Transition State of the Diels–Alder Reaction

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Abstract: A semiempirical SCF–MO calculation reveals a concerted symmetrical transition state for the Diels–Alder reaction ethylene + butadiene. An explanation is presented why MINDO-3 and related procedures yield a nonconcerted transition state for this process.

Do the typical thermal Diels-Alder (DA) reactions proceed through a concerted mechanism with a symmetrical or nearly symmetrical transition state (TS) or is this mechanism a biradical one with an open nonsymmetrical TS? Supported by numerous implicit experiments,[1-5] the idea of a concerted DA reaction underlies conventional concepts in chemical theory.[6,7] It agrees with a qualitative theoretical consideration based on the stabilization energy arguments.[8] On the other hand, various quantitative treatments lead to conflicting conclusions. We present a brief survey of these calculations on the simplest DA condensation:

$$\text{ethylene} + \text{butadiene} \rightarrow \text{cyclohexene} \qquad (1)$$

The experimental activation energy of this process amounts to about 1 eV.[9]

Salem studied reaction 1 and the dimerization of butadiene by means of a perturbational version of the extended Hückel method.[10] He considered only π electrons and investigated two geometrical variables: the lengths of the forming bonds. The results of this calculation favored a concerted mechanism. Kikuchi[11] performed a CNDO-2 calculation of symmetrical reaction path for reaction 1. Eleven degrees of freedom were optimized but no activation barrier was revealed at all. Basilevsky, Tikhomirov, and Chlenov investigated reaction 1 by a version of the SCF method which they called an "almost π-electron approximation".[12] A symmetrical reaction path was postulated and 11 degrees of freedom were varied. The saddle point so found, with the energy about 1 eV higher than that of the reactants, embodied a concerted TS having a delocalized six-electron system. This calculation was then repeated with several modifications of the underlying semiempirical assumptions and the corresponding reparametrization.[13] This led to a 30% increase of the saddle point energy but did not influence the geometry of the TS and the conclusion concerning its delocalized character.

Dewar, Griffin, and Kirschner reject a concerted mechanism of the DA reaction basing their conclusion on MINDO-3 calculations.[14] The calculated energies of nonsymmetrical TS's agree well with experimental activation energies. All internal geometrical degrees of freedom (42 for reaction 1) were optimized in this research. MINDO-2 also predicts a nonsymmetrical TS for reaction 1.[15] Burke, Leroy, and Sana[16] employing STO-3G with limited CI obtained a nearly symmetrical TS for reaction 1. At least 11 degrees of freedom were varied. A more accurate ab initio recalculation for this TS configuration yielded a satisfactory estimate of the activation energy. Finally, Townshend et al.[17] presented a rather similar but probably more extensive calculation, with 25 degrees of freedom being varied, and obtained quite similar results.

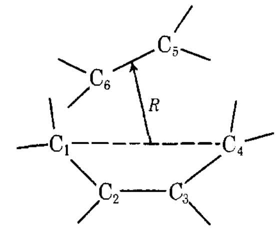
None of the above mentioned calculational procedures can be regarded as completely reliable and irreproachable when the TS's of complex reactions are concerned. So a careful analysis of their adequacy is desirable. Such an analysis is the subject of this article. Additionally, we report several new calculations.

First, we have verified that the previously revealed symmetrical TS[12] was indeed stable with respect to antisymmetrical deformations. Upon a further comparison of the symmetrical and nonsymmetrical reaction paths, the latter resulting in a biradical TS, we have found that a symmetrical DA condensation was energetically preferable. Second, we have studied the DA reaction of acetylene and cyclobutadiene by the CNDO method with the parametrization suggested by Boyd and Whitehead[18] (CNDO-BW). This calculation predicted a nonsymmetrical TS.

Since the CNDO-BW procedure can be considered as a special version of MINDO, we conclude that it is a tendency of the MINDO type procedures to favor a nonsymmetrical reaction path. We are able to give a theoretical interpretation of this fact. The MINDO type procedures prove to systematically underestimate repulsion effects in the "intermolecular" interaction region which corresponds to the separation of 2.0–2.5 Å between carbon atoms. This is just the distance range at which the symmetrical TS's found in the above discussed calculations were located, and the errors in MINDO are just of such a character that they make unstable the configurations corresponding to symmetrical TS's.

