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# THEORETICAL STUDY OF THE MECHANISM OF THE 1,3-DIPOLAR CYCLOADDITIONS

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**Abstract**—By means of the MINDO/3 method the potential energy hypersurfaces for the 1,3-dipolar cycloadditions of carbonyl and azomethine ylides to ethylene have been studied. In the first place, the synchronous formation of the two new sigma bonds has been considered. In the second place, the asynchronous region of the surface has been explored. The asynchronous mechanism appears to be more favourable, there being two transition states and an intermediate. Finally, the physical meaning of the results obtained is discussed.

At the moment, the mechanism of the 1,3-dipolar cycloaddition is the subject of a great controversy in the experimental as well as the theoretical aspect. At first two extreme theories were proposed for this reaction. A concerted mechanism, proposed by Huisgen,[1,2] with simultaneous formation in the transition state of the two new sigma bonds, and a mechanism in two steps, through a diradical intermediate, defended by Firestone.[3,4] In support of their theories, the two authors refer to a multiplicity of experimental data: stereospecifity, activation entropy, activation energy, solvent effects, periselectivity, reactivity of the dipolarophiles, regioselectivity,... In an attempt to achieve a greater concordance between theory and experiment, both authors introduce some nuances in the two mechanism. Huisgen[5,6] admits that the concerted process is compatible with an asynchronism in the formation of the two new sigma bonds. Firestone,[7] for his part, considers that the energy barrier of the second step may be zero, or almost zero. Both extreme positions, therefore, are coming closer together, so that the principal difference existing between the two mechanism may be attributed to a greater or lesser degree of asynchronism in the formation of the sigma bonds.

Numerous theoretical calculations have been carried out in this field. The cycloaddition of fulminic acid to acetylene has been studied with two different methods, producing clearly divergent results. Poppinger,[8,9] by means of "*ab initio*" calculations, reaches a slightly asynchronous transition state, whilst Dewar,[10,11] using the semi-empirical MNDO/2 method, finds a highly asynchronous transition state. On the other hand, a thorough systematic "*ab initio*" study carried out by Leroy[12–17] of a great variety of dipolarophiles and dipoles, of the propargyl-allenyl type as well as of the allyl type, shows a great synchronism in the mechanism, with slight deviations. In all these studies, a single independent variable was chosen and the rest of the geometric parameters were optimised totally or partially for each given value of the independent variable. Only Poppinger,[8,9] when studying the addition of fulminic acid to acetylene, introduces two variables into the proximity of the transition state, previously found with only one degree of freedom. Nevertheless, when he works with two independent variables, he does not achieve a complete relaxation of the system. On the other hand, Leroy,[12–17] who carries out a partial optimisation of geometry, and Poppinger,[8,9] who makes a total one, both study the potential surface in the proximity of the zone corresponding to the concerted mechanism. Dewar[10,11] alone deals with a transition state in the zone corresponding to an asynchronous mechanism. Given that in the 1,3-dipolar cycloaddition two new bonds are formed, we consider it indispensable to take as independent variables the two lengths of the sigma bonds in formation, and to study the complete potential surface.

We must emphasise from among the cases studied the cycloaddition of carbonile ylide to ethylene which, given the initial symmetry of the reagents, takes place, according to Leroy, through a perfectly synchronous transition state. Therefore, it seems interesting to study this reaction with a semiempirical method, in order to discover whether these methods favour the asynchronism of the process, as opposed to the "*ab initio*" methods. The result obtained will be highly significant, since a supposedly totally symmetrical reagent has been chosen. For the same reason the cycloaddition of azomethine ylide to ethylene has been studied. A comparison of the results obtained by means of both methods may help to clarify which of the two mechanisms proposed is closer to reality.

## *Method of calculation*

Because of the impossibility of a complete calculation of the potential hypersurface for most chemical reactions, two types of approximations have been used. The first attempts to reduce the dimensionality of the surface by eliminating certain degrees of freedom. Generally speaking, however, this supposes the introduction of unrealistic restrictions. A significant improvement in this approximation is achieved by choosing a certain number of degrees of freedom as independent variables of the potential energy, allowing the system to relax by optimising the remaining geometric parameters for each set of values of the independent variables. Nevertheless, it is necessary to proceed with great caution in the selection of these independent variables, since an inadequate selection may prevent us from reaching the true transition state. In the second type of approximation all the degrees of freedom of the system are taken into consideration, but seeks only to locate certain points of chemical interest on the potential energy surface. McIver and Komornicki[18] have suggested a method for the direct location of the transition state, without the need to construct the potential surface, thus avoiding all the dangers inherent in the introduction of the restrictions mentioned earlier. In the transition state the gradient must be null. By means of the minimisation of the square of the gradient norm, the stationary points of the potential surface are located. It must be subsequently proved that this was a true transition state. To do this the eigenvalues of the force constant matrix are calculated. In the transition state only one negative eigenvalue must exist.

