

THE THEORY OF CYCLOADDITION REACTIONS

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I. Introduction

A. SCOPE

This article will review and summarize the applications of theoretical principles and calculations to cycloaddition reactions. These reactions are defined as thermal or photochemical additions or dimerizations which result in carbocyclic or heterocyclic rings. The reverse reactions are also meant to be included within this definition. Several characteristics of cycloaddition reactions are amenable to theoretical treatment. Questions of stereoselectivity and regioselectivity, substituent and structural effects upon the rates of reaction, and the ubiquitous problem as to whether or not a particular reaction takes place in a concerted manner will be discussed in this review.

The primary recent theoretical developments in this field of cycloaddition reactions are the use of quantum perturbation theory and the direct quantum-mechanical calculation of potential energy surfaces. There have been some significant developments of empirical methods for the estimation of en-

ergies and entropies of activation. Orbital symmetry rules and correlation diagrams for concerted reactions are also of high utility in the treatment of cycloaddition reactions, but since detailed expositions have been published,¹⁻⁵ these two latter topics will not be reviewed here. The less familiar perturbational approach will be discussed in detail.

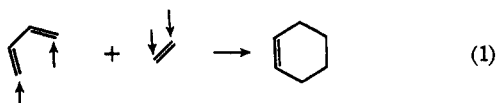
The field of cycloaddition reactions is a fertile, growing area in which nearly all organic chemists seem to have a particular interest. A large fraction of the review literature of organic chemistry is therefore devoted to the synthetic and mechanistic aspects of cycloaddition reactions. Recent reviews (1960-1970) on Diels-Alder reactions⁶⁻¹³ and other thermal cycloadditions,¹⁹⁻²⁵ photochemical cycloaddition reactions,^{20,26-57}

- (1) S. I. Miller, *Advan. Phys. Org. Chem.*, **6**, 185 (1968).
- (2) G. B. Gill, *Quart. Rev., Chem. Soc.*, **22**, 338 (1968).
- (3) J. J. Vollmer and K. L. Servis, *J. Chem. Educ.*, **45**, 214 (1968).
- (4) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970.
- (5) S. S. Novikov, G. A. Shvekhgeimer, and A. A. Dudinskaya, *Russ. Chem. Rev.*, **29**, 79 (1960).
- (6) J. G. Martin and R. K. Hill, *Chem. Rev.*, **61**, 537 (1961).
- (7) M. G. Ettliger and E. S. Lewis, *Tex. J. Sci.*, **14**, 58 (1962).
- (8) Yu. A. Titov, *Russ. Chem. Rev.*, **31**, 267 (1962).
- (9) S. B. Needleman and M. C. C. Kuo, *Chem. Rev.*, **62**, 405 (1962).
- (10) Yu. A. Arbuzov, *Russ. Chem. Rev.*, **33**, 407 (1964).
- (11) A. S. Onishchenko, "Diene Synthesis," Daniel Davey and Co., New York, N. Y., 1964.
- (12) A. Wassermann, "Diels-Alder Reactions," Elsevier, New York-N. Y., 1965.
- (13) J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **5**, 211 (1966).
- (14) J. Sauer, *ibid.*, **6**, 16 (1967).
- (15) J. Hamer, Ed., "1,4-Cycloaddition Reactions," Academic Press, New York, N. Y., 1967.
- (16) L. S. Povarov, *Russ. Chem. Rev.*, **36**, 656 (1967).
- (17) H. Kwart and K. King, *Chem. Rev.*, **68**, 415 (1968).
- (18) S. Seltzer, *Advan. Alicyclic Chem.*, **2**, 1 (1968).
- (19) J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962).
- (20) R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes," S. Patai, Ed., Interscience, London, 1964, pp 741-953.
- (21) H. Ulrich, "Cycloaddition Reactions of Heterocumulenes," Academic Press, New York, N. Y., 1967.
- (22) L. L. Muller and J. Hamer, "1,2-Cycloaddition Reactions," Interscience, New York, N. Y., 1967.
- (23) P. B. D. de la Mare, *Sci. Progr. (London)*, **56**, 243 (1968).
- (24) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **7**, 321 (1968).
- (25) R. Gompper, *ibid.*, **8**, 312 (1969).
- (26) N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, New York, N. Y., 1965, pp 194-245.
- (27) J. G. Calvert and J. N. Pitts, Jr., "Photochemistry," Wiley, New York, N. Y., 1965, pp 351-352, 502-579.
- (28) R. O. Kan, "Organic Photochemistry," McGraw-Hill, New York, N. Y., 1966.
- (29) D. C. Neckers "Mechanistic Organic Photochemistry," Reinhold New York, N. Y., 1967, pp 98-163.
- (30) A. Schönberg, "Preparative Organic Photochemistry," Springer-Verlag New York, New York, N. Y., 1968, pp 70-137, 414-424.
- (31) G. S. Hammond and N. J. Turro, *Science*, **142**, 1541 (1963).
- (32) W. C. Dauben and W. T. Wipke, *Pure Appl. Chem.*, **9**, 539 (1964).
- (33) N. C. Yang, *ibid.*, **9**, 591 (1964).
- (34) W. L. Dilling, *Chem. Rev.*, **66**, 373 (1966).

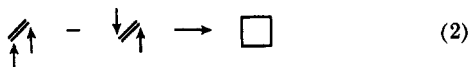
and 1,3-dipolar cycloadditions^{20,58,59} have comprehensively listed experimental facts and mechanistic inferences. For this reason, references to experimental facts that substantiate or contradict the results of particular theoretical deductions were primarily located through these review articles. Consequently, it is possible that highly pertinent experimental results may have been overlooked, but the citations of theoretical papers are hopefully complete through 1970.

B. NOMENCLATURE

A concise system for classifying cycloaddition reactions has been developed,^{4,20} and it will be used throughout this review. Two examples should define the system sufficiently. The Diels–Alder reaction of butadiene with ethylene (eq 1) may be



a concerted reaction of the π electrons of the two reactants to form two new σ bonds yielding the product cyclohexene. If the reaction takes place on the same face of both components undergoing reaction as indicated by the arrows, the reaction is a suprafacial, suprafacial process and is termed a $[\pi 4_s + \pi 2_s]$ reaction. This reaction is a symmetry-allowed reaction in the Woodward–Hoffmann sense. The antarafacial, suprafacial reaction of two ethylene molecules to yield cyclobutane (eq 2) is also an allowed reaction and would be denoted $[\pi 2_s + \pi 2_s]$.



The literature of quantum chemistry is replete with abbreviations for various theories and methods. Abbreviations that will be used are: HMO, Hückel molecular orbital; EH, ex-

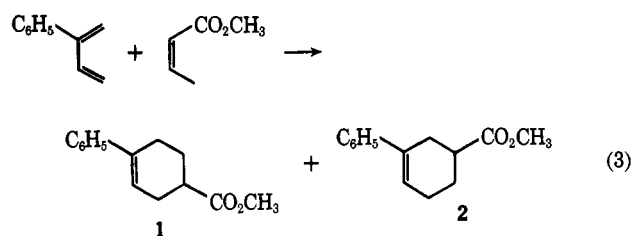
tended Hückel; PMO, perturbational MO; SCF, self-consistent field; CNDO, complete neglect of differential overlap.

II. Correlation of Theory with Experiment

Ideally, one would like to correlate experimental observations with direct *ab initio* quantum-mechanical calculations of the energy hypersurfaces connecting reactants and products, but computations of this magnitude are beyond the capabilities of computing facilities generally available. A more limited procedure is to use one of the recently developed all-valence-electron molecular orbital computer programs to calculate some details of the reaction surfaces. This type of calculation is still expensive, and only a few examples have been reported. A further degree of limitation is to choose a model for the transition state of a particular reaction, and then to calculate the total energies of ground-state reactants and the model activated complex, the difference being the activation energy. Quantum-mechanical calculations based on this approach are more numerous. Finally, one may use only information about the ground state of reactant molecules to make predictions about particular modes of reaction. Perturbation theory uses this procedure.

A calculation performed in one of the ways described above will yield more or less detailed information about the energy distribution along a reaction coordinate for a particular reaction. How is this energy information to be correlated with experimental facts?

An example will help to clarify the problem, and eq 3 illustrates a typical experimental result which might be correlated with theory. The $[\pi 4 + \pi 2]$ reaction of 2-phenylbutadiene with methyl acrylate at 150° is regioselective with a reported product ratio $1/2 = 4.5$.⁶⁰ Assuming that the products



are formed in this ratio by kinetically controlled processes, the essential problem is to estimate the two different free energies of activation for the two observed reactions, and to compare the free energy difference with the observed selectivity. The well-known expression of transition-state theory⁶¹ (eq 4)

$$k \text{ (rate constant)} = (kT/h) \exp(-\Delta G^\ddagger/RT) \quad (4)$$

could provide the mathematical connection between the calculated energies and the experiment.

The trouble is that the quantum-mechanical calculations refer to internal energy changes at 0°K in the absence of solvent. A majority of the reactions to be discussed take place in solution, many at elevated temperatures. Since detailed discussions of this situation exist, only a short outline of a semi-quantitative justification for equating calculated energies to

(35) R. N. Warrener and J. B. Bremmer, *Rev. Pure Appl. Chem.*, **16**, 117 (1966).

(36) R. Srinivasan, *Advan. Photochem.*, **4**, 113 (1966).

(37) M. Mousseron, *ibid.*, **4**, 195 (1966).

(38) P. J. Wagner and G. S. Hammond, *ibid.*, **5**, 21 (1967).

(39) D. R. Arnold, *ibid.*, **6**, 301 (1968).

(40) R. Steinmetz, *Fortschr. Chem. Forsch.*, **7**, 445 (1967).

(41) G. L. Fonken in "Organic Photochemistry," O. L. Chapman, Ed., Vol. 1, Marcel Dekker, New York, N. Y., 1967, pp 197–246.

(42) O. L. Chapman and G. Lenz, ref 41, pp 283–321.

(43) G. S. Hammond in "Reactivity of the Photoexcited Organic Molecule," Interscience Publishers, New York, N. Y., 1967, pp 119–138.

(44) W. G. Dauben, ref 43, pp 171–196.

(45) J. M. Bruce, *Quart. Rev., Chem. Soc.*, **21**, 405 (1967).

(46) R. C. Cookson, *ibid.*, **22**, 423 (1968).

(47) P. E. Eaton, *Accounts Chem. Res.*, **1**, 50 (1968).

(48) D. Elad, "Some Current Topics in Organic Photochemistry," Intra-Science Research Foundation, Santa Monica, Calif., 1968, pp 101–138.

(49) W. L. Dilling, *Chem. Rev.*, **69**, 845 (1969).

(50) N. J. Turro in "Energy Transfer and Organic Photochemistry," Interscience, New York, N. Y., 1969, pp 133–296.

(51) N. J. Turro, J. C. Dalton, and D. S. Weiss in "Organic Photochemistry," Vol. 2, O. Chapman, Ed., Marcel Dekker, 1969, pp 14–62.

(52) D. J. Trecker, ref 51, pp 63–116.

(53) N. J. Turro, *Annu. Rev. Photochem.*, **1**, 1 (1969).

(54) W. B. Hammond and G. S. Hammond, *ibid.*, **1**, 235 (1969).

(55) N. J. Turro, D. P. Pond, and F. D. Lewis, *ibid.*, **2**, 3 (1970).

(56) W. M. Horspool, *Photochemistry*, **1**, 156, 196, 202, 226 (1970).

(57) J. C. Dalton and N. J. Turro, *Annu. Rev. Phys. Chem.*, **21**, 499 (1970).

(58) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565 (1963).

(59) R. Huisgen, *ibid.*, **2**, 633 (1963).

(60) I. N. Nazarov, Yu. A. Titov, and A. I. Kuznetsova, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1270 (1959).

(61) S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes," McGraw-Hill, New York, N. Y., 1941.

experimental free energies of activation needs to be given.⁶²⁻⁶⁴ The free energy of activation is given in eq 5 in terms of the

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger \quad (5)$$

heat and entropy of activation. At absolute zero $T\Delta S^\ddagger = 0$, and the equating of ΔG^\ddagger and our calculated energies would be justifiable.

Introduction of a solvent at an elevated temperature leads to differential solvation of a ground state and transition state in a reaction. However, that part of ΔG^\ddagger due to differential solvation may be a negligible quantity. A high degree of solvation will lead to a decrease in enthalpy, but at the same time will lead to a decrease in entropy since solvent molecules are constrained by solvation. Referring to eq 5 we see that any change in solvation for two different but similar reactions leads to changes in their respective heats and entropies of activation whose contributions to their respective ΔG^\ddagger tend to cancel. We may therefore equate calculated differences in energies of activation with experimental differences in free energies of activation. One notes that it would seem to be incorrect to compare quantum-mechanical calculations with experimental heats of activation unless one is prepared to calculate differential entropies of solvation.⁶²

III. Reaction Surfaces

A. QUANTUM MECHANICAL METHODS

1. Mathematical Formulisms

The quantitative generation of a potential energy surface for a cycloaddition reaction requires the use of a method that includes at least the valence electrons of the molecules undergoing reaction. Several semiempirical MO methods exist, and critical reviews have been published.⁶⁵⁻⁷³ The most popular of the available methods are the EH,^{74,75} CNDO/2,⁷⁶ and the MINDO/2^{77,78} methods. The EH method is a straightforward application of simple MO theory using a one-electron effective Hamiltonian. Molecular orbitals are taken as linear combinations of atomic orbitals in the form of 1s, 2s, and 2p Slater orbitals. The usual variational procedure gives the secular determinant, eq 6, in which the overlap integrals S_{ij} are

$$|H_{ij} - E_i S_{ij}| = 0 \quad (6)$$

calculated from known formulas and the matrix elements are calculated by a well-known approximation, eq 7.⁷⁹ In eq 7 the

$$H_{ij} = (1.75/2)(H_{ii} + H_{jj})S_{ij} \quad (7)$$

integrals H_{ii} are taken as the negative of valence-state ionization potentials of the orbitals involved. The dependence of eq 6 and 7 on overlap, and hence on distance and orientation, gives the EH technique the potential of being able to generate a reaction surface.

The CNDO/2 and the MINDO/2 methods both attempt to apply the Hartree-Fock-Roothaan procedure⁸⁰⁻⁸⁴ to the obtention of a molecular wave function for the system under consideration. However, the Hartree-Fock operator contains both kinetic energy and potential energy operators, and the potential energy electronic operators are functions of the electronic distribution. Since one needs to know the electronic distribution in order to write the elements of the Fock matrix, analogous to eq 6, an iterative SCF procedure must be used. The CNDO method makes the approximation that the product $\phi_u \phi_v$ of any pair of orbitals is always zero if ϕ_u and ϕ_v are located on the same center (complete neglect of differential overlap). The MINDO method (modified intermediate neglect of differential overlap) restores several of the integrals neglected in the CNDO method.

The major failures of EH theory are: the calculations of charges for polar molecules are likely to be overestimated, strain energies in small-ring compounds are underestimated, and incorrect equilibrium geometries and conformations of complex molecules may be calculated. CNDO/2 calculations are unsatisfactory in the calculation of heats of formation, ionization potentials, and spectra. MINDO/2 seems to yield satisfactory heats of formation for acyclic organic compounds, but there is a tendency to overestimate the stability of cyclic compounds. Even though the quantitative inaccuracy of these approximate methods is a well-recognized fact, it is also true that calculations of this type when applied to problems of reactivity have consistently yielded interesting and qualitatively correct results.

Theoretical nonempirical calculations on moderately large organic molecules are just now beginning to appear. Some of these studies use a small set of Gaussian orbitals⁸⁵⁻⁹¹ or Slater orbitals⁹² as a basis set. Others use a large Gaussian basis set⁹³ and may also include a configuration interaction calculation.⁹⁴⁻⁹⁶ No cycloadditions have been investigated, but an

(62) M. J. S. Dewar, "The Molecular Orbital Theory of Organic Chemistry," McGraw-Hill, New York, N. Y., 1969, Chapters 6 and 8.

(63) M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **32**, 1333 (1936).

(64) R. P. Bell, *Proc. Roy. Soc., Ser. A*, **154**, 414 (1936).

(65) M. D. Newton, F. P. Boer, and W. N. Lipscomb, *J. Amer. Chem. Soc.*, **88**, 2353, 2361, 2367 (1966).

(66) L. C. Allen and J. D. Russell, *J. Chem. Phys.*, **46**, 1029 (1967).

(67) K. Fukui and H. Fujimoto, *Bull. Chem. Soc. Jap.*, **40**, 2787 (1967).

(68) G. Blyholder and C. A. Coulson, *Theor. Chim. Acta*, **10**, 316 (1968).

(69) K. Jug, *ibid.*, **14**, 91 (1969).

(70) S. Ehrensen, *J. Amer. Chem. Soc.*, **91**, 3693, 3702 (1969).

(71) H. H. Jaffé, *Accounts Chem. Res.*, **2**, 136 (1969).

(72) O. Sinanoglu and K. B. Wiberg, "Sigma Molecular Orbital Theory," Yale University Press, New Haven, Conn., 1970.

(73) J. R. Hoyland in "Molecular Orbital Studies in Chemical Pharmacology," L. B. Kier, Ed., Springer-Verlag New York, New York, N. Y., 1970, pp 31-81.

(74) R. Hoffmann and W. N. Lipscomb, *J. Chem. Phys.*, **36**, 2179, 3489 (1962); **37**, 2872 (1962).

(75) R. Hoffmann, *ibid.*, **39**, 1397 (1963).

(76) J. A. Pople and G. A. Segal, *ibid.*, **44**, 3289 (1966).

(77) M. J. S. Dewar and E. Haselbach, *J. Amer. Chem. Soc.*, **92**, 590 (1970).

(78) N. Bodor, M. J. S. Dewar, A. Harget, and E. Haselbach, *ibid.*, **92**, 3854 (1970).

(79) M. Wolfsberg and L. Helmholz, *J. Chem. Phys.*, **20**, 837 (1952).

(80) D. R. Hartree, *Proc. Cambridge Phil. Soc.*, **24**, 89, 111, 426 (1928).

(81) V. Fock, *Z. Phys.*, **61**, 126 (1930).

(82) C. C. J. Roothaan, *Rev. Mod. Phys.*, **23**, 69 (1951).

(83) R. Pariser and R. G. Parr, *J. Chem. Phys.*, **21**, 466, 767 (1953).

(84) J. A. Pople, *Trans. Faraday Soc.*, **49**, 1375 (1953).

(85) J. R. Hoyland, *J. Amer. Chem. Soc.*, **90**, 2227 (1968).

(86) R. E. Christoffersen and G. M. Maggiora, *Chem. Phys. Lett.*, **3**, 419 (1969).

(87) W. J. Hehre, R. F. Stewart, and J. A. Pople, *J. Chem. Phys.*, **51**, 2657 (1969).

(88) J. A. Pople, *Accounts Chem. Res.*, **3**, 217 (1970).

(89) S. Rothenberg, *J. Amer. Chem. Soc.*, **93**, 68 (1971).

