THE BEHAVIOR AND SEPARATION OF POLYSTYRENE IN MIXED SOLVENT SYSTEMS

A Dissertation

by

PATRICK NEAL HAMILTON

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

May 2007

Major Subject: Chemistry

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Approved by:

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

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ABSTRACT

The Behavior and Separation of Polystyrene in Mixed Solvent Systems.

(May 2007)

Patrick Neal Hamilton, B.S., Southeastern Louisiana University

Chair of Advisory Committee: Dr. David E. Bergbreiter

Non-polar phase selective solubility of modified poly(4-*n*-alkylstyrene) supports can be measured using fluorescent dyes as catalyst surrogates with thermomorphic and latent biphasic systems. By modifying the solvent compositions in heptane/ethanol and heptane/*N, N*-dimethylacetamide, increased non-polar phase selective solubility of modified polystyrene supports can be attained. Likewise, by varying the structure and length of the pendant alkyl chain, an increase in non-polar phase selective solubility is measured. These heptane soluble polymer supports can be useful for applications involving heptane soluble polymer-bound reagents and catalysts.

Various polar and non-polar polymer supports were synthesized with an attached solvatochromic catalyst surrogates to determine the solvent accessibility of the supported species in pure and mixed solvents. The results of these studies indicate that in pure solvents, the influence of both polar and non-polar polymer supports on the solvent microenvironment of these polymer-supported probes is minimal. In mixed solvent systems, a polymer-like solvent microenvironment is measured in solvent mixtures comprised of solvents the polymer has unfavorable interactions. Poly(4-*n*-alkylstyrene) and internally functionalized polyisobutylene supports are two such polymer supports that exhibit this behavior. For terminally functionalized polymers in mixed solvents, the solvatochromic behavior does not indicate a collapsed structure. In mixed solvents, there is minimal influence of the polymer support on the solvent microenvironment of these terminally functionalized polymers.

The application of soluble polyisobutylene supported copper complexes in the ATRP polymerization of styrene was investigated. Using the difference in solubility of the product polystyrene and the polyisobutylene copper complex in heptane, a solid/liquid separation of the soluble copper complex from the solid product was achieved. The results of these polymerizations indicate that the polyisobutylene copper complex behaves exactly like a low molecular weight copper complex in terms of control over molecular weight and molecular weight distribution. After the polymerizations, the polyisobutylene complexes could be separated as a heptane solution and recycled in multiple polymerizations of styrene.

DEDICATION

This dissertation is dedicated to my parents and my wife, Andrea. Thanks to my parents for always being there and helping me become the person I am today. Andrea, one sentence can't express how wonderful you are, so I'm going to spend the rest of my life reminding you.

ACKNOWLEDGMENTS

I would first and foremost like to thank Dr. Bergbreiter for providing a lab that I could call home. His support, guidance, and standards have made this whole experience worthwhile. I would also like to thank Jill for being the friendly face between us and Dr. Bergbreiter. Thanks to the three wise doctors: Dr. Andy Kippenberger, Dr. Sergio Gonzales, and Dr. Steve Furyk. Their sole advice of "Just get it done" didn't really help any, but it made for some interesting stories. However, their friendship and guidance through some rough times made it great to know them, especially when we were all sitting around a turkey fryer. Dr. Shayna Sung, good luck with your endeavors up there in NJ. Thanks to Film for being the buffer, Brandon for introducing me to 'Texas Americana', and Edmundo for using 'Wow' as the ultimate comeback. Thanks to Denisse for keeping Kippenberger in line and helping me pick on Film. Chris, I wish you the best of luck with your anger issues. Dr. Koshti and Tian, it was good working with both of you. To all other members of the Bergbreiter group, thanks for all the help you provided. Thanks to Tom Taylor for being a good roommate for some good and bad times in our first years here in graduate school. And finally, I would like to thank my wife. Even though I have dedicated this work to her, I feel that without her influence, I would not have been able to get along with most of the above people.

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CHAPTER I

INTRODUCTION

Polystyrene is inexpensive, robust, and commercially available. As a basic material, it is used not only for its physical durability, but also for its chemical inertness. Taking advantage of these two properties, many have applied polystyrene in various synthetic schemes. The innovative work of Merrifield[1] led to the idea that polymers could not only be used as a bulk material, but as a tool for synthetic chemistry. The facile separation of heterogeneous catalysts from a reaction mixture by filtration was already known to be advantageous. The synthesis and purification of peptides was greatly simplified and expedited by utilizing an easily filterable heterogeneous cross-linked polystyrene resin as a support for the growing peptide chain (**Figure 1**). A peptide can be sequentially built off of this insoluble polystyrene support. After each synthetic transformation, the product on the polymer support can be simply separated by filtration and washed to remove any un-reacted materials. At the end of the synthetic scheme, the peptide can then be easily cleaved from the polymer chain. This process produces a pure peptide completely free of its insoluble support or any polymer degradation by-products. Beginning with this initial idea of using polymers as phase "anchors", a variety of new synthetic strategies using Merrifield's resin were developed that would have otherwise been unrealistic with traditional synthetic tools.[2-4] Peptide

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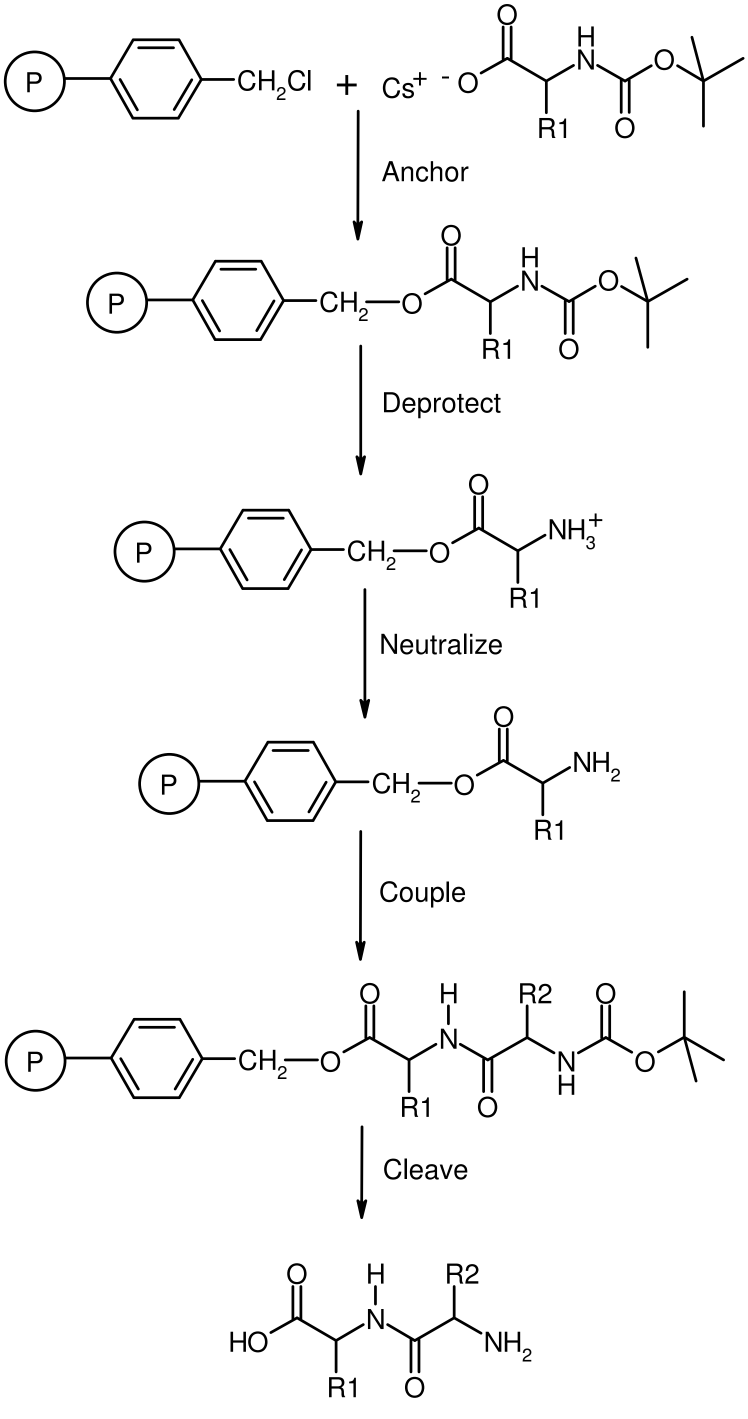


Figure 1. Merrifield synthesis of a dipeptide.

synthesis was not only greatly simplified, but now could be automated to produce vast libraries of compounds in a combinatorial fashion. Subsequently the idea of polymer "anchoring" has been applied to small molecule synthesis and catalysis.

Cross-linked polymer supports have other benefits in synthesis. For example, peptides covalently anchored to a polymer are isolated from one another. This leads to decreased rates for intermolecular reactions.[5] Further exploitation of this site isolation can be applied to transition metal catalyzed reactions. Active metal complexes are often unstable due to the formation of dimers and oligomers. Polymer resins have been found to facilitate the synthesis and/or stabilization of these complexes and can separate these active metal centers effectively from one another. Evidence of this can be seen in the carbonylation of allyl chloride by palladium amine complexes.[6] If an unsupported complex is used for catalysis, there is a limiting concentration where the active metal centers begin forming inactive oligomers. This limiting catalyst concentration is not reached with a similar supported catalyst complex, and a linear relationship of catalyst concentration and reaction rate is maintained far past the concentrations used with the unsupported metal complex. Other examples of polymer stabilization of active metal centers include preventing the dimerization of titanocene complexes.[7]

The facile separation of peptides compared to previous synthetic strategies eliminated time intensive purifications and reduced total synthesis time from weeks to hours. However, the inability to purify the peptide chains while still attached to insoluble polystyrene means that the products of any incomplete reactions will also be carried through to the next step. Attachment of each amino acid in the peptide chain must reach complete conversions to ensure the final peptide product has the correct amino acid sequence. To overcome this problem and ensure 100% conversion, excess reagents are often used. However, this method is wasteful when considering the amounts of reagents that must be used.

More efficient peptide syntheses were realized with the invention of continuous flow synthesis.[8] By eluting the reagents over the polymer support (**Figure 2**), a relatively high concentration of reagents is passed over the polymer. As coupling occurs, unused reagents are simply recycled until complete consumption of the reagent is achieved. This is determined by the in-line detector, which indirectly indicates complete formation of the polymer bound peptide product.

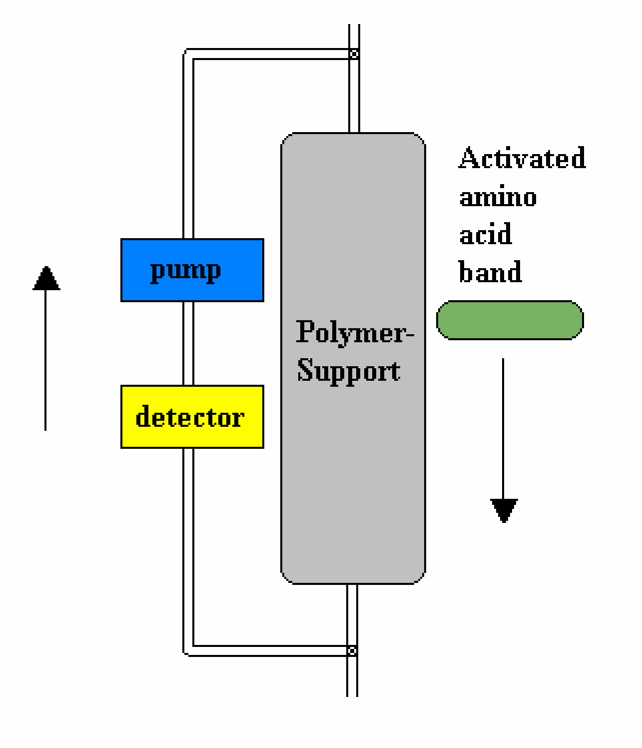
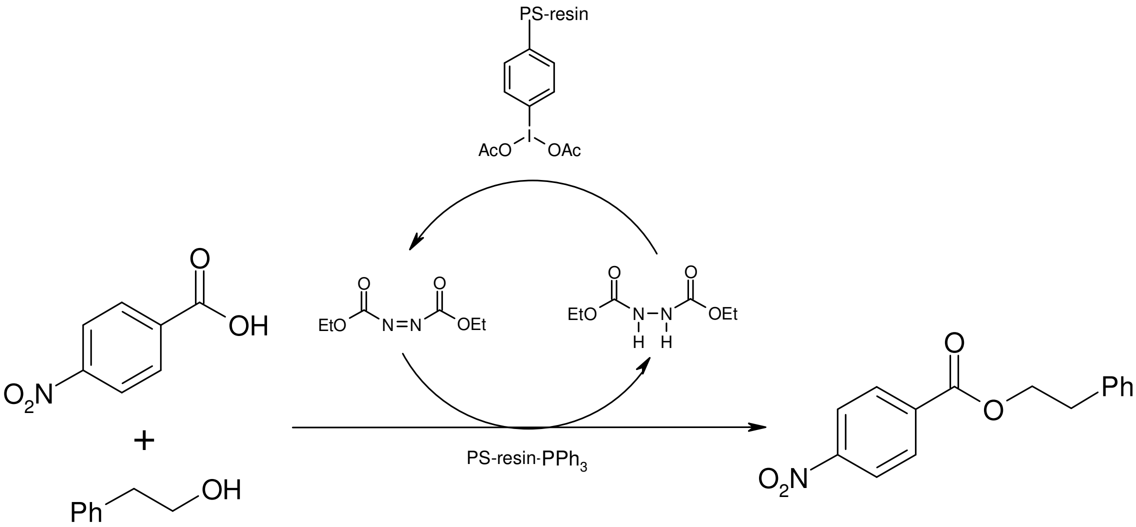


Figure 2. Continuous flow peptide synthesis.

The desire of synthetic chemists to produce compounds with a wide range of structural diversity has led to increased use of polymer supports in synthesis. Such supports are used to prepare libraries of candidate compounds for drug discovery. Often times synthesis, isolation, and purification of such drug candidates is a time consuming process. Efficient, multi-parallel synthesis using polymer supports offers a practical alternative that is readily applicable to both automation and scale-up. Such chemistry can be extended to the synthesis of natural products as well. One example is the total synthesis of the cytotoxic antitumor natural product epothilone C utilizing polymer supported reagents.[9] More recently, a multi-step synthesis of a natural product using only flow techniques was developed.[10] In this case, the synthesis of this compound was performed without the need for purification of the intermediates. This completely eliminated distillation or column chromatography steps for product purification and isolation. Other examples of this type of synthesis recently was realized in the preparation of a stage III cancer treatment drug.[11]

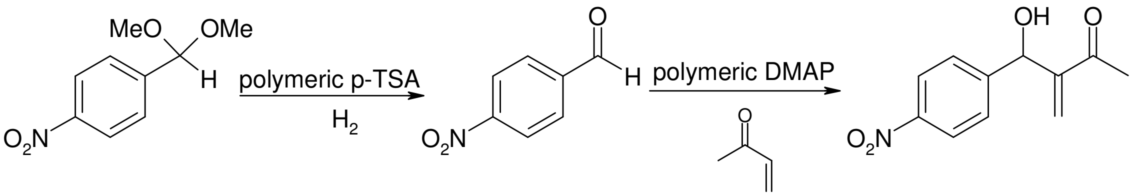
Removal of hard to purify peptides from reaction mixtures using insoluble polymers opened the door for polymeric reagents. Removal of certain reactants, reagents, and by-products from reaction mixtures can now be easily accomplished using cross-linked polystyrene. For example, trimethylamine *N*-oxide prepared from treatment of trimethylamine with hydrogen peroxide and acetic acid retains acetic acid. Oxidations of alkyl iodides to the corresponding aldehydes with this reagent often reach low yields due to the side reaction of the acetate ions to form alkyl acetates. Fréchet has described a polymer supported *N*-oxide reagent from the modification of cross-linked polystyrene with pendant chloromethyl groups.[12] Treatment of the polymer resin with deprotonated dimethylamine displaces the chloride of the polymer resin to produce a polymeric amine. Formation of the polymeric *N*-oxide reagent is accomplished with hydrogen peroxide and acetic acid. Subsequent washings with base and water allow for the complete removal of the unwanted acetate ions. Production of aldehydes from the corresponding alkyl iodides or bromides can be accomplished with reformation of the polymeric amine. More importantly, it is possible to regenerate and recycle the *N*-oxide reagent by treatment of the polymeric amine with hydrogen peroxide in the same fashion as previously mentioned.

Scheme 1. Catalytic Mitsunobu reaction



Another advantage of utilizing insoluble polymers is the ability to use two otherwise incompatible materials simultaneously in the same reaction mixture. Resin immobilization accomplishes this by kinetically isolating two otherwise reactive species. Species bound to different resins can react with species in solution, but will not react with each other due to the insolubility of the polymeric support. These type of "wolf and lamb" reactions were described in the literature over 30 years ago.[13] More recent examples of such strategies include the use of polymeric reagents to effect a simultaneous oxidation and reduction using a soluble Rh (I) catalyst and hydrogen gas with an insoluble polymer-bound Cr(VI) oxidant.[14] Toy has recently developed a cross-linked polystyrene supported (diacetoxyiodo)benzene[15] that is capable of oxidizing 1,2-dicarbethoxyhydrazine to diethyl azodicarboxylate (DEAD) and triphenylphosphine to triphenylphosphine oxide. For catalytic amounts of the diethyl azodicarboxylate to be used in a Mitsunobu reaction[16] the use of stoichiometric amounts of polymeric oxidizing reagent to regenerate the active (DEAD) in conjunction with a stoichiometric amount of

Scheme 2. "Wolf and Lamb" Baylis-Hillman reaction



cross-linked polystyrene supported phosphine would avoid the unwanted oxidation of the polymeric phosphine by the polymeric oxidizing agent. Recently, Fréchet *et al*[17] reported a one-pot sequential acetal hydrolysis and Baylis-Hillman reaction with cross-linked polymer supported *p*-toluenesulfonic acid and 4-(*N,N*-dimethylamino)-pyridine catalysts (**Scheme 2**). The control experiments confirmed that the use of soluble catalysts in conjunction with the polymeric catalyst in a one-pot synthesis excluded the formation of the desired product due to undesired interactions of the catalysts **(Figure 3**).

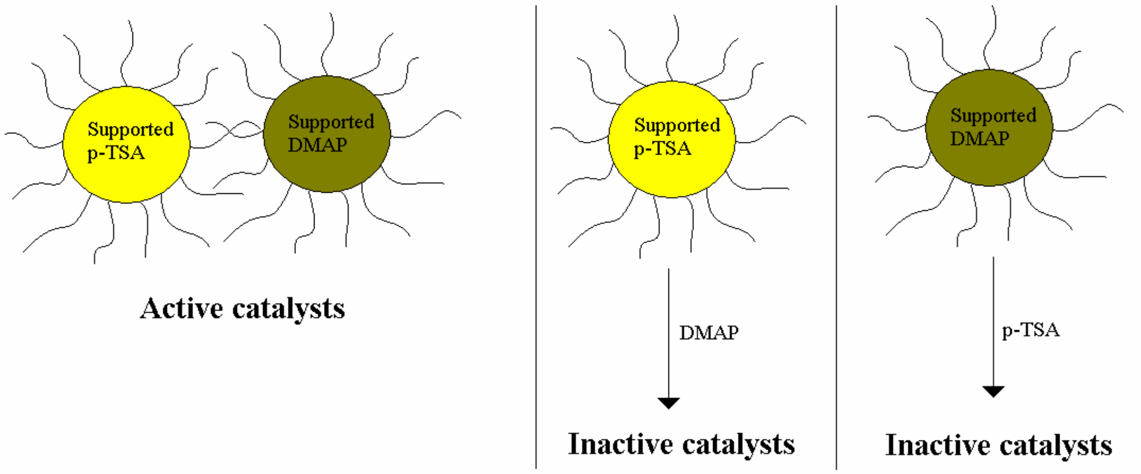
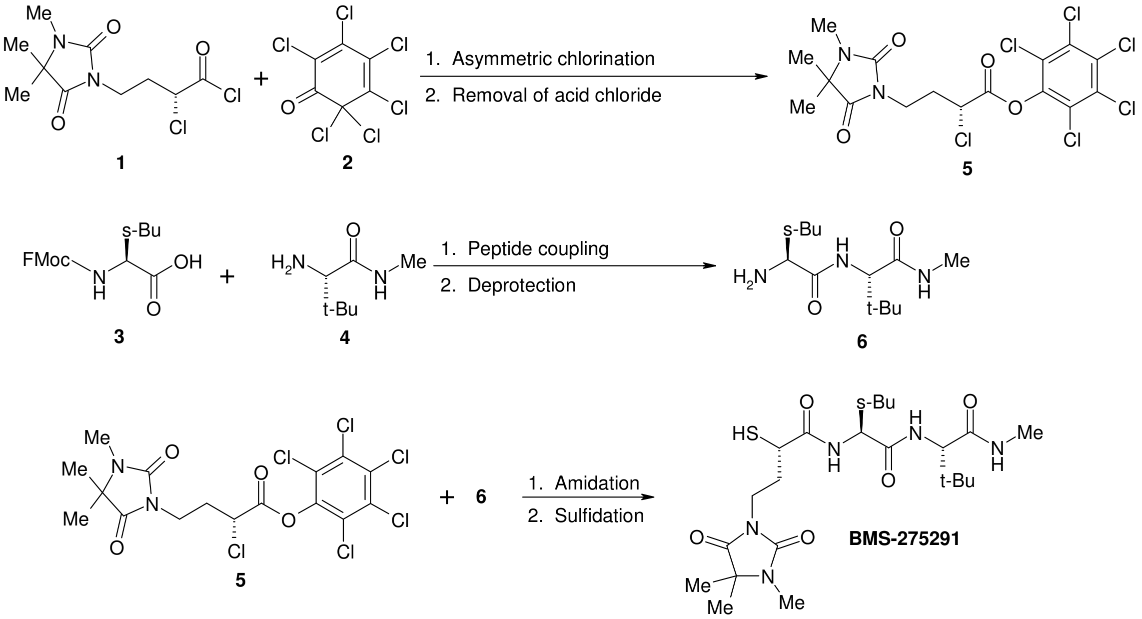


Figure 3. Situations where polymeric catalysts are or are not kinetically isolated from catalyst poisons or from species that deactivate the catalyst.

Polymeric reagents can also be used in novel ways to accelerate conventional syntheses. For example, the preparation of a peptide-containing drug candidate BMS-275291 (**Scheme 3**) is possible using a “synthesis machine”[11] (**Figure 4**) in a combination of parallel and sequential reactions. Substrates are only briefly attached to the polymeric resin as an intermediate as in the peptide coupling step. All the products are present in solution after each reaction and are eluted to the next reaction column in the series. In the synthesis of intermediate **5**, the substrates **1** and **2** were allowed to flow through the resin bound quinine and piperazine columns in series. Concurrent peptide coupling and deprotection was accomplished with the carbodiimide and tris-(2-aminoethyl) amine resins in series. Combination of intermediates **5** and **6** in the diluent Celite column was required for retardation of the flow to allow adequate time for coupling of the intermediates of the previous reaction columns. The final modification was completed using the supported ammonium reagent. For this "synthesis machine" to

Scheme 3. Synthesis of BMS-276291.



operate efficiently, optimization of reaction conditions had to be carried out. These conditions included optimizing the order of addition of substrates and optimization of flow rates to insure reactions went to completion. All the intermediate products were

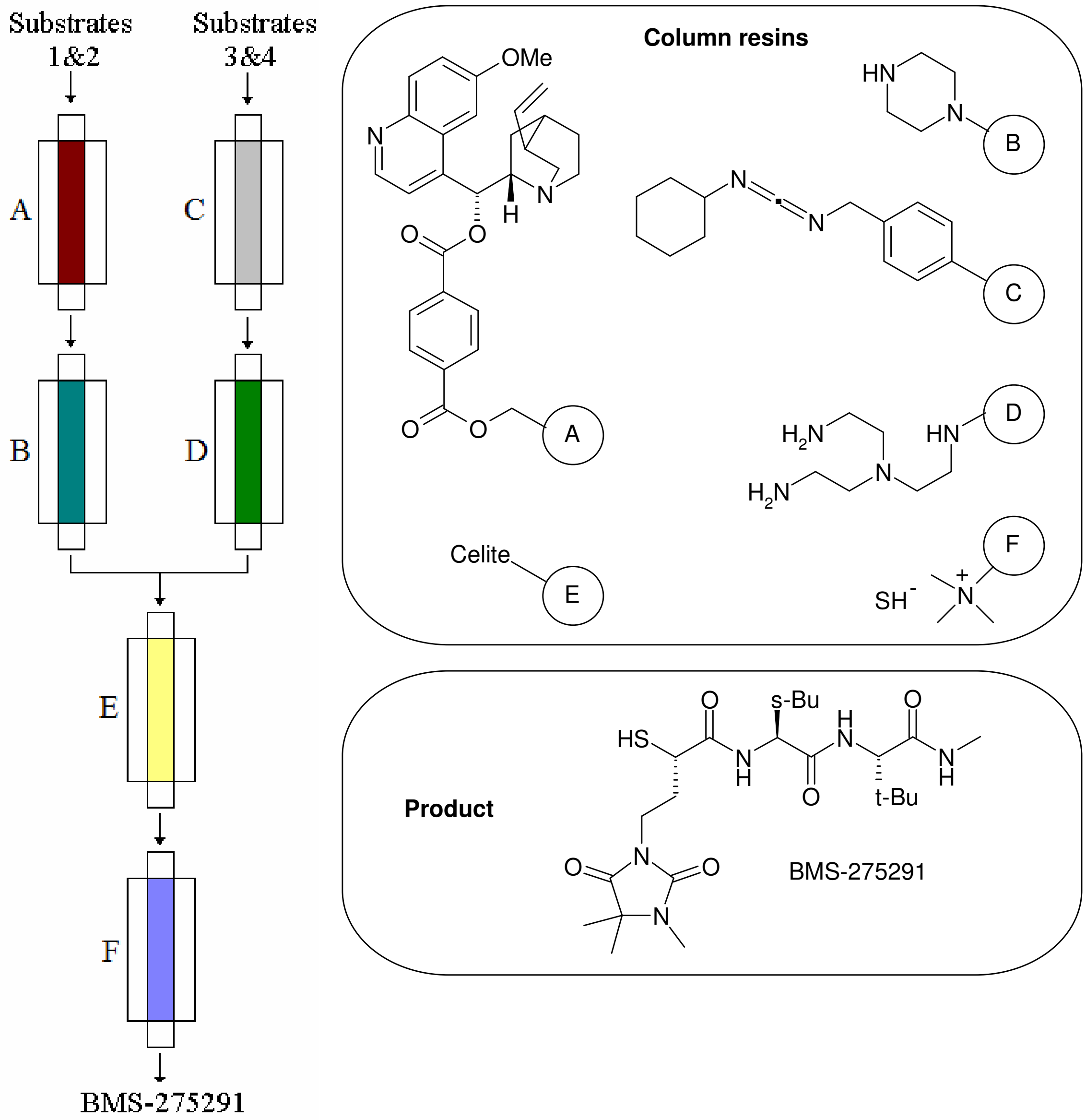
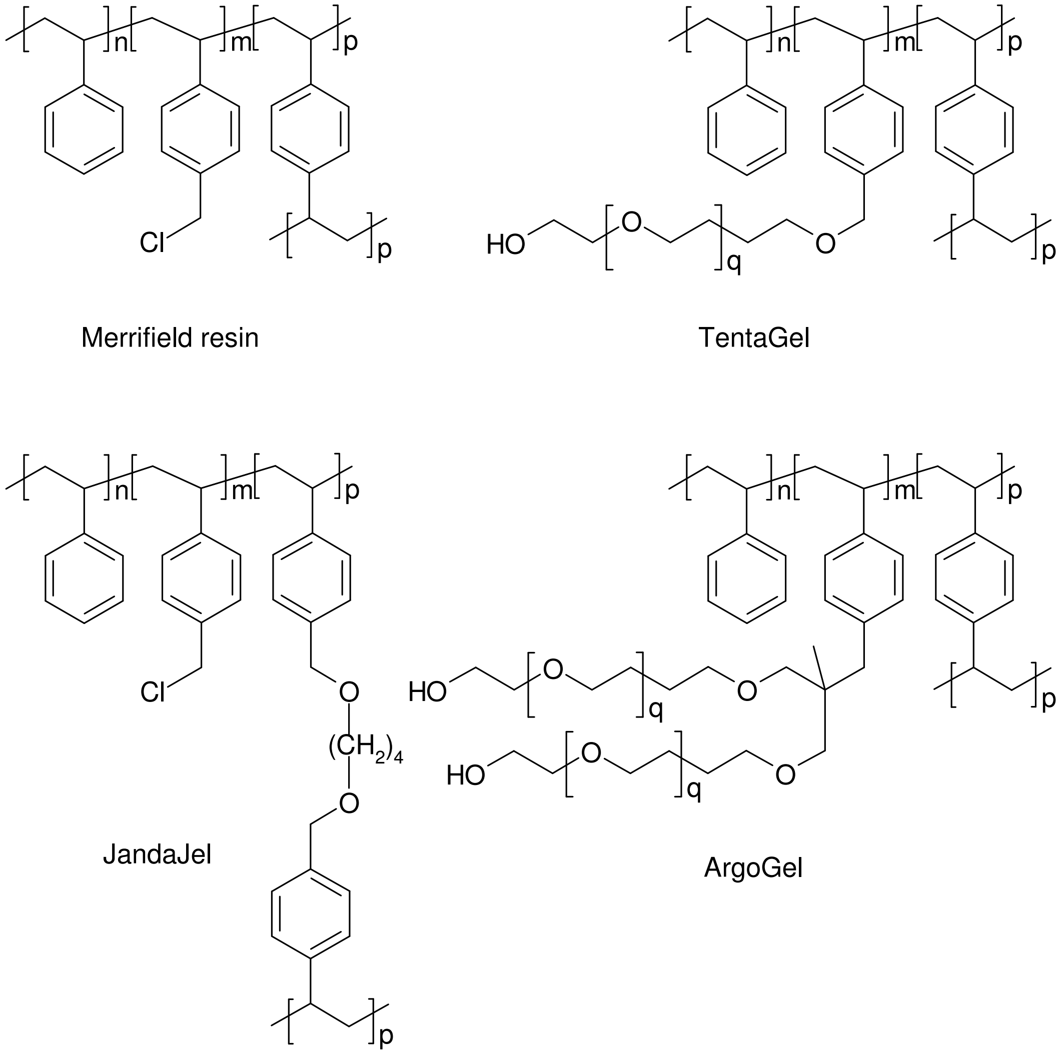


Figure 4. Solid-phase "synthesis machine" production of BMS-275291.

soluble in the eluting solvent. Since they were not bound to the polymer, analysis of the extent of reaction at each stage facilitated reaction optimization. A traditional synthesis would have required several days, but was performed in only 15 hours with the “synthesis machine”. In addition, the polymeric resins A, B, D, and F can be regenerated and used in further applications.

As previously mentioned, a homogeneous catalyst for asymmetric chlorinations has been attached to a polymeric resin. This catalyst effects the desired transformation in a recyclable reaction scheme. Industrially, this signifies that traditionally more active homogeneous catalysts can be supported on a polymer, thereby producing a commercially viable heterogeneous catalyst. As a result, much attention has been given to this topic.[18-20] However, only one example of this type of catalyst is in use industrially. A Rh(I) catalyst, $[Rh_2(CO)_2]^-$, supported on an ion exchange resin is used for the carbonylation of methanol. To minimize the amount of catalyst lost in the product phase by leaching of the active catalyst, an ion exchange guard bed had to be placed downstream of the reaction column. This column sequesters any catalyst that leaches from the original supported catalyst. This resin in the guard column bed reportedly can then be added to the original resin bed for further catalytic cycles, though that strategy is clearly not practical over extended cycles.[21]

The reason industry has failed to adopt polymer-supported catalysts reflects several problems. One reason industry has failed to introduce polymer supported homogeneous catalysts in large scale processes can be found in the way most reaction schemes depict polymer supports. The polymer is portrayed as an inert matrix with no interactions or limitations on the system. Issues such as resin swelling, steric effects, local concentration issues, the microenvironment of the supported species, and general physical properties of the resin are most often disregarded and not discussed. For example, Merrifield resin is relatively non-polar. This precludes the use of some



Merrifield resin

TentaGel

JandaJel

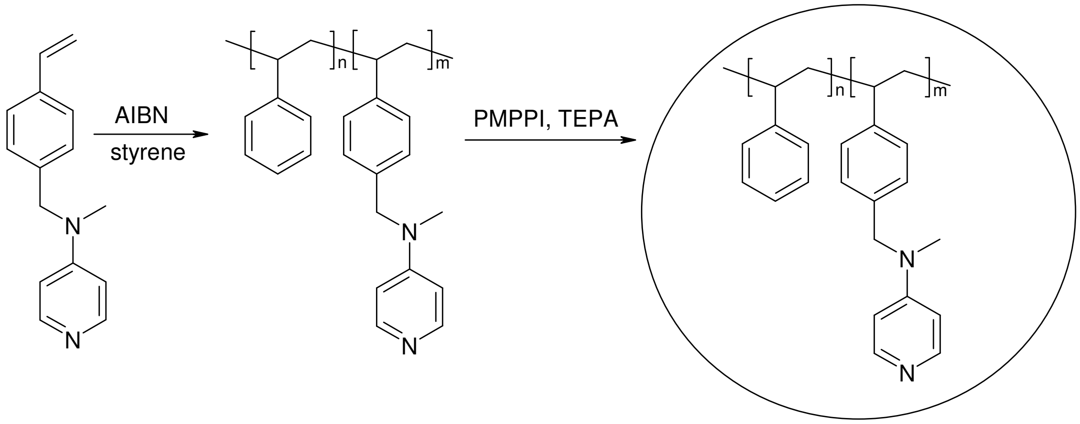
ArgoGel

Figure 5. Cross-linked resins for polymer supports.

solvents and makes some chemistry less successful. More polar versions of Merrifield resin can be prepared, examples of which include TentaGel, JandaJel, and ArgoGel (**Figure 5**). Each of these resins includes polar oxygenated species such as poly(ethylene glycol) groups.

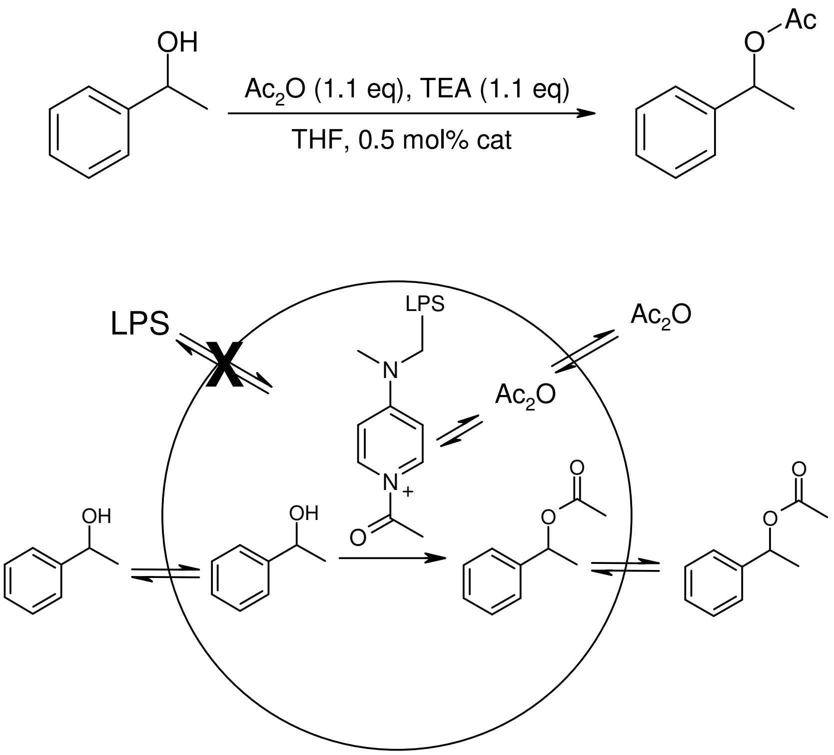
While soluble polymers are an alternative sort of support (vide infra), other approaches are still being explored that use insoluble materials. An example of this is a unique type of heterogeneous polymer recovery that was recently described.[22] Styrene was copolymerized with a 4-(*N, N*-dimethylamino)-pyridine (DMAP) modified monomer to produce a soluble polystyrene catalyst. To facilitate recovery, an insoluble shell was formed around the soluble polystyrene support using poly(methylene[polyphenyl]isocyanate) (PMPPI) and tetraethylenepentamine (TEPA) (**Scheme 4**). The resulting microencapsulated linear polystyrene was easily filtered as a

Scheme 4. Microencapsulated soluble polystyrene catalyst



free flowing solid. The heterogeneous shell allowed solvents and reagents to be shuttled from solution to the polymer bound catalyst (**Scheme 5**). Loss of the catalyst to the solution was not achieved due to the macromolecular properties of the catalyst. In comparison to commercially available cross-linked polystyrene DMAP catalysts, the microencapsulated catalyst had the same ease of separability but increased rates of reaction. However, it must be noted that the method of shell production greatly affects permeability and subsequently catalyst accessibility. This study in effect uses a soluble polymer as an alternative to a cross-linked heterogeneous support but uses the soluble

Scheme 5. Membrane separation of soluble polystyrene catalyst

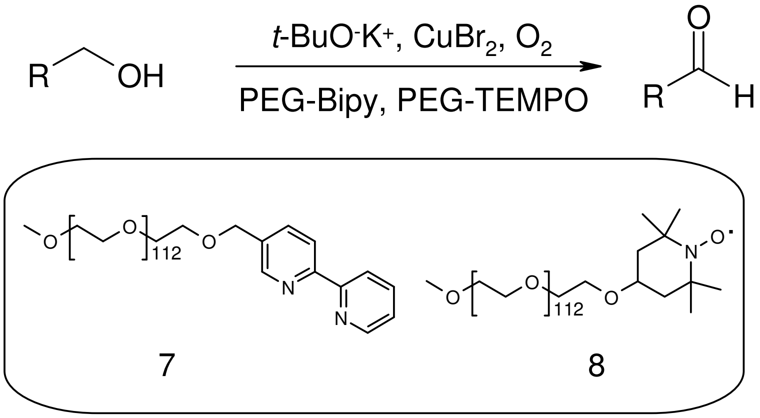


polymer in a biphasic mode. The idea of using soluble polymers had been previously been explored both by our group and others and is discussed in more detail below.

Soluble polymer supports are useful in synthesis and catalysis as they do not suffer from the problems of heterogeneity that affect characterization, reactivity, etc. They still need to have the advantage of separability from low molecular weight species, though, to be effective. Assuming strategies can be developed wherein linear soluble polymers offer the ease of separations of their cross-linked analogs, soluble polymers would offer many benefits. For example, soluble polymers have the added benefit of easy characterization such as that seen in normal synthesis. With cross-linked polymer supports, attached products must be cleaved before techniques such as traditional NMR analysis can be performed.

In the previously mentioned "wolf and lamb' reactions, multiple polymeric catalysts were used and effectively separated from the products. However, certain reactions require the direct interaction of multiple polymer-supported species before catalysis can occur. This eliminates these "wolf and lamb" approaches to perform the desired transformation. Soluble polymers would allow for effective interaction of the catalysts prior to reaction while still offering the separability of their cross-linked analogs. Toy has used poly(ethylene glycol) (PEG) supports to accomplish the selective aerobic oxidation of primary alcohols with copper/2,2'-bipyridine (**7**) and 2,2,6,6-tetramethyl-piperidyl-1-oxy (TEMPO) (**8**) complexes (**Scheme 6**).[23] The proposed mechanism (**Figure 6**) involves a complex of both polymeric ligands to produce the

Scheme 6. Oxidation with multiple soluble polymer supports.



desired transformation. This mechanism was supported by the ineffective catalysis of the alcohol substrates by not using the catalysts in conjunction. After completion of the oxidation, the polymer supports precipitate on addition of ether and can be separated from the soluble products by simple filtration. After filtration and drying, the polymer supports were recycled; however, subsequent recycling showed decreased yields of 94% to 36% from the first to the fifth catalytic cycle even upon addition of copper bromide.

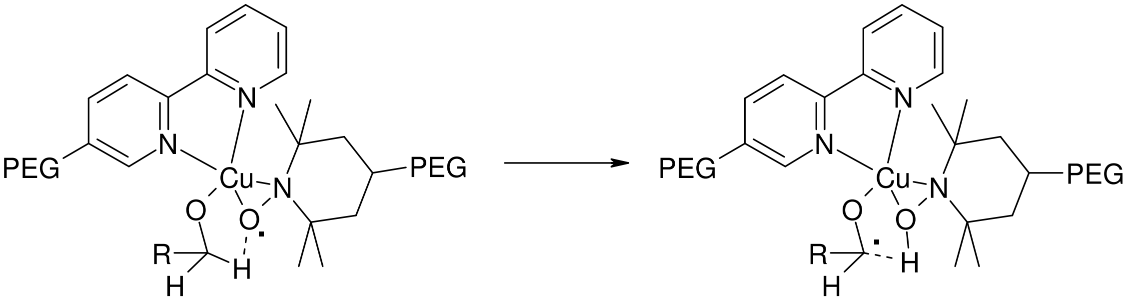


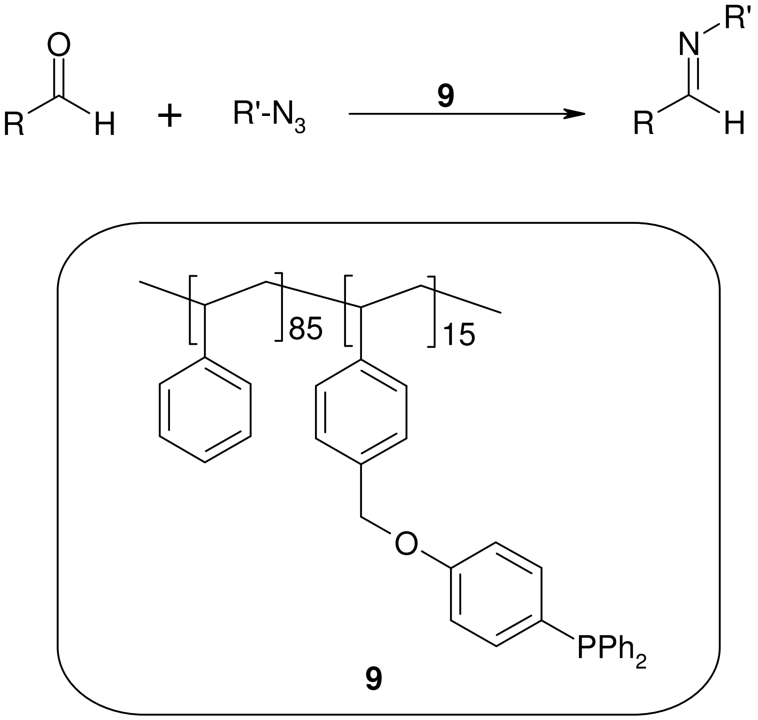
Figure 6. Proposed mechanism for oxidation of primary alcohols.

