THE USE OF SOLUBLE POLYOLEFINS AS SUPPORTS FOR

TRANSITION METAL CATALYSTS

A Dissertation

by

CHRISTOPHER EUGENE HOBBS

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

August 2011

Major Subject: Chemistry

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Approved by:

Chair of Committee,	David E. Bergbreiter
Committee Members,	Daniel A. Singleton
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	Daniel Shantz
Head of Department,	David H. Russell

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ABSTRACT

The Use of Soluble Polyolefins as Supports for Transition Metal Catalysts.

(August 2011)

Christopher Eugene Hobbs, B.S., Angelo State University

Chair of Advisory Committee: Dr. David E. Bergbreiter

Polymer supported transition metal catalysts are useful in organic chemistry as they make possible the facile separation and reuse of metal catalysts. Because of this, interest in these systems has garnered international attention in the scientific community as being "Green". Historically, insoluble, polymer-supports (i.e. Merrifield resin) were used to develop recoverable catalysts. However, these catalysts often have lower reactivity and selectivity when compared to homogeneous catalysts. Because of this, our lab has had interest in the development of soluble polymer-supports for transition metal catalysts. We have developed several separation methods for these soluble polymer-bound catalysts. These include thermomorphic liquid/liquid and solid/liquid as well as latent biphasic liquid/liquid separations. This dissertation describes the use of latent biphasic liquid/liquid and thermomorphic solid/liquid separation systems. Our lab has pioneered the use of polyisobutylene (PIB) oligomers as supports for transition metal catalysts. We have shown that these oligomers are > 99.96 % phase selectively soluble in nonpolar solvents. This has allowed us to prepare PIB-supported salen Cr(III) complexes that can be used in liquid/liquid solvent systems and can act as catalysts for

the ring opening of meso epoxides with azidotrimethylsilane (TMS-N$_3$) and can be recovered and recycled up to 6 times, with no loss in catalytic activity. Also described is the development of a PE$_{Olig}$-supported salen-Cr(III) complex that can be used as a recoverable/recyclable catalyst for the ring opening of epoxides with TMS-N$_3$ and could be reused 6 times with no loss in activity. It was also possible to prepare a PE-supported NHC-Ru complex that was able to be used as a recyclable ring closing metathesis (RCM) catalyst and could be recovered and recycled up to 10 times. Such PE$_{Olig}$-supported catalysts can perform homogeneous catalytic reactions at elevated temperatures (ca. 65 $^\circ$C), but, upon cooling, precipitate out of solution as solids while the products stay in solution. This allows for the separation of a solid catalyst from the product solution.

DEDICATION

To my family (especially my mother, for her love and support throughout this process). To my brother and sister, Eric and Heather, respectively. And to my nephew (and future chemist) Titus.

ACKNOWLEDGEMENTS

First, I would like to extend my sincerest gratitude to Professor David E. Bergbreiter for being a great teacher and mentor. I want to thank him for the opportunity to work in his laboratory and for teaching me how to be a true man of science. Through his tutelage and guidance, I have developed such a deep appreciation for science, and chemistry specifically, that I could not imagine doing anything else for the rest of my life. I would also like to thank him for his refreshing (and somewhat mysterious) good mood for the last three years of my graduate studies in his laboratory.

I would also like to thank Professor Donna K. Howell who had enough faith in a young, immature undergraduate student (who just finished his first year of college) to let him work in her laboratory. She inspired me in science and teaching greatly and has touched my life in more ways than she will ever know. Without her guidance, I would have never become a "professional" chemist. I would also like to thank her for her incredible friendship throughout the past 8 (or 9) years of my life.

I would like to express my thanks and gratitude to the members of the Bergbreiter research group, past and present. First I would like to thank Dr. Patrick Hamilton for his guidance and help as my mentor for the summer REU program and for my first year of graduate school. The lessons that he taught me have always stuck with me. I would like to thank Dr. Chayanant "Film" Hongfa for taking over for Patrick as my mentor throughout the end of my 3rd year of graduate school. Film was a joy to work with and his friendship will always be cherished. I would also like to thank some of the students that I have had the honor to mentor: Boom, Sally, Johnny and Grit. I would also

like to thank both Haw-Li Su and Yun-Chin "Jeff" Yang for their incredible scientific knowledge and advice with chemistry. Most importantly, out of this whole process, are the two closest friendships that I have developed. Without both Ollie and Victor I would have never made it past the seminar, let alone the Ph.D. program. None of the projects discussed in this dissertation would have been possible without the generous support from the Department of Chemistry at Texas A&M, The National Science Foundation, The Robert A. Welch Foundation and the Qatar National Research Fund.

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CHAPTER I

INTRODUCTION

The use of transition metal complexes in homogenous catalysis has been a main focal point in synthetic chemistry since the mid-20th century. From this interest have come many breakthroughs as transition metal complexes have been found to successfully catalyze a plethora of reactions. The search for transition metal complexes that have the ability to induce selectivity in chemical reactions has been an extremely active field of research and this activity has increased since the breakthroughs in the discovery of asymmetric oxidation[1] and hydrogenation[2] reactions by Sharpless and Noyori, respectively. Usually, stereoselectivity arises from the chiral nature of the ligands used (often times considered to be "privileged" ligands).[3] Some of these privileged ligands include: 2,2'-dihydroxy-1,1'-binaphthyl (BINOL), 2,2'-diphenylphosphino-1,1'-binaphthyl (BINAP), bis-oxazoline (Box) and salen ligands.

Even though many transition metal catalysts have high reactivity and selectivity, there are sometimes problems that arise from using such metals. These include; (i) the high cost of transition metals, (ii) the cost of the ligands or the availability of ligands only after tedious syntheses (especially in the case of chiral auxiliaries) and (iii) the potential environmental and toxicity of transition metals or ligands that are part of the homogeneous catalysts. The latter issue is especially important for synthetic processes

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This dissertation follows the style of *Journal of the American Chemical Society*.

that have application in pharmaceuticals. Because of these problems, interest dealing with the separation and recoverability/recyclability of transition metal catalysts has grown. This has been heightened by the increasing recognition by the community to issues related to "Green Chemistry" and sustainability. As science and technology move further into the 21st century, this interest in more environmentally benign chemical processes will increase. This is especially true for materials produced on an industrial scale (e.g. commodity chemicals, pharmaceuticals, agrochemicals, etc.). Thus catalyst and ligand separations are of increasing importance.

One method for the recovery and separation of catalysts is to use an insoluble or heterogeneous support. This has the advantage of allowing for separation of catalyst, ligand and product by a simple filtration. However, the heterogeneity of catalysts engendered by the insoluble support leads to problems including different reactivity and selectivity than homogeneous catalysts. This problem is inherent to systems that use heterogeneous catalysts because of the phase separation of the catalyst and substrates before, during and after a reaction. In spite of this issue, many different methods that use heterogeneous polymeric materials as solid supports have been developed ever since the revolutionary work of Merrifield[4] and Letsinger[5] in solid phase biopolymer synthesis using cross-linked polystyrene resin, work that led to Bruce Merrifield's recognition with the Nobel Prize in 1984.

In order to overcome the reactivity and selectivity problems that heterogeneous catalysts entail, much effort has been spent toward the development of systems that use soluble polymeric supports for the recovery and reuse of homogeneous catalysts.[6-8] The

obvious issue that must first be dealt with is the difficulty of separating a catalyst that is soluble from substrates or products that are also soluble. Such separation techniques preferably should be "Green"; that is, they should not involve the use of extra purification steps (i.e. column chromatography) or excessive amounts of organic solvent (i.e. solvent precipitation). Such separation/recycling techniques should also allow for the quantitative separation of the metal catalyst from products and should also not affect the catalyst so that the catalyst can be recovered and reused, retaining the same levels of reactivity from cycle to cycle. Our lab has developed several techniques for the separation of these types of polymer-bound catalysts. These methods involve either liquid/liquid separations or solid/liquid separations.[6-13]

Two of these systems heavily employed by our group and others' are (a) thermomorphic[6-8,10,11] solid/liquid or liquid/liquid separations and (b) latent biphasic[6-9,12,13] liquid/liquid separations, as shown in Figure 1. A thermomorphic solid/liquid separation system usually involves the use of a polymer-bound catalyst and substrate in a system in which the catalyst is completely insoluble at low temperature, while the substrate is in solution, but becomes monophasic upon heating.[14-16] This allows for a homogeneous reaction to occur at elevated temperatures. Simple cooling of the reaction mixture then leads to separation of the catalyst (as a solid) from the product phase. Alternatively, thermomorphic liquid/liquid can be used wherein a polymer-bound catalyst shows high phase selective solubility in either polar or nonpolar solvents that can be used in a two solvent system that when mixed, at room temperature, form a biphase, but upon heating, become monophasic.[10-11] This, again, allows for a

homogeneous reaction at elevated temperatures. After the reaction, the system is allowed to cool to room temperature so that the phases will separate and the catalyst and products are isolated in different liquid phases. Latent biphasic systems, on the other hand, involve the use of a phase-selectively soluble polymer-bound catalyst which is dissolved in a miscible or partially miscible solvent mixture of a polar and a nonpolar solvent. If solvent mixtures are chosen appropriately, they can have the property that they become biphasic after a substance induced phase perturbation. In this case, it is possible to carry out homogeneous catalysis in a mixture of two such solvents, and then perturb the system into separate phases, one containing products (polar phase), and the other containing the polymer-supported catalyst (nonpolar phase, for nonpolar polymer support). Synthetic processes that utilized these various catalyst separation systems are the main focus of this dissertation. In the following, I have discussed some of the historical and recent aspects of this chemistry reported by our group and others'. This discussion will focus on various polymers that have been used as catalyst supports that can be separated from the reaction mixture using a number of methods. Some of these polymers include; poly(ethylene glycol) (PEG), poly(*N*-isopropylacrylamide) (PNIPAM), poly(*N*-octadecylacrylamide) (PNODAM), poly(*tert*-butylstyrene) (PTBS), polyisobutylene (PIB) and polyethylene (PE).
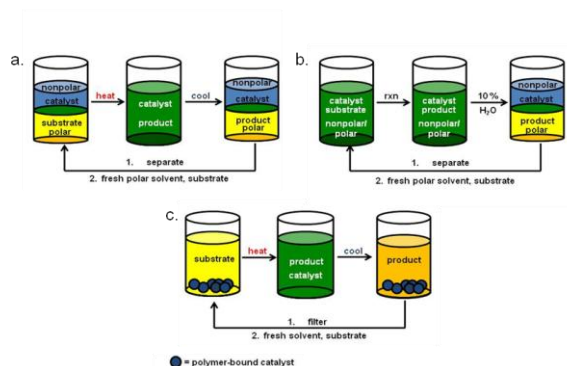
Figure 1. Schematic representation of (a) thermomorphic liquid/liquid, (b) a latent biphasic liquid/liquid separation and (c) a thermomorphic solid/liquid separation system.

Solid/Liquid Separations of Polymer-bound Catalysts

The use of supported catalysts/reagents/substrates that allow for a solid/liquid separation are among the oldest and most widely used methods that use polymers for the separation and isolation of such catalysts, reagents and substrates. Typically, such reactive species can be separated from a reaction mixture by simple filtration. In fact, this is what initially attracted the scientific community to Merrifield's initial discovery, which used cross linked polystyrene resins (Merrifield Resins) for the preparation of peptides and nucleotides.[4] These reaction systems can be considered "Green", as they reduce the amount of waste generated from excess amounts of solvent that are typically needed in lengthy purification protocols.

As mentioned earlier, even though the separation and purification of such solid supported species is relatively easy, it is often the case that chemical processes that require that reactions occur at a solid-liquid interface often show lower efficiency and

selectivity. In addition, characterization of catalysts or reagents bound to a solid matrix is more problematic as typical solution phase ^{1}H and ^{13}C NMR spectroscopy cannot be used. Because of these issues, the development of recoverable *homogeneous* polymer-bound catalysts continues to be of vast interest.

Separation of a homogeneous polymer-bound catalyst requires a different approach than the solid/liquid filtration technique used for a crosslinked resin. For example, if a solid/liquid separation is to be used, it is necessary that the polymer-bound catalyst in the *liquid phase* be induced to separate and form a *solid phase*. After such a perturbation takes place, simple filtration or centrifugation can be used to isolate the catalyst from the reaction mixture. For soluble polymers in the past this was most commonly accomplished using solvent precipitation. This process involves the addition of a solvent that is a poor solvent for the polymer-bound catalyst. Addition of such a "bad" solvent induces the soluble polymer-bound catalyst to precipitate. With an appropriate choice of solvent, the products of the reaction remain in solution. This process, although it works quite well, is unfortunately wasteful, as it generates a large amount of solvent waste. Because of this, there has been interest toward the development of methods that utilize a "greener" solid/liquid separation technique.

Our lab has developed a greener method that takes advantage of the fact that some polymers are insoluble cold, but soluble in hot solvents.[6-8, 14-16] These systems have polymers with solubility behavior that resembles conventional molecules. However, an important difference is that these polymers not only dissolve when heated, but that they precipitate as semicrystalline solids when cooled back to the original temperature in

fashion such that products are not entrained in the solid polymer. We have used such polymers' solubility to develop supports for the catalysts that exhibit thermomorphic behavior (*vide supra*). Because of the thermomorphic nature of the polymer support used, we have been able to prepare several supported catalysts that can be recovered using solid/liquid techniques without generating a large amount of excess solvent waste. Catalysts of this type will be discussed shortly.

Non-crosslinked Linear Polystyrene (NCPS)-bound Ligands/Catalysts/Reagents

Linear polystyrene has been widely used as a support for homogeneous catalysis. Inspiration for the use of NCPS as a catalyst support comes from Merrifield's initial use of crosslinked polystyrene resins (*vide supra*) for synthesis and from others' extensions of this chemistry to catalysis. These linear analogues of Merrifield resins are particularly attractive because the necessary functionalization of the polymeric supports can be introduced either directly in the polymerization process or through the use of postpolymerization modifications of the pendant phenyl groups of this polymer.[6,7] Either method can allow for the precise control over catalyst/ligand loading. In addition, these functional polymers and catalysts can often be analyzed using solution state NMR spectroscopy. These supports' solubility in various solvents such as chloroform, dichloromethane, THF, benzene and toluene also allows one to adjust reaction conditions by changing the solvent. Advantageously, NCPS shows little solubility in solvents such as hexanes and methanol, allowing NCPS-bound species to be isolated and purified using solvent precipitation methods discussed above. Linear NCPS can be prepared in a number of ways using various radical polymerization techniques. "Living"

polymerizations (e.g. atom transfer radical polymerization (ATRP)[17] or reversible addition-fragmentation chain transfer (RAFT)[18] polymerization) or conventional radical polymerizations can be used to produce the desired polystyrene or styrene copolymer (eq. 1). Either polymerization produces linear NCPS though the latter process leads to products with a broader polydispersity (PDI) as compared to living polymerization techniques.

$$n \quad \xrightarrow[\text{conditions}]{\text{initiator}} \quad n \qquad\qquad (1)$$
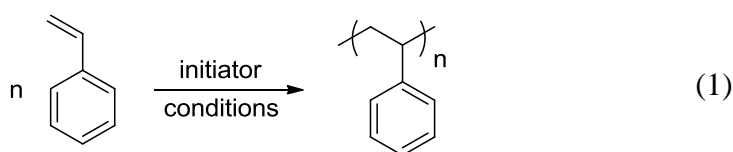
The first use of NCPS in synthesis was work that mirrored the original use of crosslinked PS resins and involved using these soluble polymers in the preparation of peptides and nucleotides[19-21]. The reasoning for this system was that, as in work using solid supports, the polymer would act as a handle to facilitate the isolation and purification of the peptide chains. In this way and NCPS was similar to Merrifield resin. However, using soluble polystyrene had an advantage in that the growing peptide chain would be kept in solution allowing for each reaction to occur homogenously. Also, such a system would allow for the growing peptide chains to be analyzed via solution state spectroscopic methods.

This application of NCPS supports is illustrated with the synthesis of a tetrapeptide. In this example, NCPS with $Mn = 200,000$ Da was prepared and used as a handle for the preparation of peptide Gly-Gly-Leu-Gly.[19] NCPS was chloromethylated by reaction of NCPS with $SnCl_4$ and chloromethylmethylether to form co-polymer **1** (eq. 2)[20]. By performing reactions in DMF followed by precipitation into water, it was

possible to prepare this tetrapeptide in 65 % yield. However, upon precipitation, it was found that some coprecipitation of other reagents was observed. In addition, crosslinking of the polymer chains in subsequent cycles was a problem.[21] In other cases low yields were encountered as a result of the incomplete precipitation of the NCPS-peptide species. The reason for this was that as the peptide chain grew longer its solubility properties began to outweigh those of the polystyrene support, so that precipitation into water was no longer efficient.[22]

(2)
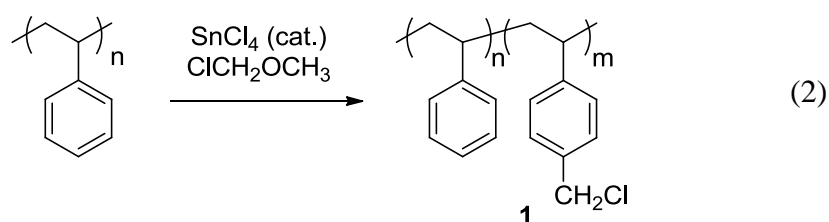
The use of linear NCPS as a supports for transition metal catalysts was investigated by Bayer as early as 1975.[23-25] Bayer *et al.* were able to show that a postpolymerization functionalization of linear NCPS (M_n = 100, 000 Da) was a feasible route to NCPS-supported phosphine ligands that could in turn be used in a ligand exchange process with excess low molecular weight complexes of Pd, Rh and Pt (eqs. 3 and 4).[23] In the case of the polymer-bound Rh complexes (**2** and **3**), the authors showed that the polymeric products of such an exchange reaction were competent in catalyzing both the homogeneous hydrogenation and hydroformylation of low molecular weight olefins. It was shown that **2** could catalyze the hydrogenation of 1-pentene and be recycled five times. Such polymer-bound catalysts could be recovered using solvent precipitation into hexanes or membrane filtration for recycling.[24]

$$\text{(3)}$$

$$\text{(4)}$$
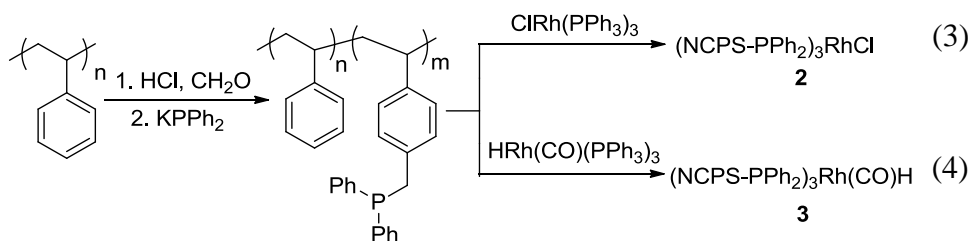
Polymer-supported species are also useful as supports for potentially toxic reagents and there are many precedents that use soluble polymers in this way as well. Recently, Toy has shown that linear NCPS-supported phosphines could be prepared through the copolymerization of styrene and 4-styryl-diphenylphosphine using AIBN to afford **4** (eq. 5). This phosphine containing copolymer was utilized as a polymeric reagent for the Mitsunobu reaction; affording reaction products in good yield.[26] In these cases, **4** was separated from the reaction products using solvent precipitation into diethyl ether, an advantage over similar reactions using triphenylphosphine.

$$\text{(5)}$$
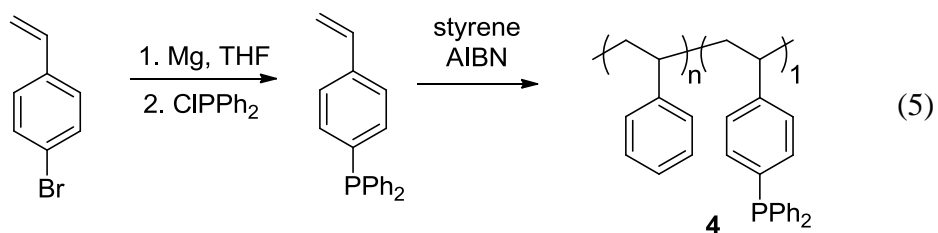
Toy and coworkers also showed that a polymeric ligand similar to the **4** could be used as a ligand for the Pd catalysts used in the Suzuki reaction. By copolymerization of styrene with 4-styryl-diphenylarsine with AIBN they were able to obtain the copolymer **5** (eq. 6).[27] They showed that **5** could be used as a ligand for Pd in the Suzuki cross coupling of various aryl halides and boronic acids to give products in good yields. The complex could then be recovered using solvent precipitation into methanol and reused four times, with no observable formation of Pd black at 75 $^\circ$C.
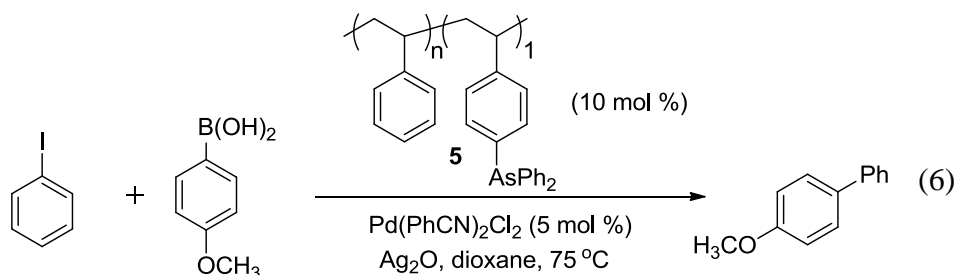
It was later shown by Garcia[28] and coworkers that NCPS could be used as a support for biaryl phosphine ligands, such as SPhos (developed by the Buchwald group[29]). In order to prepare the polymer-supported ligand **6**, they relied on the use of a postpolymerization reaction of the copolymer of styrene and vinylbenzylchloride with the HCl salt of the SPhos derivative shown below (eq. 7). In order to test the catalytic feasibility of this **6**, the authors performed palldium-catalyzed Buchwald-Hartwig cross-

coupling reactions and Suzuki reactions, as shown in eqs. 8 and 9. By reacting an aryl chloride with morpholine in the presence of **6** and Pd(OAc)$_2$, they were able to show that complete consumption of the starting materials could be achieved in 30 min. In the case of the Pd-catalyzed Suzuki reaction between 2-chloro-*m*-xylene and *o*-tolylboronic acid, the authors showed that, under similar reaction conditions, nearly complete consumption of the starting material could be achieved in 24 h. These ligands were shown to be superior to solid-supported species such as silica-bound SPhos, but much less active than PEG-supported ligands, which will be discussed later. Even though these catalysts
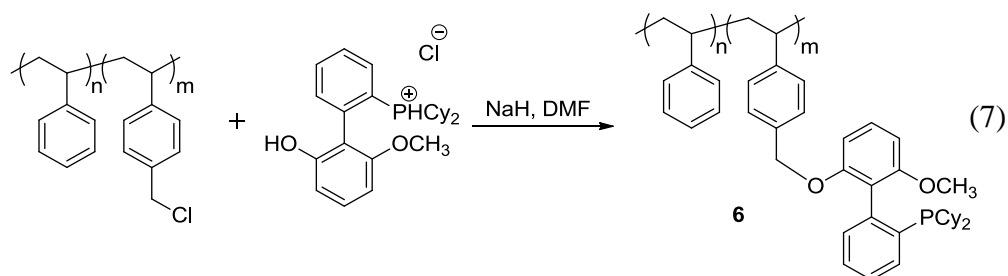
showed high activity and could be recovered easily through solvent precipitation into cold diethyl ether, phosphine oxidation precluded recycling of this catalyst.

$$\text{(8)}$$

$$\text{(9)}$$
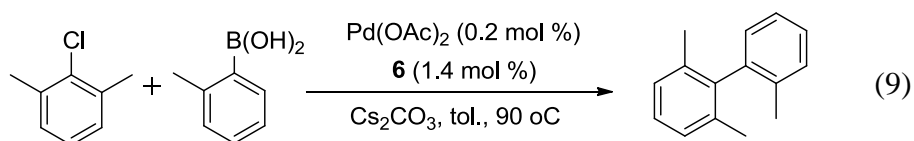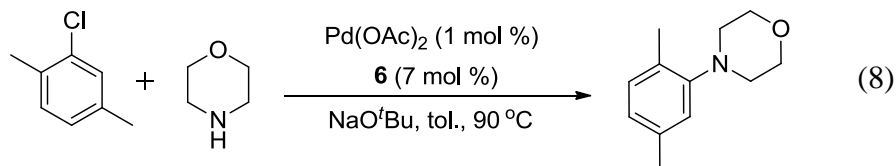
As mentioned earlier, one of the main benefits to using homogeneous catalysis is that these species often have better reactivity and better selectivity than their heterogeneous counterparts. This selectivity is most manifest in asymmetric catalysis. Because of this, much work has gone into the development of soluble polymer-supported chiral ligands and catalysts. The first examples of this work date back to the 1970's. Bayer first showed that a chiral bis-phosphine ligand could be attached to a soluble NCPS support and subsequently used to form the NCPS-bound chiral hydroformylation catalyst **7**[24], shown in eq. 10.

$$\text{(10)}$$
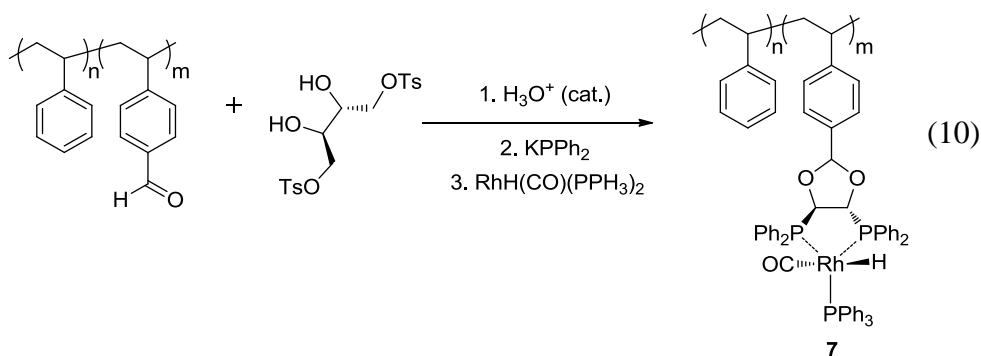
By reacting the aldehyde-containing copolymer with the chiral diol (derived from **L**-tartaric acid), the authors were able to prepare a substrate for a nucleophilic

substitution KPPh$_2$. Subsequent ligand exchange with RhH(CO)(PPh$_3$)$_3$ formed **7** which was used as a homogeneous catalyst for the hydroformylation of styrene to form the branched aldehydes in 95 % selectivity over the linear aldehydes in good yields. Although highly active, this catalyst had poor enantioselectivity giving the *R* product with *ca.* 2 % e. e. The authors reported that these results are comparable to low molecular weight catalysts under the same reaction conditions. **7** could be recovered through solvent precipitation or membrane filtration. Results published by Ohkubo's lab mirrored this initial report.[31]

It was later found by Rosling and coworkers that α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanol (TADDOL[32]) ligands could be supported by NCPS.[33] Such ligands were prepared from a suspension polymerization of styrene and a styryl-derived TADDOL monomer. The ligand **8** so formed was then used for the titanium-catalyzed addition of diethylzinc to benzaldehyde (eq. 11). Upon the addition of a solution of Ti(O^{i}Pr)$_4$ in toluene to a solution of **8**, the authors obtained a yellow solution that catalyzed the aforementioned reaction to obtain product alcohol in high yields and excellent selectivity, 80 % and 98 % e. e. Recovery of the catalyst could be achieved by precipitation into methanol and the catalyst was recycled twice.

$$(11)$$
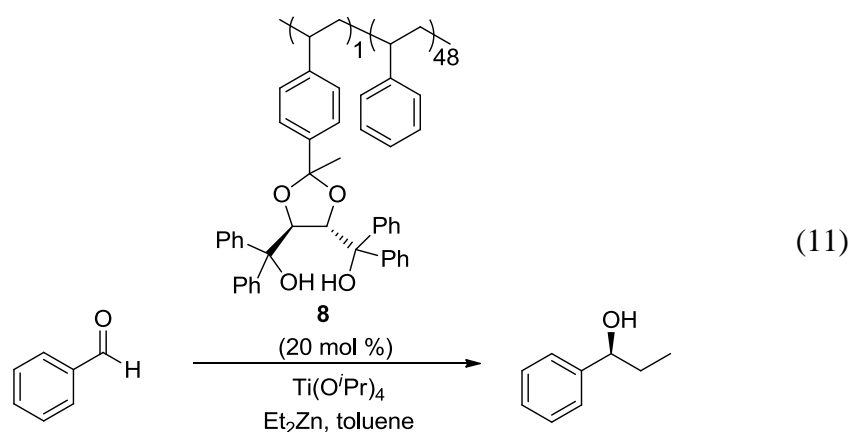
Marcus Weck's group has shown that it is possible to use NCPS-systems as supports for chiral salen ligands.[34] Weck and coworkers reported the first example of the radical copolymerization of unsymmetrical chiral salen monomers with styrene to obtain the NCPS-supported salen ligands (eq. 12). The cobalt (II) complex of the resulting polymer was treated with acetic acid and oxidized with air to form the catalytically active cobalt(III) complex **9** which was then used as recoverable/recyclable catalyst in the hydrolytic kinetic resolution (HKR) of epichlorohydrin, as shown in eq. 13.

$$(12)$$

$$\text{Cl}\diagdown\!\!\overset{\text{O}}{\triangle} \quad \xrightarrow[\text{H}_2\text{O}]{\textbf{9} \ (2.5 \ \text{mol\%})} \quad \text{Cl}\diagdown\!\!\overset{\text{O}}{\triangle} \quad + \quad \text{Cl}\diagdown\!\!\overset{\text{OH}}{\diagdown}\!\!\diagdown\text{OH} \qquad (13)$$
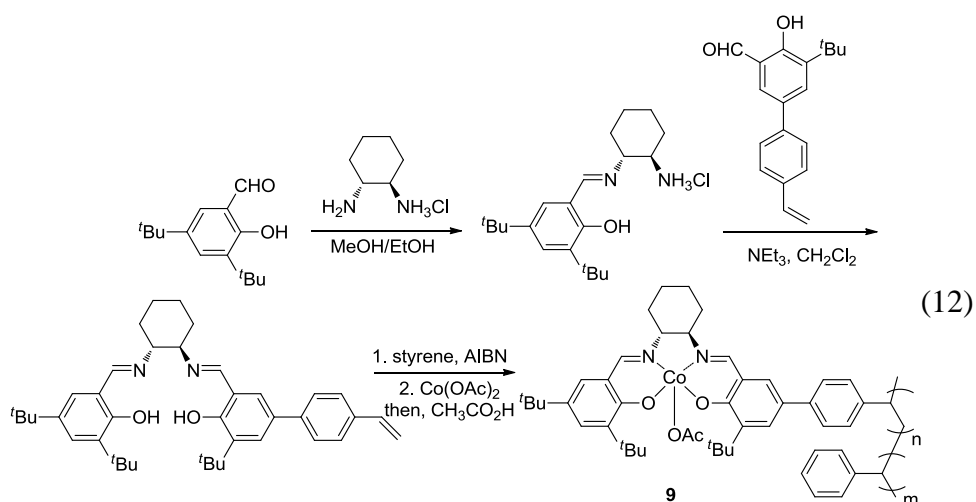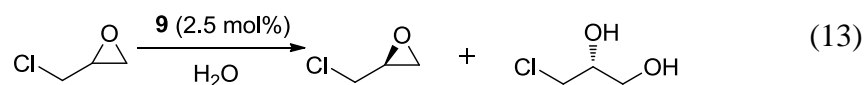
The Co(III) complex **9** described above catalyzed the HKR of epichlorohydrin with reactivities and selectivities that were comparable to results obtained with Jacobsen's catalyst; giving the ring opening product in 54 % yield and >99% e. e. after 1 h. **9** could be recovered by using a solvent precipitation into diethyl ether and could be recycled up to four times. However, in order to maintain high conversions and selectivity, the reaction time had to be increased in subsequent cycles. This was reported to be a result of loss of catalyst during to solvent precipitation.

Poly(ethylene glycol) (PEG)-supported Ligands/Reagents/Catalysts

PEG is one of the oldest (and most widely used) polymeric supports. It has been used to support various typed of ligands, reagents, organocatalysts, transition metal catalysts and has also been utilized as a nonvolatile solvent for "Greener" syntheses.[6,7,19,35] Poly(ethylene glycol) (PEG) is an end-functionalized, linear polymer formed in the anionic polymerization of ethylene oxide, as shown in eq. 14. It differs from poly(ethyleneoxide) (PEO) in that, PEG usually consists of M_n that are lower than 20,000 Da. PEG and its derivatives soluble in solvents such as DMF, CH_3CN, toluene, CH_2Cl_2 and water. The latter has been shown to be important for the development of more environmentally benign (Green) systems. Although PEG derivatives are completely soluble in these solvents, they are insoluble in solvents such as hexanes, heptane, diethyl ether and cold ethanol. Because of this, PEG derivatives can be recovered and recycled using solvent precipitation. The wide availability of inexpensive

PEG derivatives that contain either two hydroxy end groups or one hydroxy and one methoxy end group by commercial sources has made PEG's appearance in the chemical literature quite abundant.

$$\text{(14)}$$
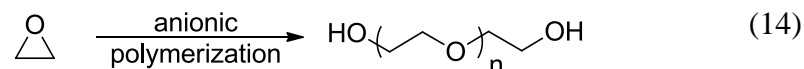
One of the earliest uses of PEG was as a soluble support for solution-phase peptide synthesis, chemistry that paralleled the earliest uses of NCPS (*vide supra*).[19] Bayer and coworkers showed that PEG did indeed serve as a useful handle for the solution phase synthesis of peptides.[21] By using ultrafiltration, they were able to successfully separate the peptide-containing PEG from the low molecular weight impurities and could prepare the small peptide H-Ile-Ala-Pro-Val-OH and pentapeptide H-Leu-Thr-Ala-Leu-Gly-OH by now what is termed liquid phase peptide synthesis.

Bayer's group also described using PEG as a support for a homogeneous catalyst.[23] They first described the preparation and use of a series of polymer-bound phosphine ligands and and showed that the Rh complexes of these PEG-bound phosphines could be used as hydrogenation catalysts.

