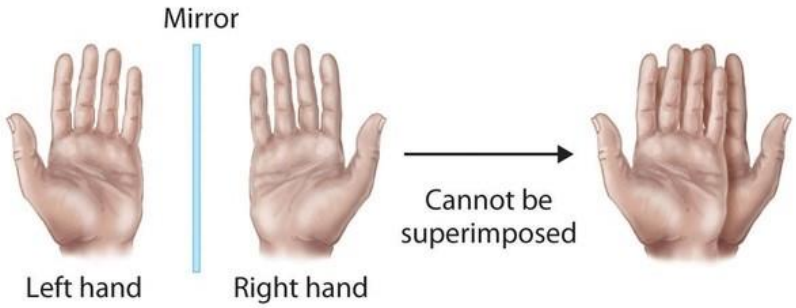
Introduction

1.1 Chirality

Chirality is a vital component in nature. Greek word cheir is the root of the phrase Lord Kelvin used to describe chirality in 1873. When racemic sodium ammonium tartrate tetrahydrate crystallised from an aqueous solution, Louis Pasteur found spontaneous resolution. This discovery was quickly acknowledged as being of utmost significance to the molecular chirality or chemistry. The optical rotation of the molecules, which have the same absolute value but the opposite sign, is the only difference between them.[1] The first method of resolving a racemate was also discovered with the spontaneous resolution of sodium ammonium tartrate. Chirality basically means '**mirror-image, non-superimposable molecules**'



As chiral molecules make up the majority of cells, chirality is a key term in biology. Amino acids and sugars are examples of small chiral compounds that serve as the building blocks for larger chiral molecules, like proteins and nucleic acids.[2] Chirality plays a crucial role in the synthesis and development of pharmaceuticals. The majority of newly discovered medicines are chiral. Interaction of drugs with biological targets such proteins, nucleic acids, and biological membranes can be used to identify their pharmacological activity. A chiral medication may have one of its two enantiomers that is a treatment for a certain ailment, whereas the other enantiomer of the molecule may not be inactive but can be harmful. As a result, chirality is important in the world of pharmaceuticals.[3]

1.1.1 Types of chirality

Chirality can be defined as “non-superimposibility of a molecule on its mirror image”. This clear definition of chirality provides a foundation that is required for chirality. Chiral

molecules may have a rotation axis, but they do not have an improper rotation axis, an inversion centre, or a plane of symmetry. [4] The existence of an asymmetric core or additional chiral components can satisfy these requirements. Based on the type of chiral entity that is present in the molecule, chiral optical active compounds can be categorised.

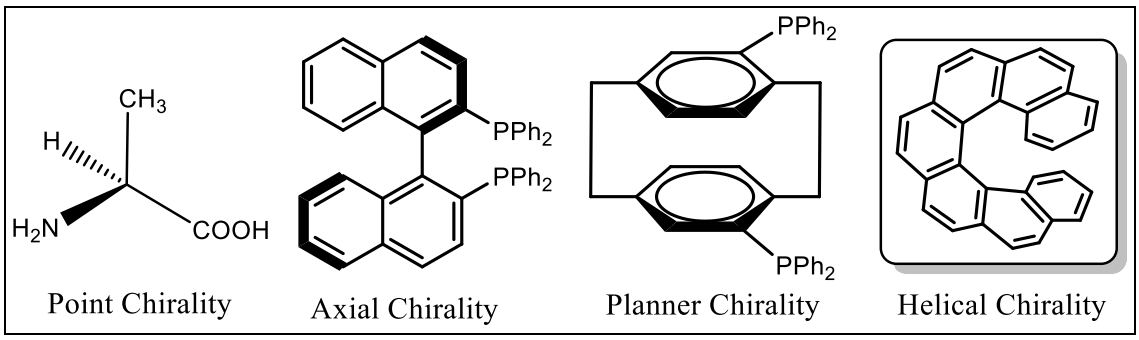


Figure 1.1: Types of Chirality

1.1.2 Point Chirality

Jacobus van't Hoff and Joseph Le Bel discovered in 1874 that a molecule with a single tetrahedral carbon atom and four distinct substituents may exist in two mirror images of one another which cannot be superimposed on each other.[5a,b]

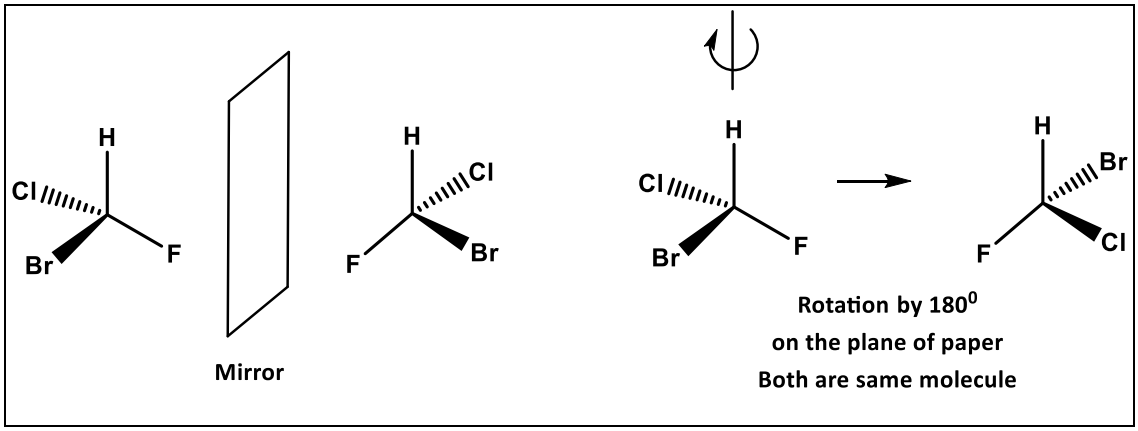


Figure 1.2: Explanation of Point Chirality

1.1.3 Axial Chirality

The non-planar pairing of four groups around a chiral axis produces axial chirality. [6] A chiral axis is a line in a chiral molecule that is retained in a non-planar arrangement around a set of four groups, producing a non-superimposable mirror image. Ortho substituted biphenyls and allenes both exhibit axial chirality.

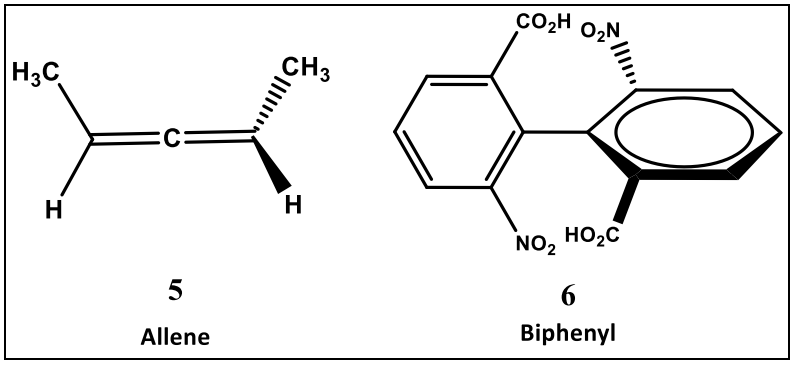


Figure 1.3: Examples of Axial Chirality

1.1.4 Planner Chirality

The first definition of planner chirality is given by Cahn, Ingold, and Prelog which states that "*a chiral plane is caused if a plane of symmetry is destroyed in such a way that chirality arises only by the difference of both sides of the plane*" [7]

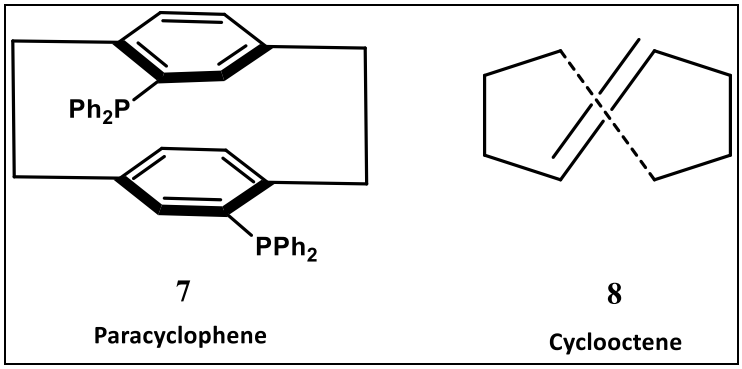


Figure 1.4: Examples of Planner Chirality

1.1.5 Helical Chirality

The most important feature of a helical molecule is its helicity, and it arises due to steric hindrance of the terminal rings which drives the molecule to go in opposite directions.[8] This renders them chiral even though they do not possess asymmetric carbon or other chiral centres.

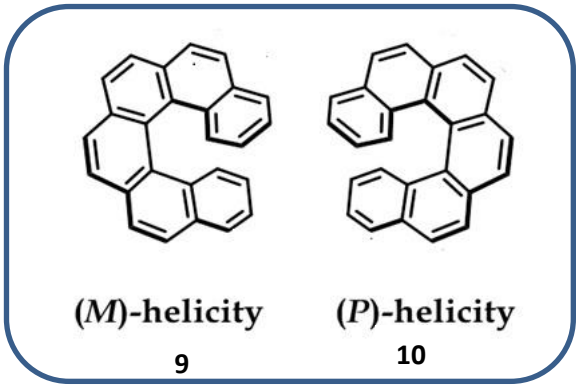
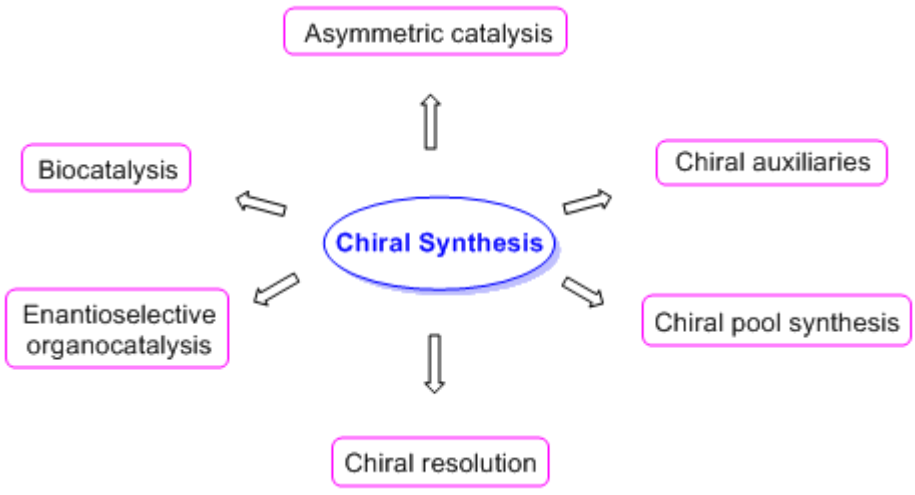


Figure 1.5: Schematic representation of Helicity

1.2 Synthesis of Chiral Compounds

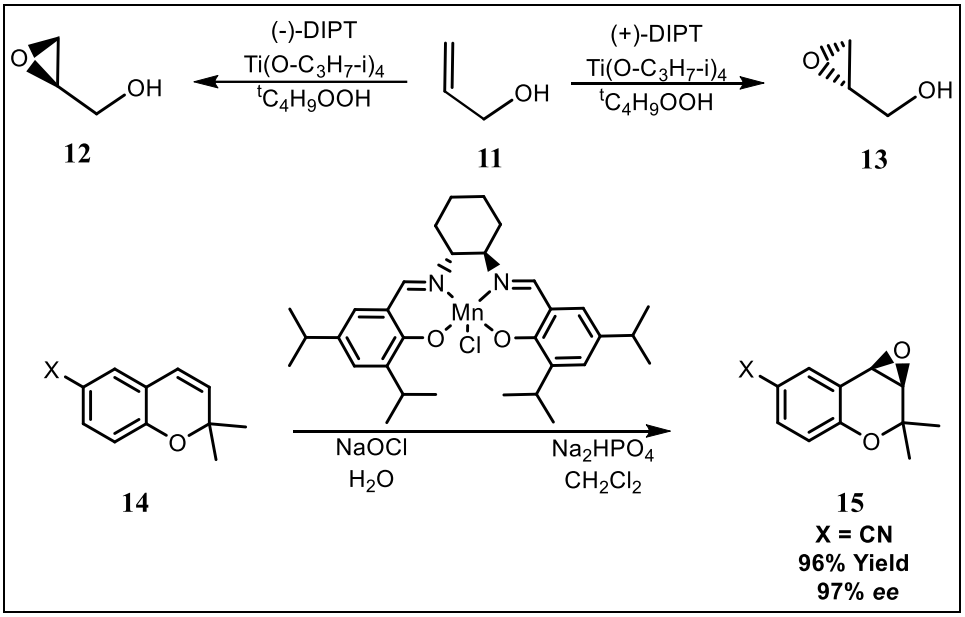
Enantioselective synthesis, also known as asymmetric synthesis or chiral synthesis, is the process of synthesize a molecule in such a way as to promote the development of a particular enantiomer or diastereomer.[9] It is a crucial procedure in contemporary chemistry and is especially significant in the area of medicinal chemistry since a molecule's various enantiomers or diastereomers can have different biological functions. For a wide range of possible uses, particularly in the pharmaceutical industry, the enantioselective synthesis of chiral compounds is essential.[10a,b]



