

**REGIOSELECTIVITY OF [2+3] CYCLOADDITION OF  
TRIPHENYLNITRONE TO NITROETHENE –  
AM1/COSMO COMPUTATIONAL STUDY<sup>+</sup>**Radomir JASIŃSKI<sup>1,\*</sup> and Andrzej BARAŃSKI<sup>2</sup>

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Two isomeric pathways for the [2+3] cycloaddition of triphenylnitron to nitroethene in a dielectric medium corresponding to the relative permittivity of toluene was evaluated in terms of AM1/COSMO calculations. It was found that reaction leading to 4-nitro-2,3,3-triphenylisoxazolidine (path A) occurs via a zwitterionic intermediate, whereas the reaction leading to 5-nitro-2,3,3-triphenylisoxazolidine (path B) takes place in concerted way. The activation parameters estimated for both reaction pathways indicate that A is favored ( $\Delta G_{\text{TSA}} = 34.33$  kcal/mol;  $\Delta G_{\text{TSB}} = 43.37$  kcal/mol). The reaction regioselectivity is in good agreement with the experimental data.

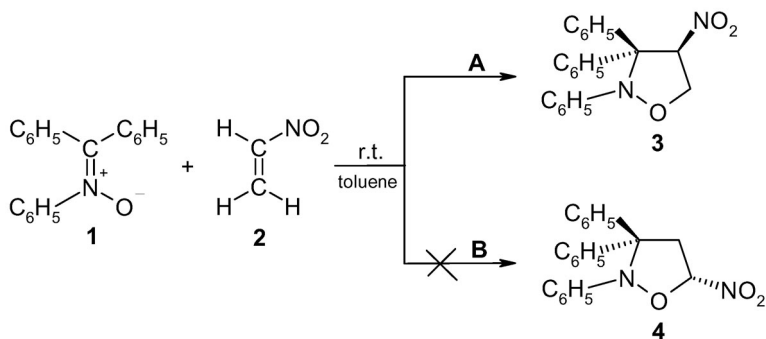
**Keywords:** [2+3] Cycloaddition; Nitron; Nitroethene; Regioselectivity; Mechanism; AM1/COSMO calculations.

Several years ago, Burdisso and Gandolfi<sup>2</sup> found that the [2+3] cycloaddition of triphenylnitron **1** to nitroethene **2** at room temperature yields 4-nitro-2,3,3-triphenylisoxazolidine (**3**) as the only reaction product (Scheme 1).

In order to explain the reaction regioselectivity, the AM1/COSMO<sup>3</sup> studies of competitive paths A and B in the dielectric medium corresponding to the relative permittivity of toluene were carried out. In particular, for each of them the kinetic and thermodynamic parameters were estimated. It is necessary to note that we successfully applied a similar approach earlier in the cycloaddition of various conjugated nitroalkenes with methyl azide<sup>4</sup>,

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formonitrile *N*-oxide<sup>5</sup>, arylnitrones<sup>6</sup>, as well as with furan<sup>7</sup> and cyclopentadiene<sup>7,8</sup>. This paper is intended as a continuation of our quantum chemical studies on the reactivity of nitroalkenes in [4+2]  $\pi$ -electron cycloadditions.



SCHEME 1

## CALCULATIONS

In the present paper, reactions A and B (Scheme 1) are treated as independent processes. Geometry optimizations of the stationary structures in the presence of solvent were carried out using AM1/COSMO<sup>3,9</sup> method implemented in MOPAC93 package. In the method, the solvent is simulated as a continuous medium, which surrounds a molecule-shape cavity, in which the solute is placed. The solvent is characterized by its relative permittivity (EPS), effective solvation radius (RSOLV), and the number of segments per atom (NSPA) which defines the solvent accessible surface area based on the van der Waals radii. In this paper we used: EPS of 2.3, RSOLV of 1 Å and NSPA of 42. Optimization of stable structures to a gradient norm less than 0.5 was performed with EF routine, whereas transition states were optimized with SADDLE routine followed by NLLSQ and TS algorithms. Stationary points were characterized by frequency calculations. The reactants, products and local minima had positive Hessian matrices. The transition states showed only one negative eigenvalue in their diagonalized Hessian matrices. The IRC calculations were carried out analogously as described recently<sup>6</sup>. In this way the minima associated with local minima **LM**, products **3**, **4** and intermediate **I** structures were localized.

