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SYNTHESIS AND PROPERTIES OF AZOLES AND AZOLE DERIVATIVES

63.* QUANTUM-CHEMICAL ANALYSIS OF [2+3] CYCLOADDITION OF 3-NITRO-1-PROPENE WITH TRIPHENYLNITRONE

R. Jasiński, E. Jasińska, and A. Barański

Quantum-chemical calculations using the semiempirical AM1/COSMO method have shown that the regioselectivity of [2+3] cycloaddition of 3-nitro-1-propene to triphenylnitrone is a function of thermodynamic factors.

Keywords: nitroisoxazolidines, [2+3] cycloaddition, AM1/COSMO, mechanism.

In previous work [2], we reported that the cycloaddition of 3-nitro-1-propene (**1**) to triphenylnitrone (**2**) proceeds regioselectivity. Of the two theoretically possible nitromethylisoxazolidines **3** and **4**, only 5-nitromethyl-2,3,3-triphenylisoxazolidine (**4**) is formed in 15% yield. However, this pathway is not the only direction for the conversion of nitroalkene **1**, which is partially converted under the reaction conditions to 1-nitro-1-propene (**5**). The reaction of propene **5** with nitrone **2** gives 4,5-*trans*-5-methyl-4-nitro-2,3,3-triphenylisoxazolidine (**6**) in 75% yield. Thus, the overall reaction is complex in nature (Scheme 1).

In order to understand the specifics of these reactions, we carried out a quantum-chemical analysis of the cycloaddition of nitropropene **1** to nitrone **2** through regioisomeric pathways **A** and **B** using the AM1/COSMO program from the MOPAC93 package [3]. In previous work [4, 5], we carried out similar calculations for the reaction of this nitrone with nitropropene **5** (pathways **C** and **D**).

The reaction analyzed was carried out without solvent with a ten-fold excess of nitroalkene **1**. Since, the dielectric constant for nitroalkene **1** is unknown, the EPS key word with value 38 was used for taking account of the solvent effect. This permits us to simulate a dielectric continuum for a reaction carried out in nitromethane [3]. (According to AM1 data, the dipole moments of nitropropene **1** and nitromethane differ only slightly and, thus, we assumed that the two compounds have similar EPS dielectric constants). Taking account of the opinion of the authors of the COSMO program [6], the NSPA parameter characterizing the solvation density, was taken equal to 42. The calculations were carried out analogously to those described in our previous work [4]. The critical structure parameters obtained as well as the activation parameters of the reactions examined are given in Table 1.

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* For Communication 62 see [1].

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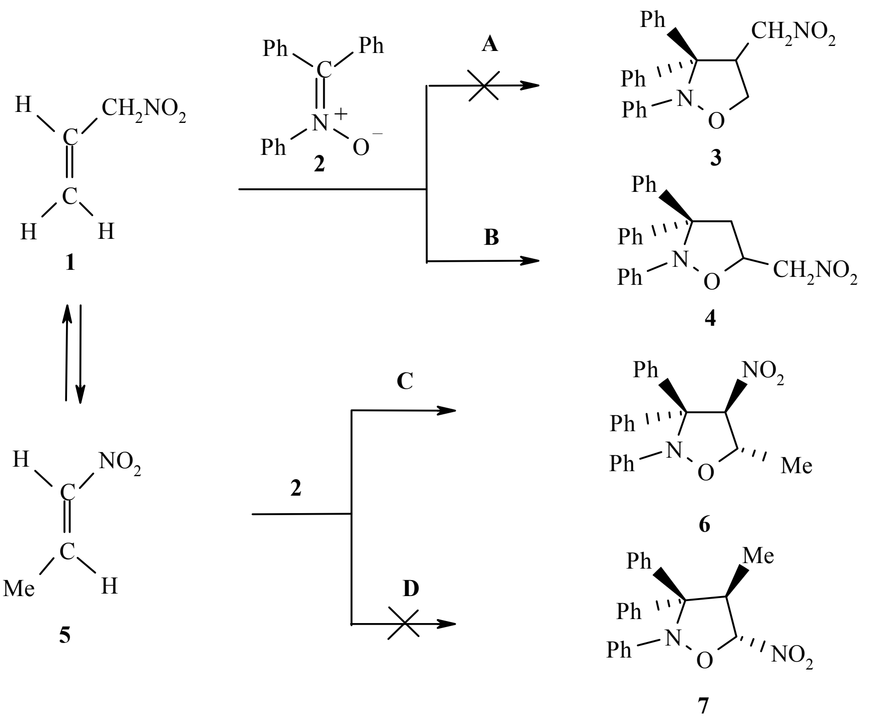

Fig. 1 implies that that the energy profiles for reaction pathways **A** and **B** are similar. In each case, there is only one transition state between the minima of the substrates and products, which confirms the concerted nature of the reaction. Both transition states have biplanar structure typical for cycloaddition

TABLE 1. Major Molecular Properties of the Critical Structures and Activation Parameters in the Cycloaddition of 3-Nitro-1-propene (**1**) to Triphenylnitrone (**2**) in Nitromethane According to an AM1/COSMO Calculation

Structure	r, Å		t*, e	ΔH_{298}, kcal/mol	ΔS_{298}, cal/mol·K	ΔG_{298}, kcal/mol	Activation parameters		
	C(3)–C(4)	C(5)–O(1)					$\Delta H^{\neq}$, kcal/mol	$\Delta S^{\neq}$, cal/mol·K	$\Delta G^{\neq}$, kcal/mol
1+2	∞	∞	—	90.69	180.8	36.79	—	—	—
TS$_A$	2.510	1.771	0.54	124.87	122.5	88.36	34.19	-58.3	51.57
3	1.576	1.458	—	79.93	117.7	44.86	—	—	—
TS$_B$	2.182	1.972	0.05	124.78	123.8	87.89	34.09	-57.1	51.10
4	1.565	1.457	—	74.27	124.8	37.07	—	—	—