1.2.1 Asymmetric Catalysis

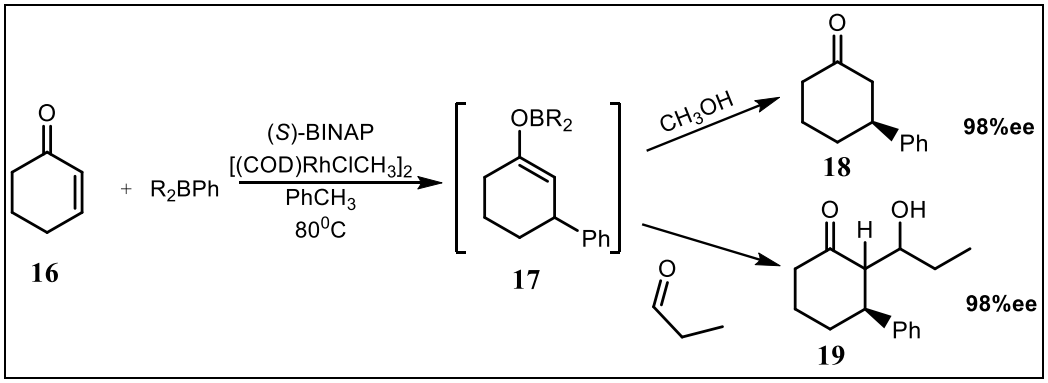
The pharmaceutical industry's growing need for optically pure chiral intermediates and the adoption of green and sustainable chemistry principles in the production of high value-added fine chemicals have spruced up the growth of asymmetric catalytic techniques.[11]

Several developments have contributed in the growth of defined transition metal complexes for asymmetric catalysis. The ability to synthesize and characterize well defined transition metal complexes improved intensely. Access to defined complexes set the stage for understanding the effect of structure for function, which resulted in the development of defined transition metal complexes, typically hybrids of organic molecules and transition metals, for chemical catalysis.[11a,b] an enantioselective chemical reaction to prepare 2,3-epoxyalcohols **12,13** from primary **11** allylic alcohols **(Scheme 1)**. The oxidizing agent is *tert*-butyl hydroperoxide. The method relies on a catalyst formed from titanium tetra(isopropoxide) and diethyl tartrate.[11c] Synthesis of the chiral epoxide **15** can be achieved using Jacobsen catalyst with high optical yield **(Scheme 1)**.[11d]



Scheme 1: Asymmetric epoxidation of allylic Alcohol

BINAP complexes of rhodium provide exceptional enantioselectivity in such modifications, again drawing on catalytic hydrogenation. Because the initially formed adduct is an enol boron species, it can be caught in a highly diastereoselective aldol process in addition to protonation, resulting in the formation of three stereogenic centres in a single asymmetric catalytic event.



Scheme 1a: Examples of Asymmetric Synthesis

1.2.2 Chiral Auxillary

A chiral auxiliary is a stereogenic group or unit that is temporarily incorporated into an organic compound in order to control the stereochemical outcome of the synthesis. Enantiomerically pure substances have frequently been synthesised using chiral auxiliaries. The majority of the readily available chiral auxiliaries are produced from substances that are found in nature, including terpenes, amino acids, and carbohydrates. However, some factors may weaken their efficient use, such as the difficulty in obtaining optically pure enantiomers on a large scale and structural limitations, making unnatural molecules is a more viable alternative. also, these naturally available molecules from chiral pool, are available in only one enantiomeric form, like amino acids are in L form, while sugars in D-form.

The choice of the suitable chiral auxiliary for each reaction can be determined by on some factors, and these must be taken into account in the development of new auxiliaries. The addition and removal steps of the auxiliary should be done easily or under mild conditions and must generate a high chemical yield and high enantioselectivity. [12]

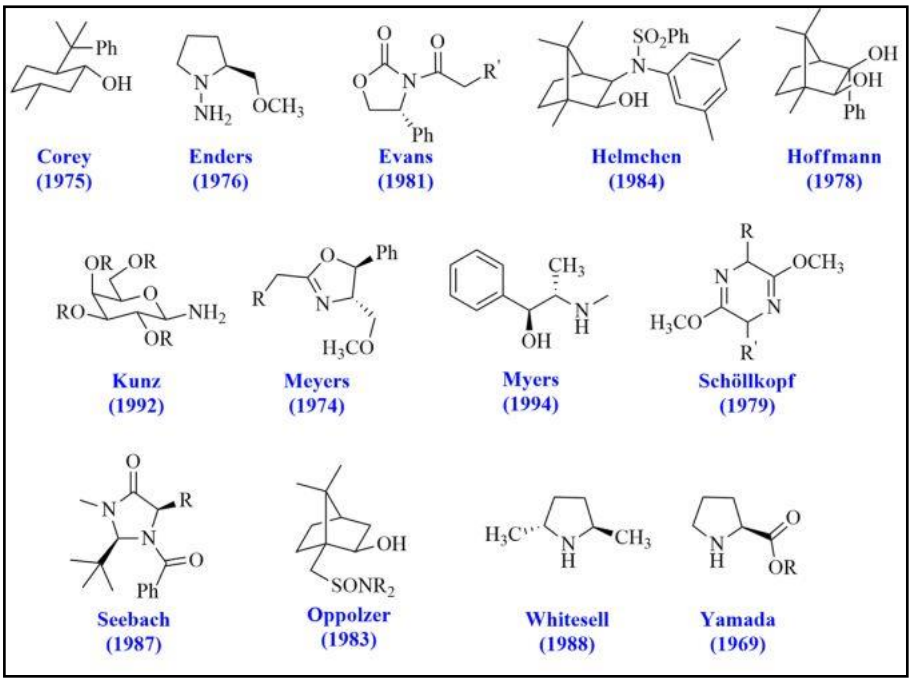
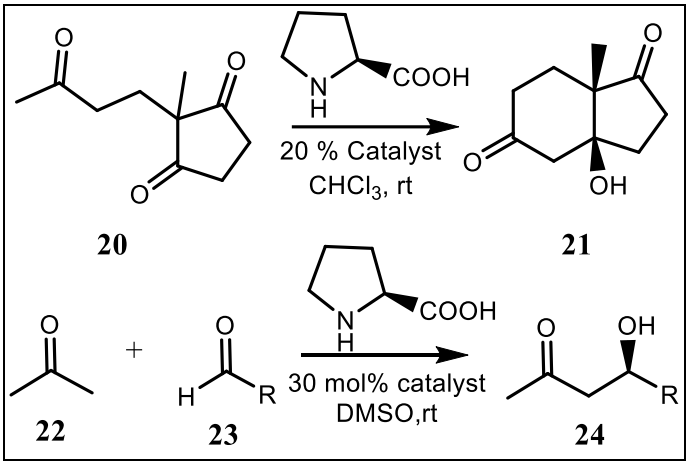


Figure 1.6; Some Wellknown Examples of Chiral Auxillaries

1.2.3 Enantioselective Organocatalysis

Enantioselective organocatalysis has become a potent synthetic paradigm that complements metal-catalyzed reactions and has sped up the creation of new processes for producing a variety of chiral compounds. The operational simplicity, ready availability of catalysts and low toxicity related with organocatalysis makes it an attractive method to synthesise complex structures.

Early in the 1970s, Hajos, Parrish, Wiechert, Eder and Sauer simultaneously reported a proline-catalyzed intramolecular aldol process (Figure 1.8), cyclization of the triketone **20** to product **21** in a high enantiomeric access and high chemical yield **(Scheme 1.1).** which raised the synthetic community's interest of the possibilities of organocatalysis.[13a,b] The suggested hydrogen connection between the carboxylic acid motif and the carbonyl electrophile is crucial to the success of this aldol reaction. List, Barbas and Lerner published a similar intermolecular process that secondary amine catalysis *via* enamines became *en vogue* in the synthetic community. The reaction of acetone **22** with substituted benzaldehyde **23** in presence of proline (30 mol %) in DMSO/acetone (4:1) at room temperature for 4 h furnished aldol product (*R*)-**24** in 68% yield and 76% ee [13] **(Scheme 1.1).**

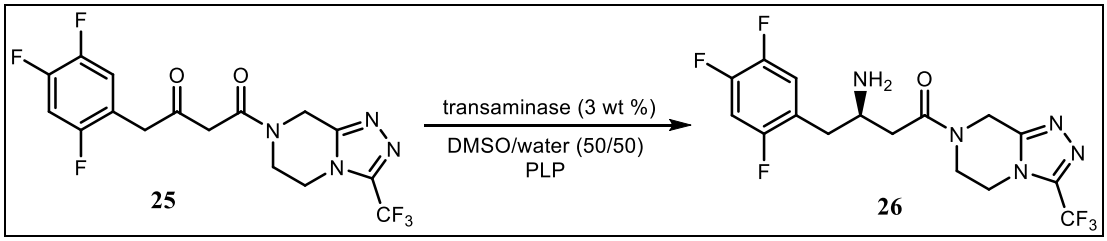


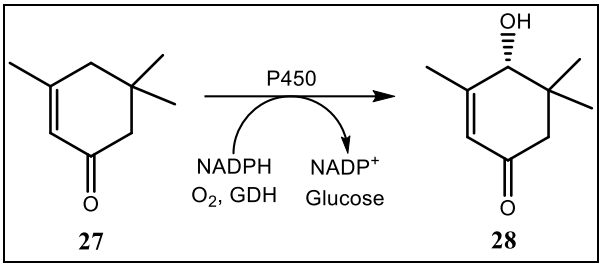
Scheme 1.1: Organocatalytic Reactions

1.2.4 Bio-Catalysis

Bio-catalysis has become a major aspect of modern organic synthesis, both in academia and across the chemical and pharmaceutical industries. Bio-catalysis has grown to be an important component of contemporary organic synthesis. Its success has been partly attributed to the rapid expansion of chemical reactions that are accessible, which has been made feasible by cutting-edge enzyme discovery methods combined with high-throughput laboratory evolution techniques for biocatalyst optimization.

