

# Theoretical Study of the Zwitterido Cleavage of 4-Azido-2-pyrrolinones: The Role of Solvent and Substituents

Dimas Suárez and Tomás L. Sordo\*

Contribution from the Departamento de Química Física y Analítica, Universidad de Oviedo, Julián Clavería 33006, Oviedo, Spain

Received February 18, 1997

**Abstract:** The zwitterido cleavage reaction of the 4-azido-2-pyrrolinones is studied using the MP2/6-31G\* and MP4SDQ/6-31G\*//MP2/6-31G\* levels of theory and taking into account the electrostatic effect of the solvent by means of a SCRF continuum model. Among the various reaction paths studied in this work, the most favored route for the thermolysis of 4-azido-2-pyrrolinone is shown to proceed through the expulsion of N<sub>2</sub> from the *trans* conformer of reactant. This N<sub>2</sub> elimination is the rate-determining step of the zwitterido process and leads to an azirine intermediate. The rearrangement of azirine to the zwitterionic intermediate may also proceed in a concerted manner no nitrene minimum being located on the MP2 PES. A reaction path through the formation of a triazole intermediate is not a competitive kinetic alternative to the N<sub>2</sub> elimination from 4-azido-2-pyrrolinone. Concerning the evolution of the zwitterionic intermediates, different competing pathways are investigated (electrocyclic closure to  $\beta$ -lactams, *gauche-trans* internal rotation, and fragmentation into cyanoketene and formalimine). The solvent provides an important electrostatic stabilization of zwitterions increasing the energy barriers for the fragmentation. The electronic and steric roles of various substituents on the evolution of zwitterionic intermediates are examined through a set of calculations at the MP2/6-31G\*//HF/6-31G\* SCRF level including mono- and multi-substituted structures. It is shown that the electron donor groups at C3 and C5 and alkyl groups at N1 in the pyrrolinone ring favor the electrocyclic closure to  $\beta$ -lactams due to their torquoelectronic effect and steric hindrance, respectively, in a cooperative manner. Therefore, the effects of substituents and solvent are required to explain theoretically the experimental results by Moore et al. on the ring contraction of the 4-azido-2-pyrrolinones to the 3-cyano-2-azetidiones.

## Introduction

The generation of reactive intermediates and the induction of concerted molecular rearrangements by the extrusion of a nitrogen molecule from organic azides have been extensively investigated.<sup>1</sup> Vinyl azides represent a special group of unsaturated azides that have become an important and synthetically useful class of organic compounds due to their high reactivity in pyrolysis, photolysis, cycloadditions, and on attack by electrophiles and nucleophiles.<sup>1c</sup> Nevertheless, the most general reaction of vinyl azides is their thermal or photolytic conversion with loss of N<sub>2</sub> leading to diverse products. On the basis of the evaluation of a large set of thermolyses of acyclic and cyclic vinyl azides, Hassner et al.<sup>2</sup> have proposed that the thermolysis of vinyl azides to isolable 1-azirines usually takes place when the  $\alpha$  substituents (R' in Scheme 1) are aryl, alkyl, a heteroatom, and often alkoxy carbonyl. If the  $\alpha$  substituent is a proton, keto-carbonyl, or a substituent destabilizing an adjacent positive charge, in the case of cyclic vinyl azides, the azirine is rarely isolated. Instead, rearrangement to nitriles or formation of heterocycles is observed.

Particularly interesting is the so-called zwitterido cleavage reaction<sup>1a,b</sup> of certain organic azides whose foundation rests on the generalized mechanism outlined in Scheme 2. This mechanistic model was proposed by Moore to predict the products obtained from the thermolysis of appropriately sub-

stituted vinyl azides. According to this model, cyclic vinyl azides of the structural type **1** cleave to the zwitterions **2** when X is a substituent capable of stabilizing a positive charge and Y and/or Z are anion stabilizing groups. The zwitterionic intermediate, **2**, can then ring close to **3** (ring contraction, path a) or cleave to **4** (fragmentation, path b).

Thus Scheme 2 depicts a strategy for cyanoketene synthesis starting from precursors in which Y is a carbonyl group and X is an appropriate leaving group, suggests an independent route to zwitterionic intermediates **2** which have also been found in the [2+2] cycloaddition reaction of ketenes with imines known as the Staudinger reaction,<sup>3</sup> and provides a rationale for the ring contraction of the 4-azido-2-pyrrolinones to the 3-cyano-2-azetidiones which constitutes an interesting synthetic route<sup>4</sup> to the biologically and clinically important  $\beta$ -lactams.<sup>5</sup> When the pyrrolinones **5** were subjected to thermolysis in refluxing benzene, the corresponding *E* isomers of the  $\beta$ -lactams, **7**, were obtained in isolated yields ranging from 55% to 90%, depending on the substituents in the 4-azido-2-pyrrolinones (see Scheme 3).

Previous theoretical work<sup>6,7</sup> on the thermolysis of vinyl azide has focused on the study of the N<sub>2</sub> expulsion. This process has been shown to proceed through a transition structure (TS) corresponding to the heterolytic rupture of the N<sub>2</sub>-N bond leading to azirine.<sup>6b,c</sup> A vinyl nitrene intermediate has been discarded as playing a significant role in this process due to its

\* Abstract published in *Advance ACS Abstracts*, October 15, 1997.

(1) (a) Moore, H. W.; Goldish, D. M. *The chemistry of Halides, Pseudo-Halides and Azides (Supplement D)*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: New York, 1983; Chapter 8. (b) Moore, H. W. *Acc. Chem. Res.* **1979**, *12*, 125–132. (c) Hassner, A. In *Azides and Nitrenes: Reactivity and Utility*; Scriven, E. F. V., Ed.; Academic Press: New York, 1984; Chapter 2.

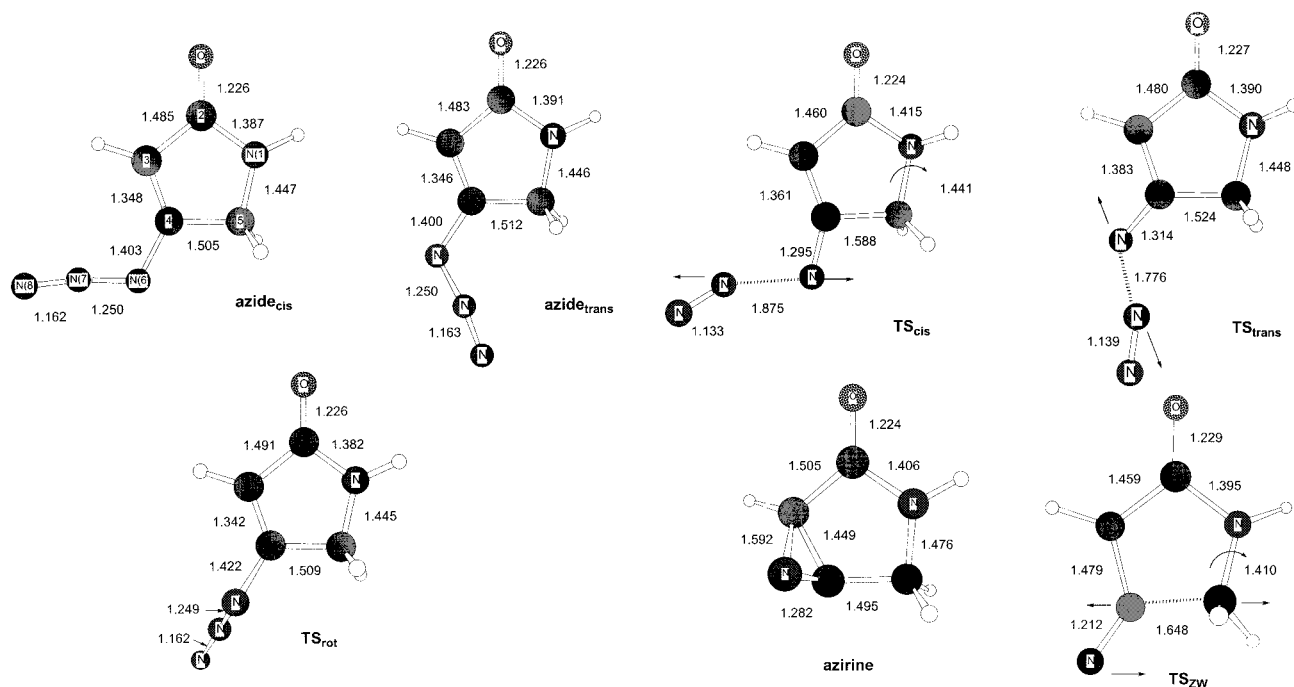
(2) Hassner, A.; Wiegand, N. H.; Gottlieb, H. E. *J. Org. Chem.* **1986**, *51*, 3176–3180.

