Electrocyclic Reactions. I. The Importance of Donor–Acceptor Interactions in Thermal Intermolecular Cycloaddition Reactions

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Abstract: A new model for thermal cycloaddition reactions involving a resonance formulation of the transition state is described. The model gives recognition to the chemical identity of the cycloaddends and reveals that intermolecular cycloadditions are part of a reactivity spectrum. Predictions about rates, stereochemistry, and solvent effects are made on the basis of the model and the suggestion is made that most intermolecular cycloadditions are concerted and not stepwise as it had been thought before. The fundamental differences between the present and past treatments of the subject are pointed out. The importance of the donor–acceptor relationship of the cycloaddends and the degree of polarity of the transition state in determining stereoselectivity is for the first time revealed.

Cycloaddition reactions have received a great deal of attention since the publication of the Woodward–Hoffmann formulation of orbital symmetry controlled reactions.[1] The notions of concerted and nonconcerted reactions were extensively utilized to rationalize the observed stereoselectivity, regioselectivity,[2] solvent effects, and rates exhibited by various cycloaddition reactions. Presently, cycloaddition reactions are regarded as proceeding in either a concerted fashion or in a nonconcerted fashion involving biradical or dipolar intermediates. We would like to suggest that a proper formulation of the transition state of cycloaddition reactions and the use of simple quantum mechanical principles lead to a totally different outlook of cycloaddition reactions from the one presently adopted. Thus, we shall first present some quantum mechanical results and apply them to a model for cycloaddition reactions which provides for the recognition of the chemical nature of the cycloaddends and accounts for the entire spectrum of behavior encountered in cycloaddition reactions.

I. Theoretical Background

We wish to derive some fundamental quantum mechanical rules applicable to cycloaddition reactions, using as an example the general case of union of two polyenes at two sites. In all subsequent discussions, we shall restrict our attention to such π–π type cycloadditions.

The union of two polyenes, A and B, at two sites will take place as the two polyenes approach each other along the lowest energy path. This lowest energy path will be the one that provides the greatest stabilization upon interaction of the two polyenes. An assessment of the magnitude of stabilization attending any number of different approaches of the two polyenes can be simply obtained through application of perturbation theory. The magnitude of the stabilization will simply depend upon the nature of interactions of the MO's of the two cycloaddends.

Let us assume that a doubly occupied MO of polyene A, namely M, interacts with an unfilled MO of polyene B, namely N, and that a doubly occupied MO of polyene B, namely K, interacts with an unfilled MO of polyene A, namely L. The result of the interaction will be to lower the energy of the occupied levels and raise the energy of the unoccupied levels. This is shown schematically in Figure 1. The stabilization energy (SE) upon interaction is then given by

$$(\mathrm{SE})_1 = N' \times \delta E_\mathrm{M} \qquad (1)$$

$$(\mathrm{SE})_2 = N' \times \delta E_\mathrm{K} \qquad (2)$$

$$(\mathrm{SE})_\mathrm{total} = (\mathrm{SE})_1 + (\mathrm{SE})_2 \qquad (3)$$

where N' stands for the number of electrons occupying the energy levels E_M and E_N corresponding to the interacting MO's M and N, and also the number of electrons occupying the energy levels E_L and E_K corresponding to the interacting MO's L and K. The value of N' can be 1 or 2 and in the present case is 2.[3]

We can now proceed to give a more explicit meaning to the expression for the stabilization energy by appropriate substitution of the quantity δE. From well-known formulas of second-order perturbation theory we can write[4]

$$\delta E_\mathrm{M} = \frac{(a_{Mr}b_{Ns}\gamma + a_{Mt}b_{Nu}\gamma)^2}{E_\mathrm{M} - E_\mathrm{N}} \qquad (6)$$

and similarly

$$\delta E_\mathrm{K} = \frac{(a_{Lr}b_{Ks}\gamma + a_{Lt}b_{Ku}\gamma)^2}{E_\mathrm{K} - E_\mathrm{L}} \qquad (7)$$

In the expressions above, a_{Mr} and a_{Mt} are the coefficients of the rth and tth p atomic orbitals of polyene A belonging to wave function M and b_{Ns} and b_{Nu} are the coefficients of the sth and uth p atomic orbitals of polyene B belonging to wave function N. Similarly,

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(1) For key references on previous and recent theoretical work on cycloaddition reactions, see: R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 8, 781 (1969).

(2) A cycloaddition reaction is termed regioselective if there is an orientational preference in the union of the two cycloaddends; see A. Hassner, *J. Org. Chem.*, 33, 2684 (1968).

(3) When $N' = 3,4$ eq 1 and 2 become

$$(\mathrm{SE})_1 = 2\delta E_\mathrm{M} + (N' - 2)\delta E_\mathrm{N} \qquad (4)$$

$$(\mathrm{SE})_2 = 2\delta E_\mathrm{K} + (N' - 2)\delta E_\mathrm{L} \qquad (5)$$

Since δE_M and δE_N and also δE_K and δE_L have different signs, the absolute magnitude of SE decreases when $N' = 3$, becoming identical with the case where $N' = 1$, and the absolute magnitude of SE becomes zero when $N' = 4$, as in the case of the interaction of unoccupied energy levels.

(4) For the derivation and application of the fundamental perturbation theory formulas, see: M. J. S. Dewar, "The Molecular Orbital Theory of Organic Chemistry," McGraw-Hill, New York, N. Y., 1969. See also: L. Salem, *J. Amer. Chem. Soc.*, 90, 543 (1968).

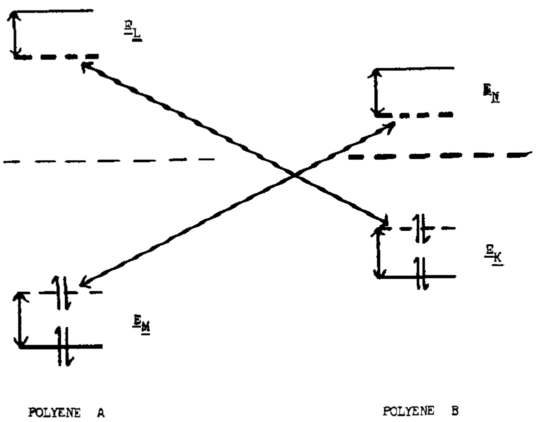


Figure 1. The effect of MO interaction upon the energy levels of the cycloaddends. Dotted lines depict the energy levels of the two molecules prior to interaction. Solid lines depict the energy levels of the two molecules after the interaction. Arrows indicate interacting energy levels. Diagram is schematic.

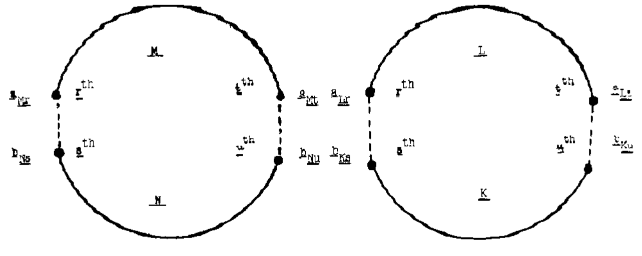


Figure 2. Union of two polyenes. The quantities involved in the calculations of the stabilization energy upon interaction of M and N and L and K. It is assumed that $\gamma_{rs} = \gamma_{tu} = \gamma$.

