Polyisobutylene Phase-Anchored Ruthenium Complexes

Haw-Lih Su,[1] *Chayanant Hongfa,*[2] *Hassan S. Bazzi,*[**2] *David E. Bergbreiter*[*1]

Summary: The use of polymers in general as ligands or sequestrants for metals has often focused on the use of cross-linked polymers or readily available soluble polar polymers like poly(ethylene glycol). Our work shows that functional nonpolar polymers like polyisobutylene are viable alternatives and can be readily used as phase selectively soluble ligands or sequestrants for commonly used transition metal catalysts. This is illustrated in this work by the synthesis of ligands and sequestrants for ruthenium catalysts widely used in ring-closing-metathesis, cross-metathesis, and ring-opening metathesis polymerization. We show that a polyisobutylene terminally functionalized with a vinyl group can be converted by electrophilic aromatic substitution into species that phase immobilize a benzylidene Ru catalyst precursor, an *N*-heterocyclic carbene ligand, or that can sequester a Ru complex by conversion of a reactive Ru alkylidene into a phase-immobilized Fischer carbene complex. In all these cases, the Ru complexes that are formed are selectively soluble in a nonpolar or weakly polar phase of a liquid/liquid biphasic system – a system that can be efficiently formed either thermomorphically, by perturbation of an initially miscible solvent mixture, or by extraction.

Keywords: catalysts; functionalization of polymers; metathesis; phase separation; ring-opening metathesis polymerization (ROMP); separation techniques

Introduction

Ever since Merrifield's ground-breaking application of cross-linked polystyrene in peptide synthesis in the 1960s,[1] insoluble polymers have received great attention in synthetic chemistry. The main benefits of solid state supports are the ease of physical separation of the polymers and their bound components from the reaction mixture, the ease of recycling (especially with expensive catalysts and ligands), and the simplification of handling a range of toxic or odorous materials. However, such a hetereogeneous system inherently has problems. For example, such systems are more difficult to characterize and the mechanical instability of most supports limits their long-term usage.[2] Therefore, alternative approaches where soluble polymers are used as supports have been studied in recent years.

Soluble polymer supports have advantages in that species bound to soluble supports can be more easily characterized and modified than species bound to heterogeneous supports. Reactive groups on such supports can better mimic the chemistry of their low molecular weight counterparts.[3–5] The most common soluble polymer used in synthesis and catalysis is poly(ethylene glycol) (PEG), a terminally functionalized polyether.[6–7] This sort of polymer is widely used because of the commercial availability of this polymer and its history of being used as a modifying group for drug delivery and for facilitation of drug bioavailability.[8] However, compared to cross-linked materials, soluble

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[1] Department of Chemistry, Texas A&M University, College Station, Texas, USA
Fax: (+1) 979-845-4719;
E-mail: bergbreiter@tamu.edu

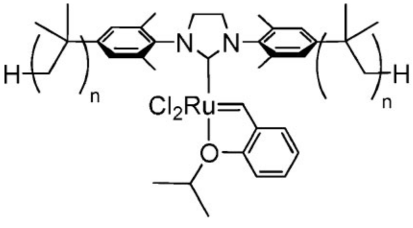
[2] Department of Chemistry, Texas A&M University at Qatar, Doha, Qatar
Fax: (+974)-423-0060;
E-mail: bazzi@tamu.edu

polymers to this point, are still used less frequently in synthesis and catalysis. This partly reflects a perception that soluble polymer supports are more difficult to use or to separate from reaction mixtures because of the similarity of the polarities of the polymer and reaction products.

