

Application of Intermolecular SCF-Perturbation Theory to the Regioselectivity in the Diels–Alder Reaction

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Intermolecular perturbation theory in the density matrix formalism is applied to investigate the directional behaviour of an electron-donating ($-\text{CH}_3$) or an electron-accepting ($-\text{CN}$) group in 1- or 2-substituted butadienes in the Diels–Alder reaction with acrylonitrile. The calculated CNDO/2 perturbation energies are analysed in three different ways by considering: a) the different perturbation energies, b) the diatomic parts of the interaction energy and c) the HOMO-LUMO contribution to the second-order energy. The regioselectivity is due to a subtle balance of charge-transfer interactions and steric effects of the substituents on the diene and the dienophile. The changes of intra- and intermolecular diatomic energy contributions are correlated with the process of bond formation and bond weakening. The intermolecular perturbation energies are dominated by pairwise interactions between the terminal C-atoms and by the secondary Woodward–Hoffmann interaction. These three localized interactions determine the endo addition and reflect the orienting power of the substituents.

Key words: Diels–Alder reaction, regioselectivity in \sim

1. Introduction

The Diels–Alder reaction [1] and its stereochemical course are of significance in the MO approaches to a rationalization of the reactivity of molecules [2]. A particular aspect of this type of reaction, the regioselectivity in the cycloaddition of asymmetrically substituted reactants, will be investigated on the basis of a perturbation procedure implemented within the framework of the CNDO/2 method [3].

If both diene and dienophile are asymmetrically substituted (4 + 2)-cycloaddition can lead to structural isomers. They may be classified according to the relative position of the substituents on the cyclohexene ring as *ortho*, *meta* or *para* products (Fig. 1). Experimentally, the reactions proceed in a regiospecific way [4]: the *ortho* isomer is formed preferentially from butadienes substituted in position 1, the *para* isomer from 2-substituted butadienes. This *o/p* orientation holds irrespective of the electron-donating or electron-accepting characteristics of the diene substituent. The stereochemistry of the reactions is characterized by *cis*-addition and the endo-rule is generally obeyed [4].

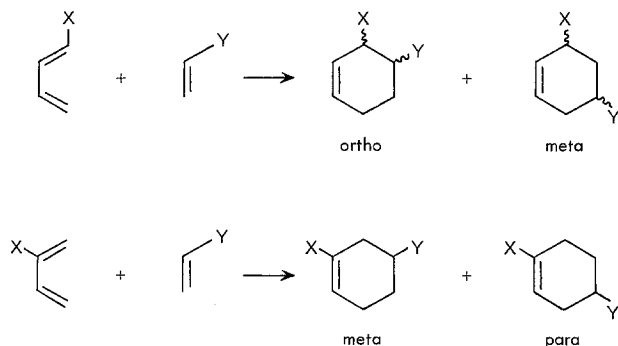


Fig. 1. Structural orientation in the Diels-Alder reaction

In order to rationalize the regioselectivity of these reactions, intermolecular perturbation theory has been applied. Feuer, Herndon and Hall [5] investigated the reaction of 1- or 2-methyl or phenyl substituted butadienes with acrylonitrile, using the PMO-method [6] in the framework of Hückel theory. The calculated interaction energies predict the formation of the *ortho* and the *para* product for the 1- and 2-substituted diene respectively, as found by experiment. The calculations, however, were limited to electron-donating diene substituents. Eisenstein *et al.* [7] were able to reproduce the observed regioselectivity in Diels-Alder reactions by using a simple rule which involves pairwise interactions of the terminal carbon atoms only. This rule has been reformulated by Houk [8] in terms of the LCAO-coefficients of the cyclo-addends and further elaborated by Epiotis [9]. For the case when the interactions of the terminal atoms in two regioisomers are equal, the rule may be extended by including secondary orbital interactions, as shown by Alston and co-workers [10, 11]. The regioselectivity in the Diels-Alder reaction catalysed by Lewis acids has been analysed by the same model [12-14]. Inukai *et al.* [15] emphasized the observation that the same structural selectivity is found independent of the polarity of the diene substituents. On the basis of Salem's theory [16] they predicted correctly the *para* orientation by all substituents in the case of the reaction of 2-substituted butadienes with methyl acrylate. However, the activation energies for the endo-mechanism exceed those of the exo-mechanism; the result is not improved by the more elaborate theory of Devaquet and Salem [17].

Bertrán *et al.* [18] discussed the regioselectivity in terms of the Hückel energies of a composite molecule formed by the reactants. Different delocalized transition state models had to be used to reproduce the directional behaviour of electron-accepting or donating groups on the diene.

None of the theoretical models mentioned covered all of the orientational and conformational aspects of the Diels-Alder reaction of the type shown in Fig. 1. Hence, a more detailed analysis of this phenomenon is attempted. By calculating specifically the interaction of 1- or 2-monosubstituted butadienes with an electron-donating ($X = \text{CH}_3$) or electron-accepting ($X = \text{CN}$) group and acrylonitrile ($Y = \text{CN}$), the interaction energy is analysed in three different ways:

- a) The total perturbational energy is separated into different characteristic contributions: the Madelung, the steric, the charge-transfer (CT) and the polarization term.

