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Are Nucleophilic Bimolecular Concerted Reactions Involving Four or More Bonds a Myth?

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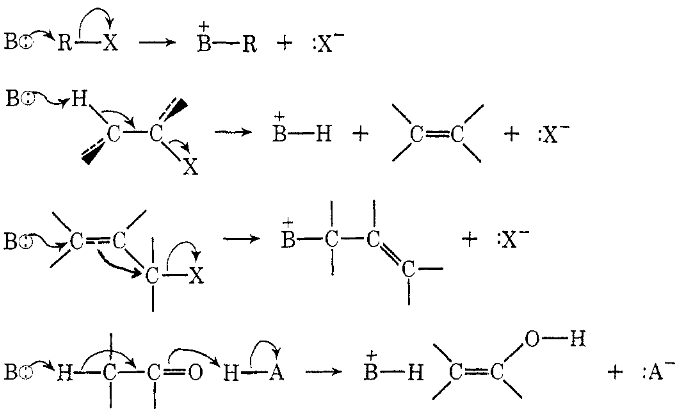
The idea that, in simple reactions of the type A + B–C → A–B + C, the A–B bond is formed at the same time that the B–C bond is broken was first suggested by Lewis.[1a] It was later given quantum mechanical expression by London.[1b] The obvious energetic economy of a process in which bond breaking is aided by simultaneous and synchronous bond making (concerted mechanism), together with the attractiveness of using a series of curved arrows to simulate a flow of electrons, led to the rapid acceptance of concerted mechanisms by organic chemists and to the representation of the majority of organic reactions as concerted processes. Examples are SN2, E2, SN2′, and enolization reactions, which are commonly depicted as shown in Chart I (B: is a base or nucleophile).

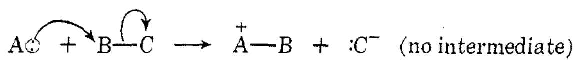
Chart I



bonds made	bonds broken	Type
1	1	SN2
2	2	E2
2	2	SN2′
3	3	

Although the concerted mechanism has logical and esthetic appeal, it is difficult in practice to find experimental criteria to distinguish between this pathway and one in which a high-energy intermediate is formed. The principal evidence supporting the concerted mechanism for bimolecular reactions is kinetic and stereochemical in nature.

Second-order kinetics establishes that both reacting species are present in the transition state for the rate-controlling step, but this condition is satisfied as well by assuming the slow or reversible formation of an intermediate as by assuming a concerted pathway. Thus, all three of the following mechanisms will obey second-order kinetics.



$$A{:} + B{-}C \xrightarrow{\text{slow}} [ABC] \xrightarrow{\text{fast}} \overset{+}{A}{-}B + {:}C^-$$

$$A{:} + B{-}C \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} [ABC] \xrightarrow{k_2} \overset{+}{A}{-}B + {:}C^- \quad (k_{-1} > k_2)$$

The concerted mechanism requires stereospecificity, and the general acceptance of concerted mechanisms has no doubt been a consequence of the observation of a high degree of stereoselectivity for many reactions.[2] This is no guarantee of a concerted mechanism, however, because a high-energy intermediate might well be expected to decompose before structural reorganization brings about a loss of stereoselectivity.

The SN2 process, where only one bond is made and one is broken, is perhaps the most generally accepted example of a nucleophilic bimolecular reaction occurring by a concerted mechanism, but even here it has

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(1) (a) G. N. Lewis, "Valence and the Structure of Atoms and Molecules," Chemical Catalog Co., New York, N. Y., 1923, p 113; (b) F. London, *Z. Elektrochem.*, **35**, 552 (1929); see also M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **34**, 11 (1938).

(2) It must be kept in mind in this respect, however, that a stereoselectivity of 90% corresponds (at 25°) to a difference of only 1.4 kcal/mol in the free energy of activation for the two reaction paths; a stereoselectivity of 99% corresponds to 2.7 kcal/mol.

been pointed out that intermediates of finite life might be formed during some SN2 reactions,[3a–e] and experimental evidence to support this view has been presented for a few reactions.[3d–g] On the other end of the scale, for the much more complex reaction, acid-catalyzed enolization, where three bonds are made and three are broken, the concerted mechanism, which was at one time favored,[4a] now is regarded as being of little, if any, importance.[4b,c]

In the past 5 years we have had occasion to examine four different types of nucleophile-initiated or base-initiated reactions involving the making of two bonds and the breaking of two bonds. In each of these reactions second-order kinetics is obeyed and, in appropriate examples, a high degree of stereoselectivity is observed. For one of these a concerted mechanism has been favored and for each of the others it has been given serious consideration; yet our experimental evidence appears to be accommodated better in every instance by a stepwise mechanism than by a concerted mechanism. This has led us to question the importance and generality of the concerted mechanism in reactions of this type. It is the purpose of this paper to summarize the evidence concerning the timing of bond making and bond breaking in these reactions.

The SN2′ Reaction

The SN2′ reaction has an amusing history. Bergmann,[5] Hughes,[6] and Winstein[7] all conceived independently the idea that attack of a nucleophile at the C=C bond of an allylic halide could result in a shifting of the position of the double bond with simultaneous ejection of the halide ion leading to an "abnormal" allylic displacement reaction. The search for such a reaction (labeled SN2′) was made in several laboratories during the next few years without any success. The groups at both the University of London and the University of California at Los Angeles examined the reaction of sodium ethoxide with α-methylallyl chloride in ethanol and concluded that displacement of chloride ion by ethoxide ion did not involve an SN2′ process.[8,9]

Numerous candidates for the SN2′ mechanistic label have been presented in the literature since that time, but the variety of pathways available for the reactions of allylic halides makes an unambiguous assignment of mechanism extremely difficult. In 1948 Catchpole, Hughes, and Ingold, as a consequence of failures to detect SN2′ reactions, suggested that the shielding of the γ-carbon atom of the allylic system by the π electrons makes it impossible for the SN2′ mechanism to be realized.[10] In 1949 Kepner, Winstein, and Young reported what they believed to be the first authentic example of an SN2′ mechanism.[11] They suggested that the SN2′ label be accepted only when second-order kinetics has been established and when it has been demonstrated that the abnormal product does not arise from rearrangement of the halide (or of an initially formed "normal" product) during the reaction.[11] Based on these criteria they proposed that their demonstration that the second-order reactions of diethyl sodiomalonate with α-methyl- and α-ethylallyl chlorides in ethanol to yield 10 and 23%, respectively, of abnormal products were the first authentic examples of the SN2′ reaction. Another example was added to the list in 1951 when it was shown by Young, Webb, and Goering that the reaction of α-alkylallyl chlorides with secondary amines in benzene followed second-order kinetics;[12] this reaction had earlier been shown to give good yields of the abnormal product.[13]

Neither example has been accepted unreservedly by the English school. Dewar suggested that the formation of the abnormal product from diethyl sodiomalonate could be explained as O-allylation followed by rearrangement.[14] Although strong arguments against this view have been given,[11b,15] de la Mare and Ingold remain unconvinced.[16,17] The second example, the reaction of diethylamine with α-methylallyl chloride in benzene,[12] Ingold believes is better classified as an SNi′ reaction than as an SN2′ reaction.[18] The reaction of piperidine with *trans*-6-alkyl-2-cyclohexen-1-yl dichlorobenzoates in *p*-xylene,[19] which has been widely accepted as demonstrating an approach by the nucleophile *cis* to the leaving group in the SN2′ reaction, is also classified by Ingold as SNi′.[18] This classification is based on the suggestion of Young, Webb, and Goering that hydrogen bonding between the hydrogen atom on nitrogen in the secondary amine and departing chloride ion occurs in the transition state.[12]

In the opinion of de la Mare[16] and of Ingold[17] the first authentic example of the SN2′ mechanism was the observation of a slow formation of the abnormal product in the reaction of radioactive lithium bromide in acetone with α-methylallyl bromide or crotyl bromide.[20] Here

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(3) (a) R. J. Gillespie, *J. Chem. Soc.*, 1002 (1952); (b) H. H. Jaffé, *J. Chem. Phys.*, **21**, 1893 (1953); (c) M. J. S. Dewar, *J. Chem. Soc.*, 2885 (1953); (d) S. Winstein, D. Darwish, and N. H. Holness, *J. Amer. Chem. Soc.*, **78**, 2915 (1956); (e) E. L. Eliel and R. S. Ro, *Tetrahedron*, **2**, 353 (1958); (f) A. J. Parker, M. Ruane, G. Biale, and S. Winstein, *Tetrahedron Lett.*, 2113 (1968); (g) R. A. Sneen and J. W. Larson, *J. Amer. Chem. Soc.*, **91**, 362 (1969).

