

Recoverable Catalysts and Reagents Using Recyclable Polystyrene-Based Supports

Catherine A. McNamara, Mark J. Dixon, and Mark Bradley*

Department of Chemistry, Southampton University, Highfield, Southampton, SO17 1BJ, United Kingdom

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Contents

1.0 Introduction	3275
1.1 Polystyrene Supports as Carriers for Reagents and Catalysts	3275
1.2 Catalyst and Reagent Attachment to Polymer Supports	3277
2.0 C–C Bond Formation Using Recyclable Resin-Based Reagents and Catalysts	3277
2.1 Palladium-Catalyzed Coupling Reactions	3277
2.2 Other Transition Metal Catalyzed Reactions	3279
2.3 Resin-Supported Olefin Metathesis	3280
2.4 Resin-Mediated Cycloaddition Reactions	3281
2.4.1 Diels–Alder Cycloadditions	3281
2.4.2 Resin-Based Catalysts for 1,3-Dipolar Cycloadditions	3282
2.5 Immobilized Chiral Ligands for Diethylzinc Additions to Aldehydes	3283
2.6 Miscellaneous: Other C–C Bond Forming Reactions	3285
3.0 Immobilized Oxidants	3286
3.1 Oxidation with Immobilized Transition Metal Complexes	3286
3.2 Alcohol Oxidation	3287
3.3 Alkene Oxidation	3289
3.3.1 Dihydroxylation	3289
3.3.2 Epoxidation	3289
3.3.3 Asymmetric Epoxidation	3290
3.3.4 Other Alkene Oxidation Reactions	3292
3.4 Potpourri: Other Immobilized Oxidants	3293
4.0 Immobilized Resin-Based Reductants	3294
4.1 General Reduction Processes	3294
4.2 Asymmetric Reduction of Ketones	3295
4.3 Alkene Reduction	3297
4.4 Resin-Based Tin and Germanium Reductants	3297
5.0 Conclusions	3297
6.0 Abbreviations	3298
7.0 Acknowledgments	3298
8.0 References	3298

1.0 Introduction

The massive increase in use and the broadening range of applications for polymeric supports in chemistry illustrate the immense significance of the technique to the chemist. The concept of performing traditional, solution-phase reactions under “pseudo homogeneous” conditions has rapidly expanded into

the domains of the medicinal, organic, organometallic, inorganic, and polymer chemist, each exploiting the benefits, first realized by the peptide chemist, for their own advantage.

Catalysts and reagents immobilized upon a range of insoluble supports have been utilized and reported since the late 1960s.¹ The advantages offered are a direct consequence of the polymer matrix. The main benefits are due to the ease of physical separation of the polymer and its bound component from the reaction mixture, the ease of recycling (especially with expensive catalysts and ligands), and the simplification of handling a range of toxic or odorous materials. Such immobilization also enables the use of high concentrations of reagents to drive reactions to completion, as byproducts or excess reagents can be easily removed by filtration, often eradicating the need for time-consuming, laborious purification steps such as chromatography, distillation, or crystallization. Another advantage is due to the unique microenvironment created for the reactants within the polymer support. Improved catalyst stability within the polymer matrix,² increased selectivity for intramolecular reactions,³ enhanced regioselectivity due to steric hindrance,⁴ and the superior activity of some supported chiral catalysts due to site cooperation⁵ have all been reported.

1.1 Polystyrene Supports as Carriers for Reagents and Catalysts

The supports that Merrifield utilized for his early work in solid-phase peptide synthesis were based on 2% divinylbenzene (DVB) cross-linked polystyrenes (PS).

PS is still one of the most popular polymeric materials used in synthesis due to its inexpense, ready availability, mechanical robustness, chemical inertness, and facile functionalization. The polymer is most commonly prepared by copolymerization with active monomers such as chloromethylstyrene or bromomethylstyrene, thus ensuring an even site distribution of the functionalized sites within the polymer matrix (Scheme 1). Various percentages and types of cross-linking agents have been incorporated into the PS resins, the most common being DVB, but other examples include ethylene glycol dimethylacrylate (EGDMA) and tetraethyleneglycol diacrylate (TEGDA) to give different solvation properties.