- b) The interaction energy is partitioned into contributions on the atoms and between the atoms. The changes of the intra- and intermolecular diatomic energies are correlated to the process of bond formation and bond weakening.
- c) By a LCMO analysis of the perturbed first-order wave function the second order SCF perturbation energy is resolved additively into pairwise interactions of molecular orbitals. In this way the energy contribution of the frontier orbitals is inferred.

2. Total Perturbation Energies

The perturbation method adopted is the SCF perturbation theory in the density matrix formulation as developed by Diercksen and McWeeny [19]. Sustmann and co-workers previously used the same formalism to evaluate first- and second-order intermolecular perturbation energies [20, 21] and to treat problems in reactivity [22, 23].

Two reacting molecules R and S are assumed to form a weak complex in the course of the reaction. The changes in the energies and wave functions, arising on formation of this model state from the isolated species, are determined by perturbation theory: given the eigenvectors $\{c_i^0\}$ and the eigenvalues $\{\epsilon_i^0\}$ of the eigenvalue problems of R and S

$$F^0 C^0 = C^0 \epsilon^0 \quad (1)$$

with

$$C^{0+} C^0 = 1, \quad (2)$$

the commutator relation for the interacting molecules is to be solved

$$RF - FR = 0, \quad (3)$$

subject to the condition of idempotency

$$RR = R, \quad (4)$$

by expanding R and F in terms of a perturbation parameter λ , $R = R^0 + \lambda R^1 + \lambda^2 R^2 \dots$, $F = F^0 + \lambda F^1 + \lambda^2 F^2 \dots$. The density matrices R^0 and R are given by summing over all projection operators $R_i^0 = c_i^0 c_i^{0+}$ and $R_i = c_i c_i^+$ respectively for the occupied orbitals. By partitioning the space into two mutually orthogonal subspaces

$$R^0 + R_u^0 = 1 \quad (5)$$

where R_u^0 defines the subspace of the unperturbed unoccupied orbitals, the n th order matrix R^n may be resolved into four projected components

$$R^n = R^0 R^n R^0 + R_u^0 R^n R_u^0 + R_u^0 R^n R^0 + R^0 R^n R_u^0 \quad (6)$$

The explicit expressions for the four components are [24]:

$$R^0 R^n R^0 = - \sum_{i=1}^{n-1} R^0 R^i R^{n-i} R^0; \quad n > 1 \quad (7a)$$

$$R_u^0 R^n R_u^0 = \sum_{i=1}^{n-1} R_u^0 R^i R^{n-i} R_u^0; \quad n > 1 \quad (7b)$$

$$\begin{aligned}
 R^0 R^n R_u^0 = & \sum_i^{\text{occ}} \sum_j^{\text{unocc}} c_i^0 c_i^{0+} F^n c_j^0 c_j^{0+} / (\epsilon_i^0 - \epsilon_j^0) \\
 & + \sum_i^{\text{occ}} \sum_j^{\text{unocc}} c_i^0 c_i^{0+} \sum_{k=1}^{n-1} (R^k F^{n-k} - F^k R^{n-k}) c_j^0 c_j^{0+} / (\epsilon_i^0 - \epsilon_j^0)
 \end{aligned} \quad (7c)$$

$$R_u^0 R^n R^0 = (R^0 R^n R_u^0)^+ \quad (7d)$$

The second sum in (7c) occurs only for $n > 1$. The matrices R^n are related to the bond order matrices P^n by $R^n = \frac{1}{2} P^n$. The expressions (6) and (7) are the working formulae to solve (3) under the constraint (4). Starting with $n = 1$ the solution is built up gradually by obtaining all matrices R^n and F^n , up to an order n sufficiently high such that all higher order corrections can be assumed to be negligible. The characteristic feature of (7c) is that the unknown matrix R^n also occurs in the F^n matrix. Thus, for every order n an iterative process is required.

The elements of the F^n -matrix are derived by developing the CNDO/2 F -matrix elements into a power series of λ and by collecting factors proportional to λ^n . An order λ^1 is assigned arbitrarily to the intermolecular integrals γ_{AB} and $\beta_{\mu\nu}$ ($A, \mu \in R$; $B, \nu \in S$)¹, so that the correct limiting behaviour of the commutator relation (3) is achieved for an infinite intermolecular distance.

The general expression for the electronic interaction energy of order n is given by [19]:

$$E^n = \frac{1}{2} \text{tr} \left[\sum_{i=0}^n P^i (H^{n-i} + F^{n-i}) \right] \quad (8)$$

Specifically, by adding the core-core repulsion, the first-order energy may be written in the form [21]

$$\begin{aligned}
 E^1 = & \sum_A^R \sum_B^S [(P_{AA}^0 - Z_A)(P_{BB}^0 - Z_B)\gamma_{AB}] + \sum_A^R \sum_B^S Z_A Z_B \left(\frac{1}{R_{AB}} - \gamma_{AB} \right) \\
 = & E_{\text{Mad}}^1 + E_{\text{Ster}}^1
 \end{aligned} \quad (9)$$

The first sum will be referred to as Madelung term [25–28]. The second sum has been denoted steric interaction [23]; this term can be derived from the electrostatic interaction of positive point charges and spatially extended electron charge distributions, assuming the CNDO/2 approximation for the penetration integrals. The second-order energy consists of the CT and the polarization term [22]

$$\begin{aligned}
 E^2 = & \sum_{\mu}^R \sum_{\nu}^S P_{\mu\nu}^1 \beta_{\mu\nu} + \frac{1}{2} \sum_A^R \sum_B^S [P_{AA}^1 (P_{BB}^0 - Z_B) + P_{BB}^1 (P_{AA}^0 - Z_A)] \gamma_{AB} \\
 = & E_{\text{CT}}^2 + E_{\text{Pol}}^2
 \end{aligned} \quad (10)$$

