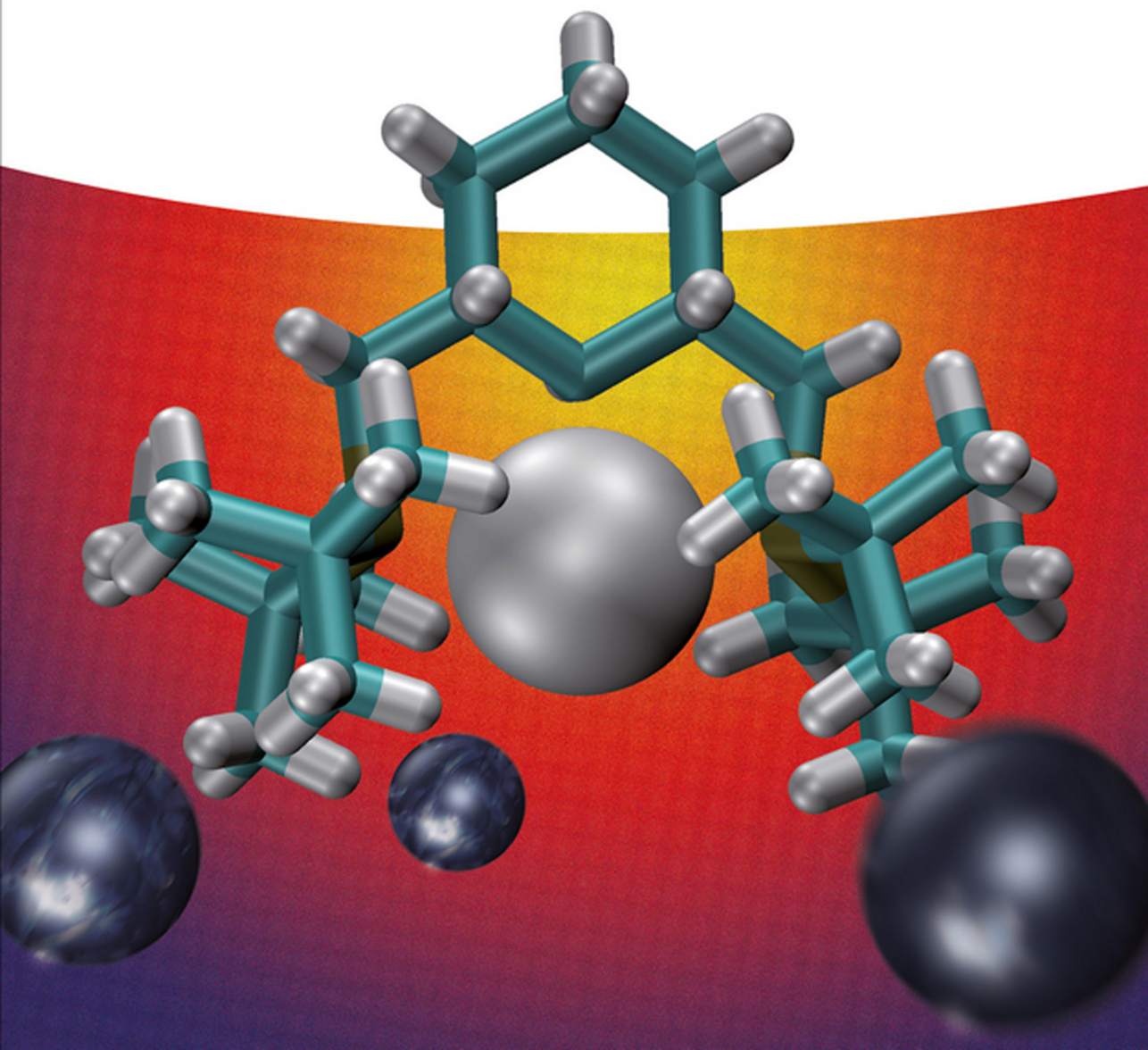


Kálmán J. Szabó and Ola F. Wendt

Pincer and Pincer-Type Complexes

Applications in Organic Synthesis and Catalysis



Edited by
Kálmán J. Szabó and
Ola F. Wendt

Pincer and Pincer-Type Complexes

Related Titles

Nolan, S.P. (ed.)

N-Heterocyclic Carbenes-Effective Tools for Organometallic Synthesis

2014

Print ISBN: 978-3-527-33490-2, also available in
digital formats

de Meijere, A., Bräse, S., Oestreich, M.
(eds.)

Metal-Catalyzed Cross-Coupling Reactions and More

2014

Print ISBN: 978-3-527-33154-3, also available in
digital formats

Molnár, Á. (ed.)

Palladium-Catalyzed Coupling Reactions

2013

Print ISBN 978-3-527-33254-0, also available in
digital formats

Andersson, P.G. (ed.)

Innovative Catalysis in Organic Synthesis

**Oxidation, Hydrogenation, and C-X Bond
Forming Reactions**

2012

Print ISBN: 978-3-527-33097-3, also available in
digital formats

Kuhl, O.

Functionalised N-Heterocyclic Carbene Complexes

2010

Print ISBN: 978-0-470-71215-3, also available in
digital formats

Edited by Kálmán J. Szabó and Ola F. Wendt

Pincer and Pincer-Type Complexes

Applications in Organic Synthesis and Catalysis

WILEY-VCH
Verlag GmbH & Co. KGaA

The Editors

Prof. Kálmán J. Szabó

Stockholm University
Arrhenius Laboratory
106 91 Stockholm
Sweden

Prof. Ola F. Wendt

Lund University
Organic Chemistry
221 00 Lund
Sweden

■ All books published by Wiley-VCH are carefully produced. Nevertheless, authors, editors, and publisher do not warrant the information contained in these books, including this book, to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

Library of Congress Card No.: applied for

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek

The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at <<http://dnb.d-nb.de>>.

© 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Print ISBN: 978-3-527-33442-1

ePDF ISBN: 978-3-527-68132-7

ePub ISBN: 978-3-527-68133-4

Mobi ISBN: 978-3-527-68131-0

oBook ISBN: 978-3-527-68130-3

Cover-Design Grafik-Design Schulz, Fußgönheim, Germany

Typesetting Laserwords Private Limited, Chennai, India

Printing and Binding Markono Print Media Pte Ltd, Singapore

Printed on acid-free paper

Contents

Preface *XI*

List of Contributors *XIII*

1 Catalysis by Pincer Complexes: Synthesis of Esters, Amides, and Peptides *1*

Chidambaram Gunanathan and David Milstein

- 1.1 Introduction and Background *1*
- 1.2 Bond Activation by Metal–Ligand Cooperation *3*
- 1.3 Synthesis of Esters *4*
- 1.3.1 Synthesis of Esters from Primary Alcohols *4*
- 1.3.2 Synthesis of Cross-Esters from Primary and Secondary Alcohols *9*
- 1.3.3 Synthesis of Esters by Acylation of Secondary Alcohols Using Esters *9*
- 1.3.4 Synthesis of Polyesters from Diols *11*
- 1.4 Synthesis of Amides *15*
- 1.4.1 Synthesis of Amides from Alcohols and Amines *15*
- 1.4.2 Synthesis of Amides from Esters and Amines *18*
- 1.4.3 Synthesis of Polyamides from Diols and Diamines *20*
- 1.5 Synthesis of Peptides from β -Amino Alcohols *24*
- 1.6 Concluding Remarks *26*
- Acknowledgments *26*
- References *27*

