

The binary collision theory derives the approximate result that

$$\tau_J \approx \tau_\omega \quad (14)$$

Equations 14 and 12 provide a simple theory for the density and temperature dependence of τ_J which can be checked by nmr experiments performed on high-density fluids. Preliminary comparison with experiment indicates that the theory is fairly accurate.^{26,34} The physical picture associated with eq 14 is reasonable. From the definition of τ_J , we expect that τ_J should be proportional to the inverse of the average collision frequency since each collision should help a molecule "forget" about its initial angular momentum. It can be shown that the collision frequency is proportional to τ_E^{-1} . Thus, we expect $\tau_J \propto \tau_E$, which is what eq 14 says.

The orientational correlation functions measured by ir experiments²⁸ (eq 15) and by Raman scatter-

$$C_1(t) = \langle \mathbf{u} \cdot \mathbf{u}(t) \rangle = \langle P_1[\mathbf{u} \cdot \mathbf{u}(t)] \rangle \quad (15)$$

ing²⁸ (eq 16) can also be described with the binary

$$C_2(t) = \langle P_2[\mathbf{u} \cdot \mathbf{u}(t)] \rangle \quad (16)$$

collision theory. In these equations, $\mathbf{u}(t)$ denotes the unit vector parallel to an axis of molecule 1 at time t , and $P_l(x)$ is the l th Legendre polynomial of x . The results of the theory are expressed most simply in terms of the Laplace transforms of $C_l(t)$; they are

$$\tilde{C}_l(s) \approx \tilde{C}_l^{(1d)}(s + \tau_\omega^{-1}) / [1 - \tau_\omega^{-1} \tilde{C}_l^{(1d)}(s + \tau_\omega^{-1})] \quad (17)$$

(34) J. DeZwaan, R. J. Finney, and J. Jonas, *J. Chem. Phys.*, **60**, 3223 (1974).

where $\tilde{C}_l^{(1d)}(s)$ denotes the Laplace transform of $C_l(t)$ for a system of ideal gas (free) molecules. Equations 17 and 14 constitute Gordon's J diffusion model approximation for $C_l(t)$.³⁵ Experimental tests indicate that the approximation is qualitatively accurate.^{26,34,36} We note that the *microscopic* theory used to derive eq 17 does not require one to adopt the unphysical assumptions that are often attributed to Gordon's results. The interested reader should see ref 26.

In summary, we have emphasized the following concept: at the high densities which characterize most of the liquid phase, the dynamic and static structures of liquids are dominated by steric (excluded volume) effects. This idea, together with the approximation that the dynamics of hard spheres can be described in terms of uncorrelated binary collisions, gives rise to specific predictions about the density and temperature dependence of several relaxation times and correlation functions. These predictions should be qualitatively accurate for high density liquids composed of fairly spherical molecules. Further, the predictions can be tested by nmr, ir, and Raman experiments. We hope that in the near future constant density and temperature experiments will be performed on dense fluids to investigate fully the strengths and limitations of the theory we have described.

The research reviewed in this article has been supported by grants from the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society. Both are gratefully acknowledged.

(35) R. G. Gordon, *J. Chem. Phys.*, **44**, 1830 (1966).

(36) R. A. Assink and J. Jonas, *J. Chem. Phys.*, **57**, 3329 (1972).

The Role of High-Pressure Kinetics in Studies of the Transition States of Diels-Alder Reactions

James R. McCabe and Charles A. Eckert*

Department of Chemical Engineering, School of Chemical Sciences, University of Illinois, Urbana 61801

Received July 9, 1973

All chemists and chemical engineers dealing in any way with a chemical reaction must eventually investigate the properties of the reaction transition state.

Charles Eckert received his S.B. and S.M. degrees from Massachusetts Institute of Technology. After completion of Ph.D. work at Berkeley under John Prausnitz in 1964, he spent a year as NATO Postdoctoral Fellow at the Laboratoire des Hautes Pressions in France, and then joined the faculty of the University of Illinois, where he is Professor of Chemical Engineering. His major research interests are the applications of molecular thermodynamics to problems in phase equilibria and chemical kinetics and high-pressure solution kinetics.

James McCabe received the Ph.D. degree from the University of Illinois, Urbana, working with Professor Eckert. He is in the Process Engineering Department of Chevron Research Company, Richmond, Calif.

Much can be and has been learned by conventional research on rates, activation energies, and solvent and substituent effects, all at atmospheric pressure. High-pressure kinetic studies, however, offer yet another probe, yielding information unobtainable by other means, yet invaluable in elucidating the structure and properties of the reaction transition state.

