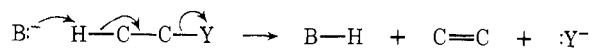# How Common Are Base-Initiated, Concerted 1,2 Eliminations?

FREDERICK G. BORDWELL

Department of Chemistry, Northwestern University, Evanston, Illinois   60201

The concept of base-initiated β-elimination reactions as constituting a general mechanistic class occurring by a single, concerted act which could be represented as

was originated by Ingold in 1927[1] and elaborated by Hughes and Ingold in their general summary of the mechanisms of elimination reactions.[2]

The well-known stereochemical preference of anti over syn elimination[3] was at first explained by the formation of a carbanion intermediate of exceedingly short lifetime which initiated an attack with inversion on the adjacent carbon atom,[4] or by assuming a slowing of syn elimination caused by repulsions between the attacking base and the leaving group.[5]   (A representation of the Winstein–Pressman–Young mechanism using current symbolism is shown.)   However, the observation of a
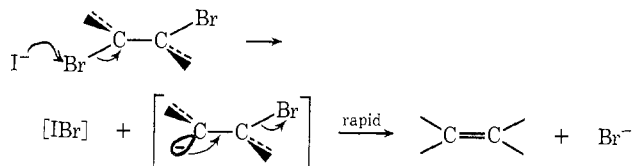
large rate preference for anti over syn elimination for benzene hexachloride isomers (10^3 to 10^4 faster rates and 9.6 to 12.5 kcal/mole lower activation energies) caused Cristol to combine the idea of inversion with Ingold's idea of a one-stage mechanism.   This gave him a "smooth, concerted pathway for anti elimination not available to syn elimination."[6]   A two-stage carbanion mechanism was suggested for syn elimination, and this was later supported by experiments demonstrating a small amount of deuterium exchange.[7]

The concerted E2 mechanism gained additional early support from the demonstration that $C_6H_5CH_2CH_2Br$ recovered after about one half-life from a reaction with NaOEt and EtOD contained no deuterium.[8]   Skell and Hauser considered only two mechanisms to be likely, namely, simultaneous removal of the β hydrogen and bromine atoms (concerted E2) or *preequilibrium* carbanion formation.   Since their experiment ruled out the latter, they felt that it constituted strong evidence for the concerted E2 mechanism.

Simultaneous removal of the β proton and the leaving group Y would require that in a given system the rate of reaction would be accelerated as the β proton becomes more acidic and as the leaving group Y^- becomes less basic.   In agreement with these expectations, the Hammett ρ values in the series $ArCH_2CH_2Y$ are positive ($+2.07$ to $+3.12$), and become more so as the leaving group becomes poorer ($I > Br > OTs > {}^+SMe_2 > F$; rates vary over a range of 26,600).[9]

Results such as those described above have convinced most authors of the ubiquity of the one-stage mechanism for base-initiated alkene-forming eliminations, as may be judged by the following quotations: *"except in a few special substrates, a concerted, rather than a stepwise, process operates"*;[10] "there is no reason to believe that more than a few special structures undergo the two-stage process";[11] "the (carbanion) mechanism does seem very uncommon, though it possibly has a certain range of validity."[12]   Although the universality of the one-stage mechanism has been generally accepted, it has become apparent that the degree of H–C and C–Y bond breaking in the transition state for most (presumably) concerted E2 eliminations cannot be equal, and current practice is to account for structure–reactivity variations in terms of transition states ranging from carbanion-like to carbonium-ion-like (variable E2 transition state theory[9c,13,14]).

For reasons given earlier I have come to question the prevalence and, in many instances, the very existence of heterolytic, one-stage mechanisms wherein as many

Frederick G. Bordwell completed both his bachelor and doctoral studies in chemistry at the University of Minnesota.   During the first part of his career as a faculty member at Northwestern University (1942 to present) he applied the training in physical organic chemistry received in his graduate studies with R. T. Arnold to problems in organic sulfur chemistry which had come to his attention during a postdoctoral year spent with C. M. Suter at Northwestern.   During the past 10 years his research has centered around the kinetic and equilibrium acidities of carbon acids (nitroalkanes, ketones, nitriles, sulfones, sulfoxides, etc.) and mechanistic studies of related reactions.

(1) W. Hanhart and C. K. Ingold, *J. Chem. Soc.*, 997 (1927).

(2) E. D. Hughes and C. K. Ingold, *Trans. Faraday Soc.*, **37**, 657 (1941).

(3) See, *e.g.*, P. Pfeiffer, *Z. Physik. Chem.*, **48**, 40 (1904); P. F. Frankland, *J. Chem. Soc.*, 654 (1912).   In the literature prior to *ca.* 1960 the terms trans and cis were used instead of anti and syn.

(4) S. Winstein, D. Pressman, and W. G. Young, *J. Amer. Chem. Soc.*, **61**, 1645 (1939).

(5) W. Hückel, W. Tappe, and G. Legutke, *Justus Liebigs Ann. Chem.*, **543**, 191 (1940).

(6) (a) S. J. Cristol, *J. Amer. Chem. Soc.*, **69**, 338 (1947); (b) S. J. Cristol, N. L. Hause, and J. S. Meek, *ibid.*, **73**, 674 (1951).

(7) S. J. Cristol and D. D. Fix, *ibid.*, **75**, 2647 (1953); J. Hine, R. D. Weimar, Jr., P. B. Langford, and O. B. Ramsay, *ibid.*, **88**, 5522 (1966).

(8) P. S. Skell and C. R. Hauser, *ibid.*, **67**, 1661 (1945).

(9) (a) C. H. DePuy and D. H. Froemsdorf, *ibid.*, **79**, 3710 (1957); (b) W. H. Saunders, Jr., and R. A. Williams, *ibid.*, **79**, 3712 (1957); (c) see J. Bunnett, *Surv. Progr. Chem.*, **5**, 53 (1969), for a summary and discussion.

(10) E. S. Gould, "Mechanisms and Structure in Organic Chemistry," Holt-Dryden, New York, N. Y., 1959, p 480 (italics are his).

(11) D. V. Banthorpe, "Elimination Reactions," Elsevier, Amsterdam, 1963, p 80.

(12) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, p 654.

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

(14) G. Biale, D. Cook, D. J. Lloyd, A. J. Parker, I. D. R. Stevens, J. Takahashi, and S. Winstein, *ibid.*, **93**, 4735 (1971).

