ENANTIOSELECTIVE SYNTHESIS MEDIATED BY CRUDE ENZYMES

A THESIS SUBMITTED FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

By
P. DHARMA RAO

SCHOOL OF CHEMISTRY
UNIVERSITY OF HYDERABAD
HYDERABAD 500 134
INDIA

APRIL 1993

CONTENTS

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, under the supervision of **Dr. D. Basavaiah.**

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

P Dharma Rao

Hyderabad **P. DHARMA RAO**

April, 1993

CERTIFICATE

Certified that the work contained in this thesis entitled **"Enantioselective synthesis mediated by Crude Enzymes"** has been carried out by Mr. P. Dharma Rao, under my supervision and the same has not been submitted elsewhere for a degree.

May 10,

D. BASAVAIAH
(THESIS SUPERVISOR)

DEAN
SCHOOL OF CHEMISTRY
UNIVERSITY OF HYDERABAD

ACKNOWLEDGEMENTS

It is with great pleasure that I express my profound gratitude to my Research Supervisor Dr.D. Basavaiah for suggesting me this problem, his invaluable guidance and encouragement. I am indebted to Dr.D. Basavaiah, from whom I learned all the basic techniques of chemical research. All the faculty members of the School of Chemistry have been extremely helpful and I thank them all.

I thank my colleagues Dr.V.V.L. Gowriswari, Dr.T.K. Bharathi, Messers. P.K.S. Sarma, P. Rama Krishna, S. Bhaskar Raju, S. Pandiyaraju. Dr.A.K.D. Bhavani and Ms.R. Suguna Hyma, for their help, encouragement and for providing amiable atmosphere.

Words are poor substitute to express the profound influence my **MOTHER** had on me in instilling confidence and dedication towards work. Her affection, guidance and encouragement have left me forever indebted to her. I express my heartfelt appreciations to my wife "JAYA" for understanding and supporting me all through. I wish to thank my son, "NIKHIL" whose entry has since brought fresh spirits to my life.

I am extremely thankful to my brother, BUJJI, for taking care of me though young. I also thank my sisters, brothers-in-law, parents-in-law and other family members for overlooking my

Sh.V. Satyanandam and my beloved cousins Ramannayya & Peddannayya, for their help and niceties shown to me when odds were against.

I thank my teachers Sh. M. Rama Chandra Murthy (alphabets), Sh.V. Trinatha Rao and Sh.N.B. Ramam who taught me lessons of life and academics.

With pleasure I appreciate the grand company provided by my seniors & contemporaries, Dr.K. Raja Reddy, Dr.M. Pulla Reddy, Dr. G.N. Reddy, G.V. Ranga Rao, Dr. M.S. Reddy, Dr. K. Vasu, Dr.B. Sreenivas, Dr.A C.S. Reddy, V.R. Pedireddi, K. Rajendar Reddy, Ch. Kishan Reddy, H.K. Reddy, M.Rama Reddy, R.Murali, D. Sekhar Reddy, V. Satish Goud, P. Bheema Rao, G.N. Sastry, Ch. Rama Krishna Rao and many others with whom I have shared memorable moments.

I gratefully acknowledge the help provided by technical and non-teaching staff, in particular Mr. S. Satyanarayana who patiently carried out my shift reagent analysis and Mrs. Asia Parwez for carrying my HPLC analysis.

Financial assistance by U.G.C. (New Delhi) is gratefully acknowledged.

P. Dharma Rao

P.Dharma Rao

ABBREVIATIONS

Ac	acetyl
Bu	butyl
CLAP	chicken liver acetone powder
DABCO	1,4-diazabicyclo(2.2.2)octane
DMAP	4-dimethylaminopyridine
E.e.	enantiomeric excess
Et	ethyl
$Eu(hfc)_3$	Tris[3-heptafluoropropylhydroxymethylene)-(-)-camphorato], europium(III) derivative
i-Bu or Bu^i	isobutyl
i-Pr or Pr^i	isopropyl
Me	methyl
MTPACl	α-methoxy-α-(trifluoromethyl)phenylacetyl chloride
Np	1-naphthyl
PCC	pyridinium chlorochromate
Ph	phenyl
PLAP	pig liver acetone powder
Py	pyridine
Rac	racemic
THF	tetrahydrofuran

ABSTRACT

The emergence of chirality as one of the key issues in pharmaceutical and agrochemical research has led to a flurry of activity among synthetic organic chemists. Consequently, enantioselective synthesis has become a major branch of organic chemistry. The biocatalytic approach to this enantioselective synthesis is currently emerging as a major tool.

This thesis describes our endeavor in developing inexpensive crude esterases as useful alternatives to the expensive isolated esterases in the synthesis of enantiomerically enriched synthons and biologically important molecules. The thesis consists of three chapters: (i) Introduction, (ii) Objectives, Results and Discussion, (iii) Experimental. The first chapter, Introduction, presents the current status of the field while according due place to fundamental contributions.

The second chapter describes objectives, results and discussion. Enzymes have been increasedly recongnised as versatile catalysts especially in the synthesis of optically active molecules. However, synthetic organic chemists remained apprehensive because of their preconceived notions about the delicacy of enzymes. Moreover non-accessability of a required enzyme often prevents one to go for an enzyme mediated

In order to provide inexpensive and simple procedures for enzyme mediated transformations, we have taken up the project "enantioselective synthesis mediated by crude enzymes". We believe that crude preparations of certain enzymes can be employed for a projected reaction as long as the other enzymes present do not interfere. Accordingly, we planned to make use of crude esterases namely pig liver acetone powder (PLAP) and chicken liver acetone powder (CLAP) for enantioselective synthesis of various molecules (98-105 & 1).

We have first taken up the resolution of secondary homoallyl alcohols, **98(a-g)**. We have first carried out the resolution of these molecules *via* enantioselective hydrolysis of corresponding acetates catalyzed by PLAP which produced the product alcohols with moderate enantiomeric purities. However, CLAP catalyzed hydrolysis of the same acetates provided the product alcohols with very high enantiomeric purities (72-98%).

Next we have taken up the resolution of anti-homoallylic alcohols, **99(a, d-h)**. This was achieved *via* CLAP catalyzed hydrolysis of corresponding acetates which produced the product alcohols in high enantiomeric purities (67->99%). We have also studied the enantioselective hydrolysis of acetates of racemic secondary propargyl alcohols, **100(a-e)**.

α-Methylene-β-hydroxypropanoates, **101(a-d)** and propane-nitriles **102(a-f)** are molecules with unique structural features

which could be exploited in the enantioselective synthesis by using them as chirons. Therefore we have subjected acetates of these racemic molecules to the PLAP catalyzed enantioselective hydrolysis producing the desired alcohols in good enantiomeric purities.

Cyclohexyl based chiral auxiliaries play a very important role in asymmetric synthesis. Therefore we turned our attention to synthesis of *trans*-2-arylcyclohexan-1-ols (**103a-g**) in homochiral form. Accordingly, we prepared variously substituted arylcyclohexanols, and their acetates were subjected to CLAP catalyzed hydrolysis to produce the required chiral auxiliaries in homochiral form.

Attracted by medicinal value of (S)-propranolol (1), we attempted its synthesis *via* enzymatically generated precursors **123** & **124**. We synthesized (±)-**123** which upon CLAP catalyzed hydrolysis produced (R)-N-ethoxycarbonylpropranolol in 40% optical purity. Then we have subjected the racemic **124** to PLAP catalyzed hydrolysis which produced the required molecules in 46% optical purity.

We have attempted the synthesis of 5-hexadecanolide (**104**), pheromone of oriental hornet, *Vespa orientalis*, *via* enzymatically produced cyclopetanol, **126**. Unfortunately the required cyclopentanol was obtained only in 42% optical purity from PLAP catalyzed hydrolysis of corresponding acetate, (±)-**126a**. We have

also attempted the synthesis of optically active (*cis*-6-methyl-tetrahydropyran-2-yl)acetic acid (105), a constituent of secretion of civet cat, *Viverra civetta*. We identified three molecules, 130, 132 & 136 as potential chiral precursors. We thought of generating these precursors *via* enzymatic hydrolysis of corresponding acetates of racemic alcohols. Unfortunately, enzymatic (PLAP/CLAP) hydrolysis of acetates of 130, 132, 136 gave only racemic products.

The third chapter deals with the experimental procedures along with the spectral data and physical constants (m.p., b.p. & optical rotations). Determination of enantiomeric purities of the compounds is also described in detail.

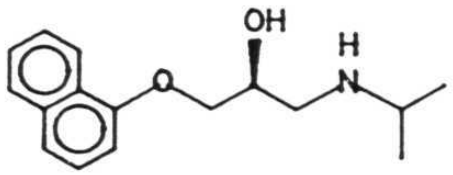
INTRODUCTION

The synthesis of optically active compounds has been a challenging area of organic synthesis with a long history.[1] In 1848, it was for the legendary Louis Pasteur[2] to carry out the first resolution of a racemate into enantiomers and to recognize subsequently, that "optical activity is a consequence of molecular asymmetry". He also developed the two important methods, diastereomer crystallization and fermentation which are still used for the industrial-scale resolution of racemates.

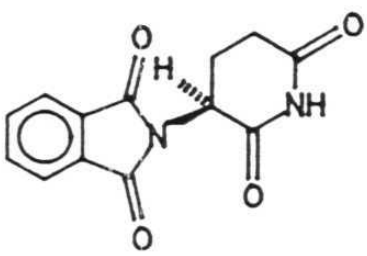
In recent years, interest in the synthesis of optically active compounds in homochiral form has gained new impetus as a consequence of ever increasing awareness about the importance of optical purity in the context of biological activity[3]. Several biologically active molecules, such as pharmaceuticals,[4] food additives, agrochemicals,[5] etc., are often chiral molecules.

Several chiral drug molecules exhibit different biological activity within their enantiomer pairs. For example, the (S)-enantiomer of the drug propranolol (1), which is used to treat hypertension, has 100 times of β-adrenergic activity of the (R)-enantiomer.[3] Similarly, the (R)-enantiomer of thalidomide is a drug used for morning sickness while the (S)-enantiomer 2 is teratogenic.[6] Such a phenomenon of property differentiation within enantiomer pairs is also exhibited by food additives and agrochemicals. For

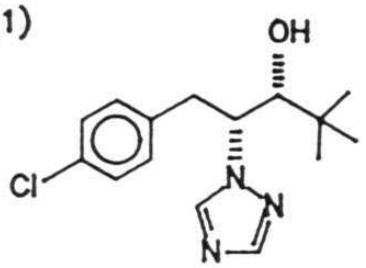
example both enantiomers of sucrose are equally sweet, but only the naturally occuring D-enantiomer is metabolized, making the synthetic L-enantiomer a potential dietary sweetener. Similarly, the (2R,3R)-enantiomer of paclobutrazol (3) is a fungicide while the (2S,3S)-enantiomer acts as a plant growth regulator.[3]



(S) – Propranolol (1)



(S) – Thalidomide (2)



(2R, 3R) – Paclobutrazol (3)

This emergence of chirality as one of the key issues in pharmaceutical[4] and agrochemical[5] research has led to a flurry of activity among synthetic organic chemists. Consequently, asymmetric synthesis,[7] once thought to be a rather esoteric subject, has become a major field of activity in both academic and industrial laboratories all over the world. Research over the last twenty years has resulted in great advances in developing efficient and economic methods for the synthesis of a variety of optically active compounds. The arsenal of synthetic organic chemists has now become very rich in chiral building blocks and methods for their preparation and elaboration.

The biocatalytic approach,[8] in particular, has recently emerged as a major tool for the synthesis of homochiral compounds with enzymes being increasedly recognized as potential chiral catalysts. Consequently, biocatalysis in organic synthesis has become a well-defined area of research. The field is served by a steady stream of monographs,[9] reviews[10-18] and specialist conferences[19-22].

Enzymes have become highly attractive catalysts mainly due to their high stereospecificity, regioselectivity, broad substrate specificity and ability to work under mild conditions.[23] Moreover, enzymes are versatile and catalyze a broad spectrum of reactions. There is an enzyme catalyzed equivalent for most types of organic reactions with few exceptions such as Diels-Alder reaction and Cope rearrangement.

The native enzymes can be modified to suit the requirements *via* immobilization,[24] chemical modification of active site[25] and site-directed mutagenesis[26] that may result in increased operational stability and change in stereoselectivity. With the advent of monoclonal antibodies, it has become possible to synthesize artificial enzymes, the abzymes or catalytic antibodies, that have been shown to catalyze required reactions in stereoselective manner.[27]

Applications of enzymes for synthesis of optically active molecules and other organic transformations have been of current interest with rich literature. As it is not possible to review

all the bibliographic material, some selective examples, that represent fundamental contributions and describe current status of the field, were chosen to illustrate the importance of enzymes in organic synthesis.

Enzymes are conventionally classified into six groups based on the type of reaction they catalyze: Oxidoreductases, transferases, hydrolases, lyases, isomerases and ligases. Oxidoreductases and hydrolases are the most widely used enzymes for the preparation of optically active molecules. Esterhydrolases[17] are of particular interest since they do not require expensive cofactors. Recent work of Klibanov[18] on the utility of these enzymes in organic media has made esterhydrolases more popular among organic chemists. These esterhydrolases have been employed for synthesis of enantiomerically enriched molecules *via*

(1) enantioselective hydrolysis of prochiral (or meso diesters) and esters of racemic carboxylic acids and acylated racemic alcohols.

(2) enantioselective esterification of racemic carboxylic acids and acylation of racemic alcohols.

(3) enantioselective transesterification of prochiral (or meso) diols, racemic alcohols and esters.

A large number of reports describing the applications of esterhydrolases to organic synthesis have appeared in literature. Since the thesis deals with the synthesis of optically active

molecules *via* hydrolysis of racemic esters, emphasis has been made for hydrolytic reactions catalyzed by esterhydrolases.

Several commercially available esterases and lipases have been employed for this purpose. Some of the more frequently used among those are:

Pig liver esterase (PLE)	Porcine pancreas lipase (PPL)
Horse liver esterase (HLE)	*Candida cylindracea* lipase (CCL)
Bacillus subtilis lipase	*Asperigillus niger* lipase (ANL)
Pseudomonas sp. lipase (PSL)	*Pseudomonas cepacia* lipase (PCL)
Pseudomonas AK lipase(Lipase AK)	*Pseudomonas* sp. SAM II lipase

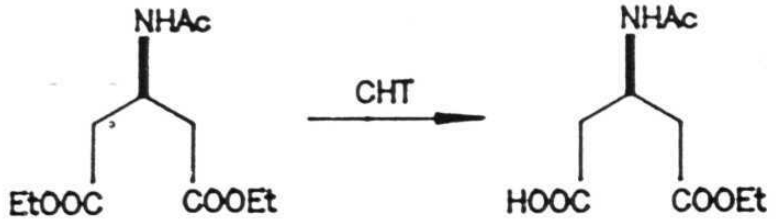
Among these pig liver esterase[28,29] is certainly the most widely used esterase for the synthesis of enantiomerically enriched compounds. PLE was employed as a catalyst for the kinetic resolution of mandelic acid ester by Dakin as early as in 1903.[30]

Enantioselective hydrolysis of prochiral diesters and diacyl prochiral diols:

Prochiral diesters:

Several esterases and lipases such as PLE, PPL, PFL, etc., are capable of catalyzing enantiotopically specific hydrolysis of prochiral diesters. One of the oldest reaction of this type is due to Cohen *et al.*[31] They showed that α-chymotrypsin (CHT) catalyzes the hydrolysis of diethyl β-acetamidoglutarate (**4a**) in enantiospecific manner resulting in the production of (R)-ethyl-

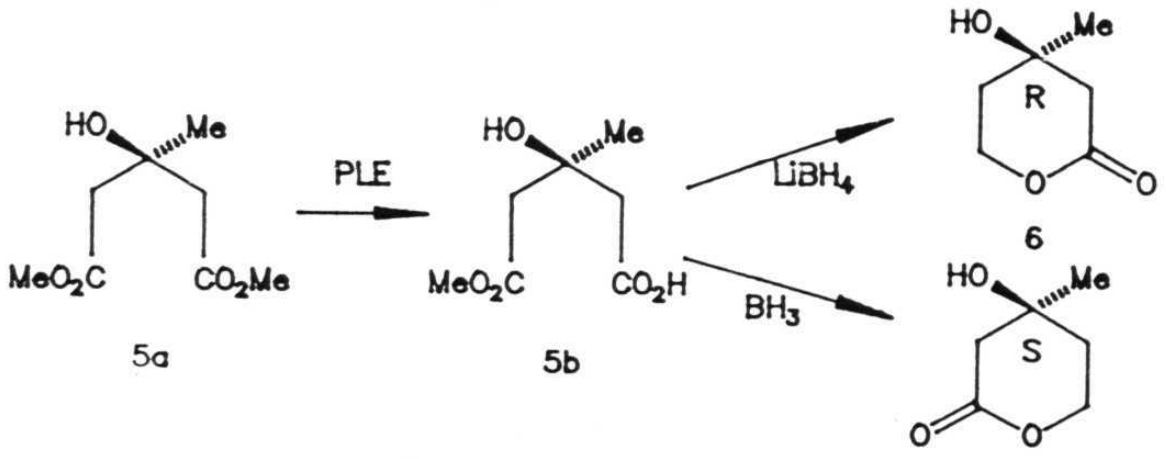
hydrogen β-acetamidoglutarate (4b) in optically pure form (Eq. 1).



4a (R)–4b (1)

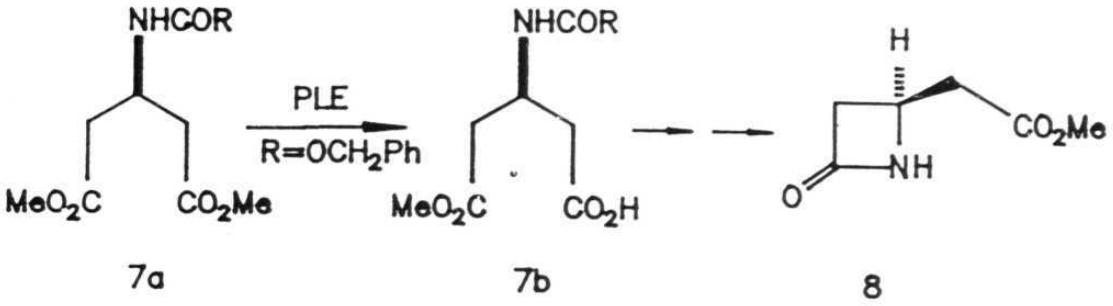
Later in 1975, Sih and coworkers[32] reported PLE catalyzed enantiospecific hydrolysis of dimethyl β-hydroxy-β-methylglutarate (5a) to produce (S)-hydrogen-methyl β-hydroxy-β-methylglutarate (5b) in 99% enantiomeric excess, which was subsequently transformed into either enantiomer of mevalonolactone (6) (Scheme 1).

SCHEME 1:



Ohno and coworkers [33]employed PLE for asymmetric hydrolysis of dimethyl β-acylaminoglutarate (7a) which gave (S)-half ester 7b in 93% enantiomeric excess. The (S)-7b was subsequently converted into the azetidinone 8, a versatile precursor for carbapenem antibiotics (Scheme 2).

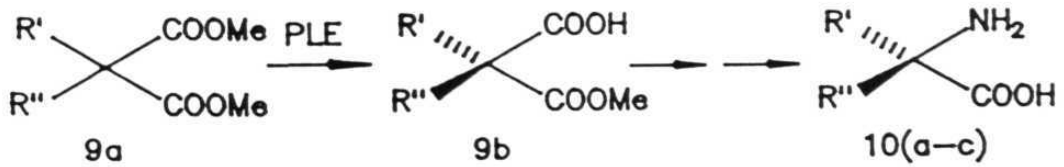
SCHEME 2:



7a 7b 8

In 1984, Schneider *et al.*[34] reported the enantioselective synthesis of monoalkyl malonates (9b) with 8-86% enantiomeric purity *via* PLE-catalyzed hydrolysis of corresponding diesters (9a). Later, Norin *et al.*[35] studied the effect of size of substituent on the enantioselectivity of PLE-catalyzed hydrolysis of dialkylated propanedioic acid esters (9a). They have also synthesized optically pure (S)-α-methylphenylalanine (10a, R' = benzyl, R" = Me), (S)-α-methyltyrosine (10b, R'= 4-hydroxybenzyl, R" = Me) and (S)-α-methyl-3,4-dihydroxyphenylalanine (10c, R' = 3,4-dihydroxybenzyl, R" = Me) employing 9b as chiral synthons (Scheme 3).[36]

SCHEME 3:

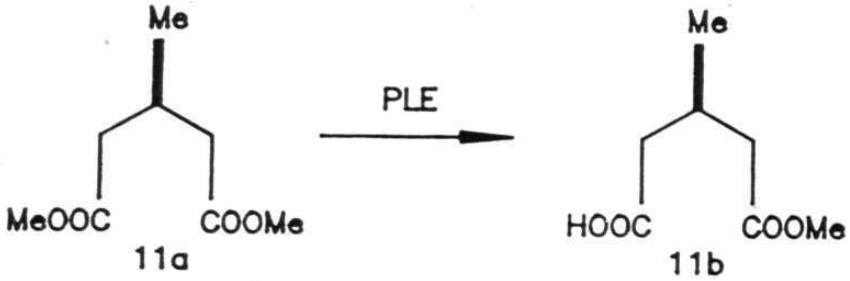


9a 9b 10(a–c)

R' = alkyl or aryl, R" = ethyl or methyl

Jones *et al.*[37] studied the effect of reaction conditions on stereoselectivity of PLE catalyzed hydrolysis of dimethyl β-methylglutarate (11a) in detail (Eq. 2). Later, Ohno *et al.*[38] reported

a similar study on the effect of size of acyl group of β-acylaminoglutarate (7a) on stereoselectivity of PLE catalyzed hydrolysis.



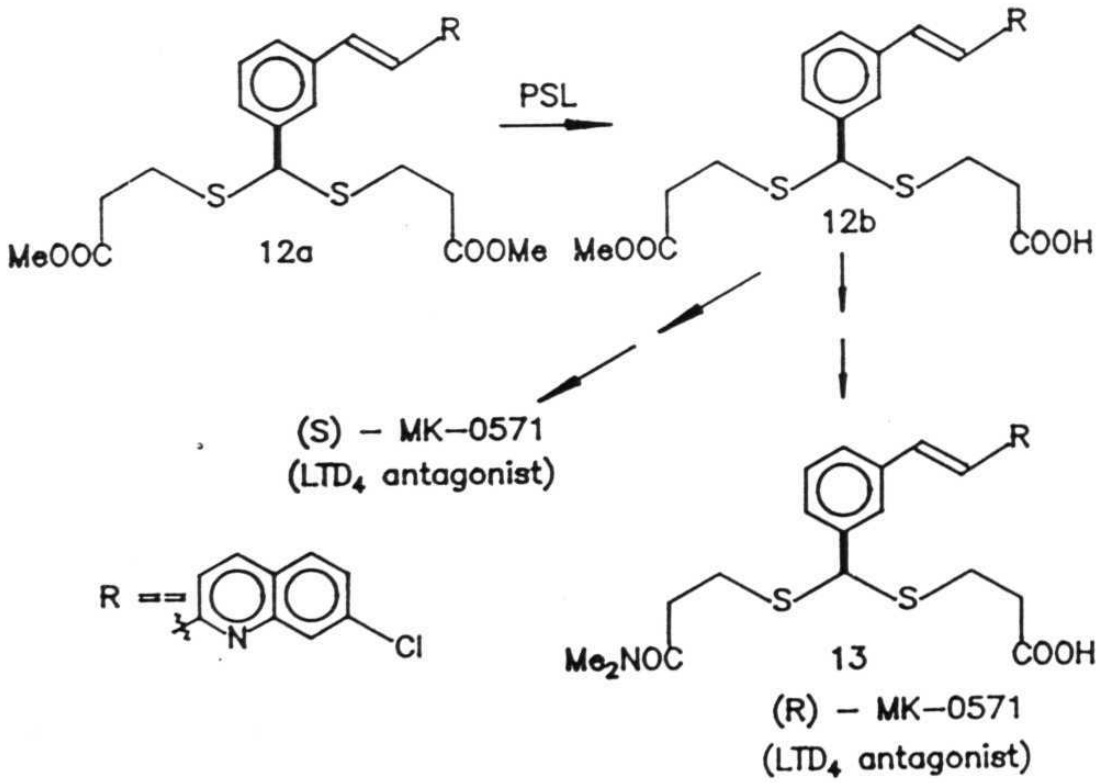
(2)

At + 20°C, pH = 7.0, MeOH = 0%, 79% e.e.

At - 10°C, pH = 7.0, MeOH = 20%, 97% e.e.

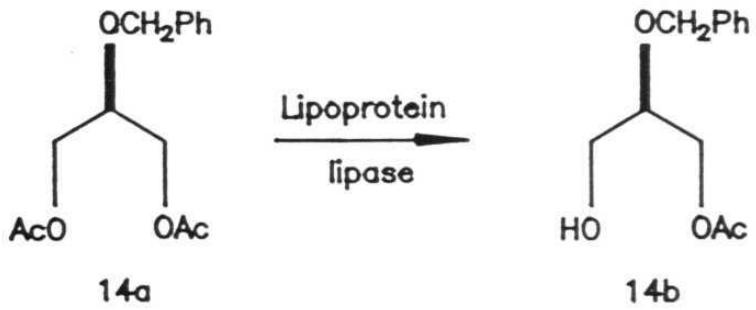
Recently, *Pseudomonas* sp. lipase (PSL) has been successfully employed for asymmetric hydrolysis of diester **12a** to produce the (R)-half ester **12b** in >98% enantiomeric excess which was subsequently transformed into either enantiomer of a potent LTD_4 antagonist 13 (Scheme 4).[39]

SCHEME 4:



Diacyl prochiral diols:

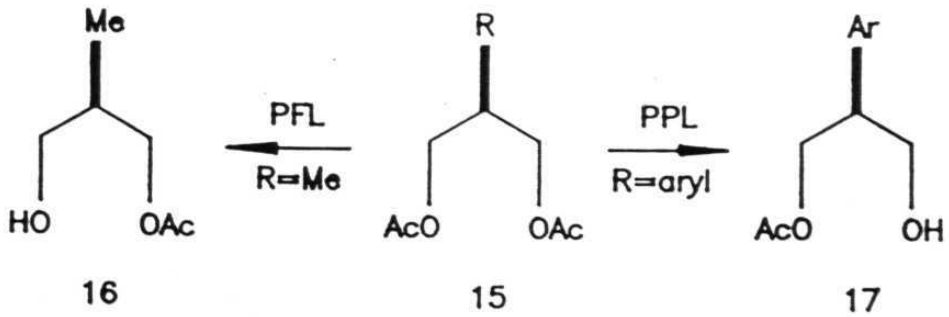
Asymmetric hydrolysis of diacyl prochiral diols catalyzed by esterhydrolases has been a well known method to provide the corresponding optically active monoacyl diols. Schneider *et al.*[40] hydrolyzed the diacetate **14a** with lipoprotein lipase to produce (R)-**14b** in 91% enantiomeric excess (Eq. 3).



14a 14b (3)

Sakai *et al.*[41] reported PFL catalyzed hydrolysis of 2-methyl-1,3-propanediol diacetate (15) (R=Me) to produce (R)-monoacetyl diol 16 in >99% enantiomeric excess. Guanti *et al.*[42] reported PPL catalyzed asymmetric hydrolysis of several 2-aryl-1,3-propanediol diacetates (15) (R=aryl) which gave the (S)-monoacetyl diols 17 in 90-96% enantiomeric excess (Scheme 5).

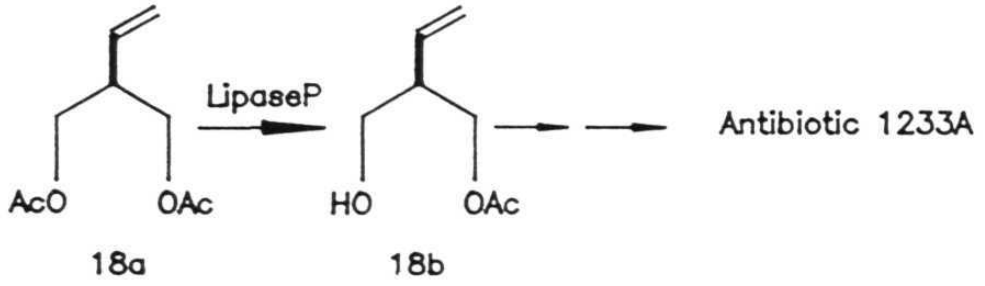
Scheme 5:



16 15 17

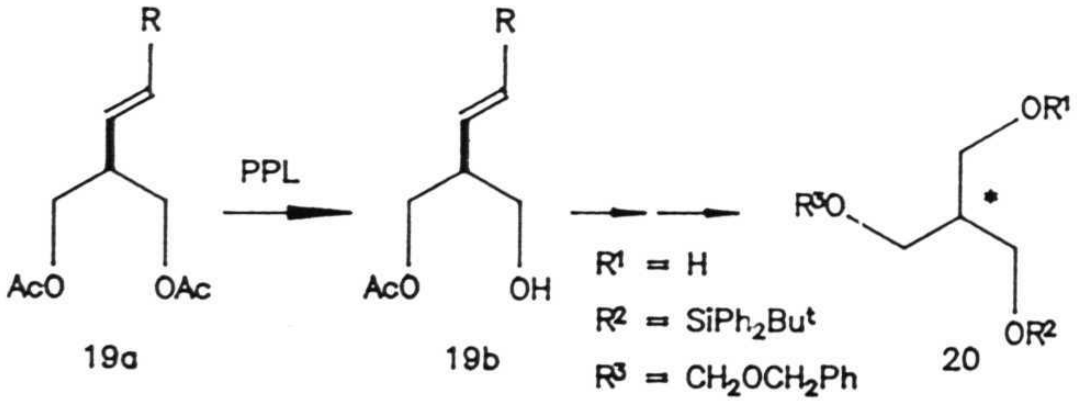
Mori *et al.*[43] employed lipase P for asymmetric hydrolysis of diacetate of 2-vinyl-1,3-propanediol (18a) to provide (R)-18b in 90% enantiomeric excess which is an important synthon for antibiotic 1233A (Scheme 6).

SCHEME 6:



Guanti *et al.*[44] during their studies to prepare new chiral building block, asymmetrized tris(hydroxymethyl)methane(THYM) (20) investigated the asymmetric hydrolysis of a variety of 2-(E)-alkenyl-1,3-propanediol diacetates (19a) catalyzed by PPL to obtain corresponding (E)-alkenyl derivatives 19b with high optical purities (>95%) (Scheme 7). The corresponding 2-(Z)-alkenyl derivatives gave less satisfactory results.

SCHEME 7:



R = n-hexyl, isopropyl, cyclohexyl.

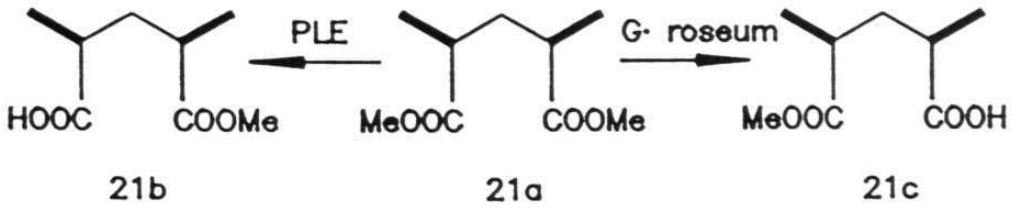
Enantioselective hydrolysis of meso diesters and diacyl meso diols:

Enzymes are now widely recognized as potential catalysts for asymmetric synthesis with their abilities to asymmetrize meso compounds *via* enantiotopic group discrimination. PLE has been the most widely used enzyme for this purpose. Other enzymes that have been employed with considerable success are PPL, PCL, SAM II, etc.

Meso diesters:

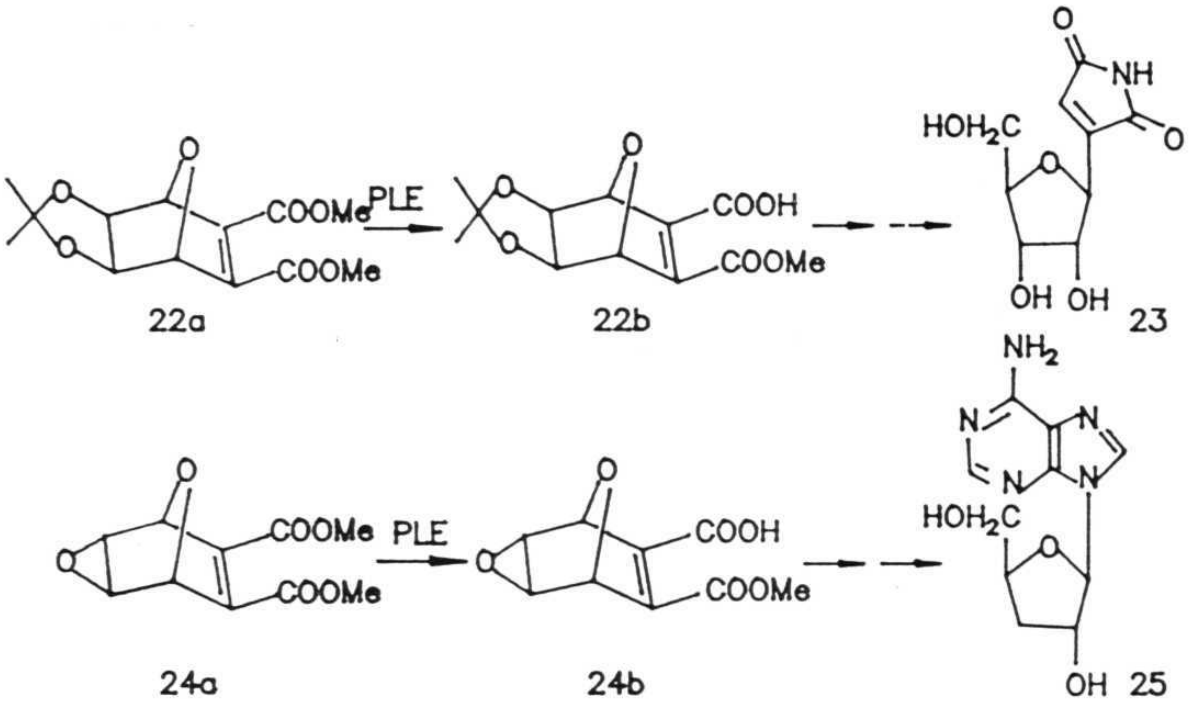
In 1981, Sih and coworkers[45] employed PLE for the first time to asymmetrize a meso diester. They asymmetrized dimethyl cis-2,4-dimethylglutarate (**21a**) *via* enantiotopically specific hydrolysis catalyzed by PLE and *Gliocladium roseum* which produced the half esters **21b** and **21c** in 64% and 98% enantiomeric excess respectively (Scheme 8).

SCHEME 8:

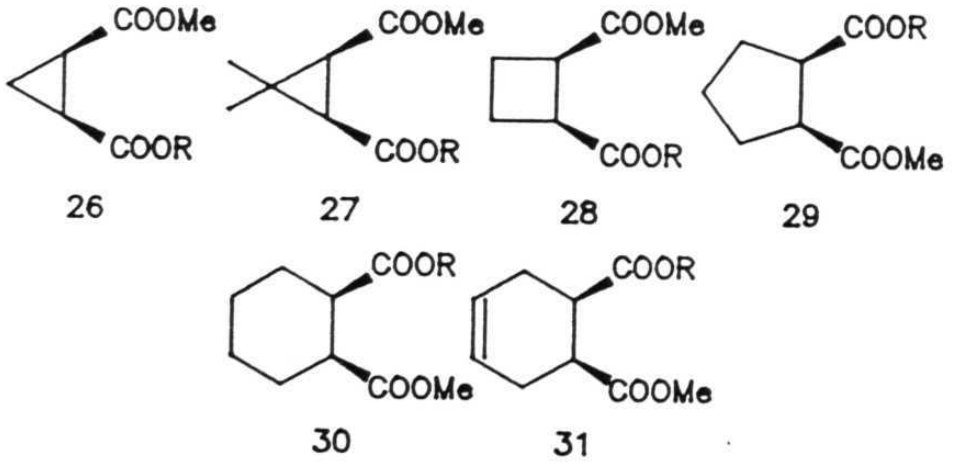


Ohno *et al.*[46] hydrolyzed the tricyclic meso diesters **22a** and **24a** using PLE as catalyst to produce the corresponding optically active mono-acid-esters **22b** and **24b** in 77% enantiomeric excess. The half esters **22b** and **24b** were subsequently converted into nucleosides showdomycin (**23**) and cordycepin (**25**) respectively (Scheme 9).

SCHEME 9:



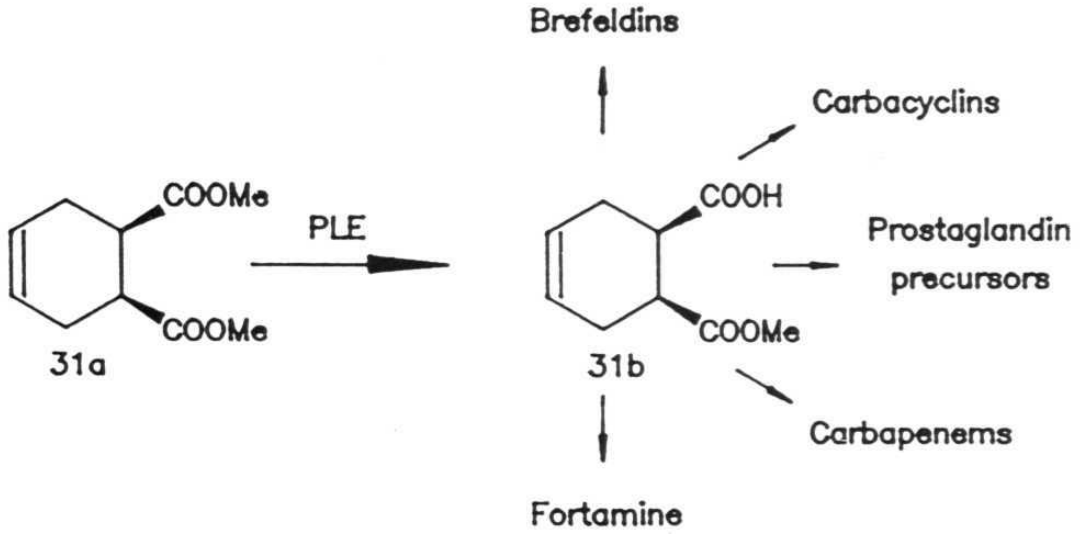
PLE catalyzed asymmetric hydrolysis of cyclic meso diesters **26a-31a** to produce the corresponding optically active half esters **26b-31b** in 9-100% enantiomeric excess was concurrently reported by Tamm *et al.*[47], Schneider *et al.*[48] and Jones *et al.*[49]



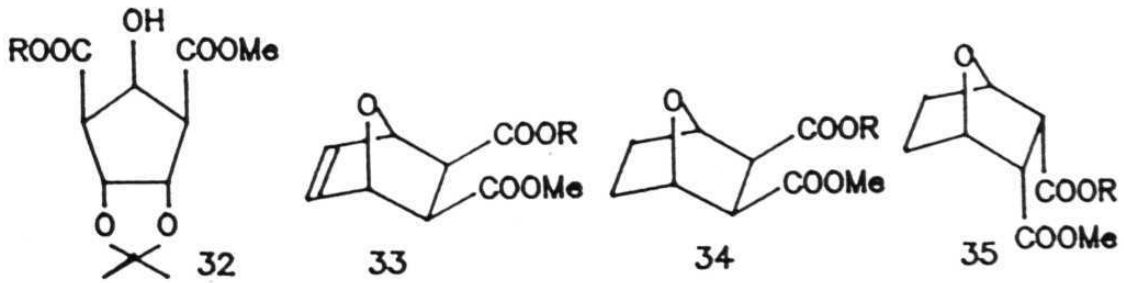
a) R = Methyl, b) R = H

Gais and coworkers[50] have demonstrated the high utility of PLE in large-scale synthesis of homochiral compounds by preparing the half ester **31b** in optically pure form in a mole-scale. The half ester **31b** is used as a chiron in the synthesis of several naturally occurring and biologically active compounds (Scheme 10).

SCHEME 10:



Zemlicka *et al.*[51] obtained the half ester **32b** in 95% enantiomeric excess from PLE catalyzed hydrolysis of meso diester **32a**. Bloch and coworkers[52] reported PLE catalyzed asymmetric hydrolysis of the bicyclic mesodiesters **33a-35a** which gave the corresponding half esters **33b-35b** in >97% enantiomeric excess.

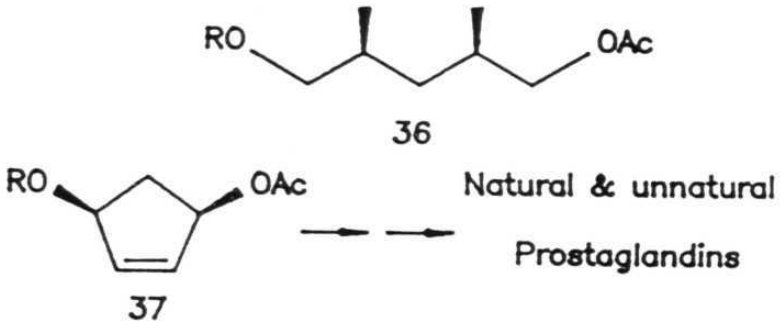


a) R = Methyl, b) R = H

Diacyl meso diols:

Sih and coworkers[53] described asymmetric hydrolysis of meso diacetates **36a** and **37a** catalyzed by PLE to produce the corresponding mono acetates **36b** and **37b** in about 80% enantiomeric excess. Later, Schneider *et al.*[54] showed PPL to be ideal enzyme for the asymmetric hydrolysis of **37a**, after screening several enzymes. The mono acetate **37b** is very valuable chiron for the synthesis of prostaglandins (Scheme 11).

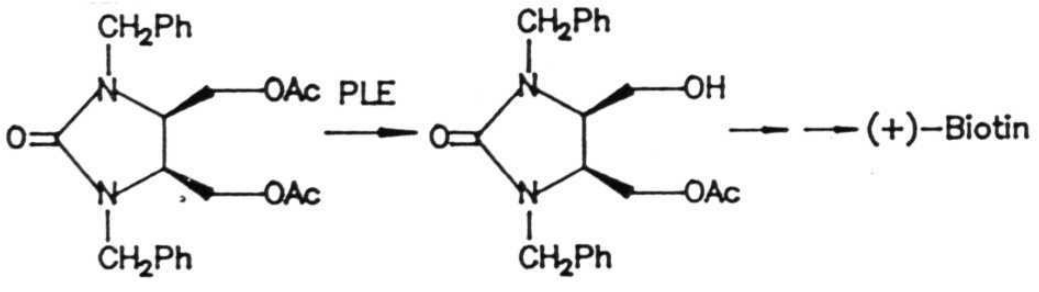
SCHEME 11:



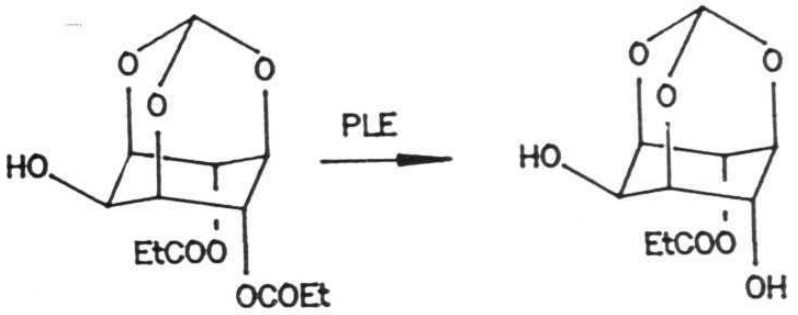
a) R = Ac, b) R = H

Wang and Sih[55] synthesized (+)-biotin in homochiral form starting from the optically active monoacetate **38b**, which in turn was obtained from PLE catalyzed enantioselective hydrolysis of corresponding diacetate 38a (Scheme 12).

SCHEME 12:

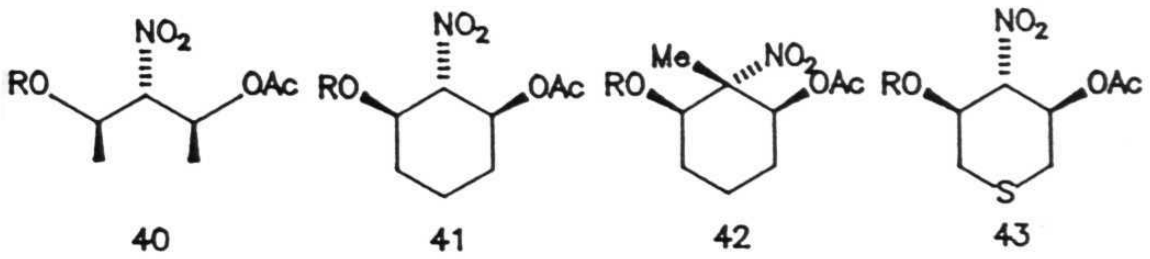


Vasella *et al.*[56] sucessfully asymmetrized the meso dipropionate **39a** *via* PLE catalyzed enantioselective hydrolysis which produced the optically active monopropionate **39b** in 95% enantiomeric excess (Eq. 4).

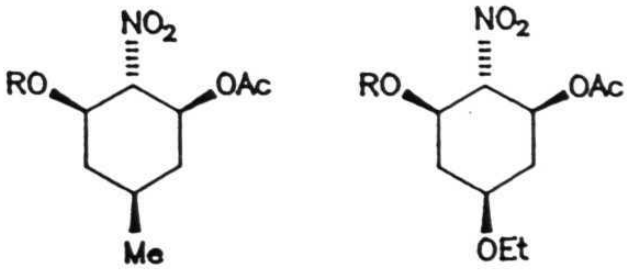


39a **39b** (4)

Seebach and coworkers[57] successfully employed pig liver acetone-methylenechloride powder (PLAMP), a crude form of PLE, for asymmetric hydrolysis of a variety of acyclic and cyclic meso 2-nitro-1,3-diols **40a-45a** to produce the corresponding optically active monoacetates **40b-45b** in 90->97% enantiomeric excess.



40 **41** **42** **43**

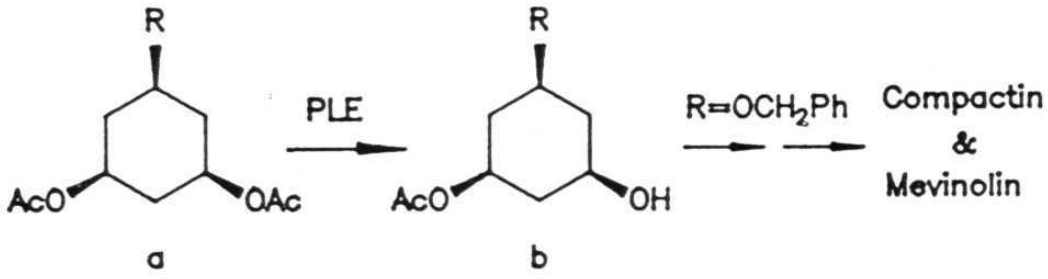


44 **45**

a) R = Ac
b) R = H

Vandewalle *et al.*[58] recently reported PLE catalyzed asymmetric hydrolysis of the meso diacetates **46a** and **47a**, which produced the monoacetates **46b** and **47b** in 95% and 80% enantiomeric excesses respectively. The monoacetate **47b** is a precursor for compactin and mevinolin (Scheme 13).

SCHEME 13:



46) R = CH_2OCH_2Ph, 47) R = OCH_2Ph

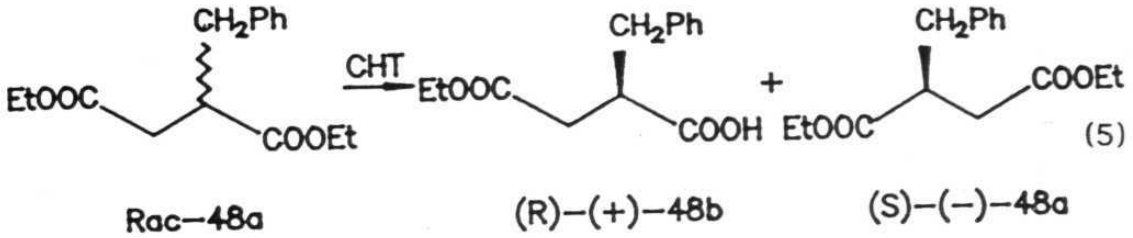
Enantioselective hydrolysis of racemic esters and acylated racemic alcohols:

The potential of esterhydrolases as catalysts for kinetic resolution of racemic carboxylic acids and alcohols *via* enantioselective hydrolysis of their esters has been well exploited. Several commercially available esterases, lipases and proteases have been employed for this purpose. Prominent among them are PLE, PPL, PSL, PCL, CCL, ANL, HLE, lipase p 30, SAM II, chymotrypsin, etc.

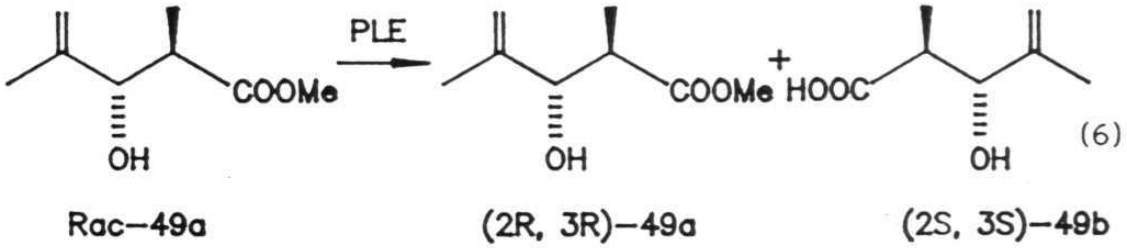
Racemic carboxylic acid esters:

In 1968, Cohen and Milovanovic[59] described a highly efficient kinetic resolution of diethyl α-benzylsuccinate (**48a**). They

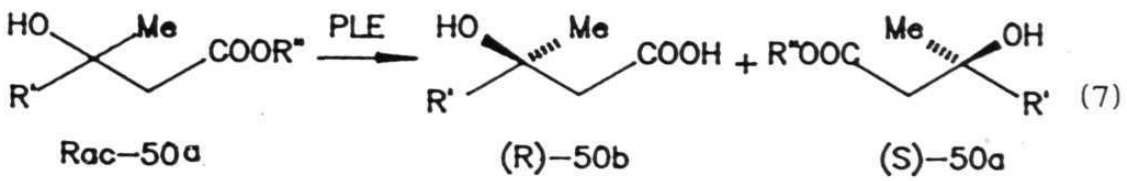
subjected the racemic diester **48a** to the α-chymotrypsin catalyzed enantioselective hydrolysis and obtained the half ester (R)-**48b** and (S)-**48a** in very high optical purities (Eq. 5).



In 1982, Sih *et al.*[60] reported kinetic resolution of racemic hydroxy ester **49a** *via* PLE catalyzed hydrolysis (Eq. 6).



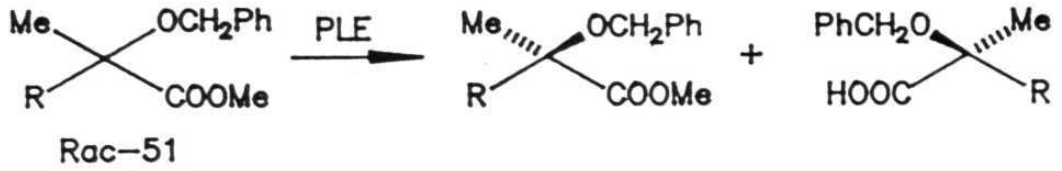
Morrow *et al.*[61] resolved several racemic β-hydroxy-β-methyl alkanoic acid esters **50a** to produce optically active acids (R)-**50b** and (S)-**50a** in 22-98% enantiomeric excess *via* PLE catalyzed hydrolysis (Eq. 7).



