Using Soluble Polymers To Recover Catalysts and Ligands

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I. Introduction

The use of soluble polymers to recover catalysts and ligands has its origins in the synthetic approaches to peptide and oligonucleotide synthesis that were developed in the labs of Merrifield and Letsinger in the 1960s.[1,2] Those discoveries revolutionalized the synthesis of biomolecules.[3,4] They also led to a significant amount of work in a variety of industrial and academic laboratories—work that was in the case of catalysis directed toward developing systems to immobilize or heterogenize homogeneous catalysts.[5] In most cases, this work focused on the same insoluble polymers Merrifield used—divinylbenzene (DVB)-cross-linked polystyrene.[5−10]

Soluble polymers were common 35 years ago, but they did not receive as much attention for use as catalyst supports as was the case for their cross-linked, insoluble analogues. Indeed, through the 1960s and 1970s reports describing the use of soluble polymers as supports for recovery and reuse of homogeneous catalysts were scattered.[10,11] This review first highlights selected examples of this early work because this work illustrates many of the ideas and separation strategies that have continued to receive attention in more recent work.[12−14] The review then discusses in a general way some of the common features of soluble polymers that differentiate them from their insoluble cousins. The review then goes on to outline in a broad way the separation strategies used to recover soluble polymeric ligands or soluble polymer-ligated homogeneous catalysts. Finally, it focuses on more recent work with several classes of soluble polymers, discussing their advantages, the separation strategies employed, and the limitations of these supports. This review does not cover biocatalysts and emphasizes examples where soluble polymers are used to recover and reuse a catalyst. Poly(alkene oxide) supports are reviewed elsewhere and are discussed to a limited extent here.

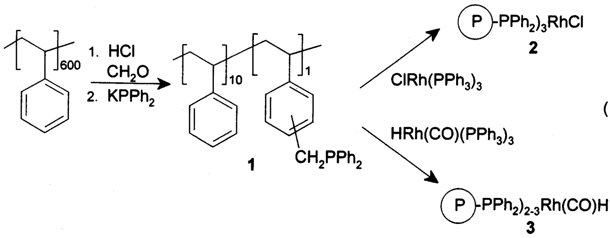
David E. Bergbreiter is an “immigrant” Texan with two “native Texan” daughters, a hyperactive chocolate Laborador, 16 acres, and a “very small” share of an oil well. After public schooling in Chicago, undergraduate work at Michigan State University, and graduate work with Professor Whitesides at the Massachusetts Institute of Technology, he and his wife Lynne moved to Texas A&M in 1974. There he rose through the ranks and is currently a professor of chemistry with interests in catalysis, organic chemistry, and polymer and surface chemistry.

II. Early Work

One of the first groups to use soluble polymers and to point out their advantages was Bayer’s group.[15−17] Much of this group’s interest was in peptide synthesis and metal complexation using soluble polymers.[18,19] However, Bayer’s group was among the first to describe soluble polymer alternatives to cross-linked polymers as catalyst supports. This work involved a variety of polymers, poly(ethylene oxide), polystyrene, poly(vinylpyrrolidine), and poly(vinyl chloride), although their initial published work focused mainly on the first two polymers. In general, Bayer’s group used relatively simple polymer modification to prepare the necessary ligands.

A. Linear Polystyrene-Bound Catalysts

In Bayer’s work, linear polystyrene (MW = 100000) was chloromethylated, and the resulting benzylic chloride was then substituted by diphenylphosphine using $KPPh_2$, chemistry analogous to that used earlier with cross-linked polystyrene resins (eq 1).[15,20]



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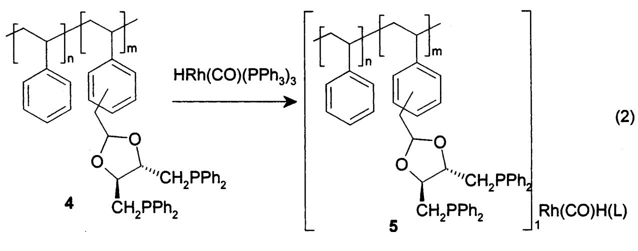
The resulting polymer **1** contained varying amounts of phosphine on the basis of elemental analyses. A typical loading is shown in eq 1. Catalysts were loaded onto these soluble diphenylphosphine-containing polymers by allowing an excess of this linear polymer to exchange with ligands of preformed Rh or Pd complexes. This exchange reaction produced a polymer-bound catalyst. $[(Rh(CO)_2(acac)]$, $Rh_2(CO)_4Cl_2$, $Rh(PPh_3)_3Cl$, $RhH(CO)(PPh_3)_3$, and $PdCl_2(PhCN)_2$ are examples of molecular complexes used in reaction with this diarylphosphinated chloromethylated polystyrene to form polymeric catalysts. The resulting polymer-bound complexes (e.g., **2** and **3**) were not extensively characterized. In some cases (e.g., in the Pd case) the products may have been polymer-modified forms of colloidal metal. Both homogeneous hydrogenation and hydroformylation reactions were carried out using these polymer-bound catalysts. For example, the rhodium hydrogenation catalyst **2** presumed to be analogous to Wilkinson's catalyst was used for five cycles of hydrogenation of 1-pentene, with catalyst recovery being effected by ultrafiltration using a polyamide membrane and a 10000 molecular weight cutoff. Solvent precipitation too was used to isolate these polymer-bound catalysts. The rhodium hydroformylation catalyst **3** had ca. 3:1 selectivity for the normal product in hydroformylation of terminal alkenes. This catalyst too was recycled twice using ultrafiltration to separate the catalysts and products. The authors report separation of the soluble polymer-bound Rh catalysts was quantitative.

B. Asymmetric Catalysis with Linear Polymer-Supported Catalysts

Bayer and Schurig[16] along with Ohkubo et al.[21] were the first to describe soluble polymers as supports for asymmetric catalysts. In Bayer's case, a DIOP (4,5-bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane) ligand was attached to a linear polystyrene, the resulting polystyrene-bound version of DIOP (e.g., **4**) was allowed to react with $HRh(CO)(PPh_3)_3$ (eq 2), and the resulting polymer-bound Rh complex **5** was used to hydroformylate styrene. Hydroformylation products were obtained (the branched product was the predominant product), but the ee was only 2%. The catalyst **5** was separable from low molecular weight materials by membrane filtration.



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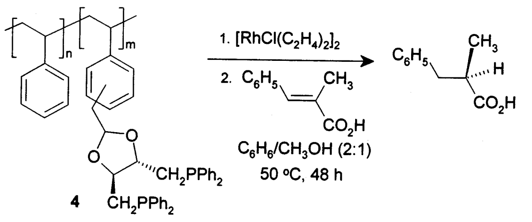
Asymmetric hydrogenation was also studied by Ohkubo, Fujimori, and Yoshinaga using other polymeric catalysts.[21] This group used the same soluble polystyrene-bound version of DIOP used earlier by Bayer's group (e.g., **4**) to prepare a rhodium(I) catalyst to hydrogenate prochiral unsaturated acids such as 2-methyl-3-phenylpropenoic acid, (*Z*)-2-methyl-2-butenedioic acid, and (*E*)-2-methyl-2-butenedioic acid (eq 3). In this case, these authors used rather small polystyrene oligomers as supports, with the largest polymer having a degree of polymerization of about 50. The smallest oligomer had a degree of polymerization of <10. Some differences in conversion and ee were noted for the differently sized polymers, but the ee values were generally <40% and the conversions were modest. Recovery and separation of the polymeric catalysts from the products was not described.



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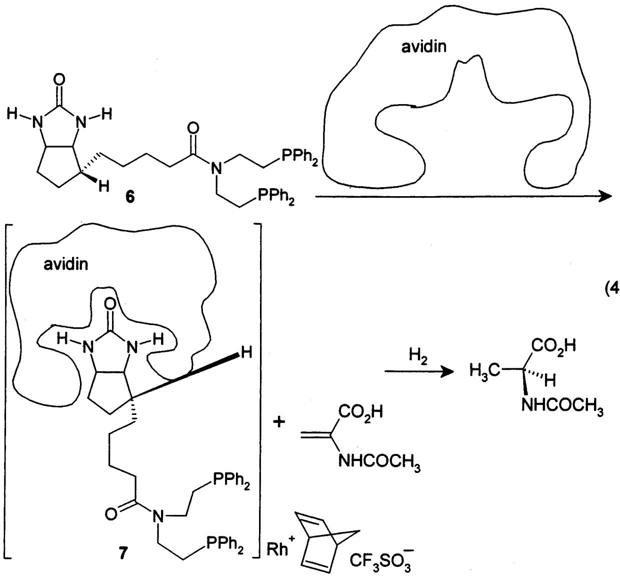
C. Water-Soluble Polymer Supports for Catalysts

1. Proteinaceous Supports

The use of environmentally more benign solvents such as water is now a subject of considerable interest in the context of "green chemistry".[22] The use of water as a solvent was also featured in some of the early work with soluble polymers. In this case, a natural polymer—a protein—was used as a water-soluble chiral support to prepare an asymmetric cationic Rh(I) hydrogenation catalyst.[23] This work also featured the use of noncovalent interactions for catalyst immobilization, taking advantage of the affinity of the protein avidin for the *N*,*N*-bis(2-diphenylphosphinoethyl)biotinamide **6** to immobilize a chiral chelating phosphine ligand. In this example, the asymmetric induction in hydrogenation of prochiral enamides using the Rh(I) catalyst prepared in eq 4 was not high enough to be practical (ca. 40–44% ee), but this work illustrates how soluble polymers confer their own solubility behavior on a ligand that would otherwise be insoluble in a particular solvent. In this case, the size of this proteinaceous



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polymer support in comparison to the products provided a way to effect catalyst separation using membrane filtration (a 10000 molecular weight cutoff ultrafiltration membrane was used). Finally, this report showed that the enantioselectivity was a result of a specific macromolecule−catalyst interaction. The presence of other proteins (e.g., lysozyme, bovine serum albumin, or carbonic anhydrase) had no influence on the enantioselectivity of **7** though these other proteins did alter **7**'s reactivity.

2. Polar Polymer Supports

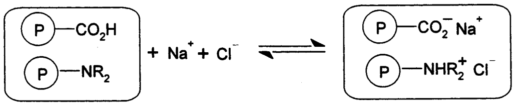
A later report by Bayer and Schumann described using linear polymers such as poly(vinylpyrrolidinone), polyethylenimine, polyacrylonitrile, and poly(ethyleniminodiacetic acid) as polychelatogens with Rh, Pd, Pt, and Ni as the actual metal catalysts.[17] These catalysts had much higher activities than the earlier catalysts described by this group and could be recovered by ultrafiltration (or by biphasic separations if water-soluble polymers were used). However, it is likely that the actual catalysts are colloidal metal rather than molecular complexes in these cases.[24]

D. Polymers Supporting Catalysts with Thermally Reversible Solubility

Temperature-dependent properties of polymers were used in early work to design a recoverable catalyst system. While the polymer in this example is never soluble, this report is relevant in the context of this review because the polymer serves as a reversible reservoir for the transition-metal catalyst. In these examples, a transition-metal salt was released from the polymer on heating. In the first instance, this involved using a thermally regenerable ion exchange polymer that reabsorbed the transition-metal salt on cooling to room temperature.[25] Here the properties of the polymer support lead to a thermally soluble/insoluble homogeneous catalyst—a scheme used subsequently by our group and others in designing soluble polymer supports for homogeneous catalysts.

1. Sirotherm Resins

The basis of the thermally soluble/insoluble catalyst system developed by Pittman was the Sirotherm ion exchange material developed earlier for desalination applications.[26] Sirotherm ion exchange resins consist of a mixture of amphoteric polymers in a water-permeable polymer matrix. The amphoteric polymers include both an acidic polymer (a poly(acrylic acid)) and a basic polymer (a polyamine such as poly(*p*-diethylaminostyrene) or poly(*N*-alkyldiallylamine)). This thermally regenerable ion resin works because the proton-transfer equilibrium 5 is temperature dependent. For example, at ambient temperature, the equilibrium favors the ionic form of the polymer and 500 mg/L sodium chloride can be absorbed from an aqueous solution that contains 1000 mg/L sodium chloride. At elevated temperature (80−90 °C), this equilibrium favors the neutral polymers and this sodium chloride is released to solution. Pittman used this same behavior to bind and release an ionic transition-metal catalyst.



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In Pittman's case, both hydroformylation and Reppe carbonylation reactions were studied. The Reppe reaction and the hydroformylation both used $RhCl_3$/Me_3N or $RhCl_3$ solutions as catalyst precursors. Rhodium carbonyl hydrides or rhodium clusters presumably form in the reaction. Pittman speculated that the active catalyst in the Reppe reactions was a rhodium carbonyl hydride anion such as **8**. This anion would complex to the Sirotherm resin like chloride does. Pittman further noted that this complexation and catalyst recovery was only efficient under neutral conditions. Under acidic (CH_3CO_2H present) or basic ($(CH_3)_3N$ present) conditions, catalyst recycling was not efficient as judged by the decreasing 1-pentene conversion in a second or third catalyst recycling. However, under neutral conditions, a suspension containing 1 g of Sirotherm resin and 30 mL of a solution of the rhodium catalyst **8** in a 1:5 (v/v) mixture of water and THF was successfully used for 16 cycles for the carbonylation shown in eq 6.

$[HRh(CO)_{n-1}]_x^-$

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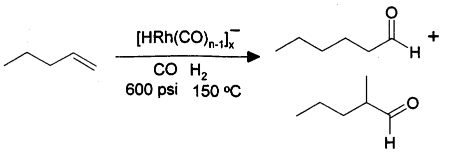

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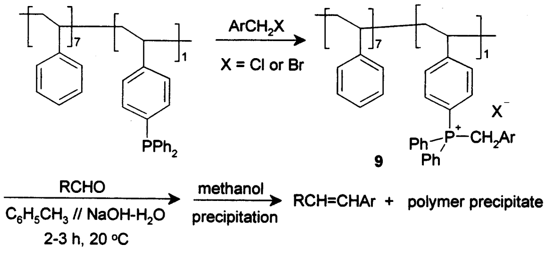
Approximately equal amounts of normal and branched products formed. About 10−20% of the product was in the form of an alcohol. The total turnover was 2500 in these 16 cycles. However, each reaction cycle required a relatively long time (10 days each), the 1-pentene conversion was modest in each cycle (ca. 60%), and a relatively high catalyst loading was present in each cycle. Nonetheless, the polymer in this example afforded a thermally reversible way to generate a homogeneous catalyst at high temperature that could then be recovered by cooling and filtration.

2. Poly(vinylpyridine) Supports

Insoluble forms of poly(vinylpyridine) have also been used to chemically bind or release a homogeneous hydroformylation catalyst in response to the presence or absence of hydrogen.[27] The polymer in this work is chemically analogous to the temperature-dependent ion exchange polymers used by Pittman. This work is one of the earliest examples where the properties of a polymer were used to recover a homogeneous catalyst.

E. Biphasic Systems Employing Soluble Polymer-Supported Catalysts

Another early example of a soluble polymer-supported catalyst from Hodge's group provided an illustration of the use of a soluble polymer as an organic catalyst in a biphasic reaction.[28] In this work, a phosphine-containing polystyrene (MW = 100000) was prepared as a copolymer of styrene and *p*-diphenylphosphinostyrene (ca. 7:1 mol/mol). Alkylation of this phosphine by benzyl chloride or by 2-bromomethylnaphthalene led to formation of the phosphonium salt **9**. This relatively acidic polymeric phosphonium salt is insoluble in aqueous base, but as a polyvalent phosphonium salt, it acts as a phase-transfer catalyst in this toluene/water mixture. Deprotonation of the phosphonium salt under these biphasic reaction conditions then produces an ylide that reacts with an aldehyde acceptor to form an alkene (eq 7). The soluble phase-transfer polymeric catalysts here—the phosphonium salts on the polystyrene—were also substrates in the subsequent Wittig reactions. However, if the polymer were used in excess, it and the byproduct polymeric polystyrenediphenylphosphine oxide could both be recovered and separated from the product alkene by precipitation using methanol.



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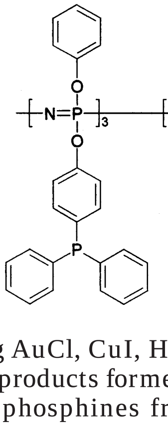
F. Inorganic Polymer Supports

1. Polyphosphazene Supports

Linear inorganic polymers too were used early on as supports for homogeneous catalysts. Examples of such chemistry include Allcock's use of polyphosphazene-bound phosphine ligands to prepare olefin isomerization and hydroformylation catalysts,[29] Awl's use of linear and ladder polysiloxanes as supports for hydrogenation catalysts,[30] and Farrell's use of siloxane polymers to support hydroformylation catalysts.[31] In Allcock's case, the polyphosphazene-bound triarylphosphine **10** was used to prepare various metal complexes using AuCl, CuI, $H_2Os_3(CO)_{10}$, and $[RhCl(CO)_2]_2$. Soluble products formed in most cases though coordination of phosphines from multiple polymers to the same metal was thought to lead to cross-linking and insolubility in some cases, with a polymer precipitate forming. ^{31}P NMR spectroscopy or IR spectroscopy (metal carbonyl complexes) served to establish that complete complexation of the polymeric phosphines by metal had been achieved. Polymer isolation by hexane precipitation often led to materials that did not redissolve. These materials may also have had coordinative cross-links involving phosphines of more than one polymer chain to the complexed metals.



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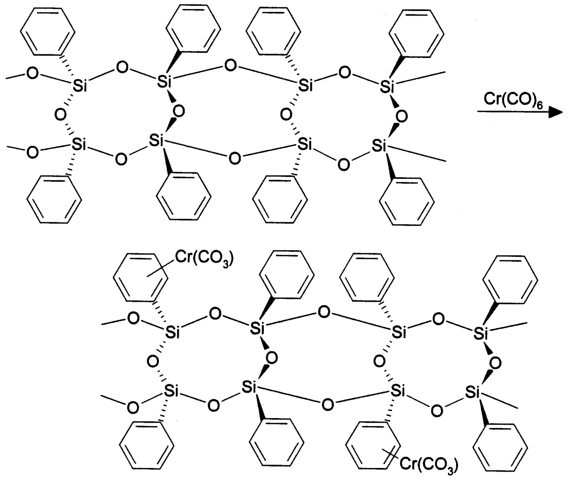
Reactions where the polyphosphazene-bound polymeric metal complexes served as catalysts were studied. In these reactions, catalyst/product separation was effected by simple distillation. However, catalyst reuse was not completely successful because of catalyst decomposition—a general problem that was recognized in part because of early attempts to recycle hydroformylation catalysts.[32]

2. Silicon-Containing Polymers as Catalyst Supports

Decomposition of a polymer-bound catalyst also frustrated the repetitive use of poly(phenylsiloxane)-complexed $-Cr(CO)_3$ as a stereoselective hydrogenation catalyst for hydrogenation of methyl sorbate to methyl (*Z*)-3-hexenoate.[30] In this case, the $-Cr(CO)_3$ groups were attached to the pendant phenyl rings of the ladder phenyl-containing siloxane polymer or to phenyl groups of a phenyl methyl silicone as shown in eq 8.



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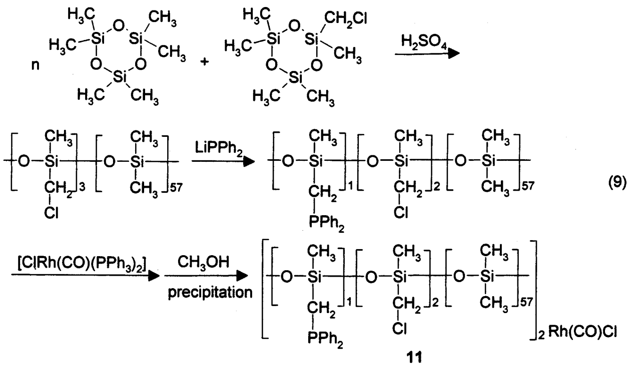
The product polymer was characterized by IR spectroscopy, elemental analysis, viscosity, GPC, and thermal analysis. However, while these soluble siloxane polymer-bound chromium carbonyl derivatives were more stable on the basis of thermal gravimetric analysis than a similar polystyrene polymer, significant loss of catalyst activity due to loss of >90% of the $-Cr(CO)_3$ groups occurred after this polymer was used in a hydrogenation and recovered by precipitation/filtration.[30]

Siloxane-supported hydroformylation catalysts were also prepared by Farrell et al. using the chemistry shown in eq 9.[31] The resulting polymers prepared by this chemistry had an M_v of 21000 and were used to prepare soluble ligands to support a rhodium carbonyl complex. However, while >90% of the polymer could be recovered after a 1-hexene hydroformylation by solvent precipitation (gravimetric analysis), elemental analysis of the recovered polymer showed that significant phosphine ligand and rhodium metal loss occurred. IR spectroscopy confirmed these results on the basis of the loss of the rhodium complex's carbonyl band at 1970 cm^{-1}. While earlier work by this group had shown significant polymer degradation in the phosphination step (especially using $LiPPh_2$ and the chloromethylated polymer), GPC showed no molecular weight loss for the polymeric catalyst **11** during a hydroformylation reaction.



Soluble rhodium complexes were also prepared by Sanger using methyl phenyl silicone polymers that were first chloromethylated ($SnCl_4$, $ClCH_2OCH_3$) and then phosphinated ($KPPh_2$).[33] This group reported IR studies not only of this polymer but also of other rhodium carbonyl complexes prepared using polymers such as $-[CH_2CH(C_6H_4PPh_2)]_{n-}$, $-[CH_2CH(C_6H_4CH_2PPh_2)]_{n-}$, and $-[CH_2CHOPPh_2)]_{n-}$. These complexes were used as hydroformylation catalysts. Issues of recycling and catalyst/product separation were not addressed and would likely have been problematic due to catalyst/ligand decomposition.

G. General Features Common to Early Work

These early papers where soluble polymers were used discuss in a general way many of the issues that are still important today in the design of new systems where polymers facilitate homogeneous catalyst recovery and reuse.[34,35] Many or most of the concepts described in more recent work have precedent in these early reports using soluble polymers as catalyst supports. However, this early work like much other work with "heterogenized" homogeneous catalysts was not widely adopted either in industry or in academia. Most often this reflected modest catalyst activity or selectivity. The separation processes were also not always well described or as mature as similar separations used today. Ultrafiltration membranes, for example, were used early on for separation and recovery of soluble polymer-bound catalysts and were even recognized as potential tools for conventional catalyst recovery.[36] However, the early examples that used ultrafiltration to recover a soluble polystyrene-bound Rh catalyst were inefficient. For example, hydrogenation of pentene with a polymer-bound Wilkinson's catalyst used over 200 mL of solvent in the overall process to hydrogenate a relatively small amount of pentene.[15] The use of membranes in reactors is now much improved with better materials, newer membranes, and practical continuous membrane reactors.[37] Catalyst loss and catalyst stability were other problems encountered in much of this early work.[31] Catalyst and ligand stability issues continue to be problems, but advances in spectroscopy make it easier to study these effects and to characterize the catalysts and ligands. Finally, it is not always clear in this early work what the catalyst was or how efficient catalyst recycling was since recycling efficiency was most often based on catalyst activity in a second or third cycle and not on trace metal analysis or studies of ligand stability. Moreover, few reports described successful use of a polymer-bound catalyst more than three times.

Most industrial and academic labs still mainly use insoluble polymer supports for catalysis and synthesis. However, the original scattered reports of the use of soluble polymer systems have substantially expanded in recent years to the point that soluble polymers are no longer uncommon as supports for catalysts and ligands.[38-40] This review's focus is these soluble polymers and the schemes that use soluble polymers for polymer-bound ligand and catalyst recovery and reuse. These issues are discussed in detail for several systems below. However, there are certain common features of all the systems, features that significantly impact the utility of soluble polymers in catalysis, catalyst recovery, and ligand synthesis. These features are briefly discussed first.

III. Characterization Advantages of Soluble Polymer Supports

One of the most significant features of soluble polymer-supported ligands and catalysts is the facility of ligand and catalyst synthesis and characterization afforded by the soluble polymer support. The use of a soluble polymer support offers advantages of homogeneity during synthesis and during characterization. In synthesis, this often means that it is possible to use synthetic procedures that directly mimic those used to prepare low molecular weight ligands and catalysts. In characterization, this means that it is relatively possible to use the range of solution-phase techniques routinely used in any synthetic operation. For example, spectroscopic procedures that work best with solutions are ^1H NMR spectroscopy and UV-vis spectroscopy, two prominent examples of techniques less readily used with an insoluble polymer support that work well with soluble polymer supports. Other NMR techniques such as ^{13}C and ^{31}P NMR spectroscopy are also very useful with soluble polymers though the advent of gel-phase NMR analyses for insoluble polymer-supported catalysts and ligands means that these other NMR procedures are not uniquely useful for soluble polymer supports.[41]

A. ^1H NMR Spectroscopy

^1H NMR spectroscopic characterization of soluble polymer-bound ligands and catalysts is most facile for ligands and catalysts present as end groups for polymers that have an equivalent weight of less than 10000. Figure 1 illustrates this with an example of a terminally bound Pd(II) catalyst, **12**, on poly(ethylene glycol) (PEG). This catalyst was prepared from an

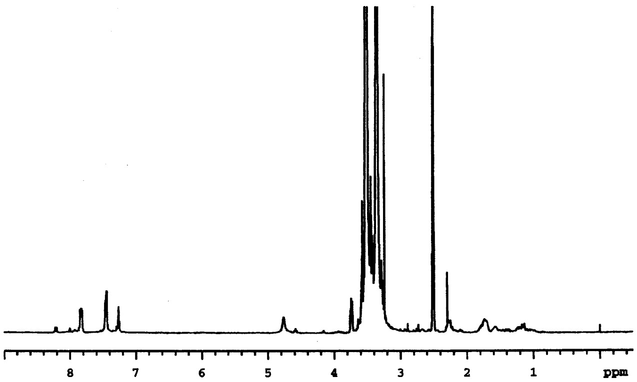
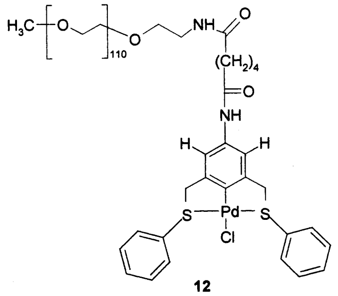


Figure 1. ^1H NMR spectrum of a polymer that contains a poly(ethylene glycol)-bound SCS−Pd(II) catalyst as the terminal group of the polymer (**12**).

amine-terminated monomethoxypoly(ethylene glycol) via amidation[42] and was analyzed by ^1H NMR spectroscopy using conditions like those used for a low molecular weight species (a 20 mg sample, 7 min of total analysis time). In this case, the poly(ethylene glycol)-bound Pd(II) catalyst with an SCS (sulfur−carbon−sulfur) ligand has an obscuring signal due to the polymer, the $-CH_2O-$ groups at δ 3.5. However, the ^1H NMR spectrum of the catalyst (and ligand) has aryl peaks in the δ 6.5−8.5 region that show up clearly.



