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Aromatic hydroxylation of Trans-cinnamic acid performed by the P450 Cinnamate-4-hydroxylase: A QMMM study

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PURPOSE OF THE ABSTRACT

Being part of the plant metabolic system, the Cinnamate 4-hydroxylase (C4H) enzyme belongs to the CYP73A family of the cytochrome P450 monooxygenase known for being a crucial biocatalyst. C4H is responsible for the hydroxylation of trans-cinnamic acid into p-coumaric acid (Scheme 1). This enzyme can have an impact on structure, development, and defense, which makes in-depth knowledge of the mechanism and interaction with the substrate during the catalytic reaction important.1 Playing different and impactful roles in plant's life, this enzyme must be properly studied in complex with their natural substrates. Trans-cinnamic acid was docked, into the active center of the C4H enzyme followed by comprehensive MD simulations and QM/MM calculations. However, unlike the hydroxylation of alkyl substrates in which the mechanism is initiated by the abstraction of the allylic hydrogen by the Iron-oxo complex, the case of aromatics is not so straightforward. Based on our QM/MM calculations, we propose to different conformations are achieved during the transition state of the aromatic hydroxylation. After a tetrahedral sigma complex formation2, the reaction proceeds through a protonated porphyrin intermediate or a direct rearrangement in comparison to the alternative epoxide and ketone pathways for aromatic hydroxylation.

FIGURES

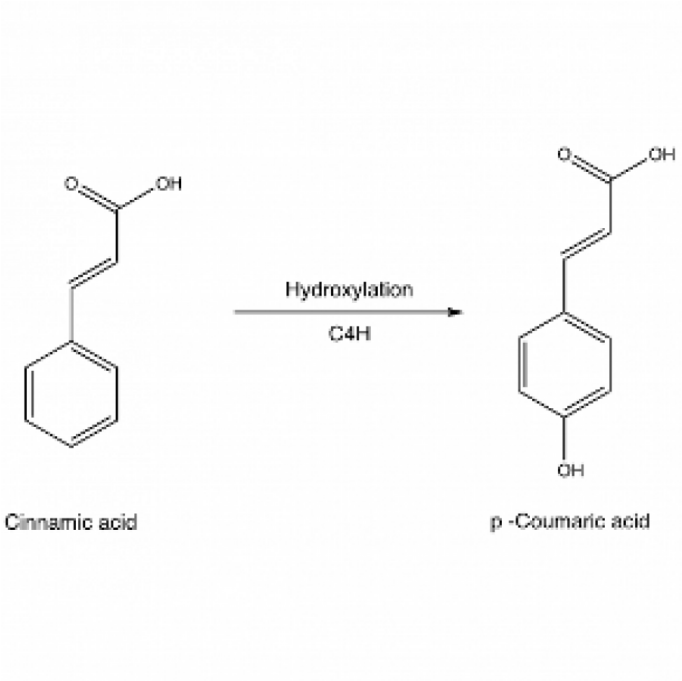

FIGURE 1

Scheme 1

FIGURE 2

KEYWORDS

Biocatalysts | Hydroxylation | Aromatic | Lignin

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