High-pressure kinetics in solution permits observation of the volume of activation of a chemical reaction

$$\Delta v^\ddagger = -RT(\partial \ln k / \partial P)_T \quad (1)$$

and this volume change has proven quite useful as an interpretive tool for determining mechanisms of reaction.¹ Rigorously,² the volume of activation is the difference in partial molal volumes between the transition state M and the reactants A and B, for a bimolecular reaction (eq 2). The partial molal vol-

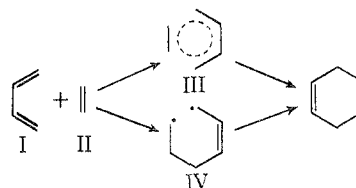
$$\Delta v^\ddagger = \bar{v}_M - \bar{v}_A - \bar{v}_B \quad (2)$$

ume of the transition state itself may be evaluated from eq 2 by separate determination of the reactant partial molal volumes. The variations of this quantity \bar{v}_M have been used in evaluating several properties of the transition state, such as dipole moment, internal secondary interactions, and specific solvent interactions.³

The purpose of this Account is to demonstrate how appropriate application of new high-pressure kinetic data has markedly enhanced our understanding of cycloaddition reactions. Specifically, we wish to report how a number of mechanistic ambiguities for Diels–Alder reactions have been resolved by recent determinations of activation volumes. The Diels–Alder reaction is of considerable importance in synthetic organic chemistry, primarily because of the ease in using it for the introduction of heterocyclic and aromatic rings, as well as the formation of bicyclic compounds. Yet, in spite of the importance of this reaction, the interpretation of its mechanism had been ambiguous until the advent of recent high-pressure kinetic studies.

The mechanistic interpretation is most straightforward for 1,2 cycloadditions, as the thermal concerted reaction is forbidden by the principle of the conservation of orbital symmetry.⁴ Theoretically, a thermal concerted 2 + 2 cycloaddition would be permitted only by means of a suprafacial–antarafacial alignment of the orbitals, but this would be virtually impossible because of the extreme distortion required in the small ring. Many investigations substantiating the two-step mechanism have been reported.⁵

On the other hand, two mechanisms are permitted for the 1,4 cycloaddition of a diene, I (which may be substituted), to a dienophile, II (generally a conjugated olefin), and the evidence for either path has often been vague or contradictory. The reaction may be a concerted four-center mechanism, with two



bonds forming in the transition state III. Alternatively, the reaction may go by a two-step route in which the first and rate-limiting step is the one-bond closure to form a true diradical intermediate, IV, which may then proceed to form the product.

Classical mechanistic studies, including atmospheric pressure kinetics, provided substantial evidence to support either of the two proposed mechanisms.⁶ The issue was further confused by early and less precise high-pressure kinetic results. It is our purpose to demonstrate in this paper the role played in understanding this reaction by newer, more accurate, high-pressure kinetic data taken in our laboratories using a new technique and to show the value of very accurate determinations of the activation volumes as a tool for studying both the structure and the properties of reaction transition states. Certainly the success of these new experimental techniques in studying Diels–Alder reactions suggests strongly that these methods should be applicable to mechanistic studies of many other reaction types.

Mechanistic Applications of High-Pressure Kinetics

The interpretation of volumes of activation as evaluated from high-pressure kinetic data by eq 1 is quite straightforward. Normally, formation of each bond corresponds to a molal volume shrinkage of 10–15 cm³, and for nonpolar reactions, solvation and electrostriction effects are generally small. Thus, for the two-step mechanism one would expect Δv^\ddagger to be –10 to –15 cm³, and for the concerted case, –20 to –30 cm³.

Early high-pressure studies⁷ of 1,4-cycloaddition reactions were interpreted with respect to the volume change on reaction (see Table I). However, the data were of limited precision, and the inconclusive results were questioned with respect to both accuracy and analysis.⁸ Walling and coworkers^{7b,c} interpreted the results of reactions 1 and 3 in terms of a two-step mechanism. Benson and Berson⁸ used a different analytical method to evaluate the activation volume from the isoprene dimerization data and obtained a value of $\Delta v^\ddagger = -38$ cm³/mol, suggesting a concerted mechanism. Similarly, Gonikberg⁹ corrected the older cyclopentadiene dimerization data for compression of reactants and products and found

(1) (a) S. D. Hamann in "High Pressure Physics and Chemistry," Vol. 2, R. S. Bradley, Ed., Academic Press, New York, N. Y., 1963, Chapter 8; (b) E. Whalley, *Advan. Phys. Org. Chem.*, **2**, 93 (1964); (c) W. J. le Noble, *Progr. Phys. Org. Chem.*, **5**, 207 (1967); (d) K. E. Weale, "Chemical Reactions at High Pressures," Spon, London, 1967; (e) R. C. Neuman, Jr., *Accounts Chem. Res.*, **5**, 381 (1972).

(2) For eq 1 to be rigorous without correction terms for compressibility, it is essential that the rate constant k be expressed in pressure-independent concentration units rather than the more conventional moles/liter.^{1a} In this work we shall express all rate constants in mole fraction concentration units.

(3) (a) H. Heydtmann, A. P. Schmidt, and H. Hartmann, *Ber. Bunsenges. Phys. Chem.*, **70**, 444 (1966); (b) J. R. McCabe, R. A. Grieger, and C. A. Eckert, *Ind. Eng. Chem., Fundam.*, **9**, 156 (1970); (c) R. A. Grieger and C. A. Eckert, *J. Amer. Chem. Soc.*, **92**, 2918, 7149 (1970); (d) J. R. McCabe and C. A. Eckert, *Ind. Eng. Chem., Fundam.*, **13**, 168 (1974).

(4) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, Weinheim, 1970.