2 The Role of Redox Processes in Reactions Catalyzed by Nickel and Palladium Complexes with Anionic Pincer Ligands *31*

Juan Cámpora and Cristóbal Melero

- 2.1 Introduction *31*
- 2.2 Pincer Complexes of Ni, Pd, and Pt in Oxidation States Different from II *34*
- 2.2.1 Complexes in the Higher Oxidation States (III, IV) *34*
- 2.2.2 Reduced Complexes of Ni, Pd, and Pt with Pincer Ligands *43*
- 2.3 Catalytic Reactions Involving Redox Processes in the Pincer-Metal Framework *46*

| | | |
|----------|--|-----------|
| 2.3.1 | Atom-Transfer Radical Addition (ATRA) and Polymerization Reactions (ATRP) | 46 |
| 2.3.2 | The Heck Reaction | 48 |
| 2.3.3 | C–C Cross-Coupling Reactions | 54 |
| 2.3.4 | Carbon–Heteroatom Coupling Reactions | 62 |
| 2.4 | Concluding Remarks | 65 |
| | Acknowledgment | 66 |
| | References | 66 |
| 3 | Appended Functionality in Pincer Ligands | 71 |
| | <i>Cameron M. Moore and Nathaniel K. Szymczak</i> | |
| 3.1 | Introduction | 71 |
| 3.1.1 | Design Criteria | 72 |
| 3.1.2 | Motivations | 72 |
| 3.1.2.1 | Transition-Metal Catalysis | 72 |
| 3.1.2.2 | Supramolecular Architectures | 73 |
| 3.2 | Appended Functionality Coplanar with the Pincer Chelate | 75 |
| 3.2.1 | Systems that Incorporate 2,2':6',2''-Terpyridine | 75 |
| 3.2.1.1 | Synthetic Strategies | 75 |
| 3.2.1.2 | Appended Lewis Acid/Bases | 77 |
| 3.2.1.3 | Appended Hydrogen-Bond Acceptor/Donors | 79 |
| 3.2.2 | Pyridine-2,6-Dicarboxamide Systems | 84 |
| 3.3 | Appended Functionality Not Coplanar to the Pincer Chelate | 86 |
| 3.3.1 | ENE Pincer Systems | 86 |
| 3.3.2 | PCP Pincer Systems | 88 |
| 3.3.3 | PEP Pincer Systems | 88 |
| 3.3.4 | Pyridine-2,6-Diimine Systems | 90 |
| 3.4 | Future Outlook and Summary | 91 |
| | References | 91 |
| 4 | C–C, C–O, and C–B Bond Formation by Pincer Complexes Including Asymmetric Catalysis | 95 |
| | <i>Kálmán J. Szabó</i> | |
| 4.1 | Introduction – Pros and Cons of Using Pincer Complexes in Catalysis | 95 |
| 4.2 | Reaction of Imines and Isocyanoacetates | 96 |
| 4.2.1 | Stereoselective Synthesis of Imidazolines | 96 |
| 4.2.2 | Application of Chiral Pincer Complexes | 99 |
| 4.2.3 | Mechanistic Considerations | 101 |
| 4.3 | C–H Functionalization of Organonitriles | 102 |
| 4.3.1 | Allylation of Imines | 102 |
| 4.3.2 | Benzyl Amine Synthesis | 103 |
| 4.4 | Reactions Involving Hypervalent Iodines | 107 |
| 4.4.1 | Arylation of Alkenes Using Pincer Complex Catalysis | 107 |
| 4.4.2 | Acetoxylation with Hypervalent Iodines | 109 |

| | | |
|----------|--|------------|
| 4.4.3 | C–H Borylation of Alkenes | 112 |
| 4.5 | Summary and Outlook | 113 |
| | References | 115 |
| 5 | Nickel-Catalyzed Cross-Coupling Reactions | 117 |
| | <i>Anubendu Adhikary and Hairong Guan</i> | |
| 5.1 | Introduction | 117 |
| 5.2 | Carbon–Carbon Bond-Forming Reactions | 118 |
| 5.2.1 | Kumada–Corriu–Tamao Coupling | 118 |
| 5.2.2 | Suzuki–Miyaura Coupling | 129 |
| 5.2.3 | Negishi Coupling | 132 |
| 5.2.4 | Sonogashira Coupling | 139 |
| 5.2.5 | Mizoroki–Heck Reaction | 140 |
| 5.2.6 | Other Miscellaneous Cross-Coupling Reactions | 141 |
| 5.3 | Carbon–Heteroatom Bond-Forming Reactions | 143 |
| 5.4 | Summary and Outlook | 144 |
| | Acknowledgments | 144 |
| | References | 144 |
| 6 | PSiP Transition-Metal Pincer Complexes: Synthesis, Bond Activation, and Catalysis | 149 |
| | <i>Laura Turculet</i> | |
| 6.1 | Introduction | 149 |
| 6.2 | PSiP Ligand Syntheses | 151 |
| 6.3 | Group 8 Metal PSiP Chemistry | 153 |
| 6.4 | Group 9 Metal PSiP Chemistry | 161 |
| 6.5 | Group 10 Metal PSiP Chemistry | 169 |
| 6.6 | Group 11 Metal PSiP Chemistry | 179 |
| 6.7 | Alternative Silyl Pincers | 180 |
| 6.8 | Summary | 183 |
| | References | 183 |
| 7 | Electronic Structures of Reduced Manganese, Iron, and Cobalt Complexes Bearing Redox-Active Bis(imino)pyridine Pincer Ligands | 189 |
| | <i>Paul J. Chirik</i> | |
| 7.1 | Introduction | 189 |
| 7.2 | Reduced Manganese, Iron, and Cobalt Complexes with Redox-Active Bis(imino)pyridines | 189 |
| 7.2.1 | Reduced Bis(imino)pyridine Manganese Chemistry | 190 |
| 7.2.2 | Reduced Bis(imino)pyridine Iron Chemistry | 193 |
| 7.2.3 | Reduced Bis(imino)pyridine Cobalt Chemistry | 200 |
| 7.3 | Conclusions and Outlook | 209 |
| | References | 209 |

