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SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES. 52*. PERISELECTIVITY OF [2+3] CYCLOADDITION OF NITRONES TO *trans*-β-CYANONITROETHYLENE IN THE LIGHT OF FMO THEORY

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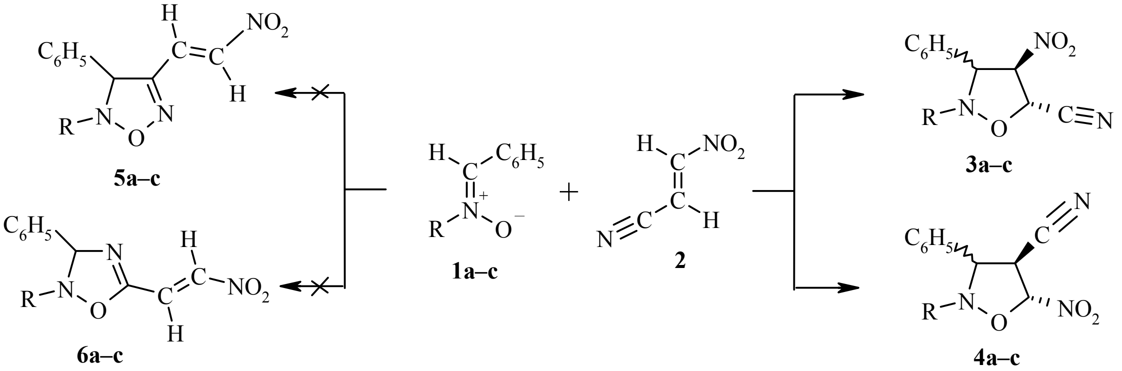
[2+3] Cycloaddition reaction of nitrones with trans-β-cyanonitroethylene may theoretically lead to regioisomeric nitroisoxazolidines and isomeric oxadiazoles. However, 4- and 5-nitroisoxazolidines were really obtained as only reaction products. Periselectivity of this reaction is rationalized in terms of the FMO theory.

Keywords: periselectivity, FMO, nitrone, nitroalkene, AM1 calculations.

Some years ago, Padwa et al. [2, 3] showed that in the [2+3] cycloaddition reaction of N-methyl-C-phenylnitrone (**1a**) and C-phenyl-N-(*t*-butyl)-C-phenylnitrone (**1b**) with trans-β-cyanonitroethylene (**2**) the alkene C=C bond participated, while the much less shielded C≡N bond remained unchanged. Consequently, regioisomeric nitroisoxazolidines **3a,b** and **4a,b** were formed as the only products. The corresponding isomeric oxadiazoles **5a,b** and **6a,b** were not found in the reaction mixture. The reaction of **2** with C,N-diphenylnitrone (**1c**) proceeds in the same way [4]. This work is an attempt to explain the observed phenomenon on the basis of Frontier Molecular Orbitals (FMO) theory [5].



a R = Me, **b** R = CMe₃, **c** R = Ph

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* Part 51 see [1].

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We began analysis of the molecular orbital interactions with the characterization of the structures of reactants **1a-c** and **2** using the AM1 method within the MOPAC 93 program package [6]. The calculations were preformed on a Pentium III (733 MHz) personal computer. In the case of nitrones and nitroalkenes, this method provides good agreement between calculated and experimental data [1, 7-9].

As shown in Table 1, the HOMO energy of **1a** is -8.45 eV. This orbital is localized on the the C, N, and O atoms of the >C=N(O)– fragment and is perpendicular to the molecular plane. LUMO has the energy -0.30 eV and is localized in the same way. Both in the case of HOMO and LUMO, the $2p_z$ coefficient on the oxygen atom is slightly higher than that on the carbon atom of the >C=N(O)– fragment. The FMO properties of **1b** are similar to those of **1a**. In this case the HOMO energy is -8.36 eV, while the LUMO energy is -0.19 eV. However, when the alkyl substituent on the nitrogen atom of the >C=N(O)- fragment is replaced by the phenyl group, the electronic structure of the FMO significantly changes. The LUMO energy decreases. Simultaneously, the $2p_z$ amplitude on the oxygen atom goes down remarkably.

The HOMO of cyanonitroethylene **2** is localized on the carbon atoms of the ethylene fragment and on the carbon and nitrogen atoms of the cyano group, perpendicularly to the molecular plane. Its energy is -12.01 eV. The $2p_z$ amplitude on the >C=C< fragment is higher than that on the –C≡N group. The corresponding LUMO, with the energy -1.81 eV, is localized in the same way. Also in this case, the $2p_z$ amplitude on the carbon atoms of the >C=C< fragment is higher than that on the carbon and nitrogen atoms of the –C≡N group.