An alternative soluble polymer support that we have recently begun to study is polyisobutylene (PIB). This sort of polymer is widely used because of its commercial materials that are used in various applications including as oil or fuel additives, synthetic rubber, adhesives, etc., PIB has the advantage of a chemically inert alkane backbone. PIB derivatives can also be readily analyzed because PIB (like PEG) has a relatively simple ^{1}H NMR spectrum where there are only two types of protons present on the polymer and where these protons appear in a relatively unimportant region of the ^{1}H NMR spectrum. PIB or at least the PIB derivatives we used[9] also has a vinyl terminus that can be modified by simple chemistry to prepare viable precursors to many sorts of soluble polymeric reagents and ligands.[10] Because PIB is noncrystalline, it is readily soluble in nonpolar and weakly polar solvents like alkanes, chlorinated alkanes, arenes, and ethers even at low temperatures. It is not soluble or only weakly soluble in polar solvents, like acetonitrile, DMF, ethanol, and water though it does dissolve in many solvent mixtures at elevated temperature. This phase selective solubility makes PIB and its derivatives attractive because the polymer and species attached to it can easily be separated from reaction mixtures by simple extraction. A particular advantage of PIB is that unlike an insoluble support, ligands and metal complexes bound to PIB can be readily characterized by solution state NMR spectroscopy. Previous work from our groups showed that PIB is a viable alternative to PEG and can be readily used to prepare phase selectively soluble ligands or sequestrants for commonly used transition metal catalysts.[10–15] Here we describe a variety of ways that PIB can be used as a phase anchor to ligate or sequester ruthenium complexes related to those widely used now in ring-closing metathesis (RCM), cross metathesis (CM), and ring-opening metathesis polymerization (ROMP) reactions.

PIB as a Support for Metathesis Catalysts

Two kinds of ligands, a benzylidene ligand and an *N*-heterocyclic carbene ligand, have been successfully bound to PIB oligomers. Both of these species have been used to prepare Hoveyda-Grubbs type catalysts **1** and **2**.[14–15] Both **1** and **2** have also been used as recyclable catalysts in ring closing metathesis reactions of dienes (Scheme 1) affording products in >90% average yields over multiple reaction cycles. Recycling was affected in two ways: either by biphasic extraction or by precipitation of the metathesis product. These results show that PIB is a viable support and that it can function as a phase anchor for the separation of Ru complexes from a polar organic solvent or a reaction mixture. In these catalytic reactions, the recyclability/recoverability of **1** was evaluated by ICP-MS analysis.



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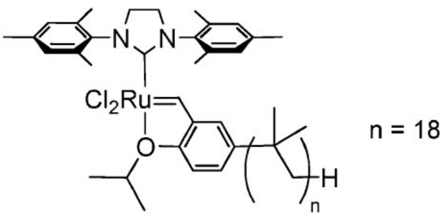

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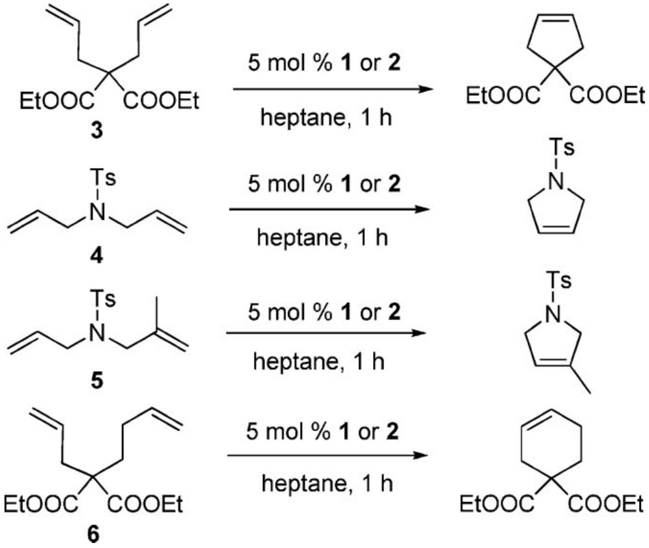
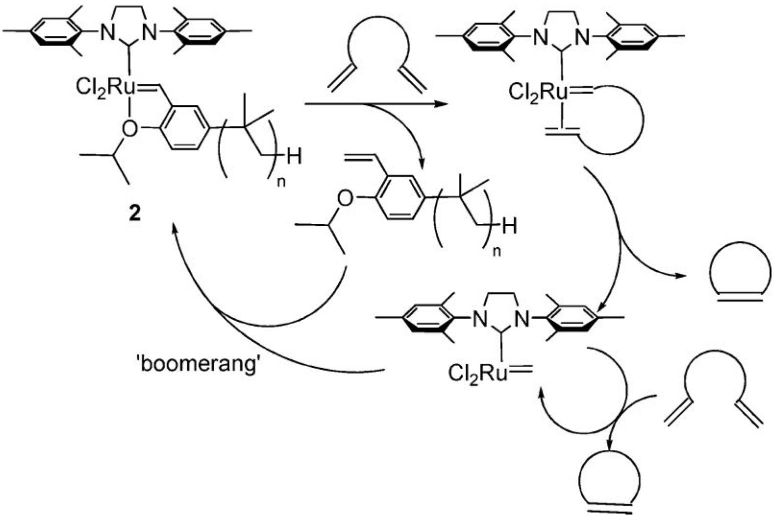
The ICP-MS results showed that only 0.28-0.54% of the starting Ru was in the product phase when **1** was used as a



