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The mechanistic role of active site residues in non-stereo haloacid dehalogenase E (DehE) (Article)

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Abstract

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Dehalogenase E (DehE) is a non-stereospecific enzyme produced by the soil bacterium, Rhizobium sp. RC1. Till now, the catalytic mechanism of DehE remains unclear although several literature concerning its structure and function are available. Since DehE is non-stereospecific, the enzyme was hypothesized to follow a 'direct attack mechanism' for the catalytic breakdown of a haloacid . For a molecular insight, the DehE modelled structure was docked in silico with the substrate 2-chloropropionic acid (2CP) in the active site . The ideal position of DehE residues that allowed a direct attack mechanism was then assessed via molecular dynamics (MD) simulation. It was revealed that the essential catalytic water was hydrogen bonded to the 'water-bearer', Asn114, at a relatively constant distance of ~2.0 Å after 50 ns. The same water molecule was also closely sited to the catalytic Asp189 at an average distance of ~2.0 Å, signifying the imperative role of the latter to initiate proton abstraction for water activation. This reaction was crucial to promote a direct attack on the α-carbon of 2CP to eject the halide ion. The water molecule was oriented favourably towards the α-carbon of 2CP at an angle of ~75°, mirrored by the formation of stable enzyme-substrate orientations throughout the simulation. The data therefore substantiated that the degradation of a haloacid by DehE followed a 'direct attack mechanism'. Hence, this study offers valuable information into future advancements in the engineering of haloacid dehalogenases with improved activity and selectivity, as well as functionality in solvents other than water. © 2019 Elsevier Inc.

SciVal Topic Prominence

Topic: Hydrolases | Enzymes | Haloalkane dehalogenases

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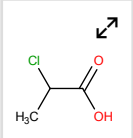
Chemistry database information

Substances



Author keywords

Catalytic mechanism | Dehalogenase E (DehE) | Haloacid | Molecular docking | Molecular dynamics (MD)

Rhizobium sp. RC1

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