

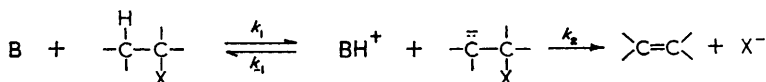
The Carbanion Mechanism of Olefin-forming Elimination

By D. J. McLennan

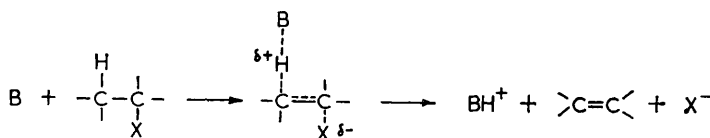
CHEMISTRY DEPARTMENT, UNIVERSITY OF AUCKLAND, NEW ZEALAND

Introduction

This Review is primarily a summary and evaluation of evidence pertaining to the carbanion or *E1cB* mechanism¹ of olefin formation. The mechanism differs from the more usual bimolecular (*E2*) mode of elimination in that it is a step-wise process, involving the intermediacy of a discrete carbanion, whereas an *E2* elimination is concerted and passes through a single transition state.^{2,3} We illustrate the case for a neutral basic species.



Scheme 1 Carbanion mechanism (*E1cB*)



Scheme 2 Bimolecular mechanism (*E2*)

By assuming a steady-state carbanion concentration in the carbanion mechanism, we obtain:

$$\text{Rate} = \frac{k_1 k_2 [\text{substrate}] [\text{B}]}{k_{-1} [\text{BH}^+] + k_2} \quad (1)$$

so that second-order kinetics: rate = k_{obs} [substrate] [B], as will be exhibited by all non-solvolytic *E2* reactions, will be observed under the following conditions (assuming that [substrate] and [B] are comparable):

(i) The first step is rate-determining, being essentially the bimolecular, irreversible formation of the carbanion, and the second step is the relatively rapid ejection of the leaving group from the α -carbon atom ($k_2 \gg k_{-1} [\text{BH}^+]$). [According to current terminology concerned with elimination reactions, the leaving group (halogen, quaternary ammonium, arenosulphonate, etc.) departs from the α -carbon atom, and the proton is removed from the β -carbon atom.]

(ii) The first step is a rapidly-attained equilibrium and the second is the rate-

¹ C. K. Ingold, 'Structure and Mechanism in Organic Chemistry', Cornell University Press, Ithaca, New York, 1953, p. 423.

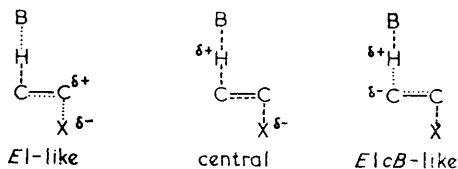
² Ref. 1, p. 422.

³ J. F. Bunnett, *Angew. Chem. Internat. Edn.*, 1962, 1, 225.

limiting, unimolecular decomposition of the carbanion ($k_{-1}[\text{BH}^+] \gg k_2$). If in this case the base **B** is not the lyate ion of the solvent, its conjugate acid, BH^+ , must be present in excess to allow the observation of second-order kinetics.

Carbanionic eliminations thus fall into two distinct mechanistic categories: one in which carbanion formation is irreversible and rate-determining, which we shall call the 'irreversible' type of mechanism, although we are considering the irreversibility of the first step only, and another in which the carbanion and substrate are in equilibrium. We shall call the latter the 'pre-equilibrium' type of carbanion mechanism. A kinetic distinction between these categories will be discussed later. Under the most commonly used conditions of base and solvent (alkoxide ions in alcohol) there are obtained second-order kinetics for both classes of carbanion mechanism and for the bimolecular mechanism, so that no kinetic criterion of mechanism is available.

Recent developments of the theory of the bimolecular mechanism view this process as comprising a spectrum of sub-mechanisms which differ subtly in transition-state character. Although C-H and C-X bond-breaking processes are necessarily coupled in that electrons partially freed by the former facilitate the latter and impart double-bond character to the transition state, the stretching of one bond may outpace that of the other in forming the transition state.³ Thus we can conceive three general types of E_2 transition state, which are illustrated in Scheme 3. The transition state may resemble a carbonium ion, the olefinic product, or a carbanion, depending on the timing of the covalency changes



Scheme 3

at the α - and β -carbon atoms. The carbonium ion and carbanion intermediates of the pure E_1 and E_1cB mechanisms are thus seen to be limiting structures in the spectrum of E_2 transition states. Reference should be made to Bunnett's paper³ for the development of the theory and a discussion of its consequences and applications.

In the absence of considerable stabilisation (which is the case in most of the reactions we discuss) the carbanion in an E_1cB reaction will be formed in an endo-energetic step so that the transition state leading to it should have carbanionic characteristics.⁴ Thus structural and environmental effects will be similar to those expected for E_2 reactions utilising E_1cB -like transition states, making experimental demonstration of the nature of the intervening species in an elimination reaction difficult. The mechanistic tests we describe in the following sections are therefore not completely unambiguous.

⁴ G. S. Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.

The list of specific applications of mechanistic criteria will not be exhaustive as experimental results for many reactions that may be *E1cB* are too meagre to allow more than speculation. The reader is referred to Banthorpe⁵ for mention of several such cases. We confine our discussion to reactions mentioned in the title. Acetylene formation from vinylic halides and the like (which almost invariably involves a carbanionic intermediate)* has been adequately reviewed by Köbrich,⁶ and while the stepwise⁷ and concerted⁸ mechanisms of halogenoform hydrolysis are analogous to the *E1cB* and *E2* mechanisms respectively, as has been demonstrated by some of the mechanistic tests described herein, we will not discuss them in any detail.

β -Hydrogen Exchange accompanying Elimination

If a pre-equilibrium carbanionic elimination is proceeding in a protic solvent, β -hydrogen atoms of the substrate will be exchanging with solvent protons at a rate which is rapid compared with that of olefin formation. Such exchange can be demonstrated by using either the substrate or solvent suitably labelled with isotopic hydrogen, allowing the reaction to proceed to partial completion, and examining recovered substrate for changes in isotopic composition. If exchange is not detected, an irreversible-type carbanion mechanism or an *E2* mechanism is indicated.

