SYNTHESES AND APPLICATIONS OF SOLUBLE POLYISOBUTYLENE (PIB)-SUPPORTED TRANSITION METAL CATALYSTS

A Dissertation

by

JIANHUA TIAN

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

DOCTOR OF PHILOSOPHY

December 2008

Major Subject: Chemistry

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Approved by:

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

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ABSTRACT

Syntheses and Applications of Soluble Polyisobutylene (PIB)-supported Transition Metal Catalysts. (December 2008)

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Chair of Advisory Committee: Dr. David E. Bergbreiter

Soluble polymer supports facilitate the recovery and recycling of expensive transition metal complexes. Recently, polyisobutylene (PIB) oligomers have been found to be suitable polymer supports for the recovery of a variety of transition metal catalysts using liquid/liquid biphasic separations after a homogeneous reaction. Our work has shown that PIB-supported Ni(II) and Co(II) β-diketonates prepared from commercially available vinyl terminated PIB oligomers possess catalytic activity like that of their low molecular weight analogs in Mukaiyama epoxidation of olefins.

Carboxylic acid terminated PIB derivatives can act as carboxylate ligands for Rh(II) cyclopropanation catalysts. An achiral PIB-supported Rh(II) carboxylate catalyst showed good activity in cyclopropanation of styrene in hydrocarbon solvents, and could be easily recycled nine times by a post reaction extraction. Further application of PIB supports in asymmetric cyclopropanation reactions were investigated using PIB-supported arenesulfonyl Rh(II) prolinates derived from L-proline as examples. The PIB-supported chiral Rh carboxylates demonstrated moderate activity and were recovered

and reused for four to five cycles. The prolinate catalyst prepared from PIB-anisole also showed encouraging enantioselectivity and about 8% ee and 13% ee were observed on *trans*- and *cis*-cyclopropanation product respectively.

Finally, PIB oligomers can be modified in a multi step sequence to prepare PIB-supported chiral bisoxazolines that can in turn be used to prepare active, recyclable PIB-supported Cu(I) bisoxazoline complexes for olefin cyclopropanation. These chiral copper catalysts showed moderate catalytic activity and good stereoselectivity in cyclopropanation of styrene. A chiral ligand prepared from D-phenylglycinol provided the most effective stereo control and gave the *trans*- and *cis*-cyclopropanation product in 94% ee and 68% ee respectively. All three PIB-supported chiral bisoxazoline-Cu(I) catalysts could be reused five to six times.

DEDICATION

To my parents and my wife, for supporting me all the way.

ACKNOWLEDGEMENTS

First of all, I would like to give my most sincere thanks to my advisor, Prof. David E. Bergbreiter, for giving me the opportunity to join his research group, for his guidance and support throughout the course of my research and for his big help in deciding the next step in my life.

I would also like to thank my committee members, Prof. Daniel A. Singleton, Prof. Marcetta Y. Darensbourg, and Prof. Daniel Shantz, for their useful advice for my research and their strong support during the course of my application for postdoctoral positions.

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CHAPTER I

INTRODUCTION

Liquid/liquid separations are ubiquitous in chemistry. Indeed most organic reactions involve a gravity separation of two phases of different density and polarity in the work-up steps. This same concept of separations also has precedent in homogeneous catalysis for separation of catalysts and products too.[1] Processes like the SHOP process and later processes like the Ruhrchemie/Rhone–Poulenc (RCH/RP) oxo process commercialized in 1980s,[1,2] advantageously immobilize a catalyst in one of the two liquid phases to facilitate catalyst recovery and reuse. More recent biphasic systems that use organic solvents,[3,4] fluorous solvents,[5] ionic liquids[6] and supercritical fluids[7] have been developed and used in a variety of catalytic transformations over the past two decades. The use of soluble polymer supports to bind a catalyst and ensure high levels of catalyst and ligand recovery in liquid/liquid separations in biphasic liquid/liquid systems is a more recent concept.

When a liquid/liquid separation is used, the polymeric catalysts are isolated as a solution at the separation stage. As was true for solid/liquid separation strategies that used soluble polymer facilitated catalysis, catalytic reactions prior to the separation process often involve single phase conditions. However, sometimes reactions are carried out under biphasic conditions. In some of those cases, partial misciblization occurs or the polymeric catalyst's phase selective solubility is different during the catalytic

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process. In cases where the reaction involves a single solvent, an extraction is used to either remove the polymeric catalyst from the product or to remove the product from the catalyst. With systems containing mixed solvents, a perturbation induced by a temperature change (a thermomorphic effect),[8] a perturbation induced by addition of a small amount of a chemical perturbant (a latent biphasic system),[9] or a perturbation induced by product formation (self disassembly)[10] can lead to liquid/liquid biphase separation which can be followed by a liquid/liquid separation of the polymer-supported catalyst and product phases. All liquid/liquid separations rely on a gravity based separation of two liquid phases to recover and separate the catalyst. All useful liquid/liquid separations require a soluble polymer-supported catalyst to have high phase selective solubility.

As is true in some solid/liquid separations, liquid/liquid separations of mixed solvent systems can often be carried out without exposing the catalyst mixture to air or water. This can be advantageous if the catalysts or their ligands are air or moisture sensitive because there is no need to open the reactor and transfer the reaction mixture to another container for a workup.

The choice of solvents and polymers for liquid/liquid separations is affected by the catalytic process of interest. First, solvents suitable for the catalytic process have to be used. Second, if miscible solvents are used, they can be miscible under the reaction conditions but it must be possible to perturb this mixture so that it is biphasic during the separation step. Third, if a thermomorphic, latent biphasic, or self disassembling separation is used, it has to be experimentally practical to separate the two liquid phases.

For example, formation of a biphase with two solvents nearly equal in density will yield an emulsion whose separation will be difficult. Likewise, a liquid/liquid separation that only occurs far from ambient temperature would make a separation less practical. Fourth, the solvents used have to be acceptable. Finally, liquid/liquid separations would not be feasible in some cases. For example, while separation of heptane and aqueous ethanol is feasible in general, but it might be impractical if a particular product acted as an emulsifying agent for heptane and aqueous EtOH.

The nature of the polymer support is another consideration if liquid/liquid separations of a polymer-supported catalyst and product are to be effective. For a liquid/liquid separation using soluble polymer supports, to be useful, the polymer-supported catalyst must preferentially dissolve in one of the two phases and products in the other. Thus, polar polymer-supported catalysts are more suitable for preparing nonpolar products and vice versa. A more subtle facet of this issue is that while a soluble polymer and hence the polymer-supported catalyst can have very high (>99.99%) phase selective solubility in one phase of a liquid/liquid biphasic system, low molecular weight products often have some solubility in both phases. Thus, some of the product is often 'lost' to the catalyst-containing phase in the first few cycles of a liquid/liquid based recycling process involving a soluble polymer-supported catalyst. This 'loss' of product can be mitigated by an extraction. It is also arguably less important when a catalyst is recycled numerous times.

Water/Organic Biphasic Systems

Water is generally considered to be the most environmental benign solvent. Many biphasic systems that include water as a solvent immobilize the catalyst in the aqueous phase.[11] Because many organic products are insoluble in water, complete separation of catalysts from products can be achieved easily. However, a biphasic catalytic process can introduce kinetic problems. In some cases, partial solubility of catalyst or substrate in the other phase or efficient mixing can alleviate these problems and reasonable reaction rates can be achieved. This is the case in the Ruhrchemie/Rhone–Poulenc (RCH/RP) oxo process for the production of butyraldehyde from propene where a water soluble triphosphine ligated Rh(I) complex is used to catalyze the hydroformylation of alkenes.[12] However, such chemistry is often restricted to a few substrates. For example, in the RCH/RP process other more lipophilic substrates, e.g. larger 1-alkenes, are not readily hydroformylated.

While many sorts of ionic or polar substituents can be used to make catalysts water soluble and thus amenable to aqueous biphasic catalysis, water-soluble polymers can be used too. The discussion below will focus on the cases where a water-soluble polymer is used as a phase tag to insure that a catalyst is phase selectively soluble so that it can be separated and recovered by a liquid/liquid separation.

Thermoregulated Phase Transfer Catalysis

Poly(ethylene glycol) (PEGs) have been used as soluble polymer supports for the recovery and recycling of catalysts in homogeneous catalysis. Like the poly(*N*-isopropylacrylamide) (PNIPAM), which will be discussed later, PEG supports also

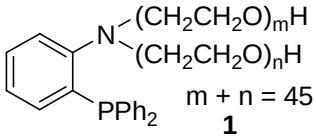
exhibit LCST (lower critical solution temperature) behavior. However, unlike PNIPAM, PEGs often separate as an oil above their LCST. This LCST behavior of PEGs in water has been used to design a process termed "thermoregulated phase-transfer catalysis" (TRPTC) by Jin's group.[13,14] Rhodium catalysts attached to these sorts of polymers have been successfully used in hydroformylation of higher olefins which are not suitable substrates in RCH/RP processes using a biphasic liquid/liquid mixture of water and an organic solvent. In these TRPTC systems, the polymer-supported catalysts' inverse temperature dependent solubility makes them soluble in an aqueous phase at a temperature below their LCST. However, at their LCST the polymer's solubility changes. Since PEGs separate as an oil-in-water emulsion at their LCST, these polymers and catalysts bound to them can partition into the organic phase that is present. In cases where the substrate is present in that organic phase, the reaction does not occur to any appreciable extent below this LCST because the catalyst concentration is low. However, above the LCST, the catalyst concentration in the organic phase increases and reaction occurs. Cooling after the reaction is complete allows the polymer-supported catalyst to partition back into the aqueous phase where it can be recovered.

An example of thermoregulated catalysis is the hydroformylation of 1-decene in a water/toluene system using the PEG-supported *P,N*-bidentate triphenylphosphine ligand **1**.[15] In this case the catalyst was generated *in situ* by reaction of $RhCl_3.3H_2O$ with **1**. Catalytic reactions were carried out using 0.1 mol% of Rh catalyst at 120 °C and, under these conditions, essentially 100% conversion of alkene to aldehydes product was

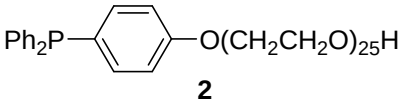
seen. A slight disadvantage to this system was a lower *n*:*iso* selectivity in the range of 0.60-0.64 due to the increased alkene isomerization at the 120 °C reaction temperature.

While the level of Rh leaching into product phase was not measured, good recycling efficiency was evident from the fact that after 20 cycles the yield of aldehyde and the TOF number of the catalyst were 94.4% and 189 h^{-1} as compared to 99% and 198 h^{-1} in the first cycle. The high recyclability of the Rh catalyst in the water phase suggests both a high phase selective solubility for the catalyst and good catalyst stability, a stability that the authors attributed to P-N chelation of Rh by the ligand.

These recycling results suggest a high phase selective solubility for Rh complexes of the ligand **1** during the catalyst/product separation step. However, this successful hydroformylation could not be solely attributed to the ligands' LCST behavior. Specifically, the biphasic hydroformylation reaction still occurred below the LCST. When a Rh catalyst was prepared using **1** (LCST = 92 °C), a ca. 40% increase in conversion from ca. 65% conversion to ca. 85% conversion was seen as the biphasic toluene/water mixture of catalyst was heated through the LCST temperature (i.e. from 90 to 100 °C).[15]



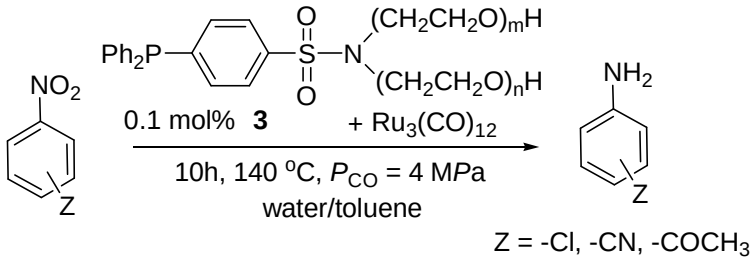
1



2

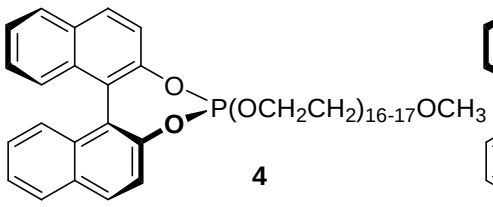
Further studies of hydroformylation using catalysts that have LCST behavior showed that even a very hydrophobic internal alkene, oleyl alcohol, afforded a good (81%) yield of aldehyde products that decreased minimally to 78% through four cycles using a very simple monovalent PEG-phosphine ligand **2**.[16]

A Ru complex of ligand **3** has also been used to reduce nitroarenes to aniline derivatives using CO as the reductant (eq. 1).[17] While no analyses for Ru were reported, only a slight loss of activity over four cycles was observed when recycling these catalysts.



(1)

Attempts at enantioselective hydroformylation of styrene under TRPTC conditions have been reported by Breuzard and co-workers.[18] In this work, the catalysts were generated *in sit*u by allowing a PEG-supported chiral phosphite ligand **4** or **5** derived from (*S*)-binaphthol to react with $[Rh(cod)_2BF_4]$ in an aqueous solution. Very modest enantioselectivity, ca. 25% ee, was achieved using ligand **5**. Moreover, recycling was unsuccessful for either polymer-supported ligand. This might be attributed to the use of relatively short PEG chains in the ligand syntheses. Alternatively, there could have been some catalyst decomposition. ^{31}P NMR spectroscopic studies of recovered catalyst/ligand or ICP analyses for Rh might have addressed this issue but were not reported.



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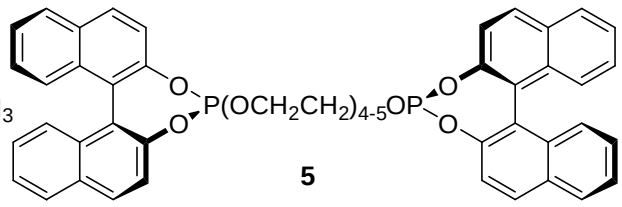


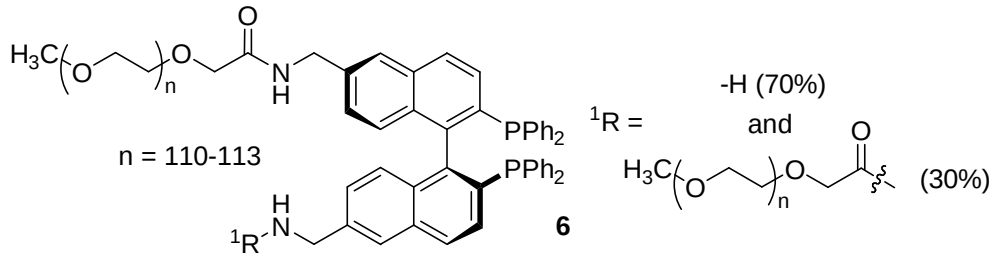
5

Smart catalyst that coupled a catalyst to a soluble responsive polymer were described by our group earlier in our efforts to develop recoverable catalysts.[19,20] More recently, Davies and Stringer found that an aqueous solution of poly(alkene oxide)s (Poloxamers) can serve as a smart reaction medium that exhibits anti- or hyper-Arrhenius behavior.[21] In these cases, the polymer was not used in a catalyst recovery step. Rather the highly temperature dependent critical micelle concentration (cmc) of these polymers was used to design systems where reactions were turned ON or OFF above a particular temperature. For example, an exothermic reaction containing hydrophobic and hydrophilic reactants was turned OFF after all the hydrophobic reactant was transferred into micellar pseudophase formed at higher temperature. It was turned back ON once the reaction mixture was cooled. More interestingly, hyper-Arrhenius behavior with a significantly accelerated reaction rate was seen in cases where the reactants and catalyst both partitioned into the micellar phase.

Aqueous Biphasic Catalysts Separable by Extraction

Saluzzo and coworkers reported another PEG-supported BINAP ligand **6** and its use in Ru-catalyzed aqueous biphasic asymmetric hydrogenation of ketones.[22] The PEG-supported Ru catalyst was prepared in DMF by reaction of $[RuCl_2(benzene)]_2$ with **6**. Initial tests of this Ru catalyst under aqueous biphasic conditions were conducted with acetophenone as a substrate in the presence of (*S*,*S*)-diphenylethylene diamine. After a biphasic reaction and pentane extraction of the product, the aqueous phase containing the Ru-catalyst was reused. Recycling was evaluated in the hydrogenation of ethyl acetoacetate to form ethyl 3-hydroxybutanoate. The polymer-supported Ru

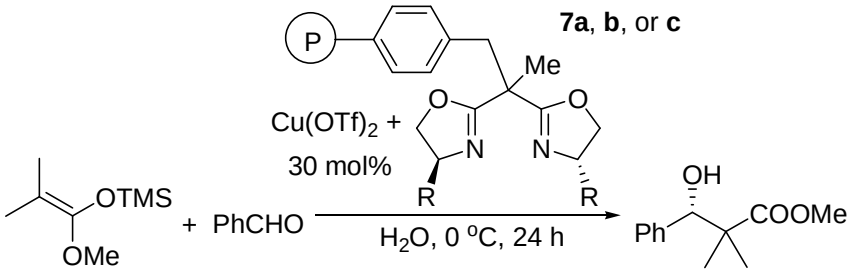
catalyst could only be reused twice with a large decrease in conversion (from 100% in cycle 1 to 20% in cycle 2) and enantioselectivity (from 75% ee in cycle 1 to 56% ee in cycle 2).



6

Another example of an aqueous biphasic system with PEG supports was described by Benaglia and coworkers.[23] In their work, PEG-supported chiral bisoxazoline (Box) ligands **7a-c** were prepared and used in $Cu(OTf)_2$ catalyzed Mukaiyama aldol reactions between the trimethylsilyl ketene acetal of methyl isobutyrate and various aldehydes in aqueous media (eq. 2). Cu(II) catalysts ligated by either **7a** or **7b** showed that the reaction of the ketene acetal and benzaldehyde proceeded with the highest enantioselectivity (55% ee) with ligand **7b,** a result that was comparable to results reported by Kobayashi with unsupported ligands in aqueous media.[24] However, poor water-solubility of the aldehyde electrophiles led to relatively low synthetic yields. The use of ligand **7c** slightly improved the enantioselectivity but did not affect the yield. Higher yields were only seen with more polar aldehydes such as 4-nitrobenzaldehyde perhaps because of solubility. These more reactive aldehydes were used to study catalyst recycling. Catalyst recycling was in this case involved separation of the organic product from the aqueous solution of the catalyst by extraction of aqueous phase with diethyl ether. The resulting aqueous phase containing the catalysts was

directly reused in a subsequent reaction cycle. These experiments showed that catalysts that used ligand **7c** could not be recycled (the ligand was partly soluble in diethyl ether). However, recycling $Cu(OTf)_2$ complexed by **7b** was successful with only modest decreases in yield (40% to 38%) and enantioselectivity (50% to 43% ee) through three cycles.



(2)

7a: R = $-CH(CH_3)_2$
7b: R = $-CH_2Ph$

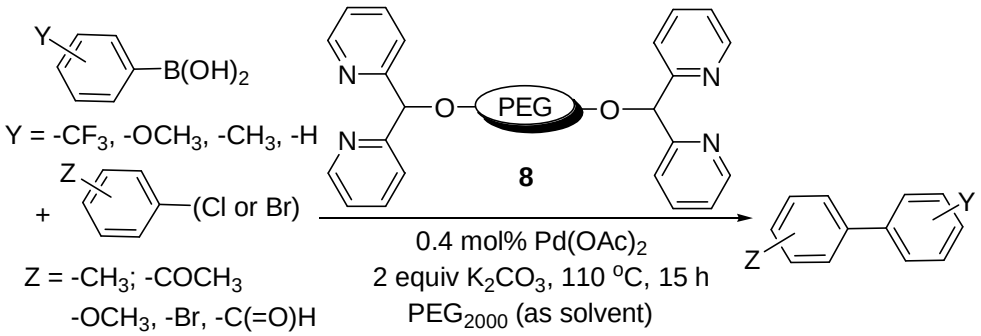
P = $MeOPEG_{5000}$—O—$(CH_2)_3O$-

7c: R = $-CH_2Ph$

P = —$(OCH_2CH_2)_{40}$—O—$(CH_2)_3O$-

Gao used a similar approach in extracting products from a PEG-supported Pd catalyst prepared from the bis(pyridylmethane) ligand **8** and $Pd(OAc)_2$ in studying cross-coupling reactions of aryl halides with either $ArB(OH)_2$ or sodium tetraphenylborate.[25] These reactions were either carried out using PEG_{2000} or a PEG_{2000}-H_2O mixture as a solvent. While the Pd catalyst ligated by **8** was successfully recycled 6 times using PEG_{2000} as solvent in cross-couplings with substituted aryl boronic acids after extracting the products with diethyl ether (eq. 3), ligand **8** was evidently not effective in stabilizing the Pd(0) catalyst in the PEG-water mixture as Pd black formed in the second cycle when water was used as a cosolvent. This observation is not at all unique to this

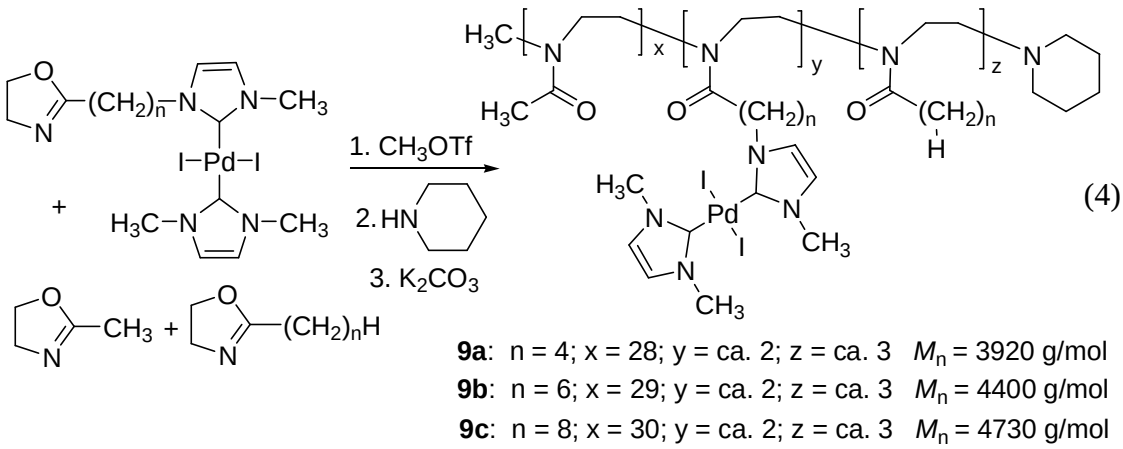
particular ligand. Adventitious catalyst decomposition or inherent catalyst instability frustrates many attempts to recycle homogeneous catalysts.



(3)

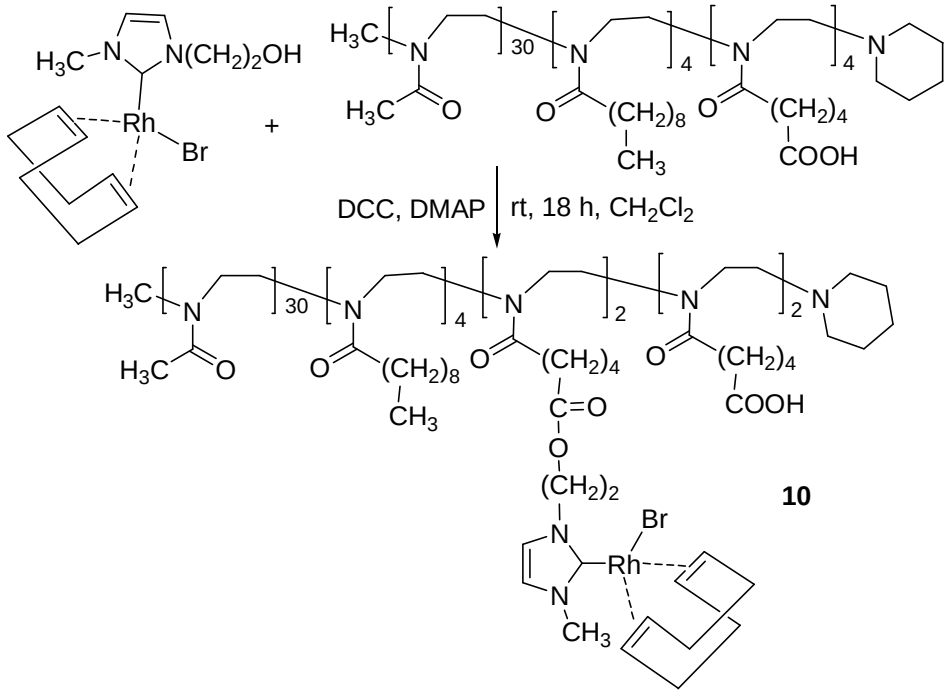
Aqueous biphasic catalysis and aqueous biphasic catalysis with polymer-supported catalysts are both successful strategies for separation of catalysts and products. However, satisfactory results with more hydrophobic substrates are problematic in either case. A possible solution to this problem is the use of amphiphilic block copolymer supports that contain a hydrophilic water-soluble block. This concept is illustrated by work where poly(2-oxazoline) copolymers were used to separate, recover, and recycle cross-coupling Pd catalysts [26,27] or Rh hydroformylation and hydrogenation catalysts.[28,29]

Poly(2-oxazoline) copolymer-supported palladium (**9)** and rhodium (**10)** catalysts were prepared as shown in eq. 4 and 5.[28,30] In these examples, the metal ligation involved an *N*-heterocyclic carbene ligand and the polymers were prepared using a Pd-complex as a comonomer or by a post-polymerization coupling of a Rh complexed functional NHC ligand to a pendant -CO_2H group.



(4)

9a: n = 4; x = 28; y = ca. 2; z = ca. 3 M_n = 3920 g/mol
9b: n = 6; x = 29; y = ca. 2; z = ca. 3 M_n = 4400 g/mol
9c: n = 8; x = 30; y = ca. 2; z = ca. 3 M_n = 4730 g/mol



(5)

10

Unlike PEGs, these amphiphilic block copolymer-supported catalysts were not completely soluble in water. Instead, these amphiphilic polymers formed micellar aggregates with a 15-nm hydrodynamic radius under the reaction conditions. The polymer-supported Pd catalyst **9a-c** showed good catalytic activity in the coupling of iodobenzene and styrene. For example, ca. 93% of *trans*-stilbene was obtained after 3 hours at 90 ºC using 0.67 mol% catalyst for **9a**, **b**, or **c**. In these cases, the spacer length

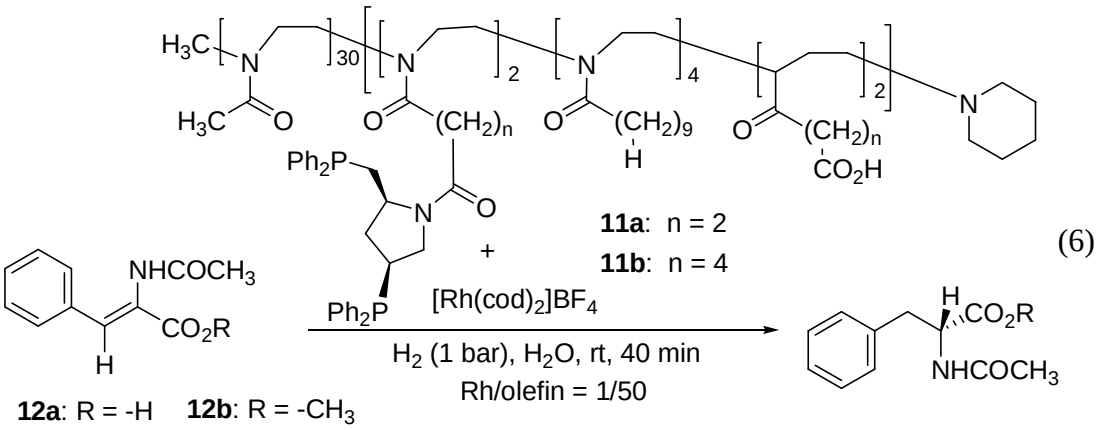
affected the catalytic activity of the pendant polymer-supported catalysts. A minimum spacer length of six methylene groups was needed to reach the highest turnover frequency (TOF = 570 h^{-1}). Recycling of catalyst **9c** was performed by a post reaction extraction with diethyl ether. The initial yield of 80% in the first cycle reduced somewhat to 68% in the third cycle. While the authors speculated that the lower activity might arise from residual diethyl ether left in the aqueous phase that prevented the solubilization of the substrates, other explanations for a decreased rate (catalyst decomposition, metal leaching) were not fully explored.

The same catalyst used in Heck couplings was also effective in the Suzuki coupling reactions between iodobenzene and phenyl boronic acid. The highest TOF number (5200 h^{-1}) was achieved by using 0.1 mol% of catalyst **9c** at 80 ºC. In this case no results on catalyst recycling were reported.[30]

The rhodium catalyst **10** was successfully reused four times in hydroformylation of 1-octene under aqueous biphasic conditions using a mixture of water and 1-octene where the substrate 1-octene was the organic phase. The organic phase consisting of the aldehyde products was separated by decantation after the reaction and the denser aqueous catalyst-containing phase was directly reused for the next cycle. Rh leaching into the product phase after the first cycle was measured by ICP-OES (inductively coupled plasma-optical emission spectroscopy). The TOF varied from 1100 h^{-1} to 2350 h^{-1} in the third cycle to 2360 h^{-1} in the fourth cycle. These TOF values were similar to those seen for an analogous low molecular weight analog in benzene (TOF = 2400 h^{-1}) measured in the same lab with a structurally similar Rh-carbene catalyst. The authors

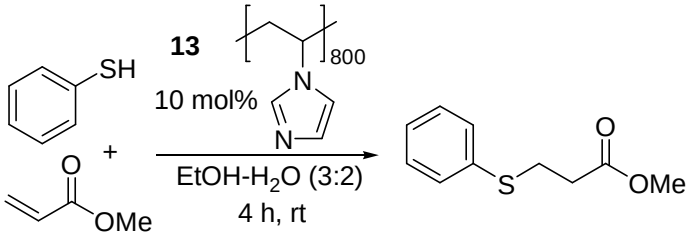
suggested that the initially lower TOF number in the first two cycles and variation of the *n*:*iso* ratio from 2.6 in the first cycle to 1.2 in the last two cycles were due to incomplete exchange of the bromide on rhodium for hydride in the initial cycles. Analyses for bromide in the recovered catalysts that would have established this were not reported. The authors also noted some hydrolysis of the ester group that coupled the Rh-NHC complex to the polymer in **10** occurs over 18 h. This resulted in a calculated loss of 2.7% of the charged Rh in each 2 h reaction cycle.

Similar water-soluble poly(2-oxazoline)-supported chiral Rh catalysts ligated by the polymers **11a** and **11b** also have been used in asymmetric hydrogenation reactions.[29] Hydrogenation of the acid **12a** was less effective than hydrogenation of the ester **12b** (eq. 6). Using **11a** as a ligand, 94% conversion and 85% ee was observed in 35 min with a Rh catalyst formed *in situ*. Using **11b**, the conversion was only slightly less (90%) with the same stereoselectivity with a similarly formed catalyst. Recycling was only studied for a catalyst ligated by **11b** and in hydrogenation of the ester **12b** and in this case only once. The only moderate conversions and no enantioselectivity seen with the acid **12a** was explained in terms of the possible micelles that this amphiphilic polymeric catalyst might form and the lower solubility of the more polar acid substrate in these micelles.



(6)

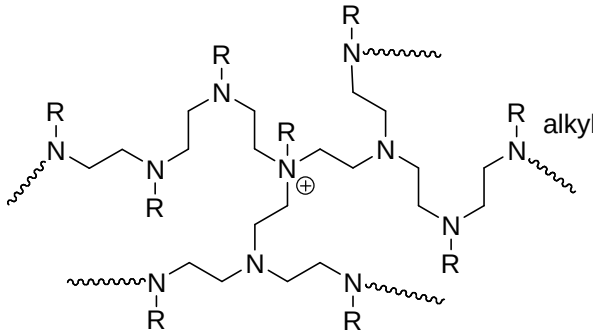
The use of poly(*N*-vinylimidazole) (PVI) (**13**) as a recyclable organocatalyst for thiol additions to α,β-unsaturated carbonyl compounds was recently described by the Beletskaya group.[31] In this reaction (eq. 7), 10 mol% of PVI (75.3 kDa) in a EtOH-water mixture was used to quantitatively effect a Michael addition of thiophenol onto methyl acrylate. After the reaction, a diethyl ether extraction removed the product. Then additional water, EtOH, or reagents were added as needed. Through four cycles the yield of thioether product was 100, 99, 100 and 100%.



(7)

In general, polymer-supported catalysts are prepared from terminally functionalized or pendent group functionalized polymer supports. Recently, Neumann and coworkers described using the interaction between atoms on the main chain and metal ions to support a homogeneous catalyst.[32] In this research, polyethyleneimine (PEI, M_w = 10,000) was first alkylated with iododododecane and iodomethane using a ratio

of substrate PEI to alkylating agents of 10.5:1:7.4 ($CH_2CH_2NH/C_{12}H_{25}I/CH_3I$). The resulting alkylated PEI only contained tertiary amines and quaternary ammonium moieties based on ^{15}N-^{1}H heteronuclear multiple bond correlation spectroscopy. Ionic immobilization of polyoxometalates such as $Na_{12}[ZnWZn_2(H_2O)_2(ZnW_9O_{34})_2]$ and $Na_3(PO_4[WO(O_2)_2]_4)$ onto these water-soluble, randomly alkylated PEI supports afforded catalysts **14** and **15** respectively. Unlike unalkylated PEI-supported polyoxometalates, these amphiphilic catalysts**14** and **15** were very effective in many hydrogen peroxide mediated oxidation reactions with hydrophobic substrates in aqueous media as shown in eqs. 8-10. High conversions (>96%) were obtained in all these reactions. The recyclability of these catalysts was demonstrated in epoxidation of cyclododecene with **14**. No apparent decrease of activity was observed over three cycles though the details of the liquid-liquid separation technique used in this case were not discussed in detail.



R = $-C_{12}H_{25}$

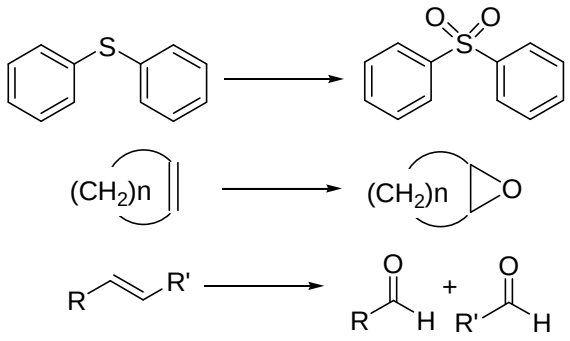
Alkylated polyethyleneimine (PEI)

alkylated PEI/$[ZnWZn_2(H_2O)_2(ZnW_9O_{34})]^{12-}$

14

alkylated PEI/$\{PO_4[WO(O_2)_2]_4\}^{3-}$

15



(8)

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(10)

Organic/Organic Biphasic Systems

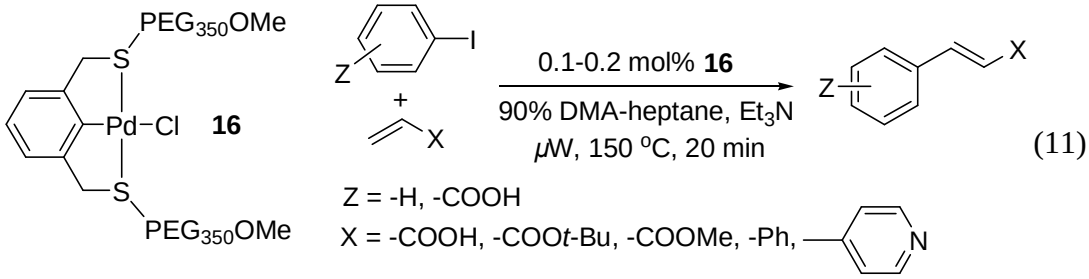
Most organic reactions are still carried out in organic media. Catalysts attached to phase selectively soluble polymer supports can be separated from products, recovered and reused in these systems just as they are in water/organic systems. Three general schemes are used. First, the reaction can be carried out in a mixture of immiscible organic solvents. If the polymer-supported catalysts were phase selectively soluble in a phase different than that favored by the product, the separation would just involve a gravity separation after the reaction. A second and possibly more useful scheme is to carry out a reaction under conditions where the solvent mixture used is a single phase. Then a phase separation could be triggered by a addition of another solvent, an additive or a temperature change. Gravity separation would then serve to separate and recover the catalyst. Again, a phase selectively soluble polymer-supported catalyst would be required and the product would have to be preferentially soluble in the non-catalyst containing phase. Finally, a reaction can be run homogeneously in a single solvent. Extraction with an immiscible solvent can then remove the product or catalyst if the catalyst is phase selectively soluble in a solvent that is not a good solvent for the product. Phase selective solubility of polymers in one or the other phase of an

organic/organic biphasic system is required for any of the above schemes to be viable. Fortunately, polymers often have excellent phase selective solubility – phase selective solubility that is subtly dependent on polymer microstructure.[33,34] Polymers can be molecularly engineered to be soluble only in a polar phase or only in a nonpolar phase. Thus, these organic/organic separation schemes can in principle be implemented in many if not most solvent mixtures.

Thermomorphic Polar Phase Selectively Soluble Polymers

Thermomorphic separations using soluble polymers were first described by our group in 1998 using polar poly(*N*-isopropylacrylamide) (PNIPAM) polymer supports.[8] Subsequent to our initial work with PNIPAM-supported catalysts under thermomorphic conditions, we prepared both PEG and PNIPAM supported SCS-Pd complexes.[35,36] The initial reports of their use in catalysis was discussed in our earlier review.[37] While later studies showed that these complexes are precatalysts and not catalysts for Pd-catalyzed cross-couplings,[38-40] low loadings of Pd complexes can be used in catalytic reactions to form products with high levels of separation of Pd from the cross-coupling products. For example, the PEG-supported SCS-Pd complex **16** was used in 90% aqueous dimethylacetamide (DMA)/heptane (1:2, vol:vol) in cross-coupling chemistry (eq. 11) under microwave conditions with reactions being complete in 10-30 min with as little as 0.01 mol% catalyst.[41] In this reaction, microwave heating caused the initial thermomorphic biphasic mixture to become miscible. After the reaction, cooling reformed the biphasic mixture. Separation of the polar phase recovered the complex **16** and four recycles were carried out. Pd leaching into the nonpolar heptane phase was

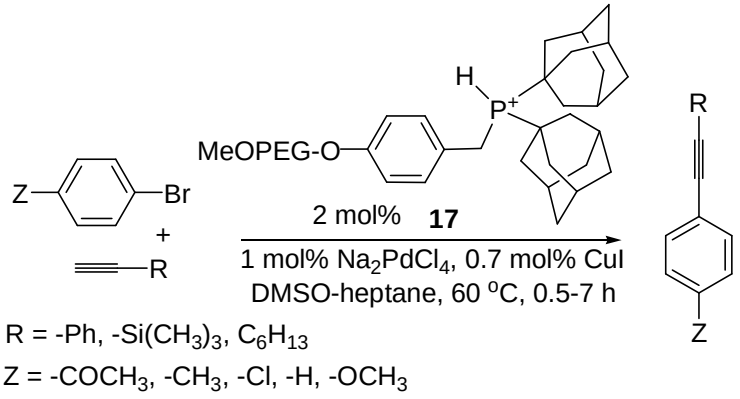
measured by ICP-MS and in a reaction using ca. 3 x 10^{-4} M Pd, the amount of Pd lost was < 0.5 % of the charged Pd.



