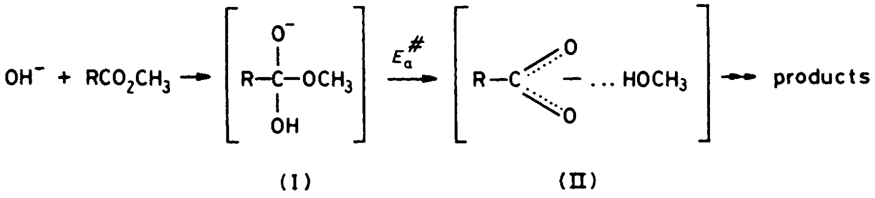
The Second Step of the $B_{AC}2$ Mechanism for Neutral Esters: a Theoretical Study

J. Joaquín Maraver * and Enrique Sánchez Marcos
Department of Physical Chemistry, Faculty of Chemistry, University of Sevilla, C/ Tramontana s/n, 41012 Sevilla, Spain
Juan Bertrán
Department of Physical Chemistry, Faculty of Science, University of Barcelona, Bellaterra, Barcelona, Spain

The semiempirical MINDO/3 method has been used to study the second step of the $B_{AC}2$ mechanism of neutral esters. Our results show that acyl–oxygen bond dissociation precedes hydroxylic hydrogen transfer.

Carbonyl addition reactions in the gas phase have been more extensively investigated than any other nucleophilic reaction.[1] From recent experiments using ion cyclotron resonance spectroscopy, the steps shown in the Scheme have been proposed[2] to describe the $B_{AC}2$ mechanism for methyl esters.



Scheme.

The gas-phase $B_{AC}2$ mechanism has been assumed to involve a tetrahedral intermediate, as in solution. In these experiments, it has been postulated that the second step, with potential barrier $E_a^{\#}$, is controlled by the passage of the hydroxylic hydrogen atom to the methoxy group of the intermediate (I) before breakage of the acyl–oxygen bond. This interpretation is based on the theoretical study carried out by Tomasi *et al.*[3] However, the problem approached by Tomasi is somewhat different in that it corresponds to the basic hydrolysis of formamide.

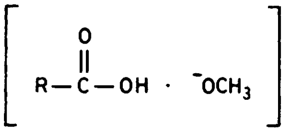
More recently, DePuy *et al.*,[4] using both ion cyclotron resonance spectroscopy and the 'flowing afterglow' technique, have suggested that this reaction ($B_{AC}2$) is most apparent if the proton-attacking base is removed by the departing methoxide ion. In this situation the potential barrier $E_a^{\#}$ is governed by the breakage of the acyl–oxygen bond, and instead of the complex (II), the complex (III) might be more relevant.

Thus there is controversy about the timing of intramolecular proton transfer to the OMe group.

The aim of the present paper is to distinguish between the aforementioned possibilities for the second step of the $B_{AC}2$ mechanism, *i.e.* whether breakage of the acyl–oxygen bond takes place before hydroxylic hydrogen transfer, or *vice versa*. In order to elucidate these points we have studied the basic hydrolysis of methyl formate, for which there are experimental results for the gas phase.[2,4]

Method

Given the impossibility of calculating the potential hypersurface for the majority of chemical reactions, a good approximation consists in taking one or two geometrical parameters as independent variables in order to reduce the dimensions of the potential hypersurface. For each value of the independent variable all the remaining geometrical parameters of the system are optimized. Because of the number of parameters to be optimized, the semiempirical MINDO/3 method[5] has been used. It has been shown that this method is adequate for the study of chemical reactivity.[6] The GEOMO program,[7] in which geometric optimization is carried out by the Rinaldi algorithm,[8] has been used.



(III)

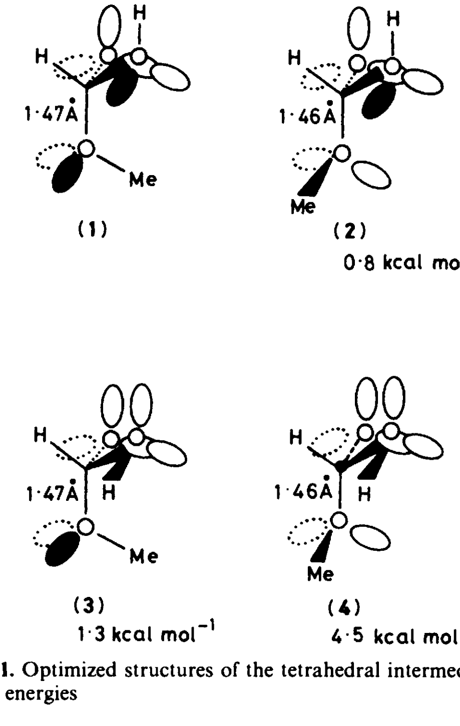


Figure 1. Optimized structures of the tetrahedral intermediate (I) and relative energies

