Ruthenium-Based Olefin Metathesis Catalysts Bearing pH-Responsive Ligands: External Control of Catalyst Solubility and Activity

Shawna Lynn Balof
University of Southern Mississippi

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RUTHENIUM-BASED OLEFIN METATHESIS CATALYSTS
BEARING PH-RESPONSIVE LIGANDS:
EXTERNAL CONTROL OF CATALYST SOLUBILITY AND ACTIVITY

by

Shawna Lynn Balof

Abstract of a Dissertation
Submitted to the Graduate School
of The University of Southern Mississippi
in Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy

May 2011
ABSTRACT
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by Shawna Lynn Balof

May 2011

Sixteen novel, Ru-based olefin metathesis catalysts bearing pH responsive ligands were synthesized. The pH-responsive groups employed with these catalysts included dimethylamino (NMe₂) modified NHC ligands as well as N-donor dimethylaminopyridine (DMAP) and 3-(o-pyridyl)propylidene ligands. These pH-responsive ligands provided the means by which the solubility and/or activity profiles of the catalysts produced could be controlled via acid addition. The main goal of this dissertation was to design catalyst systems capable of performing ring opening metathesis (ROMP) and ring closing metathesis (RCM) reactions in both organic and aqueous media.

In an effort to quickly gain access to new catalyst structures, a template synthesis for functionalized NHC ligand precursors was designed, in addition to other strategies, to obtain ligand precursors with ancillary NMe₂ groups. Kinetic studies for the catalysts produced from these precursors showed external control of catalyst solubility was afforded via protonation of the NMe₂ groups of their NHC ligands. Additionally, this protonation afforded external control of catalyst propagation rates for several catalysts. This is the first known independent external control for the propagation rates of ROMP catalysts. The incorporation of pH-responsive N-donor ligands into catalyst structures also provided the means for the external control of metathesis activity, as the protonation of these ligands resulted in an increased initiation rate based on their fast and offset.
irreversible dissociation from the metal center. The enhanced external control makes these catalysts applicable to a wide range of applications, some of which have been explored by us and/or through collaboration.

Three of the catalysts designed showed remarkable metathesis activity in aqueous media. These catalysts displayed comparable RCM activity in aqueous media to a class of water-soluble catalysts reported by Grubbs et al., considered to be the most active catalyst for aqueous olefin metathesis reactions. In ROMP reactions these particular catalysts dramatically outperformed the literature catalysts, accomplishing ROMP full conversion rates within 15 minutes compared to several hours observed with the literature catalyst. These catalysts were also able to accomplish these reactions at lower catalyst loadings than ever reported with the literature catalyst, making them the most active aqueous olefin metathesis catalysts to date.
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CHAPTER I

INTRODUCTION, BACKGROUND, AND LITERATURE REVIEW FOR OLEFIN METATHESIS AND OLEFIN METATHESIS CATALYSTS

Introduction

Over the past five decades olefin metathesis has evolved into a powerful tool in the fields of organic and polymer chemistry. The 2005 Nobel Prize in Chemistry awarded to Yves Chauvin, Richard Schrock, and Robert Grubbs for their contributions to the field clearly demonstrates the importance of olefin metathesis and acknowledges the impact of this technology on the sciences and society. Advantages of olefin metathesis for chemical synthesis include good product yields (often near quantitative) under mild reaction conditions, fewer synthetic steps to obtain the desired product, fewer side reactions when compared to many traditional methods of organic synthesis, and less generation of hazardous waste. Since the mid 1990s, much of the research has been focused on Ru-based, single-site olefin metathesis catalysts due to their high activity and tolerance toward air, moisture, and many functional groups in comparison to catalytic systems based on other transition metals.

Ru-based olefin metathesis catalyst designs have been investigated intensely over the last decade, and much progress has been made to optimize the activity and thermal stability of these complexes. The most prominent catalyst designs still feature several limitations including narrow-range solubility profiles, costly removal after use, and a lack of external activity controls. Currently no economically feasible solution exists for effective catalyst removal, and few external activity controls have been identified which can improve the applicability of these catalysts on a large, industrial scale. Also,
only a few catalyst designs are available for homogenous aqueous applications, and those which were successfully developed are limited by their cumbersome syntheses.

The focus of this dissertation is the development of new Ru-based olefin metathesis catalysts bearing pH-responsive ligands. These ligands provide the means to externally control the solubility profile and activity of the catalyst. This allows for improved catalytic performance with respect to ring opening metathesis polymerization (ROMP) and ring closing metathesis (RCM) reactions. These ligands also provide the means to enhance the applicability of these catalysts in certain applications.

Background and Literature Review

Early Developments of Transition Metal-Mediated Polymerization and Olefin Metathesis

Karl Ziegler, a German scientist, is credited with discovering the first metal-catalyzed olefin polymerization in 1953 when he made use of an ill-defined catalyst system generated from trialkyl aluminum and titanium chloride which produced relatively linear polyethylene. Similar catalysts were employed that same year by Giulio Natta for the production of mostly linear polymers from 1-alkenes, and the initial results led to the development of a wide variety of the so-called Ziegler-Natta catalysts. For their work they were both awarded the Nobel Prize in Chemistry in 1963.

Based on the initial research of Ziegler and Natta, the petrochemical industry investigated ill-defined transition metal catalysts for the production of polymers from olefins throughout the 1950s and 1960s. During these investigations some researchers obtained unexpected products that could not be explained by any known olefin polymerization reaction. One example was observed by DuPont chemist Herbert S. Eleuterio in 1956. While passing propylene feed over a molybdenum-on-aluminum catalyst in an attempt to synthesize a propylene polymer he instead obtained a
propylene-ethylene copolymer. Further analysis of the output gas showed that it was composed of a mixture of ethylene, propylene, and 2-butene. When he repeated this experiment with cyclopentene he obtained a linear, unsaturated polymer that appeared to be the opened ring joined end to end (Scheme 1) instead of a cyclopentane polymer composed of connected cyclic units.

**Scheme 1.** Results Obtained by Herbert S. Eleuterio in 1956\textsuperscript{10}

At first these reactions were not considered related to one another. It was not until four years later that it was recognized that these unexpected products were the result of a redistribution of C=C double bonds. In this redistribution one half of the C=C double bond of one olefin was exchanged for one half of the C=C double bond of a second olefin (Scheme 2). In 1967 Nissim Calderon, a chemist with Goodyear Tire Company, dubbed this reaction “olefin metathesis.”\textsuperscript{11}

**Scheme 2.** Olefin Metathesis

\[ R_1, R_2 = \text{aryl, alkyl} \]
**Mechanism of Olefin Metathesis**

Even after scientists recognized the products of olefin metathesis were formed through a redistribution of C=C bonds, the actual mechanism for the transition-metal mediated olefin metathesis reaction remained elusive. Over several years many different mechanisms were proposed. In 1971 Yves Chauvin and his student Jean-Louis Hérisson first introduced what is now the accepted mechanism of transition-metal mediated olefin metathesis (Scheme 3). This mechanism involves the [2+2]cycloaddition of a C=C double bond to a transition metal alkylidene species to form a metallacyclobutane intermediate. This metallacyclobutane intermediate then undergoes a retro [2+2]cycloaddition to give either the starting materials or a new alkene and alkylidene. The alkene’s interaction with the d$_{xz}$ or d$_{yz}$ orbitals on the metal catalyst lowers the activation energy, allowing for this reaction to proceed at moderate temperatures.

**Scheme 3. The Chauvin Mechanism**

When Chauvin’s mechanism for olefin metathesis was first published it was widely ignored. It remained that way until 1975 when Thomas Katz and his research group began publishing a series of papers that recognized and supported the Chauvin mechanism, the first entitled “Mechanism of the Olefin Metathesis Reaction.” In
these papers, Katz unambiguously showed that the metal-carbene was essential to the olefin metathesis mechanism and also provided further insight into the reasons this reaction produces such a variety of products from different starting materials. Later mechanistic work published by Robert Grubbs\textsuperscript{15} and Richard Schrock\textsuperscript{16} also supported the Chauvin mechanism. In his mechanistic studies, Grubbs used isotopically labeled olefins to track the exchange of groups. The products obtained could only be formed via the metal-carbene mechanism. Five years later, Schrock showed that metal-carbynes react with various acetylenes to give the expected alkyne metathesis products. The results of these studies resulted in an extension of, but also confirmed, the Chauvin mechanism, making it the accepted mechanism for olefin metathesis.

\textit{Types of Olefin Metathesis Reactions}

Olefin metathesis is a versatile reaction that breaks and reforms C=C double bonds, making many different types of alkene products accessible. Variations of olefin metathesis include cross metathesis (CM), ring closing metathesis (RCM), acyclic diene metathesis (ADMET), ring opening metathesis (ROM), and ring opening metathesis polymerization (ROMP) as the most prominent examples. The type of metathesis reaction that takes place is mainly determined by thermodynamics of the reaction. For example, in the case of highly strained cyclic olefins, ROM or ROMP is usually favored due to the release of energy upon the opening of the ring. Likewise RCM is often preferred by certain dienes when the product formed is a cyclic molecule with low ring strain (Scheme 4). These reactions are often reversible, so factors such as temperature or substrate concentration can be used to drive the equilibrium in favor of the desired product.\textsuperscript{17} Throughout this dissertation RCM and ROMP reactions were conducted to evaluate the activity for synthesized catalysts. The substrates for these reactions were selected to ensure that only one type of olefin metathesis reaction product was obtained.
**Scheme 4.** Thermodynamically-Driven Metathesis Reactions

RCM is an intramolecular olefin metathesis reaction of a diene that forms a cycloalkene with low ring strain. Most commonly used are α,ω-diolefins. In the first step of an RCM reaction, one C=C double bond of the diene coordinates a metal-methylidene (which is formed from any catalyst after the first reaction with an α,ω-diolefin), followed by a [2+2]cycloaddition of the alkene and metal carbene to form the metalla-cyclobutane intermediate as proposed in the Chauvin mechanism. This metalla-cyclobutane intermediate then breaks apart through a retro [2+2]cycloaddition reaction, resulting in a new metal-alkylidene complex and ethylene. The second C=C double bond of the original diene then coordinates to the metal and is followed by another [2+2]cycloaddition to form a second metalla-cyclobutane intermediate that then reverses the cycloaddition to reform the metal-methylidene complex and the desired cycloalkene product (Scheme 5). The formation of volatile ethylene drives this reaction to completion as the gas is released from the reaction mixture.\(^\text{18}\) RCM reactions are useful for the synthesis of cyclic alkenes, including macrocycles, or cyclic alkanes after hydrogenation, that are otherwise difficult to prepare by traditional synthetic methods. Hence, RCM is widely used by the pharmaceutical industry as a convenient synthetic step for the production of macrocyclic pharmaceutical products.\(^\text{1c,19}\)
ROMP is a polymerization reaction that opens strained cycloalkenes. The main thermodynamic driving force behind ROMP reactions is the relief of ring strain; therefore, this reaction is usually not reversible for most ROMP substrates. Under optimal conditions, meaning very slow catalyst decomposition resulting in a low degree of termination, this reaction can propagate almost indefinitely, making ROMP one of the few living polymerization techniques.$^{1a}$

ROMP propagates through coordination of the cyclic olefin to the metal-alkylidene with subsequent formation of the metallacyclobutane intermediate. This intermediate opens to yield a new linear metal-alkylidene, which relieves the ring strain of the original olefin. The new metal-alkylidene then continues to repeat the reaction with more substrate to produce a polymeric chain (Scheme 6). In the absence of termination reactions, propagation continues until all monomer substrate is consumed. Since the ROMP reaction is living under these conditions, the ROMP reaction will continue with the addition of more monomer. Termination often is induced externally, e.g., by chemical quenching with ethylvinyl ether.$^{20}$
ROMP is a useful synthetic tool for the production of specialized polymers, such as block copolymers.\textsuperscript{21} These polymers are synthesized by sequential addition of different monomers. For catalysts which exhibit fast initiation but only moderate propagation rates, the polymerization becomes a controlled living polymerization, meaning the molecular weights of the polymers produced can be controlled by the monomer to catalyst ratio. Since all polymer chains start growing almost simultaneously and at the same rate, the polymers produced with these catalysts also have narrow molecular weight distributions. As a consequence, linear polymers produced via controlled ROMP have well-defined material properties.

**Classes of Olefin Metathesis Catalysts**

Over the past several decades, a variety of olefin metathesis catalysts have been developed. Catalytic systems have evolved from ill-defined, heterogeneous catalysts to well-defined, single site catalysts. There have been four distinct classes of olefin metathesis catalysts: (1) “black box” catalysts, (2) Titanocene-based (Tebbe-type) catalysts, (3) Mo- and W-based (Schrock-type) catalysts, and (4) Ru-based (Grubbs-type) catalysts.

The first metathesis catalysts are often referred to as “black box” catalysts because very little was known about their structure and the mechanism by which they operated. These heterogeneous, ill-defined catalysts were derived from elements of the early transition metal series and were usually either grafted onto silica or combined with
a main group alkylation agent. They usually contain few active sites and therefore require high catalyst loadings. They are also often sensitive to air, moisture, and functional groups, which limits their applicability. Examples of “black box” catalysts still widely used today include $\text{WCl}_6/\text{SnMe}_4$ and $\text{WCl}_6/\text{Et}_2\text{AlCl}$, which are used to make a variety of plastics.

The first well-defined olefin metathesis catalysts were the Titanocene-based, Tebbe-type catalysts. These were named after DuPont chemist Fred Tebbe who, in 1978, reported the results of his investigation into the structure and reactivity of a well-defined complex synthesized from titanocene dichloride and trimethylaluminum in a toluene solution known today as the “Tebbe Complex” or “Tebbe’s Reagent” 1. Once activated with a mild Lewis base, such as pyridine, it forms an active carbene species 2 (Scheme 7). Since this catalyst was well-defined and slow to react, both the starting and propagating carbene species could be observed during a metathesis reaction, making it the first catalyst system used for mechanistic study of olefin metathesis. However, drawbacks of these catalysts were their low reactivity, sensitivity to air and moisture, and low functional group tolerance, which prevented their use in commercial applications.

Scheme 7. Activation of Tebbe’s Reagent

The catalyst activity was enormously improved with the development of the Schrock-type catalysts, which are tungsten-based and molybdenum-based carbene complexes originally developed by Richard Schrock in the mid-1980s. These catalysts even displayed a moderate functional group tolerance but still were sensitive to air and...
moisture. The most successful Schrock-type catalysts used today are the Mo-based catalysts, such as 3 (Figure 1).\textsuperscript{29} They preferentially coordinate olefins over several other functional groups such as ketones, esters, and amides.\textsuperscript{30} This makes these catalysts applicable to a wider variety of substrates than the Tebbe reagents.

![Figure 1. Mo-Based (Schrock-Type) Catalyst\textsuperscript{29}](image)

The most recent class of olefin metathesis catalysts based on Ru-carbene complexes. In the late 1980s, Robert Grubbs and Bruce Novak found that ruthenium chlorides and ruthenium tosylates could catalyze ROMP of 7-oxanobornene derivatives in water.\textsuperscript{31} In these studies, it was observed that ruthenium was significantly more tolerant toward air, moisture, and functional groups than previous generations of catalysts. In 1992 Grubbs synthesized the first Ru-based carbene complex 4 (Figure 2), which exhibited very low metathesis activity and could only perform ROMP of a few select, highly strained cyclic systems.\textsuperscript{5a} Since then, many modifications have been made to this original structure to produce a variety of functional, highly active catalysts that have revolutionized the field of olefin metathesis.
Varieties of Ru-Based Olefin Metathesis Catalysts

Over the past two decades, Ru-based olefin metathesis catalysts have been intensely studied. Most of these investigations have been centered on 16-electron, pentacoordinate Ru-alkylidene complexes, or Grubbs-type catalysts. Since the discovery of complex 4 many improvements have been made to the original catalyst design. The first of these improvements was replacing the PPh\textsubscript{3} in complex 4 with bulkier and more \(\sigma\)-donating tricyclohexylphosphine (PCy\textsubscript{3}) to give complex 5 (Figure 3) with much higher olefin metathesis activity.\textsuperscript{32} This success was followed by the synthesis of what would later be referred to as Grubbs’ first generation catalyst 9, the most active Ru-based catalyst at the time. This catalyst could be produced in a straightforward one-pot synthesis\textsuperscript{5c} in which RuCl\textsubscript{2}(=CHR)(PPh\textsubscript{3})\textsubscript{2} 8 was first generated from RuCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{3} 6 via an alkylidene transfer from an aryl diazoalkane 7 then transformed into catalyst 9 through a simple phosphine exchange with excess PCy\textsubscript{3} (Scheme 8). Catalyst 9, compared to all non-Ru-based olefin metathesis single-site catalysts at the time, exhibited superior tolerance towards air, moisture, and functional groups, though it did lack thermal stability at temperatures >60 \(^{\circ}\)C. Yet, this catalyst triggered an explosion of research in the field that has transformed olefin metathesis into a very powerful technique in organic and polymer synthesis.
Figure 3. Improved Ru-Based Carbene Catalyst 5

Scheme 8. Synthesis of Grubbs’ 1st Generation Catalyst 9

In 1998, Dixneuf et al. reported the synthesis of metathesis active, 18-electron Ru-allenylidene complexes. These complexes were synthesized by adding a bulky phosphine-containing ligand precursor to [(p-cymene)RuCl₂]. The resulting intermediate was then reacted with propargyl alcohols, with subsequent reaction with NaPF₆ and PCy₃ in methanol to yield cationic allenylidene complexes, with complex 10 (Figure 4) as a prominent example. The advantage of these catalysts was that they could be synthesized without the use of the hazardous diazoalkanes employed in the synthesis of catalyst 9 and were thermally more stable than the Grubbs-type catalysts at the time. However, these complexes never gained the same popularity as the Grubbs-catalysts due to their much lower olefin metathesis activity.
The limited thermal stability of catalyst 9 was improved upon by the development of catalysts coordinated by N-heterocyclic carbene (NHC) ligands, such as IMes\textsuperscript{34} (IMes = 1,3-bis(2,4,6-trimethylphenyl)-imidazol-2-ylidene) and H\textsubscript{2}IMes\textsuperscript{35} ligands (H\textsubscript{2}IMes = 1,3-bis(2,4,6-trimethylphenyl)-4,5-(dihydro)imidazol-2-ylidene). Herrmann \textit{et al.} reported a stable Ru-based olefin metathesis catalyst bearing an NHC ligand 11 (Figure 5) in 1998, though the activity of their catalyst was considered poor due to its extremely slow metathesis initiation rate compared to catalyst 9, requiring 12 hours to several days to initiate olefin metathesis reaction.\textsuperscript{36} However, catalyst 11 did show the potential for NHC ligands to stabilize Ru-based catalysts.

Further research into the use of NHC ligands was independently pursued by the groups of Nolan,\textsuperscript{37} Grubbs,\textsuperscript{38} and Herrmann,\textsuperscript{36,39} resulting in a variety Ru catalysts bearing NHC ligands, including Grubbs’ second generation catalyst 12, or (H\textsubscript{2}TAp)(PCy\textsubscript{3})Cl\textsubscript{2}Ru=CH-Ph.\textsuperscript{38} This catalyst exhibited unseen high thermal stability.
along with elevated activity compared to catalyst 9 as well as similar functional group tolerance. Complex 12 exhibited much slower initiation rates, typically requiring several minutes to initiate olefin metathesis reactions, but this was compensated by extraordinary propagation rates.\(^{40}\) Hence, catalyst 12 was extremely efficient in RCM reactions. The fast propagation displayed by catalyst 12 is a consequence of the bulky and strongly \(\sigma\)-donating NHC ligand.\(^{41}\) Catalyst 12 is synthesized through direct replacement of one PCy\(_3\) ligand in catalyst 9 with an H\(_2\)IMes ligand which is obtained \textit{in situ} from the dihydroimidazolium salt in the presence of a strong base (Scheme 9).\(^{42}\)

\textbf{Scheme 9.} Synthesis of Grubbs’ Second Generation Catalyst 12\(^{42}\)

Another approach for modifying these Ru-based catalysts was first realized in 1997 when it was observed that \textit{ortho}-styrenyl ethers could form stable cyclic ruthenacarbenes with these catalysts through bidentate coordination.\(^{43}\) In 2000 this carbene modification was explored independently by the groups of both Hoveyda\(^{44}\) and Blechert\(^{45}\) who simultaneously reported a phosphine-free catalyst bearing the H\(_2\)IMes ligand. This catalyst eventually became known as the Hoveyda-Grubbs catalyst 13. It was synthesized from Grubbs’ second generation catalyst 12 and \(i\)-propoxystyrene in the presence of copper chloride (Scheme 10). This catalyst had certain advantages over catalyst 12, most importantly it displayed enhanced stability in air, which is attributed to its bidentate coordination which protects the Ru-metal center from oxidation. For this reason, catalysts bearing the bidentate benzylidene ligand were developed for catalyst immobilization and recycling.\(^{46}\) Otherwise, catalyst 13 exhibited a similar activity profile
to catalyst 12, including slow initiation and fast propagation rates in comparison to first
generation catalyst 9. Modifications of complex 13 at the benzylidene moiety have also
been explored, such as $p$-substitution of the phenyl ring, which sometimes afforded
increased initiation rates in comparison to catalyst 13.$^{5d}$

**Scheme 10. Synthesis of Hoveyda-Grubbs Catalyst 13$^{44,45}$**

Another modified Grubbs-type catalyst bearing an NHC ligand is Grubbs’ third
generation catalyst 14 (Figure 6).$^{38}$ For this catalyst, which was also derived from
catalyst 12, the phosphine ligand was replaced by two weakly donating 3-bromopyridine
ligands. Because these ligands dissociated quickly to free up the necessary coordination
site for metathesis, this catalyst exhibited a fast rate of initiation, fast propagation, and
therefore extremely high overall catalytic activity. In fact, it is considered the most active
olefin metathesis catalyst to date. This catalyst was ideal for specialized ROMP
reactions but was not as widely used as catalysts 12 and 13 due to its much decreased
thermal stability and its tendency to produce undesired side products as a result of
several different types of simultaneous olefin metathesis and hydride shift reactions,
both attributed to its extremely high activity.$^{30}$
Figure 6. Grubbs’ Third Generation Catalyst 14

Modifications of the Ru-carbene moiety were also intensely investigated, leading to a multitude of active Ru-catalyst structures. In 1996, Grubbs et. al. explored several different complexes with modified carbene structures, including para-substituted benzylidene complexes, such as complex 15, methylidene complex 16, alkylidene complexes, such as complex 17, and vinylidene complex 18 (Figure 7). This study showed that para substitution of the benzylidene ligand did not have a strong effect on the overall activity of the catalyst, though faster initiation rate was observed with Grubbs’ first generation catalyst 9, which did not possess this modification. Complexes 16 and 18 were low-active in metathesis reactions when compared to catalyst 9, which was attributed to their poor catalyst initiation. As a result of this decreased activity, catalysts with these carbene modifications have not been as widely explored as the traditional benzylidene motif. Alkyl methylidene complexes 17 exhibited higher activity than catalyst 9. They were synthesized via carbene exchange from catalyst 9 using an excess of the respective alkene gas. However, complexes 17 were the only kinetic product and further converted into complex 16, which made their isolation cumbersome.
In 1999 Schanz and coworkers reported the first coordinately unsaturated 16-electron allenylidene structures 19 and 20.\textsuperscript{37c} As with some of the previous catalysts, these structures utilized strongly donating, bulky PCy\textsubscript{3} ligands, which provided the ruthenium center with a high electron density. The use of the PCy\textsubscript{3} ligands also allowed for straightforward phosphine-ligand exchange reactions, thereby giving access to NHC-ligand bearing allenylidene structures (Scheme 11). Though this class of catalysts displayed significantly lower activity than aforementioned benzylidene catalysts, as they often required several hours to several days to complete a metathesis reaction under similar reaction conditions), allenylidene catalysts were attractive because they tend to exhibit high thermal stability.\textsuperscript{37c} These catalysts were also attractive because they can be made from inexpensive, non hazardous starting materials in a straight-forward, one-step synthesis reaction\textsuperscript{33a,b,37c} and, last by not least, because the intellectual property for this class of catalyst is not protected.

**Scheme 11.** 16-Electron Allenylidene Complexes 19 and 20\textsuperscript{37c}

Simple rearrangement of allenylidene structures also granted access to indenylidene catalysts. An early example of this class of catalyst was structure 21.
(Figure 8), which was originally synthesized by Hill and co-workers.\textsuperscript{47} This complex was mistakenly first reported as a 16-electron allenylidene complex, but further studies by Jafarpour \textit{et al.}\textsuperscript{37b} determined it had an indenylidene structure, a result of an acid-catalyzed rearrangement of the C=C=C spine.\textsuperscript{37} NHC-ligated 16-electron indenylidene complexes \textsuperscript{22} and \textsuperscript{23} were also reported in the same publication (Figure 8).\textsuperscript{37b} In general, these indenylidene complexes exhibited better metathesis activity than their allenylidene counterparts combined with very high thermal stability. Today, Ru-indenylidene complexes have become the most popular alternative to the Grubbs-type benzylidene complexes. Several generations of these catalysts are commercially available and are used in a large variety of applications.\textsuperscript{48}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure8.png}
\caption{Early Indenylidene Complexes 21-23\textsuperscript{37b,47}}
\end{figure}

Another modification to the Ru-carbene moiety were the Fisher-type carbene complexes, such as those reported by Louie and Grubbs in 2002.\textsuperscript{38a} In this study, a series of Fisher-type complexes with the structure $(\text{PCy}_3)_2\text{Cl}_2\text{Ru=C(H)ER}$ or $(\text{IMes})(\text{PCy}_3)\text{Cl}_2\text{Ru=C(H)ER}$ were synthesized with a π-electron donating group directly attached to the carbene carbon. The general activity for these complexes followed the trend $E = C > N > S > O$. Many of these Fisher-type complexes were metathesis active, but displayed much lower reactivity than catalyst \textsuperscript{9}, which was not surprising considering that the generation of Fisher-type carbene complexes, such as those formed upon the addition of excess ethyl vinyl ether, are often used to quench metathesis reaction.
Further studies of Fisher carbene complexes conducted by Ozawa and company found that catalyst structures 24 and 25 (Figure 9) could perform highly selective ring opening / cross metathesis (ROCM) of certain norbornene derivatives with select vinyl chalcogenides, despite their low activity.\(^4\)

\[\text{Figure 9. Fischer-Type Carbene Complexes 24 and 25}^4\]

**Importance of Ru-Based Olefin Metathesis Catalysts**

Ru-based Grubbs-type olefin metathesis catalysts have had an enormous impact on organic synthesis. These catalysts have a high preference for carbon-carbon double bonds and often tolerate the presence of alcohols, amides, aldehydes, and carboxylic acids, making them applicable to a wide variety of substrates.\(^1\) More importantly, their use often does not require severe reaction conditions, making them an attractive technology for large-scale industrial applications. These catalysts are also useful to synthetic organic chemists for the production of unique olefins that difficult to synthesize through more traditional organic synthesis methods.

Ru-based Grubbs-type catalysts are currently used to produce a wide variety of products, including highly specialized polymeric materials such as polydicyclopentadiene (poly-DCPD) which is a high-performance, lightweight, corrosion resistant material used to make many products, including unbreakable baseball bats, corrosion resistant piping, lightweight vehicle parts, and bathroom fixtures.\(^5\) These catalysts are also used by the pharmaceutical industry to make macrocyclic compounds which are processed to
generate pharmaceuticals, such as HCV protease inhibitor BILN 2061, which is used to treat hepatitis C, as well as antitumor macrolides Pladienolide B and D. The uses for these catalysts continues to grow quickly as more application-specific improvements are made to catalyst designs.

Current Limitations of Ru-Based Olefin Metathesis Catalyst Systems

Even though Ru-based olefin metathesis catalysts have emerged as the preferred catalysts for ROMP and RCM reactions, many problems still exist with their large-scale use. One drawback to most Ru-based catalyst systems is that they are sensitive to air when in solution. While a few Ru-based olefin metathesis catalysts, such as the Hoveyda-Grubbs catalyst, can still perform somewhat effectively under non-inert conditions, most Ru-based catalysts are commonly used under inert gas conditions to guarantee optimal performance. Some catalyst designs, such as catalyst, utilize bidentate coordination ligands, which greatly improves the stability of the catalyst by protecting both the carbene ligand and the Ru-metal center. The main drawback to most of these catalyst designs is that upon initiation, metathesis and metal oxidation with molecular oxygen become competing reactions. Hence, activity loss in reactions in air is often significant.

Another limitation for most Ru-based catalysts is a lack stereoselectivity control. There are very few efficient Ru-based olefin metathesis catalysts which exhibit a high degree of cis / trans selectivity, especially in ROMP and CM reactions. Recently several groups have explored a number of structural modifications, such as bidentate, bulky, and asymmetric ligands, but high cis / trans (E/Z) control is still elusive for Ru-based systems in ROMP and CM reactions. While some catalyst designs have afforded improved enantioselectivity in certain applications, particularly for asymmetric ring-closing
metathesis (ARCM), these catalyst designs lack high enantioselectivity for a range of different substrates and applications. Though Ru-catalyst stability and stereoselectivity are important limitations being studied, this will be the extent that these are discussed as improving these limitations are not a focus in this dissertation.

One drawback that is important for this dissertation and which is displayed by most Ru-based olefin metathesis catalyst systems is their limited solubility profiles. The majority of these catalysts can only be used in organic solvents of a small polarity range. Only a few designs exist which can be used homogenously in aqueous media. Water is an attractive solvent for many applications due to its low toxicity, relative abundance, and cost-effectiveness. Reactions in aqueous media have been carried out with water-insoluble Ru-based olefin metathesis catalysts by the means of sonication, or in the presence of an organic co-solvent or surfactant, however none of these methods were very efficient or environmentally advantageous.

