



CATALYSTS FOR FINE CHEMICAL SYNTHESIS

Regio- and Stereo-
Controlled Oxidations
and Reductions

5

Editors: Stanley M. Roberts and John Whittall

C621.25
R336

Catalysts for Fine Chemical Synthesis

Volume 5

Regio- and Stereo- Controlled Oxidations and Reductions

Edited by

Stanley M. Roberts

University of Manchester, UK

John Whittall

University of Manchester, UK



John Wiley & Sons, Ltd



E2008000687

Copyright © 2007 John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester,
West Sussex PO19 8SQ, England

Telephone (+44) 1243 779777

Email (for orders and customer service enquiries): cs-books@wiley.co.uk
Visit our Home Page on www.wileyeurope.com or www.wiley.com

All Rights Reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning or otherwise, except under the terms of the Copyright, Designs and Patents Act 1988 or under the terms of a licence issued by the Copyright Licensing Agency Ltd, 90 Tottenham Court Road, London W1T 4LP, UK, without the permission in writing of the Publisher. Requests to the Publisher should be addressed to the Permissions Department, John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, England, or emailed to permreq@wiley.co.uk, or faxed to (+44) 1243 770620.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The Publisher is not associated with any product or vendor mentioned in this book.

This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is sold on the understanding that the Publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

The Publisher and the Author make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of fitness for a particular purpose. The advice and strategies contained herein may not be suitable for every situation. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of experimental reagents, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each chemical, piece of equipment, reagent, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. The fact that an organization or Website is referred to in this work as a citation and/or a potential source of further information does not mean that the author or the publisher endorses the information the organization or Website may provide or recommendations it may make. Further, readers should be aware that Internet Websites listed in this work may have changed or disappeared between when this work was written and when it is read. No warranty may be created or extended by any promotional statements for this work. Neither the Publisher nor the Author shall be liable for any damages arising herefrom.

Other Wiley Editorial Offices

John Wiley & Sons Inc., 111 River Street, Hoboken, NJ 07030, USA

Jossey-Bass, 989 Market Street, San Francisco, CA 94103-1741, USA

Wiley-VCH Verlag GmbH, Boschstr. 12, D-69469 Weinheim, Germany

John Wiley & Sons Australia Ltd, 42 McDougall Street, Milton, Queensland 4064, Australia

John Wiley & Sons (Asia) Pte Ltd, 2 Clementi Loop #02-01, Jin Xing Distripark, Singapore 129809

John Wiley & Sons Ltd, 6045 Freemont Blvd, Mississauga, Ontario L5R 4J3, Canada

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Anniversary Logo Design: Richard J. Pacifico

Library of Congress Cataloging-in-Publication Data

Regio- and stereo-controlled oxidations and reductions / edited by Stanley M. Roberts, John Whittall.
p. cm. — (Catalysts for fine chemical synthesis ; v. 5)

ISBN 978-0-470-09022-0 (cloth)

1. Oxidation. 2. Reduction (Chemistry) 3. Organic compounds—Synthesis.
4. Catalysts. I. Roberts, Stanley M. II. Whittall, John.

QD281.O9R436 2007

547'.23—dc22

2007011285

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library
ISBN 978-0-470-09022-0

Typeset in insert 10/12 pt Times by Thomson Digital Noida, India

Printed and bound in Great Britain by TJ International, Padstow, Cornwall

This book is printed on acid-free paper responsibly manufactured from sustainable forestry in which at least two trees are planted for each one used for paper production.

Catalysts for Fine Chemical Synthesis

Volume 5

Catalysts for Fine Chemical Synthesis

Series Editors

Stanley M. Roberts

University of Manchester, UK

Ivan V. Kozhevnikov

University of Liverpool, UK

Eric G. Derouane

Universidade do Algarve, Faro, Portugal

Books in this Series

Volume 1: Hydrolysis, Oxidation and Reduction

Edited by Stanley M. Roberts and Geraldine Poignant, *University of Liverpool, UK*

ISBN: 978 0 471 98123 7

Volume 2: Catalysis by Polyoxometalates

Edited by Ivan K. Kozhevnikov, *University of Liverpool, UK*

ISBN: 978 0 471 62381 6

Volume 3: Metal Catalysed Carbon-Carbon Bond-Forming Reactions

Edited by Stanley M. Roberts and Jianliang Xiao, *University of Liverpool, UK* and John Whittall and Tom E. Pickett, *The Heath, Runcorn Stylacats Ltd, UK*

