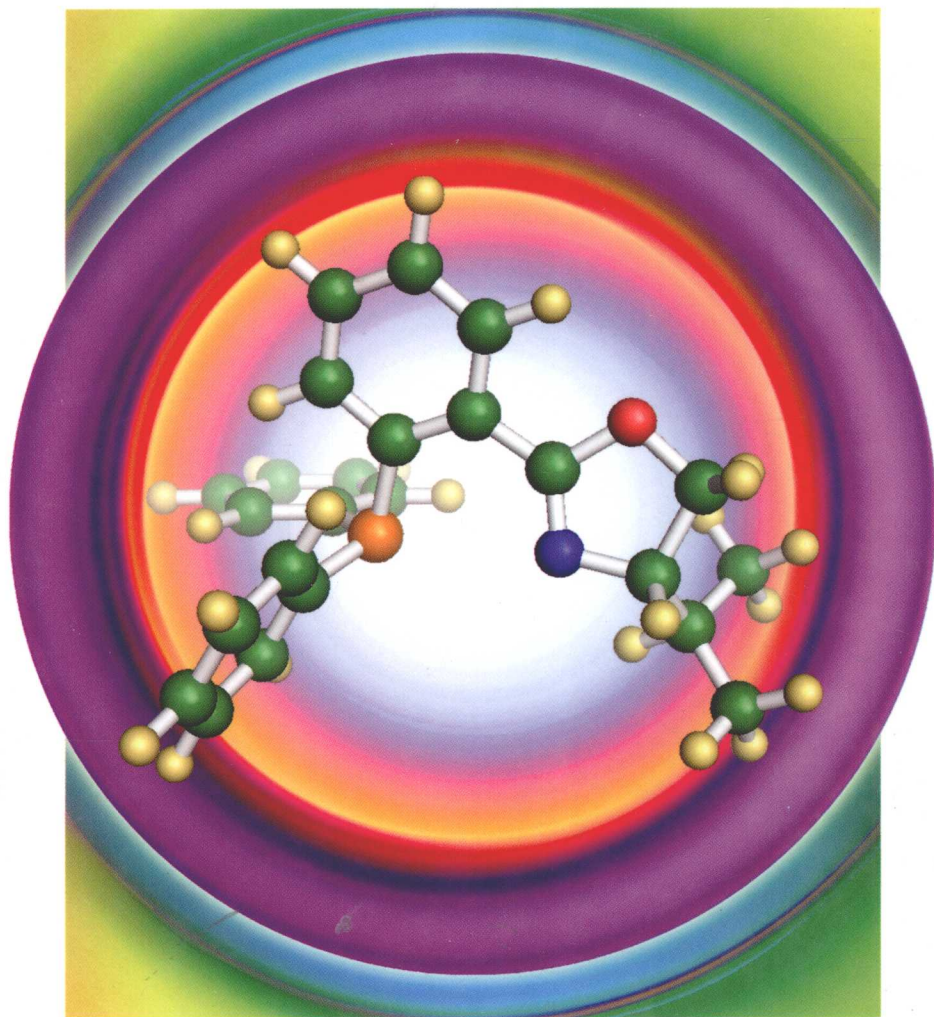


RSC Green Chemistry Series

Edited by Radovan Šebesta

Enantioselective Homogeneous Supported Catalysis



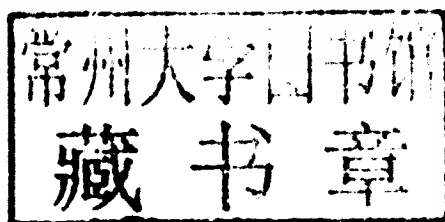
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Enantioselective Homogeneous Supported Catalysis

