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THEORETICAL STUDY OF DIELS–ALDER REACTIONS BETWEEN SUBSTITUTED DERIVATIVES OF BUTADIENE AND ETHYLENE

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Abstract—The potential surfaces for the butadiene + ethylene and 1-hydroxybutadiene + acrolein reactions, have been calculated (MINDO/2). A simplified study of the potential surface for several reactions between monosubstituted derivatives of butadiene and ethylene has also been done (MINDO/3). From the results obtained, the *endo–exo* ratio, the regioselectivity, the influence of substituents on the reaction rate and the mechanism of the process are discussed.

INTRODUCTION

Following its discovery,[1] the Diels–Alder reaction has been the object of numerous studies, both experimental[2–6] and theoretical.[7–20] Among the theoretical studies, worthy of special mention are the *endo–exo* ratio,[8–11] the regioselectivity,[12–16] the influence of substituents on the reaction rate[15,17–19] and the mechanism of the process.[10,12,20] Recently, three studies have calculated[21–24] the potential surface of the butadiene + ethylene reaction to analyze its mechanism. Dewar *et al.*,[21] using the MINDO/3 method, found that the transition state was very unsymmetrical, one new bond having been almost completely formed while the other had hardly begun to form at all. Enforcing C_s symmetry, they found a very high energy barrier which made the symmetrical mechanism very unfavourable. (These results are presently being reviewed by its author.[25]) On the other hand, the other two studies[22–24] using *ab initio* methods, found that the most favourable reaction pathway is that with a concerted and symmetrical formation of both bonds. However whilst the geometry of Leroy's transition state[22,23] prefigures the half-chair cyclohexene conformation, Salem *et al.*[24] affirm that the adduct obtained is the half-boat conformation, the formation of the half-chair adduct needing a much greater activation energy. These authors have also studied the possibility of a two-step mechanism, and have discovered the existence of a biradical with a lower energy than that of the symmetrical transition state, but the best pathway through this biradical presents a potential energy barrier that is higher than that of the symmetrical mechanism.

The results obtained for the butadiene + ethylene reaction cannot be applied to reactions with substituted dienes and dienophiles. The object of this paper is to study how the potential surface varies with the presence of substituents, to locate the transition state of each reaction, and to carry out a theoretical interpretation of the experimental results. Since this would require a considerable amount of calculation, we have used semiempirical methods without configuration interaction to keep the calculation work within reasonable limits. We feel that this approach does not undermine the conclusions of the present study owing to its comparative nature.

Figure 1 gives a general scheme of the reactions studied. 1-Hydroxybutadiene and 1-cyanobutadiene were used as substituted dienes, the former with a donor group and the latter with an acceptor group. Acrolein and cyanoethylene were used as substituted dienophiles, with two acceptor groups of differing strength. In the case of 1-hydroxybutadiene, the ketoenolic equilibrium is displaced towards the ketone form, but this molecule was considered as a model for the 1-methoxybutadiene in order to simplify the calculations.

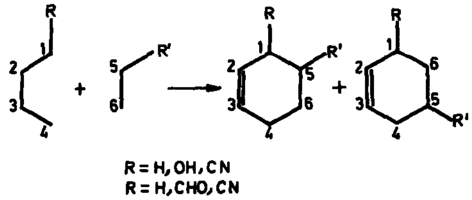

Fig. 1. Diels–Alder reactions studied.

METHOD OF CALCULATION

Owing to the impossibility of calculating the multidimensional potential energy surface for the majority of chemical reactions, two types of approximations are normally used. The first attempts to reduce the dimensionality of the surface by eliminating certain degrees of freedom. In practice, however, a sufficient reduction in these degrees of freedom is impossible without imposing unrealistic conditions. The second type of approximation involves choosing one or two degrees of freedom as independent variables of the potential energy and to allow the system to relax by optimizing the remaining degrees of freedom for each set of values of the independent variables. This second method is a considerable improvement on the first, although one has to be careful with the selection of the independent variables since an inadequate selection could prevent the correct localization of the transition state.

