

MNDO STUDY OF THE [2 + 3] CYCLOADDITION OF NITROETHENE TO FORMONITRILE N-OXIDE*

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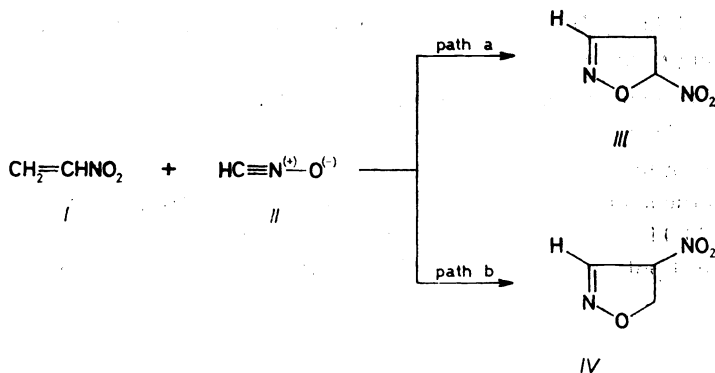
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Two regioisomeric pathways have been studied by MNDO method for nitroethene [2 + 3] cycloaddition to formonitrile N-oxide. It has been found that four critical structures are located along each of the pathways. Calculations indicate that both reactions take place in a concerted manner and that their transition states are early. Moreover, it was established that the path leading to 5-nitro-4,5-dihydro-1,2-oxazole is preferred.

In earlier papers¹⁻³ of this series we reported that the [2 + 3] cycloaddition of nitroethene to *meta* and *para* substituted benzonitrile N-oxides was a regioselective reaction, leading to 3-aryl-5-nitro-4,5-dihydro-1,2-oxazoles as the only reaction products. This fact is at variance with the expectations based on the conventional



SCHEME 1

* Part XXVIII in the series Synthesis and Properties of Azoles and Their Derivatives. Part XXVII: Khim. Geterotsikl. Soedin, in press. Some results of this work have already been presented at the IXth Symposium on the Chemistry of Heterocyclic Compounds in Bratislava, August 23-28, 1987.

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resonance theory according to which 3-aryl-4-nitro-4,5-dihydro-1,2-oxazoles should be formed preferentially. Therefore, in order to gain a better insight into the nature of the reaction, study of the critical points on the hypersurface for the [2 + 3] cycloaddition of nitroethene (*I*) to formonitrile N-oxide (*II*) (Scheme 1) was undertaken and the results are now reported.

COMPUTATIONAL PROCEDURE

For calculation purposes molecules *I* and *II* were envisaged as placed on two parallel planes with the carbon-carbon double bond of nitroethene situated symmetrically under the nitrile oxide unit and simultaneously, in a plane perpendicular to the two planes. The distance *R*, of 1 nm between the carbon atom of formonitrile N-oxide and α (path a) or β (path b) carbon atom of nitroethene was chosen arbitrarily.

The calculations were carried out using the MOPAC-3 programme package⁴ on VAX 11/750 computer. The standard MNDO hamiltonian was employed.

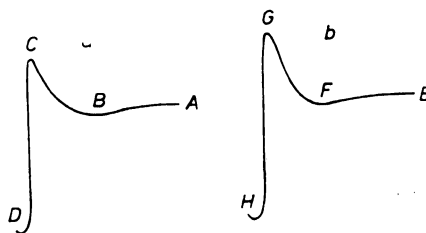
RESULTS AND DISCUSSION

In Fig. 1 the reaction profiles are illustrated with the critical points marked. Structures of these points are shown schematically in Fig. 2. Their values of the heats of formation (ΔH_{298}°), entropies (ΔS_{298}°), dipole moments (μ), charge transfer (t) and first ionization potentials (*I*) estimated by Koopman's theorem, are summarized in Table I.

From the data in Table II and Fig. 1, it is obvious that four critical structures are located along each reaction pathway.