Scheme 1.
RCM with catalyst **1** or **2**.

catalyst. This modest metal leaching is ca. 10-fold less than that observed for a Ru catalyst that used a PIB-bound benzylidene ligand (**2**) developed earlier by our group. In that case, Ru recovery was less because recovery required a 'boomerang' reaction (Scheme 2) and as much of 3% of the starting Ru was in the product phase. The improvement in Ru recovery using **1** presumably reflects the fact that the starting Ru complex, the likely methylidene catalysts, and likely even some catalyst decomposition products in the case of **1** are likely to contain the NHC ligand with two PIB groups. In the case of **2**, the starting Ru complex is phase selectively soluble, but the intermediates and any decomposition products only have a PIB group if the Ru



Scheme 2.
Metathesis and recycle mechanism of catalyst **2**.

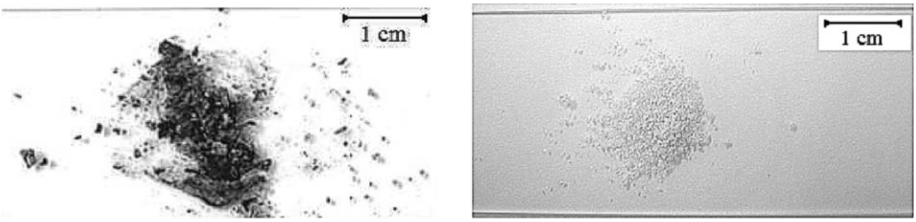


Figure 1.
The comparison between two RCM products of unsupported 2nd generation Hoveyda-Grubbs catalyst (left) and the PIB-supported ruthenium catalyst **1** (right).

alkylidene intermediates 'boomerang' back onto the starting PIB bound styrene derivative.[16]

PIB as a Sequestrant for Ruthenium Complexes

Although using polymer supported ligands for catalysts is a successful strategy for the removal of ruthenium species from a reaction mixture, the preparation of such catalysts requires a multistep synthesis. An alternative approach would be to use a functional polymer as a sequestration agent to first bind and to then remove any catalytic metal residues after a reaction. This approach to the purification of reaction mixtures has found widespread application in high-throughput syntheses where polymer bound sequestrants are used to trap excess reagents, products, or by-products.[17] It is also a general strategy used in the design of several commercially available crosslinked scavengers for other homogeneous catalysts.[18]

We have extended this idea of using polymer-supported scavengers by focusing on the design of soluble polymeric reagents that can capture the intermediates in metathesis chemistry. This idea is illustrated in Figure 2. This approach focused on using a soluble functional polymer that could react with the Ru alkylidene intermediates to form a Fischer carbene - a strategy that is already commonly used in quenching Ru-catalyzed polymerization processes. To the best of our knowledge, there are only two reports describing the use of polymers as scavengers for ruthenium species: Breinbauer *et al* used an insoluble resin-bound bisphosphine[19] and Kilbinger *et al* used poly(ethylene oxide)-poly(propylene oxide) diblock copolymers and an insoluble resin supported vinyl ether[20] to sequester ruthenium species.

