J. Org. Chem. **1998,** *63,* 9183−9189 **9183**

Toward an Understanding of the Molecular Mechanism of the Reaction between 1-Methylpyrrole and Dimethyl Acetylenedicarboxylate. An ab Initio Study

L. R. Domingo,* M. T. Picher, and R. J. Zaragozá

Departamento de Química Orgánica. Universidad de Valencia, Dr. Moliner 50, 46100 Burjassot, Valencia, Spain

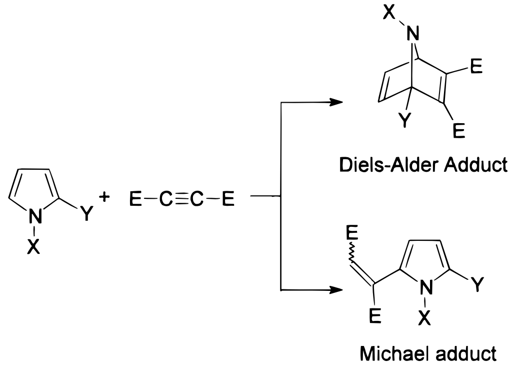
Received January 7, 1998

The molecular mechanism for the reaction between 1-methylpyrrole and dimethyl acetylenedicarboxylate (DMAD) has been studied using ab initio methods. Two alternative reaction pathways have been considered, both of which correspond to stepwise processes with initial, rate-determining formation of a common zwitterionic intermediate. This intermediate is formed by nucleophilic attack of the pyrrole ring to the carbon−carbon triple bond of DMAD. Closure of this intermediate (pathway A) affords a [4 + 2] cycloadduct, whereas intramolecular proton transfer (pathway B) affords a Michael adduct. The much larger potential energy barrier of the second step in pathway B relative to pathway A is responsible for the nonoccurrence of the former. Inclusion of solvent effects, by means of a polarizable continuum model, does not modify the electronic nature of this molecular mechanism.

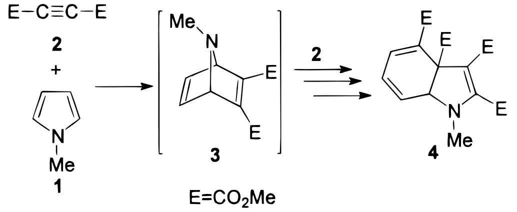
Introduction

The reactions of substituted pyrroles with electron-poor acetylenes usually follow two different pathways: (a) a Diels−Alder cycloaddition of the pyrrole ring at both of its positions (C2/C5) to yield a 7-azabicyclo[2.2.1]heptane derivative or (b) a Michael-type addition of the pyrrole derivative at one of its positions (C2 or C5) to yield a vinyl-substituted pyrrole[1] (Scheme 1). The specific outcome of the reaction is strongly dependent on the substituent at the nitrogen atom. For instance, N-substituted pyrroles bearing aryl or electron-withdrawing substituents at the nitrogen atom react with dimethyl acetylenedicarboxylate (DMAD) **2** (E = COOMe) to give [4 + 2] cycloadducts of type **3**.[2] In contrast, when the N-substituent is an alkyl group, as in 1-methylpyrrole **1**, the bicyclic 1:2 adduct **4** is formed instead (Scheme 2). This was explained by Acheson and Vernon[3] through the initial formation of an intermediate Michael adduct which then reacted with a second molecule of DMAD to yield **4**. More recently, Lee and Hahn[4] reinvestigated this reaction and proposed a different mechanism in which an initial [4 + 2] cycloaddition between **1** and DMAD takes place and affords the expected cycloadduct **3**. Reaction of the latter with another DMAD molecule finally provides **4** through a complex series of reactions. These results have to be compared with the recent findings of Visnick and Battiste.[5] These authors reported the reaction of *N*,*N*′-dipyrrolylmethane **5** with either DMAD or the acetylene derivative **2** (E = CF_3) to give bridged polycyclic compounds **7**. The formation of these adducts was explained by these authors through two sequential [4 + 2] inter-/[4 + 2] intramolecular cycloadditions of the domino type, via intermediate formation of cycloadduct **6**, not detected in the course of their study (Scheme 3).