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* Charge transfer calculated using the Leroy formula [9]

involving allylic 1,3-dipoles [7]. However, the extents of completion in the formation of new σ-bonds in both transition states differ from each other. In particular, the transition state localized on pathway **A** is more asymmetrical (Fig. 2). The difference between the C(3)–C(4) and C(5)–O(1) bond lengths in this case is greater han 0.7 Å. Such charge transfer from the 1,3-dipole substructure toward the substructure of the dipolarophile is significant. This value is 0.5 e in pathway **A**. The difference in the distances between the reaction sites C(3)–C(4) and C(5)–O(1) in the transition state localized on pathway **B** is about 0.21 Å, while the charge corresponding to transfer does not exceed 0.05 e.

The free enthalpies of activation ($\Delta G^{\neq}$) for both pathways examined are relatively high (>51 kcal/mol) (Table 1). We should note that the activation barrier thereby calculated for the reaction of nitrone **2** with nitropropene **5** in nitromethane is 45.8 kcal/mol on pathway **C** and 60.0 kcal/mol on pathway **D**, while these values in toluene are 40.8 and 51.3 kcal/mol, respectively [4, 5]. Thus, it is not remarkable that the [2+3] ycloaddition of nitrone **2** to nitropropene **5** proceeds much more readily through pathway **C**. The extent of conversion of nitrone **2** to nitroisoxazolidine **6** is apparently limited by the isomerization of nitropropene **1** to nitropropene **5**. In a previous experiment [5], we showed that this process occurs rather easily in the presence of isoxazolidines **4** and **6**. The values obtained for $\Delta G^{\neq}$ also indicate that the reaction of nitropropene **1** with nitrone **2** should give nitromethylisoxazolidines **3** and **4** in 1:3 ratio under kinetic control conditions.

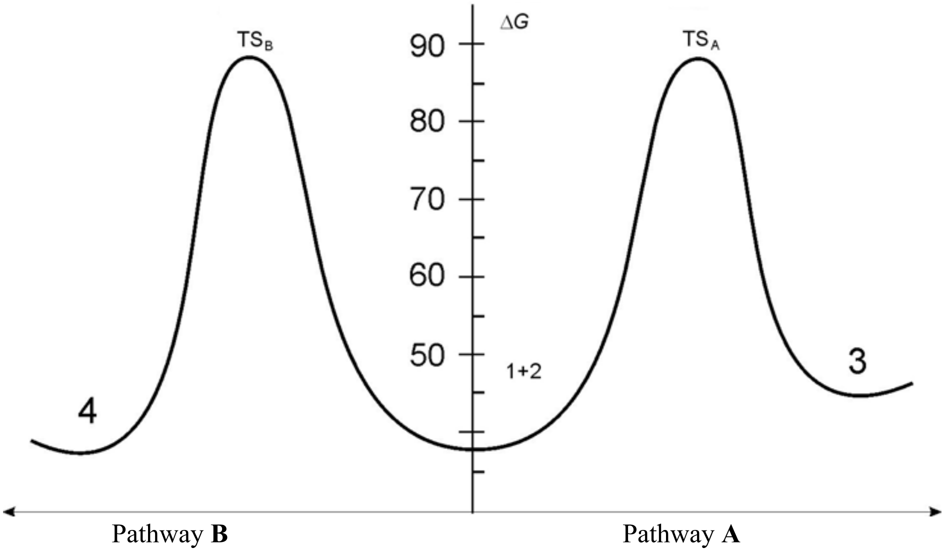

Fig. 1. Energy profile of the reaction of 3-nitro-1-propene (**1**) with triphenylnitrone (**2**).
The maxima on the curve correspond to the transition state (TS) structures.

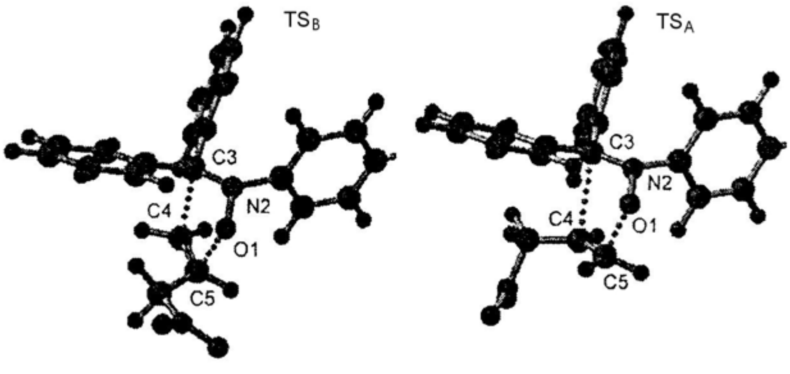

Fig. 2. Structures of the transition states of the [2+3] cycloaddition
of 3-nitro-1-propene with triphenylnitrone.

The formation of nitromethylisoxazolidine **3** is not favored, however, by thermodynamic factors. In particular, the conversion (ε^*) in the formation of nitromethylisoxazolidines **3** and **4** calculated using our previous data [8] is 0.001 and 0.216, respectively. This finding indicates that the [2+3] cycloaddition of nitrone **2** to nitropropene **1** is a thermodynamically-controlled reaction. The quantum-chemical calculation results given in this work are in good accord with our previous experimental data [2].

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