(4) (a) C. G. Swain, *ibid.*, **72**, 4578 (1950); (b) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, Chapter IX; (c) C. G. Swain, A. J. DiMilo, and J. P. Cordner, *J. Amer. Chem. Soc.*, **80**, 5983 (1958).

(5) E. Bergmann, *Helv. Chim. Acta*, **20**, 590 (1937).

(6) E. D. Hughes, *Trans. Faraday Soc.*, **34**, 185 (1938).

(7) S. Winstein, Ph.D. Dissertation, California Institute of Technology, 1938.

(8) E. D. Hughes, *Trans. Faraday Soc.*, **37**, 606 (1941).

(9) J. D. Roberts, W. G. Young, and S. Winstein, *J. Amer. Chem. Soc.*, **64**, 2157 (1942).

(10) A. G. Catchpole, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 8 (1948).

(11) (a) R. D. Kepner, S. Winstein, and W. G. Young, *J. Amer. Chem. Soc.*, **71**, 115 (1949); (b) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956).

(12) W. G. Young, I. D. Webb, and H. L. Goering, *J. Amer. Chem. Soc.*, **73**, 1076 (1951).

(13) J. Meisenheimer and J. Link, *Ann.*, **479**, 211 (1930).

(14) M. J. S. Dewar, *Bull. Soc. Chim. Fr.*, **18**, C43 (1951).

(15) S. Winstein, *ibid.*, **18**, C43 (1951).

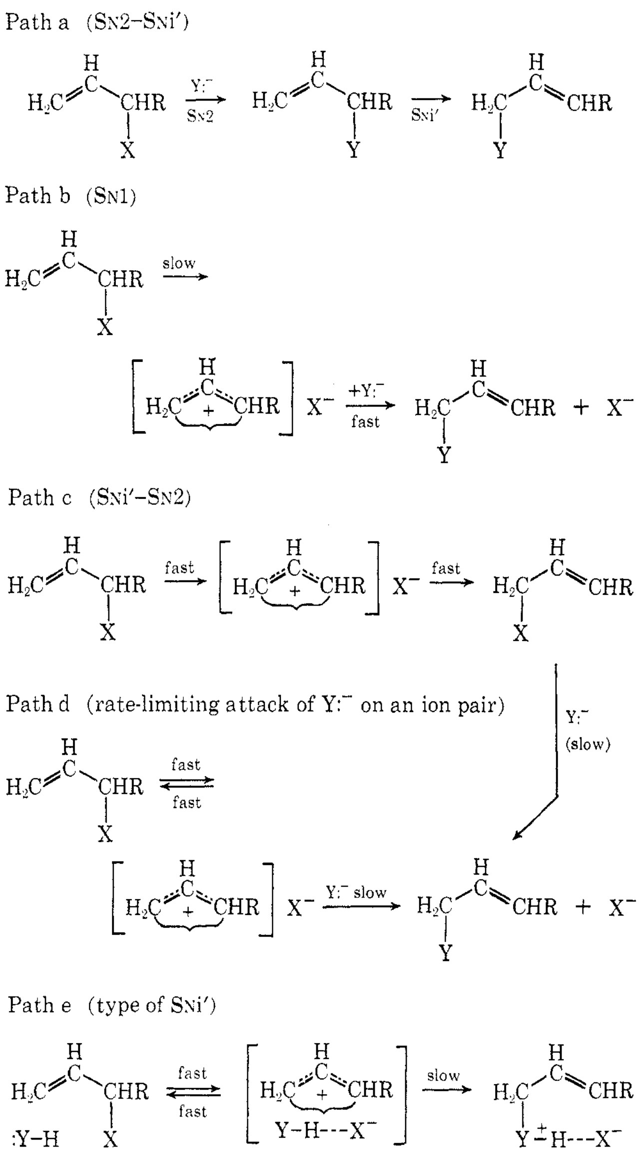
(16) P. D. de la Mare, "Molecular Rearrangements," P. de Mayo, Ed., Interscience, New York, N. Y., 1963, pp 62–68.

(17) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, pp 855–857.

(18) Reference 17, pp 859–860.

(19) G. Stork and W. N. White, *J. Amer. Chem. Soc.*, **78**, 4609 (1956).

Scheme I



the rate of SN2 reaction was determined by the rate of exchange of radioactive bromine, and the rate of SN2′ reaction was measured by the rate of appearance of the abnormal product. However, as DeWolfe and Young have pointed out,[11b] the possibility that the abnormal product arises by a lithium ion catalyzed SN1 or SNi′ reaction was not excluded. In view of the well-known susceptibility of allylic bromides to rearrangements of this type the SN1 or SNi′ mechanisms appear to be at least as likely for this example as does an SN2′ mechanism.

The difficulties involved in making a definite assignment of the SN2′ mechanistic label should be apparent from the above discussion. To summarize, the pathways other than SN2′ by which abnormal products may be formed are shown in Scheme I.

In order to make a secure assignment of the SN2′ mechanism it is necessary to exclude each of the alternative pathways, a–e. This is very difficult to do.

Path a is the alternative suggested by Dewar,[14] de la Mare,[16] and Ingold[17] for the formation of the abnormal product from diethyl sodiomalonate and α-alkylallyl chlorides.[11a] It is also the alternative path suggested by DeWolfe and Young[11b] for the formation of the abnormal product from lithium bromide and α-methylallyl or crotyl bromides.[20]

Path b is an SN1 reaction with rearrangement. It can presumably be eliminated from consideration by the observation of second-order kinetics, but the experimental error is large enough in most kinetic investigations to allow 10%, or even 20%, of abnormal product to arise from this pathway without detection, even when the kinetics appear to be second order. The classification of the reaction of diethyl sodiomalonate with α-alkylallyl chlorides[11a] as SN2′ might be questioned on these grounds.

The SNi′–SN2 pathway (c) may perhaps be ruled out by a test to show the absence of rearranged primary halide (or the like) in incomplete reactions.[11,12,19] However, if the SN2 reaction of the primary halide is 100 or more times as rapid as that of the secondary halide, which is not unreasonable, this pathway could go undetected by a test of this kind.

Path d is an alternative to the SN2′ mechanism which cannot be ruled out by any of the data on hand. Path e is a variation of path d.

Surprisingly few examples of reactions to form abnormal products where the kinetics have been established as second order have been added to those cited above. Only four additional types of nucleophiles have been used. One example where a tertiary amine (trimethylamine) is the nucleophile[21] and one where thiourea is the nucleophile[22] have been found, but a full account of the latter work has never appeared. Sodium thiophenoxide in ethanol has been used in three examples,[23] but no attempt was made in these studies to exclude the alternative SNi′–SN2 pathway. Path d also remains as a distinct possibility for these reactions. Sodium ethoxide has been used in three examples,[23c,24] but again no attempt was made to exclude the SNi′–SN2 pathway; in one of these reactions, that with α-*t*-butylallyl chloride,[24a] the kinetic criterion is barely satisfied, since the reaction becomes second order only at high sodium ethoxide concentrations.

