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Ab initio studies of gas phase asparagine conformers

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Abstract

Systematic and extensive conformational search of the gas phase asparagine has been performed for the first time. A total of 972 unique trial structures were generated by allowing for all combinations of internal single-bond rotamers. All the trial structures were optimized at the B3LYP/6-311G* level of the theory and then subjected to further optimization at the B3LYP/6-311++G** level and a total of 62 conformers were found. Single-point energies were also calculated at the MP2/6-311++G** level of theory. The relative energies, rotational constants, dipole moments, zero-point vibrational energies and some harmonic frequencies are listed for the conformers. The conformational distributions of the gas phase asparagine at various temperatures were calculated.

Keywords: Asparagine conformers; Geometry optimization; Vibrational spectra; Hydrogen bonding; Conformation distribution

1. Introduction

Asparagine, the β-amide derivative of aspartic acid, plays an important role in the biosynthesis of glycoproteins and is also essential to the synthesis of a large number of other proteins. It is an important constituent in many plant proteins. In the liver, asparagine is involved in converting one amino acid to another. Asparagine also helps to maintain an equilibrium of the central nervous system and has therapeutic properties.

Many studies have been carried out for asparagine residue [1–3] and asparagine-linked glycosylation [4,5] because of their important roles in proteins and biosynthesis of glycoproteins. Rassolian et al. [6] studied the conformations of *N*-acetyl-L-asparagine *N*-methylamide at the RHF/3-21G level of theory. Some theoretical works have also been performed for the studies of asparagine. Nakahara et al. [7] calculated the free-energy change for side-chain conformations of asparagine in solutions. Ramírez et al. [8] performed a theoretical study of the structures and vibrations of asparagine zwitterions in aqueous solution and in isolation based on the HF and SCRF theory using the 3-21G* and 6-31+G* basis sets. Zhan et al. [9] calculated C-13 NMR chemical shift tensors of asparagine and compared with experiments [10]. Alvarez-Idaboy et al. [11] studied the gas phase OH hydrogen abstraction reaction from asparagine using a quantum mechanical approach.

The molecular structural information is critical to the studies of asparagine and the reactions of asparagine in organisms. The attraction of gas phase conformation lies in the opportunity to study their intrinsic properties free of the solvent environment. Wojtkowski et al. [12] performed the conformational analysis of asparagine using specific isotope substitution. Alvarez-Idaboy et al. [11] made full geometry optimizations of a conformer using B3LYP/6-311G(d,p) method. But in most conformational studies of asparagine, the starting sets of conformations were chosen using the analysis method developed by Pachler [13]. In this method the rotamers were obtained only by rotating the C_α–C_β bond in Newman projections, so many possible rotamers were not selected and some important local minima conformers may be lost. For example, only three staggered conformers were given in Refs. [7,12]. Therefore, it is necessary to carry out a systematic and reliable theoretical study of the asparagine conformations by using an extensive set of trial conformers. The goal of this study is to locate all possible gas phase asparagine conformers with full geometry optimizations, to obtain precise knowledge about the relative stabilities of

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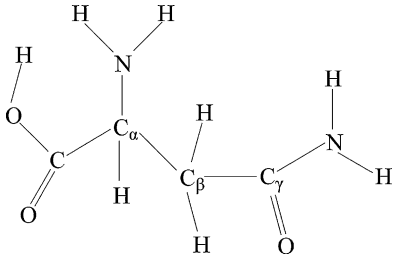

Fig. 1. Sketch of the molecular structure of asparagine.

different conformers on the energy surface, and to provide theoretical results such as rotational constants, vibrational frequencies, dipole moments of conformers and conformer distributions at various temperatures that may be helpful to future experimentalists. As DFT/B3LYP [14–16] method has been widely applied to obtain the conformational behavior, theoretical vibrational frequencies and infrared intensities of amino acids, which are in excellent agreement with the experimental data [17–19], B3LYP is used in this work as the main computational method.

2. Computational methods

Fig. 1 is a sketch of the molecular structure of asparagine. Rotating the six internal axes, i.e. the C–O, C–C_α, C_α–N, C_α–C_β, C_β–C_γ and C_γ–N bonds, results in various possible conformations. To truly characterize the molecular conformers, the initial sets of trial conformations were chosen by all possible combinations of single-bond rotamers (Fig. 2): (a) For the carboxyl group, syn and anti conformations were considered corresponding to 0° and 180° torsion; (b) Assuming a staggered conformation, one of the three groups on the α-carbon is separated from the other two groups by the plane of the carboxyl. Because the three groups on the α-carbon are different and the carboxyl is asymmetric, placement of the unique group above or bellow the carboxyl plane leads to six different rotamers; (c) Due to the symmetry of the NH_2 group, the interaction of the α-carbon and the amido leads to only three unique structures; (d) As the two hydrogen atoms on the β-carbon are equivalent, there are three possible rotamers about the C_α–C_β bond; (e) The asymmetry of acylamino leads to three different rotamers about C_β–C_γ bond; (f) The orientation of the NH_2 in the acylamino allows for three rotamers. This leads to a total of 972 trial conformations of the asparagine.

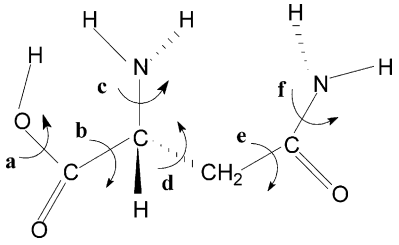

Fig. 2. Illustration of rotating the six internal single-bond axes of asparagine. *a* 2-fold: 0, 180, *b* 6-fold: 30, 90, 150, 210, 270, 330, *c* 3-fold: −60, 60, 180, *d* 3-fold: 60, 180, 300, *e* 3-fold: 60, 180, 300, *f* 3-fold: −120, 0, 120

All the 972 trial conformations were optimized at the B3LYP/6-311G* level of theory, which resulted in a set of unique conformers. The unique conformations were then subjected to further optimization at the B3LYP/6-311++G** level, and again the unique structures were identified. For the final set of unique conformations, the frequency analysis was completed at the B3LYP/6-311++G** level. Single-point energies were also calculated at the MP2/6-311++G** level for the final set of conformers.All the calculations of our work were done at our PC cluster using the GAUSSIAN 98 quantum chemistry package [20].

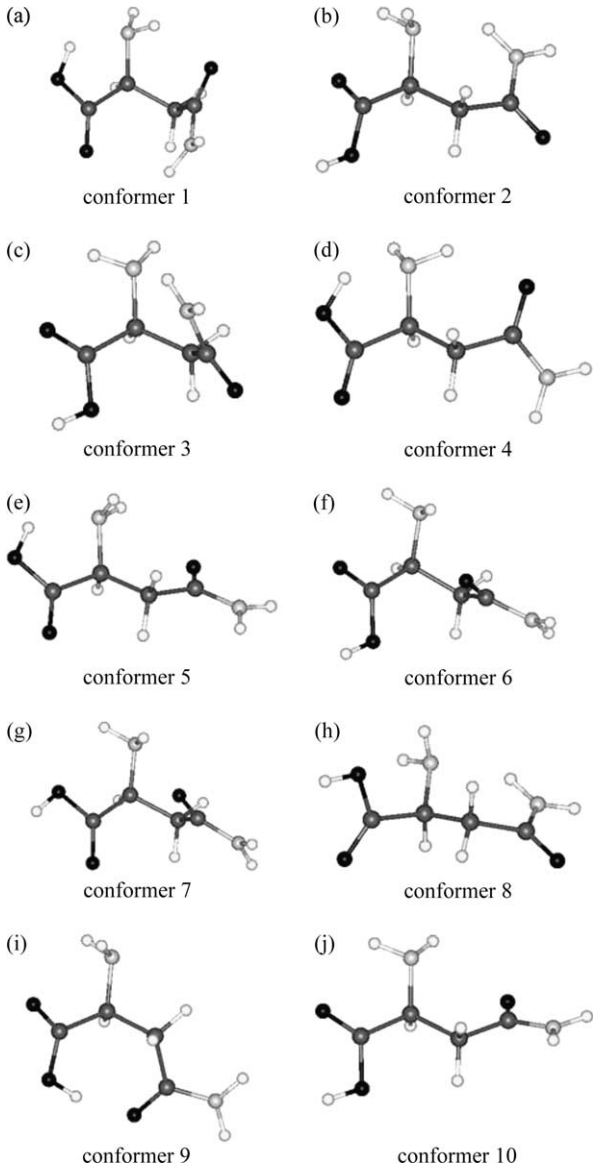

Fig. 3. Structures of the ten lowest energy conformers optimized at B3LYP/6-311++G** level.