ISBN: 978 0 470 86199 8

Volume 4: Microporous and Mesoporous Solid Catalysts

Edited by Eric G. Derouane, *Universidade do Algarve, Faro, Portugal*

ISBN: 978 0 471 49054 8

Volume 5: Regio- and Stereo-Controlled Oxidations and Reductions

Edited by Stanley M. Roberts and John Whittall, *University of Manchester, UK*

ISBN: 978 0 470 09022 0

Catalysts for Fine Chemical Synthesis

Series Preface

During the early-to-mid 1990s we published a wide range of protocols, detailing the use of biotransformations in synthetic organic chemistry. The procedures were first published in the form of a loose-leaf laboratory manual and all the protocols have been collected together and published in book form (*Preparative Biotransformations*, Wiley, Chichester, 1999).

Over the past few years the employment of enzymes and whole cells to carry out selected organic reactions has become much more commonplace. Very few research groups would now have any reservations about using commercially available biocatalysts such as lipases. Biotransformations have become accepted as powerful methodologies in synthetic organic chemistry.

Perhaps less clear to a newcomer to a particular area of chemistry is when to use biocatalysis as a key step in a synthesis, and when it is better to use one of the alternative non-natural catalysts that may be available. Therefore we set out to extend the objective of *Preparative Biotransformations*, so as to cover the whole panoply of catalytic methods available to the synthetic chemist, incorporating biocatalytic procedures where appropriate.

In keeping with the earlier format we aim to provide the readership with sufficient practical details for the preparation and successful use of the relevant catalyst. Coupled with these specific examples, a selection of the products that may be obtained by a particular technology will be reviewed. In the different volumes of this new series we will feature catalysts for oxidation and reduction reactions, hydrolysis protocols and catalytic systems for carbon-carbon bond formation *inter alia*. Many of the catalysts featured will be chiral, given the present day interest in the preparation of single-enantiomer fine chemicals. When appropriate, a catalyst type that is capable of a wide range of transformations will be featured. In these volumes the amount of practical data that is described will be proportionately less, and attention will be focused on the past uses of the system and its future potential.

Newcomers to a particular area of catalysis may use these volumes to validate their techniques, and, when a choice of methods is available, use the background

information better to delineate the optimum strategy to try to accomplish a previously unknown conversion.

S. M. ROBERTS
I. KOZHEVNIKOV
E. DEROUANE
Liverpool, 2002

Preface to Volume 5: Regio- and Stereo-Controlled Oxidations and Reductions

In recent years the world has become increasingly energy conscious. For the chemistry arena, this means that old-fashioned, inefficient processes are continually being replaced by modern methods. In turn, this fuels the search for effective catalysts to promote a wide range of transformations.

Across this range there can be no doubt that reactions resulting in either the oxidation or the reduction of a starting material are of paramount importance. In this Volume, a series of new or improved redox catalysts are featured. The catalysts have been disclosed in the recent primary literature (learned Journals) and the respective authors have amplified the disclosure of their catalysts in this Volume. Thus in each report herein, the exact method of preparation of the catalyst is described, the precise method for its use is disclosed and the breadth of substrate range is considered. A description of the equipment required as well as noteworthy safety issues form part of the description of each protocol. Finally, where potentially useful, tips and hints are appended, making these detailed “recipes” often more extensive than those found in the experimental sections of most Journals.

In order to place later chapters in proper context, the first chapter offers a comprehensive overview of industrially important catalysts for oxidation and reduction reactions. Chapters 2 and 3 describe the preparation of chiral materials by way of the asymmetric reduction of alkenes and ketones respectively. These two areas have enjoyed a significant amount of attention in recent years. Optically active amines can be prepared by imine reduction using chiral catalysts, as featured in Chapter 4, which also discloses a novel reductive amination protocol.