In view of the strong tendency of secondary and tertiary allylic halides to undergo carbonium type reactions, as in paths b–e, the behavior of allylic halides bearing an electron-withdrawing substituent seemed to offer an attractive area for studying SN2′ reactions. In such systems carbonium ion type reactions are greatly inhibited and, furthermore, the C=C bond is made more susceptible to attack by the nucleophile. Systems **1**, **2**, **3**, and **4** are examples of this type that have

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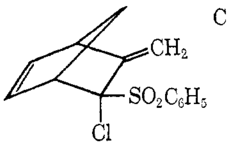
[20] (a) B. D. England and E. D. Hughes, *Nature*, **168**, 1002 (1951); (b) B. D. England, *J. Chem. Soc.*, 1615 (1955).

[21] W. G. Young, R. A. Clement, and C. H. Shih, *J. Amer. Chem. Soc.*, **77**, 3061 (1955).

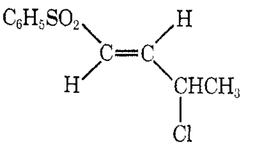
[22] Unpublished work cited in ref 11b, p 779.

[23] (a) P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.*, 3555 (1953); (b) P. B. D. de la Mare and C. A. Vernon, *ibid.*, 3331 (1952); (c) P. B. D. de la Mare and C. A. Vernon, *ibid.*, 3628 (1952).

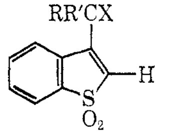
[24] (a) P. B. D. de la Mare, E. D. Hughes, P. C. Merriman, L. Pichet, and C. A. Vernon, *ibid.*, 2563 (1958); (b) P. B. D. de la Mare and C. A. Vernon, *ibid.*, 3325 (1952).



1



2



3, R = H; R′ = CH$_3$
4, R = R′ = CH$_3$

been studied to date in which the sulfonyl group provides electron withdrawal at the α position (**1**), the γ position (**2**), or the β plus γ positions (**3** and **4**).[25]

For compound **1** SN1 or SN2 reactions should be extremely slow.[27] On the other hand, SN2′ attack at the C=C bond should be facilitated by the inductive effect of the α-$C_6H_5SO_2$ group. No reaction occurred with either **1** or its epimer in a 17-hr reflux in benzene with either excess piperidine or triethylammonium thiophenoxide as reagents.[25] Under these conditions the reaction of diethylamine and α-methylallyl chloride in benzene would have gone through one half-life. Since piperidine and triethylammonium thiophenoxide are much more reactive nucleophiles than is diethylamine, it is clear that **1** and its epimer, instead of being more reactive than α-methylallyl chloride, are actually much less reactive.

In **2** we have an analog of α-methylallyl chloride in which a hydrogen atom at the γ position has been substituted by the $C_6H_5SO_2$ group. One might expect **2** to be highly susceptible to the SN2′ process since it retains all the features of the α-methylallyl halide system yet has a C=C bond that has been made much more susceptible to nucleophilic attack. Experiment showed, however, that basic nucleophiles, such as piperidine in benzene or sodium methoxide in methanol, failed to cause displacement of chloride ion, even with extended reaction times. Instead, **2** tautomerized to **2a**.

$$\underset{\mathbf{2}}{C_6H_5SO_2CH{=}CHCHClCH_3} \overset{B:}{\rightleftharpoons} \underset{\mathbf{2a}}{C_6H_5SO_2CH_2CH{=}CCH_3Cl}$$

Not only does the SN2′ process with **2** fail to compete favorably with tautomerism, but the small amount of **2** remaining at equilibrium fails to react with excess nucleophile even during protracted periods.

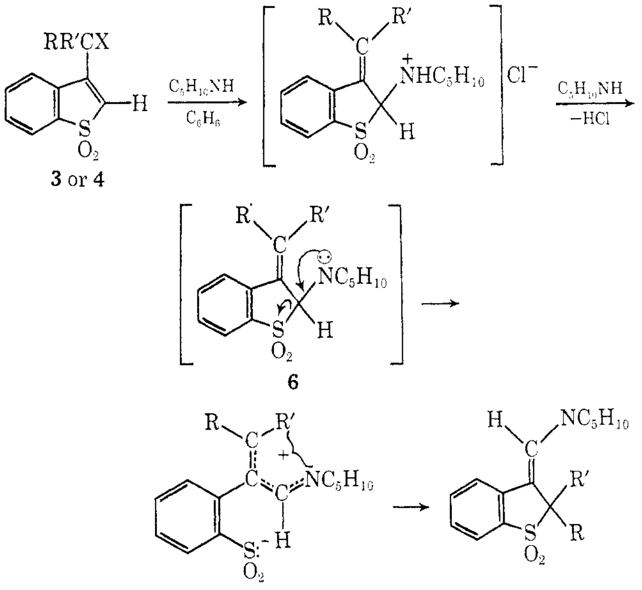
With relatively nonbasic nucleophiles, such as lithium bromide in acetone or lithium azide in DMF, displacement of chloride did occur, but SN2 displacement took precedence over SN2′ displacement. It

$$\underset{\mathbf{2}}{C_6H_5SO_2CH{=}CHCHClCH_3} \underset{(CH_3)_2CO}{\overset{LiBr}{\rightleftharpoons}} \underset{\mathbf{5}}{C_6H_5SO_2CH{=}CHCHBrCH_3}$$

should be noted that product **5** is itself capable of SN2′ displacement with LiBr in $(CH_3)_2CO$, but that none of the abnormal product was obtained even though, judging from the data of England on α-methylallyl bromide,[20] the SN2′ process should be only about 60 times slower than the SN2 process.

Various explanations for the failure of **1**, **2**, or **5** to give abnormal (SN2′-type) products on reaction with nucleophiles might be advanced. However, in our opinion the most reasonable one is that the presence of the electron-withdrawing $C_6H_5SO_2$ group has suppressed carbonium ion type reactions and that these are the source of the abnormal products from the α-alkylallyl chloride systems.

A variety of successful SN2′-like reactions have been achieved with **3** and **4**.[25] The reactions of **3** or **4** with piperidine in benzene are complicated by a subsequent rearrangement reaction involving ring opening and ring closing.[26]



Both kinetic and spectral evidence for the presence of intermediate **6** was obtained, and when certain other nucleophiles were used with **4** (LiN_3, KCN, and $C_6H_5SO_2Na$ all in dimethylformamide) products corresponding to **6** were obtained.[25] This is understandable since the N_3, CN, or $C_6H_5SO_2$ groups in these products do not have an electron pair capable of initiating a reaction to form a stable onium ion like **7**.

Although chlorides **3** and **4** react more rapidly by one or more powers of ten with secondary amines in benzene than does α-methylallyl chloride, they are much less reactive toward less basic nucleophiles such as methanol, thiourea in ethanol, or lithium bromide in acetone.[25] We attribute this lower reactivity to the inability of **3** or **4** to react by the carbonium ion type mechanisms which we believe account for the formation of abnormal products from α-methylallyl chloride with these nucleophiles.