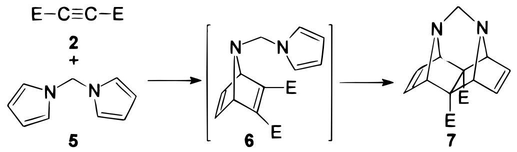
Scheme 1



Scheme 2



Scheme 3



The mechanism of the Diels−Alder reaction has been controversial for some time.[6] The archetypal Diels−Alder

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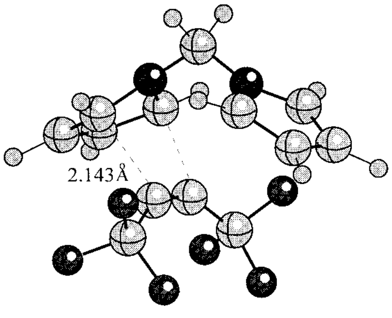


TS-F

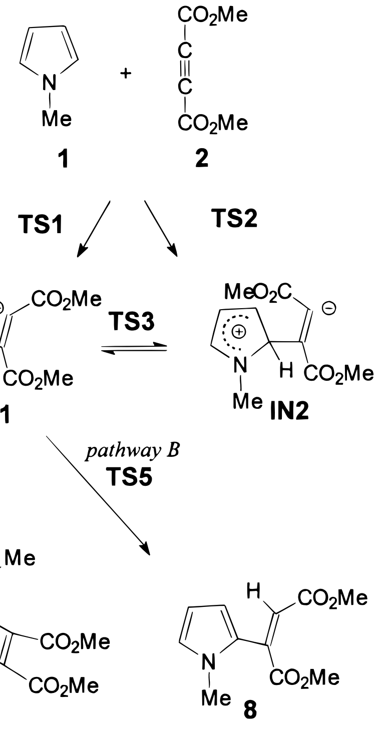
Figure 1. Synchronous transition structure for the [4 + 2] intermolecular cycloaddition between *N,N′*-dipyrrolylmethane (**5**) and **2** (E = CF_3).[12]

reaction of butadiene and ethylene[7] is exothermic by 40 kcal/mol and has a reaction barrier of 27.5 kcal/mol. It may occur via either a synchronous concerted mechanism or a stepwise mechanism involving the formation of diradical intermediates.[6] The butadiene + ethylene reaction, however, is not the typical case. In general, the Diels−Alder reaction requires opposite electronic features in the substituents at the diene and the dienophile for the reaction to be reasonably fast. Furthermore, this type of substitution on diene and dienophile favors an asynchronous concerted mechanism.

Several computational ab initio studies on this mechanism type have recently been published.[8] Sustmann et al.[9] have studied the Diels−Alder reactions of (*E*)-1-(dimethylamino)-1,3-butadiene with various dienophiles. Their results indicate that the reaction mechanism changes progressively from a concerted, asynchronous pathway to a stepwise one with increasing ability of the dienophile to stabilize a negative charge. Under suitable conditions, the intermediates of the stepwise process were trapped. It is precisely the mechanism of these cycloaditions which interests us.[10,11]

Within a research program devoted to the study of domino-type cycloadditions, we have recently presented a theoretical study of the aforementioned cycloaddition of *N,N′*-dipyrrolylmethane **5** with **2** (E = CF_3)[12] (see Scheme 3). DFT calculations allowed the conclusion that an initial [4 + 2] intermolecular cycloaddition takes place through a synchronous concerted mechanism, via the pericyclic transition structure **TS-F** (Figure 1). As a part of the same investigation, we are currently interested in the molecular mechanisms of the Diels−Alder reactions which may possibly take place via asynchronous concerted or polar stepwise mechanisms.[10,11] Among these, we are particularly interested in the reactions of substituted pyrroles with acetylene derivatives.[10,12−13] In the case now under study, the presence of electron-releasing groups on the diene (pyrrole unit) and electron-withdrawing groups on the dienophile (the carbomethoxy groups in DMAD) allows for an effective stabilization of developing electric charges of either sign, which in turn favors a stepwise mechanism via a zwitterionic intermediate (Scheme 4). In this paper, we present a theoretical study of the potential energy surface (PES) of the reaction of 1-methylpyrrole **1** with DMAD **2** (E = COOMe) with the aim of understanding why the reaction pathway takes place via an initial [4 + 2] cycloaddition instead of a Michael-type addition. The solvent effects have also been included in the study.

