THE USE OF SOLUBLE POLYOLEFIN OLIGOMERS AS TOOLS IN HOMOGENEOUS CATALYSIS

A Dissertation

by

JAKKRIT SURIBOOT

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

DOCTOR OF PHILOSOPHY

Chair of Committee,	David E. Bergbreiter
Committee Members,	Daniel A. Singleton
	Karen L. Wooley
	Melissa A. Grunlan
Head of Department,	François P. Gabbai

May 2016

Major Subject: Chemistry

Copyright 2016 Jakkrit Suriboot

ABSTRACT

Soluble polyolefins such as polyethylene (PE_{Olig}) and polyisobutylene (PIB) are useful tools in catalysis. This dissertation describes several examples that these polyolefins were used to facilitate homogeneous catalysis reactions. This include the use of PE_{Olig} as protective encapsulating agent toward acid-promoted demetalation of metal-salen complexes, the use of PE_{Olig} as a cosolvent and catalyst support in ring-opening metathesis polymerization (ROMP), the use of PIB as a post-reaction Ru removal tool in olefin metathesis, and the use of PIB as a support for a pyridine ligand on Ru(II) catalyst for ring-opening metathesis polymerization (ROMP).

The stability of polyethylene oligomer (PE_{Olig})-entrapped salen-metal complexes toward acidolysis was tested by suspending these species in acidic methanol for 24 h at 25°C. The lack of metal leaching due to acid-promoted demetalation was determined using both colorimetric and ICP-MS analyses. These results were in contrast to the reported behavior of low molecular weight salen metal complexes and to results seen with a salen complex bound to divinylbenzene (DVB) crosslinked polystyrene that demetalates under acidic conditions at room temperature.

Polyethylene oligomers (PE_{Olig}) were also used as a cosolvent and soluble catalyst support in ring-opening metathesis polymerization (ROMP) reactions. As a catalyst support, this polyolefin serves as an *N*-heterocyclic carbene ligand for a ROMP catalyst, making it soluble at 70 °C and insoluble at room temperature. As a cosolvent, unfunctionalized PE oligomers facilitate quantitative separation of PE_{Olig}-bound Ru-

catalyst residues from polymer products resulting in ROMP products with Ru contamination lower than other procedures that use soluble catalysts.

Polyisobutylene (PIB) -terminated isocyanide was prepared in two steps under mild condition with high yield. Using this reagent, the RCM product of *N*,*N*-diallyl-4-methylbenzenesulfonamide could be prepared with ruthenium content as low as 44 ppm without involving purification with silica gel. However, this protocol was unsuccessful in sequestering Ru species from ROMP reaction due to an insufficient reactivity of PIB-terminated isocyanide.

At the end, this dissertation details the use of PIB as a support for a pyridine ligand on Grubbs third generation catalyst for ROMP reactions. Using the Grubbs third generation catalyst ligated by PIB-bound pyridines does not affect the reactivity of these catalysts in ROMP chemistry. However, the Ru complexes that employ PIB-bound pyridines can prepare polymer products with significantly lower Ru contamination than those prepared with Ru complex with low molecular weight pyridines. Further increasing the non-polar character of Ru catalyst can reduce Ru leaching by ca. 60%.

DEDICATION

This work is dedicated to the two most important people in my life.

Thank you so much Mom and Dad for all of your love and support.

Thank you for always believing in me.

I could not have done this without you.

ACKNOWLEDGEMENTS

This work would not have been possible without the mentorship of my advisor, Prof. David E. Bergbreiter. I thank him for his support, guidance, motivation and numerous insightful discussions.

I would also like to thank Prof. Daniel A. Singleton, Prof. Karen L. Wooley and Prof. Melissa A. Grunlan for serving in my dissertation committee and giving me suggestions for my literature seminar, preliminary exam and writing dissertation and Prof. Lei Fang for serving as a substitute committee. I would like to thank Jill Powers and Sandy Manning (Graduate Advising).

I also would like to express my gratitude to my undergraduate advisors Prof. Warinthorn Chavasiri and Prof. Sirirat Kokpol who kept the faith in me and encouraged me for pursuing further into the field. I also would like to thank Prof. Isao Kubo and Prof. Masanori Morimoto for valuable summer research experiences. I also would like to thank all the teachers who taught me chemistry during my Bachelor's degree in the BSAC program at Chulalongkorn University, Thailand. A special thank goes to all the mentors and teachers from my primary school (Saint Gabriel's College, Thailand) to the high school (Highland High School, Missouri) who showed me how amazing science is.

I also thank Drs. Yanfei Yang "Felix", Kristine Tan, Dongmei Zhang, Yue Hu "Rachel", Christopher Hobbs (my mentor), Haw-Li Su, Yun-Chin Yang "Jeff", Nilusha Priyadarshani, and Tatyana Khamatnurova for their help in solving my research problems. I also thank future Drs. Yannan Liang, Chih-Gang Chao, Mary Layne Harrell, Peerada

Samunual, Tom Malinski, and Chris Watson for being so fun loving and spending time inside and outside chemistry lab. I would also like to thank some of the students that I have had the honor to mentor: Juan Guerrero, Justin Andrews, and William Guzman. I also thank all Bergbreiter group members for all their help and support throughout these five years. Of course, 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.

I would like to thank the Thai Student Association including my roommates Drs. Termpan Pitakbunkate, Anyanee Kamkaew, and Kantapat Chansaenpak for helping me settle down and making my life cheerful in College Station. I also would like to thank Sarin Apisaksirikul for her support in those difficult times in my academic and personal life.

Finally I would like to thank my family for their love and support on my studies towards the Ph.D. degree. I also want to thank my American family the Strub for their continuous love and care.

TABLE OF CONTENTS

		Page
ABSTRACT		ii
DEDICATION		iv
ACKNOWLEDGEMENTS		v
TABLE OF CONTENTS		vii
LIST OF FIGURES		ix
LIST OF TABLES		x
CHAPTER		
I	INTRODUCTION AND LITERATURE REVIEW	1
	Heterogeneous Supported Olefin Metathesis Catalysts	4
	Homogeneous Supported Olefin Metathesis Catalysts	25
II	PROTECTIVE ENCAPSULATION OF ACID-SENSITIVE CATALYST USING POLYETHYLENE LIGANDS	44
	Introduction	44
	Results and Discussion	57
	Conclusion	66
III	POLYETHYLENE AS A COSOLVENT AND CATALYST SUPPORT IN RING-OPENING METATHESIS POLYMERIZATION (ROMP)	67
	Introduction	67
	Results and Discussion	78
	Conclusion	88

CHAPTER Page

IV POST-REACTION RUTHENIUM REMOVAL PROCESS FOR OLEFIN METATHESIS 89

Introduction 89
Results and Discussion 98
Conclusion 104

V USING PIB-SUPPORTED PYRIDINE LIGANDS WITH Ru(II) CATALYSTS FOR RING-OPENING METATHESIS POLYMERIZATION (ROMP) 105

Introduction 105
Results and Discussion 106
Conclusion 116

VI EXPERIMENTAL SECTION 118

Materials 118
Instrumentation 118
General Experimental Procedure 119

VII CONCLUSIONS 131

REFERENCES 135

LIST OF FIGURES

FIGURE Page

1 Schematic representation of (a) thermomorphic liquid/liquid, (b) a latent biphasic liquid/liquid separation and (c) a thermomorphic solid/liquid separation system 41

2 Stability experiment wash cycles exposing PE_{Olig}-salen-metal complexes to methanolic acid 61

3 Photographs of the colorimetric assays of (a) the stability experiments of complex **114** and (b) complex **122** 62

4 Solutions of polymer **153** in CH_2Cl_2 prepared either with **2** (left) or with **145** (right) 85

5 Photograph on the left depicts the phase-selectivity of pure Hoveyda-Grubbs 2nd generation catalyst and **170** (Control). Photograph on the right depicts the before and after stages of a successful controlled quench (no monomer/polymer present) using 170 under thermomorphic heptane/DMF conditions (Quench) 100

6 Kinetic studies of ROMP reaction of **148** catalyzed by PIB-supported Ru catalysts a) **176** compared to those catalyzed by **178a** and b) **177** compared to those catalyzed by **178b** 109

7 Grubbs third generation catalyst **178a** and **178b**..... 110

8 Plot of molecular weights of polymer **153** vs monomer **148** to catalyst **177** ratios..... 111

LIST OF TABLES

TABLE Page

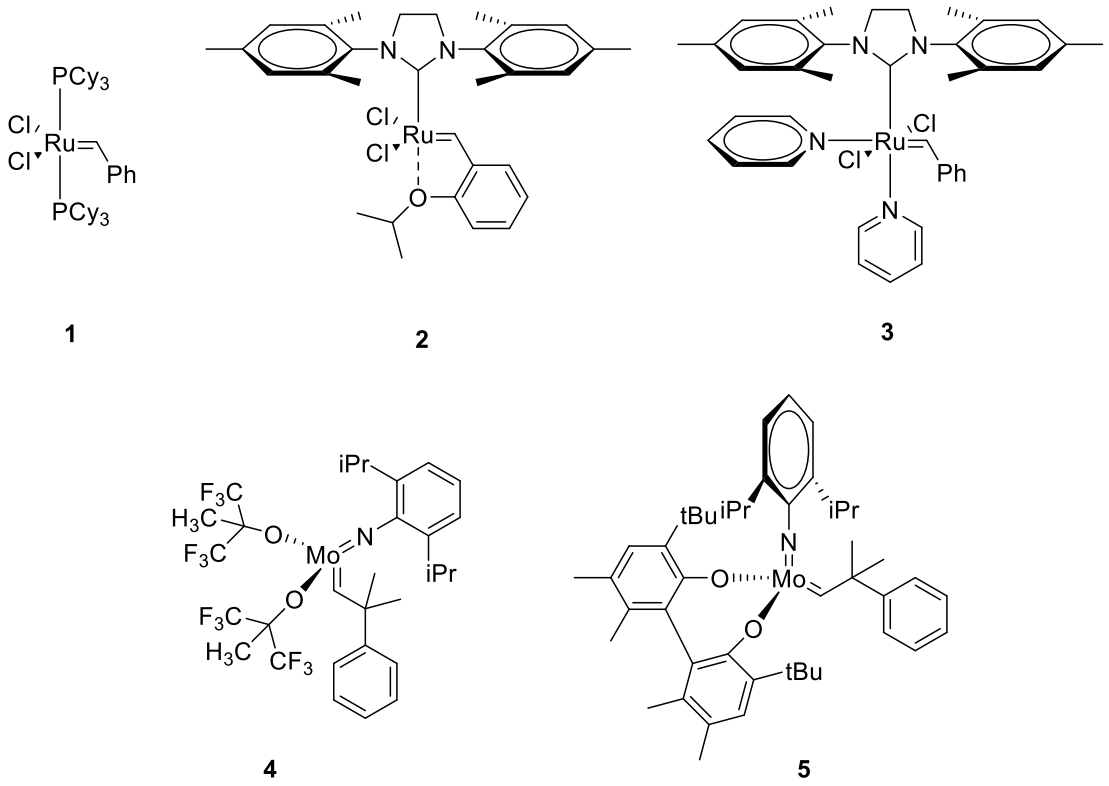
1 Results for the ROMP of Various Monomers Using Ru Complexes **145** and **158** 87

2 Results for the ROMP of Monomers **148** and **149** Using Ru Complexes **177**, **178**, and **185** 116

CHAPTER I

INTRODUCTION AND LITERATURE REVIEW

The use of metal complexes in catalysis has become a standard practice in organic synthesis. Among these catalysis reactions, olefin metathesis had been recognized as one of the most powerful tools in organic synthesis due to the facility with which this chemistry constructs carbon-carbon double bonds. The search for novel applications of olefin metathesis reaction and study of improvements of the catalysts' reactivity, stability, and selectivity have been extremely active fields since the breakthrough introduction of the current two most recognized alkylidene-types of catalyst families of ruthenium and molybdenum based complexes in 1980s by Grubbs and Schrock, respectively. The properties of these ruthenium and molybdenum olefin metathesis catalysts can be modified by alteration of the organic ligands. In the past score years, there are number of studies that introduced variety of organic ligands to both of the catalysts families. This led to a variety of novel metal complexes including (1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(*o*-isopropoxy-phenylmethylene)ruthenium (an example of a Hoveyda-Grubbs 2nd generation catalyst) **2**, [1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene]dichloro-(phenylmethylene)bis(3-bromopyridine) ruthenium(II) (a Grubbs 3rd generation catalyst) **3**, and 2,6-diisopropylphenylimido-neophylidene[(*S*)-(−)-BIPHEN]- molybdenum(VI) (an (*S*)-Schrock-Hoveyda catalyst) **5**.



Scheme 1. Some examples of olefin metathesis catalysts.

Although many studies have described how these newer versions of olefin metathesis catalysts are improved in terms of their reactivity, air and moisture stability, functional groups tolerance, and stereoselectivity, challenges still remain in using these transition metal complexes. These issues that remain challenges in search for the best solution include (i) the high cost of the transition metals especially Ru, (ii) the cost and/or tediousness of the ligand syntheses, and (iii) the potential environmental toxicological or practical concerns due to metal contamination in the product; and the waste that is often generated in the workup of these catalytic processes. The last issue is especially critical in

pharmaceutical industry, where acceptable ruthenium content in products is <10 ppm in the final compound. An efficient separation of ruthenium impurities is also important in the case of polymeric materials used in electronic or device applications. In still other cases like in synthesis of chemical intermediates, an efficient separation of ruthenium impurities is important as ruthenium residues can lead to undesirable side-reactions like hydrogenation or alkene isomerization in products.

There are several ways to approach these problems. One of these methods is to simply reduce the amount of catalyst that is used in the reaction. Originally, ring closing metathesis (RCM) reactions required catalyst loading to be 1-5 % or greater depending on specific application. However, this level of catalyst loadings seems to be an overestimate according to the work by Mol and Dinger in 2002. In their report, they found that catalyst loadings could be as low as 1 ppm or 0.0001 mol% showing that Ru-catalyzed olefin metathesis was operational at catalyst loadings with several magnitudes lower than normally reported. With suitably active catalysts, the effective TON can be as high as 600,000. While with theses catalyst loadings the reaction never reached 100% conversion, their goal was to investigate what the maximized effective TON could be. Their work emphasizing the desirability of low catalyst loadings in olefin metathesis also attracted interest from Grubbs' group and Caltech's Center of Catalysis and Chemical Synthesis. Those groups subsequently reported success in reducing the catalyst loadings to be as low as 25 ppm in ring-closing metathesis of diethyl diallylmalonate, by employing the more steric Ru-based catalysts.

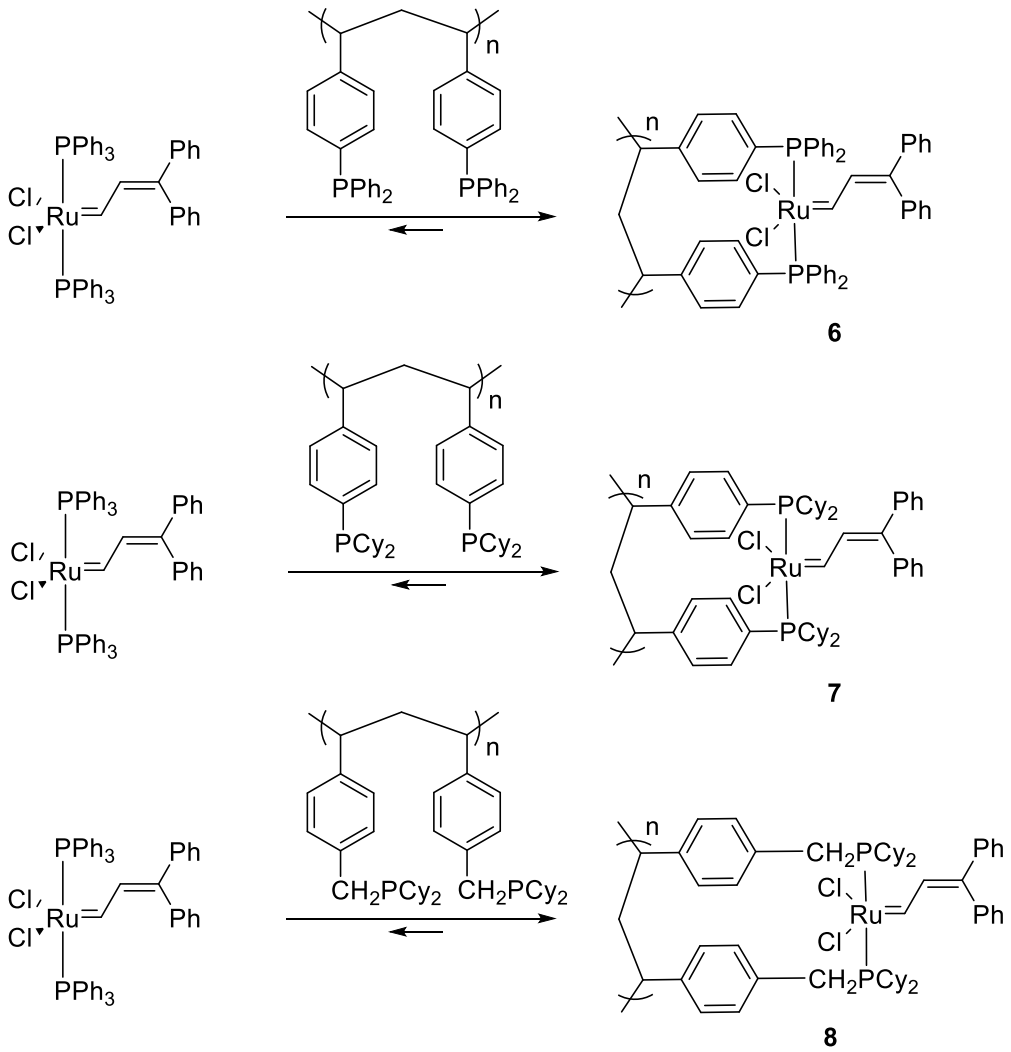
Another strategy to solve the problems arise from reaction catalyzed by transition metal complexes is to design the catalyst that can be recovered and recycled. Various methods to recover and recycle the catalyst can be used. One way is to design catalyst with insoluble tags such as silica gel or insoluble polymers (heterogeneous supports). Another way is to design a catalyst with soluble tags such as ionic liquid functionalities, or perfluorinated hydrocarbons, or soluble polymers (homogeneous supports). Ideally, these modifications should lead to an efficient metals/products separation process. This would involve simple filtration in the case of heterogeneous supports and would involve liquid/liquid extraction in the case of homogeneous supports. Both of these approaches have been used with ruthenium-based olefin metathesis catalysts.

Heterogeneous Supported Olefin Metathesis Catalysts

The use of heterogeneous/solid insoluble support is among the oldest and most widely use tool in catalyst modification for the purpose of separation and isolation of catalysts from the products. The first solid insoluble organic support introduced to the scientific community was based on the revolutionary work of Merrifield that was published in 1959, using cross-linked polystyrene resins (Merrifield's resin) in peptide and nucleotide synthesis.[1] The discovery of Merrifield led to many studies using similar heterogeneous polymeric materials as solid supports for homogeneous catalysts. As is true in peptide synthesis, solid insoluble supported catalyst that use insoluble polymer supports have the advantage of allowing for separation of catalyst and reaction mixture via simple filtration. In some cases, heterogeneous supports can also improve catalyst stability and

prevent bimolecular decomposition pathways via a phenomenon known as site isolation.[2-5] However, in other cases, catalyst activity changes in undesirable ways. Several examples of insoluble supports for olefin metathesis catalysts will be discussed shortly. These materials include cross-linked polystyrene, silica gel, and polynorbornene monolith.

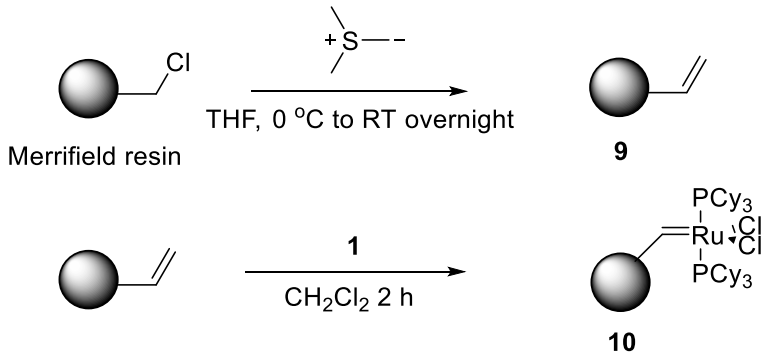
In 1995, Grubbs and Nguyen described the first well-defined polymer-supported olefin metathesis catalysts that produced living polymers in solution.[6] In this study, a series of $Cl_2(PR_3)_2Ru{=}CH{-}CH{=}CPh_2$ olefin metathesis catalysts were attached on a polystyrene-divinylbenzene (PS-DVB) support and their activities were explored. These solid-supported catalysts showed activities that were similar to that of their homogeneous analogs, with activity that varied depending on the nature of PS-supported phosphine ligands. These supported catalysts had extended lifetimes. This was ascribed to the reduced diffusivity of the catalyst molecules on the polystyrene support, which prevents a decomposition pathway that occurs via a bimolecular reaction. However, while **8** was recycled three times in a metathesis reaction of *cis*-2-pentene to form cross metathesis products of 3-hexene and 2-butene, the catalyst lost 20% of its activity after each cycle. These catalysts showed also a low initiation rate due to (i) incomplete substitution of phosphine, (ii) the diffusion limit of olefin into the cavities of crosslinked PS-DVB support, and (iii) the local high concentration of phosphine on the support.



Scheme 2. Polystyrene-divinylbenzene (PS-DVB) supported olefin metathesis catalysts **6 – 8**.

Four years after the first reported of well-defined olefin metathesis catalyst, Barrett and co-workers introduced a new concept called the "boomerang" effect. This was suggested as an improved way to use heterogeneous-supported olefin metathesis catalyst.[7] In this case, the necessary catalyst was synthesized by simply shaking of Grubbs 1st

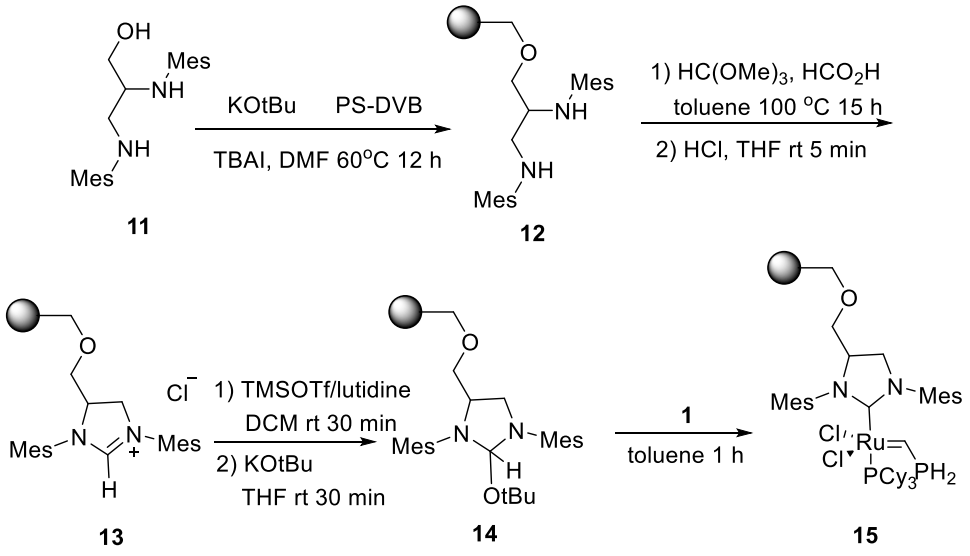
generation catalyst and vinyl polystyrene[8] for 2 h in dichloromethane followed by filtration. This catalyst, once dried, was claimed to be indefinitely stable under normal atmospheric conditions with no loss of activity.



Scheme 3. Merrifield resin-supported Grubbs 1st generation catalyst **10**.

In this so-called boomerang reaction, the catalyst reportedly leaves the heterogeneous support upon the initiation, becoming a homogeneous catalyst during the reaction of ring-closing metathesis (RCM) reaction. Then the resin recaptures it after the completion of the reaction. This behavior of the ruthenium catalyst where it flies off the resin and returns later was likened to a “boomerang”. In this work, the catalyst can be recycled up to three times with Ru contamination in the product of 500 ppm. In this recycling, the solid-supported catalyst was separated from the reaction mixture by simple filtration and the product was isolated by evaporation of the solvent. The Ru contamination level in the product can be improved by further purification step using column chromatography to be as low as 55 ppm.

Inspired by Grubbs and Barrett's works on polymer-supported catalysts and ruthenium-based alkylidene catalysts with *N*-heterocyclic carbene (NHC) ligands, Blechert and co-workers described the synthesis of permanently immobilized Grubbs 2nd generation catalysts on Merrifield-polystyrene.[9] These catalysts with *N*-heterocyclic carbene ligands have increased activity in metathesis chemistry compared to that of **1** but maintain the stability toward air and moisture, previously attributed to **1**. The *N*-heterocyclic carbene ligands are stronger Lewis base than the phosphine ligands, which dissociate from the ruthenium center to initiate catalysis. Since the NHC ligand should remain bound to the ruthenium center during and after the metathesis reaction[10] a permanently immobilized highly reactive catalyst could be prepared by attaching the *N*-heterocyclic carbene ligand of Grubbs 2nd generation catalyst to the polymeric support as shown in Scheme 4.

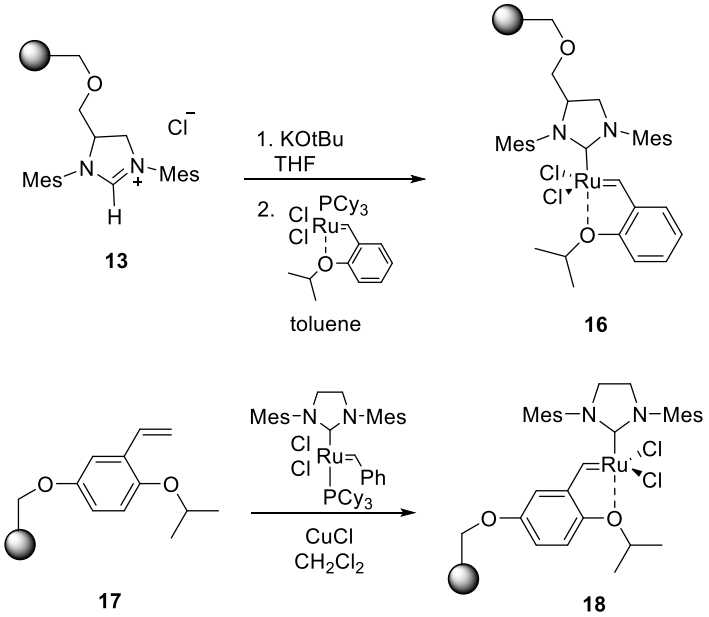


Scheme 4. Synthesis of permanently immobilized Grubbs 2nd generation catalyst **15**.

In the first example of this chemistry, the solid-supported catalyst **15** was prepared by ligand exchange between a PS-DVB-supported *N*-heterocyclic carbene ligand and the phosphine ligand on Grubbs 1st generation catalyst. The necessary PS-supported NHC ligand was synthesized by attaching diamine **11** to 1% DVB-PS by an ether linkage to yield compound **12**. The resulting Merrifield-polystyrene-supported diamine was then cyclized to form a solid-supported 3,4-dimesityl-4,5-dihydroimidazolium chloride **13**. After that compound **13** was converted to **14** by treating with TMSOTf/lutidine and the product of this reaction was then deprotected *in situ* in the presence of **1** to yield the desired supported ruthenium complex **15** as a pinkish-brown material. This heterogeneous-supported ruthenium catalyst was able to successfully catalyze different metathesis reactions including, RCM, rearrangement, and yne-ene metathesis reactions. In the case of **15**, up to four cycles of complete cyclization could be effected in an RCM reaction of diallyl malonic acid diethyl ester. The authors did not report a value of ruthenium contamination in any products only stating that the products were obtained as colorless solids or oils.

Followed the previous publication on Merrifield-supported ruthenium olefin metathesis catalyst, Blechert et al. reported improved versions of solid-supported Hoveyda-Grubbs 2nd generation complexes utilized both Merrifield and Wang resins.[11] The recycle tests of these two catalysts were conducted with the results showing that both catalysts can be recycled up to four runs in RCM reaction with even in catalytic activity. However, the ability to catalyze cross metathesis reactions of complex **18** was showed to be higher than that of complex **16**. The authors suggested that the superior activity of

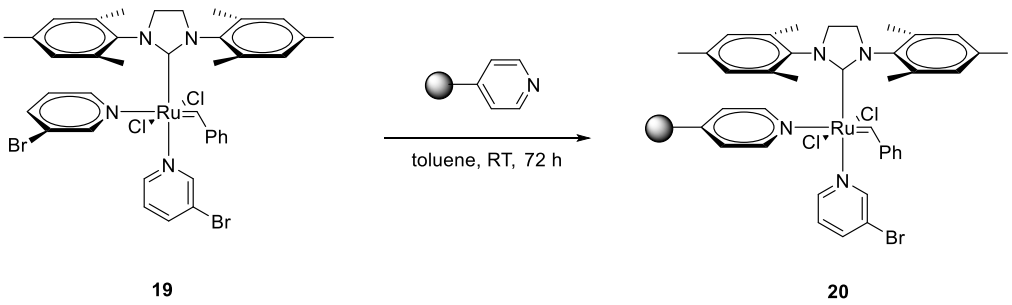
complex **18** owe to the ability of the catalyst to dissociate in solution, becoming homogeneous active species, unlike complex **16**.



Scheme 5. Synthesis of solid-supported Hoveyda-Grubbs 2nd generation catalysts **16** and **18**.

After the invention of new highly active ruthenium olefin metathesis catalyst as Grubbs 3rd generation, which can catalyze cross metathesis reaction of substrate containing nitrile group and produce a narrow polydispersity (PDI) of polymer from ring-opening metathesis polymerization, Grela and Kirschning reported a studied of the solid-supported version of this catalyst in 2005.[12] The concept of using this supported catalyst was in its potential to be used in a continuous flow process due to the ability to reload the

catalytic species onto the same solid support. The attachment has to be strong enough to minimize the leaching of ruthenium species and the solid phase can be reactivated with fresh catalyst. The cross-linked polyvinyl pyridine-divinylbenzene (PVP-DVB) was prepared by heating vinyl pyridine, divinylbenzene, and AIBN at 70 °C in non-polar solvent (C_{14}-C_{17} mixture) for 12 h followed by precipitation. The solid support PVP-DVB was then allowed to react with Grubbs 3rd generation in toluene for 72 h to yield the desire catalyst.

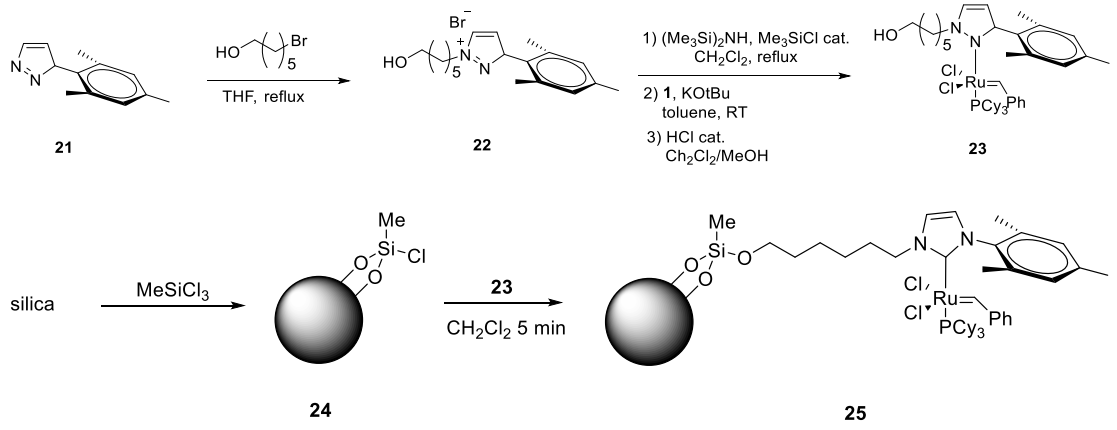


Scheme 6. Synthesis of polyvinyl pyridine-divinylbenzene (PVP-DVB) supported Grubbs 3rd generation catalyst.

The recyclability of PVP-DVB-supported Grubbs 3rd generation was tested in ring-closing metathesis reaction of diethyl diallylmalonate at 110 °C. This solid-supported catalyst showed activity up to 5 cycles with the decreasing in product yield for each run. This issue was reasoned by the authors to be due to lack of thermal stability or the problem of the leaching in each catalytic cycle. However, the advantage of this PVP-DVB-supported

Grubbs 3rd generation over other known solid phase concepts is its ability to be reactivated by washing protocol (1 N HCl, 1 N NaOH, H2O, MeOH, toluene, then addition of **19**).

Other materials commonly used as solid supports include silica-based materials. Furstner and co-workers reported the synthesis of an immobilized Grubbs 2nd generation ruthenium complex on silica gel using hydroxyalkyl groups on *N*-heterocyclic carbene ligand.[13] The preparation of this catalyst is straightforward as shown in below.

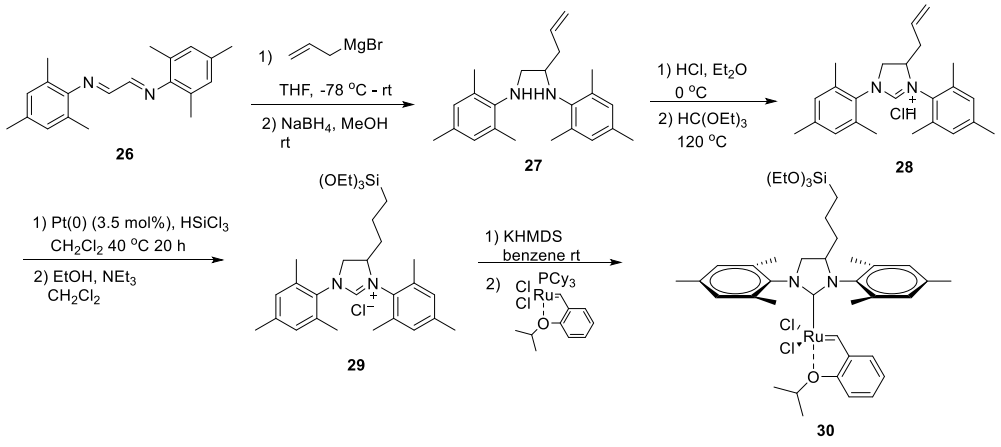


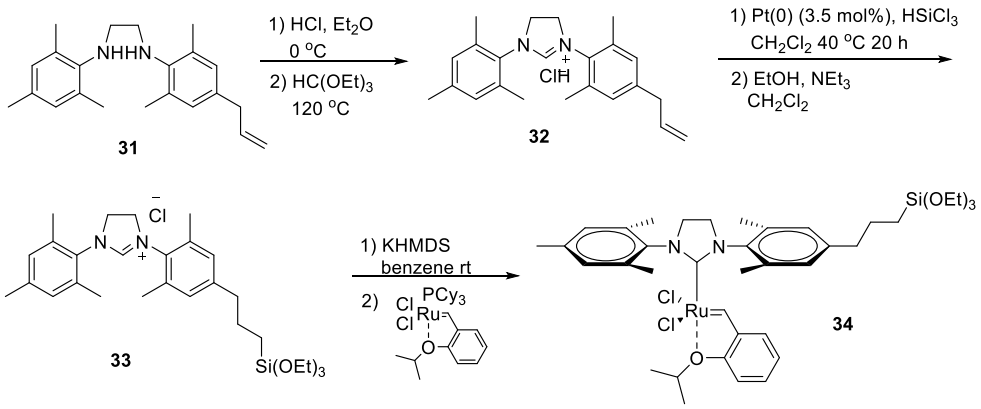
Scheme 7. Synthesis of silica-supported Grubbs 2nd generation catalyst **25**.

