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SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES

XXXVIII.* [2+3]-CYCLOADDITION OF C,C,N-TRIPHENYL AND Z-C,N-DIPHENYL NITRONE TO *n*-DEC-1-ENE IN THE LIGHT OF SEMIEMPIRICAL AM-1 CALCULATIONS

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The activation parameters of the [2+3]-cycloaddition of C,C,N-triphenyl nitrone and Z-C,N-diphenyl nitrone to n-dec-1-ene were calculated by the AM-1 method. It was shown that the paths leading to the respective isoxazolidines containing an octyl group at the C-5 position of the heterocyclic ring are preferred.

The present paper continues investigations into the reactivity of nitrones in [2+3]-cycloaddition processes [2, 3]. In particular the aim was to determine by quantum-chemical methods the activation parameters of the cycloaddition of C,C,N-triphenyl nitrone (I) and Z-C,N-diphenyl nitrone (II) to *n*-dec-1-ene (III). We expected that it would be possible on such a basis to predict the regio- and stereoselectivity of the reactions. Similar calculations [4-9] have concerned model processes involving only the simplest of nitrones and alkenes. Moreover, in most cases the obtained results were not verified experimentally.

For the calculations we employed the MOPAC-7 package [10], using the standard AM-1 version. The calculations were performed on a CONVEX 3220 computer at the Krakow computer center Cyfronet.

The structures of the initial compounds and of the theoretically possible [2+3]-cycloadducts were determined by minimizing their entropies of formation using the FPD algorithm. The transition states were obtained by means of the SADDLE, NLLSQ, and TS procedures, as supported by the presence of one negative eigenvalue of the Hessian and also by the results of analysis of the internal coordinates of the reaction [10, 11]. The geometry is shown in Figs. 1 and 2. With a knowledge of the energies of the compounds and transition states it is easy to calculate the activation parameters. The results are given in Table 1, which gives for the saddle points the values (t) of the charge transfer between the substructures of the activation complexes calculated by Leroy's formula [12], the force constants (f_{C3-C4}, f_{O1-C5}), and the relative degrees of completion of the formation of the new σ bonds ($\Delta r_1 = r_{C3-C4}/r^{\neq}_{C3-C4}$ and $\Delta r_2 = r_{O1-C5}/r^{\neq}_{O1-C5}$, where r and $r^{\neq}$ are the distances between the atoms in the product and the intermediate complex.

The reaction of triphenyl nitrone (I) with the decene (III) can theoretically lead to the regioisomeric isoxazolidines (IV) and (V):

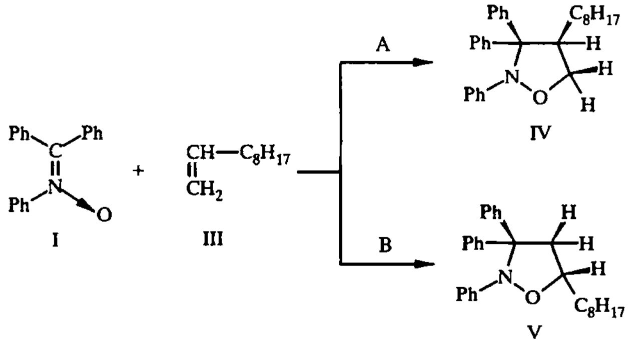

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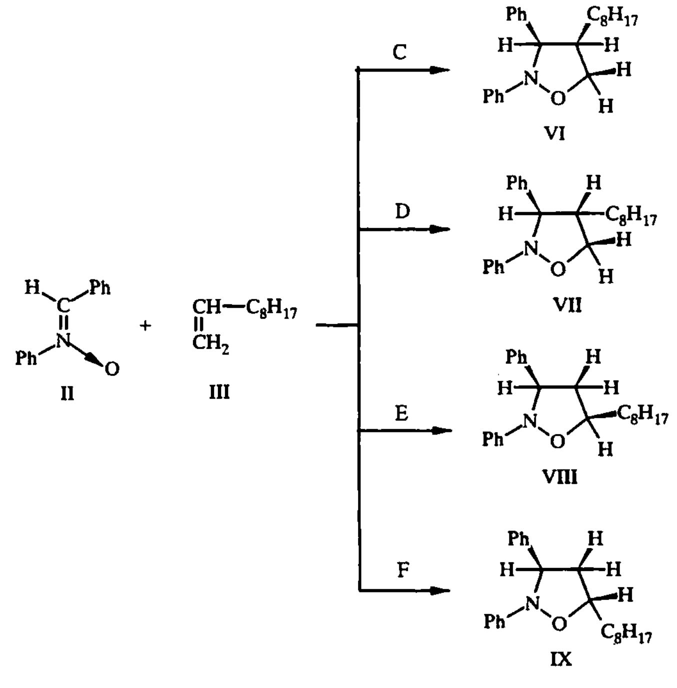
TABLE 1. Physicochemical Characteristics of the Transition States of the [2+3]-Cycloaddition of C,C,N-Triphenyl Nitrone and *Z*-C,N-Diphenyl Nitrone to *n*-Dec-1-ene, Calculated by the AM-1 Mechanism