| | |
|-----------|--|
| 8 | Pincer Complexes with Saturated Frameworks: Synthesis and Applications 213 |
| | <i>Klara J. Jonasson and Ola F. Wendt</i> |
| 8.1 | Introduction 213 |
| 8.2 | Synthesis of the Ligands 213 |
| 8.3 | Synthesis and Coordination Behavior of Carbometallated PC(sp ³)P Complexes 215 |
| 8.3.1 | Coordination Flexibility in Acyclic PC(sp ³)P Complexes 216 |
| 8.4 | Reactivity and Catalytic Applications of PC(sp ³)P Complexes 217 |
| 8.4.1 | Ammonia Activation 217 |
| 8.4.2 | Isotopic Labeling 219 |
| 8.4.3 | Reactions with Coordinated Olefins 219 |
| 8.4.4 | Carbon–Carbon Coupling Reactions 221 |
| 8.4.5 | Hydrogenation and Dehydrogenation 223 |
| 8.4.6 | CO ₂ Activation 225 |
| | References 225 |
| 9 | Heavier Group 14 Elements-Based Pincer Complexes in Catalytic Synthetic Transformations of Unsaturated Hydrocarbons 229 |
| | <i>Jun Takaya and Nobuharu Iwasawa</i> |
| 9.1 | Introduction 229 |
| 9.2 | Synthesis of Palladium Complexes Bearing PXP-Pincer Ligands (X = Si, Ge, Sn) 230 |
| 9.2.1 | Synthesis 230 |
| 9.2.2 | Structural Analyses 230 |
| 9.3 | Hydrocarboxylation 231 |
| 9.3.1 | Hydrocarboxylation of Allenes 232 |
| 9.3.2 | Hydrocarboxylation of 1,3-Dienes 234 |
| 9.4 | Reductive Aldol Type Reaction 235 |
| 9.5 | Dehydrogenative Borylation 237 |
| 9.5.1 | Dehydrogenative Borylation of Alkenes and 1,3-Dienes 237 |
| 9.5.2 | Mechanistic Considerations 239 |
| 9.6 | Synthesis and Reaction of η^2 -(Si–H)Pd(0) Complex as an Equivalent to PSiP-Palladium Hydride Complexes 241 |
| 9.6.1 | Synthesis and Structure of η^2 -(Si–H)Pd(0) 241 |
| 9.6.2 | Reaction of η^2 -(Si–H)Pd(0) Complex with an Allene 242 |
| 9.6.3 | Reaction of η^2 -(Si–H)Pd(0) Complex with Diboron 244 |
| 9.7 | Conclusions 245 |
| | References 246 |
| 10 | Experimental and Theoretical Aspects of Palladium Pincer-Catalyzed C–C Cross-Coupling Reactions 249 |
| | <i>Christian M. Frech</i> |
| 10.1 | C–C Cross-Coupling Reactions – an Indispensable Tool for the Synthesis of Complex Organic Molecules 249 |

| | | |
|-----------|--|------------|
| 10.2 | Palladium Pincer Complexes as C–C Cross-Coupling Catalysts | 250 |
| 10.3 | The Role of Palladium Pincer Complexes in Heck Reactions | 253 |
| 10.3.1 | Pd ^{II} /Pd ^{IV} Cycles and Palladium Nanoparticle Formation | 256 |
| 10.4 | Computational Investigations on the Thermal Feasibility of Pd ^{II} /Pd ^{IV} Cycles of Palladium Pincer-Catalyzed Heck Reactions | 262 |
| 10.4.1 | Possible Initial Reaction Steps of Pd ^{II} /Pd ^{IV} Mechanisms | 263 |
| 10.4.2 | Investigations on Mechanisms Initiated by Oxidative Addition of Phenyl Bromide on the Palladium(II) Center of [C ₆ H ₃ -2,6-(NHP(piperidinyl) ₂) ₂ Pd(Cl)] (10) | 263 |
| 10.4.3 | Investigations on Mechanisms Initiated by Styrene Coordination and/or Chloride Dissociation | 265 |
| 10.4.4 | Pd ^{II} /Pd ^{IV} Cycle Proposed for Palladium Pincer-Catalyzed Heck Reactions | 270 |
| 10.4.5 | Heck Reactions Catalyzed by Palladium Pincer Complexes: Pd ^{II} /Pd ^{IV} Cycles and/or Palladium Nanoparticle Formation | 274 |
| 10.5 | Theoretical Investigations on a Pincer-Catalyzed Negishi Cross-Coupling Reaction | 275 |
| 10.6 | Concluding Remarks | 277 |
| | References | 278 |
| 11 | Reactions of Square-Planar d⁸ Pincer Complexes with Oxygen and Hydrogen | 281 |
| | <i>Wilson D. Bailey, Marie V. Parkes, Richard A. Kemp, and Karen I. Goldberg</i> | |
| 11.1 | Introduction | 281 |
| 11.2 | Insertion of Molecular Oxygen into Late-Transition Metal Hydride Bonds | 284 |
| 11.3 | Hydrogenolysis of Late-Transition Metal Hydroxide and Alkoxide Complexes | 289 |
| 11.4 | Summary | 294 |
| | Acknowledgment | 294 |
| | References | 295 |
| | Index | 299 |

Preface

Transition metal catalysis has become one of the most important tools in organic synthesis, important reasons being the high selectivities and high levels of atom economy usually achieved in catalytic transformations. Pincer and pincer-like complexes are an important class of catalysts employed in organic synthesis. The main advantage of these species is the well-defined stoichiometry, which allows conscious catalyst design and fine-tuning of the reactivity and selectivity of the catalyst. Also, the tri-dentate pincer ligand gives the metal complexes an unusual thermal stability. These properties contribute to the improvement of the usual catalytic properties of the commonly used catalysts and sometimes this can give unique catalytic features, which cannot be presented without the pincer framework of the system.

The book aims to help synthetic chemists to choose and apply pincer-complex catalysts in organic transformations. It also points out the most important pincer architectures that can be used efficiently in selective synthesis. Furthermore, it discusses reactivity and mechanisms in the elementary steps of catalytic transformation, which increases our understanding thereby pointing toward completely new applications.

Chapter 1 by Milstein and Chidambaram describes a unique pincer-complex catalyzed transformation for synthesis of esters, amides, and peptides using the aromatization–dearomatization ability of the pincer ligands. Several chapters focus on the possibility of using pincer complexes to stabilize the unusual oxidation state of the metal central atom. Chapter 2 by Campora and Melero analyzes the possibilities of bringing palladium to Pd(IV) and nickel to Ni(III) states during the catalytic process. Chapter 10 by Frech is focused on application of a Pd(II)–Pd(IV) catalytic cycle in cross-coupling reactions. Chapter 3 by Szymczak and Moore describes an entirely new application area of pincer complexes, namely as scaffolds for appended functionalities, such as Lewis acids or Lewis bases (even both of these functionalities in the same complex). Another promising novel application is using saturated pincer frameworks for catalysis as described by Jonasson and Wendt in Chapter 8. Chapter 4 by Szabó is focused on pincer-complex catalyzed functionalization of imines and some C–H functionalizations including asymmetric catalysis. Chapter 5 by Adhikary and Guan describes the use of nickel pincer complexes in cross-coupling reactions and shows how these can be complementary to the traditional palladium systems. Pincer complexes

have shown very promising reactivity in the activation of small molecules, and in the contribution by Bailey, Parkes, Kemp, and Goldberg (Chapter 11), the possibilities for generation of reactive intermediates in oxidation and reduction reactions are described. In the last decade, a number of new pincer frameworks have appeared and a few of these are described in the final chapters. Although they have not always shown a lot of applications they hold a promise for completely novel transformations. Thus, Chirik in Chapter 7 describes how redox activity of the ligands can be understood and give unprecedented reactivity to base metal complexes. The use of Si, Ge, or Sn with their exceptional trans influence as the central ligating atom is explored in two chapters. Turculet in Chapter 6 gives an overview of PSiP pincer chemistry, showing the unique features of this chemistry and Takaya and Iwasawa in Chapter 9 describes the application of heavier group 14 based pincer palladium complexes in hydrocarboxylation and borylation reactions.

Hopefully, the new aspects of pincer-complex catalysis reviewed in the above chapters will contribute to a broadening of the applications of pincer complexes in organic synthesis as well as to the study of reaction mechanisms.

We would like to acknowledge the authors of this book for their enthusiasm and for sharing their knowledge on pincer chemistry with the readers and for their help in realizing the present book on applications of pincer-complex catalysis in organic synthesis.