Heats of formation for the supermolecules *A* and *E* are 80.1 and 79.8 kcal/mol, respectively. They differ from each other slightly, while for an infinite separation of the reacting moieties ($R = \infty$) they should be a priori the same and they should be equal to the sum of the heats of formation for the individual compounds *I* and *II* ($\Delta H_{298}^{\circ} = 80.0$ kcal/mol). Also ionization potentials are practically identical, whereas the dipole moments are different, what is a simple consequence of vector addition.

FIG. 1
Reaction profiles for the [2 + 3] cycloaddition of nitroethene to formonitrile N-oxide leading to 5-nitro-4,5-dihydro-1,2-oxazole (a) and 4-nitro-4,5-dihydro-1,2-oxazole (b). (Structures at the marked points are depicted in Fig. 2)



The intermediates responsible for the shallow minima on the hypersurface were found for both reaction pathways. Each of them consisted of undistorted formonitrile N-oxide on a plane nearly parallel to that of slightly distorted nitroethene. They are formed by such an arrangement of the dipoles of each reactant which results in maximum electrostatic attractions. However, no charge transfer was found inside these structures. Therefore, it appears that supermolecules *B* and *F* should be interpreted in terms of proximity pairs.

Passing from the intermediate minimum to the one for the product, only one saddle point was found in each case. Consequently, both reactions take place in a concerted manner although their transition states (TS) differ significantly. For instance, in the reaction along pathway a TS was extremely unsymmetrical, with the new σ carbon-carbon bond length of $1.83 \cdot 10^{-10}$ m and the carbon-oxygen bond length as much as $3.31 \cdot 10^{-10}$ m. In the regioisomeric pathway b it was relatively symmetrical, with bond lengths of $2.01 \cdot 10^{-10}$ m for the new σ carbon-carbon bond and $2.44 \cdot 10^{-10}$ m for the σ carbon-oxygen bond (cf. the structures *C* and *G* in Fig. 2). The nature of these TS's can be inferred from the structural changes that occur during the formation of the heterocyclic ring. For this purpose the values of three essential geometrical parameters characteristic for supermolecules *B*, *C*, *D* and *F*, *G*, *H*, namely C(1)—C(2) bond length, the sum of the C(3)—N(4) and N(4)—O(5) bond lengths and angle C(3)—N(4)—O(5), were taken under consideration and values of the parameter Δ were estimated (Table I). This last one was defined as the ratio of the difference between the values of the geometric parameter considered in the intermediate and transition state to the corresponding difference between the

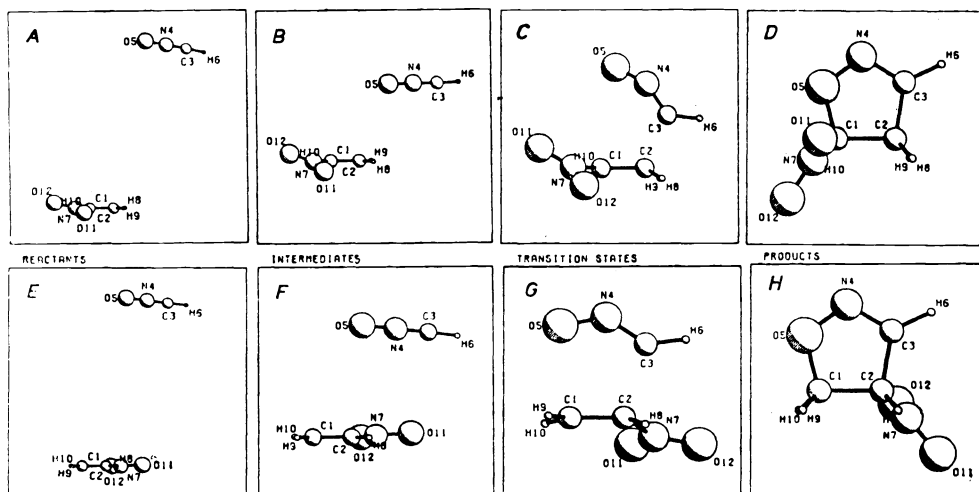


FIG. 2

The PLUTO views of the critical structures located by MOPAC-3 program

intermediate and the final product. The values of Δ , low in most cases, led us to the conclusion that TS's *C* and *G* are rather "early" ones. This fact is consistent with

