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CHAPTER 12

Elimination Reactions

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$E1cB$ Mechanisms

Results of a kinetic study of base-promoted elimination reactions of some 1,1,1-trihalo-2,2-bis(dialkoxyphenyl)ethanes in alcoholic solutions have shown that (for 3,4-dimethoxy) the tribromo derivative reacts faster than the trichloro derivative and the reactions are general-base promoted, with Brønsted β values of ca 0.6 and a kinetic isotope effect $k_H/k_D = 3.5–5.7$ for the trichloro compound.[1] Arrhenius pre-exponential factors for the alkoxy-promoted reactions provide evidence of tunnelling, but difficulty in distinguishing between $E1cB_I$ and $E2$ mechanisms is apparent; thus the leaving group effect ($k_{Br}/k_{Cl} = 22–26$) seems to be explained better by the latter (rather than as a consequence of anionic hyperconjugation) whereas the activation parameters and near identity of β values for the chloro and bromo derivatives are consistent with the former. The results support the view that the $E1cB_I$ mechanism is transformed into the $E2$ mechanism with very little change in transition-state structure.

The difficulty of distinguishing mechanisms at the $E1cB–E2$ borderline has also been discussed for reactions of secondary halides (**1-X** and **2-X**) which feature a β-hydrogen made acidic by incorporation of an α-indenyl substituent (Scheme 1).[2] 1,2-Elimination reactions of (*R*,*S*)-1-(1-X-ethyl)indene (**1-X**, X = Cl, Br, I, OBs) and the corresponding *R*,*R* isomers (**2-X**) promoted by water containing 25 vol.% acetonitrile

H(D)
OH
Me
(D)H
H
(7)
H+
Me
H
OH
H(D)
(6)
k2′
k2
H(D)
X
(D)H
H
Me
(2–X)
kE
H(D)
H
Me
(8)
+
H(D)
H
Me
(5)
kE
H(D)
X
(D)H
Me
H
(1–X)
k1′
k1
Me
H
OH
H(D)
(4)
H+
H(D)
OH
(D)H
Me
H
(3)
kS = k1 + k1′, or
kS = k2 + k2′,

SCHEME 1

occur non-stereospecifically and stereospecifically, respectively, and are in competition with solvolytic substitution via homoallylic cations formed in leaving group rate order $Br^- < I^- < BsO^-$. The kinetic deuterium isotope effects ($k_H/k_D = 4.6–6.8$) found for solvent-promoted elimination reactions of (**1-X**, X = Cl or Br) and (**2-Br**) are too large for the $E1$ mechanism and greatly exceed the values close to unity actually determined for the competing substitution reactions [to form primarily (**3**) and (**7**) from (**1-X**) and (**2-X**), respectively]. The large Brønsted coefficients [$\beta = 0.38$, 0.37, 0.47, and 0.40 for (**1-I**), (**1-Br**), (**2-Br**), and (**2-OBs**), respectively] for reaction with substituted acetate ions indicate that the reactions proceed by either $E2$ or $E1cB_I$ mechanisms; the former is favoured for (**2-Br**) and (**2-OBs**), which exhibit higher stereospecificity (95–99% *anti* elimination) than found for (**1-X**) (80–85% *anti* elimination). The *syn* elimination of (**1-X**) is apparently favoured by the absence of steric interaction of the methyl group with the adjacent phenyl hydrogens; however, the *anti* stereochemistry, which has been ascribed to the $E2$ process, increases with basicity of the added base and is favoured by negative charge on the base.

Isotope effects and element effects associated with hydron-transfer steps during methoxide promoted dehydrohalogenation reactions of p-$CF_3C_6H_4C^iHClCH_2X$ (X=Br, Cl, or F) have also been discussed, with regard to distinction between $E2$ and multi-step pathways.[3] The Arrhenius behaviour of hydrogen isotope effects was used to calculate the amounts of internal hydrogen return associated with the two-step mechanism.

The acidifying influence of the sulfonyl group, combined with its ability to transmit electronic effects is apparent from results of Hammett studies of the dehydrochlorination of p-$RC_6H_4SO_2CH_2CH_2Cl$ and $RC_6H_4SO_2CH_2CHClPh$, on reaction with Et_3N; the nearly identical positive ρ values indicate that for each series reaction proceeds via carbanion formation.[4]

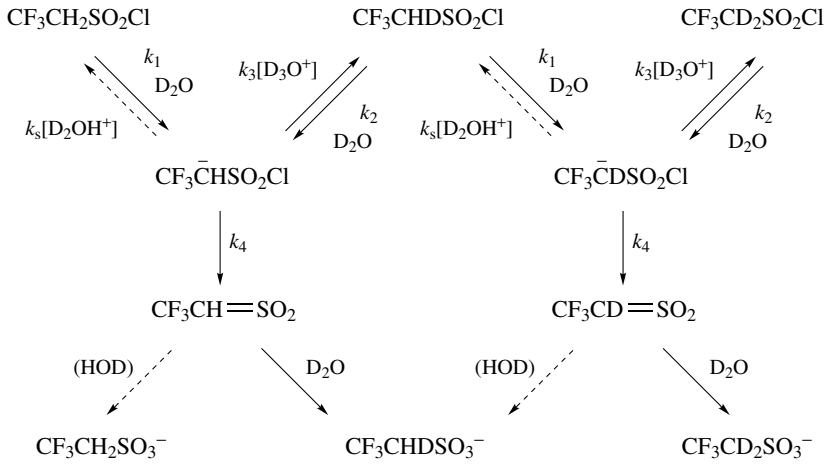
An intermediate sulfene ($CF_3CH{=}SO_2$) is formed by an irreversible $E1cB$ process during hydrolysis of 2,2,2-trifluoroethanesulfonyl chloride in water at pH 1.8–5.[5] Water acts as the carbanion-forming base in the lower pH range and hydroxide anion at higher pH; in dilute acid the hydron transfer becomes reversible and deuterium exchange of the sulfonyl chloride is observed (Scheme 2). This is believed to be the first clear demonstration of reversible and irreversible $E1cB$ reactions induced by water. The change from $E1cB_I$ to $E1cB_R$ with increasing acidity provided a means of distinguishing the $E1cB_I$ and $E2$ processes.

A change in mechanism [at pH $\approx$ pK_a of (**9**)] from $E1cB_I$ to $E1cB_R$ is also believed to account for the biphasic Brønsted plots ($\beta_1 \approx 0.7$, $\beta_2 \approx 0$) and associated entropy changes obtained for aminolysis of 4-nitrophenyl N-benzylsulfamate (**9**), apparently via $ArN{=}SO_2$, in MeCN.[6]

$$\underset{\textbf{(9)}}{ArNHSO_2ONp} + RR'NH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar\bar{N}SO_2ONp + RR'NH_2^+$$

$$Ar\bar{N}SO_2ONp \xrightarrow{k_2} ArNHSO_2NRR' + HONp$$

$Np = p\text{-}NO_2C_6H_4^-$



SCHEME 2

Non-linear kinetics have been reported for aminolysis of sulfamate esters $RNHSO_2ONp$ (Np=*p*-$NO_2C_6H_4$) in chloroform.[7] The first-order rate constants k_{obs} for reaction with imidazoles (primarily) under pseudo-first-order conditions display saturation curvature with increasing amine concentration, according to the expression

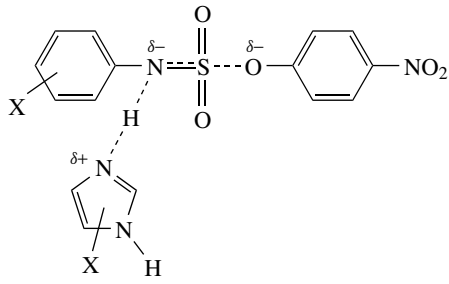
$$k_{obs} = K_m k'[\text{amine}]/(1 + K_m[\text{amine}])$$

where K_m and k' are defined by

$$\text{S} + \text{amine} \underset{}{\overset{K_m}{\rightleftharpoons}} [\text{S.amine}] \xrightarrow[\text{rds}]{k'} \text{products}$$

There was no evidence of a second-order term in amine, nor did amine self-association account for the non-linear behaviour. Hammett ρ values (for variation of $RNHSO_2$) determined for formation of the complex [S.amine] ($\rho = 1.64$) and for expulsion of the anion ($^-$ONp) ($\rho_{acyl} = -1.78$) are consistent with an *E*1*cB* process and uncomplicated by any steric effects of bound amine in the complex. The value of ρ_{acyl} is identical with that reported previously for *E*1*cB* reaction of the same esters in 50% acetonitrile–water and much greater than for their *E*2-type reactions in chloroform. Consequently, an *E*1*cB* mechanism involving extensive S–O bond cleavage with the formation of a *N*-sulfonylamine, $ArN{=}SO_2$, is supported.