In this synthesis, a hydroxyalkyl *N*-heterocyclic carbene ligand was first prepared starting from an *N*-mesitylimidazole **21** using 1-hydroxy-ω-bromopentane to form the imidazolium salt **22**. This salt was then O-silylated in the presence of hexamethyldisilazane using a catalytic amount of TMSCl in dichloromethane at reflux. The carbene ligand was then deprotonated by KOtBu in toluene and in the presence of complex **1** to afford the ruthenium complex **23**. Chlorosilane functionalities on silica gel's

surface served as an anchoring group for complex **23**. These anchoring groups were introduced by treating commercially available silica gel with $MeSiCl_3$ in dichloromethane for 30 min. In this anchoring chemistry, complex **23** was added to the suspension of the activated silica gel. In this reaction, the solution turns colorless while the silica turns red-velvet indicating deposition of the catalyst on the surface. This immobilized catalyst can be recycled in RCM reaction up to three cycles, although the immobilized catalyst had lower catalytic activity compare to its homogeneous analog.

Grubbs and co-workers described other improved versions of silica-supported olefin metathesis ruthenium catalysts.[14] The new architectures of these catalysts improve recyclability and eliminate issues associated with the decomposition of the ruthenium complex via bimolecular pathway. Such immobilized ruthenium catalysts on silica support have less intermolecular activity between the catalysts—the same phenomena reported earlier by Grubbs' group for site isolated DVB-PS supported species.



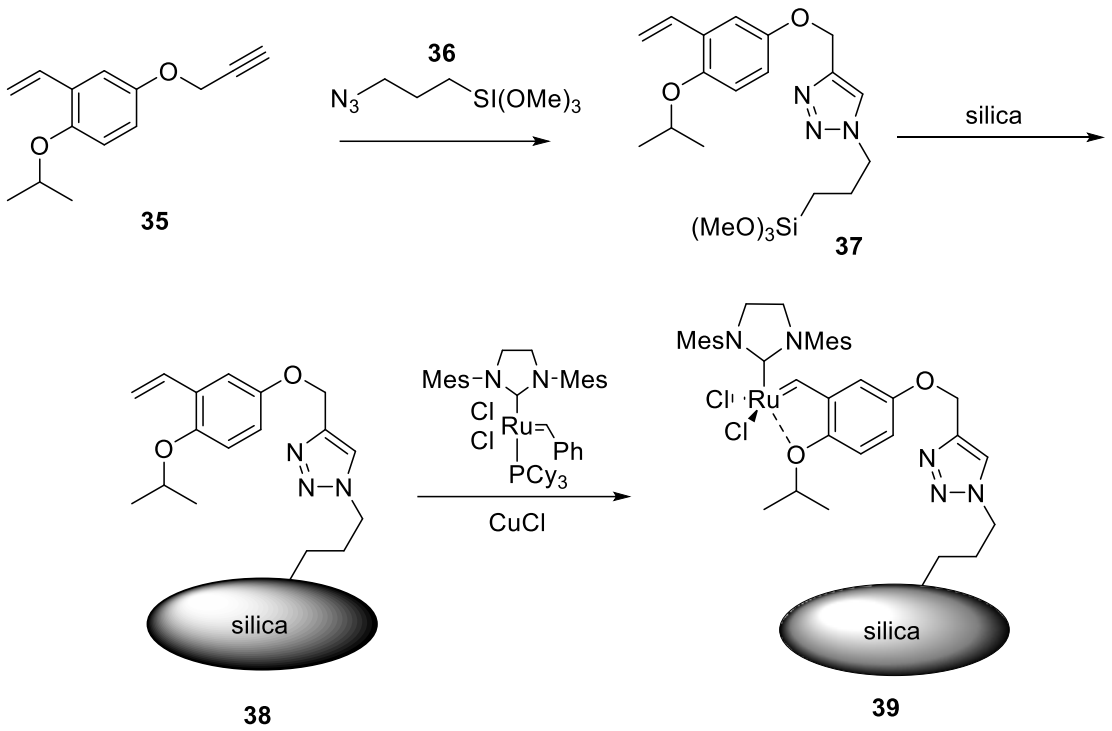


Scheme 8. Synthesis of silica-supported Hoveyda-Grubbs 2nd generation catalyst **30** and **34**.

The silica-supported complexes **30** and **34** were competent catalysts in RCM and CM reactions and were compared to their homogeneous analogs. Catalyst **34** was shown to have slightly lower catalytic activity than **30**. The ruthenium leaching studied by ICP-MS revealed the contamination level in products to be less than 5 ppb for those prepared by both **30** and **34**. The authors also showed that immobilized ruthenium catalyst **30** can be recycled up to eight times with conversion of 60% - 80% when the reaction time was 2 h and can reach 100% with reaction time of 12 h. However, the accuracy of detected Ru level is questionable, since the result number was below the detection limit of ICP-MS.

Ying et al. have also described using click chemistry for the immobilzation of Hoveyda-Grubbs type complexes on nanoporous silica.[15] The heterogeneous-supported catalyst they prepared exhibits good activity and stability as well as recyclability. In addition, these authors demonstrated that this catalyst can be used in a circulating flow reactor. The catalyst was reused in RCM reactions over 8 times with overall conversions

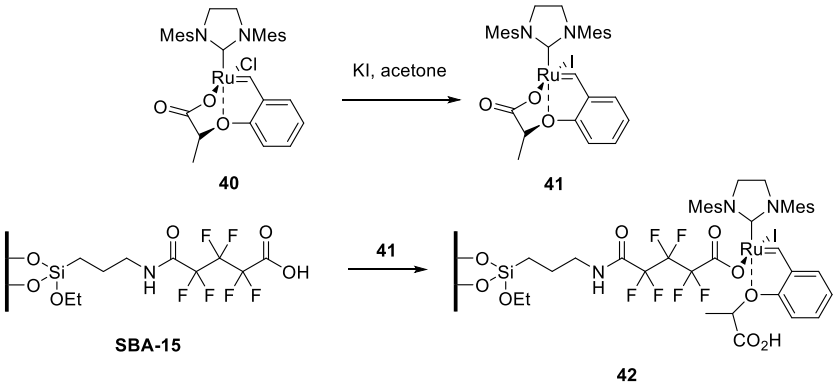
of 90% with Ru leaching levels of 11.3 ppm at the first 60 min and 1.6 ppm at 180 min based on ICP-MS analysis of the isolated products.



Scheme 9. Synthesis of silica-supported Hoveyda-Grubbs 2nd generation catalyst **39**.

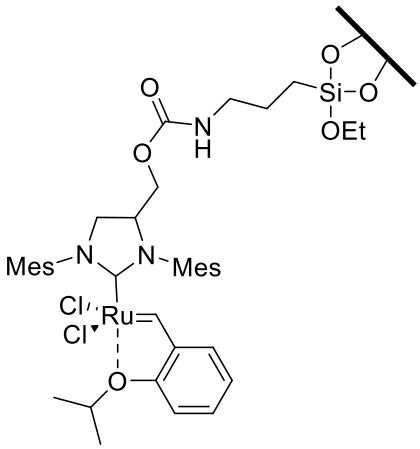
Balcar and co-workers reported the immobilization of Hoveyda-Grubbs type catalysts onto commercial molecular sieves.[16] These SBA-15 molecular sieves possess several advantages including high surface area, narrow pore size distribution, and high thermal and mechanical stability. The solid-supported ruthenium complex on such sieves was shown to be competent as RCM catalyst and the leaching of Ru into product was

found to be as low as 17 ppm. However, attempts to recycle this catalyst were unsuccessful, with the conversion reaching 90% for only two cycles.



Scheme 10. Synthesis of SBA-15-supported ruthenium olefin metathesis catalyst **42**.

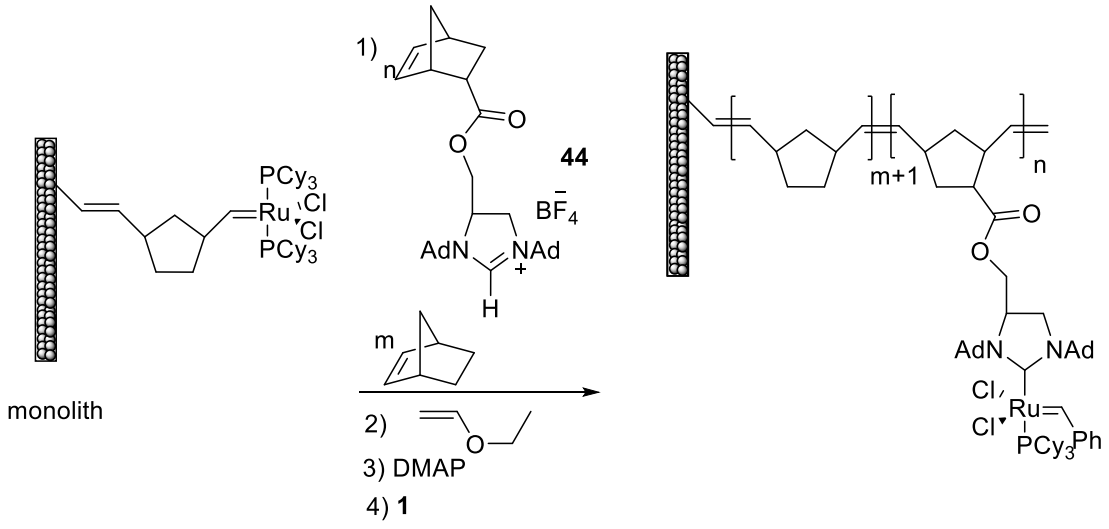
More recently, Monge-Marcet and co-workers reported a synthesis of recyclable silica-supported Hoveyda-Grubbs type complex using an NHC ligand.[17] This catalyst proved to be recyclable for alkene ring-closing metathesis and alkyne hydrosilylation reactions up to three cycles.



43

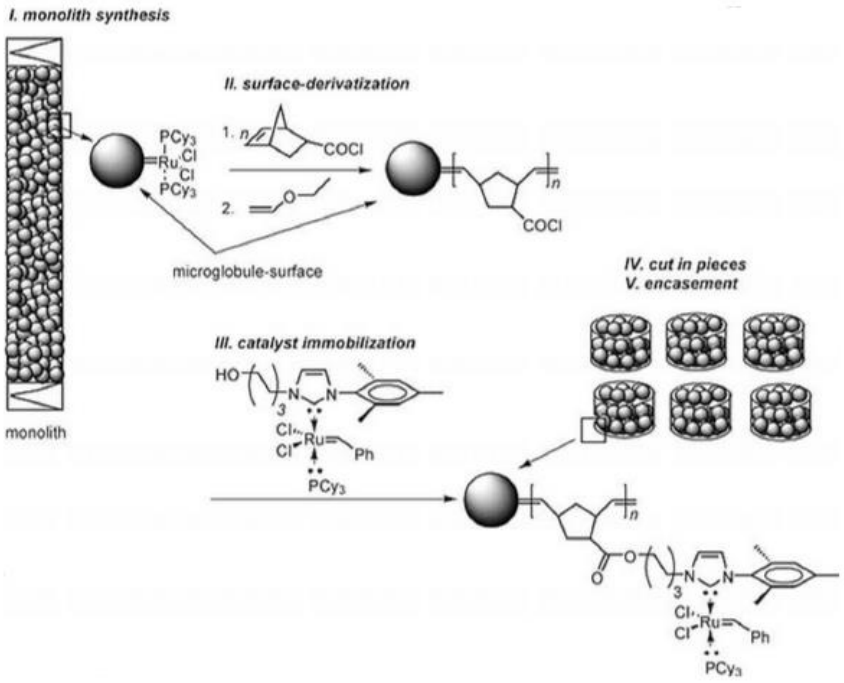
Scheme 11. Silica-supported Hoveyda-Grubbs 2nd generation catalyst **43**.

Alternative organic supports that have been used as catalysts' supports are monolithic materials. These materials have been known since 1970s[18] but have received more attention by Frechet and Svec as high-performance separation media[19,20], scavenger, and reagent supports.[21,22] Such media have been used too by Buchmeiser and co-workers. They described a synthetic route to a monolith-supported ruthenium olefin metathesis catalyst.[23] The monolith was generated through ring-opening metathesis copolymerization of norbornene (NBE) and 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo*-*endo*-dimethanonaphthalene (DMN-H6) in the presence of dichloromethane and 2-propanol within a borosilicate column. The functionalization of the catalyst onto the monolith was achieved by feeding the solid support with compound **1** in dichloromethane.



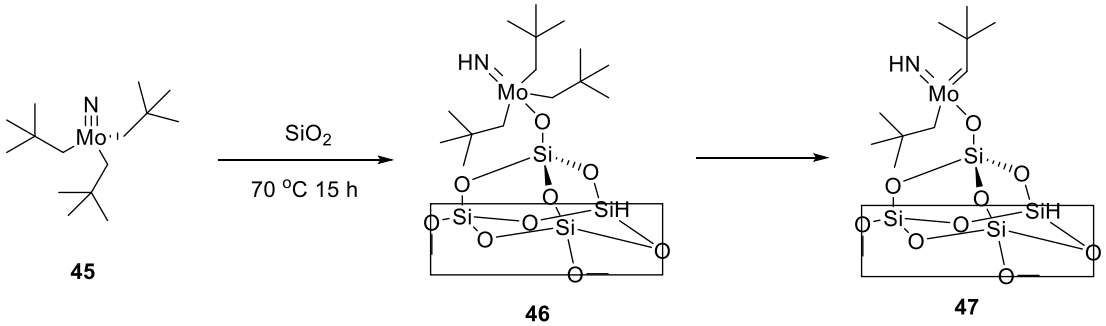
Scheme 12. Synthesis of monolith-supported ruthenium olefin metathesis catalyst.

The monolith-supported ruthenium complex showed high activity toward RCM and ROMP, where the *cis* and *trans* ratio of the polymer products are the same as those obtained using the analogous homogeneous catalyst. In addition, the leaching level of ruthenium in RCM products was shown to be 70 ppm. In subsequent work, Buchmeiser and Furstner et al. reported that a similar monolith disk-immobilized Grubbs-type catalyst could be used in RCM, ring-opening cross metathesis (ROCM), and enyne metathesis (EYM).[24] The required loading for this catalyst was as low as 0.23-0.59 mol% with the metal leaching of 3%.



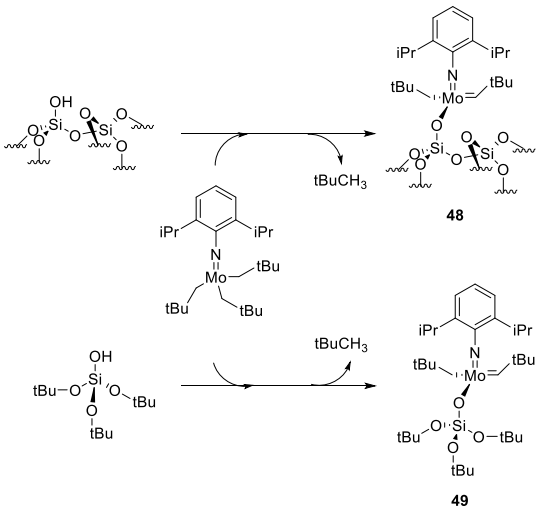
Scheme 13. Synthesis of monolith disk-supported Grubbs 2nd generation catalyst.

Schrock's molybdenum catalysts have also been made into heterogeneous complexes in order to facilitate the separation of catalyst and product, however, only few reports addressing this point exist, perhaps because of the sensitivity of these catalysts toward air and moisture. The Basset group reported the first well-defined silica-supported molybdenum olefin metathesis catalyst in 1996.[25] The molybdenum complex **45** was immobilized onto silica disc. A loss of neopentane yielded an active silica-supported catalyst **47**. The results showed that immobilized complex **47** can be used to catalyze the ROMP reactions of norbornene and *cis*-cyclooctene at temperature of 25 °C.



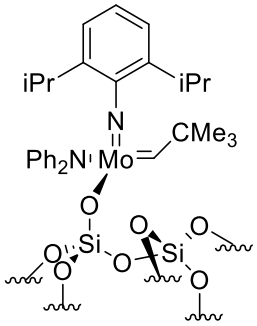
Scheme 14. Synthesis of silica-supported Schrock catalyst **47**.

In 2006, Schrock and co-workers reported the synthesis of well-defined surface immobilized molybdenum catalysts **48** and **49**.[26] These two silica-supported catalysts showed very similar in catalytic activity in cross metathesis reactions. However, the silica-supported **48** is more stable than **49**, a difference that was ascribed to site isolation of metal complexes on the silica support.



Scheme 15. Synthesis of silica-supported Schrock catalyst **48** and **49**.

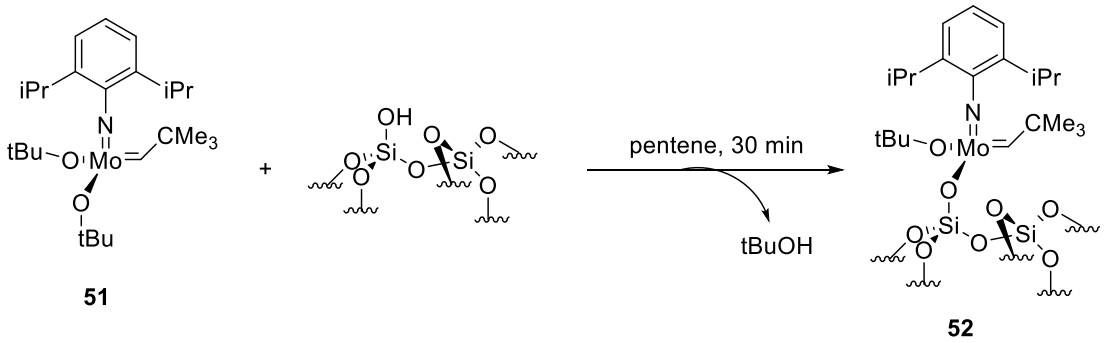
Shortly later, Schrock and co-workers developed more active, stable, and selective silica supported molybdenum olefin metathesis catalysts.[27] The increase in reactivity was achieved by replacing one imido group with a siloxy group from the surface. Keeping one remaining imido ligand enhanced the stability of the molybdenum catalyst.



50

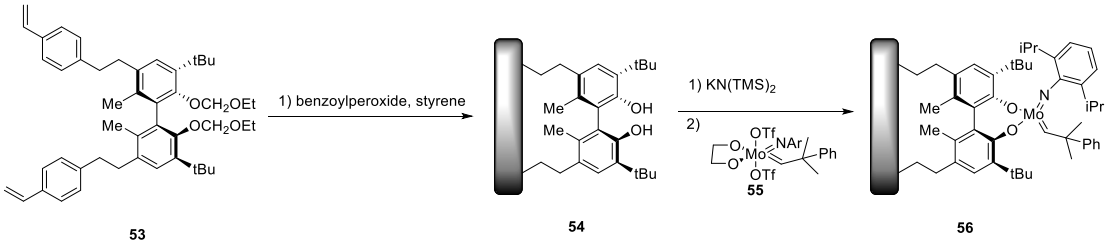
Scheme 16. Silica-supported Schrock catalyst **50**.

More recently, Schrock et al. had reported yet another silica immobilized molybdenum alkene metathesis catalyst that showed an enhancement in metathesis activity.[28] The catalyst was created by replacing one of the *t*BuO ligands with a siloxy group from the silica support as shown below.



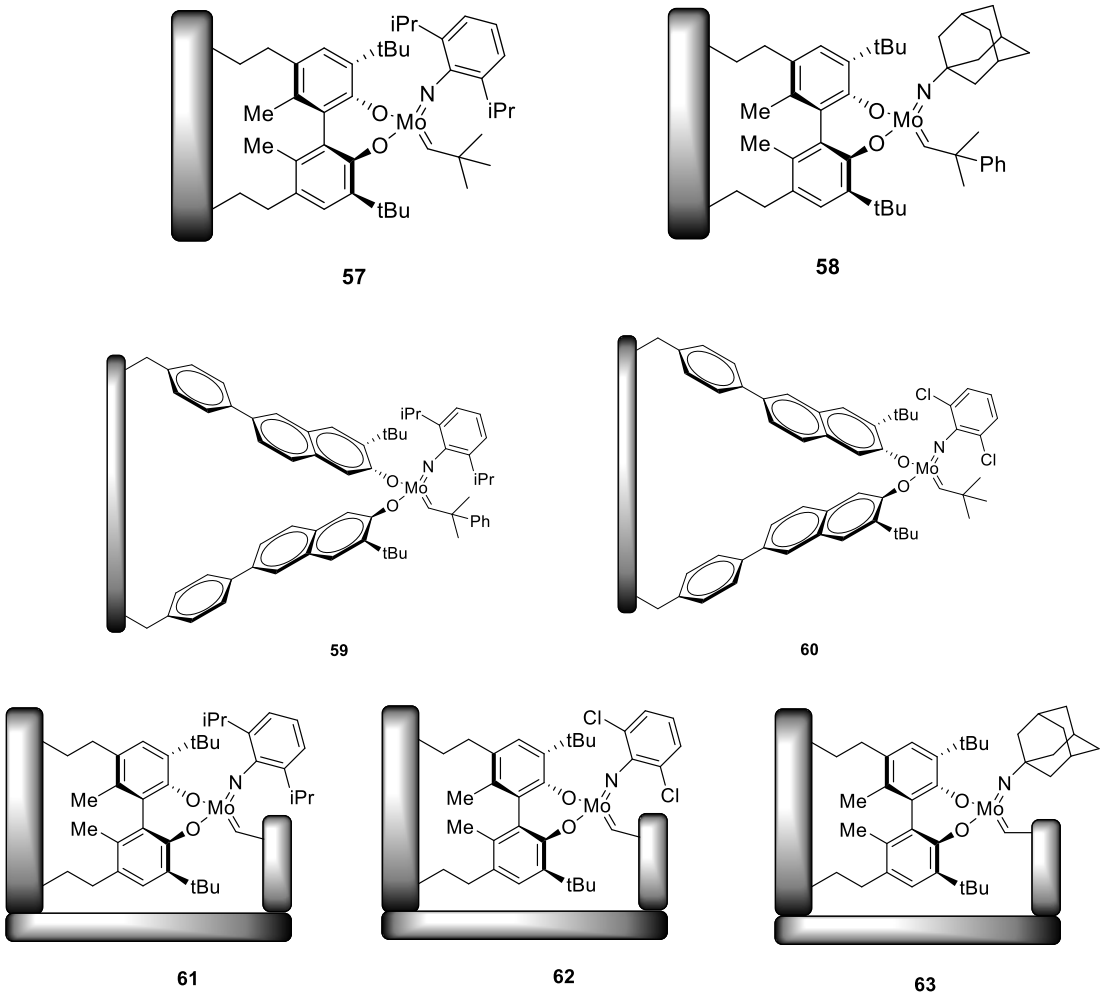
Scheme 17. Synthesis of silica-supported Schrock catalyst **52**.

In 2002, Hoveyda and Schrock et al. reported the first recyclable solid-supported chiral olefin metathesis catalyst.[29] This polystyrene-based-supported chiral catalyst was synthesized by copolymerized bis-styrene ligand **53** with styrene to form **54**. The resulting solid-supported ligand was then treated with **55** to yield dark brown color powder of catalyst **56**. This solid-supported catalyst showed similar activity to the homogeneous analog for both in terms of yield and enantioselectivity in asymmetric ring-closing metathesis reactions. The polymer-supported complex can be recycled three times with conversion significantly dropped in the third cycle. However, there was little different in enantioselectivity between each of the three cycles. This catalyst also affords good recoverability of the catalyst with only 3% leaching of molybdenum was found in the product.



Scheme 18. Synthesis of polystyrene-supported Schrock chiral catalyst **56**.

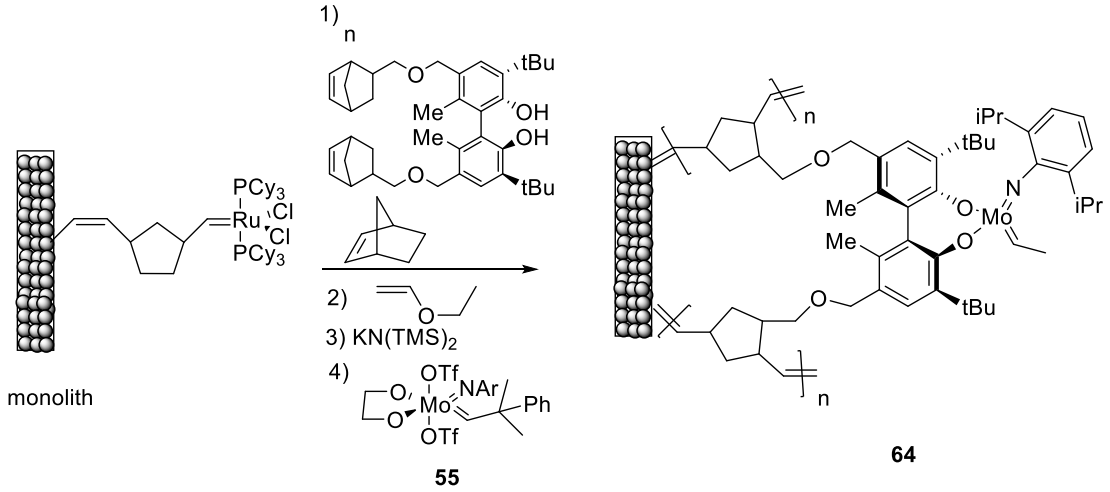
Three years after the first report from Hoveyda and Schrock et al. on solid-supported chiral molybdenum olefin metathesis catalysts, they reported a new supported catalysts using both with polystyrene- and polynorbornene-based supports, **57-60** and **61-63**, respectively.[30] These polymer-supported catalysts can be separated from the reaction mixture by simple filtration and the leaching of molybdenum in the product was found to be as low as 1%, while the reactivity and enantioselectivity were similar to homogeneous counterparts of these supported catalysts.



Scheme 19. Polystyrene-based-supported Schrock catalyst **57** – **60** and polynorbornene-based-supported Schrock catalyst **61** – **63**.

The monolith material described above that was used to support ruthenium catalysts has also used as support on Schrock-type catalysts by the groups of Buchmeiser and Furstner.[24] In order to immobilize the chiral molybdenum catalyst on a monolith support, the bis-norbornene ligand was grafted on the surface through ring-opening metathesis polymerization, followed by the treatment of resulting monolith-supported

ligand with $KN(TMS)_2$ and **55**. The monolith-supported chiral catalyst **64** was used with excellent product yields and with excellent results in term of recovery of the catalyst. In most cases, the reaction proceeded with yields that exceeded 99% with the molybdenum contamination in the products being less than 2% in all cases. The enantioselectivity was also comparable to its homogeneous analog with slightly lower in ees.



Scheme 20. Synthesis of monolith-supported Schrock catalyst **64**.

Homogeneous Supported Olefin Metathesis Catalysts

Up to this point, this discussion has focused on the immobilization of olefin metathesis catalysts on heterogeneous supports. While this has been a common technique to isolate and recycle the catalysts, it is not the only possible scheme for catalysts separation. Soluble phase tag methods have been developed as an alternative tool for

separation process between catalysts and the products. The supports for this technique do not always have to be macromolecules—small molecules like fluorous tag, or ionic tag, or redox-switchable tag have also been utilized in the catalyst separation technique.

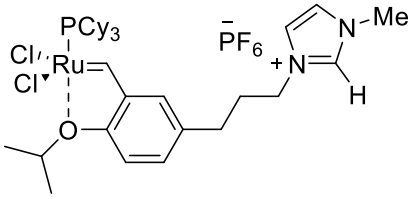
Typical problems of heterogeneized catalysts include observation that the reactivity and selectivity can differ from what is seen with homogeneous catalysts because of the heterogeneity of the catalyst. Characterization too can be a problem. These problems reflect the fact that the advantage of heterogeneous catalysts, which is the ease of separating them from the reaction mixture, is an issue not just at the separation step but also during the reaction and during the catalyst synthesis. Homogeneous catalysts in contrast have a problem in that they are in solution with the product at the end of the reaction.

One approach to deal with separation issues of homogeneous catalyst is to modify the catalyst soluble supports or tags that will allow the catalysts to perform as before in solution but that will allow the catalyst to be separated from the reaction mixtures easily and effectively.

An example of this approach is the use of ionic liquid (IL) immobilized catalysts. Ionic liquid was proposed to be used as an alternative solvent because of its unique properties including non-volatility, high stability, and good recyclability.[31] These alternative solvents are also immiscible with most of organic solvents. Thus, they can be used in catalytic reactions as a recyclable phase. Buijsman and co-workers reported the use of Grubbs 1st generation catalyst in RCM reaction in 1-butyl-3-methylimidazolium hexafluorophosphate (BMI□PF6) media. This catalyst was recycled up to three times.[32]

One year later, Dixneuf et al. also reported the use of BMI□PF6 as solvent in RCM reactions catalyzed by a ruthenium allenylidine salt and were able to recycle the catalyst for two cycles.[33]

Inspired by this work, Guillemin and co-workers introduced the ionic liquid-tagged ruthenium catalyst in order to minimize the leaching of the catalyst from the ionic liquid phase.[34]



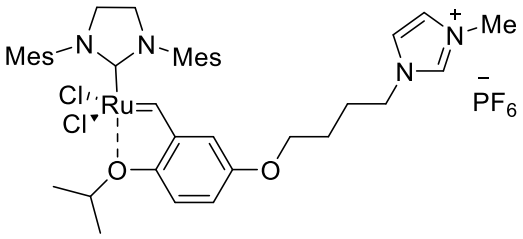
65

Scheme 21. Ionic liquid-tagged Hoveyda-Grubbs 1st generation catalyst **65**.

This ionic liquid-bound catalyst **65** complete an RCM reaction of diallyl tosylamide with BMI□PF6 as a solvent at 60 °C in 45 min using 2.5 mol% of **65**. The isolation of the product was achieved by extraction with toluene and the ionic liquid phase containing **65** was reused for an RCM reaction of diallyl tosylamide for 8 cycles. Importantly, this catalyst was stable enough to be able to catalyze the ninth cycle without any loss in activity after three months.

Yao and Sheets reported a synthesis of an ionic liquid-tagged Hoveyda-Grubbs 2nd generation catalyst **66**.[35] The catalyst and ionic liquid were recycled up to 17 cycles for

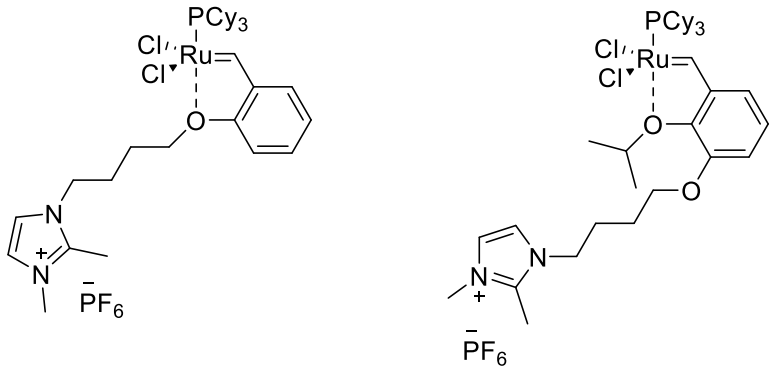
RCM reaction of diallyl tosylamide without any loss in activity, while the untagged analog of **66** lost its activity in the second and subsequent runs. The author showed that the ionic liquid tag is important for the recyclability of the catalyst in ionic liquid solution.



66

Scheme 22. Ionic liquid-tagged Hoveyda-Grubbs 2nd generation catalyst **66**.

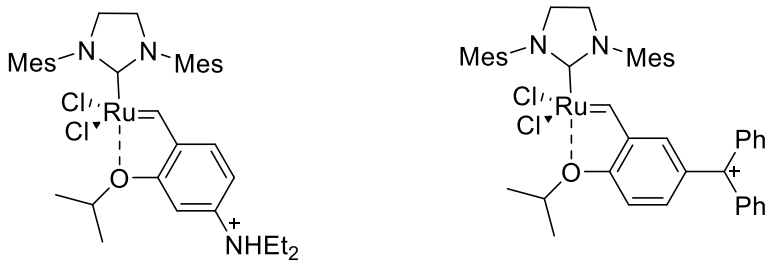
In 2007, Dixneuf and co-workers reported an attempt to improve the performance of ionic liquid-bound ruthenium complex **65** by modifying the structure of ionic liquid tag.[36] They were able to synthesize complexes **67** and **68**. However, while the activities of both catalysts were good for the first cycle, the catalyst activities significantly dropped in the second cycle.



67 **68**

Scheme 23. Ionic liquid-tagged Hoveyda-Grubbs 1st generation catalysts **67** and **68**.

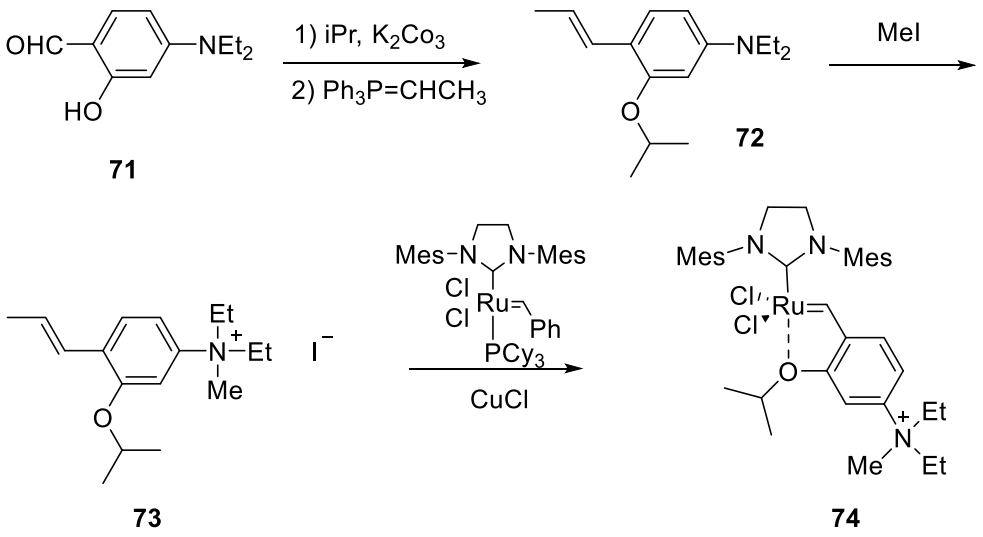
Grela and co-workers introduced two different ionic tags for ruthenium olefin metathesis catalyst in 2006.[37] These two catalysts can be activated with different conditions. The ionic-tagged complex **69** can be activated by a strong Brønsted acid or heat while complex **70** can be activated by a weak Lewis acid.



69 **70**

Scheme 24. Ionic-tagged Hoveyda-Grubbs catalysts **69** and **70**.

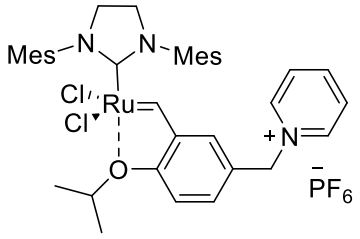
This concept proved not to be an excellent way to promote RCM and enyne metathesis reactions but also an excellent tool for green chemistry with a slight modification of the ionic tag as shown below.[38] The Hoveyda-Grubbs catalyst bearing quarternary ammonium group can catalyze RCM and enyne metathesis reactions in environmental friendly solvents like water-methanol mixture in air. However, while ruthenium content in the product is only 12-68 ppm, those values reflect purification with silica gel.



Scheme 25. Synthesis of ionic-tagged Hoveyda-Grubbs 2nd generation catalyst **74**.