(11)

While the polar polymer-supported Pd complex **16** is effective in cross-couplings of aryl iodides and acrylates, the use of less expensive aryl bromides as substrates for C-C coupling reactions is more attractive. Hindered phosphine-ligated Pd catalysts are efficient in this process[42] because the concentration of more coordinatively unsaturated Pd complexes is larger.[43,44] This aspect of homogeneous Pd chemistry has been extended to thermomorphic polymeric systems using the PEG-supported hindered phosphine **17** to form a Pd catalyst for Sonogashira coupling reactions conducted in a DMSO/heptane (eq. 12).[45] Unreactive aryl bromides were suitable substrates with this more hindered polymer-supported phosphine ligand. This polymer-supported catalyst was successfully recycled through five cycles with overall yields >90%. However, poor recyclability was seen when an aliphatic alkyne was used in place of phenyl acetylene in eq. 12. The studies of recyclability of PEG-supported Pd catalyst were more thorough than most such studies. First, the kinetics were examined for three bromoarene substrates – 4-bromoanisole, bromobenzene, 4-bromoacetophenone. The TOF in the first cycles were 336, 440, and 1150 h^{-1} versus a TOF of 252, 312, and 880 h^{-1}in the fifth cycles for these three substrates, respectively. These differences were attributed in large

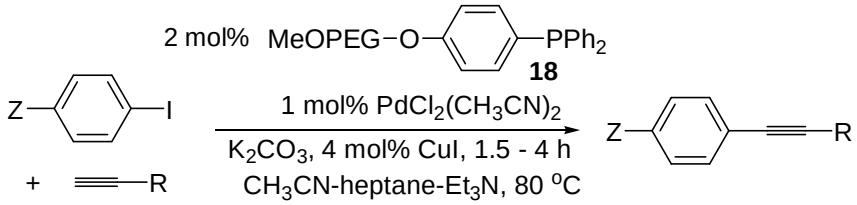
part to oxidation of the Cu(I) cocatalyst to Cu(II) since the TOF values increased when fresh CuI was added to the reaction mixture. Second, leaching of **17** or Pd into the heptane phase was negligible based on the absence of the characteristic resonance for the -CH_2O- group of PEG on ^1H NMR spectra of the nonpolar phase and analysis by X-ray fluorescence (XRF) for Pd. Based on the sensitivity of the XRF analysis, the retention of both the palladium and copper species in the DMSO phase was estimated to be > 99.995%.



(12)

Plenio's group has also reported using the PEG-supported phosphine ligand **18** in Pd-catalyzed biphasic Sonogashira coupling reactions in a thermomorphic solvent mixture of a 5:2:5 (v:v:v) of CH_3CN, Et_3N, and heptane.[45] In coupling of aryl iodides and acetylenes catalyzed with a catalyst derived from **18** (eq. 13) they noted that added Et_3N affected the temperature-induced miscibility between CH_3CN and heptane. By introducing 20 vol% Et_3N, full miscibility was achieved by heating to 80 ºC. In the absence of this additive, CH_3CN and heptane do not achieve full miscibility at this temperature. However, while this strategy worked to make two otherwise immiscible solvents miscible, this initial miscibility could not be replicated in recycling experiments

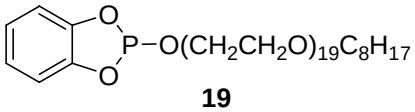
because of the formation of ammonium salt, an effect noted previously in other systems.[9] In this case, Plenio's group simply added a stronger inorganic base, K_2CO_3, that would serve to deprotonate the ammonium salt as it formed. Using this idea this group was able to recycle a Pd catalyst formed from ligand **18** five times with excellent overall yields (83% to 96%) with a variety of aryl iodides (Z = $-CH_3$, $-OCH_3$, or -Cl) and alkynes (R = $-C_4H_9$, or $-SiEt_3$, -Ph).



(13)

Recently, Wang and coworkers have reported a new thermomorphic system composed of PEG_{4000}, toluene, and heptane as a solvent mixture for the hydroformylation of *p*-isobutylstyrene by a rhodium catalyst.[46] In this system, the temperature at which miscibility is achieved is tunable by changing the weight ratio of the components. For example, a biphasic PEG_{4000}/toluene/heptane solvent system with 2/3/1 ratio of components formed a monophase at 110 ºC. Good yields (96%) and TOF numbers (384 h^{-1}) were achieved at 120 ºC when using a rhodium catalyst formed *in situ* from $RhCl_3.3H_2O$ and the PEG-phosphite derivative **19**. This PEG-phosphite-supported rhodium catalyst was recycled seven times by thermomorphic phase separation. ICP-OES analysis of the upper phase revealed about a third of the charged rhodium was leached into the product phase over the first three cycles. Leaching then dropped to 3% in each of the subsequent cycles. The origin of this leaching was not determined. It is possible that this higher metal leaching in the first several cycles might be a result of the

polydispersity of the PEG used to prepare ligand **19** since others have shown that the molecular weight of a polymer support can affect its phase selective solubility in thermomorphic separations.[36,47]. Such effects can be minimized if the polymer or the polymer-supported catalyst is first exhaustively purified using a continuous liquid/liquid extractor.[36]



19

In a follow up paper, this group described using a more PEG phase selectively soluble ligand $P[(OCH_2CH_2)_8OCH_3]_3$ (**20**).[48] In a study with the same solvents at 110 ºC but without Rh present, 0.4% of the charged ligand **20** leached into the nonpolar phase. This was a lower ligand leaching value than found for ligand **19** (2.2 %). When a Rh catalyst was formed with the PEG derivative **20**, it could be reused for nine cycles without any measurable decrease in activity. As was true for a catalyst ligated by **19**, rhodium leaching decreased after the first few cycles eventually stabilizing at ca. 1% leaching per cycle. These results suggest that Rh leaching in these systems is not solely due to ligand loss.

To further decrease rhodium leaching into the product phase of these thermomorphic hydroformylation reactions, a series of solvent mixtures were tested to determine which solvent mixture has the least ligand leaching using the PEG-supported phosphite ligand **20**.[49] A mixture of PEG_{400} and heptane (3 g each) were used as the solvents along with a series of organic cosolvents. The best results for a thermomorphic system were seen when 3.15 g of 1,4-dioxane was used as a cosolvent. In that case, a

thermomorphic system using ligand **20** showed only 0.05 mol% ligand was leached into the heptane phase under the conditions used for the hydroformylation reaction.

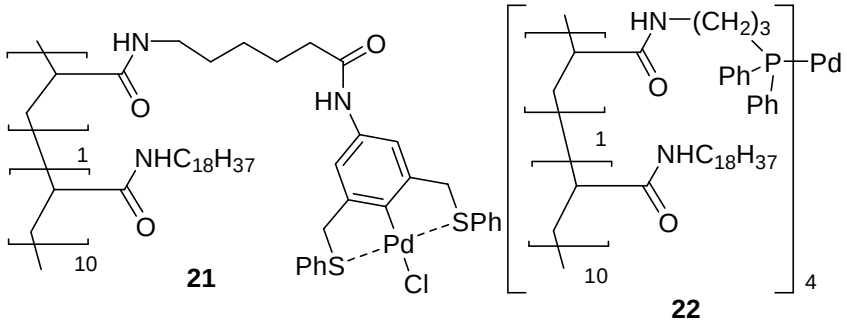
The recycling efficiency of this optimized thermomorphic system was examined in the hydroformylation of 1-dodecene using ligand **20** with 1/1000 ratio of Rh/olefin. After 23 cycles, a catalytic system containing PEG-supported ligand **20** and Rh in a mixture of PEG_{400}, heptane, and 1,4-dioxane still had high activity (94% yield). Metal analysis of product phase using ICP-AES showed that though 1.1% of Rh leaching was detected in the first cycle, the average metal loss for the rest of the cycles was about 0.65%, much less than seen previously. However, while these results are much improved, the overall loss of Rh through 23 cycles would still be ca. 15%.

Thermomorphic Nonpolar Phase Selectively Soluble Polymers

The thermomorphic separations using soluble polymers first described by our group used polar polymers like PEG and PNIPAM. However, polar polymer-supported catalysts in thermomorphic separations have an inherent problem in that both the products and byproducts of most reactions often preferentially accumulate in a polar phase. This affects the conditions necessary for miscibility in a recycling experiment. It also makes catalyst/product separation more problematic. Thus, as our group continued to explore the idea of thermomorphic separations we focused most of our attention on nonpolar polymers for separation of catalysts and products.

An advantage of poly(*N*-alkylacrylamide) supports is their phase selective solubilities are tunable by changing the structure of the alkyl substituents on the nitrogen atom.[33,34] For example, in contrast to PNIPAM, poly(*N*-octadecylacrylamide)

(PNODAM) is a lipophilic polymer that has heptane solubility. We prepared PNODAM-supported phosphine and SCS ligands using a procedure like that used earlier to prepare PNIPAM derivatives. Metalation with $Pd(PhCN)_2Cl_2$ and $Pd(dba)_2$ in refluxing THF then led to the Pd complexes **21** and **22** that had high nonpolar phase solubility. The SCS-Pd complex **21** could be used in Heck reactions just like earlier PNIPAM-supported complexes. While the actual catalyst has subsequently been shown to not be the SCS-Pd complex,[38] reactions using **21** to form cinnamic acid from iodobenzene and acrylic acid could be repeated multiple times without any additional Pd source. For example, after nine cycles conversion was still 90%.[50]

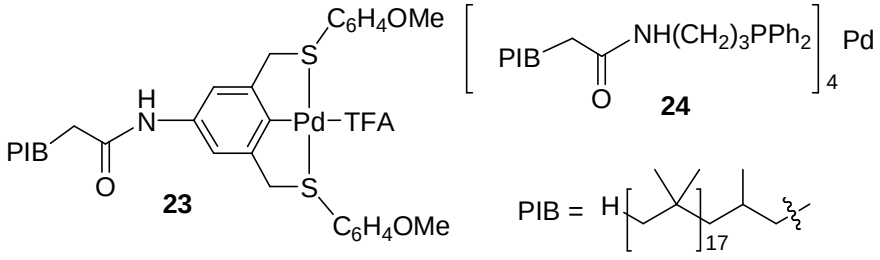


Allylic substitutions that used the Pd(0) catalyst **22** were also reported. While five cycles with this catalyst were successful, gradual deactivation of the catalyst was observed based on the increase in reaction times from 1 h in cycle 1 to 52 h in cycle 5. In this case, the use of a soluble polymer allowed us to examine the catalyst after the reaction. This ^{31}P NMR spectroscopy analysis showed that oxidation of phosphine ligands during the reaction was the proximate cause of the catalyst deactivation.

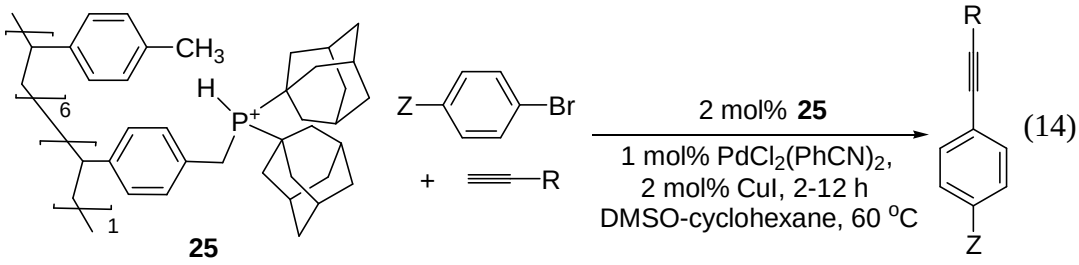
More recently, our group has begun to explore polyisobutylene (PIB) as an alternative to those polyethylene (PE) supports. Vinyl terminated PIB is commercially

available[51] and its vinyl end groups can easily be modified.[52] More usefully, these PIB oligomers are soluble in many nonpolar organic solvents at room temperature. Studies on phase selective solubility using methyl red and dansyl labeled PIB oligomers in a biphasic system consisting of 90% aqueous ethanol and heptane, revealed that these PIB derivatives are selectively soluble in heptane phase of these thermomorphic solvent mixtures to an extent of more than 99.6%.[4,52]

The utility of PIB oligomers as nonpolar soluble supports was first demonstrated in the thermomorphic systems using Pd catalyzed cross-coupling reactions. Both an SCS ligand and a phosphine ligand were attached to the terminus of a PIB oligomer and these PIB ligands were used to prepare the Pd species **23** and **24**.[40,53] Like other supported SCS-Pd(II) species, the PIB-SCS-Pd precatalyst **23** was only effective for aryl iodides as substrates in Heck chemistry that was carried out at 100 °C. In these cases, an equivolume mixture of heptane and DMA was used as solvent. This solvent mixture was miscible under the reaction conditions but immiscible at room temperature and the Pd in the heptane phase was separated and reused for three cycles without observable loss of activity. Similar results were achieved in a Sonogashira reaction conducted at 70 °C in a monophasic 90% aqueous ethanol and heptane mixture using the Pd catalyst **24** formed from a PIB-supported phosphine and $Pd_2(dba)_3$.



Plenio's group has also reported using nonpolar linear polystyrene-supported hindered phosphines **25** to form recoverable Pd catalysts.[54,55] This polymeric ligand was used in mixtures of DMSO or nitromethane with cyclohexane (eq. 14) for Sonogashira chemistry or Suzuki couplings. In the Sonogashira chemistry, the aryl bromide substrates included -$COCH_3$, -CH_3, -Cl, -H and -OCH_3 substituents and phenylacetylene or 1-octyne were used as the alkynes. In the Suzuki chemistry, $Pd(OAc)_2$ was used as the Pd source, K_3PO_4 as the base, phenylboronic acid, and aryl bromides and chlorides with -$COCH_3$, -H, -CN, and -OCH_3 substituents as substrates. In either case, the Pd catalyst ligated by the poly(4-methylstyrene)-supported hindered phosphine could be recovered in the cyclohexane phase. Five cycles were carried out. The loss of Pd into the polar phase in either example was less than 0.2% of the charged Pd based on XRF and UV spectroscopic analysis.

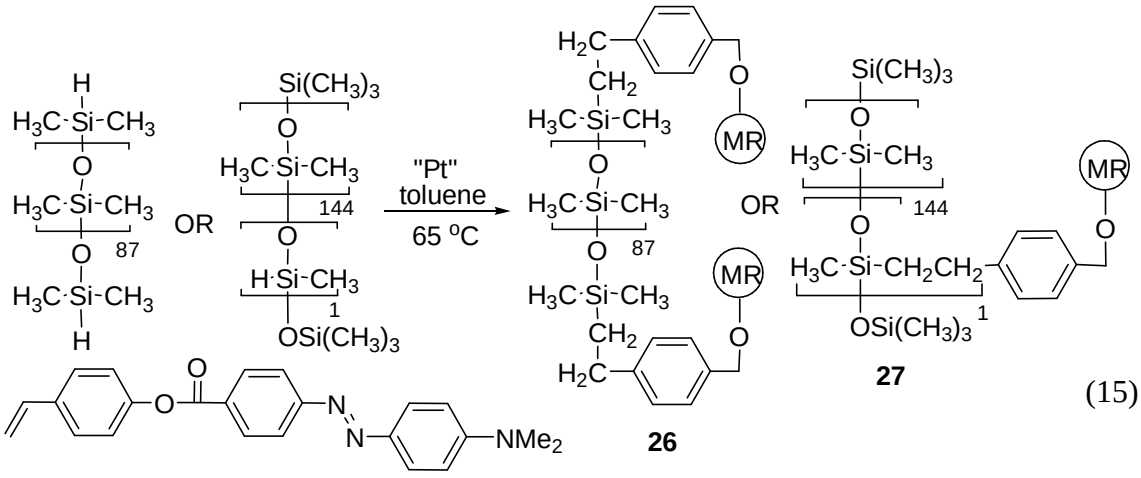


(14)

Latent Biphasic Separations

The use of temperature as a trigger to induce phase separation of solvents in a mixed solvent system is not always necessary. Product formation or small amounts of additives can have a similar effect and this strategy has been used to advantage with several sorts of soluble polymer-supported catalysts.

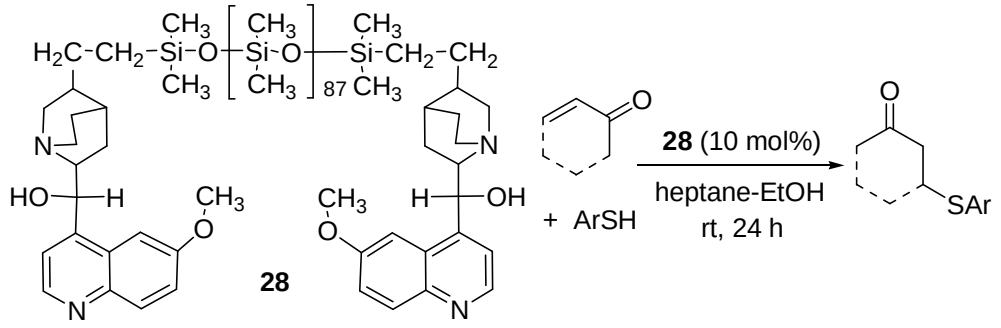
Polysiloxanes have been used as supports for the recovery of catalysts but are usually recovered by membrane filtration or solvent precipitation.[56,57] Liquid/liquid phase separations are an alternative to this approach for separation/recovery/reuse of polysiloxane-supported catalysts. The viability of this approach was demonstrated by the synthesis of several dye-labeled polydimethylsiloxanes **26** and **27** (eq. 15).[58] The feasibility of liquid/liquid biphasic separation for both **26** and **27** were studied using either a thermomorphic mixture of heptane and DMF or a latent biphasic mixture of heptane and EtOH. In these experiments, a heptane solution of the dye-labeled polymer was mixed with an equal volume of DMF or EtOH. Heating in the first case generated a monophasic solution that on cooling had 97.6% (**26**) or 99.5% (**27**) of the dye in the heptane phase. In the heptane/EtOH mixture, addition of 20 vol% water produced a biphasic mixture with 99.6% (**26**) or 99.5% (**27**) of the dye in the heptane phase.



(15)

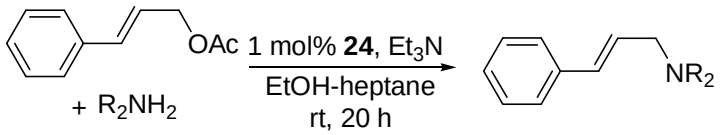
Based on these results, a silane-terminated poly(dimethylsiloxane) was used to hydrosilate a *Cinchona* alkaloid.[58] The product immobilized quinine derivative **28** was then used to catalyze Michael additions of thiophenols to α,β-unsaturated ketones and

esters (eq. 16) in a equivolume of EtOH and heptane. Recycling simply involved water addition followed by separation of the catalyst containing heptane phase. This recycled heptane phase containing the polymer-supported quinine **28** afforded 80% to 100% yields of products for each cycle through five cycles. No effort was made to optimize this chiral catalyst and only modest enantioselectivity was observed.



(16)

A polyisobutylene-supported Pd catalyst **24** was also successfully used in allylic substitution of cinnamyl acetate by secondary amines in a latent biphasic system (eq. 17). In this case, a mixture of EtOH and heptane was used as a solvent at room temperature and the separation was effected by addition of 10 vol% water. This allylic substitution catalyst was successfully recycled five times.[53]

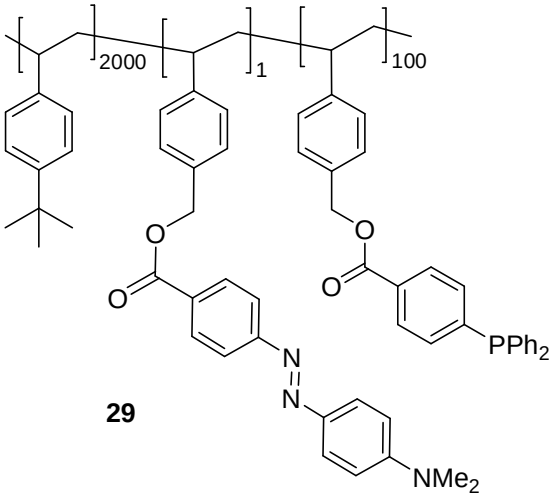


(17)

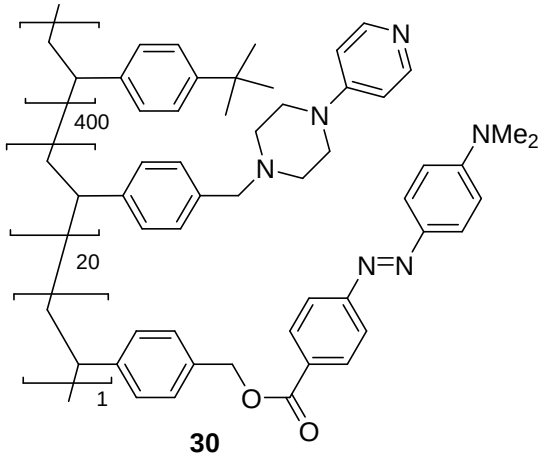
R = $-CH_2CH_3$, $-CH_2CH_2OCH_2CH_2-$

Polystyrene (PS) is an attractive soluble polymer to use to support catalysts because of the many examples that use cross-linked polystyrene as a support for catalysts, reagents, and sequestrants. However, while linear polystyrene or poly(4-methylstyrene) can be used in some liquid/liquid separations, modified polystyrenes with

larger *p*-alkyl groups are more suitable because they have greater phase selective solubility. This is illustrated by work that used poly(4-*tert*-butylstyrene) (PtBS) as a support. This polymer, unlike polystyrene itself, is very soluble in heptane supports. This was shown with the dye-labeled polymers **29** and **30**. UV-visible spectroscopy showed that polymers with ca. 95 mol% *tert*-butylstyrene groups were 99.5 % nonpolar phase selectively soluble in mixtures of heptane and polar solvents in thermomorphic or latent biphasic systems.[59]



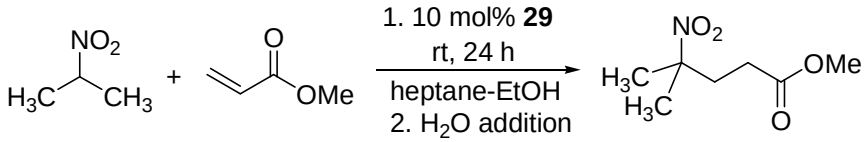
29



30

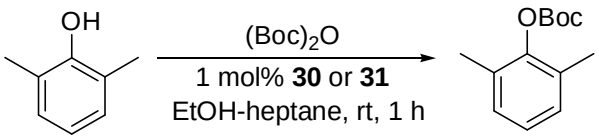
The use of PtBS in catalysis was demonstrated by the use of **29** and **30** as nucleophilic organocatalysts. When 10 mol% of **29** was added to an equivolume mixture of heptane and EtOH containing 2-nitropropane and methyl acrylate, a Michael addition product formed (eq. 18). After the reaction was complete, addition of < 10 vol% water induced biphasic separation. All of the catalyst **29** separated into the heptane phase based on visual absence dye in the polar phase. In recycling, this heptane solution was separated and a fresh EtOH solution of nitropropane and methyl acrylate was added. Five cycles in total were carried out. The yields of product in cycles 3, 4,

and 5 were 69, 72, and 71%, respectively. These yields are similar to those seen with a non-recyclable catalyst triphenylphosphine.



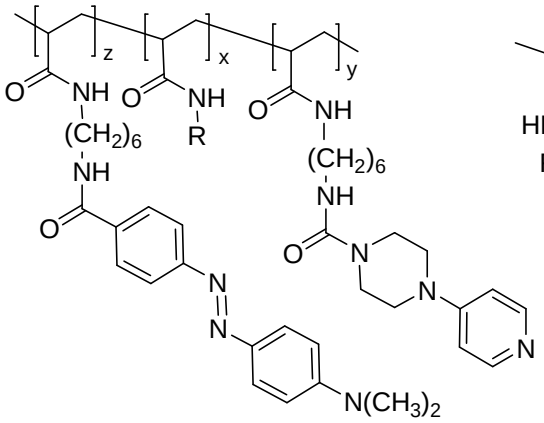
(18)

A second example of recyclability of a PtBS-supported catalyst was the use of **30** in formation of a *tert*-Boc derivative of 2,6-dimethylphenol (eq. 19). In this case, an equivolume mixture of EtOH and heptane was again used and phase separation was effected by adding a small amount of water (ca. 10% of the amount of EtOH). This polymer-supported DMAP analog was reused through 20 cycles with an average isolated yield of product of 93%/cycle. Other nonpolar polymers can be equally effective as supports for recoverable DMAP catalysts under latent biphasic conditions. The PNODAM-supported DMAP catalyst **31** for example was used and recycled 6 times for acylation of 2,6-dimethylphenol by $(Boc)_2O$. Recycling of the catalyst was conducted in a 1:1 heptane-EtOH solvent system at room temperature with water addition used to perturb the system. A thermomorphic system (heptane/DMF) could also be used to recover this catalyst.[9] Likewise, the PNIPAM-supported DMAP catalyst **32** is also recoverable and reusable in systems where reversed phase selective solubility is desired in the catalyst/product separation step (**32** is polar phase soluble).

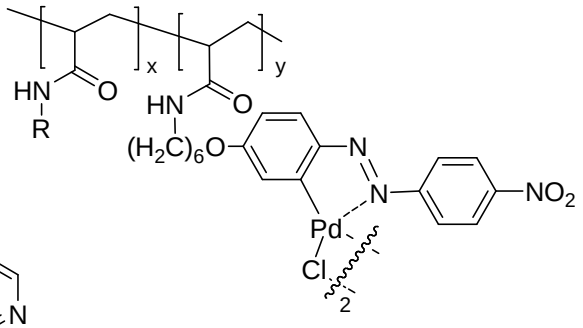


(19)

Polymer-supported palladium catalysts **33** and **34** were both successfully used in Heck reactions. These polymeric Pd catalysts were designed to be recoverable in either a nonpolar or polar phase, respectively, and incorporated a colorimetric ligand to facilitate visual analysis of catalyst recovery/separation efficiency. While visual analysis of this colored Pd catalyst separation is possible, catalyst decomposition (Pd black formation) was observed during a Heck catalysis which makes these Pd complexes less useful in cross-coupling than others.[60]



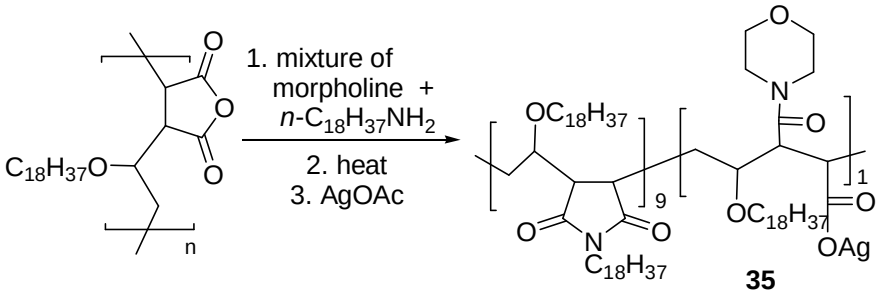
31: R = *n*-$C_{18}H_{37}$; x = 680; y = 136; z = 1
32: R = *i*-Pr; x = 4800; y = 370; z = 1



33: R = *n*-$C_{18}H_{37}$; x = 10; y = 1
34: R = *i*-Pr; x = 52; y = 3

Another example where a latent biphasic system with heptane phase recovery of a catalyst after addition of a small amount of water was used effectively is the atom efficient formation of an oxazoline from ethyl isocyanoacetate and benzaldehyde (eq. 21). This process was catalyzed both by the silver carboxylate catalyst **35** as well as by the SCS-Pd complex **21**.[9] Catalyst **35** was supported on a readily available alternating copolymer derived from maleic anhydride and an alkyl vinyl ether (eq. 20). In this example, a phase selectively soluble hydrocarbon polymer was obtained by using octadecylvinyl ether as one monomer and by treating the maleic anhydride groups with a

mixture of octadecylamine and morpholine. The amic acid derived from the primary amine could be imidized on heating and the amount of morpholine could be controlled to set the amount of -COOH groups in the product which determined the loading of Ag(I) in the eventual catalyst. Recycling of catalyst **35** was successful in a latent biphasic system of heptane and EtOH with an average loss of <0.15% of the starting Ag(I)/cycle over five cycles.



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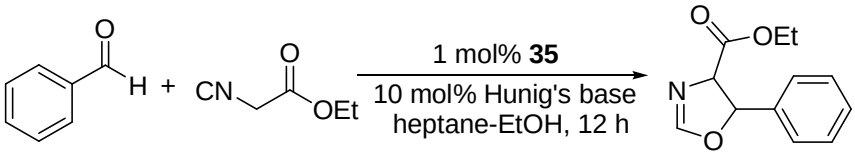

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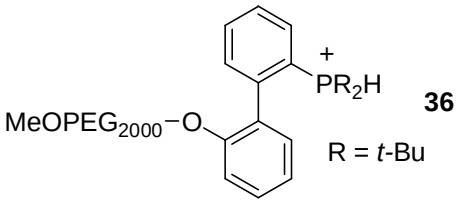
The use of **21** as a Pd source was also successful in a latent biphasic system containing DMA and heptane (1:1, vol). In this case, the phase separation was effected automatically at room temperature by the formation of triethylammonium iodide byproduct.[9] In this example, the byproduct formation advantageously effected the desired catalyst separation. However, it also illustrates the fact that byproducts not only have to be removed from a product, they can also affect the practicality of catalyst recovery efforts that depend on a phase separation event.

Catalyst Separation and Reuse by Extraction

Whether a thermomorphic or a latent biphasic scheme is used, the common feature of the above reactions is that mixed solvents are used. An alternative is to carry out a reaction in a single solvent and to rely on a soluble polymer's phase selective solubility in a subsequent extraction to separate the product from catalyst or catalyst from product. The use of this approach was demonstrated with Polymer-supported hindered phosphine ligands **17** and **36** that used in Pd-catalyzed coupling chemistry. They both can be recycled either in a thermomorphic system as discussed above or by selective product extraction. Both ligands were most effective in Pd catalysis when the coupling of an aryl halide and phenylboronic acid was carried out in pure DMSO.[61] While this single polar solvent phase gave the best yield in this cross coupling chemistry, the use of a single solvent precludes a thermomorphic separation. These PEG-containing ligands might have been recoverable by solvent precipitation. However, Plenio's group found that these catalysts could be efficiently recycled through three to six cycles by selective extraction of the products with heptane. High yields were achieved for both aryl bromides and aryl chlorides. Kinetic data were obtained in catalytic reactions using ligand **17**. Aryl bromides were more reactive with TOFs of 500 h^{-1} to 1200 h^{-1} that were dependent on the aryl halide substituents. TOF numbers for aryl chlorides were less than 100 h^{-1} in most cases. After five or six cycles, slight decreases in TOFs were seen. The leaching of Pd in product phase was below the detection limits of a colorimetric 4,4'-bis(dimethylamino)thiobenzophenone-based UV analysis for Pd.



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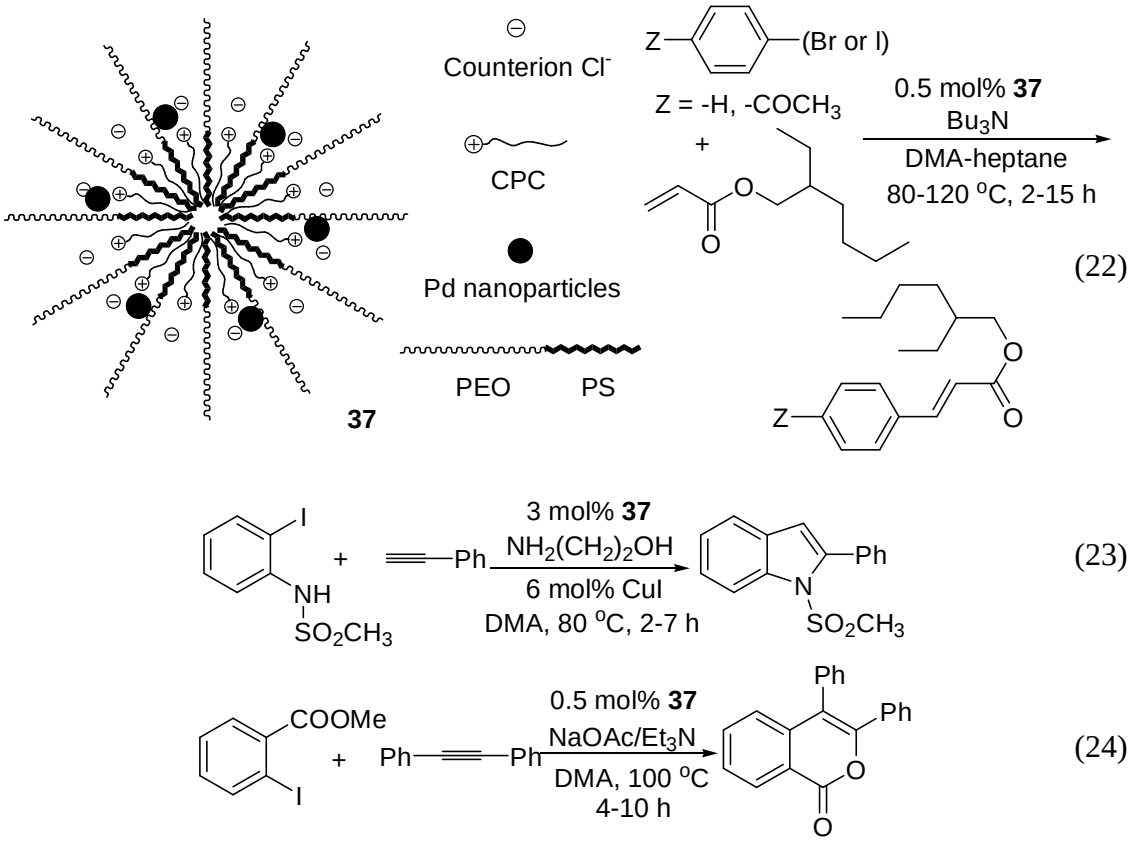
Most examples of soluble polymer-supported catalysts that are recoverable involve batch type reactions. An exception to this is the use of either **17** or **25** as a ligand for Pd in Sonogashira couplings (eqs. 12 and 14 above). Both of these ligands have been used in a continuous reactor where solvent extraction served to separate a nonpolar product from a polar polymer-supported catalyst or vice versa. This liquid/liquid separation relied on a density differences between the phase containing a polar polymer-supported Pd catalyst or a nonpolar polymer-supported Pd catalyst and the product phase to effect a continuous separation. In these two cases, the reactant was added in a nonpolar or polar phase and the product was continuously recovered from the upper less dense or lower more dense phase.[54]

Polymer Stabilized Nanoparticles

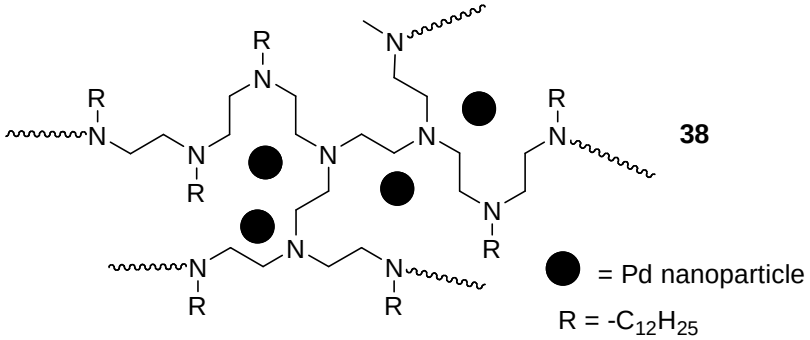
Many palladium mediated cross-coupling reactions are now thought to involve actual catalysis by traces of palladium(0) formed *in situ*.[62,63] Amphiphilic block copolymers containing hetero atoms such as nitrogen have long been known as agents that stabilize nanoparticles including catalytic Pd particles.[64,65] Linear copolymers and dendrimers which are not included in this dissertation, have more recently been used both to stabilize these sorts of particulate catalysts and to facilitate their separation, recovery, and reuse. This has included using such polymers to carry out liquid/liquid separations to recover and reuse these catalysts as discussed below.

An apt example of the how linear copolymers can be used to facilitate the recovery and reuse of nanoparticle catalysts is the work by the Beletskaya group.[66] This group described recyclable amphiphilic PS-PEO block copolymer suspensions of Pd(0) nanoparticles **37** that were effective in catalysis of Heck coupling reactions and other Pd(0)-catalyzed reactions. These Pd nanoparticles stabilized in a dendrimer-like polymeric micelle were similar to those described earlier by Fox and Whitesell,[67] but the Beletskaya group's work has demonstrated these catalysts' recyclability. In the Russian work, the catalyst system was prepared in water and the palladium nanoparticles were generated *in situ* within micelles formed by the PS-PEO block copolymer that contained a cationic cetylpyridinium chloride (CPC) surfactant that asorbed into the hydrophobic micellar core. The resulting PEO-PS-Pd(0) catalyst could be stored for one year without change. These polymer stabilized Pd colloids were used in Heck couplings (eq. 22) with activity comparable to that of a low molecular weight palladium complex ($PdCl_2(CH_3CN)_2$). These (PEO-PS-Pd(0)) colloids **37** could be used in a thermomorphic mixture of 90% aqueous DMA/heptane (1/2, v/v) three times with yields of 90, 86 and 94%. Heck chemistry with aryl bromides worked but longer reaction times and higher temperatures were required. These PEO-PS-Pd(0) colloids were also used and recycled in *N*- or *O*-heterocyclization reactions (eq. 23 and 24). In reaction in eq. 24, 0.5 mol% of PEO-PS-Pd(0) afforded the alkyne cycloaddition product in an average 70% yield over three catalytic cycles. Similar chemistry with an acetonitrile or triphenylphosphine complex of $PdCl_2$ required 5-6 mol% of a non-recyclable catalyst to achieve a similar result.



Use of 1-iodododecane to alkylate PEI (M_w = 60,000) led to a PEI derivative that could stabilize Pd nanoparticles in aqueous solution. Such alkylated-PEI-stabilized Pd nanoparticles were successfully used for hydrogenation of alkenes.[68] Analysis by ^{15}N-^{1}H heteronuclear multiple bond correlation spectroscopy showed that only secondary and tertiary amine groups remained in the alkylated PEI support. Under identical reaction conditions, higher reaction yields (>99%) and faster reaction rates were obtained in the hydrogenation of 1-octene with Pd nanoparticles stabilized by the amphiphilic alkylated PEI in an aqueous biphasic system than were seen with Pd nanoparticle catalysts stabilized by unalkylated PEI. The alkylated-PEI-Pd nanoparticles (**38**) also showed significant chemoselectivity in competition reactions between 1-octene

and 2-methyl-2-heptene or in reactions of 3-methylcyclohexene and 1-methylcyclohexene where only the less hindered substrates were hydrogenated. Recovery and recycling of the alkylated-PEI-Pd nanoparticles was also possible. In these cases, recycling simply involved decantation of the less dense alkane product phase from the aqueous phase. Over five reaction cycles were reported with 1-octene as substrate and >99% yield was obtained in each cycle.



Alkylated polyethyleneimine (PEI)

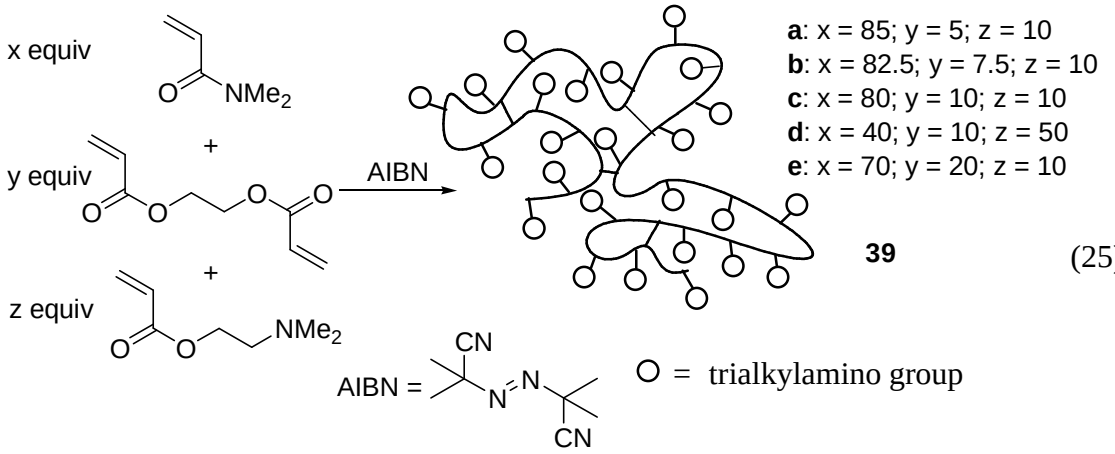
The use of soluble microgels that stabilize metal nanoparticles has recently been reported.[69-71] Such microgels can be prepared from acrylamides and/or acrylates and other functional vinyl monomers as soluble, intramolecularly cross-linked, globular-shaped macromolecules that are 10-100 nm in diameter. They dissolve in water or organic solvents such as DMF, chlorinated hydrocarbons, CH_3CN, acetone, EtOAc, THF, or toluene to form low-viscosity stable solutions. Like other functionalized polymers, microgels have pendent groups and can thus support reagents or catalysts. Such microgels are often recovered from solution and separated from products by ultracentrifugation, or ultrafiltration. A recent study has also shown that microgel-

stabilized metal nanoparticles can be separated, recovered, and reused using a liquid-liquid biphasic systems too.