TABLE I

Properties of critical structures *A–H* on the MNDO potential surface for [2 + 3] cycloadditions of nitroethene to formonitrile *N*-oxide. The bond lengths are in 10^{-10} m, angles in degrees, ΔH in kcal mol^{-1} , ΔS in e.u., dipole moments in D, ionization potentials in eV and charge transfer in e; $1 \text{ kcal mol}^{-1} = 4.184 \text{ kJ mol}^{-1}$, $1 \text{ e.u.} = 4.184 \text{ J mol}^{-1} \text{ deg}^{-1}$, $1 \text{ D} = 3.336 \cdot 10^{-30} \text{ Cm}$, $1 \text{ eV} = 1.602 \cdot 10^{-19} \text{ J}$, $e = 1.602 \cdot 10^{-19} \text{ C}$

Structure ^a	C(1)—C(2)	[C(3)—N(4)] + [N(4)—O(5)]	C(3)—N(4)— O(5)	ΔH_{298}°	ΔS_{298}°	μ	<i>I</i>	<i>t</i> ^b
Reaction path a								
<i>A</i>	1.343	2.361	179.0	80.1	128.6	7.7	10.3	0.00
<i>B</i>	1.344	2.362	178.5	79.6	116.0	7.9	10.5	0.00
<i>C</i>	1.385	2.415	152.4	109.3	96.5	6.5	9.4	-0.05
<i>D</i>	1.566	2.629	111.7	14.7	82.2	5.3	11.2	—
Δ	0.185	0.199	0.390	—	—	—	—	—
Reaction path b								
<i>E</i>	1.343	2.361	180.0	79.8	124.9	3.0	10.2	0.00
<i>F</i>	1.343	2.363	179.9	78.7	113.6	2.8	10.2	0.00
<i>G</i>	1.391	2.445	135.0	116.3	90.2	3.8	10.2	0.06
<i>H</i>	1.569	2.619	112.4	19.2	83.3	3.1	11.2	—
Δ	0.212	0.322	0.664	—	—	—	—	—

^a See Figs 1 and 2; for meaning of Δ see text. ^b Charge transfer was calculated according to expression given by Leroy et al.¹⁶

TABLE II

The activation parameters from MNDO calculations for [2 + 3] cycloadditions of nitroethene to formonitrile *N*-oxide. ΔH^{\ddagger} and ΔG^{\ddagger} are given in kcal mol^{-1} and ΔS^{\ddagger} in e.u.; $1 \text{ kcal mol}^{-1} = 4.184 \text{ kJ mol}^{-1}$ and $1 \text{ e.u.} = 4.184 \text{ J mol}^{-1} \text{ deg}^{-1}$

Critical structure	Reaction path a				Reaction path b			
	$\Delta H_{298}^{\ddagger}$	$\Delta S_{298}^{\ddagger}$	$-T\Delta S_{298}^{\ddagger}$	$\Delta G_{298}^{\ddagger}$	$\Delta H_{298}^{\ddagger}$	$\Delta S_{298}^{\ddagger}$	$-T\Delta S_{298}^{\ddagger}$	$\Delta G_{298}^{\ddagger}$
Intermediate	-0.4	-12.6	3.8	3.4	-1.1	-11.3	3.4	2.3
Transition state	29.2	-33.0	9.8	39.0	36.5	-34.7	11.3	46.8

Hammond's postulate according to which the TS for an exothermic reaction should resemble the reactant.