(3) (a) Pacansky, J.; Chang, J. S.; Brown, D. W.; Schwarz, W. *J. Org. Chem.* **1982**, *47*, 2233. (b) Moore, H. W.; Hughes, G.; Srinivasachar, K.; Fernández, M.; Nguyen, N.V.; Schoon, D.; Trahne, A. *J. Org. Chem.* **1985**, *50*, 4231.

(4) Moore, H. W.; Hernández, L.; Kuner, D. M.; Mercer, F.; Sing, A. *J. Am. Chem. Soc.* **1981**, *103*, 1769–1777.

(5) Georg, G. I.; Ravikumar, V. T. *The Organic Chemistry of  $\beta$ -Lactams*; Georg, G. I., Ed.; VCH Publishers, Inc.: New York, 1993.





**Figure 1.** MP2/6-31G\* optimized structures for the thermolysis of 4-azido-2-pyrrolinone (distances in Å). The arrows display the most important components of the transition vectors.

MP2/3-21G level by means of intrinsic reaction coordinate (IRC) calculations using the González and Schlegel method.<sup>16</sup> All the MCSCF and IRC calculations were performed using the current methods implemented in Gaussian94.<sup>10b</sup>

Quantum chemical computations on solvated molecules and TSs were carried out using a general self-consistent reaction field (SCRFF) model.<sup>17</sup> In this model, the solvent is represented by a dielectric continuum characterized by its relative static dielectric permittivity,  $\epsilon$ . The solute is placed in a cavity created in the continuum, the shape of which is chosen to fit as best as possible the solute molecular shape according to the solvent accessible surface<sup>18</sup> assuming a general cavity shape which is obtained using modified van der Waals solute atomic spheres.<sup>17a</sup> The solute charge distribution polarizes the dielectric which in turn creates an electric field that modifies both the equilibrium geometry and the electronic charge of the solute. One may take into account this interaction at the SCF level by minimizing the energy of the solute plus the electrostatic free energy change corresponding to the solvation process that is given by<sup>19,20</sup>

$$\Delta G = -\frac{1}{2}E_{\text{int}}$$

where  $E_{\text{int}}$  is the interaction energy:

$$E_{\text{int}} = \sum_{\alpha} V_{\text{el}}(\mathbf{r}_{\alpha})Z_{\alpha} - \int V_{\text{el}}(\mathbf{r})\rho(\mathbf{r}) \, \text{d}\mathbf{r}$$

In this equation,  $V_{\text{el}}$  is the electrostatic potential created by the polarized continuum in the cavity,  $\mathbf{r}_{\alpha}$  and  $Z_{\alpha}$  are the position vector and the charge of nucleus  $\alpha$ , respectively, and  $\rho(\mathbf{r})$  is the electronic density at point  $\mathbf{r}$ . The factor  $-1/2$  in the free energy arises from the fact that the positive

(16) (a) Fukui, K. *Acc. Chem. Res.* **1981**, *14*, 363. (b) González, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523.

(17) (a) Rivail, J. L.; Rinaldi, D.; Ruiz-López, M. F. In *Theoretical and Computational Model for Organic Chemistry*; Formosinho, S. J., Csizmadia, I. G., Arnaut, L., Eds.; NATO ASI Series C; Kluwer Academic Publishers: Dordrecht, 1991; Vol. 339, pp 79–92. (b) Dillet, V.; Rinaldi, D.; Angyán, J. G.; Rivail, J. L. *Chem. Phys. Lett.* **1993**, *202*, 18. (c) Dillet, V.; Rinaldi, D.; Rivail, J. L. *J. Phys. Chem.* **1994**, *98*, 5034–5039.

(18) Richards, F. M. *Annu. Rev. Biophys. Bioeng.* **1977**, *6*, 151.

(19) Claverie, P. In *Quantum Theory of Chemical Reactions*; Daudel, R., Pullman, A., Salem, L., Veillard, A., Eds.; Reidel, Dordrecht, 1982; Vol. 3, pp 151–175.

(20) Ruiz-López, M. F.; Assfeld, X.; García, J. I.; Mayoral, J. A.; Salvatella, L. *J. Am. Chem. Soc.* **1993**, *115*, 8750.

work required to polarize the medium is exactly one-half the value of the interaction energy. The computation of  $V_{\text{el}}$  may be made following different approaches. In the model used here it is obtained through a one-center expansion in terms of the spherical multipole moments of the solute including terms from order 0 to 6.<sup>17,20</sup> A relative permittivity of 2.38 was used to simulate the solvents used in the experimental work (toluene and benzene).

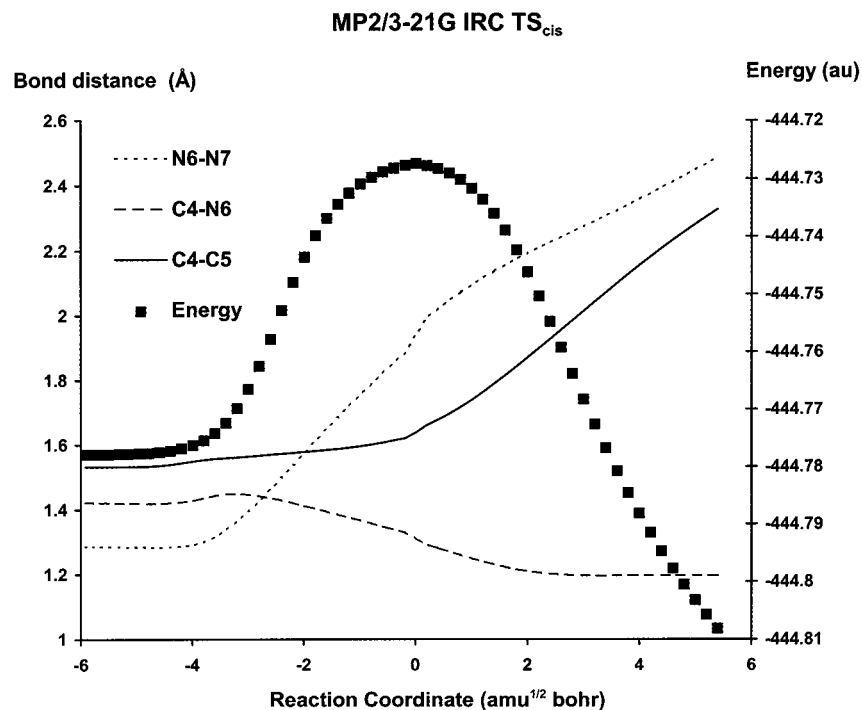
## Results and Discussion

**A. Thermolysis of the 4-Azido-2-pyrrolinone: Direct Loss of N<sub>2</sub> from the Azo Group.** Figure 1 shows the geometry of the corresponding TSs and intermediates located at the MP2/6-31G\* level for the thermolysis of the nonsubstituted 4-azido-2-pyrrolinone. Figures 2 and 3 display the structural and energetic features resulting from the MP2/3-21G IRC calculations of the most important TSs for this process. The relative energies of all the structures computed at the MP2, MP4SDQ/MP2, and MP2 SCRFF levels are contained in Table 1. Unless otherwise specified the relative energies given in the text hereafter include the ZPVE correction from the HF/6-31G\* unscaled frequencies.

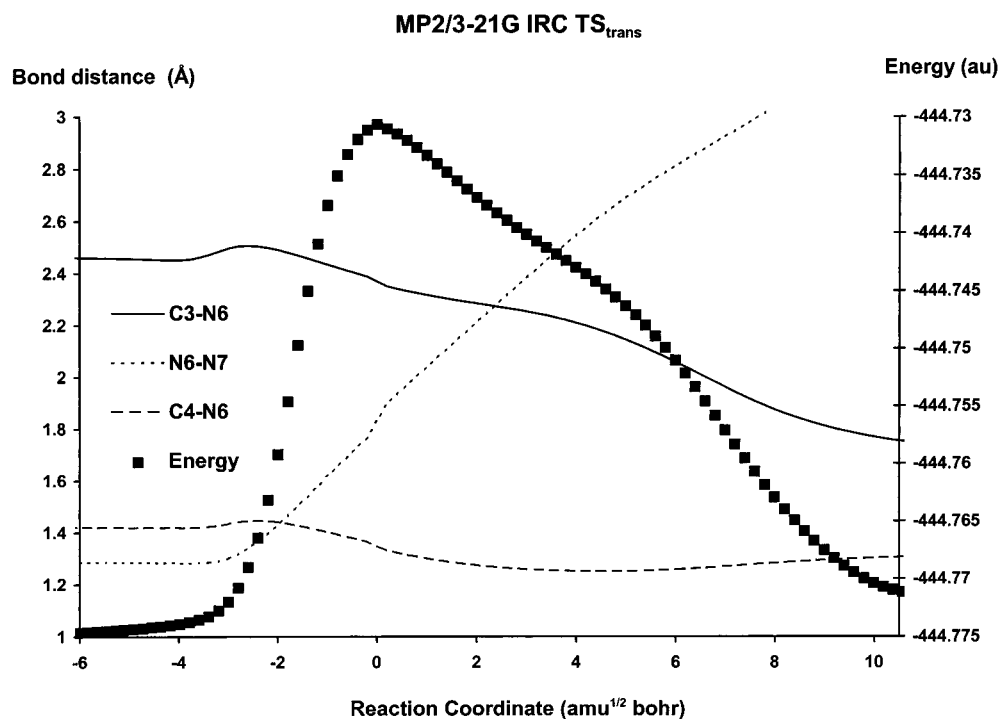
Scheme 4 sketches some of the structures involved in the reaction paths for the direct loss of N<sub>2</sub> from nonsubstituted 4-azido-2-pyrrolinone according to our MP2 calculations.

