PROTONATION CONSTANTS OF SOME ALANYL DIPEPTIDES IN 1,4-DIOXANE–WATER AND DIMETHYL SULFOXIDE–WATER MIXTURES

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Dipeptides are an interesting class of compounds constructed from relatively simple building blocks, two amino acids through a peptide bond. They are components of tissues \(^1\) exhibiting a remarkable range of biological properties acting as antibiotics, hormones, food additives, poisons or pain-killers. Furthermore, dipeptides are very attractive for drug discovery and development due to their cost-effectiveness, possibility of an oral administration and simplicity to perform molecular structural \(^2\). Stoichiometric protonation constants are among the most useful physico-chemical parameters, describing the extent of ionization of functional groups as a function of pH. They are important in a wide range of research areas such as chemistry, biochemistry and pharmaceutical drug development. For example, small peptides have acidic and basic functionalities and the extent to which the drugs enter the bloodstream is controlled by their pK\(_a\) values \(^3\). Thus the determination of protonation constants of small peptides is necessary for complete understanding of the physiochemical behaviour of dipeptide.

In this study stochiometric protonation constants (log\(_{10}K_1\) and log\(_{10}K_2\)) of some aliphatic dipeptides (Ala–Tyr, Ala–Phe, Ala–Val, Ala–Leu, Ala–Thr, Ala–Met and Ala–Pro) were determined potentiometrically in 20, 40, and 60\% (v/v) 1,4-dioxane–water and dimethyl sulfoxide–water mixtures at 25.0 (±0.1) °C with an ionic strength of 0.10 mol.L\(^{-1}\) sodium chloride. The protonation constants were calculated with the computer program PKAS and selection of the best fit chemical models is based on the statistical parameters. The effects of solvent composition on these protonation constants were discussed to determine the factors which control these processes. It has been observed that, the correlation between log\(_{10}K_1\) and log\(_{10}K_2\) with the percentage of dimethyl sulfoxide in the dimethyl sulfoxide–water mixtures are not linear in the studied solvent mixtures. The protonation constants of various alanyl dipeptides determined in this study not only are used for quantitative purposes but also can be used for the evaluation of the solute-solvent effect and predication of how the zwitterionic to neutral form ratio changes with the concentration of organic component in water–organic solvent mixtures.

KEYWORDS: Protonation constants, Dipeptides, 1,4-Dioxane, Dimethyl sulfoxide, PKAS

REFERENCES: