Abstract 9

New Artificial Imine Reductases Based on an Iridium/Vancomycin System for the Asymmetric Reduction of Cyclic Imines

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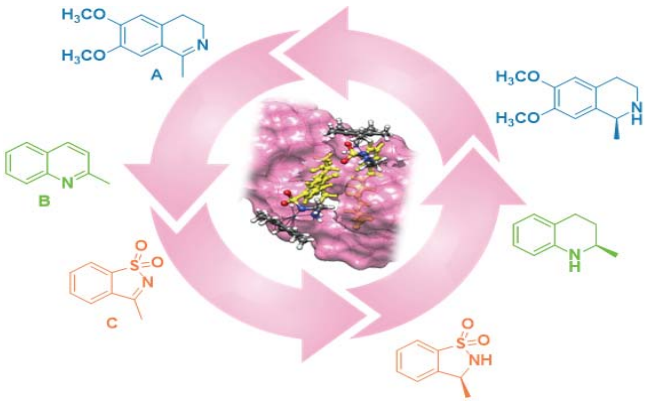
Artificial metalloenzymes, deriving from transition metal catalysts embedding within a biological environment, have recently risen up as a promising synthetic tool able to combine the reactivity of metal-based catalysis with the specificity of biocatalysis.[1] Dalbapeptides, such as vancomycin, teicoplanin and ristocetin are variously substituted heptapeptides whose antibiotic activity relies on their binding to the D-Ala-D-Ala dimer of peptidoglycan precursors thus leading to an irreversible inhibition of cell wall biosynthesis. This interaction is marked by such a low dissociation constant (K_D =~10^{-17}M) that it makes vancomycin-based systems an innovative alternative to the classical biotin/(strept)avidin technology.[2,3]

In this context, a class of aminoethylbenzensulfonamide ligands functionalized with the D-Ala-D-Ala dimer were employed for the synthesis of hybrid catalysts in association with an iridium centre. In the presence of vancomycin, a new class of artificial reductases was obtained and applied to the Asymmetric Transfer Hydrogenation (ATH) of model imine substrates in different aqueous media. An encouraging 48% (*S*) *e.e.* was obtained in the asymmetric reduction of the salsolidine precursor in CH_3COONa 0.1 M buffer at pH 5 whereas in the case of quinolines, the *meta*-artificial metalloenzyme afforded the product in a significant 70% (*S*) *e.e.* when applied to quinaldine. Moreover, an unprecedented 35% (*R*) *e.e.* in the enantioselective reduction of chiral sultam precursor 3-methylbenzo[d]isothiazole-1,1-dioxide was realized under green reaction conditions.[4]



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