Several water-soluble Ru-based olefin metathesis catalysts have been synthesized that promote metathesis reactions homogeneously in aqueous media. Some of these catalysts bear NHC ligands modified with hydrophilic groups, such as polyethylene glycol (PEG) along the NHC backbone. Hong and Grubbs published one notable example in 2006. This Hoveyda-Grubbs type catalyst 26 (Figure 10) displayed higher ROMP, RCM, and CM activity than most previous water-soluble catalysts. Other ligand modifications have incorporated charged ionic functionalities for enhanced solubility in aqueous media. This has typically been accomplished through ionic ammonium groups added to the backbone of the NHC ligand such as those present on complex 27 or through ammonium groups attached to the chelating benzylidene moiety in complexes 27 and 28 (Figure 10). Catalyst 27 is very attractive due to its relatively straightforward synthesis, but it is not highly soluble in purely aqueous media, requiring
an alcohol co-solvent for homogenous conditions. Catalysts 26 and 28, on the other hand, are highly water-soluble but require an intense synthetic effort, with up to eight additional synthetic steps. Additionally, these catalysts are limited as they do not perform well-controlled aqueous ROMP. Hence, these designs are not attractive beyond conceptual studies.

![Diagram of Ru-based olefin metathesis catalysts 26-28]

**Figure 10.** Examples of Water-Soluble Ru-Based Olefin Metathesis Catalysts 26-28

Another limitation of Ru-based olefin metathesis catalyst systems is the removal of the Ru-metal catalysts from the product stream. Because Ru-based olefin metathesis catalysts are used homogenously, catalyst removal is often difficult and costly. This is particularly problematic for the pharmaceutical industry. Currently the pharmaceutical industry performs column chromatography over silica gel for effective Ru removal. This method is very costly and time consuming, often requiring several repetitive column cycles (typically 5-10) to reduce the Ru-contamination levels below 10 ppm, the upper limit for Ru contamination in pharmaceutical products. Alternative methods for catalyst removal do exist, such as chemical scavenging and physical absorption, but to date these methods are generally not used due factors such as cost, toxicity, and long processing times. Additionally, none of these methods on their own successfully reduce the Ru-metal contamination <50 ppm, still far above the required pharmaceutical standard.
In recent years some advancements have been made with catalysts designed specifically for enhanced removal after metathesis reactions from the product stream. Several catalysts were designed for improved separation via column chromatography, though most of these designs do not sufficiently reduce the level of Ru-metal contamination below the pharmaceutical standard through just one cycle. Other catalysts have been designed with modified solubility profiles that allow for extraction of the catalyst with water or ionic liquids, but to date only a few, such as catalyst complex 29 (Figure 11), reduce the level of Ru below the required pharmaceutical standard.

Using another approach, some catalysts have been immobilized on solid support. Complex 30 (Figure 11) is the most successful example, which leaves less than 20 ppb Ru-metal contamination in its products. Though these catalyst designs were very successful at reducing Ru-metal contamination in metathesis products and could be reused several times, they still require high catalyst loadings (>2%) and an enormous synthetic effort to produce, which again makes them very little attractive for large-scale, industrial use.

![Figure 11. Catalyst Complexes 29 and 30 With Improved Removability](image)

The lack of external activity controls is another issue that is problematic in several applications. Typically, when a catalyst is added to substrate, the metathesis reaction proceeds until all substrate is consumed or the catalyst decomposes. This is
particularly problematic for the production of specialized polymers and poly-DCPD, whose physical properties and production safety suffer from this uncontrolled activity. These could be improved by externally triggering a latent catalyst, which would allow for safe mixing of substrate and catalyst.

In 2007, Schanz et al. published a method that chemically enabled the independent reversible inhibition and subsequent reactivation of a catalyst system.\textsuperscript{64} This was accomplished through the addition of N-donor ligands to catalyst 9, resulting in the formation of an inhibited species with very little ROMP activity. The method allowed for mixing of a monomer substrate and inhibited catalyst without any catalytic activity until an acid was applied to reactivate the catalyst. This was the first reversible “off/on” switch for the olefin metathesis reaction. The two ligands utilized in this inhibition with subsequent reactivation protocol were 1-methyl imidazole (MIM) and 4-dimethylaminopyridine (DMAP). The inhibition was based on the formation of low-active complex 31 additionally inhibited by free PCy\textsubscript{3} ligand until the addition of acid generates complex catalyst 32, thereby restoring the catalyst’s activity (Scheme 12). Other catalysts bearing acid-responsive donor ligands have been developed. Many of these catalysts are coordinated by pentane-2,4-dione and salicyaldimine ligands, which dissociate from the Ru-metal center upon addition of a Lewis acid or Brönsted acid, such as HCl.\textsuperscript{64,65}
Heat is another straightforward stimulus that has previously been used to trigger ROMP reactions. The catalysts used in these methods often contained a back-biting N or S-donor ligand. ROMP reactions with these catalysts start by thermally triggering the dissociation of the bidentate ligand. Although these catalysts were easily and safely handled, their application suffered from very low catalyst efficiencies due to the fact that they have to exhibit zero-activity at ambient temperature, as a result of extremely low rates of olefin metathesis initiation. Since only a very low fraction (far below 5%) of the catalyst is typically activated during the reaction, high catalyst loadings (usually ≥2%) were required, which is not very economical.

In a few studies, light has been used as external stimulus for activation of Ru-based olefin metathesis catalysts. An early study of catalyst 9 found that photolysis with light (λ = 546 nm) triggered the dissociation of one phosphine ligand, however, no further studies for catalyst 9 were conducted with respect to enhanced metathesis initiation under these conditions. Few Ru-based light-activated metathesis reactions have been described in the literature, but until quite recently the pre-catalysts used in these studies lacked the presence of an active alkylidene moiety. For these catalysts, the alkylidene was generated in situ from the substrate. The advantage of these light activated catalyst systems was that they do not rely on sophisticated and expensive Ru-
alkylidene complexes as starting materials, but their drawback was the ill-defined nature of the reactive species, which made performance optimization difficult. Additionally, these catalysts only were successfully used with substrates of extremely high ROMP activity, namely norbornene. Because thermally and light triggered catalyst systems only worked at elevated temperatures and/or require long reaction times (up to 24 hours) for catalyst initiation, they generally did not demonstrate well-control ROMP reactions or low catalyst/substrate ratios. In 2009, Grubbs et al. reported the first successful photo-activated metathesis reaction protocol for a Ru-alkylidene complex in combination with a photoacid generator, however a high catalyst/substrate ratio was required and many reactions did not go to completion.70

**Controlled Polymerizations (ROMP)**

In 1956 Szwarc defined a “living polymerization” as one that proceeds “without chain transfer or termination”.71 When no noticeable catalyst decomposition occurs, ROMP is as a living polymerization (LROMP).1a One of the earliest examples of LROMP using Ru-based olefin metathesis catalysts was published by Kanaoka and Grubbs in 1995.72 In this study, catalysts 4 (Figure 2) and 5 (Figure 3) produced homogenous polymers as well as block copolymers from silicon-containing norbornene derivatives, and several of these reactions proceeded in a somewhat controlled fashion. This method was applied in organic media, but to date only one Ru-based olefin metathesis catalysts has been reported to perform controlled ROMP homogenously in aqueous media. 6a

Key to controlled ROMP is a high ratio between the rates of initiation and propagation. A controlled polymerization must be living and additionally requires fast and complete initiation. When these conditions are met, the polymers produced have a polydispersity index (PDI) <1.5.1b,73 A few methods have been identified that enhance the initiation rate of Ru-based catalysts using Brønsted or Lewis acids.64,65 However, no
methods have been identified for external control of the rate of propagation in the LROMP reaction. The moderation of the rate of propagation could be a complementary approach to controlled LROMP, particularly considering the low thermal stability exhibited by fast ROMP initiators and the higher degree of secondary metathesis reactions exhibited by fast ROMP propagators.

**Dissertation Goals**

The main purpose of this dissertation research was to develop Ru-based olefin metathesis catalysts with pH-responsive ligands. These pH-responsive ligands provided the means to externally control the solubility profile and, in many cases, the activity of the catalyst via acid addition. External control of the catalyst's solubility allowed for use of these catalysts with a wider range of solvents and substrates, including olefin metathesis reactions in aqueous media. Some of these catalysts exhibited a reversible solubility profile, which made them useful for applications such as efficient catalyst removal after RCM reactions. External control of catalyst activity was used to alter the rate of initiation and/or propagation of the catalyst, thereby changing the overall activity of the catalyst. The overall goal of this research is to develop catalysts capable of performing RCM and ROMP reactions in both aqueous and organic media with extreme efficiency and high activity.
CHAPTER II

NHC LIGAND PRECURSOR SYNTHESIS

NHC Ligand Precursors Modified With pH-Responsive Dimethylamino Groups

Several modifications to the NHC ligands of Ru-based olefin metathesis catalysts have been made in an effort to improve several attributes of the catalyst, including solubility, activity, and selectivity.\textsuperscript{22,51} The modification of NHC ligand precursors is synthetically more straightforward than for phosphine ligands, and therefore is a more feasible approach to the synthesis of novel, Ru-based olefin metathesis catalysts.\textsuperscript{74} Typically, NHC ligands are generated \textit{in situ} via deprotonation of the NHC ligand precursor salt (A) with a strong base, such as potassium hexamethyldisilazane (KHMDS) or potassium tert-butoxide (KOT-Bu) (Scheme 13). This yields the singlet carbene species B, which is in equilibrium with the imidazoline structure C. Structure B is the free ligand species needed for the phosphine-NHC ligand exchange reaction described in Chapter I. For imidazole-2-ylidenes, such as the IMes ligand, the free carbene B is preferred, as this configuration affords 4n+2 Hückel aromaticity resulting from the four-electron three-center \( \pi \) system of the N-C-N in combination with the two \( \pi \)-electrons of the NHC ligand backbone.\textsuperscript{75,76} For dihydroimidazol-2-ylidenes, such as the H\(_2\)IMes ligand, which lack Hückel aromaticity in configuration B, imidazoline C is dominant in the equilibrium as the thermodynamically more favored structure.\textsuperscript{75,76} When neutrally charged, the NHC free carbene readily undergoes ligand exchange with the phosphine in commercially available Grubbs’ first generation catalyst 9 when low-polar solvent conditions are applied. These low-polar solvent conditions are a requirement for complete ligand exchange.\textsuperscript{41,77} This phosphine-ligand exchange provides the means to generate new olefin metathesis catalysts.
For this dissertation, several functionalized, pH-responsive NHC ligand precursors were synthesized. This was accomplished by incorporating pH-responsive dimethylamino (NMe₂) groups into the NHC ligand precursors. NMe₂ groups were ideal for this study because they are compatible with Ru-based systems and are neutrally charged, therefore they do not negatively impact the phosphine-NHC ligand exchange at the Ru-center in low-polar solvents, allowing for straightforward access to new catalyst structures. The resulting catalysts are pH-responsive, which opens up the possibility for external control of catalyst properties via acid addition. Once protonated, these NMe₂ groups become charged ionic species, which will alter catalysts’ solubility profiles. Protonation of these groups may also change the electronic environment of the ligand, depending on the position of the NMe₂ group of the ligand, hence modifying the donating ability of the ligand, thereby impacting the overall activity profile of the catalyst.

Synthesis of the H₂ITap·HCl and ITap·HCl Ligand Precursors

The first NHC ligand precursor salt synthesized for this project was H₂ITap·HCl (H₂ITap = 1,3-bis(2',6'-dimethyl-4'-dimethylaminophenyl)-4,5-dihydroimidazol-2-ylidene) containing two NMe₂ groups bound directly to the aromatic NHC ligand substituents. Precursor 37 was synthesized from commercially available starting material N,N-3,5-tetramethylaniline 33. Compound 33 was converted into phenylenediamine derivative 34 according to literature procedures with 45% overall yield. Following the literature procedure for the production of the H₂IMes ligand with a few modifications, 34 was then converted into the respective NHC ligand precursor salt...
37 in three steps (65% overall yield) via intermediates 35 and 36 (Scheme 14). In this process, an improved hydrogenation procedure was developed for diimine 35 utilizing NaBH₄ and H₃BO₃ to afford the diamine 36 in high yield and purity.⁷₉

Scheme 14. Synthesis of Ligand Precursor 37: (i) (1) NaNO₂/conc. HClₐq, 60 min, -5 °C, (2) Sn/HCl, 70 °C (45%); (ii) (CHO)₂/MeOH [HCl], 24 h, RT (85%); (iii) NaBH₄/ H₃BO₃/thf, 60 min, 30 °C (88%); (iv) HC(OEt)₃/NH₄Cl, 12 h, 130 °C (87%).

As a complimentary motif, NHC ligand precursor ITap·HCl 38 (ITap = 1,3-bis(2’,6’-dimethyl-4’-dimethylaminophenyl)imidazol-2-ylidene) was synthesized with an unsaturated backbone. ITap·HCl 38 is the unsaturated analogue to H₂ITap·HCl 37. In general, NHC ligands with unsaturated backbones (imidazole-2-ylidenes) typically have lower activity than catalysts bearing dihydroimidazol-2-ylidenes, their saturated counterparts.⁵¹ The synthesis of this ligand precursor was accomplished with a 78% yield by reacting diimine 35 with paraformaldehyde and Me₃SiCl in ethyl acetate at 70 °C using a modified literature procedure (Scheme 15).⁸¹
Ligand Precursors Using a Template Synthesis

In an effort to quickly gain access to a library of additional unique NHC ligand precursors, a template synthesis for a variety of ligand precursor salts was developed. These, like ligand precursor salts 37 and 38, also contained two ancillary NMe₂ groups. The key synthetic step to this template synthesis was the functionalization of diiodinated diamine intermediates 48-50 via Cu-mediated C-heteroatom coupling reactions, allowing for simplified access to several unique ligand precursors. In the first part of this template synthesis method, iododiamine intermediates were synthesized from commercially available anilines. The anilines chosen were 2,6-dimethylaniline 39, 2,6-diisopropylaniline 40, and 2,4-dimethyl aniline 41 (Figure 12). These anilines were first iodinated at their unsubstituted ortho or para positions. The resulting iodoaniline derivatives 42-44 were then converted into their corresponding double Schiff bases 45-47 using glyoxal. These double Schiff bases were then reduced, resulting in the desired diamine intermediates 48-50 (Scheme 16). Using this strategy, three new di(iodophenyl)diamine intermediates were generated (Figure 13).
More ligand diversity was introduced starting from the iododiamine intermediates, which were functionalized through Cu-mediated coupling reactions to obtain functionalized diamines 51-54 and 59, 60 with the aryl substituents E-CH₂-CH₂-NMe₂ (E
These ether and thioether groups possessed the pH-responsive NMe2 groups that allowed for external control of a catalyst via acid addition. Since these NMe2 groups were separated from the aryl groups of the NHC ligand substituents by an E-CH2-CH2 spacer, the electronic effect on the donor ability of the NHC ligand by protonating these groups were significantly reduced (vide infra). Four of these functionalized diamines (51-54) were successfully converted into NMe2 functionalized NHC ligand precursor salts 55-58 by performing a ring closing reaction78 with triethyl orthoformate (Scheme 17). For functionalized diamines 59 and 60 no pure NHC ligand precursor salt could be isolated due to extensive formation of unknown side products (Scheme 18). Therefore, the ortho functionalized ligand precursors were not further pursued in this project. Overall, four new NHC ligand precursors 55-58 (Figure 14) were prepared using the template synthesis. Throughout this dissertation, the ligands generated from these precursors will be referred to as IXyONMe2 (IXyONMe2 = 1,3-bis(4’-[2’’-dimethylaminoethoxy]-2’,6’-dimethylphenyl)-4,5-dihydroimidazol-2-ylidene), IXySNMe2 (IXySNMe2 =1,3-bis(4’-[2’’-dimethylaminoethanethio]-2’,6’-dimethylphenyl)-4,5-dihydroimidazol-2-ylidene), IDippONMe2 (IDippONMe2 =1,3-bis(2’,6’-diisopropyl-4’-oxo-N,N-dimethylethanaminophenyl)-4,5-dihydroimidazol-2-ylidene), and IDippSNMe2 (IDippONMe2 =1,3-bis(2’,6’-diisopropyl-4’-thio-N,N-dimethylethanaminophenyl)-4,5-dihydroimidazol-2-ylidene), respectively.
Scheme 17. Synthesis of Ligand Precursors 55-58

Scheme 18. Reaction Products Obtained from Iododiamine Intermediate 50
Figure 14. NHC Ligand Precursors 55-58
CHAPTER III

CATALYST SYNTHESIS

Ru-Based Olefin Metathesis Catalysts Bearing pH-Responsive Ligands

The purpose of this dissertation was to synthesize Ru-based olefin metathesis catalysts bearing pH-responsive ligands. The catalysts that were generated for this project bear NHC ligands modified with NMe₂ groups, as described in Chapter II. Once protonated, these groups are converted from neutral amino groups into cationic ammonium groups, allowing for external control of catalyst solubility profiles and via acid addition. For some of these catalysts, the functionalized NHC ligand also permits the external control of catalyst activity, particularly for those bearing an H₂ITap or ITap ligand, due to a change in the electronic environment and therefore overall donating ability of the NHC ligand.

Several of the catalysts generated for this study also bear basic, pH-responsive N-donor ligands. As described in Chapter I, the Schanz research group has pioneered a method that uses N-donor ligands for the inhibition of catalyst systems with subsequent reactivation via acid addition.Kinetic studies for these complexes showed that the overall reaction times for all reactivated ROMP reactions were faster than the same reactions with the precursor catalyst 9 due to the near-instant formation of a very fast-initiating species. The N-donor ligands chosen for this work were DMAP and the bidentate 3-(o-pyridyl)propylidene moiety. The use of these ligands in conjunction with NMe₂ modified NHC ligands should yield unprecedented catalyst systems that exhibit simultaneous external control of catalyst solubility and activity in metathesis reactions via the degree of protonation of the pH-responsive functionalities.
Synthesis of Catalysts Bearing pH-Responsive Ligands

**Grubbs-Type Benzylidene Catalyst Synthesis**

The first pH-responsive NHC ligand precursor used to generate the catalyst for this study was the H$_2$ITap ligand precursor salt 37. This was reacted *in situ* with Grubbs' first generation catalyst 9 in the presence of a strong base to produce the second generation-type catalyst (H$_2$ITap)(PCy$_3$)$_2$Ru=CH-Ph 61 in 70% yield via phosphine ligand exchange in accordance with literature procedure. It should be noted that a similar catalyst, with two NEt$_2$ instead of NMe$_2$ groups, was simultaneously synthesized by Plenio *et al.*, though external control of the catalyst via acid addition was not initially explored by this group. Catalyst 61 was then converted into Hoveyda-Grubbs-type catalyst (H$_2$ITap)Cl$_2$Ru=CH-(C$_6$H$_4$-O-iPr) 62, also in 70% yield, using 2-i-propoxystrene in the presence of CuCl (Scheme 19), also in accordance with literature procedures. The bidentate coordination of this catalyst’s modified benzylidene ligand has previously been shown to enhance the overall stability of the catalyst without causing a significant loss of activity compared to its PCy$_3$-coordinated benzylidene counterpart. Suitable crystals of complexes 61 and 62 were then grown, and their structures in solid state were solved via X-ray crystallography (Figures 15 and 16).
Scheme 19. Synthesis of Catalyst Complexes 61 and 62: (i) 9/KOtBu/heptane, 24 h, 60 °C (70%); (ii) 2-i-propoxystyrene/CuCl, 2 h, 35°C (70%).

Analysis of the crystal structures showed that complexes 61 and 62 exhibit a distorted square pyramidal ligand environment, which is typical for pentacoordinate Ru–carbene complexes. The base is formed by the donor ligands and the chlorides, and the benzyldiene moiety is in the apex. In catalyst 61, all bond distances and bond angles involving the ruthenium center were in the same range as for catalyst complex 63 (Figure 17) bearing a 1,3-dimesityl-1,4,5,6-tetrahydropyrimidin-2-ylidene ligand, the only other crystal structure published for a Grubbs second generation-type complex bearing an unsaturated NHC ligand backbone, within a margin of 0.01 Å and 0.6°. The only exception was the Ru-C_{NHC} distance of 2.075 Å, which was actually shorter in complex...
61 by more than 0.03 Å (2.106 Å) than observed for complex 63. This bond distance was more similar to the Ru–C_{NHC} distance of the corresponding (IMes)(PCy_3)Cl_2Ru=CHPh complex 64 (Figure 17) with a Ru-C_{NHC} distance of 2.069 Å.\textsuperscript{37a} This was not surprising as the mesityl substituents are less angled towards the metal center in catalyst 61 than in the tetrahydropyrimidin-2-ylidene complex 63 due to its shortened NHC ligand backbone. As a result, the steric interference with the benzyldiene moiety was less pronounced. This was also reflected in the longer distance between the mesityl ipso-carbon atom to the benzyldiene carbon atom in catalyst 61 compared with complex 63 (3.01 Å vs. 2.9 Å). The long distance between the aromatic ring and the carbene moiety was speculated to be responsible for lowered metathesis activity of the tetrahydropyrimidin-2-ylidene complex 64 in comparison to Grubbs’ second generation catalyst 12.\textsuperscript{85}

![Figure 17. Catalyst Complexes 63 and 64](image-url)

The unit cell of the crystal structure of catalyst 62 contained two discrete complex molecules and one molecule of CH_2Cl_2 in solvation. The averaged bond distances of both molecules were similar to those of the H_2IMes analogue 13\textsuperscript{44} (deviations <0.01 Å) with one exception. The distance between the Ru-center and the benzyldiene carbon atom was extremely short in catalyst 62 (1.735 Å), shorter by almost 0.1 Å than in catalyst Hoveyda-Grubbs catalyst 13. As the only structural difference between the two catalyst complexes was the presence of the remote p-NMe_2 groups in catalyst 62 instead of the p-methyl groups in catalyst 13, it is likely that this shortening of the metal–
carbene bond was less due to steric reasons than electronic differences. In comparison to catalyst 13, the trans bond angles at the metal center and the C–Ru–C cis angle were slightly larger in catalyst 62 by approx. 2–3°. However, the C–Ru–O cis angle for catalyst 62 (78.1°) is smaller by 1.3° than in catalyst 13. This was unexpected due to the shorter Ru–carbene bond, which should have caused a widening of this angle assuming comparable bond angles in the relatively rigid benzylidene chelate. The small C–Ru–C cis angle also caused a large distance between the mesityl ipso-carbon atom to the benzylidene carbon atom in catalyst 62 (3.08 Å) in comparison to PCy₃ coordinated complex 61.

Table 1. Selected Bond Angles [°] and Distances [Å] for Catalysts 61 and 62\textsuperscript{79}

<table>
<thead>
<tr>
<th></th>
<th>Catalyst 61</th>
<th>Catalyst 62</th>
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<tr>
<td>Ru=C(H)</td>
<td>1.826(2)</td>
<td>1.735(9)</td>
</tr>
<tr>
<td>Ru-C(NHC)</td>
<td>2.0746(19)</td>
<td>1.966(7)</td>
</tr>
<tr>
<td>Ru-O</td>
<td>-</td>
<td>2.260(5)</td>
</tr>
<tr>
<td>Ru-P</td>
<td>2.4419(6)</td>
<td>-</td>
</tr>
<tr>
<td>Ru-Cl</td>
<td>2.4080(6)</td>
<td>2.330(2)</td>
</tr>
<tr>
<td></td>
<td>2.3809(6)</td>
<td>2.339(2)</td>
</tr>
<tr>
<td>P-Ru=C(H)</td>
<td>91.45(9)</td>
<td>-</td>
</tr>
<tr>
<td>O-Ru=C(H)</td>
<td>-</td>
<td>78.1(3)</td>
</tr>
<tr>
<td>C(H)=Ru-C(NHC)</td>
<td>99.49(9)</td>
<td>103.2(3)</td>
</tr>
<tr>
<td>P-Ru-C(NHC)</td>
<td>179.41(9)</td>
<td>-</td>
</tr>
<tr>
<td>O-Ru-C(NHC)</td>
<td>-</td>
<td>178.5(3)</td>
</tr>
<tr>
<td>Cl-Ru-Cl</td>
<td>169.64(4)</td>
<td>159.69(8)</td>
</tr>
</tbody>
</table>

Catalyst 61 was also used to synthesize two catalysts with pH-responsive N-donor ligands. The first was (H₂ITap)(DMAP)₂Cl₂Ru=CH-Ph 65 (Figure 18), which was synthesized by reacting catalyst 61 in the presence of excess DMAP in t-butyl methyl ether, in accordance with the procedure developed in our laboratories.\textsuperscript{64} Since this catalyst was virtually insoluble in the reaction solvent it was isolated through vacuum filtration of the green precipitate, giving complex 65 in very high yield (90%) and purity (>99%, \textsuperscript{1}H NMR spectroscopy). The incorporation of the pH-responsive DMAP ligands allows for the control of catalyst activity via acid addition. Thus, protonation with excess
non-nucleophilic acid would cause the DMAP ligands of this catalyst to dissociate, freeing up the necessary ROMP coordination site, thereby accelerating the initiation rate of the catalyst.

![Figure 18. DMAP Catalyst Complex 65](image1)

![Figure 19. Catalyst Complex 66](image2)

(H$_2$ITap)Cl$_2$Ru(=CH-CH$_2$-CH$_2$-C$_5$H$_4$N) 66 (Figure 19) is another complex synthesized from catalyst 61 that bears a pH-responsive N-donor ligand. In this structure, the PCy$_3$ and carbene ligands of catalyst 61 were replaced by a backbiting N-donor ligand. This ligand was incorporated into the catalyst structure by reacting complex 61 in the presence of excess 2-(3-butenyl)pyridine, generating complex 66 via simple carbene exchange. This product complex 66, like DMAP complex 65, was not soluble in the reaction solvent and was isolated as a green precipitate with an 88% yield. This backbiting ligand affords much slower initiation than observed with precatalysts 9 and 61, but upon protonation the nitrogen of this ligand dissociates from the metal center, thereby accelerating the rate of catalyst activity.

The next pH-responsive ligand precursor examined for the synthesis of Grubbs-type benzylidene catalysts was ITap·HCl salt 38. This salt was first used to synthesize (ITap)(PCy$_3$)Cl$_2$Ru=CH-Ph 67, followed by complexes (ITap)Cl$_2$Ru=CH-(C$_6$H$_4$-O-iPr) 68, and (ITap)(DMAP)$_2$Cl$_2$Ru=CH-Ph 69 (Figure 20) following the procedures described for their unsaturated analogues, catalysts 61, 62, and 65. They were obtained in yields between 67-95%. Attempts to synthesize the ITap analogue to catalyst 66 were not
successful, which might be attributed to the decreased activity of its precursor complex 67.

Previous studies with complexes bearing IMes and H2IMes ligands demonstrated that catalysts possessing an unsaturated NHC backbone generally have lower activity than their counterparts with a saturated backbone. On the other hand, such catalysts frequently exhibit enhanced thermal stability, making them the preferred catalyst motif for certain applications.51 As such, we expected that complexes 67-69 would exhibit significantly lower activity than seen with complexes 61, 62, and 65.

The syntheses of Grubbs-type catalysts bearing the NHC ligand precursors 55-58 (Figure 21), which were produced via the template synthesis described in Chapter II, have proven much more difficult. To date, the only Grubbs second generation-type catalyst successfully isolated from any of these ligand precursors is (IXyONMe2)(PCy3)Cl2Ru=CH-Ph 70 (Figure 22). This complex was obtained via a ligand exchange reaction with catalyst 9 using the IXyONMe2 precursor salt 55, as was used to synthesize complex 61.79 This ligand exchange reaction required prolonged reaction time (48 hours) compared to that required for catalyst complex 61. Since catalyst 61 precipitated from solution in heptanes, isolation of the pink product proceeded via vacuum filtration. The isolated yield (40%) was lower than for catalysts 61 and 67. Though similar in structure to ligand precursor salt 55, attempts to synthesize analogous
complex 71 (Figure 22) using IXySNMe$_2$ precursor salt 56 did not afford any noticeable ligand exchange from catalyst 9, even after running the reaction for ten days. As such, other target complexes bearing the IXySNMe$_2$ ligand were not pursued.

![Diagram of structures 55-58 and 70-71](image)

**Figure 21.** NHC Ligand Precursor Salts 55-58  
**Figure 22.** Catalyst Complexes 70 and 71

Two other second generation Grubbs-type complexes, 72 and 73 (Figure 23), have been generated *in situ* from reactions with catalyst 9 and ligand precursor salts 57 and 58, respectively, but to date neither complex has been successfully isolated and purified. The presence of these complexes was indicated by both $^1$H and $^{31}$P NMR spectra obtained after solvent removal. For example, when the $^1$H NMR spectra for complex 73 was examined, the Ru=CH signal present at 19.7 ppm was indicative of the formation of a second generation-type catalyst, as was the $^{31}$P signal present at 29.0 ppm (Figures 24 and 25, obtained before completion of the reaction). However, these catalysts exhibited appreciable solubility in heptane as well as in a 1:1 mixture of 2-propanol/water, the solvents or solvent mixture which are usually used for precipitation. Attempted precipitation of complexes 72 and 73 with other solvents and solvent mixtures were not successful. Product isolation via column chromatography was also not successful as the complexes adhered to acidic, neutral, and basic stationary phases regardless of what solvent conditions were applied. It is likely that this was a result of catalyst degradation on the column.
Figure 23. Catalyst Complexes 72 and 73 Generated in situ

Figure 24. $^1$H NMR Spectrum of Complex 73 Generated in situ (300.1 MHz, 20 °C, $C_6D_6$)
Figure 25. $^{31}$P NMR Spectrum of Complex 73 Generated in situ (300.1 MHz, 20 °C, C₆D₆)

Though complexes 72 and 73 could not be isolated, attempts were made to generate Hoveyda-Grubbs-type complexes 75 and 76 (Scheme 20). One strategy was to filter the reaction solutions containing the parent complexes and to react them in situ with 2-i-propoxystrene and CuCl. Once again, $^1$H NMR indicated the presence of the desired complexes, however attempts to isolate these complexes by removing the CuCl and other impurities via column chromatography or recrystallization proved fruitless. It should be noted that removal of the Cu-based byproduct in the exchange reaction has only been accomplished via flash column chromatography to date. Hence, complexes 75 and 76, which contain very basic NMe₂ groups, very likely decomposed on a basic column, as OH⁻ ions are known to decompose Grubbs-type catalysts.⁴⁰c The catalysts also could not be separated from neutral or acidic column media due to protonation of the NMe₂ groups, which made the catalysts adhere very strongly to the stationary phase.
An alternate synthetic route based on a literature procedure developed by Grela et al. was also attempted. In this procedure, first generation Hoveyda-Grubbs complex 74 was first synthesized, isolated, and purified. Then this complex was reacted with ligand precursor salts 57 or 58 in an attempt to form catalyst complexes 75 and 76 (Scheme 20). Though fewer impurities were present in this reaction solution, attempts to isolate the product complexes via flash column chromatography were once again unsuccessful.

