BIOTRANSFORMATIONS EMPLOYING NITRILE HYDROLYZING ENZYMES TOWARDS THE ENANTIOSELECTIVE SYNTHESIS OF β-AMINO ACIDS

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Nitrile hydrolysing enzymes continue to be of great interest particularly for their pharmaceutical applications[1,2]. This work set out to utilise novel bacterial isolates containing nitrile-metabolising enzyme systems in the synthesis of a series of chiral β-amino acids with key goals to achieve high enantioselectivity and reaction efficiency.

Initial work focussed on further assessing the functional group tolerance and mechanistic action of bacterial isolate SET-1 which had been previously studied with β-hydroxynitriles by Coady et al[3,4]. Ten model β-aminonitriles, structurally related to the β-hydroxynitriles previously studied were synthesised and evaluated. In biocatalytic studies on unprotected and *N*-protected aliphatic β-amino nitriles, bacterial isolate SET-1 was disappointingly poor. The acid yields and ee were extremely low, with the highest being 0.8% and 29% respectively at pH 7. Both steadily decreased as pH increased. Studies on the *N*-protected variants of 3-aminobutyronitrile gave more promising results, particularly with the *N*-Benzyl group which produced acid in 6% yield and 75% ee, and the *N*-Tosyl group which gave the overall best result of acid product 10% yield and >99% ee.

The final stage of the project has involved working with a purified enzyme exhibiting nitrilase activity. This has been screened extensively with the unprotected nitrile, 3-aminobutyronitrile. A maximum enantioselectivity of 30% was observed which is comparable to isolate SET-1 but marginally better yields were observed. The protected variants are next to be screened with the purified enzyme which should hopefully yield better results.

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