This expression in the AO basis can be related to E^2 in the MO basis by making use of (6) and (7). One then obtains a complementary expression showing explicitly the

¹ The indices A and B refer to atoms, μ and ν to atomic orbitals.

contribution of definite pairs of MO's

$$\begin{aligned}
 E^2 = & 2 \sum_i^{\text{Rocc}} \sum_j^{\text{Sunocc}} \{F_{ij}^1\}^2 / \Delta_{ij} + 2 \sum_i^{\text{Socc}} \sum_j^{\text{Runocc}} \{F_{ij}^1\}^2 / \Delta_{ij} \\
 & + 2 \sum_i^{\text{Rocc}} \sum_j^{\text{Runocc}} \{F_{ij}^1\}^2 / \Delta_{ij} + 2 \sum_i^{\text{Socc}} \sum_j^{\text{Sunocc}} \{F_{ij}^1\}^2 / \Delta_{ij} \\
 & + 2 \sum_{i,i'}^{\text{Rocc}} \sum_{j,j'}^{\text{Runocc}} \{F_{ij}^1 / \Delta_{ij}\}^2 [J_{ii',jj'} + J_{ji',ij'}] \\
 & + 2 \sum_{i,i'}^{\text{Socc}} \sum_{j,j'}^{\text{Sunocc}} \{F_{ij}^1 / \Delta_{ij}\}^2 [J_{ii',jj'} + J_{ji',ij'}]
 \end{aligned} \quad (11)$$

whereby

$$F_{ij}^1 = c_i^{0+} F^1 c_j^0$$

$$\Delta_{ij} = \epsilon_i^0 - \epsilon_j^0$$

$$J_{kl,mn} = \sum_{\mu} \sum_{\nu} c_{k\mu}^* c_{l\mu} c_{m\nu}^* c_{n\nu} \gamma_{AB}; \quad \mu \in A, \nu \in B$$

This formula has been previously obtained by an approximate solution of the Hartree–Fock–Roothaan equations of two interacting molecules [28].

The third-order energy may be deduced in the form

$$\begin{aligned}
 E^3 = & \frac{1}{2} \text{tr} [-P^1 R^0 F^1 R^0 P^1 + P^1 R_u^0 F^1 R_u^0 P^1] \\
 & + \sum_A^R \sum_B^S P_{AA}^1 P_{BB}^1 \gamma_{AB} - \frac{1}{2} \sum_{\mu}^R \sum_{\nu}^S P_{\mu\nu}^1 P_{\mu\nu}^1 \gamma_{AB}
 \end{aligned} \quad (12)$$

The interaction energy up to third order is determined entirely by the density matrix up to first order. This result of intermolecular SCF perturbation theory is a special formulation of a general theorem in perturbation theory [29].

As representative examples Fig. 2 shows the geometries used to simulate the endo approach together with the numbering of atoms referred to below. The configurations are characterized by the symbols *O*, *M*, *P* and labelled according to the position of the substituent on the diene. Two rotamers were considered for 2-methylbutadiene: a) one H-atom of the methyl group pointing vertically upwards ($\varphi = 0^\circ$) to the molecular plane of *S*, b) two H-atoms lying above the plane of *R* ($\varphi = 60^\circ$). In the configurations corresponding to an exo-mechanism the nitrile group in the dienophile *S* is rotated around the $C_1'-C_2'$ bond by 180° . The reactants² are arranged in parallel planes such that atoms 1 and 4 of the butadienes and the atoms 1' and 2' of the acrylonitrile lie in a plane vertical to the

² The geometries of the isolated molecules were chosen as follows [30]. The bond lengths of *trans*-butadiene were transferred to the *cis*-isomer, but assuming arbitrarily bond angles of 120° . The distance between the C-atom of the methyl group and the butadiene skeleton is 1.49 Å, as found in propylene. For acrylonitrile the experimentally observed geometry was reconstructed from the data given in [31]; the same distances were used for the cyano group in the cyanobutadienes.

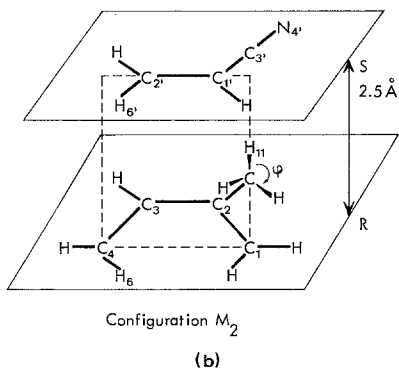
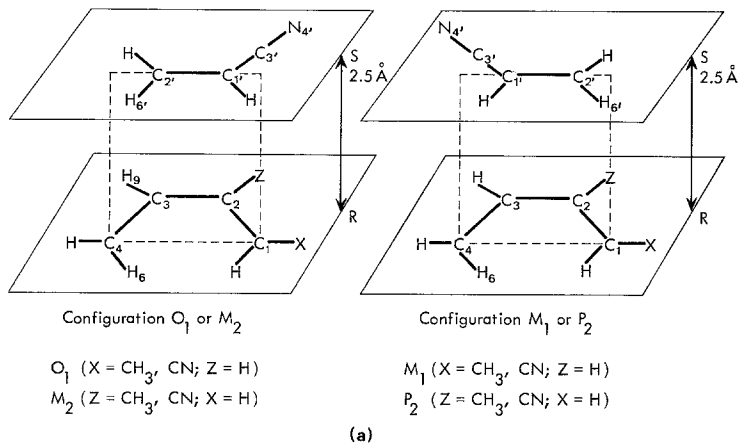


