Halohydrin dehalogenases (HHDHs) in the synthesis of chiral propargylic compounds

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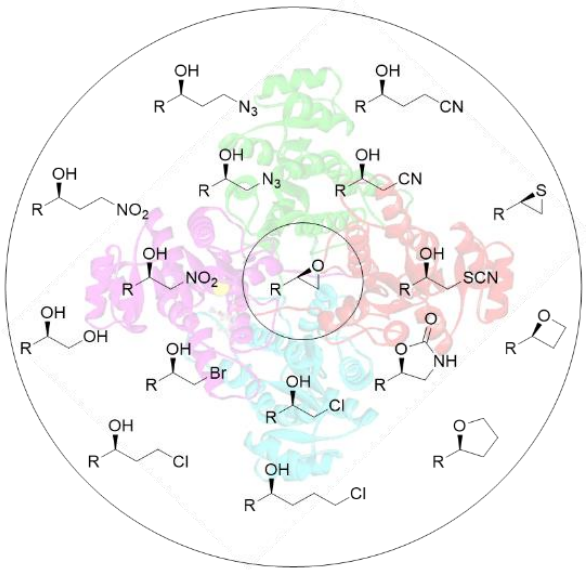
Asymmetric synthesis is an approach in organic chemistry for preparing chiral molecules that, alongside organocatalysis and metal catalysis, also employs biocatalysis to achieve high reaction selectivity through enzymes. Halohydrin dehalogenases (HHDHs) have attracted considerable attention because of their versatile biocatalytic properties, which enable a wide range of valuable synthetic transformations.[1] The natural function of HHDHs is the dehalogenation of vicinal haloalcohols (halohydrins) followed by formation of epoxides. Their chemoenzymatic potential extends further due to their ability to catalyze a wide range of bond-forming reactions, including carbon–carbon, carbon–halogen, carbon–nitrogen, carbon–oxygen, and carbon–sulfur bond formation via epoxide ring opening with various negatively charged, non-natural nucleophiles.[2] Despite limitations such as poor solubility, low substrate concentrations, and various forms of enzyme inhibition, HHDHs can be applied in a range of chemoenzymatic syntheses.

Propargylic and homopropargylic epoxides and alcohols can undergo various inter- and intramolecular reactions due to the presence of a triple bond. This versatility makes propargylic compounds desirable intermediates in organic synthesis, including in the preparation of biologically active molecules, natural products, and pharmaceuticals. Despite their importance, the stereoselective preparation of propargylic and homopropargylic epoxides and alcohols remains a challenge in organic synthesis. Using HHDH-catalyzed enzymatic resolution, we aim to develop a new, environmentally friendly, and accessible method for the efficient preparation of these valuable chiral building blocks.[3]



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