*Tetrahedron* Vol. 38, No. 12, pp. 1847 to 1852, 1982.
Printed in Great Britain.

0040-4020/82/121847-06$03.00/0

# THEORETICAL INTERPRETATION OF EXPERIMENTAL DATA ON 1,3-DIPOLAR CYCLOADDITIONS

J. M. LLUCH

Departamento de Química Física, Universidad Autónoma de Barcelona, Bellaterra, Barcelona, Spain

and

J. BERTRÁN*

Departamento de Química Física, Universidad de Sevilla, Sevilla, Spain

(*Received in U.K.* 17 *December* 1981)

**Abstract**—Using the MINDO/3 method it has been shown that the two-steps mechanism, proposed in a previous paper[1] for the 1,3-dipolar cycloadditions, is compatible with several existing experimental results. Firstly, the effects of the introduction of different substituents on the mechanism of the cycloadditions were studied. Secondly, the slight influence of the polarity of the solvent on the reaction rate has been interpreted by solvation calculations. Finally, the stereospecificity observed has been explained.

In a previous paper,[1] the cycloaddition of carbonyl and azomethine ylides to ethylene was analysed using the semiempirical MINDO/3 method. The results showed for both cycloadditions a two-step mechanism passing through two transition states separated by an intermediate. In the first transition state, where the interaction between the reactants is still weak, only the first sigma bond is being formed. The start of the formation of the second bond, having already passed through the intermediate, creates the second energy barrier. This mechanism turns out to be highly asynchronous, even when symmetrical reactants were chosen.

Huisgen,[2-5] on the other hand, in disagreeing with the two-step mechanism proposed by Firestone,[6-9] affirms that only a concentrated mechanism could explain the ensemble of existing experimental data. Among the diverse experimental facts mentioned by both authors in this controversy, we shall cite here the ones referring to the solvent effects, stereochemistry, and reactivity scale of dipolarophiles. Firstly it has been found[3] that the effect of the polarity of the solvent on the rate of 1,3-dipolar cycloadditions is very slight. Secondly, these cycloadditions are highly stereospecific.[5,10] It can be expected that the rotation of the primitively ethylenic bond could come about in the intermediate before cyclization in a two-step mechanism. Finally, it has been shown that unsubstituted alkenes and alkynes add slowly to the 1,3-dipoles, while dipolarophiles with electron-releasing or electron-attracting substituents have greater reactivity. In representing logarithms of the cycloaddition rate constants of a given 1,3-dipole with different dipolarophiles, versus the experimental ionization potential of the same, Huisgen[4,11] obtains U-shaped curves, with the minimum corresponding to the reaction with no substituents.

This fact has been interpreted using Sustmann's classification[12-13] by means of the perturbation theory within Fukui's frontier orbital approximation.[14] Sustmann classifies the 1,3-dipolar cycloaddition as three different kinds, depending on which HOMO–LUMO interaction is dominant in the reactants. Introducing any substituent alters the energy differences between the frontier orbitals. When the HOMO–LUMO energy differences are similar and both high, the rate of reaction will be minimal.

More thorough calculations of the potential surfaces of these cycloadditions have been performed by various authors.[15-18] We shall emphasize the ones done by Leroy *et al.* on a wide variety of 1,3-dipoles and dipolarophiles, evaluating the energy by an *ab initio* method.[19-26] These calculations coincide essentially with Huisgen's in attributing a variable but not very large asynchronism to the 1,3-dipolar cycloadditions. Also, the introduction of substituents which increase the charge transfer diminishes the activation barrier. Nevertheless, these calculations must be accepted with caution because of the great limitations they were carried out under. Limited basis sets are used, the correlation energy is not adequately introduced, and the enormous amount of calculation time required result in serious methodical restrictions. Therefore, Leroy has confined his study to the exploration of the synchronous zone of the surface, using one independent variable and carrying out a partial optimization of the geometry. A method that took into account the correlation energy and that permitted a complete exploration of the potential surface could probably yield different results. The conditions required with a reasonable expenditure of calculation time can only be fulfilled by using a semiempirical method like MINDO/3.