We have used the second type of approximation in our study of the Diels–Alder reaction, and we have considered as independent variables the lengths of the two forming bonds. The optimization of the remaining parameters of the system, for each value of the independent variables, has been carried out by means of a variable metric minimization method using the gradient of the potential energy. This technique starts with an initial geometry q^0 in the multidimensional space of the variable to be optimized, and a series of points q^n are successively generated according to the following formula:

$$q^{n+1} = q^n - \alpha_n A^n g^n$$

where the determination of the constant α_n and of the matrix A^n, in each iteration, depends on the method used, and g^n is the gradient vector calculated in q^n.

The calculations were carried out using the MINDO/3 program of Dewar *et al.*[26] and the GEOMO program of Rinaldi.[27] The first program used the MINDO/3 method[28] to calculate the energy value. A^n and α_n are determined by the Davidon–Fletcher–Powell[29–30] procedure that involves carrying out linear minimizations. With regard to the calculation of the gradient, the MINDO/3 program determines the partial derivatives of the energy with respect to the coordinates through finite differences. The version of the GEOMO program we used permits the optimization of geometries through the CNDO/2,[31] INDO[31] and MINDO/2[32] methods. Minimization of the energy can be carried out by any one of the methods proposed by Murtagh and Sargent,[33] Fletcher[34] or Rinaldi,[35] none of them requiring linear minimizations for the calculation of α_n. The calculation of partial derivatives is carried out using the analytical procedure proposed by Rinaldi and Rivail.[36]

RESULTS AND DISCUSSION

Since we have tried to perform a comparative study on the influence of the substituents on the Diels–Alder reaction, we had to carry out a previous calculation of the potential surface of the butadiene + ethylene reaction. The reaction was first studied assuming conservation of C_s symmetry. Figure 2 gives, for the various semiempirical methods used, the potential energy curve as a function of the length of the two forming bonds. It is to be noted that the curves obtained from the CNDO/2 and INDO methods do not present a potential barrier. This fact, in the case of CNDO/2, had already been observed by Kikuchi,[37] who attributed this failure to the nature of this semiempirical method. With the MINDO/2 method, an energy barrier of 37.5 kcal/mol is obtained for a C–C distance of 2.19 Å; with the MINDO/3 method, the corresponding values are 46.3 kcal/mol and 2.16 Å. These values are in close agreement with the *ab initio* results[22,24] and are higher than the experimental value of 27.5 kcal/mol.[38]

The next step was to calculate, by means of the MINDO/2 method, the potential surface of the butadiene + ethylene reaction as a function of the lengths of the two new bonds. The potential surface obtained is given in Fig. 3.

An asymmetrical pathway is observed which is a little more favourable than the symmetrical one, the difference between the two potential energy barriers being 1.2 kcal/mol. This difference increases to approximately 4 kcal/mol when the MINDO/3 method is used. We believe that a calculation with configuration interaction would further increase this difference, owing to the biradical-like characteristics of the asymmetrical transition state. A discussion about the symmetry or asymmetry of the transition state of this reaction will be reported elsewhere.

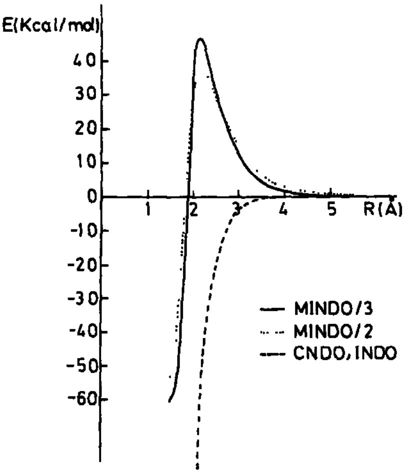

Fig. 2. Potential energy curves for the butadiene + ethylene reaction.

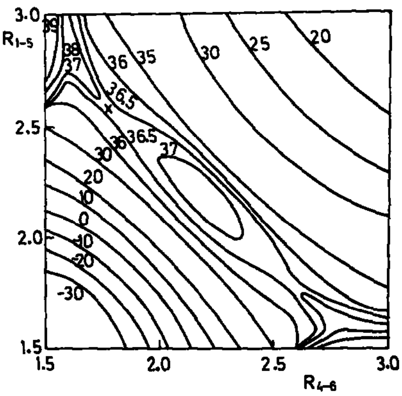

Fig. 3. Potential energy surface for the butadiene + ethylene reaction. Energy in kcal/mol (MINDO/2).