R' = CH_2CH_3, n-C_6H_{11}, CH_2CH_2OH, $CH_2CH_2OCH_2Ph$, $CH_2CH(OMe)_2$

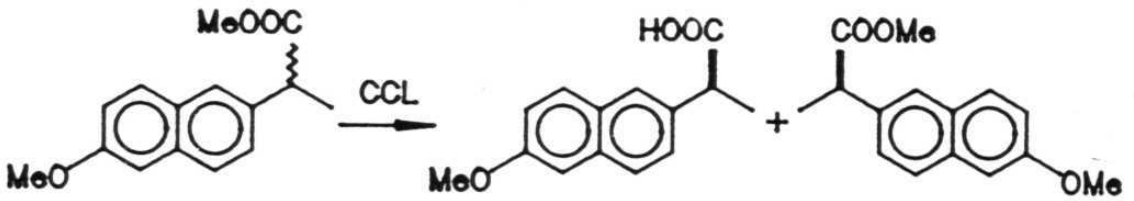
R" = Methyl or ethyl

Ohta *et al.*[62] employed PLE for resolution of several racemi α-benzyloxy-α-methylalkanoic acid esters (51) and obtained th corresponding optically active acids and esters in 60-99 enantiomeric excess (Eq. 8).



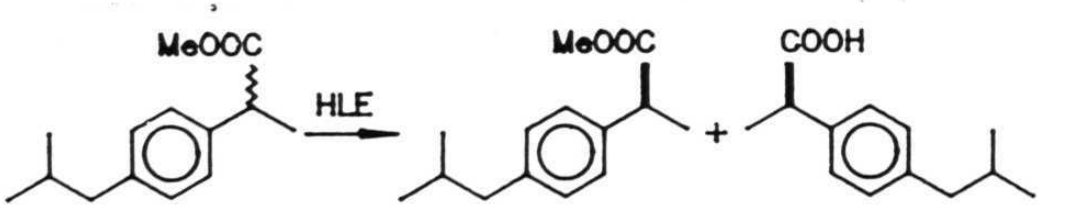
Rac–51 (8)

Sih *et al.*[63] prepared (S)-naproxen (52b)in 98% enantiomeri excess *via* CCL catalyzed enantioselective hydrolysis o corresponding racemic methyl ester 52a (Eq. 9).



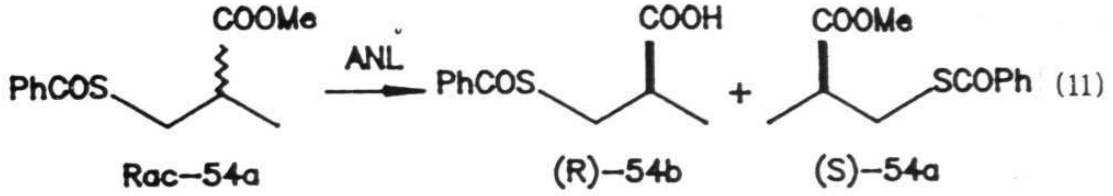
Rac–52a (S)–naproxen (52b) (R)–52a (

Bloch and coworkers[64] described efficient resolution several α-arylpropionic acids *via* HLE catalyzed hydrolysis their methyl esters. They prepared methyl ester of (S)-ibupro (53a) in >96% enantiomeric excess (Eq. 10).



Rac–53a (S)–53a (R)–ibuprofen (53b) (

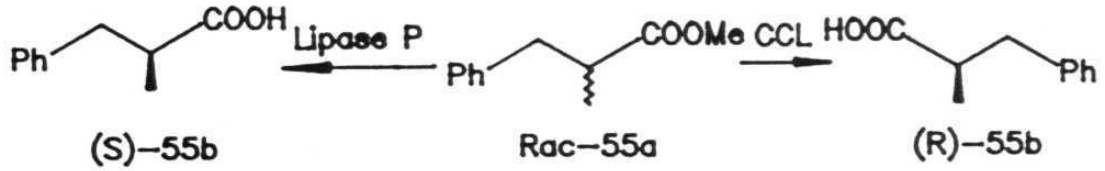
Sih and coworkers[65] utilized ANL as catalyst for enantioselective hydrolysis of racemic ester **54a** to produce the acid (R)-**54b** in 98% enantiomeric excess (Eq. 11).



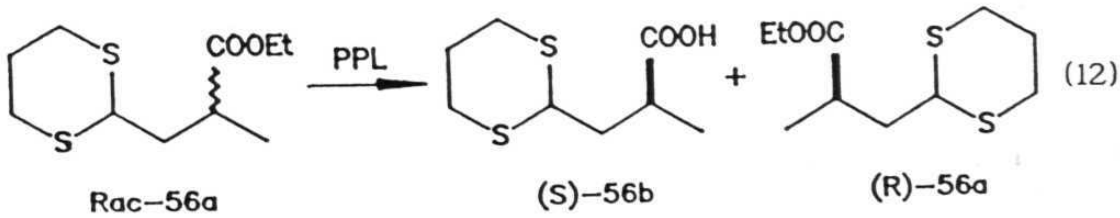
(11)

Delinck and Margolin[66] obtained both (S)- and (R)-acids **55b** with high enantiomeric excess from lipase P and CCL catalyzed hydrolyses of racemic **55a** respectively (Scheme 14).

SCHEME 14:

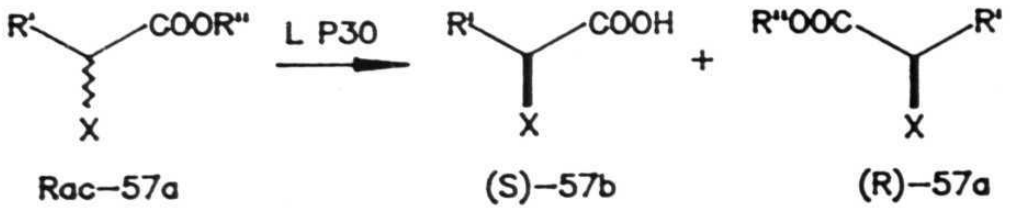


Recently Sih and Gu[67] reported kinetic resolution of racemic ester **56a** *via* PPL catalyzed enantioselective hydrolysis to produce optically pure (S)-**56b** and (R)-**56a** (Eq. 12).



(12)

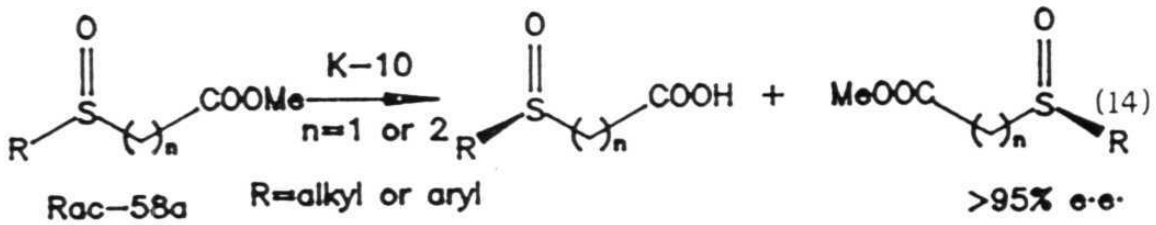
Kalaritis and coworkers[68] described enantioselective hydrolysis of alkyl esters of several racemic α-substituted alkanoic acids **57a** catalyzed by lipase P 30. They recovered the unhydrolyzed esters in 93-99% enantiomeric excess (Eq. 13).



(13)

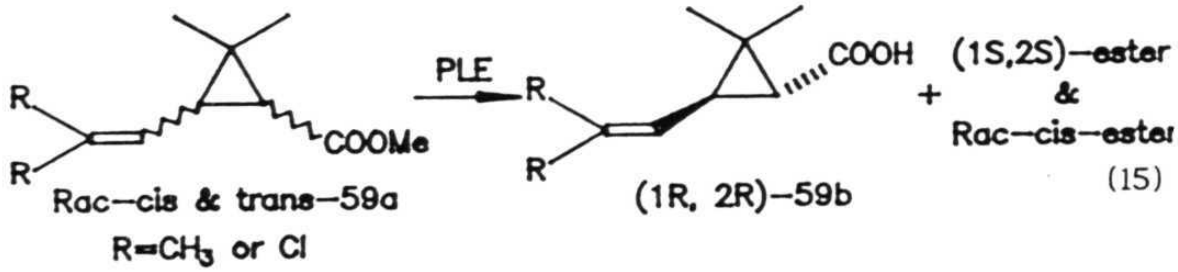
R = n-butyl, CH_2CH_2Ph; R'' = Me or Et; X = F, Br, OH

Recently, Burgess *et al.*[69] carried out resolution of several methyl sulfinyl acetates and propionates 58a *via* enantioselective hydrolysis catalyzed by *Pseudomonas* K-10 lipase. They obtained the recovered esters in >95% enantiomeric excess (Eq. 14).



(14)

Schneider *et al.*[70] reported the PLE catalyzed stereoselective hydrolysis of cyclopropane esters 59a. PLE hydrolyzes only *trans*-1R-esters to produce the corresponding (1R, 2R) acids 59b in moderate enantiomeric excesses (Eq. 15).

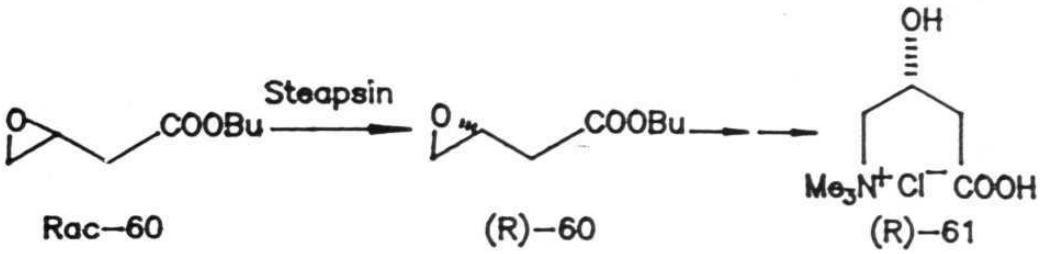


(15)

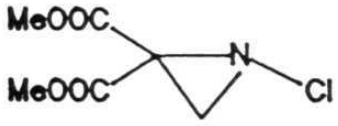
Francalanci *et al.*[71] employed steapsin for enantioselectiv hydrolysis of racemic n-butyl β,γ-epoxybutyrate (60) whic produced the unreacted ester (R)-60 in >95% enantiomeric excess

This (R)-epoxybutyrate 60 was converted into (R)-carnitine chloride (61) (Scheme 15).

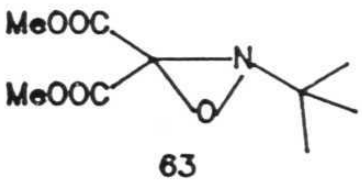
SCHEME 15:



Recently, Moretti *et al.*[72] prepared optically active diesters 62 and 63 (whose chirality is only due to trivalent nitrogen atom) in 76 and 87% enantiomeric excesses *via* enantioselective hydrolysis of the corresponding racemic diesters catalyzed by lipase from *Rhizopus delemer* and PPL respectively.

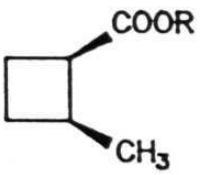


62

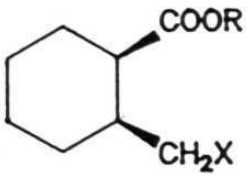


63

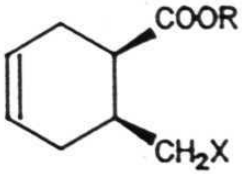
Quite recently, Jones and Toone[73] have reported an efficient synthesis of optically active esters and acids 64-66 in >97% enantiomeric excess *via* enantioselective hydrolysis of the corresponding racemic esters using PLE.



64



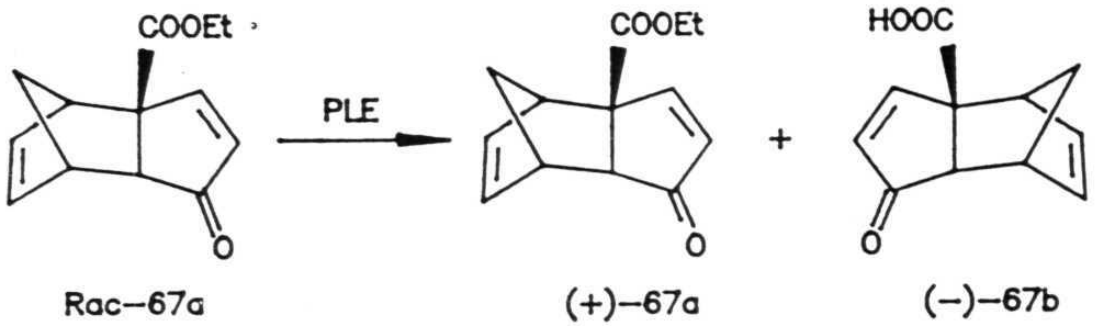
65



66

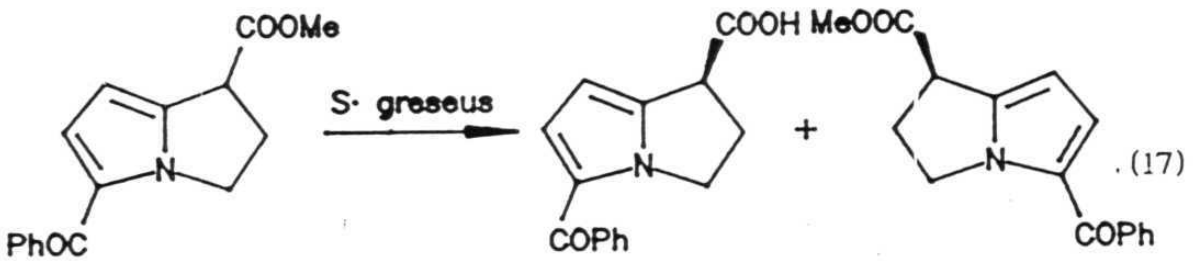
R = Me or H, X = Br or H

Zwanenburg *et al.*[74] synthesized the acid, (-)-67b in homochiral form *via* PLE catalyzed enantioselective hydrolysis of racemic ester 67a (Eq. 16).



Rac–67a (+)–67a (–)–67b (16)

Sih and Fulling[75] reported enantioselective hydrolysis of racemic ketorolac acid ester (68a) catalyzed by protease from *Streptomyces greseus* to produce both acid 68b and unreacted ester, 68a, in >96% enantiomeric excess (Eq. 17).



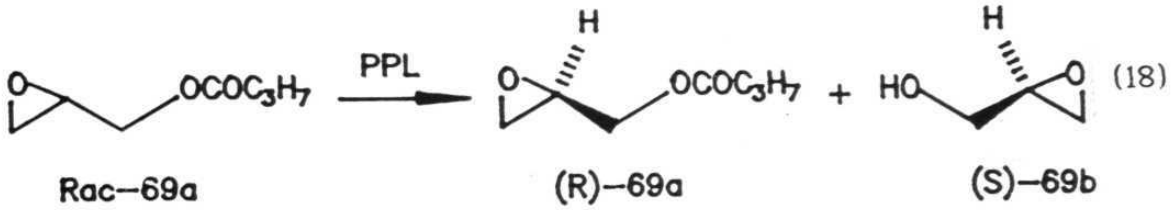
Rac–68a (S)–68b (R)–68a (17)

Acylated racemic alcohols:

Biocatalytic kinetic resolution of racemic alcohols *via* enantioselective hydrolysis of their acyl derivatives using esterhydrolases as catalysts has become a major tool for the synthesis of homochiral alcohols. Several commercially available esterhydrolases such as PLE, PPL, PFL, CCL, lipase P, lipase P 30 SAM II, etc., are capable of catalyzing the hydrolysis in enantio-

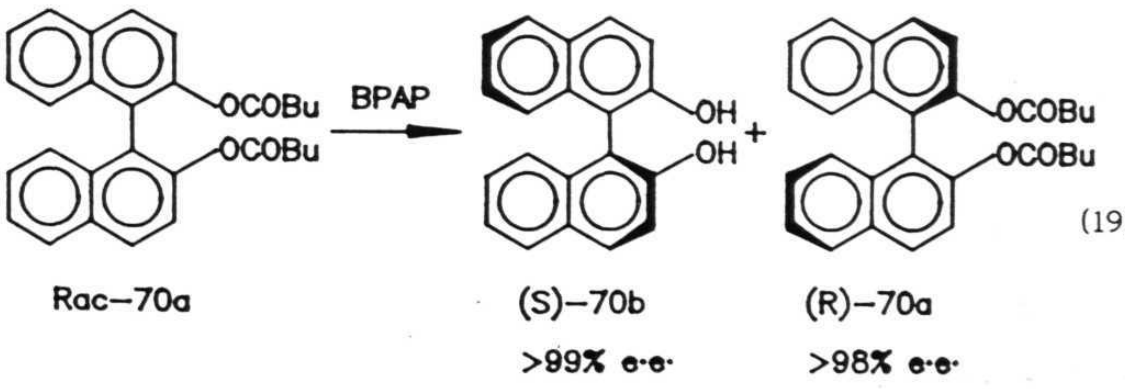
selective manner.

Whitesides and Ladner[76] reported PPL catalyzed enantioselective hydrolysis of several acylated epoxyalcohols. They obtained (R)-(-)-glycidyl butyrate (69a), a versatile chiron, in 92% enantiomeric excess (Eq. 18).



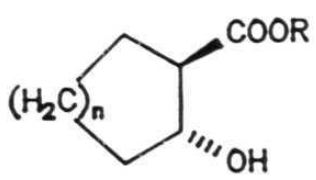
(18)

Ikekawa and coworkers[77] reported resolution of binaphthol *via* enantioselective hydrolysis of various dialkanoates of binaphthol catalyzed by *Bacillus* sp. L-75 which produced the diol and diester in high enantiomeric excess. Subsequently, Kazlauskas[78] reported a practical synthesis of both enantiomers of binaphthol *via* bovine pancreas acetone powder (BPAP) catalyzed hydrolysis of divalerate of (±)-binaphthol (70a) (Eq. 19).

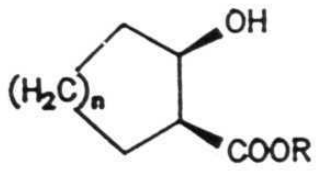


(19)

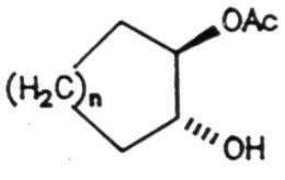
Sakai and coworkers[79,80] showed that PCL catalyzed hydrolysis of several racemic acetates of substituted cycloalkanols produced with very high enantioselectivity. The cycloalkanols 71-73 were obtained in >99% enantiomeric excess.



71



72

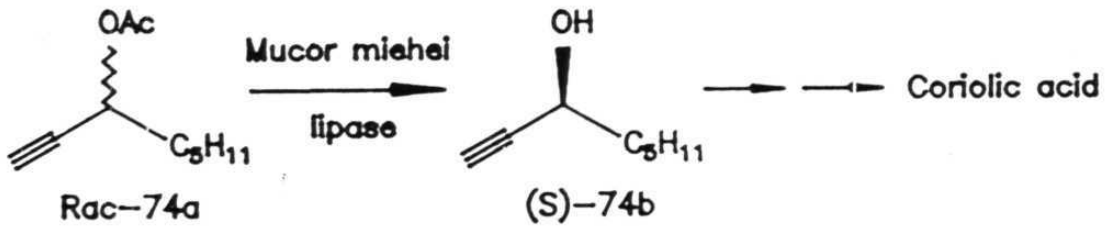


73

n = 1, 2, 3; R = Me or Et; E.e. = 99%

Roberts *et al.*[81] reported enantioselective hydrolysis of acetate of racemic oct-1-yn-3-ol (74a) catalyzed by *Mucor miehei* lipase producing (3S)-oct-1-yn-3-ol (74b) in 80% enantiomeric excess which was subsequently transformed into coriolic acid, an antifungal agent (Scheme 16).

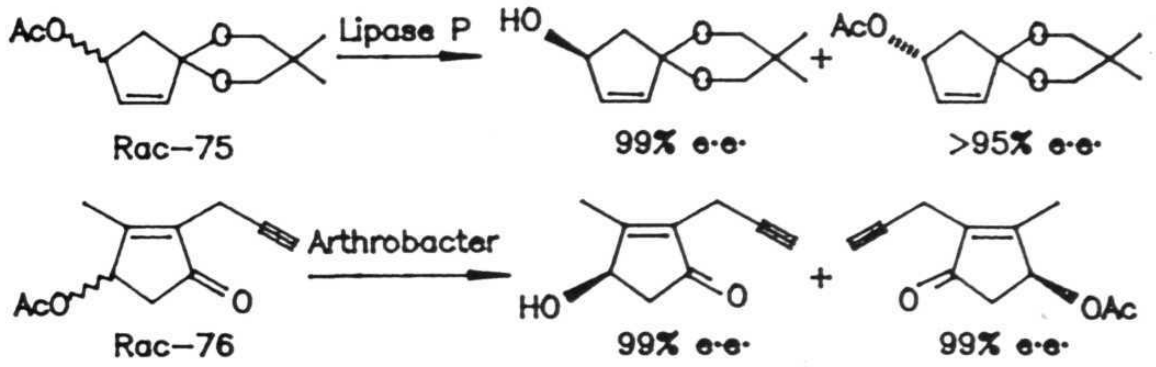
Scheme 16:



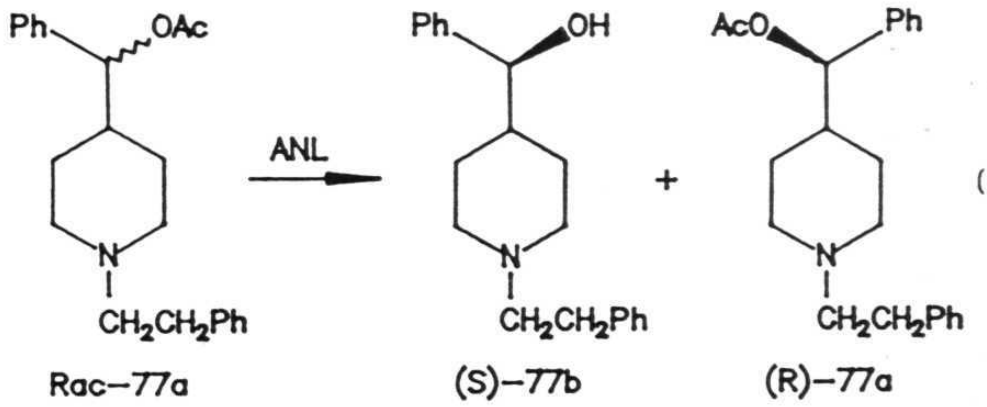
Rac–74a (S)–74b

The racemic cyclopentenyl acetates 75 and 76 were resolved *via* enantioselective hydrolysis catalyzed by lipase P[82] and *Arthrobacter* lipase[83] respectively, producing the corresponding alcohols and recovered esters in homochiral form (Scheme 17).

SCEHEME 17:

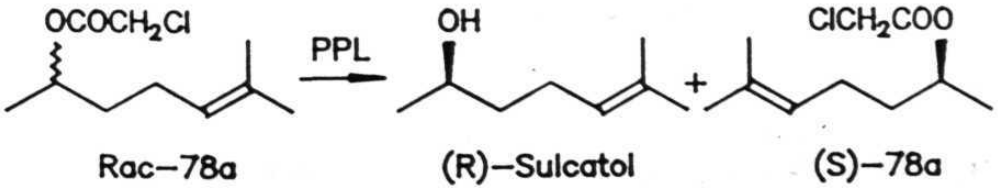


Recently, Nieduzak and Carr[84] reported the synthesis of antiarrhythmic agent **77b** *via* enantioselective hydrolysis of corresponding racemic acetate **77a** catalyzed by ANL (Eq. 20).



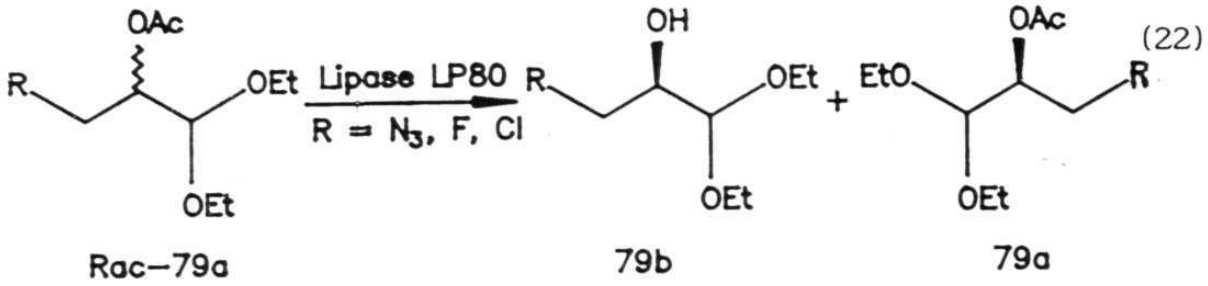
(20)

Liang and Paquette[85] described PPL catalyzed enantioselective hydrolysis of chloroacetate of racemic sulcatol **78a** which produced unreacted chloroacetate (S)-**78a** in homochiral form (Eq.21).



(21)

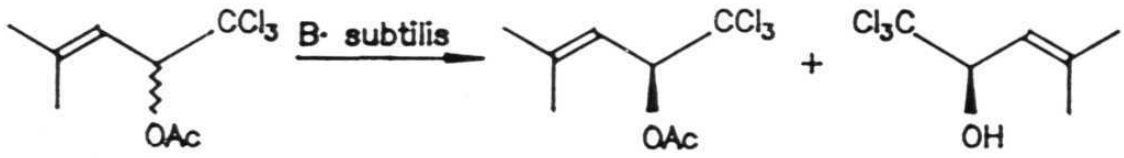
Wong and coworkers[86] developed a chemoenzymatic route to optically pure versatile chiral synthons **79(a & b)** using lipase LP-80 as catalyst for enantioselective hydrolysis (Eq. 22).



(22)

Rac–79a 79b 79a

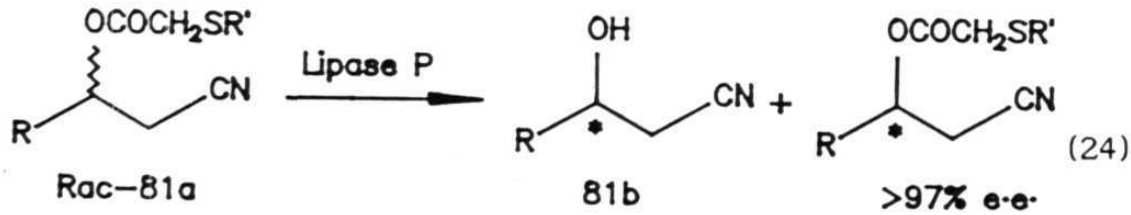
Recently, Muljiani *et al.*[87] reported *Bacillus subtilis* mediated enantioselective hydrolysis of racemic-**80a**, which produced the desired alcohol 80b in >98% enantiomeric excess (Eq. 23).



(23)

Rac–80a (S)–80a (R)–80b

Itoh *et al.*[88] reported enzymatic resolution of racemic esters **81** *via* enantioselective hydrolysis catalyzed by lipase P, which gave the unreacted esters in >97% enantiomeric excess (Eq. 24).



(24)

Rac–81a 81b >97% e.e.

R = CH_3, Ph, CH_2CH_2Ph, CH=CHPh, R' = CH_3, Ph

Esterification and transesterification:

The discovery[89,90] of the fact that lipases retain their catalytic activity in organic media of low water content (<1%) has great impact on the field of biotransformations. These lipase catalyzed reactions in organic media[18] have become very important biotransformations for the production of enantiomerically enriched compounds.

The effect of various solvents on the stereoselectivity of lipases[91-93] continues to be an interesting aspect of these biotransformations. Various solvents used for lipase catalyzed reactions are hydrocarbons (hexane, heptane, toluene, etc.) ethers (diethyl ether, diisopropyl ether, etc.), DMSO, DMF, pyridine, etc. As the literature is very vast it is very difficult to cover all the aspects, we have chosen few selected examples to indicate the importance of this class of biotransformations.

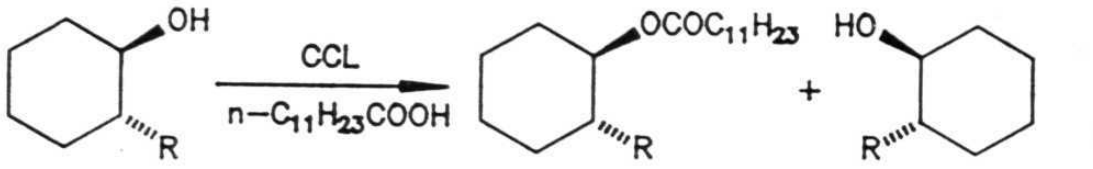
Direct esterification of carboxylic acids and alcohols:

In 1985, Klibanov and coworkers[94] reported direct esterification of various racemic α-haloacids **82a** with n-butanol in hexane catalyzed by CCL which resulted in production of optically active (R)-esters and (S)-acids (Eq. 25).

$$\underset{\text{Rac-82a}}{R_1CHXCOOH} \xrightarrow[n\text{-BuOH}]{CCL} \underset{\text{82b}}{(R)\text{-}R_1CHXCOOBu} + \underset{\text{82a}}{(S)\text{-}R_1CHXCOOH} \quad (25)$$

R = CH_3, n-C_6H_{13}, n-$C_{14}H_{29}$, Ph; X = Br, Cl, 4-Chlorophenoxy

Subsequently, Langrand *et al.*[95] described direct acylation of various racemic alcohols **83a** with lauric acid in hexane or heptane catalyzed by CCL, which gave the optically active esters and alcohols in high enantiomeric excess (Eq. 26).

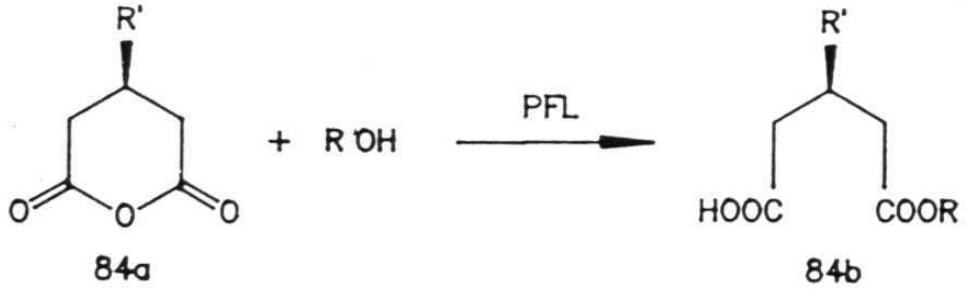


Rac-83a 83b (-)-83a (26)

R = CH_3, C_2H_5, n-C_3H_7, t-C_4H_9

Ring opening of prochiral cyclic anhydrides:

Oda *et al.*[96] reported asymmetric ring opening of various 3-substituted glutaric anhydrides (**84a**) with alcohols catalyzed by PFL producing (R)-half esters **84b** in 70-91% enantiomeric excess (Eq. 27).



84a 84b (27)

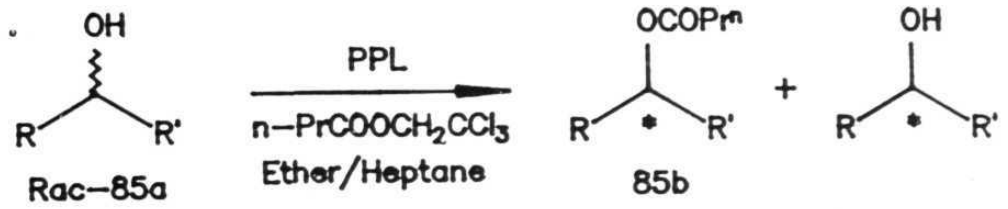
R' = CH_3, C_2H_5, n-C_3H_7, i-C_3H_7

Transesterification of racemic and prochiral or meso alcohols:

Racemic alcohols:

Kinetic resolution of racemic alcohols *via* lipase catalyzed transesterification was first reported by Klibanov *et al.* in 1985, which marked the beginning of a new field of biotransformations.[94]

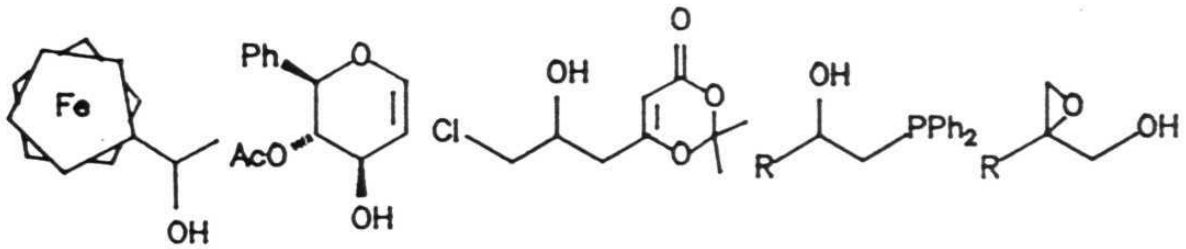
They subjected various racemic alcohols **85a** to transesterification with trichloroethyl butyrate catalyzed by PPL, producing optically active esters and alcohols in 57-100% enantiomeric excess (Eq. 28).



(28)

R = CH_3, C_2H_5; R' = alkyl, phenyl

Several important chiral molecules, for example **86-90**, have been resolved *via* enantioselective transesterification catalyzed by various lipases in organic media.[97-101]



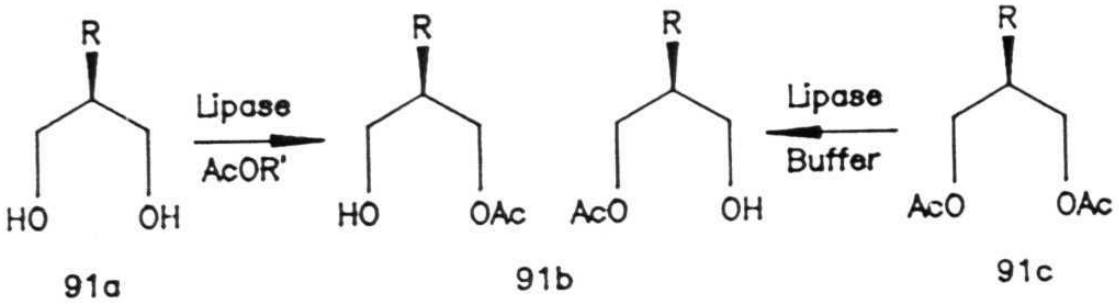
86[97] (PFL) **87**[98] (Lipase P) **88**[99] (Amano PS) **89**[100] (RGL) **90**[101] (PFL)

Prochiral and meso diols:

In 1986, Tombo *et al.*[102] showed that PPL catalyzed transesterification of prochiral diol **91a** produces corresponding optically active monoacetate **91b** while hydrolysis of corresponding diacetate **91c** catalyzed by the same enzyme gives optically active monoacetyl diol **91b** (R = alkyl) but with opposite stereochemistry, thus providing access to both the enantiomers. Later, Wong and coworkers[103] reported similar results (R = OCH_2Ph) using PSL as

the enzyme (Scheme 18).

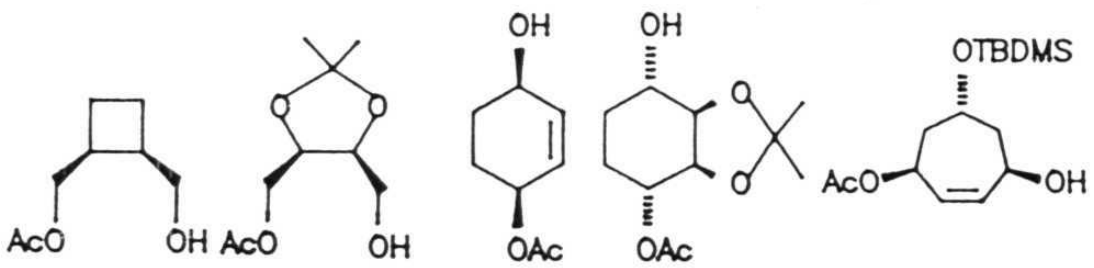
SCHEME 18:



91a 91b 91c

R = Alkyl, OCH_2Ph; R' = CH_3, $CH{=}CH_2$

Similarly, meso diols can also be asymmetrized *via* lipase mediated acylation in organic media. Using this methodology, several synthetically useful chiral molecules 92-96 were synthesized in homochiral form.[104-107]



92[104] 93[105] 94[106] 95[107] 96[107]

(Lipase SAM II) (Lipase P30) (PCL) (PCL)

Other biotransformations useful in asymmetric synthesis:

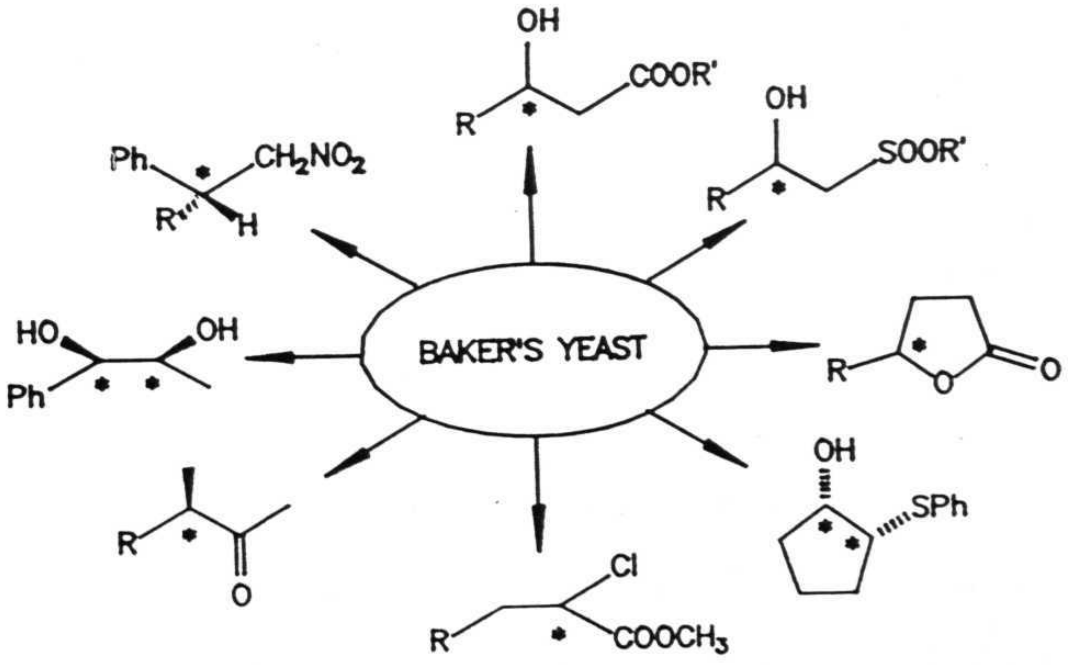
Among the synthetically useful biotransformations affected by various types of enzymes, the biocatalytic reductions and oxidations catalyzed by oxidoreductases or whole cells, and carbon-carbon bond forming reactions catalyzed by aldolases, ketolases, oxynitrilases, etc., are the most important transfor-

mations in the context of asymmetric synthesis. The biocatalytic carbon-carbon bond cleaving reactions catalyzed by whole cells are the biotransformations that seem to open new avenues in the field of asymmetric synthesis.

Asymmetric synthesis *via* biocatalytic reductions:

Biocatalytic reductions of prochiral carbonyl groups and heterotopic carbon-carbon double bonds are very important biotransformations since they result in the production of enantiomerically enriched chiral synthons. Several microorganisms and isolated enzymes have been in use for this purpose. Baker's Yeast (*Saccharomyces cerevisiae*)[108,109] catalyzed reductions are the best among several biocatalytic asymmetric reductions (Scheme 19).

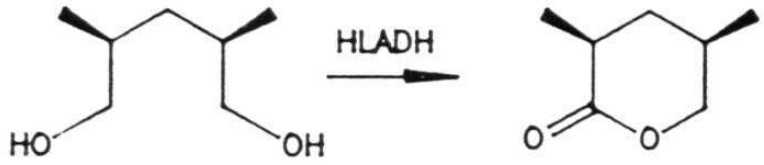
SCHEME 19:



Asymmetric synthesis *via* biocatalytic oxidations:

Biocatalytic oxidation of alcohols, hydroxylations at activated and unactivated carbons, epoxidation and Baeyer-Villiger oxidation of ketones are among the most useful biotransformations. Some selected examples have been mentioned below (Eq. 29-31, Scheme 20).

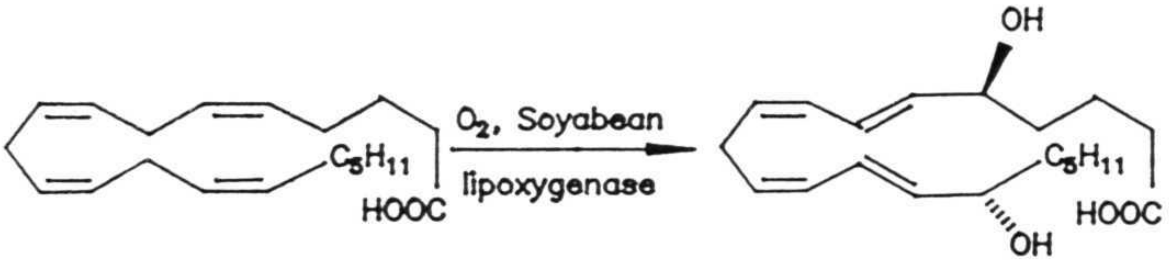
Oxidation of alcohols:[110]

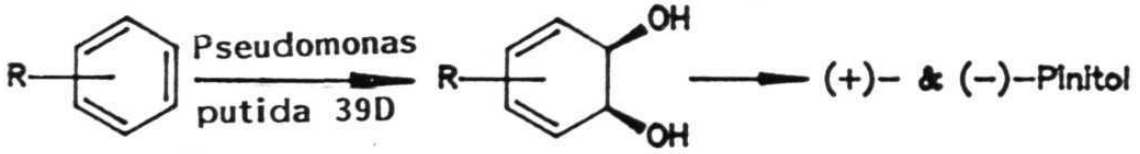


(29)

Hydroxylation at activated and unactivated carbons:[111,112]

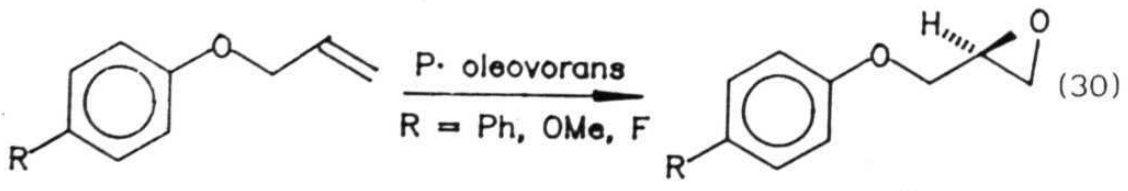
SCHEME 20:





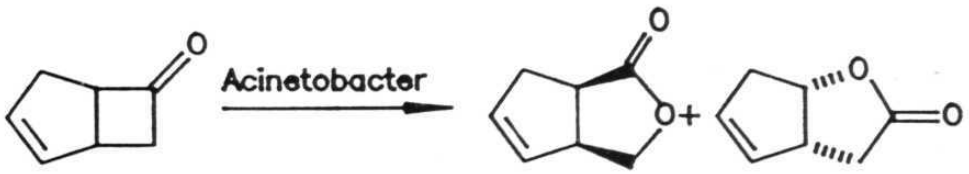
R = F, Cl, Br, alkyl

Epoxidation of olefins:[113]



(30)

Baeyer-Villiger oxidation of ketones:[114]

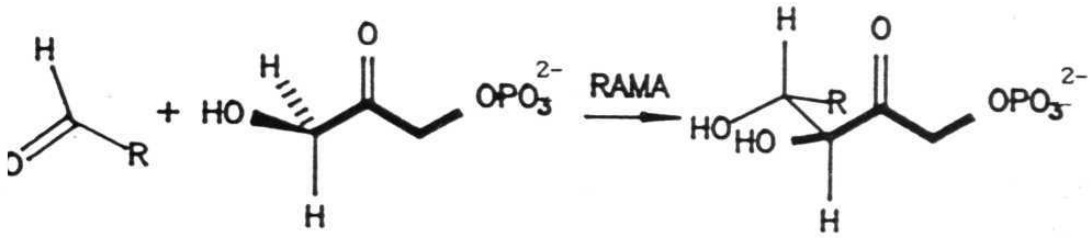


(31)

Asymmetric synthesis *via* biocatalytic C-C bond forming reactions:

Aldol reaction:

The rabbit muscle aldolase (RAMA) catalyzed aldol reaction between dihydroxyacetone phosphate (DHAP) and aldehydes that produces optically active molecules has been extensively studied and utilized by Whitesides[115] and Wong[116] (Eq. 32).



(32)

Cyanohydrin formation:

The enzymatic asymmetric addition of HCN to aldehydes[117] catalyzed by oxynitrilases has proved to be one of the highly useful biotransformations (Eq. 33).

(33)

Asymmetric synthesis *via* biocatalytic C-C bond cleavage:

Decarboxylation:

Enzymatic cleavage of a carbon-carbon bond is relatively new to organic synthesis. The recently reported[118] asymmetric decarboxylation of α-disubstituted malonic acids catalyzed by microorganism, *Alacaligenes bronchisepticus*, seems to be a highly useful biotransformation (Eq. 34).

(34)

Ar = Phenyl, 4-anisyl, 6-methoxy-2-naphthyl,

4-chlorophenyl, 2-thienyl

OBJECTIVES, RESULTS AND DISCUSSION

Objectives:

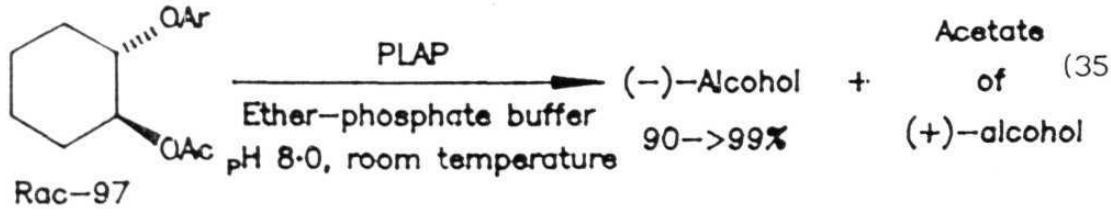
For the past five years our group has been actively involved in developing simple methods for the production of optically active compounds.[119-122] The preceding prologue enables one to conclude that enzymes have become versatile and highly potential catalysts, especially in the field of synthesis of enantiomerically enriched chiral compounds. This emergence of biotransformations as a means for the production of optically active compounds has drawn our attention sufficiently to initiate research project in this area.

Despite the high utility of biotransformations, some synthetic organic chemists remained apprehensive about the experimental techniques involved. Moreover, accessibility of a required enzyme often poses problems preventing one to go for an enzyme mediated transformation in preference to conventional reactions.

The use of purified enzymes on a regular basis could prove expensive in case of most of the enzymes. We believe that crude preparations of certain enzymes could be conveniently employed as catalysts for projected reactions if the other enzymes present in the preparation do not interfere. It has already been shown that acetone powders of pig liver,[38] horse liver,[64] bovine liver[123] and bovine pancreas[78] could be employed as catalysts with great ease

as if they were single enzymes. Porcine pancreatic lipase (25% protein) is generally used in its crude form.[76] Moreover immobilization of purified enzymes and their reuse may not always possible.

In order to provide simple and inexpensive procedures, we have initiated the project, "Enantioselective synthesis using crude enzymes." We have started with employing pig liver acetone powder (PLAP) (a crude form of PLE), an easily accessible and inexpensive enzyme. Soon, our group has come out with a report in 1990,[124] which described the PLAP-catalyzed enantioselective hydrolysis of (±)-*trans*-1-acetoxy-2-aryloxycyclohexanes (97) that produced corresponding (-)-alcohols in 90 to >99% enantiomeric excess (eq. 35). Encouraged by this initial success, we have increased our efforts in this area.[125,126]



(35)

Ar = Phenyl, 3 & 4-tolyl, 2,3, & 4-anisyl
4-t-butyl, 4-biphenyl, 2,4-dimethyl

The main objective of this work is to synthesize various enantiomerically enriched chiral synthons such as (1) homoallyl alcohols 98 & 99, (2) propargyl alcohols 100, and (3) 3-aryl-3-hydroxy-2-methylenepropionates 101 and propanenitriles

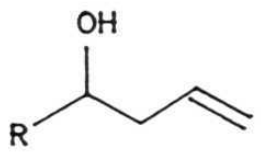
102; the chiral auxiliaries, *trans*-2-arylcyclohexan-1-ols (103); the β-adrenergic agent, (S)-propranolol (1); the pheromone of oriental hornet, (R)-hexadecanolide (104) and (*cis*-6-methyl-tetrahydropyran-2-yl)acetic acid (105), a constituent of grandular secretion of civet cat (*Viverra civetta*) *via* enzyme mediated transformations. We have planned to achieve this *via* enantioselective hydrolysis of acetates of :

1) racemic alcohols 98-103,

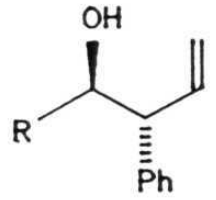
2) derivative or precursor of racemic-1 and

3) precursor-alcohols of compounds 104 & 105,

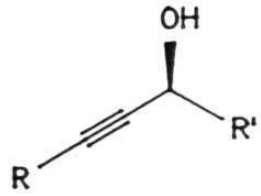
catalyzed by crude esterases such as pig liver acetone powder (PLAP) and chicken liver acetone powder (CLAP) and thereby demonstrate the potential of crude enzymes.



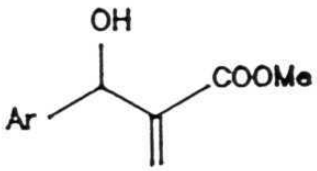
98



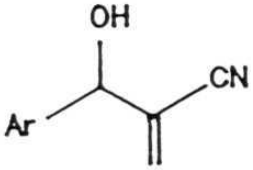
99



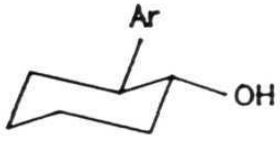
100



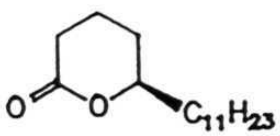
101



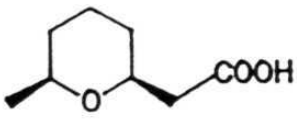
102



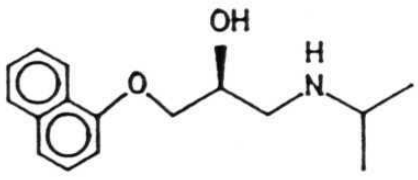
103



104



105



1

Results and Discussion:

With the aforementioned objectives in mind, we first selected PLAP as the crude enzyme for utilization in enantioselective synthesis. We have prepared PLAP in our laboratory following the procedure described by Ohno *et al.*[38] from fresh pig liver.