(5) (a) E. E. Lewis and M. A. Neylor, *J. Amer. Chem. Soc.*, **69**, 1968 (1947); (b) E. C. Coyner and W. S. Hillman, *ibid.*, **71**, 324 (1949); (c) H. W. B. Reed, *J. Chem. Soc.*, 685 (1951); (d) E. F. Silversmith, Y. Kitahara, M. C. Caserio, and J. D. Roberts, *J. Amer. Chem. Soc.*, **80**, 5840 (1958); (e) J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962); (f) P. D. Bartlett, L. K. Montgomery, and B. Seidel, *J. Amer. Chem. Soc.*, **86**, 616 (1964); (g) P. D. Bartlett, L. K. Montgomery, and K. Schueller, *ibid.*, **86**, 622 (1964).

(6) (a) J. Sauer, R. Huisgen, and R. Grashey, in "The Chemistry of Alkanes," S. Patai, Ed., Interscience, New York, N. Y., 1964; (b) H. Charton, *J. Org. Chem.*, **31**, 3745 (1966); (c) W. C. Herndon and L. H. Hall, *Tetrahedron Lett.*, **32**, 3095 (1967); (d) J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **6**, 16 (1967); (e) S. Seltzer, *Advan. Chem. Alicycl. Compounds*, **2**, 1 (1968); (f) M. Taagepera, Ph.D. Thesis, University of Pennsylvania, Philadelphia, Pa., 1970; (g) S. Kunichika, T. Okamoto, and K. Yoshikawa, *Bull. Inst. Chem. Res., Kyoto Univ.*, **49**, 109 (1971); (h) T. Inukai and T. Kojima, *ibid.*, **36**, 921 (1971).

(7) (a) B. Raistrick, R. H. Shapiro, and D. M. Newitt, *J. Chem. Soc.*, 1770 (1939); (b) C. Walling and J. Peisach, *J. Amer. Chem. Soc.*, **80**, 5819 (1958); (c) C. Walling and H. J. Schuger, *ibid.*, **85**, 607 (1963).

(8) S. W. Benson and J. A. Berson, *ibid.*, **84**, 152 (1962).

(9) (a) M. G. Gonikberg and L. F. Vereshagin, *Zh. Fiz. Khim.*, **23**, 1447 (1949); (b) M. G. Gonikberg, *ibid.*, **34**, 106 (1960).

Table I
Early Diels-Alder High-Pressure Data

Reaction	Δv^\ddagger , cm ³ /mol	Δv_{rxn} , cm ³ /mol
(1) Isoprene dimerization ^{7b}	-24.3	-45.5
(2) Cyclopentadiene dimerization ^{7a}	-22.3	-32.2
(3) 2,3-Dimethylbutadiene + butyl acrylate ^{7c}	-22.6	-42.2

Table II
Diels-Alder Activation and Reaction Volumes

Reaction, solvent, temperature, °C	Δv^\ddagger , cm ³ /mol	Δv_{rxn} , cm ³ /mol
Maleic anhydride + piperylene, 1,2-dichloroethane, 35° ^{8d}	-44.7	-33.3
Maleic anhydride + isoprene, acetone, 35° ^{18a}	-39.0	-35.9
Maleic anhydride + chloroprene, acetonitrile, 65° ^{8d}	-41.6	-36.9
Maleic anhydride + 1-methoxy- butadiene, 1,2-dichloroethane, 35° ^{18b}	-43.7	-30.4
Maleic anhydride + 2-methoxy- butadiene, acetone, 50° ^{8d}	-36.2	-34.1
Acrylonitrile + isoprene, butyl bromide, 21° ¹⁴	-33.1	-37.0
Methyl acrylate + isoprene, butyl bromide, 21° ¹⁴	-30.8	-36.9
Methyl vinyl ketone + isoprene, butyl bromide, 21° ¹⁴	-36.9	-37.1
Maleic anhydride + 1,3-cyclo- hexadiene, dichloromethane, 35° ^{3c}	-39.6	-30.3
Dimethyl acetylenedicarboxylate- cyclopentadiene, ethyl acetate, 10° ^{3c}	-30.2	-33.9

that the activation and reaction volumes were essentially equal, consistent with a one-step mechanism. Because of experimental difficulties and disagreement over the treatment of high-pressure data, as indicated above, the early results could not be regarded as mechanistically conclusive.

All of these results indicated the need for a more accurate high-pressure kinetic technique and a more rigorous, unambiguous treatment of the experimental data. Since Δv^\ddagger really represents the second derivative of the actual concentration *vs.* time raw data, the highest precision is required to minimize all uncertainties and errors. For this purpose, we developed the improved *in situ* initiation technique¹⁰ which eliminates errors due to heat of compression and starting time uncertainties.¹¹ Also, the analytical method for evaluating the derivative in eq 1 is critical. By our procedure,¹² we feel we can determine activation volumes to an uncertainty substan-

(10) R. A. Grieger and C. A. Eckert, *AIChE J.*, 16, 766 (1970).