Grela and Mauduit et al. also reported the synthesis of highly recoverable pyridinium-tagged Hoveyda-Grubbs catalyst.[39] The spacers between pyridinium and benzylidene ligand dictate the activity and recyclability of these sorts of ionically tagged

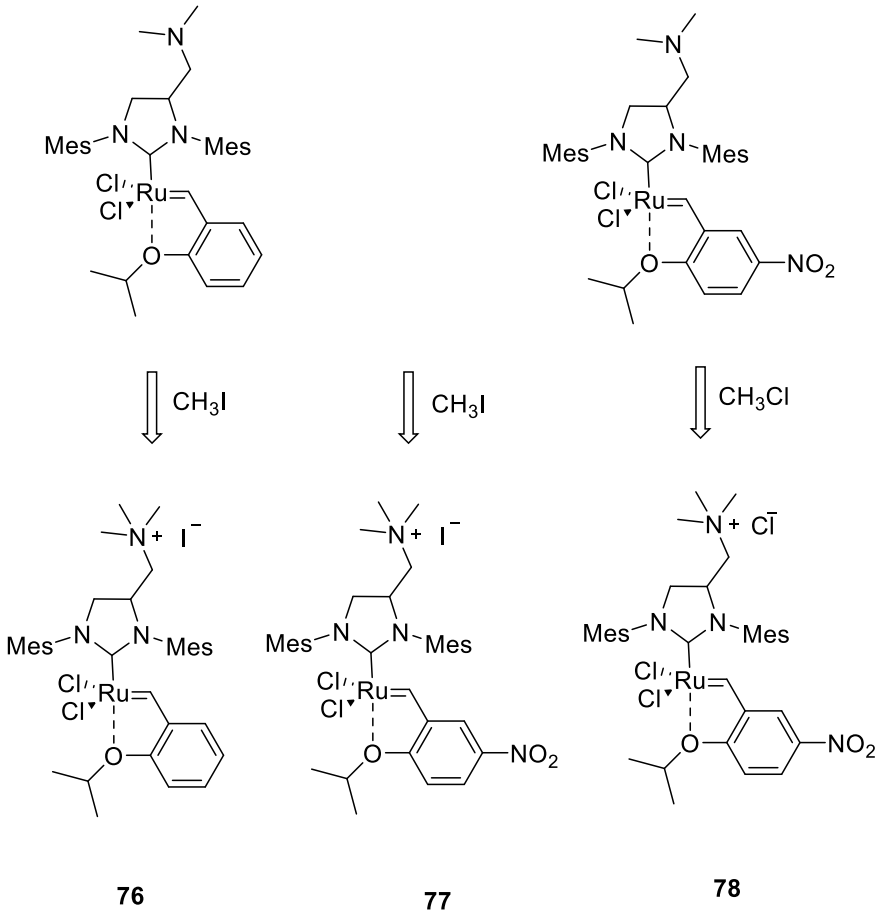
metathesis catalyst. The lower in number of the spacers the higher the activity but lower in recyclability in RCM reactions. By increasing the number of the spacers, the activity of the catalyst decreased but the recyclability would be improved. The authors claimed that with one carbon spacer between pyridinium and benzylidene ligand optimizes the performances of the catalyst. For example, complex **75** can catalyze an RCM reaction of 2-allyl-2-allyltosylamide for 6 cycles requiring 3 h for complete substrate conversion without any loss in activity over these 6 cycles. In these cases, the ruthenium contamination in the product from cycle 1, 3, and 6 were 11.5, 1.6, and 9.5 ppm, respectively. In contrast, pyridinium-tagged Hoveyda-Grubbs catalyst with no methylene spacer between pyridinium and benzylidene ligand showed a higher activity, according to the kinetic study catalyzing an RCM reaction of 2-allyl-2-methallylmalonate, but the conversion significantly dropped in the third cycle of an attempt to catalyze an RCM reaction of 2-allyl-2-allyltosylamide. Leaching for the pyridinium-tagged catalyst without spacer was not described.



75

Scheme 26. Pyridinium-tagged Hoveyda-Grubbs 2nd generation catalyst **75**.

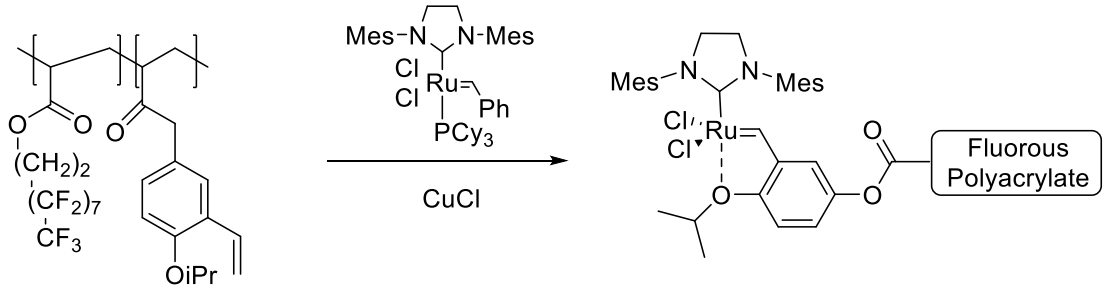
More recently, Grela and co-workers reported a family of easily separable olefin metathesis catalysts bearing polar quarternary ammonium groups.[40] These catalysts contain ionic tags bound to the *N*-heterocyclic carbene ligands. However, the statements on efficiency of the separation of this ammonium-bound catalyst is not clear since the RCM products that were analyzed were isolated with high purity only after passing the reaction mixture through a short silica gel column (silica/substrate mass ratio = 7). After that chromatography, ruthenium levels were found to be less than 5 ppm in all cases.



Scheme 27. Quarternary ammonium-bound Hoveyda-Grubbs catalyst **76** – **78**.

One of the more recent technologies in catalysts modification for recovery and recycle is the use of perfluoro-tagged catalysts in perfluorinated solvents.[41] Since the first report by Horvath[42], fluorous biphasic chemistry has been an interesting field in green chemistry research.[43] Typically, these solvents are immiscible with most organic solvents at room temperature. However, they are often thermomorphic. They can thus be used in both monophasic or biphasic condition. In either case, the catalyst can be separated from the product by a gravity-based liquid/liquid biphasic separation.

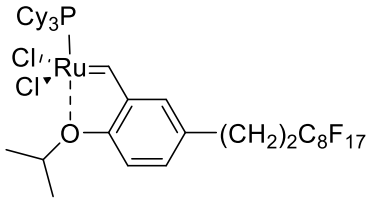
In 2004, Yao and Zhang reported the immobilization of Grubbs-type catalysts on poly(fluoroalkyl acrylate).[43] The fluoroacrylate was copolymerized with acryloyl chloride in the presence of AIBN. Then the benzylidene ligand was coupled with the poly(fluoroalkyl acrylate) to yield a polymer-supported ligand as white powder. The final fluorous-tagged catalyst **80** was obtained from this poly(fluoroalkyl acrylate) ligand by allowing **79** to react with Grubbs 2nd generation complex. The catalyst **80** that was formed was then used in RCM reactions of propene in a monophasic $PhCF_3/CH_2Cl_2$ (1:19 v/v) solvent system. Extraction of the fluorous species using perfluorohexane (FC-72) and EtOAc after each reaction allowed the catalyst to be recovered by removing FC-72 and reused. The authors were able to recycle this fluorous-tagged ruthenium catalyst for 20 cycles. However, leaching was not described.



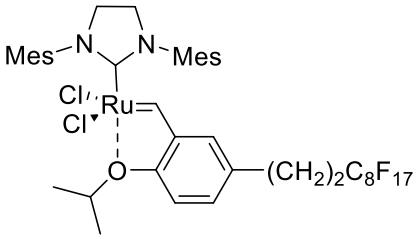
79 **80**

Scheme 28. Synthesis of poly(fluoroalkyl acrylate)-supported Hoveyda-Grubbs 2nd generation catalyst **80**.

Inspired by heavy poly(flouroalkyl acrylate) tag work by Yao and co-workers, Curran et al. reported the study of other recoverable metathesis catalysts using fluorous supports. In this case, they explored a light fluorous-tagged Hoveyda-Grubbs catalyst, which had only 17 fluorines per Ru versus 170 fluorines per Ru used by Yao and co-workers.[44] These catalysts show similar activity to their non-fluorous-bound analogs and were recovered from the products. However, these separations used chromatography using fluorous silica gel rather than a liquid/liquid extraction. Extra solvents including acetonitrile were needed to obtain the product and ether was needed to recover the fluorous-tagged catalyst. The recovered catalyst can be reused for at least five cycles with the average product yield of 97%.



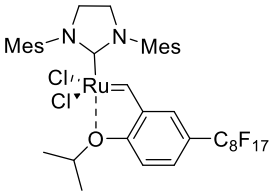
81



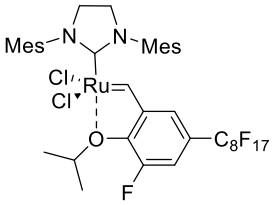
82

Scheme 29. Light fluorous-tagged Hoveyda-Grubbs catalysts **81** and **82**.

Later on, Matsugi and co-workers reported two new light fluorous-tagged catalysts. Compared to **82**, **83** had an improvement in activity with similar recyclability (90% recovery of catalyst), while **84** showed higher activity than both **82** and **83** but was not recoverable.[45] The fluorous-tagged catalyst **83** was recycled and reused in an RCM reaction of diethyl diallylmalonate for five times. The product yield was 95-100% in each cycle.



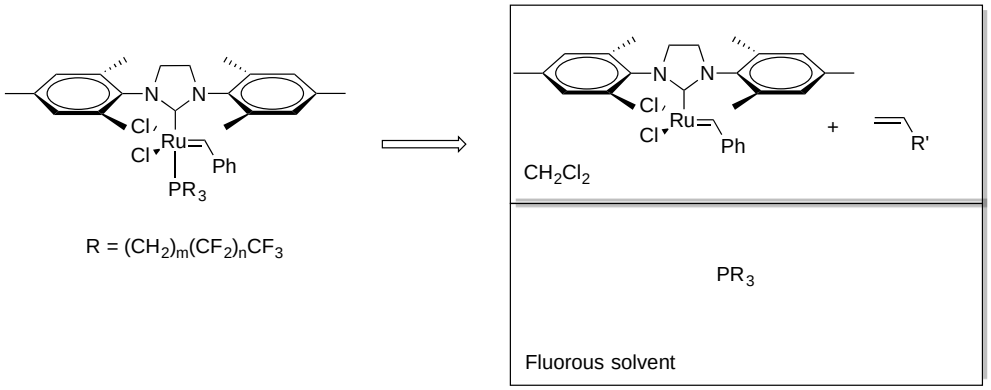
83



84

Scheme 30. Light fluorous-tagged Hoveyda-Grubbs catalysts **83** and **84**.

Another method in using fluorous-tagged ruthenium catalyst in olefin metathesis reactions was reported by Gladysz and co-worker.[46,47] Typically, the rate of the olefin metathesis reaction catalyzed by ruthenium catalyst depends on the dissociation rate of the ligand attached to the metal center. Thus, the reaction would be faster if the ligand can be scavenged. Indeed, without a scavenger, the dissociated ligand can reattach to the metal center as a reversible process that often slows the overall rate. The combination of fluorous phosphine ligand and fluorous solvent offered this quality to the ruthenium catalyst. The mechanism is depicted in Scheme below. This chemistry is analogous to the phosphine scavenging first reported by our group in 1981.[48]

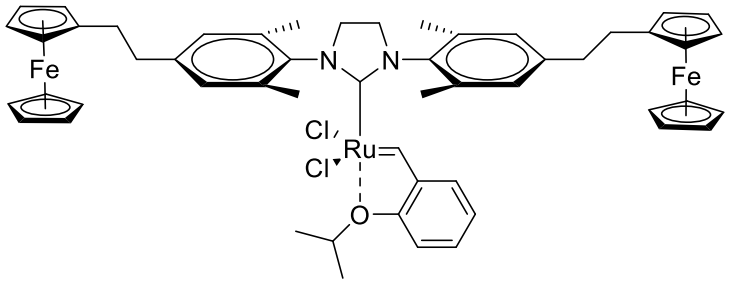


Scheme 31. Fluorous-tagged phosphine ligand scavenging mechanism in fluorous solvent.

The results showed that the initial rate of metathesis was significantly increased in fluorous media with 44% conversion of diethyl diallylmalonate to an RCM product at 2 h

versus 16% conversion of the same substrate at 2 h in CH_2Cl_2 solvent without a phosphine sequestering phase.[46] In addition to the enhancement in reaction rate, this catalyst can be recycled by extraction with $CF_3C_6F_{11}$ fluorous solvent.[47] The fluorous-tagged ruthenium catalyst was recycled for three cycles with 79% yield in each cycle and more than 85% of catalysts were recovered in the first two cycles. Although, 79% yield of RCM product was obtained in the third cycle, only 57% of catalysts were recovered. This chemistry is very similar to boomerang reaction described by Barrett,[7] which the catalyst leaves the ligand support becoming an active catalyst during the reaction and recaptures by the ligand after the completion of the reaction.

Another interesting catalyst recovery concept was reported by Plenio el al. in 2005, using only one solvent in the system but rather directing the solubility of the catalyst via redox triggering of the phase tag.[49] This ruthenium olefin metathesis catalyst was supported with two redox-switchable ferrocenyl phase tags. The catalyst **85** can be perturbed by adding 2 equivalents of oxidizing agent, $[FcCOCH_3][CF_3SO_3]$ as a 10% solution in CH_2Cl_2, and the precipitate can be reactivated by the addition of 2 equivalents of reducing agent, 1,1', 2,2', 3,3', 4,4'-octamethylferrocene ($FcMe_8$). This redox-switchable tag was acted as on/off switch for the reaction, no reaction was occurred when the ferrocenyl tags were oxidized and the reaction was continued again once the ferrocenyl tags were reduced. In addition, this redox-switchable-tagged ruthenium catalyst can be easily separated, when in the oxidized state, from the reaction mixture by filtration.

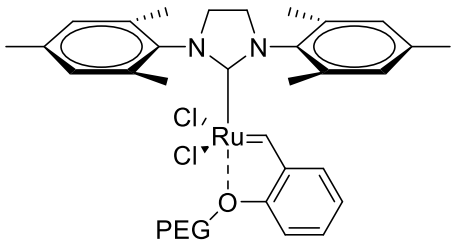


85

Scheme 32. Redox-switchable-ferrocenyl-tagged Hoveyda-Grubbs catalyst **85**.

Polyethylene glycol (PEG) is one of the most widely used as polymeric supports for reagents and organometallic complexes.[50-52] Moreover, it has also been utilized as a green solvent in organic synthesis, due to its non-volatility and non-toxicity.[53] Although PEG derivatives are soluble in many organic solvents including water, they are insoluble in solvents like hexane, diethyl ether, and cold ethanol. Thus, these PEG derivatives can be utilized as recovery and recycle tools for catalysts. The recovery of the PEG-supported catalyst from the product can be achieved by either solvent precipitation or liquid/liquid extraction.

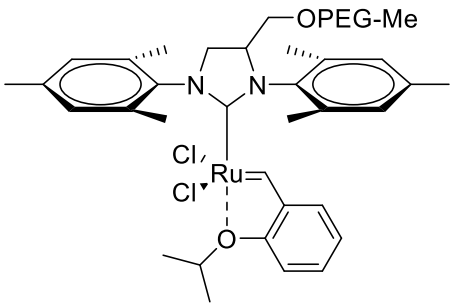
In 2003, Lamaty and co-workers described the synthesis and application of a PEG-bound ruthenium olefin metathesis catalyst.[54] The soluble support was attached to the benzylidene ligand *ortho* to the metal carbene. The recovery of this catalyst from RCM reaction was carried out by precipitation in Et_2O and filtration. Subsequently, the catalyst was recycle for four more cycles. The catalyst still exhibited high activity in the fifth run.



86

Scheme 33. PEG-supported Hoveyda-Grubbs catalyst **86**.

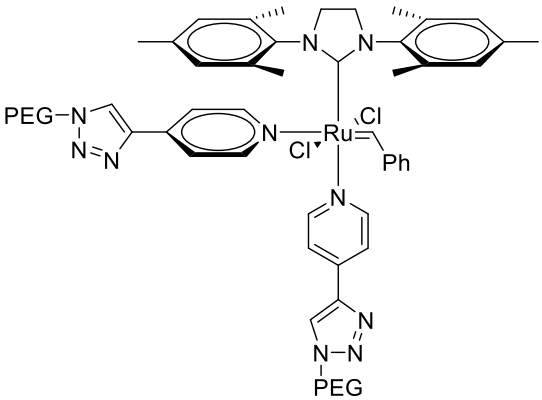
In attempting to develop a greener metathesis reaction process, Grubbs et al. reported the synthesis of highly active PEG-bound ruthenium complex that can be used in aqueous media. This complex **87** was shown to be able to catalyze RCM, CM, and ROMP reactions of substrates like 2-allyl-*N*,*N*,*N*-trimethylpent-4-en-1-aminium chloride, allyl alcohol, and *endo*-*N*-(*N*',*N*',*N*'-trimethylammonio)ethyl-bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide chloride with conversion over 95% in water as a solvent.[55] The removal of the PEG-bound ruthenium complex was examined in an RCM reaction of diethyl diallylmalonate.[56] The ruthenium level in the RCM product was found to be 41 ppm when the catalyst was removed by water extraction. This ruthenium contamination level can be reduced to less than 0.04 ppm when the extraction with water was changed to include a treatment with activated carbon.



87

Scheme 34. PEG-supported Hoveyda-Grubbs catalyst **87**.

The immobilization of highly active catalyst like Grubbs 3rd generation on PEG has also been reported.[57] Emrick and co-workers synthesized a PEG-supported Grubbs 3rd generation by ligand exchange between pyridine ligands and PEG-bound pyridine ligands. This PEG-supported catalyst **88** was used to catalyze ROMP reaction in water media. The polymer products prepared from **88** have PDI values in 1.3-1.5 range.



88

Scheme 35. PEG-supported Hoveyda-Grubbs catalyst **88**.

The Bergbreiter group has also described the use soluble polymer supports for ruthenium olefin metathesis catalysts. In their work, soluble polymers that can be more efficiently separated were used as an alternative to PEG whose separation typically generates large volumes of solvents waste during the polymer precipitation step. For example, to yield 30 mg of RCM product catalyzed by PEG-supported olefin metathesis catalyst **87**,[56] 30 g of wastes were generated from the extraction process. These alternative polymers are polyethylene (PE_{Olig}) and polyisobutylene (PIB). Our lab has developed several techniques for separation of these types of polymer-supported species including liquid/liquid separation and solid/liquid separation, as shown in Figure 1.

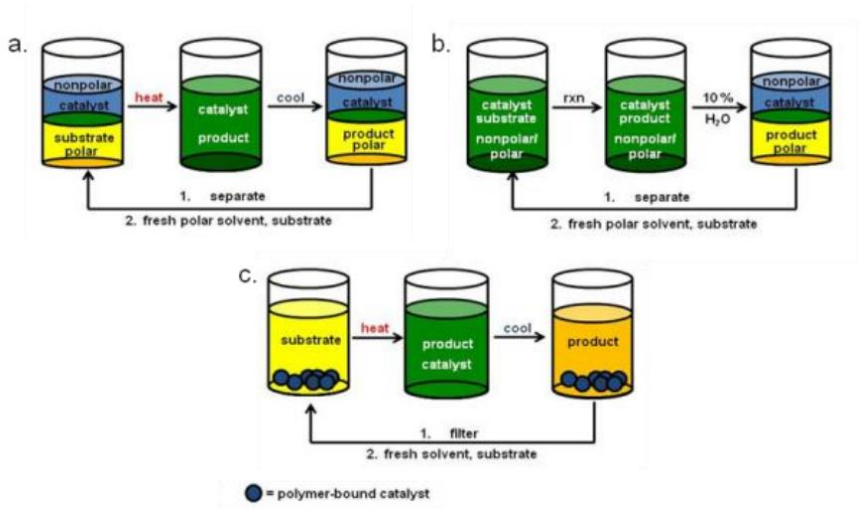
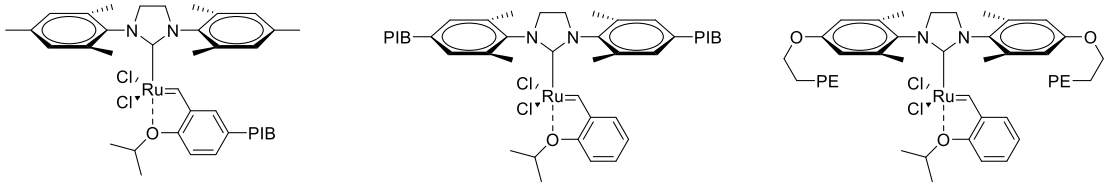


Figure 1. Schematic representation of (a) thermomorphic liquid/liquid, (b) a latent biphasic liquid/liquid separation and (c) a thermomorphic solid/liquid separation system.

We had reported the first synthesis and application of PIB-supported Hoveyda-Grubbs type catalyst in 2007.[58] The PIB was attached to the catalyst at the benzylidene ligand. This catalyst **89** was used to catalyze RCM reactions in heptane media, which the product can be extracted by acetonitrile. Noted that in some cases the product precipitated from the solution, thus, only filtration was needed to isolate the product. In term of recyclability, PIB-supported ruthenium complex **89** was allowed to be reused for at least five runs. However, the metal contamination was inconsistent for each of the product, range from 20 – 1000 ppm. In order to improve the recoverability of the PIB-supported ruthenium catalyst the PIB chains were attached to the non-dissociate *N*-heterocyclic carbene ligand of the Hoveyda-Grubbs catalyst to yield complex **90**.[59] This catalyst design allowed an improvement in ruthenium recovery with the leaching level as low as 0.37% while the catalyst **90** can be reused for 20 cycles.



89 **90** **91**

Scheme 36. Polyolefin-supported Hoveyda-Grubbs catalysts **89** – **91**.

More recent work from our group on polymer-supported olefin metathesis catalyst was the use of PE_{Olig} as catalyst supports.[60] The unique property of PE_{Olig} is that it does

not soluble in any solvent at room temperature but soluble in toluene or THF at 65 °C. Therefore, the separation technique of PE_{Olig}-supported Hoveyda-Grubbs catalyst **91** involve the heating of the reaction mixture to form monophasic condition and the reaction can be quenched by cooling the reaction mixture inducing phase separation between the solid catalyst species and the product solution. Subsequently, the catalyst can be recovered by simple filtration. PE_{Olig}-supported catalyst **91** can be reused in RCM reactions for at least eight cycles with the ruthenium leaching to be less than 0.3%.

Subsequent chapters will discuss my work focusing on the use of polyolefin oligomers as tools in metal recovery in metal catalysis reactions. First, I will discuss the use of polyethylene oligomers as protective encapsulating agent for metal salen complexes against acidic environment during a reaction workup. The use of polyethylene as solvent and support for Hoveyda-Grubbs 2nd generation complex as catalyst recovery strategy to recover catalyst from ring-opening metathesis polymerization reactions will be discussed next. Then I will describe the synthesis of polyisobutylene-bound isocyanide as ruthenium sequestering agent in metathesis reactions. Finally, I will discuss the synthesis of polyisobutylene-supported Grubbs 3rd generation complex and its use as a separable catalyst in living ring-opening metathesis polymerization reactions.

CHAPTER II

PROTECTIVE ENCAPSULATION OF ACID-SENSITIVE CATALYSTS USING POLYETHYLENE LIGANDS*

Introduction

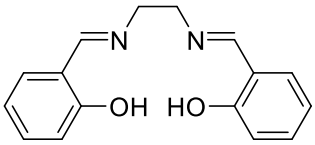
Functionalized polymers have a long history as tools for facilitating synthesis. While polymers most commonly serve to separate a catalyst or reagent from products,[51,61-63] reports have described additional roles for polymer supports wherein the support facilitates a reaction in some other way. Typically this additional functionality derives from the phase separation properties of a polymer or the polymer's intrinsic chemical properties. The use of polymer- bound smart catalysts that autonomously control an exothermic reaction,[64] the use of polymer-bound species to achieve added selectivity in a reaction,[65] the use of polymer bound species to facilitate ''pseudo'' high dilution reactions or to stabilize a reactive intermediate,[66,67] or the ways polymers facilitate multistep reactions involving incompatible reagents or catalysts[68-71] are illustrative of this broad chemistry. Here we describe another way polymer supports may be useful in catalysis. In this work, we describe how polyethylene-bound salen catalysts themselves or in the presence of added polyethylene exhibit enhanced stability as solids to acid-promoted demetalation.

---

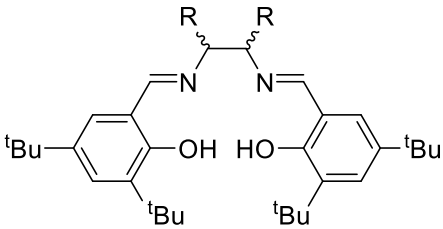
*Reprinted with permission from "Protective Encapsulation of Acid-sensitive Catalysts Using Polyethylene Ligands" by Suriboot, J.; Hobbs, C.; Yang, Y.-C.; Bergbreiter, D. E.; J. Polym. Sci. Part A: Polym. Chem. 2012, 50, 4840, Copyright 2012 by Wiley Periodicals, Inc.

In this example, the hydrophobicity and semicrystalline nature of the polyethylene support is used to protect a salen metal complex from protonation and subsequent metal leaching by a polar acid in a polar solvent that does not swell polyethylene.

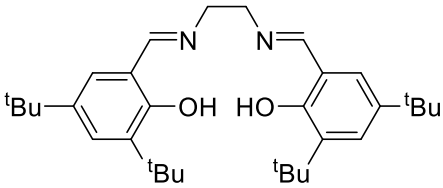
Salen ligands have a long history, having been first reported in 1933 by Pfeiffer.[72] Such ligands can be achiral (e.g. **92**) or chiral (e.g. **93**). While both sorts of ligands are important in catalysis, the broad applications and effectiveness of the chiral salen ligands in asymmetric synthesis earned their name as "privileged" ligands.[73] The name salen is short for salicylaldehyde and ethylenediamine, also known as Schiff base. Some of the most commonly known salen ligands are shown in Scheme 16. These included the original achiral salen ligand **92**, achiral **95**, and chiral ligands like **93**, **94**, and **96**. The stability of this tetradentate ligand toward hydrolysis can be increased drastically when coordinated with transition metal to form a metal-salen complex, which is very similar to the porphyrin systems present in the heme-based oxidative enzymes.



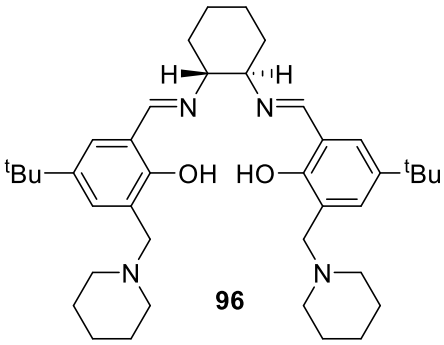
92



93) R = (*S,S*)-$CH_2(CH_2)_2CH_2$-
94) R = (*R,R*)-$CH_2(CH_2)_2CH_2$-



95

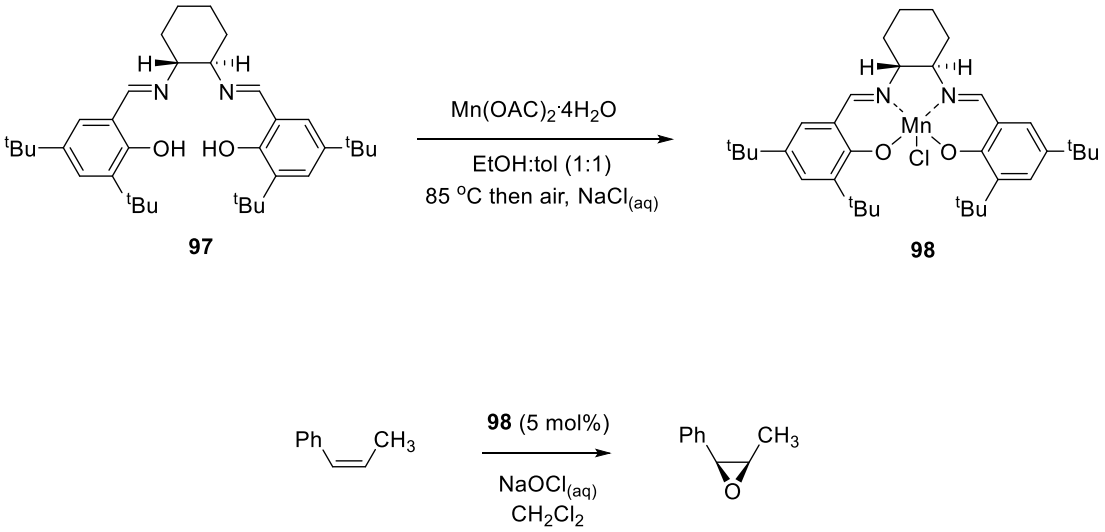


96

Scheme 16. Structures of various salen ligands.

Inspired by the porphyrin framework, Jacobsen and Katsuki had independently introduced the use of chiral salen-Mn complexes as catalysts for the asymmetric epoxidation of unfunctionalized olefins.[74,75] These breakthrough studies gained attention from the synthesis community that led to many discoveries of different salen-metal enantioselective catalysts. Transition metal-containing salen formed with a range of transition metals including Mn, Cr, Co, V, Cu, Ti, Ru, Pd, Au, Zn, and Al.[76] In addition to the ability to catalyze effective asymmetric reactions, salen ligands are popular because it is easy to synthesize and manipulate the chiral environment around the active metal center through the architecture of the diamine bridge.

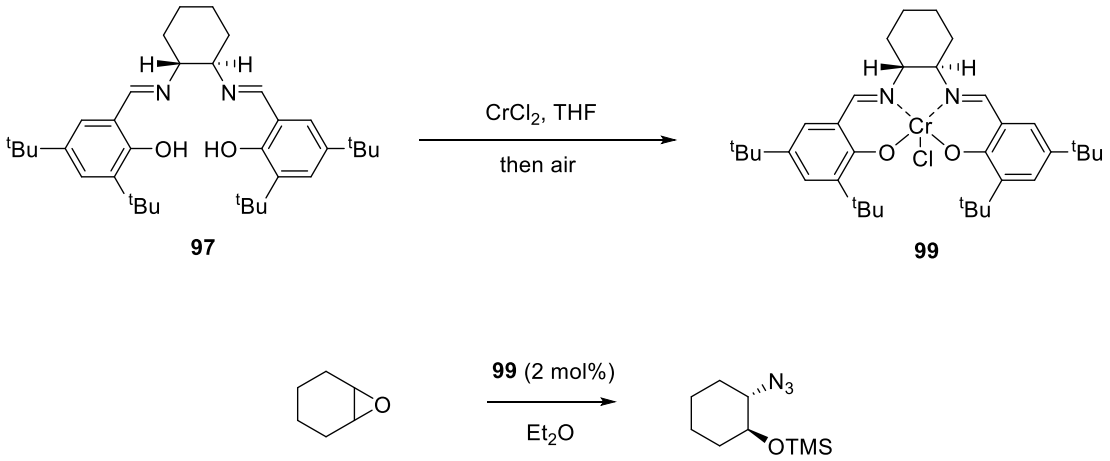
Jacobsen and co-workers described the use of salen-Mn complex **98** to catalyze *cis*-olefins using household bleach as an oxidant.[77] The epoxide product of *cis*-1-propenylbenzene can be prepared with high yield (84%) and high ee (92%) using salen-Mn catalyst **98** and NaOCl as an oxidant in dichloromethane as shown in Scheme 17.



Scheme 17. Synthesis of salen-Mn complex **98** and its application to catalyze epoxidation reaction of *cis*-1-propenylbenzene.

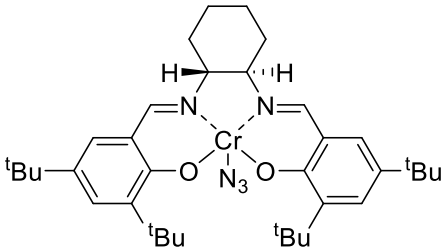
Four years later, Jacobsen et al. reported the use of a new salen-Cr complex in the new asymmetric reactions.[78] They reported that the salen-Cr complex **99** can catalyze asymmetric ring-opening reaction of cyclohexene oxide with azidotrimethylsilane as a nucleophile to yield the azido silyl enol ether in good yield (90%) and excellent enantiomeric excess (98%). Moreover, the authors reported that salen-Cr complex **99**

could be recycled and reused after vacuum distillation of the product leaving salen-Cr catalyst in the reaction flask ready to be reused by addition of fresh substrate.



Scheme 18. Synthesis of salen-Cr complex **99** and its application to catalyze ring-opening reaction of cyclohexene oxide.

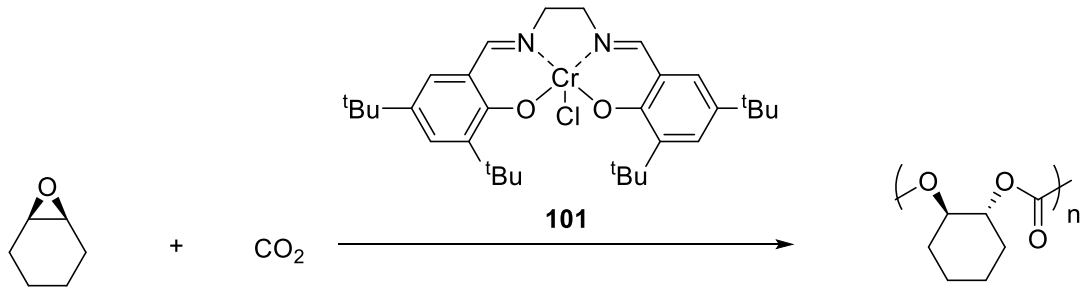
The applications of salen-metal complexes are not limited only to asymmetric synthesis evidenced by the patent filed by Jacobsen and co-workers in 2000. They reported the synthesis of polycarbonate using chiral salen-Cr complex **100** as a catalyst in reaction of (*S*)-enantiomer of racemic 1,2-epoxyhexane with one atmosphere carbon dioxide.[79]



100

Scheme 19. Chiral salen-Cr catalyst **100**.

Inspired by Jacobson's work on polycarbonate synthesized from 1,2-epoxyhexane and carbon dioxide, Darensbourg et al. reported the use of achiral salen-Cr complex as a catalyst and *N*-methylimidazole as a cocatalyst in the reaction of cyclohexene oxide and carbon dioxide to yield poly-(cyclohexylene)carbonate.[80] This study discussed about the effect of the cocatalyst on the amount of carbonate linkage on the polymer product. The optimized condition was to use 2.25 equivalent of the *N*-methylimidazole cocatalyst to afford polycarbonate with 99% carbonate linkage and a PDI of 1.4. Increasing in the amount of cocatalyst decreased the PDI of the polymer product but also reduced the amount of carbonate linkage, for example, polycarbonate prepared with 30 equivalents of *N*-methylimidazole as cocatalyst had PDI of 1.2 and 87% of carbonate linkage (13% of ether linkage).

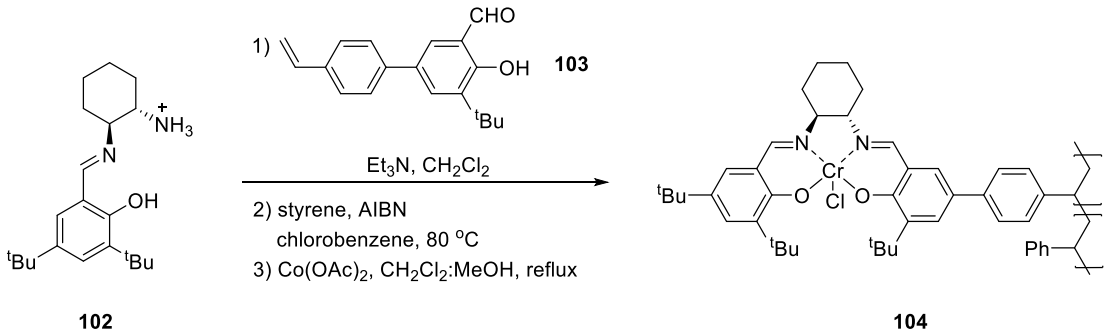


Scheme 20. Synthesis of polycarbonate from cyclohexene oxide and carbon dioxide catalyzed by **101**.