In this recent work, Biffis' group showed that in a biphasic mixture of water and CH_2Cl_2, pH-responsive microgel-stabilized Pd and Au nanoparticles selectively dissolve to the extent of > 99% in either the aqueous phase or CH_2Cl_2 phase depending on pH. These microgel-stabilized metal nanoparticles were prepared from *N*,*N*-dimethyl acrylamide (DMAA; 40 mol%), and *N*,*N*-dimethylaminoethyl methacrylate (DMAEMA; 10 mol%) and ethylene dimethacrylate (EDMA, 50 mol%) using the metal salts $Pd(OAc)_2$ or $AuCl_3$, respectively.[72] Similar switchable phase affinity was also observed for these microgel-stabilized metal nanoparticles in organic/fluorous biphasic systems via the addition of perfluorooctanoic acid or triethylamine.

The Biffis group also successfully recycled microgel-stabilized Pd nanoparticles catalysts.[73] In this case, a series of microgels (**39a**-**e**) formed by copolymerization of differing amounts of the monomers DMAA, EDMA, DMAEMA (eq. 25) was used to complex $Pd(OAc)_2$. Subsequent $NaHBEt_3$ reduction of the microgel-supported Pd(II) salt yielded Pd nanoparticles that were stabilized inside of the microgel framework. The average size of the microgel-stabilized Pd nanoparticles was found to be ca. 1.9-2.8 nm based on transmission electron microscopy. These soluble polymer-stabilized nanoparticles were shown to be useful catalysts for an aqueous phase oxidation of 1-phenylethanol to acetophenone by molecular oxygen. They showed higher or comparable activity (100% yield, 6 h, 1 mol% Pd) than Pd nanoparticles entrapped in aluminium hydroxide (90% yield, 6 h, 1 mol% Pd) or Pd nanoparticles supported on

hydroxyapatite (> 99% yield, 24 h, 0.04 mol% Pd). Separation of these microgel-supported Pd nanoparticles from product and recycling was accomplished by a post reaction extraction of the aqueous reaction media with diethyl ether. The activity through three cycles (100%, 82%, 17%) using Pd catalysts stabilized by microgel **39b** showed a large decrease due to Pd metal precipitation in the third cycle.



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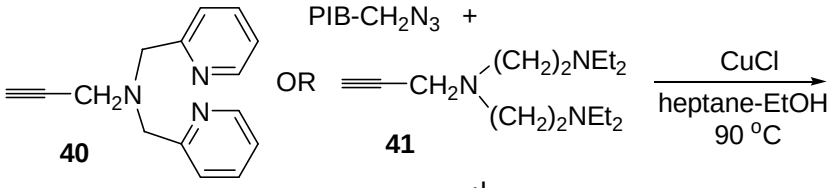
Catalyst Recovery in Self-Separating Systems

A third general way to use soluble polymers to facilitate catalyst recovery in liquid/liquid separations is similar in concept to latent biphasic chemistry. The difference is that rather than perturbing a mixed solvent system with an additive, the formation of the products induces liquid/liquid biphase formation. This is actually an old strategy that was successfully used in the SHOP process.[1] A recent report from our group where a soluble polymer is usefully used in this way is the use of the PIB-supported Cu(I) complexes in ATRP polymerization of styrene.[74]

In this report, the properties of the PIB polymer facilitate catalyst separation in two ways. First, the PIB-supported triazole catalyst was prepared in a mixture of

heptane and EtOH from an azide-terminated PIB and an alkyne containing a chelating group for copper (**40** or **41**) using Cu catalysis (eq. 26).[75] After this copper assisted alkyne azide cyclization was complete, cooling produced a biphasic mixture and the polymer-supported chelated copper complex **42a** or **42b** which was isolated as a heptane solution. The copper complex **42a** was then used in a ATRP polymerization of styrene. This polymerization was carried out using equivolume mixture of heptane and styrene with 1-bromo-1-phenylethane serving as an initiator (eq. 27).



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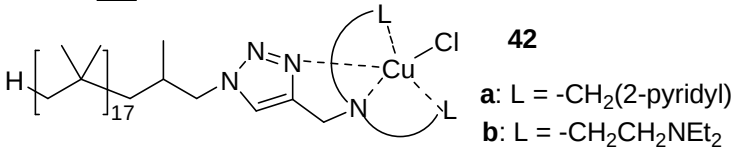

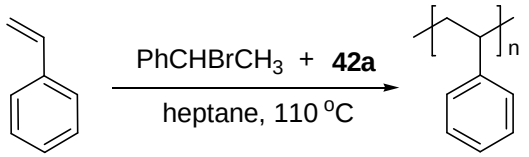

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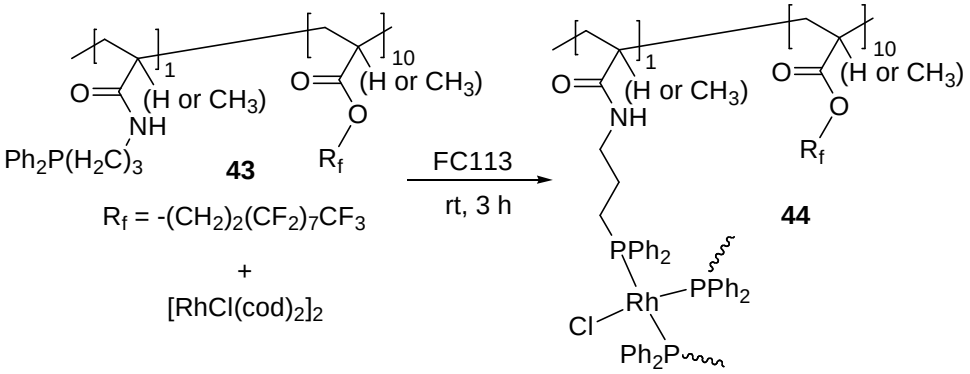
In this second polymerization step of this catalytic cascade process the miscibility of this heptane/styrene solvent mixture changed as polystyrene formed because polystyrene is insoluble in heptane. Thus, when a polymerization like eq. 27 was carried out at 110 °C to ca. 50% conversion and cooled, two phases formed with the Cu catalyst **42a** being in the upper heptane phase and the colorless polystyrene being in the lower phase. Using this approach, catalyst **42a** was successfully recycled five times in a styrene polymerization. An average of 50% conversion achieved for each cycle

with only ca. 3% of copper loss in the product was detected by ICP-MS. These results suggest that these copper catalysts and this approach should be useful in the synthesis and modification of other sorts of polymers if contamination of products by catalyst residue is of concern.

Fluorous/Organic Biphasic Catalysis

The concept of fluorous biphasic catalysis (FBS) was introduced by Horvath in 1990's,[76] and has become an attractive strategy to facilitate synthesis and catalysis. In this introduction, we have only briefly noted a few recent examples where soluble polymer-supported species are used to advantage in this sort of solvent system.

The attachment of phosphine ligands onto fluorinated polymer supports had previously been used in the synthesis of easily separated Rh catalysts for fluorous biphasic catalysis.[77,78] Similar fluoroacrylates containing alkyldiarylphosphines (e.g. **43**) have also been used react with $[RhCl(cod)_2]$ in the fluorinated solvent FC113 to form Rh complexes **44** *in situ* (eq. 28). This catalyst was then used in hydroformylation and hydrogenation of alkenes in $scCO_2$.[79-81] Catalyst recycling proved possible in this system and a total of 20 cycles were carried out for the hydrogenation of 1-octene. No Rh was detected in the octane product by neutron activation analysis.



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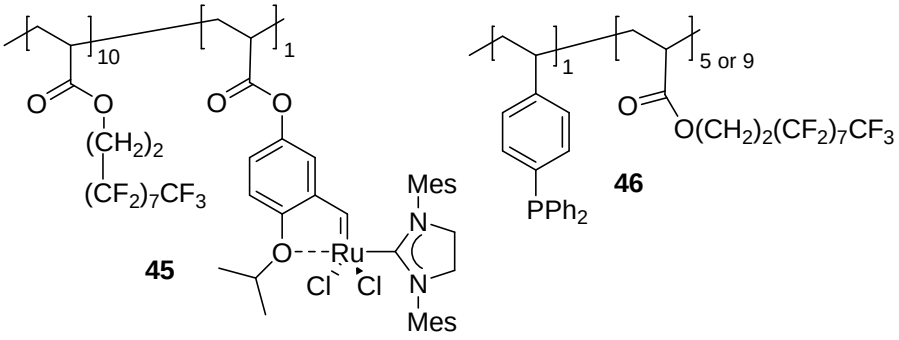
A second example where fluorinated polymer supports have facilitated catalyst separation and reuse is their use in olefin metathesis. Yao's group prepared a metathesis catalyst **45** with a Grubbs-Hoveyda Ru complex as a pendant group on a fluorinated polyacrylate similar to **43**. They then used the polymer-supported catalyst **45** in ring closing metathesis of 1,6- and 1,7- diene substrates in a mixture of $PhCF_3$ and CH_2Cl_2 (1:19, v/v) at 50 ºC.[82] They noted that this catalyst could be completely recovered by a post-reaction extraction with a fluorinated solvent (FC72) due to its excellent solubility in fluorous solvents. High conversions and recyclability of **45** through 20 reaction cycles was observed.



Fluorinated polymers containing a phosphine ligand have also been directly prepared by free radical copolymerization of styryldiphenylphosphines with fluoroacrylate monomers.[83] When the product polymer **46** was allowed to react with $[Rh(CO)_2(acac)]$ in a hexane-toluene-perfluoromethylcyclohexane (40:20:40, vol) solvent mixture, a Rh(I) catalyst that was formed *in situ* was then used in hydroformylation. In this case, the reaction was carried out under monophasic conditions at 50 ºC. Cooling separated the fluorous catalyst phase and organic product phase. This sort of thermomorphic approach to fluorous catalysis was first noted by

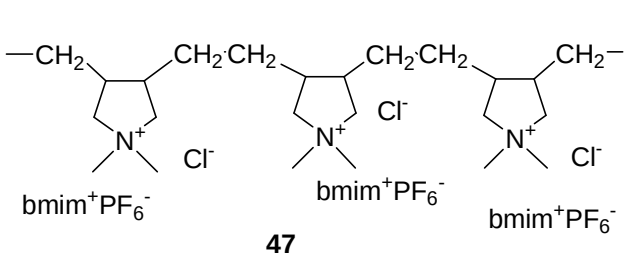
Horvath in his original description of fluorous chemistry.[76] Compared to other aqueous soluble polymer supported Rh catalysts, higher activity (TOF 136 h^{-1}) and regioselectivity (99%) were observed in the hydroformylation of 1-decene using a Rh catalyst ligated by th polymeric phosphine ligand **46**. However, catalyst recycling in this case proved to be problematic. These problems arose not because of catalyst loss or deactivation but mostly because of the continuous loss of the fluorous phase into the organic solvents over three cycles.

Polymer-Supported Catalysts in Ionic Liquids

Ionic Liquids (ILs) are of increasing interest as alternative solvents for chemical reactions in both the academia and industry.[6,84] These interesting materials have been used since the 1990s in commercial processes because they facilitate product catalyst separations.[85] Soluble polymeric materials have been used in this context too.

The most common use of higher molecular weight materials in ILs chemistry is their use as insoluble supports for supported ionic liquid phases (as SILs).[86,87] However, soluble polymers have attracted some attention too. An example of this is work by Wolfson and coworkers where a polymer supported IL-phase was formed by mixing an IL (1-butyl-3-methylimidazolium hexafluorophosphate, $bmim^+PF_6^-$) with a soluble polyelectrolyte, poly(diallyldimethylammonium chloride).[88] Hydrogenations of 2-cyclohexen-1-one and 1,3-cyclooctadiene with $(PPh_3)_3RhCl$ under biphasic conditions with this mixed ionic liquid **47** were faster (TOF = 9 and 14 h^{-1} respectively) than analogous hydrogenations with the same catalyst using a biphasic mixture of $bmim^+PF_6^-$ and diethyl ether (TOF = 2.7 and 5.9 h^{-1} respectively). Asymmetric hydrogenation of

methyl acetoacetate with BINAP-Ru catalyst (**48**) likewise was faster too. A biphasic mixture of isopropanol and the polymer-supported IL **47** containing the Ru catalyst formed product with 97% ee and with a TOF of 29 h^{-1} while the same BINAP-Ru catalyst only had a TOF = 16 h^{-1} with $bmim^+PF_6^-$ alone. In both cases, catalysts in the reactions using the ionic liquid phase **47** were reused twice with no change in activity or stereoselectivity. Atomic absorption spectroscopic analyses did not detect any leached rhodium or ruthenium in the organic product phases.



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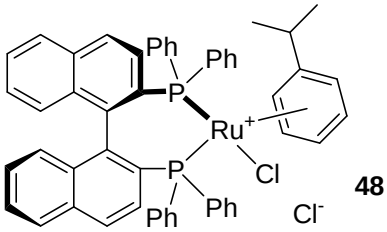

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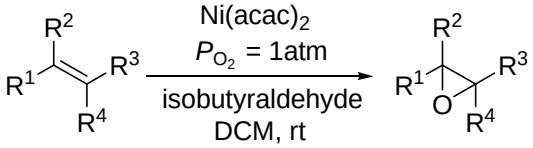
CHAPTER II

POLYISOBUTYLENE-SUPPORTED NICKEL(II) AND COBALT(II) β-DIKETONATES FOR OLEFINS MUKAIYAMA EPOXIDATION*

Introduction

The use of transition metal complexes to catalyze organic transformations has become a very powerful tool applied in modern synthetic organic chemistry. Every year, a wide variety of new reactions and new synthetic methods that use transition metals as catalysts are invented and developed.[89,90] The Ni(II) catalyzed olefin epoxidation developed by Mukaiyama and coworkers is such a reaction (eq. 29).[91]



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The Mukaiyama aerobic oxidation reaction is a simple and efficient method for the production of epoxides. While the epoxidation of olefins is catalyzed by the β-diketonato complexes of Ni(II), Fe(III), Co(II), and Cu(II) in the presence of excess of aldehydes, the Mukaiyama oxidation usefully uses molecular oxygen as the source of oxygen atoms. This makes the overall oxidation procedure safer and more practical than oxidations that use peracids. In this chemistry, product formation is complete in a few hours with high selectivity for alkene oxidation to the epoxide over allylic oxidation to

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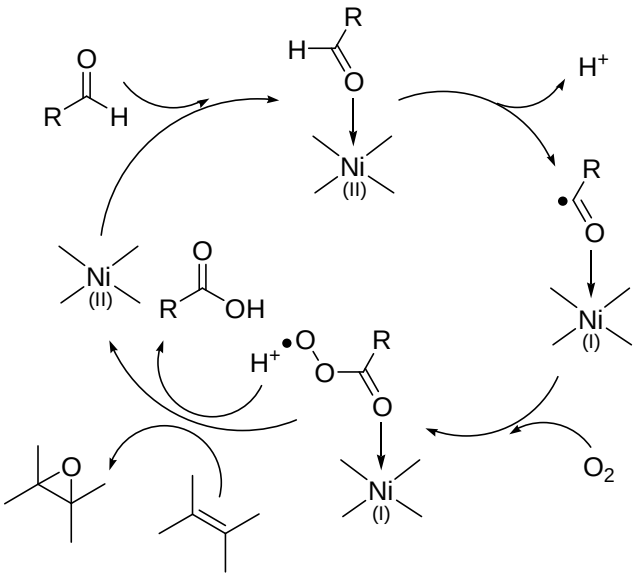
allylic alcohol or enone. Metal carboxylates of these same metals are also effective for the oxidation process but typically have slightly lower selectivity.

Mechanistic studies on the Mukaiyama epoxidation have been conducted by many groups.[92-96] The role of the transition metal catalyst in the reaction is still not very clear, and reactions may proceed by different oxygen activation mechanisms with different metals. It is widely accepted that oxidation of alkenes under Mukaiyama's conditions involves radical intermediates. Mastrorilli and coworkers have found that light could initiate the reaction under Mukaiyama's conditions even in the absence of any metal catalyst.[97] When the reaction was carried out in dark or in the presence of a radical inhibitor (*p*-hydroquinone) no product was detected. However, light was not observed to have an effect when metal complexes were used, which suggests that metal-catalyzed epoxidation proceeds by a different pathway.

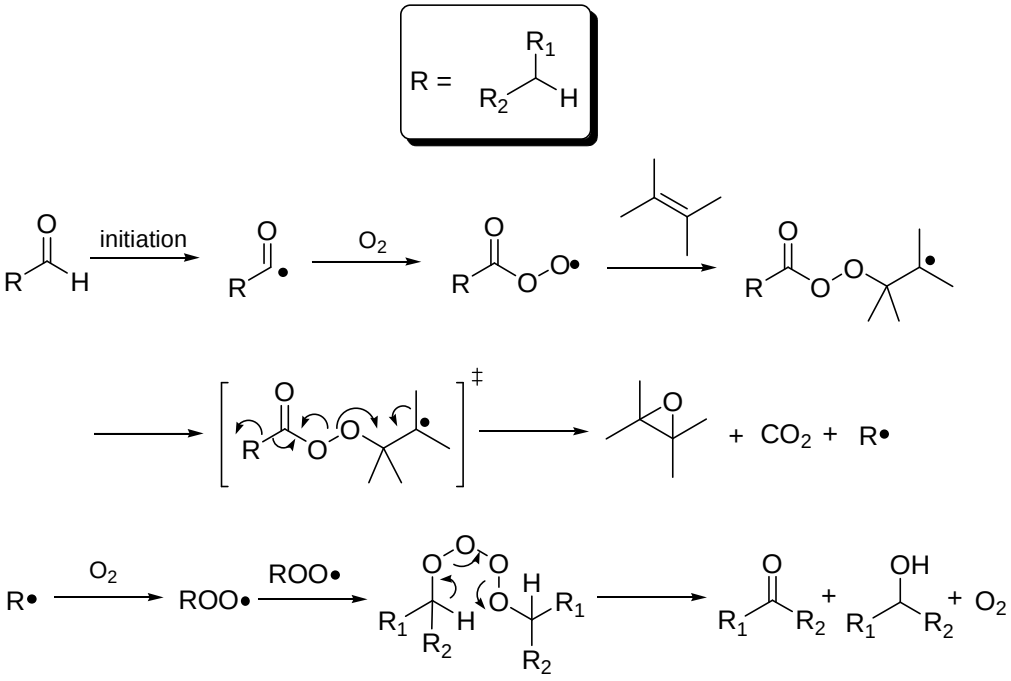
Nam and coworkers suggested that the acylperoxy radical might be the reactive species in the reaction. Alternatively, oxometal species could be another way metals with a tendency for high oxidation states could convert alkenes to corresponding epoxides.[94] A study done by Nolte's group suggested another pathway for epoxidation (Scheme 1).[95] In Nolte's mechanism, the aldehyde coordinated to the Ni(II) center first and then generated a metal stabilized acylperoxy radical that further reacted with alkene to form epoxide. Nolte's work also pointed out that the ratio of aldehyde to alkene had an significant influence on the reaction mechanism.[95,96] A 1:1 ratio of aldehyde to alkene resulted in a relatively slow reaction rate as compared to reactions that used a 3:1 ratio of aldehyde to alkene. Epoxide formation was believed to go through the aldehyde

autoxidation pathway predominantly based on the formation of byproducts such as ketone, alcohol and carbon dioxide (Scheme 2). If the ratio were lower than 0.5:1 (aldehyde:alkene), no reaction occurred because the excess alkene inhibited the aldehyde autoxidation. On the other hand, when higher ratios (3:1) of aldehyde to alkene were employed, epoxidation went smoothly and fast. In addition to epoxidation via the aldehyde autoxidation pathway, part of the epoxidation product could be formed through a peracid pathway that lead to the carboxylic acid byproduct (Scheme 3). In this case, the metal catalysts in the Mukaiyama epoxidation system would presumably affect the initiation step and accelerate the formation of acylperoxy radical. At higher aldehyde concentration, some of reactive acylperoxy radicals generated could form acylperoxy acid groups that could react with aldehyde and form two equivalents of carboxylic acid groups without formation of epoxide.

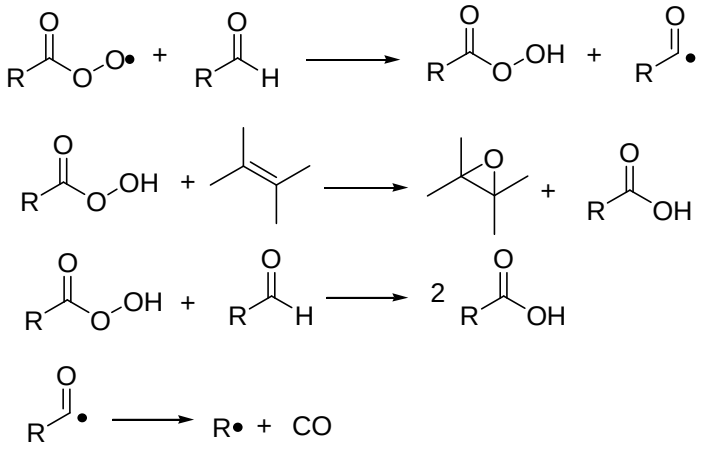
Scheme 1. Mukaiyama epoxidation mechanism proposed by Nolte



Scheme 2. Aldehyde autoxidation mechanism



Scheme 3. Peroxy acid oxidation mechanism

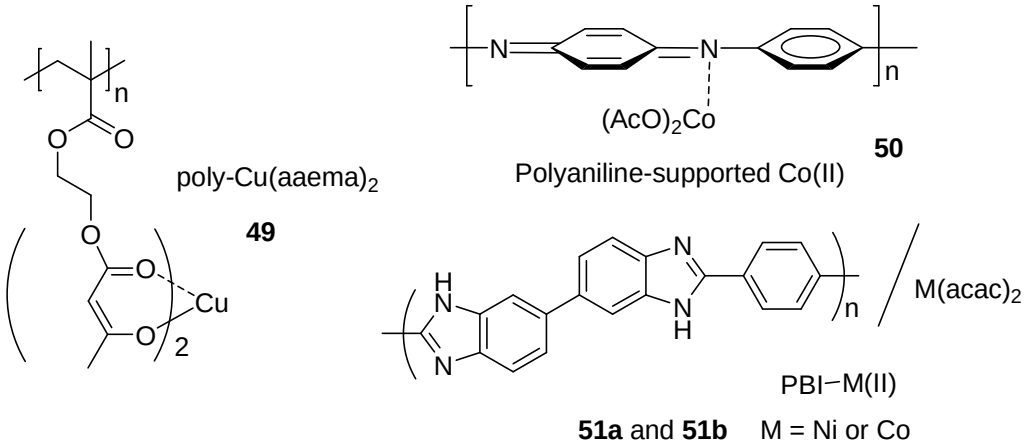


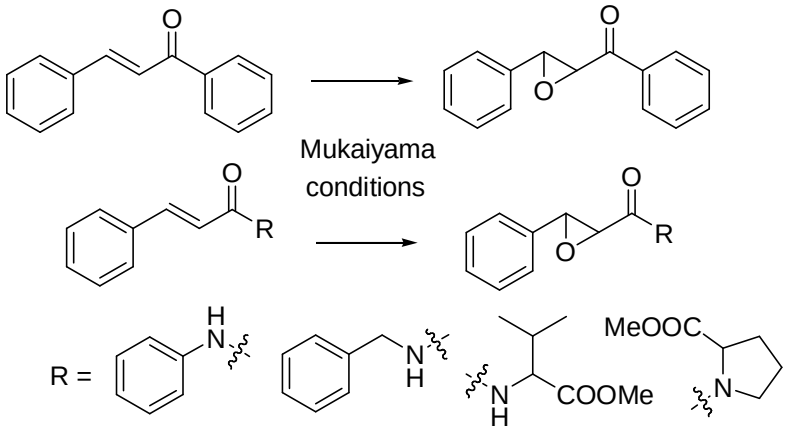
Due to its mild reaction conditions and high selectivity, the Mukaiyama method has received increasing attention in synthetic organic chemistry despite the fact that excess aldehyde has to be used in the reaction. However, while this reaction is useful, recovery and recycling of the transition metal catalysts is still an unmet challenge for this reaction. Although the nickel and cobalt β-diketonates used in Mukaiyama epoxidation are not expensive, preparation of reusable metal catalysts is still attractive in potential industrial applications and is of interest in the context of "Green" Chemistry. Pioneering works that addressed this issue before my work are discussed below.

The first polymer-supported transition metal catalyst for Mukaiyama epoxidation was **49**, a bis-2-acetoacetoxyethyl polymethacrylate copper(II) complex synthesized by Corain and Zecca in 1994.[98] While this soluble polymer-supported Cu(II) complex was active as a catalyst, its catalytic activity and selectivity in the epoxidation of cyclohexene (58% conversion, 79% selectivity) were lower than its low molecular weight analog and significant metal leaching was observed.

Iqbal's group developed a polyaniline-supported cobalt(II) acetate, where the metal ions were anchored onto the polymer through the coordination by nitrogen atoms.[99] This polymer-supported catalyst **50** was effective for aerobic oxidation of various alkenes, including the electron poor substrates, e.g. α,β-unsaturated carbonyl compounds, which are usually not reactive substrates under aerobic oxidation conditions. For example, chalcone and cinnamoyl amides could be converted to the corresponding epoxides in good yields (72% and 53-63% respectively) with this catalytic system (eq. 30 and 31). The recyclability of the catalyst was investigated with

trans-stilbene and *N*-benzyl cinnamoyl amide as substrates. Catalyst **50** could be reused up to three times by merely filtering the product solution and drying the catalyst residue before reuse. Only a small decrease in activity was observed cycle to cycle.





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(31)

More recently, polybenzimidazole (PBI)-supported transition metal acetylacetonates were synthesized by Nolte's group.[100] The results for epoxidation of limonene showed that the PBI-supported Ni catalyst **51a** was more active than the homogeneous catalyst Ni(II) $(acac)_2$ and the catalyst **51a** displayed better selectivity toward formation of limonene oxide (74% yield of epoxide at 93% conversion). PBI-supported Co **51b** was also very active but somewhat less selective. However, metal

leaching was still a problem with PBI-supported Ni. After the first cycle of (*S*)-limonene epoxidation, 20% of the original Ni species leached from the support into solution.

All three polymer-supported catalysts showed moderate recyclability. However, reaction with catalysts **50**, **51a**, and **51b** were biphasic due to the insolublility of the polymer supports. We expected that by using soluble polymer supports, the reaction efficiency would be improved while reusability of the polymer-supported transition metal catalysts could still be effective. This led us to design and synthesize soluble polymer-supported Ni(II) and Co(II) complexes for Mukaiyama olefin epoxidation as discussed below.

Results and Discussion

While most work on polymer-supported catalysts has focused on using insoluble polymer supports, an alternative approach developed by our group in the last few years that has parallels in the strategy used in fluorous biphasic catalysis is to use phase selectively soluble polymers as supports. Such polymer-supported catalysts can be used as homogeneous catalysts in a single phase with the substrate and then separated using either thermomorphic or latent liquid/liquid biphasic approaches. Either approach can be a convenient and efficient way to effect the separation of a soluble polymer-supported homogeneous catalyst from a product if the polymer selectively dissolves in a phase different than that of the product. Such separations are most practical if the polymer can be isolated as a hydrocarbon (e.g., heptane) solution, where the polymer has a phase selective solubility of 200:1, or more because most organic products of interest are more soluble in polar phases. In our previous work, nonpolar polymers poly(*N*-

octadecylacrylamide) (PNODAM) and poly(4-*tert*-butyl styrene) (PtBS) have been successfully used as nonpolar soluble supports in the palladium catalyzed Heck reactions[50] and triphenylphosphine catalyzed Michael additions[71] respectively. Such polymers showed excellent nonpolar phase selective solubility and, catalysts immobilized on these polymer could be recycled multiple times without obvious decreases in catalytic activity in a thermomorphic biphasic system. In this chapter, I am going to describe an example of this sort of approach and its application in transition metal catalyzed Mukaiyama olefin epoxidation reactions.

An alternative polyolefin support that we have recently begun to study is polyisobutylene (PIB) oligomers.[52] The PIB oligomers to be used below can be obtained from BASF under the trade name Glissopal (M_n = 1000 Da, DP = 17; M_n = 2300 Da, DP = 40). PIB has an inert carbon chain with methyl groups distributed along the backbone. These methyl groups greatly limit the crystallinity of PIB oligomers. As a result, PIB exhibits much high solubility in a variety of nonpolar or weak polar organic solvents such as hexane, toluene, dichloromethane and THF. In THF, for example, the PIB derivatives are even soluble at -78 °C. Furthermore, PIB oligomers are also soluble in a solvent mixture containing a nonpolar solvent mentioned above and a polar solvent such as DMF, methanol, ethyleneglycol diacetate (EGDA) at an elevated temperature. Such solubility enables PIB oligomers to be easily modified into ligands in good yields under various reaction conditions.

An initial use of methyl red- and dansyl-labeled PIB oligomers in different liquid/liquid biphasic systems demonstrated that PIB derivatives possessed excellent

nonpolar phase selective solubility. In the case of 90% aqueous ethanol as a polar phase and heptane as a non-polar phase, about 99.5% of the dye labeled PIB retained in the heptane phase even after several cycles of thermoregulated phase merging and separation (Table 1).[4] Another advantage of PIB is that the terminally functionalized PIB oligomers and derivatives can be easily analyzed by routine analytical techniques such as NMR spectroscopy, IR spectroscopy, and UV-vis spectroscopy (Figure 1). In specific cases PIB derivatives even can be separated by column chromatography, which provides another purification method in addition to liquid/liquid extraction.

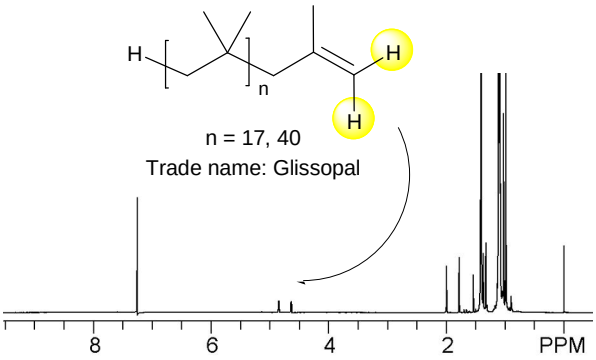


Figure 1. ^{1}H NMR spectrum of PIB-alkene.

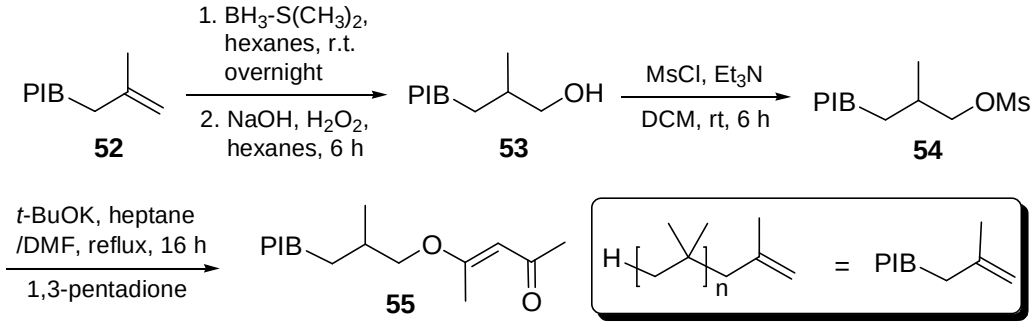
Table 1. Phase selective solubility of dye labeled PIB in heptane/polar solvent biphasic system

Polymer	Polar solvent	Phase selectivity in non-polar solvent (%)
PIB-MR 1000	90% ethanol-H_2O	99.60
PIB-dansyl 1000	90% ethanol-H_2O	99.70
PIB-MR 1000	EtOAc	93.75
PIB-MR 1000	*t*-BuOH	99.42
PIB-MR 2300	90% ethanol-H_2O	99.70
PIB-dansyl 2300	90% ethanol-H_2O	99.60
PIB-MR 2300	EtOAc	92.86
PIB-MR 2300	*t*-BuOH	98.59

MR = methyl red

β-Diketones are bidentate type ligands that are widely used to form transition metal complexes. The first PIB-β-diketone ligand we tried to prepare was designed to attach PIB chain to the '3' position of 2,4-pentadione. Its synthesis is shown in Scheme 4. Hydroboration of PIB-alkene **52** followed by oxidation under basic conditions gave rise to the PIB-alcohol **53**, a very useful intermediate in the modification of PIB. Treatment of alcohol **53** with methanesulfonyl chloride afforded PIB-mesylate **54**. However, reaction of a potassium β-diketonate with **54** instead led to a PIB-vinyl ether **55** as the major product. In this case, "O" alkylation of the ambident nucleophile is dominated.

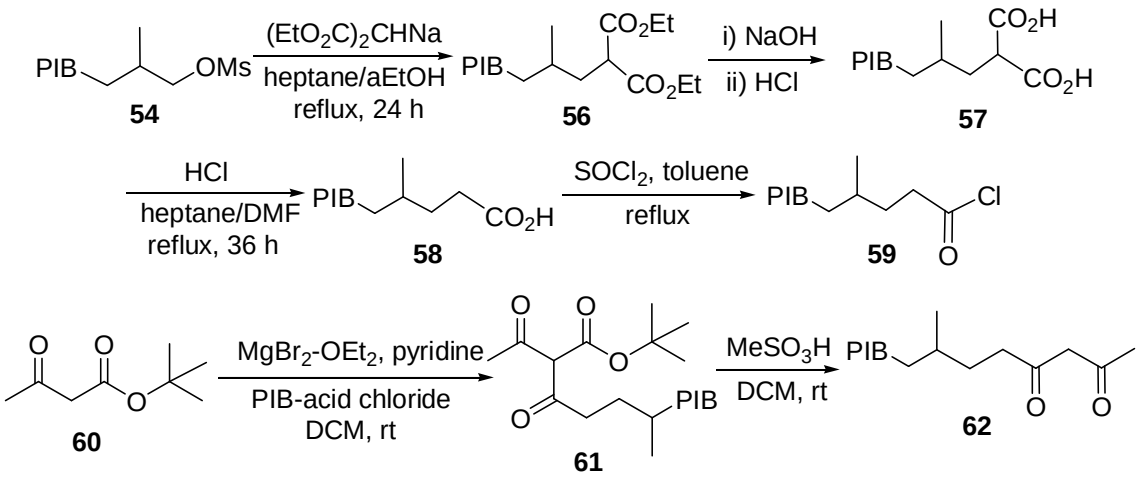
Scheme 4. Initial attempt toward synthesis of PIB-β-diketone



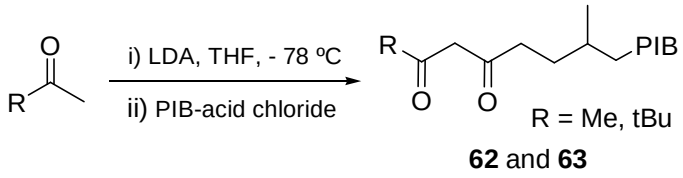
In a redesigned synthetic route, a PIB-β-diketone was prepared starting from a PIB-carboxylic acid **58** which was synthesized through the classic malonic ester synthesis route (Scheme 5). The PIB-acid chloride **59** was used as the electrophile in a reaction with the enolate of *tert*-butyl acetylacetate **60**. The nucleophilic substitution at the sp^2-hybridized carbon of the carbonyl group afforded a tricarbonyl product **61** that

could be decarboxylated after acidolysis of the *tert*-butyl ester, forming the desired PIB-supported β-diketone **62** which was characterized by ^{1}H NMR spectroscopy (Figure 2).

Scheme 5. Synthesis of PIB-β-diketone



Further experiments showed that the *tert*-butyl acetylacetate nucleophile **60** could be replaced by other methyl ketone enolates, which makes this method more general (eq. 32). Both PIB-β-diketones **62** and **63** could be prepared in this way and identified by the signals showed at δ 15-16 (enol hydrogen) and δ 5.5- 6.0 (vinyl hydrogen) in their ^{1}H NMR spectra (Figure 2).



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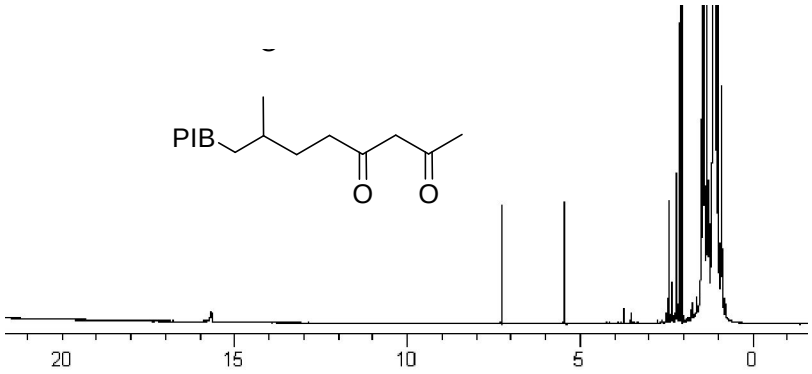
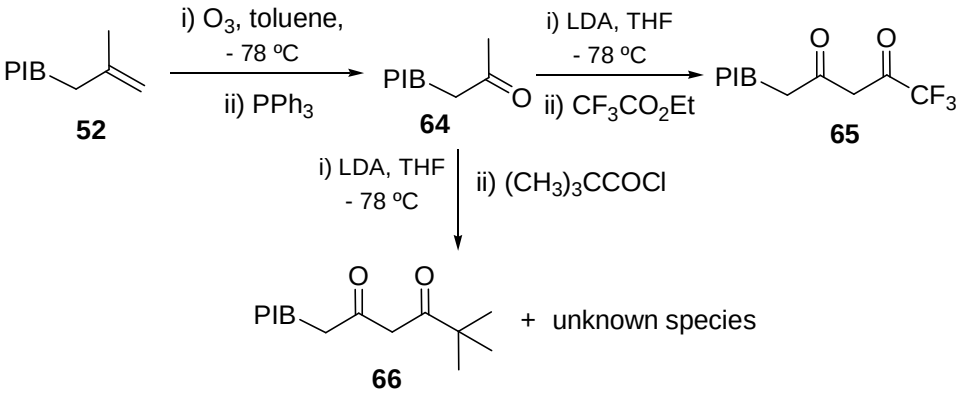


Figure 2. ^{1}H NMR spectrum of PIB-β-diketone **62**.

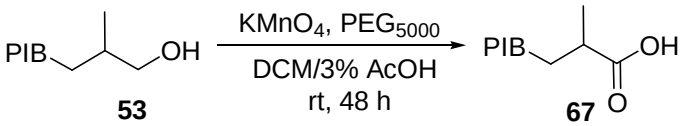
Although the above routes to PIB-β-diketone ligands were successful, the overall synthesis is experimentally tedious. To further shorten the synthesis, the PIB methyl ketone **64** formed through ozonolysis of PIB alkene was used as the precursor of nucleophile instead of low molecular weight methyl ketones. This route took advantage of the excellent solubility of PIB derivatives, which allowed the deprotonation of the PIB methyl ketone with LDA to be carried out in THF at - 78 °C. Our most successful work with this route is the chemistry shown in Scheme 6 in which ethyl trifluoroacetate was used as the electrophile and PIB-diketone **65** was prepared as the only product. An analogous reaction using pivalolyl chloride as the electrophile was less successful. While the expected β-diketone product **66** formed, presence of another unknown species was also evidenced by a singlet in the ^{1}H-NMR spectrum of the product at δ 3.7. Fortunately this PIB-supported species could be separated from the desired product by column chromatography.

Scheme 6. Alternative route to PIB-β-diketone



Other efforts to simplify the synthesis were also studied. To replace the multistep malonic ester synthesis, alternative routes to form PIB-carboxylic acids were explored. The first of these routes used $KMnO_4$ promoted oxidation of a PIB-alcohol derivative **53** to PIB-acid **67** (eq. 33). This reaction, however, only proceeded to the extent of 68%-the product was contaminated by the starting PIB-alcohol. A phase transfer agent (MeO-PEG_{5000}-OH) had to be added in this case because of the insolubility of $KMnO_4$ and the incomplete conversion can be attributed to the poor solubility of the oxidant in the reaction mixture. A second route to a carboxylic acid derivative **68** used a haloform reaction in a biphasic system consisting of THF and 6N NaOH (eq. 34). Again, addition of a phase transfer agent, tetrabutylammonium bromide (TBAB) was necessary for the reaction to occur. THF was found to be the best solvent for this reaction due to its miscibility with water. This reaction produced a carboxylic acid product that was confirmed by ^{1}H NMR spectroscopy (a single peak at δ 2.33 from the methylene group next to the carboxyl group and carbonyl group absorbence at 1706 cm^{-1} by IR). However, on esterification this product (EtOH, *p*-TsA), an ester product

was produced that had more than one type of ester group suggesting that some other unidentified acids were also present (this was not a problem with malonic ester synthesis route above).



