# A Theoretical Study of the Reaction between Cyclopentadiene and Protonated Imine Derivatives: A Shift from a Concerted to a Stepwise Molecular Mechanism

Luis R. Domingo,*,[‡] Mónica Oliva,[†] and Juan Andrés[†]

*Intituto de Ciencia Molecular, Universidad de Valencia, Dr. Moliner 50, 46100 Burjassot,*
*Valencia, Spain, and Departament de Ciéncies Experimentals, Universitat Jaume I,*
*Apartat 224, 12080 Castelló, Spain*

*domingo@utopia.uv.es*

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The reaction between cyclopentadiene and protonated pyridine-2-carboxaldehyde imine derivatives has been studied by using Hartree−Fock (HF) and B3LYP methods together with the 6-31G* basis set. The molecular mechanism is stepwise along an inverted energy profile. This results from the protonation on both nitrogen atoms of the imine group and the pyridine framework. The first step corresponds to the nucleophilic attack of cyclopentadiene on the electron-poor carbon atom of the iminium cation group to give an acyclic cation intermediate, and the second step is associated with the ring closure of this intermediate via the formation of a C−N single bond yielding the final cycloadduct. Two reactive channels have been characterized corresponding to the endo and exo approach modes of the cyclopentadiene to the iminium cation. The role of the pyridium cation substituent and the nitrogen position (ortho, meta, and para) along the reaction pathway has been also considered. Solvent effects (dichloromethane) by means of a continuum model have been taken into account to model the experimental environment.

## Introduction

The development of synthetic methodologies based on aza-Diels−Alder (ADA) reactions of imine derivatives and substituted butadienes to obtain six-membered heterocycles has attracted much interest.[1] In particular, a wide variety of imine derivatives has been successfully used along key steps in stereoselectivity synthesis of ligands and synthetic precursors.[2] These cycloadditions are highly accelerated by the addition of Bronsted and Lewis acids. This results in the formation of an iminium cation complex that rapidly undergoes cycloaddition with dienes even at very low temperature.[2a]

Recently, Andersson et al.[3] have explored the ADA cycloadditions between cyclopentadiene and a family of chiral imines containing a second nitrogen atom at a conjugated position, because in a strong acid medium the protonation of this nitrogen atom might fulfill the role of an electron-withdrawing group. In particular, when pyridine-2-carboxaldehyde, **1**, was treated with (*S*)-1-phenylethylamine, **2**, and cyclopentadiene, **4**, under acid conditions, a highly stereoselective cycloaddition takes place giving the pyridine-substituted aza-norbornene **5** in good yield[3] (see Scheme 1). Although the sequence of the major products obtained from the alternative synthetic routes are known from the experimental work,[3] there are no theoretical investigations about the detailed molecular mechanism.

The hetero-Diels−Alder reactions have been comparatively less studied from a theoretical point of view than the Diels−Alder ones.[4] Houk and co-workers[4e,f] have published several theoretical studies on the transition structures (TSs) for ADA reactions; for example, the reaction between formaldimine and butadiene has been studied at the HF/6-31G* level, and two asynchronous concerted TSs have been characterized, corresponding to the endo and exo approaches of the lone pair of the nitrogen atom to the butadiene system. The formation of the C−N bond is more advanced than that of the C−C bond at the TSs. However, for the cycloaddition between the protonated formaldimine and butadiene, the reaction presents a very asynchronous TS in which the lengths

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[‡] Universidad de Valencia.

[†] Universitat Jaume I.

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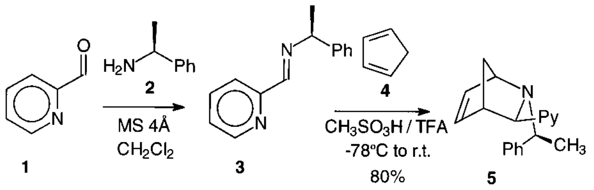
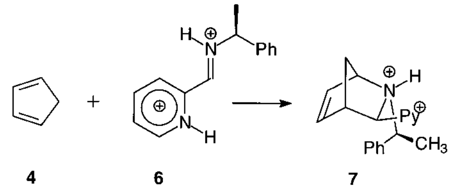
**Scheme 1**

