

# DFT INVESTIGATION OF STRUCTURES OF NITROSAMINE ISOMERS AND THEIR TRANSFORMATIONS IN GAS PHASE



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## Abstract

The geometrical structures of  $H_2NNO$  nitrosamine isomers have been obtained by geometry optimizations using the DFT method at the RB3LYP/aug-cc-pVDZ level of theory. One amino, 4 imino tautomers, 2 zwitterionic and 2 oxadiaziridine isomers of the  $H_2NNO$  nitrosamine have been found. The most stable species of the nitrosamine isomers existing as an amino form has been found. Energetics, thermodynamic properties, rate constants and equilibrium constants of all transformation reactions have been determined. The energy profile for the transformation reactions of the nitrosamine isomers has been presented.

## Introduction

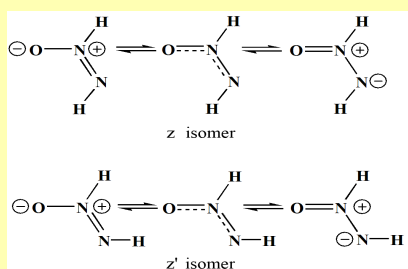
N-nitrosamines are potent carcinogens that can induce tumors in humans and animals. The International Agency for Research on Cancer (IARC) classified a number of N-nitrosamines with respect to the cancer risk for humans. Humans are exposed to N-nitrosamines from other environmental sources and from endogenous synthesis within the body. N-nitrosodimethylamine is the most commonly encountered volatile nitrosamine in many food samples.

In gas phase, volatile nitrosamines exist in several isomers. In order to get more information of the existing  $H_2NNO$  nitrosamine isomers and their behaviors in gas phase, the geometrical structures of all isomers in terms of stabilities and thermodynamic properties, rate constants and equilibrium constants of all transformation reactions have therefore been theoretically investigated and determined.

## Methods

Geometries of various isomers of the  $H_2NNO$  nitrosamine and transition states of all transformation reactions were optimized using density functional theory (DFT) method. DFT calculations have been performed with the Becke's three-parameter exchange functional (B3LYP). All geometry optimizations have been carried out using the MO computations at the RB3LYP/aug-cc-pVDZ level of theory. All minima and transition states were confirmed by real and single imaginary vibrational frequencies, respectively. All calculations were performed with the GAUSSIAN 03 program.

The standard enthalpy  $\Delta H_{298}$  and Gibbs free energy changes  $\Delta G_{298}$  of all transformation reactions between the nitrosamine isomers have been derived from the frequency calculations at the same level of theory. According to the transition-state theory, the rate constant  $k(T)$  was computed from Gibbs free energy of activation  $\Delta^\ddagger G$ .



Scheme 1.

## Results and discussion

The structures of seven isomers of the  $H_2NNO$  nitrosamine and the transition states of all transformation reactions were obtained by geometry optimizations using DFT theory at the RB3LYP/aug-cc-pVDZ level of theory as shown in Fig. 1. The  $H_2NNO$  nitrosamine isomers can be classified into four types namely amino (type a), imino (type i), zwitterionic (type z) and oxadiaziridine (type o) isomers. Two zwitterionic forms which exist as the resonance structures are depicted as shown in Scheme 1.

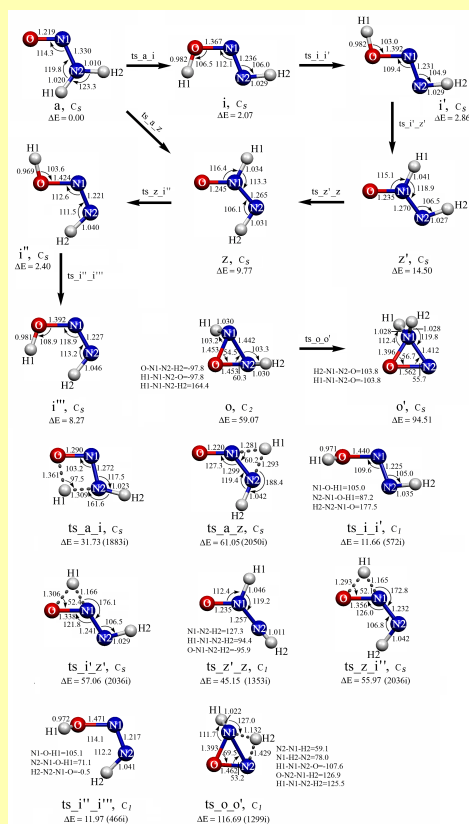


Fig. 1. The structures of the nitrosamine isomers and their transformation reactions and corresponding transition states. Bond length and bond angle are in angstrom and degree, respectively. The imaginary frequencies of transition states are in  $cm^{-1}$ . The relative energies ( $\Delta E$ ) are in kcal/mol.

The most stable form of the  $H_2NNO$  nitrosamine is an isomer a and relative stability of the nitrosamine isomers is in the decreasing order:  $a > i > i'' > i' > i''' > z > z' > o > o'$ . The energy profile for the transformation reactions of the nitrosamine isomers are shown in Fig. 2.