Fig. 2. (a) Assumed endo-configurations. (b) Definition of angle φ in configuration M_2 ($Z = CH_3$; $X = H$)

molecular planes. The distance between the molecular planes was fixed arbitrarily at 2.5 Å. From a CNDO calculation [32] and an *ab initio* calculation [33] it may be inferred that changes in the molecular structures of butadiene interacting with ethylene are appreciable only at smaller distances. However, according to another *ab initio* calculation, the rearrangement of the butadiene skeleton occurs at a very early stage of the reaction [34].

The interaction energies ΔE up to the third order are summarized in Table 1. The calculated negative ΔE values indicate no barriers of activation. Similarly, Sustmann *et al.* [23] found in the treatment of Ketene-cycloaddition, by means of SCF perturbation theory, that the CNDO/2-approximation underestimates the repulsion between molecules. The fourth and higher order perturbation corrections contribute a small and nearly constant fraction (see column 5) to the total interaction energy. Only 2-methylbutadiene in configuration M_2 ($\varphi = 0^\circ$) forms an exception; this special case is excluded from the immediate discussion and will be considered later.

The calculations show that the endo approach of the addends is energetically favoured compared to an exo-mechanism, in accordance with the endo-rule.

Table 1. Interaction energies $\Delta E = E^1 + E^2 + E^3$ (kcal/mole) between 1- or 2-substituted butadienes and acrylonitrile

Subst. X	Configuration	ΔE (endo)	ΔE (exo)	^a	Exp. Isomer Ratio [35]
1-CH ₃	<i>O</i> ₁	-15.36	-13.95	87.0	} <i>o</i> : <i>m</i> = 7.3 : 1
	<i>M</i> ₁	-15.02	-13.82	87.0	
1-CN	<i>O</i> ₁	-14.81	-13.38	87.0	} <i>ortho</i> only ^b
	<i>M</i> ₁	-14.55	-13.40	86.8	
2-CH ₃	<i>M</i> ₂ ($\varphi = 0^\circ$)	-11.75	-14.01	77.3	} <i>p</i> : <i>m</i> = 2.2 : 1
	<i>M</i> ₂ ($\varphi = 60^\circ$)	-15.21	-14.03	86.8	
	<i>P</i> ₂ ($\varphi = 0^\circ$)	-15.33	-14.11	87.2	
	<i>P</i> ₂ ($\varphi = 60^\circ$)	-15.34	-14.13	87.2	
2-CN	<i>M</i> ₂	-16.80	-14.02	87.4	} <i>para</i> only
	<i>P</i> ₂	-15.03	-13.97	86.8	

^a Percentage ΔE (endo) of the total CNDO/2 interaction energy.

^b Only data referring to the reaction with alkylacrylates are recorded in [35].

3. Analysis of the Perturbation Energies

In the case of butadienes substituted in position 1, orientation *O*₁ leads to the *ortho*-substituted cyclohexene, *M*₁ to the *meta* product. The calculations indicate that *O*₁ is the preferred approach, in agreement with the experimentally observed isomer ratio for 1-methylbutadiene. The calculated result for 1-cyanobutadiene cannot be compared with experiment directly, since only data referring to the reaction with alkylacrylates are known [35].

The interaction energies are dominated by the CT term (see Table 2) indicating that the reactions are orbitally controlled in the sense of Klopman [36]. The steric repulsion

Table 2. Contributions to the interaction energy ΔE (endo) (kcal/mole)

Subst. X	Configuration	E_{Mad}^1	E_{Ster}^1	E_{CT}^2	E_{Pol}^2	E^3
1-CH ₃	<i>O</i> ₁	-0.04	10.87	-21.33	-0.04	-4.81
	<i>M</i> ₁	0.00	10.46	-20.77	-0.03	-4.69
1-CN	<i>O</i> ₁	0.27	10.50	-20.90	-0.03	-4.64
	<i>M</i> ₁	0.07	10.41	-20.43	-0.03	-4.58
2-CH ₃	<i>M</i> ₂ ($\varphi = 0^\circ$)	-0.23	26.11	-30.22	-0.11	-7.31
	<i>M</i> ₂ ($\varphi = 60^\circ$)	-0.12	14.70	-24.22	-0.06	-5.50
	<i>P</i> ₂ ($\varphi = 0^\circ$)	-0.07	10.57	-21.04	-0.03	-4.77
	<i>P</i> ₂ ($\varphi = 60^\circ$)	-0.08	10.46	-20.95	-0.03	-4.75
2-CN	<i>M</i> ₂	0.61	11.70	-23.83	-0.06	-5.22
	<i>P</i> ₂	0.15	10.41	-20.86	-0.03	-4.70
H		0.04	10.35	-20.87	-0.03	-4.73

in configuration O_1 is greater than in M_1 , consistent with the relation of the distances between the substituents in the two complexes. The ultimate stabilization of O_1 compared to M_1 is due to the stronger bonding CT-interaction which more than compensates for the sterically unfavourable positions of the substituents. Thus, the regioselectivity is determined by a subtle balance of the steric and CT interaction.