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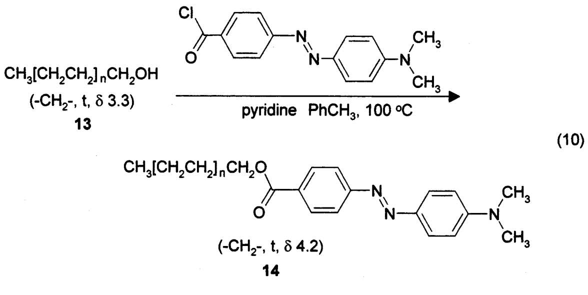
^1H NMR spectroscopic analysis of other ligands bound to terminal sites on polymers is equally feasible and makes monitoring the success of synthetic reactions easier. This has been illustrated in work with linear polyethylene-bound ligands and ligand precursors.[43] For example, when a polyethylene oligomer such as **13** with a terminal $-CH_2OH$ group was converted into a terminal acetate ester ($-CH_2OCOCH_3$) or into a phosphite ligand, a change in chemical shift of the characteristic triplet due to this hydroxymethyl group in the ^1H NMR spectrum at δ 3.3 provided a convenient way to follow the success of the reaction. In the example shown where an azo dye probe or ligand was attached to a polyethylene oligomer (eq 10), the $-CH_2OH$ methylene triplet at δ 3.3 shifted to δ 4.2 in **14**. The change in the methylene H's chemical shift, the absence of residual signals at δ 3.3, and the absence of other peaks that could have arisen from side reactions as well as the integration of the $-CH_3$ end group peak relative to the new $-CH_2O-$ and aryl C−H peaks provide conclusive evidence for the success of this reaction. In these examples, the polyethylene polymer support has a large background peak at δ 1.3. Fortunately this is a region of little interest in ^1H NMR spectroscopy. The ligand peaks show up downfield with a resolution like that of a low molecular weight compound as is the case with the catalyst **12**.



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NMR spectroscopic analyses of soluble polymeric ligands and catalysts can be limited by polymer solubility because even an oligomer support's solubility is dictated by the solubility characteristics of the polymer. In the case of a polyethylene oligomer, the ligands and subsequent catalysts are only soluble in hot solvents such as toluene-d_8 at 100 °C. This requirement for a 100 °C environment introduces some problems in analysis especially for catalysts that have dynamic behavior. For example, ligand exchange in polyethylene-bound catalysts such as **15** results in an averaged solution-state ^{31}P NMR spectrum. Dynamic behavior that averages an NMR signal in the low molecular weight analogue of **15** can be suppressed by using a lower temperature for the NMR analysis. In a polymer such as **15**, this option is precluded by the polymer's temperature-dependent solubility. As a result, dynamic behavior of this Wilkinson's catalyst analogue attached to a polyethylene oligomer can only be resolved by resorting to solid-state ^{31}P NMR spectroscopy.[44]

$[CH_3(CH_2CH_2)_nCH_2PPh_2]_3RhCl$

15

Soluble polymers with ligands and catalysts on pendant side chains are more common than soluble polymers with terminally bound ligands and catalysts. Fortunately, NMR analysis of soluble polymers with pendant side chains is also feasible. In this case, the main chain protons and carbons of the polymer encompass a broader chemical shift range and are more likely to complicate the NMR spectrum. Nonetheless, it is possible to get good ^1H and ^{13}C NMR spectra for pendant substrates, ligands, or catalysts on such polymers. If the substituents that are being added have ^1H NMR signals that do not overlap the polymer, solution-state quality spectra can be obtained when the substituent is attached with a short (e.g., 10-atom) tether. This is illustrated by the ^1H NMR spectrum shown in Figure 2a, which is a ^1H NMR spectrum of the vinyl group of an undecenylamide, **16**, on a soluble poly(*N*-isopropylacrylamide) (PNIPAM). The vinyl protons here have a line width of ca. 2 Hz, and the characteristic coupling pattern for the three protons of a vinyl group is easily discernible.[45]

B. ^{13}C NMR Spectroscopy

Solution-state ^{13}C NMR spectroscopy is also useful in following the course of reactions on soluble poly-

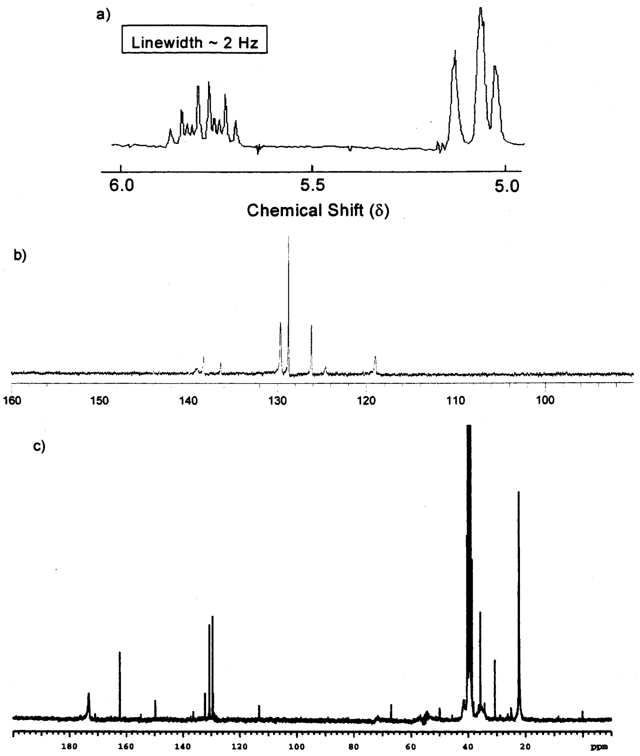
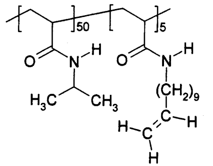


Figure 2. NMR spectra of pendant groups on soluble polymers: (a) a ^1H NMR spectrum of a poly(*N*-isopropylacrylamide)-bound 11-undecenylamine showing solution-like resolution for a vinyl group with a modestly sized spacer; (b) a ^{13}C NMR spectrum of a 1,3-thiophenylmethyl-substituted arene ligand on a poly(*N*-octadecylacrylamide) polymer showing eight distinct aryl carbons in the δ 110−150 range; (c) a ^{13}C NMR spectrum of an SCS−Pd(II) Heck catalyst on poly(*N*-isopropylacrylamide) showing the aryl carbons, the ispo carbon attached to Pd (δ 150), and larger peaks upfield due to the polymer and spacer.

mers. This is illustrated with the spectra in Figure 2b,c. These spectra of the poly(*N*-octadecylacrylamide)-bound 1,3-bis(thioarylmethyl)arene ligand **17**[46] and a similar poly(*N*-isopropylacrylamide)-bound SCS−Pd(II) Heck catalyst, **18**, show that quaternary carbons of a relatively lightly loaded (10 mol %) soluble polymer still are easily detectable. These polymers have also been characterized as solids by CP-MAS solid-state NMR spectroscopy. However, the solution-state spectra are more readily obtained and provide a direct comparison to low molecular weight compounds.



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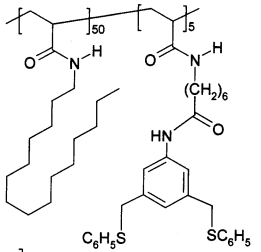

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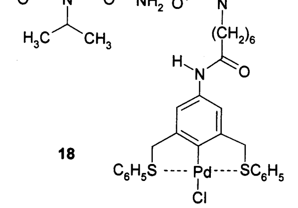

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Table 1. T_1 Relaxation Times for Methyl Groups on Pendant Chains of Soluble Polyacrylamides

molecule	T_1 (s)
hexylamine	6.8 ± 0.4
octadecylamine	4.6 ± 0.7
poly(*N*-isopropylacrylamide)	0.4 ± 0.1
poly(*N*-isopropylacrylamide)-*co*-poly(*N*-hexylacrylamide)	2.7 ± 0.8
poly(*N*-isopropylacrylamide)-*co*-poly(*N*-octadecylacrylamide)	4.1 ± 0.7

C. Relaxation Time Effects

Several studies have shown how soluble and insoluble polymers affect relaxation times of bound groups and how metal complexation affects ^{31}P NMR signals.[44,47,48] In the case of soluble polymers, such effects have been studied both with terminally functionalized polymers and with polymers containing catalysts or ligands as pendant groups (e.g., polyacrylamides).

In the case of a soluble poly(ethyldiphenylphosphine), T_1 values for phosphorus of the oligomeric phosphine **19** were similar to those of an electronically equivalent octadecyldiphenylphosphine, **20**, under the same conditions (3 and 9 s, respectively).[44] T_1 values for phosphines in soluble, insoluble, and low molecular weight ligands were also studied by Stille.[48] Stille's work showed that a soluble polystyrene-bound DIOP ligand (e.g., **4**) and a DVB-cross-linked-polystyrene-bound DIOP ligand had similar T_1 values for the phosphines in the DIOP groups, values that were an order of magnitude smaller than for the phosphines in DIOP itself. Stille's work did agree with studies of **19** in that T_1 values were generally larger for a soluble polymer-bound phosphine than for an insoluble polymer-bound phosphine.

$H_3C\text{-}[CH_2\text{-}CH_2]_{150}\text{-}CH_2PPh_2$ **19**

$H_3C\text{-}[CH_2\text{-}CH_2]_{8}\text{-}CH_2PPh_2$ **20**

T_1 relaxation times of the terminal carbon of the pendant *N*-alkyl isopropyl group of the *N*-isopropylacrylamide (NIPAM) and of methyl groups of the side chains of poly(*N*-isopropylacrylamide)-*co*-poly(*N*-hexylacrylamide) or poly(*N*-isopropylacrylamide)-*co*-poly(*N*-octadecylacrylamide) measured for solutions of these polymers in $CDCl_3$ at ambient temperature are listed in Table 1. This work and earlier work by Bayer and Fyfe suggest that the apparent differences in studies of **19** and in relaxation times seen for polystyrene-bound DIOP ligands in Stille's work are a result of the flexibility of pendant groups on a soluble (or insoluble) polymer. NMR studies of relaxation in methyl groups on polyacrylamides show that the methyl substituents on a polymer can have shorter T_1 relaxation times than analogous small molecules (Table 1). However, if a suitable spacer group is present, there is no measurable difference in the T_1 relaxation time as can be seen if one

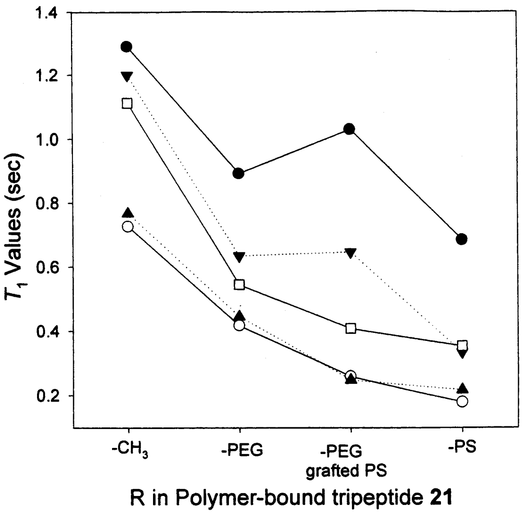
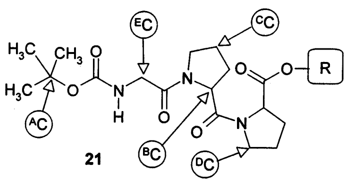


Figure 3. T_1 values for five selected carbons in a BOC-protected tripeptide, **21**, attached to various polymer supports (R = $-CH_3$, PEG, PEG−PS, or PS): ●, ^{A}C in **21**; ▼, ^{B}C in **21**; □, ^{C}C in **21**; ▲, ^{D}C in **21**; ○, ^{E}C in **21**.

compares T_1 values for the $-CH_3$ group of the free and polymer-bound octadecylamine.[45]

The results in Table 1 and for polymers **19** and **20** are similar to earlier results that directly compared T_1 values for low molecular weight compounds, a soluble PEG support, a DVB-cross-linked polystyrene with a PEG graft, and a DVB-cross-linked polystyrene (**21**; R = $-CH_3$, $-(CH_2CH_2O)_nCH_3$, PEG−polystyrene, and polystyrene, respectively).[49] The effect of these different polymers or a simple methyl group on T_1 values for the various carbons of the tripeptide **21** are illustrated in Figure 3.



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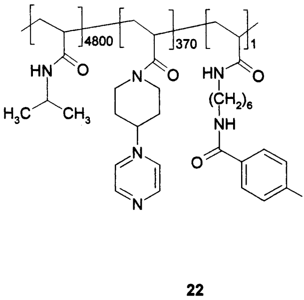
D. UV−Vis, Fluorescence, and IR Spectroscopic Studies of Soluble Polymer-Bound Ligands and Catalysts

UV−vis or fluorescence analyses of polymers with UV−vis or fluorescence spectroscopic labels is also feasible. For example, solutions of polymer **14** or of polymers such as **22** or **23** can be studied to determine the concentration of the polymer. Such dyes also provide information about solvation when the absorption maximum or emission maximum of a polymer-bound dye or fluorophore is sensitive to solvent polarity.



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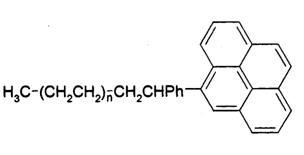

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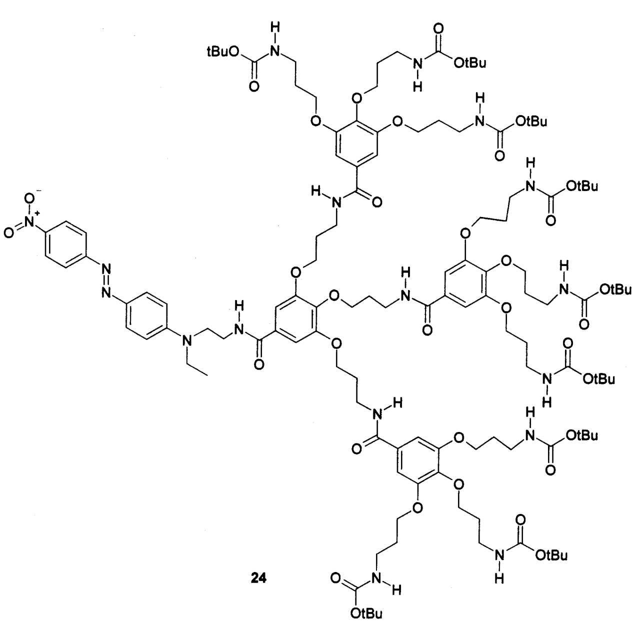
Dye-labeled soluble polymers also have other advantages. This is illustrated by recent work with **22, 23**, **27**, and **28**.[50] In the case of **22**, the extent of recovery of the organic base catalyst, a dimethylaminopyridine analogue, is easy to assay because of the presence of a small amount of dye label. A similar approach reported recently used a colored dendrimer, **24**, that was used to bind substrates and which also monitored polymer recovery.[51] In both cases, a simple colorimetric assay is facilitated by the presence of an azo dye chromophore in the soluble polymer or dendrimer. Recent work by our group has also shown that chromophoric catalyst ligands such as the azo dye ligand in **27** and **28** have additional functionality.[50] Not only does the dye label in **27** or **28** prepared in eq 11 provide a probe of where the polymer and catalyst is during recovery of the polymer and catalyst, it also provides evidence about catalyst stability. The metalated polymers **27** and **28** exhibit a pronounced bathochromic shift in their visible spectrum vis-à-vis the precursor nonmetalated poly-



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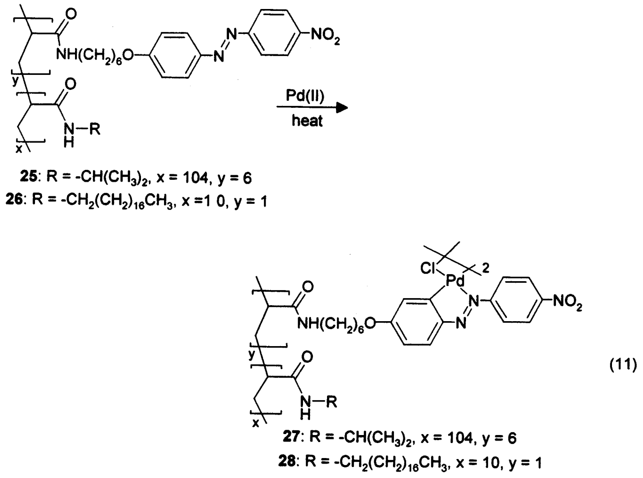


25: R = -CH(CH$_3$)$_2$, x = 104, y = 6
26: R = -CH$_2$(CH$_2$)$_{16}$CH$_3$, x =1 0, y = 1

(11)

27: R = -CH(CH$_3$)$_2$, x = 104, y = 6
28: R = -CH$_2$(CH$_2$)$_{16}$CH$_3$, x = 10, y = 1

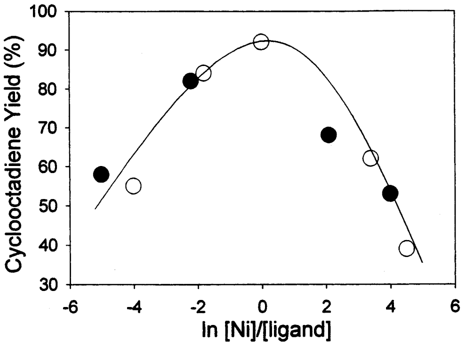


Figure 4. Selectivity in butadiene cyclodimerization to form 1,5-cyclooctadiene as a function of the ratio of a polyethylene-bound phenyl bis(2-methylphenyl) phosphite ligand to Ni (○) or as a function of the ratio of nonadecylphenyl bis(2-methylphenyl) phosphite to Ni (●).

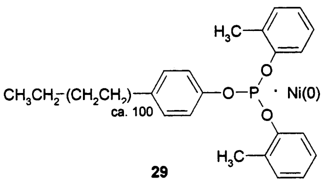
meric dyes **25** and **26**, and the loss of Pd from this azo ligand leads to changes in the UV spectrum of **27** and **28** that signal catalyst decomposition has occurred.

IR analysis of metal carbonyls on both soluble polymers is another useful analytical tool.[20,34] IR spectroscopy has also been useful with insoluble polymers. Such spectroscopic studies have the advantage that they can simply discern the coordination environment of a polymer-bound metal complex. IR spectroscopy can also be useful in analyzing catalysts after a reaction to determine catalyst stability and recyclability, especially in the case of metal carbonyl catalysts.

IV. General Features of Soluble Polymer-Supported Catalyst Activity

Soluble polymer-bound catalysts can be designed to have activity equivalent to that of their low molecular weight analogues. This is especially true for catalysts attached at the terminus of a linear polymer in a good solvent. Through the use of suitable spacer groups, catalysts attached to pendent chains too can have essentially the same reactivity as their low molecular weight counterparts.

A comparison of the selectivity of nickel(0) diene cyclooligomerization catalysts ligated by hindered triaryl phosphite ligands attached to the termini of polyethylene oligomers (**29**) to that of similar catalysts ligated by low molecular weight ligands (**30**) shows how similar polymer-bound and low molecular weight catalysts can be.[52] These results, illustrated in Figure 4, show the similarity in selectivity that can be achieved with a soluble polymer-bound catalyst with a wide variation in the relative amounts of ligand and metal.



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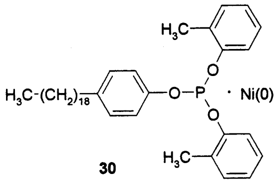

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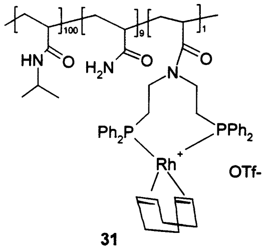
Pendant-chain-bound catalysts, especially when they contain a short spacer, can also have reactivity like that of their low molecular weight analogues. However, while soluble polymer-bound catalysts can have activities identical to those of their electronically similar low molecular weight analogues, the properties of a polymer can affect catalyst activity. Such effects were seen in early studies of asymmetric catalysis by polystyrene−DIOP−Rh(I) complexes.[21] Sometimes these effects arise because the random coil of a high molecular weight polymer can behave like a solvent or cosolvent.[34] For example, our work has shown that cationic Rh(I) hydrogenation catalysts attached to a polymer polyacrylamide polymer have activities that are lower than those of their low molecular weight analogues. This lower activity for a catalyst such as **31** was attributed to solvation of and coordination to the Rh(I) centers by amides of the polymer. Evidence for this effect is seen in experiments where **32**, a low molecular weight analogue of **31** used in the presence of PNIPAM, had a lower turnover frequency (TOF) in allyl alcohol hydrogenation.[44] Slightly lower activity in a PNIPAM organic catalyst was also noted in our recent study of PNIPAM-bound dimethylaminopyridine analogues.[50] A slight effect of the polymer on the reactivity of a terminal catalyst was also noted in our work on the asymmetric C−H insertion reaction using a polyethylene-bound Rh(II) catalyst, **33**.[53]



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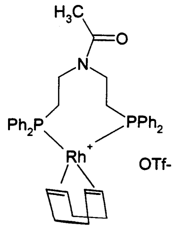

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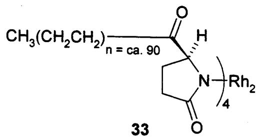

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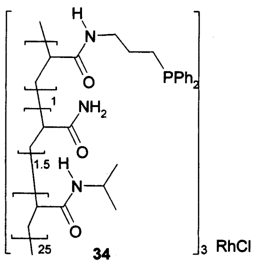
While the polyamide support in **31** decreased TOF values for allyl alcohol hydrogenation, a neutral Rh(I) catalyst, **34**, was unaffected by the polymer.[45] At 25 °C, the TOF values for hydrogenation of allyl alcohol by the low molecular weight catalyst **35** in the presence or absence of added poly(*N*-isopropylacrylamide) were 2.7 and 2.6 mol of H_2/(mol of Rh h), respectively. These values are essentially the same as the TOF for the same hydrogenation using



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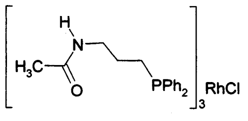

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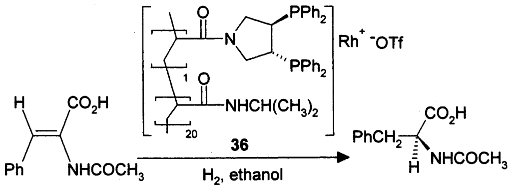
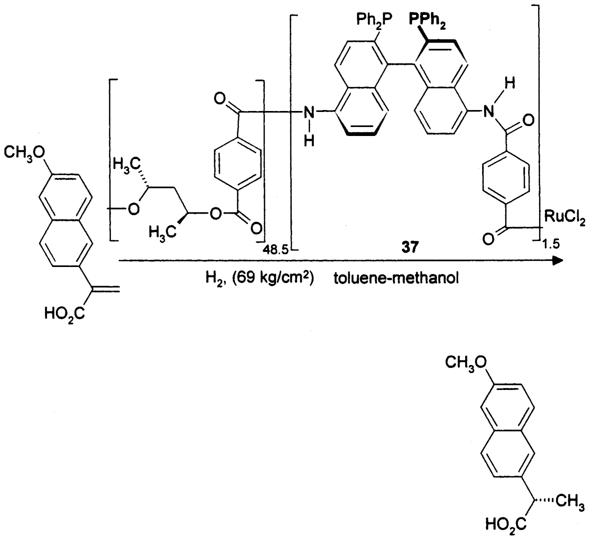
the poly(*N*-isopropylacrylamide)-bound neutral Rh(I) catalyst **34** (2.2 mol of H_2/(mol of Rh h)).

It is important to note that a soluble polymer does not always have a negative effect on catalyst selectivity even if the polymer may affect catalyst reactivity. The amides of the polymer support in the soluble poly(*N*-isopropylacrylamide)-bound chiral Rh(I) catalyst **36**, for example, have essentially no effect or a minimal effect on the percent ee in an asymmetric hydrogenation such as eq 12 where the phenylalanine product was obtained in 88% ee with a poly(*N*-isopropylacrylamide)-bound chiral hydrogenation catalyst.[54]



(12)

Soluble polymers whose main chain contains chiral catalyst ligands have also been studied, and their reactivity too can be compared to that of low molecular weight catalysts. For example, Chan has described an asymmetric hydrogenation catalyst prepared using the copolymer **37** derived from an axially chiral 5,5′-diamino-BINAP (BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) ligand, a chiral diol, and terephthalic acid.[55] The 90+% ee values seen with this catalyst in the hydrogenation shown in eq 13 are excellent and comparable to what would be obtained with a low molecular weigh Ru−BINAP catalyst.