(11) The classical technique for high-pressure kinetic studies involves compression of a premixed reaction solution, using either blank run calibration or precooling to minimize error due to heat of compression. This heat of compression is quite appreciable, such that the adiabatic heating in a typical organic solvent might amount to as much as 50° at 3000 atm. Typically the thermal half-life of high-pressure equipment is in the range of 3-5 min, so even for moderately slow reactions, large corrections are required to account for this effect. The result is appreciable error in the reaction temperature and/or time. The *in situ* method¹⁰ involves compression of the unmixed reactants followed by thermal equilibration. Then the reactants are mixed magnetically, in a few seconds, and in dilute solution the thermal effects are negligible. Moreover, in the work reported here a new high-pressure sampling technique was used,¹⁰ so that the uncertainty in reaction time was a few seconds for each point. As a result very good accuracy and precision were possible for reactions with half-lives of as little as 10 min.

(12) C. A. Eckert, J. S. Smith, and C. K. Hsieh, Abstracts, 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973.

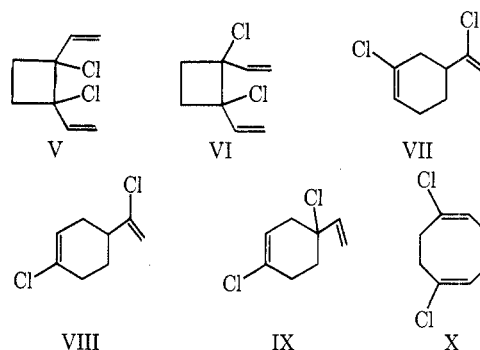
tially less than ± 1 cm³, and some typical results from our laboratories^{3c,d,13} and others¹⁴ are shown in Table II.

The large negative activation volumes reported can be interpreted only in terms of a concerted mechanism, especially when compared with the volume changes on reaction. Although one cannot say whether the partial formation of one bond is farther advanced than the other, certainly both bonds are partially formed in the transition state. The fact that in some cases the activation volume is more negative than the volume change on reaction, meaning that the transition state is actually more compact than the product, probably indicates the existence of secondary π interactions in the transition state, to be discussed below.

Competitive 1,2 and 1,4 Cycloadditions

Some cycloaddition reactions give both 2 + 2 and 2 + 4 adducts, but the variations in mechanism are clearly discernible from the available high-pressure kinetic studies. For example, Stewart¹⁵ reported that tetracyanoethylene and 4-methyl-1,3-pentadiene react under mild conditions to give both the cyclobutane and cyclohexene adducts and that the relative amounts of each were strongly solvent and temperature dependent. If both adducts were formed from a common, rate-limiting transition state, which could collapse to form either product (*i.e.*, a two-step mechanism), the product distribution would be entirely independent of these effects; thus these data indicate that two separate mechanisms must be in operation.^{5f,g,16}

The 1,2 cycloaddition does proceed by a diradical mechanism, but the case is not conclusive for either the diradical or concerted mechanism for the 1,4 addition when in competition with the 1,2 addition. Stewart¹⁷ has recently presented a good case for the existence of both mechanisms in competition from high-pressure studies of product distributions and kinetics. He showed that the thermal dimerization of chloroprene yields both cyclobutane (V, VI) and cy-



(13) R. A. Grieger and C. A. Eckert, *Trans. Faraday Soc.*, 66, 2579 (1970); (b) R. A. Grieger and C. A. Eckert, *Ind. Eng. Chem., Fundam.*, 10, 20 (1971).

(14) C. Brun and G. Jenner, *Tetrahedron*, 28, 3113 (1972).

(15) C. A. Stewart, *J. Amer. Chem. Soc.*, 84, 117 (1962).

(16) (a) P. D. Bartlett and L. K. Montgomery, *J. Amer. Chem. Soc.*, 86, 628 (1964); (b) J. C. Little, *ibid.*, 87, 4021 (1965); (c) R. E. Banks, A. C. Harrison, and R. N. Haszeldine, *Chem. Commun.*, 338, 556 (1966); (d) J. J. Eisch and G. R. Husk, *J. Org. Chem.*, 31, 589 (1966); (e) W. C. Herndon and J. Feuer, *ibid.*, 33, 417 (1968); (f) P. D. Bartlett, *Science*, 159, 833 (1968).

(17) (a) C. A. Stewart, *J. Amer. Chem. Soc.*, 93, 4815 (1971); (b) C. A. Stewart, *ibid.*, 94, 635 (1972).

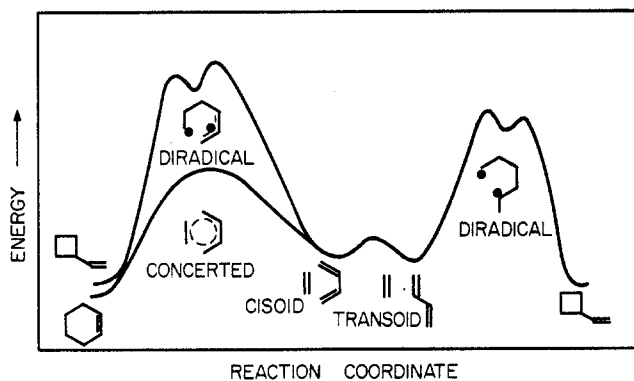


Figure 1. Energy profile for cycloaddition reactions; reactants are in the center and products on either side.