Hine, Wiesboeck, and Ramsey⁹ have shown that 1,1,1-trifluoro-2,2-dihaloethanes are dehydrofluorinated much more slowly than they undergo hydrogen exchange¹⁰ in alkaline methanol. The activating effects that the α -fluorines and β -halogens have on the β -hydrogen, together with the well-known reluctance of fluorine to depart as an anion from saturated carbon (and more so from a carbon bearing other halogens¹¹), make the intermediacy of carbanions in these eliminations highly likely, and in fact they provide us with the only examples of the *E1cB* mechanism being involved in reactions of saturated halogeno-alkanes. Breslow¹² has raised the formally correct point that,

*In some cases it has been found that *trans* elimination from a vinylic halide proceeds by a concerted mechanism whereas the analogous *cis* elimination is carbanionic (and slower) (See S. J. Cristol and W. P. Norris, *J. Amer. Chem. Soc.*, 1954, **76**, 3005; S. J. Cristol, A. Begoon, W. P. Norris, and P. S. Ramey, *ibid.*, p. 4558; G. Marchese, G. Modena, and F. Naso, *Chem. Comm.*, 1966, 492). This fact does not vitiate the arguments we advance on the stereochemistry, and its mechanistic consequences, of olefin-forming elimination, since the mechanisms and stereochemistry of displacements at unsaturated centres have little in common with those of saturated displacement reactions [see D. E. Jones, R. O. Morris, C. A. Vernon, and R. F. M. White, *J. Chem. Soc.*, 1960, 2349; J. F. Bunnett, 'Theoretical Organic Chemistry' (Kekulé Symposium) Butterworths, London, 1958, p. 144].

⁵ D. V. Banthorpe, 'Elimination Reactions', Elsevier, Amsterdam, 1963, chap. 4.

⁶ G. Köbrich, *Angew. Chem. Internat. Edn.*, 1965, **4**, 49.

⁷ J. Hine, *J. Amer. Chem. Soc.*, 1950, **72**, 2438; J. Hine and A. M. Dowell, *ibid.*, 1954, **76**, 2688.

⁸ J. Hine and J. J. Porter, *J. Amer. Chem. Soc.*, 1957, **79**, 5493; J. Hine and P. B. Langford, *ibid.*, 1957, **79**, 5497.

⁹ J. Hine, R. Wiesboeck, and O. B. Ramsey, *J. Amer. Chem. Soc.*, 1961, **83**, 1222.

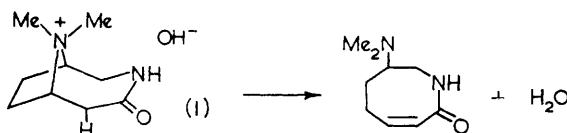
¹⁰ J. Hine, R. Wiesboeck, and R. G. Ghirardelli, *J. Amer. Chem. Soc.*, 1961, **83**, 1219.

¹¹ J. Hine, C. H. Thomas, and S. J. Ehrensens, *J. Amer. Chem. Soc.*, 1955, **77**, 3886; J. Hine, S. J. Ehrensens, and W. H. Brader, *ibid.*, 1956, **78**, 2282.

¹² R. Breslow, *Tetrahedron Letters*, 1964, No. 8, 399.

depending on the relative energetics, rapid hydrogen exchange may be an irrelevant side-reaction to *E2* olefin formation. Hine and his co-workers⁹ anticipated this argument by pointing out that if carbanions are formed, they are most likely to be intermediates in the elimination, since transfer of their free electron pairs should be more effective in promoting olefin formation than should transfer of a partially free electron pair in an *E2* transition state.

Pertaining to this concept is the observation of Paquette and Wise¹³ that pyrolysis of the ammonium hydroxide (1) is accompanied by hydrogen exchange on the carbon α to the carbonyl group. This is not unexpected in view of the presence of the keto-function, but the question remains as to whether the car-



bation is actually involved in the elimination. In the following section we discuss a clear case of an α -keto-group's assisting an *E1cB* reaction, and by inference it appears that the reaction of (1) is also *E1cB*. The poorness of the leaving group^{3,9} would also make this pathway feasible.

Carbanions are formed readily by removing a proton from the 9-position of fluorene and its derivatives as shown by exchange experiments. When a trifluoromethyl substituent is present at the 9-position, the carbanion (generated in alkaline methanol) slowly ejects fluoride ion to form the substituted fulvene.¹⁴ The usual factors [carbanion stability (caused in this case by the aromaticity of the carbanion as well as the electron-withdrawing power of the trifluoromethyl group) and the tightness of binding of the leaving group] are responsible for the *E1cB* mechanism's being preferred.

Iskander and Riad have found that the formation of *p*-nitrostyrene from 2-(*p*-nitrophenethyl)thioacetate ion is accompanied by hydrogen exchange.¹⁵ However, the relative rates of the exchange and elimination reactions are not available and further studies would be desirable before a mechanism is confidently assigned to reactions of this unusual type.

The case of β -benzene hexachloride (1,2,3,4,5,6-hexachlorocyclohexane with all chlorines equatorial) has aroused much interest. Cristol and Fix¹⁶ observed a very small amount of hydrogen exchange accompanying its dehydrochlorination and, contending that this was significant, invoked the *E1cB* mechanism. Their reaction scheme involved the rate-determining formation of a carbanion which inverted its configuration to that of the δ -isomer carbanion more rapidly than it abstracted a proton from the solvent. The δ -carbanion, after reprotona-

¹³ L. A. Paquette and L. D. Wise, *J. Org. Chem.*, 1965, 30, 228.

¹⁴ A. Streitwieser, A. P. Marchand, and A. H. Pudjaatmaka, *J. Amer. Chem. Soc.*, 1967, 89, 693.

¹⁵ Y. Iskander and Y. Riad, *J. Chem. Soc.*, 1961, 223.

¹⁶ S. J. Cristol and D. D. Fix, *J. Amer. Chem. Soc.*, 1953, 75, 2647.

tion, then could react by *E2* elimination to form the products (a mixture of trichlorobenzenes, with the 1,2,4-isomer predominating) more rapidly than the β -isomer, for stereochemical or conformational reasons.^{17,18} As pointed out by Cram,¹⁹ this mechanism requires that the products contain deuterium when the reaction is run in a deuterated medium, but subsequent investigations have shown that such deuteration is insignificant.²⁰ Thus the mechanism can be only *E2* or irreversible *E1cB*.