Edited by

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Preface

Asymmetric catalysis is arguably the most promising way to synthesize chiral compounds. The notion to use the stereoinducing component of a reaction, *i.e.* a chiral catalyst, in sub-stoichiometric amounts is important, because it is the catalyst which is usually the most expensive, in terms of time, labour or money. The research community therefore devotes considerable effort towards catalyst immobilization and recycling. Immobilization of a chiral catalyst is typically realized by means of grafting the catalyst onto a support. Catalysts can be supported either on solids or in liquid phase. The term 'heterogeneous catalysis', thus quite clearly describes all catalysts supported on solids. A broad range of solid supports have been described, especially inorganic materials, such as SiO_2 , Al_2O_3 , ZrO_2 , zeolites, clays or charcoal. Another important group of solid supports are organic polymers. Catalysts have been immobilized on these supporting materials through a number of chemical or physical interactions. Out of this flourishing field of research, a relatively new concept of liquid support for catalysts came out. Catalytic systems which act in liquid phase but can be easily recovered because of specifically tailored structure form the main part of this book. The title of this book: '**Enantioselective homogeneous supported catalysis**' thus represents recoverable catalysts operating in liquid phase. This book aims at reviewing the main concepts of this area. The emphasis is on catalysts modified with ionic, polymer and fluororous tags. New ideas in catalysis in ionic liquids and water are also discussed. The distinction between heterogeneous and supported homogeneous catalysis is not always clear, so the book also deals with dendrimeric catalysts and catalysts immobilized through weak forces on solid supports. They were included because their properties and activities often resemble catalysts in homogeneous phase.

The book is composed of eight chapters, each devoted to particular concept of enantioselective homogeneous supported catalysis. The first chapter deals with catalysts with ionic tags, especially in connection with original idea of this

concept, ionic liquids. The original idea of ionic tagging was connected with transition metal catalysts, but rapidly gained popularity also in metal-free catalysts. Therefore Chapter 2 is devoted to organocatalysts immobilized in homogeneous phases. Štefan Toma (Comenius University in Bratislava) describes not only ionically-tagged organocatalysts, but presents also some newer ideas in supported organocatalysts. Within last the few years a great number of supported organocatalysts have been developed, therefore some other chapter of the book also present additional metal-free catalytic systems.

Chapter 3, by P. Goodrich, C. Paun and C. Hardacre at Queen's University in Belfast deals with catalysis by unmodified catalyst in ionic liquids. The focus of the chapter, however, is on newer and more elaborate concepts of ionic liquid supported phases, as simple catalysis in ionic liquids have been amply described by several reviews and book chapters.

Chapter 4, written by Marco Bandini at the University of Bologna focuses on metal-based catalysts immobilized on soluble polymers.

In Chapter 5, Robertus J. M. Klein Gebbink and Morgane A. N. Virboul from Utrecht University write about catalytic dendrimers.

Chapter 6, written by Gianluca Pozzi (The National Research Council in Milan), deals with fluororous catalyst.

In Chapter 7, Szymon Buda, Monika Pasternak and Jacek Mlynarski (Jagiellonian University in Krakow) give an overview of asymmetric catalysis in aqueous media.

Chapter 8, written by J. M. Fraile, J. I. García, C. I. Herreras, J. A. Mayoral, and E. Pires (University of Zaragoza), has as its focus non-covalent immobilization.

Not all aspects of asymmetric catalysis with homogeneously supported catalysts could have been covered in this book. Because of space constraints, some new and interesting ideas have not been included, such as self-supported catalysts. An interested reader can find more details in a review by Ding and co-workers.¹ Topics presented in this book have been discussed in other more general volumes before.^{2,3} However, the field of asymmetric catalysis is developing fast with a number of new discoveries and ideas appearing rapidly. Therefore I believe that this focused collection of comprehensive reviews will be of interest to many researchers and advanced students in the field of asymmetric catalysis.

Radovan Šebesta
Bratislava

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CHAPTER 1

Ionic-tagged Transition Metal Catalysts

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1.1 Introduction

Ionic liquids are liquids consisting solely of ions. Those with melting points below 100 °C are often called room temperature ionic liquids but within this chapter simply the term ‘ionic liquids’ will be used. Their interesting physical/chemical properties stimulated the investigation of a great number of research and even technical applications. Their use in synthesis has been summarized in an excellent two-volume book edited by Wasserscheid and Welton.¹

The concept of ionically-tagged transition metal catalysts develops on the interface of homogeneous and heterogeneous catalysis. It aims to combine positive features of both worlds. The primary function of ionic tags is to enable catalyst recycling. On the other hand, appropriate reaction media offer the possibility of maintaining catalysis in the liquid phase and so benefit from high catalytic activities of homogeneous catalysts. Furthermore, the effect of ionic tags often goes beyond a simple anchor for immobilization and recycling of catalyst. Many reactions are enhanced as a result of an ionic tag installed into the catalyst structure compared to the unmodified catalyst. This effect led Lombardo and Trombini to postulate a concept of electrosteric activation.²

This means the stabilization of a transition state of a catalytic reaction by electrostatic and steric interaction with ionic tags.