Typical supports used in early studies were 2% cross-linked (microporous or gel type resins) which



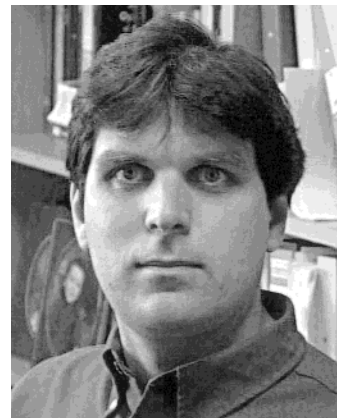
Catherine A. McNamara was born in St. Asaph, and grew up in Conwy, North Wales, before moving to Manchester, England, at the age of 15. She studied for her first degree at Southampton University and obtained her B.Sc. in Chemistry in 2000. She remained in Southampton to undertake her Ph.D. degree in the area of polymer-supported catalysts under the supervision of Professor Mark Bradley.



Mark J. Dixon was born May 17, 1976, and grew up in Rickmansworth, England. He studied for his first degree in Medicinal Chemistry at Leeds University. After graduating in 1997, he worked for 3 years for Nycomed Amersham PLC, where he was involved in the development of new radiopharmaceutical agents. Presently, he is pursuing his Ph.D. degree in chemistry at Southampton University under the guidance of Professor Mark Bradley, in the area of novel screening methodologies for combinatorial libraries.

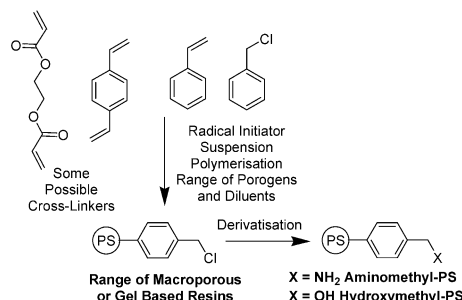
require solvent swelling for reagents to access internal functional groups.⁶ With PS resins this can sometimes be a problem, especially when protic, highly polar media such as alcohols and water are necessary, resulting in poor swelling and therefore poor site accessibility. The use of macroporous resins, which typically contain greater than 10–15% levels of the cross-linker, can overcome the need to swell the supports in a compatible solvent, due to them having a permanent pore structure.⁷ These polymers do not undergo significant swelling, and therefore reagents simply fill the pores throughout the polymer bead regardless of the reaction media. The macroporous resins can however sometimes suffer from poor loading capacity and brittleness. They must also be prepared with care to control pore size and available surface area.

To overcome some of the above limitations, 1 or 2% cross-linked polystyrene resins have been modified to improve the solvation properties of the supports. Predominant in this area has been the grafting of



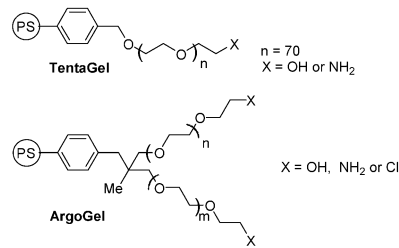
Mark Bradley was born in the United Kingdom in 1962. He received his first degree from the University of Oxford in 1986 and his Dphil degree from the same institution three years later under the supervision of Professor Sir Jack Baldwin in the area of penicillin biosynthesis. In 1989, he moved to the United States to work with Professor Chris Walsh at Harvard Medical School. He then returned to the United Kingdom and to Southampton University in 1992 as a Royal Society University Fellow. In 1997, he was made a Professor of Combinatorial Chemistry and has published in excess of 50 papers in the combinatorial area. In January 2000, he became Director of the Combinatorial Centre of Excellence now housed in Southampton. His research interests span across the whole area of combinatorial high-throughput synthesis, screening, and analysis from an academic viewpoint. This includes interests in solid-phase and small-molecule synthesis as well as combinatorial activities in the area of catalysts, dendrimers, fluorophores, and polymers. He has interests in the area of enzyme inhibition including work in the area of proteases, antibacterial agents, and antiparasitics.

Scheme 1. Synthesis and Derivatization of PS-Based Supports



poly(ethylene glycol) (PEG) onto the PS backbone. TentaGel and ArgoGel⁸ are two commercially available examples of this (Scheme 2), where the incorporation of the PEG chains dramatically increases resin compatibility with polar solvents.