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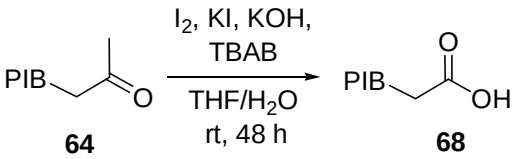
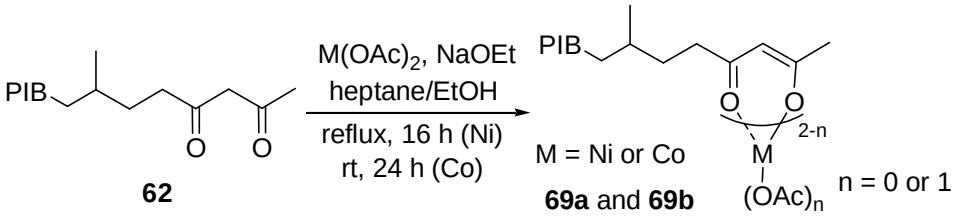


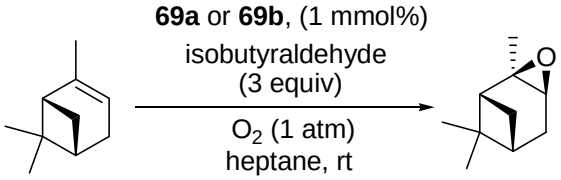
(34)

With the PIB-β-diketones in hand, the PIB-supported nickel **69a** and cobalt **69b** complexes were prepared by ligand exchange with the corresponding metal acetate salts in ethanol/heptane mixtures (eq. 35). Clear changes in the IR spectrum were seen for the products of these reactions. Characteristics of metal-β-diketonates are that the absorption frequencies of the conjugated carbonyl groups and carbon-carbon double bonds move to lower frequency due to the influence of the bonding metal ions. Typically, two absorbance peaks between 1600 cm^{-1} and 1500 cm^{-1} were seen. For example, the absorption frequencies of the carbonyl group and carbon-carbon double bond in **69a** are at 1592 cm^{-1} and 1515 cm^{-1} respectively.



(35)

The catalysts **69a** and **69b** prepared as described above were examined for catalytic activity in the epoxidation of α-(-)-pinene under Mukaiyama's conditions (eq. 36). Heptane was used as solvent to simplify the subsequent catalyst recycling. These experiments indicated that both **69a** and **69b** were highly active and selective. Only trace amounts of byproducts were found by GC analysis. To our surprise, catalyst **69b** was more reactive than **69a** with epoxidation going to complete in four hours. For **69b**, eight hours were needed to obtain 100% conversion. The reusability of the polymer-supported catalysts was also studied. In these preliminary experiments, the catalysts were recycled three times by extraction of the heptane phase with acetonitrile after each run. A fourth cycle was unsuccessful for both catalysts possibly due to metal leaching into the product phase (Table 2).



(36)

Table 2. Recycling of PIB-supported Ni and Co catalysts in Mukaiyama epoxidation of α-pinene

cycle	conversion of pinene (%)*	
	69a (**Ni**)	**69b** (**Co**)
1	100	98.7
2	97.6	96.8
3	96.6	89.0

* Determined by GC.

When compared to other insoluble polymer-supported nickel and cobalt complexes, both the PIB-supported Ni and PIB-supported Co catalysts demonstrate improved activity and selectivity. However, metal leaching is still a problem in both cases. It was also noted that some green or pink solid was formed during the reaction for the nickel or cobalt catalysts respectively. This suggests that the decomposition of PIB-supported catalysts occurred during the reaction. This may have been caused by the carboxylic acid byproduct. Another problem was in the separation of product and catalysts. Due to the low polarity of pinene oxide, extraction of the reaction solution three times with acetonitrile did not remove all the products. As much as 40% of product was still left in the heptane phase. This issue might be less problematic with a more polar substrate such as styrene or methyl acrylate.

Conclusions

Four PIB-supported-β-diketone ligands were prepared through different synthetic routes. The reaction of PIB-acid chloride as an electrophile with an enolate nucleophile derived from a low molecular weight methyl ketone turned out to be a reliable method for synthesis of PIB-β-diketones with various alkyl substituents. Switching the electrophile and nucleophile in the above synthesis scheme also afford us an efficient route to these PIB-β-diketones. In this way, polymer-supported diketone ligands could be obtained in only two steps using a PIB-methyl ketone enolate as a nucleophile using readily available low molecular weight carbonyl compounds (ester or acid chloride) as the electrophile. Subsequent ligands exchange with $Ni(OAc)_2$ or $Co(OAc)_2$ led to the

corresponding PIB-supported Ni and PIB-supported Co complexes which were catalysts in the epoxidation of α-(-)-pinene under Mukaiyama's conditions.

The experimental results indicated that both the PIB-supported Ni and PIB-supported Co complexes were highly active and selective. Only trace amounts of byproducts were observed by GC analysis. Like their low molecular weight versions, the PIB-supported Co complex was more reactive than the PIB-supported Ni complex with the epoxidation being complete in four hours. Longer reaction time was needed to get 100% conversion in the case of using PIB-supported Ni complex.

The reusability of these polymeric catalysts was also studied. In these preliminary experiments, the catalysts were recycled three times. The fourth cycles for both catalysts were unsuccessful due to the decomposition of catalysts.

CHAPTER III

POLYISOBUTYLENE-SUPPORTED RHODIUM(II) AND COPPER(II) COMPLEXES FOR OLEFIN CYCLOPROPANATION*

Introduction

The earliest example of metal catalyzed diazo compounds decomposition was reported by Silberrad and Roy in 1906.[101] Extensive studies on both applications and mechanism of the reaction only started several decades after that. In the generally accepted mechanism suggested by Yates in 1952,[102] addition of the diazo compound to a metal coordination site results in the loss of dinitrogen and generates a metal stabilized carbene *in situ*. This Fischer type of metal carbene has proven to be a very useful reactive species in many organic transformations such as olefin cyclopropanation, carbon-hydrogen insertion, ylide formation, and heteroatom-hydrogen insertion.[103,104] This chapter will focus mainly on the design and synthesis of polymer-supported transition metal catalysts and their applications in olefin cyclopropanation with diazo compounds.

Transition Metal Catalyzed Cyclopropanation of Olefins

The chemical reactivity and bonding features of cyclopropane have long fascinated organic chemists. Of further interest is the fact that derivatives of this smallest carbocycle also possess bioactivity and play a significant role in enzyme-

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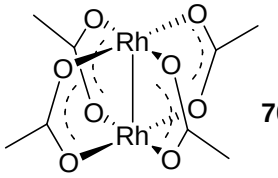
mediated reactions. It is surprising to know that such three-membered rings are kinetically and thermodynamically stable enough in many cases and this structural motif is found in molecules as diverse as fatty acids, terpenes that are formed in various biosynthetic pathways.[105]

The transition metal catalyzed cyclopropanation of alkenes with diazo compounds has been widely used in organic synthesis for the formation of cyclopropane structural subunit in natural and unnatural products. During the past few decades, a variety of achiral and chiral transition metal catalysts have been prepared and used in olefin cyclopropanation reactions. Of these catalysts, rhodium(II) carboxylates, e.g. rhodium(II) acetate dimer **70**, are the most common.[103]



70

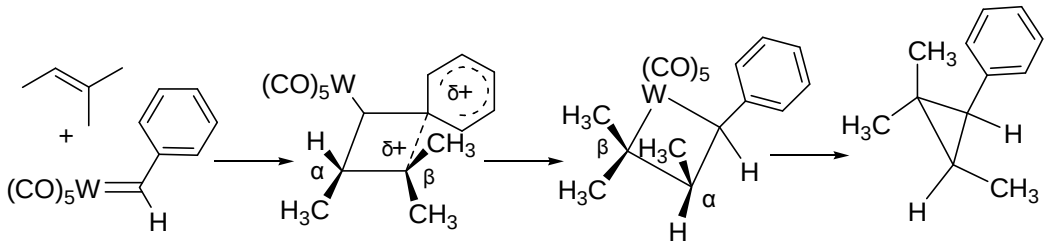
$Rh_2(OAc)_4$

Rhodium(II) carboxylates exist as binuclear compounds with D_{4h} symmetry. The 16-electron configuration on both rhodium ions provide two axial vacant coordination sites which allow the rhodium to act as a Lewis acid catalyst in reactions.[106] Generally speaking, rhodium(II) carboxylates are thermal- and air-stable. Although Lewis bases such as amines and nitriles can easily occupy the two vacant sites, such bonding is weak and the catalyst can be regenerated after removal of those inhibitors by simply heating under vacuum. However, similar coordination is not observed between alkenes and rhodium(II) carboxylate dimers in solution, except for a Rh complex containing a strong electron-withdrawing group, for example, a rhodium(II) trifluoroacetate dimer.[107,108]

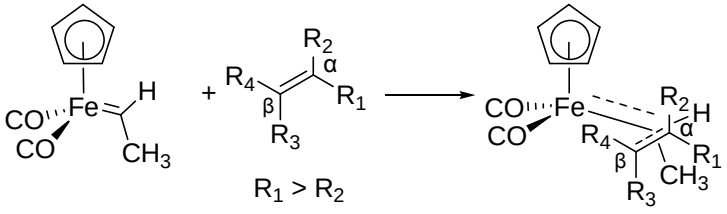
Cyclopropanation with Rh(II) carboxylates is very effective when diazocarbonyl compounds are employed. Other rhodium complexes, such as iodorhodium (III) prophyrins, hexarhodium hexadecacarbonyl, dirhodium(II) phosphates, and *ortho*-metallated phosphines are also effective for this reaction. However, this effectiveness does not extend to reactions using less stable diazomethane where palladium catalysts are more suitable for catalysis of cyclopropanation reactions (via an alkene carbene Pd(0) intermediate). In these Pd-catalyzed reactions, cyclopropanation products are formed through intramolecular rearrangement to palladacyclobutanes followed by reductive elimination.[109]

In addition to the reactivity of the diazo compounds, the difference in selectivity among different carbenoids is another issue that affects the utility of these catalysts. Casey and co-workers found that benzylidene transfer from $(CO)_5W{=}CHPh$ to alkenes predominantly yielded *cis*-cyclopropanation product.[110] This could not be fully explained by the pathway of forming a metallacyclobutane intermediate which was generally accepted as the intermediate in olefin metathesis.[111] Instead of that, they suggested that the electrophilic attack of metal carbene on C_α, the least substituted carbon, resulted in the development of positive charge at the C_β which was stabilized in the transition state via π-electron donation from the phenyl ring. The interaction between the bulky $W(CO)_5$ unit and the substituents at the C_α strongly control the stereoselectivity. The high *cis*-selectivity was a result of the co-influence of these two factors (Scheme 7).

Scheme 7. Mechanism of benzylidene transfer from $(CO)_5W{=}CHPh$ to alkene



Similar results were also obtained by Brookhart's group in the cyclopropanation of alkenes with $Cp(CO)_2Fe{=}CHPh^+$.[112] However, in their study, reaction of $Cp(CO)_2Fe{=}CHCH_3^+$ with internal alkenes also afforded *cis*-cyclopropanation isomer with high selectivity. Here there is no phenyl ring to provide the stabilization effect as discussed above. Although the precise mechanism of this ylidene transfer is still not clear, in their proposed transition state, the larger substituent R_1 at C_α adopt a position between CH_3 and H to form the intermediate with lowest energy. Subsequent synchronous $C_{carbene}$ - C_β bond formation to displace the metal unit can then lead to the *cis*-products (eq. 37).[113] Substituents R_3 and R_4 reportedly had less influence on the stereocontrol.

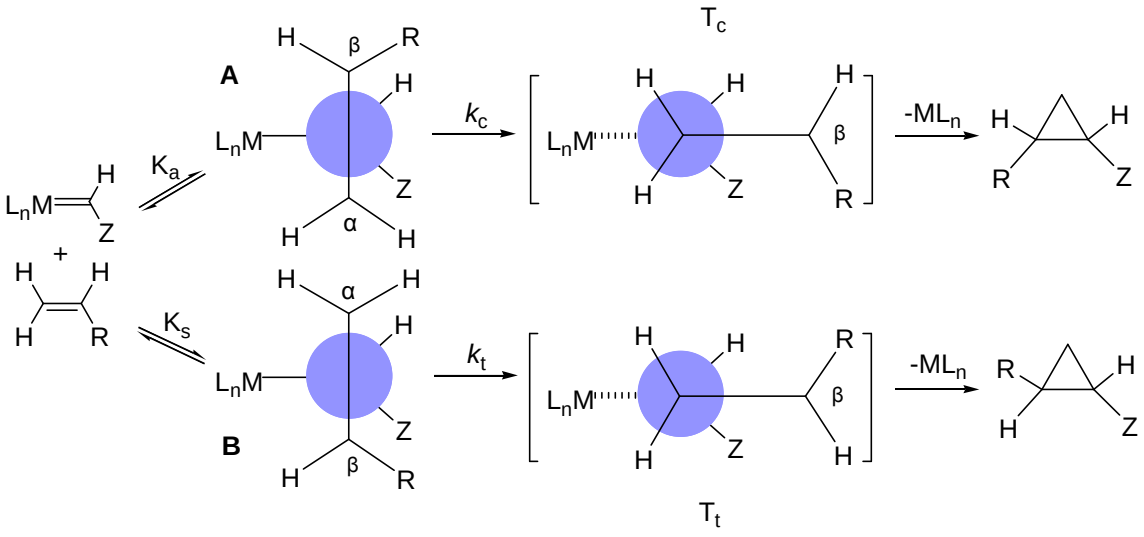


(37)

An alternative mechanistic model aimed to explain the selectivity difference was proposed by Doyle.[114] According to this model initial electronic addition of metal

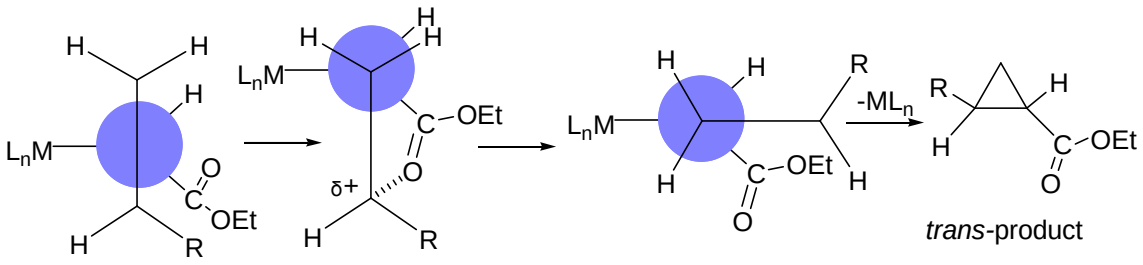
carbene to the alkene forms a π complex. Then the alkene moiety rotates around the $C_{carbene}$ - C_α bond to a position, where C_β is anti-parallel to the metal center. Formation of such alkene and metal carbene orientation is energetically favored. Subsequent backside displacement of the metal complex affords the cyclopropanation products. Stereoselectivity is mainly determined by the interaction between the substituents on the carbene center and alkene carbons (Scheme 8). The usefulness of this mechanistic model was illustrated by considering cyclopropanation of a monosubstituted alkene. In this case, if the steric repulsion between substituents R and Z is weak in the transition state, k_c can be assumed to equal to k_t and the reaction prefers to form *cis*-product through a more stable π complex **A**. Increasing the size of R group will result in a decreased k_c and further decrease the *cis*/*trans* ratio.

Scheme 8. Doyle's mechanism for olefin cyclopropanation



The most attractive feature of this model lies in its prediction of the *trans*-product in the cyclopropanation of alkene with ethyl diazoacetate. In this case, the carbonyl group next to the carbene center serves as an electron-donating group that stabilizes the positive charge developed on the C_β during the electrophilic addition of carbene to the alkene. This makes π complex **B** more favorable on energy and gives rise to the *trans*-product (Scheme 9).

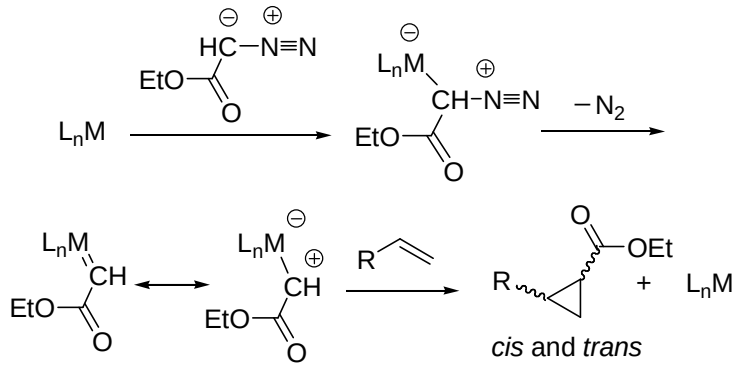
Scheme 9. Cyclopropanation with diazo carbonyl compound



Recent Development in Rhodium Catalyzed Asymmetric Cyclopropanation of Olefins

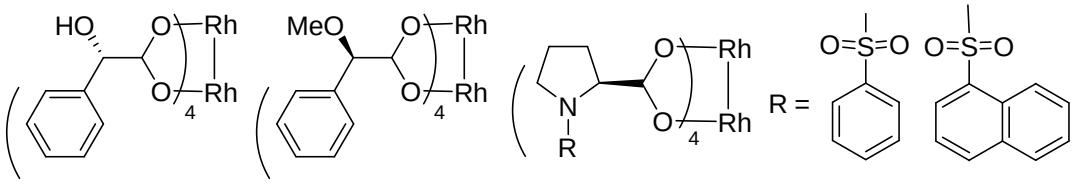
Rhodium complexes have been recognized as the most effective catalysts for olefin cyclopropanation reactions with diazo carbonyl compounds. In this reaction, four enantiomers are usually obtained from the *cis*- and *trans*-diastereomers unless very bulky or chiral derivatives of diazoacetate are employed (Scheme 10).[115] To further broaden their applications in organic synthesis, recent development in this area has been focused on the design and synthesis of chiral rhodium catalysts, catalysts that can afford a single product.

Scheme 10. Mechanism of transition metal complex catalyzed olefin cyclopropanation

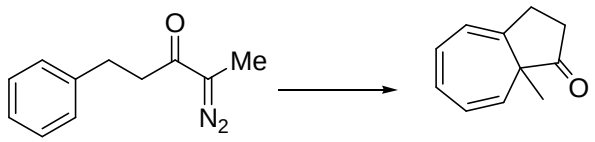


The high efficiency and simplicity of rhodium carboxylates makes them become an extensively studied topic despite the fact that stereocontrol is not efficient even if chiral carboxylate ligands are used. Early studies of chiral rhodium carboxylates included a study of the chiral rhodium carboxylates **71** and **72** by Cotton and Falvello who prepared by reaction of $RhCl_3.3H_2O$ with corresponding chiral carboxylic acids in aqueous solution.[116] However, the use of such homochiral rhodium complexes in C-C bond formation reactions with diazocarbonyl compounds was actually studied by the McKervey group.[117] In addition to complex **71**, McKervey and coworkers synthesized two new Rh carboxylates **73a** and **73b** through ligand exchange of L-proline derivatives with $Na_4Rh_2(CO_3)_4$ in aqueous solution. Three typical carbenoid reactions, e.g. intramolecular aromatic cycloaddition, C-H insertion, and alkene cyclopropanation were chosen as examples to exemplify the catalytic activity and selectivity of these catalysts. Catalyst **73b** was more efficient than **71** in aromatic cycloaddition reaction (eq. 38) and 80% yield and 33% ee were obtained. For C-H insertion reaction (eq. 39), catalyst **73a**

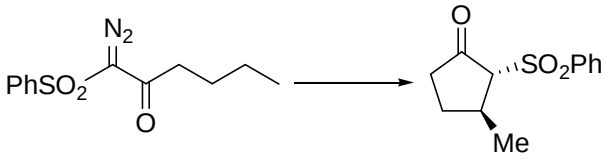
demonstrated highest activity with more than 90% yield. After treatment of the resulting cyclopentanone product mixture containing *cis*- and *trans*-isomers with NaOH(aq) followed by acidification, the *trans*-product was obtained as the only product with 12% ee. Cyclopropanation catalyzed by **71** provided a bicyclo-product in 97% yield, but only 12% ee was observed (eq. 40).



71 **72** **73a** **73b**



(38)



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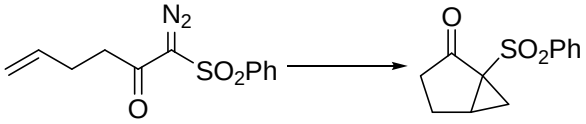
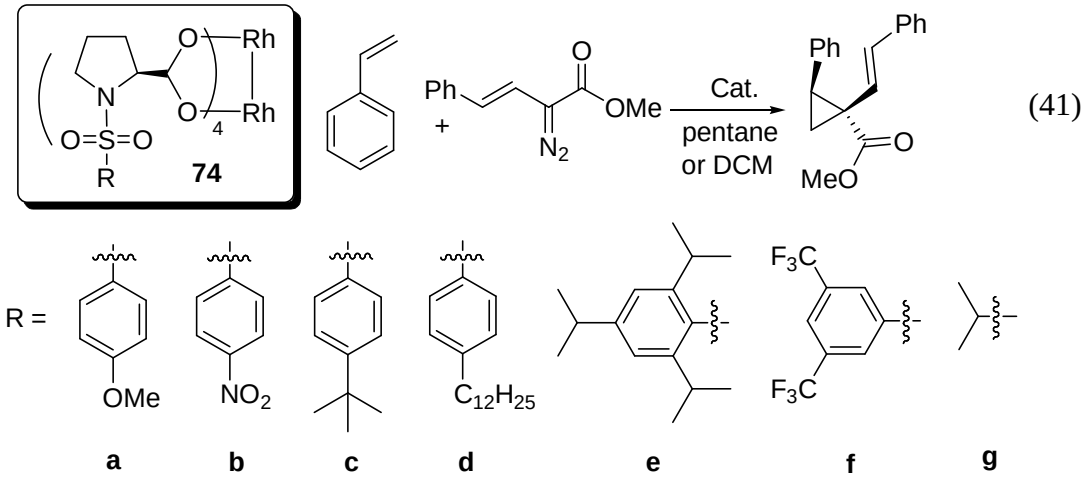


(40)

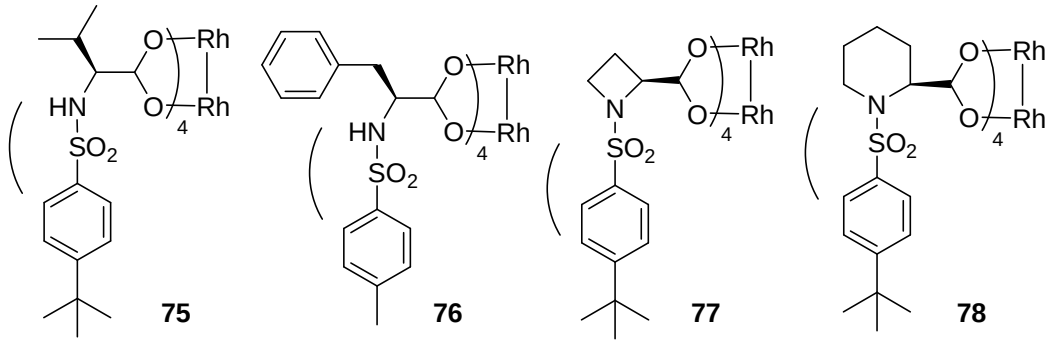
Although these preliminary results were not satisfactory, the idea of using available chiral carboxylic acid to set up a chiral environment around rhodium ions has opened the door toward the design of more successful catalysts. The most successful work with chiral rhodium(II) arenesulfonyl prolinate type catalysts was presented by Davies group.[118,119] This group described cyclopropanation of styrene with vinylcarbenoids formed by decomposition of alkyl 2-diazo-4-phenylbutenoate that

preferentially afforded *trans*-cyclopropanation product both in good yield and enantioselectivity. Such vinylcarbenoids also showed high diastereoselectivity (>20:1; *trans*:*cis*) even using $Rh_2(OAc)_4$.[120]

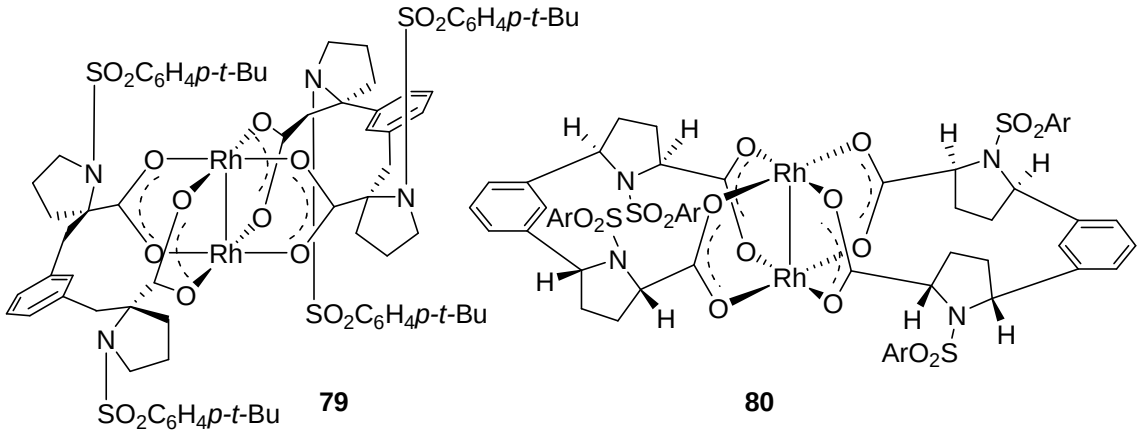
In order to evaluate the influences of chiral environment around the rhodium ions on the stereoselectivity of cyclopropanation, Davies and coworkers prepared a series of Rh(II) catalysts **74a-g** derived from L-proline with different *N*-sulfonyl groups. Catalysts with different size rings and acyclic catalysts (**75**-**78**) were also subsequently examined for stereoselectivity in the cyclopropanation of styrene with methyl 2-diazo-4-phenylbutenoate in dichloromethane or pentane (eq. 41).[119] In all cases, excellent diastereoselectivities, typically from 43:1 to 70:1 (*trans*:*cis*), were observed. It should be indicated that under the same reaction condition use of pentane as reaction solvent instead of dichloromethane led to higher enantioselectivity. Catalysts **74c** and **74d** proved to be the most effective in stereocontrol, and the resulting *trans*-products were obtained with 90-92% ee and 83-89% yields.



(41)

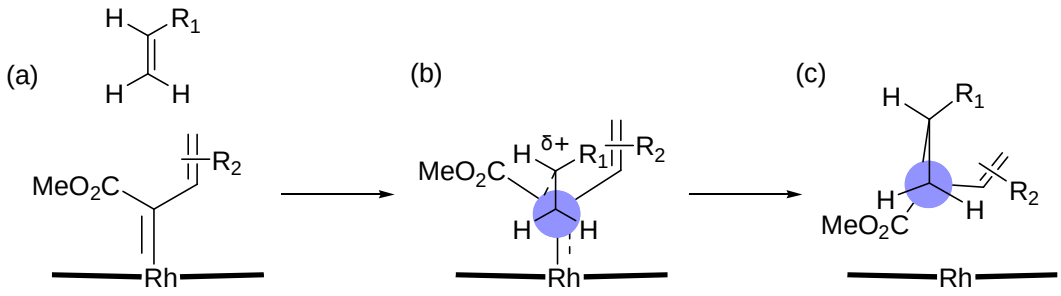


A few years later, the same group developed two new Rh(II) catalysts, **79** and **80** from L-proline.[121,122] Compared to Rh_2(*S*-DOSP)$_4$ (**74d**), catalyst **79** only showed moderate enantioselectivity (49% to 59% ee) in cyclopropanation of styrene with alkyl 2-diazo-4-phenylbutenoate. Higher selectivity (83% ee) was observed when the reaction was conducted at lower temperature (-50 ºC). Catalyst **80** (Rh_2(*S*-biTISP)$_2$) proved to be an excellent catalyst for asymmetric cyclopropanation giving up to 98% ee in cyclopropanation of styrene with methyl 2-diazo-4-phenylbutenoate in dichloromethane at -50 ºC. Unlike **74d**, catalyst **79** and **80** exhibited an opposite asymmetric induction and led to a *trans*-cyclopropanation product with the (*R*,*R*) configuration. In the former case, the (*S*,*S*) configuration predominated in the product.

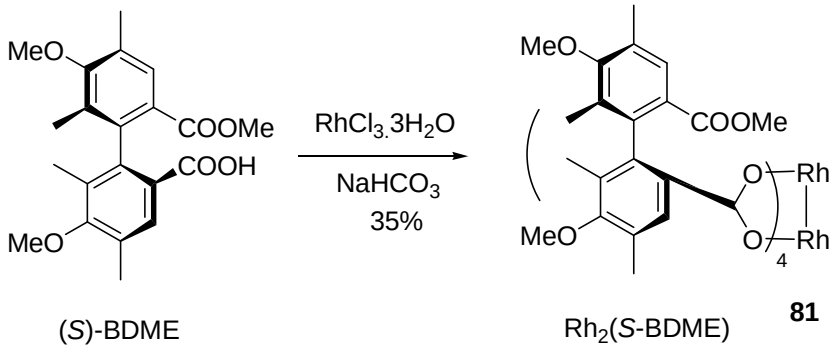


To reveal the nature of the high *trans*-stereoselectivity of vinylcarbenoids, a mechanistic study using ^{13}C kinetic isotope effects in conjunction with density functional theory calculations was conducted by Davies and Singleton.[123] Their results suggest that the alkene would take on a favored arrangement with its substituent (R^1) far from the surface of rhodium center and attack the carbene center from the direction opposite to the Rh centers. The stabilization effect of the carbenoid by the vinyl or aryl group leads to a later, less-flexible, transition state with a potential energy barrier. During this process, the R^1 will point to the alkene unit on the carbenoid to avoid the strong steric repulsion from the ester group. As a result, the alkene configuration is retained, and *trans*-isomer is achieved as the major product (Scheme 11). Compared to a side-on mechanism previously proposed by Davies,[119] where the alkene attacked the carbene center from the side of electron-withdrawing group, this end-on approach of the alkene is more reasonable. Prediction of the stereochemistry in cyclopropanation with this revised model is consistent with the experimental results.

Scheme 11. "End-on" model of olefin cycloaddition with vinylcarbenoide

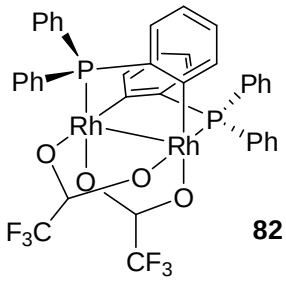


Ishitani and Achiwa designed and prepared substituted biphenyl carboxylate ligand (*S*)-BDME as candidate ligands for a chiral rhodium complex. Subsequent reaction of these chiral carboxylates with $RhCl_3.H_2O$ in the presence of sodium bicarbonate gave rise to the Rh_2(*S*-BDME)$_4$ complex **81** (eq. 42).[124] Compared to Rh_2(*S*-MEPY)$_4$ which will be discussed later, catalyst **81** showed higher catalytic activity and opposite *cis*-selectivity in asymmetric cyclopropanation of styrene with different diazoacetates and 53% ee to 99% ee were achieved on *cis*-products.



(*S*)-BDME Rh_2(*S*-BDME) **81** (42)

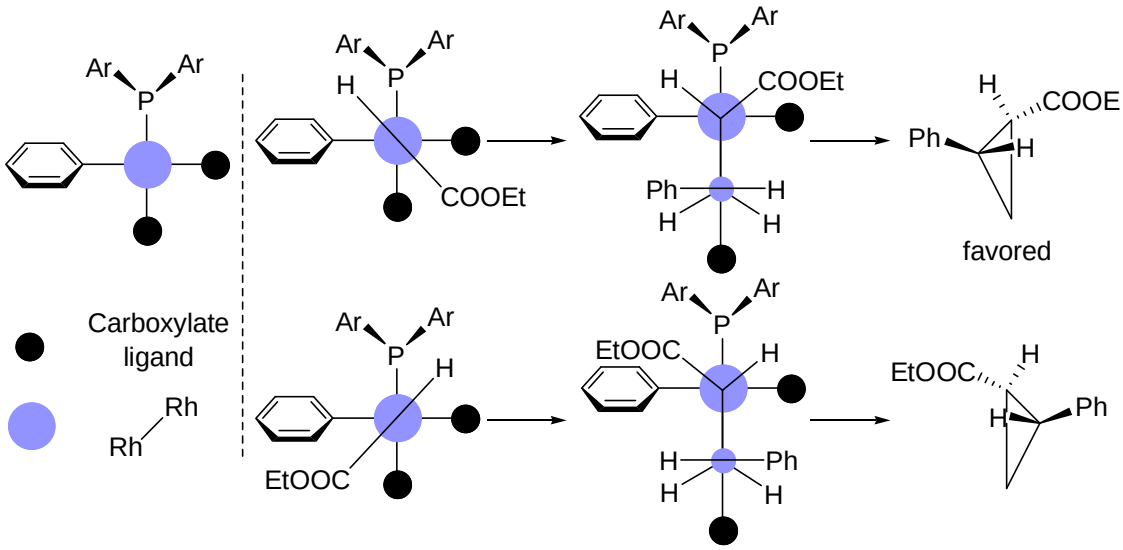
More recently, application of *M*-enantiomer of dirhodium(II) *ortho*-metalated phosphine complex **82** in cyclopropanation of styrene with diazoacetate have been reported by Barberis and coworkers.[125] Catalyst **82** gave high enantiomeric excess for both *cis*- (91% ee) and *trans*-product (87% ee) and 55% yield. Utilization of more bulky trityl group instead of trifluoromethyl group resulted in the great improvement on yield but poorer enantioselectivity. A tentative model was proposed to explain the observed experimental results (Scheme12).



82

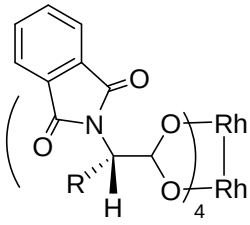
M-enantiomer

Scheme 12. Proposed transition state for the cyclopropanation of styrene catalyzed by **82**



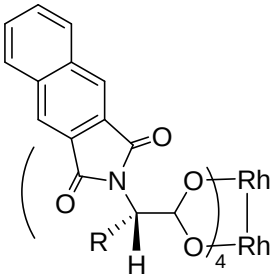
Other types of dirhodium(II) catalysts have been developed and used in carbenoid chemistry. Hashimoto's group developed a new type of chiral rhodium(II) carboxylates **83** and **84,** derived from natural amino acids. Catalysts **83** and **84** were successfully employed in 1,3-dipolar cycloaddition of α-diazo ketones[126] and Si-H insertion of methyl phenyl-diazoacetate[127] and 2,3-sigmatropic rearrangement via intramolecular formation of allylic oxonium ylides.[128] Further modification on this type of catalysts was done by Davies group.[129] Use of an adamantyl group instead of a *tert*-

butyl group at the α position afforded complex **85** which slightly improved the enantioselectivity in both intramolecular C-H insertion of the aryldiazoacetate and cyclopropanation of styrene with diazophosphonate as compared to Hashimoto's catalysts (eq. 43 and 44).



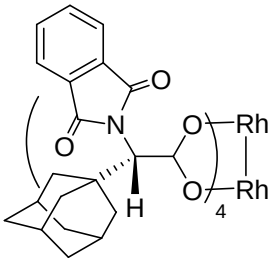
a: R = Bn; Rh_2(*S*-PTPA)$_4$
b: R = Me; Rh_2(*S*-PTA)$_4$
c: R = iPr; Rh_2(*S*-PTV)$_4$
d: R = tBu; Rh_2(*S*-PTTL)$_4$

83



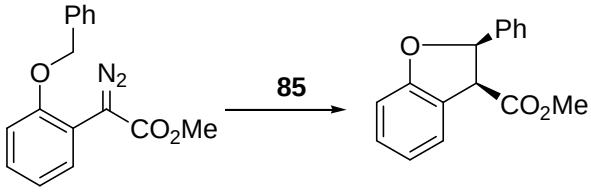
a: Rh_2(*S*-BPTPA)$_4$
b: Rh_2(*S*-BPTA)$_4$
c: Rh_2(*S*-BPTV)$_4$
d: Rh_2(*S*-BPTTL)$_4$

84

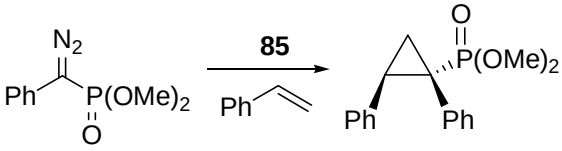


Rh_2(*S*-PTAD)$_4$

85



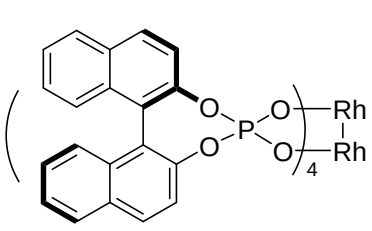
79% yield, > 94% de, 95% ee (43)



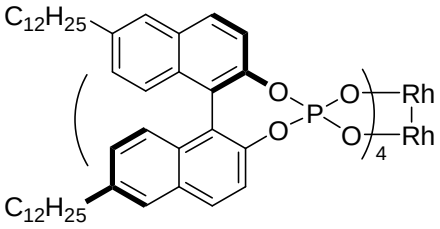
86% yield, > 94% de, 99% ee (44)

Dirhodium(II) chiral phosphate complexes **86** and **87** prepared separately by McKervey's group[130] and Pirrung's group[131] showed good activity and moderate selectivity in 2,3-sigmatropic rearrangement, C-H insertion and aromatic cycloaddition reactions. Attachment of two dodecyl groups on the 6 and 6' position of the aromatic rings dramatically enhanced both the activity and selectivity in the intramolecular tandem carbonyl ylide formation-cycloaddition of α-diazo-β-keto esters.[132] McKervey and coworkers also reported a new family of dirodium(II) carboxylates containing C_2

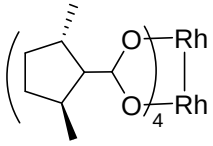
symmetry (**88**-**90**).[133] However, only modest enantiomeric control were observed (up to 29% ee) when using such C_2 symmetric rhodium complexes in intramolecular oxonium ylide-[2,3] sigmatropic rearrangement of diazo keto ester.



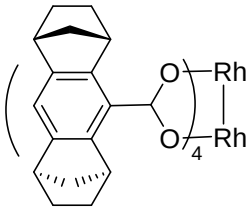
86



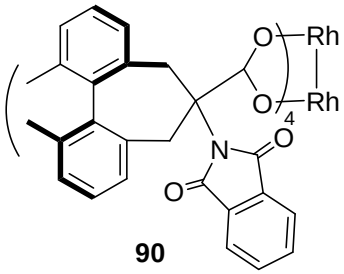
87



88



89



90

In addition to rhodium carboxylates, chiral rhodium(II) carboxamidates developed by Doyle's group are another class of effective catalysts in carbenoid reactions.[134] Although the first rhodium(II) carboxamidate (**91**) was derived from acetamide, acyclic amides are not suitable candidates for preparation of carboxamidates because of their preferred *trans*-conformation which is disfavored for ligand exchange with $Rh_2(OAc)_4$ (eq. 45). As a result, cyclic amides with *cis* form are the only good ligand source for carboxamidates. Unlike the carboxylates, carboxamidates have multiple isomers (Figure 3), but the *cis*-2,2 isomer has been found to be the dominant one. Carboxamidates are less active in the decomposition of diazocarbonyl compounds than carboxylates, but higher selectivity are usually observed due to their more rigid chiral environment around the rhodium centers.