Because salen catalysts can be utilized in variety of organic reactions and because they are relatively expensive catalysts,[81] there have been several reports that described immobilization of salen complexes onto supports like zeolites, silica gel, and soluble polymers. Since the main focus in this dissertation is on the use of soluble supports, only some examples of soluble polymer-supported salen-metal complexes will be discussed below.

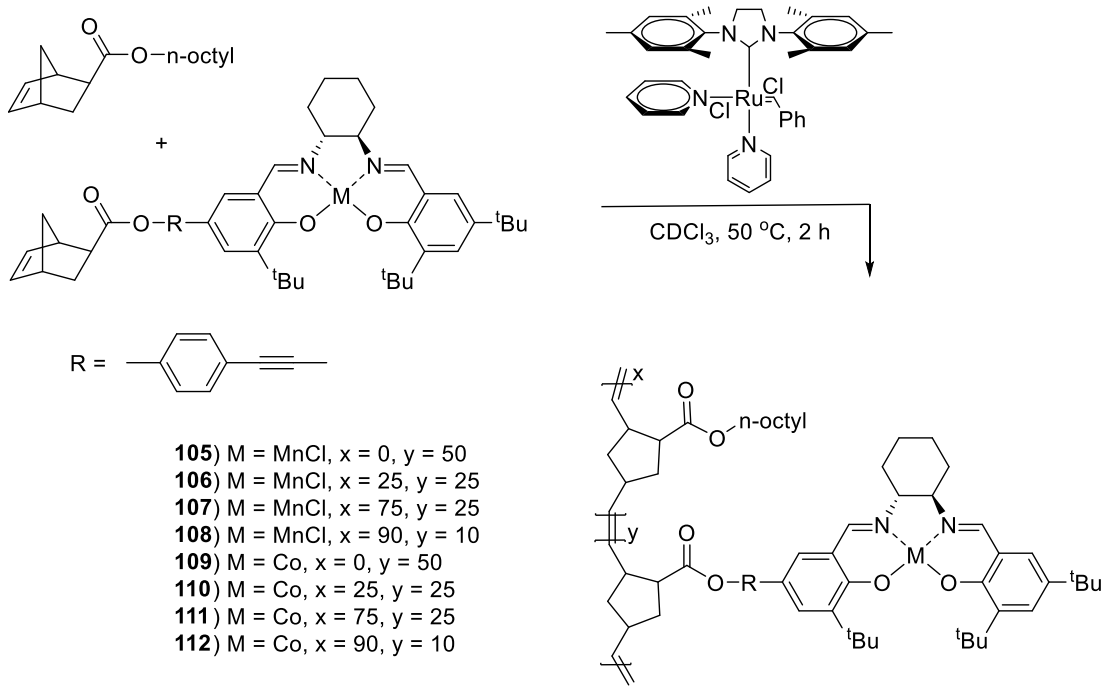
In 2006, Weck and co-workers described the synthesis and application of non-crosslinked polystyrene (NCPS)-supported salen-Co complexes.[82] These polystyrene-supported salen-Co catalysts were synthesized by free radical polymerization of a styrene-containing salen ligand with unfunctionalized styrene in chlorobenzene. Subsequently, the polystyrene-supported salen ligand was allowed to react with Co(II) acetate to yield a polystyrene-bound salen-Co(II) complex. The resulting NCPS-supported salen-Co(II) complex was oxidized to form Co(III) complex **104** before using it as a catalyst in a hydrolytic kinetic resolution of racemic epichlorohydrin. The results of this HKR reaction

showed that 99% ee of (*S*)-epichlorohydrin were formed after 54% conversion in 1 h. The catalyst can be recycled for three cycles by precipitation of the catalyst after HKR reaction of epichlorohydrin by the addition of diethyl ether. The catalyst was found to have lower activity with each cycle possibly due to physical loss of the catalysts in each precipitation process.



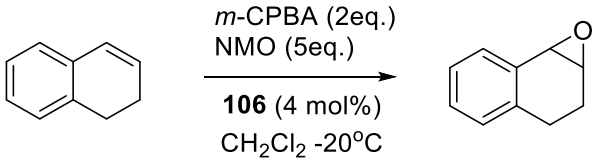
Scheme 21. Synthesis of polystyrene-supported salen-Cr catalyst **104**.

In the same year, Weck and co-worker reported that polynorbornene-supported salen-metal complexes, formed by ring-opening metathesis polymerization catalyzed by Grubbs 3rd generation catalyst, effectively catalyze epoxidation reactions of aromatic olefins.[83] The polynorbornene-supported Co(II) and Mn(III) salen complexes were prepared by copolymerization of salen-bound norbornene and octyl-bound norbornene. Typically, the degrees of polymerization (DP) of these species were 50 to 100.



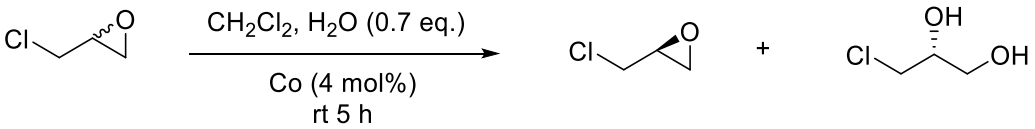
Scheme 22. Synthesis of polynorbornene-bound salen-metal complexes **105** – **112**.

The salen-Mn complexes **105** – **108** formed in this way were used in the epoxidation of aromatic olefins. For example, catalyst **106** quantitatively oxidized 1,2-dihydronaphthalene to form an epoxide product with an enantiomeric excess of 81%, which is slightly lower than the enantiomeric excess of the epoxide prepared from a low molecular weight analog of this polymeric chiral salen catalyst (88% ee). The recycling of **106** was examined, while complete conversion occurred for the second cycle, the enantiomeric excess dropped from 81% ee to 47% ee. A further decrease in performance of the polymer-supported salen complex **106** was seen in a third cycle with a conversion of 85% and an enantiomeric excess of 6%.



Scheme 23. Epoxidation of 1,2-dihydronaphthalene catalyzed by **106**.

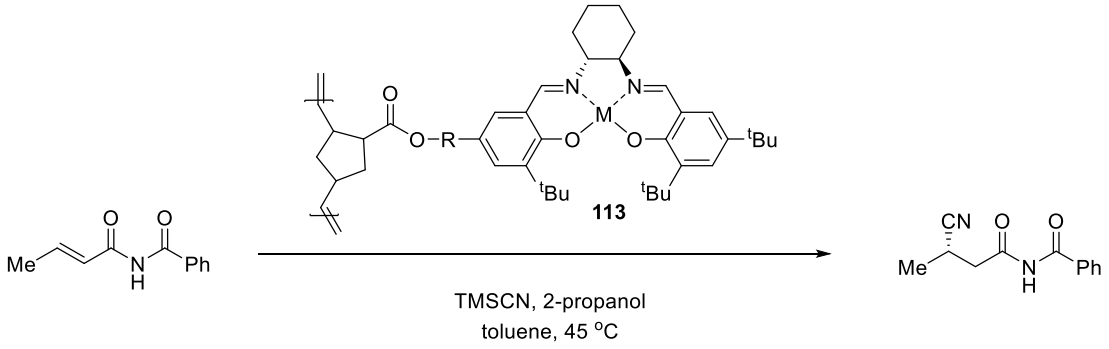
To study the ability of these salen-Co complexes in hydrolytic kinetic resolution (HKR), polymer-supported complexes **109** – **112** were oxidized with acetic acid and air to form Co(III) complexes. The obtained complexes were allowed to react with racemic epichlorohydrin under solvent-free conditions or in CH_2Cl_2 as solvent. The general results showed that the ee of the (*S*)-epoxide was 99% at a conversion of 55% when the reaction was performed using these polymer-supported salen-Co complexes, that result is very similar to low molecular weight counterpart (99% ee, 53% conversion).[84] This report also stated that site isolation was crucial as the reaction catalyzed by a homopolymer-supported complex **109** was reportedly slower than the copolymer analog.



Scheme 24. Hydrolytic kinetic resolution reaction of epichlorohydrin using salen-Co(III) catalysts **109** – **112**.

Recycling of polymer-supported salen-Co complexes was carried out by precipitation with diethyl ether. The (*R*)-3-chloro-1,2-propandiol can be removed from the mixture via water extraction leaving (*S*)-chlorohydrin in diethyl ether, which can be isolated by solvent removal. However, the recyclability of polymer-supported salen-Co acetate complex was inefficient since the longer reaction times were required for cycle to cycle due to the decreasing in catalyst's solubility.

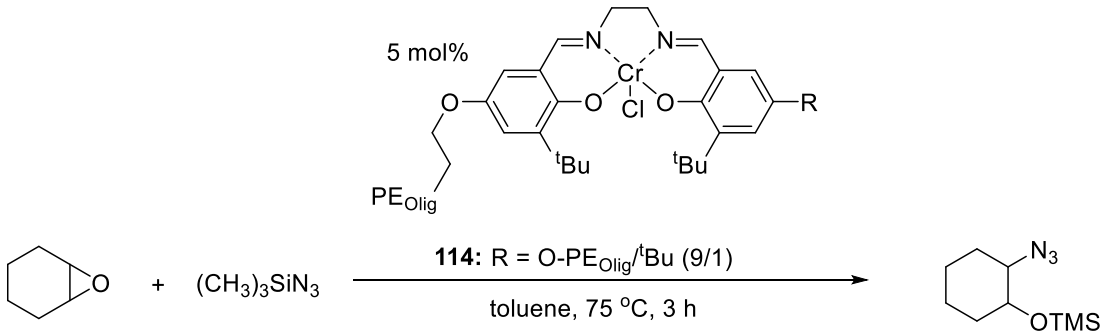
As an expansion to the work on polynorbornene-supported salen-Co(II) and Mn(III) complexes, Weck and co-workers developed polynorbornene-supported salen complex with Al(III) as the coordinated metal.[85] This complex has been shown to be competent as catalyst for 1,4-conjugate addition of cyanide to α,β-unsaturated imides. This polynorbornene-supported salen-Al complex can be recycled using solvent precipitation technique for five times while maintaining the yield and ee to be over 90%.



Scheme 25. The 1,4-conjugate addition of cyanide to α,β-unsaturated imides catalyzed by **113**.

Salen ligands and the transition metal complexes that they form are widely used in catalysis. Epoxide opening reactions, hydrolytic kinetic resolution (HKR) reactions, atom efficient polymerizations, and oxidations are among the many organic reactions carried out with such species.[86] Not surprisingly, many reports have described chemistry that uses polymers to recover and reuse these catalysts.[76,83,87-92] However, the known acid lability of the salen complexes can lead to demetalation of salen complexes which in the case of an immobilized catalyst leads to metal leaching.[76,92-94] Inspired by earlier work from our lab and more recent work at DuPont,[95-99] our lab has begun to revisit the advantages of PE_{Olig}-supported ligands/catalysts.[60,91] As part of this work, we show here that PE_{Olig}-bound salen transition metal complex precipitates alone or coprecipitated in a host polyethylene matrix are stable toward acid.

PE oligomers (PE_{Olig}) containing terminal ligands serve as thermomorphic supports for recoverable, recyclable catalysts.[60,91,95-98] and like polyethylene are insoluble at room temperature but dissolve on heating in toluene or in other solvents like toluene that dissolve polyethylene. We recently reported examples of this with PE_{Olig}-bound salen complexes that were active in salen-catalyzed ring-opening reactions of epoxides (cf. Scheme 26).[91] This strategy for catalyst immobilization has also been used in a variety of other catalytic reactions.[95-99]



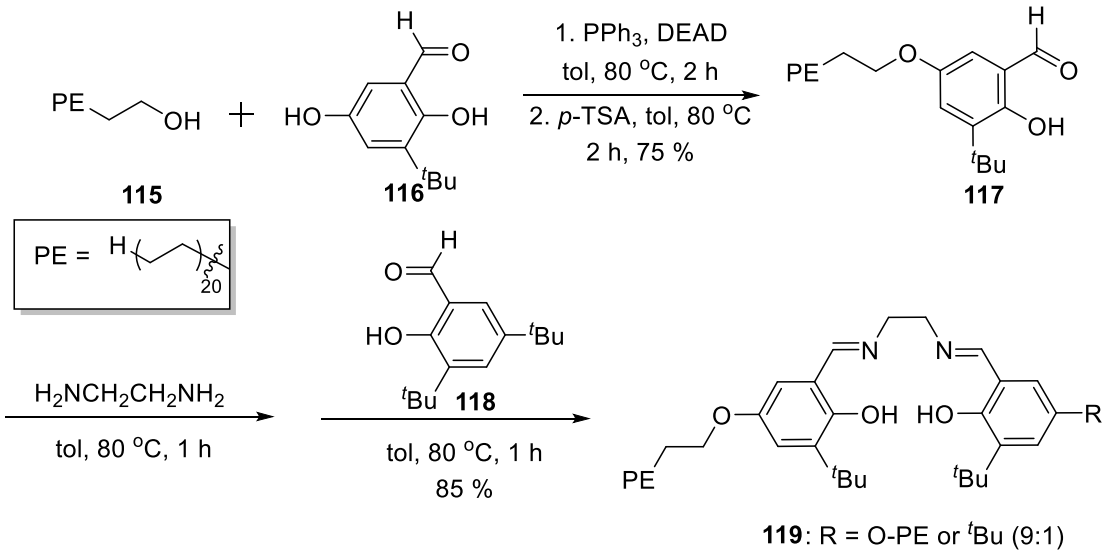
Scheme 26. Example of the catalytic reactivity of a recoverable of PE_{Olig}-salen Cr complex **114**.

Our prior work had also shown that PE oligomers coprecipitate with unfunctionalized polyethylene.[100] Depending on the loading, the precipitation process, and the surface area of the host PE, suspensions of PE containing entrapped PE oligomers have varying accessibility of the PE oligomer functional group to species in solvent. This is seen in the prior studies of entrapment functionalization of polyethylene by PE_{Olig}-bound dyes, spin labels, and fluorophores where the reactivity of PE_{Olig}-bound entrapped functional group's reactivity changed with the solvent polarity and in experiments where quenching of a PE_{Olig}-bound dansyl group by acid was decreased in polar sol- vents such as water and methanol.[101] The studies described below expand on these results to show that the stability of PE_{Olig}-supported salen and ''half-salen'' metal complexes toward acidolysis when entrapped in unfunctionalized PE oligomers is enhanced both using just the precipitated form of these catalysts or catalysts entrapped in a host PE matrix. The minimal loss of metal from the PE_{Olig}-salen complexes under these conditions shows that a PE ligand and a PE matrix can serve as a protective encapsulating agent for PE-bound

catalysts. Thus, PE ligands and a PE matrix function like paraffin wax, which is often used to stabilize reactive metals, reactive catalysts and metal hydrides toward moisture.[102,103]

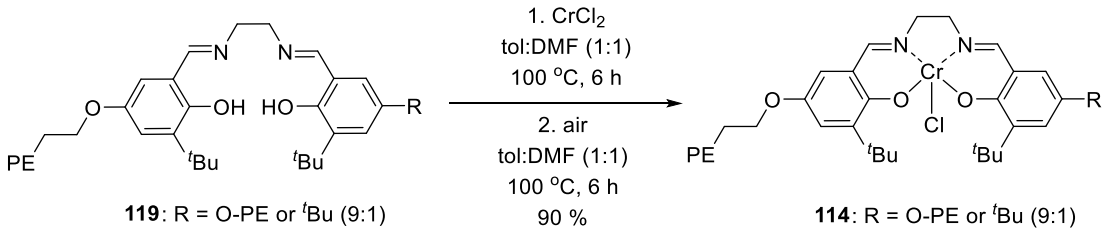
Results and Discussion

A PE_{Olig}-supported salen ligand was prepared as shown in Scheme 27. Starting from the commercially available PE_{Olig}-alcohol **115**, a regiospecific Mitsunobu reaction of **115** with 2-tert-butyl-2,5-dihydroxybenzaldehyde **116**[104] forms the PE_{Olig}-bound ether **117**.[91] The PE_{Olig}-salen ligand **119** was then prepared by a two-step process, first by treating **117** with a slight excess of ethylene diamine and then treating the product of this reaction with **118**. While an exact stoichiometric balance of **117** and ethylene diamine would directly form a bis-PE_{Olig}-ligated salen ligand, experimental problems in achieving this stoichiometry, our inability to remove any excess **117** from **119**, and the fact that one PE_{Olig} sufficed to quantitatively precipitate **119** and its metal complexes on cooling led to us to this synthetic approach. The product **119** was purified by simple cooling which lead to precipitation of the PE_{Olig}-bound species.



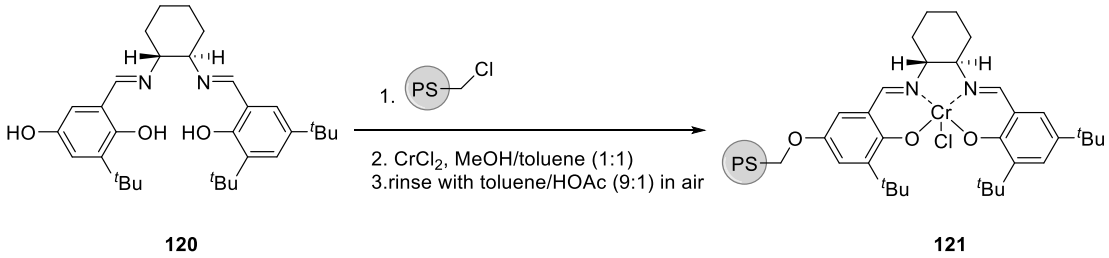
Scheme 27. Preparation of PE_{Olig}-supported salen ligand **119**

The PE_{Olig}-bound salen ligand **119** was metalated using a procedure used by a group at DuPont to metalate PE_{Olig}-bound porphyrins and phthalocyanines[99] by allowing **119** to react with $CrCl_2$ in a 1:1 mixture of toluene and *N*,*N*-dimethylformamide (DMF) at 100 °C. The Cr(II) species so formed was then oxidized with air to afford the highly colored Cr(III) complex **114**, which was isolated via vacuum filtration as a dark solid (Scheme 28). Formation of **114** was confirmed by UV- Vis spectroscopy (λ_{max} = 430 nm, toluene, 70 °C).



Scheme 28. Metalation of PE_{Olig}-supported salen **119** to form Cr^{III} complex **114**.

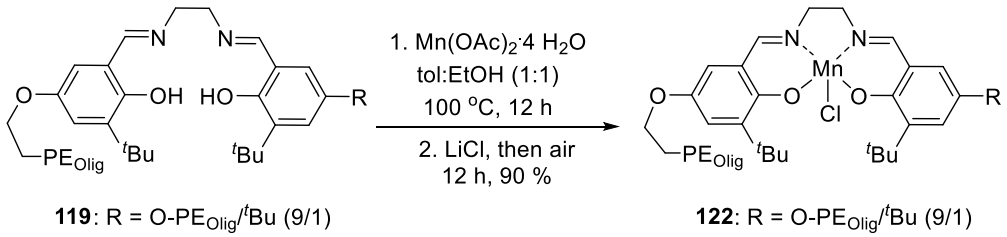
We also prepared a Cr(III) salen complex on a DVB-crosslinked polystyrene support using the chemistry shown in Scheme 29. Here a salen ligand containing a phenol group **120** was attached to Merrifield's resin via an ether bond.[5,105] The resulting PS-bound salen was then complexed with $CrCl_2$ and oxidized in air to give green-colored beads containing a salen-Cr(III) complex **121**.



Scheme 29. Synthesis of a DVB-crosslinked polystyrene-supported Cr(III)-salen complex **121**.

A PE_{Olig}-supported salen Mn(III) complex was also prepared by a procedure described by Jacobsen[5] (Scheme 30). In this case, the salen ligand **119** and

$Mn(OAc)_2 \cdot 4H_2O$ were first allowed to react in a mixture of toluene and ethanol at 100 °C. Treatment of this solution with LiCl and oxidation with air afforded a PE_{Olig}-supported salen-Mn(III) **122** as a dark solid. Formation of **122** was confirmed by UV-Vis spectroscopy (λ_{max} = 445 nm, toluene, 70 °C).



Scheme 30. Formation of a PE_{Olig}-supported salen-Mn(III) complex **122**.

Initial studies of the acid stability of PE_{Olig}-bound salen complexes used a qualitative colorimetric assay of the stability of **114** and a coprecipitate of **114**/PE_{500}. The coprecipitate of **114**/ PE_{500} was prepared by dissolving **114** and a fourfold excess of a polyethylene oligomer (Polywax-500)[106] in hot toluene. A uniformly dark colored precipitate of **114**/PE_{500} was isolated from this solution by cooling. We then tested the stability of suspensions of either the mixture of **114**/PE_{500} or **114** alone to a series of washes with methanol solutions of trifluoroacetic acid (TFA) (Fig. 2). In these studies, we stirred a suspension of **114** or **114**/PE_{500} in methanolic TFA for 24 h at 25 °C. We then separated the methanol phase. Addition of the sodium salt of ethylenediaminetetraacetic acid (EDTA) was used to colorimetrically test for leached Cr(III).[107] The results shown in

Figure 3(a) show that some leaching of metal occurred in cycle 1. We speculate that the small amount of leaching in cycle 1 may reflect a less than quantitative conversion of the PE_{Olig} salen to the PE_{Olig} salen-Cr(III) complex and the presence of some unreacted Cr salts. No visually discernible leaching was seen in cycles 2–5. These colorimetric assays did not show any difference in Cr leaching when using **114**/ PE_{500} versus **114** alone. The leaching of Cr(III) in **114** was minimal based on the unchanged color of recovered **114** (recovered from cycle 5) when it was redissolved in hot toluene. A hot toluene solution of freshly prepared **114** (4.2 mg in 15 mL toluene) had an absorbance of 0.45 at 430 nm at 70 °C. A hot toluene solution of recovered **114** after five cycles at the same concentration had an absorbance of 0.44 at 430 nm at 70 °C.

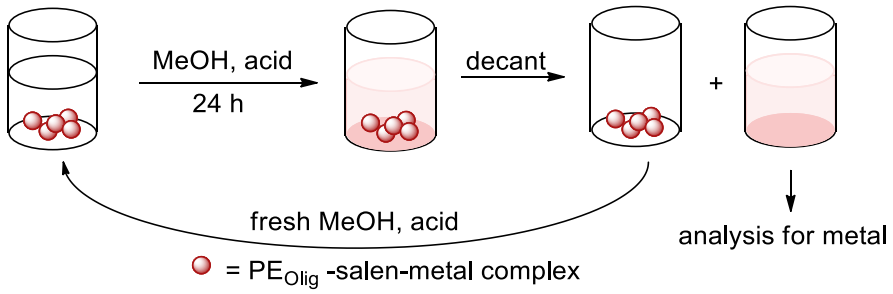


Figure 2. Stability experiment wash cycles exposing PE_{Olig}-salen-metal complexes to methanolic acid.

A colorimetric assay was similarly used to examine the stability of **122** to methanolic TFA [Fig. 3(b)]. In this case, the colorimetric assay involved treating the

methanol phase with H_2SO_4 and $NaIO_4$ to produce an orangish solution.[107] As was true for **114**, small amounts of leaching were seen in cycle 1 with no visually detectable leaching in cycles 2–5. As was true for the study of **114**, we also examined **122** that was isolated after five methanolic TFA washes by dissolving 4.2 mg of this acid washed form of **122** in hot toluene (20 mL) and comparing its absorbance at 445 nm in an 70 °C toluene solution to the absorbance of the same amount of **122** that had not been exposed to acid. In this case, an absorbance of 0.278 was observed for the sample of **122** before acid treatment and an absorbance of 0.28 was found for acid-treated **122**. This experiment showed the Mn(III) content in **122** was unchanged based on the absorbance of 4.2 mg of **122** in 20 mL of toluene at 70 °C.

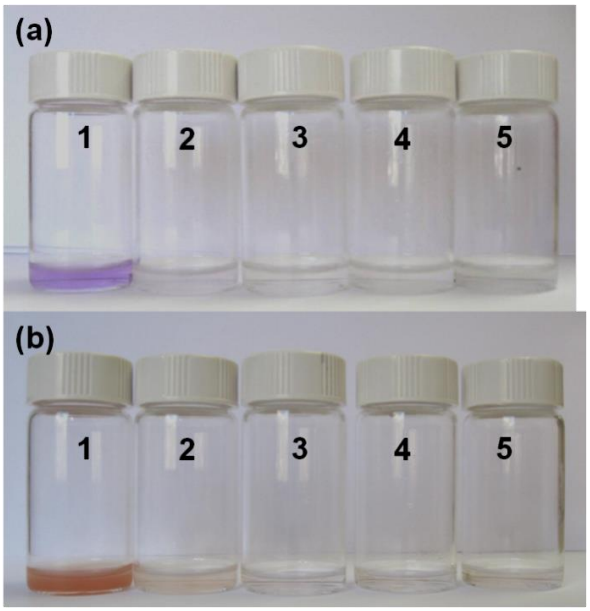


Figure 3. Photographs of the colorimetric assays of (a) the stability experiments of complex **114** and (b) complex **122**.

The qualitative stability of the PE_{Olig}-entrapped PE_{Olig}-ligated metal salen complexes to acid in methanol is in contrast to the chemistry of a low molecular weight salen complex or the polystyrene-supported salen complex. This was illustrated for the complex **121** when **121** was exposed to methanolic TFA. In this case, the solution immediately became highly colored even without EDTA treatment and the color of the polystyrene beads was bleached after exposure of **121** to methanolic TFA showing that a suspension of **121** was not as stable to acid as a suspension of **114**. However, while **114** as a solid is stable toward TFA, **114** like these other salen complexes[76,92-94] did react with TFA when **114** is in solution in hot toluene (vide infra).

To obtain more quantitative data about the extent of demetalation induced metal leaching of precipitates of PE_{Olig} metal salen complexes, we examined the stability of **114** in the presence of TFA in methanol using ICP-MS to test for leached Cr. Using the same protocol used in the experiment above, a suspension of **114** or **114**/PE_{500} was treated with TFA in methanol and allowed to stand for 1 day. After removal of supernatant by decantation, fresh methanol and TFA were added and this process was repeated four times to generate five cycles of acid treatment. The methanol phase from cycles 3 to 5 was concentrated and the residue was digested in nitric acid and sulfuric acid and analyzed by ICP-MS. In these experiments, we estimated the metal loss by comparing the leaching metal in cycles 3 to 5 with the metal content of a fully digested sample of **114** isolated after repeated five TFA/MeOH washings. We reasoned that this should be a more accurate estimate of leaching since the qualitative analyses above suggested the initial samples of **114** were contaminated with a slight excess of Cr. This analysis showed that the metal loss

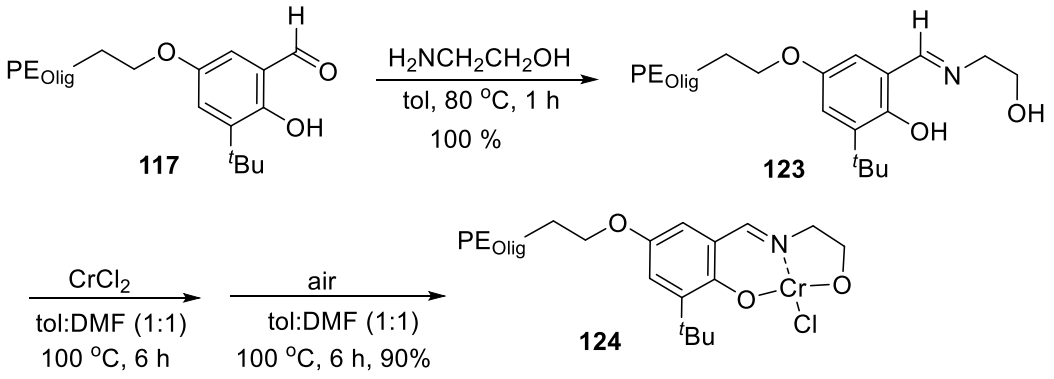
averaged 0.45% for cycles 3 to 5 (0.55% cycle 3; 0.44% cycle 4; and 0.37% cycle 5). Experiments with **114**/PE_{500} showed that the Cr loss in cycle 5 was 0.47% showing again that the PE_{Olig} ligand was itself sufficient to prevent acidolysis of **114**.

A similar experiment using ICP-MS analysis was carried out with **122**. Under the same acidolysis conditions used with **114**, complex **122** lost an average of 0.79% Mn for cycles 3 to 5 based on ICP-MS analysis (1.63% cycle 3; 0.39% cycle 4; and 0.36% cycle 5).

While literature reports describe the acid-promoted demetalation of soluble metal salen complexes occurs in solution the presence of acid,[76,92-94] we also verified that these PE_{Olig}-bound metal salen complexes in solution are demetalated with TFA. In this experiment, we suspended a sample of the Mn complex **122** from cycle 5 in the experiment described above in toluene containing 3% TFA in methanol. This suspension was then heated to 80 °C for 20 min. Cooling reprecipitated any polyethylene bound species. The remaining toluene solution was then analyzed by ICP-MS. The PE_{Olig}-bound Mn salen complex **122** contained 598 mg of Mn. The leached Mn in the toluene solution from this homogeneous TFA treatment contained 334 mg of Mn indicating that 56% of **122** was demetalated. In contrast a 24 h treatment of the solid form of this same sample of **122** by TFA in methanol led to a 0.36% loss of Mn.

A final experiment involved studying the stability of a PE_{Olig}-supported tridentate ‘‘half-salen’’ complex **124**. The ‘‘half salen’’ ligand was prepared from PE_{Olig} salicylaldehyde derivative **117** and ethanolamine in toluene at 80 °C. Upon completion of

the reaction, the mixture was cooled to room temperature at which point **123** precipitated. The product was isolated as a yellow solid in quantitative yield (Scheme 31).



Scheme 31. Synthesis of a PE_{Olig}-supported "half-salen" **123** to form Cr(III) complex **124**.

This half salen ligand **123** was then metalated using the same procedure used to form **114**. The product highly colored Cr(III) complex **124** so formed was characterized by UV-Vis spectroscopy (λ_{max} = 443 nm, toluene, 70 °C). When the solid form of this PE_{Olig}-supported Cr(III) complex **124** was subjected to the same acidolysis procedure used above, Cr leaching based on ICP-MS analysis of the methanol washings was again minimal with an average loss of chromium of 0.27% for cycles 3 to 5 (0.31% cycle 3; 0.26% cycle 4; and 0.24% cycle 5).

Conclusion

We have shown that supported salen-metal complexes prepared with PE_{Olig} ligands that have utility in catalysis also have enhanced stability toward acid promoted demetalation. PE_{Olig}-bound Cr(III)-salen and Mn(III)-salen complexes suspended in a non-swelling solvent such as methanol do not react with trifluoroacetic acid in methanol. Based on ICP-MS analysis, the levels of metal leaching into the methanol phase observed for PE_{Olig}-salen metal complexes were 0.27%, 0.45%, and 0.79% for half-salen Cr(III), salen Cr(III), and salen Mn(III) complexes, respectively. Adding the PE_{Olig}-salen complex to excess PE did not further decrease the metal leaching. The stability of these metal complexes toward acid-promoted demetalation shows that PE ligands and a PE matrix can have additional utility in recycling catalysts in that the solid state environment of the recovered species can minimize adventitious reactions that decompose a catalyst during catalyst recycling.

CHAPTER III

POLYETHYLENE AS A COSOLVENT AND CATALYST SUPPORT IN RING-OPENING METATHESIS POLYMERIZATION (ROMP)*

Introduction

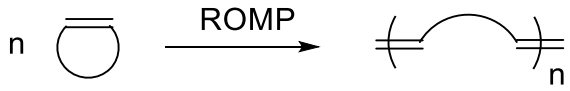
Olefin metathesis is ubiquitous both as a methodology for the synthesis of low molecular weight fine chemicals using cross metathesis (CM) or ring-closing metathesis (RCM), and for the synthesis of designer macromolecules using either polymerization chemistry including both ring-opening metathesis polymerization (ROMP) and acyclic diene metathesis polymerization (ADMET).[14,108-117] However, the presence of Ru residues in the products remains a challenge.[118,119] In the case of products from RCM and CM, Ru contamination is a problem because of the undesirability of heavy metals especially in drug candidates.[118,119] Ru catalyst residues can also lead to undesirable post-synthesis reactions like alkene isomerization.[120-123] This problem has been addressed in several ways. Sequestration of Ru residues by a post-reaction cleanup step is one approach to reduce Ru contamination in products.[124-127] We and others have also described using supported catalysts that separate catalysts from products either by solid−liquid or liquid−liquid separations.[14,40,59,60,128-132]

*Reprinted with permission from "Polyethylene as a Cosolvent and Catalyst Support in Ring-Opening Metathesis Polymerization" by Suriboot, J.; Hobbs, C.; Guzman, W.; Bazzi, H. S.; Bergbreiter, D. E. Macromolecules 2015, 48, 5511, Copyright 2015 by American Chemical Society.

For example, Balcar and Skowerski described using mesoporous molecular sieves in both RCM with Ru leaching that ranged from 0.3 to 3% of the charged Ru catalyst, and Grubbs has reported Ru leaching as low as 0.01% of the charged catalyst (<5 ppb Ru content in the product solution for catalysis with 0.4 mol % of Ru) for a silica-supported RCM catalyst. Similar approaches for ROMP chemistry were less successful with Ru leaching that was reported to be 2.8%.[14] Another alternative approach for CM and RCM reactions is to design more and more active catalysts. This approach addresses this issue best since highly active catalysts with catalyst loadings of <0.01 mol % used in a reaction of a 0.2 M substrate lead to less than 1 ppm Ru contamination even if 20% of the Ru were to leach. However, a more active catalyst does not address this problem in polymerization chemistry. The situation is especially different in polymerization reactions when the polymer products have modest degrees of polymerization. In the absence of chain transfer reactions, ROMP chemistry with a living Ru catalyst will produce 1 mmol of Ru/mmol of product. Thus, a polymerization reaction often leads to higher levels of Ru contamination.

Over the last three decades, ring-opening metathesis polymerization (ROMP) has emerges as one of the most powerful tool in synthesis of well-define polymers.[133] This chemistry has a long history since 1955 when Anderson and Merckling discovered that classical Ziegler-Natta catalysts can polymerize norbornene.[134] A major breakthrough came in 1970 when Chauvin proposed a metallacyclobutane mechanism of metathesis,[135] which then led to the synthesis of first stable alkylidene olefin metathesis catalyst by Schrock[136,137] and the synthesis of the first stable catalyst for living ring-opening metathesis polymerization by Grubbs.[138,139] The developments in high activity and

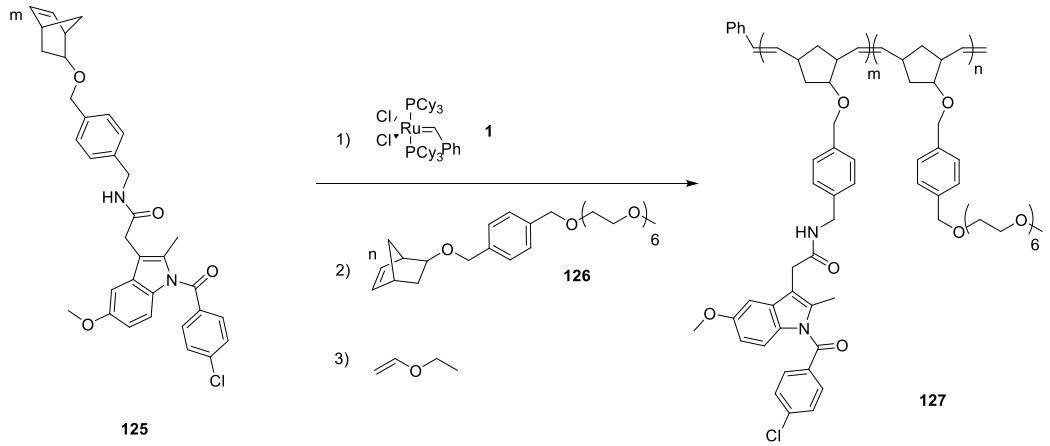
functional group tolerance of the oletfin metathesis catalysts had opened door to a new method to prepare advance materials.[140]



Scheme 32. Ring-opening metathesis polymerization (ROMP).