Sporadic reports have continued since these original studies describing other uses of PEG. For examples, Whitesides and coworkers also took advantage of the water-solubility of PEG and designed a series of water-soluble Rh-phosphine hydrogenation catalysts.[36] In still more recent work, Grubbs' laboratory reported the use of PEG as a support for *N*-heterocyclic carbene (NHC)-Ru complexes that could be used as water soluble olefin metathesis catalysts.[37]

Recently, the use of PEG as a support for chiral ligands and metal complexes has been reported as well. In 2001, Chan and coworkers anchored chiral BINAP ligands to soluble PEG oligomers.[38] These species were then be used as ligands for Ru and Rh-catalyzed asymmetric hydrogenation reactions. The preparation of such complexes started with the condensation of amino-BINAP derivative with the acid chloride of terephthalic acid followed by reaction with PEG. Subsequent reaction with [Ru(cymene)Cl$_2$]$_2$ afforded the Ru-BINAP complex **10**, as shown in eq. 15.

$$(15)$$
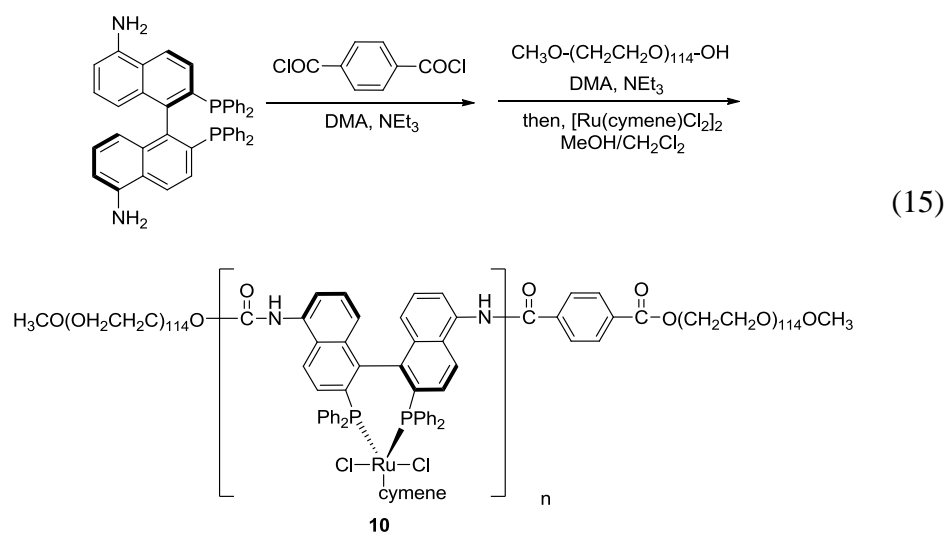
The resulting catalyst **10** catalyzed the hydrogenation of 2-(6-methoxy-2-naphthyl)-propenoic acid with complete conversion and excellent enantioselectivity (>96 % e. e.) like that of a low molecular weight catalyst. Advantageously, this soluble PEG-bound catalyst could be recycled up to three times with no loss in yield or % e. e. by using a solvent precipitation into diethyl ether.

$$(16)$$
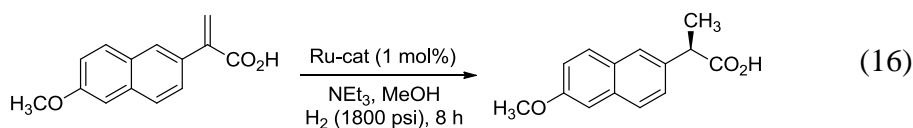
That same year, Guerreiro *et al.* also described some PEG-supported BINAP-Ru hydrogenation catalysts. These authors' ultimate goal was to prepare a catalytically active species that would accomplish hydrogenation reactions in water.[39] The preparation of the PEG-bound BINAP ligand was carried out by allowing an amino-methyl-derived BINAP to react with a PEG-glutaric acid derivative. In the presence DCC and DMAP, this condensation reaction produced the polymeric ligand in quantitative yield. The BINAP was then used to *in situ* generate the Ru complex **11** (eq. 17).

$$(17)$$
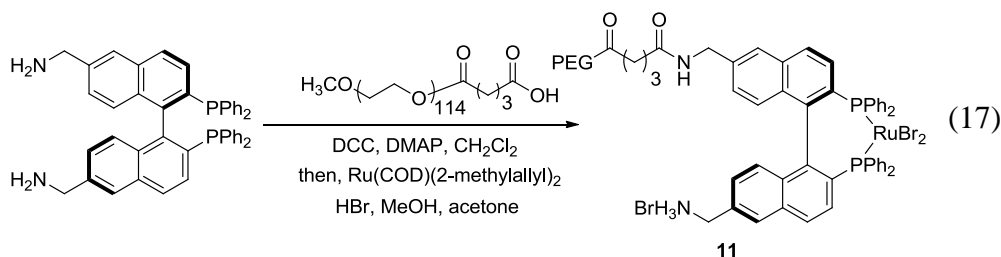
To test the utility of **11**, the authors studied the hydrogenation of various ß-ketoesters (eq. 18). These ligands also allowed these reactions to be carried out in water. However, in water the enantioselectivity was only modest (60-62 % e. e.) while the e. e. in solvents like methanol and ethylene glycol ranged up to 98 % e. e. Recovery and recycling of **11** was, however, possible using solvent precipitation into diethyl ether and the recovered catalyst was successfully used up to four times with no loss in product yield and only slight loss in product enantioselectivity (98 % e. e. in cycle 1 to 95 % e. e. in cycle 4 of the reaction in eq. 18).

$$(18)$$
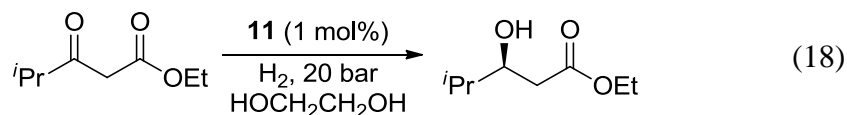
Not only can PEG be used a support for enantioselective reduction catalysts, but it can be used as a support for chiral ligands/metal complexes that can affect enantioselective oxidation reactions. Sharpless' osmium-catalyzed asymmetric dihydroxylation (AD) reaction is among the most important catalytic oxidation reactions.[1] There have been many reports on the development of insoluble polymer-supported AD catalysts,[40] but the first of using a soluble polymer support was the development of a PEG-supported cinchona alkaloid **12** ligand by Han and Janda.[41] PEG-bound cinchona alkaloid was prepared though a glutarate linker to dihydroquinone (DHQD) often used for such reactions to PEG. As shown in eq. 19, the DHQD·HCl salt was treated with base and glutaric anhydride followed by reaction with DCC, DMAP and $CH_3O(CH_2CH_2O)_{114}CH_2CH_2OH$ to give the polymer-supported ligand **12** in excellent yield (95 %).

$$\text{1. NEt}_3\text{, DMAP, glutaric anhydride} \qquad \text{2. DCC, DMAP, PEG-OH} \tag{19}$$
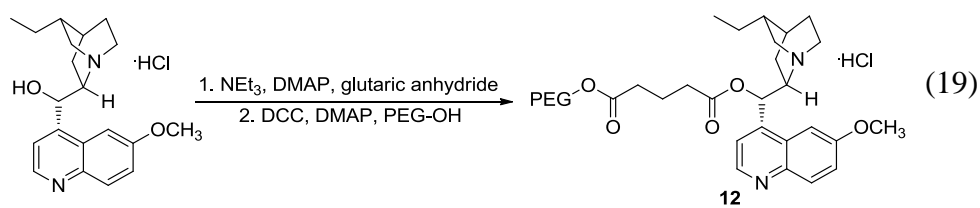
In the Sharpless AD reaction of various olefins, **12** afforded products in higher e. e. (88 % vs. 82 % e. e.) when compared to a similar insoluble-supported system, with the yields were similar (89 % vs. 87 %). Moreover, the Os complex of **12** could be quantitatively recovered through the use of a solvent precipitation into diethyl ether and the recovered catalyst was recycled up to five times with no loss in product yield or enantioselectivity.

More recently, Zhang and coworkers showed that a PEG-bound *cinchona* alkaloid **13** containing a phthalazine moiety (Scheme 1) could be produced in two steps. With OsO_4 and $K_3Fe(CN)_6$ as stoichiometric oxidant, **13**, catalyzed the dihydroxylation reaction of stilbene in excellent yield (up to 94 %) and with high stereoselectivity (up to 99 % e. e.).[42] **13** could be recovered by solvent precipitation and was recycled up to six times with no observable loss in yield or selectivity.

Scheme 1. Zhang's PEG-bound cinchona alkaloid ligand used for Sharpless' AD reaction.
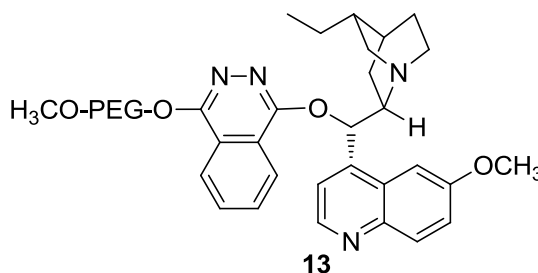
The *cinchona* alkaloids have also been shown to be important organocatalysts. Benaglia and coworkers have shown that various PEG-supported cinchona-derivatives can be used as catalysts in both amino acid alkylation and Michael addition reactions.[43] However, catalyst decomposition precluded catalyst recycling. In other work, Wang *et al*. showed that it was possible to use **14** as a recoverable, phase transfer catalyst in asymmetric epoxidation reactions of various stilbenes (eq. 20).[44] **14** was able to afford

$$(20)$$
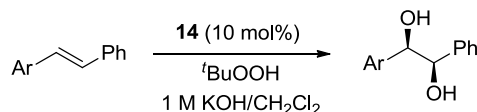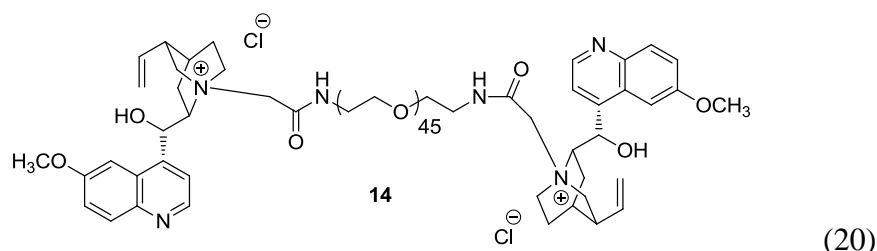
the products in good yields (80- 95 %), but the enantioselectivity was just modest (60-80 % e. e.). The catalyst could be recycled three times with no loss in yield or selectivity.

PEG-supported salen ligands/metal complexes also facilitate enantioselective catalysis. An early example came from the Janda group.[45] This study compared the reactivities and selectivities of a series of polymer-bound salen-Mn epoxidation catalysts. Both soluble (NCPS and PEG) and insoluble supports (*Janda*Jel and Merrifield resin) were studied.

$$(21)$$

$$(22)$$
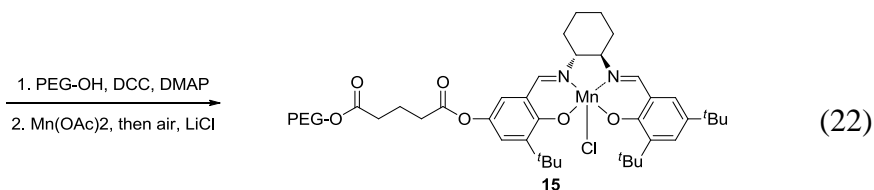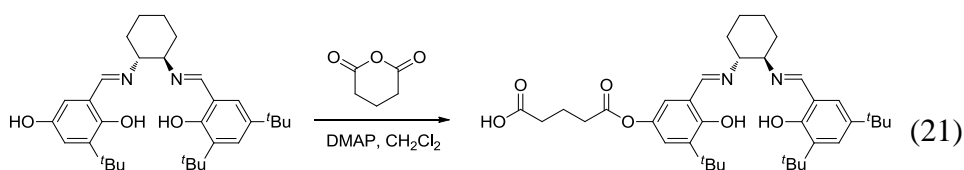
The results showed that **15** was compatible to the low molecular weight catalyst in the asymmetric epoxidation of *cis*-ß-methylstyrene with *m*-CPBA and NMO. At 4 mol%, Janda's catalyst **15** gave yields and enantioselectivities that were almost identical

to those achieved with Jacobsen's catalyst (79 % yield, 88 % e. e. and 82 % yield, 88 % e. e., respectively). This catalyst was recovered and reused twice, using solvent precipitation into cold diethyl ether. It was noted that **15** retained the same levels of reactivity and selectivity through the second cycle. However, the polymeric material recovered from the second cycle contained high amounts of chlorobenzoic acid (resulting from the reduction of *m*-CPBA) and NMO resulting in a very gummy residue, making its reuse in subsequent cycles problematic.

Shortly after this, Venkataraman's group described three other PEG-bound salen ligands.[46] Each of these was used to catalyze the asymmetric addition of diethyl zinc to aldehydes. It was found that the selectivity and reactivity of the polymer-bound catalysts was affected by the polymer chain and the nature of the linker between ligand and polymer. Ligands that were directly bound to the polymer chain produced catalysts that led to products obtained in high yields (90 %) and low enantioselectivity (32 % e. e.) in comparison to a low molecular weight catalyst (82 % e. e.). Control experiments with a low molecular weight catalyst and added PEG showed that products were obtained in high yields (88 %) and higher e. e.'s (82 %). This result indicated that the PEG had no effect on the selectivity of the reaction. When catalysts were bound to the polymer through various linkers like the glutarate spacer used in Janda's work described above, better selectivities were seen (eq. 23). In these studies, **16** could be recovered and recycled up to three times with no loss in reactivity or selectivity.

(23)
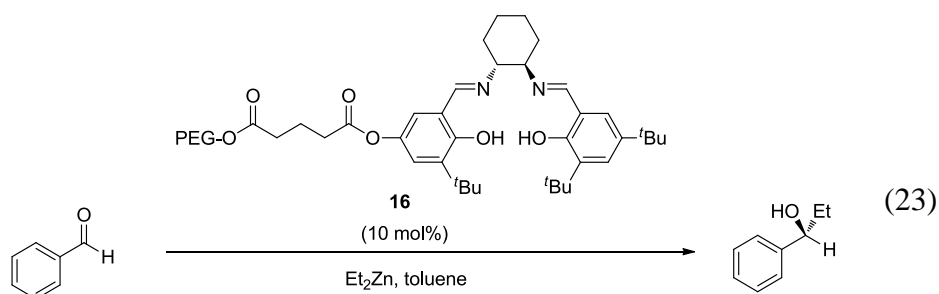
Tethering reagents to polymer supports can result in useful, green alternatives to somewhat otherwise harmful reagents. In 1997, Janda *et al.* showed that it was possible to prepare the bisphosphine **17** shown below in eq. 24.[47]

(24)
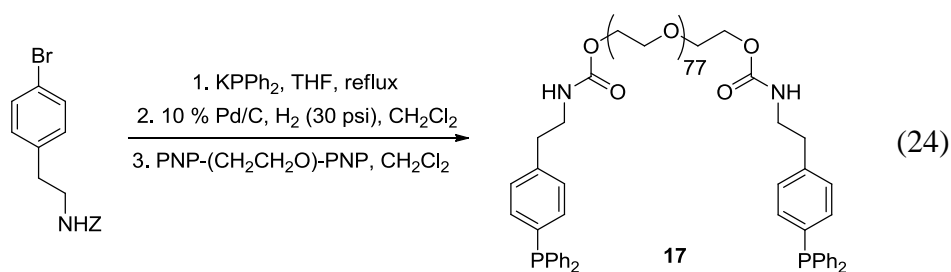
One example of a polymeric phosphine is the PEG-supported phosphine **17**. This polymeric phosphine was used in both Staudinger and Mitsunobu reactions. In the Staudinger reactions (eqs. 25 and 26), a variety of aryl and alkyl azides were reduced and **17** was reported to be superior to earlier resin-bound phosphines with **17** affording products with shorter reaction times and higher yields. In other studies, **17** was used in the Mitsunobu reaction. This reaction is widely used in synthesis but requires extra purification steps to remove the triphenylphosphine oxide byproduct. As was the case in the Staudinger reaction, it was found that reaction times were shorter and yields were higher when using **17** as a stoichiometric reagent, when compared to the solid-resin-

supported phosphines. PEG-bound byproducts were quantitatively separated from the reaction products using solvent precipitation.

(25)

(26)
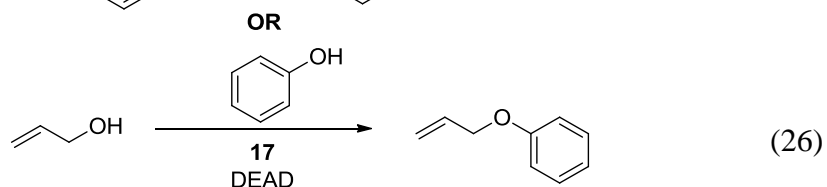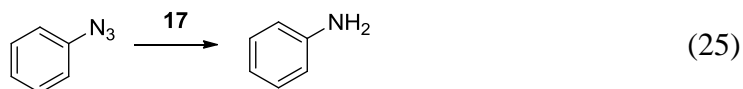
Polyethylene (PE)-supported Ligands/Reagents/Catalysts

Since the advent of the use of polymer-supports for synthesis and catalysis, reports dealing with the separation of polymer-bound ligand/reagents/catalysts from low molecular weight products/byproducts have almost always relied on solid/liquid separation strategies. This has been the case throughout the examples discussed in this dissertation so far. Most of the supported catalysts discussed up to this point have been isolated as solids after a solvent precipitation step. Such a precipitation process followed by a gravity filtration usually gives quantitative separation. However, this process is not very green because of the large amounts of solvent waste generated. In order to avoid this problem, years ago, our lab pioneered the use of polyethylene (PE)-supported ligands and catalysts.[6,8] Such catalysts exhibit thermomorphic phase behavior. Originally these ligands were prepared by anionic polymerization of ethylene gas with ^{n}BuLi. When this polymerization was quenched by addition of an electrophile, a terminally functionalized polymer-bound ligand/reagent was produced. An illustration of this

chemistry is shown below in Scheme 2. Numerous types of functionalities could be included on these oligomers, as shown below.

Scheme 2. Preparation of functionalized PE oligomers.
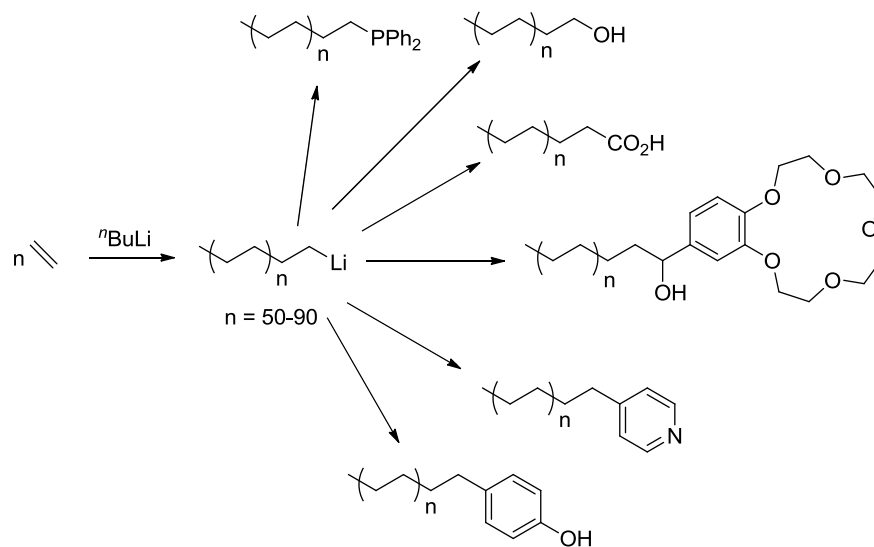
Ligands or catalysts that are attached to PE oligomers are thermomorphic in that they can be dissolved in "hot" solvents but can be quantitatively separated from the supernatant using a simple filtration. This was first shown by preparing the spin-labeled PE-oligomer shown below. This spin label dissolves in toluene at 100 $^{\circ}$C. On cooling the solution back to room temperature and filtering off the solid polymer, ESR analysis of the supernatant toluene phase showed no detectable spin label left in the solution (Scheme 3).[8]

Scheme 3. PE-bound spin label.
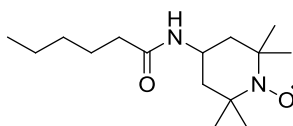
One of the earliest examples studied by our group used PE-supports in Rh(I) hydrogenation catalysis.[15] A PE-PPh$_2$ ligand was used to prepare a complex that resembled Wilkinson's catalyst. This allowed a direct comparison of the PE-bound catalyst's reactivity with that of the original low molecular weight catalyst. The preparation of the PE-bound complex is shown in eq. 27. In this chemistry PE-PPh$_2$ was

$$[ClRh(C_2H_4)_2]_2$$
$$\text{OR}$$
$$ClRh(C_2H_4)(PPh_3)_2$$
$$\text{OR}$$
$$ClRh(PPh_3)_3$$

(27)

18
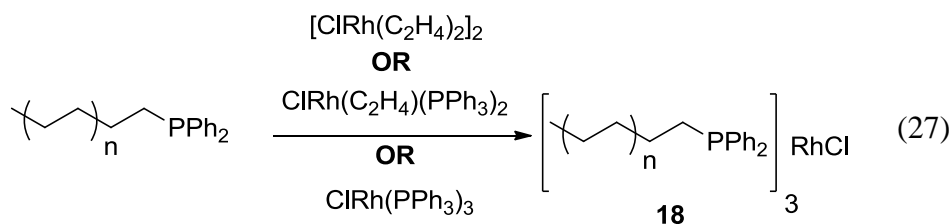
allowed to react with a chloro-rhodium ethylene dimer. The resulting exchange of PE-PPh$_2$ for PPh$_3$ and ethylene ligands or phosphine ligand produced a PE$_{Olig}$ version of Wilkinson's catalyst. The PE-bound complex **18** prepared was shown to be >10 times more reactive in olefin hydrogenation than the previously-prepared insoluble PS-bound catalyst. The catalyst could be recovered and reused up to 18 times with no loss in activity.

It was also possible to prepare PE-bound Pd(0) catalysts, using the same PE-PPh$_2$ ligand (eq. 28).[14] The use of **19** in the reaction of allyl benzoate and morpholine was to test the utility of **19** in the reaction of allylic esters with 2° amines (eq. 29). In toluene, at

100 $^{\circ}$C, the reaction was quantitative and complete within 10 min. While **19** could be used as a homogeneous solution at 100 $^{\circ}$C it was separated from the products by cooling to room temperature. The resulting solid PE_{Olig}-ligated Pd(0) catalyst was recoverable using centrifugation and was reused up to ten times with no observable loss in activity. Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) analysis showed no detectable loss of palladium.

$$\text{(28)}$$

19

$$\text{(29)}$$
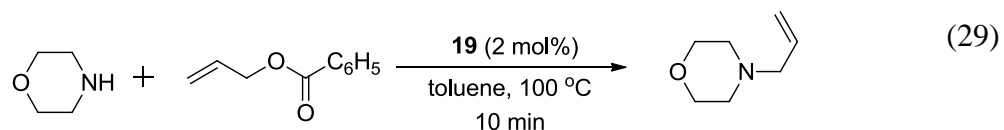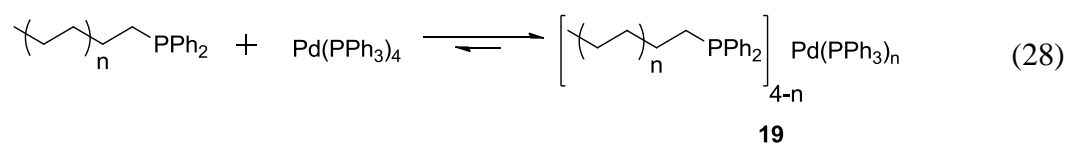
Our lab was also able to show that these strategies were very general and not limited to one type of PE-bound ligand or one type of catalyst. For example, when PE-CO$_2$H was allowed to react with [Rh(OAc)$_2$]$_2$ in a mixed solvent system of toluene and ethanol, it was possible to form a PE-supported Rh carboxylate complex. This complex was then used as a catalyst in the reaction of a diazoester and an olefin in cyclopropanation chemistry.[16] This catalyst was successfully used up to ten times with virtually no loss in activity or stereoselectivity (giving products as a 2.4:1 mixture of trans:cis isomers).

$$\text{(30)}$$
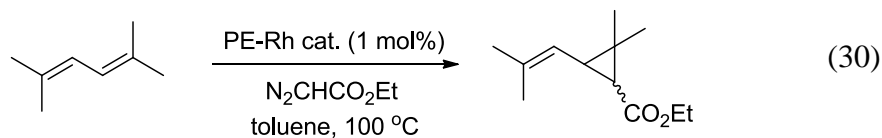
A recent example suggests that the use of such PE-supported ligand and catalysts is quite feasible in industrial applications. A group at DuPont has shown that it is possible to attach porphyrins and phthalocyanines to PE-oligomers by taking advantage of the functionality of commercially available PE-oligomers.[48] The metal complexes (Scheme 4) of such species can be used as thermomorphic, recoverable/recyclable catalysts for radical polymerizations of styrenes and methacrylates. One of the difficulties in the preparation of polymers (that will ultimately be used in commercial applications) is the removal of catalyst and metal complexes. These sorts of impurities often exist as highly colored species and therefore add color to polymer products. DuPont found, that after performing the polymerization chemistry at elevated temperatures, followed by cooling and filtering they could isolate the PE-supported catalyst and obtain products in high purity (minimal metal leaching) with no color.

Scheme 4. DuPont's PE-supported (a) porphyrin and (b) phthalocyanine metal complexes.
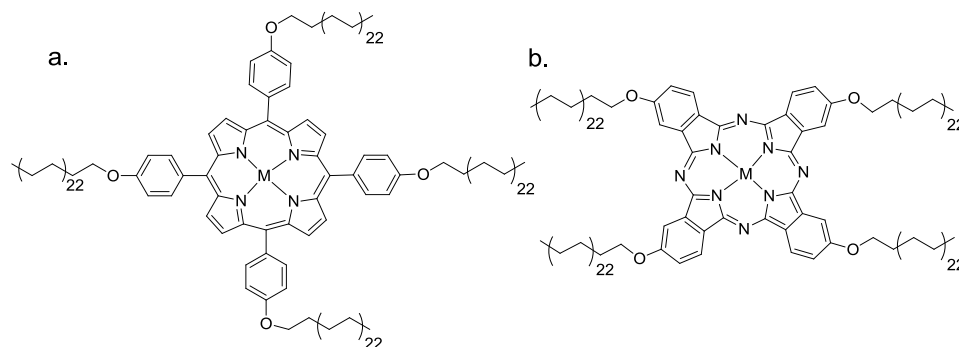
Liquid/Liquid Separations of Polymer-bound Catalysts

Up to this point, this introduction has focused on solid/liquid separation techniques for the isolation of soluble polymer-bound catalysts. While this has been the general scheme used for all polymer-supported catalysts or reagents, it is not the only possible separation scheme.[6,7,19] A method that has been developed as an alternative uses liquid/liquid separations of phase-selectively soluble polymer-bound ligands, catalysts and reagents.

Liquid/liquid separations based on density are ubiquitous in chemistry. Most organic reactions involve a procedure step that utilizes a molecule's solubility in one solvent over another wherein one solvent differs in density from a solvent that dissolves impurities instead of the product. This process is so essential to organic chemistry that it is always taught as one of the first experiments in undergraduate organic chemistry laboratory courses. Most often, these types of separation are performed using an organic/aqueous separation but an organic/organic separation is equally feasible.[6,7] Denisty based separations of other media are also common as exemplified by fluorous solvent separations[49], ionic liquids[50] and supercritical fluids such as CO_2 and water. [51]

Thermomorphic Liquid/Liquid Separation Systems

The use of thermomorphic solid/liquid separations has already been discussed in some detail. However, This idea was first developed in the Bergbreiter laboratory in the context of using liquid/liquid separations.[6,8] As briefly discussed earlier, one example of such a system would be a mixed solvent system in which two solvents are a biphase at room temperature but monophasic upon heating. This allows for a homogeneous

reaction to occur at higher temperatures with a liquid/liquid separation step after cooling and phase separation. If the catalyst and the product dissolve in different phases, gravity separation can be employed to isolate the phases that contain either the polymer-bound catalyst or the product(s).

A thermomorphic liquid/liquid system requires that the two solvents employed be immiscible cold and miscible hot. It also requires that the polymer support used be highly selectively soluble in one of the solvents over the other (phase selective solubility). Our lab has shown that it is possible to use both polar and nonpolar polymer supports for systems that require a polymer that is selectively soluble in polar solvents or nonpolar solvents, respectively. The initial reports from our lab described the use of polar poly(*N*-isopropylacrylamide) obtained from the radical polymerization of *N*-isopropylacrylamide as supports for rhodium(I) hydrogenation catalysts[10] (Scheme 5).

Scheme 5. Preparation of PNIPAM-supported phosphine-Rh complex **20**.
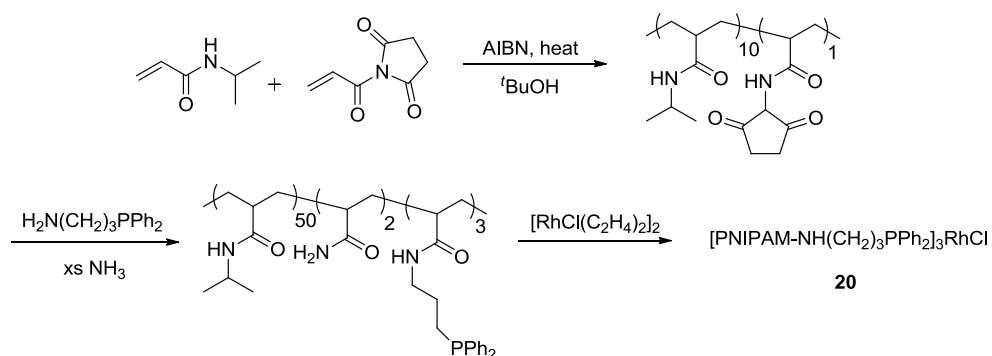
This initial report of a thermomorphic liquid/liquid system for catalysis with a polymer-bound catalyst described the hydrogenation of monosubstituted alkenes like

1-octene and 1-dodecene in a mixture of heptane and 90% ethanol/water using **20** as a catalyst. In this system, **20** was phase-selectively soluble in the polar phase of the reaction media. At room temperature, it was shown that no reaction occurred. Upon heating to 70 °C, the reaction mixture became homogeneous and reaction occurred. Recovery and recycling of **20** was achieved by cooling the reaction mixture, removing the heptane phase and adding the polar phase containing the polymer-bound **20** to a fresh solution of substrate in heptane. This catalyst was shown to be recycled up to four times with no loss in activity. It was also shown that the activity of **20** was comparable to its low molecular weight analog (Wilkinson's catalyst).

Shortly after this, the Bergbreiter group reported on the use of PNIPAM-supported Pd catalysts for thermomorphic carbon-carbon bond forming reactions. Using the same thermomorphic system described above, a Pd(0) complex bound to PNIPAM was shown to be a recoverable, recyclable catalyst for several different C-C bond forming reactions.[11] Using 2 mol% catalyst, it was possible to obtain the coupling products of various aryl iodides with *tert*-butyl acrylate (Heck reaction), phenylboronic acid (Suzuki reaction) or phenylacetylene (Sonagashira reaction). Under these conditions, the catalyst could be recycled up to three times, in some cases, with no loss in activity.

Reports discussed earlier in this chapter described the use of solid/liquid separation schemes for PEG-supported catalysts. Such catalysts can also be used under thermomorphic liquid/liquid separations. Bergbreiter and coworkers later showed, that PEG-supported SCS-pincer ligands (Scheme 6) could be used to supported Pd(II)

catalysts for Heck reactions under microwave irradiation. Using a biphasic mixture of 90 % DMF/water and heptane, Heck couplings were complete within 10-30 min. at 150 $^\circ$C using low catalyst loadings (*ca.* 0.01 mol%). ICP-MS found that <0.5 % of the palladium which was recycled as a polar phase leached into the product nonpolar phase.[51]

Scheme 6. PEG-supported SCS pincer/Pd(II) complex.
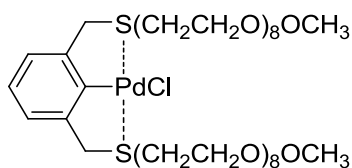
Plenio's group described the use of the highly sterically hindered PEG-bound phosphine **21** (eq. 31) for a thermomorphic biphasic Sonagashira reaction.[53] Using a solvent system of acetonitrile, triethylamine and heptane, the authors were able to effect the coupling of aryl iodides and acetylenes at 80 $^\circ$C. By adding additional K_2CO_3, they were able to recycle the catalyst up to five times with no loss in activity.

(31)
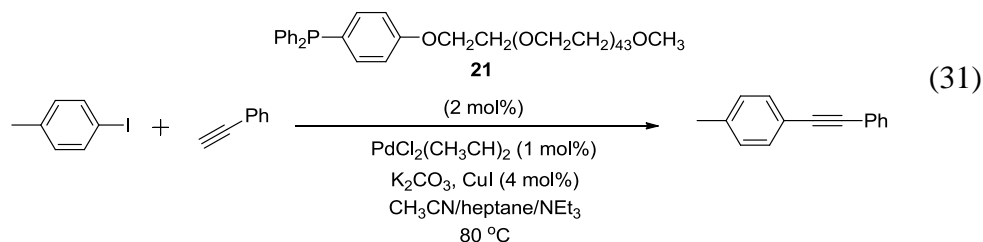
The first thermomorphic separations that were developed used polar polymers that were selectively soluble in polar solvents. This is actually a special case since heptane is usually considered to be a poor solvent for most low molecular weight

compounds. Because of this, the initial studies used reactions that employed substrates that formed products that were heptane soluble. This assured separation of products from the polar phase containing the polymer-bound catalyst. This however limits the scope of this type of system. To address this problem, our lab designed thermomorphic separation schemes that would allow for nonpolar polymer-bound catalysts to be used.

By taking advantage of PNIPAM chemistry, our lab first developed poly(*N*-octadecylacrylamide) (PNODAM), a nonpolar derivative of PNIPAM that could act as an "inverse" thermomorphic biphasic catalyst support.[6] This polymer is highly phase selectively soluble in heptane, making it an attractive thermomorphic support for formation of polar products. The extent to which these polymeric scaffolds are selective for nonpolar solvents was studied using polymer-bound dyes.[54] Based on these studies, our lab prepared PNODAM-supported phosphine ligands (prepared similar to that described above) and used their palladium complexes as recoverable catalysts for the Heck coupling of iodobenzene and acrylic acid in a homogeneous mixture of heptane and DMA at 100 $^{\circ}$C. By cooling down the reaction mixture and separating the phases, this catalyst could be recycled up to nine times.

This chemistry is relatively general, in that it can be used with other polymer supports as well. Plenio and coworkers have shown that under thermomorphic conditions (DMSO or nitromethane with cyclohexane) ligands/catalyst attached to nonpolar styrene derivatives can be recovered and recycled. They showed a palladium complex with PS-derivative **22** could be used as a recoverable catalyst for Sonagashira

coupling reactions (eq. 32). Under these conditions, the catalyst could be recycled in the cyclohexane phase and reused up to five times.[56]

$$\text{H}_3\text{CO} \text{—} \text{Br} + \text{} \equiv \text{Ph} \xrightarrow[\substack{\text{Pd(PhCN)}_2\text{Cl}_2 \text{ (1 mol\%)} \\ \text{CuI (2 mol\%)} \\ \text{Hunig's base} \\ \text{cyclohexane/DMSO}}]{\text{22 (2 mol\%)}} \text{—} \equiv \text{Ph} \qquad (32)$$
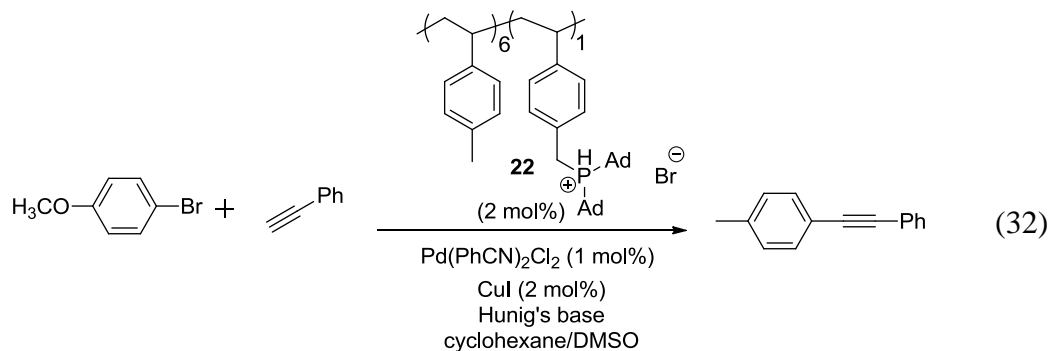
Two years later, a report came out of Yang's lab describing the use of a dendritic organic base (a DMAP derivative) that could be used as a recoverable reagent for the Morita-Baylis-Hillman reaction.[57] In order to test the efficacy of **23** as a recyclable reagent, the authors chose to study the reaction between both electron deficient aldehydes and an α,ß-unsaturated carbonyl compounds under thermomorphic conditions using DMF and cyclohexane (eq. 33). Catatyst **23** was found to be app. 98 % phase selectively soluble for the nonpolar phase. The base could be recovered and recycled by cooling the reaction mixture from 60 °C to room temperature and adding fresh DMF and substrates. Although, it was found that after the cycle the yields dropped dramatically (92 to 45 %). The reason was formation of pyridinium salts under the reaction conditions. In order to alleviate this problem, the authors found that after each isolation step, treatment of **23** with 2 M NaOH allowed them to regenerate the DMAP derivative. Using this regeneration method, **23** could be recycled up to five times with high product yields (*ca.* 90 %).

H3C(H2C)8H2CO   OCH2(CH2)8CH3

$H_3C(H_2C)_8H_2CO$

(33)

O_2N ... O_2N

DMF/cyclohexane
60 °C
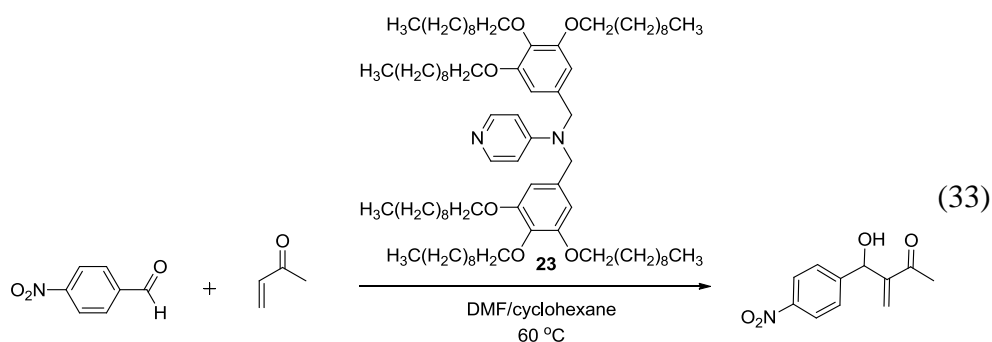
Latent Biphasic Liquid/Liquid Separation Systems

So far, the discussions in this section have dealt with the use of polymer-supported catalysts that can be recovered and recycled using thermomorphic separation techniques. An alternative is to use soluble polymer-supported catalysts in a mixed solvent system that has latent biphasic character. In this scheme, a polar solvent and a nonpolar solvent that are miscible at room temperature are used with a soluble polymer-bound catalyst to perform a homogeneous catalytic reaction at ambient temperatures. However, with an appropriate solvent mixture, the solvent mixture can be induced to separate into two phases, one containing the polymer-bound catalyst and the other the product, either by the addition of a perturbing agent or formation of a product. This method is called a latent biphasic solvent system.