Table I
Mechanistic Classification of Elimination Reactions, $B^- + H\text{-}A\text{-}E\text{-}Y^a$

	Descriptive title	Kinetic order	Symbol[b]	k^H/k^D	Element effect
↑	First-order anion	1st	$(E1)_{anion}$	1.0	Substantial
Extent of H–A bond dissociation increases	Preequilibrium anion ("reversible" anion)	2nd	$(E1cB)_R$	1.0	Substantial
	Preequilibrium ion pair (or tightly solvated anion)	2nd	$(E1cB)_{ip}$	1–2	Substantial
	Second-order anion	2nd	$(E1cB)_I$	2–8	Small
	Concerted	2nd	E2	2–8	Substantial
Extent of E–Y bond dissociation increases ↓	Preequilibrium ion pair (or tightly solvated cation)	2nd	$(E2)_{ip}$	2–5(?)	Substantial
	Ion pair (irreversible)	1st	$(E1)_{ip}$	1.0	Substantial
	Cation	1st	E1	1.0	Substantial

^{a} For classifications of carbanion elimination mechanisms see: (a) D. J. McLennan, *Quart. Rev., Chem. Soc.*, **21**, 490 (1967); (b) Z. Rappoport, *Tetrahedron Lett.*, 3601 (1968); (c) ref 11, pp 78–79; (d) F. G. Bordwell, M. M. Vestling, and K. C. Yee, *J. Amer. Chem. Soc.*, **92**, 5950 (1970). ^{b} Ingold's symbols E1 and E2, where the numerals stand for the number of species undergoing covalency change in the transition state of the rate-limiting step, *excluding solvent*, have been modified to allow for subdivision. R and I stand for "reversible" and "irreversible," and ip stands for ion pair (or tightly solvated ion). The E1cB symbol, which stands for an elimination involving a conjugate base, has also been modified to indicate whether the conjugate base is formed reversibly, irreversibly, or as part of an ion pair. In view of the plethora of symbols required for these mechanistic descriptions it is questionable whether their usage should be encouraged. The author's preference is to use word descriptions except in review articles.

as two bonds are formed and two bonds are broken simultaneously and in concert.[15] In this Account I intend to show that: (a) contrary to general opinion,[10–12] there are a large number of base-initiated alkene-forming eliminations for which two-stage mechanisms appear more attractive than the one-stage mechanism; (b) there is no evidence for a strong driving force wherein bond making aids bond breaking in a one-stage mechanism; (c) rather, there is evidence that two-stage mechanisms are favored energetically over one-stage mechanisms; and (d) when β eliminations are considered as a whole (*i.e.*, those to form C=O, C=N, N=N, N=O, C≡N, and C≡C bonds, as well as those to form C=C bonds) the two-stage mechanism is clearly much more common than the one-stage mechanism.
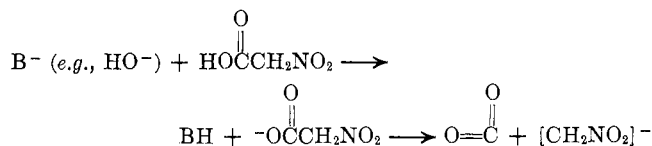
Mechanistic Classification of Elimination Reactions

Good arguments can be made for the existence of three general types of base- and/or solvent-promoted eliminations, namely, anion, concerted, and cation eliminations. The two-stage anion and cation eliminations for H–A–E–Y systems can be subdivided further on the basis of: (a) the extent of H–A or E–Y dissociation, and (b) the degree to which the dissociation is reversible under the conditions of the reaction (Table I). As might be expected, the borderlines between these mechanisms are not sharp, and a decision as to which of two mechanisms is operative is often difficult to make. The response of the various mechanistic classes

to kinetic, isotope, and leaving group probes is indicated in Table I. Additional probes will be mentioned in some of the sections in which the individual mechanisms are discussed.

The discussion of individual mechanisms will be given in terms of a generalized system H–A–E–Y (or H–A=E–Y) where A and E are C, N, or O atoms and Y is a leaving group (Cl, Br, OTs, $^+NMe_3$, OPh, OR, CN, CH_2NO_2, etc.).

First-Order Anion Eliminations, $(E1)_{anion}$. This mechanism will obtain for systems of the type $H\text{-}A_\beta\text{-}E_\alpha\text{-}Y$ which are acidic enough to give substantial (*i.e.*, non-steady-state) concentrations of $^-A\text{-}E\text{-}Y$ anions under the reaction conditions. Loss of carbon dioxide from carboxylate ions containing an appropriate leaving group, as in the synthesis of nitromethane from nitroacetic acid,[16] is a familiar, long-standing example.
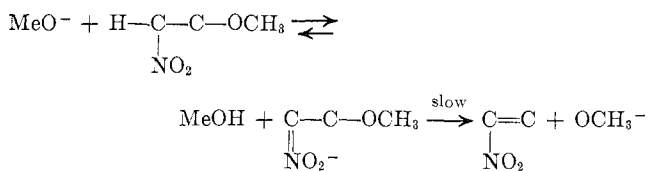
$$B^- \ (e.g., \ HO^-) + HO\overset{O}{\overset{\|}{C}}CH_2NO_2 \longrightarrow$$

$$BH + {}^-O\overset{O}{\overset{\|}{C}}CH_2NO_2 \longrightarrow O{=}\overset{O}{\overset{\|}{C}} + [CH_2NO_2]^-$$

These reactions follow overall first-order kinetics when $\Delta pK = pK_{HB} - pK_{HAEY}$ equals 2 or more. Examples where the β atom is carbon are encountered most often when the β proton is activated by the presence of two electron-withdrawing groups (EWG).[17]

(15) F. G. Bordwell, *Accounts Chem. Res.*, **3**, 281 (1970).

(16) F. C. Whitmore and M. G. Whitmore, "Organic Syntheses," Collect Vol. 1, Wiley, New York, N. Y., 1941, p 401.

(17) Z. Rappoport, *Tetrahedron Lett.*, 3601 (1968); Z. Rappoport and E. Shohamy, *J. Chem. Soc. B*, 2060 (1971).
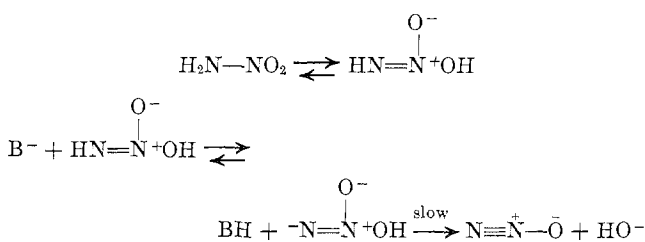
In protic solvents the only *single* EWG strong enough to permit the operation of this mechanism is nitro.[18]

$$MeO^- + H-\underset{\underset{NO_2}{|}}{C}-C-OCH_3 \rightleftharpoons$$

$$MeOH + \underset{\underset{NO_2^-}{||}}{C}-C-OCH_3 \xrightarrow{slow} \underset{\underset{NO_2}{|}}{C}=C + OCH_3^-$$
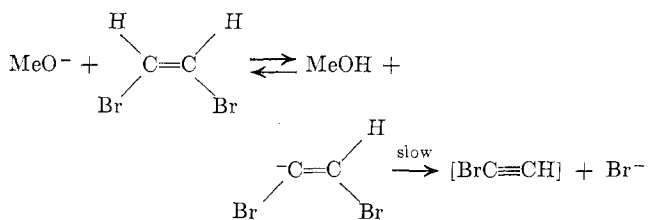
When the $H-C_\beta$ bond is less strongly activated (as by single EWG such as CH_3CO, CN, CH_3SO_2, etc.), stronger base-solvent systems would be required for the operation of this mechanism ($NaNH_2$ in liquid NH_3, $LiNEt_2$ in Et_2O, or CH_3SOCH_2K in Me_2SO should suffice).