In order to study the changes undergone by the potential energy surface of the butadiene + ethylene reaction after the addition of substituents in the diene and in the dienophile, the potential energy surface of the reaction between 1-hydroxybutadiene and acrolein, resulting in the formation of the *ortho endo* adduct, was calculated by means of the MINDO/2 method. Figure 4 shows the considerable increase in the asymmetry of the process with the result that the bond between the unsubstituted carbons closes more rapidly than that between the substituted ones. In the transition state, the lengths of the two bonds are $C_4C_6 = 1.6$ Å and $C_1C_5 = 3.0$ Å. In Table 1, the lengths of the C–C bonds in the transition state are compared with the corresponding ones in the reactants and product. Since the C_4C_6 bond has almost been formed, the C_3C_4 and C_5C_6 bonds have already lost their double bond character. The rest of the dienic fragment has also changed substantially, the central C_2C_3 bond being already shorter than the C_3C_4. From all this, we can conclude that the transition state of the 1-hydroxybutadiene + acrolein reaction corresponds to a fairly advanced stage of the process.

The calculated potential energy barrier is 28.4 kcal/mol, i.e. 7.9 kcal/mol lower than in the case of

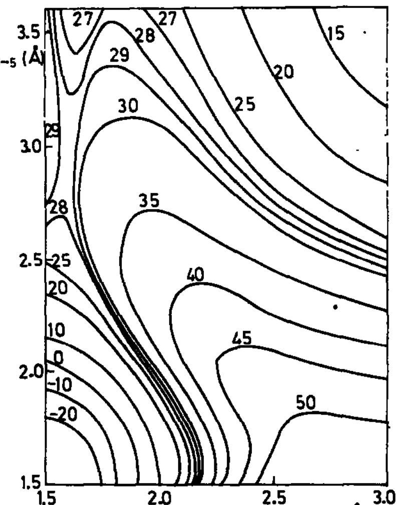

Fig. 4. Potential energy surface for the 1-hydroxybutadiene + acrolein reaction. *Orthoendo* adduct. Energy in kcal/mol (MINDO/2).

Table 1. CC Bond lengths (in Å) of the reactants, transition state and product for the 1-hydroxybutadiene + acrolein reaction (MINDO/2)

	C_4C_6	C_1C_5	C_1C_2	C_2C_3	C_3C_4	C_5C_6
Reactants	—	—	1.34	1.46	1.32	1.32
Transition state	1.6	3.0	1.38	1.39	1.43	1.43
Product	1.51	1.55	1.50	1.33	1.48	1.54

the butadiene + ethylene reaction, and is in good agreement with the empirical Alder rule about the influence of substituents on the reaction rate. A hypothetical reaction pathway where both bonds form at the same rate, would present a potential energy barrier of 43.3 kcal/mol. Therefore, it is evident that the stabilization of the transition state is closely related to the asymmetry of the process.

In the potential energy surface studied we have not been able to locate the presence of any intermediate, so it seems that the reaction proceeds in a single step from an energetic point of view. However, given the large asynchronism in the formation of the two new bonds, it is most appropriate to describe the process as a two-stage reaction as proposed by Woodward and Katz.[2]

In the reaction between 1-hydroxybutadiene and acrolein, three adducts can be formed other than the *ortho endo* one. A study of the *endo-exo* ratio and the regioselectivity would require the calculation of three more potential energy surfaces, but this is economically prohibitive. The process can be simplified by studying only those points of the potential energy surface at which the sum of the lengths of the two new bonds equals 4.5 Å. We believe that the point which corresponds to minimum energy in this slice of the potential energy surface, will give a close approximation to the transition state, because around this state the energy changes smoothly and, also, the hypothetical concerted pathways of the four reactions give an energy maximum for the same length of the two forming bonds ($C_1C_5 = C_4C_6 = 2.2$ Å). The results are given in Table 2, where ΔE represents the heat of reaction, E^*_{conc} the potential energy barrier for the bonding-concerted[39] pathway, and E* is the potential energy barrier for the asynchronous pathway going through the transition state of the reaction.