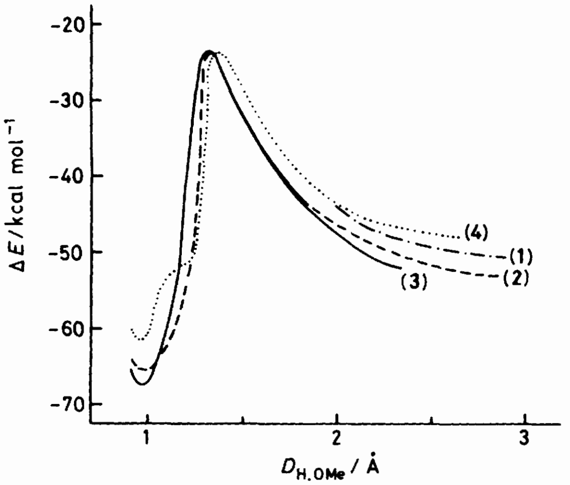


Figure 2. Potential energy curves corresponding to the structures (**1**)—(**4**), obtained by taking as independent variable the hydroxylic hydrogen–methoxylic oxygen distance. The zero energy level for each reaction has been chosen as the sum of the energies of all separate reactants

Results and Discussion

The optimization of the geometric parameters was performed on the nine different staggered conformations of the intermediate (I) by the MINDO/3 method. Figure 1 shows the four stable different conformations that have been found. The relative energies of the species (**1**)—(**4**) with respect to the most stable conformation [structure (**1**)], as well as the acyl–oxygen bond lengths, are shown in the Figure. All the conformations have closed energies. The acyl–oxygen bond, of length *ca.* 1.46 Å in all the conformations, is markedly longer than in methyl formate (1.32 Å). On the other hand, theoretical results[9] for the nine different staggered conformations of the intermediate (I; R = H) have shown a weakening and a lengthening of the acyl–oxygen bond as well as high electron densities on the methanoate group. This suggests that the fission of the acyl–oxygen bond has started in the intermediate itself.

Initially, we shall discuss the results for hydrogen transfer from the hydroxylic group to the methanoate group corresponding to the four stable conformations. We shall then discuss the results for acyl–oxygen bond fission in the same conformations.

Figure 2 shows the potential energy curves for hydrogen transfer from the hydroxylic group to the methanoate group corresponding to the four stable conformations. These energy profiles were obtained by optimizing all the remaining geometrical parameters for each value of the hydroxylic hydrogen–methoxylic oxygen distance. The range of the independent variable oscillates from an average value of 2.5 Å for the four conformations to a final value of *ca.* 1.0 Å. All the energy profiles are similar and show maxima at about 1.34 Å. The potential barriers are about 30 kcal mol^{-1}.* In these structures the intramolecular hydrogen has still not been transferred: the distance from the hydrogen atom to the methoxylic oxygen is greater (1.34 Å) than the distance to the hydroxylic oxygen (1.03 Å). After the energy maximum is reached a sharp fall in potential energy is observed. This is linked to the breaking of the C–OMe bond; only in the last phase is the hydrogen transfer from the hydroxylic group to the methanoate group achieved. The products from the four stable conformations are the same: formate anion and methanol. It is noteworthy that, in spite of our facilitating intramolecular transfer of hydrogen by the choice of independent variable, transfer is achieved only after breaking of the acyl–oxygen bond.