Preequilibrium Anion (Reversible Anion), (E1cB)$_R$. This is probably the most common elimination mechanism. It includes most base-initiated eliminations with $H-O-E-Y$, $H-N-E-Y$, and $H-N=E-Y$ systems, which are legion. (Reversals of carbonyl addition reactions generally fall in this class.) Common examples include the reversal of addition of HSO_3^- or HCN to $C=O$, reverse aldol reactions, formation of the $N=C$ bond in oximes, hydrazones, imines, etc., and the base-initiated decomposition of nitramide.

$$H_2N-NO_2 \rightleftharpoons HN=\overset{\overset{O^-}{|}}{N}{}^+OH$$

$$B^- + HN=\overset{\overset{O^-}{|}}{N}{}^+OH \rightleftharpoons$$

$$BH + {}^-N=\overset{\overset{O^-}{|}}{N}{}^+OH \xrightarrow{slow} N=\overset{+}{N}-\overset{-}{O} + HO^-$$

In most of these reactions, assignment to the (E1cB)$_R$ class is unequivocal since the cleavage of H–O and H–N bonds by bases is generally close to the diffusion-controlled limit,[19] and the corresponding base-initiated eliminations are relatively slow. When general acid-base catalysis occurs, however, a concerted mechanism may sometimes obtain.[20]

Assignment of most $H-C=E-Y$ eliminations to this class follows from the demonstration (by deuterium exchange) that this mechanism is operative for the methoxide-initiated anti elimination of HBr from *cis*-1,2-dibromoethylene.[21] It seems safe to assume

$$MeO^- + \overset{H}{\underset{Br}{}}C=C\overset{H}{\underset{Br}{}} \rightleftharpoons MeOH +$$

$${}^-\overset{}{\underset{Br}{}}C=C\overset{H}{\underset{Br}{}} \xrightarrow{slow} [BrC\equiv CH] + Br^-$$

that this mechanism will obtain also in instances where Y is a poorer leaving group than bromine.

Reverse Michael reactions belong to this general class.[12] Here the cleavage of the H–C bond is usually activated by two electron-withdrawing groups, *i.e.*, the $H-C(EWG)_2-C-Y$ system. When activation is by only one EWG the mechanism merges into (E1cB)$_{ip}$ and (E1cB)$_I$. With such $H-C(EWG)-C-Y$ systems the (E1cB)$_R$ mechanism can be detected by deuterium exchange in the substrates prior to or during elimination when Y is a poor leaving group.[22] Rate variations of over 10 powers of 10 have been observed by Crosby and Stirling for NaOEt–EtOH carbanion eliminations in $H-C(EWG)-C-OPh$ systems (EWG = NO_2, Ph_3P^+, Me_2S^+, $MeC=O$, SO_2OEt, $PhSO_2$, $MeSO_2$, CN, CO_2Et, $SO_2N(CH_2Ph)_2$, $PhS=O$, $CONH_2$, $MeS=O$, $CONEt_2$, Me_3N^+, and CO_2^-).[22d]

Preequilibrium Ion Pair (or Tightly Solvated Anion) Eliminations, (E1cB)$_{ip}$. The most clear-cut example of the operation of this mechanism is the Et_3N-initiated elimination of HX from $BrCH=CHBr$ or $ClCH=CHCl$ in DMF.[21b] Here, added $Et_3ND^+X^-$ does not affect the rate or lead to deuterium exchange, but k^H/k^D is near 1.0, and there is a substantial k^{Br}/k^{Cl} leaving group effect.

$$Et_3N + XCH=CHX \underset{DMF}{\rightleftharpoons}$$

$$Et_3\overset{+}{N}H\cdots{}^-CX=CHX \xrightarrow{slow} Et_3\overset{+}{N}H + [XC\equiv CH] + X^-$$

Miller suggests that a comparable mechanism involving a tightly solvated carbanion obtains also for several other systems where low k^H/k^D effects (<2) have been observed, including alkoxide-initiated eliminations on $PhCH(Me)CF_3$, $RCH(Me)CRR'N^+Me_3$, p-$NO_2C_6H_4CH=CHCl$, cycloalkyl-$^+NMe_3$, and $H-C(SO_2Ar)-C-OTs$ systems. The tightly solvated carbanion mechanism involving internal return has been advanced recently for the latter system on other grounds, and has been used to rationalize the stereochemistry.[23]

Second-Order Anion Eliminations, (E1cB)$_I$. Although this mechanism is probably common, it is difficult to distinguish from the concerted mechanism. Since assignment of mechanism to this class rests mainly on indirect evidence a longer discussion will be given.

The carbanion mechanisms discussed up to this point all fit the general pattern

$$B^- + H-\underset{\underset{EWG}{|}}{C}-C-Y \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B-H + {}^-\underset{\underset{EWG}{|}}{C}-C-Y \xrightarrow{k_1} \underset{\underset{EWG}{|}}{C}=C + Y^-$$

As we progress from EWG = NO_2 to weaker electron-withdrawing groups, k_1 decreases and k_{-1} increases. For EWG = NO_2 $k_1 > k_{-1}[BH]$ under most conditions (the pK_a of $H-C-NO_2$ compounds is *ca.* 9 in water and

(18) F. G. Bordwell, M. M. Vestling, and K. C. Yee, *J. Amer. Chem. Soc.*, **92**, 5950 (1970).

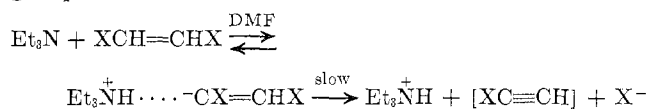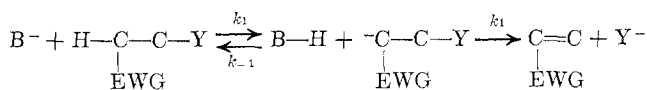(19) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, **3**, 1 (1964).

(20) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, pp 231–242.

(21) (a) S. I. Miller and W. G. Lee, *J. Amer. Chem. Soc.*, **81**, 6313 (1959); (b) W. K. Kwok, W. G. Lee, and S. I. Miller, *ibid.*, **91**, 368 (1969).

(22) (a) J. Hine, R. Wiesbock, and O. B. Ramsay, *ibid.*, **83**, 1222 (1961); (b) L. R. Fedor, *ibid.*, **91**, 908 (1969); (c) R. A. More O'Ferrall and S. Slae, *J. Chem. Soc. B*, 260 (1970); (d) J. Crosby and C. J. M. Stirling, *ibid.*, 671, 679 (1970).