Suitable reaction media for ionically-tagged catalysts can be ionic liquids, supercritical liquids, water or combinations of these. Use of biphasic set-ups is also attractive. This chapter gives an overview of enantioselective catalysis with transition metal based catalysts having an ionic moiety. Ionic catalysts used in water are, however, excluded as they are extensively covered in Chapter 7.

In this chapter, 1-butyl-3-methylimidazolium and 1-ethyl-3-methylimidazolium cations are denoted as [bmim] and [emim]; 1-butyl-2,3-dimethylimidazolium and 1-hexyl-2,3-dimethylimidazolium as [bdmim] and [hdmim]; 1-butylpyridinium cation is denoted as [bpyr]; *N*-ethyl-3-methylpiccolinium cation is denoted as [epic]. The bis(trifluoromethyl sulfonyl)imide anion is denoted as NTf₂, and triflate and tosylate as OTf and OTs.

1.2 Achiral Ionically-tagged Transition Metal Complexes

Highly polar ligands are well known in the coordination chemistry of transition metals. Such complexes were, at first, only used in water. Several reviews and books give a good overview of synthesis and applications of these hydrophilic ligands.³⁻⁶ However, it was only in 1996 when Chauvin and co-workers suggested that ligands bearing ionic moieties can be used for immobilization of metal complexes in ionic liquids.⁷ They noticed that rhodium-catalyzed hydrogenation of pent-1-ene was five times faster in [bmim]PF₆ than in acetone. Cationic rhodium complexes were well retained in ionic liquids, which could be reused. However, in rhodium-catalyzed hydroformylation, catalyst leaching was observed. After extraction of organic products, the ionic liquid was reused but part of the rhodium complex was extracted to the organic phase too. Use of mono- and trisulfonated triphenylphosphines as ligands to rhodium completely prevented catalyst leaching to the organic phase.

The concept was then further developed in a number of ways. Various cationic phosphine ligands were tested in rhodium-catalyzed hydrogenations and hydroformylations in ionic liquids or biphasic conditions. Several, structurally different, cations were successfully applied (Figure 1.1). Wasserscheid and Olivier-Bourbigou showed that guanidinium ion is particularly suitable for immobilization of rhodium complexes.^{8,9} van Leeuwen and co-workers attached two imidazolium moieties to Xantphos skeleton.^{10,11} In this way they created ligand **3**, which showed excellent recycling results and very little leaching.

Ruthenium-arene catalysts were modified by appending imidazolium moiety as well (Scheme 1.1).¹² Imidazolium ionic tags are designed by their similarity with the most common type of ionic liquids. Therefore, it is also the most frequent type of ionic tag. However, it has also a disadvantage, because the proton in position 2 is acidic; therefore, an imidazolium ion with an alkyl group substituted position 2 is often used.