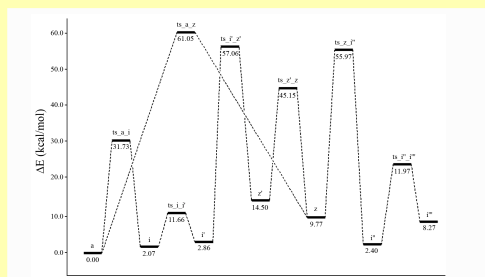


Fig. 2. The energy profile for transformations of the nitrosamine isomers. The relative energies ( $\Delta E$ ) of the nitrosamine isomers and transition states are in kcal/mol. Transition-state types for the transformation reactions are shown in parenthesis, located at top of their structures.

The highest occupied molecular orbital (HOMO) and its five minimum orbitals (HOMO-1, HOMO-2, HOMO-3, HOMO-4 and HOMO-5) based on sequentially the reaction path  $a \rightarrow i \rightarrow i' \rightarrow z' \rightarrow z \rightarrow i'' \rightarrow i'''$  as illustrated in Fig. 3 have given the following remarks. The HOMO ( $E_{HOMO}$ ) and HOMO-1 ( $E_{HOMO-1}$ ) energies for the isomers z and z' are almost the same value which is close to -8.0 eV. The HOMO and HOMO-1 orbitals of the isomer z and z' describe the occurrence of their delocalized structures which are displayed as shown in Scheme 1 and are possessed by four valence electrons of which energies are -8.0 eV. The HOMO-2 ( $E_{HOMO-2}$ ) and HOMO-3 ( $E_{HOMO-3}$ ) energies of the isomers z and z' are remarkably larger than others (see Fig. 3).

The activation energies, free energies of activation, rate constants, reaction enthalpies, free energies and equilibrium constants of the isomerizations of all the nitrosamine isomers, computed at the same level of theory are reported in Table 1.

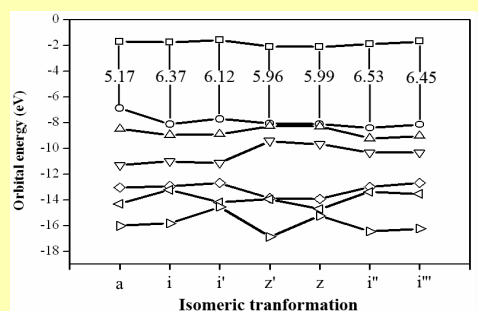


Fig. 3. The orbital energies at LUMO ( $\square-\square-\square$ ), HOMO ( $\circ-\circ-\circ$ ), HOMO-1 ( $\triangle-\triangle-\triangle$ ), HOMO-2 ( $\nabla-\nabla-\nabla$ ), HOMO-3 ( $\diamond-\diamond-\diamond$ ), HOMO-4 ( $\blacktriangleleft-\blacktriangleleft-\blacktriangleleft$ ) and HOMO-5 ( $\blacktriangleright-\blacktriangleright-\blacktriangleright$ ) of the nitrosamine isomers. The frontier molecular orbital energy gaps,  $\Delta E_{HOMO-LUMO}$  are in eV.

Table 1 Rate constants of tautomerizations and isomerizations of all the nitrosamine isomers computed at the RB3LYP/aug-cc-pVDZ level of theory

Reactions	TS types <sup>a</sup>	$\Delta^\ddagger E$ <sup>b</sup>	$\Delta^\ddagger G$ <sup>b,c</sup>	$k_{298}$ <sup>d</sup>	$\Delta E^b$	$\Delta G_{298}^b$	$\Delta H_{298}^b$	$K_{298}$
$a \rightarrow i$	I.	31.73	31.94	$2.40 \times 10^{10}$	2.07	2.23	1.83	$2.31 \times 10^7$
$a \rightarrow i'$	I.	61.05	61.25	$7.86 \times 10^{10}$	9.77	9.97	9.44	$4.93 \times 10^8$
$i \rightarrow i'$	III.	9.59	9.57	$5.98 \times 10^6$	0.79	0.77	0.83	$2.71 \times 10^3$
$i' \rightarrow i''$	III.	9.57	9.58	$5.86 \times 10^6$	5.88	5.88	5.85	$4.86 \times 10^3$
$z \rightarrow i''$	I.	46.20	46.09	$1.01 \times 10^{10}$	-7.37	-7.49	-7.19	$3.11 \times 10^6$
$z' \rightarrow i''$	II.	30.65	30.64	$2.14 \times 10^{10}$	-4.73	-4.76	-4.74	$3.09 \times 10^6$
$i'' \rightarrow i'''$	I.	54.20	54.19	$1.18 \times 10^{10}$	11.64	11.72	11.51	$2.54 \times 10^9$
$o \rightarrow o'$	I.	57.62	57.12	$8.36 \times 10^{10}$	35.44	34.98	35.49	$2.26 \times 10^{26}$

## Conclusions

The electronic properties of the nitrosamine isomers can be concluded as the following sequences.

1. Their relative stability is in the decreasing order:  $a > i > i'' > i' > i''' > z > z' > o > o'$ .
2. Their relative reactivity based on their frontier molecular orbital energy gap is in the decreasing order:  $o' > a > z' > z > i' > i > i'' > i''' > o$ .
3. Their acceptor strength is in the decreasing order:  $z > z' > i'' > i > a > i''' > i' > o' > o$ .
4. Their donor strength is in the decreasing order:  $o' > a > i' > o > z' > i > z > i'' > i'''$ .

## References

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- [2]. Wanno, B.; Ruangpornvitsuti, V. (2006) *J. Mol. Struct. Theorchem* **776**, 113-120.

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