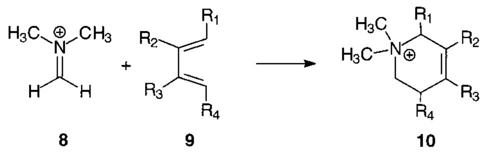
*a) Andersson's reaction.*



*b) Formally [4+2] cycloaddition of protonated imine **6**.*



**Scheme 2**



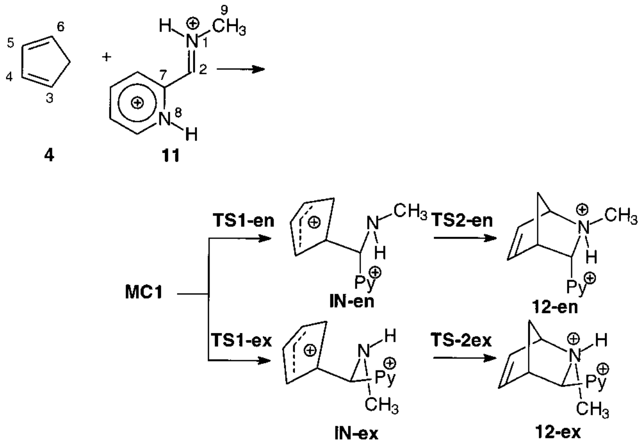
$R_1, R_2, R_3$ and $R_4$=H or $CH_3$

of C−C and C−N forming bonds are 1.919 and 3.058 Å, respectively (HF/3-21G level).[4e] These authors found also several possible intermediates associated with a stepwise mechanism. The proton acts as a strong Lewis acid increasing the electrophilic character of the carbon atom of the protonated formaldimine and, consequently, enhancing the asynchronicity of the process. The inclusion of solvent effects does not modify these findings because of the similar cationic character of both the iminium cation reactant and the TS.[4e]

Sauer and co-workers[4m] have studied recently experimentally and theoretically, using AM1 semiempirical calculations, the cycloaddition between the ylidene ammonium cation, **8**, and several substituted butadienes, **9** (see Scheme 2). These authors suggest that the aza-Diels−Alder reactions of the ylidene ammonium cation, **8**, with the acyclic 1,3-butadienes, **9**, proceed via transition structures that closely resemble those yielding intermediate allyl cations. In only the case of the reaction with cyclopentadiene, these authors conclude that the reaction takes place along a pericyclic transition state.[4m] However, a recent density functional theory (DFT) study carried out by us for the reaction between cyclopentadiene and the ylidene ammonium cation **8** points out that the reaction takes place along a highly asynchronous concerted process characterized by the nucleophilic attack of the cyclopentadiene on the ylidene ammonium cation **8** instead of a pericyclic process.[5h]

In view of these precedents, and as part of our research program devoted to the study of molecular mechanisms of the cycloaddition reactions that take place via asynchronous mechanisms,[5] we present herein the results of a theoretical study on the cycloaddition between cyclopentadiene, **4**, and the protonated *N*-methylpyridine-2-carboxaldehyde imine, **11**, as model compounds having the essential group elements intervening in the ADA reaction reported by Andersson et al. (see Scheme 3).[3] In a previous paper, a third-parametric method (PM3) study has been carried out and the limitations and weakness of this semiempirical method to analyze this type of chemical reaction have been emphasized.[5g] Therefore, our purpose is to contribute to a better understanding of the mechanistic features of these processes, especially by locating and characterizing all stationary points involved along this type of cycloaddition reaction.

**Scheme 3**



## Computational Methods and Models

All gas-phase calculations were carried out with the Gaussian 98 suite of programs.[6] An extensive characterization of the potential energy surface (PES) was carried out at the HF/6-31G*[7] level to ensure that all relevant stationary points were located and properly characterized. The stationary points were characterized by frequency calculations to verify that the transition structures have one and only one imaginary frequency. The optimizations were carried out using the Berny analytical gradient optimization method.[8] The electronic structures of stationary points were analyzed by the natural bond orbital (NBO) method.[9]

Previous theoretical studies of cycloaddition and related reactions have indicated that the activation energies calculated at the HF level are too large, while DFT[10] calculations using

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**Table 1. Total Energies (au) and Relative Energies[a] (kcal/mol, in Parentheses) for the Stationary Points Corresponding to the Reaction between Cyclopentadiene, 4, and the Protonated Imine Derivative 11**

| | HF/6-31G* | | B3LYP/6-31G* | | MP2/6-31G*// B3LYP/6-31G* | |
|---|---|---|---|---|---|---|
| **4** | −192.793 102 | | −194.102 389 | | −193.427 007 | |
| **11** | −379.211 482 | | −381.637 176 | | −380.398 689 | |
| **MC1** | −572.026 376 | (−13.7) | −575.769 680 | (−18.9) | −573.858 255 | (−20.4) |
| **TS1-en** | −572.009 007 | (−2.8) | −575.767 091 | (−17.3) | −573.861 558 | (−22.5) |
| **TS1-ex** | −572.009 678 | (−3.2) | −575.767 771 | (−17.7) | −573.862 008 | (−22.8) |
| **IN-en** | −572.044 572 | (−25.1) | | | | |
| **IN-ex** | −572.045 632 | (−25.8) | −575.772 315 | (−20.6) | −573.864 733 | (−24.5) |
| **TS2-en** | −572.038 034 | (−21.0) | | | | |
| **TS2-ex** | −572.036 199 | (−19.8) | −575.771 899 | (−20.3) | −573.862 608 | (−23.2) |
| **12-en** | −572.061 709 | (−35.8) | −575.794 903 | (−34.7) | −573.899 753 | (−46.5) |
| **12-ex** | −572.059 783 | (−34.6) | −575.793 019 | (−33.5) | −573.894 812 | (−43.4) |