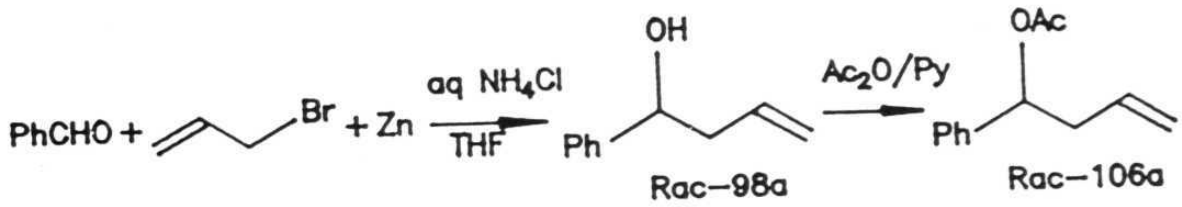
Homoallyl alcohols:

As a first step towards our target, we have started with resolution of homoallyl alcohols because homoallyl alcohols are very important chiral precursors for β- and γ-hydroxy carbonyl frame work present in many naturally occurring and pharmacologically active compounds. Moreover, the double bond present in homoallyl alcohols allows a variety of manipulations that one may wish to carry out. Enantiomerically enriched homoallyl alcohols have been prepared *via* chiral auxiliary-mediated asymmetric allyl-metalation of aldehydes and ketones.[127-129]

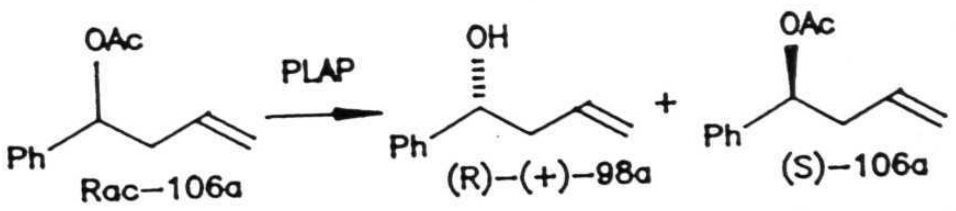
We have planned to achieve the resolution of homoallyl alcohols *via* PLAP catalyzed enantioselective hydrolysis of their racemic acetates, thinking that such a process would become simple and inexpensive method for the synthesis of optically active homoallyl alcohols. Accordingly, we prepared racemic-1-phenylbut-3-en-1-ol (**98a**) *via* Luche's method,[130] starting from benzaldehyde, allyl bromide and zinc dust in about 95% yield. The structure of

this alcohol was confirmed by IR, ^{1}H and ^{13}C NMR spectral data. This alcohol was converted into corresponding acetate **106a** by treatment with acetic anhydride in presence of pyridine and DMAP (Scheme 21).

SCHEME 21:



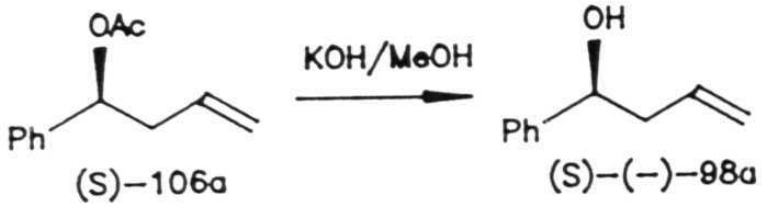
The racemic acetate **106a** was then subjected to PLAP catalyzed hydrolysis under a variety of conditions. We found that the biphasic medium which consists of ether and 0.5 M, pH 8.0 KH_2PO_4/K_2HPO_4 buffer in 1:4 ratio to be the best among all for this purpose. After 24h, during which time 59% hydrolysis was accomplished, the reaction was stopped and a mixture of product alcohol and unhydrolyzed acetate was isolated. The optically active alcohol and enantiomerically enriched acetate were separated by column chromatography (eq. 36).



(36)

The optical purity of the product, (R)-(+)-1-phenylbut-3-en-1-ol (**98a**), $[\alpha]_D^{20}$ + 27.55 (c 2.54, PhH) {Lit.[131] $[\alpha]_D^{21}$ - 39.9

(c 2.48, PhH), 84% ee, S-configuration) was determined to be 58% by comparing optical rotations. The enantiomerically enriched acetate was hydrolyzed with KOH/MeOH (eq. 37) to furnish (S)-(-)-98a, $[\alpha]_D^{20}$ -31.25 (c 1.24, PhH) in 66% optical purity.



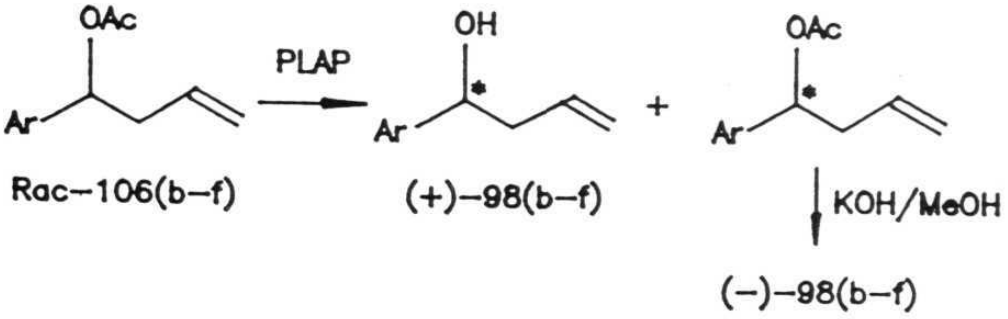
(37)

This result was encouraging. We thought that introduction of substituents into phenyl ring might produce better results. Accordingly, we prepared several variously substituted racemic-1-arylbut-3-en-1-ols (98b-98f) starting from corresponding aldehydes, allyl bromide and zinc dust following the procedure employed for (±)-98a. The structures of these alcohols were established by IR, ^1H and ^{13}C NMR spectral data. Then these alcohols were converted into corresponding acetates 106b-106f by treatment with acetic anhydride.

Ar = b) 4-tolyl, c) 4-chlorophenyl, d) 4-methoxyphenyl, e) 1-naphthyl, f) 2,4-dichlorophenyl

The racemic acetates 106b-106f were subjected to PLAP catalyzed hydrolysis under similar conditions employed for (±)-106a. The progress of the hydrolysis was monitored by HPLC. When an appropriate degree of hydrolysis was accomplished, the reactions were stopped, and the product (+)-alcohols and the enantiomerically enriched acetates were isolated (Table 1). The recovered acetates were hydrolyzed with KOH/MeOH to furnish (-)-alcohols (Scheme 22).

SCHEME 22:



The enantiomeric purities of (+)-98b (Ar= 4-tolyl), (+)-98c (Ar= 4-chlorophenyl), (+)-98d (Ar= 4-methoxyphenyl) and (+)-98e (Ar= 1-naphthyl) were determined by comparing their specific rotations with literature values[131] and found to be 67%, 65%, 64%, and 72% respectively. The optical purities of (-)-98b, (-)-98c, (-)-98d and (-)-98e were determined in the same manner and the values are given in Table 1. . The enantiomeric excess of (+)-98f (Ar = 2,4-dichlorophenyl) was determined by ^{1}H NMR analysis of

Table 1 : Enantioselective hydrolysis of (±)-106 using PLAP[a].

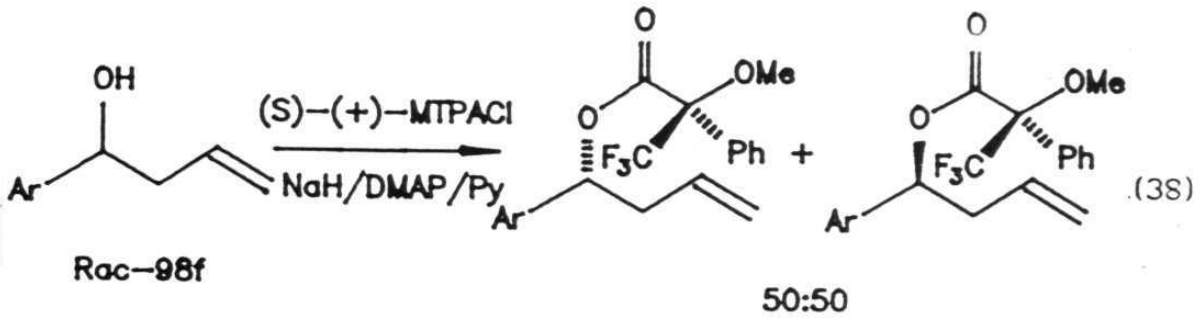
Substrate (±)-106	Time in hrs.	Conversion[b] ratio OH:OAc	(+)-98			106	
			Yield[c] (%)	$[\alpha]_D^{20}$	E.e.[d] (%)	Yield[c] (%)	E.e.[e] (%)
106a	24	59:41	61	+ 27.55 (c 2.54, PhH)	58	90	66
106b	32	43:57	90	+ 30.66 (c 1.69, PhH)	67	92	53
106c	32	39:61	87	+ 21.94 (c 2.50, PhH)	65	91	47
106d	32	43:57	74	+ 52.65 (c 7.82, PhH)	64	90	45
106e	50	50:50	88	+ 69.96 (c 3.30, PhH)	72	90	65
106f	24	38:62	77	+ 36.95 (c 3.68, PhH)	56[f]	70	30[g]

a) All reactions were carried out in 5 mM scale. b) Conversion ratio was determined by HPLC analysis. c) Yields of pure isolated products and are based on conversion ratio. d) Based on literature values[131] :for (S)-(-)-98a, Ar = phenyl, $[\alpha]_D^{21}$- 39.9 (c 2.48, PhH), 84% e.e.; for (-)-98b, Ar = 4-tolyl, $[\alpha]_D^{25}$- 37.3 (c 2.0, PhH), 82% e.e.; for (-)-98c, Ar= 4-chlorophenyl, $[\alpha]_D^{23}$ -28.4 (c3.03, PhH), 84% e.e.; for (-)-98d, Ar= 4-methoxyphenyl, $[\alpha]_D^{23}$- 65.8 (c 3.56, PhH), 80% e.e.; for (-)-98e, Ar = 1-naphthyl, $[\alpha]_D^{24}$- 77.5 (c 2.98, PhH), 80% e.e.; e) Determined by comparing observed specific rotations of (-)-alcohols, obtained after hydrolysis with KOH/MeOH, with that of literature values. f) E.e. was determined by ^{1}H NMR (200 MHz) analysis of corresponding Mosher's ester. g) Based on $[\alpha]_D$ value of corresponding (+)-alcohol.

Mosher's esters[132] of (±)- and (+)-98f following the procedure described below.

Determination of enantiomeric purity of (+)-98f:

The Mosher's ester of (±)-98f was prepared by treating the racemic alcohol with (S)-(+)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride (MTPACl) in presence of sodium hydride and DMAP using pyridine as solvent (eq. 38). In the ^{1}H NMR spectrum of Mosher's ester of (±)-98f two distinct singlets with almost



(38)

Ar = 2,4-dichlorophenyl

equal integrations, appeared at δ 3.48 and 3.58 (due to OMe group) arising from both enantiomers of homoallyl alcohol. Then, a sample of (+)-98f was converted into corresponding Mosher's ester following the procedure described for Mosher's ester of (±)-98f. The ^{1}H NMR spectrum of Mosher's ester of (+)-98f contained two distinct singlets with integrations in the ratio 12.9:3.6 appeared at δ 3.48 and 3.58 (OMe protons) indicating that the (+)-98f has an enantiomeric purity of 56% (Table 1).

The (-)-98f derived from enantiomerically enriched recovered

acetate was shown to be of 30% optical purity, by comparing the observed optical rotation with that of (+)-98f.

With the prominence of homoallyl alcohols as valuable chirons and the importance of homochirality in mind, we increased our efforts to improve the optical yields of the homoallyl alcohols. For achieving this we planned to examine the applicability of other enzyme, chicken liver acetone powder (CLAP) Accordingly, we prepared CLAP from fresh chicken liver in our laboratory in the following manner:

Chicken liver acetone powder (CLAP):

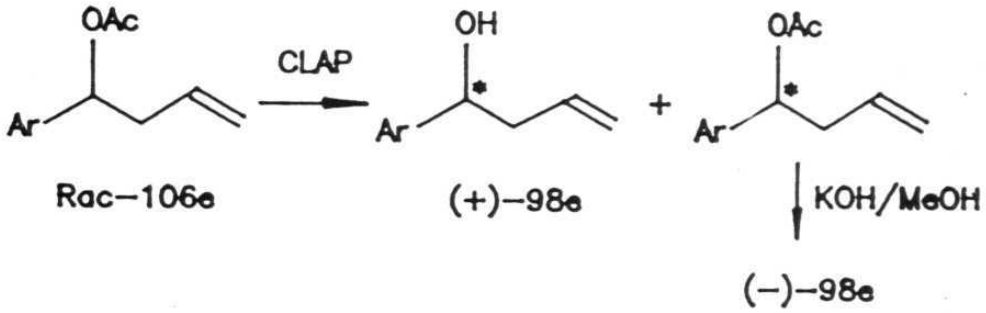
Fresh chicken liver was homogenized in chilled acetone using kitchen juicer. The brown mass, obtained after filtration of the homogenate, was air dried at room temperature and powdered using juicer. The fibrous material was removed by sieving to get CLAP as fine powder. Thus obtained CLAP was stored in refrigerator which remained active even after 3 months.

CLAP-catalyzed hydrolysis:

Hydrolysis of racemic acetate **106e** (Ar= 1-naphthyl) was examined first because this substrate with PLAP-catalyzed hydrolysis provided the best result. Of the various conditions employed, the biphasic medium which consists of ether and 0.5 M, pH 8.0, KH_2PO_4/K_2HPO_4 buffer, and room temperature were found to be the best even for CLAP-catalyzed reaction. The reaction was carried out under these conditions and it took 20h to accomplish

28% hydrolysis (HPLC) (Table 2) (Scheme 23). The product (+)-1-(1-naphthyl)but-3-en-1-ol (98e), $[\alpha]_D^{22}$ + 92.9 (c 1.26, PhH) {Lit.[131] $[\alpha]_D^{24}$ -77.5 (c 2.98, PhH), 80% ee} with 96% optical purity was isolated along with enantiomerically enriched acetate 106e, which in turn, upon hydrolysis with KOH/MeOH furnished (-)-98e, $[\alpha]_D^{22}$ -31.18 (c 0.89, PhH) with 32% optical purity.

SCHEME 23:



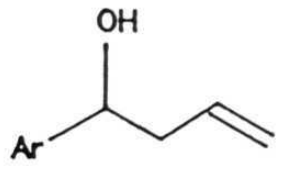
Ar = 1-naphthyl

After obtaining this highly encouraging results, we examined hydrolysis of a variety of acetates of racemic homoallyl alcohols (Table 2). The required racemic alcohols 98a, 98b, 98c, 98e, 98f, and 98g were prepared following the same Luche's procedure,[130] starting from corresponding aldehyde, allyl bromide and zinc dust. The structures of these alcohols were established by IR, ^1H & ^{13}C NMR spectral analysis. The structures of 98f and 98g were further confirmed by mass spectral analysis. These alcohols were converted into corresponding acetates 106(a-c & e-g) by treatment with acetic anhydride in presence of pyridine and DMAP.

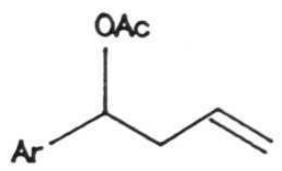
Table 2 : Enantioselective hydrolysis of (±)-106 using CLAP[a].

Substrate (±)-106	Time in hrs.	Conversion[b] ratio OH:OAc	(+)-98			106	
			Yield[c] (%)	$[\alpha]_D^{22}$	E.e.[d] (%)	Yield[c] (%)	E.e.[e] (%)
106a	35	30:70	86	+ 34.08 (c 1.11, PhH)	72	93	38
106b	40	41:59	90	+ 44.62 (c 3.83, PhH)	98	91	73
106c	22	32:68	75	+ 32.18 (c 3.20, PhH)	95	89	51
106e	20	28:72	89	+ 92.90 (c 1.26, PhH)	96	93	32
106f	40	42:58	92	+ 56.70 (c 1.30, PhH)	85[f]	93	56[g]
106g	20	31:69	88	+ 23.30 (c 2.06, PhH)	92[f]	91	46[g]

a) All reactions were carried out in 5 mM scale. b) Conversion ratio was determined by HPLC analysis. c) Yields of pure isolated products and are based on conversion ratio. d) Based on literature values[131]: for (S)-(-)-98a, Ar = phenyl, $[\alpha]_D^{21}$- 39.9 (c 2.48, PhH), 84% e.e.; for (-)-98b, Ar = 4-tolyl, $[\alpha]_D^{25}$- 37.3 (c 2.0, PhH), 82% e.e.; for (-)-98c, Ar = 4-chlorophenyl, $[\alpha]_D^{23}$ -28.4 (c 3.03, PhH), 84% e.e.; for (-)-98e, Ar = 1-naphthyl, $[\alpha]_D^{24}$- 77.5 (c 2.98, PhH), 80% e.e.; e) Determined by comparing observed specific rotations of (-)-alcohols, obtained after hydrolysis with KOH/MeOH, with that of literature values. f) E.e. was determined by ^{1}H NMR (200 MHz) analysis of corresponding Mosher's ester. g) Based on $[\alpha]_D$ value of corresponding (+)-alcohol.



Rac-98(a-c & e-g)



Rac-106(a-c & e-g)

Ar = a) Phenyl, b) 4-tolyl, c) 4-chlorophenyl, e) 1-naphthyl, f) 2,4-dichlorophenyl, g) 3,4-dichlorophenyl

Then we subjected these acetates of racemic alcohols to the CLAP-catalyzed hydrolysis under the previously mentioned conditions. The product (+)-alcohols and the enantiomerically enriched acetates were isolated after usual work-up in good chemical yields (Table 2). The recovered acetates were hydrolyzed with KOH/MeOH to furnish (-)-alcohols.

The optical purities of (+)-98a (Ar = phenyl), (+)-98b (Ar = 4-tolyl) and (+)-98c (Ar = 4-chlorophenyl) were determined by comparing their specific rotations with literature values[131] and found to be 72%, 98% and 95% respectively. The optical purities of (-)-98(a-c) were determined in the same manner and the values are given in the Table 2.

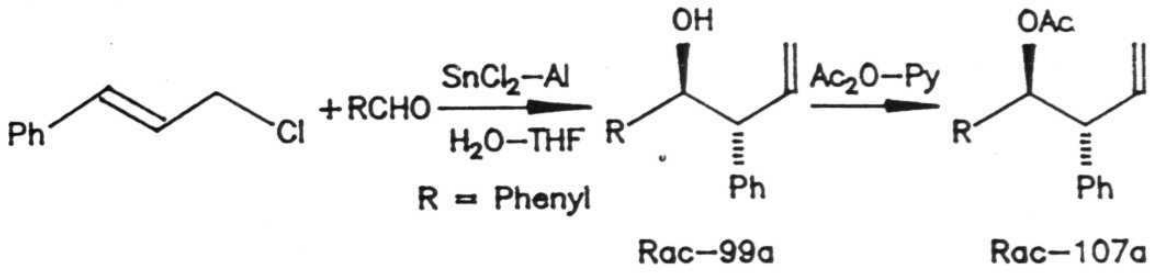
The enantiomeric excesses of (+)-98f (Ar=2,4-dichlorophenyl) and (+)-98g (Ar=3,4-dichlorophenyl) were determined by ^{1}H NMR analysis of corresponding Mosher's esters[132] following previously described procedure and found to be 85% and 92% respectively. The optical purity of (-)-alcohols, (-)-98f and (-)-98g, was determined by comparing their specific rotations with that of corresponding (+)-alcohols and found out to be 56% and 46% respectively (Table 2).

Anti-homoallyl alcohols 99:

The reasonable success achieved with the resolution of homoallyl alcohols containing one chiral center prompted us to take up the synthesis of more complex molecules in optically active form. The synthesis of optically active compounds with two or more chiral centers[133-135] has been a challenging area of present day organic synthesis because such molecules can be key intermediates for the structurally nonrigid complex molecules, such as polyethers, ansamycin and macrolide antibiotics.

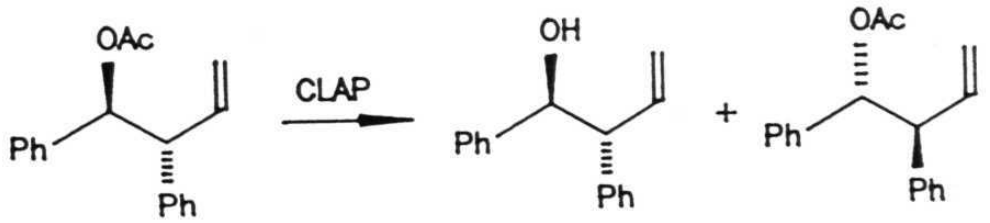
The importance of homochiral molecules with multiple chiral centers and lack of suitable methods for their large scale production prompted us to take up the resolution of anti-homoallyl alcohols 99. Obviously, we were in search of a suitable method for the synthesis of racemic-anti-homoallyl alcohols with high diastereomeric purity. Literature survey revealed that the method of Torii *et al.*[136] is one of the most convenient methods. Accordingly, we first prepared (±)-anti-1,2-diphenylbut-3-en-1-ol (**99a**) (R = Ph) by stirring a suspension of benzaldehyde, cinnamyl chloride, tin (II) chloride dihydrate and aluminium powder in THF-H_2O (5:2) at 60°C (Scheme 24). The NMR spectral data of this alcohol is in good agreement with literature data[137]. The racemic alcohol was converted into the corresponding acetate **107a** by treatment with acetic anhydride (Scheme 24).

SCHEME 24:



Rac–99a Rac–107a

The racemic acetate 107a (R= phenyl) was then subjected to CLAP catalyzed hydrolysis in biphasic medium containing ether and phosphate buffer at room temperature (eq. 39). The progress of the hydrolysis was monitored by HPLC. After 10 days, during which time 25% of hydrolysis was accomplished, the reaction was stopped. The product, (1S, 2R)-(-)-1,2-diphenylbut-3-en-1-ol (99a), $[\alpha]_D^{20}$ -14.26 (c 1.12, $CHCl_3$) {Lit.[137] $[\alpha]_D$ -12.5 (c 3.4, $CHCl_3$), 97% ee, (1S, 2R) configuration} and enantiomerically enriched acetate 107a, $[\alpha]_D^{20}$ + 11.26 (c 2.13, $CHCl_3$) were isolated.



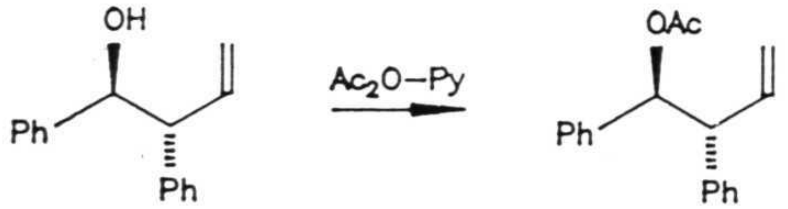
Rac–107a (–)–99a (+)–107a (39)

The enantiomeric excesses of (-)-99a and recovered acetate were also determined by ^1H NMR (200 MHz) analysis of acetates in presence of $Eu(hfc)_3$ as described in the following.

Determination of enantiomeric purity:

The ^{1}H NMR (200 MHz) spectrum of racemic acetate **107a**, in presence of Eu(hfc)$_3$, showed that the original singlet at δ 2.08 (due to CO<u>Me</u>) shifted and appeared as two distinct singlets with almost equal integrations, indicating that the two singlets arise from two enantiomers.

Then a sample of (-)-**99a** was converted into corresponding acetate by the action of acetic anhydride in presence of pyridine and DMAP (eq. 40). The ^{1}H NMR (200 MHz) spectrum of this acetate, recorded in presence of Eu(hfc)$_3$, contained two distinct singlets (OCO<u>Me</u>) with integrations in the ratio 0.6:15.1 revealing that the (-)-**99a** has an enantiomeric excess of 92%.

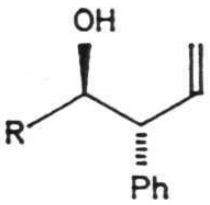


(1S, 2R)–(–)–99a (1S, 2R)–107a (40)

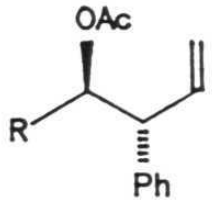
Similarly, the ^{1}H NMR spectrum of recovered acetate (+)-**107a** recorded in presence of Eu(hfc)$_3$, showed two distinct singlets (COCH$_3$) with integrations in the ratio of 8.0:3.6 indicating that the recovered acetate is enantiomerically enriched by 25%.

Encouraged by above results, we planned to examine the generality of this transformation. Accordingly, we have prepared seven more alcohols **99b-99h** changing the R group following the

previously described strategy using Torii's method. The racemic alcohols were then converted into corresponding acetates **107b-107h** by treatment with acetic anhydride. The structures of both alcohols and acetates were confirmed by IR, ^{1}H and ^{13}C NMR (Fig. 1 for **99f**) spectral data.



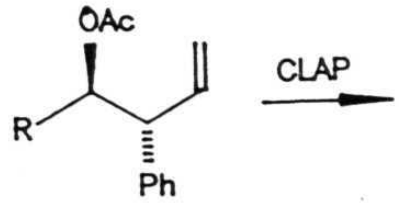
Rac-99(b-h)



Rac-107(b-h)

R = b) 4-tolyl, c) 4-chlorophenyl, d) isopropyl, e) isobutyl, f) n-butyl, g) n-pentyl, h) n-hexyl.

These acetates were then subjected to CLAP catalyzed hydrolysis in the biphasic medium (ether-phosphate buffer, pH 8.0) at room temperature. The racemic acetates **107b** and **107c** were not hydrolyzed by CLAP. The remaining acetates were smoothly hydrolyzed by CLAP-catalyzed reaction. The product (-)-alcohols and enantiomerically enriched acetates were isolated in good yields (Table 3, Eq. 41). Their enantiomeric excesses were determined by ^{1}H NMR (200 MHz) analysis of acetates in presence of $Eu(hfc)_3$.



Rac-107(d-h)

CLAP → **(−) − Alcohol + (+) − Acetate** (41)

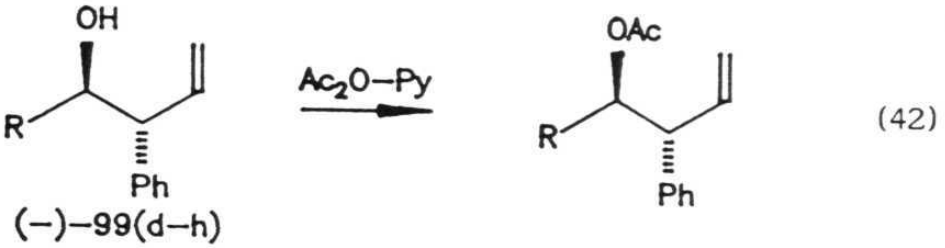
Table 3 : Enantioselective hydrolysis of (±)-107 using CLAP[a].

Substrate (±)-107	Time in hrs.	Conversion[b] ratio OH:OAc	(-)-99			(+)- 107	
			Yield[c] (%)	$[\alpha]_D^{20}$	E.e.[d] (%)	Yield[c] (%)	E.e.[e] (%)
107a	240	25:75	80	- 14.26 (c 1.12, $CHCl_3$)	92	93	25
107d	264	25:75	87	- 60.65 (c 1.83, $CHCl_3$)	67	92	19
107e	75	32:68	92	- 45.90 (c 2.20, $CHCl_3$)	>99	95	49
107f	65	22:78	89	- 57.41 (c 1.55, $CHCl_3$)	88	93	24
107g	75	35:65	89	- 44.55 (c 1.61, $CHCl_3$)	80	94	69
107h	144	35:65	86	- 46.70 (c 2.18, $CHCl_3$)	92	92	49

a) All reactions were carried out in 5 mM scale. b) Conversion ratio was determined by HPLC analysis. c) Yields of pure isolated products and are based on conversion ratio. d) Determined by ^1H NMR (200 MHz) analysis of corresponding acetates in presence of chiral shift reagent, $Eu(hfc)_3$. e) Determined by ^1H NMR (200 MHz) analysis in presence of $Eu(hfc)_3$.

Determination of enantiomeric purity:

The racemic acetate, in each case, was first subjected to ^1H NMR (200 MHz) analysis in presence of $Eu(hfc)_3$. After ensuring that the acetate signal shifts and splits into two distinct singlets, samples of (-)-alcohols were converted into corresponding acetates by treating the alcohols with acetic anhydride in presence of pyridine and DMAP (eq. 42). These acetates were then subjected to ^1H NMR (200 MHz) analysis in presence of $Eu(hfc)_3$. This showed the enantiomeric purities of (-)-**99d** (R = i-Pr), (-)-**99f** (R = n-Bu), (-)-**99g** (R = n-Pentyl) and (-)-**99h** (R = n-Hexyl) to be 67%, 88%, 80% and 92% respectively.



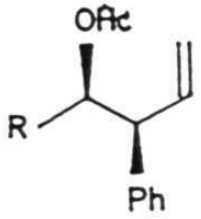
(42)

The enantiomeric purity of (-)-**99e** was however shown to be >99% as indicated by the presence of only one signal for methyl protons of acetoxy group in the ^1H NMR (200 MHz) spectrum of acetate of (-)-**99e** (Fig. 2) recorded in presence of $Eu(hfc)_3$.

Similarly, the enantiomeric excesses of enantiomerically enriched recovered acetates (+)-**107d** (R = i-Pr), (+)-**107e** (R = i-Bu), (+)-**107f** (R = n-Bu), (+)-**107g** (R = n-Pentyl) and (+)-**107h** (R = n-Hexyl) were shown to be 19%, 49%, 24%, 69% and 49%

respectively, by ^1H NMR (200 MHz) analysis in presence of $Eu(hfc)_3$.

It should be mentioned that in the ^1H NMR (200 MHz) spectrum of all the racemic acetates **107** (**a-g**), one singlet at around δ 1.8 appeared with very low intensity, possibly due to diastereomeric impurity (*syn*-isomer). The diastereomeric purity of these



syn-Diastereomer

molecules is at least 95%, as revealed by ^1H NMR analysis of racemic acetates in presence of chiral shift reagent, $Eu(hfc)_3$ during e.e determination. In all cases, COMe protons appeared as two distinct singlets due to enantiomer pairs. We also observed two additional singlets with low intensity which might be due to the corresponding *syn*-diastereomer (≤2%).

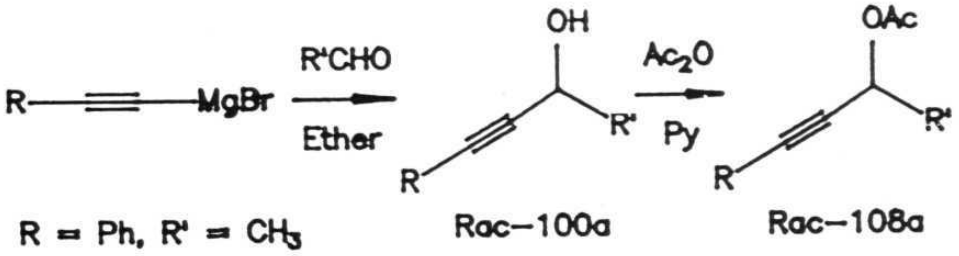
Secondary propargyl alcohols:

Homochiral propargyl alcohols **100** form an important class of synthons for a variety of biologically active molecules.[138] and for α- & β-hydroxy carboxylic acids[139]. These molecules are generally prepared *via* reduction of acetylenic ketones using chiral reducing agents,[140,141] asymmetric alkynylation of alde-

hydes[142] and reductive cleavage of chiral acetylenic acetals.[143]

Due to the importance of homochiral propargyl alcohols as chiral precursors, we next examined the possible synthesis of optically active propargyl alcohols *via* enantioselective hydrolysis of corresponding racemic acetates catalyzed by enzymes. For this purpose, we have chosen PLAP as the biocatalyst. Accordingly, we have first prepared (±)-4-phenyl-3-butyn-2-ol (**100a**) and the alcohol was converted into corresponding acetate **108a** according to the following strategy (Scheme 25).

SCHEME 25:

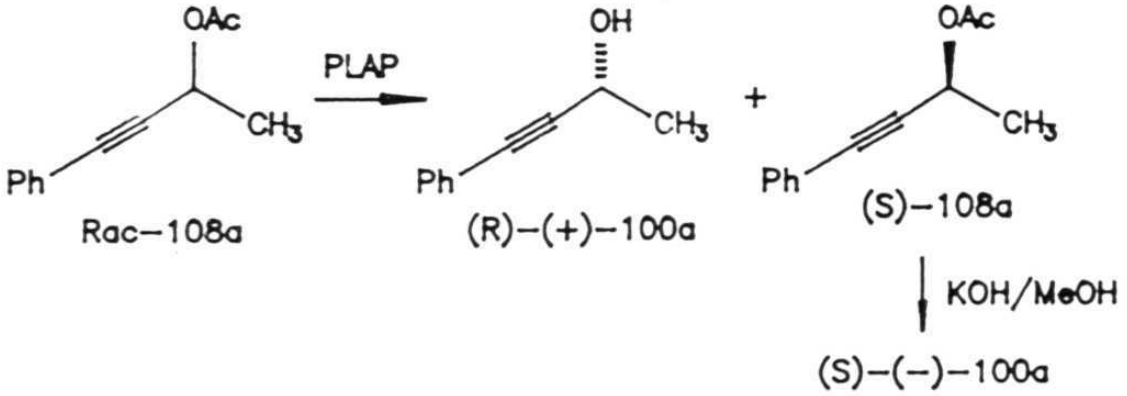


The addition of phenylethynylmagnesium bromide (which was generated *in situ* from phenylacetylene and ethylmagnesium bromide in ether) to acetaldehyde at $0^{o}C$ furnished racemic alcohol **100a** in 85% yield. The structure of this molecule was confirmed by IR, ^{1}H & ^{13}C NMR spectral data. Thus obtained racemic alcohol was converted into corresponding acetate **108a** by treating with acetic annhydride in presence of pyridine and DMAP.

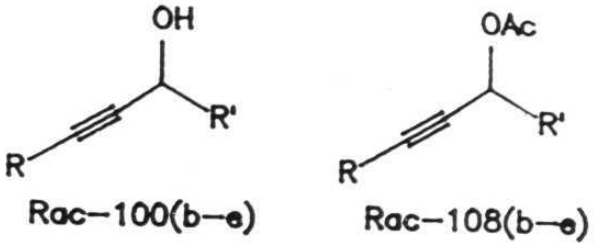
The racemic acetate **108a** was subjected to PLAP-catalyzed hydrolysis in biphasic medium (ether - phosphate buffer of pH 8.0)

at room temperature. The progress of the hydrolysis was monitored by HPLC. The reaction was stopped after 14h, during which time 48% hydrolysis was accomplished. The product, (R)-(+)-4-phenyl-3-butyn-2-ol (100a), $[\alpha]_D^{22}$ + 27.4 (c 2.7, EtOH) {Lit.[141] $[\alpha]_D^{25}$ + 30.64 (c 5.15, EtOH), 98% ee} with 88% optical purity and enantiomerically enriched acetate 108a, which in turn, upon hydrolysis with KOH/MeOH provided (S)-(-)-100a, $[\alpha]_D^{22}$ -14.15 (c 1.62, EtOH) with 45% optical purity (Scheme 26), were isolated in good chemical yields (Table 4).

SCHEME 26:



After obtaining this encouraging result, we have prepared four more racemic alcohols 100(b-e) following the previously described procedure starting from corresponding alkyne and aldehyde. The structures of these alcohols were established by IR, ^1H & ^{13}C NMR spectral data. These alcohols were converted into corresponding acetates 108(b-e) by treating the alcohols with acetic anhydride in presence of pyridine and DMAP.



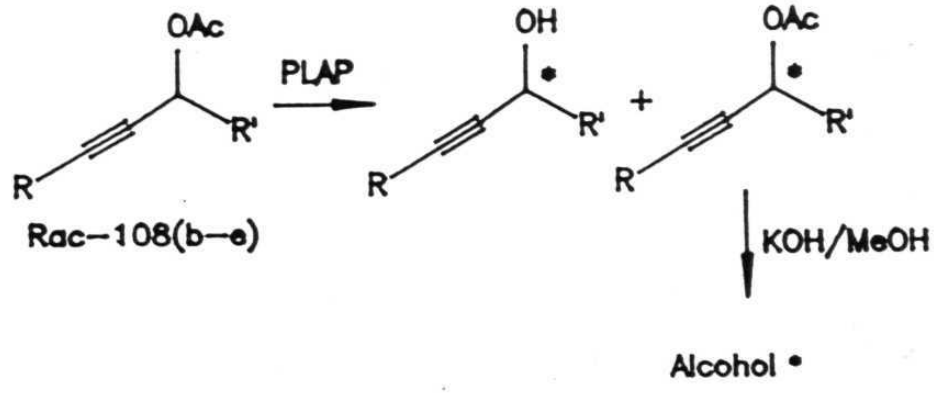
Rac-100(b-e) Rac-108(b-e)

b) R = Ph, R' = Et; c) R = Ph, R' = i-Pr;

d) R = R' = Ph; e) R = n-C_5H_{11}, R' = Ph

The racemic acetates 108(b-e) were subjected to PLAP catalyzed hydrolysis under previously described conditions (Scheme 27). The product alcohols and enantiomerically enriched unhydrolyzed acetates were isolated in good yields. The recovered acetates were converted into corresponding optically active alcohols *via* hydrolysis with KOH/MeOH. The enantiomeric purities of optically active alcohols were determined either by comparing optical rotations or by ^1H NMR analysis of corresponding acetates in presence of chiral shift reagent $Eu(hfc)_3$.

SCHEME 27:



Rac-108(b-e) Alcohol •

The optical purities of product (R)-(+)-alcohols, (+)-100b (R = Ph, R^1 = Et) and (+)-100d (R = R^1 = Ph) were determined to be

Table 4 : Enantioselective hydrolysis of (±)-108 using PLAP[a].

Substrate (±)-108	Time in hrs.	Conversion[b] ratio OH:OAc	100			108	
			Yield[c] (%)	$[\alpha]_D^{22}$	E.e. (%)	Yield[c] (%)	E.e.[d] (%)
108a	14	40:60	83	+ 27.4 (c 2.70, EtOH)	88[e]	92	45
108b	30	55:45	86	+ 3.74 (c 7.48, Ether)	15[f]	92	18
108c	40	35:65	82	- 3.08 (c 2.27, EtOH)	39[g]	92	21[h]
108d	70	30:70	89	+ 0.99 (c 6.00, $CHCl_3$)	15[i]	91	Nil
108e	26	25:75	87	- 9.17 (c 3.38, EtOH)	18[g]	93	7[h]

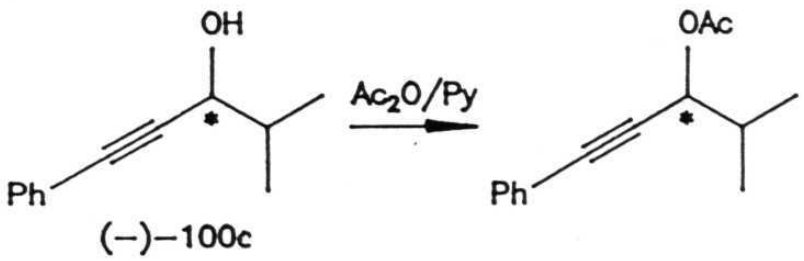
a) All reactions were carried out in 5 mM scale. b) Conversion ratio was determined by HPLC analysis. c) Yields of pure isolated products and are based on conversion ratio. d) Determined by comparing observed specificrotations of optically active alcohols obtained after hydrolysis with KOH/MeOH with those of literature values, unless otherwise specified.e) Based on literatue value[141] : for (+)-100a, $[\alpha]_D^{25}$ + 30.64 (c 5.15, EtOH), 98% e.e. f) Based on literature value[143] : for (+)-100b, $[\alpha]_D^{21}$+ 21.97(c 1.27, Ether), 90% e.e. g) Determined by ^1H NMR analysis of corresponding acetate in presence of chiral shift reagent, $Eu(hfc)_3$. h) Determined by ^1H NMR analysis in presence of $Eu(hfc)_3$. i) Based on literature value[142] for (+)-100d, $[\alpha]_D^{25}$ + 2.26 (c 6.63, $CHCl_3$), 34% e.e.

15% in each case by comparing optical rotations observed with literature values.[142,143] The optical purities of (S)-(-)-alcohols (S)-(-)-100b and (S)-(-)-100d derived from enantiomerically enriched acetates 108b & 108d were also determined in the same manner and found to be of 18% and zero, respectively (Table 4).

Determination of enantiomeric purity of (-)-alcohols 100c & 100e and recovered acetates 108c & 108e:

The ^{1}H NMR spectrum of (±)-108c recorded in presence of Eu(hfc)$_3$ showed that the original singlet at δ 2.12 (due to COMe) shifted and appeared as two distinct singlets of almost equal ntegration indicating that the two singlets arise from two enantiomers.

Then, a sample of (-)-alcohol 100c was converted into corresponding acetate by treating the alcohol with acetic anhydride in presence of pyridine and DMAP (eq. 43). The ^{1}H NMR spectrum of this acetate, recorded in presence of Eu(hfc)$_3$ showed two distinct singlets with integrations in the ratio 6.5:15 revealing that the (-)-100c has an enantiomeric excess of 39%.



(43)

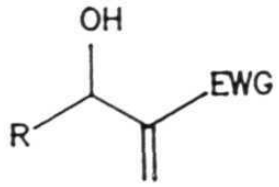
Similarly, the enantiomerically enriched 108c, precursor of

(+)-100c was analyzed by ^1H NMR analysis in presence of $Eu(hfc)_3$ and was shown to have an enantiomeric excess of 21%. The (+)-alcohol is believed to have the same enantiomeric excess.

The optical purities of (-)-100e and recovered acetate 108e were determined by ^1H NMR analysis of acetates of (±)-, (-)- and (+)-100e following the same procedure employed in case of 100c and were found to have 18 and 7% respectively (Table 4).

3-Aryl-3-hydroxy-2-methylenepropionates (101) and propanenitriles (102):

With considerable success behind, we have taken up resolution of Baylis-Hillman reaction products. Baylis-Hillman reaction[144,145] provides molecules (101, 102, 109 & 110) with unique structural features *i.e.*, they contain three functionalities providing handles for further manipulations.



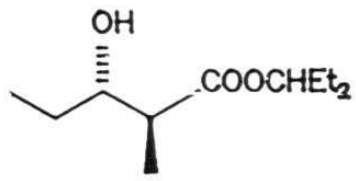
R = Alkyl or aryl

EWG = COOR (101), CN (102)

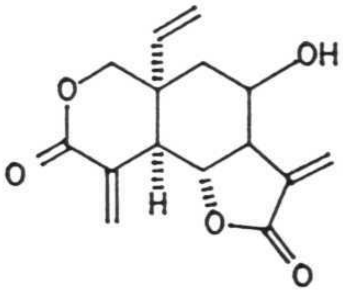
COR (109), SOOR (110)

Also the carbon frame work of these molecules is present in many naturally occurring and biologically active compounds such as

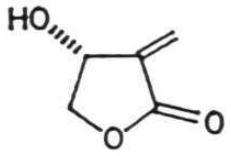
pheromones *e.g.* sitophilate (111)[146] and α-methylene-β-hydroxy-γ-butyrolactones (112-115).[147] But the potential of these Baylis-Hillman reaction products has not been exploited so far. We attribute the failure to utilize these molecules as chirons to the fact that there are no suitable methods for the large scale synthesis of these molecules in optically active form. There are, some reports[148,149] that describe the synthesis of esters (101) in optically active form but there are no methods for the synthesis of optically active nitriles (102).



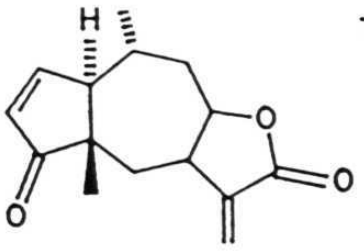
Sitophilate (111)



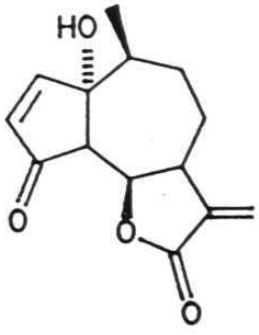
Vernolepin (113)



Thulipalin B (112)



Aromaticin (114)

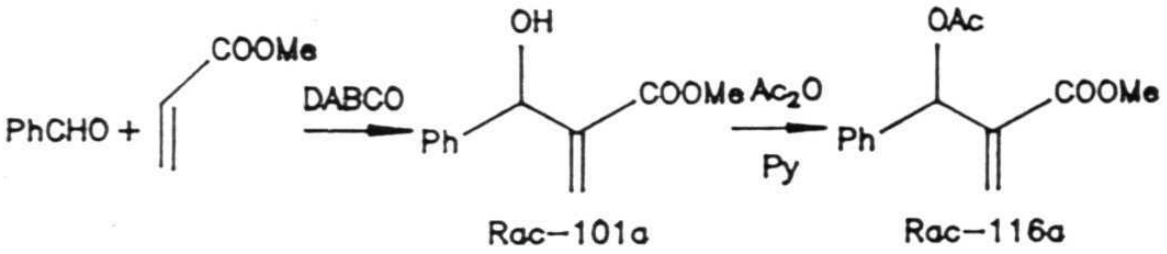


Parthenin (115)

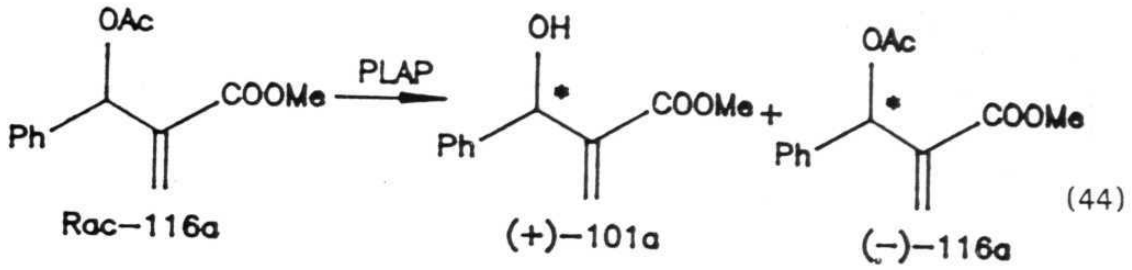
We have been trying to develop a suitable method for the synthesis of these molecules in optically active form. As part of our efforts towards achieving this, we aimed to resolve these

molecules *via* enzymatic enantioselective hydrolysis of their acetates using PLAP. Accordingly we first prepared (±)-methyl 3-hydroxy-3-phenyl-2-methylenepropionate (**101a**) *via* DABCO catalyzed reaction between methyl acrylate and benzaldehyde following literature procedure.[150] This alcohol was converted into corresponding racemic acetate **116a** by treating the alcohol with acetic anhydride in presence of pyridine and DMAP (Scheme 28).

SCHEME 28:



The racemic acetate **116a** (Ar = phenyl) was subjected to PLAP catalyzed hydrolysis in biphasic medium containing ether and 0.5 M, pH 8.0 phosphate buffer, at room temperature (eq. 44). The hydrolysis was monitored by HPLC. After 20h, during this period 41% hydrolysis was accomplished, the reaction was stopped. The product, (+)-methyl 3-hydroxy-3-phenyl-2-methylenepropanoate (**101a**) $[\alpha]_D^{20}$ + 56.13 (c 1.60, Acetone) and enantiomerically enriched acetate **116a**, $[\alpha]_D^{20}$ - 70.09 (c 2.14, Acetone) were isolated in good chemical yields. The enantiomeric excess of the (+)-**101a** was determined by ^{1}H NMR (200 MHz) analysis in presence of chiral shift reagent, Eu(hfc)$_3$ (Table 5).



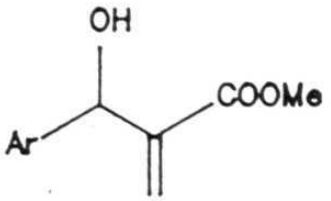
Rac–116a (+)–101a (–)–116a (44)

Determination of enantiomeric purity of (+)-101a:

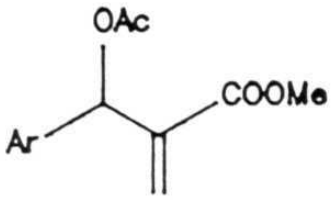
^{1}H NMR (200 MHz) analysis in presence of Eu(hfc)$_3$:

The ^{1}H NMR (200 MHz) spectrum of racemic-**101a** recorded in presence of Eu(hfc)$_3$ showed that the original singlet (for COOMe) protons) at δ 3.72 shifted and appeared as two distinct singlets with almost equal integration indicating that the two singlets arise from two enantiomers. Two singlets (for COOMe protons) with integration in 3.7:10.0 ratio, appeared in the ^{1}H NMR (200 MHz) spectrum of (+)-**101a**, recorded in the presence of Eu(hfc)$_3$, indicating that the (+)-alcohol has an enantiomeric excess of 46%.

At this stage it occurred to us that modification of aryl moiety could help in achieving high enantiomeric purities. Accordingly, we prepared three more alcohols following the previously described strategy. The structures of these alcohols were established by IR, ^{1}H and ^{13}C NMR spectral data. These racemic alcohols were converted into corresponding racemic acetates by treating the alcohols with acetic anhydride in presence of pyridine and DMAP.



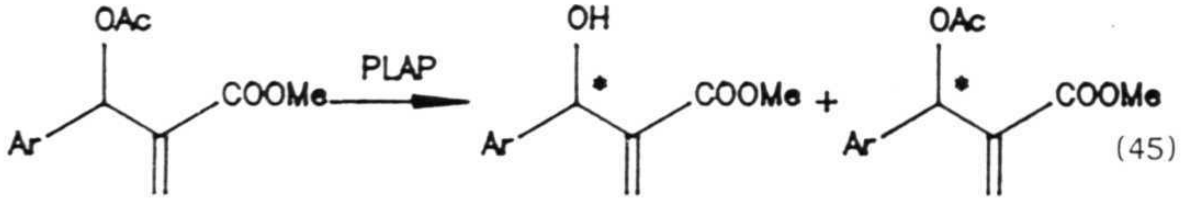
Rac–101(b–d)



Rac–116(b–d)

Ar = b) 4-tolyl, c) 4-chlorophenyl, d) 2-anisyl

These racemic acetates were subjected to PLAP-catalyzed hydrolysis in the usual manner (eq. 45). The product (+)-alcohols and enantiomerically enriched acetates were isolated in good chemical yields. The enantiomeric excesses of (+)-alcohols were determined by ^{1}H NMR (200 MHz) analysis of alcohols in presence of Eu(hfc)$_3$, following the procedure described in case of (+)-101a (Table 5). The enantiomeric excess of enantiomerically enriched acetates could not be determined because these molecules could neither be converted into corresponding alcohols nor be analyzed by ^{1}H NMR in presence of Eu(hfc)$_3$ (Table 5).