Calculations and Results

(a) The "Almost π-Electron Approximation". Ethylene + Butadiene. In the "almost π-electron approximation" the interaction energy U is evaluated as a sum of an "almost π-electron" component (Δ_π), the contribution from the energy changes of nonreacting σ bonds (Δ_σ) and the exchange repulsion (α). Thus,



$$U = \Delta_\pi + \Delta_\sigma + \alpha \qquad (2)$$

The Δ_π value is obtained from a PPP calculation, the Δ_σ is taken from empirical estimates of bond energies and some explanations concerning α are given below. The whole procedure has been derived and completely described in the preceding papers.[12,13,19] The model sufficient to deal with a symmetrical reaction path also has been described.[12] Our first purpose was to use this model to check the stability of the symmetrical TS. Hence many new geometrical variables were considered explicitly. The original model, referred to as the "almost π-electron approximation", introduced the following geometrical constraints:

(1) The planar configuration of butadiene carbon atoms C_1, C_2, C_3, C_4 was retained.

(2) The trigonal hybridization for C_2 and C_3 was assumed.

(3) The four reaction center carbon atoms, namely C_1, C_4, C_5, C_6, changed their hybridization in such a manner that local trigonal symmetry axes were always present. That is, for each of these atoms the three valence angles, while changing, remained equal to one another, and also the two adjacent C–H bonds remained equivalent. The hybridization changes may be varied independently for each of the four atoms, allowing the consideration of nonsymmetrical configurations.

The enumerated conditions result in 21 geometrical constraints. The TS was found as an energy maximum along the coordinate R, the length of the vector joining the middles of C_1–C_4 and C_6–C_5 intervals as shown in the structure. The other 20 degrees of freedom have been optimized to an energy minimum. Those representing the relative positions of the reactant molecules were introduced into the calculation explicitly. The angular variables characterizing the hybridization changes of the reaction center subject to limitations (3) were treated by a variation of the directions of the local symmetry axes.[12] The equilibrium intramolecular C–C bond lengths were found by means of the bond order–bond length relation and, finally, the equilibrium energies of C–H bonds were obtained from the known hybridization changes.[12] The latter procedure actually meant an implicit optimization of C–H bond lengths.

The main result of this calculation was that the configuration corresponding to the symmetrical TS proved to be stable under various antisymmetrical distortions. It, of course, coincided with the TS that had been found and characterized in detail previously.[12] We have thus verified that this symmetrical configuration represents true saddle point. The geometry of a nearly symmetrical TS found by Burke et al.[16b] is quite similar. For instance, the distance between C_1 and C_6 atoms (or between C_4 and C_5) equals 2.26 Å[16b] and 2.28 Å.[12]

We have also investigated a nonsymmetrical reaction path for reaction 1 with only one C–C bond forming. The cis addition was found to be energetically most preferable among various nonsymmetrical conformations in agreement with the MINDO-3 result.[14] However, contrary to that MINDO calculation, such a nonconcerted process was energetically unfavorable compared to the symmetrical concerted reaction path. The unsymmetrical interaction curve remained repulsive up to $R = 2.0$ Å, the R representing the separation of the reaction center carbon atoms. At this point the calculated energy was 10 kcal/mol over that of the symmetrical TS. We were unable to proceed further along this reaction path and investigate configurations with $R < 2$ Å, because our method, being an asymptotic one, became invalid for small intermolecular separations. This point will be discussed at greater length below.

The above formulated general qualitative conclusions remained unchanged after the calculation was modified according to ref 13 and the electron correlation was taken into account by the perturbation theory.[12]

(b) CNDO-BW Calculation. Acetylene + Cyclobutadiene. All internal degrees of freedom have been optimized in this calculation. In the coordinates R_1 and R_2, corresponding to the lengths of the two forming C–C bonds, the symmetrical reaction path proved to be a ridge of the potential surface. So the symmetrical stationary point did not represent a saddle point but was a maximum. Its energy relative to that of reactants was 16 kcal/mol.

A nonsymmetrical valley represented the cis addition and it passed through a saddle point at $R_1 = 2.16$ Å, $R_2 = 2.84$ Å, the height of the barrier being 9 kcal/mol. Another valley corresponding to the trans addition was also found; however, we did not investigate it in detail.

Discussion

Why do the MINDO type procedures and the method based on (2) give quite different results? To answer this question one has to compare the internal structure of the two methods.

Concerning MINDO, we shall neglect such details as the account of one-center exchange integrals. These are of no importance as soon as the interaction energy is considered, so the letter "I" of MINDO will be disregarded in the subsequent discussion.