Stockholm and Lund
December 2013

Kálmán J. Szabó
Stockholm University
Department of Organic Chemistry
Stockholm, Sweden

Ola F. Wendt
Lund University
Department of Chemistry
Centre for Analysis and Synthesis
Lund, Sweden

List of Contributors

Anubendu Adhikary

University of Cincinnati
Department of Chemistry
301 Clifton Court
Cincinnati
OH 45221-0172
USA

Wilson D. Bailey

University of Washington
Department of Chemistry
Seattle
WA 98195-1700
USA

Juan Cámpora

Instituto de Investigaciones
Químicas
CSIC–Universidad de Sevilla
c/ Américo Vespucio, 49
41092 Sevilla
Spain

Paul J. Chirik

Princeton University
Department of Chemistry
292 Frick Laboratory
Princeton
NJ 08544
USA

Christian M. Frech

Zürich University of Applied
Sciences
Department of Life Sciences and
Facility Management
Institute of Chemistry and
Biological Chemistry
Einsiedlerstrasse 31
CH-8820 Wädenswil
Switzerland

Karen I. Goldberg

University of Washington
Department of Chemistry
Seattle
WA 98195-1700
USA

Hairong Guan

University of Cincinnati
Department of Chemistry
301 Clifton Court
Cincinnati
OH 45221-0172
USA

Chidambaram Gunanathan

National Institute of Science
Education and Research (NISER)
School of Chemical Sciences
Bhubaneswar 751005
India

Nobuharu Iwasawa

Tokyo Institute of Technology
Department of Chemistry
2-12-1-E1-2 O-okayama
Tokyo 152-8551
Japan

Klara J. Jonasson

Lund University
Department of Chemistry
Centre for Analysis and Synthesis
Getingevägen 60
221 00 Lund
Sweden

Richard A. Kemp

University of New Mexico
Department of Chemistry and
Chemical Biology
Albuquerque
NM 87131
USA

and

Sandia National Laboratories
Advanced Materials Laboratory
Albuquerque
NM 87106
USA

Cristóbal Melero

Instituto de Investigaciones
Químicas
CSIC–Universidad de Sevilla
c/ Américo Vespucio, 49
41092 Sevilla
Spain

David Milstein

The Weizmann Institute of
Science
Department of Organic
Chemistry
Rehovot 76100
Israel

Cameron M. Moore

University of Michigan
Department of Chemistry
930 N. University
Ann Arbor
MI 48109-1055
USA

Marie V. Parkes

University of New Mexico
Department of Chemistry and
Chemical Biology
Albuquerque
NM 87131
USA

Kálmán J. Szabó

Stockholm University
Department of Organic
Chemistry
Svante Arrhenius väg 16C
SE-106 91 Stockholm
Sweden

Nathaniel K. Szymczak

University of Michigan
Department of Chemistry
930 N. University
Ann Arbor
MI 48109-1055
USA

Jun Takaya

Tokyo Institute of Technology
Department of Chemistry
2-12-1-E1-2 O-okayama
Tokyo 152-8551
Japan

Laura Turculet

Dalhousie University
Department of Chemistry
6274 Coburg Road
P.O. Box 15000
Halifax, Nova Scotia
B3H 4R2 Canada

Ola F. Wendt

Lund University
Department of Chemistry
Centre for Analysis and Synthesis
Getingevägen 60
221 00 Lund
Sweden

1

Catalysis by Pincer Complexes: Synthesis of Esters, Amides, and Peptides

Chidambaram Gunanathan and David Milstein

1.1

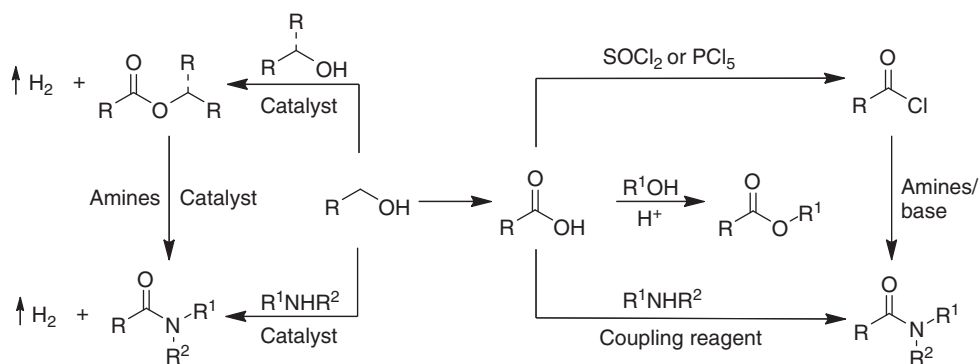
Introduction and Background

Esters, amides, amines, acetals, and peptides are important industrial chemicals. Production of these chemicals is based on multistep processes using stoichiometric amounts of acid or base promoters and coupling reagents, and involves reactive intermediates derived from alcohols or acids (Scheme 1.1), which leads to very large amounts waste [1]. Controlling overoxidation of substrates in the synthetic methods of these products is a challenge, and hence stepwise syntheses are performed (see below) [2]. Thus, green processes that can circumvent stoichiometric reagents and the generation of reactive intermediates, such as acid chlorides, and directly deliver stable and useful industrial products, such as esters and amides, in an atom-economical, selective manner without producing waste are needed.

Pincer ligands, that is, tridentate ligands that enforce meridional geometry upon complexation to transition metals, result in pincer complexes which possess a unique balance of stability versus reactivity [3]. Transition-metal complexes of bulky, electron-rich “pincer” ligands have found important applications in synthesis, bond activation, and catalysis [4, 5]. Among these, pincer complexes of ⁱPr-PNP (2,6-bis-(di-*iso*-propylphosphinomethyl)pyridine), ^tBu-PNP (2,6-bis-(di-*tert*-butylphosphinomethyl)pyridine), and PNN ((2-(di-*tert*-butylphosphinomethyl)-6-diethylaminomethyl)pyridine), PNN-BPy (6-di-*tert*-butylphosphinomethyl-2,2'-bipyridine) ligands exhibit diverse reactivity [6–8]. These bulky, electron-rich pincer ligands can stabilize coordinatively unsaturated complexes and participate in unusual bond activation and catalytic processes.

In most processes, homogeneously catalyzed by metal complexes, the ligands, while imparting critical properties on the metal center, do not participate directly in bond-making and -breaking processes with the substrates. In recent years, complexes in which the ligands actively cooperate with the metal center in bond-activation processes have been developed [9]. We have devised novel catalytic systems based on pincer complexes in which the pincer ligands cooperate with the metal center in a synergistic manner and their interplay facilitates the chemical processes. The pincer complexes are based on new pyridine- and acridine-type

pincer ligands, which undergo bond-breaking and -making processes, involving aromatization–dearomatization of the pincer ligands [8]. Such cooperative pincer complexes catalyze several unique processes, as summarized in recent reviews [6–8, 10]. Here we concentrate on the selective synthesis of esters [11–13], amides [14, 15], acetals [16], amines [17], and imines [18], directly from alcohols. Using diols, polyesters were obtained [19]; diols and diamines provided polyamides [20, 21], and aminoalcohols resulted in formation of pyrazines and peptides [22]. Cooperative pincer complexes have also catalyzed the reverse reactions of esterification and amidation; thus, hydrogenation of esters [23, 24], formates, and carbonates [25] provides the corresponding alcohols, whereas amides give amines and alcohols [26] and urea provides methanol and amines [27]. Carbon dioxide also undergoes hydrogenation to formate salts [28] by pincer catalysts.