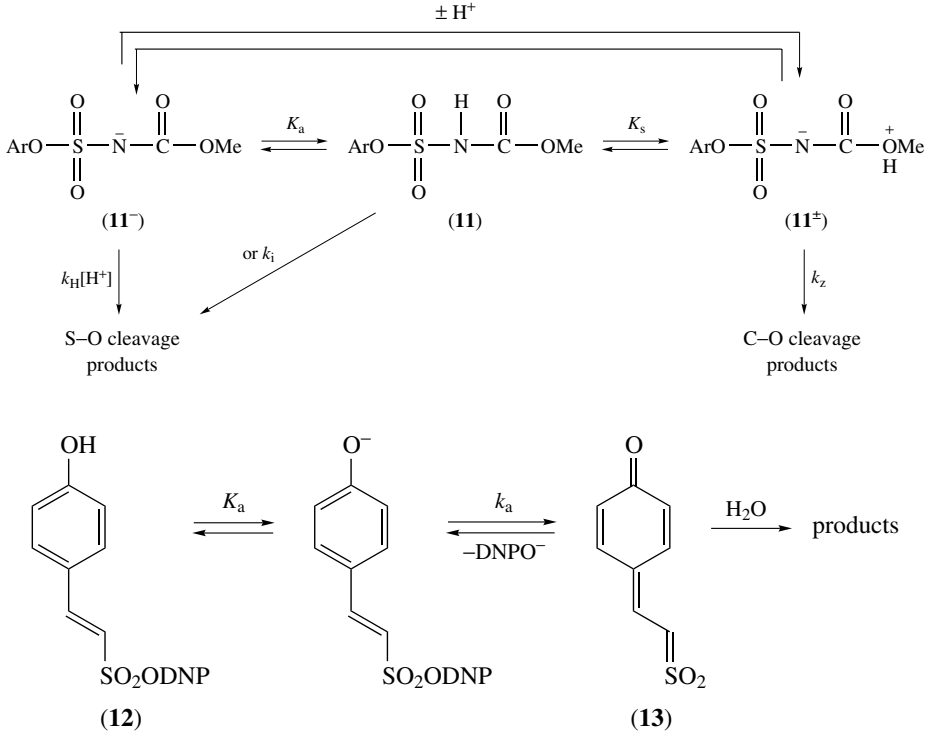
A report of a more extensive Hammett study has included estimates of values of ρ_{acyl} for aminolysis of members of the sulfamate ester series ($XC_6H_4NHSO_2ONp$) in chloroform and acetonitrile using piperidine and a set of five pyridines; variation of the pyridines allowed the determination of ρ_{pyr} values for several esters.[8] The ρ_{acyl} values become less negative with decrease in amine basicity, apparently as a consequence of diminished N_β–H cleavage and a progression from a partial carbanion-like transition state to a more central *E*2 type mechanism (**10**).



(**10**)

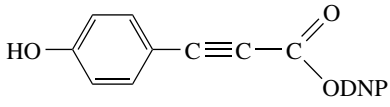
The ρ_{acyl} value for 4-dimethylaminopyridine almost doubles from −0.91 to −1.53 on change from chloroform to acetonitrile, thereby approaching the value $\rho_{acyl} \approx -1.8$ which is believed to be indicative of formation of a sulfonylimine intermediate by the $E1cB$ mechanism. The values of ρ_{pyr} (ca −1.2) suggest that there is only a small amount of positive charge on the pyridine nitrogen in the transition state; corresponding values of β_{nuc} (ca 0.2) confirm this view. General conclusions are that for the $E2$ mechanism $\beta_{nuc} = 0.2–0.6$ whereas for the $E1cB_I$ mechanism $\beta_{nuc} \geqslant 0.7$; biphasic behaviour ($\beta_{nuc} \approx 0.7$ and ca 0) is indicative of transition from $E1cB_I$ to $E1cB_R$ behaviour. This aminolysis of sulfamate esters in $CHCl_3$ and CH_3CN generally occurs by an $E2$ type mechanism which may vary from 'central' to E1cB-like. In certain cases in CH_3CN the biphasic behaviour indicative of a change from $E1cB_I$ ($\beta_{nuc} \approx 0.7$) to $E1cB_R$ ($\beta_{nuc} = 0$) is found. Aminolysis of sulfamoyl chlorides in chloroform and acetonitrile has also been found to occur by an elimination mechanism, via the corresponding N-sulfonylamine, PhN=SO_2; the $E2$ reaction is believed to become more $E1cB$-like in the more polar solvent.[9] The monosubstituted sulfamoyl chlorides react ca 10^6 times more rapidly than disubstituted sulfamoyl chlorides and primary deuterium isotope effects in the range 2.6–5.3 (Y = H) have been determined for reaction of $YC_6H_4NHSO_2Cl$ with $XC_6H_4NH_2$ in $CHCl_3$. The dependence on X is reflected in Hammett ρ values of −4.76 (Y = p-Me), −3.57 (Y = H) and −2.63 (Y = p-Cl) which are comparable to that reported previously for the related phenylmethanesulfonyl chloride system ($\rho = -3.5$).

The $E1cB$ reaction has also been invoked to account for several of the competing processes whereby aryl N-(methoxycarbonyl)sulfamates (**11**) decompose in aqueous media.[10] The pH profiles indicate a rate law that includes three terms; two pH independent terms, k_a in acid and k_p around neutral pH, with $k_a > k_p$, and a hydroxide ion-dependent term, k_{OH}. In acid, both S−O (k_{SO2}) and C−O (k_{CO}) bond cleavage reactions are involved; the former may involve either intra- or inter-molecular general-acid-catalysed decomposition of (**11**) or (**11**$^-$), respectively; the latter involves protonation of the leaving group and its expulsion from the dipolar intermediate (**11**$^\pm$) thus formed, and consequently fails to display the deuterium solvent isotope effect which characterizes a general-acid-catalysed process. The spontaneous reaction of (**11**$^-$) takes place (k_p) with exclusive S−O bond fission (to give O_2S=NCOOMe) whereas k_{OH} governs a process of HO^- attack at the carbonyl centre or at the aromatic ring.

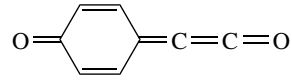


The pH profile for hydrolysis of 2,4-dinitrophenyl 4′-hydroxy-β-styrenesulfonate (**12**) in aqueous buffers (pH 5–13) features an approach to a rate plateau at high pH; this has been ascribed to a dissociative pathway, with the probable formation of a thioquinine dioxide intermediate (**13**) which benefits from the stabilizing influence of external delocalization.[11] The $\Delta S^{\neq}$ values for hydrolysis of (**12**) at various pH values are positive, as expected for a unimolecular process, and in contrast with the large negative entropy of activation for hydrolysis of 2,4-dinitrophenyl β-styrenesulfonate by an associative mechanism. The large negative value of β_{LG} (−1.85) determined through variation of the phenoxide leaving group is indicative of advanced fission of the S−OAr bond in the rate-determining transition state and within the range expected for the $E1cB$ mechanism (−1.5 to −2.4).

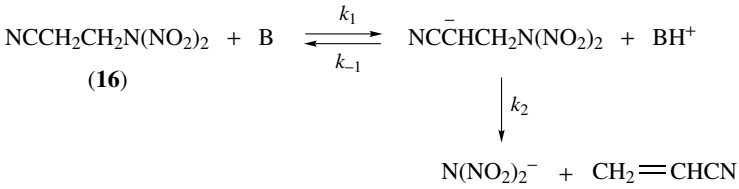
A dissociative elimination–addition pathway has also been proposed to account for the kinetics of alkaline hydrolysis of 2,4-dinitrophenyl 4′-hydroxyphenylpropionitrile in 40% (v/v) dioxane–water, although participation of the associative $B_{AC}2$ mechanism cannot be ruled out since it may be facilitated by the electronic effect of the triple bond.[12] Formation of intermediate (**15**), having a conjugated and cumulated double-bond system, should favour the $E1cB$ mechanism and thereby account for the contrasting entropies of activation found for hydrolysis of (**14**) and the corresponding 4′-methoxyphenylpropionate.



(**14**)



(**15**)



(**16**)

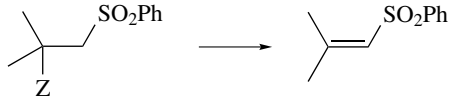
SCHEME 3

The general-base-catalysed formation of dinitramide anion, (NO_2N^-), on reaction of 2-(*N*,*N*-dinitroamino)propionitrile (**16**) in aqueous buffer solutions (pH 9.5–11.5), has been ascribed to the $E1cB_I$ mechanism ($k_2 \gg k_{-1}[BH^+]$), for which $k_{ap} = k_{OH^-}[HO^-] + k_B[B] + k_{H_2O}$. The Brønsted β value is close to unity and the entropy of activation, $\Delta S^{\neq} = 10 \pm 1\,\text{cal mol}^{-1}\text{K}^{-1}$, for reaction with hydroxide ion is consistent with the combined effects of bimolecular collision (ca $-11\,\text{cal mol}^{-1}\,\text{K}^{-1}$) and near-complete desolvation of HO^- (ca $+20\,\text{cal mol}^{-1}\,\text{K}^{-1}$).[13]

The Ad_N-*E* mechanism proposed to account for the kinetics of substitution of 9-(α-bromo-α-arylmethylene)fluorenes by thiolate ions in aqueous acetonitrile also features elimination of the leaving group in a fast step following rate-determining carbanion formation (by nucleophilic addition).[14]

*E*2 Mechanisms

Further study of the effect of strain on 1,2-elimination reactions has revealed that the formation of a carbon–carbon double bond exocyclic to a cyclopropane ring is inhibited by factors which increase from 1.4 to $10^{4.5}$ as the leaving group becomes poorer.[15] Five different leaving groups (Z = Br, Cl, SO_2Ph, SPh, and OMe) featured in the comparison of rate constants for unstrained (eq. 1) and strained (eq. 2) reactions induced by EtO^-–EtOH. It is estimated that the strain energy differences between cyclopropane and methylenecyclopropane is ca $50\,\text{kJ mol}^{-1}$ and that ca 50% of the enthalpy difference between strained and unstrained products can be induced in the elimination transition state.

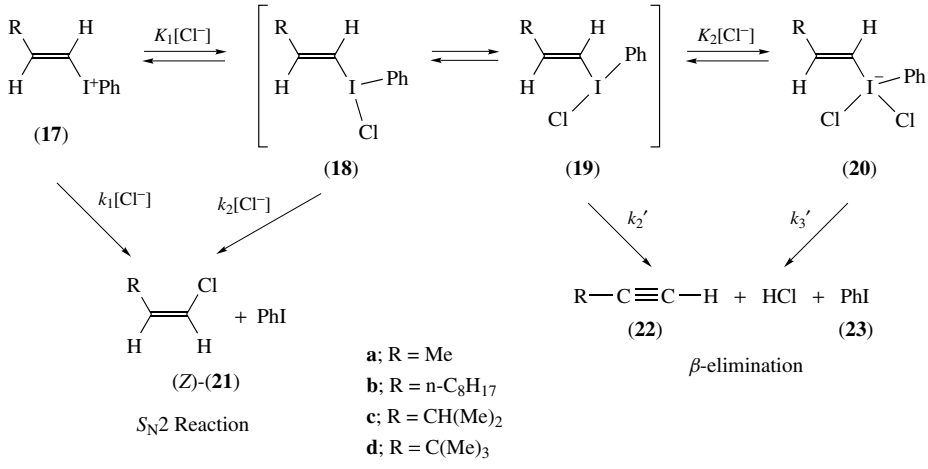


(1)

(2)

Combined use of the HSAB principle and DFT reactivity descriptors has provided a means of interpretation of the effect of basicity of *para*-substituted phenolate ions on the known elimination-substitution ratios for their reactions with *p*-nitrophenethyl bromide in 45.9% alcohol.[16] It has been concluded that *para*-substituted phenolates with higher basicity (harder), less delocalized negative charge into the fragment RC_6H_4, and a more polarizable oxygen atom (softer) have a lower (relative) attraction towards an alkyl carbon atom (soft) than towards a hydrogen atom (softer) of *p*-nitrophenyl bromide. The interactions have been explained from a local–local viewpoint which is in contrast with a global–local interpretation suggested previously.