[a] Relative to **4** + **11**. BSSE corrections have been included.

the B3LYP hybrid functional[11] have been shown to be in good agreement with experimental activation energy values.[12] Consequently, HF/6-31G* stationary points were optimized at the B3LYP/6-31G* level to obtain accurate energies for a correct characterization of the PES. Finally, single point calculations were performed at the MP2/6-31G*//B3LYP/6-31G* level to check the energetic results. The basis set superposition error (BSSE) on the computed relative energies has been estimated using the counterpoise method.[13]

The vast majority of chemical reactions are performed in solution, and because solvent effects can yield valuable information about the reaction mechanism, the need to increase our knowledge about interactions between solvent and solute remains crucial. The solvent effects have been considered by B3LYP/6-31G* optimizations of stationary points using a relatively simple self-consistent reaction field (SCRF)[14] based on the polarizable continuum model (PCM) of Tomasi's group.[15] The solvent used in the experimental work is dichloromethane. Therefore, we have used the dielectric constant at 298.0 K, $\epsilon = 8.93$.[16]

The simplified model **11** (see Scheme 3) of the chiral iminium cation **6** (see Scheme 1) has been selected to avoid conformational changes around the C9 chiral carbon atom. The chiral 1-phenylethyl group has been replaced by the achiral methyl group.

## Results and Discussions

**a. Energies.** The cycloaddition reaction between cyclopentadiene, **4**, and the iminium cation **11** can take place along two reaction pathways corresponding to the endo and exo approaches of cyclopentadiene to **11** (see Scheme 3). An analysis of the results determines that the cycloaddition takes place along a stepwise mechanism. Thus, four TSs (**TS1-en**, **TS1-ex**, **TS2-en**, and **TS2-ex**), two acyclic cation intermediates (**IN-en** and **IN-ex**), and two cycloadducts (**12-en** and **12-ex**), corresponding to the endo and exo approach modes, have been found and characterized. For the protonated pyridine−imine **11**, two planar conformations are possible corresponding to the syn and anti arrangement of the two nitrogen atoms of the iminium group and pyridinium framework. The low rotational barrier around the C2−C7 single bond allows the easy equilibration between the two conformers. For this study, we have chosen the more favorable anti arrangement.

An exhaustive exploration of the PES allows us to find also several molecular complexes (MC) associated with very early stages of the reactions and situated on a very flat region that control the access to the different reactive channels. The MC formations may take place in different arrangements of the reactants with a larger distance between **4** and **11**. Their presence on a very flat surface on the PES makes location of the MC associated with each reactive channel very difficult. Therefore, the most stable MC is included, **MC1**. The distances between the two fragments at the **MC1** are around 4−5 Å, and it is more stable than the isolated reactants **4** and **11**.

The stationary points corresponding to the formally [4 + 2] cycloaddition reaction between cyclopentadiene and the iminium cation **11** have been presented in Scheme 3 together with the atom numbering, while the total and relative energies are summarized in Table 1. The geometries of the TSs and intermediates are presented in Figure 1. The energy profiles for the most favorable exo reactive channel obtained at the different computational levels are presented in Figure 2.

An analysis of the results points out that the first step of this formally [4 + 2] cycloaddition corresponds to the nucleophilic attack of the C3 carbon atom of cyclopentadiene on the electron-poor C2 carbon atom of the iminium cation **11** to give an acyclic cation intermediate along with the formation of a new C−C bond. This process can take place along the endo or exo approaches of the conjugated π-system of **4** to the H1 hydrogen atom of **11** to give the cation intermediates **IN-en** and **IN-ex**, respectively. The values of B3LYP/6-31G* relative energies with respect to separate reactants for **TS1-en** and **TS1-ex** are −17.3 and −17.7 kcal/mol, respectively. However, if we consider the formation of the molecular complex **MC1**, the potential energy barriers (PEBs) become slightly positive (see