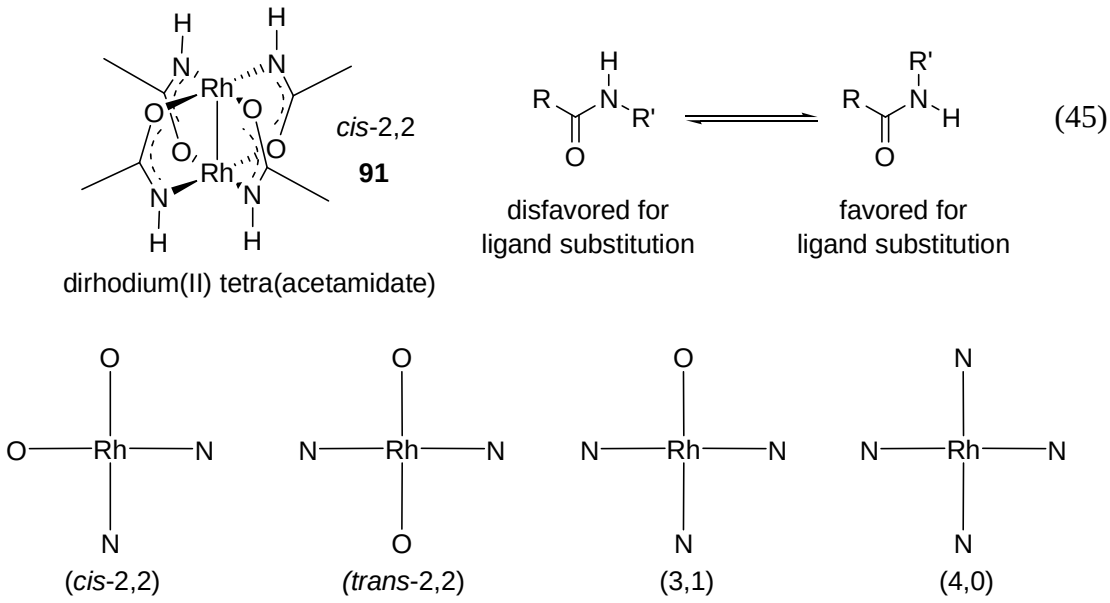
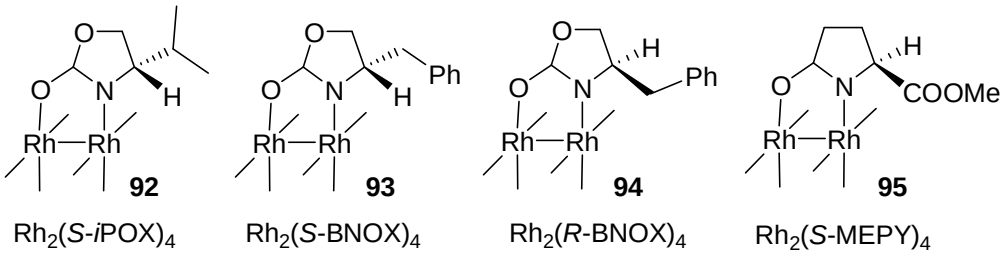
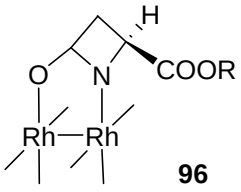


Figure 3. Possible stereo isomers of rhodium(II) carboxamidate.

During the past two decades, a variety of chiral rhodium(II) carboxamidates have been synthesized. The major contributions came from Doyle's research group. In 1990, Doyle and coworkers first synthesized four new chiral rhodium(II) carboxamidates (**92**-**95**) from chiral oxazolidinones and methyl (*S*)-(-)-2-pyrrolidone carboxylate.[135] Evaluations of these rhodium(II) carboxamidates were conducted in the cyclopropanation of styrene with D- or L-menthyl diazoacetates, and catalyst **95** (Rh_2(*S*-MEPY)$_4$) proved to be superior to any other carboxamidates in achieving high enantiomeric control.

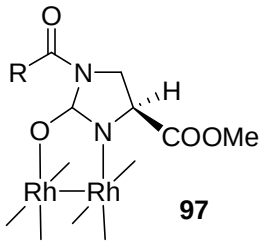


Further studies have revealed that rhodium(II) carboxamidates are more suitable for use in intramolecular cyclopropanation reactions and copper(I) bisoxazoline(Box) catalysts and rhodium(II) carboxylates are usually preferred in catalysis of intermolecular cyclopropanation reactions which will be discussed later. For example, complex **95** catalyzed intramolecular cyclopropanation of allylic diazoacetates afforded bicyclic lactones in high yield (70-93%) and enantioselectivity (>94% ee in most cases) with only few exceptions (Figure 4 and Scheme 13).[136] In the case of 2-methallyl diazoacetate, only 7% ee was observed. This low enantioselectivity was greatly improved by employing rhodium(II) carboxamidates **96** and **97** derived from imidazolidinone carboxylates[137] and oxaazetidine carboxylates respectively.[138] The best result (89% ee) was achieved with complex **97c** (Rh_2(*S*-MPPIM)$_4$). Homoallylic diazoacetates were successfully converted to the corresponding bicyclic lactones under the same conditions (Scheme 14). When using allylic or homoallylic dizaoacetamides as substrates, substitution of the extra hydrogen on the amide nitrogen with other substituents is crucial to achieve higher yield due to the formation of reaction favored conformation.



96

a: R = Me, Rh_2(*S*-MEAZ)$_4$
b: R = Bn, Rh_2(*S*-BNAZ)$_4$



97

a: R = CH_3, Rh_2(*S*-MACIM)$_4$
b: R = Bn, Rh_2(*S*-MPAIM)$_4$
c: R = $PhCH_2CH_2$, Rh_2(*S*-MPPIM)$_4$

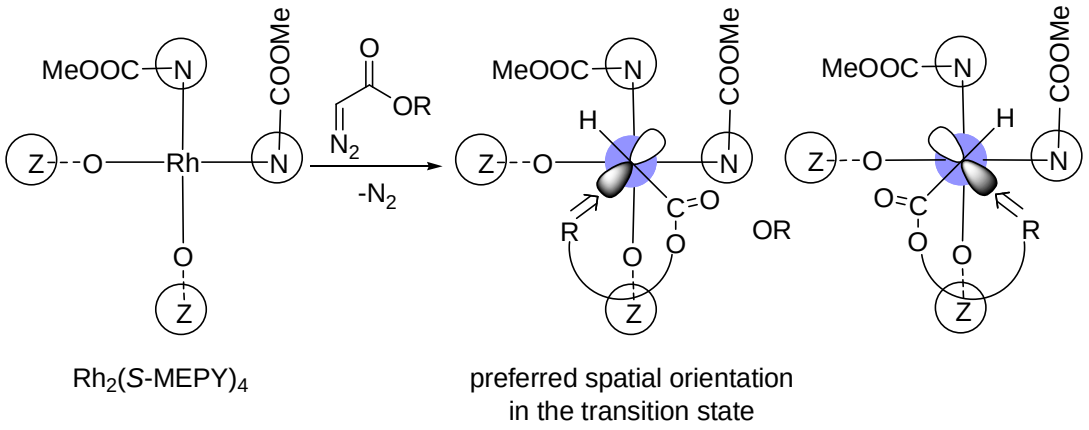
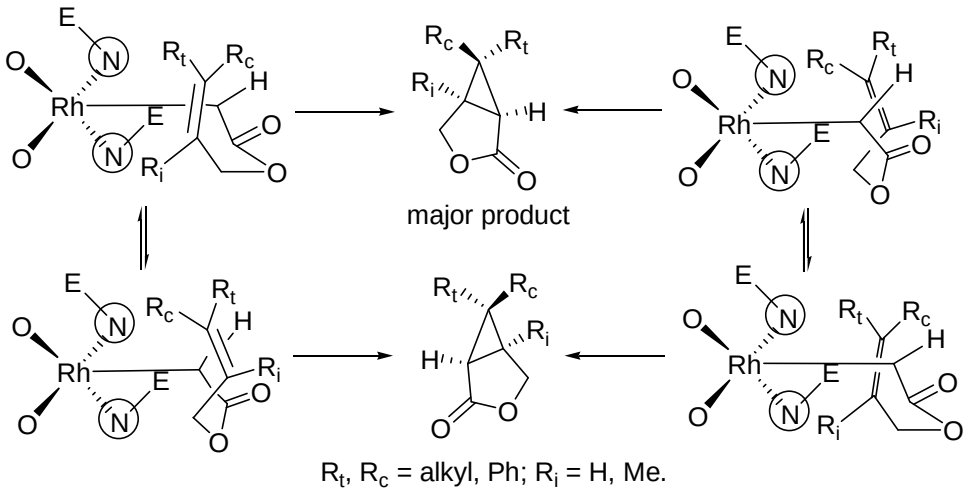
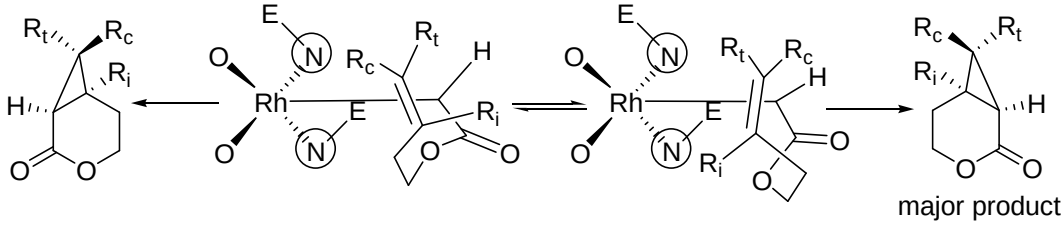


Figure 4. Preferred spatial orientation in the transition state of cyclopropanation using rhodium(II) carboxamidate.

Scheme 13. Stereocontrol in intramolecular cyclopropanation of allylic diazo acetates



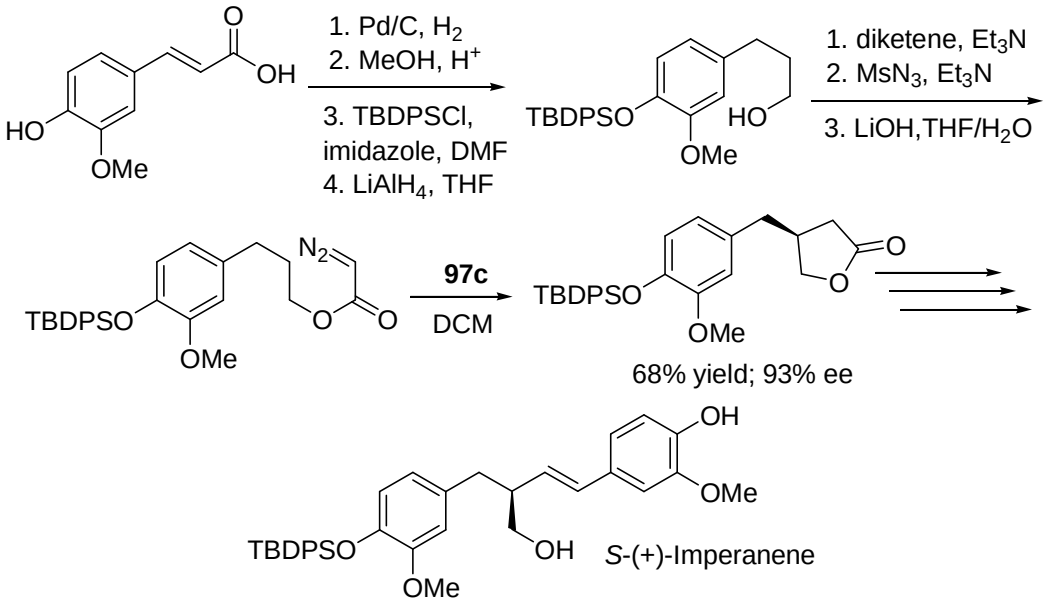
Scheme 14. Stereocontrol in intramolecular cyclopropanation of homoallylic diazo acetates



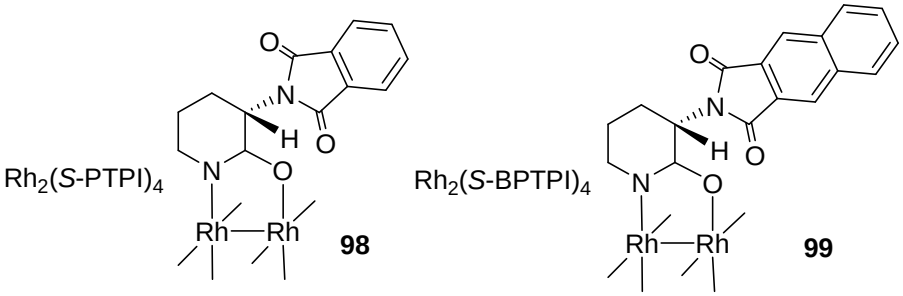
It is noteworthy that the ester groups in the catalyst framework also participate in the determination of stereochemistry through both steric interaction and electronic stabilization of carbenoids.[135] Changing the ester group to alkyl or phenyl groups resulted in the decrease in enantioselectivity.[139]

Another important application of rhodium(II) carboxamidates is the intramolecular C-H insertion reactions with diazocarbonyl compounds. Five member ring, γ-lactones are the most common products and can be obtained with good yield and high enantioselectivity.[140,141] The application of this chemistry in organic synthesis was demonstrated in the preparation of *S*-(+)-Imperanene,[142] where the only chiral center on the allylic position was set up via an enantioselective C-H insertion reaction. The use of Rh_2(4*S*-MPPIM)$_4$ complex (**97c**) provided the γ-lactone intermediate with 93% ee and 68% yield (Scheme 15).

Scheme 15. Total synthesis of *S*-(+)-imperanene



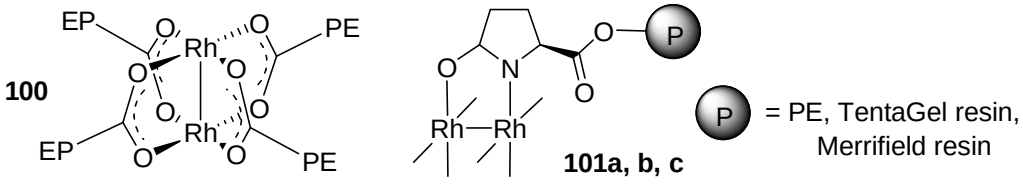
Hashimoto and coworkers designed and prepared dirhodium(II) tetrakis[3*S*-phthalimido-2-piperidinonate], complex **98**.[143] An initial evaluation of this rhodium catalyst in the intermolecular cyclopropanation of styrene and alkyl diazoacetates yielded results like those noted by Doyle's group. While utilization of diethyl ether as solvent had a positive effect on the enantiomeric control, the highest enantioselectivity (98% ee for *trans* and 96% ee for *cis*) was achieved using 2,4-dimethyl-3-pentyl diazoacetate as the carbene source. This is also the best result ever reported for a rhodium(II) carboxamidate catalyzed intermolcular cyclopropanation reactions. Complex **98** and **99** are also effective in tandem carbonyl ylide formation-intermolecular 1,3-dipolar cycloaddition of α-diazo ketones[126] and as Lewis acid catalyst for Hetero Diels-Alder reactions.[144]

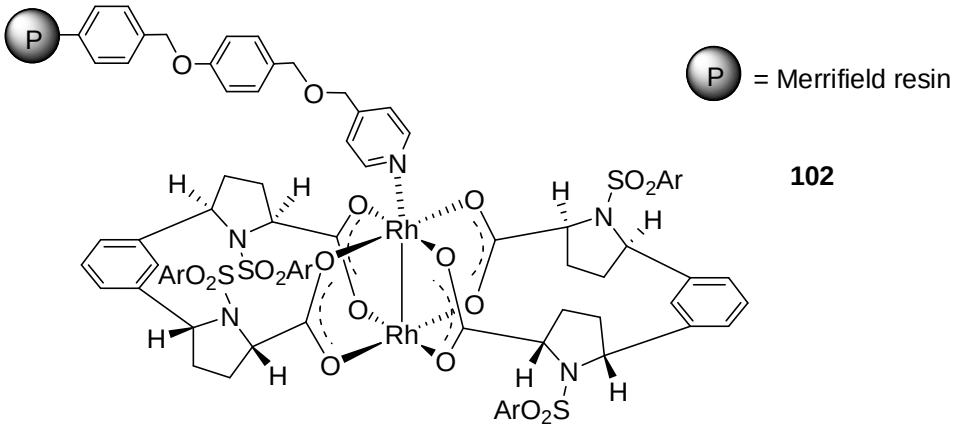


Lower production cost has been one of the goals pursued in industry. It is not surprising that recovery and recycling of precious rhodium salts and expensive chiral auxiliaries has been a challenge in both academia and industry. Attempts to recycle rhodium catalysts in fluorous biphasic systems and ionic liquids have been reported by Biffis' group[145] and Narayana's group respectively.[146] Use of polymers as supports is another alternative method to address the catalyst recycling issue. The first reusable polymer-supported rhodium catalyst (**100**) was prepared by Bergbreiter's group, where

polyethylene (PE) oligomers were used as the immobilization phase.[147] Bergbreiter and Doyle subsequently used these same PE supports in Rh_2(*S*-MEPY)$_4$ catalyzed cyclopropanation chemistry (**101a**).[148] However, with PE supports, elevated temperature is required to dissolve the polymer. That is not ideal for asymmetric catalysis since the enantioselectivities are often higher at ambient or subambient temperature.

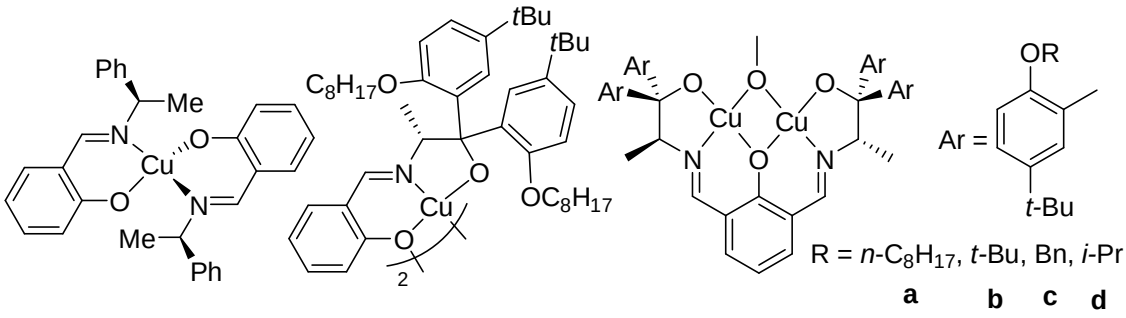
Alternative insoluble polymer supports such as NovaSyn Tentagel (TG) resin, a material in which the polystyrene backbone is grafted with poly(ethylene oxide) chains, and Merrifield resin were also used to support dirhodium carboxamidates (**101b** and **101c**) by Doy's group. These insoluble polymer-supported Rh catalysts showed good recyclability and selectivity.[149,150] A more universal and convenient immobilization method was developed by Davies' group, where various dirhodium complexes were anchored on an insoluble cross-linked polystyrene containing pyridine functionalities.[151] The coordination interaction between one of the axial vacant orbitals of the dirhodium complex and pyridine was strong enough under reaction conditions to allow these polymer-supported rhodium catalysts to be recycled via a simple solid/liquid filtration. For example, immobilized Rh_2(*S*-biTISP)$_2$ (**102**) was successfully reused up to fifteen times without any drop in yield and enantioselectivity in the cyclopropanation of styrene.





Recent Development in Copper Catalyzed Asymmetric Cyclopropanation of Olefins

In addition to rhodium complexes, copper complexes are another transition metal catalyst widely used in olefin cyclopropanation reactions. In most cases, the catalysts are prepared as stable Cu(II) complexes and reduced to reactive Cu(I) species in the reaction mixture with phenylhydrazene. After the pioneering work (**103** and **104**) introduced by Nozaki[152] and Aratani[153] respectively, considerable efforts have been done to develop new chiral ligands pursuing high enantiomeric control.

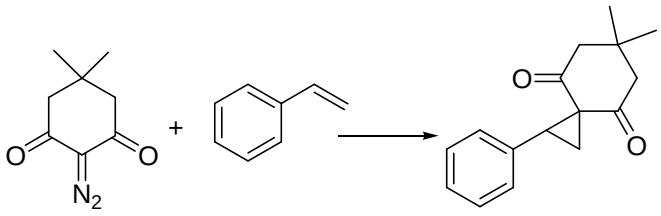


Nozaki's catalyst **103** Aratani's catalyst **104** binuclear copper(II) complexes **105**

A series of novel binuclear copper(II) complexes **105a-d** have been reported recently.[154] Compared to their mononuclear counterparts, these binuclear copper(II) catalysts like **105** exhibit moderately increased enantioselectivity in the asymmetric

cyclopropanation of styrene with ethyl diazoacetate. An average 85% ee for *trans* and 92% ee for *cis* were observed when the catalysts were modified with large alkyl groups on the alkoxide. Such enantioselectivity also showed unusual temperature independence in the reactions occurring from room temperature to 50 ºC. This was advantageous in that better yields could be obtained through running reaction at higher temperature without sacrificing the enantioselectivity.

Matlin and coworkers prepared three copper complexes derived from 3-trifluoroacetyl-(+)-camphor which showed excellent stereo control on the cyclopropanation of styrene with diazo-dimedone (eq. 46).[155] Catalyst **106** demonstrated the highest, up to 100% ee and 48% yield after one day of reaction time. A recoverable version of **106** was synthesized by immobilization of corresponding chiral ligand onto Hypersil 5 µm silica followed by ligand exchange with $Cu(OAc)_2$. Recyclability of the immobilized catalyst **107** was investigated with indene as substrate to avoid the problem of polymerization, which was observed in the case of using styrene. Three cycles were reported.



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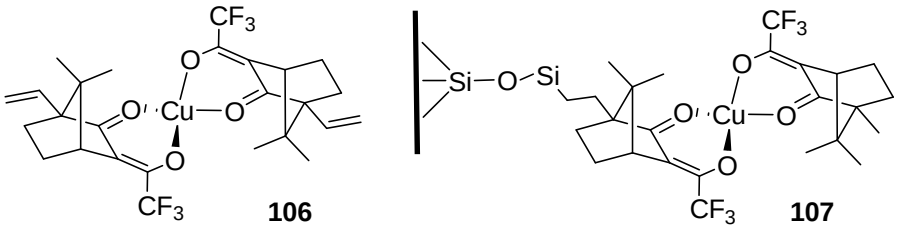


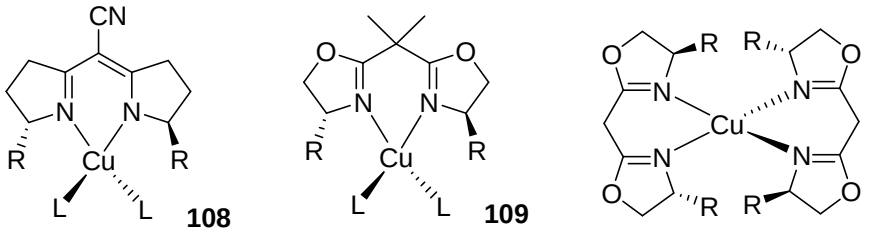
106 Cu(10-methlyenefacamH)

107 immobilized Cu catalyst

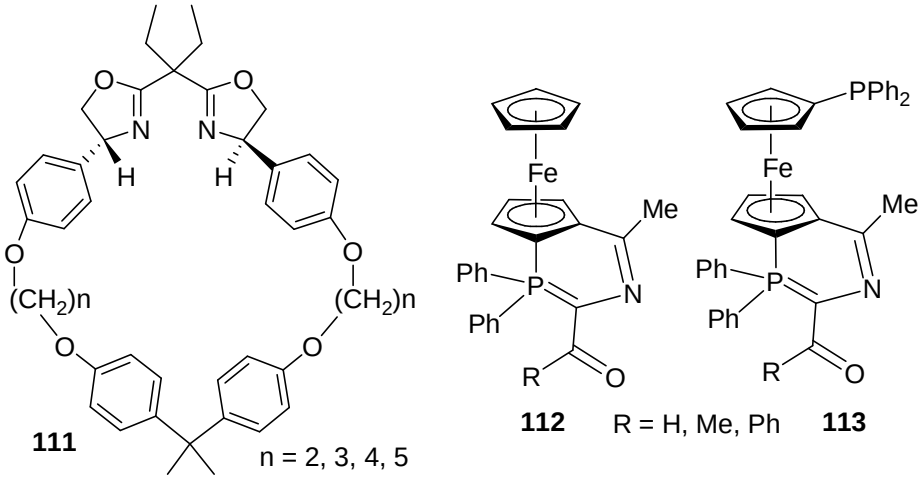
The success of Aratani's catalyst has brought more attention to the field of carbene chemistry. Economically, the utilization of relatively cheaper copper complexes instead of expensive rhodium compounds is more practical for wide application in industry if an efficient enantioselective chiral ligand was easily available in few steps. Most of recently developed ligands are derived from natural chiral amines, amino acids and amino alcohols to simplify the process of setting up chirality. Semicorrin ligand reported by Pfltaz's group is such an example.[156,157] The synthesis of this ligand involves only four steps from the commercially available pyroglutamic acid with total 30-40% yields. Good to excellent ee values (85% to 97% ee for *trans* and 68% to 95% ee for *cis*) were obtained when employing semicorrin ligated copper complex **108** in the cyclopropanation of styrene with various diazoacetates. Such high enantioselectivity was attributed to the C_2 symmetric structure in semicorrin ligands. Mechanistic studies of the copper catalyzed cyclopropanation reactions indicate that the strong repulsive interaction between the carbene ester group and the C_2 symmetric ligand determines the enantioselectivity, while the weak interaction between ester group and alkene substituents control the diastereoselectivity.[158]

Another superior C_2 symmetric chiral ligand is the bisoxazoline ligand. Copper complexes like **109** have been synthesized using this ligand by Evans' group.[159,160] Compared to semicorrins, bisoxazolines are easier to prepare and modify, and more effective in stereocontrol. When using a bisoxazoline ligand derived from *tert*-butyl leucinol, up to 99% ee can be achieved for both *cis*- and *trans*-cyclopropanation products. Another type of bisoxazoline ligand developed by Masamune's group is also

effective for the enantioselective cyclopropanation. However the stability of copper complexes **110** is not as good as with Evans' catalysts and, decomposition of **110** was observed upon standing.[161] Today a variety of chiral bisoxazoline ligands are commercially available. In addition to cyclopropanation reactions, many other reactions, such as Diels-Alder reactions, Ene-reactions, Henry reactions, and Aldol reactions are also found to proceed with good enantioselectivity in the presence of bisoxazoline ligated metal complexes.

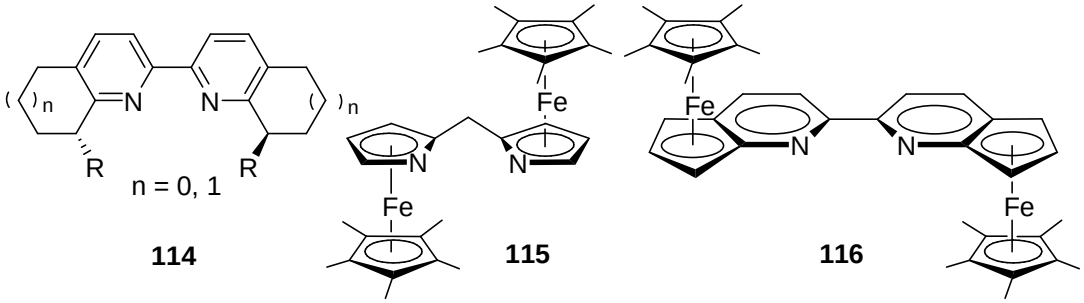


In general, low to medium diastereoselectivies with bisoxazoline ligands are usually observed because of the longer distance between the chiral centers on the ligand and substituents of alkenes. To address this issue, an interesting strategy was employed by Zinic and Sunjic, where the two C_2 symmetric centers were connected through a bridge.[162] The supramolecular copper(I) complex formed from ligand **111** contained a chiral cavity which was big enough to allow the desired transformations to occur inside. Up to 86% de (7:93, *cis*:*trans*) was observed when n=2. Kim and coworkers reported another class of catalysts with high diastereoselectivity. These ferrocene based phosphine ligands (**112** and **113**) exhibited extremely high diastereoselectivity (up to 100% de) in some cases with 2,6-di-*tert*-butyl-4-methylphenyl (BHT) azoacetate as the carbene source. However, rather low enantioselectivity was seen.[163]



111 **112** R = H, Me, Ph **113**

The use of bipyridine ligands with fixed chiral center in olefins cyclopropanation was first reported by Katsuki's group.[164,165] Moderate to good enantiomeric excess (up to 92% ee) were reported in their preliminary study. Chiral bipyridine type ligands such as **114** are structurally similar to semicorrins and bisoxazolines, and easily form complexes with various metal ions. However, these ligands are more complicated to prepare. Inspired by Katsuki's work, many chiral bipyridine ligands have been synthesized and tested in asymmetric cyclopropanation of alkenes over the past fifteen years.[166] In some cases; both enantio- and diastereoselectivity were improved. For example, planar-chiral bipyridine ligand **115** and **116** derived from ferrocene exhibited 86:14 to 96:4 (*trans*:*cis*) diastereoselectivity with 78% to 96% ee on *trans*-products.[167,168]

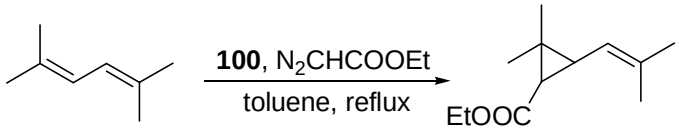


114 **115** **116**

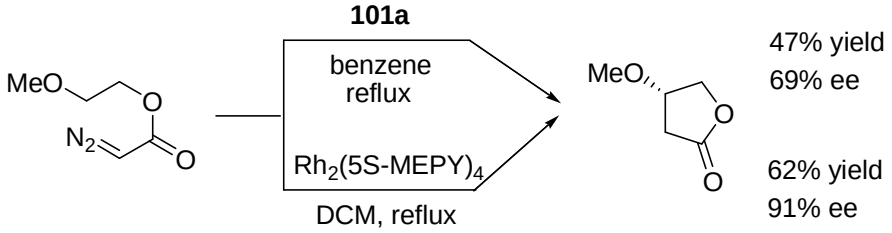
Results and Discussion

PIB-supported Achiral Rhodium(II) Carboxylate

In a previous study, a polyethylene (PE) supported rhodium(II) carboxylate dimer (**100**) was prepared and used in alkene cyclopropanation reactions. Catalyst **100** was successfully reused ten times in the cyclopropanation of 2,5-dimethyl-2,4-butadiene (eq. 47). Analysis of the product phase showed that less than 1% of the charged metal leached into product phase.[147] However, application of a PE-supported rhodium carboxamidate catalyst **101a** in intramolecular C-H insertion reaction was less successful (eq. 48). Compared to its low molecular weight analog Rh_2(*S*-MEPY)$_4$ (eq.49), catalyst **101a** showed lower activity and enantioselectivity due to the high temperature required to achieve solubility for this PE-supported catalyst.[148] Given the superior solubility of PIB in a wide range of nonpolar or weak polar solvents at or below room temperature, we envisioned that utilization of soluble PIB-supported Rh catalysts in the same carbenoid chemistry could overcome the problems observed in the case of this PE-supported Rh catalyst.

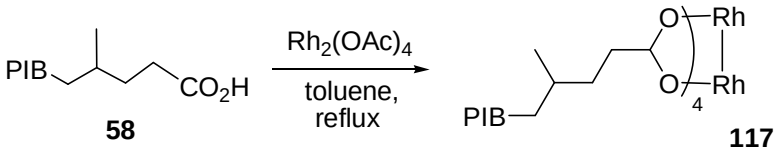


56% yield (average over ten cycles) (47)



(48) (49)

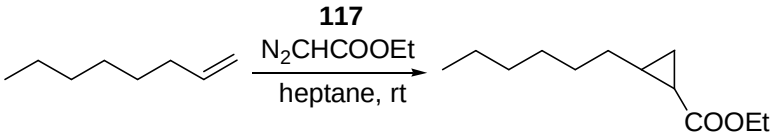
As part of an effort to develop a polyolefin-supported cyclopropanation catalyst that could be fully recovered yet used both at lower temperature and in other solvents, the PIB-supported Rh(II) carboxylate **117** was prepared as a blue-green viscous oil through ligand exchange of PIB-COOH **58** with $Rh_2(OAc)_4$ in refluxing toluene (eq. 50). ICP-MS analysis of a digested sample of this polymer-supported catalyst indicated a metal loading of 0.36 mmol of Rh/g.



Rh loading = 0.36 mmol of Rh/g (50)

Initial evaluation of the catalytic activity and recyclability of catalyst **117** was conducted using the cyclopropanation of octene with ethyl diazoacetate as an example (eq. 51). The reaction was carried out in heptane or cyclohexane in the presence of an excess of the alkene stubstrate at room temperature. A solution of ethyl diazoacetate in the same nonpolar solvent was added to the reaction mixture via a syringe pump over a set period of time. After each cycle, the nonpolar phase was extracted with ethylene

glycol diacetate (EGDA) to separate the cyclopropanation product from the PIB-supported catalyst. While this procedure was effective in isolating product and separating it from catalyst, it was not as 'Green' as the earlier procedure using the PE-supported ligand in that it required some additional solvent for the extraction. After each cycle, a portion of solvent had to be removed from the isolated nonpolar phase containing PIB-supported Rh catalyst before using it in the next cycle to avoid accumulation of the solvent and dilution of the catalyst phase. The reaction yield and diastereoselectivity for each cycle were determined by analyzing the separated EGDA phase with GC. These data are summarized in Table 3.



(51)

Table 3. Cyclopropanation of octene with Rh catalyst **117**

cycle	cyclohexahe/EGDA[a]		heptane/EGDA[b]	
	yield (%)[c]	*trans*/*cis*	yield (%)[c]	*trans*/*cis*
1	14	57/43	12	57/43
2	27		25	
3	17		31	
4	25		36	
5	30		42	
6	32		43	
7	20		41	
8			34	
8[d]			79	

[a] Use of 0.5 mmol ethyl diazoacetate. [b] Use of 1 mmol ethyl diazoacetate.
[c] Determined by GC. [d] Yield in heptane phase.

These data show that the PIB-supported Rh catalyst **117** was effective in the cyclopropanation of octene with ethyl diazoacetate in cyclohexane or heptane. The polymer-supported catalyst was readily separated and recovered by a post reaction extraction with EGDA. The desired *trans*- and *cis*-cyclopropanation products were obtained with a ratio of 53/47 (*trans*/*cis*) in either cyclohexane or heptane. Slightly higher yields were observed when using heptane as the reaction media. An average yield of 43% per cycle over eight cycles (including the product left in heptane phase) was obtained.

To evaluate the influence of solvent on the cyclopropanation reaction, the PIB-supported Rh catalyzed cyclopropanation of octene was carried out in DCM and heptane

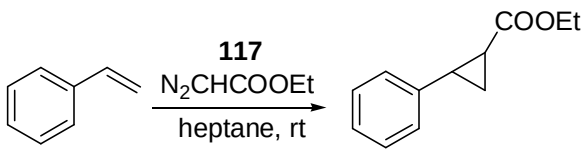
respectively. Higher yields were obtained in heptane (66%) than were observed in DCM (54%). When the reaction was carried out in heptane under the same reaction conditions without separation of the cyclopropanation product with EGDA, an overall 69% yield per cycle was obtained after four cycles. These results show that the nonpolar solvent heptane is a suitable solvent for these Rh-catalyzed olefin cyclopropanation reactions. Indeed, heptane was a better solvent than the other more polar solvents. Product yields were also lower in the mixed heptane/EGDA solvent systems formed when EGDA was used to extract the product. These lower yields observed might be attributable to the coordination of EGDA left in the nonpolar phase after the extraction in each cycle to the vacant sites on rhodium centers.

On the other hand, the presence of EGDA in the heptane phase affects the polarity of the reaction media as well. Such changes in solvent polarity might result in changes in the conformation of the PIB chain that phase anchors the catalyst in the solution. The conformation of a polymer in a solution can be significantly affected by the polarity of solvents. For example, linear polymers usually prefer a stretched out conformation when dissolved in good solvents, but adopt a contracted conformation, more like a random string ball, in poor solvents. If a similar contracted polymer chain formed for the PIB-supported catalysts, it could affect the reactivity of the catalytic centers on polymer. If that were the case, we expect that use of more active and less hindered substrates would overcome the negative effect caused by EGDA.

Another important prerequisite for recycling catalysts via a liquid/liquid biphasic system is that the polymer-supported catalysts and reaction products have to partition

into different phases. However, the octene cyclopropanation product does not show a notable polar phase selective solubility. Thus, separation of nonpolar PIB-supported Rh catalyst from the cyclopropanation product via a liquid/liquid separation was less successful in this case.

A more successful demonstration of catalyst separation/recovery/reuse with the heptane/EGDA biphasic separation system was possible using styrene as substrate (eq. 52). The stabilization effect of the phenyl ring makes styrene a very good alkene nucleophile in carbenoid-mediated electrophilic addition. Additionally, the existence of the aromatic ring in styrene enables its cyclopropanation product to possess enough polarity to selectively partition into the polar phase in a liquid/liquid extraction. Using this separation technique, the PIB-supported Rh catalyst **117** was reused through nine cycles in the cyclopropanation of styrene. The recovered heptane phase containing the polymer-supported catalyst after that cycle of catalysis still had a green color which was only a little lighter than was seen at the beginning of this series of reactions. It was also noted that the yields of product in the first two cycles (44% and 66% respectively) were apparently lower than yields for other cycles. This is because the styrene cyclopropanation product has to partition between the heptane and EGDA phases. In the earliest cycles, some of this product partitions into the heptane phase. Eventually, after ca. two cycles, the heptane phase containing the catalyst is effectively saturated with this product and an overall 75% yield is achieved in the subsequent seven cycles (Table 4).



(52)

Table 4. Cyclopropanation of styrene with Rh catalyst **117**

cycle	heptane/EGDA[a]			heptane/acetonitrile[b]		
	yield (%)[a,d]	*trans*/*cis*	metal[c] leaching	yield (%)[b,d]	*trans*/*cis*	metal[c] leaching
1	44		1.7%	53		
2	66			75		
3	79			76		
4	74			81		2.3
5	82	59/41	1.8%	70	59/41	
6	76			78		2.5
7	66			77		
8	76			82		2.4
9	75			74		2.1

[a] Use of 0.5 mmol of diazo acetate, 5 equiv. of styrene, 4 h. [b] Use of 1 mmol of diazo acetate, 9 equiv. of styrene, 5 h. [c] Determined by ICP-MS. [d] Determined by GC.

Although the recovery and recycling of the PIB-supported catalyst was successful, an inconvenience in this particular liquid-liquid biphasic system is that the high boiling point (188 ºC) of EGDA makes the isolation of styrene cyclopropanation product from the EGDA phase difficult. For this reason, such a liquid/liquid biphasic system is best considered to be a model for the study of the recyclability of PIB-supported Rh catalysts in the cyclopropanation reactions. It would, in my opinion, be less practical in a real application because product recovery and catalyst recovery have to both be practical in a application of this separation technique in industry.

In order to make the catalyst recycling system of value for practical use, a polar solvent with a lower boiling point should be used so as to facilitate isolation of the

product. To study this issue, I tested a variety of polar solvents in the liquid/liquid extraction step. Acetonitrile was found to be the most suitable solvent for separation of the polar cyclopropanation product from the nonpolar PIB-supported Rh catalyst. It has a much lower boiling point (82 ºC) than EGDA. It is also easily phase separable from a heptane rich solution at room temperature based on density. Using acetonitrile, the PIB-supported Rh catalyst **117** still could be recycled up to nine times (average 65% yield per cycle) without any obvious decrease in activity (Table 4). In a separated catalyst recycling experiment designed to obtain pure product, an overall 65% isolated yield of styrene cyclopropane product was obtained via the liquid/liquid extraction with acetonitrile over six cycles.

One important feature of utilization of liquid/liquid biphasic separation technique in these catalyses is the ability to separate a catalyst as a solution in the separation stage and to reuse the catalyst-containing phase with fresh substrate. That is evidenced in the above studies of **117** with EGDA or acetonitrile. However, a second issue is the leaching of the catalyst. In my work, I carried out extensive studies of metal leaching using ICP-MS to analyze the polar phases in both of these experiments. These analyses of the polar phase for rhodium revealed that about 1.8% and 2.3% of the charged metal leached into EGDA and acetonitrile phases, respectively, in each cycle. The higher metal leaching in the case of acetonitrile presumably reflect the better coordination ability of acetonitrile to the metal ion. This property of acetonitrile was visually evident in these experiments as the color of the solution of **117** in heptane changed from dark green to pink immediately upon addition of acetonitrile. Although the coordination of

actonitrile to rhodium ions could have led to an inactive or poisoned catalyst, the nitrile-Rh bonding interactions are very weak. Simply evaporating the acetonitirile with a nitrogen stream led to a reversal of the color change of the solution with the original dark green reforming. The regenerated PIB-Rh catalyst was as active as before and no obvious negative influences on the catalysis were observed in the presence of trace amount of acetonitrile in the recovered heptane phase.