That is the reason the MINDO/3 method has been used in this paper, our objective being to demonstrate that the two-step mechanism proposed in a previous paper[1] also explains the experimental results. To this end, the effects of the introduction of diverse substituents in the mechanism of the 1,3-dipolar cycloadditions previously analysed have been studied. Next, calculations that have allowed the theoretical influence of the solvent on these reactions to be determined were carried out. Finally, the problem of stereochemistry is discussed.

## METHOD OF CALCULATION

Since the whole evaluation of the potential hypersurface is impossible for the majority of chemical reactions of interest, two kinds of alternate methods are used to locate the transition states. Those of the first type locate them starting from the evaluation of surfaces of reduced dimensionality. So, some authors arbitrarily eliminate degrees of freedom, which generally implies too severe restrictions. Those methods which imply in some way the minimization of the potential energy are more elaborate. The most common method is the reaction coordinate one: one or two degrees of freedom are chosen as independent variables, and the rest of the geometric parameters are optimized for each set of values for the former, the energy being minimized. However, an incorrect selection of the independent variables can give rise to erroneous results. To avoid this danger, methods of the second type allow for the free and simultaneous variation of all the degrees of freedom by directly locating the transition states on the potential hypersurface, but without having to construct it. From the second type we have used McIver and Komornicki's method,[27] which locates stationary points through the minimisation of the square of the gradient norm (SIGMA program) and determines its nature by calculating the eigenvalues of the force constant matrix (FORCE program). This method is very efficient but it requires good initial estimates of the stationary points that must be located. To obtain them we have previously explored each surface with the reaction coordinate method, by means of Dewar's MINDO/3 program,[28,29] which uses the D.F.P. (Davidon, Fletcher, Powell) method[30–32] to minimise the energy.

Given that, in a previous paper,[1] the transition vectors of the two transition states showed that two new sigma bonds were formed successively, the same thing is expected to happen in the reactions with substituents. In taking as an independent variable the length of the sigma bond in formation, and optimizing the rest of the geometric parameters for each value of this variable, two energy profiles have been obtained starting from the resultant structures by introducing the substituents in the transition states of the first reactions. The two maximums and the minimum which appear in each of the reactions studied have served as a starting point for the direct locating method of the respective transition and intermediate states.

To carry out solvation calculations, the GEOMO program[33] has been used. In this program the spherical cavity model[34–36] is adopted and the SCF equations for a system of electrons and nuclei surrounded by a dielectric continuum are derived by using a multipolar expansion of the interaction energy. Apart from the constant $\epsilon$ which is assumed to be equal to the static dielectric constant of the medium, the only parameter in this model is the radius of the cavity. For neutral molecules, it has been defined by Onsager[37] as the radius of a sphere having a volume equal to the molecular volume. The choice is more ambiguous for intermediate species and transition states in which no molecular volume measurement is feasible. Within the domain of validity of the Clausius–Mossoti equation, the molecular volume appears to be proportional to the electronic polarizability $\alpha$.[38] This property will allow us to define the radius of the cavity objectively. To determine the the electronic polarizability the method used is a variational one[39] which gives rather good results even with semiempirical wavefunctions. To avoid systematic errors the following procedure has been used:[40] the electronic polarizability was computed for intermediate species, transition states, and reagents, and the ratio of the volumes was set equal to the ratio of polarizabilities. For the reagents the total experimental volume and the total theoretical polarizability are assumed to be the sum of these magnitudes for each reagent.

## RESULTS AND DISCUSSION

Firstly, we shall study cycloadditions with the inclusion of substituents, with examples of the three types given by Sustmann. In Fig. 1 the HOMO–LUMO energy differences (in eV) between the reactants are shown for each case studied. The dominant interaction in the cycloadditions of the carbonyl ylide to acrolein and acrylonitrile, and of the azomethine ylide to acrolein is HOMO (1,3-dipole)–LUMO (dipolarophile) (type I). In the cycloaddition of the formylcarbonyl ylide to ethylene both HOMO-LUMO differences are equivalent (type II). In the case of the cycloaddition of the carbonyl ylide to hydroxyethylene, the HOMO(dipolarophile)–LUMO(1,3-dipole) (type III) is dominant.