The remaining chapters deal with a variety of catalysts for effecting oxidation reactions. Chapter 5 describes three simple protocols for the controlled oxidation of primary or secondary alcohols. The importance of stereocontrolled epoxidation and hydroxylation reactions is reflected by the fact that Chapter 6, directed at this field, is one of the most extensive sections of the book. An interesting example of an enantioselective Baeyer-Villiger reaction is featured in Chapter 7, together with an industrially important ketone to enone conversion. Oxidative carbon-carbon

coupling reactions are the focus for Chapter 8, while the controlled oxidation of sulfides and sulfoxides is the topic chosen for the final chapter.

As for the previous volumes in this Series, the Editors are most grateful to the 100+ authors, who have submitted details of their work to the prescribed format for inclusion in this book. We hope that this Volume will increase exposure of their discoveries to the industrial chemical community and so contribute to the expanded employment of their catalysts in fine chemical synthesis.

STANLEY ROBERTS

JOHN WHITTALL

Manchester, 2007

Abbreviations

Ac	Acetyl
ACS	American Chemical Society
Ala	Alanine
API	Active Pharmaceutical Ingredient
aq	Aqueous
Ar	Aryl
ATH	Asymmetric Transfer Hydrogenation
atms	Atmosphere
BARF	<i>tetrakis</i> [3,5-Bis(trifluoromethyl)phenyl]borate
Bn	Benzyl
BINAP	2,2'-(Bisdiphenylphosphino)-1,1'-binaphthol
BINOL	1,1'-Binaphthol
tBME	<i>tert</i> -Butyl Methyl Ether
Boc	Butoxycarbonyl
Bu	Butyl
BuLi	Butyl Lithium
ca	<i>circa approxima</i>
CAL-B	<i>Candida antarctica</i> lipase B
CAN	Ceric Ammonium Nitrate
CATHy TM	Catalytic Asymmetric Transfer Hydrogenation
CBS	Corey-Bakshi-Shibata
COD	Cyclooctadiene
Cp	Cyclopentadienyl
DBT	Dibenzoyltartaric Acid
DCM	Dichloromethane
de	Diastereomeric Excess
DMAP	4-Dimethylaminopyridine
DMF	Dimethylformamide
DKR	Dynamic Kinetic Resolution
DPEN	1,2-Diphenylethylene 1,2-diamine
DVB	Divinylbenzene
ee	Enantiomeric Excess
EtOAc	Ethyl Acetate
eq	Equivalent

FID	Flame Ionisation Detector
GC	Gas Chromatography
HIV	Human Immunodeficiency Virus
HPLC	High Performance Liquid Chromatography
IBX	o-Iodoxybenzoic Acid
IR	Infra Red
LDA	Lithium diisopropylamide
LDBB	Lithium di- <i>tert</i> -butylbiphenylide
LDH	Layered Double Hydroxide
Me	Methyl
MOM	Methoxymethyl
Ms	Methane Sulfonyl
NAD(H)	Nicotinamide Adenine Dinucleotide (reduced)
NADP(H)	Nicotine Adenine Dinucleotide Phosphate (reduced)
Nbd	Norbornadiene
NK	Neurokinin
NMDA	N-Methyl-(D)-aspartate
NMR	Nuclear Magnetic Resonance
Oxone TM	Potassium Peroxymonosulfate
PDE	Phosphodiesterase
Ph	Phenyl
psi	Pounds Per Square Inch
PTC	Phase Transfer Catalyst
R _f	Retention Factor
R _t	Retention Time
SALEN	Salicylaldehyde Ethylenediamine Imine
SDS	Sodium Dodecylsulfate
TEMPO	2,2,6,6-Tetramethylpiperidin-1-oxyl
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMEDA	<i>N,N,N',N'</i> -Tetramethylethylenediamine
TOF	Turn Over Frequency
TON	Turn Over Number
Ts	Toluene sulfonyl
UV	Ultraviolet