Concerning the conformation of the azo group in the initial reactant, our calculations predict the *cis* form to be more stable than the *trans* one by 1.4 and 1.6 kcal/mol at the MP2 and MP4SDQ/MP2 levels, respectively (see Figure 1 and Table 1). According to a van der Waals radii analysis, the origin of this difference could be ascribed to weak steric interactions in the *trans* conformation between the N<sub>3</sub> group and the CH<sub>2</sub> fragment. A rotational TS (**TS<sub>rot</sub>** in Figure 1) connecting the *cis* and *trans* conformers was located, rendering a small energy barrier of 3.7 kcal/mol at the MP2 level (see Table 1).

A nearly planar TS (**TS<sub>cis</sub>** in Figure 1) was located for the loss of one N<sub>2</sub> molecule from the *cis* conformer of the 4-azido-2-pyrrolinone. The most important component of the transition vector of this TS corresponds to the breaking of the N<sub>2</sub>–N bond which has a bond length of 1.875 Å at **TS<sub>cis</sub>** (compared to 1.250



**Figure 2.** IRC energy profile obtained at the MP2/3-21G level for the *cis* elimination of N<sub>2</sub> from 4-azido-2-pyrrolinone. Geometrical evolution of significant interatomic distances is also shown.



**Figure 3.** IRC energy profile obtained at the MP2/3-21G level for the *trans* elimination of N<sub>2</sub> from 4-azido-2-pyrrolinone. Geometrical evolution of significant interatomic distances is also shown.

Å at the reactant) although the CH<sub>2</sub> ring puckering and a simultaneous rotation about the C5–N1 bond contribute to the reaction coordinate as well (see the transition vector sketched in Figure 1). We also note in Figure 1 that the C1–C5 and N1–C2 distances in the pyrrolinone ring are elongated in 0.079 and 0.028 Å at TS<sub>cis</sub>, respectively. The calculated energy barriers of TS<sub>cis</sub> with respect to the *cis* conformer of 4-azido-2-pyrrolinone are 44.2 and 31.2 kcal/mol at the MP2 and MP4SDQ//MP2 levels, respectively. According to MP2/3-21G IRC calculations (see Figure 2) this TS<sub>cis</sub> evolves to a cyanoketene–formaldimine complex which presents a C(ketene)–

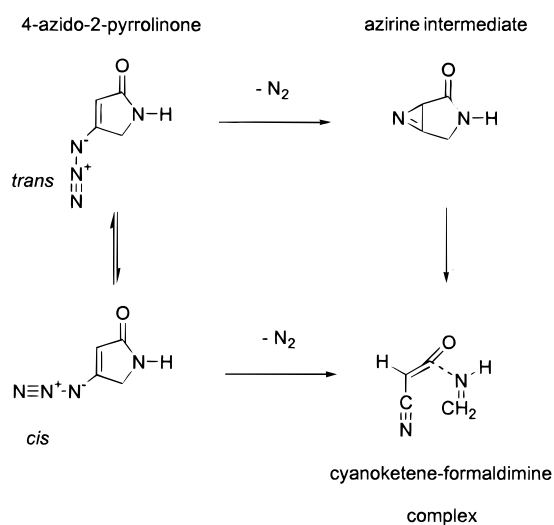
N(imine) bond distance of 2.641 Å (see **vdW<sub>g</sub>** in Figure 6) and is 20.1 and 28.6 kcal/mol more stable than reactant at the MP2 and MP4SDQ//MP2 levels, respectively. The IRC reaction path for the *cis* N<sub>2</sub> extrusion reveals that most of the cleavage of the pyrrolinone ring takes place after passing TS<sub>cis</sub> while the N6–N7 bond is appreciably broken at this TS (see Figure 2).

The loss of one N<sub>2</sub> molecule from the *trans* conformer of the 4-azido-2-pyrrolinone proceeds through a nearly planar TS (see TS<sub>trans</sub> in Figure 1). TS<sub>trans</sub> shows a more reactant-like character than TS<sub>cis</sub> given that the N6–N7 bond length is 1.776 Å and the C4–C5 bond length is increased in only 0.012 Å.

**Table 1.** Relative Energies (kcal/mol) of the Main Structures Involved in the Thermolysis of 4-Azido-2-pyrrolinone

structures	MP2	ZPVE <sup>a</sup>	MP4SDQ/MP2	MP2 SCRF <sup>b</sup> ( $\epsilon = 2.38$ )
4-azido-2-pyrrolinone <i>trans</i>	0.0	0.0	0.0	0.0 (-3.2)
<b>TS</b> azide <i>cis</i> ↔ azide <i>trans</i> ( <b>TS</b> <sub>rot</sub> )	3.9	-0.2	3.2	4.3 (-2.6)
4-azido-2-pyrrolinone <i>cis</i>	-1.5	0.1	-1.7	-1.1 (-2.8)
<b>TS</b> azide <i>cis</i> ↔ <i>gauche</i> int. ( <b>TS</b> <sub>cis</sub> )	45.6	-2.8	32.4	45.3 (-3.5)
<b>TS</b> azide <i>trans</i> ↔ azirine ( <b>TS</b> <sub>trans</sub> )	42.5	-2.4	31.5	42.4 (-3.3)
azirine intermediate	2.3	-4.1	-4.1	2.2 (-3.1)
<b>TS</b> azirine ↔ <i>gauche</i> int. ( <b>TS</b> <sub>zw</sub> )	32.1	-5.1	21.7	31.8 (-3.4)
<i>gauche</i> vdW intermediate ( <b>vdW</b> <sub>g</sub> )	-16.9	-4.6	-25.6	-16.1 (-2.3)

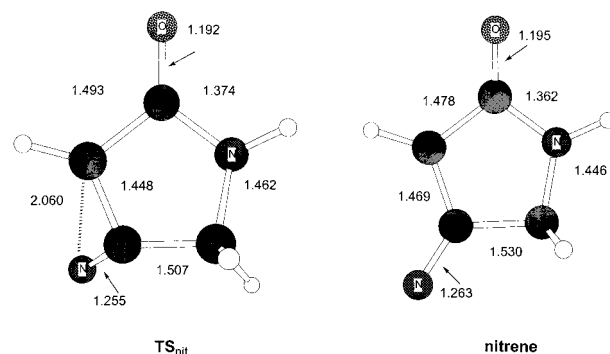
<sup>a</sup> ZPVE correction from the HF/6-31G\* frequencies. <sup>b</sup> MP2/6-31G\* SCRF single-point calculations on the gas phase geometries. Solvation energies are indicated in parentheses.

**Scheme 4**

The calculated energy barriers corresponding to **TS**<sub>trans</sub> with respect to the most stable *cis* conformer of the 4-azido-2-pyrrolinone amount to 41.5 and 30.7 kcal/mol at the MP2 and MP4SDQ/MP2 levels, respectively. Thus, **TS**<sub>trans</sub> is 2.7 and 0.5 kcal/mol more favored than **TS**<sub>cis</sub> at the same theory levels. Although these relative barriers are dependent on the theoretical method used (see Table 1), it is clear that the  $N_2$  elimination constitutes the rate-determining step in the mechanism for the zwittazido cleavage reaction of 4-azido-2-pyrrolinone.<sup>21</sup> The highest theory level used predicts energy barriers for these  $N_2$  elimination close to some experimental values for related thermolyses.<sup>2</sup> In contrast with the *cis*  $N_2$  elimination, an MP2/3-21G IRC calculation shows that the *trans*  $N_2$  elimination is accompanied by the N6–C4–C3 ring closure to yield an azirine intermediate (see Figure 3) in accordance with the favorable orientation of a N6 lone pair toward the C3 atom in **TS**<sub>trans</sub>. This azirine intermediate is 0.4 kcal/mol more stable than the *cis* vinyl azide at the MP2 level (4.3 kcal/mol at the MP4SDQ/MP2 level, see Figure 1).

