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Investigation of intermolecular hydrogen bond interactions in crystalline L-Cysteine by DFT calculations of the oxygen-17, nitrogen-14, and hydrogen-2 EFG tensors and AIM analysis

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ABSTRACT

A systematic computational study is carried out to investigate hydrogen bond (HB) interactions in the real crystalline structures of L-Cysteine at 30 and 298 K by density functional theory (DFT) calculations of electric field gradient (EFG) tensors at the sites of O-17, N-14, and H-2 nuclei. One-molecule (monomer) and nine-molecule (cluster) models of L-Cysteine are created by available crystal coordinates at both temperatures and the EFG tensors are calculated for both models to indicate the effect of HB interactions on the tensors. The calculated EFG tensors at the level of B3LYP and B3PW91 DFT methods and 6-311++G** and cc-pVTZ basis sets are converted to those experimentally measurable nuclear quadrupole resonance (NQR) parameters i.e. quadrupole coupling constants (qcc) and asymmetry parameters (η_Q). The evaluated NQR parameters reveal that the EFG tensors of ^{17}O, ^{14}N, and ^{2}H are influenced and show particular trends from monomer to the target molecule in the cluster due to the contribution of target molecule to classic N–H…O, and non-classic S–H…O and S–H…S types of HB interactions. On the other hand, atoms in molecules (AIM) analyses confirm the presence of HB interactions and rationalize the observed EFG trends. The results indicate different contribution of various nuclei to HB interactions in the cluster where O2 and N1 have major contributions. The EFG tensors as well as AIM analysis at the H6 site show that the N1-H6…O2 HB undergoes a significant change from 30 to 298 K where changes in other N–H…O interactions are almost negligible. There is a good agreement between the calculated ^{14}N NQR parameters and reported experimental data.

1. Introduction

Hydrogen bond (HB) interactions are crucial elements in the biochemical activities, and determination and stabilization of the three-dimensional structures of biological systems [1,2]. Moreover, HBs play an important role in studying structural molecular biology [3–5]. Due to the importance, the nature of these interactions has been extensively investigated by numerous either experimental or theoretical studies [6–12]. To have a better determination of the HB properties, nuclear quadrupole resonance (NQR) spectroscopy is among the most important and versatile techniques for this purpose. NQR parameters being very sensitive to HBs are useful elements in the study of hydrogen-bonded systems. Since the most characteristic nature of HB interactions is electrostatic, electric field gradient (EFG) tensors originated at the sites of quadrupole nuclei are proper elements to characterize the HB interactions in solid phase [13–15]. It is noted that quadrupole nuclei are those with spin angular moment greater than one-half ($I>1/2$) which the interaction energy of the nuclear electric quadrupole moment (eQ) and the EFG tensors is measured by NQR as a quadrupole coupling constant (qcc). Asymmetry parameter (η_Q) indicating the EFG tensors deviation from cylindrical symmetry at the site of quadrupole nucleus is also measured by NQR.

The application of the Atoms and Molecules Theory to understand the nature of the bonds such as HBs in deeper detail is an interesting approach and several excellent reviews have been published on the theory of Atoms in Molecules (AIM) developed by Bader [16–18]. Also, the analysis of the critical points (CP) of the distribution of the electronic density has demonstrated to be a potentially useful tool to study different significant chemical features such as the structure, nature, and geometry of hydrogen-bonded systems [19–22]. Thus, this analysis is used as well as EFG calculations for study of the HB interactions properties in L-Cysteine. Previously, Matta and Bader [23–25] have also studied the bond and atomic properties of amino

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acids conformers and the effect of conformation and tautomerization on these properties by using AIM theory.

Study the properties of HB interactions in amino acids and derivatives is an interesting subject due to their key role in secondary and tertiary structures of proteins. Furthermore, understanding the nature of these interactions can be a crucial step to describe the functionality of these systems in biological media at molecular level. L-Cysteine ($SH–CH_2–CH_2–NH_2COOH$) carrying an amino, a carboxylic acid, and a thiol group is capable of donating and accepting intramolecular HBs. L-Cysteine thiol or sulfhydryl (S–H) groups can contribute to the stabilization of native protein structures since they are highly polarizable and the most chemically reactive sites in proteins under physiological conditions [26–29]. The Cysteine sulfhydryl may function as either a HB donor (e.g., S–H…O) or an acceptor (e.g., H…S–H) group. Sulfhydryl HB in proteins is not well understood, primarily because such HB interactions are difficult to detect experimentally due to their weakness. L-Cysteine like all amino acids exists in gas phase mainly as neutral form but in solution and solid phase chiefly as zwitterions-neutral form with charge separation. Both X-ray and neutron diffraction studies have been carried out to characterize the HBs of the L-Cysteine crystalline structure [30–37]. These studies have revealed that L-Cysteine occurs in the crystals in the dipolar ion (zwitterions) form and the amino and thiol group hydrogen atoms participate in a three-dimensional network of HBs. Based on these studies, in solid phase, L-Cysteine crystallizes into two different polymorphs, orthorhombic [30–33] and monoclinic [34–37], which are characterized by the presence of one and two molecules of L-Cysteine in the asymmetric unit, respectively. As evidenced by X-ray [31] and neutron diffraction [32], at ambient temperature, the sulfur atoms of the thiol groups are disordered over two positions. The distances between the oxygen and sulfur atoms of the neighboring molecules in the structure are consistent with the hypothesis on the formation of the two types of intermolecular HBs (S–H…S and S–H…O). A recent structural study of L-Cysteine at 30 K [30] has shown the sulfur atoms to be completely ordered and located at those positions, which correspond to the formation of the S–H…S HBs.