Isotopic demonstrations of reversible carbanion formation in the course of elimination are rare. However, several substrates with structural features considered favorable for carbanionic elimination may have failed the hydrogen exchange test for the reason that under the conditions of alkalinity employed in the reaction, the inequality $k_{-1}[\text{BH}^+] > k_2$ did not apply.

Base Catalysis

Although elimination reactions are not base-catalysed in the true sense of the words, they adhere to rate laws consistent with recognised classes of base catalysis. The kinetics of base-catalysed reactions have been fully discussed by Bell²¹ but we shall consider them from the point of view of eqn. (1). Let us assume that a carbanionic elimination is proceeding under pseudo-first-order conditions (observed rate coefficient k_ψ) in a B-BH⁺ buffer system. In the pre-equilibrium case, $k_{-1}[\text{BH}^+] \gg k_2$, so k_ψ is given by eqn. (2) and changes of

$$k_\psi = \frac{k_1 k_2 [\text{B}]}{k_{-1} [\text{BH}^+]} \quad (2)$$

base concentration at constant buffer ratio should have no effect on k_ψ . This is specific base catalysis and reversible protonation of the carbanion should be observable. In the other extreme case, $k_{-1}[\text{BH}^+] \ll k_2$ and we obtain eqn. (3),

$$k_\psi = k_1 [\text{B}] \quad (3)$$

so k_ψ is linearly dependent on base concentration at constant buffer ratio and general base catalysis is observed. As buffer concentration is increased at constant ratio so that the kinetics change from those given by eqn. (3) to those of eqn. (2), the situation depicted in the Figure should result.

On the other hand, bimolecular reaction should be general base-catalysed throughout the range of buffer concentrations at a given pH so, in theory at least, we have a kinetic criterion of mechanism. There is the complication that a general base-catalysed reaction may exhibit kinetics qualitatively consistent with specific base catalysis if the catalytic efficiency of the lyate ion is much greater than that of any other base present, as in the *E2* reaction of DDT with benzenethiolate in methanol²² or if the base is strong enough to produce a

¹⁷ E. D. Hughes, C. K. Ingold, and R. A. Pasternak, *J. Chem. Soc.*, 1953, 3832.

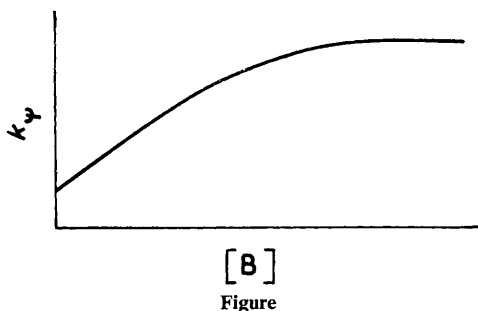
¹⁸ S. J. Cristol, N. L. Hause, and J. S. Meek, *J. Amer. Chem. Soc.*, 1951, 73, 674.

¹⁹ D. J. Cram, 'Steric Effects in Organic Chemistry', ed. M. S. Newman, Wiley, New York, 1956, p. 321.

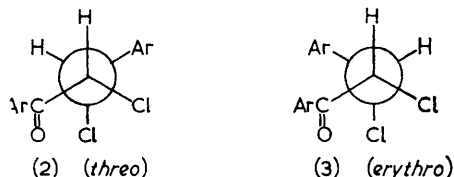
²⁰ J. Hine, R. D. Weimer, P. B. Langford, and O. B. Ramsey, *J. Amer. Chem. Soc.*, 1963, 85, 3984; 1966, 88, 5522.

²¹ R. P. Bell, 'The Proton in Chemistry', Cornell University Press, Ithaca, New York, 1959, p. 134.

kinetically significant concentration of lyate ions, as when phenoxides are used as bases in $E2$ reactions.^{22,23}



The dehydrochlorinations of the diastereoisomeric 4,4'-dichlorochalcone dichlorides (2 and 3; Ar = $p\text{-Cl-C}_6\text{H}_4$) are not stereospecific.²⁴ The *threo* dichloride yields chiefly the *trans* olefin as expected for a 'trans' elimination through an *anti*-periplanar transition state (see section on stereochemistry) while the *erythro* substrate gives a 2 : 1 mixture of the *trans*- and *cis*-olefins. This in itself is not sufficient evidence for the formation of a carbanion with sufficient lifetime to permit partial rotation about the central carbon-carbon bond, but it was also



shown that the kinetics of the reactions in buffered ethanolic solutions were consistent with a refined form of eqn. (1). A clear demonstration of the carbanion mechanism was thus constituted. Other halogenochalcones eliminate in a non-stereospecific fashion²⁵ although some reactions of this type, reported by Southwick *et al.*,²⁶ are not direct eliminations.

The decomposition of the Michael adduct of 4-nitrochalcone and malononitrile in neutral and acidic methanol exhibits kinetics that are consistent with a carbanion mechanism.²⁷ Similar results for the decomposition of 1,1,1,3-tetranitro-2-phenylpropane have been reported by Hine and Kaplan²⁸ and again the $E1cB$ mechanism was invoked.

Related to mechanisms of base catalysis are the basicity functions (H_-) of

²² B. D. England and D. J. McLennan, *J. Chem. Soc. (B)*, 1966, 696.

²³ R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1964, 5.

²⁴ T. I. Crowell, A. A. Wall, R. T. Kemp, and R. E. Lutz, *J. Amer. Chem. Soc.*, 1963, **85**, 2521.

²⁵ R. E. Lutz, D. F. Hinckley, and R. H. Jordan, *J. Amer. Chem. Soc.*, 1951, **73**, 4647.

²⁶ P. L. Southwick, A. K. Colter, R. J. Owellen, and Y.-C. Lee, *J. Amer. Chem. Soc.*, 1962, **84**, 4299.

²⁷ S. Patai, S. Weinstein, and Z. Rappoport, *J. Chem. Soc.*, 1962, 1741.