Although these cycloadditions present diverse characteristics, they maintain the same common denominator as the cycloadditions with no substituents discussed in a previous paper:[1] all of them occur in two steps with the successive formation of both sigma bonds, and as a result, with a very high asynchronism. In Table 1 the sigma bond lengths (Å), the increase in energy (kcal/mol) with respect to the reactants, and the charge transfer for the three stationary points of each cycloaddition, including for comparative purposes the cycloadditions without substituents, are shown. In all cases the transition vec-

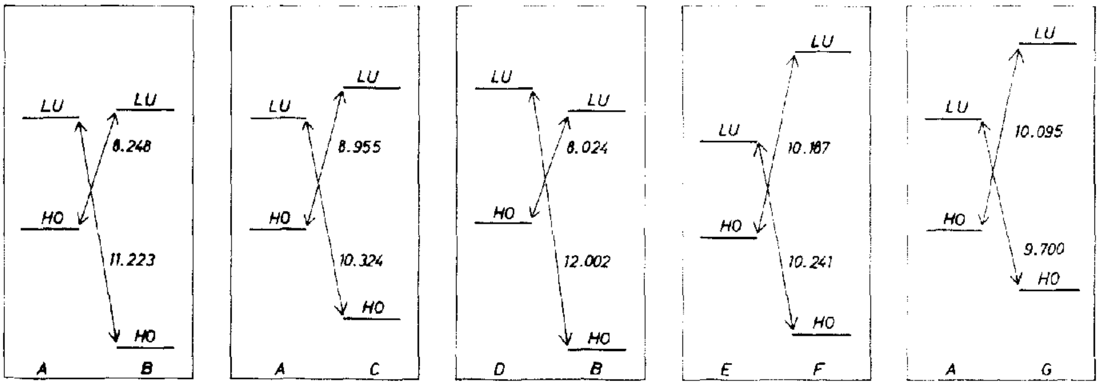

Fig. 1. Energy disposition of the frontier orbitals of the reactants of the different cycloadditions. (*A*) Carbonyl ylide; (*B*) acrolein; (*C*) acrylonitrile; (*D*) azomethine ylide; (*E*) formylcarbonyl ylide; (*F*) ethylene; (*G*) hydroxyethylene.

Table 1. Sigma bond lengths, increase in energy and charge transfer for the stationary points of each cycloaddition

| | | TS 1 | | | | Intermediate | | | | TS 2 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | C2C4 | C3C5 | Δ E | t | C2C4 | C3C5 | Δ E | t | C2C4 | C3C5 | Δ E | t |
| Carbonyl + Ethylene | | 2.10 | 4.30 | 12.2 | -0.006 | 1.62 | 3.90 | 6.6 | 0.068 | 1.59 | 3.12 | 7.9 | 0.070 |
| Carbonyl + Acrolein | Subst. side | 4.27 | 1.94 | 18.7 | 0.029 | 4.09 | 1.69 | 17.7 | 0.100 | 3.08 | 1.63 | 19.9 | 0.135 |
| | Non-subst. side | 2.23 | 4.27 | 10.7 | 0.044 | 1.53 | 3.63 | -7.9 | 0.585 | 1.54 | 3.11 | -7.2 | 0.538 |
| Carbonyl + Acrylonitrile | | 2.16 | 4.28 | 11.7 | 0.017 | 1.58 | 3.91 | 1.6 | 0.201 | 1.56 | 3.15 | 2.3 | 0.230 |
| Carbonyl + Hydroxyethylene | | 2.14 | 4.37 | 11.7 | -0.055 | 1.60 | 4.11 | 3.0 | -0.251 | 1.58 | 3.19 | 4.8 | -0.365 |
| Formylcarbonyl + Ethylene | Subst. side | 3.89 | 1.85 | 21.26 | 0.071 | 3.83 | 1.73 | 21.19 | 0.089 | 3.09 | 1.66 | 22.2 | 0.105 |
| | Non-subst. side | 2.06 | 4.13 | 12.9 | -0.045 | 1.62 | 3.70 | 8.46 | -0.056 | 1.61 | 3.43 | 8.49 | -0.051 |
| Azomethine + Ethylene | | 1.96 | 4.06 | 17.5 | 0.092 | 1.68 | 3.79 | 16.2 | 0.217 | 1.63 | 2.94 | 18.2 | 0.250 |
| Azomethine + Acrolein | | 2.20 | 4.23 | 12.0 | 0.093 | 1.54 | 3.86 | -6.9 | 0.686 | 1.55 | 2.72 | -1.4 | 0.526 |