(90) W. A. Lathan, W. J. Hehre, and J. A. Pople, *ibid.*, **93**, 808 (1971).

(91) R. E. Cristoffersen, D. W. Genson, and G. M. Maggiora, *J. Chem. Phys.*, **54**, 239 (1971).

(92) R. M. Pitzer, *ibid.*, **47**, 965 (1967).

(93) E. Clementi and D. R. Davis, *ibid.*, **45**, 2593 (1966).

(94) R. J. Buenker and S. D. Peyerimhoff, *ibid.*, **48**, 354 (1968).

(95) S. D. Peyerimhoff and R. J. Buenker, *ibid.*, **51**, 2528 (1969).

(96) R. J. Buenker and S. D. Peyerimhoff, *J. Amer. Chem. Soc.*, **91**, 4342 (1969).

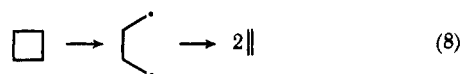
interesting study of the electrocyclic opening of cyclobutene to butadiene⁹⁷ will be described.

2. Applications to Cycloaddition Reactions

EH theory has been used to explore a number of reaction surfaces. The addition of methylene to ethylene along with several related problems was considered in some detail.⁹⁸ The calculated results were in qualitative agreement with previous postulates about the mechanisms of methylene addition to olefins.⁹⁹ Dimerizations of methylenes and nitroso compounds¹⁰⁰ and the potential surface for the decarbonylation of cyclopropanone¹⁰¹ have also been studied. In general the results show that the least-motion, most symmetrical geometry of approach of two molecules is, in these cases, not the preferred reaction path. Unsymmetrical relative approaches with unsymmetrical degrees of intermediate bonding are favored.

It should be noted that the correlation diagrams for these reactions show that the reactions are orbital symmetry forbidden in the least-motion geometry. Other non-least-motion reaction pathways can be followed. It is pointed out¹⁰⁰ that the semiempirical MO calculations are necessary to define the allowed reaction pathway. The forbiddenness of the symmetrical approach only defines a very small part of the reaction surface. Even the EHMO calculation may not locate the correct reaction pathway for two reasons. First, all degrees of freedom for the reacting system are not allowed to vary, so this may prejudice the results. Second, as discussed above, the EHMO method may not be sufficiently accurate for calculation of the energetic changes which occur in these reactions. Even with these objections, the results are still interesting.

Tetramethylene biradicals have been postulated as transient intermediates in several thermal and photochemical cycloadditions. For example, the activation energy for retrocycloaddition, 63 kcal/mol,^{102, 103} of cyclobutane to yield ethylene, is consistent with intermediate formation of tetramethylene, eq 8. A recent calculation¹⁰⁴ of the potential energy surface for

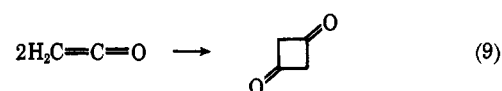


this reaction gave an unusual and unexpected result. According to the calculation, the intermediate biradical species did not exist as a minimum in the many-dimensional potential energy reaction surface. The reaction coordinate for eq 8 had only two minima, corresponding to cyclobutane and two ethylene molecules. The intermediate region characteristic of the ring-opened cyclobutane was a large flat area of the energy surface in which single bonds could be rotated from their equilibrium position with very little cost in energy. This surface was termed a "twixtyl" and it was suggested that experimental distinguishability from a true intermediate would be impos-

sible. The results of this calculation certainly indicate that organic chemists may need to redefine some mechanistic concepts in at least one area of cycloaddition chemistry.

Some previous limited EH investigations of dimers of ethylene in ground and excited states have been published.^{105, 106} The ground state of the dimer was found to be unstable with respect to two ethylene molecules, and there was an intermolecular attraction in the excited state. Correspondence with the Woodward-Hoffmann rules⁴ for cycloaddition [$\pi 2_s + \pi 2_s$] is obvious. These studies are limited because, generally, only a few variations in the respective orientation and the intermolecular distance are allowed in order to make the calculations more tractable.

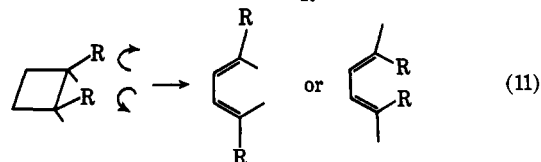
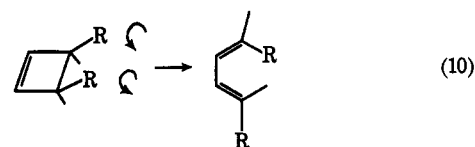
Another example is a study of the dimerization of ketene to yield the head-to-tail dimer, cyclobutane-1,3-dione (eq 9).¹⁰⁷



EH wave functions and energies were calculated at several different intermolecular distances, and the various internal angles within the ketene moiety were varied, but the entire system was maintained in C_{2h} symmetry. A calculated level crossing of vacant and occupied orbitals with the same symmetry was noted, and in agreement with expectation the reaction is therefore orbital symmetry forbidden.⁴ The possibility of calculating symmetry-allowed reaction pathways was interdicted by requiring the highly symmetrical approach of the two molecules.

3. Electrocyclic Reactions

Electrocyclic reactions can be thought of as internal cycloaddition reactions, so it is certainly germane to review the calculations of potential energy surfaces in this closely related area. A typical reaction is the opening of cyclobutene, thermally or photochemically, to yield butadiene. *A priori*, the reaction can proceed either in a conrotatory fashion⁴ (eq 10) or in a disrotatory fashion (eq 11),⁴ and the two reaction path-



ways are experimentally distinguishable. The thermal symmetry-allowed motion is conrotatory in this case.⁴

Several EH calculations were carried out during development of the Woodward-Hoffmann rules^{108, 109} in order to confirm results of symmetry arguments, but the details have not been published. However, the reactions given in eq 10 and 11

(97) K. Hsu, R. J. Buenker, and S. D. Peyerimhoff, *J. Amer. Chem. Soc.*, **93**, 2117 (1971).

(98) R. Hoffmann, *ibid.*, **90**, 1475 (1968).

(99) P. S. Skell and A. Y. Garner, *ibid.*, **78**, 5430 (1956).

(100) R. Hoffmann, R. Gleiter, and F. B. Mallory, *ibid.*, **92**, 1460 (1970).

(101) D. M. Hayes, C. A. Zeiss, and R. Hoffmann, *J. Phys. Chem.*, **75**, 340 (1971).

(102) R. W. Carr and W. D. Walters, *ibid.*, **67**, 1370 (1963).

(103) R. W. Vreeland and D. F. Sweinhart, *J. Amer. Chem. Soc.*, **85**, 3349 (1963).

(104) R. Hoffmann, S. Swaminathan, B. G. Odell, and R. Gleiter, *ibid.*, **92**, 7091 (1970).

(105) R. Polak and J. Paldus, *Theor. Chim. Acta*, **4**, 37 (1966).

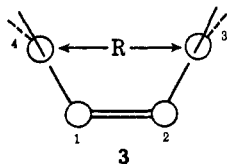
(106) M. G. Sucre and A. Tallet, *ibid.*, **7**, 277 (1967).

(107) H.-D. Scharf and J. Fleischauer, *Tetrahedron Lett.*, 5867 (1968).

(108) R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, **87**, 395 (1965).

(109) R. Hoffmann and R. B. Woodward, *ibid.*, **87**, 2046 (1965).

have been the object of probably the most ambitious theoretical calculations of reaction surfaces to date.⁹⁷ Nonempirical SCF calculations using a large Gaussian orbital basis set with configuration interaction were carried out. At each stage along the reaction coordinate, which was defined as a function of the C₁-C₄ bond distance *R* in **3** and the out-of-plane rotation



angle of the CH₂ groups, an intensive effort was made to minimize the total energy with respect to all other molecular structure parameters. A good approximation to the Hartree-Fock energy of the system was obtained, with the calculated energy difference between cyclobutene and butadiene being +11.5 kcal/mole,⁹⁷ in close agreement with the experimental difference $\Delta\Delta H_f^\circ(0^\circ\text{K}) = 10.5 \pm 0.5$ kcal/mol. The experimental value is estimated from recent heats of combustion^{110,111} and the difference in molar heat capacities at 300°K.¹¹² The small error is not important, and it may be due to a failure to satisfactorily optimize all of the molecular geometrical parameters. One factor which was not considered is the fact that the *s-cis* conformation of butadiene has been shown to possess a chiral nonplanar C₂ configuration.¹¹⁸ This would increase the discrepancy in energies of ground-state reactant and product.

The major conclusions of the research are very unlikely to be affected by small criticisms as noted above. The most important conclusion has to do with the timing of the stretching of the carbon-carbon bond and the twisting of the CH₂ groups. Instead of a process involving simultaneous stretching and rotation, the reaction proceeds through an essentially stepwise process. *R* is first varied about 60% of the way from its equilibrium value in cyclobutene to its butadiene value. Then, preferred conrotatory rotation of the methylene groups occurs without further change in *R*, and finally *R* continues its variation toward the equilibrium value in the product. The calculated activation energy is about 46 kcal/mol⁹⁷ as compared to the experimentally determined ΔH^\ddagger of 33 kcal/mol.¹¹⁴ The discrepancy here should not be judged as indicating irreconcilable disagreement of experiment and theory. Better calculations and experiments may modify both values in time.

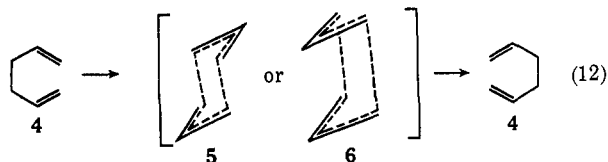
The conrotatory mode of rotation was more favorable than the disrotatory mode by about 14 kcal/mol⁹⁷ at the energy maxima in the potential surfaces. It is important to note that in some of the possible reaction mechanisms involving synchronous elongation of *R* and twisting of the methylene groups, the disrotatory motion was of lower energy. The mode of reaction calculated to be preferred depends upon the nature of the reaction path, so it is very critical to determine the correct minimum energy interconversion path. Previous EH cal-

culations¹⁰⁸ on this system in which the rotation was carried out entirely within the butadiene framework gave disrotatory motion as the favored rotation, and one can now understand the reason for the incorrect prediction. A second EH calculation¹¹⁵ which assumed a concerted bond stretching-rotational motion was of temporary interest but must now be discounted.

The thermal reaction of bicyclo[1.1.0]butane to yield butadiene and cyclobutene has been investigated using CNDO/2 calculations.¹¹⁶ Calculated ground-state properties were in good agreement with experimental values, and the modes of ring opening which are allowed by orbital-symmetry rules were calculated to be of lower energy than the forbidden reactions. However, only a few models of possible reaction pathways were examined, and the energies were not minimized for these models with respect to molecular parameters.

One conclusion that must be drawn from all of the preceding work is that it is very difficult to arbitrarily choose a correct reaction pathway for the purposes of making a calculation. In another example, an analysis of the thermal *cis-trans* isomerization of diimide has been carried out using EH theory.¹¹⁷ Three possible transition states were considered, a three-atom colinear planar form, a completely linear form, and a 90° twisted form. However, calculations on a similar system, N₂F₂,^{118,119} have shown that analogous postulated transition states are not energy maxima. In CNDO/2 calculations, twisting the N₂F₂ molecule while maintaining C₂ symmetry leads to a maximum energy at a dihedral angle of 95° rather than 90°. Accurate guesses as to the structure of a transition are not possible even in this very simple case. In the theoretical approach presently under discussion, it appears that the entire energy surface for any particular reaction must be investigated before quantitative conclusions are possible.

The MINDO/2 procedure has been used^{120,121} to investigate several examples of Cope¹²²⁻¹²⁴ rearrangements. One can infer from an illuminating experiment¹²⁵ that the degenerate Cope rearrangement of bialllyl (eq 12) takes place *via* a transition



state which is chairlike (**5**) rather than boatlike (**6**). Orbital symmetry arguments indicate that the rearrangement is an allowed reaction and transition state **6** may be destabilized relative to **5** by secondary orbital interactions.⁴ For the calculations^{120,121} the energies of the symmetrical structures **5** and **6** were minimized with respect to all bond lengths and angles. The calculated difference in energy between **5** and **6** was 6.6

(110) E. J. Prosen, F. W. Maron, and R. D. Rossini, *J. Res. Nat. Bur. Std.*, **42**, 269 (1949).

(111) K. B. Wiberg and R. A. Fenoglio, *J. Amer. Chem. Soc.*, **90**, 3395 (1968).

(112) S. W. Benson, F. R. Cruickshank, D. M. Golden, G. R. Haugen, M. E. O'Neal, A. S. Rodgers, R. Shaw, and R. Walsh, *Chem. Rev.*, **69**, 279 (1969).

(113) E. W. Garbisch, Jr., Abstracts of Papers, 159th National Meeting of the American Chemical Society, Houston, Tex., Feb 1970, No. ORGN-055.

(114) R. W. Carr and W. D. Walters, *J. Phys. Chem.*, **69**, 1073 (1965).

(115) G. Feler, *Theor. Chim. Acta*, **12**, 412 (1968).

(116) K. B. Wiberg, *Tetrahedron*, **24**, 1083 (1968).

(117) J. Alster and L. A. Burnelle, *J. Amer. Chem. Soc.*, **89**, 1261 (1967).

(118) W. C. Herndon, J. Feuer, and L. H. Hall, *Theor. Chim. Acta*, **11**, 178 (1968).

(119) M. S. Gordon and H. Fischer, *J. Amer. Chem. Soc.*, **90**, 2471 (1968).

(120) A. Brown, M. J. S. Dewar, and W. Schoeller, *ibid.*, **92**, 5516 (1970).

(121) M. J. S. Dewar and W. W. Schoeller, *ibid.*, **93**, 1481 (1971).

(122) S. J. Rhoads in "Molecular Rearrangements," Part 1, P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1963, pp 684-694.

(123) E. Vogel, *Angew. Chem., Int. Ed. Engl.*, **2**, 1 (1963).

(124) W. von E. Doering and W. R. Roth, *ibid.*, **2**, 115 (1963).

(125) W. von E. Doering and W. R. Roth, *Tetrahedron*, **18**, 67 (1962).

kcal/mol, close to the experimental estimate of 5.7 kcal/mol for 3,4-dimethyl-1,5-hexadiene rearrangement.¹²⁴ The calculated difference in energy (activation energy) between bialllyl and **5** (24 kcal/mol)¹²⁰ is less than the observed value (35.5 kcal/mol¹²⁶).



- 7, X = -CH=CH-
 8, X = -CH₂-
 9, X = -

The degenerate rearrangements of bullvalene (**7**), barbaralane (**8**), and semibullvalene (**9**) were also assumed to have symmetrical transition states, in these cases necessarily boat-like.¹²¹ Quoted experimental values for the activation energy for rearrangement of **7** range from 11.7 to 13.1 kcal/mol¹²⁷⁻¹³⁰ and the calculated value is 11.3 kcal/mol.¹²¹ For **8**, experimental results are 8.6¹³¹ and 10.4¹³² kcal/mol as compared with a calculated 5.9 kcal/mol.¹²¹ Semibullvalene has a calculated energy difference between the assumed transition state and the ground state of 2.3 kcal/mol;¹²¹ for octamethylsemibullvalene, 6.4 kcal/mol.^{132a} Again the calculated activation energies are less than the experimental values, but in better agreement than for the rearrangement of bialllyl. The better agreement was attributed to the fact that MINDO/2 calculations overestimate the stability of cyclic compounds, these overestimations canceling in the cases of **7-9**.

Considering the results which have been obtained from the more complete calculations of energy surfaces cited earlier,^{97,104} one can suggest another likely source of error. It is probable that the geometries chosen as transition states in these latter reactions may not correspond to energy maxima, but instead are stable intermediates along the reaction coordinate. The fact that the energy of the intermediate states are minimized with respect to *all* bond length and angles supports this contention, for a change along the reaction coordinate would necessarily increase the energy of the system. A more complete investigation of the reaction surface is needed. The Cope rearrangement has been studied by empirical methods to be discussed later, and there it is also found that the symmetrical boat and chair intermediate forms for bialllyl correspond to transition states.

4. Charge-Transfer Complexes and Excimers

Two identical or different molecules in either ground or excited states may associate with each other to form a stable molecular complex. The formation of these complexes could be an initial step in a reaction sequence leading to a cyclo-

adduct. Recent reviews¹³³⁻¹⁴¹ comprehensively survey experimental and theoretical work in the area, so only a few investigations particularly related to the present topic of reaction surfaces will be mentioned.

EH calculations on a tetracyanoethylene-benzene complex¹⁴² at several different intermolecular distances and in several different relative conformations of the two molecules failed to reproduce the known stability of the complex. In any conformation where the interplanar distance was between 2 and 3.5 Å, the intermolecular potential was repulsive. CNDO/2 calculations on the same system¹⁴³ did yield a binding energy for the complex at distances of less than 3.5 Å. However, the energy curve showed too deep a minimum (125 kcal/mol more stable than separated components) at too short an interplanar distance (1.75 Å). Agreement with experiment could probably be improved in both cases if extensive reparameterizations were carried out. In their present form neither the EH or the CNDO/2 method seems to be useful for obtaining accurate quantitative information about energy surfaces for these kinds of interactions.

Benzene, toluene, and *p*-xylene excimers have been studied with EH calculations.¹⁴⁴ For two eclipsed benzene molecules the ground-state dimer was unstable at distances less than 4.0 Å. The excimer was stable, 4.4 kcal/mol at an interplanar distance of 3.4 Å. Translation or rotation of the rings decreased the stability. Toluene, which forms an excimer, showed a minimum in energy, 1.2 kcal/mol at 3.7 Å. *p*-Xylene, which does not seem to form an excimer, gave only a very shallow (0.2 kcal/mol) minimum at 4.3 Å. The agreement with experiment is nice, but may be accidental.

B. EMPIRICAL REACTION SURFACES

1. Background

Nearly all bimolecular reactions have an activation energy, so that if the potential energy of a system is plotted along a reaction coordinate from reactants to products, a maximum in the energy will be found. Figure 1 shows a simplified reaction coordinate-potential energy diagram. The configuration of the atoms comprising the system at the maximum energy point corresponds to the species called the activated complex or transition state, and the energy difference between reactants and activated complex is called the activation energy. The heat of reaction, ΔH , is also indicated on Figure 1. In actual

- (126) W. von E. Doering and J. C. Gilbert, *Tetrahedron Suppl.*, 397 (1966).
 (127) M. Saunders, *Tetrahedron Lett.*, 1699 (1963).
 (128) G. Schroder, R. Merenyi, and J. F. M. Oth, *ibid.*, 773 (1964).
 (129) G. Schroder, J. F. M. Oth, and R. Merenyi, *Angew. Chem., Int. Ed. Engl.*, 4, 752 (1965).
 (130) A. Allerhand and H. S. Gutowsky, *J. Amer. Chem. Soc.*, 87, 4092 (1965).
 (131) W. von E. Doering, J. Jones, and M. Saunders, *Tetrahedron*, 23, 3943 (1968).
 (132) G. Schroder and J. F. M. Oth, *Angew. Chem., Int. Ed. Engl.*, 6, 414 (1967).
 (132a) F. A. L. Anet and G. E. Schenck, *Tetrahedron Lett.*, 4237 (1970).