The high order of reactivity of **3** and **4** toward basic nucleophiles in SN2′-like processes must be due to the ability of the sulfonyl group to provide conjugative electron withdrawal at the β position (*via* the benzene ring).[28] (The sulfonyl group provides inductive electron withdrawal at the γ position, but the unreactivity

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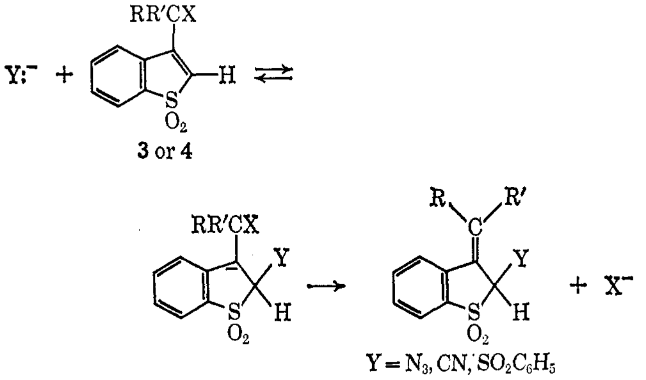
(25) The experiments with systems 1 and 2 were carried out in this laboratory by T. G. Mecca (unpublished results); experiments with systems 3 and 4 were initiated by R. W. Hemwall and D. A. Schexnayder[26] and extended by T. G. Mecca (unpublished results).

(26) (a) F. G. Bordwell, R. W. Hemwall, and D. A. Schexnayder, *J. Org. Chem.*, **33**, 3233 (1968); (b) F. G. Bordwell and D. A. Schexnayder, *ibid.*, **33**, 3236 (1968); (c) F. G. Bordwell and D. A. Schexnayder, *ibid.*, **33**, 3240 (1968).

(27) F. G. Bordwell and G. D. Cooper, *J. Amer. Chem. Soc.*, **73**, 5184 (1951); F. G. Bordwell and B. B. Jarvis, *J. Org. Chem.*, **33**, 1182 (1968).

of **2** shows that this type of activation is ineffective.) This effect must be one of delocalizing the charge at the β position, and it seems likely that a carbanion intermediate is formed.

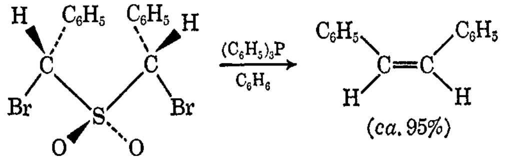


Although it is difficult to exclude a concerted SN2′ mechanism with bond making proceeding well ahead of bond breaking, the data on hand with respect to leaving group effects, solvent effects, and relative nucleophilicities ally these reactions much more closely with nucleophilic aromatic or vinylic substitutions, where there is good evidence for stepwise mechanisms,[29] than with SN2 reactions.[25]

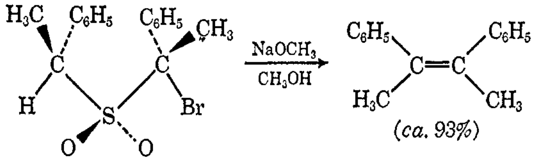
In summary, there appear to be no unambiguous examples of the SN2′ concerted mechanism. Reactions of α-alkylallyl chlorides represented as occurring by this mechanism can be explained by carbonium ion type reactions or other alternative paths. When dissociation to give carbonium ions is suppressed by substitution of an electron-withdrawing group at the α, β, or γ position of the allylic halide abnormal displacement either fails to occur or occurs by a carbanion-type mechanism.[30] We conclude that the concerted SN2′ mechanism may well be a myth.[31]

The Ramberg–Bäcklund Reaction

The base-initiated elimination of HX and, subsequently, of SO_2 from an α-halo sulfone to give an alkene (the Ramberg–Bäcklund reaction) has been found to obey second-order kinetics.[32a–c] Recently several such reactions have been shown to occur with a high degree of stereoselectivity and with inversion at each of the reaction centers.[32d–f]

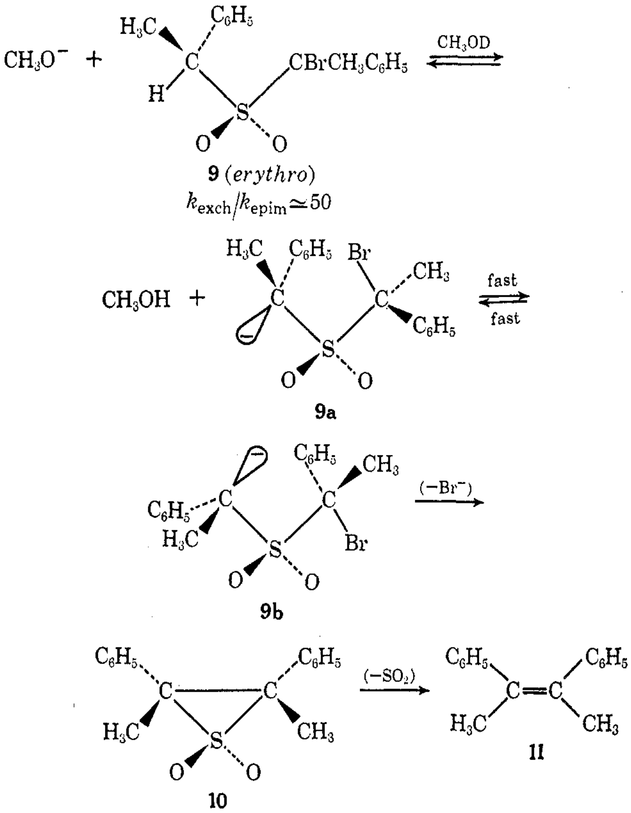


8 (*meso* isomer: the *dl* isomer gave *ca.* 95% of *trans*-$C_6H_5CH{=}CHC_6H_5$)[32d]



9 (*erythro* isomer: the *threo* isomer gave *ca.* 95% of *trans*-$C_6H_5CH_3C{=}CCH_3C_6H_5$)[32e]

Convincing evidence for the presence of carbanion intermediates in these reactions has been presented,[32e] and it has been suggested the reactions follow the course outlined for **9**.



Deprotonation of **9** is believed to occur selectively (as shown) from a conformation in which the proton is flanked by the two oxygen atoms of the sulfone grouping. The deprotonation was demonstrated to be reversible by recovery of deuterated **9** from an incomplete reaction carried out in CH_3OD. The recovered deuterated **9** contained about 2% of the (deuterated) *threo* isomer, and calculation shows $k_{\text{exch}}/k_{\text{epim}} \cong 50$; this is comparable to the k_e/k_α values obtained with $C_6H_{11}C^*H(CH_3)SO_2C_6H_5$ and $C_6H_5C^*H(CH_3)SO_2C_6H_5$ under similar conditions.[33] The asymmetric pyramidal

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[28] G. Maury, E.-M. Wu, and N. H. Cromwell, *J. Org. Chem.*, **33**, 1900 (1968), have shown that a β-carbonyl group also promotes SN2′-like reactions.

[29] See S. D. Ross, *Progr. Phys. Org. Chem.*, **1**, 31 (1963), for a review of nucleophilic aromatic substitution; see Z. Rappoport, *Advan. Phys. Org. Chem.*, **7**, 1 (1969), for a recent review of nucleophilic vinylic substitution.

[30] Evidence has been presented recently to show that reactions of nucleophiles with fluoroalkenes which had previously been thought to proceed by concerted SN2′ pathways actually involve carbanion intermediates; see H. F. Koch and A. J. Kielbania, Jr., *J. Amer. Chem. Soc.*, **92**, 729 (1970).

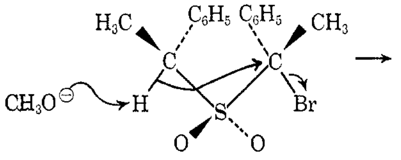
[31] "A traditional story, often in explanation of some natural phenomenon, useful to historians principally for what it reveals of the culture of the peoples among whom it was current" (paraphrased from Funk and Wagnalls Standard College Dictionary, Harcourt, Brace and World, Inc., New York, N. Y., 1963).