Recently, ROMP has been attracting attention from many researchers for its applications in biological and pharmaceutical. The need for well-controlled polymers and functional groups tolerance of the method in therapeutic applications made ROMP an excellent candidate. Thus, some example of using ROMP as a method to prepare therapeutic materials will be discussed shortly below.

In 2004, Nguyen and co-workers synthesized a series of amphiphilic polynorbornene based nanoparticles containing indomethacin and investigated their potential as drug delivery vehicles.[141] The synthesis of amphiphilic block copolymer was achieved through ring-opening metathesis polymerization of norbornene-based incorporated indomethacin and hexaethylene glycol monomethyl ether norbornene using Grubbs 1st generation **1**, followed by quenching with ethyl vinyl ether.

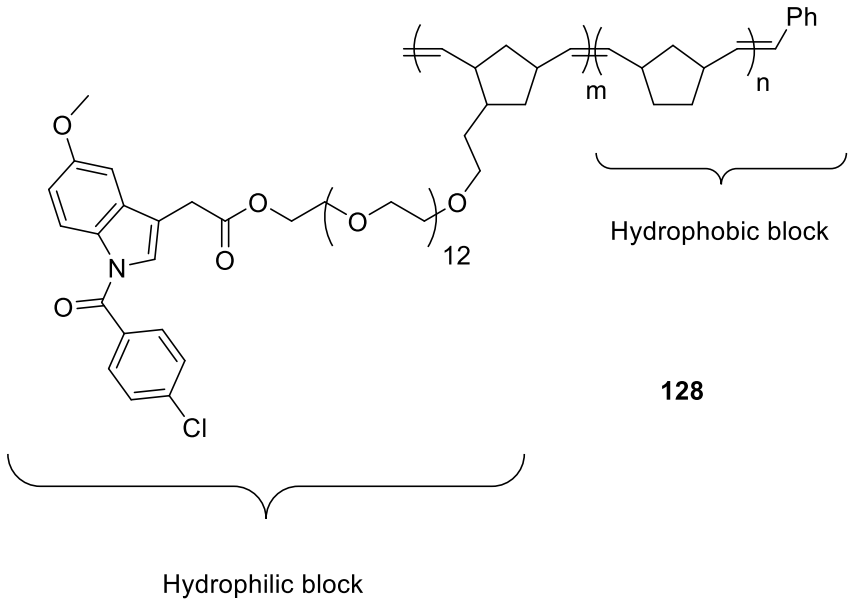


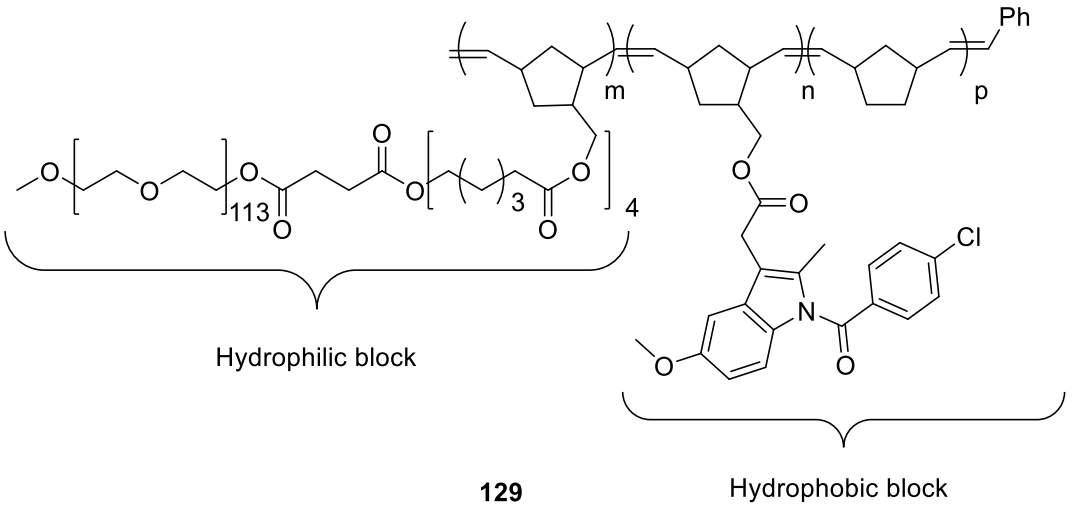
Scheme 33. Synthesis of amphiphilic block copolymers **127**.

The authors demonstrated that amphiphilic block copolymer of hexaethylene glycol norbornene and indomethacin-containing norbornene could form polymeric core-shell nanoparticles in water. These nanoparticles have average diameter in the range of 90 – 1000 nm determined by transmission electron microscopy (TEM). The ability to release indomethacin of block copolymer consists of 17% of hexaethylene glycol norbornene was investigated. It was found that 12% of indomethacin was released when incubated in HCl-adjusted mixture of H_2O/DMSO (pH = 3.0, 20 wt % H_2O) at 25 °C in 48 h and the level of indomethacin released was increased to 20% when incubated at 37 °C with the same incubation time.

Another approach in using polynorbornene-based nanoparticles as drug delivery vehicles was described by Gnanou and co-workers.[142] Two types of drug delivery methods had been discussed; (i) indomethacins were carried at periphery, and (ii) indomethacins were carried at their core. In the first case, indomethacins were attached to the periphery

of the nanoparticles shell through ester linkage that can be released when the environment is acidic enough. The latter case, indomethacins were attached to the polynorbornene chains that are part of the nanoparticle core shell, which can also be released when the environment is adequately acidic. Both strategies showed promising results in indomethacins releasing level. Polynorbornene nanoparticles with indomethacins attached on the periphery released 80% of the drugs via degradation of ester bonds after 48 h. On other hand, the shell of polymer **129** was initially disrupted from the degradation of hydrophilic block in acidic environment exposing the inner core of the nanoparticle which then allow 85% of the drug to be released after 48 h.

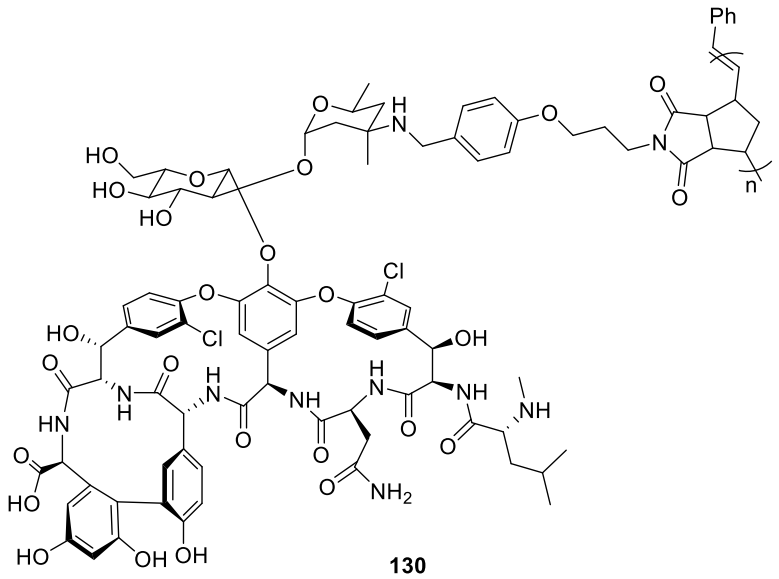




Scheme 34. Periphery-containing indomethacin polynorbornene **128** and core-containing indomethacin polynorbornene **129**.

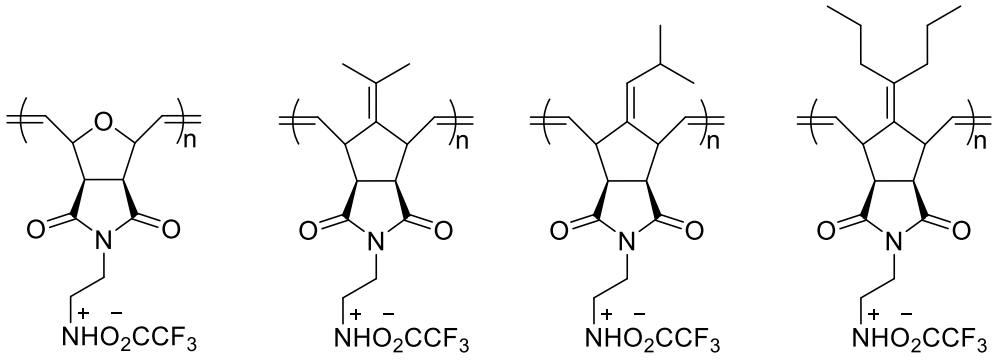
Arimoto and co-workers reported the synthesis of vancomycin-conjugated norbornene homopolymer.[143] Initially, the polymer was synthesized in aqueous emulsion

condition yielding only 4% of the product (molecular weights of the polymer product were ranged from 8.2 – 17.2 Da). However, the yield was improved to 60% when the polymerization was carried out in methanol media (molecular weights of the polymer product were ranged from 8.2 – 66.3 Da). The antibacterial property of vancomycin-conjugated norbornene homopolymer prepared from aqueous emulsion process showed to be comparable to those of normal vancomycin toward bacteria such as *S. aureus* (MIC of 0.2 μg/mL), *Enterococcus faecalis* (MIC of 0.5 μg/mL), Van-A VRE (MIC of 250 μg/mL), and Van-B VRE (MIC of 125 μg/mL). This result suggested that the incorporation of polynorbornene does not damage the antibacterial property of vancomycin. However, the incorporation of vancomycin to polynorbornene through methanol method enhanced the antibacterial property by 8 to 60 fold (MIC of 31 μg/mL in the case of Van-A VRE; MIC of 2 μg/mL in the case of Van-B VRE). The reason behind this outcome was not clear but the authors suggested that the polymer weight distribution played an important role in this phenomenon.



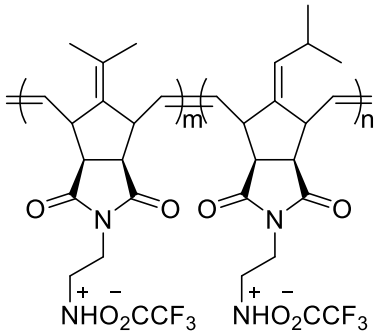
Scheme 35. Vancomycin-conjugated norbornene homopolymer **130**.

Coughlin and co-workers successfully described the incorporation of antibacterial amphiphilic cationic species onto the main chain of polynorbornene.[144] The structure of polymer with hydrophobic end and protected cationic group showed phospholipid-disruption activity suitable for antibacterial application. A series of this type of polymer were prepared by ring-opening metathesis polymerization catalyzed by Grubbs 3rd generation catalyst yielding polymers with molecular weight between 1,600-137,500 g/mol and polydispersities in a range of 1.1-1.3.



Scheme 36. Amphiphilic cationic polynorbornenes **131** – **134**.

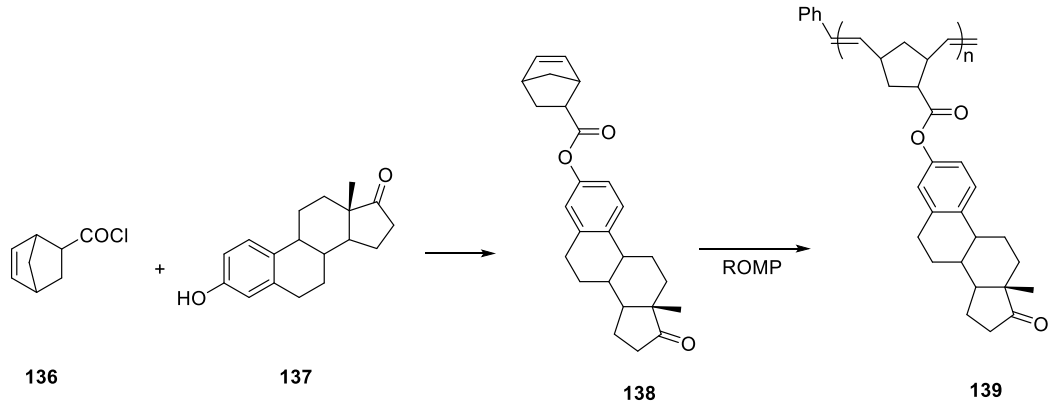
Antibacterial activity and hemolytic activity of these polymers were investigated using growth-inhibition assay. It was found that all of the polymers with hydrophobic character and cationic group exhibited good antibacterial activity and even better especially in the case of polymers with the molecular weight between 4,500-64,000 Da. The antibacterial activity and hemolytic activity of the polymer could be tuned by selecting appropriate co-monomers. For example, by copolymerizing between low hemolytic activity of **132** and high antibacterial activity of **133** with 9/1 ratio of **132**/**133**, this random copolymer **135** possesses low hemolytic activity close to that of **132** (caused 15% hemolysis at 4000 μg/mL) and strong antibacterial activity close to that of **133** (MIC of 40 μg/mL for both *E. coli* and *B. subtilis*).



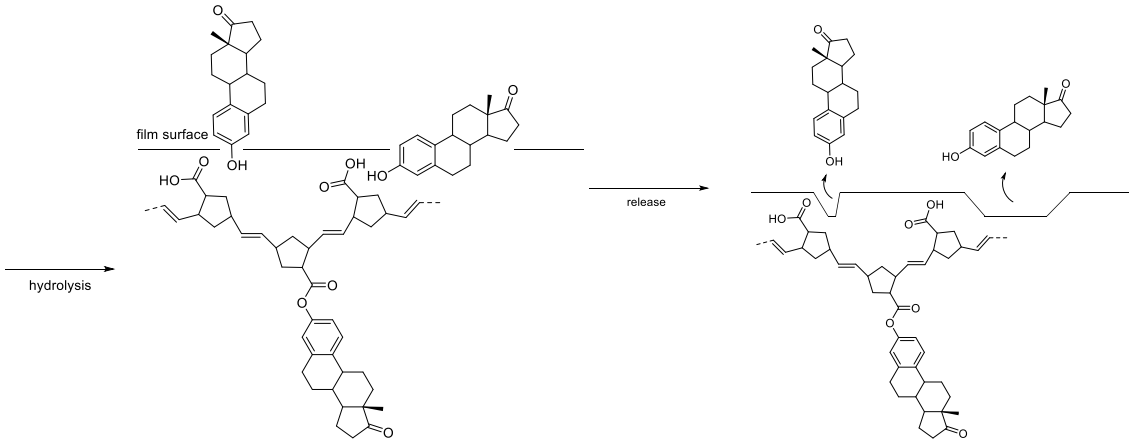
135

Scheme 37. A random amphiphilic copolymer that exhibit selective disruption of bacterial membranes in the presence of red blood cells.

More recently, Wakatsuki and co-workers described another example of using ROMP in therapeutic application.[145] The authors reported the use of Grubbs 2nd generation complex to catalyze ring-opening metathesis polymerization of estrone-conjugated norbornenes. The product polymers were then cast into thin films and followed by the examination of releasing rate of estrone under mild condition (pH of 5.5 or 3.0 at 37 °C), human sweat has pH of 4.0 – 6.0. The examination was performed with two types of samples, flake, and film. The fine-flake sample released 11% of estrone over the course of 80 h while the film type showed significantly slower rate, 2% of estrone released over 130 h. Although the releasing rate of estrone was steady for both types of the sample, the slower releasing rate observed in the film sample was due to the smaller surface area. Interestingly, there was no effect on the estrone-releasing rate when changing the pH from 3.0 to 5.5.



Scheme 38. Synthesis of polynorbornene-supported estrone **139**.



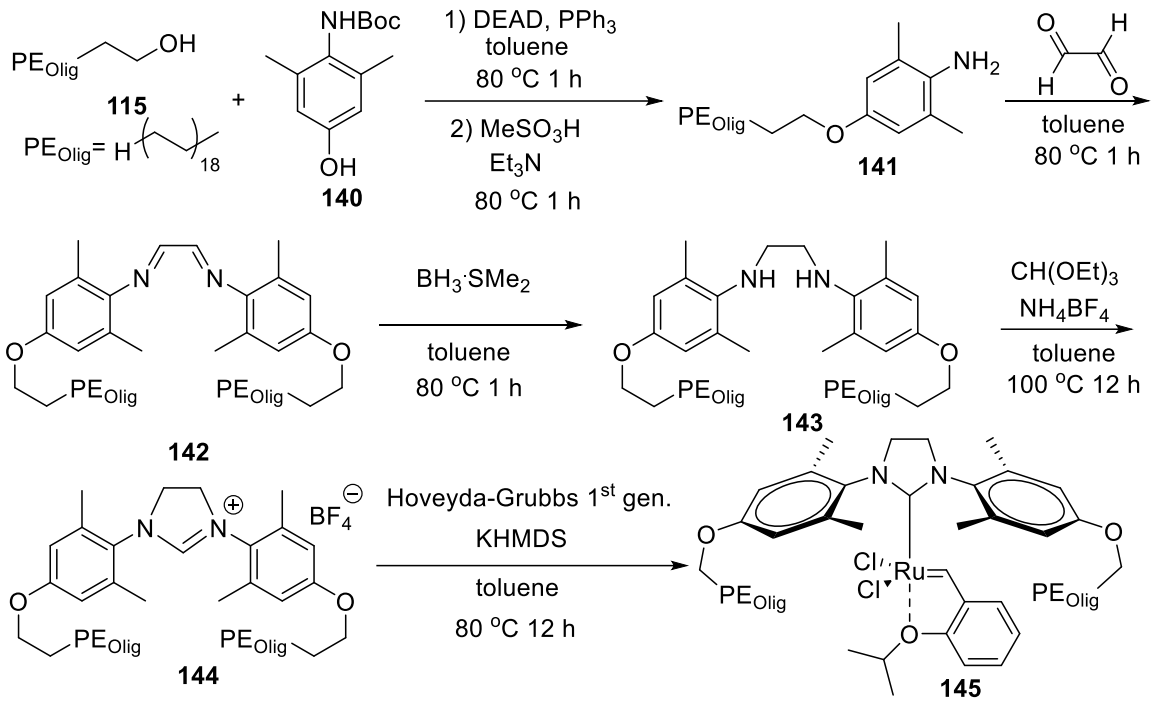
Scheme 39. Proposed releasing scheme of estrone from **139**.

Our groups and others have been interested in the development of recyclable/reusable ring-closing metathesis (RCM) catalysts[59,60] as well as in developing procedures for ROMP that eliminate Ru contamination in products while minimizing the use of additional solvents or processing steps.[146] We recently showed that a polyisobutylene-supported Hoveyda−Grubbs catalyst can be used in ROMP reactions of

various monomers.[146] This soluble PIB-phase anchored NHC-ligated catalyst allows for polymerizations to proceed normally. It then facilitates the sequestration and separation of nonpolar PIB-NHC-ligated Ru contaminants from the more polar ROMP polymers using a biphasic solvent extraction method.[146] Here we describe a significantly improved thermomorphic separation system that separates >99.5% of catalyst residues from products without using excess solvent by using unfunctionalized polyethylene oligomers (Polywax) as a cosolvent with a polyethylene (PE_{Olig})-NHC ligated metathesis catalyst previously described by our lab.[60] While this system requires elevated temperatures to dissolve the PE oligomers which could be a problem for some catalysts, it overall leads to polymer products with lower Ru contamination.

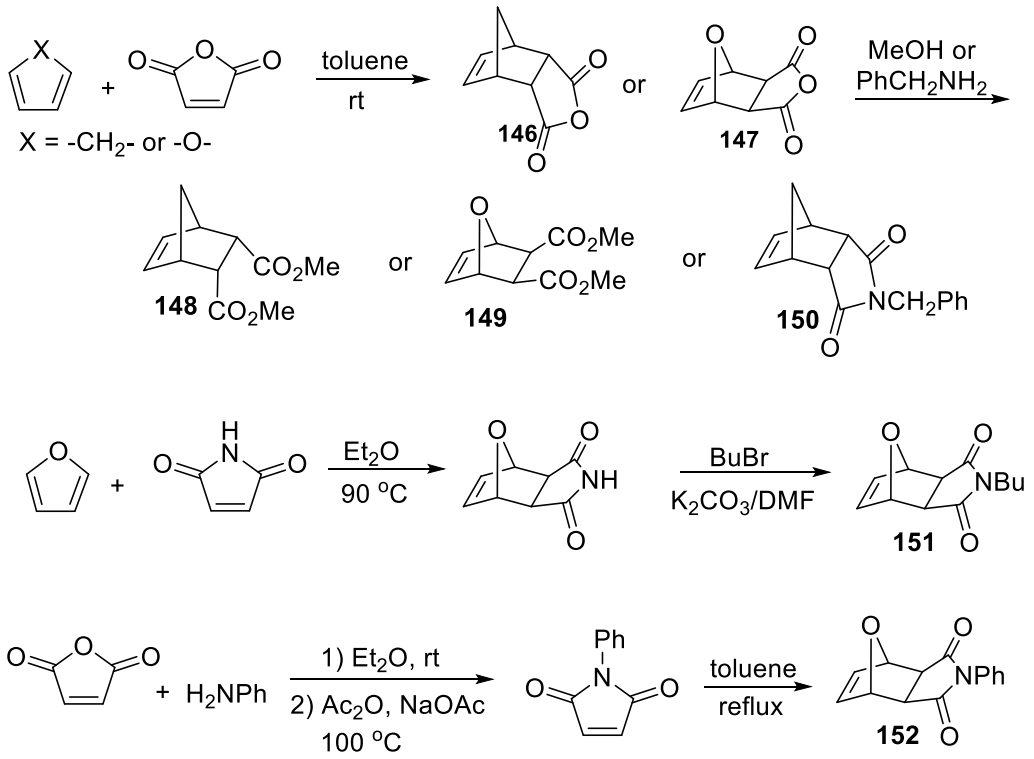
Results and Discussion

The PE_{Olig}-supported Hoveyda−Grubbs second generation catalyst **145** that we used in this paper for ROMP reactions was synthesized from the commercially available PE_{Olig}-alcohol **115** and N-Boc-4-amino-3,5-xylenol **140** using a Mitsunobu reaction to form the PE_{Olig}-aniline **141**. After formation of the protected arylamine, deprotection led to the aniline **141** which was used to form PE_{Olig}-bisimine **142**. The bright yellow powder so formed was then reduced using excess $BH_3{\cdot}SMe_2$ in THF to form the PE_{Olig}-bisamine **143**. Treatment of **143** with $CH(OEt)_3$, NH_4BF_4, and a catalytic amount of formic acid formed the PE_{Olig}- imidazolinium salt **144**. The catalyst **145** was then synthesized by the addition of KHMDS and Hoveyda−Grubbs first-generation catalyst to PE_{Olig}-imidazolinium salt, as shown in Scheme 40.[60]



Scheme 40. Synthesis of PE_{Olig}-supported Hoveyda-Grubbs 2nd generation catalyst **145**

The ROMP monomers used in this study were synthesized as shown in Scheme 41 using known reactions. Diels−Alder reactions of maleic anhydride with cyclopentadiene or furan afforded anhydrides **146** or **147**[14,132] that were in turn used to prepare monomers **148**, **149**, and **150** by reactions with MeOH or $PhCH_2NH_2$.[146-148] Monomer **151** was prepared using SN_2 chemistry from furan−maleimide Diels−Alder adduct, and monomer **152** was prepared by a Diels−Alder reaction of *N*-phenylmaleimide with furan in toluene.[149,150]

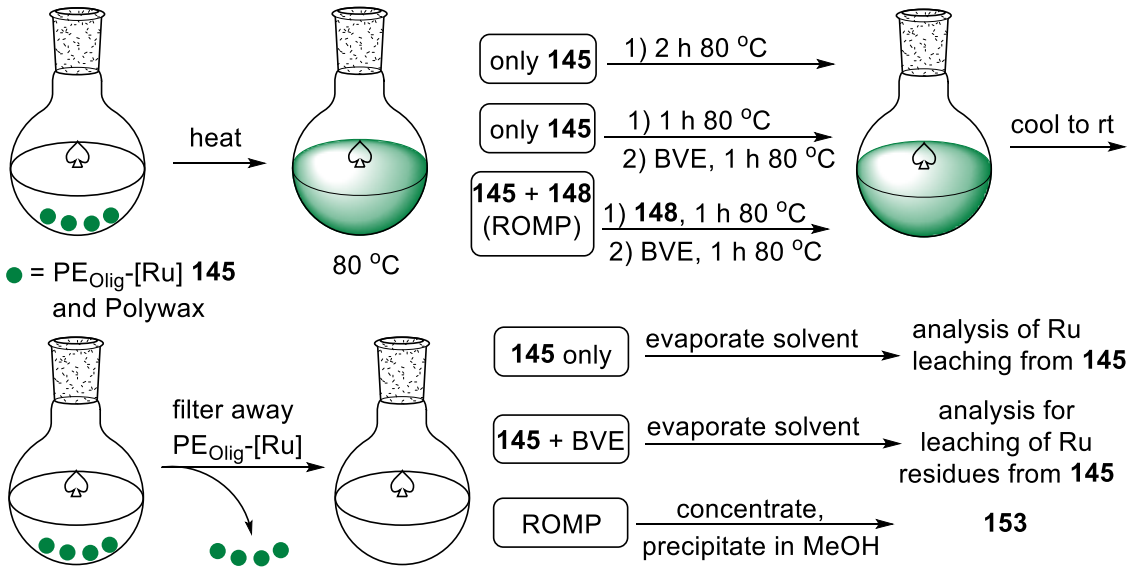


Scheme 41. Synthesis route to monomers **148-152**

To test whether a thermomorphic PE_{Olig}-bound Ru alkylidine complex could be effectively quenched with vinyl ether and to determine if the Ru residues could be easily separated from products, we carried out two control reactions. In the first experiment, 0.01 mmol of the Ru complex **145** (ca. 1 mg of Ru) was suspended in ca. 5 g of THF, and the resulting suspension was heated to 80 °C until a solution formed. This solution was then stirred for 1 h, at which point it was cooled. This led to precipitation of **145**. We initially hoped to simply separate this precipitate of **145** from the solution, but the precipitate that formed contained very fine particles that were difficult to separate. Filtration of these solutions followed by inductively coupled plasma mass spectrometry (ICP-MS) analyses

of the residue showed Ru contamination at levels that seemingly randomly varied from 4 to 16 ppm (ca. 2−8% Ru leaching). While this is only a modest amount of leaching, the variability from experiment to experiment was problematic. To alleviate this problem, we added a small amount of narrow dispersity polyethylene (PE) oligomer as a cosolvent (Polywax-400, PDI 1.08). We and others had previously used this strategy of adding unfunctionalized polyethylene to increase the mass of the recovered catalyst which facilitates catalyst recycling and separation. We had also shown that this type of unfunctionalized PE was itself an alternative to heptane as a hydrocarbon solvent in recycling similar Ru catalysts in RCM chemistry.[151-154] In this second experiment, 0.01 mmol of the Ru complex **145** (ca. 1 mg of Ru) and 100 mg of Polywax 400 were suspended in ca. 5 g of THF, and the resulting suspension was heated to 80 °C until a solution formed. This solution was also stirred for 2 h, at which point it was cooled, and the resulting coprecipitate of **145**/Polywax proved much easier to filter through Celite and a 0.2 μm filter. The resulting THF solution contained only 0.08 ppm Ru (0.04% of the starting Ru). A second control experiment was also carried out. Since the ROMP experiments below require reaction of the terminal Ru vinylidene on the polymer with alkyl vinyl ether, we carried out a second control experiment that was identical to the first experiment but that included a step where the solution of the hot Ru complex **145** was allowed to react with excess butyl vinyl ether. This simulating the step where vinyl ether cleaves the Ru from the polymer chain at 80 °C. As was the case in the first control experiment above, this solution was cooled to form a coprecipitate of the residues of Ru complex **145** and Polywax. Filtration of these residues through Celite and a 0.2 μm filter yielded a THF

filtrate that contained 0.84 ppm Ru (0.42% of the starting Ru). This ca. 10-fold increase in Ru residues still yields a solution with minimal Ru leaching. We presume some soluble Ru byproduct or byproducts formed in this quenching reaction but did not attempt to determine the structure of the ca. 0.5% of this soluble Ru byproduct.

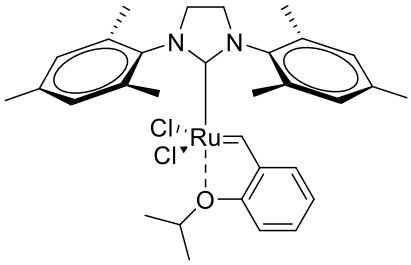


Scheme 42. Scheme to examine Ru leaching from **145**, from residues of **145** formed in a butyl vinyl ether (BVE) quenching step, and from a polymerization using **145**.

Our initial studies of the utility of PE$_{Olig}$ supports in minimizing Ru leaching in ROMP used the PE$_{Olig}$-supported Hoveyda–Grubbs second-generation catalyst **145** and monomer **148**. The polymerization was carried out using unfunctionalized polyethylene (Polywax) as a cosolvent in the reaction mixture as shown in Scheme 42 since the experiments above showed that this added cosolvent facilitated filtration and Ru recovery.

Polymer **153** was prepared on 1 mmol scale in THF with using 2.5% (w/w) of Polywax-400 as a cosolvent. The polymerization was carried out at 80 °C for 1 h using 1 mol % of **145**. The reaction was then terminated by the addition of butyl vinyl ether and stirred for an additional hour. At this point, cooling led to coprecipitation of the Polywax cosolvent phase, and the Ru species derived from **145**. That Polywax phase containing PE_{Olig}-NHC-ligated residue was removed from product solution by filtration through Celite and a 0.2 μm filter. The homopolymer was then isolated by precipitation in MeOH. The amount of Ru residues in product polymer was analyzed by ICP-MS. The result showed that the Ru content in polymer **153** is 26 ppm. This Ru leaching of 0.5% is comparable to the leaching seen in the absence of a polymerization using only a hot butyl vinyl ether quench of **145** (vide infra).

The experiments described above used a modest amount of the linear polyethylene oligomer cosolvent. In the case of monomers **148** − **152**, increasing the amount of this Polywax cosolvent led to problems in that the polymer products precipitated. However, in the case of monomer **148**, we were able to increase the amount of Polywax 10-fold in reactions forming polymer **148**. In this case, the amount of Ru leaching with 1 g of the Polywax cosolvent was 25 ppm – a result that is essentially the same as the 26 ppm seen with 0.1 g of the Polywax cosolvent.



2

Scheme 43. Hoveyda-Grubbs 2nd generation catalyst **2**.

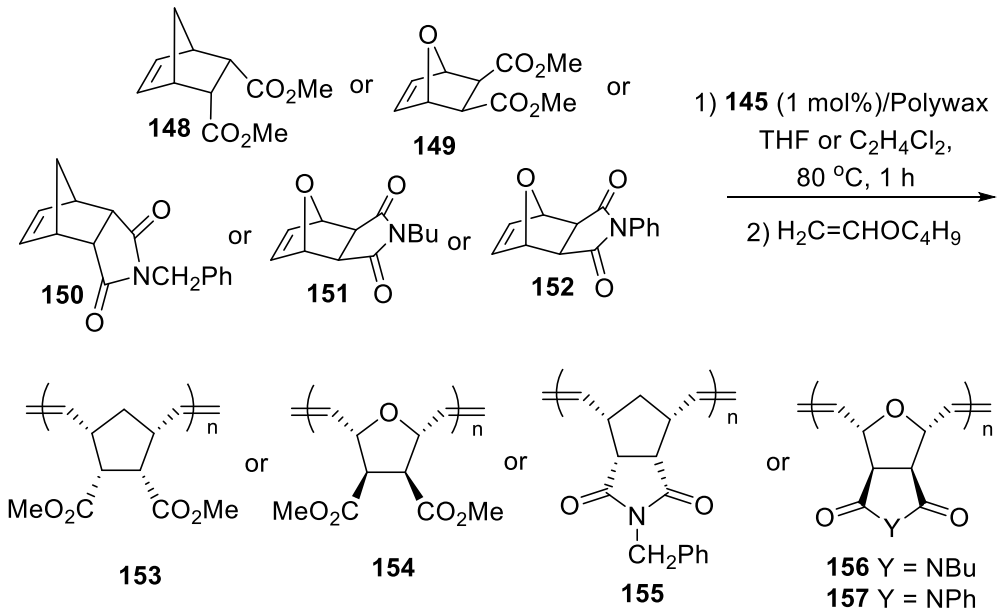
To compare the PE_{Olig}-bound catalyst with its low molecular weight counterpart, polymers **153** were made using 1 mol % of the low molecular weight Hoveyda−Grubbs catalyst second generation **2** on 1 mmol scale. In this case, the product solution was concentrated, and the homopolymer product was isolated as solid by precipitation from THF using MeOH. Unlike the experiment above, the polymer **153** prepared from **2** was reprecipitated twice more from THF using MeOH. These experiments and precipitations used the same amount of polymer, THF, and MeOH as was used in isolating polymer **153** prepared using **145**. Polymer samples after each precipitation were collected and analyzed by ICP-MS. The analysis showed that the Ru content in the polymer samples was 768, 478, and 349 ppm for the first, second, and third precipitation, respectively. While these results suggest that the Ru content in polymer product can be reduced by solvent precipitation, the results with even with three precipitations and are still inferior to the much lower contamination seen for the polymer prepared with PE_{Olig}-supported catalyst **145**. The colors of the solutions of polymers prepared from **145** versus **2** were also different and indicative of the different levels of Ru contamination. We also noted that the

isolated polymer 15 prepared with catalyst **2** after two precipitations appeared white. However, a solution of this polymer in CH_2Cl_2 was colored. This is in contrast to a CH_2Cl_2 solution of polymer **153** prepared with the PE_{Olig}- supported catalyst **145**, which was a colorless as shown in Figure 4.

Figure 4. Solutions of polymer **153** in CH_2Cl_2 prepared either with **2** (left) or with **145** (right).

To further establish the utility of **145** and to show that **145** was equivalent to **2** as a catalyst for ROMP chemistry, we explored polymerization of a series of monomers using this PE_{Olig}-supported Ru catalyst (Scheme 44). Polymerizations of **149** and **151** were carried out in THF, and polymerization of **150** and **152** was carried out in 1,2-dichloroethane (1,2-DCE) on 1 mmol scales. After the termination and isolation process, the resulting polymers **154**−**157** were analyzed by GPC and ICP-MS for M_n, PDI, *E*/*Z* ratios in the product polymers, and Ru leaching in the polymer products (Table 1). The analysis showed that Ru contaminant contents in polymers prepared from **145** were in the

range 19 − 26 ppm as shown in when the insoluble PE precipitates were carefully filtered the product polymer solutions. In these cases, the Ru leaching was quite similar to that seen in a control reaction where the only chemistry was treatment of the starting Ru complex **145** with butyl vinyl ether. In all cases, Ru leaching was much lower than that seen with the conventional catalyst **2**. The data in Table 1 include polymerizations using both **145** and **2**. They show that the use of a PE_{Olig}-bound Ru complex has no significant effect on M_n, PDI, or *E*/*Z* ratios in the products in polymerizations that use similar conditions and similar catalyst loadings. Our results also showed that the PE_{Olig}-bound precatalyst **145** works with a variety of monomers. The only significant difference between polymerizations using **145** versus **2** is the lower Ru leaching with the PE_{Olig}-bound catalyst.



Scheme 44. Ring-opening metathesis polymerization of **148-152** using **145**

Table 1. Results for the ROMP of Various Monomers Using Ru Complexes **145** and **158.**

Polymers	Yield (%)[a]	M_n	PDI	*E*:*Z* Ratio[b]	Ru Content (ppm)[c]
153	80	30,400	1.48	-[d]	26 (0.51)[e]
154	87	33,300	1.55	36:64	23 (0.45)[e]
155	85	62,000	1.23	-[d]	19 (0.37)[e]
156	89	26,000	1.51	48:52	25 (0.49)[e]
157	76	197,500	1.84	53:47	26 (0.51)[e]
153a[f]	80	23,600	1.35	-[d]	349 (6.84)[e,g]
154a[f]	80	26,400	1.34	38:62	461 (9.04)[e,g]
155a[f]	98	58,700	1.65	-[d]	263 (5.16)[e,g]
156a[f]	95	28,100	1.71	47:53	348 (6.83)[e,g]
157a[f]	85	147,000	1.53	52:48	300 (5.88)[e,g]

[a]Yield of polymer isolated after one precipitation from THF (or DCE) into the poor solvent MeOH. [b]Polymers **154**, **155**, and **156** had distinguishable *E* and *Z* isomers (chemical shifts are noted in Chapter VII). The *E*/*Z* ratio was determined by integrating ^{1}H NMR signals for these isomers. [c]Ru analysis based on ICP-MS analysis. [d]The *E* and *Z* isomers had overlapping ^{1}H NMR signals. [e]The percent of the original Ru that was present as a contaminant in the polymer product. [f]This polymer was prepared using catalyst **2**. [g]This polymer was precipitated 3 times from MeOH.