In the case of 2-substituted butadienes the interaction energies deserve a more detailed discussion. In configuration M_2 of 2-methylbutadiene the interaction energy depends strongly on the relative orientation of the H-atoms on the methyl group to the acrylonitrile molecule, increasing with the torsional angle φ defined in Fig. 2b. The biplanar transition state guaranteeing maximum π overlap is not the energetically favoured approach. The analysis of the various energy contributions (Table 2) reveals that the destabilization is caused by the steric repulsion due to the small distance of atom H_{11} from the plane of the acrylonitrile molecule. Despite the larger CT-term for the *meta* product, the steric effect is decisive in directing the reaction to the *para* product. Indeed, with increasing steric requirements of alkyl groups in 2-substituted butadienes the relative proportion of the *para* isomer increases [35]. However, some kinetic data are not consistent with the interpretation that the steric factor determines the isomer composition. The second-order rate constants of the reaction of maleic anhydride with 2-alkyl butadienes increase continuously with the size of the alkyl substituent [37]. Furthermore, according to Inukai and Kojima [38], the *s-cis-s-trans* equilibrium constant in the case of 2-substituted butadienes seems to be dominant in determining the relative rates of the uncatalysed reaction.

2-Cyano butadiene should react with acrylonitrile to yield the *meta* product, since orientation M_2 is stabilized in comparison to P_2 by a large increase in CT energy exceeding the first-order repulsive interaction. Experimentally, however, only the *para* isomer has been isolated from the reaction products [35]. The failure of the model calculation will be discussed later.

4. Role of the Interacting Centres

The approximations inherent in the CNDO/2 method lead to an "energy breakdown" into monatomic and diatomic contributions [39]

$$E = \sum_A E_A + \sum_{A < B} E_{AB} \quad (13)$$

The relevance of these E_{AB} values has been examined; they were found to be transferable and to be correlated with the strength of the chemical bond [40]. Thus, it may be conjectured that the changes E_{AB}^n calculated by perturbation theory measure the strengthening or weakening of the bonds in the weak complex.

The perturbational quantities E_A^n and E_{AB}^n can be derived by using the expression for E_A and E_{AB} given in [39], developing the density matrix into powers of λ and by comparing the coefficients of equal powers of λ^n . The diatomic energies are further partitioned into an electrostatic and a bonding contribution. The expressions are ordered according to the location of A and B in the molecules R and S .

The intramolecular contributions are:

$$E_A^n = \sum_{i=0}^n \sum_{\mu, \nu}^A \frac{1}{2} P_{\mu\mu}^i P_{\nu\nu}^{n-i} \gamma_{AA} + \sum_{\mu}^A P_{\mu\mu}^n \left[-\frac{1}{2} (I_{\mu} + A_{\mu}) - (Z_A - \frac{1}{2}) \gamma_{AA} \right] - \frac{1}{4} \sum_{i=0}^n \sum_{\mu, \nu} P_{\mu\nu}^i P_{\mu\nu}^{n-i} \gamma_{AA} \quad (14a)$$

$$E_{AB_{e1}}^n = \sum_{i=0}^n P_{AA}^i P_{BB}^{n-i} \gamma_{AB} - Z_A P_{BB}^n \gamma_{AB} - Z_B P_{AA}^n \gamma_{AB} \quad (14b)$$

$$E_{AB_{bond}}^n = \sum_{i=0}^n -\frac{1}{2} \sum_{\mu}^A \sum_{\nu}^B P_{\mu\nu}^i P_{\mu\nu}^{n-i} \gamma_{AB} + \sum_{\mu}^A \sum_{\nu}^B 2 P_{\mu\nu}^n \beta_{\mu\nu} \quad (14c)$$

An approximate relation is expected to hold for the changes in monoatomic contributions, when they are summed over all atoms and over all orders in perturbation theory. The interaction energy of two molecules is approximately proportional to the gradient of the total energy with respect to the nuclear coordinates of the atoms in the direction of approach. Now the gradient of the energy is equal to the force on the nuclei [41]. Since it has been shown that the forces due to the E_A terms in the CNDO/2 method vanish [42], the added contributions $\sum_{n=1}^{\infty} \sum_A E_A^n$ should nearly cancel.