Table III
Chloroprene Dimerization Isomers

	Isomer				
	V	VI + X	IX	VII	VIII
% isomer, 1 atm	4.2	12	13	17	16
% isomer, 10,000 atm	4.6	2.8	3	59	30
$-\Delta v^\ddagger$, cm ³ /mol	22	22	22	31	29
$-\Delta v_{rxn}$, cm ³ /mol	27	(27)	32	32	32

clohexene adducts (VII, VIII, IX), and some cyclooctadiene adduct (X), as shown in Table III.

A comparison of the isomer distributions and activation volumes clearly indicates that there are two different mechanisms occurring. Isomers V, VI, and X should result from a diradical reaction, which is favored only with head-to-head orientation of the reacting molecules. Isomers VII and VIII are made by a concerted reaction, favored only with the unsubstituted vinyl group serving as a dienophile. If all isomers resulted from a common transition state, the distribution would be independent of pressure, but the results in Table III indicate a large increase in the percentage of VII and VIII isomers with pressure. The difference of 7–9 cm³/mol in activation volumes is about what would be expected as the difference between the formation of one bond and of two bonds in the transition state. Also, the activation and reaction volumes are nearly the same for the VII and VIII isomers, a typical circumstance with concerted Diels–Alder reactions (see Table II), but the activation volumes for the diradical isomers are 5–10 cm³/mol less than the reaction volumes, indicating that only one bond is completely formed in the transition state. Stewart's work indicates the value of high-pressure studies in elucidating a complex reaction mechanism in a situation where ordinary atmospheric pressure evidence could be inconclusive. As a result, we may now paint a reasonable picture of competitive 1,2 and 1,4 cycloadditions. The situation can best be visualized by considering a free-energy diagram proposed by Bartlett¹⁸ as shown in Figure 1.

The diene can exist in either the cisoid or the transoid form, with the transoid form having a lower energy level. The Diels–Alder 1,4 addition occurs only with the cisoid diene *via* a concerted mechanism, as predicted by the Woodward–Hoffmann orbital symmetry rules. However, a diradical is possible, although at a higher energy level, which can lead to

both 1,2- and 1,4-addition products. The transoid diene reacts thermally only *via* a diradical mechanism to form the cyclobutane adduct.

Secondary Interactions

The possibility of secondary interactions between nonbonding sites in the transition state was first proposed by Woodward and Katz.¹⁹ Woodward and Hoffmann²⁰ have also shown that the orbital interactions between unsaturated centers in a concerted cycloaddition reaction, such as that between a cyclic diene and a cyclic dienophile, will tend to lower the energy of the endo transition and thus determine the stereospecificity of the reaction. Houk²¹ has found that the presence of a second double bond in the dienophile in cycloadditions with cyclic reactants transforms a nonselective process into a stereoselective one. This last finding is seen as the result of stabilization of the transition state by secondary orbital interactions.

High-pressure kinetic studies of several Diels–Alder reactions (see Table II) show strong evidence for secondary interactions in that, for all of the reactions of maleic anhydride, the volume of activation was more negative than the volume change on reaction. This results in a transition state more compact than the adduct, and a typical volume profile along the reaction coordinate is shown in Figure 2. This effect can be visualized for the transition state for 1,4-diene addition to maleic anhydride in Figure 3 where carbon atoms 1' and 3 and 4' and 4 are bond-forming centers, while secondary interactions occur between atoms 3' and 5 and between 2' and 2.

The last reaction shown in Table II, cyclopentadiene + dimethyl acetylenedicarboxylate, does not exhibit a volume minimum in the transition state. This is to be expected if the volume minimum is due to secondary interactions, since the nonbonding carbons in the acetylenic dienophile are situated such that they do not allow secondary π interactions with the diene to occur. Also, no minima are observed for the three reactions reported by Brun and Jenner,¹⁴ but these all involve singly conjugated dienophiles, which thus have only a single site available for secondary interaction as opposed to two in the maleic anhydride.

Table IV indicates how diene substituents affect the secondary interactions occurring in the transition state. It can be seen that 1-substitutions in the diene lead to a more compact transition state than 2-substitutions. This seems unusual since it is the 2 and 3 positions in the diene which would be involved in secondary interactions, as indicated in Figure 3. However, it should be noted that the methyl and methoxy groups are both electron donors in the 1 position. Since a partial transfer of charge from the electron-rich diene to the electron-deficient dienophile occurs in the course of most Diels–Alder reactions, electron-donating groups on the bond-forming carbon 1 should enhance this electron flow. This may explain the larger effects of secondary interactions observed with 1-substitutions.

(19) R. B. Woodward and T. J. Katz, *Tetrahedron*, 5, 70 (1959).

(20) R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, 87, 4388 (1965).

(21) K. N. Houk, *Tetrahedron Lett.*, 30, 2621 (1970).

(18) P. D. Bartlett, *Quart. Rev. Chem. Soc.*, 24, 473 (1970).