(13)

V. Strategies for Separation and Recovery of Soluble Polymer-Bound Ligands and Catalysts

Separation schemes for recovering a soluble polymer-bound catalyst or ligand, separating it from the product, and reusing it are primarily based on gas/liquid, liquid/solid, or liquid/liquid separation techniques (Figure 5).

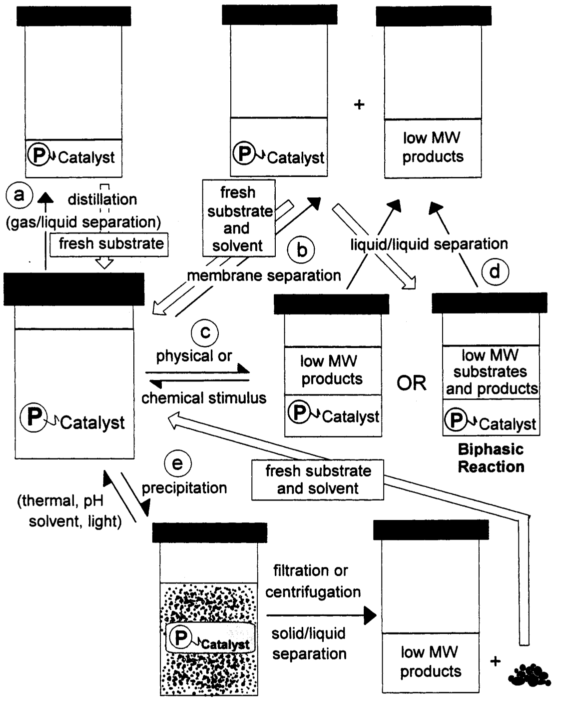


Figure 5. General schemes for separation, recovery, and reuse of soluble polymer-bound catalysts: (a) gas/liquid separation of products by distillation; (b) separation of low molecular weight products from a high molecular weight soluble polymer-bound catalyst and ligand using a semipermeable membrane; (c) use of a physical or chemical stimulus to induce formation of two immiscible liquid phases that are subsequently separated so as to separate products from a solution of a soluble polymer-bound catalyst and ligand; (d) use of a reaction mixture that is always biphasic, with the catalysts residing in a phase different from that in which the substrates/products reside; (e) use of a physical change, a chemical reaction, or a solvent change to induce formation of a precipitate of a polymer-bound catalyst and ligand followed by a solid/liquid separation using centrifugation or filtration to isolate a reusable catalyst.

Distillation (Figure 5a) is a simple and effective procedure. It is generally applicable to many sorts of catalytic reactions. Polymeric ligands are not necessary in this case, and such separations are equally effective with ordinary homogeneous catalysts. A potential problem with gas/liquid separations is catalyst or ligand thermal instability.

Macromolecules can also be separated from low molecular weight components on the basis of size. Membrane filtration (Figure 5b) provides a useful liquid/liquid separation technique that was used in some of the earliest work using soluble polymer-bound catalysts.[15] Semipermeable membranes have a long history in macromolecular chemistry and are ubiquitously used in separations of biomacromolecules from low molecular weight species.[37,56] Such techniques are particularly well adapted to separation of dendrimer-bound catalysts because of the globular structure of these hyperbranched polymers. Membrane systems also offer an engineering advantage in that they can be designed so that catalysts can be used in continuous reactions, a possible process advantage over other separations that depend on using catalysts in batch-type processes.[37,56,57]

Liquid/liquid separations (Figure 5c) that are based on the selective solubility of a polymer in one phase of a biphasic mixture can also be used to recover soluble polymer-bound catalysts and ligands. For example, fluorinated polymers that have selective solubility in a fluorous phase of a biphasic organic/fluorocarbon system can be designed to recover and reuse catalysts. In this case, the system would be biphasic throughout the process. Alternatively, it is possible to design polymers that have thermomorphic phase-selective solubility in either a polar or nonpolar phase of a biphasic system.[46,58−60] If an appropriate solvent system were then chosen, a soluble polymer-bound catalyst or ligand could be used under monophasic conditions (e.g., at elevated temperature). If, after reaction, this miscible mixed solvent system were perturbed (e.g., by cooling), a biphasic mixture could re-form. Then liquid/liquid separation could be used to recover the catalyst and separate it from the products. Examples of such liquid/liquid separations with acrylates, polar acrylamides, and nonpolar acrylamides are all described below.

Precipitation of a polymeric ligand or polymeric catalyst (Figure 5d) followed by a filtration or some other sort of liquid/solid separation is the most common separation scheme used with soluble polymer-bound catalysts. The way in which a soluble polymer-bound catalyst is precipitated can vary. Precipitation of a soluble polymer can almost always be accomplished by the addition of an excess of a poor solvent. Alternatively, if the soluble polymer is amphoteric, precipitation can be achieved by protonation or deprotonation. Soluble polymers that precipitate on cooling can also be used and recovered by filtration or centrifugation. Finally, there are examples where soluble polymers have inverse temperature-dependent solubility. In these latter cases, increasing temperatures can be used to precipitate a soluble polymer-bound catalyst. Examples of each of these sorts of separations are discussed below.

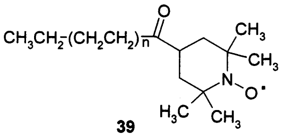
A. Solid/Liquid Separations of Polyethylene-Bound Catalysts

Polymers can have profound temperature-dependent solubility. Polyethylene is a common example of a polymer with strong temperature-dependent solubility. Even in what would be considered a “good” solvent, polyethylene has no detectable solubility at room temperature. However, on heating, polyethylene readily dissolves to form solutions that can contain as much as 1 g of polymer/10 mL of solvent. Such concentrations of polymer are much more than sufficient to provide a platform for a catalyst support since 0.4 mmol of catalyst/g of polyethylene is a loading that can readily be achieved. For example, solutions of the polyethylene-bound diphenylphosphine-ligated Rh(I) hydrogenation catalyst **15** in toluene could be prepared such that the catalyst concentration was >10^{-2} M at 100 °C.[44]

Our group was the first to take advantage of the temperature-dependent solubility of polyethylene in designing recoverable but soluble polymer supports for catalysts. The examples below show that polyethylene oligomers are effective and general supports for ligands and catalysts. The necessary functional oligomers are available by anionic polymerization of ethylene.[43] While such anionic polymerization does not lead to polymers with good materials properties, the oligomeric ligands that derive from the synthesis shown in eqs 14 and 15 have chemistry that is equivalent to that of their low molecular weight octadecyl or nonadecyl analogues. As noted above, multistep syntheses such as those in eqs 14 or 15 can be followed by ^{1}H NMR spectroscopy since the end group concentration is relatively high for ethylene oligomers such as these ($n \leq 200$) in hot deuterated toluene. Studies with dye-labeled polyethylene oligomers **14**, spin-labeled polyethylene oligomers **39**, and pyrene-labeled polyethylene oligomers **23** verified that these materials are soluble in hot solvent but have no detectable solubility in any solvent at room temperature. The lack of room-temperature solubility in these spectroscopically labeled polymers, in the phosphine and phosphite ligands **19**, **29**, and **38** above, and in catalysts attached to these polymers is a direct consequence of the solubility characteristics of the polyethylene portion of this polymer. In these cases, the terminally functionalized polyolefin functions as a solubility handle in much the same way as the poly(ethylene oxide) polymers used early on by Bayer served as solubility handles for catalysts and amino acids.[16] The anionic oligomerizations used to prepare these polyethylene oligomer ligands are suitable for synthesis of small quantities (<10 g) of the necessary polymers. More recent chemistry including living polymerization of ylides and functionalization of vinyl-terminated ethylene or propylene oligomers yields more monodisperse oligomers that would be an alternative more economic route to larger quantities of the necessary end-functionalized polyolefins.[61,62]

$$H_2C{=}CH_2 \xrightarrow[\text{TMEDA}]{\text{BuLi}} CH_3CH_2(CH_2CH_2)_nLi \xrightarrow{ClPPh_2} \underset{\textbf{19}}{CH_3CH_2(CH_2CH_2)_nPPh_2} \qquad (14)$$

$$CH_3CH_2(CH_2CH_2)_nLi \xrightarrow[2.\ H_3O^+]{1.\ CO_2} CH_3CH_2(CH_2CH_2)_nCO_2H \xrightarrow[2.\ \text{BuLi}]{1.\ BH_3\text{-}S(CH_3)_2} \qquad (15)$$
$$\xrightarrow{P(OAr)_3} \underset{\textbf{38}}{CH_3CH_2(CH_2CH_2)_nCH_2OP(OAr)_2}$$



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Many sorts of catalysts have been attached to polyethylene polymers by a number of groups. Examples are listed in Table 2. In all cases, the catalysts dissolve in a solvent suitable for polyethylene at elevated temperature. However, while such catalysts are homogeneous at elevated temperature, all such catalysts are completely insoluble at room temperature. The general scheme used in catalysis and catalyst recovery with the polyethylene-bound catalysts and ligands listed in Table 2 is illustrated in Figure 6. Typically, the catalyst is used homogeneously in a suitable solvent at high temperature and recovered by filtration or centrifugation as a solid polyethylene powder at room temperature. In these examples, the polyethylene ligands selectively pre-

Table 2. Polyethylene-Bound Transition-Metal Catalysts Used Homogeneously and Recovered at Room Temperature by a Solid/Liquid Separation[a]

reaction	catalyst	recovery (%)
alkene hydrogenation[44]	L_3RhCl	>99.9
alkene hydroformylation[63,64]	$L_2Rh(CO)Cl$	>99.9
allylic acetate substitution[65]	L_4Pd	>99.98
alkene cyclopropanation[66]	$[(LCO_2)_2Rh]_2$	>99.9
asymmetric cyclopropanation/CH insertion[53]	$[(LCO_2)_2Rh]_2$	
alcohol carbonylation[67]	L_2PdX_2	>99.98
butadiene polymerization[68]	$(LCO_2)_3Nd$	>99.98
butadiene cyclodimerization/cyclotrimerization[52]	$LC_6H_4OP(OAr)_2Ni$	>99.99
primary alcohol oxidation[69]	$(LCO_2)Ru_6{}^+LCO_2{}^-$	>99.9
tin halide reductions[70]	$LSn(C_4H_9)_2Cl$	
ATRP polymerizations[71−73]	LCu	
Kharasch reactions[74]	L_3RuCl_2	
alkyne carboxylations[75]	L_3RuCl_2	
butadiene dimerization[65]	L_2PdX_2	>99.98
multistep oxidation/reduction[76]	L_3RhCl/cross-linked PVP−$Cr_6{}^+$	
phase-transfer catalysis[77,78]	$LXR_3{}^+$ (X = N, P (or crown ether))	

[a] L is a polyethylene-oligomer-bound ligand.

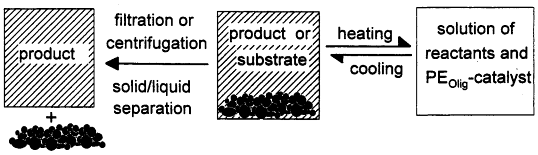
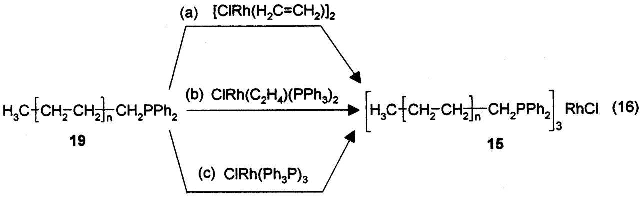


Figure 6. Scheme used with polyethylene-ligated catalysts that are homogeneous in a hot solution of substrate and that are insoluble and separable from a room-temperature solution of products.

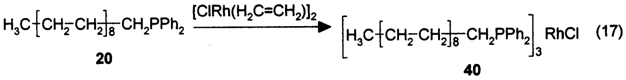
cipitate. The precipitates that form include all polyethylene-containing species. However, these semicrystalline solids do not entrain extraneous materials, so products or starting materials that are not associated with a polyethylene oligomer do not contaminate the recovered catalyst.

1. Rhodium(I) Hydrogenation Catalysts on Polyethylene Supports

Rh(I) hydrogenation was one of the first reactions studied for a polyethylene-bound catalyst.[44] In this case, direct comparisons were made between the activity and selectivity of this soluble polymer-bound catalyst **15**, its low molecular weight analogue $(C_{18}H_{37}PPh_2)_3RhCl$, **40**, and an insoluble DVB-cross-linked polystyrene-bound catalyst. The polyethylene-bound catalyst **15** was prepared from a diphenylphosphine-terminated polyethylene oligomer using one of three processes (eqs 16a−c)—phosphine ligand exchange



with Wilkinson's catalyst, phosphination of a chlororhodium ethylene dimer, or exchange of polyethylenediphenylphosphine for phosphine and ethylene ligands in a monomeric catalyst. Each route generated an equivalent catalyst. Solution-state ^{31}P NMR spectroscopy showed that no triphenylphosphine was present after the catalyst had been recycled several times, a result predicted by the expected favorable entropy for polymer−rhodium complexation.[69,79] The use of $[ClRh(H_2C{=}CH_2)]_2$ (eq 16a) was deemed to be the best synthesis procedure for this catalyst, and this route was used to prepare the low molecular weight analogue **40** (eq 17).



$$\underset{\mathbf{20}}{H_3C{-}[CH_2{-}CH_2]_8{-}CH_2PPh_2} \xrightarrow{[ClRh(H_2C=CH_2)]_2} \underset{\mathbf{40}}{[H_3C{-}[CH_2{-}CH_2]_8{-}CH_2PPh_2]_3RhCl} \quad (17)$$

The $(CH_3CH_2(CH_2CH_2)_{ca.\ 100}CH_2CH_2PPh_2)_3RhCl$ so prepared was an order of magnitude more reactive than a commercially available insoluble polystyrene-bound catalyst.[44] It was about as active as its octadecyl analogue, typically having 80% of the activity of the octadecyldiphenylphosphine-ligated catalyst. The polyethylene-bound catalyst could be reused multiple times. Recycling experiments showed that the catalyst could be used up to 18 times with no significant loss in activity. Recycling in these cases used the protocol shown in Figure 6, with the polyethylene-bound catalysts typically being recovered by filtration.

These polyethylene-bound catalysts were characterized by NMR spectroscopy as described above. The reactivity of these catalysts with various alkenes was also compared in kinetic studies. The relative reactivity with mono-, di-, and trisubstituted alkenes and toward a larger alkene was comparable to that of a low molecular weight electronically equivalent Rh catalyst, $(C_{18}H_{37}PPh_2)_3RhCl$ (**40**). "Used" catalyst was examined spectroscopically (^{31}P NMR at elevated temperature) and was found to be equivalent to "fresh" catalyst. The only change after multiple recycle/recovery experiments was a small (ca. 10%) increase in the intensity of the phosphine oxide peak.

The extent of recovery of the polymeric ligand (and catalyst) in this reaction was estimated to be >99.9% on the basis of earlier results with analogous polymers that contained spectroscopic labels. Analysis of the filtrate for Rh by inductively coupled plasma analysis confirmed this estimate and showed that there was no detectable rhodium in the filtrate. This corresponded to loss of <0.1% of the charged rhodium catalyst. These quantitative measures of rhodium recovery were in agreement with estimates of catalyst recovery based on persistent activity in the recycling experiments.

a. Three-Phase Test of Catalyst Stability. An important issue in recycling catalysts is catalyst stability. A concern with hydrogenation catalysts is the possible formation of colloidal metal.[24] Earlier and continuing reports describe many examples of polymer-ligated metal colloids that are active hydrogenation catalysts.[80−83] In the case of the polyethylene-bound Rh(I) hydrogenation catalyst a three-phase test was used to test for the formation and presence of rhodium metal colloids and, indirectly, to test catalyst stability.[84] In this case, a 2% DVB-cross-linked polystyrene was modified to contain a styrene group. Then this insoluble alkene substrate was treated with H_2 and either with the polyethylene-bound Rh(I) catalyst **15** or with $(C_{18}H_{37}PPh_2)_3RhCl$. Both catalysts reduced the alkene on the polymer. Both fresh and used polyethylene-bound catalysts were measurably less reactive than the low molecular weight catalyst, but this relative difference in reactivity is expected since a macroscopic substrate is being reduced by a polymeric catalyst. Similar effects of solvent and polymer size in reactivity have been seen previously.[85]

b. Simultaneous Multistep Oxidation/Reduction Using a Polyethylene-Bound Rhodium(I) Hydrogenation Catalyst. The use of polymeric systems to achieve site isolation has been recognized in many contexts.[86] The role of site isolation in carrying out multistep reactions with insoluble polymers was recognized early on as a promising aspect of polymer-supported chemistry that was not feasible in solution-phase synthesis.[87] Soluble polymers also lend themselves to such chemistry. It is well-known that mixing of polymers with one another is often energetically unfavorable. This is especially true if the polymers have very different characters. For example, a nonpolar polymer such as polyethylene is unlikely to be miscible or compatible with a polar polymer.

The incompatibility of polyethylene with polar polymers was used to advantage using polyethylene-bound catalysts and oxidation reagents on polar ion exchange polymers to design a multistep simultaneous oxidation/reduction procedure.[76] In this multistep reaction scheme (Figure 7), the polyethylene-bound Rh(I) hydrogenation catalyst and phosphine ligand were used in the presence of an insoluble poly(vinylpyridinium chlorochromate) (PVPCC) reagent. Both the Rh(I) and the phosphine are always associated with a poly(vinylpyridinium)-incompatible polyethylene oligomer and are thus kinetically isolated from this insoluble polymer-bound oxidant. Control experiments with $ClRh(PPh_3)_3$ showed that this low molecular weight catalyst was decomposed by this same PVPCC oxidant. With $ClRh(PPh_3)_3$, no hydrogen uptake occurred and the phosphine ligands were shown to have been oxidized to form triphenylphosphine oxide. Since the penultimate reductant, H_2, is kinetically inactive with the poly(vinylpyridinium chlorochromate) oxidant, this mixed phase system consisting of **15** and PVPCC could be used to carry out a simultaneous oxidation/reduction (eq 18). After the reaction, filtration of the hot solution separated the solution containing product and polyethylene-oligomer-bound ligand and catalyst from the insoluble oxidant. Cooling and filtration or centrifugation then separated the recyclable polyethylene-bound catalyst from the aldehyde product.

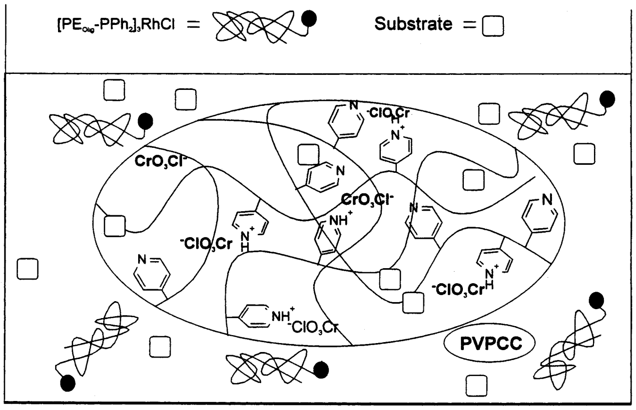
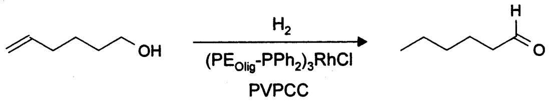


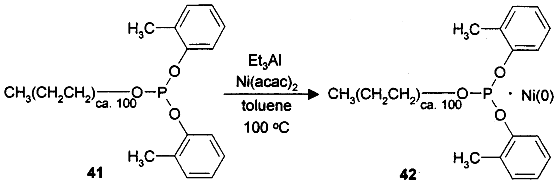
Figure 7. Simultaneous use of a recoverable polyethylene-bound Rh(I) hydrogenation catalyst containing a polyethylene-bound phosphine, **19**, with an insoluble, poly(vinylpyridinium)-bound Cr(VI) oxidant.



(18)

2. Polyethylene-Bound Nickel(0) Diene Cyclooligomerization Catalysts

The separation and reuse of soluble polyethylene-bound diaryl phosphite or polyethylene-bound phenyl diaryl phosphite to ligate nickel(0) diene oligomerization catalysts provided an early illustration of the utility of polyethylene ligands to recover active homogeneous catalysts whose activity mirrored that of low molecular weight analogues.[52] In these recycling experiments, a solution of the nickel(0) polyethylene phosphite catalyst was prepared by in situ formation of a Ni(0) catalyst from a mixture of the polyethylene ligand, $Ni(acac)_2$, and triethylaluminum. The amber-colored solution so prepared was visually homogeneous. Catalysts such as **29** or **42** formed in this way (eq 19) converted butadiene to cyclooligomerization products in 3−5 h at 100 °C in toluene. Cooling typically produced a light yellow polyethylene solid and a clear toluene solution of product. Centrifugation or filtration avoiding oxygen exposure produced a product solution and a solid polyethylene-bound catalyst that could be reused without triethylaluminum activation. Up to three cycles were carried out. Analysis of the product solution from the second cycle after catalyst precipi-



(19)

tation using inductively coupled plasma analysis showed that <0.01% of the charged nickel catalyst had been leached. This corresponded to a <5 ppb concentration of Ni in the product solution. Experiments analyzing for nickel in control experiments where no nickel catalyst was present show that this level of Ni corresponded to the minimum detectable level of Ni under these conditions.

Catalyst and ligand integrity is a general concern and proved to be problematic in the case of these Ni(0)-catalyzed diene oligomerizations. Catalyst stability was initially tested simply by monitoring catalyst reactivity in the recycled catalyst. A slight decrease in activity through three cycles indicated some loss of catalyst or catalyst decomposition. The absence of leached nickel suggested that the observed gradual decrease in catalyst effectiveness was not due to catalyst leaching. Subsequent experiments heating the polyethylene-bound catalysts in the absence of substrate suggested that phosphite ligands such as **41** were not as thermally stable under our reaction conditions as desired. Indeed, heating the polyethyl diaryl phosphite **41** in toluene for extended periods showed that irreversible changes in the ligand occurred on the basis of ^{31}P NMR spectroscopy. Such changes included the formation of some phosphonate and formation of a trialkyl phosphite. The nickel catalysts too are very reactive. Such catalysts could decompose by adventitious oxidation in the repetitive recovery and recycling oxidations. The lability of these nickel complexes to oxygen and moisture impurities had been established previously.[88]

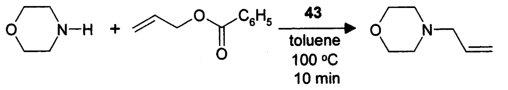
As noted above, these polyethylene-bound Ni(0) catalysts have reactivity that is essentially the same as that of their electronically similar octadecyl analogues (Figure 4). Product selectivity maps show that this similarity in activity is maintained for wide variations in the ratio of ligand to nickel. However, only at ligand:metal ratios that are >1:1 is catalyst recovery and reuse practical. Unlike the case where the polyethyl diaryl phosphite-ligated catalyst is used, catalysts in reactions using the octadecyl diaryl phosphite-ligated catalyst cannot be recycled.

3. Polyethylene-Bound Palladium(0) Catalysts

Diphenylphosphine-terminated polyethylene oligomers have been used with a variety of Pd(0) and Pd(II) catalysts to prepare allylic substitution,[65] diene dimerization,[65] and carbonylation catalysts[64,67] that can be successfully recovered and reused using the protocol in Figure 6. Such recycling was most extensively studied with the Pd(0) catalyst prepared using the exchange reaction in eq 20. This preparative reaction worked very well. Heating a 4:1 (mol/mol) ratio of the $PE_{Olig}PPh_2$ with the yellow-orange solution of the triphenylphosphine-ligated Pd(0) formed a yellow-orange solution that in turn formed a light yellow precipitate and a colorless solution on cooling to room temperature. The resulting polyethylene powder had a faint yellow color. This precipitation process was quantitative. No polyethylene ligand remained in solution.

$$\underset{\mathbf{19}}{CH_3CH_2(CH_2CH_2)_nPPh_2} + (Ph_3P)_4Pd \rightleftharpoons \underset{\mathbf{43}}{(CH_3CH_2(CH_2CH_2)_nPPh_2)_{4-n}Pd(PPh_3)_n} + PPh_3 \quad (20)$$

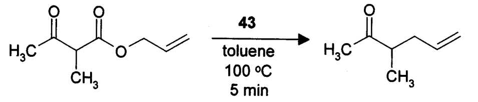
When the initially formed polyethylene-bound catalyst **43** was allowed to react with an allyl ester such as allyl benzoate and a secondary amine such as morpholine or piperidine, a quantitative conversion of the allylic ester into an allylic amine occurred in 10 min at 100 °C in toluene (eq 21). Cooling precipitated the polyethylene catalyst, and the precipitate was isolated by centrifugation. Centrifugation was used instead of filtration to separate the catalyst from the product solution to minimize possible oxygen exposure of this oxygen-sensitive catalyst. The catalyst isolated in this fashion could be reused through 10 cycles in reaction 21 with no diminution in activity. ICP analysis of the filtrate after the first reaction showed no detectable Pd in comparison to a blank. The estimated loss of palladium to solution was <0.001% of the charged palladium.



