Atoms-in-molecules Investigation of the C5 Hydrogen-bond in Amino Acids and Tripeptides

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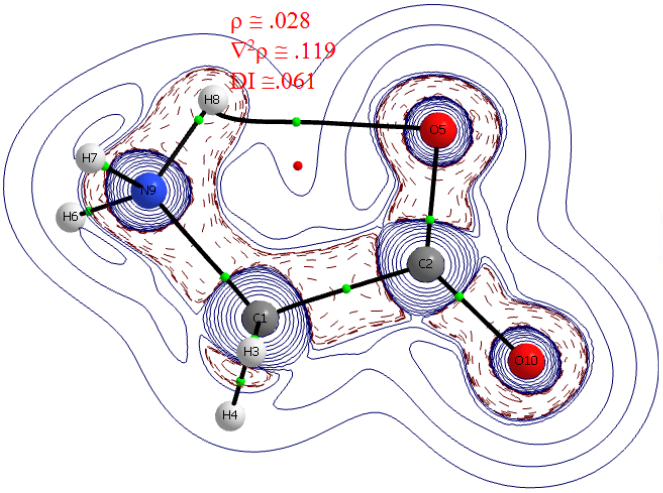
The quantum theory of atoms-in-molecules (QTAIM) was used to investigate the C5 intramolecular hydrogen-bond in amino acids between the amide proton and carbonyl oxygen. These hydrogen-bonds are of interest because of their potential influence on the folding of peptides and proteins, especially in β-sheets. The H···O bond length as well as properties of the electron density topology, including the electron density (ρ) and the Laplacian of the electron density ($\nabla^2\rho$) at the bond critical point (BCP) and the delocalization index (DI) of the bond, were compared with simple hydrogen-bonded molecules XH···YH (X,Y=F, OH, NH_2). Hydrogen-bonds, like many other "closed-shell" interactions, are characterized by values of $\rho \lesssim 0.03$ e·bohr^{-3}, $\nabla^2\rho \lesssim 0.1$ e·bohr^{-5}, and DI ≅ 0.02 - 0.08. The potential hydrogen-bonds were surveyed for 20 proteinogenic amino acids in the neutral form in the gas phase, in the zwitterionic form in aqueous solution (PCM), and in the simple tripeptides Gly-Aaa-Gly (Aaa = 20 amino acids) in aqueous solution. Perhaps not surprisingly, the zwitterions showed the greatest tendency to form notable hydrogen-bonds, and some tripeptides did as well, but the gas phase canonical structures did not.

Zwitterionic form in aqueous solution



Neutral form in the gas phase