The intermolecular contributions are:

$$E_{AB_{e1}}^1 = (P_{AA}^0 - Z_A) (P_{BB}^0 - Z_B) \gamma_{AB} + Z_A Z_B \left(\frac{1}{R_{AB}} - \gamma_{AB} \right) \quad (15a)$$

$$E_{AB_{e1}}^n = \sum_{i=1}^{n-2} P_{AA}^i P_{BB}^{n-1-i} \gamma_{AB} + P_{AA}^{n-1} (P_{BB}^0 - Z_B) \gamma_{AB} + P_{BB}^{n-1} (P_{AA}^0 - Z_A) \gamma_{AB}; \quad n = 2, 3, 4, \dots \quad (15b)$$

$$E_{AB_{bond}}^n = \sum_{\mu}^A \sum_{\nu}^B \left[\sum_{i=0}^{n-1} \frac{1}{2} P_{\mu\nu}^i P_{\mu\nu}^{n-1-i} \gamma_{AB} + 2 P_{\mu\nu}^{n-1} \beta_{\mu\nu} \right]; \quad n = 2, 3, \dots \quad (15c)$$

The sum in (15b) occurs only for values $n \geq 3$. From (15a) and (9) it is deduced that the first-order electrostatic energy summed over all pairs of atoms on R and S is identical to the total perturbation energy of first order. Consequently, the sum of the first-order intramolecular terms of R and S is zero. A further relation between intra- and intermolecular contributions can be derived for the second-order terms. By comparison of Eq. (10) with (15b) and (15c) for $n = 2$, it is deduced that twice the total interaction energy is contained in the sum over all terms (15b) and (15c). It follows that half the sum of the intermolecular contributions compensates the sum of the intramolecular contributions.

E_{AB}^n values of some selected intermolecular pairs of atoms are listed in Table 3. They refer to the complex of 1-methylbutadiene with acrylonitrile in configuration O_1 (see Fig. 2). According to these values a concerted, but slightly asymmetric bond closure should occur, the (4-2') bond being formed faster than (1-1'). *Ab initio* calculations indicate a minimal energy demand for the symmetrical approach of the unsubstituted

Table 3. Intermolecular diatomic energy contributions (kcal/mole) of 1-methylbutadiene and acrylonitrile in configuration O_1

Pairs (RS')	Distance [Å]	$E_{RS'}^1$	$E_{RS'}^2$	$E_{RS'}^3$	Sum
C ₁ C _{1'}	2.61	1.55	-12.69	-3.88	-15.01
C ₄ C _{2'}	2.61	1.64	-16.85	-5.31	-20.52
C ₂ C _{3'}	2.60	1.49	-11.01	-2.62	-12.14
C ₂ C _{1'}	2.76	0.78	- 2.62	-0.83	- 2.67
C ₃ C _{2'}	2.76	0.76	- 4.97	-1.36	- 5.57
C ₂ N ₄	3.01	0.30	1.10	0.13	1.54
C ₁ C _{3'}	2.77	0.84	- 3.47	-0.69	- 3.31
H ₆ C _{2'}	2.68	0.21	- 0.71	-0.13	- 0.64
Total		10.82	-42.74	-14.44	-46.36

reactants [33, 34]. In contrast, a MINDO/3 calculation [43] predicts a highly asymmetrical transition state. From an analysis of the substituent effects on rate constants [44], the secondary deuterium isotope effects [45], and high pressure kinetic data [46], a concerted mechanism with a nearly symmetrical transition state has been inferred for related Diels–Alder reactions. The (2-3') interaction contributes significantly in stabilizing the configuration O_1 . The summed values $E_{AB}^{1+2+3} \equiv E_{AB}^1 + E_{AB}^2 + E_{AB}^3$ for the three dominant pairs (4-2'), (1-1') and (2-3') nearly equal the total intermolecular interaction energy, indicating thus an almost complete cancellation of all other intermolecular contributions. The same holds to a lesser degree when the E_{AB}^2 values are considered alone. In the exo approach the interaction of the pair (1-3') assists the bond closing centres, but despite a very similar distance the interaction is smaller than that of the (2-3') pair in the endo orientation. Thus, the E_{AB}^2 as well as the E_{AB}^{1+2+3} values reflect the qualitative arguments of Woodward and Hoffmann [47] based on the symmetry of the HOMO and LUMO in butadiene.

The intramolecular E_{AB}^n values (Table 4) follow the changes of bond lengths in the isolated molecules when forming the final cyclohexene product. The (1-2), (3-4) and

Table 4. Intramolecular diatomic energy contributions (kcal/mole) of 1-methylbutadiene and acrylonitrile in configuration O_1

Pairs (AB)	Distance [Å]	E_{AB}^2	E_{AB}^3	Sum
C ₁ C ₂	1.34	7.18	3.26	10.44
C ₂ C ₃	1.48	-4.14	-1.66	-5.80
C ₃ C ₄	1.34	6.01	2.73	8.74
C ₄ H ₆	1.08	0.55	0.18	0.73
C ₃ H ₉	1.08	-0.08	-0.02	-0.10
Total R		13.76	6.26	20.02
C _{1'} C _{2'}	1.34	4.07	2.91	6.98
C _{1'} C _{3'}	1.43	3.33	0.27	3.60
C _{3'} N _{4'}	1.16	0.24	0.87	1.11
C _{2'} H _{6'}	1.09	0.78	0.28	1.06
Total S		7.61	3.37	10.98

(1'-2') double bonds are lengthened, the (2-3) bond is shortened, and the corresponding diatomic contributions are altered accordingly. These perturbational E_{AB}^n quantities parallel the variations of the E_{AB} 's calculated by Kikuchi [32] from the total energies along an energy-minimized reaction path of the unsubstituted reactants. The E_{CH}^n values may be ordered into two groups. In the first group, involving H-atoms bonded to the terminal C-atoms of the π systems where rehybridization from sp^2 to sp^3 hybrids occurs, the changes are small but appreciable. In the second group, referring to centres where no new bonds are formed, the changes are almost negligible.