²⁸ J. Hine and L. A. Kaplan, *J. Amer. Chem. Soc.*, 1960, **82**, 2915.

alkaline solutions, which are analogous to the Hammett acidity functions (H_0). Ridd and More O'Ferrall²⁹ have obtained H_- values for concentrated methanolic solutions of sodium methoxide and have found that $\log k_{\psi}$ for the hydrolysis of chloroform is proportional to the H_- value of the medium. This was expected since proton transfer in this carbanionic α -elimination is under thermodynamic control, and rates of such specific base-catalysed reactions should correlate with H_- .²⁹ On the other hand, the rates of the *E2* dehydrochlorination of 2-phenethyl chloride and 1-chloro-3,3-dimethylbutane (general base-catalysed reactions) were proportional to the base concentrations and not to the H_- values of the alkaline solutions. This mechanistic criterion is not widely applicable at present as H_- scales have been established for only a few solutions. In any case, the same objections that have been raised against drawing mechanistic conclusions from H_0 correlations³⁰ may apply to the use of H_- .

The catalytic constants (k) of *constitutionally related* bases reacting by general base catalysis with a given substrate can be related to their base strengths (K_b) by the Brønsted equation (4), in which the β parameter, which normally has values

$$\log k = \beta \log K_b + \text{const.} \quad (4)$$

between zero and unity, is usually taken as a measure of the degree of transfer of the proton from the substrate to the base in the transition state.³¹ If an irreversible type of carbanion mechanism (general base-catalysed) in which the transition state resembles the carbanion, is operative, β should be close to unity, and should ideally be unity if a pre-equilibrium type of *E1cB* reaction occurs, as rate constants of specific base-catalysed reactions are directly proportional to the basicity constants of the attacking bases.³² These predictions await experimental verification in so far as elimination reactions are concerned.

Brønsted exponents have recently been used to diagnose the nature of *E2* transition states. It is found that relatively high values of β (0.6–0.9) are associated with carbanion-like transition states, while lower β parameters (0.2–0.4) result when an *E2* transition state has partial carbonium-ion character.^{22,23,33}

Isotope Effects

A. Deuterium Isotope Effects.—The deuterium isotope effect (k_H/k_D) of a three-centre proton transfer should be the theoretical maximum (about seven at room temperature in the absence of tunnelling) when the donor and acceptor molecules exert equal control over the proton in the transition state.³⁴ Several *E2* reactions which probably pass through central-type transition states exhibit this maximum isotope effect.³⁵ If the character of the transition state is shifted

²⁹ J. H. Ridd and R. More O'Ferrall, *J. Chem. Soc.*, 1960, 5030, 5035.

³⁰ J. F. Bunnett, *J. Amer. Chem. Soc.*, 1961, **83**, 4956, 4968, 4973, 4978.

³¹ J. F. Bunnett, *Ann. Rev. Phys. Chem.*, 1963, **14**, 271.

³² R. P. Bell, ref. 21, ch. 10.

³³ D. J. McLennan, *J. Chem. Soc. (B)*, 1966, 705, 709.

³⁴ F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265.

³⁵ (a) V. J. Shiner, *J. Amer. Chem. Soc.*, 1952, **74**, 5285; (b) V. J. Shiner and M. L. Smith, *J. Amer. Chem. Soc.*, 1961, **83**, 593; (c) W. H. Saunders and D. H. Edison, *J. Amer. Chem. Soc.*, 1960, **82**, 138.

towards the carbanion or carbonium ion extremes the isotope effect should decrease and should be at or near unity if proton transfer is either practically complete or has hardly commenced when the transition state is attained, as in the *E1cB* and *E1* mechanisms respectively. A low isotope effect should also be observed when the pre-equilibrium carbanion mechanism is operative, for a β -deuterated substrate will exchange most of its deuterium for hydrogen from a protic solvent before olefin formation becomes appreciable.

Measurement of the deuterium isotope effect has enabled the irreversible-type carbanion mechanism to be identified as the pathway of the dehydrofluorination of 1,1,1-trifluoro-2-methyl-3-phenyl propane in alkaline alcoholic solution.³⁶ The value of 1.2 is the lowest yet reported for an olefin-forming elimination. The pre-equilibrium mechanism is invalidated by the lack of β -hydrogen exchange and the fact that optically active substrate can be recovered unracemised after partial reaction. The isotope effects in the pre-equilibrium carbanionic dehydrofluorination of $\text{CF}_3\cdot\text{CHCl}_2$ and $\text{CF}_3\cdot\text{CHBrCl}$ are 1.26 and 1.41 respectively,¹⁰ and these values are consistent with the assigned mechanism. Eliminations involving expulsion of fluorine from a trifluoromethyl group thus appear to be particularly favourable for the observation of the carbanion mechanism, although the resulting olefins are prone to isomerise³⁶ or suffer addition of solvent.^{10,14,37}

There remains much scope for the measurement of deuterium isotope effects in reactions of doubtful mechanism, some of which we will mention later in the section on stereochemistry.

B. Leaving-group Isotope Effects.—These have not been exploited as much as deuterium isotope effects as mechanistic criteria, and there are only two examples of interest.

The nitrogen isotope effect for elimination from the 2-phenethyltrimethylammonium ion in aqueous alkaline solution is experimentally indistinguishable from unity,³⁸ yet when the medium is alkaline ethanol the isotope effect is about 30% of that expected for complete C–N rupture in the transition state.³⁹ This could mean that the mechanism changes from *E2* to *E1cB* as the base–solvent system is changed from OEt^- – EtOH to OH^- – H_2O , but arguing against this interpretation is the fact that the deuterium isotope effect (3.0) is the same in both alkaline ethanol and 50% aqueous ethanol^{35c} (where the base is largely present as hydroxide⁴⁰). A more likely explanation is that the difference in nitrogen isotope effect is associated with the greater solvation energy to be overcome when the C–N bond is stretched in water. The bimolecular transition state will shift further in the carbanion direction with increasing solvent polarity,^{3,41} with a consequent decrease in the degree of C–N rupture.

³⁶ D. J. Cram and A. S. Wingrove, *J. Amer. Chem. Soc.*, 1964, **86**, 5490.

³⁷ W. T. Miller, E. W. Fager, and P. H. Griswold, *J. Amer. Chem. Soc.*, 1948, **70**, 431.