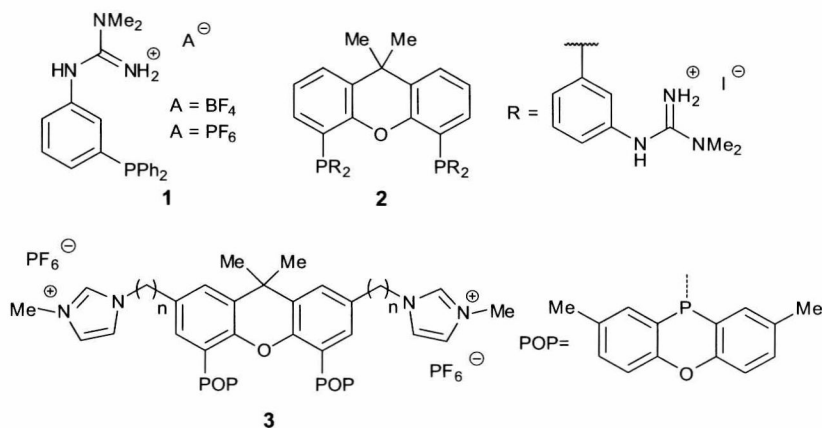
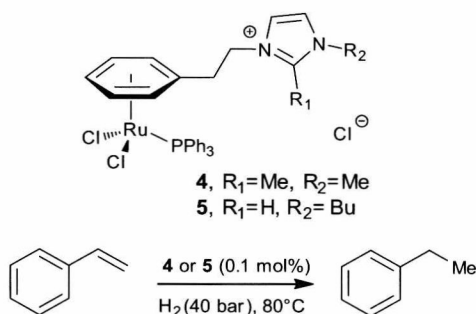


Figure 1.1 Achiral phosphine ligands with ionic tags for hydrogenations and hydroformylations.



Scheme 1.1

Palladium-catalyzed Suzuki and Stille couplings¹³ as well as Heck reaction¹⁴ were successfully performed with various ionically-tagged catalysts (Figure 1.2). These catalysts have good catalytic activities and at the same time significantly reduced metal leaching from ionic liquid.

The usefulness of the ionic-tagging strategy for catalyst immobilization was also amply demonstrated in ruthenium-catalyzed olefin metathesis.^{15–20} Both Grubbs catalyst of the first and second generation (8–13) have been modified with ionic tags. Usually imidazolium ions have been selected. Figure 1.3 shows various ways in which ionic tags can be introduced into metathesis catalysts.

Achiral Mn-Schiff base **14** was used as an epoxidation catalyst,²¹ or porphyrin **15** derivatized with four pyridinium moieties was used for the oxidation of styrene (Figure 1.4).²²

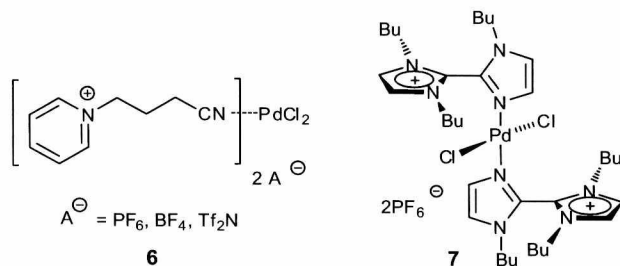


Figure 1.2 Ionically modified ligands for palladium-catalyzed cross-couplings.

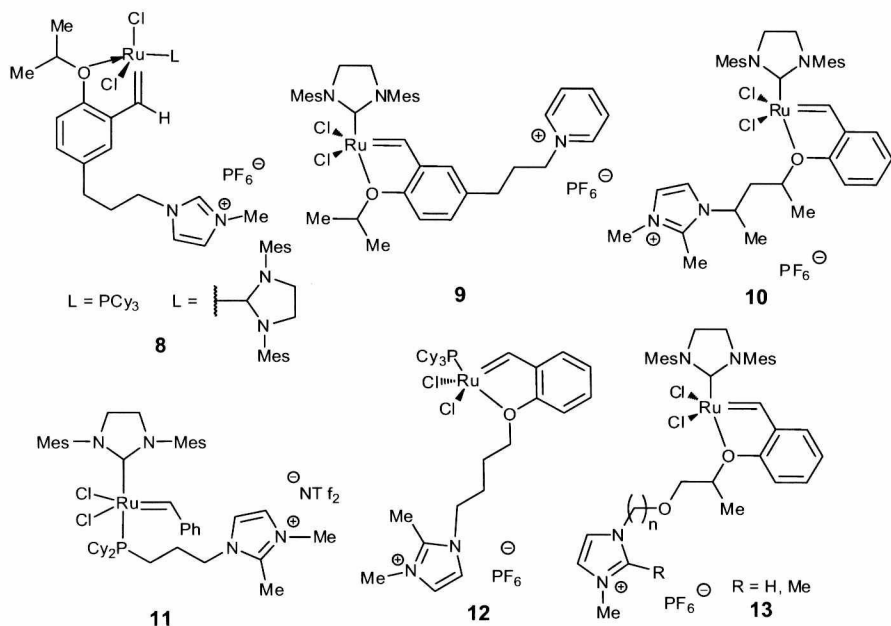


Figure 1.3 Ru complexes with ionic tags for olefin metathesis.

