

P007 Nitrilase Catalysed Desymmetrisation of 3-Hydroxyglutaronitrile:
Preparation of a Statin Side Chain Intermediate
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Atorvastatin (Lipitor) is a HMG-CoA reductase inhibitor that is used for the treatment of hypocholesterolemia and atherosclerosis. Launched in 1997, it is now the world's largest grossing drug (2004 sales of \$12 bn). One of the most challenging parts of the synthesis of this molecule is the development of a route to the side chain. Ethyl (*R*)-4-cyano-3-hydroxybutyrate, a useful intermediate in the synthesis of the side chain, can be accessed via a nitrilase-catalysed desymmetrisation of the *meso*-dinitrile species 3-hydroxyglutaronitrile in a volume efficient, high yielding biotransformation. This poster describes a synthesis of ethyl (*R*)-4-cyano-3-hydroxybutyrate utilizing this biotransformation. All steps in the synthesis are readily scaleable, including preparation of the biocatalyst, which is obtained in very high yield of soluble, active protein after expression in a strain of *Pseudomonas fluorescens*.