This loss of activity of the supports was attributed to decomposition of the poly(ethylene glycol) catalyst complex.

To effectively recover poly(ethylene glycol) supported species, the poly(ethylene glycol) must have a molecular weight of 2000 Da to facilitate suitable precipitations for filtration.[3] Attachment of catalyst and substrates only by end-group modifications, in conjunction with this molecular weight restriction, limits the maximum theoretical loading level to 1 mmol/g for these supports. Other problems associated with poly(ethylene glycol) are poor solubility at low temperatures and difficult removal of inorganic impurities such as transition metal cations. An alternative support is polystyrene. Polystyrene has a theoretical maximum loading of approximately 9.6 mmol/g if all the aromatic rings are substituted. Polystyrene is also soluble in a range of solvents at various temperatures. For these reasons, polystyrene is a more versatile linear polymer support.

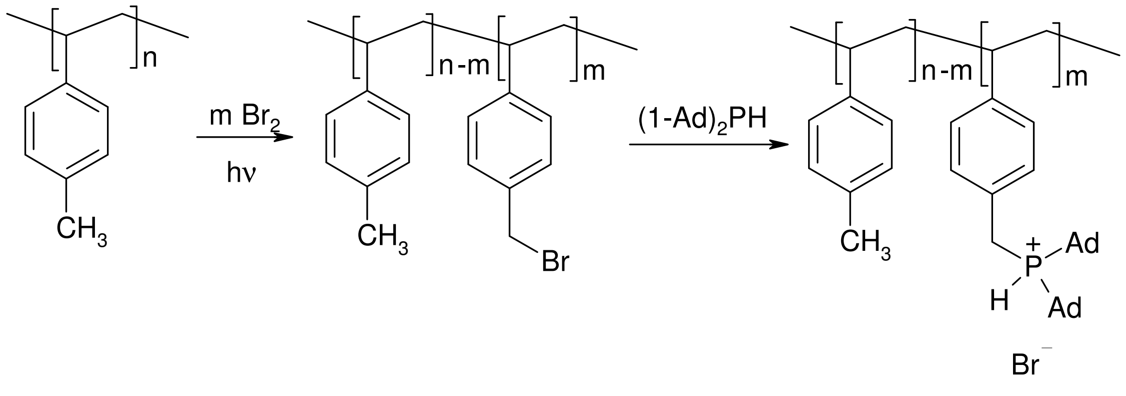
Linear polystyrene has been used in peptide synthesis[24] as well as in small molecule synthesis and catalysis.[25-27] Recently, a linear polystyrene supported phosphine (**9**) was synthesized to facilitate removal of the phosphine oxide by-product from a Staudinger/Aza-Wittig reaction (**Scheme 7**).[28] Poly(ethylene glycol) bound phosphines were not considered due to the low loading and solubility issues of the support. The polystyrene bound phosphine was prepared in three steps to produce a soluble phosphine reagent. This phosphine reagent could be used in the synthesis of imines with reactivities higher than those compared to triphenylphosphine. At the end of the reaction, precipitation of the polymer support allowed for complete removal of the phosphine oxide by-product.

Scheme 7. Staudinger/Aza-Wittig reaction with polystyrene bound phosphine



Other modified polystyrene-supported phosphines have been prepared and used as ligands in organometallic reactions.[29] A soluble poly(4-methylstyrene) support was synthesized and modified by free radical bromination of the pendant methyl groups. The resulting poly(4-methylstyrene)-co-poly(4-bromomethylstyrene) supports were allowed to further react with an electron rich phosphine, diadamantylphosphine $(1\text{-Ad})_2PH$ (**Scheme 8**). The subsequent use of this copolymer supported phosphine (**10**) in palladium catalyzed carbon-carbon coupling reactions was then described. The active palladium-

Scheme 8. Poly(4-methylstyrene) supported phosphine.



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phosphine complexes that formed were used in multiple catalytic cycles. The polymeric catalyst complex was efficiently separated by nanofiltration. Products from Sonogashira and Suzuki coupling reactions were produced in excellent yields and the polymer support was recycled nine times with minimal polymer leaching (<0.05%). However, use of polar aprotic solvents in the Heck catalysis was detrimental as it damaged the polymeric membranes used for filtration.

Precipitation and membrane filtration are the two most common methods for separating soluble polymer supported catalysts, ligands and reagents from the reaction mixture.[26,30-37] However, in many cases these methods are not practical. Solvent precipitation typically requires excess solvent usage that decreases the overall efficiency. The extended times that are needed for membrane filtration and the as yet incompletely realized general ability of membranes to be used in the many milieu that synthetic chemists use excludes this method for many synthetic processes outside the academic laboratory. Therefore, new ways for recovering soluble supports in synthesis and catalysis are needed.

In normal organic synthesis, it is common to employ a simple organic/aqueous liquid/liquid separation to purify compounds. These liquid/liquid separations are achieved using only gravity and a pair of immiscible solvents of differing densities. This concept can also be applied to polymers. For example, the removal of salt impurities from linear polystyrene can be achieved by dissolution of the polystyrene in toluene and removal of the aqueous soluble impurities in an easily separable liquid/liquid separation. By having a mixture of catalyst and product that prefer the opposing immiscible solvents, effective separations can be achieved in the same manner. This concept is not exclusive to polymers as this type of liquid/liquid separation of products from catalysts already has its foundations in industry without the use of polymers as phase “anchors”. The Ruhrchemie/Rhône-Poulenc (RCH/RP) hydroformylation process (**Figure 7**) is a well-known industrial example that utilizes catalysts that are firmly ‘anchored’ in a polar catalyst phase with non-polar products being effectively separated.

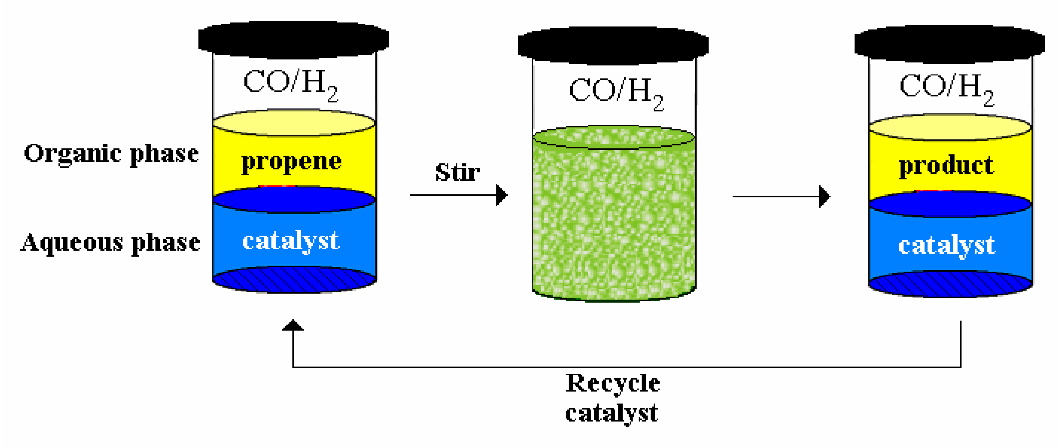
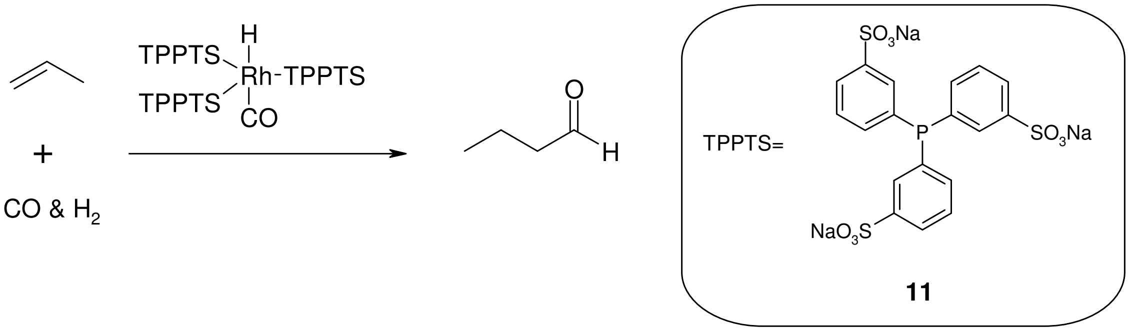


Figure 7. RCH/RP hydroformylation of propene to butyraldehyde.

With the RCH/RP process, a biphasic aqueous/organic system is maintained throughout the entire process. Triphenylphosphine ligands with attached sodium sulfonate residues (**11**) are used to maintain the exclusive solubility of the rhodium catalyst in the aqueous phase. Sufficient stirring of this catalytic system with propene and synthesis gas (CO and H_2) produces butyraldehyde (**Scheme 9**).[38] The butyraldehyde can then be separated from the catalyst by a simple liquid/liquid separation of the product containing organic phase from the catalyst containing polar phase. However, this system is limited since it is specifically designed for the production of butyraldehyde. For example, the RCH/RP process cannot effectively perform the hydroformylation of 1-hexene due to the insolubility of the substrate in the aqueous phase.[39,40]

To circumvent the problems of solubility of the reagents, a combination of homogeneous reaction conditions and biphasic separations would be ideal. It is known

Scheme 9. Aqueous soluble rhodium catalyst in RCH/RP hydroformylation of propene.



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that mixtures of fluorocarbon solvents such as perfluorinated alkanes, ethers, and amines produce biphasic mixtures with many organic solvents such as toluene, acetone, and tetrahydrofuran. These fluorous/organic solvent mixtures produce easily separable systems such as aqueous/organic solvent mixtures. However, unlike their aqueous analogs, these fluorous/organic solvent mixtures will become miscible at elevated temperatures (**Figure 8**). This phenomenon of two immiscible solvents becoming miscible with the application of heat or immiscible upon cooling is described as thermorphic behavior. Application of this solvent behavior allows a chemist to combine the features of homogeneous reaction conditions with the simplicity of a gravity-based liquid/liquid biphasic separation.

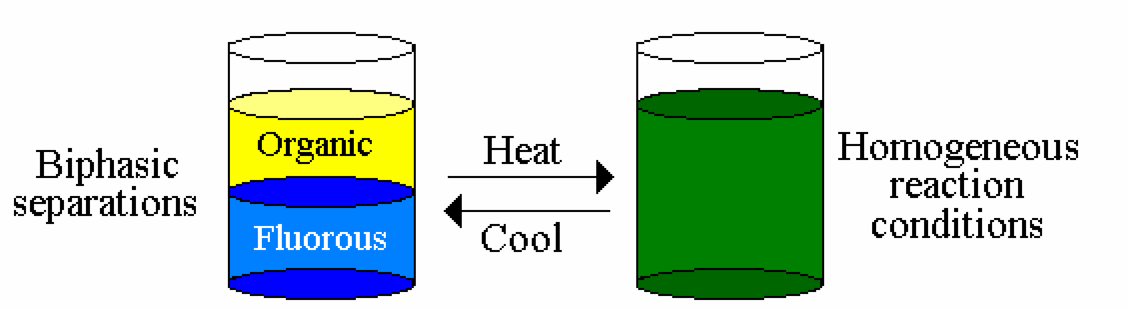
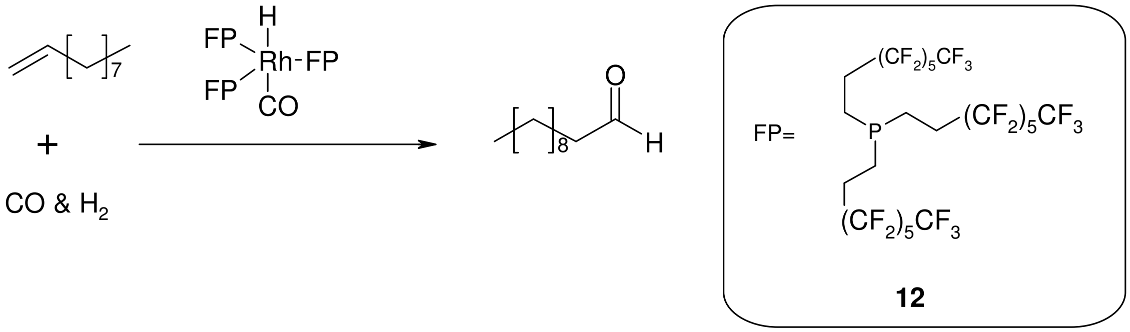


Figure 8. Thermomorphic behavior of fluorous/organic solvent mixtures.

In an example of using thermomorphic conditions to address the previous problems with substrate solubility in the RCH/RP process, Horváth described a hydroformylation process for the conversion of higher alkenes such as 1-decene to undecanal.[41] With both the catalyst and more non-polar substrates being in solution at elevated temperatures, complete conversions were achieved. Upon cooling, a biphasic system developed that allowed for the same facile separations as the aqueous/organic RCH/RP hydroformylation process. As in the RCH/RP process, a modified phosphine ligand (**12**) was used to 'anchor' the rhodium catalyst in the fluorous phase. In this particular example, perfluoromethylcyclohexane and toluene were used as solvents, and the hydroformylation of 1-decene was successfully completed at 100 °C (**Scheme 10**). In this particular example, cooling of this reaction mixture to room temperature produced a biphasic reaction mixture with the rhodium catalyst residing in the lower fluorous phase and the product in the upper toluene phase.

Scheme 10. Thermomorphic fluorous/organic hydroformylation of 1-decene.



While effective, these fluorous techniques have problems that may limit their widespread adoption in industry. The two main concerns are cost and environmental issues. While this hydroformylation scheme is effective, the high cost of fluorous solvents makes industrial use cost prohibitive. Also, the persistence of perfluorinated chemicals in the environment makes waste disposal an issue.

There are a number of organic solvent mixtures that demonstrate homogeneous reaction conditions and biphasic separations without the use of expensive fluorinated solvents.[42] For example, an equivolume mixture of heptane and *N, N*-dimethylformamide (DMA) will produce a biphasic system when mixed at room temperature. Heating of this solvent mixture above 70 ˚C will produce a homogeneous solvent system that will reform into a biphasic solvent system upon cooling to ambient temperatures. In cases where homogeneous conditions are needed at ambient or sub-ambient temperatures, latent biphasic mixtures can be used (**Figure 9**). These solvent

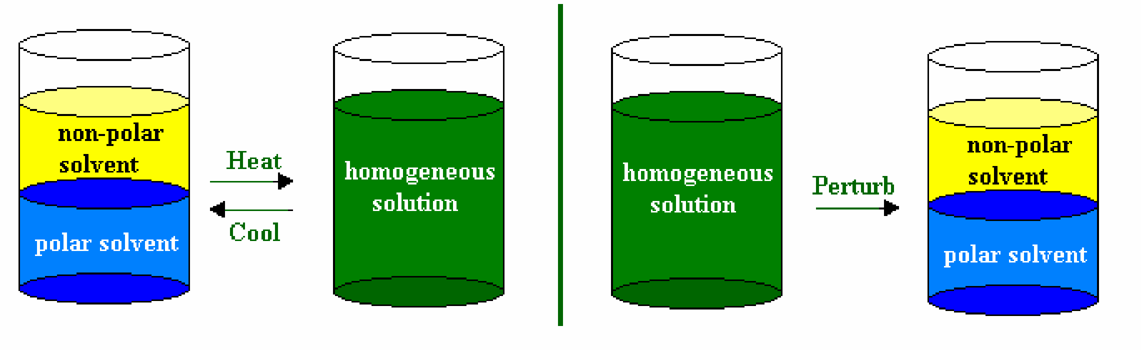


Figure 9. Thermomorphic (left) and latent biphasic (right) liquid/liquid separations.

mixtures exist as homogeneous solutions that are at the cusp of immiscibility. To induce a biphasic system for separations, the addition of solvents, salts, or even the product formation can perturb the solvents into an immiscible mixture. An example of this system is an equivolume mixture of heptane and 95% ethanol. At room temperature, heptane and 95% ethanol are miscible, but heptane and 90% ethanol-water are immiscible. Therefore, the transition from homogeneous to biphasic systems can be easily performed by the simple addition of a few drops of water to heptane and ethanol mixtures.

For these systems to function effectively in a catalytic system, the differential solubility of the products from the catalyst must occur as in the previously mentioned RCH/RP hydroformylation process. Our group and others have demonstrated that polymers can have highly selective solubility in thermomorphic and latent biphasic systems.[43] Depending on the polarity of the product formed, either non-polar and polar polymer supports can be used that have differential and highly phase selective solubility relative to the products formed (**Figure 10**). Much in the same way as the sulfonated

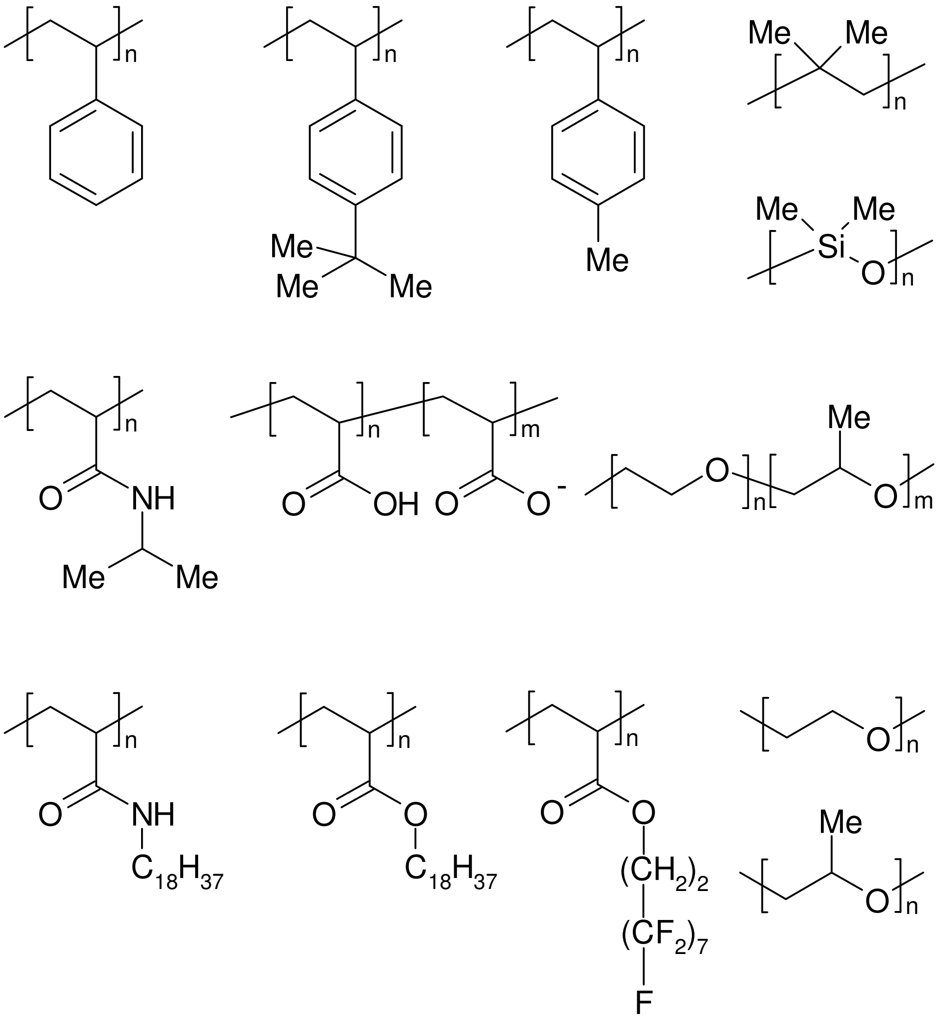
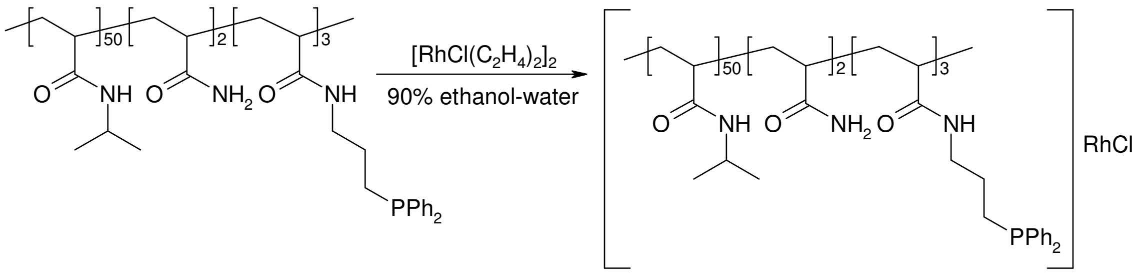


Figure 10. Soluble polymer supports.

residues of the triphenylphosphine ligands in the RCH/RH hydroformylation process allow for selective solubility of the rhodium catalyst in the polar phase, variation of the polymer's backbone or pendant groups can be used to afford supports that can be selectively soluble in various solvent mixtures. Estimation of a polymer's phase selective solubility in a biphasic solvent mixtures can be easily achieved without running a catalytic reaction by fluorescence or UV-vis spectroscopy of a solution of a polymer supported dye[44]. By measuring the intensity of a polymer-supported dye in the different solvent phases, a clear determination of the extent of partitioning of the polymer support in the two phases can be made. In many cases, selective solubilities that exceed 99.9 mol% of polymer in a polar or non-polar phase can be achieved.

The Bergbreiter group was the first to demonstrate the practicality of liquid/liquid thermomorphic separation techniques with soluble polymer-supported catalysts. In this first report, a poly(*N*-isopropylacrylamide) (PNIPAM) polymer support was prepared that contained an attached phosphine.[45] Complexation of a Rh (I) species produced a soluble polymeric Wilkinson's catalyst (**13**) (**Scheme 11**) which could be used in the hydrogenation of 1-octadecene or 1-dodecene. A heptane/90% ethanol-water solvent which was initially biphasic was used as the reaction mixture. On heating to 70 °C this solvent mixture became miscible to produce a homogeneous reaction mixture. Upon cooling, a biphasic system reformed and the non-polar products were recovered in the heptane phase. The polymer remained in the polar phase and the polymer rich ethanol phase was used up to four subsequent catalytic cycles with no loss in activity.

Scheme 11. PNIPAM Wilkinson's catalyst



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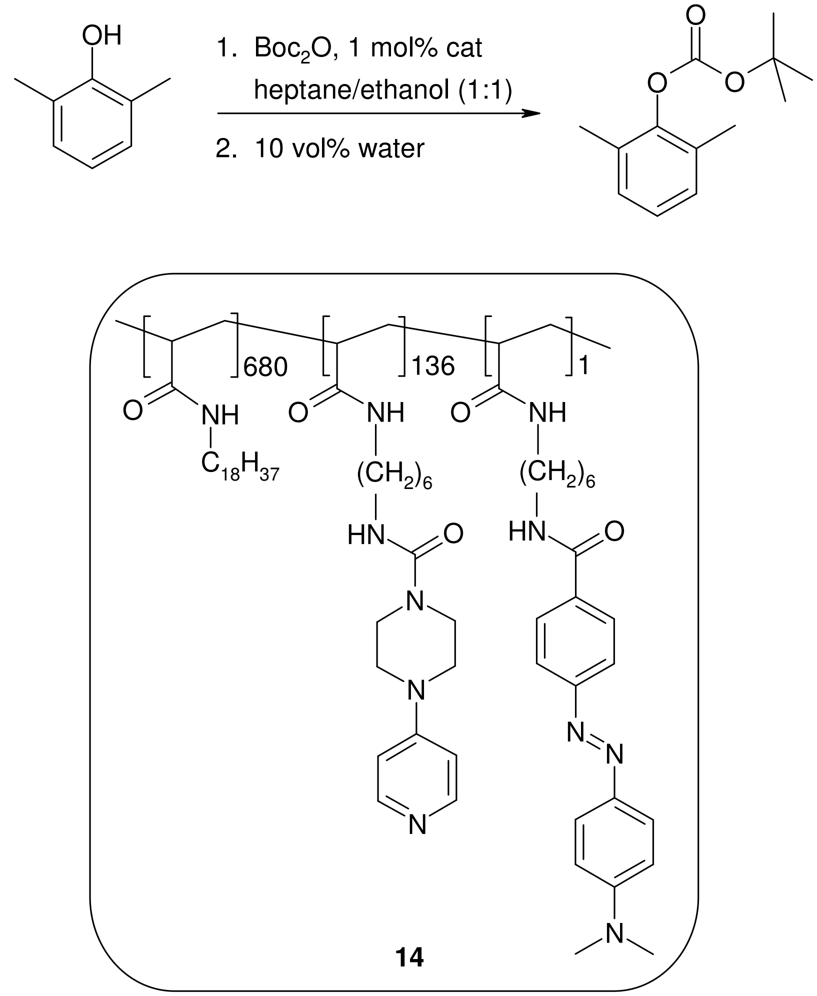
While the previous example provided a recyclable soluble polymer supported catalyst, this approach is limited to reactions where a non-polar product formed. An additional problem was that if reactions produced polar by-products, fouling of the polymer catalyst phase could occur. For these reasons, our group began to study modified polyacrylamides where the isopropyl pendant alkyl chain was replaced with more hydrophobic octadecyl groups. Incorporation of this pendant group allowed for the synthesis of a heptane soluble poly(*N*-octadecylacrylamide) (PNODAM) supported DMAP catalyst (**14**) which could be used in the acylation of 2,6-dialkylphenols (**Scheme 12**).[46] This polymer supported catalyst was successfully used in both thermomorphic and latent biphasic systems and was recycled up to six times with yields in the final cycles reaching 99% and with minimal leaching of the polymer support. The distribution of the polymer supports in these biphasic solvents was determined by the incorporation of *p*-methyl red, a UV-vis dye. The exact partitioning of the poly(*N*-octadecylacrylamide) (PNODAM) supported DMAP (**14**) catalyst in the heptane phase

Scheme 12. Acylation of phenols with PNODAM DMAP catalysts.



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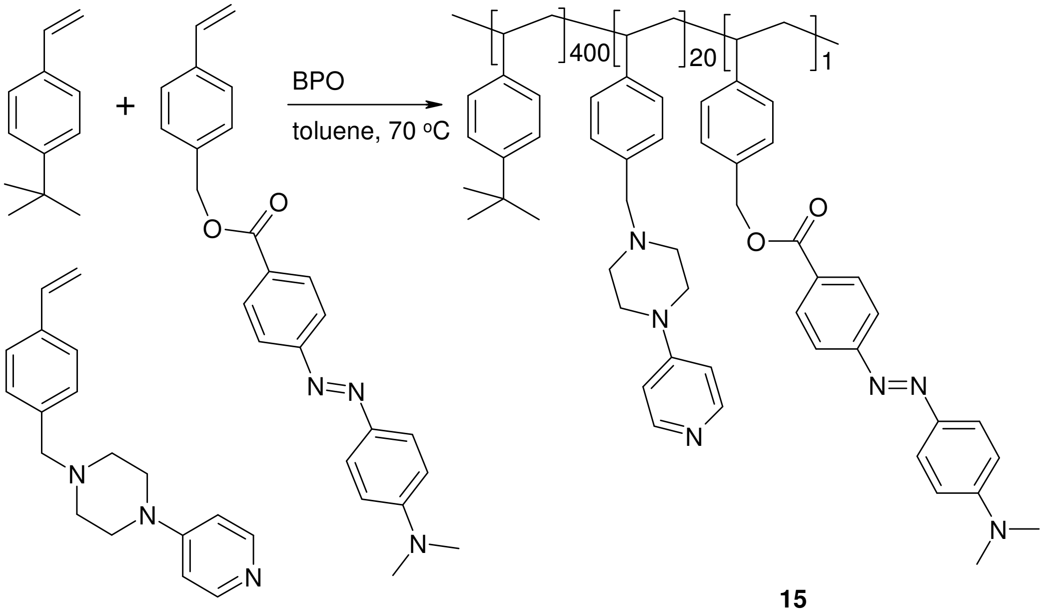
versus ethanol-water or *N,N*-dimethylformamide was ascertained by UV-vis inspection of the non-polar and polar solvent phases. Quantitative recovery of the polymer support from the products was indicated by the absence of any detectable absorbance of the polymer bound UV-vis dye in the product phases.

To eliminate the possibility of interactions of the polar functionalities of the polymer backbone of polyacrylamides in thermomorphic or latent biphasic polymer supported catalysis, I studied alternative non-polar polystyrene supports. Concurrent with my studies, reports by Plenio[47] described polymerization of 4-methylstyrene leading to poly(4-methylstyrene) supports that were soluble in cyclohexene and could be separated by liquid/liquid separations from dimethylsulfoxide. These alkylstyrene supports exhibited more useful solubility than polystyrene itself because polystyrene is insoluble in alkane solvents. This result had earlier been noted in earlier work by the Bergbreiter group where commercially available 4-*t*-butylstyrene was used to prepare very hydrocarbon soluble poly(4-*t*-butylstyrene) support. This heptane soluble poly(4-*t*-butylstyrene) polymer was used to prepare a supported DMAP catalyst (**15**) (**Scheme 13**) whose reactivity was similar to that of the previously described poly(*N*-octadecylacrylamide) supported DMAP catalyst. This poly(4-*t*-butylstyrene) catalyst

Scheme 13. PTBS bound DMAP catalyst



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was used in the same acylation reactions, with recycling of the catalyst for over 20 catalytic cycles. Quantitative recovery of the polymer support in heptane/90% ethanol-water latent biphasic systems was again determined by an absence of any absorbance of the polymer bound UV-vis dye in the polar product phase.[48]

Subsequent to these studies, other examples of these types of liquid/liquid separations of soluble polymers exist with thermomorphic,[45,49-55] latent biphasic,[46] and fluorous biphasic separations have been reported.[41,56-60] In all of these cases, separations use solvent mixtures where one phase selectively dissolves the polymer support.

In the chapters to follow, I will describe a series of studies wherein hydrocarbon soluble polymers suitable for support of catalysts are prepared and studied. These studies will include studies of modified polystyrene supports, studies of the solvation of pendant groups on polystyrene in miscible polar/non-polar solvent mixtures and strategies that use hydrocarbon-soluble polymers in catalysis.

CHAPTER II

LIQUID/LIQUID SEPARATIONS OF MODIFIED POLYSTYRENE SUPPORTS

Introduction

Soluble polymer supports impart macromolecular properties to supported materials while still maintaining the advantage of simple analysis. In many cases, soluble supported catalyst analogs are as active and as selective as the low molecular weight catalysts they replace.[43-60] Linear polystyrene is an useful soluble polymer because it is a direct analog of the more widely used insoluble cross-linked polystyrene. Incorporating functionality onto a soluble polymer like polystyrene can be accomplished by copolymerization of chloromethylstyrene and styrene, just as is done with cross-linked polystyrene (Merrifield's resin).[1] This leads to copolymers with reactive benzylic chloromethyl groups that can be substituted post-polymerization either directly with a catalyst or with a ligand that is then used to complex a catalyst. These catalysts attached to linear polystyrene dissolve in appropriate solvents to form a homogeneous solution. The extent of loading of functionality on soluble polystyrene can be adjusted by changing the ratio of co-monomers used in the polymerization reaction. An advantage of soluble-polystyrene is that a wide variety of functional groups can be introduced to the polymers using the chloromethyl modified polystyrene as a starting material.

Linear polystyrene has already been used by others in a variety of chemistry. However, precipitation or membrane filtration has typically been the only methods used for polymer and substrate/reagent/catalyst recovery.[3] The alternative approach discussed in this dissertation of using liquid/liquid separations has received less study.

While linear polymer supports can be separated from solution, there are problems with the existing polymer separation strategies. With solid/liquid separations (**Figure 11**), the polymer support is forced to precipitate from the reaction. Typically, the addition of solvents the polymer support is insoluble in will force the polymer out of solution. This makes filtration of the polymer support possible. However, this can require large volumes of solvent. Other methods to precipitate polymers from solution rely on critical solution temperatures of the polymer support. For example, polyethylene oligomers have an upper critical solution temperature (UCST). At temperatures higher than 100 °C in toluene, polyethylene oligomers are completely soluble. Upon cooling below this upper critical solution temperature, polyethylene oligomers will completely precipitate into a filterable solid polymer phase. Poly(*N*-isopropylacrylamide) is another polymer support that has a temperature dependent solubility. In this case aqueous solutions of the poly(*N*-isopropylacrylamide) are homogeneous at ambient temperature. This polymer support in solution exhibits a lower critical solution temperature (LCST) and can be heated to induce precipitation of the polymer support. While these critical solution temperatures are known for polystyrene,[61] no examples of using this method of precipitation exist for the quantitative recovery of polystyrene because these temperatures are inconvenient (e.g the LCST for polystyrene in toluene is above the melting point of polystyrene). In addition, while most prior examples where soluble polymers are used as catalyst supports involve their removal by a solid/liquid filtration,[62] some chemistry is not amenable to precipitation as a form of polymer recovery.[63]

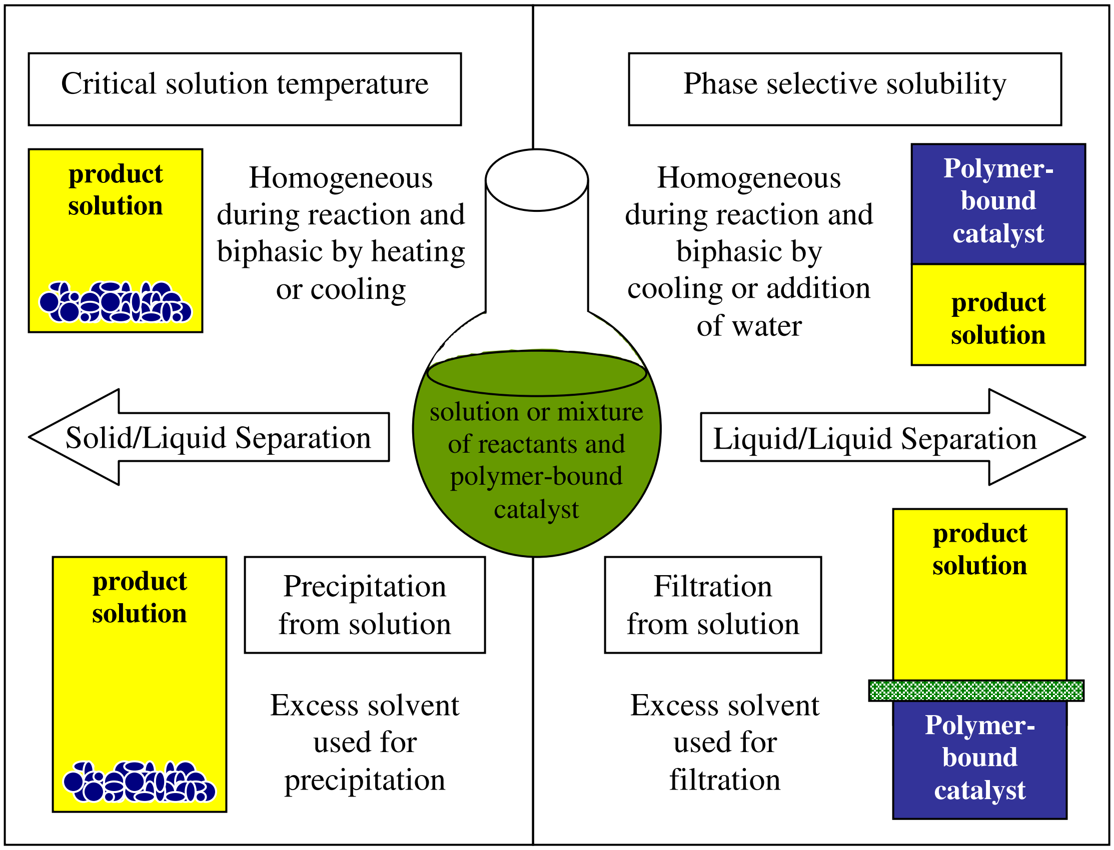


Figure 11. Possible strategies for separation of polymeric phases from products using solid or liquid biphasic separations.

Membrane filtration is an alternative way to recover a polymer that does not involve filtration of a solid polymer phase. This separation is based on the size of the macromolecule in solution and the fact that macromolecules are generally larger than the substrates and products in synthesis. In these cases, a liquid separation can be achieved that effectively separates the polymer from the product solution being filtered. Plenio, has used this methodology to remove poly(4-methylstyrene)-supported catalysts from the products of Sonogashira and Suzuki coupling reactions.[29] With this methodology, there is no need to invoke a phase change of the polymer support. Therefore, batch synthesis with precipitations can be avoided and the soluble polymer support can be used in systems for continuous reactions. While this method effectively can separate certain polymers such as the poly(4-methylstyrene), the size, structure, and polarity of the macromolecule as well as the properties of the solution being filtered greatly affect the ease of separations with membrane filtration.[35] For example, in a reported example where Heck catalysis was performed using poly(4-methylstyrene)-supported palladium complexes, degradation of the polymeric membrane precluded the use of membrane filtration as a practical method for effective separations of the catalyst from the products.

The Bergbreiter group has described alternative strategies that simplify reaction work-ups of soluble polymer supports that avoid precipitation and membrane filtration and allow for catalyst removal with a liquid/liquid separation as seen in **Figure 11**.[43-46,48,49] The key feature of all of these strategies is to carry out a reaction under homogeneous conditions to eliminate the liquid/liquid and liquid/solid limitations of biphasic or heterogeneous reactions. Liquid/liquid biphasic conditions are only established at the end of the reaction at the separation step.

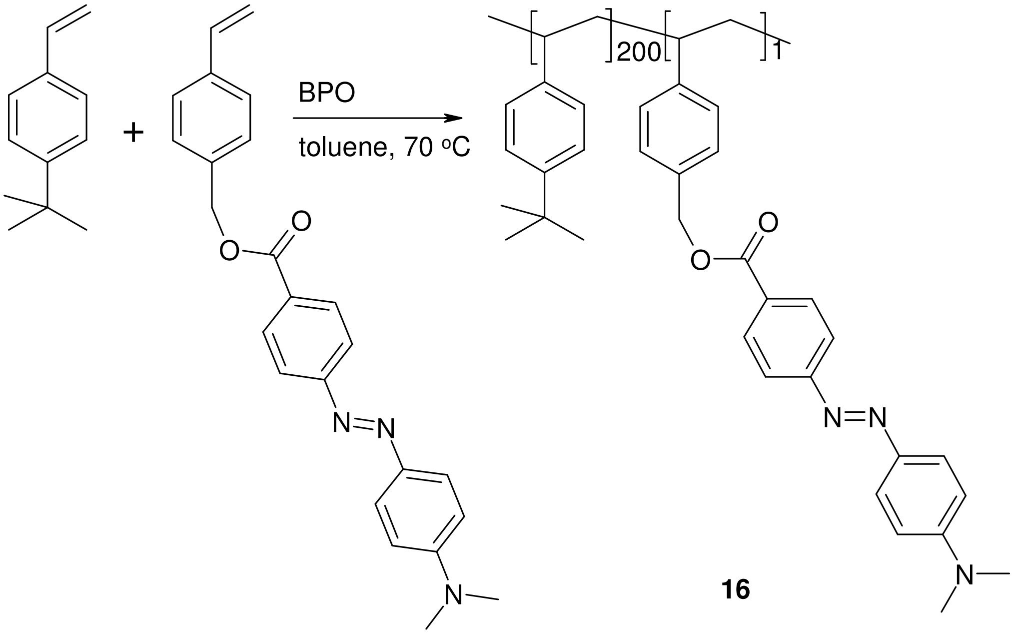
One of the strategies involves a latent biphasic system where two or more solvents are miscible but at the cusp of miscibility. An example of such a latent biphasic reaction scheme would incorporate an equal volume of heptane and ethanol. Such a mixture is monophasic at room temperature. Linear polymers with supported catalysts can be dissolved in this mixture and reactions can be then performed under homogeneous conditions. The addition of greater than 5% by volume of water induces a phase separation as seen in **Figure 11**. In this chemistry, one could use either a polar phase soluble polymer or a non-polar phase soluble polymer. However, since organic products are typically decorated with functional groups and are more selectively soluble in the polar phase of this final biphasic liquid/liquid mixture, polymers soluble in the heptane phase are needed to effectively separate them from the polar product phase.

Alternatively heptane/ethanol/water mixtures with heptane soluble polymer supports can be used in non-polar thermomorphic systems schematically shown in **Figure 11**. For example, under conditions where the initial volume ratio of heptane/ethanol/water is 10/9/1, the initial solvent mixture is biphasic at room temperature. Heating this mixture above 70 ˚C produces a monophasic solution that separates back into a biphasic system upon cooling to room temperature.