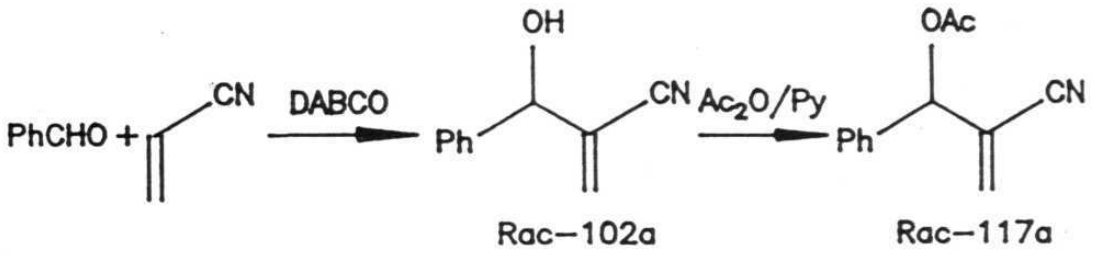
(45)

Rac–116(b–d) (+)–101(b–d) (–)–116(b–d)

After the limited success with propionates 101, we turned our attention to propanenitriles 102. We first prepared (±)-3-hydroxy-3-phenyl-2-methylenepropanenitrile (102a) *via* DABCO catalyzed reaction between acrylonitrile and benzaldehyde following the

procedure developed in our laboratory[151]. The structure of this alcohol was established by IR, ^{1}H & ^{13}C NMR spectral data. This racemic alcohol was then converted into corresponding racemic acetate **117a** by treating the alcohol with acetic anhydride at $0^{o}C$ in presence of pyridine and DMAP (Scheme 29).

SCHEME 29:



The racemic acetate **117a** was then subjected to PLAP catalyzed hydrolysis under the usual conditions. The progress of the hydrolysis was monitored by HPLC. After 9h, during which time 42% hydrolysis was accomplished, the reaction was stopped. The product (+)-3-hydroxy-3-phenyl-2-methylenepropanenitrile (**102a**), $[\alpha]_D^{20}$ + 19.54 (c 1.22, Acetone) and enantiomerically enriched acetate **117a**, $[\alpha]_D^{20}$ - 6.64 (c 1.65, Acetone) were isolated in good chemical yields (Eq. 46).

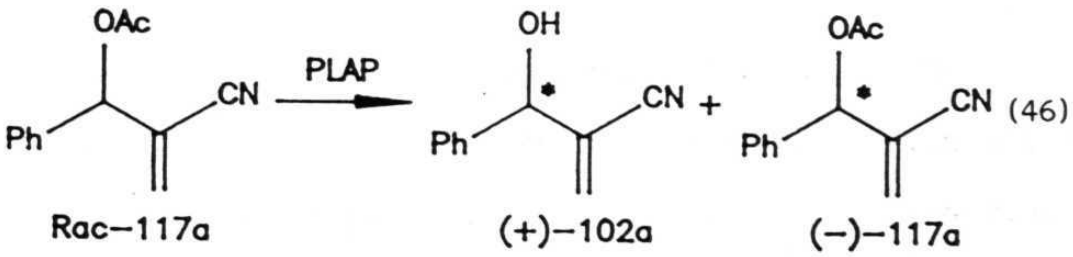


Table 5 : Enantioselective hydrolysis of (±)-116/117 using PLAP[a]

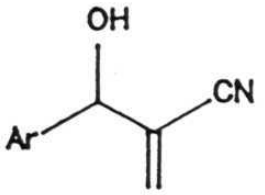
Substrate racemic 116/117	Time in hrs.	Conversion[b] ratio OH:OAc	(+)-101 or 102			Recovered 116/117[e] Yield[c](%)
			Yield[c] (%)	$[\alpha]_D^{20}$	E.e.[d] (%)	
116a	20	41:59	90	+ 56.13 (c 1.60, Acetone)	46	90
116b	28	35:65	89	+ 76.62 (c 1.29, Acetone)	65	90
116c	28	42:58	86	+ 71.55 (c 1.09, Acetone)	62	89
116d	10	24:76	79	+ 26.33 (c 1.21, Acetone)	50	93
117a	9	42:58	81	+ 19.54 (c 1.22, Acetone)	60	87
117b	9	35:65	84	+ 27.30 (c 1.13, Acetone)	70	89
117c	14	34:66	88	+ 13.28 (c 0.82, Acetone)	59	89
117d	10	35:65	88	+ 43.60 (c 1.03, Acetone)	64	92
117e	14	25:75	90	+ 23.90 (c 1.02, Acetone)	70	88
117f	24	29:71	87	+ 60.42 (c 0.66, Acetone)	86	95

a) All reactions were carried out in 5 mM scale. b) Conversion ratio was determined by HPLC analysis. c) Yields of pure isolated products and are based on conversion ratio. d) E.es. of 101 were determined by ^{1}H NMR (200 MHz) analysis in presence of chiral shift reagent, Eu(hfc)$_3$ and that of 102 were determined by HPLC analysis using chiral column, CHIRALCEL OD (Daicel, Jpn) and were further confirmed by ^{1}H NMR (200 MHz) analysis of corresponding acetates in presence of Eu(hfc)$_3$. e) E.es. were not determined as the enantiomeric enrichment would not be appreciable.

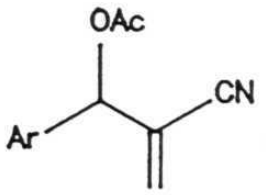
Determination of enantiomeric purity of (+)-102a:

The enantiomeric purity of (+)-102a was determined to be 60% by HPLC analysis of (±)- and (+)-102a using chiral column, CHIRALCEL OD (25 cm, Daicel, Jpn.) and 5% išopropanol in hexane as eluent (0.4 mL per min.). The two enantiomers have retention times 36 and 38 minutes. This was further confirmed ^{1}H NMR analysis of corresponding acetates in presence of $Eu(hfc)_3$ (Table 5).

In order to examine the generality and enantioselectivity of the transformation, we planned to modify the aryl moiety, which may also help in achieving high enantiomeric purities. Accordingly, we prepared five more alcohols following the previously described strategy changing the aldehyde. The structures of these alcohols were established by IR, ^{1}H and ^{13}C NMR spectral data. These racemic alcohols were converted into corresponding racemic acetates by treating the alcohols with acetic anhydride in presence of pyridine and DMAP.



Rac–102(b–f)

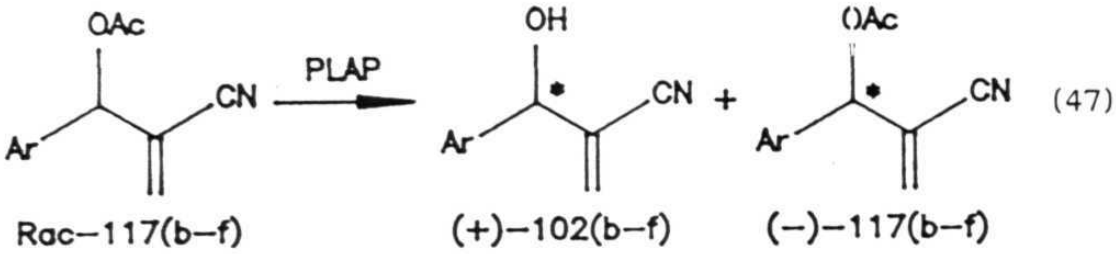


Rac–117(b–f)

Ar = b) 4-tolyl, c) 4-chlorophenyl, d) 2-anisyl,
e) 4-isopropylphenyl, f) 1-naphthyl.

These racemic acetates were subjected to PLAP-catalyzed hydrolysis in the usual manner (eq. 47). The product (+)-alcohols

and enantiomerically enriched acetates were isolated in good chemical yields. The enantiomeric excesses of (+)-alcohols were



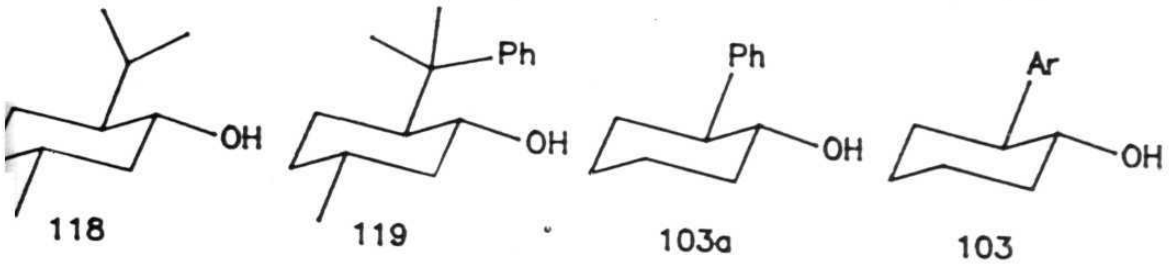
(47)

Rac–117(b–f) (+)–102(b–f) (–)–117(b–f)

determined by HPLC analysis on chiral column, CHIRALCEL OD (Fig. 3 for 102c) and were further confirmed by ^{1}H NMR (200 MHz) analysis of corresponding acetates in presence of $Eu(hfc)_3$ (Table 5). The enantiomeric excess of recovered acetates was not determined as the enantiomeric enrichment would not be appreciable.

Homochiral (-)-*trans*-2-arylcyclohexan-1-ols (103), versatile chiral auxiliaries:

The exponential growth of asymmetric synthesis[7] in the last two decades resulted mainly from the rational designing of a large variety of chiral auxiliaries and their utilization in a large number of reaction types. Among the various chiral auxiliaries, the cyclohexyl-based chiral auxiliaries[152] such as menthol (118),[153] Corey's 8-phenylmenthol (119)[154] Whitesell's *trans*-2-phenylcyclohexan-1-ol (103a)[155] occupy a special position because of their versatility and the high levels of absolute stereocontrol they offer.



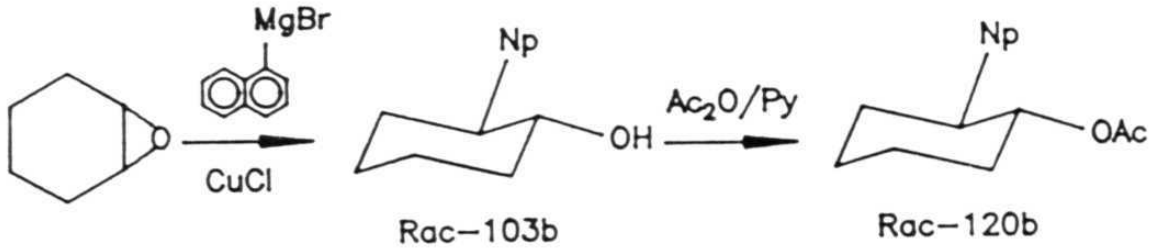
118 119 103a 103

The *trans*-2-phenylcyclohexan-1-ol (**103a**), in particular, has been extensively used in a wide variety of asymmetric reactions such as ene-reaction, Diels-Alder reaction, Zinc-Reformatsky reaction, Pauson-Khand reaction, Darjen's glycidic ester condensation reaction, *etc.*, with remarkable stereocontrol.[121,152] This high potential chiral auxiliary, *trans*-2-phenylcyclohexan-1-ol (**103a**) can be obtained with homochirality in both (+)- and (-)-forms *via* enzymatic resolution[155-157] or directly *via* asymmetric hydroboration of 1-phenylcyclohexene.[158] But there has been no access to its analogs of the type **103**, that might offer better levels of control as a consequence of increased bulkiness of aromatic moiety.

We were interested in developing an efficient and economical method for the resolution of analogs of *trans*-2-phenylcyclohexan-1-ol of the type **103** that could prove handy in our pursuit for the development of new asymmetric methodologies. Accordingly, we first prepared (±)-*trans*-2-(1-naphthyl)cyclohexan-1-ol (**103b**) *via* copper-catalyzed opening of cyclohexene oxide by 1-naphthylmagnesium bromide and converted the same into corresponding acetate **120b** by treating (±)-**103b** with acetic anhydride in presence of

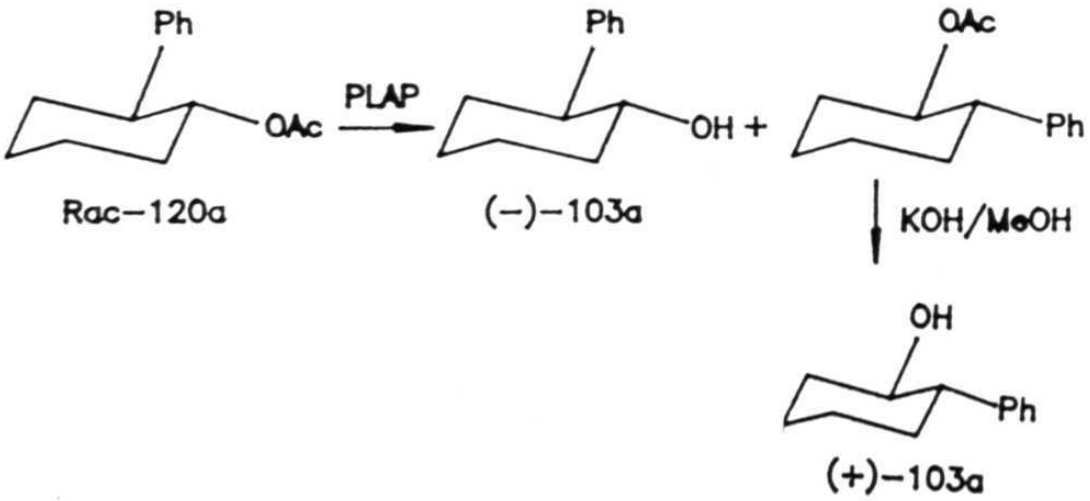
pyridine and DMAP following the procedure described by Whitesell *et al*[155]. (Scheme 30). The structures of alcohol and acetate were established by IR, ^{1}H (Fig. 4) & ^{13}C NMR (Fig. 5), and Mass spectral data.

SCHEME 30:



Whitesell *et al.*[155] have synthesized optically pure *trans*-2-phenylcyclohexan-1-ol (103a) in both (+)- and (-)-forms *via* PLAP-catalyzed enantioselective hydrolysis of (±)-*trans*-1-acetoxy-2-phenylcyclohexane (120a) (Scheme 31).

SCHEME 31:

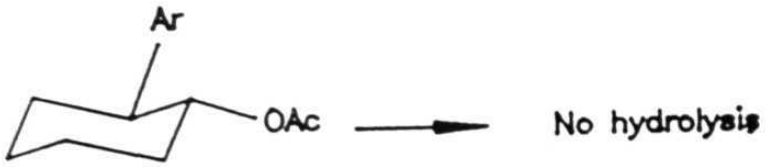


It occurred to us that (±)-*trans*-1-acetoxy-2-(1-naphthyl)-cyclohexane (120b) could be enantioselectively hydrolyzed by PLAP. Accordingly, the racemic acetate **120b** was subjected to PLAP catalyzed hydrolysis under the usual conditions. To our surprise, no hydrolysis took place even after 5 days (Eq. 48). Then we carried out the same reaction under various conditions (variation in pH and changes in organic solvent). All our attempts met with failure.

Rac–120b

(48)

Then we thought that naphthyl group may not have suited for this enzyme and substrates with other aromatic groups could be better for PLAP. Accordingly, we prepared a variety of *trans*-2-arylcyclohexan-1-ols (103c-103g) following the scheme 30. These alcohols were characterized by IR, ^{1}H & ^{13}C NMR spectral data. The racemic alcohols were converted into corresponding racemic acetates **120c-120g** by treating the alcohols with acetic anhydride in presence of pyridine and DMAP. These racemic acetates were subjected to PLAP-catalyzed hydrolysis under various conditions (Eq.49). All attempts met with failure. With this, we came to the conclusion that PLAP cannot tolerate substitution on phenyl ring.



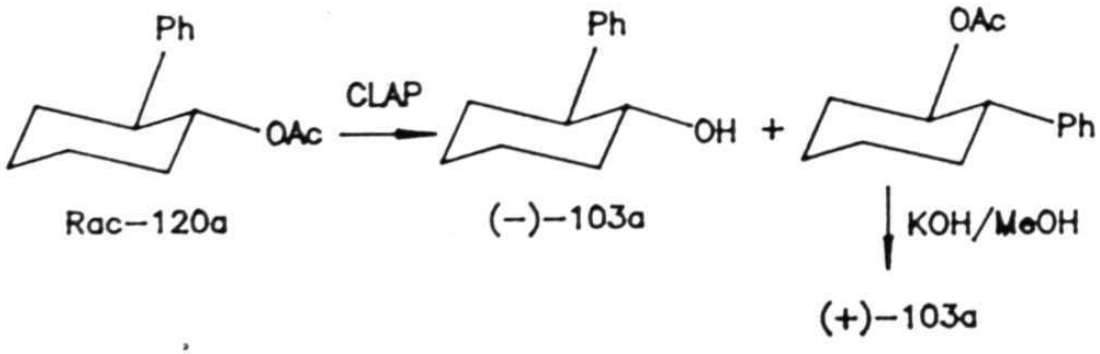
(49)

Rac–120(c–g)

Ar = c) 4-tolyl, d) 2-tolyl, e) mesityl,
f) 4-methoxyphenyl, g) 4-bromophenyl.

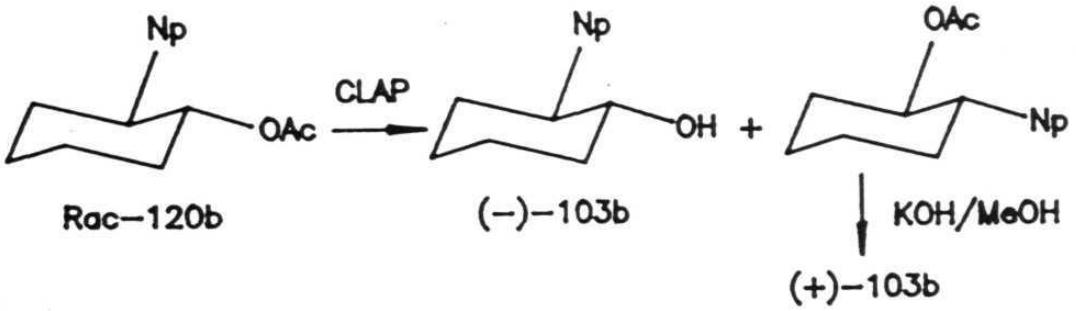
In our relentless efforts, we switched over to CLAP. We first examined the CLAP-catalyzed enantioselective hydrolysis of (±)-120a (Ar = phenyl) in two phase medium consisting ether and 0.5 M, pH 8.0, $KH_2PO_4 \backslash K_2HPO_4$ buffer, at room temperature. The progress of the hydrolysis was monitored by HPLC. In 10 days, 35% hydrolysis was accomplished and then the reaction was quenched. The product (-)-(103a) Ar = phenyl, $[\alpha]_D^{22}$ -58.66 (c 1.19, MeOH) {Lit.[155] $[\alpha]_D^{27}$ -58.4 (c 10.0, MeOH), for (1R,2S)-enantiomer} with >99% optical purity and enantiomerically enriched acetate 120a, which in turn, upon hydrolysis with KOH\MeOH provided (+)-103a, $[\alpha]_D^{22}$ + 29.20 (c 2.46, MeOH) {Lit.[155] $[\alpha]_D^{23}$ + 58.3 (c 10.0, MeOH), for (1S,2R)-enantiomer)} with 50% optical purity were isolated in good yields (Table 6) (Scheme 32).

SCHEME 32:



We next subjected the racemic acetate **120b** (Ar = 1-naphthyl) to CLAP catalyzed hydrolysis under previously described conditions (Scheme 33). In two days time, we noticed the start of hydrolysis and was monitored by HPLC. The reaction was quenched after 12 days, by when 26% hydrolysis was accomplished. The product alcohol and unhydrolyzed acetate were obtained in good yields. The enantiomeric excess of product (-)-alcohol **103b**, $[\alpha]_D^{22}$ -72.94 (c 1.47, MeOH) and the (+)-alcohol, $[\alpha]_D^{22}$ +28.4 (c 1.51, MeOH), obtained after hydrolysis of recovered acetate **120b** with KOH\MeOH, were determined in the following manner.

SCHEME 33:



Determination of enantiomeric purity of (-)- and (+)-103b:

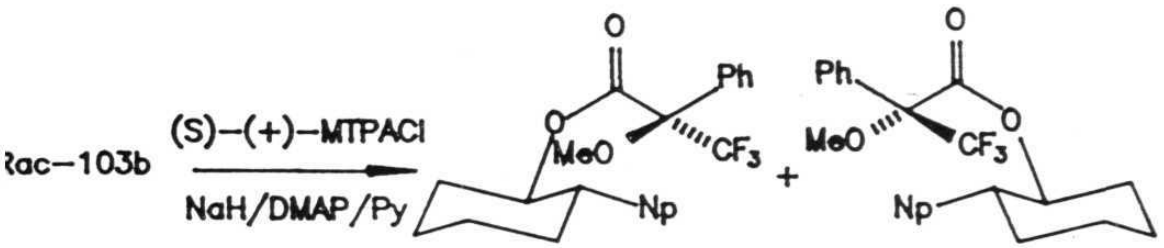
This was achieved *via* ^{1}H NMR (200 MHz) analysis of Mosher's esters of (±)-, (-)- and (+)-**103b** (Ar = 1-naphthyl). The (±)-**103b** was treated with (S)-(+)-MTPACl in presence of sodium hydride and DMAP using pyridine as solvent to provide the required Mosher's ester (eq. 50). The ^{1}H NMR (200 MHz) spectrum (Fig. 6) of this

Table 6 : Enantioselective hydrolysis of (±)-120 using CLAP[a].

Substrate (±)-120	Time in days	Conversion[b] ratio OH:OAc	(-)-103			Recovered 120	
			Yield[c] (%)	$[\alpha]_D^{22}$	E.e.[d] (%)	Yield[c] (%)	E.e.[e] (%)
120a	10	35:65	85	- 58.66 (c 1.19, MeOH)	>99[f]	86	50[f]
120b	12	26:74	83	- 72.94 (c 1.47, MeOH)	>99	91	39
120c	10	40:60	82	- 59.50 (c 1.37, MeOH)	>99	88	65
120d	10	28:72	79	- 63.96 (c 1.45, $CHCl_3$)	90[g]	83	34[g]
120e	12	25:75	84	- 32.48 (c 1.26, MeOH)	>99	87	30
120f	10	37:63	86	- 55.40 (c 1.46, MeOH)	>99	89	55
120g	12	28:72	80	- 26.28 (c 1.67, $CHCl_3$)	>99	85	42

a) All reactions were carried out in 5 mM scale. b) Conversion ratio was determined by HPLC analysis. c) Yields of pure isolated products and are based on conversion ratio. d) E.es. were determined by ^1H NMR (200 MHz) anal- ysis of corresponding Mosher's esters, unless otherwise specified. e) E.es were determined by ^1H NMR (200 MHz) analysis of Mosher's esters of (+)-alcohols obtained after hydrolysis with KOH/MeOH. f) Based on literatue value[155] : for (-)-103a, $[\alpha]_D^{27}$ - 58.4 (c 10.0, MeOH) & for (+)-103a, $[\alpha]_D^{23}$ + 58.3 (c 10.0, MeOH). g) Based on literature value[159] : for (-)-103d, $[\alpha]_D^{26}$ -71.1

compound shows two distinct singlets with almost equal integration at δ 2.84 and 3.10 for OMe protons arising from two enantiomers.



(50)

50:50

Then we prepared Mosher's ester of (-)-**103b** (Ar= 1-naphthyl) and its ^{1}H NMR spectrum shows absence of other enantiomer indicating that the (-)-alcohol has an enantiomeric excess of >99%. Then (+)-alcohol was converted into corresponding Mosher's ester and its ^{1}H NMR spectrum shows two distinct singlets at δ 2.84 and 3.10 (OMe protons) with integration in the ratio 6.5:15 indicating that the (+)-alcohol has an enantiomeric excess of 39%.

Encouraged by these results, the racemic acetates **120c-120g** were subjected to CLAP catalyzed hydrolysis under the usual conditions to produce (-)-alcohols and enantiomerically enriched acetates. The enantiomerically enriched acetates were hydrolyzed with KOH\MeOH to produce corresponding (+)-alcohols. The enantiomeric excesses of (-)-**103c** (Ar= 4-tolyl), (-)-**103f** (Ar= 4-methoxyphenyl) and (-)-**103g** (Ar= 4-bromophenyl) were determined by ^{1}H NMR (200 MHz) analysis of corresponding Mosher's esters and found out

to be >99% in all three cases. The enantiomeric excesses of (+)-alcohols, **103c**, **103f** & **103g** were also determined in the same manner and were found to be 65, 55 and 42% respectively.

The enantiomeric excesses of (-)-**103d** (Ar = 2-tolyl), $[\alpha]_D^{22}$ - 63.96 (c 1.45, $CHCl_3$) {Lit.[159] $[\alpha]_D^{26}$ - 71.1 (c 10.0, $CHCl_3$), for (1R,2S)-enantiomer} and (+)-**103d**, $[\alpha]_D^{22}$ + 24.56 (c 2.52, $CHCl_3$) {Lit.[159] $[\alpha]_D^{26}$ + 70.6 (c 10.0, $CHCl_3$), (1S,2R)} were determined by comparing specific rotations with literature values and were found to be 90 and 34% respectively. The enantiomeric excesses of (-)-**103e** (Ar = mesityl), $[\alpha]_D^{22}$ -32.48 (c 1.26, MeOH) and (+)-**103e** were determined according to the following procedure.

Determination of enantiomeric purities of (-)- & (+)-103e:

The Mosher's ester of (±)-**103e** was prepared from MTPACl and corresponding alcohol following the procedure described in case of Mosher's ester of (±)-**98f**. The ^1H NMR spectrum of Mosher's ester of (±)-**103e**, did not provide any information about its diastereomeric purity. However, the ^1H NMR spectrum of Mosher's ester of (±)-**103e**, recorded in presence of $Eu(hfc)_3$, showed that the original singlet at δ 3.20 (merged with multiplet) shifts and splits into two distinct singlets with equal integrations indicating that the two singlets arise from the two enantiomers.

The Mosher's esters of (-)- & (+)-**103e** were then prepared and the ^1H NMR spectra of these Mosher's esters, recorded in presence of $Eu(hfc)_3$, revealed that the alcohols (-)- & (+)-**103e**

have enantiomeric excesses >99 and 30% respectively.

The absolute configurations for (-)-**103b**, (-)-**103c**, (-)-**103e** (-)-**103f** and (-)-**103g** were tentatively assigned as (1R,2S) in analogy with (-)-**103a** (Ar = Ph) & (-)-**103d** (Ar = 2-tolyl). Based on this presumption, the structures of these molecules were drawn.

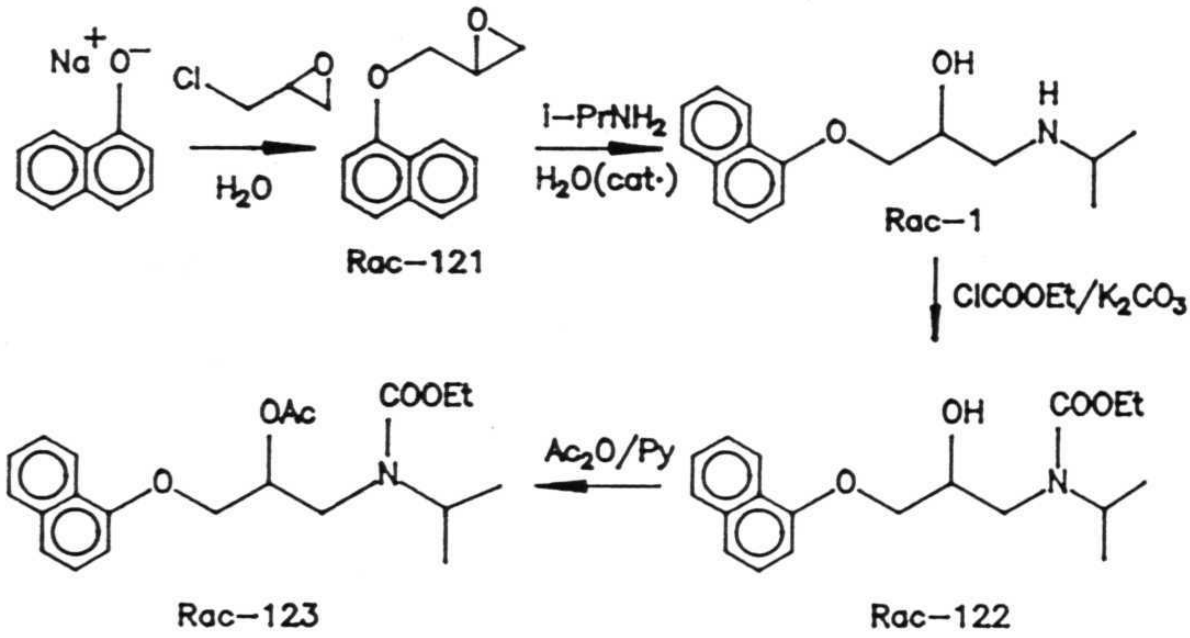
Attempted synthesis of (S)-propranolol (1):

Propranolol (1) has been used as a β-adrenergic agent in its racemic form. However, the (S)-enantiomer[160] was shown to be more active when compared to racemate or (R)-enantiomer. This importance of chirality in its pharmacological activity and its commercial importance has stimulated lot of research in the direction of developing simple and efficient methods for the synthesis of (S)-propranolol (1). Recently, Sharpless and coworkers[161] and Achiwa *et al.*[162] reported efficient non-enzymatic methods for the synthesis of (S)-propranolol (1). (S)-propranolol (1) has also been synthesized starting from homochiral precursors such as D-mannitol.[163] Several reports describing synthesis of (S)-propranolol, that rely on enzymatically produced chirons such as cyanohydrins,[164] glycerol derivatives,[165] halohydrins,[166] *etc.*, have appeared in recent literature.

Owing to the medicinal importance of (S)-propranolol, we became interested in developing a convenient method for its prepa-

ration. Since the synthesis of (±)-propranolol is very easy and cheap process, a direct resolution of propranolol may prove to be economical. We have identified the racemic acetate **123** as the potential substrate for enzymatic enantioselective hydrolysis catalyzed by PLAP or CLAP. Accordingly, we planned its synthesis as outlined in the Scheme 34.

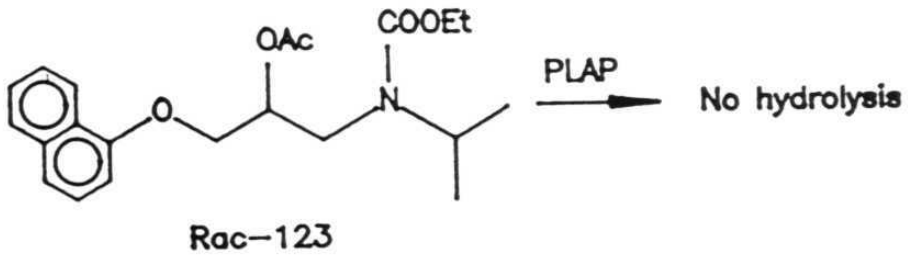
SCHEME 34:



The glycidyl 1-naphthyl ether (121) was prepared from 1-naphthol and epichlorohyrdin following literature procedure.[167] This racemic epoxide **121** was converted into racemic propranolol (**1**) by refluxing a mixture of (±)-121, isopropylamine and catalytic amount of water following Sharpless' procedure.[161] Then the secondary amino functionality was protected by converting it into the ethyl carbamate **122** *via* treatment with ethyl

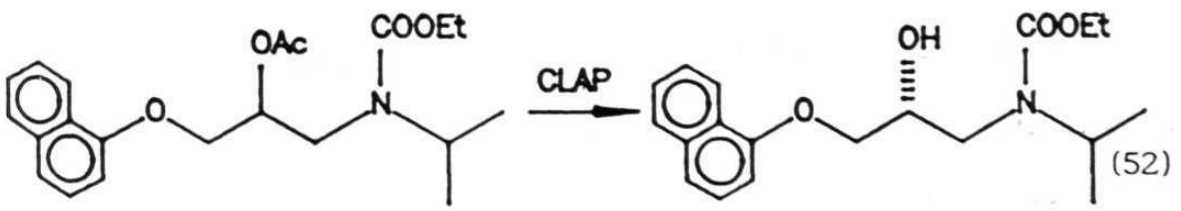
chloroformate in aqueous K_2CO_3. N-Protected racemic propranolol **122** was then converted into corresponding racemic acetate **123** by treatment with acetic anhydride in presence of pyridine and DMAP. The structures of (±)-121, (±)-1, (±)-122 and (±)-123 were in full agreement with IR, ^1H (Fig. 7) and ^{13}C NMR (Fig. 8) spectral data.

The racemic acetate 123 was subjected to PLAP-catalyzed hydrolysis under usual conditions (ether:0.5 M, pH 8.0, KH_2PO_4/ K_2HPO_4 buffer in 1:4). Unfortunately, no hydrolysis was observed even after 5 days (eq. 51).



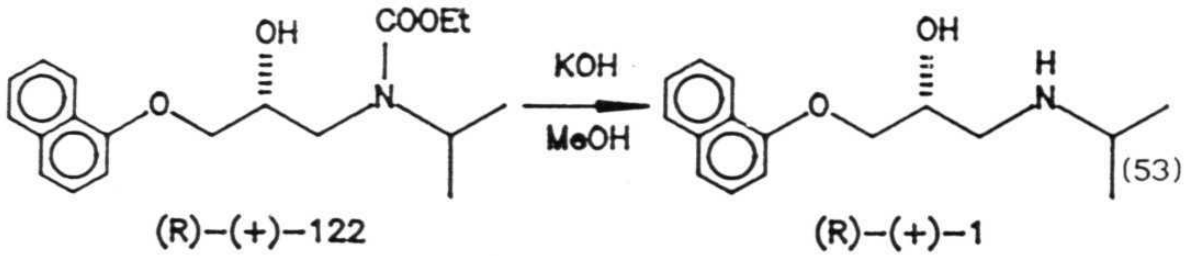
Rac–123 (51)

Afterwards, we subjected the racemic acetate **123** to CLAP catalyzed hydrolysis under usual conditions (eq. 52). We noticed the start of hydrolysis within 3 days and the progress of hydrolysis was monitored by HPLC. After 8 days, 15% of hydrolysis was accomplished.



Rac–123 (R)–(+)–122 (52)

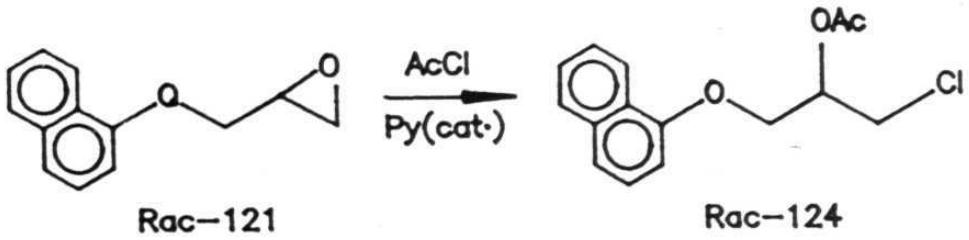
The (+)-N-protected (R)-propranolol (122), $[\alpha]_D^{20}$ + 10.86 (c 1.84, $CHCl_3$) with 40% optical purity was isolated. The optical purity of this compound was established by converting (+)-122 to the (R)-(+)-propranolol (1) $[\alpha]_D^{20}$ + 4.27 (c 0.70, EtOH), 40% e.e. {Lit.[168] $[\alpha]_D^{20}$ + 10.6 (c 1.02, EtOH) optically pure} *via* hydrolysis with KOH\MeOH and comparing the optical rotation of (R)-propranolol with literature value (Eq. 53).



(R)–(+)–122 (R)–(+)–1 (53)

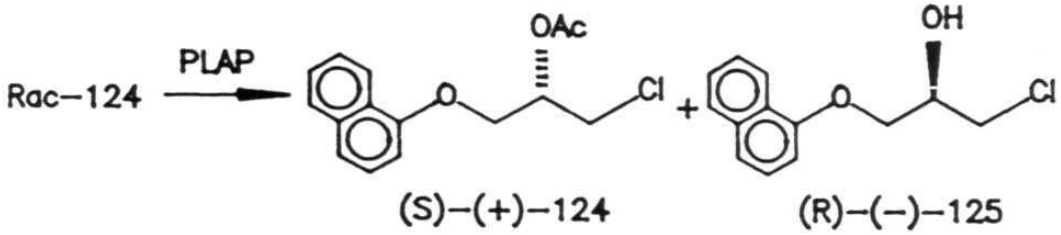
Since the optical purity and the configuration of propranolol obtained are not what we were hoping for, we directed our attention towards the synthesis of a suitable precursor for the preparation of homochiral (S)-propranolol. We have chosen the acetate of chlorohydrin 124, as a suitable precursor. We prepared (±)-2-acetoxy-1-chloro-3-(1-naphthoxy)propane (124) in one step directly from the (±)-glycidyl 1-naphthyl ether (121) by treatment with acetyl chloride in presence of catalytic amount of pyridine (eq. 54). The structure of this compound was confirmed by IR, ^1H & ^{13}C NMR spectral data. It is worthwhile to mention here that the synthesis of (S)-(-)-propranolol *via* lipase PS catalyzed

enantioselective transesterification of (±)-124 was reported by Bevinakatti *et al.* recently.[166]



(54)

We subjected the racemic acetate 124 first to PLAP catalyzed hydrolysis under usual conditions (eq. 55). HPLC analysis showed accomplishment of 35% hydrolysis in 45h. The (R)-(-)-chlorohydrin 125 , $[\alpha]_D^{20}$ - 4.37 (c 1.6, EtOH) {Lit.[166] $[\alpha]_D^{25}$ +9.0 (c 1.9 EtOH),



(55)

>95% ee} obtained has 46% optical purity and the (S)-(+)-acetate 124, $[\alpha]_D^{20}$ + 5.9 (c 0.84, EtOH) {Lit.[166] $[\alpha]_D^{25}$ - 19.9 (c 2.4, EtOH), >95% ee} has 28% optical purity. Efforts are under progress in our laboratory to improve the optical purities of these products by making some structural changes.

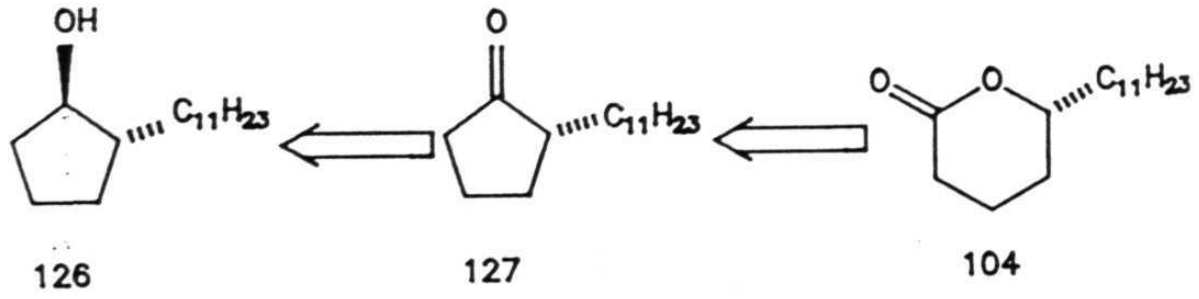
Towards the synthesis of optically active 5-hexadecanolide (104), pheromone of *Vespa orientalis*:

Optically active substituted δ-valerolactones constitute an important class of natural products *e.g.* pheromones.[169] The title

compound, 5-hexadecanolide (104), pheromone of the oriental hornet, *Vespa orientalis* has attracted attention of many organic chemists.[170] Several syntheses of this molecule that rely either on naturally occurring homochiral precursors[171] or hydroxy acids generated *via* hydrogenation of keto acids using chiral catalysts[172] or Baker's yeast[173] have been reported in literature. This moelcule has also been synthesized *via* Baeyer-Villiger oxidation of optically active cyclopentanone, generated *via* reductive cleavage chiral acetal.[174]

We plan to synthesize optically active 5-hexadecanolide (104) using enzymatic methodology. We have identified the (±)-*trans*-2-undecylcyclopentan-1-ol (126) as the key intermediate since this alcohol can be resolved *via* enantioselective hydrolysis of its acetate 126a, catalyzed by enzymes. The optically active alcohols thus procured, can be converted into the required lactone *via* Baeyer-Villiger oxidation of the corresponding ketone 127 (Scheme 35).

SCHEME 35:

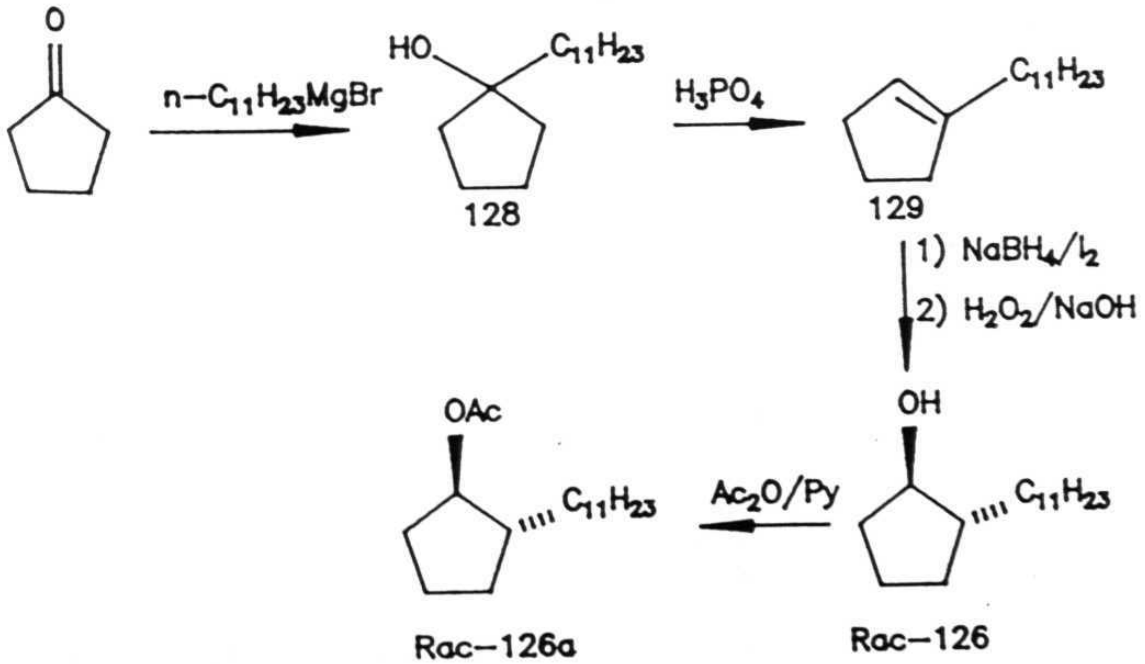


126 127 104

The synthesis of (±)-1-acetoxy-2-(n-undecyl)cyclopentane

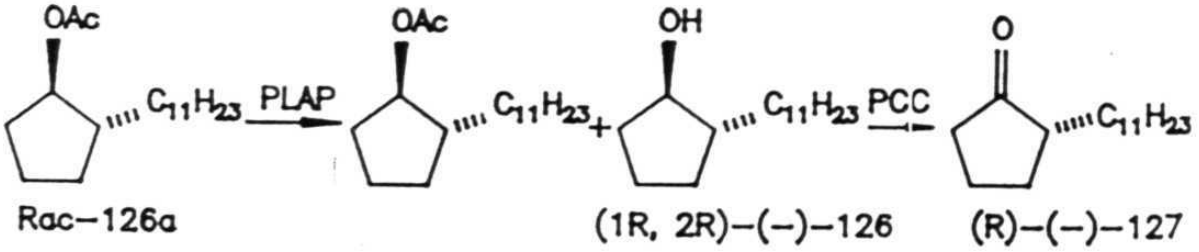
(126a) was achieved using the strategy outlined in the Scheme 36. The tertiary alcohol 128 was obtained in 50% yield by the addition of n-undecylmagnesium bromide on cyclopentanone in THF at $0^{o}C$. This cyclopentanol 128 upon dehydration with H_3PO_4 afforded 1-(n-undecyl)cyclopentene (129) in 85% yield. This cyclopentene was converted into (±)-*trans*-2-(n-undecyl)cyclopentan-1-ol (126) *via* hydroboration with $NaBH_4$-I_2 (following the procedure reported by Periasamy *et al*[175]) followed by oxidation with H_2O_2\NaOH in 80% yield. This cyclopentanol 126 was converted into corresponding racemic acetate 126a by treating the alcohol with acetic anhydride in presence of pyridine and DMAP. The structures of the molecules 126, 126a, 128, 129 were established by IR, ^{1}H & ^{13}C NMR spectral data.

SCHEME 36:



The racemic acetate **126a** was then subjected to PLAP catalyzed hydrolysis in biphasic medium containing ether and phosphate buffer of pH 8.0 in 1:4 ratio and at room temperature. The progress of the hydrolysis was monitored by GC. After 5 days, (25% hydrolysis), the reaction was quenched and products were isolated. The product, (-)-*trans*-2-(n-undecyl)cyclopentan-1-ol (**126**), $[\alpha]_D^{20}$ - 10.2 (c 1.66, $CHCl_3$) was isolated in 76% chemical yield. It produced (R)-(-)-2-(n-undecyl)cyclopentan-1-one (**127**), $[\alpha]_D^{20}$ - 35.09 (c 2.97, ether), {Lit.[174] $[\alpha]_D^{24}$ + 81.0 (1.04, ether), 97% ee} with 42% optical purity, upon oxidation with PCC.[176] This shows that the absolute configuration of the alochol (-)-**126** to be (1R, 2R) with 42% optical purity (Scheme 37). The enantiomerically enriched acetate was not analyzed as the enantiomeric excess of the product alcohol was not upto satisfactory levels.

SCHEME 37:

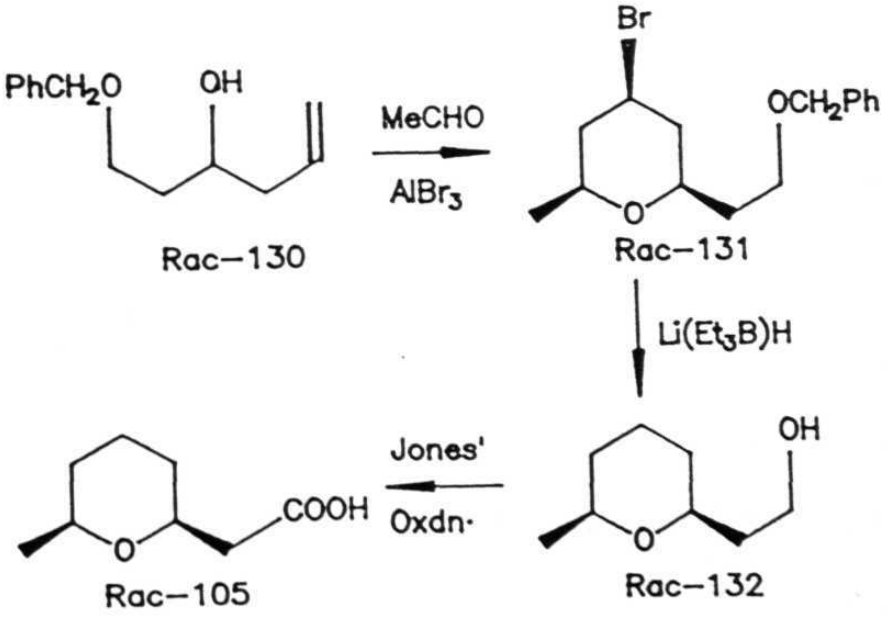


In fact, the conversion of optically active 2-undecylcyclopentan-1-one to 5-hexadecanolide *via*, Baeyer-Villiger oxidation with mCPBA was reported in the literature.[174] However, we have not proceeded further as optical purity of the ketone **127** is not satisfactory.

Towards synthesis of optically active (*cis*-6-methyltetrahydropyran-2-yl)acetic acid (105):

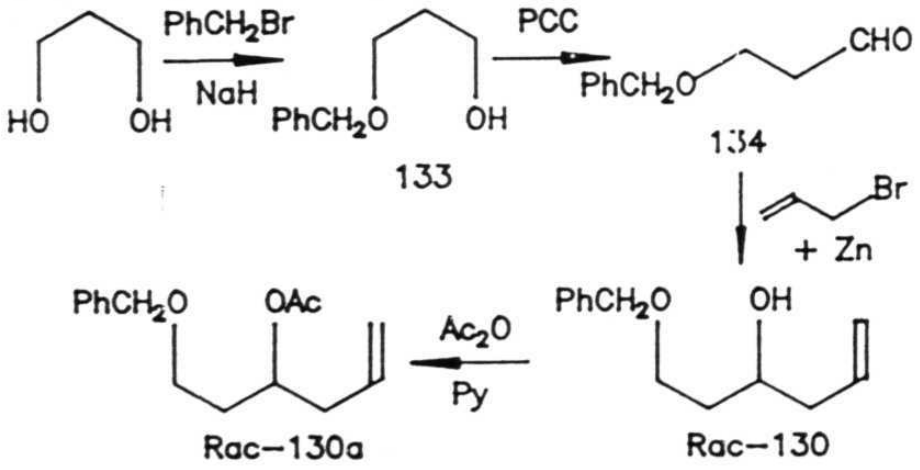
The (+)-S,S-(*cis*-6-methyltetrahydropyran-2-yl)acetic acid (105) is a constituent of glandular secretion of civet cat (*Viverra civetta*).[177] The synthesis of 105, both optically active[178-180] and racemic,[181] has attracted considerable attention owing to the stereocontrol required by it. Of these, only the syntheses of Kenian *et al.*[179] and Jones *et al*[180] are based on chirons generated enzymatically. Taddei *et al.*[181] recently reported an elegant synthesis of (±)-105 (Scheme 38). It occurs to us the intermediates 130, 131, and 132 could be precursors of substrates for enzymatic hydrolysis in order to obtain them in optically active form so that the synthesis of optically active 105 would be achieved.

SCHEME 38:



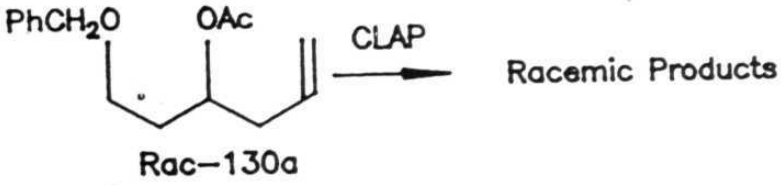
Accordingly, the compound 130 was prepared as outlined in Scheme 39. The 1,3-propanediol was converted into monobenzyl ether 133 *via* monoalkylation with benzyl bromide in presence of sodium hydride. The monobenzyl ether of propanediol was converted into corresponding aldehyde 134 *via* PCC oxidation.[176] The Luche's allylation reaction[130] on this aldehyde afforded (±)-1-benzyloxy-5-hexen-3-ol (130). The racemic alcohol 130 was converted into corresponding acetate 130a by treating it with acetic anhydride in presence of pyridine and DMAP (Scheme 39). Structures of compounds 130, 133, 134, and 130a have been established by IR, ^{1}H & ^{13}C NMR spectral data.

SCHEME 39:



The racemic acetate 130a was subjected to CLAP-catalyzed hydrolysis under previously described conditions (eq. 56). We have chosen CLAP because racemic acetates of homoallyl alcohols are good substrates for CLAP. Hydrloysis has taken place but the product alcohol and unhydrolyzed acetate from this reaction turned

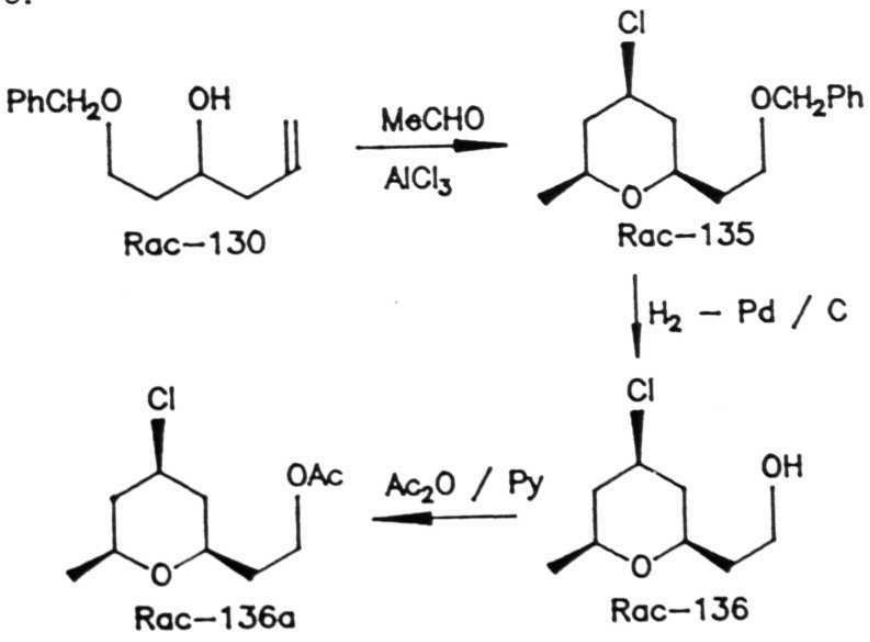
ut to be optically inactive.