In order to strengthen evidence in favour of the proposition that concerted in-plane S_N2 displacement reactions can occur at vinylic carbon the kinetics of reactions of some β-alkyl-substituted vinyliodonium salts (**17**) with chloride ion have been studied.[17] Substitution and elimination reactions with formation of (**21**) and (**22**), respectively, compete following initial formation of a chloro-λ^3-iodane reaction intermediate (**18**). Both (**17**) and (**18**) undergo bimolecular substitution by chloride ion while (**18**) also undergoes a unimolecular (intramolecular) β-elimination of iodobenzene and HCl. The [**21**]/[**22**] ratios for reactions of (**18a–b**) increase with halide ion concentration, and there is no evidence for formation of the *E*-isomer of (*Z*)-alkene (**21**); iodonium ion (**17d**) forms only the products of elimination, (**22d**) and (**23**).



Ring opening of an epoxide with a strong non-nucleophilic base is often used for the synthesis of allylic alcohols and incorporation of a silyl group is known to induce regioselective cleavage of the C–O bond α to silicon.[18] In order to broaden understanding of the reason for the regiochemistry of eliminative ring opening of α,β-epoxysilane, the products of reaction of non-nucleophilic bases with epoxides bearing the bulky trimethylsilyl group (unlikely to coordinate with base) have been determined. The observed preference for eliminative α-opening of these epoxysilanes has been correlated with the character of the AM1 LUMO isosurface.

Gas-Phase Base-Promoted Elimination Reactions

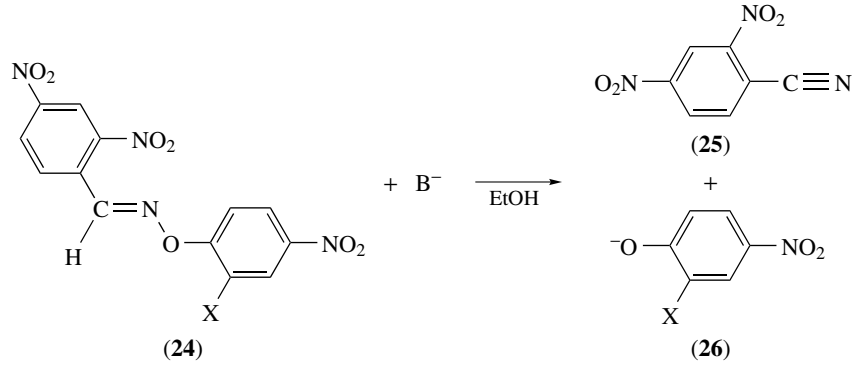
There have been several studies of gas-phase $E2$ reactions.[19–21] Results of *ab initio* calculations, up to the MP2/6–31 + G** level, on gas-phase reactions of fluoride ion with 3-chlorocyclohexene and 3-fluorocyclohexene predict that the lowest energy barrier is for *anti* 1,4-elimination but that the barriers to *syn* 1,4-elimination and *anti* 1,2-elimination are within 2.5 cal mol^{-1} of the preferred path;[19] the barriers for S_N2 and S_N2' reactions are comparable but much higher than for elimination processes. Transition states have also been located for fluoride ion promoted reactions of chlorocyclopropane;[20] the barrier for *syn* elimination is only 3.6 kcal mol^{-1} larger than for *anti* elimination as a consequence of the inherent periplanarity of the transition state for the former and the disadvantage of torsional ring strain in that for the latter. However, the S_N2 pathway dominates ($E_a = 7.3$ kcal mol^{-1}) over the $E2$(anti) pathway ($E_a = 18.6$ kcal mol^{-1}).

Ab initio methods using the 6–31 + G* basis sets have been used in a theoretical study of competing S_N2 and $E2$ reactions of $NCCH_2CH_2Cl$ with HO^- and HS^- in the gas phase.[21] The antiperiplanar elimination transition state, which is favoured over those for S_N2 and $E2$(*gauche*) reactions, is more $E1cB$-like than that for the slower $E2$(*anti*) reaction of ethyl chloride.

Formation of Double and Triple Bonds to a Heteroatom

$E2$ elimination reactions of *O*-substituted oximes have received further attention.[22–25] Thus, reaction of (*E*)-2,4-dinitrobenzaldehyde *O*-pivaloyloxime with $R_2NH/R_2NH_2^+$ buffer in 70% MeCN (aq.) exhibits second-order kinetics and general-base catalysis with Brønsted $\beta = 0.45$; the decrease in Hammett ρ value from 1.6 to 2.3 with change of the base–solvent system to DBU in MeCN is also believed to be consistent with the concerted mechanism.[22] Reactions of (*E*)-2,4-dinitrobenzaldehyde *O*-aryloximes (**24a–c**) promoted by RO^-–ROH buffers in EtOH have been shown to give 2,4-dinitrobenzonitrile (**25**) and aryl oxides (**26**) as the only products.[23] The Brønsted $\beta = 0.55$–0.75 decreases as the leaving group is made more nucleofugic and $|\beta_{lg}| = 0.39$–0.48 increases as the base becomes weaker; the interpretation in terms of a positive interaction coefficient provides further support for the $E2$ mechanism.

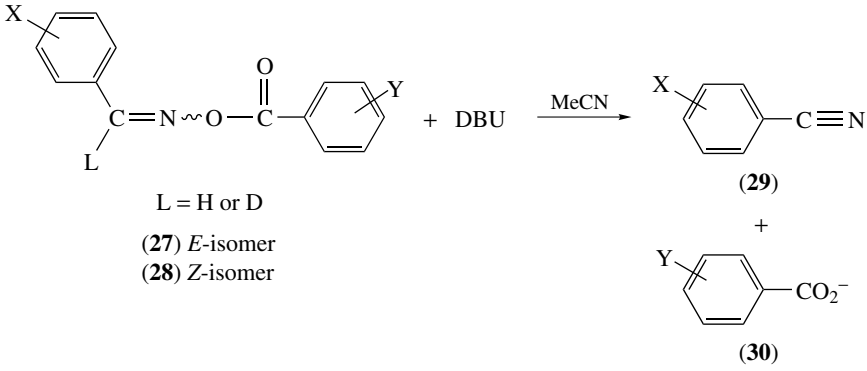
Nitrile-forming eliminations from (**28**), promoted by DBU in MeCN, have been found to occur 36 000-fold faster than for (**27**) via more symmetrical transition states, with less negative charge development at the β-carbon and smaller degrees of proton transfer and N_α–OC(O)Ar bond cleavage.[24] This is evidenced by the following values determined for reaction of (**27**), $k_H/k_D = 3.3 \pm 0.2$, Hammett $\rho = 2.19 \pm 0.05$, $\beta_{lg} = -0.49 \pm 0.2$, $\Delta H = 10.4 \pm 0.6$ kcal mol^{-1} and $\Delta S^{\neq} = -34.3 \pm 2.6$ cal mol^{-1} K^{-1}, when compared with the corresponding values for (**28**), $k_H/k_D = 7.3 \pm 0.2$, $\rho = 1.21 \pm 0.05$, $\beta_{lg} = -0.40 \pm 0.1$, $\Delta H = 6.8 \pm 0.6$ kcal mol^{-1} and $\Delta S^{\neq} = -25.8 \pm 1.9$ cal mol^{-1} K^{-1}, respectively. The extent of proton transfer and negative charge density at the β-carbon decreases with a better leaving group, and the extent of leaving group departure decreases with the electron-withdrawing ability of the β-aryl substituent. The results have been interpreted with reference to a More



(**24**) (**25**) + (**26**)

X = **a**; H, **b**; Cl, **c**; NO_2

B^- = EtO^-, PhC(Me)=NO^-/PhC(Me)=NOH, $CF_3CH_2O^-$/CF_3CH_2OH



L = H or D

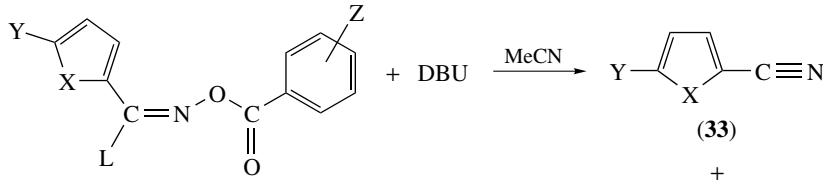
(**27**) *E*-isomer

(**28**) *Z*-isomer

(**29**) + (**30**)

O'Ferrall–Jencks diagram and *ab initio* calculations with the 6–31 G basis set. It is concluded that the transition state is slightly *E*1c*B*-like for (**27**) and more symmetrical for (**28**).

Nitrile-forming *anti* eliminations from the (*Z*)-oximes (**31**) and (**32**) have also been found to proceed by the *E*2 mechanism; the symmetrical transition state is little



(**31**) X = S

(**32**) X = O

L = H, D; Y = various

(**33**) + (**34**)

affected by the aromatic resonance energy of the β-substituent, becomes slightly more product like with a larger degree of proton transfer, more negative charge development at the β-carbon, and a greater extent of leaving group departure as the substituent is changed from phenyl to thienyl to furyl (relative rates 1:1.1:0.6); this trend is evidenced by the corresponding increase in k_H/k_D, ρ and $|\beta_{lg}|$ values.[25] The following respective values were determined for (**31**) and (3**2**): $k_H/k_D = 8.2 \pm 0.1$ and 8.8 ± 0.2, $\rho = 1.22 \pm 0.19$ and 1.87 ± 0.05, $\beta_{lg} = -0.43 \pm .01$ and -0.55 ± 0.1, $\Delta H^{\neq} = 5.9 \pm 0.1$ and 6.5 ± 0.1 kcal mol^{-1}, and $\Delta S^{\neq} = -28.5 \pm 0.3$ cal mol^{-1} K^{-1} and -29.0 ± 1.5 cal mol^{-1} K^{-1}.