Scheme 4



Computing Methods

All gas-phase calculations were carried out with the Gaussian94 suite of programs.[14] An extensive characterization of the potential energy surface was carried out at the HF/3-21G[15] level to ensure that all relevant

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stationary points were located and properly characterized. The stationary points were characterized by frequency calculations in order to verify that the transition structures have one and only one imaginary frequency. The HF/3-21G frequencies were used as a starting point in the search of the HF/6-31G* [15] structures. The optimizations were carried out using the Berny analytical gradient optimization method.[16] The transition vectors (TV),[17] that is, the eigenvector associated to the unique negative eigenvalue of the force constants matrix, have been charactized. Optimized geometries of all the structures are available from the authors.

Previous theoretical studies of Diels−Alder reactions have indicated that the activation energies calculated at the HF level are too large, whereas MP2 calculations tend to underestimate them. However, energy calculations for stationary points using MP3/6-31G* are in accord with experimental values.[11,18] Recently, DFT calculations using the B3LYP hybrid functional[19] have been shown to be in good agreement with experimental activation energy values and to give a similar potential energy barrier to that obtained using time-consuming MP3 calculations.[12,20] Consequently, all HF/6-31G* stationary points were optimized at the B3LYP/6-31G* level to obtain accurate energies for a correct characterization of the PES.[21]

The solvent effects have been considered by B3LYP/6-31G* single point calculations using a relatively simple self-consistent reaction field (SCRF)[22] method, based on the Onsager model,[23] in which the solvation energy is calculated from the electrostatic energy between the solute, modelized as a dielectric sphere of radius ao, and the solvent, described as a continuum of dielectric constants (ϵ). The solvent used in the experimental work is diethyl ether.[4] Therefore, we have used the dielectric constant at 293.2 K, $\epsilon = 4.27$.

Results and Discussion

Figure 2 displays a schematic representation of the energy profile and the location of the stationary points for the reaction between 1-methylpyrrole **1** and DMAD **2**: reactants **1** + **2**; products **3**, **4**, and **8**; intermediates **IN1** and **IN2**; and the transition structures **TS1**, **TS2**, and **TS3** (common to pathways A and B), **TS4** (corresponding to [4 + 2] cycloaddition processes), and **TS5** (corresponding to the electrophilic substitution on the pyrrole ring) along two reactive pathways. Figure 3 presents the geometry of these TSs, including the selected geometrical parameters, while Table 1 shows the total and relative energies of the stationary points. In Table 2, the imaginary frequency, the Hessian unique negative eigenvalue and main TV components, and corresponding geometric parameters are reported for the TSs. Geometries of the stationary points along the PES obtained with the different methods are very similar. Geometrical values given throughout correspond to the HF/6-31G* optimized structures, while energetic values correspond to the B3LYP/6-31G* calculations. Table 1 shows that HF/6-31G* energies overestimate the potential energy barriers, whereas B3LYP/6-31G*//HF/6-31G* calculations give values very close to B3LYP/6-31G*.

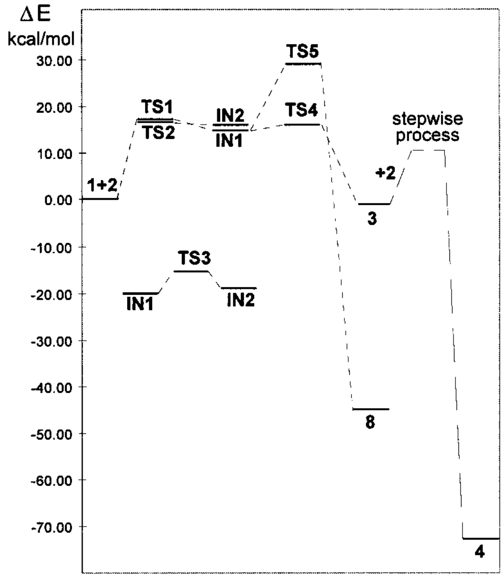

Figure 2. Schematic representation of the energy profile for the reaction between 1-methylpyrrole (**1**) and DMAD (**2**). **TS3** is off the scale.

