Secondary structure of H-bonded Polyalanine peptides in vacuo: Computational spectroscopy and Density Functional Theory

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Hydrogen bonds are essential in stabilizing the secondary structure of polypeptides in vacuo. We here address the structure of Alanine-based peptides Ac-Ala_n-LysH+ (n=5,10,15), for which a helical secondary structure was indicated by earlier gas-phase experiments [1].

Using van der Waals corrected [2] density-functional theory (DFT) as implemented in the all-electron FHI-aims code [3], we present vibrational "computational spectroscopy" for all three molecules. Our results are corroborated by comparing calculated vibrational spectra to multiple photon IR spectroscopy data, obtained at the FELIX free electron laser for the molecules at room temperature. For the longer molecules (n=10,15), \alpha-helical structure models provide good qualitative agreement between theory and experiment already in the harmonic approximation.

For Ac-Ala_5-LysH+, an unambiguous helical structure assignment is questioned in the literature [4]. We thus perform an extensive conformational search, pre-screening O(10^5) conformers, using the opls-aa force field and different H-bond constraints in order to explore different structure families. A wide range of the resulting structure candidates (125 structures total) was post-relaxed in DFT.

The predicted lowest energy structure ("g-1") in van der Waals corrected DFT (PBE, revPBE and BLYP) is not a simple helix, showing instead an "inverted" hydrogen bond (oriented against a possible helix dipole). The qualitative differences between the harmonic spectra of different structure prototypes (g-1, \alpha- or 3_10-helical) do not yet allow for an unambiguous structure verification. Computing anharmonic spectra through Born-Oppenheimer molecular dynamics and the dipole-dipole autocorrelation function (300 K), there are marked improvements, and the predicted "g-1" conformer is clearly consistent with experiment and expected to be relevant even at finite T, where different conformers might coexist.

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