**Scheme 20.** Synthesis of Complexes 75 and 76 via an Alternate Synthetic Route

Synthesis and isolation of DMAP derivatives ([IDippONMe₂](DMAP)Cl₂Ru=CHPh 77 and ([IDippSNMe₂](DMAP)Cl₂Ru=CH-Ph 78 (Figure 26) from complexes 72 and 73 proved much more fruitful. As with the initial attempts to synthesize Hoveyda-Grubbs-type catalysts, derivative complexes 77 and 78 were obtained via direct filtration of the reaction solutions of the parent complexes 72 and 73, followed by subsequent reaction *in situ* with excess DMAP. The new solutions were then either sonicated or stirred for periods of 2-24 hours. Complexes 77 and 78 then precipitated from solution, allowing for their isolation via filtration. As with catalyst complexes 65 and 69, complexes 77 and 78 contain a DMAP ligand and a pH-responsive NMe₂, allowing for external control of solubility and activity. However, complexes 77 and 78 only bear one DMAP ligand, very likely as a result of the larger steric bulk provided by the NHC ligands. Pentacoordinate Ru-alkylidene complexes bearing only one N-donor ligand have been isolated before.
and the DMAP ligand is always coordinated trans to the NHC donor ligand in these complexes.

![Figure 26: DMAP Catalyst Complexes 77 and 78](image)

Because catalyst complexes 70, 77, and 78 possess an unsaturated NHC ligand backbone, they were expected to have similar activity to their H₂IMes ligand bearing analogues 61 and 65 under non-acidic conditions. Under acidic conditions, however, the NHC ligation of these catalysts were anticipated to exhibit less influence on the activity due to the proximity of their NMe₂ groups from the aryl substituents of their NHC ligands by an E-CH₂-CH₂ spacer, where E = O or S. This spacer minimizes the interference of the protonated N⁺HMe₂ with the electron donating properties of the NHC ligands. This allows for the external control of catalyst solubility with pH-responsive N-donor ligands being the only influence on the catalyst activity upon protonation where present (vide infra). The alkyl NMe₂ groups of these NHC ligands are also much more basic than the aryl NMe₂ groups of the H₂IMes ligand, so gradual protonation of complexes 77 and 78 should afford protonation of these NMe₂ groups before significant protonation at the N-donors occurs.
Synthesis of Catalysts With a SPh Modification to the Carbene Ligand

Previous studies have shown that catalysts containing Ru-carbenes modified with SPh groups are capable of some degree of substrate selectivity under certain conditions. These catalysts have also shown decreased activity when compared to their traditional benzylidene counterparts, though this decreased activity could be an advantage when applied to substrates that exhibit very high metathesis activity since reduced catalyst activity also means a lower degree of side reactions. These properties make the SPh modified Ru-carbene catalysts an interesting alternative to the benzylidene Ru-carbene catalysts which were the main focus of this dissertation for the use in specialty applications. By incorporating NMe$_2$ modified NHC ligand precursors H$_2$ITap or ITap, these phenylthiomethylidene catalysts should also exhibit externally controllable activity and solubility profiles.

Hence, catalyst complexes (H$_2$ITap)(PCy$_3$)$_2$Cl$_2$Ru=CH-SPh 79, and (ITap)(PCy$_3$)$_2$Cl$_2$Ru=CH-SPh 80 (Figure 27) were synthesized from catalyst precursor 24 (Figure 9) using ligand precursor salts 37 and 38 respectively, employing protocols very similar to those employed to generate corresponding benzylidene catalysts. Because SPh precatalysts are much slower initiators than their benzylidene counterparts, complete phosphine-ligand exchange required much more time (4-6 days) to obtain complete conversion to obtain second generation products when compared to the synthesis of catalyst 61. The isolated yields obtained were also lower, with 68% for complex 79 and 78% for complex 80. By reacting these products with excess DMAP, structures 81, (H$_2$ITap)(DMAP)$_2$Cl$_2$Ru=CH-SPh, and 82, (ITap)(DMAP)$_2$Cl$_2$Ru=CH-SPh, were also synthesized (Figure 27) in very high yields (>90%). Dissociation of these DMAP ligands via acid addition was expected to improve catalyst initiation, thereby improving the overall activity of these catalysts.
Suitable crystals were obtained for catalyst complex 81, and its structure in solid state was solved via X-ray crystallography (Figure 28). As expected, analysis of the crystal structure showed that this hexacoordinate complex exhibits a slightly distorted octahedral geometry. When compared with (H₂IMes)(DMAP)₂Cl₂Ru=CH-Ph 83 (Figure 29), a similar NHC-ligand bearing DMAP catalyst complex previously published by the Schanz research group,⁸⁷ the results showed that all bond distances in 81 are slightly shorter (0.01-0.06 Å) than in catalyst 83 with the exception of one of the Ru-Cl bonds. The Ru-N distance to the DMAP trans to the alkylidene was shorter by 0.06 Å in complex 81 than 83, suggesting that this DMAP ligand should be more labile in complex 83 (Table 2). The bond angles also showed a few more significant differences between the structures. First was the trans bond angle between the same DMAP and the Ru-carbene, which was nearly 180° in complex 83 but bent more by 13° in complex 81. The second noticeable difference was the trans angle between NHC ligands and the other DMAP ligand, which was nearly linear in complex 81 but smaller by 15° in complex 83. The differences suggested that less internal geometric strain exists in complex 81.
between the alkylidene and the NHC ligand, very likely due to the presence of the sulfur, which increases the distance between the phenyl group and the metal center, allowing for a tighter arrangement (shorter distances) of the ligands around the Ru-metal center without significantly distorting the octahedral arrangement. This was also reflected by the trans chloride ligands of complex 81, which had nearly identical bond lengths and more linearity to their trans bond angle when compared to those of complex 83.

**Figure 28.** ORTEP Diagram of Catalyst 81

**Figure 29.** DMAP Catalyst Complex 83
Table 2. Selected Bond Angles [°] and Distances [Å] for Catalysts 81 and 83

<table>
<thead>
<tr>
<th></th>
<th>81</th>
<th>83</th>
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<td></td>
<td>2.272 (3)</td>
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</tr>
<tr>
<td>Ru-Cl</td>
<td>2.4132 (9)</td>
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<td></td>
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<td>2.4372 (5)</td>
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<tr>
<td>Cl-Ru-Cl</td>
<td>179.25 (4)</td>
<td>177.54 (2)</td>
</tr>
</tbody>
</table>

Attempts were also made to generate complexes 84, 85, and 86 (Figure 30) using ligand precursor salts 55, 57, and 58, respectively. Though these catalysts would also be low active catalysts, they were expected to exhibit enhanced stability. This quality would have been advantageous for applications in aqueous media upon protonation of the NMe$_2$ groups of their NHC ligands. Unfortunately, none of these ligand precursors afforded complete ligand exchange with catalyst precursor 24, with only 30-70% conversion to product obtained. Attempts to isolate these products from the starting complex were unsuccessful.

Figure 30. Target Complexes 84, 85, and 86
**Synthesis of Indenylidene Catalyst Complexes**

Indenylidene Ru-catalyst complexes are also an attractive alternative to the traditional benzylidene (Grubbs-type) catalysts. These catalysts are easily obtained via acid-catalyzed rearrangement of the C=C=C spine of allenylidene catalysts structures, which makes them as commercially attractive as their allenylidene counterparts. Many of these complexes display high activity, though they are often not quite as active as benzylidene catalysts. Their main advantage over most of their benzylidene counterparts is their high thermal stability, which makes them the preferred catalysts for many applications, in particular at elevated temperatures.

Another advantage is the stability of the (PPh₃)₂Cl₂Ru-3-phenyldienylidene precursor catalyst 21. Hence, catalyst modifications may avoid the use of the expensive PCy₃ ligand, which usually is sacrificed in later catalyst modifications. So far, the only indenylidene complexes that could be generated in the project were made using ITap ligand precursor salt 38. To synthesize these complexes, phenylindenylidene parent complex 21 was first synthesized according to literature procedure. Complex 21 was then used to generate (ITap)(PPh₃)Cl₂Ru-3-phenyldienylidene 87 in moderate yield (67%) via phosphine ligand exchange. An excess of DMAP was then added to this complex to generate (ITap)(DMAP)₂Cl₂Ru-3-phenyldienylidene 88, which was afforded in 87% yield (Scheme 21). For complexes 87 and 88 the protonation of their pH-responsive groups was expected to change their solubility and activity. They were also expected to exhibit higher thermal stability than benzylidene counterparts 67 and 69.
**Scheme 21.** Synthesis of Phenyl Indenyldene Catalyst Complexes 87 and 88

For this dissertation, many different catalyst structures were attempted. Most of these were benzylidene-carbene (Grubbs-type) catalysts, though other alkylidene motifs were also explored. All of the catalysts generated bear pH-responsive NMe₂ modified NHC ligands, though some also possess pH-responsive DMAP or 3-(o-pyridyl)propyldiene N-donor ligands. In all, a total of 16 new catalyst complexes were synthesized, isolated, and characterized. Most of these were generated using H₂ITap or iTap ligands precursor salts 37 and 38. Catalysts made with ligand precursor salts 55-58 proved much more difficult to synthesize and isolate, and hence, they are only found in three of the new catalyst structures.
CHAPTER IV
KINETIC STUDIES IN ORGANIC MEDIA

Substrates and Methods for Relative Kinetic Studies in Organic Media

To assess the basic olefin metathesis activity for each of the new catalysts described in Chapter III, ROMP and RCM reactions were conducted in organic media. The substrates selected for these studies were chosen in order to avoid competing secondary metathesis reactions. The activity of the new catalysts was compared to commercially available catalysts under the same reaction conditions. Relative kinetic studies for some of these catalysts were also conducted in the presence of acid to assess the change in catalyst solubility and activity afforded by their pH-responsive ligands upon protonation.

The substrates selected for ROMP reactions in organic media included cyclooctene (COE) and exo-7-oxanorbornene derivative 89 (Scheme 22). Experiments with COE were conducted small scale in an NMR tube, and the progress of the reaction was directly monitored via $^1$H NMR.$^{79}$ To monitor conversion of norbornene substrate 89 to poly-89, kinetic studies were conducted by quenching aliquots of a reaction solution collected over specific time intervals with ethyl vinyl ether,$^{20}$ which were then individually analyzed via $^1$H NMR spectroscopy after solvent removal. The relative amounts of monomer and polymer present were determined by integration of the sufficiently separated monomer and polymer signals for select hydrogen atoms of each substrate at specific time intervals. Unless otherwise stated, all ROMP reactions were conducted in benzene with [Ru] = 0.5 mM and 0.5% catalyst loadings. In a few reactions, polymers were produced on a larger scale and isolated according to literature procedures.$^{64}$ The isolated polymers were then analyzed via gel permeation chromatography (GPC) to determine the average molecular weights and polydispersity indices (PDIs) of the
polymers produced in order to establish the degree of control and initiation efficiency provided under specific conditions.

**Scheme 22.** ROMP Substrates

For RCM reactions, diethylallylmalonate (DEDAM) and 3,3-diallylpentane-2,4-dione (DAP) were the substrates chosen for kinetic studies in organic media (Scheme 23). These two substrates dramatically favor their cyclopentene RCM products 90 and 91 over all other olefin metathesis products under most reaction conditions. For these substrates, as with COE, small-scale reactions were monitored directly in an NMR tube, and conversion to product was determined via $^1$H NMR by integration of sufficiently separated substrate and product signals for their allylic hydrogens. Unless otherwise stated, these reactions were conducted in benzene with [Ru] = 1.0 mM and 1.0% catalyst loadings. It has been established that terminal olefins, such as those found in DEDAM and DAP, are generally more reactive substrates for olefin metathesis than the 1,2-disubstituted olefins used in ROMP, therefore initiation is faster in RCM than in ROMP. This increase in activity, however, does come at a price, as many RCM reactions never reach full conversion to product due to the formation of unstable Ru-methylidene intermediate complexes that degrade noticeably in the reaction solution, in particular when the RCM activity is low. According to our observations, DMAP ligated catalysts generally exhibit faster decomposition in RCM reactions than other pyridine complexes. The reason for this is not known for certain, but the elevated nucleophilicity of the DMAP in comparison to far less basic pyridines is likely the most important factor. The result is a very low stability for the corresponding Ru-methylidene complex generated during the RCM reaction.
Scheme 23. RCM Substrates

Once ROMP and RCM kinetic profiles were obtained for each of the new catalysts, they were then compared to those obtained for commercially available catalysts under similar reaction conditions. The commercially available catalysts selected were Grubbs second generation catalyst 12 and Hoveyda-Grubbs catalyst 13 (Figure 31). These catalysts were chosen not only for their structural similarity to many of the catalysts that were examined, but also because they are widely used for commercial applications. Therefore, catalysts 12 and 13 provide a standard for comparing the relative profiles of the new catalysts, based on their modified NHC ligands.

Figure 31. Commercially Available Catalysts 12 and 13

After obtaining kinetic profiles under standard, non-acidic conditions, many of these studies were repeated in the presence of various equivalents of acid. The two acids that were chosen include H₃PO₄ and p-toluenesulfonic acid (TsOH). Non-nucleophilic acids were chosen because they do not significantly affect the coordination at the Ru-center, which is sometimes observed in the presence of nucleophilic acids. These studies were conducted to determine the degree of external control on the solubility and activity profiles for these catalysts afforded via protonation of their pH-responsive ligands. Specific emphasis was placed on the study of ROMP kinetic profiles,
particularly on the rates of initiation and propagation relative to those acquired under standard conditions, to evaluate the change in activity upon protonation of the pH-responsive groups.

Kinetic Studies

*Kinetic Studies of Benzylidene Catalysts Bearing an H$_2$ITap Ligand*

The first two catalysts evaluated using ROMP and RCM reactions were (H$_2$ITap)(PCy$_3$)Cl$_2$Ru=CH-Ph 61 and (H$_2$ITap)Cl$_2$Ru=CH-(C$_6$H$_4$-O-iPr) 62 (Figure 32). Their catalytic activity was then compared to that of commercially available catalysts 12 and 13 under similar reaction conditions. Since the overall structure of catalysts 61 and 62 were very similar to their commercially available counterparts, they were expected to exhibit similar activity profiles under standard conditions. Any differences in activity were attributed to the electronic effects afforded by the NMe$_2$ groups of their H$_2$ITap ligands.

![Fig 32. Complexes 61 and 62](image)

Relative kinetic results showed that both H$_2$ITap catalysts 61 and 62 were very active in olefin metathesis and performed ROMP of COE with similar activity to their commercially available counterparts (Figure 33). Evaluation of the kinetic profiles suggested that catalyst 62 had a faster rate of initiation, as catalyst 13 exhibited a significantly longer induction period before the dramatic rate increase was observed. Such long induction times are typical for slow-initiating but fast-propagating olefin metathesis catalysts and thus strongly affect the overall reaction rates. The kinetic results also showed that both PCy$_3$ ligated complexes 12 and 61 initiated at significantly faster rates than Hoveyda-Grubbs-type catalysts 13 and 62.
RCM reactions of DEDAM were then conducted in benzene (Figure 34).

Examination of these kinetic profiles showed catalysts 12 and 61 performed at nearly identical rates. As with the ROMP reactions, both of these catalysts exhibited a much faster rate of initiation, as shown by the faster initial conversion, compared to catalysts 13 and 62. Interestingly, commercially available catalyst 13 was slightly more active than catalyst 62 in the RCM reaction, which is in contrast to the performances observed for the ROMP reaction. It should be noted that catalysts 12 and 13 are considered highly active olefin metathesis catalysts,\textsuperscript{22,51} therefore the kinetic results from both the ROMP and RCM reactions mean that catalysts 61 and 62 also belong in the same category.
To evaluate the effect of protonation of the NMe₂ groups of the H₂ITap ligand on the activity profile of catalysts 61 and 62, additional ROMP reactions using exo-7-oxanorbornene derivative 89 were conducted in the presence of variable amounts of p-toluenesulfonic acid (TsOH).\(^{88}\) TsOH was chosen for this study because it is a non-nucleophilic acid that does not cause precipitation of the catalysts from the organic reaction medium via formation of an insoluble salt. These reactions were conducted in 1.0 mM catalyst solutions with 1.0 % catalyst loadings in polar organic solvents (CD₂Cl₂ and CDCl₃) to maintain solubility of the protonated species. The results (Figures 35 and 36) showed that the rate of ROMP conversion for both catalysts slowed dramatically with increasing equivalents of acid. This was counterintuitive to all previous reports, where addition of acid to a Ru-based olefin metathesis catalyst accelerated the overall rate.\(^{58a,64,77,89}\)

The effect of different substitution in the 4-position of the phenyl rings on the NHC ligand properties has been studied by Plenio et al. by generating a small library of symmetric and unsymmetric ligands.\(^{84,90}\) Through these studies, it was found that the
change from electron-withdrawing to donating groups in the phenyl-para position had a significant impact on the redox potentials of Ir and Ru complexes. NHC-Ir complexes bearing σ-donating NEt₂ groups had the lowest cathodic redox potential in the series indicating significantly enhanced donating properties of this ligand.⁸⁹b This effect also translated into elevated RCM and CM activities of the corresponding NHC-Ru carbene complexes.⁸⁴ In light of this information, we hypothesized that transformation of the π-donating NMe₂ group into a σ-withdrawing NMe₂H⁺ moiety must have caused significant electronic changes in the H₂ITap ligand that also impacted the overall catalyst’s electronic environment and thus caused reduced metathesis activity. This allowed for a novel and unique external activity control for the ROMP reaction via degree of protonation.

![Figure 35. ROMP of 88 With Catalyst 61 in CD₂Cl₂](image_url)

Figure 35. ROMP of 88 With Catalyst 61 in CD₂Cl₂ ([Ru] = 1.0 mM, 1.0% Catalyst Loading, Room Temperature)
To determine whether the observed deceleration of the ROMP reaction with complexes 61 and 62 upon acid addition was mostly due to a change initiation rate or propagation rate, poly-89 was also produced on a larger scale under identical reaction conditions as the kinetic investigations and analyzed by GPC analysis (Table 3). Due to the unfavorable ratio of the rates of initiation and propagation, the H$_2$IMes ligated catalysts 12 and 13 do not promote controlled ROMP, meaning that the polymer molecular weights obtained with these catalysts are substantially higher than the theory.$^{51}$ Since catalysts 61 and 62 exhibit a similar reactivity profile, the measured average molecular weights (M$_{p}$) of poly-89 (Table 3) in the absence of acid were likewise significantly larger (> 150,000 for catalyst 61, 80,000 for catalyst 62) than the theory (27,600), indicating incomplete initiation under these reaction conditions (Table 3). However, with increased TsOH amounts present in the ROMP reaction, the average molecular weights of the polymers produced grew progressively smaller. For catalyst 61, the M$_{p}$ was reduced to 55,500 (approx. one third of the M$_{p}$ obtained for the acid-free ROMP) when two equivalents of TsOH was added. For catalyst 62, the addition of 1.6
equiv. of TsOH produced poly-89 with an $M_p$ of 34,600, which is very close to the theoretical value. Further addition of TsOH reduced the molecular weights far below the theoretical value, which was partially due to incomplete polymerizations attributed to catalyst decomposition. The improved molecular weight control indicates that the acid addition mostly affected the rates of propagation, which resulted in more favorable $k_{\text{initiation}} / k_{\text{propagation}}$.

Table 3. GPC Results for ROMP Polymers (Poly-89) From TsOH Studies

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>TsOH (equiv.)</th>
<th>Time [min] (&gt;95% conv.)</th>
<th>$M_p$ (theory)</th>
<th>$M_p$ (GPC)</th>
<th>$PDI$</th>
</tr>
</thead>
<tbody>
<tr>
<td>61&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>14</td>
<td>27,600</td>
<td>&gt; 150,000</td>
<td>1.23</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>32</td>
<td></td>
<td>138,700</td>
<td>1.34</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>56</td>
<td></td>
<td>141,000</td>
<td>1.31</td>
</tr>
<tr>
<td></td>
<td>1.2</td>
<td>210</td>
<td></td>
<td>119,200</td>
<td>1.33</td>
</tr>
<tr>
<td></td>
<td>1.6</td>
<td>600</td>
<td></td>
<td>95,900</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>-</td>
<td></td>
<td>55,500</td>
<td>1.73</td>
</tr>
<tr>
<td>62&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0</td>
<td>8</td>
<td>80,000</td>
<td>80,000</td>
<td>1.64</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>14</td>
<td>75,300</td>
<td></td>
<td>1.57</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>20</td>
<td>68,200</td>
<td></td>
<td>1.52</td>
</tr>
<tr>
<td></td>
<td>1.2</td>
<td>24</td>
<td>66,800</td>
<td></td>
<td>1.46</td>
</tr>
<tr>
<td></td>
<td>1.6</td>
<td>60</td>
<td>34,700</td>
<td></td>
<td>1.63</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>100</td>
<td>9,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>1.8</td>
</tr>
</tbody>
</table>

<sup>a</sup> with CH$_2$Cl$_2$ as solvent; <sup>b</sup> with CHCl$_3$ as solvent; <sup>c</sup> incomplete polymerization attributed to catalyst decomposition

Slowing the propagation in olefin metathesis usually is not desired for most applications since it reduces the activity and also the potential turnover numbers, making the reaction less efficient. However, decreased propagation rates can be advantageous for controlled ROMP reactions, where a low propagation/initiation ratio is desired to ensure a simultaneous start of all growing polymer chains. Unfortunately the PDIs for the polymers produced in these reactions did not give a consistent picture of the improved ROMP control that was expected with the improved propagation control of catalysts 61 and 62 upon the addition of TsOH. Catalyst 62 exhibited the expected development of the PDIs for the better controlled ROMP reactions with increasing acid amounts present.
during the polymerization up to 1.2 equivalents of TsOH were added, reducing the values from 1.64 to 1.46. Further increase of the TsOH amount then led to a higher PDI’s again (1.8 for 2.0 equiv. of acid). For catalyst 61, the increased ROMP propagation control was not reflected in lower PDIs. However, the “uncontrolled” ROMP with the acid-free catalyst produces a polymer with an amazingly low PDI of 1.23, which is in stark contrast to the high experimental $M_p$. The PDIs then gradually increased to 1.73 with increased TsOH amounts present during the reaction. Very likely, despite the lowered propagation rates, the ROMP reaction with catalysts 61 and 62 was not sufficiently controlled to give well-defined polymeric materials.

To confirm these findings of the external propagation control with acid, DFT calculations performed by Dr. Yong Zhang (The University of Southern Mississippi) were used to determine the Mulliken atomic charges for model complexes 93, 93a and 93b (Figure 37) which bear a PMe$_3$ ligand instead of the PCy$_3$ ligand and differ in the degree of protonation at the H$_2$ITap ligand (Table 4). The charges were calculated using a B3LYP method with a large basis (6-311++G(2d.2p)) for first coordination shell atoms on geometries optimized by using the mPW1PW91/sdd method (details in Chapter VIII), which were found to give good predictions of geometric and electronic properties for late transition metal complexes.$^{91}$ A recent report described a correlation between the Mulliken atomic charges at the metal center in Ru-carbene complexes and the rate of metathesis initiation.$^{92}$ In this report it was demonstrated that the Ru-center in slow-initiating Grubbs’ second generation catalyst 12 in fact is more positively charged than in fast-initiating Grubbs’ first generation catalyst 9. This was used as a rational to explain the influence of the remaining donor ligand (NHC versus PCy$_3$) on the dissociation rates of the other PCy$_3$ ligand which determines the initiation rate. For this reason, the calculations also included catalysts 91 and 92 (Figure 37), the PMe$_3$-ligated counterparts
of complexes 9 and 12, for comparison. Similar to the reported calculations,\textsuperscript{92} the Ru-center was found to be more positively charged in the NHC ligated complex 92 than in complex 91. The Mulliken atomic charges for the Ru-center in complex 93 were nearly identical to complex 92 which was not surprising with respect to the similar activities for catalysts 12 and 61 in the ROMP and RCM reactions. More interestingly, the charges became less positive with increasing protonation to complexes 93a and 93b, however, these charges were still more positively charged than complex 91. This was somewhat surprising since the H$_2$ITap ligand became positively charged and thus an increase in the charge at the metal center was expected. Following the rational of the previous calculations,\textsuperscript{92} it can only mean that the $\pi$-acceptor capability of the H$_2$ITap ligand was reduced upon protonation. These results also meant that the initiation rates of model complexes 93a and 93b should not be lower in comparison to complex 93. Therefore, these calculations confirmed that the reduced overall activity exhibited by gradual protonation of catalysts 61 and 62 was a result of slower ROMP propagation.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{complexes.png}
\caption{Complexes Used for DFT Calculations}
\end{figure}
<table>
<thead>
<tr>
<th>complex</th>
<th>$q_{MK}$</th>
<th>$\Delta q_{MK}(90)$</th>
<th>$\Delta q_{MK}(91)$</th>
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<tbody>
<tr>
<td>91</td>
<td>0.313</td>
<td>-</td>
<td>-0.621</td>
</tr>
<tr>
<td>92</td>
<td>0.834</td>
<td>+0.621</td>
<td>-</td>
</tr>
<tr>
<td>93</td>
<td>0.851</td>
<td>+0.638</td>
<td>+0.017</td>
</tr>
<tr>
<td>93a</td>
<td>0.831</td>
<td>+0.618</td>
<td>-0.003</td>
</tr>
<tr>
<td>93b</td>
<td>0.712</td>
<td>+0.499</td>
<td>-0.122</td>
</tr>
</tbody>
</table>

As further proof, the relative initiation rates for complexes 61 and 62 were determined experimentally without and in the presence of TsOH. This was accomplished by monitoring the conversion of the Ru-species with ethylvinyl ether (EVE). The reaction affords only one turnover to form the metathesis-inactive Fischer-carbene complexes 93 (Scheme 24) and hence is only dependent on the metathesis initiation. We monitored the changes for the $^1$H NMR signal for the benzylidene-H atom ($\delta = 19.02$ ppm for 61; $\delta = 16.80$ ppm for 62). PCy$_3$-containing complex 61 was converted into the respective ethoxymethylidene species 94 which was observed via the methylidene-H signal at $\delta = 13.73$ ppm. Reactions with TsOH did not afford a stable ethoxymethylidene complex containing a $^1$H NMR signal which could be reliably integrated. With TsOH, a species at $\delta = 13.73$ ppm was observed with complex 61, however, over time the signal disappeared, very likely due to degradation. Complex 62 solutions generated multiple broad signals in the range between 9 and 16 ppm in the presence of EVE. Hence, the conversion was monitored by the reduction of the benzylidene-H signal versus an internal standard in these reactions.

Scheme 24. Conversion of Catalysts 61 and 62 with EVE into Ethoxymethylidene Complexes 94
As expected, the catalyst conversion increased slightly with increased acid amounts. Only 24% of catalyst 61 initiated in 60 min without TsOH, but the presence of 1 equivalent of TsOH afforded 52.7% conversion. With 2 equiv. of TsOH, > 50% conversion was reached after 5 min, but after 30 min a plateau at 67% conversion was observed (Figure 38), most likely a result of catalyst decomposition. Catalyst 62 generally exhibited faster initiation than catalyst 61, though the differences in the conversion of EVE in the presence of TsOH were much less pronounced (Figure 38). However, the overall trend showed that the EVE conversion proceeded marginally faster at higher acid concentrations. For example, after 6 min complex 62 was converted by 52.0% (acid-free), 58.2% (1 equiv. TsOH) and 63.3% (2 equiv. TsOH). All conversions with complex 62 went > 95%. These results, when combined with the results from the ROMP reactions and DFT calculations, unambiguously show the decreased activity observed for catalysts 61 and 62 was exclusively due to a decrease in propagation rate. To the best of our knowledge, this is the first example of external control of the ROMP propagation rates, almost independent from the initiation values.

Figure 38. Conversion of Catalysts With 100 Equivalents EVE
a) Catalyst 61 [Ru] = 4 mM, CD2Cl2, 20 °C, b) Catalyst 62 [Ru] = 2 mM, CDCl3, 20 °C
The next benzylidene catalyst bearing a pH-responsive H$_2$ITap ligand examined was DMAP catalyst 65, or (H$_2$ITap)(DMAP)$_2$Cl$_2$Ru$\equiv$CH-Ph. Because this catalyst had multiple protonation sites, we expected gradual protonation with non-nucleophillic acid would produce several complexes (65, 65a, and 65b), each with a different ROMP reaction activity profile (Scheme 25), allowing for external control of catalyst activity via acid addition. The order of anticipated protonation was based on the approximate pKa values of the conjugate acids for the pH responsive ligands, with the more basic DMAP ligands (DMAPH$^+$ pKa = 9.2) dissociating before protonation of the aryl amines (aryl ammonium pKa ~ 4-6). In contrast to catalysts 61 and 62, this catalyst was expected to exhibit lower olefin metathesis activity than commercially available catalyst 12 under standard, non-acidic conditions due to the presence of the inhibiting DMAP ligands. Upon dissociation of these DMAP ligands via addition of two equivalents of non-nucleophillic acid, highly active, fast initiating complex 65b would then be formed. Acid addition beyond two equivalents would then protonate the NMe$_2$ groups, thereby slowing catalyst propagation, as seen with catalyst 61 and 62.

Scheme 25. Gradual Protonation of Catalyst Complex 65

The anticipated activity profile for catalyst complex 65 was confirmed by performing ROMP reactions of COE with zero, two, and four equivalents of H$_3$PO$_4$ (Figure 39). Catalyst complex 65 displayed slightly lower activity than commercially
available catalyst complex 12 under similar reaction conditions. Based on previous studies by the Schanz research group, the high ROMP activity of hexacoordinate NHC(DMAP)$_2$Ru alkylidene complexes is caused by relatively fast initiation rates compared to catalysts 12 but slower propagation$^{64}$. As expected, upon the addition of two equivalents of H$_3$PO$_4$, catalyst activity for complex 65 was greatly enhanced, dramatically exceeding the activity for catalyst 12, with 96.8% conversion to ROMP polymer achieved within 15 minutes. Upon protonation of the DMAP ligand, the predicted effect was observed, generating species 65a with significantly faster initiation and propagation. When four equivalents of H$_3$PO$_4$ were added, the initial activity observed for catalyst 65b were very similar to those seen with catalyst 12, however the conversion quickly reached a plateau and precipitation of the catalyst complex was observed, resulting in only 41.3% conversion to polymer after 30 minutes. It is likely that the precipitation was a result of rapid degradation of the fast initiating species 65b.