Geometries, Energies, and TVs. The transition structures **TS1** and **TS2** correspond to a nucleophilic attack of the C2 center of the pyrrole ring on the conjugated acetylenic system of the DMAD to give the zwitterionic intermediates **IN1** and **IN2**. The presence of two electron-withdrawing carboxyl groups on the acetylenic system facilitates the delocalization of the charge transferred from the pyrrole ring, allowing DMAD to act as an electrophile. The potential energy barriers associated with **TS1** and **TS2** are 16.7 and 16.2 kcal/mol, respectively. These potential energy barriers are lower than that for **TS-F** (18.7 kcal/mol),[12] due to the greater electron-withdrawing character of the CO_2Me groups than the CF_3 groups. The lengths of the C2−C7 bond being formed in **TS1** and **TS2** are 1.956 and 1.869 Å, respectively, whereas the distance between C5 and C8 are 2.946 and 3.262 Å, indicating that these atoms do not bond in this step. In these TSs, the carboxyl group at C7 is in the plane of the C7−C8 double bond being formed, whereas the carboxyl group at C8 is perpendicular (for **TS1** and **TS2**, the C8−C7−C9−O10 dihedral angles are 196.5° and 196.7°, and the C7−C8−C13−O14 dihedral angles are 89.6° and −93.0°, respectively). This arrangement, which is also present in intermediates **IN1**

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(21) B3LYP/6-31G* full optimization of the structures **TS2** and **IN2** was unsuccessful, giving DFT calculations a very flat PES (see Figure 2). However, DFT restricted optimizations allowed us to obtain accurate energies.

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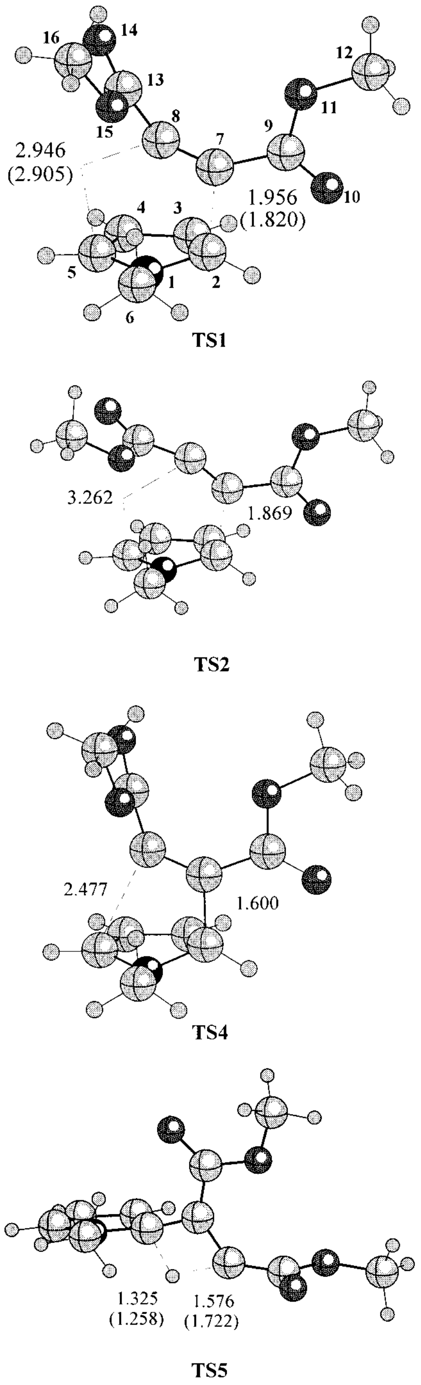

Figure 3. Selected geometrical parameters for transition structures corresponding to the reaction between 1-methylpyrrole (**1**) and DMAD (**2**). The lengths of the C−C bonds directly involved in the reaction obtained at the RHF/6-31G* and B3LYP/6-31G* (in parentheses) levels are given in angstroms.

and **IN2**, allows for the effective delocalization of the negative charge being formed at C8. The values of the C8−C7−C9 and C7−C8−C13 bond angles in **TS1** are 141.9° and 145.5°, and in **TS2**, they are 133.5° and 153.6°, respectively. These bond angles show that there is a change of hybridization at C7 and C8 as they go from reactants to intermediates. Both the smaller C8−C7−C9 bond angle and the shorter C2−C7 bond being formed in **TS2** indicate that the bond formation is more advanced in **TS2** than **TS1**.

The main component of the TVs for **TS1** and **TS2** is associated with the C2−C7 bond being formed (0.77 and 0.85, respectively). For these TSs, the components associated with bond angles C2−C7−C9 and dihedral angles H2−C2−C3−C4 also have an important weight in the TVs (see Table 2). These components are associated with the change of hybridization of the C2 and C7 centers along the bond formation process.