We may note that for the *ortho endo* adduct, the value of the potential energy barrier calculated by this method (28.3 kcal/mol) almost coincides with that calculated from the complete potential energy surface (28.4 kcal/mol). This fact seems to enhance the validity of the simplification used. Regarding the regioselectivity, it is confirmed that the *ortho* adducts are kinetically more favourable than the *meta* adducts. It is also observed that the potential energy barrier corresponding to the formation of the *ortho endo* adduct is less than that corresponding to the formation of the *ortho exo* adduct, in spite of the fact that the latter is slightly more stable. All these results are in good agreement with the *endo* rule and with the *ortho* orientation observed experimentally in most Diels–Alder reactions.[4,5]

Table 2. Heats of reaction and potential barriers (in kcal/mol) for the 1-hydroxybutadiene + acrolein reaction (MINDO/2)

Adduct	ΔE	E^*_{conc}	E*
Ortho endo	−33.0	43.4	28.3
Ortho exo	−33.4	43.4	30.5
Meta endo	−31.8	45.2	43.2
Meta exo	−30.8	45.7	41.4

A study of several reactions using other substituents confirms the conclusions reached for the 1-hydroxybutadiene + acrolein reaction. As in this case, we have likewise considered only those points of the potential energy surface at which the sum of the lengths of the two new bonds equals 4.5 Å. To justify this approximation, we have calculated the bonding-concerted pathway for all the reactions studied. We have found that the energy maximum always appears at the same length values of the two new bonds.

Table 3 gives the results obtained with the MINDO/3 method for all the reactions studied. In this table, ΔE, E^*_{conc} and E* have the same meaning as in Table 2, $HOMO^D$ and $LUMO^D$ are the energies of the frontier orbitals of the diene, $HOMO^F$ and $LUMO^F$ are the corresponding energies of the dienophile, and *t* is the charge transfer between the diene and the dienophile calculated as the sum of the net charges on the dienophile atoms. From Table 3, several interesting remarks can be made about the *endo–exo* ratio, the regioselectivity, the influence of substituents on the reaction rate and the mechanism of the process.

The *endo–exo* ratio has been studied, using the MINDO/3 method, for the butadiene + acrolein reaction. With *s-trans* acrolein, the same potential energy barrier was obtained for the formation of both adducts. With *s-cis* acrolein, however, the formation of the *endo* adduct is slightly more favourable, thus agreeing with the increase in the secondary interactions. However, the difference between both potential barriers is small, as could be expected from the acyclic nature of the dienes and dienophiles.

The regioselectivity can be studied from the 1-hydroxybutadiene + acrolein, 1-hydroxybutadiene + cyanoethylene and 1-cyanobutadiene + acrolein reactions. In all three cases, the potential energy barrier for the *ortho* adduct is considerably lower than that for the *meta* adduct, thus agreeing with the experimental rule.[4,5] The 1-cyanobutadiene + acrolein reaction is of special interest. For dienes with acceptor substituents, the HOMO coefficients for the two terminal carbon atoms are quite close. The MINDO/3 calculation, in particualr, indicates that the substituted carbon coefficient is higher. The frontier orbital method predicts, therefore, the predominant formation of the *meta* adduct, while the potential energy barriers obtained in our calculations establish that the *ortho* adduct is clearly more favourable. Our results coincide with experimental data for a similar reaction of 1-cyanobutadiene.[40]

In order to discuss the influence of substituents on the reaction rate, it is convenient to use the classification of Diels–Alder reactions proposed by Sustmann.[41] Comparing the two HOMO–LUMO interactions that appear in Table 3, one can observe that the interaction between the HOMO of the diene and the LUMO of the dienophile clearly predominates in the majority of reactions studied (Diels–Alder reactions with normal electron demand). The only exceptions are the butadiene + ethylene and the 1-cyanobutadiene + ethylene reactions which may be considered as neutral since both interactions are similar.