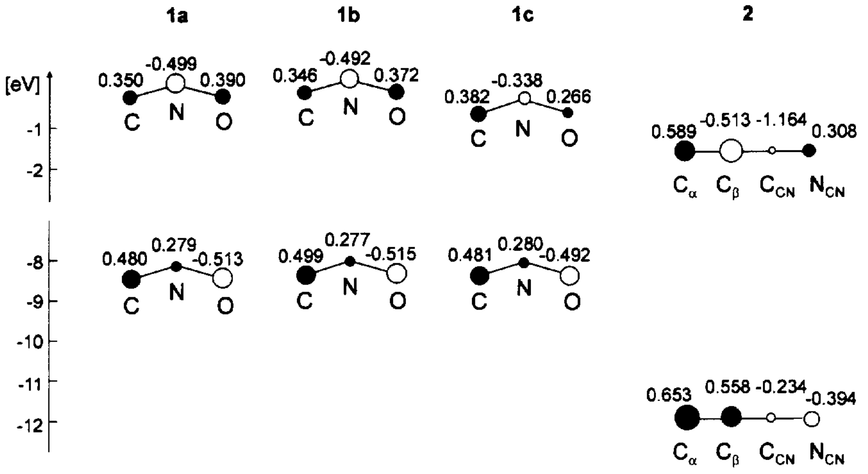
Figure 1 shows the FMO interaction diagram of the reactions studied, elaborated on the basis of the electronic properties of the addends. As shown, in the case of all of the nitrones studied, the $\text{HOMO}_{\text{nitrone}}$–$\text{LUMO}_{\text{alkene}}$ energy gap is significantly smaller than the $\text{HOMO}_{\text{alkene}}$–$\text{LUMO}_{\text{nitrone}}$ gap. Hence, according to the Sustmann classification [10], these are the reactions with normal orbital control.

According to the Fukui and Fujimoto rule [11], in the cycloaddition reactions new σ-bonds are formed between those atoms where the difference between atomic orbital (AO) coefficients is the lowest. As shown in Fig. 1, the AO coefficients of the HOMO of nitrone **1a** are 0.480 and -0.513 for carbon and oxygen atoms of the >C=N(O)– fragment, respectively. When these data are compared with the corresponding data for the LUMO of cyanonitroethylene **2**, it can be noticed that the values of the HOMO coefficients are clearly much closer to the LUMO coefficients on carbon atoms of the ethylene fragment, than to the coefficients on the atoms of the –C≡N group. Comparison of the AO coefficients of the LUMO of alkene **2** with those of the HOMO of nitrones **1b** and **1c** leads to similar conclusion. Hence, in all of the cases analyzed, the C=C bond in the ethylene fragment of the alkene should react preferentially in the cycloaddition reaction. This conclusion is perfectly consistent with the periselectivity observed experimentally [2-4].

The FMO method, which is a simplification of the Molecular Orbital Perturbation method [12, 13], does not take into account all of the factors that influence reactivity of chemical compounds. It happens in practice that beside the orbital effects, sometimes the reaction periselectivity is controlled by steric effects and/or by charge distribution on reagents. The [2+3] cycloaddition reactions of diarylnitrones and tetracyanoethylene are examples of such control [14]. However, the FMO method predicts well the periselectivity of the reactions of *trans*-β-cyanonitroethylene with N-alkyl-C-phenylnitrones and C,N-diphenylnitrone.

TABLE 1. Essential Properties of Frontal Molecular Orbitals of Nitrones **1a-c** and Cyanonitroethylene **2**

Compound	HOMO					LUMO				
	Eigenvectors				E [eV]	Eigenvectors				E [eV]
	C/C_α	N/C_β	O/C_{CN}	N_{CN}		C/C_α	N/C_β	O/C_{CN}	N_{CN}	
1a	0.480	0.279	-0.513	—	-8.45	0.350	-0.499	0.390	—	-0.30
1b	0.499	0.277	-0.515	—	-8.36	0.346	-0.492	0.372	—	-0.19
1c	0.481	0.280	-0.492	—	-8.40	0.382	-0.338	0.266	—	-0.73
2	0.653	0.558	-0.234	-0.394	-12.01	0.513	-0.589	-0.164	0.308	-1.81



6.64	6.55	6.59	$\Delta E_1 = \lvert E_{HOMO\ nitrone} - E_{LUMO\ alkene} \rvert$
11.71	11.82	11.28	$\Delta E_2 = \lvert E_{HOMO\ alkene} - E_{LUMO\ nitrone} \rvert$
5.07	5.27	4.69	$\Delta\Delta E = E_2 - E_1$

Fig. 1. FMO interaction diagram for [2+3] cycloaddition of nitrones **1a-c** to cyanonitroethylene **2**. Data for diagram taken from Table 1.

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