An $E2$ mechanism has been proposed to account for the kinetics of formation of 3-azabicyclo[3.3.0]oct-2-ene on dehydrohalogenation of *N*-chloro-3-azabicyclo[3.3.0]octane in alkaline medium.[26]

The vicarious nucleophilic substitution of carbo- and hetero-cyclic nitroarene hydrogen by a hydroxyl group, on reaction with silylhydroperoxide anions, has been shown to proceed via nucleophilic addition of ROO^- followed by base induced elimination of ROH by an $E2$-type mechanism; the required orientation of the hydroxylation can be controlled by the conditions selected.[27]

Although no rates have been determined, the results of semiquantitative experiments involving competition between displacement of hydrogen and halogen have been interpreted in terms of the following equation for the VNS process:

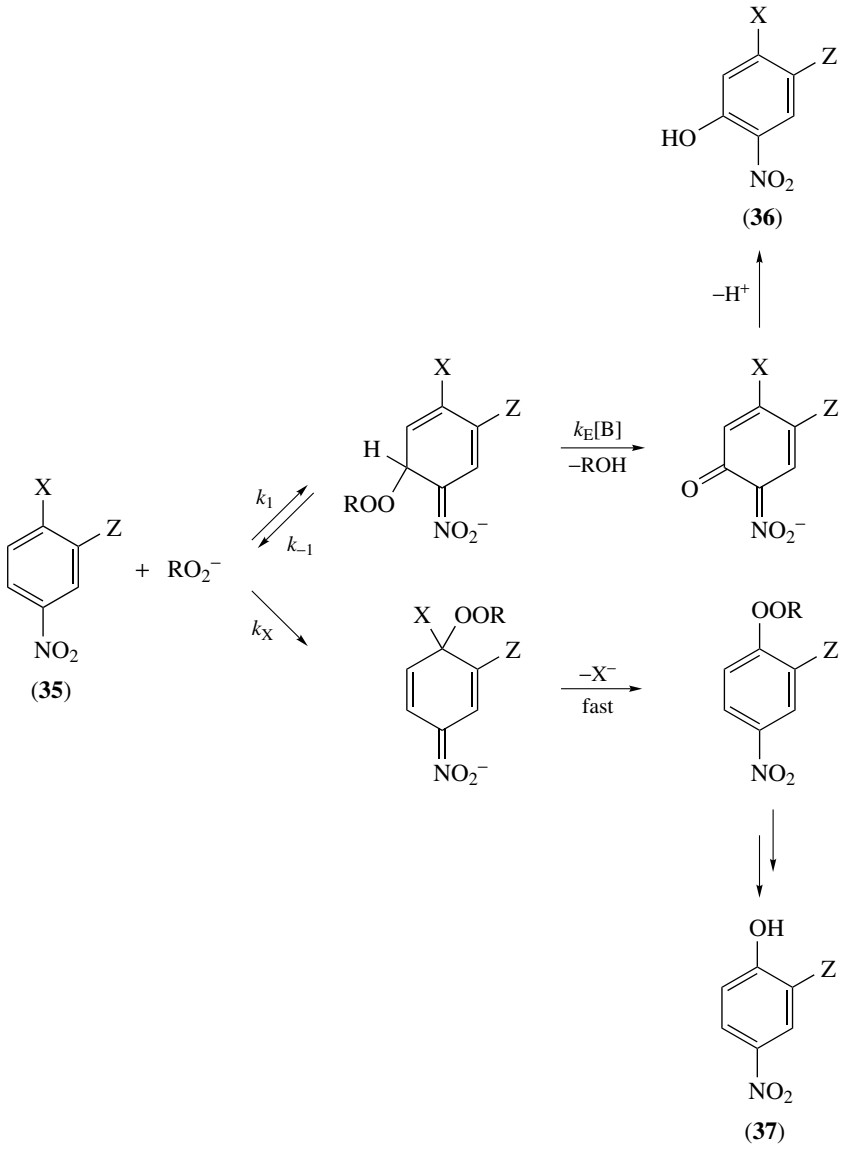
$$HArNO_2 + RO_2^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RO_2(H)Ar{=}NO_2^- \xrightarrow[-ROH]{k_E[B]} O{=}Ar{=}NO_2^-$$

$$v = k_{obs}\,[HArNO_2][RO_2^-] \qquad \text{where } k_{obs} = k_1k_E[B]/(k_{-1} + k_E[B])$$

The ratio of products (**36**) and (**37**) from VNS of hydrogen (P_H) and substitution of halogen (P_X), respectively (Scheme 4), will depend on the strength and concentration of base, provided that the elimination is a kinetically important step in the VNS reaction, namely $P_H/P_X = k_1k_E[B]/k_{-1}k_X$. The influence of base will decrease until a constant value $P_H/P_X = k_1/k_X$ is reached as $k_E[B] \gg k_{-1}$. This has been demonstrated for 4-chloronitrobenzene, which undergoes exclusive substitution of chlorine unless strong base is present to favour the VNS process. The deuterium isotope effect for VNS hydroxylation by Bu^{t}OOH, determined as the ratio of H versus D substitution of 1-deutero-2,4-dinitrobenzene, varied from 7.0 ± 0.3 to 0.98 ± 0.01 as the base in NH_3 was changed from NaOH to Bu^{t}OK; the former value is consistent with a rate determining $E2$ process.

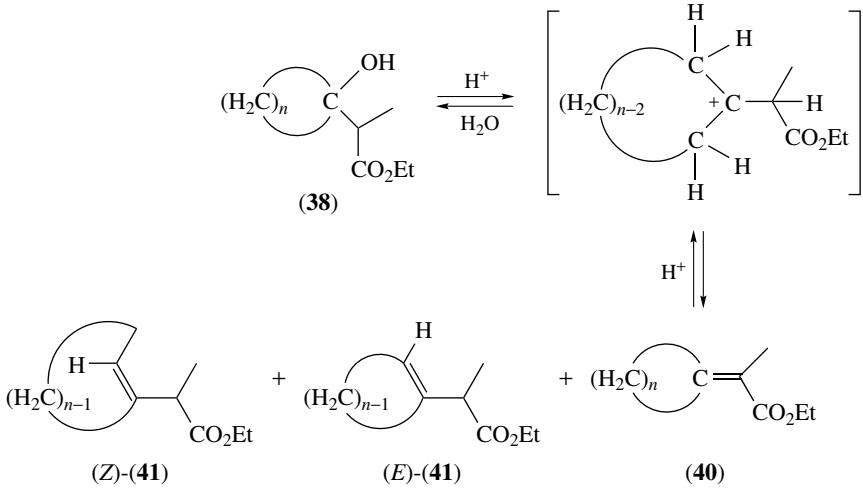
Solvolytic Reactions

Salt effects on monomolecular heterolysis reactions (S_N1, $E1$, $F1$, solvolysis) have been reviewed[28] and the effects of salts on the rate of dehydrobromination of 3-bromocyclohexene have been interpreted.[29] The regiochemistry and stereochemistry



SCHEME 4

of elimination of water from tertiary alcohols (**38**) of ring size $(n + 1) = 5–16$ have been reported (see Table 1).[30] The reaction is presumed to proceed via an intermediate carbenium ion which then deprotonates to give isomeric alkenes (**40**) and (*E*)- or (*Z*)-(**41**). The behaviour of the medium sized rings can be explained in terms of I-strain.



(**38**)

(*Z*)-(**41**) (*E*)-(**41**) (**40**)

TABLE 1. Distribution (%) of alkenes formed from (**38**)

$n+1$	(**40**)	(*E*)-(**41**)	(*Z*)-(**41**)
5	34	66	0
6	0	100	0
7	20	80	0
8	8	92	0
9	2	96	2
10	0	100	0
11	1	89	10
12	1	86	13
13	4	68	28
14[a]	15	60	25
15	28	54	18
16	7	73	20

[a]Results calculated by extrapolation.

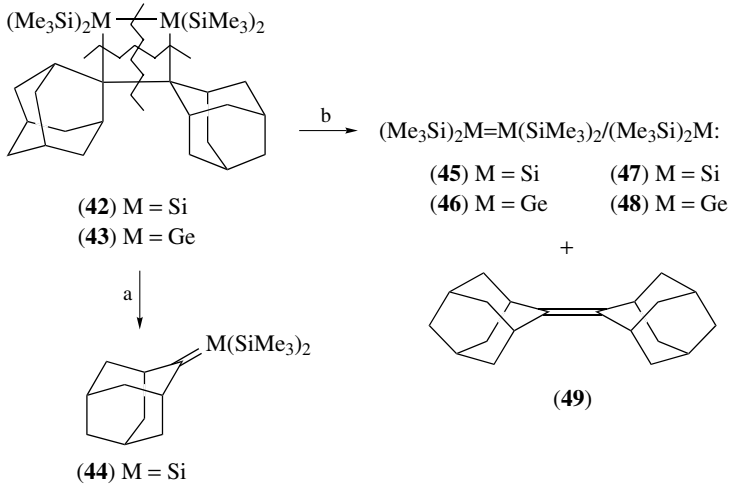
Specific acid-catalysed solvolysis of 1-methoxy-1,4-dihydronaphthalene or 2-methoxy-1,2-dihydronaphthalene in 25% acetonitrile in water has been found to yield mainly the elimination product, naphthalene, along with a small amount of 2-hydroxy-1,2-dihydronaphthalene, there being no trace of either the 1-hydroxy-1,4-dihydronaphthalene or the rearranged ether.[31] The nucleophilic selectivity, $k_{N3}/k_{HOH} = 2.1 \times 10^4$, between added azide ion and solvent water has been estimated for the relatively stable ($k_w = 1 \times 10^7$ s^{-1}) intermediate benzallylic carbocation for which the barrier to dehydronation is unusually low ($k_e = 1.6 \times 10^{10}$ s^{-1}), as evidenced by the large elimination-to-substitution ratio with solvent water as base/nucleophile. The kinetics of acid-catalysed solvolysis of 1-hydroxy-1,4-dihydronaphthalene and 2-hydroxy-1,2-dihydronaphthalene have also been studied.