Other solvent combinations other than the heptane/ethanol systems discussed are also available which allow for a range of possible polarities and separation temperatures to be used in these sorts of separations.[42,64] For example, an equivolume mixture of heptane and *N, N*-dimethylformamide (DMF) is biphasic at room temperature but thermomorphically forms a miscible solution on heating. Cooling reforms the original biphasic mixture of a heptane-rich and DMF-rich phase. In this instance, the solvents are all aprotic unlike the heptane/ethanol systems.

As previously mentioned, separations from typical products in these liquid/liquid systems requires the use of heptane soluble polymers to separate them from the polar products. Unsubstituted polystyrene is not the most suitable polymer for use in a liquid/liquid biphasic separation because it is not soluble in heptane. Thus, it is necessary to prepare a modified polystyrene support if heptane solubility is to be achieved. To make polystyrene soluble in heptane, previous workers in the Bergbreiter group used the commercially available 4-*t*-butylstyrene as a monomer to prepare a substituted heptane-soluble polystyrene. To test the phase selective solubility of this polymer, a (10:1) copolymer of 4-*t*-butylstyrene and 4-vinzylbenzyl *p*-methyl red was synthesized (**16**) (**Scheme 14**). In this copolymer, the attached dye serves as a catalyst

Scheme 14. Synthesis of poly(4-*t*-butylstyrene) with attached UV-dye



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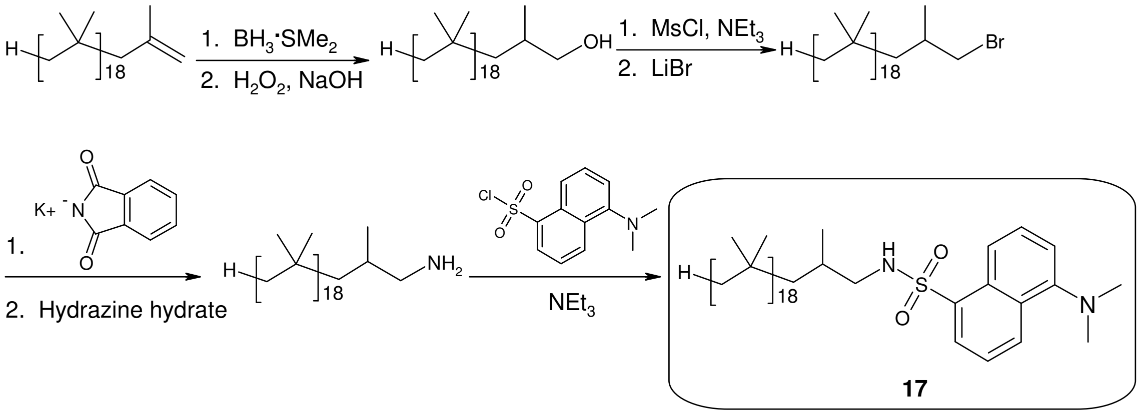
surrogate, testing separations separately from studying reaction chemistry. The results based on UV-visible spectroscopic analysis of each phase after a biphasic separation showed that poly(4-*t*-butylstyrene) (**16**) as a support has a high, >99%, selectivity for the heptane-rich phase of a heptane/90% ethanol-water mixture.[48] This extent of separation is sufficient for the separation of common polar products and by-products prepared in most syntheses from the polymer support. High phase selective solubility of this support is seen in other solvent mixtures such as heptane/*N, N*-dimethylacetamide and heptane/*t*-butyl alcohol.[44]

Polymers with pendant hydrophobic groups like the alkyl group in poly(4-*t*-butylstyrene) copolymers with pendant azo dyes are one sort of phase selectively soluble polymer that can be separated as a heptane solution under latent biphasic or thermomorphic conditions. Such polymers contain functionality as pendant functional groups randomly incorporated along the polymer chain.

Another sort of polymeric material that can be separated in either a non-polar (e.g. heptane) or a polar solution would be a terminally functionalized polymer. Several examples have been described.[3,65] Terminally functionalized polyisobutylene oligomers are one example of a terminally functionalized heptane-soluble polymer. In this case, the polymer is available with a terminal vinyl group which can be modified to incorporate a dye like a dansyl fluorophore which can be used to determine the solubility preference of this polymer in heptane/90% ethanol-water (**Scheme 15**). In this case, when a polyisobutylene oligomer (**17**) was dissolved in heptane and added to an equivolume of 90% ethanol-water and this biphasic system was heated above 70 °C, a homogeneous solution formed. Upon cooling, two phases reform. The measurement of the fluorescent intensity of the oligomer supported fluorophore in the two phases indicated a high phase selective solubility of the polyisobutylene 1000 Da oligomer in heptane (99.70%) versus 90% ethanol-water mixture (0.3%).

Scheme 15. Synthesis of fluorescently labeled polyisobutylene **17**.



Possible problems with liquid/liquid biphasic polymer recovery systems are the loading and nature of the attached substrates. While the polymer can exhibit good non-polar solubility, if the attached molecules are too polar or if they are too large representing more than ca. 5-10 mol% or weight percent of the polymer, they could diminish the heptane phase selective solubility of the polymer.[3] It is postulated that these issues may be minimized by increasing the size of the non-polar polymer or by increasing the non-polar character of the polymer support – a hypothesis I have investigated as discussed below.

To explore possible polymer modifications for heptane-soluble polystyrenes, we examined the effects of changing the pendant *t*-butyl group of linear polystyrene with more hydrophobic *n*-alkyl groups. Various *n*-alkylstyrene monomers and polymers were synthesized and labeled post-polymerization with a fluorescent dye. The heptane phase selective solubility of these supports was then determined in both latent biphasic and thermomorphic solvent systems by comparison of the ratio of fluorescence intensity of the two phases. The effects these *n*-alkyl substituents have on the non-polar phase selective solubility of polystyrene supports as well as ways to improve separations are described in this chapter.

Results and Discussion

As mentioned previously, the synthesis of a non-polar phase selectively soluble polymer support can be achieved with the commercially available monomer 4-*t*-butylstyrene. These modified polystyrene supports had a phase selective solubility of > 1000:1 (99.9 %). While their phase selective solubility was good, it was likely that with other more polar catalysts or ligands, or that with other solvent systems that their phase selective solubility could drop. Indeed, in cases where the *p*-methyl red was in its conjugate acid form, it was possible to visually see some leaching of the support into the polar phase. To develop a more phase selectively soluble polymer, we sought to both change the polymer and to change the probe we used to monitor phase selective solubility.

The approach that was taken had several features. First, we designed what we thought would be more heptane soluble analogs of poly(4-*t*-butylstyrene). Second, we designed materials that could incorporate a probe of phase selective solubility post-polymerization as the loading of the dye onto the polymer would then mimic the chemistry that would likely be used to load a catalyst, ligand, substrate, reagent, or sequestrant. Finally, while *p*-methyl red dyes work as a convenient visual probe, the extinction coefficient of this dye is such that it is difficult to quantitatively measure phase selective solubilities of greater than 1000:1. Thus, we designed a dansyl fluorescent dye that could be attached to a substituted polystyrene by nucleophilic substitution post-polymerization and had a linear relationship of fluorescence intensity versus concentration at low concentrations (µM to nM) as is seen in **Figure 12**. As is discussed below, a series of substituted polystyrenes including poly(4-*n*-butylstyrene), poly(4-*n*-dodecylstyrene), and poly(4-*n*-octadecylstyrene) were prepared from their monomers and the polymers were tested under various thermomorphic and latent biphasic conditions using heptane/*N, N*-dimethylacetamide and heptane/ethanol-water systems to determine the extent of polymer phase selective solubility in these solvent systems.

The synthesis of the various 4-*n*-alkylstyrene monomers was carried out as shown in **Scheme 16.** Since Friedel-Crafts alkylation of benzene would likely generate a mixture of isomers due to rearrangement of the intermediate carbocation, alkylation of the aromatic ring was accomplished through coupling of an aryl Grignard reagent to a primary alkyl bromide using ferric chloride as a catalyst. While this synthesis could be reportedly extended to secondary alkyl groups, our work was limited to incorporating *n*-alkyl substituents. This synthesis proved much simpler experimentally than two

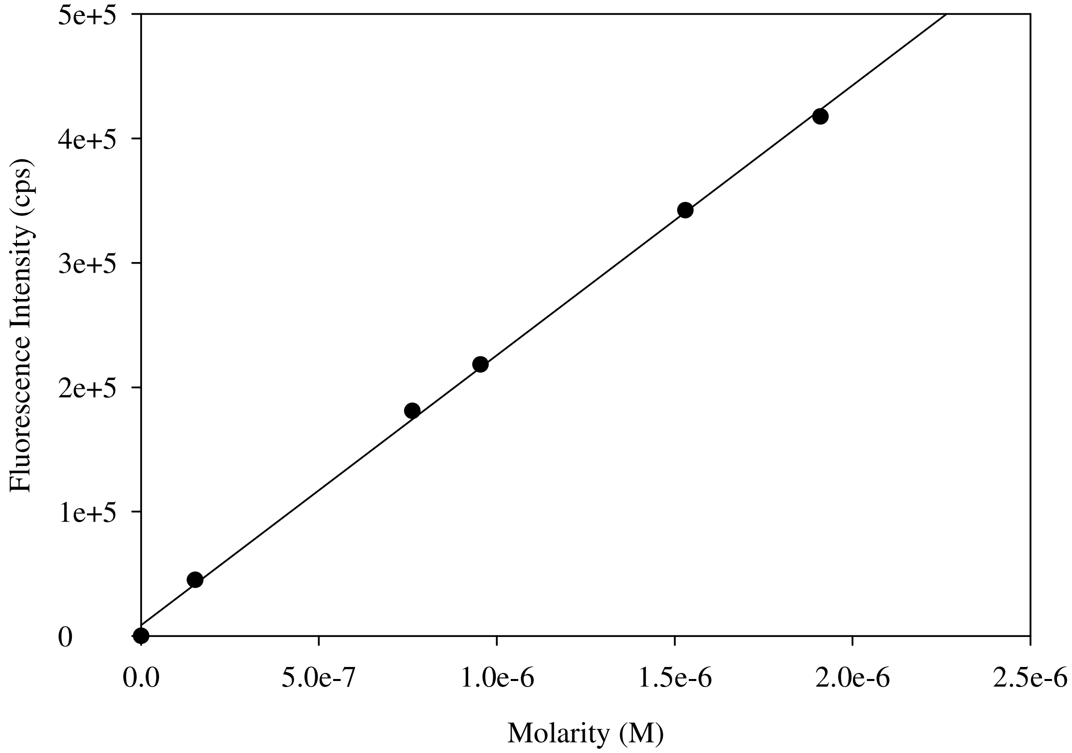
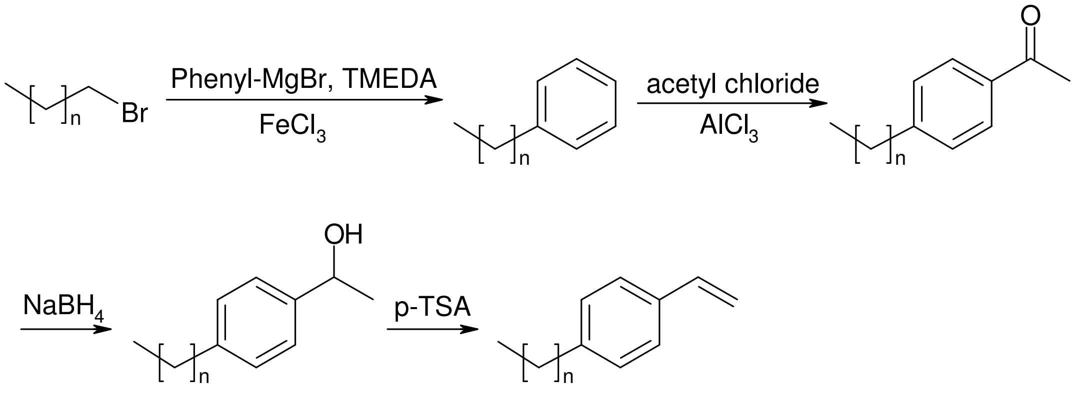


Figure 12. Calibration curve for the *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide fluorescence intensity versus concentration as a heptane solution. An R^2 value of 0.996 was obtained using the software provided in Microsoft Excel®.

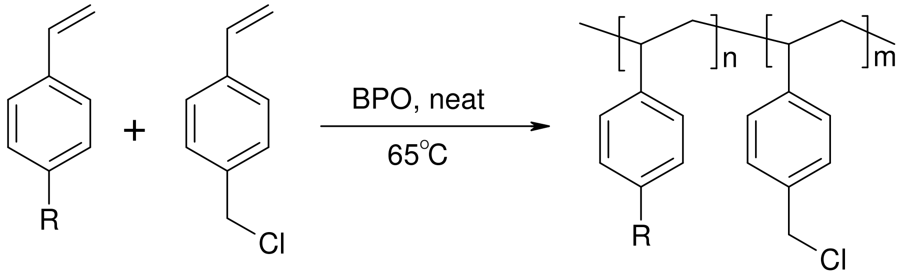
Scheme 16. Synthesis of 4-*n*-alkylstyrenes



alternative routes involving Gilman reaction of alkyllithium reagents with benzyl chloride or cuprate coupling of phenyllithium with alkyl halides. Once the *n*-alkylbenzene was prepared, a second series of reactions were used to incorporate a two-carbon substituent that could ultimately be transformed into the vinyl moiety. This was achieved *via* Friedel-Crafts acylation of the newly formed *n*-alkylbenzenes with acetyl chloride. The 4-*n*-alkylacetophenone products of this reaction were reduced to the corresponding alcohol by treatment with sodium borohydride. Acid catalyzed dehydration of the alcohol produced the desired styrene.

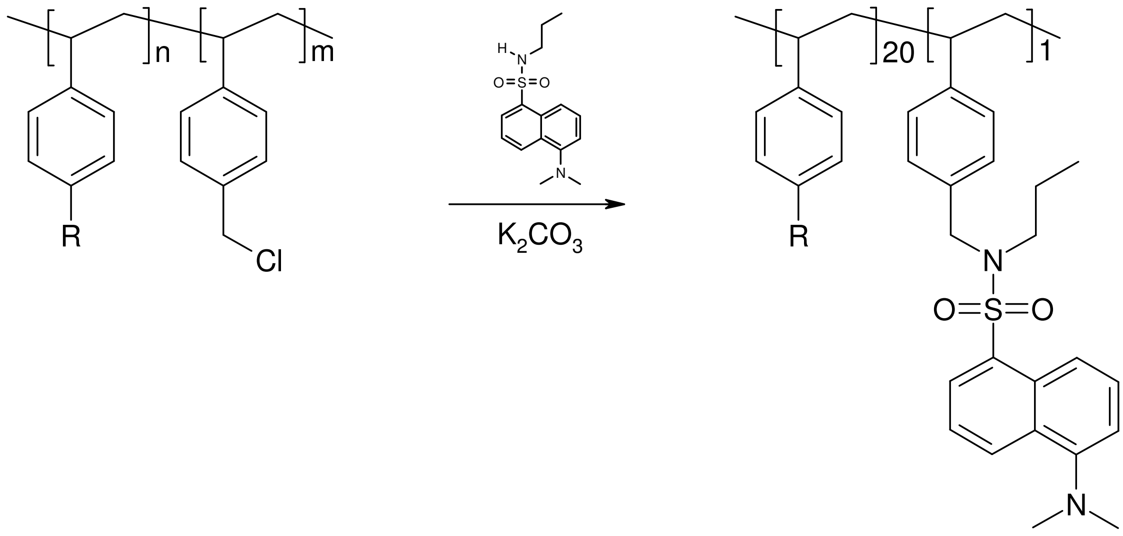
Bulk copolymerization of these 4-*n*-alkylstyrenes with 4-vinyl benzyl chloride was achieved using benzoyl peroxide as the radical initiator to produce the desired substituted polystyrenes (**Scheme 17**). For example, in the preparation of 4-*n*-butylstyrene copolymers, a 10:1 molar ratio of 4-*n*-butylstyrene: 4-vinyl benzyl chloride was added to a dry Schlenk tube with benzoyl peroxide. After degassing the sealed flask by four cycles of freeze/pump/thaw, the reaction was heated at 65 ˚C for 24 h. Visual inspection of the now solid reaction mixture indicated polymerization had occurred. The solid poly(4-*n*-butylstyrene)-co-poly(4-vinyl benzyl chloride) could be dissolved in chloroform and precipitated into methanol to remove low molecular weight oligomers and unused monomer. Analysis of this copolymer by ^{1}H NMR indicated a 13:1 poly(4-*n*-butylstyrene)-co-poly(4-vinyl benzyl chloride) copolymer based on comparison of the pendant benzylic protons (2.5 ppm) of the *n*-alkylstyrene repeat unit with the polymeric pendant benzylic protons (4.5 ppm) of the 4-vinyl benzyl chloride repeat unit. Gel permeation chromatography of the copolymer indicated a number average molecular weight of 20000 Da with a polydispersity index (M_w/M_n) of 2.3.

Scheme 17. Synthesis of poly(4-*n*-alkylstyrene) copolymers.

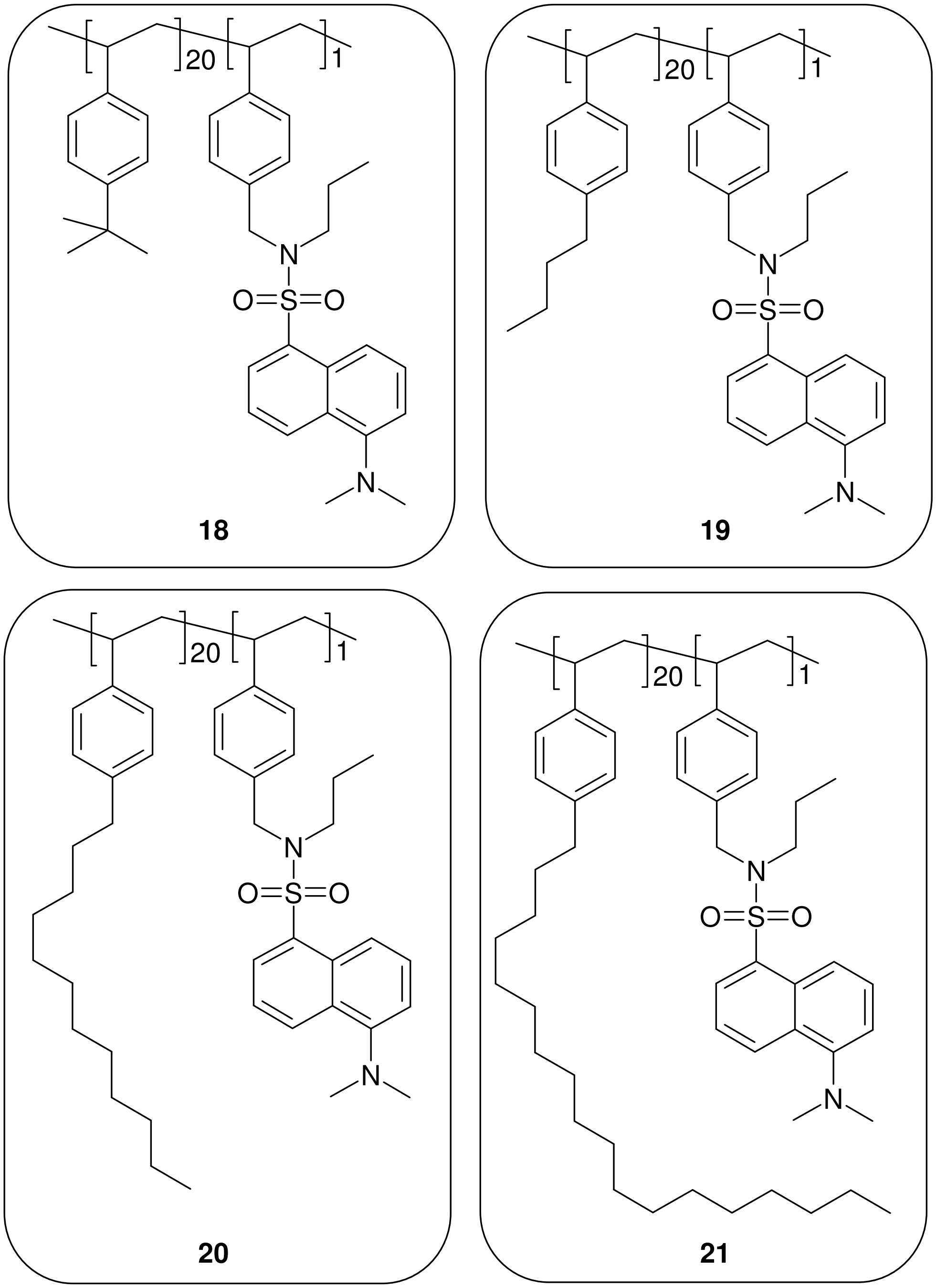


As noted above, we typically have used labeled polymers where a dye serves as a catalyst surrogate to measure polymer phase selective solubility in liquid/liquid mixtures.[44,48,66] Since fluorescence is a more sensitive technique than UV-visible spectroscopy, we prepared a fluorescence dye that could be incorporated into the copolymer products of **Scheme 17** by a nucleophilic substitution reaction. A dye that met this requirement, *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide, was synthesized according to a literature procedure.[67] This fluorophore was then attached to various soluble polystyrene supports (**Scheme 18**) by carrying out a nucleophilic substitution reaction in a thermomorphic heptane/N, N-dimethylformamide solvent mixture at 80 ˚C. The nucleophilic substitution reaction was performed under homogeneous conditions. Unreacted fluorophores that were not soluble in heptane were separated in the DMF phase after the reaction. The *N*-propyl-dansyl-labeled polystyrene

Scheme 18. Attachment of fluorescent probe to polymer



was soluble in the heptane-rich phase. The substituted polystyrenes (**18-21**) that were prepared in this way are shown in **Figure 13**. By visual inspection, heating a biphasic heptane-DMF mixture that contained these polymers to 80 °C produced a completely



18 **19** **20** **21**

***Figure 13*.** Fluorescently labeled poly(4-alkylstyrene) supports.

homogeneous solution. After cooling, this thermomorphic solvent mixture separated into two phases.

Next we quantitatively measured the non-polar phase selective solubility of these polymers. All polymers and solvent systems were first visually tested to insure that they reversibly form monophasic and biphasic systems. Then in the actual quantitative analysis, the polymer support was dissolved in heptane and either DMF or ethanol were then added. A 2:1 (vol:vol) mixture of these non-polar:polar solvents was chosen as the optimal solvent composition to form homogeneous and biphasic systems for testing of the phase selective solubility of these polymer supports in both the thermomorphic and latent biphasic systems.

As previously mentioned, the (10:1) copolymer of 4-*t*-butylstyrene and 4-vinyl benzyl *p*-methyl red (**16**) exhibited greater than 99% heptane selectivity in biphasic/monophasic systems (heptane/90% ethanol-water).[60] This polymer support was therefore chosen as a point of comparison for this study. The phase selective solubility of the *N*-propyl-dansyl labeled poly(4-*t*-butylstyrene) (**18**) under latent biphasic conditions was measured by mixing 8 mL of a heptane solution of this polymer with 4 mL of ethanol. After stirring for 30 min, the homogeneous solution was induced to form a biphasic system by the addition of 0.4 mL water (10 vol% based on ethanol). Upon separation of the layers, the heptane phase was mixed with a fresh sample of ethanol to reform a miscible solution. Addition of water to this second solution again produced a biphasic mixture. Repetition of this cycle of dissolution/phase separation was carried out three times. As can be in seen **Table 1**, the resulting heptane phase selective solubility measured is consistent with previous investigations. The selectivity seen for this heptane/ethanol-water system was 30000/1 with the poly(4-*t*-butylstyrene) copolymer (**18**) preferring the heptane phase.

Next, a polymer support that had a varied pendant group was studied. Using *N*-propyl-dansyl-labeled poly(4-*n*-butylstyrene) (**19**) in the same solvent as described above, we measured a phase selective solubility of 100000/1 phase preference for heptane over 90% ethanol-water.

Table 1. Phase selective solubility measurements of poly(4-butylstyrene) supports **18** & **19** in heptane/90% ethanol-water.[a]

Poly(4-*t*-butylstyrene) (**18**)			Poly(4-*n*-butylstyrene) (**19**)		
Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]	Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]
1	3.7×10^{-7}	3000/1	1	1.1×10^{-8}	100000/1
2	5.7×10^{-8}	20000/1	2	1.6×10^{-8}	100000/1
3	4.4×10^{-8}	30000/1	3	7.7×10^{-9}	100000/1
4	3.8×10^{-8}	30000/1	4	1.1×10^{-8}	100000/1

[a] The polymer supports were prepared as 1.2 mM (**18**) and 1.3 mM (**19**) solutions of the polymer-bound dansyl in heptane. The solvent volume ratios in the heptane/ethanol/water solvent mixtures were 2/1/0.1.

[b] Calculated using the calibration curve in **Figure 12** and the fluorescence intensity in the polar phase. The error in the fluorescence intensity of the dilute polar phases is expected to be (±) 5% of the measured value.

[c] Calculated as the ratio of the fluorescence intensity of the non-polar/polar phase.

Altering the solvent system could produce different results. Indeed, when the experiments above were repeated for both the *N*-propyl-dansyl-labeled poly(4-*t*-butylstyrene) (**18**) and poly(4-*n*-butylstyrene) (**19**) increasing the quantity of water used to induce phase separation from 0.4 mL to 0.8 mL (10% to 20% by volume relative to the ethanol), both polymers behave in the exact same manner (**Table 2**). Under this second set of conditions, both polymers have a heptane phase selective solubility of 1000000/1 which is a selectivity that is at the limit of detection in this fluorescence assay.

While the phase selective solubility of the polymer supports (**18 & 19**) could be increased by the addition of water, it was of interest to determine if the phase selective solubility could be decreased by the use of a reduced amount of water in subsequent cycles. In cycles 1-4 of **Table 3**, 8 mL of heptane was used to dissolve the poly(4-*n*-butylstyrene) support (**19**) and 4 mL of ethanol was added to produce a homogeneous solvent system. Addition of 0.8 mL of water produced a biphasic heptane/80%-ethanol

Table 2. Phase selective solubility measurement of poly(4-butylstyrene) supports **18** & **19** in heptane/80% ethanol-water.

Poly(4-*t*-butylstyrene) (**18**)			Poly(4-*n*-butylstyrene) (**19**)		
Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]	Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]
1	1.0×10^{-8}	100000/1	1	7.6×10^{-9}	200000/1
2	7.9×10^{-9}	100000/1	2	1.6×10^{-9}	800000/1
3	2.1×10^{-9}	300000/1	3	9.7×10^{-10}	1000000/1

[a] The polymer supports were prepared as 1.2 mM (**18**) and 1.3 mM (**19**) solutions of the polymer-bound dansyl in heptane. The solvent volume ratios in the heptane/ethanol/water solvent mixtures were 2/1/0.1.

[b] Calculated using the calibration curve in **Figure 12** and the fluorescence intensity in the polar phase. The error in the fluorescence intensity of the dilute polar phases is expected to be (±)5% of the measured value.

[c] Calculated as the ratio of the fluorescence intensity of the non-polar/polar phase.

water system. Removal and recycling of the heptane phase and repetition of this addition of ethanol and then water produced an optimal heptane phase selective solubility of 1000000/1 as seen in the previous experiment. At this point, this heptane phase was used in cycles 5-8 with the addition of 4 mL of ethanol, but with addition of 0.4 mL of water to induce biphasic separations. The heptane phase selective solubility of the polymer support (**19**) was gradually reduced to 100000/1 in cycle 8.

The gradual increase in phase selective solubility in cycles 1-4 shown in **Table 3** presumably is due in part fractionation of the polymer. The initial polymer support, based on its polydispersity index, contains a range of polymers of varying molecular

Table 3. Phase selective solubility measurements of poly(4-*n*-butylstyrene) **19** in 80% and 90% ethanol-water mixtures.

Heptane:80% EtOH / 2:1 vol:vol			Heptane:90% EtOH / 2:1 vol:vol		
Cycle[a]	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]	Cycle[d]	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]
1	2.8×10^{-8}	40000/1	5	1.1×10^{-8}	100000/1
2	7.5×10^{-9}	200000/1	6	1.6×10^{-8}	100000/1
3	1.4×10^{-9}	800000/1	7	7.7×10^{-9}	100000/1
4	9.7×10^{-10}	1000000/1	8	1.1×10^{-8}	100000/1

[a] The polymer support was prepared as a 1.3 mM solution of the polymer-bound dansyl in heptane. The solvent volume ratios in the heptane/ethanol/water solvent mixtures were 2/1/0.2.

[b] Calculated using the calibration curve in **Figure 12** and the fluorescence intensity in the polar phase. The error in the fluorescence intensity of the dilute polar phases is expected to be (±)5% of the measured value.

[c] Calculated as the ratio of the fluorescence intensity of the non-polar/polar phase.

[d] The solvent volume ratios in the heptane/ethanol/water solvent mixtures were 2/1/0.1.

size. As the experiments in **Table 3** progress from cycle to cycle, some of lower molecular weight oligomers of the polymeric support that have a lower phase selective solubility may be lost from the heptane solution. This would explain the slight increase in phase selective solubility in each subsequent cycle, as the remaining higher molecular weight polymer species would be more selective to the non-polar phase. Another factor is that the polymeric heptane phase is becoming saturated with more polar solvent molecules such as water from cycle 1 to cycle 4. When a point is finally reached where the complete saturation of the polymeric heptane solution is achieved, the optimal amount of polar solvent molecules is present to produce the most ideally separating biphasic mixture. This latter explanation would further account for the slow decrease in the polymer support's heptane phase selective solubility when changing the ethanol-water solutions from 80% to 90% by volume. In these experiments, the heptane phase of cycle 4 is presumably saturated with a 80% ethanol water mixture. After separation of the heptane phase of cycle 4, the addition of fresh ethanol again forms a homogeneous solution which presumably contains trace amounts of water from the saturated heptane phase. Addition of the 0.4 mL of water produces a biphasic heptane/ethanol-water solvent system. This residual water from the heptane phase should be more phase selectively soluble in ethanol over heptane. As subsequent cycles are performed, the ethanolic phase slowly abstracts the small amount of water that is saturating the heptane phase. After two subsequent cycles, a point is finally reached where the all the residual water from cycles 1-4 are sufficiently abstracted and the heptane phase selective solubility of the polymer support reflects a heptane/90% ethanol-water biphasic separation rather than a heptane/80% ethanol-water biphasic separation.

The heptane phase selective solubility achieved with the poly(4-butylstyrene) supports **18** & **19** in the heptane/90% ethanol-water latent biphasic systems was more than adequate even with the fluorescently tagged polymers; therefore, further investigations with the more hydrophobic supports was unnecessary. However, a mixed solvent system that would produce lower heptane phase selective solubility of the polymer supports could also be studied and such a system could be a better way to determine the exact effects the various pendant *n*-alkyl groups had on the heptane phase selective solubility of the modified polystyrene supports.

As previously stated, thermomorphic systems of heptane/*N, N*-dimethylformamide (DMF) have been used in non-polar polymer separations in catalytic reactions. However, the heptane phase selective solubility of the polymer supports was found to decrease upon switching from ethanol to *N, N*-dimethylformamide as the polar solvent. In the studies of solvent mixtures below, we found that *N, N*-dimethylacetamide (DMA) was experimentally a better choice as a polar solvent than DMF. Heptane/DMA solvent mixtures produced the desired thermomorphic behavior for the selectivity measurements with the all polymer supports used. All polymer supports **18-21** studied were added to an initially biphasic mixture, which upon heating resulted in a homogeneous solvent system.

Poly(4-*t*-butylstyrene) (**18**) was again used as a standard for this series of polymer solvent selective solubility measurements. The heptane phase selective solubility of this support was likely not to be higher than other more hydrophobically modified polystyrene supports under investigation. Dissolution of the polymer to be studied in 8 mL of heptane and addition of this solution to a flask containing 4 mL *N, N*-dimethylacetamide formed a biphasic solvent system. After heating the stirred solvent mixture to 80 °C, a homogeneous solvent system developed. Cooling the solvent system induced separation of the phases, and the heptane phase selective solubility of the polymer support was determined. The heptane layer was once again subjected to the same conditions until a point was reached where the heptane phase selective solubility of the polymer support was consistent cycle to cycle. The poly(4-*t*-butylstyrene) support **18** exhibited a limiting value for non-polar phase selective solubility of 99.8787% (**Table 4**). The same experimental conditions were repeated for poly(4-*n*-butylstyrene) **19**. The results showed the polymer support exhibiting an optimal non-polar phase selective solubility of 2000/1.

One possible explanation for this increase in non-polar phase selective solubility in switching from the *t*-butyl to *n*-butyl pendant groups is the ease of solvation of the polymer supports. The poly(4-*n*-butylstyrene) **19** may allow for better hydrophobic solvation of the polymer support as compared to the poly(4-*t*-butylstyrene) **18**. Studies of the LCST behavior using *n*-propyl versus *i*-propyl poly(*N*-alkylacrylamide)s in our group has previously shown that *n*-alkyl groups behave like more hydrophobic groups. Regardless of the origin of the effect though, a clear difference was exhibited between these two polymer supports. This suggested that further investigations of the heptane phase selective solubility with the more hydrophobic long chain alkyl groups would yield interesting results.

Table 4. Phase selective solubility measurement of poly(4-butylstyrene) supports **18** & **19** in heptane/DMA.[a]

Poly(4-*t*-butylstyrene) (**18**)			Poly(4-*n*-butylstyrene) (**19**)		
Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]	Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]
1	8.2×10^{-6}	100/1	1	4.0×10^{-6}	500/1
2	4.5×10^{-6}	400/1	2	1.2×10^{-6}	1000/1
3	2.0×10^{-6}	700/1	3	1.5×10^{-6}	1000/1
4	1.7×10^{-6}	800/1	4	1.3×10^{-6}	2000/1
5	1.8×10^{-6}	800/1	5	6.5×10^{-7}	1000/1

[a] The polymer supports were prepared as 1.4 mM (**18**) and 1.5 mM (**19**) solutions of the polymer-bound dansyl in heptane. The solvent volume ratios in the heptane/*N*, *N*-dimethylacetamide solvent mixtures were 2/1. The solutions were made homogeneous by the heating of the solvent mixtures above 80 °C and again biphasic by cooling the solutions to room temperature.

[b] Calculated using the calibration curve in **Figure 12** and the fluorescence intensity in the polar phase. The error in the fluorescence intensity of the dilute polar phases is expected to be (±) 5% of the measured value.

[c] Calculated as the ratio of the fluorescence intensity of the non-polar/polar phase.

Poly(4-*t*-butylstyrene) **18** exhibited a non-polar phase selective solubility of 800/1 which was slightly worse than that observed in the previous experiment with heptane/ethanol systems. As water is theorized to be a driving force for optimal separations, it was envisioned that manipulation of the solvent composition could further improve the preference of poly(4-*t*-butylstyrene) **18** for the non-polar phase. After examining the phase selective solubility of this support in the previous solvent system, the heptane phase was subjected to the same thermomorphic solvent conditions. Upon cooling 0.08 mL water (2% by volume of water relative to *N, N*-dimethylacetamide) was added and the resulting phases were separated and measured for the partitioning of the polymer support. An order of magnitude increase in selectivity was achieved with this addition of water, with the results depicted in **Table 5** with a selectivity of roughly 7000/1 versus 800/1 phase preference of the polymer support for heptane over *N, N*-

Table 5. Phase selective solubility measurement of poly(4-*t*-butylstyrene) support **18** in heptane/DMA-water.[a]

Heptane/DMA			Heptane/98% DMA-Water		
Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]	Cycle[d]	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]
1	7.8 x 10^{-6}	100/1	6	8.0 x 10^{-8}	7000/1
2	4.2 x 10^{-6}	400/1	7	7.0 x 10^{-8}	7000/1
3	1.9 x 10^{-6}	700/1			
4	1.6 x 10^{-6}	800/1			
5	1.7 x 10^{-6}	800/1			

[a] The polymer support was prepared as a 1.4 mM solution of the polymer-bound dansyl in heptane. The solvent volume ratios in the heptane/*N*, *N*-dimethylacetamide solvent mixtures were 2/1. The solutions were made homogeneous by the heating of the solvent mixtures above 80 °C and again biphasic by cooling the solutions to room temperature.

[b] Calculated using the calibration curve in **Figure 12** and the fluorescence intensity in the polar phase. The error in the fluorescence intensity of the dilute polar phases is expected to be (±) 5% of the measured value.

[c] Calculated as the ratio of the fluorescence intensity of the non-polar/polar phase.

[d] The same procedure was followed as in previous cycles except for the addition of water upon cooling to adjust the final solvent ratio of heptane/*N*, *N*-dimethylacetamide/water to 2/1/0.02.

dimethylacetamide. This would indicate that in cases where the reaction was not sensitive to water, an improvement in recovery could be attained simply by the addition of a small amount of water.

The non-polar phase selective solubility of other 4-*n*-alkylstyrene polymer supports **20 & 21** was investigated utilizing the same thermomorphic heptane/*N, N*-dimethylacetamide system described above to determine the effect of larger *n*-alkyl groups. As in the previous experiments, the polymer supports were cycled through a series of separations until a limiting phase selective solubility was observed. As can be seen from the results in **Table 6**, there is an increase in the preference of the polymer support for the heptane phase as the pendant alkyl chain is lengthened. As can be seen in **Figure 14**, the concentration of the polymer-supported dansyl in the polar phase of these biphasic separations is greatly diminished with the supports **20** & **21**.

The results above establish that the hydrophobicity of the polymer support can measurably affect the phase selective solubility of separations of these polymer supports in the heptane phase of a thermomorphic system. This effect can be thought of in much the same way as the addition of water in previous results with the latent biphasic and thermomorphic separations. In the previous experiments with poly(4-*t*-butylstyrene) **18**, the polar phase of the solvent systems were made increasingly polar leading to better separations polymeric heptane phase from the polar phase. Similarly, the non-polar character of the heptane phase was increased in these systems. Instead of addition of a small molecule into the solution, the molecule was built into the polymer support,

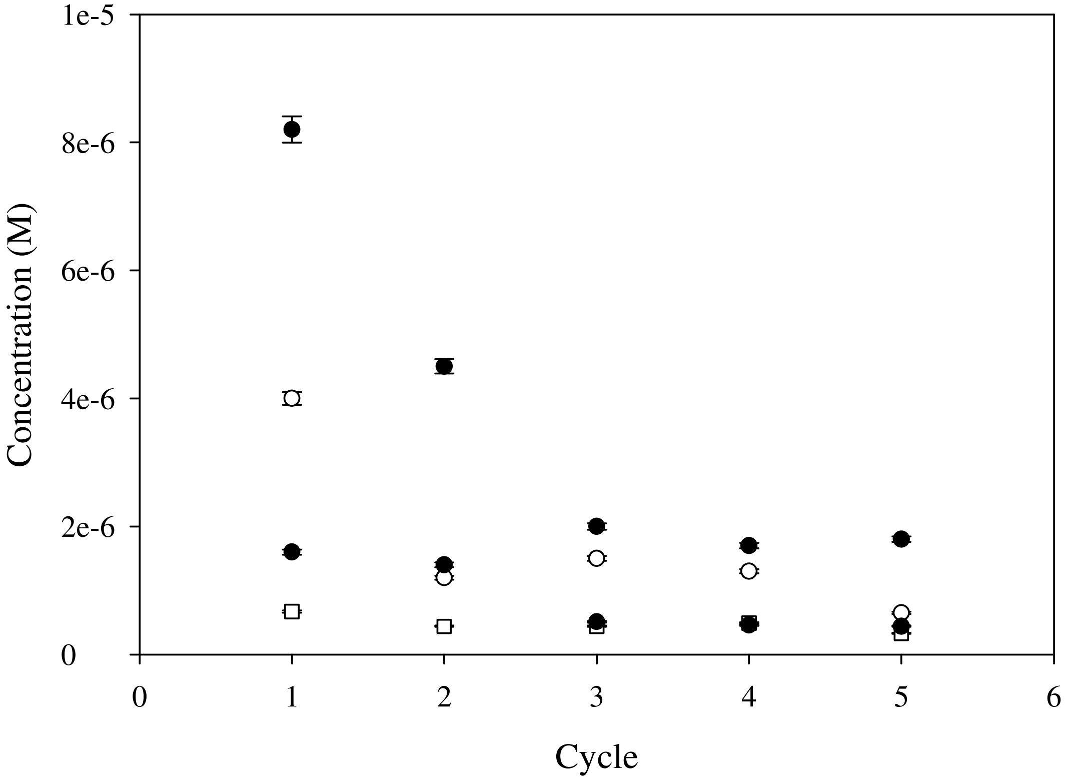


Figure 14. Plot of the concentration of polymer-bound dansyl probes versus cycle. The dansyl probes are represented as poly(4-*t*-butylstyrene) **18** (●), poly(4-*n*-butylstyrene) **19** (○), poly(4-*n*-dodecylstyrene) **20**, (■), and poly(4-*n*-octadecylstyrene) **21** (□).

eliminating the need for further manipulations of the system. Also, the addition of water could be avoided in reaction schemes where water would be detrimental.

Table 6. Phase selective solubility measurement of poly(4-alkylstyrene) supports **20** & **21** in heptane/DMA.[a]

Poly(4-*n*-dodecylstyrene) (**20**)			Poly(4-*n*-octadecylstyrene) (**21**)		
Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]	Cycle	Polymer-bound fluorophore in polar phase (M)[b]	Phase selective solubility in heptane/EtOH[c]
1	6.7×10^{-7}	7000/1	1	1.6×10^{-6}	3000/1
2	4.4×10^{-7}	10000/1	2	1.4×10^{-6}	4000/1
3	4.4×10^{-7}	10000/1	3	5.1×10^{-7}	10000/1
4	4.9×10^{-7}	10000/1	4	4.6×10^{-7}	10000/1
5	3.2×10^{-7}	10000/1	5	4.4×10^{-7}	10000/1

[a] The polymer supports were prepared as 4.9 mM (**20**) and 5.4 mM (**21**) solutions of the polymer-bound dansyl in heptane. The solvent volume ratios in the heptane/*N*, *N*-dimethylacetamide solvent mixtures were 2/1. The solutions were made homogeneous by the heating of the solvent mixtures above 80 °C and again biphasic by cooling the solutions to room temperature.