Figure 39. ROMP of COE With Complexes 12, 65, 65a, 65b
[Ru] = 0.5 mM, 0.5% Catalyst Loading, 20 °C
Table 5. RCM of DEDAM With Catalysts 12 and 65

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Equivalents of H₃PO₄</th>
<th>Time (min)</th>
<th>% Conversion to Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>0</td>
<td>3</td>
<td>1.2</td>
</tr>
<tr>
<td>12</td>
<td>0</td>
<td>15</td>
<td>15.8</td>
</tr>
<tr>
<td>12</td>
<td>0</td>
<td>30</td>
<td>30.2</td>
</tr>
<tr>
<td>65</td>
<td>0</td>
<td>3</td>
<td>1.9</td>
</tr>
<tr>
<td>65</td>
<td>0</td>
<td>30</td>
<td>7.2</td>
</tr>
<tr>
<td>65a</td>
<td>2</td>
<td>3</td>
<td>31.5</td>
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<tr>
<td>65a</td>
<td>2</td>
<td>15</td>
<td>43.5</td>
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<td>65b</td>
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</tr>
<tr>
<td>64b</td>
<td>4</td>
<td>15</td>
<td>13.3</td>
</tr>
<tr>
<td>64b</td>
<td>4</td>
<td>30</td>
<td>14.4</td>
</tr>
</tbody>
</table>

RCM reactions of DEDAM with catalyst 65 (Table 5) confirmed the change in the activity and solubility tends observed in the ROMP reactions. For the RCM reactions, catalyst 65 displayed noticeably lower RCM activity than catalyst 12 in the absence of acid, rather than the comparable activity seen in the ROMP reactions. Once again, upon addition of two equivalents of H₃PO₄ the activity rate of catalyst 65 initially increased beyond catalyst 12, however, this was soon followed by significant catalyst degradation which was observed as a plateau in conversion within 15 minutes, as well as significant precipitation of the catalyst. With four equivalents of H₃PO₄, decreased activity and significant catalyst precipitation was observed, similar to the ROMP reaction. This once again implies that the fast-initiating catalyst species most likely degraded quickly in solution.

Catalyst 66, or (H₂ITap)Cl₂Ru(=CH-CH₂-CH₂-C₅H₄N), was the final benzylidene catalyst bearing an H₂ITap ligand that was evaluated. This catalyst contained a pH-responsive, backbiting 3-(o-pyridyl)propyldene N-donor ligand in addition to the NMe₂ groups of its NHC ligand. We hypothesized that this back-biting ligand would cause very low catalyst activity until protonation via addition of excess non-nucleophilic acid caused dissociation of the coordinated nitrogen from the metal center, thereby forming activated
catalyst complex 66a (Scheme 26). The anticipated degree of inhibition afforded by the 3-(o-pyridyl)propylidene in catalyst 66 was expected to be much greater than the inhibition observed with the DMAP ligands of catalyst 65. Unlike catalyst 66, gradual protonation studies were not conducted with catalyst 66 because the aryl NMe₂ groups and the N-donor ligand were expected to exhibit similar pKa values, therefore gradual protonation would most likely have produced a mixture of complexes, each with a different kinetic profile.

**Scheme 26. Activation of Catalyst Complex 66**

Kinetic profiles obtained for ROMP of COE (Figure 40) with catalyst 66 confirmed that stronger inhibition of catalyst activity was observed for catalyst 66 than seen for DMAP catalyst 65. As expected, with the addition of four equivalents of H₃PO₄ an increase in activity was observed. This was most likely due to an increase in initiation, but because protonation of the NMe₂ groups also reduce the catalyst’s propagation rates, complex 66a still performs at lower rates than those seen for catalysts 12 and 61. Catalyst 66 also displayed lower activity than catalyst 62, but upon acidification complex 66a displayed significantly increased rates initiation compared to catalyst 62, as indicated by the sudden increase in ROMP activity, which is present from the very beginning of the reaction with complex 66a. Also, as with complex 65b, significant precipitation of the catalyst complex was observed, which implies that fast-initiating complex degrades quickly.
Figure 40. ROMP of COE With Complexes 12, 61, 62, 66, and 66a
[ Ru ] = 0.5 mM, 0.5% Catalyst Loading, 20°C

RCM of DEDAM was also conducted with catalyst 66. Conversion rates with DEDAM in the absence of H₃PO₄ of complex 66 were very low, with only 6.2 % conversion to product observed after 30 minutes. The addition of excess H₃PO₄, afforded only a slight improvement, with 12.9% conversion after 30 minutes. Once again, precipitation of the catalyst was observed, which likely accounted for the extremely low rate of RCM conversion observed with complex 66a.

Kinetic Studies of Benzylidene Catalysts Bearing ITap Ligands

The next catalysts studied in the standard ROMP and RCM reactions in organic media were benzylidene catalysts 67-69 bearing ITap ligands (Figure 41). Since catalysts with unsaturated NHC ligand backbones are generally less active than their counterparts with saturated backbones,¹¹ (ITap)(PCy₃)Cl₂Ru=CH-Ph 67, (ITap)Cl₂Ru=CH-(C₆H₄-O-iPr) 68, and (ITap)(DMAP)₂Cl₂Ru=CH-Ph 69 were expected to perform ROMP of COE and RCM of DEDAM at much slower rates than observed with unsaturated analogues 61, 62, and 65. ROMP and RCM kinetic results at room temperature confirmed this hypothesis (Tables 6 and 7). Because catalysts with
unsaturated backbones tend to exhibit enhanced thermal stability, kinetic studies were also conducted at elevated temperature (60 °C) with catalyst 67 and 69. This elevated temperature provided an extraordinary improvement in the conversion rates for ROMP of COE with both of these catalysts, as well as a superior RCM reaction for phosphine-ligated catalyst 67. Acceleration of kinetic rates at elevated temperature was expected and has been demonstrated before with other catalyst systems.\textsuperscript{51,67,68} However, the activity was improved by at least two orders of magnitude, and the overall activity is significantly higher than the activity of catalysts 12 and 13 at ambient temperature. This is without precedence for this moderate temperature increase. Very likely, most of this activity jump is caused by much elevated initiation rates, thus generating a larger number of active species.

![Catalyst Complexes 67-69](image)

**Figure 41.** Catalyst Complexes 67-69

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Time (min)</th>
<th>Temperature (°C)</th>
<th>% Conversion to Polymer</th>
</tr>
</thead>
<tbody>
<tr>
<td>67</td>
<td>60</td>
<td>20</td>
<td>8.5</td>
</tr>
<tr>
<td>67</td>
<td>120</td>
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</tr>
<tr>
<td>69</td>
<td>5</td>
<td>60</td>
<td>95.5</td>
</tr>
</tbody>
</table>

**Table 6.** ROMP of COE With Catalysts 67-69

\([\text{Ru}] = 0.5 \text{ mM, 0.5\% Catalyst Loading}\)
Table 7. RCM of DEDAM With Catalysts 67-69

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Time (min)</th>
<th>Temperature (˚C)</th>
<th>% Conversion to Product</th>
</tr>
</thead>
<tbody>
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<td>67</td>
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<td>6</td>
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<td>64.7</td>
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<td>120</td>
<td>20</td>
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<tr>
<td>69</td>
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<td>30.6</td>
</tr>
</tbody>
</table>

**Kinetic Studies of Benzylidene Catalysts Bearing Other pH-Responsive Ligands**

Kinetic studies in organic media were also conducted with 

(IXyONMe$_2$)(PCy$_3$)$_2$Ru=CH-Ph 70, (IDippONMe$_2$)(DMAP)Cl$_2$Ru=CHPh 77, and 

(IDippSNMe$_2$)(DMAP)$_2$Cl$_2$Ru=CH-Ph 78 (Figure 42) to establish their metathesis activity under standard conditions. Though the electronic influence of the NMe$_2$ groups of these catalysts was considered minimal with these catalysts, it was unknown how the steric of these bulky NHC ligand precursors would affect the metathesis activity of the catalyst.

DMAP catalysts 77 and 78 were expected to have lower metathesis activity than Grubbs second generation catalyst 12, since this has been previously observed for analogous IMes ligated DMAP complex 83. This catalyst exhibited a reduced rate for ROMP od COE by a factor of 0.57 from those observed for homologous catalyst 12. 87
A study of the relative kinetic profiles obtained through ROMP of COE showed catalysts 70, 77, and 78 each have lower ROMP metathesis activity than catalyst 12 (Figure 43). Compared to the other catalysts, complex 70 exhibited a much lower rate of initiation, as seen by the delay in initial conversion, as well as an unexpectedly low ROMP activity compared to complex 12. Catalysts 77 and 78 exhibited nearly identical activities, as was expected by their very similar structure. They were faster in the ROMP reaction than complex 70, and showed only slightly lower activity than seen with catalyst 12, though this decrease in activity was much less than what was previously reported for complex 83. However, the activities of 77 and 78 were not quite unexpected. Although DMAP Ru-alkylidene complexes are generally slower than their second generation counterparts, the bulky o-iPr groups in the NHC ligand have been shown to accelerate both the rates of initiation and propagation compared to their o-CH3 substituted counterparts. Furthermore, the pentacoordinate structure containing only one DMAP ligand is also expected to generate a lower amount of free DMAP in the reaction mixture, and it was shown that increased amounts of N-donor ligand reduced the conversion rates in ROMP reactions with Ru-alkylidene complexes. Hence, the reduced reactivity
due to the presence of the DMAP ligand in these catalysts was more than compensated by the bulkier NHC ligand and the low DMAP content of the catalyst. Therefore, these catalysts exhibited a higher activity than catalyst 70.

The RCM reactions with DEDAM exhibited a markedly different activity trend for this group of catalysts (Table 8). Catalyst 78 dramatically outperformed catalyst 12, with >95% conversion within one hour. Catalyst 77 accomplished only 36.5% conversion observed at one hour, which was slightly less than standard setting catalyst 12. This difference in activity between catalysts 77 and 78 was unexpected due to their structural similarities as well as the nearly identical activity seen in their ROMP reactions. Catalyst 70 displayed very little RCM metathesis activity, with only 2.1% conversion observed within the same time frame, indicating the very slow initiation also observed in the ROMP reaction.

Table 8. RCM Reactions of DEDAM With Catalysts 12, 70, 77, and 78

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Time (min)</th>
<th>% Conversion to Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>60</td>
<td>46.1</td>
</tr>
<tr>
<td>70</td>
<td>60</td>
<td>2.1</td>
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<td>77</td>
<td>60</td>
<td>36.5</td>
</tr>
<tr>
<td>78</td>
<td>56</td>
<td>95.2</td>
</tr>
</tbody>
</table>
Kinetic Studies of Phenylthiomethylidene (Ru=CH-SPh) Catalysts

Previous studies of phenylthiomethylidene (Ru=C-SPh) catalysts have shown that these catalysts perform at much slower rates than their benzylidene counterparts in ROMP and RCM metathesis reactions. As such, the activity profiles for (H₂Ir)(PCy₃)₂Cl₂Ru=CH-SPh 79, (Ir)(PCy₃)₂Cl₂Ru=CH-SPh 80, (H₂Ir)(DMAP)₂Cl₂Ru=CH-SPh 81, and (Ir)(DMAP)₂Cl₂Ru=CH-SPh 82 were expected to show much lower activity in ROMP and RCM reactions than observed with their benzylidene counterparts, complexes 61, 65, 67, and 69, respectively. The experimental data supports this prediction, with very little activity observed for most of these complexes at room temperature (Tables 9 and 10). When these reactions were repeated at elevated temperatures, all of these catalysts displayed dramatically improved metathesis activity, which should be attributed mostly to an increase of catalyst initiation rates. It should be mentioned that the nature of the alkylidene group only influences the initiation, since the first metathesis turnover generates the same propagating species from different Ru-alkylidene catalysts. Hence, once initiated, these catalysts should exhibit the same activity as their otherwise equally ligated counterparts which display much faster metathesis reactions at ambient temperature as seen throughout this chapter. For catalyst 81, two and four equivalents of H₃PO₄ were added, and the ROMP and RCM reactions were monitored at both 20°C and 60°C. This was implemented in an effort to improve catalyst activity by means of dissociation of the DMAP ligands, however no metathesis activity was observed in any of these reactions with acid, likely due to catalyst degradation in the presence of acid. Since no metathesis activity was observed for these reactions, it is likely that complex 81a, formed upon dissociation of the DAMP ligand, rapidly decomposed following the known dimerization pathway, in particular if this process for this pathway is faster than the first catalyst turnover (Scheme 27).
Figure 44. Catalyst Complexes 79-82

Table 9. ROMP Reactions of COE With Catalysts 79-82
[Ru] = 0.5 mM, 0.5% Catalyst Loading

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Time (min)</th>
<th>Temperature (°C)</th>
<th>% Conversion to Polymer</th>
</tr>
</thead>
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<td>79</td>
<td>24</td>
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<td>80</td>
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<td>39.6</td>
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<tr>
<td>80</td>
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<td>20</td>
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<td>60</td>
<td>60</td>
<td>77.0</td>
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<td>60</td>
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Table 10. RCM Reactions of DEDAM With Catalysts 79-82

<table>
<thead>
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<th>Catalyst</th>
<th>Time (min)</th>
<th>Temperature (˚C)</th>
<th>% Conversion to Product</th>
</tr>
</thead>
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<tr>
<td>82</td>
<td>60</td>
<td>60</td>
<td>16.7</td>
</tr>
</tbody>
</table>

Scheme 27. Failed Initiation of Catalyst 81 With H₃PO₄

*Kinetic Studies of Indenylidene Catalyst Complexes*

The final catalysts tested in organic media were (ITap)(PPh₃)Cl₂Ru-3-phenylindenylidene 87 and (ITap)(DMAP)₂Cl₂Ru-3-phenylindenylidene 88 (Figure 45). Because indenylidene catalyst structures typically exhibit enhanced thermal stability when compared to their benzylidene counterparts, we hypothesized that these catalysts would remain stable under acidic conditions as well as at elevated temperatures. As such, ROMP and RCM reactions were conducted with catalyst under acidic conditions and at elevated temperature (60 ˚C) in addition to the standard kinetic studies. For catalyst complex 87, results showed this complex exhibited very low activity in both ROMP and RCM reactions (Tables 12 and 13). Additionally, reactions conducted at elevated temperatures did not afford any metathesis products, most likely due to an
advanced rate of decomposition. This was in very stark contrast to results observed for benzylidene counterpart 67, which showed a dramatic increase in activity at elevated temperature. The addition of H₃PO₄ did improve the metathesis activity for complex 87, though faster rates of catalyst degradation were also observed, which resulted in a lower overall yield in the ROMP reaction.

![Figure 45. Phenylindenylidene Catalyst Complexes 87 and 88](image)

**Table 11. ROMP Reactions of COE With Catalyst Complex 87**

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Equivalents of H₃PO₄</th>
<th>Time (h)</th>
<th>% Conversion to Polymer</th>
</tr>
</thead>
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<td>&lt;1</td>
</tr>
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<td>0</td>
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<td>&lt;1</td>
</tr>
<tr>
<td>20</td>
<td>2</td>
<td>5</td>
<td>10.6</td>
</tr>
</tbody>
</table>

**Table 12. RCM Reactions of DEDAM With Catalyst Complex 87**

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Equivalents of H₃PO₄</th>
<th>Time (h)</th>
<th>% Conversion to Product</th>
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<td>&lt;1</td>
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<td>0</td>
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<td>3</td>
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Since the DAMP ligands of catalyst complex 88 are much more basic than the aryl NMe₂ groups of its ITap NHC ligand, we hypothesized that the addition of just 2 equivalents of H₃PO₄ would yield fast initiating, fast propagating complex 88a (Scheme 28) as seen with DMAP catalyst complex 65. Examination of the ROMP kinetic profile (Figure 46) shows that this is indeed the case, as catalyst complex 88a displays a much
higher activity than 88 in neutral solution based on the much faster rates of initiation, and therefore higher overall activity. In fact, catalyst 88a is slightly more active than catalyst 12, which is extraordinary considering the unsaturated backbone of the ITap ligand, which usually provides catalysts with a significantly reduced activity compared to catalysts bearing NHC ligands with saturated backbones. Surprisingly, DMAP catalyst 88 also showed higher ROMP activity than its PPh3 ligated precursor 87 under both non-acidic and acidic conditions. Increased activity was also observed in the RCM reactions with two equivalents of H3PO4, with complex 88a displaying higher rates of initiation and higher overall activity when compared to complexes 12 and non-acidified complex 83 (Figure 47). This confirms that the activity profile of catalyst 88 can be externally controlled via addition of acid. More importantly, the somewhat sluggish performance of catalyst 88 can be externally stimulated to make it comparable in performance to catalyst 12, a catalyst considered to have excellent activity.

**Scheme 28. Protonation of Catalyst 88**

```
Me2N     Me2N
\|      \|
NMe2-Ru-Cl-Ph-NMe2
\|      \|
NMe2     NMe2

88
Slow Initiator
Fast Propagator

2H+    D = H3PO4, H2O
------
-2DMAPH+

Me2N     Me2N
\|      \|
NMe2-Ru-Cl-Ph-NMe2
\|      \|
NMe2     NMe2

88a
Fast Initiator
Fast Propagator
```
Summary

Kinetic studies were conducted in organic media to assess the metathesis activity for each of the new catalysts bearing NMe$_2$ modified NHC ligands. This activity was determined through a series of ROMP and RCM reactions using appropriate metathesis substrates. The kinetic profiles that were generated were then compared to those obtained for commercially available catalysts under similar reaction conditions to assess the relative rates of activity. The general trend observed was that in the absence of acid in organic solution catalysts bearing the H$_2$ITap ligand were more active than their counterparts bearing other pH-responsive NHC ligands synthesized in this project, with a few even outperforming their commercially available counterparts 12 and 13, which are
considered the standard of high metathesis activity. As expected, benzylidene carbene catalysts outperformed the phenylthiomethylidene complexes, though the performance of these catalysts was improved, for some by several orders of magnitude, at elevated temperature (60 °C). Under standard conditions, the indenylidene complexes also exhibited lower activities than their homologous benzylidene carbene catalysts though, unlike the phenylthiomethylidene complexes, no major increase in metathesis activity was observed at elevated temperature.

For several of these catalysts, additional kinetic studies were conducted in the presence of non-nucleophillic acid in order to determine the influence on the catalyst activity by the protonation of their pH-responsive groups. For those catalysts bearing the H₂ITap ligand, protonation of this ligand typically reduced catalyst activity. (H₂ITap)(PCy₃)Cl₂Ru=CH-Ph (61) and (H₂ITap)Cl₂Ru=CH-(C₆H₄-O-iPr) (62) were used to conduct ROMP polymer studies and relative initiation kinetics with EVE, which, when coupled with DFT calculations for several model complexes, unambiguously confirmed that this decrease in catalyst activity was a result of a reduced rate of propagation. To the best of our knowledge, this is the only example of independent propagation control of a metathesis reaction to date.

For several of the catalysts additionally coordinated by N-donor ligands, selective protonation was used to determine the ROMP kinetic profiles afforded by protonation of specific pH-responsive groups. Upon dissociation of the N-ligands via acid addition, all catalysts exhibited faster initiation, which was expected based on previous studies by the Schanz research group.⁶⁴ For (H₂ITap)(DMAP)₂Cl₂Ru=CH-Ph 65, (H₂ITap)Cl₂Ru(=CH-CH₂-CH₂-CH₂-C₅H₄N) 66, and (ITap)(DMAP)₂Cl₂Ru-3-phenylindenylidene 88 this resulted in an increase in overall catalyst activity. For phenylindenylidene catalyst 88, this increase in activity was particularly dramatic, as it was converted from a very sluggish catalyst to one with comparable activity to catalyst
12 upon the addition of acid. However, (H$_2$ITap)(DMAP)$_2$Cl$_2$Ru=CH-SPh 81 and (ITap)(PPh$_3$)$_2$Cl$_2$Ru-3-phenylindenylidene 87 experienced fast decomposition with the addition of acid, resulting in very low conversion into metathesis products.
CHAPTER V
KINETIC STUDIES IN ACIDIC PROTIC MEDIA

Substrates and Methods for Relative Kinetic Studies in Acidic Protic Media

The main goal of this dissertation was to generate Ru-based olefin metathesis catalysts capable of performing ROMP and RCM reactions in both organic and aqueous media. To this end, several target catalysts were synthesized, each bearing an NHC ligand modified with pH-responsive NMe₂ groups. These NMe₂ groups provided the means for external control of catalyst solubility profiles via acid addition, which converts these basic NMe₂ groups into ionic ammonium groups (N⁺HMe₂). Benzylidene catalyst (H₂ITap)Cl₂Ru(=CH-CH₂-CH₂-C₅H₄N) 66, phenylthiomethylidene catalysts (H₂ITap)(PCy₃)Cl₂Ru=CH-SPh 79, (H₂ITap)(DMAP)₂Cl₂Ru=CH-SPh 81, and phenylindenylidene catalysts phenyl(ITap)(PPh₃)Cl₂Ru-3-phenylindenylidene 87, (ITap)(DMAP)₂Cl₂Ru-3-phenylindenylidene 88 all exhibited insufficient solubility in acidic aqueous media, so kinetic studies with these catalysts were not conducted. The other catalysts exhibited sufficient solubility in acidic protic media, and they were employed in homogenous ROMP and RCM reactions with water-soluble substrates.

The following metathesis reactions were conducted: ROMP of exo-7-oxanorbornene derivatives 95 and 96 and RCM of diallylmalonic acid 97 (Scheme 29). Acidic protic solvents selected for the metathesis reactions conducted in these studies included 1 M HClₐq–2-propanol (1:9 v/v) or 0.1M HClₐq. Because these substrates are solids, accurate addition to an NMR tube was not feasible. Hence, relative kinetic studies were only conducted by taking aliquots of the reaction solution in precise time intervals, quenching them with ethyl vinyl ether (EVE), 20 followed by removal of the volatiles. The samples were then dissolved in D₂O and individually analyzed via ¹H NMR spectroscopy (300 MHz, 20 °C) by integrating signals representing the substrate and product.
Kinetic Studies

Aqueous Metathesis Reactions for Catalysts Bearing H₂ITap and ITap Ligands

The first two catalysts examined for metathesis reactions in acidic protic and aqueous media were complexes 61, \((\text{H}_2\text{ITap})(\text{PCy}_3\text{)}\text{Cl}_2\text{Ru}^{=\cdot}\text{CH-Ph})\), and 62, \((\text{H}_2\text{ITap})\text{Cl}_2\text{Ru}^{=\cdot}\text{CH-(C}_6\text{H}_4\text{-O-iPr})\). Both of these complexes appeared to exhibit an externally controllable solubility profile, as they both precipitated from organic solutions upon the addition of two equivalents of DCl, which made them very attractive candidates for this study. However, catalyst 61 exhibited low solubility in purely aqueous media when protonated with two equivalents of DCl. \(^1\text{H} \)NMR analysis indicated this was partially due to the incomplete protonation of the NMe₂ groups of its NHC ligand. Instead, a mixture of complexes 61a-61d was formed (Scheme 30), including unstable phosphine-deficient complexes plus the \(\text{PCy}_3\text{D}^+\) cation, formed by partial protonation of the phosphine ligand, which was observed by \(^{31}\text{P} \)NMR spectroscopy. The mixture exhibited low stability, as it decomposed within a few hours in solution. \(^{79}\) Catalyst 62 was soluble in 0.1M DCl / D₂O and formed complex 62a (Scheme 31), which exhibited very slow hydrolysis of the Ru-NHC bond (51% in 7 d).
Based on these results, ROMP of cationic exo-7-oxanorbornene derivative 95 and RCM reactions of diallylmalonic acid 97 were carried out in acidic protic media with a 1 M HCl<sub>aq</sub>–2-propanol (1:9 v/v) solution for catalyst 61 and a 0.1 M HCl<sub>aq</sub> solution for catalyst 62. The catalyst loadings were 4% in each of these experiments, with [Ru] = 2.0 mM and a reaction temperatures of 50 °C. The catalytic performance of both catalysts 61 and 62 in acidic protic media was quite disappointing, as neither complex produced any noticeable amounts of polymer during the ROMP reaction. Furthermore, the RCM of 97 reached only 56% for catalyst 61 and 44% for catalyst 62 in 30 minutes at 50 °C. Additional reaction times did not afford further conversions, likely due to catalyst decomposition. As shown in Chapter IV, converting the π-donating NMe<sub>2</sub> groups into σ-withdrawing NMe<sub>2</sub>H<sup>+</sup> moieties had decreased catalyst activity. The fact that the ROMP
activity was almost zero must be attributed to the solvent since the deprotonated species 61 and 62 exhibit metathesis activity in organic solvents (vide supra). In our experience, reactions in water are sluggish. We believe that water may act as an inhibitor to many catalysts, including 61 and 62.93 Hence, as a result of slower propagation of species 62a and 61b-d, respectively, and additional H2O inhibition, the tested ROMP reactions did not afford noticeable amounts of product.

The next catalyst studied was (H2ITap)(DMAP)2Cl2Ru=CH-Ph 65. In Chapter IV, a gradual protonation scheme (Scheme 25) was proposed in which fast initiating, slow propagating complex 65b would be formed upon protonation with four equivalents of acid. A similar methodology was attempted, using an excess of acid to form this complex (Scheme 32). Upon protonation in 0.1M solutions of acid in water this catalyst was soluble, though small amounts of catalyst did precipitate. As with catalyst complexes 61 and 62, no noticeable amounts of polymer were produced during the ROMP reaction of norbornene substrate 96 under similar reaction conditions. RCM reactions of substrate 97 did afford conversion, though at low levels (Table 13). The low observed activity in aqueous media was likely caused by extremely slow propagation based on the presence of the N’HMe2 groups. For all ROMP and RCM reactions, catalyst loadings were 4%, with [Ru] = 2.0 mM and a reaction temperatures of 50 °C. The higher conversion with H3PO4 may be a result of a lower degree of protonation by the weaker acid, which may have resulted in a faster propagating species. However, at this point, this is pure speculation.
Scheme 32. Protonation of Catalyst Complex 65 With Excess Acid

Table 13. RCM of 97 With Catalyst 65

<table>
<thead>
<tr>
<th>Acid</th>
<th>Time (min)</th>
<th>% Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₃PO₄</td>
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<td>25.2</td>
</tr>
<tr>
<td>HCl</td>
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</tr>
<tr>
<td>HCl</td>
<td>60</td>
<td>10.3</td>
</tr>
</tbody>
</table>

The same effect was observed for all of the complexes bearing an ITap ligand (Figure 48). For all of these reactions catalyst loadings were 4%, in 0.1M HClaq, with [Ru] = 2.0 mM, and reaction temperatures of 60 °C. For these complexes, (ITap)(PCy₃)Cl₂Ru=CH-Ph 67, (ITap) (ITap)Cl₂Ru=CH-(C₆H₄-O-iPr) 68, (DMAP)₂Cl₂Ru=CH-Ph 69, (ITap)(PCy₃)Cl₂Ru=CH-SPh 80, and (ITap)(DMAP)₂Cl₂Ru=CH-SPh 82, some precipitation of the catalyst was observed. ROMP reactions of norbornene derivative 96 afforded no ROMP activity with any these catalysts. Lower conversion rates were also observed for RCM reactions of 97 than was seen for catalysts 61 and 62 with similar reaction conditions (Table 14). The kinetic results for these ITap bearing catalysts further emphasize the strong influence that acidification of the aryl NMe₂ of the NHC ligand substituent has on the activity profile of catalysts with these types of modified NHC ligands.
Table 14. RCM of DAM With Catalysts Bearing ITap Ligands

<table>
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<th>Catalyst</th>
<th>Time (min)</th>
<th>% Conversion</th>
</tr>
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<tr>
<td>(ITap)(DMAP)₂Cl₂Ru=CH-SPh</td>
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</table>

Aqueous Metathesis Reactions for Catalysts Bearing NHC Ligand With Remote NMe₂ Groups

ROMP and RCM reactions for catalysts bearing NHC ligands modified with remote NMe₂ groups were also conducted in aqueous media. For these catalysts (70, 77, and 78), the NMe₂ groups were separated from the aryl substituents of the NHC ligand by an E-CH₂-CH₂ spacer, where E = O or S. For these catalysts, their activity in organic solvents was significantly lower than their H₂ITap counterparts. In aqueous media, however, it was anticipated that the formation of the NMe₂H⁺ groups should not dramatically affect the electronic catalyst environment. Thus, these catalysts were expected to exhibit a faster propagation in aqueous media than the H₂ITap and ITap ligand bearing catalysts.
The first of these catalysts to be studied was (IXyONMe₂)(PCy₃)Cl₂Ru=CH-Ph 70 (Scheme 33). Similar to catalyst complex 61, sufficient catalyst solubility was accomplished using 1 M HClaq-2-propanol (1:9 v/v), so this was the solvent chosen for aqueous olefin metathesis reactions with this catalyst. As before aqueous ROMP and RCM reactions for this catalyst were initially conducted with [Ru] = 2.0 mM solution with 4% catalyst loading. The results for ROMP reactions of norbornene substrate 96 with catalyst 70 were surprising (Table 15). The ROMP reaction was first conducted at 60 °C, which afforded >99% conversion to polymer within 15 minutes. This reaction was then repeated at room temperature using the same concentrations, which yielded almost the same conversion. Decreasing the catalyst loading to 2% did result in a slight decrease in the conversion, and no further conversion was observed after 15 minutes, indicating a loss of activity due to catalyst degradation. However, the conversions observed were a dramatic improvement over catalyst 61. In fact, in these ROMP reactions catalyst 70 even outperformed Grubbs’ water soluble catalyst 26 (Figure 49), which is considered to be the most active Ru-based olefin metathesis catalyst for use in homogenous aqueous olefin metathesis applications. That catalyst, by comparison, required three hours to achieve the same ROMP conversion of a similar substrate, at similar catalyst loadings, afforded by catalyst 70 within 15 minutes. Catalyst 97 was less active in the RCM reaction of DAM in acidic protic media, with only 75.1% conversion achieved after 15 minutes at 60 °C with no further conversion after this time, however, this result was comparable to those observed with catalyst 26 after several hours with other α,ω-diolefins.⁶a Based on these results, catalyst 70 is definitely a highly active olefin metathesis catalyst in protic media.
Table 15. ROMP of Norbornene Substrate 96 With Catalyst 70

<table>
<thead>
<tr>
<th>% Catalyst Loading</th>
<th>Temperature (°C)</th>
<th>Time (min)</th>
<th>% Conversion to Polymer</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>60</td>
<td>15</td>
<td>99.38</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>15</td>
<td>98.17</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>15</td>
<td>86.53</td>
</tr>
</tbody>
</table>

The last two catalysts examined via ROMP and RCM olefin metathesis reactions in aqueous media were (IDippONMe₂)(DMAP)Cl₂Ru=CH-Ph 77 and (IDippSNMe₂)(DMAP)₂Cl₂Ru=CH-Ph 78. Like catalyst 70, these two catalysts possess remote NMe₂ groups. These catalysts additionally bear pH-responsive DMAP ligands, resulting in higher initiation rates upon acid addition. The simultaneous protonation of the NMe₂ groups and the DMAP ligands of catalyst complexes 77 and 78 produced water soluble complexes 77a and 78a (Scheme 34). We hypothesized that these two complexes could afford an unprecedented olefin metathesis catalyst system capable of performing both ROMP and RCM reactions in aqueous media, especially considering the high activity exhibited by catalyst 70.
Aqueous ROMP and RCM reactions were conducted with catalysts 77 and 78 using 0.1M HCl\textsubscript{aq}. The ROMP and RCM reactions proceed fast at room temperature. RCM of 97 ([Ru] = 2 mM with 4% catalyst loading) only reached 62.9% and 52.5% conversion, respectively, after 30 minutes. Again, further conversion was not observed, indicating catalyst decomposition due to the fast initiation. The ROMP reactions with substrate 96 proceeded to complete conversion at extraordinary rates, with >95% ROMP conversion achieved in each reaction within 15 min (Table 16). This extremely high activity clearly demonstrates that these two catalyst systems dramatically outperform Grubbs’ water soluble catalyst 26 in aqueous media,\textsuperscript{6a} making them the most active catalysts for aqueous olefin metathesis applications to date.