Another specific aim in my research was to find new biphasic systems that may have potential applications for recycling polymer-supported catalysts. As I mentioned above, EGDA may not be a good solvent for isolating a high-boiling-point polar product dissolved in it. However, use of EGDA as a polar phase to immobilize a polar polymer-supported catalyst for preparation a nonpolar product would be possible. In this case, the separation of products can be effected by liquid/liquid extraction with low-boiling-point hydrocarbons. In addition, the heptane/EGDA solvent mixture has the feature that it also exhibited thermomorphic character. A 1/1 (v/v) mixture of these solvents is immiscible at room temperature but completely miscible at 65 ºC. This also suggests that the phase selective soluble polymer-supported catalyst used in the mixture of heptane and EGDA can be recovered and recycled in a thermomorphic conditions as well. Another solvent mixture containing pentadecane and dimethyl carbonate also demonstrated a temperature-dependent miscibility between room temperature and 45 ºC. Phase selective study using methyl red labeled poly(N,N-dialkylacrylamide) in these two novel thermomorphic system has already been investigated by other people in our group.[169]

Isolation of reaction products in dimethyl carbonate is much easier than that in EGDA due to its relatively lower boiling point (80 ºC). However, application of this solvent in a cyclopropanation of styrene using ethyl diazoacetate was not successful and only trace amounts of the cyclopropanation products were formed based on GC analysis of the dimethyl carbonate phase. The reasons for this lack of reaction were not studied further since the acetonitrile/heptane solvent system described above already worked well with this PIB-supported Rh catalyst **117**.

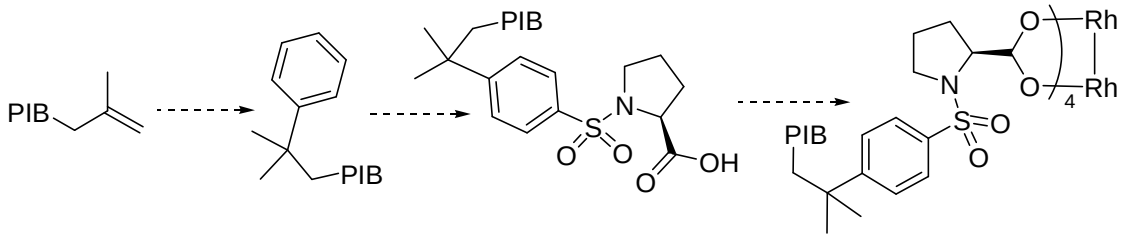
PIB-supported Chiral Rhodium(II) Carboxylates

Asymmetric catalytic methods have become a powerful tool for inducing stereo-control in organic synthesis. In light of our success in recycling achiral PIB-supported Rh(II) carboxylate in cyclopropanation of styrene, we attempted to extend the same recycling protocol to chiral Rh(II) carboxylates. Several candidate complexes were considered for recycling. Among the numerous chiral Rh(II) carboxylates, Rh(II) arenesulfonyl prolinates developed by McKervey and coworkers were found to be the simplest to prepare.[117] These sorts of Rh carboxylates demonstrate excellent enantioselectivity in the cyclopropanation of styrene with alkyl 2-diazo-4-phenylbutenoates. Moreover, in most cases, high *trans*-selectivities are also obtained.[118,119] Based on these reported results, I decided to use these catalysts as examples to investigate the potential applicability of PIB supports in asymmetric catalysis.

It is reported that Rh(II) arenesulfonyl prolinate catalysts with a *tert*-butyl or dodecyl group at the *para*-position of the benzene ring gave the best enantio-

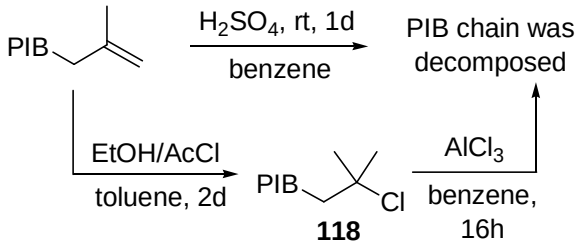
selectivity.[119] This suggests that a catalyst with a longer alkyl group in place of a *tert*-butyl of dodecyl group would also be effective. Since other in our group have used vinyl terminated PIB-oligomers as substrates in electrophilic aromatic substitution, I pursued the possible synthesis of a PIB-*tert*-butyl benzene via an electrophilic aromatic substitution. This chemistry shown in Scheme 16 if successful would make preparation of PIB-supported Rh(II)-*tert*-butyl benzenesulfonyl prolinate straightforward. Thus the synthesis of PIB-*tert*-butyl benzene becomes the initial focus of my work in this area.

Scheme 16. Potential synthesis route to PIB-supported Rh(II) *tert*-butyl benzenesulfonyl prolinate



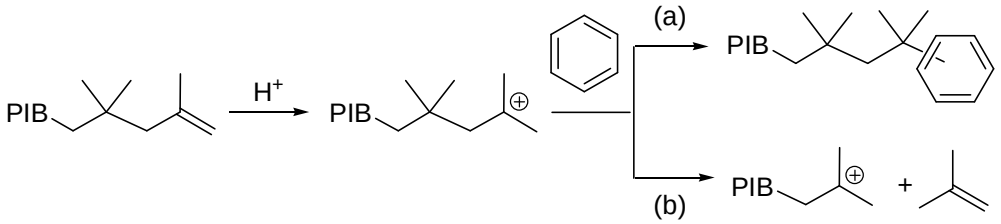
However, the initial synthesis of PIB-supported *tert*-butyl benzene, the key intermediate for the synthesis of the desired catalyst, was not successful (Scheme 17). Alkylation of benzene with PIB-alkene or PIB-*tert*-butyl chloride (**118**) under Friedel-Crafts conditions did not give the desired product. What was seen was that the PIB carbon chain decomposed. In fact, *tert*-butyl benzene was generated as one of the major products.

Scheme 17. Synthesis of PIB-*tert*-butyl benzene



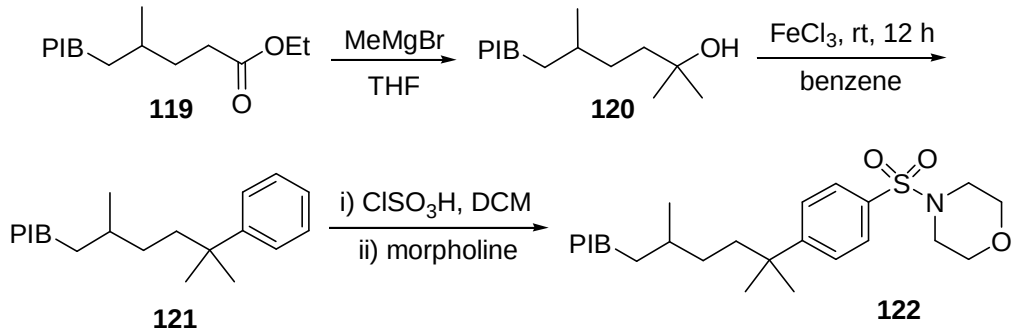
A subsequent literature survey showed that similar results were also reported by Ipatieff and Sanford respectively when using diisobutylene or triisobutylene as alkylating agent.[170,171] Based on the fact that the same alkylation procedure worked very well for activated aromatic substrates such as phenol and anisole, I believe that the relatively low reactivity of benzene is the main reason for the decomposition of PIB chain. Under Friedel-Crafts conditions, the PIB-alkene or PIB-*tert*-butyl chloride is converted to a tertiary carbocation terminated polymer (Scheme 18). This carbocation once formed can either react with the arene or can depolymerize. The pathway of π-complex that proceeds to form a σ-complex would form the desired substituted aromatic product (pathway a); pathway b that involves degradation of the polyisobutyl cation releases isobutylenes that can be protonated under the reaction conditions to competitively form *tert*-butyl benzene. Further complicating the picture is the fact that the alkylation of the arene can be reversible. Thus even if a PIB arene is formed, it can dealkylate under the same reaction conditions as well.

Scheme 18. Possible pathways for PIB chain decomposition



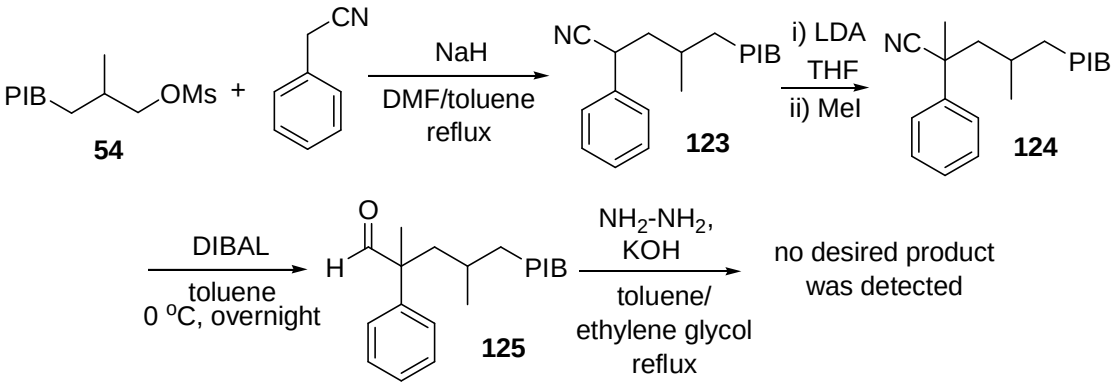
To test this hypothesis, I first prepared a PIB-tertiary alcohol **120** by a double alkylation of PIB-ester **119** with CH_3MgBr. In this case, there is no diisobutylene repeat unit in the end group of alcohol **120**. Thus, if the tertiary carbocation formed from **120** were to lose isobutylene, it would have to form an unstable primary carbocation instead of the tertiary carbocation formed in Scheme 18. Subsequent alkylation of benzene with **120** in the presence of $FeCl_3$ afforded PIB-*tert*-butyl benzene **121** which was identified by ^1H NMR spectrum. The resulting PIB-*tert*-butyl benzene **121** was subsequently chlorosufonated followed by treatment with morpholine to afford the desired PIB-sulfonamide **122** (Scheme 19).

Scheme 19. Alternative route to PIB-*tert*-butyl benzene



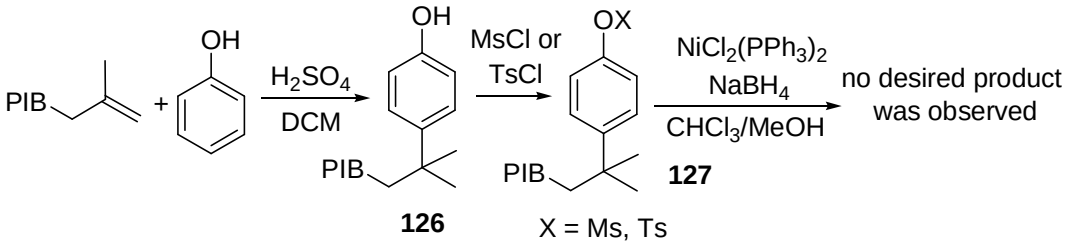
As part of this work, an alternative route to PIB-*tert*-butyl benzene shown in Scheme 20 was also explored. This route involved as an initial step alkylation of benzylnitrile with PIB-OMs (**54**) and MeI form the PIB alkylated methyl benzylnitrile **124**. The nitrile group in **124** was then reduced to aldehyde (**125**) with DIBAL-H at 0 ^{o}C. However, subsequent Wolf-Kishner reduction of aldehyde **125** in a solvent mixture of toluene and ethylene glycol under reflux did not yield the expected PIB-*tert*-bulyl benzene. This might be attributed to the use of a nonpolar solvent and a low reaction temperature in our procedure (180-190 ^{o}C is usually required for Wolf-Kishner reduction to occur in ethylene glycol). Other reducing agents such as BH_3, $NaBH_4$, and $LiAlH_4$ may be an alternative that would make this synthetic scheme viable as a route to the desired PIB-*tert*-butyl benzene.[172] But this possibility was not explored.

Scheme 20. Another possible route to PIB-*tert*-butyl benzene



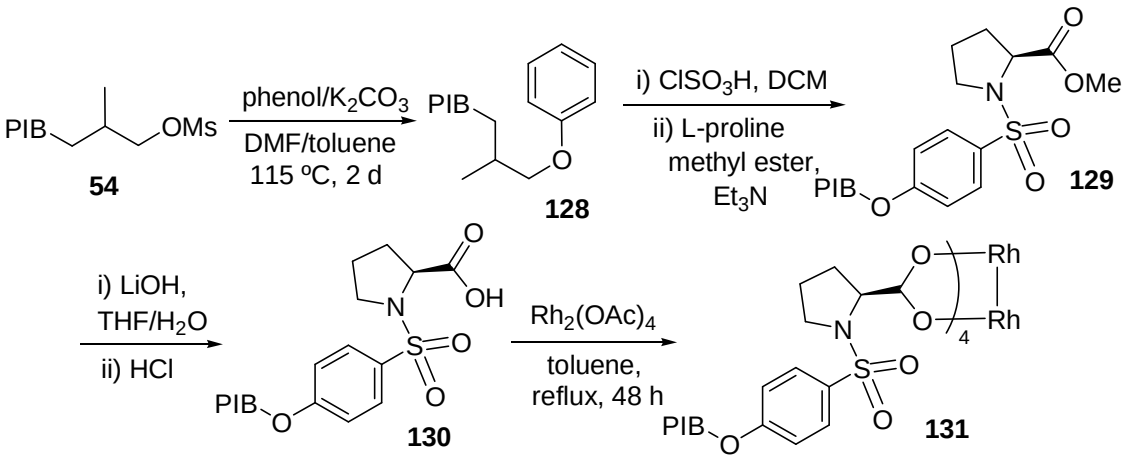
A final proposed synthesis of PIB-*tert*-butyl benzene is shown in Scheme 21. This chemistry is based on our success in preparing PIB derivatives of phenol. Converting the hydroxyl group in PIB-phenol (**126**) to a leaving group followed by a transition metal (Pd or Ni complexes) catalyzed reductive cleavage of the carbon-oxygen bond is a third possible route to PIB-*tert*-butyl benzene. We briefly explored this route but did not get success (Scheme 21). This might be ascribed to the use of less reactive mesylate and tosylate (**127a** and **b**). Using a better leaving group such as a triflate group in conjunction with soluble transition metal complexes the synthesis scheme shown below may be successful.[173]

Scheme 21. Possible route to PIB-*tert*-butyl benzene through deoxygenation of PIB-phenol



An alternative scheme used the PIB-phenyl ether **128** as an analog of PIB-*tert*-butyl benzene (Scheme 22). Chlorosulfonation on the *para*-position of the benzene ring of this activated PIB-supported arene followed by reaction of the intermediate, PIB-arene sulfonyl chloride, with L-proline methyl ester led to the PIB-supported benzenesulfonyl methyl prolinate **129**. The resulting ester was then hydrolyzed to carboxylic acid **130**. Subsequent ligand exchange with $Rh_2(OAc)_4$ afforded the PIB-supported Rh(II) prolinate **131** as a blue-green viscous oil.

Scheme 22. Synthesis of PIB-supported chiral Rh(II) arenesulfonyl prolinate (**131**)



The polymeric Rh catalyst **131** was then examined for activity and recyclability in the cyclopropanation of styrene with ethyl diazoacetate. Separation of the polymer-supported catalyst from cyclopropanation product was conducted by a post reaction extraction with EGDA. The experimental results for these studies are collected in Table 5.

Table 5. Cyclopropanation of styrene with Rh catalyst **131**

cycle	yield (%)[a]	*trans* ee (%)[c]	*cis* ee (%)[c]	*trans*/*cis*
1	39			
2	73			
3	58	N/A	N/A	53/47
4	60			
5	43			

[a] EGDA was used as the polar phase. [b] Determined by GC. [c] Determined by GC with a chiral column.

The positive result of these studies was that catalyst **131** demonstrated moderate catalytic activity and could be easily reused through five cycles. However, no detectable enantioselectivity for either the *trans*- or *cis*-products was observed. That however, is perhaps not unexpected given results seen for low molecular weight catalysts like **74a**. To address this issue, PIB chain was directly attached onto anisole at *para*-position to increase the steric hindrance on the aromatic ring (Scheme 23). Using the synthetic strategy described in Scheme 22, a more hindered PIB-supported Rh(II) prolinate **135** was thus prepared. While reaction of L-proline methyl ester at the *ortho*-position of PIB-anisole **132** in the presence of triethyl amine only provided trace amount of **133**, the use of a stronger inorganic base K_2CO_3 in combination with running the reaction at an elevated temperature did afford the PIB-supported methyl prolinate **133** in good yield. Experimental results on using of catalyst **135** in cyclopropanation are summarized in Table 6.

Scheme 23. Synthesis of PIB-supported chiral Rh(II) arenesulfonyl prolinate (**135**)

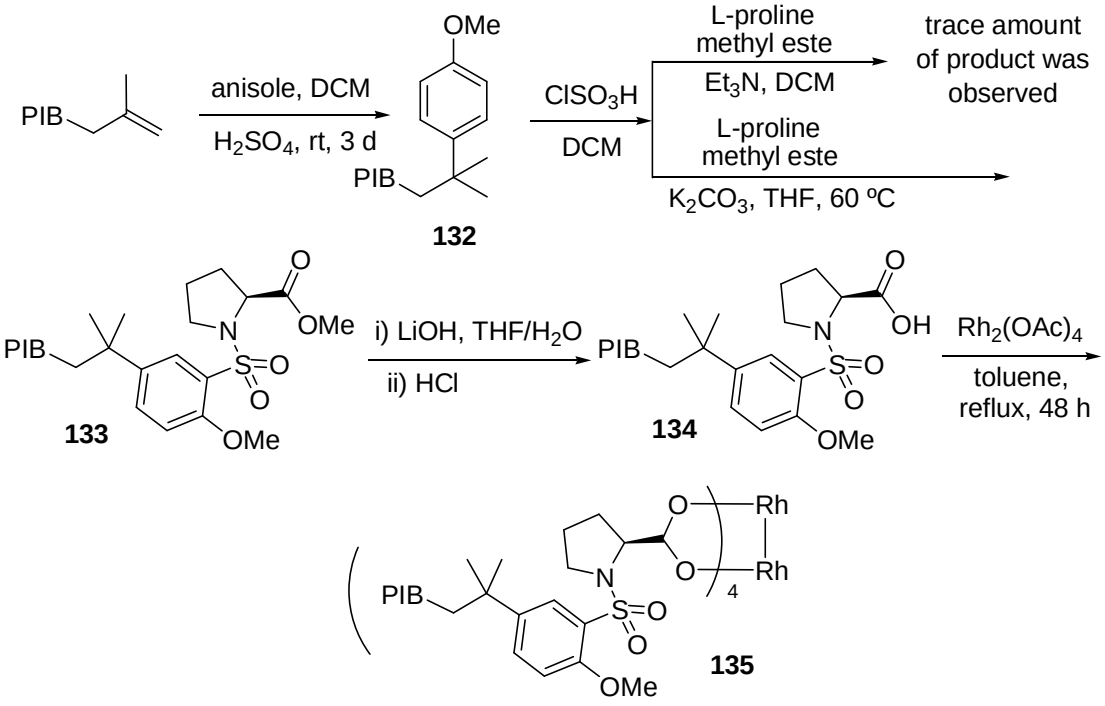


Table 6. Cyclopropanation of styrene with Rh catalyst **135**

cycle	yield (%)[a,b]	*trans* ee (%)[c]	*cis* ee (%)[c]	*trans*/*cis*
1	42	7	13	51/49
2	68			54/46
3	69	10	13	56/44
4	43			60/40

[a] Acetonitrile was used as the polar phase. [b] Determined by GC. [c] Determined by GC with a chiral column.

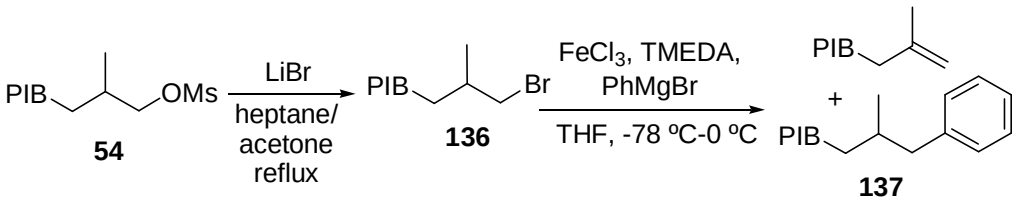
As was true for catalyst **131**, catalyst **135** also showed moderate activity in olefin cyclopropanation. In this case some enantioselectivity, ca. 8% ee and 13% ee were observed for the *trans*- and *cis*-products respectively. Although such enantioselectivity is lower than the 6% ee seen for the *trans*-product and 30% ee seen for the *cis*-product when a similar low molecular weight analog **74c** was used,[118] these results are encouraging.

In addition to the low enantioselectivity seen with PIB-supported Rh catalysts **131** and **135**, their recyclability was not as good as we expected. After four to five cycles, the color of the heptane phase containing the polymeric Rh catalyst was observed to change to light pink from its original blue-green color. Moreover, when using acetonitrile as the polar solvent in the liquid/liquid extraction, the ratio of *trans* to *cis* changed as the cycle number increased. This diastereoselectivity change from 51/49 in the first cycle to 60/40 in the forth cycle and the color change suggested to us that the structure of the Rh complex and/or the oxidation state of rhodium ion might be changing during the recycling process.

We have also noted that the observed lower enantioselectivity in the cyclopropanation of styrene may also be due to the reaction studied. Specifically, the ethyl diazoacetate is not always the best carbene source for the case of Rh(II) benzenesulfonyl prolinate catalysts. Higher enantio- and diastereoselectivity could be obtained by using alkyl 2-diazo-4-phenylbutenoate or alkyl phenyldiazoacetate. The reason for this was discussed in the introduction section.

A final route to a PIB-arene-supported cyclopropanation catalyst received a cursory examination and is shown in Scheme 24. This chemistry involved an iron-catalyzed cross-coupling of PIB-Br **136** and phenyl Grignard reagent and was based on a successful work by others in the group who used this chemistry to make 4-alkystyrenes. My preliminary study showed that this is indeed another way to form PIB-benzene. A possible problem is that the desired PIB-benzene **137** is formed along with about 22% of PIB-alkene as an elimination product based on ^{1}H NMR spectrum. Nonetheless, this PIB-benzene **137** could still be used as a precursor for a PIB-supported version of Rh_2(*S*-DOSP)$_4$ (**74d**), a catalyst that has been reported to be effective at achieving enantiomeric control in olefin cyclopropanation reactions.

Scheme 24. Synthesis of PIB-benzene

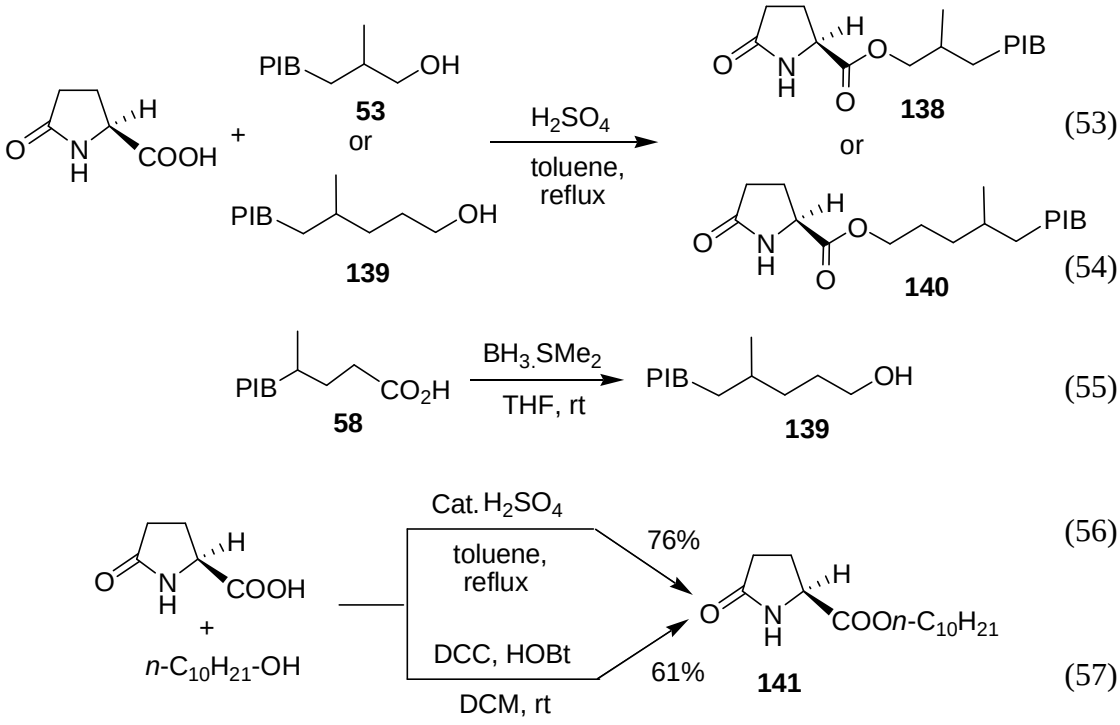


PIB-supported Chiral Rhodium(II) Carboxamidate

Recovery and recycling of chiral Rh(II) carboxamidates developed by Doyle's group is another attractive goal for my research because of these catalysts' excellent performance in asymmetric olefin cyclopropanation, C-H insertion and other carbenoid based reactions. As noted above, polyethylene has been used to support these catalysts. However, its use required elevated temperature, a disadvantage in this process. The use of other soluble polymer supports in rhodium carboxamidates chemistry has not been

reported by far. The discussion below summarizes my preliminary results on using soluble PIB supports in this chemistry.

The PIB-supported *S*-MEPY ligand **138** and **140** were prepared by a Fischer esterification of *S*-pyrrolidone-5-carboxylic acid (eq. 53-54). These alcohols **53** and **139**, differ from one another in a potentially important way. Specifically, **139** which is prepared through reduction of PIB-COOH (eq. 55), has two extra methylene spacers which place the racemic center of the polymeric support further away from the chiral environment around Rh centers in the catalyst. However, it was not clear if the acid catalyst used in the Fischer process would affect the chiral center in *S*-pyrrolidone-5-carboxylic acid. To test this, ester **141**, a low molecular weight analog of PIB-supported *S*-MEPY ligands, was prepared via Fischer esterification and a DCC-HOBt protocol respectively (eq. 56 and 57). The DCC-HOBt coupling method is a very mild procedure for ester formation and under these esterification conditions, the chiral center in pyrrolidone-5-carboxylic acid is retained in the product. The ester **141** prepared from the two different methods showed similar optical activity ($[\alpha]^{21.6}_{D}$ = -0.69°, *c* = 1, EtOH, Fischer condition; $[\alpha]^{20.6}_{D}$ = -0.49°, *c* = 1, EtOH, DCC-HOBt). This result suggests that a catalytic amount of acid did not affect the chirality in the product ester **141** or in the PIB-supported *S*-MEPY ligands **138** and **140**. We believe that transesterification between PIB-alcohols and methyl *S*-pyrrolidone-5-carboxylate using the same acid catalyst would work in the same way.

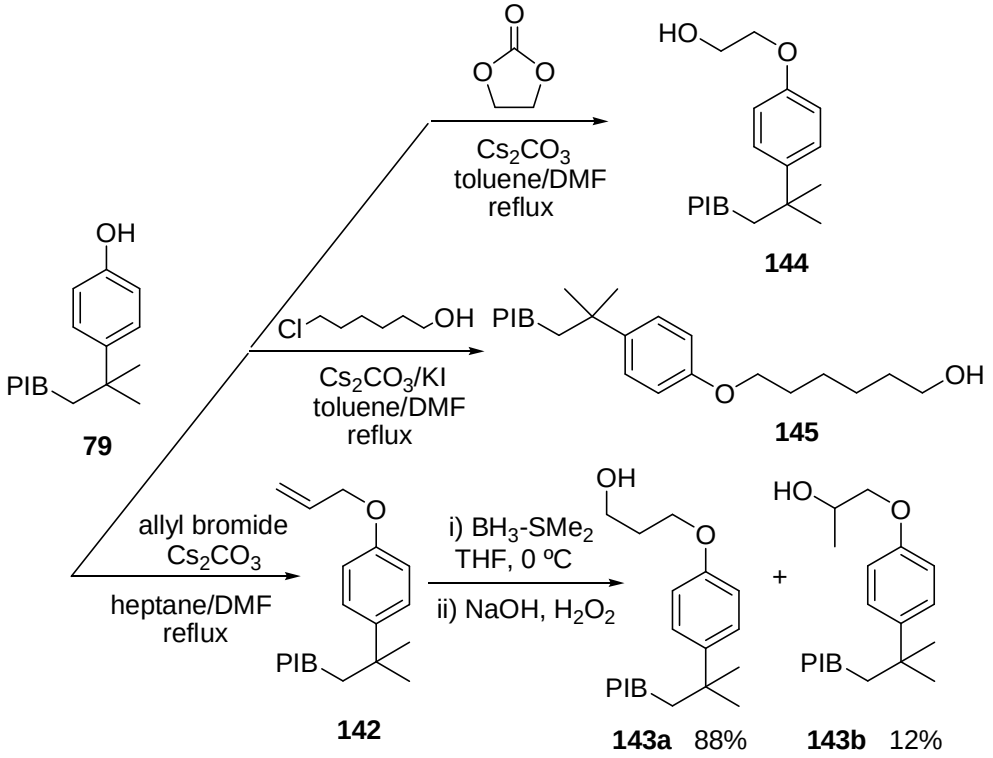


Although alcohol **139** might be better than alcohol **53** for preparation of chiral Rh carboxamidate catalysts, the synthesis of the necessary starting carboxylic acid **58** is tedious. Thus I also looked at alternative ways to make an achiral PIB-alcohol efficiently.

Based on all the PIB intermediates we have, PIB-phenol proved to be the best candidate for synthesis of an achiral alcohol as it has no chiral centers. My first effort to use this PIB derivative to make an alcohol used hydroboration chemistry as shown in Scheme 25. Allylation of PIB-phenol **79** yielded PIB-phenyl allyl ether **142** quantitatively. However, the subsequent hydroboration of PIB-phenyl allyl ether **142** generated regioisomers. In addition to the desired primary alcohol **143a** (88% yield based on ^{1}H-NMR spectrum), 12% of the secondary alcohol **143b** was obtained as a byproduct. A better route to a single primary alcohol derivative from PIB-phenol was

the reaction of PIB-phenol with ethylene carbonate or 6-chloro hexanol which led to the PIB-alcohols **144** and **145** respectively. However, while these routes led to primary alcohols, my attempts at transesterifications of *S*-MEPY with them were relatively unsuccessful. Transesterification of *S*-MEPY with alcohol **144** did not yield an ester product and transesterification using the alcohol **145** gave ester in less than 50% conversion even when the reaction was carried out for two days or longer.

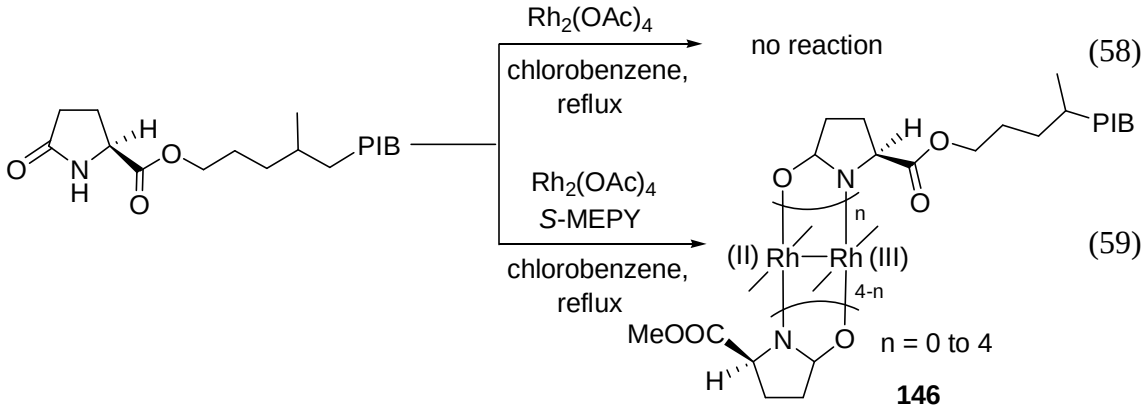
Scheme 25. Alternative routes to synthesize achiral PIB-alcohols



Compared to rhodium(II) carboxylates, rhodium(II) carboxamidates has been less studied due to the difficulties encountered in their synthesis and purification. This situation did not change until a new preparative route was developed by Doyle in 1990. In this new synthesis procedure, the acetic acid byproduct was continuously evaporated

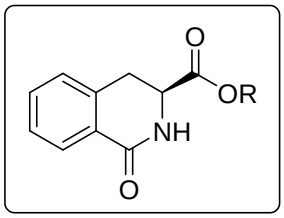
and absorbed by a base trap. That process drove the reaction to completion. It was also reported that rhodium(II) carboxamidates more easily oxidize to Rh(II)-Rh(III) dimer. This process is usually visually obvious based on the color change from deep blue to dark pink,[134] and is a problem because the oxidized rhodium carboxamidates are not effective in olefin cyclopropanation reactions unless the Rh(III) is reduced to Rh(II) again.

In general, polymer-supported rhodium carboxamidates are synthesized through ligand exchange of polymeric ligands with low molecular weight rhodium carboxamidates. To avoid the high cost purification step, we tried to carry out a ligand exchange directly using the PIB-supported ligand **140** and rhodium(II) acetate dimer in refluxing chlorobenzene (eq. 58). This initial attempt was not successful due to the poor solubility of rhodium acetate in chlorobenzene. Addition of small amount of *S*-MEPY ligand to the reaction mixture as a phase transfer agent did initiate the ligand exchange (eq. 59), but the reaction rate was very slow. After three days, there was still a large amount of rhodium acetate left in the bottom of the flask. Increasing the amount of *S*-MEPY accelerated the reaction rate but in turn resulted in the formation of undesired low molecular weight rhodium carboxamidate in the reaction mixture. However, after a simple work-up based on extraction followed by flash chromatography, the desired PIB-supported Rh carboxamidate **146** was obtained as purple viscous oil. The color suggested that the Rh(II)-Rh(III) dimer was formed.



Synthesis of 1-Oxo-1,2,3,4-tetrahydroisoquinoline-3-carboxylates

Most of chiral rhodium carboxamidates currently used are derived from lactams, oxazolidinones, and imidazolidinones with four- or five-membered ring scaffolds. Only one example based on six-membered ring 3-amino-2-piperidinone was reported by Hashimoto and coworkers.[143] As part of my work, I also looked at a new class of chiral lactam ligands, 1-oxo-1,2,3,4-tetra-hydroisoquinoline-3-carboxylate **149a** and **149b**, that could potentially be used to prepare Rh carboxamidatates. Tetrahydroisoquinoline derivatives **149a** and **149b** possess similar functionalities as *S*-MEPY ligand except the ring size. We believe such structural similarity would lead us to a new chiral Rh carboxamidate.



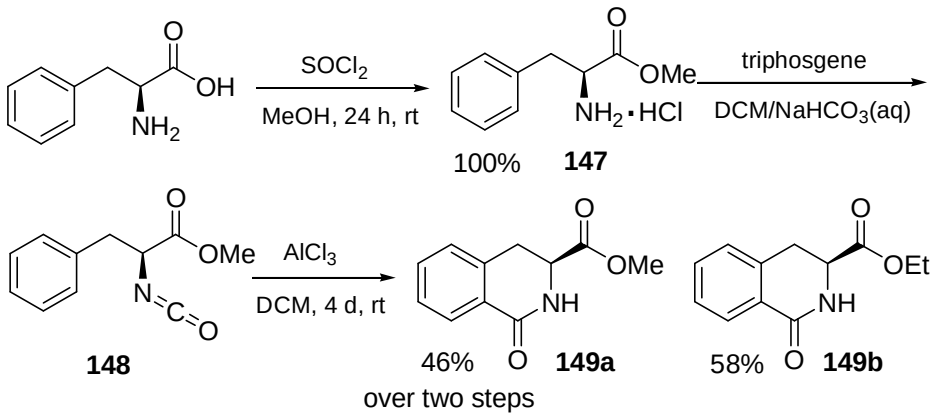
R = Me or Et

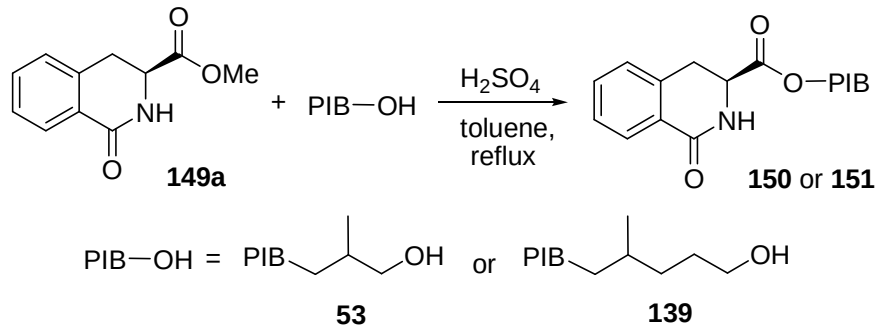
149a and **149b**

1-oxo-1,2,3,4-tetrahydroiso-quinoline-3-carboxylate

The synthesis of tetrahydroisoquinoline derivative **149a** from L-phenylalanine is shown in Scheme 26. Treatment of phenylalanine with $SOCl_2$ in anhydrous methanol at room temperature for 24 hours quantitatively yielded ester **147**. The amino group in **147** was then converted to the isocyanate **148** by reaction with triphosgene. Subsequent $AlCl_3$ promoted ring closure of isocyanate **148** led to the lactam **149a** in 46% yield with optical activity ($[\alpha]^{21}_D$ = 78°, *c* = 0.9, MeOH). Using the same procedure, lactam **149b** was also obtained in 58% yield. Transesterification of **149a** with PIB-alcohol **53** or **139** afforded PIB-supported chiral lactam ligand **150** and **151** respectively (eq. 60). Use of **149b** in transesterification was not successful perhaps due to the slightly higher steric hindrance on the ethyl group.

Scheme 26. Synthesis of 1-oxo-tetrahydroisoquinoline-3-carboxylates **149**





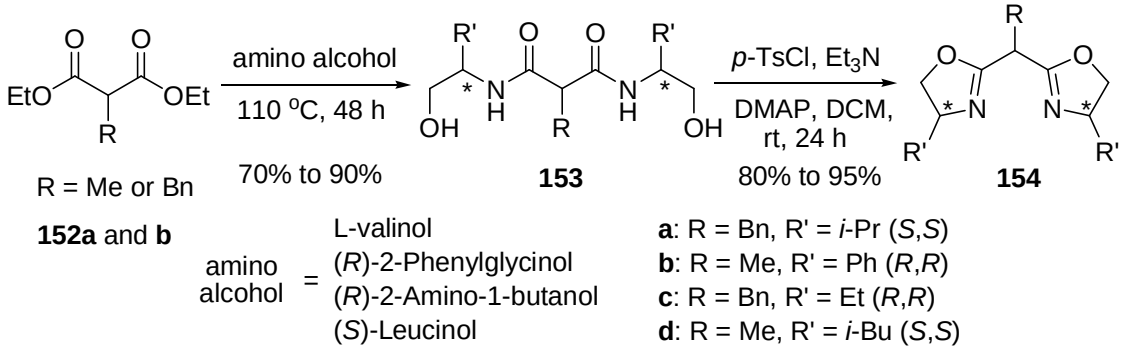
(60)

PIB-supported Chiral Bisoxazoline-ligated Copper Triflates

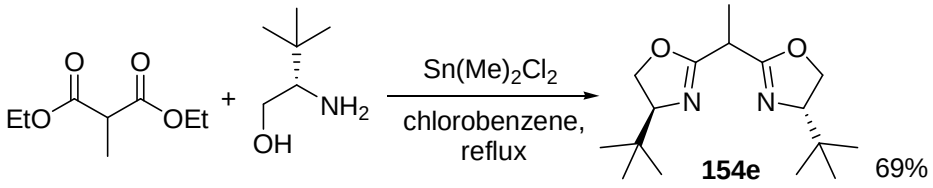
Chiral bisoxazoline ligands are recognized as a broadly useful class of chiral ligands and they have been used in a large number of asymmetric transformations. Usually the catalysis is conducted at room temperature or below, with 1-10 mol % of bisoxazoline-ligated transition metal catalyst. Given the cost of the chiral bisoxazoline ligands, the accepted desirability of recovering transition metal catalysts, and the utility of the PIB-supported catalysts at room temperature and below, I extended my work with PIB-supported Rh catalysts to include the synthesis of chiral bisoxazoline-ligated catalysts.