Scheme 2. TentaGel and ArgoGel Supports



Reaction rates are generally presumed to be slower for polymer-supported reagents and catalysts compared to the analogous solution alternative. Some groups have studied the use of linear PS (no DVB) as a soluble “solid” support,⁹ the aim being to make

the heterogeneous species more solution-like. Although reaction rates might be improved, the polymers can be difficult to recover, often contaminating the product and complicating reuse. As in the area of synthesis on soluble polystyrenes, where the technique was largely abandoned in the early 1980s, this method seems unlikely to have much long-term utility.

1.2 Catalyst and Reagent Attachment to Polymer Supports

Three main methods of immobilization have been reported and discussed. These include: (a) entrapment, where a preformed catalyst is enveloped within a PS network, (b) ion-pairing where cations or anions are bound to complementary resin sites, and (c) covalent binding. Of these the latter two are by far the most commonly used due to their broad applicability, the fact that insignificant leaching is usually observed, and that stable, active catalysts and reagents are formed. Binding is usually effected in two ways: (a) grafting the catalyst or reagent onto the prederivatized support or (b) copolymerization of the active species with styrene and DVB. Both methods have been well documented.

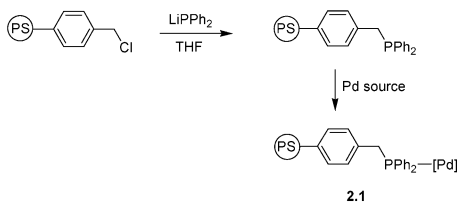
This article reviews the use of PS-based recyclable reagents and catalysts and has been arranged by reaction type. Where appropriate, stereoselective examples have been discussed as has the extent of viable recycling.

2.0 C–C Bond Formation Using Recyclable Resin-Based Reagents and Catalysts

2.1 Palladium-Catalyzed Coupling Reactions

Jang¹⁰ has reported the use of polymer-bound palladium catalyst **2.1** in the Suzuki coupling of a number of organoboranes with alkenyl bromides, iodobenzene, and aryl triflates, with the polymer-supported catalyst being prepared from Merrifield resin in two steps (Scheme 3). Selected results for

Scheme 3. Preparation of PS-Supported Pd Catalyst **2.1**



the reaction between a number of organoboranes and various alkenyl bromides (Scheme 4) are given in

Scheme 4. Suzuki Coupling of Organoboranes with Alkenyl Bromides Catalyzed by PS-Supported Pd Catalyst **2.1**

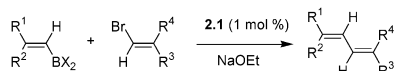


Table 1. The results obtained were good with isolated yields in the range 78–96%. Catalytic activity was

Table 1. Suzuki Coupling of Organoboranes with 1-Alkenyl Bromides with PS-Supported Pd Catalyst **2.1**

entry	R ¹	R ²	X	R ³	R ⁴	yield (%)
1	Ph	H	BDOB ^a	H	Ph	96
2	Bu	H	BDOB	Ph	H	91
3	Bu	H	BDOB	H	Ph	94
4	Bu	H	BDOB	Hex	H	89
5	Ph	H	BDOB	Me	Me	81

^a BDOB = benzodioxaborole.

at least comparable to homogeneous Pd(PPh₃)₄, and in some cases was significantly improved. The catalyst was reused more than 10 times with no decrease in activity, showing the huge utility of these supported catalysts.

Le Drian¹¹ investigated metal loss from the polymer **2.1** during the Suzuki reaction and also showed that variation of the Pd salt or complex used to prepare the catalyst had a significant effect on catalyst performance in the model reaction between phenylboronic acid and 4-bromopyridine (Table 2). The best catalysts were obtained from Pd(PPh₃)₄ (Table 2, entry 1). Even with very low levels of catalyst, good yields were achieved (Table 2, entry 2). In contrast, the catalyst prepared from PdCl₂ gave a yield of only 72% with a relatively large level of catalyst (Table 2, entry 3). Between 0.60 and 0.65% of the polymer-bound Pd was observed to be lost during a typical reaction. The catalysts were stable to heat and air and were reused five times without loss in activity.