The calculations presented at this paper were carried out for 293 K. The absolute entropy of all structures was calculated from a complete vibrational analysis. Enthalpies were corrected to Gibbs free energies using the

calculated entropies. The molecular properties obtained from the critical structures are shown in Table I.

## RESULTS AND DISCUSSION

The AM1/COSMO calculations show that in both reaction pathways the interactions of addition species initially lead to local minima **LM** (Fig. 1) without the necessity of overcoming the activation barrier.

Their existence on the PES is related to the reduction of the enthalpy of the reaction system by 2.09 kcal/mol for **LM<sub>A</sub>** and 2.70 kcal/mol for **LM<sub>B</sub>** (Table II). The minima found are only enthalpic. Due to the entropy factor ( $T\Delta S$ ), the Gibbs energies of both structures at 293 K are positive ( $\Delta G_{\text{LM}_A} - \Delta G_{1+2} = 12.89$  kcal/mol,  $\Delta G_{\text{LM}_B} - \Delta G_{1+2} = 13.50$  kcal/mol). Within the **LMS**, the reaction centres do not adopt the spatial orientation found later in transition complexes (Fig. 2). The latter are not orientation complexes according to Huisgen's terminology<sup>11</sup>. Nor they have any features of charge transfer complexes (CT) postulated by Konovalov<sup>12</sup> because there is no charge transfer between substructures ( $t = 0.0$ ).

Further movement of the addition species along the intrinsic coordinates of reactions A and B leads to transition complexes **TS<sub>A</sub>** and **TS<sub>B</sub>** (Fig. 1). Their nature is confirmed by the existence of one imaginary eigenvalue of the Hessians. The energy expense needed to achieve a required critical

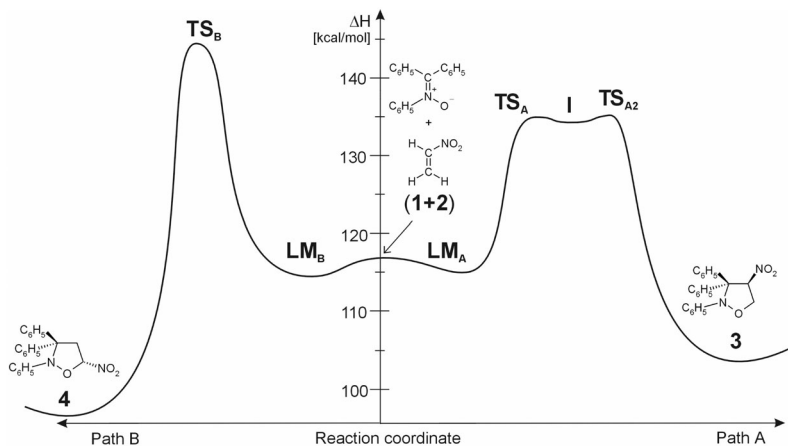


FIG. 1

Reaction profiles for the [2+3] cycloaddition of triphenylnitron **1** to nitroethene **2**. The structures are depicted in Fig. 2

TABLE I  
Essential molecular properties from the AM1/COSMO calculations of stationary structures for the [2+3] cycloaddition of triphenylnitroene **1** to nitroethene **2** (in toluene, T = 293 K)

Path	Structure	Distance, Å			Angle, ° C3-O1-C5-C4	$\Delta H$ kcal/mol	$\Delta S$ cal/mol K	$\Delta G$ kcal/mol	$\mu$ D	$t^a$ e
		$d_{C3-C4}$	$d_{C4-C5}$	$d_{C5-O1}$						
<b>1</b>		-	-	-	107.27	105.5	76.36	5.06	-	
<b>2</b>		-	1.336	-	9.64	69.2	-10.65	5.52	-	
<b>LM<sub>A</sub></b>		5.993	1.336	3.279	53.85	123.6	78.60	11.12	0.00	
<b>TS<sub>A</sub></b>		4.300	1.394	1.832	86.65	120.2	100.04	10.61	0.21	
<b>I</b>		3.230	1.440	1.536	30.87	120.1	98.55	12.73	0.57	
<b>TS<sub>A2</sub></b>		2.679	1.449	1.521	7.44	120.2	99.62	11.49	0.53	
<b>3</b>		1.589	1.536	1.452	4.76	120.8	67.56	4.61	-	
<b>1</b>		-	-	-	107.27	105.5	76.36	5.06	-	
<b>2</b>		-	1.336	-	9.64	69.2	-10.65	5.52	-	
<b>LM<sub>B</sub></b>		5.716	1.336	3.263	107.03	119.4	79.22	5.27	0.00	
<b>TS<sub>B</sub></b>		2.115	1.399	1.983	5.62	120.0	109.08	7.00	0.08	
<b>4</b>		1.566	1.527	1.434	7.26	116.9	62.16	5.24	-	

<sup>a</sup> Charge transfer was calculated according to Leroy<sup>10</sup>.