[32] (a) F. G. Bordwell and G. D. Cooper, *J. Amer. Chem. Soc.*, **73**, 5187 (1951); (b) F. G. Bordwell and J. M. Williams, Jr., *ibid.*, **90**, 435 (1968); (c) see L. A. Paquette, *Accounts Chem. Res.*, **1**, 209 (1968), for a review; (d) F. G. Bordwell, B. B. Jarvis, and P. W. R. Corfield, *J. Amer. Chem. Soc.*, **90**, 5298 (1968); (e) F. G. Bordwell, E. Doomes, and P. W. R. Corfield, *ibid.*, **92**, 2581 (1970); (f) E. Doomes, unpublished results.

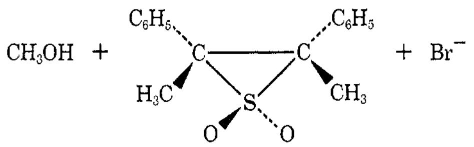
[33] (a) See D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic, New York, N. Y., 1965, pp 105–113; (b) E. J. Corey and T. H. Lowry, *Tetrahedron Lett.*, 803 (1965); (c) F. G. Bordwell, D. D. Phillips, and J. M. Williams, Jr., *J. Amer. Chem. Soc.*, **90**, 426 (1968).

carbanion resulting from deprotonation of **9** (*e.g.*, **9a**) is pictured as maintaining its asymmetry by virtue of a barrier to rotation. Rapid inversion at the carbanionic center is believed to be possible, as is rapid rotation around the S–CBrCH$_3$C$_6$H$_5$ bond, making the interconversion **9a** ⇄ **9b** rapid. This results in the carbanion being "effectively planar" and allows the conversion of **9** to **10** to occur with inversion at the C–Br center. Decompositions of episulfones to alkenes, such as **10** → **11**, are known to be highly stereoselective.[34]

The demonstration that carbanions are formed during eliminations, such as in the methoxide-initiated dehydrobromination of **9** to form **10**, does not necessarily mean that these carbanions are on the reaction pathway.[35] It could be that their formation is merely coincidental to the concerted mechanistic path.

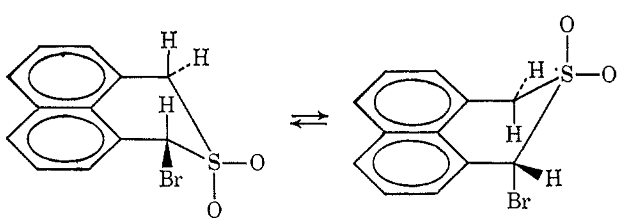


9



10

It is difficult to distinguish experimentally between the stepwise and concerted paths. The concerted path might be expected to have a negative activation entropy since it requires a coplanar alignment of the H–C–S–C–Br atoms in the transition state. The activation parameters observed for the reaction **9** → **10** ($E_a = 21$ kcal/mol and $\Delta S^{\ddagger}_{25} = 3$ eu)[32b] do not bear out this expectation, but it is difficult to rule out the concerted mechanism on this basis in the absence of a known model. One approach is to examine the behavior of a system in which this alignment of atoms is made facile (or mandatory) for stereochemical reasons. 1-Bromo-2-thia-2,3-dihydrophenalene 2,2-dioxide (**13**) is a molecule of this type which would be expected to give a Ramberg–Bäcklund reaction.[36]



13a **13b**

The signal for the benzylic hydrogen atoms in the nmr spectrum of the parent sulfone, 2-thia-2,3-dihydrophenalene 2,2-dioxide, appears as a singlet, which indicates that conformations comparable to **13a** and **13b** are in mobile equilibrium. Conformation **13a**, in which the H–C–S–C–Br atoms are coplanar, as required in the W-type double inversion mechanism, should then be easily accessible. Conditions would appear, then, to be ideal for the operation of a concerted mechanism. Comparison of the kinetic data for this system with those of the open-chain analog, C$_6$H$_5$CH$_2$SO$_2$CHBrC$_6$H$_5$ (**14**), is made in Table I.

Table I

Comparison of the Kinetic Data for the Reactions of 1-Bromo-2-thia-2,3-dihydrophenalene (13) and α-Bromobenzyl Benzyl Sulfone (14) with Sodium Methoxide in Methanol at 25°

Substrate	k_{obsd}, M^{-1} sec^{-1}	E_a, kcal/mol	$\Delta S^{\ddagger}$, eu
13[a]	(1.0×10^{-2})[b]	25.5	16
14[a]	(7.5×10^{-2})[c]	25	17

[a] Deuterium exchange was complete from an incomplete reaction in CH$_3$OD. [b] E. Doomes, unpublished results. [c] Reference 32b.

If the Ramberg–Bäcklund reaction of **14** is occurring by a concerted mechanism one might have expected that the incorporation of the reactive centers into a ring, as in **13**, would have a favorable effect. In conformation **13a** the H–C–S–C–Br atoms are held in a coplanar alignment and there should be relatively little additional rigidity imposed on the system in the transition state for the concerted 1,3-W elimination. The kinetic data in Table I show, however, that **13** undergoes the Ramberg–Bäcklund reaction 7.5 times more *slowly* than does **14**, and that the activation parameters are nearly identical. This result does not appear to be consistent with the concerted mechanism.

The Favorskii Rearrangement

The Favorskii rearrangement involves a base-initiated 1,3 elimination of HX from the α and α′ positions of an α-halo ketone to form a cyclopropanone (or like) intermediate. It is comparable in this respect to the Ramberg–Bäcklund reaction. Second-order kinetics have been observed in all the systems studied to date.[37] The reaction with *cis*- and *trans*-1-chloro-1-acetyl-2-methylcyclohexane and sodium ethoxide in ethanol has been shown to be stereospecific with inversion at the C–Cl bond,[38a] but a nonstereospecific reaction occurs with sodium methoxide in methanol.[38b] Although a cyclopropanone intermediate has been generally accepted for the Favorskii rearrangement, it has not been clear whether this is formed by loss of halide ion from a carbanion or by a concerted elimination of HX from the halo ketone.[39,40] The stereospecificity observed in the reactions of 1,1-dibromo ketones has been explained as

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[34] F. G. Bordwell, J. M. Williams, Jr., E. B. Hoyt, Jr., and B. B. Jarvis, *J. Amer. Chem. Soc.*, **90**, 429 (1968).

[35] J. Hine, R. Wiesboeck, and O. B. Ramsay, *ibid.*, **83**, 1222 (1961); R. Breslow, *Tetrahedron Lett.*, 399 (1964).

[36] C. Y. Meyers, A. M. Malte, and W. S. Matthews, *J. Amer. Chem. Soc.*, **91**, 7510 (1969).

[37] (a) F. G. Bordwell, R. R. Frame, R. G. Scamehorn, J. G. Strong, and S. Meyerson, *ibid.*, **89**, 6704 (1967); (b) F. G. Bordwell and R. G. Scamehorn, *ibid.*, **90**, 6751 (1968); (c) F. G. Bordwell, R. G. Scamehorn, and W. R. Springer, *ibid.*, **91**, 2087 (1969); (d) F. G. Bordwell, M. W. Carlson, and A. C. Knipe, *ibid.*, **91**, 3949 (1969); (e) F. G. Bordwell and M. W. Carlson, *ibid.*, **91**, 3951 (1969).

[38] (a) G. Stork and I. J. Borowitz, *ibid.*, **82**, 4307 (1960); (b) H. O. House and W. F. Gilmore, *ibid.*, **83**, 3980 (1961).

[39] R. B. Loftfield, *ibid.*, **73**, 4707 (1951); ref 24.

