

Communications

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,¹ *N*-Nitrosamines are of widespread interest. The stereochemistry of *N*-nitrosamines has been studied utilizing various experimental techniques,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.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.⁴ The crystal structure reveals that the *N*-nitrosamine moiety is ordered, and adopts the *E* conformation.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.⁵ Its displacement from the plane containing the three attached atoms is 0.038(2) Å.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.⁶

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 planar. 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)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.³ 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 evidence³ 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.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

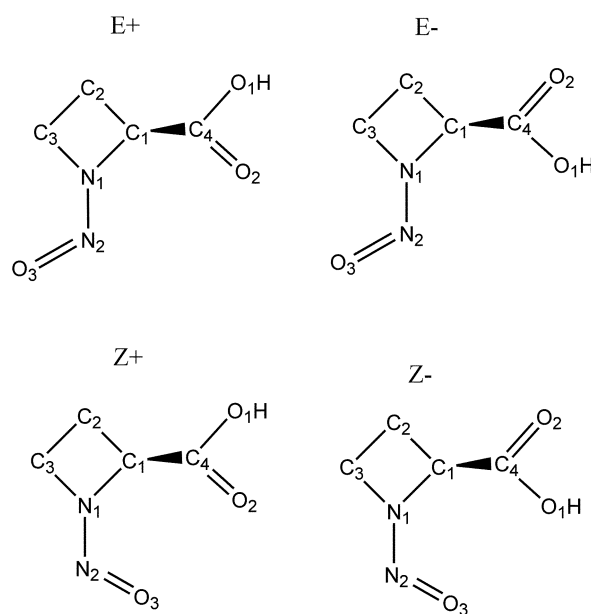


Figure 1. Four stable conformations of *N*-Nitrosoazetidine-2-carboxylic acid.

Table 1. Calculated Energies^a of the conformers

Basis sets	Gas Phase			
	Conformers			
	E+	E-	Z+	Z-
6-31+G*	-488.3601335	-488.3601876	-488.3600579	-488.360315
6-31++G**	-488.3746655	-488.3746685	-488.3744839	-488.3747068

Basis sets	SCRF (CPCM) Calculation			
	Conformers			
	E+	E-	Z+	Z-
6-31+G*	-488.3873768	-488.3860219	-488.3863927	-488.386541
6-31++G**	-488.3876814	-488.386059	-488.3862957	-488.3865638

^aenergies in Hartree units**Table 2.** Selected Geometric parameters of E+ conformer

Geometric Parameters	Methods		
	Exptl ^a	6-31+G*	6-31++G**
		Bond Length ^b	
O1-C4	1.200(2)	1.1864	1.1866
O2-C4	1.311(3)	1.3257	1.3246
O3-N2	1.254(2)	1.1936	1.1940
N1-N2	1.285(2)	1.2923	1.2913
N1-C1	1.468(3)	1.4482	1.4475
C1-C4	1.507(3)	1.5141	1.5139
C1-C2	1.548(3)	1.5606	1.5607
C2-C3	1.544(3)	1.5498	1.5502
		Bond Angle ^c	
N2-N1-C1	133.81(18)	130.81	131.00
O3-N2-N1	111.61(18)	114.69	114.69
N1-C1-C2	87.14(16)	86.72	86.72
C4-C1-C2	116.42(18)	114.49	114.55
C3-C2-C1	89.60(16)	88.76	88.79
O1-C4-O2	125.0(2)	123.57	123.55
O1-C4-C1	122.0(2)	123.40	123.27
		Dihedral Angle ^d	
C3-N1-N2-O3	-4.1(3)	-11.16	-9.65
N2-N1-C1-C4	-69.7(3)	-53.93	-55.42
N1-C1-C2-C3	2.54(16)	4.58	3.99
		Out of plane ^e	
C1-C3-N2-N1	0.038(2)	0.230	0.242

^aTaken from ref. 3. ^bIn Å units. ^c^dIn degree units. ^eIn Å units. The displacements of N1 are from the plane containing C1, C3, and N2.

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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