Vinyl nitrenes have also been proposed as intermediates for the thermolysis of vinyl azides.<sup>1c</sup> Given that a vinyl nitrene for the thermolysis 4-azido-2-pyrrolinone is located at the HF/6-31G\* level but does not exist on the MP2/6-31G\* PES, it seems convenient to investigate the role of nondynamical electron correlation on this part of the PES. CAS-MCSCF/6-31G\* optimizations on the singlet state were carried out using

(21) To investigate a possible biradical character of this TS, a CAS-MCSCF/6-31G\*/MP2/6-31G\* single-point calculation was performed using a (8,8) active space of 8 electrons and 6  $\pi/\pi^*$  and 2  $\sigma/\sigma^*$  orbitals more directly involved in the bond making and breaking. The HF electronic configuration was observed to clearly dominate the multideterminant expansion of the CAS-MCSCF wave function in which the corresponding coefficient has a value of 0.91. Therefore, nondynamical electronic correlation is expected to play a minor role in this part of the PES.

**Figure 4.** CAS-MCSCF(4,4)/6-31G\* optimized structures of the nitrene intermediate and the TS for its ring closure to azirine.

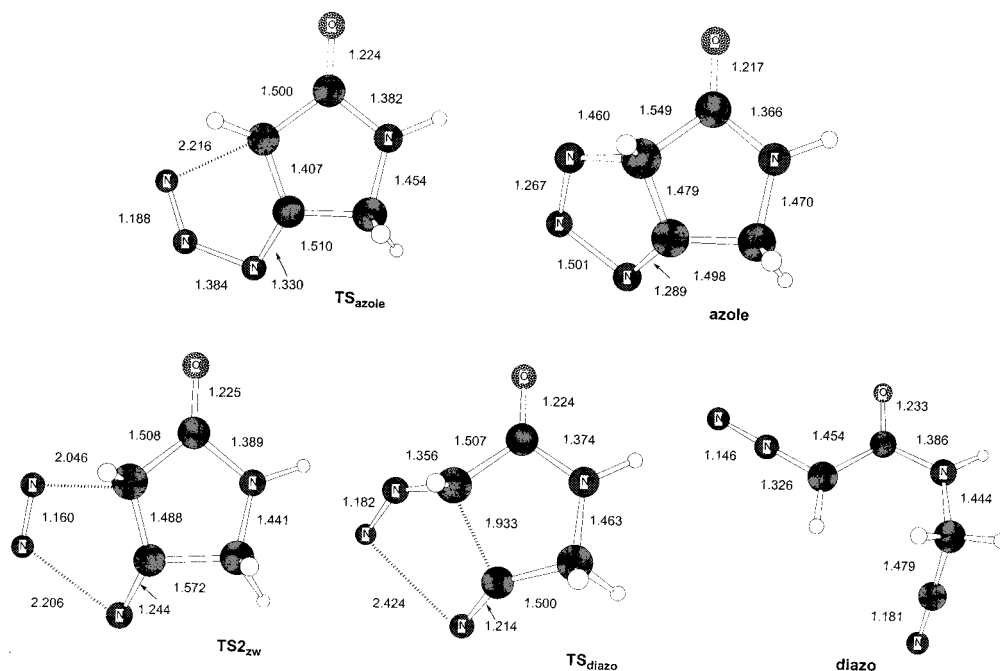
a complete (4,4) active space which consists of four  $\pi/\pi^*$  orbitals located on the C3–C4–N6 atoms. The CAS-MCSCF method predicts that the vinyl nitrene is a minimum (see Figure 4). According to the expansion of the CAS-MCSCF(4,4)/6-31G\* wavefunction, the resultant nitrene minimum has an electronic structure resonant between vinyl nitrene and imine carbene structures. At the CAS-MCSCF(4,4)/6-31G\* level only 3.3 kcal/mol are required for the ring closure of this intermediate to azirine through **TS**<sub>nit</sub> (see Figure 4). Considering the crucial importance of including the dynamical electron correlation in predicting relative energies,<sup>22</sup> MR-MP2/6-31G\* single-point calculations<sup>15</sup> were also performed on vinyl nitrene and **TS**<sub>nit</sub>, rendering an almost negligible energy barrier for the ring closure of 0.4 kcal/mol without ZPVE correction. Moreover, when the ZPVE correction calculated at the HF/6-31G\* level is included, **TS**<sub>nit</sub> turns out to be 0.8 kcal/mol more stable than the nitrene. Thus, in agreement with previous work,<sup>6c,7</sup> we find that dynamical electronic correlation discards the vinyl nitrene route for the thermolysis of 4-azido-2-pyrrolinone.

According to MP2 calculations the ring opening of the azirine intermediate gives the cyanoketene–formaldimine through **TS**<sub>zw</sub> in Figure 1. The transition vector of this TS is analogous to that for **TS**<sub>cis</sub> presenting a C3–C4–N6 bending motion and a more pronounced contribution from the CH<sub>2</sub> ring puckering and rotation about the C5–N1 bond. These last motions would play an important role to avoid the small-angle strain in the ring opening of pyrrolinone. The calculated energy barrier for the ring opening of azirine is 28.8 (MP2), 24.8 (MP4SDQ/MP2), and 21.3 (MP4SDTQ/MP2) kcal/mol with respect to azirine. These values lie in the typical range observed for pericyclic reactions.<sup>23</sup> It is interesting to note that following the definition proposed by Herges,<sup>24</sup> **TS**<sub>zw</sub> could be considered as an example of a *coarctate* TS for the lone pair–five-membered ring terminators processes.

(22) Borden, W. T.; Davidson, E. R. *Acc. Chem. Res.* **1996**, *29*, 67–75.

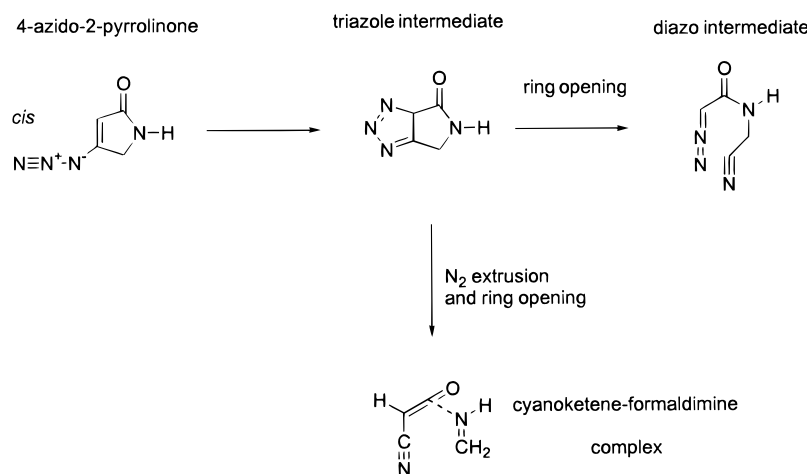
(23) Houk, K. N.; Li, Y.; Evanseck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682–708.

(24) Herges, R. *Ang. Chem., Int. Ed. Engl.* **1994**, *33*, 255–276.



**Figure 5.** MP2/6-31G\* optimized structures for the thermolysis of 4-azido-2-pyrrolinone through a triazole intermediate (distances in Å).

### Scheme 5



The calculated solvation energies for all the structures located along the reaction coordinate from vinyl azides to the azirine or cyanoketene–formaldimine intermediates have moderate values around 3 kcal/mol at MP2 SCRF level using the gas-phase geometries (see Table 1). Thus solvation energies do not introduce important changes in the relative energies of those structures. The most significant changes in solution occur for the energy difference between the *cis* and *trans* conformations of the azo group in vinyl azides which is reduced in 0.4 kcal/mol, and the  $N_2$  *cis* elimination from 4-azido-2-pyrrolinone which is slightly favored by 0.2 kcal/mol at the MP2 SCRF level.

**B. Thermolysis of the 4-Azido-2-pyrrolinone: Triazole Route.** Scheme 5 summarizes the mechanism for the thermolysis of 4-azido-2-pyrrolinone *via* a triazole intermediate according to our calculations. Figure 5 shows the located structures for the rearrangement and fragmentation of the bicyclic triazole intermediate, while Table 2 contains the corresponding relative energies at the different levels of theory.