(23) F. G. Bordwell, J. Weinstock, and T. F. Sullivan, *J. Amer. Chem. Soc.*, **93**, 4728 (1971).

ca. 15 in Me$_2$SO), and, when Y is a poor leaving group such as OR, $k_1 \gg k_{-1} \gg k_2$. Mechanism (E1)$_{\text{anion}}$ then obtains; the intermediate anion (nitronate ion) is formed in high concentrations and can be observed spectroscopically.[24] As Y becomes a better leaving group k_2 increases to the point where $k_2 \gg k_{-1}$, and only steady-state concentrations of the intermediate ion are present. Since with EWG = NO$_2$ k_{-1} remains small, no example where both the starting material and the intermediate nitronate ion are present in appreciable concentrations can be realized. In other words, the mechanism passes directly from (E1)$_{\text{anion}}$ to (E1cB)$_{\text{I}}$, without passing through the (E1cB)$_{\text{R}}$ stage (consult Table I). Even the (E1cB)$_{\text{ip}}$ mechanism probably will be by-passed, except perhaps for reactions initiated by weak, uncharged bases in poorly dissociating solvents. For example, as Y is changed from OCH$_3$ to OAc (MeO$^-$ base) we pass directly from the (E1)$_{\text{anion}}$ to the (E1cB)$_{\text{I}}$ mechanism. The principal evidence favoring the latter carbanion mechanism over a concerted E2 mechanism is that the k^H/k^D isotope effect remains the same for the change in leaving groups, and that the syn elimination for Y = OAc is slightly faster than the anti elimination in the cyclohexyl system.[18]

Y = OMe; $k^H/k^D = 7.5$ Y = OAc; $k^H/k^D = 8.0$
Y = OAc; $k^H/k^D = 8.0$
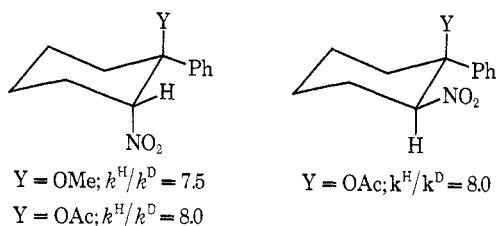
With EWG = RC=O, $k_1 < k_{-1}$ under most conditions (the pK_a of CH$_3$COCH$_3$ is *ca.* 20 in water and *ca.* 24 in Me$_2$SO), and the (E1cB)$_{\text{R}}$ mechanism holds with OCH$_3$ or OPh leaving groups.[22b,d] With OAc as the leaving group the absence of deuterium exchange and the observation of general base catalysis rule out this mechanism:[25] the (E1cB)$_{\text{ip}}$ or (E1cB)$_{\text{I}}$ mechanism now probably obtains.

With EWG = RSO$_2$, $k_1 < k_{-1}$ in all but the most strongly basic media (the pK_a of CH$_3$SO$_2$CH$_3$ is *ca.* 28.5 in Me$_2$SO). Initially formed carbanions will be tightly hydrogen bonded in protic solvents, and internal return is expected to be extensive.[26] It is not surprising, then, that tests for preequilibrium carbanion formation which require exchange with the solvent prior to elimination, such as specific lyate ion catalysis[27] and deuterium exchange,[27b] are negative when a good leaving group (*e.g.*, OTs) is present. Here the mechanism is likely to be (E1cB)$_{\text{ip}}$.[21b,23] The small leaving

group effects observed in certain instances indicate, however, that the (E1cB)$_{\text{I}}$ mechanism may also be operative.[23]

Concerted E2 Eliminations. In ethoxide-initiated eliminations from ArCH$_2$CH$_2$Y systems the presence of a sizable k^H/k^D isotope effect (5–7) *coupled with* a substantial element effect provides convincing evidence that cleavage of both H–C and C–Y bonds has progressed to at least some degree in the transition state.[19] Evidence of a similar nature is available for base-initiated elimination of NO$_2^-$ from C$_6$H$_5$CH$_2$ONO$_2$.[28] The concerted mechanism no doubt obtains also for eliminations from nonactivated primary systems, RCH$_2$CH$_2$Br, although such eliminations compete poorly with S$_N$2 processes when Y is OTs (*e.g.*, 99% ether and 1% alkene are formed at 40° from *n*-C$_{16}$H$_{33}$-CH$_2$CH$_2$OTs and *t*-BuOK–*t*-BuOH[29]).

Base-initiated reactions with many secondary systems, R'CH$_2$CH(R)Y, probably also proceed by concerted mechanisms, although here the mechanism can merge imperceptibly into (E2)$_{\text{ip}}$ or E1 mechanisms as ionization of the C–Y bond is made easier and as the base is made weaker. Note, for example, that strong electron-releasing R groups, such as R$_2$N, RO, or RS, evoke E1 (or S$_N$1) reactions in protic solvents.

Preequilibrium Ion-Pair (or Tightly Solvated Cation) Eliminations, (E2)$_{\text{ip}}$. Winstein's ion-pair mechanism for solvolyses of tertiary halide, and like, substrates now seems firmly established.[30] There is also strong

$$R\text{—}X \rightleftharpoons R^+X^- \rightleftharpoons R^+ \,||X^- \rightleftharpoons R^+ + X^-$$
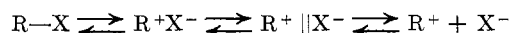
evidence to show that the alkenes formed in these solvolyses arise, at least in part, from attack of the solvent *and* of the "gegenion" on ion pairs (3 or 4).[31] Furthermore, judging from trapping experiments with azide ion, it now appears that even in solvolyses classified as **Lim** according to the Sneen azide reactivity–selectivity probe[32] the reactions with azide ion occur with ion pairs, as well as with the free carbonium ion.[33] It seems reasonable to suppose that lyate ions introduced into such solvolyses will initiate elimination reactions by attack on ion pairs, rather than on the covalent substrate, particularly since ion pairs are undoubtedly *far* better proton donors than are covalent substrates.[34] If the ion pairs are in equilibrium with the covalent substrate, this will lead to a second-order component in the rate expression, *i.e.*, an ion-pair E2 mechanism: (E2)$_{\text{ip}}$.

(24) F. G. Bordwell, K. C. Yee, and A. C. Knipe, *J. Amer. Chem. Soc.*, **92**, 5945 (1970).

(25) L. R. Fedor, *ibid.*, **89**, 4479 (1967).

(26) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, Chapter IV; W. T. Ford and D. J. Cram, *J. Amer. Chem. Soc.*, **90**, 2606, 2612 (1968).

(27) (a) J. Weinstock, R. G. Pearson, and F. G. Bordwell, *ibid.*, **78**, 3473 (1956); (b) W. M. Jones, T. G. Squires, and M. Lynn, *ibid.*, **89**, 318 (1967).