Pyrolytic Reactions

Cycloreversions

The retro-Diels–Alder reaction has been reviewed.[32] A fully concerted cyclic transition state has been proposed for conrotatory opening of cyclobutenes, in order to account for the low activation entropy and unexpected activation volume of ca -2 to $-3\ cm^3\ mol^{-1}$.[33]

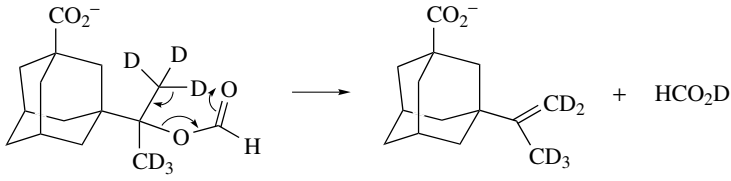
2 + 2-Cycloreversions of a 1,2-disilacyclobutane (**42**) and a 1,2-digermacyclobutane (**43**) have been induced in solution both thermally and photochemically; fragmentation of sterically congested (**42**) follows Scheme 5 paths a and b, respectively; fragmentation of (**43**) yields (**46**) (which photodissociates to **48**) in each case.[34]



SCHEME 5

Acid Derivatives

Further evidence has been reported in favour of the loss of neutrals (even-electron) from even-electron anions by a charge-remote process.[35] Thus, the parent $(M-H)^-$ ion (**50**), in which the 1- and 3-substituents on adamantane can neither interact through bonds nor approach through space, has been found to fragment by exclusive loss of HCO_2D. The corresponding carboxylate cation $(M-H)^+$, generated by charge reversal of anion (**50**), has been shown to behave likewise.

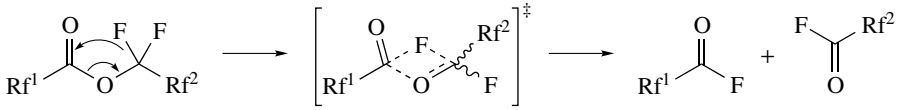


(**50**) (**51**)

Unimolecular pyrolysis of the tautomers of monothioformic acid (two conformers of thiol- and two conformers of thiono-) have been studied by *ab initio* methods with STO-3 G and 6–31 G** basis sets.[36] The barrier heights for dehydrogenation (via a four-centre transition state) and dehydrogensulfidation (via a three-centre transition state) of thiol formic acid are 67.47 and 67.09 kcal mol^{-1}, respectively. Dehydration of *s-cis*-HCSOH occurs via a three-centre transition state with an activation energy of 81.18 kcal mol^{-1}; this is much greater than for dehydration of the *s-trans* form, which occurs via a four-centre transition state with a barrier of only 68.83 kcal mol^{-1}.

Results of HF/3–21 G theoretical studies of gas-phase dehydration of α-hydroxy acids suggest that the reaction is favoured by electron-donating substituents via a three-membered ring intermediate formed via a five-membered ring transition state; a three-membered ring transition state governs formation of product in the second step.[37]

Certain perfluoro esters (**52**) (incapable of the eliminative fragmentation, with β-hydrogen migration, commonly displayed by hydrocarbon esters) have been shown to decompose at elevated temperature (230–250 °C).[38] AM1 semiempirical calculations suggest that a four-membered transition state (**53**) featuring transfer of α-fluorine to the carbonyl carbon is involved; this is consistent with the negative entropy of activation and relatively high activation energy.



(**52**) (**53**)

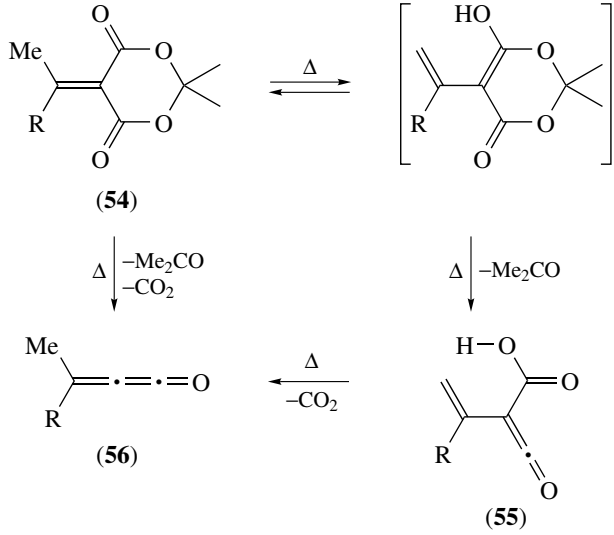
Further theoretical study of the mechanism of decomposition of β-propiolactone and β-butyrolactone, to form CO_2 and ethene or propene, respectively, has concluded that the process can best be described as asynchronous and concerted.[39] Calculations also suggest that concerted processes are preferred for both decarbonylation and decarboxylation of η-thiobutyrolactone.[40]

Direct evidence has been reported for the formation of methoxyvinyl- and methylthiovinyl-(carboxy)ketenes (**55c** and **55d**) upon flash vacuum thermolysis of Meldrum's acid derivatives (**54c**) and (**54d**), respectively;[41] the intermediates decarboxylate readily to give (**56c**) and (**56d**), respectively, and are more transient than those obtained previously from (**54a,b**).

First-order kinetics have been reported for gas-phase thermal decomposition of nitroethyl carboxylates to give nitroethylene and the corresponding aliphatic acid.[42]

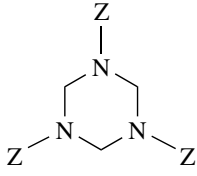
Nitrogen Compounds

Activation parameters have been determined for eliminative thermal decomposition of hexahydro-1,3,5-trinitro-1,3,5-triazine and related compounds, under high pressure in dilute solution.[43] The negative activation volumes, low enthalpies of activation,

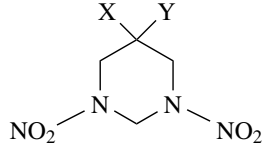


a; R = H, **b**; R = Me, **c**; R = MeO, **d**; R = MeS

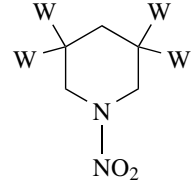
order of thermal stability and detection of aromatic products suggest that these cyclic nitramines and nitrosamines decompose through elimination of HNO_2 or HNO by a non-homolytic pathway which is dependent on reaction conditions and structural features. The order of stability (**58a > 57b > 57a > 58b > 59**) is consistent with the expected decrease in acidities of the methylene hydrogens.



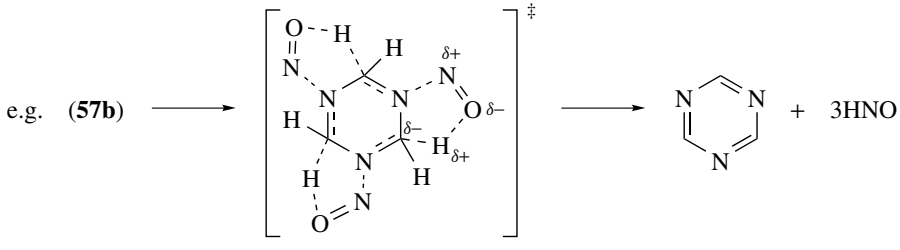
(**57a**) Z = NO_2
(**57b**) Z = NO



(**58a**) X = Me, Y = NO_2
(**58b**) X = NO_2, Y = NO_2

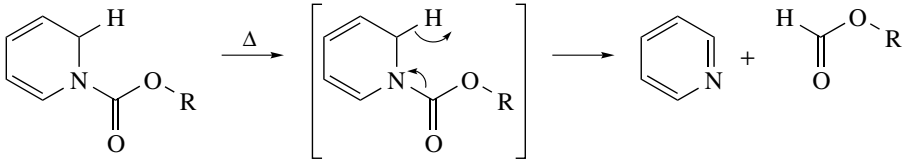


(**59**) W = NO_2



Formation of 2*H*-azirines by thermal decomposition of vinyl azides has been shown to exhibit small entropy of activation and insensitivity to solvent polarity; acyclic vinyl azides decompose more readily than analogous cyclic ones and it is advantageous to have a hydrogen atom *cis* to the azido group (*E*-are more reactive than *Z*-isomers).[44] These results and the linear correlation found for ring-substituent effects on decomposition of α-styryl azides are consistent with a nonconcerted mechanism in which elimination of nitrogen and cyclization into a three-membered ring proceeds synchronously.

It is clear from a study of thermal and radical-induced decompositions of *N*-alkoxycarbonyldihydropyridines that radical processes are of minor importance, and that pyridine formation is probably a consequence of 1,2-elimination of formate (Scheme 6).[45] It has also been concluded that the rate of 1,4-elimination of formate from *N*-alkoxycarbonyl-1,4-dihydropyridines at higher temperatures is too rapid to be explained by a homolytic process.

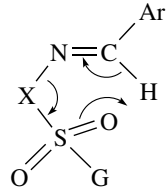


SCHEME 6

The thermodynamics and shock-tube kinetics of pyrolysis of azetidine, in argon at high dilution, have been compared with those for trimethylene oxide, sulfide and imine.[46]

Thermochemical parameters estimated by semiempirical AM1 calculations have been found to support the proposal that isobutene formation on gas-phase thermolysis of *N*-methyl-*N*-phenyl-*tert* -butylsulfenamide and morpholinyl-*tert* -butylsulfenamide occurs by a unimolecular mechanism involving a four-centre cyclic transition state and co-formation of the corresponding thiohydroxylamines.[47]

Kinetics and mechanisms of gas-phase pyrolysis of sulfonyl hydrazones and their oxime analogues have been reported for the first time;[48] it is proposed that cyanoarene formation arises in each case via a six-membered transition state (**60**). The lower limit



(**60**)

e.g. Ar = Ph, G = *p*-Tol, X = O or NH

for rate enhancement on replacing the hydrazone N−NH bond by the oxime N−O bond is $6-9 \times 10^4$ and the Hammett ρ value for the hydrazones is negligible (ca 0.01).