[b] Calculated using the calibration curve in **Figure 12** and the fluorescence intensity in the polar phase. The error in the fluorescence intensity of the dilute polar phases is expected to be (±) 5% of the measured value.

[c] Calculated as the ratio of the fluorescence intensity of the non-polar/polar phase.

Phase selectivity studies of polymer supports other than poly(4-alkylstyrene) have been reported (**Table 7**).[44,68] In these studies, *N, N*-dimethylformamide and ethanol were used as the polar solvents to study the phase selective solubility of polyisobutylene oligomers (**17**) with attached dansyl, and polysiloxanes (PAS) and poly(octadecylmethacrylates) (PODMA) with supported *p*-methyl red. As *N, N*-dimethylformamide (DMF) and *N, N*-dimethylacetamide (DMA) are similar, the results from the two solvent systems for phase selective solubility can be compared. **Table 7** compares the results of this chapter's findings with those reported in literature. As can be seen, the polystyrene supports **18-21** are superior in heptane phase selective solubility

Table 7. Phase selectivity measurement of polymer supports in heptane/polar solvent mixtures.[a]

Polymer support	Polar solvent	Phases selective solubility in heptane (%)
polysiloxane	90% ethanol	200/1
polyisobutylene (**17**)	90% ethanol	300/1
poly(octadecylmethacrylate)	90% ethanol	>2000/1
poly (4-*t*-butylstyrene) (**18**)[b]	90% ethanol	30000/1
poly (4-*n*-butylstyrene) (**19**)[b]	90% ethanol	100000/1
polysiloxane	DMF	300/1
poly (4-*t*-butylstyrene) (**18**)[c]	DMA	800/1
poly (4-*n*-butylstyrene) (**19**)[c]	DMA	2000/1
poly(octadecylmethacrylate)	DMF	>2000/1
poly (4-*n*-dodecylstyrene) (**20**)[c]	DMA	100000/1
poly (4-*n*-octadecylstyrene) (**21**)[c]	DMA	100000/1

[a] The phase selective solubility in heptane are converted from the percentage reported in literature for polyisobutylene oligomers with a supported dansyl,[44] polysiloxane with a supported *p*-methyl red,[68] and poly(octadecylmethacrylate)[44] with a supported *p*-methyl red.

[b] The highest obtained value in **Table 1**.

[c] The highest obtained value in **Tables 4** and **6.**

to previous polymeric examples in heptane/ethanol systems. For example, substituted polystyrene possesses superior heptane phase selective solubility in comparison to polysiloxane (PAS) supports in the thermomorphic systems. However, similar phase selective solubilities are achieved with the poly(4-*n*-butylstyrene) **19** and a poly(octadecyl methacrylate) (PODMA) support. If better heptane phase selective solubility is required in this solvent system, implementation of the poly(4-*n*-dodecylstyrene) **20** and poly(4-*n*- octadecylstyrene) **21** would be more suitable for recoveries of polymer supported species in heptane.

Conclusions

Non-polar phase selective solubility can be measured using fluorescent dyes as catalyst surrogates with thermomorphic and latent biphasic systems. By modifying the solvent compositions in heptane/ethanol and heptane/*N, N*-dimethylacetamide, increased non-polar phase selective solubility of polystyrene supports can be attained. Likewise, by varying the structure of the pendant alkyl chain, a slight increase in non-polar phase selective solubility is realized as seen in the poly(4-*n*-butystyrene) and poly(4-*t*-butylstyrene) studies. Further increase in non-polar phase selective solubility is found upon increasing the alkyl chain length. This is theorized to occur by the increase in non-polar character of the heptane solvent mixture by the dissolved modified polystyrene support, thus allowing for better separations. These supports can be expected to be useful in the recovery and recycling of catalysts or reagents in thermomorphic or latent biphasic systems where heptane is used as the solvent for polymer recovery and separation.

CHAPTER III

PROBING THE SOLUTION MICROENVIRONMENT OF PENDANT GROUPS ON SOLUBLE 4-SUBSTITUTED POLYSTYRENE SUPPORTS

Introduction

Cost efficient and environmentally friendly chemical processes are important goals of the chemical industry. Various insoluble catalyst supports have been made using materials such as cross-linked polymers. These supports allow for easy recovery of catalysts by filtration without the use of excess solvents. They also allow for catalysts to be used in continuous processes.[69,70,71] However, there are disadvantages to using heterogeneous catalysts. These include diffusion-limited mass transfer, non-uniform reaction rates, difficult functionalization[72], and problems with characterizing and analyzing species on insoluble supports.[73] Using soluble polymer-bound catalysts is an alternative strategy that avoids or minimizes many of these problems. Soluble polymer supports provide the same simplicity of separation as the insoluble support when ultracentrifugation, precipitation, or extraction is used as a means of recovery. They have the advantage of simple analysis. In many cases, these soluble supported catalysts analogs are as active as the soluble low molecular weight catalysts.[44,46,48,62,66,74,75]

Soluble polar and non-polar polymer supports have been used in catalysis. Poly(ethylene glycol) oligomers have been extensively used in a number of catalytic systems.[3,62,76,77] This commercially available polymer can be used to support and dissolve a number of catalysts in a variety of polar solvents by attachment of the catalyst to the polymer *via* a reactive end-group. Catalysts and reagents can easily be supported on one or both ends of the polymer support and characterized like their low molecular weight counterparts. Polyisobutylene oligomers, a non-polar analog of poly(ethylene glycol), have also been used in a variety of applications as successful soluble polymeric supports.[65] Through the use of simple functional group interconversions, a plethora of catalysts and reagents can be attached to these soluble polymer supports. However, the fact that both poly(ethylene glycol) and polyisobutylene are end functionalized only allows for attachment of only one or two catalysts or reagents per polymer chain – limiting the amount of catalyst or reagent loading. In contrast, the use of polystyrene copolymers like those mentioned in the previous chapter can incorporate ligands, catalysts, reagents or substrates as pendant groups and can permit one to use a broader range of catalyst/reagent loadings by varying the functional copolymer ratios in the preparation of these supports.

Polyisobutylene oligomers and the poly(4-alkylstyrene) copolymers both have non-polar phase selective solubilities that can be utilized in thermomorphic and latent biphasic solvent systems (**Figure 15**). However, while either of these polymers as supports facilitate the recovery and characterization of a non-polar phase selectively soluble polymer supported species, there are other factors involved when incorporating macromolecules as catalyst supports. For example, it has been shown that certain soluble polymeric 4-(*N, N*-dimethylamino)pyridine (DMAP) analogs possess slightly

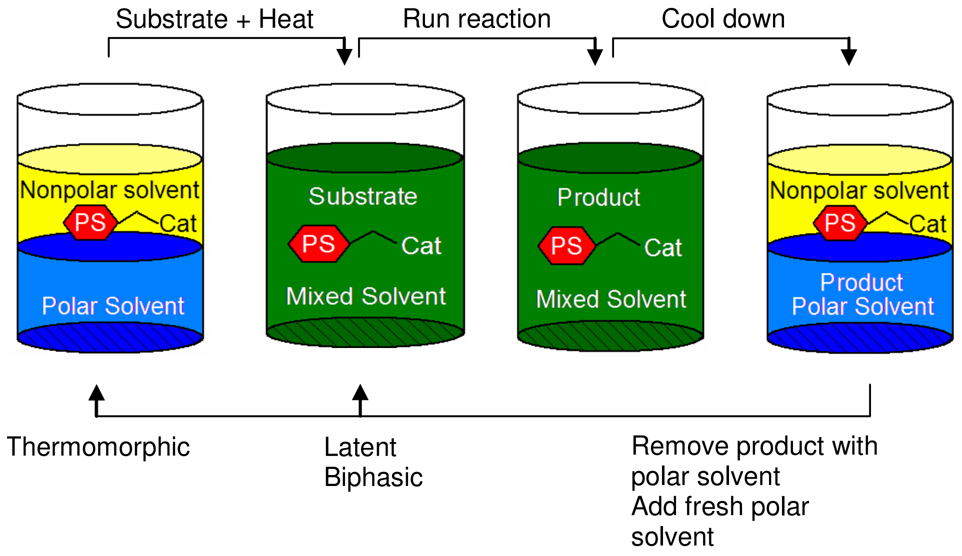
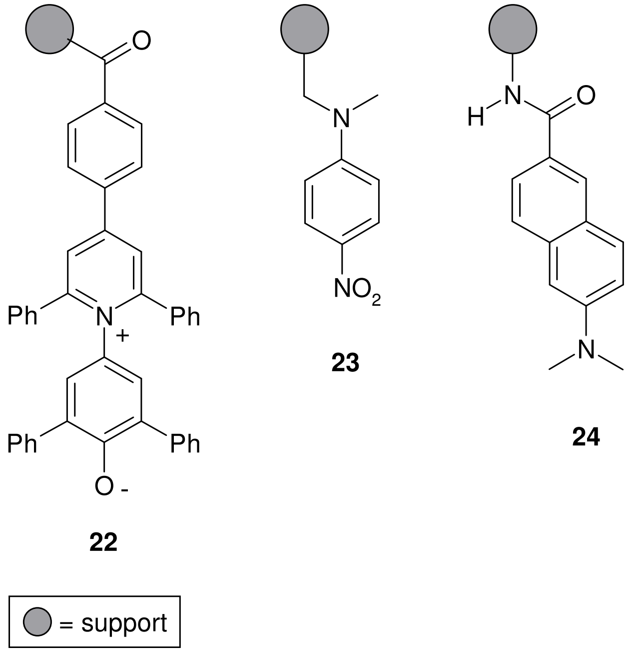


Figure 15. Soluble recovery scheme for non-polar soluble polymer catalysis with biphasic liquid/liquid separations.

lower activities than unbound DMAP[66] while other macromolecular supports outperform DMAP considerably.[78] One possible explanation for this is that solvation of the supported species is sensitive to the polymer structure and to the solvent milieu. Either the polymer's backbone or solvation may indirectly or directly affect a supported species. For example, changes in catalyst microenvironment could retard rates of reaction if the transition state were polar and if the microenvironment were non-polar. Alternatively, the creation of a more "enzyme-like" pocket around the polymer-bound catalyst might increase rates.[79] Recently, it was shown that manipulation of the nanoenvironment of a dendrimer supported DMAP altered the catalytic properties of the supported DMAP analog. The results were thought to be directly related to preferential solvation of the supported catalyst.[78]

Poly(4-*n*-alkylstyrene) supports were designed to be used in thermomorphic and latent biphasic solvent systems. Such solvent systems are normally mixtures of solvents. Since solvent mixtures afford a different polarity than the pure solvent components and since solvent polarity can affect reaction rates, we sought to probe how solvent mixtures might affect a poly(4-*n*-alkylstyrene)-bound catalyst. Rather than directly use poly(4-*n*-alkylstyrene) supports in a catalytic system and study yields to assay catalyst microenvironment, a direct measurement of the solvent microenvironment around the polymer bound species was sought. If such studies were successful, they could be useful in that it might be possible to estimate the optimal reaction solvent systems for a particular polymer support before a catalytic reaction was actually performed.

To carry out this study, we decided to use a solvatochromic dye as a catalyst surrogate. Solvatochromic shifts of dyes have been extensively used in a number of studies to determine solvent polarity scales for various pure and mixed solvent systems. Such studies have involved species as diverse as DNA, polymer surfaces, cross-linked polymers, soluble polymers, polymer blends and dendrimer systems.[80-87] Various sorts of dyes have been used. Some examples include analogs of UV-visible dyes such as Reichardt's betaine dye (**22**) and 4-(*N, N*-dimethylamino)-1-nitrobenzene (**23**) and fluorescent dyes such as 6-(*N, N*-dimethylamino)-2-acylnaphthalene (**24**) shown in **Figure 16**. While any of these dyes might work for our purpose, we already had used a fluorescent dansyl moiety in the earlier studies of polymer phase selective solubility (cf. Chapter II). The fluorescent dansyl molecule used in that work is a suitable probe of microenvironments as it exhibits a strong solvatochromic shift of its fluorescent emission λ_{max} as a function of solvent with shifts to longer wavelengths with more polar solvents and shifts to shorter wavelengths with more non-polar solvents.[80,88] Covalent attachment of this moiety to non-polar and polar polymer supports as was used before would thus provide a catalyst surrogate for determining the solution microenvironment of soluble polymer bound species.



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23

24

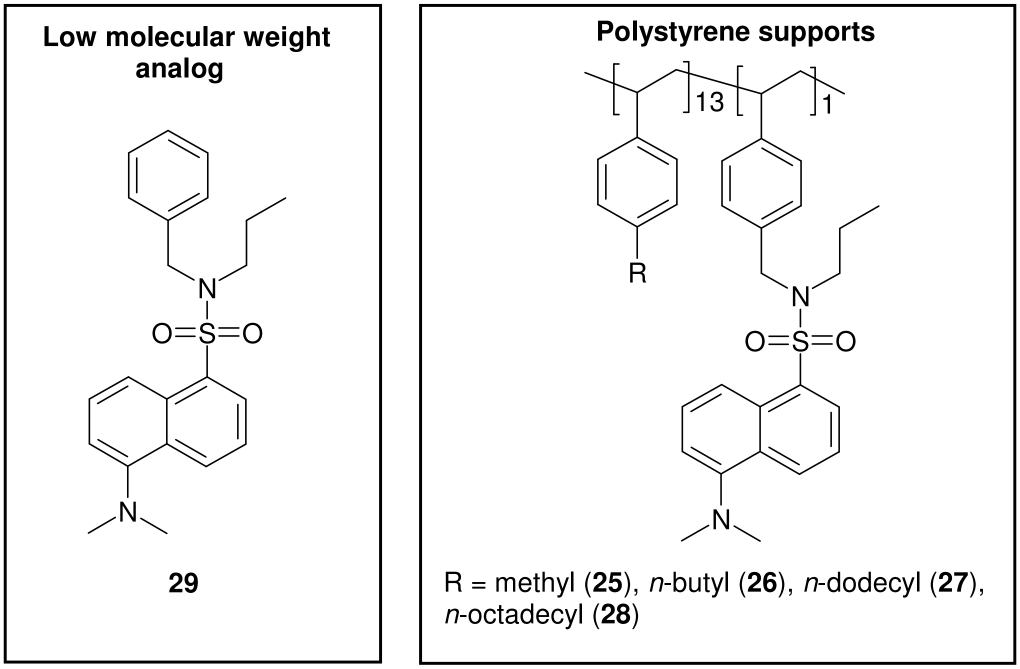
Figure 16. Solvatochromic dyes for solvent microenvironment studies.

Shea and coworkers had earlier prepared a variety of cross-linked and linear polystyrenes covalently labeled with a solvatochromic dansyl probe and used this dye to determine site accessibility of solvents with these supports. It was found that in non-solvents for polystyrene such as methanol and ethanol, the solvatochromic shifts of linear polystyrene supported probe correlated with an environment of the supported dye similar to dry polymer. This suggested a collapsed structure rather than a solvated polymer-dansyl structure.[80] Reagents and catalysts supported on polystyrene in these solvents would then be sequestered from solution by a polymer microenvironment, making them effectively heterogeneous. Perhaps more important, the greater polarity of solvents for reactions of such species would not affect a reaction in these systems since the polymer-bound species does not see the solvent environment. Since similar polar solvents are employed in thermomorphic and latent biphasic systems, the possibility of this differential solvation of the dansyl solvatochromic dye supported on various soluble polymer supports in mixed solvent systems was a particular subject of interest.

Results and Discussion

The synthesis of the poly(4-*n*-alkylstyrene) supports was described in the previous chapter. The substitution reactions used to incorporate a dansyl fluorophore onto supports for studies of solvation microenvironments were carried out in the same fashion as described in that chapter. The copolymers (**25-28**) prepared has a copolymer ratio of 4-alkylstyrene to dansyl-supported probe of 13:1 as determined by ^{1}H NMR analysis. A low molecular weight analog (**29**) of these copolymers (**Figure 17**) was also synthesized using the reaction of benzyl chloride with the *N*-propyl-dansyl probe in *N, N*-dimethylformamide.

In addition to a low molecular weight probe, we also studied two linear polymers that incorporated dansyl groups as probes. One of these polymers was poly(ethylene glycol) and the other polymer used was polyisobutylene. Two synthetic routes were employed to incorporate dansyl probes onto poly(ethylene glycol) (PEG) and polyisobutylene (PIB) oligomers. End-group functionalization was used in both cases. However, in the first case, the final product had the dansyl group as the terminal group at the end of a single polymer chain. In the second approach, the dansyl was incorporated such that it was at the termini of two polymer chains making it effectively an internal rather than a terminal functional group. The *N*-propyl-dansyl probe previously described was used in the nucleophilic substitution of PEG (2000 Da) and PIB (2300 Da) oligomers (**Scheme 19**) to prepare the end-functionalized polymers **30 & 31** in the first



Low molecular weight analog

29

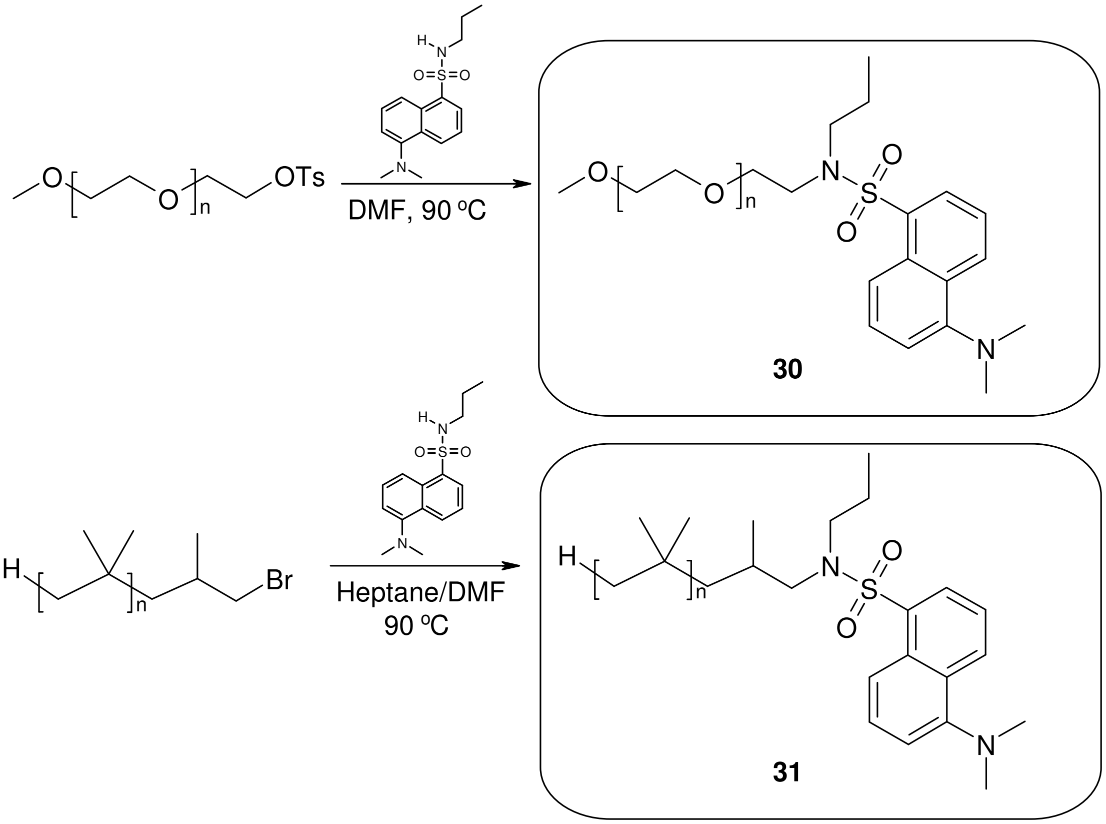
Polystyrene supports

R = methyl (**25**), *n*-butyl (**26**), *n*-dodecyl (**27**), *n*-octadecyl (**28**)

Figure 17. Low molecular weight dansyl analog and polymer-supported dansyl copolymers.

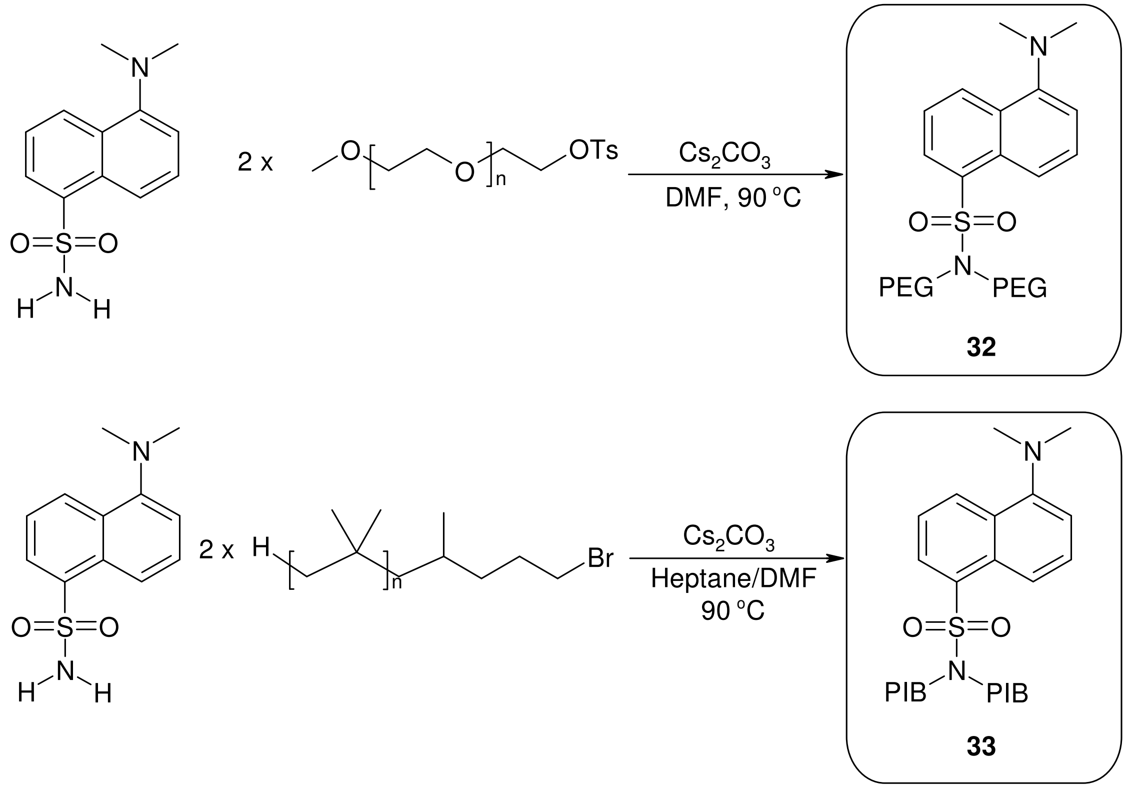
case. The incorporation of two polymers to make the dansyl probe reside in the middle of a longer linear polymer support was also effected by nucleophilic substitution. In this case, a double displacement by the unalkylated dansyl probe was used with two equivalents of the terminally functionalized oligomer. Poly(ethylene glycol) tosylate terminated (2000 Da) and polyisobutylene bromide terminated (2300 Da) oligomers were reacted with 5-dimethylaminonaphthalene-1-sulfonamide in this way to make a

Scheme 19. Synthesis of terminal polymer supported dansyl.



dansyl probe that had two oligomers (**Scheme 20**). In both synthetic routes employing the poly(ethylene glycol) supported dansyl probe, the polymer solutions had to be thoroughly washed and dried to remove trace impurities such as water. A significant advantage was also realized in this case with the polyisobutylene derivatives in that the simplicity and effectiveness of thermomorphic systems could be employed with the polyisobutylene supports to facilitate isolation of the products. As already noted, the use of heptane soluble polymers in thermomorphic systems allows for facile separations of these non-polar supports from polar impurities by simple liquid/liquid separations.

Scheme 20. Internally functionalized polymer supported dansyl.



32

33

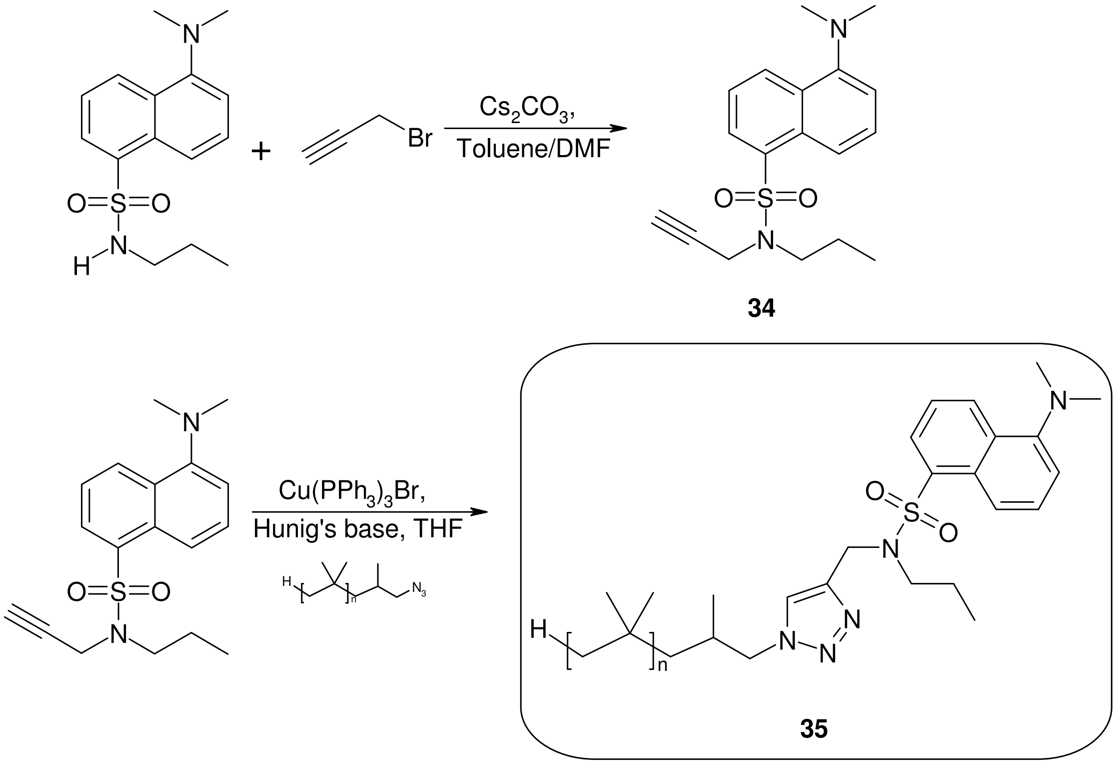
Since the polyisobutylene oligomers are phase selectively soluble in the heptane phase of heptane/*N, N*-dimethylformamide solvent mixture, they could be easily separated from the polar impurities by a liquid/liquid biphasic separation. This greatly speeded up the synthesis and purification of these non-polar oligomers as compared to the synthesis of polar poly(ethylene glycol) oligomers.

A fourth sort of polymer-bound dansyl dye was also prepared. This dansyl probe was like those prepared previously on polyisobutylene but incorporated a more polar group at the end of the polyisobutylene to determine if it is the polymer itself that affects solvatochromic behavior or if a polar group in the vicinity of the probe alone is sufficient to mitigate the effects of the polymer chain on the environment of a dansyl probe as measured by the dansyl's solvatochromic behavior. To carry out this synthesis, we used the non-polar polyisobutylene support and a polar triazole moiety to attach the dye to the support (**Scheme 21**). Solvatochromic studies of this material could then be compared to the directly functionalized polyisobutylene oligomer to give an indication into the actual effects of polymer backbone versus method of attachment. In this case, a modified dansyl probe had to be synthesized to make it suitable for this reaction scheme.

The nucleophilic substitution of propargyl bromide with the *N*-propyl-dansyl probe produced the required alkyne-functionalized probe (**34**) for the subsequent attachment to the polyisobutylene support. A so-called 'Click' reaction involving a copper catalyzed (3+2) cycloaddition was used to modify an azide terminated polyisobutylene oligomer (2300 Da) with the *N*-propargyl-*N*-propyl-dansyl probe. This produced a polyisobutylene-supported dansyl (**35**) where the 1,4-disubstitued-1,2,3-

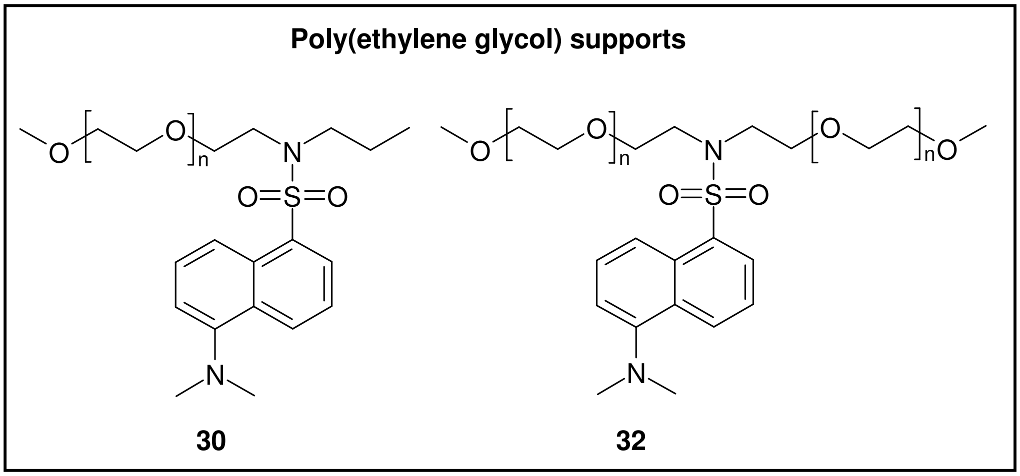
polyisobutylene triazole linked the fluorophore to the polymer with the polar triazole in close proximity to the attached probe. This polar functionality directly adjacent to the probe would therefore give a clear indication in solvatochromic studies if the microenvironment of the supported species would be affected.

Scheme 21. Synthesis of 1,2,3-triazole linked PIB-dansyl probe.



Pure Solvents

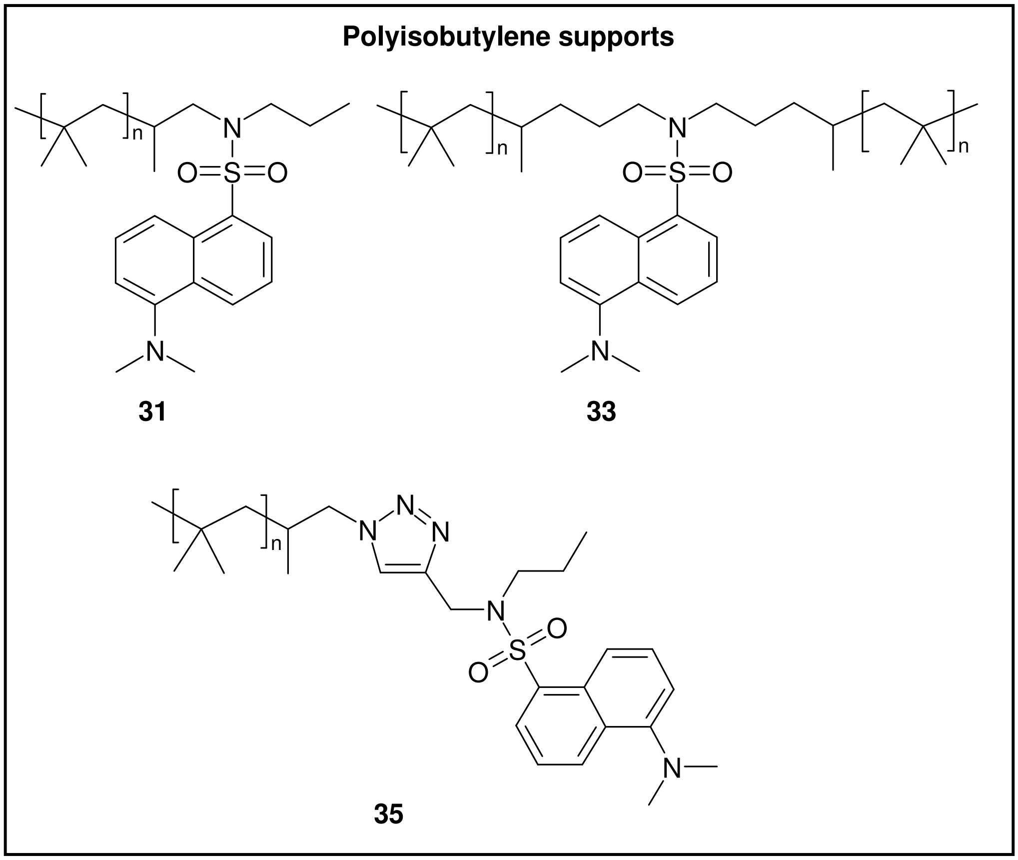
With the availability of a variety of poly(ethylene glycol), polyisobutylene, and poly(4-*n*-alkylstyrene) derivatives (**Figures 17 & 18**) containing covalently bonded



Poly(ethylene glycol) supports

30

32



Polyisobutylene supports

31

33

35

Figure 18. Terminal and internal oligomer supported dansyl probes.

solvatochromic fluorescent dansyl probes attached either terminally, internally, or as a pendant group in hand, it was possible to begin a systematic study of dansyl group solvation of dansyl-labeled polymers or oligomers in both pure and mixed solvents. In pure solvents, any variations of the emission λ_{max} of the dansyl moiety attached to the different polymers would indicate the interference of the support with the solvation of the covalently attached probe. Dilute solutions (1 mg of polymer supported probe in 100 mL of solvent) of these polymers were prepared and the emission λ_{max} was measured in various pure solvents. The results of this set of experiments can be seen in **Table 8**. Graphical representations of these results are shown in **Figures 19-21**. In examining the behavior of these supports in the various solvents, a difference in the emission λ_{max} due to solvatochromic effect of different solvation of the supported probes is observed. This effect is discussed below.

The polymers solutions were all prepared such that the dansyl probes and the polymer supports were present at in low concentrations. Therefore, the solvatochromic shifts can be attributed to influences of the polymer affecting the probe rather than an effect due to intermolecular polymer entanglements. As was thought in the previous chapter, supports with longer alkyl chains should increase the non-polar nature of the

Table 8**.** Solvatochromic studies of polymer supported dansyl fluorophore.[a]

		λ_{max}(nm)	
Dansyl Probe	Tetrahydrofuran	Toluene	Cyclohexane
N-benzyl- *N*-propyl dansyl **29**	498	478	450
Polystyrene supports			
25	494	481	466
26	493	479	464
27	492	478	460
28	490	477	458
Polyisobutylene supports			
31	490	475	447
33	488	470	446
35	496	478	452
Poly(ethylene glycol) supports			
30	497	484	--
32	502	488	--

[a]The pure solvent-dansyl solutions were all prepared with 1 mg of the appropriate dansyl probe in 100 mL of the solvent. All the solutions were excited at 357 nm and the emission λ_{max} was recorded.

solution. Therefore, it would be expected that as the length of the alkyl group is increased, an increasingly hypsochromic shift in the probe's fluorescence would be observed. In **Figures 19-21**, a decrease in the emission λ_{max} of the poly(4-*n*-alkylstyrene) supported probes with increasing alkyl chain length is observed. Poly(4-methylstyrene) **25** has a measured emission λ_{max} of 481 in pure toluene. Poly(4-*n*-octadecylstyrene) **28** has a emission λ_{max} of 477 nm. This 4 nm shift is consistent with the notion that the dansyl groups experience a more non-polar microenvironment with longer *n*-alkyl groups of poly(4-*n*-alkylstyrene) polymer supported pendant probe.

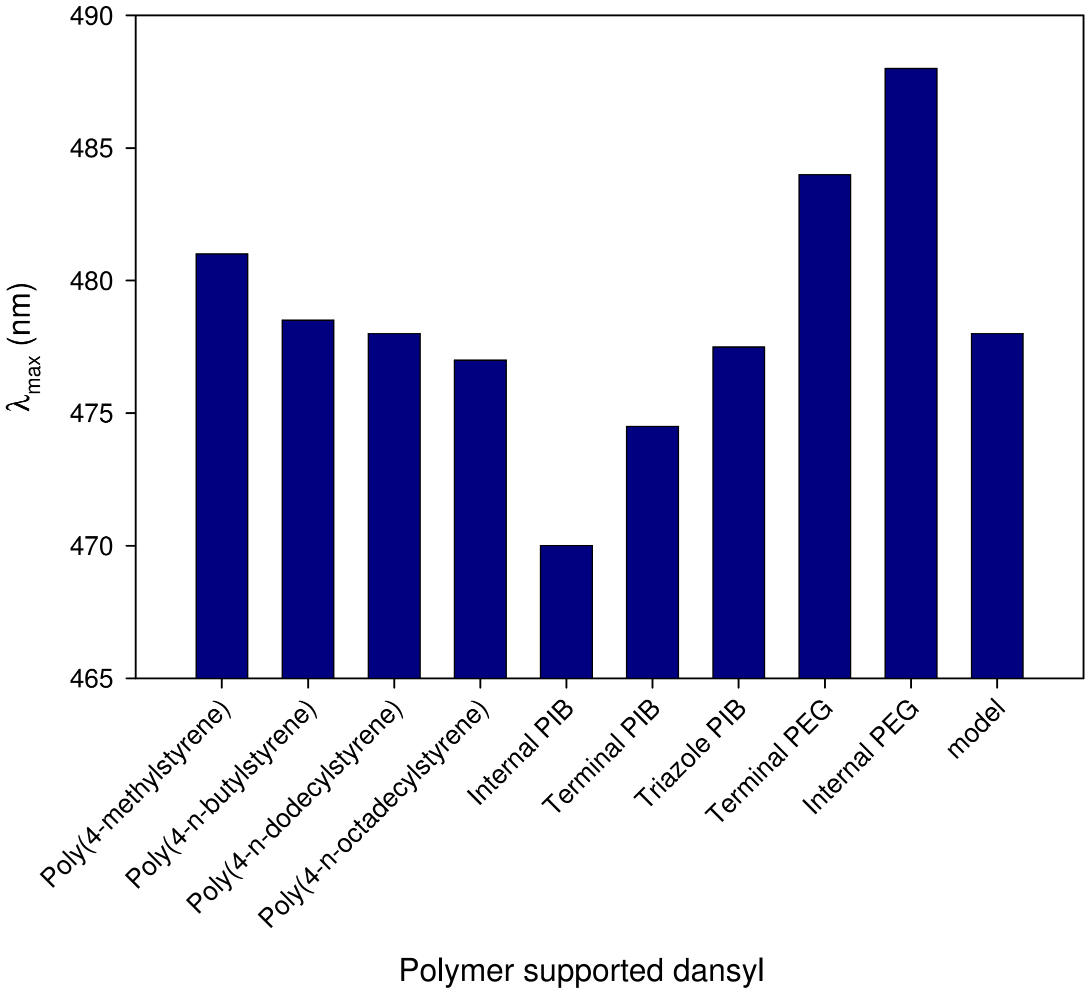


Figure 19. Emission λ_{max} of polymer supported dansyl probes in toluene.

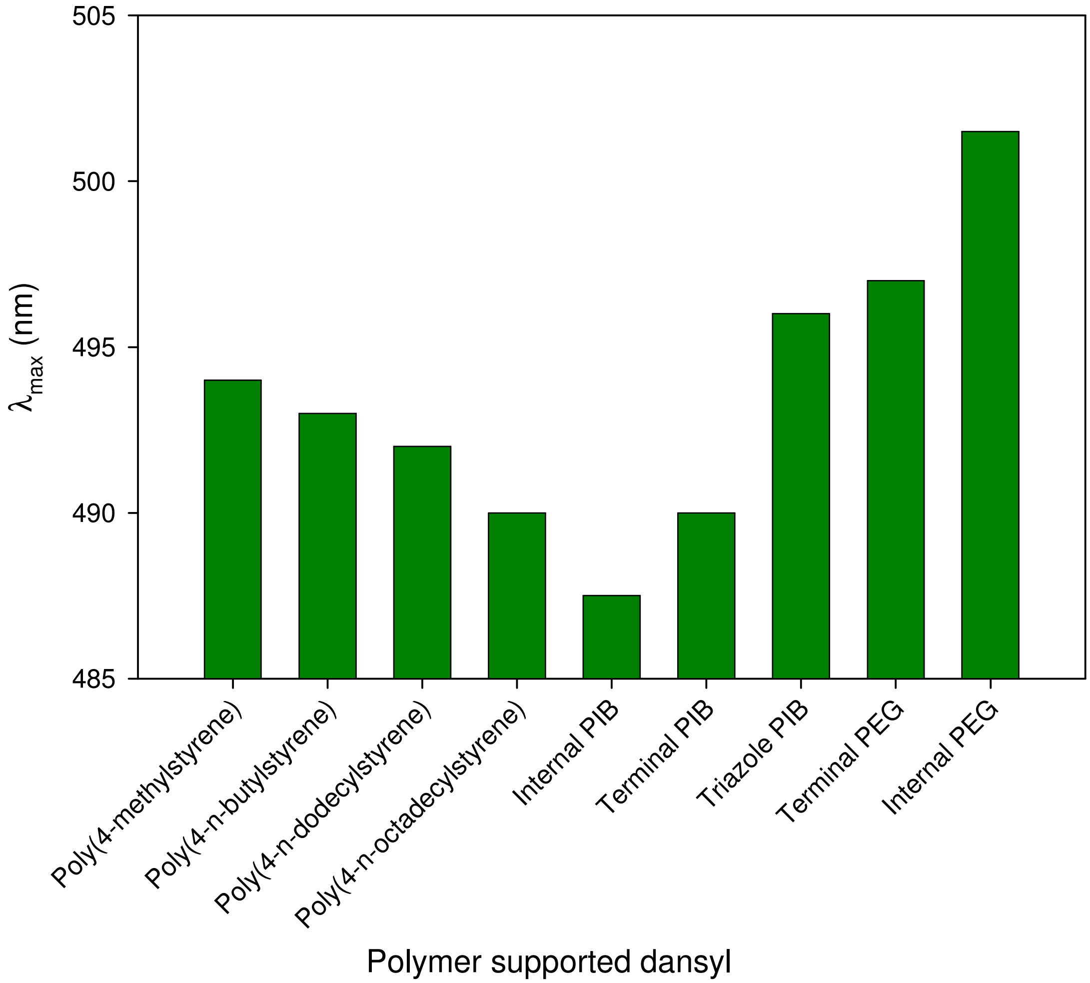


Figure 20. Emission λ_{max} of polymer supported dansyl probes in tetrahydrofuran.