According to our calculations the corresponding TS for ring closure from *cis* 4-azido-2-pyrrolinone to the bicyclic triazole structure (**TS<sub>azole</sub>** in Figure 5) is clearly a highly destabilized structure in which the azo group is very distorted and the C3–

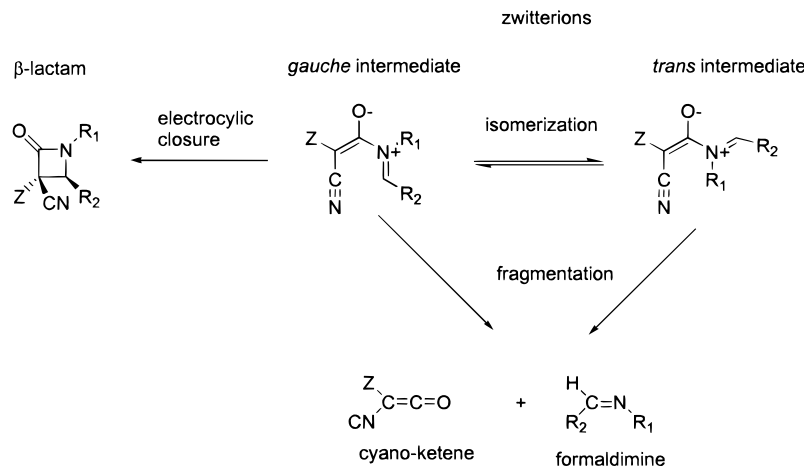
**Table 2.** Relative Energies (kcal/mol) of the Main Structures Involved in the Thermolysis of 4-Azido-2-pyrrolinone through a Triazole Intermediate

structures	MP2	ZPVE <sup>a</sup>	MP4SDQ//MP2	MP2 SCRF <sup>b</sup> ( $\epsilon = 2.38$ )
4-azido-2-pyrrolinone <i>cis</i>	0.0	0.0	0.0	0.0 (−2.8)
<b>TS azide <i>cis</i> ↔ triazole (TS<sub>azole</sub>)</b>	39.0	−1.3	40.1	38.9 (−2.9)
triazole intermediate	13.9	1.6	6.2	12.2 (−4.4)
<b>TS triazole ↔ <i>gauche</i> int. (TS<sub>2zw</sub>)</b>	29.3	−2.8	35.7	28.1 (−4.0)
<b>TS triazole ↔ diazo int. (TS<sub>diazo</sub>)</b>	23.2	−1.6	30.0	21.9 (−4.1)
diazo intermediate	0.9	−1.6	−3.4	−0.7 (−4.3)

<sup>a</sup> ZPVE correction from the HF/6-31G\* frequencies. <sup>b</sup> MP2/6-177408n\* page single-point calculations on the gas phase geometries. Solvation energies are indicated in parentheses.

N8 forming bond is not much advanced. The IRC reaction path at the MP2/3-21G level confirms that **TS<sub>azole</sub>** connects both minima, giving energy barriers of 37.0 and 38.8 kcal/mol at the MP2 and MP4SDQ//MP2 levels, respectively. At the MP2 and MP4SDQ//MP2 levels the triazole intermediate (see Figure

## Scheme 6



5) is less stable than the *cis* 4-azido-2-pyrrolinone by 15.5 and 7.8 kcal/mol, respectively (see Table 2).

Scheme 5 shows two possible pathways for the subsequent evolution of the triazole intermediate. The extrusion of an  $N_2$  molecule from the triazole to yield a cyanoketene–formaldimine complex proceeds in a concerted manner through  $TS_{2zw}$  (see Figure 5). MP2/3-21G IRC calculations show that most of the opening of the pyrrolinone ring takes place after the extrusion of the  $N_2$  molecule. The energy barriers for this process with respect to the triazole intermediate amount to 11.0 and 25.0 kcal/mol at the MP2 and MP4SDQ//MP2 levels of theory, respectively. The ring opening of the triazole intermediate can also occur *via* a 1,3-dipolar intramolecular cycloreversion TS ( $TS_{diaz}$  in Figure 5) which leads to an open-chain intermediate (**diazo** in Figure 5). This pericyclic TS is a more stable structure than  $TS_{2zw}$ , presenting energy barriers of 6.1 and 20.6 kcal/mol at the MP2 and MP4SDQ//MP2 levels, respectively. The resultant diazo compound has a relative energy with respect to triazole of  $-16.2$  and  $-12.8$  kcal/mol at the same theory levels.

Concerning the electrostatic effect of solvent along the reaction coordinate passing through the triazole intermediate, the calculated MP2/6-31G\* SCRF relative energies do not show important changes with respect to those in gas phase apart from a moderate stabilization of 1–2 kcal/mol of the triazole and diazo compounds (see Table 2).

According to the results presented above, the energy profile *via* a triazole intermediate is clearly more unstable than that for the  $N_2$  elimination from 4-azido-2-pyrrolinone. Thus, the triazole route does not constitute a competitive kinetic alternative to the  $N_2$  elimination from the initial reactant leading to the cyanoketene–formaldimine complex as the first step of the zwitterionic cleavage reaction.

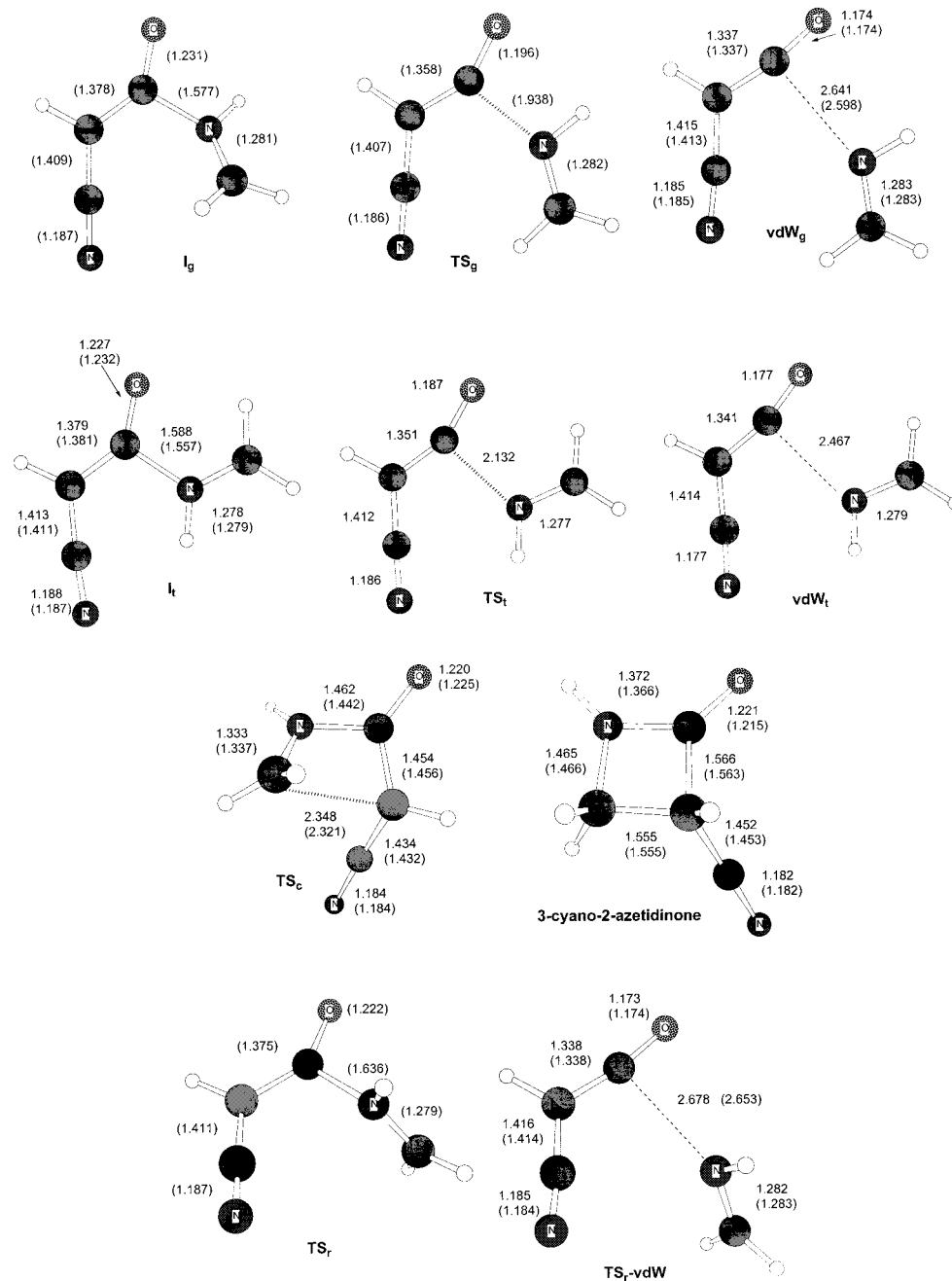
**C. Evolution of the Cyanoketene–Formaldimine Zwitterionic Intermediates.** Scheme 6 depicts several paths for the evolution of the cyanoketene–formaldimine zwitterionic intermediates. Figure 6 shows the geometry of the corresponding TSs and intermediates located both in vacuum and in solution at the MP2/6-31G\* level. The relative energies of these structures are contained in Table 3.