tors of both transition states clearly show the two steps in which the reactions occur. As a typical example, the two transition states for the cycloaddition of the azomethine ylide to acrolein have been drawn (Fig. 2), indicating the direction and module of the transition vector for each atom. In the first transition state a strong displacement of atoms 2 and 4 is produced, corresponding to the formation of the $C_2C_4$ bond, while the $C_3C_5$ bond formation starts much more slowly. But in the second transition state, atoms 3 and 5 are the ones which form the $C_3C_5$ bond more rapidly, while $C_2C_4$ is unaltered.

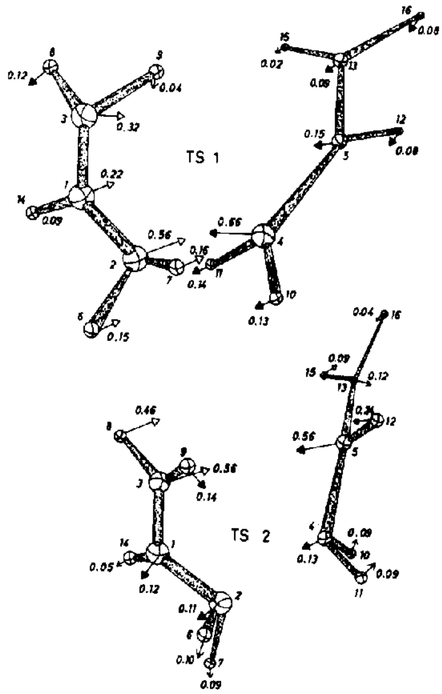

Fig. 2. Cycloaddition of azomethine ylide to acrolein. First and second transition state, with the transition vector components for each atom.

Regarding the energy, as in the nonsubstituted case, an energy profile analogous to the one proposed by Firestone[6–9] is obtained, with the second transition state presenting a second very small energy barrier respecting the intermediate. To interpret this profile theoretically, the value of the increase in energy of the stationary points respecting the reactives has been broken down into two contributions: the geometric distortion energy of the initial fragments and the interaction energy between them. The values obtained, including the cycloadditions with no substituents, are given in Table 2. It can be observed that, in general, the distortion energy increases as the reaction goes on, which corresponds to the change of geometry that the reactants undergo as the process progresses towards the products. At the same time, as Fukui established, the frontier orbitals of both fragments draw near to each other as the distortion increases. The interaction energy is repulsive in the first transition states, which indicates that the exchange term is stronger than the charge transfer one, which remains small at the beginning of the reaction. This becomes important as of the zone of the intermediate, when the frontier orbitals are already quite near and the overlap between the molecular orbitals of both reactives is large. Accordingly, the charge transfer is stronger than the repulsive term, in the intermediate as well as in the second transition state, therefore the interaction energy is negative. As a result of the evolution of all these

Table 2. Decomposition of the increase in energy of the stationary points with respect to the reactives