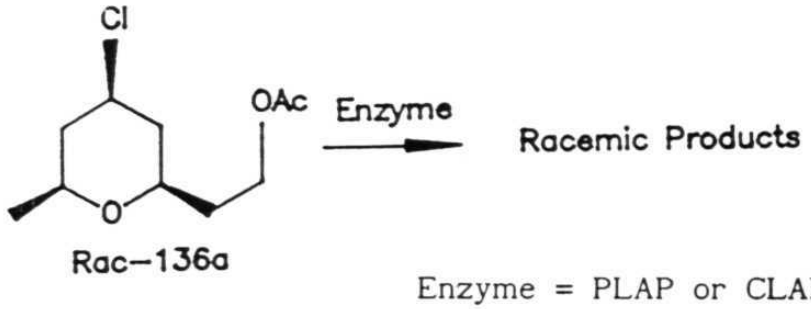
(56)

Then we turned our attention towards the second compound 131. We prepared corresponding chloro-compound 135 instead of 31, according to the scheme 40. The racemic alcohol 130 was converted into the all-*cis*-tetrahydropyran compound 135 by allowing a mixture of (±)-130, acetaldehyde and aluminium chloride (anhydrous) in benzene at 0-5^{O}C following the procedure described by Taddei *et al*[181]. The racemic 135 was debenzylated *via* hydrogenolysis catalyzed by 5% palladium on carbon to get the racemic alcohol 136. The racemic alcohol 136 upon treatment with acetic anhydride in presence of pyridine and DMAP produced the required racemic acetate 136a (Scheme 40).

SCHEME 40:



This racemic acetate 136a was first subjected to CLAP catalyzed hydrolysis which produced only racemic alcohol and acetate. Here we thought of changing the enzyme. Accordingly, we subjected the racemic acetate 136a to PLAP catalyzed hydrolysis which too produced racemic alcohol and acetate (Eq. 57).

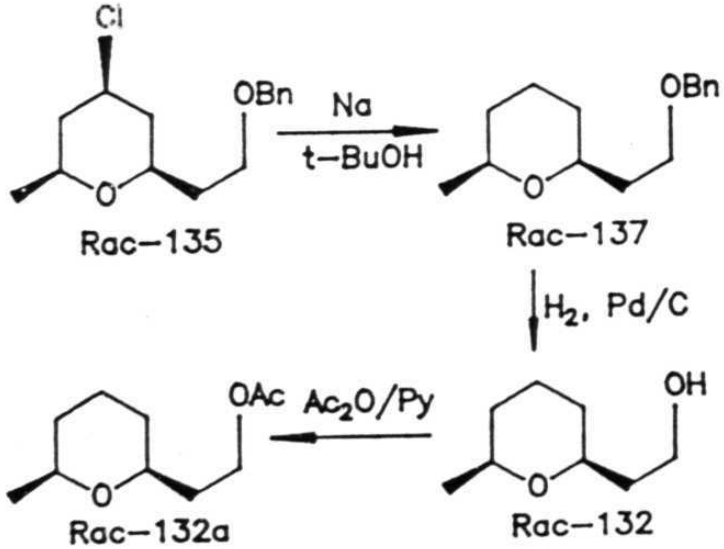


(57)

Enzyme = PLAP or CLAP

Next we thought of employing the third compound, the (±)-132 as starting material for the enzymatic substrate. Accordingly we prepared compound 132 using the following strategy (Scheme 41).

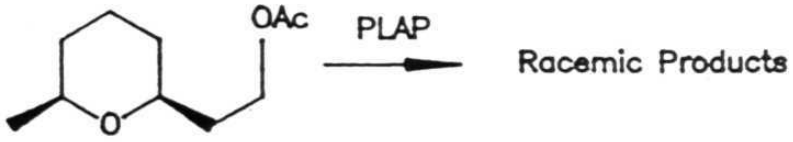
SCHEME 41:



We first dechlorinated the (±)-all-*cis*-tetrahydropyran compound 135 by treating it with sodium metal in presence of t-butyl

alcohol and then the dechlorinated compound 137 was debenzylated *via* hydrogenolysis catalyzed by 5% palladium on charcoal to get (±)-2'-(*cis*-6-methyltetrahydropyran-2-yl)ethanol (132). This alcohol was converted into the corresponding racemic acetate **132a** by treatment with acetic anhydride.

The racemic acetate **132a** was subjected to PLAP catalyzed hydrolysis which produced racemic alcohol and acetate (Eq. 58). These studies demonstrate that the substrates 130a, 132a and **136a** are not suitable to enzymatic enantioselective hydrolysis using PLAP.



Rac–132a (58)

About active sites of PLE and CLE:

In the abscence of X-ray structure, it is difficult to predict the steric course of enzymatic transformation of a new substrate relying on literature analogies. It can often lead to erroneous conclusions. Such a case was presented by PLE-catalyzed enantioselective hydrolysis. PLE was so fickle, often exhibiting reversal of stereoselectivities triggered by apparently trivial changes even within structurally similar series of substrates. But the advent of active-site model, developed by Jones *et al.*,[182] has

changed the scenario completely. With the aid of Jones' active-site model of PLE, almost all the previously reported anamalous results could be explained.

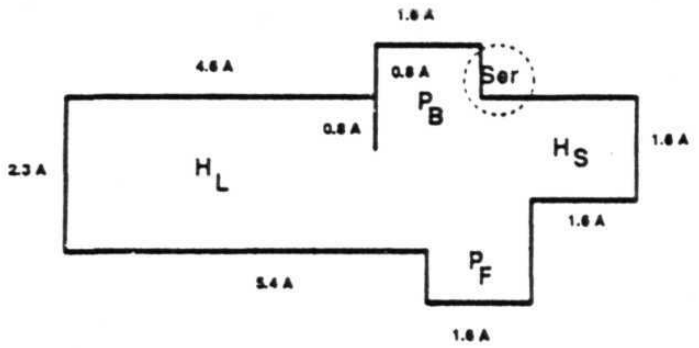


Fig: Top perspective of active-site model of PLE (Jones et al.)[182].

Though we do not have any evidence for the structure of active-site of esterase(s) present in chicken liver acetone powder which is responsible for enantioselective hydrolysis, we can speculate a possible active-site model for esterase(s) in CLAP on the basis of our experimental results, particularly, in the case of (±)-*trans*-1-acetoxy-2-arylcyclohexanes (**120a-g**). PLAP hydrolyzes only (±)-*trans*-1-acetoxy-2-phenylcyclohexane (**120a**) and fails to hydrolyze other (±)-*trans*-1-acetoxy-2-arylcyclohexanes (**120b-g**). Where as CLAP hydrolyzes a variety of (±)-*trans*-1-acetoxy-2-arylcyclohexanes (**120a-g**). Therefore we believe that the esterase(s) in CLAP has larger pockets when compared to PLE which can accomdate sterically bulkier substrates.

Conclusion:

Our prime objective of utilizing crude esterases, *viz.*, pig liver acetone powder (PLAP) and chicken liver acetone powder (CLAP) as alternatives to expensive isolated esterases has met with considerable success. We have succeeded in providing simple and inexpensive procedures for the synthesis of optically active secondary homoallyl alcohols (98) and *anti*-homoallyl alcohols (99) with very high enantiomeric purities. We have succeeded in producing a variety of homochiral *trans*-2-arylcyclohexan-1-ols (103), versatile chiral auxiliaries, *via* CLAP mediated hydrolysis of corresponding racemic acetates. We have made a good study of PLAP catalyzed enantioselective hydrolysis of acetates of racemic α-methylene-β-hydroxypropanoates (101) and propanenitriles (102). More study is required to achieve synthesis of enantiomerically pure (S)-propranolol (1). We believe that crude enzymes will be future reagents of choice for obtaining enantiomerically pure compounds.

EXPERIMENTAL

Melting points: Melting points were recorded on a Buchi 510 apparatus and are uncorrected.

Boiling points: Boiling points refer to the temperatures measured using short path distillation units and are uncorrected.

Infrared Spectra: Infrared spectra were recorded on Perkin-Elmer model 1310 or 297 spectrophotometers. All the spectra were calibrated against polystyrene absorption at 1601 cm^{-1}. Solid samples were recorded as KBr wafers and liquid samples as film between NaCl plates.

Nuclear Magnetic Resonance Spectra: Proton magnetic resonance spectra (100 or 200 MHz) and carbon-13 magnetic resonance spectra (25 or 50 MHz) were recorded either on JEOL-FX-100 or Brucker 200 spectrometer. Spectra for all the samples were measured in chloroform-d solution with tetramethylsilane(δ = 0 ppm) as internal reference. Spectral assignments are as follows: (1) Chemical shift on the δ scale, (2) Standard abbreviation for multiplicity, i.e., s = singlet, d = doublet, t = triplet, q = quartet, br = broad, (3) Number of hydrogens integrated for the signal, (4) Coupling constant J in Hertz.

Mass spectral analysis: Mass spectra were recorded on Finnigon MAT instrument (70 ev, 100 A, 180^{o}C).

Optical rotations: Optical rotations were measured either on Autopol II automatic polarimeter or Jasco DIP 370 Digital

polarimeter at the wavelength of the sodium D-line (589 nm) and at ambient temperatures.

Chromatography: Analytical thin layer chromatography (TLC) was performed on glass plates (7 x 2 cm) coated with Acme's silica gel G (250 mμ) containing 13% calcium sulphate as binder. Visualization of spots was achieved by exposure to iodine vapor. Column chromatography was carried out using Acme's silica gel (100-200 mesh). High pressure liquid chromatography (HPLC) analysis was carried out either on Waters Associates Liquid Chromatograph equipped with model 440 absorbance detector (for conversion ratio determination) or Shimadzu C-R4A Chromatopac equipped with SPD-10A UV-VIS detector (for e.e. determinations) using special grade solvents. E.e determinations were carried out using chiral column, CHIRALCEL OD supplied by Daicel, Jpn. Gas chromatography analysis was carried out on a CHEMITO Gas chromatograph equipped with a flame ionization detector on SE-30 or carbowax column using nitrogen as carrier gas.

General: All reactions were monitored by TLC while enzymatic reactions were monitored by HPLC. Moisture sensitive reactions were carried out using standard syringe-septum techniques under nitrogen atmosphere. All the solvents used were dried and distilled using suitable drying agents before use. The yields of products of enzymatic hydrolysis are based on conversion ratios.

(±)-1-Phenyl-3-buten-1-ol (98a):

This was prepared according to Luche's method.[130]

To a saturated aqueous NH_4Cl solution (100 mL), zinc dust (7.8 g, 120 mM), and a mixture of allyl bromide (10.4 mL, 120 mM) and benzaldehyde (10.2 mL, 100 mM) in THF (20 mL) were added. The resulting suspension was stirred at room temperature for 1h. Then the suspension containing zinc salts was extracted with ether and the ether layer was dried over anhydrous sodium sulphate. Removal of solvent followed by distillation under reduced pressure yielded pure alcohol as a colourless liquid.

Yield : 14 g (95%)

b.p. : 96°C at 3 mm (Lit.[183] b.p. 71°C at 0.75 mm)

IR (neat): 3375 cm^{-1}

^1H NMR : δ 2.22 (br, 1H, D_2O washable), 2.48 (t, 2H, J = 6 Hz), 4.68 (m, 1H), 4.88-5.24 (m, 2H), 5.50-6.00 (m, 1H), 7.30 (s, 5H).

^{13}C NMR : δ 42.59, 73.35, 118.12, 125.94, 127.47, 128.36, 134.59, 144.06

(±)-1-(4-Methylphenyl)-3-buten-1-ol (98b):

This compound was prepared from 4-tolualdehyde, allyl bromide and zinc dust following the same procedure as described for compound **98a**, as a colourless liquid.

Yield : 92%

b.p. : 92°C at 2.5 mm (Lit.[183] b.p. 74-75°C at 0.42 mm)

IR (neat): 3375 cm^{-1}

^1H NMR : δ 2.20-2.60 (m, 6H, 1H D_2O washable), 4.60 (t, 1H, J = 6 Hz), 4.88-5.20 (m, 2H), 5.44-6.00 (m, 1H), 7.12 (m, 4H).

^{13}C NMR : δ 20.70, 43.29, 73.06, 117.30, 125.77, 128.77, 134.65, 136.59, 141.06.

(±)-1-(4-Chlorophenyl)-3-buten-1-ol (98c):

This compound was prepared from 4-chlorobenzaldehyde, allyl bromide and zinc dust according to the procedure described for compound **98a**, as a colourless liquid.

Yield : 94%

b.p. : 122°C at 1.5 mm (Lit.[183] b.p. 98.5-99°C at 0.30 mm)

IR (neat): 3375 cm^{-1}

^1H NMR : δ 2.40 (t, 2H, J = 6 Hz), 2.80 (br, 1H, OH), 4.58 (t, 1H, J = 6 Hz), 4.88-5.20 (m, 2H), 5.44-5.92 (m, 1H), 7.20 (m, 4H).

^{13}C NMR : δ 43.53, 72.59, 118.53, 127.24, 128.48, 133.04, 134.01, 142.36.

(±)-1-(4-Methoxyphenyl)-3-buten-1-ol (98d):

This compound was prepared from 4-anisaldehyde, allyl bromide and zinc dust following the same procedure as described

for compound **98a**, as a colourless liquid.

Yield : 90%

b.p. : 122°C at 1.5 mm (Lit.[183] b.p. 102-103°C at 0.35 mm)

IR (neat): 3400 cm^{-1}

^1H NMR : δ 2.16 (br, 1H, OH), 2.44 (t, 2H, J= 6 Hz), 3.76 (s, 3H), 4.62 (t, 1H, J= 6 Hz), 4.88-5.24 (m, 2H), 5.60-6.08 (m, 1H), 6.80 (d, 2H, J = 8 Hz), 7.20 (d, 2H, J = 8 Hz).

^{13}C NMR : δ 43.12, 54.65, 72.71, 113.35, 117.12, 126.88, 134.59, 136.12, 158.53.

(±)-1-(1-Naphthyl)-3-buten-1-ol (98e):

This compound was prepared from 1-naphthaldehyde, allyl bromide and zinc dust following the same procedure as described for compound **98a**, as a colourless oil.

Yield : 94%

b.p. : 148°C at 1.5 mm

IR (neat): 3375 cm^{-1}

^1H NMR : δ 2.12 (br, 1H, OH), 2.36-2.92 (m, 2H), 5.00-5.28 (m, 2H), 5.48 (m, 1H), 5.64-6.16 (m, 1H), 7.28-8.16 (m, 7H).

^{13}C NMR : δ 42.94, 70.24, 119.00, 123.36, 125.77, 126.24, 128.12, 129.24, 130.65, 134.04, 135.34, 140.01.

(±)-1-(2,4-Dichlorophenyl)-3-buten-1-ol (98f):

This compound was prepared from 2,4-dichlorobenzaldehyde, allyl bromide and zinc dust following the same procedure as described for compound **98a**. This was obtained as a crystalline solid.

Yield : 95%

m.p. : 51-52^{o}C

IR (KBr) : 3250 cm^{-1}

^{1}H NMR : δ 2.04-2.72 (m, 3H, 1H D_2O washable), 4.84-5.32 (m, 3H), 5.60-6.04 (m, 1H), 7.04-7.60 (m, 3H).

^{13}C NMR : δ 41.76, 69.18, 118.77, 127.30, 128.06, 129.06, 132.18, 133.42, 133.83, 139.89.

Mass(M^+) : 216 and 218.

(±)-1-(3,4-Dichlorophenyl)-3-buten-1-ol (98g):

This compound was prepared from 3,4-dichlorobenzaldehyde, allyl bromide and zinc dust following the same procedure as described for compound **98a**, as a colourless liquid.

Yield : 91%

b.p. : 126^{o}C at 1 mm

IR (neat): 3350 cm^{-1}

^{1}H NMR : δ 2.44 (m, 3H, 1H D_2O washable), 4.64 (t, 1H, J = 6 Hz) 4.88-5.26 (m, 2H), 5.40-5.96 (m, 1H), 6.96-7.36 (m, 3H).

^{13}C NMR : δ 43.41, 72.06, 118.88, 125.30, 127.89, 130.30, 131.18, 132.41, 133.59, 144.24.

Mass(M^+) : 216 and 218.

(±)-1-Acetoxy-1-phenyl-3-butene (106a):

To a solution of racemic 1-phenyl-3-buten-1-ol (7.4 g, 50 mM) in dry dichloromethane (50 mL) were added pyridine (8.9 mL, 110 mM) and 4-dimethylaminopyridine (0.122 g, 1 mM). To this acetic anhydride (9.4 mL, 100 mM) was added dropwise with stirring. After 3h stirring at room temperature, the reaction mixture was taken up in ether (150 mL) and washed successively with ice cold 2N HCl (3 x 30 mL) and saturated K_2CO_3 solution. The organic layer was dried over anhydrous Na_2SO_4. The liquid obtained after concentration was purified by column chromatography (10 % ethyl acetate in hexane) to afford pure racemic acetate as a colourless liquid.

Yield : 8.5 g (90%)

IR (neat): 1740 cm^{-1}

^1H NMR : δ 2.04 (s, 3H), 2.60 (m, 2H), 4.88-5.24 (m, 2H), 5.44-5.92 (m, 2H), 7.28 (s, 5H).

(±)-1-Acetoxy-1-(4-methylphenyl)-3-butene (106b):

This compound was prepared by treating (±)-**98b** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**, as a colourless liquid.

Yield : 92 %

IR (neat): 1740 cm^{-1}

^1H NMR : δ 2.02 (s, 3H), 2.30 (s, 3H), 2.40-2.68 (m, 2H), 4.80-5.16 (m, 2H), 5.40-5.88 (m, 2H), 7.16 (m, 4H).

(±)-1-Acetoxy-1-(4-chlorophenyl)-3-butene (106c):

This compound was prepared by treating (±)-98c with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 106a, as a colourless liquid.

Yield : 89%

IR (neat): 1740 cm^{-1}

^1H NMR : δ 2.06 (s, 3H), 2.40-2.64 (m, 2H), 4.84-5.16 (m, 2H), 5.28-5.90 (m, 2H), 7.24 (s, 4H).

(±)-1-Acetoxy-1-(4-methoxyphenyl)-3-butene (106d):

This compound was prepared by treating (±)-98d with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 106a, as a colourless liquid.

Yield : 93%

IR (neat): 1740 cm^{-1}

^1H NMR : δ 2.02 (s, 3H), 2.32-2.82 (m, 2H), 3.76 (s, 3H), 4.84-5.16 (m, 2H), 5.40-5.88 (m, 2H), 6.82 (d, 2H, J= 8 Hz), 7.22 (d, 2H, J = 8 Hz)

(±)-1-Acetoxy-1-(1-naphthyl)-3-butene (106e):

This compound was prepared by treating (±)-98e with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 106a, as a colourless oil.

Yield : 92%

b.p. : 162°C at 0.5 mm

IR (neat): 1740 cm^{-1}

^1H NMR : δ 2.08 (s, 3H), 2.76 (t, 2H, J = 6 Hz), 4.88-5.24 (m, 2H), 5.48-6.04 (m, 1H), 6.60 (t, 1H, J = 6 Hz), 7.32-8.24 (m, 7H).

(±)-1-Acetoxy-1-(2,4-dichlorophenyl)-3-butene (106f):

This compound was prepared by treating (±)-98f with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 106a, as a colourless liquid.

Yield : 92%

b.p. : 120°C at 0.9 mm

IR (neat): 1740 cm^{-1}

^1H NMR : δ 2.08 (s, 3H), 2.54 (t, 2H, J = 6 Hz), 4.84-5.24 (m, 2H), 5.44-5.96 (m, 1H), 6.12 (t, 1H, J = 6 Hz), 7.04-7.52 (m, 3H).

(±)-1-Acetoxy-1-(3,4-dichlorophenyl)-3-butene (106g):

This compound was prepared by treating (±)-98g with acetic anhydride in the presence of pyridine and DMAP following the same

procedure as described for compound **106a**, as a colourless liquid.

Yield : 89%

IR (neat): 1740 cm^{-1}

^1H NMR : δ 2.08 (s, 3H), 2.52 (m, 2H), 4.84-5.16 (m, 2H), 5.40-5.84 (m, 2H), 7.00-7.44 (m, 3H).

Pig liver acetone powder (PLAP):

This was prepared according to the procedure reported by Ohno *et al.*[38]

Freshly purchased pig liver (500 g) was homogenised in chilled acetone (2 L) using kitchen juicer. The brown mass obtained after filtration was air dried at room temperature and powdered using juicer. Fibrous material was removed by sieving to furnish 100 g of PLAP as fine powder. This powder can be stored for 2-3 months in refrigerator without any significant loss of activity.

General procedure:

PLAP/CLAP-catalyzed hydrolysis of racemic acetates:

To 0.5 M, pH 8.0, KH_2PO_4/K_2HPO_4 buffer (40 mL), racemic acetate (5 mM) in ether (10 mL) was added with stirring at room temperature. After 10 min., PLAP/CLAP (1 g) was addded and the stirring was continued. The progress of the hydrolysis was monitored by HPLC/GC. When an appropriate degree of hydrolysis was accomplished, the reaction was quenched with 2N HCl (10 mL)

To this sodium chloride (5 g) and dichloromethane (50 mL) were added and the resulting suspension was vigorously stirred for 0.5h. Then the enzyme was removed by filtration with suction and the layers were separated. The aqueous layer was extracted with dichloromethane (3 x 20 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Removal of solvent followed by column chromatography (silica gel, 10% ethyl acetate in hexane) of the crude liquid obtained, afforded optically active alcohol and enantiomerically enriched unhydrolyzed acetate.

General procedure:

Hydrolysis of recovered acetates with KOH:

To a solution of 85% KOH (0.5 g, 7.5 mM) in MeOH (5 mL) was added recovered acetate (3 mM) and stirred for 3h at room temperature. Then methanol was removed under vacuum and the residue was diluted with water (5 mL) and extracted with ether (3 x 10 mL). The ether layer was dried over anhydrous Na_2SO_4 and concentrated. The crude liquid obtained was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to afford pure (-)-alcohol.

PLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-phenyl-3-butene (106a):

Hydrolysis of racemic-106a (0.95 g, 5 mM) with PLAP (1 g)

afforded (R)-(+)-alcohol and unhydrolyzed acetate in 59:41 ratio.

Reaction time : 24h

Yield of (+)-alcohol : 0.26 g (61%)

Optical rotation : $[\alpha]_D^{20}$ + 27.55 (c 2.54, PhH), 58% e.e.

{Lit.[131] $[\alpha]_D^{21}$ - 39.9 (c 2.48, PhH), 84% e.e.}

Yield of recovered acetate: 0.36 g (90%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (-)-alcohol.

Yield of (-)-alcohol : 0.24 g (94%)

Optical rotation : $[\alpha]_D^{20}$ - 31.25 (c. 1.24, PhH), 66% e.e.

{Lit.[131] $[\alpha]_D^{21}$ - 39.9 (c 2.48, PhH), 84% e.e.}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

PLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(4-methylphenyl)-3-butene (106b):

Hydrolysis of racemic-**106b** (1.02 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 43:57 ratio.

Reaction time : 32h

Yield of (+)-alochol : 0.32 g (90%)

Optical rotation : $[\alpha]_D^{20}$ + 30.66 (c 1.69, PhH), 67% e.e.

{Lit.[131] $[\alpha]_D^{25}$ - 37.3 (c 2.0, PhH), 82% e.e}

Yield of recovered acetate: 0.53 g (92%)

The above recovered acetate upon hydrolysis (KOH/MeOH)

afforded (-)-alcohol.

Yield of (-)-alcohol : 0.37 g (90%)

Optical rotation : $[\alpha]_D^{20}$ - 24.20 (c. 2.74 PhH), 53% e.e.

{Lit.[131] $[\alpha]_D^{25}$ - 37.3 (c 2.0, PhH), 82% e.e}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

PLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(4-chlorophenyl)-3-butene (106c):

Hydrolysis of racemic-106c (1.12 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 39:61 ratio.

Reaction time : 32h

Yield of (+)-alcohol : 0.31 g (87%)

Optical rotation : $[\alpha]_D^{20}$ + 21.94 (c 2.5, PhH), 65% e.e.

{Lit.[131] $[\alpha]_D^{23}$ - 28.4 (c 3.03, PhH), 84% e.e.}

Yield of recovered acetate: 0.62 g (91%).

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.46 g (92%)

Optical rotation : $[\alpha]_D^{20}$ - 15.92 (c 5.26, PhH), 47% e.e.

{Lit.[131] $[\alpha]_D^{23}$ - 28.4 (c 3.03, PhH), 84% e.e.}.

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

PLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(4-methoxyphenyl)-3-butene (106d):

Hydrolysis of racemic-**106d** (1.1 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 43:57 ratio.

Reaction time : 32h

Yield of (+)-alcohol : 0.28 g (74%)

Optical rotation : $[\alpha]_D^{20}$ + 52.65 (c 7.82, PhH), 64% e.e.

{Lit.[131] $[\alpha]_D^{23}$ - 65.8 (c 3.56, PhH), 80% e.e.}

Yield of recovered acetate: 0.56 (90%)

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.4 g (89%)

Optical rotation : $[\alpha]_D^{20}$ - 37.1 (c 6.96 PhH), 45% e.e.

{Lit.[131] $[\alpha]_D^{23}$ - 65.8 (c 3.56, PhH), 80% e.e.}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

PLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(1-naphthyl)-3-butene (106e):

Hydrolysis of racemic-**106e** (1.2 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 50:50 ratio.

Reaction time : 50h

Yield of (+)-alcohol : 0.435 g (88%)

Optical rotation : $[\alpha]_D^{20}$ + 69.96 (c 3.3, PhH), 72% e.e.

{Lit.[131] $[\alpha]_D^{24}$ - 77.5 (c 2.98, PhH) 80% e.e.}

Yield of recovered acetate: 0.54 g (90%)

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.4 g (92%)

Optical rotation : $[\alpha]_D^{20}$ - 63.07 (c 6.29, PhH), 65% e.e.

{[Lit.[131] $[\alpha]_D^{24}$ - 77.5 (c 2.98, PhH, 80% e.e.}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

PLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(2,4-dichlorophenyl)-3-butene (106f) :

Hydrolysis of racemic-**106f** (1.29 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 38:62 ratio.

Reaction time : 24h

Yield of (+)-alcohol : 0.32 g (77%)

Optical rotation : $[\alpha]_D^{20}$ + 36.95 (c 3.68, PhH), 56 % e.e.

Yield of recovered acetate: 0.56 g (70%).

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.43 g (92%)

Optical rotation : $[\alpha]_D^{20}$ - 19.80 (c 2.02, PhH), 30 % e.e.

(based on $[\alpha]_D$ value of (+)-**98f**)

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

Determination of enantiomeric purity of (+)-(98f):

Mosher's ester of (±)-98f:

To a suspension of oil free sodium hydride (10 mg, 0.4 mM) in pyridine (0.5mL) at room temperature were added (±)-98f (11 mg, 0.05 mM) and DMAP (5mg) and stirred for 15 min. To this 0.1 M solution of (+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPACl) in dichloromethane (1 mL, 0.1 mM) was added and stirred for 24 hr. Then the reaction mixture was poured into cold 4N HCl (5 mL) and extracted with ether (3 x 5 mL). The ether layer was washed with saturated K_2CO_3 solution and dried over anhydrous Na_2SO_4. Removal of solvent followed by column purification (silica gel, 10% ethyl acetate in hexane) of the residue afforded pure Mosher's ester.

^{1}H NMR (200 MHz) : δ 2.60 (t, 2H), 3.48 & 3.58 (two singlets, 3H), 4.95-5.20 (m, 2H), 5.50-5.90 (m, 1H), 6.35-6.55 (m, 1H), 7.25-7.50 (m, 8H).

Two distinct singlets at δ 3.48 and 3.58 are of equal integration indicating that the compound is a 50:50 mixture of two diastereomers.

Mosher's ester of (+)-98f:

Mosher's ester of (+)-98f was prepared from (+)-MTPACl and the corresponding alcohol following the same procedure as described for Mosher's ester of (±)-98f. The ^{1}H NMR spectrum of this compound contained two singlets at δ 3.48 and 3.58 with

integration in the ratio 12.9:3.6 establishing the enantiomeric purity of (+)-98f to be 56%.

Chicken liver acetone powder (CLAP):

Freshly purchased chicken liver (500 g) was homogenised in chilled acetone (2 L) using kitchen juicer. The brown mass obtained after filtration was air dried at room temperature and powdered using juicer. Fibrous material was removed by sieving to afford 100 g of CLAP as fine powder. This powder can be stored for 2-3 months without any significant loss of activity.

CLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(1-naphthyl)-3-butene (106e):

Hydrolysis of racemic-106e (1.2 g, 5 mM) with CLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 28:72 ratio.

Reaction time : 20h

Yield of (+)-alcohol : 0.25 g (89%)

Optical rotation : $[\alpha]_D^{22}$ + 92.9 (c 1.26, PhH), 96% e.e.

{Lit.[131] $[\alpha]_D^{24}$ - 77.5 (c 2.98, PhH), 80% e.e.}

Yield of recovered acetate: 0.8 g (93%).

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.6 g (92%)

Optical rotation : $[\alpha]_D^{22}$ - 31.18 (c 0.89, PhH), 32% e.e.

{Lit.[131] $[\alpha]_D^{24}$ - 77.5 (c 2.98, PhH), 80% e.e.}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

CLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-phenyl-3-butene (106a):

Hydrolysis of racemic-106a (0.95 g, 5 mM) with CLAP (1 g) afforded (R)-(+)-alcohol and unhydrolyzed acetate in 30:70 ratio.

Reaction time : 35h

Yield of (+)-alcohol : 0.19 g (86%)

Optical rotation : $[\alpha]_D^{22}$ + 34.08 (c 1.11, PhH), 72% e.e.

{Lit.[131] $[\alpha]_D^{21}$ - 39.9 (c 2.48, PhH), 84% e.e.}

Yield of recovered acetate: 0.62 g (93%).

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.46g (95%)

Optical rotation : $[\alpha]_D^{22}$ - 18.42 (c 1.84, PhH), 38% e.e.

{Lit.[131] $[\alpha]_D^{21}$ - 39.9 (c 2.48, PhH), 84% e.e.}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

CLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(4-methylphenyl)-3-butene (106b):

Hydrolysis of racemic-106b (1.02 g, 5 mM) with CLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 41:59 ratio.

Reaction time : 40h

Yield of (+)-alcohol : 0.3 g (90%)

Optical rotation : $[\alpha]_D^{22}$ + 44.62 (c 3.83, PhH), 98% e.e.

{Lit.[131] $[\alpha]_D^{25}$ - 37.3 (c 2.00, PhH), 82% e.e.}

Yield of recovered acetate:0.53 g (91%).

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.4g (92%)

Optical rotation : $[\alpha]_D^{22}$ - 33.20 (c 1.13, PhH), 73% e.e.

{Lit.[131] $[\alpha]_D^{25}$ - 37.3 (c 2.0, PhH), 82% e.e.}.

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

CLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(4-chlorophenyl)-3-butene (106c):

Hydrolysis of racemic-106c (1.12 g, 5 mM) with CLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 32:68 ratio.

Reaction time : 22h

Yield of (+)-alcohol : 0.22 g (75%)

Optical rotation : $[\alpha]_D^{22}$ + 32.18 (c 3.20, PhH), 95% e.e.

{Lit.[131] $[\alpha]_D^{23}$ - 28.4 (c 3.03, PhH), 84% e.e.}

Yield of recovered acetate: 0.68 g (89%).

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.51 g (93%)

Optical rotation : $[\alpha]_D^{22}$ - 17.37 (c 2.24, PhH), 51% e.e.

{Lit.[131] $[\alpha]_D^{23}$ - 28.4 (c 3.03, PhH), 84% e.e.}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

CLAP-catalyzed hydrolysis of (±)-1-acetoxy-1-(2,4-dichlorophenyl)-3-butene (106f):

Hydrolysis of racemic-**106f** (1.29 g, 5 mM) with CLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 42:58 ratio.

Reaction time : 40 h

Yield of (+)-alcohol : 0.42 g (92%)

m.p. : 58-59°C

Optical rotation : $[\alpha]_D^{22}$ + 56.70 (c 1.30, PhH), 85 % e.e.

Yield of recovered acetate: 0.7 g (93%).

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.54 g (92%)

Optical rotation : $[\alpha]_D^{22}$ - 37.51 (c 1.35 PhH), 56 % e.e.

(based on $[\alpha]_D$ value of (+)-**98f**)

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

Determination of enantiomeric purity:

Mosher's ester of (+)-98f:

Mosher's ester of (+)-98f was prepared from (+)-MTPACl and the corresponding alcohol following the same procedure as described for Mosher's ester of (±)-98f. The ^{1}H NMR (200 MHz) spectrum of this compound contained two singlets at δ 3.48 and 3.58 with integration in the ratio 4.6:0.4 establishing the enantiomeric purity of (+)-98f to be 85%.

CLAP-catalyzed hydrolysis of (±)-1-acetoxy-(3,4-dichlorophenyl)-3-butene (106g):

Hydrolysis of racemic-106g (1.29 g, 5 mM) with CLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 31:69 ratio.

Reaction time : 20h

Yield of (+)-alcohol : 0.29 g (88%)

Optical rotation : $[\alpha]_D^{22}$ + 23.30 (c 2.06, PhH), 92 % e.e.

Yield of recovered acetate: 0.81 g (91%).

The above recovered acetate upon hydrolysis (KOH/MeOH) afforded (-)-alcohol.

Yield of (-)-alcohol : 0.61 g (90%)

Optical rotation : $[\alpha]_D^{22}$ - 11.79 (c 2.18, PhH), 46 % e.e.

(based on $[\alpha]_D$ value of (+)-98g)

Both (+)-alcohol and (-)-alcohol have IR, ^{1}H & ^{13}C NMR data identical with that of the corresponding racemic compound.

Determination of enantiomeric purity:

Mosher's ester of (±)-98g:

This was prepared from (±)-98g and (+)-MTPACl following the same procedure as described for Mosher's ester of (±)-98f.

^{1}H NMR (200 MHz) : δ 2.60 (m, 2H), 3.45 & 3.57 (two singlets, 3H), 4.95-5.20 (m, 2H), 5.45-6.00 (m, 2H), 7.00-7.60 (m, 8H).

Two singlets at δ 3.45 and 3.57 are of almost equal integration indicating that the compound is a 50:50 mixture of two diastereomers.

Mosher's ester of (+)-98g:

Mosher's ester of (+)-98g was prepared from (+)-MTPACl and the corresponding alcohol following the same procedure as described for Mosher's ester of (±)-98g. The ^{1}H NMR (200 MHz) spectrum of this compound contained two singlets at δ 3.45 and 3.57 with integration in the ratio 4.7:0.2 establishing the enantiomeric purity of (+)-98g to be 92 %.

(1E)-1-Chloro-3-phenylprop-2-ene (cinnamyl chloride) :

To a solution of cinnamyl alcohol (38.5 mL, 300 mM) in dry ether (300 mL) at 0^{o}C, thionyl chloride (32.8 mL, 450 mM) was added dropwise over 30 min. with stirring. After 1h stirring at 0^{o}C, the reaction mixture was allowed to warm to room temperature and stirred for 5h. Then the solvent and excess thionyl chloride were removed under reduced pressure. The crude liquid was distilled under reduced pressure to afford pure cinnamyl chloride as a pale yellow liquid.

Yield : 39 g (85%)

b.p. : 70-74^{o}C at 2 mm (Lit.[184] b.p. 83-84^{o}C at 1-2 mm)

IR (neat): No hydroxyl absorption.

^{1}H NMR : δ 5.16 (d, 2H, J = 6 Hz), 5.96-6.72 (m, 2H), 7.28 (m, 5H).

(±)-*anti*-1,2-Diphenylbut-3-en-1-ol (99a):

This compound was prepared following literature procedure.[136]

To a mixture of cinnamyl chloride (11.1 mL, 80 mM) and benzaldehyde (10.2 mL, 100 mM) in THF (100 mL), water (40 mL) was added and the resulting suspension was heated to 60^{o}C. Then aluminium powder (2.16 g, 80 mM) and tin (II) chloride dihydrate (9.02 g, 40 mM) were added in quick succession with vigorous stirring. Then the reaction mixture was stirred for 3h at 60^{o}C. The reaction mixture was cooled to room temperature and diluted with 2N HCl (50 mL). The reaction mixture was extracted with ether (3 x 50 mL). The combined organic layer was washed with saturated $NaHCO_3$ solution and dried over anhydrous Na_2SO_4. Removal of solvent followed by column chromatography (silica gel, 10% ethyl acetate in hexane) of the crude afforded pure alcohol as a colourless liquid.

Yield : 14 g (78%)

IR (neat): 3375 cm^{-1}

^{1}H NMR : δ 2.36 (br, 1H, OH), 3.44 (t, H, J= 8 Hz), 4.68 (d, 1H, J= 8H), 4.88-5.22 (m, 2H), 5.84-6.34 (m, 1H), 6.96-7.36 (m, 10H).

^{13}C NMR : δ 58.94, 77.12, 118.18, 126.53, 126.71, 127.36, 127.89, 128.30, 137.94, 140.71, 142.01.

(±)-*anti*-1-(4-Methylphenyl)-2-phenylbut-3-en-1-ol (99b):

This compound was prepared from 4-tolualdehyde and cinnamyl chloride following the same procedure as described for compound **99a**, as a pale yellow liquid.

Yield : 75%

IR (neat): 3375 cm^{-1}

^{1}H NMR : δ 1.52 (br, 1H, OH), 2.26 (s, 3H), 3.52 (t, 1H, J= 8 Hz) 4.76 (d, 1H, J= 8 Hz), 4.96-5.36 (m, 2H), 5.92-6.52 (m, 1H), 6.80-7.48 (m, 9H).

^{13}C NMR : δ 19.88, 57.71, 75.82, 116.83, 125.36, 125.53, 127.18, 127.36, 127.47, 135.71, 137.06, 138.06, 139.89.

(±)-*anti*-1-(4-Chlorophenyl)-2-phenylbut-3-en-1-ol (99c):

This compound was prepared from 4-chlorobenzaldehyde and cinnamyl chloride following the same procedure as described for compound **99a**, as a pale yellow liquid.

Yield : 80%

IR (neat): 3400 cm^{-1}

^{1}H NMR : δ 2.36 (s, 1H, OH), 3.44 (t, 1H, J= 8 Hz), 4.78 (d, 1H, J= 8 Hz) 4.96-5.44 (m, 2H), 5.92-6.48 (m, 1H), 6.84-7.40 (m, 9H).

^{13}C NMR : δ 59.23, 76.59, 118.77, 126.95, 128.24, 128.48, 126.65, 133.12, 137.77, 140.48, 140.71.

(±)-*anti*-2-methyl-4-phenylhex-5-en-3-ol (99d):

This compound was prepared from isobutyraldehyde (4 equivalents) and cinnamyl chloride (1 equivalent) following the same procedure as described for compound **99a**, as a colourless liquid.

Yield : 73%

IR (neat): 3400 cm^{-1}

^{1}H NMR : δ 0.68-1.04 (m, 6H), 1.32-1.96 (m, 2H, 1H D_2O washable), 3.16-3.64 (m, 2H), 4.92-5.28 (m, 2H), 5.84-6.32 (m, 1H), 6.96-7.40 (m, 5H).

^{13}C NMR : δ 15.76, 20.06, 29.70, 54.59, 78.47, 116.53, 126.59, 128.06, 128.77, 138.89, 142.18.

(±)-*anti*-6-Methyl-3-phenylhept-1-en-4-ol (99e):

This compound was prepared from isovaleraldehyde (3 equivalents) and cinnamyl chloride (1 equivalent) following the same procedure as described for compound **99a**, as a colourless liquid.

Yield : 72%

b.p. : 98-100°C at 1 mm

IR (neat): 3425 cm^{-1}

^1H NMR : δ 0.68-1.00 (m, 6H), 1.00-1.96 (m, 4H, 1H D_2O washable), 3.20 (t, 1H, J= 8 Hz), 3.84 (m, 1H), 4.92-5.28 (m, 2H), 5.80-6.32 (m, 1H), 6.88-7.40 (m, 5H).

^{13}C NMR : δ 21.64, 23.76, 24.53, 43.88, 57.82, 72.18, 117.65, 126.71, 128.30, 128.77, 138.65, 142.18.

(±)-*anti*-3-Phenyloct-1-en-4-ol (99f):

This compound was prepared from valeraldehyde (3 equivalents) and cinnamyl chloride (1 equivalent) following the same procedure as described for compound **99a**, as a colourless liquid.

Yield : 74%

b.p. : 116-118°C at 2 mm

IR (neat): 3350 cm^{-1}

^1H NMR : δ 0.80 (distorted t, 3H), 1.30 (m, 6H), 1.72 (br, 1H, OH), 3.20 (t, 1H, J= 8 Hz), 3.72 (m, 1H), 4.84-5.24 (m, 2H), 5.72-6.22 (m, 1H), 6.92-7.36 (m, 5H).

^{13}C NMR : δ 13.91, 22.50, 27.83, 34.16, 57.11 73.97, 117.36, 126.42, 127.99, 128.48, 138.34, 141.85.

(±)-*anti*-3-Phenylnon-1-en-4-ol (99g):

This compound was prepared from capronaldehyde (2.5 equivalents) and cinnamyl chloride (1 equivalent) following the same procedure as described for compound **99a**, as a colourless liquid

Yield : 70%

b.p. : 110-112°C at 2 mm

IR (neat): 3400 cm^{-1}

^1H NMR : δ 0.84 (distorted t, 3H), 1.28 (br, 8H), 1.72 (br, 1H, OH), 3.20 (t, 1H, J= 7.5 Hz), 3.76 (m, 1H), 4.92-5.28 (m, 2H) 5.80-6.28 (m, 1H), 6.96-7.40 (m, 5H).

^{13}C NMR : δ 14.00, 22.59, 25.47, 31.82, 34.59, 57.23, 74.12, 117.53, 126.65, 128.34, 128.71, 138.59, 142.12.

(±)-*anti*-3-Phenyldec-1-en-4-ol (99h):

This compound was prepared from n-heptaldehyde and cinnamyl chloride following the same procedure as described for compound **99a**, as a colourless liquid.

Yield : 74%

b.p. : 120-122°C at 1 mm

IR (neat): 3425 cm^{-1}

^1H NMR : δ 0.84 (distorted t, 3H), 1.22 (m, 10H), 1.76 (br, 1H, OH), 3.20 (t, 1H, J= 8 Hz), 3.76 (m, 1H), 4.96-5.28 (m, 2H), 5.80-6.32 (m, 1H), 6.92-7.44 (m, 5H).

^{13}C NMR : δ 17.94, 22.47, 25.59, 29.11, 31.70, 34.41, 57.18, 74.00, 117.59, 126.53, 128.06, 128.65, 138.48, 141.94.

(±)-*anti*-4-Acetoxy-3,4-diphenylbut-1-ene (107a):

This compound was prepared by treating (±)-**99a** with acetic anhydride in presence of pyridine and DMAP following the same

procedure as described for compound **106a**, as a colourless liquid.

Yield : 92%

IR (neat): 1730 cm^{-1}

^1H NMR (200 MHz) : δ 1.85 & 2.08 (two singlets in 1:99, 3H), 3.75 (t, 1H, J = 8 Hz), 5.05-5.26 (m, 2H), 5.91-6.30 (m, 2H), 6.87-7.40 (m, 10H).

^{13}C NMR : δ 21.11, 56.65, 78.35, 117.30, 126.83, 127.30, 127.89, 128.16, 128.48, 128.59, 137.77, 138.68, 140.01, 170.24.

(±)-*anti*-4-Acetoxy-4-(4-methylphenyl)-3-phenylbut-1-ene (107b):

This compound was prepared by treating (±)-**99b** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**, as a colourless liquid.

Yield : 94%

IR (neat): 1730 cm^{-1}

^1H NMR : δ 2.08 (s, 3H), 2.28 (s, 3H), 3.76 (t, 1H, J = 8 Hz), 4.88-5.32 (m, 2H), 5.88-6.36 (m, 2H), 6.76-7.40 (m, 9H).

^{13}C NMR : δ 21.17, 56.65, 78.06, 117.30, 126.88, 127.47, 128.59, 128.71, 128.93, 136.06, 137.51, 138.18, 140.30, 170.18.

(±)-*anti*-4-Acetoxy-4-(4-chlorophenyl)-3-phenyl-but-1-ene (107c):

This compound was prepared by treating (±)-**99c** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**, as a colourless liquid

Yield : 91%

IR (neat): 1730 cm^{-1}

^1H NMR : δ 2.04, (s, 3H), 3.64 (t, 1H, J= 8 Hz), 4.84-5.24 (m, 2H), 5.80-6.40 (m, 2H), 6.76-7.36 (m, 9H).

^{13}C NMR : δ 21.06, 56.58, 77.47, 117.59, 127.06, 128.36, 128.65, 128.77, 133.65, 137.54, 139.65, 170.06.

(±)-*anti*-4-Acetoxy-5-methyl-3-phenylhex-1-ene (107d):

This compound was prepared by treating (±)-**99d** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**, as a colourless liquid.

Yield : 92%

IR (neat): 1730 cm^{-1}

^1H NMR (200 MHz) : δ 0.90 (two d, 6H, J = 6 Hz), 1.52-1.71 (m, 1H), 1.82 & 2.04 (two singlets in 1:99, 3H), 3.54 (t, 1H, J = 8 Hz), 5.05-5.25 (m, 3H), 5.90-6.15 (m, 1H), 7.20-7.40 (m, 5H).

^{13}C NMR : δ 15.42, 19.53, 20.58, 28.59, 52.88, 79.00, 116.18, 126.59, 127.77, 128.59, 138.53, 141.00, 170.47.

(±)-*anti*-4-Acetoxy-6-methyl-3-phenylhept-1-ene (107e):

This compound was prepared by treating (±)-**99e** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**, as a colourless liquid.

Yield : 93%

IR (neat): 1740 cm^{-1}

^1H NMR (200 MHz) : δ 0.82 (two doublets, 6H, J = 5 Hz), 1.05-1.65 (m, 3H), 1.86 & 2.04 (two singlets in 2:98, 3H), 3.35 (t, 1H, J = 8 Hz), 5.05-5.18 (m, 2H), 5.24-5.40 (m, 1H), 5.94-6.14 (m, 1H), 7.15-7.40 (m, 5H).

^{13}C NMR : δ 20.70, 21.29, 23.11, 24.29, 41.29, 55.71, 73.82, 116.36, 126.59, 127.89, 128.53, 138.24, 140.89, 170.11.

(±)-*anti*-4-Acetoxy-3-phenyloct-1-ene (107f):

This compound was prepared by treating (±)-99f with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 106a, as a colourless liquid.

Yield : 92%

IR (neat): 1730 cm^{-1}

^1H NMR (200 MHz) : δ 0.80 (distorted t, 3H), 1.10-1.51 (m, 6H), 1.86 & 2.04 (two inglets in 3:97, 3H), 3.40 (t, 1H, J = 8 Hz), 5.02-5.30 (m, 3H), 5.90-6.12 (m, 1H), 7.22 (m, 5H).

^{13}C NMR : δ 13.29, 20.41, 21.76, 26.84, 31.41, 54.65, 75.24, 116.12, 126.36, 127.65, 128.24, 137.83, 140.65, 168.73.

(±)-*anti*-4-Acetoxy-3-phenylnon-1-ene (107g):

This compound was prepared by treating (±)-99g with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 106a, as a colourless liquid.

Yield : 94%

IR (neat): 1730 cm^{-1}

^1H NMR (200MHz) : δ 0.85 (distored t, 3H), 1.12-1.50 (m, 8H), 1.88 & 2.05 (two singlets in 2:98, 3H), 3.40 (t, 1H, J = 8 Hz), 5.05-5.30 (m, 3H), 5.95-6.15 (m, 1H), 7.15-7.40 (m, 5H).

^{13}C NMR : δ 13.82, 21.00, 22.35, 24.88, 31.41, 32.17, 55.12, 75.82, 116.65, 126.83, 128.12, 128.71, 138.30, 141.12, 170.77.

(±)-*anti*-4-Acetoxy-3-phenyldec-1-ene (107h):

This compound was prepared by treating (±)-**99h** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 106a, as a colourless liquid.

Yield : 94%

IR (neat): 1740 cm^{-1}

^1H NMR (200 MHz) : δ 0.85 (distorted t, 3H), 1.12-1.50 (m, 10H), 1.85 & 1.85 & 2.08 (two singlets, 3H), 3.40 (t, 1H, J = 8 Hz), 5.05-5.30 (m, 3H), 5.90-6.20 (m, 1H), 7.15-7.40 (m, 5H).

^{13}C NMR : δ 13.76, 20.76, 22.29, 25.06, 28.76, 31.41, 32.12, 55.06, 75.59, 116.47, 126.71, 128.01, 128.18, 128.59, 138.24, 141.00, 170.47.

CLAP-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-3,4-diphenylbut-1-ene (107a):

Hydrolysis of racemic-**107a** (1.33 g, 5 mM) with CLAP (2 g) afforded (-)-alcohol and unhydrolyzed acetate in 25:75 ratio.

Reaction time : 10 days

Yield of (-)-alcohol : 0.22 g (80%)

Optical rotation : $[\alpha]_D^{20}$ - 14.26 (c 1.12, $CHCl_3$), 92 % e.e.

{Lit.[137] $[\alpha]_D$ - 12.5 (c 3.4, $CHCl_3$), 97% e.e.}

Yield of recovered acetate: 0.93 g (93%)

Optical rotation : $[\alpha]_D^{20}$ + 11.26 (c 2.13, $CHCl_3$), 25 % e.e.

Both (-)-alcohol and (+)-acetate have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

Determination of enantiomeric purity:

Acetate of (-)-99a:

This was prepared by treating (-)-**99a** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**107a**.

Yield : 92%

This compound has IR, ^1H NMR data identical with that of corresponding racemic compound.

^1H NMR (200 MHz) analysis in the presence of $Eu(hfc)_3$:

The ^1H NMR spectrum of (±)-**107a** (5 mg) was recorded in the presence of $Eu(hfc)_3$ (40 mg). It was observed that the original singlet at δ 2.08 due to $COCH_3$ group shifts and splits into two distinct singlets of equal integration indicating that the two singlets arise from two enantiomers. Similarly, acetate of

(-)-**99a** was subjected to ^{1}H NMR analysis in presence of $Eu(hfc)_3$. The signal of acetoxy-methyl shifts and splits into two distinct singlets but with integration in the ratio 0.6:15.1 indicating that (-)-**99a** is 92% enantiomerically pure. The recovered acetate was subjected to same analysis which showed that its optical purity is 25%.

CLAP-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-5-methyl-3-phenyl-hex-1-ene (107d):

Hydrolysis of racemic-**107d** (1.16 g, 5 mM) with CLAP (2 g) afforded (-)-alcohol and unhydrolyzed acetate in 25:75 ratio.