TABLE II  
Kinetic and thermodynamic parameters calculated for the [2+3] cycloaddition of triphenylnitron **1** to nitroethene **2** (in toluene, T = 293 K)

Transition	Activation parameters			Thermodynamic parameters				
	$\Delta H^\ddagger$ kcal/mol	$\Delta S^\ddagger$ cal/mol K	$\Delta G^\ddagger$ kcal/mol	$\Delta H_T$ kcal/mol	$\Delta S_T$ cal/mol K	$\Delta G_T$ kcal/mol	log K	$\gamma^*$
<b>(1+2) → LM<sub>A</sub></b>	-	-	-	-2.09	-51.11	12.89	-9.55	0.00
<b>(1+2) → I</b>	18.36	-54.51	34.33	16.83	-54.61	32.83	-24.33	0.00
<b>I → 3</b>	1.09	0.04	1.08	-30.80	0.64	-30.99	22.97	1.00
<b>(1+2) → 3</b>	-	-	-	-13.97	-53.97	1.84	-1.37	0.02
<b>(1+2) → LM<sub>B</sub></b>	-	-	-	-2.70	-55.29	13.50	-10.01	0.00
<b>(1+2) → 4</b>	27.32	-54.76	43.37	-20.50	-57.82	-3.56	2.64	0.95

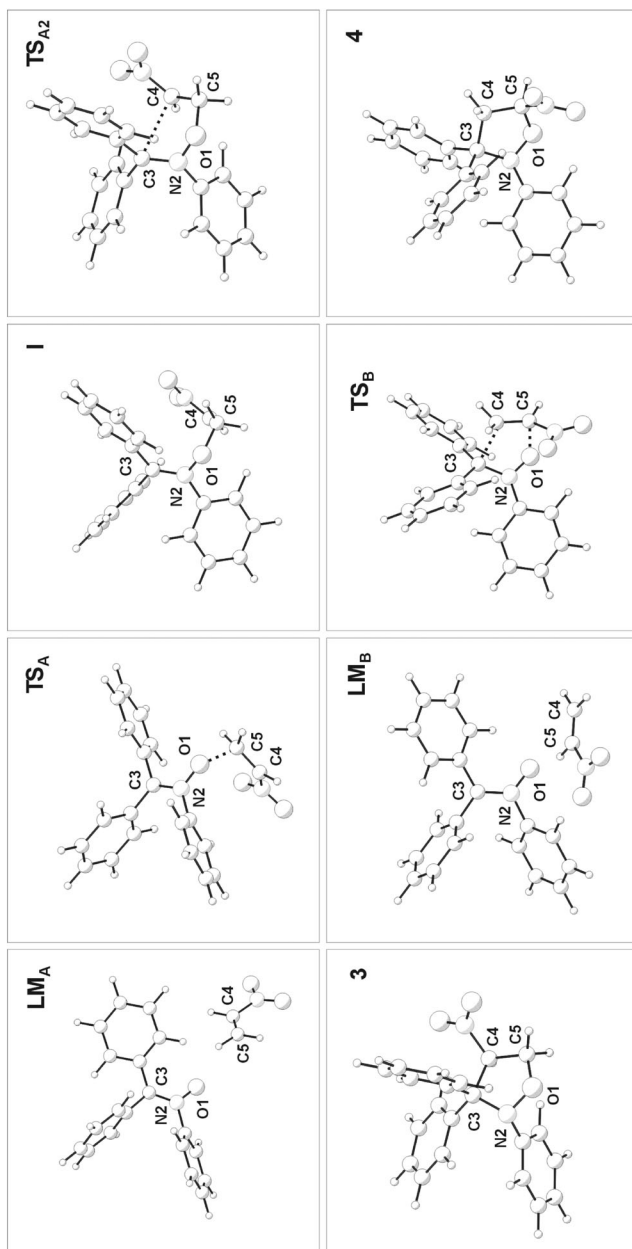


FIG. 2  
 PLUTO views of stationary structures for the [2+3] cycloaddition of triphenylnitrene **1** with nitroethene **2** in toluene solution screening in paths A and B