Other Pyrolytic Reactions

Comparison of results of single-pulse shock-tube experiments with those from an earlier study suggest that the existing rate expression for HF elimination from 1,1,1-trifluoroethane may need to be re-evaluated.[49]

The transition state for elimination of HF from hydrofluorocarbons has been probed by determining threshold energies and unimolecular rate constants for such reactions of chemically activated $CF_3CH_2CH_3$ and $CF_3CH_2CF_3$.[50] Chemically activated $CF_3CH_2CH_3$* containing 95 and 101 kcal mol^{-1} internal energy can be produced by combination of $CF_3CH_2^{\bullet}$ with $CH_3^{\bullet}$, or $CF_3^{\bullet}$ with $CH_3CH_2^{\bullet}$, respectively. The unimolecular elimination rate constants calculated from RRKM theory were fitted to the experimental values in order to obtain threshold energies, E_0, of 73 kcal mol^{-1} for $CF_3CH_2CF_3$ and 62 kcal mol^{-1} for $CF_3CH_2CH_3$; these, on comparison with those for CF_3CH_3 and CF_3CH_2Cl, show that replacement of H of $CF_3CH_3$by a methyl substituent lowers E_0 by ca 5 kcal mol^{-1}. The chlorine and fluorine substituents have the same effect on E_0 as a CF_3 group. Approach to the transition state for HF elimination apparently involves a flow of electron density from the departing hydrogen to the β-carbon, and from the β- to the α-carbon and to the α-carbon from its substituents; most of the incoming electron-density is passed from the α-carbon to the departing fluorine. Thus, electron-withdrawing substituents on either carbon raise E_0 because they hinder the flow of electron density.

Results of a PEPICO study of the dissociation dynamics of 2-bromobutane ions have been analysed with tunnelling-corrected RRKM statistical theory using vibrational frequencies obtained from *ab initio* MO calculations.[51] It has been concluded that the slow rate of loss of HBr, to form the but-2-ene ion, occurs via a concerted mechanism in which tunnelling is a feature of the proton transfer.

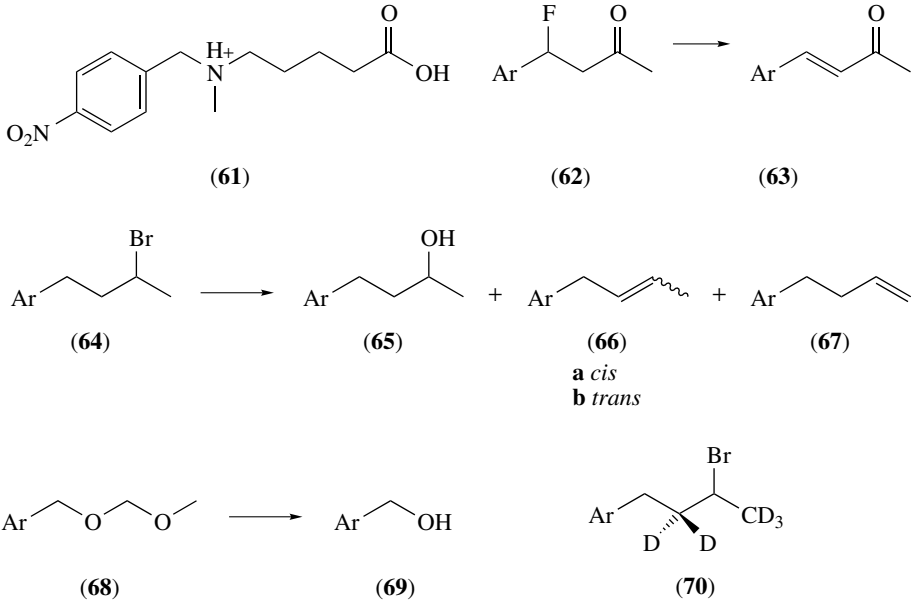
Theoretical predictions, based on AM1 MO theory, for gas-phase elimination reactions of 3-chloropropanoic and 2-chlorobutanoic acids are consistent with experimental results; four-, five-, and six-membered transition states have been discussed.[52]

o-Quinone methide is formed as a common intermediate on very low-pressure pyrolysis (550−1210 K) of *o*-hydroxybenzyl alcohol, 3,4-dihydro-2*H*-1-benzopyran (chroman) and 1,4-benzodioxin.[53] The respective processes involve dehydration, ethene elimination following initial cleavage of the phenoxy−carbon bond, and phenyl−vinoxy bond cleavage leading to formation of a four-ring intermediate which decarbonylates.

Reactions Catalysed by Biomolecules

Hapten design strategy for generation of an active site with a suitable catalytic residue has been further demonstrated. Thus, catalytic antibody 43D4−3D12, which was generated against the tertiary amine (**61**), has been found to catalyse the selective

elimination of HF from β-fluoro ketone (**62**) in aqueous medium and without competing substitution.[54] $Glu^{H}50$ acts as a general base at the active site; likewise, the antibody effects conversion of (**64**) to (**66a**) (18%), (**66b**) (72%), (**67**) (1%), and (**65**) (9%) by selective abstraction of the proton β- to the nitrophenyl ring. Reactions of the pentadeutero substrate (**70**) are subject to kinetic isotope effects of 2.9 and 4.1 for *cis* and *trans* elimination reactions, respectively. In contrast, $Glu^{H}50$ is believed to act as a general acid in catalysing hydrolysis of acetal (**68**) to the alcohol (**69**). The reactions share the nitrophenyl ring as a common recognition element and proton transfer as a mechanistic feature.



π-Stacking interactions and solvation effects within the highly preorganized cleft of a bifunctional C-shaped host are believed to benefit the base-promoted conversion of 5-nitrobenzisoxazole to 2-cyano-5-nitrophenolate relative to the acetate-promoted reaction; structural variation of the host has been explored.[55]

Elimination Reactions in Synthesis

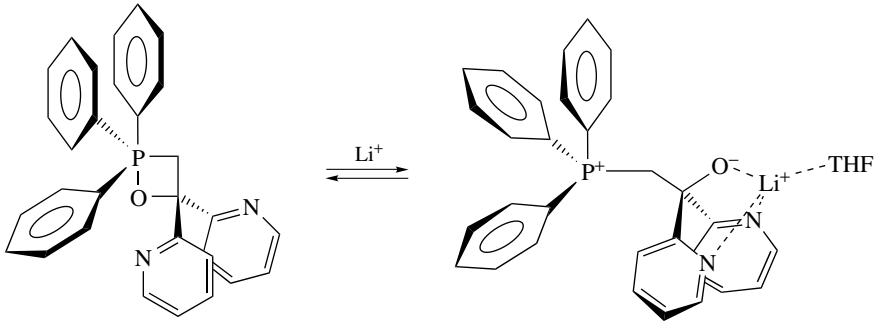
High-level quantum mechanical calculations have been used to explore the Horner–Wandsworth–Emmons reaction in the gas phase and also with a solvation contribution evaluated using the PCM/DIR method.[56] Ring closure of the P–O bond (TS2), to form oxaphosphetane, is rate determining in the absence of solvation; however, the oxyanion becomes a true intermediate, at an energy minimum on the reaction path, only in response to the effects of solvation, whereupon its formation by carbonyl addition (TS1) becomes rate limiting. Formation of *E*-product is always

favoured by TS2, whereas TS1 shifts the preference towards *Z*-selectivity if the phosphorus bears hydrogen-bond-donor ligands. The results emphasize the importance of addressing the relative stabilities of TS1 and TS2 in any interpretation of *E*/*Z* selectivities.

The *ab initio* MO(HF/3–21 G*) method and density functional (B3LPY/6–31 G*) theory have been used in higher level calculations for a range of oxaphosphetane reactions of MeCHO and PhCHO.[57] For both non-stabilized (alkylidene) and semi-stabilized (benzylidene) ylides it has been found that *cis* and *trans* oxaphosphetanes are formed via puckered and nearly planar transition states, respectively. However, in contrast with previous semiempirical calculations and in agreement with known product distributions, the puckered transition state is found to be favoured by the latter, on reaction with benzaldehyde. For reaction between PhCHO and $Ph_3P{=}CHPh$ the computed carbonyl kinetic isotope effect (at HF/3–21 G*) is 1.051 at 0 °C and in agreement with the experimental KIE; in contrast, disagreement between the computed value (1.039) and the experimental value (1.0) for reaction with $Ph_3P{=}CHPr$ suggests that some rate-determining alternative to the puckered transition state may apply for formation of *cis*-oxaphosphetane from this non-stabilized ylide.

Ab initio (HF and MP2) and MNDO-PM3 theoretical studies of the reaction of unstabilized ($Me_3P{=}CHCH_3$), semi-stabilized ($Me_3P{=}CHC{\equiv}CH$), and stabilized ($Me_3P{=}CHCN$) ylides with acetaldehyde have also been reported.[58] It has been concluded that oxaphosphetane formation proceeds by a very asynchronous cycloaddition (borderline two-step mechanism) in which the alignment of P, C, C, and O atoms is almost planar in the transition state; the extent of C–C bond formation ranges from 44% (unstabilized case) to 60% (stabilized case), whereas the degree of P–O bond formation is insignificant. Oxaphosphetane decomposition (retrocycloaddition) is also very asynchronous, with P–C bond breakage running ahead of C–O bond breakage. Unfortunately, the energy barriers calculated for the formation, pseudorotation, and decomposition of oxaphosphetane were very dependent on the level of theory employed.