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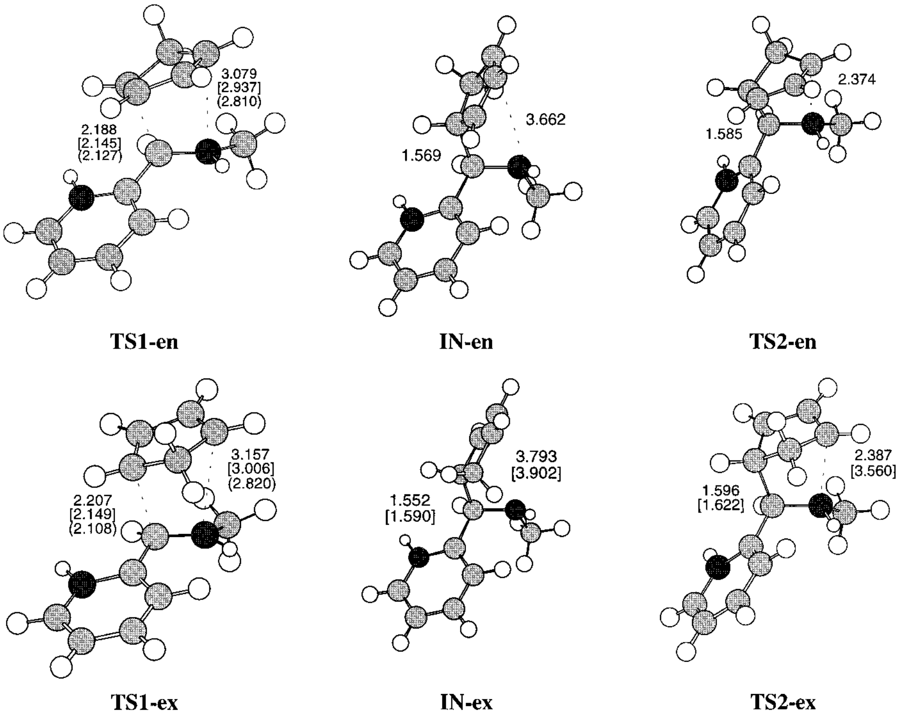


**TS1-en** **IN-en** **TS2-en**

**TS1-ex** **IN-ex** **TS2-ex**

**Figure 1.** Selected geometrical parameters for transition structures and intermediates corresponding to the reaction between cyclopentadiene, **4**, and the iminium cation **11**. The values of the lengths of the bonds directly involved in the reaction obtained at the RHF/6-31G*, B3LYP/6-31G* (numbers in brackets), and B3LYP/6-31G* in dichloromethane (numbers in parentheses) are given in angstroms.

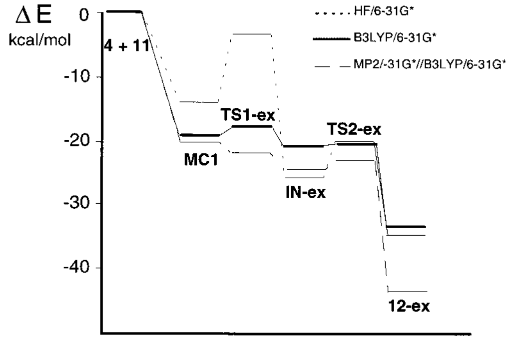
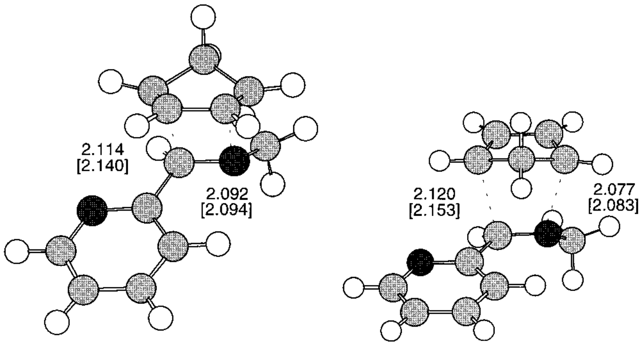


**Figure 2.** Inverted energy profiles for the exo reactive channel corresponding to the cycloaddition reaction between cyclopentadiene, **4**, and the iminium cation **11**.

Table 1). There is an inverted energy profile, and the corresponding values of the barrier heights are 1.6 and 1.2 kcal/mol, respectively (see Figure 2). **TS1-ex** is 0.4 kcal/mol more favorable than **TS1-en**. Formation of the acyclic cation intermediate **IN-ex** from **MC1** is lightly exothermic; however, the very low PEB found at the B3LYP/6-31G* level for the second step corresponding to nucleophilic attack of the N1 nitrogen atom on the C6 position of the allyl cation, 0.3 kcal/mol, favors the rapid transformation into the cycloadduct **12-ex** via **TS2-ex**. This region on the potential energy surface is very flat, and attempts to locate the corresponding stationary point along the endo channel, **IN-en** and **TS2-en,** were unsuccessful at the B3LYP/6-31G* computational level.

