

Ab Initio and DFT Study of the Reaction Mechanism of Diformylketene with Formamide

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Ab initio and DFT calculations have been carried out to study the reaction mechanism between diformylketene and formamide. Gas-phase calculations show that the mechanism is concerted in contrast to the results of a previous paper. However, although it appears there is one single transition state, the characteristics of its structure reveal a very asynchronous reaction mechanism. The reaction is clearly exothermic and as well has a rather small activation energy. Its pseudopericyclic character has been confirmed by calculation of magnetic properties. The effect of solvent has been analyzed by using the Onsager and PCM methods: substantial changes have not been found in solution.

Introduction

The reactions between ketenes and nucleophiles have attracted the attention of many experimental and theoretical chemists.^{1–4} Specifically, the α -oxoketenes are intermediates in several organic reactions and they are a subject of interest from different points of view.^{5–8} In several studies, Birney et al. have emphasized the unusual reactivity of α -oxoketenes because of the preference for [4+2] reactions against the most common [2+2] reactions of ketenes.^{9,10} According to these authors the reactions between formylketene and nucleophiles such as water (similar to that studied in the present paper) have a pseudopericyclic behavior. Working on the original definition of Lemal et al.,¹¹ Birney et al. have examined a large number of pseudopericyclic reactions, which they have found to possess three essential features, namely: very low or zero activation energies, that no pseudopericyclic reaction can be forbidden, and usually planar transition structures.¹⁰ This later feature contrasts with typical pericyclic reactions in hydrocarbons where the need for keeping the orbital overlap leads to very distorted transition structures. Our research group has performed computational studies to elucidate the pericyclic/pseudopericyclic character in several reactions.^{12–15}

One of the many applications of the quantum chemistry is the study of reaction mechanisms, as is the case of the present work. The starting point is the paper by Saripinar et al.¹⁶ where an analysis of the reaction mechanism of *s*-EZ-diformylketene with formamide (Figure 1) is performed by AM1¹⁷ semiempirical calculations. According to their results these authors propose a stepwise mechanism. There are two transition states (TS1 and TS2) and an intermediate of zwitterionic nature (IN). The calculated energies relative to reactants R1 and R2 are the following: TS1, 16.57 kcal/mol; IN, 15.95 kcal/mol; TS2, 24.79 kcal/mol; P, -19.47 kcal/mol. The preceding values lead us to raise the next question: Considering that the energetic difference between TS1 and IN is very small (0.62 kcal/mol) and that semiempirical methods have an insufficient reliability, is it

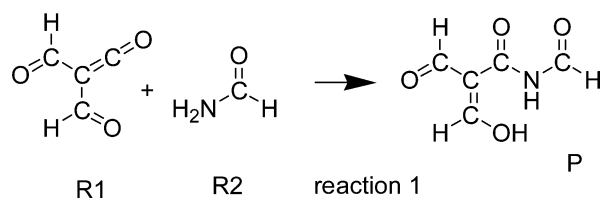


Figure 1. Reaction between diformylketene and formamide.

possible to obtain an improvement in the calculation to give rise to a concerted mechanism? To elucidate this question, in this work we use more reliable methods such as Hartree–Fock and DFT. In addition, trying to reproduce the experimental conditions, we study solvent effects on the mechanism.

Computational Details

Initially the AM1 semiempirical calculations of Saripinar et al. were reproduced. From this starting approximation, successive improvements were performed: first with the Hartree–Fock method and the 3-21G basis set; later with the 6-31G(d,p) basis set; and finally with the 6-31+G(d,p) basis set and the density functional theory (specifically, the Becke3LYP functional). This DFT method involves a substantial improvement since it already incorporates electronic correlation. B3LYP combines the hybrid functional for the exchange energy (dependent on three coefficients) proposed by Becke (B3)¹⁸ with the correlation functional proposed by Lee, Yang, and Parr (LYP).^{18,19} All stationary points were characterized as minima or transition structures by calculating the harmonic vibrational frequencies, using analytical second derivatives. Also, the pathway for the reaction was obtained at the Becke3LYP/6-31+G(d,p) level by using the intrinsic reaction coordinate (IRC) with mass-weighted coordinates.^{20–22} Starting from the transition structure, the reactants and products are unequivocally identified.

Finally the effect to include a solvent was studied. To model the solute–solvent interactions several methods have been proposed. One family of models is referred to as Self-Consistent Reaction Field (SCRf) methods. In this work we use two of these methods: the simple Onsager model²³ and the more

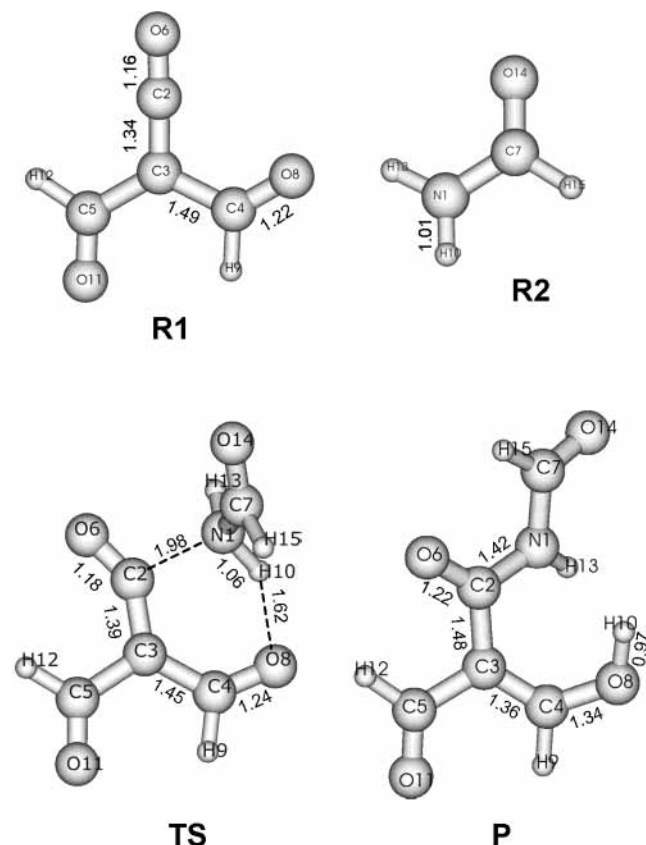
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TABLE 1: Calculated Energies (kcal/mol) Relative to the Reactants

	AM1 ^a	B3LYP/6-31+G(d,p)
TS1 (TS)	16.57	2.22 (2.05) ^b
IN	15.95	
TS2	24.79	
P	-19.47	-15.94 (-23.78) ^b

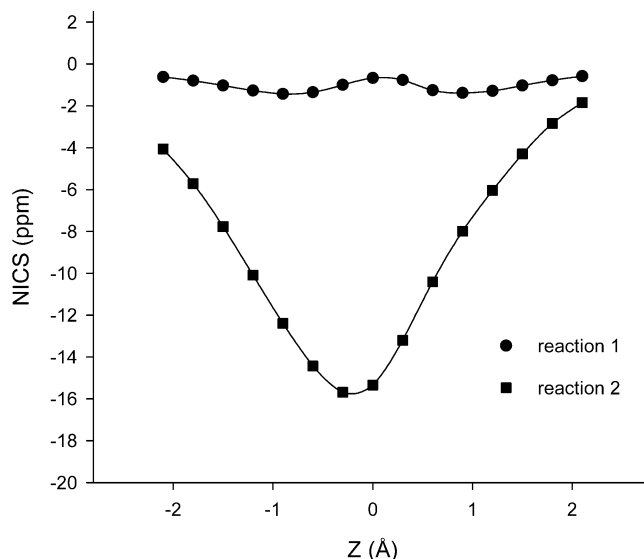
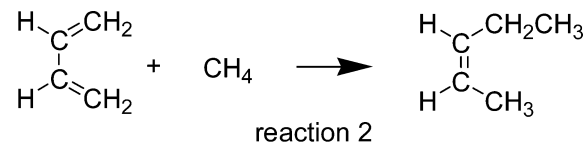
^a Calculated by Saripinar et al.¹⁶ ^b With ZPE correction.**Figure 2.** Geometries obtained at the B3LYP/6-31+G(d,p) level (distances in Å).

sophisticated Tomasi's PCM (Polarized Continuum Model) procedure.²⁴ In both methods the solvent is considered as a "continuum" without structure of uniform dielectric constant ϵ : the *reaction field*. The solute is inside the solvent in a cavity and its dipole moment interacts with the environment creating an induced dipole moment, which electrostatically stabilizes the solute. For the Onsager model the cavity is a sphere of radius a_0 , and for the PCM model the cavity is made up of the union of a series of interlocking atomic spheres. The effect of polarization of the solvent continuum is represented numerically: it is computed by numerical integration rather than by an approximation to the analytical form used in the Onsager model.