Table 16. ROMP Reactions of Norbornene Substrate 96 With Catalysts 77 and 78

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>% Catalyst Loading</th>
<th>Time (min)</th>
<th>% Conversion to Polymer</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>4</td>
<td>15</td>
<td>&gt;99</td>
</tr>
<tr>
<td>77</td>
<td>1</td>
<td>15</td>
<td>97.2</td>
</tr>
<tr>
<td>78</td>
<td>4</td>
<td>15</td>
<td>97.6</td>
</tr>
</tbody>
</table>

For catalyst 77, >99% ROMP reaction conversion was even achieved with catalyst concentrations as low as 1.0 mM at 1.0% catalyst loading, a concentration more often applied to reactions with ROMP substrates in organic media. Very few examples can be found in the literature of Ru-based olefin metathesis catalysts for efficient ROMP in aqueous media.\textsuperscript{6a,51} The closer examination of the kinetics of this reaction indicated
that this is, in fact, a fast initiating catalyst, as no long induction period is observed prior to the sudden onset in activity (Figure 50). This likely accounts for the increased activity displayed by these catalysts, showing that external control of catalyst solubility was afforded via protonation and subsequent dissociation of the DMAP ligand. The logarithmic plot is linear which indicates that the ROMP followed pseudo first order kinetics for much of the reaction, though some deviation is seen at high conversions and long reaction times, indicating slow catalyst decomposition (Figure 51). Catalyst 77 can be considered the most active catalyst for aqueous ROMP to date. The efficient initiation may make this catalyst suitable for controlled aqueous ROMP, however, detailed polymer analyses are needed to confirm these kinetic results.

Figure 50. ROMP of Norbornene Substrate 96 With Catalyst 77
[Ru] = 1.0 mM, 1.0% Catalyst Loading, in 0.1M HClaq, 20 °C
Summary

ROMP and RCM reactions were conducted both acidic protic and aqueous media using catalysts bearing pH-responsive ligands. Many, but not all, catalysts exhibited solubility in acidic aqueous or aqueous/alcoholic media confirming our goal to generate a catalyst with an externally controllable solubility profile. For catalysts bearing H$_2$ITap or ITap ligands, a dramatic loss of activity was observed upon protonation of the aryl NMe$_2$ groups of their NHC ligands, which clearly showed that conversion of the their π-donating dimethylamino groups into σ-withdrawing ammonium groups significantly reduced their catalyst activity. For systems with these aryl NMe$_2$ groups, no noticeable ROMP activity was achieved in aqueous media, and no RCM reaction was observed accomplishing >56% substrate conversion. In most cases, complete catalyst decomposition was observed.

Much higher activities were exhibited by catalyst systems with remote NMe substituted NHC ligands in aqueous media. The ROMP reactions with these catalysts were very fast, often giving >95% within 15 minutes or less, making them the fastest ROMP catalysts for aqueous metathesis to date. Catalyst 77 (Figure 52) was
particularly impressive, achieving nearly complete conversion to ROMP polymer in aqueous media at concentrations as low as 1.0 mM with 1.0% catalyst loading in 60 minutes at room temperature. Previously published catalysts by Grubbs et al.\textsuperscript{6a} did not even remotely exhibit such high activity. Closer examination of the ROMP kinetic profile for this reaction showed that this catalyst may be suitable for controlled polymerization in aqueous media due to the fast dissociation its pH-responsive DMAP ligand, however, analysis of the polymers obtained in this reaction has not yet been completed to substantiate this theory.

![Figure 52. pH-Responsive Catalyst 77](image)
CHAPTER VI
APPLICATIONS FOR OLEFIN METATHESIS CATALYSTS WITH PH-RESPONSIVE LIGANDS

There are many practical applications available for catalysts with externally controllable solubility and activity profiles. The ability to perform homogenous olefin metathesis reactions in aqueous and acidic protic media, as explored in Chapter V, greatly expands the substrate availability for Ru-based olefin metathesis catalyst systems. Catalysts systems with reversible solubility profiles, externally controlled via acid addition, might be very economical, as these systems could be used to perform olefin metathesis reactions in both organic and aqueous media with a large variety of substrates of different solubilities. Interest has steadily grown to use olefin metathesis in aqueous and biological media. This chapter describes practical applications that were or are currently being explored in our laboratories or via collaboration.

In a collaboration with Dr. Andrea Robinson (Monash University, Australia) we have provided (H$_2$ITap)Cl$_2$Ru=CH-(C$_6$H$_4$-O-/Pr) 62 to synthesize oligopeptides containing unnatural amino acids grafted on solid support. The analogous natural peptides have therapeutic value as potential drugs and antidotes to natural venoms but suffer from rapid digestion in the human body based on breaking their labile S-S bonds. These S-S bonds enforce the active tertiary bicyclic structures. Thus, their replacement with HC=CH bonds is highly desirable, since they provide much elevated stability of the peptide under physiological conditions. The –CH=CH- moieties are generated via RCM. The use of aqueous media in the synthesis is much more benign to the peptides than organic solvents, thus an olefin metathesis catalyst was needed which can perform under these conditions. The project is still ongoing and we have not received any preliminary results.
The external control of the catalyst solubility afforded by the pH-responsive ligands in these catalyst systems was also proven useful when employed for the removal of the Ru-metal catalyst from olefin metathesis reactions in organic media. The effective removal of Ru-metal has become an important issue for the pharmaceutical industry, which currently uses very expensive column chromatography to remove Ru-metal contamination from their products.\textsuperscript{6b,59} The pH-responsive catalyst systems developed for this dissertation are obviously very attractive for this process, as they have been shown to precipitate from organic reaction media upon acid addition, which would allow for easier catalyst removal.

We applied this concept by developing a protocol for catalyst 62 which reduces the Ru-metal contamination in RCM reaction mixtures (Scheme 35).\textsuperscript{79} Catalyst 62 was selected because of its enhanced hydrolytic stability and low solubility in organic media upon protonation, a result of the formation of low-soluble dicationic Ru-species 62a (Scheme 35). For this study, RCM reactions of diethylidendalylmalonate (DEDAM) and 3,3-diallyl-2,4-pentanedione (DAP) (Figure 53) ([Ru] = 3.3 mM, 2% catalyst loading) were carried out in either toluene or ethyl acetate at 50 °C for 30 minutes. All reaction provided >99\% conversion. These reactions were then quenched through addition of ethyl vinyl ether. After 10 minutes, concentrated acid (HCl or H\textsubscript{2}SO\textsubscript{4}) was added via microliter syringe (approximately 10 equivalents with respect to the catalyst). This caused precipitation of the Ru-metal species within seconds of acid addition (Scheme 36). The slurry was then filtered through a plug of Na\textsubscript{2}SO\textsubscript{4}, followed by solvent removal under reduced pressure. The complete RCM conversion was verified via \textsuperscript{1}H NMR spectroscopy before aliquots of 20–22 mg were taken and digested with concentrated HNO\textsubscript{3} for analysis by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). The residual product that remained after the aliquots were taken was then extracted with t-BuOMe and washed with water. The solvent was once again removed under reduced
pressure and additional aliquots of 20–22 mg were once again taken and digested with concentrated HNO₃ for ICP-MS analysis.

![Figure 53. Substrates for Catalyst Removal Studies](image)

**Scheme 35. Precipitation of Catalyst 62 via Acid Addition**

![Scheme 36. Catalyst Removal Method](image)

The results showed that products obtained from substrate DEDAM contained significantly lower amounts ruthenium than the products obtained from substrate DAP (Table 17). The results also showed that products obtained via filtration with subsequent extraction in water exhibit improved Ru-removal when compared to filtration alone, but significant amounts of the RCM product are also lost through this extra step. The conditions with lowest residual Ru-metal content in the RCM products were observed when the removal protocols were applied to a reaction solution with DEDAM as substrate, in toluene, and H₂SO₄ as acid. The residual Ru levels under these conditions of 24 ppm (after filtration only) and 11 ppm (after filtration and subsequent wash) are very close to the pharmaceutical standard of ≤ 10 ppm. This represents the most
effective, single-step Ru-removal protocol for homogenous metathesis reactions to date, including column chromatography and all scavenging methods.\textsuperscript{60,61} Hence, this method could be a very attractive alternative to column chromatography in the pharmaceutical industry based on its effectiveness and economic feasibility. It should be noted that attempts to reuse the precipitated catalyst after deprotonation with \textit{NEt}_3 were not successful.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|}
\hline
Substrate & Acid & Solvent & Method\textsuperscript{a} & Yield (\%)\textsuperscript{b} & ppm Ru \\
\hline
DEDAM & HCl & Toluene & F & 86.5 & 82 \\
DEDAM & HCl & Toluene & W & 58.8 & 48 \\
DEDAM & H\textsubscript{2}SO\textsubscript{4} & Toluene & F & 72 & 24 \\
DEDAM & H\textsubscript{2}SO\textsubscript{4} & Toluene & W & 60.3 & 11 \\
DEDAM & HCl & AcOEt & F & 76.9 & 34 \\
DEDAM & HCl & AcOEt & W & 52.9 & 45 \\
DEDAM & H\textsubscript{2}SO\textsubscript{4} & AcOEt & F & 85.7 & 140 \\
DEDAM & H\textsubscript{2}SO\textsubscript{4} & AcOEt & W & 45.7 & 48 \\
DAP & HCl & Toluene & F & 43.2 & 498 \\
DAP & HCl & Toluene & W & 68.9 & 160 \\
DAP & H\textsubscript{2}SO\textsubscript{4} & Toluene & F & 79.1 & 213 \\
DAP & H\textsubscript{2}SO\textsubscript{4} & Toluene & W & 44.5 & 80 \\
DAP & HCl & AcOEt & F & 78.2 & 335 \\
DAP & HCl & AcOEt & W & 63.3 & 144 \\
DAP & H\textsubscript{2}SO\textsubscript{4} & AcOEt & F & 68.1 & 149 \\
DAP & H\textsubscript{2}SO\textsubscript{4} & AcOEt & W & 44.3 & 90 \\
\hline
\end{tabular}
\caption{Results for Studies of Ru-Metal Removal After RCM Reactions [Ru] = 3.3 mM, 2\% Catalyst Loading, 50 °C}
\end{table}

\textsuperscript{a} F = filtration alone, W = filtration with subsequent extraction; \textsuperscript{b} Isolated yields for W were based on the extraction step alone.

In collaboration with Dr. Kevin Müller of BASF (Ludwigshafen, Germany), several catalysts produced for this dissertation were investigated for emulsion ROMP,\textsuperscript{97} which has little precedence in literature.\textsuperscript{2c,96} The scope of studies with water-soluble catalysts was limited to highly strained norbornene,\textsuperscript{7a} since less reactive monomers did not result in high conversions. Also, the catalyst loadings were high (3.3\%). The current studies by BASF demonstrated that catalysts (\textit{H}_2)ITapRu=CH-Ph, and 79-82 were capable of polymerizing cyclooctene (COE) and dicyclopentadiene (DCPD) in emulsion under acidic conditions to afford complete polymerization with loadings as low as 180 ppm. Stable latexes were successfully generated for not only COE and DCPD, but also for
copolymers from mixtures of these two monomers. For the first time, other, less-reactive monomers than norbornene (the most active ROMP monomer known) were successfully polymerized with this technique. Also, the catalyst loading could be lowered by two orders of magnitude than in previous examples.\(^\text{98}\) A patent application for this process has been submitted and no detailed results have been released by our partner.\(^\text{97}\)

Additionally, the effect of acid addition to pH-responsive catalysts 65 and 79-82 (Figure 54) on gelation times of ROMP substrates was also investigated by BASF.\(^\text{97}\) The gelation times for DCPD (in hexadecane) and COE was monitored with these catalysts (66 mg per 5.35g of substrate, or 0.16-0.17% catalyst loading for DCPD and 0.14% catalyst loading for COE) at room temperature. The same experiments were then conducted in the presence of excess toluenesulfonic acid (TsOH) (0.2g). The results show that gelation times responded differently to the acid addition, depending on the nature of the catalyst and the substrate. It was observed that gelation times for DCPD are faster in the presence of acid with all catalysts tested. With COE, gelation times for catalysts bearing H\(_2\)ITap ligands were also faster in the presence of acid, particularly for Ru=CH-SPh catalysts 79 and 82. For catalysts bearing ITap ligands (catalysts 90 and 91), gelation times were longer in the presence of acid, which was in stark contrast to what was observed with DCPD. Most contradictory are the results for catalyst 82. With this catalyst, the increase in gelation time was for COE was dramatic, which took two hours in the presence of acid versus 0.5 min observed without acid.
Table 18. Gelation Studies\textsuperscript{a} of DCPD and COE

\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Catalyst} & \textbf{DCPD}\textsuperscript{b} & & \textbf{COE} & \\
 & \textbf{No Acid} & \textbf{TsOH}\textsuperscript{c} & \textbf{No Acid} & \textbf{TsOH}\textsuperscript{c} \\
\hline
65 & 0.03 & 0.03 & 1.1 & 0.03 \\
79 & 0.8 & 0.03 & 46.0 & 0.7 \\
80 & 10.6 & 0.8 & 2.2 & 3.9 \\
81 & 1.1 & 0.3 & 120 & 3.3 \\
82 & 5.0 & 1.5 & 1.5 & 120 \\
\hline
\end{tabular}

\textsuperscript{a} 66 mg catalyst / 5.35 g substrate at room temperature (0.16-0.17% catalyst loading for DCPD, 0.14% catalyst loading for COE); \textsuperscript{b} in hexadecane; \textsuperscript{c} 0.2 g TsOH

The data from these gelation studies provides some interesting implications for ROMP reactions conducted with these catalysts bearing pH-responsive ligands. As with previous kinetic studies, this data shows that the rate of ROMP reactions, and therefore overall catalyst activity profiles, may be altered through protonation of these catalysts with pH-responsive ligands in different directions for different monomers. Because different activity trends were observed for catalysts 80 and 82 with COE and DCPD, acid addition may additionally change the catalyst affinity for one substrate over another. This implies the degree of protonation may be a parameter which could be adjusted to produce truly statistical co-polymers of monomers whose reactivity with certain catalysts
change in different directions upon protonation. This, for the first time, could allow for the generation of statistical ROMP co-polymers with different compositions. Detailed studies of this phenomenon beyond the gelation studies, however, were not conducted.
CHAPTER VII

SUMMARY

For this dissertation, novel Ru-based olefin metathesis catalysts bearing pH-responsive ligands were produced. These pH responsive ligands provided the means by which the solubility and activity profiles of the catalyst could be externally controlled via acid addition. All of the catalysts generated for this dissertation contain pH-responsive, NMe₂ modified NHC ligands. Additionally, some of the catalysts produced also contained pH-responsive N-donor ligands. The overall goal of this project was to generate catalyst systems capable of performing olefin metathesis reactions in both organic and aqueous media.

To achieve this goal, a series of NMe₂ modified NHC ligand precursor salts 37, 38, and 55-58 (Figure 55) were first produced. H₂ITapHCl 37 and ITapHCl 38 were made by following literature procedures, with slight modifications, for similar imidazolin-2-ylidene and imidazole-2-ylidene complexes, after the dimethylamino groups were introduced to the starting aniline compound. Both of these ligand precursors bear NMe₂ groups attached directly to the aryl substituents of their NHC ligands. By contrast, IXyONMe₂HCl 55, IXySNMe₂HCl 56, IDippONMe₂HCl 57, and IDippSNMe₂HCl 58 each bear NMe₂ groups that are removed from the aryl group of the NHC ligand by an E-CH₂-CH₂ spacer (E = O or S). These precursors were synthesized via a template synthesis, based on the synthesis of precursor salt 37, which was developed in an attempt to gain fast access to a library of ligand precursors. Key to this template synthesis is the formation of diiodinated diamine intermediates which could be functionalized through Cu-mediated C-heteroatom coupling reactions, enabling a straightforward access to several unique ligand precursors.
After these NHC ligand precursors were synthesized, they were used to make novel Ru-based olefin metathesis catalysts. These NHC ligands were incorporated into these structures via ligand exchange reactions with phosphine-ligand bearing precatalysts. In addition, some of the product catalysts were reacted with excess N-donor ligand, which produced other derivative catalyst complexes. Most of the catalysts produced for this dissertation were benzyldiene-carbene (or Grubbs-type) complexes, though phenylthiomethylidene, phenylindenylidene, and bidentate propylidene complexes were also generated.

Most of the catalysts produced for this dissertation bear either an H$_2$ITap or ITap ligand (Figures 56 and 57), the catalyst syntheses were straightforward in accordance with literature procedures. By contrast, complexes with remote NMe$_2$ groups on their NHC ligands proved much more difficult to synthesize and isolate. Alternative synthesis methods attempted with these ligand precursors, but were unsuccessful. As a result, only three of the catalysts generated for this study bear this NHC ligand motif (Figure 58). In total, 16 novel catalyst complexes were generated for this study.
Figure 56. Catalysts Bearing an H$_2$ITap Ligand

Figure 57. Catalysts Bearing an ITap Ligand
To assess the olefin metathesis activity of these catalysts in comparison to literature catalyst complexes, ROMP and RCM reactions were conducted in organic media. The kinetic profiles that were generated were then compared to those obtained for commercially available catalysts 12 and 13 under similar reaction conditions to assess the relative activities. In the absence of acid, metathesis reactions in organic showed that H₂ITap ligand ligand bearing counterparts were more active than catalysts bearing other pH-responsive ligands synthesized in this project. As expected, benzylidene-carbene catalysts outperformed analogous phenylthiomethylidene catalysts and phenylindenylidene-carbene complexes. However, with the phenylthiomethylidene complexes, catalyst performance was dramatically improved with elevated temperature (60 °C).

For some catalysts generated in this study, kinetic studies in organic media were also conducted in the presence of non-nucleophilic to assess the change in catalyst solubility and activity profiles afforded via protonation of the pH-responsive groups. The first to be examined in the acid studies were catalysts 61 and 62. Under standard, non-acidic conditions, these two catalysts exhibited very similar activity profiles to their commercially available counterparts, catalysts 61 and 62. However, upon protonation of
their pH-responsive NMe₂ groups with increased concentrations of TsOH, a significant decrease in activity was observed. Analysis of polymers produced in ROMP reactions under these conditions indicated that the slowing of catalyst activity was due to a decrease in the rate of propagation, since better molecular weight control was afforded with increased amounts of acid. Additional DFT calculations were used to determine the Mullikan atomic charges for similar model complexes. These indicated that the π-acceptor capability of the H₂ITap ligand was reduced upon protonation, showing that the protonation of the NMe₂ groups of the ITap ligand greatly interfered with the electronic environment of the ligand, thus causing an overall decrease in catalyst activity. Initiation kinetics conducted by reacting complexes 61 and 62 with EVE confirmed that slightly increased rates of initiation were observed when acid was added. Combined, these results unambiguously showed that the decrease of activity upon protonation of the NMe₂ groups of the H₂ITap ligand was a result of decreased rates of propagation. To our knowledge this is the first example of an external control for propagation in metathesis reactions.

Kinetic studies upon the addition of acid were also conducted with catalysts bearing pH-responsive N-donor ligands. As expected, an increase in the rate of initiation in ROMP and RCM reactions was observed when these N-donor ligands were dissociated from the metal center upon acid addition. For catalysts 65, 66, and 88, dissociation of the DMAP ligand not only resulted in increased initiation efficiency, but also in an increase in overall catalyst activity. For catalyst 88 this increase was extraordinary, since this phenylindenylidene complex was converted from a slow catalyst system into one with activity similar to commercially available catalyst 12, which is considered to have excellent metathesis activity. This was not unexpected, as these trends had previously been observed in literature for other DMAP catalyst systems.⁴⁹,⁶₄
Unfortunately, for catalysts 81 and 87 decreased metathesis conversions were observed, most likely due to increased catalyst decomposition in the presence of acid.

Since the main goal in this dissertation was to generate catalysts capable of performing metathesis reactions in aqueous media, the catalysts made for this project were tested in aqueous ROMP and RCM reactions. The protonation of the NMe$_2$ groups of the NHC ligand of these catalysts afforded complexes bearing two cationic NMe$_2$H$^+$ groups, which, for most catalysts produced in this project, provided sufficient catalyst solubility in aqueous or acidic protic media. Therefore, external control of catalyst solubility was established via protonation of the pH-responsive groups. For catalyst systems with H$_2$ITap and ITap ligands, the conversion of the π-donating dimethylamino groups into σ-withdrawing ammonium groups upon protonation once again resulted in a dramatic slowing of catalyst propagation. For systems with these aryl NMe$_2$ groups, no noticeable ROMP activity was observed in acidic aqueous media, and no RCM reaction provided more than 56% substrate conversion with a 4% catalyst loading. In most cases, significant catalyst decomposition was also observed.

Much better activity was observed with catalysts bearing NHC ligands modified with remote NMe$_2$ groups in acidic, protic media. These catalysts (70, 77, and 78) each completed ROMP reactions faster than Grubbs water-soluble catalyst 26, which is considered to be the most active catalyst in aqueous olefin metathesis reactions. This catalyst has been reported to afford full ROMP conversion of norbornene substrates in a little over three hours with 3.3% catalyst loading. All three of our catalysts, by comparison, allow for the same conversion in just 15 minutes at 4% catalyst loading. Catalyst 70 was also shown to exhibit nearly complete conversion to ROMP polymer with the same norbornene substrate within 15 minutes at just 2% catalyst loading, lower than ever observed with catalyst 26, as well as comparable RCM activity to catalyst 26. Catalyst 77 also performs ROMP of norbornene substrate at lower concentrations, with
97.2% conversion to polymer observed with just [Ru] = 1.0 mM with 1.0% catalyst loading, which is more similar to reaction conditions applied in organic media and is significantly lower than what has ever been observed with Grubbs’ catalyst 26. This catalyst is by far the most active aqueous ROMP catalysts ever reported to date.

Many applications exist for our catalyst systems that exhibit externally controllable solubility and activity profiles. One application developed in our laboratories has enabled the removal of Ru-metal contamination after RCM reactions by way of external manipulation of catalyst solubility profile via acid addition. Another application currently being explored in collaboration with Dr. Andrea Robinson (Monash University, Australia) is the use of these catalysts to graft cyclic oligopeptides containing unnatural amino acids. Other collaborations with BASF have found application for use in the synthesis of stable latexes of COE, DCPD, and mixtures of the two. Other exciting results generated by our collaborators at BASF include gelation studies of these two monomers using our catalysts both in the presence and absence of TsOH. The results of this study imply that acid addition might not just afford an external control of activity and solubility, but may additionally change the catalyst affinity for one substrate over another. However, no further studies have yet been conducted to explore this phenomenon.
CHAPTER VIII

EXPERIMENTALS

General Procedures

All experiments with organometallic compounds were performed under a dry nitrogen atmosphere using standard Schlenck techniques or in an MBraun dry-box (O₂ <2 ppm). NMR spectra were recorded on a Varian Inova instrument (300.1 MHz for ¹H, 75.9 MHz for ¹³C, and 121.4 MHz for ³¹P). ¹H and ¹³C NMR spectra were referenced to the residual solvent, ³¹P NMR spectra were referenced using H₃PO₄ (δ = 0 ppm) as external standard. For sonication a Fischer Scientific Ultrasonic Cleaner FS 30 was used. The bath temperature was set to 30 °C. ICP-MS analyses were conducted by Dr. Alan M. Shiller. X-ray crystallography was conducted by Dr. Edward J. Valente. Absolute Size-Exclusion Chromatography (ASEC) of ROMP polymers was conducted by Dr. Andrew B. Lowe and Dr. Bing Yu. DFT calculations were conducted by Dr. Yong Zhang. Size exclusion chromatographic analysis was performed on a Waters system comprised of a Waters 515 HPLC pump, Waters 2487 Dual λ absorbance detector, and Waters 2410 RI detector equipped with a PolymerLabs PLgel 5µm guard column and a PolymerLabs PLgel 5µm MIXED-C column, in THF stabilized with 281 ppm BHT at a flow rate of 1.0 mL/min. The column was calibrated with a series of narrow molar mass distribution poly(methyl methacrylate) standards. The data was analyzed with Empower Pro 1154.

DFT calculations were conducted using the Gaussian 03 program.¹⁰⁴ All atoms in the model complexes were considered in the calculations. Geometries were optimized by using the hybrid DFT method mPW1PW9¹⁰⁶ together with an effective-core potential basis SDD¹⁰⁶ which were found to give good geometries for late transition metal complexes.⁹¹ To compute the Mulliken charges, a hybrid DFT method B3LYP together with a large basis set was used, namely a full-electron basis DGDZVP for Ru, a 6-
311++G(2d,2p) for first coordination shell atoms, and 6-31G(d) for the rest part of the atoms. The same approach was used to calculate various electronic properties of late transition metal complexes. In case of the monoprotonated 93b, structures of protonating the NMe2 group in both sides of the NHC ligands were considered and their Mulliken charges were found to be very similar. The average value was reported.

Materials and Methods

All solvents for manipulations under inert gas (heptane, thf, CH2Cl2, tBuOMe, toluene) were dried by passage through solvent purification (MBraun-Auto-SPS). Water was filtered, deionized (DI), and distilled prior to use. All NMR solvents used in combination with catalyst complexes (D2O, DCl–D2O, CD2Cl2, CDC13) were degassed prior to use. Other solvents were used as purchased. Reagents were purchased from commercial sources were degassed and stored in the dry-box when directly used in combination with organometallic complexes, and otherwise were used without further purification. 2-i-Propoxystyrene, diethylidiallylmalonate (DEDAM) 79, diallylmalonic acid (DAM) 80, and 3,3-diallylpentane-2,4-dione (DAP) 81 and monomer 77 were synthesized according to literature procedures. Grubbs’ catalyst 1 was purchased from Aldrich, degassed and stored in the dry-box. Phenylindenylidene catalyst precursor 21 was synthesized in accordance with literature procedure. BASF provided Ru=CH-SPh catalyst precursor 24. Purity of all complexes was determined via 1H NMR spectroscopy.

ICP MS Analyses

The aliquots of RCM product were digested in hot conc. HNO3 (1 mL). The solid residue was then dissolved in 0.16 M HNO3 containing 2 ppb In as an internal standard. The final analytical solution contained about 0.67 mg of product per mL acid. [Ru] was determined in this solution using a sector-field ICP-MS (ThermoFinnigan Element 2). Equivalent results were obtained from five different Ru isotopes (masses 99, 100, 101,
102, and 104); likewise, no difference was noted between results obtained in low resolution \((m/Δm = 300)\) or medium resolution \((m/Δm = 4000)\), suggesting a lack of interferences. Blank samples of the digested starting materials gave Ru contents of <0.1 ppm (DEDAM) and 0.6 ppm (DAP) Ru-content.

*Synthesis of N,N-3,5-Tetramethyl-1,4-phenylenediamine (34)*

A solution of NaNO\(_2\) (9.922 g, 143.8 mmol) in water (20 mL) was added slowly to a solution of \(N,N\)-3,5-tetramethylaniline \(33\) (20.032 g, 134.4 mmol) in conc. HCl\(_{aq}\) (50 mL) under vigorous stirring via a capillary which was immersed in the reaction solution at -5 °C over a period of 60 min. During the addition, a yellow precipitate (4-nitroso-\(N,N\)-3,5-tetramethylaniline-HCl) was formed. After the addition, the slurry was stirred for another 60 min at 0 °C and then filtered cold through a Buchner funnel. The yellow residue (4-nitroso-\(N,N\)-3,5-tetramethylaniline-HCl) was washed with ethanol (3 x 50 mL) and suction-dried for 60 min. Then the powdered filter residue was added in small portions to a slurry of powdered tin (7.360 g, 61.8 mmol) in conc. HCl\(_{aq}\) (50 mL) at 70°C. While adding the nitrosoaniline the solution turned intensely yellow in color and reverted back to colorless within a few seconds. Once all tin was consumed, the yellow color persisted. The residual nitrosoaniline salt not used in the conversion was stored for a later transformation. It should be noted that this procedure avoids the addition of excess tin. Otherwise an insoluble precipitate is formed during the basic work-up, and this causes a significant reduction of the yield. The resulting slightly yellow solution was slowly added to ice-cold 3 M aqueous NaOH (300 mL). The aqueous phase was extracted with CH\(_2\)Cl\(_2\) (3 x 50 mL), and the organic phases were combined and dried over NaSO\(_4\). The solvent was removed to give compound \(34\) (9.770 g, 60.3 mmol, 45%) in over 98% purity (\(^1\)H NMR) as a golden-colored viscous liquid.