Finally, to test the energetic results, single point calculations were made at the MP2/6-31G* level. These calculations give a similar inverted energy profile to that obtained at the B3LYP/6-31G* level (see Figure 2).[5h] However, the MP2 calculations stabilize **TS1-ex** more effectively than **MC1**; now **MC1** energy lies above that of **TS1-ex**, and consequently, at the MP2 level, **MC1** is not a minimum on the PES. The reaction pathway from separated reactants to the intermediate presents a barrierless reaction profile.

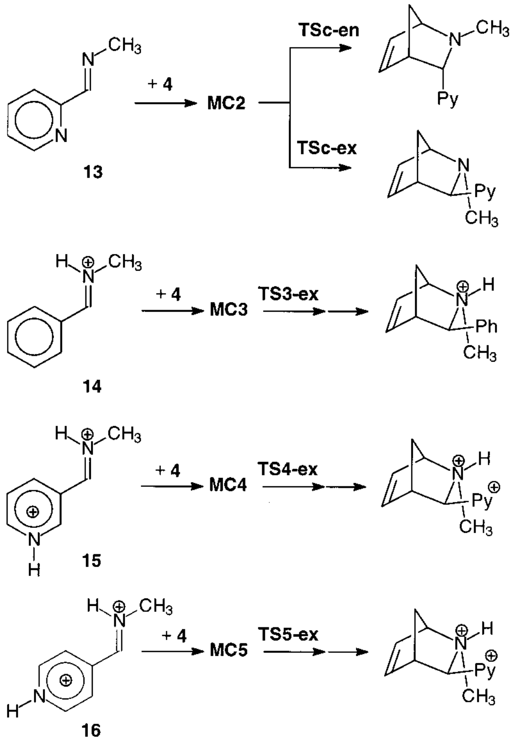
It is well know that the iminium salts are more reactive than neutral imines.[2a,3] On the other hand, the presence of electron-releasing groups on the imine group deactivates the imine for the cycloaddition with unactivated dienes. Therefore, to evaluate the effects of the protonation (acid conditions) on the molecular mechanism for these disfavored cycloaddition processes, the reaction between cyclopentadiene and the pyridine-2-carboxaldehyde imine **13** has been also considered. A detailed exploration of the PES for this [4 + 2] cycloaddition allows identification of one MC, **MC2**, and two TSs, **TSc-en** and **TSc-ex**, corresponding to the endo and exo approaches, respectively (see Scheme 4). The geometries of the TSs are presented in Figure 3. This cycloaddition takes place along a concerted process in which both C−C and C−N forming bonds are formed in a synchronous fashion along a pericyclic transition state. The PEBs associated with **TSc-en** and **TSc-ex** are 32.0 and 28.8 kcal/mol, respectively (B3LYP/6-31G* results). Therefore, there is a pronounced exo stereoselectivity for this [4 + 2] cycloaddition[4e,f,j,l] because of unfavorable interactions between the N1 lone pair of the imine fragment and the $\pi$-system of cyclopentadiene along the endo approach.[4f] Thus, with the protonation of the nitrogen atom of the imine group, these unfavorable interactions disappear, lowering the exo selectivity for the protonated process. A comparison of these PEBs with those obtained for acid medium, **4** + **11**, shows that the barrier for the iminium cation is ca. 28 kcal/mol less energetic than that for the imine. Thus, the C−C bond formation along the nucleo-



**TSc-en** **TSc-ex**

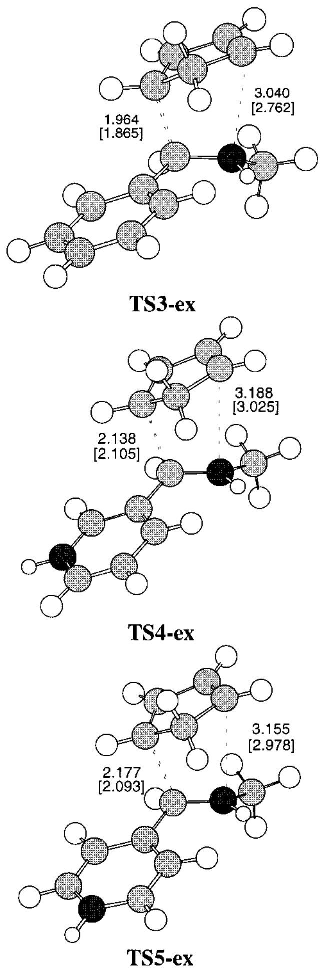
**Figure 3.** Selected geometrical parameters for transition structures corresponding to the reaction between cyclopentadiene, **4**, and the imine **13**. The values of the lengths of the bonds directly involved in the reaction obtained at the RHF/6-31G* and B3LYP/6-31G* (numbers in brackets) are given in angstroms.

