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Discovery, functional characterization and synthetic applications of a promiscuous ketoreductase from an Icelandic hotspring metagenome

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PURPOSE OF THE ABSTRACT

In the search of novel thermostable hydroxysteroid dehydrogenases (HSDHs), enzymes able to regio- and stereoselectively oxidize/reduce steroidal compounds,[1] by (meta)genome mining, we recently discovered in an Icelandic hot spring metagenome a novel Short-chain Dehydrogenase/Reductase (SDR), named Is2-SDR. Surprisingly, despite the high sequence similarity shared with HSDHs, this enzyme showed no activity in the oxidation of steroid substrates, e.g., cholic acid. On the other hand, remarkably, Is2-SDR was able to reduce with high regio- and stereoselectively a diversified panel of carbonylic substrates, including bulky ketones, α- and β-ketoesters, and α-diketones of pharmaceutical relevance, proving to be a very active and versatile ketoreductase.[2-4]

Moreover, Is2-SDR showed both a high thermophilicity (Topt = 70 °C) and thermostability (TM = 75 °C), these data being consistent with the environmental conditions of collection of the starting metagenomic DNA (hot spring, 85–90 °C). A broad tolerance to both water-miscible and water-immiscible organic solvents was demonstrated as well, thus, confirming the potential of this new biocatalyst for its synthetic application.[5]

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FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

enzyme discovery | biocatalysis | metagenomics | ketoreductases

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