Scheme 1.1 Conventional versus catalytic synthesis of esters and amides.

Deprotonation of a pyridinylmethylenic proton of pyridine- and bipyridine-based pincer complexes can lead to dearomatization. The dearomatized complexes can then activate a chemical bond ($\text{H}-\text{Y}$, $\text{Y} = \text{H}$, OH , OR , NH_2 , NR_2 , C) by cooperation between the metal and the ligand, thereby regaining aromatization (Figure 1.1). The overall process does not involve a change in the metal's oxidation state [6–8]. In this chapter, we describe the novel, environmentally benign catalytic synthesis of esters, amides, and peptides that operate via this new metal–ligand cooperation based on aromatization–dearomatization processes.

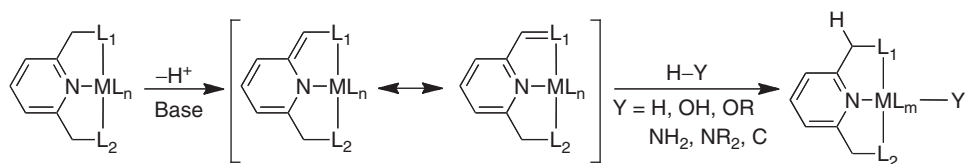
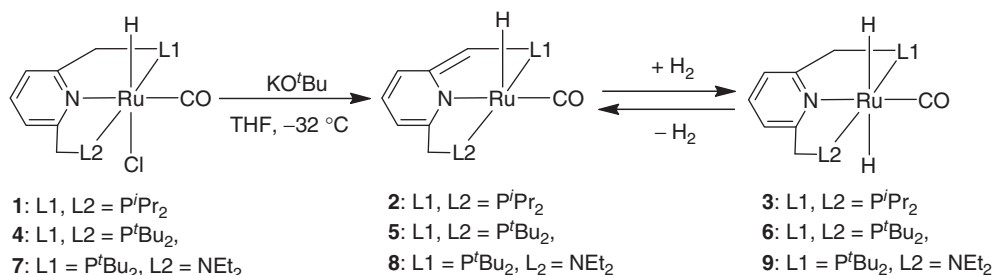


Figure 1.1 Metal–ligand cooperation based on aromatization–dearomatization.

1.2

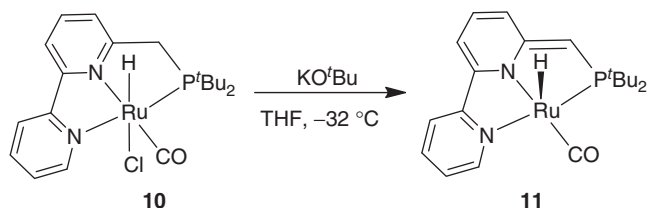
Bond Activation by Metal–Ligand Cooperation

We have discovered a new mode of bond activation by metal–ligand cooperation based on aromatization–dearomatization of pyridine- and acridine-based heteroaromatic pincer complexes (Figure 1.1) [6–8, 29]. Recently, we have observed that bipyridine-derived PNN-Bipy ligands also exhibit similar metal–ligand cooperativity (Scheme 1.2) [13, 24–27]. Such reactivity, which is not possible with the corresponding aryl-based PCP pincer complexes, is made possible in pyridine-based pincer complexes by (i) the relatively low resonance energy of pyridine (28 kcal mol^{−1}; compared to benzene, 36 kcal mol^{−1}), (ii) the acidity of pyridinyl methylene protons in the pyridine-based pincer complexes, and (iii) stabilization of the dearomatized ligand by the metal center.



Scheme 1.2 Preparation of dearomatized pyridine-based PNP and PNN pincer complexes and their reversible reaction with H₂.

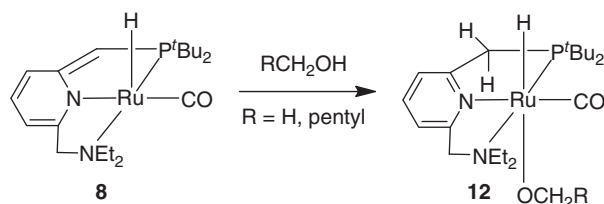
For example, the pyridine-based pincer complexes **1**, **4**, **7**, and **10** undergo smooth deprotonation to provide complexes **2**, **5**, **8**, and **11** (Schemes 1.2 and 1.3). NMR studies of **2**, **5**, **8**, and **11** indicate dearomatization, as the pyridine protons are shifted to lower frequency (olefinic region). Moreover, the structure of complex **2** is unequivocally corroborated by single-crystal X-ray diffraction studies [23]. Importantly, the dearomatized complexes of **2**, **5**, and **8** activate dihydrogen by cooperation between the ruthenium center and the deprotonated phosphine arm, resulting in aromatization to quantitatively yield the ruthenium *trans*-dihydride complexes of **3**, **6**, and **9**, respectively (Schemes 1.2). The magnetically equivalent



Scheme 1.3 Preparation of dearomatized bipyridine-derived PNN pincer complex **11**.

trans-dihydrides resonate as triplets in complexes **3** and **6** at -4.96 ppm ($^2J_{\text{PH}} = 20.0$ Hz) and -4.90 ppm ($^2J_{\text{PH}} = 17.0$ Hz), respectively, whereas they display doublets at -4.06 ppm ($^2J_{\text{PH}} = 17.0$ Hz) for complexes **9**. The *trans*-dihydride complexes **3**, **6**, and **9** slowly lose H_2 at room temperature to regenerate complexes **2**, **5**, and **8**, respectively.

In addition to the activation of dihydrogen [29d, 30], the dearomatized pyridine-derived pincer complexes also activate O–H bonds of alcohols [11–18, 31] and water [29e, 32], N–H bonds of amines and ammonia [29f,h], sp^3 C–H [29c] and sp^2 C–H bonds [29a,g], and carbon dioxide [33]. Among these various bond-activation reactions, of particular interest here is the O–H bond activation of alcohols, as complex **8** reacts with alcohols to provide the aromatic coordinatively saturated hydrido-alkoxy complexes **12** (Scheme 1.4), indicating the possibility of catalytic transformations based on dehydrogenation of alcohols.



Scheme 1.4 O–H activation by the dearomatized PNN pincer complex **8**.

Such dearomatization and aromatization of these electron-rich ligand systems in cooperation with metal centers present new opportunities for homogeneous catalysis.

1.3

Synthesis of Esters

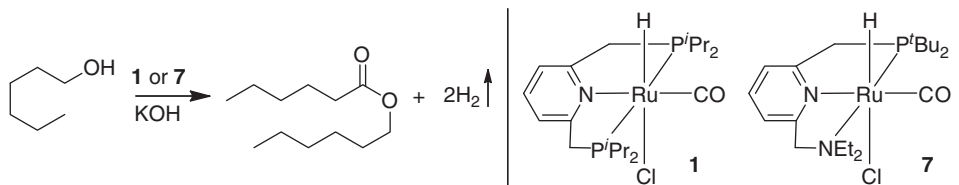
Esterification is an important reaction in organic synthesis. It has an assortment of applications in the production of synthetic intermediates, biologically active natural products, fragrances, polymers, polyesters, plasticizers, fatty acids, paints, and pharmaceuticals. Environmentally benign esterification methods catalyzed by pincer complexes that operate via metal–ligand cooperation are described in this section.