The component associated with the distance between C5 and C8, which are not being bonded in this first step, has a low value in **TS1** (0.10) and a negligible one in **TS2**. This low value in **TS1** can account for a favorable electrostatic interaction between the developing electric charges of either sign at neighboring C5 and C8 centers. The unique imaginary frequencies for **TS1** and **TS2** have the values 446i and 539i cm^{-1}, respectively. These low values indicate that these TSs are associated with the motion of heavy atoms.

The zwitterionic intermediates **IN1** and **IN2** are two configurational stereoisomers that differ in the relative position of the carboxyl group at C8. In these intermediates, the C2−C7 bond lengths are 1.549 and 1.553 Å, respectively, and the C8−C7−C9 bond angles are 130.2° and 124.2°, respectively. The distance between the C8 and C5 atoms in these intermediates (3.474 and 3.641 Å, respectively) indicates that these atoms are not bonded. The values of the C7−C8−C13 bond angles (123.2° and 131.6° for **IN1** and **IN2**, respectively) show that C8 presents an sp^2 hybridization, with one of the sp^2 lobes filled by the electron density transferred from the pyrrole ring to DMAD. The intermediate **IN1** has a lower energy than **IN2** (1.8 kcal/mol), due to a favorable electronic interaction between the electron pair located in the sp^2 lobe and also to the positive charge delocalized in the π-system of the pyrrole ring in **IN1**. The two intermediates are connected via the transition structure **TS3**. This process has a low potential energy barrier (4.0 kcal/mol), and it is associated with the configurational inversion of the C8 center, which changes hybridization: sp^2−sp−sp^2. The C2−C7 bond length in **TS3** is 1.584 Å, and the C7−C8−C13 bond angle is 178.7°. The value of this bond angle indicates that the C8 center presents an sp hybridization in which the charge located at C8 occupies a p atomic orbital. The main component of the TV for **TS3** (0.85) is associated with the C9−C7−C13 bond angle, showing the change of hybridization of the C8 center. This TS presents a very low imaginary frequency (127i cm^{-1}), associated with the configurational change in the C8 center.

The intermediates **IN1** and **IN2** are unstable and can undergo several transformations. The nucleophilic attack of the anionic C8 center of the intermediate **IN1** on the C5 atom of the pyrrole ring via **TS4** gives the cycloadduct **3**. For 1-methylpyrrole, in which the C5 position is not substituted, this cyclization process presents a very small potential energy barrier. The length of the C5−C8 bond being formed in **TS4** is 2.477 Å. In this transition structure, the N1 atom is located outside the C2−C3−C4−C5 molecular plane, a consequence of the rehybridization of C5 from sp^2 to sp^3. Due to the repulsion of the bond being formed and the lone pair of the nitrogen atom in the syn arrangement, only the configurational stereoisomer **3** is formed, making this process highly stereoselective (syn and anti arrangement refer to the relative arrangement of the lone pair of the nitrogen atom relative to the bonds being formed).

Table 1. Total Energies (au) and Relative Energies (kcal/mol, in Parentheses) for the Stationary Points of the Reaction between 1-Methylpyrrole (1) and DMAD (2)

	HF/6-31G*	B3LYP/6-31G*//HF/6-31G*	B3LYP/6-31G*
1 + 2	−777.935 258, (0.0)	−782.544 598, (0.0)	−782.553 252, (0.0)
IN1	−777.901 924, (20.9)	−782.512 348, (20.2)	−782.527 155, (16.4)
IN2	−777.895 885, (24.7)	−782.513 375, (19.6)	−782.524 269, (18.2)
3	−777.944 864, (−6.0)	−782.553 670, (−5.7)	−782.554 601, (−0.9)
8	−778.000 975, (−41.2)	−782.616 117, (−44.9)	−782.624 854, (−44.9)
4	−1308.142 438, (−69.5)	−1315.727 011, (−71.5)	
TS1	−777.882 610, (33.0)	−782.518 711, (16.2)	−782.526 571, (16.7)
TS2	−777.880 803, (34.2)	−782.519 538, (15.7)	−782.527 372, (16.2)
TS3	−777.882 609, (33.0)	−782.509 307, (22.2)	−782.520 780, (20.4)
TS4	−777.892 362, (26.9)	−782.518 748, (16.2)	−782.527 358, (16.3)
TS5	−777.854 667, (50.6)	−782.494 952, (31.2)	−782.500 122, (33.3)

