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Substrate scope and selectivity of hydroxysteroid dehydrogenases in the biocatalyzed reduction of 1,2-diketones

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PURPOSE OF THE ABSTRACT

The biocatalytic reduction of 1,2-diketones to give chiral α-hydroxy ketones and/or vicinal diols has been previously studied using different alcohol dehydrogenases (ADHs) from various sources [1].

In our recent works, we have investigated the substrate promiscuity of a specific subfamily of ADHs, i.e., hydroxysteroid dehydrogenases (HSDHs), NAD(P)H-dependent oxidoreductases acting on their natural substrates, such as neutral steroids, bile acids and other steroid derivatives, with exquisite stereo- and regioselectivity [2].

These studies showed that selected HSDHs from our in-house collection, including novel biocatalysts from extreme environments identified by (meta)genome mining, can accept a wide range of different substrates, for example α-keto esters, tetralones and the racemic synthon Wieland-Miescher ketone [3].

In this work, we have extended our investigation of HSDHs promiscuity to a set of representative 1,2-diketones, i.e., the symmetric aliphatic/aromatic diketones 1 and 2 and the asymmetric synthon 1-phenyl-1,2-propanedione 7 (Scheme 1). The reactions were set up in the presence of a B. megaterium glucose dehydrogenase (BmGDH)-glucose system for NAD(P)H cofactor regeneration and analyzed at scheduled times to assess both substrate conversion and selectivity.

Additionally, docking studies were carried out to get a deeper insight in the stereochemistry of 1,2-diketones reduction catalyzed by selected HSDHs.

FIGURES

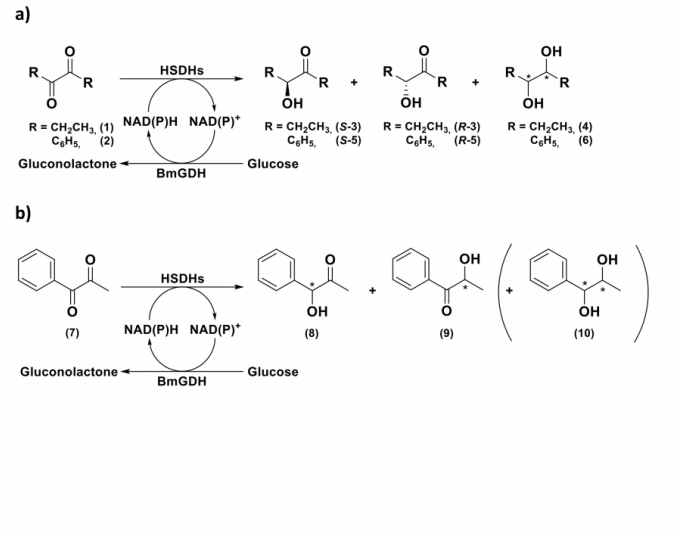

FIGURE 1

Scheme 1

HSDHs-catalyzed reduction of either symmetric (a) or asymmetric (b) 1,2-ketones.

FIGURE 2

KEYWORDS

hydroxysteroid dehydrogenases | selectivity | substrate promiscuity | 1,2-diketone reduction

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