1.3.1

Synthesis of Esters from Primary Alcohols

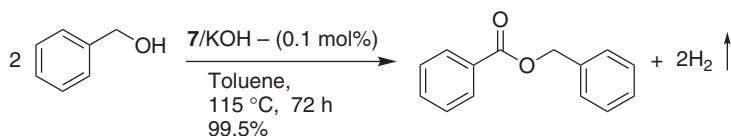
When primary alcohols were heated with a catalytic amount of complex **1**, in the presence of a catalytic amount of base, an unusual dehydrogenative coupling to form esters with evolution of H_2 was observed [11]. Thus, refluxing a hexanol (bp 157°C) solution containing complex **1** and KOH (0.1 mol% each) under argon in

Table 1.1 Catalytic conversion of alcohols to esters by PNP (**1**) and PNN (**7**) complexes in the presence of catalytic base.

|  | | | | | |
|--|---------|------|------------------|-----------|-----|
| Catalyst | Solvent | Time | Temperature (°C) | Yield (%) | TON |
| 1/KOH (0.1 mol%) | — | 24 | 157 | 67 | 670 |
| 7/KOH (0.1 mol%) | Toluene | 24 | 115 | 95 | 950 |

an open system for 24 h resulted in formation of hexyl hexanoate in 67% yield. The PNN complex **7**, which possesses a hemilabile amine “arm,” was a significantly better catalyst (still in the presence of an equivalent of base) than the corresponding PNP complex **1**, leading to 95% (950 turnovers) hexyl-hexanoate after 24 h at 115 °C (Table 1.1) [11].

Good turnover numbers (TONs) and yields of esters were obtained with various alcohols at 115 °C. Reaction follow-up with benzyl alcohol indicated that 91% benzyl benzoate was formed already after 6 h, with turnover frequency (TOF) reaching 333 h^{-1} at the level of 50% benzyl benzoate. Formation of the ester became very slow after 6 h, perhaps because of retardation of the reaction by the high ester concentration. However, almost quantitative formation of benzyl benzoate was obtained (Scheme 1.5).

**Scheme 1.5** Catalytic conversion of benzyl alcohol to benzyl benzoate by PNN complex **7**.

Further improvement in the reaction was possible by exclusion of the need for base. Thus, reaction of complex **7** with KO^tBu resulted in the formation of the coordinatively unsaturated, 16e^- Ru(II) neutral complex **8**. Indeed, **8** is an excellent catalyst for the dehydrogenative coupling of alcohols to esters and the reaction proceeds with liberation of H_2 under neutral conditions [11]. Table 1.2 provides a few examples. GC analysis of the reaction mixtures indicated that aldehydes were formed only in trace amounts. This catalytic reaction provided a new “green” pathway for the synthesis of esters directly from alcohols. Considerably less efficient methods had been reported previously for this transformation [34].

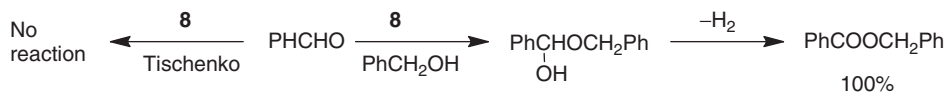
Table 1.2 Examples of dehydrogenative coupling of alcohols to form esters and dihydrogen catalyzed by dearomatized Ru PNN complex **8**.

| $2 \text{ R-OH} \xrightarrow[\text{Toluene, reflux}]{\textbf{8 (0.1 mol\%)}} \text{R-CO-O-R} + 2\text{H}_2 \uparrow$ | | | | |
|--|--------|-----------------|----------|-----------|
| | | | | |
| Entry | R | Ester | Time (h) | Ester (%) |
| 1 ^a | Propyl | Butyl butyrate | 5 | 90 |
| 2 | Pentyl | Hexyl hexanoate | 6 | 99 |
| 3 | Ph | Benzyl benzoate | 4 | 92 |

Conditions: 0.01 mmol catalyst **8**, 10 mmol alcohol, and toluene (2 ml) were refluxed (115 °C) under Ar flow.

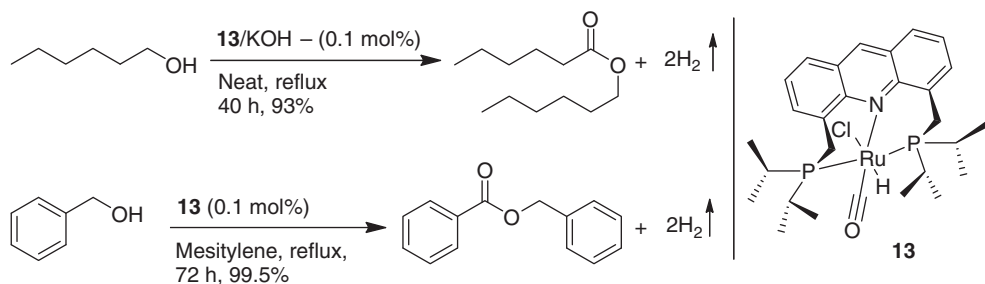
^aNeat reaction, heated at 117 °C.

There are two potential pathways by which an ester can be formed, both involving an intermediate aldehyde, namely a Tischenko-type condensation [35] or hemiacetal formation followed by its dehydrogenation [34]. Our results establish that the second pathway is operative, at least in the case of benzyl alcohol [11]. Thus, employing benzaldehyde (in absence of alcohol) did not yield any ester. On the other hand, reaction of benzaldehyde with 1 equivalent of benzyl alcohol led to quantitative formation of benzyl benzoate (Scheme 1.6).

**Scheme 1.6** Formation of ester via hemiacetal intermediary.

Using the acridine-derived PNP pincer complex **13**, primary alcohols can be directly transformed into acetals under neutral conditions [16, 36]. When the reactions were carried out in the presence of 1 equivalent of base (relative to complex **13**, 0.1 mol%), the corresponding esters were obtained in very good yields (Scheme 1.7). Mechanistic studies revealed that a β-hydrogen is essential for the acetal formation; thus, alcohols such as benzyl alcohol provided benzyl benzoate in 99.5% yield, rather than acetal, even under neutral conditions [16].

Recently, Gusev and coworkers [37] reported the PNN ruthenium pincer complex **14** with an aliphatic backbone, which displayed impressive catalytic activity in the presence of a base (KO^tBu, 0.5 mol%) for the conversion of simple alcohols such as ethanol and propanol. Although the reactions worked at temperatures below 100 °C, good conversions required heating at higher temperatures (Table 1.3,



Scheme 1.7 Esterification of primary alcohols by acridine PNP ruthenium pincer complex **13**.

Table 1.3 Dehydrogenative coupling of alcohols to form esters and dihydrogen catalyzed by the Ru PNN complex **14**.

| Entry | R | T (°C) | Time (h) | Conversion (%) |
|-------|----------------|--------|----------|----------------|
| 1 | Me | 78 | 7.5 | 30 |
| 2 | Et | 96 | 8 | 73 |
| 3 | Pr | 118 | 3 | 78 |
| 4 | <i>i</i> -Amyl | 131 | 2.5 | 92 |
| 5 | Hexyl | 158 | 1 | 86 |

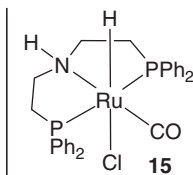
entries 4–5). An analogous dehalogenated osmium-based dimeric pincer complex was also reported to have comparable activity to that of complex **14**.