Bisoxazolines **154a–d** were synthesized as shown in Scheme 27. The dihydroxy malonodiamides **153a–d** were readily prepared from diethyl methyl-, or benzylmalonate **152a** or **152b** and corresponding chiral amino alcohols in good to excellent yields. The cyclization was accomplished by a one pot literature method involving activation of the terminal hydroxyl groups with *p*-toluenesulfonyl chloride, followed by a DMAP promoted ring closure.[160]

Scheme 27. Synthesis of low molecular weight bisoxazoline ligands



Synthesis of bisoxazoline ligand derived from *S*-*tert*-leucinol with the same ring closing procedure discussed above was not successful due to the higher steric hindrance from the adjacent *tert*-butyl group. Another ring closing procedure developed by Masamune's group worked very well in this case.[174] In this procedure, activation of the amide with dimethyltin dichloride followed by dehydration afforded the bisoxazoline **154e** in 69% yield (eq. 61).

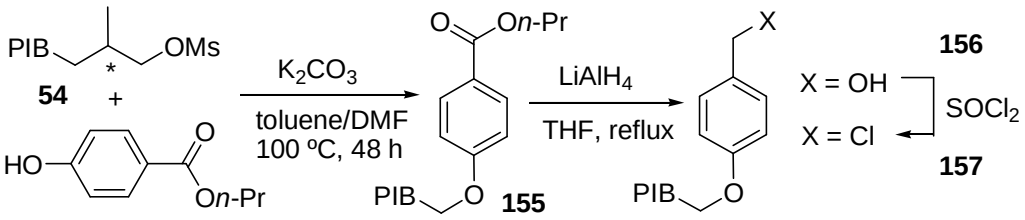


(61)

The PIB-mesylate **54** was prepared as a racemic compound. To eliminate the possible interference from the racemic center of PIB on the catalysis, we added a 4-oxy-benzyl linker between the polymer chain and bisoxazolines. The synthesis of PIB-benzyl chloride **157** is shown in Scheme 28. PIB-mesylate **54** was converted to the PIB-supported *n*-propyl benzoate **155** by a S_N2 substitution. The ester group on **155** was then

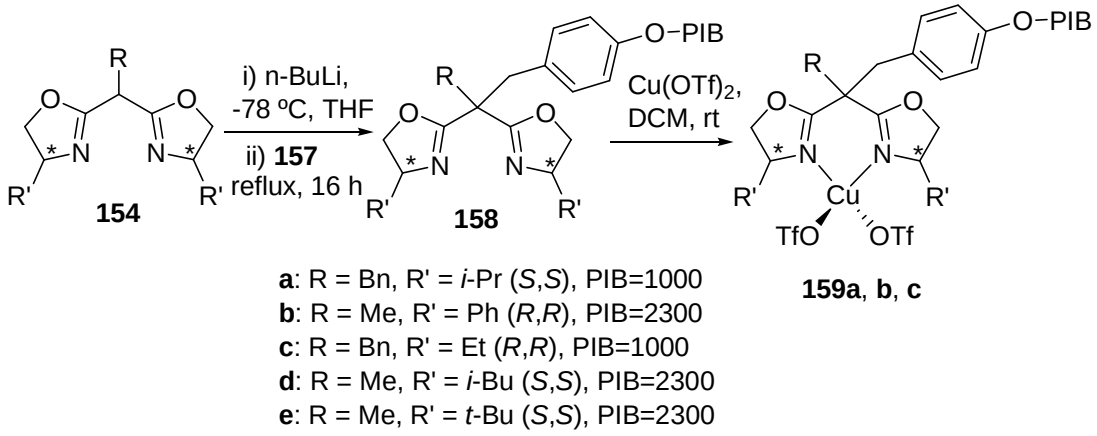
reduced by $LiAlH_4$. The resulting alcohol **156** was treated with $SOCl_2$ to afford the desired PIB-benzylchloride **157**.

Scheme 28. Synthesis of PIB-benzyl chloride



With PIB-benzylchloride **157** and bisoxazoline **154a-e** in hand, PIB supported ligands **158a–e** were prepared by alkylation of corresponding bisoxazolines with **157** (Scheme 29). All of these reactions of PIB had the attractive feature that they could be analyzed by solution state ^1H NMR spectroscopy. These analyses verified that the conversions of **154a-e** to **158a-e** were quantitative. Figure 5 shows a portion of the ^1H NMR spectrum of **158b**, illustrating that solution state resolution is attainable in analyses of these terminally functionalized PIB oligomers.

Scheme 29. Synthesis of PIB-supported bisoxazoine ligated copper(II) triflates



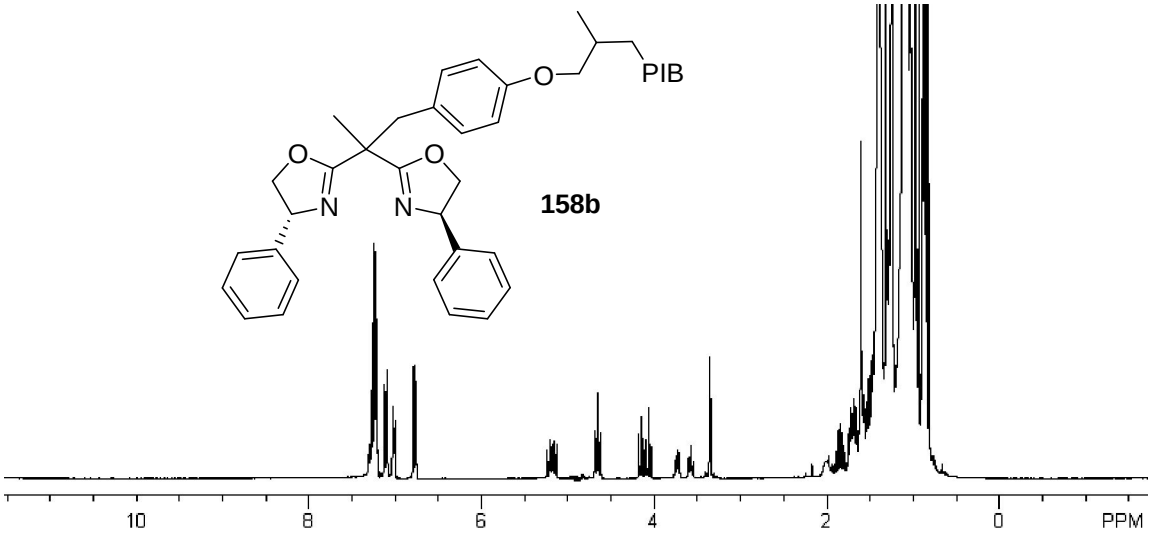


Figure 5. ^{1}H NMR spectrum of PIB-supported bisoxzaoline ligand **158b**.

These syntheses were also facilitated by the heptane solubility of the PIB derivatives which reduced purification to a simple heptane extraction step. Reaction of **158a-c** with $Cu(OTf)_2$ in dichloromethane at room temperature led to the copper

complexes **159a–c** with metal loadings of 0.50, 0.21 and 0.44 mmol of Cu/g, respectively (based on ICP-MS analysis). The resulting copper complexes **159a-c** were studied as asymmetric catalysts for the cyclopropanation of styrene with ethyl diazoacetate. Results of these cyclopropanation reactions are collected in Table 7.

Table 7. Asymmetric cyclopropanation of styrene with PIB-supported bisoxazoline ligated copper triflates

cycle	**159a** (1.9 mol%)				**159b** (1 mol%)				**159c** (1.9 mol%)			
	yield (%)[b]	trans /cis	trans ee (%)[c]	cis ee (%)[c]	yield (%)	trans /cis	trans ee (%)	cis Ee (%)	yield (%)	trans /cis	trans ee (%)	cis ee (%)
1	68	72/28			32	83/17	94	68	42	66/34	71	40
2	63	69/31	37	70	53	81/19	93	72	60	66/34		
3	61	69/31			53	81/19	92	66	68	66/34	65	42
4	56	69/31	36	71	54	81/19	92	67	52	67/33		
5	52	68/32			42	81/19	90	66	53	66/34	67	38
6[a]					56	80/20	92	69	48	67/33		

[a] Ethyl dizaoacetate was added in 10 hours. [b] Determined by GC. [c] Determined by GC with a chiral column.

All three PIB-supported bisoxazoline ligands showed moderate catalytic activity and modest to very good stereoselectivity. Of these catalysts, **159b** demonstrated the highest diastereoselectivity (trans/cis 81/19) and good enantioselectivity for both the *cis*- and *trans*-cyclopropanation products (68% and 92% ee, respectively). Cyclopropanation of styrene with ethyl diazoacetate using catalyst **159a** afforded the *cis*-product in 70% ee while a similar reaction with catalyst **159c** yielded the *trans*-product in 68% ee. These

results are encouraging. They show that a soluble PIB support and its use in heptane-rich solutions is compatible with an asymmetric catalytic reaction at room temperature.

Both catalysts **159b** and **159c** could be reused up to six times without a decrease in the enantio- and diastereoselectivity. The PIB_{2300}-supported copper catalyst **159b** showed slightly lower catalytic activity compared to the PIB_{1000} version. In the case of using **159c**, 33%, 16% and 5% of metal leaching was observed in the EGDA phases for the 1st, 2nd and 5th cycles, respectively, by ICP-MS analysis. We believe this reflects mass transfer of a portion of the PIB-supported copper catalyst **159c** to the polar phase because the polar part of these ligands is relatively large in comparison to the size of the non-polar PIB group. This makes the catalysts less phase selectively soluble. The decrease in leaching through several cycles is presumed to reflect a greater loss of less phase selectively soluble lower molecular weight fractions of the polydisperse PIB-supported catalyst in the initial biphasic separations. The loss of PIB-supported copper species into the polar phase is thus both greater than that seen for PIB-Rh catalyst **117** and decreases as the number of cycles increases.

We also analyzed EGDA phases in another recycling experiment using the higher molecular weight PIB-supported catalyst **159b**. This catalyst too was reusable through multiple cycles. Metal leaching for the 1st, 2nd, 3rd, 4th and 6th cycles was 13%, 7%, 6% 7% and 7% of the charged catalyst, respectively. These leaching rates are larger than we wished. Nonetheless, they show that the recyclability of PIB_{2300} supported Cu(I) catalysts is better than that seen for PIB_{1000} supported catalysts, a result which we ascribe to the larger nonpolar PIB chain in **159b**.

To confirm that the observed leaching reflected the inherent phase selective solubility of these oligomeric PIB-supported bisoxazoline catalysts in liquid/liquid biphasic separations, separate experiments examining the phase selective solubility of **159b** in a heptane/EGDA biphasic extraction were conducted in the absence of a catalytic reaction. EGDA was added to a heptane solution of **159b** and the concentration of **159b** in both the heptane and EGDA phases was analyzed by UV–visible spectroscopy using the absorbance of **159b** at 720 nm. Assuming that the extinction coefficient of **159b** in the heptane and EGDA phases is the same, we estimate the phase selective solubility of **159b** in the first two cycles in this experiment where the condition that no reaction occurs is ca. 14% and 7%, respectively. These UV–visible spectroscopy results match our ICP-MS results. They support the hypothesis that the lower phase selectivity of the PIB-supported catalyst is the origin of the catalyst leaching problem. If metal loss from the bisoxazoline had occurred, the ICP-MS results that analyze for metal would have differed more from these UV-visible spectroscopy results which directly assay for the presence of the metal ligand complex. This suggests that a higher molecular weight PIB will afford a more recyclable catalyst.

Conclusions

In summary, both PIB-supported achiral rhodium carboxylates and chiral rhodium prolinates have been synthesized and used in olefin cyclopropanation reactions. Catalyst reusability was demonstrated in both heptane/EGDA and heptane/acetonitrile solvent systems. Oligomeric PIB-carboxylate ligands were used to prepare achiral rhodium(II) cyclopropanation catalysts that work at room temperature and that can be

recycled and reused in both heptane/EGDA and heptane/acetonitrile solvent systems with liquid/liquid catalyst recovery and separation. Up to nine cycles with ca. 2% metal leaching were seen in a typical cyclopropanation. PIB-supported chiral arenesulfonyl Rh prolinates prepared from PIB-phenyl ether and PIB-anisole respectively, also demonstrated moderate activity and enantioselectivity in cyclopropanation reactions, but gradual deactivation of the catalysts was seen over cycles.

As an extension of rhodium catalyzed alkene cyclopropanation chemistry, PIB-supported *S*-MEPY ligands were synthesized and used in the preparation of PIB-supported Rh carboxamidate catalysts. However, formation of oxidized rhodium species, Rh(II)-Rh(III), were observed during the catalyst preparation. A new class of chiral lactam ligands derived from L-phenylalanine was synthesized as potential chiral ligands for preparation of Rh carboxamidates. Attachment of such chiral lactam onto PIB supports was accomplished by acid catalyzed transesterification.

The most stereoselective catalysts were prepared using bisoxazoline ligands. PIB-supported bisoxazoline-Cu(I) complexes were prepared and were shown to have moderate to good activity and enantioselectivity at room temperature. Catalyst **158b** was the most effective of these catalysts affording the *cis*- and *trans*-cyclopropanation product in 68% ee and 92% ee respectively and in an average 48% yield over six cycles. However, while these bisoxazoline ligands on PIB allowed us to prepare more stereoselective catalysts, leaching for PIB-supported copper catalysts is more problematic due to the higher mass percent loading of the polar groups in these oligomeric catalysts with regard to the PIB polymer. Recyclability can be improved by

increasing the length of PIB chain but metal leaching is still a problem with PIB groups having a degree of polymerization of 40–50, that suggests to us that PIB with higher degrees of polymerization should be examined in this specific case.

CHAPTER IV

EXPERIMENTAL

Materials: polysiobutylene (PIB) oligomers were obtained from BASF Co. with molecular weight 1000 and 2300 (n = 17 and 40). All other reagents were purchased from commercial sources and used without further purification unless otherwise specified. ^{1}H NMR spectra were recorded on Varian Mercury 300 or Inova 300 spectrometers at 300 MHz and reported in ppm referenced to $CDCl_3$ or *d*-DMSO. ^{13}C NMR spectra were obtained on Mercury 300 or Inova 300 spectrometer at 75 MHz and reported in ppm referenced to $CDCl_3$. 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), and m (multiplet). The PIB derivatives generally contained peaks in the d 0.8-1.6 range that are assigned to the protons of the oligomer chain. Crude products also often contained alkane solvents that appeared in this region, but even crude PIB products can be readily characterized by examining the end groups whose functional groups' protons inevitably appeared downfield of the alkane region. IR spectra were obtained on a Bruker Tensor 27 FT-IR. The phase selective solubility studies on PIB-supported metal complexes were performed on a Cary 100 UV/vis spectrophotometer. Yields in catalytic reactions were analyzed by gas chromatography used a Shimadzu GC-2010 instrument with a nonpolar ZB-5MS column (length: 30 m; inner diameter: 0.25 mm; film thickness: 0.50 μm). Eanatiomeric excess of chiral cyclopropanation products were determined by GC using a chiral cyclodextrin 2,3-di-*O*-

methyl-6-*O*-propyldimethylsilyl-β-CD column (length: 30 m; inner diameter: 0.25 mm; film thickness: 0.25 μm). Metal analysis was conducted on a Perkin Elmer DRC II ICP-MS instrument. All reactions were carried out under an inert atmosphere unless otherwise noted.

PIB-CH_2OH (**53**).

The starting vinyl-terminated PIB (7.4 g, 7.4 mmol) was dissolved in 30 mL of hexane and then was allowed to react with 2M BH_3-SMe_2 in THF (2 mL, 4 mmol) at room temperature. After 24 h, the reaction mixture was cooled to 0 °C and 10 mL of ethanol, 3 mL of 4 N NaOH, and 3 mL of 30% H_2O_2 were added slowly and sequentially to the flask. The reaction mixture was then allowed to stir at room temperature for 30 min and to reflux for two hours. After cooling down to room temperature, 50 mL of water was added to the flask. The reaction mixture was extracted with hexane (40 mL x 3), and the combined organic phase was then washed with water (15 mL x 3), brine (30 mL). The organic phase was dried over Na_2SO_4, filtered and solvents were removed under reduced pressure. After drying under vacuum for 24 h, a total yield of 6.6 g (88%) of product (PIB-CH_2OH) was obtained. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.75-1.46 (m, 276H), 3.27-3.32 (dd, *J* = 7.5, 10.2 Hz, 1H), 3.44-3.49 (dd, *J* = 5.4, 10.2 Hz, 1H).

PIB-CH_2OMs (**54**).

PIB-CH_2OH (10 g, 9.8 mmol) was dissolved in 100 mL of DCM and cooled to 0 ºC. Then methanesulfonyl chloride (2.3 mL, 29 mmol) and triethylamine (4.3 mL, 31 mmol) were added dropwise. The reaction mixture was allowed to stir for 6 h after warming to room temperature. The solvent was removed under reduced pressure and the resulting

mixture was taken up with 300 mL of hexane. After removal of the insoluble ammonium salts by filtration, the hexane solution was washed with 90% EtOH (50 mL x 4). The organic phase was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. A total yield of 10.5 g (97.8%) of product was obtained after drying under vacuum for 24 h. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.88-1.46 (m, 211H), 1.95 (m, 2H), 2.96 (s, 3H), 3.85-3.90 (dd, *J* = 7.5, 9.3 Hz, 1H), 4.03-4.08 (dd, *J* = 5.4, 9.3 Hz, 1H).

PIB-OC(CH$_3$)=CHCOCH$_3$ (55).

A reaction mixture containing PIB-OMs (1 g, 0.9 mmol), 2,4-pentadione (0.6 mL, 5.8 mmol), K_2CO_3 (1.2 g, 8.7 mmol), 25 mL of heptane, and 25 mL of DMF was heated to reflux. After 24 h, the reaction mixture was allowed to cool down to room temperature. The isolated heptane phase was washed with 90% EtOH three times and dried over Na_2SO_4. After removal of heptane, 0.81 g (80%) of light yellow viscous oil was obtained. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 368 H), 2.13 (s, 3H), 2.27 (s, 3H), 3.41-3.47 (dd, *J* = 7.5, 9.3 Hz, 1H), 3.54-3.59 (dd, *J* = 5.7, 9.3 Hz, 1H), 5.41 (s, 1H).

PIB-CH$_2$CH(COOEt)$_2$ (56).

Sodium (1.6 g, 68.9 mmol) was allowed to react with EtOH (100 mL) to form a solution of EtONa in EtOH. Then diethyl malonate (11.4 mL, 74 mmol) was added and the resulting solution was stirred at room temperature for 30 min. A solution of PIB-CH_2OMs (7 g, 6.4 mmol) in 50 mL of heptane was also prepared and 35 mL of the ethanolic solution of the sodium diethyl malonate was added to this mesylate solution. After heating at 80 ºC for 12 h, the reaction mixture was cooled to room temperature,

200 mL of hexane was added, and the hexane solution was washed with water (30 mL x 2) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the product was dried under vacuum for 24 h to yield 6.5 g (87.6%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.88-2.0 (m, 226H), 3.35-3.40 (dd, *J* = 6.3, 8.7 Hz, 1H), 4.12-4.21 (m, 4H).

PIB-$CH_2CH(COOH)_2$ (**57**).

A mixture of PIB-$CH_2CH(COOEt)_2$ (6.5 g, 5.6 mmol) and sodium hydroxide (2.6 g, 65 mmol) was dissolved in 50 mL of ethanol and 50 mL of heptane, and the solution was heated to 80 ºC for 40 h. After cooling to room temperature, the solution was neutralized by concentrated HCl. Then 50 mL of water was added, the organic phase was separated and the water phase was extracted by hexane (40 mL x 3). The combined organic phases were washed by DMF (10 mL x 3), 90% EtOH (10 mL x 3), and finally dried over Na_2SO_4. After the solvents were removed under reduced pressure, the product was dried under vacuum for 24 h to give 5.4 g (87.3%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.76-2.0 (m, 370H), 1.98 (m, 2H), 3.47-3.52 (dd, *J* = 6.3, 8.4 Hz, 1H); IR (neat, cm^{-1}) 1722.

PIB-CH_2CH_2COOH (**58**).

The diacid **57** was then decarboxylated by adding the diacid product **57** (5 g, 4.53 mmol) to a mixture of 5 mL of concentrated HCl, 5 mL of H_2O in 50mL of DMF and 50 mL of heptane and heating this mixture at 120 ºC for 40 h. After cooling to room temperature, the heptane-rich phase was isolated. The DMF-rich phase was extracted with hexane (30 mL x 3). The combined heptane and hexane phases were washed by 90% EtOH (20

mL x 2), brine (20 mL) and dried over Na_2SO_4. The solvents were removed under reduced pressure and the product was dried under vacuum for 24 h to give 4 g (83.2%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.76-2.0 (m, 274H), 2.30-2.36 (m, 2H); ^{13}C NMR ($CDCl_3$, δ): 14.1, 22.3, 29.1, 31.5, 32.1, 34.1, 36.2, 38.2, 53.2, 57, 57.9, 58.4, 59.3, 179.5; IR (neat, cm^{-1}) 1711.

PIB-CH_2CH_2COCl (**59**).

A sample of PIB-CH_2CH_2COOH (1.2 g, 1.1 mmol) and 20 mL of toluene (dry) was added to a 100-mL flask. Then thionyl chloride (2 mL, 27 mmol) was added to this solution dropwise at room temperature. The reaction mixture was heated to 115 ºC for 4 h. After cooling, the solvent was removed under reduced pressure and the residue was examined by IR (1802 cm^{-1}) after drying under vacuum for 2 h. The PIB-acid chloride so obtained was typically used in further steps without further analysis.

PIB-$CH_2CH_2COCH(COCH_3)COO$*t*-Bu (**61**).

In a 100-mL, two-necked dry flask equipped with a magnetic stir bar, was placed $MgBr_2.OEt_2$ (1.55 g, 6 mmol) and 30 mL of dichloromethane under nitrogen. The resulting heterogeneous mixture was cooled down to 0 ºC using an ice bath, and then *tert*-butyl acetoacetate (0.7 mL, 4 mmol) was added to the reaction mixture by a syringe with vigorous stirring. Then pyridine (0.7 mL, 8 mmol) was slowly added to the heterogeneous mixture. After the mixture was stirred for 15 min at 0 ºC, a solution of PIB-acid chloride (from PIB-acid 5**8**, 2 g, 2 mmol) in 25 mL of dichloromethane was added dropwise to the flask via a syringe. The resulting mixture was stirred for 15 min at 0 ºC and 24 h at room temperature. The solvent was removed under reduced pressure

and the residue was dissolved in 40 mL of hexanes. The hexane phase was washed with 6 M HCl (10 mL x 2), DMF (10 mL x 4) and 90% EtOH (10 mL x 3). After drying over sodium sulfate, the solvent was removed under reduced pressure to give 2.0 g, (85.5%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.43 (m, 461H), 2.26 (s, 3H), 2.5-2.7 (m, 2H), 17.43 (s, 1H).

PIB-$CH_2CH_2COCH_2COCH_3$ (**62**).

The tricarbonyl compound **61** (1 g, 0.83 mmol) was treated with methanesulfonic acid (2 mL) in 20 mL of DCM at 30-40 °C for 16 h. Then the DCM was removed and the residue was dissolved in 50 mL of hexane. The hexane solution was washed with 90% EtOH (10 ml x 3), water (10 mL x 3), and dried over Na_2SO_4. Removal of hexane led to isolation of 0.75 g (82%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.49 (m, 330H), 2.05 (s, enol CH_3), 2.15 (s, keto CH_3), 2.25 (m, PIB-CH_2-CO- of the enol tautomer), 2.46 (m, PIB-CH_2-CO- of the keto tautomer), 3.56 (s, -$COCH_2CO$- of the keto tautomer), 5.48 (s, =CH- of the enol tautomer), and 15.5 (br s, -OH of the enol tautomer).

PIB-$CH_2CH_2COCH_2COC(CH_3)_3$ (**63**).

To a solution of diisopropylamine (1.3 mL, 9 mmol, freshly distilled) in 10 mL of dry THF was added dropwise 5.3 mL of a 1.6 M solution of *n*-BuLi (8.4 mmol) in hexane at -78 ºC. After 30 min, pinacolone (1.1 mL, 9 mmol) was added dropwise to the solution of LDA in THF above made at -78 ºC (a white solid was precipitated, which is the enolate of pinacolone). After another 30 min, when deprotonation of pinacolone was complete, the reaction mixture was warmed up to room temperature to form a

homogeneous solution. Then 15 mL of a THF solution of PIB-acid chloride (from the acid **57**, 3 g, 2.8 mmol) was added dropwise to this enolate solution using a syringe. The reaction mixture was then cooled to 0 ºC with an ice-water bath and stirred overnight. The reaction mixture was quenched with 6 M HCl, and the solvent was removed under reduced pressure. The residue was dissolved in 60 mL of hexanes and washed with 90% EtOH (15 mL x 2), DMF (15 mL x 3) and 90% EtOH (15 mL x 3). The resulting solution was dried over Na_2SO_4 overnight. The solvents were removed under reduced pressure and the residue was dried in vacuum for 24 h to give 2.8 g (88%) of product **63** as a viscous yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 341H), 2.27 (m, PIB-CH_2-CO- of the enol tautomer), 2.48 (m, PIB-CH_2-CO- of the keto tautomer), 3.62 (s, -$COCH_2CO$- of the keto tautomer), 5.6 (s, =CH- of the enol tautomer), 15.82 (s, -OH of the enol tautomer). The principle species present (ca. 93%) was the enol form of the β-diketone. Diketone **62** was prepared following a procedure analogous to that shown above for **63**.

PIB-$COCH_3$ (**64**).

Polyisobutylene (PIB) (18.3 g, 18.3 mmol) was dissolved in 150 mL of toluene in a 500-mL flask. This reaction mixture was then cooled to -78 ºC and treated with ozone in an ozonolysis apparatus for 30 min. After the residual ozone was removed by degassing with N_2 for 20–30 min, triphenylphosphine (24 g, 91 mmol) was added to the cold reaction mixture. To insure complete reduction of the ozonide, this reaction mixture was allowed to stir at room temperature for 12 h. At this point, the absence of peroxides was verified with a peroxide test. Then most of the toluene was removed under reduced

pressure and the residue was taken up with 150 mL of heptane. Filtration was used to remove the solid (triphenylphosphine and triphenylphosphine oxide). To the resulting heptane phase was added 150 mL of DMF. To facilitate removal of any residual triphenylphosphine, this solvents mixture was heated to reflux in air for 12 h (to oxidize the triphenylphosphine) and finally cooled to room temperature. The heptane phase of the biphasic mixture was separated. If any triphenylphosphine remained in this solution, more DMF was added and the reflux was continued. Otherwise, the heptane phase containing **64** was washed with DMF (20 mL x 2), water (20 mL x 2), brine (20 mL), dried over Na_2SO_4. Finally the solvent was removed under reduced pressure to give 17 g (93%) of product 18. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.84-1.48 (m, 180H), 2.10 (s, 3H), 2.42 (s, 2H); IR (neat, cm^{-1}) 1722.

PIB-$COCH_2COCF_3$ (65).

To a solution of diisopropylamine (4.6 mL, 32.6 mmol) in 35 mL of dry THF was added dropwise 19 mL of 1.6 M solution of *n*-BuLi (30.4 mmol) in hexane at -78 ºC. After 30 min, 10.2 g (10.2 mmol) of PIB methyl ketone **64** in 25 mL of THF was added dropwise at -78 ºC to the solution of LDA in THF above made. After another 30 min, when deprotonation was completed, ethyl trifluoroacetate (2.4 mL, 20.4 mmol) was slowly added to the reaction mixture via a syringe. The reaction mixture was kept at -78 ºC for 2 h and then warmed up to room temperature overnight. The reaction mixture was quenched with 6 M HCl. After the reaction, the solvents were removed at reduced pressure, the residue was dissolved in 100 mL of hexanes and the hexane solution was washed with 90% EtOH (20 mL x 2), DMF (20 mL x 2) and 90% EtOH (20 mL x 3).

The final hexane phase was dried over Na_2SO_4 and the hexane was removed to yield 10.3 g (96.6%) of product 28. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.43 (m, 292H), 2.35 (s, 2H), 5.82 (s, 1H); ^{13}C NMR ($CDCl_3$, δ): 97.95 (s), 117.2 (q, *J* = 284.12 Hz), 177.5 (q, *J* = 36.21 Hz), 195.45 (s); IR (neat, cm^{-1}) 1697, 1599.

PIB-$CH_2COCH_2COC(CH_3)_3$ (**66**).

This compound was prepared from PIB methyl ketone **64** and pivaloyl chloride using the procedure used to prepare diketone **65**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.5 (m, 288H), 2.29 (s, 2H), 3.71 (s, unknown), 5.53 (s, 1H), 15.01 (s, 1H).

PIB-CH_2COOH (**67**) by oxidation of **PIB-CH_2OH 53**.

In a 100-mL flask equipped with a stir bar, PIB-CH_2OH **53** (0.5 g, 0.49 mmol) was dissolved in 15 mL of dichloromethane, and then 15 mL of 3% acetic acid aqueous solution, $KMnO_4$ (0.3 g, 2 mmol) and PEG_{5000} (0.05 g, 0.01 mmol) were added to the flask. The resulting two-phase reaction mixture was vigorously stirred for 24 h at room temperature. The byproduct MnO_2 was removed by filtration, and the organic phase was separated from aqueous phase. After evaporation of dichloromethane, the residue was dissolved in 30 mL of hexanes and washed with 3 M HCl (10 mL x 2), 90% EtOH (10 mL x 5), and water (10 mL x 2). The hexane phase was then dried over Na_2SO_4 and the solvent was removed under reduced pressure to yield 0.5 g of PIB oligomer, which was a mixture of starting material and oxidized product (68.7% conversion) based on ^{1}H NMR spectroscopy. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-2.0 (m, 244H), 2.55 (m, 2H, -CH_2COOH).

PIB-COOH (**68**) from iodoform reaction.

To a solution of **64** (1.35 g, 1.35 mmol) in 40 mL of THF in a 250-mL flask was added 30 mL of 5 M KOH and of tetrabutylammonium bromide (TBAB, 0.3 g, 1 mmol). The resulting mixture was stirred for 1.5 h at room temperature. Then 10 mL of 0.5 M I_2/KI (5 mmol) in water was added to the reaction mixture. After 48 h, the reaction mixture was separated and the organic solvent was removed under reduced pressure. The residue was taken up in 40 mL of hexanes and then filtrated to remove TBAB. The organic phase was first washed with 6 M HCl (10 mL x 2), DMF (15 mL x 3) and 90% EtOH (15 mL x 3). The organic phase was finally dried over Na_2SO_4 and the solvent was removed under reduced pressure to yield 1.28 g (94.1%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.9 (m, 231H), 2.33 (s, 2H); IR (neat, cm^{-1}) 1706.

PIB-supported Ni(II) β-diketonate (**69a**).

PIB-β-diketone **62** (109.3 mg, 0.1 mmol) was dissolved in 15 mL of heptane. EtONa (10 mg, 0.15 mmol) was added to this solution and the resulting mixture was stirred for 20 min at room temperature. Then a solution of $Ni(OAc)_2.4H_2O$ (13.6 mg, 0.05 mmol) in 15 mL of absolute alcohol was added to the flask containing the PIB-diketonate and the reaction mixture was heated to reflux for 20 h. After cooling down to room temperature, about 2 mL of water was added to the reaction mixture to effect the phase separation. The heptane phase was washed with 90% EtOH (5 mL x 3) and dried over Na_2SO_4. Evaporation of the solvent afforded 100.6 mg of product as green oil.

(*Note: The PIB-Ni(II) complex used in catalysis was prepared using a 1 to 1 ratio of PIB-diketone and nickel acetate, so some low molecular weight carboxylate ligand

might be present in the formed PIB-supported Ni species. The nickel loading of **69a** was 1.2 mmol/g based on ICP-MS analysis. IR (neat, cm^{-1}) 1592, 1515.

PIB-supported Co(II) β-diketonate (**69b**).

This polymer-supported catalyst was prepared from $Co(OAc)_2$ using the above procedure except the reaction was conducted at room temperature and with a 1 to 1 ratio of PIB-β-diketone and $Co(OAc)_2$. The desired product was obtained as dark yellow-green viscous oil in 79% yield.

General procedure for Mukaiyama olefin epoxidation.

The Mukaiyama olefin epoxidation reaction was carried out in heptane under 1 atm of molecular oxygen using 1 mol % of a PIB-supported catalyst. For one equivalent of olefin, three equivalents of isobutyraldehyde were employed as coreagent. After the reaction was complete (4 h for Co(II) complex and 8 h for Ni(II) complex), the heptane phase was extracted with acetonitrile three times. The heptane phase was used in the next cycle directly and the combined acetonitrile phase was analyzed by GC.

General procedure for preparation of PIB-supported Rh(II) carboxylates (117 and **135)**.

The PIB-supported Rh(II) carboxylates were prepared according to a procedure previously published. To a toluene solution of PIB carboxylic acid **57** or **134** (4 equivalents) was added a solution of $Rh_2(OAc)_4$ (1 equivalent) in EtOH. The reaction mixture was kept under reflux for 3 h. Then the EtOH was gradually removed by distillation and the resulting toluene solution was allowed to reflux for 2 d. Evaporation of toluene afforded a blue-green viscous oil which was dissolved in hexane for work-up.

Low molecular weight Rh species could be efficiently removed by liquid/liquid extraction of a hexane phase containing PIB-supported Rh species with 90% EtOH.

$(PIB\text{-}COO)_2Rh$ (117).

This compound was prepared from PIB-acid **58** and $Rh_2(OAc)_4$ using the procedure above. This rhodium complex was made twice and metal loading was 0.36 mmol/g (first batch) and 0.35 mmol/g (second batch, after column chromatography, DCM/MeOH = 95/5 to 90/10). IR (neat, cm^{-1}) 1697, 1573.

PIB-*tert*-butyl chloride (118).

To a solution of PIB_{2300}-alkene (1.73 g, 0.75 mmol) in 15 mL of toluene was added acetyl chloride (0.92 mL, 14 mmol), EtOH (0.7 mL, 12.5 mmol) slowly and sequentially. The resulting reaction mixture was allowed to stir at room temperature for 2 d. Then, the toluene was removed under reduced pressure, and the residue was dissolved in 50 mL of hexane. After washing with 90% EtOH twice, the hexane solution was dried over Na_2SO_4. Evaporation of hexane afforded the desired product. ^1H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.5 (m, 396H), 1.67 (s, 6H), 1.97 (s, 2H).

PIB-*tert*-butanol (120).

To a solution of the ethyl ester of PIB-acid **119** (1.1 g, 1 mmol) in 10 mL of THF was added MeMgBr (3M in diethylether, 1.4 mL, 4.2 mmol) at 0 ºC. The reaction mixture was then allowed to warm up to 40 ºC and stirred overnight. The THF was removed and the residue was dissolved in 50 mL of hexane. The hexane solution was washed with 90% EtOH for three times and dried over Na_2SO_4. The conversion was 100% complete

based on ^{1}H NMR spectrum. There were no characteristic signals showing up except those signals from PIB-backbone.

PIB-*tert*-butylbenzene (**121**).

PIB-*tert*-butanol (**120**) (210.8 mg, 0.2 mmol) was dissolved in 3 mL of benzene. To this solution was added anhydrous $FeCl_3$ (110 mg, 0.68 mmol), and the resulting reaction mixture was stirred overnight at room temperature. After removing benzene, the residue was dissolved in 30 mL of hexane and washed with 0.5 M HCl (10 mL x 1), 90% EtOH (10 mL x 3), and dried over Na_2SO_4. Conversion was 100% complete based on ^{1}H NMR spectrum. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 362), 7.18 (m, 1H), 7.24-7.33 (m, 4H).

PIB-*tert*-butylbenzene-sulfonylamide (**122**).

This compound was prepared using the same procedure used to prepare the compound **133** except use of morpholine instead of methyl prolinate. Conversion was 100% complete based on ^{1}H NMR spectrum. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.8 (m, 252H), 2.97 (m, 4H), 3.73 (m, 4H), 7.47 (d, J = 9.3 Hz, 2H), 7.63 (d, J = 9.3 Hz, 2H).

PIB-phenylacetonitrile (**123**).

A reaction mixture containing PIB-OMs **54** (1 g, 0.91 mmol), phenylacetonitrile (158 μL, 1.37 mmol), NaH 60% in mineral oil (51 mg, 1.27 mmol) and 8 mL of toluene and 8 mL of DMF was heated to reflux for 2 d. The toluene was removed under reduced procedure, and 50 mL of hexane was added to the residue. The hexane phase was separated and washed with DMF (10 mL x 1), 90% EtOH (10 mL x 3). The yield was not recorded, but the conversion was almost complete based on ^{1}H NMR spectrum.

Moreover, trace amount of PIB-OMs, PIB-OH byproduct (7 %), and some PIB-alkene were also observed. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-2.0 (m, 375H), 3.68-3.73 (t, *J* = 7.91 Hz, 1H), 3.74-3.81 (dd, *J* = 4.84, 11.84 Hz, 1H), 7.25-7.39 (m, 5H). (Note: Two diastereomers were observed corresponding to *syn*- and *anti*-product respectively.)

PIB-methyl-phenylacetonitrile (**124**).

A LDA solution (0.48 mmol in 3 mL of THF) was prepared according to the procedure above. To this solution was added a solution of PIB-phenylacetonitrile **123** (312.8 mg, 0.28 mmol) in 7 mL of THF at -78 ºC and the reaction mixture was allowed to warm up to room temperature. After 20 min, methyl iodide (0.1 mL, 1.6 mmol) was added to the reaction solution, and the resulting reaction mixture was stirred overnight. The THF was evaporated and the residue was dissolved in hexane and washed with 90% EtOH for three times and dried over Na_2SO_4. After removing the solvent, 270 mg (86%) crude product was obtained. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-2.0 (m, 312H), 7.26-7.31 (m, 1H), 7.33-7.38 (m, 2H), 7.38-7.43 (m, 2H).

PIB-methyl-phenylacetaldehyde (**125**).

To a solution of PIB-methyl-phenylacetonitrile (**124**) (0.62 g, 0.55 mmol) in 5 mL of toluene was added DIBAL-H (1 M in toluene, 0.83 mL, 0.83 mmol) at 0 ºC. The reaction solution was allowed to warm up to room temperature and stirred overnight. The toluene was removed under reduced pressure, and the residue was dissolved in 50 mL of hexane. The hexane phase was washed with 0.5 M HCl (10 mL) and 90% EtOH (10 mL x 3) and dried over Na_2SO_4. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-2.0 (m, 438),

7.24-7.37 (m, 5H), 9.46 (s, 1H), 9.48 (s, 1H). (Note: Two diastereomers were observed corresponding to *syn*- and *anti*-aldehyde respectively.)

PIB-C_6H_4OH (**126**).

To a 500-mL of flask was added polyisobutylene (10 g, 10 mmol) and phenol (19 g, 200 mmol) in 100 mL of dichloromethane. The reaction mixture was cooled to 0 ºC, 6 mL of concentrated H_2SO_4 was added slowly, and the resulting mixture was stirred first at 0 ºC for 1 h and then at room temperature for 60 h. The solvent was removed under reduced pressure and the crude product was dissolved in 200 mL of hexane. This hexane-rich phase was washed with 90% EtOH (30 mL x 2), DMF (30 mL x 2), and then washed with 90% EtOH until no phenol residue left in hexane phase. After drying over Na_2SO_4, the hexane was removed under reduced pressure to yield 9 g (82%) of product after drying for 24 h under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.79-1.49 (m, 180H), 1.81 (s, 2H), 4.99 (br s, 1H), 6.72 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H).

PIB-C_6H_4-OMs (**127a**).

This compound was prepared from PIB-phenol **126** using the procedure used to prepare the PIB-OMs **54**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 210H), 1.85 (s, 2H), 3.17 (s, 3H), 7.21 (d, *J* = 9.76 Hz, 2H), 7.42 (d, *J* = 9.76 Hz, 2H).

PIB-C_6H_4-OTs (**127b**).

This compound was prepared from PIB-phenol **126** using the procedure used to prepare the PIB-OMs **54**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.4 (m, 206H), 1.75 (s, 2H), 2.40 (s, 3H), 6.79 (d, *J* = 8.21 Hz, 2H), 7.20 (d, *J* = 8.05 Hz, 2H), 7.22 (d, *J* = 8.21 Hz, 2H), 7.61 (d, *J* = 8.05 Hz, 2H).

PIB-OPh (**128**)**.**

A reaction mixture containing phenol (660 mg, 7 mmol), PIB-OMs **54** (4.03 g, 3.68 mmol), toluene (30 mL), DMF (25 mL), and K_2CO_3 (5.5 g, 40 mmol) was heated at 100-110 ºC for 2 d. After cooling down to room temperature, toluene was removed under reduced prssure and, 100 mL of hexane and 10 mL of water was added to the residue. The DMF phase was separated and the hexane phase was washed with 90% EtOH (15 mL x 5) and dried over Na_2SO_4. 3.42 g of crude product was obtained after removing solvent. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-2.0 (m, 255H), 3.57-3.64 (t, *J* = 8.4 Hz, 1H), 3.72-3.79 (dd, *J* = 5.4, 9.0 Hz, 1H), 6.83-6.91 (m, 3H), 7.20-7.28 (m, 2H).