Contents

Series Preface.	xvii
Preface to Volume 5	xix
Abbreviations	xxi
1 Industrial Catalysts for Regio- or Stereo-Selective Oxidations and Reductions A Review of Key Technologies and Targets	1
<i>John Whittall</i>	
1.1 Introduction	2
1.2 Reduction of Carbon-Carbon Double Bonds	3
1.2.1 Privileged structures: α -amino acids and itaconic acids	4
1.2.2 β -Amino acids	5
1.2.3 α -Alkyl substituted acids	6
1.2.4 α -Alkoxy substituted acids	8
1.2.5 Unsaturated nitriles	9
1.2.6 Alkenes and allyl alcohols	10
1.2.7 α,β -Unsaturated aldehyde reduction.	10
1.3 Ketone and Imine Reduction	12
1.3.1 Catalytic hydrogenation of ketones and imines	12
1.3.2 Asymmetric transfer hydrogenation (ATH) catalysts	15
1.3.3 Modified borane reagents	20
1.3.4 Biocatalysts (alcohol dehydrogenases and ketoreductases)	21
1.4 Oxidation.	23
1.4.1 Sharpless chiral epoxidation of allyl alcohols	23
1.4.2 Dioxirane catalyzed epoxidation	23
1.4.3 Amines and iminium salts	25
1.4.4 Phase transfer catalysts	25
1.4.5 The Juliá-Colonna method (polyleucine oxidation).	26
1.4.6 Organocatalytic α -hydroxylation of ketones	27
1.4.7 Baeyer–Villiger oxidation.	27
1.4.8 Chiral sulfoxides.	28
References	29
2 Asymmetric Hydrogenation of Alkenes, Enones, Ene-Esters and Ene-Acids	35
2.1 (<i>S</i>)-2,2'-Bis{[di(4-methoxyphenyl)phosphinyl]oxy}-5,5',6,6',7,7', 8,8'-octahydro-1,1'-binaphthyl as a ligand for rhodium-catalyzed asymmetric hydrogenation	36
<i>Ildiko Gergely, Csaba Hegedüs and Jozsef Bakos</i>	

2.1.1	Synthesis of (<i>S</i>)-5,5',6,6',7,7',8,8'-Octahydro-1,1'-bi-2-naphthol . .	37
2.1.2	Synthesis of (<i>S</i>)-2,2'-Bis{[di(4-methoxyphenyl)phosphinyl]oxy}-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl.	38
2.1.3	Asymmetric hydrogenation of Dimethyl itaconate.	40
	Conclusion.	41
	References.	41
2.2	Synthesis and application of phosphinite oxazoline iridium complexes for the asymmetric hydrogenation of alkenes	42
	<i>Frederik Menges and Andreas Pfaltz</i>	
2.2.1	Synthesis of (4 <i>S</i> ,5 <i>S</i>)-2-(5-Methyl-2-phenyl-4,5-dihydro-oxazol-4-yl)-1,3-diphenyl-propan-2-ol	42
2.2.2	Synthesis of (4 <i>S</i> ,5 <i>S</i>)-O-[1-Benzyl-1-(5-methyl-2-phenyl-4,5-dihydro-oxazol-4-yl)-2-phenyl-ethyl]-diphenylphosphinite	43
2.2.3	Synthesis of (4 <i>S</i> ,5 <i>S</i>)-[(η^4 -1,5-Cyclooctadiene)-{2-(2-phenyl-5-methyl-4,5-dihydro-oxazol-4-yl)-1,3-diphenyl-2-diphenylphosphinite-propane}iridium(I)-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate	45
2.2.4	Asymmetric hydrogenation of <i>trans</i> - α -Methylstilbene	46
	Conclusion.	47
	References.	48
2.3	Synthesis and application of heterocyclic phosphine oxazoline (HetPHOX) iridium complexes for the asymmetric hydrogenation of alkenes	48
	<i>Frederik Menges and Pier Giorgio Cozzi</i>	
2.3.1	Synthesis of (4 <i>S</i>)- <i>tert</i> -Butyl-2-(thiophene-2-yl)-4,5-dihydrooxazole	49
2.3.2	Synthesis of (4 <i>S</i>)- <i>tert</i> -Butyl-2-(3-diphenylphosphino-thiophene-2-yl)-4,5-dihydrooxazole	50
2.3.3	Synthesis of (4 <i>S</i>)-[(η^4 -1,5-Cyclooctadiene)-{4- <i>tert</i> -butyl-2-(3-diphenylphosphino-thiophene-2-yl)-4,5-dihydrooxazole}iridium(I)-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate	52
2.3.4	Asymmetric hydrogenation of <i>trans</i> - α -Methylstilbene	53
	Conclusion.	54
	References.	54
2.4	(<i>R</i>)-2,2',6,6'-Tetramethoxy-bis[di(3,5-dimethylphenyl)phosphino]-3,3'-bipyridine [(<i>R</i>)-Xyl-P-Phos] as a ligand for rhodium-catalyzed asymmetric hydrogenation of α -dehydroamino acids.	55
	<i>Jing Wu and Albert S.C. Chan</i>	
2.4.1	Synthesis of 3-Bromo-2,6-dimethoxypyridine	55
2.4.2	Synthesis of Bis(3,5-dimethylphenyl)phosphine chloride	56
2.4.3	Synthesis of 3-Bromo-2,6-dimethoxy-4-di(3,5-dimethylphenyl)phosphinopyridine	57
2.4.4	Synthesis of 3-Bromo-2,6-dimethoxy-4-di(3,5-dimethylphenyl)phosphinopyridine	59
2.4.5	2,2',6,6'-Tetramethoxy-bis[di(3,5-dimethylphenyl)phosphinoyl]-3,3'-bipyridine	60
2.4.6	Optical resolution of (\pm)- 6 with (–) or (+)-2,3- <i>O,O'</i> -Dibenzoyltartaric acid monohydrate [(<i>R</i>)- 6 or (<i>S</i>)- 6]	61
2.4.7	(<i>R</i>)-2,2',6,6'-Tetramethoxy-bis[di(3,5-dimethylphenyl)phosphino]-3,3'-bipyridine [(<i>R</i>)-Xyl-P-Phos, (<i>R</i>)- 1]	62
2.4.8	Preparation of the stock solution of [Rh(<i>R</i> -Xyl-P-Phos)(COD)]BF ₄	63
2.4.9	A typical procedure for the asymmetric hydrogenation of methyl (<i>Z</i>)-2-Acetamidocinnamate.	64
	References.	65