Our lab was the first to describe this method.[9,54] In 2003, we showed that this was a viable, general separation system. We were able to test the efficiency of such a separation by preparing various polymer-bound chromophores and fluorophores as catalyst surrogates that allowed us to measure the extent of separation using UV-visible spectroscopy and fluorescence spectroscopy, respectively. Because of the issues stated earlier, our work focused on the use of nonpolar phase-selectively soluble polymers. In

order to determine the amount of selectivity these polymers had, we first prepared, both, PNODAM-supported methyl red and dansyl dyes, shown below (Scheme 7).

Scheme 7. Structures of both PNODAM-bound dansyl and methyl red dyes.
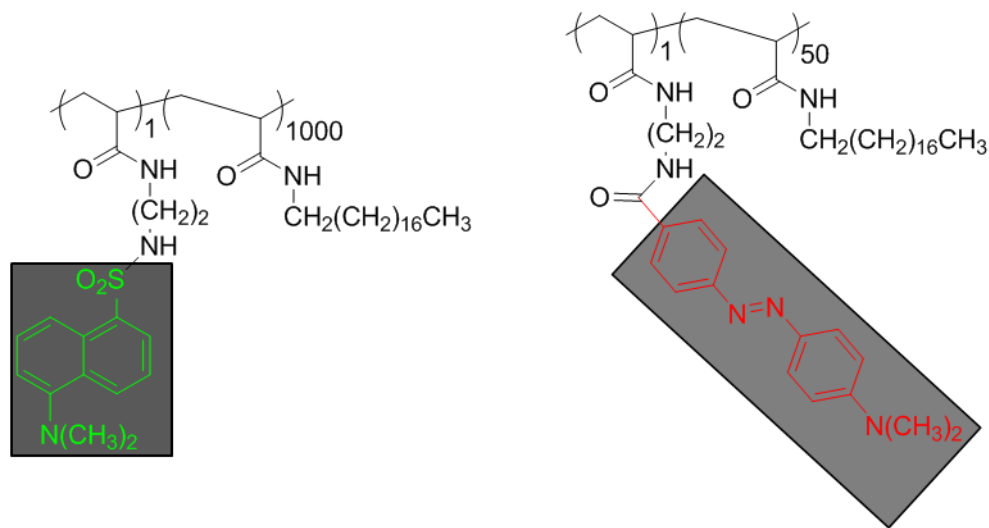
By dissolving these polymer-bound dyes in a mixture of toluene and 95 % ethanol/water followed by the addition of 5 % water, we were able to show that the polymers had a phase selective solubility for the nonpolar phase of >99.9 %. We also showed that there are many solvent mixtures that can be used including heptane/ethanol or TBME/ethanol/water.

After the efficiency of this separation system was determined, we then turned to the use of such polymers as supports for transition metal catalysts. The initial work used supported SCS-pincer/Pd complexes in catalysis. Starting with a PNODAM-pincer/Pd complex, we carried out a Heck coupling between acrylic acid and iodobenzene. After a homogeneous reaction at 120 °C in heptane and DMA, addition of *ca.* 5 % water

induced phase separation and the product was isolated by a gravity separation. The catalyst was recoverd in heptane and the product was in the polar phase. This method was also used to recover and recycle a PNODAM-supported DMAP catalyst **24** (eq. 34). This catalyst was recycled six times with no loss in catalytic activity.

(34)
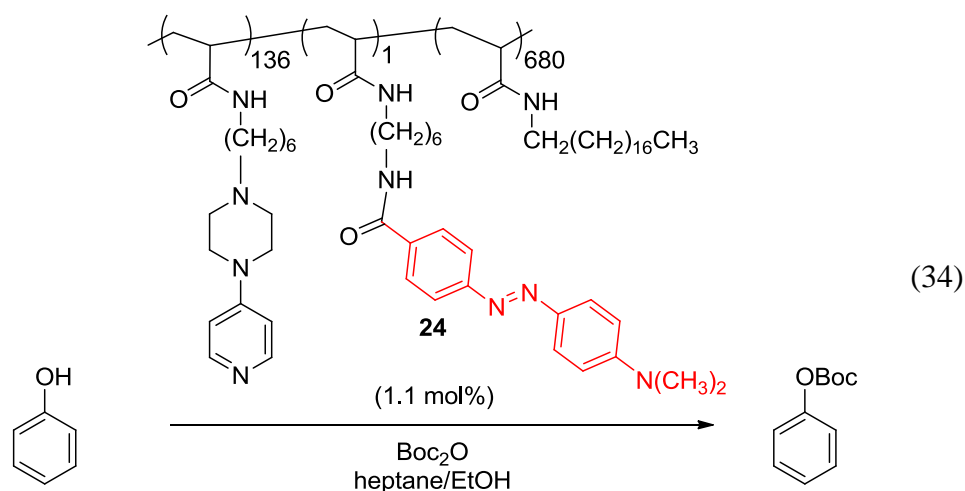
A few months after this initial report, we described the use of nonpolar linear polystyrene (poly(*tert*-butylstyrene) or PTBS) derivatives.[58] In this work, we first prepared a series of methyl red-labeled poly(*tert*-butylstyrene)'s containing either phosphine or aromatic amine functionality. Unlike the linear NCPS supports described earlier, the "greasier" *tert*-butyl analogs were found to be highly soluble in nonpolar solvents (such as heptane) and slightly soluble solvents (such as THF). Because of this high solubility in heptane, catalysts or reagents bound to these polymers could be recovered using a latent biphasic solvent system. In order to test the efficiency of the selective solubility of this polymer system, a co-polymer of tert-butylstyrene and a methyl red containing styrene were prepared. Similar to what was discussed earlier, the

phase selective solubility could be studied using UV-visible spectroscopy. The selectivity was shown to be >99.5 % for the nonpolar over the polar phase in a latent biphasic mixture of heptane and ethanol.

After the selectivity was determined, we studied catalysts attached to this type of polymer. We were able to show that the PTBS-bound triphenylphosphine derivative **25** could catalyze the Michael addition of 2-nitropropane and methylacrylate under latent biphasic reaction conditions using heptane and ethanol as the reaction media (eq. 35). Using the same method as above, the catalyst could be recovered and recycled four times with no loss in product yield.

(35)
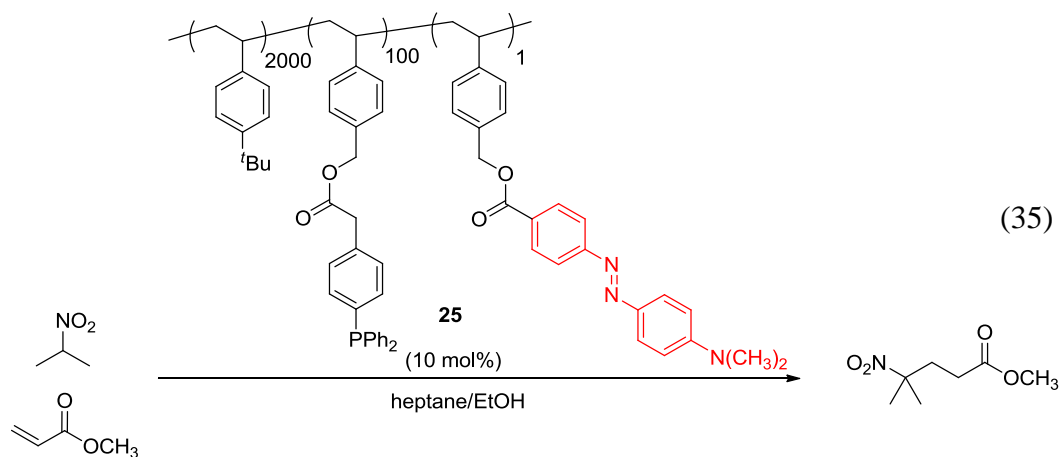
The generality of this chemistry can be further extended to the use of inorganic polymers as well. In 2006 we reported the use of polysiloxanes as supports for homogeneous catalysis under latent biphasic reaction conditions.[59] This was an improvement on previous chemistry that required the use of solvent precipitation or membrane filtration to recover catalysts bound to polysiloxanes.[60] This chemistry too used a methyl red-labeled poly(dimethylsiloxane) (PDMS) to first verify the was phase

selectivity of this polymer in a latent biphasic reaction mixture of heptane and ethanol (the phase selectivity was found to be > 99.5%). A PDMS-supported cinchona alkaloid **26** was then prepared and used a recoverable/recyclable catalyst for the Michael addition of thiophenols and α,ß-unsaturated ketones and esters. By simply adding *ca.* 20 % water to the reaction mixture, the phases could be induced to separate and the heptane phase (containing **26**) could be isolated and reused up to five times with no loss in activity (eq. 36).

(36)
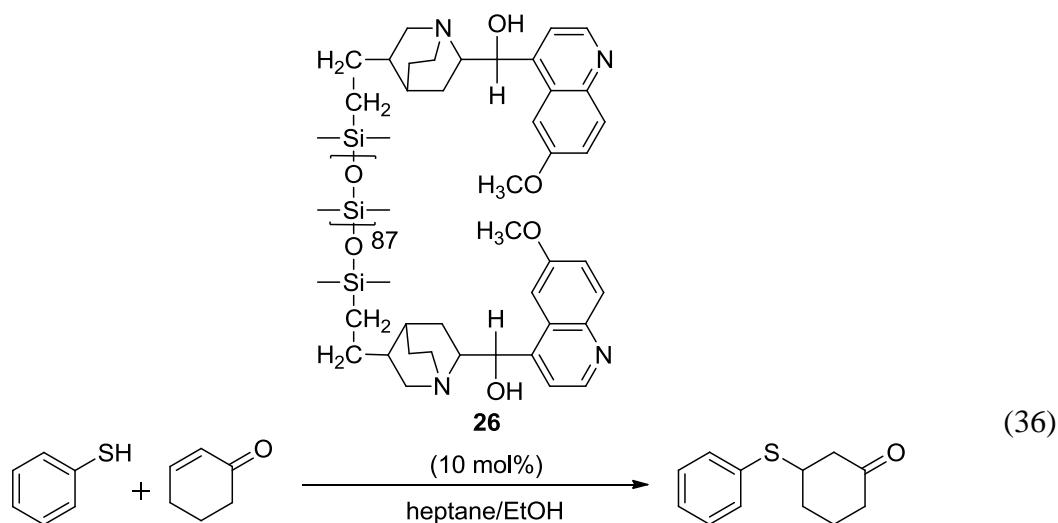
Polyisobutylene-supported Ligands/Catalyst

As discussed earlier, catalysts attached to polyolefins, such as polyethylene, can be readily recovered and recycled. However, there are problems that arise using PE supports in that the catalyst has absolutely no solubility in any solvent at room temperature. Furthermore, PE has very poor solubility in many solvents, especially polar solvents. Polyisobutylene (PIB) is an alternative polyolefin support for transition metal catalysts.[7,12,13,35,61,62,63,64,65,66] PIB oligomers are attractive both because they are very

soluble and because they are commercially available from BASF, under the trade name of Glissopal (M_n of 1000-2300).[61] These oligomers are sold such that the oligomer contains a 90:10 mixture of di-tri-substituted olefin end groups. We have shown that relatively simple organic transformations can be used to create many functional groups from these PIB derivatives. Often, these syntheses involve relatively easy purification methods (i.e. no column chromatography). These derivatives can serve as ligands (or ligand precursors) for a variety of catalyst systems.[62,63,64, 6566] An advantage in this chemistry is that we can link the PIB to a ligand through stable, inert carbon-carbon bonds, a more attractive concept than using heteroatom linkages as heteroatom bonds can decompose under some reaction conditions. Also, these oligomers have very high solubility in many nonpolar and slightly polar solvents (heptane, hexanes, methylenechloride, chloroform, toluene, THF, diethyl ether, etc.) at room temperature or below. Indeed, PIB remains in solution in many solvents at temperatures as low as -78 °C.[35] Due to this high solubility, PIB oligomers and their derivatives can be easily analyzed by ^{1}H and ^{13}C NMR spectroscopy (Figure 2). Also, unlike many other polymer supports, spectra of PIB-supported groups are virtually identical to their low molecular weight analogs. Our lab has shown that PIB derivatives have a very high phase selective solubility (>99.6 %) for nonpolar solvents over polar ones in both latent biphasic and thermomorphic solvent systems.
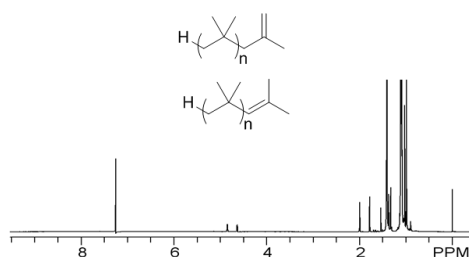
Figure 2. Structure and ^{1}H NMR spectra of PIB-alkene.

It was briefly discussed earlier that many studies have shown that insoluble crosslinked polystyrene supported ligands and catalysts differ in various ways from their low molecular weight soluble analogs in their rates of reaction and in their selectivities in catalysis. Similar questions often times arise about whether or not soluble, terminally-functionalized polymer-supported ligands are "different" than their low molecular weight counterparts.[35] Our lab has suggested that such polymer-supported species (such as PIB-bound groups) afford terminal groups the same environment as unsupported ones, at least in reactions with low molecular weight substrates. This hypothesis is supported by studies that examine the activities and selectivities of terminal polymer-bound supported catalysts vis-a-vis their low molecular weight counterparts. Spectroscopic experiments including solvatochromic studies of the activity of polymer-bound fluorophores and NMR spectroscopy of dynamics of ligand exchange rates[66,67] have also been used to support our arguments about the similarity of low molecular weight and terminally-substituted polymeric ligands. Recently, we reported the use of variable-temperature (VT) NMR spectroscopy to study the kinetics of Ag-phosphine exchange processes of PIB-bound phosphine ligands versus low molecular weight

phosphine ligands. The spectroscopic data (experimental and theoretical), the rate constants for the exchange reactions and the activation energies of these processes were virtually identical to the electronically-similar, low molecular weight species.

The first reports detailing the utility of PIB oligomers as supports in catalysis appeared in 2004[62] and 2005[63]. That report showed that it was possible to prepare PIB-bound phosphines and SCS pincer ligands that could be used as ligands for palladium cross coupling catalysts. The preparation of these ligands is outlined in eqs. 37 and 38. The syntheses started with the hydroboration/oxidation followed by conversion of the hydroxyl group into the bromide through a mesylation followed by substitution with LiBr. Reaction with *n*-BuLi and a phosphine/borane complex followed by removal of borane with morpholine provided the PIB-bound phosphine **27** shown below. From the PIB-OMs the PIB-SCS ligand could be formed through a malonic acid synthesis followed by reaction with ethylchloroformate. Subsequent reaction with the low molecular weight SCS-precursor formed **28**. Both PIB-bound ligands were then used to form Pd(0) or Pd(II) complexes and the resulting complexes were used in Heck and Sonagashira cross-coupling reactions. Under either thermomorphic or latent biphasic conditions, these catalysts were recycled up to three times.

H⎯(PIB)⎯C(CH₃)₂CH₂C(=CH₂)CH₃

$\xrightarrow[\text{2. H}_2\text{O}_2,\text{ NaOH}]{\text{1. BH}_3\cdot\text{Me}_2\text{S}}$

H⎯(PIB)⎯CH₂CH(CH₃)CH₂OH

$\xrightarrow{\text{MsCl}}$

(37)

H⎯(PIB)⎯CH₂CH(CH₃)CH₂OMs

$\xrightarrow{\text{LiBr}}$

$\xrightarrow[\text{2. morpholine}]{\substack{\text{1. }^n\text{BuLi then,}\\ \text{Ph}_2\text{PH}\cdot\text{BH}_3}}$

H⎯(PIB)⎯CH₂CH(CH₃)CH₂PPh₂

27

H⎯(PIB)⎯CH₂CH(CH₃)CH₂OMs

$\xrightarrow[\substack{\text{2. NaOH}\\ \text{3. H}_3\text{O}^+,\text{ heat}}]{\substack{\text{1. diethylmalonate}\\ \text{EtONa}}}$

$\xrightarrow[\text{2.}]{\text{1. ClCO}_2\text{Et}}$

(38)

H₂N⎯C₆H₃(CH₂SC₆H₄OCH₃)₂

H⎯(PIB)⎯CH₂CH(CH₃)CH₂C(=O)NH⎯C₆H₃(CH₂SC₆H₄OCH₃)₂

28
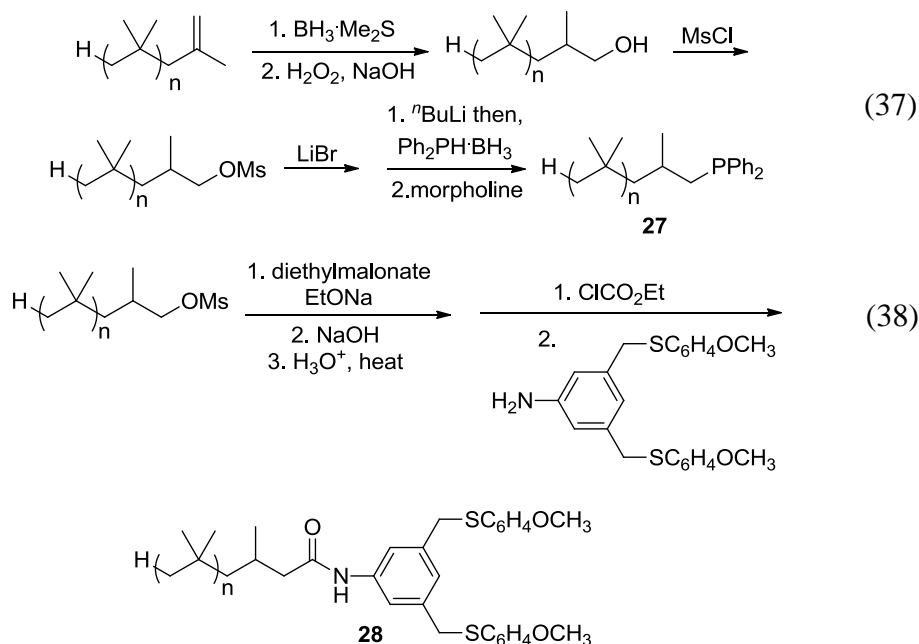
Our lab has also had success in the development of self-separating systems based on PIB-bound catalysts.[12,13,65] These systems are a version of the latent biphasic system discussed above and take advantage of the high solubility of PIB in heptane vs. the low solubility of NCPS in heptane (eq. 39). In the seminal example of this chemistry we prepared a PIB-supported copper complex **29**, shown below, using a copper catalyzed "click" reaction. This complex **29** was then used in an ATRP reaction of styrene in heptane at 110 °C. Upon cooling, the product polystyrene precipitated while the **29** stayed in solution. This catalyst could be recovered by forced siphon and was reused 5 times without any significant loss in activity. ICP-MS showed that *ca.* 3 % of the copper was found in the polystyrene product.

$$(39)$$
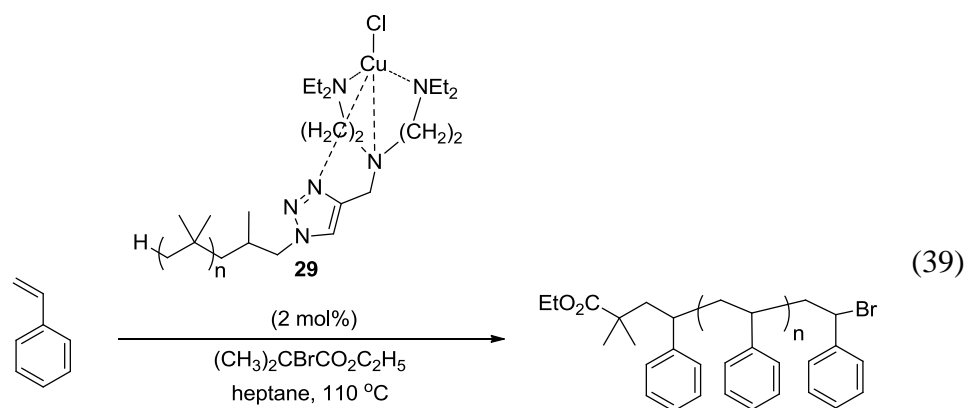
Similar self-separation events can occur when synthesizing low molecular weight species, too. We have had interest in polymer-bound Ru complexes useful as recoverable ring-closing metathesis (RCM) (pre)catalysts.[12,13] An early example of this work used the PIB-bound Ru complex shown in eq. 40. This synthesis used Friedel-Crafts alkylation reactions to functionalize PIB (*vide infra*). This chemistry was followed by an acid-catalyzed Cannizaro reaction, a Williamson ether synthesis and a Wittig reaction to give the styrene derivative. Reaction with the Grubbs' 2nd generation catalyst yielded the PIB-supported Hoveyda-Grubbs 2nd generation catalyst shown below.[12] In early work with this catalyst, a ring-closing metathesis reaction of the sulfonamide using the PIB-Ru complex in heptane produced a dihydropyrrole product that precipitated from a heptane solution of the catalyst and substrate. Forced siphon separated the heptane solution of the catalyst that was recycled 5 times (eq. 41).
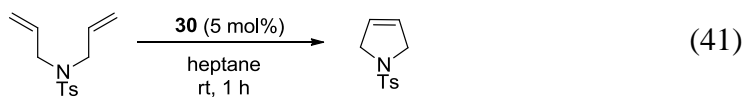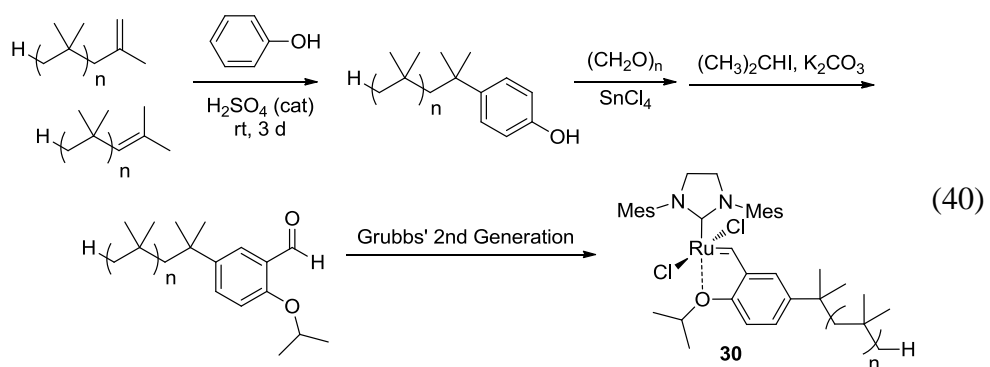
Much of the chemistry in our lab is focused mainly, not on the development of new chemistry, but the development of new ways to use and improve existing chemical processes. This involves taking advantage of a polymer's physiochemical properties and applying them toward the development of "Green" methods for the recovery and isolation of homogeneous catalysts and products that they form. The following dissertation describes, in detail, processes that we have developed using both PIB and PE_{Olig}-supports for the preparation of recoverable/recyclable ligands and transition metal catalysts.

CHAPTER II

PREPARATION OF A PIB-SUPPORTED BINOL

Introduction

Over the past few decades, the enantiomeric atropoisomers of 2,2'-dihydroxy-1,1'-binaphthol (BINOL) **34** have become widely used as chiral auxiliaries for transition metal catalysts.[68] Racemic BINOL was first prepared and described over 130 years ago, by von Richter.[69] Because of stability of each of its atropisomers (with barriers of rotation of *ca.* 24 kcal/mol), BINOL has been found to be a useful chiral ligand for a vast number of chemical transformations. Some of these include; enantioselective reductions[70] and oxidations[71], ene reactions[72], aldol reactions[73-79], Diels-Alder reactions[80-82] and hetero-Diels-Alder reactions.[83,84]

The synthesis of BINOL can be carried out through an oxidative coupling of 2-naphthol **31**, using various metal salts. Suitable oxidants include: $FeCl_3$[85], $K_3Fe(CN)_6$[86], $Mn(acac)_3$[87] or Cu-amine complexes.[88] In the latter case, the use of chiral amines allows for the preparation of optically pure (*R*)- or (*S*)-BINOL, often times with e. e. > 90 %. The mechanism for this coupling reaction is shown in Scheme 8.

Scheme 8. Mechanism of the formation of BINOL from 2-naphthol.
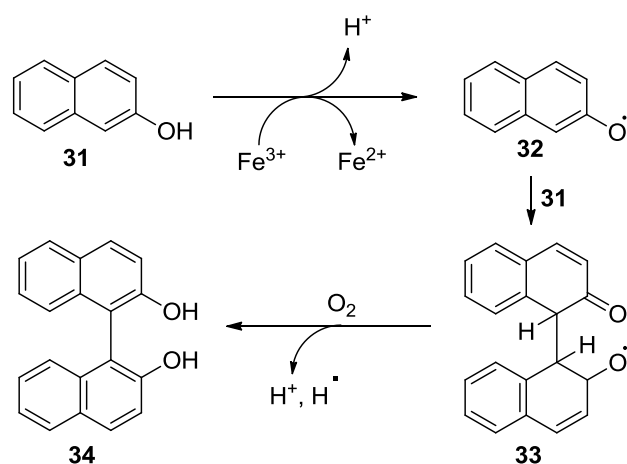
These coupling reactions are not catalytic and often require more than a stoichiometric amount of metal salt. The mechanism of this reaction first involves the one electron oxidation of **31** to give the naphthol radical **32** which can then undergo a coupling reaction with another equivalent of neutral **31** to form the new C-C bond which generates the new radical **33**. This radical can then eliminate $H^{\bullet}$ and then go on to be oxidized by atmospheric O_2 to release a proton to regain aromaticity to form racemic BINOL **34**.[68]

Enantiomerically pure (*R*)- or (*S*)- BINOL has been extensively studied and can be either be isolated by resolution or prepared by an asymmetric synthesis. Resolution can be accomplished in a number of ways, including, by chemical[68,89] or enzymatic[68,90] resolution of (±)-BINOL (which will not be discussed in detail). The first example of the synthesis of enantiomerically pure BINOL was reported by Wynberg and coworkers.[91] They showed that, by allowing **31** to reaction with 1 equiv. of Cu(NO$_3$)$_2$·3H$_2$O and (*S*)-

phenylethylamine (eq. 42), they could obtain (*S*)-BINOL ((*S*)-**34**) in 63 % yield. However, this asymmetric synthesis, unfortunately, only gave the product in 3 % e. e.

(42)
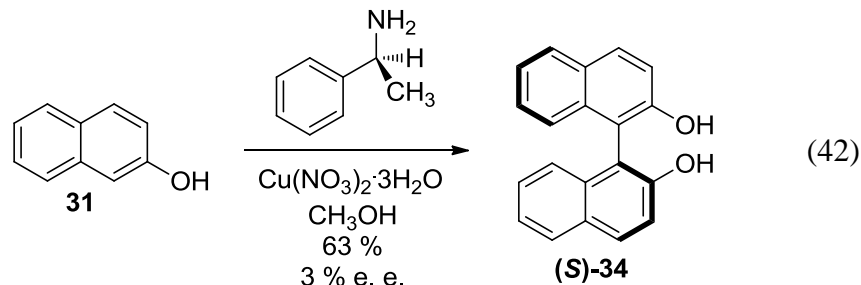
Shortly after this, Brussee's group discovered that the stereoselectivity could be increased by changing the chiral auxiliary from (*S*)-phenylethylamine to amphetamine.[92] Using this method, eq. 43, they were able to obtain (*S*)-**34** in 94 % yield and 96 % e. e.

(43)
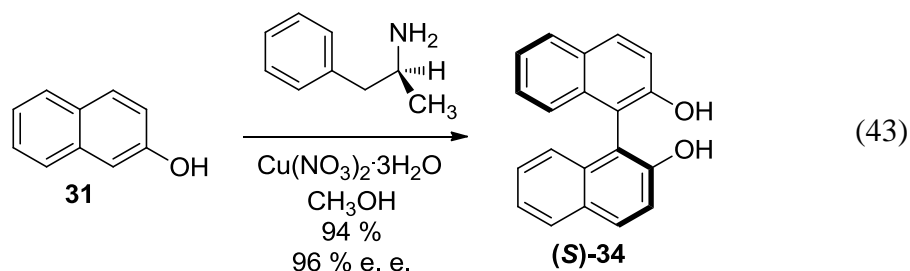
Even though this procedure is an improvement on Wynberg's chemistry, it is still problematic in that, it requires stoichiometric amounts of chiral ligand and transition metal salt; making this process less attractive because of the cost and the toxicity of the copper salt. To improve this chemistry, there have been some catalytic methods developed for the preparation of either (*R*)- or (*S*)-**34**.[93-98] Some of these processes involve the use of chiral oxovanadium complexes **35**-**37** and can afford enantiomerically pure (*R*)- or (*S*)-**34** in moderate to good yields and enantioselectivities (Scheme 9).

Scheme 9. Chiral oxovanadium complexes **35**-**37** used for the catalytic asymmetric preparation of BINOL.
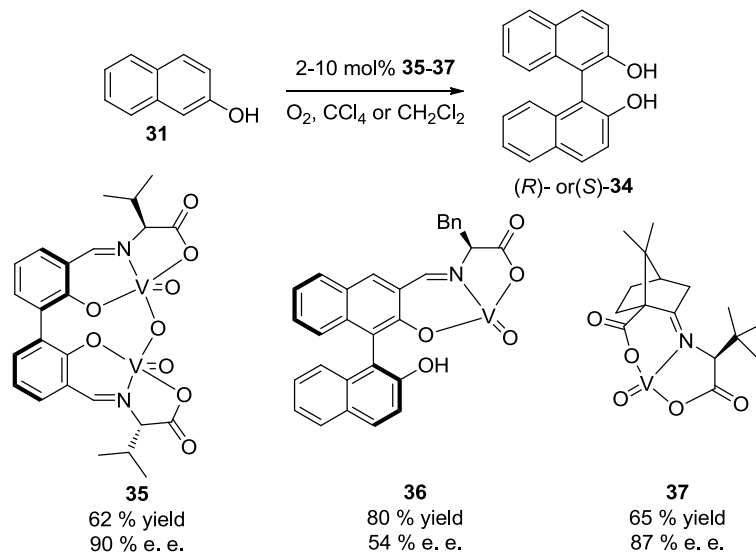
BINOL is among one of the most widely known axially chiral molecules and has been shown to be a highly competent catalyst for many asymmetric catalytic reactions.[68] Because of its ability to induce high levels of enantioselectivity in many different reactions, BINOL is considered by some to be in a special class of "privileged" ligands.[99] Examples of some of the reactions catalyzed by BINOL complexes are described below.

One of the most-studied asymmetric catalytic reactions is the enantioselective reduction of carbonyl compounds. Tang and coworkers reported the synthesis of a novel BINOL-phospho-borane complex (*S*)-**38** (eq. 44) that was shown to be capable of reducing ketones with high levels of enantioselectivity.[70] This complex, at 6 mol%, was shown to catalyze the reduction of ketones such as phenyl methyl ketone in the presence

of a $BH_3 \cdot THF$ complex in toluene at 100 $^{\circ}$C to afford the secondary alcohol products in high yield and selectivity (94 %, 99 % e. e.), as shown in eq. 45.

$$(44)$$

$$(45)$$
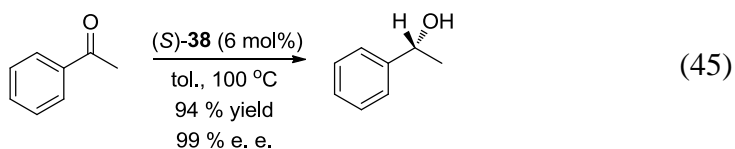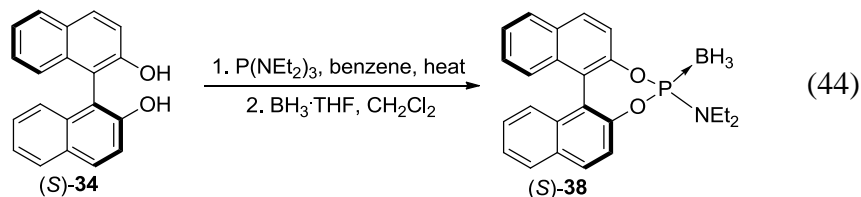
The use of (R)- or (S)-34 is not limited to asymmetric reductions This chiral ligand has proven to be useful in many oxidation reaction as well. Shibasaki and coworkers reported the preparation of an (R)-BINOL-La complex (R)-39[71] (eq. 46) that could catalyze the asymmetric epoxidation of olefins with *tert*-butyl hydroperoxide (TBHP) to afford optically active epoxy ketones in yields up to 99 % and in 99 % e. e.

$$(46)$$
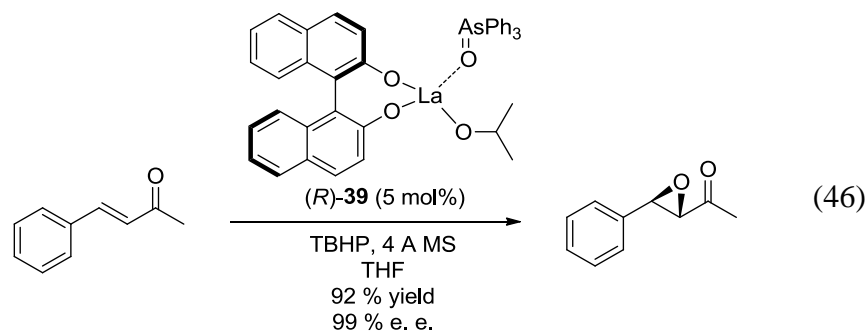
An important goal of synthetic chemistry is to develop methodologies for the formation of C-C bonds. A classical example of such methodology is the ene reaction. This reaction was first discovered by Alder in 1943.[74] He reported that when propene and maleic anhydride are mixed together and subjected to high temperature and pressure

the resulting product is allylic succinic anhydride. While the ene reactions initially studiedrequired the use of high temperatures and pressures, this situation changed when Colonge[75] and Normant[76] reported the first Lewis-acid catalyzed Ene reaction between isobutylene and chloral with 10 mol% AlCl$_3$.

The first example of an asymmetric ene cyclization reaction utilizing BINOL was reported by Yamamoto *et al*. They showed that (*R*)-BINOL-Al complex, (*R*)-**40**, (generated in situ from (*R*)-**34** and AlMe$_2$) promoted the cyclization shown in eq. 47. As is the case with most of these early examples, this reaction was not catalytic; complex (*R*)-**40** had to be used as a

$$(47)$$
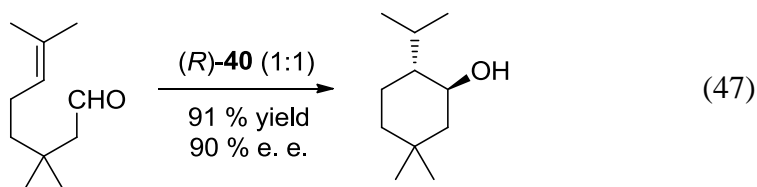
stoichiometric reagent. Nakai and Mikami[77] later found that, through extensive catalyst screening, that a BINOL-Ti complex ((*R*)-**41**, generated *in situ* from (*R*)-**34** and TiBr$_2$(O*i*-Pr)$_2$) was   an excellent catalyst for the intermolecular ene reaction between olefins and glyoxylate esters (eq. 48). As shown in eq. 48, reaction of olefin and methyl glyoxylate catalyzed by complex (*R*)-**41** (formed in situ), at 5 mol%, provided the ene adduct in high yield and excellent e. e. (98 %).

$$(48)$$
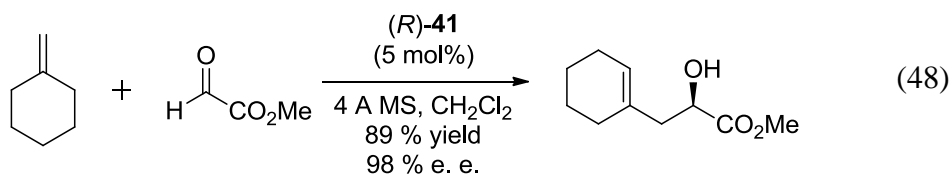
Reetz[78] later found that a complex similar to (R)-**41** could catalyze Mukaiyama aldol reactions as well. Reaction of various aldehydes and silyl enol ethers provided products with poor e. e. (*ca.* 8 % e. e.). Mukaiyama found, shortly after this, that the (R)-**42** complex[79], shown in eq. 49, was able to afford aldol products in e. e.'s up to 85 %.

(49)
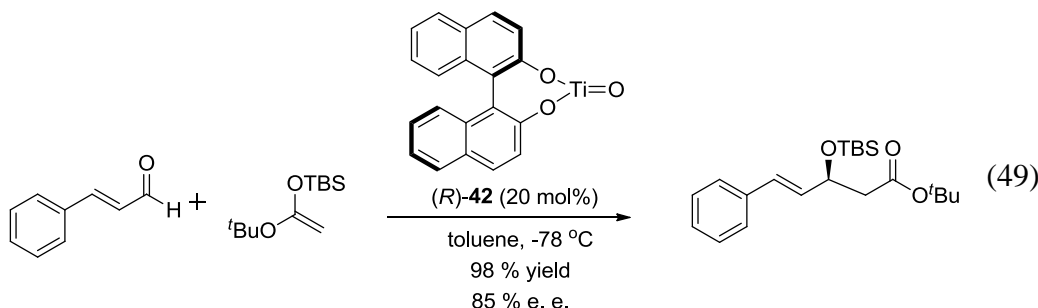
About 3 decades ago, the first example of a Lewis acid-catalyzed enantioselective Diels-Alder reaction was reported by Guseinov[68], followed by work from Koga and coworkers.[80] The two earliest examples of the use of BINOL complexes are credited to Seebach[81] and Reetz[77]. Both of these labs utilized BINOL-Ti complexes (BINOL-TiCl$_2$(O*i*-Pr)$_2$ ((R)-**43**) and BINOL-TiCl$_2$ ((R)-**44**) respectively), with Reetz' complex affording Diels-Alder adducts in higher e. e.'s (eq. 50).

(50)
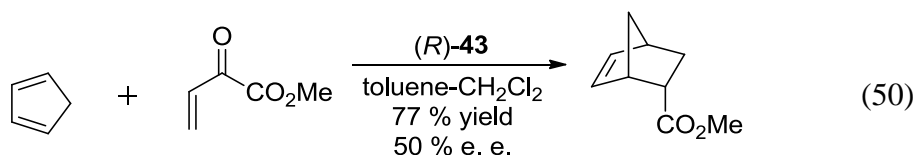
A late improvement to BINOL-Ti catalyzed Diels-Alder chemistry was reported from Mikami's lab.[82] Their group showed that the reaction between 1,3-dienyol derivatives and methacrolein could be catalyzed with complex (R)-**43** to afford Diels-Alder adducts in moderate yields (*ca.* 60 %) and moderate to high e. e.'s (71-94 %) (eq. 51).

$$\text{(51)}$$
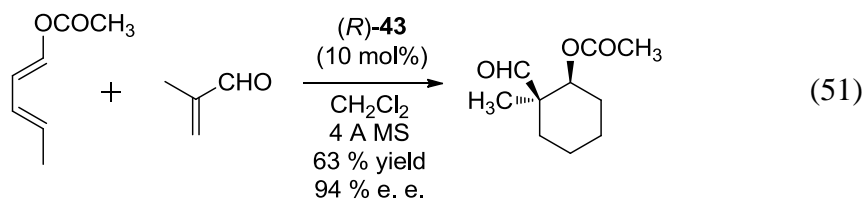
Jorgensen and coworkers found that BINOL-Al complexes (such as (S)-BINOL-AlMe$_3$ complex (S)-**45**) can serve as competent catalysts for Hetero-Diels-Alder reactions as well as the reaction described above.[83] By reacting isoprene with various glyoxylate esters in the presence of an (S)-BINOL-Al complex (S)-**45** (formed in situ), they were able to preferentially form the Hetero-Diels-Alder adducts over the ene adducts in high e. e.'s (94-97 %) but in rather modest yields (*ca.* 30 %) for most substrates (eq. 52).

$$\text{(52)}$$
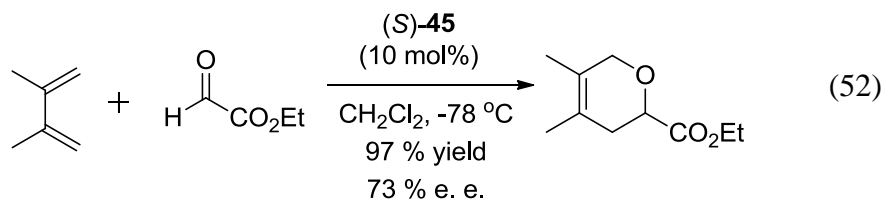
PIB-bound BINOL

As illustrated in this chapter so far, transition and main groups metal complexes of (R)- or (S)-**34**, have been important in the development of many different asymmetric catalytic systems. Often times, these catalysts induce a high level of stereoselectivity within the products while affording those products in good yields. Because of this importance, it has been of some interest to prepare polymer-supported BINOL ligands that can be used as recoverable, recyclable catalysts for some of the reactions described above. There have been numerous examples and reviews detailing the preparation and use of polymer-bound BINOL's as ligands, catalysts and materials.[6,7,68, 100, 101] Below

are described just a few examples of soluble polymer-supported BINOL-metal complexes from the recent literature.

As described in detail in Chapter I, functionalized PEG oligomers are among the most widely used soluble polymer-supports for ligands and transition metal catalysts. Because of the importance of BINOL ligands, Kumaraswamy and coworkers reported the preparation of a PEG-bound (*R*)-BINOL-Ca complex (*R*)-**47** (eq. 53).[102]
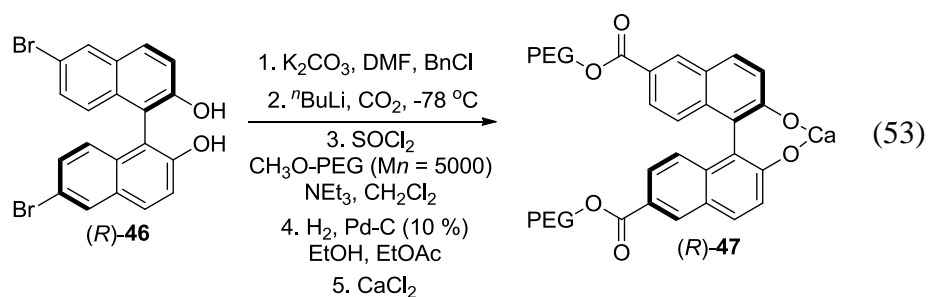
The preparation of the PEG-bound BINOL-Ca complex, (*R*)-**47**, started with the protected dibenzyl ether of bromo BINOL (*R*)-**46** (formed in the reaction of (*R*)-**34** with Br_2). Low-temperature lithium-halogen exchange with *n*-BuLi followed by reaction with CO_2 and an aqueous work up led to the BINOL-carboxylic acid. This species was then converted into the acid chloride and allowed to react with PEG (M_n = 5000). Hydrogenolysis then afforded the PEG-bound BINOL ligand. This ligand was then deprotonated and reacted with $CaCl_2$ to obtain the Ca complex (*R*)-**47**. This complex was then used as a catalyst for asymmetric Michael addition reactions (eq. 54). (*R*)-**47** was able to provide the Michael adducts in good yields but in modest to low e. e.'s. The catalyst was recovered using solvent precipitation into diethyl ether and was reused three times with no observed loss in product yield.

$$\text{(R)-47 (15 mol\%)}$$

Ph—CH=CH—C(O)Ph + H$_3$CO—C(O)—CH$_2$—C(O)—OCH$_3$ $\xrightarrow[\substack{0\ ^\circ C \\ 86\ \%\ yield \\ 25\ \%\ e.e.}]{(R)\text{-}47\ (15\ mol\%)}$ Ph—C(O)—CH$_2$—CH(Ph)—CH(CO$_2$CH$_3$)$_2$ (54)
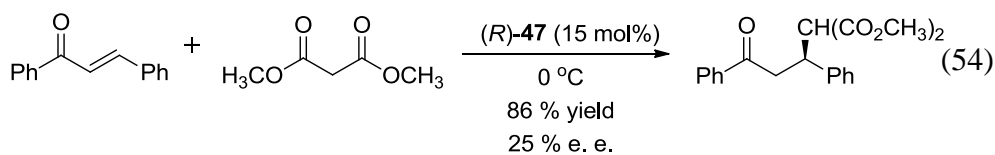
Complex (*R*)-**47** was also used as a catalyst for asymmetric epoxidation reactions of α,ß-unsaturated ketones with *tert*-butyl hydroperoxide as an oxidant (eq 55). Again, high yields were observed for these reactions, but only modest levels of enantioselectivity were seen. Recycling data for the epoxidation reactions were not reported.

$$\xrightarrow[\substack{^tBuOOH,\ 4\ A\ MS \\ 0\ ^\circ C \\ 93\ \%\ yield \\ 47\ \%\ e.e.}]{(R)\text{-}47\ (10\ mol\%)}$$ (55)
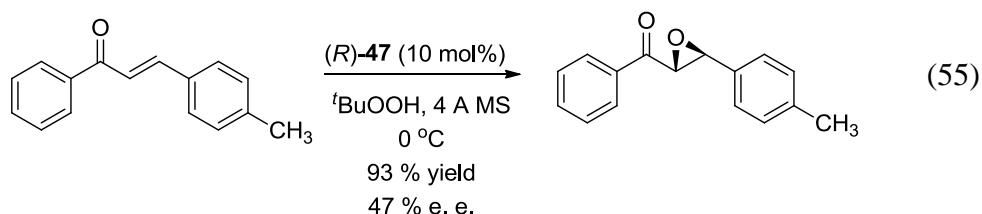
It has also been possible to prepare linear polymers that contain a BINOL unit as a pendant group. This was shown in the preparation of a NCPS-supported BINOL ligand ((*R*)-**49**). The synthesis of (*R*)-**49** started with the reaction between (*R*)-**34** and Br$_2$ in CH$_2$Cl$_2$ at -78 $^\circ$C to afford the mono-brominated species. This was followed with protection and a low temperature lithium-halogen exchange followed by formylation with DMF. Reduction with NaBH$_4$ yielded (*R*)-**48**, which was followed by a reaction with 4-vinyl benzylchloride and deprotection to afford a BINOL-styrene derivative (eq. 56). This monomer could then be subjected to a radical (initiator = AIBN) copolymerization with styrene to form the linear NCPS (*R*)-**49** shown below (eq. 57).[103]

$$(56)$$

$$(57)$$
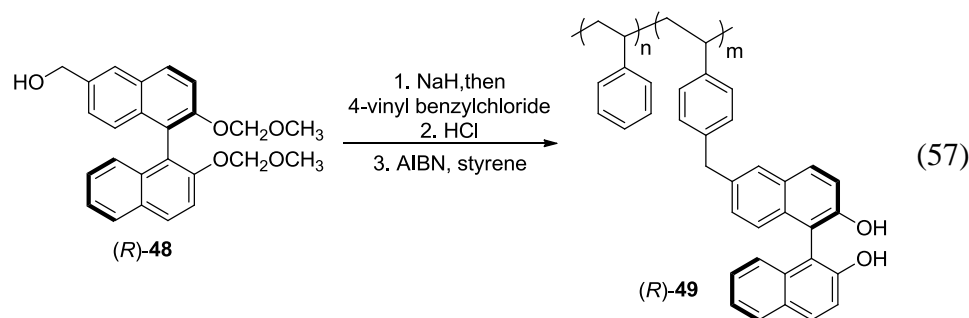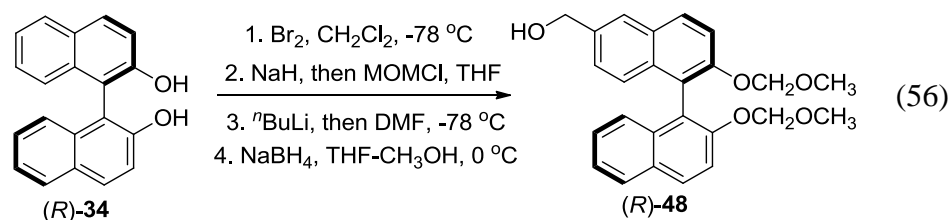
Addition of Ti(Oi-Pr)$_4$ to a solution of (R)-**49** afforded a Ti complex which was then used as a catalyst for the asymmetric addition of Et$_2$Zn to benzaldehyde. Reaction of benzaldehyde in CH$_2$Cl$_2$ at -20 $^\circ$C afforded the alcohol in moderate to good yields (*ca.* 60 %) and e. e.'s up to 84 %. The complex formed from Ti(Oi-Pr)$_4$ and (R)-**49** could be recovered using a solvent precipitation but because of co-precipitation of metal salt contaminants, recycling of the catalyst was not effective.

Results and Discussion[*]

As mentioned in Chapter I of this dissertation, our lab has been interested in the use of functionalized PIB oligomers as non polar analogues of PEG. Such polymer-bound species can be used as recoverable/recyclable, phase-selectively soluble ligands for homogeneous catalysts in liquid/liquid separation systems. The utility of PIB as a

polymer support was briefly discussed, as a few examples of our previous work were shown and it was mentioned that because of the terminal olefin of PIB, we can use a wide variety of simple organic transformations to prepare many different PIB-supported substrates.[7,12,13,35,61-63,104] This is illustrated in Scheme 10.

Scheme 10. Varity of functionality that can be appended to PIB oligomers.
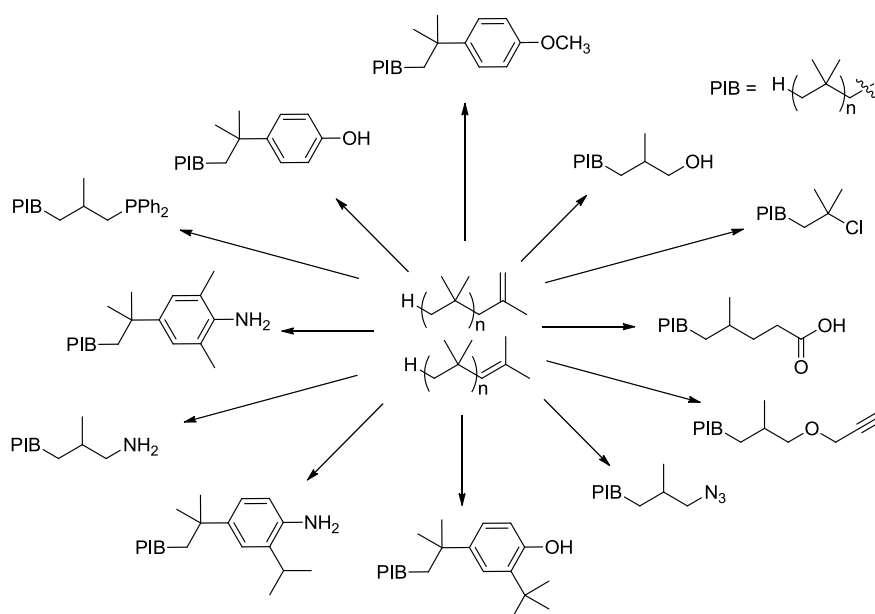
As shown above, there are numerous functionalities that can be attached to PIB using basic organic transformations. Reactions like hydroboration/oxidation, malonic ester synthesis and Williamson ether synthesis are all effective transformations that serve as building blocks for the preparation of numerous functional PIB's.

Reactions shown in Scheme 10 produce PIB-supported arenes are particularly interesting in connection with BINOL ligand chemistry. We had earlier shown that the

use of Friedel-Crafts alkylation chemistry is a general approach to the synthesis of a variety of PIB-bound aryl groups, usually in good yields and without the need for extra purification steps. Initial work in our lab focused on the electrophilic substitution of phenol and phenol derivatives. Subjecting commercially available PIB to reaction with an excess of phenol in CH_2Cl_2 in the presence of a catalytic amount of sulfuric acid afforded the PIB-phenol derivatives (**50** and **51**) in high yields; after removal of the solvent and a work up with hexanes followed by several washings with a polar solvent afforded 4-polyisobutylphenol that was pure by ^1H and ^{13}C NMR spectroscopy. The regiochemistry was also shown to be very high; the only product isolated from the hexanes phase was the 4-polyisobutylated arene. Not only has been possible to prepare the phenol derivatives shown, but using chemistry similar to that in eq. 57, we have been

$$50 = R = H$$
$$51 = R = {}^tBu$$
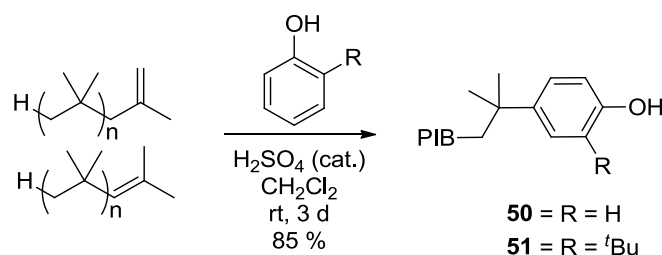
able to prepare PIB-bound anisoles and anilines as well. However, all of these are highly activated; they all contain highly electron donating substituents on the ring. This makes them especially reactive towards electrophilic aromatic substitution (EAS) reactions. We were curious as to whether or not it was possible to prepare PIB-arene ligands from less activated aromatic species like benzene or toluene. Unfortunately, all attempts at performing the Friedel-Crafts alkylation chemistry on these arenes using the starting PIB

olefin failed. This was even the case when the arenes were used as solvents in large excess. The reason for this is discussed below.

Even though we (usually) observed none of the desired products, some alkylated arenes did form. Upon analysis of the reaction mixture, it was found that, in the reaction of PIB and benzene, 4-*tert*-butylbenzene was present (Scheme 11). Formation of the low molecular weight byproduct suggested that depolymerization of the polyisobutyl-cation intermediate **52** formed in the first step of the EAS reaction was the reason for a lack of success in polyisobutylation of benzene or toluene. In this explanation, **52**would form. While **52** could react with the arene to form a σ-complex (a relatively high energy barrier, especially in the case of unactivated arenes) and form the PIB-arene product, the reversible nature of these reactions would reform **52** and the starting arene..Any **52** formed either by a dealkylation of the σ-complex of PIB and naphthol or **52** that did react with the arene could also undergo an entropy-favored depolymerization reaction in which the polymer chain loses a unit of gaseous isobutylene, forming a new tertiary polyisobutyl-cation (**52$_{n-1}$**) of chain length n-1. It was possible that this depolymerization could proceed until the reaction media is effectively saturated with isobutylene. The isobutylene would then be able to undergo an EAS reaction with the arene, leading to the *tert*-butylated product. This proposed explanation for the lack of formation of polyisobutylbenzene or toluene chemistry also has precedence in older literature reports.[105,106]

Scheme 11. Reaction and mechanism of the formation of 4-*tert*-butylbenzene from the reaction of PIB and benzene.
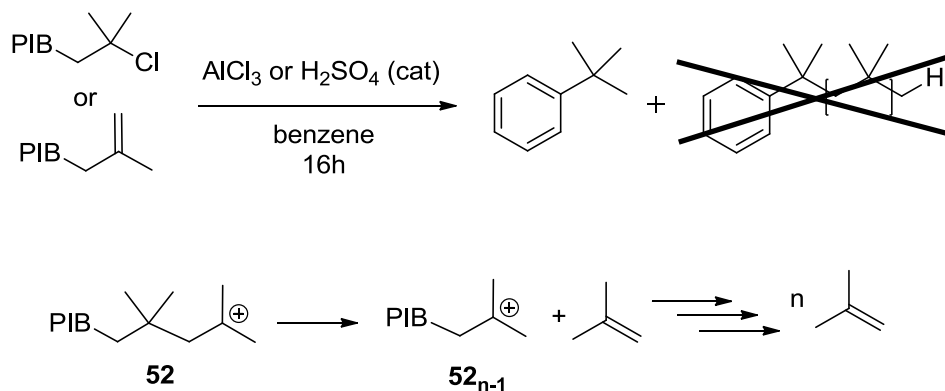
This issue is relevant as it affected our attempted preparation of PIB-supported naphthol and BINOL ligands. ^{1}H NMR spectroscopic analysis of attempts to prepare PIB-bound BINOL directly from the reaction of PIB olefin with 10 eq. of (±)-BINOL ((±)-**34**) with either a Lewis or protic acid in CH_2Cl_2 showed no product formation even after prolonged stirring (3 d) or upon microwave irradiation. This was the case under a
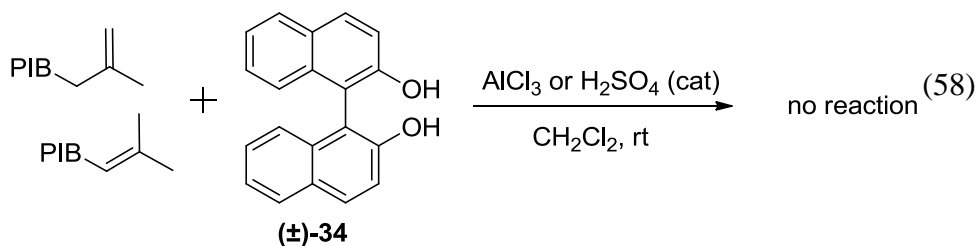
variety of reaction conditions (i.e. using either PIB alkene or a preformed PIB-chloride). Since reaction of **34** and polyisobutylene was unsuccessful, we examined the EAS reaction of PIB-alkene and 2-naphthol **31** (eq. 59). In principle, the product of this reaction could be used to form the PIB-BINOL through an oxidative coupling reaction

(*vide supra*). To our surprise, this reaction also failed under prolonged reaction or microwave irradiation. We did have, however, modest success in forming 6-polyisobutyl-2-naphthol (**53**) by the reaction of preformed PIB-chloride and **31**. This reaction yielded the desired product in low yields (*ca.* > 15 %).
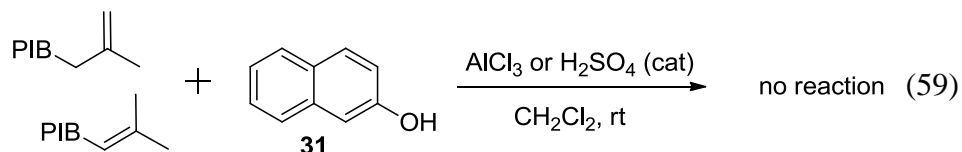
A more careful analysis of the reaction mixture showed that large amounts of the 6-*tert*-butyl-2-napthol were formed presumably by the depolymerization mechanism discussed above. This was also the case in the reaction with BINOL. While the yield of **53** from of the reaction between PIB-chloride and 2-naphthol was low, **53** could be isolated by washing a heptane solution of the product and with a polar solvent such as acetonitrile. Therefore, we proceeded to probe the formation of 6,6'-di(polyisobutyl)-2,2'-binaphthol (±)-**54** through the oxidative coupling of this species with CuCl$_2$ (eq. 60). Even though we found that it was possible to form (±)-**54,** the low yields of the preparation of **53** renders this process unattractive.
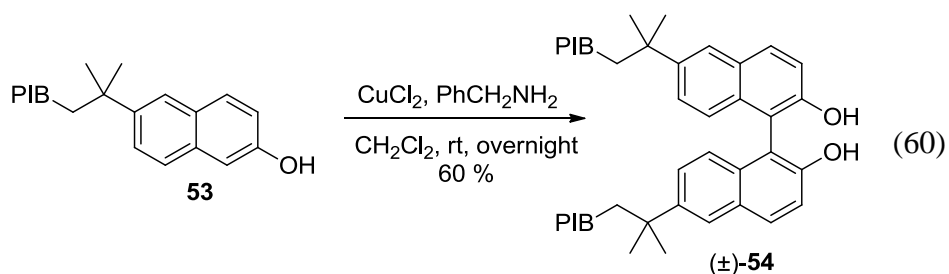
We next examined an alternative route for the preparation of a PIB-supported BINOL. Prior work had shown that BINOL derivatives undergo AlCl$_3$-mediated Friedel-

Crafts acylation reactions with acid chlorides to generate aryl ketones.Reasoning that the intermediate acylium ion attached to the terminus of the PIB would not undergo the depolymerization process described above we prepared a PIB-acid chloride according to Scheme 12 to test this hypothesis.

Scheme 12. Preparation of PIB-BINOL through Freidel-Crafts acylation chemistry.
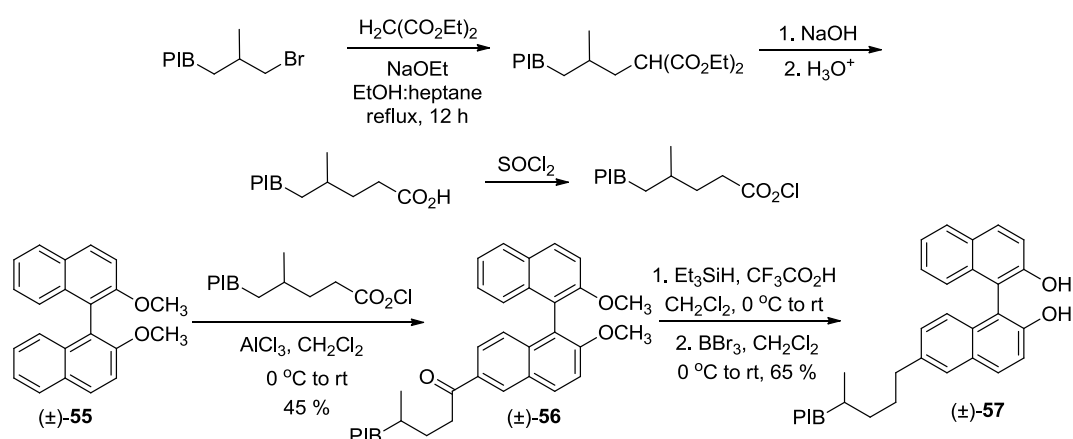
The Friedel-Crafts acylation of bis-methoxy BINOL (±)-**55** with PIB-acid chloride was carried out using $AlCl_3$ in CH_2Cl_2 at 0 °C. After warming to room temperature, the PIB-BINOL ketone (±)-**56** was formed in modest yield (45 %). Column chromatographic separation was used to isolate the desired product, which could then be reduced using triethylsilane and TFA, followed by deprotection of the methyl ethers with BBr_3 to afford the PIB-BINOL (±)-**57** in 65 % yield. The diol (±)-**57** was selectively soluble in nonpolar solvents and could be prepared on a multi-gram scale. Although this was the case, because of the long synthesis (9 steps in all) and the need for chromatographic purification, developments toward more direct routes would be more

appropriate if one wanted to develop and use recoverable catalysts based on PIB-supported BINOL's. This is especially true for the preparation of enantiomerically pure PIB-BINOL, as the starting BINOL is expensive compared to the racemic form.

Conclusions

The studies discussed in this chapter show that it is possible to prepare numerous PIB-supported arenes through the use of Friedel-Crafts alkylations; so long as the arene species involved is highly activated. The preparation of PIB-supported arenes that are less activated was shown to be more problematic as a depolymerization mechanism of the PIB oligomer occurs in these cases. This was especially true in the attempted preparation of PIB-supported naphthol and PIB-supported BINOL species. In order to overcome this problem, an AlCl$_3$-mediated Friedel-Crafts acylation reaction between a methylated BINOL and a PIB-acid chloride was performed to obtain PIB-BINOL ketone (±)-**56**. Such a reaction was more successful because the intermediate PIB-acylium ion cannot undergo the same depolymerization mechanism. This species could be reduced and deprotected to yield (±)-**57** that was phase selectively soluble in nonpolar solvents such as heptane. As mentioned above, such a synthetic scheme is not attractive because of the number of steps and purification methods involved. Because of this, the development of more direct routes to both racemic and enantiomerically pure **57** warrants further investigation.

CHAPTER III

POLYOLEFIN-SUPPORTED TRI-AND TETRADENTATE SCHIFF BASE-CONTAINING LIGANDS/METAL COMPLEXES[*]

Introduction

Salen ligands and the transition metal complexes that they form are widely used in catalysis. They can be used in a variety of reactions to convert simple organic starting materials into useful products. Some of the most well known transformations mediated by salen metal complexes are asymmetric epoxidations, epoxide opening and hydrolytic kinetic resolution (HKR) reactions. The latter two processes are especially common[107-109] and are the basis of chemistry that has led to important new asymmetric syntheses. Similar epoxide opening chemistry is also the basis of new greener polymerization chemistry affording polycarbonates from carbon dioxide and epoxides.[110] The broad utility and effectiveness of chiral salen ligands is evidenced by their description in the literature as members of a class of "privileged" ligands.[99]

Salen ligands have been known for over 70 years ever since the first reported preparation of a salen by Pfeiffer in 1933.[111] The easy synthesis of this class of ligand has led to extensive studiesof metal complexes containing these species. The name salen is derived from the ligand precursors, salicylaldehyde and ethylenediamine, and the pro-

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65

duct's tetradentate binding resembles those seen in porphyrin systems found in many heme-based enzymes. Some of the most commonly used salen ligands are shown in Scheme 13. These include the originally defined "salen" **58**, the tetra-*tert*-butyl derivative **59** and the chiral variants, **60** and **61**.

Scheme 13. Structures of various salen ligands.
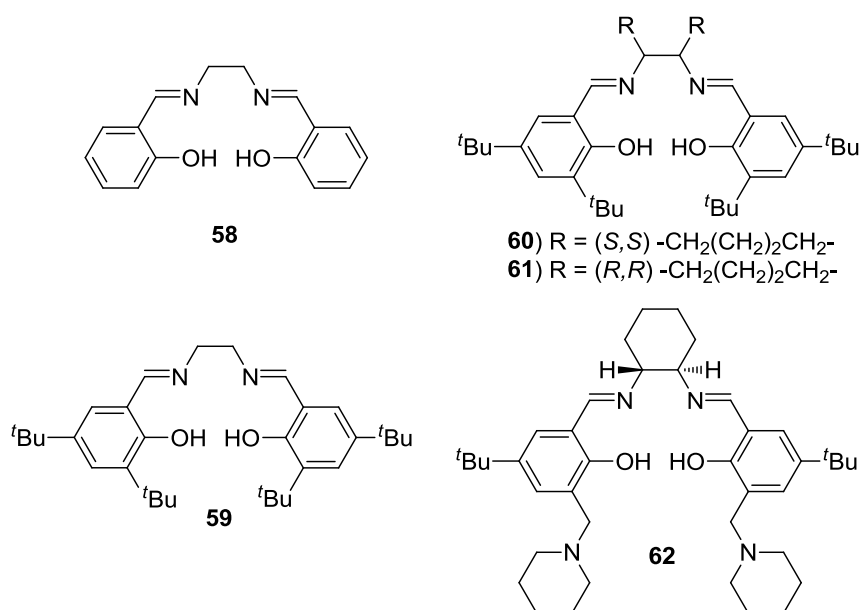
While the classical salen ligand **58** and analogous species like **59** are achiral, a variety of chiral salen ligands can be prepared with chiral 1,2-diamines. Species like **60** or **61** are examples and have been widely used asymmetric catalysis. More recently, piperidyl derivative **62** was developed by Nozaki *et al.* The cobalt complex of this ligand can be used for the copolymerization of epoxides and CO_2.[112]Examples of chiral transition metal complexes of salen ligands include complexes of Mn, Cr, Co, V, Cu, Ti,

Ru, , Zn, Zr and Al.[109,113]Described below are representative examples of some of these complexes and the reactions that they catalyze.

One of the most noted successes of salen/metal complexes in asymmetric catalysis is in asymmetric epoxidations of unfunctionalized olefins. This catalytic process was first reported in 1990 independently by Jacobsen[114] and Katsuki.[115] Both of these reports reports utilized chiral salen-Mn complexes as catalysts with iodosylarenes as stoichiometric oxidants. Later, Jacobsen and coworkers reported on the use of Mn(III)-complex **63** that could catalyze the asymmetric epoxidations of simple *cis*-olefins in the presence of household bleach as an oxidant (eq. 61).[116] This method produced epoxides in good yield (up to 84 %) and high enantioselectivty (up to 92 % e. e.). Jacobsen's and Katsuki's

(61)
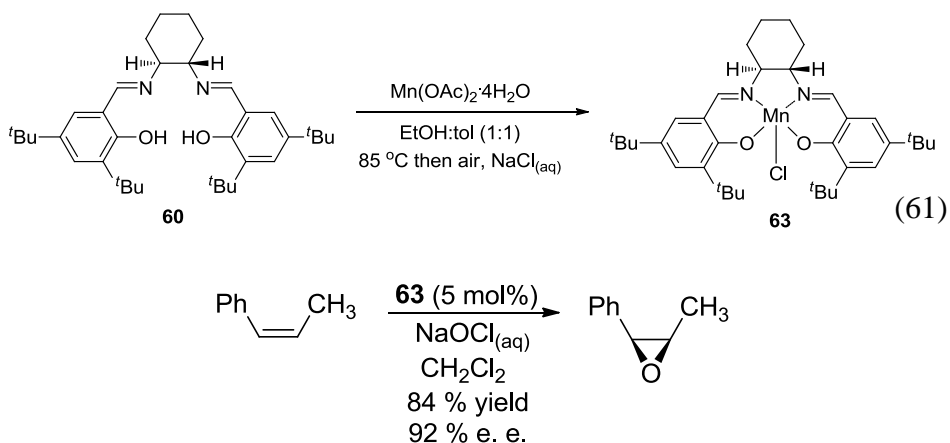
original successes in this area have since led to many other schemes for asymmetric epoxidations using chiral salen complexes. These examples have been reviewed recently.[108]

Four years after the seminal report of the epoxidation described above, Jacobsen and coworkers hypothesized that since this ligand system worked so well for the

asymmetric epoxidation, similar systems may be able to mediate the asymmetric opening of epoxides as well.[117] They reported that salen-Cr(III) complexes such as **64** were indeed capable of catalyzing the asymmetric ring opening of epoxides with azidotrimethylsilane as a nucleophile to yield the azido silyl enol ethers in good yields (up to 90 %) and excellent enantioselectivity (up to 98 % e. e.).

(62)

(63)
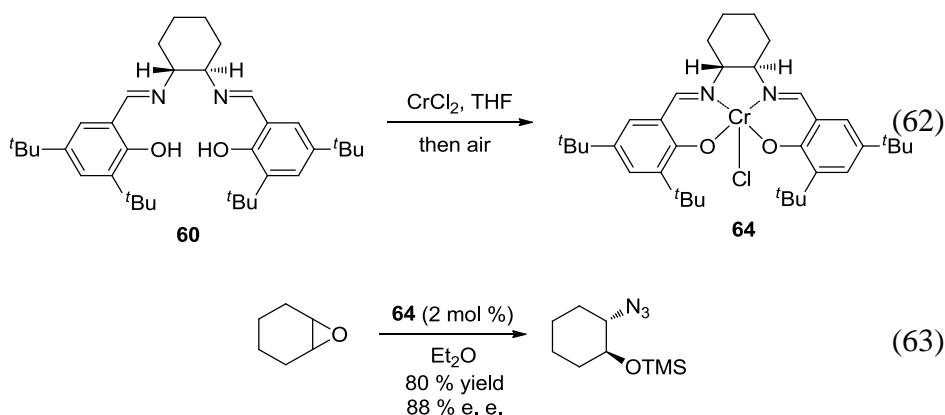
It was found that the complex **64** could be recycled by vacuum distillation of the azido product followed by addition of fresh substrate to the catalyst. Interestingly, elemental analysis of the complex after cycle 1 found no chloride and a nitrogen:chromium ratio of 5:1. This led the authors to the conclusion that **64** simply served as a precatalyst and that the active catalyst was actually **65**; which, more than likely, would not have been the case if **64** acted simply as a chiral Lewis acid, activating the epoxide. This prompted Jacobsen to investigate the mechanism for the reaction in more detail.

65
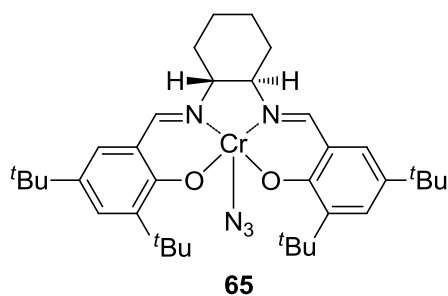
A year later, they found that the catalyst performed both activation of the epoxide towards reaction with the nucleophile and acted as an azide transfer agent.[118] Testing the kinetics of the reaction between cyclopentene oxide and HN_3, they found that, in a 5-fold excess of epoxide, the kinetics revealed a zero-order rate dependence in HN_3. However, the rate constant (k_{obs}) was correlated in a linear fashion to the square of the catalyst concentration. This indicated that the reaction was 2nd order with respect to the catalyst. This prompted Jacobsen and coworkers to propose the mechanism outlined below in Scheme 14.

Scheme 14. Proposed mechanism of the asymmetric epoxide opening with Cr-salen complex.
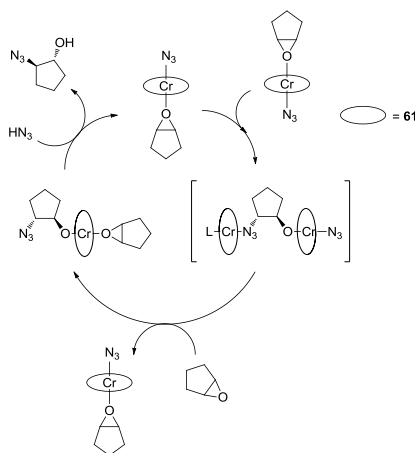
It was found that salen-Co(III) complexes (generated in situ from the salen-Co(II) complex, air and benzoic acid) could also catalyze epoxide opening with carboxylic acids in moderate to good enantioselectivity (up to 99 % e. e.).[119] Studies that examined the kinetic resolution of *meso*-epoxides revealed that epoxide opening was in competition with epoxide hydrolysis, which occurred from the adventitious presence of water . It was found that the diols obtained were formed in high e. e.'s (*ca.* 95 %). This led the authors to believe that a highly selective hydrolytic kinetic resolution (HKR) of the epoxide was occurring. Indeed, terminal epoxides react rapidly with water in the presence of catalyst **66** and acetic acid (eq. 64).[120]
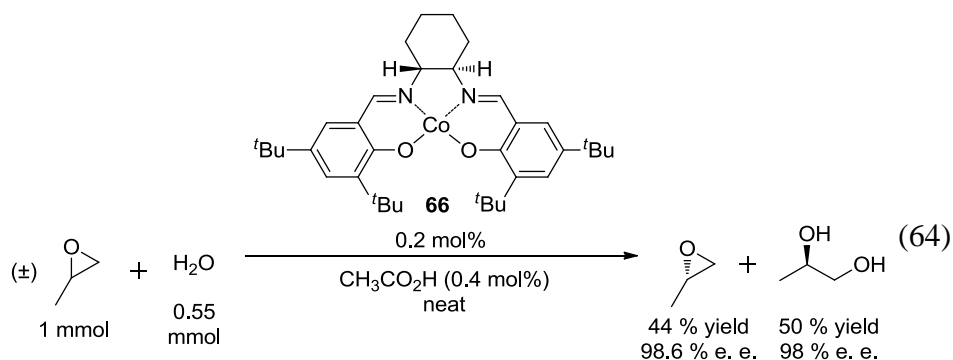
PIB-and PE_Olig-bound Salen-metal Complexes as Recyclable Catalysts for Ring-opening Reactions of Epoxides

Because of the broad utility of salen transition metal complexes of ligands such as **60** and **61** in catalysis, a variety of reactions and approaches for catalyst and ligand recovery have been explored.[6,7,113,121,122] Three general strategies to recover, reuse, or separate the catalyst and product have been used in these studies. The first strategy uses a support that is insoluble before, during, and after the reaction.[123] These approaches have typically used cross-linked polymer supports or inorganic solid supports. A second

strategy is to use a biphasic system liquid/liquid system. Examples of this approach include the use of ionic liquid[124] phase-immobilized catalysts and biphasic fluorous soluble supports.[125] A third strategy has been to use soluble but phase-separable polymeric supports. This has involved polymers with pendant salen ligands or polymers that contain salen ligands that are repeating units in the polymer structure. The most successful examples of this strategy use salen complexes that are repeating units of the polymer backbone structure.[113] In the cases where achiral or chiral salen metal complexes are supported on soluble polymers, the salen ligands and catalysts are typically separated from products after a reaction as solids using solvent precipitation.

An early report on the use of polymer-supported salen-metal complexes came from Jacobsen's laboratory and described the use of solid crosslinked polystyrene (PS) resins and solid silca supports for salen-Co complexes for the HKR of terminal epoxides. The PS-bound catalyst provided products in yields up to 52 % and selectivities as high as 99 %. The solid catalyst could be reused up to 5 times with no observable loss in yield or enantioselectivity.[126]

Weck and Holbach extended the chemistry described earlier (eqs. 12 and 13) to include the well defined polynorbornene-bound salen complexes shown below (eq. 65).[121,122] The use of a controlled polymerization technique, such as ROMP, allowed the authors to control the extent of site isolation of each catalytic species. Also, they showed that the preformed complexes were compatible with Grubbs' 3rd generation catalyst, thereby allowing them to prepare the polymer-supported catalysts without the need for post-polymerization steps to functionalize the polymer. Typically, the degrees of

polymerization (DP) of these species were 50 to 100. To study the ability of these complexes in the HKR, **67**-**70** were oxidized with acetic acid and air, the Co(III) complexes obtained were allowed to react with (±)-epichlorohydrin in CH_2Cl_2 or under neat (solvent-free) conditions. They reported that the typical results obtained with complexes such as **68** and **70** gave yields of the diol of 55 % and the e. e. of the resulting (*S*)-epoxide was 99 %. The authors reported that the site isolation of the Co complex was important as they noted that reaction with homopolymer **67** was slower than reaction with the copolymers, but that the enantioselectivity was similar. This may be due to decreased flexibility in the polymer backbone. However, when catalyst concentration on the polymer is lower, the activity is diminished (43 % conversion and 80 % e. e.); most likely due to impeding the bimetallic mechanism proposed by Jacobsen (Scheme 14). Such catalysts could be recovered by precipitation into diethyl ether. However, recycling was problematic as catalyst solubility decreased and the HKR reaction times increased from cycle to cycle.

(65)

67: x = 0, y = 50
68: x = 25, y = 25
69: x = 75, y = 25
70: x = 90, y = 10
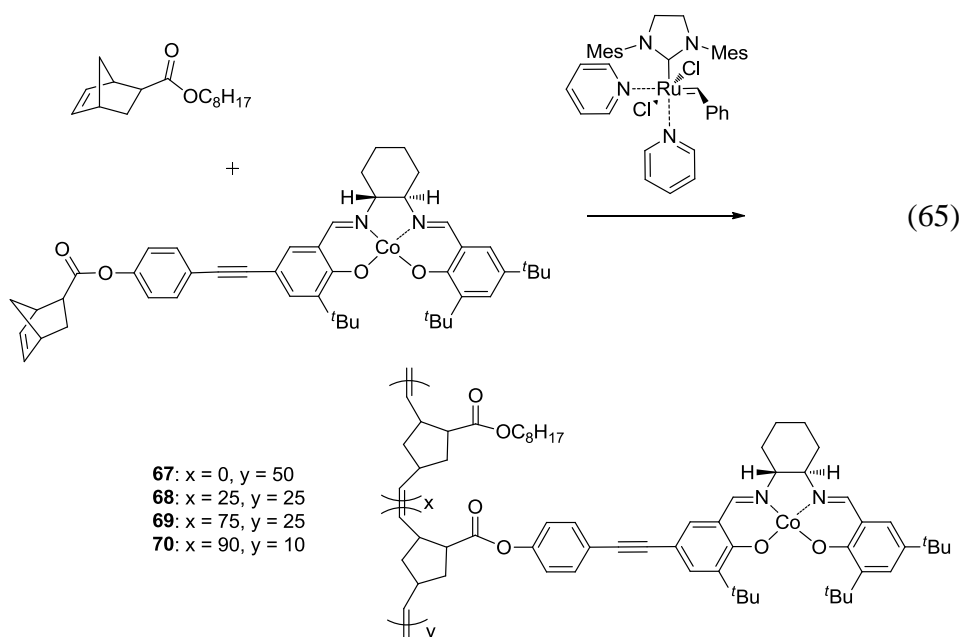
Weck's group later described the use of a polynorbornene-supported salen-Al(III) complex **71**. This complex was shown to catalyze the asymmetric conjugate addition of CN to α,ß-unsaturated imides (eq. 66) to give products in good yields (*ca.* 90 %) and high enantioselectivity (*ca.* 90 % e. e.). The polymer-bound catalyst could be recovered using solvent precipitation and recycled 5 times with no loss in product yield or enantioselectivity.[127]

(66)
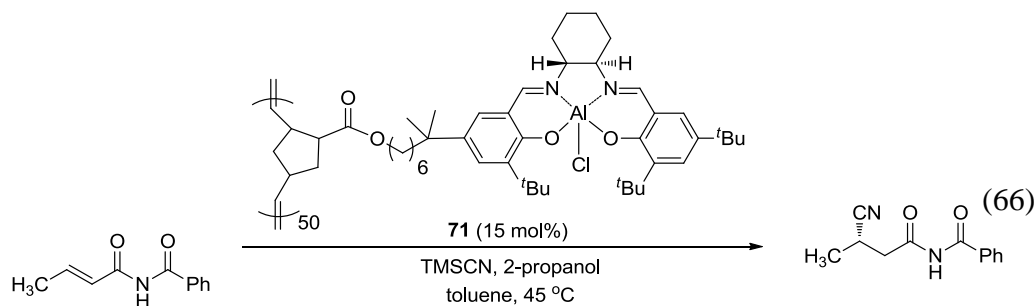
This catalytic system proved to be efficient, however the authors noted that, while 5 mol% catalyst loading would suffice, the need for larger amounts of catalyst

were required for efficient recycling. This could potentially be problematic on large scale syntheses. This process also required repeated solvent precipitations, rendering it environmentally detrimental.

In 1999, Jacobsen showed that Cr(III) complexes of other Schiff base-containing ligands were capable of catalyzing the Hetero-Diels-Alder reaction between various dienes and carbonyl compounds. Because of the structural resemblance of these ligands to that of salen, such compounds are named "half-salen" ligands.[128] The preparation of the Cr(III) complexes of these tridentate ligands is straightforward and similar to that of the salen ligands and involves imine formation between a salicylaldehyde derivative and (1*R*,2*S*)-1-amino-2-indanol followed by standard metallation procedures (eq. 62). Jacobsen reported that complex **72** could catalyze the HDA reaction shown below to give rise to exclusively *cis* tetrahydropyranones in good yields (88 %) and high enantioselectivy (99 % e. e.) (eq. 67). HDA reactions were run at room temperature and required the use of 4 Å MS for reaction to occur. The reason for this was so a coordination site could be opened for reaction to occur (according to X-Ray crystallographic data, the coordination site was blocked by a molecule of water). Literature reports of the preparation and use of polymer-supported half-salen catalysts are scarce. The examples that have been described all involve the use of insoluble polymer supports.[129-132]

$$\text{(67)}$$
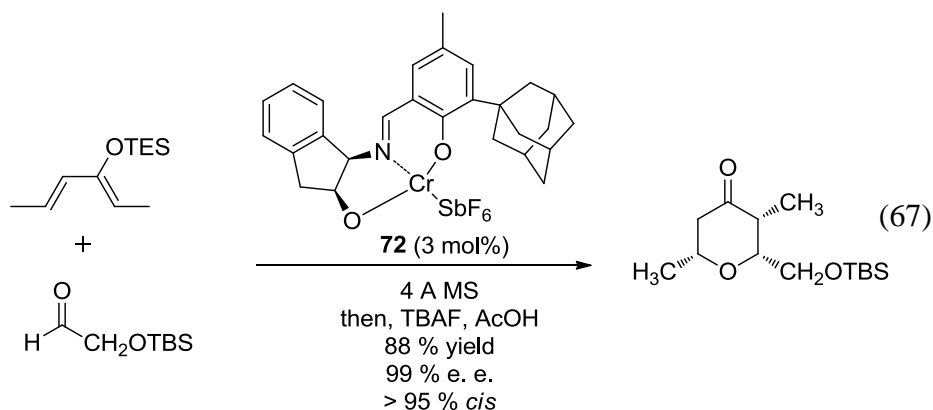
The use of solvent precipitation for the recovery of soluble polymer supports is an effective way to separate a polymer from other materials but it carries with it the disadvantages discussed earlier. This chapter describes the advantages and limitations of an alternative approach using polyolefin-bound salen ligands and salen metal complexes that phase separate from a single phase reaction either as a separable liquid phase or as solids. These soluble polymeric species enable the use of common organic solvents with either a thermomorphic or latent biphasic separation of a catalyst after a monophasic homogeneous reaction with minimal use of solvent. The results below show that this is an alternative and effective way to recover and reuse Cr-salen catalysts in epoxide ring-opening reactions. It is also a viable approach to immobilize catalysts for other salen metal complex mediated reactions. However, the use of these materials as effective asymmetric catalysts is frustrated by an inability to achieve sufficiently high catalyst concentrations.

Results and Discussion

Past work in our group has emphasized two general strategies for recycling catalysts that use soluble polymers as phase handles. The first of these strategies uses

polymer supports that afford a monophasic mixture of solvents, substrate, and catalyst during a reaction with a subsequent polymer-facilitated liquid/liquid catalyst/ligand separation after the reaction is complete. The two general schemes that we have found most effective are shown in parts a and b of Figure 1 and either involve a thermomorphic phase separation where a polymer-bound catalyst and products separate into different density liquid phases after a change in temperature, or use a latent biphasic mixed solvent system that is perturbed with small amounts of an additive to become a biphasic mixture. In either case, the catalyst and product are separable by a gravity-based separation so long as the catalyst is phase selectively soluble in a different phase than the product.

The other general strategy we have developed is based on the thermomorphic solubility of polymers like polyethylene. In this case (Figure 1 c), a terminally functionalized polyethylene oligomer or polymer is modified so that it can bind to a catalyst. Because polyethylene is completely insoluble in organic solvents at room temperature but soluble hot, such catalysts can be used in a heated solution as homogeneous catalysts but recovered on cooling by a solid/liquid separation. In this case, the product remains in solution while the catalyst self-separates as a solid.

To use the liquid/liquid separation strategies shown in Figure 1 in salen complex-catalyzed reactions requires an appropriate polymer-bound salen ligand. As described here, salen ligands **7** and **8** can be prepared by using a common intermediate **51** that was formed in a Friedel−Crafts alkylation, using the acid-catalyzed reaction of commercially available polyisobutylene oligomers containing terminal alkene groups with 2-*tert*-

butylphenol as shown in Scheme 15.[133,134] The product 4-polyisobutyl-2-*tert*-butylphenol **51** was converted to a salicylaldehyde derivative **73** by an acid-catalyzed alkylation and Cannizzaro reaction with use of paraformaldehyde. Subsequent imine formation then afforded both achiral **74** and chiral **75** salen ligands from suitable 1,2-diamines. These achiral and chiral ligands were then converted into metal complexes (**76** and **77**) by using the same chemistry used in the syntheses of structurally similar low molecular weight salen metal complexes.[117,134]

Scheme 15. Preparation of PIB-supported Cr(III)-salen complexes 7**6** and **77**.
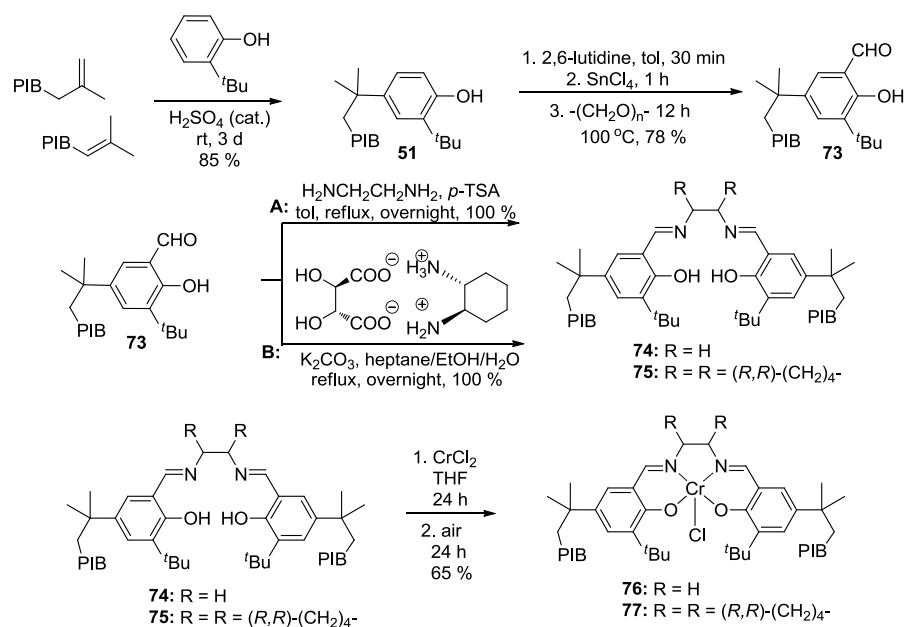
Given the availability of the PIB-bound salicylaldehyde **73**, we briefly examined its use in the synthesis of other salen-like metal complexes. For example, the intermediate 3-*tert*-butyl-5-polyisobutylsalicylaldehyde **73** formed in Scheme 15 was

used to prepare a "half-salen" ligand **75** as shown in eq. 68. This ligand, like the salen

ligands **74** and **75**, could be metalated by using procedures like those used with low

molecular weight analogues to form Cr complex **79**.[128]

(68)
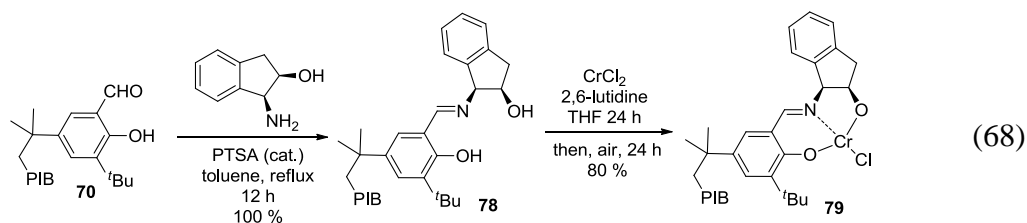
Electrophilic substitution of phenol by vinyl-terminated polyisobutylene has the

potential to be a general route to elaborated salen ligands too. This is shown by the

chemistry in Scheme 16 where 3-(piperindylmethyl)-5-polyisobutyl-salen ligands **82** and

83 were prepared from 4-polyisobutylphenol via multiple acid-catalyzed formylations by

using chemistry modeled after the chemistry reported by Kozlowski.[135]

Scheme 16. Preparation of 3-(piperindylmethyl)-5-polyisobutyl-salen ligands **82** and **83**.
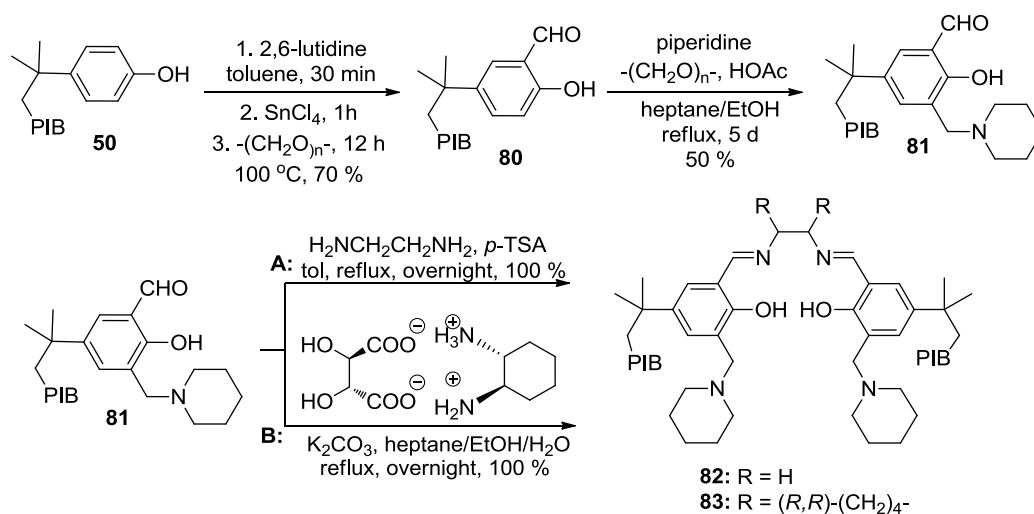
The second strategy for separation of polyolefin-bound catalysts and products is based on the thermomorphic properties of polymers like polyethylene that are soluble hot and insoluble cold. In this case, we prepared salen ligands and salen metal complexes using terminally functionalized thermomorphic polyethylene oligomers as supports. These studies stem from our prior successes with polyethylene oligomer (PE_{Olig})-bound catalysts and were prompted by the success of a DuPont group that used commercially available terminally functionalized PE oligomers in the synthesis of PE_{Olig}-bound porphyrin and phthalocyanine metal complexes. These complexes could be used as thermomorphic catalysts for free radical polymerizations or copolymerizations of styrenes and methacrylates. An example of such PE_{Olig}-bound porphyrin complexes is the Co(II) complex **84** which could be prepared by an S_N2 reaction of PE_{Olig}-OMs and a tetra-phenol porphyrin derivative, followed by metallation with $Co(OAc)_2 \cdot 4H_2O$ (eq. 69).[48]

$$(69)$$
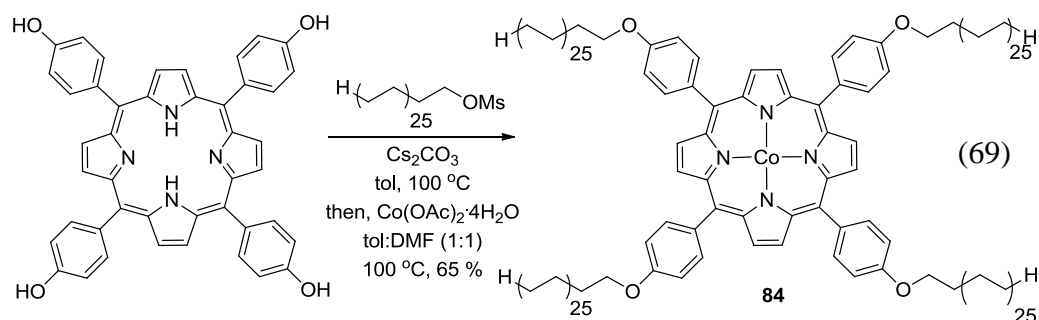
Inspired by these results, we set out to prepare thermomorphic, PE_{Olig}-supported salen ligands. To prepare PE_{Olig}-bound salen ligands we used a regioselective Mitsunobu reaction of the less hindered hydroxyl group of 3-*tert*-butyl-5-hydroxysalicylaldehyde with the terminal hydroxyl group of a commercially available

hydroxyl-terminated polyethylene oligomer[136] to prepare the salen ligand precursor **85**. The reason for this is, even though quite successful for the preparation of complexes like **84**, typical S_N2 procedures using 3-*tert*-butyl-5-hydroxysalicylaldehyde, Cs_2CO_3 and PE_{Olig}-OMs resulted in low conversions (> 20 %) of the desired PE_{Olig}-salicyladehyde. In these cases, the conditions for diimine formation that we used to form **74** from the PIB-substituted salicylaldehyde **73** led to formation of the diimine contaminated with 5−10% of the monoimine resulting from incomplete imine formation from the diamine. Quantitative formation of the bisimine from a diamine was possible by using 10 mol % excess of the PE_{Olig}-bound salicylaldehyde. However, in this case, we could not easily separate the unreacted salicylaldehyde **85** from the bisimine. Any mixtures of mono- and diimines occasionally seen in syntheses of a PIB-bound species could be separated by chromatography because of the high solubility of the PIB support. Chromatographic separation is not possible with polyethylene oligomeric ligands as the insolubility of the PE oligomers at room temperature makes chromatographic separation of these two products impractical. To obtain PE_{Olig}-bound product free of the salicylaldehyde or monoimine impurity we chose to use a slight excess of the diamine and to convert the 9:1 mixture of di- and monoimines that formed into a phase separable PE_{Olig}-bound salen ligand by reaction of the mixture of di- and monoimines with excess 3,5-di-*tert*-butylsalicylaldehyde. This in effect produces a more polydisperse but equally thermomorphic PE_{Olig}-bound salen ligand **86** as a mixture. Metallation of this product mixture in the DMF-toluene mixture used in metallation of PE_{Olig}-bound porphyrins and

phthlalocyanines[48] then afforded a PE_{Olig}-bound salen-Cr complex **87** (Scheme 17), which was isolated as a dark brown solid.

Scheme 17. Preparation of PE-bound salen-Cr(III) complex **87**.
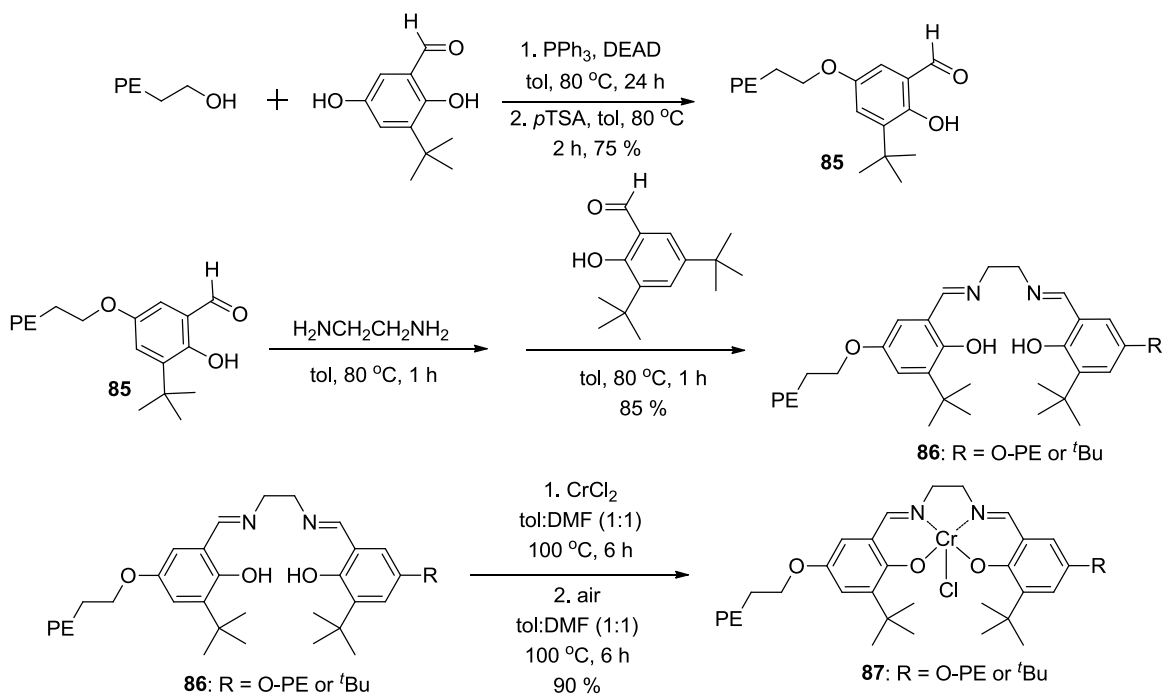
The properties of polyolefins like polyisobutylene and polyethylene both have advantages and impose some limitations in these syntheses. First, PIB's solubility makes it feasible to separate PIB-containing intermediates from more polar low molecular weight starting materials or byproducts by a simple solvent extraction. This makes it possible to use excess reagents in ligand syntheses and to separate unreacted reagents from the PIB products by an extraction without a chromatographic separation. Likewise, PE_{Olig}-bound species separate from excess reagents as a solid. Second, both the PIB- and

PE$_{Olig}$-bound intermediates can be readily analyzed by solution-state NMR spectroscopy.[6,8,14,15,48] However, there are also limitations associated with the use of polyolefin supports. For example, neither the PIB nor the PE supports can be used in a polar solvent like ethanol to form the salen ligands from a 1,2-diamine and the salicylaldehyde precursor because of their insolubility in ethanol. Instead, mixed solvent systems (e.g., heptane−ethanol) must be used. Finally, as was true in the synthesis of salen ligands from PE oligomers, it can be difficult to separate polymer-bound byproduct from the desired polymer product. This is not a problem for derivatives of the very soluble PIB supports, which can often be separated from one another by column chromatography and methods to address this problem for thermomorphic PE oligomer supports can be devised as described above. Nonetheless, byproduct separation remains a possible limitation for syntheses of other polyolefin-bound ligands.

As noted above, polyolefin supports like PIB and PE have precedent in separation, recovery, and reuse of a variety of catalysts.[6,7] Past work has shown that PIB is effective at making the Ru alkylidene complexes phase selectively soluble in the heptane phase of biphasic mixtures of heptane and polar organic solvents to facilitate recovery, separation, and reuse of ring-closing metathesis catalysts.[12,13] PIB was equally effective in effecting phase separation of salen complexes like **76** or **77**. This is visually apparent by comparison of the photographs in Figure 3. In this example, a highly colored single phase mixture of absolute ethanol and heptane containing **76** (Figure 3 a) is perturbed into a biphasic solvent mixture (Figure 3 b) by the addition of 10 vol % water. Similar efficiency in phase separation of these PIB salen complexes was also achieved

by using **76** in a thermomorphic mixture of heptane and *N,N′*-dimethylformamide (DMF). When a mixture of heptane and DMF was used, the PIB-bound salen complex **76** was soluble in a hot miscible mixture of these solvents at 80 °C. This solution was monophasic and deeply colored like that in Figure 3 a. However, in the case of this DMF/heptane mixture, cooling this deeply colored monophasic solution produced a biphasic liquid/liquid mixture with the salen complex **76** separating into the less dense heptane-rich phase. The extent of phase separation was evaluated by UV−visible spectroscopy. On the basis of the absorbance of **76** at 350 nm, <0.1% of the salen complex remained in the polar DMF-rich phase after this thermomorphic liquid/liquid separation.

PE is also effective at thermomorphic phase separation of the salen complex **87**. In this case, the PE_{Olig}-salen complex of Cr forms a dark brown solution on heating to 70 °C (Figure 3 c). Cooling this solution produces a water white supernatant and a dark brown PE solid (Figure 3 d), chemistry that is analogous to that reported by a DuPont group that used similar ligands to thermomorphically separate highly colored PE_{Olig}-bound Co complexes of porphyrins and phthalocyanines from solution on cooling (Scheme 4).
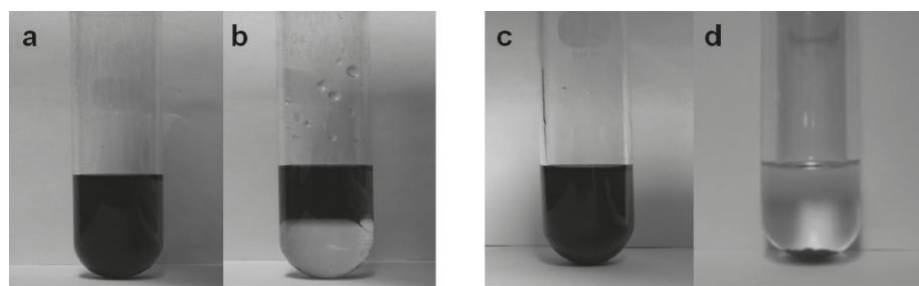
Figure 3. Photograph showing the separation of **76** in a mixture of heptane and ethanol (a) before and (b) after the addition of *ca.* 10 % water and **87** in toluene at (c) 75 °C and (d) after cooling to room temperature and centrifugation.

The penultimate test of the utility of these salen ligands is the ability of their metal complexes to effect reactions that their low molecular weight analogues promote. In preliminary experiments reported previously, we noted that the achiral catalyst **76** is as competent as its low molecular weight analogue in the polymerization of cyclohexene oxide and CO_2.[133,134] These studies showed that **76** is kinetically very similar to a low molecular weight Cr salen catalyst that had a *tert*-butyl group in the 5 position (versus the 5-polyisobutyl group in **76**) in CO_2−epoxide polymerization. The fact that this PIB-bound salen species was also readily separated from the catalyst and that the polycarbonate product was isolated with low Cr-contamination (so long as an acid workup that decomposes the Cr-salen complex was avoided) suggested that polyolefin-bound salen complexes **76**, **77**, **79**, and **87** should be similarly useful as recyclable separable catalysts in a variety of ring-opening reactions of low molecular weight epoxides or in other salen complex-mediated catalysis. This is indeed the case though catalyst concentration imposes some limitations on this chemistry as noted below.

Our initial studies focused on the utility of the achiral complex **76** as a recyclable catalyst for the ring-opening of epoxides with various thiolphenols.[133] These studies employed a heptane/ethanol solvent mixture and latent biphasic conditions for recovery and recycling of **76** in a liquid/liquid separation/recovery system. In this chemistry, we used a miscible mixture of heptane and ethanol which dissolved both catalyst **76** and the epoxide and thiophenol reactants. Ring-opening reactions of epoxides were carried out with three different epoxides and two different aromatic thiols. It was found that PIB-bound catalyst **76** was as effective as an electronically analogous low molecular weight catalyst in this chemistry and that catalyst recycling and separation from product was feasible. In these recycling experiments, phase separation and catalyst recovery was achieved by the addition of 10 vol % water to the homogeneous reaction mixture after the reaction was complete. This added water produced a biphasic heptane/aqueous ethanol mixture. Gravity filtration of the less dense catalyst-containing nonpolar phase afforded a recyclable solution of the catalyst. The products of the reactions were isolated by removal of the solvent and characterized by ^{1}H and ^{13}C NMR spectroscopy and were >95% pure without the need for any chromatographic separation of catalyst residues.[63,133]

Reuse of the catalyst **76** was affected by simply adding fresh ethanol and substrates to the recovered heptane-rich phase. The PIB-supported catalyst could be recycled through at least 4 cycles with no observed loss in catalytic activity. The extent of catalyst leaching was also tested using inductively coupled plasma mass spectroscopy (ICP-MS) analysis of the product phase. This analysis showed that products from the

reaction between glycidol and 4-methylthiophenol showed only 0.26% chromium loss per cycle.

After the discovery that **76** could be used as a recyclable catalyst for the ring-opening of epoxides with thiols, we examined the use of complex **77** (Scheme 15) as a catalyst for the asymmetric ring-opening (ARO) of epoxides.[117] We first tested the use of **77** as a catalyst for reaction of cyclohexene oxide and azidotrimethylsilane (eq. 70). As expected based on the success of **76** in epoxide-thiol reactions (*vide supra*), complex **77** was able to catalyze the opening of cyclohexene oxide with azidotrimethylsilane to afford the azido alcohol product (eq. 69). The PIB-supported catalyst **77** was successfully recycled six times using the same latent biphasic conditions to recover the **76** (*vide supra*).

Table 1. ARO of cyclohexene oxide with azidotrimethylsilane catalyzed by **77**.

$$\text{(cyclohexene oxide)} + (CH_3)_3SiN_3 \xrightarrow[\substack{\text{heptane:EtOH} \\ \text{rt, 12 h}}]{\textbf{77} \text{ (5 mol\%)}} \text{(azido alcohol)} \qquad (70)$$
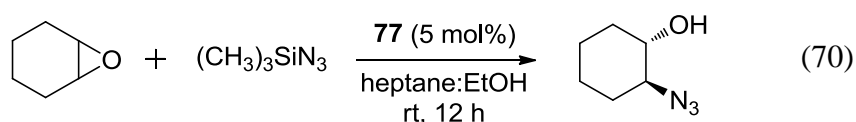
entry	cycle	yield (%)	e. e. (%)
1	1	42	10
2	2	54	13
3	3	70	22
4	4	79	14
5	5	90	12
6	6	95	15

However, while **77** proved to be a recyclable catalyst, it was unfortunately not a very stereoselective catalyst, based on chiral HPLC analysis of a chromophore-labeled

derivative of the product from eq. 69.[137] In these cases, analyses of the reaction's enantioselectivity based on chiral HPLC analysis of products showed very low enantioselectivity as noted in Table 1.

The low enantioselectivity for the reaction in eq. 69 can be explained by the low concentration of catalyst **77** in the reaction system. Jacobsen and co-workers have reported the best enantioselectivities for these Cr-salen catalyzed reactions are obtained under solvent-free conditions using neat substrate where catalyst concentrations are *ca.* 0.20 M.[117,118,137] In the case of the PIB-bound catalyst **77**, the insolubility of **77** in substrate required that a solvent be used. Thus, concentrations of **77** in these heptane−ethanol solutions were almost a factor of 10 lower (0.03 M). Control experiments suggest that the lower enantioselectivity seen with **77** is mainly due to this lowered catalyst concentration as opposed to the presence of the PIB oligomer. Two control experiments with Jacobsen's catalyst **64** were performed. First, when the low molecular weight catalyst **64** was used in place of **77** at 0.032 M, the enantioselectivity of the reaction was 19%. The 19% e. e. seen with a 0.032 M concentration of **64** as a catalyst is very close to the average 14% e. e. reported in Table 1. A second experiment examined the reaction of cyclohexene oxide with azidotrimethylsilane catalyzed by 5 mol % of **64** in methylene chloride. When **64** was present at 0.035 M, ring-opened product was obtained with 33% e. e. While these results suggest a slight solvent effect, these control experiments suggest that the diminished enantioselectivity seen with **77** is in large part due to the lower catalyst concentration. Catalyst concentration affects

selectivity because of the importance of the bimolecular reaction mechanism proposed by Jacobsen.[118]

Given the success of the polyolefin-bound salen complexes in epoxide ring-opening reactions, we also briefly studied the use of a PIB-bound "half-salen"[128] Cr complex (**79**) as a catalyst for other reactions. Low molecular weight analogues of **79** have previously been used as catalysts for a number of transformations (*vide supra*). We set out to investigate the activity of **79** by attempting to catalyze the reaction of crotonaldehyde and ethyl vinyl ether (eq. 71).

$$(71)$$
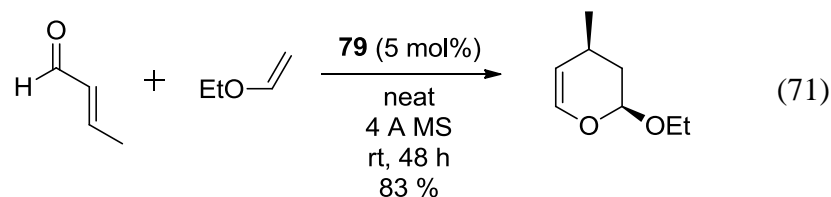
In this study, the PIB-bound catalyst **79** was dissolved in ethyl vinyl ether and crotonaldehyde was added to the solution and the reaction mixture was allowed to stir for 2 days. Separation was effected by the removal of solvent and the addition of heptane and acetonitrile to the reaction flask. This produced a biphasic mixture with the polymer-bound catalyst in the heptane-rich phase and the product in the polar acetonitrile-rich phase. Even though preliminary trials of this catalytic system seemed promising (83% yield and > 20:1 d. r.), recycling of the polymer-bound catalyst was not feasible. Diminished yields of the product (*ca.* 25%) were seen in cycle 2. In this case, ^{1}H NMR analysis showed that the reason for these diminished yields was decomposition of the catalyst due to the 4 Å MS present in the reaction mixture. Because of this, further

investigations of this system were not continued and the enantioselectivity was not evaluated.

