

Histidine protonation states are key in the LigI catalytic reaction mechanism

LINA ZHAO¹, Dibyendu Mondal², Weifeng Li³, Yuguang Mu⁴, and Philipp Kaldis¹

¹Lund University

²University of California San Francisco

³Shandong University

⁴Nanyang Technological University

March 12, 2021

Abstract

Lignin is one of the world's most abundant organic polymers, and 2-pyrone-4,6-dicarboxylate lactonase (LigI) catalyzes the hydrolysis of 2-pyrone-4,6-dicarboxylate (PDC) in the degradation of lignin. The pH has profound effects on enzyme catalysis and therefore we studied this in the context of LigI. We found that changes of the pH mostly affects surface residues, while the residues at the active site are more subject to changes of the surrounding microenvironment. In accordance with this, a high pH facilitates the deprotonation of the substrate. Detailed free energy calculations by the empirical valence bond (EVB) approach revealed that the overall hydrolysis reaction is more likely when the three active site histidines (His31, His33 and His180) are protonated at the ϵ site, however, protonation at the δ site may be favored during specific steps of reaction. Our studies have uncovered the determinant role of the protonation state of the active site residues His31, His33 and His180 in the hydrolysis of PDC.

Hosted file

ligI_V15.pdf available at <https://authorea.com/users/401213/articles/513382-histidine-protonation-states-are-key-in-the-ligi-catalytic-reaction-mechanism>