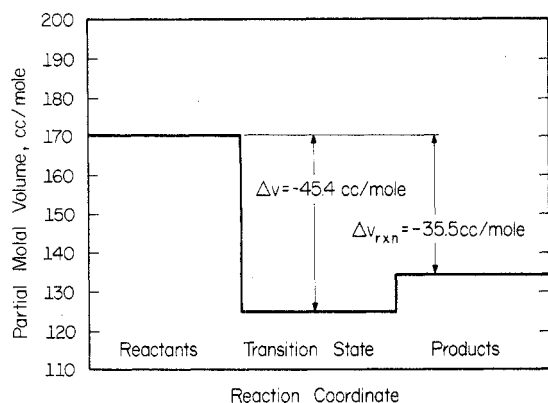


Figure 2. Volume profile along the reaction coordinate for the reaction of maleic anhydride with 1-methoxybutadiene in *n*-butyl chloride at 35.00°.

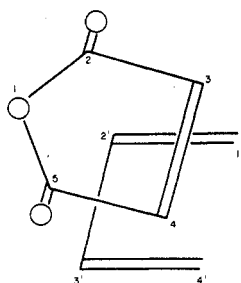


Figure 3. The transition state for Diels-Alder diene additions to maleic anhydride.

Table IV
Substituent Effects on Secondary Interactions

Reaction	Vol minimum, ^a cm ³ /mol	Act. energy, ^a kcal
Maleic anhydride + 1-methylbutadiene ^{3d}	-11.6	11.0
Maleic anhydride + 2-methylbutadiene ^{3o, 13a}	-2.4	13.1
Maleic anhydride + 1-methoxybutadiene ^{13b}	-11.8	10.0
Maleic anhydride + 2-methoxybutadiene ^{3d}	-1.9	13.9
Maleic anhydride + 2-chlorobutadiene ^{3d}	-4.7	15.3

^a Average of values in six to nine solvents.

The strong secondary interactions noted with 1-substituted dienes also seem to have the effect of stabilizing the transition state and lowering the activation energy with respect to the reactions with 2-substituted dienes. As indicated in Table IV, the activation energies of the reactions with 1-substituted dienes are 2–5 kcal/mol lower than those with 2-substituted dienes. Houk²¹ has also reported a stabilizing effect of 2.5–5 kcal/mol for reactions which exhibit stereoselectivity due to secondary orbital interactions.

Substituent Effects

Many studies of substituent effects on rates of Diels-Alder reactions have been reported,^{6a,d,e,22}

(22) (a) E. J. Dewitt, C. T. Lester, and G. A. Ropp, *J. Amer. Chem. Soc.*, 78, 2101 (1956); (b) D. Craig, J. J. Shipman, and R. B. Fowler, *ibid.*, 83, 2885 (1961); (c) J. Sauer, D. Lang, and A. Mielert, *Angew. Chem.*, 74, 352 (1962); (d) D. Lang, Ph.D. Thesis, University of Munich, 1963; (e) C. A. Stewart, Jr., *J. Org. Chem.*, 28, 3320 (1963); (f) J. Sauer, H. Wiest, and A. Mielert, *Chem. Ber.*, 97, 3183 (1964); (g) T. Inukai and T. Kojima, *Chem. Commun.*, 1334 (1969).

Table V
Relative Solvent Effects

Reaction	Trans state μ_M , Debyes	Sol eff, k_A/k_B^a	Relative rate constant ^b
Maleic anhydride + 1-methoxybutadiene	7	6.1	95
Maleic anhydride + 2-methoxybutadiene	4	7.4	3
Maleic anhydride + 1-methylbutadiene	4	3.9	19
Maleic anhydride + 2-methylbutadiene	3	3.9	11
Maleic anhydride + 2-chlorobutadiene	3	6.5	0.4

^a A = acetonitrile, $\epsilon = 37.5$; B = *n*-butyl chloride, $\epsilon = 7.4$.
^b Average value for six to nine solvents.

but in general such results yield little conclusive information about how the properties of the transition state itself are influenced by substituents; we can elucidate substantially more information if the effect of pressure on the reaction rate is also measured.

As mentioned above, the partial molal volume of the transition state itself, \bar{v}_M , as found from eq 2, is frequently useful in ascertaining properties of the transition state, such as, for example, its dipole moment. Application of the Kirkwood²³ approach for an ideal dipole μ in a dielectric continuum of dielectric constant ϵ can be used to yield a relationship for the solvent dependence of the activation volume on the dielectric properties of the solvent. The limitations involved in the simplifying assumptions of this technique are many, but it does provide the only basis currently available for semiquantitative estimation of dipole moments of reaction transition states.

The Kirkwood relationship has the form

$$\bar{v}_M = \bar{v}_M^0 - \frac{\mu_M^2}{r_M^3} \frac{\partial}{\partial P} \left(\frac{\epsilon - 1}{2\epsilon + 1} \right) \quad (3)$$

where \bar{v}_M^0 is the partial molal volume of the transition state in the absence of electrostriction and $(\partial/\partial P)[(\epsilon - 1)/(2\epsilon + 1)]$ is a property of the solvent. Permitting the many assumptions involved in deriving eq 3, then a plot of \bar{v}_M vs. $(\partial/\partial P)[(\epsilon - 1)/(2\epsilon + 1)]$ should be linear with a slope proportional to μ_M^2 .²⁴ If the radius of the transition state is approximated from the molar volume, μ_M may be estimated.