Table 2. Effect of the Pd Source on the Suzuki Reaction Coupling Efficiency of Phenylboronic Acid with 4-Bromopyridine

entry	Pd source	mol % Pd	yield (%)
1	Pd(PPh ₃) ₄	3	94
2	Pd(PPh ₃) ₄	0.1	90
3	PdCl ₂	13.5	72
4	Pd(CH ₃ CN) ₂ Cl ₂	4.4	85
5	Pd(dba) ₂	1	90
6	Na ₂ PdCl ₄	1	87

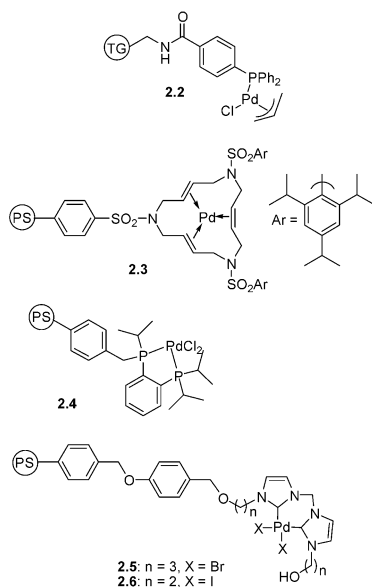
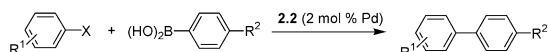
The same PS-supported Pd catalyst has been incorporated into resin beads sintered within an inert high-density polyethylene matrix (to give so-called resin “plugs”, that enable the handling of discrete packages of resin).¹² Synthesis of the Pd catalyst was completed as in Scheme 3, using Pd(PPh₃)₄ as the Pd source. Use of the “plugs” during a Suzuki coupling reaction of boronic acids and aryl iodides was investigated and compared to solution based Pd(PPh₃)₄.¹³ Yields were in the range 71–92%, and the two methods were comparable (Table 3). Repeated reuse (four times demonstrated) showed only a small decrease in yield.

The PS–PEG-supported triarylphosphine-palladium complex **2.2** (Scheme 5) has been used to catalyze allylic substitutions, the Suzuki reaction, and the hydroxycarbonylation of aryl halides.^{14–16} Thus, when **2.2** was examined in the reaction of a series of aryl halides and arylboronic acids (Scheme 6) yields were generally good (70–91%) (Table 4). It is of note that, in the presence of **2.2**, the reaction proceeded at a significantly lower temperature (25 °C) than usually

Table 3. Comparison of Yields for the Suzuki Coupling of Aryl Iodides and Boronic Acids Using Pd "Plugs" and Pd(PPh₃)₄

entry	RB(OH) ₂	RI	yield ^a (%)
1	C ₆ H ₅	<i>p</i> -Me C ₆ H ₅	82 (83)
2	C ₆ H ₅	<i>p</i> -NHAc C ₆ H ₅	78 (81)
3	<i>p</i> -Me C ₆ H ₅	C ₆ H ₅	86 (86)
4	<i>p</i> -Me C ₆ H ₅	<i>p</i> -NHAc C ₆ H ₅	71 (78)
5	<i>p</i> -OMe C ₆ H ₅	<i>p</i> -NHAc C ₆ H ₅	87 (87)
6	<i>p</i> -OAc C ₆ H ₅	C ₆ H ₅	92 (95)

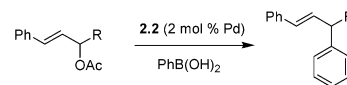
^a Yields in parantheses are for those obtained with Pd(PPh₃)₄

Scheme 5. PS-Supported Pd Catalysts 2.2–2.6**Scheme 6. Suzuki Coupling of Aryl Halides and Aryl Boronic Acids Catalyzed by PS-PEG-Supported Triarylphosphine Pd Complex 2.2****Table 4. Suzuki Coupling of Aryl Halides with Aryl Boronic Acids Catalyzed by PS-PEG-Supported Triarylphosphine-Pd Complex 2.2**

entry	R ¹	X	R ³	yield (%)
1	C ₆ H ₅	I	H	88
2	C ₆ H ₅	I	Me	91
3	C ₆ H ₅	I	OMe	72
4	C ₆ H ₅	Br	H	77
5	C ₆ H ₅	Br	Me	82
6	C ₆ H ₅	Br	OMe	70
7	<i>o</i> -Me C ₆ H ₅	I	Me	80
8	<i>p</i> -Me C ₆ H ₅	I	Me	79

required when soluble Pd-phosphine complexes are employed (typically 80 °C or more).¹⁷