| | TS 1 | | | Intermediate | | | TS 2 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Dist. | Interac. | Δ E | Dist. | Interac. | Δ E | Dist. | Interac. | Δ E |
| Carbonyl + Ethylene | 3.6 | 8.6 | 12.2 | 20.7 | -14.1 | 6.6 | 29.3 | -21.4 | 7.9 |
| Carbonyl + Acrolein | 2.8 | 7.9 | 10.7 | 43.8 | -51.7 | -7.9 | 39.6 | -46.8 | -7.2 |
| Carbonyl + Acrylonitrile | 3.3 | 8.4 | 11.7 | 23.1 | -21.5 | 1.6 | 30.9 | -28.6 | 2.3 |
| Carbonyl + Hydroxyethylene | 3.5 | 8.2 | 11.7 | 26.2 | -23.2 | 3.0 | 40.9 | -36.1 | 4.8 |
| Formylcarbonyl + Ethylene | 3.9 | 9.0 | 12.9 | 22.49 | -14.03 | 8.46 | 25.14 | -16.65 | 8.49 |
| Azomethine + Ethylene | 8.1 | 9.4 | 17.5 | 19.2 | - 3.0 | 16.2 | 25.5 | - 7.3 | 18.2 |
| Azomethine + Acrolein | 4.4 | 7.6 | 12.0 | 52.5 | -59.4 | -6.9 | 40.9 | -42.3 | -1.4 |

contributions it can be concluded that the first energy barrier is mainly due to the interaction energy and, therefore, due to the exchange energy, which reflects the effect of the steric impediment. On the other hand, the second energy barrier is due to the geometric distortion of the reactants.

Another general point has to do with the order of formation of the sigma bonds. In dealing with cycloadditions in which one of the reactants is asymmetric, and since the mechanism is in two steps, two possible asynchronous paths exist by which cycloaddition can take place, depending on which end of the asymmetric reactant the first sigma bond is formed. According to the frontier orbital approximation,[14] the first sigma bond should be formed at the end of the asymmetric reactant which has a greater coefficient for the dominant HOMO–LUMO interaction.

Next we shall analyse the particular characteristics of each type of cycloaddition. In a first group of reactions, substituents which reinforced the normal direction of the charge transfer in the reactions that had none, were included. Electron-attracting substituents (–CN, –CHO) were introduced in ethylene, and the three type I cycloadditions referred to before (Fig. 1) were studied. Since the charge transfer in these cases will be towards the dipolarophile, and since the nonsubstituted carbons in acrolein as well as in acrylonitrile are the ones that have the greater LUMO coefficients, the first sigma bond should be formed on the side opposite the substituent. In effect, this was verified for the cycloaddition of the carbonyl ylide to acrolein, the two series of stationary points corresponding to the two possible asynchronous paths (Table 1) being present. If the first sigma bond is formed by the substituted carbon of acrolein, the charge transfer is small, because the normal cyclic evolution of the electrons takes place in the opposite direction. The first transition state appears very late in the reaction coordinate and with a substantial distortion that elevates its energy considerably, although the second transition state is the one that imposes a barrier to the reaction. But, the energy consumption is much smaller if the first sigma bond is formed by the nonsubstituted side of acrolein, in agreement with the frontier orbital approximation.[14] In conclusion, the introduction of electron-attracting substituents in ethylene, which therefore reduce the HOMO–LUMO difference, causes an increase in charge transfer and a stabilization of the whole energy profile, with respect to the corresponding cycloadditions without substituents. In sum, the first transition state is found sooner in the reaction path, since the charge transfer term rapidly compensates for the repulsive terms, imposing a smaller energy barrier to the reaction. The increase in the charge transfer is especially important in the zone of the intermediate and in the second transition state, both of which are delayed but which appear to be enormously stabilized. This is better appreciated in the case of the cycloaddition of the azomethine ylide to acrolein, where the second transition state, having no substituents, was the one that imposed the barrier. Its first transition state has more energy when the –CHO group is introduced in ethylene.