First suppose the interaction of the reactants to be relatively small, that is to say, intramolecular overlap integrals are supposed to be larger than intermolecular ones. Then a perturbational treatment is valid, and the interaction energy, as a result of the NDO assumption, involves only three contributions: the resonance, the polarization, and the Coulomb energies.[8] For nonpolar hydrocarbon systems all the net atomic charges approximately vanish, and that leads to vanishing of the polarization energy. The Coulomb contribution still remains, because of the difference between the nuclear repulsion energy and the repulsion of electrons localized at their AO's (γ_{IJ}). The differences between γ_{IJ} and the respective core attraction integrals, that is the penetration integrals, are neglected according to MINDO.

As a consequence of the fact that the Coulomb energy arises only due to the nuclear repulsion, it can be added at the final stage of a MINDO calculation. So, as a first stage, it suffices to consider only the resonance energy.

We shall deal with such deformations of the reactant molecules as the changes of their bond lengths and the distortions of their planar geometry. The latter distortions are appropriate to treat in terms of the changes of the trigonal hybridization of carbon atoms. Then the "optimal hybrid π orbitals" can be introduced[8,12] and, in principle, a MINDO calculation could be performed using this special AO basis. The resonance energy obtained in such a hypothetical calculation would be mainly due to the interactions of those "π orbitals", the σ–σ and σ–π resonance being relatively small at intermolecular distances. This energy can be easily identified with the Δ_π term of (2). To make the coincidence complete we note that instead of a perturbational treatment one could make a variational calculation, which for such an "almost π system" would reduce to a usual PPP treatment.[8]

Another contribution to the MINDO resonance energy would come from the hybridization changes of the σ bonds and also from the changes of their lengths. When these are small, the arising energy changes can be treated by perturbation theory. They then appear as an additive correction Δ_σ to the variational Δ_π energy. Having in mind the approximate invariance properties of MINDO under unitary one-center transformations of the AO basis,[23] this reasoning shows that in the case of consistent parametrization, which is supposed, the sum $\Delta_\pi + \Delta_\sigma$ of (2) will almost coincide with the MINDO estimation of the resonance energy.

Now let us consider the additional repulsive term α in (2). It involves the contributions of three types: the corrections to the NDO scheme, the penetration integrals, and the corrections coming from a special parametrization of nuclear repulsion energies, which are implied to be different from γ_{IJ}. The following estimation can be derived for nonpolar systems:[8]

$$\alpha = \sum_{\mathrm{IJ}} \alpha_{\mathrm{IJ}};\ \alpha_{\mathrm{IJ}} = \gamma \sum_{\substack{i\epsilon \mathrm{I} \\ j\epsilon \mathrm{J}}} S_{\mathrm{ij}}{}^2 \tag{3}$$

Here S_{ij} are the overlap integrals and the summation involves all valence AO's of the carbon atoms; γ is an empirical parameter.

Of the above mentioned three effects only one is involved in MINDO, namely, the last one. We can restrict our treatment to only those geometrical arrangements of the reacting system for which intermolecular C–H and H–H MINDO interactions prove to be negligibly small. Indeed, the inspection shows that the configurations close to a symmetrical reaction path satisfy this condition up to the saddle point. Then the same form as (2) can be taken for the MINDO interaction energy with the α term involving only C–C interactions and redefined as

$$\alpha_{\mathrm{MINDO}} \equiv \alpha_{\mathrm{M}} = \sum_{\mathrm{IJ}} \alpha_{\mathrm{M,IJ}}$$

$$\alpha_{\mathrm{M,IJ}} = 16(R_{\mathrm{IJ}}^{-1} - \gamma_{\mathrm{IJ}}) \exp(-\xi R_{\mathrm{IJ}}) \qquad (4)$$

Here R_{IJ} represent the distances between C atoms and ξ is an empirical parameter for which different MINDO versions suggest different values.[18,20,21]

As shown previously[8] and as is also clear from the preceding discussion, (2) using (3) for α is a reasonable approximation for the interaction energy for configurations obeying the following limitations: (1) the hybridization changes are small, (2) the intermolecular overlap integrals are far less than 1, and (3) the intermolecular C–h and H–H interactions in α can be neglected. These conditions are satisfied at the initial and intermediate stages of π-addition reactions, up to the distance of about 2 Å between the C atoms of reactants. For such configurations the principal disagreement between the calculations described in the preceding section of this paper and the MINDO ones is expected to arise from the difference of (3) and (4) for α. The formal structure of these expressions is the same but the distance dependences of separate terms differ, mainly because the empirical exponent index ξ in (4) is smaller than the Slater exponent which determines the S^2 values in (3). The MINDO ξ values are the result of an empirical calibration in the range of equilibrium geometries of isolated reactant molecules. So the extrapolation of (4) onto the intermolecular interaction region has no satisfactory justification.