- (133) G. Briegleb, "Elektronen-Donator-Acceptor-Komplexe," Springer-Verlag, Berlin, 1961.
 (134) L. J. Andrews and R. M. Keefer, "Molecular Complexes in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964.
 (135) J. Rose, "Molecular Complexes," Pergamon Press, New York, N. Y., 1967.
 (136) R. S. Mulliken and W. B. Person, "Molecular Complexes," Wiley, New York, N. Y., 1969.
 (137) R. Foster, "Organic Charge-Transfer Complexes," Academic Press, New York, N. Y., 1969.
 (138) E. G. McRae and M. Kasha in "Fundamental Process in Radiation Biology," L. Augenstein, B. Rosenberg, and R. Mason, Ed., Academic Press, New York, N. Y., 1964.
 (139) M. Kasha, H. R. Rawls, and M. A. El-Bayoumi, *Pure Appl. Chem.*, 11, 371 (1965).
 (140) A. A. Lamola in "Energy Transfer and Organic Photochemistry," A. A. Lamola and N. J. Turro, Ed., Interscience, New York, N. Y., 1969, pp 58, 77, 104.
 (141) J. E. Leonard and G. S. Hammond, *Annu. Survey Photochem.*, 2, 189 (1970).
 (142) S. Wold, *Acta Chem. Scand.*, 20, 2377 (1966).
 (143) D. B. Chesnut and P. E. S. Wormer, *Theor. Chim. Acta*, 20, 250 (1971).
 (144) D. B. Chesnut, C. J. Fritchie, and H. E. Simmons, *J. Chem. Phys.*, 42, 1127 (1965).

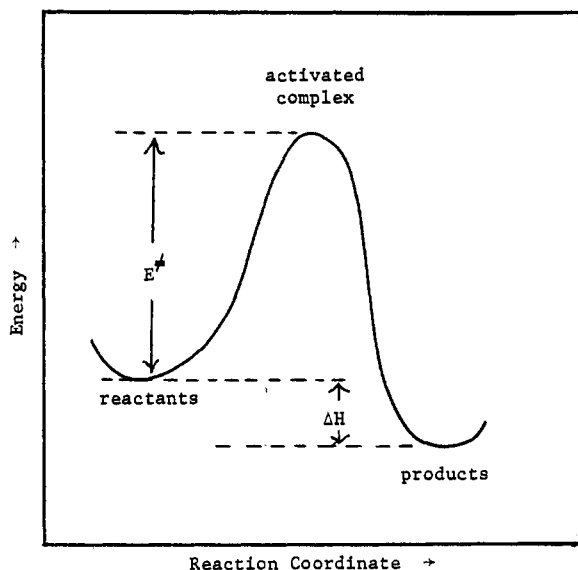


Figure 1. Simplified reaction-potential energy diagram.

fact, the reacting species are polyatomic molecules with several possible internal motions, and the reaction itself may involve numerous changes in relative external and internal positions. Therefore, in reality there is a potential energy hypersurface of many dimensions connecting reactants to activated complex to products.

The activated complex can be treated as a normal molecule in equilibrium with the reactants. Then the classical treatment of the transition-state theory⁶¹ allows one to write a relationship between the rate constant for a reaction and the entropy ΔS^\ddagger and heat of activation ΔH^\ddagger (eq 13; also see eq 4). In eq 13 k , h , R , and T are the Boltzman constant, Planck's con-

$$k = (kT/h)(\exp \Delta S^\ddagger/R)(\exp -\Delta H^\ddagger/RT) \quad (13)$$

stant, the gas constant, and the absolute temperature, respectively. This section of this review is concerned with the empirical methods which have been devised to estimate ΔH^\ddagger and ΔS^\ddagger .

The first applications of transition-state theory were made using a semiempirical approach,^{61,145,146} combining some empirical information and elementary quantum mechanics in the treatment of the $H + H_2$ bimolecular exchange reaction. A later, more empirical development called the method of intersecting potential energy surfaces^{147,148} is more apropos to the present discussion. A simplified diagram for the bimolecular reaction of two molecules R and S to yield a final adduct P is given in Figure 2. The potential energy levels of R and S in their normal state (infinite separation) and P are indicated by dashed lines. The variation of the energies of R and S as their internal nuclear configurations change to values characteristic of the product is represented by a surface I. Surface II is raised in energy above I by the repulsion energy between R and S . Surface III represents the change in energy for the product P as bond lengths and angles change toward values characteristic of the reactants. The point where surfaces II

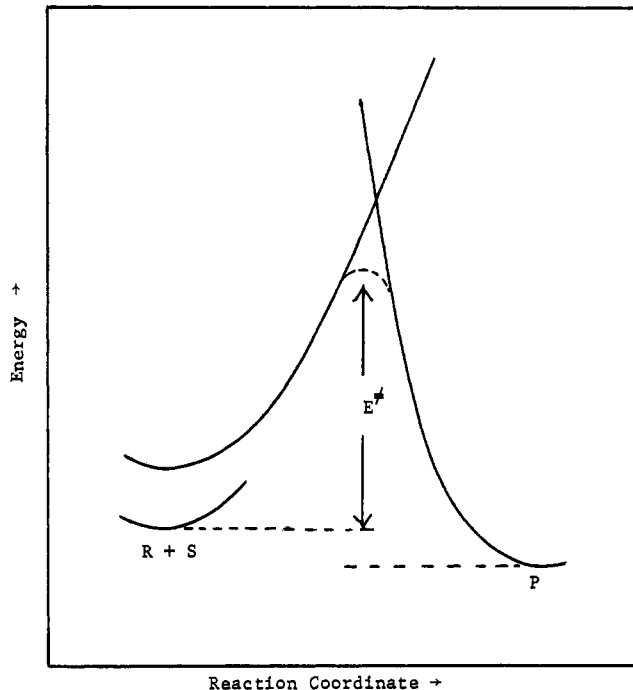


Figure 2. Bimolecular reaction-potential energy diagram.

and III cross is an activated state from which the energy of activation may be obtained. An exchange or resonance between the two different configurations near the crossing point may lower the energy and the activation energy would then be given by E^\ddagger in Figure 2.

Once the energy of activation has been calculated and a model for the transition state obtained, the entropy of activation would be calculated by standard statistical thermodynamical techniques. In this case, one would not correlate the calculated energy of activation with an experimental free energy of activation. The empirical information used in constructing the diagram is potential energy information appropriate to determining the heat of activation at the temperature where reaction takes place. The entropy of activation must now be estimated in order to calculate the rate of a reaction according to eq 13.

2. Earlier Work on Cycloadditions

There were several early attempts to calculate the activation parameters of reactions of interest in the present context. The work until 1941 is summarized in the famous book on the transition-state theory by Glasstone, Laidler, and Eyring.⁶¹ Several of the conclusions must be modified in the light of later theory and criticism, but the work is still of high interest and pertinence.

The reaction $H_2 + I_2 \rightleftharpoons 2HI$ was treated as a classical bimolecular homogeneous exchange reaction,¹⁴⁸ with a planar symmetrical transition state. The semiempirical calculated value for the activation energy was higher than the experimental value, but with some empirical adjustments of vibrational frequencies in the transition state good agreement of experimental and calculated rate constants was obtained. These results are now only of historical interest since the major part of this reaction has been shown to involve a heterogeneous

(145) H. Eyring and M. Polanyi, *Z. Phys. Chem.*, **B12**, 279 (1931).

(146) H. Eyring, *Chem. Rev.*, **10**, 103 (1932).

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

(148) M. G. Evans, *ibid.*, **35**, 824 (1939).

chain mechanism.¹⁴⁹ Of course, in the geometrical arrangement chosen for the calculations,¹⁵⁰ the reaction is a [$\sigma_2s + \sigma_2s$] process which is forbidden by the orbital symmetry rules.^{4, 151} Semiempirical MO calculations¹⁵² of the potential-energy surface confirm this viewpoint. Arguments for¹⁵³ and against¹⁵¹⁻¹⁵⁴ trapezoidal bimolecular transition states have also been presented.

The reactions of ethylene with iodine, bromine, and chlorine^{155, 156} and the dimerization of ethylene¹⁵⁷ were also analyzed by the methods of transition-state theory, and reasonable agreements with experimental activation parameters were obtained. Symmetrical planar four-center transition states were chosen for the halogen-olefin reactions, and these geometrics are again orbital-symmetry forbidden.

The 1,4 addition of bromine to butadiene (eq 14) is an al-

$$\text{Br}_2 + \text{CH}_2=\text{CHCH}=\text{CH}_2 \longrightarrow \text{BrCH}_2\text{CH}=\text{CHCH}_2\text{Br} \quad (14)$$

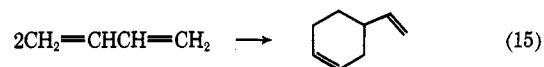
lowed [$\pi_4s + \sigma_2s$] process, and an activation energy of 31 kcal/mol was calculated for a completely planar transition state.^{158, 159} An angle of approach of the bromine molecule perpendicular to the plane of the butadiene gave an activation energy of 65 kcal/mol. This unrealistic geometric prediction is probably the result of some faulty assumptions about potential functions.

Several calculations were made on Diels-Alder reactions,^{148, 160-164} and most of the calculations used the method of intersecting potential energy surfaces. A few vibrations of the molecules were chosen as critical vibrations along the reaction coordinate, the others were assumed not to change, and the force constants for the critical vibrations were obtained from vibrational spectra. The initial calculation on the reaction, ethylene + butadiene \rightarrow cyclohexene,^{147, 160} ascribed too much weight to repulsion of the two molecules if they were to approach in parallel planes. Consequently, an all-planar cyclic transition state was assumed, the calculated activation was very high compared to the experimental value, and resonance in the transition state was invoked to account for the discrepancy.¹⁴⁸ Calculations were also made assuming a biradical intermediate, but the activation energy was much higher than in the case of a cyclic transition state.

A later calculation¹⁶⁴ pertaining to the same cycloaddition assumed the more familiar transition state in which the π orbitals of the two reactant molecules overlap. Good agreement with the experimental activation energy was obtained only if an unsymmetrical approach of the two molecules was

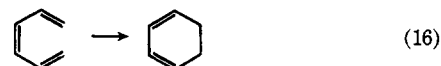
assumed, with one new bond of the product forming faster than the second. This type of model has been discussed by other workers,^{165, 166} and the discussion is certainly not settled by these calculations. Exchange energy would be larger for the symmetrical complex, and this is neglected in the above calculation on stereochemical grounds which are not valid.

Calculations on the Diels-Alder dimerization of butadiene (eq 15) have been quite interesting in that results have been



obtained which support both a concerted mechanism^{148, 162, 163} and a two-step biradical pathway.¹⁶¹ It was claimed that the experimental value of the ΔS^\ddagger of the reaction was in agreement with a calculated value for a reaction leading to an open transition state,¹⁶¹ but two later recalculations with revised values for several reaction coordinate vibrational frequencies showed agreement with a cyclical transition state.^{162, 163} The correct mechanism for the dimerization of butadiene is not known, and some arguments which may be interpreted as favoring a biradical intermediate will be discussed in the next section.

As far as could be determined, only one other type of organic reaction has been treated by the method of intersecting potential energy surfaces. The thermal closure of 1,3,5-hexatriene to yield cyclohexadiene (eq 16) was analyzed in great



detail for comparison with some very precise experimental data.¹⁶⁴ The calculated preexponential factor in the Arrhenius equations agreed within a factor of 2 with the experimental value. Calculated and experimental energies of activation were also in agreement assuming a symmetrical transition state. The experimental activation energy is *ca.* 5 kcal/mol higher than in the cyclization of ethylene with butadiene. This is primarily attributed to the smaller exothermicity of the unimolecular reaction.

All of the work discussed in this section suffers the disadvantages of excessive assumptions and unsystematic applications. In several cases, the experimental data may also have been, at that time, too imprecise to provide a good test for theory.

3. Thermochemistry and Chemical Kinetics

During the past decade there have been significant developments of empirical methods for estimating the thermodynamic properties of organic compounds.^{112, 167-173} Many of these

(149) J. H. Sullivan, *J. Chem. Phys.*, **46**, 73 (1967).

(150) A. Wheeler, B. Topley, and H. Eyring, *ibid.*, **4**, 178 (1936).

(151) R. Hoffmann, *ibid.*, **49**, 3739 (1968).

(152) L. C. Cusachs, M. Krieger, and C. W. McCurdy, *ibid.*, **49**, 3740 (1968).

(153) R. M. Noyes, *ibid.*, **49**, 3741 (1968).

(154) J. N. Murrell and K. J. Laidler, *Trans. Faraday Soc.*, **64**, 371 (1968).

(155) A. Sherman and C. E. Sun, *J. Amer. Chem. Soc.*, **56**, 1096 (1934).

(156) A. Sherman, O. T. Quimby, and O. Sutherland, *J. Chem. Phys.*, **4**, 732 (1936).

(157) F. P. Jahn, *J. Amer. Chem. Soc.*, **61**, 798 (1939).

(158) H. Eyring, A. Sherman, and G. E. Kimball, *J. Chem. Phys.*, **1**, 586 (1933).

(159) L. S. Kassel, *ibid.*, **1**, 749 (1933).

(160) M. G. Evans and E. Warhurst, *Trans. Faraday Soc.*, **34**, 614 (1938).

(161) G. B. Kistiakowski and W. W. Ransom, *J. Chem. Phys.*, **7**, 725 (1939).

(162) A. Wassermann, *J. Chem. Soc.*, 612 (1942).

(163) D. Rowley and H. Steiner, *Discuss. Faraday Soc.*, **10**, 198 (1951).

(164) K. E. Lewis and H. Steiner, *J. Chem. Soc.*, 3081 (1964).

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

(166) M. J. S. Dewar and R. S. Pyron, *J. Amer. Chem. Soc.*, **92**, 3098 (1970).

(167) C. T. Mortimer, "Reaction Heats and Bond Strengths," Pergamon Press, London, 1962.

(168) H. A. Skinner and G. Pilcher, *Quart. Rev., Chem. Soc.*, **17**, 264 (1963).

(169) G. R. Somayajulu, A. P. Kudchadker, and B. J. Zwolinski, *Annu. Rev. Phys. Chem.*, **16**, 213 (1965).

(170) A. J. Kalb, A. L. H. Chung, and T. L. Allen, *J. Amer. Chem. Soc.*, **88**, 2938 (1966).

(171) G. J. Janz, "Thermodynamic Properties of Organic Properties," Academic Press, New York, N. Y., 1967.

(172) S. W. Benson, "Thermochemical Kinetics," Wiley, New York, N. Y., 1968.

(173) P. v. R. Schleyer, J. E. Williams, and K. R. Blanchard, *J. Amer. Chem. Soc.*, **92**, 2377 (1970).

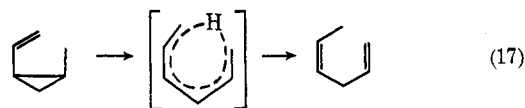
methods are based upon additivity schemes in which the basic units are the atoms or bonds or groups which comprise the organic molecule. A theoretical justification for these methods has slowly been emerging as the quantum-mechanical concepts of equivalent and localized molecular orbitals have been developed.¹⁷⁴

Group additivity methods have been the most successful schemes developed.¹¹² For saturated and unsaturated hydrocarbons, it certainly seems possible by these methods to estimate the heats of formation (ΔH_f°), heat capacities (C_p°), and entropies (S°) to a high degree of accuracy. Error limits of the order of ± 1.0 kcal/mol in ΔH_f° and ± 1.0 gibbs/mol in S° are reasonable. Known correction factors for ring strain, steric factors, and resonance effects can be introduced with a similar degree of accuracy. So heats of reaction can be calculated to within ± 2.0 kcal/mol.

Within the framework of the transition-state theory, a chemical reaction simply involves the passage of molecular species along a reaction surface. The heats of formation and the entropies of the reactants and the products are easily calculated as described above. Why can't the thermodynamic properties of intermediates and transition complexes be calculated in a similar way by group additivity methods? Of course, this would involve the development of strain, resonance, and relative stability parameters for unstable species, but after several decades of experimental work on the kinetics of organic reactions, this development should now be possible.

Benson has been the principle architect of principles and methods for carrying out kinetic calculations based on transition-state theory and group-additivity methods. He has summarized his ideas in several articles,¹⁷⁵⁻¹⁷⁸ and in a very useful book,¹⁷² so only a brief outline of results pertinent to the subject of cycloaddition reactions will be given. The main criticism that one could make of this type of work is similar to the criticism that one should apply to the earlier work in transition-state theory. A specific model must be chosen before its heat of formation and entropy may be calculated. Only a few details of the structure of the model are specified, its bonds, barriers to internal rotation, and degree of resonance stabilization. One seeks to remove a degree of arbitrariness by calculating properties of at least two transition complexes, say a biradical or a cyclic transition state, for comparison with experimental values. Still, the precise nature and geometry of any calculated intermediate may be open to argument. This quasi-thermodynamic method also cannot reveal any aspects of quantum-mechanical forbiddenness or allowedness⁴ or orbital symmetry required motions⁴ which might pertain to the reaction. However, even with these objections, highly useful and provocative results can still be obtained.

The kinetics of dissociation, structural isomerization, and geometrical isomerization for a large number of cyclopropane and cyclobutane derivatives have been examined.¹⁷⁷ Retro [2 + 2] cycloadditions and Cope rearrangements of ring-substituted small ring compounds are included. With the exception of cyclobutene isomerizations and the hydrogen transfer reaction for 1-alkyl-2-vinylcyclopropanes (eq 17), all reactions are qualitatively and quantitatively consistent with biradical

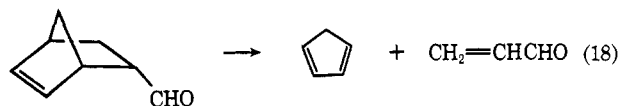


intermediates. This is generally in accord with mechanisms which have been suggested for these reactions.^{179, 180}

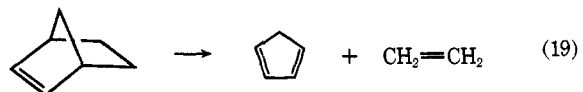
The kinetic data on Cope rearrangements, ester pyrolyses, and dehydrohalogenations of alkyl halides are summarized and examined from the standpoint of cyclic transition states.¹⁷⁵ The Arrhenius parameters are calculated, and the experimental values are generally in agreement with the proposed mechanisms. Some discrepancies are attributed to faulty experimental data.