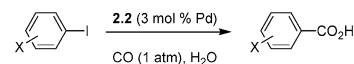
2.2 was found to catalyze the allylic arylation of primary and secondary allyl acetates in aqueous media with phenylboronic acid (Scheme 7), with good results (Table 5). For the reaction of 1-phenyl-3-acetoxybutene, the yield obtained with **2.2** (Table 5, entry 2) compared very favorably with those obtained with either TPPTS, a water soluble Pd complex (Table 5, entry 3), or with Pd(PPh₃)₄ (Table 5, entry 4). The recovered catalyst was reused, after a simple washing procedure, with no loss of activity.

Scheme 7. Allylation of Phenylboronic Acid Catalyzed by PS-PEG-Supported Triarylphosphine Pd Complex 2.2**Table 5. Catalysis of the Allylic Arylation of Allyl Acetates in Aqueous Media by PS-PEG-Supported Triarylphosphine-Pd Complex 2.2**

entry	R	catalyst	yield (%)
1	H	2.2	99
2	Me	2.2	99
3	Me	Pd/TPPTS ^a	15
4	Me	Pd(PPh ₃) ₄	14
5	Et	2.2	90
6	Hex	2.2	85

^a Derived in situ by mixing di(*μ*-chloro)bis-(*η*-3-allyl)dipalladium(II) and phosphine.

2.2 was also found to be an effective catalyst for the hydroxycarbonylation of aryl halides (Scheme 8).¹⁸ Under optimum conditions, a variety of aryl

Scheme 8. Hydroxycarbonylation of Aryl Iodides Catalyzed by PS-PEG-Supported Triarylphosphine Pd Complex 2.2

iodides were converted to the corresponding carboxylic acids in good to quantitative yield (Table 6). Reuse of the catalyst was investigated using iodobenzene. No decrease in yield was observed after 30 reactions using the same catalyst, while the average yield over these 30 reactions was 97%!

Table 6. Hydroxycarbonylation of Aryl Iodides in Water Catalyzed by PS-PEG-Supported Triarylphosphine-Pd Complex 2.2^a

entry	X	base	yield (%)
1	H	K ₂ CO ₃	97
2	<i>o</i> -CH ₃	KOH	96
3	<i>m</i> -CH ₃	K ₂ CO ₃	99
4 ^b	<i>p</i> -CH ₃	KOH	100
5 ^b	<i>p</i> -OCH ₃	KOH	96
6 ^{b,c}	<i>p</i> -Cl	K ₂ CO ₃	99
7 ^b	<i>o</i> -Br	K ₂ CO ₃	100
8 ^b	<i>p</i> -NO ₂	K ₂ CO ₃	100
9	<i>m</i> -COOEt	K ₂ CO ₃	93

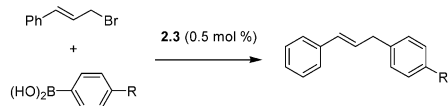
^a All reactions carried out in water under carbon monoxide (1 atm) at 25 °C for 12–20 h, unless otherwise stated.

^b Benzene used as a co-solvent. ^c Reaction for 40 h.

Miyaura¹⁹ has investigated the use of PS-bound Pd **2.1** in cross-coupling reactions and successfully extended the range of applicable substrates. Tollyboronic acid was thus coupled to a number of chloropyridines, activated chloroarenes, and chloroquinoline. Yields were generally in the region of 90%, and the catalyst was reused six times without loss of activity, although the appearance of the polymer was reported to change from yellow to gray.

The PS-bound 15-membered, cyclic triolefin Pd complex **2.3** has been used as a catalyst in Suzuki-type couplings of cinnamyl bromide with a number

Scheme 9. Suzuki Coupling of Cinnamyl Bromide with Arylboronic Acids Catalyzed by Cyclic Triolefin Pd Complex 2.3



of aryl boronic acids (Scheme 9).²⁰ The coupling reaction for each substrate was repeated five times, recycling the same resin for each subsequent reaction. Results are summarized in Table 7.