We display in Figure 1 the ratio $\alpha_{\mathrm{M}}/\alpha$ and the ratios of their first and second derivatives $\mathrm{d}\alpha/\mathrm{d}R \equiv \alpha'$ and $\mathrm{d}^2\alpha/\mathrm{d}R^2 \equiv \alpha''$ as functions of the separation R. The main conclusions are:

(1) The function $\alpha_{\mathrm{M}}(R)$ behaves rather satisfactorily within a wide range of distances and in particular in the region of 2.0–2.5 Å, where the TS's of π-addition reactions may be expected.

(2) In the same range of distances the empirical quantity $\alpha_{\mathrm{M}}'' \equiv \mathrm{d}^2\alpha_{\mathrm{M}}/\mathrm{d}R^2$ in the case of MINDO-3 is four times as small as that based on (3) theoretical estimation and 20 times as small for MINDO-2.

One can better appreciate the significance of the latter difference by recalling the general results concerning the stability of symmetrical TS's.[8] The potential curves corresponding to their antisymmetrical deformations pass through a maximum or through a minimum at the symmetrical reference configurations, depending on the absolute values of the second derivatives of the Δ_π and α terms. For a symmetrical configuration Δ_π'' and α'' (differentiation respective to an antisymmetrical deformation) have different signs, the α'' being positive. Therefore it is just the α term which allows a symmetrical TS to be stable. Clearly, the underestimation of α'' is a great danger because it can turn into an imaginary maximum, the true minimum of the energy curve corresponding to an antisymmetrical motion. Then the respective symmetrical TS will become "forbidden", leading to a wrong conclusion concerning the reaction mechanism. Such a situation seems to occur in the MINDO calculation of DA reactions.

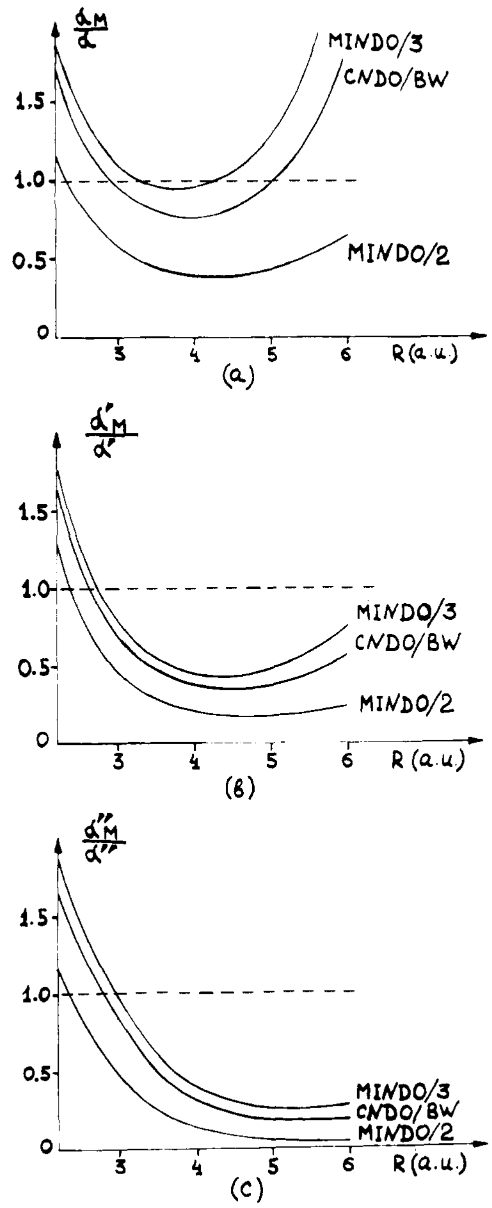


Figure 1. Distance dependence of the empirical equivalents of exchange repulsion (a) and its first (b) and second (c) derivatives appearing in the MINDO/2, MINDO/3 and Boyd–Whitehead version of CNDO.