According to Alder's empirical rule, the rate of a normal Diels-Alder reaction is increased by electron-donating substituents in the diene and by electron-withdrawing substituents in the dienophile. The results in Table 3 are in excellent agreement with this rule. For example, if we consider the reaction between butadiene and *s-trans* acrolein, we may observe that the introduction of a donor group in the diene (the hydroxyl group) decreases the potential energy barrier of the reaction, while the introduction of a weak acceptor group (the cyano group) increases it slightly. Similarly, if we substitute the ethylene by acrolein or by cyanoethylene in the 1-hydroxybutadiene + ethylene reaction, we have in both cases a decrease in the potential energy barrier. In the reaction between butadiene and ethylene, the reaction rate increases when any substituent is introduced in the diene or in the dienophile, as could be expected given that in this reaction both HOMO-LUMO interactions are similar.

We may also observe in Table 3 that there is good correlation between the potential energy barrier, the $LUMO^F$–$HOMO^D$ energy difference and the charge transfer between the diene and the dienophile. This correlation allows us to interpret Alder's empirical rule from the configuration interaction analysis proposed by Epiotis.[7] In fact, the smaller the $LUMO^F$–$HOMO^D$ difference, the larger the stabilization of the transition state due to charge transfer and the lower the potential energy barrier of the reaction.

The data in Table 3 clearly show that the influence of substituents on the reaction rate is closely related to the

Table 3. Results for the Diels-Alder reactions studied (MINDO/3)

Diene	Dienophile	Adduct	ΔE	$E^{\neq a}_{conc}$	$E^{\neq a}$	$LUMO^F$–$HOMO^{D\,b}$	$LUMO^D$–HOMOF^b	t
Butadiene	Ethylene		−60.8	45.9	41.2	11.32	11.55	0.0111
1-Hydroxybutadiene	Ethylene		−48.4	48.8	40.5	10.63	11.72	−0.0831
1-Cyanobutadiene	Ethylene		−47.1	50.3	40.9	11.20	10.93	0.0412
Butadiene	Acrolein (*s-cis*)	*Endo*	−45.4	50.8	35.6	9.64	11.98	−0.2294
		Exo	−45.8	51.3	36.1	9.64	11.98	−0.2216
Butadiene	Acrolein (*s-trans*)	*Endo*	−45.2	51.1	37.1	9.60	12.02	−0.2179
		Exo	−46.1	51.3	37.1	9.60	12.02	−0.2169
1-Hydroxybutadiene	Acrolein (*s-trans*)	*Ortho endo*	−32.8	53.7	30.6	8.90	12.20	−0.4043
		Meta endo	−32.6	54.6	49.2	8.90	12.20	−0.1610
1-Cyanobutadiene	Acrolein (*s-trans*)	*Ortho endo*	−29.6	57.0	38.0	9.47	11.40	−0.2010
		Meta endo	−32.1	55.8	50.1	9.47	11.40	−0.1788
1-Hydroxybutadiene	Cyanoethylene	*Ortho endo*	−34.8	54.5	37.5	9.66	11.25	−0.2068
		Meta endo	−33.6	55.6	52.2	9.66	11.25	−0.0154

[a] in kcal/mol. [b] in eV.

asynchronous formation of the two new bonds. In fact, we may observe that the butadiene + ethylene reaction is the most exothermic one and that it would be the fastest if all the reactions proceeded through a concerted pathway in which both bonds were formed at the same rate. However, we find that this reaction is the slowest one as indicated by the E^* values. The E^*_{conc}–E^* difference may be taken as a measure of the increase in stabilization due to the asynchronous formation of the two new bonds. We may observe that this energy difference depends on the substituents introduced in the diene and dienophile. For a given diene and dienophile the E^*_{conc}–E^* difference corresponding to the formation of the *meta* adduct is always lower than that corresponding to the formation of the *ortho* adduct. Hence, the regioselectivity of the Diels–Alder reaction is also related to the asynchronism of the process.

In conclusion then, we may affirm that the presence of substituents in the diene or in the dienophile introduces large changes in the potential energy surface, increasing the asymmetry of the process. In spite of the different closing rate of the two new bonds, the reaction seems to be concerted from an energetic point of view. However, given that our calculations do not include configuration interaction, we cannot definitely exclude the possibility of a two-step process with a biradical intermediate. As for the *endo–exo* ratio, the regioselectivity and the influence of substituents on the reaction rate, the results of the present study are in close agreement with the experimental ones.

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