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## Semiempirical MO Calculation of Hetero Atom Three-Membered Ring Compounds (II) · N-Nitroso-azirine and -diaziridine

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Fully optimized MNDO molecular orbital calculations are performed for N-nitroso-azirine (I) and -diaziridine (II). The ground state geometries show the nonplanar configuration around the imino nitrogen. The nitroso group rotational energy barriers and the ring inversion energy barriers are also discussed.

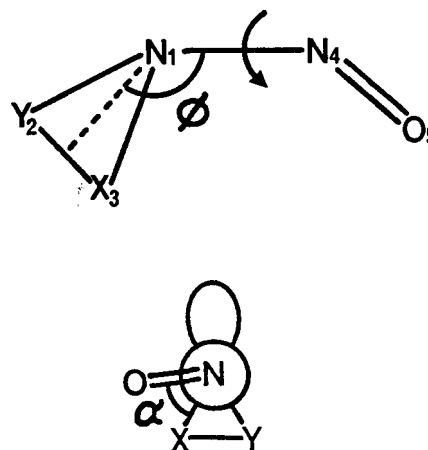
### Introduction

Nitrosamines are biologically important compounds as cancer suspect agents.<sup>1</sup> Also N-nitrosamines are widely included in many consumer products.<sup>2</sup>

Since three-membered ring compound has large ring strain, three-membered ring with nitrosamine compounds are structurally interesting compounds. Structural studies<sup>3-7</sup> of N,N-dimethyl nitrosamine show a planar heavy atom structure. This heavy atom planarity has been explained by partial double bond character between the amino and nitroso nitrogen. Also this partial double bond character inhibits the nitroso group rotation around the N-N bond and makes high nitroso group rotational energy barrier. Previous study<sup>8</sup> showed the ground state conformations, the nitroso group rotational energy barriers and aziridine ring inversion barriers of N-nitroso-aziridine, -oxaziridine, and -dioxaziridine. Here three-membered ring nitrosamine studies were extended to the N-nitroso-azirine (I), and -diaziridine (II).

### Calculation Method

MNDO<sup>9</sup> MO method in the AMPAC<sup>10</sup> program package was used throughout. The AMPAC program was modified for the CDC CYBER 180/860 and run at NOS/VE. All calculations were performed by using standard RHF SCF procedures in the AMPAC. I and II were fully optimized during the calculation to find the ground state conformations. For the transition state of the three-membered ring inversion process, the imino nitrogen was set to planar configuration. Since there are two imino nitrogens in the N-nitroso-diaziridine, N<sub>1</sub> and N<sub>3</sub>, two different ring inversion transition states can be calculated. For the energy profile of the nitroso group internal rotation, the nitroso group was set to be eclipsed with the N<sub>1</sub>-X<sub>3</sub> bond (see Figure 1) in the three-membered ring and then the nitroso group was rotated counterclockwise 10° increment. In the nitroso group rotational energy barrier calculations, all geometric parameters were allowed to opti-

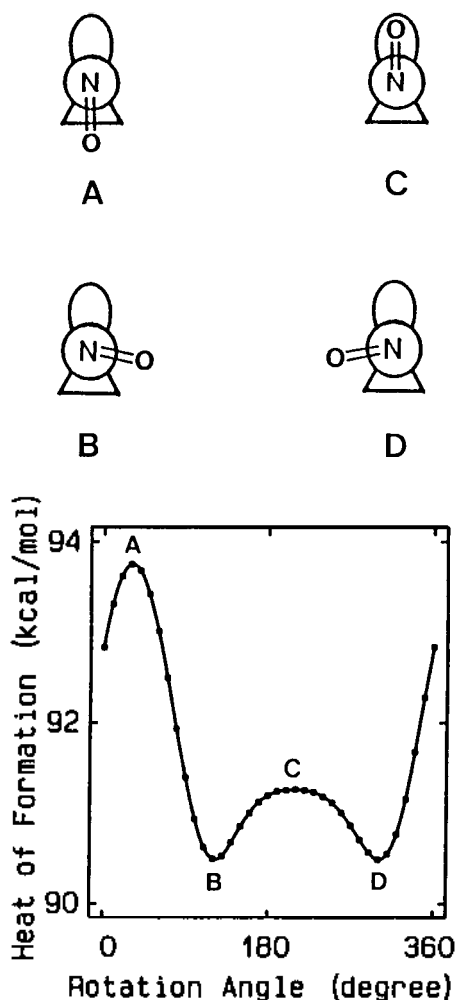


**Figure 1.** Numbering scheme of atoms and definitions of the angle  $\alpha$  and  $\phi$ : a) X=Y=CH: N-Nitroso-azirine (I). b) X=NH, Y=CH<sub>2</sub>: N-Nitroso-diaziridine (II).

mize except the nitroso group twisting angle. To find the nitroso group rotational transition state, the nitroso group twisting angle was rotated 1° increment around the energy maximum and finally rotated 0.1° increment. All transition states were confirmed by one and only one negative eigen value in the Hessian matrix.