Conclusion

In summary, we have shown that a PE_{Olig}-supported Hoveyda−Grubbs second-generation Ru complex is a competent catalyst in ROMP with a variety of furan- and cyclopentadiene-derived monomers in dichloroethane or THF at 80 °C. Using **145** along with unfunctionalized polyethylene (Polywax) as a cosolvent does not change the nature of the polymer products in any significant way other than to significantly decrease Ru contamination of the polymer products. While this linear polyolefin cosolvent can affect solubility of the polymer products if its concentration is too high, its use at modest concentrations simplifies catalyst separations. Control experiments suggested that most of the leaching of Ru species that is seen results not from the polymerization process but rather from byproducts formed during a terminating step that uses butyl vinyl ether.

CHAPTER IV

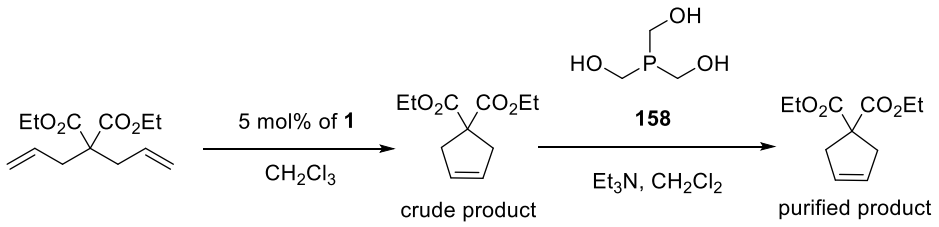
POST-REACTION RUTHENIUM REMOVAL PROCESS FOR OLEFIN METATHESIS

Introduction

The development of modern Ru metathesis catalysts such as Grubbs and Hoveyda-Grubbs types have been the primary tools in widespread applications of organic synthesis that required carbon-carbon double bond construction.[110] These applications include the synthesis of pharmaceuticals,[155] the preparation of cancer-targeting nanoparticles,[156] and the synthesis of insect pheromones as environmental friendly pest-control agents.[110] However, one of the issues common to all metathesis procedures is the removal of the ruthenium at the end of the process. Such ruthenium residues can lead to an increasing in toxicity of the final product, isomerization of the product double bonds, and decomposition of the material over time. Thus, many researchers have been focusing on the development of an efficient and practical procedure to remove highly-colored ruthenium complexes from the products of olefin metathesis reactions.

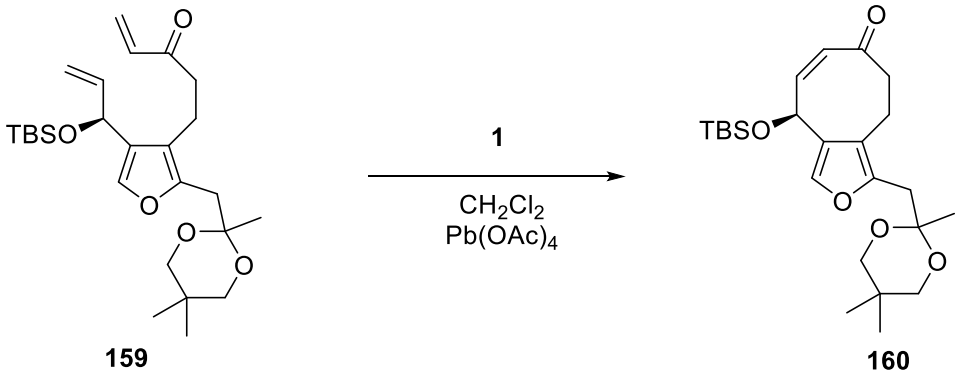
In 1999, Grubbs and Maynard described the use of commercially available water-soluble phosphines as ruthenium sequestering agents for Grubbs first generation catalysts.[127] The removal process was performed by adding crude product of an RCM reaction of diethyl diallylmalonate to a solution of tris(hydroxymethyl)phosphine (86 eq.) and triethylamine in methylene chloride. The color of the resulting solution changed from brown to pale yellow within five minutes, indicating that the phosphine was coordinated

with ruthenium to form a water-soluble ruthenium complex. Then ruthenium species were then removed by extraction with water leaving the product in methylene chloride phase. The amount of ruthenium contamination level was analyzed from 5 mg of RCM product by ICP-MS. The result showed that this purification procedure could reduce the amount of ruthenium from 14920 ppm (crude product) to 1144 ppm. Increasing the amount of tris(hydroxymethyl)phosphine however did not lead to any significant decrease in the Ru contamination. However, two additional washes of the phosphine-ruthenium solution with water reduced the ruthenium contamination level to 670 ppm. To further reduce the level of ruthenium contamination in the product, the crude RCM product of diethyl diallylmalonate was stirred with triethylamine, and an excess of silica gel. This formed phosphine-ruthenium-silica gel species were then removed from the product by simple filtration. The amount of residual ruthenium in the sample after this step was 206 ppm. These results suggested that the part of the problem of this method was not the efficiency of the coordination between phosphine ligand and ruthenium complex but the separation efficiency between phosphine-ruthenium complex and the product. A second problem was that the ultimate Ru concentration was > 1000 ppm, a value that is too high for any pharmaceutical product.[56,157]



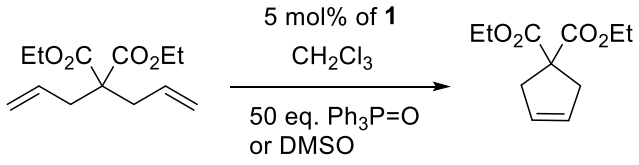
Scheme 45. Ruthenium removal process for RCM reaction of diethyl diallylmalonate using water-soluble phosphine **158**.

Paquette and co-workers reported the use of lead(IIII) acetate as a ruthenium removal tool.[158] The lead acetate that was used as a scavenging agent was added to the completed RCM reaction of **159** and stirred overnight at room temperature in an inert atmosphere. The mixture was then passed through a pad of silica gel (10 g/0.005 mmol of catalyst). The final RCM product was then isolated as a white solid by solvent evaporation and analyzed for Ru and Pb levels by ICP-MS. The results of ruthenium levels in the product showed no significant difference between 1.25 equivalents (300 ppm), and 1.50 equivalents (310 ppm) used of lead(IIII) acetate. However, lead level was lower by fourfold in the latter condition (1 ppm).



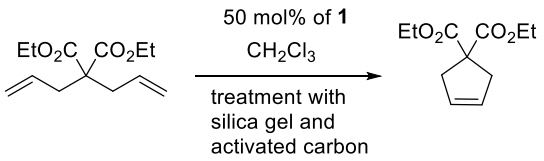
Scheme 46. Ruthenium removal process for RCM reaction of **159** using $Pb(OAc)_4$.

Later, Georg and co-workers reported a mild oxidative procedure that converted Grubbs first generation catalyst into a polar undefined product using either triphenylphosphine oxide or dimethyl sulfoxide (DMSO) that can be removed by a column of silica gel.[159] The crude RCM product of diethyl diallylmalonate was treated with triphenylphosphine oxide or dimethyl sulfoxide for 12 h. The resulting mixture was subsequently passed through a column of silica gel affording purified RCM product. The results of ruthenium levels analyzed by ICP-MS were 240 ppm when 50 equivalent of triphenylphosphine oxide was used and 362 ppm in the case of DMSO (50 eq.).



Scheme 47. Ruthenium removal process for RCM reaction of diethyl diallylmalonate by converting **1** into a polar undefined product using either triphenylphosphine or DMSO.

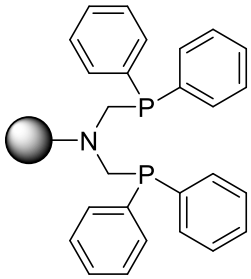
In 2003, Kim and Cho described a ruthenium cleanup procedure for high catalyst loading (50 mol%) RCM reactions using combination of activated carbon and silica gel.[160] This procedure involved a three-step treatment of RCM crude product. For example, the crude mixture of a completed RCM reaction of diethyl diallylmalonate was absorbed on silica gel and passed through silica gel pad, followed by the treatment with 100 equivalents of activated carbon for 12 h at room temperature. The residue was purified for the final time via silica gel column chromatography. The purified product was then analyzed for ruthenium level by ICP-MS. The result was 60 ppm.



Scheme 48. Ruthenium removal process for high catalyst loading RCM reaction of diethyl diallylmalonate.

Breinbauer and co-workers described the used of inexpensive resin **161** to scavenge the Ru from an RCM reaction that used a Grubbs first generation catalyst.[161] This phosphine resin is stable at room temperature in air for at least 6 months. The ruthenium species were removed from an RCM reaction of diethyl diallylmalonate by stirring the reaction mixture with 20 equivalents of **161** for 17 h. The color of mixture was changed from purple to yellow and the off-white beads of phosphine resin became brown.

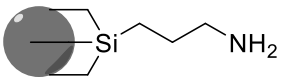
The resin-sequestered Ru was removed from the mixture by simple filtration. Residual ruthenium in the product analyzed by ICP-MS was 2000 ppm. The ruthenium contamination level was reduced to 1660 ppm when the reaction was treated with 5 equivalents of **161** with a secondary treatment that used a silica gel column. Ruthenium content in RCM product was further reduced to 1120 ppm of sample when charcoal was used instead of silica gel.



161

Scheme 49. Phosphine resin **161** as a scavenger for Grubbs 1st generation catalyst.

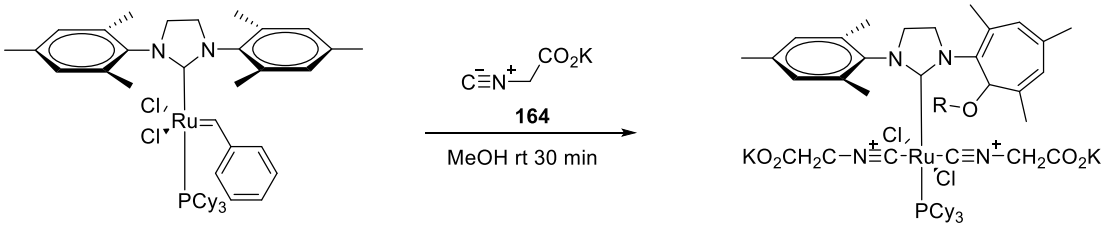
Crudden et al. reported a ruthenium removal procedure using amine-functionalized mesoporous silicate.[162] Grubbs first generation catalysts were removed from an RCM reaction of diethyl diallylmalonate by the stirring the reaction mixture with 10-fold excess of aminopropyltriethoxysilane-derivatized silicates for 1 h at room temperature. The solution was then filtered to remove the scavenging agent. The residual ruthenium in the RCM product analyzed by ICP-MS was 1672 ppm. This result can be improved to 776 ppm by treating the sample with the second aliquot of silicate for 1 h.



162

Scheme 50. Aminopropyltriethoxysilane-derivatized silicates **162** as a scavenger for Grubbs 1st generation catalyst.

Shortly after, Diver and co-workers described a rapid cleanup procedure for metathesis reactions using polar isocyanide as quenching agent.[163] The authors reported that a polar isocyanide could rapidly react with **163** through Büchner insertion to form complex **165**.

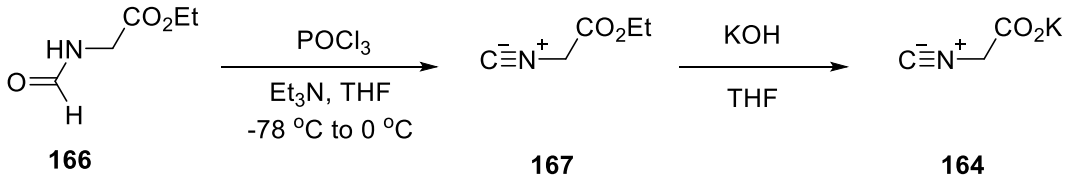


163 **165**

Scheme 51. Quenching process of **163** with isocyanide **164**.

A polar isocyanide was prepared starting from refluxing glycine ethyl ester hydrogen chloride in anhydrous trimethyl orthoformate for 2 h. The resulting formamide **166** was then dehydrated with triethylamine and $POCl_3$ to yield isocyanide **167**. The isocyanide **167** was then converted to an isocyanide salt **164** by reacting **167** with KOH

followed by evaporation of the solvent mixture to afford white solid. The ability of isocyanide **164** to serve as a quenching agent was evaluated in a cross enyne metathesis reaction between 1-hexene and 1-benzoyloxy-2-propyne catalyzed by a Grubbs second generation catalyst. At 50% conversion of the reaction, 8.8 equivalent of isocyanide **164** was added and the color of the reaction was immediately changed from purple to yellow. Further conversion was not observed, indicating that the reaction was rapidly quenched.



Scheme 52. Synthesis of isocyanide **164**.

The crude product from the RCM reaction of diethyl diallylmalonate catalyzed by a Grubbs second generation catalyst was treated with 4.4 equivalent of isocyanide **164** for 30 min at room temperature, followed by plug filtration using silica gel. The ruthenium content in the product analyzed by ICP-MS was 1662 ppm. Increasing the quenching periods did not improve the separation efficiency. This cleanup protocol was also effective in workup of cross metathesis reactions. For example, ruthenium contamination level in the cross metathesis product of methyl vinyl ketone and 1-hexene catalyzed by Grubbs second generation catalyst was 116 ppm.

Although there have been a number of reports on ruthenium cleanup protocols, most of the procedures required the use of an excess silica gel as part of the procedure. This procedure produces silica gel wastes and solvent water that is undesirable. Moreover, in the best of these procedures the Ru contamination was only reduced to 60 ppm. It is our interest to develop an effective and easy to use ruthenium cleanup protocol that can avoid or eliminate the use of silica gel as part of the cleanup steps with a goal of a simple efficient separation process that leads to Ru contamination in products at ca. 10 ppm for a reaction that use 5 mol% of Ru catalyst.

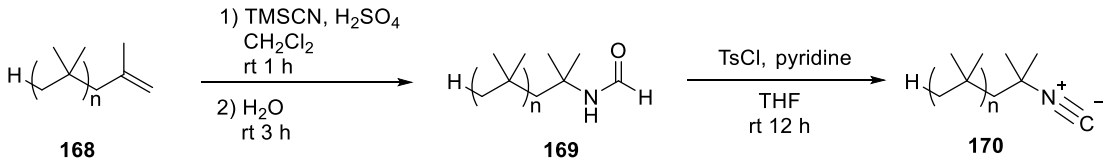
In previous work, Bergbreiter and co-workers described the synthesis of a polyisobutylene (PIB) supported Hoveyda-Grubbs second generation catalyst that was used to achieve Ru contamination levels of 77 ppm in the RCM reaction product of diethyl diallylmalonate and 111 ppm in the ROMP reaction product of norbornene derivatives.[59,146] These Ru contamination levels reflected the use of 5 mol% catalyst and correspond to leaching of 0.63% for the RCM reaction, and the use of 1 mol% catalyst and correspond to leaching of 1.44% for the ROMP reaction. PIB is selectively soluble in non-polar alkane solvents. By extension, compounds it is bound to ought to have similar solubility. This characteristic is useful in homogenous catalysis when combined with thermomorphic or latent biphasic solvent chemistry as it facilitates an efficient purification method. Because PIB-bound compounds are selectively soluble in the non-polar phase of the thermomorphic system, they can be removed by a simple gravitational liquid/liquid biphasic separation.[164] Additional benefits of PIB include availability and being non-toxic material (LD_{50} = 5 g/kg of rats).[165]

PIB-bound quenching agents are an alternative way to sequester Ru. Indeed, our group made a PIB-bound ethyl vinyl ether that was successfully used as a quenching agent after ROMP and RCM.[166] However, while this sequestrant was shown to be kinetically equivalent to low molecular weight vinyl ether, this sequestrant required a multistep synthesis.

Inspired by Diver's and our previous work, we explored the synthesis of a polyisobutylene-terminated isocyanide and its application as a quenching agent for ruthenium olefin metathesis catalyst catalyzed reaction. The synthesis of PIB-terminated isocyanide is straightforward, only two steps were needed to obtain high yield of the final product **170**. The cleanup protocol that use **170** is simple since quenched PIB-bound ruthenium species can be separated from the product by precipitation in an excess amount of hexane.

Results and Discussion

The polyisobutylene-terminated isocyanide **170** that we used in this experiment was synthesized from commercially available PIB alkene **168** using a Ritter reaction by treating **168** with trimethylsilyl cyanide to form PIB-formamide **169**. The resulting formamide **169** was then dehydrated with tosyl chloride and pyridine in THF at room temperature to yield PIB-terminated isocyanide **170** as light yellow viscous liquid as shown in Scheme 53.



Scheme 53. Synthesis of PIB-terminated Isocyanide **170**.

The ability of PIB-terminated isocyanide as a quenching agent was evaluated with Hoveyda-Grubbs second generation catalyst without carrying out any metathesis reaction. This primary experiment was performed by adding a 2 mL solution of Hoveyda-Grubbs second generation catalyst in DMF to a 4 mL scintillation vial. To this vial, a 2 mL solution of 8.8 equivalent of PIB-terminated isocyanide in heptane was added. At room temperature, the mixture was biphasic. The contents of the vial were heated to 80 °C and the two phases became miscible forming a bright green monophasic solution. The color of the mixture changed from green to light yellow within a minute after the mixture became monophasic. Upon cooling to room temperature, the mixture became biphasic again. However, the DMF phase that was once green became colorless while the heptane phase was still yellow. The inactive catalyst was clearly phase-selectively soluble in the heptane phase. These qualitative results indicate that the PIB-terminated isocyanide was successful at inserting itself into the metal center changing the polarity of the ruthenium complex anchoring the Ru in the non-polar heptane phase.

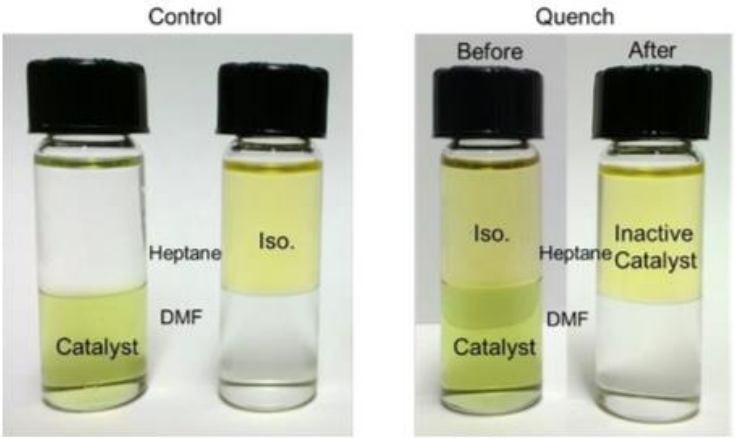
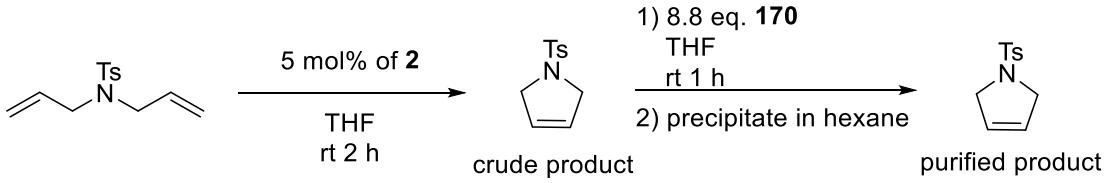


Figure 5. Photograph on the left depicts the phase-selectivity of pure Hoveyda-Grubbs 2nd generation catalyst and **170** (Control). Photograph on the right depicts the before and after stages of a successful controlled quench (no monomer/polymer present) using **170** under thermomorphic heptane/DMF conditions (Quench).

Next, the cleanup protocol was examined in an RCM reaction of *N*,*N*-diallyl-4-methylbenzenesulfonamide catalyzed by 5 mol% of Hoveyda-Grubbs second generation catalyst. A 1 mmol scale RCM reaction of *N*,*N*-diallyl-4-methylbenzenesulfonamide was carried out in THF at room temperature for 2 h. At this point, 8.8 equivalent of PIB-terminated isocyanides **170** were added to the reaction mixture and allowed to stir for 1 h at room temperature. The mixture was then precipitated in hexane whereas the RCM product precipitated out and recovered as a white solid, which subject to analyze by ICP-MS for ruthenium content. The ruthenium level in isolated the RCM product was 44 ppm.

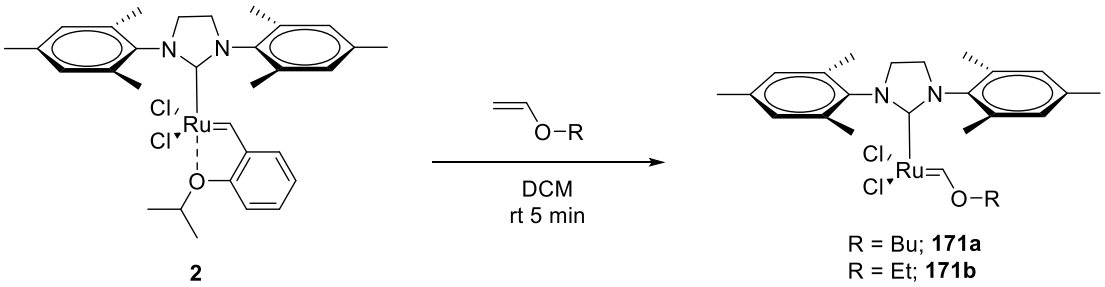


Scheme 54. Ruthenium removal process from RCM reaction using PIB-terminated isocyanide **170**.

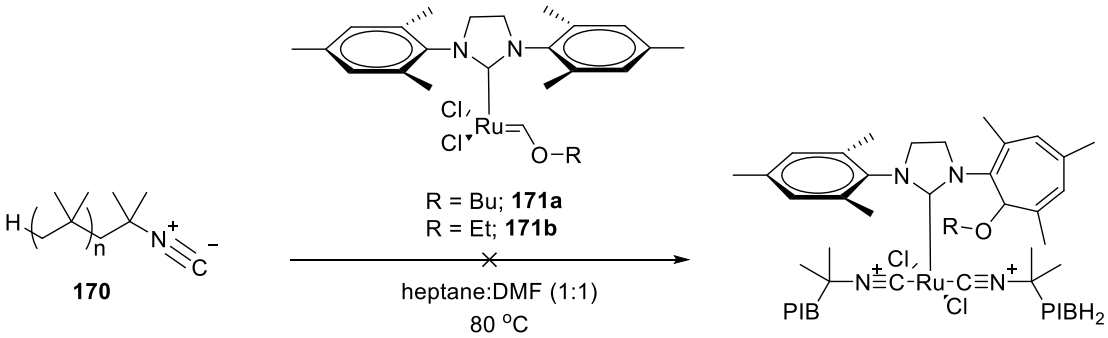
To further establish the utility of **170**, several attempts to remove Hoveyda-Grubbs catalyst from ring-opening metathesis polymerization reaction were made. Since the quenching mechanism of ruthenium olefin metathesis catalyst using isocyanide involved Büchner insertion of alkylidene species to *N*-heterocyclic carbene ligand, the cleavage of the polymer product from ruthenium complex is required before the ruthenium scavenging step using isocyanide can be carried out.

In an experiment using a Hoveyda-Grubbs second generation catalyst, the scavenging protocol for Ru from a ROMP reaction using the PIB-terminated isocyanide **170** was examined with Hoveyda-Grubbs second generation catalyst that had been quenched with butyl vinyl ether. The quenched catalyst **171a** was dissolved in DMF in a 4 mL scintillation vial, followed by the addition of 10 equivalents of PIB-terminated isocyanide in heptane. This biphasic mixture was then heated to 80 °C to form monophasic mixture. After 5 min, the mixture was allowed to cool to room temperature reforming the biphasic heptane/DMF mixture. However, the colors were remained the same as before the heating, yellow in the heptane phase and brown in the DMF phase. This suggested that the PIB-terminated isocyanide reaction with the quenched ruthenium complex **171a** failed.

Increasing the heating time period to 1 h or changing the cleaving agent from butyl vinyl ether to ethyl vinyl ether did not led to a successful scavenging of the quenched Hoveyda-Grubbs second generation catalyst **171**.



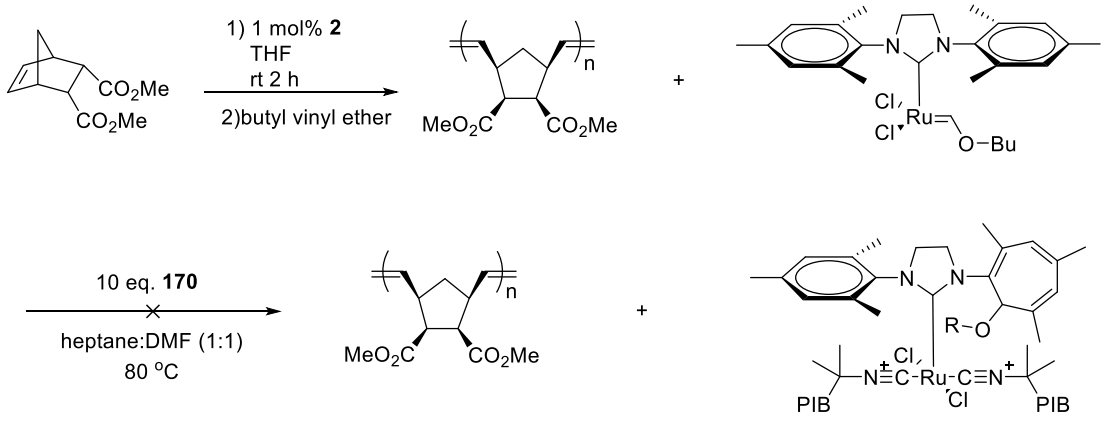
Scheme 55. Reaction of **2** with vinyl ether to form either **171a** or **171b**.



Scheme 56. Attempts to scavenge **171** with PIB-terminated isocyanide **170**.

We also examined the scavenging ability of PIB-terminated isocyanide in ROMP reaction of norbornene derivative **148** catalyzed by Hoveyda-Grubbs second generation catalyst. The norbornene monomer **148** was polymerized by Hoveyda-Grubbs second generation catalyst in THF for 2 h at room temperature. The reaction was quenched by an

excess amount of butyl vinyl ether for 1 h at room temperature, followed by the removal of THF and excess butyl vinyl ether via reduced pressure to yield product polymer that contains ruthenium complex residues. To this mixture, the biphasic solution of 10 equivalent of PIB-terminated isocyanide **170** in 1:1 heptane/DMF was added. The mixture was heated to 80 °C and stirred for 5 min. After cooling the mixture to room temperature, the DMF phase was remained highly-colored, indicating that the attempt to scavenge the ruthenium complex **171a** was unsuccessful. As was true in the experiment above, increasing the stir time to 1 h did not change the result.



Scheme 57. An attempt to scavenge **171a** from ROMP reaction of **148** using PIB-terminated isocyanide **170**.

The complex **171** is known to be one of the least active form of ruthenium olefin metathesis complexes.[167] Thus, the reason underlying these unsuccessful attempts to scavenge the ruthenium complex **171** with PIB-terminated isocyanide might be a

consequence of the lower reactivity of isocyanide species to an electron-rich Ru alkylidene that forms after a vinyl ether quenching process.

Conclusion

In summary, we have shown that PIB-terminated isocyanide **170** can be prepared in two steps under mild conditions in high yield. While this PIB-terminated isocyanide **170** can rapidly quench Hoveyda-Grubbs second generation catalyst and scavenge a Hoveyda-Grubbs second generation catalyst from a RCM reaction of *N*,*N*-diallyl-4-methylbenzenesulfonamide in THF at room temperature, it was unsuccessful in sequestering Ru species from a ROMP reaction. Using this reagent, the RCM product of *N*,*N*-diallyl-4-methylbenzenesulfonamide could be prepared with ruthenium content as low as 44 ppm without involving purification with silica gel. However, attempts to scavenge the ruthenium catalyst from ROMP reaction using PIB-terminated isocyanide **170** were not successful due to an insufficient reactivity of isocyanide species.

CHAPTER V

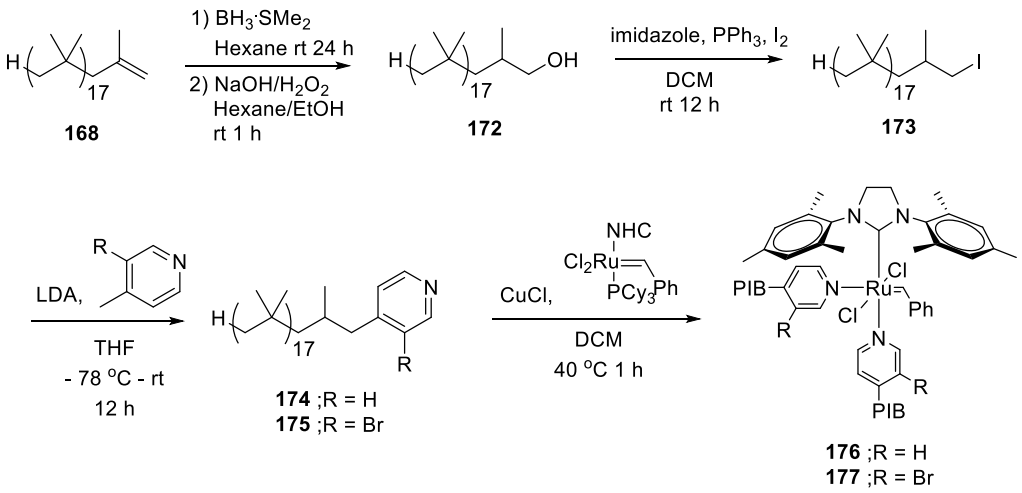
USING PIB-SUPPORTED PYRIDINE LIGANDS WITH Ru(II) CATALYSTS FOR RING-OPENING METATHESIS POLYMERIZATION (ROMP)

Introduction

Soluble polymer supports are useful tools in homogeneous catalysis.[51,164,168] The applications of soluble supports include the use of polymer-supported smart catalysts that autonomously control an exothermic reaction,[64] the use of polymer-supported species to achieve added selectivity in a reaction,[65] the use of polymer-bound sequestering agent to remove metal catalysts from products,[163] the use of polymer-supported species to facilitate "pseudo" high dilution reactions,[66] the use of polymer-bound species to reduce by-products from reactions and as antileaching agents to facilitate homogeneous catalysis.[169] This work shows that the use of phase-selective polyisobutylene (PIB) as Grubbs third generation catalysts supports can facilitate the separation between catalysts and products in ROMP reactions. Moreover, these PIB supports did not interfere with a catalyst's activities in ring-opening metathesis polymerization evidenced from the kinetic study of ROMP reaction using PIB-bi-supported Grubbs third generation catalyst versus the ROMP reaction of the same monomer using non-supported counterpart. This study also shows that the efficiency of the separation between PIB-supported catalyst and polymer product can be improved by increasing the non-polar character of polyisobutylene supports on the catalyst.

Results and Discussion

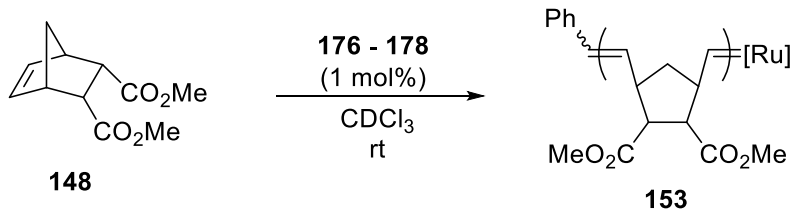
A 4-polyisobutylpyridine (PIB-picoline) ligand **174** and the 3-bromo-4-polyisobutylpyridine (PIB-Br-picoline) ligand **175** were synthesized from the commercially available PIB alkene **168** using a hydroboration reaction to form the PIB-alcohol **172**. Then the PIB-alcohol **172** was converted to a PIB-terminated iodide **173** using imidazole, triphenylphosphine, and iodine in dichloromethane. Then 2 equivalents of a lithiated 4-picoline or 3-bromo-4-picoline prepared by reaction of 4-picoline or 3-bromo-4-picoline with lithium diisopropylsilylamide was allowed to react with this PIB-iodide. This formed the PIB-picoline **174** or the PIB-Br-picoline **175**, respectively. These PIB-bound pyridine ligands were then used to prepare PIB-supported Grubbs third generation catalysts **176** or **177** by allowing Grubbs second generation catalyst to react with either **174** or **175** in the presence of CuCl at 40 °C for 1 h (Scheme 58). The resulting catalysts **176** or **177** were fully characterized by ^{1}H and ^{13}C NMR spectroscopy. Both catalysts were soluble in heptane at room temperature.

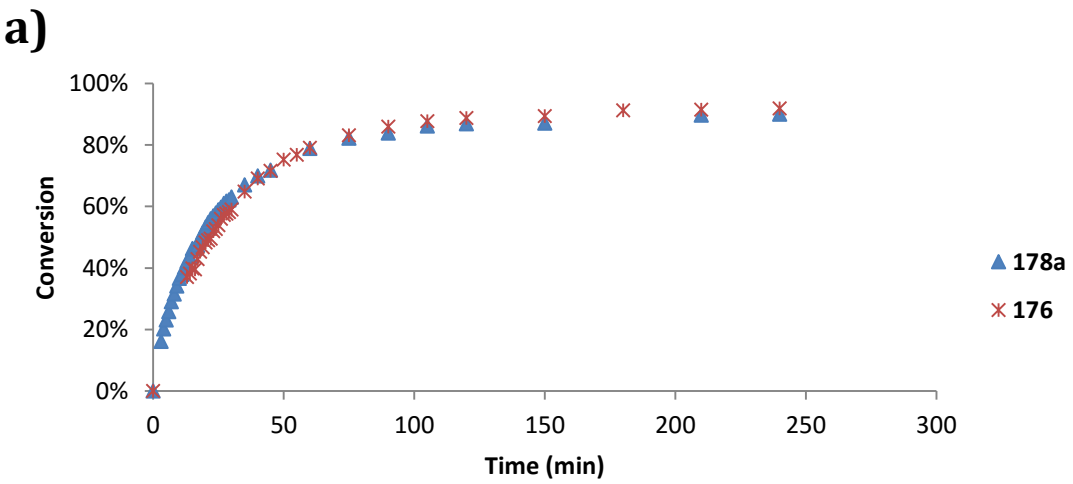


Scheme 58. Synthesis route of PIB-bi-supported Grubbs third generation **176** and **177**.

Prior studies comparing the reactivity of low molecular weight catalysts or low molecular weight reagents with polyethylene oligomer-bound Rh hydrogenation catalysts,[96] with PIB-bound salen polycarbonate polymerization catalysts,[170] with PIB-vinyl ether quenching agents for Ru carbenes,[166] and in ^{13}C NMR studies of phosphine ligand exchange at Ag(I) centers[171] all have shown little or no change in reactivity for a terminal polymer-supported ligand or reagent versus a low molecular weight analog. Nonetheless, our initial efforts in studying PIB-bound pyridines **176** and **177** aimed to test whether phase selective PIB-bi-supported Grubbs third generation catalysts **176** and **177** have the same activities as their low molecular weight counterparts. To probe this issue we carried out kinetic studies using a ROMP reaction of norbornene derivative **148** in 0.6 ml of $CDCl_3$ (1 mol% of catalyst with concentration of 0.5 mM) at room temperature using ^{1}H NMR spectroscopy. The activities of the Grubbs third generation catalysts **176** and **177**

containing PIB-bound pyridine ligands were then monitored by ^{1}H NMR by observing the disappearance of the norbornene alkene peak at 6.23 ppm and the appearance of the alkene peak at 5.55 ppm for the polynorbornene product. The conversion of **148** to polymer **153** was then plotted against time as shown in Figure 6. The results showed that Grubbs third generation catalysts **176** and **177** containing PIB-bound pyridine ligands possess the same activity as their low molecular weight counterparts toward ROMP reaction of norbornene derivative **148**. Grubbs had previously noted that the initiation rate of ROMP reactions catalyzed by Grubbs third generation catalysts depends on the dissociation rate of the pyridine ligand. In low molecular weight complexes, this dissociation rate increases with electron deficient pyridine ligands and the rate of the ROMP reaction increases.[172] This same effect was seen in ROMP reaction of **148** catalyzed by Grubbs third generation catalyst **177**.