In our study we shall explore the potential surface by minimisation of energy, taking as independent variables the two lengths of the two new sigma bonds in formation. We shall deal first with the concerted zone, and go on to the asynchronous zone. This preliminary study of the potential surface will be taken as a starting point for the application of the McIver and Komornicki[18] method of direct location of stationary points. The preliminary exploration of the surface is carried out by calculating the potential energy by means of Dewar's[19] semiempirical method MINDO/3,[20] which has no disadvantages with regard to compounds which do not have adjacent atoms with lone pairs. As an optimisation procedure, MINDO/3 uses the D.F.P.[21-23] (Davidon, Fletcher, Powell) method, based on Fletcher–Powell's algorithm. It is an iterative technique which begins with an initial geometry $x_0$ in the multidimensional space of the variables which are optimised and generates a series of successive points $x_i$ by means of the formula

$$x_{i+1} = x_i - \alpha_i H_i g_i$$

where $\alpha_i$ is a parameter obtained by cubic interpolation, $H_i$ a matrix which tends to the inverse of the Hessian matrix, and $g_i$ the gradient.

## RESULTS AND DISCUSSION

We will first present the results obtained for the 1,3-dipolar cycloaddition of carbonyl ylide to ethylene. Next the case of azomethine ylide will be described. Finally we will discuss the physical meaning of the results obtained.

In order to explore the concerted region of the surface of the carbonyl ylide cycloaddition to ethylene the $R_{24}$ and $R_{35}$ lengths of the two new sigma bonds in formation have been kept equal each to other. Two distinct tetrahydrofuran conformers may be obtained as final products: the planar and the half-boat conformers, in which the oxygen is clearly removed from the plane determined by the four carbon atoms. Leroy[12] defines two ways of approximation of the reagents: type *P* approximation, with both reagents situated on parallel planes, and type *C* approximation, in which all the heavy atoms are coplanar. The second is preferred energetically at short distances, whilst type *P* is favoured at long distances. In this study using MINDO/3 different results have been obtained. Starting with reagents situated initially on parallel planes at long distances, two clearly differentiated reaction paths appear, as shown in Fig. 1. The one in a full line passes through a transition state to $R = 2.45$ Å, far removed from coplanarity, to arrive at the half-boat conformation of tetrahydrofuran. The one in a dashed line passes through a transition state also at $R = 2.45$ Å, much closer now to the coplanar situation, leading to the planar conformer of tetrahydrofuran. Therefore our results present the situation in a completely different aspect from Leroy, for whom only one way existed, the type *P* approximation at long distances and the type *C* being adopted at short distances. In fact, there are two distinct channels through which the reaction takes place, following different ways of approximation for each one, the final result obtained being a different conformer of tetrahydrofuran for each channel. The barrier existing between both conformers and along the whole path of reaction is what gives its individual identity to each of the paths studied. Nevertheless, these maximum points are transition states only if we confine ourselves to the synchronous region of the potential surface, but they are not true transition states when the complete potential surface is taken into consideration. This may be seen when the asynchronous region of the surface is explored, allowing that the lengths of bonds $R_{24}$ and $R_{35}$ are different one from the other, though keeping their sum constant. As is shown in Fig. 2, the energy goes down as we move away from the central point, corresponding to the synchronous path.

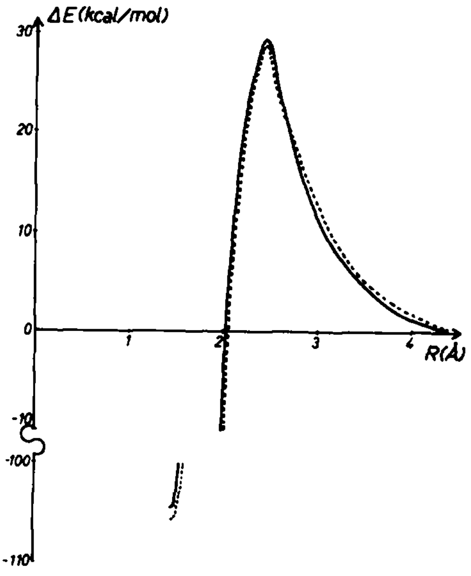

Fig. 1. Synchronous reaction paths for the carbonyl ylide cycloaddition to ethylene, leading to half-boat conformation of the tetrahydrofuran (———) and planar conformation (— — —).