In our approach, an alkene-terminated PIB was first converted to PIB alcohol, which subsequently underwent vinyl ether exchange in the presence of a palladium catalyst to afford the PIB vinyl ether **7** in good yield (Scheme 3). This vinyl ether was fully characterized by ^{1}H and ^{13}C NMR spectroscopy and proved to have reactivity analagous to that of its low molecular weight counterpart.

In order to probe the reactivity between **7** and ruthenium species, PIB vinyl ether **7**

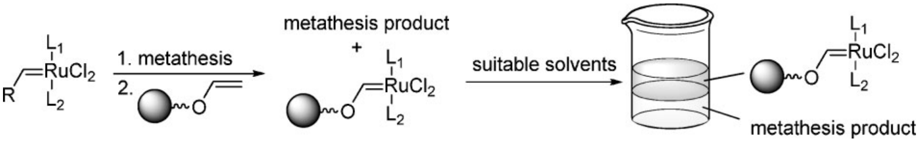
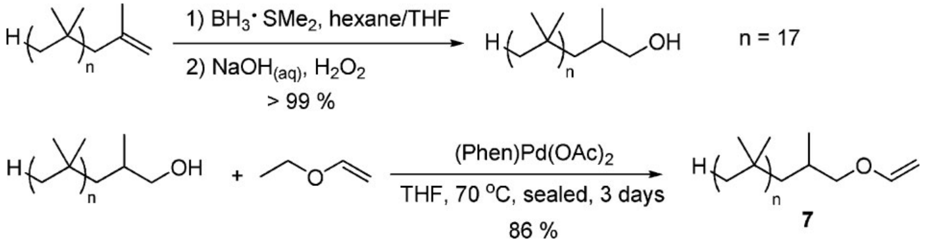


Figure 2.
Illustration of using a polymer-supported scavenger.



Scheme 3.
Synthesis of PIB vinyl ether.

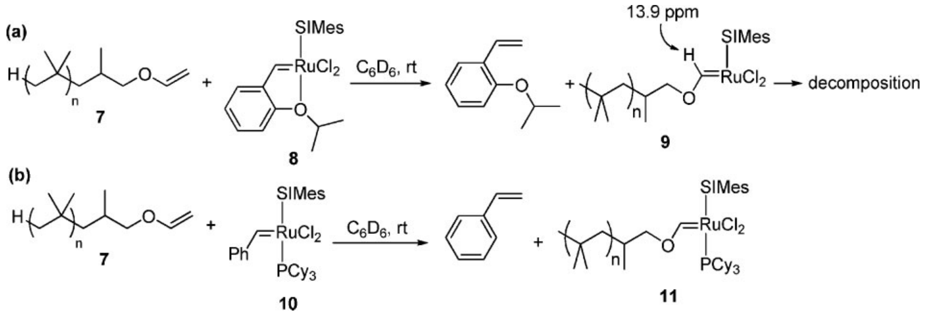
was tested as a sequestratant for the 2nd generation Hoveyda-Grubbs catalyst **8**. Kinetic studies using ^{1}H NMR spectroscopy showed that a new peak at δ 13.9 ppm formed but diminished over time. This result suggested that the Fischer carbene **9** was formed but decomposed quickly. We speculated that the Fischer carbene **9** formed but that decomposition of this Fischer carbene occurred due to the instability this 14-electron species (Scheme 4). If these were the case, a Fischer carbene **9** would be stable if other ligands were present. Therefore, a similar experiment was carried out using the 2nd generation Grubbs catalyst **10** and **7**. If our hypothesis were correct, the phosphine formed *in situ* should provide an additional ligand for the ruthenium to stabilize the Fischer carbene formed as a product by metathesis with the PIB vinyl ether **7**.