Enzymes involved in the synthesis of particular metabolites, or natural products, are largely useful as promotor for bio-catalysis. Natural products tend to have diverse chemical structures, and studies on the biosynthesis of such natural products have unveiled a correspondingly diverse set of biosynthetic enzymes. Consequently, enzymes that synthesise natural products are a possible source of a variety of catalysts. The synthesis of the drug for treating diabetes Sitagliptin **26** by Merck from the prochiral precursor pro-Sitagliptin **25.** Hydroxylation of α-isophorone **27** can be done to (R)-4-hydroxy isophorone **28** by a P450-monooxygenase from Bacillus megaterium expressed in E. coli **(Scheme 1.2)** [14]

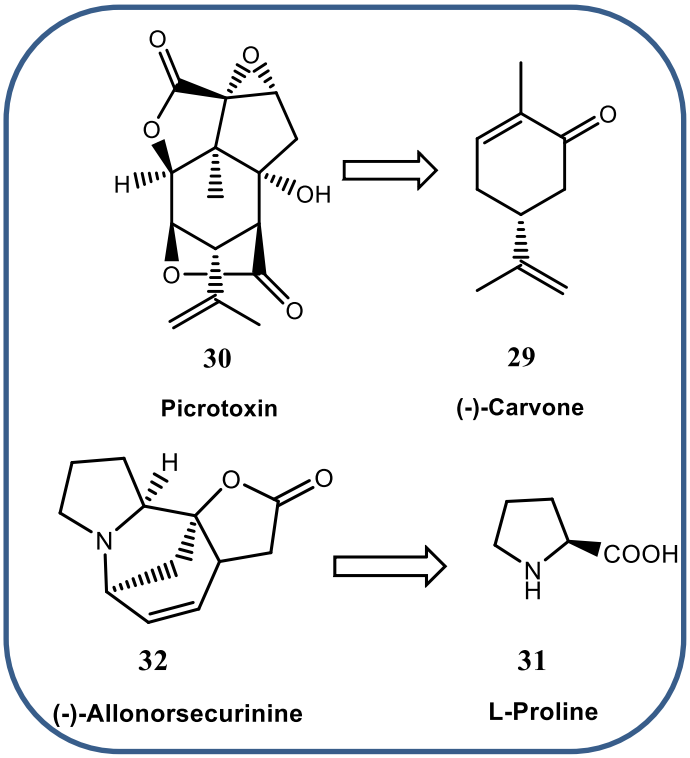




Scheme 1.2: Asymmetric synthesis of Sitagliptin **26** using a transaminase (ATA) and Hydroxylation of α-isophorone **27**

1.2.5 Chiral pool

The chiral pool, which is used in organic synthesis, is a "collection of numerous enantiopure building blocks provided by nature." A collection of enantiomerically pure molecules that can be found in nature is referred to as a chiral pool. Amino acids, chiral carboxylic acids, and monosaccharides are examples of common chiral starting materials found in nature. By using this methodology in organic synthesis, an enantiopure substance can be added to the molecule to provide the desired chiral centre. For instance, naturally occurring enantiopure amino acids can be transformed into antibacterials, cytotoxic substances and protease inhibitors.[15] Corey's 1979 synthesis of picrotoxinin **30** from **(-)** carvone **29** [15a] and preparation of (-)-allonorsecurinine **32** from L-Proline **31** [15b] are some of the examples of the important chiral pool synthesis of natural products.



Scheme 1.3: Synthesis of Picrotoxine and (-)-Allonorsecurinine

1.3 Chiral Resolution

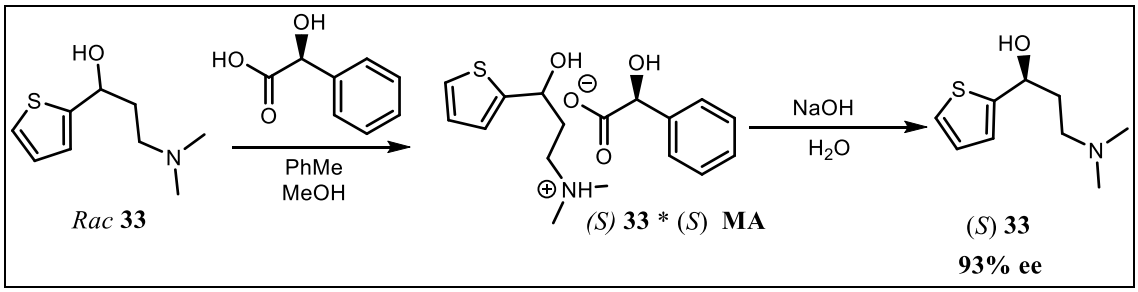
Enantiomeric resolution, also known as chiral resolution, is a stereochemical technique for separating racemic substances into their enantiomers. It is a crucial tool for creating optically active compounds.

Two enantiomers in a racemic mixture can be distinguished by the process of kinetic resolution. An enantioenriched sample of the less reactive enantiomer is produced when two enantiomers react chemically with a chiral catalyst or reagent at differing reaction rates.

kinetic resolution where 100% of a racemic reactant can be converted into an enantiopure product is called Dynamic kinetic resolution.

Due to its relative simplicity and scalability, chiral resolution by diastereomeric salt production or biocatalysis continues to be one of the most used technologies. In instance, 100% yield with 100% enantiomeric excess (pure enantiomer) can be reached when racemization loops or-even better-dynamic kinetic approaches-can be used for compounds with racemization-prone functionalities

Resolution by diastereomeric salt formation is commonly applied to amines and acids as they have reactive groups that can form salts with chiral resolving agents. Biocatalysts are frequently used to resolve alcohols. Biocatalysis is used for polar molecules such as alcohols, many amines, thiols, and sulphides.[16a] (±)-Alcohol **33** was combined with (S)-mandelic acid in PhMe-MeOH, (S)-**33** was allowed to form a diastereomeric salt with (S)-mandelic acid in a highly reproducible manner to give (S)- alcohol **33** in 41% yield and 93% ee .[16a]



Scheme 1.4: Eli Lilly's synthesis of (S)-3-(N,N-dimethylamino)-1-(2-thienyl)propan-1-ol **33**

1.4 Biocatalytic Transformation,

The term "bio-catalysis" refers to the utilisation of organic materials, such as enzymes from biological sources or complete cells, to accelerate chemical reactions. Numerous events, such as the generation of alcohols through fermentation and cheese through the breakdown of milk proteins, depend heavily on the catalysis of enzymes. The first enzyme was identified in 1833 and is a combination of amylases, a group of enzymes that catalyse the breakdown of starch into sugars like glucose and maltose. It is crucial for fermentation.

The phrase "bio catalytsis" refers to enzyme-mediated processes, biotransformations, and fermentations. Secondary alcohols that are enantiomerically pure can be used as active pharmaceutical intermediates and in the production of a variety of natural compounds (API). Much progress has been made in the fields of asymmetric synthesis and catalysis as a result of the great demand for these chiral molecules. By using a biological system, compounds (like sugar and starch) and specific adducts (like amino acids and fatty acids) are converted into more complex target products during fermentation. The word "biotransformation" refers to the process of turning specified reactants or substrates into desired target products while using entire or dormant cell systems. Enzyme catalysis is frequently employed when crude extracts, partially purified enzyme or immobilised enzyme on solid support are used to achieve the desire transformation.[17]

1.5 Enzymatic Resolution

The resolution of racemic starting materials has been an important technique for the synthesis of useful chiral chemicals since Pasteur first described the separation of the enantiomers of tartaric acid *via* the sodium ammonium and sodium potassium rac-tartrates in 1848. While numerous elegant approaches for the synthesis of enantioenriched building blocks have been developed as a result of advances in asymmetric catalysis, kinetic resolution continues to be a crucial technique that is frequently applied in both academia and industry.

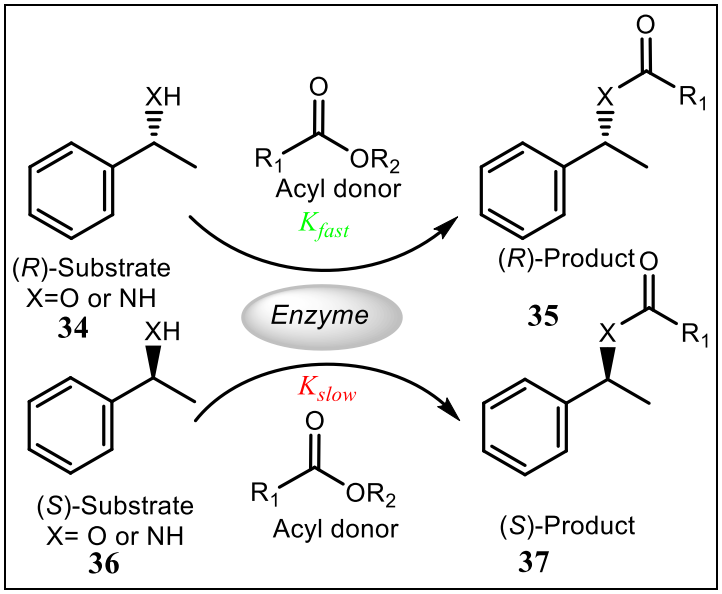
It is advantageous for their use in KR because enzymes in nature frequently evolve to catalyse reactions of particular substrates or specific substrate types. An enzyme's active site, whether in the wild-type or variations with certain mutations, can accomplish highly enantio-discriminating catalysis by creating an inherently chiral environment, leading to

efficient resolutions when faced with racemic substrates. The mirror-image link between the substrate enantiomers and the enzyme is incidental; they are completely different molecules. Though such enzymatic approaches provide access to more effective and elegant syntheses, bio-catalytic reactions are becoming recognised as a vital component of the main stream organic chemist's toolkit, possibly only still being used after traditional chemistry has failed.

When seminal reviews first came out in the early 2000s, hydrolases (like lipase CAL-B) or amidases (such penicillin acylase and Subtili-sin) were still the most commonly used biocatalysts for the kinetic resolution of chiral primary and secondary alcohols, amines, or carboxylic acids. By using asymmetric reduction of prochiral ketones, keto reductases (KREDs), a subgroup of alcohol dehydrogenases (ADHs), were used to produce chiral secondary alcohols. The long-established nitrile hydratase (NHase) technique to produce acrylamide from acrylonitrile was likely the most well-known large-scale industrial biocatalytic process. [18]

Due to its great activity and selectivity, enzymatic KR of racemic mixtures is the most popular method for obtaining enantiomerically pure alcohols and amines on an industrial scale. If a lipase or a serine protease is used as the enzymatic resolving agent, the process can be made either (R) - or (S) -selective for the KR of these molecules. The enzyme resolves the racemic substrate in the majority of the alcohol and amine KR protocols that have been published by selectively acylating one of the enantiomers. This enables the isolation of the enantiopure alcohol or amine using standard purification methods.

The acyl group transferred from the enzyme to the substrate originates from a so-called acyl donor, which is added to the reaction in an amount at least equimolar to favor the substrate. Since this trans-esterification process is fully reversible, highly activated esters or enol esters are commonly used as acyl donors to drive the reaction to form the acylated product.[18a]



Scheme 1.5: Example of a enzymatic Resolution of Secondary Alcohols and Primary Amines

Synthesis of single enantiomers of pharmaceutical intermediates is becoming increasingly important in the pharmaceutical industry. Organic synthesis is one of the methods for synthesizing single enantiomers, and bio-catalysis offers an additional dimension and great opportunity to generate pharmaceutically useful chiral compounds. The advantage of bio-catalysis over chemical catalysis is that enzyme-catalyzed reactions are stereoselective and regioselective and can be carried out at ambient temperature and atmospheric pressure. Bio-catalytic processes can be carried out in both organic solvent and aqueous environments, allowing both polar organic and water-soluble compounds to be selectively and efficiently modified with enzymes or bio-catalytically active cells. Different classes of enzymes can be used to catalyze different types of chemical reactions to produce a wide variety of chiral compounds.

Enzyme-catalyzed reactions can be categorized into six main groups according to the International Union of Biochemistry. [19]

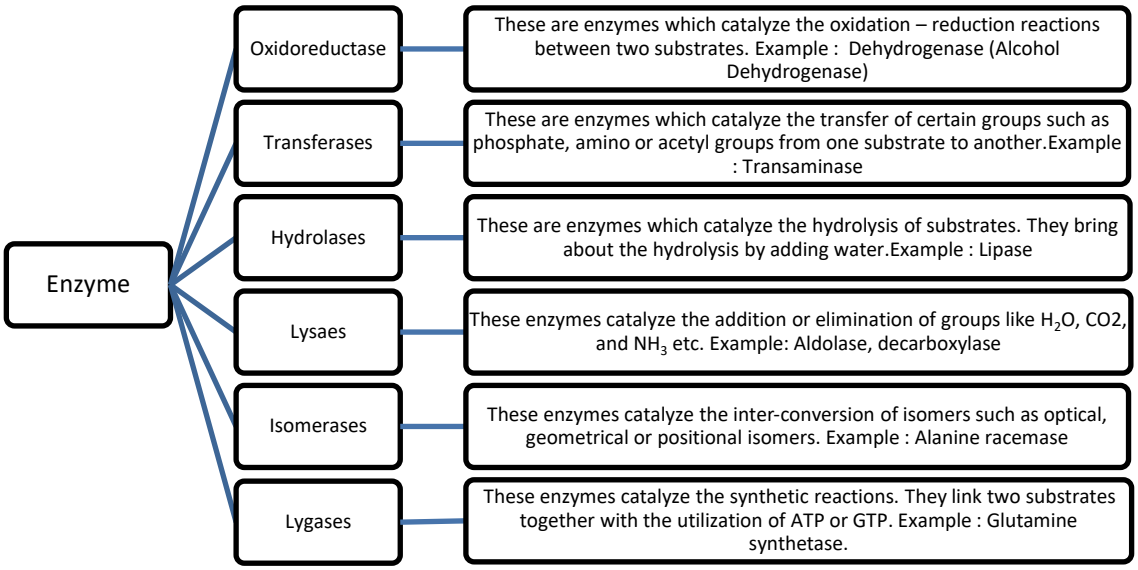


Figure 1.7: Types of Enzymes and their Function

1.5.1 Advantages of biocatalyst

The use of enzymes or entire cells as biocatalysts for industrial synthetic chemistry can be widely referred to as bio-catalysis. They have been employed for many centuries in the enzymatic breakdown of milk proteins to produce cheese as well as alcohol through fermentation. The variety of bio-catalytic applications has expanded as a result of significant advancements in our understanding of the relationship between protein structure and function over the past few decades.

