Summary

The focus of this thesis is to study the enzymatic kinetic resolution of alcohol and diol which have different shape. The study is focused on the development of efficient condition for kinetic resolution of roof shape alcohol, and diol, along with enzymatic desymmetrisation of roof shape *meso* diol is also studied. The resolved molecules are converted into chiral amine, diamines and amides. The synthesised amine diamines and amide are screened as chiral solvating agents in NMR. We also present our efforts to scan roof shape alcohol as possible chiral auxiliary.

The work is arranged in four chapters, with an introduction to biocatalyst in Chapter **1**.

Chapter 2 deals with the application of lipase for the preparation of useful and unusual chiral molecules. Enzymatic resolution is main focus of chapter 1, which is further divided into two sections. Chapter 2 begins with the discussion on molecules with different shape and size and particular property due to their structure. We are interested in resolution of molecules with unusual shape and size of alcohol and diol. The basic introduction for the synthesis of roof shape molecules will be discussed. We prepared three different types of roof shape molecules using Diels-Alder reaction with anthracene with different dienophiles. The roof shape alcohol and *trans*-diol are subjected for lipase mediated kinetic resolution. Absolute configuration of roof shape alcohol was confirmed by single crystal X-ray analysis. The roof shape alcohol and diol are converted into amine and diamines by simple chemical transformations. Along with enzymatic resolution, enzymatic desymmetrisation of *meso* diol is also studied. The product obtained after desymmetrisation shows *P*-helical motif due to the extended intermolecular hydrogen bonding. The *cis*-isomers undergo loss of its optical purity due to the internal acyl transfer process. To prevent isomerization of *cis* isomer a protocol of *in situ* conversion to stable isomer using Mitsunobu reaction was applied.

In section II enzymatic resolution of fluorinated alcohol is also studied. One of the limitations of kinetic resolution is maximum 50 % yield.

To overcome this difficulty a strategy of combination of enzymatic resolution followed by Mitsunobu reaction has been applied. With the aid of Mitsunobu protocol greater than 50 % yields are achieved. The resolved fluorinated alcohol is further converted into chiral amides.

Chapter 3 focuses on the chiral discrimination and the measurement of enantiomeric excess. The NMR approach to discriminate enantiomers using chiral auxiliaries such as, solvating agents, derivatizing agents, lanthanide shift reagents, the choice of such auxiliaries and the limitations are discussed in detail. The main focus is utilization of the synthesized amine, diamine and amide for possible application as chiral solvating agents for various functional groups. The chapter is accordingly divided into four sections. In the first section, application of various roof shape amine and diamine as chiral solvating agents is discussed for α functionalized acids. The present protocol of roof shape amines as CSA is also tested for hetro nuclei NMR in section II. In section-III roof shape anchored crown ether as possible CSA for ammonium cation are tested. In section IV hydrogen bond interactions are probed for different functionality such as sulphoxide, amide, keto alcohol and acids to test discrimination in ^{1}H NMR. The study revealed that introduction of electron withdrawing group enhances chiral discrimination property. The CSA has been scanned for few chiral drugs and drug intermediates with good separations. Few examples of the separation of signals in ^{19}F NMR are also studied.

Chapter 4 is about application of roof shape alcohol as chiral auxiliary for preparation of halo acids. Esterification reaction of roof shape chiral alcohol and racemic α-halo acids in presence of DCC, DMAP furnished diastereomers of ester in non-racemic form.

The detailed discussion of each of these studies is contained in the appropriate chapters and only a brief discussion on the concepts of kinetic resolution and desymmetrisation is given in chapter 1 as introductory note.

The enzymatic work presented in this thesis has been performed with the use of steapsin lipase purchased from Sisco Research Laboratories, Mumbai and CAL-B as Novozyme-435, manufactured by Novozyme (Denmark). This enzyme immobilized on macro porous acrylic resin. Novozyme commercial manufacturing of Novozyme

435 (*Candida antarctica Lipase*-B [CAL-B]) is done by gene expression in an Aspergilius microorganism. As indicated by its name the yeast was isolated in *Antarctica* with the aim of finding enzyme. *Candidia rugasa* lipase (CRL) was obtained from Sigma-Aldrich. This steapsin and *CRL* lipase were purchased and used as such, while Novozyme-435 was a generous gift from Novozyme, Bangalore, India.