[40] A. W. Fort, *ibid.*, **84**, 2620 (1962); see also ref 33a, pp 243–249.

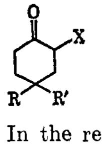
involving a concerted *trans*-antiparallel 1,3 elimination of HX,[41] and it has been suggested that the stereospecificity observed with cyclic α,α'-dibromo ketones is most readily explained by a concerted *cis* 1,3 elimination of HX.[42]

In certain Favorskii rearrangements, including those with $NaOCH_3$–CH_3OH and 2-chloro-4,4-diphenylcyclohexanone, α-chlorobenzyl methyl ketone, or benzyl chloromethyl ketone, essentially complete deuterium exchange occurs at the α and α' positions during the reaction.[37a–c] Although carbanions (enolate ions) are clearly present in these reactions, it is again difficult to be sure that their presence is not merely coincidental to a concerted mechanism.[35] In this instance there are two kinds of experimental evidence that argue against this view. Firstly, there is the observation that in the examples studied to date the size of the k_{Br}/k_{Cl} leaving group effect always parallels the extent of deuterium exchange, *i.e.*, a large Br/Cl rate ratio always coincides with extensive deuterium exchange and *vice versa.*[37] Secondly, there is the observation that methyl substitution at the carbon atom holding X in $ArCH_2COCH_2X$ has a striking effect on the reaction characteristics.[37d]

A large leaving group effect ($k_{Br}/k_{Cl} = 116$) was observed for the 2-halo-4,4-diphenylcyclohexanone system.[37a] This is explicable on the basis of either a concerted mechanism or one involving formation of an equilibrium concentration of carbanion. (If the mechanism involves formation of the carbanion in a *rate-limiting step*, the k_{Br}/k_{Cl} ratio should be about unity.[37d]) If the concerted mechanism is correct, one would not expect the k_{Br}/k_{Cl} ratio to vary much when relatively minor structural changes are made. This mechanism is not consistent, therefore, with the experimental results obtained with 2-halocyclohexanones shown in Table II.

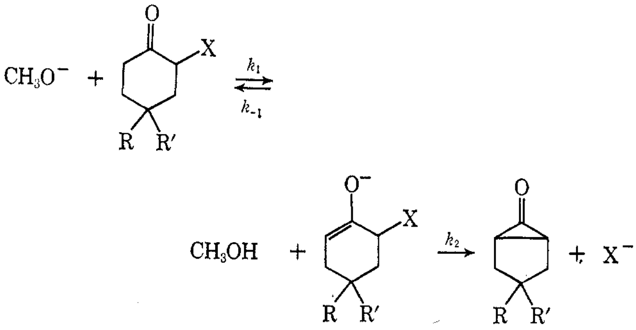
Table II

Correlation of Leaving Group Effects with Deuterium Exchange in the Reactions of 2-Halocyclohexanones with CH_3ONa in CH_3OH (or CH_3OD)

2-Halocyclohexanone	R	R′	k_{Br}/k_{Cl}	% d_3[a]
	C_6H_5	C_6H_5	116	100
	C_6H_5	CH_3	52	50
	H	H	Low[b]	19

[a] In the recovered chloro ketone for runs made in CH_3OD. [b] Rate data are not available, but the yield of ethyl cyclopentanecarboxylate obtained from a reaction of 2-bromocyclohexanone with sodium ethoxide in ethanol is only 21% as compared to 65–70% from 2-chlorocyclohexanone.[39] Assuming that k_{Br}/k_{Cl} for by-product formation (largely epoxy ether) is *ca.* 100 [see C. L. McCabe and J. C. Warner, *J. Amer. Chem. Soc.*, **70**, 4031 (1948)], this indicates that k_{Br}/k_{Cl} is *ca.* 30.

The correlation between a decreasing k_{Br}/k_{Cl} ratio and decreasing deuterium exchange at the α' position can be accounted for if it is assumed that elimination of halide ion occurs from a carbanion (enolate ion) intermediate with a rate constant k_2, and that the k_{-1}/k_2 ratio increases with the size of the substituents in the 4 position.[37a]



In the $ArCH_2COCH_2X$ system $k_{Br}/k_{Cl} = 63.5$ (Ar = C_6H_5) for reaction with sodium methoxide in methanol.[37c] If this is a concerted 1,3 elimination one would hardly expect substitution of a methyl group at the α position to have much of an effect on the k_{Br}/k_{Cl} ratio or on other aspects of the reaction, such as the Hammett ρ value or the response to changing methoxide ion concentration. The differences in the behavior of the two systems shown in Table III are therefore not consistent with a concerted mechanism.

Table III

Effect of Methyl Substitution on the Reaction of $ArCH_2COCH_2X$ with Sodium Methoxide in Methanol[37d]

	$ArCH_2$-$COCH_2X$ (15)	$ArCH_2CO$-$CHXCH_3$ (16)
Relative rates (X = Cl)[a]	1	>250[b]
Deuterium exchange,[c] %	~80	~5
k_{Br}/k_{Cl}	63	0.9
Hammett ρ	−5.0	+1.36
k (50% H_2O-CH_3OH)/k(CH_3OH)	110	6
Product with		
2 *M* $NaOCH_3$	100% **17**[e]	100% **18**
0.05 *M* $NaOCH_3$	100% **17**	**18** and **19**
0.0001 *M* $NaOCH_3$[d]	100% **17**	100% **19**

[a] For chloride ion release. [b] This is a minimum value; a change in rate-determining step precludes an exact determination.[37d] [c] Exchange prior to loss of chloride ion. [d] Addition of 0.05 *M* $NaOCH_3$ over a 6-hr period to a solution of **15** or **16** in methanol. [e] **17**, $ArCH_2CH_2CO_2CH_3$; **18**, $ArCH_2CH(CH_3)CO_2CH_3$; **19**, $ArCH_2COCH(OCH_3)CH_3$.

On the other hand, the changes recorded in Table III are explicable on the basis of the stepwise mechanism outlined in Scheme II.

First, note that the change from $C_6H_5CH_2COCH_2X$ (**15**) to $C_6H_5CH_2COCHXCH_3$ (**16**) caused the k_{Br}/k_{Cl} ratio to drop from 63 to 0.9. This is accompanied by a drop in the extent of deuterium exchange at the benzylic position from *ca.* 80% to *ca.* 5% and a change in Hammett ρ from −5.0 to + 1.36. Since **15** undergoes extensive deuterium exchange, $k_{-1} > k_2$, which makes k_2 rate limiting. The large leaving group effect and the large negative ρ are consistent with this view, as is the sensitivity of the rate to increased ionizing power of the solvent (the rate increases 110-fold in changing from

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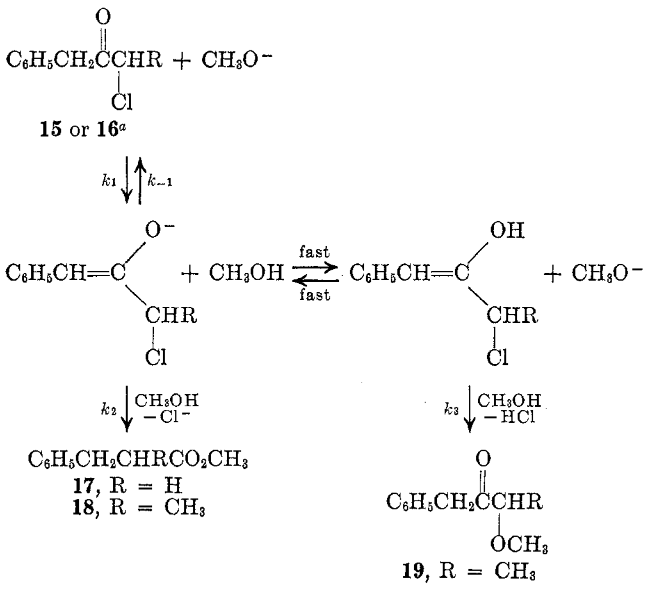
(41) J. Kennedy, N. J. McCorkindale, R. A. Raphael, W. T. Scott, and B. Zwanenburg, *Proc. Chem. Soc. London*, 148 (1964).