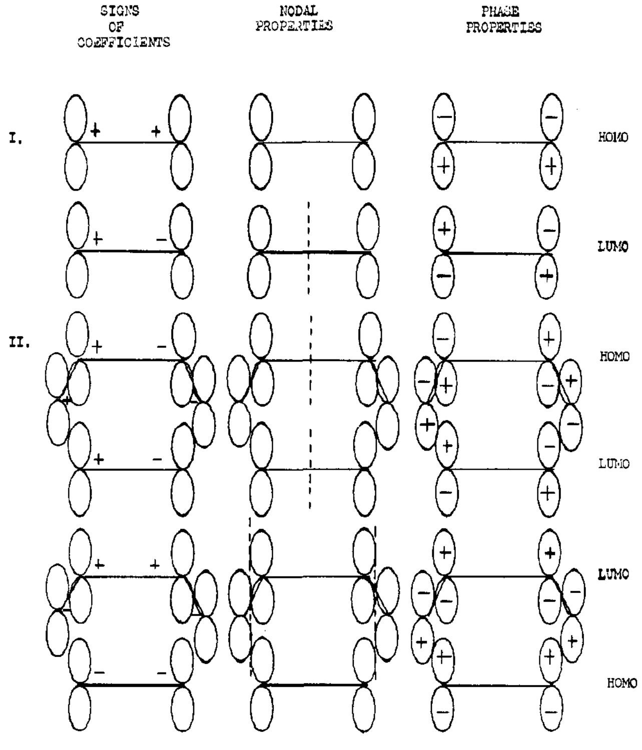


Figure 3. Three ways of viewing pictorially the MO interactions of two cycloaddends. The HOMO–LUMO interactions only are depicted, since they make the dominant contribution to the stabilization energy because the corresponding energy levels are the ones most closely spaced. (I) The 2s + 2s cycloaddition; the coefficient products have different signs; thus, reaction is unfavorable; (II) the 4s + 2s cycloaddition; the coefficient products have identical signs; hence, reaction is favorable.

a_{Lr} and a_{Lt} are the coefficients of the *r*th and *t*th p atomic orbitals of polyene A belonging to wave function *L* and b_{Ks} and b_{Ku} are the coefficients of the *s*th and *u*th p atomic orbitals of polyene B belonging to wave function *K*. Union of the two polyenes involves union of the *r*th and the *s*th p orbitals and the *t*th and the *u*th p orbitals of the two polyenes. Figure 2 shows the union of the two polyenes, the interacting MO's and the appropriate coefficients of the uniting orbitals. Furthermore, γ stands for the resonance integral between the two interacting p atomic orbitals at the union sites. The rest of the symbols have their usual meaning. Equations 6 and 7 can finally be substituted into the expression for the total stabilization in which case we have

$$\mathrm{SE} = N'\left[(a_{Mr}b_{Ns} + a_{Mt}b_{Nu})^2\gamma^2\frac{1}{E_{\mathrm{M}} - E_{\mathrm{N}}}\right] + N'\left[(a_{Lr}b_{Ks} + a_{Lt}b_{Ku})^2\gamma^2\frac{1}{E_{\mathrm{K}} - E_{\mathrm{L}}}\right] \quad (8)$$

Equation 8 is a central equation of organic chemistry. On the basis of this equation we can make an enormous number of predictions about the qualitative aspects of chemical reactivity. It is obvious that SE will exhibit a variation depending upon the following four factors.

(a) The magnitude of quantities $E_{\mathrm{M}} - E_{\mathrm{N}}$ and $E_{\mathrm{K}} - E_{\mathrm{L}}$ or, in other words, the proximity of the interacting energy levels: it is obvious that the closer the spacing of two energy levels of two different molecules, the stronger the interaction of the corresponding MO's will be, and, in general, the greater the stabilization energy will also be. It is the energy level proximity factor that the organic chemist usually is referring to when he talks about electronic effects. In our discussions, we shall consistently use the term energy level proximity effect rather than the less specific term electronic effect whereever appropriate.

(b) The second factor, the magnitude of quantities $(a_{Mr}b_{Ns} + a_{Mt}b_{Nu})^2$ and $(a_{Lr}b_{Ks} + a_{Lt}b_{Ku})^2$, will, of course, depend on the relative sign of the coefficient products. The latter will depend upon the individual signs of a_{Mr}, a_{Mt}, b_{Ns}, and b_{Nu}, and the individual signs of a_{Lr}, a_{Lt}, b_{Ks}, b_{Ku}. These individual signs of the coefficients are in fact determined by the nodal properties of the appropriate wave functions. The nodal properties of the wave functions also dictate their corresponding phase properties. Thus, one has three equivalent ways of determining the relative signs of the coefficient products by looking either at the signs of the individual coefficients, or by noting the number of nodes of each of the interacting molecular orbitals, or by examining the phase compatibility of the uniting atomic orbitals. These three equivalent ways are exemplified in Figure 3. It can be seen that in the case of the 2s + 2s or 2a + 2a cycloaddition the signs of the two coefficient products are different, because the individual signs of the relevant coefficients dictate so, or because the interacting MO's possess an odd number of nodes with respect to the uniting fragments, or because the phases of the uniting p orbitals are incompatible. This implies that the value of SE will be near zero since the value of the terms $(a_{Mr}b_{Ns} + a_{Mt}b_{Nu})^2$ and $(a_{Lr}b_{Ks} + a_{Lt}b_{Ku})^2$ will be near zero. Hence, re-

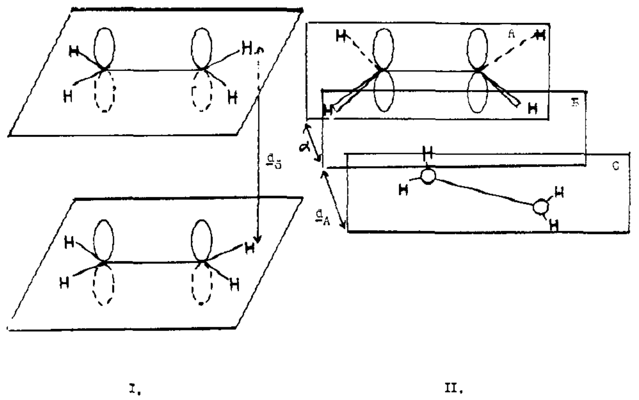


Figure 4. The geometry of the s + s (I) and s + a (II) transition states. Planes are parallel in case I; all planes are parallel in case II. Plane A includes the C–C bond and is perpendicular to the ethylenic framework. Plane B includes the two ethylenic hydrogens. Plane C includes all atoms of the ethylenic framework.

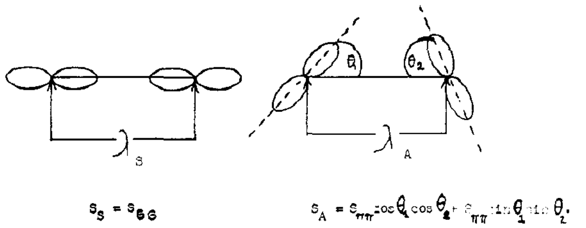
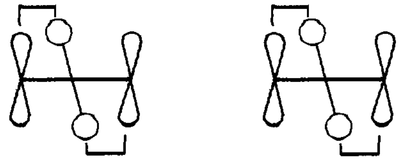


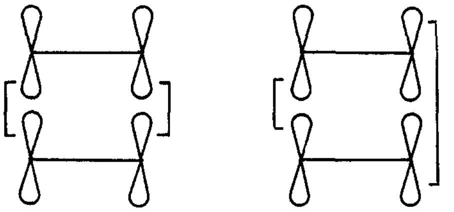
Figure 5. The geometry of orbital overlap in the s + s and s + a transition states of the 2 + 2 cycloaddition of two ethylenes. The values of $S_{\sigma\sigma}$ and $S_{\pi\pi}$ corresponding to a particular value of λ can be found in Kopineck's tabulation. The values of λ, θ_1, θ_2 can be obtained by simple trigonometric computation.

action will be unfavorable in a 2s + 2s or 2a + 2a fashion, and another mode of cycloaddition will be sought. Accordingly, the cycloaddition will occur in a 2s + 2a or 2a + 2s fashion, which in effect renders the signs of the coefficient products identical. On the other hand, in the case of the 4s + 2s or 4a + 2a cycloaddition the signs of the two coefficient products are identical, because the individual signs of the relevant coefficients dictate so, or because the interacting MO's possess an even number of nodes with respect to the uniting fragments, or because the phases of the uniting p orbitals are compatible. This implies that the value of SE will be large since the value of the terms $(a_{M_r}b_{N_s} + a_{M_t}b_{N_u})^2$ and $(a_{L_r}b_{K_s} + a_{L_t}b_{K_u})^2$ will be large. Hence, reaction will be favorable in a 4s + 2s or 4a + 2a fashion.

