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Enzyme catalysed enantiospecific hydrolysis of silyl ether bonds

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PURPOSE OF THE ABSTRACT
Reversible formation of silyl ethers is widely used in organic synthesis to protect hydroxyl functions from unwanted reactions.[1] Extension of the application of silyl ethers from mere protecting groups to the simultaneous kinetic resolution of racemic mixtures of alcohols has been an object of intensive research for many years.[2] Despite considerable advances with various chemo catalysts, however, stereospecificity is still not satisfactory. A solution might provide the use of enzyme catalysts, which due to their special active sites often enable high stereospecificity in addition of being a greener alternative to chemical catalysts.

The ability of enzymes to mediate conversion of silyl ethers has been reported for quite some time[3], but mostly without (enantio-)specificity. We recently showed that literature-described lipase-mediated conversion of silyl ethers is unspecific and independent of its catalytic triad. Therefore, we were looking for enzymes specifically catalysing silyl ether conversion.

Here we present two newly identified enzymes cleaving the silyl ether bond of TMS-protected 1-phenylethanol with opposite enantiospecificity.

After purification of these proteins from their natural source, identifying them by in-gel digest and LC-MS/MS and heterologous expression in E.coli, we aimed to analyse their catalytic mechanism by introducing site-specific mutations. Thereby, we could identify a few amino acids leading to partly or complete loss of function. Comparison of both enzymes might further allow us to understand the origin of their enantiospecificity.

Although their biological function remains unknown, homologous proteins seem to be widely distributed in nature, and by that give us a whole repertoire of possible enzymatic catalysts for silyl ether conversion. Moreover, they allow us to gain further understanding of the needs of enzymatic catalysts specifically acting on silyl ether bonds.

FIGURES

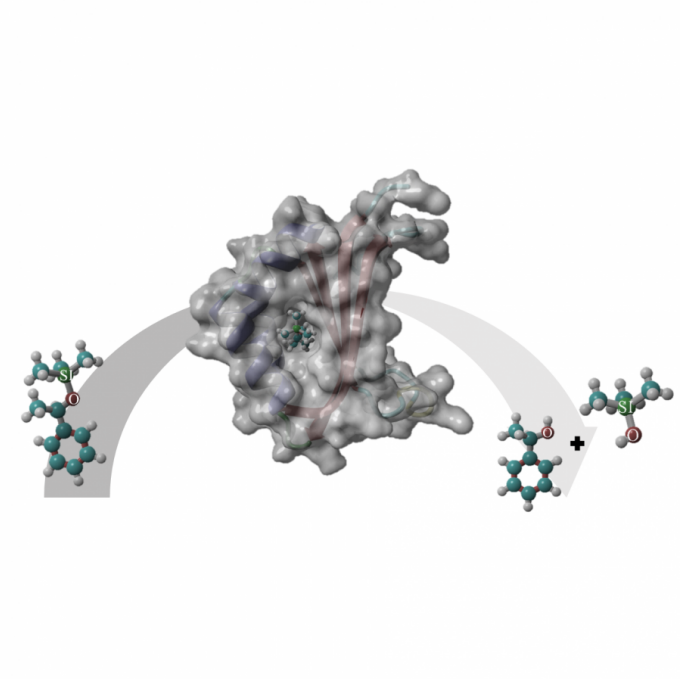

FIGURE 1

Enzymatic catalysed hydrolysis of trimethylsilyl-protected 1-phenylethanol.

FIGURE 2

KEYWORDS

silyl ether | protection group cleavage | enzyme discovery | enantiospecific catalysis

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