CONFORMATIONAL STUDIES OF DIPEPTIDE ANALOGS

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As the conformational flexibility of a molecule is increased one would expect the number of low energy conformers to increase dramatically. To the contrary, our work on a series of monomers of increasing complexity has found that the number of thermally populated conformational isomers does not growth with the molecular size. A wide array of techniques including: LIF, Fluorescence Dip Infrared Spectroscopy (FDIRS), UV-UV Hole Burning and IR-UV Hole Burning, have been used to identify the most stable conformations under supersonic expansion conditions of three tryptophan derivative dipeptide analogues: N-acetyl trytophan ethyl ester (NATE), N-acetyl trytophan amide (NATA) and N-acetyl trytophan methyl amide (NATMA). To establish the geometry of the different conformers found, quantum chemical calculations were performed on these three molecules. Due to the high number of structures in conformational space, various molecular mechanics force fields were tested as a screening method to identify low lying structures for ab initio calculations. The accuracy of several Force Fields (OPLS/AA, MM3, and MMFF) describing these species was checked and compared with Hartree Fock and Density Functional Theory calculations. For the three molecules investigated, two families of geometries (corresponding to C7 and C5 structures) have been found to be stable at supersonic expansion conditions. Their relative stabilities are governed by the interactions between the indole-containing side chain and the peptide backbone. The sensitivity and conformational specificity of the FDIRS spectra to these interactions makes it a very powerful tool in assigning of the experimental conformers to the calculated geometries.