*Synthesis of Glyoxalbis(4-dimethylamino-2,6-dimethylphenyl)imine (35)*
Compound 34 (6.373 g, 39.4 mmol) was added to a solution of 40% aqueous glyoxal (3.852 g, 26.6 mmol) in methanol (100 mL) and one drop of conc. HCl$_{\text{aq}}$ (approx. 20 mL) and stirred for 24 hrs at room temperature. During the reaction, a deep-yellow colored precipitate was formed. The slurry was filtered, the residue was washed with methanol (3 x 20 mL), dried on the filter, and then dried in the vacuum oven at 60 °C for 3 h to give compound 35 (5.874 g, 16.8 mmol, 85%) in >99% purity ($^1$H NMR) as a golden-yellow powder. $^1$H NMR (300.1 MHz, 20 °C, CDCl$_3$): $\delta$ 8.11 (s, 2 H, N=C=H), 6.50 (s, 4 H, C$_6$H$_2$), 2.94 (s, 12 H, N(CH$_3$)$_2$), 2.24 (C$_6$H$_2$–CH$_3$); $^{13}$C NMR (75.9 MHz, 20 °C, CDCl$_3$): $\delta$ 162.5 (N=CH), 148.1, 140.6, 128.9, 112.8 (C$_6$H$_2$), 40.8 (N(CH$_3$)$_2$), 19.2 (C$_6$H$_2$–CH$_3$).

Synthesis of N,N-Bis(4'-dimethylamino-2',6'-dimethylphenyl)ethylene-1,2-diamine (36)

A solution of compound 35 (3.380 g, 9.66 mmol) in thf (100 mL) containing NaBH$_4$ (0.821 g, 21.6 mmol) and boric acid (1.781 g, 28.8 mmol) was stirred at 30 °C over a period of 60 min. In this time period the solution turned colorless. The solution was cooled to room temperature and water (40 mL) was added carefully and then conc. HCl$_{\text{aq}}$ (10 mL) was added dropwise until the solution stopped developing gas. The solution was warmed to 50 °C under stirring for 10 min and then cooled to room temperature. The thf was removed under reduced pressure and the aqueous solution was neutralized with Na$_2$CO$_3$. The aqueous phase was extracted with tBuOMe (60 mL), and the organic layer was washed with brine (3 x 40 mL). The organic phase then was dried over Na$_2$SO$_4$ and filtered. The solvent was removed under reduced pressure with a rotary evaporator, and the residue was dried in the vacuum oven at 60 °C for 2 h to give compound 36 (3.000 g, 8.47 mmol, 88%) as a colorless, viscous liquid in >98% purity ($^1$H NMR) which solidified at room temperature over 12 h. $^1$H NMR (300.1 MHz, 20 °C, CDCl$_3$): $\delta$ 6.51 (s, 4 H, C$_6$H$_2$), 3.11 (s, 4 H, NH–CH$_2$), 2.89 (s, 12 H, N(CH$_3$)$_2$), 2.34 (s, 12
Synthesis of 1,3-Bis(2',6'-dimethyl-4'-dimethylaminophenyl)-4,5-dihydroimidazolinium chloride, \( \text{H}_2\text{ITap-HCl (37)} \)

A solution of diamine 36 (2.567 g, 7.25 mmol) and ammonium chloride (0.380 g, 7.22 mmol) in triethyl ortho-formate (30 mL) was heated under stirring at 130 °C for 16 h. The excess triethyl ortho-formate was distilled under reduced pressure (0.1 Torr) and collected to be reused. Cyclohexane (30 mL) was added to the solid residue and sonicated for 30 min at 30°C. The slurry was filtered, washed with cyclohexane (3 x 20 mL), sucked dry on the filter for 10 min and dried in the vacuum oven at 60°C for 3 h to give ligand precursor 37 (2.499 g, 6.31 mmol, 87%) as a slightly off-white powder in >99% purity (\(^1\)H NMR). \(^1\)H NMR (300.1 MHz, d\(_6\)-DMSO): \( \delta \) 8.97 (s, 1 H, N=C=H-N), 6.55 (s, 4H, \( \text{C}_6\text{H}_2 \)), 4.37 (s, 4H, N=C=H-N), 2.92 (s, 12 H, N(\( \text{C}_6\text{H}_3 \))\(_2\)), 2.32 (s, 12 H, ary-C\(_6\text{H}_3\)); \(^{13}\)C NMR (75.9 MHz, d\(_6\)-DMSO): \( \delta \) 160.8 (N=C=H-N), 150.8, 135.9, 122.2, 111.7 (\( \text{C}_6\text{H}_2 \)), 51.3 (N-\( \text{C}_6\text{H}_3 \)), 40.0 (N(\( \text{C}_6\text{H}_3 \))\(_2\)), 17.8 (\( \text{C}_6\text{H}_2-\text{C}_6\text{H}_3 \)).

Synthesis of 1,3-Bis(2',6'-dimethyl-4'-dimethylaminophenyl)imidazoliun chloride, ITap HCl (38)

Under non-inert conditions, a solution of chlorotrimethylsilane (0.345 g, 3.20 mmol) in ethyl acetate (20 mL) was added to a solution of diimine 35 (1.086 g, 3.09 mmol) in ethyl acetate (50 mL) containing paraformaldehyde (0.139 g, 4.64 mmol) under stirring at 70 °C over a period of 5 h. After the addition, the reaction was kept under stirring at 70 °C for another 16 h. During this time, a slightly reddish-purple precipitate formed. After cooling to room temperature, the slurry was filtered, the residue was washed with ethyl acetate (2 x 10 mL) and dried in the vacuum oven at 60 °C to give ligand precursor 38 (0.998 g, 2.50 mmol, 78%) as a slightly off white powder in >99% purity (\(^1\)H NMR). \(^1\)H NMR (300.1 MHz, CDCl\(_3\), 20 °C): \( \delta \) 10.09 (t, \(^3\)J\(^1\)H\(^1\)H = 1.5 Hz, 1H),
7.67 (d, 3J[1H,1H] = 1.5 Hz, 2H, C$_3$H$_3$N$_2$), 6.46 (s, 4H, 2 x C$_6$H$_2$), 3.00 (s, 6H, N(CH$_3$)$_2$), 2.17 (s, 6H, 2 x C$_6$H$_2$(CH$_3$)$_2$); $^{13}$C NMR (75.9 MHz, CDCl$_3$, 20 °C): δ 151.3, 138.9, 121.8, 111.6 (C$_6$H$_2$), 134.7, 125.3 (C$_3$H$_3$N$_2$), 40.2 (N(CH$_3$)$_2$), 18.2 (C$_6$H$_2$(CH$_3$)$_2$).

Synthesis of 4-iodo-2,6-dimethylbenzenamine (42)$^{108}$

Iodine (22.622 g, 89.1 mmol) was added to a solution of compound 2,6-dimethylaniline (10.027 g, 82.7 mmol) and NaHCO$_3$ (8.367 g, 99.5 mmol) in 250 mL CH$_2$Cl$_2$–H$_2$O 1:1 v/v in air with stirring at -5 °C over a period of 60 min. After the addition was complete, the reaction was stirred for 60 min at room temperature. Sodium thiosulfate (9.000 g, 36.2 mmol) was added and the reaction was stirred an addition 10 min to reduce the residual iodine. The organic phase was separated, washed with H$_2$O (3 x 100 mL), and the organic phase was separated and dried over NaSO$_4$. The solvent was removed to give compound 42 (19.610 g, 79.3 mmol, 96%) in >98% purity ($^1$H NMR) as a dark-colored solid.

Synthesis of 4-iodo-2,6-diisopropylbenzenamine (43)$^{109}$

Iodine (22.015 g, 86.7 mmol) was added to a solution of 2,6-diisopropylaniline (14.552 g, 82.1 mmol) and NaHCO$_3$ (8.308 g, 98.9 mmol) in 250 mL CH$_2$Cl$_2$–DI H$_2$O 1:1 (v/v) in air with stirring at -5 °C over a period of 60 min. After the addition was complete, the reaction was stirred for 60 min at room temperature. Sodium thiosulfate was added and the reaction was stirred an addition 10 min to reduce the residual iodine. The organic phase was separated, washed with H$_2$O (3 x 100 mL), and the organic phase was separated and dried over NaSO$_4$. The solvent was removed to give compound 43 (19.610 g, 79.3 mmol, 96%) in >97% purity ($^1$H NMR) as a dark-colored solid.

Synthesis of 2-iodo-4,6-dimethylbenzenamine (44)$^{110}$

Iodine (17.818 g, 70.2 mmol) was added to a solution of 2,4-dimethylaniline (7.008 g, 57.9 mmol) and NaHCO$_3$ (5.881 g, 70.0 mmol) in 120 mL CH$_2$Cl$_2$–DI H$_2$O 1:1 (v/v) in air with stirring at -5 °C over a period of 60 min. After the addition was complete,
the reaction was stirred for 60 min at room temperature. Sodium thiosulfate was added and the reaction was stirred an addition 10 min to reduce the residual iodine. The organic phase was separated, washed with H$_2$O (3 x 100 mL), and the organic phase was separated and dried over NaSO$_4$. The solvent was removed to give compound 44 (17.070 g, 69.1 mmol, 94%) in >96% purity (1H NMR) as a dark-colored solid.

**Synthesis of Glyoxalbis(4-iodo-2,6-dimethylphenyl)imine (45)**

Aniline 42 (9.800 g, 32.9 mmol) was added to a solution of 40% aqueous glyoxal (3.982 g, 27.5 mmol) in methanol (100 mL) and one drop of conc. HCl$_{aq}$ and stirred for 24 hrs at room temperature. During the reaction, a deep-yellow colored precipitate was formed. The slurry was filtered, the residue was washed with methanol (3 x 20 mL), sucked dry and the dried in the vacuum oven at 60 °C for 3 h to give compound 45 (5.562 g, 10.8 mmol, 54%) in >98% purity (1H NMR) as a yellow powder. 1H NMR (300.1 MHz, 20 °C, CDCl$_3$): δ 8.06 (s, 2H, N=C), 7.44 (s, 4H, C$_6$H$_2$), 1.57 (s, 12H, C$_6$H$_2$–CH$_3$); 13C NMR (75.9MHz, 20 °C, CDCl$_3$): δ 163.4 (N=C), 149.7, 137.2, 129.1, 89.3 (C$_6$H$_2$), 18.1 (CH$_3$).

**Synthesis of Glyoxalbis(4-iodo-2,6-diisopropylphenyl)imine (46)**

Aniline 43 (4.323 g, 14.2 mmol) was added to a solution of 40% aqueous glyoxal (2.059 g, 14.3 mmol) in methanol (50 mL) and one drop of conc. HCl$_{aq}$ and stirred for 24 hrs at room temperature. During the reaction, a deep-yellow colored precipitate was formed. The slurry was filtered, the residue was washed with methanol (3 x 20 mL), sucked dry and the dried in the vacuum oven at 60 °C for 3 h to give compound 46 (5.432 g, 5.61 mmol, 79%) in >98% purity (1H NMR) as a golden-yellow powder. 1H NMR (300.1 MHz, 20 °C, CDCl$_3$): δ 8.03 (s, 2H, N=C), 7.44 (s, 4H, C$_6$H$_2$), 2.84 (m, 4H, iPr–CH$_2$), 1.18 (d, 3J[H,H] = 6.9 Hz, 24H, iPr–CH$_3$); 13C NMR (75.9MHz, 20 °C, CDCl$_3$): δ 160.4 (N=C), 147.8, 139.5, 132.7, 90.5 (C$_6$H$_2$), 28.5 (iPr–CH$_3$), 23.4 (iPr–CH$_3$).

**Synthesis of Glyoxalbis(2-iodo-4,6-dimethylphenyl)imine (47)**
Aniline 44 (12.454 g, 41.9 mmol) was added to a solution of 40% aqueous glyoxal (6.096 g, 42.1 mmol) in methanol (100 mL) and one drop of conc. HCl\textsubscript{aq} and stirred for 24 hrs at room temperature. During the reaction, a deep-yellow colored precipitate was formed. The slurry was filtered, the residue was washed with methanol (3 x 20 mL), sucked dry and the dried in the vacuum oven at 60 °C for 3 h to give compound 47 (5.562 g, 10.8 mmol, 54%) in >96% purity (\textsuperscript{1}H NMR) as a yellow powder.

\textsuperscript{1}H NMR (300.1 MHz, 20 °C, CDCl\textsubscript{3}): δ 8.14 (s, 2H, N=C\textsubscript{6}H\textsubscript{2}), 7.57 (s, 2H, C\textsubscript{6}H\textsubscript{2}), 7.03 (s, 2H, C\textsubscript{6}H\textsubscript{2}), 2.29 (s, 6H, C\textsubscript{6}H\textsubscript{2}–C\textsubscript{H}\textsubscript{3}), 2.21 (s, 6H, C\textsubscript{6}H\textsubscript{2}–C\textsubscript{H}\textsubscript{3}); \textsuperscript{13}C NMR (75.9MHz, 20 °C, CDCl\textsubscript{3}): δ 165.3 (N=\textsubscript{C}H), 156.7, 138.3, 137.9, 130.4, 133.2, 84.6 (C\textsubscript{6}H\textsubscript{2}), 24.1 (CH\textsubscript{3}), 15.3 (CH\textsubscript{3}).

\textit{Synthesis of N,N'-Bis(4'-iodo-2',6'-dimethylphenyl)amino-1,2-ethane (48)}

A solution of compound 45 (4.822 g, 9.31 mmol) in thf (100 mL) containing NaBH\textsubscript{4} (0.932 g, 24.6 mmol) and boric acid (1.568 g, 25.3 mmol) was stirred at 30 °C over a period of 90 min. In this time period the solution turned colorless. The solution was cooled to room temperature and water (40 mL) was added carefully and then conc. HCl\textsubscript{aq} (16 mL) was added dropwise until the solution stopped developing gas. The solution was warmed to 50 °C under stirring for 10 min and then cooled to room temperature. The thf was removed under reduced pressure and the aqueous solution was neutralized with Na\textsubscript{2}CO\textsubscript{3}. The aqueous phase was extracted with tBuOMe (60 mL), and the organic layer was washed with brine (3 x 50 mL). The organic phase then was dried over Na\textsubscript{2}SO\textsubscript{4} and filtered. The solvent was removed under reduced pressure with a rotary evaporator, and the residue was dried in the vacuum oven at 60 °C for 2 h to give compound 48 (4.500 g, 8.71 mmol, 94%) as an off-white solid in >98% purity. \textsuperscript{1}H NMR (300.1 MHz, 20 °C, CDCl\textsubscript{3}): δ 7.33 (s, 4H, C\textsubscript{6}H\textsubscript{2}), 3.31 (br, 2H, NH), 3.17 (s, 4H, NH–C\textsubscript{6}H\textsubscript{2}), 2.25 (s, 12H, C\textsubscript{6}H\textsubscript{2}–C\textsubscript{H}\textsubscript{3}); \textsuperscript{13}C NMR (75.9MHz, 20 °C, CDCl\textsubscript{3}): δ 145.9, 137.6, 132.1, 85.4 (C\textsubscript{6}H\textsubscript{2}), 48.8 (NH–C\textsubscript{6}H\textsubscript{2}), 18.6 (CH\textsubscript{3}).
**Synthesis of N,N'-Bis(4'-iodo-2',6'-diisopropylphenyl)amino-1,2-ethane (49)**

A solution of compound 46 (5.003 g, 8.02 mmol) in thf (100 mL) containing NaBH₄ (1.587 g, 15.9 mmol) and boric acid (1.3300 g, 21.1 mmol) was stirred at 30 °C over a period of 90 min. In this time period the solution turned colorless. The solution was cooled to room temperature and water (40 mL) was added carefully and then conc. HClₐq (17 mL) was added dropwise until the solution stopped developing gas. The solution was warmed to 50 °C under stirring for 10 min and then cooled to room temperature. The thf was removed under reduced pressure and the aqueous solution was neutralized with Na₂CO₃. The aqueous phase was extracted with tBuOMe (60 mL), and the organic layer was washed with brine (3 x 50 mL). The organic phase then was dried over Na₂SO₄ and filtered. The solvent was removed under reduced pressure with a rotary evaporator, and the residue was dried in the vacuum oven at 60 °C for 2 h to give compound 49 (4.661 g, 7.41 mmol, 93%) as an opaque solid in >98% purity (¹H NMR).

¹H NMR (300.1 MHz, 20 °C, CDCl₃): δ 7.39 (s, 4H, C₆H₂), 3.26 (br., 2H, NH), 3.20 (m, 4H, iPr–CH), 3.10 (s, 4H, NH–CH₂), 1.22 (d, 3JH¹H = 7.2 Hz, 24H, iPr–CH₃); ¹³C NMR (75.9MHz, 20 °C, CDCl₃): δ 145.3, 143.3, 133.1, 88.9 (C₆H₂), 52.2 (NH–CH₂), 28.0 (iPr–CH), 24.3 (iPr–CH₃).

**Synthesis of N,N'-Bis(2'-iodo-4',6'-dimethylphenyl)amino-1,2-ethane (50)**

A solution of compound 47 (5.174 g, 10.0 mmol) in thf (100 mL) containing NaBH₄ (2.0670 g, 54.7 mmol) and boric acid (1.695 g, 27.4 mmol) was stirred at 30 °C over a period of 90 min. In this time period the solution turned colorless. The solution was cooled to room temperature and water (40 mL) was added carefully and then conc. HClₐq (16 mL) was added dropwise until the solution stopped developing gas. The solution was warmed to 50 °C under stirring for 10 min and then cooled to room temperature. The thf was removed under reduced pressure and the aqueous solution was neutralized with Na₂CO₃. The aqueous phase was extracted with tBuOMe (60 mL),
and the organic layer was washed with brine (3 × 50 mL). The organic phase then was
dried over Na₂SO₄ and filtered. The solvent was removed under reduced pressure with a
rotary evaporator, and the residue was dried in the vacuum oven at 60°C for overnight to
give compound 50 (3.928 g, 7.51 mmol, 75%) as an off-white solid in >98% purity (¹H
NMR). ¹H NMR (300.1 MHz, 20 °C, CDCl₃): δ 7.43 (s, 2H, C₆H₂), 6.91 (s, 2H, C₆H₂), 3.49
(br, 2H, NH) 3.15 (s, 4H, NH–CH₂), 2.34 (s, 6H, C₆H₂–CH₃), 2.20 (s, 6H, C₆H₂–CH₃); ¹³C
NMR (75.9MHz, 20 °C, CDCl₃): δ 151.6, 137.6, 130.8, 128.4, 126.6, 81.2 (C₆H₂), 49.1
(NH–CH₂), 23.9 (CH₃), 20.5 (CH₃).

Synthesis of N,N′-Bis(4′-[2′′-dimethylaminoethoxy]-2′,6′-dimethylphenyl)amino-1,2-
ethane (51)

Diamine 48 (2.105 g, 4.00 mmol) was added to a solution of KOtBu (1.820 g,
16.2 mmol) in N,N-Dimethylethanolamine (30 mL) and stirred under inert gas conditions
at 60 °C for 60 min. After 60 min, CuCl (1.01, 10.2 mmol) was added under N₂ gas. Then
vacuum was applied and the reaction was stirred at 130 °C overnight. tBuOMe (100 mL)
and aqueous ammonia (1.5M, 100 mL) was added and the solution was stirred in air at
room temperature for 60 min. The yellow-colored organic phase was separated, washed
with brine (6 x 100 mL), then dried over Na₂SO₄ and filtered. The solvent was removed
from the filtrate under reduced pressure with a rotary evaporator, and the residue was
dried in the vacuum oven at 60 °C for 3 h to give compound 51 (1.438 g, 3.23 mmol,
80%) as a dark-colored solid in >98% purity (¹H NMR). ¹H NMR (300.1 MHz, 20 °C,
CDCl₃): δ 6.61 (s, 4H, C₆H₂), 4.01 (t, ³J[¹H¹H] = 5.7 Hz, 4H, O-CH₂), 3.49 (br, 2H, N-H),
3.08 (s, 4H, NH-CH₂), 2.70 (t, ³J[¹H¹H] = 5.7 Hz, 4H, CH₂-NMe₂), 2.32 (s, 12H, C₆H₂–
CH₃), 2.29 (s, 12H, N(CH₃)₂); ¹³C NMR (75.9MHz, 20 °C, CDCl₃): δ 146.3, 137.8, 127.6,
112.2 (C₆H₂), 65.3 (O-CH₂), 59.6 (CH₂-NMe2), 52.6 (NH-CH₂), 46.2 (N(CH₃)₂), 16.2
(CH₃).
**Synthesis of N,N'-Bis(4'-[2''-dimethylaminoethanethio]-2',6'-dimethylphenyl)amino-1,2-ethane (52)**

Diamine 48 (2.005 g, 3.90 mmol) was added to a solution of 2-(Dimethylamino)ethanethiol hydrochloride (1.643 g, 12.0 mmol) and KOtBu (3.479 g, 31.0 mmol) in 1-methyl-2-pyrrolidinone (60 mL) and stirred under inert gas conditions at 60 °C for 60 min. After 60 min, CuCl (1.187 g, 12.0 mmol) was added under inert gas atmosphere. Vacuum was applied for 10 sec and the flask was sealed off. The reaction was stirred under vacuum at 110 °C for 16 h. tBuOMe (100 mL), aqueous ammonia (100 mL) and 0.1 M NaOH (4 mL) was added and the solution was stirred in air at room temperature for 2 hrs. The organic phase was separated, washed with 0.1 M NaOH (3 x 80 mL) and brine (5 x 80 mL), and then dried over Na$_2$SO$_4$. The solvent was removed under reduced pressure with a rotary evaporator, and the residue was dried in the vacuum oven at 60 °C for overnight to give compound 52 (1.409 g, 3.01 mmol, 77%) as a light yellow powder with >96% purity ($^1$H NMR). $^1$H NMR (300.1 MHz, 20 °C, CDCl$_3$): $\delta$ 8.80 (s, 4H, C$_6$H$_2$), 3.39 (br, 2H, N-H), 3.18 (s, 4H, NH-CH$_2$), 2.96 (t, $^3$$J$[H'H] = 8.1 Hz, 4H, S-CH$_2$), 2.52 (t, $^3$$J$[H'H] = 8.1 Hz, 4H, CH$_2$-NMe$_2$), 2.30 (s, 12H, N(CH$_3$)$_2$), 2.26 (s, 12H, C$_6$H$_2$-CH$_3$); $^{13}$C NMR (75.9MHz, 20 °C, CDCl$_3$): $\delta$ 145.1, 131.5, 130.4, 127.9 (C$_6$H$_2$), 59.1 (CH$_2$-NMe2), 48.9 (S-CH$_2$), 45.6 (NH-CH$_2$), 33.1 (N(CH$_3$)$_2$), 18.8 (CH$_3$).

**Synthesis of N,N'-Bis(4'-[2''-dimethylaminoethoxy]-2',6'-diisopropylphenyl)amino-1,2-ethane (53)**

Diamine 49 (4.007 g, 6.32 mmol) was added to a solution of KOtBu (1.493 g, 13.3 mmol) in N,N-dimethylethanolamine (25 mL) and stirred under inert gas conditions at 60 °C for 60 min. After 60 min, CuCl (1.318, 13.3 mmol) was added under N$_2$ gas. Then vacuum was applied and the reaction was stirred at 120 °C for 16 h. tBuOMe (100 mL) and aqueous ammonia (1.5M, 100 mL) was added and the solution was stirred in air at room temperature for 60 min. The organic phase was separated, washed with brine (8
x 100 mL), then dried over Na$_2$SO$_4$ and filtered. The solvent was removed from the filtrate under reduced pressure and the filtrate residue was dried in the vacuum oven at 60 °C for 3 h to give compound 53 (2.792 g, 5.04 mmol, 79%) as a viscous brown liquid in >95% purity (1H NMR). 1H NMR (300.1 MHz, 20 °C, CDCl$_3$): δ 6.70 (s, 4H, C$_6$H$_2$), 4.06 (t, 3J[1H1H] = 6.0 Hz, 4H, O-CH$_2$), 3.37 (sept, 3J[1H1H] = 6.9 Hz, 4H, iPr-C$_2$H), 3.06 (s, 4H, NH-C$_2$H), 2.73 (t, 3J[1H1H] = 6.0 Hz, 4H, NMe$_2$-CH$_2$), 2.35 (s, 12H, N(C$_3$H$_3$)$_2$), 1.67 (br, 2H, N-H), 1.24 (d, 3J[1H1H] = 6.0 Hz, 24H, iPr-C$_3$H$_3$); 13C NMR (75.9 MHz, 20 °C, CDCl$_3$): δ 155.7, 144.7, 136.7, 109.8 (C$_6$H$_2$), 65.9 (O-CH$_2$), 58.7 (N-C$_2$H), 52.8 (NH-C$_2$H), 46.2 (N(C$_3$H$_3$)$_2$), 28.2 (iPr-CH), 24.5 (iPr-CH$_3$).

Synthesis of N,N’-Bis(4’-[2”-dimethylaminoethanethio]-2’,6’-diisopropylphenyl)amino-1,2-ethane (54)

Diamine 49 (3.041 g, 4.82 mmol) was added to a solution of 2-(Dimethylamino)ethanethiol hydrochloride (14.921 g, 14.8 mmol) and KOtBu (3.358 g, 29.9 mmol) in 1-methyl-2-pyrrolidinone (80 mL) and stirred under inert gas conditions at 60 °C for 60 min. After 60 min, CuCl (1.500, 15.2 mmol) was added under inert gas atmosphere. The reaction was stirred under vacuum at 110 °C 16 h. tBuOMe (100 mL), aqueous ammonia (1.5M, 100 mL) and 0.1 M NaOH (4 mL) was added and the solution was stirred in air at room temperature for 2 hrs. The organic phase was separated, washed with 0.1 M NaOH (3 x 80 mL) and brine (4 x 80 mL), and then dried over Na$_2$SO$_4$. The solvent was removed under reduced pressure with a rotary evaporator, and the residue was dried in the vacuum oven at 60 °C for 3 h to give compound 54 (2.091 g, 3.63 mmol, 74%) as a dark-colored oil which slowly solidified at room temperature to give the desired compound with >98% purity (1H NMR). 1H NMR (300.1 MHz, 20 °C, CDCl$_3$): δ 7.13 (s, 4H, C$_6$H$_2$), 3.31 (sept, 3J[1H1H] = 7.2 Hz, 4H, iPr-CH), 3.21 (s, 2H, N-H), 3.14 (s, 4H, NH-CH$_2$), 3.02 (t, 3J[1H1H] = 6.9 Hz, 4H, S-CH$_2$), 2.57 (t, 3J[1H1H] = 6.9 Hz, 4H, CH$_2$-NMe$_2$) 2.24 (s, 12H, N(CH$_3$)$_2$), 1.24 (d, 3J[1H1H] = 6.6 Hz,
24H, iPr-CH₃); ¹³C NMR (75.9MHz, 20 °C, CDCl₃): δ 143.6, 135.4, 126.2, 114.3 (C₆H₂),
59.4 (N-CH₂), 55.6 (NH-CH₂), 46.1 (N(CH₃)₂), 31.6 (S-CH₂), 28.9 (iPr-CH), 24.2 (iPr-
CH₃).

**Synthesis of Ligand Precursor Salt 55 (IXyONMe₂·HCl)**

Diamine 51 (1.200 g, 2.70 mmol) and ammonium chloride (0.183 g, 3.42 mmol) was heated in a mixture of triethyl ortho-formate (13 mL) and ethanol (5 mL) under reflux at 110 °C for 16 h. Then the solvent was distilled off under reduced pressure (0.1 Torr), and the unreacted triethyl-ortho-formate was collected to be reused. CH₂Cl₂ (5 mL) was added to dissolve the solid residue. Ethyl acetate (30 mL) was added, and the CH₂Cl₂ was removed under reduced pressure. The resulting slurry was sonicated for 30 min at 30 °C then filtered, washed with ethyl acetate (3 x 20 mL), sucked dry on the filter for 10 min and dried in the vacuum oven at 60 °C for 3 h to give NHC ligand precursor 55 (1.00 g, 2.04 mmol, 75%) as a white solid with >98 % purity (¹H NMR). ¹H NMR (300.1 MHz, 20 °C, CDCl₃): δ 9.18 (s, 1H, N–CH=N), 6.68 (s, 4H, C₆H₂), 4.58 (s, 4H, N-CH₂),
4.04 (t, J[H₁H] = 5.7 Hz, 4H, O-CH₂), 2.72 (t, J[H₁H] = 5.7 Hz, 4H, NMe₂-CH₂), 2.41
(s, 12H, C₆H₂-CH₃), 2.33 (s, 4H, N(CH₃)₂); ¹³C NMR (75.9MHz, 20 °C, CDCl₃): δ 160.4
(N-CH=N), 159.7, 137.0, 125.8, 115.2 (C₆H₂), 66.2 (O-CH₂), 58.4 (CH₂-NMe₂), 52.3 (=N-
CH₂), 46.1 (N(CH₃)₂), 18.5 (C₆H₂-CH₃).

**Synthesis of Ligand Precursor Salt 56 (IXySNMe₂·HCl)**

Diamine 52 (1.297 g, 2.73 mmol) and triethyl ammonium chloride (0.571 g, 4.16 mmol) was heated in a mixture of triethyl ortho-formate (13 mL) and ethanol (5 mL) under reflux at 100 °C for 16 h. Then the solvent was distilled off under reduced pressure (0.1 Torr), and the unreacted triethyl-ortho-formate was collected to be reused. CH₂Cl₂ (5 mL) was added to dissolve the solid residue. Ethyl acetate (30 mL) was added, and the CH₂Cl₂ was removed under reduced pressure. The resulting slurry was sonicated for 30 min at 30 °C then filtered, washed with ethyl acetate (3 x 20 mL), sucked dry on
the filter for 10 min and dried in the vacuum oven at 60 °C for 3 h to give NHC ligand precursor 56 (1.025 g, 1.97 mmol, 72%) as a white solid with >95 % purity (\(^1\)H NMR). \(^1\)H NMR (300.1 MHz, 20 °C, CDCl\(_3\)): δ 10.21 (s, 1H, N–CH=N), 7.19 (s, 4H, C\(_6\)H\(_2\)), 4.50 (s, 4H, N-CH\(_2\)), 3.23 (t, \(^3\)J\(^1\)H\(^1\)H\(_2\) = 7.8 Hz, 4H, S–CH\(_2\)), 2.91 (t, \(^3\)J\(^1\)H\(^1\)H\(_2\) = 6.0 Hz, 4H, NMe\(_2\)-CH\(_2\)), 2.59 (s, 12H, C\(_6\)H\(_2\)-CH\(_3\)), 2.43 (s, 4H, N(CH\(_3\))\(_2\)); \(^13\)C NMR (75.9MHz, 20 °C, CDCl\(_3\)): δ 160.7 (N–CH=N), 140.3, 136.2, 130.3, 128.3 (C\(_6\)H\(_2\)), 58.1 (S-CH\(_2\)), 52.0 (CH\(_2\)-NMe\(_2\)), 45.3 (=N-CH\(_2\)), 30.6 (N(CH\(_3\))\(_2\)), 18.5 (C\(_6\)H\(_2\)-CH\(_3\)).