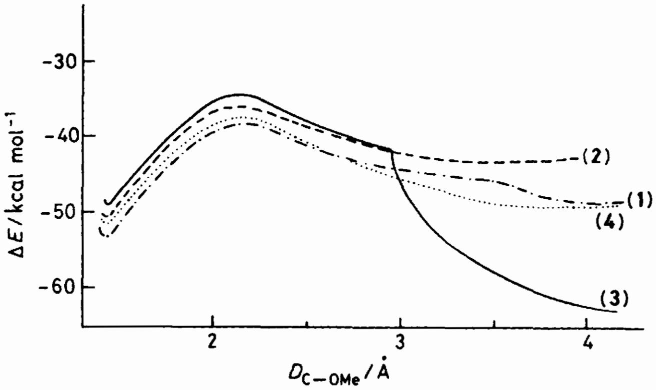


Figure 3. Potential energy curves corresponding to the structures (**1**)—(**4**), obtained by taking as independent variable the carbon–methoxylic oxygen distance

Let us now analyse the results for the decomposition of the intermediate (I; R = H), taking the length of the carbon–methoxylic oxygen bond as the independent variable. Figure 3 shows the potential energy curves obtained for the four stable conformations of the intermediate (I; R = H). Again all the curves are similar. For a carbon–methoxylic oxygen distance of 2.2 Å, the curves show a potential barrier of *ca.* 14 kcal mol^{-1} with respect to the energy of the intermediates. In view of the slow fall of the potential curves after the respective transition states, the geometrical parameter taken is regarded as a good representation of the reaction co-ordinate, in contrast with the previous case.

On the other hand, there is a clear difference in the evolution of one of the potential energy curves during the last step of the process. For a value of the variable-independent distance of 3 Å, the potential energy curve of intermediate (**3**) shows a strong stabilization, corresponding to hydrogen transfer from the hydroxylic group to the methanoate group. Thus for the conformation (**3**) the final products are formate anion and methanol, in good agreement with the gas-phase experimental results.[2] In contrast, for other stable conformations of the intermediate (I; R = H), formic acid and methanoate anion are the final products. Looking at the hydroxylic hydrogen–methoxylic oxygen distance (2.5—3.8 Å) for this particular value (3 Å) of the independent variable, we can understand the difference in behaviour of the various stable conformations of the intermediate (I) in the last step of the process. The small value corresponds to the structure belonging to the potential energy curve of conformation (**3**). These results explain why hydrogen transfer in the last step of the process is not observed for the conformations (**1**), (**2**), and (**4**) of the intermediate (I) when we take the carbon–methoxylic oxygen distance as an independent variable.

From the analysis of the potential energy curves obtained taking the aforementioned independent variable, it is obvious that the C–OMe distance suitably describes the reaction co-ordinate for the first phase of the process, whereas the hydroxylic hydrogen–methoxylic oxygen distance is more appropriate for the last phase. If the potential barriers obtained in Figures 2 and 3 (30 and 14 kcal mol^{-1}, respectively) are compared, the breaking of the acyl–oxygen bond is seen to be energetically the more favourable process.

In conclusion, the results presented provide a deeper insight into the second step of the $B_{AC}2$ mechanism. It has been shown theoretically that the breakage of the acyl–oxygen bond occurs before hydrogen transfer to the OMe group. Thus, easy break-

---

* 1 cal = 4.184 J.

age of the C–OMe bond followed by proton transfer would explain the absence of carbonyl oxygen exchange recently observed by Riveros.[10] A complete description of this pathway, which would require the use of *ab initio* calculations with polarization basis set and correlation energy, has not been attempted because of the semiempirical character of this study. Nevertheless, the theoretical implications concerning the timing of the proton transfer may be a good starting point for future research.

References

1 N. M. M. Nibbering, *Recl. Trav. Chim. Pays-Bas*, 1981, **100**, 297.
2 K. Takashima and J. M. Riveros, *J. Am. Chem. Soc.*, 1978, **100**, 6128.
3 G. Alagona, E. Scrocco, and J. Tomasi, *J. Am. Chem. Soc.*, 1975, **97**, 1285.
4 C. H. DePuy, J. J. Grabowski, V. M. Bierbaum, S. Ingemann, and N. M. M. Nibbering, *J. Am. Chem. Soc.*, 1985, **107**, 1093.
5 R. C. Bingham, M. J. S. Dewar, and D. M. Lo, *J. Am. Chem. Soc.*, 1975, **97**, 1285.
6 M. J. S. Dewar, *Chem. Br.*, 1975, **11**, 97.
7 D. Rinaldi, Quantum Chemistry Program Exchange no. 290, 1976.
8 D. Rinaldi, *Comput. Chem.*, 1976, **1**, 109.
9 J. J. Maraver, E. S. Marcos, and J. Bertrán, *An. Quím.*, in the press.
10 K. Takashima, S. M. José, A. T. Do Amaral, and J. M. Riveros, *J. Chem. Soc., Chem. Commun.*, 1983, 1255.

Received 23rd *September* 1985; *Paper* 5/1647