HF calculations render a *gauche* zwitterionic intermediate  $I_g$  which is 27.8 kcal/mol more stable than the *cis* 4-azido-2-pyrrolinone. This intermediate could also be formed by a *syn* attack of formaldimine on cyanoketene. The *anti* structure<sup>8f</sup> is not considered in this work since only the *syn* structure can be obtained in the thermolysis of the 4-azido-2-pyrrolinones. The inclusion of electronic correlation at the MP2 level causes  $I_g$  to disappear from the PES. The only minimum energy structure

located on this area of the MP2 PES in gas phase is a planar vdW complex,  $vdW_g$ , which results from the opening of the pyrrolinone ring (see Figure 6). In contrast, a planar *trans* zwitterionic intermediate,  $I_t$  in Figure 6, appears on the MP2 PES in which the C(ketene)–N(imine) bond distance has a value of 1.588 Å and is 0.6 kcal/mol less stable than  $vdW_g$  at the MP2 level (see Table 3). At the MP2 level the fragmentation of this *trans* intermediate requires only 0.6 kcal/mol through  $TS_t$  in Figure 6 and leads to a planar vdW structure ( $vdW_t$  in Figure 6). At the MP2 level,  $vdW_t$  and  $vdW_g$  have nearly the same energy and are connected to each other through a conformational rotation TS ( $TS_{vdW}$  in Figure 6) with an energy requirement of 1.7 kcal/mol. Both  $vdW_g$  and  $vdW_t$  complexes can directly dissociate without an energy barrier into isolated cyanoketene and formaldimine, which are about 7 kcal/mol higher in energy than the vdW complexes (see Table 3).

The minimum energy path for the formation of β-lactams from the zwitterionic intermediates proceeds, as in the Staudinger reaction,<sup>8a</sup> along a conrotatory electrocyclic closure. Figure 6 shows the optimized TS,  $TS_c$ , for the ring closure of the *gauche* vdW intermediate to give 3-cyano-2-azetidione. In this TS, the cyano group presents an *inward* orientation<sup>8d,f</sup> as a consequence of the *syn* relationship between cyano and formaldimine groups at the intermediate. The energy barrier corresponding to  $TS_c$  with respect to the  $vdW_g$  structure is 27.5 kcal/mol at the MP2 level, similar to the MP4//MP2 predicted value of 28.3 kcal/mol. The reaction energy corresponding to this ring contraction computed at MP2 level amounts to  $-26.7$  kcal/mol ( $-25.3$  at the MP4//MP2 level) relative to  $vdW_g$ .

In contrast with the thermolysis of vinyl azides discussed above, the electrostatic influence of solvent appears to play a decisive role in the nature of the cyanoketene–formaldimine intermediates, as expected from the large charge polarization present in these structures. This crucial effect of solvent has been previously recognized in the study of the Staudinger reaction between ketenes and imines.<sup>8b,c</sup> Therefore, we carried out optimizations in solution at the MP2/6-31G\* SCRF level ( $\epsilon = 2.38$ ) in order to estimate properly the role of solvent in the nature and evolution of the cyanoketene–formaldimine intermediates. Figure 6 and Table 3 display the geometric and energetic data of the located intermediates and TSs in solution. The most remarkable outcome of the optimization in solution is that a stable nonplanar *gauche* zwitterionic intermediate  $I_g$  is located on the MP2 SCRF PES in contrast with the gas-phase PES where no such structure was found (see Figure 6). This donor–acceptor intermediate has a C(ketene)–N(imine) bond distance of 1.577 Å and presents a nonplanar structure due to



**Figure 6.** MP2/6-31G\* optimized structures both in gas phase and in solution for the evolution of the zwitterionic intermediates (distances in Å, and values in parentheses correspond to MP2/6-31G\* SCRF optimized structures).

**Table 3.** Relative Energies (kcal/mol) of the Main Structures Involved in the Evolution of the Nonsubstituted Zwitterionic Intermediates

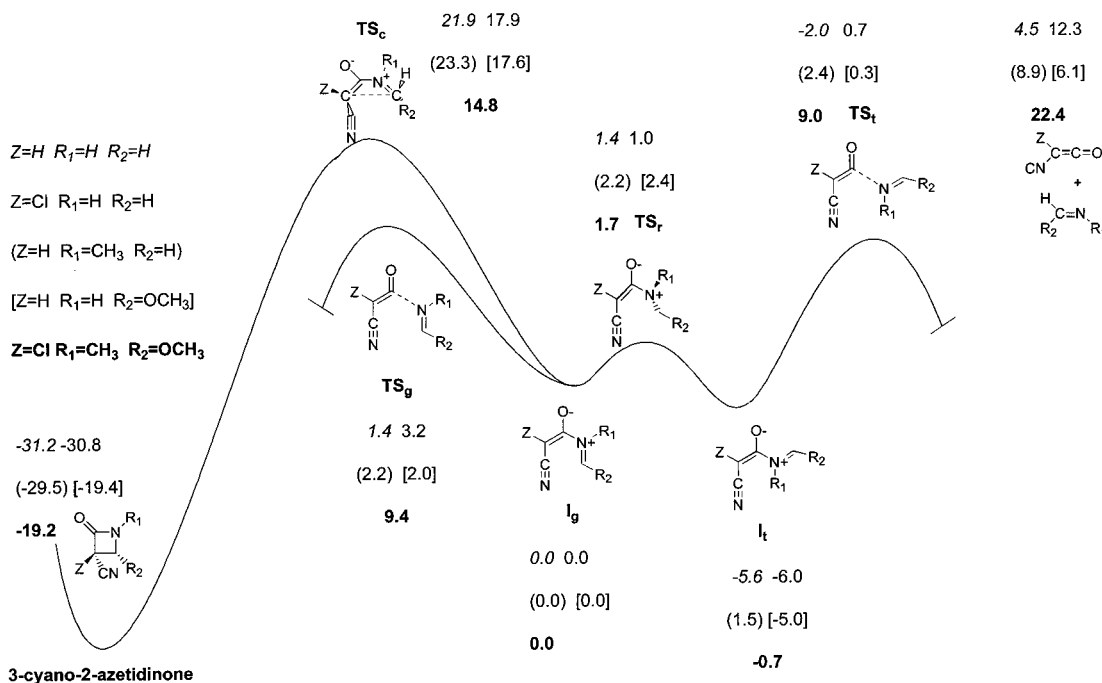
structures	MP2	ZPVE <sup>a</sup>	MP4SDQ//MP2	MP2 SCRF <sup>b</sup> ( $\epsilon = 2.38$ )
gauche intermediate ( <b>I<sub>g</sub></b> )	—	0.0	—	0.0
<b>TS<sub>g</sub></b> gauche int. ↔ gauche vdW int. ( <b>TS<sub>g</sub></b> )	—	-1.2	—	2.0
gauche vdW intermediate ( <b>vdW<sub>g</sub></b> )	0.0	-2.4	0.0	-0.4 (-2.3)
trans intermediate ( <b>I<sub>t</sub></b> )	-2.2	0.4	-0.6	-5.9 (-5.5)
<b>TS<sub>t</sub></b> trans int. ↔ trans vdW int. ( <b>TS<sub>t</sub></b> )	0.2	-1.4	0.4	—
trans vdW intermediate ( <b>vdW<sub>t</sub></b> )	0.0	-2.5	-0.1	—
<b>TS<sub>r</sub></b> gauche int. ↔ trans int. ( <b>TS<sub>r</sub></b> )	—	-0.6	—	1.7
<b>TS<sub>r</sub></b> gauche vdW ↔ trans vdW (gas phase) ( <b>TS<sub>r</sub>vdW</b> )	2.2	-2.9	2.3	1.3 (-2.7)
gauche vdW ↔ trans int. (solution) ( <b>TS<sub>r</sub>vdW</b> )	—	—	—	—
<b>TS<sub>c</sub></b> electrocyclic closure ( <b>TS<sub>c</sub></b> )	25.8	-0.7	26.6	22.9 (-4.7)
3-cyano-2-azetidinone	-30.7	1.6	-27.3	-32.7 (-3.8)
formaldimine + cyanoketene	8.6	-3.6	8.3	6.7 (-3.7)

<sup>a</sup> ZPVE correction from the HF/6-31G\* frequencies. <sup>b</sup> Optimization in solution at the MP2/6-31G\* SCRF level. Solvation energies are indicated in parentheses.

the steric interaction between the cyano group and the formaldimine moiety. At the MP2 SCRF level, 0.8 kcal/mol are

required to dissociate this intermediate through **TS<sub>g</sub>** to yield a vdW complex which is 2.8 kcal/mol more stable than **I<sub>g</sub>** (see





**Figure 7.** Sketch of the main substituted structures involved in the evolution of the zwitterionic intermediates. Relative energies (kcal/mol) at the MP2/6-31G\* SCRF ( $\epsilon = 2.38$ ) level using the HF/6-31G\* gas-phase geometries and including ZPVE correction from HF/6-31G\* frequencies are also indicated.

Figure 6). A TS for the internal rotation about the C(cyanoketene)–N(imine) bond ( $TS_r$  in Figure 6) connects  $I_g$  with  $I_t$  in solution, giving an energy barrier of 1.1 kcal/mol with respect to  $I_g$ . In addition, the MP2 SCRF optimization shows that the C(ketene)–N(imine) bond distance in solution is 0.031 Å shorter in the *trans* intermediate than in the corresponding gas-phase structure.  $vdW_t$  and  $TS_t$  structures which were already very close in structure and in energy in the MP2 gas-phase PES (see Table 3 and Figure 6) coalesce in solution when optimizing at the MP2 SCRF level. In solution  $TS_r$  connects  $I_t$  and  $vdW_g$  structures with an energy barrier of 1.2 kcal/mol with respect to the *gauche* vdW cyanoketene–formaldimine structure.