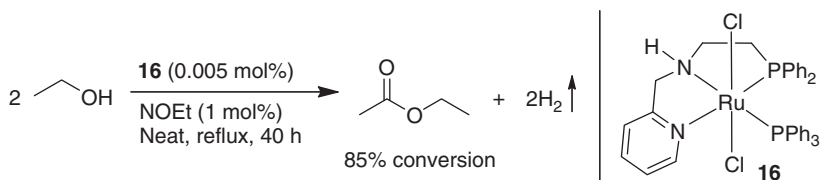
Though in moderate yield, the reported conversion of ethanol to ethyl acetate by complex **14** and a related osmium dimer complex [37] by Gusev generated interest in the catalytic synthesis of ethyl acetate from ethanol because it is a widely used fine chemical. Very recently, Beller *et al.* [38] screened the catalytic activity of various known pincer complexes for this transformation and found that Takasago's complex **15**, known as *Ru-MACHO catalyst*, is very efficient and the reaction in the presence of a base resulted in very good TON (Table 1.4).

Simultaneously, Spasyuk and Gusev [39] also reported a similar finding; among the various screened pincer complexes, complex **16** showed impressive reactivity with 85% conversion of ethanol (Scheme 1.8).

In addition to these transformations by well-defined pincer complexes, the complexes assembled *in situ* from the metal precursor $[\text{Ru}(\text{COD})(\text{methylallyl})_2]$ (COD, cyclooctadiene) and PNP or PNN pincer ligands (used for complexes

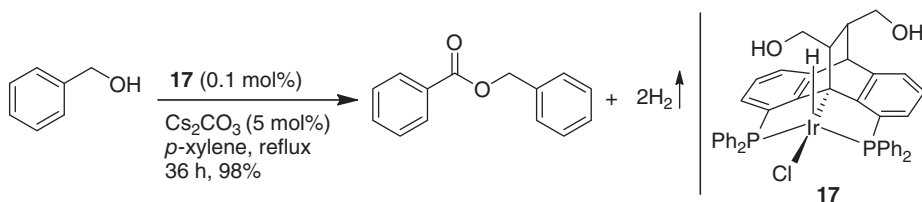
Table 1.4 Synthesis of ethyl acetate from ethanol by Ru-MACHO catalyst.

| $2 \text{ CH}_3\text{CH}_2\text{OH} \xrightarrow[\text{reflux}]{\begin{array}{l} \mathbf{15} \text{ (0.05–0.005 mol\%)} \\ \text{NOEt (0.6–1.3 mol\%)} \end{array}} \text{CH}_3\text{COOCH}_2\text{CH}_3 + 2\text{H}_2 \uparrow$ | | | | | | |
|--|-----------|--------------|----------|--------|-----------|--------|
|  | | | | | | |
| Entry | 15 (mol%) | NaOEt (mol%) | Time (h) | T (°C) | Yield (%) | TON |
| 1 | 0.05 | 1.3 | 6 | 90 | 81 | 1 620 |
| 2 | 0.05 | 1.3 | 24 | 70 | 70 | 1 400 |
| 3 | 0.005 | 0.6 | 46 | 90 | 77 | 15 400 |

**Scheme 1.8** Synthesis of ethyl acetate from ethanol by the PNN ruthenium pincer complex **16**.

4 and **7**, respectively) also catalyzed the dehydrogenative coupling of alcohol into esters successfully [40]. The catalytically active complex (which could be complex **8**, the CO ligand generated from intermediate aldehyde) displayed similar reactivity as that of complex **8**. PNP and PNN ruthenium(II) hydrido borohydride complexes [(PNX)RuH(BH₄), X = P, N] [41] and PNS ruthenium complexes [(PNS^{tBu})RuHCl(CO)] [42], analogs to complex **7**, also show catalytic reactivity for the esterification of alcohols.

In 2011, Gelman and coworkers [43] reported a PC_{Sp}³P iridium pincer complex (**17**), which exhibited efficient catalytic activity for the conversion of benzyl alcohol to benzyl benzoate (Scheme 1.9) and was suggested to operate via a novel metal–ligand cooperation mode. Both electron-withdrawing and electron-donating substituents

**Scheme 1.9** Acceptor-less dehydrogenative coupling of benzyl alcohols to form esters and dihydrogen catalyzed by the Ir(III) PC_{Sp}³P complex **17**.

on the aromatic ring are tolerated, and the corresponding esters were obtained in good yields (88–97%).

1.3.2

Synthesis of Cross-Esters from Primary and Secondary Alcohols

When a toluene solution of complex **11** (1 mol%) was refluxed with equimolar amounts of 1-hexanol and cyclohexanol, cyclohexyl hexanoate was obtained in 79% yield, together with 16% hexyl hexanoate, resulting from self-coupling of 1-hexanol, and 12% of cyclohexanone by dehydrogenation of cyclohexanol [13]. Despite the use of equimolar amounts of primary and secondary alcohols, the formation of the ester cyclohexyl hexanoate as the major product from dehydrogenative cross-esterification is noteworthy. The yield of the cross-esterification products significantly improved when an excess of secondary alcohols was used in the reaction. Thus, in a similar reaction, refluxing a toluene solution containing cyclohexanol and 1-hexanol in a molar ratio of 2.5/1 with complex **11** (1 mol%), cyclohexyl hexanoate was obtained in 93% yield (based on 1-hexanol). Cyclohexanone (34%) was also formed, and the products were isolated by column chromatography. The synthetic potential and substrate scope of this selective dehydrogenative cross-esterification process were demonstrated [13] with various cyclic and acyclic secondary alcohols and other primary alcohols, and the results are summarized in Table 1.5.

1.3.3

Synthesis of Esters by Acylation of Secondary Alcohols Using Esters

The transesterification reaction is a useful transformation that converts esters to other esters upon reaction with alcohols, as a result of exchange of alkoxy groups, avoiding the use of air- and moisture-sensitive reagents, such as acid chlorides. Further, ester-to-ester transformation is particularly useful when the carboxylic acid and their activated derivatives are not readily available [44]. In general, transesterification of secondary alcohols is slower than that of primary alcohols. The reaction is not atom-economical, as it produces, in addition to the desired ester, an equivalent of alcohol. Circumventing this undesired path, we have devised a novel method for transesterification in which dihydrogen is formed as the only byproduct, rather than alcohols, upon reaction of symmetrical esters with secondary alcohols.

Thus, refluxing a benzene solution of complex **8** (1 mol%), ethyl acetate (5 mmol) and cyclohexanol (15 mmol) under an argon atmosphere for 28 h resulted in complete consumption of ethyl acetate [12]. Cyclohexyl acetate was the only product formed (95%, Table 1.6) as observed by GC analysis and further confirmed by characterization of the isolated product. Similarly, refluxing a toluene solution containing 1 equivalent of an ester, such as hexyl hexanoate, pentyl pentanoate, and butyl butyrate, and 3 equivalent of various secondary alcohols in the presence of 1 mol% of complex **8** resulted in cross-esters in very good yields (Table 1.6). Somewhat lower yields of products were obtained when only 2 equivalent of secondary alcohols was used.