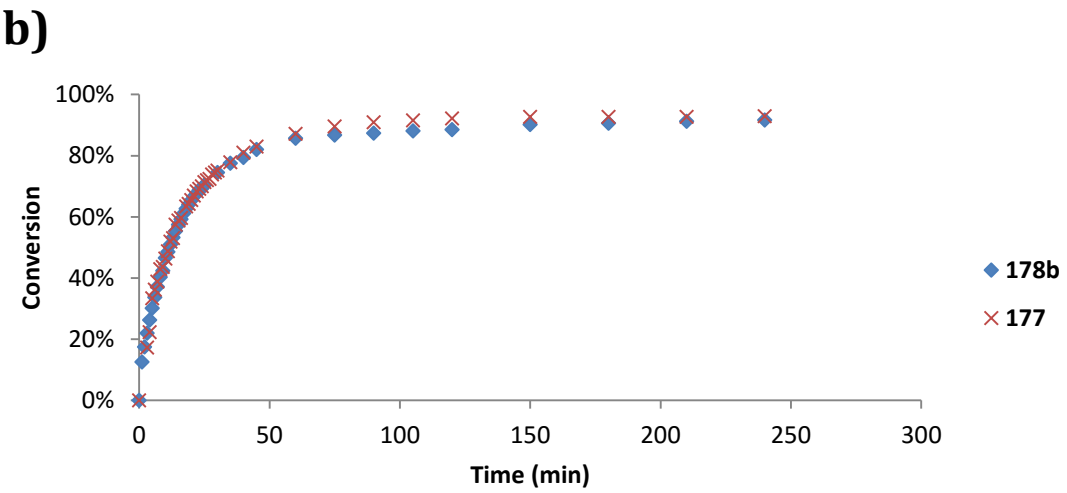
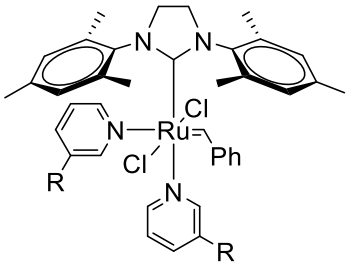


Figure 6. Kinetic studies of ROMP reaction of **148** catalyzed by PIB-supported Ru catalysts a) **176** compared to those catalyzed by **178a** and b) **177** compared to those catalyzed by **178b**.

An important property of third generation Grubbs' ruthenium catalysts is their ability to control molecular weight of the polymer product.[173] Since one metal center generates only one polymer chain, the molecular weight of the polymer product can be controlled by adjusting the monomer to catalyst ratio. To show that this same effect is seen with a Grubbs third generation catalyst containing PIB-bound pyridine ligands, we carried out five different ROMP reactions of norbornene derivative **148** polymerized by the Grubbs' third generation catalyst **177** containing 3-bromo-4-polyisobutylpyridine ligands. These reactions were carried out in dichloromethane using, 2 mol%, 1.5 mol%, 1 mol%, 0.5 mol%, and 0.28 mol% of catalyst loading. The resulting molecular weights of polymer products were increased proportionally to the number of monomer to catalyst ratio. A plot of molecular weights of polymer products versus monomer to catalyst ratio (Figure 8) shows that the ROMP reaction of **148** using **177** was controllable in the same way as is a ROMP reaction using 4-bromopyridine as a ligand in the Ru complex **178b**.



178a ;R = H
178b ;R = Br

Figure 7. Grubbs third generation catalyst **178a** and **178b**.

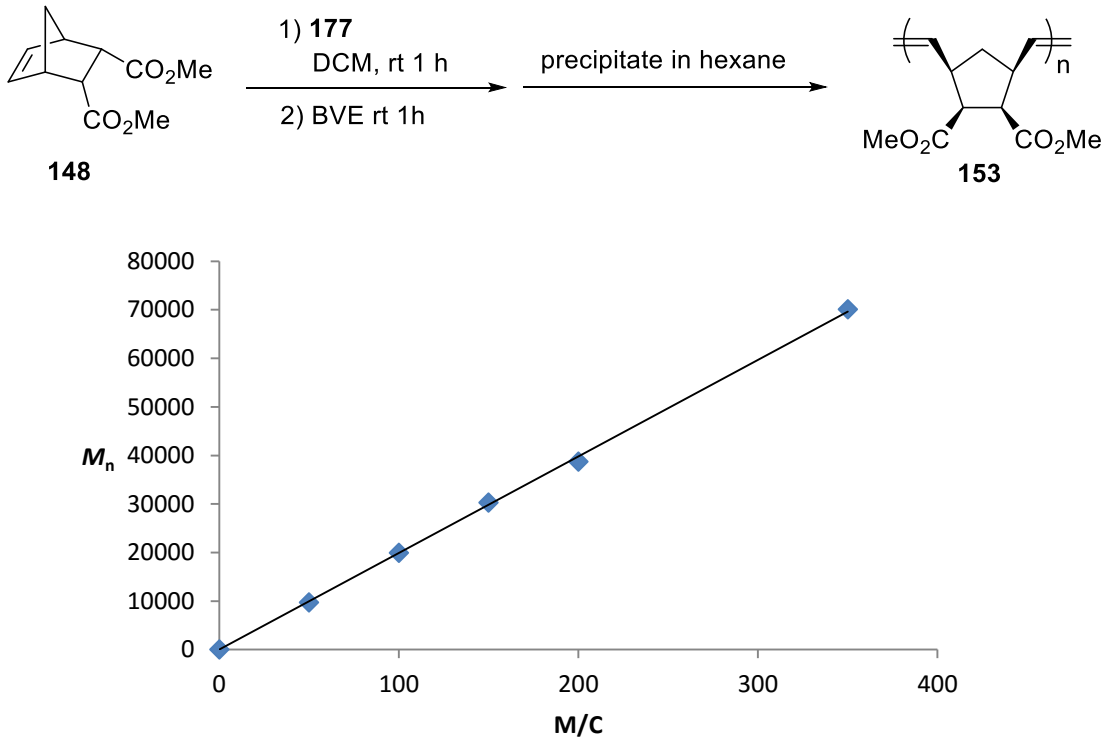
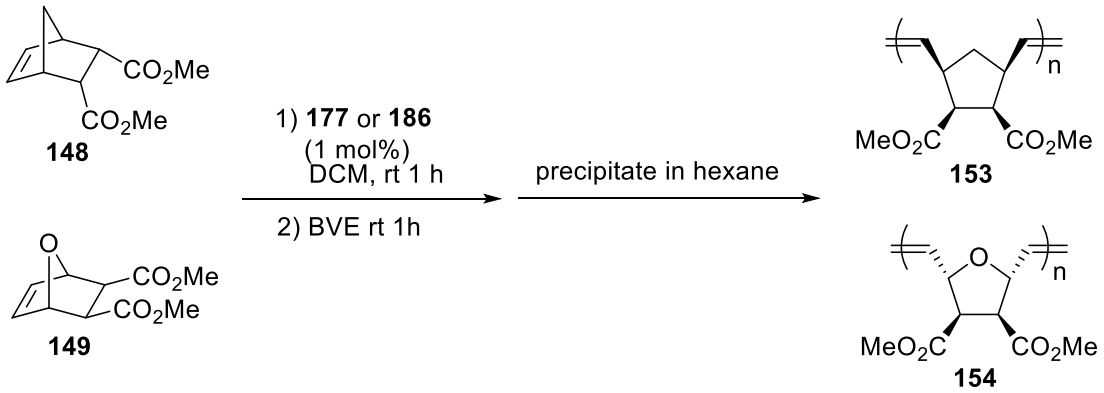


Figure 8. Plot of molecular weights of polymer **153** vs monomer **148** to catalyst **177** ratios.

To further establish the utility of **177** as a recoverable catalyst, we carried out ROMP reaction of **148** using 1 mol% of **177** in dichloromethane at room temperature for 1 h. After this point, an excess amount of butyl vinyl ether was added to the reaction mixture and continue stirring for additional hour. The polymer product was then precipitated using a 10-fold excess of hexane. This product polymer was then analyzed for ruthenium content by ICP-MS and its dispersity (PDI) was analyzed by GPC. The ICP-MS analysis showed that the ruthenium contaminant content in polymer prepared from **177** was 159 ppm. The PDI of the polymer was 1.07, which is comparable to those

polymers prepared with low molecular Grubbs third generation catalyst **178b** (PDI < 1.10).[173] A second polymerization of another monomer **149** was carried out using **177** using the same procedure as was used in polymerization of **148** with complex **177**. The polymer product **154** derived from monomer **149** was again isolated by a precipitation and analyzed by ICP-MS and GPC. In this case, the polymer **154** had a Ru contaminant level of 156 ppm. Its dispersity was 1.05.



Scheme 59. ROMP reactions of **148** and **149** catalyzed by **177** or **186**.

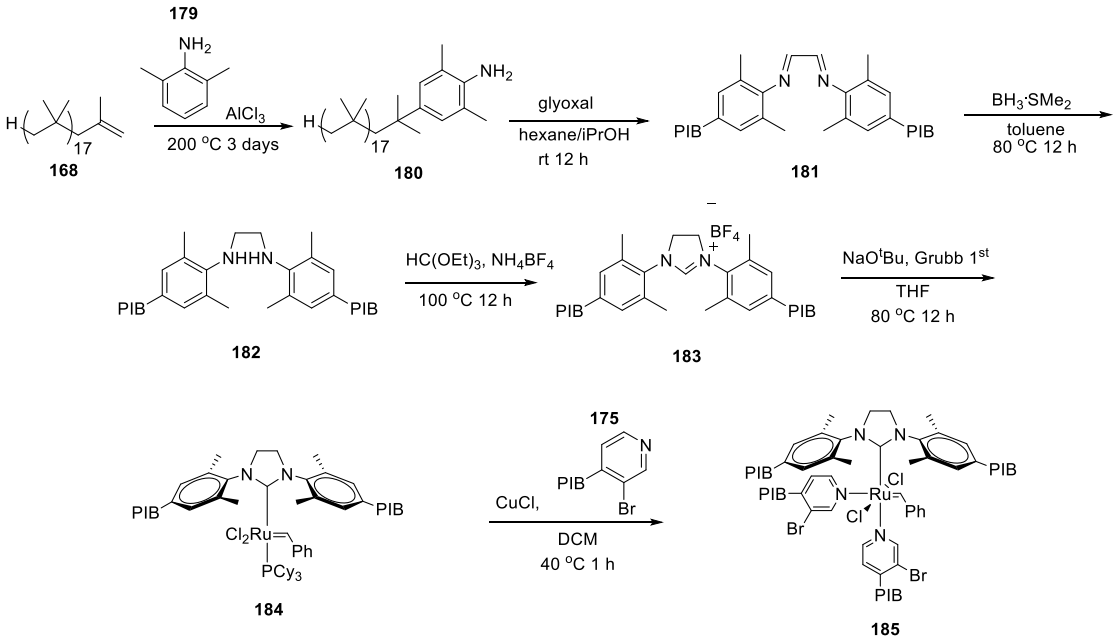
To compare these results with results for ROMP polymer products prepared from Grubbs third generation catalyst **178b**, polymerization of **148** and **149** to form polymers **153** and **154** was carried out. These polymers were isolated by precipitation in a 10-fold excess of methanol. In these cases, ICP-MS analysis showed that the polymers prepared using the PIB-supported Ru catalyst **177** had lower Ru contaminant contents (159 and 156 ppm, respectively) than those prepared from non-supported Grubbs third generation

catalyst (823 and 821 ppm), suggesting that PIB character of PIB-supported Ru catalyst facilitated the separation of Ru species from the product in the precipitation step.

Other studies had earlier shown that PIB-supported NHC ligands also decrease Ru contamination in polymer products. We thus hypothesized that further increasing the number of PIB groups in the Ru complex could result in an even lower Ru contamination in the product. To test this hypothesis, we endeavored to prepare a PIB-quad-supported Grubbs third generation catalyst **186** and to use this catalyst to prepare polymers **153** and **154** and to then analyze Ru contamination in the product polymers.

We proposed to effect the synthesis of a PIB-quad-supported Grubbs third generation catalyst **185** by reaction of a known PIB-supported Grubbs second generation catalyst **184** with the PIB-supported picoline **175** in the presence of CuCl at room temperature for 1 h. To accomplish this, we had to first prepare the PIB-supported Grubbs second generation catalyst **184**. This synthesized was carried out using a reported procedure.[174] This procedure began by allowing the commercially available PIB-terminated alkene **168** to react with 2,6-dimethylaniline **179** in the presence of $AlCl_3$ to form PIB-aniline **180**. Then this PIB-bound aniline **180** was allowed to react with glyoxal to form the bright yellow liquid PIB-bisimine **181**. The bisimine product was then reduced to form PIB-bisamine **182** using excess $BH_3{\cdot}SMe_2$. This bisamine was then converted into the colorless PIB-supported imidazolium tetrafluoroborate salt **183** by heating **182** with NH_4BF_4 in $CH(OEt)_3$ at 100 °C for 12 h. The precatalyst **184** was then synthesized by the addition of sodium *t*-butoxide and Grubbs first generation catalyst to PIB-imidazolium salt **183**, as shown in Scheme 60. Finally, a PIB-quad-supported Grubbs third generation

catalyst **185** was synthesized by treating PIB-supported Grubbs second generation catalyst **184** with PIB-supported picoline **175** in the presence of CuCl at 40 °C for 30 min. The product complex **185** was characterized by ^{1}H NMR spectroscopy.



Scheme 60. Synthesis route of PIB-quad-supported Grubbs third generation catalyst **185**.

The major problem of this synthesis was the stability of PIB-supported Grubbs second generation catalyst **184** toward air and moisture. We found that it is difficult to carry out the last step in Scheme 60 without experiencing the decomposition of **184** even with Schlenk techniques. However, this catalyst decomposition issue was addressed by performing the purification step of **184** and subsequent step of the synthesis of catalyst **185** in the glovebox.

While the synthesis had problems, we were eventually able to prepare the desired catalyst **185**. With this catalyst in hand, we carried out ROMP reactions of norbornene **148** and oxanorbornene **149** using 1 mol% of **185** in dichloromethane at room temperature. After 1h, an excess amount of butyl vinyl ether was added to the reaction mixture. After an additional hour of stirring, mixture was added to a 10-fold excess, relative to the amount of DCM in the mixture, of hexane to isolate polymer products **153** and **154** as white solids that were analyzed by GPC and ICP-MS for M_n, PDI, *E*/*Z* ratio in the product polymers, and Ru leaching in the polymer product. The analysis showed that Ru contaminant contents in polymers **153** and **154** prepared from **185** were 93 and 88 ppm, respectively.

While polymers prepared with quad PIB-supported Ru catalyst **185** had ca. 60% less Ru contamination than those prepared with **177**, this procedure proved not to be the best in term of minimizing the Ru content in the ROMP products. In Chapter III, we described a scheme that use PE_{Olig}-supported NHC Ru complex to prepare ROMP products with Ru contamination of ca. 20 ppm. The practicality of using quad PIB-supported Ru catalyst **185** to prepare ROMP product with low Ru content is questionable, considering its modest effect on minimizing Ru contamination level and the difficulty in catalyst synthesis as mentioned earlier.

Table 2. Results for the ROMP of Monomers **148** and **149** Using Ru Complexes **177**, **178**, and **185**.

Catalysts	Polymers	Yield (%)[a]	M_n	PDI	*E*:*Z* Ratio[b]	Ru Content (ppm)[c]
177	**153**	76	19,900	1.07	-[d]	159 (2.51)[e]
177	**154**	92	22,900	1.05	36:64	156 (3.01)[e]
185	**153**	48	22,600	1.06	-[d]	93 (0.93)[e]
185	**154**	74	27,600	1.06	36:64	88 (1.37)[e]
178b	**153**	70	20,500	1.05	-[d]	823 (11.98)[e]
178b	**154**	93	19,800	1.08	38:62	821 (16.03)[e]

[a]Yield of polymer isolated after one precipitation from DCM into the poor solvent hexane (or MeOH). [b]Polymer **154** had distinguishable *E* and *Z* isomers (chemical shifts are noted in Chapter VII). The *E*/*Z* ratio was determined by integrating ^{1}H NMR signals for these isomers. [c]Ru analysis based on ICP-MS analysis. [d]The *E* and *Z* isomers had overlapping ^{1}H NMR signals. [e]The percent of the original Ru that was present as a contaminant in the polymer product.

Conclusion

In summary, we have shown that PIB-supported Grubbs third generation Ru complexes **177** and **185** are competent catalysts in ROMP reactions of norbornene **148** and oxanorbornene **149** in DCM at room temperature. Using the Grubbs third generation catalyst ligated by PIB-bound pyridines does not affect the reactivity of these catalysts in ROMP chemistry. Indeed, catalysts with PIB-bound pyridines and low molecular weight pyridines have essentially identical kinetic behavior. The catalyst with 3-bromo-4-polyisobutylpyridine ligands also has the same control over molecular weight and

dispersity as a Ru complex formed using 4-bromopyridine. However, the Ru complexes that employ the PIB-bound pyridines can prepare polymer products with significantly lower Ru contamination than those prepared with its low molecular weight counterpart. These results suggest that it is not necessary to put PIB groups on ligands that strongly associate with a Ru center to reduce Ru contamination in metathesis products. Unfortunately, further increasing the non-polar character of Ru catalyst by preparing a catalyst with two PIB-bound pyridines and with an NHC ligand containing PIB groups only reduced Ru contamination by ca. 60% compared to those prepared with Grubbs third generation catalyst containing only 3-bromo-4-polyisobutylpyridine ligands. While this quad PIB-supported Ru catalyst had ca. 60% less Ru contamination, other schemes described in Chapter III that use polyethylene-supported NHC complexes produce polymer products with still lower Ru contamination. Further, the quad PIB supported catalyst synthesis was in our hands experimentally difficult so it is not practical to use this chemistry to further increase the number of PIB groups on the Ru catalyst to reduce Ru leaching into the polymer product.

CHAPTER VI

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 °C. Chemical shifts were reported in parts per million (δ) relative to residual proton resonances in the deuterated chloroform ($CDCl_3$), deuterated benzene (C_6D_6), deuterated or deuterated toluene (C_7D_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. 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.

Preparation of PE_{Olig}/PE_{500} Mixtures. To a 20 mL vial, PE_{Olig}-supported salen complex **114** or **122** (50 mg), PE_{500} (200 mg), and toluene (10 mL) were added and heated at 80 °C for 10 min. Then solution mixture was cooled to room temperature, filtered, and washed with tolene (5 mL) and acetone (5 mL) to afford a solid mixture of the PE_{Olig}-supported salen complex and PE_{500}.

General Procedures for Stability Tests Using TFA. A PE_{Olig} complex (32 mg) or a PE_{Olig}/PE_{500} mixture (135 mg) that was to be tested was weighed into a 20 mL vial. Methanol (10 mL) and TFA (0.3 mL) were added to the vial. After 24 h, the supernatant solution was removed by a pipette and filtered through a pad of Celite. Methanol and TFA were evaporated under reduced pressure and the residue was digested and analyzed by ICP-MS for metal content. Fresh methanol and TFA were added to the vial. The same operation was repeated for four more times.

Digestion Procedures for ICP-MS Analysis. The sample that was to be analyzed and 4 g of concentrated nitric acid were added to a glass vial. The mixture was heated to 120 °C for 24 h. At this point, 4 g of concentrated sulfuric acid was added to the solution at room temperature and the system was again heated to 120 °C for 2 days. The clear solution that formed was then allowed to cool to room temperature and was diluted with 1% nitric acid aqueous solution as necessary to produce a ICP-MS analysis sample. The diluted sample

solution was then analyzed by ICP-MS which allowed us to determine the ppm of metal in the diluted ICP-MS sample which could be converted by simple math into the mg of metal/g of analysis sample and into the total mg of metal in the bulk sample. This analysis showed that the samples of **114**, **122**, and **124** after four 24 h TFA/MeOH treatments had 18, 18, and 36 mg of Cr, Mn, and Cr per g of **114**, **122**, and **124**, respectively.

PE$_{Olig}$-Supported Salen-Mn(III) Complex 122. Toluene (4 mL) and 6 (0.50 g, 0.32 mmol) were added to a 25-mL, round-bottomed flask equipped with a magnetic stirrer, reflux condenser and a pressure-equalized addition funnel. This apparatus was flushed with N_2 and heated to 100 °C with an oil bath. The mixture was allowed to stir until **119** dissolved. At this point, a solution of Mn(OAc)2□4H2O (0.24 g, 0.98 mmol) in ethanol (4 mL) was added to the reaction mixture in a dropwise fashion via the addition funnel. The reaction mixture was then allowed to stir for 12 h. At this point, LiCl (0.085 g, 2.0 mmol) was added to the reaction flask and the reaction mixture was allowed to stir for a further 8 h with exposure to air. Cooling to room temperature, led to precipitation of **122** which was isolated via vacuum filtration and was washed with toluene (25 mL) and THF (25 mL) to give 0.46 g of **122** as a dark solid in 90% yield. UV-Vis spectroscopy (toluene, 70 °C, λ_{max} = 445 nm with ε = 3499 M^{-1} cm^{-1}).

PE$_{Olig}$-Supported ‘‘Half-salen’’ 123. To a 10-mL, round-bottomed flask, equipped with a magnetic stirrer and a rubber septum was added **117** (0.10 g, 0.14 mmol) and toluene (1.4 mL). This mixture was then placed under N_2, heated to 80 °C with an oil bath, and stirred until **117** dissolved. At this point ethanolamine (0.025 mL, 0.42 mmol) was added to the reaction mixture via a syringe. The resulting yellow reaction mixture was stirred 1

h more and then cooled to form a precipitate of **123**. This precipitate was isolated by filtration as a light yellow powder and was then washed with toluene (5 mL) and acetone (5 mL) to afford 0.11 g (100% yield) of 10. ^{1}H NMR (500 MHz, toluene-d_8, 100 °C) δ: 7.89 (s, 1 H), 6.53 (s, 2 H), 3.84 (t, *J* = 6.7 Hz, 2 H), 3.38 (t, *J* = 4.1 Hz, 2 H), 3.20 (t, *J* = 4.1 Hz, 2 H), 1.81 (m, 2 H), 1.58 (s, 9 H), 1.39–1.28 (brs, 200 H) and 0.90 (t, *J* = 6.9 Hz, 3 H). ^{13}C NMR (125 MHz, toluene-d_8, 100 °C) δ: 167.68, 155.86, 152.10, 139.75, 119.91, 119.24, 114.54, 114.29, 35.65, 32.60, 26.97, 23.26, 14.23.

PE$_{Olig}$-Supported ''Half-salen'' Cr(III) Complex 124. To a 10-mL round-bottomed flask, equipped with a magnetic stirrer and a rubber septum was added 10 (0.11 g, 0.14 mmol), $CrCl_2$ (0.020 g, 0.16 mmol), toluene (0.7 mL), and DMF (0.7 mL). This reaction mixture was placed under N_2, heated to 100 °C with an oil bath, and stirred for 6 h. At this point, the reaction mixture was exposed to air and allowed to stir for another 6 h. At which point, the reaction mixture was allowed to cool to room temperature. The PE$_{Olig}$-bound product which precipitated was isolated via vacuum filtration as a brown powder and was washed with toluene (5 mL), methanol (5 mL), and acetone (5 mL) to give 0.11 g (90% yield) of **124**. UV-Vis spectroscopy (toluene, 70 °C, λ_{max} = 435 nm with ε = 4612 M^{-1} cm^{-1}).

Polystyrene-Supported Salen Cr(III) Complex 121. To a 20 mL vial, Merrifield resin (0.500 g, 0.4 mmol), DMF (5 mL), salen ligand **120** (0.304 g, 0.59 mmol), DMAP (0.049 g, 0.4 mmol), and DIPEA (0.14 mL, 0.8 mmol) were added. The reaction mixture was shaken for 1.5 h at room temperature. Then a MeOH/toluene (5 mL, 1:1) solution of $CrCl_2$ (0.098 g, 0.8 mmol) was added to the resin beads (0.500 g, 0.4 mmol) followed by a further

1 h of shaking at room temperature. The beads were then filtered and rinsed sequentially with MeOH, CH_2Cl_2, 9:1 toluene/HOAc, CH_2Cl_2, MeOH, and CH_2Cl_2 and then dried in vacuo to yield the product as green beads. The IR spectrum contains strong absorbance at 1666 cm^{-1}.

General Procedure of Colorimetric Analysis for Chromium Leaching. The methanol phase from the stability studies of **114** or **114**/ PE_{500} that was to be analyzed was decanted and transferred to a 20 mL vial. Then the solvent was removed under reduced pressure. At this point, methanol (1 mL) was added to the vial followed by the addition of an aqueous solution (1 mL) of Na_2EDTA (prepared from the reaction of EDTA (0.10 g, 3.4 mmol) and NaOH (0.020 g, 5.0 mmol) in 20 mL of water). At this point, the solution was heated at 90 °C for 5 min.

General Procedure of Colorimetric Analysis for Manganese Leaching. The methanol phase from the stability studies of **122** or **122**/ PE_{500} that was to be analyzed was decanted and transferred to a 20 mL vial. At this point, methanol (1 mL) was added to the vial followed by the addition of 1 mL of 10 % H_2SO_4 aqueous solution and $NaIO_4$ (0.10 g, 0.47 mmol). The solution was then heated at 90 °C for 5 min.

Procedure for Control Experiment 1. To a 50 mL centrifuge tube, 25 mg (0.01 mmol) of PE_{Olig}-[Ru] **145** and 0.1 g of Polywax were charged with a magnetic stir bar and sealed with a rubber septum and copper wire. After this tube was evacuated and filled with N_2 three times, 5 mL of THF was added to the mixture. The initial suspension was stirred and heated to 80 °C for 2 h. The solution that formed was then cooled to room temperature to form a precipitate of **145**/Polywax. At this point, the solid/liquid biphasic mixture was

filtered through Celite and 0.2 μm filter to yield a clear solution. This entire was transferred to a 20 mL vial. The solvent was removed at reduced pressure. Any residue left in the vial was digested and prepared for ICP-MS analysis. This analysis showed that the residue contained 0.08 ppm of Ru (0.04% of the Ru) in the catalyst **145**.

Procedure for Control Experiment 2. To a 50 mL centrifuge tube, 25 mg (0.01 mmol) of PE_{Olig}-[Ru] **145** and 0.1 g of Polywax were charged with a magnetic stir bar and sealed with a rubber septum and copper wire. After this tube was evacuated and filled with N_2 three times, 5 mL of THF was added to the mixture. The initial suspension was stirred and heated to 80 °C for 2 h. The solution that formed was then allowed to react with 0.05 mL of butyl vinyl ether (BVE). Stirring was continued for an additional 2 h, at which point the solution was cooled to room temperature to form a precipitate of a Ru-complex/ Polywax. At this point, the solid/liquid biphasic mixture was filtered through Celite and 0.2 μm filter to yield a clear solution. This entire was transferred to a 20 mL vial. The solvent was removed at reduced pressure. Any residue left in the vial was digested and prepared for ICP-MS analysis. This analysis showed that the residue contained 0.84 ppm of Ru (0.42% of the Ru in **145** used initially).

General Procedure for ROMP Reactions Catalyzed by PE_{Olig}-[Ru] 145. To a 50 mL centrifuge tube, 25 mg (0.01 mmol) of PE_{Olig}-[Ru] **145** and 0.1 g of Polywax were charged with magnetic stir bar and sealed with a rubber septum and copper wire. After this tube was evacuated and filled with N_2 three times, 2 mL of solvent (THF in the case of monomers **148**, **149**, and **151** or 1,2-dichloroethane (DCE) in the case of monomers **150** and **152**) was added to the mixture and stirred at 80 °C until the solution became

homogeneous. At this point, the solution of 1 mmol monomer in an additional 2 mL of THF or DCE was added to the reaction mixture. The polymerization was allowed to continue at 80 °C for 1 h. After that 0.05 mL of butyl vinyl ether (BVE) was added to quench the reaction. After 1 h the reaction mixture was allowed to cool to room temperature, inducing phase separation of the PE_{Olig}-ligated Ru/Polywax matrix and polymer product solution. This solid/liquid biphasic mixture was filtered through 0.2 μm filter to yield a clear solution. Then the product polymer solution was concentrated using reduced pressure to approximately 1 mL, and this solution was added to 10 mL of MeOH to precipitate the ROMP polymer product. The product was then characterized by gel permeation chromatography, ^{1}H NMR and ^{13}C NMR spectroscopy, and by ICP-MS analysis for Ru contamination.

Polymer 153. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.55 (2H, br), 3.62 (6H, br), 3.12 (2H, br), 2.81 (2H, br), 1.90 (2H,br) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.4, 131.5, 51.3, 44.6, 39.5, 38.0 ppm.

Polymer 154. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90 (1H, br, *trans*), 5.60 (1H, br, *cis*), 5.08 (1H, br, *cis*), 4.69 (1H, br, *trans*), 3.65 (6H, br), 3.09 (2H, br) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.0, 132.5, 131.0, 80.5, 80.2, 53.3, 52.9, 52.6 ppm.

Polymer 155. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25 (5H, br), 5.58 (2H, br), 4.60 (2H, br), 3.22 (2H, br), 2.90 (2H, br), 1.83 (2H, br) ppm. ^{13}C NMR (75 MHz, CDCl3): δ 178.1, 136.3, 129.3, 128.9, 128.1, 49.2, 45.2, 42.3, 40.3, 37.8 ppm.

Polymer 156. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.09 (1H, br; *trans*), 5.80 (1H, br, *cis*), 5.04 (1H, br, *cis*), 4.48 (1H, br, *trans*), 3.48 (2H, br), 3.33 (2H, br), 1.56 (2H, br), 1.29 (2H, br),

0.90 (3H, br) ppm. ^{13}C NMR (75 MHz, CDCl3): δ 175.7, 131.0, 81.1, 53.3, 52.2, 38.8, 29.7, 20.0, 13.6 ppm.

Polymer 157. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40−7.00 (5H, br), 5.93 (1H, br, *trans*), 5.62 (1H, br, *cis*), 5.05 (1H, br, *cis*), 4.50 (1H, br, *trans*), 3.22 (2H, br) ppm. ^{13}C NMR (75 MHz, CDCl3): δ 175.1, 133.8, 131.8, 129.3, 128.8, 126.6, 81.2, 53.6, 53.4 ppm.

General Procedure for ROMP Reactions Catalyzed by 2. This procedure was identical to that used with **145** except that the MeOH precipitation process was repeated three times to yield ROMP polymer product for characterization by gel permeation chromatography, ^{1}H NMR and ^{13}C NMR spectroscopy, and ICP-MS analysis.

Digestion Procedure of 153 – 157 for ICP-MS Analyses. The sample that was to be analyzed and 2 g of concentrated nitric acid were added to a glass vial. The mixture was heated to 120 °C for 24 h. At this point, 2 g of concentrated sulfuric acid was added to the solution at room temperature, and the system was again heated to 120 °C for 24 h. The clear solution that formed was then allowed to cool to room temperature and was diluted with 1% nitric acid aqueous solution as necessary to produce an ICP-MS analysis sample. The diluted sample solution was then analyzed by ICP-MS which allowed us to determine the ppm of metal in the diluted ICP-MS sample which could be converted by simple math into the μg of metal/g of analysis sample (ppm).

PIB-terminated Formamide 169. To a 5 mL round bottom flask, polyisobutylene **168** (0.5 g, 1 mmol) and tetramethylsilyl cyanide (0.5 g, 10 mmol) were charged and dissolved in 2 mL of DCM. After that, sulfuric acid was then added drop-wise to the PIB/TMSCN solution and stirred for 1 h. At this point, 1 mL of water was added to the reaction solution

and stirred for 12 h. After that, the solvent was removed and the PIB species were dissolved in 5 mL of hexane and 5 mL of acetonitrile. The polar water and acetonitrile phases were removed, leaving behind the hexane phase. The hexane phase was neutralized with $NaHCO_3$ (3 x 5 mL) and brine (1x 5 mL). The product of was isolated as colorless liquid (85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.05 (s, 1H), 5.20 (s, 1H), 1.83 (s, 2H), 1.55(s, 6H), 1.45 - 0.99 (140H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$) δ: 160.97, 160.69, 158.51, 57.68, 36.21, 29.32 ppm.

PIB-terminated Isocyanide 170. To a 25 mL round bottom flask, **169** (4.15 g, 3.77) and pyridine (2.98 g, 37.3 mmol) were dissolved in 8 mL of THF and stirred for 15 min. After that, tosyl chloride (2.87 g, 15.1) was then added to the solution and allowed to react for 12 h. The product was filtered via Buchner funnel, and washed with water and brine. The product was concentrated and yielded a yellow, tacky compound 3 (75 % yield) was recovered from the process. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.87 (s, 2H), 1.64 (s, 6H), 1.48 - 0.89 (140H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$) δ: 154.92, 109.83, 57.62, 38.35, 31.26 ppm.

RCM Procedure Using 2nd Generation Grubbs Catalyst and PIB-Isocyanide 170 as a Ru Removal Tool. *N*,*N*-diallyl-4-methylbenzenesulfonamide (0.26 g, 1 mmol) was dissolved in 2 mL of DCM and purged with N_2. To this mixture, **2** (0.04 g, 0.05 mmol) in 2 mL of DCM was added and stirred at room temperature for 2 h. At this point, **170** (0.62 g, 0.44 mmol) in 1 ml of DCM was added to the reaction solution and stirred at room temperature for 1 h. After that, the reaction mixture was condensed to approximately 1

mL and precipitated in 10 mL of hexane to recover the product as a white solid. The product was then analyzed for Ru contamination by ICP-MS.

PIB-terminated Alcohol 172. To a 100 mL round bottom flask, 5 g (5 mmol) of **168** and 10 mL of hexane were charged. To the solution, 0.17 mL (1.7 mmol) of $BH_3 \cdot SMe_2$ was added and stirred at room temperature for 24 h. Then the mixture was cool to 0 °C and 1.4 mL of 4 N NaOH in 4 mL of EtOH was added. After that 0.8 mL of 30% H_2O_2 was added to the reaction and stirred at room temperature for 3 h. At this point, 30 mL of H_2O was added to the reaction mixture and the extracted with hexane (5 x 10 mL) and washed with H_2O (3 x 5 mL), and brine (1 x 10 mL). The organic phase was then dried with $NaSO_4$ and the solvent was removed via reduce pressure to yield product as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.49- 3.44 (dd, J = 5.4 Hz, 1H), 3.32-3.26 (dd, J = 7.5 Hz, 1H), 1.46-0.75 (m, 180H).

PIB-terminated Iodide 173. To a 50 mL round bottom flask, **172** (1.4 g, 1.4 mmol), PPh_3 (0.477 g, 1.82 mmol), imidazole (0.124 g, 1.82 mmol), iodine (0.459 g, 1.82 mmol), and 14 mL of DCM were charged. The mixture was stirred at room temperature for 12 h. At this point, the solvent was removed via reduce pressure and the mixture was redissolved in 10 mL of hexane. The mixture was filtered through Celite to yield colorless solution. After hexane was removed via reduce pressure, the crude product was then purified by column chromatography (hexane) to yield colorless liquid (67% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.31- 3.26 (dd, J = 9.5, 4.2 Hz, 1H), 3.17-3.13 (dd, J = 10.24, 6.45 Hz, 1H), 1.46-0.75 (m, 180H).