The relative polarities of the transition states of five substituted butadienes reacting with maleic anhydride have been evaluated from eq 3^{3d} and are shown in Table V. Only the transition state with 1-methoxybutadiene is significantly more polar than either reactants or products. In general, the effect of substituents on transition-state polarity appears to be $\text{OCH}_3 > \text{CH}_3 > \text{Cl}$, with substitution at the 1 or bond-forming position resulting in a more polar transition state than 2-substitution.

The discovery of a quite polar transition state in a Diels-Alder reaction suggests that perhaps the reaction will show kinetic solvent effects more typical of

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(24) Although this method is really only semiquantitative at best, due to the limiting assumptions involved in the Kirkwood treatment, it is clearly superior to other methods proposed^{3a} involving plots of difference quantities, such as k , Δv^\ddagger , or Δs^\ddagger , vs. dielectric properties, which have been shown to yield much poorer estimates of μ_M .^{3d}

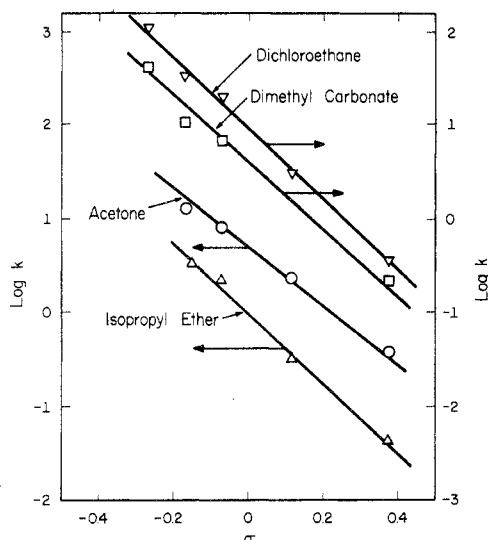


Figure 4. A Hammett σ - ρ plot for the addition of substituted 1,3-butadienes to maleic anhydride in four different solvents. Values of σ_{para} are used for 1-substitution and of σ_{meta} for 2-substitution.

polar reactions. However, the relative solvent effects observed indicate that this is not the case (see Table V). With a polar reaction one would expect to see the largest solvent effect with an increase in solvent polarity for the reaction having the most polar transition state. The fact that the reaction with the least polar transition state (maleic anhydride + chloroprene) shows a greater kinetic solvent effect than the most polar one confirms the nonpolar nature of this Diels-Alder reaction.

Moreover, the relative rates correlate rather poorly with the values of μ_M , but fall in the exact order of the activation energies (see Table IV). Thus, it appears that the kinetic substituent effects are primarily due to the electron-donating and -withdrawing characteristics of the substituents rather than any effects they may have on the transition-state polarity.

This conclusion is further substantiated by the success of various linear free energy models in predicting substituent effects on rates.^{6b,h,22f,25} Our high-pressure studies have led to an excellent correlation of the substituent effects for reactions of substituted 1,3-butadienes with maleic anhydride by the Hammett ρ - σ equation,^{3d} and an example is given in Figure 4. Similar agreement was found with the data sets from the literature.^{22b,c} The average ρ calculated from these plots is about -3.5 . This large negative value of σ indicates that the reaction rate will be greatly enhanced by electron-donating substituents, which have a negative value of σ .

The success of the Hammett equation with the essentially nonaromatic Diels-Alder reaction is in excellent agreement with the results of the high-pressure kinetic studies, which have shown Diels-Alder reactions to proceed *via* a concerted, four-center mechanism. The transition state resembles a quasiaromatic conjugated ring, and thus is similarly affected by the electron withdrawal and donation of

substituents. The large negative ρ , compared with typical Hammett ρ values, is likely the result of substituents being situated directly on the "ring" rather than somewhat removed on a side chain.

Comparison of the polarities of the reactants with those of the transition states as estimated from high-pressure kinetic data, as well as the kinetic substituent effects, both substantiate the essentially nonpolar nature of Diels-Alder reactions. These results have also led to a good correlative and predictive technique for kinetic solvent effects^{3d,26} based on regular solution theory.²⁷ An example of such prediction is shown in Figure 5.

Catalyzed Reactions

Finally, another important example of the application of high-pressure kinetics to the elucidation of the structure of a transition state is provided by studies of the mechanism of the catalyzed Diels-Alder reaction. Although the results of many atmospheric pressure investigations, mostly product studies, led to ambiguous or inconclusive conjectures about the mechanism, the activation volume measurements are quite conclusive.

Many examples have been reported²⁸ in which AlCl_3 or other Lewis acids were useful in catalyzing Diels-Alder reactions, especially for those cases where the dienophile contained a conjugated carbonyl group. It appears clear that the mechanism of catalysis involves complex formation of the AlCl_3 with the carbonyl oxygen, withdrawing electrons from the conjugated system and rendering the dienophile (the electron acceptor in the normal Diels-Alder addition) more reactive. This conclusion is supported by infrared studies of complexes between ethyl acetate and group III and group IV halides,²⁹ as well as by the reaction kinetics.³⁰ For cases where the dienophile has a conjugated carbonyl group, the initial rate has been found to be second order overall, first order in diene and first order in the dienophile.