(21)

Polyethylene ligands were also successfully used with Pd/C catalysts to prepare in situ catalysts that mimic the reactivity of $(Ph_3P)_4Pd$ in allylic substitution chemistry.[83,89−91] While the identity of the catalyst in these experiments is not clear, the $PE_{Olig}PPh_2$ ligand functions at elevated temperature with the Pd/C catalyst and the mixture of Pd/C and polyethylene ligand can be recovered by filtration and reused as long as adventitious oxidation of the $PE_{Olig}PPh_2$ by oxygen is avoided.

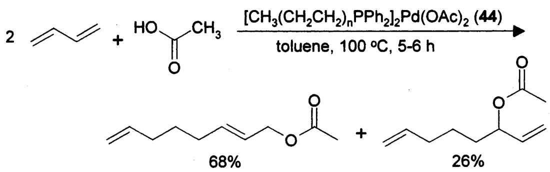
The polyethylene-ligated Pd(0) catalyst **43** was also successfully used and recycled in 10 cycles of a decarboxylative allylic substitution (eq 22) using a variety of substituted acetoacetic acid allyl esters. Typical catalyst loadings were 2 mol %. However, since the reaction was complete within 5 min, these loadings could be reduced significantly.



(22)

4. Polyethylene-Bound Palladium(II) Catalysts

Pd(II) catalysts ligated by polyethylene can be successfully prepared and recycled too. In this case, $Pd(OAc)_2$ was first added to a reactor. Then 2 equiv of $PE_{Olig}PPh_2$ was added. Heating the resulting mixture to 100 °C formed the catalyst **44**, which was successfully used through five cycles in dimerization of butadiene to form a mixture of allylic acetates (eq 23).[65] Recycling and recovery of **44** was possible after



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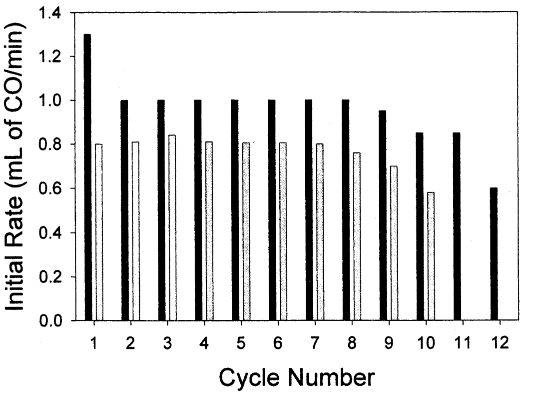
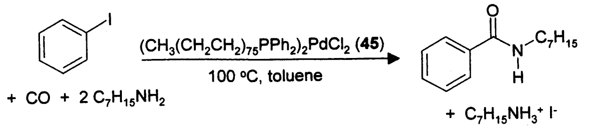


Figure 8. Recovery of catalyst **45** as a stoichiometric polyethylenediphenylphosphine−Pd(II) complex (black bars) or in the presence of excess polyethylenediphenylphosphine ligand (gray bars) in iodobenzene carboxamidation (eq 24).

cooling using centrifugation to separate **44** from the allyl ester product mixture.

The Kharkhanov group at Moscow State University also used polyethylene-complexed Pd(II) catalysts in carbonylation chemistry (eq 24).[64,67] The necessary Pd(II) catalyst ligated by an oligomeric phosphine was obtained by heating $Cl_2Pd(PPh_3)_2$ with a stoichiometric quantity of the oligomeric phosphine ligand **19** at 100 °C in toluene. The oligomeric catalyst was then separated from triphenylphosphine and any uncomplexed catalysts by cooling and filtration.

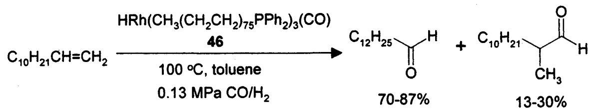


(24)

When a stoichiometric amount of the oligomeric phosphine (relative to Pd) was used in aryl iodide carbonylations (eq 24), the catalyst **45** was about 60% as active as $Cl_2Pd(PPh_3)_2$. This activity was maintained for 11 runs with a gradual decrease in catalyst activity in cycles 10−12 (Figure 8). The decrease in catalyst activity was attributed to inadvertent phosphine ligand oxidation. In accord with this suggestion, the authors noted that a catalyst mixture that was prepared using excess phosphine ligand **19** was slightly less active than the complex prepared with stoichiometric amounts of the oligomeric phosphine ligand but the resulting homogeneous catalyst mixture was more stable (Figure 8).

5. Polyethylene-Bound Hydroformylation Catalysts

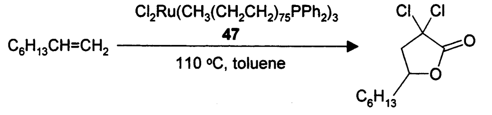
Hydroformylation catalysts ligated by polyethylenediphenylphosphine ligands were studied both by the Bergbreiter group and by the Moscow State University group.[63,64] For example,[64] the Moscow State University group used an oligomerically ligated Rh(I) catalyst in hydroformylation of alkenes including 1-dodecene, cyclododecene, styrene, and 1,5-cyclooctadiene (eq 25). The ratio of linear to branched product in the 1-dodecene hydroformylation was sensitive to syn gas pressure and to the presence of excess oligomeric ligand. In the case of the stoichiometric complex **46**, the linear product was about 70% of the product mixture. Increasing the amount of oligomeric ligand relative to the rhodium catalyst **46** increased the percentage of linear product to 87% and also increased the stability of the catalyst solution. Catalyst solutions containing excess phosphine ligand were recycled at least 10 times successfully using the precipitation/filtration protocol shown in Figure 6. Such recycling maintains the phosphine:Rh(I) ratio because both the excess ligand and catalyst are equally efficiently recovered on cooling.



(25)

6. Polyethylene-Bound Ruthenium Catalysts

a. Catalysts for the Kharasch Reaction. Recoverable polyethylenediphenylphosphine-bound ruthenium(II) catalysts have been studied by several groups. Joint work between Weinreb's group and Bergbreiter's group has shown that $Cl_2Ru(PE_{Olig}PPh_2)_3$ catalysts can be prepared by exchange of $PE_{Olig}PPh_2$ with the triphenylphosphine groups of $Cl_2Ru(PPh_3)_3$.[74] This phosphine exchange reaction produced a clear solution that contained triphenylphosphine on the basis of ^{31}P NMR spectroscopy. The catalyst so formed was completely insoluble at room temperature. These groups showed that the resulting soluble polyethylene-bound Karasch reaction catalysts have activity and selectivity similar to those of their low molecular weight analogues. These soluble polyethylene-bound Ru(II) catalysts are also practical catalysts. Such catalysts readily dissolve in hot toluene and were successfully recycled several times without any measurable change in reactivity (eq 26).

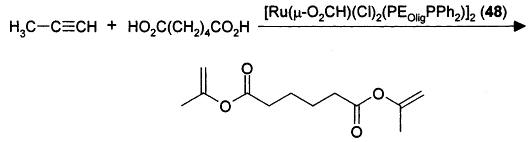


(26)

For example, in reaction 26 the yield of the halogenated γ-lactone using $Cl_2Ru(PPh_3)_3$ as catalyst was 81% and was 80% in each of three cycles with the $Cl_2Ru(PE_{Olig}PPh_2)_3$ catalyst. The soluble polymer-bound catalyst was also shown to be comparable to the low molecular weight catalyst in intramolecular Kharasch cyclizations. There were slight changes in product stereoselectivity seen in intramolecular cyclizations—changes that were either due to the use of an alkyldiphenylphosphine or due to environmental effects of the nonpolar polyethylene ligand. However, the catalyst **47** was recyclable both in intramolecular Kharasch reactions and intermolecular reactions such as reaction 26. The effectiveness of the polymer-bound catalyst in these reactions can be judged by the scale of the reactions; a typical Kharasch reaction was carried out on a 50 mmol scale using <1 mol % catalyst.

b. Catalysts for Alkyne Carboxylation. Dimeric ruthenium catalysts containing both phosphine ligands and bridging carboxylate groups were also prepared by reaction of **19** with $[Ru(\mu\text{-}O_2CH)(CO)_2)]_n$.[75] The resulting catalyst, $[Ru(\mu\text{-}O_2CH)(CO)_2(PE_{Olig}PPh_2]_2$

(**48**), was then used to prepare vinyl esters by carboxylation of terminal alkynes with various carboxylic acids (eq 27). The effectiveness of the catalyst recycling protocol shown in Figure 6 for these polyethylene-ligated alkyne carboxylation Ru catalysts can be seen in results where the same recovered catalyst was used successively in a series of reactions. Specifically, one 0.1 mmol sample of the catalyst **48** was successively recovered and reused in a series of reactions, first forming vinyl diesters of propyne and adipic acid, hexyne and succinic acid, propyne and adipic acid, hexyne and succinic acid, propyne and adipic acid, propyne and succinic acid, propyne and succinic acid, hexyne and adipic acid, hexyne and phthalic acid, hexyne and phthalic acid, and hexyne and adipic acid. This sequence of successive reactions led to 55 mmol of the various diesters, none of which were contaminated by vinyl esters from earlier reactions.



(27)

c. Ruthenium Carboxylate Cluster Catalysts for Alcohol Oxidation. The work described above used polyethylene ligands to recover catalysts and relied on phosphorus-containing polyethylene ligands to coordinate to a transition metal. Polyethylene with terminal anionic carboxylate groups too can be used as a counterion to recover metal salts active in catalysis.[66,68,69,79] Indeed, carboxylic acid-terminated polyethylene oligomers have proven to be especially useful in transition-metal catalyst recovery. This was apparent in early work designed to prepare a recoverable, reusable polymer-bound oxidation catalyst.[69] The formation of the catalyst in this case relied on the exchange equilibrium shown in eq 28. Heating a 1:1 (equiv/equiv) ratio of $PE_{Olig}CO_2H$ to $[(CH_3CH_2CO_2)_6Ru_3O(H_2O)_3]^+CH_3CH_2CO_2^-$ in toluene at 100 °C followed by cooling to room temperature converted the initially dark green solution of the propionate ruthenium complex **49** into a suspension of a green polyethylene powder in a colorless supernatant. ICP analysis showed that this green powder had 1.09% Ru, suggesting that the powder contained a mixture of polyethylene carboxylate and propionate ligands on the recovered polymer-ligated Ru_3 cluster **50**. When the polyethylene-bound catalyst so formed was redissolved in chlorobenzene with a primary or secondary alcohol in the presence of oxygen, aldehyde or ketone formed. While recovery of these polyethylene carboxylate triruthenium clusters was efficient, the oxidation activities of these catalysts were modest. Recycling of this catalytic oxidant was accomplished by cooling (reprecipitation) and redissolution (heating). ICP analysis of the filtrate after the second cycle showed <2% of the charged Ru was lost to solution. Control experiments showed that the propionate cluster was not entrapped in virgin polyethylene; a polyethylene ligand was required if the clusters were to be recovered and recycled. However, catalyst decomposition limited catalyst recyclability. Such thermal decomposition had been previously noted for the propionate complex[92] and also affected the polyethylene-bound clusters. The catalyst deactivation in this case could be followed by UV−vis spectroscopy. The polyethylene carboxylate-bound Ru_3 cluster's UV−vis spectrum had a λ_{max} of 658 (this λ_{max} was shifted from the 686 nm λ_{max} of the propionate cluster, possibly because of the nonpolar $PE_{Olig}CO_2^-$ ligands). This λ_{max} of 658 nm changed to 640 nm after prolonged heating of the catalyst, indicating catalyst decomposition had occurred.

$$\underset{}{CH_3CH_2(CH_2CH_2)_nCO_2H} + \underset{\mathbf{49}}{[(CH_3CH_2CO_2)_6Ru_3O(H_2O)_3]^+CH_3CH_2CO_2^-} \rightleftharpoons$$

$$\underset{\mathbf{50}}{[(CH_3CH_2(CH_2CH_2)_nCO_2)_{6-n}(CH_3CH_2CO_2)_nRu_3O(H_2O)_3]^+} \begin{bmatrix} CH_3CH_2CO_2^- \text{ or} \\ CH_3(CH_2CH_2n)CO_2^- \end{bmatrix} \qquad (28)$$

7. Polyethylene-Bound Europium(III) Complexes

The color change seen in the exchange reaction 28 (dark green solution to colorless solution with a green polyethylene precipitate) could have been the result of the polyethylene carboxylate being a better ligand than a propionate ligand. However, separate experiments with octadecanoate and polyethylene carboxylate-bound Eu(III) clusters showed that the effectiveness of complexation of this Ru cluster by polyethylene ligands in the presence of low molecular weight propionate ligands is a result of entropic effects—entropic effects that can be used to advantage in catalyst recovery and use.

Fluorescence spectroscopic analyses of europium(III) carboxylate solutions containing as carboxylate ligands mixtures of $PE_{Olig}CO_2^-$ or $C_{17}H_{35}CO_2^-$ were used to demonstrate the equivalence of a polyethylene and low molecular weight ligand and to quantify the entropic advantages for metal complex recovery that result from the use of these room-temperature insoluble polyethylene ligands.[79] The amount of europium(III) carboxylate remaining in solution after heating and precipitation of mixtures of $(C_{18}H_{37}CO_2)_3Eu$ and $PE_{Olig}CO_2H$ was used to estimate equilibrium constants for eqs 29−31. By varying the molar ratios of $(C_{18}H_{37}CO_2)_3Eu$ to $PE_{Olig}CO_2H$ from 1:6 to 6:1, mixtures were prepared that had from 66% to <0.09% of the original Eu(III) left in solution as measured by fluorescence. These experimental values for the percentage of remaining soluble $(C_{18}H_{37}CO_2)_3Eu$ after dissolution, equilibration, and precipitation of the $(C_{18}H_{37}CO_2)_3Eu$ and $PE_{Olig}CO_2H$ mixtures were then compared to calculated percentages for the remaining $(C_{18}H_{37}CO_2)_3Eu$ assuming various equilibrium constants for equilibria 29−31. The results indicated that $C_{18}H_{37}CO_2H$ and $PE_{Olig}CO_2H$ were roughly equivalent as ligands. Further experiments showed that quantitative recovery of the Eu(III) by $PE_{Olig}CO_2H$ was possible after 2−5 cycles of dissolution, equilibration, and precipitation even when stoichio-

$$\boxed{\text{POLY-L}} + \text{(ligand)}_3\text{Metal} \rightleftharpoons \boxed{\text{(POLY-L)Metal(ligand)}_2} + \text{ligand} \qquad (29)$$

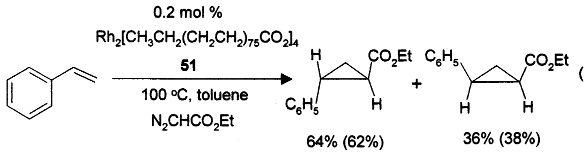
$$\text{POLY-L} + \boxed{\text{(POLY-L)Metal(ligand)}_2} \rightleftharpoons \boxed{\text{(POLY-L)}_2\text{Metal(ligand)}} + \text{ligand} \qquad (30)$$

$$\text{POLY-L} + \boxed{\text{(POLY-L)}_2\text{Metal(ligand)}} \rightleftharpoons \boxed{\text{(POLY-L)}_3\text{Metal}} + \text{ligand} \qquad (31)$$

metric amounts of the two carboxylic acids were used in the initial exchange reaction. If the octadecanoate ligand was a minor component, no detectable Eu(III) remained in solution because entropic factors favor formation of one of the boxed complexes in equilibria 29−31. These complexes in boxes in eqs 29−31 all contain at least one polyethylene ligand that ensures the complex precipitates.

8. Polyethylene-Bound Rhodium(II) Cyclopropanation Catalysts

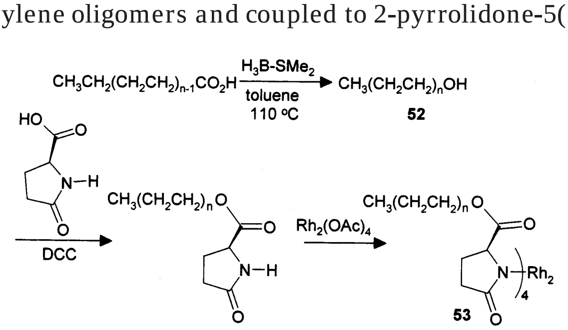
The use of a polyethylene carboxylic acid to support a transition-metal salt was successfully used in the preparation of practical catalysts using $Rh_2(OAc)_4$ as a catalyst precursor. Rhodium(II) carboxylates are known as effective catalysts for cyclopropanation reactions of alkenes, and using $PE_{Olig}CO_2H$ as the oligomeric ligand and $Rh_2(OAc)_4$ as the Rh(II) source, we successfully prepared $Rh_2(PE_{Olig}CO_2)_4$ (**51**) catalysts that were effective in cyclopropanation reactions such as that shown in eq 32.[66] In this case, the stereoselectivity (trans/cis) seen with the oligomeric catalyst at 100 °C mirrored that of the low molecular weight $Rh_2(OAc)_4$ as catalyst at 25 °C (values in parentheses in eq 32). Copper(II) salts of this carboxyl-terminated polyethylene oligomer, $Cu(PE_{Olig}CO_2)_2$, were equally effective in this olefin cyclopropanation chemistry. These catalysts could be recycled by precipitation and filtration and used through 10 cycles without any loss in activity.



(32)

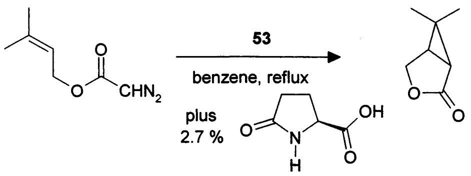
9. Polyethylene-Bound Chiral Rhodium(II) Catalysts

Extensions of this chemistry wherein an anionic polyethylene ligand is used to complex and recover a transition-metal catalyst led to one of the earliest and most successful examples of a recoverable homogeneous asymmetric catalyst that produced product with practical ee values. This work coupled the successful development by Doyle's group of chiral catalysts for asymmetric cyclopropanation and C−H insertion with the use of polyethylene carboxylates as ligands for recoverable Rh(II) carboxylate catalysts.[53] In this chemistry, the polyethylene oligomers containing terminal carboxyl groups that had been used in the formation of the $[(PE_{Olig}CO_2)_2Rh]_2$ above were converted into hydroxymethyl-terminated polyethylene oligomers and coupled to 2-pyrrolidone-5(*S*)-carboxylic acid (PYCA) via an ester bond. A Rh(II) catalyst, $PE_{Olig}Rh_2(5(S)\text{-}PYCA)_4$ (**53**), was then prepared by ligand exchange (eq 33) at elevated temperature. Cooling precipitated the polyethylene and led to isolation of the resulting catalyst. The catalyst so formed was successfully used in asymmetric C−H insertion reactions and in intramolecular cyclopropanations. Good enantioselectivity and isolated yields were seen in repeated runs with seven successful cycles of eq 34. Some erosion of the initially high enantioselectivity (98% ee) was seen, with the percent ee gradually decreasing to 61% by run 7.



(33)

The entropically favored presence of at least one polyethylene ligand per rhodium catalyst even in the presence of some of the low molecular weight ligand was advantageously used in this case to increase enantioselectivity in the insertion chemistry (eq 34).



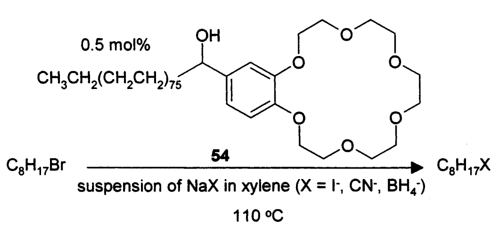
(34)

This addition of a small amount (ca. 2.7%) of the low molecular weight ligand as an additive in this case did not compromise catalyst recovery. On the basis of the earlier studies of Ru_3 cluster chemistry and the studies of competitive complexation and recovery of europium(III) carboxylates by $PE_{Olig}CO_2H$, the catalyst **53** was expected to always have at least one polyethylene ligand, so rhodium leaching did not occur even if small amounts of additives were added.

10. Polyethylene-Bound Phase-Transfer Catalysts

Ionic catalysts in the form of phosphonium salts are widely used as phase-transfer catalysts.[93] Polyethylene ligands have been successfully used to bind phosphonium salts, ammonium salts, and crown ethers for use as recoverable, recyclable phase-transfer catalysts.[77,78] Kinetic studies of polyethylene-bound phase-transfer catalysts prepared from anionically oligomerized ethylene show that the polyethylene-bound catalysts' activities in these reactions are comparable to those of their low molecular weight analogues.[77] An important consideration in this case is that kinetic studies showed that the polymer-bound catalyst was quite active. The reported rates were such that reaction half-lives of 1−8 h were readily attained at oligomeric catalyst concentrations of 3×10^{-3} M. Catalyst recovery was effected by cooling, precipitation, and filtration. As was true in the other catalytic chemistry described above, these catalysts could be used in multiple sequential reactions to form different products without cross-contamination of one product by another as measured by GC analysis.

The most convenient way to use these oligomeric polyethylene-bound phase-transfer catalysts proved to be in solid/liquid phase-transfer reactions. In these cases, 0.5 mol % polyethylene-bound crown ether catalyst **54** was dissolved in a solvent such as xylene along with the substrate. The nucleophile in the form of a sodium salt was present as a suspension. Simple heating to 110 °C and magnetic stirring then effected complete conversion of the substrate to product over the course of 16 h (eq 35). Hot filtration or decantation separated the excess sodium salt of the nucleophile from the organic solution. Cooling and filtration then produced a precipitate of the polyethylene-bound crown ether **54** that was recovered by filtration. Using this protocol, three successive preparative reactions on a 50 mmol scale were carried out using 1-bromooctane and sodium iodide, octanal and sodium borohydride, and 1-bromooctane and sodium cyanide with no contamination of the products from one reaction to the next. Isolated yields in these reactions were 90%, 93%, and 85%, respectively.



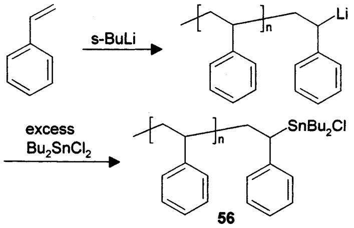
(35)

Soluble polyethylene-bound phase-transfer catalysts have also been prepared using commercially available oxidized polyethylene as a support.[78] In this case, bifunctional catalysts containing ammonium groups and a polyether were prepared by amidation of the carboxylic acid groups of oxidized polyethylene using commercially available α,ω-diaminopoly(alkene oxide)s. By using an excess of this reagent, a polyethylene-bound poly(alkene oxide) amine could be prepared and isolated. Subsequent quaternization with butyl bromide yielded a tetraalkylammonium phase-transfer catalyst that has polyethylene-like temperature-dependent solubility and activity similar to that of phase-transfer catalysts in nucleophilic substitutions of primary alkyl halides with NaCN.

11. Polyethylene-Bound Tin Catalysts

Polyethylene oligomers can also be used to support other organic catalysts. A comparison of the utility of soluble polystyrene- and polyethylene-supported tin halides **55** and **56** as catalysts for reductions of aryl and alkyl bromides and iodides using sodium borohydride as the penultimate reductant has been reported.[70] In this chemistry, the soluble polymer-bound tin halides were prepared by anionic oligomerization of ethylene or styrene followed by treatment of the reactive organolithium oligomers so formed with excess Bu_2SnCl_2 (eqs 36 and 37). The products were characterized by both ^1H and ^{119}Sn NMR spectroscopy. Loadings were also estimated by integrating the ^{119}Sn NMR peaks versus a soluble tin standard (Bu_4Sn). Typical loadings estimated by NMR spectroscopy were in the 0.1–0.4 mmol of tin/g of oligomer range, values that were in rough agreement with the results of elemental analyses for tin that showed loadings were in the range of 0.3–0.6 mmol of tin/g of oligomer.

$$H_2C{=}CH_2 \xrightarrow{\text{BuLi, TMEDA}} CH_3CH_2(CH_2CH_2)_nLi \xrightarrow{\text{excess } Bu_2SnCl_2} \underset{\textbf{55}}{CH_3CH_2(CH_2CH_2)_nSn(Bu)_2Cl} \quad (36)$$



56

(37)

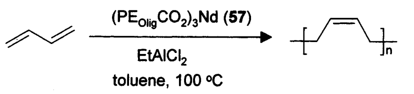
Catalysts **55** and **56** were successfully used in alkyl and aryl bromide reductions (eq 38). In these reactions, the polyethylene-bound tin catalyst was recovered and reused following the protocol described in Figure 6. The polystyrene-bound catalyst had reactivity analogous to that of the polyethylene-bound catalyst in bromide reductions. However, the cooling–precipitation process used to recover the polyethylene-bound catalyst was more convenient than solvent precipitation that was required for recovery/reuse of the polystyrene-bound catalyst. Recycling experiments consequently mainly used the polyethylene-bound catalyst. Kinetic studies showed that catalysts **55** and **56** had comparable reactivity.

$$n\text{-}C_{12}H_{25}Br \xrightarrow[\text{NaBH}_4\text{, 20 mol\% benzo-15-crown-5; toluene, 110 °C, 16 h}]{\text{10 mol\% PE}_{Olig}\text{SnBu}_2\text{Cl } (\textbf{55})} n\text{-}C_{12}H_{26} \quad (38)$$

12. Polyethylene-Bound Polymerization Catalysts

Polymerization catalysts are often not separated from the product polymer; their presence is often at very low levels or is inconsequential for the eventual polymer end use. Ziegler–Natta and metallocene olefin polymerization catalysts provide a widely used example of efficient catalysts that are not recovered or reused. However, in some cases where the catalyst residue can affect a polymer's stability or properties, there is interest in recovering and reusing polymerization catalysts.