(28) P. J. Smith and A. N. Bourns, *Can. J. Chem.*, **44**, 2553 (1966).

(29) P. Veeravagu, R. T. Arnold, and E. W. Eigenmann, *J. Amer. Chem. Soc.*, **86**, 3072 (1964).

(30) See C. D. Ritchie, "Solute-Solvent Interactions," J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, 1969, Chapter 4, for a detailed discussion and an estimation of rates.

(31) M. Cocivera and S. Winstein, *J. Amer. Chem. Soc.*, **85**, 1702 (1963); D. J. Cram and M. R. V. Sahyun, *ibid.*, **85**, 1257 (1963); P. S. Skell and W. L. Hall, *ibid.*, **85**, 2851 (1963).

(32) R. A. Sneen, J. V. Carter, and P. S. Kay, *ibid.*, **88**, 2594 (1966).
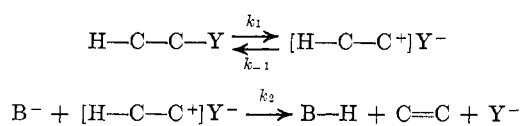
(33) C. D. Ritchie, *ibid.*, **93**, 7324 (1971).

(34) Consider, for example, that a positively charged annular nitrogen atom activates an aromatic ring for deprotonation *via* ylide formation by a factor of over 10^{10} (relative to an uncharged aromatic ring) [see R. A. Olofson, J. M. Landesberg, K. H. Houk, and J. S. Michelman, *ibid.*, **88**, 4265 (1966); J. A. Zoltewicz and L. S. Helmick, *ibid.*, **92**, 7547 (1970)].

$$H—C—C—Y \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [H—C—C^+]Y^-$$

$$B^- + [H—C—C^+]Y^- \xrightarrow{k_2} B—H + C=C + Y^-$$

The $(E2)_{ip}$ mechanism has on occasion been considered to explain the second-order components in the rate expression for tertiary halides, which appear only at high base concentrations. For example, the $(E2)_{ip}$ mechanism for the second-order component appearing at high concentrations of NaOMe in the methanolysis of benzyldimethylcarbinyl chlorides was considered, but it was rejected on the basis of ρ values ($+1$ for the E2 vs. -1.2 for the E1 component) and a slightly larger k^H/k^D isotope effect (2.6 for E2 vs. 1.9 for E1).[9c] It is true that a negative ρ would be expected for formation of the ion pair, but a positive ρ would be expected for the reaction of the ion pair with base. The *overall* ρ might well be positive, then, for the $(E2)_{ip}$ reaction.

Some supporting evidence for the $(E2)_{ip}$ mechanism is provided by a study of the reaction of the tertiary allylic bromide $p\text{-}MeC_6H_4SO_2CH=CHC(Me)_2Br$ (1) with solvents and with nucleophiles.[35] Based on differences in the behavior of 1, as compared to primary halides, in seven different mechanistic probes, it was concluded that the substitution reactions, which predominate with weakly basic nucleophiles such as azide ion, thiocyanate ion, aniline, and thiourea, were occurring by ion-pair S_N2 mechanisms. It follows that the accompanying elimination reactions are probably occurring by ion-pair E2 mechanisms. With more strongly basic nucleophiles, such as piperidine or thiophenoxide ion, 1 gave predominantly elimination products (according to our analysis, 70% $(E2)_{ip}$ and 30% $(S_N2)_{ip}$ with C_6H_5SK in MeOH).[35b]

(1)

(30%) + (49%) + (21%)
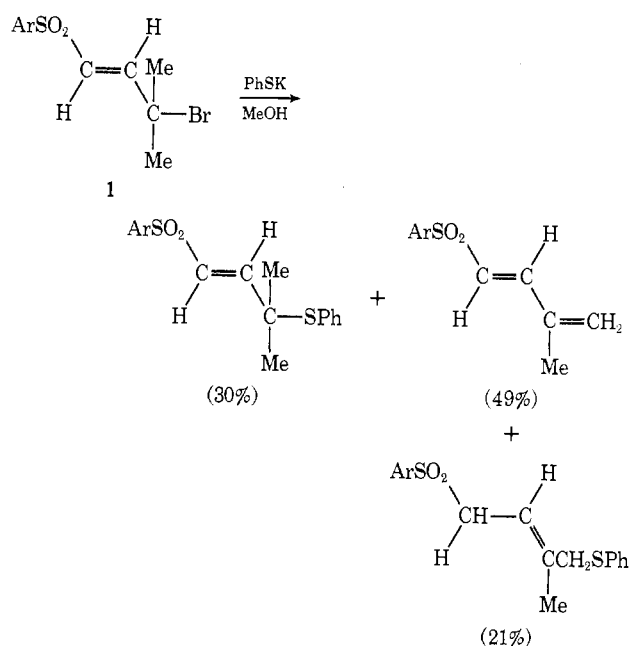
Thiophenoxide ion has recently been shown to be the most reactive of all anions tested in cation–anion com-

bination reactions (over 10^5 better than MeO^-).[36] If we accept the preliminary evidence cited above that thiophenoxide ion also has a strong tendency to deprotonate cations in ion pairs, we can rationalize the remarkable ability of this ion in promoting E2 reactions that has been noted previously and has been the subject of considerable speculation. *Thus, it is reasonable to suppose that the greater ability of $C_6H_5S^-$ (or RS^-) than MeO^- to promote E2 reactions from tert-butyl chloride*[37a,b] *or benzyldimethylcarbinyl chlorides*[37c] *is due to its superior ability to attack the cation in the $(E2)_{ip}$ mechanism.* The importance of the ionizing power of the medium in such reactions is brought out by the observation that the E2 reaction (ion-pair E2, in our opinion) of $C_6H_5CH_2CMe_2Br$ with alkoxide ion is seven times faster with EtONa–EtOH than with t-BuOK–t-BuOH.[38]

The $(E2)_{ip}$ mechanism also accounts for the ability of thiophenoxide ion (or other nucleophiles) to promote E2 reactions in dipolar aprotic solvents.[39] Winstein rationalized the nearly equal ability of nucleophiles such as PhSNa and LiBr to promote substitution and elimination reactions with cis-4-$tert$-butylcyclohexyl tosylate in acetone in terms of a "merged S_N2–E2 mechanism." His suggestion of a common *intermediate* leading to S_N2 and E2 products has been modified to one wherein there is simultaneous bonding in the *transition state* to the β hydrogen atom and α carbon atom.[40] Eck and Bunnett have presented evidence against the merged S_N2–E2 mechanism by showing that the rate of E2 reactions for t-BuMe$_2$CBr in acetone promoted by halide ions is *faster* than for Me_3CBr, despite the greater steric effect.[41] The faster rate is, of course, consistent with the $(E2)_{ip}$ mechanism.