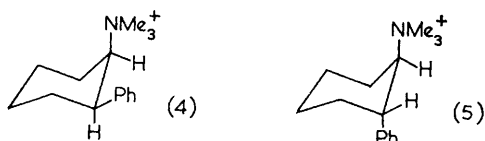
³⁸ S. Ašperger *et al.*, quoted by D. V. Banthorpe and J. H. Ridd, *Proc. Chem. Soc.*, 1963, 225.

³⁹ G. Ayrey, A. N. Bourns, and V. A. Vyas, *Canad. J. Chem.*, 1963, **41**, 1759.

⁴⁰ R. G. Burns and B. D. England, *Tetrahedron Letters*, 1960, No. 24, 1.

⁴¹ D. V. Banthorpe, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 1960, 4056.

The second case involves elimination from the isomeric 2-phenylcyclohexyl-trimethylammonium ions to yield 1-phenylcyclohexene.⁴² *Anti*-Elimination from the *cis* isomer (4) has a nitrogen isotope effect of 1.2% (theoretical maximum for



complete C–N rupture in the transition state would be about 3%) which is indicative of an *E2* mechanism. However, the isotope effect for *syn* elimination from the *trans* isomer (5) is only 0.2%, so it appears that the *anti* elimination is *E2* and the *syn* elimination is *E1cB*. Cristol and Stermitz had earlier assigned these mechanisms on stereochemical grounds.⁴³

Carbon-14 isotope effects can be measured for displacement at both the α - and the β -carbon atom, but as yet only investigations on *E2* reactions have been carried out.⁴⁴

C. Solvent and Secondary Isotope Effects.—Deuterioxide ion in D_2O is a stronger base than hydroxide in water by a factor of about 1.6 at 80°, and Steffa and Thornton⁴⁵ have reported solvent isotope effects [$k(D_2O)/k(H_2O)$] of 1.57 and 1.79 for the respective *E2* reactions of the 2-phenethyl-dimethylsulphonium and -trimethylammonium ions at this temperature. These effects demonstrate the change in *E2* transition state character that has been so amply illustrated in the 2-phenethyl series,^{35c,46} and such a method should be capable of detecting a carbanion mechanism. The solvent isotope effect for the hydrolysis of chloroform⁴⁷ (an α -elimination proceeding *via* a reversibly-formed carbanion) is 1.74, and this figure could be taken as a guide for the *E1cB* reactions of neutral substrates.

A secondary (α) deuterium isotope effect of unity is expected for a carbanion mechanism, but since elimination from the 2-phenethyl-dimethylsulphonium ion, a known *E2* reaction, has an α -isotope effect of 1.00,⁴⁸ this particular criterion holds little promise.

The Hammett Equation

Rates of elimination of substrates bearing suitably substituted α - or β -bound phenyl groups can be correlated by the Hammett equation. For β -bound aryl

⁴² G. Ayrey, E. Buncel, and A. N. Bourns, *Proc. Chem. Soc.*, 1961, 458.

⁴³ S. J. Cristol and F. R. Stermitz, *J. Amer. Chem. Soc.*, 1960, **82**, 4962.

⁴⁴ H. Simon and G. Müllhofer, *Pure Appl. Chem.*, 1964, **8**, 385.

⁴⁵ L. Steffa and E. R. Thornton, *J. Amer. Chem. Soc.*, 1963, **85**, 2680.

⁴⁶ W. H. Saunders and R. A. Williams, *J. Amer. Chem. Soc.*, 1957, **79**, 3712, C. H. DePuy and D. H. Froemsdorf, *ibid.*, 1957, **79**, 3710, C. H. DePuy and C. A. Bishop, *ibid.*, 1960, **82**, 2532, 2535.

⁴⁷ J. R. Jones, *Trans. Faraday Soc.*, 1965, **61**, 95.

⁴⁸ S. Ašperger, N. Ilakovac, and D. Pavlović, *J. Amer. Chem. Soc.*, 1961, **83**, 5032.

groups the value of the reaction parameter ρ increases as structural and environmental conditions are changed so as to shift $E2$ transition states in the $E1cB$ direction.⁴⁶ Thus a high positive value of ρ is expected to obtain for a carbanionic elimination, since negative charge density on the β -carbon atom in the transition state will be at a maximum.

The question of how high a ρ value to expect for a $E1cB$ reaction is in doubt. DePuy *et al.*⁴⁹ suggested that the value of 5.0, obtained from rates of carbanionic polymerisation, be used as a guide, and while this seems reasonable, a model process more similar to elimination reactions would be desirable.

Stereochemistry of Elimination Reactions

If it is accepted that all $E2$ reactions follow an *anti* ('*trans*')* stereochemical course, then any elimination proceeding with different stereochemistry (*e.g.*, *syn*, or '*cis*' elimination) must necessarily have a different mechanism, and the carbanion mechanism is most frequently cited in this regard. It is the purpose of this section to examine critically the empirical and theoretical basis of the above assumption. In doing so, we will show that it is only partially correct, by presenting evidence in favour of the availability of a *syn*-stereochemical course to $E2$ reactions, which thereby removes the necessity of suggesting another (*e.g.*, carbanion) mechanism for reactions that are not *anti*-stereospecific.

First based on experimental observations,⁵⁰ the ' $E2$ Rule' has recently been rationalised on the basis of a conceptual mechanistic dissection⁵¹ and by molecular orbital descriptions and calculations.⁵² It is clear that in an $E2$ transition state, the partial bonds joining the β -hydrogen and the leaving group to the central carbons should be as nearly coplanar as possible in order that p -orbital overlap to form the developing π -bond be maximised, but this simple consideration leaves the question of *anti* against *syn* coplanarity open. In a recent treatment, *anti* elimination is justified by a consideration of the magnitude of the resonance integral between the atoms or groups whose departure effects double-bond formation.⁵³

The experimental evidence for the ' $E2$ Rule' usually involves the fact that eliminations from a suitable diastereoisomeric pair are *anti*-stereospecific or that the formation of 1-R-cycloalkene by *anti* elimination of HX from *cis*-1-R-2-X-cycloalkane is faster than the corresponding *syn* elimination from the *trans* isomer.