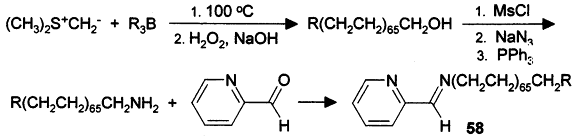
a. Polyethylene-Bound Diene Polymerization Catalysts. Lanthanide catalysts for stereoselective polymerization of butadiene were one of the first examples of a polyethylene-bound polymerization catalyst that was successfully recovered and reused.[68] In this case, a $(PE_{Olig}CO_2)_3Nd$ catalyst was used with Et_3Al or $EtAlCl_2$ as a reducing agent to stereospecifically polymerize butadiene (eq 39). While the resulting catalysts had activity equivalent to that of a divinylbenzene-cross-linked-polystyrene-bound neodymium carboxylate, separation of the catalyst was a problem. When this polymerization was carried out to produce a concentrated solution of poly(*cis*-1,4-butadiene) product, the cooled solution was too viscous for filtration or centrifugation to recover the polyethylene-bound catalyst. Catalyst filtration (or centrifugation) to recover the polyethylene-bound catalyst **57** was only possible if the reaction mixture was first diluted with excess solvent. This require-



(39)

ment for additional solvent at the end of the reaction makes catalyst recovery less useful for a practical process. In this case, solvent addition is not being used as a way to precipitate a soluble polymer; it is only reducing the viscosity of the product solution prior to the necessary filtration or centrifugation step.

b. Polyethylene-Bound Catalysts for Atom-Transfer Radical Polymerization. More recently polyethylene oligomers were used to design ligands for copper(I) catalysts used in atom-transfer radical polymerization.[71] This latter chemistry used an alternative route to prepare the polyethylene oligomers based on ylide oligomerization (eq 40).[61] The resulting end-functionalized oligomers are more monodisperse than the oligomers prepared by anionic oligomerization (eq 14), but they have the same solubility properties (Figure 6). After the hydroxyl-functionalized oligomer was converted into an amine and then into an imine derivative of 2-pyridinecarboxaldehyde, the product chelating ligand was used to complex CuBr in an atom-transfer radical polymerization (ATRP) reaction.[94] A hot toluene solution containing a 2:1:1 ratio of the ligand **58** to CuBr to ethyl 2-bromoisobutyrate was then used to initiate a methyl methacrylate polymerization (eq 41). The result was a "living" radical polymerization and formation of poly(methyl methacrylate) polymer with a relatively narrow polydispersity (1.22−1.45). Decantation after cooling to 0 °C was used to separate the product polymer solution from the polyethylene-ligated Cu(I) catalyst **59**, and the product polymer was then isolated from the toluene solution by precipitation with methanol. The conclusion that the copper catalyst was removed quantitatively was based on visual inspection of the color of the product polymer solution.



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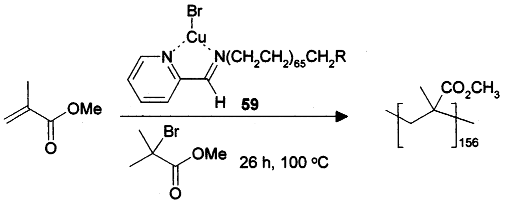
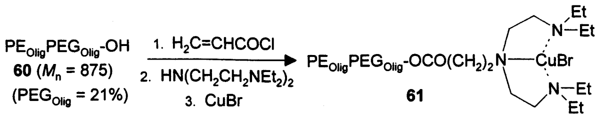


(41)

While catalyst separation in this case simply involved cooling and decantation, this is probably not a solution to the problem of removing catalyst from ATRP polymerizations. This is because the catalyst's activity was not ideal, especially when a significant portion of the monomer had been consumed. The authors speculated that deviations from ideality seen at higher conversions reflect slower propagation rates. This is a possible kinetic problem not seen in the catalysis involving low molecular weight substrates and is due to the requirement that a high molecular weight polymer end group react with a polymeric catalyst. While it is expected that a terminally functionalized polymer should have good reactivity with a low molecular weight substrate, macromolecule−macromolecule reaction rates can be lower even when both macromolecules are soluble. A second problem is that, to achieve good solution properties (e.g., low viscosity), the polymerization requires relatively dilute monomer. In the example reported, the methyl methacrylate was $<10^{-2}$ M.

Subsequent work by Zhu expanded on the use of soluble polymers as supports for ATRP polymerizations.[72,73] In this most recent work, commercially available block copolymers of polyethylene and poly(ethylene oxide) (**60**) were used to prepare the supports (eq 42). Though the starting oligomers were reported to be soluble at room temperature, the polyethylene block in the catalyst after the reaction provides the sort of solubility used in the other reactions above that use polyethylene oligomers as ligand supports. Thus, in a polymerization (eq 43), the green block-copolymer-bound catalyst **61** was removed from a 20 wt % solution of poly(methyl methacrylate) by cooling to room temperature. Separation of the resulting green solid from product solution was accomplished by centrifugation. UV−vis analysis of the second and third cycles showed that <2% of the initial copper catalyst remained in the colorless poly(methyl methacrylate) toluene solution. Significantly, dispersities in recycled runs were constant. The differences between these catalysts and those studied earlier by Brittain were studied in more detail in a subsequent paper. The conclusion of that paper was that the presence of a polyethylene-incompatible PEG block and the lower molecular weight of the copolymer **60** may make this catalyst behave more like its low molecular weight analogue. A larger polyethylene support negatively impacted propagation rates, an affect that was ameliorated by the presence of the PEG block.



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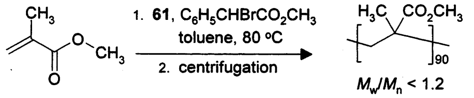


(43)

B. Solid/Liquid Separations of Catalysts on Polymers with Inverse Temperature-Dependent Solubility

Most polymers have "normal" temperature-dependent solubility and are like the polyethylene oligomer above. In cases such as polyethylene where the material's solubility is profoundly different at different temperatures, this solubility change can be used to advantage for catalyst recovery. There are also polymers with "inverse" temperature-dependent solubility. These polymers are soluble cold and insoluble hot. In cases where these polymers' solubility is profoundly different at different temperatures, such

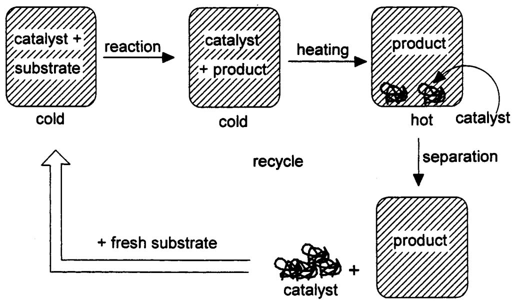


Figure 9. Scheme for recovery, separation, and reuse of a polymer-bound catalyst when the polymer has inverse temperature-dependent solubility and is insoluble warm and soluble cold.

polymers can be used to recover catalysts on heating using the processes shown in Figure 9.

The most common examples of polymers that precipitate or phase separate from solution on heating are seen in aqueous solutions where the phenomenon occurs in the 0−100 °C temperature range. The temperature at which such phase separation occurs is termed the lower critical solution temperature (LCST).[95] Phase separation of polymers from solutions is known in other solvents too.[96] However, in other solvents, phase separation usually occurs above the boiling point of the solvent and is thus only seen in a pressurized apparatus.

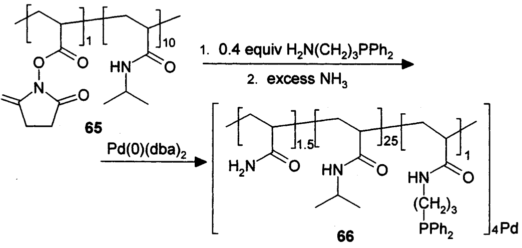
1. “Smart” Thermally Responsive Catalysts

Phase separation on heating was first used not to recover catalysts but to engineer “smart” behavior into homogeneous catalysts and substrates.[45,97−99] This effect was first shown using triblock copolymers of poly(ethylene oxide)−poly(propylene oxide)−poly(ethylene oxide) (**62**) that contained phosphine-ligated Rh(I) hydrogenation catalysts at their termini (**64**).[91,92] Such polymers and the ligands and catalysts derived from them have LCSTs that are determined by the relative sizes of the hydrophilic ethylene oxide and hydrophobic propylene oxide blocks. In essence, the copolymers combine the solubility characteristics of poly(ethylene oxide)—soluble in water up to 100 °C—and poly(propylene oxide)—insoluble in water. The nonpolar phosphine ligand end groups of **63** also affect the LCST, lowering the LCST of the copolymer product. In hydrogenation reactions, these polymer-bound Rh(I) catalysts are active cold and inactive hot (above their LCSTs). This on/off activity is fully reversible, and such phase separation of a soluble polymer-bound catalyst provides a way to control an exothermic reaction. However, the polymeric catalyst **64** in these cases was not recycled. Catalyst recovery in the case of these poly(alkene oxide) supports was difficult because the poly(alkene oxide) polymers phase separated as an oily phase on heating. While a separation of such a catalyst phase is possible in principle, in practice it was not feasible to separate and recover a small amount of this oily phase from the bulk aqueous phase.

2 Poly(N-isopropylacrylamide)-Bound Catalysts

a. Poly(*N*-isopropylacrylamide)-Bound Palladium(0) Catalysts. Poly(alkene oxide)s generally phase separate from water as an oil in water emulsion, but other polymers separate as solids from water solution on heating.[100] We have reported using this property for polyacrylamides such as **65** to make polymeric ligands and in turn water-soluble Pd(0) catalyst **66** that is recoverable on heating. Such a catalyst was successfully used in allylic substitution reactions or in alkyne−aryl iodide couplings.[101]

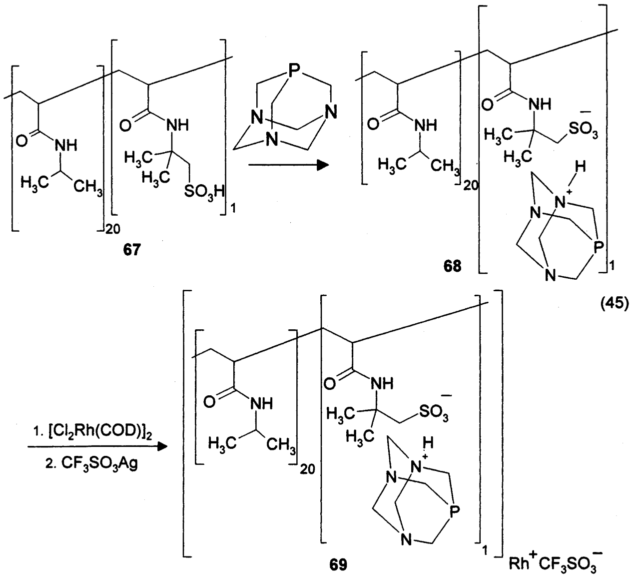
Recovery and reuse of the catalyst **66** was accomplished by heating an aqueous solution of **66** above the polymer’s LCST. This required that **66** be soluble in cold water. This posed a problem in this case because of the hydrophobicity of the aminopropyldiphenylphosphine that was being used to prepare the polymeric ligands in eq 44. In fact, use of a stoichiometric amount of aminopropyldiphenylphosphine in eq 44 yielded a polymeric ligand with a high loading of phosphine groups, but the product polymer was too hydrophobic to be soluble in water. To avoid this problem, a substoichiometric amount of this aminated phosphine ligand was used to consume a portion of the active ester groups in **65**. The remaining active ester groups were then converted to more hydrophilic acrylamide groups, balancing out the hydrophobicity of the aminopropyldiphenylphosphine groups in the product polymer. This scheme of using an active-ester-containing polymer and a mixture of amines to tune the solubility of the product copolymer ligands is a general approach to engineering a particularly desired solubility into polyacrylamides.



(44)

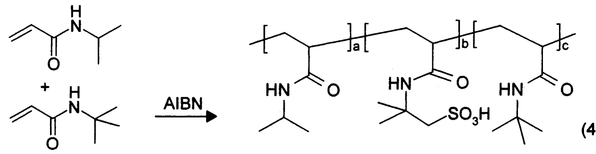
The poly(*N*-isopropylacrylamide)-ligated Pd(0) catalysts prepared in eq 44 could also be recycled by solvent precipitation. For example, if, after the reaction were complete, the mixture of polymeric catalyst **66** and product in acetonitrile were poured into hexane, the polymeric catalyst would precipitate and could be isolated by filtration. Using such recycling approaches, the Pd(0) catalyst **66** was successfully recycled 15 times in allylic substitution of allyl acetates with *p*-toluenesulfinate or with secondary amine nucleophiles. The same catalyst was also recycled five times in couplings of terminal alkynes to aryl iodides.

b. Poly(*N*-isopropylacrylamide) Derivatives as Ionic Supports for Rhodium(I) Hydrogenation Catalysts. The strong acid-containing polymer **67** has also been used to ionically immobilize a basic phosphine-containing ligand to form the polymer **68**.[45] This polymer was in turn used to prepare a cationic Rh(I) catalyst, **69**, that was soluble in a 3 × 10^{-4} M solution at 22 °C and insoluble at 55 °C. Hot centrifugation could recover this catalyst that had no activity at this higher temperature.



67 **68** **69** (45)

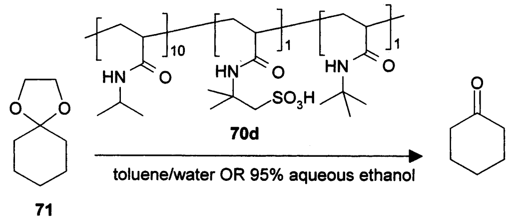
c. Poly(*N*-isopropylacrylamide)-Bound Sulfonic Acid Catalysts. Acid catalysts on polymers are common but usually involve insoluble cross-linked polymers (e.g., sulfonated cross-linked polystyrene). Recoverable acid catalysts on soluble polymers however can be prepared too.[45] In this case, a polymer such as **67** is not suitable for use as a thermally recoverable catalyst in water because its LCST is >100 °C. However, by synthesizing terpolymers **70** that contain a more hydrophobic *N-tert*-butylacrylamide (eq 46), the LCST and hence the recoverability of this soluble acid catalyst can be engineered so that the precipitation occurs in a convenient temperature range.



(46)

	a:b:c	LCST
70a: =	1:1:1	45 - 47 °C
70b: =	10:2:5	38 - 40 °C
70c: =	10:1:1	33 - 35 °C
70d: =	20:1:0	43 - 45 °C

The recoverable poly(*N*-isopropylacrylamide)-bound strong acid catalyst **70** can be completely recovered on heating above its LCST as evidenced by experiments where a purified, high molecular weight version of **70** was allowed to react with an aqueous solution of a basic azo dye methyl red. Below **70**'s LCST, the dye is protonated by this polymeric acid. Above the LCST of **70**, the dye is not protonated. Such acid catalysts have been shown to catalyze typical hydrolysis reactions such as the hydrolysis of the dioxospirodecane **71** (eq 47) in a mixed phase toluene/water or aqueous ethanol solvent mixture.



70d **71** (47)

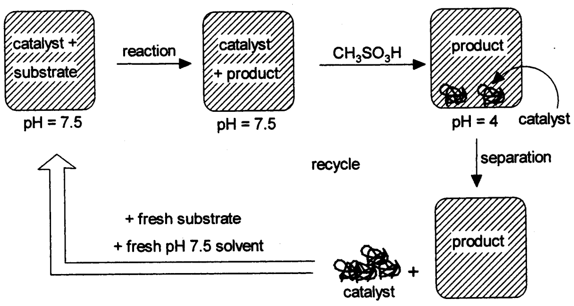
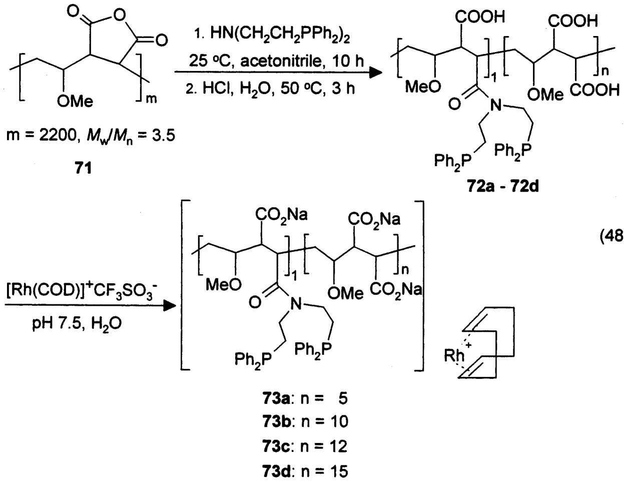


Figure 10. Scheme for recovering, separating, and reusing a soluble polymer-bound catalyst attached to a polymer with pH-dependent solubility.

d. Poly(*N*-isopropylacrylamide)-Bound Biological Catalysts. Enzymes, while not the subject of this review, are the most common sort of catalyst attached to inverse temperature-dependent soluble polymers. They can be recovered by mild heating. A recent report illustrates how this approach can be used in the synthesis of biologically interesting peptides and oligosaccharides.[102] Such chemistry has been reviewed.[103,104]

C. Solid/Liquid Separations of Catalysts on Acid- and Base-Soluble Polymers

Polymers such as poly(acrylic acid) and polyethylenimine have pH-dependent solubility, and this pH-dependent solubility has been used to advantage to prepare ligands and catalysts that can be dissolved by adjusting the pH of a solution.[105,106] In such cases, a change in pH leads to a precipitate and a solid/liquid separation can then isolate a catalyst or ligand that can be reused as a homogeneous catalyst if a fresh solution of the appropriate pH is used (Figure 10). pH precipitation could in principle be used with a variety of water-soluble catalysts (vide infra). However, the explicit use of pH changes to recover a catalyst is surprisingly limited. Such a recovery procedure was recently used with soluble catalysts derived from maleic anhydride–methyl vinyl ether

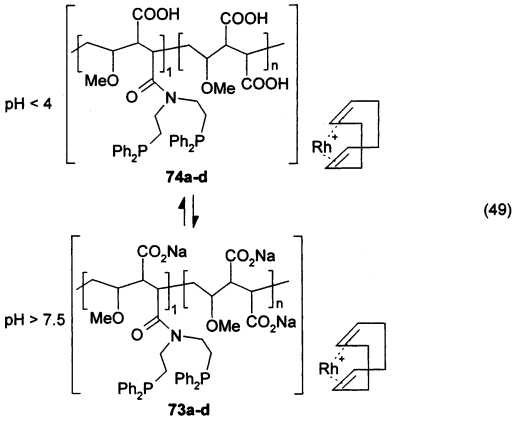


71 **72a - 72d** (48)

73a: n = 5
73b: n = 10
73c: n = 12
73d: n = 15

copolymer **71**.[107] In this case, phosphine ligands were attached to polymers to form carboxylic acid-containing polymeric phosphine ligands **72a**–**72d** that had pH-sensitive solubility (eq 48). Complexation of these polymeric phosphine ligands to a cationic Rh(I) species then formed cationic polymer-bound Rh(I) hydrogenation catalysts **73a**–**73d**. The polymer-bound catalyst so formed was soluble above pH 7.5 and insoluble below pH 4.

The resulting polymer-bound catalyst **73** could be used to carry out hydrogenation of a water-soluble substrate homogeneously in a pH 7.5 solution. Addition of a small amount of acid (e.g., CH_3SO_3H) after the reaction was complete converted the carboxylate groups of **73** into carboxylic acid groups (**74**) (eq 49), and the polymer precipitated (Figure 10). Separation of the polymer from the solution using centrifugation followed by addition of fresh substrate in a pH 7.5 solution redissolved the catalyst and allowed the catalyst to be used in subsequent reaction cycles. Hydrogenation rates with the catalyst **73** were comparable to but lower than rates with a low molecular weight analogue of **73**. For example, hydrogenation of allyl alcohol was ca. 50% as fast with **73** and hydrogenation of *N*-isopropylacrylamide was about 90% as fast as hydrogenations with low molecular weight catalysts.



(49)

pH-sensitive solubility has been reported for other polymeric ligands and catalysts.[50,105,106] However, the explicit use of pH adjustment to recover a catalyst has not always been emphasized as a catalyst recovery technique. pH-induced recovery of polymer-bound catalysts should have some general utility though, since pH adjustment around pH 7 requires such a small amount of added acid or base.

D. Solid/Liquid Separations of Catalysts after Solvent Precipitation of Polymers

Adding a solution of a polymer in a good solvent to an excess of a poor solvent is probably the most general way to induce polymer/solution phase separation (Figure 11). When this separation process leads to a filterable precipitate, it is a valuable way to isolate a polymer from solution, and if the polymer has a catalyst attached to it, solvent precipitation is a valuable and general way to recover soluble polymer-bound catalysts. Such approaches were among the earliest methods used for soluble polymer-bound catalyst recovery and are the most common way poly(ethylene oxide)-bound catalysts and ligands are recovered from solution.[108]

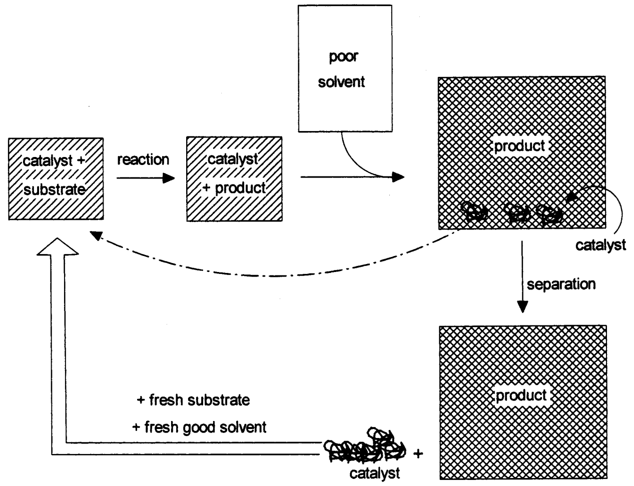
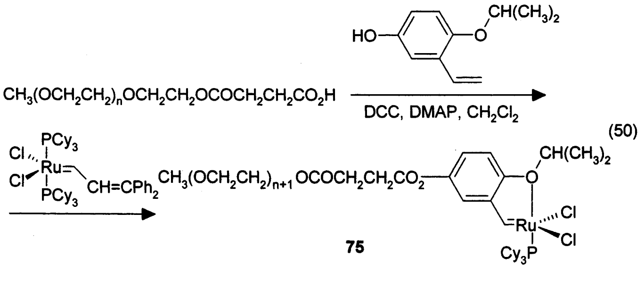


Figure 11. Scheme for recovering, separating, and reusing a soluble polymer-bound catalyst using an excess of poor solvent to precipitate a polymer.

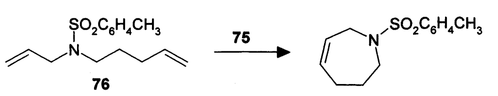
1. Poly(alkene oxide)-Bound Catalysts

Recycling of PEG-supported catalysts is most commonly accomplished by solvent precipitation and is reviewed elsewhere in this issue. While this chemistry is covered in Janda's review, an example of recycling of a PEG-based ruthenium metathesis catalyst, **75**, illustrates the general ideas underlying this approach to recovering catalysts bound to these sorts of soluble polymers.[109] In this example, a carboxylic acid-terminated PEG polymer was first prepared using succinic anhydride. The resulting carboxylic acid was then used to immobilize a phenol that had a styrene moiety that could be used to immobilize a ruthenium ring-closing metathesis catalyst. The resulting catalyst **75** so formed (eq 50) is analogous to catalysts that Hoveyda had earlier shown to be exceptionally stable.[110] This PEG-bound catalyst **75** was soluble in CH_2Cl_2. After a metathesis reaction had been carried out in this solvent using 5 mol % **75**, the reaction mixture was added to excess diethyl ether to precipitate the PEG polymer. Filtration isolated the catalyst that could then be redissolved in CH_2Cl_2 and reused. This catalyst was successfully used for ring-closing metathesis such as that shown in eq 51 using a variety of substrates in vessels open to air. In the specific case of substrate **76**, the catalyst **75** was recycled eight times with



(50)

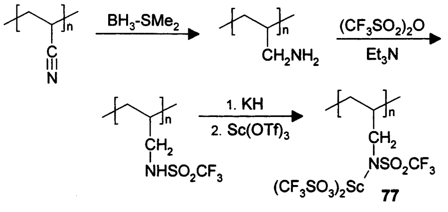
conversions that varied from 98% in the first run to 92% in the last run.



(51)

2. Polyacrylonitrile-Bound Scandium Catalysts

Solvent precipitation is the most general way to recover a soluble polymer, and it has been used with many other examples of soluble polymeric catalysts. An example of this is the polymer-supported scandium catalyst **77**.[111] This catalyst was prepared from polyacrylonitrile using the chemistry in eq 52. It was then used in the synthesis of a library of quinoline derivatives using a three-component coupling reaction involving an alkene, an aldehyde, and an aniline derivative (eq 53). The polymer-bound catalyst was at least partially soluble in the CH_2Cl_2/CH_3CN mixed solvent system used for this coupling reaction. Addition of hexane at the conclusion of the reaction precipitated the catalyst, and the precipitate so formed could be removed from the product by filtration and recycled.