2.5	(<i>R,R</i>)-2,3-Bis(<i>tert</i> -butylmethylphosphino)quinoxaline (QuinoXP*) as a ligand for rhodium-catalyzed asymmetric hydrogenation of prochiral amino acid and amine derivatives	65
	<i>Tsuneo Imamoto and Aya Koide</i>	
2.5.1	Synthesis of (<i>R</i>)- <i>tert</i> -Butyl(hydroxymethyl)methylphosphine–borane	66
2.5.2	Synthesis of (<i>R</i>)-Benzoyloxy(<i>tert</i> -butyl)methylphosphine–borane	67
2.5.3	Synthesis of (<i>S</i>)- <i>tert</i> -Butylmethylphosphine–borane	69
2.5.4	(<i>R,R</i>)-2,3-Bis(<i>tert</i> -butylmethylphosphino)quinoxaline (QuinoxP*)	70
2.5.5	Asymmetric hydrogenation of Methyl (<i>E</i>)-3-acetylamino-2-butenolate catalyzed by Rh(I)-(<i>R,R</i>)-2,3-Bis(<i>tert</i> -butylmethylphosphino)quinoxaline	71
	Conclusion	72
	References	73
2.6	Rhodium-catalyzed asymmetric hydrogenation of indoles	73
	<i>Ryoichi Kuwano and Masaya Sawamura</i>	
2.6.1	Synthesis of (<i>R</i>)-2-[(<i>S</i>)-1-(Dimethylamino)ethyl]-1-iodoferrocene	73
2.6.2	Synthesis of (<i>R</i>)-2-[(<i>S</i>)-1-(Diphenylphosphinyl)ethyl]-1-iodoferrocene	75
2.6.3	Synthesis of (<i>R,R</i>)-2,2'-Bis[(<i>S</i>)-1-(diphenylphosphinyl)ethyl]-1,1''-biferrocene	78
2.6.4	Synthesis of (<i>R,R</i>)-2,2''-Bis[(<i>S</i>)-1-(diphenylphosphino)ethyl]-1,1''-biferrocene [abbreviated to (<i>S,S</i>)-(<i>R,R</i>)-PhTRAP]	80
2.6.5	Catalytic asymmetric hydrogenation of <i>N</i> -Acetyl-2-butyldole	82
2.6.6	Catalytic asymmetric hydrogenation of 3-Methyl- <i>N</i> -(<i>p</i> -toluenesulfonyl)indole	84
	Conclusion	85
	References	86
3	Asymmetric Reduction of Ketones	87
3.1	(<i>R,R</i>)-Bis(diphenylphosphino)-1,3-diphenylpropane as a versatile ligand for enantioselective hydrogenations	89
	<i>Natalia Dubrovina and Armin Börner</i>	
3.1.1	Synthesis of (<i>S,S</i>)-1,3-Diphenylpropane-1,3-diol	89
3.1.2	Synthesis of (<i>S,S</i>)-Methanesulfonyloxy-1,3-diphenylpropane-1,3-diol	91
3.1.3	Synthesis of (<i>R,R</i>)-Bis(diphenylphosphino)-1,3-diphenylpropane	91
	Conclusion	93
	References	93
3.2	Synthesis of both enantiomers of 1-Phenylethanol by reduction of acetophenone with <i>Geotrichum candidum</i> IFO 5767	93
	<i>Kaoru Nakamura, Mikio Fujii and Yoshiteru Ida</i>	
3.2.1	Cultivation of <i>G. candidum</i> IFO 5767	94
3.2.2	Synthesis of (<i>S</i>)-1-Phenylethanol	95
3.2.3	Synthesis of (<i>R</i>)-1-Phenylethanol	95
	Conclusion	97
	References	97
3.3	Titanocene-catalyzed reduction of ketones in the presence of water. A convenient procedure for the synthesis of alcohols via free-radical chemistry	97
	<i>Antonio Rosales, Juan M. Cuerva and J. Enrique Oltra</i>	
3.3.1	Titanocene-catalyzed reduction of Acetophenone in the presence of water	98

