Artificial transfer hydrogenases based on the biotin-(strept)avidin technology : fine tuning the selectivity by saturation mutagenesis of the host protein

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Incorporation of biotinylated racemic three-legged d6-piano stool complexes in streptavidin yields enantioselective transfer hydrogenation artificial metalloenzymes for the reduction of ketones. Having identified the most promising organometallic catalyst precursors in the presence of wild-type streptavidin, fine-tuning of the selectivity is achieved by saturation mutagenesis at position S112. This choice for the genetic optimization site is suggested by docking studies which reveal that this position lies closest to the biotinylated metal upon incorporation into streptavidin. For aromatic ketones, the reaction proceeds smoothly to afford the corresponding enantioenriched alcohols in up to 97% ee (R) or 70% (S). On the basis of these results, we suggest that the enantioselection is mostly dictated by CH/π interactions between the substrate and the η6-bound arene. However, these enantiodiscriminating interactions can be outweighed in the presence of cationic residues at position S112 to afford the opposite enantiomers of the product.
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