1.3 Chiral Transition Metal Catalysts with Ionic Tag

Chiral transition metal catalysts can be immobilized through ionic forces in ionic liquids. This is enabled by charge carried by a metal ion. Numerous examples of this approach have been described.^{23–27} Such systems, however, often suffer from considerable metal leaching during work-up operations. The introduction of an auxiliary ionic moiety into the ligand has been suggested as a possible solution to this problem. The installation of an ionic tag into the ligand structure, indeed, helps prevent metal leaching. Catalytic activities are usually comparable or better than that of unmodified catalysts.

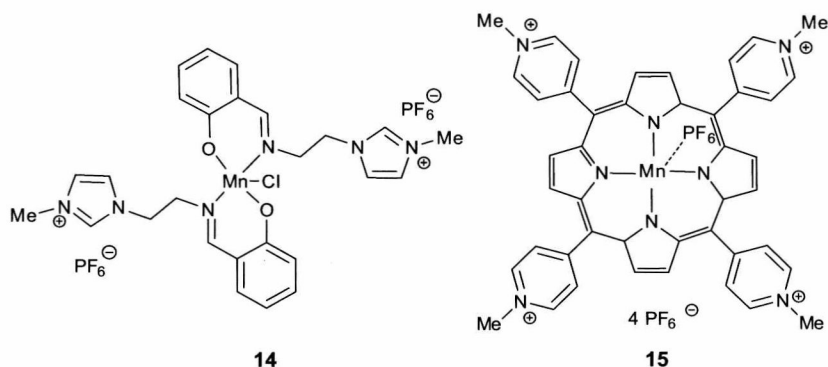


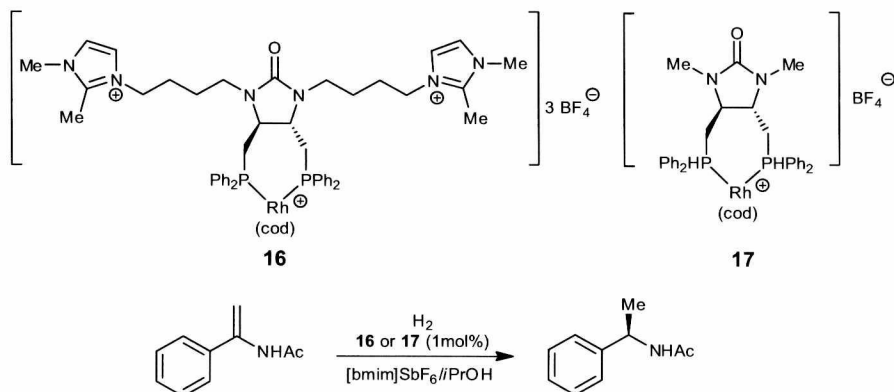
Figure 1.4 Achiral Mn-based oxidation catalysts.

1.3.1 Catalysts for Enantioselective Reduction

Enantioselective hydrogenations are one of the most widely employed asymmetric transformations. Expensive rhodium, ruthenium and iridium complexes are the most active hydrogenation catalysts. This motivated great effort for the synthesis of immobilized catalysts. Also, the concept of ionically-tagged catalysts has been developed and tested on hydrogenation reactions. Several researchers therefore tried to immobilize rhodium and ruthenium complexes with the help of ionic tags. An important factor is also good solubility of hydrogen ionic liquids. However, prototypical hydrogenation catalysts, Rh-BINAP complexes, are too air-sensitive and therefore have not been used in ionic liquids. Rhodium complexes with DIOP⁷ or DUPHOS²⁸ have been successfully used in ionic liquids for hydrogenation of functionalized olefins.