Reaction time : 11 days

Yield of (-)-alcohol : 0.2 g (87%)

Optical rotation : $[\alpha]_D^{20}$ - 60.65 (c 1.83, $CHCl_3$), 67% e.e.

Yield of recovered acetate: 0.8 g, (92%)

Optical rotation : $[\alpha]_D^{20}$ + 15.61 (c 2.69, $CHCl_3$), 19 % e.e.

Both (-)-alcohol and (+)-acetate have IR, ^{1}H & ^{13}C NMR data identical with that of the corresponding racemic compound.

Determination of enantiomeric purity:

Acetate of (-)-99d:

This was prepared by treating (-)-**99d** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**107a**.

Yield : 91%

This compound has IR, ^1H NMR data identical with that of corresponding racemic compound.

^1H NMR (200 MHz) analysis in the presence of $Eu(hfc)_3$:

The ^1H NMR spectrum of (±)-**107d** (5 mg) was recorded in the presence of $Eu(hfc)_3$ (40 mg). It was observed that the original singlet at δ 2.04 due to $COCH_3$ group splits into two distinct singlets of equal integration indicating that the two singlets arise from the enantiomers. Where as in the ^1H NMR spectrum of acetate of (-)-**99d** recorded in presence of $Eu(hfc)_3$, we observed two singlets in the ratio 1.5:5.5 for acetoxy-methyl protons showing the enantiomeric purity of (-)-**99d** to be 67%. The recovered acetate was subjected to same analysis and its enantiomeric purity was found to be 19%.

CLAP-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-6-methyl-3-phenyl-hept-1-ene (107e):

Hydrolysis of racemic-**107e** (1.23 g, 5 mM) with CLAP (2 g) afforded (-)-alcohol and unhydrolyzed acetate in 32:68 ratio.

Reaction time : 75 h

Yield of (-)-alcohol : 0.3 g (92%)

Optical rotation : $[\alpha]_D^{20}$ - 45.90 (c 2.2, $CHCl_3$), >99% e.e.

Yield of recovered acetate: 0.8 g (95%)

Optical rotation : $[\alpha]_D^{20}$ + 21.03 (c 2.04, $CHCl_3$), 49 % e.e.

Both (-)-alcohol and (+)-acetate have IR, ^1H & ^{13}C NMR data

identical with that of the corresponding racemic compound.

Determination of enantiomeric purity:

Acetate of (-)-99e:

This was prepared by treating (-)-99e with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**107a**.

Yield : 93%

This compound has IR, ^{1}H NMR data identical with that of corresponding racemic compound.

^{1}H NMR (200 MHz) analysis in the presence of Eu(hfc)$_3$:

In the ^{1}H NMR spectrum of (±)-**107e** (5 mg), recorded in the presence of Eu(hfc)$_3$ (40 mg), the original singlet at δ 2.04 due to $COCH_3$ group splits into two distinct singlets of equal integration indicating that the two singlets arise from two enantiomers. Similarly, acetate of (-)-**99e** was subjected to ^{1}H NMR analysis in presence of Eu(hfc)$_3$. The singlet due to $COCH_3$ remained intact (as singlet) indicating that (-)-**99e** is enantiomerically pure. The recovered acetate was subjected to same analysis. Its enantiomeric purity was found to be 49%.

CLAP-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-3-phenyloct-1-ene (107f):

Hydrolysis of racemic-**107f** (1.23 g, 5 mM) with CLAP (2 g) afforded (-)-alcohol and unhydrolyzed acetate in 22:78 ratio.

Reaction time : 65 h

Yield of (-)-alcohol : 0.20 g (89%)

Optical rotation : $[\alpha]_D^{20}$ - 57.41 (c 1.55, $CHCl_3$), 88% e.e.

Yield of recovered acetate: 0.9 g (93%)

Optical rotation : $[\alpha]_D^{20}$ + 27.39 (c 1.89, $CHCl_3$), 24 % e.e.

Both (-)-alcohol and (+)-acetate have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

Determination of enantiomeric purity :

Acetate of (-)-99f:

This was prepared by treating (-)-**99f** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**107a**.

Yield : 92%

This compound has IR, ^1H NMR data identical with that of corresponding racemic compound.

^1H NMR (200 MHz) analysis in the presence of Eu(hfc)$_3$:

The ^1H NMR spectrum of (±)-**107f** (5 mg) was recorded in the presence of Eu(hfc)$_3$ (40 mg). It was observed that the original singlet at δ 2.04 (due to $COCH_3$ group) splits into two distinct singlets of equal integration indicating that they arise from two enantiomers. Similarly, the acetate of (-)-**99f** was subjected to ^1H NMR analysis in presence of Eu(hfc)$_3$. The singlet of acetoxy-methyl group splits into two distinct singlets in the ratio 0.9:15, indicating that (-)-**99f** is 88% enantiomerically

pure. The recovered acetate was subjected to same analysis which showed that its enantiomeric purity is 24%.

CLAP-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-3-phenylnon-1-ene (107g):

Hydrolysis of racemic-**107g** (1.3 g, 5 mM) with CLAP (2 g) afforded (-)-alcohol and unhydrolyzed acetate in 35:65 ratio.

Reaction time : 75 h

Yield of (-)-alcohol : 0.34 g (89%)

Optical rotation : $[\alpha]_D^{20}$ - 44.55 (c 1.61, $CHCl_3$), 80% e.e.

Yield of recovered acetate: 0.80 g (94%)

Optical rotation : $[\alpha]_D^{20}$ + 33.89 (c 2.12, $CHCl_3$), 69 % e.e.

Both (-)-alcohol and (+)-acetate have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

Determination of enantiomeric purity :

Acetate of (-)-99g:

This was prepared by treating (-)-**99g** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**107a**.

Yield : 92%

This compound has IR, ^1H NMR data identical with that of corresponding racemic compound.

^1H NMR (200 MHz) analysis in the presence of Eu(hfc)$_3$:

The ^1H NMR spectrum of (±)-**107g** (5 mg) was recorded in the

presence of $Eu(hfc)_3$ (40 mg). It was observed that the original singlet at δ 2.05 due to $COCH_3$ group shifts and splits into two distinct singlets of equal integration indicating that the two singlets arise from two enantiomers. Similarly, acetate of (-)-**99g** was subjected to ^1H NMR analysis in presence of $Eu(hfc)_3$. The singlet due to acetoxy-methyl protons splits into two distinct singlets in the ratio 1.4:13.0, indicating that (-)-**99g** is 80% enantiomerically pure. The recovered acetate, after same analysis, was found to be 69% enantiomerically pure.

CLAP-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-3-phenyldec-1-ene (107h):

Hydrolysis of racemic-**107h** (1.37g, 5 mM) with CLAP (2 g) afforded (-)-alcohol and unhydrolyzed acetate in 35:65 ratio.

Reaction time : 6 days

Yield of (-)-alcohol : 0.35 g (86%)

Optical rotation : $[\alpha]_D^{20}$ - 46.70 (c 2.18, $CHCl_3$), 92% e.e.

Yield of recovered acetate: 0.82 g (92%)

Optical rotation : $[\alpha]_D^{20}$ + 23.33 (c 2.48, $CHCl_3$), 49 % e.e.

Both (-)-alcohol and (+)-acetate have IR, ^1H & ^{13}C NMR data identical with that of the corresponding racemic compound.

Determination of enantiomeric purity:

Acetate of (-)-99h:

This was prepared by treating (-)-**99h** with acetic anhydride

in presence of pyridine and DMAP following the same procedure as described for (±)-**107a**.

Yield : 92%

This compound has IR, ^{1}H NMR data identical with that of corresponding racemic compound.

^{1}H NMR (200 MHz) analysis in the presence of Eu(hfc)$_3$:

The ^{1}H NMR spectrum of (±)-**107h** (5 mg) was recorded in the presence of Eu(hfc)$_3$ (40 mg). It was observed that the original singlet at δ 2.08 due to $COCH_3$ group shifts and splits into two distinct singlets of equal integration indicating that the two singlets arise from two enantiomers. Similarly, acetate of (-)-**99h** was subjected to ^{1}H NMR analysis in presence of Eu(hfc)$_3$. The singlet due to acetoxy-methyl protons splits into two distinct singlets in the ratio 0.35:9.0, indicating that (-)-**99d** is 92% enantiomerically pure. The recovered acetate was found to be 49% enantiomerically pure by same analysis.

(±)-4-Phenyl-3-butyn-2-ol (100a):

To a solution of bromomagnesium phenylacetylide (100 mM) {prepared from phenylacetylene (11.2 mL, 102 mM) ethylmagnesium bromide (7.5 mL, 100 mM)} in dry ether (100 mL), acetaldehyde (6.7 mL, 120 mM) in dry ether (20 mL) was added dropwise at 0^{o}C. After stirring for 1h at 0^{o}C, the reaction mixture was allowed to warm to room temperature and was stirred further for 1h. Then the

reaction was quenched with saturated NH_4Cl solution. The organic layer was separated and dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue was distilled under reduced pressure to afford pure racemic alcohol as a colourless liquid.

Yield : 12.4 g (85%)

b.p. : 81°C at 2 mm (Lit.[185] b.p. 89-92°C at 3 mm)

IR (neat): 3325, 2230 cm^{-1}

^1H NMR : δ 1.52 (d, 3H, J = 6 Hz), 2.16 (br, 1H, D_2O washable), 4.72 (m, 1H), 7.08-7.52 (m, 5H).

^{13}C NMR : δ 24.17, 58.41, 83.71, 91.24, 122.71, 128.24, 131.65.

(±)-1-Phenyl-1-pentyn-3-ol (100b):

This compound was prepared from bromomagnesium phenylacetylide and propionaldehyde following the same procedure as described for compound **100a**, as a colourless liquid.

Yield : 82%

b.p. : 110°C at 1 mm (Lit.[186] b.p. 133-134°C at 10.5 mm)

IR (neat): 3350, 2250 cm^{-1}

^1H NMR : δ 1.06 (t, 3H, J = 6 Hz), 1.52-2.10 (m, 3H, 1H D_2O washable), 4.52 (t, 1H, J = 6 Hz), 7.00-7.48 (m, 5H).

^{13}C NMR : δ 9.35, 30.76, 63.94, 85.92, 90.06, 122.71, 128.24, 131.65.

(±)-4-Methyl-1-phenyl-1-pentyn-3-ol (100c):

This compound was prepared from bromomagnesium phenyl-

acetylide and isobutyraldehyde following the same procedure as described for compound **100a**, as a colourless liquid.

Yield : 84%

b.p. : 112°C at 1 mm (Lit.[187] b.p. 95°C at 0.5 mm)

IR (neat): 3350 cm^{-1}

^1H NMR : δ 1.06 (two doublets, 6H, J = 6 Hz), 1.48-2.16 (m, 2H, 1H D_2O washable), 4.36 (d, 1H, J = 6 Hz), 7.08-7.48 (m, 5H).

^{13}C NMR : δ 17.41, 18.11, 34.53, 68.12, 85.35, 89.12, 122.83, 128.24, 131.65.

(±)-1,3-Diphenyl-2-propyn-1-ol (100d):

This compound was prepared from bromomagnesium phenylacetylide and benzaldehyde following the same procedure as described for compound **100a**, as a colourless viscous liquid.

Yield : 81%

b.p. : 170°C at 1 mm (Lit.[185] b.p. 165-168°C at 0.5 mm)

IR (neat): 3350, 2210 cm^{-1}

^1H NMR : δ 2.24 (br, 1H, OH), 5.68 (s, 1H), 7.16-7.76 (m, 10H)

^{13}C NMR : δ 64.88, 86.53, 89.00 126.83, 128.36, 128.65, 131.83, 140.83.

(±)-1-Phenyl-2-octyn-1-ol (100e):

This compound was prepared from 1-heptynylmagnesium bromide

and benzaldehyde following the same procedure as described for compound **100a**, as a colourless liquid.

Yield : 88%

b.p. : 130°C at 1 mm (Lit.[188] b.p. 180-182°C at 16 mm)

IR (neat): 3350 cm^{-1}

^1H NMR : δ 0.88 (distorted t, 3H), 1.00-1.72 (m, 6H), 1.92-2.36 (m, 3H, 1H D_2O washable), 5.40 (br, 1H), 7.08-7.60 (m, 5H).

^{13}C NMR : δ 13.76, 18.64, 22.00, 28.11, 30.94, 64.53, 80.12, 87.35, 126.65, 128.01, 128.41, 129.53, 133.89, 141.47.

(±)-3-Acetoxy-1-phenylbut-1-yne (108a):

This compound was prepared by treating (±)-**100a** with acetic anhydride in the presence of pyridine and DMAP following the same procedure as described for compound **106a**, as a colourless liquid.

Yield : (90%)

b.p. : 84°C at 2 mm

IR (neat): 1740, 2250 cm^{-1}

^1H NMR : δ 1.56 (d, 3H, J = 6 Hz), 2.08 (s, 3H), 5.64 (q, 1H, J = 6 Hz), 7.04-7.52 (m, 5H).

(±)-3-Acetoxy-1-phenylpent-1-yne (108b):

This compound was prepared by treating (±)-**100b** with acetic anhydride in the presence of pyridine and DMAP following the same

procedure as described for compound **106a**, as a colourless liquid.

Yield : 88%

b.p. : 92°C at 2 mm

IR (neat): 1740, 2250 cm^{-1}

^1H NMR : δ 1.08 (t, 3H, J = 7 Hz), 1.88 (m, 2H), 2.10 (s, 3H), 5.52 (t, 1H, J = 7 Hz), 7.08-7.52 (m, 5H).

(±)-3-Acetoxy-4-methyl-1-phenylpent-1-yne (108c):

This compound was prepared by treating (±)-**100c** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**, as a colourless liquid.

Yield : 91%

b.p. : 118°C at 2.5 mm

IR (neat): 1740 cm^{-1}

^1H NMR : δ 1.06 (two d, 6H, J = 7 Hz), 1.80-2.24 (m, 4H), 5.40 (d, 1H, J = 5 Hz), 7.00-7.52 (m, 5H).

(±)-3-Acetoxy-1,3-diphenylprop-1-yne (108d):

This compound was prepared by treating (±)-**100d** with acetic anhydride in the presence of pyridine and DMAP following the same procedure as described for compound **106a**, as a viscous liquid.

Yield : 89%

b.p. : 172°C at 2 mm

IR (neat): 1740, 2250 cm^{-1}

^{1}H NMR : δ 2.12 (s, 3H), 6.66 (s, 1H), 7.04-7.64 (m, 10H)

(±)-1-Acetoxy-1-phenyloct-2-yne (108e):

This compound was prepared by treating (±)-100e with acetic anhydride in the presence of pyridine and DMAP following the same procedure as described for compound **106a,** as a colourless liquid.

Yield : 90%

b.p. : 152°C at 4 mm

IR (neat): 1740, 2250 cm^{-1}

^{1}H NMR : δ 0.84 (distorted t, 3H), 0.96-1.68 (m, 6H), 2.04 (s, 3H), 2.20 (m, 2H), 6.40 (m, 1H), 7.08-7.60 (m, 5H).

PLAP-catalyzed hydrolysis of racemic-3-acetoxy-1-phenylbut-1-yne (108a) :

Hydrolysis of racemic-**108a** (0.94 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 40:60 ratio.

Reaction Time : 14h

Yield of (+)-alcohol: 0.24 g, (83%)

Optical Rotation : $[\alpha]_D^{22}$ + 27.4 (c 2.7, EtOH), 88% e.e.

{Lit.[141] $[\alpha]_D^{25}$ + 30.64 (c 5.15, EtOH), 98% e.e.}

Yield of unhydrolyzed acetate: 0.52 g (92%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (-)-alcohol.

Yield of (-)-alcohol: 0.31 g (89%)

Optical Rotation : $[\alpha]_D^{22}$ - 14.15 (c 1.62, EtOH), 45% e.e.

{Lit[141]. $[\alpha]_D^{25}$ + 30.64 (c 5.15, EtOH), 98% e.e.}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the racemic alcohol.

PLAP-catalyzed hydrolysis of racemic-3-acetoxy-1-phenylpent-1-yne (108b):

Hydrolysis of racemic-108b (1.01 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 55:45 ratio.

Reaction Time : 30h

Yield of (+)-alcohol: 0.38 g, (86%)

Optical Rotation : $[\alpha]_D^{22}$ + 3.74 (c 7.48, Ether), 15% e.e.

{Lit.[143] $[\alpha]_D^{21}$ + 21.97 (c 1.27, Ether), 90% e.e.}

Yield of unhydrolyzed acetate: 0.42 g (92%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (-)-alcohol.

Yield of (-)-alcohol: 0.30 g (90%)

Optical Rotation : $[\alpha]_D^{22}$ - 4.42 (c 5.20, Ether), 18% e.e.

{Lit.[143] $[\alpha]_D^{21}$ + 21.97 (c 1.27, Ether), 90% e.e.}

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the racemic alcohol.

PLAP-catalyzed hydrolysis of racemic-3-acetoxy-4-methyl-1-phenyl-

pent-1-yne (108c):

Hydrolysis of racemic-108c (1.08 g, 5 mM) with PLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 35:65 ratio.

Reaction Time : 40h

Yield of (-)-alcohol: 0.25 g, (82%)

Optical Rotation : $[\alpha]_D^{22}$ - 3.08 (c 2.27, EtOH), 39% e.e.

Yield of unhydrolyzed acetate: 0.65 g (92%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.48 g (92%)

Optical Rotation : $[\alpha]_D^{22}$ + 1.59 (c 2.51, EtOH), 21% e.e.

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of the racemic alcohol.

Determination of enantiomeric purity:

Acetate of (-)-100c:

This was prepared by treating (-)-100c with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-106a.

Yield : 91%

This compound has IR , ^1H NMR data identical with that of (±)-108c.

^1H NMR analysis in the presence of $Eu(hfc)_3$:

The ^1H NMR spectrum of (±)-108c (5 mg) was recorded in the presence of $Eu(hfc)_3$ (20 mg). It was observed that original

singlet at δ 2.12 (due to $COCH_3$ group) shifts and splits into two distinct singlets of equal integration indicating that the two singlets arise from two enantiomers. Similarly, acetate of (-)-100c was subjected to ^1H NMR analysis using $Eu(hfc)_3$. The singlet due to $COCH_3$ separated into two distinct singlets of 6.5:15 integration indicating that the enantiomeric excess of (-)-100c to be 39%. The recovered acetate was subjected to the same analysis which showed that its optical purity is 21%.

PLAP-catalyzed hydrolysis of racemic-3-acetoxy-1,3-diphenylprop-1-yne (108d):

Hydrolysis of racemic-108d (1.25 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 30:70 ratio.

Reaction Time : 70h

Yield of (+)-alcohol: 0.28 g, (89%)

Optical Rotation : $[\alpha]_D^{22}$ + 0.999 (c 6.0, $CHCl_3$), 15% e.e.

{Lit.[142] $[\alpha]_D^{25}$ + 2.26 (c 6.63, $CHCl_3$), 34% e.e.}

Yield of unhydrolyzed acetate: 0.8 g (91%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished almost racemic alcohol.

Yield of alcohol : 0.61 g (90%)

Optical Rotation : Nil

{Lit.[142] $[\alpha]_D^{25}$ + 2.26 (c 6.63, $CHCl_3$), 34% ee}

Both (+)-alcohol and the alcohol obtained from recovered

acetate have IR, ^{1}H & ^{13}C NMR data identical with that of the racemic alcohol.

PLAP-catalyzed hydrolysis of racemic-1-acetoxy-1-phenyloct-2-yne (108e):

Hydrolysis of racemic-108e (1.22 g, 5 mM) with PLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 25:75 ratio.

Reaction Time : 26h

Yield of (-)-alcohol: 0.22 g, (87%)

Optical Rotation : $[\alpha]_D^{22}$ - 9.17 (c 3.38, EtOH), 18% e.e.

Yield of unhydrolyzed acetate: 0.85 g (93%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.64 g (91%)

Optical Rotation : $[\alpha]_D^{22}$ + 4.09 (c 1.46, EtOH), 7% e.e.

Both (+)-alcohol and (-)-alcohol have IR, ^{1}H & ^{13}C NMR data identical with that of the racemic alcohol.

Determination of enantiomeric purity:

Acetate of (-)-100e:

This was prepared from (-)-100e and acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-106a.

Yield : 91%

This compound has IR ^{1}H NMR data identical with that of

(±)-108e.

^{1}H NMR analysis in the presence of Eu(hfc)$_3$:

The ^{1}H NMR spectrum of (±)-108e (5 mg) was recorded in the presence of Eu(hfc)$_3$ (20 mg). It was observed that original singlet at δ 2.04 due to $COCH_3$ group shifts and splits into two distinct singlets of equal integration indicating that the two singlets arise from two enantiomers. Similarly, acetate of (-)-100e was subjected to ^{1}H NMR analysis using Eu(hfc)$_3$. The singlet due to $COCH_3$ separated into two distinct singlets with 7:10 integration indicating that the enantiomeric excess of (-)-100e to be 18%. The recovered acetate was subjected to similar ^{1}H NMR analysis which showed that its enantiomeric purity is 7%.

(±)-Methyl 3-hydroxy-3-phenyl-2-methylenepropanoate (101a):

This was prepared following literature procedure.[150]

A mixture of benzaldehyde (10.15 mL, 100 mM), methyl acrylate (13.5 mL, 150 mM) and DABCO (1.68 g, 15 mM) was allowed to react at room temperature for 7 days. The reaction mixture was dissolved in ether (150 mL) and the solution was washed with 2N hydrochloric acid, water and aqueous sodium bicarbonate solution in that order. The ether layer was dried over anhydrous Na_2SO_4. Removal of solvent and excess methyl acrylate on a rotary evaporator followed by distillation of the crude under reduced

pressure afforded pure racemic alcohol as a colourless liquid.

Yield : 16.3 g (85%)

b.p. : 100°C at 0.5 mm

IR (neat): 3450, 1710 cm^{-1}

^1H NMR (200 MHz) : δ 2.98 (d, 1H, OH, J = 5 Hz), 3.72 (s, 3H), 5.56 (d, 1H, J = 5 Hz), 5.80 (m, 1H), 6.30 (s, 1H), 7.32 (s, 5H).

^{13}C NMR : δ 51.82, 72.94, 125.89, 126.77, 127.89, 128.48, 141.59, 142.36, 166.89.

(±)-Methyl 3-hydroxy-3-(4-methylphenyl)-2-methylenepropanoate (101b):

This compound was prepared from 4-tolualdehyde, methyl acrylate and DABCO following the same procedure as described for (±)-**101a,** as a colourless liquid.

Reaction Time : 8 days

Yield : 75%

b.p. : 122°C at 1 mm

IR (neat): 3450, 1710 cm^{-1}

^1H NMR (200 MHz) : δ 2.32 (s, 3H), 2.95 (d, 1H, OH, J = 5 Hz), 3.73 (s, 3H), 5.54 (d, 1H, J = 5 Hz), 5.86 (s, 1H), 6.32 (s, 1H), 7.20 (m, 4H).

^{13}C NMR: δ 20.76, 51.53, 72.35, 125.18, 126.59, 128.89, 137.18, 138.53, 142.36, 166.65.

(±)-Methyl 3-hydroxy-3-(4-chlorophenyl)-2-methylenepropanoate (101c):

This compound was prepared from 4-chlorobenzaldehyde, methyl acrylate and DABCO following the same procedure as described for compound (±)-**101a**, as a colourless liquid.

Reaction Time : 6 days

Yield : 78%

b.p. : 126^{o}C at 1 mm

IR (neat): 3425, 1710 cm^{-1}

^{1}H NMR (200 MHz) : δ 3.06 (d, 1H, OH, J = 6 Hz), 3.72 (s, 3H), 5.50 (d, 1H, J = 6 Hz), 5.80 (s, 1H), 6.32 (s, 1H), 7.30 (s, 4H).

^{13}C NMR : δ 51.70, 72.18, 125.94, 127.89, 128.36, 133.42, 139.83, 141.71, 166.57.

(±)-Methyl 3-hydroxy-3-(2-methoxyphenyl)-2-methylenepropanoate (101d):

This compound was prepared from 2-methoxybenzaldehyde, methyl acrylate and DABCO following the same procedure as described for compound (±)-**101a**, as a colourless liquid.

Reaction Time : 6 days

Yield : 72%

b.p. : 130-132^{o}C at 2 mm

IR (neat): 3450, 1710 cm^{-1}

^{1}H NMR : δ 3.36 (d, 1H, OH, J = 6 Hz), 3.74 (s, 3H), 3.83 (s,

(200 MHz)

3H), 5.71 (s, 1H) 5.84 (d, 1H, J = 6 Hz), 6.28 (s, 1H), 6.72-7.44 (m, 4H).

^{13}C NMR : δ 51.76, 55.41, 68.18, 110.77, 120.83, 125.59, 127.77, 129.00, 129.47, 141.77, 156.83, 167.24.

(±)-Methyl 3-acetoxy-3-phenyl-2-methylenepropanoate (116a):

This compound was prepared by treating (±)-**101a** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**106a**, as a colourless liquid.

Yield : 87%

b.p. : 126^{o}C at 1 mm

IR (neat): 1730 cm^{-1}

^{1}H NMR : δ 2.08 (s, 3H), 3.68 (s, 3H), 5.82 (s, 1H), 6.36 (s, 1H), 6.64 (s, 1H), 7.31 (s, 5H).

(±)-Methyl 3-acetoxy-3-(4-methylphenyl)-2-methylenepropanoate (116b):

This compound was prepared by treating (±)-**101b** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**106a**, as a colourless liquid.

Yield : 85%

b.p. : 142^{o}C at 5 mm

IR (neat): 1730 cm^{-1}

^{1}H NMR : δ 2.06 (s, 3H), 2.30 (s, 3H), 3.66 (s, 3H), 5.82 (s,

1H), 6.34 (s, 1H), 6.60 (s, 1H), 7.16 (m, 4H).

(±)-Methyl 3-acetoxy-3-(4-chlorophenyl)-2-methylenepropanoate (116c):

This compound was prepared by treating (±)-**101c** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**106a**, as a colourless liquid.

Yield : 89%

b.p. : 124°C at 0.6 mm

IR (neat): 1730 cm^{-1}

^1H NMR : δ 2.08 (s, 3H), 3.70 (s, 3H), 5.86 (s, 1H), 6.38 (s, 1H), 6.62 (s, 1H), 7.29 (s, 4H).

(±)-Methyl 3-acetoxy-3-(2-methoxyphenyl)-2-methylenepropanoate (116d):

This compound was prepared by treating (±)-**101d** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**106a**, as a colourless liquid.

Yield : 83%

IR (neat): 1730, 1240 cm^{-1}

^1H NMR : δ 2.08 (s, 3H), 3.72 (s, 3H), 3.82 (s, 3H), 5.61 (s, 1H), 6.36 (s, 1H), 6.76-7.08 (m, 3H), 7.12-7.40 (m, 2H).

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-3-phenyl-2-methylene-

propanoate (116a):

Hydrolysis of racemic-**116a** (1.17 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 41:59 ratio.

Reaction time : 20h

Yield of (+)-alcohol : 0.36 g (90%)

Optical rotation : $[\alpha]_D^{20}$ + 56.13 (c 1.60, Acetone), 46% e.e.

Yield of recovered acetate: 0.62 g (90%)

Optical rotation : $[\alpha]_D^{20}$ - 70.09 (c 2.14, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

^1H NMR (200 MHz) analysis in presence of Eu(hfc)$_3$:

The (±)-**101a** (5 mg) was subjected to ^1H NMR analysis in the presence of Eu(hfc)$_3$ (10mg). It was observed that the singlet at δ 3.72, arising from OMe (COOMe) group shifts and splits into two distinct singlets of equal integration indicating that it is a racemate.

Then the (+)-alcohol was subjected to same analysis under identical conditions. The singlet due to OMe protons now splits into two distinct singlets with integration in 3.7:10.0 ratio, showing that the enantiomeric excess of (+)-**101a** to be 46%.

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-3-(4-methylphenyl)-2-methylenepropanoate (116b):

Hydrolysis of racemic-116b (1.24 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 35:65 ratio.

Reaction time : 28h

Yield of (+)-alcohol : 0.32 g (89%)

Optical rotation : $[\alpha]_D^{20}$ + 76.62 (c 1.29, Acetone), 65% e.e.

Yield of recovered acetate: o.72 g (90%)

Optical rotation : $[\alpha]_D^{20}$ - 88.47 (c 1.97, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

^1H NMR (200 MHz) analysis in presence of Eu(hfc)$_3$:

The ^1H NMR spectrum of (±)-101b (5 mg) was recorded in the presence of Eu(hfc)$_3$ (10 mg). The original singlet at δ 3.73 due to OMe (COOMe) protons splits into two singlets in 1:1 ratio arising from both enantiomers. Similar analysis of (+)-alcohol showed two singlets in the ratio 2.0:9.3 for COOMe protons establishing its enantiomeric purity to be 65%.

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-3-(4-chlorophenyl)-2-methylenepropanoate (116c)

Hydrolysis of racemic-116c (1.34 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 42:58 ratio.

Reaction time : 28h

Yield of (+)-alcohol : 0.41 g (86%)

Optical rotation : $[\alpha]_D^{20}$ + 71.55 (c 1.09, Acetone), 62% e.e.

Yield of recovered acetate: 0.69 g (89%)

Optical rotation : $[\alpha]_D^{20}$ - 85.61 (c 1.64, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

^1H NMR analysis using Eu(hfc)$_3$:

The original singlet at δ 3.72 due to OMe (COOMe) protons appeared as two distinct singlets in 50:50 ratio in the ^1H NMR spectrum of (±)-**101c** (5 mg) recorded in the presence of Eu(hfc)$_3$ (20mg) while that of (+)-**101c** showed two distinct siglets in the ratio 3.2:13.7 indicating that its enantiomeric purity is 62%.

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-(2-methoxyphenyl)-2-methylenepropanoate (116d):

Hydrolysis of racemic-**116d** (1.32 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 24:76 ratio.

Reaction time : 10h

Yield of (+)-alcohol : 0.21 g (79%)

Optical rotation : $[\alpha]_D^{20}$ + 26.33 (c 1.21, Acetone), 50% e.e.

Yield of recovered acetate: 0.94 g (93%)

Optical rotation : $[\alpha]_D^{20}$ - 7.21 (c 1.38, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

^1H NMR (200 MHz) analysis in presence of Eu(hfc)$_3$:

In the ^1H NMR spectrum of (±)-101d (5 mg) recorded in the presence of $Eu(hfc)_3$ (10 mg) the original singlet of OMe (COOMe) protons at δ 3.74, appeared as two distinct singlets of equal integration, indicating that they arise from two enantiomers. On the other hand ^1H NMR spectrum of (+)-101d recorded in presence of $Eu(hfc)_3$ showed two distinct singlets with integration in 9.7:3.2 ratio revealing its enantiomeric purity to be 50%.

(±)-3-Hydroxy-3-phenyl-2-methylenepropanenitrile (102a):

This was prepared following the procedure developed in our laboratory.[151]

A mixture of benzaldehyde (10.2 mL, 100 mM), acrylonitrile (9.87 mL, 150 mM) and DABCO (1.68 g, 15 mM) was allowed to react at room temperature for 40h. The reaction mixture was dissolved in ether (150 mL) and the solution was washed with 2N HCl, water and aqueous sodium bicarbonate solution in that order. The ether layer was dried over anhydrous Na_2SO_4. Removal of solvent and excess acrylonitrile on a rotavapor followed by distillation of the crude under reduced pressure afforded pure racemic alcohol, as a colourless liquid.

Yield : 12.7 g (80%)

b.p. : 120-124°C at 1.5 mm (Lit.[151] b.p. 110°C at 0.95 mm)

IR (neat): 3450, 2240 cm^{-1}

^1H NMR : δ 2.80 (br, 1H, D_2O washable), 5.22 (s 1H), 5.96 (s,

1H), 6.04 (s, 1H), 7.36 (s, 5H).

^{13}C NMR: δ 73.59, 117.00, 125.94, 126.41, 128.21, 130.36, 139.12

(±)-3-Hydroxy-3-(4-methylphenyl)-2-methylenepropanenitrile (102b):

This compound was prepared from p-tolualdehyde, acrylonitrile and DABCO following the same procedure as described for **(±)-102a**, as a colourless liquid.

Reaction time : 50h

Yield : 78%

b.p. : 138-142°C at 0.5 mm

IR (neat): 3440, 2240 cm^{-1}

^{1}H NMR : δ 2.36 (s, 3H), 2.80 (br, 1H, OH), 5.16 (s, 1H), 5.96 (d, 1H, J = 1 Hz), 6.04 (d, 1H, J =1 Hz), 7.20 (m, 4H).

^{13}C NMR : δ 22.53, 75.06, 118.71, 127.83, 128.01, 131.00, 131.47, 131.47, 137.89, 140.01.

(±)-3-Hydroxy-3-(4-chlorophenyl)-2-methylenepropanenitrile (102c):

This compound was prepared from p-chlorobenzaldehyde, acrylonitrile and DABCO following the same procedure as described for **(±)-102a**, as a colourless liquid.

Reaction time : 40h

Yield : 83%

b.p. : 146-148°C at 1.5 mm

IR (neat): 3425, 2225 cm^{-1}

^{1}H NMR : δ 2.60 (br, 1H, OH), 5.24 (s, 1H), 6.02 (d, 2H, J = 6 Hz), 7.30 (s, 4H).

^{13}C NMR : δ 72.32, 116.77, 125.53, 127.83, 128.71, 130.89, 134.12, 137.71.

(±)-3-Hydroxy-3-(2-methoxyphenyl)-2-methylenepropanenitrile(102d):

This compound was prepared from 2-methoxybenzaldehyde, acrylonitrile and DABCO following the same procedure as described for (±)-**102a**, as a colourless liquid.

Reaction time : 40h

Yield : 76%

b.p. : 135-137^{o}C at 1 mm

IR (neat): 3450, 2240 cm^{-1}

^{1}H NMR : δ 3.56 (br, 1H, OH), 3.76 (s, 3H), 5.44 (br, 1H), 5.92 (m, 2H), 6.68-7.40 (m, 4H).

^{13}C NMR : δ 55.00, 68.82, 110.59, 117.06, 120.65, 125.47, 127.06, 129.47, 129.89, 156.24.

(±)-3-Hydroxy-3-(4-isopropylphenyl)-2-methylenepropanenitrile (102e):

This compound was prepared from 4-isopropylbenzaldehyde, acrylonitrile and DABCO following the same procedure as described for (±)-**102a**, as a colourless liquid.

Reaction time : 60h

Yield : 86%

b.p. : 142-144^{o}C at 1 mm

IR (neat): 3450, 2240 cm^{-1}

^{1}H NMR (200 MHz) : δ 1.25 (d, 6H, J= 4 Hz), 2.28 (d, 1H, OH, J= 2 Hz), 2.92 (m, 1H), 5.30 (d, 1H, J= 1 Hz), 6.04 (s, 1H), 6.15 (s, 1H), 7.30 (m, 4H).

^{13}C NMR : δ 23.87, 33.85, 73.97, 117.09, 126.57, 126.96, 129.64, 136.69, 149.70.

(±)-3-Hydroxy-3-(1-naphthyl)-2-methylenepropanenitrile (102f):

This compound was prepared from 1-naphthaldehyde, acrylonitrile and DABCO following the same procedure as described for **(±)-102a**. The crude liquid thus obtained was purified by column chromatography (silica gel, 25% ethyl acetate in hexane) to afford pure alcohol as a viscous liquid.

Reaction time : 75h

Yield : 76%

IR (neat): 3400, 2225 cm^{-1}

^{1}H NMR : δ 3.24 (br, 1H, OH), 5.80 (m, 1H), 5.92 (s, 2H), 7.12-8.00 (m, 7H).

^{13}C NMR : δ 70.59, 117.30, 123.24, 125.24, 125.36, 125.94, 126.53 129.00, 129.42, 130.36, 131.36, 133.83, 134.30.

(±)-3-Acetoxy-3-phenyl-2-methylenepropanenitrile (117a):

This compound was prepared by treating (±)-**102a** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-106a, as a colourless liquid.

Yield : 85%

b.p. : 115°C at 0.5 mm

IR (neat): 2225, 1740 cm^{-1}

^1H NMR (200 MHz) : δ 2.18 (s, 3H), 6.01 (s, 1H), 6.10 (s, 1H), 6.32 (s, 1H), 7.38 (s, 5H).

(±)-3-Acetoxy-3-(4-methylphenyl)-2-methylenepropanenitrile (117b):

This compound was prepared by treating (±)-**102b** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-106a, as a colourless liquid.

Yield : 87%

b.p. : 132°C at 6 mm

IR (neat): 2225, 1740 cm^{-1}

^1H NMR (200 MHz) : δ 2.14 (s, 3H), 2.34 (s, 3H), 5.96 (d, 1H, J = 1 Hz), 6.04 (d, 1H, J = 1 Hz), 6.29 (s, 1H), 7.22 (m, 4H).

(±)-3-Acetoxy-3-(4-chlorophenyl)-2-methylenepropanenitrile (117c):

This compound was prepared by treating (±)-**102c** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**106a** as a colourless liquid.

Yield : 84%

b.p. : 138°C at 2 mm

IR (neat): 2225, 1740 cm^{-1}

^1H NMR (200 MHz) : δ 2.16 (s, 3H), 6.05 (d, 1H, J = 1 Hz), 6.10 (d, 1H, J = 1 Hz), 6.30 (s, 1H), 7.34 (s, 4H).

(±)-3-Acetoxy-3-(2-methoxyphenyl)-2-methylenepropanenitrile(117d):

This compound was prepared by treating (±)-102d) with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-106a, as a colourless liquid.

Yield : 86%

b.p. : 141°C at 2 mm

IR (neat): 2240, 1740 cm^{-1}

^1H NMR (200 MHz) : δ 2.16 (s, 3H), 3.82 (s, 3H), 5.96 (d, 2H, J = 2 Hz), 6.68 (s, 1H), 6.70-7.46 (m, 4H).

(±)-3-Acetoxy-3-(4-isopropylphenyl)-2-methylenepropanenitrile (117e):

This compound was prepared by treating (±)-102e with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-106a, as a colourless liquid.

Yield : 86%

b.p. : 146°C at 2 mm

IR (neat): 2240, 1740 cm^{-1}

^1H NMR : δ 1.22 (d, 6H, J = 6 Hz), 2.18 (s, 3H), 2.90 (m. 1H).

5.96 (s, 1H), 6.08 (s, 1H), 6.30 (s, 1H), 7.12-7.36 (m, 4H).

(±)-3-Acetoxy-3-(1-naphthyl)-2-methylenepropanenitrile (117f):

This compound was prepared by treating (±)-**102f** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for (±)-**106a**, as a colourless liquid.

Yield : 90%

IR (neat): 2240, 1740 cm^{-1}

^1H NMR (200 MHz) : δ 2.20 (s, 3H), 5.92 (d, 1H, J = 1.2 Hz), 6.10 (d, 1H, J = 1.2 Hz), 7.06 (s, 1H), 7.36-8.08 (m, 7H).

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-3-phenyl-2-methylene-propanenitrile (117a):

Hydrolysis of racemic **117a** (1 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 42:58 ratio.

Reaction time : 9h

Yield of (+)-alcohol : 0.27 g (81%)

Optical rotation : $[\alpha]_D^{20}$ + 19.54 (c 1.22, Acetone), 60% e.e.

Yield of recovered acetate: 0.5 g (87%)

Optical rotation : $[\alpha]_D^{20}$ - 6.64 (c 1.65, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

By HPLC anlysis using chiral column:

The enantiomeric excess of (+)-102a was determined to be 60% by HPLC analysis using chiral column, CHIRALCEL OD (25 cm)

Conditions employed:

Substrate	Eluent iPrOH:Hexane	Flow rate mL/min.	Retention time(min.)	Ratio of enantiomers	E.e. %
(±)-102a	5:95	0.4	36.39	49:51	
			38.29		
(+)-102a	5:95	0.4	36.08	19.8:80.2	60
			37.99		

By ^{1}H NMR (200 MHz) analysis in presence of Eu(hfc)$_3$:

The (±)-117a (5 mg) was subjected to ^{1}H NMR analysis in the presence of Eu(hfc)$_3$ (25 mg). It was observed that one of the two singlets at δ 6.01 and 6.10, due to olefinic protons, splits into two distinct singlets of equal integration indicating that it is a racemate.

Then the (+)-alcohol was converted into the corresponding acetate following the same procedure as described for (±)-106a and subjected to ^{1}H NMR analysis under identical conditions. The singlet of olefinic proton now splits into two distinct singlets with integration in 3:12.4 ratio showing the enantiomeric excess of (+)-alcohol to be 61%.

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-3-(4-methylphenyl)-2-methylenepropanenitrile (117b):

Hydrolysis of racemic **117b** (1.075 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 35:65 ratio.

Reaction time : 9h

Yield of (+)-alcohol : 0. 25 g (84%)

Optical rotation : $[\alpha]_D^{20}$ + 27.3 (c 1.13, Acetone), 70% e.e.

Yield of recovered acetate: 0.62 g (89%)

Optical rotation : $[\alpha]_D^{20}$ - 8.16 (c 1.22, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

By HPLC anlysis using chiral column:

The enantiomeric excess of (+)-**102b** was determined to be 70% by HPLC analysis using chiral column, CHIRALCEL OD (25 cm).

Conditions employed:

Substrate	Eluent iPrOH:Hexane	Flow rate mL/min.	Retention time(min.)	Ratio of enantiomers	E.e. %
(±)-**102b**	10:90	0.5	27.342	49.3:50.7	
			29.934		
(+)-**102b**	10:90	0.5	27.119	14.5:85.4	70
			29.615		

By ^1H NMR (200 MHz) analysis in presence of Eu(hfc)$_3$:

The enantiomeric excess of (+)-**102b** was also determined by ^1H NMR analysis of (±)-**117b** and acetate of (+)-**102b** in the presence of Eu(hfc)$_3$ and found to be 72% (on the basis of integrations of separated signals of olefinic protons).

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-3-(4-chlorophenyl)-2-methylenepropanenitrile (117c):

Hydrolysis of racemic-117c (1.18 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 34:66 ratio.

Reaction time : 14h

Yield of (+)-alcohol : 0.29 g (88%)

Optical rotation : $[\alpha]_D^{20}$ + 13.28 (c 0.82, Acetone), 59% e.e.

Yield of recovered acetate: 0.69 g (89%)

Optical rotation : $[\alpha]_D^{20}$ - 6.60 (c 1.81, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^{1}H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

By HPLC anlysis using chiral column:

The enantiomeric excess of (+)-102c was determined to be 59% by HPLC analysis using chiral column, CHIRALCEL OD (25 cm).

Conditions employed:

Substrate	Eluent iPrOH:Hexane	Flow rate mL/min.	Retention time(min.)	Ratio of enantiomers	E.e. %
(±)-102c	10:90	0.5	46.38 50.95	49.6:50.4	
(+)-102c	10:90	0.5	46.00 49.55	20.3:79.6	59

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-(2-methoxyphenyl)-2-methylenepropanenitrile (117d):

Hydrolysis of racemic-117d (1.15 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 35:65 ratio.

Reaction time : 10h

Yield of (+)-alcohol : 0.28 g (88%)

Optical rotation : $[\alpha]_D^{20}$ + 43.60 (c 1.03, Acetone), 64% e.e.

Yield of recovered acetate: 0.69 g (92%)

Optical rotation : $[\alpha]_D^{20}$ - 9.54 (c 1.46, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

By HPLC anlysis using chiral column:

The enantiomeric excess of (+)-**102d** was determined to be 64% by HPLC analysis using chiral column, CHIRALCEL OD (25 cm).

Conditions employed:

Substrate	Eluent iPrOH:Hexane	Flow rate mL/min.	Retention time(min.)	Ratio of enantiomers	E.e. %
(±)-102d	10:90	0.5	30.94	49.1:50.9	
			35.26		
(+)-102d	10:90	0.5	31.70	20.4:79.6	64
			35.92		

By ^1H NMR (200 MHz) analysis in presence of Eu(hfc)$_3$:

^1H NMR analysis of (±)-**117d** and acetate of (+)-**102d** in the presence of Eu(hfc)$_3$ was carried out and the enantiomeric purity of (+)-**102d** was found to be 67% (on the basis of integrations of separated signals of olefinic protons).

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-3-(4-isopropylphenyl)-2-methylenepropanenitrile (117e):

Hydrolysis of racemic-**117e** (1.28 g, 5 mM) with PLAP (1 g) afforded (+)-alcohol and unhydrolyzed acetate in 25:75 ratio.

Reaction time : 14h

Yield of (+)-alcohol : 0.22 g (90%)

Optical rotation : $[\alpha]_D^{20}$ + 23.90 (c 1.02, Acetone), 70% e.e.

Yield of recovered acetate: 0.83 g (88%)

Optical rotation : $[\alpha]_D^{20}$ - 6.79 (c 1.85, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

By HPLC anlysis using chiral column:

The enantiomeric excess of (+)-102e was determined to be 70% by HPLC analysis using chiral column, CHIRALCEL OD (25 cm).

Conditions employed:

Substrate	Eluent iPrOH:Hexane	Flow rate mL/min.	Retention time(min.)	Ratio of enantiomers	E.e. %
(±)-102e	05:95	0.5	32.63	49.8:50.2	70
			34.61		
(+)-102e	05:95	0.5	32.56	14.7:85.2	
			34.49		

PLAP-catalyzed hydrolysis of (±)-3-acetoxy-3-(1-naphthyl)-2-methylenepropanenitrile (117f):

Hydrolysis of racemic-**117f** (1.25 g, 5 mM) with PLAP (1 g)

afforded (+)-alcohol and unhydrolyzed acetate in 29:71 ratio.

Reaction time : 24 h

Yield of (+)-alcohol : 0.26 g (87%)

Optical rotation : $[\alpha]_D^{20}$ + 60.42 (c 0.66, Acetone), 86% e.e.

Yield of recovered acetate: 0.84 g (95%)

Optical rotation : $[\alpha]_D^{20}$ - 14.2 (c 1.12, Acetone)

Both (+)-alcohol and (-)-acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

Determination of enantiomeric purity:

By HPLC anlysis using chiral column:

The enantiomeric excess of (+)-102f was determined to be 86% by HPLC analysis using chiral column, CHIRALCEL OD (25 cm).

Conditions employed:

Substrate	Eluent iPrOH:Hexane	Flow rate mL/min.	Retention time(min.)	Ratio of enantiomers	E.e. %
(±)-102f	30:70	0.5	15.24	51:49	
			23.41		
(+)-102f	30:70	0.5	15.37	6.8:93.2	86
			23.33		

By ^1H NMR (200 MHz) analysis in presence of $Eu(hfc)_3$:

The enantiomeric excess of (+)-102f was determined to be 86% by ^1H NMR analysis of (±)-117f and acetate of (+)-102f in presence of $Eu(hfc)_3$ based on integrations of separated signals of olefinic protons.

(±)-*trans*-2-Phenylcyclohexan-1-ol (103a):

This compound was prepared following the same procedure as reported by Whitesell *et al.*[155]

To a stirred solution of phenylmagnesium bromide (100 mM) in dry THF (100 mL) [prepared from bromobenzene (10.5 mL, 100 mM) and magnesium turnings (2.43 g, 100 mM)] at -20°C, cuprous chloride (0.49 g, 5 mM) was added. After 10 min., a solution of cyclohexene oxide (10.1 mL, 100 mM) in dry THF (10 mL) was added dropwise at the same temperature. After the addition is complete, the reaction mixture was allowed to warm to 0°C. After stirring 2h at 0°C, the reaction was quenched with saturated $(NH_4)_2SO_4$ solution. Organic layer was separated and washed with saturated $(NH_4)_2SO_4$ solution until the aqueous layers were no longer blue. The combined aqueous layer was extracted with ether (3 x 50 mL). The extracts were combined and dried over anhydrous Na_2SO_4 and concentrated. The solid obtained, was crystallized from pentane to furnish the racemic alcohol as a white crystalline solid.

Yield : 14 g (79%)

m.p. : 56-57 (Lit.[155] m.p. 56-57°C)

IR (KBr) : 3300 cm^{-1}

^1H NMR (200 MHz) : δ 1.27-2.17 (m, 9H, 1H D_2O washable), 2.37-2.48 (m, 1H), 3.60-3.71 (m, 1H), 7.20-7.38 (m, 5H).

^{13}C NMR : δ 25.11, 26.06, 33.41, 34.43, 53.18, 74.29, 126.83, 128.12, 128.77, 143.71.

Mass(M^+) : 176

(±)-*trans*-2-(1-Naphthyl)cyclohexan-1-ol (103b):

This compound was prepared from 1-naphthylmagnesium bromide and cyclohexene oxide following the same procedure described for compound **103a**. The crude solid obtained, was crystallized from hexane to furnish racemic alcohol, as a white crystalline solid.

Yield : 65%

m.p. : 129-130°C (Lit.[189] m.p. 129-130°C)

IR (KBr) : 3220 cm^{-1}

^1H NMR (200MHz) : δ 1.49-2.30 (m, 9H, 1H D_2O washable), 3.40 (m, 1H), 4.00 (m, 1H), 7.40-8.25 (m, 7H).

^{13}C NMR : δ 25.24, 26.49, 33.99, 34.96, 47.03, 74.28, 122.94, 123.35, 125.64, 125.71, 126.02, 127.07, 128.99, 132.81, 134.29, 139.70.

Mass(M^+) : 226

(±)-*trans*-2-(4-Methylphenyl)cyclohexan-1-ol (103c):

This compound was prepared from p-tolylmagnesium bromide and cyclohexene oxide following the same procedure as described for compound **103a**. The crude solid obtained, was crystallized from hexane to furnish racemic alcohol as a white crystalline solid.

Yield : 74%

m.p. : 70-72°C (Lit.[190] m.p. 72-73°C)

IR (KBr) : 3250 cm^{-1}

^1H NMR (200MHz) : δ 1.25-2.14 (m, 9H, 1H D_2O washable), 2.32 (s, 3H), 2.32-2.44 (m, 1H), 3.58-3.63 (m, 1H), 7.14 (s, 4H).

^{13}C NMR : δ 21.00, 25.06, 26.06, 33.47, 34.47, 52.76, 74.35, 127.89, 129.47, 136.30, 140.48.

Mass(M^+) : 190

(±)-*trans*-2-(2-Methylphenyl)cyclohexan-1-ol (103d):

This compound was prepared from o-tolylmagnesium bromide and cyclohexene oxide following the same procedure as described for compound **103a**. The crude oil obtained was distilled under reduced pressure to afford pure racemic alcohol as a colourless liquid.

Yield : 70%

b.p. : 96°C at 2 mm (Lit.[159] b.p. 81-82°C at 0.2 mm)

IR (neat): 3400 cm^{-1}

^1H NMR (200 MHz) : δ 1.20-2.20 (m, 9H, 1H D_2O washable), 2.38 (s, 3H), 2.68-2.86 (m, 1H), 3.70-3.90 (m, 1H), 7.00-7.40 (m, 4H).

^{13}C NMR : δ 19.64, 24.94, 26.06, 32.94, 34.35, 47.53, 74.06, 125.47, 126.00, 126.30, 130.41, 137.00, 141.65.

Mass(M^+) : 190

(±)-*trans*-2-(2,4,6-Trimethylphenyl)cyclohexan-1-ol (103e):

This compound was prepared from mesitylmagnesium bromide and cyclohexene oxide following the same procedure as described for

compound **103a**. The crude solid obtained, was crystallized from hexane to furnish racemic alcohol, as a white crystalline solid.