(42) E. W. Garbisch, Jr., and J. Wohllebe, *Chem. Commun.*, 306 (1968).

Scheme II



[a] For **15**, R = H, $k_{-1} > k_2$; for **16**, R = CH_3, $k_{-1} < k_2$.

CH_3OH to 50% (v/v) CH_3OH–H_2O). Ionization of halide ion from the enolate ion is greatly accelerated by the presence of a methyl group (compare **16** with **15**), so much so that for **16** $k_{-1} < k_2$, which makes k_1 rate limiting. This explains the absence of a leaving group effect, the lack of deuterium exchange, the change in sign for ρ from − to +, and the relative lack of sensitivity of the rate to increased ionizing power of the solvent (the rate increases by only sixfold in changing from CH_3OH to 50% (v/v) CH_3OH–H_2O). The change in product distribution observed for **16** when the reaction is carried out at low methoxide concentrations is accounted for as methanolysis of an enol allylic chloride intermediate.[37d,e] It is difficult, if not impossible, to reconcile the data for either **15** or **16** with a concerted mechanism.

An additional strong argument for a stepwise carbanion mechanism can be made on the basis of the large value and negative sign of ρ for the $ArCH_2COCH_2Cl$ system, and the fact that a much better correlation coefficient was obtained for a plot constructed from a modified Hammett equation which takes into account the prior equilibrium than from an ordinary Hammett equation which assumes, in essence, that the reaction occurs in one step.[37c]

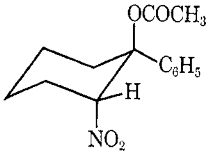
Our conclusion from the studies on the Ramberg–Bäcklund and Favorskii rearrangement reactions is that carbanion-type 1,3 eliminations are greatly preferred to concerted pathways, and that here, too, the concerted pathway could well be a myth.[43]

Carbanionic-Type 1,2-Elimination Reactions

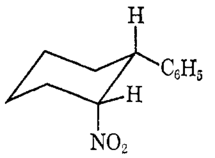
The current view of E2 reactions is that they occur by a spectrum of concerted mechanisms which differ in the extent to which bond making and bond breaking occurs in the transition state.[44,45] The E2 mechanism merges imperceptibly on the one side to carbonium ion type eliminations (E1) where the C–X bond breaks completely prior to the loss of the proton to the base (or solvent), and on the other side to carbanion-type eliminations ("E1cb"[46]) where the H–C bond breaks completely prior to loss of the halide ion (Scheme III).

The timing of these bond cleavages is hard to ascertain, and mechanistic classification of these reactions is difficult. A comparison in our laboratory of the rates of carbanion formation in the presence and absence of a potential leaving group has allowed us to contribute to this question.

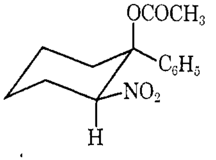
Several years ago we observed that the piperidine-initiated *syn* elimination of a molecule of acetic acid from **20** was 3.5-fold faster than the comparable *anti* elimination from **22**. Since *anti* eliminations in cyclohexane systems are usually much faster than *syn* eliminations it was concluded that the *syn* elimination with **20** was occurring by way of a carbanion (nitronate ion) intermediate. Inasmuch as the reactions of **20** and **22** were nearly identical with respect to solvent, salt, deuterium isotope, and substituent effects on the rates, carbanion mechanisms were suggested for both of these eliminations.[47] Faith in this interpretation was shaken somewhat, however, by comparison of the methoxide ion initiated rates of elimination for **20** and **22** with methoxide ion initiated rates of proton abstraction for the corresponding nitroalkanes, **21** and **23**, respectively.[48]



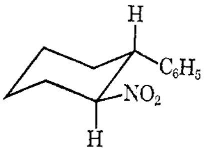
20 (70)



21 (350)



22 (60)



23 (1.0)

(numbers in parentheses are relative second-order rates with $NaOCH_3$–CH_3OH)

It will be noted that the methoxide ion promoted elimination reaction of **22** is 60 times as rapid as proton abstraction from the corresponding nitroalkane, **23**, whereas the elimination reaction for **20** is actually five times slower than proton abstraction from **21**. At first sight one might be tempted to ascribe the 60-fold rate

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(43) A corollary to this conclusion is that, if the presence of carbanions can be demonstrated in 1,3-elimination reactions, these carbanions will be on the reaction path. This conclusion probably also holds true for 1,2-elimination reactions, although this point is difficult to prove.[35]

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

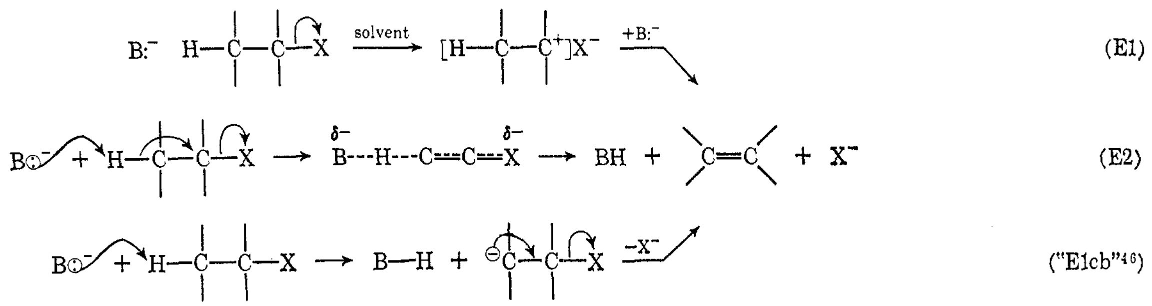
(45) J. F. Bunnett, *Angew. Chem. Int. Ed. Engl.*, **1**, 225 (1962); *Angew. Chem.*, **74**, 731 (1962); *Surv. Progr. Chem.*, **5**, (1969).

(46) (a) This symbol was devised for *reversible* carbanion formation. (b) There are actually three types of carbanion mechanisms. For examples, see F. G. Bordwell, M. M. Vestling, and K. C. Yee, *J. Amer. Chem. Soc.*, in press.

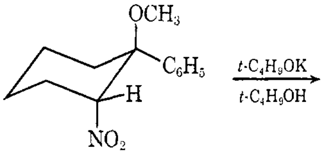
(47) F. G. Bordwell, R. L. Arnold, and J. B. Biranowski, *J. Org. Chem.*, **28**, 2496 (1963).

(48) F. G. Bordwell and M. M. Vestling, *J. Amer. Chem. Soc.*, **89**, 3906 (1967).