(c) The third factor is the magnitude of γ. In a typical π cycloaddition the magnitude of γ will vary depending upon the geometry of the transition state, or, in other words, the nature of orbital overlap. In general, in an s + a and an a + s cycloaddition the magnitude of the two resonance integrals of the uniting p orbitals will be the same in each case. This is shown below. On the contrary, in an s + s and an a + a



cycloaddition the magnitude of the two resonance integrals of the uniting p orbitals will be the same in the former case and different in the latter case. This is shown below. It can be seen that in the case of an



a + a cycloaddition one of the resonance integrals is zero. Accordingly, a π cycloaddition will preferentially occur in an s + s rather than an a + a fashion. At this point, it should be mentioned that an a + a mode of cycloaddition could become prominent in cases where an appreciable bending of the orbital lobes materializes. This is not expected to be the case in typical π cycloadditions. It is predicted then that on the basis of the three determinants of reactivity discussed above, a π cycloaddition will occur in an s + s or an s + a fashion. We shall distinguish between two types of γ, namely the resonance integral characteristic of an s + a union of the cycloaddends, γ_A, and the resonance integral characteristic of an s + s union of the cycloaddends, γ_S. Because of the geometry of the s + s and s + a transition states and because γ depends on the overlap of the uniting p orbitals at the transition state, one generally expects that $\gamma_S > \gamma_A$, if everything else is kept constant. Thus, assuming that the two reacting olefins approach each other so that repulsive interactions between the double bond ligands are minimized, one can calculate the ratio γ_S/γ_A from simple formulas.[5] We shall illustrate by an appropriate calculation for the case of the 2 + 2 cycloaddition of two ethylenes. Figure 4 shows the geometry of the two transition states and the crucial parameters for the calculation. In Figure 4, d_A and d_S are the minimum energy nonbonded distances between the two ethylenic frameworks. It can be seen that d_A and d_S can be set equal to the equilibrium nonbonded distance between two hydrogen atoms. The values of d_A and d_S are readily available from already existing calculations.[6] Furthermore, the distance α can be easily calculated from knowledge of the C–H bond length of an ethylene molecule and related angles. By simple trigonometry, one can then calculate the distance and angles between the overlapping p orbitals and by reference to tabulated values of the $S_{\sigma\sigma}$ and $S_{\pi\pi}$ overlap integrals,[7] one can arrive at the result $\gamma_S/\gamma_A = 12.5$. The basic features of the calculation are shown in Figure 5. If one considers the fact that the stabilization energy depends upon the square of the resonance integral of the uniting p orbitals, it becomes clear that on simple overlap considerations the 2s + 2s transition state is strongly favored over the 2s + 2a transition state.[8]

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(5) J. D. Roberts, "Molecular Orbital Calculations," W. A. Benjamin, New York, N. Y., 1961, p 82.

(6) For review and tabulation, see J. E. Williams, P. J. Stang, and P. v. R. Schleyer, *Annu. Rev. Phys. Chem.*, 19, 531 (1968).

(7) H. J. Kopineck, *Z. Naturforsch. A*, 5, 420 (1950). Extrapolated values were used in some instances.

(8) One is led to similar conclusions with regard to the 4 + 2 cycloaddition of butadiene and ethylene.

We have discussed the variation of γ with the geometry of the transition state of the cycloaddition reaction by assuming that cycloaddition takes place *via* an approach of the cycloaddends which minimizes nonbonded steric repulsions; thus we were able to calculate γ_S/γ_A. Alternatively, the assumption could have been made that cycloaddition takes place *via* an approach that maximizes orbital overlap; thus one would have been able to calculate the difference in steric energy arising from nonbonded repulsive interactions between the 2s + 2s and 2s + 2a transition states. The two procedures are, naturally, equivalent. In discussing cycloaddition reactions we shall consistently use the term orbital overlap effect as being more specific than the alternative term steric effect wherever appropriate. One should be conscious, however, as to how those effects find their theoretical justification in accordance with our simple perturbational viewpoint.

(d) The fourth factor is the value of N. The value of SE is significant for $N = 2$, significant for $N = 1$ (identical with the case of $N = 3$), and zero for $N = 0$ (identical with the case of $N = 4$).

The analysis given above shows that any pattern of cycloaddition reactivity will have to be due to a combination of more than one factor. Up to now, the "concertedness," and by implication the energetics, of a cycloaddition were inferred by most organic chemists only from consideration of the phase compatibility and degree of overlap of the appropriate MO's of the cycloaddends. A reference to eq 8 will convince the reader that this is a necessary but not sufficient condition for "concertedness." The energy separation of the interacting MO's of the cycloaddends is, in fact, the key factor which determines the extent by which a concerted union of the cycloaddends will be favored over a nonconcerted one. This determining factor of organic reactivity becomes unrecognizable in any analysis of cycloaddition pathways *via* correlation diagrams which relate orbital symmetry but not energies. We shall utilize the perturbational approach developed above in order to gain new insight about cycloaddition reactions which cannot readily be afforded by the symmetry approaches of the past.

Finally, a note of caution. A full perturbational treatment involves the evaluation of all possible interactions of the MO's of the cycloaddends which contribute to the stabilization energy of either the s + s or the s + a transition state. The consideration of only the most important set of interactions of the MO's of the cycloaddends is a shortcut to laborious calculations but the conclusions reached by such a treatment are generally reliable and very simple to reach. It should be noted that the neglect of all but the dominant interactions between the MO's of the two reactants has been an implicit assumption in all frontier orbital approaches to reactivity which were so successful in correlating a large number of organic chemical observations. Henceforth, we shall adopt this approximate treatment.

II. Interaction Diagrams

In the following discussion of cycloaddition reactions, we shall consider the dominant transition-state interactions of the relevant MO's of the two partners involved in the cycloaddition process. This can be most conveniently accomplished by the construction of interaction diagrams.[9] An interaction diagram depicts the following: (a) the relevant MO energy levels of the two reactants, namely the π MO energy levels of the two reactants;[10] (b) the distribution of electrons in the relevant MO energy levels of each of the two reactants; (c) the dominant interactions of the MO's of the two cycloaddends, the strength of which can be ascertained by noting the degree of proximity of the energy levels corresponding to the interacting MO's.

On the basis of an interaction diagram, predictions about the stereochemical outcome of the reaction can be made by noting the phase properties of the MO's which interact most strongly. Furthermore, as interactions become stronger the energy of the corresponding s + s or s + a transition state is lowered since the stabilization energy increases; hence, the reaction becomes faster. Thus, both stereochemistry and rate variations can be predicted with the use of interaction diagrams. Figure 6 shows two typical interaction diagrams for the cases of ethylene thermal and photochemical dimerizations.

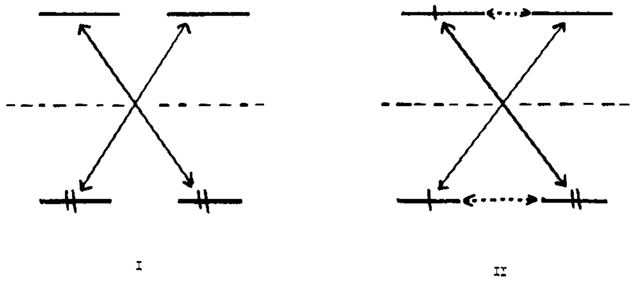

Figure 6. (I) The thermal dimerizations of ethylene. Dominant interactions are shown by solid arrows and stabilize the s + a transition state. (II) The photochemical dimerization of ethylene. Dominant interactions are shown by broken arrows and stabilize the s + s transition state. Proximity of interacting energy levels defines dominant interaction. Diagrams are schematic.

A word about the construction of interaction diagrams is in order. An interaction diagram can be very simply constructed *via* the utilization of computation or experimental data. Specifically, a calculation of the MO energy levels of the individual cycloaddends can directly lead to the construction of an interaction diagram. Alternatively, and more reliably, ionization potentials and electronic transitions of the individual cycloaddends can be utilized in order to specify the relative energies of the occupied and unoccupied MO's of the two cycloaddends. In utilizing such data one assumes equal final energies of the ion radicals and equates the energies of the absorption maxima to electronic transitions between the zero vibrational energy levels of the two electronic states. The construction of an interaction diagram from ionization potential and spectroscopic data is shown in Figure 7. In this work, interaction diagrams have been constructed on the basis of the available experimental data.

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(9) Such interaction diagrams have previously appeared elsewhere. See, for example, 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. See also ref 4.

(10) In this paper we consider only π–π cycloadditions. An extension of our treatment can very simply accommodate σ–π cycloadditions.

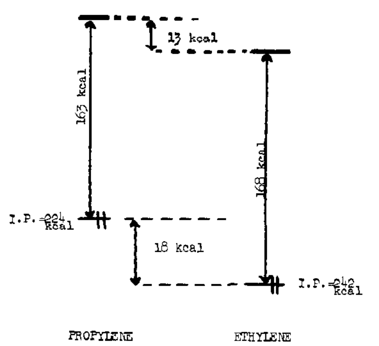

Figure 7. Construction of an interaction diagram for the case of the propylene–ethylene cycloadditions. Ionization potentials and π–π^* transitions are in kilocalorie units. Ionization potential data are from D. W. Turner, *Advan. Phys. Org. Chem.*, **4**, 31 (1966). Spectroscopic data are from P. G. Wilkinson and R. S. Mulliken, *J. Chem. Phys.*, **23**, 1895 (1955); J. C. Jones, Jr., and R. W. Taylor, *Anal. Chem.*, **27**, 228 (1955).

