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Computational Prediction of the pKas of Small Peptides through Conceptual DFT Descriptors

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Abstract

The experimental pKa of a group of simple amines have been plotted against several Conceptual DFT descriptors calculated by means of different density functionals, basis sets and solvation schemes. It was found that the best fits are those that relate the pKa of the amines with the global hardness η through the MN12SX density functional in connection with the Def2TZVP basis set and the SMD solvation model, using water as a solvent. The parameterized equation resulting from the linear regression analysis has then been used for the prediction of the pKa of small peptides of interest in the study of diabetes and Alzheimer disease. The accuracy of the results is relatively good, with a MAD of 0.36 units of pKa.

Keywords: Computational Chemistry, Peptides, Conceptual DFT

1. Introduction

Protein glycation is initiated by a nucleophilic addition (nonenzymatic glycation or Maillard reaction), reaction between a free amino group from a protein and a carbonyl group from a reducing sugar to form a freely reversible Schiff base. Glycated proteins can undergo further reactions, giving rise to some structures called advanced glycation endproducts (AGEs) [1]. The formation of

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