All the calculations were performed with the Gaussian98 software package.²⁵

Results and Discussion

Stationary Points. The calculated energies relative to the reactants R1 and R2 are showed in Table 1. Only AM1 predicts a stepwise mechanism. All other methods (of better reliability) lead to a concerted mechanism. Figure 2 shows the geometries of reactants, transition state, and product obtained at the B3LYP/6-31+G(d,p) level.

**Figure 3.** NICS computed along a z -axis defined as perpendicular to the six-atom ring (C2–N1–H10–O8–C4–C3) for the transition structure of reaction 1. Similar calculation for the analogous pericyclic reaction 2.**Figure 4.** Pericyclic reaction analogous to reaction between diformylketene and formamide.

On the other hand, all methods show that the reaction is very exothermic. The activation energy is small: 4.20 kcal/mol with the B3LYP/6-31+G(d,p) method. This value together with the planarity of the transition structure are typical features of pseudopericyclic reactions, as Birney et al. suggested.¹⁰ Figure 2 shows that atoms directly involved in reaction (N1, C2, C3, C4, O8, and H10) are practically coplanar in the transition structure. Another feature of pseudopericyclic reactions is the lack of aromaticity associated with the process. The cyclic loop of pericyclic reactions is known to give rise to aromatic transition states,^{26–30} and the typical disconnection of pseudopericyclic reactions prevents this aromaticity. In a simple way, this fact can be studied by analysis of magnetic properties of the transition structure.³¹ For this purpose we calculate two of these properties: the nucleus independent chemical shift (NICS) reported by Schleyer et al.³² and the anisotropy of the current-induced density (ACID) recently developed by Herges and Geuenich.³³

The magnetic properties were calculated by computing the NMR shielding tensors at the B3LYP/6-31+G(d,p) level, using the CSGT (Continuous Set of Gauge Transformations) method.³⁴

In general, large negative NICS values are associated with aromatic character. Figure 3 shows NICS computed along a z -axis defined as perpendicular to the six-membered ring (C2–N1–H10–O8–C4–C3) and crossing the center of this ring. For comparison, a similar calculation was performed for the most analogous pericyclic reaction (reaction 2 in Figure 4). Whereas reaction 2 shows a marked π aromaticity involving one ring current, reaction 1 (diformylketene with formamide) does not show appreciable aromatization.

The ACID method is a efficient tool for the investigation and visualization of delocalization and conjugation. A cyclic topology in an ACID plot indicates a pericyclic reaction.

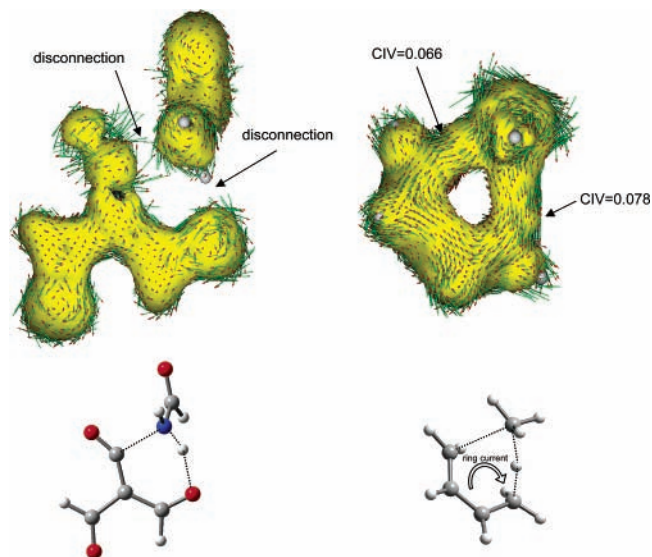


Figure 5. ACID plots for the transition states of reactions 1 and 2. The current density vectors (green arrows with red tips) are plotted onto the isosurface of value 0.03. The vector of the magnetic field is pointing upward. In TS_2 these vectors exhibit a closed circle in the six-membered ring and no disconnection. In TS_1 the topology of delocalized electrons exhibits two clear disconnections.

Disconnections that are characteristic for pseudopericyclic systems are immediately visible by a disconnection in the contiguous system of the ACID boundary surface. Figure 5 presents the ACID isosurface of the transition structures for reactions 1 and 2. TS_2 does not exhibit any disconnection. Moreover, the current density vectors plotted onto the isosurface show the pericyclic nature of the delocalized system: the diatropic ring current forms a loop around the six-membered ring as expected for an aromatic system. The extent of conjugation can be quantified by giving the critical isosurface value, CIV, at which the topology of the ACID boundary surface changes. The values for the two forming bonds in TS_2 are very large (0.066 and 0.078), showing a substantial conjugation. In contrast to TS_2 , the transition structure for reaction 1 shows two clear disconnections.