Some of the retro-Diels-Alder reactions which have been examined have kinetic parameters consistent with calculated biradical intermediates.^{175, 178} These include the thermal decomposition of 4-vinylcyclohexene (dimerization of butadiene) which has been discussed in detail in a long paper.¹⁷⁵ A biradical intermediate is also suggested for cyclohexene pyrolysis (butadiene + ethylene). All of these reactions are allowed to be concerted by orbital-symmetry rules.⁴ The retro-Diels-Alder reactions of bicyclo[2.2.1]heptene, bicyclo[2.2.1]heptadiene, and the endo and exo isomers of dicyclopentadiene are estimated as more likely to be concerted reactions.¹⁷⁸ In every case, the calculated heats of formation of biradicals and concerted transition complexes are close in energy, of the order of 5-10-kcal/mol differences. The possibility exists that judicious substitution of radical stabilizing groups would tip the balance toward the biradical intermediate, assuming that these groups would not stabilize a concerted transition complex to as large an extent, which seems to be a reasonable assumption.

The thermal decomposition of *endo*-methylene-2,5-tetrahydrobenzaldehyde (eq 18) as compared to the thermal de-



composition of bicyclo[2.2.1]heptene (eq 19) could provide a



test. Experimental activation energies are 33.6¹⁸¹ and 42.8¹⁸² kcal/mol, respectively, and this difference of 9.2 kcal/mol is larger than the stabilization energy, 8.7 kcal/mol, which is assigned to conjugation of the carbonyl group with one center of the biradical intermediate.¹⁷⁸ Both reactions are predicted to be concerted,¹⁷⁸ so the substituent surprisingly has a larger electronic effect on the concerted reaction than it would have on a biradical reaction.

The only conclusion one can draw from the above example is that in spite of all the mechanistic work that has been done on Diels-Alder reactions, and in spite of the usefulness and simplicity of the thermochemical-kinetic schemes, the argu-

(174) For a recent review, see ref 72, pp 209-220.

(175) S. W. Benson, *J. Chem. Phys.*, **46**, 4920 (1967).

(176) H. E. O'Neal and S. W. Benson, *J. Phys. Chem.*, **71**, 2903 (1967).

(177) H. E. O'Neal and S. W. Benson, *ibid.*, **72**, 1866 (1968).

(178) H. E. O'Neal and S. W. Benson, *Int. J. Chem. Kinet.*, **2**, 423 (1970).

(179) H. M. Frey, *Advan. Phys. Org. Chem.*, **4**, 147 (1966).

(180) H. M. Frey and R. Walsh, *Chem. Rev.*, **69**, 103 (1969).

(181) G. B. Kistiakowsky and J. R. Lacher, *J. Amer. Chem. Soc.*, **58**, 123 (1936).

(182) W. C. Herndon, W. B. Cooper, Jr., and M. J. Chambers, *J. Phys. Chem.*, **68**, 2016 (1964).

Table I
Activation Parameters for Cope Rearrangements^a

<i>E_q</i>	Transition state	ΔH^\ddagger (calcd 0°K), kcal/mol	ΔH^\ddagger (exptl), kcal/mol	ΔS^\ddagger (calcd 423°K), gibbs/(deg mol)	ΔS^\ddagger (exptl), gibbs/(deg mol)	Ref
21	Chairlike	22.8	35.5	-16.6	-10.4	126
21	Boatlike	28.1	~41	-16.7		131
22	Boatlike	17.2	~21	-8.5		131
23	Boatlike	16.7	23.1	-10.0	-11.7	189

^a All calculated values from ref 187.

ment about concerted and biradical reactions may still be carried on. More precise experimental work is needed, and a first-class *ab initio* SCF-CI quantum calculation on the energy surface of a simple Diels-Alder reaction would be especially useful.

4. Energy Surfaces from Empirical Potential Functions

During the decade 1960-1970, an approach to the conformational analysis of organic compounds was developed which required the use of digital computers to minimize the sum of energies obtained from an extensive set of classical potential functions.¹⁸³⁻¹⁸⁵ Practitioners of conformational analysis had always held the viewpoint that a molecule was a system of particles held together by classical forces, but the complexity of the mathematical treatment limited early efforts to simple considerations of group interaction terms like the *gauche n*-butane interaction term.¹⁸⁶ The relative potential energy of two different conformations of the same molecule was obtained by summing over the requisite interaction terms.

In the newer methods of quantitative conformational analysis, the conformational energy is analyzed by partitioning the energy into several parts as in eq 20. E_r and E_θ are the bond-

$$E = E_r(r) + E_\theta(\theta) + E_\phi(\phi) + E_n(d) \quad (20)$$

length and bond-angle deformation energies; the potential functions for these energies are obtained from vibrational analyses. E_ϕ is energy due to torsional strain, and its functional dependence upon geometry is obtained from rotational barrier studies. The nonbonding energy, E_n , is the hardest quantity to estimate, and potential functions of several different types have been suggested. The problems of choosing potentials and the computational problems of minimizing the energy in eq 20 with respect to molecular geometry are discussed extensively in a recent review,¹⁸⁴ and the history and procedures will not be repeated here. It can simply be stated that the relative potential energies of a transition state and a ground state are just as easily obtained from a computer as are the relative energies of two conformations of the same molecule. The requisite inputs are a set of potential functions and nuclear coordinates.

(183) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **83**, 4537 (1961); **84**, 3355 (1962); **86**, 4854 (1964); **89**, 7036 (1967).

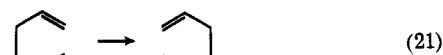
(184) K. B. Wiberg, *ibid.*, **87**, 1070 (1965).

(185) J. E. Williams, P. J. Stang, and P. v. R. Schleyer, *Annu. Rev. Phys. Chem.*, **19**, 531 (1968).

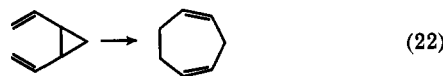
(186) R. B. Turner, *J. Amer. Chem. Soc.*, **74**, 2118 (1952).

(187) M. Simonetta and G. Favini, *Tetrahedron Lett.*, 4837 (1966).

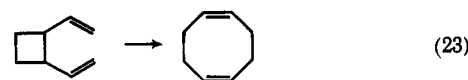
(188) M. Simonetta, G. Favini, C. Mariani, and P. Gramaccioni, *J. Amer. Chem. Soc.*, **90**, 1280 (1968).



(21)



(22)



(23)

Only three reactions related to cycloadditions have been studied by these methods.^{187,188} All three reactions are similar Cope rearrangements shown in eq 21-23.^{126,181,189} The rupture of the σ bond defined the reaction coordinate, and the bond-making process was assumed to vary linearly with the progress of reaction, λ . Other molecular parameters were varied to minimize the energy at each stage of advancement of the reaction. For 1,5-hexadiene the transition state was calculated to occur at $\lambda = 0.5$, the other reactions had transition states close to that point. The activation entropies were obtained by standard statistical mechanical methods using the geometries and bond orders in the calculated transition states. Experimental and calculated activation parameters are compared in Table I.

It is difficult to make an assessment of these results. The difference in energy between chair and boat transition states is nicely calculated, in agreement with the previously cited experimental value.¹²⁶ MINDO/2 calculations^{120,121} described in an earlier section were also satisfactory in this regard. However, both MINDO/2 and these present calculations are low on the activation energies. Contrary to the assertions of the researchers in the area,¹⁸⁸ an error of 7-14 kcal/mol in activation energies can not be considered satisfactory agreement with experiment. In the present case, it seems unlikely that a change in the chosen reaction mechanism would change the calculated activation energies to any significant extent. Energies were calculated and minimized at $\lambda = 0.05$ intervals, so there does not seem to be any chance that a sizable energy barrier is hidden because of the geometric restrictions on the calculations.

The predictive reality of these types of calculations can certainly be questioned. Additional development is needed.

IV. Perturbational Molecular Orbital Theory

Traditionally, MO discussions of organic reactions have been confined to π -electronic systems, and have largely been based upon concepts like bond orders, electronic charges, free va-

(189) G. S. Hammond and C. D. Deboer, *ibid.*, **86**, 899 (1964).

lences, localization energies, etc.^{62, 190-195} In considering cycloaddition reactions, the limitation of MO theory to π electrons does not greatly hamper us since most cycloadditions involve the addition of one π -molecular system to another. However, the employment of reactivity indexes of the type listed above might be a serious handicap. Each of these reactivity indexes is a function of the eigenvectors of the molecular wave function for a single isolated molecule. The mutual interaction of two molecules, which necessarily controls the rate and orientation of a cycloaddition reaction, cannot be estimated by such methods.

The problem of calculating the interaction energy between two molecules has a long quantum-mechanical history. One of the first goals of quantum chemists was to gain an understanding of the attractive van der Waals forces between neutral molecules,^{196, 197} and a later objective was to explain the attractive force which led to the formation of charge-transfer complexes. Perturbation theory is especially suited for the calculation of intermolecular forces, and both problems have been extensively investigated using perturbation methods.

The basic idea is that one may start with molecular wave functions for isolated, separated molecules, and then calculate the energy change resulting from the mutual perturbing influence of one molecule upon the other. A different quantum-mechanical approach would be to calculate the energy of the composite system using the variational method, and to then obtain the interaction energy as the difference between the isolated molecule energies and the composite system energy. The perturbational method is computationally simpler, and also leads to more accurate calculated interaction energies, since the total energies of molecular system cannot be determined to a high degree of accuracy, even by highly sophisticated methods.

The extension of these theoretical concepts to cycloaddition reactions is a natural evolution. The methodology had its genesis in early articles on the mathematical principles of MO theory, and the energy changes that occur when structural differences are introduced into a π -electronic system.¹⁹⁸⁻²⁰⁰ In MO terminology these structural changes would be represented by quantitative variations of certain Coulomb integrals and resonance integrals within the π system. The corresponding energy variations were calculated by perturbation theory. Several later articles by Dewar²⁰¹⁻²⁰⁵ elaborated the

procedures, and a simple theory of the perturbation energy that arises from the merger of two conjugated π systems was developed. A general PMO theory of reactivity ensued from this work.^{62, 203, 206-208}

At the same time, Fukui and his coworkers were evolving the "frontier orbital" theory,²⁰⁹⁻²¹² which correlated reactivity with properties of the highest filled and lowest vacant orbitals of a reactant molecule. Mathematical correlations of the frontier orbital concepts with perturbation theory were easily demonstrated,^{212, 213} and the relationship of both PMO theory and the frontier orbital method to the orbital-symmetry reactivity concepts has also been extensively discussed (ref 62, 207, 208, 214-222).

After discussing the theoretical formalisms of PMO theory, applications to thermal and photochemical cycloaddition reactions and related areas will be described. In each case, earlier works which employed MO theory will also be listed.

A. THEORY AND ASSUMPTIONS

1. Simplified Theory

The central points of PMO reactivity theory can be elucidated by considering the change in energy which occurs as two molecules, R and S, react to form a united molecule R-S (Figure 3).

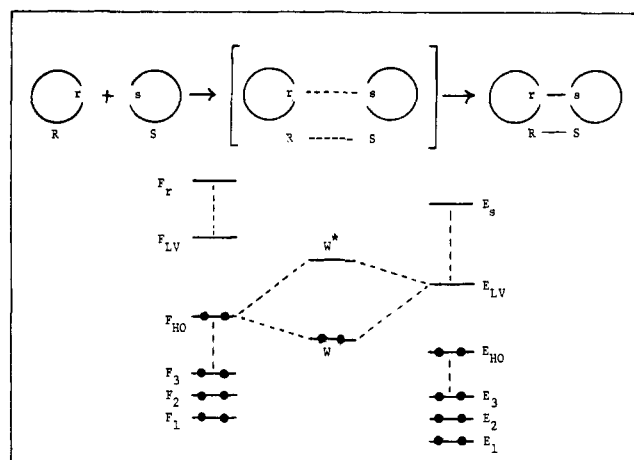


Figure 3. Intermolecular reaction of R and S.

(190) R. Daudel, R. Lefebvre, and C. Moser, "Quantum Chemistry, Methods and Applications," Interscience, New York, N. Y., 1959.

(191) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961.

(192) J. D. Roberts, "Notes on Molecular Orbital Calculations," W. A. Benjamin, New York, N. Y., 1961.

(193) K. Higasi, H. Baba, and A. Rembaum, "Quantum Organic Chemistry," Interscience, New York, N. Y., 1965.

(194) L. Salem, "The Molecular Orbital Theory of Conjugated Systems," W. A. Benjamin, New York, N. Y., 1966.

(195) R. L. Flurry, Jr., "Molecular Orbital Theories of Bonding in Organic Molecules," Marcel Dekker, New York, N. Y., 1968.

(196) J. O. Hirschfelder and W. J. Meath, *Advan. Chem. Phys.*, **12**, 3 (1967).

(197) H. Margenau and N. R. Kestner, "Theory of Intermolecular Forces," Pergamon Press, London, 1969, Chapter 1.

(198) C. A. Coulson and G. S. Rushbrooke, *Proc. Cambridge Phil. Soc.*, **36**, 193 (1940).

(199) C. A. Coulson and H. C. Longuet-Higgins, *Proc. Roy. Soc., Ser. A*, **191**, 39 (1947); **192**, 16 (1947); **193**, 447, 456 (1948); **195**, 188 (1948).

(200) H. C. Longuet-Higgins, *J. Chem. Phys.*, **18**, 265, 275, 283 (1950).

(201) M. J. S. Dewar, *Proc. Cambridge Phil. Soc.*, **45**, 638 (1949).

(202) M. J. S. Dewar, *J. Chem. Soc.*, 2329 (1950).

(203) M. J. S. Dewar, *J. Amer. Chem. Soc.*, **74**, 3341, 3345, 3350, 3353, 3355, 3357 (1952).

(204) M. J. S. Dewar, *J. Chem. Soc.*, 3532 (1952).

(205) M. J. S. Dewar, *ibid.*, 1617 (1954).

(206) M. J. S. Dewar, *Advan. Chem. Phys.*, **8**, 65 (1965).

(207) M. J. S. Dewar, *Tetrahedron, Suppl.*, **8**, (1), 75 (1966).

(208) M. J. S. Dewar, *Chem. Soc. Spec. Publ.*, No. 21, 177 (1967).

(209) K. Fukui, T. Yonezawa, and H. Shingu, *J. Chem. Phys.*, **20**, 722 (1952).

(210) K. Fukui, T. Yonezawa, C. Nagata, and H. Shingu, *ibid.*, **22**, 1433 (1954). Subsequent articles are listed in ref 211.

(211) K. Fukui, "Molecular Orbitals in Chemistry, Physics and Biology," P. O. Löwdin and B. Pullman, Ed., Academic Press, New York, N. Y., 1964, pp 513-537.

(212) K. Fukui in "Modern Quantum Chemistry," Part I, O. Sinanoglu, Ed., Academic Press, New York, N. Y., 1965, pp 49-84.

(213) K. Fukui, C. Nagata, T. Yonezawa, H. Kato, and K. Morokuma, *J. Chem. Phys.*, **31**, 287 (1959).

(214) K. Fukui, *Tetrahedron Lett.*, 2009 (1965).

(215) K. Fukui, *Bull. Chem. Soc. Jap.*, **39**, 498 (1966).

(216) K. Fukui and H. Fujimoto, *Tetrahedron Lett.*, 251 (1966).

(217) K. Fukui and H. Fujimoto, *Bull. Chem. Soc. Jap.*, **39**, 2116 (1966).

(218) K. Fukui and H. Fujimoto, *ibid.*, **40**, 2018 (1967).

(219) K. Fukui and H. Fujimoto, *ibid.*, **41**, 1989 (1968).

(220) K. Fukui and H. Fujimoto, *ibid.*, **42**, 3399 (1969).

(221) K. Fukui and H. Fujimoto in "Mechanisms of Molecular Migrations," Vol. 2, B. S. Thyagarajan Ed., Interscience, New York, N. Y., 1969, pp 117-190.

(222) K. Fukui, *Top. Curr. Chem.*, **15**, 1 (1970).

For the present, the discussion will be limited to the change in π -electronic energy, and the main objective is to estimate the difference in electronic energy between separated molecules and transition state.

The energy levels of R are $F_1, F_2, F_3, \dots, F_r$, with the highest occupied level being F_{HO} . Similarly the energy levels of S are $E_1, E_2, E_3, \dots, E_s$, the lowest vacant level being E_{LV} . Each MO of R and S is an orthonormal linear combination of basis atomic orbitals of the form of eq 24, and these functions are

$$\Psi_j^{\text{R}} = \sum_i C_{ij} \phi_i \quad (24)$$

assumed to be known. The energy (eigenvalue) associated with a particular MO is given by eq 25, where \mathbf{H}^{R} is the Hamiltonian

$$F_j = \int \Psi_j^{\text{R}} \mathbf{H}^{\text{R}} \Psi_j^{\text{R}} dT \quad (25)$$

operator appropriate to the isolated molecule R.

In the transition complex, the total intermolecular interaction is a sum of the interactions of each specific molecular energy level of R with each individual level of S. As the levels of the two reactants interact, the levels repel each other and this leads to level splittings. One of the important level splittings, between highest occupied MO (HOMO) of R and lowest unoccupied MO (LUMO) of S, is illustrated in Figure 3. The necessary mathematics to deduce the energy levels of the transition state will be simplified to an examination of this important interaction. We will impose the zero-overlap approximation as in Hückel MO theory¹⁹¹ ($S_{\text{RS}} = 0$), and will assume that the reaction involves the formation of a single new bond between orbitals r of R and s of S.

The MO's of the transition complex are taken as linear combinations of the MO's of the separated species (eq 26). The

$$\Psi^{\text{RS}} = a\Psi^{\text{R}} + b\Psi^{\text{S}} \quad (26)$$

best approximate energy of the interacting state will be obtained by applying the variational theorem, which leads first to a set of secular equations, and finally to a secular determinant (eq 27), where W is the energy level value (s) for the

$$\begin{vmatrix} F_{\text{HO}} - W & \Gamma_{\text{RS}} \\ \Gamma_{\text{RS}} & E_{\text{LV}} - W \end{vmatrix} = 0 \quad (27)$$

transition complex, and Γ_{RS} is the resonance (exchange) integral for the specific interaction between R and S.

The solution of eq 27 is given by eq 28, which is equivalent

$$W = \frac{1}{2} \left[F_{\text{HO}} + E_{\text{LV}} \pm \sqrt{(E_{\text{HO}} + E_{\text{LV}})^2 - 4F_{\text{HO}}E_{\text{LV}} + 4\Gamma_{\text{RS}}^2} \right] \quad (28)$$

to eq 29. Expanding the square-root term in eq 29 as a series

$$W = \frac{1}{2} \left[F_{\text{HO}} + E_{\text{LV}} \pm (F_{\text{HO}} - E_{\text{LV}}) \sqrt{1 + (2\Gamma_{\text{RS}})^2 / (F_{\text{HO}} - E_{\text{LV}})^2} \right] \quad (29)$$

and taking the first two terms gives eq 30 for the lower energy

$$W = F_{\text{HO}} + (\Gamma_{\text{RS}})^2 / (F_{\text{HO}} - E_{\text{LV}}) \quad (30)$$

level W (Figure 3) of the interacting state.