Spectroscopic evidence for formation of a betaine lithium salt adduct during the course of a Wittig reaction has been reported for the first time.[59] The ylide $Ph_3P{=}CH_2$ formed oxaphosphetane (**71**) on treatment with 2,2′-dipyridyl ketone at −60 °C in

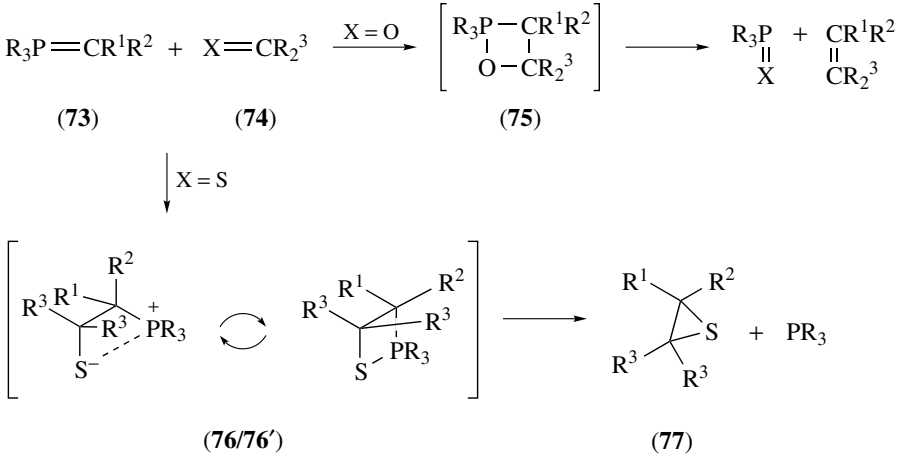


(**71**) (**72**)

THF; the ^{31}P NMR reveals only a singlet at $\delta_P = -63.2$, which, on addition of LiBr, gives way to a weak singlet at $\delta_P = +23.7$ which has been ascribed to the rather insoluble betaine (**72**).

A transition between thiaphosphetane- and *gauche*-betaine-type structures of intermediates in the thio-Wittig reaction of ylides $R_3P{=}CR^1R^2$ with $S{=}CR^3_2$ has been detected by ^{31}P NMR spectroscopy and predicted by computational study.[60] Thus *ab initio* calculations for reaction of (**73b**) with (**74b**) (X = O) reveal the formation of a conventional oxaphosphetane intermediate (**75b**) that features a planar four-membered ring, whereas the intermediate of the corresponding thio-Wittig reaction (X = S) is characterized by a large P−S separation and departure from planarity. The betaine character of the intermediate decreases upon reducing the phosphonium stabilization electronically, by substituting the Me_3P moiety consecutively by H_3P (**76c**) and $(CF_3)_3P$ (**76d**). The intermediate (**76a**) formed on reaction of ylide (**73a**) with thioketone (**74a**) in toluene at 233 K exhibits a ^{31}P NMR signal at −40 ppm in the range expected for a thiaphosphetane structure, whereas the product in dichloromethane features a signal at δ +1.0 ppm (at 243 K); both products decompose at slightly elevated temperatures to produce Ph_3PS and $Ph_2C = CH_2$ via a 2,2-diphenylthiirane intermediate (**77a**) and Ph_3P (Scheme 7). The ^{31}P NMR chemical shift of (**76a/76a′**) in toluene–dichloromethane mixtures varies continuously with solvent composition.

It has been suggested that the preferential formation of (*E*)-alkene on Wittig reaction of amide-substituted phenyl 3-pyridyl ketones with non-stabilized phosphorus ylides which contain a carboxyl terminus is a consequence of either hydrogen bonding or salt



a, $R^1 = R^2 = H$, $R = R^3 = Ph$

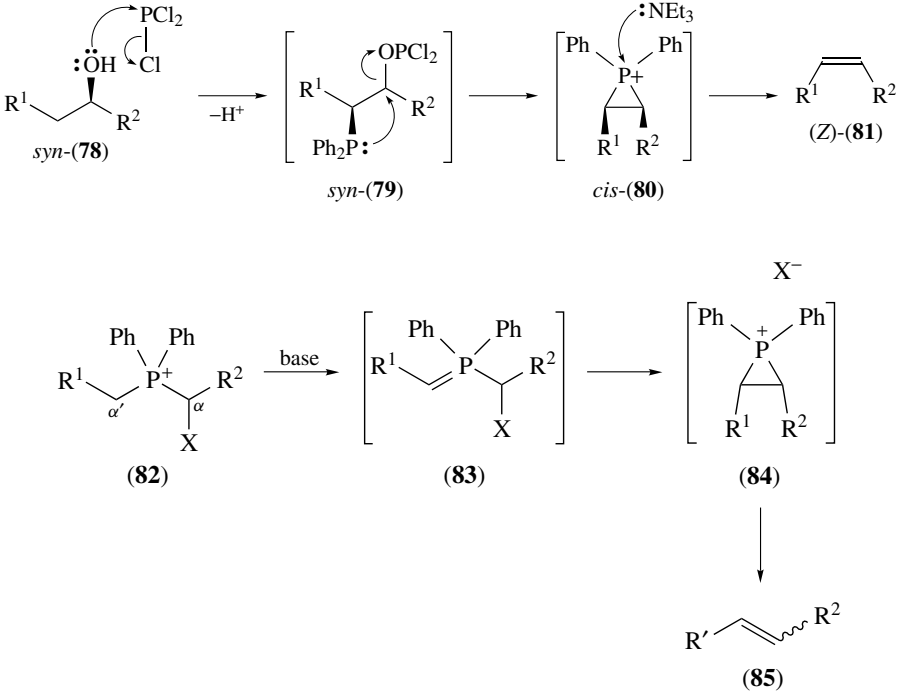
b, R = Me, **c**, R = H, **d**, $R = CF_3$, where $R^1 = R^2 = H$ and $R^3 = Me$

e, $R^3 = p\text{-}C_6H_4NMe_2$, **f**, $R^3 = p\text{-}C_6H_4OMe$, where $R^1 = H$, $R^2 = Me$ and R = Et

SCHEME 7

bridge formation between the amide group and the carboxyl terminus during formation of the oxaphosphetane intermediate.[61]

A means of forming alkenes by *anti* β-elimination of OH and a heteroatom group X on adjacent carbon atoms has been developed.[62] The reaction involves an *anti* Wittig elimination via an *epi*-phosphonium species (**80**); the reaction is induced by reacting *anti*- or *syn*-1,2-phosphinyl alcohols (**78**) with PCl_3 and Et_3N to give (*E*)- and (*Z*)-alkenes, respectively. The *epi*-phosphonium intermediate (**80**) undergoes nucleophile-induced extrusion of the phosphorus atom. Support for this suggestion has been gained by development of a phosphorus Ramberg–Bäcklund-type reaction (Scheme 8).[63] Treatment of (**82**, $R^1 = R^2 = Ph$, $X = Br$) with Et_3N gave stilbene (**85**) with *cis*-selectivity ($Z:E \approx 78:22$) that is comparable to that observed in the conventional Ramberg–Bäcklund reaction; the *E*/*Z* ratios determined for a series (**82**, $R^1 = Ph$, $R^2 = YC_6H_4$, $X = Br$) do not correlate with known effects of substituent Y.



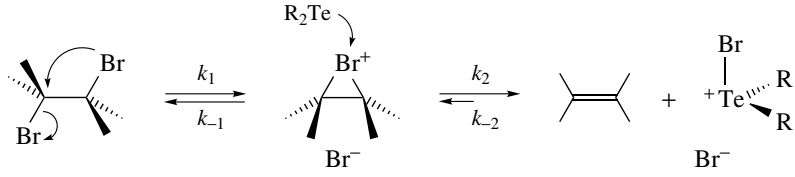
SCHEME 8

A new and convenient method of preparation of trichloro- and trifluoromethyl sulfones has found application in β-elimination of haloform via an unusually facile Ramberg–Bäcklund rearrangement under extremely mild and non-aqueous conditions.[64] Thus, 9-fluorenyl trichloromethyl sulfone in $CHCl_3$ affords

9-dichloromethylenefluorene in quantitative yield at room temperature on treatment with DBU, Et_3N, DABCO, morpholine, or even 2,6-lutidine. The expected β-elimination of $CHCl_3$ and accompanying sulfene formation did not occur, nor could they be achieved by using alternative benzylic or benzhydrylic trichloromethyl sulfones.

The effects of solvent, temperature, and bulk of the silyl and carbamate functionalities on the stereochemistry of Peterson olefinations of silylated benzyl carbamates (to give substituted vinyl carbamates) has been investigated.[65] Steric/electronic bulk of the triphenylsilyl moiety appears to be the overriding factor in promoting *Z*-selectivity.

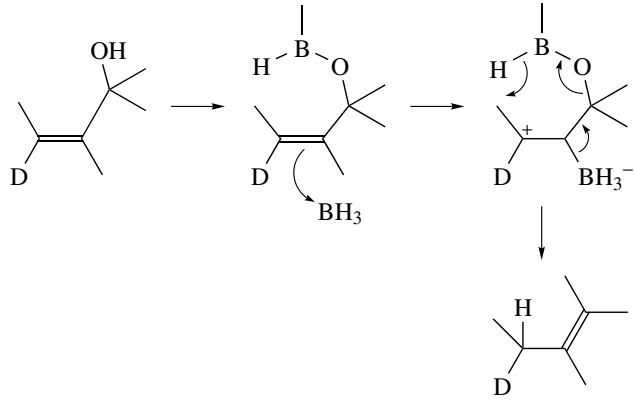
A study of debrominations of *vic*-dibromides promoted by diaryl tellurides and di-*n*-hexyl telluride has established several key features of the elimination process: the highly stereoselective reactions of *erythro*-dibromides are much more rapid than for *threo*-dibromides, to form *trans*- and *cis*-alkenes, respectively; the reaction is accelerated in a more polar solvent, and by electron-donating substituents on the diaryl telluride or carbocation stabilizing substituents on the carbons bearing bromine.[66] Alternative mechanistic interpretations of the reaction, which is of first-order dependence on both telluride and *vic*-dibromide, have been considered. These have included involvement of $TeAr_2$ in nucleophilic attack on carbon (with displacement of Br^- and formation of a telluronium intermediate), nucleophilic attack on bromine (concerted *E*2-like debromination) and abstraction of Br^+ from an intermediate carbocation. These alternatives have been discounted in favour of a bromonium ion model (Scheme 9) in which the role of $TeAr_3$ is to abstract Br^+ in competition with reversal of the preequilibrium bromonium ion formation. The insensitivity of reaction rate to added LiBr suggests that the bromonium ion is tightly paired with Br^-.