point on the PES is rather variable. As for reaction A, the activation Gibbs energy is 34.33 kcal/mol, and for reaction B it is as high as 43.37 kcal/mol. This means that cycloadduct **3** should be the kinetically preferred product at room temperature ( $\Delta G_{\text{TSB}} - \Delta G_{\text{TSA}} = 9.04$  kcal/mol). This correlates well with the results of experimental studies<sup>2</sup>.

Furthermore, the complexes found also differ in their structures (Fig. 2). In particular, the  $\text{TS}_B$  structure is of a biplanar type<sup>13</sup>. This means that both  $\sigma$  bonds needed for the formation of the azolidine ring are formed simultaneously, even though the degree of their formation varies ( $d_{\text{C3-C4}} = 2.115$  Å,  $d_{\text{C5-O1}} = 1.983$  Å). The movement of the addition species from the  $\text{TS}_B$  area along the reaction coordinate leads directly to the cycloadduct **4** minimum. Unlike the  $\text{TS}_B$  complex,  $\text{TS}_A$  is not of a biplanar type. Only one  $\sigma$  bond forms within its structure. This bond is located between reaction centres C5 and O1 ( $d_{\text{C5-O1}} = 1.832$  Å). The distance between centres C3 and C4 ( $d_{\text{C3-C4}} = 4.300$  Å) is much longer than the typical bond length in transition complexes of cycloaddition reactions between nitrones and simple alkenes<sup>14</sup>. The transition from the  $\text{TS}_A$  region to the product **3** minimum leads through a shallow minimum of intermediate **I** ( $\Delta G_{\text{I}} - \Delta G_{\text{TSA}} = -1.50$  kcal/mol). The high dipole moment ( $\mu = 12.73$  D) and the value of the charge transfer from the nitron to the nitroalkene substructure ( $t = 0.57$ ) indicate its zwitterionic nature. Inclusion of 3\*3 CI in the calculations of **I** structure causes decrease their heats of formation only by ca. 0.3 kcal/mol relative to the SCF value of 133.74 kcal/mol. This fact excludes a biradical character of **I**.

Intermediate **I** is converted to cycloadduct **3** after overcoming a minor activation barrier ( $\Delta G = 1.08$  kcal/mol) related to the system's entering the  $\text{TS}_{A2}$  transition state region. Within  $\text{TS}_{A2}$ , a  $\sigma$  bond forms necessary for closing the azolidine ring ( $d_{\text{C3-C4}} = 2.679$  Å). Therefore, the AM1/COSMO calculations indicate that the reaction leading to cycloadduct **3** does not follow the concerted mechanism. This may not be ruled out in the case of the [2+3] cycloaddition of extremely  $\pi$ -deficient alkenes to nitrones with the strongly hindered reaction centre<sup>15</sup>. It is necessary to note at this point, that the ionization potential of nitroethene determined using the PES equals 11.14 eV<sup>16</sup>.

As it should be expected, the heterocycle in cycloadducts **3** and **4** is not flat (Fig. 2). Moreover, Gibbs energy of **3** differs from that of **4** (Table I). This causes that the equilibrium degree of conversion  $\gamma^*$ <sup>17</sup> for path B equals 0.95, whereas that for path A is only 0.02. At room temperature, however, the regioselectivity of the reaction studied is not determined by the thermochemical factors but by the height of activation barriers (Fig. 1, Table II).

## CONCLUSIONS

The AM1/COSMO calculations satisfactorily account for the regioselectivity of the [2+3] cycloaddition of triphenylnitron with nitroethene observed within the experimental studies<sup>2</sup>. Furthermore, they suggest that the reaction leading to 4-nitro-2,3,3-triphenylisoxazolidine occurs via a zwitterionic intermediate, whereas the reaction leading to 5-nitro-2,3,3-triphenyl-5-nitroisoxazolidine takes place in the concerted way. However, it is necessary to note that the AM1/COSMO method is of a semi-empirical type and the quantitative aspects of the results obtained should be treated with caution<sup>18</sup>.

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