**Synthesis of Ligand Precursor Salt 57 (IDippONMe\(_2\)HCl)**

Diamine 53 (2.604, 4.70 mmol) and ammonium chloride (0.306 g, 5.72 mmol) was heated in a mixture of triethyl ortho-formate (13 mL) and ethanol (5 mL) was heated under reflux at 110 °C for 16 h. Then the solvent was distilled off under reduced pressure (0.1 Torr), and the unreacted triethyl-ortho-formate was collected to be reused. CH\(_2\)Cl\(_2\) (5 mL) was added to dissolve the solid residue. Ethyl acetate (30 mL) was added, and the CH\(_2\)Cl\(_2\) was removed under reduced pressure. The slurry was sonicated for 30 min at 30 °C then filtered, washed with ethyl acetate (3 x 20 mL), sucked dry on the filter for 10 min and dried in the vacuum oven at 60 °C for 3 h to give ligand precursor 57 (0.952 g, 1.51 mmol, 31%) as a white powder with >98 % purity (\(^1\)H NMR). \(^1\)H NMR (300.1 MHz, 20 °C, CDCl\(_3\)): δ 8.09 (s, 1H, N–CH=N), 6.78 (s, 4H, C\(_6\)H\(_2\)), 4.80 (t, \(^3\)J\(^1\)H\(^1\)H\(_2\) = 11.4 Hz, 4H, N-CH\(_2\)) 4.08 (t, \(^3\)J\(^1\)H\(^1\)H\(_2\) = 5.7 Hz, 4H, O–CH\(_2\)), 3.00 (sept, \(^3\)J\(^1\)H\(^1\)H\(_2\) = 10.4 Hz, 4H, iPr–CH\(_3\)), 2.75 (t, \(^3\)J\(^1\)H\(^1\)H\(_2\) = 5.7 Hz, 4H, NMe\(_2\)-CH\(_2\)), 2.36 (s, 12H, N(CH\(_3\))\(_2\)), 1.22 (d, \(^3\)J\(^1\)H\(^1\)H\(_2\) = 6.6 Hz, 12H, iPr–CH\(_3\)), 1.37 (d, \(^3\)J\(^1\)H\(^1\)H\(_2\) = 6.9 Hz, 12H, iPr–CH\(_3\)); \(^13\)C NMR (75.9MHz, 20 °C, CDCl\(_3\)): δ 161.0 (N–CH=N), 158.9, 147.9, 122.2, 111.0 (C\(_6\)H\(_2\)), 66.1 (O-CH\(_2\)), 58.4 (N-CH\(_2\)), 55.7 (=N-CH\(_2\)), 46.1 (N(CH\(_3\))\(_2\)), 29.6 (iPr–CH\(_3\)), 25.6, 23.9 (i-Pr–CH\(_3\)).

**Synthesis of Ligand Precursor Salt 58 (IDippSNMe\(_2\)HCl)**

Diamine 54 (2.091, 3.61 mmol) and ammonium chloride (0.235 g, 4.40 mmol) in a mixture of triethyl ortho-formate (13 mL) and ethanol (5 mL) was heated under reflux at
110 °C for 16 h. Then the solvent was distilled off under reduced pressure (0.1 Torr), and the unreacted triethyl-ortho-formate was collected to be reused. CH₂Cl₂ (5 mL) was added to dissolve the solid residue. Ethyl acetate (30 mL) was added, and the CH₂Cl₂ was removed under reduced pressure. The slurry was sonicated for 30 min at 30 °C then filtered, washed with ethyl acetate (3 x 20 mL), sucked dry on the filter for 10 min and dried in the vacuum oven at 60 °C for 3 h to give ligand precursor 58 (1.112 g, 1.91 mmol, 52%) as a white powder with >97 % purity (¹H NMR). ¹H NMR (300.1 MHz, 20 °C, CDCl₃): δ 8.96 (s, 1H, N–C=CH=N), 7.09 (s, 4H, C₆H₄), 4.64 (s, 4H, N–CH₂), 3.04 (t, 3J[¹H¹H] = 6.6 Hz, 4H, S–CH₂), 2.89 (sept, 3J[¹H¹H] = 6.9 Hz, 4H, C₆H(CH₃)₂), 2.59 (t, 3J[¹H¹H] = 6.6 Hz, 4H, Me₂N–CH₂), 2.26 (s, 12H, N(CH₃)₂), 1.30 (d, 3J[¹H¹H] = 6.9 Hz, 12H), 1.19 (d, 3J[¹H¹H] = 6.9 Hz, 12H, CH(CH₃)₂), 1.30 (d, 3J[¹H¹H] = 6.9 Hz, 12H, CH(CH₃)₂), 1.19 (d, 3J[¹H¹H] = 6.9 Hz, 12H, CH(CH₃)₂); ¹³C NMR (75.9MHz, 20 °C, CDCl₃): δ 159.2 (N–C=CH=N), 146.3, 141.2, 126.6, 123.6 (C₆H₄), 58.0 (=N–CH₂), 55.0 (Me₂N–CH₂), 45.3 (N(CH₃)₂), 30.6 (S–CH₂), 29.1 (CH(CH₃)₂), 25.2, 23.4 (CH(CH₃)₂).

Synthesis of N,N'-Bis(2'-[2"-dimethylaminoethoxy]-4',6'-dimethylphenyl)amino-1,2-ethane (59)

Diamine 50 (1.650 g, 3.23 mmol) was added to a solution of KtBu (1.067 g, 9.51 mmol) in N,N-dimethylethanolamine (25 mL) and stirred under inert gas conditions at 60 °C for 60 min. After 60 min, CuCl (0.944, 9.52 mmol) was added under inert gas atmosphere. Then vacuum was applied and the reaction was stirred at 120 °C for 16 h. tBuOMe (100 mL) and aqueous ammonia (1.5M, 100 mL) was added and the solution was stirred in air at room temperature for 60 min. The organic phase was separated, washed with brine (8 x 100 mL), then dried over Na₂SO₄ and filtered. The solvent was removed under reduced pressure and the residue was dried in the vacuum oven at 60°C for 3 h to give compound 59 (0.854 g, 1.79 mmol, 56%) as a viscous brown liquid in >93% purity. ¹H NMR (300.1 MHz, 20 °C, CDCl₃): δ 7.10 (s, 2H, C₆H₂), 6.86 (s, 2H, C₆H₂), 4.42 (br, 2H, N-H), 3.19 (s, 4H, NH-CH₂), 2.87 (t, 3J[¹H¹H] =
7.8 Hz, 4H, O-CH₂), 2.48 (t, 3 J[^1H][^1H] = 6.6 Hz, 4H, CH₂-NMe₂), 2.30 (s, 6H, C₆H₂-CH₃), 2.30 (s, 6H, C₆H₂-CH₃), 2.27 (s, 6H, C₆H₂-CH₃), 2.23 (s, 12H, N(CH₃)₂). ¹³C NMR data was not determined for this compound.

*Synthesis of N,N'-Bis(2''-[2'''-dimethylaminoethanethio]-4',6''-dimethylphenyl) amino-1,2-ethane (60)*

Diamine 50 (1.529 g, 2.92 mmol) was added to a solution of 2-(Dimethylamino)ethanethiol hydrochloride (1.275 g, 9.00 mmol) and KOtBu (2.603 g, 23.2 mmol) in 1-methyl-2-pyrrolidinone (35 mL) and stirred under inert gas conditions at 60 °C for 60 min. After 60 min, CuCl (0.891 g, 9.04 mmol) was added under inert gas atmosphere. Vacuum was applied for 10 sec and the flask was sealed. The reaction was stirred under vacuum at 110 °C 16 h. tBuOMe (60 mL), aqueous ammonia (1.5M, 60 mL) and 0.1 M NaOH (3 mL) was added and the solution was stirred in air at room temperature for 2 hrs. The organic phase was separated, washed with 0.1 M NaOH (4x 60 mL) and brine (3 x 60 mL), and then dried over Na₂SO₄. The Na₂SO₄ was removed via filtration. The solvent was removed from the filtrate under reduced pressure with a rotary evaporator, and the residue was dried in the vacuum oven at 60 °C for 16 h to give compound 60 (0.902 g, 1.90 mmol, 66%) as a viscous brown liquid in >90% purity (¹H NMR). ¹H NMR (300.1 MHz, 20 °C, CDCl₃): δ 6.60 (s, 2H, C₆H₂), 6.41 (s, 2H, C₆H₂), 4.46 (br, 2H, N-H), 3.31 (s, 4H, NH-CH₂), 2.91 (m, 4H, O-CH₂), 2.68 (m, 4H, CH₂-NMe₂), 2.38 (s, 6H, C₆H₂-CH₃), 2.34 (s, 6H, C₆H₂-CH₃), 2.21 (s, 6H, C₆H₂-CH₃), 2.23 (s, 12H, N(CH₃)₂). ¹³C NMR data was not determined for this compound.

*Synthesis of (H₂ITap)(PCy₃)Cl₂Ru=CH-Ph (61)*

Ligand precursor 37 (0.637 g, 1.61 mmol) and KOtBu (0.178 g, 1.60 mmol) were heated under stirring to 60 °C in n-heptane for 60 min under inert gas conditions. After cooling to room temperature, Grubbs’ first generation catalyst 9 (1.003 g, 1.22 mmol) was added and the slurry was heated to 65 °C for 24 h also under inert gas conditions.
In this time period an orange-brownish precipitate was formed. The solution then was cooled to room temperature, the solvent was removed under reduced pressure and methanol was added under non-inert conditions. The resulting slurry was sonicated for 30 min in air and then filtered. The filter residue was washed with water (10 mL) and methanol (3 x 10 mL). The resulting light brown powder was dried in the vacuum oven at 60°C for 60 min to give catalyst 61 (0.794 g, 0.86 mmol, 70%) in >98% purity (\(^1\)H and \(^{31}\)P NMR spectroscopy). \(^1\)H NMR (300.1 MHz, 20 °C, CD\(_2\)Cl\(_2\)): δ 19.02 (s, 1 H, Ru=CH), 8.95 (br, 2 H), 7.07 (br, 3 H,C\(_6\)H\(_5\)), 6.49 (s, 4 H,C\(_6\)H\(_2\)), 3.91 (br, 4H,N–CH\(_2\)), 2.96 (s, 12H,N(C\(_3\)H\(_3\))), 2.72 (s, 12H,C\(_6\)H\(_2–\)C\(_6\)H\(_5\))), 2.42–2.60 (br m, 4 H, NHC\(_3\)), 1.92–2.05 (br m, 3 H), 1.29–1.55 (br m,12 H), 0.92–1.12 (br m, PCy\(_3\)), \(^1\)H NMR (300.1 MHz, 20 °C, CD\(_2\)Cl\(_2\)): δ 294.1 (br, Ru=CH), 221.4 (d, \(^2\)J\(^{31}\)P\(^{13}\)C = 80.1 Hz, NHC\(_3\)), 164.4, 129.7, 128.0, 127.5 (s, =CH–C\(_6\)H\(_5\)), 152.1, 150.5, 150.1, 140.0 (br), 137.6 (br), 128.3, 112.3, 111.7 (s, NHC-Ph-CH), 53.1 (d, \(^4\)J\(^{31}\)P\(^{13}\)C = 3.3 Hz), 52.1 (s, N–C\(_6\)H\(_5\)), 40.5, 40.4 (s, N(CH\(_3\))\(_2\)), 20.9 (s), 19.3 (br, C\(_6\)H\(_2\)), 31.7 (d, \(^1\)J\(^{31}\)P\(^{13}\)C = 16.5 Hz), 29.6 (br), 28.3 (d, \(^3\)J\(^{31}\)P\(^{13}\)C = 10.2 Hz), 26.8 (s, PCy\(_3\)-C); \(^{31}\)P NMR (121.4 MHz, 20 °C, CD\(_2\)Cl\(_2\)): δ 30.2 (s).

**Synthesis of \((H_2ITap)Cl_2Ru=CH-(C_6H_4-O-iPr) (62)***

Catalyst 61 (0.303 g, 0.33 mmol) in CH\(_2\)Cl\(_2\) (15 mL) was stirred at room temperature under inert gas conditions with CuCl (0.036 g, 0.40 mmol) and 2-\(\text{-i-}\)propoxystyrene (0.054 g, 0.33 mmol) for 2 h. The solution turned from brown to green in this time period. Then the solvent was removed under reduced pressure and the residue was taken up in 10 mL of a mixture of CH\(_2\)Cl\(_2\)–heptane 1:1 v/v in air. The solution was filtered, and then was loaded onto a flash column with silica gel. The column was washed with a mixture of CH\(_2\)Cl\(_2\)–ethanol 95:5 v/v until all green color was removed from the stationary phase. The solvent was removed under reduced pressure and the residue was taken up in CH\(_2\)Cl\(_2\) (10mL). Heptane (30 mL) was added and the residual CH\(_2\)Cl\(_2\)
was removed under reduced pressure. The product precipitated and the slurry was filtered. The filter residue was washed with n-heptane (3 x 10 mL), sucked dry for 5 min and dried in the vacuum oven at 60°C for 60 min to give catalyst 62 (0.162 g, 0.23 mmol, 70%) as a green powder in >98% purity (1H NMR). 1H NMR (300.1 MHz, 20 °C, CDCl₃): δ 16.80 (s, 1 H, Ru=CH), 7.47(m, 1H), 7.01 (m, 1H), 6.85(m, 1H), 6.78 (m, 1H, C₆H₄), 6.58 (s, 4 H, NHC₆H₂), 4.15 (s, 4 H, N–C₆H₂), 3.00 (s, 12 H, N(C₆H₃)₂), 2.44 (br, 12 H, C₆H₂–CH₃), 4.89 (sept., 3J[¹H¹H] = 6.0 Hz, 1H, CH(CH₃)₂), 1.28 (d, 3J[¹H¹H] = 6.0 Hz, 6 H, CH(CH₃)₂); 13C NMR (75.9 MHz, 20 °C, CDCl₃): δ 299.0 (Ru=CH), 211.7 (N=C–N), 161.0, 150.8, 122.8, 122.2, 112.9, 112.2 (s, =CH–C₆H₄), 152.2, 145.5, 129.3, 112.2 (s, C₆H₂), 74.8 (CH(CH₃)₂), 26.9 (CH(CH₃)₂), 40.8 (s, N(CH₃)₂), 21.1 (C₆H₂–CH₃).

Crystal Structure Determination of Catalysts 61 and 62

Deep brown crystals of 61 are triclinic, a = 9.6949(5) Å, b = 13.969(2) Å, c = 17.5080(7) Å, α = 99.287(7)°, β = 99.451(4)°, γ = 90.001(7)°, volume = 2307.4(4)Å³, two molecules per cell in space group P-1 (#2); very small green crystals of 62 are monoclinic, a = 19.6502(11) Å, b = 10.9433(5) Å, c = 33.440(2) Å, β = 104.928(7)°, volume = 6948.2(7)Å³, eight molecules per cell in space group P2(1)/a (#14). Data was collected with MoKα radiation (λ = 0.71073Å) at 295(2)K, and an analytical absorption correction was applied. Structures were solved with SHELXS-86;¹⁰ non-H atoms were modeled with anisotropic vibrational parameters, H-atoms were located in difference electron density maps but placed in idealized positions with isotropic vibrational parameters 20% larger than the equivalent isotropic vibrational factor of the adjacent carbon atom. In each structure, aryl methyl H’s are disordered over alternate trigonal positions; these were modeled by refining occupancy factors. Structural models were refined to convergence by full-matrix least-squares using SHELXL-97.¹¹ Final R for 61...
was 0.040 for 9628 reflections with I > 2σI, 513 parameters, goodness-of-fit 1.04; for 62, final R was 0.086 for 5128 reflections with I > 2σI, 774 parameters, goodness-of-fit 0.99.

*Synthesis of (H₂ITap)(DMAP)₂Cl₂Ru=CH-Ph (65)*

4-Dimethylaminopyridine (DMAP, 0.488 g, 4.00 mmol) was added to a slurry of catalyst 61 (1.232 g, 1.36 mmol) in t-butyl methyl ether (50 mL) and the solution was stirred for 16 h. In this time, a bright green precipitate formed and the supernatant solution turned colorless from a previous light brown. The precipitate is filtered in air and washed once with a 1 mM solution of DMAP in t-butyl methyl ether (20 mL) and the residue was dried in the vacuum oven at 60 °C for 2 h to give compound 65 (1.065 g, 1.22 mmol, 90 %) in >99 % purity (¹H NMR).

¹H NMR (300.1 MHz, C₆D₆, 20 °C): δ 19.81 (s, Ru=CH), 8.57 (d, J¹H¹H = 7.2 Hz, 2H), 7.23 (t, J¹H¹H = 8.4 Hz, 1H), 7.01 (m, 2H, =CH-C₆H₅), 8.29 (d, J¹H¹H = 7.5 Hz, 2H), 8.18 (d, J¹H¹H = 6.3 Hz, 2H), 6.08 (d, J¹H¹H = 7.5 Hz, 2H), 5.43 (d, J¹H¹H = 6.3 Hz, 2H, 2 × C₆NH₂), 6.59 (s, 2H), 6.34 (s, 2H, 2 × C₆H₂), 3.57 (m, 2H), 3.48 (m, 2H, CH₂-C₆H₂), 3.01 (s, 6H), 2.61 (s, 6H), 2.58 (s, 6H), 2.54 (s, 6H, 4 × N(CH₃)₂), 2.20 (s, 6H), 1.80 (s, 6H, 2 × C₆H₂(CH₃)₂). ¹³C NMR (75.9 MHz, 20 °C, C₆D₆): δ 309.8 (Ru=CH), 221.2 (N-C-N), 153.7, 153.5, 152.5 (2 signals), 152.1, 150.5 (2 signals), 150.4, 140.8, 138.7, 130.9, 130.6, 128.9, 128.6, 113.1, 112.6, 106.7, 106.2 (aryl-C), 51.9, 51.1 (N-CH₂-CH₂-N), 40.5, 40.3, 38.2, 37.8 (N-CH₃), 21.7, 19.6 (C₆H₂(CH₃)₂).

*Synthesis of (H₂ITap)Cl₂Ru(=CH-CH₂-CH₂-CH₂-C₆H₄N) (66)*

Complex 61 (0.100 g, 0.110 mmol) and 2-but-3'-enylpyridine (0.022 g, 0.17 mmol) were stirred in tBuOMe (20 mL) for 16 h at room temperature. After this time, the resulting greenish slurry was filtered in air, and the residue washed with tBuOMe (2 × 10 mL) and dried in the vacuum oven (60 °C, 4 h) to give complex 66 (0.064 g, 0.097 mmol, 88%) as a gray-green powder in >96% purity (¹H NMR).

¹H NMR (300.1 MHz, 20 °C,
C₆D₆: δ 18.99 (t, 3J¹H¹H] = 2.5 Hz, 1H, Ru=CH), 8.26 (m, 1H), 6.56 (m, 1H), 6.27 (m, 1H), 6.16 (m, 1H, C₆H₄N), 6.59 (s, 4H, C₆H₂), 3.53 (s, 4H, N-CH₂CH₂N), 3.41 (t, 3J¹H¹H] = 6.0 Hz, 2H), 2.84 (m, 2H, CH₂CH₂), 2.77 (br, 12H, C₆H₂(C₆H₃)₂), 1.73 (br. m, 6H), 1.55 (br. m, 9H), 1.12 (br. m, 15H, PCy₃); ¹³C NMR (75.9 MHz, CD₂Cl₂, 20 °C): δ 334.4 (Ru=CH), 217.8 (N-C-N), 162.2, 150.5, 150.2, 140.1, 138.6, 135.5, 123.3, 120.8, 112.4 (aryl-C), 53.9 (CH₂), 51.7 (CH), 40.2 (N(CH₃)₂), 34.0 (CH₂), 22.3 (CH₃), 19.6 (CH₃).

Synthesis of (ITap)(PCy₃)Cl₂Ru=CH-Ph (67)

ITap ligand precursor 38 (0.303 g, 0.76 mmol) and Potassium bis(trimethylsilyl)amide (0.158 g, 0.79 mmol) were heated under stirring to 60 °C in n-heptane for 60 min under inert gas conditions. After cooling to room temperature, Grubbs’ 1st Generation catalyst 9 (0.400 g, 0.49 mmol) was added and the slurry was heated to 60°C for 24 h also under inert gas conditions. In this time period the solution turned brown. The solvent was removed under reduced pressure. A mixture of 2-propanol and water 1:1 v/v (50 mL) was added under non-inert conditions. The resulting slurry was sonicated for 30 min in air and then filtered. The filter residue was washed with water (3 x 10 mL) and methanol (2 x 10 mL). The resulting light orange-brown powder was dried in the vacuum oven at 60°C for 16 h to give catalyst 67 (0.379 g, 0.42 mmol, 95%) in >97% purity (¹H NMR and ³¹P NMR spectroscopy). ¹H NMR (300.1 MHz, 20 °C, C₆D₆): δ 20.01 (s, Ru=CH), 7.19 (br. m, 1H), 7.12 (br. m, 2H, =CH-C₆H₅), 7.02 (br. m, 2H), 6.53 (br. s, 4H, C₆H₂), 6.35 (m, 1H), 6.30 (m, 1H, N-CH=CH-N), 2.68 (s, 12H, 2 x N(CH₃)₂), 2.47 (s, 12H, 2 x C₆H₂(C₆H₃)₂), 2.60 (m, 3 H) 1.73 (br. m, 6H), 1.55 (br. m, 9H), 1.12 (br. m, 15H, PCy₃); ³¹C NMR (75.9 MHz, CD₂Cl₂, 20 °C): δ 294.7 (br., Ru=CH), 190.4 (d, 2J³¹P⁻¹³C] = 84.8 Hz, N-C-N), 152.1, 150.6, 150.2, 138.8, 137.4, 137.3, 128.9, 128.0, 127.7, 125.3 (2 signals), 124.9, 111.3, 110.7 (aryl-C + N-CH=CH-N), 40.1 (2 signals, N-CH₃), 20.2, 18.8 (C₆H₂(CH₃)₂), 31.5 (d, 1J³¹P⁻¹³C] = 17.2 Hz), 29.4 (br. s), 28.0 (d, 2J³¹P⁻¹³C] = 9.6 Hz), 26.5 (s, PCy₃); ³¹P NMR (121.4 MHz, C₆D₆, 20 °C): δ 32.4 (s).
Synthesis of (ITap)Cl₂Ru=CH-(C₆H₄-O-iPr) (68)

Complex 67 (0.301 g, 0.33 mmol) was stirred at room temperature under inert gas conditions with 2-i-propoxystyrene (0.190 g, 1.17 mmol) and CuCl (0.042 g, 0.43 mmol) for 16 h. Then the solvent was removed under reduced pressure and the residue was taken up in 3 mL of CH₂Cl₂ in air. The solution was filtered, and then loaded onto a flash column with silica gel. The column was washed cyclohexane (30 mL). This filtrate was discarded. The column was then washed with a mixture of ethyl acetate–cyclohexane 90:10 v/v until all of a thick brown band was removed from the stationary phase. The solvent was removed under reduced pressure and the residue was taken up in CH₂Cl₂ (10 mL). Heptane (30 mL) was added and the residual CH₂Cl₂ was removed under reduced pressure. The product precipitated and the slurry was filtered. The filter residue was washed with n-heptane (3 x 10 mL), sucked dry for 5 min and dried in the vacuum oven at 60°C overnight to give catalyst 68 (0.152 g, 0.22 mmol, 67%) as a green powder in > 96% purity (¹H NMR). ¹H NMR (300.1 MHz, 20 °C, C₆D₆): δ 17.01 (s, 1H, Ru=C₆H), 7.34 (m, 1H), 7.10 (m,1H), 6.67 (m,1H), 6.31 (m, 1H, C₆H₄), 6.58 (s, 4H, C₆H₂), 6.38 (s, 2H, N-CH=CH-N), 4.49 (sept., ³J[¹H¹H] = 6.0 Hz, 1H, iPr-CH₂), 2.63 (s, 12H, N(CH₃)₂), 2.51 (s, 12H, C₆H₆(CH₃)₂), 1.43 (d, ³J[¹H¹H] = 6.0 Hz, 6H, CH(CH₃)₂). ¹³C NMR (75.9 MHz, 20 °C, C₆D₆): δ 287.7 (Ru=C), 177.7 (N=C–N), 152.7, 151.4, 146.1, 139.0, 135.2, 124.8, 122.1, 122.0, 113.1, 112.1, (aryl-C), 111.8 (N=C=C-N), 75.0 (CH(CH₃)₂), 40.3 (N(CH₃)₂), 21.4 (CH(CH₃)₂), 20.1 (CH₃), 18.3 (CH₃).

Synthesis of (ITap)(DMAP)₂Cl₂Ru=CH-Ph (69)

4-Dimethylaminopyridine (DMAP, 0.165 g, 1.36 mmol) was added to a slurry of complex 67 (0.300 g, 0.33 mmol) in t-butyl methyl ether (80 mL) and the solution was sonicated at 30 °C for 2 h and then stirred at room temperature for another 16 h. The grayish-green precipitate was filtered in air, washed once with a 1 mM solution of DMAP in t-butyl methyl ether (20 mL) and the residue was dried in the vacuum oven at 60°C for
2 h to give compound 69 (0.251 g, 0.28 mmol, 84 %) in a purity of >99 % pure. $^1$H NMR (300.1 MHz, 20 °C, C$_6$D$_6$): δ 20.18 (s, 1H, Ru=C$_{13}$H), 8.82 (br., 2H), 7.26 (m, 1H), 7.04 (m, 2H, =CH-C$_6$H$_5$), 8.36 (d, $^3$J$[^1]$H$[^1]$H = 7.5 Hz, 2H), 8.18 (d, $^3$J$[^1]$H$[^1]$H = 7.2 Hz, 2H), 6.00 (d, $^3$J$[^1]$H$[^1]$H = 7.5 Hz, 2H), 5.43 (d, $^3$J$[^1]$H$[^1]$H = 6.3 Hz, 2H, 2 × C$_6$NH$_4$), 6.50 (s, 2H, N-C=CH=CH=N), 6.45 (br., 2H), 6.38 (br., 2H, 2 × C$_6$H$_2$), 2.87 (exp. s, 6H), 2.58 (s, 12H), 2.51 (br. s, 6H, 4 × N(CH$_3$)$_2$), 2.12 (s, 6H), 1.76 (s, 6H, 2 × C$_6$H$_2$(CH$_3$)$_2$). $^{13}$C NMR (75.9 MHz, 20°C, C$_6$D$_6$): δ 311.8 (Ru=C$_{13}$H), 188.1 (N-C-N), 153.3, 153.1, 152.0, 150.7, 150.5, 131.0, 128.4, 124.6, 112.1, 106.4, 105.9 (aryl-C), 139.4, 138.2 (N-C=CH=N), 40.2 (N(CH$_3$)$_2$), 38.1 (C$_6$H$_4$-N(CH$_3$)$_2$), 37.7 (C$_6$H$_4$-N(CH$_3$)$_2$), 20.9 (CH$_3$), 19.6 (CH$_3$).

Synthesis of (IXyONMe$_2$)(PCy$_3$)Cl$_2$Ru=CH-Ph (70)

Ligand precursor salt 55 (0.260 g, 0.53 mmol) and potassium bis(trimethylsilyl)amide (0.111 g, 0.55 mmol) were heated under stirring to 60 °C in n-heptane for 60 min under inert gas conditions. After cooling to room temperature, Grubbs’ 1st Generation Catalyst 9 (0.357 g, 0.43 mmol) was added and the slurry was heated to 60 °C for 48 h also under inert gas conditions. The solution was then filtered, and the filter residue was dried in a vacuum oven at 60 °C. The solvent was removed from the filtrate. The filtrate residue was sonicated in 2-propanol – DI H$_2$O 1:1 v/v (20 mL) for 30 min. The filter residue was washed with water (3 × 10 mL) and methanol (1 × 10 mL). The resulting light pink powder was dried in the vacuum oven at 60 °C for overnight to give catalyst 70 (0.171 g, 0.17 mmol, 40 %) in >99% purity ($^1$H NMR). $^1$H NMR (300.1 MHz, 20 °C, C$_6$D$_6$): δ 19.71 (s, Ru=CH$_3$), 7.23 (m, 3H), 7.10 (m, 2H), 6.84 (br., 4H, 2 × C$_6$H$_2$), 3.94 (t, $^3$J$[^1]$H$[^1]$H = 5.7 Hz, 2H), 3.61 (t, $^3$J$[^1]$H$[^1]$H = 6.0 Hz, 2H, 2 × O-CH$_2$), 3.30 (br., 6H), 2.75 (br., 6H, 2 × N(CH$_3$)$_2$), 2.62 (t, $^3$J$[^1]$H$[^1]$H = 5.7 Hz, 2H), 2.54 (t, $^3$J$[^1]$H$[^1]$H = 6.0 Hz, 2H, 2 × O-CH$_2$), 2.19 (s, 12H, 2 × C$_6$H$_2$(CH$_3$)$_2$), 2.55 (br., m, 3H), 1.60 (br., m, 12H), 1.15 (br. m, 18H, PCy$_3$); $^{13}$C NMR (75.9 MHz, 20 °C, d$_6$-benzene): δ 272.6 (br., Ru=CH$_3$), 189.5 (d, $^2$J$[^3]$P$[^13]$C = 87.6 Hz, N-C-N), 150.8, 150.0, 141.9, 139.3, 138.0,
Synthesis of (IDippONMe2)(DMAP)Cl2Ru=CH-Ph (77)

Ligand precursor 57 (0.332 g, 0.55 mmol) and KOtBu (0.066 g, 0.59 mmol) were stirred under vacuum at 90 °C in n-heptane for 5 h. After cooling for 5 min, Grubbs’ first generation catalyst 9 (0.301 g, 0.36 mmol) was added and the slurry was stirred at 60 °C for 48 h under vacuum. The solution was then filtered under inert gas into a schlenk flask containing 4-Dimethylaminopyridine (DMAP) (0.1512 g, 1.24 mmol). The solution was then sonicated for 3 h under inert gas conditions. The resulting slurry was cooled on ice for 30 min, then filtered in air. The filter residue was washed with heptane (3 x 10 mL). The resulting green powder was dried in the vacuum oven at 60 °C for overnight to give catalyst 77 (0.215 g, 0.20 mmol, 55%) in >95% purity (1H NMR).