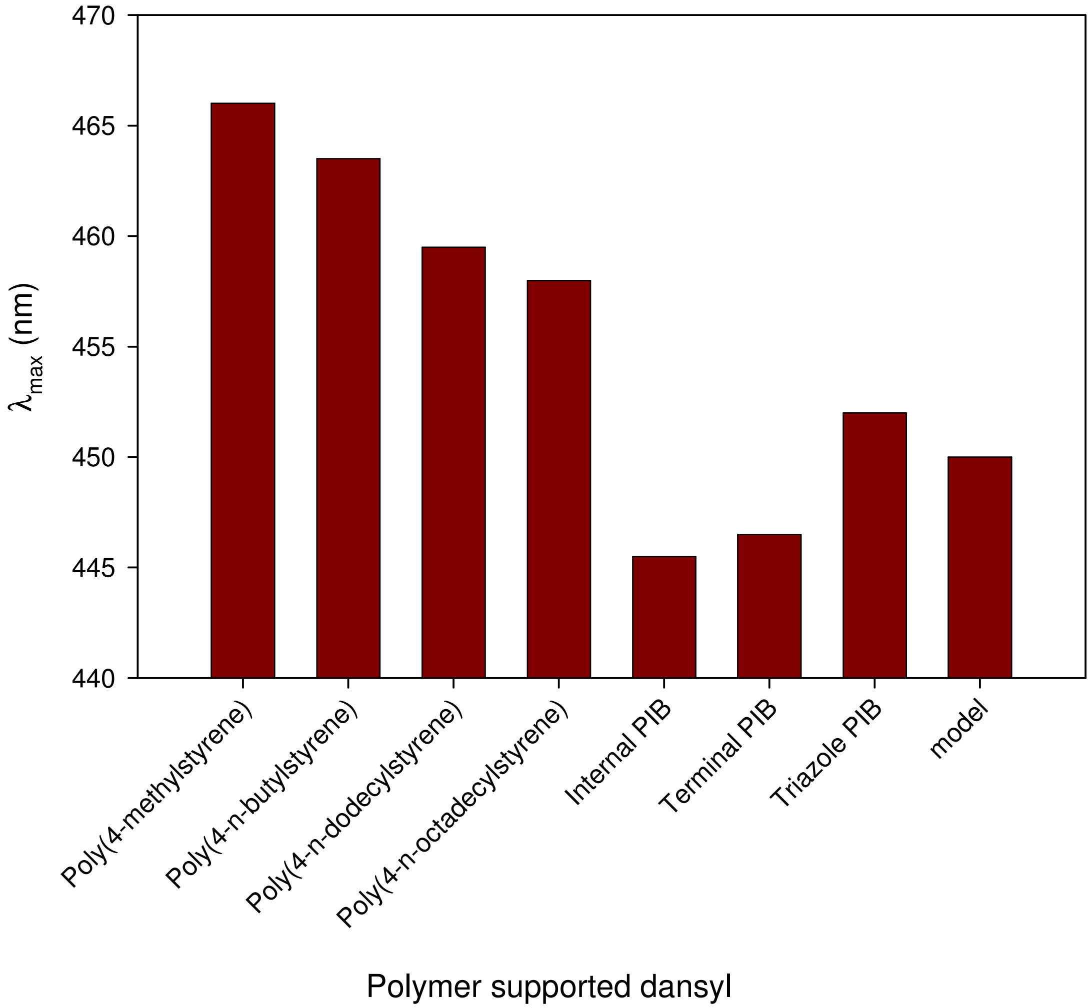


Figure 21. Emission λ_{max} of polymer supported dansyl probes in cyclohexane.

In this study of pure solvents, it should also be possible to determine if the poly(4-*n*-alkystyrene) supported dansyl probe was sufficiently accessible to the solution environment. With **29**, an emission λ_{max} of 478 nm is observed in toluene. When this low molecular weight probe is dissolved in a more polar solvent such as tetrahydrofuran, an emission λ_{max} of 498 nm is observed. This 20 nm shift in emission λ_{max} of the probe is expected since a more polar microenvironment of the probe should be measured in more polar solutions. Therefore, the degree to which a polymer supported probe's emission λ_{max} shifts in comparison to **29** would give some indication to the extent the polymer support influenced the probe's microenvironment in various pure solvents. In switching from non-polar to polar solvents, a variable solvatochromic shift should be experienced by using different polarity solvents to dissolve the polymer support. This was seen with the poly(4-methylstyrene) **25** when its emission λ_{max} in the pure solvents studied. In this case **25** has an emission λ_{max} of 494 nm when dissolved in tetrahydrofuran. In switching to more non-polar solvents, the emission λ_{max} changed to 481 nm when the support was dissolved in toluene and 466 nm when it was dissolved in cyclohexane. This 13 nm solvatochromic shift in switching from tetrahydrofuran to toluene and a 28 nm solvatochromic shift in switching from tetrahydrofuran to cyclohexane were approximately 70% of those of *N*-propyl-*N*-benzyl dansyl **29** (20 nm and 48 nm respectively), indicating a modest but measurable difference in solvent dependent microenvironment of **25** versus **29**. The observed change shows that the solvents studied did interact though with the polymer supported probe.

The solvatochromic shifts observed for the dansyl probe in **25** are less than those for the low molecular weight probe **29**. This indicated that this polymer support does affect the microenvironment of the supported dansyl probe in different solvents. However, the pendant group of this support is only a methyl group. Longer alkyl chains could have a greater effect. This proved not to be the case. All the poly(4-*n*-alkylstyrene) supports **25-28** exhibited essentially the same solvatochromic shifts of approximately 14 nm in switching from tetrahydrofuran to toluene and 30 nm in switching from tetrahydrofuran to cyclohexane. Based on the model compounds solvatochromic behavior in cyclohexane, the influence of the pendant *n*-alkyl chains on the probe could have had a significant effect. However, comparison of these polymer supports to the results for the *N*-propyl-*N*-benzyl dansyl probe **29** indicate that these pendant *n*-alkyl groups of poly(4-*n*-alkylstyrene) supports do not in and of themselves change the solution environment of the supported probe any more than a methyl group.

It was speculated solvatochromic shifts of the non-polar polystyrene supported dansyl probes in **25-28** might differ from those seen with the more polar poly(ethylene glycol) supported dansyl probes in **30** and **32**. The polar poly(ethylene glycol) supports **30** and **32** were expected to increase the polarity around the dansyl probe as both these polymer supports are more polar than poly(4-*n*-alkylstyrene) supports. The effect of the support on the probe can involve an effect of the support on the emission λ_{max} or an effect on the solvatochromic shifts of a supported probe or both effects can be observed. In comparison to the most non-polar polystyrene support **28**, a bathchromic shift was observed for the poly(ethylene glycol) supported probes in **30** and **32**. In toluene, the emission λ_{max} changed from 477 nm with the poly(4-*n*-octadecylstyrene) supported probe **28** to 484 nm with the terminal poly(ethylene glycol) supported probe in **30**. This 7 nm solvatochromic shift indicated a more polar microenvironment was experienced by the probe in **30**. An even greater shift of 11 nm was measured with the more polar internally functionalized poly(ethylene glycol) supported probe **32**. These findings indicate that non-polar versus polar supports do affect the emission λ_{max} of the probe.

Next, the solvatochromic shifts of these poly(ethylene glycol) supported dansyl probes in different pure solvents were evaluated. Since poly(ethylene glycol) is only soluble in toluene and tetrahydrofuran, only one comparison could be made. With the poly(4-*n*-alkylstyrene) supported dansyl probes in **25-28** a 13 nm solvatochromic shift versus a 20 nm shift for the *N*-propyl-*N*-benzyl dansyl probe **29** was measured by switching from the solvents tetrahydrofuran to toluene. Since the probe was located on the terminus of the poly(ethylene glycol) chain, less interference by the polymer backbone was expected for **30** and a solvatochromic shift of < 13 nm was expected. The terminally functionalized poly(ethylene glycol) supported dansyl **30** had a fluorescence emission λ_{max} of 484 nm in toluene and 497 nm in tetrahydrofuran. This 13 nm shift was exactly the same as that observed for studies with the poly(4-*n*-alkylstyrene) supports. Apparently the poly(ethylene glycol) support affects the emission λ_{max} but the effect of the poly(ethylene glycol) on solvation of the dansyl is no different than the effects of the styrene supports on dansyl groups on the polystyrenes. In the case of an internally functionalized polymer support (**32**) where the dansyl is in the middle of two poly(ethylene glycol) chains, the dansyl emission λ_{max} changed from 488 to 502 nm on switching from the non-polar toluene to the more polar tetrahydrofuran solvent for dissolution of **32**. In this case, the placement of the polymer on both sides of the dansyl probe also caused a 14 nm bathochromic shift of the probe's solvent microenvironment in both toluene and tetrahydrofuran. Since similar solvatochromic shifts were seen in the pure solvent studies for both non-polar and polar polymers, these studies provide no evidence that the polymer significantly affects solvation of a pendant group in a pure solvent.

A final set of experiments looked at the polyisobutylene oligomers **31**, **33**, and **35** in the various pure solvents to determine if similar effects would be seen for dansyl groups on these supports. A non-polar influence similar to the poly(4-*n*-alkylstyrene) supports was expected for the emission λ_{max}. The polyisobutylene supported probes were expected to produce a hypsochromic shift as compared to polystyrene supports. Indeed, in both toluene and cyclohexane, the emission λ_{max} was 7 nm lower for the internally placed polyisobutylene probe **33** than compared to the poly(4-*n*-octadecylstyrene) supported probe **28**, indicating a more non-polar microenvironment for the probe.

With triazoles becoming more popular as a means to attach various species to polymers[76], the influence this polar functionality has on neighboring reagents and catalysts was also studied. In this case, a 1,2,3-triazole containing polyisobutylene probe (**35**) could be compared to a probe with only two polyisobutylene groups. As expected, the emission λ_{max} of the dansyl group in the probe with the triazole was greater reflecting a more polar environment. However, in studies of solvents on the emission λ_{max}, the effects of the directly functionalized **31** versus the triazole linked **35** polyisobutylene support were essentially identical.

Previous comparisons of the solvatochromic shifts of poly(4-*n*-alkylstyrenes) **25-28** and poly(ethylene glycol) supported probes **30** and **32** indicated no advantages of using either support in different pure solvent systems. Polyisobutylene supported probes were therefore expected to behave in a similar manner. To the contrary, a 17 nm solvatochromic shift of **31**, **33**, and **35** in switching from tetrahydrofuran to toluene was observed as compared to the 13 nm shifts seen in both poly(4-*n*-alkylstyrene) and poly(ethylene glycol) supports. Interestingly, the *N*-propyl-*N*-benzyl dansyl probe **29** experienced a 20 nm solvatochromic shift, which was very close to the value determined for the polyisobutylene supports. Similar solvatochromic shifts were also seen in switching from toluene to cyclohexane **31**, **33**, and **35**. With the poly(4-*n*-alkylstyrene) supports **25-28**, an average solvatochromic shift of 17 nm was determined. Again, the *N*-propyl-*N*-benzyl dansyl probe **29** and polyisobutylene supports **31**, **33**, and **35** had very similar solvatochromic shifts of 28 nm and 26 nm respectively.

Results obtained in pure solvents for poly(ethylene glycol) **30** and **32** and poly(4-*n*-alkylstyrene) probes **25-28** suggest that these supports behave in a similar manner. Differences in solution polarity can be measured with these polymer-supported probes much in the same way as a *N*-propyl-*N*-benzyl dansyl probe **29**. The extent of solvatochromic shift is slightly lower with these supports. This slight difference is due to an influence of the polymer support on the solvent microenvironment of the supported probe. With polyisobutylene supports **31**, **33**, and **35**, the solvatochromic shifts are almost exactly that of the *N*-propyl-*N*-benzyl dansyl probe **29**. Therefore, in pure solvents, species supported on polyisobutylene are suspected to free from influence by this support.

Mixed Solvents

The influences of the polymer supports on the solvatochromic shifts in the previous experiments with pure solvents were at least in the case of polystyrene supports **25-28** and poly(ethylene glycol) supports **30** and **32** mainly a result of the influence of the polymer on the probe emission λ_{max}. Solvents produce a solvatochromic shift in both cases but the magnitude of that effect is not significantly affected by the polymer. The results for polyisobutylene supports **31**, **33**, and **35** were similar, though there the polymer effects on the solvatochromic behavior of the probe were comparable to the *N*-propyl-*N*-benzyl dansyl probe **29**.

The effect of mixed solvents such as those used in thermomorphic and latent biphasic systems was of more interest and was also investigated since mixed solvents may not behave like pure solvents. Specifically, since non-solvents of polystyrene such as ethanol are used in these thermomorphic and latent biphasic systems and since polystyrenes of the sort I have discussed above are insoluble in ethanol, more drastic changes in the microenvironment of polymer supported species might occur as the volume percent of ethanol in the solvent mixture changes from 0 – 100%. Such behavior is expected and should be similar to that seen as solvent mixtures change in precipitation of polymer supports from solution. For example, the addition of a concentrated chloroform solution of polystyrene into an excess volume of methanol causes the polystyrene to change conformation from a soluble polymer species to a non-solvated precipitate because of the unfavorable interaction of the methanol solvent molecules with the polystyrene macromolecules. In thermomorphic and latent biphasic systems, non-solvents for a modified polystyrene supports could similarly change the conformation and solution structure of the polystyrene supports (**Figure 22**). Such effects are of interest when pendant groups are used in catalytic systems. The extent of this change in conformation of the polymer support would give insight into how polar solvent systems could be used without reducing polymer-bound solvent interactions.

To mimic the conditions of thermomorphic and latent biphasic mixed solvent systems, a series of polymeric solutions were prepared as in the previous experiments with pure solvents. However, in this investigation of solvatochromic behavior of the polymer supported dansyl probes, the solvatochromic shifts measured would be induced by adding solvents the polymer support was either poorly or completely insoluble in. This process is similar to what was done in Shea's work,[80] but was being done with homogeneous polymer solutions. In Shea's work, the studies involved polymer precipitates. Here studies were discontinued if the polymer precipitated because we were interested in mixed solvent effects on soluble polymer supported species where the dye was serving as a surrogate for a polymer-supported catalyst species. For comparison

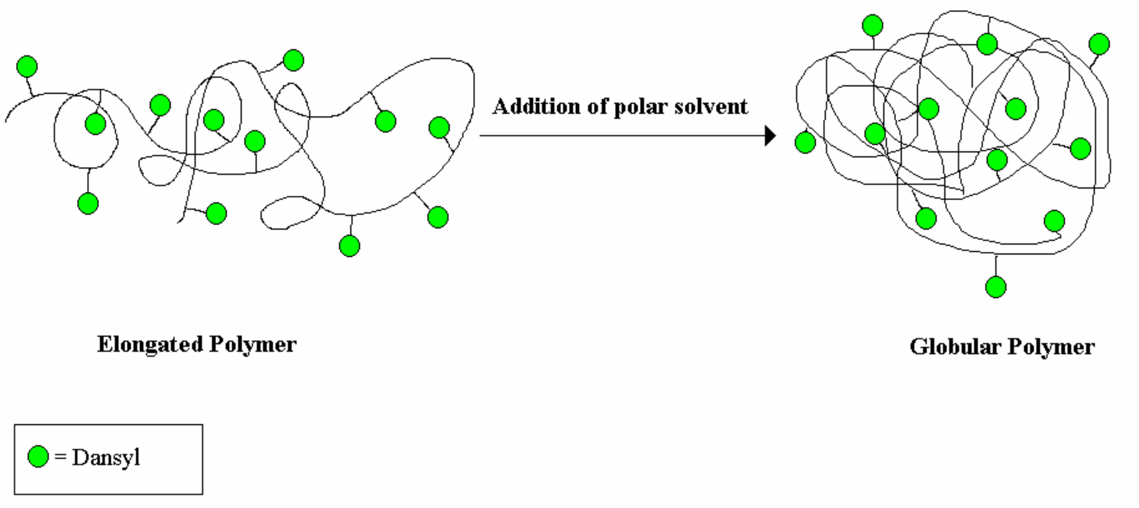


Figure 22. Changes in polymer conformations in solution based on unfavorable interactions of polar solvent molecules with the polymer support.

purposes, a fully soluble low molecular weight model **29** was used to establish the behavior of the free solvatochromic probe in solution. Any variations in the solvatochromic shifts in comparison to *N*-propyl-*N*-benzyl dansyl probe **29** could then be attributed to intramolecular polymer entanglements that at least hypothetically are a result of a polymer conformational change.

The previous studies of poly(4-*n*-alkylstyrene) supported dansyl dyes showed that the polymer support has an effect on the relative position of the dansyl probe's emission λ_{max} compared to the *N*-propyl-*N*-benzyl dansyl probe **29**. The effects of changing from a non-polar to a polar solvent were attenuated relative to **29** but those effects were the same for all the polystyrene and poly(ethylene glycol) supports. However, the supports do have significant differences in solubility in mixed solvents with the non-polar nature of the pendant alkyl chain likely to lead to different solvent compositions at which the solvent mixture could induce a polymer conformation change. For example, poly(4-methylstyrene) supported dansyl **25** is the most polar of the poly(4-*n*-alkylstyrene) supports and is expected to have the most compatibility with polar solvents. In contrast, poly(4-*n*-octadecylstyrene) supported dansyl **28** is the most non-polar polymer and should have the most incompatibility with the polar solvents used.

All solvent mixture used were miscible at room temperature. The following miscible solvent mixtures were chosen: cyclohexane/ethanol, cyclohexane/acetone, ethyl acetate/*N,N*-dimethylacetamide, tetrahydrofuran/ethanol, toluene/ethanol, and toluene/*N,N*-dimethylacetamide. A dilute solution of the polymer (1 mg of polymer supported probe in 100 mL of solvent) was prepared as in the previous experiments, and then the non-solvent would be added at various volume ratios. Precipitation of the polymer supports in these mixed solvent systems did not occur. No precipitates were visually apparent. Additional evidence for the solubility of the polymer supports was the essentially constant fluorescence intensity of the polymer-supported fluorophore in all the solutions. This was suggestive of complete solubility of the polymer-supported fluorophore because experiments where the polymer-bound dansyl precipitates have different fluorescence intensities.

Increasing the polar solvent composition of the solvent mixtures (**Figures 23-33**) led to a gradual but continuous change in the emission λ_{max} of **29**. However, in the case of the polystyrene-supported species, a deviation from this behavior was seen. The point at which the polymer supported probe's solvatochromic shift deviates from that set by **29** depends on the nature of the alkyl side chain. This deviation point varies with the percent cyclohexane and occurs at larger cyclohexane concentrations for the longer alkyl chains. For example, in the toluene/ethanol solvent mixtures (**Figure 24**), at a solvent composition of 100% toluene there is approximately only a 1 nm solvatochromic shift in comparison of **29** to poly(4-methylstyrene) **25** and poly(4-*n*-octadecylstyrene) **28**. At a solvent composition of equal parts toluene and ethanol, a more noticeable difference in the polymer supports is seen. For poly(4-methylstyrene) **25** a 7 nm solvatochromic shift compared to **29** is measured. However, poly(4-*n*-octadecylstyrene) supported dansyl **28** experiences a solvatochromic shift of 16 nm as compared to **29**, twice that experienced with the poly(4-methylstyrene) **25**. Finally, at a solvent composition of 90% ethanol by volume, **29** has a measured emission λ_{max} of 518 nm. At the same solvent composition, the poly(4-*n*-octadecylstyrene) supported dansyl **28** has a measured emission λ_{max} of 476 nm, a difference of over 40 nm as compared to 34 nm for the poly(4-methylstyrene) **25**. These results correlate the hypothesis that a polymer conformation change is occurring. Presumably at these polar solvent compositions, the polymer conformation changes to produce a more polymer-like microenvironment around the supported solvatochromic probe – a microenvironment that excludes much of the polar solvent, which is reflected in the greater solvatochromic shifts for dyes on the polymers as compared to **29**.

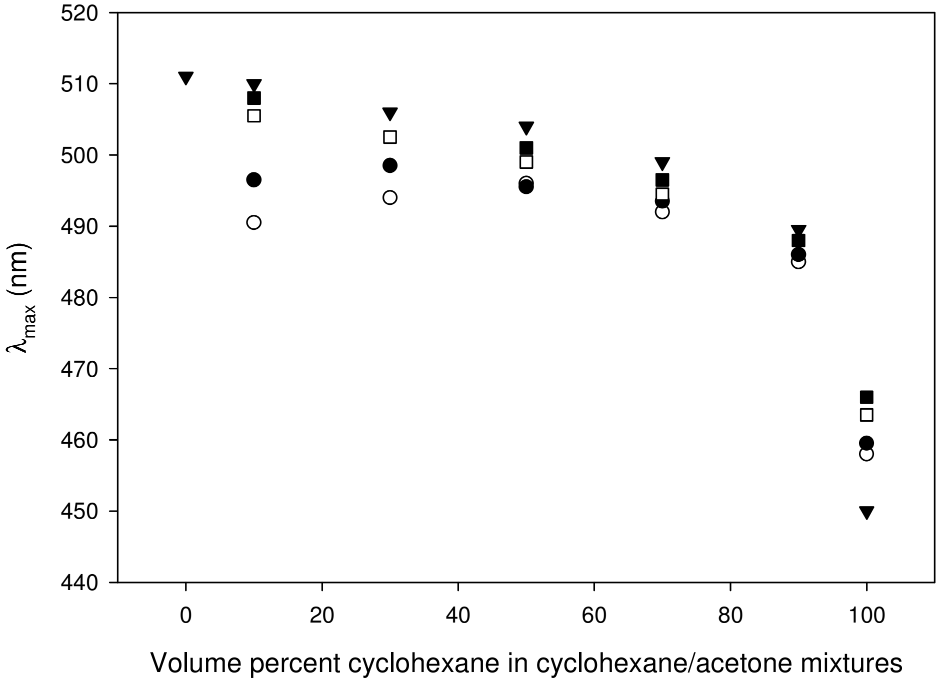


Figure 23. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent cyclohexane in cyclohexane/acetone solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(4-methylstyrene) **25** (■), poly(4-*n*-butylstyrene) **26** (□), poly(4-*n*-dodecylstyrene) **27** (●), and poly(4-*n*-octadecylstyrene) **28** (○).

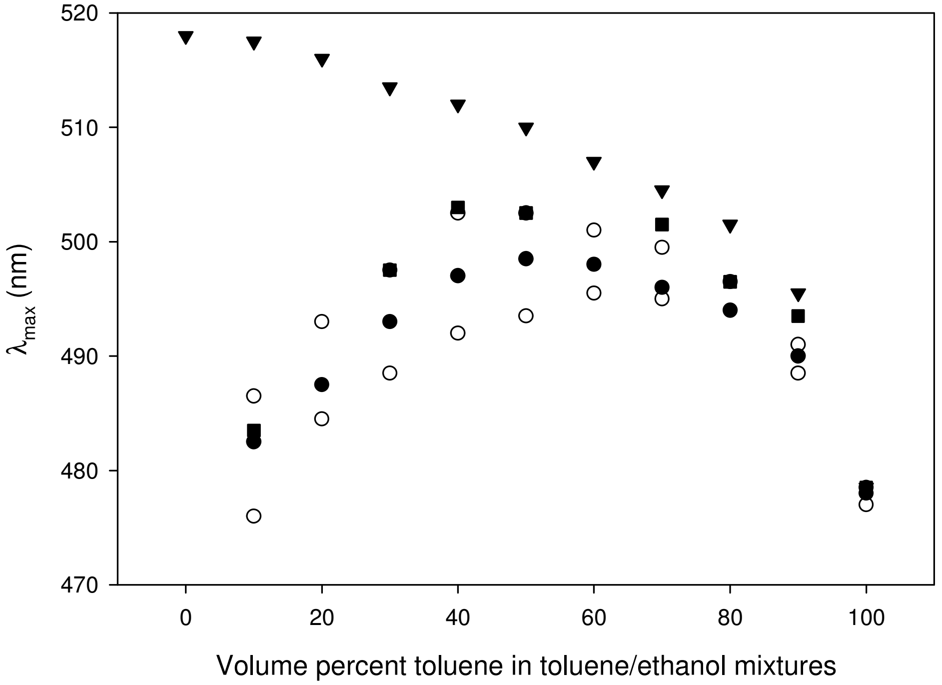


Figure 24. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent toluene in toluene/ethanol solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(4-methylstyrene) **25** (■), poly(4-*n*-butylstyrene) **26** (□), poly(4-*n*-dodecylstyrene) **27** (●), and poly(4-*n*-octadecylstyrene) **28** (○).

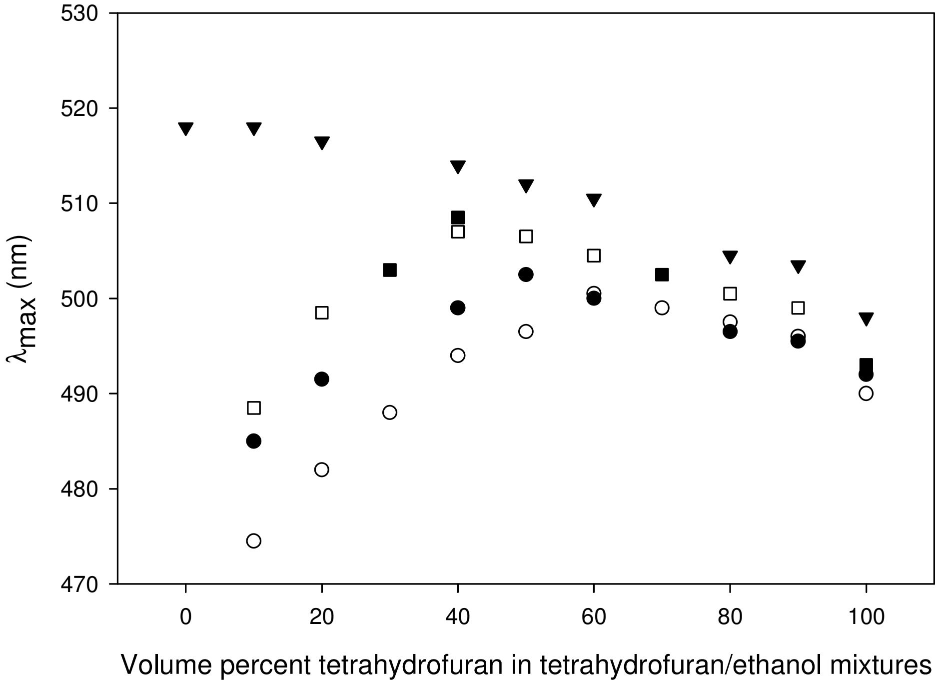


Figure 25. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent tetrahydrofuran in tetrahydrofuran/ethanol solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(4-methylstyrene) **25** (■), poly(4-*n*-butylstyrene) **26** (□), poly(4-*n*-dodecylstyrene) **27** (●), and poly(4-*n*-octadecylstyrene) **28** (○).

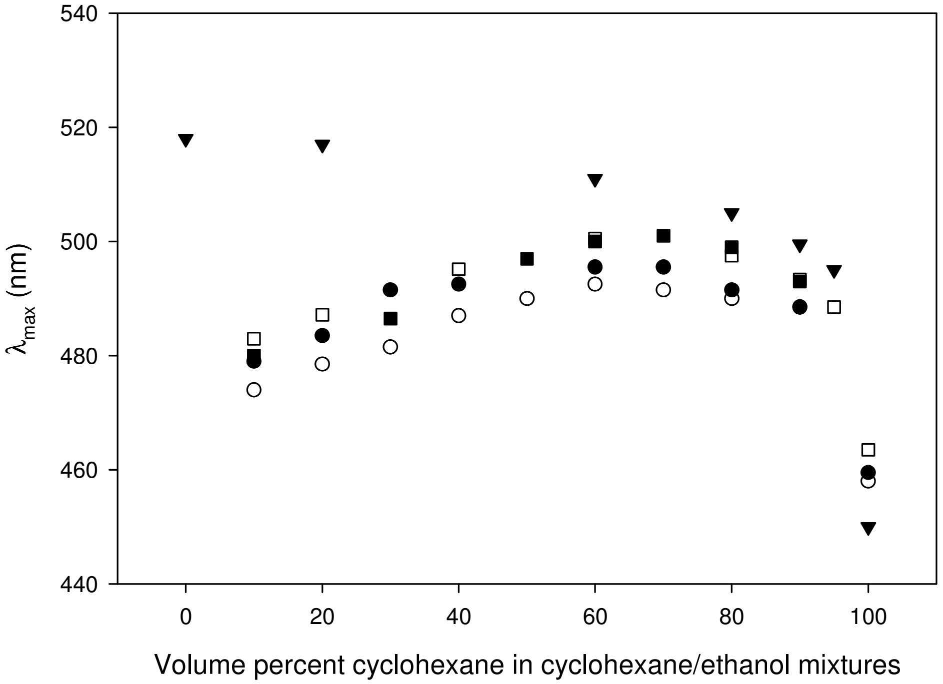


Figure 26. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent cyclohexane in cyclohexane/ethanol solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(4-methylstyrene) **25** (■), poly(4-*n*-butylstyrene) **26** (□), poly(4-*n*-dodecylstyrene) **27** (●), and poly(4-*n*-octadecylstyrene) **28** (○).

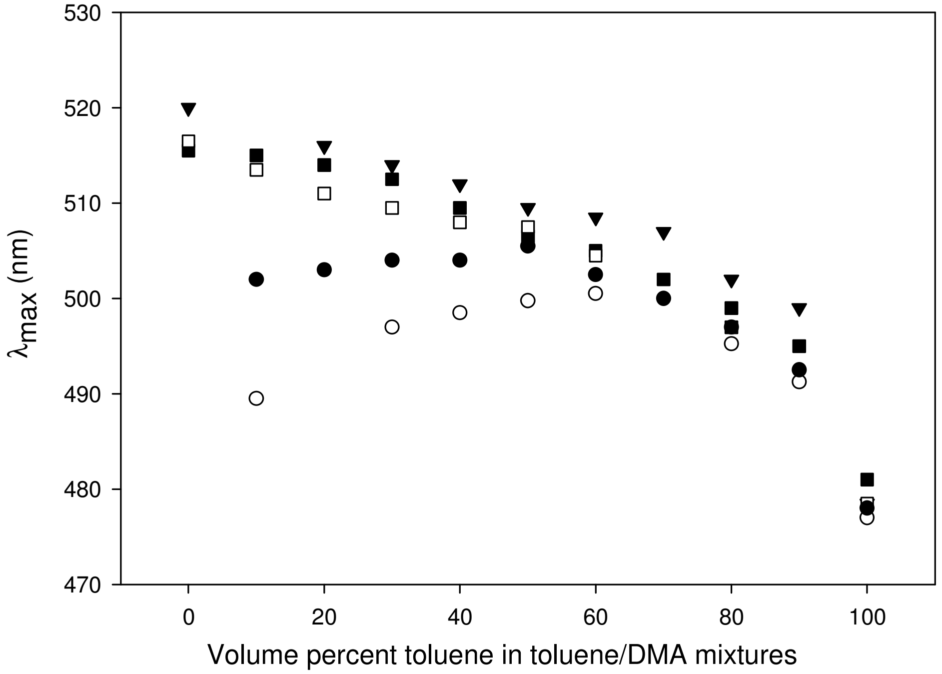


Figure 27. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent toluene in toluene/*N*, *N*-dimethylacetamide solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(4-methylstyrene) **25** (■), poly(4-*n*-butylstyrene) **26** (□), poly(4-*n*-dodecylstyrene) **27** (●), and poly(4-*n*-octadecylstyrene) **28** (○).

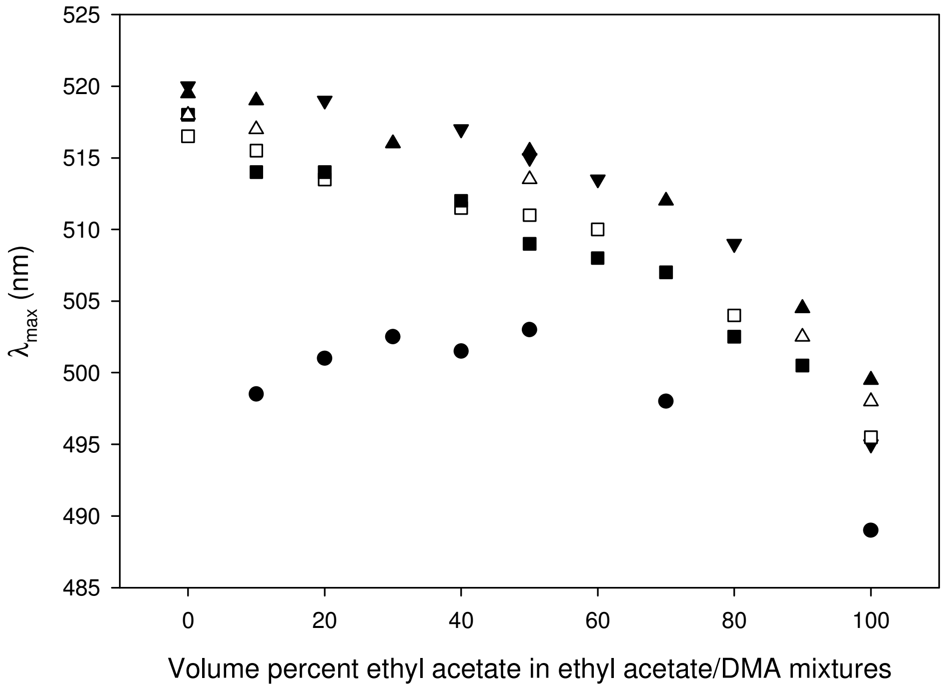


Figure 28. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent ethyl acetate in ethyl acetate/*N*, *N*-dimethylacetamide solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(4-methylstyrene) **25** (■), poly(4-*n*-butylstyrene) **26** (□), poly(4-*n*-dodecylstyrene) **27** (●), poly(ethylene glycol) **30** (△), and polyethylene glycol **32** (▲).

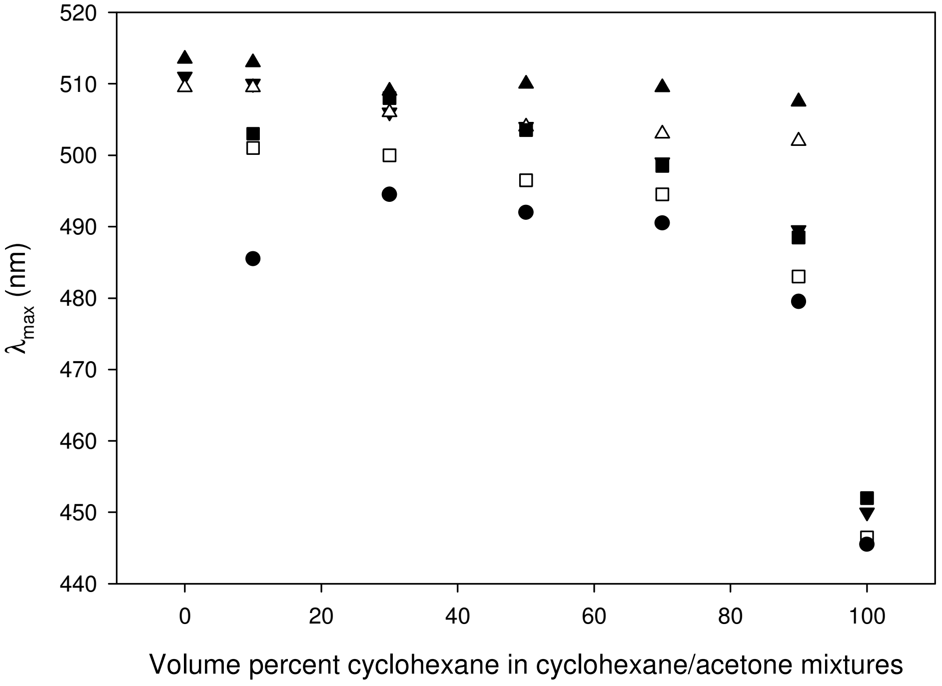


Figure 29. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent cyclohexane in cyclohexane/acetone solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(ethylene glycol) **30** (△), polyethylene glycol **32** (▲) polyisobutylene **31** (□), polyisobutylene **33** (■), and polyisobutylene **35** (●).

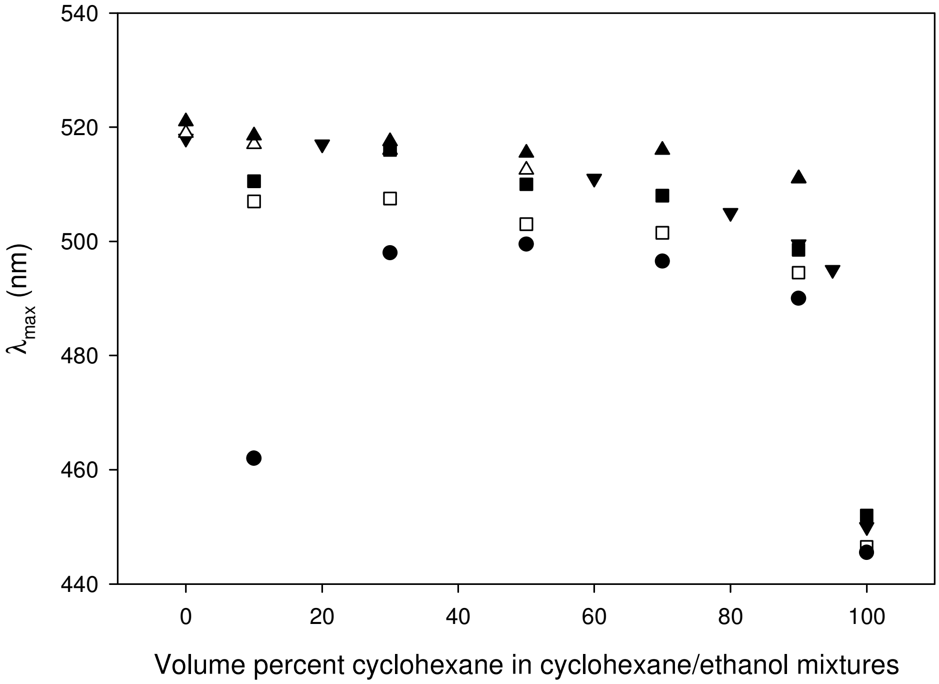


Figure 30. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent cyclohexane in cyclohexane/ethanol solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(ethylene glycol) **30** (△), polyethylene glycol **32** (▲) polyisobutylene **31** (□), polyisobutylene **33** (■), and polyisobutylene **35** (●).

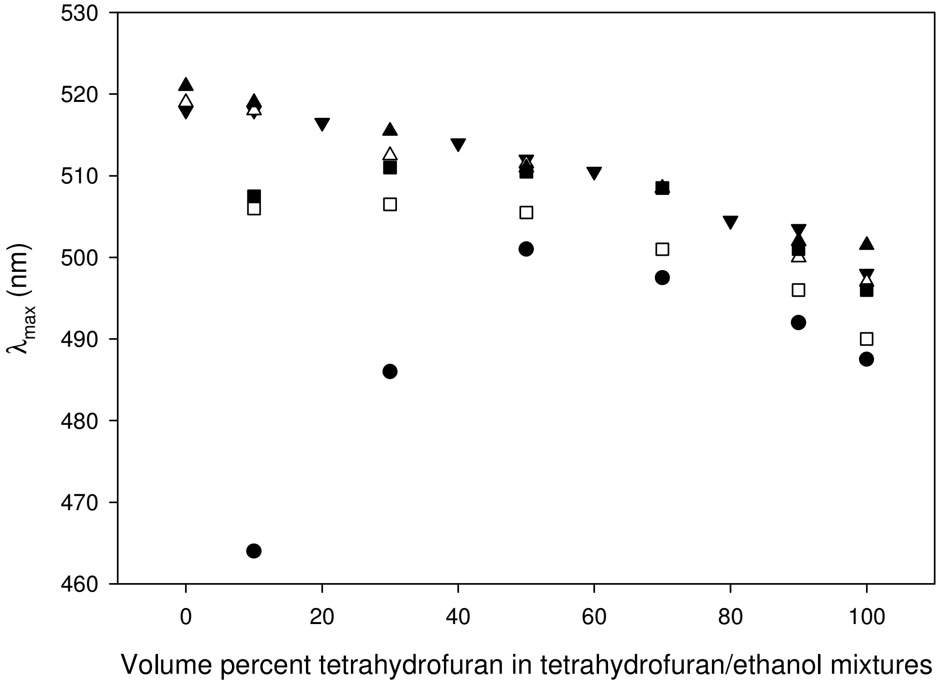


Figure 31. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent tetrahydrofuran in tetrahydrofuran/ethanol solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(ethylene glycol) **30** (△), polyethylene glycol **32** (▲) polyisobutylene **31** (□), polyisobutylene **33** (■), and polyisobutylene **35** (●).