Initial compounds	Path	$\Delta H^{\#}_{298}$ (kcal/mole)	$\Delta S^{\#}_{298}$ (cal/mole)	$\Delta G^{\#}_{298}$ (kcal/mole)	Δr_1	Δr_2	t, d, e.	$f_{C(3)-C(4)}$ (mdyn/A)	$f_{O(1)-C(5)}$ (mdyn/A)
I + III	A	32,1	-54,9	48,5	0,64	0,73	-0,08	0,57	1,35
	B	28,2	-53,5	44,0	0,69	0,73	-0,08	0,75	1,07
II + III	C	25,5	-49,9	40,4	0,69	0,73	-0,05	0,69	1,04
	D	24,3	-53,0	40,1	0,70	0,73	-0,06	0,71	1,07
	E	22,2	-51,1	37,3	0,73	0,71	-0,06	0,88	0,87
	F	24,0	-54,5	40,2	0,72	0,71	-0,05	0,91	0,86

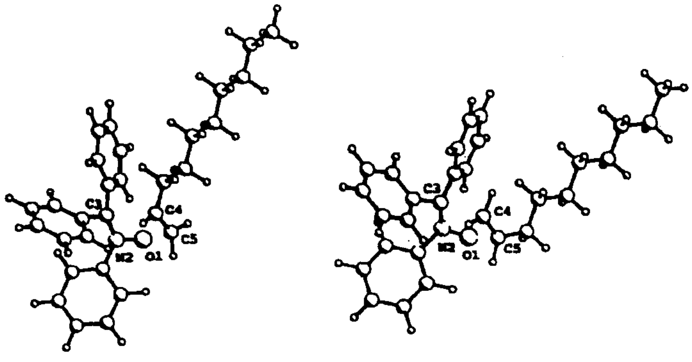
The calculations showed that for path A, exactly like path B, there is only one transition state. This fact indicates a concerted reaction mechanism. In both transition states (Fig. 1) the octyl radical and the phenyl groups are deflected from the reaction centers. This is due to rehybridization of the AOs of the atoms between which the new σ bonds are formed, and the processes are close to completion to different degrees, as shown by the values of Δr_1 and Δr_2. In path A the asymmetry of the transition states is greater, and the difference in the degrees of completion of the formation of the new bonds amounts to ~15%. Irrespective of the type of regioisomer that forms, the O_1 and C_5 atoms always interact more strongly than C_3 and C_4. This is demonstrated by the values of the force constants $f_{C(3)-C(4)}$ and $f_{O(1)-C(5)}$.

Both the enthalpy ($\Delta H^{\#}_{298}$) and the thermodynamic potential of activation ($\Delta G^{\#}_{298}$) indicate the preferential formation of the adduct (V). The difference between the activation barriers for paths A and B is so large ($\Delta\Delta G^{\#}_{298}$ ~4.4 kcal/mole) that the formation of the adduct (IV) is formally forbidden. Our previous laboratory investigations of the reaction (2) are in full agreement with the results of the quantum-chemical calculations. It must, however, be borne in mind that the experiments were conducted in toluene ($\varepsilon = 2.38$), whereas the calculations relate to the individual molecules in vacuum ($\varepsilon = 1$).

In the case of the [2+3]-cycloaddition of diphenyl nitrone (II) to the decene (III) four paths, leading to the isomeric isoxazolidines (VI-IX), are theoretically possible:

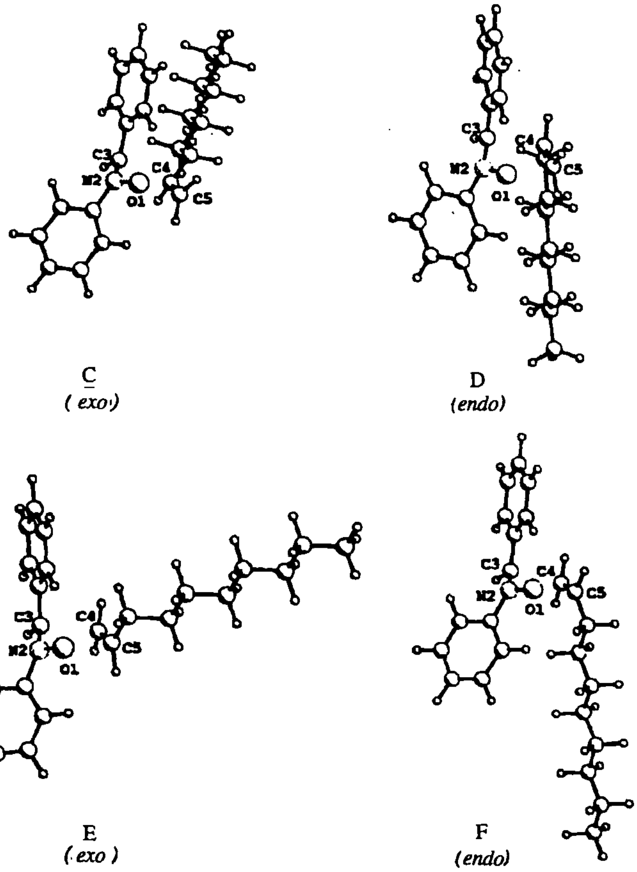


These isomers differ not only in the position of the octyl radical but also in the stereochemical configuration of the substituents. The octyl radical and the phenyl group at the $C_{(3)}$ atom can be located on the same side or on opposite sides of the nominal plane of the isoxazolidine ring. The obtained states (Fig. 2, Table 1) are distinguished by higher symmetry than the transition states of the reaction of (I + III), and for paths E and F the interaction between the $C_{(3)}$ and $C_{(4)}$ atoms is stronger than that between $O_{(1)}$ and $C_{(5)}$, whereas the opposite situation is observed for paths C and D.



A B

Fig. 1. Structure of the intermediate compounds of the reactions of compounds (I + II).



C (exo) D (endo)

E (exo) F (endo)

Fig. 2. Structures of the transition states of the reactions of (II) + (III).

If the enthalpy of activation is chosen as a parameter characterizing the reactivity, the formation of adducts with the octyl radical at the $C_{(5)}$ atom of the isoxazolidine ring seems preferable. Two such adducts (VIII, IX) can be obtained, depending on whether the 1,3-dipole attacks the double bond of the dipolarophile on the *exo* or on the *endo* side (Fig. 2). It follows from the calculations, however, that *exo*-addition must take place considerably more quickly. This is probably due to steric factors. In the case of *endo*-addition more compact packing of the atoms within the limits of the transition states occurs, and this is thermodynamically unfavorable.

If the transition states leading to the adducts (VI) and (VII) are considered, it is found that *endo*-addition will predominate for the same reasons. In this case the orientation of the octyl radical toward the side of the 1,3-dipole is more favorable. Inclusion of the entropy of activation changes the preference for the reaction paths a little, since the energy barrier on path F is raised.

However, the transition state E is preferred, irrespective of the method of assessing the reactivity, and the transition states C, D, and F differ little in energy (Table 1). The described analyses have found support in laboratory investigations. As a result of the reaction of the diphenyl nitrone (II) with the decene (III) we obtained a 20:1 mixture of the *cis* (VIII) and *trans* (IX) isomers of 2,3-diphenyl-5-octylisoxazolidines [3]. However, it should be mentioned that this reaction, like the reaction mentioned above, was carried out in toluene.

The earlier analysis in terms of PMO theory [2] made it possible to suggest that the nitrones (I) and (II) only differ little in reactivity. The thermodynamic potentials of the reaction calculated in the present work indicate, however, that the cycloaddition of (I) + (III) must take place much more slowly than (II) + (III). This indicates that steric factors have a strong effect on the process. Kinetic measurements [3] confirmed unambiguously the higher activity of the nitrone (II) in reaction with *n*-dec-1-ene.

Thus, the activation parameters calculated by the AM-1 method reflect the experimental observed activity of the nitrones (I) and (II) in reaction with the decene (III). The AM-1 method can probably be recommended for analysis of the regioselectivity in the cycloaddition of nitrones to alkenes.

In conclusion we mention that the calculated indices of charge transfer t indicate only a small displacement of electrons in the intermediate complexes from the dipolarophile to the 1,3-dipole. This makes it possible according to Sustman's classification [13] to assign the investigated reactions [2+3]-cycloaddition of the second or third type.

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