**Scheme 4**



philic attack of cyclopentadiene on the iminium cation **11** via **TS1-ex** is strongly favored relative to the C−C and C−N bond formations along the pericyclic process via **TSc-ex**.

Andersson et al. suggested that the presence of the pyridinium cation in the iminium group might fulfill the role of an electron-withdrawing group, favoring the reaction.[3] Therefore, the next step was to study the role of the pyridinium cation substituent on the barrier. The selected model was the reaction of cyclopentadiene and the protonated benzaldimine **14**, in which the pyridinium cation present in **11** has been replaced by the neutral phenyl group (see Scheme 4). In Figure 4 the geometry of **TS3-ex**, corresponding to the nucleophilic attack of cyclopentadiene on iminium cation **14**, is displayed. The PEB associated with **TS3-ex** with respect to its corresponding MC, **MC3**, is 17.2 kcal/mol. This value is larger than that associated with **TS1-ex**, indicating that the electron-withdrawing character of the pyridinium cation has a key role in decreasing the barrier height. In addition, the experimental results show that the position of the nitrogen atom on pyridinium ring (ortho, meta, or para) can have also an important role in the reaction.[3] When carboxaldehyde imine is in an ortho or para position, the cycloadducts are formed with a large yield; however, when it is located in a meta position, the cycloadduct is not observed.[3] Therefore, to determine the role of the position of the nitrogen pyridinium atom, the reactions between cyclopentadiene and the protonated meta and para pyridine−carboxaldehyde imine derivatives, **15** and **16**, respectively, have been also studied (see Scheme 4). In Figure 4, the geometries of **TS4-ex** and **TS5-ex**, corresponding to the more favorable exo reaction channels, are presented. The values of the B3LYP/6-31G* barrier heights relative to the corresponding MCs, **MC4** and **MC5**, are 3.2 and 0.7 kcal/mol, respectively. These energetic values show that the reaction pathways for the ortho and para position of the nitrogen atom, via **TS1-ex** and **TS5-ex**, are more favorable than that for the meta position, via **TS4-ex**, in agreement with the experimental data.[17] These comparative studies indicate



**TS3-ex**

**TS4-ex**

**TS5-ex**

**Figure 4.** Selected geometrical parameters for **TS3-ex**, **TS4-ex**, and **TS5-ex**. The values of the lengths of the bonds directly involved in the reaction obtained at the RHF/6-31G* and B3LYP/6-31G* (numbers in brackets) are given in angstroms.

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[17] Although the meta **TS4-ex** has also a very low barrier, the presence of a competitive polymerization reaction can be responsible for the nonformation of the corresponding cycloadduct.[3]

**Table 2. HF/6-31G* Wiberg Bond Indices (BO) and Net Charges (*Q*, au) for Transition Structures and Intermediates Corresponding to the Reactions between Cyclopentadiene, 4, and the Imine Derivatives 11, 13, and 15**

| | TS1-en | TS1-ex | TS4-ex | IN-en | IN-ex | TS2-en | TS2-ex | TSc-en | TSc-ex |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | BO | | | | |
| C−C | 0.44 | 0.36 | 0.40 | 0.97 | 0.96 | 0.93 | 0.94 | 0.42 | 0.42 |
| C−N | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.22 | 0.23 | 0.38 | 0.38 |
| | | | | | *Q* | | | | |
| **CP** | 0.54 | 0.43 | 0.44 | 0.97 | 0.95 | 0.84 | 0.84 | 0.19 | 0.19 |
| **IM** | 0.52 | 0.60 | 0.58 | 0.11 | 0.12 | 0.22 | 0.21 | −0.15 | −0.14 |
| **Py** | 0.94 | 0.96 | 0.98 | 0.93 | 0.93 | 0.94 | 0.95 | −0.05 | −0.04 |

that the pyridinium cation has a large electron-withdrawing effect, which can be decomposed into two contributions: (i) the electronegative character of the charged pyridinium cation decreases drastically the value of the barrier height, and (ii) the conjugate position of the protonated nitrogen atom in the pyridinium fragment has a minor effect.

**b. Geometries and Frequency Analysis.** In the TSs corresponding to the nucleophilic attack of cyclopentadiene on the iminium cation **11**, **TS1-en** and **TS1-ex**, the lengths of the C2−C3 forming bond are 2.188 and 2.207 Å, respectively, while the distances between the N1 and C6 atoms are 3.079 and 3.157 Å (geometrical data correspond to the HF/6-31G* structures). Similar values are obtained at the B3LYP/6-31G* level (see Figure 1). The values of the unique imaginary frequency of **TS1-en** and **TS1-ex** are 363i and 366i cm$^{-1}$, respectively. Analysis of the atomic motion along these vibrational frequencies indicates that these TSs are mainly associated with the motion of the C2 and C3 carbon atoms along the C−C bond-formation process.