III. The Importance of Donor–Acceptor Relationships in Cycloaddition Reactions

We would like now to consider some specific properties of the cycloaddends and relate them to the stereochemical and rate aspects of the cycloaddition reaction.

In every cycloaddition reaction, except in the case of dimerizations, we can always define one of the partners in the cycloaddition process as the donor and the other as the acceptor. If one considers cycloaddends I and II, then, if $E_{\mathrm{HOMO\ I}} - E_{\mathrm{LUMO\ II}} < E_{\mathrm{HOMO\ II}} - E_{\mathrm{LUMO\ I}}$, it will always follow that cycloaddend I is the donor and cycloaddend II is the acceptor. This criterion can be reliably used in defining donor and acceptor cycloaddends, irrespective of the nature of cycloaddition.

We can now proceed to define the spectrum of interactions between cycloaddends expected in a cycloaddition reaction. For that purpose, we shall use the letters of the alphabet to denote the extent of similarity of the cycloaddends in terms of their electron donating and electron accepting abilities. Thus, an AA pair will denote two cycloaddends of identical electron accepting and donating abilities, an AM pair will denote cycloaddends of substantially different electron accepting and donating abilities, and an AZ pair will denote cycloaddends of extremely different electron accepting and donating abilities. In going from an AA pair to an AZ pair, the quantity $E_{\mathrm{HOMO\ donor}} - E_{\mathrm{LUMO\ acceptor}}$ will decrease in general. In other words, the spectrum of cycloaddend interactions will range from those of nonpolar type, *e.g.*, AD cycloadditions, to those of polar type, *e.g.*, AX cycloadditions. We reserve the use of the symbols AA and AZ for denoting the limiting cases of a dimerization and a near-ionic cycloaddition, respectively. It is important to realize that the quantity $E_{\mathrm{HOMO\ donor}} - E_{\mathrm{LUMO\ acceptor}}$ provides an index for locating a cycloaddition on the reactivity spectrum. This quantity can be determined by calculation, or preferably, by reference to ionization potential and spectroscopic data as discussed before.

Finally, we consider two cycloaddends d and a where d denotes the donor molecule and a the acceptor molecule. We shall define their interaction at the transition state by a resonance hybrid involving no-bond (NB) and charge-transfer (CT) contributing structures.

$$\mathrm{d\cdots a(NB)} \longleftrightarrow \mathrm{d^{+}\cdots a^{-}(CT)}$$

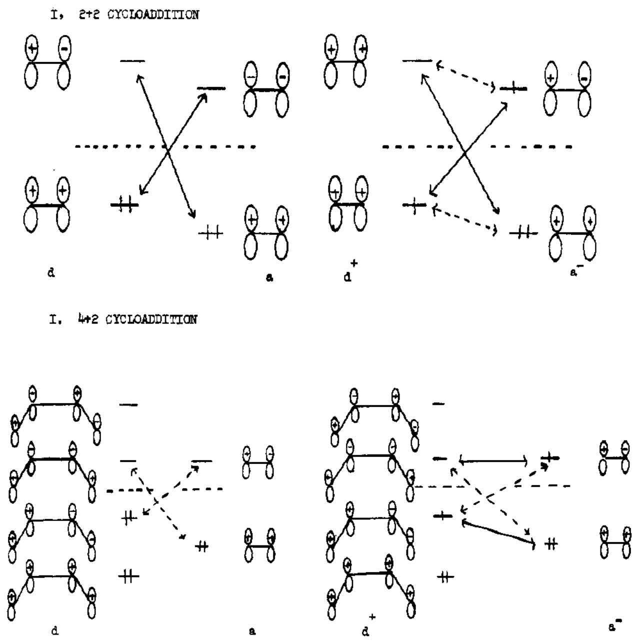

Figure 8. The resonance formations of the transition state of a cycloaddition reaction. Solid arrows indicate dominant interactions stabilizing the s + a transition state, while broken arrows indicate dominant interactions stabilizing the s + s transition state. Diagrams are schematic.

It is clear that in the case of AD-like cycloaddition the contribution of the CT structure will be negligible, while in the case of an AX-like cycloaddition the contribution of the NB structure will be negligible. Figure 8 demonstrates the resonance formulation of the transition state of a cycloaddition reaction through the use of interaction diagrams.

An examination of the phase compatibility of the appropriate wave functions corresponding to the interacting energy levels reveals the following trends. (a) In the case of the 2 + 2 cycloaddition the s + s transition state is increasingly stabilized as the importance of contributor $\mathrm{d^{+}\cdots a^{-}}$ is increased. On the contrary, the s + a transition state is stabilized whether contributor $\mathrm{d\cdots a}$ or $\mathrm{d^{+}\cdots a^{-}}$ makes the most important contribution to the resonance hybrid. (b) In the case of the 4 + 2 cycloaddition, the s + s transition state is stabilized whether contributor $\mathrm{d\cdots a}$ or $\mathrm{d^{+}\cdots a^{-}}$ makes the most important contribution to the resonance hybrid. On the contrary, the s + a transition state is increasingly stabilized as the importance of contributor $\mathrm{d^{+}\cdots a^{-}}$ is increased.

According to the above generalizations, one can then distinguish between extreme types of cycloadditions which display different characteristics. In the case of the 2 + 2 cycloaddition, the two extremes are represented by the nonpolar, or AD-like, cycloaddition and the polar, or AX-like, cycloaddition. In the case of the 4 + 2 cycloaddition, the two extremes are represented by the semipolar, or AM-like, cycloaddition and the polar, or AX-like, cycloaddition.[11] We shall

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(11) The assumption that a 4 + 2 cycloaddition ranges from an AM to an AX type is based on both experiment and theory. According to our theory the quantity $E_{\mathrm{HOMO\ donor}} - E_{\mathrm{LUMO\ acceptor}}$ is smaller for the reaction of unsubstituted butadiene with ethylene than for the reaction of simple ethylenes; thus, the former reaction typifies an AM-like cycloaddition while the latter an AD-like cycloaddition. From the experimental standpoint, it is generally true that the 4 + 2 cycloaddition is preceded by charge-transfer complex formation even when the cyclo-

examine how the degree of polarity of the transition state affects the stereochemical outcome of the 2 + 2 and 4 + 2 cycloaddition reactions.

AD-Like 2 + 2 Cycloadditions. A typical AD cycloaddition transition state will be described by a resonance hybrid of an NB and a CT structure, but the contribution of the latter structure will be considered to be negligible. Thus, one can simply describe a nonpolar, AD-like, cycloaddition transition state by a single structure, the NB structure. From Figure 8, one can readily see that under those circumstances the only stabilizing MO interactions of the cycloaddends are those stabilizing the s + a transition state. Thus, an AD-like cycloaddition will take place in a predominantly s + a fashion, unless multisubstitution of the cycloaddends by bulky substituents makes such a union impossible.

AX-Like 2 + 2 Cycloadditions. A typical AX cycloaddition will be described by a resonance hybrid of an NB and a CT structure. The contribution of the NB structure will be considered to be negligible. Thus, we can describe a polar, AX-like, cycloaddition transition state by a single structure, the CT structure. From Figure 8, one can readily see that under those circumstances there will be two kinds of stabilizing MO interactions, namely, those stabilizing the s + a and those stabilizing the s + s transition state. The preferred transition state will then be determined by the relative magnitude of the two kinds of stabilizing interactions.

In order to evaluate the electronic preference for the antarafacial or suprafacial transition state, we consider two important factors: (a) the proximity of the energy levels corresponding to the interacting MO's, the interaction of which stabilizes the s + s or s + a transition states; (b) the extent of orbital overlap attainable at the s + s or s + a transition state.

