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COMPUTATIONAL INVESTIGATION OF HISTIDINE-ARGININE PAIRS IN ENZYME CATALYZED MORITA-BAYLIS-HILLMAN REACTIONS

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PURPOSE OF THE ABSTRACT

The Morita–Baylis–Hillman (MBH) reaction is a C-C coupling reaction in which simple starting materials are converted into functionalized products in a catalytic process. It has numerous applications, especially in the synthesis of pharmaceutically important compounds. Despite the great synthetic potential, the practical application of the MBH reaction is rather limited due to low catalytic efficiencies. Use of biocatalysts could offer a promising solution to these challenges. Recent studies in the use of enzymes in organic synthesis have led to the exploration of promiscuous biocatalytic routes to the MBH reaction. Joshi et al. reported that lysozyme C, myoglobin and a couple of proteins containing a suitably positioned histidine and arginine pair in proximity catalyzed the MBH reaction with notable efficiencies.[1] 14 rounds of directed evolution on a de novo designed MBH enzyme based on a histidine nucleophile has introduced an arginine motif in the active site, suggesting the importance of arginine as an oxyanion hole motif.[2] In this study, the importance of histidine and arginine pairs for the catalytic activity was explored using quantum mechanical theozyme models.[3] Generated catalytic atom maps based on these theozymes were screened in the protein database to identify natural proteins that can present the catalytic amino acids in the three-dimensional arrangement required for optimal catalysis of the MBH reaction.[4] In light of the obtained results, new proteins with potential promiscuous activity towards the MBH reaction were proposed for experimental testing.

FIGURES

KEYWORDS

Morita-Baylis-Hillman Reaction | Promiscuous Enzymes | Biocatalyst | Enzyme Design

BIBLIOGRAPHY