The previous quantum mechanical calculations on L-Cysteine include studies of protonation and ionization potential [38], a comparison of PCILO and SCF results [39], grand state vibrational spectra [40,41], minimum energy conformations [42,43], and electronic excitations of Cysteine conformers [44]. Recently, Pawlukojc et al. [45] have carried out neutron spectroscopy, Raman, IR, and ab initio calculations on L-Cysteine. Their work suggests that the presence of a three-dimensional network of HBs affects the structural and dynamical parameters of the molecule in the crystal to such extent that the "free molecule" approximation reflects the geometry of the L-Cysteine

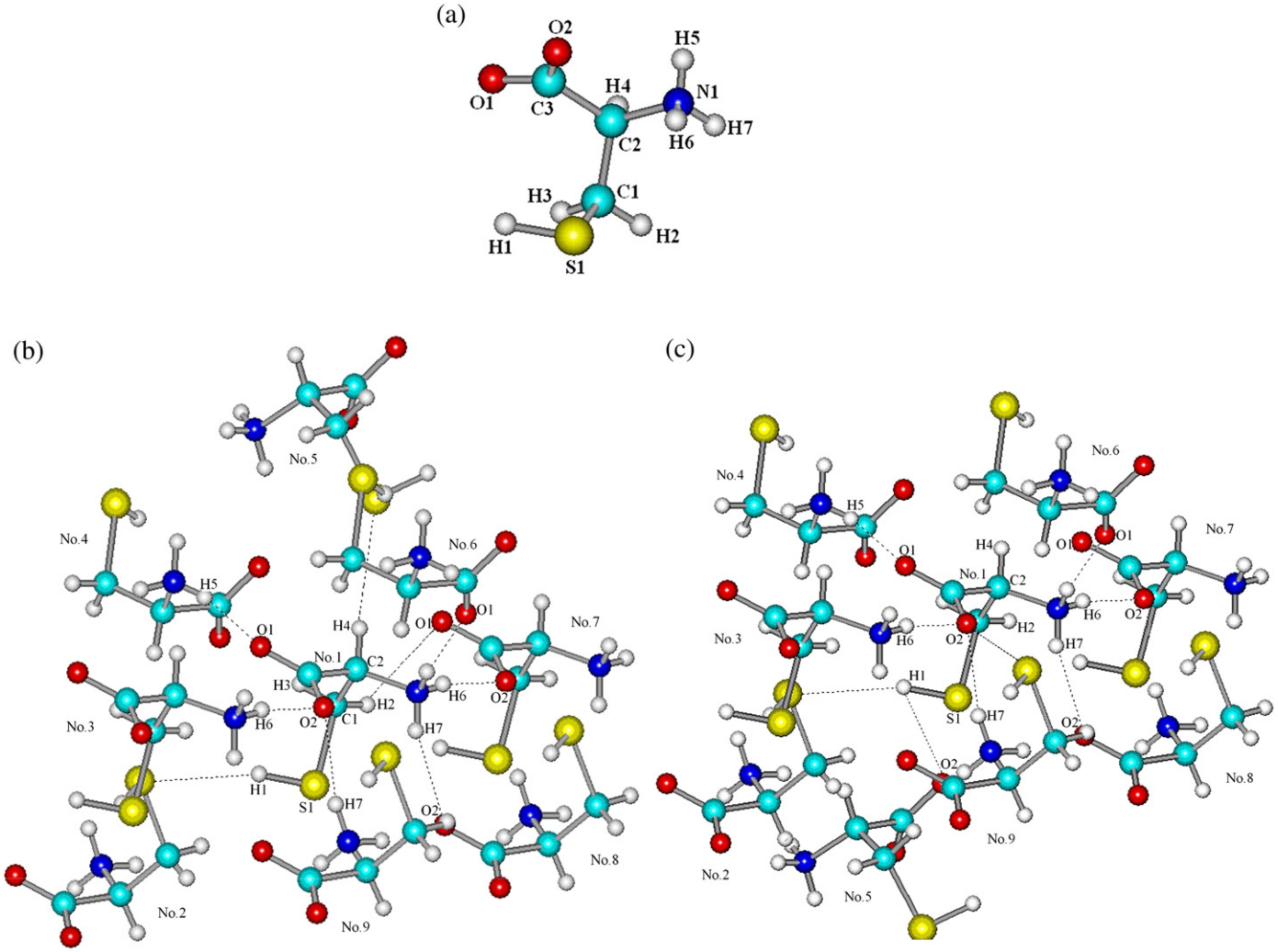

Fig. 1. (a) Monomer, and (b) and (c) nine-molecule clusters of L-Cysteine at 30 and 298 k, respectively. No.1 (Target molecule): (x,y,z); No.2: ($1/2-x,2-y,-1/2+z$); No.3: ($3/2-x,2-y,1/2+z$); No.4: ($1/2+x,3/2-y,1-z$); No.5: ($1-x,-1/2+y,3/2-z$); No.6: ($x,y,1+z$); No.7: ($1+x,y+1/2,z$); No.8: ($x+1/2,y,z$); No.9: ($-1/2+x,y,z$). At 298 K, No.5: ($-1/2+x,1-yz-1/2$). Dashed lines show the HBs (Table 2).