Yield : 78%

m.p. : 76°C (Lit.[191] m.p. 76.5°C)

IR (KBr) : 3400 cm^{-1}

^1H NMR (200MHz) : δ 1.22-2.18 (m, 9H, 1H D_2O washable), 2.23 (s, 3H), 2.33 (s, 3H), 2.45 (s, 3H), 2.92-3.05 (m, 1H), 4.13-4.23 (m, 1H), 6.82 (d, 2H, J= 9 Hz).

^{13}C NMR : δ 20.64, 21.76, 21.94, 25.33, 26.26, 29.82, 35.53, 49.23, 71.35, 129.77, 131.53, 135.36, 135.77, 136.18, 138.59.

Mass(M^+) : 218

(±)-*trans*-2-(4-Methoxyphenyl)cyclohexan-1-ol (103f):

This compound was prepared from 4-anisylmagnesium bromide and cyclohexene oxide following the same procedure as described for compound **103a**. The crude solid obtained was crystallized from hexane to furnish racemic alcohol as a white crystalline solid.

Yield : 71%

m.p. : 70-72°C (Lit.[191] m.p. 71-72°C)

IR (KBr) : 3400 cm^{-1}

^1H NMR (200 MHz) : δ 1.25-2.14 (m, 9H, 1H D_2O washable), 2.30-2.41 (m, 1H) 3.54-3.62 (m, 1H), 3.78 (s, 3H), 6.83-6.90 (m, 2H), 7.13-7.20 (m, 2H).

^{13}C NMR : δ 24.94, 26.00, 33.41, 34.41, 52.18, 55.06, 74.35, 114.06, 128.77, 135.42, 158.47.

Mass(M^+) : 206

(±)-*trans*-2-(4-Bromophenyl)cyclohexan-1-ol (103g):

This compound was prepared from 4-bromophenylmagnesium bromide and cyclohexene oxide following the same procedure as described for compound **103a**. The crude solid obtined was crystallized from hexane to furnish racemic alcohol, as a white crystalline solid.

Yield : 60%

m.p. : 107°C

IR (KBr) : 3250 cm^{-1}

^1H NMR (200MHz) : δ 1.25-2.14 (m, 9H, 1H D_2O washable), 2.33-2.46 (m, 1H), 3.57-3.65 (m, 1H), 7.09-7.16 (m, 2H), 7.41-7.48 (m, 2H).

^{13}C NMR : δ 26.23, 27.11, 34.53, 35.94, 53.26, 75.41, 121.72, 131.00, 133.06, 144.01.

Mass(M^+) : 254 and 256

(±)-*trans*-1-Acetoxy-2-phenylcyclohexane (120a):

This compound was prepared by treating racemic-**103a** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**. The crude liquid obtained, was distilled under reduced pressure to produce pure

racemic acetate **120d** as a colourless liquid.

Yield : 92%

b.p. : 90-92^{o}C at 0.5 mm

IR (neat): 1740 cm^{-1}

^{1}H NMR : δ 0.96-2.24 (m, 11H), 2.32-2.80 (m, 1H), 4.64-5.12 (m, 1H), 7.16 (s, 5H).

(±)-*trans*-1-Acetoxy-2-(1-naphthyl)cyclohexane (120b):

This compound was prepared by treating racemic-**103b** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**. The crude oil obtained was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to furnish pure racemic acetate **120b** as a colourless viscous oil.

Yield : 96%

IR (neat): 1740 cm^{-1}

^{1}H NMR : δ 1.20-2.32 (m, 11H), 3.32-3.72 (m, 1H), 4.96-5.40 (m, 1H), 7.08-8.24 (m, 7H).

(±)-*trans*-1-Acetoxy-2-(4-methylphenyl)cyclohexane (120c):

This compound was prepared by treating racemic-**103c** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**. The crude solid obtained, was crystallized from hexane to get pure racemic acetate

120c as crystalline solid,

Yield : 83%

m.p. : 46-48^{o}C

IR (neat): 1740 cm^{-1}

^{1}H NMR : δ 1.04-2.32 (m, 14H), 2.40-2.76 (m, 1H), 4.68-5.08 (m, 1H), 7.04 (s, 4H).

(±)-*trans*-1-Acetoxy-2-(2-methylphenyl)cyclohexane (120d):

This compound was prepared by treating racemic-**103d** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**. The crude liquid obtained, was distilled under reduced pressure to afford pure racemic acetate **120d** as a colourless liquid.

Yield : 92%

b.p. : 98-99^{o}C at 1 mm

IR (neat): 1740 cm^{-1}

^{1}H NMR : δ 1.02-2.40 (m, 14H), 2.64-3.08 (m, 1H), 4.70-5.16 (m, 1H), 6.84-7.28 (m, 4H).

(±)-*trans*-1-Acetoxy-2-(2,4,6-trimethylphenyl)cyclohexane (120e):

This compound was prepared by treating racemic-**103e** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**. The crude oil obtained, was column purified (silica gel, 10% ethyl acetate in

hexane) to produce pure racemic acetate **120e** as a viscous oil that solidified on standing for long period.

Yield : 92%

m.p. : 63-64°C

IR (neat): 1740 cm^{-1}

^1H NMR : δ 0.96-2.48 (m, 20H), 2.84-3.32 (m, 1H), 5.16-5.56 (m, 1H), 6.72 (s, 2H).

(±)-*trans*-1-Acetoxy-2-(4-methoxyphenyl)cyclohexane (120f):

This compound was prepared by treating racemic-**103f** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound **106a**. The crude solid obtained, was crystallized from hexane to get pure racemic acetate as a white crystalline solid.

Yield : 91%

m.p. : 56-57°C

IR (KBr) : 1720 cm^{-1}

^1H NMR : δ 1.04-2.28 (m, 11H), 2.36-2.76 (m, 1H), 3.76 (s, 3H), 4.68-5.08 (m, 1H), 6.80 (d, 2H, J = 8 Hz), 7.08 (d, J = 8 Hz).

(±)-*trans*-1-Acetoxy-2-(4-bromophenyl)cyclohexane (120g):

This compound was prepared by treating racemic-**103g** with acetic anhydride in presence of pyridine and DMAP following the

same procedure as described for compound **106a**. The crude liquid obtained, was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to furnish pure racemic acetate as colourless liquid.

Yield : 95%

IR (neat): 1740 cm^{-1}

^1H NMR : δ 0.68-2.20 (m, 11H), 2.32-2.76 (m, 1H), 4.64-5.08 (m, 1H), 6.80-7.60 (m, 4H).

CLAP-catalyzed hydrolysis of (±)-*trans*-1-acetoxy-2-phenylcyclohexane (120a):

Hydrolysis of racemic-**120a** (1.09 g, 5 mM) with CLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 35:65 ratio.

Reaction Time : 10 days

Yield of (-)-alcohol: 0.26 g (85%)

m.p. : 64-65°C (Lit.[155] m.p. 64-65°C)

Optical Rotation : $[\alpha]_D^{22}$ - 58.66 (c 1.19, MeOH), >99% e.e.
{Lit.[155] $[\alpha]_D^{27}$ -58.4 (c 10.0, MeOH)}

Yield of unhydrolyzed acetate: 0.6 g (86%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.47 g (97%)

Optical Rotation : $[\alpha]_D^{22}$ + 29.20 (c 2.46, MeOH), 50% e.e.
{Lit.[155] $[\alpha]_D^{27}$ + 58.3 (c 10.0, MeOH)}

Both (+)-alcohol and (-)-alcohol have IR, ^{1}H & ^{13}C NMR data identical with that of racemic alcohol.

CLAP-catalyzed hydrolysis of (±)-*trans*-1-acetoxy-2-(1-naphthyl)-cyclohexane (120b):

Hydrolysis of racemic-120b (1.34 g, 5 mM) with CLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 26:74 ratio.

Reaction Time : 12 days

Yield of (-)-alcohol: 0.24 g (83%)

m.p. : 101-102°C

Optical Rotation: : $[\alpha]_D^{22}$ - 72.94 (c 1.47, MeOH), >99% e.e.

Yield of unhydrolyzed acetate: 0.9 g (91%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.72 g (95%)

Optical Rotation : $[\alpha]_D^{22}$ + 28.40 (c 1.51, MeOH), 39% e.e.

Both (+)-alcohol and (-)-alcohol have IR, ^{1}H & ^{13}C NMR data identical with that of racemic alcohol.

Determination of enantiomeric purity:

Preparation of Mosher's ester of (±)-103b:

To a suspension of oil free sodium hydride (10 mg, 0.4 mM) in pyridine (0.5mL) were added (±)-103b (11 mg, 0.05 mM) and DMAP (5mg) and stirred for 15 min at room temperature. To this 0.1 M solution of (+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride

(MTPACl) in dichloromethane (1 mL, 0.1 mM) was added and stirred for 24 h. Then the reaction mixture was poured into cold 4N HCl (5 mL) and extracted with ether (3 x 5 mL). The ether layer was washed with saturated K_2CO_3 solution and dried over anhydrous Na_2SO_4. Removal of solvent followed by column purification (silica gel, 10% ethyl acetate in hexane) of the residue afforded pure Mosher's ester.

^{1}H NMR (200 MHz) : δ 1.40-2.40 (m, 8H), 2.84 & 3.10 (two singlets, 3H), 3.60-3.80 (m, 1H), 5.48-5.70 (m, 1H), 6.88-8.15 (m, 12H).

Two distinct singlets of almost equal integration appeared at δ 2.84 and 3.10 due to OMe protons indicating that the compound is a 50:50 mixture of two diastereomers.

Mosher's esters of (-)-103b & (+)-103b :

Mosher's ester of (-)-103b was prepared from (+)-MTPACl and the corresponding alcohol following the same procedure as described for Mosher's ester of (±)-103b. The ^{1}H NMR spectrum of this compound showed only one singlet at δ 2.84 (OMe protons) establishing the enantiomeric purity of (-)-103b to be >99%. Similar analysis of Mosher's ester of (+)-103b established the enantiomeric purity of (+)-103b to be 39%.

CLAP-catalyzed hydroslysis of (±)-*trans*-1-acetoxy-2-(4-methylphenyl)cyclohexane (120c):

Hydrolysis of racemic-120c (1.16 g, 5 mM) with CLAP (1 g)

afforded (-)-alcohol and unhydrolyzed acetate in 40:60 ratio.

Reaction Time : 10 days

Yield of (-)-alcohol: 0.31 g (82%)

m.p. : 54-55°C

Optical Rotation: : $[\alpha]_D^{22}$ - 59.50 (c 1.37, MeOH), >99% e.e.

Yield of unhydrolyzed acetate: 0.61 g (88%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.48 g (98%)

Optical Rotation : $[\alpha]_D^{22}$ + 39.12 (c 1.89, MeOH), 65% e.e.

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of racemic alcohol.

Determination of enantiomeric purity:

Mosher's ester of (±)-103c:

This compound was prepared from (+)-MTPACl and (±)-103c following the same procedure as described for Mosher's ester of (±)-103b.

^1H NMR (200 MHz) : δ1.20-2.40 (m, 11H), 2.60-2.80 (m, 1H), 3.15 and 3.25 5.16-5.36 (m, 1H), 6.94-7.32 (m, 9H).

The two singlets at δ 3.15 and 3.25 arising from OMe protons are of equal intensities indicating that they arise from two diastereomers.

Mosher's esters of (-)-103c & (+)-103c :

Mosher's ester of (-)-103c was prepared from (+)-MTPACl and

the corresponding alcohol following the same procedure as described for Mosher's ester of (±)-**103b**. The ^{1}H NMR (200 MHz) spectrum of this compound contained only one singlet at δ 3.15 (OMe protons) establishing the enantiomeric purity of (-)-**103c** to be >99%. On the otherhand, the enantiomeric excess of (+)-**103** was found to be 65% by similar analysis.

CLAP-catalyzed hydrolysis of (±)-*trans*-1-acetoxy-2-(2-methylphenyl)cyclohexane (120d):

Hydrolysis of racemic-**120d** (1.16 g, 5 mM) with CLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 28:72 ratio.

Reaction Time : 10 days

Yield of (-)-alcohol: 0.21 g (79%)

Optical Rotation: : $[\alpha]_D^{22}$ - 63.96 (c 1.45, $CHCl_3$), 90% e.e.

{Lit.[159] $[\alpha]_D^{26}$ - 71.1 (c 10.0, $CHCl_3$)}

Yield of unhydrolyzed acetate: 0.69 g (83%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.53 g (95%)

Optical Rotation : $[\alpha]_D^{22}$ + 24.56 (c 2.52, $CHCl_3$), 34% e.e.

{Lit.[159] $[\alpha]_D^{26}$ + 70.6 (c 10.0, $CHCl_3$)}

Both (+)-alcohol and (-)-alcohol have IR, ^{1}H & ^{13}C NMR data identical with that of racemic alcohol.

CLAP-catalyzed hydrolysis of (±)-*trans*-1-acetoxy-2-(2,4,6-trimethylphenyl)cyclohexane (120e):

Hydrolysis of racemic-120e (1.30 g, 5 mM) with CLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 25:75 ratio.

Reaction Time : 12 days

Yield of (-)-alcohol: 0.23 g (84%)

m.p. : 81-82°C

Optical Rotation: : $[\alpha]_D^{22}$ - 32.48 (c 1.26, MeOH), >99% e.e.

Yield of unhydrolyzed acetate: 0.85 g (87%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.67 g (95%)

Optical Rotation : $[\alpha]_D^{22}$ + 9.78 (c 1.40, MeOH), 30% e.e.

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of racemic alcohol.

Determination of enantiomeric purity:

Mosher's ester of (±)-103e:

This compound was prepared from (+)-MTPACl and (±)-103e following the same procedure as described for Mosher's ester of (±)-103b.

^1H NMR : δ 1.08-2.60 (m, 17H), 3.00-3.48 (m, 4H), 5.60-6.00 (m, 1H), 6.56-7.44 (m, 7H).

^1H NMR (100 MHz) analysis in presence of Eu(hfc)$_3$:

The ^1H NMR (100 MHz) spectrum of Mosher's ester of (±)-103e

(5 mg), recorded in presence of $Eu(hfc)_3$(30 mg), revealed that the original singlet at δ 3.20 (merged with multiplet) arising from OMe group, shifts and splits into two distinct singlets with almost equal integration indicating that the Mosher's ester is a 50:50 mixture of two diastereomers.

Mosher's esters of (-)-103e & (+)-103e :

Mosher's ester of (-)-**103e** was prepared from (+)-MTPACl and the corresponding alcohol following the same procedure as described for Mosher's ester of (±)-**103b**. The ^1H NMR (200 MHz) spectrum of this compound, recorded in presence of $Eu(hfc)_3$, revealed that the original singlet at δ 3.20 shifts but remains intact as singlet establishing the enantiomeric purity of (-)-**103e** to be >99%. Similar analysis established the enantiomeric purity of (+)-**103e** to be 30%.

CLAP-catalyzed hydrolysis of (±)-*trans*-1-acetoxy-2-(4-methoxyphenyl)cyclohexane (120f):

Hydrolysis of racemic-**120f** (1.24 g, 5 mM) with CLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 37:63 ratio.

Reaction Time : 10 days

Yield of (-)-alcohol: 0.33 g (86%)

m.p. : 83-84°C

Optical Rotation: : $[\alpha]_D^{22}$ - 55.40 (c 1.46, MeOH), >99% e.e.

Yield of unhydrolyzed acetate: 0.7 g (89%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.55 g (95%)

Optical Rotation : $[\alpha]_D^{22}$ + 30.82 (c 1.63, MeOH), 55% e.e.

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of racemic alcohol.

Determination of enantiomeric purity:

Mosher's ester of (±)-103f:

This compound was prepared from (+)-MTPACl and **(±)-103f** following the same procedure as described for Mosher's ester of **(±)-103b.**

^1H NMR (200MHz) : δ 1.20-2.30 (m, 8H), 2.56-2.78 (m, 1H), 3.18 and 3.28 (two singlets, 3H), 3.78 and 3.80 (two singlets, 3H) 5.10-5.28 (m, 1H), 6.80-7.30 (m, 9H).

Two singlets with almost equal integration at δ 3.18 and 3.28 (OMe protons) indicate the presence of two diastereomers in 1:1 ratio.

Mosher's ester of (-)-103f & (+)-103f :

Mosher's ester of **(-)-103f** was prepared from (+)-MTPACl and the corresponding alcohol following the same procedure as described for Mosher's ester of (±)-**103b.** The ^1H NMR (200 MHz) spectrum of this compound contained only one singlet at δ 3.18 (OMe protons) establishing the enantiomeric purity of **(-)-103f** to be >99%. On the otherhand, the enantiomeric purity of **(+)-103f**

was shown to be 55% by a similar analysis.

CLAP-catalyzed hydrolysis of (±)-*trans*-1-acetoxy-2-(4-bromophenyl)cyclohexane (120g):

Hydrolysis of racemic-**120g** (1.49 g, 5 mM) with CLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 28:72 ratio.

Reaction Time : 12 days

Yield of (-)-alcohol: 0.285 g (80%)

m.p. : 121-122°C

Optical Rotation: : $[\alpha]_D^{22}$ - 26.28 (c 1.67, $CHCl_3$), >99% e.e.

Yield of unhydrolyzed acetate: 0.9 g (85%)

The above recovered acetate upon hydrolysis (KOH/MeOH) furnished (+)-alcohol.

Yield of (+)-alcohol: 0.74 g (96%)

Optical Rotation : $[\alpha]_D^{22}$ + 11.18 (c 1.42, $CHCl_3$), 42% e.e.

Both (+)-alcohol and (-)-alcohol have IR, ^1H & ^{13}C NMR data identical with that of racemic alcohol.

Determination of enantiomeric purity:

Mosher's ester of (±)-103g :

This compound was prepared from (+)-MTPACl and **(±)-103g** following the same procedure as described for Mosher's ester of (±)-**103b**.

^1H NMR (200MHz) : δ 1.20-2.40 (m, 8H), 2.60-2.85 (m, 1H), 3.22 and 3.38 (two singlets, 3H), 5.10-5.30 (m, 1H), 6.90-7.60 (m, 9H).

The two singlets with almost equal integration appeared at δ 3.22 and 3.38 (OMe protons) indicate the presence of two diastereomers in equal concentration.

Mosher's esters of (-)-103g & (+)-103g :

Mosher's ester of (-)-103g was prepared from (+)-MTPACl and the corresponding alcohol following the same procedure as described for Mosher's ester of (±)-103b. The ^{1}H NMR (200 MHz) spectrum of this compound contained only one singlet at δ 3.22 (OMe protons) establishing the enantiomeric purity of (-)-**103g** to be >99%. The (+)-**103g** was shown to be 42% enantiomerically pure by a similar analysis.

(±)-1,2-Epoxy-3-(1-naphthoxy)propane (121):

To a solution of sodium 1-naphthoxide {prepared from 1-naphthol (14.4 g, 100 mM) and 1N NaOH solution (100 mL)} epichlorohydrin (11.7 mL, 150 mM) was added with stirring at room temperature. After 6h the reaction mixture was extracted with ether and the organic layer was washed with 5% NaOH solution. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed on a rotary evaporator. Fractional distillation of the crude liquid under reduced pressure afforded pure (±)-**121**.

Yield : 16 g (80%)

b.p. : 160°C at 3 mm (Lit.[167] b.p. 148-50°C at 2 mm)

IR (neat): 1600 cm^{-1}

^{1}H NMR : δ 2.64-3.00, (m, 2H), 3.44 (m, 1H), 3.92-4.44 (m, 2H), 6.76 (m, 1H), 7.12-7.52 (m, 4H), 7.56-7.84 (m, 1H), 8.04-8.36 (m, 1H).

^{13}C NMR : δ 44.00, 49.74, 68.59, 104.83, 120.53, 121.89, 125.12, 125.42, 125.65, 126.30, 127.30, 134.36, 154.06.

(±)-Propranolol (1):

To a solution of racemic-121 (10 g, 50 mM) in isopropylamine (50 mL), water (2 mL) was added and the reaction mixture was refluxed for 3h. Removal of excess isopropylamine followed by recrystallization of the crude solid from 20% benzene in hexane afforded racemic propranolol in pure form.

Yield : 11 g (85%)

IR (melt): 3300 cm^{-1}

^{1}H NMR : δ 1.12 (d, 6H, J = 5 Hz), 2.64-3.20 (m, 5H, 2H D_2O washable), 3.96-4.48 (m, 3H), 6.64-6.88 (m, 1H), 7.12-7.56 (m, 4H), 7.60-7.88 (m, 1H), 8.04-8.32 (m, 1H).

^{13}C NMR : δ 22.11, 49.03, 49.47, 68.00, 70.65, 104.88, 120.48, 121.80, 125.18, 125.47, 125.83, 126.36, 127.47, 134.48, 154.29.

(±)-N-Ethoxycarbonylpropranolol (122):

To a mixture of 2N K_2CO_3 solution (25 mL) and (±)-1 (5.2 g, 20 mM) in acetone (5 mL), ethyl chloroformate (2.9 mL, 30 mM) was

added at $0^{o}C$ with stirring. After 2h, the reaction mixture was extracted with ether and the organic layer was dried over anhydrous Na_2SO_4. Removal of solvent afforded pure N-protected propranolol **122,** as a colourless liquid.

Yield : 6 g (90%)

IR (neat): 3400, 1660 cm^{-1}

^{1}H NMR : δ 1.04-1.40 (m, 9H), 1.60 (br, 1H, OH), 3.52 (d, 2H, J= 4 Hz), 3.96-4.40 (m, 6H), 6.76 (m, 1H), 7.12-7.52 (m, 4H), 7.56-7.84 (m, 1H), 8.00-8.24 (m, 1H).

^{13}C NMR : δ 14.47, 20.35, 20.64, 46.88, 48.47, 61.76, 69.88, 71.35, 104.83, 120.65, 121.71, 125.24, 125.53, 125.89, 126.41, 127.59, 134.53, 154.24.

(±)-1-(N-Ethoxycarbonylisopropylamino)-2-acetoxy-3-(1-naphthoxy)-propane (123);

To a solution of racemic-**122** (5 g, 15 mM) in dichloromethane (25 mL), pyridine (2.8 mL, 35 mM) and DMAP (36 mg, 0.3 mM) were added. To this acetyl chloride (2.1 mL, 30 mM) was added dropwise with stirring at $0^{o}C$. After 2h stirring, the reaction mixture was taken up in ether (40 mL) and washed successively with 2N HCl (3 x 10 mL), $NaHCO_3$ solution and water. The organic layer was dried over anhydrous Na_2SO_4. Removal of solvent followed by column chromatography (silica gel, 30% ethyl acetate in hexane) afforded pure racemic-**123** as a viscous liquid.

Yield : 5 g (89%)

IR (neat): 1740, 1680 cm^{-1}

^1H NMR (200 MHz) : δ 1.25 (m, 9H), 2.10 (s, 3H), 3.40-3.75 (m, 2H), 4.08-4.40 (m, 5H), 5.60 (m, 1H),6.80 (d, 1H, J = 4 Hz) 7.30-7.56 (m, 4H), 7.80 (m, 1H), 8.25 (m, 1H).

^{13}C NMR : δ 14.58, 20.50, 20.88, 20.99, 44.38, 48.96, 61.30, 67.90, 71.46, 104.90, 120.79, 121.88, 125.32, 125.73, 126.44, 127.48, 134.60, 154.31, 156.44, 170.33.

CLAP-catalyzed hydrolysis of racemic-123:

Hydrolysis of racemic-123 (1.12 g, 3 mM) with CLAP (1.5 g) afforded (+)-alcohol and unhydrolyzed acetate in 15:85 ratio.

Reaction Time : 8 days

Yield of (+)-alcohol: 0.13 g (87%)

Optical rotation : $[\alpha]_D^{20}$ + 10.86 (c 1.84, $CHCl_3$), 40% e.e.

{based on optical purity of (R)-(+)-1}

Yield of recovered acetate: 0.9 g (94%)

Both (+)-alcohol and recovered acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

(R)-(+)-Propranolol (1):

To a solution of KOH (0.1 g) in MeOH (2 mL), was added (+)-122 {obtained from CLAP catalyzed hydrolysis of (±)-123)} (0.13 g) and stirred for 2 h. Then MeOH was removed under reduced pressure, and the residue was dissolved in water and extracted

with ether. The ether layer was dried over anhydrous Na_2SO_4. Removal of solvent followed by recrystallization from hexane afforded colourless crystals.

Yield : 0.07 g (89%)

m.p. : 66-67 ^{o}C (Lit.[168] m.p. 73 ^{o}C)

Optical rotation: $[\alpha]_D^{20}$ + 4.27 (c 0.7, EtOH), 40% e.e.

{ Lit.[168] $[\alpha]_D^{20}$ + 10.6 (c 1.02, EtOH)}

This compound has spectral data identical with that of (±)-propranolol(1)

(±)-1-Chloro-3-(1-naphthoxy)prop-2-yl acetate (124):

To a mixture of (±)-121 (8 g, 40 mM) and pyridine (0.3 mL, 4 mM) in dry benzene (40 mL) acetyl chloride (7.1 mL, 100 mM was added with stirring at room temperature. After 3h stirring, the reaction mixture was diluted with ether (40 mL) and washed thoroughly with water and saturated K_2CO_3 solution. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. Distillation of the crude oil under reduced pressure afforded pure acetate as a colourless viscous oil.

Yield : 8 g (71%)

b.p. : 164^{o}C at 1 mm

IR (neat): 1740 cm^{-1}

^1H NMR : δ 2.12 (s, 3H), 3.88 (d, 2H, J = 4 Hz), 4.32 (d, 2H, J = 4 Hz), 5.50 (m, 1H), 6.80 (m, 1H), 7.20-7.56 (m,

4H), 7.64-7.88 (m, 1H), 8.04-8.28 (m, 1H)

^{13}C NMR : δ 20.64, 42.59, 66.29, 71.00, 104.94, 121.00, 121.71, 125.42, 125.71, 126.53, 127.53, 134.48, 153.83, 170.13.

PLAP-catalyzed hydrolysis of racemic-1-chloro-3-(1-naphthoxy)-prop-2-yl acetate (124):

Hydrolysis of racemic-**124** (1.39 g, 5 mM) with PLAP (1 g) afforded (R)-(-)-chlorohydrin (**125**) and unhydrolyzed acetate in 35:65 ratio.

Reaction time : 45h

Yield of (+)-alcohol: 0.35 g (85%)

IR (neat) : 3400 cm^{-1}

^{1}H NMR : δ 2.68 (br, 1H, D_2O washable), 3.60-3.96 (m, 2H), 4.00-4.48 (m, 3H), 6.76 (m, 1H), 7.12-7.56 (m, 4H), 7.60-7.84 (m, 1H), 8.00-8.24 (m, 1H).

^{13}C NMR : δ 46.18, 68.65, 69.88, 105.06, 121.00, 121.65, 125.42, 125.83, 126.53, 127.65, 134.53, 153.89.

Optical rotation : $[\alpha]_D^{20}$ - 4.37 (c 1.6, EtOH), 46% e.e.

{Lit.[166] $[\alpha]_D^{25}$ + 9.0 (c 1.9, EtOH), >95% e.e.}

Yield of recovered acetate: 0.85 g (94%)

Optical rotation : $[\alpha]_D^{20}$ + 5.9 (c 0.84, EtOH), 28% e.e.

{Lit.[166] $[\alpha]_D^{25}$ - 19.9 (c 2.4, EtOH), >95% e.e.}

The recovered acetate has IR, ^{1}H & ^{13}C NMR data identical with that of corresponding racemic compound.

1-(n-Undecyl)cyclopentan-1-ol (128) :

To a solution of n-undecylmagnesium bromide (50 mM) in THF (50 mL) {prepared from n-undecyl bromide (11.1 mL, 50 mM) and magnesium (1.21 g, 50 mM)} was added dropwise a solution of cyclopentanone (4.4 mL, 50 mM) in THF (10 mL) at 0°C. After stirring for 2 h at room temperature, the reaction was quenched with saturated NH_4Cl solution. The organic layer was separated and the aqueous phase was extracted with ether (2 x 25 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated on a rotavapor. The crude product obtained was column purified (silica gel, 5% ethyl acetate in hexane) to furnish pure tertiary alcohol as a colourless liquid.

Yield : 6 g (50 %).

IR (neat): 3400 cm^{-1}.

^{1}H NMR : δ 0.84 (distorted t, 3H), 1.24-1.60 (m, 29H).

^{13}C NMR : δ 13.23, 21.94, 23.11, 24.00, 28.64, 28.94, 29.59, 31.17, 38.82, 40.88, 81.65.

1-(n-Undecyl)cyclopent-1-ene (129) :

A suspension of tertiary alcohol 128 (4.8 g, 20 mM) and iosphoric acid (5 mL) was heated for 1h at 120 °C. The reaction

mixture was allowed to cool to room temperature, diluted with water (10 mL) and extracted with hexane. The organic layer was washed with 5% NaOH solution followed by water and dried over anhydrous Na_2SO_4. Removal of solvent followed by column purification (silica gel, hexane) afforded pure **129** as a colourless liquid.

Yield : 3.8 g (85%).

IR (neat): 3050 cm^{-1} (weak).

^1H NMR : δ 0.88 (distorted t, 3H), 1.00-2.00 (m, 27H), 5.28 (br, 1H).

^{13}C NMR : δ 13.35, 22.06, 23.82, 27.23, 28.76, 29.06, 30.59, 31.35, 31.41, 34.41, 122.41, 144.48.

(±)-*trans*-2-(n-Undecyl)cyclopentan-1-ol (126) :

This was prepared following the hydroboration/oxidation procedure reported by Periasamy *et al.*[175]

To a suspension of sodium borohydride (0.27 g, 7 mM) in THF (25 mL) under nitrogen atmosphere, was added the cycloalkene **129** (3.33 g, 15 mM) and cooled to 0 ^oC . Then a solution of iodine (0.9 g, 3.5 mM) in THF (15 mL) was added dropwise at 0 ^oC. After stirring for 3 h, the reaction was quenched with water (1 mL) and added 2.5 N NaOH solution (15 mL). Then 30% aqueous H_2O_2 solution (14 mL) was added dropwise with stirring at 0^oC and the contents were stirred overnight at room temperature. The contents were

extracted with ether (3 x 30 mL). The ether layer was dried over anhydrous Na_2SO_4 and concentrated on a rotavapor. The crude product obtained was purified by column chromatography (silica gel, 5 % ethyl acetate in hexane) to afford pure alcohol as a colourless liquid.

Yield : 2.9 g (80%).

IR (neat): 3350 cm^{-1}.

^1H NMR : δ 0.88 (distorted t, 3H), 1.10-2.10 (m, 28H), 3.64-3.92 (m, 1H).

^{13}C NMR : δ 14.00, 21.88, 22.70, 28.35, 29.41, 29.76, 30.00, 32.00, 34.00, 34.47, 48.23, 79.06.

(±)-*trans*-1-Acetoxy-2-(n-undecyl)cyclopentane (126a) :

This compound was prepared by treating (±)-126 with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 106a, as a colourless liquid.

Yield : 92%

IR (neat): 1740 cm^{-1}.

^1H NMR (200 MHz) : δ 0.87 (distorted t, 3H), 1.25 (s, 20H), 1.50-2.00 (m, 7H), 2.04 (s, 3H), 4.70-4.80 (m, 1H).

^{13}C NMR : δ 13.82, 20.94, 22.47, 27.88, 29.23, 29.53, 30.00, 31.76, 33.53, 45.18, 81.30, 170.60.

PLAP-catalyzed hydrolysis of (±)-126a :

Hydrolysis of racemic-**126a** (0.7 g, 2.5 mM) with PLAP (1 g) afforded (-)-alcohol and unhydrolyzed acetate in 25:75 ratio.

Reaction time: 5 days

Yield of (-)-alcohol: 0.11 g (76%)

Optical rotation : $[\alpha]_D^{20}$ -10.2 (c 1.66, $CHCl_3$), 42% e.e.

Yield of recovered acetate: 0.47 g (89%)

The (-)-alcohol and recovered acetate have IR, ^1H & ^{13}C NMR data identical with that of corresponding racemic compounds.

(R)-(-)-2-(n-Undecyl)cyclopentan-1-one (127) :

To a stirred suspension of pyridinium chlorochromate (0.22g, 1 mM) in dichloromethane (5 mL), a solution of (-)-126 (0.11 g, 0.45 mM) in dichloromethane (2 mL) was added in one portion at 0^oC. After stirring for 2 h ,the reaction mixture was diluted with dry ether (10 mL). The supernatant solution was decanted from the black gum. The inorganic black gum was washed with dry ether (3 x 2 mL). The combined organic layer was passed through a short column of florisil. Removal of solvent provided pure (R)-(-)-**127** as colourless liquid.

Yield : 0.09 g (85%).

IR (neat): 1740 cm^{-1}.

^1H NMR : δ 0.88 (distorted t, 3H), 1.28-2.36 (m, 27H).

^{13}C NMR : δ 13.82, 20.53, 22.47, 27.35, 29.17, 29.41, 31.70, 37.88, 48.88, 220.89.

Optical rotation : $[\alpha]_D^{20}$ - 35.09 (c 2.97, ether), 42% e.e.

{Lit.[174] $[\alpha]_D^{24}$ + 81.0 (c 1.04, ether), 97% e.e.}.

3-Benzyloxypropan-1-ol (133):

To a suspension of oil free sodium hydride (4.8 g, 200 mM) in dry benzene (200 mL) at reflux propan-1,3-diol (14.5 mL, 200 mM) was added with stirring. After refluxing for 1h, benzyl bromide (23.8 mL, 200 mM) was added slowly. The reaction mixture was further refluxed for 2h. Then the reaction mixture was cooled to room temperature and diluted with water. The layers were separated and the aqueous layer was extracted with ether (2 x 30 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated on a rotavapor. The crude liquid obtained, was distilled under reduced pressure to get pure alcohol, 133.

Yield : 20 g (60%)

b.p. : 122-124°C at 2.5 mm (Lit.[192] b.p. 155°C at 23 mm)

IR (neat): 3350 cm^{-1}

^1H NMR : δ 1.84 (m, 2H), 2.10 (br, 1H, D_2O washable), 3.48-3.84 (m, 4H), 4.50 (s, 2H), 7.30 (s, 5H).

^{13}C NMR : δ 32.47, 60.71, 68.59, 73.24, 127.89, 128.65, 138.53.

3-Benzyloxypropanal (134):

To a stirred suspension of pyridinium chlorochromate (PCC)

(38.8 g, 180 mM) in dichloromethane (200 mL), 3-benzyloxypropanol (19.9 g, 120 mM) in dichlormethane (20 mL) was added in one portion at room temperature. After stirring for 2h, the reaction mixture was diluted with dry ether (100 mL). The supernatant solution was decanted from the black gum. The inorganic black gum was washed with dry ether (3 x 30 mL). The combined organic layer was passed through a short column of florisil. Removal of solvent followed by distillation of the residual liquid under reduced pressure furnished pure aldehyde.

Yield : 17.7 g (90%)

b.p. : 106-108^{o}C at 2.5 mm (Lit.[193] 109^{o}C at 3.0 mm)

IR (neat): 1720 cm^{-1}

^{1}H NMR : δ 2.66 (m, 2H), 3.79 (t, 2H, J = 5 Hz), 4.51 (s, 2H), 7.28 (s, 5H), 9.77 (m, 1H).

^{13}C NMR : δ 43.47, 63.59, 72.82, 127.47, 128.24, 137.89, 201.01

(±)-1-Benzyloxy-5-hexen-3-ol (130):

This was prepared following Luche's procedure.[130]

To a saturated aqueous NH_4Cl solution (100 mL), zinc dust (7.8 g, 120 mM) and a mixture of allyl bromide (10.4 mL, 120 mM) and 3-benzyloxypropanaldehyde (16.4 g, 100 mM) in THF (15 mL) were added with stirring at room temperature. After 2h , the reaction mixture was extracted with ether (3 x 30 mL). The ether layer was dried over anhydrous Na_2SO_4 and concentrated to produce racemic

alcohol **130**, as a colourless liquid.

Yield : 19.5g (95%)

IR (neat): 3400 cm^{-1}

^1H NMR : δ 1.76 (q, 2H, J = 6 Hz), 2.24 (t, 2H, J = 6 Hz), 2.80 (br, 1H, D_2O washable), 3.52-3.96 (m, 3 H), 4.52 (s, 2H), 4.84-5.20 (m, 2H), 5.56-6.04 (m, 1H), 7.30 (s, 5H).

^{13}C NMR : δ 35.64, 41.59, 68.17, 69.35, 72.77, 117.06, 127.42, 128.12, 134.71, 137.89.

(±)-4-Acetoxy-6-benzyloxyhex-1-ene (130a):

To a solution of (±)-130 (5.15 g, 25 mM) in dichloromethane (25 mL) were added pyridine (4.5 mL, 55 mM) and DMAP (60 mg, 0.5 mM). To this acetic anhydride (4.7 mL, 50 mM) was added slowly with stirring at room temperature. After stirring for 3h, the reaction mixture was taken up in ether (75 mL) and washed successively with 2N HCl (3 x 15 mL) and saturated K_2CO_3 solution. The organic layer was dried over anhydrous Na_2SO_4. Removal of solvent afforded pure racemic acetate as a colourless liquid.

Yield : 5.4g (87%)

IR (neat): 1740 cm^{-1}

^1H NMR : δ 1.64-2.08 (m, 5H), 2.30 (t, 2H, J = 6 Hz), 3.46 (t, 2H, J = 6 Hz), 4.44 (s, 2H), 4.84-5.20 (m, 3H), 5.48-6.00 (m, 1H), 7.28 (m, 5H).

^{13}C NMR : δ 20.35, 33.17, 38.23, 65.88, 70.18, 72.35, 117.35, 127.18, 127.89, 133.24, 138.01, 169.95.

(±)-all-cis-2-(2′-Benzyloxyethyl)-4-chloro-6-methyltetrahydropyran (135):

This was prepared following literature procedure.[181]

To a suspension of anhydrous $AlCl_3$ (6.66 g, 50 mM) in dry benzene (20 mL) a mixture of (±)-1-benzyloxy-5-hexen-3-ol (130) (10.3 g, 50 mM) and acetaldehyde (2.8 mL, 50 mM) in dry benzene (100 mL) was added dropwise with stirring at 0°C. The reaction mixture was stirred for 3h at 0°C. Then the reaction was quenched with 0.1 M phosphate buffer of pH 7.4 (150 mL) and the resultant suspension was extracted with ether. The organic layer was dried over anhydrous Na_2SO_4 and concentrated on a rotavapor. The crude liquid obtained was column purified (silica gel, 10% ethyl acetate in hexane) to afford pure (±)-135.

Yield : 6.8 g (59%)

IR (neat): 1120 cm^{-1}

^{1}H NMR : δ 1.16 (d, 3H, J = 6 Hz), 1.20-2.20 (m, 6H), 3.20-4.12 (m, 5H), 4.44 (s, 2H), 7.28 (m, 5H).

^{13}C NMR : 21.58, 36.12, 42.41, 44.23, 55.76, 66.41, 72.59, 72.88, 73.53, 127.65, 128.48, 138.89.

(±)-all-cis-2-(2′-Hydroxyethyl)-4-chloro-6-methyltetrahydropyran (136):

A solution of racemic-135 (5.37 g, 20 mM) in ethyl acetate (20 mL), was shaken with 10% palladium on charcoal (200 mg) at 35 lbs/sq. inch pressure at room temperature in a Parr hydrogenator until the required pressure drop had taken place. The catalyst was filtered off. Removal of solvent afforded pure racemic alcohol as a colourless liquid.

Yield : 3.3 g (93%)

IR (neat): 3350 cm^{-1}

^1H NMR : δ 1.20 (d, 3H, J = 6 Hz), 1.28-2.24 (m, 6H), 2.52 (s, 1H, D_2O washable) 3.16-4.16 (m, 5H).

^{13}C NMR : δ 21.29, 37.65 41.88, 43.65, 55.06, 59.88, 72.71, 75.53.

(±)-all-cis-2-(2′-Acetoxyethyl)-4-chloro-6-methyltetrahydropyran (136a):

This compound was prepared by treating (±)-136 with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound 130a, as a colourless liquid.

Yield : 92%

IR (neat): 1730 cm^{-1}

^1H NMR : δ 1.20 (d, 3H, J = 6 Hz), 1.28-2.24 (m, 9H), 3.20-3.60 (m, 2H), 3.80-4.32 (m, 3H).

^{13}C NMR : δ 20.58, 21.17, 34.59, 41.88, 43.76, 55.18, 60.82, 72.47, 73.06, 170.71.

(±)-cis-2-(2′-benzyloxyethyl)-6-methyltetrahydropyran (137):

To a solution of racemic-**135** (5.37 g, 20 mM) in dry THF (30 mL) were added t-butyl alcohol (5 mL) and freshly cut sodium metal pieces (5 g). The contents were refluxed for 3h. Then the reaction mixture was allowed to cool and the supernatant liquid was decanted. The flask containing sodium pieces were rinsed with dry ether (2 x 20 mL). The combined organic solution was washed twice with brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The crude liquid obtained was column purified (silica gel, 10% ethyl acetate in hexane) to provide pure dechlorinated tetrahydropyran compound **137**, as a colourless liquid.

Yield : 3.2 g (70%)

IR (neat): 1080 cm^{-1}

^1H NMR : δ 1.12 (d, 3H, J = 5 Hz), 1.24-1.96 (m, 8H), 3.20-3.68 (m, 4H), 4.48 (s, 2H), 7.28 (m, 5H).

^{13}C NMR : δ 22.00, 23.59, 31.29, 33.23, 36.59, 66.76, 72.71, 73.59, 74.59, 127.36, 127.47, 128.24, 138.77.

(±)-cis-2-(2′-Hydroxyethyl)-6-methyltetrahydropyran (132):

This compound was prepared by hydrogenolysis of compound **136a** using Pd-C as catalyst following a similar procedure described for hydrogenolysis of **135**. This was obtained as a colourless liquid.

Yield : 94%

IR (neat): 3350 cm^{-1}

^1H NMR : δ 1.16 (d, 3H, J = 6 Hz), 1.24-1.96 (m, 8H), 2.80 (s, 1H, D_2O washable), 3.28-3.64 (m, 2H), 3.76 (t, 2H, J = 4 Hz).

^{13}C NMR : δ 21.41, 22.70, 30.53, 32.35, 37.53, 60.29, 73.29, 77.12

(±)-cis-2-(2′-Acetoxyethyl)-6-methyltetrahydropyran (132a):

This compound was prepared by treating racemic alcohol **132** with acetic anhydride in presence of pyridine and DMAP following the same procedure as described for compound-**132,** as a colourless liquid.

Yield : 90%

IR (neat): 1730 cm^{-1}

^1H NMR : δ 1.16 (d, 3H, 6 Hz), 1.28-1.88 (m, 8H), 2.04 (s, 3H), 3.20-3.60 (m, 2H), 4.18 (t, 2H, J = 6 Hz).

^{13}C NMR : δ 20.76, 21.88, 23.47, 31.17, 33.06, 35.35, 61.41, 73.65, 74.35, 171.00

CLAP-catalyzed hydrolysis of (±)-4-acetoxy-6-benzyloxyhex-1-ene (130a):

Hydrolysis of racemic-130a (1.24 g, 5 mM) with CLAP (1 g) afforded alcohol and unhydrolyzed acetate in 40:60 ratio.

Reaction time : 23 h

Yield of alcohol : 0.38 g (92%)

Optical rotation : Nil

Yield of recovered acetate: 0.67 g (90%)

Optical rotation : Nil

Both alcohol and acetate have IR, ^{1}H & ^{13}C NMR data identical with that of corresponding racemic compounds.

PLAP-catalyzed hydrolysis of racemic-(±)-all-cis-2-(2'-acetoxy-ethyl)-4-chloro-6-methyltetrahydropyran (136a):

Hydrolysis of racemic-**136a** (0.44 g, 2 mM) with PLAP (0.5g) afforded alcohol and unhydrolyzed acetate in 85:15 ratio as determined by GC analysis.

Reaction time : 3h

Yield of alcohol : 0.25 g (85%)

Optical rotation : Nil

Yield of recovered acetate: 0.06 g (90%)

Optical rotation : Nil

Both alcohol and acetate have IR, ^{1}H & ^{13}C NMR data identical with that of corresponding racemic compounds.

CLAP-catalyzed hydrolysis of racemic-(±)-all-cis-2-(2'-acetoxy-ethyl)-4-chloro-6-methyltetrahydropyran (136a):

Hydrolysis of racemic-**136a** (0.44 g, 2mM) with CLAP (0.5 g)

afforded (+)-alcohol and unhydrolyzed acetate in 80:20 ratio as determined by GC analysis.

Reaction time : 3h

Yield of alcohol : 0.25 g (88%)

Optical rotation : Nil

Yield of recovered acetate: 0.08 g (90%)

Optical rotation : Nil

Both alcohol and acetate have IR and ^{1}H NMR data identical with that of corresponding racemic compounds.

PLAP-catalyzed hydrolysis of racemic-(±)-cis-2-(2'-acetoxyethyl)-6-methyltetrahydropyran (132a):

Hydrolysis of racemic-**132a** (0.18 g, 1 mM) with PLAP (0.2 g) afforded alcohol and unhydrolyzed acetate in 30:70 ratio as determined by GC analysis.

Reaction time : 4h

Yield of alcohol : 0.038 g (92%)

Optical rotation : Nil

{Lit.[178] $[\alpha]_D$ + 24.6 ($CHCl_3$)}

Yield of recovered acetate: 0.12 g (95%)

Optical rotation : Nil

Both alcohol and acetate have IR and ^{1}H NMR data identical with that of corresponding racemic compounds.

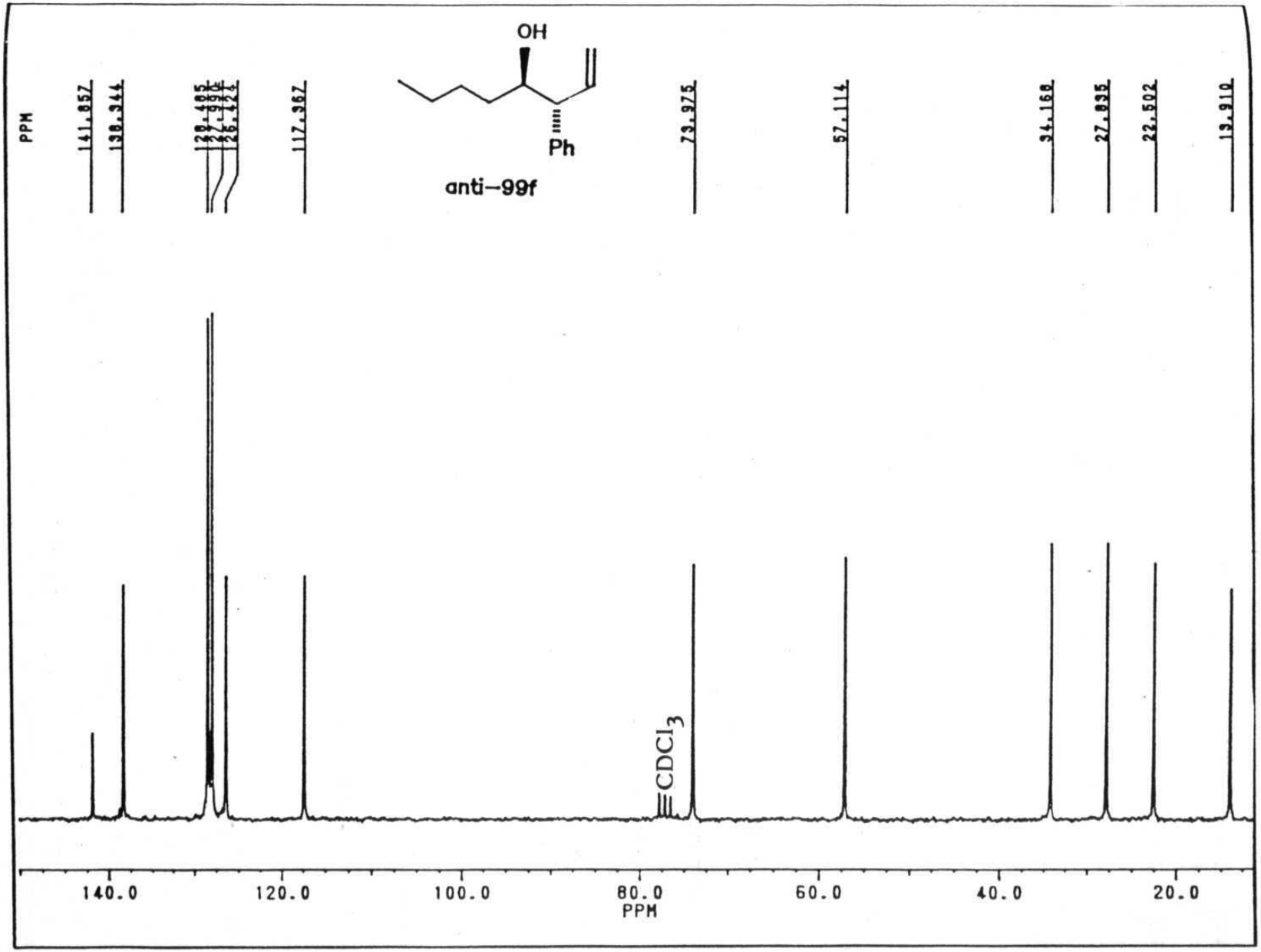


Fig. 1: ^{13}C NMR spectrum of **99f**

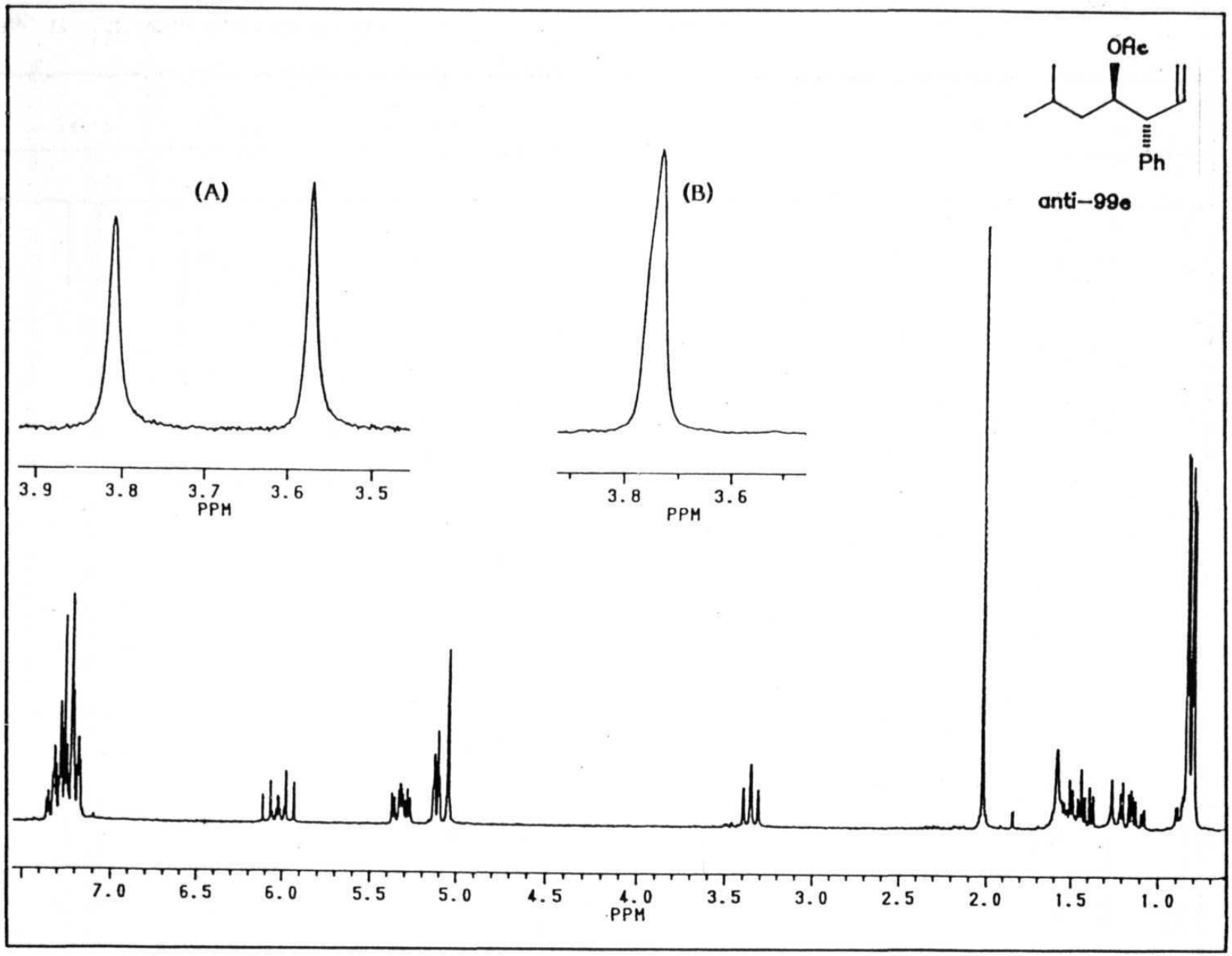


Fig. 2. ^1H NMR spectrum of **107e**. (A) Splitting of $OCOCH_3$ signal of (+)-**107e**. (B) Splitting of $OCOCH_3$

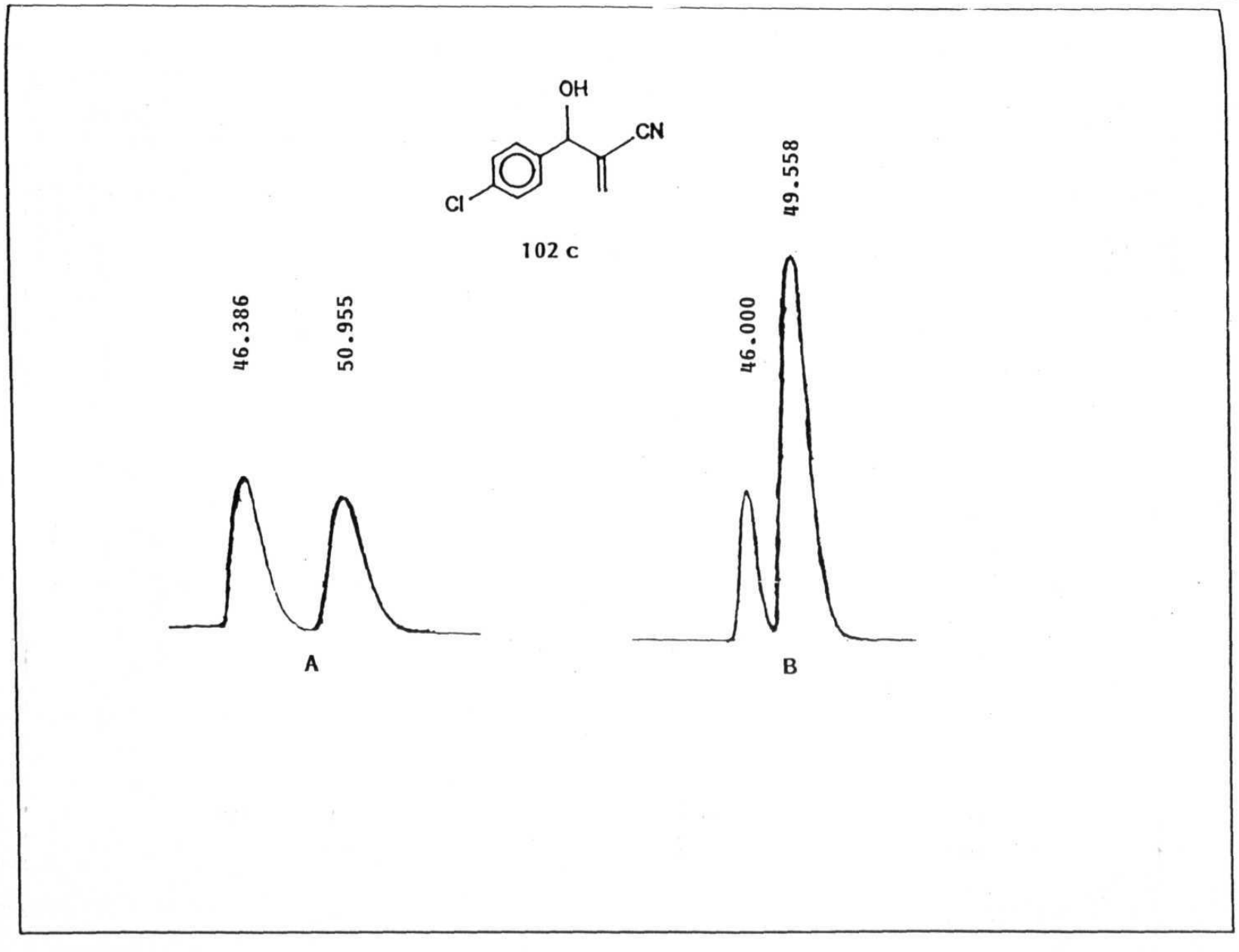


Fig. 3: HPLC analysis of 102c on chiral column, Chiralcel OD. (A) Chromatogram of (±)-102c. (B) Chromatogram of (+)-102c, 59% e.e.