This supposition proved correct. ^{1}H NMR spectroscopy showed that the formation of the Fischer carbene **11** occurred and that the carbene **11** that formed was stable under an inert atmosphere (Figure 3).

Kinetic studies that compare the rate of formation of a Fischer carbene by reaction of **10** with PIB vinyl ether **7** (Scheme 4) and the rate of formation of a Fischer carbene by reaction of **10** with ethyl vinyl ether are shown in Figure 4. These rates were measured by ^{1}H-NMR spectroscopy and are virtually identical.

After the reaction of **10** with **7** to form a Fischer carbene was complete, acetonitrile and hexanes were added to the reaction mixture to examine the phase selectivity of the product PIB-bound Fischer carbene **11**. As shown in Figure 5, the PIB Fischer carbene **11** was selectively soluble in the nonpolar phase of a biphasic mixture of hexane and acetonitrile.

Since PIB vinyl ether was found to be a successful scavenger for the Grubbs catalyst **11**, it was subsequently tested in both ring-closing metathesis (RCM) and ring-opening metathesis polymerization (ROMP) chemistry (Scheme 5). Unfortunately, while **7**



Scheme 4.
Reactions of PIB vinyl ether with (a) 2nd generation Hoveyda-Grubbs catalyst (b) 2nd generation Grubbs catalyst.

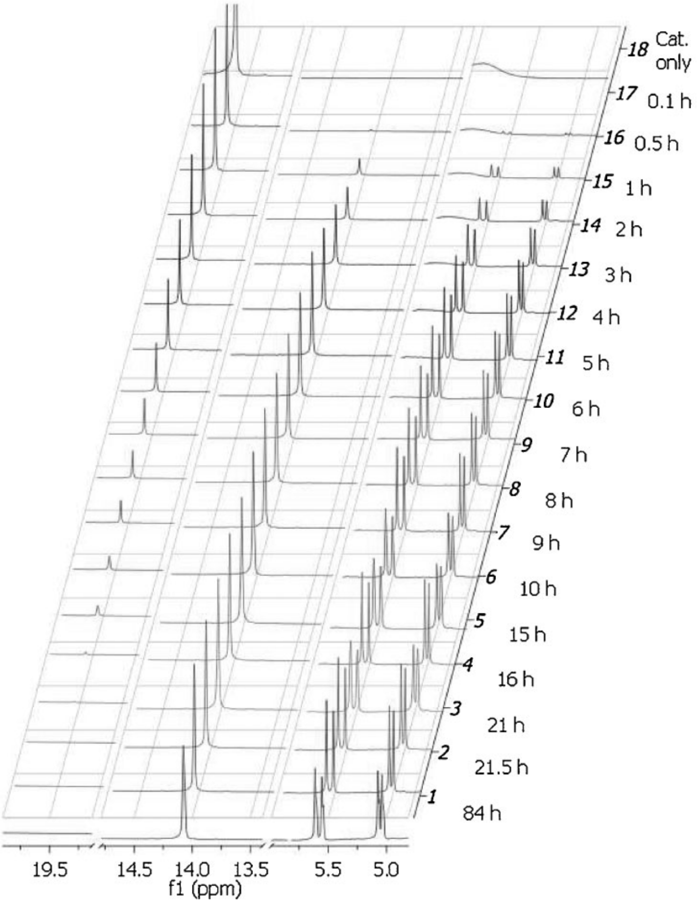


Figure 3.
Kinetic study of the reaction of PIB vinyl ether with 2nd generation Grubbs catalyst **10** by ^{1}H NMR spectroscopy. δ 19.6 ppm is the benzylidene proton of 2nd generation Grubbs catalyst **10**. δ 14.1 ppm indicates the alkylideneproton of the so-formed PIB-bound Fischer carbene **11**. Two doublet peaks at δ 5.6 and 5.1 ppm indicate the formation of styrene.