We also explored the use of the thermomorphic polyethylene-supported Cr-salen complex **87** as a recyclable catalyst for the ring-opening of cyclohexene oxide with azidotrimethylsilane (eq. 72). This chemistry involved the use of thermomorphic solubility of polyethylene and a solid/liquid separation (Figure 1 c) to separate the PE$_{Olig}$-bound catalyst **83** from product. In the event, we first dissolved 5 mol % of **87** in 3 mL of toluene at   75 °C under N$_2$. After a homogeneous solution was obtained, cyclohexene oxide and azidotrimethylsilane were sequentially added to the reaction flask with a syringe. The reaction mixture was then stirred 3 h under N$_2$ at 75 °C. Workup and catalyst separation and recovery was then accomplished by simply cooling the reaction mixture to room temperature. Phase separation of solvent containing the product and polymer-bound catalyst was visually apparent. At this point an additional 5 mL of toluene was added and the supernatant solution containing the product was separated from the PE$_{Olig}$-bound **87**. To ensure quantitative recovery of the product, this isolation procedure was repeated twice. Recycling of the solid catalyst was achieved by then dissolving the recovered solid **87** in 3 mL of fresh toluene at 75 °C and treating this solution with fresh substrate.

$$\text{(72)}$$
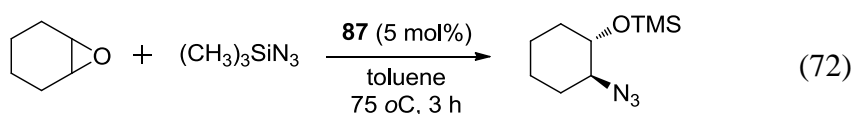
Table 2. Ring-opening reaction of cyclohexene oxide with azidotrimethylsilane catalyzed by **83**.

entry	cycle	yield (%)
1	1	88
2	2	90
3	3	100
4	4	100
5	5	100
6	6	100

As can be seen in Table 2, complex **87** was very successful as a recyclable separable catalyst in this ring-opening reaction. The efficiency of catalyst **87** is shown by the recycling data in Table 2. PE_{Olig}-supported catalyst **87** could be recycled six times with no loss in catalytic activity; as determined from the isolated mass yields of each cycle. The effectiveness of this process in minimizing catalyst leaching was also tested by using inductively coupled plasma mass spectroscopy (ICP-MS) analysis of the pure product. After removal of the solvent and digestion in HNO_3 the analysis showed that for the reaction in Table 2, metal leaching was found to be *ca.* 0.3 %.

It is well known that both the imine functionality and salen-metal complexes can undergo decomposition in acidic media,[110,134] either by hydrolysis or cleavage of the metal from the organic ligand framework resulting from acidolysis, respectively. This problem can be substantial in the manufacturing of commodity chemicals, such as polymers, in which the leaching of metal into the products is undesirable because of their toxicity and highly colored nature.

An example is shown below, a salen-Cr(III) complex can be used to catalyze the formation of a polycarbonate from cyclohexene oxide and CO_2 with PPNCl (bis(triphenylphosphoranylidene)ammonium chloride) as a cocatalyst.[110] The copolymer, so-formed, is typically highly colored. The reason for this is that the acidolysis step that is required to cleave the product polymer from the metal center inadvertently strips much of the metal away from the ligand, resulting in a polymer that has high levels of metal contamination. Several precipitations are needed to rid the product of the colored metal species; however this generates large amounts of solvent waste.
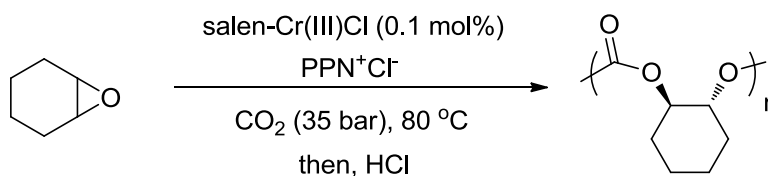
Previous work in our lab has shown that PIB-salen-Cr(III) complex **73** can be used as a phase handle for the sequestration of the highly colored metal contaminates from the polymer product; which can be isolated (by precipitation into heptane) as white powder. Although the metal loss was much lower than that previously observed using low molecular weight catalysts, the loss of chromium (resulting from the acidolysis step) was still substantial as catalyst recycling was found to be inefficient.[134] Because PE_{Olig}-supported species, such as **87**, exist as highly colored solids at room temperature (as can be seen from Figure 3c,d), we hypothesized that this property could be taken advantage of. Knowing that these complexes are highly susceptible to acidic decomposition in

solution, it was proposed that materials such as **87**, in the solid state, would be less likely to undergo acidolysis. The reasoning was that the PE_{Olig} matrix could potentially serve as protection of the ligand-metal framework from the acidic media. Advantageously, the chromophoric property of the metal contaminants could potentially serve as a colorimetric test for the stability of these materials to acidolysis. As shown in Figure 4, preliminary experiments were performed by submerging the PE_{Olig} material (**87**) in a non-swelling solvent (i.e. methanol) followed by the addition of trifluoroacetic acid (TFA). The mixture was allowed to sit overnight. At this point, the acidic methanol was
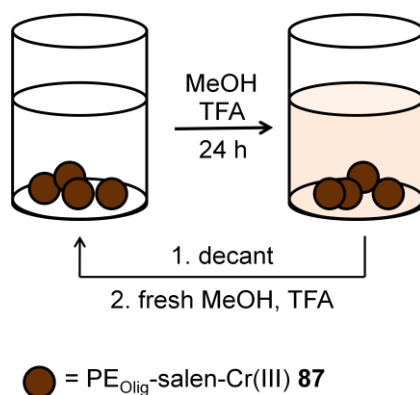
Figure 4. Schematic representation of stability studies of complex **87** toward acidolysis in methanol.

removed, followed by the addition of fresh methanol and TFA to the vial containing **87**, this process was repeated 4 more times. After each cycle, the methanol phase that was isolated typically had no color associated with it, which supports the initial hypothesis. This process could be extended to other PE_{Olig}-salen-metal complexes, as well. As

mentioned earlier, Mn(III) complexes are some of the most well known transition metal complexes of salen ligands.[114,115] These complexes were first prepared in the early 1990's and are among the best catalysts for epoxidation reactions of unfunctionalized olefins. Because of this, having some knowledge of the stability of polymer-supported salen-Mn(III) complexes is vital. We were able to prepare the PE$_{Olig}$-supported salen-Mn(III) Cl complex **88**, as shown in.
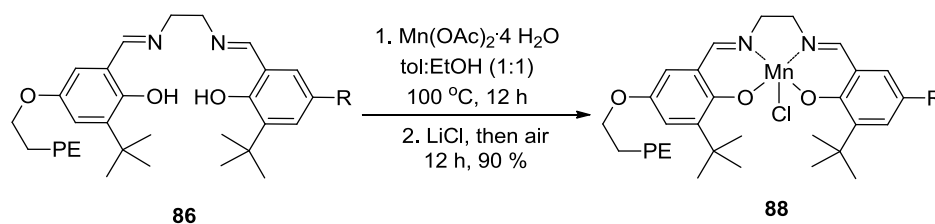
Starting from PE$_{Olig}$-salen **86**, Mn(III) complex **88** could be prepared in one step from reaction with Mn(OAc)$_2$·4H$_2$O in a mixture of toluene and ethanol followed by reaction with LiCl and oxidation with air. The process provided **88** in good yield (90 %) as a dark brown powder. Acidolysis stability studies were carried out using the same procedure that was used for complex **88** (*vide supra*) and provided methanol phases that were colorless, even upon oxidation to the permanganate species (a common qualitative test for manganese). Also, ICP-MS analysis of the methanol phase (after removal of the solvent and digestion in HNO$_3$) showed little loss (*ca.* 2.9 % for cycle 1to 0.15 % for cycle 5) of Mn from solid **88**.

Conclusions

We have shown that recovery and recycling of salen ligands and their metal complexes can be facilitated with the use of soluble polyolefin oligomers as phase anchors for such ligands/catalysts. Using PIB-bound salen-Cr complexes, we have shown that ring-opening of various epoxides with thiols and an azide source can be facilitated and the catalyst can be recycled with minimal metal leaching. However, applications of this chemistry to asymmetric catalysis are limited by the low enantioselectivity achieved because of the polyolefin catalyst's concentration. Other PIB-bound salen ligands as well as a "half-salen" catalyst were also prepared. The latter "half-salen" catalyst effectively catalyzed a hetero-Diels−Alder reaction but could not be recycled because of the instability of the ligand to the reaction conditions. The preparation of a PE$_{Olig}$-bound salen ligand was also achieved by using a regioselective Mitsunobu reaction and the products were converted into a PE$_{Olig}$-bound salen-Cr(III) complex. This complex was used as a soluble thermomorphic catalyst in the ring-opening of cyclohexene oxide with azidotrimethylsilane at 75 °C and was recycled six times with no loss in catalytic activity. Preliminary data also suggest that PE$_{Olig}$-supported salen metal complexes show stability to acidolysis in the solid state. This is evident from experiments in which the solid material is exposed to an acidic environment (in a non-swelling solvent) for extended periods of time. After, the solvent (which is colorless) was isolated and analyzed by ICP-MS. In the case of Mn complex **88**, metal loss due to acidolysis was quite low (*ca*. 0.15 %).

CHAPTER IV

PE_{Olig}-SUPPORTED *N*-HETEROCYCLIC CARBENE LIGANDS/METAL COMPLEXES FOR RING-CLOSING METATHESIS (RCM) REACTIONS[*]

Introduction

Olefin metathesis has a rich, fascinating history.[138,139] Early on, it came to play an important role in the chemical industry in both the Phillips Triolefin Process and the Shell Higher Olefin Process (SHOP).[138,139,140,141,142] It is defined as a carbon-carbon rearrangement reaction of alkenes and was first described by Anderson and Merckling in 1955 when they discovered the first carbon-carbon rearrangement in the Ti-catalyzed norbornene polymerization.[143] A few years later, it was investigated by Truett and coworkers.[144] They observed that, using a titanium-based catalyst, norbonene could undergo a ring-opening reaction that resulted in polymer-formation. Although not often credited for the description of the mechanism of olefin metathesis, the authors described a mechanism that closely resembled what would later become the generally accepted mechanism.[145] Truett *et al.* described a process that involved: activation of the norbornene "by coördination (*sic*) with the reduced titanium center through the π-electrons of the double bond…subsequent rearrangement step is thought of as a

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[*] Reprinted with permission from "Thermomorphic Polyethylene-Supported Olefin Metathesis Catalysts" by Hobbs, C.; Yang, Y.-C.; Ling, J.; Nicola, S.; Su, H.-L.; Bazzi, H. S.; Bergbreiter, D. E. *Org. Lett.* **2011**, *As Soon as Publishable*. Copyright 2011 by the American Chemical Society.

concerted process involving a minimum of charge separation. Thus, as the bond between carbon atoms 1 and 2 breaks with these electrons rejoining the double bond, the original carbon-to-titanium bond breaks and a new carbon-carbon bond is formed at the 1-position of the norbornene and a new carbon-to-titanium bond is formed…This process regenerates the active titanium center for further coördination (*sic*) and activation of norbornene units." (Scheme 18).

Scheme 18. Mechanism proposed by Truett and coworkers.
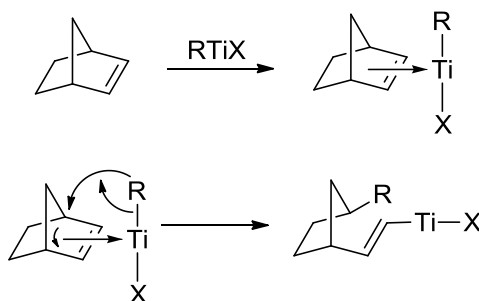
Seven years later, Calderon and coworkers described that when an internal olefin (such as 2-pentene) was exposed to a catalyst composed of WCl_6, ethylaluminum and ethanol, an interchange mechanism resulted and a formation of a mixture of 2-butene, 2-pentene and 3-hexene was observed.[146,147] The authors called this process "olefin metathesis". The name is derived from the Greek "μετάθεσις" which means "change of position".

As mentioned above, there is now a generally accepted mechanism of this process that was originally proposed by Chauvin and Hérisson in 1970.[145] They proposed that olefin metathesis proceeds through the intermediate metallacyclobutanes

which are generated by the coordination of olefins to a metal alkylidene species. This process can be achieved through a series of alternating [2 + 2] cycloaddition and cycloreversion reactions, as shown in Scheme 19.

Scheme 19. Mechanism proposed by Chauvin and Hérisson.
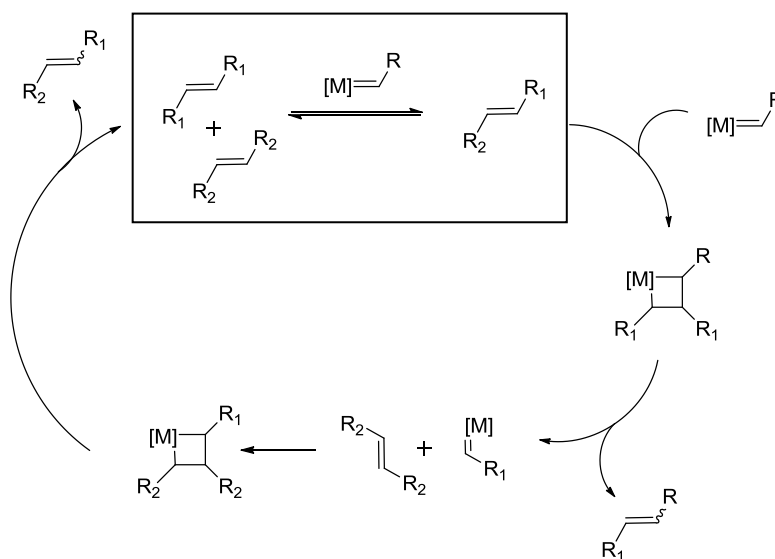
These early types of catalysts typically consisted of multicomponent systems formed from transition metal halides and metal alkyl species as cocatalysts. The most widely known examples include catalysts based off of tungsten salts such as $WCl_6/EtAlCl_2$ and WCl_6/Bu_4Sn. However, species such MoO_3/SiO_2 were also used.[138,1139] Later examples include the first single-component catalysts based off of titanium[148], tantalum[149] and tungsten[150] and then well defined molybdenum catalysts.[151] Such early examples suffered from sensitivity to both moisture and oxygen and also had relatively low functional group tolerance. As shown in Table 3, complexes based off of

titanium and tungsten are very reactive toward protic species (such as acids and alcohols), water and carbonyl compounds. Molybdenum is less reactive toward these species, however, it can be seen that ruthenium complexes are vastly superior with regards to functional group compatibility as they react preferentially with olefins.

Table 3. The reactivity of transition metals typically used for olefin metathesis toward common functional groups.

Ti	W	Mo	Ru	
Acids	Acids	Acids	**Olefins**	
Alcohols, Water	Alcohols, Water	Alcohols, Water	Acids	Reactivity
Aldehydes	Aldehydes	Aldehydes	Alcohols, Water	
Ketones	Ketones	**Olefins**	Aldehydes	
Esters, Amides	**Olefins**	Ketones	Ketones	
Olefins	Esters, Amides	Esters, Amides	Esters, Amides	

The earliest examples that used Ru-based catalysts were reported nearly half a century ago. This early work utilized transition metal salts (such as $RuCl_3(H2O)_n$ and $IrCl_6(NH_4)_2$) as catalysts for the ROMP of norbornene.[152] For whatever reason, it wasn't until 1988 that the use of Ru was again reported by Grubbs' laboratory.[153,154] The same group also found that the active species was actually a Ru-alkylidene, prompting Grubbs' laboratory to prepare complex **89** (eq. 73).[155]

$$\text{Cl} \cdots \underset{\underset{PPh_3}{|}}{\overset{\overset{PPh_3}{|}}{Ru}} \cdots PPh_3 \quad + \quad \underset{\triangle}{\overset{Ph \quad Ph}{\diagdown}} \quad \xrightarrow{CH_2Cl_2/C_6H_6} \quad \text{Cl} \cdots \underset{\underset{PPh_3}{|}}{\overset{\overset{PPh_3}{|}}{Ru}} = \diagup \overset{Ph}{\underset{Ph}{}} \quad (73)$$

89
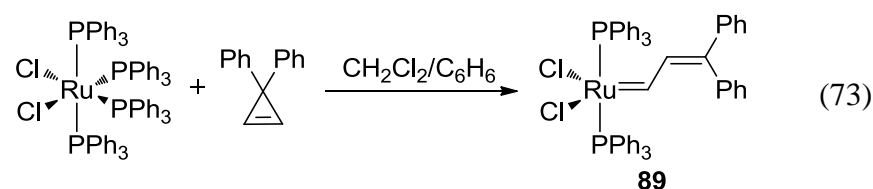
Grubbs and coworkers found that reaction of $RuCl_2(PPh_3)_4$ with a strained olefin, such as 3,3-diphenylcyclopropene, produces the Ru-Fischer carbene complex **89** (eq. 73). This complex was shown to be indefinitely stable under inert atmosphere and stable for several minutes under air. Furthermore, because of the high functional group tolerance of Ru-metathesis catalysts, complex **89** was stable in solution (CH_2Cl_2/C_6H_6) in the presence of alcohols, water, or HCl. **84**, unfortunately, showed low reactivity and was only effective in the polymerization of highly strained cyclic olefins, such as norbornene.[138,155]

A few years later this chemistry was improved with the preparation of complexes **90-96** (eq. 74).[156] Such complexes could be prepared in high yields (75 – 80 %) in one pot starting from $RuCl_2(PPh_3)_4$ followed by addition of 2.2 equiv. of a trialkylphosphine. These complexes, especially **90** (now known as Grubbs 1st generation catalyst), were shown to be much more active as ROMP initiators and were even more tolerant to other functional groups compared to those catalysts bearing two PPh₃ ligands.

$$RuCl_2(PPh_3)_4 \xrightarrow[\text{CH}_2\text{Cl}_2]{\substack{\text{PhCHN}_2 \text{ (2 equiv.)} \\ \text{then, PCy}_3 \text{ (2.2 equiv.)}}}$$

PCy₃ | Cl
Ru
Cl | PCy₃

X

90 = H
91 = N(CH₃)₂
82 = OCH₃
93 = CH₃
94 = F
95 = Cl
96 = NO₂

(74)
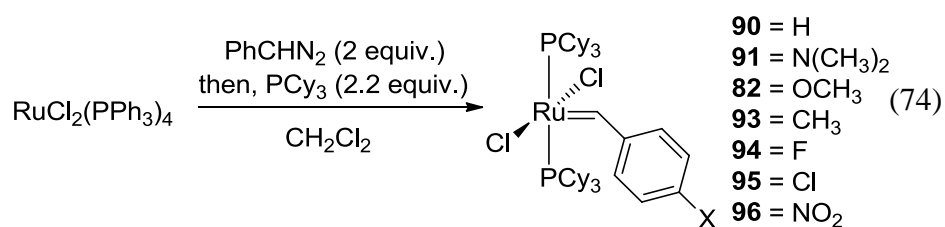
Even further improvement was made when the groups of Nolan[157] and Grubbs[158] simultaneously discovered that one of the tricyclohexylphosphine ligands could be replaced with an *N*-heterocyclic carbene (NHC) ligand (giving rise to what are now known as Grubbs 2nd generation catalysts). Because of the necessity for the stereoelectonic properties of bulky phosphines to impart stability to the active metal

catalyst, Nolan and coworkers hypothesized that a bulky nucleophilic NHC ligand could also be used. Such a ligand, if successful, may improve Ru-catalysts by stabilizing the metal center (because of the increased σ-donatation) and remedy the phosphine ligand degradation. Nolan found that complexes bearing 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes) as a ligand (such as **98**), were indeed superior to earlier phosphine ligands; they were shown to have higher catalyst performance due to the increased σ-donatation of the NHC ligand versus Phosphine ligand and because of the increased steric bulk of the NHC ligand the rate of catalyst decomposition was decreased. Grubbs *et al*. showed that the **98** was a very efficient catalyst for RCM reactions of various dienes; in some cases, showing higher catalyst activity than complex **90**. The preparation of complexes bearing NHC's is shown below (eq. 75) and proceeds by reaction of complex **90** and the persistent carbene **97**.

$$(75)$$
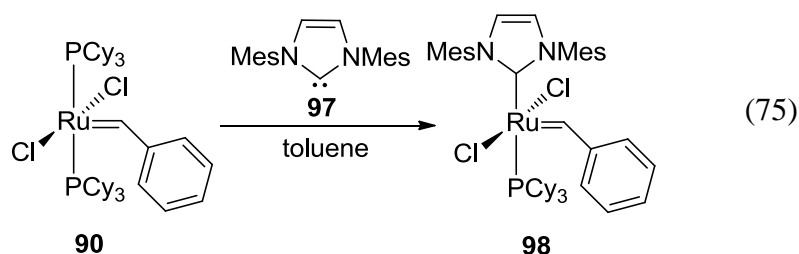
Later that same year, it was found by Grubbs' laboratory that changing the electronic nature of the NHC could lead to further improvement in catalytic activity. Grubbs and coworkers hypothesized that by using NHC ligands that lacked unsaturation in the backbone, stabilization of the carbene from the π-system would be diminished; producing a more basic (σ-donating) ligand.[159] Such a system would potentially lead to

higher catalytic activity. The preparation of complexes based off of 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidenes (SIMes) is shown in Scheme 20.

Scheme 20. Preparation of complex SIMes-Ru complex **99**.
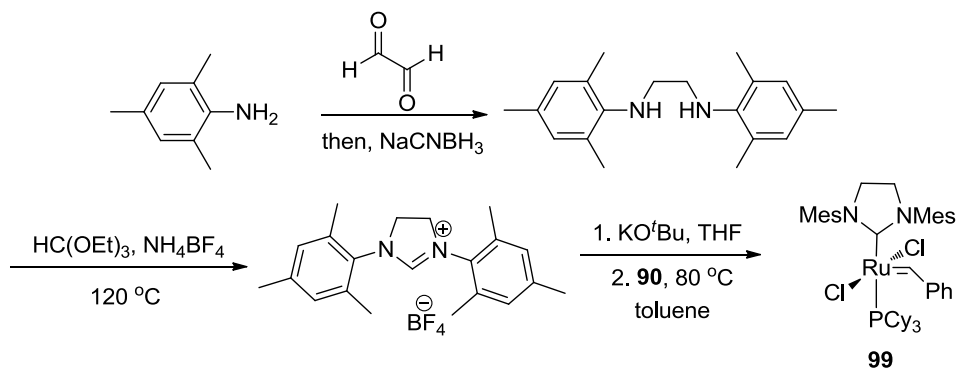
The synthesis of **99** was carried out by the condensation of mesitylamine with aqueous glyoxal followed by reduction of the imines using NaCNBH$_3$. Cyclization was then carried out with triethyl orthoformate and ammonium tetrafluoroborate to give the imidazolinium salt. Deprotonation followed by reaction of the carbene with complex **90** afforded complex **99**. It was shown that, in some cases that the RCM activity of **99** was higher than that of **90**. The reason is twofold; for dienes containing protic functional groups, **99** was superior because of its increased functional group tolerance and because of its increased reactivity **99** was able to perform RCM on substrates bearing disubstituted olefins (for the preparation of tri- and tetrasubstituted alkenes) and more sterically demanding R groups (i.e. *tert*-butyl).

Hoveyda and coworkers found that, in the course of their studies of chromene syntheses from styrenyl ethers that it was possible to produce recyclable Ru-based

metathesis catalysts through the use of chelating ligands.[160] The authors found, that

many metathesis reactions are not effective in the presence of styrenyl ethers, such as the

ROMP of cyclooctene, eq. 76. This result led them to the conclusion that complexes

such as **100** were being formed *in situ*.

$$\text{OPh} \quad \xrightarrow[\text{90 (5 mol\%)}]{} \quad < 2 \text{ \% desired product} \qquad \textbf{100} \qquad (76)$$
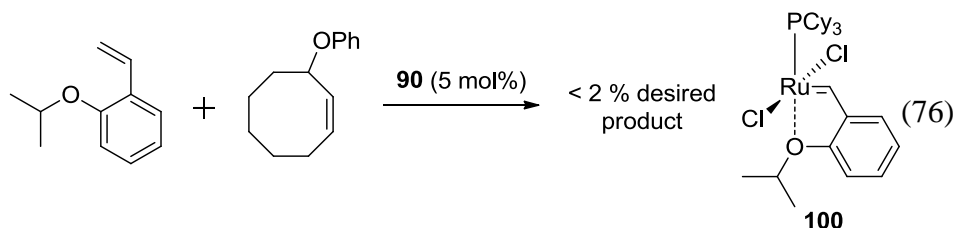
After this discovery, the authors described a synthesis to form complex **100**

directly. Reacting complex **90** with the styrenyl ether (eq. 77), they were able to isolate

100 in 65 % yield. They noted that the complex (now referred to as Hoveyda-Grubbs 1st

generation catalyst) is "exceptionally robust" as it can be purified using column

chromatography.

$$\xrightarrow[\text{24 h}]{\text{90, CH}_2\text{Cl}_2} \qquad \textbf{100} \qquad (77)$$
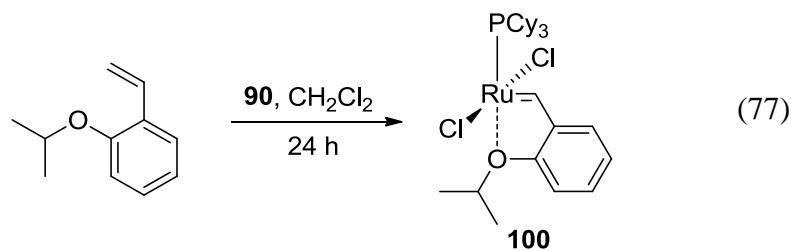
Because of the chelation from the oxygen atom, complex **100** was shown to be

very stable. A solution of **100** in chloroform under air showed only 2 % decomposition

after 2 weeks. This complex is also a very competent catalyst for the RCM of various

dienes and was also recyclable; the catalyst could be recovered from silica gel column

chromatography and reused a second time.

The next year, the same group reported on the preparation of complex **101**. This complex contained the same chelating ether ligand as **100**, but, instead of a tricyclohexyl phosphine, it contained an NHC ligand (eq. 78).[161] The synthesis of complex **101** was similar to that of complex **100**; it consisted of a reaction between complex **99** and the same styrenyl ether. With the use of CuCl (as a phosphine scavenger) the authors were able to obtain **101** in 85 % yield, as a deep green solid. It was found that complex **101** is just as active a RCM catalyst as is complex **99**, but **101** can be recovered and reused, because of the stability of the chelating ligand system.
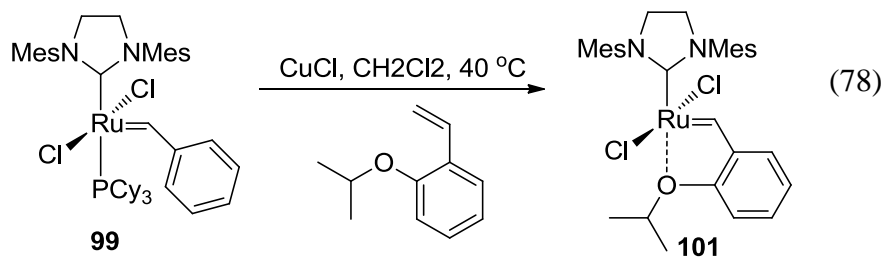
Because of these seminal studies, olefin metathesis has risen to be one of the largest and most exciting fields of organic chemistry. Due to the high reactivity, stability and functional group tolerance of **101**, this complex has become among the most widely used olefin metathesis catalyst; prompting the preparation of polymer-supported versions of **101** that can be recovered and recycled.

PE$_{Olig}$-bound NHC Ligands/metal Complexes for Ring-closing Metathesis (RCM) Reactions

As discussed early on, one of the most popular methods of catalyst recovery is to use a solid support. However, the use of soluble supports has several disadvantages (*vide supra*). Despite these disadvantages, there are numerous reports that detail the use of

various insoluble supports (i.e. crosslinked polystyrene or silica gel) to immobilize Ru-based metathesis catalysts.[138,162] The focus herein, however, will be to describe the use of soluble polymer supported Ru-metathesis catalysts.

An early example of the use of soluble polymeric supports was disclosed by Hoveyda and coworkers.[161-163] They were able to prepare a dendritic scaffold which supported 4 catalytically active Ru complexes. The preparation of this dendrimer (**102**) is shown in eq. 79. The authors reported that this tetravalent catalyst was a highly active catalyst for RCM, giving the products in high yields (up to 99 %). This dendritic catalyst could also be recovered and recycled through 6 cycles, with little los in catalyst activity. The authors did note that relatively high amounts of Ru leaching were observed (*ca.* 50 % in cycle 6). Furthermore, although the catalyst was recyclable, it relied on the use of column chromatography as a means of isolation of the catalyst, making this process not ideal.
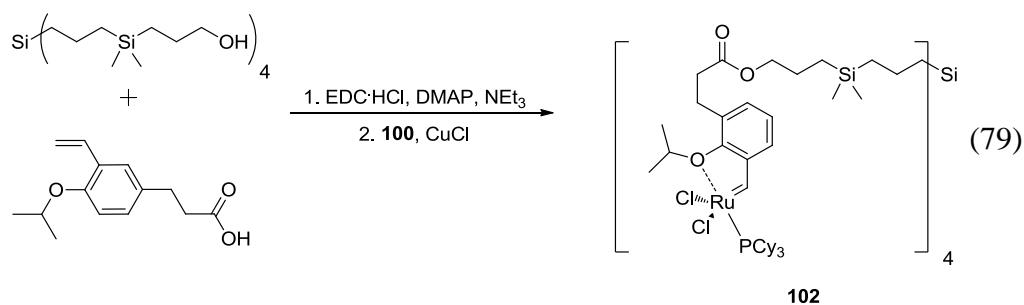
Shortly after this, Blechart *et al*. reported the preparation of a poly(oxanorbornene)-bound catalyst **105**.[164] **105** was prepared from the ROMP of **103** and **104** with Grubbs 2nd generation catalyst and CuCl (as a phosphine scavenger) as shown in eq. 80. Under these conditions, it was possible to regenerate the metal by

sequestration with the styrenyl pendant groups and use the newly formed complex as a RCM catalyst.
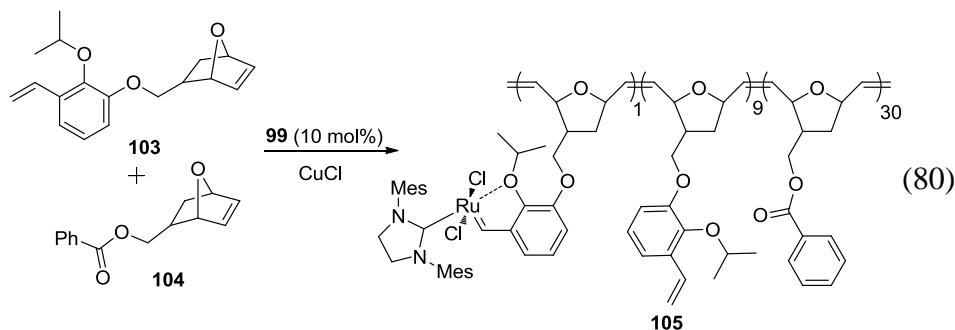
Complex **105** was described as a having a high level of "self-generation" as it contains a relatively large amount of styrenyl groups that act as excess ligand. This excess ligand can regenerate the catalyst through a metal exchange, or boomerang-type mechanism. **105** was shown to be a highly recoverable/recyclable RCM catalyst. It was able to be recovered by precipitation into diethyl ether or hexanes and could be recycled 7 times with no loss in activity. Because of the excess styrenyl groups present, **105** showed very little loss of metal.

The attachment of these types of catalysts as end groups on a polymer is possible as well. The first example of using PEG as a polymer support was reported by Yao in 2000.[165] He showed it was possible to prepare a recoverable catalyst by anchoring the Hoveyda-Grubbs 1st generation catalyst to PEG through the benzylidene moiety. This catalyst (**106**) could be recovered using solvent precipitation and reused 5 times, with no loss in product yield. It was reported that the reaction times in subsequent cycles had to be extended, most likely due to the loss of metal.

106
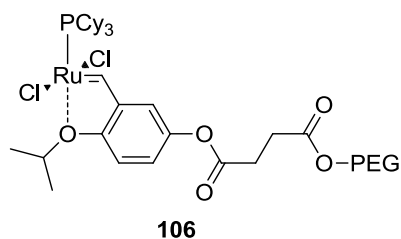
Similar work was disclosed by Lamaty *et al.* several years later. This was the first report of a PEG-supported Hoveyda-Grubbs 2nd generation catalyst.[166] The authors reported that complex **107** could catalyze various RCM reactions and could be reused up to 5 times. However, a loss of activity was observed due to metal loss.

107
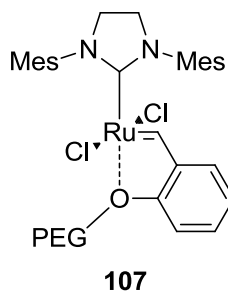
Both of these complexes (**106** and **107**) are inherently flawed; recovery of the metal catalyst relies on a "boomerang" type mechanism. That is, the active catalytic species is actually not attached to the polymer support. Having a system that relies on recapturing the active catalyst can lead to relatively large amount of metal leaching. Through their work towards the development of water soluble metathesis catalysts, Grubbs *et al.* found that anchoring Hoveyda-Grubbs 2nd generation-like complexes to PEG through the NHC ligand greatly diminishes the amount of metal leaching from the catalyst to the products.[67,167] The reason for this is that the active, 14-electron catalyst remains attached to the NHC ligand throughout the catalytic cycle. Complex **108** was shown to be a highly active catalyst for RCM, cross metathesis and ROMP in aqueous

media. It was also shown to be an excellent sequestration agent, giving products that contained with as little as 0.04 ppm Ru contamination.

108
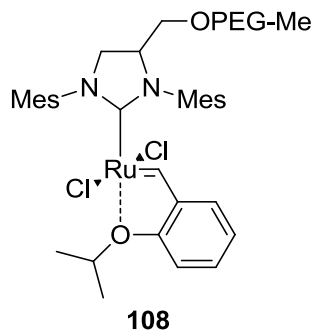
    As mentioned earlier in Chapter I, our lab has had interest in the development of polymer-supported Ru-complexes that can be recovered/reused using liquid/liquid separation systems.[12] The use of a PIB-bound benzylidene as a catalyst phase handle was described earlier. Catalyst **30** could be used to facilitate the RCM of various substrates and, in some cases, could even be used as a "self-separating" catalyst. However, it was found that Ru contamination in the products was relatively high (*ca.* 1000 ppm). In order to reduce the amount of Ru leaching into the products, our lab developed a PIB-supported NHC-Ru complex **109**.[13] This ligand could be used to form transition metal complexes of both, Ag and Ru. The preparation of **109** is shown in Scheme 21. Reaction of commercially available PIB and 2,6-dimethylaniline in the presence of AlCl$_3$ afforded the PIB-supported aniline species. This was then coupled with oxalyl chloride to afford the bisamide which was then reduced using BH$_3$·SMe$_2$ followed by cyclization and reaction with Hoveyda-Grubbs 1st generation catalyst to afford complex **109**.