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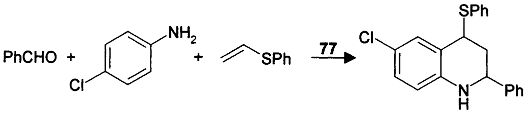
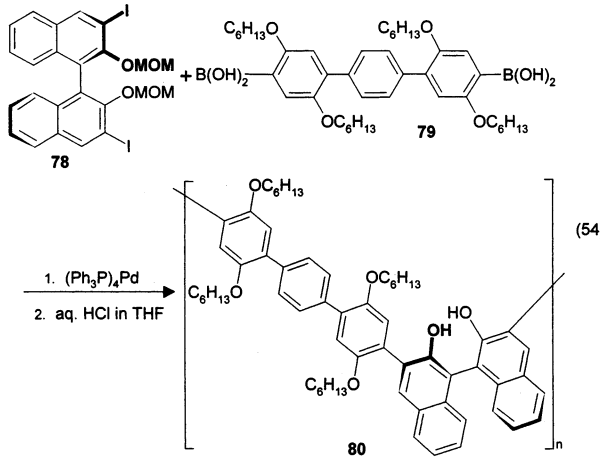


(53)

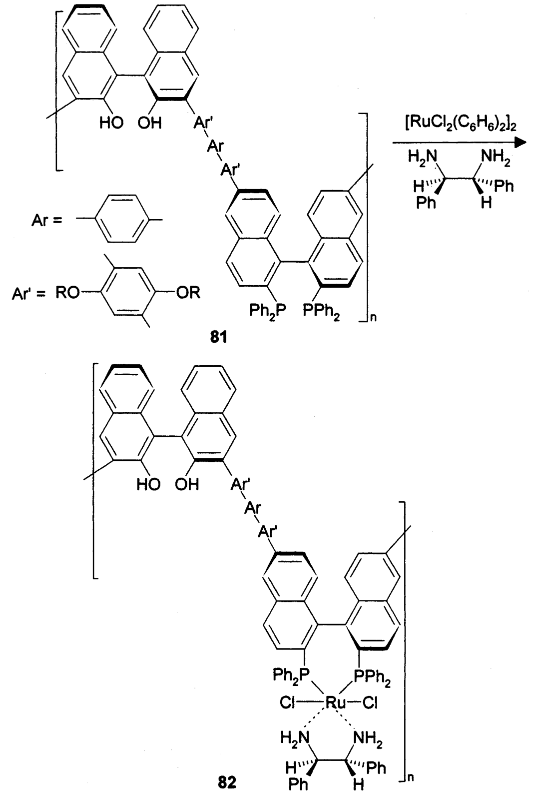
3. Chiral Rigid-Rod Polymers Containing Binaphthyl Groups as Catalyst Supports

Soluble polymer-bound chiral ligands where the chiral groups are part of the polymer's main chain have also been used as recoverable catalysts. Pu's group has provided a number of examples of such catalysts that can be used in asymmetric 1,2-additions of diorganozinc reagents to carbonyl compounds and in other asymmetric reactions.[112] For example, Pu has described the preparation of polymer **80** using chiral binaphthyl monomers such as **78** and a boronic acid derivative of the terphenyl compound **79** as precursors. A Suzuki coupling then yields **80** (eq 54). This rigid-rod polymer can in turn be used to promote 1,2-addition of Et_2Zn to aryl aldehydes to yield an alcohol product with ee values in the high 90% range.[112,113] One of the features of this system is the use of a rigid-rod polymer. The idea here is that the lack of polymer flexibility precludes these polymers coiling—conformational ambiguities that can lead to the introduction of stereochemically irregular sites. Some support for the idea that soluble rigid-rod polymer-supported catalysts can have activity different from that of more flexible soluble polymer-supported catalysts can be found in earlier work using a phosphinated derivative of the rigid-rod polymer poly(1,4-naphthalene) as a support for osmium clusters.[114] Pu's work also illustrates that these soluble polymer-bound catalysts can also be recovered and reused. Recycling by precipitation of the catalyst **80** with methanol was carried out, and the resulting catalyst after three recycles had essentially the same yield and stereoselectivity as fresh catalyst in the reduction of acetophenone.



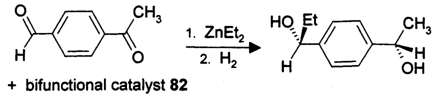
(54)

Bifunctional, rigid-rod polymers have been reported both by Pu and later by Chan to prepare recoverable polymers that can promote multiple reactions.[115,116] The general idea is illustrated by the 1,1′-bi-2-naphthol (BINOL)−BINAP polymer **81** prepared by Pu. This polymer contains both a chiral BINOL group that can be used to promote asymmetric 1,2-addition of Et_2Zn to aryl aldehydes and a BINAP phosphine that can be used to form chiral ruthenium complexes for asymmetric reduction of alkyl aryl ketones. The necessary polymer **81** was prepared using Suzuki couplings such as those used in eq 54 and was



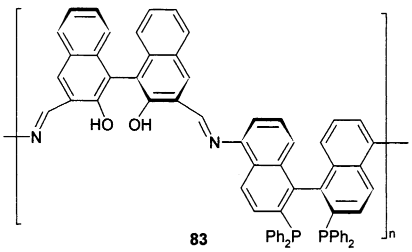
(55)

converted into a chiral ruthenium complex, **82**, by reaction with $[RuCl_2(C_6H_5)_2]_2$ and (*R*,*R*)-1,2-diphenyl-1,2-diaminoethane (eq 55). The product of this reaction was characterized by solution-state ^{31}P NMR spectroscopy which showed that this soluble polymeric ruthenium complex was very similar to the monomeric BINAP−diamine complex described by Noyori.[117] Subsequent use of **82** in reaction 56 led to formation of two chiral centers in a tandem alkylation/reduction reaction. The copolymer catalyst in these cases was recovered by precipitation with methanol and on reuse had similar high conversions and stereoselectivity.



(56)

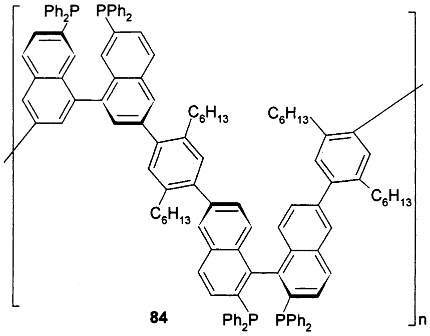
A very similar soluble rigid-rod polymer containing BINOL and BINAP ligands has been prepared by Fan et al.[116] The main difference between this polymer (**83**) and that prepared by Pu is that the polymerization involves aldimine formation instead of a Suzuki C−C-bond-forming reaction. This polymer was used in both asymmetric Et_2Zn addition to aldehydes and in asymmetric hydrogenations of 2-arylacrylic acids. After a reaction, the polymer was quantitatively precipitated using methanol. Filtration yielded a recovered catalyst that had stereoselectivity and activity equivalent to those of the original catalyst.



83

As might be expected from the results with rigid-rod polymers such as **80** and **82**, other rigid-rod polymers with BINAP alone in the main chain or with BINOL as a pendant group on a polystyrene polymer can be prepared and used as soluble ligands and catalysts.[118,119] Examples include the poly(BINAP) polymer **84** and the linear polystyrene-bound BINOL ligand **85**. The poly(BINAP) polymer was successfully used in asymmetric hydrogenations of enamides and in aryl alkyl ketone reductions using a cationic Rh(I) or a chiral diamine−Ru complex, respectively.[118] The polymer was recovered by methanol precipitation, and the recovered polymeric catalyst had the same activity and stereoselectivity as the virgin soluble polymer catalyst.

The polystyrene-bound version of BINOL (**85**) was used to prepare titanium BINOL-ate and aluminum lithium bis(binaphthoxide) catalysts for asymmetric alkylation of aldehydes by Et_2Zn and for asymmetric Michael addition reactions of dibenzyl malonate to cyclohexenone.[119] However, recovery of the catalyst in this case by precipitation was complicated by coprecipitation of other titanium and zinc compounds which make reuse of this catalyst less effective. While solvent precipitation is a general method for soluble polymer and soluble polymeric catalyst recovery, this recovery method can lead to entrainment of impurities in a recovered catalyst as attested to by this example.



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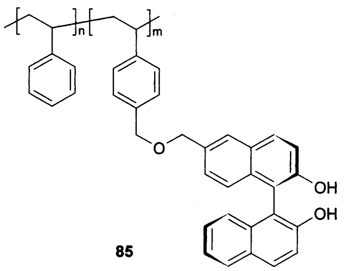
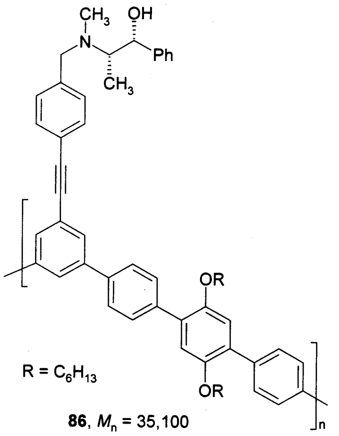


85

A rigid-rod main chain chiral soluble polymeric catalyst containing ephedrine groups has been prepared by Hu.[120] This catalyst (**86**) was successfully used in addition of Et_2Zn to chiral aromatic aldehydes. In a typical reaction such as addition of Et_2Zn to benzaldehyde, the stereoselectivity was 76% ee (94% yield). When a CH_2Cl_2 solution of this catalyst from this reaction was added to excess methanol, **86** precipitated and could be isolated by filtration. The recovered catalyst was then used in this same addition reaction, yielding 1-phenylpropanol product in 82% yield with 76% ee.



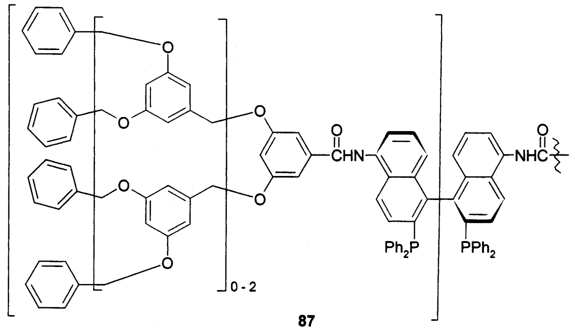
R = C_6H_{13}

86, M_n = 35,100

Main chain polyamide−polyester copolymers prepared using terephthalic acid, (*S*,*S*)-1,3-pentanediol, and a chiral 5,5′-diamino-BINAP monomer complexed to Ru (**37**) have excellent activity and stereoselectivity in asymmetric hydrogenation (vide supra).[55] These catalysts like the catalysts on the polyarylene polymers described by Pu, Hu, and Chan are recoverable by solvent precipitation using methanol.

4. Binaphthyl-Containing Dendritic Polymer-Supported Catalysts in Asymmetric Hydrogenation

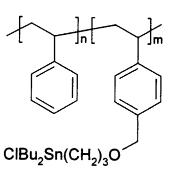
Recyclable catalysts for hydrogenation that employed Frechet-type dendrimers with a BINAP core have been reported by Fan and Chan.[121] These dendrimers (**87**) were converted into a ruthenium catalyst with $[Ru(cymene)Cl_2]_2$ in situ and the resulting catalysts used in asymmetric hydrogenation of 2-arylacrylic acids such as 2-(4-(2-methyl-1-propyl)-phenyl)propenoic acid to form ibuprofen with enantioselectivities of >90%. Catalyst recycling by solvent precipitation with no effect on conversion or ee was demonstrated for three cycles.



87

5. Linear Polystyrene-Bound Catalysts

Soluble polystyrene-bound catalysts are generally recovered by solvent precipitation or by membrane filtration. Another example of this is an alternative to the soluble polymer-bound tin chloride catalysts described above that was developed by Enholm.[122] This linear polystyrene-bound tin catalyst (**88**) along with $NaBH_4$ as the penultimate reductant was successfully used in a wider variety of solvents (e.g., benzene, THF, dimethylacetamide, and ethyl acetate) than the soluble polyethylene-bound catalyst **55**. Moreover, unlike the terminally functionalized polystyrene polymer **56** described above, this soluble polymer had a higher loading of tin since the tin was incorporated as a pendant group. It however could be recycled by solvent precipitation using cold methanol. Using only 1−2 mol % polymeric tin species **88**, aryl and alkyl bromides could be reduced to give up to 93% isolated yields of hydrocarbon product. An extension of Enholm's work led to a polymeric allylstannane reagent analogous to **88**.[123] While this reagent (**89**) was not a catalyst but rather a stoichiometric source of allyl groups, it and the corresponding tin byproducts from allyl-transfer chemistry were quantitatively recovered by methanol precipitation.



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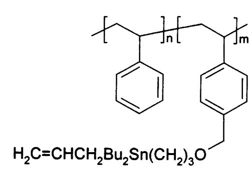
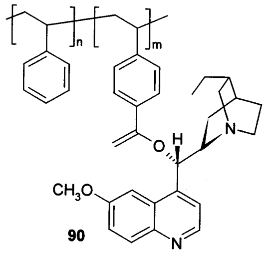


89

Janda's review elsewhere in this issue discusses various sorts of soluble polymer-supported asymmetric dihydroxylation catalysts. While most of these catalysts are attached to PEG derivatives and recovered by solvent precipitation,[124] there are several reports where other polymers or copolymers containing acrylates, styrene, or acrylonitrile groups are used. These reports almost uniformly describe using these polymers under conditions where the polymer is insoluble though in the case of the catalysts **90** and **91** the polymer-ligated osmium catalyst dissolved in the course of the reaction and was recovered by precipitation with water and filtration.[125] However, while these reports emphasize heterogeneous conditions for the oxidation, many of these polymers are not cross-linked and conceivably could be used as soluble ligands for osmium oxidants under other conditions.[126−128]



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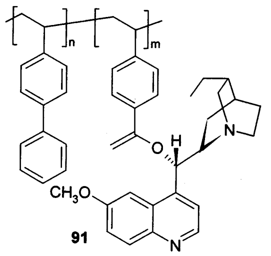
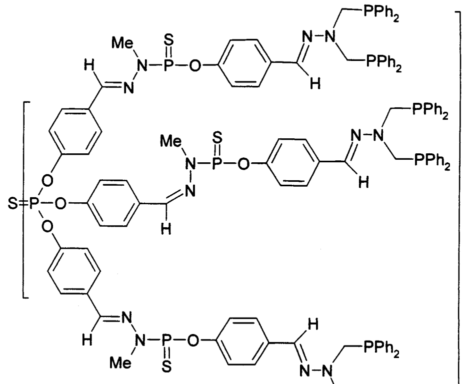


91

6. Dendrimer-Supported Catalysts

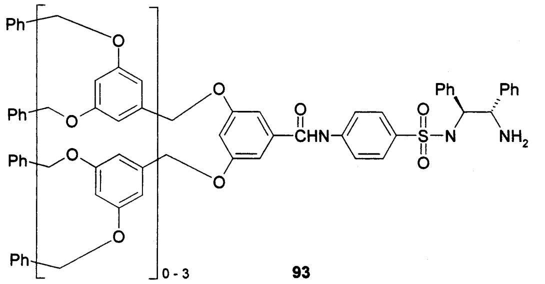
Dendrimer-supported catalysts have also been recovered and reused by solvent precipitation. A variety of dendrimers can be used for this purpose. Several examples of higher generation dendrimers derived from phosphorus-containing dendrimers based on a thiophosphonate core (cf. **92**) were modified to have the $-PPh_2$ groups on their surface complexed to $-PdCl_2$ or $-RuH_2(PPh_3)_2$ and used as recoverable catalysts for Stille couplings, Knoevenagel condensations, and Michael additions.[129] These catalysts were recovered by adding a reaction mixture to excess ether. Recycled catalysts were successfully used with little or no loss in activity, suggesting a good level of catalyst recovery. Metal analyses of the product solutions for leached palladium or ruthenium were, however, not reported.



92

A recyclable dendritic catalyst containing a ruthenium diamine complex was prepared from [Ru-

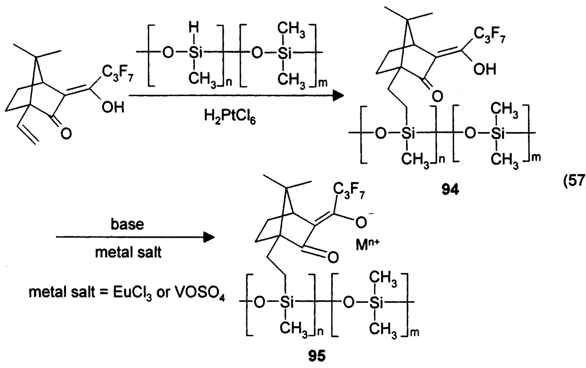
(cymene)$Cl_2]_2$ and the chiral dendritic analogue of (*S*,*S*)-*N*-(*p*-tolylsulfonyl)-1,2-diphenylethylenediamine (**93**).[130] After removal of the reaction solvent (CH_2Cl_2), the catalyst was precipitated with methanol. The recovered catalyst was used up to five times with enantioselectivities that varied from 96.5% ee (first cycle) to 95% ee (fifth cycle).



93

7. Poly(dimethylsiloxane)-Supported Catalysts

Recent work has described the use of poly(dimethylsiloxane) chains to covalently immobilize Lewis acid catalysts based on chiral 1,3-diketonate ligands.[131] Using an oxovanadium(IV) or europium(III) metal salt as a precursor and 3-heptafluorobutanoylcamphorato ligand bound to a poly(dimethylsiloxane), **94**, soluble polymers containing Lewis acids and a chiral β-diketonate ligand, **95**, were prepared (eq 57). These polymer-bound Lewis acids were then used in hetero-Diels–Alder reactions of 1-methoxy-3-(trimethylsilyloxy)-1,3-butadiene with benzaldehyde. The polymeric catalyst containing the oxovanadium catalyst had activity that was comparable to that of the monomeric bis[3-heptafluorobutanoylcamphorate]-ligated oxovanadium(IV) catalyst. However, the monomeric and polymeric catalyst notably yielded products of opposite chirality. Modest stereoselectivity was seen for the Eu(III) catalyst, and in this case the polymeric and monomeric catalysts produced the same products.



94 **95**

(57)

Precipitation of the polymer-attached catalyst **95** can be used to recover the catalyst from the reaction mixture, and the catalyst can be reused in subsequent catalytic runs. Essentially 100% of the catalyst's activity was retained through seven cycles. However, while this catalyst and support are interesting, it is the reversal of stereoselectivity on supporting a catalyst on a polymer described here that is most notable. Such a stereochemical reversal has some precedent in other polymer systems (vide infra) but is still unusual. Such altered stereoselectivity suggests significant changes in the metal coordination environment occur in the presence of the polymer.

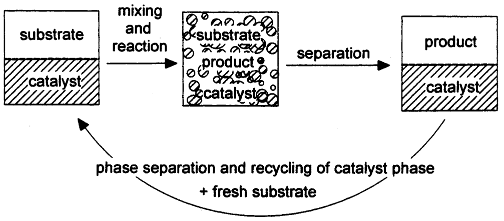
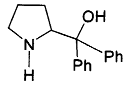


Figure 12. Scheme for recovering, separating, and reusing a soluble polymer-bound catalyst under aqueous biphasic conditions where the polymer-bound catalyst is designed to reside in the aqueous phase.

8. Polyacrylate-Supported Catalysts

Changes in enantioselectivity have also been seen in other polymer-supported systems.[132] Specifically when the chiral amino alcohol **96** was coupled to a copolymer of octadecyl methacrylate and 2-hydroxyethyl methacrylate, the enantioselectivity and the sense of the stereoselectivity of addition of Et_2Zn to benzaldehyde varied with the initial substrate ratio. Excess nucleophile (Et_2Zn) led to the (*S*)-1-phenylethanol product dominating, while an excess of benzaldehyde electrophile led to the (*R*)-1-phenylethanol product predominating.



96

E. Liquid/Liquid Separation of Water-Soluble Polymer-Bound Catalysts under Aqueous Biphasic Conditions

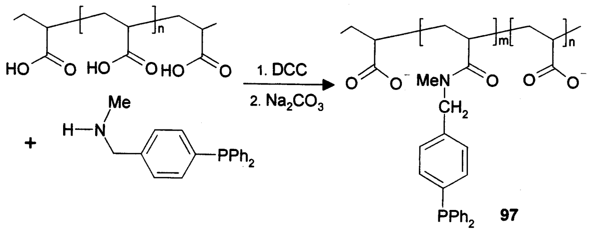
The use of environmentally benign solvents such as water for catalytic reactions is an attractive alternative to the use of organic solvents.[22] Most examples where homogeneous catalysts are used in water employ low molecular weight ligands that contain a polar group—tri- and monosulfonated triphenylphosphine being among the most common examples of a ligand that can be used to render a traditional transition-metal catalyst water soluble. Polymers too can serve this role. Examples of this include catalysts such as **7**, **12**, or **34**. Other examples include ligands and catalysts on pH-sensitive polymers. In some cases with polar substrates, monophasic aqueous chemistry can be used. However, in most cases, the hydrophobicity of most interesting organic materials dictates that biphasic conditions be used with water-soluble catalysts.

While water-soluble polymers have been used as macromolecular ligands to engineer water solubility into catalysts for reactions in water, the more common role of such polymers (and analogous low molecular weight ligands) is in aqueous biphasic catalysis. In this scheme (Figure 12), two phases are always present. The reaction can occur in the organic phase where the substrate resides, in the aqueous phase, or most commonly at the interface of the two phases.

The catalyst remains in the aqueous phase and is recycled simply by a liquid/liquid separation and reuse of the aqueous catalyst solution.

1. Water-Soluble Polymer-Bound Hydrogenation Catalysts Derived from Poly(acrylic acid) or Polyethylenimine Used under Biphasic Conditions

Andersson's group described both basic and acidic polymer supports that function in either of these roles.[105,106,133,134] The necessary phosphinated polymers were prepared using the chemistry in eqs 58 and 59 starting with either poly(acrylic acid) or poly(ethylenimine).



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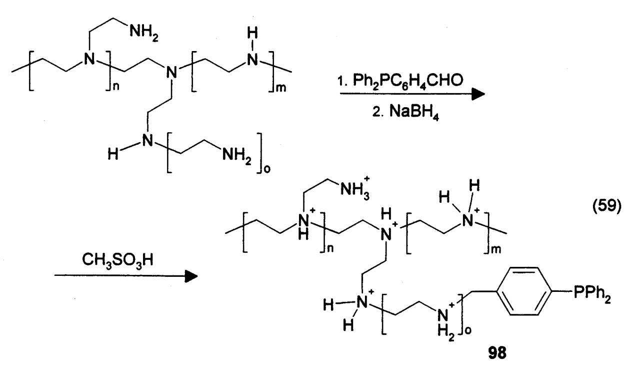
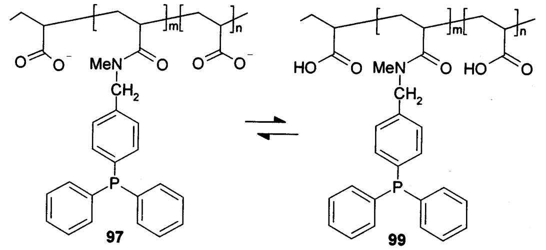


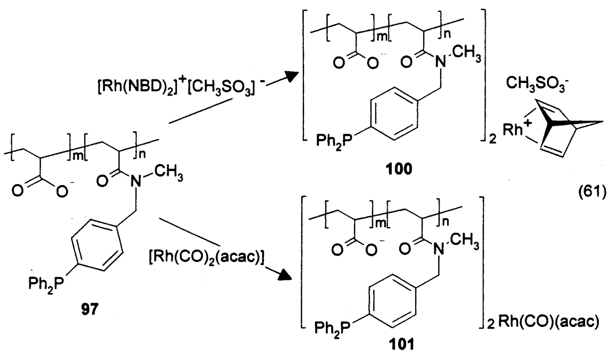
(59)

The solubility of ligand **97** or **98** depends on the phosphine loading and the pH of the solution. Under acidic conditions, the carboxylic acid groups of **97** are protonated and **99** forms (eq 60). In this state, the ligand has little solubility in water though it is soluble in methanol and some other organic solvents. Under basic conditions (pH > 7), the carboxylic acid groups of **97/99** are in the form of carboxylate groups and the resulting ligand prepared with a $-CO_2Na$:$-PPh_2$ molar ration of ca. 5:1 is soluble in water at a concentration of 0.17 N in phosphine at pH 8. The ligand derived from polyethylenimine has inverted pH-dependent solubility, being soluble only at pH < 6. At pH 3 a ligand with a N:P ratio of 7 has a solubility such that the phosphine ligand concentration is 0.21 N.



(60)

The ligands **97** and **98** were converted into water-soluble catalysts **100**−**103** using $[Rh(NBD)_2]^+CH_3SO_3^-$ or $[Rh(CO)_2(acac)]$ (eqs 61 and 62). The resulting hydrogenation or hydroformylation catalysts were soluble in water under basic conditions (**100**, **101**) or acidic conditions (**102**, **103**). The hydrogenation catalysts **100** and **102** were both active in biphasic hydrogenation of water-miscible substrates. Hydrogenation of a less water-soluble alkene such as 1-hexene required the addition of surfactants. The catalysts were suitable for biphasic hydrogenations, but recovery and recycling studies were not extensively described. Under some conditions, rhodium colloids form, complicating homogeneous catalyst recovery and reuse.