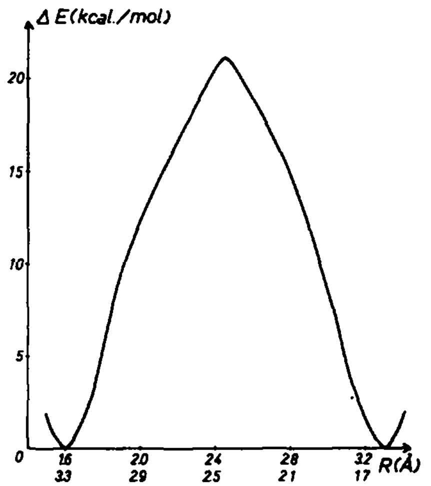

Fig. 2. Energetic profile in function of $R_{24}$ and $R_{35}$ lengths, keeping their sum constant.

We reach two lateral minimums situated in the asynchronous region of the surface, with bond lengths of 1.6 Å and 3.3 Å. These points are taken as a starting point for the direct location method of McIver and Komornicki, mentioned earlier.

The principal results obtained are given in Table 1, in which the values found for the increase in energy (kcal/mol) from separated reagents and the bond distances (Å) $R_{24}$ and $R_{35}$ are set out, by means of different methods, in the addition of carbonyl ylide to ethylene. In the first five columns the bond lengths $R_{24}$ and $R_{35}$ are kept equal in relation to each other, which indicates that this is the study of the synchronous zone of the surface. In the first three, Leroy's results obtained by "*ab initio*" methods using different basis sets are shown. In the next two, those obtained in this study with MINDO/3 are given, both for the path of reaction leading to the half-boat conformer of tetrahydrofuran and for the one leading to the planar conformer. Even though the bond distances are analogous with those given by Leroy, the energies are much greater. This is due not only to the difference between the methods used, but mainly to the fact that we started with completely optimised carbonyl ylide, which is 14.5 kcal/mol more stable than the planar structure taken into consideration by Leroy. The existence of a more stable structure than the planar one had already been pointed out by Houk.[24]

In the asynchronous region of the surface three stationary points have been located. From the calculation of the eigenvalues of the force constant matrix two transition states and one intermediate are identified. The first transition state has the 2–4 bond which is in formation, possessing a length already clearly lower than the lengths $R_{24}$ and $R_{35}$ obtained for the synchronous transition states. The other bond, 3–5, has still not begun to close. Immediately there appears an intermediate with an already almost completely constituted bond and another which still has not begun its formation. Finally there exists a second transition state, with the 2–4 bond already formed and the 3–5 bond now beginning to close. The structures of these two transition states can be much better visualised in Figs. 3 and 4. At the side of each atom the module of the amplitude of displacement of each one is registered, corresponding to the direction of the reaction coordinate, obtained by means of the diagonalisation of the force constant matrix. In the first transition state (Fig. 3), the modules are clearly greater in the C atoms involved in the 2–4 bond, which is in formation, than in the right-hand part, corresponding to the 3–5 bond. This indicates that the intensity of movement is much greater around the bond which closes during this step. In contrast, an examination of the same numbers for the second transition state (Fig. 4), shows values of greater size around the 3–5 bond, which is now beginning to close, than in the zone around the 2–4 bond, already completely formed. This therefore indicates a more intense amplitude of displacement around the 3–5 bond, which is the one which closes during this second step.