Bio-catalysts work similarly to other catalysts in that they accelerate reactions. However, they have several distinctive advantages over traditional catalysts. High selectivity is a bio-catalyst's most significant benefit. This selectivity is frequently chiral, or stereo-selectivity, positional, or functional group-specific (i.e., chemo-selectivity). In chemical synthesis, such high selectivity is desired since it may provide various advantages like reduced or no use of protective groups, less side reactions, simpler separation, and fewer environmental issues. In commercial applications, other benefits like high catalytic efficiency and comfortable operating conditions are also quite desirable. Bio-catalytic reactions can be carried out in an aqueous environment, reducing the use and the disposing/recycling cost of solvents. Also, from a safety point of view, the use of water as a reaction solvent is industrially advantageous. In commercial applications, other

benefits like high catalytic efficiency and comfortable operating conditions are also quite desirable.

Parallel to this, examples of enzymes being used in conjunction with organic solvents have proliferated in recent years. Higher substrate loading is possible during bio-catalytic reactions in biphasic systems and with pure organic solvents. These reactions also stop water-sensitive compounds from being hydrolyzed and frequently disrupt the thermodynamic equilibrium of several reactions.

Since enzymes are proteins, they normally remain stable under the same conditions that proteins do, such as moderate temperatures and moderate pH levels.[20] They are capable of being very active in these circumstances. Many enzymes can achieve extraordinarily high turnover frequencies since they are only constrained by the diffusion of the starting material to the active site.

The 3-dimensional architectures of the enzymes used in these processes offer the regio- and enantioselectivity, resulting in the generation of optically pure molecules and isomers. Notably, the chemical strategy failed to carry out certain reactions, or the bio-catalytic methods performed better. Many of the examples were used in place of earlier chemical methods. It's interesting that many of these reactions take place in organic solvents, either as a single organic phase or as a biphasic system.

1.5.2 Limitations of biocatalyst

The use of enzymes in organic transformation has some restrictions and downsides. For instance, enzymes are commercially expensive, thus their disposal after using a single use in an organic reaction is not cost-effective. Co-factors are necessary for many enzymes to function properly. Heat, some organic solvents, acids, and bases, among other things, are incompatible with the enzymes. [21]

In comparison to other solvent systems, aqueous media perform better during the enzymatic process. The majority of organic transformations, however, do not function well with water as a solvent since many organic molecules are not even soluble in aqueous conditions. Enzyme removal from water is also far more labor-intensive than enzyme removal from organic solvents. [22]

1.5.3 Hydrolase

The promise of bio-catalysis as an efficient and environmentally friendly method for contemporary chemical synthesis is gradually coming to light. The field of bio-catalytic promiscuity, which extends the use of enzymes in organic synthesis, has gained a lot of attention and grown quickly in recent years. The use of biocatalytic transformation focuses mostly on the catalytic activities of enzymes with alternate Organic conversions and artificial substrates. Creating enzyme-catalyzed unusual reactions might improve already-existing catalysts and open up new, previously unattainable synthesis pathways. Since they exhibit considerable activity for some surprising reactions like the aldol reaction and other unique carbon-carbon and carbon-heteroatom bond-forming reactions, hydrolase (such as lipase, protease, and acylase) has undoubtedly drawn particular attention among these enzymes.

A new frontier extending the use of enzymes in organic transformation has drawn a lot of attention in the last ten years. Pyruvate decarboxylase, which not only decarboxylates pyruvate but also forms a connection between acetaldehyde and benzaldehyde to produce R-phenylacetylcarbinol, as famous example of a promiscuous enzyme process. Since its initial study in 1921, pyruvate decarboxylase has been used in industry to create carbon-carbon bonds, a process that does not happen naturally.[23a] Enzymatic applications for reactions such as aldol couplings, Michael(-type) additions, Mannich reactions, Henry reactions, and Knoevenagel condensations were discussed by Miao et al. in their review. [23b] In the same year, Gotor-Fernández et al. also emphasised the hydrolase-catalyzed processes for unconventional conversions. [23c]

Due to their many appealing properties, including stability in organic solvents, the lack of a need for cofactors, a wide range of substrate tolerance, commercial availability, and high chemo-, regio-, and stereoselectivity, hydrolases (such as lipase, protease, and acylase) have attracted the most attention as biocatalysts. In hydrolysis, transesterification, aminolysis processes, etc., hydrolases have demonstrated a high degree of flexibility. Rather than the well-known hydrolytic function, catalytic activity for unexpected reactions may potentially play a natural role in hydrolase evolution, according to research. [23d]

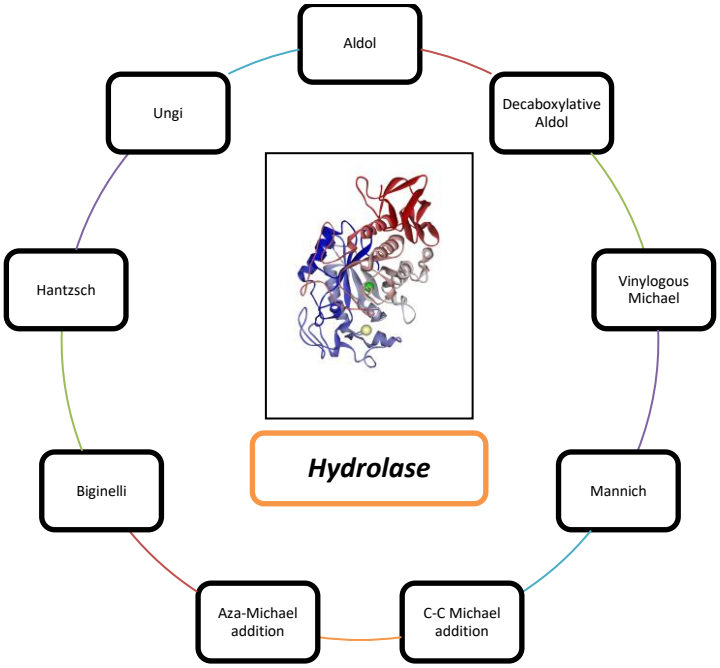


Figure 1.8: Application of Hydrolase catalyse Reaction

1.5.4 Application of Lipase

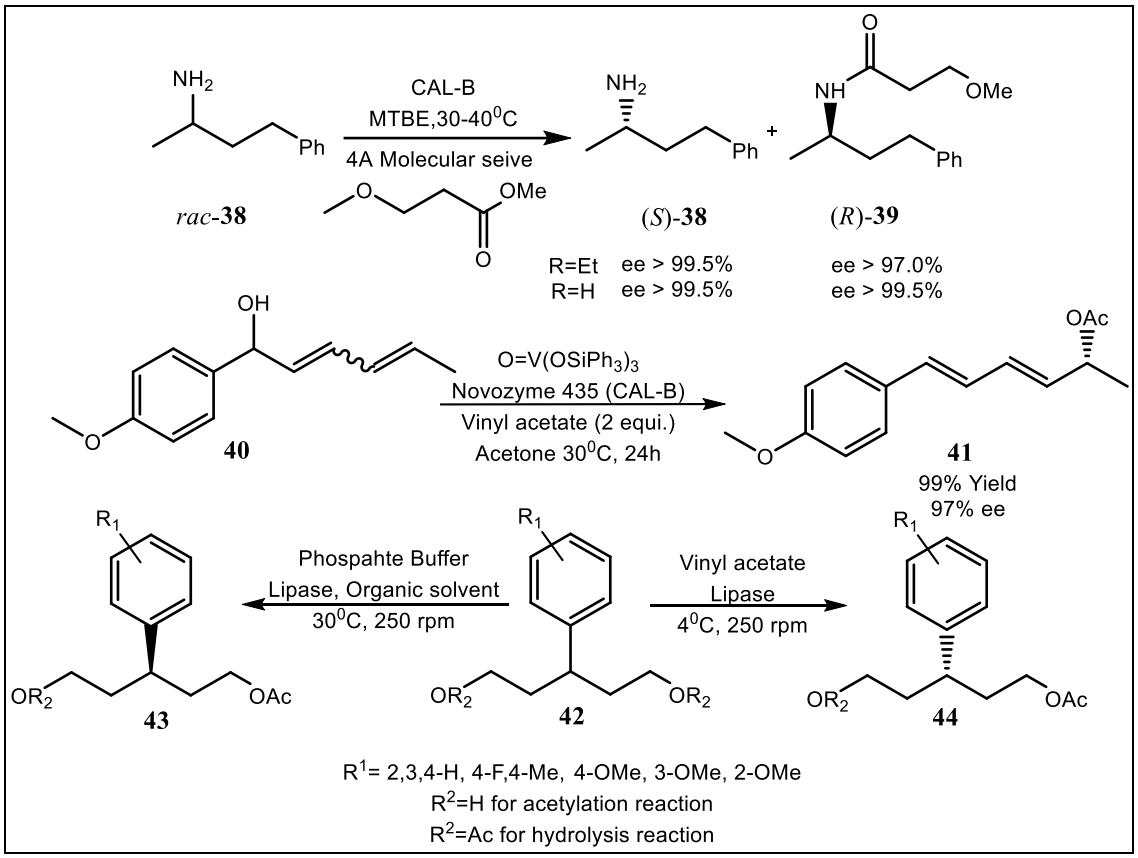
Triacylglycerol acylhydrolase, or lipases (EC 3.1.1.3), are members of the hydrolase family and operate on carboxylic ester linkages. They belong to the class of serine hydrolases and don't need a cofactor. Lipases have a molecular weight that ranges from 19 to 60 kDa. Serine hydrolases, also referred to as the lipase enzyme and members of the triacylglycerol ester hydrolase family, are widely distributed (EC 3.1.1.3). They are known as carboxylesterases, and they can catalyse the hydrolysis (and synthesis) of long-chain triglycerides to fatty acids, diacylglycerol, monoacylglycerol, and glycerol. They also exhibit interesterification, esterification, aminolysis, and alcoholysis activity in addition to hydrolysis, all of which contribute to a variety of businesses. In a non-aqueous media, lipase produces esters from glycerol and long-chain fatty acids.

Because of the wide range of catalytic actions they may perform and the high yields they can produce, microbial lipases are more valuable than those derived from plants or animals. Burkholderia glumae, Candida anatarctica B, and Pseudomonas aeruginosa all had a lead, but they did not exhibit interfacial activation.[24a,b] Lipases catalyse conversion reactions such as esterification, transesterification, interesterification, acidolysis, alcoholysis, and aminolysis. [24c]

Bacterial strains such as *Pseudomonas alcaligenes, P. aeruginosa, P. fragi, P. fuorescens BJ-10, Bacillus subtilis, B. nealsonii S2MT* and some species of fungi are *Penicillium expansum, Trichoderma, Penicillium chrysogenum; Aspergillus niger* produces lipases in higher quantities.

