than the methoxide-promoted reaction *via* the ion pair (Table 2 and equation 18). Apparently, the methoxide-promoted reactions are very close to the borderline where both mechanisms have the same activation energy. This borderline does not correspond to merging of transition-state structures.[30]

Is it also possible that the uncatalysed elimination to give (11) is a one-step solvent-promoted concerted *E*2 reaction? No, since the isotope effect k^{H}_{E}/k^{D6}_{E} is 1.50 in methanol but decreases to 1.16 in the presence of 2M sodium methoxide. The expected value for this secondary β-deuterium isotope effect on a one-step reaction should be very close to unity for reaction both with and without added base. The values strongly indicate a stepwise mechanism for the reaction with pure solvent and elimination mainly through an *E*2 mechanism in the presence of a substantial amount of lyate anion. Moreover, a parallel stepwise preassociation mechanism (equation 16), or an enforced concerted mechanism with a carbocation-like transition state, for the methoxide-promoted reaction is not a reasonable alternative to the *E*2 mechanism for the same reason.

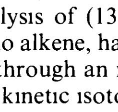
6.2 Other Systems

A study of a related system, eliminated from t-BuCl in basic methanol or methanol–Me_2SO mixtures, has revealed that EtS is a more efficient base than methoxide in pure methanol but not in solvent mixtures having a high proportion of Me_2SO.[31] The results may be interpreted by a stepwise mechanism with an ion-pair intermediate formed in a pre-equilibrium step or with mixed stepwise and concerted elimination. If the reactions are concerted, there is no need to invoke the *E*2C mechanism since the results of the base-promoted reactions are compatible with the theory of the variable *E*2 transition state theory.[31]

Shiner and co-workers have concluded that the solvolysis of cyclopentyl *p*-bromobenzenesulfonate in aqueous hexafluoroisopropanol involves reversible formation of the contact ion pair.[32] The stereochemistry of the elimination was studied by use of specifically deuteriated substrate.

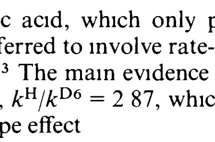
The solvolysis of (13) in acetic acid, which only provides elimination to alkene, has been inferred to involve rate-limiting elimination through an ion pair.[33] The main evidence was the value of the kinetic isotope effect, $k^{H}/k^{D6} = 2.87$, which is too large for a purely secondary isotope effect.

The elimination may also occur through a reversibly formed ion–molecule pair. Bordwell[26] has suggested that the hydroxide-promoted elimination from neomenthyl trimethylammonium ion (14) in water occurs *via* a 'tightly solvated cation'. Even strongly alkaline conditions could not completely suppress the competing first-order reaction. The possible role of the basic leaving group trimethylamine as the hydron abstractor has not been investigated. However, Bunton and co-workers have found



$(EtO)_2P(O)C(Me)_2OMs$

(13)

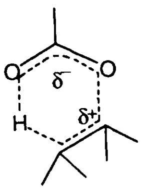


(14)

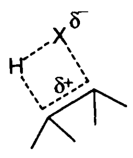
that added amines are efficient in promoting elimination from ferrocenylalkyl carbocations in 50% acetonitrile in water [34]

7 Concerted Pericyclic Elimination (E_i)

This mechanism has a cyclic transition state, *e g* (15) and (16), in which intramolecular hydron transfer to the leaving group is concerted with C–X bond cleavage

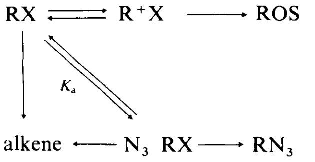


(15)



(16)

It was suggested recently that destabilization of the carbocation intermediate of the stepwise solvolysis of cumyl derivatives, $RArCMe_2X$, by electron-withdrawing ring substituent R, leads to a change in mechanism to concerted pericyclic elimination [35] Thus, it was found that destabilization of the carbocation intermediate increases the amount of alkene product in 50 vol% trifluoroethanol in water This was interpreted as elimination through the ion pair which competes with nucleophilic substitution by the solvent (at the ion-pair stage or through the free carbocation) Large destabilization, $\sigma_R^+ \geqslant 0$ 34, yields a substantial amount of alkene Addition of 0 50 M sodium azide provides 20—30% of the azide substitution product but has no acceleration effect on the overall rate Moreover, it was found that the fraction of alkene is independent of azide anion concentration, only the amounts of alcohol and ether decrease The substitution reaction with azide was concluded to proceed by a concerted preassociation mechanism (equation 19)



(19)

This mechanistic interpretation requires that a large part of the substrate is associated with azide anion as a preassociation complex and that this species reacts to give olefin with a rate similar to that of the un-preassociated substrate

An alternative interpretation might be a mechanism in which the contact ion pair reacts *only* to elimination product and the substitution products originate from solvent-separated and free carbocation Consistently, the measured Hammett and Winstein–Grunwald parameters of $\rho^+ = -4$ 6 and $m_{\text{elim}} = 0$ 7, respectively, for *para*-substituted chlorides suggest a polar transition state Another speculative mechanistic interpretation is concerted solvent-promoted elimination The absence of detectable catalysis with strong base may be due to a very small Brønsted β-parameter, *i e* , the catalysis from a solvent molecule is similar to that of an added strong base that is present at a much lower concentration

Acknowledgement The Swedish Natural Science Research Council supported this work

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