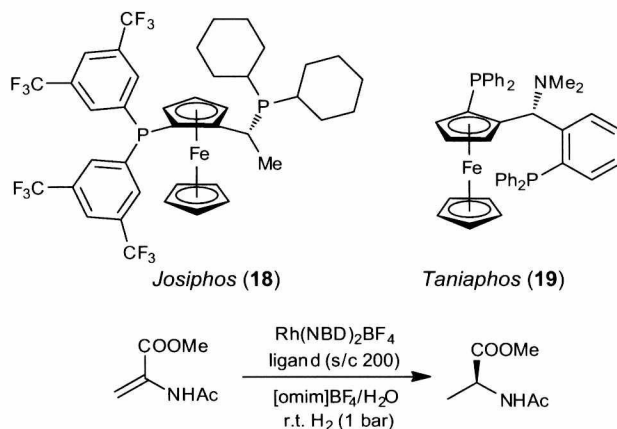
The first rhodium catalyst with an ionic tag was prepared by Lee and co-workers. They attached two imidazolium moieties onto a rhodium-disphosphine complex.²⁹ The resulting catalyst **16** showed excellent catalytic activities in asymmetric hydrogenation of enamides. In the two-phase system [bmim]SbF₆/*i*-PrOH, enamide was hydrogenated with 97% ee with full conversion within 1 hour. The catalyst **16** was recycled four times with very little loss of catalytic activity (95% ee, 85% conversion in 1 h). In comparison, hydrogenation with unmodified complex **17** resulted in a similarly enantioselective reaction in the first run, but in subsequent runs enantioselectivity and conversion decreased considerably (4th run, 88% ee, 85% conversion in 12 h). After the first run the *i*-PrOH layer was investigated by inductively coupled plasma atomic emission spectroscopy (ICP-AES). In experiment with complex **16** no rhodium (<1 ppm) or phosphorus (<3 ppm) leaching from the ionic liquid was detected, whereas with complex **17** it was found that 2% rhodium and 6% phosphorus was leached from the ionic liquid. A control experiment with low catalyst loading (0.5 mol% of complex **17**) showed that rhodium leaching is not the sole reason for decreased catalytic performance of the catalyst. Improved stability of the catalyst **16** in

ionic liquid was suggested as a possible explanation of its superior catalytic activity (Scheme 1.2).



Scheme 1.2

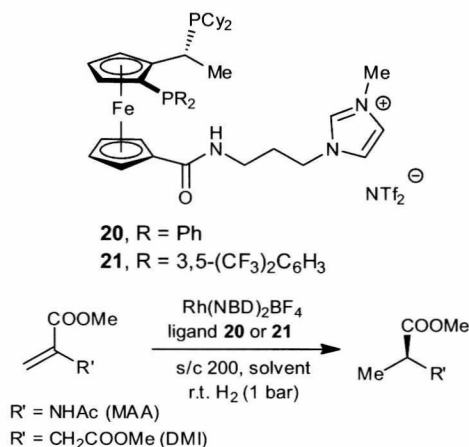
Ferrocenyl diphosphine ligands serve in a number of excellent hydrogenation systems, including industrial applications.^{30,31} Solvias and Novartis researchers tested ferrocenyl diphosphines, such as Taniaphos, Josiphos, Walphos or Mandyphos, in rhodium-catalyzed hydrogenation in ionic liquids as well as mixtures of ionic liquid with organic solvents or water.³² The most promising results were obtained in mixtures of ionic liquids with water – wet ionic liquid. For instance, in a mixture of [omim]BF₄/H₂O ligands Taniaphos and Josiphos afforded enantioselectivities of 99% ee (Scheme 1.3). Josiphos was reused six times with constant ee and only in the seventh run did the reaction time have to



Scheme 1.3

be prolonged from 20 to 40 min to reach full conversion. Enantioselectivity, however, remained unchanged (99% ee). Inductively coupled plasma mass spectrometry (ICP-MS) found only 0.9 ppm Rh in the water phase, so the decrease in activity was attributed to catalyst decomposition, rather than to leaching of the catalyst.

Inspired by these promising results, they also synthesized modified Josiphos ligands with imidazolium tag **20** and **21**.³³ These diphosphanes were successfully employed in rhodium-catalyzed asymmetric hydrogenation of methyl acetamidoacrylate (MAA) and dimethyl itaconate (DMI) (Scheme 1.4).

