

Computational Studies of Phosphorylated Amino Acids and Corresponding Amides

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Phosphorylation is a common post-translational modification in proteins and is involved in cell signaling. Phosphorylation involves the addition of a phosphate group to a protein and can occur at -OH, -NH, and -SH groups. The gas and solution phase acidities and gas phase heats of formation have been predicted at the G3(MP2) level of theory for ten phosphorylated amino acids (arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, lysine, serine, threonine, and tyrosine) and their corresponding amides providing the first reliable set of these values. Extensive conformational sampling was performed using density functional theory. Many low energy conformers exist in the neutrals and anions. The lowest energy conformations always maximize the hydrogen bonding. The most abundant phosphorylated amino acids are phosphoserine, -threonine, and -tyrosine. The gas phase acidities (GAs) of these three phosphorylated amino acids and their corresponding amides were determined by using proton transfer reactions in a Fourier transform ion cyclotron mass spectrometer by the Cassady group. Excellent agreement was found between the experimental GAs and the predicted GAs for these six molecules. In general, the phosphorylated amino acids are 13 to 27 and 1 to 7 kcal/mol more acidic than their corresponding non-phosphorylated amino acids and phosphorylated amino acid amides respectively. They are also significantly more acidic than the parent phosphoric acid and can become similar to the strong gas phase acid H_2SO_4 . The results will be used to develop anionic proteomic approaches. The pK_a values for the phosphorylated amino acids and their corresponding amides are within 3 pK units. The heats of formation of the neutral compounds were calculated from the atomization energies at the G3(MP2) level and isodesmic reactions and excellent agreement was found between the two methods. This work is sponsored by the U.S. National Science Foundation.