3.3.2	Titanocene-catalyzed synthesis of Methyl 4-deuterio-4-phenyl-4-hydroxybutanoate.	99
	References.	100
3.4	Xyl-tetraPHEMP: a highly efficient biaryl ligand in the [diphosphine RuCl ₂ diamine]-catalyzed hydrogenation of simple aromatic ketones	101
	<i>Paul H. Moran, Julian P. Henschke, Antonio Zanotti-Gerosa and Ian C. Lennon</i>	
3.4.1	Synthesis of Tri(3,5-dimethylphenyl)phosphine oxide	102
3.4.2	Synthesis of Bis(3,5-dimethylphenyl)-(2-iodo-3,5-dimethylphenyl)phosphine oxide	103
3.4.3	Synthesis of <i>rac</i> -4,4',6,6'-Tetramethyl-2,2'-bis[bis(3,5-dimethylphenyl)phosphino]-biphenyl	105
3.4.4	Synthesis of <i>rac</i> -4,4',6,6'-Tetramethyl-2,2'-bis[bis(3,5-dimethylphenyl)phosphino]-biphenyl [abbreviated to (<i>rac</i>)-Xyl-tetraPHEMP]	106
3.4.5	Synthesis of [(<i>R</i>)- <i>N,N</i> -Dimethyl(1-methyl)benzylamino-C ² ,N]-{ <i>rac</i> -4,4',6,6'-tetramethyl-2,2'-bis[bis(3,5-dimethylphenyl)phosphino]-biphenyl}-palladium(II) tetrafluoroborate and separation of the diastereomers.	107
3.4.6	Synthesis of (<i>S</i>)-4,4',6,6'-Tetramethyl-2,2'-bis[bis(3,5-dimethylphenyl)phosphino]-biphenyl: [abbreviated to (<i>S</i>)-Xyl-tetraPHEMP] and (<i>R</i>)-4,4',6,6'-Tetramethyl-2,2'-bis[bis(3,5-dimethylphenyl)phosphino]-biphenyl [abbreviated to (<i>R</i>)-Xyl-tetraPHEMP]	108
3.4.7	Synthesis of [(<i>R</i>)-Xyl-tetraPHEMP RuCl ₂ (<i>R,R</i>)-DPEN] and [(<i>S</i>)-Xyl-tetraPHEMP RuCl ₂ (<i>S,S</i>)-DPEN]	110
3.4.8	Reduction of Acetophenone using [(<i>S</i>)-Xyl-tetraPHEMP RuCl ₂ (<i>S,S</i>)-DPEN] as a precatalyst	111
	Conclusion.	112
	References.	112
3.5	<i>N</i> -Arenesulfonyl- and <i>N</i> -Alkylsulfamoyl-1,2-diphenylethylenediamine ligands for ruthenium-catalyzed asymmetric transfer hydrogenation of activated ketones	113
	<i>Michel (Massoud S.) Stephan and Barbara Mohar</i>	
3.5.1	Synthesis of <i>N</i> -Arenesulfonyl-1,2-diphenylethylenediamines	113
3.5.2	Preparation of Ru(II)- <i>N</i> -arenesulfonyl-1,2-diphenylethylenediamine complexes	114
3.5.3	Asymmetric transfer hydrogenation of Ethyl benzoylacetate	115
	Conclusion.	116
	References.	116
3.6	The synthesis and application of BrXuPHOS: a novel monodentate phosphorus ligand for the asymmetric hydrogenation of ketones	116
	<i>Martin Wills, Yingjian Xu, Gordon Docherty and Gary Woodward</i>	
3.6.1	Synthesis of (<i>S</i>)-BrXuPHOS	117
3.6.2	Synthesis of (<i>S,S,SS</i>)-BrXuPHOS-Ru-DPEN	119
3.6.3	General procedure of asymmetric hydrogenation of acetophenone	120
	Conclusion.	121
	Acknowledgement	121
	References.	121
3.7	<i>In Situ</i> formation of ligand and catalyst: application in ruthenium-catalyzed enantioselective reduction of ketones.	121
	<i>Jenny Wettergren and Hans Adolfsson</i>	
3.7.1	Synthesis of (<i>S</i>)-3-Fluoro-1-phenylethanol	122