In the second phase, substituents with electronic effects in a direction opposite to the normal charge transfer with no substituents were introduced. In the first place, the –CHO group in the carbon ylide and then the –OH group in ethylene (Fig. 1). The introduction of the –CHO group in the ylide practically makes the two HOMO–LUMO energy differences equal, obtaining a type II cycloaddition. Both interactions are therefore equivalent, the formation of the first sigma bond on a different side of the asymmetric reactive being favoured by each of them. It was necessary to locate the two series of stationary points corresponding to both possibilities. If the first sigma bond is formed on the substituted side of the ylide, which has the greater HOMO coefficient, the charge transfer is small (Table 1) and towards ethylene, but the energy profile imposes a strong barrier to the reaction. On the other hand, if the first sigma bond is formed on the non-substituted side, which has the greater LUMO coefficient, the charge transfer, which sustains itself at a low level, is reversed, and the reaction goes on the more favourable path. In comparison with the non-substituted cycloaddition, the inclusion of the –CHO group in the ylide destabilizes the energy profile. The first transition state is delayed, imposing a greater barrier to the reaction. It must be emphasized in this particular case that, although a second transition state exists mathematically, the energy barrier that separates it from the intermediate is so small that, from a chemical point of view, it has more to do with a reaction in two stages than in two steps. On the other hand, the introduction of the –OH group in ethylene makes the HOMO(dipolarophile)–LUMO(1,3-dipole) reaction dominant (Fig. 1), obtaining a type III cycloaddition. Since the non-substituted carbon of hydroxyethylene is the one which has the greater HOMO coefficient, the first sigma bond must be formed by this side. The charge transfer is reversed, becoming quite significant as of the intermediate, with the consequential stabilization of the entire energy profile with respect to the non-substituted case. In sum, the first transition state is formed sooner in the reaction path and imposes a smaller energy barrier.

It can be deduced from the set of reactions studied that the introduction of substituents which alter the relative energy of the frontier orbitals varies the rate of the reaction, which is minimal for type II cycloaddition, where both HOMO–LUMO energy differences are great. This conclusion may be better appreciated if the energy barriers of the cycloadditions of the carbonyl ylides to different dipolarophiles are represented, versus the energy of the HOMO or the LUMO of the same, where each of their U-shaped curves, analogous to the experimental ones given by Huisgen versus the ionization potential, are obtained. In Fig. 3 one of these curves is shown, the one corresponding to the representation versus the LUMO. Actually, the only representation that would make sense is the one the most favorable HOMO–LUMO energy difference. However, since the HOMO of the carbonyl ylide is fixed, diminishing the energy of the LUMO of the dipolarophile diminishes the HOMO(carbonyl)–LUMO(dipolarophile) difference, accelerating the reaction and obtaining the right side of the curve represented in Fig. 3. On the other hand, increasing the energy of LUMO, in the case of hydroxyethylene, increases the HOMO energy, so much that the HOMO(dipolarophile)–LUMO(carbonyl) interaction becomes dominant, decreasing the barrier and creating the left side.

Another experimental aspect to be studied was the one having to do with the solvent effects. The values of the increase in energy for the cycloadditions of the carbonyl and azomethine ylides to ethylene and acrolein in solvents of different dielectric constants have been

Table 3. Effect of different solvents in the cycloaddition of the azomethine ylide to ethylene

| | TS 1 | | Intermediate | | TS 2 | |
|---|---|---|---|---|---|---|
| $\varepsilon$ | $\Delta$ E | Transfer | $\Delta$ E | Transfer | $\Delta$ E | Transfer |
| 1 | 17.5 | 0.092 | 16.2 | 0.217 | 18.2 | 0.250 |
| 2 | 17.4 | 0.109 | 15.1 | 0.268 | 17.5 | 0.293 |
| 5 | 17.2 | 0.128 | 13.6 | 0.325 | 16.7 | 0.340 |
| 10 | 17.1 | 0.138 | 12.8 | 0.352 | 16.2 | 0.361 |
| 78 | 16.9 | 0.149 | 11.8 | 0.381 | 15.7 | 0.383 |

recalculated, using the GEOMO program and maintaining the geometries of the different stationary points and reactives fixed. As a representative example, the results obtained for the cycloaddition of the azomethine ylide to ethylene, on introducing the effects of solvents characterized by different $\epsilon$, from $\epsilon = 1$, in the case of vacuum, to $\epsilon = 78$, in the case of water, are given in Table 3. The values of the increase in energy and the charge transfer for each of the three stationary points are also given. As $\epsilon$ increases, the charge transfer does, and the energy profile is stabilized. This indicates that the effect of the solvent is analogous to the one produced by the introduction of a substituent that reinforces the normal charge transfer. The effect of the first transition state, which is the one that imposes the barrier, is very slight, which agrees with the weak experimental influence of the solvent polarity on the rate. The stabilization is much greater in the second transition state, which in this particular case and as happened with the introduction of substituents, ceases to be the highest energy point of the profile. The influence is maximum on the intermediate, where there is a greater charge separation, augmenting in this way the two step nature of the cycloaddition. All these characteristics are general for the set of 1,3-dipolar cycloadditions studied. In the case of the cycloadditions to acrolein the effects are qualitatively identical, although of greater quantity, due to the sum of the two factors which operate in the same direction: the solvation and the -CHO group in ethylene.