reacts rapidly with **11**, it was found that after metathesis, the formation of a Fischer carbene was much slower ($t_{1/2} \sim 40$ h) at room temperature. This decrease of the quenching reaction rate may be due to the formation of a less reactive ruthenium species during the course of the metathesis reaction. Indeed, when monitoring a RCM reaction by ^{1}H NMR spectroscopy, we observed a new peak formed at δ 18.4 ppm during the reaction. We have assigned this peak at δ 18.4 ppm to the methylidene protons of compound **12** (Scheme 6). The Ru-complex **12** has been isolated previously by Grubbs *et al* in 2001,[21] and

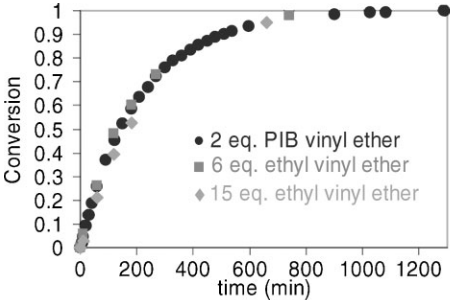


Figure 4.
Kinetic studies of the reactions of PIB vinyl ether **7** and different amounts of ethyl vinyl ether with 2nd generation Grubbs catalyst **10**. The conversion was based on the residual benzylidene signal intensity of ^{1}H-NMR spectroscopy.

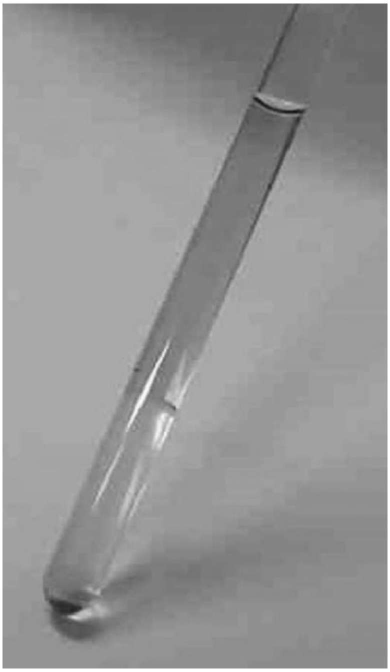


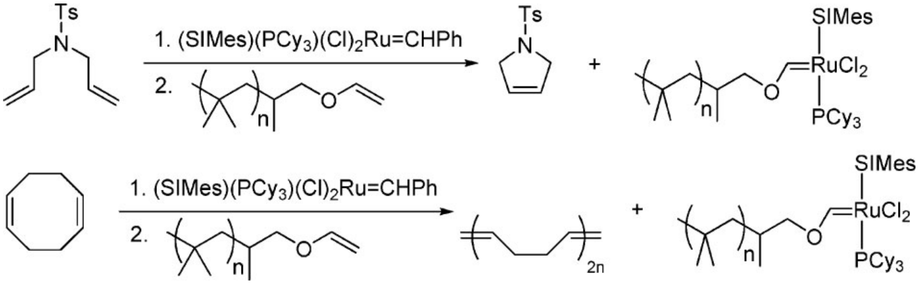
Figure 5.
PIB Fischer carbene was phase selectively soluble in nonpolar phase in a hexane-acetonitrile biphasic mixture.

the benzylidene proton of compound **12** was reported to have a chemical shift of δ 18.41 ppm in benzene-d_6. Compound **12** was also reported to have a very low dissociation rate constant (1e-3 s^{-1} at 85 °C). Since phosphine dissociation is presumably required for formation of a Fischer carbene, **7** is not very effective in quenching the Ru intermediate in this RCM or ROMP chemistry to form a species like **11**.