### Results and Discussion

**N-Nitroso-azirine (I).** The nitroso group rotational energy profile of I is shown in Figure 2. There are two equivalent ground state conformers, B and D. The rotational energy barrier of nitroso group is calculated to be 0.67 kcal/mol. The structure of the rotational transition state of I shows that the nitroso group is eclipsed with the lone pair of the imino nitrogen in the azirine ring, as shown in the previous study.<sup>8</sup> In the ground state of I, the nitroso group is twisted 47.0° from the N<sub>1</sub>-C<sub>2</sub> bond in the azirine ring toward the



**Figure 2.** The nitroso group internal rotational energy profile of the N-nitroso-azirine (I). A: The maximum. C: The rotational transition state (TS-Rot). B and D: The equivalent ground state (GS).

lone pair of the imino nitrogen. This twisting is general phenomenon in this type of compounds, three-membered ring nitrosamines.<sup>8</sup> The angle between the  $N_1-N_3$  bond and the ring plane ( $\phi$  in Figure 1) is calculated to be  $128.5^\circ$  in the ground state, compared to the corresponding angle in 1H-azirine,<sup>11</sup>  $110.9^\circ$ . Thus one can conclude planarity around imino nitrogen is increased when the azirine ring is incorporated with the nitroso group. The structure of the azirine ring inversion transition state shows a planar configuration around the imino nitrogen. The azirine ring inversion energy barrier is calculated to be 11.42 kcal/mol, which is compared to that of N-nitroso-aziridine, 3.98 kcal/mol. This high azirine ring inversion energy barrier can be explained by the antiaromatic effect in the ring inversion transition structure of I. Since the structure of the ring inversion transition state of I has four  $\pi$  electrons and that of the ground state has two  $\pi$  electrons, the former shows antiaromaticity and the latter shows aromaticity. The ground state of I is more stable than that of N-nitroso-aziridine and the azirine ring inversion transition state of I is less stable than that of N-nitroso-aziridine. Consequently the three-membered ring inversion energy barrier of I is larger than that of N-nitroso-aziridine.

**Table 1.** Calculated Heat of Formations and Energy Barriers (kcal/mol)

Compounds	Heat of Formations			Energy Barriers	
	Gs	TS-Rot	TS-Inv <sup>a</sup>	Rot	Inv <sup>a</sup>
N-Nitroso-azirine (I)	90.60	91.27	102.02	0.67	11.42
N-Nitroso-diaziridine (II)					
II <sub>anti</sub>	48.76 <sup>b</sup>	52.78	61.63 (N <sub>1</sub> )	2.40 <sup>d</sup>	12.85 (N <sub>1</sub> ) <sup>e</sup>
II <sub>anti</sub>	52.15 <sup>c</sup>		75.49 (N <sub>3</sub> )	1.16 <sup>f</sup>	26.71 (N <sub>3</sub> ) <sup>g</sup>
II <sub>syn</sub>	56.17 <sup>b</sup>	58.67	61.63 (N <sub>1</sub> )	2.50 <sup>d</sup>	5.41 (N <sub>1</sub> ) <sup>e</sup>
II <sub>syn</sub>	56.41 <sup>c</sup>		75.49 (N <sub>3</sub> )	2.26 <sup>f</sup>	19.32 (N <sub>3</sub> ) <sup>g</sup>

<sup>a</sup> Parentheses show inversion site. <sup>b</sup> Heat of formation of the ground state. <sup>c</sup> Heat of formation of the local minimum. <sup>d</sup> Energy barrier from the ground state to the local minimum. <sup>e</sup> Energy barrier from the local minimum to the ground state. <sup>f</sup> Energy barrier from the II<sub>anti</sub> to the II<sub>syn</sub>. <sup>g</sup> Energy barrier from the II<sub>anti</sub> to the II<sub>anti</sub>.