We can express Γ_{RS} as a function of the coefficients of the atomic orbitals of the original separated molecules. This is

done in eq 31 where ϕ_r and ϕ_s are the atomic orbitals in the

$$\Gamma_{\text{RS}} = \langle \Psi_{\text{R}} | \mathbf{P} | \Psi_{\text{S}} \rangle = \langle c_r^{\text{HO}} \phi_r | \mathbf{P} | c_s^{\text{LV}} \phi_s \rangle = c_r^{\text{HO}} c_s^{\text{LV}} \langle \phi_r | \mathbf{P} | \phi_s \rangle = c_r^{\text{HO}} c_s^{\text{LV}} \gamma \quad (31)$$

original basis set, c_r and c_s are the respective eigenvectors in the LCAO-MO's, γ is the atomic orbital transition state resonance integral, and \mathbf{P} is the perturbation Hamiltonian.

Extending this treatment to all interacting nondegenerate levels of R and S leads to the usual equation of second-order perturbation theory (eq 32)²⁰³ for the change in energy which

$$\Delta_2 = k \left(\sum_{\text{R}}^{\text{occ}} \sum_{\text{S}}^{\text{vac}} - \sum_{\text{R}}^{\text{vac}} \sum_{\text{S}}^{\text{occ}} \right) \frac{(c_r c_s)^2 \gamma^2}{E_{\text{R}} - E_{\text{S}}} \quad (32)$$

occurs as R and S interact. k is an occupancy number, 1 or 2, depending upon whether the interaction involves one electron or two electrons, respectively.

If a vacant or partially vacant energy level of S is degenerate in energy with a filled or partially filled level of R, a first-order perturbation energy term arises. In many photochemical reactions this term may be the overriding factor which determines the energy change concurrent with the reaction being calculated. Substitution in secular determinant (eq 27) with $F = E$ gives the new energy levels as $F \pm \Gamma$. Then using eq 31 for the more explicit form of Γ , one obtains eq 33 for the first-order change in energy.

$$\Delta_1 = kc_r c_s \gamma \quad (33)$$

In cycloaddition reactions, bond formation may occur simultaneously at two or more reaction sites. Equations 32 and 33 can be modified by summing the quadratic terms over all reaction sites as in eq 34 and 35.

$$\Delta_1 = k \sum_{rs} c_r c_s \gamma_{rs} \quad (34)$$

$$\Delta_2 = k \left(\sum_{\text{R}}^{\text{occ}} \sum_{\text{S}}^{\text{vac}} - \sum_{\text{R}}^{\text{vac}} \sum_{\text{S}}^{\text{occ}} \right) \frac{\left(\sum_{rs} c_r c_s \gamma_{rs} \right)^2}{E_{\text{R}} - E_{\text{S}}} \quad (35)$$

To compare first-order perturbation energies with second-order energies, one must assume a value for γ in terms of the units of Hückel MO theory. A convenient choice is $\gamma = \beta/2$ where β is the usual Hückel resonance integral. The energy units of first-order terms will then be twice those of second-order terms. A smaller value of γ would lead to a larger ratio of first-order to second-order units. So one deduces that first-order terms may be dominant during the early stages of a reaction.

The first- and second-order perturbation energies are positive; that is, the π energy of the transition state is larger (more stable) than that of the separated molecules. The reactivities of molecules are assumed to parallel the π stabilization energy. One might expect that this assumption would be most correct when comparing two (or more) different reaction sites in the same molecule. The most stable transition state, given by the largest π stabilization energy, would point out the preferred reaction pathway.

Two other assumptions deserve some discussion. Equation 30 is only obtainable as a tenable approximation if the matrix element Γ_{RS} is small compared to the energy difference between interacting MO levels. This will only be true at an early point along the reaction coordinate. This means that calculations and predictions may be reliable only during the start of a reaction. If, for two related reactions, the free energy reac-

tion surfaces parallel each other up to large extents of reaction, valid predictions are expected. These reactions would obey a reactivity "non-crossing" rule.²²³ Reactions not exhibiting this behavior could not be interpreted with PMO theory.

The effects of Coulombic repulsion and attraction are neglected in this simple treatment, and this fact coupled with the zero-overlap approximation precludes using this form of the theory to consider the reactions of highly polar substances. The neglect of overlap also leads to a neglect of the intermolecular repulsive interactions of filled levels. Therefore, it would seem most appropriate to use this simplest PMO theory only when the starting MO's are Hückel MO's calculated with the same basic assumptions.

2. General Theory

Several derivations of a more complete and general PMO theory of intermolecular interactions have been published.^{219, 222, 224-231} A natural parallel to the evolution of MO theory itself can be discerned. First, there is a development of an independent electron Hückel-type method for π systems as described in the preceding section. Then come methods which include or can be applied to all the valence electrons of reacting molecules. Overlap is retained in the perturbation formalism^{226, 227} just as in extended Hückel MO theory,⁷⁵ and the important effects of electron and nuclear Coulombic repulsions and attractions are explicitly treated.^{219, 225} Finally, a perturbation theory based upon an SCF formalism is derived.^{219, 225, 228-231} Then the calculations can be carried out in the framework of one of the common valence-shell SCF schemes like the CNDO⁷⁶ or MINDO⁷⁷ methods.

A more elaborate theory is desirable for many reasons. The most important reason may be because an elaborate theory is capable of being dissected into several parts, to each of which a theoretical or physical interpretation may be given. The subtle details of chemical reactions are often determined by a balance among diverse factors, and an analysis of these factors might be facilitated by a partition of the theory. Early studies of the dispersion forces between unsaturated molecules like ethylene, butadiene, etc., and benzene are interesting from this viewpoint.²³²⁻²³⁴ Highly parameterized calculations based solely on the π electrons gave reasonable values of the interaction energies, but a later investigation²³⁵ including the σ electrons gave the σ - π and the σ - σ interactions as much more important in the total dispersion forces between small olefins and polyolefins. These results were obtained at an intermolecular distance of 10 Å and in several relative orientations, and it is possible that the relative amounts of the three contributions to the dispersion force might change at shorter distances. However, it is clear that the implication of the σ electrons

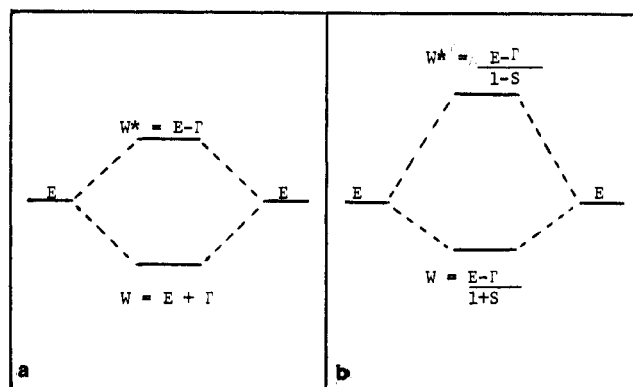


Figure 4. Interaction of two closed-shell molecules.

could not have been perceived without the later elaboration of theory. Incidentally this case also indicates a need for an all-valence-electron MO treatment of intermolecular forces.

Overlap is introduced²²⁶ because a Hückel-type perturbation treatment including the zero-overlap approximation does not lead to any repulsion between the interacting species, even for as simple a system as two closed-shell helium atoms (Figure 4a). Inclusion of overlap gives the antibonding intermolecular level as more stabilized than the bonding intermolecular level is stabilized (Figure 4b), giving a net repulsion between the two occupied shells of electrons.

The mathematical treatment is straightforward.²²⁶ A secular determinant (eq 36) with overlap included, for the interaction of MO's F of R and E of S , is solved for the interaction energy,

$$\begin{vmatrix} F - W & \Gamma_{RS} - S_{RS}W \\ \Gamma_{RS} - S_{RS}W & E - W \end{vmatrix} = 0 \quad (36)$$

Δ (eq 37). If the intermolecular interaction integral is ex-

$$\Delta = -4 \sum_{R \neq S}^{\text{occ}} \sum_{S}^{\text{occ}} \Gamma_{RS} S_{RS} + 2 \sum_R^{\text{occ}} \sum_S^{\text{vac}} (\Gamma_{RS} - S_{RS}F)^2 / (F - E) + 2 \sum_S^{\text{occ}} \sum_R^{\text{vac}} (\Gamma_{RS} - S_{RS}E)^2 / (E - F) \quad (37)$$

pressed as a function of overlap and the eigenvectors of the MO's of the separate molecules, eq 37 can be transformed into eq 38 after a few straightforward approximations. In eq 38, q_r and q_s are the Hückel electron densities at positions

$$\Delta = - \sum_{rs} (q_r + q_s) \gamma_{rs} S_{rs} + 2 \left(\sum_R^{\text{occ}} \sum_S^{\text{vac}} - \sum_R^{\text{vac}} \sum_S^{\text{occ}} \right) \frac{\left(\sum_{rs} C_r C_s \gamma_{rs} \right)^2}{E_R - E_S} \quad (38)$$

r and s , and each will be close to unity if R and S are neutral organic molecules. Equation 38 and eq 32 are identical except for the repulsive first term in eq 38 which is not a Coulombic interaction. This term arises because each molecule has a closed-shell structure into which other electrons cannot penetrate. The larger the electron density on an atom, the larger this "exclusion shell." Applications will be discussed later, but one can see that this repulsive term might allow one to delineate the shape of an energy surface for a cycloaddition reaction. Also, eq 38 is easily extended to a consideration of all the valence electrons,²²⁷ rather than just the π electrons.²²⁶

If the molecules are polar, the Coulombic energy terms can simply be appended to eq 32 or 38. These would take the form

- (223) R. D. Brown, *Quart. Rev., Chem. Soc.*, **6**, 63 (1952).
 (224) R. F. Hudson and G. Klopman, *Tetrahedron Lett.*, 1103 (1967).
 (225) G. Klopman and R. F. Hudson, *Theor. Chim. Acta*, **8**, 165 (1967).
 (226) L. Salem, *J. Amer. Chem. Soc.*, **90**, 543 (1968).
 (227) A. Imamura, *Mol. Phys.*, **15**, 225 (1968).
 (228) A. Devaquet and L. Salem, *J. Amer. Chem. Soc.*, **91**, 3793 (1969).
 (229) A. Devaquet, *Mol. Phys.*, **18**, 233 (1970).
 (230) R. Sustmann and G. Binsch, *ibid.*, **20**, 1 (1971).
 (231) R. Sustmann and G. Binsch, *ibid.*, **20**, 9 (1971).
 (232) F. London, *J. Phys. Chem.*, **46**, 305 (1942).
 (233) C. A. Coulson and P. L. Davies, *Trans. Faraday Soc.*, **48**, 777 (1952).
 (234) P. L. Davies, *ibid.*, **48**, 789 (1952).
 (235) E. F. Haugh and J. O. Hirschfelder, *J. Chem. Phys.*, **23**, 1778 (1955).

given in eq 39,²⁸⁶ where Q_r and Q_s are the total initial charges

$$\Delta Q = - \sum_{rs} Q_r Q_s \Omega / \epsilon \quad (39)$$

on atoms r and s , respectively, Ω is the Coulomb repulsion integral and ϵ is the local dielectric constant.²⁸⁴ The problems associated with defining some of these quantities are obvious.

The SCF formulation of intermolecular perturbation theory leads to equations which are very similar to the foregoing equations. In the region of small overlap and assuming both an SCF perturbation operator and the zero-differential overlap approximation, the interaction energy takes the form given in eq 40, where each term is understood to be correctly summed

$$\Delta = -Q_r Q_s \Omega / \epsilon + \frac{2(C_r C_s \gamma)^2}{F - E} + C_r C_s \gamma + (E_x \text{ and } P) \quad (40)$$

over all interactions between the two molecules. The first term is a first-order Coulombic energy term which can be calculated in terms of the atomic charges. The second-order term represents an attractive energy due to the mixing of occupied orbitals of one molecule with vacant orbitals of the other molecule. This energy has been called the delocalization energy or charge-transfer energy. The first-order delocalization energy term, $C_r C_s \gamma$, only arises if two partially occupied orbitals are degenerate or nearly degenerate in energy. The literature should be consulted for the form of the less important exchange (E_x) and polarization (P) terms which remain.^{219, 225, 229, 236}

The neglect of overlap in the SCF treatment (*cf.* first term in eq 38) should not be a serious omission. This approach is almost always adopted in valence-shell SCF calculations which have been quite successful in several applications. However, this does mean that eq 40 should only parallel reality at an early stage of the cycloaddition reaction.

3. Charge and Frontier-Orbital Control of Reactivity

General treatments of chemical reactivity have been described which are based on intermolecular PMO theory.^{215-222, 224, 225, 286, 237} First we consider the case in which a large energy gap separates filled and vacant levels of the two molecules undergoing reaction. The donor molecule retains its electrons strongly, and the acceptor molecule has a low tendency to gain electrons. In the second-order term of eq 40, the denominator may be replaced by an average energy difference, A . Then the intermolecular energy will be given by eq 41, and we see that this reaction would primarily be con-

$$\Delta = -Q_r Q_s \Omega / \epsilon + 2(C_r)^2 (C_s)^2 \gamma^2 / A \quad (41)$$

trolled by charge distribution.²⁸⁶ It is difficult to conceive of a cycloaddition reaction which would exhibit this behavior.

More usually, the two organic molecules undergoing a cycloaddition reaction would have frontier orbitals, HOMO's and LUMO's, which are fairly close in energy. Facile cycloadditions might be the result of interacting degenerate orbitals, and the total perturbation energy would then be approximated by the first-order delocalization term of eq 40 as given by eq 42. In general, such a reaction would be controlled by a

$$\Delta = 2C_r^{\text{HOMO}} C_s^{\text{LUMO}} \gamma \quad (42)$$

single interaction, that of the highest occupied orbital of one reagent with the lowest unoccupied of the other reagent. We would call this reaction a frontier-orbital controlled reaction, and photochemical cycloaddition reactions are likely to be of this type.

Many cycloaddition reactions of nonexcited molecules could be intermediate in character. Equation 40 then indicates that the interaction of HOMO (R) with LVMO (S) might not be a dominating factor, especially if the molecules are large with filled and vacant manifolds of closely spaced energy levels. However, it has been suggested^{220, 222} that, even in these cases, the interactions of the frontier orbitals may still be a predominant influence. By inference and from actual numerical calculations, it is demonstrated that frontier-electron density increases as the reaction proceeds. At the same time, a narrowing of the energy gap between frontier orbitals occurs. Both of these effects would increase the importance of the frontier orbitals. It is suggested that this effect could only be apparent during the very initial stages of a reaction, but this is the very period when orientation, selectivity, or relative reactivity might be determined.

The numerical calculations were carried out on the system 1,3-butadiene and ethylene.²²⁰ As the terminal bonds in butadiene are stretched and the central bond compressed, the highest-occupied antisymmetric orbital of butadiene does increase in energy, and correspondingly the lowest vacant orbital of ethylene is lowered in energy by bond elongation.²²² However, the stabilizing influence of delocalization on the butadiene MO is not included. As the reaction proceeds, one mixes a part of the vacant antisymmetric orbital of ethylene into the filled antisymmetric orbital of butadiene, and this must oppose the destabilizing effect described above.

Empirically, the evidence seems to favor an emphasis upon the frontier orbitals of a molecule as controlling factors in reactivity. Several examples of the success of reactivity indices based upon the frontier orbital coefficients could be cited,^{62, 191, 288} and it may be that full calculations and the frontier-orbital results would parallel each other. A critical test has not been devised.

B. APPLICATIONS OF PMO THEORY

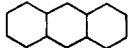
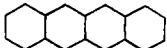
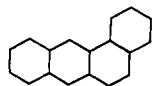
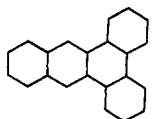
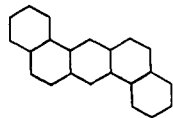
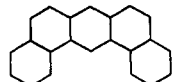
PMO theory can provide a detailed picture of a reaction surface, or it can be used to correlate relative reactivities and selectivities from a qualitative or semiquantitative point of view. Examples of the latter aspect of use are more numerous and are often more useful to the chemist in testing his conjectures about the mechanisms of reactions. Neither application has reached a mature and final state of development. This fact will become obvious as we review several of the applications of PMO theory which have been published. The experienced organic chemist may feel that the correlations of experimental facts and the conclusions which are drawn are redundant in certain cases, since explanations in terms of the ordinary electronic theory of organic chemistry may be available. The important point is that PMO theory can provide quantitative correlations and explanations in many cases where only qualitative inferences were previously possible.

(236) G. Klopman, *J. Amer. Chem. Soc.*, **90**, 223 (1968).

(237) K. Fukui, H. Hao, and H. Fujimoto, *Bull. Chem. Soc. Jap.*, **42**, 348 (1969).

(238) R. D. Brown, *J. Chem. Soc.*, 691, 2730 (1950).

Table II
Rate Constants and Localization Energies for Diels-Alder Reactions of Maleic Anhydride^a

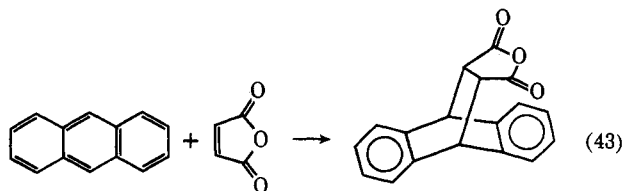
Diene		Rate constant, l./(mol sec)	N_{14}^b (arbitrary units)	L_{14}^c , eV	L^d , eV
	Anthracene	75.2	2.530	(0)	(0)
	Naphthalene	1380	2.052	-0.232	-0.392
	Benz[a]anthracene	6.92	2.790	0.237	-0.003
	Dibenz[a,c]anthracene	3.58	3.007	0.395	0.088
	Dibenz[a,h]anthracene	0.747	3.079	0.440	0.087
	Dibenz[a,j]anthracene	0.675	3.037	0.440	0.022

^a Diethyl succinate solution at 129.7°. ^b Reactivity numbers. ^c SCF-MO method. ^d SCF-MO method, most reactive position. ²⁴⁴

1. Diels-Alder Reactions

The 4 + 2 → 6 cycloaddition reaction of an unsaturated dienophile to a diene⁵⁻²⁰ has been a favorite subject for theoreticians. This is natural because many examples of the reaction are known in which reaction occurs simply upon mixing in inert solvents or in the gas phase. Solvent effects are minimized or absent, and calculations can be compared with experiments with some hope that the calculated results are reliable.