(*Note: Phenol was purified using azeotropic method to remove water before use. Trace amounts of PIB-OMs were still left after two days reaction time and PIB-OH was also found as an elimination product. The PIB-OPh was used without further purification.)

PIB–$C_6H_4OCH_3$ (**132**).

A solution of polyisobutylene (10 g, 10 mmol) in 100 mL of anisole was carefully combined with 5 mL of concentrated H_2SO_4 at 0 ºC and this reaction mixture was stirred first at 0 ºC for 1 h and then at room temperature for 60 h. The excess anisole was removed under reduced pressure. The resulting organic product was dissolved in 200 mL of hexane and washed with 90% EtOH (30 mL x 2), DMF (30 mL x 2), 90% EtOH (30 mL x 3), and finally dried over Na_2SO_4. After the solvent was removed and the product was dried under vaccum for 12 h, 10 g (90%) of product **132** was obtained. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.82-1.49 (m, 180H), 1.81 (s, 2H), 3.79 (s, 3H), 6.84 (d, *J* = 9.0 Hz, 2H), 7.29 (d, *J* = 9.0 Hz, 2H).

PIB-anisolesulfonyl-methyl prolinate (**133**).

To a solution of PIB-anisole **132** (1 g, 0.9 mmol) in 10 mL of DCM was added $ClSO_3H$ (0.18 mL, 2.7 mmol). The resulting solution was stirred overnight at room temperature. DCM was removed under reduced pressure and 15 mL of THF and K_2CO_3 (1.11 g, 9 mmol) was added to the flask. Then the reaction mixture was heated to 50 ºC for 1 d. The THF was removed and the residue was redissolved in 60 mL of hexane. The hexane phase was washed with 90% EtOH (10 mL x 3) and dried over Na_2SO_4. After removing hexane, a total yield of 0.88 g (75%) of product was obtained. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.75-1.7 (m, 200H), 1.79 (s, 3H), 2.02 (m, 3H), 3.22-3.29 (m, 1H), 3.50-3.58 (m, 1H), 3.67 (s, 3H), 3.92 (s, 3H), 4.59 (dd, *J* = 4.2, 7.5 Hz, 1H), 6.89 (d, *J* = 9.0 Hz, 2H), 7.46 (dd, *J* = 2.7, 9.0 Hz, 1H), 7.91 (d, *J* = 2.7 Hz, 1H).

PIB-anisolesulfonyl-proline (**134**).

PIB-supported prolinate **133** (0.8 g, 0.62 mmol) and LiOH (26 mg, 0.62 mmol) were dissolved in a solvent mixture containing THF (8 mL) and water (2 mL). The resulting reaction mixture was stirred for 24 h at room temperature. The THF was then removed under reduced pressure, and the residue was redissolved in 50 mL of hexane and washed with 90% EtOH (10 mL x 3) and dried over Na_2SO_4. Evaporation of hexane yielded 0.79 g (98%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.7 (m, 227H), 1.73-1.9 (m, 4H), 2.01-2.16 (m, 1H), 2.21-2.35 (m, 1H), 3.19-3.32 (m, 2H), 3.93 (s, 3H), 4.68 (dd, *J* = 8.4, 3.3 Hz, 1H), 6.95 (d, *J* = 8.7 Hz, 1H), 7.52 (dd, *J* = 2.4, 8.7 Hz, 1H), 7.92 (d, *J* = 2.4 Hz, 1H).

(*Note: the product can be further purified by column chromatography (flush sequence: hexane, DCM, DCM/MeOH = 9/1)

PIB-benzenesulfonyl-methyl prolinate (**129**)**.**

This compound was prepared from PIB phenyl ether **128** using the procedure used to prepare the compound **133** except running the reaction at room temperature and using Et_3N as base. The desired product was obtained in 72% yield. ^1H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.8 (m, 396H), 1.81-2.12 (m, 5H), 3.22-3.31 (m, 1H), 3.40-3.48 (m, 1H), 3.62-3.73 (m, 4H), 3.77-3.84 (dd, *J* = 5.7, 8.7 Hz, 1H), 4.27 (dd, *J* = 8.2, 3.4 Hz, 1H), 6.94 (d, *J*=8.7 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 2H).

PIB-benzenesulfonyl-proline (**130**).

This compound was prepared from PIB-methyl prolinate **129** using the procedure used to prepare the compound **134**. The desired product was obtained in 64% yield after column chromatography (flush sequence: hexane, DCM, DCM/MeOH 90/10). ^1H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 372H), 1.64-1.78 (m, 2H), 1.78-1.94 (m, 2H), 1.97-2.1 (m, 1H), 2.17-2.28 (m, 1H), 3.14-3.23 (q, *J* = 8.4 Hz, 1H), 3.46-3.56 (m, 1H), 3.66-3.71 (t, *J* = 8.3 Hz, 1H), 3.82 (dd, *J* = 5.7, 9.0 Hz, 1H), 4.19 (dd, *J* = 8.1, 3.3 Hz), 6.98 (d, *J* = 9.0 Hz, 2H), 7.78 (d, *J* = 9.0 Hz, 2H).

PIB-supported *p*-benzenesulfonyl Rh(II)-L-prolinate (**131**).

The PIB-supported *p*-benzenesulfonyl-L-proline (**130**) (0.57 g, 0.45 mmol) was dissolved in 30 mL of toluene. To this solution $Rh_2(OAc)_4$ (40 mg, 0.18 mmol) was added as a solution in 20 mL of EtOH. The reaction mixture was heated to reflux for 2 h, and then the EtOH was distilled out. The resulting toluene solution was kept refluxing

for 24 h. Toluene was removed under reduced pressure and the dark green residue was redissolved in 60 mL of hexane and washed with 90% EtOH until the washings were colorless. The hexane solution was dried over Na_2SO_4 and filtrated through cotton. After evaporation of hexane, 0.61 g of product was obtained as blue-green viscous oil with metal loading 0.32 mmol/g based on ICP-MS analysis.

PIB-supported anisolesulfonyl Rh(II)-L-prolinate (**135**).

This compound was prepared from PIB-anisolesulfonyl-proline **134** using the procedure above except running the reaction in refluxing chlorobenzene. The metal loading was 0.34 mmol/g based on ICP-MS analysis.

PIB-CH_2Br (**136**).

PIB-CH_2OH (**53**) (7.1 g, 7 mmol) and Et_3N (2.5 mL, 18 mmol) were dissolved in 80 mL of CH_2Cl_2. The mixture was cooled to 0 °C. To this mixture was added MsCl (1.1 mL, 14 mmol) dropwise. Then the temperature was allowed to warm up to room temperature and the reaction mixture was stirred for 6 h. After evaporation of CH_2Cl_2, 50 mL of heptane, 50 mL of actone, and LiBr (6.46 g, 74 mmol) were added to the flask. The resulting reaction mixture was heated to reflux for 18 h. Then the solvent was removed under reduced pressure. The residue was taken up in 120 mL of hexane. The insoluble salts were removed by filtration. The hexane phase was washed with 90% EtOH (30 mL x 3), water (20 mL x 3), and dried over Na_2SO_4. Evaporation of hexane yielded 6.3 g (84%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.5 (m, 205H), 3.22-3.28 (dd, J = 9.6, 6.9 Hz, 1H), 3.37-3.41 (dd, J = 9.6, 4.8 Hz, 1H).

PIB-CH_2Ph (**137**).

A mixture containing phenylmagnesium bromide (5.6 mmol), *N*,*N*,*N*',*N*'-tetramethyl-ethylenediamine (TMEDA) (0.76 mL, 5.7 mmol), PIB-CH_2Br (0.97 g, 0.9 mmol), and 15 mL of THF was cooled to -78 °C. Anhydrous $FeCl_3$ (10 mg, 0.06 mmol) was added to this cold solution. The resulting reaction mixture was then immersed in an ice-water bath and stirred for 1 h at 0 °C. Then the ice-bath was removed and the reaction mixture was stirred at room temperature for 18 h. THF was then removed under reduced pressure and the residue was dissolved in 50 mL of hexane. The insoluble inorganic salts were removed by filtration. The resulting hexane solution was washed with DMF (10 mL x 2), 90% EtOH (10 mL x 4), and dried over Na_2SO_4. In addition to the desired PIB-benzene **137** PIB-alkene was also formed as an elimination byproduct in 22% yield based on peaks at δ 4.8 and 5.3 in the ^{1}H-NMR spectrum of the product. The reaction product was also contaminated with biphenyl. ^{1}H-NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 374H), 2.26-2.37 (dd, *J* = 12.8, 8.8 Hz, 1H), 2.58-2.64 (dd, *J* = 12.8, 6.4 Hz, 1H), 7.15-7.31 (m, 5H).

Decyl-(*S*)-2-Pyrrolidinone-5-carboxylate (**141**).

(a) *Fischer method.*

A reaction mixture containing decyl alcohol (420 mg, 2.65 mmol), (*S*)-2-pyrrolidone-5-carboxylic acid (330 mg, 2.56 mmol), H_2SO_4 (1 drop), and 30 mL of toluene was heated reflux for 24 h. After evaporation of toluene, the residue was purified by column chromatography (EtOAc/petroleum = 4/3) and afforded 524 mg (76%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.85 (t, *J* = 7.2 Hz, 3H), 1.18-1.34 (br s, 14H), 1.56-1.66

(m, 2H), 2.15-2.28 (m, 1H), 2.30-2.40 (m, 2H), 2.41-2.52 (m, 1H), 4.13 (t, *J* = 6.6 Hz, 2H), 4.22 (dd, *J* = 8.7, 5.1 Hz, 1H), 5.86 (br s, 1H). $[\alpha]^{21.6}_{D}$ -0.69° (*c* 1.00, EtOH).

(b) *Dicyclohexylcarbodiimide (DCC)-1-hydroxybenzotriazole (HOBt) coupling method.*

A reaction mixture containing decyl alcohol (420 mg, 2.65 mmol), (*S*)-2-pyrrolidone-5-carboxylic acid (331 mg, 2.56 mmol), DCC (792 mg, 3.84 mmol), HOBt (519 mg, 3.84 mmol), and 25 mL of DCM was allowed to stir at room temperature for 3 d. The reaction mixture was then filtrated to remove solid. The DCM was evaporated and the residue was dissolved in 50 mL of hexane. The hexane solution was filtrated again to remove insoluble byproducts. The resulting solution was concentrated and purified by column chromatography (EtOAc/petroleum = 4/3) and yielded 432 mg (61%) of product. $[\alpha]^{20.7}_{D}$ -0.49° (*c* 1.00, EtOH).

PIB-$CH_2CH_2CH_2$-OH (**139**) from **PIB-CH_2CH_2COOH 58**.

A solution of PIB-acid **58** (2.1 g, 2 mmol) in 15 mL of THF was cooled to 0 ºC with an ice-water bath. To this solution 1.5 mL (3 mmol) of 2M BH_3-SM_2 in THF was added drowise and the solution was then stirred overnight. The excess of BH_3 was decomposed by addition of 10 mL of wet THF (containing 0.5 mL of H_2O). The resulting solution was dried over Na_2SO_4 and concentrated to afford 1.95 g (95%) of desired product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 265H), 3.61 (t, *J* = 6.9 Hz, 2H).

PIB-C_6H_4O-allyl (142).

A reaction mixture containing PIB-phenol **126** (2.71 g, 2.48 mmol), allyl bromide (1.07 mL, 12.4 mmol), Cs_2CO_3 (1.62 g, 4.96 mmol), DMF (15 mL), and heptane (15 mL) was

heated to reflux for 48 h. After standard liquid/liquid extraction work-up, the desired product **142** was obtained. Yield was not recorded. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.78-1.5 (m, 298H), 1.78 (s, 2H), 4.49 (d, *J* = 5.7 Hz, 2H), 5.25 (d, *J* = 10.0 Hz, 1H), 5.38 (d, *J* = 16.8 Hz, 1H), 6.15 (m, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 7.25 (d, *J* = 8.7 Hz, 2H).

PIB-C_6H_4O-CH_2CH_2OH (144).

This compound was prepared from PIB-phenol **126** and ethylene carbonate using the procedure above except using toluene/DMF mixture as reaction media. Yield was not recorded. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.78-1.6 (m, 219H), 1.83 (s, 2H), 3.97 (m, 2H), 4.12 (t, *J* = 4.5 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H).

PIB-C_6H_4O-$(CH_2)_6OH$ (145).

This compound was prepared from PIB-phenol **126** and 6-chloro-1-hexanol using the procedure above. Yield was not recorded. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.78-1.65 (m, 364H), 1.78 (s, 2H), 3.63 (q, *J* = 4.4 Hz, 2H), 3.93 (t, *J* = 6.4 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H).

1-oxo-1,2,3,4-tetrahydroisoquinoline-3-methyl-carboxylate (149a).

To a solution of the methyl ester of L-phenylalanine (2 g, 9.3 mmol) in 40 mL of DCM was added 40 mL of saturated $NaHCO_3$ solution and triphosgen (0.95 g, 3.2 mmol) at 0 ºC. The resulting biphasic reaction mixture was allowed to stir for 15 min at 0 ºC, and then the DCM phase was separated and the aqueous phase was extracted with DCM (10 mL x 2). The combined organic phase was dried over Na_2SO_4. After removing DCM, the isocyanate intermediate **148** was used in the next step without further purification.

^{1}H NMR (300 MHz, $CDCl_3$, δ): 2.98-3.07 (dd, *J* = 7.5, 14.1 Hz, 1H), 3.12-3.18 (dd, *J* = 4.8, 14.1 Hz, 1H), 3.79 (s, 3H), 4.23-4.28 (dd, *J* = 4.8, 7.5 Hz, 1H), 7.18 (m, 2H), 7.24-7.36 (m, 3H).

The isocyanate intermediate **148** was dissolved in 100 mL of dried DCM and the resulting solution was then cooled down to 0 ºC with an ice-water bath. To this solution $AlCl_3$ (4.35 g, 32.6 mmol) was added in one portion and the reaction mixture was allowed to warm up to room temperature and to stir for 4 d. After cooling the reaction mixture down to 0 ºC, 20 mL of 0.5 M HCl was added to the mixture and the mixture was stirred for 1 h at this temperature. The DCM phase was separated and washed with 0.5 M HCl (20 mL x 1). All the aqueous phase was back extracted with DCM (10 mL x 2). The combined organic phase was dried over Na_2SO_4 and then concentrated and purified by column chromatography (hexane/EtOAc = 3/4). A total yield of 0.9 g (47%) of pure product was obtained as light yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 3.14-3.23 (dd, *J* = 10.2, 15.9 Hz, 1H), 3.26-3.34 (dd, *J* = 5.4, 15.6 Hz, 1H), 3.79 (s, 3H), 4.37-4.42 (m, 1H), 6.34 (br s, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.46 (dt, *J* = 7.5, 1.5 Hz, 1H), 8.62 (dd, *J* = 7.8, 1.5 Hz, 1H). $[\alpha]^{21}_D$ +78° (*c* 0.90, MeOH).

1-oxo-1,2,3,4-tetrahydroisoquinoline-3-ethyl-carboxylate (149b).

This compound was prepared from ethyl ester of L-proline in 58% yield using the procedure above. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.25 (t, *J* = 7.1 Hz, 3H), 3.13-3.21 (dd, *J* = 10.2, 15.9 Hz, 1H), 3.24-3.33 (dd, *J* = 5.4, 15.9 Hz, 1H), 4.18-4.27 (q, *J* = 7.1

Hz, 2H), 4.33-4.4 (m, 1H), 6.57 (br s, 1H), 7.21 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 8.03 (dd, *J* = 7.5, 1.5 Hz, 1H).

PIB-tetrahydroisoquinoline-carboxylate (150).

To a solution of PIB-CH_2OH **53** (3.05 g, 3 mmol) in 50 mL of toluene was added tetrahydroisoquinoline-3-methyl-carboxylate (492 mg, 2.4 mmol) and four drops of H_2SO_4. The resulting solution was heated to reflux for 48 h. After the reaction was complete, the toluene was removed under reduced pressure and the residue was redissolved in 80 mL of hexane and washed with DMF (15 mL), 90% EtOH (15 mL x 4), and dried over Na_2SO_4. The solution was concentrated and purified by column chromatography (flush sequence: hexane, DCM) to yield 1.78 g (63%) of product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.8 (m, 209H), 1.9 (m, 1H), 3.17-3.23 (dd, *J* = 9.9, 15.6 Hz, 1H), 3.26-3.35 (dd, *J* = 5.7, 15.6 Hz, 1H), 3.83-3.92 (m, 1H), 3.98-4.07 (m, 1H), 4.36-4.42 (m, 1H), 6.32 (br s, 1H), 7.23 (d, *J* = 6.6 Hz, 1H), 7.36 (t, *J* = 6.6 Hz, 1H), 7.46 (dt, *J* = 7.2, 1.5 Hz, 1H), 8.07 (dd, *J* = 7.5, 1.5 Hz, 1H).

PIB-tetrahydroisoquinoline-carboxylate (151).

This compound was prepared from PIB-$(CH_2)_3OH$ **139** in 34% yield using the procedure above. (Column chromatography, flush sequence: hexane, DCM, DCM/EtOAc = 7/3; PIB-alcohol contain two much PIB-alkene and other unknown unfunctionalized PIB derivatives). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 231H), 3.12-3.21 (dd, *J* = 9.9, 15.6 Hz, 1H), 3.23-3.32 (dd, *J* = 5.7, 15.6 Hz, 1H), 4.18 (t, *J* = 6.3 Hz, 2H), 4.34-4.4 (m, 1H), 6.37 (br s, 1H), 7.22 (d, *J* = 6.5 Hz, 1H), 7.34 (t, *J* = 6.5 Hz, 1H), 7.43 (dt, *J* = 7.4, 1.5 Hz, 1H), 8.05 (dd, *J* = 7.5, 1.5 Hz, 1H).

PIB-(*S*)-2-Pyrrolidinone-5-carboxylate (138).

This compound was prepared from PIB-alcohol **53** and (*S*)-2-pyrrolidinone-5-carboxylic acid using the procedure used to prepare compound **150**. Conversion was higher than 90% based on ^{1}H NMR spectrum. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 210H), 1.89 (m, 1H), 2.18-2.27 (m, 1H), 2.32-2.4 (m, 2H), 2.41-2.5 (m, 1H), 3.78-3.87 (m, 1H), 3.95-4.04 (m, 1H), 4.21-4.27 (dd, *J* = 8.7, 5.1 Hz, 1H), 6.22 (br s, 1H).

PIB-(*S*)-2-Pyrrolidinone-5-carboxylate (140).

This compound was prepared from PIB-alcohol **139** and (*S*)-2-pyrrolidinone-5-carboxylic acid or its methyl ester in 41% to 45% yield (reaction was not complete) using the procedure used to prepare compound **150**. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 221H), 2.17-2.27 (m, 1H), 2.31-2.39 (m, 2H), 2.41-2.52 (m, 1H), 4.21 (t, *J* = 6.5 Hz, 2H), 4.23 (dd, *J* = 8.6, 5.1 Hz, 1H), 5.83 (br s, 1H).

PIB-supported Rh_2(*S*-MEPY)$_4$ (146).

PIB-(*S*)-2-pyrrolidinone-5-carboxylate **140** (1.33 g, 1.14 mmol) and (*S*)-methyl-2-pyrrolidinone-5-carboxylate (*S*-MEPY) (172 mg, 1.2 mmol) were dissolved in 80 mL of freshly distilled chlorobenzene. To this solution was added $Rh_2(OAc)_4$ (159 mg, 0.36 mmol). The resulting reaction mixture was refluxed under a nitrogen atmosphere in a Soxhlet extraction apparatus. The extractor thimble was charged with oven-dried Na_2CO_3 and sand in a 2:1 ratio. The reaction mixture was refluxed for 6 d. Then the chlorobenzene was removed under reduced pressure, leaving a purple viscous oil. This residue was dissolved in 100 mL of hexane. The resulting dark pink solution was washed with 90% EtOH (20 mL x 5) and dried over Na_2SO_4. The hexane solution was

then concentrated and purified by column chromatography (flush sequence: hexane, DCM/MeOH 95/5 to 90/10) and afforded 1.22 g of dark pink viscous oil.

General procedure for olefin cyclopropanation.

In a typical cyclopropanation reaction, 1 mol % of the PIB-supported catalyst was used and the reaction was carried out in heptane or cyclohexane with a 5- to 10-fold excess of alkene substrate at room temperature. The solution of ethyl diazoacetate in the same nonpolar solvent was added to the reaction mixture via a syringe pump over 5-8 h period. After each cycle, the nonpolar phase was extracted with ethyleneglycol diacetate (EGDA) or acetonitrile to separate the cyclopropanation product from the PIB-supported catalyst. After that, a portion of the nonpolar solvent was evaporated and fresh substrate was added for the next cycle. The yield in each cycle was determined by analyzing the isolated polar phase containing the cyclopropanation product with GC using an internal standard (dodecane or undecane). For copper catalyzed cyclopropanation reactions, the active copper(I) species were generated *in situ* by reducing copper(II) with phenylhydrazine (5% in DCM, v/v), and EGDA was used to extract the cyclopropanation products from the heptane phase. The enantiomeric excess of product was determined using a chiral cyclodextrin-β-CD column.

General procedure for digestion.

The sample that was to be analyzed (10-30 mg) was added to a 20 mL vial along with 4 g of concentrated nitric acid (68%). The mixture was heated to 120-130 ºC until everything dissolved. At this point, 4 g of concentrated sulfuric acid (98%) was added to the solution. The resulting acidic solution was then heated up to 120-130 ºC for 24

hours. After cooling down to room temperature, the concentrated acidic aqueous solution was transferred to a 50 mL plastic bottle and diluted to c.a. 50 mL with 1% nitric acid solution. If the metal content in the sample is too high, it can be diluted again to ensure the ion concentration is within the range of standard curve. Then, the diluted sample solution was analyzed by ICP-MS.

$PhCH_2CH((CO)NH\text{-}CH(i\text{-}Pr)\text{-}CH_2OH)_2$ (153a).

A mixture of diethyl benzylmalonate (4.38 g, 17.5 mmol) and L-valinol (3.8 g, 36.9 mmol) was heated at 100-110 ºC for 48 h. The reaction mixture was solidified on cooling. The yellow solid so formed was then dissolved in 15-20 mL of hot EtOH. To this hot solution was added 180 mL of cold hexane. The resulting mixture was cooled to room temperature and kept in a freezer overnight. Filtration of the mixture yielded 4.65 g (73%) of diamide as white solid. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 0.63 (d, J = 8.7 Hz, 3H), 0.68 (d, J = 8.7 Hz, 3H), 0.8 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.9 Hz, 3H), 1.8 (m, 2H), 2.94-3.08 (m, 2H), 3.23-3.4 (m, 4H), 3.47-3.53 (dd, J = 6.9, 8.1 Hz, 1H), 3.54-3.62 (m, 2H), 4.58 (t, J = 5.1 Hz, 1H), 4.62 (t, J = 5.1 Hz, 1H), 7.16-7.27 (m, 5H), 7.49 (dd, J = 2.1, 9.3 Hz, 2H).

$PhCH_2CH((CO)NH\text{-}CH(Et)\text{-}CH_2OH)_2$ (153c).

This compound was prepared from diethyl benzylmalonate and (*R*)-(-)-2-amino-1-butanol using the procedure above. The desired product was ontained as white solid in 77% yield. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 0.61 (t, J = 7.2 Hz, 3H), 0.76 (t, J = 7.2 Hz, 3H), 1.11-1.29 (m, 2H), 1.39-1.58 (m, 2H), 2.97 (d, J = 7.8 Hz, 2H), 3.05-3.37 (m,

5H), 3.47-3.61 (m, 2H), 4.61-4.90 (m, 2H), 7.10-7.23 (m, 5H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 1H).

$CH_3CH((CO)NH\text{-}CH(Ph)\text{-}CH_2OH)_2$ (153b).

This compound was prepared from diethyl methylmalonate and (*R*)-(-)-2-phenylglycinol using the procedure above. The desired product was ontained as white solid in 90% yield. ^{1}H NMR (300 MHz, DMSO-d_6, δ): 1.18 (d, *J* = 7.2 Hz, 3H), 3.4 (q, *J* = 7.2 Hz, 1H), 3.48-3.61 (m, 4H), 4.77-4.86 (m, 2H), 4.98 (t, *J* = 5.1 Hz, 2H), 7.19-7.35 (m, 10H), 8.34 (dd, *J* = 2.1, 7.5 Hz, 2H).

$CH_3CH((CO)NH\text{-}CH(i\text{-}Bu)\text{-}CH_2OH)_2$ (153d).

This compound was prepared from diethyl methylmalonate and (*S*)-(+)-leucinol using the procedure above. The desired product was ontained as white solid in 92% yield after column chromatography (DCM/MeOH = 9/1). ^{1}H NMR (300 MHz, DMSO-d_6, δ): 0.79-0.87 (m, 12H), 1.18 (d, *J* = 7.3 Hz, 3H), 1.2-1.35 (m, 4H), 1.44-1.58 (m, 2H), 3.0.8 (q, 1H, *J* = 7.2 Hz), 3.11-3.25 (m, 4H), 3.70-3.81 (m, 2H), 4.65 (q, *J* = 6.9 Hz, 2H), 7.43 (d, *J* = 9.2 Hz, 1H), 7.51 (d, *J* = 9.2 Hz, 1H).

Box-Ph (154b).

To a solution of dihydroxymalonodiamide (**153b**) (6.5 g, 18.2 mmol) and DMAP (222 mg, 1.82 mmol) in 60 mL of DCM was added dropwise Et_3N (11.2 mL, 80.1 mmol) and *p*-TsCl (7.37 g, 37.9 mmol). The bright yellow solution was stirred at room temperature for 24 h. A white crystalline solid (ammonium salts) was formed during the reaction. After one day reaction time, the reaction mixture was diluted with 100 mL of DCM. The white crystalline formed was completely dissolved again. The resulting light yellow

solution was washed with saturated aqueous NH_4Cl (60 mL), water (30 mL). The combined aqueous NH_4Cl and water phase was extracted with DCM (30 mL x 3). The combined organic phase was washed with 50 mL of saturated aqueous $NaHCO_3$, dried over Na_2SO_4, filtered through cotton, and concentrated in vacuum to give a yellow-white solid. The resulting solid was purified by column chromatography twice (MeOH/DCM = 5/95, hexane/EtOAc = 3/2) and yielded 5.55 g (95%) of product (containing some unknown impurities which did not affect the next step reaction) as light pink oil which was found polymerized upon standing. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.62 (d, *J* = 7.8 Hz, 3H), 3.81 (q, *J* = 7.8 Hz, 1H), 4.11-4.19 (m, 2H), 4.61-4.70 (dd, *J* = 10.2, 7.8 Hz, 2H), 5.28 (dd, *J* = 8.7, 9.6 Hz, 2H), 7.2-7.36 (m, 10H).

Box-*i*-Pr (154a).

This compound was prepared from diamide **153a** using the procedure above. The desired product was obtained in 91% yield (crude). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.74 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H), 1.55-1.80 (m, 2H), 3.16-3.31 (m, 2H), 3.79 (t, *J* = 8.1 Hz, 1H), 3.84-4.0 (m, 4H), 4.16-4.25 (m, 2H), 7.12-7.28 (m, 5H).

Box-*i*-Bu (154d).

This compound was prepared from diamide **153d** using the procedure above. The desired product was obtained in 73% yield. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.87 (d, *J* = 6.9 Hz, 6H), 0.89 (d, *J* = 6.9 Hz, 6H), 1.19-1.29 (m, 2H), 1.43 (d, *J* = 7.5 Hz, 3H), 1.52-1.63 (m, 2H), 1.64-1.75 (m, 2H), 3.46 (q, *J* = 7.5 Hz, 1H), 3.8 (dt, *J* = 8.1, Hz, 2H), 4.05-4.16 (m, 2H), 4.29 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.32 (dd, *J* = 7.8, 1.8 Hz, 1H).

Box-Et (154c).

This compound was prepared from diamide **153c** using the procedure above. The desired product was obtained in 81% yield (crude). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.61 (t, *J* = 8.1 Hz, 3H), 0.79 (t, *J* = 8.1 Hz, 3H), 1.35-1.65 (m, 4H), 3.21-3.36 (m, 2H), 3.78 (t, *J* = 8.1 Hz, 1H), 3.85-3.94 (m, 2H), 3.98-4.11 (m, 2H), 4.28-4.36 (m, 2H), 7.2-7.34 (m, 5H).

Box-*t*-Bu (154e).

Methyl diethyl malonate (295 mg, 1.69 mmol) and (*S*)-*tert*-leucinol (405 mg, 3.38 mmol) were dissolved in 14 mL of xylene. The resulting solution was heated to reflux for 4 h with a Dean-Stark trap. Then 13 mg (0.06 mmol) of dichlorodimethyl stannane was added to the solution and the reaction mixture was allowed to reflux for 48 h. Most of xylene was removed under reduced pressure and the concentrated residue was purified by column chromatography on neutral alumina (EtOAc/hexane = 3/2) to afford 329 mg (69%) of the desired product as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.85 (s, 9H), 0.86 (s, 9H), 1.45 (d, *J* = 7.5 Hz, 3H), 3.52 (q, *J* = 7.5 Hz, 1H), 3.8-3.87 (m, 2H), 4.02-4.08 (m, 2H), 4.12-4.19 (m, 2H).

PIB-CH_2O-C_6H_4-$COOCH_2CH_2CH_3$ (155).

PIB-OMs **54** (6.92 g, 6.3 mmol) and 4-hydroxyl *n*-propylbenzoate (1.7 g, 9.45 mmol) were dissolved in a solvent mixture of toluene (60 mL) and DMF (40 mL). After addition of K_2CO_3 (4.35 g, 31.5 mmol), the reaction mixture was heated up to 110-120 ^oC and kept at that temperature for 2 d (5 d for PIB-2300). Toluene was evaporated under vacuum and the residue was extracted with hexane (50 mL x 3). The combined

hexane phase was washed with 90% EtOH (15 mL x 4) and then dried over Na_2SO_4. Evaporation of hexane gave rise to 7.3 g (98%) of product as viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 219H), 1.77 (q, *J* = 7.3 Hz, 2H), 1.97-2.07 (m, 1H), 3.63-3.69 (dd, *J* = 8.7, 7.2 Hz, 1H), 3.78-3.83 (dd, *J* = 8.7, 6.0 Hz, 1H), 4.23 (t, *J* = 7.3 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 7.97 (d, *J* = 8.7 Hz, 2H).

PIB-CH_2O-C_6H_4-CH_2OH (156).

PIB-benzoate **155** (7.3 g, 6.2 mmol) was dissolved in 25 mL of anhydrous THF. After the solution was cooled to 0 ºC, $LiAlH_4$ (324 mg, 8.1 mmol) was added to the solution carefully. The reaction mixture was then allowed to reflux overnight. After the reaction was complete, the excess $LiAlH_4$ was decomposed by addition of small amount of water. The mixture was stirred at room temperature until the color of the mixture turned to white. Then the mixture was diluted with 50 mL of hexane. The white precipitate was removed by filtration and the resulting solution was dried over Na_2SO_4. Evaporation of solvent yielded 6.45 g (93%) of the desired product as colorless viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.6 (m, 206H), 2.96-2.08 (br s, 1H), 3.60 (dd, 1H, *J* = 9.0, 8.2Hz), 3.76 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.59 (d, *J* = 6 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H).

PIB-CH_2O-C_6H_4-CH_2Cl (157).

To a solution of PIB-benzylalcohol (5.2 g, 4.63 mmol) in 20 mL of DCM was added dropwise $SOCl_2$ (1 mL, 13.9 mmol) and two drops of DMF at 0 ºC. The resulting solution was stirred at room temperature for 2 h. After decomposing the excess $SOCl_2$ with small amount of water (ca. 0.5 mL), the solution was then diluted with 100 mL of

DCM and transferred to a separation funnel. The DCM phase was washed with water (10 mL x 5), $NaHCO_{3(sat.)}$ (10 mL x 2) and water (10 mL x 3). (Note: During the work-up, if serious emulsion is formed, it will be better to use centrifuge to get good separation.) The organic phase was then dried over Na_2SO_4, and 5.25 g (99%) of product was obtained after removal of solvent: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.8–1.8 (m, 214H), 1.9-2.3 (m, 1H), 3.58-3.64 (dd, *J* = 7.5, 9.0 Hz, 1H), 3.73-3.79 (dd, *J* = 5.7, 9.0 Hz, 1H), 4.54 (s, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H).

PIB_{2300}-benzylchoride.

This compound was prepared from PIB_{2300} using the procedure used above to prepare PIB_{1000}-benzylchloride **157**.

PIB-Box-(Ph) (158b).

A solution of Box-Ph (1.45 g, 4.52 mmol) in 6 mL of THF was cooled to -78 ºC with a dry ice-acetone bath. To the cold solution was added dropwise 1.58 M *n*-BuLi (2.86 mL, 4.52 mmol). After stirring for 30 min, the solution was allowed to warm to room temperature. Then a solution of PIB_{2300}-benzylchloride (8.18 g, 3.35 mmol) in 25 mL of THF was added to this lithio anion. The resulting reaction mixture was allowed to reflux for 36 h. Then the THF was removed under reduced pressure, and the residue was redissolved in 150 mL of hexane. The hexane phase was washed with water (15m), DMF (15 mL x 3), 90% EtOH (20 mL x 3) and dried over Na_2SO_4. Evaporation of the solvent afforded 8.71 g (95%) of PIB-supported Box ligand as light yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.8-2.0 (m, 700H), 3.37 (s, 2H), 3.54-3.61 (t, *J* = 7.8 Hz, 1H), 3.7-3.77 (dd, *J* = 8.7, 5.4 Hz, 1H), 4.07 (t, *J* = 8.1 Hz, 1H), 4.15 (t, *J* = 8.1 Hz, 1H),

4.62-4.69 (m, 2H), 5.14-5.24 (m, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 7.02 (m, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 7.18-7.32 (m, 8H); ^{13}C NMR ($CDCl_3$, δ): 22.9, 25.5, 29.4, 31.5, 32.7, 34.9, 36.1, 38.4, 41.6, 44.1, 50.0, 57.0, 59.6, 69.7, 74.4, 75.4, 114.4, 126.9, 127.0, 127.7, 127.8, 128.4, 128.8, 128.9, 131.7, 142.4, 142.6, 158.6, 169.4, 169.6.

PIB-Box-(Et) (158c).

This compound was prepared from PIB_{1000}-benzylchloride **157** and Box ligand **154c** using the procedure used to prepare PIB-supported Box ligand **158b**. The desired product was obtained in 66% yield. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.9 (m, 235H), 1.95-2.1 (m, 1H), 3.22-3.38 (m, 4H), 3.61 (t, *J* = 7.7 Hz, 1H), 3..75-3.89 (m, 3H), 3.95-4.08 (m, 2H), 4.25-4.13 (m, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 7.19 (d, *J* = 8.7 Hz, 2H), 7.2-7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, δ): 20.7, 28.5, 29.3, 29.5, 31.4, 32.6, 32.8, 36.1, 38.4, 48.5, 49.9, 57.0, 59.7, 67.7, 72.2, 74.5, 114.1, 126.8, 128.1, 128.2, 128.8, 130.6, 130.7, 131.6, 137.2, 158.3, 166.6.

PIB-Box-(*i*-Pr) (158a).

This compound was prepared from PIB_{1000}-benzylchloride **157** and Box ligand **154a** using the procedure used to prepare PIB-supported Box ligand **158b**. The desired product was obtained in 67% yield. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.8 (m, 256H), 1.98-2.11 (m, 1H), 3.22 (d, *J* = 14.1, 1H), 3.26 (d, *J* = 14.1, 1H), 3.37-3.46 (t, *J* = 14.4 Hz, 2H), 3.59-3.64 (t, *J* = 7.2 Hz, 1H), 3.78-3.83 (m, 1H), 3.84-98 (m, 4H), 4.12-4.23 (m, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 7.19 (d, *J* = 8.7 Hz, 2H), 7.24-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, δ): 18.2, 19.2, 20.6, 29.4, 31.3, 31.5, 32.8, 36.1, 38.4, 38.8, 39.5, 48.6, 49.9,

57.0, 58.4, 59.0, 59.7, 69.9, 72.1, 74.4, 114.1, 126.7, 128.0, 128.9, 130.7, 131.6, 137.3, 158.2, 166.5.

PIB_{2300}-Box-(*i*-Bu) (158d).

This compound was prepared from PIB_{2300}-benzylchloride **157** and Box ligand **154d** using the procedure used to prepare PIB-supported Box ligand **158b**. The desired product was obtained in 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.85 (m, 694H), 1.92-2.03 (m, 1H), 3.16 (d, *J* = 13.8 Hz, 1H), 3.24 (d, *J* = 13.8 Hz, 1H), 3.52-3.6 (t, *J* = 7.8 Hz, 1H), 3.69-3.76 (m, 1H), 3.84 (t, *J* = 7.5 Hz, 2H), 4.06-4.16 (m, 2H), 4.28-4.35 (m, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, δ): 14.3, 20.7, 21.2, 21.6, 23.0, 23.4, 25.8, 31.5, 34.8, 36.1, 38.6, 43.9, 45.8, 59.5, 64.7, 73.6, 73.8, 74.3, 114.1, 128.6, 131.7, 158.2, 167.8, 167.9.

PIB_{2300}-Box-(*t*-Bu) (158e).

This compound was prepared from PIB_{2300}-benzylchloride **157** and Box ligand **154e** using the procedure used to prepare PIB-supported Box ligand **158b**. The desired product was obtained in 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.8-1.8 (m, 586H), 1.91-2.03 (m, 1H), 3.14 (d, *J* = 13.5 Hz, 1H), 3.3 (d, *J* = 13.5 Hz, 1H), 3.52-3.6 (m, 1H), 3.69-3.76 (m, 1H), 3.77-3.92 (m, 2H), 3.98-4.19 (m, 4H), 6.74 (d, *J* = 8.7 Hz, 2H), 7.06 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, δ): 14.2, 20.5, 21.1, 21.7, 23.0, 25.9, 26.1, 31.6, 32.4, 34.1, 34.7, 36.0, 38.3, 43.9, 59.6, 68.9, 75.9, 114.2, 128.7, 131.9, 158.2, 167.8, 170.1.

PIB-Box-(*i*-Pr)-Cu(II)(OTf)$_2$ (159a).

A reaction mixture containing PIB-Box-(*i*-Pr) **158a** (0.89 g, 0.59 mmol), Cu(OTf)$_2$ (213 mg, 0.59 mmol), and DCM (7 mL) was stirred at room temperature for 24 h. Evaporation of DCM afforded a blue-green viscous oil. Then this crude product was dissolved in 30 mL of anhydrous heptane. The resulting suspension was allowed to pass through a short celite column (1.5 cm) to remove unreacted copper salt. The desired copper complex was obtained as blue-green viscous oil (1.07 g, containing some heptane solvent) after removal of heptane under reduced pressure (this process was carried out below 50 ºC to avoid the decomposition of the copper complex).

PIB-Box-(Ph)-Cu(II)(OTf)$_2$ (159b) and **PIB-Box-(Et)-Cu(II)(OTf)$_2$ (159c)** were also prepared from the PIB-supported Box ligands **158b** and **158c**, respectively, using the procedure used to prepare PIB-supported copper complex **159a**.

CHAPTER V

SUMMARY

Various PIB-supported transition metal catalysts were synthesized. Two specific reactions, Mukaiyama olefin epoxidation and olefin cyclopropanation, were chosen as the model reactions to study the catalytic activity and recyclability of these polymeric catalysts. In a standard procedure, the reactions were carried out in heptane. Recovery and recycling of these polymeric catalysts were accomplished via a simple post reaction extraction with a polar solvent such as ethyleneglycol diacetate and acetonitrile. The excellent nonpolar phase selective solubility of PIB supports enables the PIB-supported catalysts retain in the heptane phase and separate from the products that were partioned into the polar phase.

Our preliminary results showed that all these PIB-supported catalysts were comparable to their low molecular weight analogs in activity and selectivity, and could be easily recovered and reused multiple times in both selected reactions. However, metal leaching was still a major problem for these PIB-supported catalysts, especially for PIB-supported Cu catalysts. In that case, the relatively higher molecular weight of the polar part (Box ligated Cu triflates) in comparation with the nonpolar PIB chain decreased the nonpolar phase selective solubility of the PIB-supported Cu catalyst. As a result, higher metal leaching was observed. This problem can be partially solved by either using a longer PIB chain as support or attaching multiple PIB chains on one catalyst.

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