The calculated heat of formations and energy barriers are shown in Table 1. Selected geometric parameters, atomic charges, total dipole moments and bond orders are shown in Table 2.

**N-Nitroso-diaziridine (II).** Since the hydrogen atom at N<sub>3</sub> (see Figure 1) in the diaziridine ring is nonsymmetric, there are two possible conformers for the N-nitroso-diaziridine (II). The hydrogen atom attached the N<sub>3</sub> in the diaziridine ring can have anti (II<sub>anti</sub>) and syn (II<sub>syn</sub>) conformation *vs.* the nitroso group. Figure 3 and 4 show the nitroso group rotational energy profile of II<sub>anti</sub> and II<sub>syn</sub>, respectively. The smallest heat of formation in II<sub>syn</sub>, which is the ground state, is always larger than that of any state in II<sub>anti</sub>. One can see the nitroso group rotational energy profile of II<sub>anti</sub> (see Figure 3) has two energy minima, which are the ground state, D, and the local minimum, B. The ground state structure of II<sub>anti</sub> shows that the nitroso group is placed between the lone pair of the imino nitrogen N<sub>1</sub> and the N<sub>1</sub>-N<sub>3</sub> bond in the diaziridine ring. The nitroso group prefers the more electronegative side, the N<sub>1</sub>-N<sub>3</sub> bond, than the less electronegative side, the N<sub>1</sub>-C<sub>2</sub> bond in the diaziridine ring, which is called anomeric effect. The heat of formations are 48.78 and 52.15 kcal/mol for the ground state D and the local minimum B in II<sub>anti</sub>, respectively. The structure of the nitroso group rotational transition state in II<sub>anti</sub> shows that the nitroso group is nearly eclipsed with the lone pair of the imino nitrogen N<sub>1</sub>. The heat of formation of the nitroso group rotational transition state in II<sub>anti</sub> is 52.78 kcal/mol. Thus the rotational energy barriers of the nitroso group in II<sub>anti</sub> are calculated to be 0.63 kcal/mol from the local minimum to the ground state and 4.00 kcal/mol from the ground state to the local minimum.

There are two minima in II<sub>syn</sub> (see Figure 4), the ground state, B, and the local minimum, D. The structure of the ground state in II<sub>syn</sub> shows that the nitroso group is placed between the lone pair of the imino nitrogen N<sub>1</sub> and the N<sub>1</sub>-C<sub>2</sub> bond. Since the nitroso group prefers the more electronegative side, so-called the anomeric effect, this result seems unreasonable. Probably the syn-hydrogen in N<sub>3</sub> repulsion

**Table 2.** Geometric Paramtres, Atomic Charges, Total Dipole Moments and Bond Orders of N-Nitroso-azirine (I) and -diziridine (II)<sup>a</sup>

	I			II					
	GS	TS-Rot	TS-Inv	$\Pi_{anti}$		$\Pi_{syn}$		TS-Inv	
				GS	TS-Rot	GS	TS-Rot	N <sub>1</sub>	N <sub>3</sub>
Distances <sup>b</sup>									
N <sub>1</sub> -C <sub>2</sub>	1.478	1.496	1.448	1.477	1.491	1.475	1.482	1.436	1.520
N <sub>1</sub> -C <sub>3</sub>	1.488	1.496	1.461						
N <sub>1</sub> -N <sub>3</sub>				1.405	1.408	1.402	1.409	1.389	1.366
N <sub>1</sub> -N <sub>4</sub>	1.377	1.404	1.307	1.382	1.411	1.373	1.413	1.324	1.384
N <sub>4</sub> =O <sub>5</sub>	1.166	1.161	1.174	1.161	1.158	1.163	1.158	1.165	1.164
Angles <sup>c</sup>									
C <sub>2</sub> N <sub>1</sub> C <sub>3</sub>	52.8	52.0	54.6						
C <sub>2</sub> N <sub>1</sub> N <sub>3</sub>				61.6	60.8	61.8	61.2	64.5	58.6
N <sub>1</sub> N <sub>4</sub> O <sub>5</sub>	117.2	113.5	116.9	117.5	112.4	117.6	113.5	117.9	118.4
φ	128.5	116.8	180.0	129.3	119.1	135.1	123.8	180.0	127.3
α	47.0	151.2	0.0	50.3	157.7	41.8	107.0	3.5	44.6
Atomic charges <sup>d</sup>									
N <sub>1</sub>	-0.273	-0.277	-0.420	-0.262	-0.272	-0.249	-0.243	-0.402	-0.143
N <sub>4</sub>	0.195	0.131	0.316	0.223	0.201	0.224	0.161	0.339	0.175
O <sub>5</sub>	-0.196	-0.128	-0.311	-0.151	-0.118	-0.175	-0.092	-0.244	-0.177
Total dipole moment <sup>e</sup>									
	3.314	3.229	4.511	2.822	2.503	3.137	2.897	3.455	2.779
Bond orders									
N <sub>1</sub> -N <sub>4</sub>	1.00	0.94	1.14	0.97	0.92	0.99	0.92	1.04	0.98
N <sub>4</sub> =O <sub>5</sub>	1.93	1.99	1.74	1.97	2.00	1.94	2.00	1.84	1.94