The $(E2)_{ip}$ mechanism is probably operative also with many other tertiary and secondary systems. Sneen and Larsen have shown that, under conditions where the rate of solvolysis of 2-octyl mesylate in aqueous dioxane is nearly independent of $[N_3^-]$, the azide product has an inverted configuration, just as it does for 2-octyl brosylate in a solvent of lesser ionizing power where the rate becomes dependent on $[N_3^-]$.[42] These results appear to be best interpreted in terms of an ion-pair S_N2 mechanism: an $(E2)_{ip}$ mechanism is thereby implicated for the accompanying elimination reactions.[42b] The authors suggest that ion-pair mech-

(35) (a) F. G. Bordwell and T. G. Mecca, *J. Amer. Chem. Soc.*, 94, 2119 (1972); (b) T. G. Mecca, Ph.D. Dissertation, Northwestern University, 1971.

(36) C. D. Ritchie and P. O. I. Virtanen, unpublished results reported at the Linear Free Energy Conference, Tallahassee, Fla., Feb 1972.

(37) (a) P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.*, 41 (1956); (b) D. J. McLennan, *J. Chem. Soc. B*, 705, 709 (1966); (c) J. F. Bunnett, G. T. Davis, and H. Tanida, *J. Amer. Chem. Soc.*, 84, 1608 (1962).

(38) C. H. DePuy, D. L. Storm, J. T. Frey, and C. G. Naylor, *J. Org. Chem.*, 35, 2746 (1970).

(39) (a) E. L. Eliel and R. S. Ro, *Chem. Ind. (London)*, 251 (1956); (b) S. Winstein, D. Darwish, and N. J. Holness, *J. Amer. Chem. Soc.*, 78, 2915 (1956); (c) A. J. Parker, *Chem. Tech.*, 1, 302 (1971).

(40) A. J. Parker, M. Ruane, G. Biale, and S. Winstein, *Tetrahedron Lett.*, 2113 (1968).

(41) D. Eck and J. F. Bunnett, *J. Amer. Chem. Soc.*, 91, 3099 (1969).

(42) (a) R. A. Sneen and J. W. Larsen, *ibid.*, 91, 362 (1969); (b) R. A. Sneen and H. M. Robbins, *ibid.*, 91, 3100 (1969).

anisms are general for secondary, and even primary, substrates.[42] Although the evidence they presented does not exclude the classical S_N2 and E2 mechanisms,[43] the ion-pair mechanisms do seem probable for many secondary substrates. For example, a two-stage mechanism can account for the superiority of PhS^- over EtO^- in promoting elimination from cyclohexyl tosylate,[37b] and for the "anomalous" formation of predominantly Saytzeff product in the Hofmann degradation of neomenthyltrimethylammonium ion (2).[44] In the

2

88%   12%
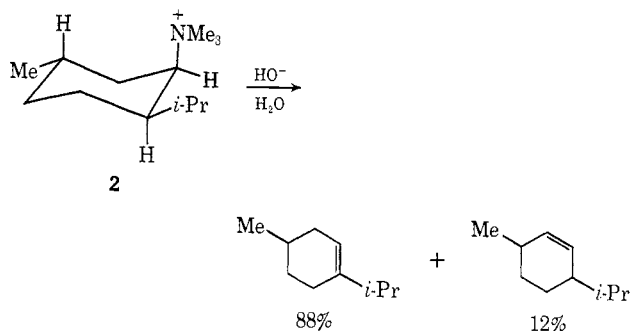
latter reaction the E1 mechanism could not be suppressed *even under strongly alkaline conditions.*[44] A tightly solvated cation is obviously present here and also in NaOEt–EtOH solution where the E2 reaction can be observed with little interference from the E1 reaction. It seems reasonable to assume that a two-stage mechanism is operative here, and also for analogous situations such as in the ethanolysis of menthyl chloride where the concentration of NaOEt had to be increased to 1 M in order to make the second-order component contribute more than 90% to the elimination reaction.[45]

We conclude, in agreement with Sneen,[42] that the ion-pair E2 mechanism represents a common mechanistic path that has been hitherto largely unappreciated.

Concerning Driving Forces for Base-Initiated Elimination Reactions

The idea of Evans and Polanyi[46] that part of the energy released in bond formation can be utilized in (simultaneous) bond breaking to provide a *driving force* for a chemical reaction can be given qualitative support in that in eliminations to form the stronger (by *ca.* 30 kcal/mole) C=O bonds much more basic leaving groups can be ejected than in eliminations to form (the weaker) C=C bonds. Thus attack of base on H–O–C–Y systems can easily eject strongly basic Y^- anions such as CN^-, $SO_3{}^{2-}$, HO^-, $CH_3COCH_2{}^-$, $C_6H_5CO^-$, etc. (reversals of carbonyl addition reactions), whereas eliminations to form C=C bonds cannot. In eliminations to form C=O bonds one bond is broken and one bond is formed in the rate-limiting step, which is ionization of Y^- from the $Y-C-O^-$ anion (Table I). Strongly

basic Y^- groups can also be ejected in the formation of C=C bonds: note, for example, the ejection of PhO^- and RO^- in carbanion eliminations from H–C(EWG)–C–Y systems.[22d] When the C=C bond being formed is incorporated as part of an aromatic system the powerful driving force provided by these aromatizing eliminations commonly gives rise to the ejection of strongly basic anions (HO^-, $NH_2{}^-$, and even R^-). An example where an (incipient) methyl anion is ejected is shown.[47]
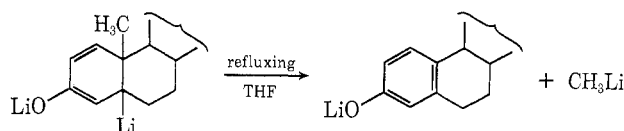
It would appear from these examples that part of the energy released in the formation of a multiple bond can be used to assist breaking of the C–Y bond, at least in carbanion eliminations. In concerted eliminations with H–C–C–Y systems initiated by a base, B^-, one could anticipate, then, that the energy released in formation of the B–H and C=C bonds might aid in the breaking of the H–C and C–Y bonds. Indeed, the large driving force seemingly inherent in anti eliminations, but not syn eliminations,[6] was one of the most convincing early arguments for the concerted E2 mechanism. It was pointed out that the anti geometry provided an opportunity for maximum orbital overlap for the development of the π bond, and that this provided a driving force for breaking of the H–C and C–Y bonds. The evidence for a large driving force favoring *anti* eliminations came, however, chiefly from work on the benzene hexachloride system,[6] and this has not been supported by work on other systems. For example, when the β-hydrogen atom is activated by the $ArSO_2$ group, activated syn elimination in the cyclohexane system completely overshadows nonactivated anti elimination,[48] and this holds true even for the weakly electron-withdrawing phenyl group.[49] Further doubts concerning a large driving force favoring anti eliminations are raised by the evidence indicating that the high anti/syn ratios are not present in cyclopentane systems[23,27] or in medium-ring systems,[50] and that the high anti/syn ratios in some cyclohexane systems may be caused as much by a retardation of syn elimination, due to conformational effects, as by an acceleration of anti elimination.[23] Also, the 10^5-fold faster dehydrobromination of *cis-* than of *trans-*1,2-dibromoethylene by methoxide ion *cannot* be attributed to a superior

(43) D. J. Raber, J. M. Harris, R. E. Hall, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **93**, 4821 (1971); D. J. McLennan, *Tetrahedron Lett.*, 2317 (1971).