With regard to the first factor, proximity of energy levels, it can be seen from Figure 9 that the s + a transition state is stabilized more than the s + s transition state. This is so because the spacing of the energy levels corresponding to the MO's, the interaction of which stabilizes the s + a transition state, is smaller than the spacing of the energy levels corresponding to the MO's, the interaction of which stabilizes the s + s transition state. On the other hand, on the basis of the consideration of the extent or orbital overlap, it can be shown that the s + s transition state is overwhelmingly favored over the s + a transition state. We recall that the ratio γ_S/γ_A, which depends on the extent of orbital overlap at the corresponding transition states, had a value of 12.5 when the cycloaddition of two unsubstituted ethylenes was considered.[12] In AX cycloadditions, the substituents on the two olefins necessarily have different electronic properties and because of the dominance of the CT structure in the transition-state resonance hybrid, additional electrostatic interactions between the two partners become important. Since an s + s transition state involves the interaction of two olefins lying in parallel planes while an s + a transition state involves the interaction of two olefins lying in perpendicular planes, electrostatic attraction will be maximal for an s + s transition state and smaller for an s + a transition state. Hence, the degree of orbital overlap for an s + s transition state is further enhanced relative to that for an s + a transition state because of electrostatic attraction. Accordingly, the ratio γ_S/γ_A is, in general, expected to increase whenever an AX cycloaddition takes place. One should not forget that the stabilization energy depends upon the square of the resonance integral, γ, of the uniting p orbitals; thus, differences in the extent of orbital overlap at the s + s and the s + a transition states result in magnified differences in the stabilization energy of the corresponding transition states. Thus, the opposing nature of the energy level proximity effect and the orbital overlap effect gives rise to a decisive preference for the s + s transition state, since the orbital overlap effect by far outweighs the importance of energy level proximity effect. This has been verified by model calculations which take into account the electron distribution in the MO's of the two cycloaddends in the case of an AX cycloaddition. Thus, polar, AX-like cycloaddition reactions will take place in a predominantly s + s fashion.

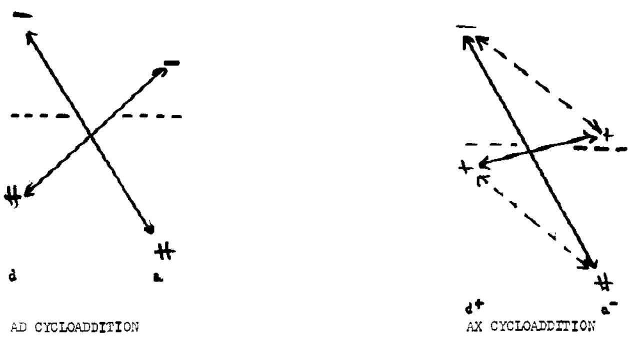

Figure 9. The electronic differences between an AD and an AX cycloaddition. Solid arrows show interacting MO energy levels stabilizing the s + a transition state. Broken arrows show interacting MO energy levels stabilizing the s + s transition state. Diagrams are schematic.

AM-Like 4 + 2 Cycloadditions. A typical AM cycloaddition transition state will be described by a resonance hybrid of an NB and a CT structure. The importance of the CT structure nearly equals the importance of the NB structure. From Figure 8, one can readily see that under those circumstances there will be two kinds of stabilizing MO interactions, namely, those stabilizing the s + a transition state originating from the CT contributor, and those stabilizing the s + s transition state originating from both the CT and the NB contributors. Thus, the s + s transition-state stabilizing interactions are more widespread than the s + a transition-state stabilizing interactions. If one considers the fact that orbital overlap considerations overwhelmingly favor the s + s transition state, as we have similarly seen in the case of the 2 + 2 cycloadditions, one can come to the conclusion that the s + s transition state will be preferred over the s + a transition state.

AX-Like 4 + 2 Cycloadditions. A typical AX cycloaddition transition state will be described by a

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addends are slightly perturbed by substituents. Hence, the contribution of the charge-transfer structure to the transition-state resonance hybrid should be important. On the other hand, charge-transfer complexes do not precede 2 + 2 cycloadditions when the cycloaddends are only slightly perturbed by substituents.

(12) The value of the γ_S/γ_A ratio might vary as one goes from the cycloaddition of two unsubstituted ethylenes to the cycloaddition of two heavily substituted ethylenes. In general, the variation is not expected to be great since the effect of substitution upon the size and shape of the orbitals will affect both s + s and s + a orbital overlap in the same direction.

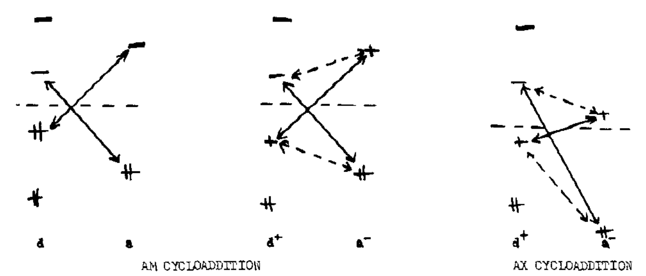


Figure 10. The electronic differences between an AM and an AX cycloaddition. Solid arrows indicate dominant interactions stabilizing the s + s transition state. Broken arrows indicate dominant interactions stabilizing the s + a transition state. Diagrams are schematic.

resonance hybrid of an NB and a CT structure. The importance of the NB structure will be considered as negligible. Thus, we can describe a polar, AX-like, cycloaddition transition state by a single structure, the CT structure. From Figure 8, one can readily see that under those circumstances there will be two kinds of interactions, namely, those interactions stabilizing the s + s transition state and those interactions stabilizing the s + a transition state. The preferred transition state will then be determined by the relative magnitude of the two kinds of stabilizing interactions. In this case, application of both the proximity of energy levels criterion and the orbital overlap criterion indicates that the s + s transition state will be preferred. This is shown in Figure 10.

We now summarize our conclusions in Table I. It can be seen that a 2 + 2 cycloaddition should range from a predominantly s + a reaction to a predominantly s + s reaction with all the in-between gradations. On the other hand, a 4 + 2 cycloaddition is always s + s.

Table I. The Spectrum of Thermal 2 + 2 and 4 + 2 Cycloadditions

Type of cycloaddition	Designation	Preferred union of cycloadducts
2 + 2 AD	Nonpolar	s + a
2 + 2 AM	Semipolar	s + a and s + s
2 + 2 AX	Polar	s + s
4 + 2 AM	Semipolar	s + s
4 + 2 AX	Polar	s + s

IV. The Nature of Antarafacial Union

There is one additional facet of the cycloaddition reaction which merits consideration. While in the s + s mode of cycloaddend union the stereochemistry around the double bonds is maintained, in the case of the s + a union rotation of a bond must occur in one of the cycloaddition partners. It is obvious that bond rotation will occur within the one partner which sustains the greatest double bond loosening due to its interaction with the second partner. We shall show that one can simply relate donor–acceptor properties to the stereochemical outcome of an s + a union of two cycloaddends.

Let us consider the cycloaddition of propylene to ethylene and inquire about which of the two partners will preferentially sustain bond rotation in the course of the s + a union. One is reminded that the reaction is a typical 2 + 2 AD cycloaddition and will be predisposed toward s + a reaction. One can write two distinct transition states as shown in Figure 11. It can be seen that transition-state I involves rotation in the acceptor moiety, the ethylene molecule. The strongest interaction, involving the HOMO of the donor and the LUMO of the acceptor, loosens the π bond of the rotating fragment, while the weakest interaction, involving the HOMO of the acceptor and the LUMO of the donor, does not greatly contribute to the loosening of the π bond of the rotating fragment. On the other hand, transition-state II involves rotation in the donor moiety, the propylene molecule. The strongest interaction, involving the HOMO of the donor and the LUMO of the acceptor, does not greatly contribute to the loosening of the π bond of the rotating fragment, while the weakest interaction, involving the HOMO of the acceptor and the LUMO of the donor, loosens the π bond of the rotating fragment. Hence, transition-state I, which involves the loosening of the acceptor π bond *via* the strongest interaction of the MO's of the cycloaddends, would be of lower energy than transition-state II. We can generalize the above result by saying that in an s + a union rotation will preferentially occur within the acceptor moiety and the exhibited preference will increase as the difference in strength of the two major interactions stabilizing the s + a transition state of the cycloaddition increases. Thus, in going from an AD to an AX type of cycloaddition, rotation within the acceptor moiety will increasingly be favored whenever s + a union of the cycloaddends occurs. This is illustrated in Figure 12. It is extremely important to stress that in the above discussion we have uniformly assumed that orbital overlap effects are comparable for both antarafacial transition-state configurations.