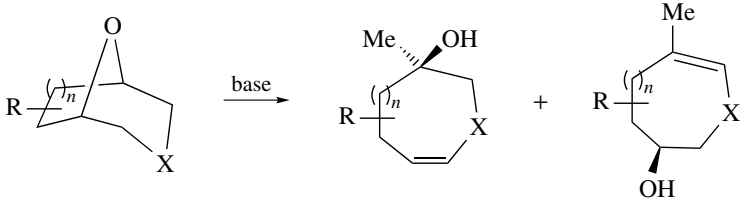
SCHEME 9

A modification of an earlier procedure for debromination of *vic*-dibromides in the presence of catalytic amounts of diorganotellurides has allowed the synthesis of terminal alkenes and *cis*- and *trans*-1,2-disubstituted alkenes from appropriate precursors;[67] the relative substrate reactivities suggest that, as for the stoichiometric reaction, the catalytic reaction involves intermediate bromonium ion formation. The Te(IV) dibromides formed in the debrominative elimination are reduced back to the catalysts by either sodium ascorbate or the thiol glutathione.

Hydroboration of a 5β-hydroxyandrost-3-ene has been found to induce facile elimination of the 5β-hydroxy group; results of a deuterium labelling study of the fate



SCHEME 10



(**86**) (**87**) (**88**)

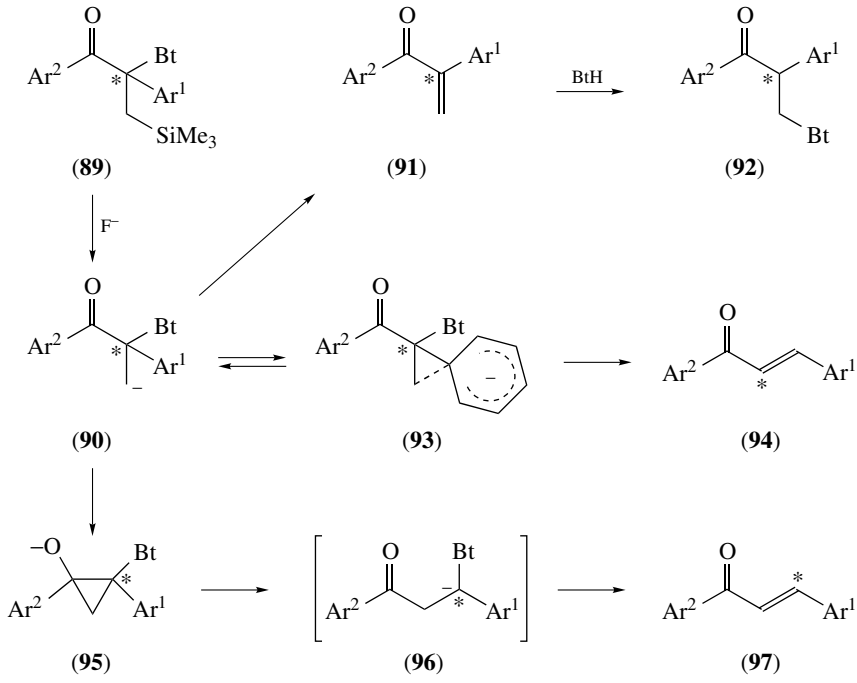
X = S, SO_2, *N*-Boc
n = 1,2

of deuterium at C(3) suggest that this may involve a *trans*-diaxial borane–borinate elimination coupled with a *syn* transfer of hydrogen from the bromide (Scheme 10).[68]

A study of ring opening of hetero-oxabicyclic [3.2.1] and [3.3.1] systems (**86**) has established that for X = SO_2 or *N*-Boc the selectivity is low.[69] Preferential formation of (**87**) rather than (**88**) is dependent on selective removal of the axial versus the equatorial proton.

Other Reactions

A carbon labelling study has elucidated the rearrangement mechanism for formation of chalcone (**97**) which accompanies formation of (**91**) by the expected vicinyl elimination of trimethylsilyl and benzotriazolyl groups from 2-benzotriazolyl-2-aryl-3-ketopropylsilanes, on reaction with fluoride ion in DMF.[70] Thus, it has been possible to distinguish between the two alternative mechanisms depicted in Scheme 11 (via intermediates (**93**) or (**95**), respectively, by determining the fate of the labelled quaternary carbon of substrate (**89**). The results are consistent with the formation of a cyclopropane intermediate (**95**) which subsequently ring opens, with relief of strain, to form delocalized carbanion (**96**), from which the chalcone (**97**) is obtained (labelled



SCHEME 11

β- to the carbonyl group) following protonation and β-elimination of triazole. Formation of (**95**), and hence (**97**), are favoured by aryl (Ar^2) substituent effects which increase the electrophilicity of the adjacent carbonyl group

On acetolysis in the presence of NaOAc, triterpenoid tosylates have been found to form substitution products by bimolecular processes (S_N2 on carbon, S_AN on sulfur) and elimination products often via intermediates formed by hydride and/or methyl shifts.[71]

Rate and equilibrium constants for ring opening of 2-[(4-dimethylamino)phenyl]-1,3-thiazolidine to an imminium ion in aqueous solution at 25 °C have been compared with literature values for *N*-Bu-and *N*-Ph-substituted thiazolidines derived from 4-dimethyaminocinnamaldehyde and discussed with reference to Baldwin's rules.[72] The rate of ring opening (which is greatest for the N−H thiazolidine) varies by 10^8-fold, mainly as a consequence of steric interactions between the substituents at N and C(2) in the ring-opening transition state; the corresponding variations in equilibrium constants are small.

The mechanism of formation of $PhC{\equiv}CCO_2H$ from *trans*-$PhCH{=}CHCO_2H$ by stepwise bromination–dehydrobromination has been explored.[73]

Nucleophilic attack of hydroxide ion on the α-carbon atom, with subsequent cleavage of the $C_\alpha-C_\beta$ bond, has been proposed to account for the kinetics of retro-aldol reaction of substituted benzylidene malononitriles with hydroxide ion in 90%

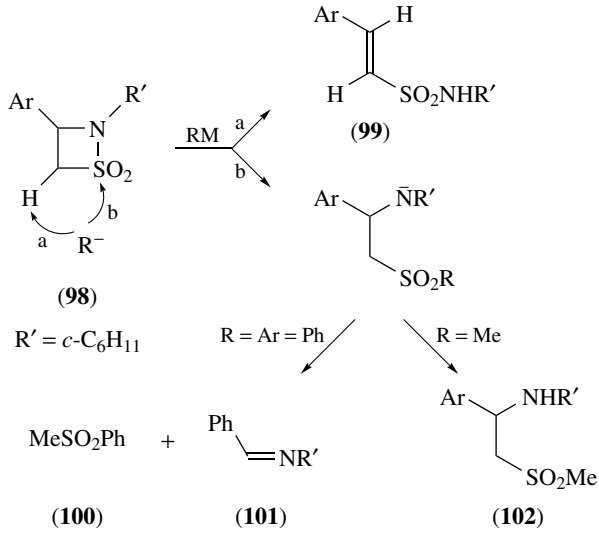
MeOH–10% H_2O.[74] The reaction rates, which are increased by electron-withdrawing aryl substituents, have been correlated using the Hammett equation.

The leaving group dependence of activation parameters found for reaction of 2-(β,β-dihalovinyl)-5-nitrothiophenes with NaOMe in MeOH ($\Delta S^{\neq}$ negative for Cl, zero for Br, and positive for I) suggest that the substitution reaction proceeds via an addition–elimination mechanism, with formation of an intermediate haloalkyne, for the bromide and iodide.[75]

A search for examples of charge-remote reactions of even-electron organic negative ions in the gas phase has featured collision-induced decompositions of 3-substituted adamantanecarboxylate anions.[76] Fragmentations of the 3-substituent (which the CO_2^- group is unable to approach) is likely to occur when there is no suitable lower energy decomposition channel directed by the charged site. Charge-remote radical losses from 3-$CH(Et)_2$ and 3-CO_2Me are observed and elimination of MeOD and HCO_2D from 3-$C(CD_3)_2$(OMe) and 3-$C(CD_3)_2$(OCH=O), respectively, has been studied.

4-Non-substituted β-sultams (**98**) undergo eliminative formation of (*E*)-vinylsulfonamides (**99**) on reaction with MeLi but are subject to competing substitution (with ring opening) to give (**102**) when MeMgBr is used.[77] 4-Monosubstituted β-sultams react with organometallics, MeLi, PhLi, MeMgBr, by stereoselective formation of only (*E*)-vinylsulfonamides regardless of the configuration of the 3- and 4-substituents.

The pH–rate profile for reaction of nitrosobenzene with *N*-methylhydroxylamine (to form only 1-methyl 2-phenyldiazene-2-oxide) has been found to exhibit a negative break between pH 0.5 and 3.0. This has been ascribed to a change in rate-determining step from nucleophilic attack on nitrosobenzene at low pH to dehydration of the *N*,*N*′-dihydroxy intermediate at higher pH;[78] the dehydration is subject to general-acid catalysis ($\alpha = 0.34$) and specific and general-base catalysis ($\beta = 0.20$). The pH–rate profile is similar to that for reaction of *N*-methylhydroxylamine with



p-chlorobenzaldehyde, which is also believed to proceed by an ionic (rather than free radical) mechanism. However, the behaviour of MeNHOH contrasts with that for analogous reaction of nitrosobenzene with phenylhydroxylamine for which dehydration of the addition intermediate is rate determining throughout the pH range. Comparison of the rate constants for the oxonium-ion-catalysed reactions of PhNO with MeOH and PhNHOH provides further indication that special factors apply to the latter (as found previously for reaction with benzaldehyde); a pre-association mechanism has been discussed.

Results of *ab initio* studies lend support to a mechanism, involving initial formation of Me_3C^+, CO_2 and $Me_3COC(O)N{=}N^-$, proposed to account for oxidative fragmentation of di-tert-butyl azodicarboxylate promoted by thianthrenium perchlorate.[79]

Results of a study of acid-catalysed epimerization of indolo [2,3-*a*]quinolizidine derivatives support a mechanism involving nitrogen lone pairs in an eliminative ring opening–ring closure.[80]

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