In the acyclic intermediates **IN-en** and **IN-ex**, the C2−C3 bond length, 1.569 and 1.552 Å, respectively, indicates that this C−C bond is already formed, while the N1−C6 distance, 3.662 and 3.793 Å, respectively, presents a larger value than that in the previous TSs. In these intermediates, while both the C2 and C3 carbon atoms are completely pyramidalized, the C4, C5, and C6 atoms have a planar arrangement in agreement with sp$^2$ hybridization for these carbon atoms. Moreover, the C4−C5 and C5−C6 bond lengths, ca. 1.4 Å, agree with an allyl arrangement for the C4, C5, and C6 carbon atoms. The H1−N1−C2 bond angle, ca. 111°, agrees with an sp$^3$ hybridization for the N1 nitrogen atom. The change of hybridization, it is sp$^2$ in the iminium cation **8**, is caused by the charge transferred along the nucleophilic attack of cyclopentadiene on the iminium group that is mainly located at the N1 nitrogen atom.

In the TSs corresponding to the cyclization process, **TS2-en** and **TS2-ex**, the lengths of the N1−C6 forming bond are 2.374 and 2.387 Å, respectively; in the cyclopentadiene framework, while the C4−C5 bond progresses to a double bond, the C5−C6 progresses to a single bond. The values of the unique imaginary frequency of **TS2-en** and **TS2-ex** are 152i and 153i cm$^{-1}$, respectively. Analysis of the atomic motion along these vibrational frequencies indicates that these TSs are mainly associated with the motion of the N1 nitrogen and C6 carbon atoms along the C−N bond-formation process. A quite different result is obtained for **TS2-ex** at the B3LYP/6-31G* level. In this TS, the length of the N1−C6 forming bond, 3.560 Å, is near to that found in **IN-ex**, 3.902 Å, in agreement with the very low barrier found for the cyclization process.[18]

A comparison of the lengths of the forming bonds for the meta **TS4-ex** and para **TS5-ex** with those corresponding to the ortho **TS1-ex** shows that there are not significant geometrical differences (see Figures 1 and 4). Finally, for the concerted **TSc-en** and **TSc-ex**, the lengths of the two forming bonds are 2.114 and 2.120 Å (for the C2−C3 bonds), respectively, and 2.092 and 2.077 Å (for the N1−C6 bonds), respectively (see Figure 3).

**c. Bond Orders and Charge Analysis.** 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.[5e] To follow the nature of these processes, the Wiberg bond indices[19] have been computed at the HF/6-31G* level by using the NBO analysis as implemented in Gaussian 98. The results are included in Table 2.

For **TS1-en** and **TS1-ex**, the BO values for the C2−C3 forming bond are ca. 0.4, while the BO values between the N1 and C6 atoms are 0.0. These results indicate that only the C2−C3 bond is being formed in these TSs. For **IN-en** and **IN-ex**, the BO values of the C2−C3 bond, 1.0, indicate that these C−C single bonds are already formed, while the N2−C6 BO values, 0.0, show that these atoms are not bonded in these intermediates. The BO values for the C4−C5 and C5−C6 bonds (1.5 and 1.4, respectively) point out an allyl structure for the C4−C5−C6 framework which allows a favorable stabilization of the positive charge generated at the cyclopentadiene residue along the nucleophilic attack. For **TS2-en** and **TS2-ex**, the BO values of the N1−C6 forming bonds are 0.2. These low values indicate that the TSs for the cyclization processes are early.

For concerted **TSc-en** and **TSc-ex**, the BO values of the N1−C6 and C2−C3 forming bonds are ca. 0.4. These data point to a synchronous bond formation along a pericyclic process.

The natural population analysis[20] allows us to evaluate the charge transferred along these cycloaddition processes. The HF/6-31G* atomic charges have been shared among the donor cyclopentadiene, **CP**, the acceptor iminium cation framework, **IM**, and the pyridinium cation substituent, **Py** (see Table 2). The values of the charge transferred from the cyclopentadiene to the iminium cation along the stepwise process are around 0.4 au (for **TS1-en** and **TS1-ex**), 1.0 au (for **IN-en** and **IN-ex**), and 0.8 au (for **TS2-en** and **TS2-ex**). These values indicate an increasing of the charge transferred along the nucleophilic attack of the cyclopentadiene on the electron-poor iminium cation up to formation of the allyl cation intermediates, in which the **CP** residue supports one positive charge. The positive charge at the pyridinium cation substituent, **Py**, remains unchanged