In the acyclic case, *anti* elimination can proceed through as many staggered

*We prefer to discuss the steric relationships of groups across a single bond in terms of the nomenclature of W. Klyne and V. Prelog, *Experientia*, 1960, 16, 521, and to reserve the *cis-trans* nomenclature for cases of geometric isomerism.

⁴⁹ C. H. DePuy, G. F. Morris, J. S. Smith, and R. J. Smat, *J. Amer. Chem. Soc.*, 1965, 87, 2421.

⁵⁰ C. K. Ingold, ref. 1, p. 467; D. J. Cram, ref. 19, chap. 6.

⁵¹ C. K. Ingold, *Proc. Chem. Soc.*, 1962, 265.

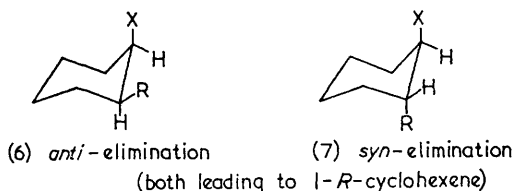
⁵² G. H. Stewart and H. Eyring, *J. Chem. Educ.*, 1958, 35, 550; K. Fukui and H. Fujimoto, *Tetrahedron Letters*, 1965, No. 48, 4303.

⁵³ E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis', Interscience Publishers, New York, 1965, p. 482.

(low-energy) conformations of the initial and transition states as there are hydrogens on the β -carbon atom, but for *syn* elimination, an eclipsed (higher energy) conformation must lie on the reaction co-ordinate. If we take the 3 kcal./mole potential barrier to rotation of ethane as the minimum difference in energy between the *anti*-periplanar and *syn*-periplanar transition states for elimination from a substrate where *anti* elimination will produce one olefin and *syn* elimination another, we find that the former reaction will be favoured by a rate factor of at least 160. In other words, without having made any assumptions regarding stereochemical rate preferences in elimination, we have calculated that conformational factors will cause the product mixture to contain 99.4% of the olefin arising from *anti* elimination. More sensitive techniques than those commonly used in the past would be necessary to detect the minor product.

It will be noted that the foregoing only applies to fully concerted *E2* reactions, and that alternative activation processes and transition-state conformations may be available when either *E1*-like or *E1cB*-like transition states are involved.⁵¹

We turn from product comparisons in the acyclic case to the rate determinations that have demonstrated the preference for *anti* elimination from alicyclic compounds. For cyclohexanes, it is known that the leaving group must be axial for easy *anti* elimination to occur,⁵⁴ and if by analogy we assume that the leaving group in a *syn* elimination must also be axial, we find that *anti* elimination is diaxial and *syn* elimination is axial-equatorial.* The two initial state conformations for reaction are thus (6) and (7) respectively, in which R is a hydrogen-activating group (e.g., Ar, ArSO₂). It can be seen immediately that *syn* elimination from the *trans* isomer (7) will be comparatively unfavorable



because of the necessity of having two bulky groups in the axial positions in the reactive conformation, which will thus be sparsely populated. Again a rough calculation is informative. If we assume that both the above conformations eliminate HX at the *same* rate, that eliminations from the conformations with equatorial X can be neglected, and that the difference in free energy between (6) and (7) is 3.5 kcal./mole (reasonable for large R and X), we find that the measured rate of *anti* elimination from the *cis* isomer is about 370 times greater

*Recent work in a conformationally frozen 2-*p*-tolyl sulphonylcyclohexyl toluene-*p*-sulphonate system has shown that the leaving group in a *syn* elimination indeed prefers the axial orientation for departure (W. M. Jones, T. G. Squires, and M. Lynn, *J. Amer. Chem. Soc.*, 1967, **89**, 318). No further evidence supporting the operation of the *E1cB* mechanism can be adduced from these authors' results (cf. refs. 56, 57, 59, and 60).

⁵⁴ D. H. R. Barton, *J. Chem. Soc.*, 1953, 1027.

than that of *syn* elimination from the *trans* isomer. This observed rate ratio is not a consequence of the inherent preference for *anti* elimination. It arises out of differences in the position of conformational equilibria. Banthorpe⁵⁵ has considered this matter from a slightly different viewpoint, but the same conclusion can be drawn from his illustrative data, namely, that the observed preference for *anti* elimination may be wholly or partly an artefact arising out of initial-state conformational differences. *syn*-Periplanar transition states for a cyclohexyl *syn* elimination are available only when boat-form conformations are attainable, and the even greater energy of these can further accentuate the apparent preference for *anti* elimination. (See N. O. Brace, *J. Amer. Chem. Soc.*, 1964, **86**, 2428.)

Implicit in the above is the assumption that *E2 syn* elimination is possible, and we now cite evidence to that effect. Deuterium isotope effect and Hammett studies by DePuy and his co-workers⁴⁹ have shown that the formation of 1-phenylcyclopentene from *cis*- and *trans*-2-phenylcyclopentyl toluene-*p*-sulphonates (by *anti* and *syn* eliminations respectively) follows the *E2* mechanism. The important point was that k_{anti}/k_{syn} had the low value of 14, whereas with the cyclohexyl analogues (6 and 7; R = Ph, X = OTs) this kinetic preference for *anti* elimination was greater than 10,000. The difference, which appears in other cyclopentyl-cyclohexyl reaction systems,⁵⁶ has been rationalised in terms of *E2* elimination rates' being at a maximum when the dihedral angle between the H-C and C-X bonds is either 180° (*anti* elimination) or 0° (*syn*-periplanar elimination), and decreasing to a minimum as the angle approaches 90°. The dihedral angle in cyclopentyl *syn* eliminations is clearly less than in the corresponding cyclohexyl cases, thus affording a greater chance for partial π -bond formation to occur without undue torsional strain. When neutral bases are used, there is also an electrostatic contribution to the preference for cyclopentyl *syn* elimination.^{56b}

It has already been mentioned that when the leaving group is NMe_3^+ (6 and 7; R = Ph, X = NMe_3^+) the *E1cB* mechanism apparently prevails in the *syn* elimination while the *anti* elimination is *E2*.^{42,43} This is not necessarily a general result since the positively charged leaving group will be more able to stabilise carbanionic charge than will a neutral atom or group.

