Chemistry Central Journal

Poster presentation

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Molecular modeling studies of lipase-catalyzed β-lactam polymerization

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from 4th German Conference on Chemoinformatics
Goslar, Germany. 9–11 November 2008

Published: 5 June 2009

Chemistry Central Journal 2009, **3**(Suppl 1):P57 doi:10.1186/1752-153X-3-S1-P57

This abstract is available from: http://www.journal.chemistrycentral.com/content/3/S1/P57

Enzymatic polymerization has emerged over the last 5 years as a field of considerable interest and commercial promise. The reaction proceeds with high regio-, enantio-, and chemoselectivity under relatively mild conditions. Enzymes have been used so far to synthesize polyesters, polysaccharides, polycarbonates, polyphenols, polyanilines, vinyl polymers, and poly-amino acids [1]. Particularly, lipase B of *Candida antarctica* immobilized on polyacrylic resin (Novozyme 435) has proven to be a very versatile catalyst and has successfully been used for the synthesis of polyesters from various substrates [2][3][4]. Little, however, has been reported on the enzyme catalyzed synthesis of polyamides [5].

While it has been shown that nylons can chemically be produced from the corresponding amino acids or by anionic ring-opening polymerization of 5–13 membered unsubstituted lactams, poly-β-alanine has not yet been obtained by either polymerization of β-alanine or β-lactam (2-azetidinone). Using lipase B of *Candida antarctica* we have recently been successful in the production of unbranched poly-βalanine starting from unsubstituted β-lactam [6].

Here we report preliminary molecular modeling studies of the lipase catalyzed ringopening polymerization of β-lactam towards an understanding of the underlying enzymatic mechanism. We can show that amide formation initially follows the well-known enzymatic acylation of Ser105 by β-lactam using Asp187 and His224 of the catalytic centre and Thr40 and Gly106 as oxy-anion hole. The elongation of the chain, however, utilizes different parts of the active site. The mechanism is only applicable for β-lactam and can not be utilized by β-alanine and suggests a reasoning for the experimental finding that β-alanine can not be polymerized enzymatically but rather inhibits the polymerization in a copolymerization experiment with β-lactam and β-alanine.

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