Table 2. HF/6-31G* Imaginary Frequencies (cm^{-1}), Hessian Unique Negative Eigenvalues (au), Main Components of the Transition Vector (C, au), and Corresponding Geometric Parameters (G, Bonds in Å, Angles in deg) for the Transition Structures Corresponding to the Reaction between 1-Methylpyrrole (1) and DMAD (2)

TS1			TS2			TS4		
446.4i[a]			539.0i[a]			209.3i[a]		
−0.0648[b]			−0.0709[b]			−0.0222[b]		
	C	**G**		**C**	**G**		**C**	**G**
C2−C3	−0.111	1.416	C2−C3	−0.135	1.425	C5−C8	0.888	2.477
C2−C7	0.771	1.956	C2−C7	0.852	1.869	C5−C8−C13	0.212	142.7
C5−C8	0.101	2.946	C3−C2−C7	−0.111	97.9	N1−C5−C4−C3	0.200	−17.0
C3−C2−C7	−0.116	95.4	C2−C7−C9	−0.122	103.9	C7−C2−C3−C4	−0.188	−85.0
C2−C7−C9	−0.145	103.7	C5−C5−C13	0.244	77.0	H5−C5−C4−C3	−0.109	−181.8
C5−C8−C13	−0.483	128.5	H2−C2−C3	0.127	123.6	H1−C1−C2−C3	−0.140	148.9
H2−C2−C3−C4	0.239	156.3	H2−C2−C3−C4	0.277	149.3			

TS3			TS5		
126.7i[a]			2081.3i[a]		
−0.4748[b]			−0.4783[b]		
	C	**G**		**C**	**G**
C2−C7	−0.144	1.584	N1−C2	0.128	1.418
C5−C8	0.144	3.457	C2−C3	0.158	1.427
C2−C7−C9	0.302	108.9	C3−C4	−0.111	1.370
C9−C7−C13	0.850	128.4	C4−C5	0.114	1.403
C2−C3−C4−C5	0.113	−3.7	H1−C8	0.690	1.576
C7−C2−C3−C4	0.202	−110.2	C2−C7−C8	−0.235	106.6
C8−C9−C7−C13	0.126	0.1	C7−C8−C13	−0.182	127.2
C5−C8−C13−O14	−0.127	−80.6	H1−C8−C7	−0.562	73.5
			N1−C3−C2−C7	0.131	−155.4

[a] Imaginary frequency. [b] Eigenvalue.

The main component of the TV for **TS4** is associated with the C5−C8 bond being formed (0.88). For this TS, the components associated with the bond angle C5−C8−C13 and the dihedral angle N1−C5−C4−C3 also have an important weight (see Table 2). These components are associated with the change of hybridization of the C5 and C8 centers along the C5−C8 bond formation. The unique imaginary frequency for **TS3** has the value of 209i cm^{-1} and is related to the motion of heavy atoms along the closure process.

Due to the loss of aromatic character of the pyrrole ring in this cycloadditition, the overall process is slightly exothermic (−0.9 kcal/mol). In fact, the potential energy barrier for the inverse process is 17.2 kcal/mol. In consequence, the formation of **3** from **1** and **2** can be easily reversed. However, the presence of an excess of **2** in the reaction mixture causes the formation of the 1:2 adduct **4** via **3**, as proposed by Lee and Hahn.[4] Calculations at either the HF/6-31G* or the B3LYP/6-31G*//HF/6-31G* level predict a very exothermic process. In consequence, the formation of **4** from **1** and **2** can be considered essentially irreversible.

All attempts to find a concerted [4 + 2] transition structure for the cycloaddition between 1-methylpyrrole **1** and DMAD **2** were unsuccessful. Optimization of a transition structure using the C_2 symmetry for the C2−C7 and C5−C8 bond being formed (2.139 Å) leads to a structure that is 4.1 kcal/mol higher than that of **TS1**. So, the higher potential energy barrier associated with the pericyclic process relative to the electrophilic addition of DMAD to the pyrrole ring via **TS1** inhibits this pathway.