Let us now consider the energy aspect of Table 1. An energy profile analogous to the one described by Firestone has been obtained. There exists a first transition state which implies an energy barrier of 12.2 kcal/mol, much less than for a synchronous mechanism. A fall in energy is produced which corresponds to the closing of a first bond in order to reach the intermediate, and a second transition state appears, with a very small barrier, of 1.3 kcal/mol, owing to the beginning of the formation

Table 1. Results for the carbonyl ylide cycloaddition to ethylene

| | "Ab initio" | | | MINDO/3 | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | STO-3G | 7s-3p | 4-31G | Half-Boat | Planar | TS1 | Intermediate | TS2 | Cyclorreversion |
| ΔE | 6.0 | 1.0 | 10.3 | 29.3 | 29.0 | 12.2 | 6.6 | 7.9 | 9.6 |
| $R_{24}$ | 2.35 | 2.35 | 2.35 | 2.45 | 2.45 | 2.10 | 1.62 | 1.59 | - - |
| $R_{35}$ | 2.35 | 2.35 | 2.35 | 2.45 | 2.45 | 4.30 | 3.90 | 3.12 | - - |

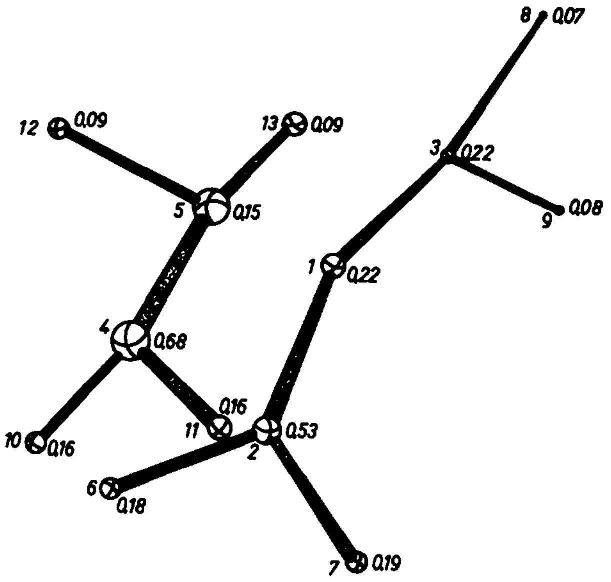

Fig. 3. Structure of the first transition state, with the modules of the amplitudes of displacement of each atom.

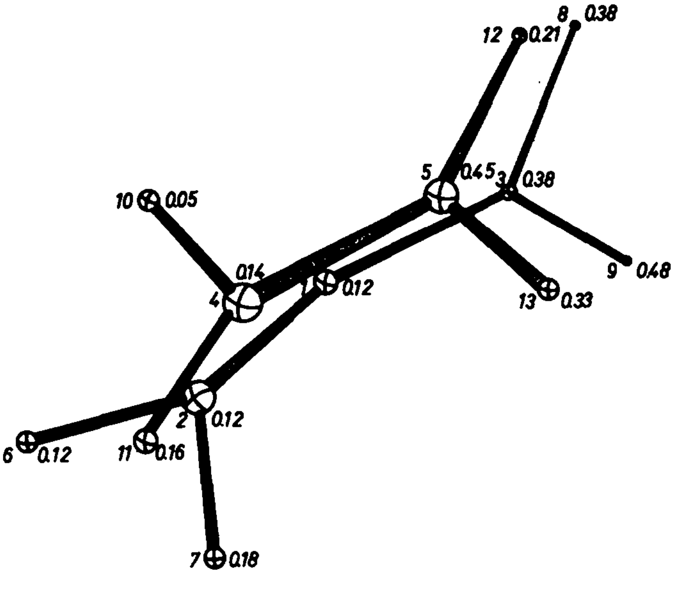

Fig. 4. Structure of the second transition state.

of the second bond. Also given in the table is the value of the activation energy of the cyclorreversion of carbonyl ylide to oxirane, from which it proceeds. In this way, only an asynchronous mechanism possesses a reaction rate, according to the barrier of the first transition state, which may make cicloaddition competitive with cyclorreversion.

Let us analyse the results obtained for the addition of azomethine ylide to ethylene. The mode of procedure is similar to the one used with the carbonyl ylide. Only one planar conformer of pyrrolidine exists, except for an angular displacement of the hydrogen bonded to the nitrogen. This causes the appearance of a single path of reaction when the synchronous region of the surface is explored. In Table 2 the numerical results obtained for this case are presented. In the first column the energy barrier and the bond distances corresponding to the synchronous path are given. In the transition state both reagents form an intermediate angle between the coplanar and parallel planes situations. As in the previous case, this maximum point is not a true transition state if the complete surface is considered, since the force constant matrix presents two negatives eigenvalues, owing to the fact that the energy goes down as the lengths of the two sigma bonds vary from one another. When the asynchronous region is explored three stationary points are obtained, corresponding, as in the previous case, to two transition states separated by an intermediate. There appears a transition state with the 2–4 bond at an advanced degree of formation, and the 3–5 bond, whose closing has not yet begun. Subsequently an intermediate is found with the 2–4 bond already almost formed and the 3–5 bond which has not begun to form. Finally, there exists a second transition state with