An interesting aspect of theory has to do with the relative reactivities of aromatic hydrocarbons with a common dienophile. The reaction of anthracene with maleic anhydride is a typical example (eq 43). MO approaches to this problem first



appeared in 1950²³⁸ and have continued to appear up to the present.^{203, 210, 211, 223, 239-244} The most simplistic viewpoint assumes that energy of activation will parallel the heat of reaction, which in turn parallels the π energy loss in the reaction.^{62, 63} The π -energy loss defines a reactivity index called the

paralocalization energy, L_{14} .^{288, 245-247} Semiquantitative correlations of L_{14} and the rates of Diels-Alder reactions are well known.^{191, 203, 211, 223}

The rates of the maleic anhydride additions to five polycyclic aromatic hydrocarbons were recently determined,²⁴⁴ and the data are summarized in Table II. Localization energies were calculated for either attack at the single most reactive positions (L), or for simultaneous attack at the most reactive 1,4 position (L_{14}) using a semiempirical SCF-MO method.²⁴⁸ The table also lists reactivity numbers (N_{14}) which were rapidly calculated by hand using the first-order perturbation method introduced by Dewar several years ago.²⁰³ When the logarithms of the rate constants are correlated with the localization energies, the correlation coefficients are $N_{14} = 0.986$, $L_{14} = 0.988$, and $L = 0.865$. This result is taken to mean that the transition state is essentially cyclic and symmetric,²⁴³ in agreement with the general formulation of Diels-Alder reactions as allowed concerted [$\pi 4_s + \pi 2_s$] processes.⁴

Localization energies can be related to the generalized PMO theory by assuming that the reaction is frontier-orbital controlled.^{211, 222} Using eq 40, the first term would be constant, and the reactivity differences would be controlled by the second-order interaction term, as shown in eq 44, or eq 45, if

$$\Delta = C + 2 \frac{[C_{1r}^{\text{HO}} C_{1s}^{\text{LV}} + C_{4r}^{\text{HO}} C_{2s}^{\text{LV}}]^2}{E_R^{\text{HO}} - F_S^{\text{LV}}} \gamma^2 \quad (44)$$

$$\Delta = C_1 + C_2 [C_{1r} + C_{4r}]^2 \quad (45)$$

(239) R. D. Brown, *J. Chem. Soc.*, 1612 (1951).

(240) A. Pullman and G. Berthier, *C. R. Acad. Sci.*, **241**, 2563 (1956).

(241) H. Hopff and H. R. Schweizer, *Helv. Chim. Acta*, **42**, 2315 (1959).

(242) I. R. Epstein, *Trans. Faraday Soc.*, **63**, 2085 (1967).

(243) H. Sofer, O. E. Polansky, and G. Derflinger, *Monatsh. Chem.*, **99**, 1879 (1968).

(244) M. J. S. Dewar and R. S. Pyron, *J. Amer. Chem. Soc.*, **92**, 3098 (1970).

(245) R. D. Brown, *Aust. J. Sci. Res., Ser. A*, **2**, 564 (1949).

(246) R. D. Brown, *J. Chem. Soc.*, 3249 (1950).

(247) R. D. Brown, *Trans. Faraday Soc.*, **45**, 296 (1949); **46**, 146 (1950).

(248) M. J. S. Dewar and T. Morita, *J. Amer. Chem. Soc.*, **91**, 796 (1969).

$C_{1s} = C_{2s}$, and if the energy gap between HFMO of aromatic reactant and LVMO of maleic anhydride is relatively constant. Equation 45 is equivalent to the reactivity index called approximate superdelocalizability,²¹¹ and must therefore also be linearly related to all of the other reactivity indexes which have been suggested for aromatic compounds.^{211, 223, 249-251}

It may also be that the full calculations of the intermolecular perturbation energy would give values which parallel the localization energies, but this has not yet been demonstrated. However, it has been shown that there is an almost exact correlation between the para localization energy²³⁸ and the extra delocalization energy of a complex of diene and dienophile, as exemplified in eq 46 for the complex of maleic anhydride and benzene.²⁵² The complex is treated as a supermolecule within the Hückel approximations.²⁵² It is assumed

$$E(\text{delocalization}) = E(\text{complex}) - E(\text{benzene}) - E(\text{maleic anhydride}) \quad (46)$$

that the supermolecule has two additional bonds, joining the carbon atoms of the double bond of maleic anhydride to 1,4 positions in the aromatic compound, and the resonance integrals for these bonds are assumed to be proportional to overlap integrals. This kind of model for a π complex has been used often in the studies of charge-transfer complexes,²⁵³⁻²⁶⁰ and in applications to Diels-Alder reactions.²⁶¹⁻²⁶⁴ Perturbation energies (eq 44) are approximations to the delocalization energies (eq 46), so one might reasonably expect a correlation of PMO results with para localization energies.

Equations 44 and 45 also make clear the importance of a relationship between the phases of the MO's which are interacting, in this case, electronic interaction of HFMO of diene and LVMO of dienophile ($\Psi_R^{HO} \rightarrow \Psi_S^{LV}$). The product of the coefficients of the MO's must add in phase for the perturbation energy to be large.²¹¹ In Figure 5, this relationship is illustrated for the reaction of butadiene with ethylene. This necessary phase relationship between the frontier orbitals defines a selection rule for the Diels-Alder reaction,^{4, 211, 222, 265} and all known examples of the reaction satisfy this rule. The description of the reaction as a suprafacial, suprafacial process⁴ is also contained in this selection rule since the interacting orbitals are p-type, antisymmetric in the plane of the molecule.

As one introduces substituents into the diene and dienophile, or if one allows the structures of the reactants to differ in a major way, the frontier orbital energy difference in the denominator of eq 44 will not approximate a constant value.

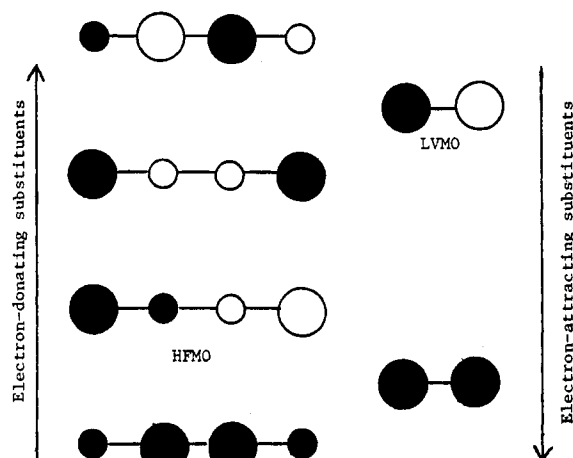


Figure 5. HMO diagrams for butadiene and ethylene. Shaded areas indicate positive coefficients.

The size of the energy gap, related to the difference between the ionization potential of the diene and the electron affinity of the dienophile, could then serve as a rough kind of reactivity index.^{222, 265, 266} The diagram in Figure 5 illustrates the concept for substituted butadiene and ethylene. All electronic levels of butadiene are raised by introducing an electropositive substituent, and all levels of ethylene are lowered by introducing an electronegative substituent. In effect, butadiene will become a better donor and ethylene a better acceptor molecule, and the energy gap HOMO (butadiene) \rightarrow LVMO (ethylene) will be decreased. The overall effect is to increase the second-order stabilization PMO energy calculated by eq 44. It can easily be seen that the inverse substitution pattern decreases the energy gap HOMO (ethylene) \rightarrow LVMO (butadiene) in a similar way so either pattern of substitution should lead to increased rates of Diels-Alder reactions. Traditional effects of substitution are therefore accommodated by this aspect of the theory, and, in addition, the occurrence of reactions with inverse electron demand^{11, 14, 267, 268} is nicely explained.

No energy gap-reactivity index quantitative correlations have appeared in the literature. However, the logarithms of the rates of the reaction of several aromatic dienes with a common dienophile have been compared with the ionization potentials of the aromatic compound, and a linear plot was observed.²⁶⁹ Even in the case of a series of 9,10-disubstituted anthracenes reacting with maleic anhydride, an excellent linear correlation was obtained.²⁶⁹ In this second case one might have expected some steric effects to be present. In analogous experiments, with cyclopentadiene as diene, the dienophile was varied, and the logarithm of the rate of cycloaddition was compared with the electron affinity of the dienophile.²⁷⁰ There was a very wide variation in the structure of the dienophile, and the correlation of the data was correspondingly not as good as in the diene-variation cases. In all this work, ionization potentials and elec-

(249) H. H. Greenwood, *Trans. Faraday Soc.*, **48**, 585 (1952).

(250) J. Koutecky, R. Zahradnik, and J. Cizek, *ibid.*, **57**, 170 (1961).

(251) H. H. Greenwood and R. McWeeny, *Advan. Phys. Org. Chem.*, **4**, 73 (1966).

(252) N. Tyutyulkov and P. Markov, *Monatsh. Chem.*, **99**, 861 (1968).

(253) R. L. Flurry, Jr., *J. Phys. Chem.*, **69**, 1927 (1965); **73**, 2111 (1969).

(254) R. L. Flurry, Jr., and P. Politzer, *ibid.*, **73**, 2787 (1969).

(255) S. Wold, *Acta Chem. Scand.*, **20**, 2377 (1966).

(256) M. Sundbom, *ibid.*, **20**, 1608 (1966).

(257) R. Roos, *ibid.*, **20**, 1673 (1966); **21**, 1608 (1967).

(258) D. B. Chesnut and R. W. Moseley, *Theor. Chim. Acta*, **13**, 230 (1969).

(259) D. B. Chesnut and P. E. S. Wormer, *ibid.*, **20**, 250 (1971).

(260) K. Sundaram and W. P. Purcell, *Int. J. Quantum Chem.*, **5**, 101 (1971).

(261) N. Tyutyulkov and P. Markov, *Monatsh. Chem.*, **96**, 2030 (1965).

(262) P. Markov and N. Tyutyulkov, *ibid.*, **97**, 1229 (1966).

(263) P. Markov and P. N. Skancke, *Acta Chem. Scand.*, **23**, 1295 (1969).

(264) P. Markov, *Dokl. Bolg. Akad. Nauk*, **22**, 419 (1969).

(265) K. Fukui, *Tetrahedron Lett.*, 2009 (1965).

(266) R. D. Brown, *J. Chem. Soc.*, 2224, 2232 (1959).

(267) W. E. Bachmann and N. C. Deno, *J. Amer. Chem. Soc.*, **71**, 3062 (1949).

(268) J. Sauer and H. Wiest, *Angew. Chem., Int. Ed. Engl.*, **1**, 269 (1962).

(269) A. I. Konvalov and V. D. Kiselev, *Zh. Org. Khim.*, **2**, 142 (1966).

(270) A. I. Konvalov, V. D. Kiselev, and O. A. Vigdorovich, *ibid.*, **3**, 2085 (1967).

tron affinities were estimated from the energies of charge-transfer bands, a technique which is in common use.^{271, 272}

There is a well-known qualitative relationship between the ability of dienes and dienophiles to form charge-transfer complexes and the rates of their Diels–Alder reactions.^{12, 14, 18, 20} Electron-donating groups in the diene (donor) coupled with electron-attracting groups in the dienophile (acceptor) facilitate both processes. There is also a well-known mechanistic question as to whether or not a molecular charge-transfer complex of diene and dienophile is a necessary precursor to the transition state of the Diels–Alder reaction.^{273–275} It is difficult to see how simplified PMO theory could answer this question, since an intermolecular perturbation energy would result in either case.

In some ways, the question is a semantic one. There is no doubt that π -molecular complexes exist. They are always formed exothermically from their precursors.^{133–137} There is also no doubt that a “complex” of diene and dienophile traverses a reaction surface in the Diels–Alder reaction, since the reaction is always bimolecular. But the concept of a stable molecular complex closer to the transition state than separated addenda is not a tenable one.²⁷⁶

Calculations of the geometries of π -molecular complexes may have a bearing. Some of these calculations were carried out in the supermolecule approach,^{252–260} and others used perturbational techniques.^{279, 280} In most cases, all valence electrons were treated. In many cases, particularly with tetracyanoethylene complexes, the calculated most stable relative geometries of donor and acceptor were not the geometries which would lead to a Diels–Alder adduct.^{259, 279, 280} If this situation exists during a Diels–Alder reaction, the stable molecular complex is simply a side effect, which may be eliminated from mechanistic considerations. However, some of the forces which stabilize molecular complexes will also help determine the height of energy barriers in Diels–Alder reactions.

The two factors of electron-transfer ability and localization energies have been combined in a recent discussion of reactivity in diene syntheses.²⁸¹ Diene reactivity is determined by the 1,4-localization energy and the donor capacity (ionization potential), while dienophile reactivity is determined by 1,2-localization energy and the electron-acceptor capacity (electron affinity). Hückel MO calculations showed that decreasing 1,4-localization energies paralleled decreasing ionization potentials, but decreasing 1,2-localization energies had an inverse relationship to electron-accepting capacity. Therefore two donor molecules with the same ionization potential like benzene and butadiene are expected to have different reactivities because their 1,4-localization energies differ to a large extent, but the reactivity of butadiene and ethylene as dienophiles, with localization energies of 2.47 and 2.00 β , respectively, is controlled by their differing electron affinities. These

suggestions certainly seem reasonable, but a quantitative test has yet to be reported.

The PMO theory incorporates elements of all of the previously discussed work in this section, and can also treat the additional factor of charge interactions if the molecules are polar (*cf.* eq 40). Only a few PMO calculations have been carried out. The first reported results^{282, 283} were concerned with the various dimerizations and cross-additions of cyclopentadiene (CPD), cyclopentadienone (CPDO), and maleic anhydride (MA). Hückel MO calculations gave the wave functions and energy levels for the separate molecules, and all interactions except at the two primary bonding sites were neglected. The high reactivity of CPDO and several of its derivatives was primarily attributed to a very low-lying LVMO. The high tendency of CPDO to dimerize had earlier been attributed to very low 1,4-localization and 1,2-localization energies.²⁸⁴

The results of the PMO calculations are summarized in the last column of Table III, where perturbation energies are all

Table III

PMO Energies for Diels–Alder Reactions

Reaction		Energies, kcal/mol		
Diene	Dienophile	Endo geometry ^a	Exo geometry ^a	Unspecified ^b
CPD	+CPD	(0.0)	+2.3	(0.0)
CPD	+MA	-7.1	-2.7	-7.3
CPD	+CPDO	-16.2		-12.9
CPDO	+CPD	-10.0		-3.0
CPDO	+MA	-8.8	-1.4	-6.9
CPDO	+CPDO	-29.9	-17.4	-15.9

^a EHMO,²⁸⁶ ^b Hückel.²⁸³

given relative to the calculated energy for CPD dimerization. The calculated values²⁸³ are generally in agreement with experiment. CPDO is expected to react with CPD solely as a dienophile (-12.9 kcal/mol), rather than as a diene (-3.0 kcal/mol).²⁸⁵ A diffusion-controlled rate is predicted²⁸³ for CPDO dimerization, and experiments indicate that the rate of dimerization is very fast.²⁸³ When a electrostatic interaction energy of -12.4 kcal/mol is added to the second-order PMO energy for the reactions CPDO + MA, MA is predicted to trap CPDO more efficiently than CPD, but the converse has been observed.²⁸⁵

The remainder of the data in Table III is the result of EHMO-PMO calculations using eq 35.²⁸⁶ Endo and exo parallel planes configurations of the reaction pairs were investigated. The intermolecular resonance integrals were taken proportional to overlap integrals, and all interactions between the π electrons contributed to the PMO energy. The differences in PMO calculated energies and experimental results is quite good. For example, the difference in transition state energies for formation of *endo*- and *exo*-dicyclopentadiene is estimated to be 2.3 kcal/mol, and the experimental value is 4.5

(271) J. B. Birks and M. A. Slifkin, *Nature (London)*, **191**, 761 (1961).

(272) G. Brigleb, *Angew. Chem.*, **76**, 326 (1964).

(273) R. B. Woodward, *J. Amer. Chem. Soc.*, **64**, 3058 (1942).

(274) L. J. Andrews and R. M. Keefer, *ibid.*, **77**, 6284 (1955).

(275) M. J. S. Dewar, *Tetrahedron Lett.*, 16 (1959).

(276) J. A. Berson and W. A. Mueller, *J. Amer. Chem. Soc.*, **83**, 4940 (1961).

(277) B. A. Arbuzov and A. I. Konovalov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1290 (1965).

(278) J. Sauer and B. Schröder, *Angew. Chem., Int. Ed. Engl.*, **4**, 711 (1965).

(279) W. C. Herndon and J. Feuer, *J. Amer. Chem. Soc.*, **90**, 5914 (1968).

(280) M. J. Mantione, *Theor. Chim. Acta*, **11**, 119 (1968); **15**, 141 (1969).

(281) A. I. Konovalov, *Zh. Org. Khim.*, **5**, 1713 (1969).

(282) E. W. Garbisch, Jr., and R. F. Sprecher, *J. Amer. Chem. Soc.*, **88**, 3436 (1966).

(283) E. W. Garbisch, Jr., and R. F. Sprecher, *ibid.*, **91**, 6785 (1969).

(284) R. D. Brown, *J. Chem. Soc.*, 2670 (1951).

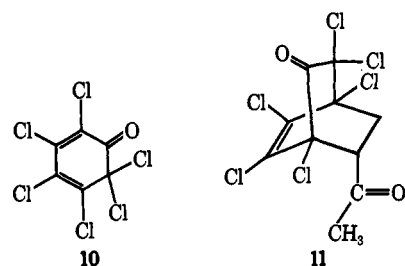
(285) C. H. DePuy, M. Isaks, K. L. Eilers, and G. F. Morris, *J. Org. Chem.*, **29**, 3503 (1964).

(286) W. C. Herndon and L. H. Hall, *Theor. Chim. Acta*, **7**, 4 (1967).

kcal/mol.²⁸⁷ The calculation also accounts for the fact that CPDO undergoes dimerization (-29.9 kcal/mol) rather than reaction with maleic anhydride (-8.8 kcal/mol).²⁸⁸

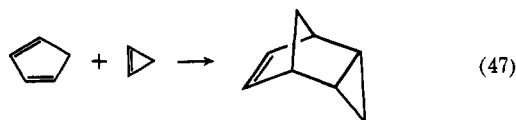
The endo specification of all the reactions are accounted for by secondary interactions between orbitals not formally bonded in the adduct.^{288, 289} If only p orbitals are considered, a PMO calculation has indicated that primary overlap in an endo geometry may be larger than primary overlap in an exo geometry.²⁹⁰ There is no direct experimental evidence to support this contention, but the role of secondary interactions seems well established. The formation of exo adducts in [6 + 4] cycloaddition reactions is an especially compelling fact.^{289, 291} The role of other secondary forces such as attractive dispersion forces or van der Waals repulsive forces has not been clarified.²⁹²⁻²⁹⁴

Calculations similar to those summarized in Table III have been performed on the pair of reactants methyl vinyl ketone and 2,3,4,5,6-hexachloro-2,4-cyclohexadiene (**10**).²⁹⁵ The product of the reaction is an endo-ortho adduct (**11**),²⁹⁶ but the



calculations predict that an exo-ortho adduct would be the major product. Whether this result arises from unidentified steric factors or from faulty theory is an important point which needs to be investigated. PMO calculations on the dimerization of benzocyclobutadiene and its reaction with cyclopentadiene²⁹⁷ did predict the correct order of reactivity, but no details of the calculations are given.

A very interesting aspect of selectivity manifests itself in the reaction of cyclopentadiene with cyclopropene,²⁹⁸ which yields an endo-methylene product exclusively (eq 47). An SCF-



PMO calculation using all-valence-electron MINDO results as the basis functions has been described in detail.²⁹¹ When

(287) W. C. Herndon, C. R. Grayson, and J. M. Manion, *J. Org. Chem.*, **32**, 526 (1967).