1.5.5 Lipase in Resolution

Lipase-mediated reactions of Racemates, which are frequently employed, can be carried out using techniques including Kinetic Resolutions (KR),[25a] Dynamic Kinetic Resolutions[25b], Desymmetrisation[26] and. A chiral (bio) catalyst is used in the process of kinetic resolution, which is based on the different reaction rates of the enantiomers. Because it gives users access to the two enantiomers individually, EKR has a particular importance in the production of optically active chemicals.[25]



Scheme 1.6: Kinetic Resolution, Dinemic Kinetic Resolution, and Desymmetrisation

1.5.6 Kinetic Resolution

Utilizing a biocatalyst to distinguish between the enantiomers and increase the rate of hydrolysis or esterification of one rather than the other is referred to as "enzymatic kinetic resolution." This technique is unique in that the highest required conversion is 50%, which means that one enantiomer must react with selectivity to separate the other one. [26]

1.5.7 Dynamic Kinetic Resolution

It is simple and effective to access enantiomerically pure alcohol and amine derivatives *via* dynamic kinetic resolution (DKR). The following conditions must be met; hence designing an effective DKR system is far from straightforward:

(I) The enantioselectivity of the KR must be sufficient (E value 24 = k_{fast}/k_{slow} 20).
(ii) The enzyme and the catalyst for racemization must work well together.
(iii) The rate of racemization (k_{rac}) must be at least ten times quicker than the reaction of the slow-reacting enantiomer, which is catalysed by an enzyme (k_{slow})
(iv) The catalyst for racemization must not interact with the resolution-derived product.[27]

1.5.8 Desymmetrisation

In stereochemistry, desymmetrization is the modification of a molecule that causes the loss of one or more symmetry components. The introduction of chirality is a typical use for this class of reactions. Formally, these conversions needed to get rid of an improper axis of rotation (mirror plane, centre of inversion, rotation-reflection axis). In other words, desymmetrisations result in the chiral product of prochiral precursors. [28]

It is a potent synthetic technique in which desymmetrization of an achiral or meso molecule to produce enantiomerically enhanced products. A chiral reagent or catalyst can be used to discriminate two enantiotopic functional groups in order to achieve an enantioselective symmetry breaking synthetic process. [29]

1.5.9 Transesterification Reaction

In line with the fundamentals of sustainable chemistry, biocatalysis has evolved as a sophisticated synthetic technology that enables the development of environmentally

beneficial processes. Enantiomers of a given molecule should be viewed as two distinct entities in terms of their biological function, particularly their pharmacological features, over the past ten years. Among the various techniques, enzyme-catalyzed techniques like kinetic resolution of racemates or asymmetrical synthesis from prochiral precursors are intriguing. Arylated amines, esterified alcohols, and acids, as well as other derivatives, were the basis for the first generation of procedures that were created. Enantioselective synthesis and transesterification processes carried out in organic media have been thoroughly investigated and characterised recently. Compared to hydrolysis, these processes provide a number of benefits. One example is solubility. For instance, solubility issues can be resolved more quickly than in aqueous solutions, and there is the potential to reduce the number of processes. Higher stereoselectivity in the synthesis mode and increased enzyme stability in organic solvents have both been reported. The ratio of the two enantiomers' reaction rates determines the enantioselectivity in any kinetic resolution process.

Short chain esters have a significant role in both artificial and natural tastes and perfumes owing to the modest response requirements. The synthesis of these compounds is a good candidate for enzyme catalysis. Terpene alcohols have been trans-esterified and esterified by lipase in supercritical carbon dioxide and solvents, respectively. The extent of conversion of racemic substrate (c), the optical purity, expressed as enantiomeric excess (ee) of the product or the remaining substrate, and the enantiomeric ratio (E).

As a result, only at the same level of conversion it is useful to compare the enantiomeric purities of two KRs. Sih et al. [30] have developed equation to calculate the inherent enantioselectivity of the biocatalytic KR. The enatomeric ratio (E), a measure of enantioselectivity, assesses an enzyme's capacity to differentiate between two isomers. The E value is handy for quickly comparing the selectivity of kinetic resolution because it remains constant throughout the process. The following three equations can be used to empirically compute E for an irreversible enzymatic KR by taking measurements of two of the three parameters: conversion (c), ee of the product, and ee of the unreacted starting material.

For irreversible reaction and no side-reactions take place, the parameters of kinetic resolution (*ee(P)*, *ee(S)*, Conv. and *E*) are all interrelated according to equations [31]

$$Conv. = \frac{\mathrm{ee(S)}}{\mathrm{ee(S)+ee(P)}} \qquad \text{……..Equation (1)}$$

$$E = \frac{\ln[(1-Conv.)(1+ee(R))]}{\ln[(1-Conv.)(1-ee(R))]}$$ ……..Equation (2)

Or

$$E = \frac{\ln[(1-Conv.)(1-ee(S))]}{\ln[(1-Conv.)(1+ee(S))]}$$

$$E = \frac{\{\ln[\frac{ee(P)(1-ee(S))}{ee(S)+ee(P)}]\}}{\{\ln[\frac{ee(P)(1+ee(S))}{ee(S)+ee(P)}]\}}$$ ……..Equation (3)

E levels in the range of 15 to 30 are generally regarded as moderate to good, and above these numbers they are beneficial. As a general rule, E values below 15 are unsatisfactory for practical applications. E > 200 kinetic resolutions are regarded as being extremely selective. E values above 200 are challenging to measure precisely and call very sophisticated analytical techniques.[32]

1.6 Acylating Reagent in Lipase catalysed Reaction

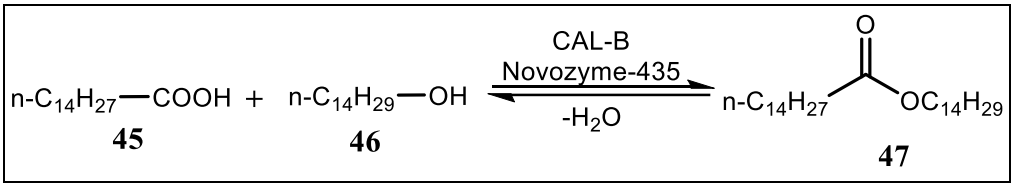
The acyl donor can affect the lipase's enantioselectivity through either its acyl or alkyl moiety. According to several investigations, this behaviour was rationalised on the grounds that the migratory group would imprint the enzyme during the formation of the acyl-enzyme intermediate, so affecting the enzyme's selectivity. This substrate matching strategy is referred to as a novel method for efficiently increasing the enantioselectivity of lipases in organic solvents. The enantioselectivity of lipases can be explained and predicted using a mix of molecular modelling and kinetic studies, and structural variables that enhance enzyme-substrate affinities and have an impact on enantioselectivity have been found.

These findings demonstrate that the reactivity and selectivity of the lipases are greatly influenced by the structure of vinyl esters. The synthesis of the acyl enzyme is likely prevented in the cases of vinyl pivalate and vinyl benzoate by the steric hindrance of the esters. The stereo-pocket structure, whose form might vary depending on the lipase, is where the enantioselectivity originates. The substrate structure is a major determinant of the lipase from P. cepacia's stereopreference, and the stereoselectivity is dependent on the atomic specifics of interactions between the substrate and lipase. Schulz et al. discovered a straightforward model to forecast the enantioselectivity of P. cepacia lipase toward a variety of secondary alcohols. The slow enantiomer's average minimised structure for the [O-H] hydrogen bond distance serves as the basis for this model. Another

explanation is that the accessibility of R and S differs in the energy curve of the enzyme/substrate interaction.[33]

1.6.1 Carboxylic Acid as acylating agent

The enzymatic condensation of an alcohol and an acid needs to be done under continuous removal of the water, in order to shift the equilibrium towards the product. On a lab scale, this protocol—which necessitates visibly high temperatures—is rarely used; instead, activated acyl donors are typically used at milder circumstances. However, there are some highly intriguing uses for using carboxylic acids as acylating agents in enzymatic reactions that are applied widely. One such example is the preparative-scale synthesis of myristyl myristate **47** with long chain alcohol **46** and acid **45**.[34]



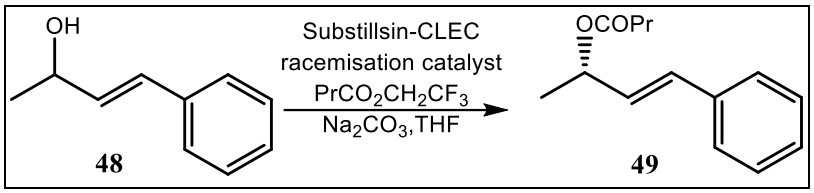
Scheme 1.71: Synthesis of myristyl myristate **47**

1.6.2 Tri Halo Esters as acylating agent

Early in the 1990s, in the first acylation investigations in organic solvents, 2,2,2-trichloroethyl groups were introduced as activated acyl donors. Because of the inadequate activation, transesterifications proceed slowly. As a result, there are few instances of this departing group being utilised in literature (none in the past five years).

2,2,2-Trifluoroethyl esters are much less used than vinyl esters, although being slightly more activated than their trichloro counterparts.

Their synthesis can be completed quickly either by coupling acids and alcohols with carbohydrides or by combining acid chlorides and the alcohol. Dynamic Kinetic Resolution of a series of allylic alcohols **48** using 2,2,2-trifluoroethyl butanoate in the presence of Subtilisin-CLEC to give ester **49.** [35]



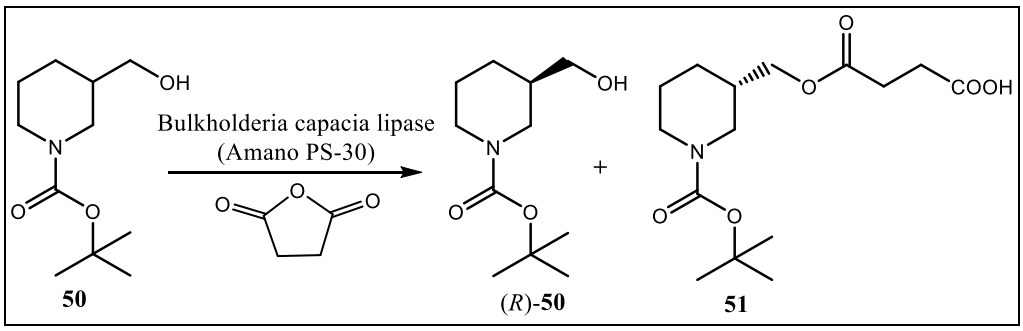
Scheme 1.72: Resolution of allylic alcohol using 2,2,2-trifluoroethyl butanoate **49**

1.6.3 Anhydride as acylating agent

Acyclic anhydrides have been used in enzymatic processes since the beginning, but they are mostly used in enzyme-mediated ester synthesis.

Even so, on an industrial scale, cyclic anhydrides (such as succinic anhydride) are more frequently used than their acyclic counterpart for the kinetic resolution of alcohols.