On the other hand, the electrostatic effect of solvent decreases the energy barrier connecting the zwitterionic intermediates with the  $\beta$ -lactam whereas the energy barriers for fragmentation to yield the corresponding van der Waals complexes are increased. Thus, at the MP2 level the energy barrier for the electrocyclic closure of the  $vdW_g$  complex in gas phase is 27.5 kcal/mol while in solution the ring closure takes place from a moderately stable *gauche* zwitterionic intermediate with an energy barrier of 22.2 kcal/mol. It appears then that the electrostatic effect of solvent favors the formation of the  $\beta$ -lactams from the zwitterionic intermediates. However, the solvent effect in the cyanoketene–formaldimine system result is clearly insufficient to explain a significant stereochemical ring closure to form  $\beta$ -lactams given that the energy barrier for the dissociation of the *gauche* intermediate structure (0.8 kcal/mol at the MP2 SCRF level) is much smaller than that for the electrocyclic closure (22.2 kcal/mol at the same level). Therefore, a crucial role must be played by substituents in the evolution of the zwitterionic intermediates.

**D. Evolution of the Substituted Zwitterionic Intermediates.** We shall discuss now the effect of substitution at three different positions of the cyanoketene–formaldimine zwitterionic intermediates. The following groups were chosen: Z = Cl, R<sub>1</sub> = CH<sub>3</sub>, and R<sub>2</sub> = CH<sub>3</sub>O (see Scheme 3). Owing to the size of the substituted systems and on the basis of the good

performance of the MP2//HF calculations on the nonsubstituted system, calculations were carried out optimizing the substituted structures at HF level in the gas phase and performing MP2 single-point calculations on the HF structures both in the gas phase and in solution.<sup>25</sup> Furthermore, the experience gained from the topology of the PES in the nonsubstituted case allowed us to focus our attention on the most chemically significant critical points for the substituted systems. Figure 7 shows the substituted structures that were studied along the reaction coordinate and indicates their relative energies calculated at the MP2/6-31G\*//HF/6-31G\* SCRF level, including the ZPVE correction from the HF/6-31G\* frequencies (unless otherwise indicated, energies cited in the text hereafter correspond to this theory level). Some molecular properties of the different substituted  $I_g$  structures are collected in Table 4. First, the effect of each substituent is discussed separately, and subsequently the simultaneous effects of two and the three substituents will be considered.

The presence of the chlorine atom provokes a greater interaction between Cl–cyanoketene and formaldimine moieties in the zwitterionic intermediates: the C(ketene)–N(imine) bond distance is slightly shortened in 0.021 Å at  $I_g$ , and the HF NBO<sup>26</sup> charge transfer from the formaldimine moiety to cyanoketene is increased in 0.029 au with reference to the nonsubstituted case (see Table 4). This can be understood in terms of the electron-withdrawing effect of the chlorine atom conferring a greater acceptor capability to the substituted cyanoketene whose LUMO orbital energy decreases by 0.04 au. On the other hand, the  $\pi$ -donor effect and the *outward* alignment of the chlorine atom stabilize the TS for the electrocyclic closure,  $TS_c$ , by means

(25) In general, for the nonsubstituted systems studied in this work, the MP2//HF and MP2 relative energies manifest a good agreement. In addition, the solvation energy calculated on gas-phase optimized structures (not detailed here) compare well with that calculated on structures optimized in solution and reported in Table 3.

(26) (a) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735. (b) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

**Table 4.** Molecular Properties of the Substituted *gauche* Intermediates ( $I_g$ ) Optimized at the HF/6-31G\* Theory Level in the Gas Phase

properties	Z = H, R <sub>1</sub> = H, R <sub>2</sub> = H	Z = Cl, R <sub>1</sub> = H, R <sub>2</sub> = H	Z = H, R <sub>1</sub> = H, R <sub>2</sub> = OCH <sub>3</sub>	Z = H, R <sub>1</sub> = CH <sub>3</sub> , R <sub>2</sub> = H	Z = Cl, R <sub>1</sub> = CH <sub>3</sub> , R <sub>2</sub> = H	Z = H, R <sub>1</sub> = CH <sub>3</sub> , R <sub>2</sub> = OCH <sub>3</sub>	Z = Cl, R <sub>1</sub> = H, R <sub>2</sub> = OCH <sub>3</sub>	Z = Cl, R <sub>1</sub> = CH <sub>3</sub> , R <sub>2</sub> = OCH <sub>3</sub>
C(ketene)–N(imine) bond distance (Å)	1.564	1.543	1.531	1.560	1.540	1.532	1.514	1.518
imine → ketene NBO charge transfer (au)	0.509	0.538	0.550	0.517	0.547	0.578	0.552	0.579
dipole moment (debyes)	6.78	8.65	8.52	6.84	8.74	7.87	10.55	9.96
$\Delta E_0^\ddagger$ <sup>a</sup> for fragmentation (kcal/mol)	0.9	3.2	2.0	2.2	5.7	4.8	5.4	9.4
$\Delta E_0^\ddagger$ <sup>a</sup> for electrocyclic closure (kcal/mol)	22.6	(2.2) 17.9	(1.1) 17.6	(1.3) 23.3	(4.8) [1.3] 18.6	(3.9) [1.5] 18.4	(4.5) [2.1] 13.9	(8.5) [4.8] 14.8
mean life $\tau \times 10^{13}$ (s) <sup>b</sup>	2.8	(-4.7) 38	(-5.0) 5.2	(0.7) 7.4	(-4.0) [0.0] 7.4·10 <sup>2</sup>	(-4.2) [0.1] 2.7·10 <sup>2</sup>	(-8.7) [1.0] 3.2·10 <sup>2</sup>	(-7.8) [1.2] 1.1·10 <sup>5</sup>

<sup>a</sup> Energy barriers computed at the MP2/6-31G\*\*/HF/6-31G\* level including ZPVE correction from HF/6-31G\* frequencies and solvation energy ( $\epsilon = 2.38$ ).  $\delta\Delta E_0^\ddagger$  between the substituted and nonsubstituted  $I_g$  structure are shown into parentheses. ( $\delta\Delta E_0 - \sum\delta\Delta E_{0,mono}$ ) is a measure of the cooperative effect of substituents in the energy barriers and is shown in brackets for the two- and three-substituted  $I_g$  structures. <sup>b</sup> See ref 29.

of the so-called torquoelectronic effect.<sup>8df,27</sup> Therefore, the 2-fold electronic role of the chlorine atom results in an increase of 1.8 kcal/mol in the energy barrier for the fragmentation of  $I_g$  and a diminution of 4.0 kcal/mol in the energy barrier for the electrocyclic closure with respect to the nonsubstituted system.

The effect of the CH<sub>3</sub>O group on the evolution of the zwitterionic intermediates is mainly related to the stabilization of these intermediates supplied by the electron-donor ability of methoxy. The donor–acceptor interaction between formaldimine and cyanoketene at the  $I_g$  structure is slightly strengthened according to the calculated reduction of the C(ketene)–N(imine) bond distance (0.033 Å) and the increase of 0.041 e of the HF NBO<sup>26</sup> charge transfer from the fomaldimine moiety to cyanoketene with respect to the nonsubstituted system (see Table 4). Thus, the barrier for the dissociation of  $I_g$  shows a moderate increment of 0.6 kcal/mol.<sup>28</sup> A more prominent effect of the methoxy group is found in  $TS_c$  where CH<sub>3</sub>O is placed in an *outward* orientation stabilizing this TS due to the above mentioned torquoelectronic effect.<sup>8d,f</sup> The barrier for the electrocyclic closure with respect to  $I_g$  amounts to 17.6 kcal/mol at the MP2//HF level (4.3 kcal/mol lower than the nonsubstituted system).

The most important effect of the methyl group is a consequence of its steric requirements. From data in Figure 7 it can be seen that the methyl group favors the  $I_g$  intermediate due to important steric interactions between methyl and cyano groups in the *trans* conformation. In this case, the *trans* intermediate,  $I_t$ , has a nonplanar structure (C=C···N=C: 149.5°) and is 1.5 kcal/mol (MP2//HF) less stable than  $I_g$ . Hence, the presence of the methyl group inverts the previously observed trend regarding the relative stability of *gauche* and *trans* intermediates. The rest of the relative energies and molecular properties for R<sub>1</sub> = CH<sub>3</sub> do not show significant changes with respect to their corresponding nonsubstituted structures.

Concerning the effect of solvent on the monosubstituted systems it can be noted that the stabilization of the zwitterionic intermediates by the electrostatic interaction with solvent is slightly reinforced by chlorine and methoxy substituents owing to the increase in the dipole moments induced by these groups (see Table 4). When compared with MP2//HF calculations in gas phase, the MP2//HF SCRF single-point calculations predict increments of 3.0 and 2.7 kcal/mol in the fragmentation barriers

(27) Dolbier, W. R.; Koronial, H.; Houk, K. N.; Sheu, C. *Acc. Chem. Res.* **1996**, *29*, 471–477.