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**Table 3. B3LYP/6-31G* Total Energies (au) and Relative Energies[a] (kcal/mol, in Parentheses) for the Stationary Points Corresponding to the Reaction between Cyclopentadiene, 4-s, and the Protonated Imine Derivative 11-s in Dichloromethane**

| | B3LYP/6-31G* in dichloromethane | |
|---|---|---|
| **4-s** | −194.102 505 | |
| **11-s** | −381.880 694 | |
| **MC1-s** | −575.985 066 | (−1.2) |
| **TS1-en-s** | −575.987 157 | (−2.5) |
| **TS1-ex-s** | −575.987 118 | (−2.5) |
| **12-en-s** | −576.018 396 | (−22.1) |
| **12-ex-s** | −576.020 188 | (−23.2) |

[a] Relative to **4-s** + **11-s**.

along the stepwise process, 0.9 au. Therefore, the negative charge is located mainly at the iminium N1 nitrogen atom. The concerted TSs (**TSc-en** and **TSc-ex**) show a low value of the charge transfer, 0.2 au, which flows from the cyclopentadiene to the imine indicating a low polar process.

Finally, a comparative analysis of bond orders, charge transfers (see Table 2), and geometries (see Figures 1 and 4) for the ortho **TS1-ex** and meta **TS4-ex** shows that both TSs have similar features. Thus, the relative position, ortho, meta, and para, of the iminium group on the pyridinium system does not modify substantially the asynchronicity of the bond formation processes. These results agree with the energetic data and point out that the conjugation does not have a decisive role in decreasing the barrier height.

**d. Solvent Effects.** Solvent effects on cycloaddition reactions are well-known and have received considerable attention, especially in the past few years. The solvent effects have been considered by B3LYP/6-31G* optimizations of stationary points using a relatively simple SCRF method, based on the PCM method of Tomasi's group.[15] Table 3 reports the total and relative energies of the reactants (**4-s** and **11-s**), the molecular complex (**MC1-s**), the first TSs of the stepwise mechanism (**TS1-en-s** and **TS1-ex-s**), and the products (**12-en-s** and **12-ex-s**) obtained with the inclusion of solvent effects, while the geometrical parameters are included in Figure 1.

With the inclusion of the solvent effects, the separate reactants are preferentially stabilized because of a larger localization of the positive charge on the iminium cation **11-s**. Now the **MC1-s** energy lies above the **TS1-en-s** and **TS1-ex-s**; in consequence, **MC1-s** is not a minimum on the PES and the relative energies of these TSs with respect to the separate reactants are −2.5 kcal/mol. In this computational model, inclusion of solvent effects does eliminate the exo selectivity because of a large stabilization of the endo **TS1-en-s**.[5e]

Finally, a comparison of the geometrical parameters of the TSs given in Figure 1 shows that the inclusion of solvent effects on the geometry optimization does not modify substantially the geometries obtained in a vacuum;[5h] the value of the N1−C6 forming bond decreases approximately 0.12−0.18 Å.

## Conclusions

The molecular mechanism of the formally [4 + 2] cycloaddition reaction between cyclopentadiene and protonated pyridine-2-carboxaldehyde imine derivatives has been studied by using HF/6-31G* and B3LYP/6-31G* methods. The results indicate that this cycloaddition takes place along a polar stepwise mechanism. The first step corresponds to the nucleophilic attack of cyclopentadiene on the electron-poor carbon atom of the iminium cation group to give an acyclic cation intermediate, while the second step is associated with the ring closure of this intermediate along with the formation of a C−N single bond yielding the final cycloadduct. Two reactive channels have been characterized corresponding to the endo and exo approach modes of the cyclopentadiene to the iminium cation.

In neutral conditions, the cycloaddition between cyclopentadiene and the imine takes place along a synchronous concerted mechanism. The large activation energy associated with the pericyclic process hinders the formation of the corresponding cycloadduct. Protonation of both pyridine and imine nitrogen atoms increases strongly the electrophilicity of the dienophile, and the cycloaddition takes place along a favorable inverted energy profile, allowing justification of the large acceleration of the reaction in a strong acid medium. Cyclopentadiene and protonated pyridine-2-carboxaldehyde imine derivatives act as nucleophile and electrophile, respectively, in these polar processes. The electronegative character of the charged pyridinium cation decreases drastically the value of the barrier height, and the relative position of the nitrogen atom (ortho, meta, or para) in the pyridinium ring has a marginal effect. The inclusion of solvent effects yields a negligible variation of the energy profile. The present theoretical study identifies the different factors controlling the reactive outcome.

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**Supporting Information Available:** Cartesian coordinates with the computed total energies of the B3LYP/6-31G* stationary points. This material is available free of charge via the Internet at http://pubs.acs.org.

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