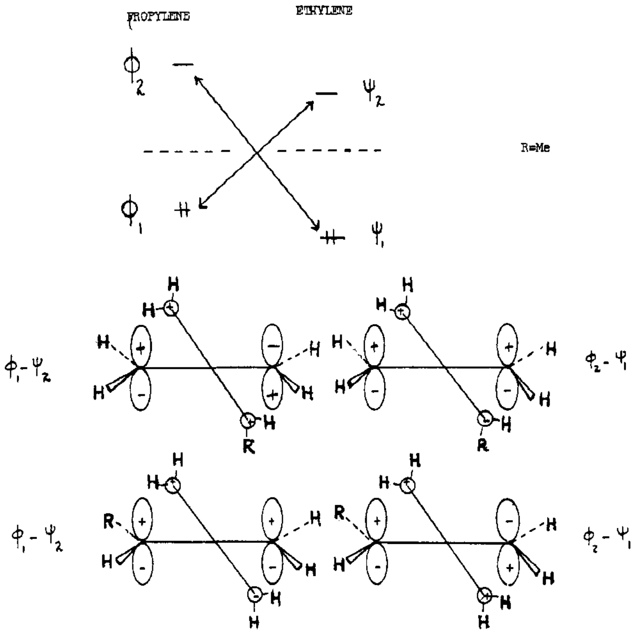


Figure 11. The AD s + a cycloaddition of propylene (donor) and ethylene (acceptor). Interaction diagram reveals the relative strength of the $\phi_1\psi_2$ and $\phi_2\psi_1$ interactions. The two possible transition states of the cycloaddition are shown. Diagram is schematic.

We now want to explicitly consider why the HOMO–LUMO interaction between two cycloaddends in the case of a 2 + 2 cycloaddition loosens preferentially the π

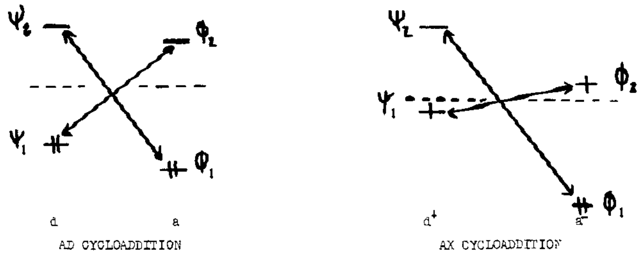


Figure 12. Illustration of rotational preference in an s + a cycloaddition. In the AD case the difference in the strength of interaction $\psi_1\phi_2$ and $\psi_2\phi_1$ is small. In the AX case the difference in the strength of interaction $\psi_1\phi_2$ and $\psi_2\phi_1$ is large. The criterion is the proximity of the corresponding energy levels. Diagrams are schematic.

bond of one and not both of the cycloaddends as we have assumed above. One can reasonably assume that at infinite distance separating the two cycloaddends there are two electrons occupying the HOMO of one cycloaddend and zero electrons occupying the LUMO of the other cycloaddend. As the two molecules are brought within a distance of modest orbital overlap, then a modest interaction between the HOMO of the first and the LUMO of the second cycloaddend gives rise to charge transfer from the HOMO of the first to the LUMO of the second cycloaddend. At this stage of weak perturbation of the two molecules, which in fact is the one considered as the prototype for the theoretical discussion of cycloaddition reactions, the π bonds of *both* cycloaddends are weakened due to charge transfer. As a result of charge transfer the first cycloaddend now possesses $2 - \epsilon$ bonding electrons and the second cycloaddend now possesses ϵ antibonding electrons, where ϵ can be a fractional number. Finally, as the two cycloaddends are brought within a distance which equals the sum of the covalent radii of the uniting atomic centers, then the HOMO of the first molecule fully overlaps the LUMO of the second molecule. At this stage of strong perturbation of the two molecules the two electrons initially occupying the HOMO of one cycloaddend are now simultaneously occupying the HOMO of one and the LUMO of the other cycloaddends. As a result the π bond of *only one* cycloaddition partner is weakened and this will be the cycloaddend which provides the LUMO for the interaction to take place. The conclusion is then reached that as one goes from weak to strong perturbation of the cycloaddends, or, as one goes from reactant to products in an antarafacial 2 + 2 cycloaddition, the π bond of one of the cycloaddends is preferentially loosened. Additional applications of this concept will be described elsewhere.

Let us next consider the cycloaddition of 1,3-butadiene and ethylene and inquire about which of the two partners will preferentially sustain bond rotation in the course of a hypothetical s + a union. One is reminded that the reaction is a typical 4 + 2 AM cycloaddition and will thus take place predominantly in an s + s fashion. One can write two distinct transition states as shown in Figure 13. By following the same reasoning as before, it can be seen that for each of the two possible s + a transition states there exist two possible interactions, namely, an interaction which gives rise to loosening of the bonds of both cycloaddends

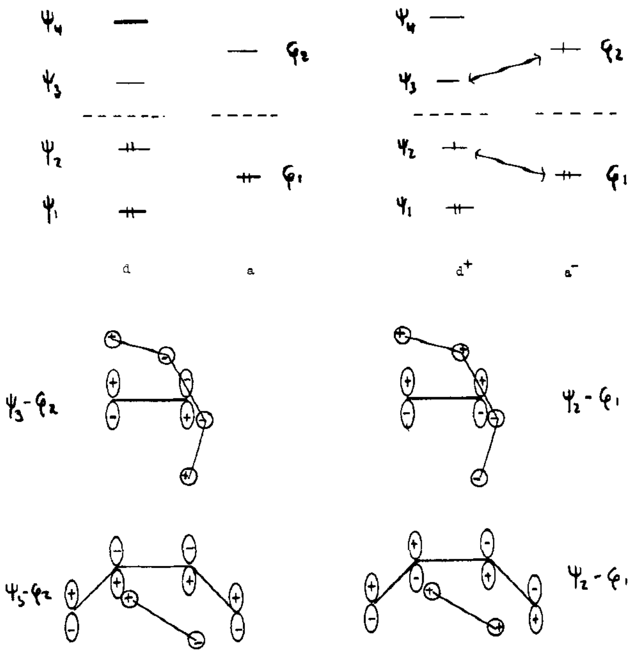


Figure 13. The AM s + a cycloaddition of 1,3-butadiene and ethylene. The two possible transition states of the cycloaddition are shown. The interactions stabilizing the s + a transition state are shown by solid lines on the interaction diagrams. Diagrams are schematic.

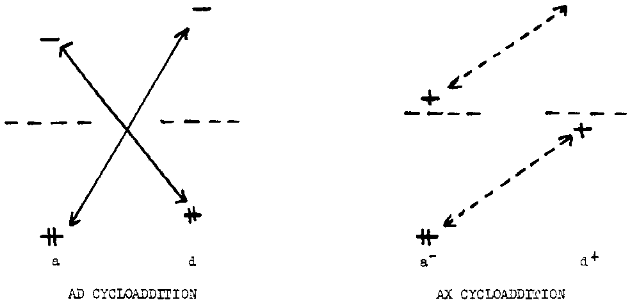


Figure 14. The energy level proximity effect in the cases of AD and AX cycloadditions. Broken arrows indicate interacting energy levels stabilizing s + s unions while solid arrows indicate interacting energy levels stabilizing s + a unions. Orbital overlap is more favorable in the case of the s + s unions than in the case of the s + a unions. Diagrams are schematic.

and an interaction which also gives rise to loosening of the bonds of both cycloaddends. Accordingly, there will be no significant electronic preference on the basis of the above considerations for either of the two possible s + a transition states. Again it should be stressed that in the above discussion we have assumed that orbital overlap effects are comparable for both conceivable s + a transition-state configurations.

We are now prepared to consider the major questions of cycloaddition reactions with respect to: (a) rates of cycloaddition reactions; (b) stereochemistry of cycloaddition reactions; and (c) solvent effects on the rate and stereochemistry of cycloaddition reactions.