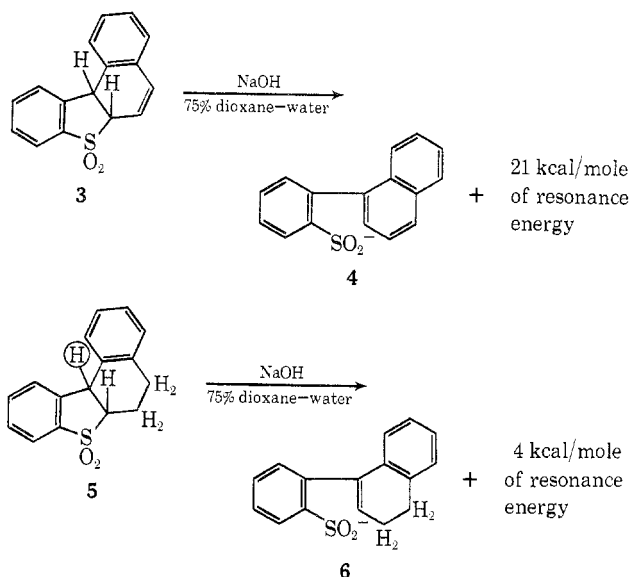(44) E. D. Hughes and J. Wilby, *J. Chem. Soc.*, 4094 (1960).

(45) E. D. Hughes, C. K. Ingold, and J. B. Rose, *ibid.*, 3839 (1953).

(46) M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **34**, 11 (1938).

(47) H. L. Dryden, Jr., G. M. Webber, and J. J. Wieczorek, *J. Amer. Chem. Soc.*, **86**, 742 (1964).

(48) F. G. Bordwell and R. J. Kern, *J. Amer. Chem. Soc.*, **77**, 1141 (1955).

(49) (a) J. Weinstock and F. G. Bordwell, *ibid.*, **77**, 6706 (1955); (b) S. J. Cristol and F. R. Stermitz, *ibid.*, **82**, 4692 (1960); (c) A. C. Cope, G. A. Berchtold, and D. L. Ross, *ibid.*, **83**, 3859 (1961); (d) G. Ayrey, E. Buncel, and A. N. Bournes, *Proc. Chem. Soc. London*, 458 (1961); (e) S. J. Cristol and D. I. Davies, *J. Org. Chem.*, **27**, 293 (1962); (f) C. H. DePuy, G. F. Morris, and R. J. Smat, *J. Amer. Chem. Soc.*, **87**, 2421 (1965).

(50) (a) J. Sicher and J. Zavada, *Collect. Czech. Chem. Commun.*, **32**, 2122 (1967); **33**, 1278 (1968); (b) J. L. Coke and M. P. Mourning, *J. Amer. Chem. Soc.*, **90**, 5561 (1968).

driving force resulting from a concerted anti elimination, since the anti elimination has been shown to proceed by a carbanion mechanism.[21]

Comparison of the rates of ethoxide-initiated carbanion elimination of PhOH from $C_6H_5SO_2CH_2CH_2$-OPh[22d] with the concerted elimination of HBr from $C_6H_5CH_2CH_2Br$[51] shows that the *carbanion process is ca. 1000 fold faster.* This is remarkable, indeed, when one considers that the difference in leaving group effects (OPh *vs.* Br) would have been expected to favor the concerted process by at least a factor of 10^5, judging from leaving group effects in S_N2 reactions.[52] It seems evident from these data that the carbanion process is favored from an energetic standpoint. It would appear that with the $ArCH_2CH_2Y$ system the concerted process is brought into play only because carbanion formation is very difficult in this particular instance ($pK^{PhCH_3} - pK^{PhSO_2CH_3} \geq 10$). Furthermore, the driving force provided by the concerted mechanism must be relatively small.

Recently we have examined an aromatizing elimination reaction wherein arenesulfinate ion 4 was produced from sulfone 3, and have compared it with the non-aromatizing elimination of the dihydro derivative of 3, *i.e.*, 5 → 6.[54]

3 was only about twice as fast as the rate of *exchange* for 5. We conclude that the elimination reaction of 3 must also be occurring by a carbanion mechanism, $(E1cB)_I$. The twofold faster rate of carbanion formation from 3 could be caused by such factors as inductive acceleration by the C=C bond or less internal return for the carbanion derived from 3. It is significant that, despite the large amount of energy released in the formation of the C=C bond in the aromatizing elimination, the reaction does not adopt the concerted course that would allow this potentially large driving force to be utilized for breaking of the H–C and C–SO₂ bonds. We must conclude either that the carbanion process is strongly favored from an energetic standpoint or, if we accept a concerted mechanism for the conversion of 3 to 4, that the concerted process has relatively little driving force.

In the $(E1cB)_I$ mechanism $k_2 \gg k_{-1}$, and k_1 is rate limiting. If ejection of the leaving group from the carbanion is a highly energetically favorable process, as we believe it is, then it would be possible to explain the *preferential* formation of an unstable C=C bond by this mechanism. A particularly striking example is the formation of *trans*-cyclooctene (8) as the major product from the Hofmann degradation of cyclooctyltrimethylammonium hydroxide (7),[55] despite the fact that 8 is 9.3 kcal/mole less stable, judging from heats of hydrogenation,[56] than is the cis isomer 9. Assuming an $(E1cB)_I$ mechanism it is understandable that the nature of the product can be dictated by the higher relative kinetic acidity of the cis (diastereotopic) β-hydrogen atom. A syn[50] carbanion elimination gives *trans*-cyclooctene (8). On the other hand, it appears
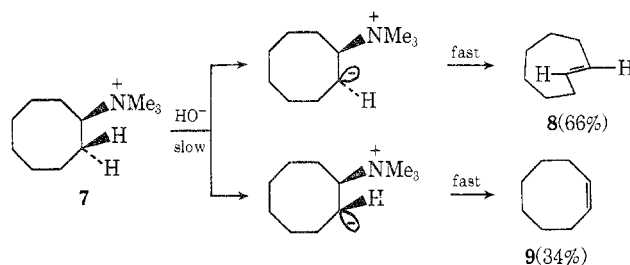
highly unlikely that highly strained 8 would be formed *in preference* to 9 if these eliminations are concerted.