The intermediate **IN1** may also undergo an alternative process, pathway B, that leads to the formation of the Michael adduct **8**. This process corresponds to an intramolecular proton transfer from C2 to the anionic C8 center with aromatization of the pyrrole ring and is associated with the second step of an electrophilic substitution on the pyrrole ring. However, this intramolecular proton-transfer process, via the transition structure **TS5**, presents a high potential energy barrier (16.9 kcal/mol) relative to the second step of the stepwise [4 + 2] cycloaddition, making the transformation of the intermediate **IN1** into the Michael adduct **8** via this pathway unlikely and allowing us to discard this intramolecular process.

The transition structure **TS5** corresponds to a four-membered transition structure in which the length of the

Table 3. B3LYP/6-31G* Wiberg Bond Indices for Transition Structures and Intermediates along the Reaction Pathway between 1-Methylpyrrole (1) and DMAD (2)

TS1		**TS2**		**IN1**		**IN2**		**TS4**		**TS5**	
	BO		BO		BO		BO		BO		BO
C2−C7	0.44	C2−C7	0.50	C2−C7	0.89	C2−C7	0.91	C2−C7	0.84	C7−Ht	0.41
C5−C8	0.11	C5−C8	0.08	C5−C8	0.04	C5−C8	0.06	C5−C8	0.31	C8−Ht	0.37
C7−C8	2.24	C7−C8	2.20	C7−C8	1.79	C7−C8	1.77	C7−C8	1.90	C7−C8	1.77
C8−C13	1.10	C8−C13	1.16	C8−C13	1.15	C8−C13	1.21	C8−C13	1.09	C8−C13	1.05
C7−C9	1.01	C7−C9	1.01	C7−C9	1.02	C7−C9	1.04	C7−C9	1.01		

C2−H17 bond being broken is 1.325 Å and the C8−H17 bond being formed is 1.576 Å. A part of the high energy of **TS5** relative to **IN1** is due to the angular strain associated with the formation of this transition structure, which requires the reduction of the C2−C7−C8 bond angle (the values for this bond angle in **IN1** and **TS5** are 120.0° and 106.6°, respectively).

The main components of the TV for **TS5** are associated with the H1−C8 bond being formed (0.69) and with the H1−C8−C7 bond angle (−0.52). The components associated with the bonds of the pyrrole ring show the change of bond order along the aromatization of the pyrrole ring. Finally, the component associated with the C8−C7−C2 bond angle is associate with the strain that appears along the formation of this four-membered TS. This transition structure presents a very high imaginary frequency (2081i cm^{-1}), indicating that this process is associated mainly with the motion of the H1 atom from C2 to C8 centers.

Bond Orders and Charge Analysis. A more balanced measure of the extent of bond formation or bond breaking along a reaction pathway is provided by the concept of bond order (BO). This theoretical tool has been used to study the molecular mechanism of chemical reactions.[24] To follow the nature of this process, the Wiberg bond indices[25] have been computed by using the Natural Bond Orbital[26] analysis as implemented in Gaussian94. The results are also included in Table 3.

For **TS1** and **TS2**, the values of the C2−C7 BOs are 0.44 and 0.50, whereas the values of the C5−C8 BOs are 0.11 and 0.08, respectively. These data are in agreement with the C2−C7 bond formation. The low value of the C5−C8 BO in **TS1** is a consequence of the arrangement of the C8 center relative to the C5 position of the pyrrole ring. The values of the C7−C8 BOs in these TSs (2.24 and 2.20, respectively) show the double bond formation from the triple bond present in DMAD.

For **IN1** and **IN2**, the values of the C2−C7 BOs (0.89 and 0.91, respectively) indicate that the C2−C7 single bond is already formed, whereas the C5−C8 BOs (0.04 and 0.06, respectively) present lower values than in the previous TSs. These data are in agreement with the longer C5−C8 distance in these intermediates than those in the corresponding TSs and can account for stabilizing electronic factors in the latter.

For **TS4**, the values of the C2−C7 and C5−C8 BOs (0.84 and 0.31, respectively) are in agreement with the C5−C8 bond formation along the closure of the zwitterionic intermediate **IN1**. The C2−C7 BO is lower than that in **IN1** and agrees with the increase of bond length found in **TS4**.

For **TS5**, the value of the C7−H1 and C8−H1 BOs (0.41 and 0.37, respectively) show a concerted bond breaking−formation process for the intramolecular proton transfer.