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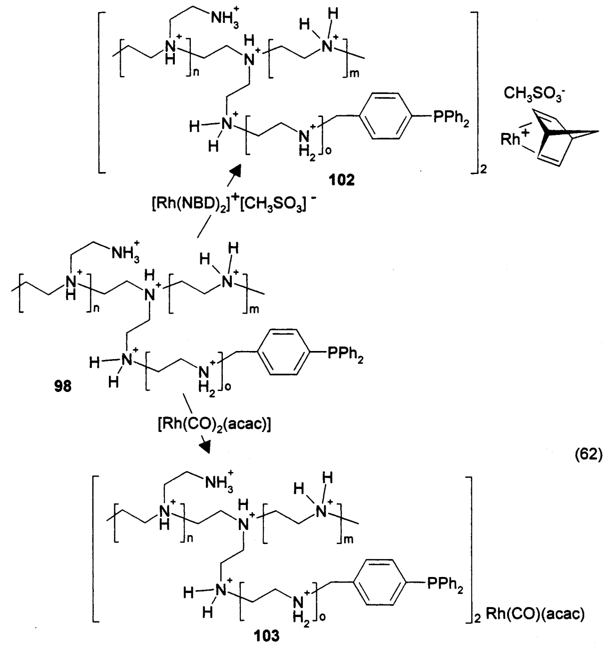


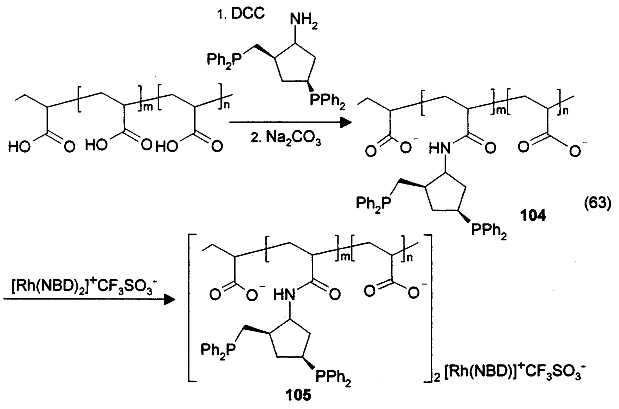
(62)

2. Water-Soluble Polymer-Bound Hydroformylation Catalysts Derived from Poly(acrylic acid) or Polyethylenimine Used under Biphasic Conditions

Hydroformylation with catalysts **101** and **103** was also attempted. However, while **101** was a competent hydroformylation catalyst under biphasic conditions and while it could be recovered using aqueous biphasic catalysis conditions with a basic aqueous solution, **103** was not suitable for hydroformylation. It was suggested that the acidic conditions required to dissolve **103** led to decomposition of the rhodium hydride intermediates.

3. Water-Soluble Polymer-Bound Asymmetric Hydrogenation Catalysts Used under Biphasic Conditions

Andersson was more successful preparing an asymmetric hydrogenation catalyst (eq 63) and then using this catalyst **105** in asymmetric hydrogenation under aqueous biphasic conditions (eq 64).[134] In this case, the aqueous catalyst solutions were separated and recovered using the scheme in Figure 12, washing the aqueous phase with organic solvent to remove any product. The enantioselectivity of the catalyst **105** was ca. 89% under biphasic conditions in hydrogenation of an α-acetoamidocinnamic acid, a value like that of the low molecular weight ligand. Rhodium concentrations in these biphasic asymmetric hydrogenations were in the 1−2 mM range.



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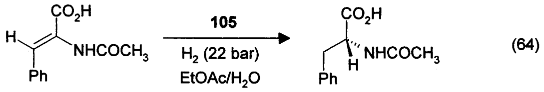
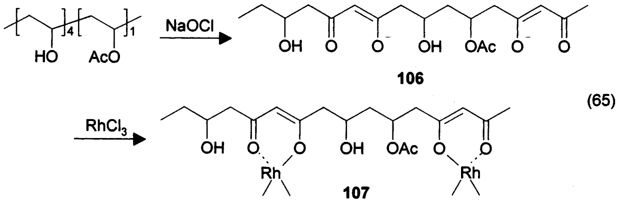


(64)

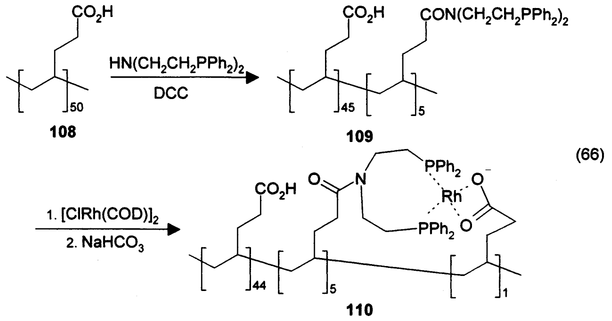
4. Modified Polymers as Supports for Hydroformylation Catalysis under Biphasic Conditions

Alper has described two approaches to the design of water-soluble polymer-supported catalysts for alkene hydroformylation under aqueous biphasic conditions.[135,136] In the first of these papers,[135] Alper and Chen used known oxidation chemistry to prepare a poly(enolate-*co*-vinyl alcohol-*co*-vinyl acetate) support starting with 80% hydrolyzed poly(vinyl acetate) (eq 65). This oxidation produced the polymer **106** that contained *β*-diketone groups. Such groups under basic conditions form a polymeric version of an acetylacetonate ligand that can in turn be used to form a Rh complex. The resulting catalyst **107** was successfully used in hydroformylation of 1-octene, converting 49% of this alkene in 28 h to a roughly equal mixture of 2-methyloctanal and nonanal. Using the recycling scheme in Figure 12, the catalyst was recycled three times without any effect on the activity or selectivity. No catalysis occurred in the organic phase, and this was used as evidence that the soluble polymer-bound Rh(I) catalyst resided exclusively in the aqueous phase. Kinetic studies showed that his system had TOFs (ca. 2×10^{-4} kmol (kg of Rh)$^{-1}$ s^{-1}) that were comparable to those measured for a biphasic hydroformylation of 1-octene using HRh(CO)(TPPTS)$_3$. Styrene and styrene derivatives were converted into aldehydes with good selectivity at 40 °C. However, under these conditions, conversions were low (<20% conversion in 22 h).



(65)

Alper subsequently showed that ligands derived from poly(4-pentenoic acid) (prepared by catalytic hydrocarboxylation of 1,2-polybutadiene) were better water-soluble supports for styrene hydroformylation catalysts.[136] Starting with poly(4-pentenoic acid) **108** (MW = 4900, PDI = 2.96), he prepared a chelating phosphine ligand using DCC and bis[(2-diphenylphosphino)ethyl]amine (eq 66). The resulting product **109**, which was characterized by ^{31}P NMR spectroscopy, contained a ca. 9:1 ratio of carboxylic acid to phosphinated carboxamide groups. Subsequent treatment of this phosphinated poly(4-pentenoic acid) polymer with [ClRh(COD)]$_2$ yielded a yellow solution of a Rh(I) complex, **110**. This Rh(I)-containing polymer was soluble in THF but could be isolated as an aqueous solution on treatment with aqueous bicarbonate. After removal of the water, the product was characterized by ^{31}P NMR (D$_2$O), ^{13}C NMR, and XPS spectroscopy. Elemental analysis showed that the phosphine loading was 0.58 mmol of phosphorus/g.



(66)

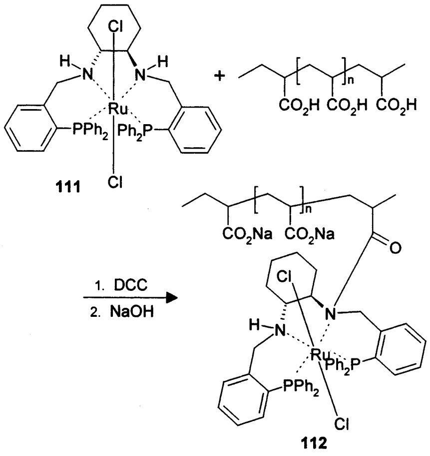
Use of this catalyst in hydroformylation of 1-octene and 1-dodecene was successful with complete conversion of these alkenes to a 2:1 mixture of linear/branched aldehydes occurring in 16 h at 90 °C. Vinyl ether substrates yielded predominately or exclusively branched aldehyde products, but in these cases the conversions were lower. The most promising results were obtained with vinyl arenes. Substrates such as styrene, 4-methoxystyrene, 4-halostyrene, and 2-vinylnaphthalene all yielded predominately high (>95%) yields of predominately (>10:1) branched products in 24 h at 70 °C using just 0.15 mol % catalyst **110**. These aqueous-phase catalysts were recycled three times with no change in activity and selectivity in the recovered catalyst. Atomic absorption analyses of the organic product phases showed no detectable rhodium, indicating that the catalysts did not leach detectable amounts of rhodium under the reaction conditions.

5. Proteins as Supports for Hydroformylation Catalysis under Biphasic Conditions

Proteins were used in early work to immobilize a homogeneous asymmetric hydrogenation catalyst.[22] They have also been used in aqueous biphasic hydroformylation reactions.[137] Human serum albumin was used as a macromolecular support to immobilize $Rh(CO)_2(acac)$ for hydroformylations carried out in a pentane/water mixture. While the structure and binding sites for Rh(I) in these proteins were not described, recycling of these protein-complexed catalysts was very efficient. The catalyst was recycled through 10 cycles, and atomic absorption analyses showed that only 8 ppm rhodium was lost into the organic phase.

6. Poly(acrylic acid)-Supported Ruthenium Transfer Hydrogenation Catalysts

Asymmetric transfer hydrogenations using a chiral ruthenium catalyst, **111**, attached to water-soluble poly(acrylic acid) using the chemistry shown in eq 67 were also successful.[138] The resulting catalyst **112** gave excellent yields (95%) and enantioselectivity (96% ee) in the reaction of acetophenone using 2-propanol as the solvent. While this catalyst was not used in an aqueous biphasic reaction, its high polarity and water solubility ensured that it completely precipitated on addition of hexane to the reaction solution. The recovered catalyst however had somewhat lower yields (89% and 80%) and enantioselectivities (80% and 77% ee) in the second and third cycles.



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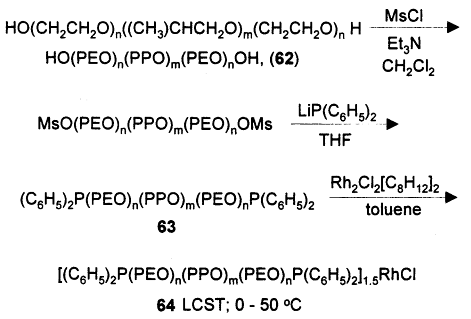
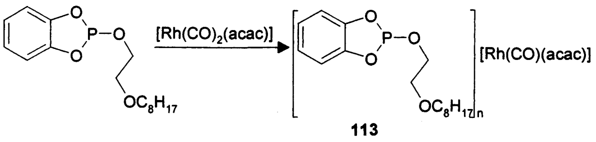
7. Polymers with Thermoregulated Solubility as Supports in Catalysis under Biphasic Conditions

Thermoregulated phase-transfer catalysis is an alternative to normal biphasic catalysis.[139,140] In this chemistry, heating is used to change the solubility of a catalyst in a biphasic mixture. By using polymeric supports whose water solubility decreases with temperature (e.g., the polymers with an LCST, vide supra), catalysts can be prepared that are at least partially soluble in the organic phase hot and only soluble in the aqueous phase cold. Such catalysts are used much like ordinary aqueous biphasic catalysts, but the problems of interfacial reactions or diffusion are minimized since the mixing process in Figure 12 essentially involves the catalyst dissolving in the organic phase. This chemistry has been reviewed.[139] It typically involves using poly(alkene oxide)-bound catalysts similar to those described in Scheme 1. Its advantage is that it avoids the problems of other biphasic reactions—diffusion of a hydrophobic organic substrate into a polar solvent or to an interface—since, under the reaction conditions, the catalyst goes to the phase where the substrate is (i.e., the organic phase).

Scheme 1. Synthesis of Poly(alkene oxide)-Triblock-Copolymer-Supported Catalysts That Have "Smart" Activity and Inverse Temperature-Dependent Solubility in Water[97]



A specific example of this thermoregulated phase-transfer catalysis that parallels some of the other biphasic chemistry discussed here is the use of the nonionic water-soluble poly(ethylene oxide)-bound phosphite-ligated rhodium catalyst for hydroformylation of styrene.[140] This catalyst was prepared using the chemistry in eq 68. The catalyst **113** prepared in this manner was not characterized but was presumed to be a phosphite-ligated Rh(I) compound. This catalyst was active both in hydrogenation and in hydroformylation chemistry. In hydrogenation of allyl alcohol in pure water, this Rh(I) catalyst exhibited the same on/off anti-Arrhenius behavior described earlier for other "smart" catalysts. In the case of **113**, hydrogenation of allyl alcohol ceased at 70 °C (above **113**'s LCST). Hydrogenation resumed at lower temperature (30 °C). This process was reversible.



(68)

The inverse temperature-dependent solubility of the polymer-bound catalyst **113** was used to advantage in the hydrogenation of styrene in a two-phase heptane/water mixture. In this mixture, hydroformylation of styrene was very efficient at 80 °C. Conversions were >99% in 6 h with 5 mPa of a 1:1 CO/H_2 mixture. The predominant product (ca. 80%) was the branched product 2-phenylpropanal. Heptane was judged to be a better solvent than toluene in these reactions on the basis of the observation that some color characteristic of the Rh(I) catalyst appeared in the toluene phase of a toluene/water mixture on cooling. Recycling in these cases involves a liquid/liquid separation and reuse of the aqueous phase.

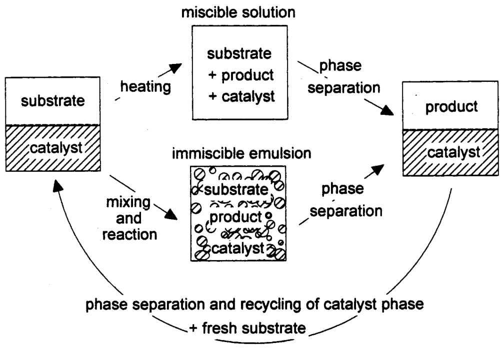


Figure 13. Scheme for recovering, separating, and reusing a soluble fluorinated polymer-bound catalyst under fluorous biphasic conditions where the polymer-bound catalyst is designed to reside in the fluorous phase. Reactions can be performed either in a biphasic emulsion or homogeneously by heating suitable thermorphoric fluorocarbon/organic mixtures that become miscible when hot.

8. Dendrimers as Supports for Catalysts under Biphasic Conditions

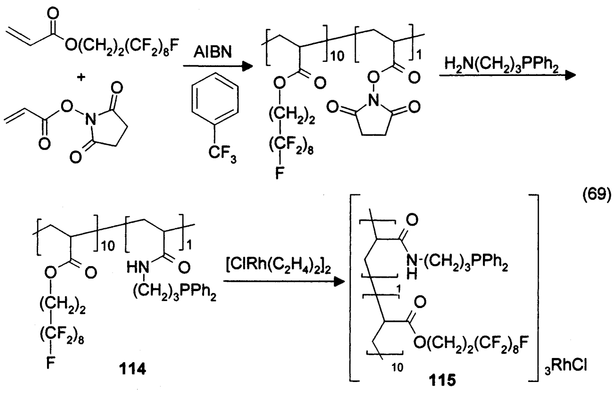
Water-soluble dendrimers can also be used in biphasic catalysis chemistry to engineer water solubility and phase separability into a catalyst. This area has recently been reviewed.[141]

F. Liquid/Liquid Separation of Fluorinated Polymer-Bound Catalysts under Biphasic Conditions

1. Fluorinated Acrylate Polymers as Fluorous-Phase-Soluble Supports

Fluorinated polymers have received less attention than other polymers in catalysis because of their lack of swellability and solubility. However, fluorous-phase catalysis has received significant attention as a simple way to carry out biphasic chemistry and as a simple method for catalyst separation and recovery.[142,143] As might be expected, fluorinated polymers can be used under these conditions and, as shown in Figure 13, they serve as generic fluorous-phase handles for catalysts.[144]

To prepare fluoropolymer-bound catalysts, copolymerization of a fluorinated acrylate ester with a reactive acrylate ester, *N*-acryloxysuccinimide (NASI), has proved to be a useful route to fluorous-phase-soluble polymers including phosphine-containing polymer **114** that can be used to complex Rh(I) and Pd(0) (eq 69).[145-147] Similar polymers can also be prepared with hydroxamic acid ligands and azo dyes.[60] All these polymers and the resulting catalysts are soluble in fluorinated solvents and insoluble in common organic solvents.



(69)

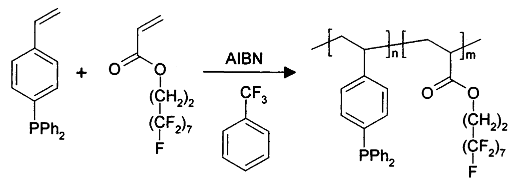
The Rh(I) hydrogenation catalysts were successfully used in hydrogenations both at atmospheric pressure and in a Parr hydrogenation apparatus (60 psi).[145] Turnover numbers for the catalyst **115** were in the 5000−10000 range (mmol of alkene hydrogenated/mol of Rh(I)). Catalyst activities in these biphasic systems were modest; turnover frequencies ranged from 16 to 60 mmol of H_2/(mmol of Rh(I) h). Exact TOFs varied depending on the polymer used and the alkene substrate. Most commonly less substituted alkenes were more reactive. The specific catalyst **115** shown above was recycled 15 times with no measurable loss in activity. Recycling involved simply allowing the biphasic organic/fluorocarbon mixture to stand and phase separate. The upper organic phase containing the product was then removed by forced siphon, fresh alkene substrate solution was added, the reaction vessel was repressurized, and the reaction was continued. In a typical experiment, In these recycling experiments, 0.05 g (~3 μmol of Rh) of the polymer-bound catalyst **115** in 5 mL of FC-77 and 2 mmol of various alkenes in 5 mL of THF were transferred quickly to the N_2-flushed hydrogenation vessel. The hydrogenation reaction was allowed to proceed overnight to ensure complete conversion of alkene to alkane, as evidenced by ^1H NMR analysis. Liquid separation of the fluorous phase containing **115** from the THF phase containing the alkane product was followed by introduction of another THF solution of substrate. Other catalysts prepared using a methacrylate monomer or with other fluoroacrylate esters were similarly recyclable.

2. Fluorinated Polyacrylates as Supports for Catalysts in Supercritical Carbon Dioxide

The fluorinated acrylate-bound ligands used successfully in hydrogenations in fluorous solvents can also be used to prepare homogeneous catalysts that dissolve in the environmentally benign solvent supercritical carbon dioxide, $scCO_2$. Recently Fackler and Akgerman reported that Rh(I) catalysts on these polymers can also be used for hydrogenation of 1-octene in $scCO_2$.[148] Hydrogenation of 1-octene in $scCO_2$ in the presence of such a fluoracrylate-ligated catalyst resulted in a quantitative conversion of 1-octene to octane within 12 h (reaction conditions: 33 °C, 2500 psi, catalyst:1-octene ratio (equiv/equiv) of 1:100). The catalyst was reportedly recoverable at the end of the reaction though details of the recovery process were not explicitly described in this preliminary report.[148]

3. Fluorinated Polyacrylate-co-Polystyrene Polymers as Fluorous-Phase-Soluble Supports

Fluorinated acrylate−styrene copolymers too have been used in fluorous-phase catalysis.[147] The necessary polymeric ligands were prepared by copolymerization of 4-diphenylphosphinostyrene with a fluoroacrylate (eq 70). Then a 2-fold excess of this fluorinated polymer (**116**) was dissolved in perfluoromethylcyclohexane and added to a toluene/hexane mixture containing [Rh(CO)$_2$(acac)]. Heating this mixture to 50 °C formed a single yellow phase that separated into two phases on cooling. Under biphasic conditions, all the Rh(I) was apparently attached to the polymer on the basis of the color of the fluorous and organic phases. TOFs of 136 (mol of aldehyde h^{-1})/mol of rhodium catalyst were obtained at 100 °C. The catalyst formed in situ from **116** and [Rh(CO)$_2$(acac)] is especially active and can be recovered. The activity of these catalysts in hydroformylation of hexane was such that the total turnover number of 140000 was obtained when the polymeric catalyst was allowed to react with a large excess of hexane for 58 h. Recovery of the catalyst involved simple phase separation and recycling as illustrated in Figure 13. Analysis of the organic phases indicated a loss of 1 ppm rhodium—a problem that the authors speculate can be solved by varying the organic solvent. A more pragmatic problem was loss of fluorocarbon solvent in recycling experiments.



116: n:m = 1:5 or 1:9

(70)

G. Liquid/Liquid Separation of Polymer-Bound Catalysts with Thermomorphic Solvent Mixtures

Liquid/liquid separations of nonpolar and polar solvents are very common in synthesis. Indeed, even when a synthetic procedure involves a distillation, a filtration, or a recrystallization, there are often intermediate separation steps that involve extraction. While most procedures for recovery of soluble polymers emphasize solid/liquid separations, liquid separations may have broad potential too because polymers in a biphasic system often have a profound phase preference for one phase over the other. Such a phase preference has already been described for the water-soluble and fluorous-phase-soluble polymers discussed above. However, both aqueous and fluorous biphasic catalysis typically involve reactions that occur under biphasic conditions—conditions that can pose kinetic limitations because of substrate solubility and interfacial reactivity issues.

1. Polar Polymers as “Normal” Thermomorphic Biphasic Catalyst Supports

To address the problems of biphasic reactivity but to advantageously use the biphasic separation properties of a polymer support, we recently introduced a thermomorphic scheme for catalyst recovery and reuse.[46,58,59] Figures 14 and 15 illustrate the two ways this scheme can be used for soluble polymer-bound catalyst separation, recovery, and reuse. In this scheme, polymers that have thermomorphic phase-selective solubility are used. Such polymers can be designed to be soluble in either a polar or nonpolar phase of a system that is biphasic at rest.[46,58] When an appropriate solvent system is chosen, heating produces a miscible solvent mixture from an initially immiscible biphasic system. In such cases, cooling of a hot miscible mixed solvent system then re-forms the biphasic mixture. Catalysts or ligands bound to soluble polymers in such a system can thus be used under monophasic conditions (e.g., at elevated temperature) if the polymer remains in solution. After reaction and cooling, these polymers and their associated ligands and catalyst can be recovered and separated from the product solution because the polymeric catalyst and products are in different phases of a biphasic mixture.

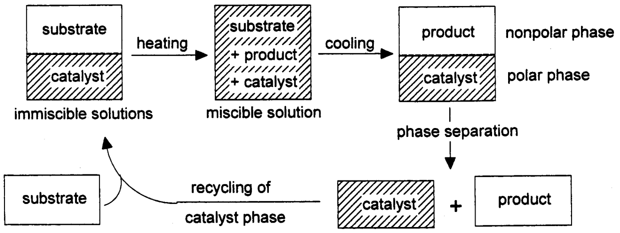


Figure 14. Scheme for recovering, separating, and reusing a thermomorphic soluble polymer-bound catalyst. In this normal thermomorphic system, a polar-phase soluble polymer is used so that the polymer and catalyst remain in the polar phase under biphasic conditions. On heating, the initially biphasic solvent mixture becomes miscible. The polymer-bound catalyst stays in solution, and a homogeneous monophasic reaction occurs. Cooling regenerates the biphasic conditions, and the polymer-bound-catalyst-containing phase is separated and recycled.

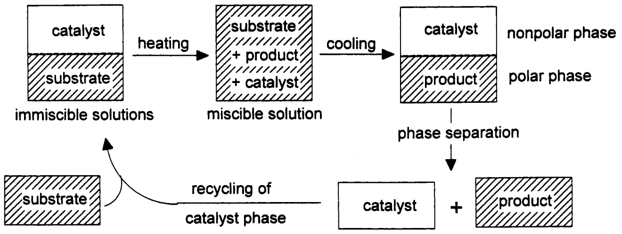
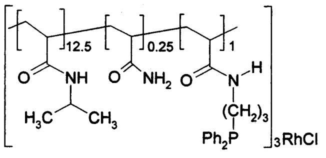


Figure 15. Scheme for recovering, separating, and reusing a thermomorphic soluble polymer-bound catalyst. In the inverse of this thermomorphic system, a nonpolar-phase soluble polymer is used so that the polymer and catalyst remain in the nonpolar phase under biphasic conditions. However, on heating, the initially biphasic solvent mixture becomes miscible. Since the polymer-bound catalyst stays in solution, homogeneous monophasic reactions occur. Cooling regenerates the biphasic conditions, and the polymer-bound-catalyst-containing phase is separated and recycled.

Solid/liquid separations may also be carried out in thermorphic systems (Figures 14 and 15). Though our work has focused on biphasic systems whose miscibility changes with temperature, Gladysz has noted that dramatic solubility/temperature dependence can also be seen with insoluble catalysts that have ca. 100-fold differences at hot versus cold temperatures.[149] This group correctly notes that these phase changes can be very useful in catalyst recovery. Polymers have already been used in this context (Figure 6).

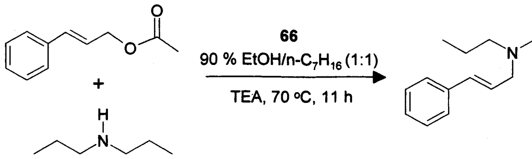
Polar polymers that have been used in normal thermomorphic separation include poly(ethylene oxide), poly(*N*-isopropylacrylamide), and dendrimers.[46,58] In the initial reports,[58,59] poly(*N*-isopropylacrylamide)-bound rhodium and palladium catalysts **18**, **66**, and **118** were prepared from a poly((*N*-isopropylacrylamide)-*co*-poly(*N*-acryloxysuccinimide) copolymer (cf. eq 44). These catalysts bound to a polar polymer dissolve in polar solvents such as ethanol, *N*,*N*-dimethylformamide (DMF), *N*,*N*-dimethylacetamide (DMA), and water. They are not soluble in solvents such as heptane or toluene. When these soluble polymer-bound catalysts are added to biphasic mixtures of heptane and ethanol/water (90% ethanol) or biphasic mixtures of heptane and DMF or DMA at room temperature, the polymer-bound catalysts are exclusively in the polar phase. These biphasic mixtures have complicated compositions reflecting some solubility of the nonpolar solvent in the polar solvents and some solubility of the polar solvent in the nonpolar solvent. However, the distribution coefficient of the polymer can be controlled so that all of the polymer (and all of the catalyst) is in a single phase. Such phase-selective solubility is easily tested using a dye-labeled polymer (e.g., a polymer such as **25** or **26**).