Uncertainty has existed, however, about the mechanism of the catalyzed Diels-Alder reaction. For example, due to the very high polarity of the dienophile- AlCl_3 complex, one was tempted to propose a two-step mechanism involving a dipolar open-chain intermediate.³¹ Also a significant body of evidence also existed suggesting concerted mechanism for this catalyzed reaction,³² so, as in the study of the unca-

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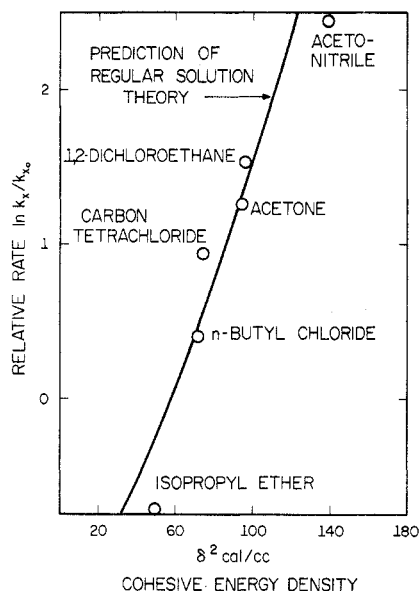


Figure 5. Kinetic solvent effects predicted by regular solution theory for the Diels-Alder reaction of 2-methoxybutadiene with maleic anhydride at 50.00°.

talyzed reaction, the exact nature of the mechanism was ambiguous. However, a recent high-pressure study³³ of the mechanism of the AlCl_3 catalyzed Diels-Alder addition of 2,3-dimethylbutadiene to *n*-butyl acrylate has shown clearly that this reaction follows a single-step, concerted mechanism.

As pointed out above, single-bond formation leads to a value of Δv^\ddagger of -10 to -15 cm^3/mol , compared to about twice that shrinkage for a concerted two-bond forming reaction. For example, for the Friedel-Crafts reaction between benzene and benzoyl chloride in the presence of AlCl_3 to give benzophenone, the volume change on reaction is -40 to -45 cm^3/mol and the activation volume is -13.4 cm^3/mol .³⁴ This is consistent with the fact that the Friedel-Crafts reaction occurs by a two-step process with the first step rate-determining. Thus, information about the volume of activation for the reaction, both with and without a catalyst, should indicate whether the reaction is one step or two, and even more clearly whether the addition of the catalyst alters the mechanism. The volumes of activation and reaction reported by Poling and Eckert³³ are shown in Table

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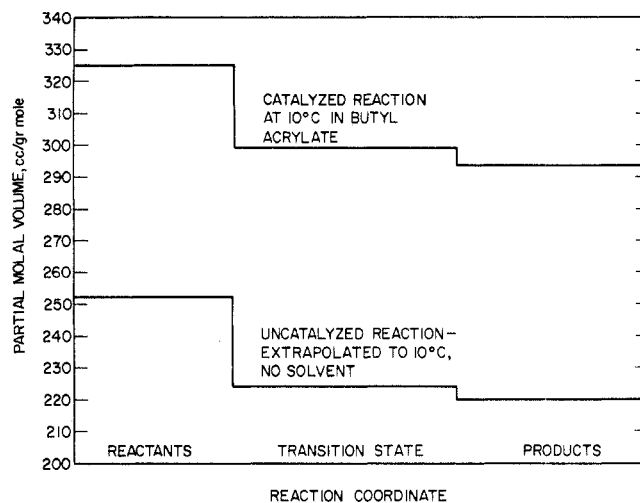


Figure 6. Volume profiles along the reaction coordinate for the addition of 2,3-dimethylbutadiene to *n*-butyl acrylate, both with and without AlCl_3 catalyst.

Table VI
Catalyzed and Uncatalyzed Diels-Alder Activation Volumes in Reaction of Dimethylbutadiene with Butyl Acrylate

	Catalyzed	Uncatalyzed
Δv^\ddagger , cm^3/mol	-25.7	-28.6
Δv_{rxn} , cm^3/mol	-29	-32

VI, and show clearly the concerted mechanism, forming two bonds in the activation process.

The relative partial molal volume profiles along the reaction path are compared in Figure 6. The volume profiles of both catalyzed and uncatalyzed reactions are essentially identical except that the catalyzed reaction is shifted upward by approximately 73 cm^3/mol due to the presence of the AlCl_3 . This not only suggests that the two reactions proceed by the same mechanism but also substantiates the role of the AlCl_3 in the catalyzed reaction. Figure 6 indicates that, as the reaction proceeds, the AlCl_3 remains complexed with the transition state, and only at some later time does the AlCl_3 become available for reuse as a catalyst by dissociation of the complex with adduct.

This reaction provides an excellent example of the manner in which the results from high-pressure kinetic studies can be used to clarify uncertain and ambiguous mechanistic evidence. However, one should be cautioned that specific results such as these cannot necessarily be extended to all Diels-Alder and related reactions.

The authors gratefully acknowledge the continued financial support of this work by the National Science Foundation.