Reaction Pathway. Starting from the transition structure obtained with the B3LYP method a IRC calculation was done to confirm that the reaction path links the reactants (R1 + R2) with the product P. As Figure 6 shows, no direction was completed, but the end points we reached in both directions allow us to assume that TS_1 is the correct transition state for the reaction. Toward reactants the compounds diformylketene and formamide are clearly distinguished. Toward products a structure where N1 and C2 are bonded and H10 has been transferred to O8 is reached. The optimization of this structure leads to product P. From this structure only a rotation around the N1–C7 bond is needed to reach P: the real reaction is completed and only a conformational arrangement remains to be done. The length of this process was the reason that our repeated attempts to arrive at P failed. Anyway, the section of the path obtained is enough to set TS_1 as the correct transition state for the reaction.

Toward products Figure 6 shows a rather flat region (approximately between r.c. = 0 and r.c. = 2) where energy falls smoothly, then it falls suddenly. This fact could be interpreted as a tendency to form an intermediate, although it finally does not take place.

One of the features of the mechanism is its asynchronicity. So, although DFT calculations indicate one single step, the two

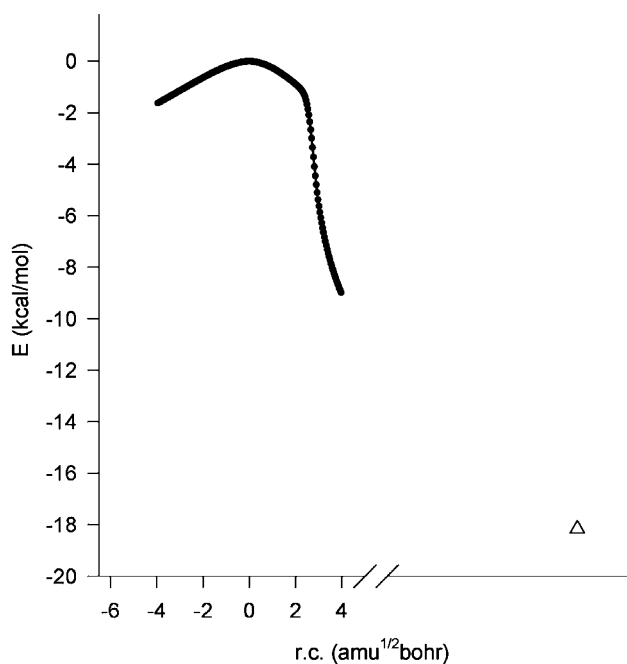


Figure 6. Calculated IRC at the B3LYP/6-31+G(d,p) level. The energies (kcal/mol) are relative to TS. The point marked with a small triangle corresponds to P.

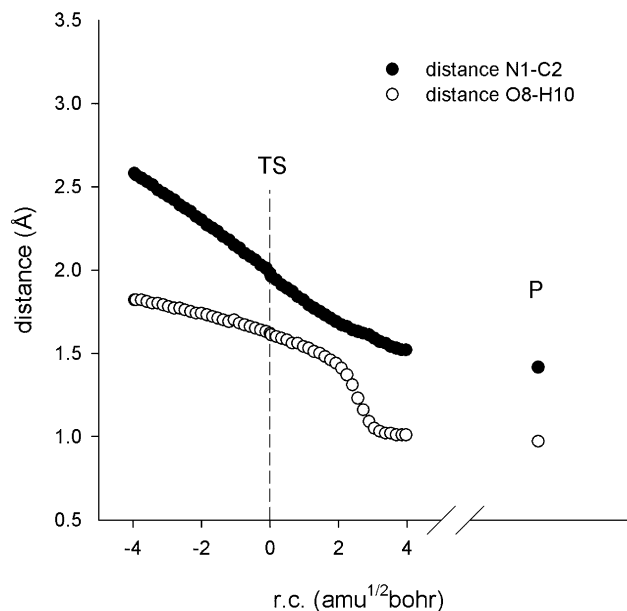


Figure 7. Evolution of the N1–C2 and O8–H10 bond lengths along the reaction coordinate calculated at the DFT level.

fundamental processes of the reaction (the bond of N1 with C2 and the transfer of H10 from N1 to O8) do not take place at the same rate. In this asynchronous reaction first basically N1 and C2 bond together, then H10 is transferred. This asynchronicity takes place in other similar reactions of α -oxoketenes.^{35,36} To make this fact clear Figure 7 shows the variation of N1–C2 and O8–H10 distances along the reaction. The N1–C2 bond length decreases in a more pronounced way before the TS, then the fall is smoother. The behavior of the O8–H10 bond length is appreciably different: until the reaction coordinate is 2 $amu^{1/2}$ bohr it decreases smoothly, then in a short interval it falls suddenly to practically reach its final value. This graph is another evidence that H10 transfer is almost done when the incomplete IRC stops.