The pattern in the inter- and intramolecular diatomic contributions of the example selected is equally recognizable in all other calculated configurations. The interactions (4-2'), (1-1') and (2-3') in orientations O_1 and M_2 , and (4-1'), (1-2') and (3-3') in M_1 and P_2 , are predominant in the intermolecular perturbation energies. Using the sum of these contributions as a measure of reactivity, the experimentally observed structural directivity of the methyl and cyano group [35] is reproduced, both the E_{AB}^2 and the E_{AB}^{1+2+3} values lead to the same conclusion (Table 5). By partitioning the E_{AB}^n 's further

Table 5. Sum of the energy contribution of the terminal C-atom pairs and of the secondary Woodward–Hoffmann interaction (kcal/mole)

Subst. X	Configuration	$\Sigma E_{RS'}^2$	$\Sigma E_{RS'}^{1+2+3}$
1-CH ₃	O_1	-40.55	-47.68
	M_1	-40.13	-46.78
1-CN	O_1	-39.73	-45.96
	M_1	-39.23	-45.59
2-CH ₃	M_2 ($\varphi = 0^\circ$)	-39.01	-45.02
	M_2 ($\varphi = 60^\circ$)	-39.37	-45.43
	P_2 ($\varphi = 0^\circ$)	-40.78	-47.68
	P_2 ($\varphi = 60^\circ$)	-40.68	-47.55
2-CN	M_2	-38.68	-44.47
	P_2	-40.50	-47.22

in electrostatic and bonding terms, the analysis of the numerical values reveals that the diatomic contributions are almost entirely determined by the bonding terms, in particular the E_{AB}^2 's by the CT term. Thus, ultimately the model of Eisenstein *et al.* [7] of considering only the CT interactions of the terminal C-atom pairs is recovered. However, at least in the case of 2-cyanobutadiene, it must be supplemented by the subsidiary secondary interaction proposed by Woodward and Hoffmann [47] in order to predict the experimentally preponderant isomer.

Whereas E_{AB}^2 and E_{AB}^{1+2+3} quantities always indicate the major product when restricted to definite pairs of centres, the total perturbation energies fail to predict the observed isomer in the reaction of 2-cyanobutadiene and acrylonitrile. The analysis of E_{AB}^n values in this case shows a strong second-order CT interaction between the cyano groups. These additional specific interactions may be an artifact of the semiempirical method used, even though the CNDO method correctly describes the strongly activating character

of the cyano group and its less-pronounced directional power [48]; this is shown by the smaller difference in interaction energy between O_1-M_1 or M_2-P_2 configurations (Table 1) compared with the difference in interaction of butadiene with acrylonitrile (-15.33 kcal/mole) and with ethylene (-12.24 kcal/mole). Alternatively, the case of 2-cyanobutadiene may indicate a failure of the one-step prereaction complex model. Support for this interpretation are the results obtained by Bertrán *et al.* [18] on 2-butadienes with electron-accepting groups. For this class of diene reactants an asymmetrically delocalized transition state, characterized by a bonding interaction between only one pair of terminal C-atoms, had to be assumed.

5. LCMO Analysis

The first-order LC coefficients which describe the mixing of the unperturbed orbitals due to the intermolecular perturbation can be derived from the correction P^1 to the density matrix P^0 by combining the resolution (6)

$$P^1 = (R_u^0 P^1 R^0)^+ + (R_u^0 P^1 R^0) \quad (16)$$

with the expression [49]

$$P^1 = 2R^1 = 2 [C_{\text{occ}}^0 C_{\text{occ}}^{1+} + C_{\text{occ}}^1 C_{\text{occ}}^{0+}] \quad (17)$$

The C_{occ}^1 matrix is the first-order correction to the occupied unperturbed eigenvectors C_{occ}^0 . Insertion of (17) into the last term on the right-hand side of (16) gives

$$R_u^0 P^1 R^0 = 2R_u^0 [C_{\text{occ}}^0 C_{\text{occ}}^{1+} + C_{\text{occ}}^1 C_{\text{occ}}^{0+}] R^0 \quad (18)$$

Now C_{occ}^1 is developed in the complete set of eigenvectors C^0 on the lines of a LCMO procedure [49]:

$$C_{\text{occ}}^1 = C^0 A_{\text{occ}}^1 \quad (19)$$

Inserting the expansion (19) in (18) and using the orthonormality condition (2), one obtains

$$R_u^0 P^1 R^0 = 2C_{\text{unocc}}^0 A_{\text{III}}^1 C_{\text{occ}}^{0+} \quad (20)$$

Referring to (16), only the submatrix A_{III}^1 of A_{occ}^1 which mixes occupied with unoccupied unperturbed orbitals is needed for the determination of P^1 . Conversely, given P^1 , A_{III}^1 can be obtained by means of

$$A_{\text{III}}^1 = \frac{1}{2} C_{\text{unocc}}^{0+} P^1 C_{\text{occ}}^0 \quad (21)$$

The elements $A_{\text{III}ij}^1$ determine the charge transferred between the molecules, if the unperturbed density matrix P^0 is changed by P^1 . The information regarding the reorganization of the charge between the molecules is accessible from R^2 . Using the resolution (6), together with (7), the change in charge on molecule R , $N_{R \rightarrow S}^2$ is given by

$$\text{tr} [R_I^2] = \frac{N_{R \rightarrow S}^2}{2} = \text{tr} [R_{\text{II}}^1 R_{\text{III}}^1 R_{\text{II}}^0] - \text{tr} [R_{\text{II}}^1 R_{\text{III}}^1 R_I^0] \quad (22)$$

