STUDIES ON LIPASE CATALYZED ESTERIFICATION/TRANS-ESTERIFICATION REACTIONS FOR RESOLUTION OF RACEMIC ACIDS AND ALCOHOLS IN MICROAQUEOUS MEDIUM

by

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CERTIFICATE

This is to certify that the thesis entitled ***"Studies on lipase catalyzed esterification / trans-esterification reactions for resolution of racemic acids and alcohols in microaqueous medium"*** being submitted by ***Jaspreet Pannu*** to the Indian Institute of Technology Delhi, for the award of degree of Doctor of Philosophy, has been prepared under my supervision and guidance in conformity with the rules and regulations of Indian Institute of Technology Delhi. The research report and the results presented in this thesis have not been submitted to any other University or Institute for the award of any degree or diploma.

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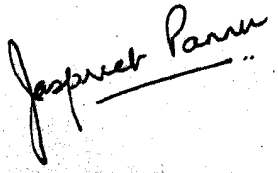

(Jaspreet Pannu)

Abstract

Lipase catalyzed synthetic reactions like esterification/trans-esterification in microaqueous medium are increasingly being used for resolution of racemic molecules which are used in synthesis of optically active drugs and agrochemicals. In our study, we have selected three racemic substrates (DL-Menthol, RS-Ibuprofen and DL-Lactic acid) to study the role of physicochemical properties of the bulk medium on enzyme activity and selectivity.

Lipases from ***Candida cylindracea*** was used to catalyze enantioselective trans-esterification of DL- Menthol and esterification of RS - Ibuprofen with vinyl acetate and 1-propanol respectively. Lipase from ***Pseudomonas*** spp. was used to catalyze the esterification of DL - Lactic acid with n- butanol. L - Menthol, S - Ibuprofen and L - Lactic acid were the preferred isomers. In order to permit enzyme recovery and reuse, immobilization on hydrophobic macroporous supports like Accurel EP-100 was carried out. Hydrophobic solvents at low water activities (a_W of 0.33) were found to work best as bulk medium for carrying out the above reactions (both in terms on initial reaction rate and enantioselectivity). Enantioselectivity was found to be high for all the three reactions in highly hydrophobic solvents, This was confirmed by determining the energies of activation associated with these reactions in different solvents. Based on our observations, a rational explanation for high enzyme selectivity for the preferred isomer in hydrophobic solvents has been provided.

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Different reactor configurations (batch, continuous stirred tank and packed bed) with the provision for continuous control of water activity were used to carry out the selected reactions. Their performance was tested in terms of productivities obtained in each case. The PBR was found to display higher productivities than the other two. The enantiomeric preference of the enzyme was found to be maintained in all the reactor types.

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