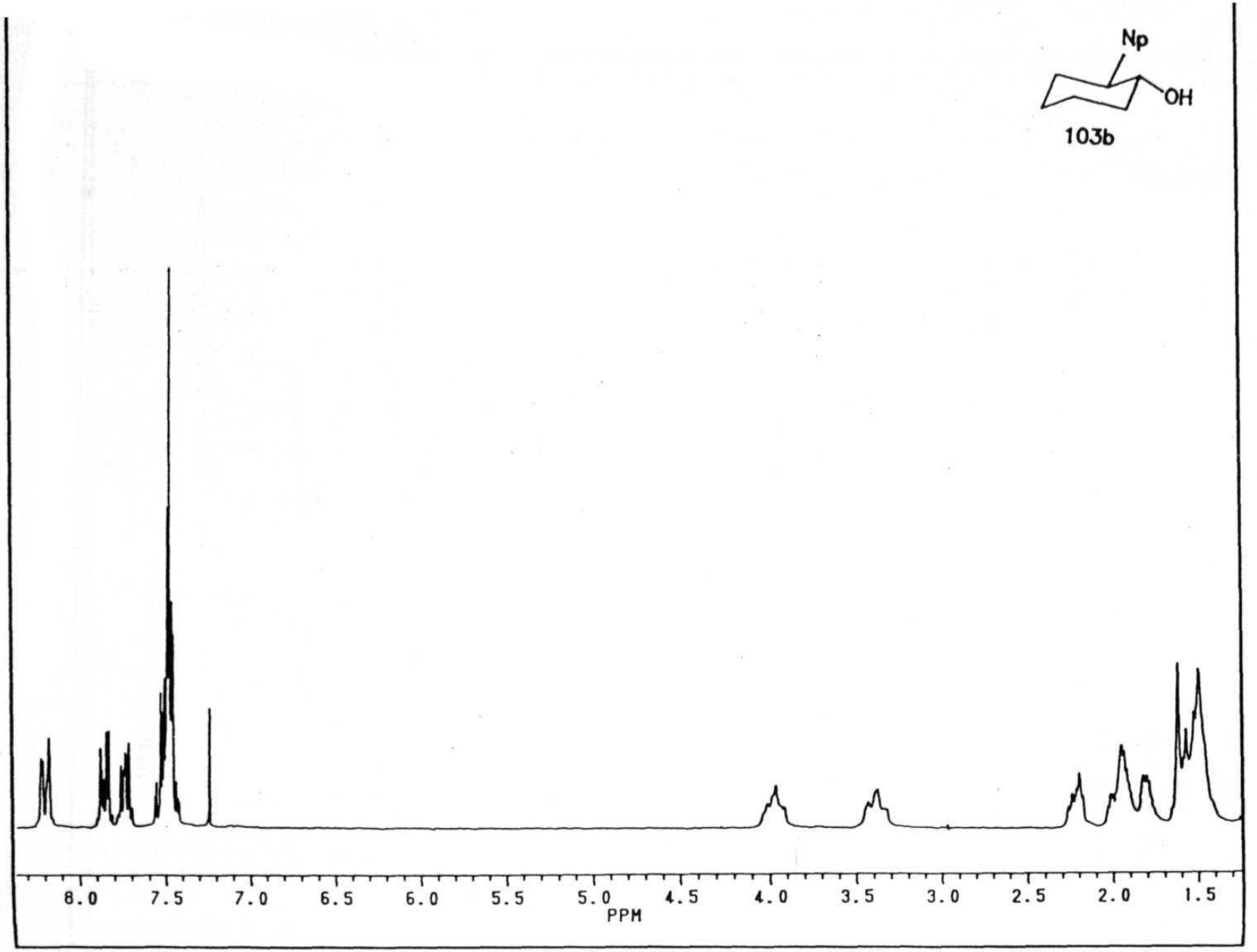


Fig. 4: ^{1}H NMR spectrum of **103b**.

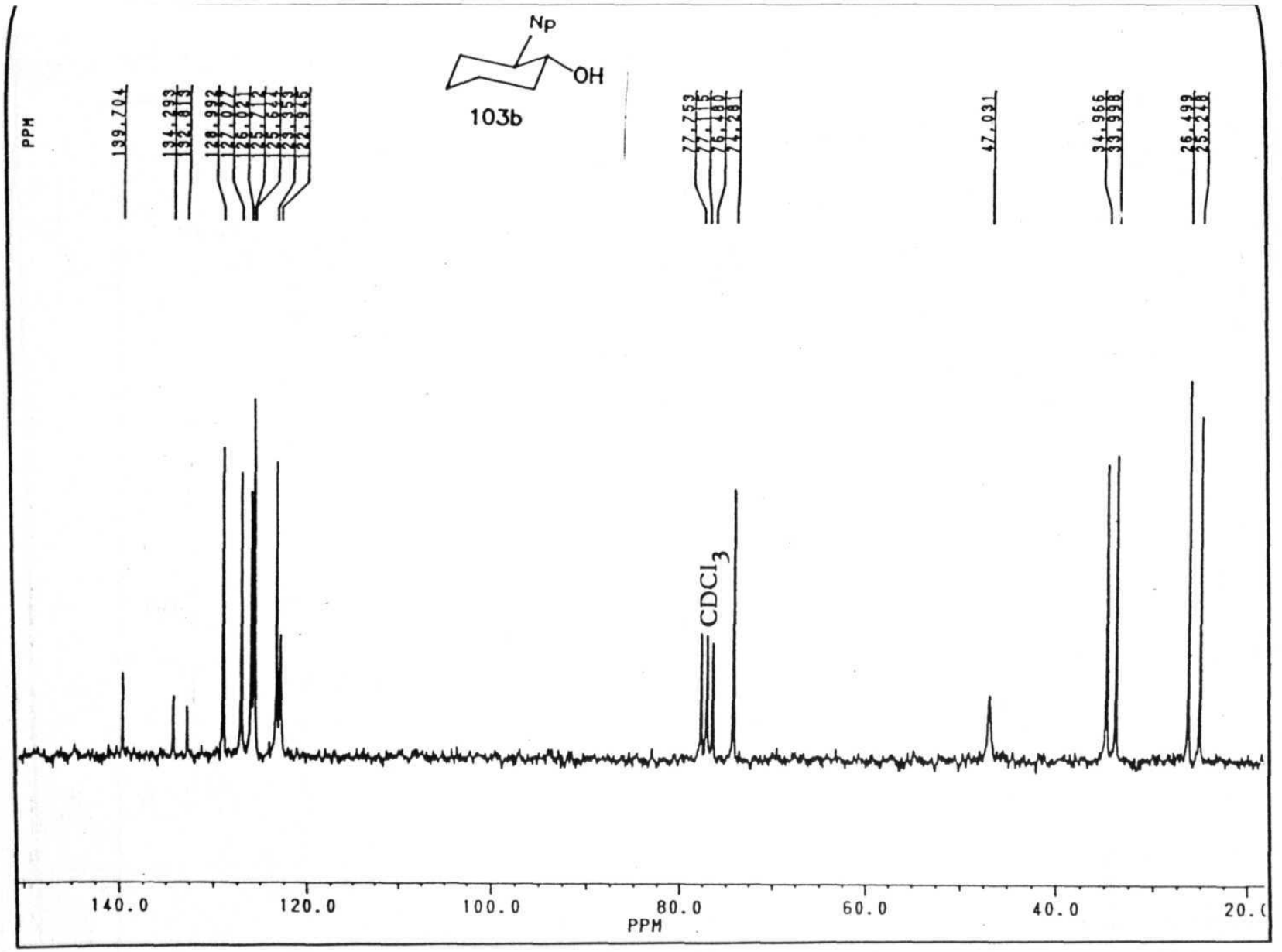


Fig. 5: ^{13}C NMR spectrum of **103b.**

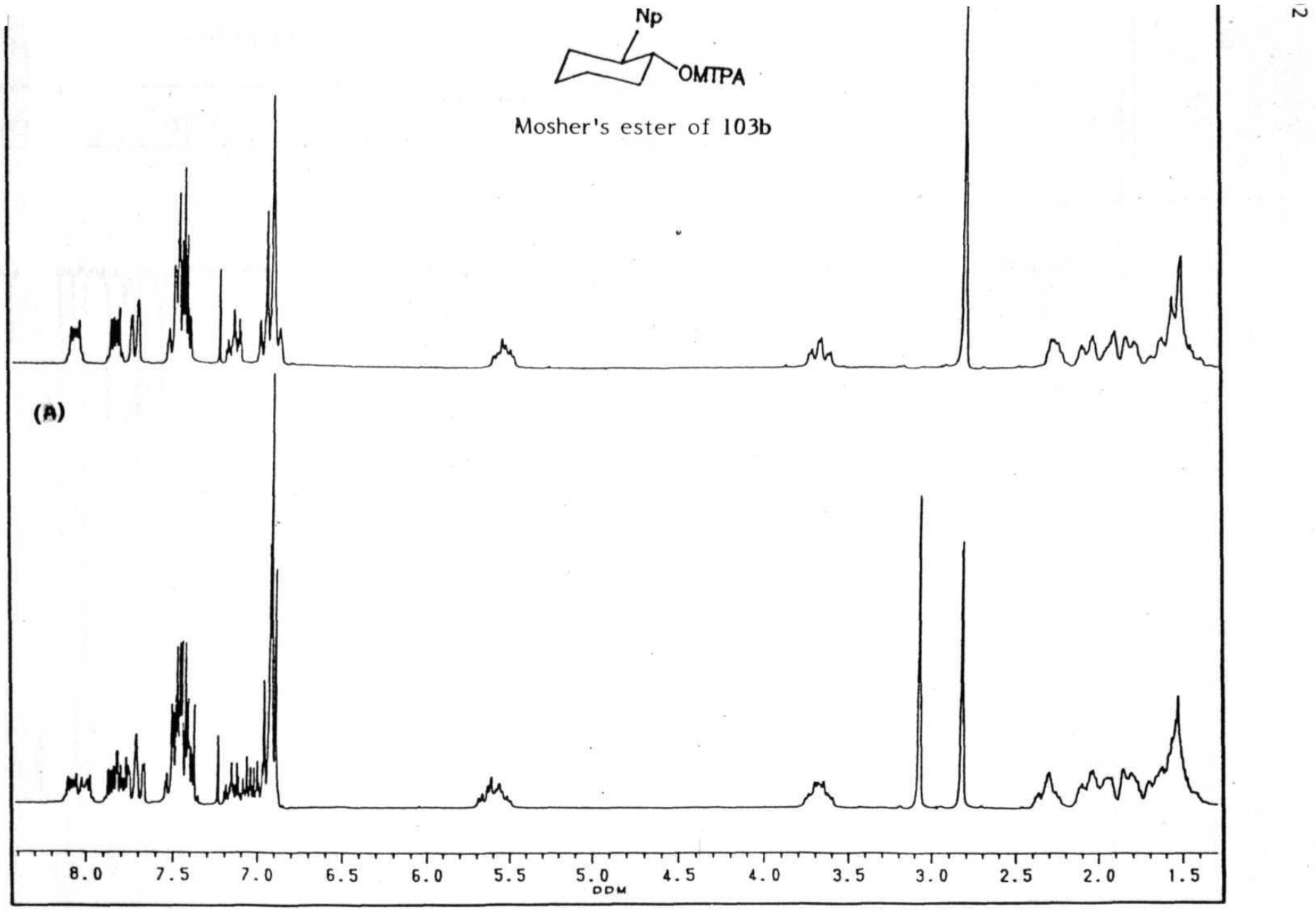


Fig. 6: (A) ^{1}H NMR spectrum of Mosher's ester of (±)-**103b**. (B) ^{1}H NMR spectrum of Mosher's ester of (-) 103b

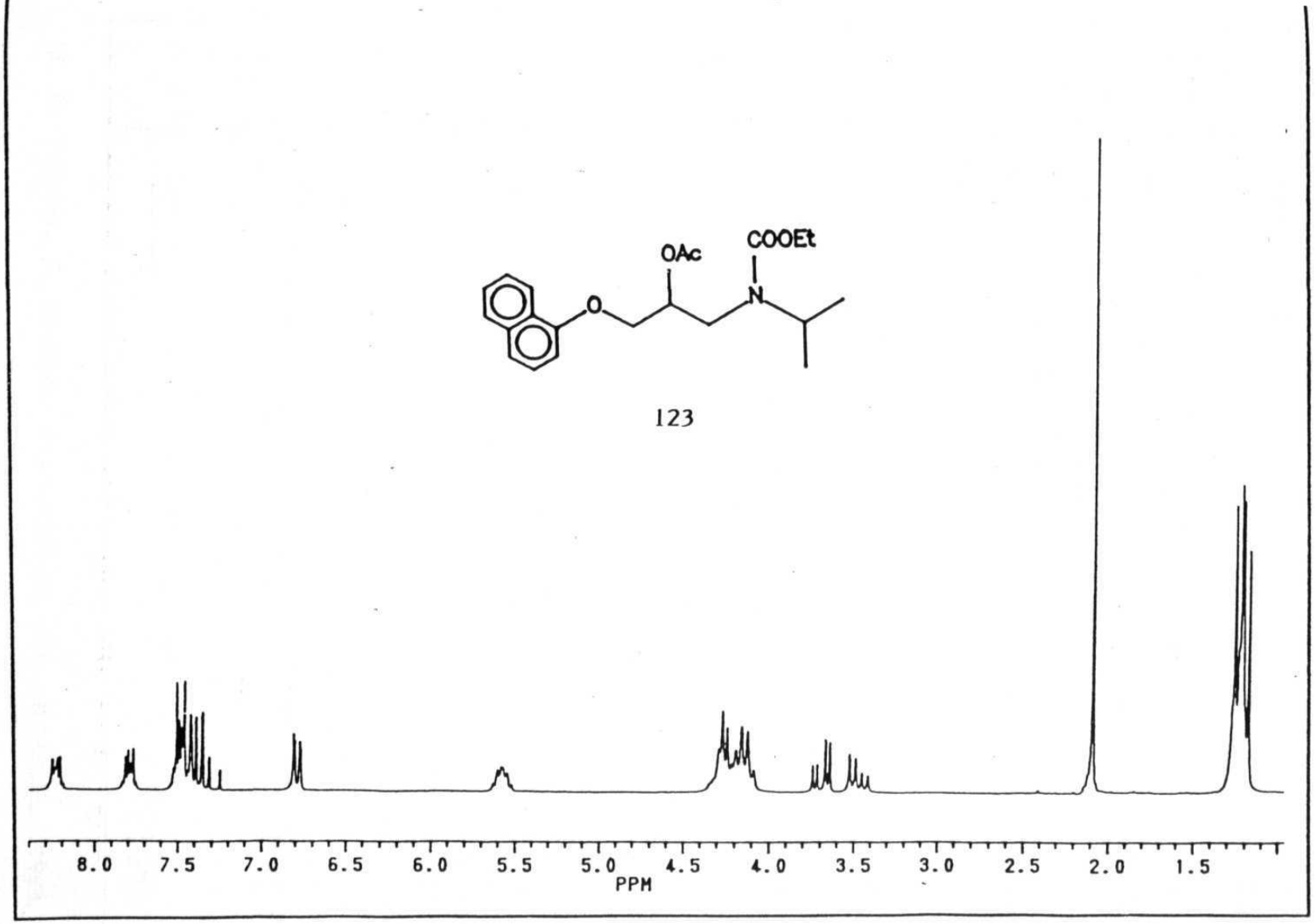
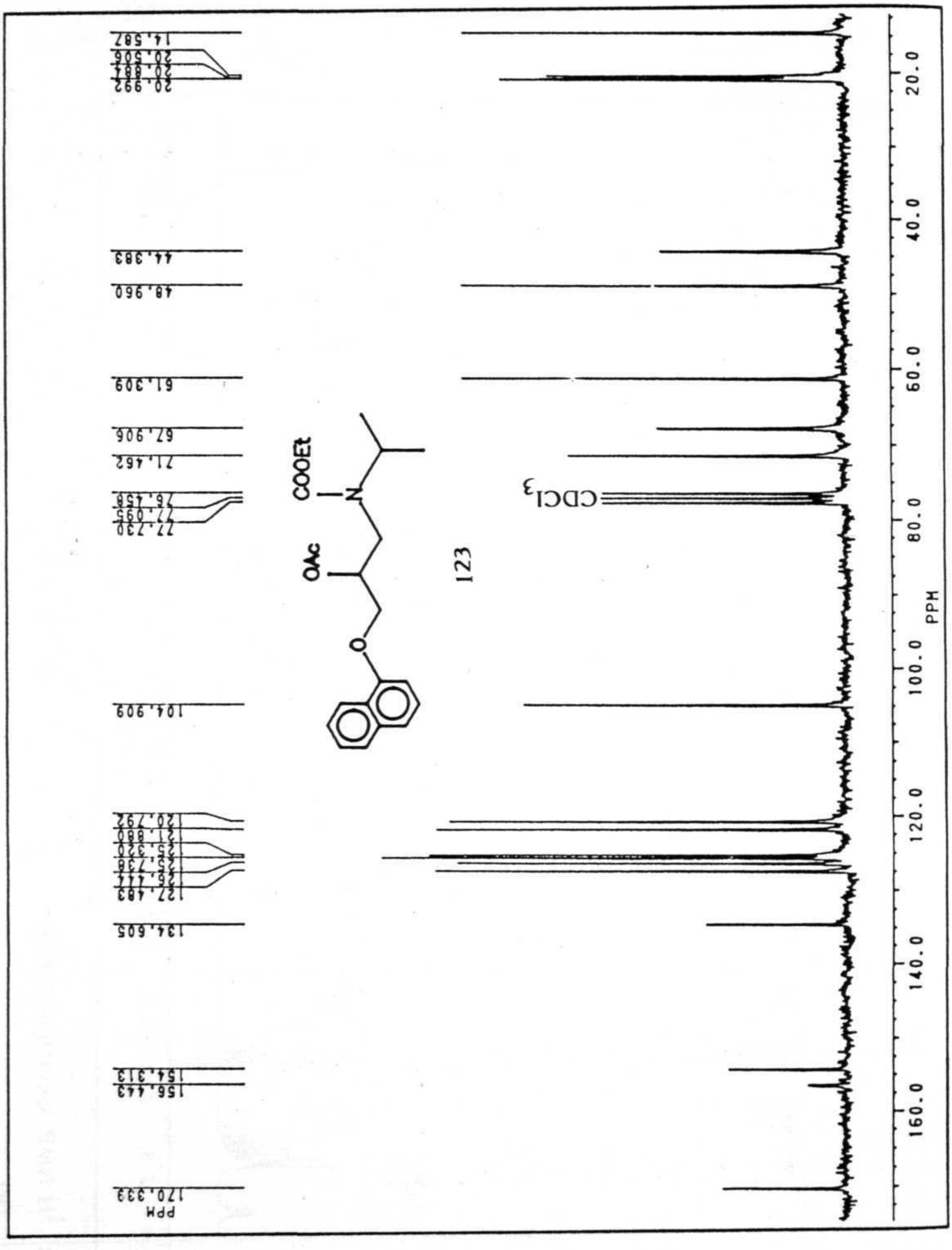


Fig. 7: ^{1}H NMR spectrum of **123.**



14.582
20.506
20.884
20.992
44.383
48.960
61.309
67.906
71.462
76.458
77.095
77.730
104.909
120.792
121.880
125.320
125.738
126.414
127.483
134.605
154.313
156.443
170.339
PPM
OAc
COOEt
N
O
123
CDCl3
20.0
40.0
60.0
80.0
100.0
120.0
140.0
160.0
PPM

REFERENCES

1. E.L. Eliel, *Stereochemistry of Carbon Compounds*, McGraw-Hill, New York, 1962.
2. S.F. Mason, *Molecular optical activity and the chiral discriminations*, Cambridge University Press, Cambridge, 1982, 6.
3. J. Crosby, *Tetrahedron*, 1991, **47**, 4789.
4. S.C. Stinson, *Chem. & Eng. News (Washington)*, 28 Sept 1992, 46.
5. G.M.R. Tombo, D. Bellus, *Angew. Chem. Int. Ed. Engl.*, 1991, **30**, 1193.
6. R.A. Sheldon, P.A. Porskamp, W. ten Hoeve in J. Tramper, H.C. van der Plas, P. Linko (Editors), *Biocatalysts in Organic Syntheses*, Elsevier, Amsterdam, 1985, 59.
7. J.D. Morrison (Editor), *Asymmetric Synthesis*, Academic Press, New York, 1983-1985, Vol 1-5.
8. E. Santaniello, P. Ferraboschi, P. Grisenti, A. Manzocchi, *Chem. Rev.*, 1992, **92**, 1071.
9. H.G. Davies, R.H. Green, D.R. Kelly, S.M. Roberts, *Biotransfomations in Preparative Organic Chemistry*, Academic Press, London, 1989.
10. G.M. Whitesides, C.-H. Wong, *Angew. Chem. Int. Ed. Engl.*, 1985, **24**, 617.
11. J.B. Jones, *Tetrahedron*, 1986, **42**, 3351.
12. S. Butt, S.M. Roberts, *Nat. Prod. Rep.* 1986, **3**, 489.
13. H. Yamada, S. Shimizu, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 622.

14. C.-S. Chen, C.J. Sih, *Angew. Chem. Int. Ed. Engl.*, 1989, **28**, 695.

15. C.-H. Wong, *Science*, 1989, **244**, 1145.

16. D.H.G. Crout, M. Christen, in R. Scheffold (Editor) *Modern Synthetic Methods*, Springer-Verlag, Berlin, 1989, Vol.**5**, 1.

17. W. Boland, C. Froβl, M. Lorenz, *Synthesis*, 1991, 1049.

18. A.M. Klibanov, *Acc. Chem. Res.*, 1990, **23**, 114.

19. International Symposium on *Biocatalysts in Organic Synthesis*, Noordwijkerhout, The Netherlands, 14-17 April 1985.

20. Ciba Foundation Symposium 111, *Enzymes in Organic Synthesis*, 1985

21. NATO Advanced Research Workshop, Enzymes as Catalysts in Organic Synthesis, 1986.

22. IUPAC-NOST International Symposium on *Enzymes in Organic Synthesis,* New Delhi, India, 6-9 Jan. 1992.

23. W.P, Jencks, *Catalysis in Chemistry and Enzymology*, McGraw-Hill, New York, 1969.

24. I. Chibata (Editor), *Immobilized Enzymes, Research and Development*, Kodansha, Tokyo, 1978.

25. C. Radziejewski, D. Hilvert, E.T. Kaiser, *The Construction of Semisynthetic Enzymes*, in J. Tramper, H.C. van der Plas, P. Linko (Editors), *Biocatalysts in Organic Synthesis*, Elsevier, Amsterdam, 1985, 81.

26. D. Botstein, D. Shortle, *Science,* 1985, **229**, 1193.

27. P.G. Schultz, *Acc. Chem. Res.*, 1989, **22**, 287.

28. M. Ohno, M. Otsuka, in A.S. Kende (Editor), *Organic Reactions,* 1989, **37**, 1.

29. L.-M. Zhu, M.C. Tedford, *Tetrahedron*, 1990, **46**, 6587.

30. H.D. Dakin, *Proc. Chem. Soc. London*, 1903, **19**, 161.

31. S.G. Cohen, E. Khedouri, *J. Am. Chem. Soc.,* 1961, **83**, 1093.

32. F.-C. Huang, L.F.H. Lee, R.S.D. Mittal, P.R. Ravikumar, J.A. Chan, C.J. Sih, E. Caspi, C.R. Eck, *J. Am. Chem. Soc.,* 1975, **97**, 4144.

33. M. Ohno, S. Kobayashi, T. Iimori, Y.-F. Wang, T. Izawa, *J. Am. Chem. Soc.,* 1981, **103**, 2405.

34. M. Schneider, N. Engel, H. Boensmann, *Angew. Chem. Int. Ed. Engl.*, 1984, **23**, 66.

35. F. Bjorkling, J. Boutelje, S. Gatenbeck, K. Hult, T. Norin, P. Szmulik, *Tetrahedron*, 1985, **41**, 1347.

36. F. Bjorkling, J. Boutelje, S. Gatenbeck, K. Hult, T. Norin, *Tetrahedron Lett.*, 1985, **26**, 4957.

37. L.K.P. Lam, R.A.H.F. Hui, J.B. Jones, *J. Org. Chem.*, 1986, **51**, 2047.

38. K. Adachi, S. Kobayashi, M. Ohno, *Chimia,* 1986, **40**, 311.

39. D.L. Hughes, J.J. Bergan, J.S. Amato, M. Bhupathy, J.L. Leazer J.M. McNamara, D.R. Sidler, P.J. Reider, E.J.J. Grabowski, *J. Org. Chem.,* 1990, **55**, 6252.

40. D. Breitgoff, K. Laumen, M.P. Schneider, *J. Chem. Soc., Chem. Commun.*, 1986, 1523.

41. Z.-F Xie, H. Suemune, K. Sakai, *J. Chem. Soc., Chem. Commun.*, 1988, 1638.

42. G. Guanti, E. Narisano, T. Podgorski, S. Thea, A. Williams, *Tetrahedron*, 1990, **46**, 7081.

43. K. Mori, Y. Takahashi, *Liebigs. Ann. Chem.*, 1991, 1057.

44. G. Guanti, L. Banfi, E. Narisano, *Tetrahedron Lett.*, 1989, **30**, 2697; *idem*, *Tetrahedron: Asymmetry*, 1990, **1**, 721; *idem*, *Tetrahedron Lett.*, 1990, **31**, 6421.

45. C.-S. Chen, Y. Fujimoto, C.J. Sih, *J. Am. Chem. Soc.*, 1981, **103**, 3580.

46. Y. Ito, T. Shibata, M. Arita, H. Sawai, M. Ohno, *J. Am. Chem. Soc.*, 1981, **103**, 6739.

47. P. Mohr, N. Waespe-Sarcevic, C. Tamm, K. Gawronska, J.K. Gawronski, *Helv. Chim. Acta.*, 1983, **66**, 2501.

48. M. Schneider, N. Engel, P. Honicke, G. Heinemann, H. Gorisch, *Angew. Chem. Int. Ed. Engl.*, 1984, **23**, 67.

49. G. Sabbioni, M.L. Shea, J.B. Jones, *J. Chem. Soc., Chem. Commun.*, 1984, 236.

50. H.-J. Gais, K.L. Lukas, *Angew. Chem. Int. Ed. Engl.*, 1984, **23**, 142.

51. J. Zemlicka, L.E. Craine, M.-J. Heeg, J.P. Oliver, *J. Org. Chem.*, 1988, **53**, 937.

52. R. Bloch, E. Guibe-Jampel, C. Girard, *Tetrahedron Lett.*, 1985, **26**, 4087.

53. Y.-F. Wang, C.-S. Chen, G. Girdaukas, C.J. Sih, *J. Am. Chem. Soc.*, 1984, **106**, 3695.

54. K. Laumen, M.P. Schneider, *J. Chem. Soc., Chem. Commun.*, 1986, 1298.

55. Y.-F. Wang, C.J. Sih, *Tetrahedron Lett.*, 1984, **25**, 4999.

56. G. Baudin, B.I. Glanzer, K.S. Swaminathan, A. Vasella, *Helv. Chim. Acta.*, 1988, **71**, 1367.

57. M. Eberle, M. Egli, D. Seebach, *Helv. Chim. Acta.*, 1988, **71**, 1.

58. M. Carda, J. Van der Eycken, M. Vandewalle, *Tetrahedron : Asymmetry*, 1990, **1**, 17.

59. S.G. Cohen, A. Milovanovic, *J. Am. Chem. Soc.*, 1968, 90, 3495.

60. C.-S. Chen, Y. Fujimoto, G. Girdaukas, C.J. Sih, *J. Am. Chem. Soc.*, 1982, **104**, 7294.

61. W.K. Wilson, S.B. Baca, Y.J. Barber, T.J. Scallen, C.J. Morrow, *J. Org. Chem.*, 1983, **48**, 3960.

62. T. Sugai, H. Kakeya, H. Ohta, *J. Org. Chem.*, 1990, **55**, 4643.

63. Q.-M. Gu, C.-S. Chen, C.J. Sih, *Tetrahedron Lett.*, 1986, **27**, 1763.

64. M. Ahmar, C. Girard, R. Bloch, *Tetrahedron Lett.*, 1989, **30**, 7053.

65. Q.-M. Gu, D.R. Reddy, C.J. Sih, *Tetrahedron Lett.*, 1986, **27**, 5203.

66. D.L. Delinck, A.L. Margolin, *Tetrahedron Lett.*, 1990, **31**, 6797.

67. R.-L. Gu, C.J. Sih, *Tetrahedron Lett.*, 1990, **31**, 3283.

68. P. Kalaritis, R.W. Regenye, J.J. Partridge, D.L. Coffen, *J. Org. Chem.*, 1990, **55**, 812.

69. K. Burgess, I. Henderson, K.-K. Ho, *J. Org. Chem.*, 1992, **57**, 1290.

70. M. Schneider, N. Engel, H. Boensmann, *Angew. Chem. Int. Ed. Engl.*, 1984, **23**, 64.

71. D. Bianchi, W. Cabri, P. Cesti, F. Francalanci, M. Ricci, *J. Org. Chem.*, 1988, **53**, 104.

72. M. Bucciarelli, A. Forni, I. Moretti, F. Prati, *J. Chem. Soc., Chem. Commun.*, 1988, 1614; *idem*, *Tetrahedron : Asymmetry*, 1990, **1**, 5.

73. E.J. Toone, J.B. Jones, *Tetrahedron : Asymmetry*, 1991, **2**, 207.

74. A.J.H. Klunder, W B. Huizinga, A.J.M. Hulshof, B. Zwanenburg, *Tetrahedron Lett.*, 1986, **27**, 2543.

75. G. Fulling, C.J. Sih, *J. Am. Chem. Soc.*, 1987, **109**, 2845.

76. W.E. Ladner, G.M. Whitesides, *J. Am. Chem. Soc.*, 1984, **106**, 7250.

77. Y. Fujimoto, H. Iwadate, N. Ikekawa, *J. Chem. Soc., Chem. Commun.*, 1985, 1333.

78. R.J. Kazlauskas, *J. Am. Chem. Soc.*, 1989, **111**, 4953.

79. Z.-F. Xie, H. Suemune, K. Sakai, *J. Chem. Soc., Chem. Commun.*, 1987, 830.

80. Z.-F. Xie, I. Nakamura, H. Suemune, K. Sakai, *J. Chem. Soc., Chem. Commun.*, 1988, 966.

81. C. Chan, P.B. Cox, S.M. Roberts, *J. Chem. Soc., Chem. Commun.*, 1988, 971.

82. H. Danda, A. Maehara, T. Umemura, *Tetrahedron Lett.*, 1991, **32**, 5119.

83. P. Washausen, H. Grebe, K. Kieslich, E. Winterfeldt, *Tetrahedron Lett.*, 1989, **30**, 3777.

84. T.R. Nieduzak, A.A. Carr, *Tetrahedron:Asymmetry*, 1990, **1**, 535.

85. S. Liang ,L.A. Paquette, *Tetrahedron:Asymmetry*, 1990, 1, 445.

86. R.L. Pederson, K.K.-C. Liu, J.F. Rutan, L. Chen, C.-H. Wong, *J. Org. Chem.*, 1990, **55**, 4897.

87. Z. Muljiani, S.R. Gadre, S. Modak, N. Pathan, R.B. Mitra, *Tetrahedron : Asymmetry*, 1991, **2**, 239.

88. T. Itoh, Y. Takagi, S. Nishiyama, *J. Org. Chem.*, 1991, **56**, 1521.

89. A. Zaks, A.M. Klibanov, *Science*, 1984, **224**, 1249.

90. A. Zaks, A.M. Klibanov, *Proc. Natl. Acad. Sci.* USA., 1985, **82**, 3192.

91. A. Zaks, A.M. Klibanov, *J. Am. Chem. Soc.*, 1986, **108**, 2767.

92. T.Sakurai, A.L. Margolin, A.J. Russell, A.M. Klibanov, *J. Am. Chem. Soc.* 1988, **110**, 7236.

93. H. Kitaguchi, P.A. Fitzpatrick, J.E. Huber, A.M. Klibanov, *J. Am. Chem. Soc.*,1989, **111**, 3094.

94. G. Kirchner, M.P. Scollar, A.M. Klibanov, *J. Am. Chem. Soc.*, 1985, **107**, 7072.

95. G. Langrand, M. Secchi, G. Buono, J. Baratti, C. Triantaphylides, *Tetrahedron Lett.*, 1985, **26**, 1857.

96. K. Yamamoto, T. Nishioka, J. Oda, *Tetrahedron Lett.*, 1988, **29**, 1717.

97. N.W. Boaz, *Tetrahedron Lett.*, 1989, **30**, 2061.

98. D.B. Berkowitz, S.J. Danishefsky, *Tetrahedron Lett.*, 1991, **32**, 5497.

99. J. Sakaki, H. Sakoda, Y. Sugita, M. Sato, C. Kaneko, *Tetrahedron : Asymmetry*, 1991, **2**, 343.

100. H.B. Kagan, M. Tahar, J.-C. Fiaud, *Tetrahedron Lett.*, 1991, **32**, 5959.

101. P. Ferraboschi, D. Brembilla, P. Grisenti, E. Santaniello, *J. Org. Chem.*, 1991, **56**, 5478.

102. G.M.R. Tombo, H.-P. Schar, X. Fernandez, I. Busquets, O.Ghisalba, *Tetrahedron Lett.*, 1986, **27**, 5707.

103. Y.-F. Wang, J.J. Lalonde, M. Momongan, D.E. Bergbreiter, C.-H. Wong, *J. Am. Chem. Soc.*, 1988, **110**, 7200.

104. U. Ader, D. Breitgoff, P. Klein, K.E. Laumen, M.P. Schneider, *Tetrahedron Lett.*, 1989, **30**, 1793.

105. M. Pottie, J. Van der Eycken, M. Vandewalle, *Tetrahedron : Asymmetry*, 1991, **2**, 329.

106. K.J. Harris, Q.-M. Gu, Y.-E. Shih, G. Girdaukas, C.J. Sih,

Tetrahedron Lett., 1991, **32**, 3941.

107. C.R. Johnson, J.P. Adams, S.J. Bis, R.L. De Jong, A. Golebiowski, J.R. Medich, T.D. Penning, C.H. Senanayake, D.H. Steensma, M.C. Van Zandt, *Pure & Appl. Chem.*, 1992, **64**, 1115.

108. S. Servi, *Synthesis*, 1990, 1.

109. R. Csuk, B.I. Glanzer, *Chem. Rev.*, 1991, **91**, 49.

110. J.B. Jones, in P.A. Frey (Editor), *Mechanisms of Enzymatic Reactions : Stereochemistry*, Elsevier, Amsterdam, 1986, 3.

111. E.J. Corey, W.-G. Su, M.B. Cleaver, *Tetrahedron Lett.* 1989, **30**, 4181.

112. T. Hudlicky, R. Fan, H. Luna, H. Olivo, J. Price, *Pure & Appl. Chem*, 1992, **64**, 1109.

113. H. Fu, M. Newcomb, C.-H. Wong, *J. Am. Chem. Soc.*, 1991, **113**, 5878.

114. V. Alphand, R. Furstoss, *J. Org. Chem.*, 1992, **57**, 1306.

115. M.D. Bednarski, E.S. Simon, N. Bischofberger, W.-D. Fessner, M.-J. Kim, W. Lees, T. Saito, H. Waldmann, G.M. Whitesides. *J. Am. Chem. Soc.*, 1989, **111**, 627.

116. D.G. Drueckhammer, W.J. Hennen, R.L. Pederson, C.F. Barbas. III, T. Krach, C.-H. Wong, *Synthesis*, 1991, 499.

117. F. Effenberger, T. Ziegler, S. Forster, *Angew. Chem. Int. Ed. Engl.*, 1987, **26**, 458.

118. K. Miyamoto, H. Ohta, *J. Am. Chem. Soc.*, 1990, **112**, 4077.

119. D. Basavaiah, V.V.L. Gowriswari, P.K.S. Sarma, P. Dharma Rao,

Tetrahedron Lett., 1990, **31**, 1621.

120. D. Basavaiah, T.K. Bharathi, *Synth. Commun.*, 1989, **19**, 2035.

121. D. Basavaiah, T.K. Bharathi, *Tetrahedron Lett.*, 1991, **32**, 3417.

122. D. Basavaiah, T.K. Bharathi, P. Rama Krishna, *Synth. Commun.*, 1992, **22**, 941.

123. D. Basavaiah, S. Bhaskar Raju, *Bioorg & Med. Chem. Lett.*, 1992, **2**, 955.

124. D. Basavaiah, P. Rama Krishna, T.K. Bharathi, *Tetrahedron Lett.*, 1990, **31**, 4347.

125. D. Basavaiah, S. Bhaskar Raju, *Synth. Commun.*, 1991, **21**, 1859.

126. D. Basavaiah, P. Rama Krishna, *Pure & Appl. Chem.*, 1992, **64**, 1067.

127. H.C. Brown, P.K. Jadhav, *J. Am. Chem. Soc.*, 1983, **105**, 2092.

128. R.W. Hoffmann, T. Herold, *Chem. Ber.*, 1981, **114**, 375.

129. E.J. Corey, C.-M. Yu, S.S. Kim, *J. Am. Chem. Soc.*, 1989, **111**, 5495.

130. C. Petrier, J.-L. Luche, *J. Org. Chem.* 1985, **50**, 910.

131. N. Minowa, T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 3697.

132. J.A. Dale, D.L. Dull, H.S. Mosher, *J. Org. Chem.*, 1969, **34**, 2543.

133. R.W. Hoffmann, *Angew. Chem. Int. Ed. Engl.* 1987, **26**, 489.

134. Y. Yamamoto, K. Maruyama, *Heterocycles*, 1982, **18**, 357.

135. S. Masamune, W. Choy, J.S. Petersen, L.R. Sita, *Angew. Chem. Int. Ed. Engl.*, 1985, **24**, 1.

136. K. Uneyama, H. Nanbu, S. Torii, *Tetrahedron Lett.*, 1986, **27**, 2395.

137. A. Hafner, R.O. Duthaler, R. Marti, G. Rihs, P. Rothe-Streit, F. Schwarzenbach, *J. Am. Chem. Soc.*, 1992, **114**, 2321.

138. J.J. Partridge, N.K. Chadha, M.R. Uskokovic, *J. Am. Chem. Soc.*, 1973, **95**, 7171.

139. M.M. Midland, P.E. Lee, J. Org. Chem., 1981, **46**, 3933.

140. R. Noyori, I. Tomino, M. Yamada, M. Nishizawa, *J. Am. Chem. Soc.*, 1984, **106**, 6717.

141. H.C. Brown, G.G. Pai, *J. Org. Chem.*, 1985, **50**, 1384.

142. S. Niwa, K. Soai, *J. Chem. Soc., Perkin. Trans.*I, 1990, 937.

143. K. Ishihara, A. Mori, I. Arai, H. Yamamoto, *Tetrahedron Lett.*, 1986, **26**, 983.

144. A.B. Baylis, M.E. D. Hillman, *German Patent* 2155113 (1972), *Chem. Abstr.*, 1972, **77**, 34174q.

145. S.E. Drewes, G.H.P. Roos, *Tetrahedron*, 1988, **44**, 4653.

146. K. Mori, *Tetrahedron*, 1989, **45**, 3233.

147. H.M.R. Hoffmann, J. Rabe, *Angew. Chem. Int. Ed. Engl.*, 1985, **24**, 94.

148. M. Kitamura, I. Kasahara, K. Manabe, R. Noyori, H. Takaya, *J. Org. Chem.*, 1988, **53**, 708.

149. K. Burgess, L.D. Jennings, *J. Org. Chem.*, 1990, **55**, 1138.

150. H.M.R. Hoffmann, J. Rabe, *Angew. Chem. Int. Ed. Engl.*, 1983, **22**, 795.

151. D. Basavaiah, V.V.L. Gowriswari, *Synth. Commun.*, 1987, **17**, 587.

152. J.K. Whitesell, *Chem. Rev.*, 1992, **92**, 953.

153. A. Misumi, K. Iwanaga, K. Furuta, H. Yamamoto, *J. Am. Chem. Soc.* 1985, **107**, 3343.

154. E.J. Corey, H.E. Ensley, *J. Am. Chem. Soc.*, 1975, **97**, 6908.

155. J.K. Whitesell, R.M. Lawrence, *Chimia*, 1986, **40**, 318.

156. A. Schwartz, P.B. Madan, E. Mohasci, J.P.O'Brien, L.J. Todaro, D.L. Coffen, *J. Org. Chem.*, 1992, **57**, 851.

157. K. Laumen, D. Breitgoff, R. Seemayer, M.P. Schneider, *J. Chem. Soc., Chem. Commun.*, 1989, 148.

158. H.C. Brown, J.V.N. Vara Prasad, A.K. Gupta, R.K. Bakshi, *J. Org. Chem.*, 1987, **52**, 320.

159. D.R. Galpin, A.C. Huitric, *J. Pharm. Sci.*, 1968, **57**, 447.

160. B.G. Main, S.M. Tucker in S.M. Roberts, B.J. Price (Editors), *Medicinal Chemistry-The Role of Organic Chemistry in Drug Research*, Academic Press, London, 1985, 69.

161. J.M. Klunder, S.Y. Ko, K.B. Sharpless, *J. Org. Chem.*, 1986, **51**, 3710.

162. H. Takahashi, S. Sakuraba, H. Takeda, K. Achiwa, *J. Am. Chem. Soc.*, 1990, **112**, 5876.

163. J. Jurczack, S. Pikul, T. Bauer, *Tetrahedron*, 1986, **42**, 447.

164. Y.-F. Wang, S.-T. Chen, K.K.-C. Liu, C.-H. Wong, *Tetrahedron Lett.*, 1989, **30**, 1917.

165. Y. Terao, M. Murata, K. Achiwa, *Tetrahedron Lett.*, 1988, **29**, 5173.

166. H.S. Bevinakatti, A.A. Banerji, *J. Org. Chem.*, 1991, **56**, 5372.

167. A.P. Terent'ev, M.A. Volodina, M.L. Smironova, V.G. Mishina, *Chem. Abst.*, 1960, **54**, 15353i.

168. R. Howe, R.G. Shanks, *Nature*, 1966, **210**, 1336.

169. R. Ikan, R. Gottlieb, E.D. Bergmann, J. Ishay, *J. Insect Physiol.*, 1969, **15**, 1709.

170. M. Utaka, H. Watabu, A. Takeda, *Chem. Lett.*, 1985, 1475.

171. M. Larcheveque, J. Lalande, *Tetrahedron*, 1984, **40**, 1061.

172. T. Kikukawa, A. Tai, *Chem. Lett*, 1984, 1935.

173. M. Utaka, H. Watabu, A. Takeda, *J. Org. Chem.*, 1987, **52**, 4363.

174. A. Mori, H. Yamamoto, *J. Org. Chem.*, 1985, **50**, 5444.

175. A.S.B. Prasad, J.V.B. Kanth, M. Periasamy, *Tetrahedron*, 1992, 48, 4623.

176. E.J. Corey, J.W. Suggs, *Tetrahedron Lett.*, 1975, 2647.

177. J.P. Ward, D.A. van Dorp, *Experientia*, 1981, **37**, 917.

178. Y. Masaki, Y. Serizawa, K. Nagata, K. Kaji, *Chem. Lett.*, 1983, 1601.

179. E. Keinan, K.K. Seth, R. Lamed, *J. Am. Chem. Soc.*, 1986, **108**, 3474.

180. J.B. Jones, R.S. Hinks, *Can. J. Chem.*, 1987, **65**, 704.

181. L. Coppi, A. Ricci, M. Taddei, *J. Org. Chem.*, 1988, **53**, 911.

182. E.J. Toone, M.J. Werth, J.B. Jones, *J. Am. Chem. Soc.*, 1990, **112**, 4946.

183. G.G. Smith, K.J. Voorhees, *J. Org. Chem.*, 1970, **35**, 2182.

184. L.J. Andrews, S.L. Linden, *J. Am. Chem. Soc.*, 1947, **69**, 2091.

185. C.U. Pittman, Jr., G.A. Olah, *J. Am. Chem. Soc.*, 1965, **87**, 5632.

186. A.Klages, *Ber. Deut. Chem. Gesell.*, 1906, **39**, 2587.

187. H. Normant, T. Cuvigny, *Soc. Chim. Fr. Bull.*, 1957, 1447.

188. M.M.C. Moureu, H. Desmtos, *Bull. Soc. Chim. Paris.*, 1902, **27**, 366

189. J.W. Cook, C.L. Hewett, C.A. Lawrence, *J. Chem. Soc.*, 1936, 71.

190. B.C. McKusick, *J. Am. Chem. Soc.*, 1948, **70**, 1976.

191. A. Alexakis, D. Jachiet, J.F. Normant, *Tetrahedron*, 1986, **42**, 5607.

192. M.L. Mihailovic, M. Miloradovic, *Tetrahedron*, 1966, **22**, 723.

193. A. Gaiffe, C. Launay, *Chem. Abst.*, 1968, 69, 26707k.

VITAE

The author was born on 18th october 1964 at Inavilli, Andhra Pradesh. Following his earlier education, he joined SKBR college, Amalapuram and obtained B.Sc. degree from Andhra University. Later he joined Kurukshetra University and recieved his M.Sc. degree in 1986. Subsequently he joined the Ph.D. program in 1987 in School of Chemistry, University of Hyderabad, Hyderabad. He was awarded JRF and SRF by UGC, New Delhi.

LIST OF Publications:

1. Sulfuric acid catalyzed decarbonylation of alkoxyacetyl chlorides: D.Basavaiah, P.Dharma Rao, V.V.L.Gowriswari, Synth. Commun., **1988**, 18, 1411.

2. Chiral acrylates as substrates in Baylis-Hillman reaction: D.Basavaiah, V.V.L.Gowriswari, P.K.S.Sarma, P.Dharma Rao, Tetrahedron Lett., **1990**, 31,1621.

3. Enantioselective hydrolysis of racemic acetates of homo-allyl alcohols by crude pig liver acetone powder (PLAP): D.Basavaiah, P.Dharma Rao, Synth. Commun., **1990**, 20, 2945.

4. Resolution of α-methylene-β-hydroxy esters and nitriles with crude pig liver acetone powder (PLAP): P.Dharma Rao, D. Basavaiah, Presented (oral) in IUPAC-NOST International symposium on Enzymes in Organic Synthesis, New Delhi, **1992**