Indeed, they have the benefit of making it simple to separate the product monoester from the unreacted alcohol via base extraction. Additionally, acylations with cyclic anhydrides have an atom economy of 100%; however, it should be noted that the resulting hemiester is typically not the desired end product and an additional step (the hydrolysis) has to be performed.[34] One such example (Scheme 5) is given by the resolution of (R,S)-N-(tert-butoxycarbonyl)-3-hydroxymethylpiperidine **50** with succinic anhydride and BCL.[36]

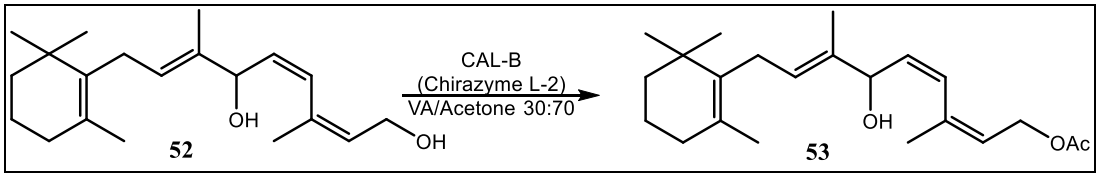


Scheme 1.73: Resolution of (R,S)-N-(tert-butoxycarbonyl)-3-hydroxymethylpiperidine **50**

1.6.4 Vinyl acetate as acylating agent

On a small scale, enol esters such vinyl acetate, isopropenyl acetate and ethoxyvinyl esters are by far the best activated and most /widely used acyl donors (see Table 1). 29– The leaving group is an enol, which instantaneously tautomerizes to the keto form. Since there is no longer a nucleophile, the reaction is now irreversible. Due to their utility as

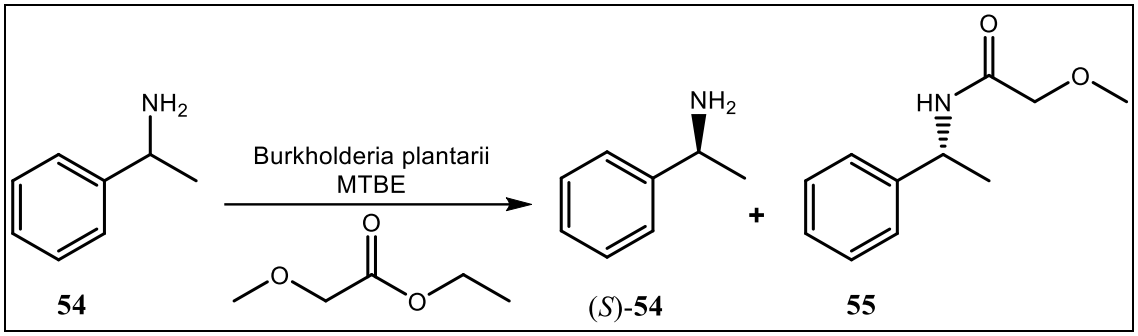
building blocks in polymer chemistry and as acylating agents in non-enzymatic processes, certain vinyl esters and IPA are commercially accessible. The transformation of these bulk compounds into the required vinyl or isopropenyl esters is ensured by Pd- or acid-catalyzed transesterifications. Using other Ru catalysts, alkoxyvinyl esters can also be created from the appropriate acid and acetylene. The use of a solvent is not necessary because these acyl donors—especially the inexpensive VA—are frequently utilised in excessive amounts.[34] Vinyl acetate is used for the Chirazyme L-2 mediated acetylation of an intermediate for Vitamin A synthesis.[37]



Scheme 1.74: Enzymatic acetylation of an intermediate for Vitamin A **53**

1.6.5 Acetate as acylating agent

Researchers from BASF developed ethylmethoxyacetate for the enzymatic resolution of chiral amines in the 1990s. Since that time, optically pure aliphatic and benzyl amines, amino alcohols, and other chemicals have been produced on a large scale using methoxyacetic acid esters. The initial acylation rate for ethylmethoxyacetate is 100 times faster than the same reaction with, for instance, ethyl butyrate due to the methoxy substituent's remarkable enhancement of the carbonyl reactivity. Additionally, the selectivity of these acyl donors is unmatched and is particularly improved when esters of secondary alcohols such isopropyl methoxyacetate are used.[34] Equimolar amounts of 1-phenylethylamine and ethylmethoxy acetate are converted in to methoxy acetates in the presence of Burkholderia plantarii lipase.[38]

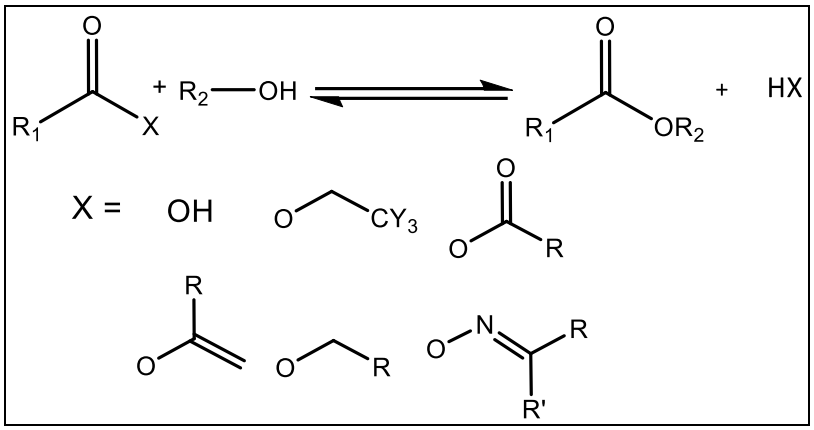


Scheme 1.75: Enzymatic acetylation of 1-phenylethyl amine **54** by ethyl methoxy acetates

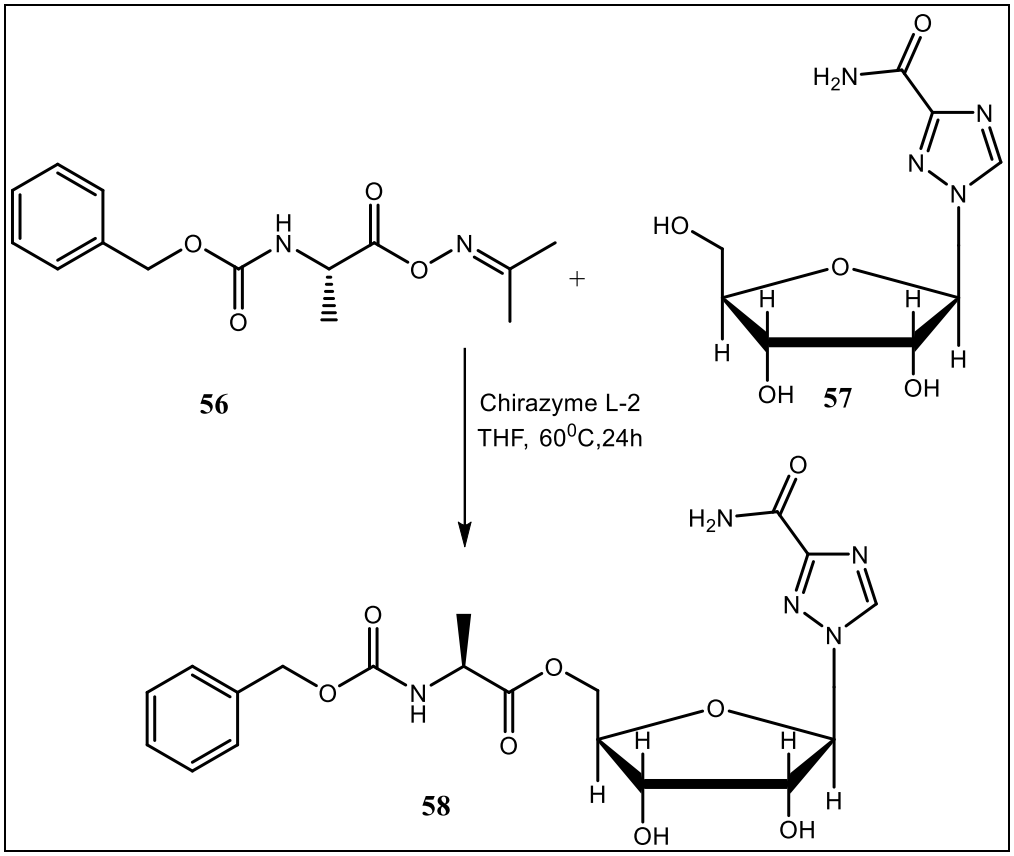
1.6.6 Oxime as acylating agent

In the past five years, oxime esters, which were initially described in 1989, have barely been employed. Despite the fact that reversible behaviour has occasionally been seen, they are typically regarded as irreversible acyl donors. In addition to the straightforward acetone oxime, more complex oxime esters have lately been proposed and have succeeded even better. Their manufacture entails the condensation of oximes and acid chlorides or the DCC coupling of oximes and acids.

Schering-pilot-scale Plough's acylation of Ribavirin's alcohol with Cbz-protected L-alanyl oxime ester in the presence of CAL-B (Chirazyme) is an intriguing illustration of an oxime ester's industrial use.[34] An interesting example of industrial application of an oxime ester is the acylation of the primary alcohol of Ribavirin with Cbz-protected L-alanyl oxime ester in the presence of CAL-B (Chirazyme).[39]



Scheme 1.77: General Enzymatic Resolution with different acylating agent



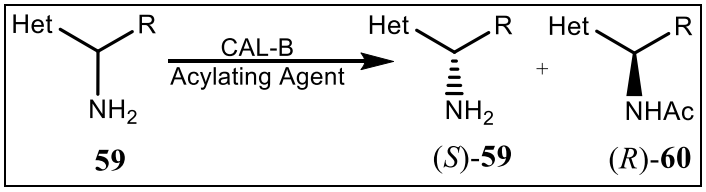
Scheme 1.76: Enzymatic acylation of the primary alcohol of Ribavirin **56**

1.7 Enzymatic Resolution of Alcohol

Racemic alcohol's kinetic resolution (KR) with an acyl donor under lipase catalysis in organic Solvents have drawn more and more attention as an effective way to make optically active chemicals. Several liturare examples are shown below.

1.7.1 Enzymatic Resolution of Bicyclic 1-Heteroarylamines

The (R)- and (S)-enantiomers of a structurally diverse series of bicyclic 1-heteroaryl primary amines were needed for drug development, and the utilisation of enzymatic techniques for resolving racemic amine substrates has quickly acquired popularity, especially for large-scale commercial applications. Candida antarctica lipase B6 is an enzyme that has been utilised extensively in the resolution of alcohols (CALB, available immobilised on polyacrylamide as Novozyme 435). In general, CALB exhibits strong selectivity for the (R)-enantiomer of secondary alcohols while leaving the (S)-enantiomer unaltered as a transesterification catalyst.[40,40a]



Scheme 1.79 Example of Enzymatic Resolution of bicyclic 1-heteroaryl primary amines

1.7.2 Enzymatic Resolution of Loxoprofen

For the synthesis of (S)-profens, a significant number of biocatalytic approaches have been established to date; nevertheless, because of the commercial significance of these medications, more effective and sustainable techniques are required. A NSAI medication with anti-inflammatory, analgesic, and antipyretic properties, loxoprofen **62** is a (S)-2-(4-(R)-2-oxo-cyclopentylmethyl)phenyl propionic acid. Due to the fact that the equivalent trans-alcohol metabolite is loxoprofen's active form, it is a pro-drug.

The racemic alcohol 2-(p-[(p-methoxy phenyl)methoxy]methylphenyl)propanol **61** was enzymatically resolved into loxoprofen through a transesterification reaction in the presence of lipase from Burkholderia cepacia (lipase-PS), molecular sieves 4, DIPE as a solvent, and vinyl acetate as an acyl donor (Scheme1.80). After 12 hours, the matching (S)-acetate and (R)-alcohol could be obtained with 98% and 94% enantiomeric excess, respectively. Following the required configuration of (S)-acetate, loxoprofen was synthesised.[40] Irreversible enzymatic transesterification with vinylacetate was applied to racemic (**61**) by using Lipase-PS (Burkholderia cepacia) in DIPE (iPr2O) as a solvent to afford the (S)-**(62)**-acetate and the (R)-alcohol with good enantioselectivity.[41]

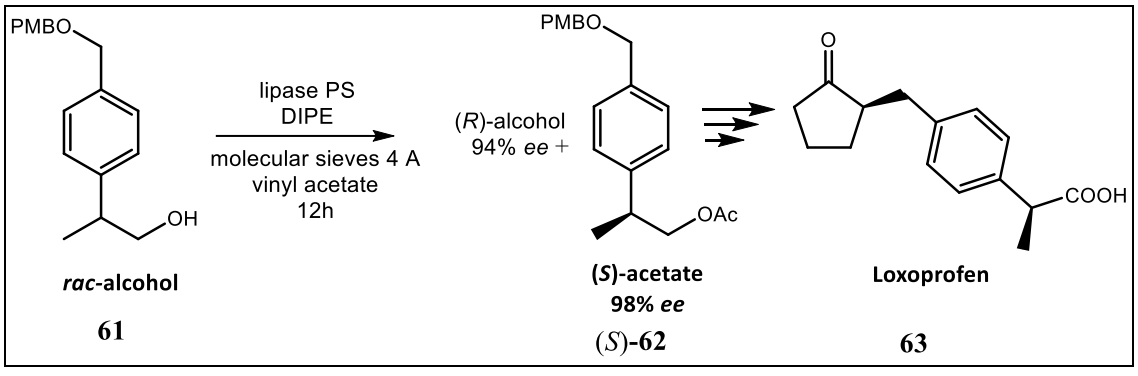


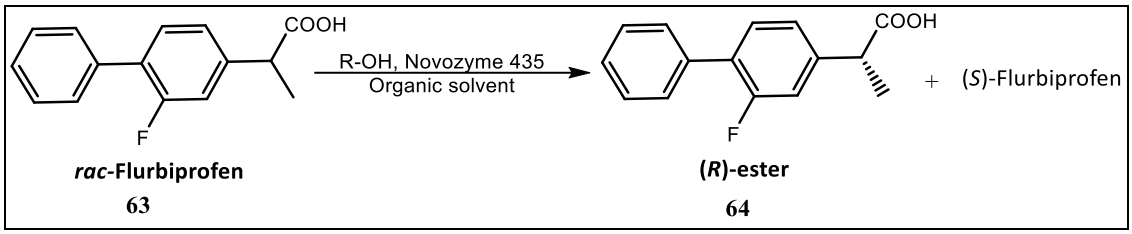
Figure 1.80: Enzymatic Resolution step in a synthesis of Loxoprofen

1.7.3 Enzymatic Resolution of Flurbipropen

Using dry Aspergillus oryzae, MIM mycelia as biocatalysts, racemic flurbiprofen was kinetically resolved. Following the optimization of the reaction conditions (organic solvent, type of alcohol, and temperature), (R)-Flurbiprofen ester was produced with a range of conversion and enantioselectivity. Later, kinetic resolution of the same racemic drug was carried out in a flow reactor, which is thought to be an intriguing method for the development of the lipase-catalyzed synthesis of enantiopure molecules. It's also important to note that these automated systems support continuous bioprocesses, make it simple to optimise reactions (including factors like residence time), enable multistep reactions, and enable inline product recovery and purification. Direct esterification in organic solvent utilising a commercial enzyme (Novozym 435) and the entire microbe (A. oryzae, MIM) were therefore contrasted with the conventional batch technique as a proof of concept.

