Ab initio MO Study on N-Nitrosoazetidine-2-carboxylic Acid

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Due to its important biological characters such as carcinogenic and mutagenic properties,\textsuperscript{1} N-Nitrosamines are of widespread interest. The stereochemistry of N-nitrosamines has been studied utilizing various experimental techniques,\textsuperscript{2} because the molecular geometry of these compounds critically influences their biological activity. In particular, non-planarity and, connected with it, inherent chirality of the N-nitrosamine chromophore exhibit interesting geometric characters and relative stability between isomers. Recently, an X-ray crystallographic study of (S)-N-nitrosamino-2-carboxylic acid revealed its structural details.\textsuperscript{3}

Experimental evidence shows the following geometric characteristics. 1) Due to a restricted rotation about the partially double N-N bond, the molecule can exist as either the E or Z stereoisomer (Figure 1). In an aqueous solution, the E conformer is more stable than Z conformer.\textsuperscript{4} The crystal structure reveals that the N-nitrosamine moiety is ordered, and adopts the E conformation.\textsuperscript{3} (2) The N atom of the N-nitrosamino group of the molecule included in a strained four-membered ring may lead to its pyramidal configuration and the intrinsic chirality of a chromophore.\textsuperscript{5} Its displacement from the plane containing the three attached atoms is 0.038(2) Å.\textsuperscript{3}

To more correctly interpret this data, an ab initio Molecular Orbital study of N-Nitrosoazetidine-2-carboxylic acid has been performed. All ab initio molecular orbital calculations were carried out at the level of HF theory using the Gaussian 98 package.\textsuperscript{5}

Due to the restriction between the N-N partial double bond, both E and Z conformations were considered. Since the rotational barrier of C2-C1-C4-O2 is high, the optimized geometry depends on the initial torsion angle of C2-C1-C4-O2 during the geometry optimization. Two possible C2-C1-C4-O2 orientations (+ and −) are considered for each E and Z conformers. Therefore, four types of stable conformers (E+, E−, Z+ and Z−) were considered for the calculations (Figure 1).

During the geometry optimization, no geometric constraints were used such as assuming that the ring is a planner. For each conformation, gas phase geometry optimizations and energy calculations were performed at the Hartree Fock level with 6-31+G* and 6-31++G** basis sets. With optimized geometries, the Self-Consistent Reaction Field (SCRF) calculations using the conductor-like polarizable continuum model (CPCM)\textsuperscript{7} has been carried out to see the solvent effects on the conformation.

Among the conformers, Z− and E+ conformers are the most stable conformations in the gas phase and in the aqueous solution, respectively (Table 1). Experimental evidence shows that the E+ conformer is observed in X-ray crystallographic study.\textsuperscript{5} Due to polar environments caused by other molecules in the crystal, the molecule prefers the E conformation rather than the Z conformation. With the experimental evidence\textsuperscript{3} and the calculations done in this work, it is concluded that N-nitrosoazetidine-2-carboxylic acid prefers the E conformation in polar environments and the Z conformation in non-polar environments.

Calculated geometric values of the E+ conformer are represented in Table 2 and compared with its experimental values.\textsuperscript{3} The crystal structure of N-Nitrosoazetidine-2-carboxylic acid corresponds well with the calculated geometry of the E+ conformer which is the lowest energy conformation with SCRF calculation. The displacement from the plane of the N atom of the N-nitrosamino group

![Figure 1](https://via.placeholder.com/150)

**Figure 1.** Four stable conformations of N-Nitrosoazetidine-2-carboxylic acid.
containing the three attached atoms is 0.230 Å and 0.242 Å with 6-31+G* and 6-31++G**, respectively. It shows little deviation from its experimental value of 0.038 Å. However, overall geometric values show good agreement with the experimental values.

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References