When the potential surfaces of nonconcerted reactions, such as radical additions, are dealt with, then the valleys corresponding to the approach of reactants display a rather sharp relief, contrary to shallow valleys characteristic of the symmetrical reaction path of DA reactions. The error in the second derivative of the interaction energy still can distort the shape of a nonsymmetrical valley; however, it cannot turn a valley into a ridge as in the DA case. For such processes a MINDO calculation gives correct qualitative predictions of reaction paths. The radical addition TS's found by MINDO and those calculated using (2) are practically the same.[22]

Conclusion

For the majority of usual [4 + 2] DA additions the symmetrical reaction path is expected to be stable and energetically preferable. The converse statement is expected to be true for [2 + 2] concerted reactions, whose symmetrical transition configurations are not only forbidden in a Woodward–Hoffmann sense (that is their energies are much too high) but are also unstable to antisymmetrical motions, as follows from the stabilization energy arguments.[8]

To complete the comparison of the MINDO calculations of TS's and those using the "almost π-electron approximation" we would like to make one more comment. Equation 2 is theoretically justified only in the region of intermediate intermolecular separations, and our method is fit for treatment of selected chemical systems in a limited range of configurations.

One has to reckon on the luck of finding the desired TS in the allowed region. In contrast, the empirical MINDO-type procedures are universal and well suited for dealing with equilibrium molecular geometries, but their extrapolation into the intermolecular interaction region can result in very serious errors. The need for a reliable semiempirical method to treat chemical reactions is still far from being exhausted.

References and Notes

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(23) The invariance is slightly disturbed because an empirical parametrization of one-center exchange integrals cannot exactly reproduce the transformational properties of AO's. However, we have agreed to neglect these integrals.

Proton–Electron Hyperfine Coupling Constants of the Chlorophyll *a* Cation Radical by ENDOR Spectroscopy

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Received April 12, 1976

Abstract: In this paper we describe the assignment of the major coupling constants in monomer chlorophyll *a* cation free radical by ENDOR spectroscopy. To facilitate chemical manipulation methylpyrochlorophyllide *a* has been used as a stand-in, and a suite of six selectively deuterated derivatives have been subjected to ENDOR investigation. Details of the synthesis of these compounds are described. To study the effect of structural features on the spin distribution in the free radicals, six additional chlorophyll derivatives have been studied. Five coupling constants have been assigned, which account for about 80% of the observed electron spin resonance line width in the chlorophyll *a* monomer cation radical. The spin distribution appears to be highly asymmetric.

ENDOR[1] spectroscopy has provided important support[2-8] for the original ESR interpretation[9-11] that the primary donor of photosynthesis contains two special chlorophylls. Detailed comparisons of in vivo and in vitro ENDOR data have provided an experimental basis for a variety of special pair chlorophyll models[9,12-24] as the primary donor in photosynthesis. In all previous ENDOR studies an interpretation of the spin density distribution in terms of a specific molecular structure has not been documented. For conclusions based on the in vivo ENDOR to be the most convincing, the ENDOR spectrum should account for the whole of the unpaired spin density rather than reflect only a small fraction of an electron distribution. Incomplete interpretation is a likely possibility since all sites of spin density are not necessarily observable by ENDOR spectroscopy.[25] Thus a molecular basis for assignment of the ENDOR spectra of the chlorophyll cations is important.

In this paper we report the detailed analysis of the proton-ENDOR spectrum of the cation radical of chlorophyll *a* (**1**), methylpyrochlorophyllide *a* (**9**), and of a series of related magnesium chlorins. These data provide a clear description of specific assignments of the electron–proton hyperfine coupling constants of in vitro chlorophyll *a* π cation free radical and provide firm support for the view that the ENDOR spectrum of the $Chl\cdot^{+}$ free radical accounts essentially for all of the protons on the chlorophyll macrocycle. Comparisons between in vivo and in vitro ENDOR data therefore do in fact appear to be essentially complete.

The model compound (**9**) is essentially identical to chlorophyll *a* insofar as spin distribution in the cation free radicals is concerned, but it offers a much greater variety of possibilities for structural modifications and for the selective introduction of deuterium. The results of the ENDOR spectroscopy on a wide range of selectively deuterated and structurally modified chlorins establish that chlorophyll *a* π cation free radical has low spin density at the four methine bridges and the nitrogen atoms of the pyrrole rings. Although the results are in general agreement with open shell calculations for chlorins, the chlorophyll *a* cation radical shows a strongly asymmetric spin distribution that cannot as yet be completely accounted for by current theory. Finally we show experimentally that this asymmetry is the result of ring V of the chlorophyll macrocycle and is not a result of other various functional side groups.

Experimental Section

Spectra. ENDOR spectra were recorded on a Varian E-700 spectrometer with a Varian large access cavity and at a temperature of 100 K on samples prepared on the vacuum line. Compounds (0.5–1 mg) were first dried by dissolution in benzene, followed by evaporation