Scheme 21. Preparation of PIB-supported complex **109**.
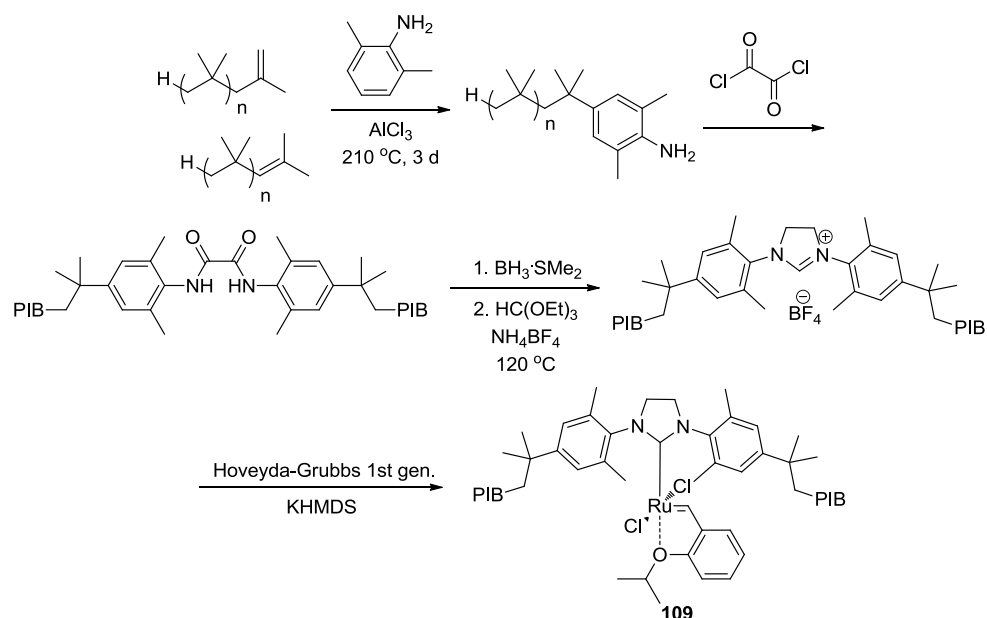
PIB-bound complex **109** served as a highly phase selectively soluble, recoverable/reusable catalyst for the RCM reactions of several substrates. **109** could be recycled up to 20 times, giving pure products in high yields (> 95 %). The Ru contamination was found to be 10 times lower than what was observed using catalyst **30**; the chemistry of which relied on a boomerang mechanism for catalyst recovery. However, the isolation of the products is often not quantitative as the products have slight solubility in the nonpolar, polymer phase. This is not the case when using solid/liquid separations mentioned above, but these systems suffer from their detrimental effects on the environment. Described below is the first example of a recoverable/recyclable, thermomorphic, polymer-bound RCM catalyst that allows for the quantitative phase separation of the catalyst as a solid (Figure 4).

Results and Discussion

Our group pioneered the use of polyethylene oligomers as catalyst supports a number of years ago.[6-8,46] Terminally-functionalized oligomers of PE are completely insoluble in any solvent at room temperature, but, are soluble upon heating. When the hot solution is cooled back to room temperature, the PE$_{Olig}$ precipitates out of solution and can be quantitatively isolated using vacuum filtration or centrifugation. This maks functionalized PE$_{Olig}$ species viable candidates as ligands for the development of thermomorphic catalysts. Such species can be used as supports for transition metal complexes that can perform homogeneous catalysis at elevated temperatures and thereafter, can be isolated as a solid upon cooling. After several years, interest in our lab for this chemistry was again rekindled when a group at DuPont reported the preparation of PE$_{Olig}$-bound porphyrin and phthalocyanine metal complexes that can be used as catalysts for radical polymerizations.[47] Their report prompted us to prepare PE$_{Olig}$-supported salen/metal complexes[63] and PE$_{Olig}$-supported NHC ligands, which can be used as thermomorphic, recoverable Ru RCM catalysts (*vide infra*) that are soluble at elevated temperatures but precipitate upon cooling (Figure 5). Such complexes were prepared from commercially available functionalized PE-oligomers.[136]
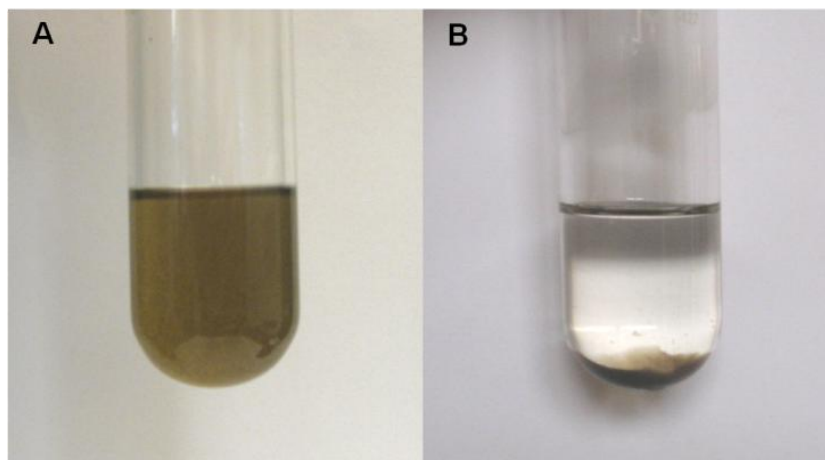
Figure 5. Picture showing the thermomorphic solubility property of **119** in toluene at (**A**) 75 °C and (**B**) after cooling to room temperature followed by centrifugation.

The desired PE_{Olig}-bound NHC-Ru complex 5 was prepared from commercially available PE_{Olig}-OH and Hoveyda Grubbs 1st generation catalyst as shown in Scheme 22. PE_{Olig}-mesylate (PE_{Olig}-OMs[46]) was allowed to react with *N*-mesityl imidazole in refluxing toluene for 24 h to give the PE_{Olig}-imidazolium mesylate which was then subjected to a counter anion exchange with LiCl in a mixture of toluene and THF at reflux to yield the imidazolium chloride **110** as a white powder in quantitative yield. These products were isolated by cooling the reaction mixture followed by gravity filtration and were characterized by solution state variable temperature (VT) ^{1}H and ^{13}C NMR spectroscopy. With **110** in hand, the PE_{Olig}-NHC-Ru complex **111** was synthesized by reaction of **110** with potassium bis(trimethylsilyl)amide (KHMDS) and **100** in toluene at 80 °C for 8 h. **111** was isolated via vacuum filtration as a brownish/green

powder. Formation of **111** was determined by the characteristic benzylidene proton shift at 16.6 ppm in the ^{1}H NMR spectrum.

Scheme 22. Preparation of PE-supported NHC-Ru complex
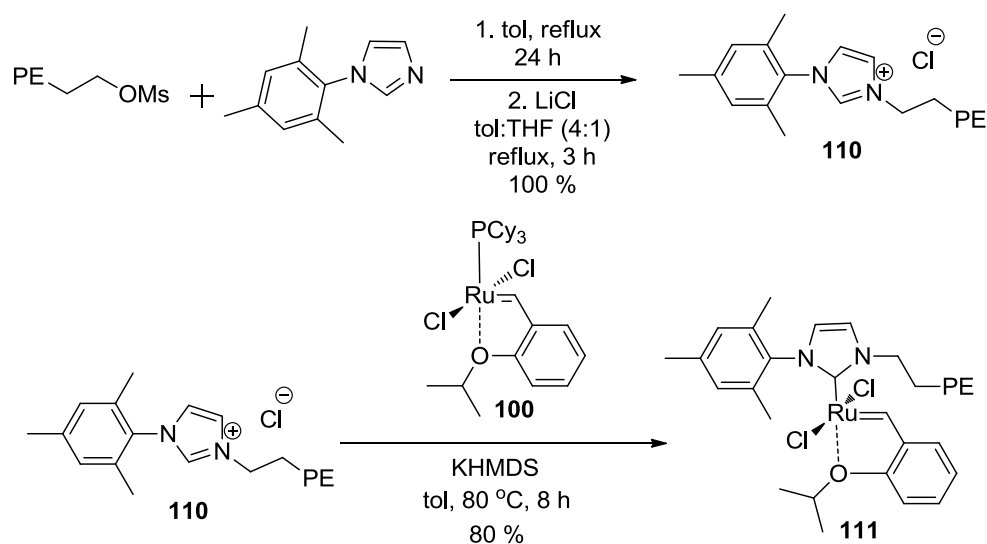
We were interested in probing the ability of **111** as a recoverable/recyclable catalyst for the RCM reactions of various substrates under thermomorphic reaction conditions. As shown in eq. 81, three different substrates were used in separate experiments. These experiments were conducted at 65 °C in degassed toluene and were typically complete within 5 min. These reactions could be monitored by the evolution of ethylene gas. Recovery of the PE$_{Olig}$-bound catalyst **111** was affected by cooling the reaction mixture to room temperature, which induced phase separation of **111** as a solid, followed by the addition of toluene (10 mL) and centrifugation. The toluene solution (which contained the product) could then be removed using a forced siphon. Toluene (10

mL) addition and centrifugation was then repeated to remove any residual product. The toluene was removed and the supernatants were combined and the solvent was removed under reduced pressure to yield the RCM products in high purity, without the need for any further purification. The process of recycling of small amounts of PE_{Olig} catalyst was facilitated by adding additional PE that had not been functionalized with catalyst or ligand. This simplified handling of the small amount of precipitated powder. Using this method, complex **111**, in some cases, was recovered and reused up to four times in good yields, as shown in Table 4.

$$\text{(81)}$$

112: n = 1, X = C(CO$_2$Et)$_2$
113: n = 1, X = NTs
114: n = 2, X = NTs
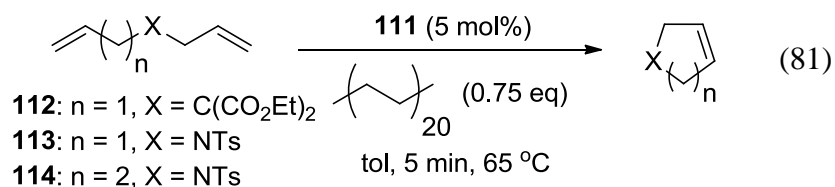
Table 4 Recycling data for various RCM reactions using **106** as a catalyst.

Substrate[a]	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
112	98	96	95	92	63
113	94	93	83	50	-
114	99	93	80	71	-

The efficiency of the ability of **111** to sequester Ru contaminants from the products was evaluated by inductively coupled mass spectrometry (ICP-MS). Analysis of the RCM product from substrate **113**, which was digested in sulfuric and nitric acid,

showed the presence of < 0.63 % of charged Ru (*ca.* 74 ppm) in the product after removal of the solvent; 10 times lower than our previous reports.[12] This is comparable to studies that utilize low molecular weight catalysts in which Ru contamination *after silica gel flash chromatography* was found to be *ca.* 100 ppm.[138,168] Ru contamination is also visually evident in the pictures below, in Figure 6, where the products of substrate **113** that resulted from the reactions using three different catalysts are depicted. As can be seen from the picture, the product that was isolated from the reaction with the low molecular weight Hoveyda-Grubbs 2nd generation catalyst **101** is highly colored, as is the product that is isolated from reaction with a PIB-bound catalyst previously reported from our lab.[12] As can be seen, this complex contains a polymer-support that is anchored through the benzylidene moiety; rendering the recovery of this catalyst dependent on a "boomerang" mechanism. However, use of complex **111**, in which the polymer-support is attached to the NHC ligand of the complex, gives rise to a product that is water-white, indicating that the Ru contamination is much lower, rendering further purification steps unnecessary.

Although complex **111** was a competent catalyst for the RCM reaction, the recyclability was somewhat limited possibly because of decomposition of the catalyst. It has been shown that, in general, complexes with unsymmetrical NHC ligands that contain an *N*-alkyl group are prone to faster rates of decomposition than complexes that contain a bulkier NHC ligand (IMes or SIMes).[138,139]. In order to improve the recyclability, we set out to prepare a PE$_{Olig}$-supported SIMes-like ligand that could be used to facilitate the recovery of catalytically active Ru complexes.
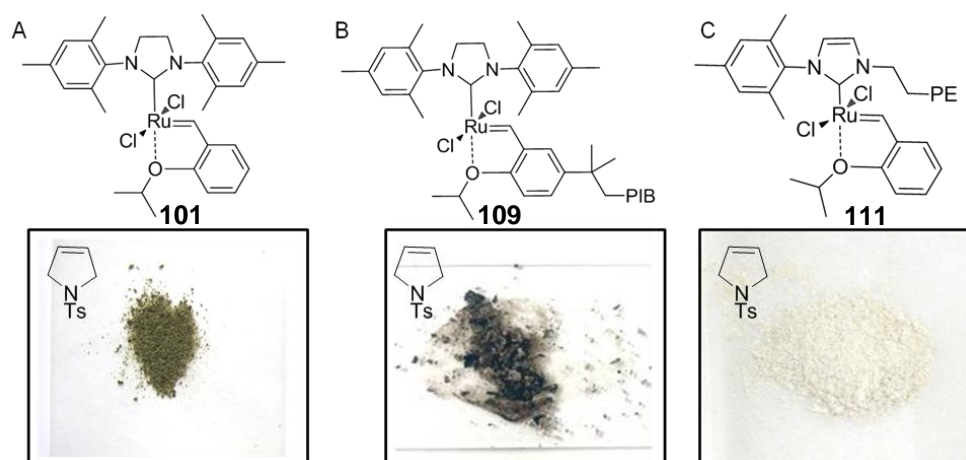
Figure 6 Comparison of the color of the product from reaction of **113** with (A) Hoveyda-Grubbs 2nd generation catalyst **101**, (B) PIB-supported catalyst **109**[12] and (C) PE-supported complex **111**.

The preparation **119** started with the Mitsunobu[63] reaction of commercially available PE_{Olig}-OH[136] with *N*-boc-4-amino-3,5-xylenol with triphenylphosphine and diethyl azodicarboxylate (DEAD) in toluene at 80 °C followed by deprotection with methanesulfonic acid afforded PE_{Olig}-supported aniline **115** as a light brown powder in quantitative conversion (Scheme 23). **115** could then be subjected to reaction with aqueous glyoxal in a mixture of toluene and 2-propanol (3:1) at 75 °C to quantitatively afford the bisimine **116** as a bright yellow solid. Reduction of **116** followed by standard cyclization procedures of **117** (triethylorthoformate, formic acid (cat.) and ammonium tetrafluoroborate) afforded the PE-supported imidazolinium salt **118** as a white powder in quantitative conversion. All the intermediates were confirmed by ^{1}H and ^{13}C NMR

spectroscopy. **119** showed singlet in the ^{1}H NMR spectrum for the methine proton of *ca.* 5.95 ppm in C_6D_6. Reaction of **119** with KHMDS and **100** in anhydrous toluene at 80 $^\circ$C afforded complex **119** as a pale green powder in excellent yield. Formation of **119** was confirmed by a singlet at *ca.* 16.9 ppm in the ^{1}H NMR spectrum corresponding to the benzylidene proton.

Scheme 23 Preparation of PE$_{Olig}$-supported Ru complex **119**
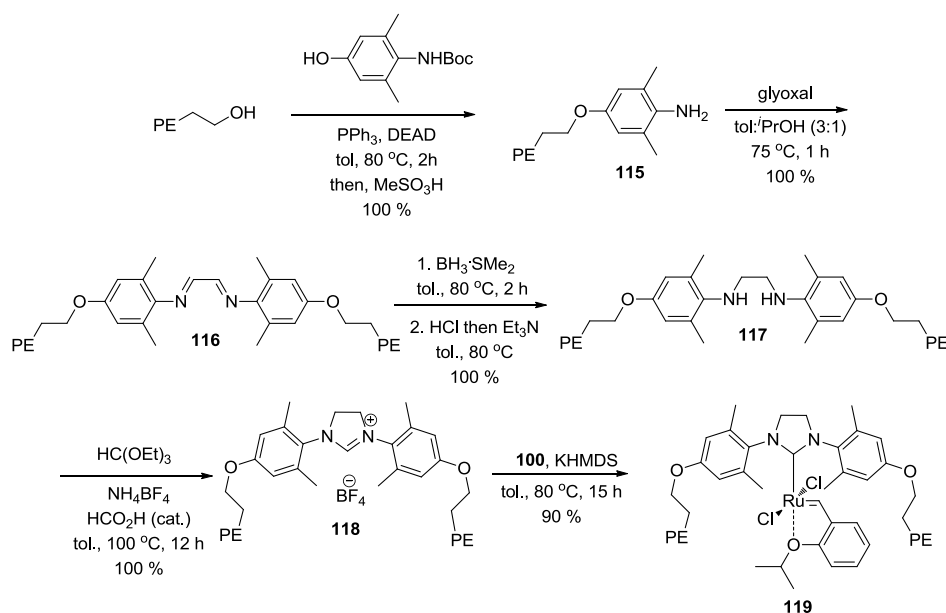
After the successful preparation of complex **119**, we next probed its ability to serve as a recoverable catalyst for various RCM reactions, in order to compare its recyclability with complex **106**. The results are shown below in Table 5.

$$\text{(82)}$$

112: R = H, X = C(CO$_2$Et)$_2$
113: R = H, X = NTs
120: R = CH$_3$, X = NTs

119 (2.5 mol%)

(0.75 eq)

tol, 5 min, 65 °C
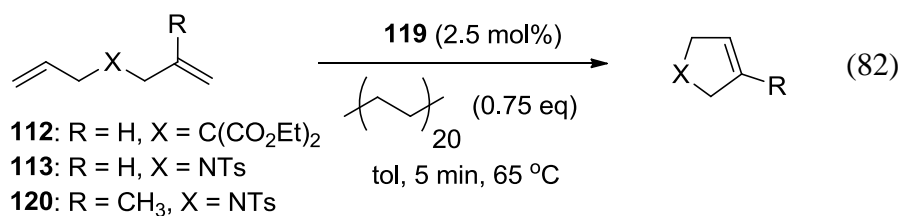
Table 5 Recycling data for various RCM reactions using **119** as a catalyst.

substrate	Cycle 1 (%)	Cycle 2 (%)	Cycle 3 (%)	Cycle 4 (%)	Cycle 5 (%)	Cycle 6 (%)	Cycle 7 (%)	Cycle 8 (%)
112	99	98	99	99	98	98	94	94
113	99	99	99	99	99	99	95	81
120	99	99	99	99	99	97	95	83

As shown in Table 5, **119** was a competent RCM catalyst, typically yielding products in 5 min. Recovery of **119** was performed in the exact same manner as discussed for complex **111** (*vide supra*). Similarly, concentration of the toluene layers under reduced pressure afforded the RCM products in high purity. Under these conditions, complex **119** was able to be recycled up to 8 times in excellent yields. Reaction of substrate **112** could be extended to 10 cycles with reaction times of 15 min. each (average yield = 96 %). In terms of recyclability, it can be concluded that catalyst **119** is superior to **111**. Catalyst decomposition typically occurred around cycle 7 or 8, as observed by the diminished conversion of products. To test the efficiency of this process, ICP-MS was again used to determine the amount of Ru contamination. It was found that the product of **113** contained *ca.* 0.3 % (*ca.* 99 ppm) of charged Ru, again, roughly 10 times lower than our previous reports.[12]

Often, when using soluble, polymer-bound catalysts, performing sequential reactions of different substrates with the same batch of catalyst is difficult and impractical. This becomes especially true when utilizing a liquid/liquid separation technique (as described above) because the phase containing the catalyst becomes saturated with product.[12,13,63,67] This should not be the case with thermomorphic complex **119** because, upon cooling, **119** precipitates out of solution, while the products remain soluble – a hypothesis that has support in the prior work that used PE_{Olig}-bound Ru catalysts in the synthesis of a series of different vinyl esters.[169] This allows for complete removal of product solution. As a proof-of-concept, we tested the applicability of complex **119** in a "one-pot" catalytic procedure in which, after phase separation and isolation of the product, a different substrate is added to the reaction flask and allowed to react with the same batch of catalyst. This allows for the one batch of catalyst to perform more than one different reaction in the same pot (Scheme 24).

In this experiment, **119** was allowed to react with **112** for 5 min. in toluene at 65 °C (reaction **A**). The mixture was allowed to cool to room temperature and then 10 mL of toluene was added to the flask. Following, centrifugation and removal of the toluene solution by forced siphon was carried out. This process was repeated to remove traces of residual product. Isolation of the product phase followed by removal of the solvent afforded the RCM product in quantitative yield. **120** was then added to the reaction flask and allowed to react at 65 °C for 5 min. (**B**). The same product isolation procedure was performed and ^{1}H NMR showed quantitative formation of the RCM product with < 5 %

Scheme 24. "One-pot" catalytic procedure using **119** to catalyze the RCM of three different substrates.

contamination from **A**. Finally, **113** was added to the reaction flask (**C**).Utilizing the same reaction and product isolation procedure, the product from this reaction was obtained quantitatively and contained < 5 % of residual product from the preceding reaction(s).

As part of an ongoing project, we have briefly examined the ability of PE_{Olig}-supported Ru complex **111** to initiate the ring-opening metathesis polymerization (ROMP) of strained cyclic olefins. ROMP was one of the earliest commercial applications of olefin metathesis (vide supra). With the development of well-defined Ru-

based initiators over the years, ROMP has become one of the most widely used living polymerization methods for the construction of various macromolecules with well controlled molecular weights. Although the use of polymer-supported species that initiate ROMP cannot be recycled, it is important to develop methods for the sequestration of Ru contaminates because of the detrimental effects of such metal species. Work that utilizes insoluble polymer-supported ROMP initiators has recently been reviewed; many of these systems utilize solid silica-supported initiators.

Because of the advantages of homogeneous catalysts (or initiators) over heterogeneous systems (as discussed in Chapter I) we were interested in preparing a thermomorphic ROMP initiator. Such a species could potentially be used to mediate the polymerization reactions at elevated temperatures. After quenching the polymerization and allowing the reaction mixture to cool, the polymer-supported Ru complex could be isolated as a solid while the product polymer would stay in solution; a concept similar to a "self-separating" ATRP catalyst reported by our group based off of a PIB-supported-Cu(I) complex. Preliminary results suggest that complex **111** can successfully serve as a recoverable initiator for the ROMP of strained cyclic olefins (eq. 83).

$$M_n = 19{,}890 \text{ Da} \tag{83}$$
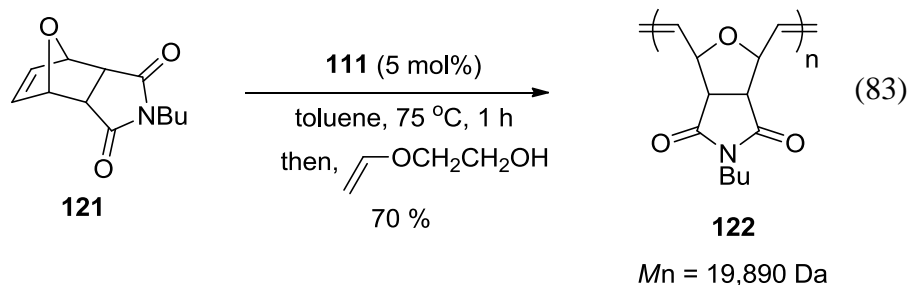
As shown in eq. 83, addition of substrate **121** to initiator **111** (5 mol%) in toluene at 75 °C resulted in formation of polymer **122** in under 1 h in good yield (70 %).

Typically, such polymerization procedures require that the "living" polymer chain be quenched by termination with ethyl vinyl ether. However, since the reactions initiated by **111** require the use of elevated temperatures, ethyl vinyl ether could not be used as its boiling point is 36 °C. In order to quench the reaction in eq. 83, the use of a higher boiling vinyl ether was required. Ethyleneglycol vinyl ether, as a quenching agent, was sufficient for our purposes. After quenching the polymerization, the reaction mixture was cooled to room temperature and the reaction mixture was subjected to a solvent precipitation into methanol and **122** was isolated as a white powder. Analysis of **122** by gel permeation chromatography (GPC) showed **122** to have a number-average molecular weight (M_n) of 19, 890 Da. These results are comparable to reaction of **121** with low molecular weight **101**, which, under the same reaction conditions, gave 122 with $M_n =$ 22,615 Da. To test the efficiency of **111** to sequester the metal contaminates out of the product, ICP-MS was again utilized. The analysis showed that polymer **122** contained *ca.* 4.5 % of charged Ru from **111**.

Conclusions

In conclusion, we have shown that the use PE$_{Olig}$-supports is an efficient way to recover and recycle RCM catalysts. This report of PE$_{Olig}$-supported Ru complexes constitutes the first examples of Ru-RCM catalysts that can be recovered/recycled using a thermomorphic solid/liquid separation. In toluene at 65 °C, RCM reactions catalyzed by such complexes were complete within 5 min. and the catalysts could be recycled up to 10 times. Furthermore, ICP-MS analysis showed that the Ru contamination of the RCM products was on the order of 10 times lower than with complex **109**. Furthermore,

the Ru content was lower than previous studies that utilize low molecular weight catalysts that rely on column chromatography to remove any Ru contamination. Because of the thermomorphic nature of these materials, we were able to design a "one-pot" reaction system in which complex **119** was able to catalyze the RCM reaction of three different substrates sequentially, affording the respective products in high conversions and with low contamination from the previous reaction(s). Preliminary results show that it was also possible to such PE$_{Olig}$-supported Ru catalysts as initiators for the ROMP of cyclic olefin **121**. By using **111** as a recoverable initiator, polymer product **122** can be isolated as a white powder in good yield (70 %) with relatively low Ru contamination (*ca.* 4.5 %).

CHAPTER V

EXPERIMENTAL SECTION

Materials

All solvents were purchased from EMD or Sigma-Aldrich and used as received. All chemicals were purchased from Sigma-Aldrich or Alfa-Aesar and used as received. Polyisobutylene and polyethylene were gifts from BASF and Baker-Hughes, respectively.

Instrumentation

The ^{1}H-NMR spectra were recorded on an Inova 500 MHz spectrometer operating at 499.95 MHz and Inova 300 MHz spectrometer operating at 299.91 MHz. ^{13}C-NMR spectra were recorded on an Inova 500 MHz spectrometer operating at 125.72 MHz and Inova 300 MHz spectrometer operating at 74.987 MHz. NMR spectra in the case of PE$_{Olig}$-bound substrates were obtained at 70 $^\circ$C. Chemical shifts were reported in parts per million (δ) relative to residual proton resonances in the deuterated chloroform (CDCl$_3$), deuterated benzene (C$_6$D$_6$), deuterated or deuterated toluene (C$_7$D$_8$). Coupling constants (J values) were reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), and m (multiplet). UV-Vis spectra were obtained using a Varian Cary 100 spectrometer. IR spectra were obtained using a Bruker Tensor 27 FT-IR. The % e. e.

values were determined by chiral HPLC analysis (ChiralCel OD, hexanes/isopropanol (8:2)). ICP-MS data were obtained using a Perkin Elmer DRC II instrument.

General Experimental Procedure

All reactions were carried out under an inert atmosphere of N_2 using standard Schlenk techniques, unless otherwise noted. Catalyst loadings are based off of metal content and were determined by UV-vis spectroscopy or ICP-MS analysis.

4-polyisobutylphenol 50. To a 500-mL round-bottomed flask equipped with a stir bar and rubber septum were added phenol (15 g, 160 mmol), PIB-alkene (8.9 g, 8.9 mmol) in CH_2Cl_2 (200 mL), and conc. H_2SO_4 (1.05 g, 10.7 mmol). The mixture was then stirred under N_2 for three days at room temperature. At this point, the solvent was removed under reduced pressure and 250 mL of hexanes was added to the viscous oil. The hexanes solution was washed with 3-150 mL portions of *N,N*-dimethylformamide and 3-150 mL portions of 90% ethanol/water. The organic phase was dried over $NaSO_4$, filtered and solvent was removed under reduced pressure to give 8.27 g of **50** as a viscous, light yellow oil, 90 %. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 6.75 (d, *J* = 8.8 Hz, 2H), and 7.23 (d, *J* = 8.8 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 153.19, 142.99, 127.52, 114.75, multiple peaks between 58 - 60, 38 - 38.5, and 30.75 - 33.

2-*tert*-butyl-4-polyisobutylphenol 51. This compound was prepared by using the same procedure used to prepare **50** and was isolated as a viscous, light yellow oil, 85 %. ^{1}H-NMR (300 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 6.6 (d, *J* = 7.8 Hz, 1H),

7.05 (m, 1H), and 7.3 (s, 1H). ^{13}C NMR (125 MHz, CDCl$_3$), δ: 151.83, 142.07, 135.04, 125.42, 124.53, 115.91, multiple peaks between 58 - 60, and 22 – 39.

6-polyisobutyl-2-naphthol 53. To a flame dried, 250 mL, round-bottomed flask equipped with a stir bar and rubber septum was added 2-naphthol (2.746 g, 19 mmol) in 43 mL of methylenechloride and was cooled to 0 °C. AlCl$_3$ (0.31 g, 2.34 mmol) was added and the reaction mixture was stirred for 10 min. Upon addition of AlCl$_3$, the reaction mixture turned dark red. Next, the preformed PIB-chloride (2.01 g, 2.02 mmol), in methylenechloride (10 mL), was added drop wise via syringe. The reaction was placed under N$_2$ and allowed to warm to room temperature was stirred for an additional 18 h. The solvent was removed under reduced pressure to give a viscous oil and to this residue was added hexanes (100 mL). The organic phase was then washed with 5-50 mL portions of 90% ethanol/water and dried over Na$_2$SO$_4$. The solvent was then removed under reduced pressure to give a viscous oil that was purified by column chromatography (silica gel, hexanes followed by methylenechloride) to yield 0.3 g of **53** as a light yellow oil, 15 %. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 0.8-1.6 (m, 152H), 1.9 (s, 6H), 7.02-7.09 (d, J = 7.5 Hz, 1H), 7.10-7.12 (s, 1H), 7.5-7.54 (d, J = 9.0 Hz, 1H), 7.6-7.74 (m, 3H).

6,6'-bis(Polyisobutyl)-2,2'-binaphthol 54. To a flame-dried, 25 mL, round-bottomed flask equipped with a stir bar and a rubber septum was added CuCl$_2$ (0.25 g, 1.85 mmol), benzylamine (1 mL, 9.17 mmol) in CH$_2$Cl$_2$ (5 mL). The reaction mixture was then placed under N$_2$ and allowed to stir for 30 min. At this time, **53** (0.91 g, 0.795 mmol) in CH$_2$Cl$_2$ (5 mL) was added via syringe and the reaction mixture was allowed to stir

overnight. The solvent was removed under reduced pressure to yield a viscous oil. To the crude product was added hexanes (100 mL). The organic phase was then washed with 3-50 mL portions of a saturated ammonium hydroxide solution, 3-50 mL portions of 90% ethanol/water and the organic phase was dried over Na_2SO_4. The solvent was then removed under reduced pressure to yield 0.54 g of **54** as viscous, brown oil, 59%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.8-1.8 (m, 300H), 1.9 (s, 12H), 7.117-7.135 (d, J = 5.4 Hz, 2H), 7.36-7.39 (m, 4H), 7.79 (s, 2H), 7.93-7.95 (d, J = 5.4 Hz, 2H).

PIB-bimethoxy-BINOL ketone 56. To a flame dried, 100 mL, round-bottomed flask equipped with a stir bar and a rubber septum was added (±)-**55** (1.72 g, 5.47 mmol) in CH_2Cl_2 (22 mL) and place under N_2. The reaction flask was then cooled to 0 °C in an ice-water bath. Then, $AlCl_3$ (0.51 g, 3.86 mmol) was added to the flask and the reaction mixture instantly turned dark red. The reaction mixture was allowed to stir for 10 min before the PIB-acid chloride (2 g, 1.85 mmol) in CH_2Cl_2 (5 mL) was added. The dark brown reaction mixture was allowed to warm to room temperature and was allowed to stir for an additional 48 h. The solvent was then removed under reduced pressure to yield a dark viscous oil. To this crude product was added hexanes (200 mL) and the organic phase was then washed with 1-100 mL portion of water, 3-100 mL portions of acetonitrile and the organic phase was then dried over Na_2SO_4 and the solvent was removed under reduced pressure to give a light yellow, viscous oil. This crude product was purified by column chromatography (silica gel, hexanes: ethylacetate: triethylamine (93:5:2)) to yield 0.9 g of **56** as a light yellow viscous oil, 45%. ^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.8-1.8 (m, 162H), 3.0-3.08 (m, 2H), 3.76 (s, 3H), 3.80 (s, 3H), 7.06 (d, J =

12.0 Hz, 1H), 7.13-7.35 (m, 1H), 7.45-7.53 (m, 2H), 7.75 (d, J = 9.0 Hz, 3H), 7.87 (d, J = 9.0 Hz, 1H), 7.99 (d, J = 9.0 Hz, 1H), 8.11 (d, J = 9 Hz, 1H), 8.51 (s, 1H).

6-polyisobutyl-2,2'-hydroxy-1,1'-binaphthol 57. To a flame dried, 25 mL, round-bottomed flask equipped with a stir bar and a rubber septum was added **56** (1.6 g, 1.15 mmol) in CH_2Cl_2 (5mL) and was then placed under N_2 and cooled to 0 °C on an ice-water bath. Trifluoroacetic acid (1.3 mL, 17.25 mmol) was then added to the reaction mixture dropwise via syringe. Upon addition, the reaction immediately turned dark brown. At this point, triethylsilane (0.5 mL, 2.88 mmol) was added to the reaction mixture dropwise via syringe. The dark reaction mixture was warmed to room temperature and was allowed to stir for an additional 48 h. The solvent was then removed under reduced pressure to yield a viscous oil. To this crude product was added hexanes (200 mL) and the organic phase was washed with 1-100 mL portion of water, 3-100 mL portions of 90% ethanol/water and the organic phase was then dried over Na_2SO_4 and the solvent was removed under reduced pressure to give 1.12 g of **57** as a viscous yellow oil, 70 %. ^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.8-1.8 (m, 158H), 2.38-2.75 (m, 2H), 3.76 (s, 3H), 3.80 (s, 3H), 7.02-7.09 (m, 2H), 7.13 (d, J = 7.4 Hz, 1H), 7.21 (t, J = 7.1 Hz, 1H), 7.32 (t, J = 7.4 Hz, 1H), 7.43 (s, 1H), 7.48 (s, 1H), 7.65 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.92, (d, J = 8.9 Hz, 1H), 7.99 (d, J = 8.9 Hz, 1H). This product (1.05 g, 0.764 mmol), in CH_2Cl_2 (23 mL) was then added to a flame dried, 100 mL, round-bottomed flask equipped with a stir bar and a rubber septum and was then placed under N_2 and cooled to 0 °C on an ice-water bath. At this point, BBr_3 (0.2 mL, 2.29 mmol) was slowly added in a dropwise fashion via a gas-tight syringe. Upon addition, the reaction

mixture turned black. The reaction was slowly warmed to room temperature and allowed to stir for an additional 48 h. At this point, water (5 mL) was added to the reaction mixture followed by the addition of CH_2Cl_2 (25 mL) and the layers were separated and the organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure to yield a dark, viscous oil. To this crude product was added hexanes (200 mL) and this organic phase was washed with 3-100 mL portions of 90% ethanol/water and 1-50 mL portion of brine. The organic phase was then dried over Na_2SO_4 and the solvent was removed under reduced pressure to yield 1 g of **57** as a dark oil, 95%. ^{1}H NMR (500 MHz, CDCl$_3$), δ: 0.8-1.8 (m, 160H), 2.38-2.75 (m, 2H), 7.10 (d, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.31-7.42 (m, 4H), 7.69 (s, 1H), 7.92 (t, *J* = 7.8 Hz, 2H), 7.98 (d, *J* = 9.8 Hz, 1H).

2-hydroxy-4-*tert*-butyl-5-(polyisobutyl)benzaldehyde 73. To a 100-mL round-bottomed flask equipped with a stir bar, rubber septum, and a water-jacketed reflux condenser were added **51** (3.42 g, 3.13 mmol) and 2,6-lutidine (0.58 g, 5 mmol) in toluene (40 mL). The mixture was stirred at room temperature for 30 min. At this time, SnCl$_4$ (0.15 mL, 1.25 mmol), in 10 mL of toluene, was added dropwise via syringe. The reaction mixture was then stirred at room temperature for 1 h. At this point, paraformaldehyde (0.56 g, 18.78 mmol) was added to the flask. The reaction mixture was then placed on an oil bath regulated at 100°C and stirred for 12 h. The reaction mixture was then cooled to room temperature and acidified to pH 2 with 2 M HCl. The organic phase was isolated and solvent was removed under reduced pressure. 250 mL of hexanes was added to the viscous oil and was washed with 3-150 mL portions of *N,N*-

dimethylformamide and 3-150 mL portions of 90% ethanol/water. The organic phase was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to give 2.8 g of **73** as a viscous, yellow oil, 76%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 7.32 (s, 1H), 7.57 (s, 1H), 9.9 (s, 1H), and 11.62 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 197.55, 159.30, 140.89, 137.40, 133.20, 128.74, 120.19, multiple peaks between 58 - 60, and 22 - 39.