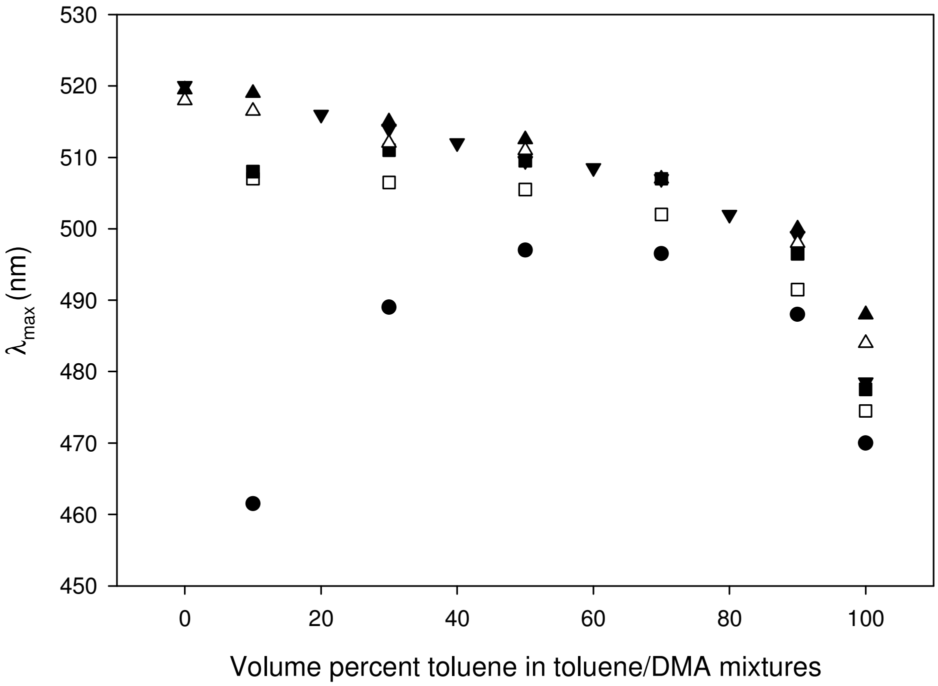


Figure 32. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent toluene in toluene/*N*, *N*-dimethylacetamide solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(ethylene glycol) **30** (△), polyethylene glycol **32** (▲) polyisobutylene **31** (□), polyisobutylene **33** (■), and polyisobutylene **35** (●).

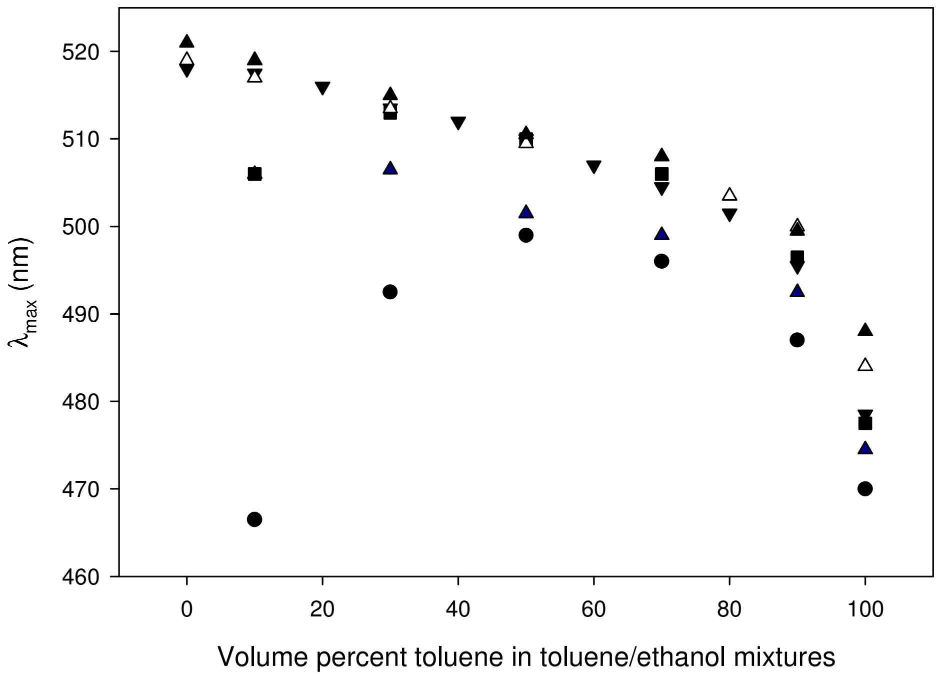


Figure 33. Plot of the observed emission λ_{max} of dansyl probes as a function of volume percent toluene in toluene/ethanol solvent mixtures. The dansyl probes are represented as *N*-benzyl-*N*-propyl dansyl **29** (▼), poly(ethylene glycol) **30** (△), polyethylene glycol **32** (▲) polyisobutylene **31** (□), polyisobutylene **33** (■), and polyisobutylene **35** (●).

With polymer conformation changes presumably occurring, the non-polar nature of the polystyrene supports can be exploited in these solvent systems to produce a solvent microenvironment around a supported species in solution by adjustment of the solvent composition. Given that conformational changes were occurring with polymer supports such as poly(4-*n*-octadecylstyrene) **28**, it is possible that certain solvent mixtures could be prepared that would utilize this conformational change to measure an even more non-polar microenvironment around the supported species than could be achieved by the solvent mixture alone. As in the previous example, at a solvent composition of 90% by volume of ethanol in a toluene/ethanol solvent mixture, poly(4-

n-octadecylstyrene) **28** had a measured emission λ_{max} of 476 nm which was close to the starting value of 477 nm for the emission λ_{max} of **28** in pure toluene. In the cyclohexane/ethanol (**Figure 26**) solvent mixtures, the introduction of ethanol at a solvent composition of 90% by volume of ethanol produced a similar value for emission λ_{max} of 474 nm for poly(4-*n*-octadecylstyrene) **28**. To ultimately prove that these observed drops in emission λ_{max} were the result of a conformational change, a solvent microenvironment lower that that produced by the *N*-benzyl-*N*-propyl dansyl probe **29** and the poly(4-*n*-octadecylstyrene) **28** dissolved in the pure solvent would have to be measured at relatively polar solvent compositions. In tetrahydrofuran/ethanol mixed solvent systems, the lowest obtainable emission λ_{max} of **29** was 498 nm in pure tetrahydrofuran. With the poly(4-*n*-octadecylstyrene) supported probe **28**, the emissionλ_{max} of 490 nm was measured in pure tetrahydrofuran. While lower than that measured for the low molecular weight probe, the solvent composition could be made increasingly polar and an even lower emission λ_{max} of 474 nm could be obtained. As this value of emission λ_{max} is more like a toluene than a tetrahydrofuran environment, the idea that the dansyl probe is surrounded exclusively by the polystyrene support versus the solvent environment is more likely. As can be seen in **Figures 24 & 25**, at relatively polar solvent compositions, poly(4-*n*-octadecylstyrene) supported dansyl **28** becomes increasingly isolated from the solution environment and a increasingly non-polar polymer microenvironment is experienced by the dansyl probe **28**. In these examples, a dansyl probe that is encapsulated by the polymer and is increasingly isolated completely from solution while still being part of the overall solution is observed.

As mentioned previously, the polystyrene supports used are soluble in a variety of solvents. With ethanol being a known poor solvent for these supports, *N, N*'-dimethylacetamide was also used since the poly(4-methylstyrene) **25** is soluble and poly(4-*n*-butylstyrene) **26** is sparingly soluble in this solvent. Therefore the deviations in the solvent microenvironment of the polymer supported dansyl should not be seen for these two polymers when *N, N*-dimethylacetamide is used as the more polar component of the solvent mixtures. In the toluene/*N, N*-dimethylacetamide (**Figure 27**) and ethyl acetate/*N, N*-dimethylacetamide (**Figure 28**) solvent mixtures, both polymers probes behave exactly as *N*-benzyl-*N*-propyl dansyl probe **29** as expected with only roughly a 5 nm solvatochromic shift from the trend set by **29**. In comparison, poly(4-*n*-dodecylstyrene) **27** experienced almost a 20 nm difference in solvatochromic shift relative to **29** since poly(4-*n*-dodecylstyrene) **27** is completely insoluble and ultimately not compatible with this polar solvent.

A collapsed polymer structure could be induced with the polystyrene supported probes **25-28** in the previous experiments. However, solvatochromic probes attached to the terminal end of one oligomer supports should not experience this phenomenon since the oligomer should be less capable of encapsulating the probe as with the previous polystyrene examples. As seen in **Figure 28**, poly(ethylene glycol) **30** behaved exactly as the *N*-benzyl-*N*-propyl dansyl probe **29** with only a 5 nm solvatochromic shift in pure ethyl acetate and a 1 nm difference in pure *N, N*-dimethylacetamide. Even at equal volume mixtures of these two solvents only a 1 nm difference in solvatochromic shift could be measured in comparison to **29**. This behavior was expected with the terminal functionalized polymer **30**, but the polymer support **32** was expected to possibly exhibit some collapsed structure since the probe was placed between two poly(ethylene glycol) chains. However, similar results were also obtained for **32** in this solvent mixture. Since both the poly(ethylene glycol) supported probes **30** and **32** were soluble in both solvents of the ethyl acetate/*N, N*-dimethylacetamide solvent mixture, the same linear behavior as that seen by poly(4-methylstyrene) **25** and poly(4-*n*-butylstyrene) **26** was expected. Therefore, non-solvents for **30** and **32** needed to be used if a conformational change in the polymer could be used to induce more solvent dependence for the emission λ_{max} for the dansyl probe in **32**.

With the poly(ethylene glycol) supported probes in these cyclohexane/acetone systems (**Figures 29**), there is very little difference in the emission λ_{max} of the poly(ethylene glycol) probes **30** and **32** from that of *N*-benzyl-*N*-propyl dansyl probe **29** initially (approximately 1-2 nm difference in emission λ_{max}). An increase in this difference is observed with the addition of increasing amounts of cyclohexane. At a solvent composition of 90% cyclohexane in this solvent system, an emission λ_{max} of 490, 502, and 508 nm were measured for **29**, **30**, and **32** respectively. Since poly(ethylene glycol) is insoluble in cyclohexane, this 13-18 nm solvatochromic shift was not surprising. While a more polar microenvironment is being measured in **30** and **32**, the lack of change in the emission λ_{max} as the solvent composition changes in assays of the emission λ_{max} of dansyl probes in both **30** and **32** in various cyclohexane/acetone mixtures is more likely a result of the influence of the polymer support rather than an polymer encapsulated structure.

The results of the previous experiments with poly(ethylene glycol) supports showed no measurable difference between probes with the oligomer chains placed on one or both sides of the probe. Similar experiments were performed with the non-polar polyisobutylene supports. For the polyisobutylene supported probes, it was determined that the terminal polymer supported probe **31** experienced little influence of its solvation by the polymer support. For example, in cyclohexane/ethanol solvent mixtures (**Figure 30**), in pure cyclohexane only a 3 nm solvatochromic shift is experienced by using the *N*-benzyl-*N*-propy dansyl probe **29** versus **31**. Upon increasing the polar nature of the solvent mixture, at 80% by volume ethanol, a solvatochromic shift of approximately 3 nm is still observed. As can be seen **Figures 29-33** with the two terminally functionalized polyisobutylene supported probes **31** and **35**, there is only a small hypsochromic shift from the solvatochromic trend set by **29**. This slight shift was expected since the polymer supports have already exhibited a similar shift in the pure solvent systems. One variation with the polyisobutylene probe **35** was experienced. In all solvent systems, a hypsochromic shift was detected, but only at solvent compositions of high polarity. This behavior cannot be completely explained. However, since it falls between the trends set by **29** and the other terminally functionalized polyisobutylene probe **31**, this behavior is not thought to be the result of some collapsed structure as seen in the polystyrene supports.

With the previous dansyl probe placed between two poly(ethylene glycol) chains, no reasonable conclusions could be drawn as to whether a collapsed structure had formed. This is not the case for the probe attached between two polyisobutylene chains

(33). In all solvent mixtures examined (**Figures 29-33**), it can be seen that there is a very marked difference in the emission λ_{max} for 33. The supported probe's behavior is identical in nature to what is seen in poly(4-*n*-octadecylstyrene) **28**. For example, in toluene/ethanol solvent mixtures (**Figure 33**) at polar solvent compositions of 90% ethanol, **29**, **28**, and **33** have a measured emission λ_{max} of 518, 476, and 467 nm respectively. In this system an even more non-polar microenvironment (an approximately 50 nm solvatochromic shift) is seen by the probe placed internally in a polyisobutylene chain than a similar probe supported as a pendant group on poly(4-*n*-octadecylstyrene). In solvent mixtures using toluene and tetrahydrofuran (**Figures 31-33**), an emission λ_{max} lower than that observed in pure solvents was again observed at relatively polar solvent compositions. In these solvent mixtures, the formation of a polyisobutylene polymer micelle around the probe could be forming. Regardless of its exact structure, a collapsed structure is expected with the internally supported polyisobutylene probe in solution when highly polar solvent compositions are used.

In mixed solvent systems, the supports derived from polystyrene and polyisobutylene produced a number of solvatochromic changes. Polymer confirmation changes were suspected to form in solvent mixtures the polymer support was incompatible with. While the supported dansyl probe was still in solution, a solvent microenvironment that reflected a probe completely isolated from the solution could be measured with polymer supports such as poly(4-*n*-octadecylstyrene) **28** and polyisobutylene **33**. With polymer supports **30**, **31**, **32**, and **35**, no influence on the dansyl microenvironment by the polymer support could be measured that would indicate this collapsed structure. Therefore, at various solvent mixtures, these supports would allow for complete accessibility of supported species to the solution environment.

Conclusions

The chemical nature of the polymer support is a factor that must be acknowledged when supporting reagents and catalysts. Soluble polymer supports are seen as a way to maintain homogeneity of the supported reagent or catalyst while introducing the advantage of a more efficient macromolecular recovery. With the polarity of solvents and substrates playing an important role in many reactions, the influence of these polymer supports must be taken into consideration.

I have described the synthesis and evaluation of a variety of soluble polymer supported solvatochromic catalyst surrogates. The results of these studies indicate that modified polystyrene and poly(ethylene glycol) supports with pendant species allow adequate solvent accessibility in pure solvents. Based on the nature of the support, the polystyrene supports undergo a change in conformation depending on the interaction of the support with the solution. In solutions the polystyrene support is increasingly incompatible with, supported species will be trapped in a polymer-encapsulated structure. For the poly(ethylene glycol) oligomers, it was determined that a supported species can be attached and the solvent accessibility will be minimally affected by the method of attachment either terminally or internally in both pure and mixed solvents. With the terminally functionalized polyisobutylene supports, it was shown that the use of polar linkages has a mild effect on solvent microenvironment in pure solvents. However, there is little difference in supporting of a probe terminally by either direct or polar linkage to the polyisobutylene oligomer in terms of solvent accessibility in both pure and mixed solvents. And finally, with the use of internally functionalized polyisobutylene supported species, it was determined that they behave in a manner similar to the polystyrene supports, with polymer conformations being induced that entangle the supported species in a polymer-like microenvironment.

CHAPTER IV

SEPARATION OF POLYISOBUTYLENE COPPER COMPLEXES IN THE ATOM TRANSFER RADICAL POLYMERIZATION OF STYRENE

Introduction

Atom transfer radical polymerization (ATRP) has become the predominant method of controlled radical polymerization since its initial discovery in 1995. In the last decade, the number of publications dedicated to this topic is a clear indication of the interest in these systems for polymer synthesis. Atom transfer polymerizations have the advantages of producing polymers with controlled molecular weights and molecular weight distributions. The inherent end-group control of this type of polymerization leaves a reactive functionality at the end of a polymerization that can be exploited to further synthesize block copolymers. The nature of this polymerization also facilitates the production of a variety of polymer architectures with various functionalized monomers. This robust nature of this type of polymerization is also apparent in the array of solvents that can be used in the production of these polymers.

The production of commercial polymers by ATRP by industry is slowly coming about. The capability to control the different structural aspects of polymers produced by ATRP allows for fine-tuning of a polymer’s physical characteristics. Such polymers as materials can be used in applications such as lubricants, membranes, in drug delivery, and as electronic materials.[89] However, with ATRP being used in the production of these materials, metal contamination is problematic since typical concentrations of the highly colored transition metal catalyst in bulk monomer are roughly 0.1 M. At these levels, certain polymeric materials cannot be made by traditional ATRP polymerization unless an efficient and practical means of removal of the transition metal complexes can be achieved.

The high amount of catalyst used is a consequence of the nature of the polymerization system (**Figure 34**). As the name indicates, radicals are produced by a reversible transfer of a radically transferable atom, a halogen atom, from a monomeric or polymeric alkyl halide initiator to a transition metal complex in a lower oxidation state. This forms an organic radical and a transition metal complex in a higher oxidation state.[90] Typically, stoichiometric amounts of transition metal catalysts relative to the

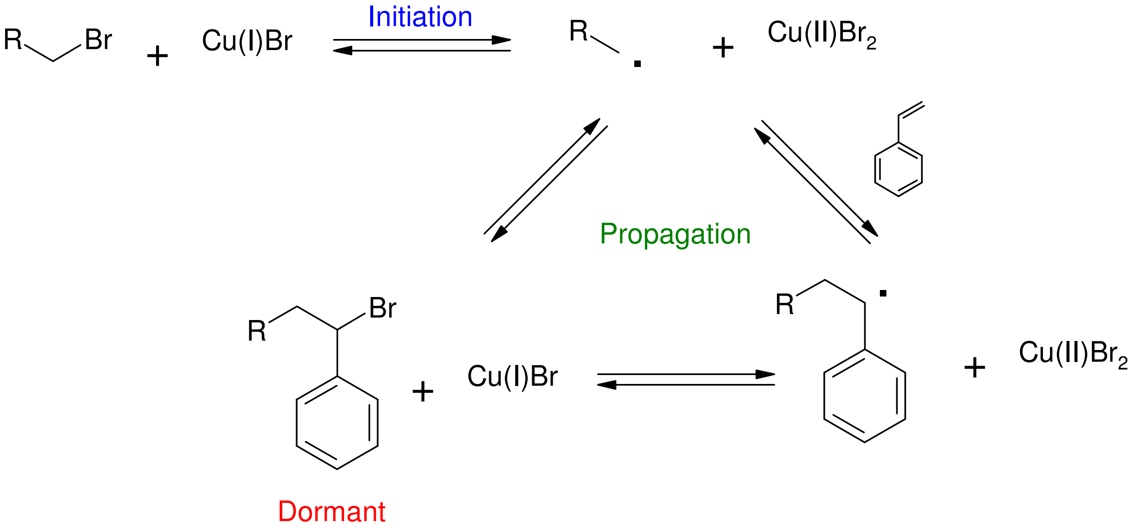
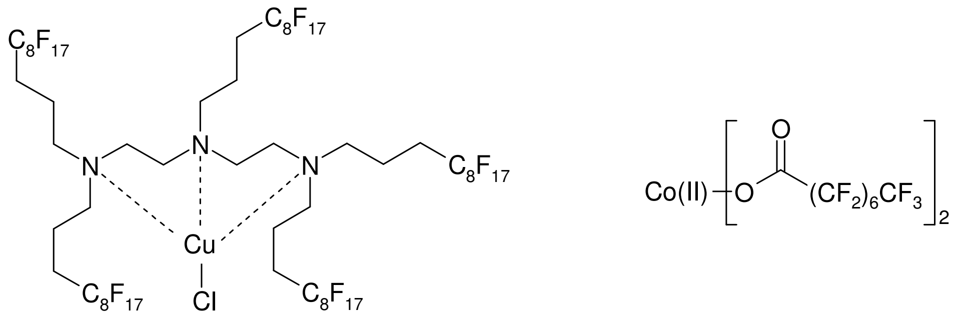


Figure 34. Copper catalyzed transfer of a halogen atom to form active and dormant species in a typical ATRP by a copper (I) redox system.

initiator are used to efficiently accomplish this redox process and to produce the desired polymerization results. At the end of a typical ATRP polymerization, the extent of control over the polymerization reaction can be verified by the molecular weight and molecular weight distribution. Typically all initiator molecules form a reactive radical which can interact with the monomers in solution to form the growing polymer chain. Since the propagating polymer chains all propagate at the same rate, a linear correlation between monomer consumption and molecular weight can be seen. Therefore, if efficient initiation and propagation occurs, the molecular weights of the product polymer correlate to the predicted molecular weights. The predicted molecular weight is calculated by the molar ratio of monomer to initiator used at the start of the polymerization multiplied by the conversion of monomer to polymer. Since propagation is controlled by the copper complex in this polymerization, the propagation of the growing polymer chains is slower than a typical free radical polymerization. However, as propagation is now occurring at a constant rate, the distribution, or polydispersity, of polymer molecular weights approaches unity in these systems (M_w/M_n=1.0-1.4). This high control over final polymer properties makes these systems highly sought after for applications where control of molecular weight of the polymer is needed as mentioned earlier.

In an academic setting, column chromatography or ion exchange is often used to remove the unwanted copper contaminants from the final product polymer. However, methods that reduce the amount of transition metal used in the process or removes or potentially recycles the metal complex after the polymerization are more desirable for this process to be commercially applicable. One such method involves the liquid/liquid separation of the transition metal complexes from the product in an organic/aqueous solvent system. As mentioned in previous chapters, polymers are known to exhibit phase selectively solubility in liquid/liquid biphasic systems. This property was recently taken advantage of and a biphasic system involving toluene and water was utilized for the ATRP polymerization of styrene.[91] Under these biphasic conditions, styrene and polystyrene are phase selectively soluble in toluene over water. The ATRP polymerization of styrene produced a product polystyrene with a molecular weight of 15,000 Da and a polydispersity (M_w/M_n) of 1.15. In this system a copper (I) halide/amine complex was used to effect the desired polymerization. This polar catalyst complex could therefore be easily removed in the aqueous phase of the reaction mixture and little contamination of this complex in the product polystyrene was measured (6 ppm residual copper in product). While separable, this polymerization scheme was limited. The production of various molecular weight polystyrene products with the same control over final molecular weight properties could not be achieved with this system because it is biphasic at the beginning, end, and during the reaction.

Given the limitations of this always biphasic system, it could be expected that other systems including fluorous thermomorphic systems described in earlier chapters have been investigated. Using these systems it was hoped that a homogeneous reaction scheme with a biphasic separation would accomplish the goal of producing polymers with controlled molecular weights and allow for efficient separations of the active transition metal complex. A variety of groups have designed various ligands and complexes that can be phase selectively soluble in fluorous solvents (**Figure 35**). Haddleton was the first to report a fluorous biphasic ATRP catalysis system for the removal of copper species in the fluorous phase.[92] Using perfluoromethylcyclohexane and toluene, this solvent system was expected to produce a homogeneous polymerization solution with a biphasic separation at the end removing the fluorous amine copper complex **36**. The ATRP polymerization of methyl methacrylate was achieved using **39**. Unfortunately, the thermomorphic behavior of this solvent system was not exhibited as the solvent system remained biphasic even at elevated temperatures. This resulted in polymerization times slower than typical ATRP polymerizations. Other systems utilizing fluorous solvents that effectively afford the desired homogeneous polymerization conditions have been investigated and include a 1:1:1 equivolume mixture of toluene, cyclohexane, and perfluorodecalin.[93] In the reported example, a



Fluourous copper (I) ligand

36

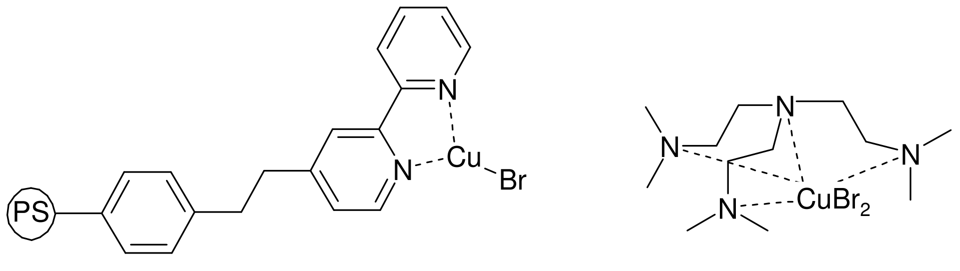
Fluorous cobalt complex

37

Figure 35. Fluorous-tagged ligands for use in fluorous biphasic separations of active ATRP metal complexes from the product polymer.

fluorous cobalt complex **37** was used in the homogeneous ATRP polymerization of styrene with removal of the cobalt complex in the fluorous phase after the polymerization reaction. However, the maximum molecular weight of 2500 Da that was seen in this system for the production of polystyrene is undesirable. This limitation was ascribed to the formation of a biphasic system at higher conversions of styrene to polystyrene. At higher conversions the concentration of polystyrene which is presumably increasingly insoluble in this homogeneous reaction resulted in a biphasic system developing in much the same way the small addition of water causes a heptane/ethanol system to become biphasic.

Immobilized/soluble polymer hybrids[90] have also been used to support these active catalyst complexes for solid/liquid separations after polymerizations (**Figure 36**). These recoverable systems have been designed with these catalyst systems that produce



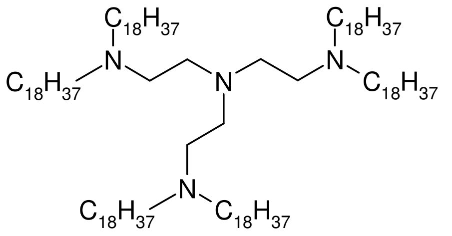
38 **39**

PS = Cross-linked polystyrene

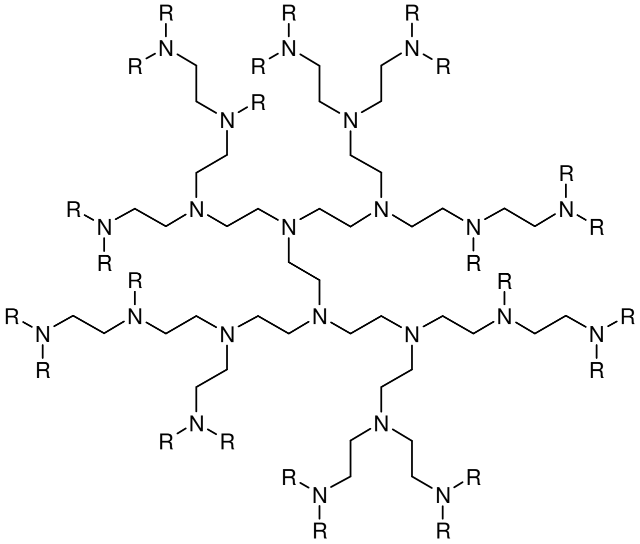
Figure 36. Immobilized/soluble copper complexes for use in ATRP polymerization.

methyl methacrylate polymers with controlled molecular weights and molecular weight distributions, and reduced amounts of copper in the product polymers. However, to establish control over this system, a soluble copper (II) species **39** has to be present as a deactivator of the propagating polymer chain. In systems only using the immobilized polymer supported copper complex **38**, limited control is exhibited by the copper complex on the controlled radical polymerization of methyl methacrylate. Using **38** and **39** concurrently in the polymerization does result in control of the final product polymer's molecular weight. The polymer supported species could be effectively separated from the product polymer by a filtration. However, excessive washings of the catalyst after filtration prior to recycling were still required in this system. Also, the soluble copper (II) deactivator complex **39** was completely soluble in the product polymer and would have to be removed by other methods.

In the previous example, a soluble copper complex was needed to establish control over the polymerization. With removal of soluble amine complexes only being achieved with tedious methods such as column chromatography, still other methods have been investigated that use soluble copper ligands which can be separated by a solid/liquid separation. Alkylated amines such as those shown in **Figure 37** were prepared and used in the ATRP polymerization of methyl methacrylate in 1,4-dioxane. These copper complexes could be removed from the product polymer at the end of the polymerization. Two different approaches to a solid/liquid separation illustrate the advantages and problems of these systems. The first sort of solid/liquid separation is one that used the temperature dependent solubility of **40** in 1,4-dioxane. This thermoresponsive ligand was prepared by alkylation of a simple amine with hydrophobic octadecyl groups.[94] This hydrophobic amine chelate has an upper critical solution temperature and its copper (I) complex is completely soluble in 1,4-dioxane at 70 ˚C. Therefore running the polymerization of methyl methacrylate at this elevated temperature proceeded with a soluble **40**/copper (I) complex. Cooling this reaction mixture down to 10 ˚C induced precipitation of the **40**/copper (I) complex. Filtration removed the amine complex from the polymeric solution. However, 200 ppm residual copper remained in the product polymer after this filtration, possibly because the precipitation is not complete.



40



41

Figure 37. Thermoresponsive copper ligand (left) and hyperbranched PEI copper ligand (right).

A second sort of soluble amine ligand was also synthesized that could be separated from the product polymer, but in a different fashion as that previously described. Alkylated hyperbranched polyethyleneimine (PEI) **41** can be readily prepared from the commercially available polyamine.[95] Use of copper (I) complexes of **41** could be used in the ATRP polymerization of methyl methacrylate in 1, 4-dioxane to produce polymers with controlled molecular weight and polydispersity. However, at the end of the reaction, the **41**/copper (I) complex could be removed by precipitation of the product polymer rather than the ligand. In polar solvents such as methanol, the **41**/copper complex is completely soluble and poly(methyl methacrylate) is completely insoluble. Taking advantage of this difference in solubility, the **41**/copper complex could be removed from the product polymer by precipitation and removal of the **41**/copper complex as a methanol solution. Copper contamination was measured to be 16.5 ppm of residual copper in the poly(methyl methacrylate) product. However, for this scheme to be effective, excess solvent had to be used to precipitate the product polymer and effectively separate it from the soluble **41**/copper complex.

The previous examples used polymer supported copper complexes that had to be used in conjunction with a soluble deactivator. To overcome this limitation, different polymer supports that offered better solubility of the supported copper complex were investigated. Brittain and coworkers have examined the use of several polymeric supported ligands in ATRP polymerizations (**Figure 38**). With JandaJel offering increased swelling in solution as compared to normal polystyrene supports, the use of this resin to synthesize a more soluble polymeric imine (**42**) copper complex was investigated.[96] Use of **42**/copper complexes in the ATRP polymerization of styrene resulted in polystyrene with good molecular weight control but limited control over polydispersity (M_w/M_n=1.5). This limited control was attributed to the lack of sufficient solution accessibility of the copper (II) complex to interact with propagating radicals on the polymer chain. With these diffusion limitations of catalyst complex, the ineffective deactivation would cause an increased polydispersity of the product polymer.

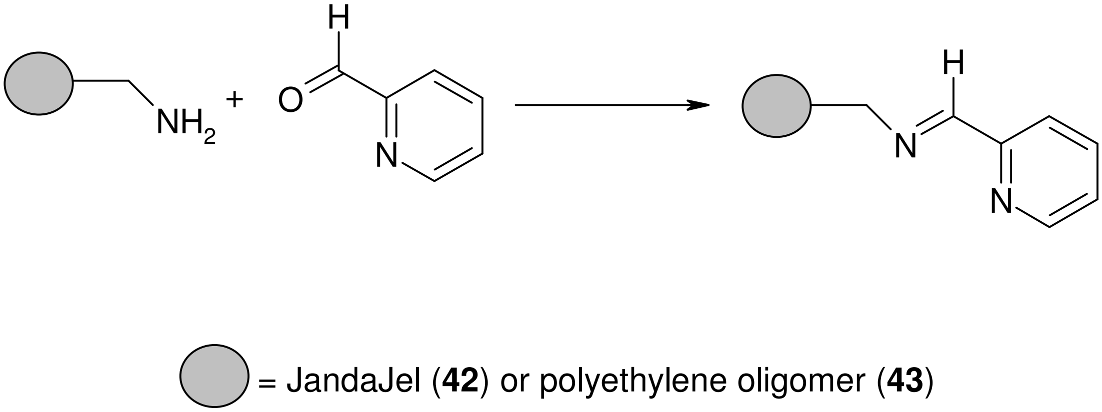


Figure 38. Pyridine-based imine copper ligands **42** and **43** for use in ATRP polymerizations.

To avoid these limitations, a soluble polymer support (**43**) was investigated. Polyethylene oligomers can be used as both a soluble and insoluble support based on their upper critical solution temperature. At elevated temperatures, the **43**/copper complex is completely soluble in the reaction solution. Upon cooling, the copper complex supported on polyethylene precipitates from solution and can be recovered by a filtration. Therefore, polyethylene oligomers that were modified with an appropriate imine ligand were used in ATRP polymerization reactions.[97] In an ATRP polymerization of polystyrene with a ligand like that used on the JandaJel, the same control over molecular weight was achieved. However, limited control over the polydispersity (M_w/M_n=1.5) was still seen. It was suggested that in this system, some interference of reaction conditions or the polyethylene support on the effective catalysis of the supported copper complex must be occurring though such effects had not been observed in other catalytic reactions including polymerizations.[98]

In all of the examples described above of supported ATRP catalysts, a stoichiometric amount of copper had to be used in the controlled radical polymerizations using these supports. This is not the case with recent examples using low molecular weight copper ligands, as they can now be used in sub-stoichiometric amounts to produce polymers with controlled molecular weight and polydispersity. Also, with these examples of supported catalysts, the recycling of these supports was limited. At best 3-4 polymerization cycles of methyl methacrylate could be carried out before a loss in control over the molecular weight or polydispersity occurred. The work below sought to address this problem and to develop a new approach to polymer-supported ATRP polymerization of styrene.

The previous examples of supported catalysis for ATRP polymerization generally had problems with solubility of the catalysts. As indicated in the previous chapter, polyisobutylene oligomers have solubility properties such that they can behave exactly as a low molecular weight species but are still separable. If that were also true in

ATRP polymerizations, the use of this polymer support in the ATRP polymerization of styrene should produce sufficient control in this reaction.

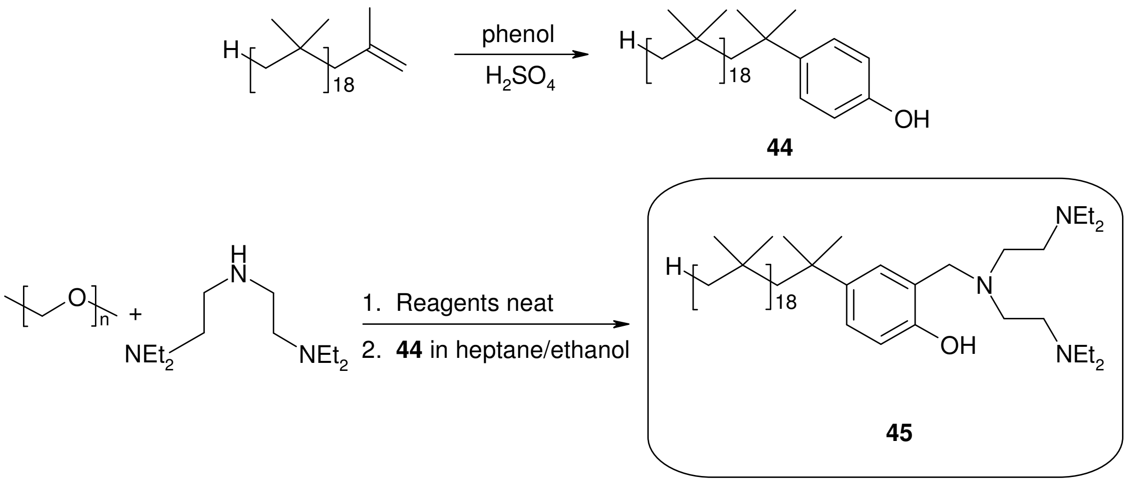
Given the phase selective solubility of polyisobutylene in heptane, a “smart” catalyst separation was envisioned that employed the differing solubilities of styrene and polystyrene in heptane. This separation is precedented in the earlier fluorous phase studies but could be more practicable and tunable in an all organic system. Under the initial conditions in the polymerization of styrene in heptane, the monomer is completely soluble in the reaction mixture. However, as the polymerization occurs, production of increasingly higher molecular weight polystyrene ensues. This increasingly high molecular weight product polymer species is increasingly insoluble presenting the biphasic solution. Indeed, at high enough conversions, this product polystyrene would induce the heptane/styrene mixture to self-separate to produce a biphasic liquid/liquid, liquid/gel, or solid/liquid system. As shown in the previous chapters, polyisobutylene oligomers are highly soluble supports in biphasic systems involving heptane. However, under biphasic liquid/liquid conditions, these non-polar oligomers exhibit a high phase selective solubility in heptane over other more polar solvents. Also, in the previous chapter it was shown that polyisobutylene oligomers have terminal groups that behave much like a low molecular weight species in mixed solvent systems. Indeed, the terminal groups studied in Chapter III on polyisobutylene were more comparable to a low molecular weight species that similar species on other polymer supports. Therefore, use of this oligomer support with sub-stoichiometric amounts in the ATRP polymerization of polystyrene with heptane as a solvent should allow for efficient catalysis and separation of active copper complexes from the product polymer. Once removed from the product polystyrene, the polyisobutylene supported complexes should then be able to be easily recycled in further ATRP polymerization of styrene by the addition of fresh monomer.

Results and Discussion

Soluble polyisobutylene oligomers were chosen to investigate if an active catalyst complex supported on this support terminally would behave as predicted in the previous chapter. Since polyisobutylene supports are soluble in a wide range of organic solvents mixtures, the synthesis of copper ligands for use in ATRP polymerizations could be carried out in the same manner as low molecular weight ligands. Also, given the heptane phase selective solubility of polyisobutylene, the synthesis of these polymer supported ligands would be greatly expedited since the unsupported ligands are themselves polar and can be separated from the non-polar support using a thermomorphic or latent biphasic system.

The first polyisobutylene supported ligands investigated were those derived from a simple alkyl amine ligand. *N,N,N',N'*-tetraethyldiethylenetriamine (TEDETA) was chosen as the amine ligand and supported on polyisobutylene *via* two synthetic routes. In choosing the synthetic route, it was advantageous to devise a scheme that produced the polyisobutylene terminated ligand with the highest fidelity and least number of modifications to the supported ligand system. Therefore, the first synthetic route arrived at the desired complex in two synthetic steps from the starting polyisobutylene (**Scheme 22**). First the electrophilic aromatic substitution of phenol by the polymeric alkene was used to afford the polyisobutylene *p*-substituted phenol **44**. Formation of **44** was verified by the presence of the 1,4-disubstituted aromatic protons appearing as doublets at 6.7 and 7.2 ppm upon ^{1}H NMR analysis of the polymer support and by the complete disappearance of the polyisobutylene alkene protons centered around 4.7 ppm. **44** could then be treated with TEDETA and paraformaldehyde to afford the desired polyisobutylene-phenol ligand **45**. The formation of **45** was verified by the shift in aromatic protons of the supported phenol and the appearance of the ligand protons in the ^{1}H NMR spectrum of the polyisobutylene support. This polyisobutylene ligand could be treated with copper to form a heptane soluble copper complex for use in a controlled radical polymerization. The formation of the copper complex could not be verified by NMR but was evidenced by the color change of the colorless **45**/ heptane solution to a green homogeneous solution on the addition of copper (II) chloride.

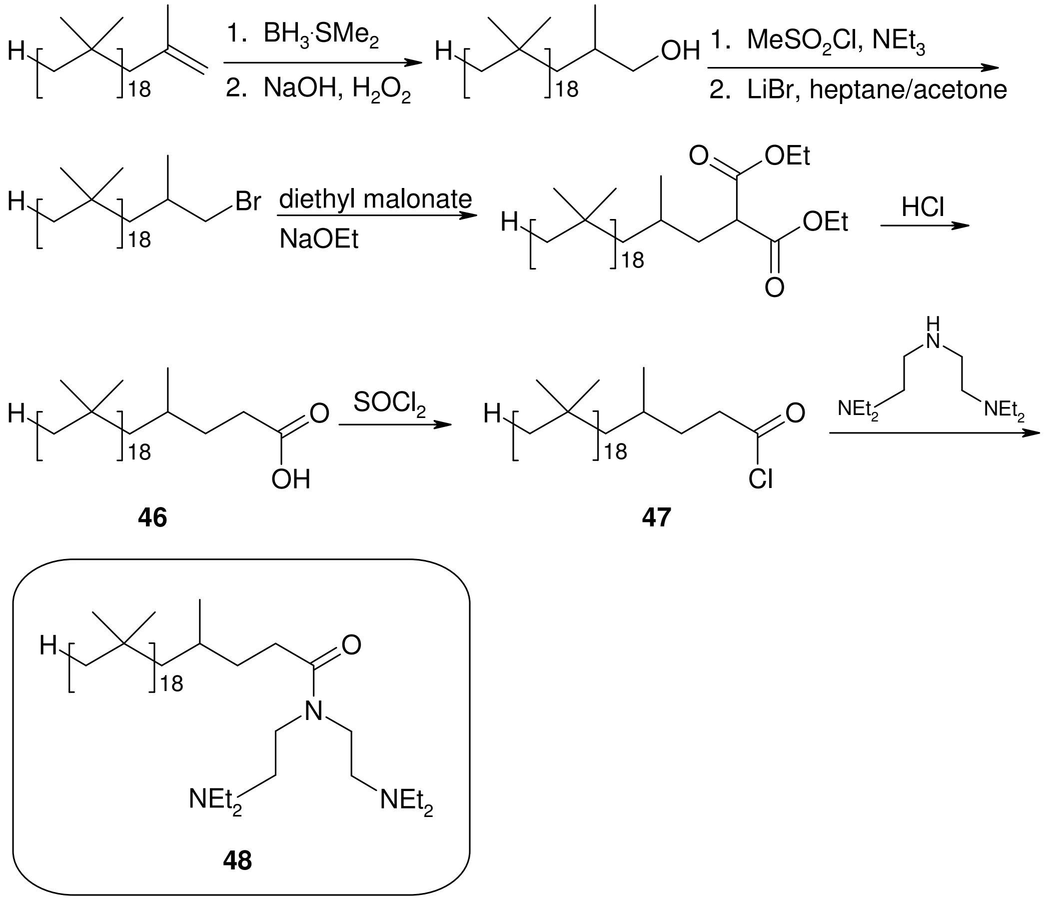
Scheme 22. Synthesis of polyisobutylene-phenol ligand **45**.