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

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

(290) W. C. Herndon and L. H. Hall, *ibid.*, 3095 (1967).

(291) K. N. Houk and R. B. Woodward, *J. Amer. Chem. Soc.*, **92**, 4143, 4145 (1970).

(292) W. C. Herndon and J. M. Manion, *J. Org. Chem.*, **33**, 4504 (1968).

(293) Y. Kobuke, T. Fueno, and J. Furukawa, *J. Amer. Chem. Soc.*, **92**, 6548 (1970).

(294) K. L. Williamson and Y.-F. L. Hsu, *ibid.*, **92**, 7385 (1970).

(295) K. Somekawa, T. Matsuo, and S. Kumamoto, *Bull. Chem. Soc. Jap.*, **42**, 3499 (1969).

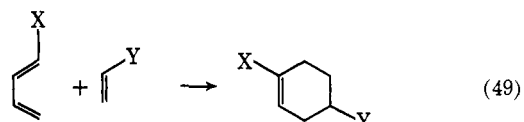
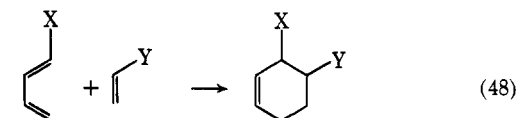
(296) K. Somekawa, H. Uemura, and S. Kumamoto, *Kogyo Kagaku Zasshi*, **72**, 2012 (1969).

(297) M. D. Gheorghiu and M. Avram, *Rev. Roum. Chim.*, **12**, 1063 (1967).

(298) K. E. Wiberg and W. J. Bartley, *J. Amer. Chem. Soc.*, **82**, 6375 (1960).

the reacting molecules were arranged in parallel planes 4.0 Å apart, the endo configuration was more stable than the exo by 1.65 kcal/mol. At shorter intermolecular distances the minimum energy configuration for both endo and exo geometries required the methylene group of the cyclopropene to be rotated away from the other reactant molecule. An important fact is that in both endo and exo configurations the proximal hydrogen atoms of the methylene groups of both reactants were the most important contributors to the second-order stabilization energy. Also, in both cases, the first-order repulsion terms involving these hydrogen atoms were determining factors in the overall perturbation energy.²⁹¹ This repulsion energy is suggested to be the origin of the phenomenon called "steric hindrance," and the assignment of a steric factor as the principle reason for preferential formation of an endo product in this case²⁸⁹ is therefore confirmed.

Another aspect of the stereochemistry of the Diels-Alder reaction which has intrigued organic chemists since its discovery is the orientation effects (regioselectivities) that are observed when the diene and the dienophile are both asymmetrically substituted.^{7,8,11,14} PMO calculations on 1- and 2-phenylbutadienes and 1- and 2-methylbutadienes reacting with acrylonitrile, methyl acrylate, acrolein, and styrene have been published.²⁹⁹ Hückel MO wave functions were used as basis functions and a cyclic concerted mechanism was assumed. The preferred orientation of addition was calculated correctly in every case, as illustrated in eq 48 and 49. Also, in



every case, the interaction of HOMO of diene and LVMO of dienophile was sufficient as a qualitative criterion for the direction of addition.

Problems of orientation and relative reactivities have also been investigated using PMO theory including overlap.^{298, 300} The more elaborate theory allows one to obtain a much more detailed picture of certain addition reactions than can be obtained from a simpler theory. Using eq 38 and a reasonable expression which interrelates the exchange interaction integral to overlap integrals (eq 50),³⁰⁰ one can express the interaction

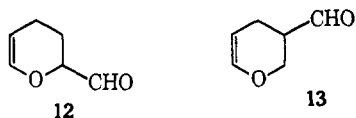
$$\gamma_{rs} = 3\beta S_{rs} \quad (50)$$

energy for a cycloaddition in terms of atomic overlap integrals, which in turn are a function of distance and orientation. In this way the dimerization reactions of butadiene to yield divinylcyclobutanes and 1,5-cyclooctadiene were shown to involve repulsive interactions in the ground states of the reactants. The Diels-Alder reactions of butadiene with ethylene, butadiene dimerization, and acrolein dimerization were all calculated to undergo a concerted bond closure to yield adduct. Attractive secondary interactions had to be invoked to give the correct order of PMO energies for the first two reactions.

(299) J. Feuer, W. C. Herndon, and L. H. Hall, *Tetrahedron*, **24**, 2575 (1968).

(300) L. Salem, *J. Amer. Chem. Soc.*, **90**, 553 (1968).

Two reactions of acrolein are possible to yield compounds **12** and **13**. Concerted, asymmetric mechanisms were found to



be the best reaction pathways, but the PMO energy for formation of **13** was more favorable than for formation of **12**, whereas **12** is the only actual product of the reaction.³⁰¹ A later calculation²²⁸ using π SCF-MO's and including the first-order charge interactions (eq 39) was in agreement with experiment. Although the electrostatic energies were a large part (60–70%) of the total PMO energies, the reversal of the predictions is not due solely to their inclusion. With the SCF orbitals, the second-order PMO energies also favored formation of **12**, and the previous failure³⁰⁰ to agree with experiment is attributed to the unreliability of Hückel MO's.

2. Cycloadditions Involving Excited States

The applications of MO reactivity indexes to molecules in their excited states have been reviewed during 1970.^{302, 303} Consequently, only those topics directly concerned with photocycloaddition reactions will be mentioned. Before citing specific examples, an important question needs to be discussed. Is it appropriate for excited-state reactivity to use a perturbational approach, rationalized as an approximation to transition-state theory? The risks involved in using transition-state theory to describe a process which involves decay of an electronically excited molecule have been clearly pointed out.^{302–305} Many photoreactions may not involve activation barriers.

A logical picture of photoreaction processes includes the following sequence of events: vertical excitation of the reactant, vibrational decay of the excited molecule toward its lowest excited state configuration, deexcitation from the potential energy surface of the excited state to a ground-state potential energy surface of a photoproduct.^{306–309} A clear picture of the deexcitation process has been developed from valence-bond calculations on the cyclobutene-butadiene system.^{308, 310} The photoreaction can occur most readily when a large barrier in the ground-state potential energy surface passes close to a minimum in the excited-state surface.

It seems clear that a reaction surface involving an excited molecule might have a negative slope. With this in mind, PMO energies can be reinterpreted as a measure of the slope of the energy surface at the beginning of the reaction.³⁰² Furthermore, it is reasonable to expect that the products of a reaction or the relative reactivity in a similar series of compounds will be determined at an early stage of the reaction (deactivation)

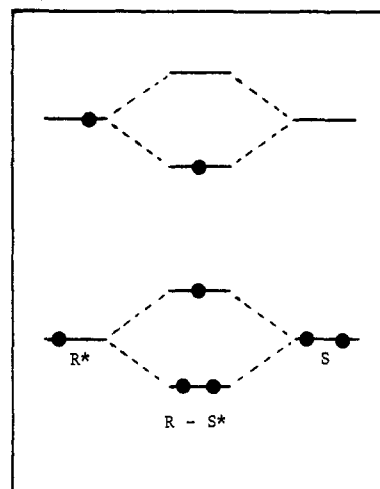
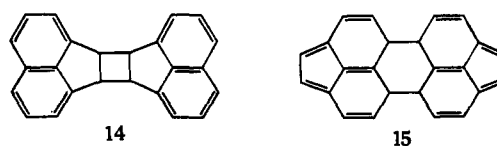


Figure 6. Perturbed energy levels for the photoaddition of two identical molecules.

process. A perturbational approach to reactivities of excited molecules might very well be more soundly based than the same approach to ground-state chemistry. An important difficulty arises as to what functions will be used to represent the unperturbed excited wave functions. This problem has been circumvented in most cases to be discussed by use of a virtual-orbital approximation.

PMO calculations for excited-state reactions are similar in most respects to the calculations already described. However, in a cycloaddition involving an excited reactant with another excited molecule, partially occupied orbitals of the excited species will be nearly degenerate in energy with corresponding orbitals in the unexcited reactant. An energy level diagram for the photoaddition of two identical molecules, one of which is in its first excited state, is given in Figure 6. The interaction of the degenerate orbitals will give use to a first-order perturbation energy (eq 34), which may be the dominant stabilizing factor in a photochemical reaction. General aspects of the theory, including the differences between triplet and singlet excited-state reactivities, were summarized in a pioneering article,³¹¹ and in several articles already discussed.^{226, 228, 229}

The first photochemical addition reactions to be treated by PMO theory were the dimerizations of anthracene, tetracene, pentacene, and acenaphthylene.³¹¹ Anthracene was correctly calculated to dimerize at its 9,10 positions,³¹² and acenaphthylene was correctly predicted to form a cyclobutane photodimer³¹³ (**14**). Earlier calculations³¹⁴ of the free valence at various positions in the excited- and ground-state acenaphthylene molecule had shown that **15** would have been pre-



(301) C. W. Smith, D. G. Norton, and S. A. Ballard, *J. Amer. Chem. Soc.*, **73**, 5274 (1951).

(302) R. Daudel, *Advan. Quantum. Chem.*, **5**, 1 (1970).

(303) O. Chalvet, R. Daudel, and G. H. Schmid, *Tetrahedron*, **26**, 365 (1970).

(304) K. J. Laidler, "The Chemical Kinetics of Excited States," Oxford University Press, New York, N. Y., 1955, p 41.

(305) G. S. Hammond, *Advan. Photochem.*, **7**, 373 (1969).

(306) W. C. Dauben, *Chem. Weekbl.*, **60**, 381 (1964).

(307) J. P. Malrieu, *Photochem. Photobiol.*, **5**, 291 (1966).

(308) W. Th. A. M. v. d. Lugt and L. J. Oosterhoff, *Chem. Commun.*, 1235 (1968).

(309) R. C. Dougherty, private communication.

(310) W. Th. A. M. v. d. Lugt and L. J. Oosterhoff, *J. Amer. Chem. Soc.*, **91**, 6042 (1969).

(311) K. Fukui, K. Morokuma, and T. Yonezawa, *Bull. Chem. Soc. Jap.*, **34**, 1178 (1961).

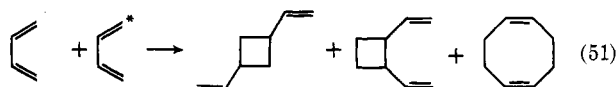
(312) A. Mustafa, *Chem. Rev.*, **51**, 1 (1952).

(313) E. L. Bowen and J. D. F. Marsh, *J. Chem. Soc.*, 109 (1947).

(314) V. A. Crawford and C. A. Coulson, *ibid.*, 1990 (1948).

dicted as the product if free valence was a correct reactivity index for this case. The dimerization of acenaphthylene was interpreted successfully in terms of frontier electron densities.³¹⁵ Agreement of PMO and frontier electron results is expected since the leading term in the PMO energy is a first-order term involving the product of the coefficients of the HFMO at the reactive sites, which is equal to the frontier electron density.

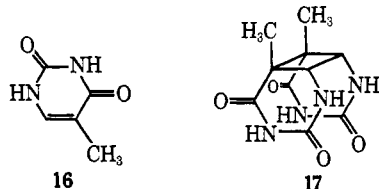
Detailed energy surfaces for the photodimerization reactions of butadiene (eq 51) have been calculated by PMO theory in-



cluding overlap.³⁰⁰ Both reactions to yield divinylcyclobutanes were calculated to be concerted in nature but with one bond closing faster than the other. The PMO stabilization energy to yield the 1,3 isomer is smaller than that calculated for the reaction to yield the 1,2 isomer. The reaction to yield 1,5-cyclooctadiene is calculated to be highly favorable if two *s-cis*-butadiene moieties collide. The best calculated mechanism is concerted and symmetric. The photochemical [4 + 2] addition is found to require a two-step closure with a large activation energy for the second bond closure. No experiments directly bearing on this last prediction have been reported.

The photodimerization of two linear steroidal dienones has been successfully correlated with PMO calculations.²²⁸ Triplet $\pi-\pi^*$ states were assumed, SCF-MO wave functions for 3,5-hexadienone were used as basis orbitals, and molecular models were used to indicate where steric hindrance might outweigh a favorable calculated electronic stabilization energy. An interesting discussion of the reactivity differences to be expected from other excited states is also given.

The photochemistry of thymine (16) and similar compounds^{316, 317} is a subject of intense interest to spectroscopists and biochemists. The dimer of thymine (17) was the first heat-



stable photoproduct to be isolated from the photolysis of nucleic acid derivatives.^{318, 319} Most theoretical studies of reactions of this type have been concerned with the properties of the isolated singlet and triplet excited states of reactant molecules. The results suggest that the double bond in all excited states is highly reactive.³²⁰⁻³²⁴ The relative ease of photo-

cyclodimerization for several pyrimidine bases has been shown to parallel unpaired electron densities at the double bond,³²⁰⁻³²⁴ and decreased excited-state bond orders.³²¹⁻³²⁴ An all-valence-electron iterative EHMO study of thymine³²⁵ gives results which compare favorably with the previous π -electron calculations.

Simple calculations of the first-order PMO energies (eq 34) for interaction of an excited molecule with a second unexcited molecule of the same species for uracil, thymine, cytosine, and several aromatic compounds have been reported.³²⁶ Hückel MO's were employed and a concerted reaction scheme was assumed. Both uracil and thymine gave a higher π -PMO energy than acenaphthylene or anthracene, which should indicate that they form dimers easily. The PMO energy to yield a head-to-head dimer, 17, was also more favorable than that calculated for head-to-tail dimerization.

A very complete theoretical study of thymine photodimerization which should serve as a model for calculations of this type was presented at a recent symposium.³²⁵ The total interaction between molecules was decomposed into four terms: (1) an overlap interaction due to intermolecular π -electron delocalization, (2) an intermolecular electrostatic charge interaction, (3) a polarization term, and (4) a σ -bond dispersion energy term. Term 2 was estimated by using charges obtained from iterative EHMO calculations. Term 3 was calculated using the net charges on the atoms and bond polarizabilities,³²⁷ while the dispersion energy was also calculated in a bond polarizability approximation. The delocalization energy (term 1) was calculated according to eq 38, but including first-order terms.²²⁶ Parallel planes head-to-head and head-to-tail, *cis* and *trans* configurations of ground-state and $\pi-\pi^*$ excited-state dimers were examined, and the intermolecular distances were varied from 1 to 5 Å. Excited-state dimers were 12 to 15 kcal/mol more stable than the separated reactants, with the *cis* head-to-head dimer being the most stable. A weak attractive interaction, of the order of 2 kcal, was calculated for the ground-state dimers. When all interactions are included, the order of stability is the same as that calculated from the π PMO energies alone. One other important aspect of the dimerization process was investigated. The attractive PMO energy grew larger as the molecules were tilted into a nuclear geometry approaching that of the final ground-state dimer.

All of this work taken together supports a mechanism in which the molecules are aligned by small stabilizing forces in the ground state, with excitation and slight nuclear rearrangement giving a more stable excited species which can decay later to the ground-state dimer. A concerted nature for the reaction is implied, but other reaction pathways involving two-step mechanisms were not calculated. Additional work in this area would be of interest. A comparison between different excited states could be carried out using SCF orbitals, and it would be interesting to compare results for several pyrimidine bases.

Photocycloaddition reactions involving two different reactant molecules constitute a large and growing area of organic photochemistry. Research in this area has concentrated on the useful synthetic aspects of the reactions and determinations of

(315) K. Fukui, T. Yonezawa, and C. Nagata, *Bull. Chem. Soc. Jap.*, **34**, 37 (1961).

(316) J. G. Burr, *Advan. Photochem.*, **6**, 193 (1968).

(317) K. C. Smith and P. C. Hanawalt, "Molecular Photobiology: Inactivation and Recovery," Academic Press, New York, N. Y., 1969.

(318) R. Beukers, J. Ijlst, and W. Berends, *Recl. Trav. Chim. Pays-Bas*, **79**, 101 (1960).

(319) A. Wacker, H. Dellweg, and D. Weinblum, *Naturwissenschaften*, **47**, 477 (1960).

(320) M. J. Mantione and B. Pullman, *Biochim. Biophys. Acta*, **91**, 387 (1964).

(321) V. I. Danilov, *Photochem. Photobiol.*, **6**, 233 (1967).

(322) A. Denis and A. Pullman, *Theor. Chim. Acta*, **7**, 110 (1967).

(323) V. A. Kuprievich, *Int. J. Quantum Chem.*, **1**, 561 (1967).

(324) B. Pullman, *Photochem. Photobiol.*, **7**, 525 (1968).

(325) R. Sayre, J. P. Harlos, and R. Rein in "Molecular Orbital Studies in Chemical Pharmacology," L. B. Kier, Ed., Springer-Verlag New York, New York, N. Y., 1970, pp 207-237.

(326) C. Nagata, A. Imamura, Y. Tagashira, and M. Kodama, *J. Theor. Biol.*, **9**, 357 (1965).

(327) J. O. Hirschfelder, C. F. Curtis, and R. B. Bird, "Molecular Theory of Gases and Liquids," Wiley, New York, N. Y., 1954.

the particular excited states responsible for chemical reaction in isolated cases. A few reactions have been examined from a perturbational standpoint, and several qualitative arguments may be illustrated by reference to Figure 7, which depicts the

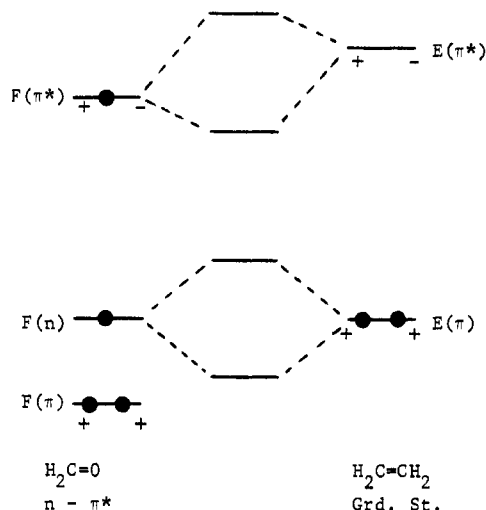


Figure 7. Perturbed energy levels for the photoaddition of formaldehyde to ethylene.

interaction of a simple carbonyl compound with an olefin; the reaction which ensues yields an oxetane and is known as the Paterno-Büchi reaction.³⁹

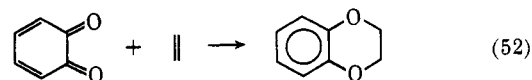
The experimental evidence, summarized in recent papers,³²⁸⁻³³¹ clearly defines two different reaction mechanisms, both processes eventually giving the same oxetane-type product. The largest number of examples involve $n-\pi^*$ excited states of the carbonyl compounds. The triplet state of an aryl ketone or aldehyde reacts with electron-rich olefins *via* an electrophilic attack of the radicaloid lone electron on oxygen to generate a triplet biradical intermediate. A subsequent closure to ground-state oxetane must be accompanied by a spin inversion to a singlet species. Cases involving alkyl carbonyl compounds and electron-poor olefins seem to require a mechanism in which the π electrons of the carbonyl $n-\pi^*$ singlet state and the π electrons of the olefin participate in a concerted type of reaction to yield an oxetane. The intervention of a singlet biradical intermediate which undergoes closure to oxetane before significant steric rearrangement within the intermediate can take place cannot be eliminated from consideration in this second case.