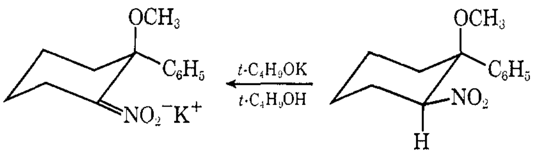
Scheme III



acceleration of **22** over **23** to a concerted *anti* E2 elimination and the 5-fold rate retardation to some factor disfavoring a nonconcerted *syn* elimination. However this analysis ignores the reason for the 350-fold difference in rates between **21** and **23**. Comparison with other nitrocyclohexane systems has shown that the rate for **21** is "normal," whereas that for **23** is retarded. Determinations of the Hammett ρ values for deprotonation of **21** and **23** (Ar in place of C_6H_5) and comparison with analogous ρ values for five-membered ring and acyclic analogs have shown that the retardation effect is associated with deformation of the chair in **23**.[49] This deformation allows the equatorial nitro and phenyl groups to move away from one another and causes the phenyl group to shield the acidic hydrogen atom. It seemed probable that this deformation should be less in **22** than in **23** because relief of the repulsion between the nitro and phenyl nitro groups in **22** is achieved only at the expense of increased repulsions between the nitro and acetoxy groups. This hypothesis was tested by preparing the methoxy analogs of the acetoxy compounds **20** and **22**. The methoxyl group in these analogs (**24** and **25**) should simulate the steric behavior of the acetoxy group, but the methoxyl group is such a much poorer leaving group that nitronate ion formation should be observable. This proved to be the case.[46b]

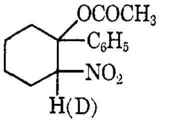


24 (relative rate = 1.0)



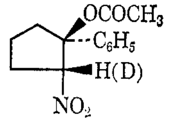
25 (relative rate = 1.4)

It will be observed that in this instance the isomer in which the nitro and phenyl groups are equatorial (**25**) actually reacts slightly *faster* than does **24** where the acidic hydrogen atom is equatorial. These results support the view that the methoxide-initiated reactions of **20** and **22** involve carbanion (nitronate ion) intermediates. This view is supported further by the similarity of the isotope effects (k_H/k_D) for the reactions of **20**, **22**, **26**, **27**, and **28** with methoxide ion.[46]



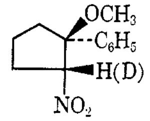
20 or 22

$k_H/k_D = 8.0$



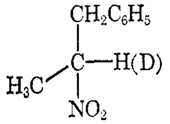
26

$k_H/k_D = 6.3$



27

$k_H/k_D = 7.4$



28

$k_H/k_D = 7.5$

isotope effects for reaction with $NaOCH_3$-CH_3OH at 25°

The reactions of **27** and **28** with methoxide ion unquestionably involve carbanion (nitronate ion) formation. If the elimination reactions of **20**, **22**, and **26** involve the formation of carbanion intermediates in steady-state concentrations one would expect primary isotope effects of a similar order of magnitude for those eliminations to those observed for nitronate ion formation from **27** and **28**. On the other hand, if the elimination reactions are concerted, one would expect a different, probably smaller, primary isotope effect. The data from the isotope effects, therefore, support the carbanion mechanism for the elimination reactions.

The failure of nitro acetate **22** to avail itself of the *anti* E2 mechanism is worthy of special comment. The sizable k_H/k_D ratio points to appreciable H–C bond breaking in the transition state. An appreciable negative charge must be building up on carbon in the transition state, but this negative charge is *not* delocalized to any very large extent to the oxygen atoms of the nitro group since the rate of formation of nitronate ions in other, comparable, instances has been found *not* to parallel nitronate ion stability.[49,50] It is surprising, then, that the negative charge is not dissipated by ejection of the acetate ion and simultaneous formation of a C═C bond (E2 mechanism). That it is not must mean that this process is energetically unfavorable. It is evidently more favorable energetically to form the nitronate ion, which subsequently ejects the acetate ion. In other words, it is energetically more economical to convert the two adjacent sp^3 carbon atoms to sp^2 carbon

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(49) F. G. Bordwell and K. C. Yee, *J. Amer. Chem. Soc.*, in press.

(50) F. G. Bordwell, W. J. Boyle, Jr., and K. C. Yee, *ibid.*, in press.

atoms one at a time than in a concerted fashion. This seems to indicate that structural reorganization is the costly factor in this reaction, and that the *preferred mechanism will be that requiring the least structural reorganization* (principle of least motion[51]). Carried to its extreme the principle of least motion predicts that most base- (or solvent)-initiated 1,2- or 1,3-elimination reactions will proceed by two-stage mechanisms and that the concerted mechanism will be relatively rare.[52] This prediction can be broadened to include all reactions where two (or more) bonds are formed and two (or more) bonds are broken.

Our conclusion is that two types of nucleophilic bimolecular concerted reactions may actually be myths (S_N2' reactions and base-initiated 1,3 eliminations) and that this mechanistic pathway may be much less common than has been assumed heretofore for other reactions in which two (or more) bonds are formed and two (or more) bonds are broken (such as 1,2-elimination reactions).

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(51) See J. Hine, *J. Org. Chem.*, **31**, 1236 (1966), and *J. Amer. Chem. Soc.*, **88**, 5525 (1966), for a discussion.

(52) There is strong evidence to indicate that base-initiated 1,2-elimination reactions with simple secondary alkyl halides are concerted,[53] but the status of the much more numerous elimination reactions where the hydrogen atom is rendered more acidic by the presence of an electron-withdrawing group in the 2 position or the tendency of the halogen to ionize is increased by the presence of an electron-releasing group at the 1 position is not so clear. Such reactions may well be stepwise.

(53) See, for example, R. A. Bartsch and J. F. Bunnett, *J. Amer. Chem. Soc.*, **90**, 408 (1968).

Petroleum Nitrogen Compounds and Oxygen Compounds

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Petroleum technologists have an obvious interest in the chemical structure of their basic raw material. However, concern for what petroleum is— and how it was formed—extends well beyond the oil industry. Its considerable abundance in the earth's crust along with oil shale and coal accounts for part of this broad interest. As the "molecular fossils" of ancient plant deposits, petroleum provides an intriguing link between the plant biochemistry of today and that of 100 million years ago. The apparent alteration of this original plant mass in the course of geological time has raised basic questions as to the kinds of chemistry that could have been involved in the formation of petroleum. As our knowledge of the composition of petroleum increases, moreover, we should receive fresh insights into the lipid composition of present plants.

The distillable fraction of petroleum is composed mainly of hydrocarbons, with variable amounts of sulfur compounds as the principal other constituents. Lesser amounts of nitrogen compounds and oxygen compounds make up the balance. Despite their smaller concentrations, these nitrogen and oxygen compounds play an important role in the science of petroleum. Their greater reactivity compared with that of the hydrocarbons makes them more sensitive indicators of the physicochemical environment of petroleum during its long storage in the ground. Similarly their greater structural complexity provides more stringent checks on proposed relationships between petroleum components and past or present plant constituents.

Finally, nitrogen compounds are important to the petroleum refiner. They poison many refining catalysts and cause undesirable deposits in finished products such as gasoline and jet fuel. A knowledge of the nature of these nitrogen compounds should prove useful in the development of processes for their removal and of additives for their control. Although the composition of the hydrocarbons and sulfur compounds in petroleum has been understood in general terms for about 15 years (*e.g.*, see ref 1), a similar understanding of the nitrogen compounds and oxygen compounds has unfolded only during the past 2 years. It is this story which shall now concern us.

The structural range of petroleum hydrocarbons is illustrated in Figure 1 as a three-dimensional, continuous array. Generally each of the compound types implied by Figure 1 occurs in a given petroleum as a continuous homologous series. Figure 2 diagrams the two main families of sulfur compounds found in petroleum, the sulfides and thiophenes. Other sulfur compound types (mercaptans, polysulfides, etc.) occur, but in generally smaller concentrations. Numerous individual hydrocarbons and sulfur compounds have been identified in petroleum (see ref 2). Within a given

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(1) (a) F. W. Melpolder, R. A. Brown, and T. A. Washall, *Anal. Chem.*, **26**, 1904 (1954); (b) H. E. Lumpkin and B. H. Johnson, *ibid.*, **26**, 1719 (1954).

(2) (a) M. A. Bestougeff in "Fundamental Aspects of Petroleum Geochemistry," B. Nagy and U. Colombo, Ed., Elsevier, Amsterdam