In the previous studies of polyisobutylene supported solvatochromic probes, the method of attachment had a slight influence over the microenvironment of the supported probe. Therefore, another synthetic method to attach TEDETA to polyisobutylene was used to determine if such differences could affect in an actual catalytic process. Since the previous ligand had a phenol in close proximity to the ligand, another synthetic scheme was developed where TEDETA was attached to PIB *via* an amide bond as seen in **Scheme 23**. The synthesis of a polyisobutylene terminated carboxylic acid **46** was previously reported.[65] Treatment of **46** with thionyl chloride produced the polyisobutylene terminated acid chloride **47**. Infrared spectroscopy established that formation **47** occurred based on the complete disappearance of the characteristic carbonyl peak of **46** (1710 cm^{-1}) and the appearance of the desired carbonyl peak of the acid chloride **47** (1800 cm^{-1}). Rather than isolating **47**, it was allowed to react directly with TEDETA to produce the desired polyisobutylene-terminated amide **48** as determined by the new carbonyl peak of the amide (1640 cm^{-1}) as well as the ^1H NMR analysis of the final product.

The separation strategy envisioned for the separation of these polyisobutylene supported copper complexes from the product polymer envisioned the use of heptane to induce a phase separation of the product polystyrene from a heptane phase containing the polyisobutylene copper complex. However, it was equally important to establish that these ligands were effective in ATRP chemistry. To test the efficiency of these ligands in a controlled radical polymerization, a literature procedure was duplicated to ensure

Scheme 23. Synthesis of polyisobutylene amide ligand **48**.



these ligands were suitable for use in the controlled radical polymerization of styrene prior to using our separation scheme. An ATRP procedure using anisole as a solvent and a copper (II) species was employed. Matyjaszewski recently reported using oxidatively stable copper (II) complexes that can be reduced *in situ* to form the active copper (I) complexes needed in normal ATRP.[99] This method of generating the active copper species *in situ* was of interest to us ultimately since our polyisobutylene supported ligands could be metalated with stable copper (II) species and stored for extended periods of time before use. This procedure employed the use of tin (II) 2-ethylhexanoate ($Sn(EH)_2$) to reduce copper (II) chloride to copper (I) chloride. Since this compound is an FDA approved anti-oxidant, the use of this tin (II) species as an oxygen scavenger could be utilized in our polymerizations too. With this scavenger present, stringent degassing would not be required. Finally, using this method, the controlled radical polymerization of styrene can reportedly be effected using reduced amounts of copper complexes. Therefore, the use of polyisobutylene copper complexes could be used in sub-stoichiometric amounts in this polymerization scheme, greatly reducing the amount of possible copper contamination in the use and facilitating recycling of this support.

With the exception of the ligand, the same reaction conditions reported by Matyjaszewski were used in this polymerization. The polyisobutylene terminated ligand (**45** or **48**) was added as an anisole solution to a dry Schlenk flask containing copper (II) chloride. The flask was then sealed and heated for 15 min at a temperature of 110 °C. After sufficient stirring, a green homogeneous solution formed indicating a soluble polyisobutylene terminated copper (II) complex had formed. This solution was then allowed to cool to room temperature and purified styrene was added and allowed to stir with the soluble polymeric copper (II) complex. At this time, an anisole solution of tin (II) 2-ethylhexanoate was added and the flask was sealed with a rubber septum. The solution was then sparged with nitrogen gas for 15 min. Then ethyl-2-bromoisobutyrate initiator which had been previously degassed was added *via* syringe and the reaction flask was immediately placed in an oil bath which at 110 °C. After allowing the polymerization to proceed for 9.5 h with **45** and 20 h with **48**, the now viscous reaction mixture was allowed to cool to room temperature. Excess monomer and solvent were then removed by vacuum distillation. The product was then isolated with the included copper complexes of **45** or **48**, as was evident by the highly colored solid polystyrene product. The yield of these reactions was calculated based on the mass of styrene used divided by the mass of recovered polymer and the theoretical molecular weight was calculated based on the molar ratio of initial styrene to initiator multiplied by both the molecular weight of styrene and the conversion of monomer to polymer. Actual molecular weights were measured by gel permeation chromatography using polystyrene standards. The exact results for the polyisobutylene terminated copper complexes of **45** and **48** in the controlled radical polymerization of styrene can be seen in **Table 9**.

Table 9. ATRP polymerization of styrene using polyisobutylene phenol **45** and polyisobutylene amide ligand **48** copper (II) complexes in anisole.[a]

Ligand	Conversion[b] (%)	Time (h)	M_n (calc)[c] (Da)	M_n[d] (Da)	M_w/M_n[d]
48	50.2	20.0	10k	160k	1.36
45	27.9	9.5	6k	74k	1.61

[a] All polymerizations were run at 110 °C with a styrene concentration of 6.5M in anisole. The ratio of monomer/initiator/$CuCl_2$/Ligand/Sn(EH)2 was 200/1/0.1/0.1/0.1.

[b] The percent conversion was calculated based on the initial mass of monomer used divided by the mass of polystyrene recovered.

[c] The calculated molecular weights were based on the initial monomer to initiator ratio multiplied by the conversion and the molecular weight of styrene.

[d] The molecular weights and polydispersity of the polystyrene products were determined by gel permeation chromatography using a GMHx1 column set with THF as the eluting solvent.

With a low molecular weight species in this polymerization, the reported polymerization of styrene occurred to yield product molecular weights close to calculated values (M_n=17,000 Da and M_n(calc)=14,000 Da) with good control over polydispersity (M_w/M_n=1.12).[98] The polyisobutylene phenol ligand **45**/copper (II) complex did not exhibit similar results, exhibiting both a lack of control over both molecular weight and polydispersity. This indicates that inefficient initiation and deactivation of radicals in this polymerization occurred. As can be seen from the results of these polymerizations, the calculated molecular weight is far from the actual molecular weights measured (M_n=74,000 Da and M_n(calc)=6,000 Da). However, examination of the polydispersity in the case of the polyisobutylene-supported amide **48**/copper (II) complex (M_w/M_n=1.36) indicated that efficient deactivation of the propagating radical species during polymerization could be occurring. Nonetheless, this complex too showed a lack of control over molecular weight. This can be attributed to inefficient activation of the initiator by the polyisobutylene copper (II) complexes.

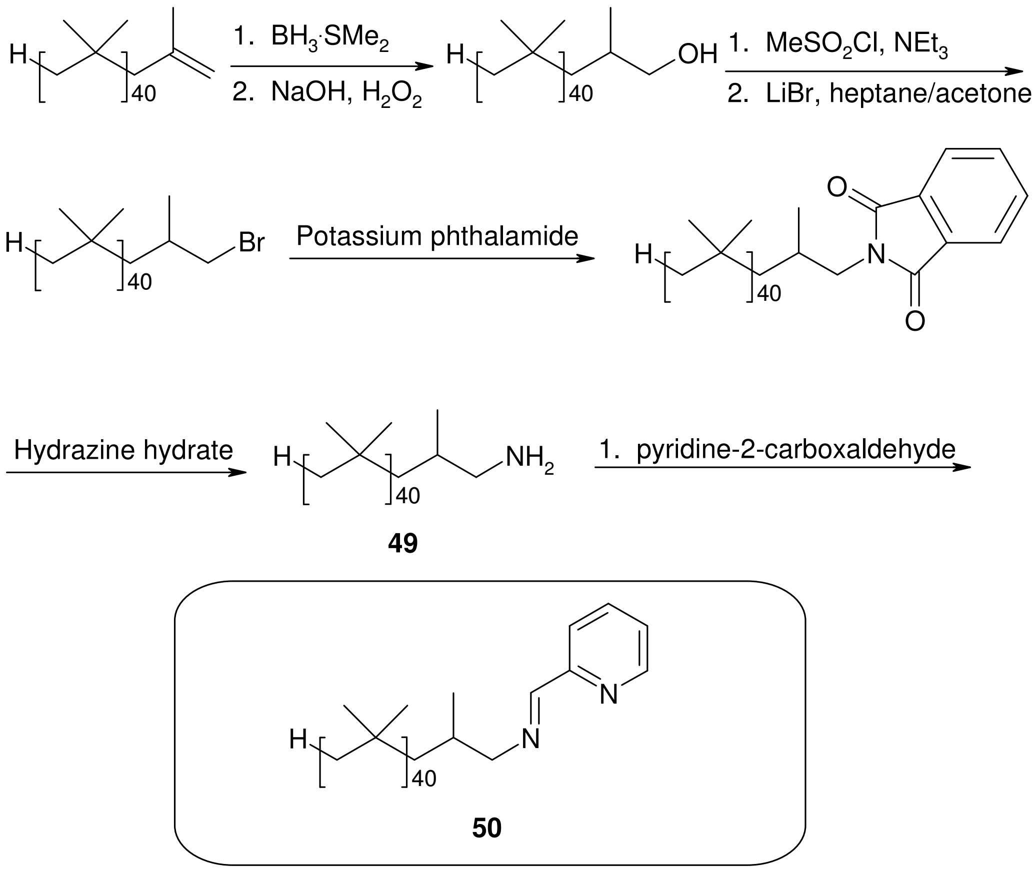
With previous polymer supported copper complexes, inefficient deactivation by the supported complex was observed because of diffusional limitations of the support to effectively interact with the propagating polymer chain. Since the polydispersity in the case of the polyisobutylene-amide copper complex was low, this diffusional limitation was not a problem with this support. Therefore, it was concluded that the choice of polymer support was not the limiting issue in this polymerization scheme. With low molecular weight copper complexes, the structure of the copper ligand influences both the activation and deactivation properties of copper species in ATRP polymerizations.

Therefore, it was suspected that the replacement of the TEDETA ligand with a different sort of copper ligand could produce more favorable results. We supposed that the use of a different copper ligand could allow for more efficient activation of the initiator and allow us to gain control over the molecular weight of the product polymer.

Synthesis of a polyisobutylene pyridine imine copper complex was next investigated (**Scheme 24**). The necessary polyisobutylene terminated amine **49** starting material was first formed by methods previously reported by our group using a series of functional group interconversions that could be easily monitored by ^{1}H NMR spectroscopy.[65] The facile purification of these polyisobutylene intermediates was again greatly expedited by the heptane phase selective solubility of polyisobutylene support. This amine was then coupled with 2-pyridinecarboxaldehyde in the same manner as reported by Brittain[96,97] to product the desired ligand **50**. The same polymerization procedure as previously used was performed with this new polyisobutylene terminated pyridine imine ligand **50** as a copper (II) complex. The results of using this ligand in the ATRP polymerization of styrene can be seen in **Table 10**.

As mentioned previously, the structure of the copper ligand used in these polymerizations can have varying effects on both initiation and deactivation efficiencies. As seen from the initial polymerization using anisole as a solvent, a molecular weight close to the predicted value (M_n=10,000 Da and M_n(calc)=14,000 Da) indicated that efficient activation of the initiator had occurred. However, increased polydispersity of the product polystyrene (M_w/M_n=1.99) indicated that poor deactivation by the polyisobutylene **50**/copper complex was occurring. A possible explanation for this

Scheme 24. Synthesis of polyisobutylene terminated pyridine imine ligand **50**.



could be the choice of solvent. While soluble in anisole, some unfavorable interactions of the slightly polar anisole solvent molecules could impose limitations on the use of polyisobutylene oligomers. Therefore other solvents **50** was readily soluble in were studied too. As can be seen in the experiments in **Table 10**, control over molecular weight (M_n=24,000 Da and M_n(calc)=21,000 Da in heptane) and polydispersity (M_w/M_n=1.28 in heptane) was exhibited by polyisobutylene **50**/copper complex when more non-polar solvents were used. This confirmed that polyisobutylene **50** could be

Table 10. ATRP polymerization of styrene using polyisobutylene pyridine imine **50**/copper (II) complex in various solvents.[a]

Solvent	Conversion[d] (%)	Time (h)	M_n (calc)[e] (Da)	M_n[f] (Da)	M_w/M_n[f]
anisole[b]	49.5	14.0	10k	14k	1.99
toluene[b]	50.1	15.0	10k	14k	1.49
heptane[c]	61.9	15.0	21k	24k	1.28

[a] All polymerizations were run at 110 °C with a styrene concentration of 6.5M in solvent.
[b] The ratio of monomer/initiator/$CuCl_2$/**50**/Sn(EH)2 was 200/1/0.1/0.2/0.2.
[c] The ratio of monomer/initiator/$CuCl_2$/**50**/Sn(EH)2 was 320/1/0.1/0.3/0.2.
[d] The percent conversion was calculated based on the initial mass of monomer used divided by the mass of polystyrene recovered.
[e] The calculated molecular weights were based on the initial monomer to initiator ratio multiplied by the conversion and the molecular weight of styrene.
[f] The molecular weights and polydispersity of the polystyrene products were determined by gel permeation chromatography using a GMHx1 column set with THF as the eluting solvent.

used in the same fashion as a low molecular weight ligand to produce ATRP-active copper complexes for controlled radical polymerizations.

Unlike low molecular weight complexes, these polyisobutylene terminated copper complexes have potential advantages in terms of their separation after a reaction. Based on the phase selectively soluble properties of these supports in heptane, removal of the polyisobutylene supports can be achieved in principle without post-polymerization precipitation by excess solvent or column chromatography. This separation efficiency was realized in the polymerization of styrene performed in heptane. At the onset of the polymerization, a heptane soluble polyisobutylene terminated transition metal catalyst complex and styrene are both part of a homogeneous solution. As the reaction proceeded, an increasingly insoluble polystyrene is produced. Stopping the reaction midway and allowing it to cool to room temperature produced a viscous reaction mixture that on centrifugation produced an easily separable biphasic system with a soluble polyisobutylene-ligand/copper heptane phase, and a polystyrene-rich lower phase as seen in **Figure 39**.

This ease of separation is a significant advantage for these polyisobutylene bound ATRP catalysts. However, another important feature of this system is the reusability of the catalyst. The heptane solution containing the polyisobutylene **50**/copper complex could be added to fresh monomer and used in subsequent polymerizations. The recycling of the polyisobutylene imine ligand **50**/copper (II) complex in the ATRP polymerization of styrene in heptane can be seen in **Table 11.** For the recycling, the first polymerization cycle was performed as described previously. The reaction mixture

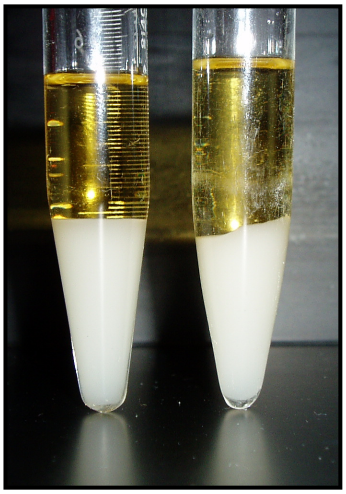


Figure 39. Separation of polystyrene from heptane soluble polyisobutylene terminated copper complexes.

produced a biphasic system after centrifugation, and the heptane phase was removed and added to a fresh solution of styrene. A fresh amount of tin (II) 2-ethylhexanoate ($Sn(EH)_2$) was added to reduce any copper (II) species in solution and scavenge oxygen present in solution. After sparging with nitrogen gas and addition of initiator as previously described, the reaction solution was again placed in an oil bath held at 110 °C. The subsequent steps polymerizations were carried out exactly as already described and the recycling of the heptane phase was carried out for three polymerizations.

This polyisobutylene **50** supported copper complex could indeed be recycled. However, as seen in **Table 11** the recycling led to less control over both molecular weight and polydispersity (M_n=102,000 Da , M_n(calc)=22,000 Da , and M_w/M_n=1.92 in cycle 3). This could possibly be explained by decomposition of the copper species in solution. However, we observed that the solution color remained constant so this was not the likely problem. Another possible explanation for this behavior could be the amount of tin (II) 2-ethylhexanonate ($Sn(EH)_2$) that was being used. This material could be building up in concentration in the heptane phase. Each subsequent polymerization uses a fresh amount of this reagent which could be accumulating in the heptane phase with reagent from prior cycles. To avoid this problem, copper (I) chloride was used to prepare the starting copper catalyst complex.

Table 11. Recycling of polyisobutylene pyridine imine **50**/copper (II) complex in the ATRP polymerization of styrene in heptane.[a]

Cycle	[Sty]/[I]	Conversion[b] (%)	Time (h)	M_n (calc)[c] (Da)	M_n[d] (Da)	M_w/M_n[d]
1	330	61.9	14.0	21k	24k	1.28
2	330	53.5	10.0	19k	38k	1.69
3	330	64.5	9.0	22k	102k	1.92

[a] All polymerizations were run at 110 °C with a styrene concentration of 6.5M in heptane. The ratio of initiator/$CuCl_2$/**50**/$Sn(EH)_2$ was 1/0.1/0.3/0.2.
[b] The percent conversion was calculated based on the initial mass of monomer used divided by the mass of polystyrene recovered.
[c] The calculated molecular weights were based on the initial monomer to initiator ratio multiplied by the conversion and the molecular weight of styrene.
[d] The molecular weights and polydispersity of the polystyrene products were determined by gel permeation chromatography using a GMHx1 column set with THF as the eluting solvent.

With a polyisobutylene **50**/copper (I) complex in hand, a polymerizations was carried out in the same manner as previously described. Tin (II) 2-ethylhexanoate was still used, since its oxygen scavenging properties were still of interest. As can be seen in **Table 12**, the control over molecular weight in these polymerizations upon recycling from cycle 1 to cycle 3 (M_n=7,000 Da and, M_n(calc)=7,000 Da in cycle 3) was regained. However, the polydispersity control of this system was still not consistent cycle to cycle (M_w/M_n=1.28-1.92 in cycles 1-3).

Table 12. Recycling of polyisobutylene **50**/copper (I) complex in the ATRP polymerization of styrene in heptane.[a]

Cycle	[Sty]/[I]	Conversion[b] (%)	Time (h)	M_n (calc)[c] (Da)	M_n[d] (Da)	M_w/M_n[d]
1	330	33.0	21.0	11k	16k	1.63
2	330	56.3	21.0	19k	18k	1.16
3	280	24.6	21.0	7k	7k	1.44

[a] All polymerizations were run at 110 °C with a styrene concentration of 6.5M in heptane. The ratio of initiator/CuCl/**50**/Sn(EH)$_2$ was 1/0.1/0.3/0.05.

[b] The percent conversion was calculated based on the initial mass of monomer used divided by the mass of polystyrene recovered.

[c] The calculated molecular weights were based on the initial monomer to initiator ratio multiplied by the conversion and the molecular weight of styrene.

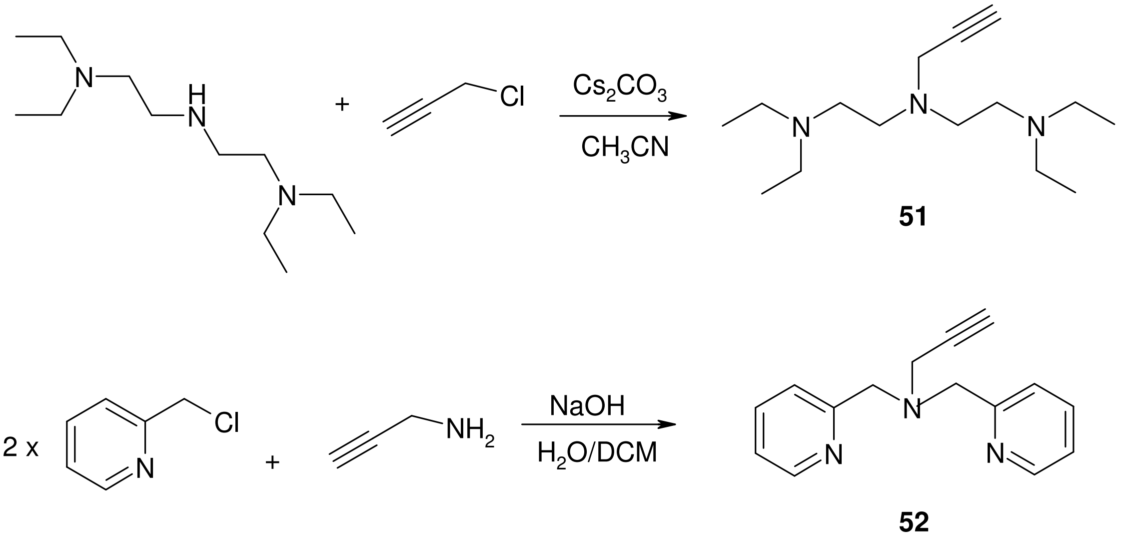
[d] The molecular weights and polydispersity of the polystyrene products were determined by gel permeation chromatography using a GMHx1 column set with THF as the eluting solvent.

To address this issue lack of polydispersity control, a new ligand was again investigated. In the previous chapter, a 1,2,3-triazole was used as a means of linking a dye that served as a catalyst surrogate to polyisobutylene. A recent report has indicated that appropriately functionalized 1,4-disubstituted-1,2,3-triazoles made from this copper (I) catalyzed reaction can catalyze their own formation from alkynes and azides and that they both bind and stabilize copper (I) species under aerobic aqueous conditions.[100] Since others have reported use of this 'Click' cycloaddition in applications such as the modification of macromolecules[101] and the synthesis of other ligand/metal complexes,[102-105] we incorporate these various concepts to produce a polymer-supported copper(I) complex by a similar route.

The methodology we envisioned for the synthesis of this new polyisobutylene copper (I) complex would have advantages over the previous synthetic schemes. The synthesis could not only be autocatalytic, but would directly produce and complex the copper (I) species. According to the literature, similar complexes stabilize the copper complex as well. To carry out this synthesis, an alkyne-functionalized copper (I) ligand was first prepared. Two possible ligands for use in this scheme were synthesized as shown below (**Scheme 25**).

Since it was already known that TEDETA could complex copper (I) species, an alkyne-functionalized TEDETA ligand (**51)** was synthesized by nucleophilic displacement of propargyl chloride by the cesium salt of TEDETA. However, since better results had been achieved in polymerizations using aromatic amines rather than TEDETA, another pyridine based ligand was also synthesized using propargyl amine

Scheme 25. Synthesis of alkyne-functionalized copper ligands.



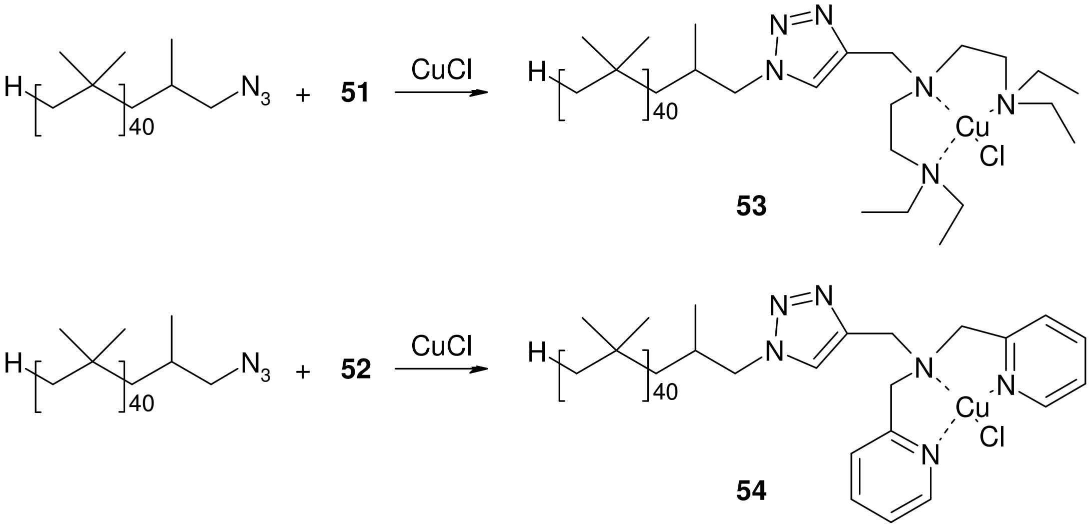
51

52

and 2-(chloromethyl)-pyridine (**52**). Both of these ligands were polar and completely soluble in ethanol. Thus reaction of a heptane soluble polyisobutylene terminated azide with these ethanol soluble ligands in a latent biphasic heptane/ethanol system proved to be a practical route for synthesis of the desired metal complexes (**Scheme 26**). These reactions are both autocatalytic and self-separating reaction schemes as described below.

The autocatalytic and self-separating nature of the polyisobutylene-supported copper (I) complex syntheses above was established by running the reaction with sub-stoichiometric amounts of the copper (I) salt in a heptane/ethanol solvent system. For example, **51** (1.1eq) could be dissolved in ethanol and added to a flask containing CuCl (0.1eq). Addition of polyisobutylene terminated azide (1.0eq) as a heptane solution to this now colored ethanol solution formed a homogeneous solvent mixture. This reaction mixture could then be heated at 65 °C overnight. After complete reaction in a homogeneous heptane/ethanol solvent system, a small amount of water was added to the reaction mixture to produce a biphasic system. The exclusive solubility of polyisobutylene **53** allowed for removal of the newly formed homogeneous polymer-supported copper (I) complex from any excess **51** *via* a liquid/liquid separation. Further washing with polar solvents such as ethylene glycol diacetate could be used to visually demonstrate the heptane phase selective solubility of the polyisobutylene copper complexes **53** and **54** (**Figure 40**).

Scheme 26. Synthesis and concurrent metalation of polyisobutylene triazole copper complexes **53** and **54**.



While the solution of the polyisobutylene-bound copper complex was itself a catalyst for alkyne-azide cyclization (and for polymerization, vide infra), ^{1}H NMR spectroscopic analysis and characterization of the newly formed polyisobutylene complex **53** required column chromatography to remove any paramagnetic copper salts from the polyisobutylene-bound copper complex. After this purification step, the characteristic diastereotopic protons of polyisobutylene adjacent to the triazole appear as a doublet of doublets centered around 4.1 ppm with complete disappearance of the starting protons centered around 3.1 ppm for the polyisobutylene terminated azide.

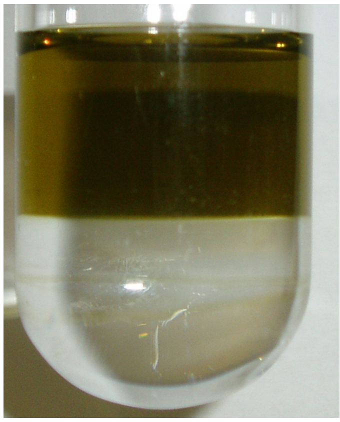


Figure 40. Separation of a heptane soluble **54** in a biphasic separation with ethylene glycol diacetate.

Also, the presence of the 5-H-triazole proton at 7.5 ppm indicates formation of the 1,4-disubstituted-1,2,3-triazole product. In cases where the polyisobutylene copper complexes **53** and **54** were to be used in further polymerization reactions, the above reaction was run with stoichiometric amounts of copper (I) to allow for synthesis and complete metalation of the polymer-metal complex. In these cases, characterization of the final polyisobutylene copper complexes was accomplished by infrared spectroscopy and was based on the complete disappearance of both the polyisobutylene terminated azide (2097 cm^{-1}) and alkyne-functionalized ligands **51** and **52** (2120 cm^{-1}) stretches. Inductively coupled plasma mass spectroscopy (ICP-MS) was used to determine the exact metal loadings of the polyisobutylene triazole copper complexes after complete digestion of the polymer-copper species. The polyisobutylene **53** complex had a copper metal loading of 0.416 mmol copper/g of polyisobutylene complex while the polyisobutylene **54** complex had a metal loading of 0.115 mmol copper/g of polyisobutylene complex. In the latter case, copper loading of the ligand is likely incomplete.

With the previous use of polyisobutylene ligands **45** and **48** derived from TEDETA, little control over the ATRP polymerization of styrene was exhibited. However, the interaction of the triazole with the copper species was of interest since it too could bind the copper (I) species and change the character of the copper (I) complex. Therefore, the use of these pre-metalated polyisobutylene triazole copper (I) complexes in the controlled radical polymerization of styrene was investigated. For use in the ATRP polymerization of styrene, a heptane solution of each of the polyisobutylene copper complexes **53** and **54** was prepared. The heptane solutions of both polyisobutylene copper complexes in heptane were initially green. On heating, the color changed from green to yellow with complex **53** and from green to red with **54**. These colors obtained for these solutions did not change further. In a polymerization reaction, the solution of a copper complex so formed was added to a Schlenk flask containing a measured amount of styrene. The reaction flask was sealed and sparged with nitrogen gas for 15 min. Tin (II) 2-ethylhexanoate ($Sn(EH)_2$)was added under nitrogen to scavenge residual oxygen. A previously degassed amount of ethyl 2-bromoisobutyrate initiator was added *via* syringe and the sealed reaction flask was placed in an oil bath at 110 °C. The polymerizations were allowed to proceed for a designated amount of time and the reaction mixture was worked up by cooling to room temperature. Centrifugation produced two phases. The upper heptane phase containing either complex **53** or **54** could be separated from the white product polystyrene as can be seen in **Figure 41**. For the **53**, the polymerization results were similar to those previously seen with the other polyisobutylene TEDETA ligand analogs **45** and **48**. An actual molecular weight that was over 10 times larger than that calculated was measured (M_n=200,000 Da and M_n(calc)=13,000 Da). However, this was not the case with the polyisobutylene triazole pyridine copper complex **54**. Good control over molecular weight (M_n=18,000 Da and M_n(calc)=26,000 Da) and a reasonable polydispersity (M_w/M_n=1.34) was observed in the first use of this polyisobutylene copper complex. The results where this copper complex was used in a series of three sequential polymerizations are listed in **Table 13**.

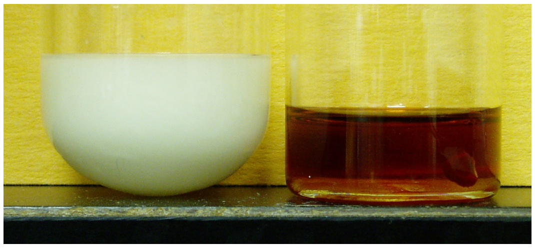


Figure 41. Separation of polyisobutylene **54** copper complexes from product polystyrene.

Our goal to not only make a polymer supported copper complex that could be used in the ATRP polymerization of styrene, but to also develop an efficient method to remove and recycle the supported copper complex. From visual inspection of the product polystyrene from the previously described polymerizations, the white polystyrene product had no apparent contamination of copper was produced as seen in

Table 13. Recycling of polyisobutylene triazole pyridine copper (I) complex **54** in the ATRP polymerization of styrene in heptane.[a]

Cycle	[Sty]/[I]	Conversion[b] (%)	Time (h)	M_n (calc)[c] (Da)	M_n[d] (Da)	M_w/M_n[d]
1	330	53.6	21.0	26k	18k	1.34
2	330	55.1	21.0	22k	18k	1.26
3	330	38.7	21.0	13k	17k	1.37

[a] All polymerizations were run at 110 °C with a styrene concentration of 6.5M in heptane. The ratio of initiator/CuCl/**54**/Sn(EH)$_2$ was 1/0.1/0.3/0.05.

[b] The percent conversion was calculated based on the initial mass of monomer used divided by the mass of polystyrene recovered.

[c] The calculated molecular weights were based on the initial monomer to initiator ratio multiplied by the conversion and the molecular weight of styrene.

[d] The molecular weights and polydispersity of the polystyrene products were determined by gel permeation chromatography using a GMHx1 column set with THF as the eluting solvent.

Figure 41. ICP-MS analysis of the polystyrene produced from the first use of this polymeric copper complex however showed that there was some (23 ppm) copper in theproduct polystyrene. This is a fraction of the ca. 660 ppm copper used in the polymerization. While this represents a significant reduction of the amount of copper in these systems and avoids the use solvent precipitation which require the use of a large excess of solvents, the results are only a modest success.

With the above results, the level of copper contamination was considerably higher (ca. 5% of the initial quantity initially used) than anticipated. The high heptane phase selective solubility of these supports has been discussed (>99.7% for heptane) in biphasic solvent mixtures involving heptane/90% ethanol systems. The highly colored polyisobutylene complex **54** has also exhibited a high heptane phase selective solubility as seen in **Figures 40** and **41** involving both liquid/liquid and solid/liquid separations of the complex. Therefore, the copper contamination exhibited in these systems is not a result of the incomplete separation of the ligand as seen in previous supported examples, but rather is likely a result of formation of some copper species not bound to the polyisobutylene support which is partitioned in the product polymer phase.

At this point, our methodology was comparable if not better than previously reported examples of polymer-supported copper complexes for the use, recovery and separation of copper catalysts in ATRP polymerizations. However, further advantages of our polyisobutylene ligand systems would be seen if better control over polydispersity could be achieved. Therefore, a combination of polyisobutylene ligands was used to further optimize the polymerization results. The previously reported polyisobutylene ligand **50** exhibited good control over both molecular weight and polydispersity initially, but suffered in subsequent recycling, possibly due to metal leaching from the complex or decomposition of the active copper (I) species. Since the polyisobutylene copper (I) complex **54** has shown reasonable recyclability, the combination of polyisobutylene **50** and **54** could produce a mixed ligand system with even further polydispersity control and recyclability.

The use of polyisobutylene ligand **50** and polyisobutylene copper complex **54** in the same polystyrene polymerization reactions produced polymers with good control over both molecular weight (M_n=8,000 Da and M_n(calc)=4,000 Da in cycle 1) and polydispersity (M_w/M_n = 1.12 in cycle 1) in cycles 1-3 (**Table 14**). It must be noted that a low yield was obtained from the first use of this mixed polyisobutylene ligand system.

This could not be explained, but an increase in yields to 30-50% in later cycles was consistent with previous experiments. Recycling of the heptane phase containing the polyisobutylenes **50** and **54** copper complex past three polymerization cycles produced polymers with a higher polydispersity than desired (M_w/M_n = 1.58 in cycle 5). Since leaching of the metal was not suspected, deactivation of the active copper (I) complex must be occurring. Since tin (II) 2-ethylhexanoate was being used in the polymerizations, formation of copper (II) halides is unlikely. However, only sparging with nitrogen gas and use of tin (II) 2-ethylhexanoate were used to remove oxygen in the previous polymerizations so copper (II) formation cannot be completely excluded.

Table 14. Recycling of polyisobutylene ligand **50** and polyisobutylene copper complex **54** in the ATRP polymerization of styrene in heptane.[a]

Cycle	[Sty]/[I]	Conversion[b] (%)	Time (h)	M_n (calc)[c] (Da)	M_n[d] (Da)	M_w/M_n[d]
1	430	8.5	22.0	4k	8k	1.12
2	330	44.6	22.0	15k	19k	1.17
3	330	34.9	22.0	12k	17k	1.16
4	330	52.4	22.0	18k	23k	1.43
5	330	55.9	22.0	19k	24k	1.58

[a] All polymerizations were run at 110 °C with a styrene concentration of 6.5M in heptane. The ratio of initiator/CuCl/**50&54**/Sn(EH)$_2$ was 1/0.1/0.3/0.05.

[b] The percent conversion was calculated based on the initial mass of monomer used divided by the mass of polystyrene recovered.

[c] The calculated molecular weights were based on the initial monomer to initiator ratio multiplied by the conversion and the molecular weight of styrene.

[d] The molecular weights and polydispersity of the polystyrene products were determined by gel permeation chromatography using a GMHx1 column set with THF as the eluting solvent.

Table 15. Recycling of polyisobutylene **50** and **54** copper (I) complex with in the ATRP polymerization of styrene in heptane using freeze/pump/thaw degassing.[a]

Cycle	[Sty]/[I]	Conversion[b] (%)	Time (h)	M_n (calc)[c] (Da)	M_n[d] (Da)	M_w/M_n[d]
1	330	51.8	21.0	18k	23k	1.11
2	330	59.3	21.0	20k	22k	1.14
3	330	61.1	21.0	21k	24k	1.15
4	330	43.0	21.0	15k	17k	1.25
5	330	47.3	21.0	16k	17k	1.26

[a] All polymerizations were run at 110 °C with a styrene concentration of 6.5M in heptane. The ratio of initiator/CuCl/**50&54**/Sn(EH)$_2$ was 1/0.1/0.3/0.05.

[b] The percent conversion was calculated based on the initial mass of monomer used divided by the mass of polystyrene recovered.

[c] The calculated molecular weights were based on the initial monomer to initiator ratio multiplied by the conversion and the molecular weight of styrene.

[d] The molecular weights and polydispersity of the polystyrene products were determined by gel permeation chromatography using a GMHx1 column set with THF as the eluting solvent.

With the previous experiments, the amount of tin (II) 2-ethylhexanoate (Sn(EH)$_2$) was reduced to improve control over the molecular weight of the polystyrene polymers reduced. While this species can be used in various amounts in the first polymerization reaction without any adverse side-effects, the removal of any traces of oxygen by other means was also explored using repeated freeze/pump/thaw cycles. When the same experimental procedure for the polymerization of styrene was performed, results like those seen in **Table 15** were obtained. This set of experiments demonstrated both good control over molecular weight (M_n=17,000 Da and M_n(calc)=16,000 Da in cycle 5) and polydispersity (M_w/M_n = 1.26 in cycle 5) in the polymerization of styrene for over 5 cycles of recycling of the polyisobutylene mixed ligand copper complex.

Conclusions

The diffusion limitations of previously reported copper (I) ligands supported on various soluble and insoluble materials was overcome by utilizing soluble polyisobutylene oligomers supports. Various synthetic methods were employed to produce polyisobutylene terminated ligands that could be used to form copper (I) and copper (II) complexes for use in the controlled radical polymerization of styrene. The insolubility of the product polystyrene in heptane was integrated into a polymerization scheme that allowed for simple removal of heptane soluble copper containing ligands. These ligands were supported on a heptane phase selectively soluble polyisobutylene support that could be removed by centrifugation of the polymerization mixture to form a biphasic system. The heptane phase containing polyisobutylene copper complexes could be separated and recycled for up to 5 polymerization cycles with good control being exhibited over both molecular weight and polydispersity. The amount of copper present in the final product was greatly reduced and required only a simple liquid/liquid separation to effectively remove the copper complex sequestered as a polyisobutylene complex in heptane.

During the ligand synthesis, a new catalytic cascade synthesis of a copper(I) complex was also developed that involved autocatalytic synthesis of a triazole-attached copper complexes that was also self-separating at the end of reaction based on the heptane phase selective solubility of the polyisobutylene group. These complexes could then be used directly in the polymerization of styrene.

CHAPTER V

SUMMARY OF EXPERIMENTS

Experimental

General Procedures

Polyisobutylene was obtained from BASF. All other reagents and solvents were obtained from commercial sources and used without further purification unless otherwise specified. Two types of polyisobutylene were used, Glissopal 1000 and Glissopal 2300. ^{1}H NMR spectra were obtained on Varian Inova 300 or Mercury 300 spectrometers at 300 MHz and reported in ppm referenced to $CDCl_3$. ^{13}C NMR spectra were obtained on Varian Inova 300 or Mercury 300 spectrometers at 75 MHz and reported in ppm referenced to the chloroform contaminant in $CDCl_3$ unless otherwise stated. All phase selectivity measurements and solvent microenvironment studies were performed with a Fluorolog 2 spectrofluorometer. Centrifugation with a Jouan CT422 centrifuge was used to more efficiently separate the phases. IR spectra were obtained on a Bruker Tensor 27 FT-IR spectrometer. Gel permeation chromatography was performed using a Viscotek triple detector system using a GMHx1 column set with tetrahydrofuran as the eluting solvent. A flow rate of 1 mL/min was used and molecular weights and polydispersity were determined using polystyrene standards using the software supplied by Viscotek.

General procedure for phase selectivity studies

Since our typical applications of polymer supports involve using soluble polymers as catalysts supports in thermomorphic or latent biphasic solvent systems, polymer concentrations that were used for the phase selective solubility studies were calculated by determining the quantity of polymer that would be necessary in a catalytic reaction if the polymer were to later be used as a catalytic support. Substrate ranges falling between 0.1 M to 0.5 M would commonly require catalyst concentrations of 0.1 mol% to 2 mol%. Therefore, a 1.0 – 6.0 mM (based on mol% of dansyl fluorophore supported) solutions of the polymer-bound fluorophore were prepared and tested for heptane phase selective solubility. Standard curves were first prepared to determine the concentration of dyes that preserved the linearity for quantitative analyses. The error associated with the fluorescence measurements of the polymer-bound fluorophore in the dilute polar phases was determined by taking four consecutive measurements of the fluorescence intensity of the same polymer-bound fluorophore in the polar solution. The standard deviation for these measurements was routinely 5 % of the average value. The poly(4-*n*-alkystyrene) supported *N*-propyl-dansyl probes were dissolved in the heptane phase and the second polar phase added after the polymer had dissolved in the heptane. In latent biphasic systems, the system at this point was homogeneous. In thermomorphic systems, the system at this point was biphasic and in those cases heat was applied to induce phase miscibility. Once a homogenous solution was obtained, cooling (thermomorphic systems) or some perturbation (e.g. water addition to a latent biphasic mixture) was used to induce phase separation. Centrifugation was used if the phase separation was problematic or slow. The solvent layers after centrifugation or standing were then separated and serially diluted with the predominant solvent for that phase until the fluorescence reading fell within the previously determined linear range of the fluorophore. Extinction coefficients were considered to be unaffected by solvent media and phase selectivity preference was calculated as a ratio of the fluorescence intensity at the λ_{max} of emission measured for each phase of a system which was excited at 357 nm.