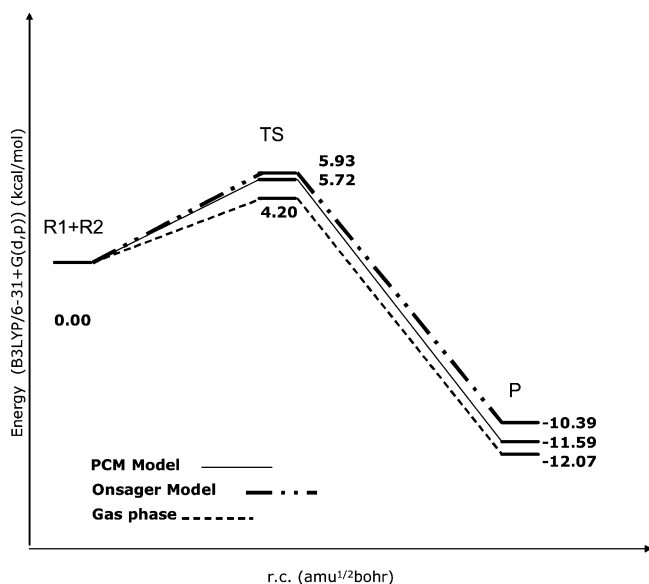


Figure 8. Comparison between results in the gas phase and in solution. Calculations were performed at the B3LYP/6-31+G(d,p) level including the ZPE correction.

TABLE 2: DFT Dipole Moments (D) for the Different Species in the Gas Phase and in Solution

	gas phase	solution	
		Onsager	PCM
R1	2.718	3.049	3.047
R2	4.114	4.401	4.551
TS	1.675	1.789	1.497
P	1.817	2.074	2.209

Solvent Effect. Saripinar et al. carried out almost all their experiments between α -oxoketenes and formamide using benzene as solvent.¹⁶ For this reason, this solvent was chosen to study the effect of solvent on the reaction mechanism.

First we applied the Onsager method. With this model as well as geometrical optimizations we can obtain analytical frequencies. Prior to the SCRF calculations it is necessary to estimate the radius a_0 for the solute cavity in a separate job. The results at the B3LYP/6-31+G(d,p) level show very small differences with regard to gas-phase calculations (see Figure 8). Only a minor increase of TS and P energies is found. The effect of the reaction field generated by the solvent is evident in the almost general increase of dipole moments of all species (see Table 2).

The PCM model involves a substantial improvement because it implies the use of a more realistic cavity for solute. Nevertheless, the results are very similar to those of the Onsager method (see Figure 8). The dipole moment does not change too much either (Table 2). That is, in this particular case there is not much difference between representing the cavity as a single sphere or as a superposition of atomic spheres. So, the presence of an apolar solvent like benzene does not contribute to the existence of an intermediate for the reaction mechanism as was predictable. Therefore, and according to our calculations as much in the gas phase as in solution, the reaction mechanism is concerted.

Conclusions

Only the semiempirical AM1 method predicts a stepwise mechanism for the studied reaction. Ab initio and DFT calculations lead to a concerted mechanism. According to the B3LYP/6-31+G(d,p) calculations this is an exothermic reaction

with a very small activation energy. Another significant feature is its asynchronous character: the two bond lengths that better characterize the reaction (N1–C2 and H10–O8) do not change in a synchronized way. Although undoubtedly there is only a single step, in the first stage basically N1 connects to C2 and in the next stage fundamentally H10 transfers from N1 to O8.

According to the results the reaction can be easily classified as pseudopericyclic: small activation energy, an almost planar six-membered ring in the transition state, and no aromatic character of this transition state. This lack of aromaticity is clear when the behavior is compared with that of an analogous pericyclic reaction.

Finally, the effect of the solvent was studied by using SCRF methods: no significant repercussion was found.

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Supporting Information Available: Geometries of all the structures obtained with the different calculation methods, visualization of the reaction pathway, and imaginary frequencies for the transition structures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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