The Rates of 2 + 2 Cycloaddition Reactions. In going from an AD-like to an AX-like 2 + 2 cycloaddition reaction, both energy level proximity effects and orbital overlap effects become more favorable. This is shown in Figure 14. Thus, a polar cycloaddition, in our terminology an AX cycloaddition, will be much

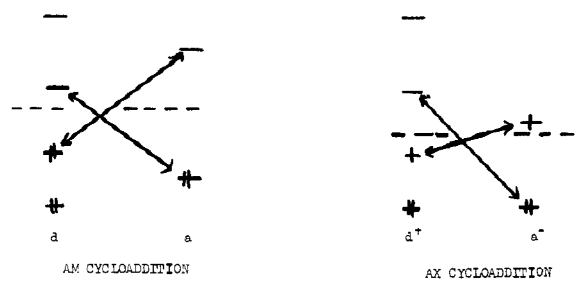


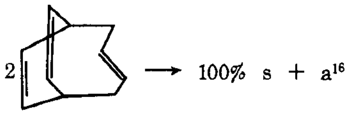
Figure 15. The energy level proximity effect in the cases of AM and AX cycloadditions. Orbital overlap is more favorable in the AX than the AM case since the increased importance of the charge-transfer structure to the transition-state resonance hybrid increasingly gives rise to electrostatic attractive interactions between the cycloaddends which counteract nonbonded repulsions and, thus, give rise to increasingly more favorable orbital overlap. All 4 + 2 cycloadditions occur suprafacially. Diagrams are schematic.

faster than a nonpolar cycloaddition, in our terminology an AD cycloaddition. This has been amply demonstrated to be so.[13] Indeed, strongly electrophilic olefins may cycloadd to electron-rich olefins under surprisingly mild conditions, without the influence of light or heat. On the contrary, cycloadditions of nonpolar olefins and dimerization reactions require comparatively high temperatures to be accomplished.[14]

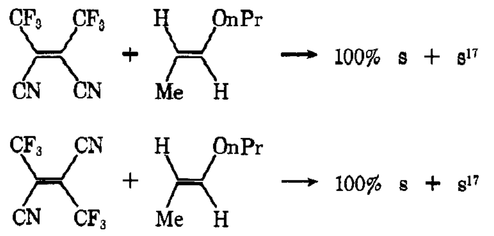
The Rates of 4 + 2 Cycloaddition Reactions. In going from an AM- to an AX-like 4 + 2 cycloaddition reaction, both energy level proximity effects and, to some extent, orbital overlap effects become more favorable. This is shown in Figure 15. Thus, the rate of 4 + 2 cycloaddition reaction will increase in that order. Pertinent rate data in accord with our expectations are compiled in an excellent review of cycloaddition reactions.[15]

The Stereochemistry of 2 + 2 Cycloaddition Reactions. According to our formulation, a dimerization (AA-type cycloaddition) or a nonpolar cycloaddition (AD-type cycloaddition) will take place in an antarafacial fashion, and bond rotation will preferentially occur within the acceptor partner. On the other hand, polar cycloaddition (AX-type cycloaddition) will take place in a suprafacial fashion.

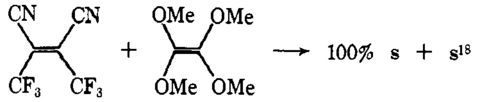
(a) Simple Olefins. Examples of the 2 + 2 cycloaddition of simple olefins drawn from the literature are shown below.



AA-type cycloaddition



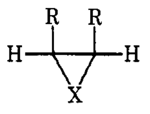
AX-type cycloaddition



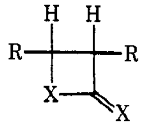
AZ-type cycloaddition

(b) Ketenic Molecules. In all cases of cycloaddition of ketenes to good electron donors, the ketenic moiety plays the role of the acceptor and thus *either* s + s or s + a union will give rise to retention of the stereochemical features around the donor double bond in the final cycloadduct. This has been demonstrated to be the case in a great number of examples.[19]

(c) Extrusion Reactions. Reactions of the following types (eq 9 and 10) are predicted to be syn



$\mathrm{RHC{=}CHR} + \mathrm{X}:$
$\mathrm{X} = \mathrm{SO}, \mathrm{SO_2}, \mathrm{N_2}, \mathrm{NNO}$ (9)
R = electron-releasing group



$\mathrm{RHC{=}CHR} + \mathrm{CX_2}$
$\mathrm{X} = \mathrm{O}, \mathrm{S}$ (10)
R = electron-releasing group

stereospecific since in all cases the donor moiety will be the olefin and the acceptor moiety will be the "small molecule." Thus, either s + s or s + a cleavage will give rise to retention of the stereochemical features around the carbon–carbon bond undergoing the reaction. The situation is similar to that encountered in the case of ketene cycloaddition. A number of experiments confirm these expectations.[20]

The Stereochemistry of 4 + 2 Cycloaddition Reactions. The 4 + 2 cycloaddition will always occur in an s + s manner, irrespective of the polarity of the transition state. This has been known to be so for a long time.

The Effect of Solvent on the Rates and Stereochemistry of Cycloaddition Reactions. We have seen that in the case of the 4 + 2 cycloaddition either the NB or the CT contributor to the resonance hybrid provides stabi-

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(13) J. K. Williams, D. W. Wiley, and B. C. McKusick, *J. Amer. Chem. Soc.*, **84**, 2210 (1962).

(14) J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962).

(15) R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes," S. Patai, Ed., Interscience, New York, N. Y., 1964.

(16) K. Kraft and G. Koltzenburg, *Tetrahedron Lett.*, 4357, 4723 (1967).

(17) S. Proskow, H. E. Simmons, and T. L. Cairns, *J. Amer. Chem. Soc.*, **88**, 5254 (1966). See also additional examples of stereospecific 2 + 2 polar cycloadditions reported therein. It is significant that when the donor olefin has the cis configuration instead of the trans configuration, then the combination trans acceptor–cis donor and cis acceptor–cis donor becomes 54% s + s and 41% s + a, respectively. It is important to notice that in both cases rotation occurs in the acceptor molecule while the substituents of the donor retain their stereochemical relationships in the product as anticipated by our theory. The increased preference for s + a addition when a cis donor is employed is probably due to an orbital overlap effect.

(18) R. W. Hoffman, *Angew. Chem.*, **80**, 823 (1968). Admittedly, in this example, the evidence is incomplete since the retention or nonretention of donor stereochemistry cannot be revealed.

(19) J. C. Martin, V. W. Goodlet, and R. D. Burpitt, *J. Org. Chem.*, **30**, 4309 (1965); G. Binsch, L. A. Feiler, and R. Huisgen, *Tetrahedron Lett.*, 4497 (1968); R. Huisgen, L. A. Feiler, and G. Binsch, *Angew. Chem.*, **76**, 892 (1964); *Angew. Chem., Int. Ed. Engl.*, **3**, 753 (1964). For addition of good donors to isocyanates, see: E. J. Moriconi and J. F. Kelly, *Tetrahedron Lett.*, 1435 (1968); F. Effenberger and G. Keifer, *Angew. Chem., Int. Ed. Engl.*, **6**, 951 (1967).

(20) F. G. Bordwell, J. M. Williams, Jr., E. B. Hoyt, Jr., and B. B. Jarvis, *J. Amer. Chem. Soc.*, **90**, 429 (1968); D. S. Noyce and E. H. Banitt, *J. Org. Chem.*, **31**, 4043 (1966).

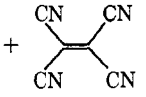
lization for the favorable s + s union of the cycloaddends, while in the case of the 2 + 2 cycloaddition only the CT contributor provides stabilization for the favorable s + s union of the cycloaddends. We can anticipate that by changing the solvent polarity we change the importance of the contribution of the CT structure to the transition-state resonance hybrid. A change in solvent polarity is not significantly sensed by the 4 + 2 cycloaddition since stabilization of the s + s transition state arises to a comparable extent from either NB or CT contributor. On the other hand, the 2 + 2 cycloaddition dramatically depends on the contribution of the CT structure to the transition-state resonance hybrid, since it is the CT contributor which gives rise to the stabilization of the favorable s + s transition state. Hence, as solvent polarity is increased, the importance of the CT contributor increases and so does the stabilization of the s + s transition state. Accordingly, both 4 + 2 and 2 + 2 cycloadditions should be faster in polar solvents since in both cases electrostatic attraction of the cycloaddends arising from the increased contribution of the CT structure to the transition state provide for more favorable orbital overlap, but the 2 + 2 cycloaddition should be more sensitive to solvent changes than a 4 + 2 cycloaddition.