PIB-bound Picoline 174 or Br-Picoline 175. To a 100 mL flame dried flask, 4-picoline (0.387 mL, 3.98 mmol) or 3-bromo-4-picoline (0.453 g, 3.98 mmol), and 5 mL of THF were charged. To this mixture, LDA (2.65 mL, 5.3 mmol) was added at – 78 °C and stirred for 1 h. At this point, **173** (3 g, 2.65 mmol) in 5 mL of THF was added to the reaction flask in drop-wise fashion. Then the reaction mixture was warmed to room temperature and stirred for 12 h. After that, 30 mL of sat. NH_4Cl and 30 mL of H_2O were added to the mixture (the reaction color immediately changed from dark purple to light yellow). Then the mixture was extracted with hexane (2 x 30 mL), washed with MeCN (2 x 20 mL), H_2O (2 x 10 mL), and brine (2 x 10 mL). The organic phase was then dried with $NaSO_4$ and the solvent was removed via reduce pressure to yield the product **174** (92 % yield) or **175** (86 % yield) as yellow liquid.

174 ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.51 (d, *J* = 5.81, 2H), 7.13 (d, *J* = 5.81 Hz, 2H), 2.66 (m, 2H), 1.63 – 0.6 (m, 160H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$) δ: 152.16, 149.62, 124.00, 59.61, 38.54, 38.15, 32.44, 31.26 ppm.

175 ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.67 (d, *J* = 2.88, 1H), 8.41 (d, *J* = 2.88, 1H), 7.17 (d, *J* = 4.61 Hz, 1H), 2.71 (m, 2H), 1.63 – 0.6 (m, 160H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$) δ: 151.84, 151.19, 148.17, 125.04, 59.61, 38.54, 38.15, 32.44, 31.26 ppm.

Grubbs 3rd Generation Containing 174 or 175. To a 10 mL flame dried round bottom flask, **174** (0.49 g, 0.300 mmol) or **175** (0.50 g, 0.300 mmol), Grubbs 2nd generation catalyst (0.115 g, 0.136 mmol), CuCl (0.013 g, 0.136 mmol), and dry DCM (4 mL) were charged. The mixture was stirred at 40 °C for 1 h (the color changed from purple to green in 5 min). At this point, the solution was cooled to room temperature and passed through

Celite to yield green color filtrate. The solvent was removed via reduce pressure to yield product **176** or **177** as green liquid which is not stable to air but can be stored in glovebox for at least 6 months.

176 ^{1}H NMR (500 MHz, $CDCl_3$) δ: 19.10 (s, 1H), 8.58 (br, 4H), 7.69 (br, 2H), 7.64 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.4 Hz, 4H), 7.08 (d, *J* = 7.4 Hz, 4H), 6.80 (d, *J* = 5.86, 2H), 6.78 (br, 2H), 4.14 (m, 4H), 2.66 (s, 12H), 2.25 (s, 6H), 2.01 – 0.6 (m, 280H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$) δ: 313.21, 220.80, 218.75, 151.86, 149.97, 130.18, 129.68, 127.74, 124.09, 77.28, 77.03, 76.78, 58.84, 58.22, 56.92, 53.46, 40.40, 38.13, 32.45, 31.26, 30.80, 22.57, 14.04 ppm.

177 ^{1}H NMR (500 MHz, $CDCl_3$) δ: 19.12 (s, 1H), 8.67 (br, 2H), 8.42 (br, 2H), 7.92 (br, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.15 (br, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.91 (m, 1H), 6.78 (br, 4H), 4.78 (s, 12H), 4.14 (m, 4H), 2.66 (s, 12H), 2.25 (s, 6H), 2.01 – 0.6 (m, 280H) ppm. ^{13}C NMR (500 MHz, $CDCl_3$) δ: 315.56, 220.46, 217.75, 151.86, 149.97, 130.18, 129.68, 127.74, 124.09, 77.28, 77.03, 76.78, 58.84, 58.22, 56.92, 53.46, 40.40, 38.13, 32.45, 31.26, 30.80, 22.57, 14.04 ppm

General Procedure for Kinetic Study of ROMP Reaction of 148. To an NMR tube, a solution of **148** (0.06 g, 0.3 mmol), 0.003 mmol of **174**, **175**, or **178**, and 0.6 mL of $CDCl_3$ were charged. The kinetic was followed by ^{1}H NMR spectroscopy.

PIB-quad-supported 3rd Generation Grubbs Complex 185. A mixture of 29 mg (0.01 mmol) PIB-supported 2nd generation Grubbs complex **184**, 37 mg (0.022 mmol) 3-bromo-4-(polyisobutyl)pyridine **175** and 1 mg (0.01 mmol) CuCl in 1 mL of chloroform-d_1 was heated at 40 ^{o}C in a sealed NMR tube for 30 min, at which point the reaction was complete

as indicated by ^{1}H NMR. The resulting green solution was then filtrated through celite and used directly for ROMP reactions. ^{1}H NMR(300 MHz, $CDCl_3$) δ: 19.05 (s, 1H), 8.64 (br, 2H), 8.38 (d, J = 5.1 Hz, 2H), 7.49 (m, 1H), 7.20 (s, 2H), 7.13 (d, *J* = 5.1 Hz, 2H), 7.11 (s, 2H), 7.01 (m, 4H), 4.06 (m, 4H), 2.67 (br, 6H), 2.25 (br, 6H), 2.01-0.6 (m, 560H).

General Procedure for ROMP Reactions Catalyzed by 177or 178b or 185. To a 10 mL round bottom flask, 0.01 mmol of Ru catalysts were charged with magnetic stir bar. After this tube was evacuated and filled with N_2 three times, 1 mL of DCM was added to the mixture and stirred at room temperature until the solution became homogeneous. At this point, the solution of 1 mmol monomer in an additional 1 mL of DCM was added to the reaction mixture. The polymerization was allowed to continue at room temperature for 1 h. After that 0.05 mL of butyl vinyl ether (BVE) was added to quench the reaction. After 1 h the reaction mixture concentrated using reduced pressure to approximately 1 mL, and this solution was added to 10 mL of hexane (MeOH in the case of **178b**) to precipitate the ROMP polymer product. The product was then characterized by gel permeation chromatography, ^{1}H NMR and ^{13}C NMR spectroscopy, and by ICP-MS analysis for Ru contamination.

CHAPTER VII

CONCLUSIONS

This dissertation describes the use of soluble polyolefins such as polyethylene (PE_{Olig}) and polyisobutylene (PIB) as tools to facilitate catalysis in several ways. PE_{Olig} can be used as encapsulating agents that protect metal catalysts such as salen-Cr, salen-Mn, and half-salen-Cr complexes from acid promoted demetalation. The stability of these PE_{Olig}-supported complexes toward acid promoted demetalation was tested by suspending these complexes in a non-swelling solvent methanol containing trifluoroacetic acid at room temperature for 24 h. Based on ICP-MS analysis, the level of metal leaching into the methanol phase abserved for PE_{Olig}-salen metal complexes were 0.27%, 0.45%, and 0.79% for half-salen Cr(III), salen Cr(III), and salen Mn(III) complexes, respectively. Although, PE matrix can enhance the stability of salen-metal complexes toward acid promoted demetalation, adding the PE_{Olig}-salen complex to excess PE did not further improve their stability. In contrast, DVB-crosslinked polystyrene-supported Cr(III)-salen complex was demetalated immediately after exposed to methanolic TFA. The stability of these metal complexes toward acid-promoted demetalation shows that PE ligands and a PE matrix can have additional utility in recycling catalysts in that the solid state environment of the recovered species can minimize adventitious reactions that decompose a catalyst during catalyst recycling.

It was also possible to use PE_{Olig} as a tool to recover transition metal catalysts from the products. We have shown that PE_{Olig}-supported Hoveyda–Grubbs second-generation

Ru complex **145** is a competent catalyst in ROMP with a variety of furan- and cyclopentadiene-derived monomers in dichloroethane or THF at 80 °C. Using **145** along with unfunctionalized polyethylene (Polywax) as a cosolvent does not change the nature of the polymer products in any significant way other than to significantly decrease Ru contamination of the polymer products. Based on ICP-MS analysis, Ru contamination levels in the ROMP products were in the range of 19 – 26 ppm, which translate in to the percent Ru leaching of 0.37 – 0.51%. In addition, these polymer products had no significant different in M_n, PDI, or *E*/*Z* ratios than those prepared with the low molecular weight Ru catalyst. While this linear polyolefin cosolvent can affect solubility of the polymer products if its concentration is too high, its use at modest concentrations simplifies catalyst separations. Control experiments suggested that most of the leaching of Ru species that is seen results not from the polymerization process but rather from byproducts formed during a terminating step that uses butyl vinyl ether.

As an alternative Ru removal method for metathesis reactions, PIB-terminated isocyanide **170** was prepared. This quenching agent can be prepared in two steps under mild conditions in high yield. While this PIB-terminated isocyanide **170** can rapidly quench Hoveyda-Grubbs second generation catalyst and scavenge a Hoveyda-Grubbs second generation catalyst from a RCM reaction of *N*,*N*-diallyl-4-methylbenzenesulfonamide in THF at room temperature, it was unsuccessful in sequestering Ru species from a ROMP reaction. Using this reagent, the RCM product of *N*,*N*-diallyl-4-methylbenzenesulfonamide could be prepared with ruthenium content as low as 44 ppm without involving purification with silica gel. However, attempts to

scavenge the ruthenium catalyst from ROMP reaction using PIB-terminated isocyanide **170** were not successful due to an insufficient reactivity of isocyanide species.

We also have shown that PIB ligands can be used as a tool to facilitate the separation of Ru species from the ROMP products. Using the Grubbs third generation catalyst ligated by PIB-bound pyridines does not affect the reactivity of these catalysts in ROMP chemistry. Indeed, catalysts with PIB-bound pyridines and low molecular weight pyridines have essentially identical kinetic behavior. The catalyst with 3-bromo-4-polyisobutylpyridine ligands also has the same control over molecular weight and dispersity (PDI < 1.10) as a Ru complex formed using 4-bromopyridine. However, the Ru complexes that employ the PIB-bound pyridines can prepare polymer products with significantly lower Ru contamination (159 and 156 ppm) than those prepared with its low molecular weight counterpart (823 and 821 ppm). These results suggest that it is not necessary to put PIB groups on ligands that strongly associate with a Ru center to reduce Ru contamination in metathesis products. Unfortunately, further increasing the non-polar character of Ru catalyst by preparing a catalyst with two PIB-bound pyridines and with an NHC ligand containing PIB groups only reduced Ru contamination by ca. 60% compared to those prepared with Grubbs third generation catalyst containing only 3-bromo-4-polyisobutylpyridine ligands. While this quad PIB-supported Ru catalyst had ca. 60% less Ru contamination, the use of polyethylene-supported NHC complex **145** can produce polymer products with still lower Ru contamination. Further, the quad PIB supported catalyst synthesis was in our hands experimentally difficult so it is not practical to use this

chemistry to further increase the number of PIB groups on the Ru catalyst to reduce Ru leaching into the polymer product.

In all, this dissertation described examples of how soluble polymers can be used to minimize the decomposition rate of the catalyst during catalyst recycling by enhancing its stability at resting state, or to facilitate the separation between metal catalyst and product in order to afford high purity product that can be used in pharmaceutical applications. Such work can aid in the future development of new practical catalysis processes that will utilize soluble polymer as their tools.

REFERENCES

(1) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149-2154.

(2) Collman, J. P.; Belmont, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1983**, *105*, 7288-7294.

(3) Drago, R. S.; Pribich, D. C. *Inorg. Chem.* **1985**, *24*, 1983-1985.

(4) Töllner, K.; Popovitz-Biro, R.; Lahav, M.; Milstein, D. *Science* **1997**, *278*, 2100-2102.

(5) Annis, D. A.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1999**, *121*, 4147-4154.

(6) Nguyen, S. T.; Grubbs, R. H. *J. Organomet. Chem.* **1995**, *497*, 195-200.

(7) Ahmed, M.; Barrett, A. G. M.; Braddock, D. C.; Cramp, S. M.; Procopiou, P. A. *Tetrahedron Lett.* **1999**, *40*, 8657-8662.

(8) Sylvain, C.; Wagner, A.; Mioskowski, C. *Tetrahedron Lett.* **1998**, *39*, 9679-9680.

(9) Schürer, S. C.; Gessler, S.; Buschmann, N.; Blechert, S. *Angew. Chem. Int. Ed.* **2000**, *39*, 3898-3901.

(10) Weskamp, T.; Kohl, F. J.; Hieringer, W.; Gleich, D.; Herrmann, W. A. *Angew. Chem. Int. Ed.* **1999**, *38*, 2416-2419.

(11) Randl, S.; Buschmann, N.; Connon, S. J.; Blechert, S. *Synlett* **2001**, *2001*, 1547-1550.

(12) Mennecke, K.; Grela, K.; Kunz, U.; Kirschning, A. *Synlett* **2005**, *2005*, 2948-2952.

(13) Prühs, S.; Lehmann, C. W.; Fürstner, A. *Organometallics* **2004**, *23*, 280-287.

(14) Allen, D. P.; Van Wingerden, M. M.; Grubbs, R. H. *Org. Lett.* **2009**, *11*, 1261-1264.

(15) Lim, J.; Seong Lee, S.; Ying, J. Y. *Chem. Commun.* **2010**, *46*, 806-808.

(16) Bek, D.; Gawin, R.; Grela, K.; Balcar, H. *Catal. Commun.* **2012**, *21*, 42-45.

(17) Monge-Marcet, A.; Pleixats, R.; Cattoën, X.; Wong Chi Man, M. *Tetrahedron* **2013**, *69*, 341-348.

(18) Hansen, L. C.; Sievers, R. E. *J. Chromatogr. A* **1974**, *99*, 123-133.

(19) Hjertén, S.; Liao, J.-L.; Zhang, R. *J. Chromatogr. A* **1989**, *473*, 273-275.

(20) Hjerten, S.; Yi-Ming Li, Y.; Liao, J.-L.; Mohammad, J.; Nakazato, K. i.; Pettersson, G. *Nature* **1992**, *356*, 810-811.

(21) Tripp, J. A.; Stein, J. A.; Svec, F.; Fréchet, J. M. J. *Org. Lett.* **2000**, *2*, 195-198.

(22) Tripp, J. A.; Svec, F.; Fréchet, J. M. J. *J. Comb. Chem.* **2001**, *3*, 216-223.

(23) Mayr, M.; Mayr, B.; Buchmeiser, M. R. *Angew. Chem. Int. Ed.* **2001**, *40*, 3839-3842.

(24) Mayr, M.; Wang, D.; Kröll, R.; Schuler, N.; Prühs, S.; Fürstner, A.; Buchmeiser, M. R. *Adv. Synth. Catal.* **2005**, *347*, 484-492.

(25) Herrmann, W. A.; Stumpf, A. W.; Priermeier, T.; Bogdanović, S.; Dufaud, V.; Basset, J.-M. *Angew. Chem. Int. Ed.* **1996**, *35*, 2803-2805.

(26) Blanc, F.; Copéret, C.; Thivolle-Cazat, J.; Basset, J.-M.; Lesage, A.; Emsley, L.; Sinha, A.; Schrock, R. R. *Angew. Chem. Int. Ed.* **2006**, *45*, 1216-1220.

(27) Blanc, F.; Thivolle-Cazat, J.; Basset, J.-M.; Copéret, C.; Hock, A. S.; Tonzetich, Z. J.; Schrock, R. R. *J. Am. Chem. Soc.* **2007**, *129*, 1044-1045.

(28) Blanc, F.; Rendon, N.; Berthoud, R.; Basset, J.-M.; Coperet, C.; Tonzetich, Z. J.; Schrock, R. R. *Dalton Trans.* **2008**, 3156-3158.

(29) Hultzsch, K. C.; Jernelius, J. A.; Hoveyda, A. H.; Schrock, R. R. *Angew. Chem. Int. Ed.* **2002**, *41*, 589-593.

(30) Dolman, S. J.; Hultzsch, K. C.; Pezet, F.; Teng, X.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **2004**, *126*, 10945-10953.

(31) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667-3692.

(32) Buijsman, R. C.; van Vuuren, E.; Sterrenburg, J. G. *Org. Lett.* **2001**, *3*, 3785-3787.

(33) Semeril, D.; Olivier-Bourbigou, H.; Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **2002**, 146-147.

(34) Audic, N.; Clavier, H.; Mauduit, M.; Guillemin, J.-C. *J. Am. Chem. Soc.* **2003**, *125*, 9248-9249.

(35) Yao, Q.; Sheets, M. *J. Organomet. Chem.* **2005**, *690*, 3577-3584.

(36) Thurier, C.; Fischmeister, C.; Bruneau, C.; Olivier-Bourbigou, H.; Dixneuf, P. H. *J. Mol. Catal. A: Chem.* **2007**, *268*, 127-133.

(37) Gułajski, Ł.; Michrowska, A.; Bujok, R.; Grela, K. *J. Mol. Catal. A: Chem.* **2006**, *254*, 118-123.

(38) Michrowska, A.; Gulajski, L.; Kaczmarska, Z.; Mennecke, K.; Kirschning, A.; Grela, K. *Green Chem.* **2006**, *8*, 685-688.

(39) Rix, D.; Caijo, F.; Laurent, I.; Gulajski, L.; Grela, K.; Mauduit, M. *Chem. Commun.* **2007**, 3771-3773.

(40) Skowerski, K.; Wierzbicka, C.; Szczepaniak, G.; Gulajski, L.; Bieniek, M.; Grela, K. *Green Chem.* **2012**, *14*, 3264-3268.

(41) Fustero, S.; Simón-Fuentes, A.; Barrio, P.; Haufe, G. *Chem. Rev.* **2015**, *115*, 871-930.

(42) Horváth, I. T.; Rábai, J. *Science* **1994**, *266*, 72-75.

(43) Yao, Q.; Zhang, Y. *J. Am. Chem. Soc.* **2004**, *126*, 74-75.

(44) Matsugi, M.; Curran, D. P. *J. Org. Chem.* **2005**, *70*, 1636-1642.

(45) Matsugi, M.; Kobayashi, Y.; Suzumura, N.; Tsuchiya, Y.; Shioiri, T. *J. Org. Chem.* **2010**, *75*, 7905-7908.

(46) Correa da Costa, R.; Gladysz, J. A. *Chem. Commun.* **2006**, 2619-2621.

(47) da Costa, R. C.; Gladysz, J. A. *Adv. Synth. Catal.* **2007**, *349*, 243-254.

(48) Bergbreiter, D. E.; Bursten, M. S. *J. Macromol. Sci., Chem.* **1981**, *16*, 369-381.

(49) Süßner, M.; Plenio, H. *Angew. Chem. Int. Ed.* **2005**, *44*, 6885-6888.

(50) Bergbreiter, D. E. *Chem. Rev.* **2002**, *102*, 3345-3384.

(51) Bergbreiter, D. E.; Tian, J.; Hongfa, C. *Chem. Rev.* **2009**, *109*, 530-582.

(52) Gravert, D. J.; Janda, K. D. *Chem. Rev.* **1997**, *97*, 489-510.

(53) Heldebrant, D. J.; Jessop, P. G. *J. Am. Chem. Soc.* **2003**, *125*, 5600-5601.

(54) Varray, S.; Lazaro, R.; Martinez, J.; Lamaty, F. *Organometallics* **2003**, *22*, 2426-2435.

(55) Hong, S. H.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 3508-3509.

(56) Hong, S. H.; Grubbs, R. H. *Org. Lett.* **2007**, *9*, 1955-1957.

(57) Samanta, D.; Kratz, K.; Zhang, X.; Emrick, T. *Macromolecules* **2008**, *41*, 530-532.

(58) Hongfa, C.; Tian, J.; Bazzi, H. S.; Bergbreiter, D. E. *Org. Lett.* **2007**, *9*, 3259-3261.

(59) Hongfa, C.; Su, H.-L.; Bazzi, H. S.; Bergbreiter, D. E. *Org. Lett.* **2009**, *11*, 665-667.

(60) Hobbs, C.; Yang, Y.-C.; Ling, J.; Nicola, S.; Su, H.-L.; Bazzi, H. S.; Bergbreiter, D. E. *Org. Lett.* **2011**, *13*, 3904-3907.

(61) Albericio, F.; Tulla-Puche, J. *The Power of Functional Resins in Organic Synthesis*; Wiley, 2008.

(62) Benaglia, M. In *Recoverable and Recyclable Catalysts*; John Wiley & Sons, Ltd: 2009, p 301-340.

(63) Parrish, C. A.; Buchwald, S. L. *J. Org. Chem.* **2001**, *66*, 3820-3827.

(64) Bergbreiter, D. E.; Case, B. L.; Liu, Y.-S.; Caraway, J. W. *Macromolecules* **1998**, *31*, 6053-6062.

(65) Niu, Y.; Yeung, L. K.; Crooks, R. M. *J. Am. Chem. Soc.* **2001**, *123*, 6840-6846.

(66) Bédard, A.-C.; Collins, S. K. *J. Am. Chem. Soc.* **2011**, *133*, 19976-19981.

(67) Zhao, M.; Helms, B.; Slonkina, E.; Friedle, S.; Lee, D.; DuBois, J.; Hedman, B.; Hodgson, K. O.; Fréchet, J. M. J.; Lippard, S. J. *J. Am. Chem. Soc.* **2008**, *130*, 4352-4363.

(68) Chi, Y.; Scroggins, S. T.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2008**, *130*, 6322-6323.

(69) Cohen, B. J.; Kraus, M. A.; Patchornik, A. *J. Am. Chem. Soc.* **1981**, *103*, 7620-7629.

(70) Gembus, V.; Bonnet, J.-J.; Janin, F.; Bohn, P.; Levacher, V.; Briere, J.-F. *Org. Biomol. Chem.* **2010**, *8*, 3287-3293.

(71) Muratore, M. E.; Shi, L.; Pilling, A. W.; Storer, R. I.; Dixon, D. J. *Chem. Commun.* **2012**, *48*, 6351-6353.

(72) Pfeiffer, P.; Breith, E.; Lübbe, E.; Tsumaki, T. *Liebigs Ann.* **1933**, *503*, 84-130.

(73) Yoon, T. P.; Jacobsen, E. N. *Science* **2003**, *299*, 1691-1693.

(74) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801-2803.

(75) Irie, R.; Noda, K.; Ito, Y.; Matsumoto, N.; Katsuki, T. *Tetrahedron Lett.* **1990**, *31*, 7345-7348.

(76) Baleizão, C.; Garcia, H. *Chem. Rev.* **2006**, *106*, 3987-4043.

(77) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063-7064.

(78) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897-5898.

(79) Jacobsen, E. N.; Tokunaga, M.; Larrow, J. F.; US Patent 2,000,009,463: February 24, 2000.

(80) Darensbourg, D. J.; Mackiewicz, R. M.; Rodgers, J. L.; Fang, C. C.; Billodeaux, D. R.; Reibenspies, J. H. *Inorg. Chem.* **2004**, *43*, 6024-6034.

(81) Xia, Q. H.; Ge, H. Q.; Ye, C. P.; Liu, Z. M.; Su, K. X. *Chem. Rev.* **2005**, *105*, 1603-1662.

(82) Zheng, X.; Jones, C. W.; Weck, M. *Chem. Eur. J.* **2006**, *12*, 576-583.

(83) Holbach, M.; Weck, M. *J. Org. Chem.* **2006**, *71*, 1825-1836.

(84) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307-1315.

(85) Madhavan, N.; Weck, M. *Adv. Synth. Catal.* **2008**, *350*, 419-425.

(86) Gupta, K. C.; Sutar, A. K. *Coord. Chem. Rev.* **2008**, *252*, 1420-1450.

(87) Yao, X.; Chen, H.; Lü, W.; Pan, G.; Hu, X.; Zheng, Z. *Tetrahedron Lett.* **2000**, *41*, 10267-10271.

(88) Dhal, P. K.; De, B. B.; Sivaram, S. *J. Mol. Catal. A: Chem.* **2001**, *177*, 71-87.

(89) Hajji, C.; Roller, S.; Beigi, M.; Liese, A.; Haag, R. *Adv. Synth. Catal.* **2006**, *348*, 1760-1771.

(90) Gill, C. S.; Venkatasubbaiah, K.; Jones, C. W. *Adv. Synth. Catal.* **2009**, *351*, 1344-1354.

(91) Bergbreiter, D. E.; Hobbs, C.; Hongfa, C. *J. Org. Chem.* **2011**, *76*, 523-533.

(92) Jones, C. *Top. Catal.* **2010**, *53*, 942-952.

(93) Lloret, F.; Moratal, J.; Faus, J. *J. Chem. Soc., Dalton Trans.* **1983**, 1743-1748.

(94) Hernández-Molina, R.; Mederos, A.; Gili, P.; Domínguez, S.; Núñez, P. *Polyhedron* **1997**, *16*, 4191-4196.

(95) Bergbreiter, D. E.; Chandran, R. *J. Am. Chem. Soc.* **1985**, *107*, 4792-4793.

(96) Bergbreiter, D. E.; Chandran, R. *J. Am. Chem. Soc.* **1987**, *109*, 174-179.

(97) Bergbreiter, D. E.; Walker, S. A. *J. Org. Chem.* **1989**, *54*, 5138-5141.

(98) Bergbreiter, D. E.; Weatherford, D. A. *J. Org. Chem.* **1989**, *54*, 2726-2730.

(99) Older, C.; Kristjansdottir, S.; Ritter, J.; Wilson, T.; Grady, M. C. *Chem. Ind.* **2009**, *123*, 319-328.

(100) Bergbreiter, D. E.; Chen, Z.; Hu, H. P. *Macromolecules* **1984**, *17*, 2111-2116.

(101) Bergbreiter, D. E.; Hein, M. D. *Macromolecules* **1990**, *23*, 764-769.

(102) Taber, D. F.; Nelson, C. G. *J. Org. Chem.* **2006**, *71*, 8973-8974.

(103) Sather, A. C.; Lee, H. G.; Colombe, J. R.; Zhang, A.; Buchwald, S. L. *Nature* **2015**, *524*, 208-211.

(104) Larrow, J. F.; Jacobsen, E. N. *Org. Synth.* **1998**, *75*, 1.

(105) Angelino, M. D.; Laibinis, P. E. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 3888-3898.

(106) Polywax, B. H. I.; Vol. 2015.

(107) Berthold, M. E., Sr.; Huchital, D. *J. Chem. Educ.* **1973**, *50*, 340.

(108) Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746-1787.

(109) Bielawski, C. W.; Grubbs, R. H. *Prog. Polym. Sci.* **2007**, *32*, 1-29.

(110) *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH Verlag GmbH, 2003.

(111) Leitgeb, A.; Wappel, J.; Slugovc, C. *Polymer* **2010**, *51*, 2927-2946.

(112) Sutthasupa, S.; Shiotsuki, M.; Sanda, F. *Polym. J.* **2010**, *42*, 905-915.

(113) Bunz, U. H. F.; Mäker, D.; Porz, M. *Macromol. Rapid Commun.* **2012**, *33*, 886-910.

(114) Hemelaere, R.; Carreaux, F.; Carboni, B. *J. Org. Chem.* **2013**, *78*, 6786-6792.

(115) Peng, Y.; Decatur, J.; Meier, M. A. R.; Gross, R. A. *Macromolecules* **2013**, *46*, 3293-3300.

(116) Lehman, S. E.; Wagener, K. B. In *Handbook of Metathesis*; Wiley-VCH Verlag GmbH: 2008, p 283-353.

(117) Reimann, S.; Baumeister, U.; Binder, W. H. *Macromol. Chem. Phys.* **2014**, *215*, 1963-1972.

(118) Vougioukalakis, G. C. *Chem. Eur. J.* **2012**, *18*, 8868-8880.

(119) Chu, D. S. H.; Schellinger, J. G.; Shi, J.; Convertine, A. J.; Stayton, P. S.; Pun, S. H. *Acc. Chem. Res.* **2012**, *45*, 1089-1099.

(120) Courchay, F. C.; Sworen, J. C.; Ghiviriga, I.; Abboud, K. A.; Wagener, K. B. *Organometallics* **2006**, *25*, 6074-6086.

(121) Alcaide, B.; Almendros, P.; Luna, A. *Chem. Rev.* **2009**, *109*, 3817-3858.

(122) Hong, S. H.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2004**, *126*, 7414-7415.

(123) Schmidt, B. *Eur. J. Org. Chem.* **2004**, *2004*, 1865-1880.

(124) Deraedt, C.; d'Halluin, M.; Astruc, D. *Eur. J. Inorg. Chem.* **2013**, *2013*, 4881-4908.

(125) Rosen, E. L.; Varnado Jr, C. D.; Arumugam, K.; Bielawski, C. W. *J. Organomet. Chem.* **2013**, *745–746*, 201-205.

(126) Lambeth, R. H.; Pederson, S. J.; Baranoski, M.; Rawlett, A. M. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 5752-5757.

(127) Maynard, H. D.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 4137-4140.

(128) Szczepaniak, G.; Kosinski, K.; Grela, K. *Green Chem.* **2014**, *16*, 4474-4492.

(129) Ferraz, C. P.; Autenrieth, B.; Frey, W.; Buchmeiser, M. R. *ChemCatChem* **2014**, *6*, 191-198.

(130) Buchmeiser, M. R. *Chem. Rev.* **2009**, *109*, 303-321.

(131) Pastva, J.; Skowerski, K.; Czarnocki, S. J.; Žilková, N.; Čejka, J.; Bastl, Z.; Balcar, H. *ACS Catalysis* **2014**, *4*, 3227-3236.

(132) Balcar, H.; Bek, D.; Sedláček, J.; Dědeček, J.; Bastl, Z.; Lamač, M. *J. Mol. Catal. A: Chem.* **2010**, *332*, 19-24.

(133) Smith, D.; Pentzer, E. B.; Nguyen, S. T. *Polym. Rev.* **2007**, *47*, 419-459.

(134) Anderson, A. W.; Merckling, N. G. US. Patent 2,721,189, October 18, 1955

(135) Jean-Louis Hérisson, P.; Chauvin, Y. *Macromol. Chem. Phys.* **1971**, *141*, 161-176.

(136) Schrock, R. R. *J. Am. Chem. Soc.* **1974**, *96*, 6796-6797.

(137) Schrock, R. R. *J. Am. Chem. Soc.* **1975**, *97*, 6577-6578.

(138) Gilliom, L. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1986**, *108*, 733-742.

(139) Howard, T. R.; Lee, J. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 6876-6878.

(140) Rutenberg, I. M.; Scherman, O. A.; Grubbs, R. H.; Jiang, W.; Garfunkel, E.; Bao, Z. *J. Am. Chem. Soc.* **2004**, *126*, 4062-4063.

(141) Bertin, P. A.; Watson, K. J.; Nguyen, S. T. *Macromolecules* **2004**, *37*, 8364-8372.

(142) Quémener, D.; Héroguez, V.; Gnanou, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 217-229.

(143) Arimoto, H.; Nishimura, K.; Hayakawa, I.; Kinumi, T.; Uemura, D. *Chem. Commun.* **1999**, 1361-1362.

(144) Ilker, M. F.; Nüsslein, K.; Tew, G. N.; Coughlin, E. B. *J. Am. Chem. Soc.* **2004**, *126*, 15870-15875.

(145) Ogawa, S.; Takano, S.; Fujimori, H.; Itoh, T.; Kaita, S.; Iida, T.; Wakatsuki, Y. *React. Funct. Polym.* **2010**, *70*, 563-571.

(146) Al-Hashimi, M.; Hongfa, C.; George, B.; Bazzi, H. S.; Bergbreiter, D. E. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 3954-3959.

(147) Goll, J. M.; Fillion, E. *Organometallics* **2008**, *27*, 3622-3625.

(148) Heath, W. H.; Palmieri, F.; Adams, J. R.; Long, B. K.; Chute, J.; Holcombe, T. W.; Zieren, S.; Truitt, M. J.; White, J. L.; Willson, C. G. *Macromolecules* **2008**, *41*, 719-726.

(149) Wilson, G. O.; Caruso, M. M.; Schelkopf, S. R.; Sottos, N. R.; White, S. R.; Moore, J. S. *ACS Applied Materials & Interfaces* **2011**, *3*, 3072-3077.

(150) Musa, O. M. US. Patent 20,110,065,880, March 30, 2011

(151) Camm, K. D.; Martinez Castro, N.; Liu, Y.; Czechura, P.; Snelgrove, J. L.; Fogg, D. E. *J. Am. Chem. Soc.* **2007**, *129*, 4168-4169.

(152) Clevenger, R. C.; Turnbull, K. D. *Synth. Commun.* **2000**, *30*, 1379-1388.

(153) Olson, C. L.; Caserio, M. C.; Roberts, J. D. *Org. Synth.* **1973**, *5*, 944.

(154) Anderson, W. K.; Milowsky, A. S. *J. Org. Chem.* **1985**, *50*, 5423-5424.

(155) McCauley, J. A.; McIntyre, C. J.; Rudd, M. T.; Nguyen, K. T.; Romano, J. J.; Butcher, J. W.; Gilbert, K. F.; Bush, K. J.; Holloway, M. K.; Swestock, J.; Wan, B.-L.; Carroll, S. S.; DiMuzio, J. M.; Graham, D. J.; Ludmerer, S. W.; Mao, S.-S.; Stahlhut, M. W.; Fandozzi, C. M.; Trainor, N.; Olsen, D. B.; Vacca, J. P.; Liverton, N. J. *J. Med. Chem.* **2010**, *53*, 2443-2463.

(156) Matson, J. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **2008**, *130*, 6731-6733.

(157) Garrett, C. E.; Prasad, K. *Adv. Synth. Catal.* **2004**, *346*, 889-900.

(158) Paquette, L. A.; Schloss, J. D.; Efremov, I.; Fabris, F.; Gallou, F.; Méndez-Andino, J.; Yang, J. *Org. Lett.* **2000**, *2*, 1259-1261.

(159) Ahn, Y. M.; Yang, K.; Georg, G. I. *Org. Lett.* **2001**, *3*, 1411-1413.

(160) Cho, J. H.; Kim, B. M. *Org. Lett.* **2003**, *5*, 531-533.

(161) Westhus, M.; Gonthier, E.; Brohm, D.; Breinbauer, R. *Tetrahedron Lett.* **2004**, *45*, 3141-3142.

(162) McEleney, K.; Allen, D. P.; Holliday, A. E.; Crudden, C. M. *Org. Lett.* **2006**, *8*, 2663-2666.

(163) Galan, B. R.; Kalbarczyk, K. P.; Szczepankiewicz, S.; Keister, J. B.; Diver, S. T. *Org. Lett.* **2007**, *9*, 1203-1206.

(164) Bergbreiter, D. E. *ACS Macro Letters* **2014**, *3*, 260-265.

(165) Andersen, F. A. *Int. J. Toxicol.* **2008**, *27*, 83 -106.

(166) Su, H.-L.; Hongfa, C.; Bazzi, H. S.; Bergbreiter, D. E. *Macromolecular Symposia* **2010**, *297*, 25-32.

(167) Louie, J.; Grubbs, R. H. *Organometallics* **2002**, *21*, 2153-2164.

(168) Bandini, M. *Green Chemistry Series* **2012**, *15*, 94-122.

(169) Liang, Y.; Harrell, M. L.; Bergbreiter, D. E. *Angew. Chem. Int. Ed.* **2014**, *53*, 8084-8087.

(170) Hongfa, C.; Tian, J.; Andreatta, J.; Darensbourg, D. J.; Bergbreiter, D. E. *Chem. Commun.* **2008**, 975-977.

(171) Su, H.-L.; Pérez, L. M.; Lee, S.-J.; Reibenspies, J. H.; Bazzi, H. S.; Bergbreiter, D. E. *Organometallics* **2012**, *31*, 4063-4071.

(172) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2002**, *41*, 4035-4037.

(173) Choi, T.-L.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2003**, *42*, 1743-1746.

(174) Al-Hashimi, M.; Bakar, M. D. A.; Elsaid, K.; Bergbreiter, D. E.; Bazzi, H. S. *RSC Advances* **2014**, *4*, 43766-43771.