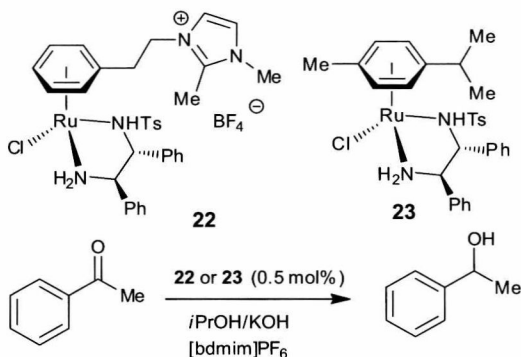


Scheme 1.4

Modified ligands **20** and **21** paralleled catalytic behaviour of unmodified ligands in the asymmetric hydrogenation in classical organic solvents as well as under biphasic conditions. Hydrogenation of MAA using ligand **21** proceeded with 99% ee, and for reduction of DMI ligand **20** was superior (99% ee). Imidazolium tagged ligands showed much better reusability in *t*-BuOMe/[bmim]BF₄ biphasic system compared with unmodified Josiphos ligands (approx. 15% decrease of TOF for the 8th cycle, with constant enantiomeric purity of the product).

Ruthenium-catalyzed transfer hydrogenation of ketones is an important alternative to classical hydrogenation methods.³⁴ Several attempts were made to prepare reusable ruthenium catalysts with ionic tags. Geldbach and Dyson succeeded in the introduction of the imidazolium moiety onto η⁶-arene of the Ru complex.³⁵ Catalyst **22** was slightly less active than unmodified catalyst **23** in the absence of ionic liquid. More importantly, enantioselectivity was significantly lower (58% ee) compared to *p*-cymene ligand **23** (98% ee). On the other hand, with catalyst **22**, dissolved in 1-butyl-2,3-dimethylimidazolium hexafluorophosphate [bdmim]PF₆, hydrogenation of acetophenone in a biphasic system (ionic liquid and propan-2-ol/KOH) proceeded well (Scheme 1.5).

Using ionic catalyst **22**, enantioselectivity was as high as with traditional *p*-cymene ligand **23** (98% ee). Recycling of the catalytic system led to decreased conversion (52% in the 4th run compared with 99% in the 1st run) of the reaction, but enantioselectivity remained the same. Decrease in catalytic activity was explained by partial leaching of the catalyst from ionic liquid due to decomposition of the ruthenium complex. As an alternative hydride donor to propan-2-ol/KOH, formic acid/triethylamine azeotrop was also used. Enantioselectivities were even higher (99% ee) but again a decrease in conversion between recycling experiments was observed.



Scheme 1.5

A different approach to functionalization of Ru-TsDPEN catalyst **25** was chosen by Ohta and co-workers.³⁶ They introduced the imidazolium moiety into the diamine part of the ruthenium complex. Using the catalyst **24**, transfer hydrogenation of acetophenone with formic acid/triethylamine in [bmim]PF₆ proceeded with high enantioselectivity (92% ee) and high conversion (98%). Unmodified Ru-TsDPEN catalyst **25** gave similar results (93% ee, 96% conversion) but after the 4th cycle conversion decreased gradually (4th cycle, 88%; 5th cycle, 63%). In comparison, catalyst **24** showed slightly better results (4th cycle, 92%; 5th cycle, 75%) (Figure 1.5).

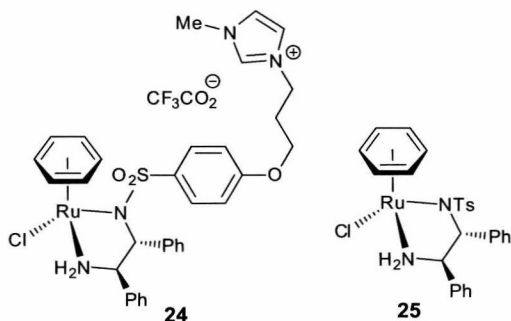


Figure 1.5 Ru-TsDPEN catalysts for transfer hydrogenation.