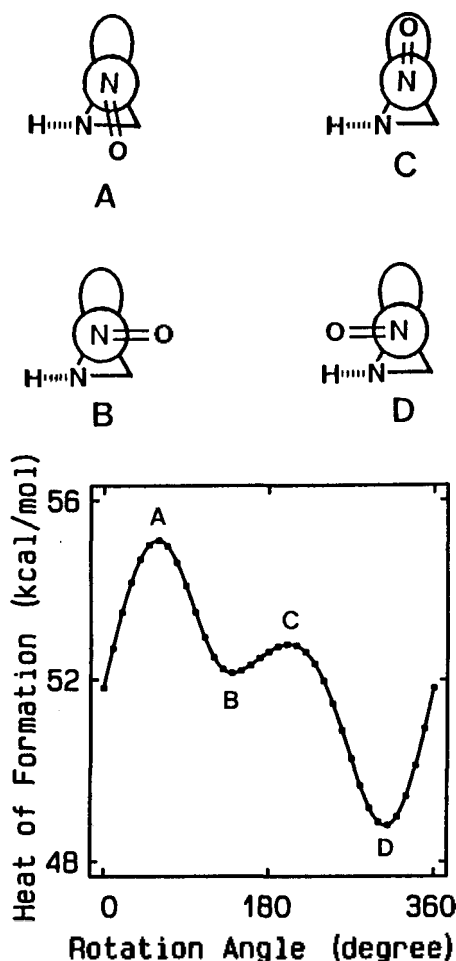
<sup>a</sup>See Figure 1. for the numbering of the atoms. <sup>b</sup>Distance in Å. <sup>c</sup>Angle in degrees. <sup>d</sup>Electronic unit. <sup>e</sup>Unit in debye.

with the nitroso group competes with the anomeric effect of the nitroso group. Consequently this syn-hydrogen in N<sub>3</sub> repulsion with the nitroso group is slightly more effective than the anomeric effect of the nitroso group. One can see that the heat of formations of the ground state and the local minimum are very similar. This small difference of heat of formation is different from the case of  $\Pi_{anti}$  which the anomeric effect prevails. The heat of formations are 56.17 and 56.41 kcal/mol for the ground state and the local minimum in  $\Pi_{syn}$ , respectively. The structure of the nitroso group rotational transition state in  $\Pi_{syn}$  shows that the nitroso group is nearly eclipsed with the lone pair of the imino nitrogen N<sub>1</sub>. The heat of formation of the nitroso group rotational transition state in  $\Pi_{syn}$  is 58.67 kcal/mol. The rotational energy barriers of the nitroso group in  $\Pi_{syn}$  are calculated to be 2.26 kcal/mol from the local minimum to the ground state and 2.50 kcal/mol from the ground state to the local minimum.

Since N-nitroso-diaziridine has two imino nitrogens in the diaziridine ring, there are two nitrogen inversion sites, N<sub>1</sub> and N<sub>3</sub> (see Figure 1). Either of imino nitrogen inversion causes interconversion of  $\Pi_{anti}$  to  $\Pi_{syn}$  and *vice versa*. The structure of the inversion transition state shows that the imino nitrogen, N<sub>1</sub> or N<sub>3</sub>, has planar configuration. The heat of formations of the inversion transition states are 61.63 and 75.49 kcal/mol for the N<sub>1</sub> and N<sub>3</sub> sites, respectively. The structure of the N<sub>1</sub> inversion transition state shows that the nitroso group is nearly eclipsed with the diaziridine ring. However, the structure of the N<sub>3</sub> inversion transition state