Finally, we shall study the third experimental fact, referring to the stereochemistry of the reaction. If the primitively double bond of the ethylenic dipolarophile were already a single bond in the intermediate, it would have a small rotation barrier, for which reason a rotation could occur before the intermediate cyclised. Nevertheless, Mulliken's population analysis[41] shows for all the cycloadditions studied that the bond in question maintains a high double-bond character, not only in the intermediate, but even in the second transition state. So, for example, for the cycloaddition of the carbonyl ylide to ethylene, this index is 2.116 in isolated ethylene, 1.786 and 1.728, respectively, in the intermediate and the second transition state, and going down to 1.191 in the final product. This should create a rotation barrier large enough to maintain the stereospecificity. In effect, this was verified by studying the rotation barrier of the C-C bond of ethylene in the intermediate of this cycloaddition. A value of 16 kcal/mol was obtained, which is very high if compared with the 1.3 kcal/mol required to form the second sigma bond.

In conclusion, the mechanism in two steps, derived from our theoretical calculations by means of the MINDO/3 method, is compatible with the experimental results referring to the solvent effects, stereochemistry, and reactivity scale of dipolarophile. However, from a theoretical point of view, and given the limitations of the calculation method used, for this mechanism to attain a definitive value, an *ab initio* calculation would have to be done with a sufficiently extended basis set, introducing the correlation energy and carrying out a complete optimization of the geometry in the asynchronous zone of the potential surface. Unfortunately, at present, the realisation of such a project is impossible because of the enormous amount of calculation time required.

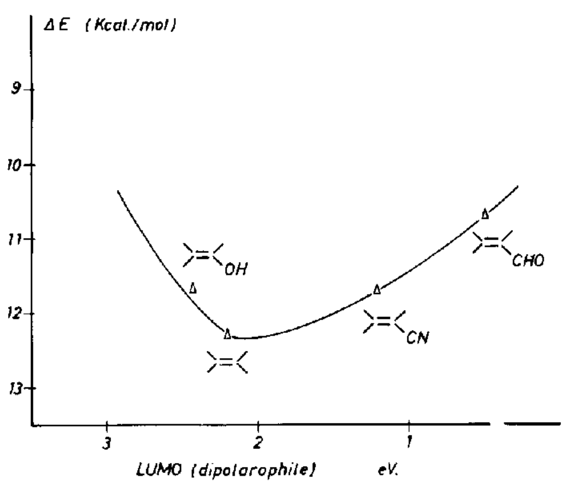

Fig. 3. Energy barriers of the cycloadditions of the carbonyl ylide to different dipolarophiles, versus the energy of the LUMO of these.

## REFERENCES

[1] J. M. Lluch and J. Bertrán, *Tetrahedron* **35**, 2601 (1979).
[2] R. Huisgen, *Angew. Chem. Int. Ed. Engl.* **2**, 565 (1963).
[3] R. Huisgen, *Ibid* **2**, 633 (1963).
[4] R. Huisgen, *J. Org. Chem.* **33**, 2291 (1968).
[5] R. Huisgen, *Ibid.* **41**, 403 (1976).
[6] R. A. Firestone, *Ibid.* **33**, 2285 (1968).
[7] R. A. Firestone, *J. Chem. Soc., A* 1570 (1970).
[8] R. A. Firestone, *J. Org. Chem.* **37**, 2181 (1972).
[9] R. A. Firestone, *Tetrahedron* **33**, 3009 (1977).
[10] R. Huisgen, *Pure and Appl. Chem.* **53**, 171 (1981).
[11] W. Bihlmaier, R. Huisgen, H. V. Reissing and S. Voss, *Tetrahedron Letters* 2621 (1979).
[12] R. Sustmann, *Ibid.* 2717, 2721 (1971).
[13] R. Sustmann and H. Trill, *Angew. Chem. Int. Ed. Engl.* **11**, 838 (1972).
[14] K. Fukui, *Fortschr. Chem. Forsch.* **15**, 1 (1970); K. Fukui, T. Yonezawa and H. Shingu, *J. Chem. Phys.* **20**, 722 (1952); K.