(28) In view of the effect of the electronic correlation on this part of the PES for the nonsubstituted system, this particular barrier was further investigated by means of MP2/6-31G\* optimizations of the  $I_g$  and  $TS_g$  structures substituted with R<sub>2</sub> = OCH<sub>3</sub>. These two critical points were confirmed to exist at MP2 level, the resultant barrier being 0.4 kcal/mol.

for the Cl- and methoxy-substituted  $I_g$  structures, respectively. The corresponding calculated increments of the energy barriers for the electrocyclic closure are 3.3 and 1.1 kcal/mol, respectively.

The inclusion of two substituents and solvent simultaneously induces in all the cases an increase of about 2 kcal/mol in the energy barriers for the fragmentation of the  $I_g$  structures (see Table 4). The most remarkable effect on the electrocyclic closure occurs when Cl and CH<sub>3</sub>O groups are present, rendering an energy barrier of only 13.9 kcal/mol due to the nearly additive character of the torquoelectronic effect of both substituents.

When the three substituents are present and the solvent is taken into account, the energy barrier for dissociation of the  $I_g$  structure has a value of 9.4 kcal/mol, the  $I_t$  structure is only 0.7 kcal/mol more stable than  $I_g$ , and the energy barrier for the electrocyclic closure of the  $I_g$  structure is 14.8 kcal/mol (see Table 4). These computational results indicate that the fragmentation and the electrocyclic closure of the fully substituted  $I_g$  structure could be kinetically competitive processes, the  $\beta$ -lactams being the thermodynamically favored products by 41.6 kcal/mol with respect to the isolated Cl-cyanoketene and methoxy-*N*-methylformaldimine fragments.

When the data in Figure 7 are compared for the fully substituted system with those for the monosubstituted systems, it is clear that the similar stability of *gauche* and *trans* zwitterionic intermediates is related to the presence of the methyl group. Similarly, the combined electronic effect of the Cl and CH<sub>3</sub>O groups on the electrocyclic closure accounts for the observed diminution in the corresponding energy barrier. However, the most striking results are the computed barriers for dissociation of the *gauche* and *trans* intermediates. The magnitude of these energy barriers (approximately 11 and 8 kcal/mol at MP2//HF level with and without estimation of solvent effects, respectively) reveals that the effect of the substituents is not strictly additive and consequently, an important cooperative effect may be claimed. This is clearly shown by  $\delta\Delta E_0^\ddagger - \sum_{mono}\delta\Delta E_0^\ddagger$  as a measure of the cooperative effect in the energy barriers for fragmentation and electrocyclic closure (see Table 4 for the details). When passing from the monosubstituted systems to the 2-fold substituted ones, the cooperative effect on the energy barrier for fragmentation is about 1–2 kcal/mol. However, this cooperative effect rises sharply up to 4.8 kcal/mol when the three substituents are included. The importance of this cooperative effect is also reflected by the mean life for fragmentation of the  $I_g$  structures in solution which was estimated using the conventional transition state theory.<sup>29</sup> As Table 4 shows, the separate incorporation of the substituents hardly increases the mean life of the substituted intermediates which is around 10<sup>-13</sup> s. For the disubstituted

structures, the computed mean life increases to  $10^{-12}$  s. Notably, the simultaneous effect of the three substituents dramatically increases the computed mean life up to  $10^{-8}$  s. This large value of the mean life would allow for equilibration of the internal energy of the zwitterionic intermediate facilitating the access of the system to the electrocyclic closure channel in competition with fragmentation. Thus, the observed yield of 55% reported by Moore et al.<sup>4</sup> for the ring contraction to  $\beta$ -lactam of the three-substituted azidopyrrolinones studied in the present work ( $Z = \text{Cl}$ ,  $R_1 = \text{CH}_3$ ,  $R_2 = \text{OCH}_3$ ) could be explained. On the other hand, when  $R_1 = \text{CH}_3$  is replaced by  $R_1 = \text{CH}_2\text{CH}_3$  or  $R_1 = \text{CH}(\text{CH}_3)_2$ , yields around 88–90% have been obtained. This is in accord with our finding that the steric effect of the  $R_1$  group favors the *gauche* zwitterionic intermediate which is the precursor for the electrocyclic closure. In this way, the *trans* channel for dissociation becomes disfavored and the yield of the alternative cyclization increases. Replacement of  $R_2 = \text{CH}_3\text{O}$  by  $R_2 = \text{CH}_3\text{CH}_2\text{O}$  barely modifies the observed yield to a 60% in agreement with the similar electron-donor character of these substituents.

### Summary

The kinetic controlling step of the zwittazido cleavage of 4-azido-2-pyrrolinone corresponds to the loss of a  $\text{N}_2$  molecule from the *trans* conformer of the initial vinyl azide leading to the azirine intermediate. For the nonsubstituted system, the MP4SDQ/6-31G\*\*//MP2/6-31G\* energy barrier for this process has a value of 29.1 kcal/mol including ZPVE correction from the HF/6-31G\* frequencies. Taking into account the dynamical and nondynamical electronic correlation, the appearance of a vinyl nitrene as a critical point on the PES is discarded in favor of the azirine intermediate. The azirine intermediate rearranges to a more stable zwitterionic intermediate passing through a TS which presents an energy barrier of 24.8 and 21.3 kcal/mol at the MP4SDQ/6-31G\*\*//MP2/6-31G\* and MP4SDTQ/6-31G\*\*//MP2/6-31G\* levels including ZPVE correction from the HF/6-31G\* frequencies, respectively. A reaction path through the

(29) The mean lifes of the zwitterionic intermediates  $\mathbf{I}_g$  were estimated as  $\tau = 1/k_{\text{diss}}$ , where  $k_{\text{diss}}$  is the kinetic constant for the fragmentation of the  $\mathbf{I}_g$  structures through the corresponding  $\mathbf{TS}_g$ .  $k_{\text{diss}}$  was computed using the conventional transition state theory:

$$k_{\text{diss}} = \frac{kT}{h} \frac{Q_{\text{TS}_g}^\ddagger}{Q_{\mathbf{I}_g}} \exp\left(\frac{-\Delta E_0^\ddagger}{RT}\right)$$

$\Delta E_0^\ddagger$  is the activation barrier for fragmentation as shown in Table 5, and the selected temperature was 90 °C.

formation of a triazole intermediate is not a competitive kinetic alternative to the  $\text{N}_2$  elimination from 4-azido-2-pyrrolinone. The *gauche* zwitterionic intermediate may undergo either an electrocyclic closure to a  $\beta$ -lactam or a dissociation into formalimine and cyanoketene. Although SCRF calculations reveal that the zwitterionic structures are clearly favored by the electrostatic interaction with solvent, our calculations show that fragmentation of the nonsubstituted zwitterions presents very low barriers compared to the electrocyclic closure.

At the MP2/6-31G\*\*//HF/6-31G\* SCRF level including the ZPVE correction from the HF/6-31G\* frequencies, it has been shown that the role played by substituents is critical on the evolution of the zwitterionic intermediates. The  $R_2 = \text{CH}_3\text{O}$  and  $Z = \text{Cl}$  substituents slightly strengthen the charge transfer interaction between cyanoketene and formalimine fragments while the  $R_1 = \text{CH}_3$  group destabilizes the *trans* zwitterions with respect to the *cis* ones due to steric repulsions. The presence of Cl and  $\text{CH}_3\text{O}$  substituents reduces the energy barrier for the ring contraction of zwitterions to  $\beta$ -lactams by the torquoelectronic effect. The simultaneous inclusion of the three substituents is required in order to rationalize the experimental data by Moore et al.<sup>4</sup> Thus, the computed energy barriers for fragmentation and electrocyclic closure of the nonsubstituted or monosubstituted zwitterionic intermediates are 2–3 and 18–22 kcal/mol, respectively, whereas for the three-substituted structures the corresponding values are 9.4 and 14.8 kcal/mol, respectively. Consequently, when the three substituents are included and solvent is taken into account, the mean life of the zwitterionic intermediates before fragmentation is notably increased, thus allowing a significant formation of the thermodynamically favored  $\beta$ -lactam ring in agreement with experiment. Therefore the formation of  $\beta$ -lactams through the zwittazido cleavage reaction would be favored by using  $Z$  and  $R_2$  strong electron-donor substituents and  $R_1$  substituents destabilizing the *trans* conformation of the zwitterionic intermediates through steric hindrance.

**Acknowledgment.** The authors thank Dr. R. López (University of Oviedo), Dr. M. F. Ruiz-López (University of Nancy) and one of the referees for helpful comments and suggestions, and the CICYT (Spain) for computer time on the Cray YMP at the CIEMAT and are grateful to the DGICYT for financial support (PB94-1314-C03-01). D.S. also thanks the DGICYT (Spain) for a grant.

JA970517J