1H NMR (300.1 MHz, 20 °C, C6D6): δ 19.63 (s, 1 H, Ru=C), 8.21 (d, 3J[1H1H] = 6.6 Hz, 2 H, DMAP), 8.10 (d, 3J[1H1H] = 7.5 Hz, 2 H, o-Ph), 7.18 (m, 2H, m-Ph), 7.03 (m, 1H, p-Ph), 6.98 (s, 4H, C6H2), 5.48 (d, 3J[1H1H] = 6.6 Hz, 2 H, DMAP), 4.36 (m, 4H, CH2), 4.02 (m, 4H, CH2), 3.81 (m, 4H, CH2), 2.66 (m, 4H, CH-CH3), 2.21 (6H, N(CH3)2), 2.14 (6H, N(CH3)2), 1.78 (6H, N(CH3)2), 1.73 (d, 3J[1H1H] = 5.7 Hz, 6 H, CH-CH3), 1.36 (d, 3J[1H1H] = 6.0 Hz, 6 H, CH-CH3), 1.22-1.28 (m, 12H, CH-CH3). 13C NMR (75.9 MHz, 20 °C, d6-benzene): δ 310.1 (Ru=C), 224.2 (N-C-N), 160.3, 159.9, 153.5, 152.5, 152.1, 152.0, 149.7, 132.0, 130.1, 129.5, 111.0, 110.3, 106.2 (aryl-C), 66.9, 66.4 (O-CH2), 58.7 (N-CH2-CH2-N), 54.8, 54.0 (N-CH2), 46.1 (4 x N(CH3)2), 37.8 (N(CH3)2), 29.8, 28.7 (4 x CH), 27.5, 26.7, 26.5, 24.1 (CH-CH3).

Synthesis of (IDippSNMe2)(DMAP)Cl2Ru=CH-Ph (78)

Ligand precursor 58 (0.256 g, 0.41 mmol) and potassium bis(trimethylsilyl)amide (0.086 g, 0.43 mmol) were heated under stirring to 60°C in n-heptane for 60 min under
inert gas conditions. After cooling to room temperature, Grubbs' first generation catalyst 9 (0.262 g, 0.32 mmol) was added and the slurry was heated to 60 °C for 24 h also under inert gas conditions. The solution was then filtered under inert gas. 4-Dimethylaminopyridine (0.159 g, 1.32 mmol) was added to the filtrate and sonicated in tBuOMe for 60 min under inert gas conditions. In this time period, a bright green precipitate was formed. The resulting slurry was stirred at room temperature 16 h, then sonicated an additional 60 min and filtered. The filter residue was washed with a 1 mM DMAP solution in tBuOMe (3 x 10 mL). The resulting green powder was dried in the vacuum oven at 60 °C for overnight to give catalyst 78 (0.084 g, 0.10 mmol, 24%) in >95% purity (1H NMR). 1H NMR (300.1 MHz, 20 °C, C6D6): δ 19.51 (s, 1H, Ru=C6H), 8.12 (d, 3J1H1H = 7.2 Hz, 2H), 8.03 (d, 3J1H1H = 7.2 Hz, 2H), 7.06 (d, 3J1H1H = 7.2 Hz, 2H), 5.57 (d, 3J1H1H = 7.2 Hz, 2H, 2 × C5N4H4), 7.65 (s, 2H), 7.41 (s, 2H, 2 x C6H2), 7.17 (m, 2 H), 7.09 (m, 3H, =CH-C6H5), 4.26 (m, 2 H), 4.00 (m, 2H, N-C6H2), 3.78 (m, 4H, CH(CH3)2), 3.03 (m, 4H, S–C6H5), 2.61 (m, 4H, Me2N-C6H2), 2.06 (s, 12H), 1.81 (s, 6 H), 1.19 (s, 6H, 4 x N(CH3)2), 1.65 (d, 3J1H1H = 5.7 Hz, 12H), 1.29 (d, 3J1H1H = 6.0 Hz, 12H, 4 x CH(CH3)2); 13C NMR (75.9 MHz, 20 °C, C6D6): δ n.o. (Ru=CH), 222.4 (N-C-N), 158.0, 153.0, 140.0, 128.6, 127.0, 125.7, 114.2, 114.1, 106.2, 105.9 (aryl-C), 66.4, 65.8, 58.6, 58.5, 51.8 (N-CH2-CH2-N), 46.1 (N(CH3)2), 38.1, 37.7, 27.1, 27.0, 26.7(CH3), 26.6(CH3), 20.3 (CH3), 20.0 (CH3).

**Synthesis of (H2ITap)(PCy3)Cl2Ru=CH-SPh (79)**

H2ITapHCl 37 (0.374 g, 0.93 mmol) and KOtBu (0.120 g, 1.07 mmol) were heated to 80 °C in heptane (60 mL) for 30 min. After the slurry cooled to room temperature, precatalyst 24 (0.606 g, 0.77 mmol) was added and the mixture was stirred at 60°C for 6 d in a closed vacuum. In this time period, a light-pink precipitate was formed. The reaction mixture was cooled to room temperature and then filtered in air. The residue was washed with heptanes (2 x 10 mL) and then dried in the vacuum oven.
at 60 °C for 4 h. A mixture of 2-propanol and 0.5 M aqueous ammonium chloride (3:1 v/v, 50 mL) was added to the dry residue under non-inert conditions and the mixture was sonicated at 30 °C for 60 min. The slurry was filtered in air, the residue was washed with methanol (2 × 10 mL) and then dried in the vacuum oven at 60°C for 2 h to give compound 79 (0.474 g, 0.50 mmol, 65 %) in >99 % purity (1H NMR). 1H NMR (300.1 MHz, 20°C, C6D6): δ 17.98 (s, Ru=CH), 7.21 (d, 3J[1H1H] = 7.2 Hz, 2H), 6.97 (t, 3J[1H1H] = 8.4 Hz, 1H), 6.88 (m, 2H, =CH-C6H5), 6.50 (s, 2H), 6.13 (s, 2H, 2 × C6H5), 3.35 (m, 4H, CH2-C6H5), 2.90 (s, 6H), 2.75 (s, 6H, 2 × N(CH3)2), 2.60 (s, 6H), 2.28 (s, 6H, 2 × C6H2(CH3)2), 2.57 (br., m, 3H), 1.88 (br., m, 6H), 1.65 (br., m, 6H), 1.55 (br., m, 3H), 1.45-1.02 (br., m, 18H, PCy3). 13C NMR (75.9 MHz, 20°C, d6-benzene): δ 272.2 (br., Ru=CH), 219.4 (d, 2J[31P13C] = 81.6 Hz, N-C-N), 150.5, 149.5, 141.8, 140.4, 138.6, 129.3, 128.7, 126.5, 125.5, 125.4, 112.7, 111.9 (s, aryl-C), 52.3, 52.1 (s, N-CH2-CH2-N), 40.5, 40.3, 40.0, 39.6 (N-CH3), 21.0, 20.0 (C6H2(CH3)2), 32.3 (d, 1J[31P13C] = 15.6 Hz), 29.7 (s), 28.1 (d, 2J[31P13C] = 10.2 Hz), 26.7 (s, PCy3); 31P NMR (121.4 MHz, 20°C, C6D6): δ 23.4 (s).

Synthesis of (ITap)(PCy3)Cl2Ru=CH-SPh (80)

ITapHCl 38 (0.599 g, 1.50 mmol) and KOtBu (0.193 g, 1.72 mmol) were heated to 80°C in heptane (120 mL) for 30 min. After the slurry cooled to room temperature, precatalyst 24 (0.992 g, 1.16 mmol) was added and the mixture was stirred at 60 °C for 96 h in a closed vacuum. In this time period, a light-pink precipitate was formed. The reaction mixture was cooled to room temperature and then filtered in air. The residue was washed with heptanes (2 x 10 mL) and then dried in the vacuum oven at 60°C for 4 h. A mixture of 2-propanol and 0.5 M aqueous ammonium chloride (3:1 v/v, 50 mL) was added to the dry residue under non-inert conditions and the mixture was sonicated at 30 °C for 60 min. The slurry was filtered in air, the residue was washed with methanol (2 × 10 mL) and then dried in the vacuum oven at 60°C for 2 h to give compound 80 (0.820 g,
0.91 mmol, 78\%) in >99 \% purity (\textsuperscript{1}H NMR). \textsuperscript{1}H NMR (300.1 MHz, 20 °C, C\textsubscript{6}D\textsubscript{6}): \textit{δ} 18.21 (s, Ru=CH), 7.25 (d, \textit{J}\textsuperscript{1}H\textsuperscript{1}H] = 7.5 Hz, 2H), 6.99 (t, \textit{J}\textsuperscript{1}H\textsuperscript{1}H] = 7.5 Hz, 2H), 6.89 (t, \textit{J}\textsuperscript{1}H\textsuperscript{1}H] = 7.5 Hz, 1H), 6.27 (m, 1H, N-CH=CH-N), 2.73 (s, 3H), 2.60 (s, 3H), 2.57 (s, 3H), 2.28 (s, 3H, 2 × N(C\textsubscript{6}H\textsubscript{3}))\textsubscript{2} + 2 × C\textsubscript{6}H\textsubscript{2}(C\textsubscript{6}H\textsubscript{3})\textsubscript{2}), 2.61 (br., m, 1H), 1.93 (br., m, 6H), 1.64 (br., m, 6H), 1.52 (br., m, 3H), 1.45-1.08 (br., m, 18H, PCy\textsubscript{3}). \textsuperscript{13}C NMR (75.9 MHz, 20 °C d\textsubscript{6}-benzene): \textit{δ} 272.6 (br., Ru=CH), 189.5 (d, \textit{J}\textsuperscript{31}P\textsuperscript{13}C] = 87.6 Hz, N-C-N), 150.8, 150.0, 141.9, 139.3, 138.0, 129.2, 128.7, 127.1, 125.6, 125.4, 124.9, 124.8, 112.0, 111.3 (s, aryl-C + N-CH=CH-N), 39.9, 39.5, (N\textsubscript{-}C\textsubscript{6}H\textsubscript{4}), 20.7, 19.8 (C\textsubscript{6}H\textsubscript{2}(C\textsubscript{6}H\textsubscript{3})\textsubscript{2}), 32.5 (d, \textit{J}\textsuperscript{31}P\textsuperscript{13}C] = 16.1 Hz), 29.8 (s), 28.1 (d, \textit{J}\textsuperscript{31}P\textsuperscript{13}C] = 10.2 Hz), 26.7 (s, PCy\textsubscript{3}); \textsuperscript{31}P NMR (121.4 MHz, 20°C, C\textsubscript{6}D\textsubscript{6}): \textit{δ} 26.0 (s).

\textit{Synthesis of (H\textsubscript{2}ITap)(DMAP)\textsubscript{2}Cl\textsubscript{2}Ru=CH-SPh (81)}

4-Dimethylaminopyridine (DMAP, 0.412 g, 3.38 mmol) was added to a slurry of catalyst 79 (1.237 g, 1.32 mmol) in t-butyl methyl ether (80 mL) and the solution was sonicated at 30°C for 2 h and then stirred at room temperature for another 16 h. The grayish-green precipitate was filtered in air, washed once with a 1 mM solution of DMAP in t-butyl methyl ether (20 mL) and the residue was dried in the vacuum oven at 60°C for 2 h to give compound 81 (1.110 g, 1.23 mmol, 93 \%) in >98 \% purity (\textsuperscript{1}H NMR). \textsuperscript{1}H NMR (300.1 MHz, 20 °C, CDCl\textsubscript{3}): \textit{δ} 17.33 (s, Ru=CH), 8.26 (br., 2H), 7.16 (br., 2H), 6.49 (br., 2H), 6.22 (br., 2H, 2 × C\textsubscript{6}NH\textsubscript{4}), 6.47 (s, 2H), 6.15 (s, 2H, 2 × C\textsubscript{6}H\textsubscript{2}), 7.13 (m, 5H, S-C\textsubscript{6}H\textsubscript{5}), 4.11 (m, 2H), 3.98 (m, 2H, CH\textsubscript{2}-CH\textsubscript{2}), 3.00 (s, 6H), 2.96 (s, 6H), 2.90 (s, 6H), 2.69 (s, 6H, 4 × N(C\textsubscript{6}H\textsubscript{3})\textsubscript{2}), 2.60 (s, 6H), 2.40 (s, 6H, 2 × C\textsubscript{6}H\textsubscript{2}(C\textsubscript{6}H\textsubscript{3})\textsubscript{2}). \textsuperscript{13}C NMR (75.9 MHz, 20 °C, CDCl\textsubscript{3}): The compound was not sufficiently soluble in C\textsubscript{6}D\textsubscript{6}. Thus, the spectra were recorded in CDCl\textsubscript{3}. The compound suffered from partial degradation during the recording time (approx. 20\% in 16 h). This was observed for all bis-DMAP Ru-carbene complexes in chlorinated solvents thus far. However, several signals for the compound
were observed. 220.9 (n-C-N), 154.2, 152.6, 150.3, 149.3, 138.7, 129.2, 128.4, 127.8, 127.2, 126.7, 112.2, 111.4, 106.5 (s, s, aryl-C), 52.3 (DMAP-CH$_3$), 40.7, 40.1, 39.8, 39.2 (N-(CH$_3$)$_2$), 20.9, 19.6 (C$_6$H$_2$(CH$_3$)$_2$).

_Crystal Structure Determination of Catalyst 81_

Dark red or brown crystals of 81 are triclinic, $a = 10.2523(5)$ Å, $b = 12.3752(6)$ Å, $c = 18.3356(6)$ Å, $\alpha = 86.269(4)^\circ$, $\beta = 88.750(4)^\circ$, $\gamma = 78.653(4)^\circ$, volume = 2275.91(19)Å$^3$, space group P-1 (#2). Data was collected with MoK$_\alpha$ radiation ($\lambda = 0.71073$Å) at 300(2)K, and an analytical absorption correction was applied. Structures were solved with SHELXS-86 and refinements were done using SHELXL-97; non-H atoms were modeled with anisotropic librational factors, H-atoms were located in difference electron density maps but placed in idealized positions with isotropic displacement parameters of 120% of the U (eq) of the attached atom.$^{82}$ Final R for 81 was 0.0555 for 4827 reflections with I > 2$\sigma$(I), 520 parameters, goodness-of-fit 1.009.

_Synthesis of (iTap)(DMAP)$_2$Cl$_2$Ru=CH-SPh (82)_

4-Dimethylaminopyridine (DMAP, 0.244 g, 2.00 mmol) was added to a slurry of catalyst 80 (0.601 mg, 0.64 mmol) in $t$-butyl methyl ether (30 mL) and the solution was sonicated at 30 °C for 2 h and then stirred at room temperature for another 16 h. The bright-green precipitate was filtered in air, washed once with a 1 mM solution of DMAP in $t$-butyl methyl ether (10 mL) and the residue was dried in the vacuum oven at 60 °C for 2 h to give compound 82 (0.498 g, 0.55 mmol, 86 %) in >99 % purity ($^1$H NMR). $^1$H NMR (300.1 MHz, 20 °C, CDCl$_3$): $\delta$ 17.68 (s, 1H, Ru=CH), 7.17 (m, 5H, S-C$_6$H$_5$), 6.85 (br., 2H, N-CH=CH-N), 8.61 (br., 2H), 8.03 (br., 2H), 6.09 (br., 8H, 2 × C$_6$NH$_4$ + 2 × C$_6$H$_2$), 2.93 (br., 12H), 2.77 (br., 6H), 2.65 (br., 6H, 4 × N(CH$_3$)$_2$), 2.27 (br., 12H, 2 × C$_6$H$_2$(CH$_3$)$_2$).

$^{13}$C NMR (75.9 MHz, 20 °C, CDCl$_3$): The compound was not sufficiently soluble in C$_6$D$_6$. Thus, the spectra were recorded in CDCl$_3$. The compound suffered from partial
degradation during the recording time (approx. 20% in 16 h). This was observed for all bis-DMAP Ru-carbene complexes in chlorinated solvents thus far. However, several signals for the compound were observed. $\delta$ 288.0 (br., Ru=CH), 187.5 (N-C-N), 151.3, 149.1, 130.1, 128.1, 124.5, 111.8, 106.6 (s, aryl-C + N-CH=CH-N), 40.1 (2 x N-CH$_3$), 39.1 (4 x N(CH$_3$)$_2$), 26.9 (C$_6$H$_2$-CH$_3$), 19.6 (C$_6$H$_2$-CH$_3$).

**Synthesis of (ITap)(PPh$_3$)Cl$_2$Ru-3-phenylindenylidene (87)**

ITapHCl ligand precursor 38 (0.678 g, 1.67 mmol) and KOtBu (0.220 g, 1.96 mmol) were heated under stirring to 60 °C in toluene (50 mL) for 60 min under inert gas conditions which resulted in the formation of a relatively clear solution with small salt crystals settling quickly. After cooling to room temperature, catalyst 21 (1.154 g, 1.30 mmol) was added and the slurry was heated to 60 °C for 24 h also under inert gas conditions. The solvent was then removed under reduced pressure. A mixture of 2-propanol and water 1:1 v/v (50 mL) was added under inert conditions. The resulting slurry was sonicated for 60 min and then filtered. The filter residue was washed with methanol (4 x 10 mL). The resulting light deep purple powder was dried in the vacuum oven at 60 °C overnight to give catalyst 87 (0.811 g, 0.82 mmol, 63%) in >97% purity (1H NMR). 1H NMR (300.1 MHz, 20 °C, CDCl$_3$): $\delta$ 7.80 (d, $^3$$J$[1H,1H] = 7.5 Hz, 1H), 7.62 (m, 2H), 7.51 (m, 1H), 7.34 (m, 2H) 7.20 (m, 9H), 7.06 (m, 6H), 6.90 (m, 1H), 6.86 (t, $^3$$J$[1H,1H] = 7.5 Hz, 1H), 6.66 (2 x s, 2 x 1H), 6.65 (s, 1H), 6.64 (s, 1H), 6.46 (s, 1H), 5.94 (m, 1H), 5.61 (m, 1H), 3.61 (s, 6H), 2.67 (s, 6H, 2 x N(CH$_3$)$_2$), 2.53 (s, 3 H) 2.47 (s, 3H), 2.01 (s, 3H), 1.73 (s, 3H, aryl-CH$_3$); 13C NMR (75.9 MHz, 20 °C, CDCl$_3$, significant signals): $\delta$ 300.7 (d, $^3$$J$[31P,13C] = 12.9 Hz, Ru=C), 185.1 (d, $^2$$J$[31P,31P] = 96.0 Hz, N-C-N), 40.4, 39.9 (N-CH$_3$), 20.6, 19.0 (C$_6$H$_2$(CH$_3$)$_2$); 31P NMR (121.4 MHz, 20 °C,C$_6$D$_6$): $\delta$ 28.8 (s).
Synthesis of (ITap)(DMAP)$_2$Cl$_2$Ru-3-phenylindenylidene (88)

4-Dimethylaminopyridine (DMAP, 0.209 g, 1.71 mmol) was added to a slurry of complex 87 (0.414 g, 0.42 mmol) in t-butyl methyl ether (50 mL) and the solution was stirred at 50 °C for 24 h. The reddish-purple precipitate was filtered in air, washed once with a 1 mM solution of DMAP in t-butyl methyl ether (20 mL) and the residue was dried in the vacuum oven at 60 °C for 2 h to give compound 88 (0.355 g, 0.37 mmol, 87 %) in >96% purity ($^1$H NMR).

$^1$H NMR (300.1 MHz, 20 °C, C$_6$D$_6$): 10.08 (1H), δ 9.37 (m, 2H), 9.19 (m, 2H), 8.44 (m, 1H), 8.07 (m, 4H) 7.72 (m, 2H), 7.18 (m, 2H), 7.12 (m, 2H), 6.80-7.07 (m, 5H), 6.58 (m, 1H), 6.53 (m, 1H), 6.33 (m, 1H), 6.26 (m, 1H), 5.96 (m, 2H), 5.73 (m, 2H), 5.64 (m, 1H), 2.79 (s, 3H), 2.70 (s, 3H) 2.70 (s, 6H), 2.35 (s, 6H), 2.26 (s, 3H), 1.99 (s, 3H, 4 × N(CH$_3$)$_2$), 2.07 (s, 3 H) 2.06 (s, 9H, aryl-CH$_3$); $^{13}$C NMR (75.9 MHz, 20°C, CDCl$_3$, significant signals): δ 301.0 (s, Ru=C), 185.7 (s, N-C=N), 40.4, 40.1, 38.5 (2 signals, N-CH$_3$), 21.6 (2 signals), 19.7, 19.6 (C$_6$H$_2$(CH$_3$)$_2$).

General Procedure for ROMP of COE

COE (7.8 mL, 60 mmol) was added to the catalyst solution (0.60 mL, 0.50 mM, 0.30 mmol, organic solvent) under inert conditions via a microlitre syringe and the monomer conversion was monitored via $^1$H NMR spectroscopy (300.1 MHz, 20 °C) by integration of the sufficiently separated multiplet signals at δ = 5.51 ppm (COE, =CH–) and 5.46 ppm (polymer, =CH-) in regular intervals over a period of 15 min to 10 days.

General Procedure for RCM of DEDAM

DEDAM (14.4 mL, 60 mmol) was added to the catalyst solution (0.60 mL, 1.00 mM, 0.60 mmol, organic solvent) under inert gas conditions via a microlitre syringe and the monomer conversion was monitored via $^1$H NMR spectroscopy (300.1 MHz, 20 °C) by integration of the sufficiently separated multiplet signals at δ = 2.87 ppm (DEDAM, allyl-CH$_2$) and 3.16 ppm [90, ring allyl-CH$_2$] in regular intervals over a period of 1 h to 3 days.
General Procedure for ROMP of 89 With Various Amounts of TsOH

Monomer 89 (15.9 μL, 60 μmol) in CH₂Cl₂ or CHCl₃ was added to the catalyst solution (0.60 mL, 1.0 mM, 0.60 μmol [61 in CH₂Cl₂; 62 in CHCl₃]) containing various molar equivalents of a 0.12 M solution of p-Toluenesulfonic acid in the same solvent (2.0 μL, 0.24 μmol, 0.4 equiv.) which were added 2 minutes prior via microliter syringe. The monomer conversion was monitored via ¹H NMR spectroscopy (300.1 MHz, 20 °C) by integration of the signals δ 6.46 ppm (s, 2H, monomer 89) and δ 5.91, 5.51 ppm (m, 2 cis-H and trans-H, poly-89).

General Procedure for Synthesis of Poly-89

A stock solution of monomer 89 (0.10 M, 2.0 mL, 0.20 mmol) in CH₂Cl₂ or CHCl₃ was added to a catalyst stock solution (1.0 mM, 2.0 mL, 2.0 μmol [61 in CH₂Cl₂; 62 in CHCl₃]) containing various molar equivalents of a 0.25 M solution of TsOH in 2-propanol (3.2 μL = 0.4 equivalents) which were added 2 minutes prior via microliter syringe. After appropriate time intervals (20 min – 10 h), the reactions were quenched with ethylvinyl ether and dried under vacuum. The resulting residue was dissolved in ethyl acetate (from catalyst 61) or CH₂Cl₂ (from catalyst 62), filtered through a short flash column of silica gel (1 cm) and additional solvent (5 ml) was used for elution. The solvent was removed from the filtrate in the vacuum oven (60 °C) and the residue was analyzed via ASEC.

General Procedure for the Reaction of Catalysts 61 and 62 With EVE

Ethylvinyl ether (EVE) (31 μL, 320 μmol) in CH₂Cl₂ or CHCl₃ was added to the catalyst solution (0.60 mL, 4.0 mM, 3.2 μmol [61 in CD₂Cl₂; 62 in CDCl₃]) containing various molar equivalents of a 0.60 M solution of p-Toluenesulfonic acid in 2-PrOH (0.60 M, 4.0 μL = 1 equiv.) which were added 2 minutes prior via microliter syringe. The monomer conversion was monitored via ¹H NMR spectroscopy (300.1 MHz, 20 °C) by integration of the signals δ 19.02 ppm (s, 1H, 61) or δ 16.25 ppm (s, 1H, 62) and δ 13.73
ppm (s, 1H, for catalyst 61 without acid), δ 7.50 ppm (m, 1H, 2-i propoxybenzylidene/styrene, for catalyst 62 without acid) or δ 7.86 ppm (m, 2 H, TsOH).

General Procedure for ROMP of Monomers 95 and 96

The catalyst (8 mmol) and monomer 95 (67.8 mg, 0.50 mmol) or monomer 96 (40.5, 0.5 mmol) were dissolved in the protic solvent (either in 2-PrOH–1 M HCl\textsubscript{aq} 9 : 1 v/v or 0.1 M HCl\textsubscript{aq}, 2.0 mL) under inert gas conditions and the solution was heated to 50 °C under stirring. An aliquot (0.3 mL) was taken after 30 min, quenched with ethylvinyl ether, dried under vacuum, and the monomer conversion was monitored via \(^1\text{H} \text{NMR}\) spectroscopy (300.1 MHz, 20 °C, D\textsubscript{2}O) by integration of the signals δ 6.49 ppm (m, 2 H, 95), δ 5.97 ppm (m, 2 \text{trans-H}, polymer) and δ 5.81 ppm (m, 2 \text{cis-H}, polymer) for monomer 95 and δ 6.46 ppm (m, 2 H, 96), δ 5.99 ppm (m, 2 \text{trans-H}, polymer) and δ 5.79 ppm (m, 2 \text{cis-H}, polymer) for monomer 96.

General Procedure for RCM of 97

The catalyst (8 mmol) and 97 (36.8 mg, 0.20 mmol) were dissolved in the protic solvent (2-PrOH–1M HCl\textsubscript{aq} 9 : 1 v/v or 0.1 M HCl\textsubscript{aq}, 2.0 mL) under inert gas conditions and the solution was heated to 50 °C under stirring. Aliquots (0.3 mL) were taken after 30 min and 60 min, quenched with ethylvinyl ether, dried under vacuum, and the product conversion was monitored via \(^1\text{H} \text{NMR}\) spectroscopy (300.1 MHz, 20°C, D\textsubscript{2}O) by integration of the signals δ 2.58 (97-CH\textsubscript{2}) and δ 2.98 ppm (cyclopentene-CH\textsubscript{2}).

\(^1\text{H} \text{NMR Investigation of the Hydrolytic Stability of 61a}

Complex 61a (2.0 mg, 3 mmol) was dissolved in 0.1 M DCI/D\textsubscript{2}O in air and kept at room temperature in an NMR tube. \(^1\text{H} \text{NMR}\) spectra were recorded in certain time intervals and the intensities were monitored for the corresponding NMR signals for complex 61 and the hydrolysis product 61a. \(^1\text{H} \text{NMR}\) (300.1 MHz, 20 °C, 0.1 M DCI/D\textsubscript{2}O) δ 16.29 (s, 1 H, Ru=C\text{H}), 7.04 (s, 4 H, C\text{6H}\text{2}), 7.11 (m, 1 H), 6.49 (m, 1 H), 6.43 (m, 2 H, C\text{6H}\text{4}), 4.46 (m, 1H, CH(CH\text{3})\text{2}), 3.64 (s, 4 H, N–CH\text{2}), 2.81 (s, 12 H, N(CH\text{3})\text{2}), 1.91 (s, 12
H, aryl-CH₃), 0.58 (m, 6 H, CH(CH₃)₂), 13C NMR (75.9 MHz, 20 °C, 0.1 M DCl/D₂O) δ (Ru=C, n.o.), 207.2 (N=C–N), 139.2, 132.1, 122.6, 122.0, 113.7 (1 signal n.o., =CH–C₆H₄), 152.0, 145.0, 142.3, 120.4 (s, C₆H₂), 74.8 (CH(CH₃)₂), 26.9 (CH(CH₃)₂), 40.8 (s, N(CH₃)₂), 21.1 (C₆H₂–CH₃).

General Procedure for RCM of DEDAM / DAP With Subsequent Ru Removal

The substrate (DEDAM: 96 mg, 0.40 mmol; DAP: 108 mg, 0.60 mmol) was added to a solution of catalyst 61 (DEDAM: 5.4 mg, 8 mmol; DAP: 8.1 mg, 12 mmol) in toluene or ethyl acetate (DEDAM: 2.0 mL; DAP: 3.0 mL) under inert gas conditions and the solution was kept stirring for 60 min at 50 °C. Then the solution was cooled to room temperature and acid (4 mL, conc. HClₐq or H₂SO₄ [96%]) was added under inert gas atmosphere and stirred for another 2 min causing the formation of a precipitate. The solution was filtered through Na₂SO₄, washed with the solvent (3 x 2 mL), and the solvent was removed under reduced pressure. The product was dried in the vacuum (0.1 Torr) for 30 min. Isolated yields were obtained in the range of 72–87% (DEDAM) and 43–79% (DAP). ¹H NMR (300.1 MHz, 20 °C, D₂O) was used to determine the conversion (all >99%) by integration of distinct signals for the starting material and RCM product [(δ 2.86 ppm (DEDAM-CH₂) vs. δ 3.16 ppm (cyclopentene-CH₂); δ 2.65 ppm (DAP-CH₂) vs. δ 2.91 ppm (cyclopentene-CH₂)]. An aliquot of 20–22 mg was taken from each reaction for Ru analysis via ICP MS. The residual product was dissolved in t-butylmethylether (20 mL) and washed with water (3 x 20 mL), the organic phase was dried over Na₂SO₄ and the solvent was removed and the product was dried in the vacuum (0.1 Torr) for 30 min. Product recoveries after the washing steps were between 44–69%. Aliquots of 20–22 mg were taken for Ru analysis via ICP MS.
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