Table 2. Results for the azomethine ylide cycloaddition to ethylene

| | MINDO/3 | | | | |
|---|---|---|---|---|---|
| | TS synchronous | TS 1 | Intermediate | TS 2 | Cyclorreversion |
| $\Delta E$ | 28.2 | 17.5 | 16.2 | 18.2 | 27.3 |
| $R_{24}$ | 2.33 | 1.96 | 1.68 | 1.63 | - - |
| $R_{35}$ | 2.33 | 4.06 | 3.79 | 2.94 | - - |

the 2–4 bond already practically constituted, and the 3–5 bond which is already beginning to close. The closing of both bonds presents a degree of asynchronism somewhat less than in the case of carbonyl ylide. For this reason, from an energetical point of view, the difference between the synchronous and asyncronous mechanisms is less than in the previous case. An intermediate appears situated in a shallow well of potential, at 1.3 kcal/mol from the first transition state and at 2 kcal/mol from the second. The asynchronous mechanism is the reason why cycloaddition is preferred to the cyclorreversion of azomethine ylide to aziridine, whose energy barrier is indicated in the last column.

In short, for both carbonyl ylide and azomethine ylide, transition state are obtained with MINDO/3 analogous to those already described by Dewar,[10,11] using MNDO/2, for the addition of fulminic acid to acetylene. Nevertheless, they are completely different from the synchronous transition states found by "*ab initio*" methods.[15] Our results present two energy barriers, the second being very small. This favours the diradical mechanism suggested by Firestone.

Let us now discuss the physical meaning of the results obtained. Both kinds of method present important limitations. The semiempirical ones are parametrized for distances of equilibrium and not for situations removed from them, such as appear in the course of the reaction. It has been proved only that the "*ab initio*" methods with a limited basis sets and without introducing the correlation energy, such as those applied to the theoretical study of the 1,3-dipolar cycloaddition, present acceptable results for distances of equilibrium. Besides, owing to the great time required for calculation, a complete relaxation of geometry cannot, in general, be attained.

The fact that the "*ab initio*" methods tend to favour synchronous transition states, whilst the semiempirical ones favour the asynchronous, in cycloadditions, has been already recently analysed in different papers.[11,25–27] Houk[26] points out that the methods which use the ZDO approximation favour asinchronous transition states, since when overlap is neglected the closed-shell repulsion is not taken into account and this destabilisation is greater for asynchronous structures. This objection is only partially true for the MINDO/3 method, whose parametrization compensates for these errors for the distances of equilibrium. Even though this argument favours the results of the "*ab initio*" methods, another factor exists which acts in the opposite direction, the correlation energy. This is already included in the MINDO/3 parametrization, whilst it has to be introduced explicitly into an "*ab initio*" method, either through configuration interaction or other methods. There is no lack of examples in the bibliography[28] in which the introduction of the correlation energy has dramatically changed the relative stability of different compounds. It is to be hoped that in the 1,3-dipolar cycloaddition the correlation energy favours the asynchronous transition states, for two reasons. In the first place, because the frontier orbitals of the system in the reaction studied come together as the asynchronism increases, because of which a configuration interaction will favour the asynchronous structures. In the second place, because the asynchronous transition states present a greater electronic localisation, and it has been pointed out in the bibliography[29,30] that the correlation energy is greater as the localisation increases.

In conclusion, in spite of the limitations of the method used, for the addition of both carbonyl and azomethine ylides to ethylene, a highly asynchronous transition state may be expected, given the great difference of energy between the two mechanism. This conclusion is more obvious for the case of carbonyl ylide. A mechanism in two steps, such as the one which appears in the present calculations, must be affirmed with greater reservations, since the second energy barrier is smaller.

In order to give a definitive value to the conclusions of this study we consider it indispensable to make an "*ab initio*" calculation, with a sufficiently extended basis set, introducing the correlation energy and effecting a complete relaxation of geometry, in the asynchronous zone of the potential surface.

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