Table 1.5 Dehydrogenative cross-coupling of primary and secondary alcohols catalyzed by **11**.^a

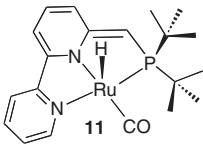
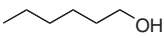
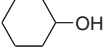
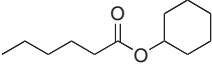
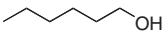

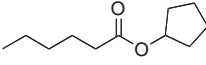
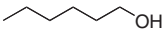
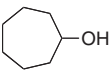
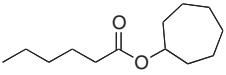
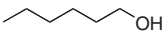

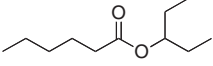
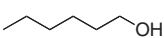
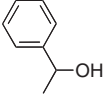
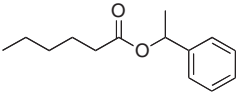

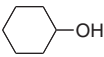
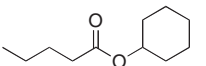


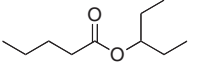

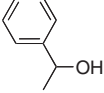
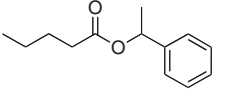
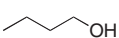
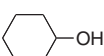
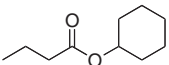
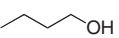

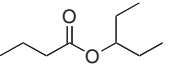
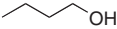
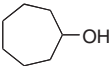
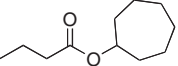
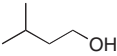
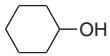
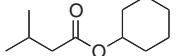
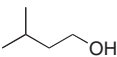

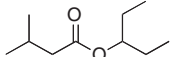
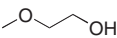
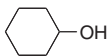
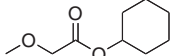
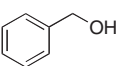
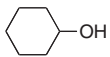
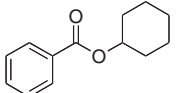
| $R^1-CH_2OH + R^2-CH(OH)-R^3 \xrightarrow[\text{Toluene, reflux}]{\mathbf{11} \text{ (1 mol\%)}} R^1-CH_2-C(=O)-O-CH(R^2)-R^3 + 2H_2 \uparrow$ <div style="display: inline-block; vertical-align: middle; text-align: center;">  <p>11</p> </div> | | | | | |
|--|---|---|---|----------|-----------|
| Entry | 1° alcohol | 2° alcohol | Cross ester | Time (h) | Yield (%) |
| 1 |  |  |  | 24 | 93 |
| 2 |  |  |  | 26 | 63 |
| 3 |  |  |  | 26 | 90 |
| 4 |  |  |  | 26 | 93 |
| 5 |  |  |  | 26 | 58 |
| 6 |  |  |  | 25 | 95 |
| 7 |  |  |  | 24 | 96 |
| 8 |  |  |  | 38 | 46 |
| 9 |  |  |  | 25 | 95 |
| 10 |  |  |  | 26 | 93 |

Table 1.5 (Continued)

| Entry | 1° alcohol | 2° alcohol | Cross ester | Time (h) | Yield (%) |
|-------|---|---|---|----------|-----------|
| 11 |  |  |  | 26 | 70 |
| 12 |  |  |  | 25 | 99 |
| 13 |  |  |  | 25 | 95 |
| 14 |  |  |  | 24 | 98 |
| 15 |  |  |  | 24 | 91 |

^aComplex 11 (0.03 mmol), primary alcohol (3 mmol), secondary alcohol (7.5 mmol), and toluene (2 ml) were refluxed under argon. Yields of products were determined by GC using *m*-xylene as an internal standard.

When the unsymmetrical ester ethyl butyrate was reacted with 3-pentanol in the presence of **8** (1 mol%) under refluxing toluene, 75% conversion of ethyl butyrate took place to yield 73% of 3-pentyl butyrate (entry 14, Table 1.6). 3-Pentyl acetate, which was expected to be formed from the ethanol intermediate, was observed only in trace amounts, perhaps as a result of the loss of ethanol under reflux conditions. Likewise, the reaction of methyl hexanoate with cyclohexanol results in 42% conversion with the formation of 42% cyclohexyl hexanoate (entry 15).

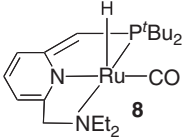

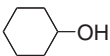
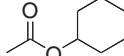
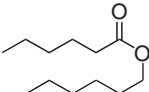
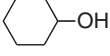
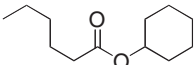
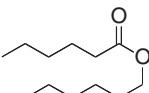

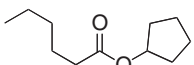
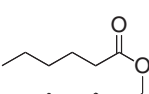
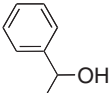
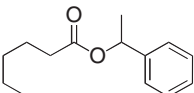
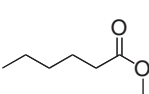

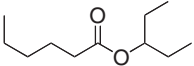
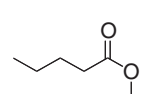
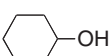
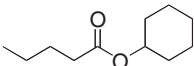
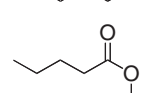

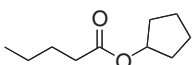
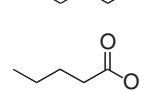
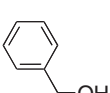
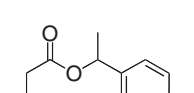
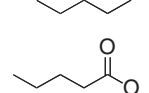


Dehydrogenation of the secondary alcohol to the corresponding ketone is a slower reaction than the dehydrogenative coupling of the primary alcohol to ester, and thus most of the secondary alcohol reacts with the ester, although some ketone formation is observed as excess of alcohol is used. When symmetrical esters are used, both acyl and alkoxy parts of the substrate ester are incorporated into the product ester with liberation of hydrogen, providing an atom-economical and environmentally benign method for the transesterification reactions [12].

1.3.4

Synthesis of Polyesters from Diols

Polyesters are generally synthesized by a step-growth polycondensation reaction or through chain-growth ring-opening polymerization. However, achieving high molecular weights by the known methods for the synthesis of polyesters is

Table 1.6 Acylation of secondary alcohols catalyzed by the complex **8**.^a

| $2 \text{ R}^2\text{-CH(OH)-R}^1 + \text{R-CO-O-R} \xrightarrow[\text{Toluene, reflux}]{\textbf{8 (1 mol\%)}} 2 \text{ R}^2\text{-CH(R}^1\text{)-CO-O-R} + 2\text{H}_2 \uparrow$ <div style="display: inline-block; vertical-align: middle; text-align: center;">  <p>8</p> </div> | | | | | | |
|---|---|---|---|------|------------|-----------|
| Entry | Ester | Alcohol | Cross-esters | Time | Conversion | Yield (%) |
| 1 ^b |  |  |  | 28 | 100 | 95 |
| 2 |  |  |  | 26 | 96 | 95 |
| 3 |  |  |  | 26 | 71 | 70 |
| 4 |  |  |  | 36 | 50 | 49 |
| 5 |  |  |  | 26 | 91 | 90 |
| 6 |  |  |  | 36 | 93 | 93 |
| 7 |  |  |  | 36 | 87 | 85 |
| 8 |  |  |  | 18 | 51 | 49 |
| 9 |  |  |  | 26 | 91 | 90 |