When the arylsulphonyl group is used to activate the β -proton (6 and 7; R = ArSO_2 , X = OTs) the situation is unchanged, and the preference for *anti* elimination is again less strong with the corresponding cyclopentyl compounds.⁵⁶ The pre-equilibrium carbanion mechanism was ruled out by the finding of general base catalysis,^{56b} and rates of carbanion formation from the cyclopentyl compounds were shown to be too slow to account for the *syn* elimination,⁵⁷ which must therefore be *E2*. When trimethylamine was used as base, stereochemical preference was almost completely absent from the cyclopentyl series.^{56b}

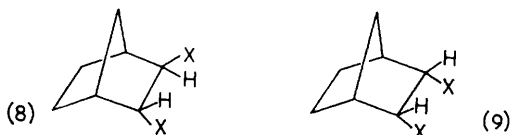
⁵⁵ D. V. Banthorpe, ref. 5, p. 90.

⁵⁶ (a) J. Weinstock, R. G. Pearson, and F. G. Bordwell, *J. Amer. Chem. Soc.*, 1956, **78**, 3468; (b) *J. Amer. Chem. Soc.*, 1956, **78**, 3472.

⁵⁷ J. Weinstock, J. L. Bernoulli, and R. G. Pearson, *J. Amer. Chem. Soc.*, 1958, **80**, 4961.

Hine and Ramsey, using a Taft equation⁵⁸ approach, have shown indirectly that the rates of carbanion formation and *syn* elimination from the cyclohexyl *trans* isomer are about equal,⁵⁹ and have thereby secured proof of the carbanion mechanism, albeit from a three-point linear free-energy plot. The corresponding *trans*-chloride is about as reactive in *syn* elimination as the sulphonate,⁶⁰ and while this is difficult to understand in terms of an *E2* mechanism, where secondary sulphonates are invariably more reactive than halides, the *E1cB* mechanism affords a ready explanation since the activation step involves proton ionisation, and OTs and Cl have similar electron-withdrawing powers.⁵⁹ However, the relative rates of displacement of halide and sulphonate ions are variable, and there are aspects of sulphonate eliminations that are not well understood.⁶¹

Turning now to the 2,3-dihalogenonorbornanes, we find that *syn* elimination from the *trans*-dihalides (8; X = Hal) is *faster* than *anti* elimination from the *endo-cis* isomers (9; X = Hal).^{62,63} Measurements of deuterium isotope effects show that the *E2* mechanism prevails,⁶³ in contradiction of an earlier suggestion



of the carbanion mechanism.⁶² Removal of *exo* groups in the *syn* elimination is the preferred stereochemical course,⁶³ and the tentative explanation is in terms of steric effects. DePuy's hypothesis explains the unusual steric preference nicely, as coplanarity can be achieved in the transition state for *syn* elimination, but the geometric rigidity of the system prevents this in the *anti* dehydrohalogenation.

The carbanion mechanism has also been invoked to explain the same reactivity order, *syn* > *anti*, in the dehydrochlorination of the 11,12-dichloro-11,12-dihydro-9,10-ethanoanthracenes⁶⁴ (10 and 11) but the necessary tests to confirm this have not been performed. The effect of substituting an acid-strengthening *p*-tolylsulphonyl group for one of the chlorines is to increase the rates of dehydrochlorination about a million-fold and to cause *anti* elimination to predominate by a small rate factor.⁶⁴ This is intelligible in terms of the carbanion

⁵⁸ R. W. Taft 'Steric Effects in Organic Chemistry', ed. M. S. Newman, Wiley, New York, 1956, ch. 13.

⁵⁹ J. Hine and O. B. Ramsey, *J. Amer. Chem. Soc.*, 1962, **84**, 973.

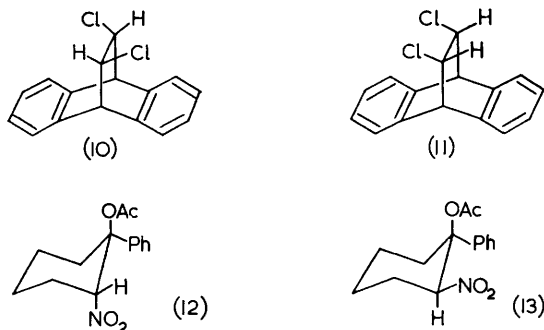
⁶⁰ H. L. Goring, D. I. Relyea, and K. L. Howe, *J. Amer. Chem. Soc.*, 1957, **79**, 2502.

⁶¹ (a) H. M. R. Hoffmann, *J. Chem. Soc.*, 1965, 6753, 6762; (b) D. H. Froemdsdorf, W. Dowd, and K. E. Leimer, *J. Amer. Chem. Soc.*, 1966, **88**, 2345; J. F. Bunnett and R. A. Bartsch, unpublished results.

⁶² S. J. Cristol and E. F. Hoegger, *J. Amer. Chem. Soc.*, 1957, **79**, 3438.

⁶³ N. A. LeBel, P. D. Beirne, E. R. Karger, J. C. Powers, and P. M. Subramanian, *J. Amer. Chem. Soc.*, 1963, **85**, 3199; N. A. LeBel, P. D. Beirne, and P. M. Subramanian, *ibid.*, 1964, **86**, 4144; H. Kwart, T. Takeshita, and J. L. Nyce, *ibid.*, p. 2606.

⁶⁴ S. J. Cristol and N. L. Hause, *J. Amer. Chem. Soc.*, 1952, **74**, 2193; S. J. Cristol and R. P. Arganbright, *ibid.*, 1957, **79**, 3441.



mechanism as discussed by Cristol and his co-workers, but an *E2* explanation is also available. The substituent could cause an *E2* transition state to shift in the *E1cB* direction, where the bond changes are relatively uncoupled, and this may result in the stereochemical consequences of geometric rigidity being overcome. If the mechanism is in fact *E2*, DePuy's hypothesis receives further confirmation.

Bimolecular *syn* elimination has been suggested in order to explain apparently anomalous *cis:trans* olefin ratios in the reactions of secondary arenesulphonates⁶⁵ and 'onium salts.⁶⁶ Other *syn* eliminations recently shown to be operative in the reactions of cycloalkyl 'onium salts⁶⁷ could, from the pattern of results, very well be caused by the incursion of an α' - β (ylide)⁶⁸ mechanism,⁶⁹ although no elimination reaction in alkaline solution has yet been shown to proceed by this mechanism.