The Roman subscripts denote submatrices of the density matrices blocked according to

$R = \begin{pmatrix} R_I & R_{II} \\ \dots & \dots \\ R_{III} & R_{IV} \end{pmatrix}$; I and IV refer to the molecule R and S respectively, II and III to the interaction elements. By means of (16), (20) and the orthonormality of the unperturbed eigenvectors (2), the final expression is obtained

$$N_{R \rightarrow S}^2 = -2 \sum_i^{R_{\text{occ}}} \sum_j^{S_{\text{unocc}}} \{A_{IIIij}^1\}^2 + 2 \sum_i^{S_{\text{occ}}} \sum_j^{R_{\text{unocc}}} \{A_{IIIij}^1\}^2 \quad (23)$$

Some LCMO coefficients showing the resolution of the first-order perturbed MO's in terms of the unperturbed MO's are listed in Table 6. The quantities $a_{\text{HO-LU}}$ and $a_{\text{LU-HO}}$ are particular elements of the A_{III}^1 matrix; the first MO label refers to the butadiene, the second to the acrylonitrile. The coefficient $a_{\text{HO-LU}}$ exceeds $a_{\text{LU-HO}}$ in

Table 6. LCMO coefficients and HOMO-LUMO energy contribution (kcal/mole)

Subst. X	Configuration	$a_{\text{HO-LU}}$	$a_{\text{LU-HO}}$	$N_{R \rightarrow S}^2$	$E_{\text{HO-LU}}^2$
1-CH ₃	O_1	0.1059	0.0404	-0.0232	-8.03
	M_1	0.1040	0.0374	-0.0233	-7.75
1-CN	O_1	0.0971	0.0399	-0.0202	-6.92
	M_1	0.0960	0.0332	-0.0209	-6.76
2-CH ₃	M_2 ($\varphi = 0^\circ$)	0.1241	0.0246	-0.0268	-11.34
	M_2 ($\varphi = 60^\circ$)	0.1164	0.0362	-0.0260	-9.97
	P_2 ($\varphi = 0^\circ$)	0.1060	0.0388	-0.0235	-8.27
	P_2 ($\varphi = 60^\circ$)	0.1065	0.0386	-0.0235	-8.35
2-CN	M_2	0.1098	0.0480	-0.0195	-9.08
	P_2	0.1000	0.0405	-0.0206	-7.53

accordance with the dienic and dienophilic nature of the butadiene and the acrylonitrile. The other coefficients in A_{III}^1 are appreciably smaller. $N_{R \rightarrow S}^2$, the net charge transferred between the molecules is almost entirely determined by $a_{\text{HO-LU}}$. Thus, all other contributions of $R \rightarrow S$ and the back-donated charge $S \rightarrow R$ nearly cancel. However, in the second-order energy only a relatively small fraction, about 40%, is determined by $a_{\text{HO-LU}}$. This energy contribution, $E_{\text{HO-LU}}^2$, correlates only with the experimentally observed isomer ratios (see Table 1) for 1- but not for 2-substituted butadienes. This failure persists, even if $E_{\text{LU-HO}}^2$ is added to $E_{\text{HO-LU}}^2$.

By considering the frontier orbitals [50], but restricting the interactions to a few definite pairs of atoms, the regioselectivity in the Diels-Alder reaction has been discussed [7-14]. Given two atoms on R and S , the product of the LCAO coefficients of the corresponding p -orbitals in π -HOMO of the diene and in π^* -LUMO of the dienophile is assumed to be a measure of the interaction. In the case of 2-substituted butadienes the experimentally preponderant isomer is predicted from the interaction of the terminal C-atoms alone. Secondary Woodward-Hoffmann interaction has to be added in the case of 1-substituted butadienes in order to favour the *ortho* isomer [14]. Thus, the frontier orbital model successfully correlates the regioselectivity with the magnitude of the LCAO coefficients in HOMO and LUMO, whereas the energy contribution of the frontier

orbitals including the interaction between all centres fails to predict the observed regioisomers. The second-order intermolecular diatomic CT contribution, as given by the second term in (15c), includes all the MO contributions. These E_{AB}^2 quantities, summed for the same pairs of atoms as in the frontier orbital model, account for almost all the intermolecular perturbation energy and reproduce the observed regioselectivity.

6. Conclusion

If the bonding interactions in the weak complex as calculated by the CNDO/2 method are assumed to be of relevance for the kinetic behaviour, the following conclusions emerge from the threefold analysis of the perturbation energies. The regioselectivity in the Diels–Alder reaction is due to a complex interplay of CT interactions and steric effects of the substituents on the diene and on the dienophile. This agrees with the conclusion derived empirically by Titov [35] from a compilation of experimental data. The intermolecular perturbation energies are dominated by the contributions of three pairs of atoms, namely the two terminal pairs of C-atoms, which form new bonds, and by the secondary Woodward–Hoffmann interaction, for all the other intermolecular diatomic contributions roughly cancel each other. These three localized interactions determine the endo-addition and the regioselectivity of the substituents, irrespective of their electron donating or accepting characteristics.

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