By varying the reaction conditions (temperature and residence time), the protocol inflow reactor demonstrated a significant reduction in reaction time (from 6 h to 15-60 min), and it produced both the (S)-Flurbiprofen and (R)-Flurbiprofen butyl ester with 90% ee (chemical purity >98%), as shown in **(Scheme 1.81)**. [40]

Inflow reactor showed a significant reduction of the reaction time (from 6 h to 15–60 min) and yielded both the (*S*)-Flurbiprofen and (*R*)-Flurbiprofen butyl ester with ≥90% *ee* (chemical purity >99) [42]

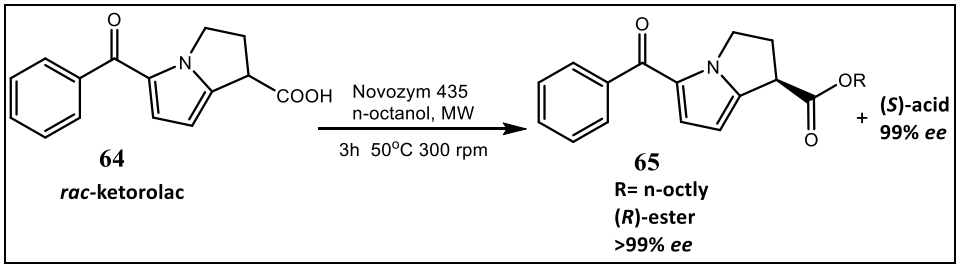


Scheme 1.81: Enzymatic Resolution of Flurbipropen

1.7.4 Enzymatic Resolution of Ketorolac

A powerful NSAI medication from the class of heterocyclic acetic acid derivatives, ketorolac (rac-5-benzoyl-1,2-dihydro-3H pyrrolo[1,2-a]pyrrole-1-carboxylic acid) is used extensively as an analgesic. Utilizing various immobilised lipases, such as Novozym 435, Lipozyme TL IM, Lipozyme RM IM, lipase Amano AS, and lipase AYS

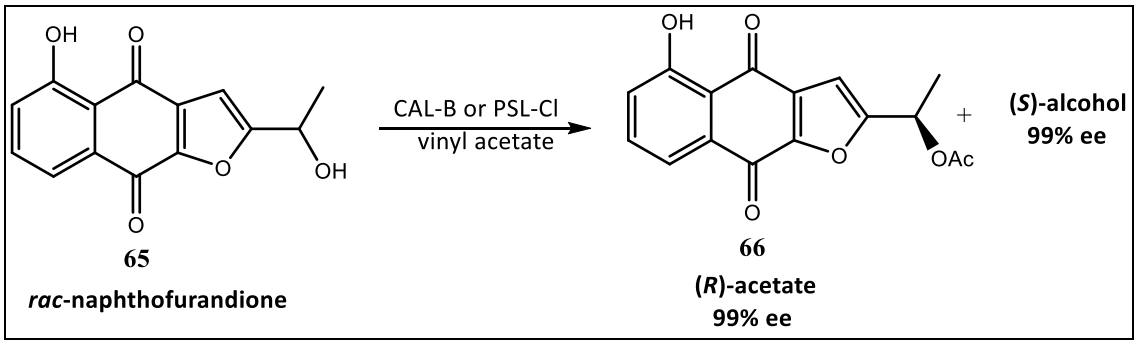
Amano, the kinetic resolution of this molecule by microwave (MW) was studied. Novozym 435, among others, catalysed the enantioselective acylation of rac-Ketorolac in 3 hours at 50 degrees Celsius and 300 RPM with a high ee value (>99%) for both the residual (S)-acid and (R)-ester. Additionally, it was discovered that the reaction followed the Ping-Pong bi-bi mechanism and that n-octanol blocked it. [43]



Scheme 1.82: Enzymatic Resolution of Ketorolac

1.7.5 Enzymatic Resolution of naphthofurandione derivative

The bark of Tabebuia impetiginosa included naphthofurandione (S)-5-hydroxy-2-(1-hydroxyethyl)naphtho[2,3-b]furan-4,9-dione, a secondary metabolite with anticancer effects (Bignoniaceae). From commercially available 1,5-dihydroxynaphthalene, racemic naphthofurandione was produced by a series of chemical processes. The rac-naphthofurandione was subjected to enzymatic kinetic resolution through the acetylation process. The lipases from Pseudomonas cepacia and Candida antarctica B (Novozym 435) performed the best (PSL-CI, 3 hours of reaction). In order to produce (S)-alcohol and the matching (R)-acetate with 99% ee for both and E > 200, the reaction required vinyl acetate as the acyl donor, THF as the solvent, 250 rpm, and 30 C as the reaction temperature. [44]

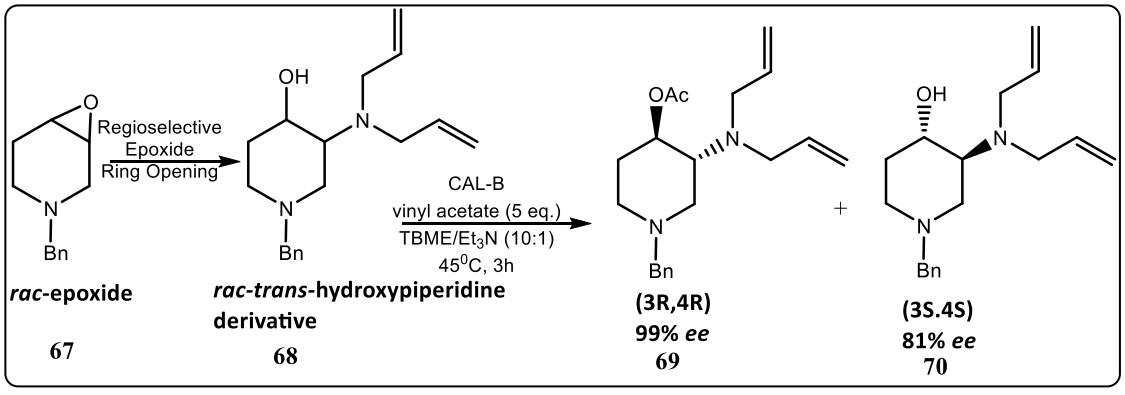


Scheme 1.83: Enzymatic Resolution of naphthofurandione derivative

1.7.6 Enzymatic Resolution of Aminohydroxypiperidine Derivatives

Some bioactive substances, such as an inhibitor of non-receptor tyrosine kinase (Scheme 40) that is used to treat auto-immune illnesses, have the trans-3-amino-4-hydroxypiperidine moiety in their structures. By using lipase to catalyse the kinetic acylation of the matching racemate, it was possible to produce enantiopure, orthogonally protected (3R,4R)-3-amino-4-hydroxypiperidine acetate. The regioselective opening of the epoxide at the rac-1-benzyl-3,4-epoxypiperidine (rac-epoxide) with diallylamine produced the racemic trans-N-benzyl-3-(diallylamino)-4-hydroxypiperidine (trans-hydroxypiperidine derivative). Following that, it was put through an enzymatic transesterification reaction using vinyl acetate (5 eq.) as the acyl donor, lipases from Candida antarctica types A (lipase NZL-101) and B (Novozym 435), Burkholderia cepacia (PSL IM), Pseudomonas fluorescens (AK), and Thermomyces lanuginosus (TL IM), in TBME as the solvent, and at 30^0C.

The conversions were only moderate (11%-31%), despite the fact that all lipases catalysed the acylation of the substrate with the same stereochemical preference, (3R,4R)-product and (3S,4S)-substrate. Thus, in order to increase the reaction rate utilising the lipases CAL-A and CAL-B, the influence of several reaction parameters (organic solvent, temperature, and triethylamine as an additive) was investigated. TBME/Et_3N (10:1) as the solvent, three days of reaction time, and a temperature of 45 ^{0}C produced the greatest results. In this instance, the kinetic resolution produced the (3S,4S)-substrate and (3R,4R)-product with enantiomeric excess of >99% and 81%, respectively, c 45%, and E > 200.



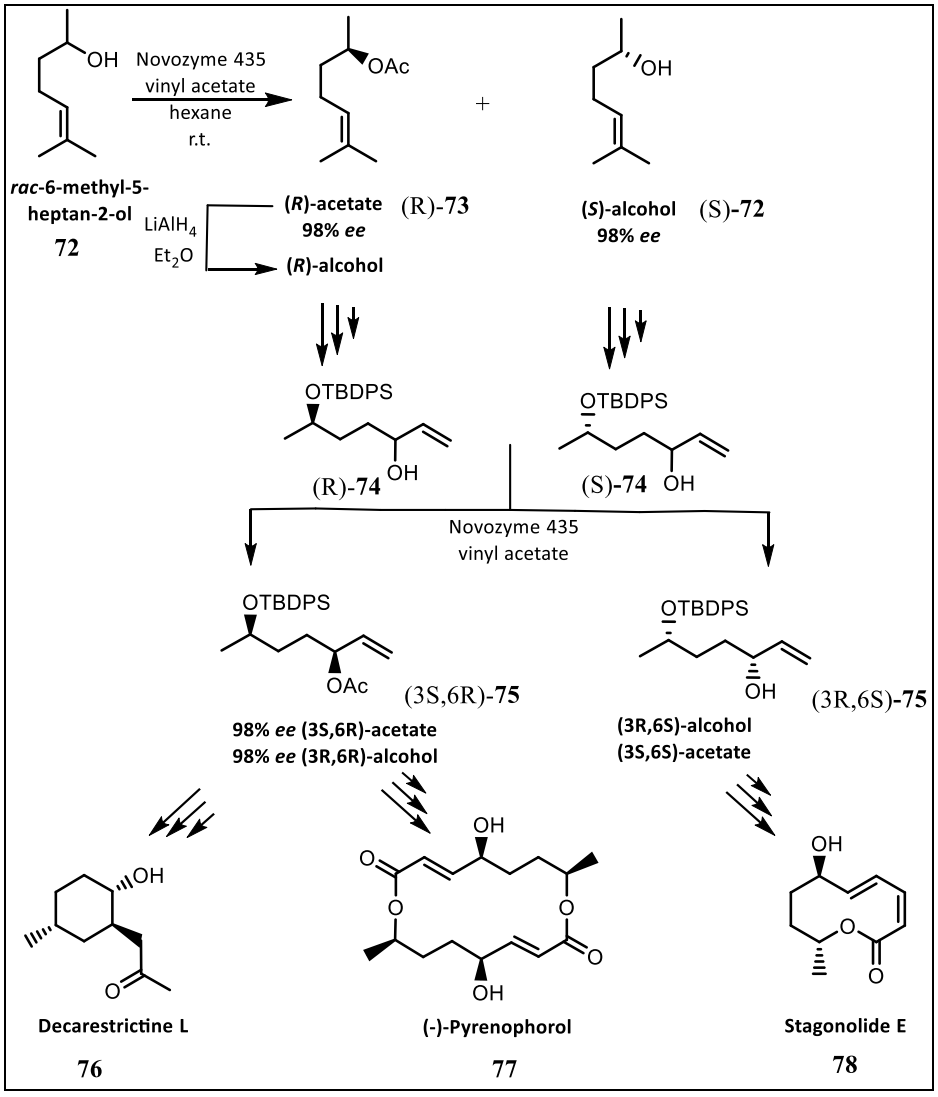
Scheme 1.84: Enzymatic Resolution of Aminohydroxypiperidine Derivatives

It should be noted that when the reaction was conducted without triethylamine as an addition, a considerable drop in the reaction rate was found. [45]

1.7.7 Enzymatic Resolution of Intermediates of Stagonolide E, Pyrenophorol and Decarestrictine L

By acetylating the corresponding racemates under the action of lipase, enantiomerically pure hept-6-ene-2,5-diol derivatives were produced. These intermediates were crucial in the synthesis of the bioactive substances decarestrictine L **75,** pyrenophorol **76**, and stagonolide E **77**, (Scheme 1.85), which were all isolated from filamentous fungi. After 50% conversion, acetylation of racemic 6-methyl-5-hepten-2-ol with Novozym 435 and vinyl acetate in hexane at room temperature produced both the (R)-acetate **73** and (S)-alcohol **72** with 98% ee (E > 195). Additionally, the (R)-alcohol was created by treating (R)-acetate with $LiAlH_4$. The hydroxyl group was then protected with tert-butyldiphenylsilyl (TBDPS), and the resulting aldehydes were then subjected to ozonolysis and a reaction with vinylmagnesium bromide to produce the allylic alcohols (3S,6R) **74** and (S)-alcohols, respectively (3R,6S) **74**.