Fukui, T. Yonezawa, C. Nagata and H. Shingu, *Ibid.* **22**, 1433 (1954).
[15]D. Poppinger, *J. Am. Chem. Soc.* **97**, 7486 (1975).
[16]D. Poppinger, *Aust. J. Chem.* **29**, 465 (1976).
[17]M. J. S. Dewar, *Disc. Faraday Soc.* **62**, 197 (1977).
[18]M. J. S. Dewar, S. Olivella and H. S. Rzepa, *J. Am. Chem. Soc.* **100**, 5650 (1978).
[19]G. Leroy and M. Sana, *Tetrahedron* **31**, 2091 (1975).
[20]G. Leroy, M. T. Nguyen and M. Sana, *Ibid.* **34**, 2459 (1978).
[21]G. Leroy and M. Sana, *Ibid.* **32**, 709 (1976).
[22]G. Leroy, M. T. Nguyen and M. Sana, *Ibid.* **32**, 1529 (1976).
[23]G. Leroy, M. Sana, L. A. Burke and M. T. Nguyen, *Contribution to the Theoretical Study of Reactions Mechanism*, in *Quantum Theory of Chemical Reactions*, (Edited by R. Daudel, A. Pullman, L. Salem and A. Veillard), Vol. 1, p. 91. Reidel, Dordecht, Holland (1980).
[24]G. Leroy and M. Sana, *Tetrahedron* **32**, 1379 (1976).
[25]G. Leroy, *Ann. Soc. Sci. Bruxelles* **92**, 79 (1978).
[26]N. Minh Tho, Doctoral Thesis, Louvain-La-Neuve (1980).
[27]J. W. McIver and A. Komornicki, *J. Am. Chem. Soc.* **94**, 2625 (1972).
[28]R. C. Bingham, M. J. S. Dewar and D. H. Lo, *Ibid.* **97**, 1285 (1975).
[29]M. J. S. Dewar, H. Metiu, P. J. Student, A. Brown, R. C. Bingham, D. H. Lo, C. A. Ramsden, H. Kollmar, P. Werner and P. K. Bischof, Program QCPE No. 279.
[30]W. C. Davidon, *Comput. J.* **10**, 406 (1968).
[31]R. Fletcher, *Ibid.* **3**, 33 (1965).
[32]R. Fletcher and M. J. D. Powell *Ibid.* **6**, 163 (1963).
[33]D. Rinaldi, *Comput. & Chem.* **1**, 108 (1976) and GEOMO (QCPE No. 290).
[34]J. Hylton, R. E. Christoffersen, G. G. Hall, *Chem. Phys. Lett.* **24**, 501 (1974); *Ibid.* **26**, 501 (1974).
[35]J. Hylton, R. E. Christoffersen and G. G. Hall, *J. Am. Chem. Soc.* **98**, 7191 (1976).
[36]J. L. Rivail and D. Rinaldi, *Chem. Phys.* **18**, 233 (1976).
[37]L. Onsager, *J. Am. Chem. Soc.* **58**, 1486 (1936).
[38]J. Barriol and A. Weisbecker, *C.R. Acad. Sci.* **259**, 2831 (1964).
[39]D. Rinaldi and J. L. Rivail, *Theor. Chim. Acta* **32**, 243 (1974).
[40]J. Bertrán, A. Oliva, D. Rinaldi and J. L. Rivail, *Noveau Journal de Chimie* **4**, 209 (1980).
[41]R. S. Mulliken, *J. Chem. Phys.* **23**, 1833 (1955).