shows that the nitroso group is twisted 44.6° which is similar to the ground state structure. The N<sub>1</sub> imino nitrogen inversion energy barriers in II are 12.85 kcal/mol from the  $\Pi_{anti}$  to the  $\Pi_{syn}$  and 5.54 kcal/mol from the  $\Pi_{syn}$  to the  $\Pi_{anti}$ . The N<sub>3</sub> imino nitrogen inversion energy barriers in II are 26.41 kcal/mol from the  $\Pi_{anti}$  to the  $\Pi_{syn}$  and 19.40 kcal/mol from the  $\Pi_{syn}$  to the  $\Pi_{anti}$ . The calculated heat of formations and energy barriers are shown in Table 1. Selected geometric parameters, atomic charges, total dipole moments and bond orders are shown in Table 2.

There are three major effects considered here, i) the conjugation between the lone pair of the imino nitrogen N<sub>1</sub> and the nitroso group double bond, ii) the dipole-dipole repulsion between the lone pair of the imino nitrogen N<sub>1</sub> and the lone pair of the nitroso nitrogen N<sub>4</sub>, and iii) steric hindrance between the nitroso group and three-membered ring. When the imino nitrogen N<sub>1</sub> shows planar configuration, which is the inversion transition state of I and II, maximum conjugation can be possible between the lone pair of the imino nitrogen N<sub>1</sub> and the nitroso group double bond. Thus the inversion transition states of I and II are stabilized by this conjugation. Also in the ground state structure of I and II, the nitroso group makes nearly 90° with the lone pair of the imino nitrogen N<sub>1</sub>. And then the nitroso group double bond makes nearly parallel with the lone pair of the imino nitrogen N<sub>1</sub>, which shows maximum conjugation. When the nitroso group is placed middle in the three-membered ring, the dipole-dipole repulsion is maximum and I and II show the maximum energy state. At the maximum energy state,



**Figure 3.** The nitroso group internal rotational energy profile of the N-nitroso-diaziridine-anti( $II_{anti}$ ). A: The maximum. B: The local minimum. C: The rotational transition state (TS-Rot). D: The ground state (GS).

the steric hindrance is moderate, not severe. The rotational transition states of I and II show that the nitroso group is nearly eclipsed with the lone pair of the imino nitrogen  $N_1$ . At the nitroso group rotational transition state, the dipole-dipole repulsion is not severe and the steric hindrance is moderate also.

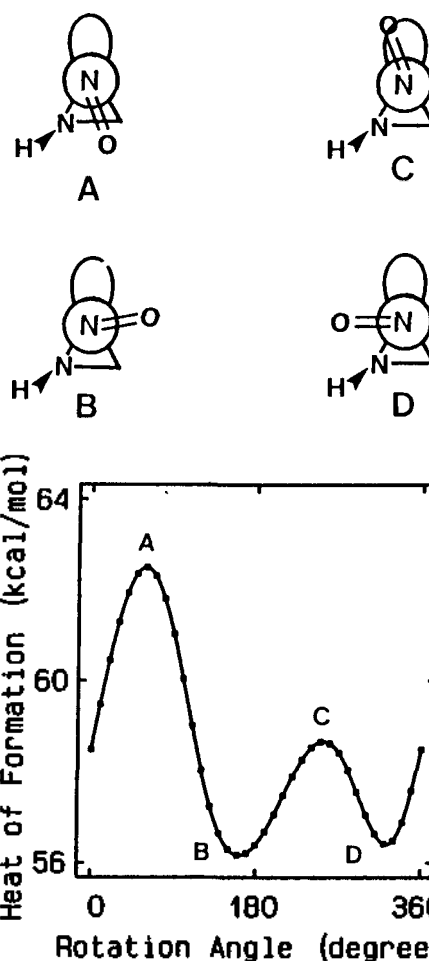
### Conclusion

The ground states geometry of N-nitroso-azirine (I) and -diaziridine (II) show that the imino nitrogen  $N_1$  has nonplanar configuration. Also in the ground states of I and II the nitroso group is not eclipsed with the three-membered ring. The nitroso group rotational transition states of I and II show that the nitroso group is nearly eclipsed with the lone pair of the imino nitrogen  $N_1$ .  $II_{anti}$  conformation is more stable than  $II_{syn}$  conformation.

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**Figure 4.** The nitroso group internal rotational energy profile of the N-nitroso-diaziridine-syn( $II_{syn}$ ). A: The maximum. B: The local minimum. C: The rotational transition state (TS-Rot). D: The ground state (GS).

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