The enzyme-catalyzed acylation of these allylic alcohols followed a similar procedure . In this scenario, high enantioselectivity (E > 195), or 50%, was used to produce both critical intermediates (3S,6R)-acetate **75** and (3R,6S)-alcohol **75**. In the creation of stagonolide E, **78** the (3R,6S)-alcohol, which is enantiomerically pure, served as an intermediary. Enantiomerically pure allylic (3S,6R)-acetate served as a crucial step in the chemoenzymatic synthesis of Pyrenophorol **77** and Decarestrictine L **76**. [46]



Scheme 1.85: Enzymatic Resolution of Intermediates of Stagonolide E, Pyrenophorol and Decarestrictine L

1.8 Enzymatic Desymmetrisation

Enzymes are regarded as some of the most potent and selective catalysts for the synthesis of optically active substances.[47] One reason for this appeal is that they are environmentally friendly, and chemo-, regio-, and stereoselective in their action. In comparison to nonenzymatic procedures, side reactions such as isomerization, racemization, epimerization, and molecular rearrangement have less of an impact on enzymatic reactions due to the moderate circumstances under which they function. However, organic chemists have typically been averse to using biocatalysts in their syntheses. This is mostly due to the fact that most enzymes are extremely sensitive catalysts that perform their functions primarily in aqueous solutions in their native state.

Additionally, managing them calls for some biochemistry understanding. However, certain recent developments in the field of biocatalysis have "approached" the use of enzymes in organic synthesis: They have the following advantages: (a) they can function in nonaqueous fluids accepting a variety of substrates [48] (b) immobilisation procedures boost their stability and make handling them easier [49]. As a result, many enzymes are now available for purchase and usage as any other chemical. Asymmetric Synthesis and Kinetic Resolution of racemic mixtures are two major groups of stereoselective biotransformations (KR). They are conceptually different from one another in that a KR is based on a transformation, making it simpler to separate the two enantiomers of the racemic substrate, whereas asymmetric synthesis presumes the creation of one or more chirality elements in a substrate.

This fact entails a practical distinction, only half of the initial substance is utilised in a kinetic resolution. One drawback of KRs is that only one enantiomer of a substrate is necessary, and many strategies have been proposed to get around this restriction.[50] The dynamic KR,[51] which entails performing an *in situ* continuous racemization of the substrate so that, theoretically, all of the racemic starting material can be utilised for transformation into one enantiomer, has recently received greater attention. Many of the substrates used in enzyme-catalyzed kinetic processes, however, are not subject to racemization. Desymmetrization of symmetric compounds entails a modification that gets rid of one or more of the substrate's symmetry components. Enantioselectivity is possible if the symmetry components that prevent chirality are removed.[52]

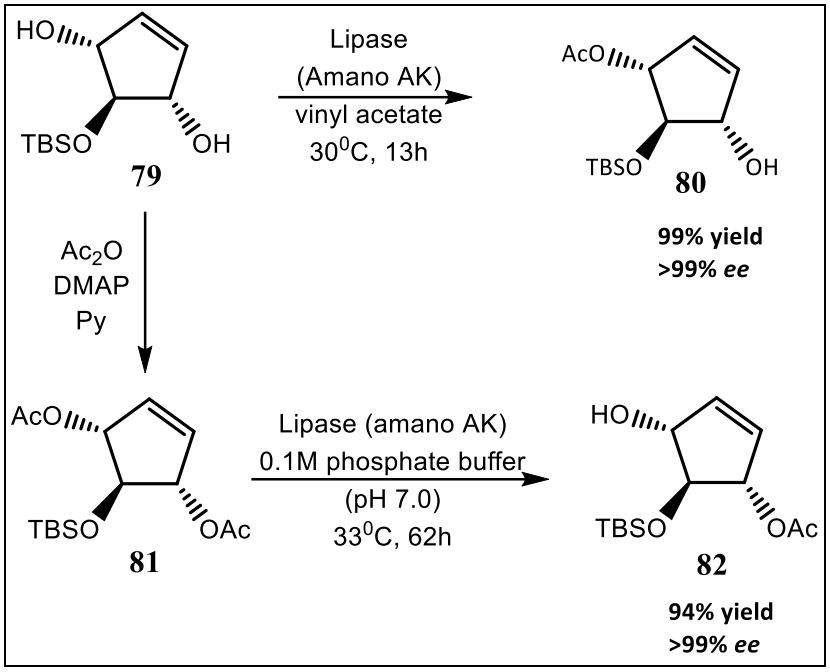
Enantioselective Enzymatic Desymmetrizations (EEDs), which fall under the category of asymmetric synthesis, are capable of producing a maximum yield of 100%.[53] This makes them a very intriguing alternative to KRs for the synthesis of optically active chemicals, as evidenced by the rise in the number of enzymatic desymmetrizations used in synthesis that have been reported in the literature in recent years. This study discusses the advancements made, particularly from 1999 onward, in the utilisation of biocatalysts for the desymmetrization of *meso* and prochiral chemicals.

It is organised from a synthetic perspective as opposed to a biocatalytic perspective, and as a general rule, only examples that are helpful from a synthetic perspective are included, such as EEDs that constitute or can constitute a key step in a synthetic route or help to rationalise the substrate specificity of an enzyme or the desymmetrization of a particular

class of compounds. Enantioselectivity and the yield of the EED, which should be higher than 50% so that the desymmetrization suggests a clear advantage over KRs, hence significant parameters that have received attention.

1.8.1 Examples of Enzymatic Desymmetrisation

Enzymatic desymmetrization of triol and its derivative allowed for the facile preparation of both enantiomers of *trans*-4,5-dihydroxy-2-cyclopenten-1-one in the enantioselective synthesis of the core system of the neocarzinostatin chromophore. Meso 5-tert-butyldimethylsilyloxy-2-cyclopentene-1,4-diol **79** was successfully transesterified by lipase AK (Amano), and its diacetate was hydrolyzed. High yields and enantiopurity were achieved for both monoesters.[54]

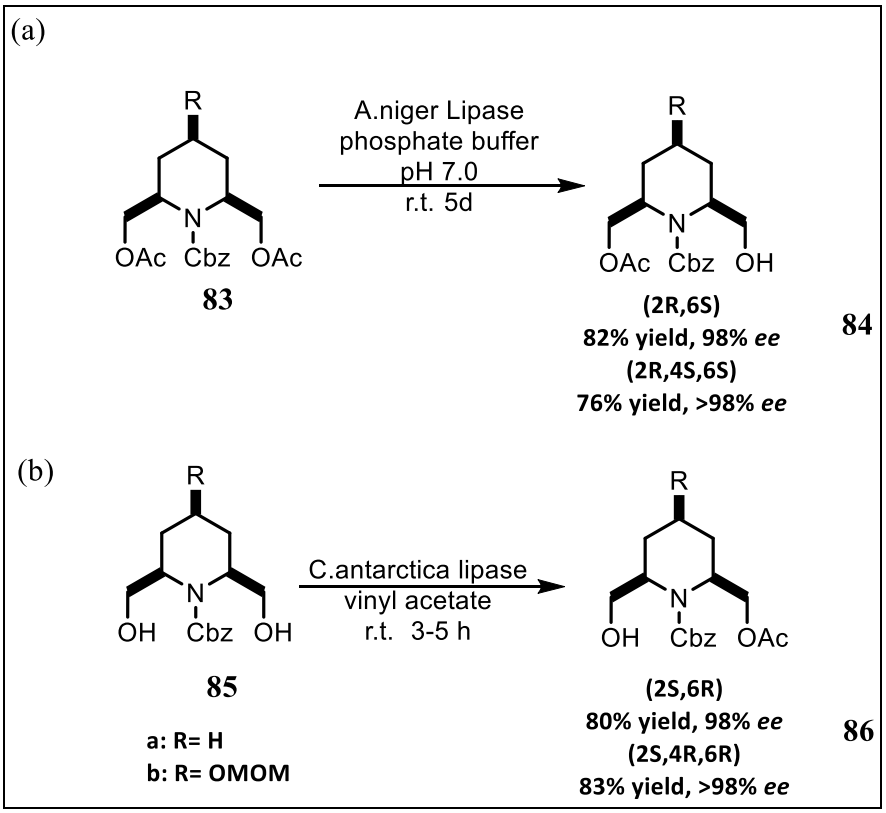


Scheme 1.86: Enzymatic Desymmetrisation of 5-tert-butyldimethylsilyloxy-2-cyclopentene-1,4-diol **79**

A common structural component of substances that are physiologically active is the piperidine ring. In this context, Chenevert and coworkers' desymmetrization techniques have been used to generate both enantiomers of various *cis*-2,6- and *cis,cis*-2,4,6-substituted piperidines.[55,56] In particular, the hydrolyses of the diacetates by Aspergillus niger lipase produced substantial yields of enantiopure monoacetates at a modest pace.

Candida antarctica lipase's stereoselective acylation of the corresponding diols produced the opposite enantiomeric series, again in high yields and ee's, at a noticeably faster. The

usage of these acquired chiral building blocks in the synthesis of various physiologically active molecules illustrated their value. [57]



Scheme 1.87: Enzymatic Desymmetrisation of substituted piperidines

Chapter 1

Introduction of this thesis contain importance of enzymes used in different reactions to synthezed important optically active natural products which has potential applications in pharmaceutical industries.

Chapter 2

The focus of this chapter is to study the enzymatic kinetic resolution of alcohol and on the development of efficient condition for kinetic resolution of substituted Secondary alcohols, The resolved molecules are converted into chiral Kagan's type amides. The synthesised amides are screened as chiral solvating agents in NMR to study an effect of substitution of fluorine at different position or aryl ring in supramolecular interaction.

Chapter 3 [I]

Section I of the chapter 3 deals with the one pot kinetic resolution-Mitsunobu Reaction to overcome the main disadvantage of enzyme kinetic resolution. In this methodology we studied effect of different Acylating reagent on a yield and optical purity of product in reaction.

Chapter 3 [II]

In Section II, we studied Conversion of alcohols to carbonate observed under the mild conditions of Mitsunobu reaction in presence of silver salt. An investigation is undertaken to explore this unexpected observation, we explore this observation on different substrates, reagents and also studied its Stereochemical aspects.

Chapter 4

This chapter includes synthesis and study of optically active thiourea based organocatalysts and explored its application in various Asymmetric reactions like Baylis Hillman Reaction and Aldol Reaction. We also investigated its supramolecular interaction (as a Chiral Solvating Agent) with different Analytes.

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