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Novel artificial metalloenzymes for olefin metathesis based on modified Grubbs-Hoveyda complexes

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PURPOSE OF THE ABSTRACT

Artificial metalloenzymes represent an attractive approach for the design of novel biocatalysts by combining homogeneous catalysis and enzyme catalysis.[1,2] A successful example for artificial metalloenzymes are ruthenium-based Grubbs-Hoveyda complexes incorporated into protein scaffolds which catalyse olefin metathesis, a powerful C-C bond formation reaction with numerous applications in organic chemistry which no natural enzyme is reported to catalyse. In previous studies, we reported the covalent conjugation of Grubbs-Hoveyda type complexes with maleimide functionalised NHC backbone to the β-barrel protein nitrobindin from Arabidopsis thaliana via thiol-ene reaction with a free cysteine residue. The engineered cavity of the protein provides a defined hydrophobic second coordination sphere around the central ruthenium atom, which improves the turnover number of the catalyst compared to the free metal complex.[3,4] This approach also enables cascade reactions with an artificial hydrogenase[5] and a fatty acid decarboxylase[6] which do not proceed with the free metal complex due to inactivation issues.

Artificial metalloenzymes often suffer from comparably low activities and total turnover numbers in comparison to natural enzymes. Consequently, there is a high interest in strategoes for their optimisation. On one hand engineering of these artificial metalloenzymes by directed evolution of the protein scaffold gained increased attention.[7] On the other hand, a deep understanding about the behaviour of the metal catalyst in aqueous solutions, which is often different compared to dry organic solvents, is crucial for the effective design of these de novo biocatalysts as well.

In this work, we present novel artificial metalloenzymes for olefin metathesis based on Grubbs Hoveyda complexes with substituted halide ligands cojugated to nitrobindin variants which we characterised by ESI-MS, CD-spectroscopy and UV-vis spectroscopy. We studied the effect of common parameters in aqueous biotransformations such as buffer, pH-value, salt additives and organic co-solvents on the catalyst activity and stability. In order to elucidate the effect of the substituted halide ligands in interaction with the protein scaffold, we compared the catalytic performance to free catalysts with the same substitution pattern.

FIGURES

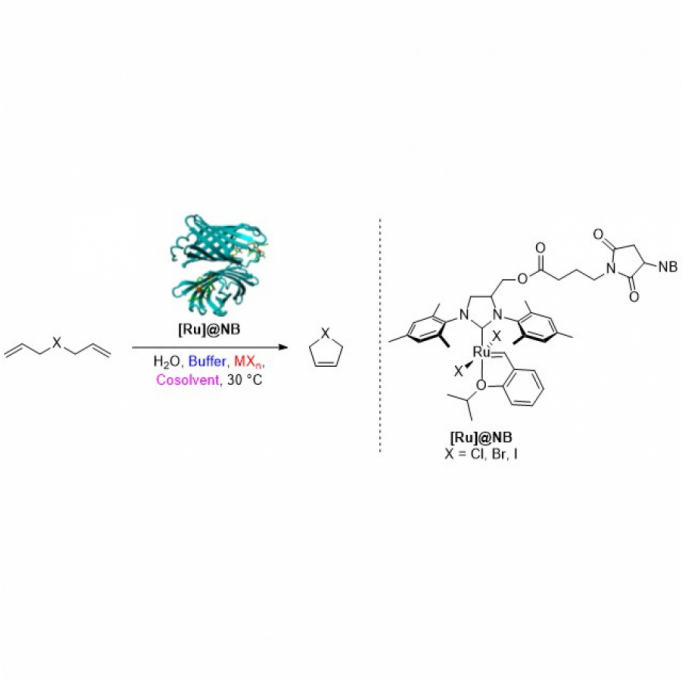

FIGURE 1

FIGURE 2

Figure 1

Ring-closing metathesis with artificial metalloenzymes based on halide-substituted Grubbs-Hoveyda catalysts.

KEYWORDS

artificial metalloenzymes | olefin metathesis | β-barrel protein

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