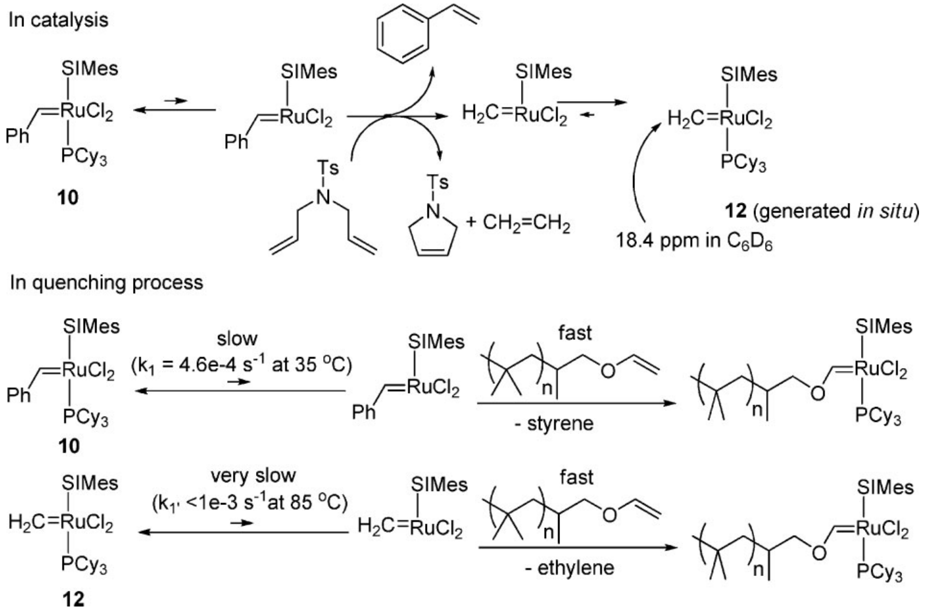
Given the low phosphine dissociation rate of compound **12** at ambient temperature, we also studied the quenching process (Scheme 6) at 60 °C. At 60 °C, the quenching reaction was complete in 10 h. Under these conditions the quenching reaction and formation of the Fischer carbene proceeded to completion. After the quenching reaction completed, hexanes and acetonitrile were added to separate the PIB bound Fischer carbene species from reaction mixture. Both phases were analyzed with ^{1}H NMR spectroscopy. We found no RCM product in the nonpolar phase and all of the PIB-bound Fischer carbene was present in the non polar phase. None of the PIB-bound Fischer carbene was present in the polar phase based on ^{1}H NMR spectroscopy.

Conclusion

In summary, the studies here show that polyisobutylene oligomers are good nonpolar phase selectively supports for Ru species like those used in metathesis chemistry. This soluble polymer can be used to form both ligands and sequestrants for ruthenium-based metathesis catalysts. In all cases, the Ru complexes formed were selectively soluble in a nonpolar or weakly polar phase of a liquid/liquid biphasic system. When PIB is used as a support to prepare a vinyl ether sequestrant to form Fischer carbenes from a Ru alkylidene, kinetic analyses showed the activity of the PIB vinyl ether is identical to ethyl vinyl



Scheme 5.
PIB vinyl ether as a scavenger for ruthenium residue after RCM and ROMP.



Scheme 6.
After RCM reaction, PIB vinyl ether was added as a scavenger. Because of the slow dissociation rate of compound **10**, the quenching process was very slow.

ether. This kinetic reactivity and phase selective solubility make PIB supports useful as separable Ru sequestrants of these sorts of Ru complexes. The use of these supports and a liquid/liquid phase separation provide a simple method to separate deep colored and metal-containing byproducts from metathesis reaction mixtures.

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