There is also one example of *syn* elimination being faster than *anti* elimination in a conformationally mobile system. Bordwell, Arnold, and Biranowski⁷⁰ have reported that removal of acetic acid from compound (12) by a *syn*-clinal elimination (60° dihedral angle) is 3.5 times faster than *anti* elimination (180° dihedral angle) from its isomer (13) when piperidine is used as base in an ethanol-chloroform solvent. This fact is inexplicable in terms of the *E2* mechanism as neither conformational considerations nor DePuy's hypothesis can accommodate it. Using kinetic parameters, Hammett reaction constants, and the effects of 4,4-dimethyl substituents as supplementary evidence, Bordwell and his co-workers invoked the *E1cB* mechanism, noting that the strongly electron-withdrawing nitro-group would facilitate this. At first sight, the deuterium isotope effect for elimination from both compounds (4-9) seems to be too high

⁶⁵ C. H. Snyder and A. R. Soto, *Tetrahedron Letters*, 1965, No. 37, 3261. For difficulties in interpreting product results from arenesulphonate eliminations in dimethylsulphoxide, see ref. 61b.

⁶⁶ J. Zavada and J. Sicher, *Proc. Chem. Soc.*, 1963, 96; *Coll. Czech. Chem. Comm.*, 1965, 30, 438.

⁶⁷ J. Sicher, J. Závada, and J. Krupička, *Tetrahedron Letters*, 1966, No. 16, 1619; J. Závada, M. Svoboda, and J. Sicher, *ibid.*, 1966, No. 16, 1627.

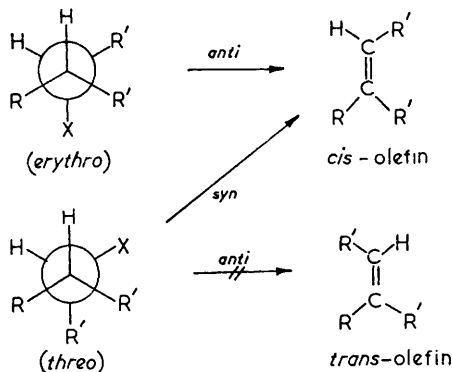
⁶⁸ D. V. Banthorpe, ref. 5, p. 101.

⁶⁹ J. F. Bunnett, personal communication.

⁷⁰ F. G. Bordwell, R. L. Arnold, and J. B. Biranowski, *J. Org. Chem.*, 1963, 28, 2496.

for carbanionic elimination, but Lewis has found that such isotope effects in the formation of carbanions by pyridine-catalysed deprotonation of nitroalkanes can be as high as 25.⁷¹ This is attributed to a proton tunneling effect.

We now consider so-called stereoconvergent²⁶ eliminations, in which a pair of diastereoisomers eliminate, one necessarily by a *syn* elimination, to give the same olefin, as illustrated in Scheme 4. Cram, Greene, and DePuy have discovered such a reaction in the 1,2-diphenyl-1-X-propane system (R = Me; R' = Ph) where in the medium t-butoxide-t-butyl alcohol, the trimethylammonium salts (X = NMe₃⁺), both yield the *trans*-olefin (their scheme is



Scheme 4

opposite to that shown in our Scheme 4) and at virtually identical rates.⁷² As the starting materials are of approximately equal stability,⁷³ the transition states must be of comparable energy, making the carbanion mechanism, also favoured by structural and medium features, a strong possibility. Whether the carbanion in the overall *syn* elimination is formed in a *syn*-stereospecific step, or whether the proton *anti* to the leaving group is removed, to be followed by rotation, is not known. When ethoxide in ethanol is the base, *anti*-stereospecificity is restored and the *threo*-ion becomes 57 times more reactive than the *erythro* as a result of the *E2* transition state's shifting towards the central region, where phenyl eclipsing effects are important. The reactions in t-butyl alcohol warrant further investigation, and studies of isotope and phenyl-substituent effects could prove fruitful.

Cristol and Pappas⁷⁴ report that the *threo*- and *erythro*-chlorides (R = ArSO₂, R' = Ph, X = Cl in Scheme 4) both yield the *cis*-olefin on dehydrochlorination, with *anti* elimination from the *erythro*-chloride being much faster than *syn* elimination from the *threo*-substrate. This could be a case of *E2 anti* elimination

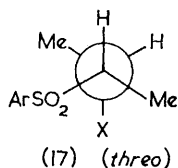
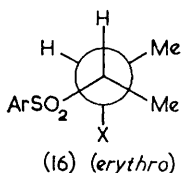
⁷¹ E. S. Lewis and J. D. Allen, *J. Amer. Chem. Soc.*, 1964, **86**, 2022; L. Funderburk and E. S. Lewis, *ibid.*, 1964, **86**, 2531.

⁷² D. J. Cram, F. D. Greene, and C. H. DePuy, *J. Amer. Chem. Soc.*, 1956, **78**, 790.

⁷³ F. A. Abd Elahafez and D. J. Cram, *J. Amer. Chem. Soc.*, 1953, **75**, 339.

⁷⁴ S. J. Cristol and P. Pappas, *J. Org. Chem.*, 1963, **28**, 2066.

known to retain their configuration,⁷⁷ and if formed in these eliminations would be expected to decompose by an *anti*-stereospecific pathway.



Conclusion

It can be seen that clear examples of the carbanion mechanism are rare. Of the criteria we have discussed, stereochemistry of elimination is, at present, the least reliable, since there is now evidence that *E2* reactions are not necessarily *anti* stereospecific. This means that it no longer suffices to conclude, from stereochemical findings alone, that a mechanism other than *E2* is operative when *anti* elimination does not prevail. Many of the reactions that proceed with unusual stereochemistry, and to which the carbanion mechanism has consequently been assigned, must therefore be re-examined by use of other available criteria before the mechanistic question can be considered solved.

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⁷⁷ D. J. Cram, D. A. Scott, and W. D. Neilsen, *J. Amer. Chem. Soc.*, 1961, **83**, 3696.