Conclusion	123
References	124
3.8 Synphos and Difluorpos as ligands for ruthenium-catalyzed hydrogenation of alkenes and ketones	125
<i>S��verine Jeulin, Virginie Ratovelomanana-Vidal and Jean-Pierre Genet</i>	
3.8.1 Synthesis of [RuCl((S)-SYNPHOS)(<i>p</i> -cymene)]Cl	125
3.8.2 Synthesis of [RuCl((S)-DIFLUORPHOS)(<i>p</i> -cymene)]Cl	126
3.8.3 Synthesis of [RuI((S)-DIFLUORPHOS)(<i>p</i> -cymene)]I	127
3.8.4 Synthesis of [NH ₂ R ₂] [(RuCl(P*P)) ₂ (μ-Cl) ₃] P*P = SYNPHOS or DIFLUORPHOS and R = Me or Et	127
3.8.5 Synthesis of [NH ₂ Me ₂][RuCl-(S)-DIFLUORPHOS] ₂ [μ-Cl] ₃	128
3.8.6 Synthesis of <i>in situ</i> generated [RuBr ₂ ((S)-SYNPHOS)] and [RuBr ₂ ((S)-DIFLUORPHOS)]	129
Conclusion	131
References	131
3.9 An arene ruthenium complex with polymerizable side chains for the synthesis of immobilized catalysts	132
<i>Estelle Burri, Silke B. Wendicke, and Kay Severin</i>	
3.9.1 Synthesis of 2-Methyl-cyclohexa-2,5-dienecarboxylic acid 2-(2-methyl-acryloyloxy)-ethyl ester	133
3.9.2 Synthesis of [η ⁶ -(2-Methyl-benzoic acid 2-(2-methyl-acryloyloxy)-ethyl ester)RuCl ₂] ₂	134
Conclusion	135
References	135
3.10 Selective reduction of carbonyl group in β, γ-unsaturated α-alpha-ketoesters by transfer hydrogenation with Ru-(<i>p</i> -cymene) (TsDPEN)	135
<i>Minjie Guo, Dao Li, Yanhui Sun and Zhaoguo Zhang</i>	
3.10.1 Synthesis of Di-μ-chloro-bis[chloro(η ⁶ -1-isopropyl-4-methyl-benzene)ruthenium(II)]	136
3.10.2 Synthesis of (±)-Monotosylate-1,2-diphenyl-1,2-ethylenediamine	136
3.10.3 Synthesis of Ru complex Ru(<i>p</i> -cymene)(TsDPEN)	138
3.10.4 Ru-TsDPEN catalyzed transfer hydrogenation reaction of β,γ-unsaturated-α-ketoesters	139
Conclusion	140
References	141
3.11 Preparation of polymer-supported Ru-TsDPEN catalysts and their use for the enantioselective synthesis of (S)-fluoxetine	141
<i>Liting Chai, Yangzhou Li and Quanrui Wang</i>	
3.11.1 Synthesis of the supported ligand 9	141
3.11.2 Synthesis of ligand 17	148
3.11.3 General procedure for asymmetric transfer hydrogenation	150
3.11.4 Preparation of (S)-Fluoxetine hydrochloride	151
Conclusion	154
References	154
3.12 Polymer-supported chiral sulfonamide-catalyzed reduction of β-keto nitriles: a practical synthesis of (R)-Fluoxetine	155
<i>Guang-yin Wang and Gang Zhao</i>	
3.12.1 Synthesis of (R)-3-Amino-1-phenyl-propan-1-ol	155
3.12.2 Synthesis of (R)-ethyl 3-hydroxy-3-phenylpropylcarbamate	156
3.12.3 Synthesis of (R)-3-(Methylamino)-1-phenylpropan-1-ol	157
3.12.4 Synthesis of (R)-Fluoxetine	158