Figure 7 shows³³² that the most important stabilizing perturbation of the reacting species is the degenerate interaction of the hole on oxygen with the π electrons of the olefin for the triplet carbonyl reaction ($E(\pi) \rightarrow F(n)$). Similarly the singlet carbonyl species concerted reaction is controlled by an in-phase almost degenerate interaction between the half-occupied π^* level of carbonyl compound and the π^* level of the olefin ($F(\pi^*) \rightarrow E(\pi^*)$). The effects of substituent groups

can be deduced by tracing the energy level variations introduced by the substituents. For example, electron-donating substituents (alkyl groups) on the carbonyl group raise the π and π^* level, leaving the energy of the lone electron on oxygen relatively unchanged. If electron-attracting groups (cyano groups) are simultaneously introduced into the olefin, π and π^* levels of the olefin are lowered, and the perturbation favoring a concerted mechanism is intensified while that favoring a biradical intermediate is diminished in magnitude. The agreement with the postulated mechanism is remarkable for such a simple treatment, and several other aspects of Paterno-Büchi reactions can be correlated in this way.³³²

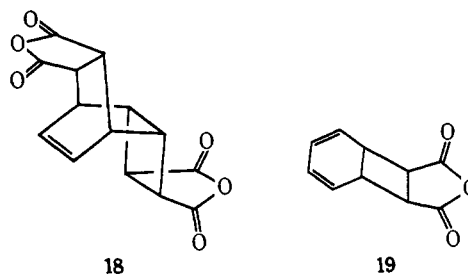
More complete calculations on Paterno-Büchi reactions using Hückel MO wave functions and the simplest form of PMO theory³³³ agree with experimental results in almost every respect. Of course, these calculations do not discriminate between the reactivities of singlets and triplets and do not consider competing radiationless transformations of possible intermediates of exciplexes which may occur during the sequence of steps which comprise the reaction.

Other reactions for which the same type of calculations have been carried out are the photochemical and thermal cycloaddition reactions of quinones with olefins (eq 52)³³⁴ and the



photocycloaddition reactions of excited coumarins to DNA bases.³³⁵ In the latter case, it is predicted that the furanyl double bond of psoralen will be significantly less reactive than the coumaryl double bond in the ${}^3n-\pi^*$ state, in agreement with the observed relative yields of photoproducts.³³⁵⁻³³⁷

The stereochemistry of the addition of maleic anhydride to benzene, which results in a 2:1 adduct with stereochemistry shown in **18**,³³⁸ has been correlated with PMO calculations in-



cluding overlap, and also including secondary interactions.³³⁹ Experimentally, the first step of the reaction seems to involve a 1,2 addition of excited maleic anhydride to benzene, perhaps after formation of an exciplex.³⁴⁰ The PMO calculations gave an excited-state complex as 8.4 kcal/mol more stable than a ground-state complex. In the excited state 1,2 addition is favored over 1,4 addition by 55.9 kcal/mol, and secondary in-

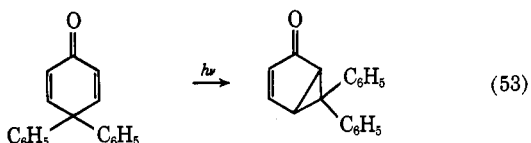
(328) N. J. Turro and P. W. Wriede, *J. Amer. Chem. Soc.*, **92**, 320 (1970).
 (329) J. C. Dalton, P. A. Wriede, and N. J. Turro, *ibid.*, **92**, 1318 (1970).
 (330) I. H. Kochevar and P. J. Wagner, *ibid.*, **92**, 5742 (1970).
 (331) N. C. Yang and W. Eisenhardt, *ibid.*, **93**, 1277 (1971).
 (332) W. C. Herndon, *Tetrahedron Lett.*, 125 (1971).

(333) W. C. Herndon and W. B. Giles, *Mol. Photochem.*, **2**, 277 (1970).
 (334) W. C. Herndon and W. B. Giles, *Chem. Commun.*, 497 (1969).
 (335) P.-S. Song, M. L. Harter, T. A. Moore and W. C. Herndon, *Photochem. Photobiol.*, **13**, 521 (1971).
 (336) C. H. Krauch, D. M. Kramer, and A. Wacker, *ibid.*, **6**, 341 (1967).
 (337) F. Dall'acqua, S. Marciari, F. Bordin, and R. Bevilacqua, *Ric. Sci.*, **38**, 1094 (1968).
 (338) E. Grovenstein, Jr., D. V. Rao, and J. W. Taylor, *J. Amer. Chem. Soc.*, **83**, 1705 (1961).
 (339) M.-H. Whangbo and I. Lee, *J. Korean Chem. Soc.*, **13**, 273 (1969).
 (340) W. H. Hardham and C. S. Hammond, *J. Amer. Chem. Soc.*, **89**, 3200 (1967).

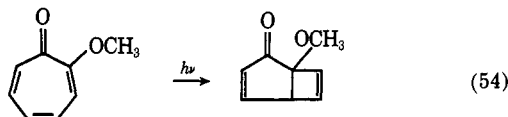
teractions destabilize the endo configuration for the preferred 1,2 reaction by 21.5 kcal/mol. The butadiene moiety of the intermediate **19** can then react with maleic anhydride. The calculations give a PMO energy of 37.2 kcal/mol for an addition of excited maleic anhydride to **19**, and 20.2 kcal/mol for addition of ground-state maleic anhydride. This is not in accord with the suggested mechanism,³⁴⁰ which postulates a thermal [2 + 4] reaction for the second step almost simultaneous with the first step. Secondary interactions were not included in the second set of calculations, and it is very likely that secondary interactions of an excited maleic anhydride molecule would be destabilizing. Another factor which decreases the usefulness of the results is the assumption of a $\pi-\pi^*$ excited state for the maleic anhydride, instead of the more likely $n-\pi^*$ state.

The cycloaddition of $n-\pi^*$ excited dimethyl maleate to cyclohexene has been discussed qualitatively in terms of the interactions of π^* level of maleate with π^* level of cyclohexene.³⁴¹ It is pointed out that reaction is a "half-allowed" reaction in contrast to the reaction of a $\pi-\pi^*$ excited maleate which would be wholly allowed. The latter reaction would have a stabilizing orbital interaction involving the π levels of the two reactants; cf. Figure 6, missing in the reaction of the $n-\pi^*$ state.

One other area of organic photochemistry, internal cyclization, has received a great deal of theoretical attention, although PMO calculations *per se* have not been reported. Well-studied examples include the photochemical rearrangements of 2,5-cyclohexadienones (eq 53)³⁴²⁻³⁴⁵ and the photo-



chemical isomerizations of monocyclic tropolones³⁴⁶⁻³⁴⁸ and cycloheptatrienes to bicyclic compounds^{36, 349, 350} (eq 54 and 55). Each of these reactions can be interpreted by examining the

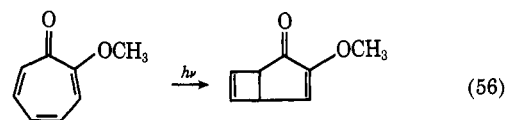


changes in bond order which occur upon excitation at the sites where intramolecular cyclizations take place.^{115, 302, 307, 345, 351, 352} This is essentially a first-order PMO

treatment since the first-order change in energy upon uniting two orbitals within a molecular system is directly proportional to the bond order between those orbitals.¹⁹⁹

In the 2,5-cyclohexadienone rearrangement (eq 53), the initial postulated steps are n,π^* excitation, followed by bond formation between positions 3 and 5.³⁴²⁻³⁴⁵ The total 3,5 bond orders are: ground-state -0.070 , $\pi-\pi^*$ excited state -0.058 , and $n-\pi^*$ excited state $+0.114$.³⁴⁵ The observed bond formation is only in agreement with the predicted behavior of the n,π^* state. The use of partial bond orders, utilizing only the highest occupied MO, would not discriminate between the various states, since each partial bond order is positive. A calculation of the change in bond order upon excitation is also not informative in this case.

Cyclization of dienes, dienones, cyclic trienes, and cyclic trienones have been treated using the change in π bond order with excitation as a criterion for reaction.^{302, 352} In all of these reactions there is a positive change in bond order upon excitation, corresponding to the observed reaction. However, the directive influence of substituent groups is not well correlated by these calculations. For example, α -tropolone cyclizes internally to yield the bicyclic product shown in eq 54, but the π -bond-order change upon excitation to the n,π^* state is largest for the opposite sense of closure,³⁵² illustrated in eq 56. Per-



haps, calculations of the total bond orders involved would resolve this discrepancy. Even in the case of cycloheptatriene cyclizations, where a simple explanation in terms of excited state polarizations has been offered,³⁵³ calculations of bond orders would be useful and interesting.

3. Related Topics

Some important developments of theory are occurring that are closely related to the foregoing discussions.

A favorable unimolecular reaction pathway for a particular molecule can be correlated with a vibrational mode that has a small force constant. It has been shown that this vibrational mode will have a symmetry identical with that of a low-lying electronic excited state.^{354, 355} Expressions for the energy of the molecule as reaction occurs can be derived in terms of the magnitude of displacement along the reaction coordinate and the molecular wave functions using perturbation theory. The expression for the energy contains a term, second order in the potential-energy charge, which must be integrated over the wave function for the ground state and an excited state. These integrals can only be different from zero if any two elements of the integrand contain the representation of the third.

More rigorous discussions of the conditions relating favorable reaction pathways to low-lying electronic states have appeared,³⁵⁶⁻³⁶⁰ and the theory has been applied to the pyrolyses

- (341) G. Ahlgren and B. Akermark, *Tetrahedron Lett.*, 1885 (1970).
 (342) H. E. Zimmerman and D. I. Schuster, *J. Amer. Chem. Soc.*, **83**, 4484 (1961); **84**, 4527 (1962).
 (343) H. E. Zimmerman, *Advan. Photochem.*, **1**, 183 (1963).
 (344) K. Schaffner, *ibid.*, **4**, 81 (1966).
 (345) H. E. Zimmerman and J. S. Swenton, *J. Amer. Chem. Soc.*, **89**, 906 (1967).
 (346) E. J. Forbes, *J. Chem. Soc.*, 3864 (1955).
 (347) W. G. Dauben, K. Koch, S. L. Smith, and O. L. Chapman, *J. Amer. Chem. Soc.*, **85**, 2616 (1963).
 (348) K. F. Koch, *Advan. Alicyclic Chem.*, **1**, 257 (1966).
 (349) W. G. Dauben and R. L. Cargill, *Tetrahedron*, **12**, 186 (1961).
 (350) O. L. Chapman, *Advan. Photochem.*, **1**, 323 (1961).
 (351) Z. Simon, *Zh. Fiz. Khim.*, **38**, 1609 (1964); *Chem. Abstr.*, **61**, 9084d (1964).
 (352) J. P. Malrieu, *Photochem. Photobiol.*, **5**, 301 (1966).

- (353) A. R. Brember, A. A. Gorman, R. L. Leyland, and J. B. Sheridan, *Tetrahedron Lett.*, 2511 (1970).
 (354) R. F. W. Bader, *Mol. Phys.*, **3**, 137 (1960).
 (355) R. F. W. Bader, *Can. J. Chem.*, **40**, 1164 (1962).
 (356) L. Salem, *Chem. Phys. Lett.*, **3**, 99 (1969).
 (357) L. Salem, *Chem. Brit.*, **5**, 449 (1969).
 (358) L. Salem and J. S. Wright, *J. Amer. Chem. Soc.*, **91**, 5947 (1969).
 (359) R. G. Pearson, *ibid.*, **91**, 1252, 4947 (1969).
 (360) R. G. Pearson, *Theor. Chim. Acta*, **16**, 107 (1970).

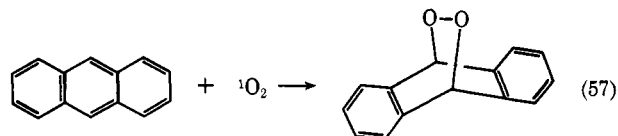
of cyclobutane and cyclohexene.^{357, 358} Detailed outlines of the molecular motions necessary for decomposition are developed. In the retro-Diels-Alder reaction of cyclohexene, the force constant for the allowed concerted motion is not much smaller than the force constant for a two-step reaction. It is concluded that the tendency for the Diels-Alder retrogression to be a concerted reaction may be weak.³⁵⁸

The Woodward-Hoffmann rules⁴ can be rederived from this theory,^{357, 360} and it is shown that a qualitative understanding of allowed or forbidden motions can be obtained from very rough MO wave functions.³⁶⁰ Applications to the problem of predicting the stable structure of a molecular species have also been discussed.³⁵⁹ In general, agreement with other more empirical theory³⁶¹ is found.

A different and interesting new analysis of concerted reactions has been applied to several cycloaddition reactions.³⁶²⁻³⁶⁴ The central point of this new method is that nuclear motions during a reaction may twist, stretch, and bend MO's but will not introduce new nodes into the orbitals. A mapping operator, conceptually similar to an evolution operator,³⁶⁵ is used to transform the molecular wave functions of the reactants into new wave functions characteristic of the nuclear geometry of the product. These new mapped wave functions are produced without topological change so that the nodal properties of the reactant are retained. If the wave functions obtained by mapping the reactant MO's overlap strongly with the ground-state MO's of the product, the reaction is "allowed" in the Woodward-Hoffmann⁴ sense. Overlap may range from zero to unity, and the value of the overlap is associated with a degree of permissibility for the calculated reaction. This method allows one to obtain semiquantitative delineations of mechanisms of reactions with only a minimum number of quantum-mechanical calculations. It can also be easily applied to those reactions which cannot be treated by symmetry arguments due to the unsymmetrical nature of the reactant molecules.

In applications³⁶⁴ CNDO wave functions were taken as starting orbitals, and an approximate mapping operator which is capable of reflecting the effects of bond bending and twisting was constructed. The stereospecificity of the closure of butadiene to cyclobutene is shown to depend principally on the π orbitals, and the more elaborate theory corroborates the Woodward-Hoffmann arguments concerning the requisite stereochemistry associated with the reaction. The bicyclobutane-butadiene rearrangement is also elucidated with results in agreement with previous potential-surface calculations.¹¹⁶ The overlap function for the concerted thermal addition of formaldehyde to ethylene is small, but not zero, indicating that the reaction might be observable. Other [2 + 2] cycloaddition reactions are discussed. The Diels-Alder reaction of ethylene with butadiene is analyzed,³⁶⁴ and a very interesting experimental inhibition of the reaction by neighboring hydroxyl group³⁶⁶ is explained.

With regard to the use of perturbation theory as opposed to a transition-state model encompassing orbitals of all the reactants, a detailed comparison for radical, nucleophilic, and electrophilic attack on some aromatic systems has been published.^{367, 368} The trends predicted by both methods are similar. Two photoreactions, the photodeuteration of aromatic compounds and the photooxidation of polycyclic aromatic compounds (eq 57), are treated by the supermolecule transition-



state model.^{363, 369} The effects of substituents on the cycloaddition reaction have been investigated extensively,^{370, 371} and the results are correctly correlated by these MO calculations. Molecular oxygen also reacts with monoolefins and conjugated dienes,³⁷⁰ and an extensive development of state correlation diagrams has been used to investigate the various factors which control the reactivity of ground and excited states of oxygen toward several different molecules.³⁷²⁻³⁷⁴

Perturbational MO approaches to chemical problems are being explored in several areas of chemistry not directly related to cycloaddition reactions. Mass spectrometric, thermolytic, and photolytic fragmentation reactions have been discussed on this basis.³⁷⁵ The activities of drugs, and the drug-receptor interactions have been correlated using PMO theory.³⁷⁶ The ability of sensitizers to excite certain other molecules is correlated with the HFMO of sensitizer and the LVMO of receptor molecule,^{377, 378} a concept clearly related to a perturbational treatment. Lastly, recent developments of perturbational^{379, 380} approaches to the interpretation of electronic spectra^{379, 380} and the assignment of photoelectron ionization values^{381, 382} should be mentioned. An increasing use of PMO and related methods in elucidating diverse aspects of chemistry is expected.

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(361) L. S. Bartell, *J. Chem. Educ.*, **45**, 754 (1963).

(362) C. Trindle and O. Sinanoglu, *J. Amer. Chem. Soc.*, **91**, 4054 (1969).

(363) C. Trindle, *ibid.*, **92**, 325 (1970).

(364) C. Trindle, *ibid.*, **90**, 3255 (1970).

(365) A. Messiah, "Quantum Mechanics," North Holland Publishing Co., Amsterdam, 1962, pp 310-312, 722-724, 801.

(366) A. T. Austin and B. Pearson, *Chem. Ind. (London)*, 1228 (1966); *Nature (London)*, **221**, 949 (1969).

(367) J. Bertran, O. Chalvet, R. Daudel, T. F. W. McKillop, and G. H. Schmid, *Tetrahedron*, **26**, 339 (1970).

(368) O. Chalvet, R. Daudel, and T. F. W. McKillop, *ibid.*, **26**, 349 (1970).

(369) O. Chalvet, R. Daudel, C. Ponce, and J. Rigaudy, *Int. J. Quantum Chem.*, **2**, 521 (1968).

(370) K. Gollnick and G. O. Schenck, ref 15, pp 255-344.

(371) J. Rigaudy, *Pure Appl. Chem.*, **16**, 169 (1968).

(372) A. U. Khan and D. R. Kearns, *Advan. Chem. Ser.*, No. 77, 143 (1968).

(373) D. R. Kearns and A. U. Khan, *Photochem. Photobiol.*, **10**, 193 (1969).

(374) D. R. Kearns, *J. Amer. Chem. Soc.*, **91**, 6554 (1969).

(375) R. C. Dougherty, *ibid.*, **90**, 5780, 5788 (1968).

(376) A. Commarata, ref 72, pp 156-190.

(377) E. F. Ullman and N. Baumann, *J. Amer. Chem. Soc.*, **90**, 4158 (1968).

(378) E. F. Ullman and N. Baumann, *ibid.*, **92**, 5892 (1970).

(379) H. J. Maria, D. Larsor, N. E. McCarville, and S. P. McGlynn, *Accounts Chem. Res.*, **3**, 368 (1970).

(380) J. W. Rabalais, J. M. McDonald, V. Scherr, and S. P. McGlynn, *Chem. Rev.*, **71**, 73 (1971).

(381) F. A. Davis, M. J. S. Dewar, R. Jones, and S. D. Worley, *J. Amer. Chem. Soc.*, **91**, 2094 (1969).

(382) M. J. S. Dewar and S. D. Worley, *J. Chem. Phys.*, **51**, 263 (1969).