Finally, the natural bond orbital analysis allows us to evaluate the charge transferred along the cycloaddition process. The atomic charges have been shared between the donor pyrrole and the acceptor DMAD systems. The values of the charge transferred in **TS1**, **IN1**, and **TS4** are 0.36, 0.71, and 0.49 au, respectively. These values indicate an increase of the charge transferred along the nucleophilic attack of pyrrole ring to DMAD up to formation of the zwitterionic intermediates.

The values of the dipole moments for **TS1**, **IN1**, and **TS4** are 3.50, 7.05, and 3.50 D, respectively. The low dipole moment for **IN1**, relative to the value of similar zwitterionic species,[10] can be understood as an effective charge delocalization along pyrrole ring and carboxylate groups in these species.

Solvent Effects. Solvent effects on [4 + 2] cycloadditions are well known[27] and have received considerable attention, especially in the past few years.[10,28,29] Thus, finally we have carried out SCRF B3LYP single point calculations over the B3LYP geometries to study the solvent effects on PES. Although, according to the hypothesis of Tomasi et al.,[30] in the case of minima, the approximation of frozen geometries can often be considered as adequate, in the case of TSs, this can be more questionable. However, in a recent paper devoted to the study of the solvent effects in the cycloaddition reaction between 1-methyl-2-vinylpyrrole and DMAD, we pointed out that only small geometry modifications for these TSs are detected.[10]

Table 4 reports the B3LYP/6-31G* relative energies with inclusion of solvent effects. These data show that the inclusion of the solvent effects does not cause any qualitative change along the two competitive channels. Intermediates and transition structures are stabilized by ca. 5 kcal/mol. These results are due to the low variation of the dipole moments along the reactive channels and are related to the effective delocalization of the charge

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Table 4. Total Energies (au) and Relative Energies (kcal/mol, in Parentheses) for the Stationary Points of the Reaction between 1-Methylpyrrole (1) and DMAD (2), Including the Solvent Effects

1 + 2	−782.546 072	(0.0)	**TS1**	−782.526 735	(12.1)
IN1	−782.527 344	(11.8)	**TS2**	−782.527 553	(11.6)
IN2	−782.524 634	(13.5)	**TS3**	−782.521 025	(15.7)
3	−782.554 699	(−5.4)	**TS4**	−782.527 510	(11.6)
8	−782.625 047	(−49.6)	**TS5**	−782.500 417	(28.7)

transferred along the nucleophilic attack of DMAD to 1-methylpyrrole.

Conclusions

In this study, we have carried out an ab initio study of the potential energy surface for the cycloaddition reaction of DMAD to 1-methylpyrrole. The following conclusions can be drawn from the results reported in this study: (i) For the reaction of 1-methylpyrrole with DMAD, two alternative reaction pathways have been found corresponding to a [4 + 2] cycloaddition and an electrophilic substitution reaction on the pyrrole ring to give a Michael-type adduct. (ii) For the alternative pathways, there is a common well on the PES corresponding to an intermediate with pronounced zwitterionic characteristics. The formation of this intermediate is the rate-determining step. (iii) The higher potential energy barrier for the intramolecular proton-transfer process associated with the second step of the electrophilic substitution relative to closure of the zwitterionic intermediate favors the cycloaddition process. (iv) The formation of this intermediate provides an explanation why different substituted pyrroles afford Michael adducts instead of Diels−Alder cycloadducts. Thus, when the closure step is hindered (presence of 2-substituents), the electrophilic substitution mechanism can be improved. (v) Although both CF_3 and CO_2Me may act as electron-withdrawing groups, the higher effective ability of the carboxylate group for charge delocalization favors a stepwise mechanism instead of a concerted synchronous mechanism associated with a pericyclic [4 + 2] cycloaddition.

Acknowledgment. The authors dedicate this paper to Professor R. Alan Jones in acknowledgment of his contribution to the study of pyrrole chemistry. Financial support from the Universidad de Valencia through the project UV97-2219 is gratefully acknowledged. We thank professor J. A. Marco for helpful comments. All calculations were performed on a IBM POWER PC-250 workstation of the Departamento de Química Orgánica of the Universidad de Valencia and on a Cray−Silicon Graphics Origin 2000 with 64 processors of the Servicio de Informática de la Universitat de València. We are most indebted to this center for providing us with computer capabilities.

JO980036Y