***N,N′*-Bis(3-*tert*-butyl-5-(polyisobutyl)salicylidene)-1,2-ethylenediamine 74.** To a 50-mL round-bottomed flask equipped with a stir bar, a rubber septum and water-jacketed reflux condenser with a Dean-Stark trap was added **73** (3.0 g, 2.6 mmol), ethylenediamine (0.08 g, 1.3 mmol), and a catalytic amount of PTSA in toluene (30 mL). The reaction mixture was stirred at reflux overnight. The solvent was removed under reduced pressure and then 150 mL of hexanes was added to the viscous residue. The hexane solution was washed with 3-100 mL portions of *N,N*-dimethylformamide, then 3-100 mL portions of 90% ethanol/water. The organic phase was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to give 6.1 g of **74** as a viscous, yellow oil, 100 %. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 280H), 1.8 (s, 4H), 3.95 (s, 4H), 7.05 (s, 1H), 7.40 (s, 1H), and 8.43 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 168.10, 158.20, 139.80, 136.50, 128.40, 127.70, 118.20, multiple peaks between 58 - 60, and 22 - 39.

(*R,R*)-*N,N′*-Bis(3-*tert*-butyl-5-(polyisobutyl)salicylidene)-1,2-cyclohexanediamine 74. To a 50-mL round-bottomed flask equipped with a stir bar and a water-jacketed reflux condenser and a 10-mL addition funnel was added the L-tartrate salt of

cyclohexenediamine (0.265 g, 1 mmol), K_2CO_3 (1.66 g, 2 mmol) and water (3 mL). Then absolute ethanol (11 mL) was added and the suspension was heated to reflux and became homogenous. Then, **73** (2.965 g, 2 mmol), in heptane (5.5 mL), was added dropwise via an addition funnel. The yellow reaction mixture was allowed to stir at reflux for 12 h under N_2. At this point, the reaction mixture was cooled to room temperature and worked up with 100 mL of hexanes. The layers were separated and the organic phase was washed with 3 50-mL portions of 90% ethanol/water. The organic phase was then dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to yield 2.73 g of **74** as a viscous, yellow oil, 100 %. ^{1}H NMR (300 MHz, CDCl3), δ: 8.31 (s, 2H), 7.29 (s, 2H), 6.94 (s, 2H), 3.37-3.30 (m, 2H), 1.8-0.8 (m, 380H). ^{13}C NMR (125 MHz, CDCl$_3$), δ: 164.91, 156.96, 137.85, 134.92, 126.92, 125.72, 116.82, multiple peaks were present between 57-60 and 20-40.

N,N′-Bis(3-*tert*-butyl-5-(polyisobutyl)salicylidene)-1,2-ethylenediamino-Cr(III)

chloride 76. To a 50-mL round-bottomed flask equipped with a stir bar and rubber septum were added **74** (6.62 g, 2.78 mmol) and $CrCl_2$ (0.374 g, 3.05 mmol) in THF (30 mL). The reaction mixture was then stirred under N_2 at room temperature for 24 h then stirred under air for 24 h. The solvent was removed under reduced pressure and then 150 mL of hexane was added to the viscous residue. The hexane solution was washed with a solution of 3-100 mL portions of a saturated aqueous solution of NH_4Cl, and then with 3-100 mL portions of a saturated aqueous solution of NaCl. The organic phase was dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure to give 4.30 g of **76** as a dark-brown, viscous oil, 65%. IR (neat): cm[-1] 1625 (m), 1535 (s), 1467

(s), 1394 (s), 1364 (s), and 1235 (m). UV-visible spectroscopy (λ_{max} = 350 nm, ε = 4514 $M^{-1}cm^{-1}$).

(*R,R*)-*N,N'*-Bis(3-*tert*-butyl-5-(polyisobutyl)salicylidene)-1,2-cyclohexanediamine-Cr(III) chloride 77. This complex was prepared by using the same procedure used to prepare complex **76** and was isolated as a dark, viscous oil, 65 %.

ARO of cyclohexene oxide with TMS-N$_3$ catalyzed by 77. To a 50-mL Schlenk tube equipped with a stir bar and rubber septum was added **77** (1 g, 0.35 mmol) in a mixture of 5 mL of heptane and 5 mL of ethanol. To this solution was added cyclohexene oxide (0.7 mL, 7.08 mmol) and TMS-N$_3$ (1 mL, 7.78 mmol). The dark reaction mixture was allowed to stir for 12 h under N$_2$, at which time stirring was stopped and 0.5 mL of water was added to the reaction mixture to induce phase separation. The aqueous layer was removed and dried over Na$_2$SO$_4$ and solvent was removed from this polar phase under reduced pressure to yield the azido alcohol as a yellow oil in corresponding yields and e. e. values reported in Table 1. Spectroscopic analyses were identical with those previously reported.[117] E. e. values in Table 1 were determined by chiral HPLC analysis of a chromophoric derivative of the ARO product.[63] ^{1}H NMR (300 MHz, CDCl$_3$) δ: 3.28-3.16 (m, 1H), 3.06-2.97 (m, 1H), 1.94-1.79 (m, 3H), 1.66-1.46 (m, 2H), 1.3-0.97 (m, 4H). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 74.0, 67.0, 30.0, 29.5, 24.1, 23.5. FT-IR (neat, cm-1) 3350, 2940, 2860, and 2098. Recycling of the catalyst was achieved by simply adding fresh ethanol and substrates to the organic phase.

3-(*tert*-butyl)-2-hydroxy-5-(polyisobutyl)salicylidene-(1*R*,2*S*)-(1-amino-2-indanol) imine 78. To a two-necked, 50-mL round-bottomed flask equipped with a stir bar,

water-jacketed reflux condenser and a Dean-Stark trap was added **70** (2.94 g, 2.028 mmol), in toluene (21 mL), and (1*R*,2*S*)-1-amino-2-indanol (0.333 g, 2.230 mmol) and a catalytic amount of PTSA. The reaction mixture was stirred with azeotropic removal of water for 12 h and then cooled to room temperature. The solvent was then removed under reduced pressure and to the viscous oil was added hexanes (150 mL). The solution was washed with 3 100-mL portions of DMF and 3 100-mL portions of 90% ethanol/water. The organic phase was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to yield 3.19 g of **78** as a viscous, yellow oil, 100 %. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 8.62 (s, 1H), 7.40 (s, 1H), 7.35-7.17 (m, 4H), 7.12 (s, 1H), 4.80 (d, *J* = 5.32 Hz, 1H), 4.73 (bs, 1H), 3.25 (m, 2H), 1.80-0.80 (m, 160H). ^{13}C NMR (125 MHz, CDCl$_3$), δ:168.3, 158.0, 141.0, 140.8, 139.5, 136.5, 128.6, 127.2, 127.0, 125.5, 125.0, 117.7, 75.8, 75.3, multiple poorly resolved peaks were present between 77 and 60 and 20-40.

3-(*tert*-butyl)-2-hydroxy-5-(polyisobutyl)salicylidene-(1*R*,2*S*)-(1-amino-2-indanol) imine-Cr(III)Cl 79. To a 50-mL round-bottomed flask equipped with a stir bar and rubber septum was added **78** (2.74 g, 1.73 mmol) and CrCl$_2$ (0.233 g, 1.90 mmol) in THF (21 mL). The dark reaction mixture was allowed to stir under N$_2$ for 24 h at room temperature. At which point, the reaction system was exposed to air and stirred for 24 h. The solvent was removed under reduced pressure and hexanes (150 mL) was added to the dark, viscous oil. The hexanes-solution was then washed with 3-50 mL portions of a saturated aqueous solution of NH$_4$Cl and 3-50 mL portions of a saturated aqueous solution of NaCl. The organic phase was dried over Na$_2$SO$_4$ and the solvent was

removed under reduced pressure to yield 2.82 g of **79** as a dark, viscous oil, 100 %. UV-visible spectroscopy (λmax =348 nm).

2-hydroxy-5-polyisobutylbenzaldehyde 80. This compound was prepared by using the same procedure used to prepare **73** and was isolated as a viscous, yellow oil, 70% . ^{1}H NMR (500 MHz, CDCl$_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 6.94 (d, J = 8.5 Hz, 1H), 7.48 (m, 1H), 7.57 (dd, J = 2.4, 8.5 Hz, 1H), 9.9 (s, 1H), and 10.88 (s, 1H). ^{13}C NMR (125 MHz, CDCl$_3$), δ: 197.07, 159.65, 142.40, 135.74, 130.73, 120.21, 117.24, multiple peaks between 58 - 60, 38 - 38.5, and 30.75 - 33.

2-hydroxy-4-methylpiperidyl-5-(polyisobutyl)benzaldehyde 81. To a 50-mL, round-bottomed flask equipped with a stir bar, rubber septum and a water-jacketed reflux condenser was added piperidine (0.44 mL, 4.46 mmol) and paraformaldehyde (0.15 g, 4.90 mmol) in glacial acetic acid (3.19 mL). The mixture was stirred at room temperature for 3 h. At this point, **80** (5 g, 4.46 mmol) in a mixture of heptane and ethanol (1:1, 13 mL) was added to the reaction flask and placed on an oil bath regulated at 90 $^\circ$C and allowed to stir for 5 d. At this point, the reaction was cooled to room temperature and hexanes (50 mL) was added. The mixture was washed with 1-25 mL portion of saturated NaHCO$_3$(aq) and 3-25 mL portions of 90% ethanol/water. The organic phase was dried over NaSO$_4$, filtered and solvent was removed under reduced pressure to give a viscous, yellow oil which was then purified by column chromatography (silica, hexanes:ethylacetate (9:1)) to give 2.6 g of **81**, 50 %. ^{1}H NMR(500 MHz, CDCl$_3$) δ 10.40 (s, 1H), 7.65 (d, J = 2.5 Hz, 2H), 7.22 (d, J = 2.4 Hz, 2 Hz), 3.70 (s, 2H), 2.55 (m, 4H), 1.8 (s, 2H), and 0.8-1.6 (m, 140H). ^{13}C NMR (125 MHz,

CDCl$_3$) δ 191.7, 159.7, 140.9, 133.8, 125.4, 122.2, multiple poorly resolved peaks between 58 and 60, 38-39, and 30-33.

***N,N′*-Bis((3-piperidylmethyl)-5-polyisobutylsalicylidene)-1,2-ethylenediimine 82**. This compound was prepared by using the same procedure used to prepare **74** and was isolated as a viscous, yellow oil, 100 %. ^{1}H NMR (500 MHz, CDCl$_3$) δ: 8.39 (s, 2H), 7.31 (s, 2H), 7.19 (s, 2H), 3.70 (s, 2H), 2.60 (m, 8H), 1.8 (s, 4H), and 0.8-1.6 (m, 300H). ^{13}C NMR (125 MHz, CDCl$_3$) δ: 166.3, 157.1, 139.9, 132.0, 127.2, 124.1, 117.8, multiple poorly resolved peaks between 58 and 60.0, 38-39, and 30-33.

(*R,R*)-N,N′-Bis((3-piperidylmethyl)-5-polyisobutyl)salicylidene-1,2-cyclohexanediimine 83. This compound was prepared by using the same procedure used to prepare **77** and was isolated as a viscous, yellow oil, 100 %. ^{1}H NMR (500 MHz, (CDCl$_3$) δ: 8.31 (s, 2H), 7.36 (s, 2H), 7.03 (s, 2H), 3.60 (d, *J* = 12.7 Hz, 2H), 3.47 (d, *J* = 12.7 Hz, 2H), 3.3 (m, 2H), 2.60 (m, 8H), 1.8 (s, 4H), and 0.8-1.6 (m, 300H). ^{13}C NMR (125 MHz, CDCl$_3$) δ: 163.9, 156.1, 138.7, 130.8, 127.4, 126.5, 116.7, multiple poorly resolved peaks between 58 and 60, 38-39, and 30-33.

PE$_{Olig}$-bound salicylaldehyde derivative 85. To a 150-mL, round-bottomed flask equipped with a stir bar, pressure-equalized addition funnel, and a rubber septum was added 3-*tert*-butyl-5-hydroxysalicylaldehyde (1.88 g), PE$_{Olig}$-OH (1.33 g, 6.84 mmol), and triphenylphosphine (3.47 g, 17.09 mmol) in toluene (34 mL). The mixture was placed in an oil bath regulated at 80 °C and the contents were allowed to dissolve. At this point, a solution of DEAD (2.69 mL, 17.09 mmol) in toluene (10 mL) was added dropwise with the addition funnel. The dark reaction mixture was allowed to stir at 80

°C for 24 h. Then the reaction mixture was cooled to room temperature whereupon the PE$_{Olig}$-bound product precipitated. This product was collected by vacuum filtration and washed with toluene (50 mL) and THF (50 mL). This product was then placed in a 25-mL round-bottomed flask equipped with a stir bar and rubber septum and 10 mL of toluene containing 0.5 mL of water was added to this flask along with 0.45 g of PTSA. The flask was placed on an oil bath at 80 °C for 2 h. This procedure converted any imine derivative of the aldehyde group of **85** back into an aldehyde group. The PE$_{Olig}$-bound product **85** that precipitated on cooling of the reaction mixture at this point was collected by vacuum filtration and washed with toluene (50 mL) and THF (50 mL) to yield 1.1 g of **85** as a light orange solid, 80 %. ^{1}H NMR (500 MHz, benzene-d_6, 70 °C) δ 11.87 (s, 1H), 9.38 (s, 1H), 7.26 (d, J = 3.1 Hz, 1H), 6.43 (d, J = 1.9 Hz, 1H), 3.71 (t, J = 6.3 Hz, 2H), 1.71 (m, 1H), 1.49-1.30 (bs, 230H), 0.91 (t, J = 6.6 Hz, 5H). ^{13}C NMR (125 MHz, benzene-d_6, 70 °C) δ: 196.0, 155.9, 151.7, 139.9, 123.9, 120.1, 113.1, 68.6, 34.8, 31.9, 29.7, 29.3, 29.2, 28.9, 26.1, 22.5, 13.9.

PE$_{Olig}$-bound salen derivative 86. To a 25-mL, round-bottomed flask equipped with a stir bar and a rubber septum was added **85** (0.80 g) in toluene (6 mL). The mixture was placed under N$_2$ and the reaction flask was placed on an oil bath regulated at 80 °C. To the reaction mixture was added ethylenediamine (0.011 mL, 0.163 mmol). Upon addition of ethylenediamine, the reaction became bright yellow. The reaction was allowed to stir for 1 h, at which point 3,5-di-tert-butylsalicylaldehyde (0.25 g, 1.30mmol) was added to the reaction mixture, which was allowed to stir for an additional hour. At this point, the reaction was cooled to room temperature and the

product was collected by vacuum filtration, then washed with toluene (20 mL) and THF (20 mL) to give 0.7 g of **86** as a yellow solid (as a mixture of the bis-PE$_{Olig}$ and mono-PE$_{Olig}$-bound species), 90%. ^{1}H NMR (500 MHz, benzene-d_6, 70 $^\circ$C) δ: 7.86 (s, 2H), 7.54 (s,1H), 6.51 (m, 2 H), 3.83 (t, J = 6.4 Hz, 4 H), 3.35 (s, 4 H), 1.49-1.30 (bs, 420H), 0.91 (t, J = 6.6 Hz, 5H)). ^{13}C NMR (125 MHz, benzene-d_6, 70 $^\circ$C) δ 167.5, 166.9, 155.1, 151.3, 143.6, 139.9, 138.9, 119.0, 118.2, 113.1, 68.6, 59.1, 34.9, 31.8, 31.2, 30.8, 29.6, 29.4, 29.2, 26.1, 22.5, 13.6.

PE$_{Olig}$-bound salen-Cr(III) complex 87. To a 10-mL, round-bottomed flask equipped with a stir bar, a rubber septum, and a water-jacketed reflux condenser were added **86** (0.7 g), CrCl$_2$ (0.086 g, 0.7 mmol), toluene (2 mL), and DMF (2 mL) and the flask was placed under N$_2$. The mixture was placed on an oil bath regulated at 100 $^\circ$C and allowed to stir for 12 h. At this point, the flask was exposed to air and the reaction allowed to stir for 12 h. The reaction was then allowed to cool to room temperature and the product was collected by vacuum filtration and washed with THF (100 mL) to give 0.63 g of **87** as a brownish/yellow solid, 90%. UV-visible spectroscopy (toluene, 70 $^\circ$C, λ_{max} = 366 nm). Separate UV-visible analysis of **62** in toluene showed it had a λ_{max} of 366 nm with ε = 7566 M-1 cm-1, and this extinction coefficient was used to calculate the Cr(III) loading of **87**.

PE$_{Olig}$-bound salen-Mn(III) complex 88. To a 25-mL, round-bottomed flask equipped with a stir bar, a rubber septum, a pressure-equalized addition funnel and a water-jacketed reflux condenser were added **86** (0.5 g) and toluene (4 mL). The flask was placed under N$_2$ and the mixture was placed on an oil bath regulated at 100 $^\circ$C and

allowed to stir until dissolution of **86** was observed. At this point, a solution of Mn(OAc)$_2$·4H$_2$O (0.24 g, 0.33 mmol) in ethanol (2 mL) was added in a dropwise fashion via addition funnel. The reaction mixture was allowed to stir for 12 h. At this point, the flask was exposed to air and the reaction mixture was allowed to stir for 8 h. At this point, LiCl (0.013 g, 0.36 mmol) was added to the flask and the reaction mixture was allowed to stir for 12 h. The reaction was then allowed to cool to room temperature and the product was collected by vacuum filtration and washed with THF (100 mL) to give 0.5 g of **88** as a brownish/yellow solid, 100%. UV-visible spectroscopy (toluene, 70 °C, λ_{max} = 450 nm).

Ring-opening of cyclohexene oxide with TMS-N$_3$ catalyzed by 87. To a 50-mL round-bottomed Schlenk tube equipped with a stir bar and rubber septum were added complex **83** and toluene (3 mL). The reaction vessel was then placed under N$_2$ and placed on an oil bath regulated at 75 °C. Once dissolution of the solid was achieved, cyclohexene oxide (0.097 mL, 0.95 mmol) was added by syringe followed by azidotrimethylsilane (0.126 mL, 0.95 mmol). The reaction mixture was allowed to stir at 75 °C for 3 h. At this point, the reaction vessel was removed from the oil bath and allowed to cool to room temperature, inducing precipitation of the catalyst. The reaction vessel was then exposed to air and 5 mL of toluene was added. The system was then subjected to centrifugation for 10 min at 1100 rpm. The solvent was decanted and the process was repeated. The toluene layers were combined and the solvent was removed under reduced pressure to yield the product as a light yellow oil. Spectra were identical with those found in the

literature.[117] To facilitate recycling of the catalyst, toluene (3 mL) was added to the recovered catalyst and the entire process was repeated.

***N*-polyethyl-*N′*-mesitylimidizolium chloride 110.** To a 25-mL, round-bottomed flask equipped with a magnetic stir bar, a water-jacketed reflux condenser and rubber septum were added *N*-mesityl imidazole (1.06 g, 5.68 mmol) and polyethylmethane sulfonate (PE$_{Olig}$-OMs) (1.19 g, 1.89 mmol) and toluene (10 mL). The reaction vessel was placed in an oil bath regulated at 120 ℃ and allowed to stir under nitrogen for 24 h. At this point, the reaction was allowed to cool to room temperature. The precipitated product was isolated via vacuum filtration and washed with toluene (20 mL) and THF (20 mL) to give 1.6 g of the imidazolium salt as a white powder, 100 %. ^{1}H NMR (500 MHz, benzene-*d$_6$*, 70 ℃) δ: 10.20 (s, 1H), 7.65 (s, 1H), 6.63 (s, 2H), 6.34 (s, 1H), 4.71 (t, *J* = 7.4 Hz, 2H), 2.79 (s, 3H), 2.03 (s, 3H), 1.89 (s, 6H), 1.87-1.84 (m, 2H), 1.39-1.28 (b, 100H) and 0.90 (t, *J* = 5.5 Hz, 3H). ^{13}C NMR (125 MHz, benzene-*d$_6$*, 70 ℃) δ: 140.09, 139.54, 134.50, 129.35, 129.28, 50.07, 31.86, 30.55, 29.94, 26.05, 22.61, 16.87 and 13.73. To a 25 mL, round-bottomed flask equipped with a magnetic stir bar, water-jacketed reflux condenser and rubber septum was added *N*-mesityl-*N′*-polyethylimidazolium methanesulfonate (0.360 g, 0.440 mmol), LiCl (0.187 g, 4.40 mmol), toluene (9.50 mL) and THF (2.40 mL). The mixture was heated to reflux on an oil bath and allowed to stir under nitrogen for 3 h. At this point, the reaction flask was allowed to cool to room temperature. The precipitated product was isolated via vacuum filtration and washed with water (30 mL) and THF (30 mL) to yield 0.330 g of **110** as a white powder, 100 %. ^{1}H NMR (500 MHz, benzene-*d$_6$*, 70 ℃) δ: 11.14 (s, 1H), 7.75 (s,

1H), 6.66 (s, 2H), 6.39 (s, 1H), 4.83 (t, J = 6.6 Hz, 2H), 2.06 (s, 3H), 1.95 (s, 6H), 1.90-1.83 (m, 2H), 1.37-1.27 (b, 110H) and 0.90 (t, J = 5.5, 3H). ^{13}C NMR (125 MHz, benzene-d_6, 70 °C) δ: 139.90, 134.69, 131.58, 129.45, 129.41, 31.91, 29.78, 30.51, 29.78, 26.25 and 22.61.

PE$_{Olig}$-NHC-Ru complex 111. To a 50-mL, round-bottomed Schlenk tube equipped with a stir bar was added **110** (0.2g, 0.25 mmol) and the flask was then placed in the glovebox and charged with **100** (0.18 g, 0.29 mmol) and KHMDS (0.06 g, 0.25 mmol). The flask was then equipped with a rubber septum and brought out of the glovebox. At this point, degassed anhydrous toluene (4 mL) was added to the flask via syringe and the reaction flask was then placed on an oil bath regulated at 80 °C and allowed to stir for 8 h. At this point, the reaction mixture was allowed to cool to room temperature, inducing phase separation of the solid-PE$_{Olig}$ product. **111** was then isolated by vacuum filtration, washed with toluene (10 mL) and acetone (10 mL) to yield 0.2 g of **111** as a brownish-green powder, 80 %. ^{1}H NMR (500 MHz, benzene-d_6, 70 °C) δ: 16.60 (s, 1H), 6.84 (s, 2H), 6.72 (t, J = 7.2 Hz, 1H), 6.63 (s, 1H), 6.53 (d, J = 7.9 Hz, 1H), 6.26 (s, 1H), 4.95 (t, J = 8.6 Hz, 2H), 4.80-4.72 (m, 1H), 2.24 (s, 3H), 2.11 (s, 6H), 2.09 (s, 6H), 1.37-1.27 (b, 400H), 0.90 (t, J = 5.5, 11H). ^{13}C NMR (125 MHz, toluene-d_8, 100 °C) δ: 192.77, 139.82, 134.81, 129.53, 31.81, 29.62, 26.78, 22.49, 13.59.

General procedure for the ring-closing metathesis using complex 111. To a 50-mL, round-bottomed centrifuge tube, equipped with a magnetic stir bar and rubber septum was added **111** (0.022 g, 0.027 mmol) and polyethylene (0.22 g). The flask was evacuated and refilled with N$_2$ three times before degassed toluene (2.5 mL) was added

via syringe. The flask was then placed on an oil bath regulated at 65 °C. Once dissolution of the catalyst was observed diene (0.414 mmol) was added via syringe. Upon addition of the diene, the evolution of ethylene gas was observed and the reaction was allowed to stir for five minutes. After this, degassed toluene (10 mL) was added to the reaction flask via forced siphon and the system was allowed to cool to room temperature before being subjected to centrifugation for 20 minutes. The toluene layer was then removed via forced siphon and degassed toluene (10 mL) was added once more and the system was again subjected to centrifugation for 20 minutes. The toluene layer was removed via forced siphon and the supernatents were combined. The solvent was removed under reduced pressure to give pure product. Recycling of the catalyst was achieved by simply adding more of the starting diene.

PE-bound aniline 115. To a 25-mL, round-bottomed flask, equipped with a magnetic stir bar, pressure-regulated addition funnel and a rubber septum was added PE$_{Olig}$-OH (Unilin® 550, M$_n$ = 550) (1.8 g, 3.3 mmol), *N*-boc-4-amino-3,5-xylenol (1.55 g, 6.53 mmol), PPh$_3$ (1.33 g, 6.53 mmol) and toluene (25 mL). The reaction flask was placed under nitrogen and placed on an oil bath regulated at 75 °C and stirred until dissolution of all the reagents. At this time DEAD (1 mL, 6.53 mmol), in toluene (10 mL) was added in a dropwise fashion via an addition funnel. The reaction was allowed to stir for 2 h. At this time, the reaction flask was allowed to cool to room temperature affecting precipitation of PE$_{Olig}$ product. The product was isolated, as a light brown powder, via vacuum filtration and was washed with toluene (10 mL) and THF (10 mL). The product was then placed in a round-bottomed flask equipped with a stir bar. To this flask was

added toluene (5 mL) and the reaction mixture was placed on an oil bath regulated at 80 °C until dissolution of the PE was observed. At this point, methanesulfonic acid (3 mL) was added to the flask and was allowed to stir for 1 h. Water (1 mL) was added to the reaction flask and was allowed to stir vigorously for 5 min. At this time, the aqueous phase was removed via pipette and the reaction mixture was neutralized with NEt_3 (3 mL). At this point, the reaction flask was allowed to cool to room temperature, affecting precipitation of PE_{Olig} product. The product was isolated via vacuum filtration and was washed with toluene (10 mL) and acetone (10 mL) to give 1.75 g of **115** as a light brown powder, 100 %. ^1H NMR (500 MHz, benzene-d_6, 70 °C) δ: 6.66 (s, 2H), 3.82 (t, $J = 6.7$ Hz, 2H), 1.94 (s, 6 H), 1.72 (m, 2H), 1.49 − 1.20 (bs, 164H), 0.91 (t, $J = 6.6$ Hz, 5H). ^{13}C NMR (125 Hz, benzene-d_6, 70 °C) δ: 157, 136.5, 114, 103. 68, 34.8, 31.9, 29.7, 29.3, 29.2, 28.9, 26.1, 22.5, 14.0.

PE-bound bis-imine 116. To a 10-mL, round-bottomed flask, equipped with a stir bar and a rubber septum was added **115** (0.5 g, 0.55 mmol) and toluene (4 mL). The reaction mixture was then placed under N_2 and placed on an oil bath regulated at 75 °C. The mixture was stirred until complete dissolution of **115** was observed. At this point a 40 % aqueous solution of glyoxal (0.01 g, 0.38 mmol), in 2-propanol (1 mL) was added. Upon addition of glyoxal, the reaction mixture became bright yellow within 5 min. indicating formation of the bis-imine. The reaction was allowed to stir for 1 h. at which point, it was allowed to cool to room temperature, inducing phase separation of **116**. The product was isolated by vacuum filtration, washed with toluene (10 mL) and acetone (10 mL) to yield 0.51 g of **116** as a bright yellow solid, 100 %. ^1H NMR (500 MHz, benzene-d_6, 70

ºC) δ: 8.19 (s, 2H), 6.75 (s, 4H), 3.82 (t, J = 6.7 Hz, 4H), 2.18 (s, 12H), 1.80-1.60 (m, 4H), 1.49-1.20 (bs, 314H), 0.91 (t, J = 6.6 Hz, 8H). ^{13}C NMR (125 MHz, toluene-d_8, 100 ºC) δ: 163.07, 156.75, 115.0, 114.81, 68.17, 54.24, 34.8, 31.9, 29.7, 29.3, 29.2, 28.9, 26.1, 22.5, 14.0

PE-bound bis-amine 117. To a 10-mL, round-bottomed flask, equipped with a stir bar and rubber septum was added **116** (0.5 g, 0.27 mmol) and toluene (2 mL). The reaction flask was placed on an oil bath regulated at 75 °C and allowed to stir until complete dissolution of **116** was observed. At this point, BH$_3$·SMe$_2$ (1 mL, 10.6 mmol) was added via syringe. Upon addition, the reaction mixture immediately turned deep red then immediately colorless. The reaction was allowed to stir for 1 h. At this point, aqueous HCl (5 mL) was added to the reaction flask and the mixture was allowed to stir for 10 min. At this point, the aqueous phase was removed via pipette and then the reaction mixture was neutralized with NEt$_3$ (5 mL). At this point, the reaction flask was allowed to cool to room temperature, inducing phase separation of **117**. The product was isolated by vacuum filtration, washed with toluene (10 mL) and acetone (10 mL) to yield 0.49 g of **117** as a white solid, 100 %. ^{1}H NMR (500 MHz, benzene-d_6, 70 ºC) δ: 6.68 (s, 4H), 3.82 (t, J = 6.7 Hz, 4H), 2.95 (s, 4H), 2.21 (s, 12H), 1.80-1.60 (m, 4H), 1.49-1.20 (bs, 314H), 0.91 (t, J = 6.6 Hz, 8H). ^{13}C NMR (125 MHz, toluene-d_8, 100 ºC) δ: 158.49, 134.16, 133.79, 116.10, 115.73, 68.30, 47.41, 32.05, 29.59, 26.27, 22.71, 137.4, 9.56.

PE-bound imidizolinium salt 118. To a 5-mL, round-bottomed flask, equipped with a stir bar and a rubber septum were added **117** (0.3 g, 0.236 mmol), toluene (2 mL), HC(OEt)$_3$ (0.8 mL, 3.54 mmol), NH$_4$BF$_4$ (0.03 g, 0.283 mmol) and a catalytic amount of

formic acid (1 drop). The reaction flask was placed an oil bath regulated at 100 °C and allowed to stir for 16 h. At this point, the reaction flask was allowed to cool to room temperature, inducing phase separation of **118**. The product was isolated by vacuum filtration, washed with toluene (10 mL) and acetone (10 mL) to yield 0.32 g of **118** as a white powder, 100 %. ^{1}H NMR (500 MHz, benzene-d_6, 70 °C) δ: 6.55 (s, 4H), 5.93 (s, 1H), 4.11 (s, 4H), 3.73 (t, J = 6.6 Hz, 4H), 2.09 (s, 12H), 1.80-1.60 (m, 4H), 1.49-1.20 (bs, 314H), 0.91 (t, J = 6.6 Hz, 8H). ^{13}C NMR (125 MHz, benzene-d_6, 70 °C) δ:

PE-NHC-Ru complex 119. This complex was formed using the same procedure for the preparation of complex **111**. Vacuum filtration afforded **119** as a pale green solid (90 % yield). ^{1}H NMR (500 MHz, benzene-d_6, 70 °C) δ: 6.55 (s, 4H), 5.93 (s, 1H), 4.11 (s, 4H), 3.73 (t J = 6.6 Hz, 4H), 2.09 (s, 12H), 1.80-1.60 (m, 4H), 1.49-1.20 (bs, 314H), 0.91 (t, J = 6.6 Hz, 8H). ^{13}C NMR (125 MHz, toluene-d_8, 100 °C) δ: 214.60, 159.60, 153.68, 140.68, 122.08, 121.60, 114.83, 68.37, 51.56, 34.8, 31.9, 29.7, 29.3, 29.2, 28.9, 26.1, 22.5, 14.0.

General procedure for the ring-closing metathesis using complex 119. To a 50-mL, round-bottomed centrifuge tube, equipped with a magnetic stir bar and rubber septum was added **119** (0.033 g, 0.0104 mmol) and polyethylene (0.22 g). The flask is evacuated and refilled with N_2 three times before degassed toluene (2.5 mL) was added via syringe. The flask was then placed on an oil bath regulated at 65 °C. Once dissolution of the catalyst was observed the diene (0.414 mmol) was added via syringe. Upon addition of the diene, the evolution of ethylene gas was observed and the reaction was allowed to stir for five minutes. After this, degassed toluene (10 mL) was added to the reaction flask

via syringe and the system was allowed to cool to room temperature before being subjected to centrifugation for 20 minutes. The toluene layer was then removed via syringe and degassed toluene (10 mL) was added once more and the system was again subjected to centrifugation for 20 minutes. The toluene layer was removed as before and the supernatents were combined and the solvent was removed under reduced pressure to give pure product. Recycling of the catalyst was achieved by the addition of the starting diene or an equivalent of a different diene (in the case of the "one-pot" procedure in Scheme 24).

ROMP of 121 initiated with complex 111. To a 50-mL, round-bottomed Schlenk tube, equipped with a magnetic stir bar and rubber septum was added **111** (0.022 g) and **121** (0.1 g, 0.426 mmol). The flask was then evacuated and purged with N_2 3 times. At this point, dry, degassed toluene (3 mL) was added and the reaction flask was placed on an oil bath regulated at 70 $^{\circ}$C. The reaction mixture was allowed to stir for 1 h before ethyleneglycol vinyl ether (1.5 mL) was added to the reaction flask via syringe. The reaction mixture was allowed to stir for 8 h to ensure that the living polymer was completely quenched. At this point, THF (1 mL) was added to the reaction flask and the reaction mixture was allowed to cool to room temperature. At this point, the product **122** was precipitated by adding the reaction mixture in a dropwise fashion to into methanol (30 mL). **122** was isolated via vacuum filtration as a 0.07 g of a white solid, 70 %. GPC analysis shows: M_n = 19, 890 Da, M_w/M_n = 1.4.

CHAPTER VI

CONCLUSIONS

In summary, the work presented in this dissertation shows that it is possible to use soluble polyolefins (such as PIB and PE_{Olig}) as supports for homogeneous catalysts. PIB oligomers can be used as phase tags for ligands such as BINOL. The preparation of PIB-supported BINOL **57** relied on the Friedel-Crafts acylation of bis-methoxy BINOL **55** with PIB-acid chloride followed by reduction of the resulting ketone **56** and deprotection of the methoxy groups. It was also possible to prepare PIB-salen-Cr(III) complexes such as **77**. The syntheses of such ligands and metal complexes are relatively straight forward and began with the Friedel-Crafts alkylation of 2-*tert*-butylphenol with PIB-alkene to give a PIB-bound phenol derivative **51**. This was followed with formylation with $SnCl_4$ and paraformaldehyde. The resulting aldehyde **73** was then coupled with the **L**-tartrate salt of cyclohexene diamine followed by metallation with $CrCl_2$ and oxidation to give the salen-Cr(III) complex **77**. This complex was used as recoverable/reusable catalysts for the ring opening reactions of epoxides with TMS-N_3. Using a latent biphasic liquid/liquid separation system of ethanol and heptane, this catalyst can be recycled 6 times, with no loss in product yield. However, as a result of the relatively diluted reaction conditions, the enantioselectivity of this complex was diminished; most likely due to the obstruction of the bimetallic mechanism that is essential for high levels of stereoselectivity. It was also possible to develop polyolefin-bound salen-metal complexes that can be recovered using a thermomorphic solid/liquid separation technique. This was accomplished by preparing a PE_{Olig}-supported salen-

Cr(III) complex **87** starting from a regioselective Mitsunobu reaction of commercially available PE$_{Olig}$-OH to form a PE$_{Olig}$-bound salicylaldehyde derivative **85**. **85** was then coupled with ethylenediamine followed by metallation with CrCl$_2$ and oxidation to form the Cr(III) complex **87**. This complex can catalyze the ring opening reactions of epoxides under thermomorphic solid/liquid separation conditions at 80 °C. When the reaction is cooled, the catalyst precipitates and it can be isolated as a solid. This complex can be recycled 6 times with no loss in product yield. Such complexes can also serve as viable metal sequestration agents, giving products with low metal content (*ca.* 0.3 %) as shown by ICP-MS. It was also possible to prepare thermomorphic NHC ligands as well. This was achieved by preparing PE$_{Olig}$-imidazolium and imidazolinium salts, **110** and **118**, respectively. The syntheses of both were straightforward. **110** was prepared from the reaction of PE$_{Olig}$-OMs with mesitylimidazole followed by reaction with KHMDS and Hoveyda-Grubbs 1st generation **100** catalyst to give complex **111**. **119**, however, was prepared from the Mitsunobu reaction of PE$_{Olig}$-OH and *N*-boc-4-amino-3,5-xylenol followed by coupling with glyoxal. Reduction of the resulting imine followed by cyclization with triethyl orthoformate gave **118**. This species could be reacted with KHMDS and Hoveyda-Grubbs 1st generation catalyst **100** to give complex **119**. These Ru complexes were able to catalyze the RCM reactions of various substrates at 65 °C and could be recovered and reused up to 10 times with little loss in product yield. Because of the thermorphic nature of these oligomers, it was possible to perform three different reactions sequentially in a "one-pot" procedure. Each reaction product had minimal contamination from the previous reaction because as the catalyst precipitates,

the products remain in solution, allowing for their quantitative separation. ICP-MS analysis showed that the Ru leaching was *ca.* 0.63 % and 0.3 % for complexes **111** and **119**, respectively. As part of an ongoing project, we are interested in using such complexes as initiators for the ring-opening metathesis polymerization (ROMP) of strained cyclic olefins. Preliminary results show that complex **111** can successfully be used as a recoverable initiator for the polymerization of **121**. Product polymer **122** can be obtained as a white powder in decent yield with relatively low (*ca.* 4.5 %) Ru content. These polyolefin-supported catalysts enable the utilization of "Green" chemistry principles and ideas; a goal of ever-increasing interest in mainstream chemistry.

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