SITE-SPECIFIC CONFORMATIONAL RAMAN AND IR SPECTRA STUDIES OF SELECTIVELY ISOTOPIC LABELED PEPTIDES

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In an effort to determine any underlying interactions that might discriminate between the two most common helical protein structures, α helix and 3_{10} helix, we have carried out detailed spectral analysis and quantum mechanical simulations based on density functional theory (DFT) computations of the amide vibrational force fields (FF) and intensities for Raman and IR spectra, at various levels of theory, mostly BPW91/6-31G*. Short structures cannot develop stable helical conformations,consequently, parameters from these ab initio calculations on short peptides were then transferred onto corresponding larger oligopeptides (normally 20 residues) of the same conformation which are representative of molecules studied experimentally. To visualize intricate structural differences between the two types of helices, selected amide positions were isotopically labeled with ^{13}C=O and ^{15}N on the amide link or ^{13}C and ^{18}O on the amide C=O. The spacing between these labels along the sequence was varied, one residue at a time, to test position sensitivity. A similar approach was followed for 3_1 helices and β sheets. There is a distinct difference in adjacent and alternate labels in a helical sequence, since the sign of the coupling constant changes, which makes the more intense component of the exciton coupled pair opposite in the two cases and leads to a shift in frequency for the apparent ^{13}C=O Raman or IR band. In terms of discriminating between structures, this sign change is the same in α and 3_{10} helices, however the intensity distribution is somewhat different, indicating the mixing of modes shifts in the two structures. The coupling constants are of the same order of magnitude as well. There is little apparent shift of the amide III, even with ^{15}N labeling, presumably due to the extensive mixing of these modes. This work is supported by the National Science Foundation, (grant CHE07-18043 to TAK).