Conclusion.	159
References.	159
4 Imine Reduction and Reductive Amination	161
4.1 Metal-free reduction of imines: enantioselective Brønsted acid-catalyzed transfer hydrogenation using chiral BINOL-phosphates as catalysts	162
<i>Magnus Rueping, Erli Sugiono, Cengiz Azap and Thomas Theissmann</i>	
4.1.1 Synthesis of (<i>R</i>)-2,2'-Bis-methoxymethoxy-[1,1'] binaphthalene (MOM-BINOL)	162
4.1.2 Synthesis of (<i>R</i>)-3,3'-Diiodo-2,2'-bis(methoxymethoxy)-1, 1'-binaphthalene	164
4.1.3 Synthesis of 3,3'-Bis-(3,5'-bis-trifluoromethyl-phenyl)-2, 2'-bismethoxymethoxy [1,1'-binaphthalene]	165
4.1.4 Synthesis of (<i>R</i>)-3,3'-[3,5-Bis(trifluoromethyl)phenyl]- 1,1'-binaphthylphosphate	166
4.1.5 General procedure for the transfer hydrogenation of ketimines.	167
4.1.6 Synthesis of [1-(2,4-Dimethyl-phenyl)-ethyl]- (4-methoxy-phenyl)-amine	167
Conclusion.	168
References.	170
4.2 Metal-free Brønsted acid-catalyzed transfer hydrogenation: enantioselective synthesis of tetrahydroquinolines.	170
<i>Magnus Rueping, Thomas Theissmann and Andrey P. Antonchick</i>	
4.2.1 General procedure for the transfer hydrogenation of quinolines	170
4.2.2 Synthesis of 7-Chloro-4-phenyl-1,2,3,4-tetrahydroquinoline	172
4.2.3 Synthesis of (<i>S</i>)-2-Phenyl-1,2,3,4-tetrahydroquinoline	172
4.2.4 Synthesis of (<i>R</i>)-2-(2-(Benzo[1,3]dioxol-5-yl)ethyl)-1,2,3, 4-tetrahydro-quinoline	173
Conclusion.	174
References.	174
4.3 A highly stereoselective synthesis of 3 α -Amino-23, 24-bisnor-5 α -cholane via reductive amination.	175
<i>Sharaf Nawaz Khan, Nam Ju Cho and Hong-Seok Kim</i>	
4.3.1 Synthesis of Tris[(2-ethylhexanoyl)oxy]borohydride	177
4.3.2 Synthesis of 3 α -Acetamino-23,24-bisnor-5 α -cholane	177
4.3.3 Synthesis of 3 α - <i>N</i> -1-[<i>N</i> (3-[4-Aminobutyl])-1, 3-diaminopropane]-23,24-bisnor-5 α -cholane	179
Conclusion.	181
Acknowledgements.	181
References.	181
5 Oxidation of Primary and Secondary Alcohols.	183
5.1 Copper(II) catalyzed oxidation of primary alcohols to aldehydes with atmospheric oxygen	183
<i>Suribabu Jammi and Tharmalingan Punniyamurthy</i>	
5.1.1 Synthesis of copper(II) complex 1	184
5.1.2 Typical procedure for the oxidation of primary alcohols to aldehydes	185