118

a. Hydrogenation Reactions Using Rhodium(I) Catalysts under Thermomorphic Conditions. The initial reactions that were studied under thermomorphic conditions were hydrogenations and allylic substitutions. Hydrogenations of alkenes such as 1-dodecene and 1-octene with a Rh(I) catalyst such as **118** in a mixture of 90% EtOH/H_2O and heptane were carried out. In this solvent mixture at 25 °C, no reaction occurred; the substrate alkene was exclusively in the heptane phase (K_D(alkene) > 1000 for $[\text{dodecene}]_{\text{heptane}}/[\text{dodecene}]_{\text{EtOH/H}_2\text{O}}$), and the polymer-bound catalyst was in the polar EtOH/H_2O phase (K_D(catalyst) < 0.002 for $[\text{catalyst}]_{\text{heptane}}/[\text{catalyst}]_{\text{EtOH/H2O}}$). However, at 70 °C, the heptane/EtOH/H_2O mixture containing the polymer-bound catalyst **118** and alkene substrate became homogeneous and reaction occurred. Under these homogeneous conditions, the catalyst was comparable to but slightly less active than $RhCl(PPh_3)_3$. However, unlike $RhCl(PPh_3)_3$, the polymer-bound catalyst **118** was successfully recycled by simply cooling and separating the polar and nonpolar phases. Addition of fresh substrate in heptane to the recovered ethanol phase containing the catalyst resulted in a fresh reaction. Recycling the catalyst four times in this manner resulted in no changes in activity.

b. Allylic Substitutions Using Palladium(0) Catalysts under Thermomorphic Conditions. The Pd(0) catalyst **66** was similarly recyclable. This catalyst was used in the allylic substitution shown in eq 71. The allylic tertiary amines prepared from cinnamyl acetate were formed regioselectively and were isolated from the heptane phase of a heptane/EtOH/H_2O mixture simply by removal of the heptane solvent. The catalyst was recyclable five times as long as adventitious oxidation of the oxygen-sensitive catalyst **66** was avoided. One potentially undesirable feature of this process is that isolated product yields in the first cycle or first few cycles are not always as high as in later cycles. This is because of some miscibility of the products in the polar phase—a problem that can be addressed by adding an extraction step. In multiple cycles this is not a problem because the other phase becomes saturated. This effect was first noticed with the allylic substitution shown in eq 71 where the isolated yields of *N*,*N*-dipropylcinnamylamine from the heptane phase were 80%, 98%, 98%, 100%, and 100% in cycles 1−5. Loss of a small amount of product in the first few cycles would not be a problem if the catalyst were recycled multiple times, and if desired, the material in the polar phase can be recovered by a heptane extraction.



(71)

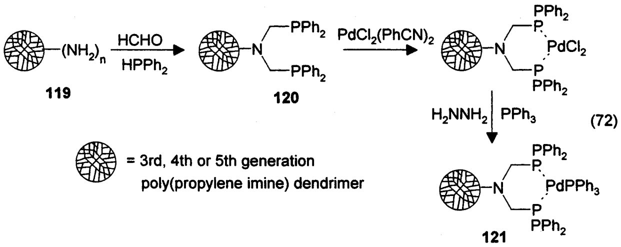
c. Heck Catalysis Using Palladium(0) and Palladium(II) Catalysts under Thermomorphic Conditions. In subsequent work, we extended the idea of using thermomorphic systems for soluble polymer-bound catalyst recovery and reuse to other Pd-catalyzed carbon−carbon-bond-forming reactions.[59] In this case, the catalysts used included **12**, **18**, and **66**.

Recyclable Heck, Suzuki, and Sonogashira couplings could be carried out using the Pd(0) catalyst **66** in a thermomorphic mixed solvent system using the protocol discussed above. Yields in the second or third cycle were all in the 95+% range. Conversions of the limiting iodobenzene reagent were quantitative by GC. While the thermomorphic heptane/EtOH/H_2O system discussed above proved suitable for iodobenzene couplings with *tert*-butyl acrylate, phenylboronic acid, or phenylacetylene, the styrene reaction did not occur readily in this solvent. A 1:1 (v/v) mixture of dimethylacetamide and heptane at 90 °C was used in this case. The use of a different solvent mixture in this case suggests that many other solvent mixtures can be used. Moreover, other work described in this paper showed that solvent mixtures where complete miscibility is not achieved are also practical for thermomorphic catalysis and catalyst recycling.

An important conclusion from this chemistry was that stable catalysts are more attractive in these recycling experiments. While a Pd(0) catalyst such as **66** was useful in this work, acting as a recoverable, recyclable catalyst in the conversion of aryl halides in a set of C−C-bond-forming chemistry, this catalyst is oxygen sensitive. It promotes phosphine ligand oxidation with trace amounts of oxygen. Such ligand oxidation is a general problem encountered in many recycling studies (vide supra), and when it occurs, it precludes further catalyst recycling. The catalysts **12** and **18** avoid this problem These catalysts too carry out Heck and Suzuki couplings with aryl iodides and are oxygen- and heat-stable.

2. Dendrimers as "Normal" Thermomorphic Biphasic Catalyst Supports

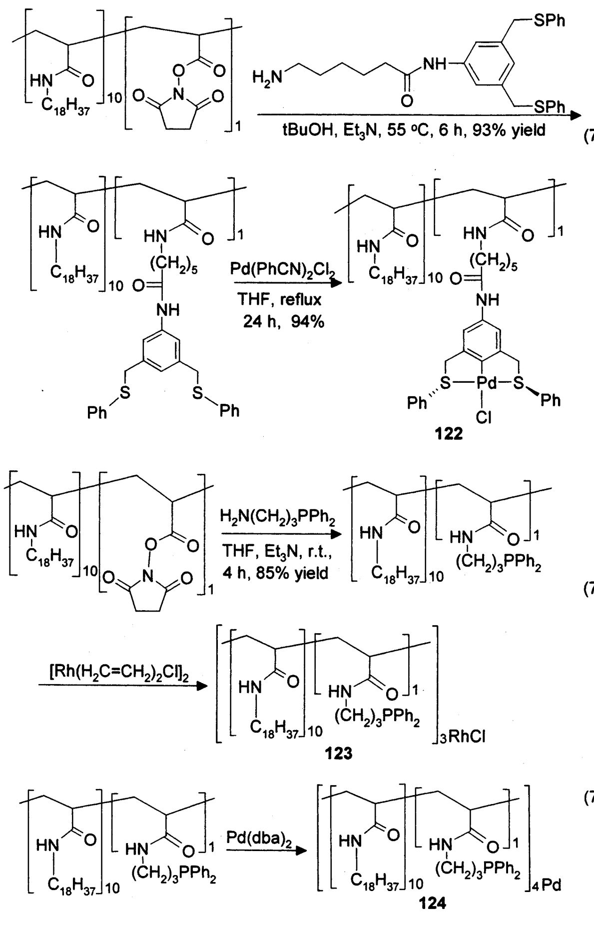
The idea of using a polymer as a phase anchor in a biphasic system whose miscibility changes with temperature should be broadly applicable and can be extended to polymers other than polyacrylamides. Indeed, poly(ethylene oxide)-supported Pd(II) catalyst was one of the catalysts used in the work discussed above. A recent report describing the use of recoverable, soluble polypropylenimine dendrimer-bound Pd(0) catalyst **121** prepared from an amine-terminated third-, fourth-, or fifth-generation polypropylenimine dendrimer, **119**, in allylic substitution chemistry in a thermomorphic heptane/*N*,*N*-dimethylformamide system further supports this premise.[150] In this case, dendrimer **120** with up to 64 diphenylphosphine groups on its periphery was prepared (eq 72) and used to complex a Pd(0) catalyst. The polar dendrimer-bound catalyst was found to be selectively soluble in the polar DMF phase of a DMF/heptane mixture at room temperature but remained in solution when these phases became homogeneous at 75 °C. In an allylic substitution with cinnamyl acetate and morpholine, this catalyst was recycled three times. On cooling, the polar and nonpolar phases phase separated and the dendrimer-bound catalyst was exclusively in the polar phase on the basis of ICP analysis that failed to detect Pd in the heptane phase (detection limit of 0.1 ppm). Liquid/liquid separation and addition of a fresh solution of substrate in heptane to the recovered DMF phase containing the dendrimer-bound catalyst allowed the catalyst to be recycled three times. In this case, thermomorphic recycling was found to be more convenient than solvent precipitation or membrane filtration.



(72)

3. Nonpolar Polymers as "Inverse" Thermomorphic Biphasic Catalyst Supports

The loss of product to the polar phase which was noted in some of the thermomorphic catalytic reactions discussed above can pose a more significant problem in cases where polar or heptane-insoluble products are formed. Moreover, many of the Pd-catalyzed reactions discussed above generate salt byproducts (e.g., $Et_3NH^+I^-$ in Heck reactions where Et_3N is used as a base). The development of inverse thermomorphic systems using nonpolar polymers addresses these issues.[46] In this case, the structural diversity inherent in the polymer support was used to prepare a polymer with profoundly different resting solubility in a biphasic resting system (Figure 15). Even subtle changes in polymer structure can significantly affect polymer solubility (e.g., the water solubility of poly(ethylene oxide) versus the water insolubility of poly(propylene oxide)), so it is expected that the use of poly(*N*-octadecylacrylamide)-*co*-poly(*N*-acryloxysuccinimide) in eqs 73–75 should produce polymer-bound catalysts whose solubility would be quite different from the solubility of **18**. Indeed the catalysts **122**–**124** are all insoluble in polar solvents and very soluble in heptane, and these catalysts can thus be used in an "inverse" thermomorphic system where the catalyst is recovered as a heptane solution after a Rh(I)-catalyzed hydrogenation or a Pd(0)- or Pd(II)-catalyzed carbon–carbon-bond-forming reaction. The success of such recycling is evidenced in a reaction such as eq 76 where the poly(*N*-octadecylacrylamide)-bound SCS–Pd(II) catalyst **122** (PNODAM–SCS–Pd(II)) was used successfully in nine cycles without any change in catalyst activity.



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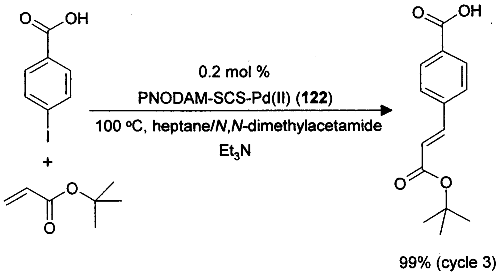

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H. Membrane Separations of Soluble Polymer-Bound Catalysts

Ultrafiltration techniques were used in some of the earliest work to recover soluble polymer-bound cata-

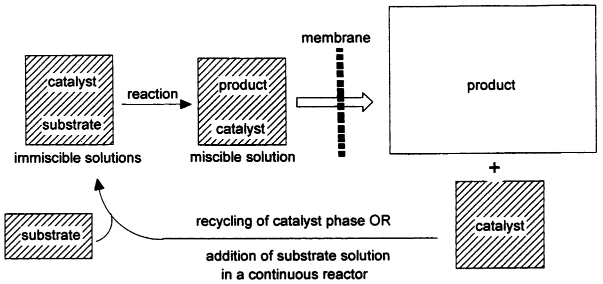
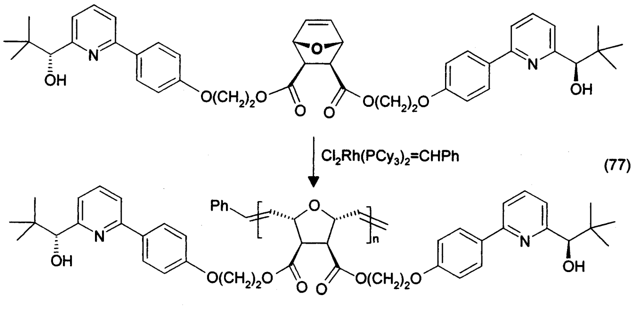


Figure 16. Membrane filtration of a soluble polymer- or dendrimer-bound catalyst from low molecular weight products. Recycling can involve either reuse of the clean catalyst solution or, in a continuous reactor, continuous addition of fresh substrate solution.

lysts.[15,36] This same approach continues to be of interest for recovery and reuse of soluble polymer-bound catalysts.[57] Most if not all of the examples of polymeric supports described above can be recovered and reused in this way though the efficiency of recovery may not always be high enough for practical use in a continuous reactor. Figure 16 schematically illustrates this approach to separation of soluble polymer-bound catalysts from products. Illustrative examples of various classes of polymer-supported catalysts recovered in this way are discussed below.

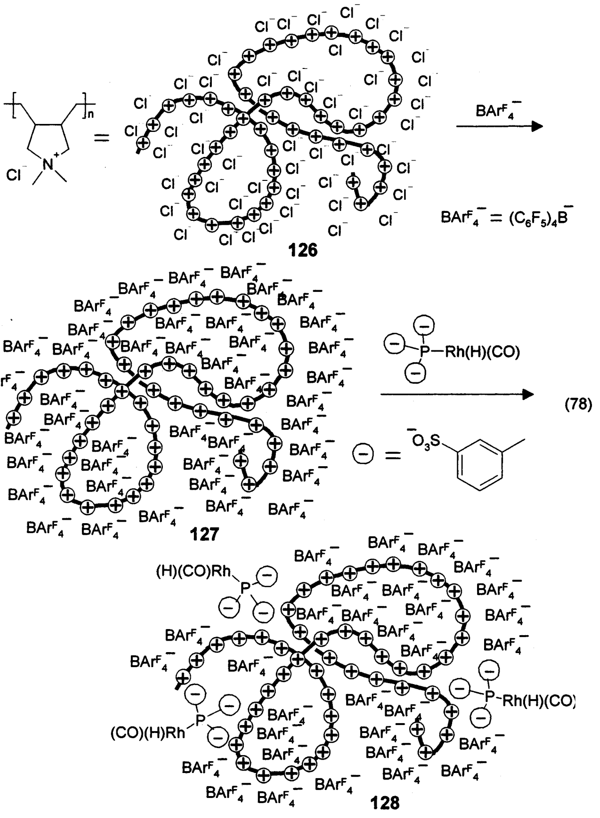
An example of a new type of polymer that has been used to support a catalyst that was recovered using ultrafiltration is the polymer **125** derived from a metathesis polymerization (eq 77).[151] This polymer contains a chiral hydroxypyridinyl ligand that was shown to be useful in Et_2Zn additions to benzaldehyde.[112] The size of this polymer was such that it could be separated from the products by ultrafiltration, and the authors noted that it thus might have application in a continuously operating flow reactor.



(77)

125: n = 20 - 100

Ultrafiltration was also used to recover catalytically active Rh(I) complexes that were ionically tethered to soluble polyelectrolytes.[152] The soluble polymer used in this example is poly(diallyldimethylammonium chloride) **126**. This polymer contains undesirable chloride anions that were first exchanged for $\mathrm{BAr^F}_4{}^-$ anions to form **127**. Exchange of some of these $\mathrm{BAr^F}_4{}^-$ anions ($(C_6F_5)_4B^-$) by $[HRh(CO)(NaTPPTS)_3]$ was then used to generate a polymer, **128**, with Rh(I) electrostatically bound to a methanol-soluble polymer (eq 78). The resulting catalyst was used in the hydroformylation of hexene. The activities of the resulting catalysts (TOFs of 160 mol/h) were comparable to those of a low molecular weight catalyst. In workup, a 50000 molecular weight cutoff poly(ether sulfone) membrane was used. A 10-fold amount of solvent with respect to the cell volume was pumped through the cell to separate the catalyst from the hydroformylation products. Atomic absorption spectroscopy showed that ca. 98% of the Rh(I) was recovered. While this is a retention of 99.8% of the Rh(I) per cell volume, the need for larger amounts of solvents and even a 0.2% loss of Rh(I) is probably not acceptable in an industrial process. However, the authors note that this loss of Rh(I) probably reflects adventitious phosphine ligand oxidation due to the excess solvent used and the handling. They speculate that this would not be a problem in a continuous reactor.



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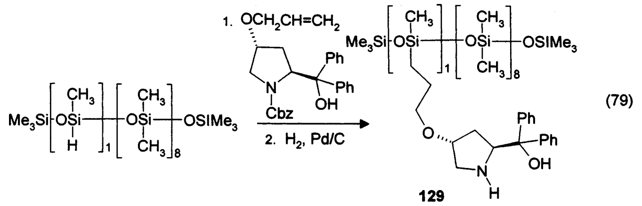
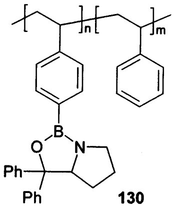
The effectiveness and durability of various membrane materials and membranes in recycling of Rh(I) attached to high molecular weigh soluble phosphinated polystyrene (MW = 270000) has been studied.[153] Partially hydrolyzed acetylcellulose, polysulfonamide, polyamide, and poly(vinylidene fluoride)-*co*-poly(tetrafluoroethylene) membranes were examined. The polysulfonamide membranes retained their productivity and permeability over almost a year in these experiments.

An oxazaborolidine catalyst, **129**, prepared from a methylhydrosiloxane–dimethylsiloxane copolymer containing 15% chiral *trans*-4-hydroxyproline monomer



(79)

(eq 79) has been used for asymmetric reductions of alkyl aryl ketones to the corresponding alcohols. Enantioselectivities in this reaction are high (>89%) as are the chemical yields. After such an asymmetric reduction, this soluble inorganic polymer-supported catalyst ligand was separated from the products and recovered by nanofiltration. These sorts of soluble polymeric ligands could be used in a continuously operated membrane reactor with good enantiomeric excess and high space−time yields. This particular system has also been compared and contrasted to a similar enzymatic reaction using a natural macromolecular catalyst, dehydrogenase, in a membrane reactor.[154] Other work from this same group showed that similar polystyrene-supported oxazaborolidine **130** could also be recycled in a continuously operated membrane reactor with measurably higher retention (99.94% for **130** versus 98.5% for **129**).[155,156]



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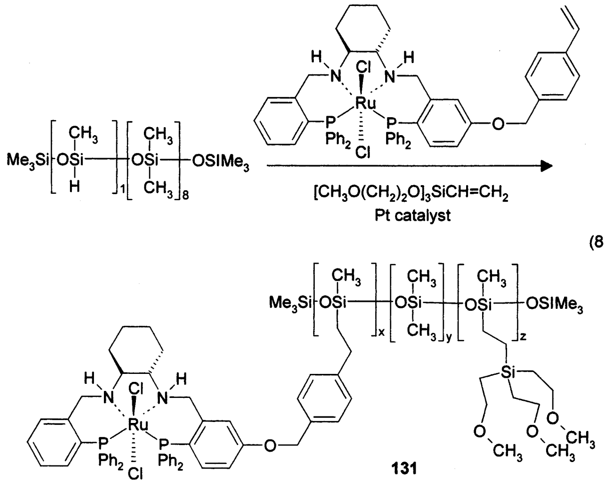
Siloxane polymer **131** prepared by hydrosilylation of a styrene derivative of a phosphinated chiral cyclohexane-1,2-diamine derivative (eq 80) were also used in a membrane reactor for transfer hydrogenation of acetophenone by the chiral ruthenium catalyst using 2-propanol as the hydrogen source.[157] Several aspects of this chemistry were noteworthy. First, the synthesis of **131** employed a hydrosilylation reaction with a mixture of the phosphinated cyclohexane-1,2-diamine substrate and $[(CH_3OCH_2CH_2)_3SiCH{=}CH_2]$. By varying the ratio of the diamine substrate to the vinylsilane, it was possible to "tune" the solubility of the resulting poly(dimethylsiloxane)-bound catalyst in much the same way solubilities of polyacrylamides were tuned (cf. eq 44). Second, in this example, the synthetic catalyst in a continuous membrane reactor was directly compared to a carbonyl reductase enzyme that also used 2-propanol as a reducing agent. The conclusion was that while the organic catalyst has some advantages with some substrates, the enzyme still had a higher total turnover number (TTN). The principle reason for this was that the enzyme was better retained by the membrane and more stable. In this case retention of **131** was 99.5%. Increasing this value to 99.9% would have increased this TTN value almost 6-fold.



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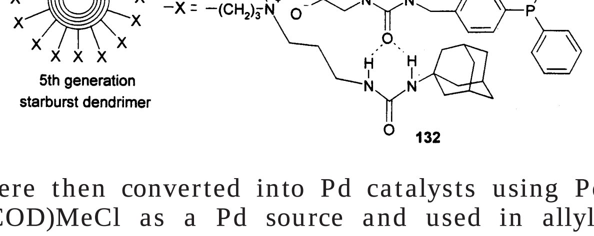
I. Separations of Soluble Catalysts on Dendrimers

Dendrimer-bound catalysts are especially attractive soluble polymer-bound catalysts since the polymer support is so well defined. Several recent reviews summarize this chemistry,[141,158−160] so only selected examples of dendrimer-supported catalysts that illustrate general separation issues are discussed here. In general, dendrimer supports provide several ways to separate and recover catalysts. The functional groups on their periphery can be used to alter the solubility of a catalyst immobilized in the dendrimer interior. In such cases, catalysts are typically recovered by one of the biphasic approaches discussed above or via a thermomorphic process.[150] Alternatively, dendrimers can be separated from low molecular weight products by membrane filtration. This was the original approach proposed in the earliest examples of dendrimer-supported catalysis.[161] Advantages of membrane separation of dendrimers has also been noted in combinatorial chemistry.[162]

Crooks has been a pioneer in developing dendrimer-bound colloidal catalysts.[163] The preparation of fluorous-phase-soluble dendrimers is one of the approaches his group has used to design recoverable catalysts. In these cases, the interior amine groups of a polypropylenimine dendrimer are first used to sorb a metal salt. Reduction then produces metal clusters that have catalytic activity. These dendrimers retain their peripheral amine groups, groups that can be modified with fluorinated surfactants that engender fluorous-phase or supercritical CO_2 solubility into the dendrimer-encapsulated metal catalyst. These soluble dendrimer-bound palladium clusters have been used both for Heck chemistry and in hydrogenations.[164−166]

DeGroot recently described modification of fifth-generation poly(ethyleneimine) dendrimers using urea groups.[167] The resulting peripherally modified dendrimers were then used to immobilize a phosphine ligand using urea acetic acid groups that could bind to the surface of these dendrimers by hydrogen bonds. The resulting phosphinated dendrimers **132** were then converted into Pd catalysts using Pd(COD)MeCl as a Pd source and used in allylic substitution of allylic acetates by secondary amines.



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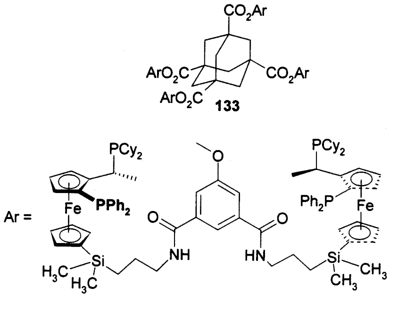
Good conversions were obtained. These noncovalently modified dendritic catalysts were recycled using a Koch MPF-60 NF membrane that had a 400000 molecular weight cutoff. Retention values as high as 99.9% were reported. The principle problem limiting the utility of this catalyst is a small amount of catalyst deactivation.

Dendrimer-bound chiral phosphine-based rhodium asymmetric hydrogenation catalysts that can be recovered by nanofiltration have been described.[168] Using known chiral ferrocenyldiphosphine ligands, the dendrimer **133** was prepared using an adamantane core. Then a cationic rhodium catalyst was prepared from this dendrimer that contained eight diphosphines on its periphery using $[Rh(COD)_2]BF_4$ as the rhodium source. This catalyst was active at 1 mol % loading in methanol, hydrogenating dimethyl itaconate in 98% ee. Reportedly this dendrimer-bound rhodium catalyst was "completely retained" using a membrane with a pore size of 3 kD. However, activities of the recycled catalyst were not described.



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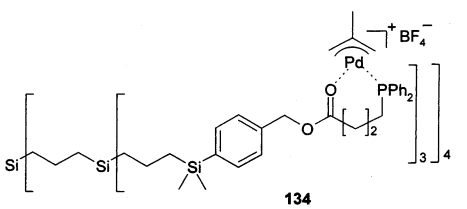
Main group organometallic carbosilane dendrimers provide another versatile platform for recovering and reusing catalysts. Such dendrimers have been studied in a variety of formats, supporting a variety of catalysts.[169] They can commonly be recovered using a membrane reactor. An example of this system is a recently reported palladium catalyst for hydrovinylation of styrene. This catalyst was based on a phosphinated carbosilane dendrimer, **134**. Again, the limitation for catalyst recycling seems to be catalyst stability.



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VI. Summary

Many approaches exist for batch and continuous recycling of soluble polymer-bound catalysts. This range of available procedures makes recovering a soluble polymer-bound catalyst both experimentally straightforward and practical. Such recovery operations are no more difficult than catalyst recycling using insoluble polymers. Soluble polymer-supported catalysts often have advantages of more facile characterization and very predictable reactivity. It is apparent that analogues of low molecular weight catalysts can now routinely be prepared that have activities and selectivities as high as those of their low molecular weight counterparts. Optimization of an individual process for a specific catalyst is still required though. Some other general problems remain. Soluble polymers still can affect catalyst activity. Extra synthetic work is typically necessary to immobilize a catalyst or to prepare the requisite ligand, and appropriate polymer supports are not as readily available commercially. Finally, there is a separate problem in that many homogeneous catalysts are not as inherently recyclable as desired. Such reuse problems sometimes are due to experimental problems associated with use and reuse of a catalyst (e.g., adventitious oxidation). In other cases, catalyst decomposition or ligand decomposition are inherent features of a given catalyst—features that might not always be apparent when a catalyst is used in a single use but that affect catalysts that have to be used multiple times.

VII. References

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