A corollary of the above is that in the case of a 2 + 2 cycloaddition increased solvent polarity leads not only to enhanced rates, but also increased amounts of cycloadducts arising from s + s union of the cycloaddends. It is also apparent that in going from an AD to an AX 2 + 2 cycloaddition, the magnitude of the solvent effect should increase as the two interacting partners possess an increasingly higher potential for change transfer. Figure 16 shows schematically the effect of solvent on the rate of the 2 + 2 and 4 + 2 cycloaddition reactions. It follows from Figure 16 that in going from an AA to an AZ type of cycloaddition, increasing solvent polarity will progressively enhance the rate of the 2 + 2 cycloaddition relative to the rate of the 4 + 2 cycloaddition to an increasingly greater extent. We shall exemplify the above predictions with pertinent cases.

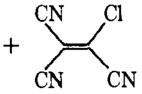
(a) Rate Response to Solvent Changes.[15] In the case of a 4 + 2 cycloaddition, rates typically vary up to a factor of 5–10 over a range of solvent polarity. In the case of a 2 + 2 cycloaddition, rates typically vary up to a factor of 10^5 over a range of solvent polarity.

(b) Solvent Effects in Relation to Type of Cycloaddend Interaction. In the case of a 4 + 2 cycloaddition in going from an AM to an AX pair of cycloaddends, an increase in solvent polarity is expected to produce an increasingly higher rate enhancement. However, since this higher rate enhancement arises from increasingly more favorable orbital overlap as a result of increased electrostatic interaction at the transition state, and since the spectrum of AM to AX 4 + 2 cycloadditions is characterized by a dominant contribution of the CT structure to the transition-state resonance hybrid, then the magnitude of the effect is expected to be small. There has been no systematic study to test this prediction. In the case of a 2 + 2 cycloaddition in going from an AD to an AX pair of interacting cycloaddends, an increase in solvent polarity produces an increasingly greater rate enhancement. This is shown with the following examples.[21]

$\dfrac{k_{\text{acetonitrile}}}{k_{\text{cyclohexane}}}$

p-methoxystyrene +


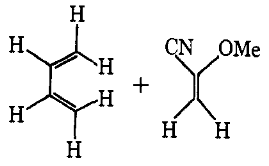
6.3×10^4

p-methoxystyrene +


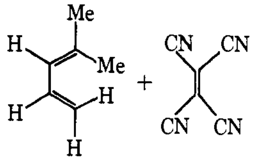
200

(c) Solvent Effect on the Competition of 4 + 2 and 2 + 2 Cycloaddition. An inspection of Figure 16 indicates that the rate enhancement of the 2 + 2 cycloaddition due to increased solvent polarity rapidly increases relative to the corresponding rate enhancement of the 4 + 2 reaction as you go from an AA to an AZ pair of interacting cycloaddends. Of course, this means that 2 + 2 cycloaddition will tend to be preferred over 4 + 2 in polar solvents in cases where competition between the two mechanisms exists. This is shown with the following examples.[22]

Type of interaction — Reactants

AM


$$\left[\frac{k_{\text{nitromethane}}}{k_{\text{cyclohexane}}}\right]_{2+2} \simeq \left[\frac{k_{\text{nitromethane}}}{k_{\text{cyclohexane}}}\right]_{4+2}$$

AX


$$\left[\frac{k_{\text{nitromethane}}}{k_{\text{cyclohexane}}}\right]_{2+2} \simeq 50\left[\frac{k_{\text{nitromethane}}}{k_{\text{cyclohexane}}}\right]_{4+2}$$

(d) Solvent Effect on Reaction Stereospecificity. It is predicted that as solvent polarity increases, the stereochemistry of the 2 + 2 cycloaddition is affected and s + s union of cycloaddends is enhanced. The following example illustrates the above prediction.[17]

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(21) J. K. Williams, D. W. Wiley, and B. C. McKusick, *J. Amer. Chem. Soc.*, **84**, 2210 (1962); J. K. Williams, D. W. Wiley, and B. C. McKusick, *ibid.*, **84**, 2216 (1962).

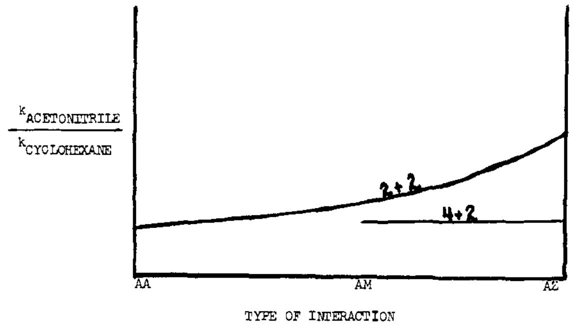
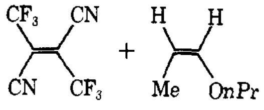


Figure 16. Variations of magnitude of solvent effect with type of cycloaddend interaction. Diagram is schematic.

Reaction	*% s + s product*	
	Ethyl acetate solvent 46%	acetonitrile solvent 56%

It is also predicted that as solvent polarity increases, the stereochemistry of the 4 + 2 cycloaddition reaction should remain unaffected. This, in fact, has been found in almost all cases studied up to now.

Conclusion

A realization of the importance of donor–acceptor interactions and a resonance formulation of the transition state of a cycloaddition reaction led us to the description of the entire spectrum of cycloaddend interactions.[23] The theoretical apparatus consisted of the construction of appropriate interaction diagrams and applications were, for simplicity's sake, restricted to the cases of the 4 + 2 and 2 + 2 cycloaddition reactions as exemplary of $4N + 2$ and $4N$ electron processes.

The substantial and very important differences between the present formulation and that of Woodward and Hoffmann are apparent in several respects. First, a major implication of the present treatment, to be further substantiated in future publications, is that random behavior (*e.g.*, nonstereospecificity) might be the outcome of several well defined and competing processes rather than the indication of the existence of a partially or totally indiscriminating intermediate, *e.g.*, a biradical. This contrasts sharply with the division of reactivity into "concerted" and "nonconcerted" types as advocated by Woodward and Hoffmann.[1] In our view, the majority of cycloaddition reactions are "concerted," in other words, synchronous overlap of the p orbital at both sites of union is taking place at the transition state and the stereochemical consequences of the reaction simply depend on the properties of the cycloaddends. Second, the Woodward–Hoffmann approach can be seen to be applicable to a special case of the 2 + 2 cycloaddition (AA type of 2 + 2 cycloaddition) and uniformly to all cases of the 4 + 2 cycloaddition. It is exactly the failure of the Woodward–Hoffmann approach to reproduce the spectral behavior of cycloaddition reactions which gives rise to a distinction of "concerted" and "nonconcerted" reactions. While undoubtedly two-step intermolecular cycloadditions occur, we believe that in most cases the nonstereoselectivity of a cycloaddition is not an indication of the existence of an intermediate at some point along the reaction coordinate but rather the result of more than one concerted pathway.

A final and most important question remains to be asked, namely, what are the circumstances under which a genuine two-step cycloaddition will occur? We have seen that concerted cycloadditions belong to a reactivity spectrum. It is then reasonable to expect that the activation energy difference between a one-step and a two-step cycloaddition will be different at different points of the reactivity spectrum. Specifically, it is expected that when the MO interactions between the cycloaddends are strong the two-step mechanism will be disfavored while when they are weak the two-step mechanism will be favored. We have seen *via* interaction diagrams that in both 2 + 2 and 4 + 2 cycloadditions the weakest interactions between the MO's of the cycloaddends occur toward the extreme nonpolar end of the spectrum since the interacting energy levels are separated by relatively large energy gaps. On the other hand, the strongest interactions between the MO's of cycloaddends in both 2 + 2 and 4 + 2 cycloadditions occur toward the polar end of the spectrum since the interacting energy levels are separated by relatively small energy gaps. Accordingly, a two-step cycloaddition is to be expected toward the nonpolar end of the 2 + 2 and 4 + 2 cycloaddition spectrum. Thus, certain nonpolar AA 2 + 2 cycloadditions might proceed *via* the intermediacy of biradicals not only because the steric requirements of the s + a transition state are stringent but primarily because the interaction of the appropriate MO's of the cycloaddends is weak.[24] Similarly, certain extreme semipolar AM 4 + 2 cycloadditions could conceivably proceed *via* the intermediacy of biradicals. Indeed, thermochemical calculations show that certain semipolar Diels–Alder reactions can proceed *via* biradical intermediates.[25]

In this work we described the spectrum of thermal 2 + 2 and 4 + 2 concerted cycloadditions and identified the type of 2 + 2 and 4 + 2 cycloadditions where a stepwise mechanism might be operative. In another work we shall extend our treatment to photochemical cycloadditions.

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