The calculations predict that the dipole moment of TS for path *a* is smaller than that, for the intermediate, whereas for path *b* the opposite is true. Thus, in accordance with current theories of the solvent effects^{5,6}, the formation of nitroisoxazoline *III* should be faster in less polar solvents while the reverse should be true for the formation of nitroisoxazoline *IV*. Unfortunately, no experimental data are available for direct comparison. However, it should be noted at this point that [2 + 3] cycloaddition of nitroethene to benzonitrile N-oxide in tetrachloromethane ($\mu = 0.0$ D) is faster⁷ than in nitromethane ($\mu = 3.7$ D) by more than a factor of 2.

An interesting conclusion can be drawn from the values of the charge transfer. It was found that for structure *C* it takes place in the direction from N-oxide to nitroethene, whereas for structure *G* the direction is opposite – from nitroethene to N-oxide. Hence, a group donating electrons to a –CNO fragment should favour the reaction along path *a* and at the same time hinder the reaction along path *b*. Actually, when passing from *p*-methoxybenzonitrile N-oxide to *p*-nitrobenzonitrile N-oxide, reaction rate constant of the addition to nitroethene (at 25°) decreases³ by a factor of 1.9.

Heats of formation of the final products *D* and *H* are 14.7 and 19.2 kcal/mol, respectively. The ionization potentials of both products agree closely and their heterocyclic rings are nearly planar. Here again no experimental data are available for comparison, as compounds *III* and *IV* are still unknown.

Table II summarizes the predicted activation parameters. As it can be seen, the formation of intermediates *B* and *F* is exothermic by 0.4 and 1.1 kcal/mol, respectively. The true experimental enthalpies should be, however, lower, since MNDO overestimates the repulsion between atoms when they are separated by 1.5–2.5 times longer bond between them⁸ than normal. The ΔG^\ddagger values indicate that the two intermediates are not likely to correspond to free energy minima at room temperature.

Concerning the transition states, it can be seen that activation enthalpy calculated for path *a* is by 7.3 kcal/mol lower than that for path *b*. Consequently, the reaction leading to nitroisoxazoline *IV* should be formally forbidden. Thus, the predicted regioselectivity is in full agreement with those for the [2 + 3] cycloaddition of nitroethene to benzonitrile N-oxides mentioned in the introduction. Activation enthalpies, 29.2 and 36.5 kcal/mol, agree well with those of 28.8 kcal/mol evaluated by Robb et al.⁹ for [2 + 3] cycloaddition of formonitrile N-oxide to ethene by means of MC SCF method with the standard 4-31G basis set. The same result was also obtained by Poppinger^{10,11} from *ab initio* calculations with minimal STO-3G basis set.

Our estimated entropies of activation are –33.0 and –34.7 e.u. and the heats of the reaction –65.4 and –60.4 kcal/mol for path *a* and *b*, respectively. The evalua-

tion of these quantities is not easy, since the enthalpies and the entropies of activation, as well as the exothermicity of the reaction under consideration, have not yet been experimentally determined.

Finally, it should be noted that inclusion of 2×2 CI causes decrease in the heats of formation of both transition structures. However, the energy of structure *G* decreases only by 0.4 kcal/mol relative to the SCF value of 116.3 kcal/mol, whereas the energy of structure *C* decreases by as much as 18.7 kcal/mol relative to the SCF value of 109.0 kcal/mol indicates partially a biradical character of the reaction along path *a*. This last conclusion is interesting from the point of view of the mechanism of the reaction^{12,13}.

Summarizing the results reported here, it seems that MNDO is a suitable semi-empirical method for prediction of regioselectivity in cycloaddition of nitroalkenes to nitrile N-oxides. We hope that results obtained will be useful for further predictions of the regioselectivity of nitrile N-oxide [2 + 3] cycloadditions, in particular, with help of PMO approach^{14,15}.

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