General procedure for solvent microenvironment studies

Dilute solutions of all supported dansyl probes were made by the dissolution of the supported probes in an appropriate solvent at a concentration of approximately 1 mg of supported dansyl probe in 100 mL of solvent. These solutions were made with a variety of pure solvents and the fluorescence emission λ_{max} of these solutions were recorded after exciting the solution at 357 nm. For the mixed solvent studies, non-polar and polar solvent mixtures were used. The supported probe was dissolved in the specified solvent at a concentration of 1 mg of supported probe in 100 mL of solvent. Then specified amounts of this solution were added to the appropriate solvent and again the fluorescence emission λ_{max} of these solutions were recorded after exciting the solution at 357 nm.

General procedure for the ATRP polymerization of styrene

Polyisobutylene **54** (0.098 g, 0.038 mmol) and polyisobutylene **50** (0.048 g, 0.020 mmol) were dissolved in 2 mL of heptane and placed in a 25 mL Schlenk tube along with styrene (4.5 g, 43 mmol). Nitrogen was then bubbled through this solution for 15 minutes, and a solution of tin (II) 2-ethylhexanoate (10.4 mg, 0.03 mmol) in 0.3

mL of heptane was then added. The solution was then sealed by a rubber septum and the reaction solution degassed by 3 cycles of freeze/pump/thaw under vacuum to remove oxygen. Previously degassed ethyl 2-bromoisobutyrate (20 μL, 0.13 mmol) was added *via* syringe and the reaction was immediately immersed in an oil bath that was preset to the specific reaction temperature (110 °C). After a set reaction time, the reactions were allowed to cool to room temperature and transferred to a 50 mL centrifuge tube. The mixture was then centrifuged at 1500 rpm at 5 °C for 1 h to ensure complete separation of the product from the heptane phase. The resulting heptane phase was removed and 2 mL of fresh heptane was added to the product polystyrene phase to remove any residual catalyst. After removal of residual solvents under reduced pressure, a sample of polymer was analyzed for residual copper content by ICP-MS. Measured amounts of polystyrene were also redissolved in tetrahydrofuran, filtered through a PTFE filter (0.45 μm), and analyzed by gel permeation chromatography (GPC).

Recycling of polyisobutylene copper complexes in the ATRP polymerization of styrene

In a typical recycling experiment, all the heptane phases from a given cycle were combined and concentrated to yield a polyisobutylene copper complex residue which was then redissolved in heptane. This heptane solution was used as the catalyst solution in the next cycle.

Synthesis of *n*-Alkylbenzenes

These compounds were synthesized according to a literature procedure.[67] Yields and NMR spectroscopy data for each of the products prepared are listed below.

4-*n*-Dodecylbenzene. (22.0 g, 74.0% yield) ^{1}H NMR (CDCl$_3$): δ 0.89 (t, *J* = 7.3 Hz, 3H), 1.23-1.36 (br m, 18H), 1.60 (m, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 7.13-7.29 (m, 5H). ^{13}C NMR (CDCl$_3$): δ 14.1, 22.7, 29.4, 29.5, 29.6, 29.8, 31.5, 31.9, 36.0, 125.5, 128.2, 128.4, 143.0.

4-*n*-Octadecylbenzene. (32.8 g, 82.2% yield) ^{1}H NMR (CDCl$_3$): δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.20-1.38 (br m, 30H), 1.60 (m, 2H), 2.58 (t, *J* = 7.7 Hz, 2H), 7.14-7.30 (m, 5H). ^{13}C NMR (CDCl$_3$): δ 14.1, 22.7, 29.4, 29.5, 29.6, 29.8, 31.6, 31.9, 36.0, 125.5, 128.2, 128.4, 143.0.

Representative Synthesis of 4′-*n*-Alkylacetophenones

To a dry 2-necked round-bottomed flask was added aluminum chloride (34.95 g, 0.262 mol) and 160 mL of dichloromethane under a positive flow of nitrogen. This reaction mixture was cooled to -10 °C and acetyl chloride (18.6 mL, 0.262 mol) was added dropwise. After the addition was complete, the reaction mixture was allowed to stir for 10 min. *n*-Butylbenzene (29.32 g, 0.218 mol) in 40 mL of dichloromethane was then added dropwise over a 30 min period. The solution was then stirred at 0 °C for 1.5 h and then allowed to stir for an additional 4 h at room temperature. The solution was then poured over an ice/HCl (100 mL/30 mL) slurry and allowed to stir for 1 h. This solution was extracted with 3 x 100 mL of dichloromethane. The organic phase was then washed with 100 mL of 0.1 M HCl, 2 x 100 mL of saturated aqueous NaHCO$_3$, and 3 x 100 mL of distilled water. The organic phase was then dried over MgSO$_4$ overnight, filtered, and the solvent was removed under reduced pressure in a rotary evaporator to yield 34.6 g (89.1 % yield) of 4′-*n*-butylacetophenone (89.05 % yield). ^{1}H NMR

($CDCl_3$): δ 0.92 (t, *J* = 7.4 Hz, 3H), 1.35 (m, 2H), 1.60 (m, 2H), 2.57 (s, 3H), 2.66 (t, *J* = 7.7 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 7.87 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 13.9, 22.3, 26.5, 33.2, 35.6, 128.4, 128.6, 134.8, 148.8, 197.9.

Synthesis of 4′-*n*-Alkylacetophenones

These compounds were synthesized according to the procedure used for 4′-*n*-butylacetophenone above. Yields and NMR spectroscopy data for each of the products used are listed below.

4′-*n*-Dodecylacetophenone. (24.5 g, 95.3 % yield) ^{1}H NMR ($CDCl_3$): δ 0.87 (t, *J* = 7.2 Hz, 3H), 1.19-1.36 (br m, 18H), 1.61 (m, 2H), 2.58 (s, 3H), 2.65 (t, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.87 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 26.5, 29.2, 29.3, 29.4, 29.5, 29.6, 31.1, 31.9, 36.0, 128.4, 128.6, 134.9, 148.8, 197.9.

4′-*n*-Octadecylacetophenone. (16.9 g, 92.6 % yield) ^{1}H NMR ($CDCl_3$): δ 0.91 (t, *J* = 6.8 Hz, 3H), 1.25-1.40 (br m, 30H), 1.66 (m, 2H), 2.61 (s, 3H), 2.69 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.91 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 24.4, 29.2, 29.4, 29.8, 29.5, 29.6, 29.7, 31.9, 38.6, 128.0, 128.5, 132.8, 137.1, 200.6.

Representative Synthesis of 4′-*n*-Alkylphenylmethylcarbinols

The 4′-*n*-butylacetophenone (34.61 g, 0.196 mol) was dissolved in 500 mL of EtOH. $NaBH_4$ (11.12 g, 0.293 mol) was slowly added to this solution and the reaction mixture was refluxed for 1.5 h. After cooling, the solvent was removed under reduced pressure in a rotary evaporator and the crude product was dissolved in 300 mL of hexanes. Water was slowly added to the hexanes solution until no more gas evolved. The water was then separated and the organic phase was washed with 0.1 M HCl (3 x

100 mL), then brine (3 x 100 mL). The organic phase was then dried over $MgSO_4$. The solution was filtered and the solvent removed under reduced pressure in a rotary evaporator to yield 31.89 g (90.7 % yield) of 4′-*n*-butylphenylmethylcarbinol. ^{1}H NMR ($CDCl_3$): δ 0.92 (t, *J* = 7.4 Hz, 3H), 1.34 (m, 2H), 1.48 (d, *J* = 6.6 Hz, 3H), 1.58 (m, 2H), 1.83 (d, *J* = 2.5 Hz, 1H), 2.59 (t, *J* = 8.0 Hz, 2H), 4.85 (dq, *J* = 6.6 Hz and 2.5 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 13.9, 22.3, 25.0, 33.7, 35.3, 70.3, 125.3, 128.5, 142.2, 143.0.

Synthesis of 4′-*n*-Alkylphenylmethylcarbinols

These compounds were synthesized according to the procedure used for 4′-*n*-butylphenylmethylcarbinol above. Yields and NMR spectroscopy data for each of the products used are listed below.

4′-*n*-Dodecylphenylmethylcarbinol. (23.9 g, 96.8 % yield). ^{1}H NMR ($CDCl_3$): δ 0.87 (t, *J* = 7.1 Hz, 3H), 1.21-1.37 (br m, 18H), 1.48 (d, *J* = 6.3 Hz, 3H), 1.59 (m, 2H), 1.75 (d, *J* = 3.7 Hz, 1H), 2.58 (t, *J* = 7.8 Hz, 2H), 4.86 (dq, *J* = 6.3 Hz and 3.7 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 25.0, 29.3, 29.5, 29.6, 29.7, 31.5, 31.9, 35.6, 70.3, 125.3, 128.5, 142.3, 143.0.

4′-*n*-Octadecylphenylmethylcarbinol. (15.09 g, 98.6 % yield) ^{1}H NMR ($CDCl_3$): δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.16-1.37 (br m, 30H), 1.48 (d, *J* = 6.3 Hz, 3H), 1.58 (m, 2H), 1.74 (d, *J* = 3.0 H, 1H), 2.58 (t, *J* = 8.0 Hz, 2H), 4.86 (dq, *J* = 6.3 Hz and 3.0 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 25.0, 29.3, 29.5, 29.6, 29.7, 31.5, 31.9, 35.6, 70.2, 125.3, 128.5, 142.2, 143.0.

Representative Synthesis of 4-*n*-Alkylstyrenes

4′-*n*-Butylphenylmethy-carbinol (31.89 g, 0.179 mol) was dissolved in 500 mL of toluene and *p*-TSA (0.756 g, 3.97 mmol) was added. This solution was allowed to stir under reflux with an attached Dean-Stark trap for 2 h. The solution was then cooled and washed with 500 mL of water and then 250 mL of brine. After drying over $MgSO_4$ and filtering, the solvent was removed under reduced pressure in a rotary evaporator. The product was then purified by column chromatography (hexanes) to yield 28.7 g (90.0 % yield) of 4-*n*-butylstyrene. ^1H NMR ($CDCl_3$): δ 0.92 (t, *J* = 7.4 Hz, 3H), 1.34 (m, 2H), 1.58 (m, 2H), 2.58 (t, *J* = 7.8 Hz, 2H), 5.18 (d, *J* = 10.7 Hz, 1H), 5.69 (d, *J* = 17.6 Hz, 1H), 6.68 (dd, *J* = 17.6 Hz and 10.7 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 14.0, 22.3, 33.6, 35.4, 112.8, 126.1, 128.6, 135.0, 136.7, 142.7.

Synthesis of 4-*n*-Alkylstyrenes

These compounds were synthesized according to the procedure used for 4′-*n*-butylstyrene above. Yields and NMR spectroscopy data for each of the products used are listed below.

4-*n*-Dodecylstyrene. (17.5 g, 78.1 % yield) ^1H NMR ($CDCl_3$): δ 0.87 (t, *J* = 6.7 Hz, 3H), 1.20-1.35 (br m, 18H), 1.58 (m, 2H), 2.57 (t, *J* = 7.7 Hz, 2H), 5.18 (d, *J* = 11.0 Hz, 1H), 5.69 (d, *J* = 17.7 Hz, 1H), 6.68 (dd, *J* = 17.7 Hz and 11.0 Hz, 1H), 7.13 (d, *J* = 7.7 Hz, 2H), 7.32 (d, *J* = 7.7 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 14.1, 22.7, 29.3, 29.4, 29.5, 29.6, 29.7, 31.5, 31.9, 35.7, 112.7, 126.1, 128.6, 134.5, 136.7, 142.7.

4-*n*-Octadecylstyrene. (13.6 g, 94.6 % yield) ^{1}H NMR (CDCl$_3$): δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.16-1.37 (br m, 30H), 1.58 (m, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 5.17 (d, *J* = 10.7 Hz, 1H), 5.69 (d, *J* = 17.5 Hz, 1H), 6.68 (dd, *J* = 17.5 Hz and 10.7 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (CDCl$_3$): δ 14.1, 22.7, 29.3, 29.4, 29.5, 29.6, 29.7, 31.5, 31.9, 35.7, 112.8, 126.1, 128.6, 134.5, 136.7, 142.8.

Representative Synthesis of Poly(4-*n*-Alkylstyrene)-co-Poly(4-Vinyl Benzyl Chloride)

4-*n*-Butylstyrene (1.5 g, 9.4 mmol) and 4-vinyl benzyl chloride (0.143 g, 0.94 mmol) were added to a dry Schlenk tube. Benzoyl peroxide (0.0453 g, 0.187 mmol) was added and the flask was sealed. The mixture was then degassed by 4 cycles of freeze/pump/thaw. After warming to room temperature, the reaction was heated at 65 °C for 24 h. After cooling, approximately 40 mL of chloroform was added to the flask and the polymer was precipitated into 400 mL of stirring MeOH. The solid polymer was then filtered to yield 1.4 g, (85.2 % yield M_n = 20k, M_w/M_n = 2.3) of the 13:1 poly(4-*n*-butylstyrene)-co-poly(4-vinyl benzyl chloride) copolymer. The 13:1 mol:mol ratio of 4-*n*-butylstyrene:4-vinyl benzyl chloride repeat units was determined by integrating the peaks at 2.47 ppm (benzylic protons of 4-*n*-butylstyrene) and 4.45 ppm (benzylic protons of 4 vinyl benzyl chloride). ^{1}H NMR (CDCl$_3$): δ 0.86 (br t, *J* = 6.9 Hz, 39H), 0.98-2.13 (br m, 94H), 2.47 (br s, 26H), 4.45 (br s, 2H), 6.11-7.12 (br m, 56H).

Synthesis of Poly(4-*n*-Alkylstyrene)-co-Poly(4-Vinyl Benzyl Chloride) Copolymers

These compounds were synthesized according to the procedure used for the poly(4-*n*-butylstyrene)-co-poly(4-vinyl benzyl chloride) copolymer above. Yields and NMR spectroscopy data for each of the products used are listed below.

Poly(4-Methylstyrene)-co-Poly(4-Vinyl Benzyl Chloride). (4.08 g, 91.5 % yield. M_n = 20k, M_w/M_n = 1.6) ^{1}H NMR ($CDCl_3$): δ 0.99-2.11 (br m, 42H), 2.25 (br s, 39H), 4.45 (br s, 2H), 6.13-7.11 (br m, 56H).

Poly(4-*t*-Butylstyrene)-co-Poly(4-Vinyl Benzyl Chloride). (1.5 g, 47.0 % yield. M_n = 21k, M_w/M_n = 1.9). ^{1}H NMR ($CDCl_3$): δ 0.98-2.13 (br m, 159H), 4.45 (br s, 2H), 6.11-7.12 (br m, 56H).

Poly(4-*n*-Dodecylstyrene)-co-Poly(4-Vinyl Benzyl Chloride). (1.2 g, 56.6 % yield. M_n = 20k, M_w/M_n = 2.5). ^{1}H NMR ($CDCl_3$): δ 0.86 (br t, J = 6.9 Hz, 39H), 0.98-2.13 (br m, 302H), 2.47 (br s, 26H), 4.45 (br s, 2H), 6.11-7.12 (br m, 56H).

Poly(4-*n*-Octadecylstyrene)-co-Poly(4-Vinyl Benzyl Chloride). (2.94 g, 91.3 % yield M_n = 48k, M_w/M_n = 1.7). ^{1}H NMR ($CDCl_3$): δ 0.86 (br t, J = 6.9 Hz, 39H), 0.98-2.13 (br m, 458H), 2.47 (br s, 26H), 4.45 (br s, 2H), 6.11-7.12 (br m, 56H).

Representative Synthesis of Poly(4-*n*-Alkylstyrene)-co-Poly(4-Vinyl Benzyl Dansyl)

A mixture of *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide[67] (0.1347 g, 0.46 mmol) and potassium carbonate (0.0620 g, 0.45 mmol) in 10 mL of dry DMF was placed in a flame-dried flask. The reaction was stirred under nitrogen for 1 h before the addition of a solution of the 13:1 poly(4-*n*-butylstyrene)-co-poly(4-vinyl benzyl chloride) copolymer (0.598 g, 0.22 mmol) in 20 mL of dry heptane. The biphasic reaction mixture was then heated to 90 °C to form a single phase which was allowed to stir for 72 h. Upon cooling, 100 mL of hexanes was added and the DMF phase was removed. The hexanes/heptane layer was washed with distilled water (1 x 100 mL) and then with 90% EtOH (4 x 100 mL). The organic phase was dried over 3 Å molecular sieves, filtered, and the solvent was removed under reduced pressure in a rotary evaporator to yield 0.411g (82% yield) of product **(26)**. ^{1}H NMR ($CDCl_3$): δ 0.59 (br s, 3H), 0.91 (br t, J = 6.8 Hz, 39H), 1.03-2.10 (br m, 31H), 2.51 (br s, 26H), 2.88 (s, 6H), 3.09 (br s, 2H), 4.36 (br s, 2H), 6.06-7.22 (br m, 57H), 7.56 (br m, 2H), 8.19 (br s, 1H), 8.38 (br s, 1H), 8.52 (br s, 1H).

Synthesis of Poly(4-*n*-Alkylstyrene)-co-Poly(4-Vinyl Benzyl Dansyl) Copolymers

These compounds were synthesized according to the procedure used for the poly(4-*n*-butylstyrene)-co-poly(4-vinyl benzyl dansyl) copolymer above. Yields and NMR spectroscopy data for each of the products used are listed below.

Poly(4-*t*-Butylstyrene) (18). (0.400 g, 81 % yield). ^{1}H NMR ($CDCl_3$): δ 0.3-2.5 (br m, 249H), 2.91 (s, 6H), 3.13 (br s, 2H), 4.8-4.2 (br m, 3H),6.00-7.28 (br m, 87H), 7.55 (br m, 2H), 8.18(br s, 1H), 8.5 (br s, 1H), 8.36 (br s, 1H).

Poly(4-Methylstyrene) (25). (0.06 , 60 % yield). ^{1}H NMR ($CDCl_3$): δ 0.57 (br s, 3H), 0.99-2.11 (br m, 44H), 2.25 (br s, 39H), 2.86 (s, 6H), 3.05 (br s, 2H), 4.33 (br s, 2H), 6.13-7.11 (br m, 57H), 7.56 (br m, 2H), 8.18 (br s, 1H), 8.35 (br s, 1H), 8.51 (br s, 1H).

Poly(4-*n*-Dodecylstyrene) (27). (0.092 g, 92 % yield). ^{1}H NMR (CDCl$_3$): δ 0.59 (br s, 3H), 0.91 (br t, *J* = 6.8 Hz, 39H), 1.03-2.10 (br m, 302H), 2.51 (br s, 26H), 2.88 (s, 6H), 3.09 (br s, 2H), 4.36 (br s, 2H), 6.06-7.22 (br m, 57H), 7.55 (br m, 2H), 8.19 (br s, 1H), 8.38 (br s, 1H), 8.52 (br s, 1H).

Poly(4-*n*-Octadecylstyrene) (28). (0.18 g, 94.0 % yield). ^{1}H NMR (CDCl$_3$): δ 0.59 (br s, 3H), 0.91 (br t, *J* = 6.8 Hz, 39H), 1.03-2.10 (br m, 460H), 2.51 (br s, 26H), 2.88 (s, 6H), 3.09 (br s, 2H), 4.36 (br s, 2H), 6.06-7.22 (br m, 57H), 7.55 (br m, 2H), 8.19 (br s, 1H), 8.38 (br s, 1H), 8.52 (br s, 1H).

Synthesis of *N*-Benzyl-*N*-Propyl-5-Dimethylaminonapthalene-1-Sulfonamide (29)

A mixture of *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide (0.5 g, 1.7 mmol) and potassium carbonate (0.236 g, 1.7 mmol) in 10 mL of dry DMF was placed in a flame-dried flask. The reaction was stirred under nitrogen for 1 h before the addition of benzyl chloride (0.181 g, 1.4 mmol). The reaction mixture was heated at 80 °C and stirred for 24 h. Upon cooling, 100 mL of ethyl acetate was added and the DMF phase was separated. The ethyl acetate layer was washed with distilled water (2 x 100 mL) then with brine (1 x 100 mL). The organic phase was dried over 3 Å molecular sieves, filtered, and the solvent was removed under reduced pressure in a rotary evaporator. The product was then purified by column chromatography (3:1, hexanes:ethyl acetate). The solvent was removed under reduced pressure in a rotary evaporator and the product was dried under vacuum overnight to yield 0.263 g (48.0 % yield). ^{1}H NMR (CDCl$_3$): δ 0.78 (t, *J* = 7.3 Hz, 3H), 1.54 (m, 2H), 2.08 (t, *J* = 2.4 Hz, 1H), 2.82 (s, 6H), 3.32 (t, *J* = 7.6 Hz, 2H), 4.52 (s, 2H), 7.13 (d, *J* = 7.5 Hz, 1H), 7.33

(m, 5H), 7.49 (m, 2H), 8.20 (d, *J* = 7.5 Hz, 1H), 8.31 (d, *J* = 8.5 Hz, 1H), 8.50 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (CDCl$_3$): δ 11.0, 22.9, 45.1, 45.4, 50.9, 115.1, 118.7, 123.2, 126.8, 128.1, 128.3, 128.4, 129.4, 129.7, 130.0, 130.4, 134.5, 137.5, 151.5.

Synthesis of Poly(ethylene glycol) Monomethyl Ether Tosylate

Poly(ethylene glycol) monomethyl ether (Mw=2000 Da) (20.22 g, 0.01011 mol) was added to a round-bottomed flask and dissolved in 35 mL of dichloromethane. Triethylamine (2.56 g, 0.0253 mol) was added and the reaction was placed in an ice bath. After cooling, *p*-toluenesulfonyl chloride (4.82 g, 0.0253 mol) was added in four portions in 15 min intervals. After the additions were complete, the reaction was allowed to warm to room temperature and stir for an additional 18 h. The reaction was then filtered, and the filtered solid was washed with an additional 100 mL of dichloromethane. The dichloromethane solutions were combined and washed with 2 x 50 mL of 3 M HCl, 50 mL of 1 M HCl, 50 mL of saturated aqueous NaHCO$_3$ solution, 2 x 50 mL of brine, then dried over anhydrous Na$_2$SO$_4$ overnight. The solution was then filtered and the solvent removed under reduced pressure in a rotary evaporator to yield 14.66 g (67.3 % yield) of the poly(ethylene glycol) monomethyl ether tosylate. ^{1}H NMR (CDCl$_3$): δ 2.44 (s, 3H), 3.37 (s, 3H), 3.50-3.72 (br m, 204H), 4.15 (t, *J* = 4.9 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.8 (d, *J* = 8.6 Hz, 2H).

Synthesis of Dansyl-Terminated Poly(ethylene glycol) (30)

A mixture of *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide (0.0893 g, 0.306 mmol) and cesium carbonate (0.0997 g, .306 mmol) in 10 mL of dry DMF was placed in a flame-dried flask. The reaction was stirred under nitrogen for 1 h before the addition of a solution of poly(ethylene glycol) monomethyl ether tosylate (0.1657 g, .0764 mmol) in 10 mL of dry DMF. The reaction mixture was then heated to 90 °C and was allowed to stir for 48 h. Upon cooling, 100 mL of distilled water was added and the water/DMF solution was washed with diethyl ether (3 x 100 mL). The water/DMF was then extracted with dichloromethane (3 x 50 mL). The dichloromethane extracts were then combined and allowed to dry over 3 Å molecular sieves, filtered, and solvent was removed under reduced pressure in a rotary evaporator to yield 0.092 g (48.9 % yield) of product. ^{1}H NMR ($CDCl_3$): δ 0.77 (t, *J* = 7.3 Hz, 3H), 1.55 (m, 2H), 2.87 (s, 6H), 3.31 (t, *J* = 7.8 Hz, 2H), 3.37 (s, 3H), 3.43-3.74 (br m, 204H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.51 (m, 2H) 8.15 (d, *J* = 7.5 Hz, 1H), 8.28 (d, *J* = 8.5 Hz, 1H), 8.51 (d, *J* = 8.5 Hz, 1H).

Synthesis of Dansyl-Terminated Polyisobutylene (31)

A mixture of *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide (0.0651 g, 0.22 mmol) and cesium carbonate (0.0725 g, 0.22 mmol) in 10 mL of dry DMF was placed in a flame-dried flask. The reaction mixture was allowed to stir at room temperature for 1 h. A solution of bromide-terminated polyisobutylene[65] (0.137 g, 0.058 mmol) in 20 mL of heptane was added and the mixture was heated at 90 °C for 48 h. The reaction mixture was then allowed to cool and 100 mL of hexanes was added. The DMF layer was removed and the hexanes/heptane layer was washed with distilled water (1 x 100 mL) then with 90% EtOH (4 x 100 mL). After drying over 3 Å molecular sieves, the solution was filtered and solvent removed under reduced pressure in a rotary evaporator to yield 0.1182 g (77.2 % yield) of product. ^{1}H NMR ($CDCl_3$): δ 0.65 (t, *J* = 7.4 Hz, 3H), 0.77-1.80 (br m, 335H), 2.88 (s, 6H), 3.00 (m, 2H), 3.25 (m, 2H), 7.17 (d, *J*

= 7.0 Hz, 1H), 7.52 (m, 2H), 8.16 (d, *J* = 7.0 Hz, 1H), 8.27 (d, *J* = 8.5 Hz, 1H), 8.52 (d, *J* = 8.5 Hz, 1H).

Synthesis of Internally Functionalized Poly(ethylene glycol) Dansyl (32)

A mixture of 5-dimethylaminonaphthalene-1-sulfonamide (0.0479 g, .191 mmol) and cesium carbonate (0.1309 g, .402 mmol) in 10 mL of dry DMF was placed in a flame-dried flask. The reaction mixture was stirred under nitrogen for 1 h before the addition of a solution of poly(ethylene glycol) monomethyl ether tosylate (0.8301 g, 0.383 mmol) in 10 mL of dry DMF. The reaction mixture was then heated to 90 °C and was allowed to stir for 48 h. Upon cooling, 100 mL of distilled water was added and the water/DMF was washed with diethyl ether (3 x 100 mL). The water/DMF was then extracted with dichloromethane (3 x 50 mL). The dichloromethane extracts were combined and allowed to dry over 3 Å molecular sieves, filtered, and the solvent was removed under vacuum using a rotary evaporator to yield 0.6 g (68.3% yield) of product. ^{1}H NMR ($CDCl_3$): δ 2.87 (s, 6H), 3.37 (s, 6H), 3.43-3.74 (br m, 408H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.51 (m, 2H), 8.15 (d, *J* = 7.6 Hz, 1H), 8.28 (d, *J* = 8.5 Hz, 1H), 8.51 (d, *J* = 8.5 Hz, 1H).

Synthesis of Hydroxy-terminated Polyisobutylene (PIB-$(CH_2)_3OH$)

To solution of carboxylic acid-terminated polyisobutylene (PIB-$(CH_2)_2COOH$) (2.0 g, 0.85 mmol) in 50 mL of diethyl ether was added lithium aluminum hydride (32 mg, 0.85 mmol). The reaction mixture was allowed to stir for 12 h. The mixture was filtered and washed successively with H_2O (1 x 10 mL), 0.1 M HCl (1 x 10 mL), and then with brine (3 x 10 mL). After drying over Na_2SO_4, the solvent was removed under vacuum under vacuum using a rotary evaporator to yield 1.4 g (70% yield) of PIB-$(CH_2)_3OH$. ^1H NMR ($CDCl_3$): δ 0.71-1.61 (br m, 335H), 1.83 (m, 1H), 3.63 (t, *J* = 5.2 Hz, 2H).

Synthesis of Bromide-Terminated Polyisobutylene (PIB-$(CH_2)_3Br$)

A solution of PIB-$(CH_2)_3OH$ (1.4 g, 0.597mmol) in 50 mL of dichloromethane was cooled to 0 °C. Triethylamine (0.202 g, 2.00mmol) and then methanesulfonyl chloride (0.209g, 1.82mmol) were added to the solution dropwise. The reaction was allowed to warm to room temperature and stirred for an additional 6 h. The solvent was removed under reduced pressure using a rotary evaporator and the residue was dissolved in 20 mL of a 1:1 heptane/acetone mixture containing LiBr (0.5 g, 5.77 mmol). The reaction mixture was heated to 80 °C for 24 h. The mixture was cooled to room temperature and added to 100 mL of hexanes. The organic phase was then washed successively with H_2O (1 x 50 mL), DMF (5 x 10 mL), and again with H_2O (2 x 20 mL). After drying over Na_2SO_4, the solvent was removed under vacuum using a rotary evaporator to yield 1.220 g (87% yield) of PIB-$(CH_2)_3Br$. ^1H NMR ($CDCl_3$): δ 0.71-1.61 (br m, 335H), 1.83 (m, 1H), 3.37 (t, *J* = 6.8 Hz, 2H).

Synthesis of Internally Functionalized Polyisobutylene Dansyl (33)

A mixture of 5-dimethylaminonaphthalene-1-sulfonamide (0.0162 g, 0.065 mmol) and cesium carbonate (0.210 g, 0.644 mmol) in 10 mL of dry DMF was placed in a flame-dried flask. The mixture was allowed to stir at room temperature for 1 h. A solution of PIB-$(CH_2)_3Br$ (0.3112 g, 0.129 mmol) in 20mL of heptane was added and the solution was heated at 90 °C for 48 h. The reaction mixture was then allowed to cool and 100 mL of hexanes was added. The DMF layer was removed and the hexanes/heptane layer was washed with distilled water (1 x 100 mL) then with 90% EtOH (4 x 100 mL). After drying over 3 Å molecular sieves, the solution was filtered and solvent removed under vacuum using a rotary evaporator to yield 0.309 g (94.4 % yield) of product. ^{1}H NMR (CDCl$_3$): δ 0.69-1.88 (br m, 670 H), 2.88 (s, 6H), 3.25 (m, 4H), 7.19 (d, *J* = 7.0 Hz, 1H), 7.53 (m, 2H) 8.30 (d, *J* = 7.0 Hz, 1H), 8.31 (d, *J* = 8.3 Hz, 1H), 8.53 (d, *J* = 8.3 Hz, 1H).

Synthesis of *N*-Propargyl-*N*-Propyl-5-dimethylaminonapthalene-1-sulfonamide (34)

A mixture of *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide (0.8734 g, 3.0 mmol) and cesium carbonate (1.169 g, 3.6 mmol) in 10 mL of dry DMF was placed in a flame-dried flask. The mixture was allowed to stir at room temperature for 1 h. An 80% by weight toluene solution of propargyl bromide (4.45 g, 30 mmol) was added and the reaction mixture was heated at 80 °C for 48 h. The reaction mixture was then allowed to cool and solvent was removed at reduced pressure using a rotary evaporator. The crude product was then purified by silica gel column chromatography (3:1, hexanes:ethyl acetate) to yield 0.874 g (88.6 % yield) of product. ^{1}H NMR (CDCl$_3$): δ 0.78 (t, *J* = 7.3 Hz, 3H), 1.54 (m, 2H), 2.08 (t, *J* = 2.4 Hz, 1H), 2.82 (s, 6H), 3.32 (t, *J* = 7.6 Hz, 2H), 4.15 (d, *J* = 2.4 Hz, 2H), 7.13 (d, *J* = 7.0 Hz, 1H), 7.49 (m, 2H), 8.20 (d, 7.0 Hz, 1H), 8.31 (d, 8.3 Hz, 1H), 8.50 (d, 8.3 Hz, 1H). ^{13}C NMR (CDCl$_3$): δ 10.8, 20.5, 35.4, 45.2, 47.9, 73.2, 77.1, 114.9, 119.4, 122.9, 127.8, 129.4, 129.8, 130.0, 130.3, 134.5, 151.4.

Synthesis of Dansyl Triazole-Terminated Polyisobutylene (35)

N-Propargyl-*N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide (31 mg, 0.094 mmol) and Hunig's base (21 mg, 0.17 mmol) were added to a solution of the PIB-azide[65] (0.2 g, 0.085 mmol) in 5 mL of THF. Tris(triphenylphoshine) copper(I) bromide (8 mg, 0.1 mmol) was added and N_2 was bubbled though the reaction for 30 min. The reaction was heated for 48 h at 55 °C. After cooling, the solvent was removed and the product was taken up in 50 mL of hexanes and washed with three 5-mL portions of DMF, three 5-mL portions of brine, dried over Na_2SO_4, and concentrated under reduced pressure using a rotary evaporator. The product was then passed through a plug of silica gel and eluted with additional dichloromethane. After removing the solvent under reduced pressure using a rotary evaporator, the residue was then dissolved in 3 mL of heptane and 1 mL of acetone and Merrifield's resin (100 mg, 1.3 meq benzyl chloride/g resin) and LiBr (100 mg, 1.15 mmol) were added and stirred for 12 h to remove traces of triphenylphosphine. After filtration, the solvent was removed under reduced pressure using a rotary evaporator to give 0.074 g (37%) of the polyisobutylene terminated dansyl triazole. ^{1}H NMR ($CDCl_3$): δ 0.65 (t, *J* = 7.4 Hz, 3H), 0.77-1.80 (br m, 335H), 2.88 (s, 6H), 3.20 (t, *J* = 7.8 Hz, 2H), 3.93 (dd, *J* = 13.6 Hz and 8.4 Hz, 1H), 4.14 (dd, *J* = 13.6 Hz and 6.8 Hz, 1H), 4.60 (s, 2H), 7.17 (d, *J* = 7.0 Hz, 1H), 7.37 (s, 1H), 7.52 (m, 2H), 8.16 (d, *J* = 7.0 Hz, 1H), 8.27 (d, *J* = 8.3 Hz, 1H), 8.52 (d, *J* = 8.3 Hz, 1H).

Synthesis of Polyisobutylene-Phenol Ligand (45)

Paraformaldehyde (0.0179 g, 0.60 mmol) and *N*,*N*,*N'*,*N'*-tetraethyldiethylenetriamine (0.1297 g, 0.60 mmol) were added to a round-bottomed flask and heated for 1 h at 90 °C and then allowed to cool under a flow of N_2 to room temperature. Polyisobutylene-phenol **44**[65] (0.5426 g, 0.50 mmol) as a solution in 10 mL of heptane was then added to this cooled reaction mixture along with 5 mL of ethanol. This solution was then allowed to reflux for 24 h. After cooling to room temperature, 50 mL of hexanes and 10 mL of water was added to induce a phase separation of the heptane and ethanol phases. The upper heptane/hexanes phase was removed and washed once with 50 mL of DMF, then 3 x 50 mL of MeOH. After drying over 3 Å molecular sieves, the solvent was removed under reduced pressure using a rotary evaporator to yield 0.57 g (87.0 % yield) of the desired product. ^{1}H NMR ($CDCl_3$): δ 0.79-1.39 (m, 192 H), 2.40-2.80 (br m, 16 H), 3.69 (s, 2 H), 6.75 (d, *J* = 8.3 Hz, 1 H), 6.94 (s. 1H), 7.14 (d, *J* = 8.3 Hz, 1 H).

Synthesis of Polyisobutylene Amide Ligand (48)

Polyisobutylene terminated carboxylic acid (**46**)[65] (2.65 g, 2.42 mmol) was dissolved in 30 mL of toluene. Thionyl chloride (3.0 mL, 41 mmol) was added to this solution dropwise and the reaction mixture was refluxed for 4 h. After cooling, the solvent was removed under reduced pressure and the residue was analyzed by IR spectroscopy (carbonyl stretch of acid chloride at 1802 cm^{-1}) after drying under vacuum for 2 h. The polyisobutylene acid chloride (**47**) so obtained was not further purified but was dissolved in 30 mL of fresh toluene. *N*,*N*,*N′*,*N′*-Tetraethyldiethylenetriamine (0.5996 g, 2.78 mmol) was then added dropwise and the reaction was allowed to stir at room temperature for 2 h. IR spectroscopic analysis showed complete disappearance of the acid chloride peak (1802 cm^{-1}) and the appearance of the characteristic amide carbonyl stretch at 1650 cm^{-1}. An additional 100 mL of toluene was then added and this solution was washed with 2 x 50 mL of 90% EtOH then 2 x 50 mL of water. After drying over 3 Å molecular sieves, the toluene was removed under reduced pressure using a rotary evaporator to provide 2.7 g of **48** (84 % yield). ^{1}H NMR (CDCl$_3$): δ 0.79-1.39 (m, 192 H), 2.31(m, 2H), 2.57 (br m, 12H), 3.39 (m, 4H).

Synthesis of Polyisobutylene Pyridine Imine Ligand (50)

Polyisobutylene amine (**49**)[65] (1.05 g, 0.45 mmol) was dissolved in 50 mL of toluene. 2-Pydridine carboxaldehyde (0.105 g, 0.98 mmol) was then added and the solution was stirred and heated at reflux with an attached Dean-Stark trap. After 2 h, the reaction was allowed to cool and the solvent was removed under reduced pressure using a rotary evaporator. The resulting residue was then dissolved in 100 mL of hexanes and washed with 3 x 50 mL of 90% ethanol and then dried over 3 Å molecular sieves. After filtration, the solvent was removed under reduced pressure using a rotary evaporator to give 0.95 g (87 % yield) of the desired polyisobutylene pyridine imine ligand **50**. ^{1}H NMR (CDCl$_3$): δ 0.77-1.80 (br m, 335H), 3.38 (dd, J = 13.4 and 8.3 Hz, 1H,), 3.66 (dd, J = 13.4 and 6.1 Hz, 1H), 7.32 (m, 1H), 7.75 (m, 1H), 8.02 (m, 1H), 8.36 (s, 1H), 8.65 (m, 1H).

Synthesis of 1, 3-*N*,*N*,*N′*,*N′*-Tetraethyl-2-*N″*-Propargyldiethylenetriamine (51)

A mixture of *N*,*N*,*N′*,*N′*-tetraethyldiethylenetriamine (1.07 g, 4.99 mmol), propargyl chloride (0.372 g, 4.99 mmol), potassium iodide (10 mg, 0.06 mmol) and cesium carbonate (1.625 g, 4.98 mmol) in acetonitrile (15 mL) was stirred at room temperature for 72 h. The solids of the reaction mixture were filtered off. The solvent was then removed under reduced pressure using a rotary evaporator to produce a residue that was extracted with diethyl ether (20 mL). The diethyl ether was then removed under reduced pressure using a rotary evaporator to yield 1.02 g of the desired alkyne functionalized ligand **51** (81 % yield) as a pale yellow liquid. ^{1}H NMR ($CDCl_3$): δ 1.02 (t, *J* = 6.0 Hz, 12H), 2.19 (t, *J* = 2.4 Hz, 1H), 2.57 (m, 16H), 3.46 (d, *J* = 2.4 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 11.7, 42.9, 47.4, 51.0, 52.0, 73.0, 78.6.

Synthesis of *N, N*-Bis(2-Pyridylmethyl)-*N*-Propargylamine (52)

A sample of 2-picolyl chloride hydrochloride (2.06 g, 12.6 mmol) was dissolved in a methanol/water mixture (20 mL/10 mL) in a pressure vessel and propargyl amine (0.34 g, 6.2 mmol) was added. After briefly flushing with nitrogen, the reaction solution was sealed and heated at 65 °C for 12 h. After removing the solvent under reduced pressure with a rotary evaporator, 10 mL of water was added and the aqueous phase was separated. The aqueous phase was extracted with 3 x 40 mL of dichloromethane. The organic phases were combined and washed once with 20 mL of 3 M NaOH and then dried over $MgSO_4$. After filtering, 100 mL of anhydrous diethyl ether was added and the resulting mixture was filtered. Removal of the solvent under reduced pressure using a rotary evaporator yielded 1.17 g (79.5% yield) of the desired alkyne product **52**. ^{1}H NMR ($CDCl_3$): δ 2.33 (t, *J* = 2.4 Hz, 1H), 3.46 (d, *J* = 2.4 Hz, 2H), 3.95 (s, 4H), 7.20 (m, 2H), 7.55 (m, 2H), 7.69 (m, 2H), 8.60 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 42.5, 59.4, 67.9, 73.6, 122.1, 123.1, 136.5, 149.2, 158.7.

Synthesis of TEDETA Triazole Terminated Polyisobutylene Ligand

To a pressure vessel, PIB azide[65] (1.02 g, 0.43 mmol) and **51** (0.22 g, 0.86 mmol) were added to 20 mL of a heptane/ethanol (1:1/v:v) and CuCl (0.005 g, 0.04 mmol) mixture. Nitrogen was bubbled through the solution for 15 min. The reaction was then sealed and heated at 65 °C for 16 h. After cooling, water was added to produce a biphasic mixture. The heptane solution was then removed and an additional 100 mL of hexanes was added. This heptane/hexanes solution was then washed with acetonitrile, DMF, diethylene glycol diacetate and methanol (50 mL each) respectively. This heptane/hexanes solution was then passed through a silica plug to remove any chelated copper. The solvent was then removed under reduced pressure using a rotary evaporator to give 0.91g (81% yield) of the desired polyisobutylene terminated TEDETA triazole ligand. ^{1}H NMR ($CDCl_3$): δ 0.77-1.80 (br m, 347H), 2.57 (br m, 16H), 3.89 (s, 2H), 4.03 (dd, J = 13.2 and 8.8 Hz, 1H,), 4.23 (dd, J = 13.2 and 6.1 Hz, 1H), 7.46 (s, 1H).

Synthesis of Polyisobutylene Triazole Copper Complexes 53 and 54

A procedure similar to that above was used with a stoichiometric amount of CuCl to produce the desired complexes. IR analysis of the polyisobutylene copper complexes showed complete disappearance of both the polyisobutylene terminated azide stretch (2097 cm^{-1}) and the alkyne-functionalized ligands' stretch (2120 cm^{-1}). Inductively coupled plasma mass spectroscopy (ICP-MS) was used to determine the exact metal loadings of the polyisobutylene triazole copper complexes. The polyisobutylene copper complex **53** used had a copper metal loading of 0.416 mmol copper/g of polyisobutylene complex while the polyisobutylene copper complex **54** had a metal loading of 0.115 mmol copper/g of polyisobutylene complex.

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