The concerted mechanism has often been considered to provide a driving force for fragmentation reactions involving the formation and breaking of four or more bonds, which may be represented as

$$\overset{\ominus}{a}-b-\overset{}{c}-d-\overset{}{X} \longrightarrow \overset{+}{a}=b + c=d + X^- {}^{57}$$

As evidence it is pointed out that the solvolysis of 4-bromoquinuclidine (11) in 80% EtOH at 40° is almost

The mechanism for the nonaromatizing elimination from 5 was established as preequilibrium carbanion, $(E1cB)_R$, by the observation of complete exchange of the β hydrogen (circled in the formula) under conditions where little or no elimination occurred. In contrast, sulfone 3 did not give a detectable amount of exchange of the β proton during elimination. Interestingly enough, however, the rate of *elimination* for
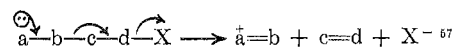
(51) W. H. Saunders, Jr., and D. H. Edison, *J. Amer. Chem. Soc.*, 82, 138 (1960).

(52) For MeO⁻ + CH₃Y, Y = Br is better by 10⁴·⁵ than Y = OAc.[53] Data are not available for Y = OPh.

(53) E. R. Thornton, "Solvolysis Mechanisms," Ronald Press, New York, N. Y., 1964, p 165.

(54) F. G. Bordwell, G. D. Cooper, and D. A. R. Happer, *Tetrahedron Lett.*, 2759 (1972).

(55) K. Ziegler and W. Wilms, *Justus Liebigs Ann. Chem.*, 567, 1 (1950); A. C. Cope, R. A. Pike, and C. F. Spencer, *J. Amer. Chem. Soc.*, 75, 3212 (1953).

(56) R. B. Turner and W. R. Meador, *ibid.*, 79, 4133 (1957).

(57) See, for example, E. M. Kosower, "An Introduction to Physical Organic Chemistry," Wiley, New York, N. Y., 1968, pp 94–97. Lack of participation during fragmentation of an open-chain analog has been demonstrated by C. A. Grob, F. Ostermayer, and W. Raudenbusch, *Helv. Chim. Acta*, 45, 1672 (1962).

10^5 faster than that of 1-bromo[2.2.2]bicyclooctane (10).[57] It should be noted, however, that the rate of solvolysis of 11 is actually over 10 times *slower* than that of *tert*-butyl bromide.[58] It seems likely, then, that the faster rate for 11 as compared to 10 is caused primarily by circumvention of internal return from the ion pair initially formed from 11, rather than by a driving force resulting from simultaneous bond formation and bond breaking.

circumvention of
internal return by fragmentation
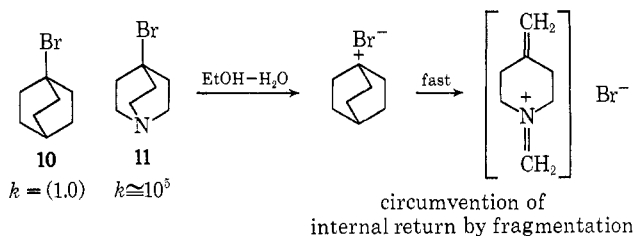
General Conclusions

Our general conclusions are that: (1) most base-initiated β eliminations which involve breaking of a bond of the type H–O, H–N, H–N=, H–C(EWG), or H–C(EWG)$_2$, where EWG = NO$_2$, CN, COR, SO$_2$R, or the like, proceed by anion mechanisms rather than a concerted mechanism; (2) although there is evidence for a driving force for C–Y bond cleavage from anions of the type $^-$O–C–Y, $^-$C–C–Y, and the like, there is no evidence for a driving force wherein O=C or C=C bond formation aids H–O or H–C bond breaking; (3) many examples of β eliminations heretofore classified as occurring by concerted E2 mechanisms probably occur by ion-pair E2 mechanisms; (4) when viewed as a whole, there are many more examples of two-stage than of one-stage β eliminations.[59]

(58) R. C. Fort and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 86, 4194 (1964); *Chem. Rev.*, 64, 277 (1964), report the solvolysis rate of 10 in 80% EtOH to be 10^6 slower than that of *t*-BuBr.
(59) The rarity of the heterolytic, one-stage β-elimination mechanism is not surprising when one considers that the microscopic re-

One-stage β eliminations are probably uncommon for one or all of the following reasons: (a) torsional strain is introduced by eclipsing effects in the transition state; (b) an unfavorable entropy effect is introduced in the transition state by the freezing of rotations around three bonds of the substrate;[61] and (c) energy is required to lengthen and shorten bonds, and to change bond angles in the rehybridization process. Two-stage β eliminations in which ionic intermediates are formed presumably have the advantage that solvent and structural reorganization can occur in two stages rather than in one fell swoop.[62]

In view of the evident preference for the majority of β eliminations to follow two-stage mechanisms it appears appropriate to question many of the mechanistic assignments made in the literature, not only for β eliminations, but also for other reactions where as many as two bonds have been assumed to be formed and two bonds broken in concert.

verse of this mechanistic type is rare; *i.e.*, most electrophilic and nucleophilic additions to C=C, C=O, C=N, etc., bonds occur by two-stage mechanisms. Miller has recently used this argument effectively in reaching the conclusion that iodide-initiated debrominations occur by two-stage rather than one-stage mechanisms.[60]
(60) C. S. T. Lee, I. M. Mathai, and S. I. Miller, *J. Amer. Chem. Soc.*, 92, 4602 (1970).
(61) It is surprising to note in this regard that the entropies of activation for (presumably) concerted alkene-forming eliminations are generally much more positive than for accompanying S$_N$2 reactions (see, *e.g.*, ref 11, pp 46–48).
(62) This advantage, at least as a first approximation, can be considered to be an example of the application of the principle of least molecular deformation. For more critical analyses of this principle, however, see: J. Hine, *J. Org. Chem.*, 31, 1236 (1966); J. Hine, *J. Amer. Chem. Soc.*, 88, 5525 (1966); S. I. Miller, *Advan. Phys. Org. Chem.*, 6, 185 (1968); O. S. Tee, *J. Amer. Chem. Soc.*, 91, 7144 (1969); O. S. Tee and K. Yates, *ibid.*, 94, 3074 (1972).

Pressure Effects as Mechanistic Probes of Organic Radical Reactions

ROBERT C. NEUMAN, JR.

Department of Chemistry, University of California, Riverside, California 92502

Received March 29, 1972

Activation parameters are useful in understanding

Robert Neuman received the Ph.D. from Cal Tech under the direction of George Hammond and then spent the 1962–1963 academic year as an NSF postdoctoral fellow with Cheves Walling at Columbia University. His active interest in high-pressure studies developed during this latter period. Besides the topic of this Account, another research area has been nmr studies of hindered rotation reactions. He has been at University of California at Riverside since 1963 and is now Professor of Chemistry.

chemical reactions since they provide information about the nature of the activated complexes formed from the reactants. Enthalpies and entropies of activation (ΔH^* and ΔS^*) are routinely determined because they are easily obtained *via* the temperature dependence of rate constants. The volume change of activation (ΔV^*) is much less frequently reported, but in principle