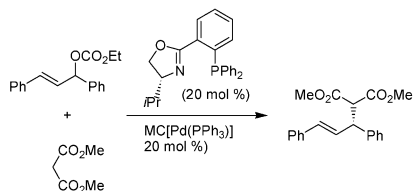
Table 7. Suzuki Coupling of Cinnamyl Bromide and Aryl Boronic Acids Catalyzed by Cyclic Triolefin Pd Catalyst 2.3^a

entry	R	yield (%) ^b
1	CF ₃	85–98
2	Br	83–95
3	Cl	84–92
4	H	85–98
5	OMe	82–97

^aAll reactions carried out in toluene at 80 °C. ^bYield represents range of five reuses.

Kobayashi²¹ has reported the use of microencapsulated (MC) Pd(PPh₃)₄ for catalysis of both Suzuki coupling and allylic substitution reactions. The catalyst was prepared by the addition of Pd(PPh₃)₄ to a cyclohexane solution of linear PS (*M_w* ca. 280 000) at 40 °C followed by cooling to 0 °C. After addition of hexane to harden the polymer capsule the MC catalyst was collected by filtration. Reaction conditions were optimized for the reaction between allyl methyl carbonate and dimethyl phenylmalonate. Best results were achieved using 20 mol % of catalyst and 20 mol % of PPh₃ as an external ligand. These conditions were then used for a series of allylic substitution reactions between allylic carbonates and either malonates or β-ketoesters. Yields were generally high and the palladium catalyst was recovered quantitatively and reused with no loss of activity after five cycles of use. The catalyst was also shown to be active in the Suzuki coupling of boronic acids with aryl bromides. In addition, asymmetric allylation was carried out using MC Pd and a soluble chiral ligand (Scheme 10). The reaction was found to proceed in good yield (87%) and e.e. (83%).

Scheme 10. Asymmetric Allylation Using MC Pd(PPh₃)₄



PS-supported 1,2-bis(diisopropylphosphino)benzene Pd(II) complex **2.4** (Scheme 5) has been shown to catalyze the Heck reaction.²² The polymer-supported catalyst was found to have a higher turnover number than either its solution analogue or Pd(OAc)₂/PPh₃. This finding was attributed to deactivation of the soluble catalysts by aggregation or by

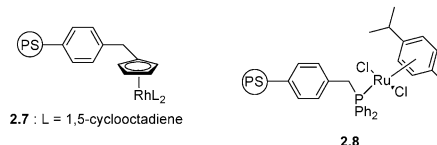
equilibration to a sterically blocked tetraphosphino complex. The catalyst was stable to air and was reused five times with no appreciable loss of activity.

The PS-supported “carbene” Pd complexes **2.5** and **2.6**, linked to the polymer support via the Wang linker, have been reported to be efficient air-stable, recyclable catalysts for the Heck reaction during the coupling of a number of aryl halides and alkenes.²³

2.2 Other Transition Metal Catalyzed Reactions

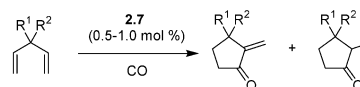
Eilbracht has reported the preparation of PS-supported rhodium complex **2.7** (Scheme 11) and its

Scheme 11. PS-Supported Catalysts 2.7 and 2.8



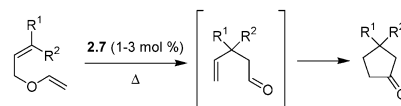
application for the synthesis of cyclopentanones.²⁴ Initially, the hydrocarbonylative cyclization of substituted 1,4-dienes was investigated (Scheme 12). The

Scheme 12. Hydrocarbonylative Cyclization of Substituted 1,4-Dienes Catalyzed by PS-Supported Rh Complex 2.7



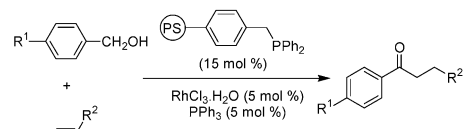
desired cyclopentanones were obtained in high overall yield, and the ratio of saturated and unsaturated products could be controlled by varying the pressure of carbon monoxide and the reaction time. Reuse of the catalyst was reported with no loss of activity. In an alternative approach, cyclopentanones were prepared in a one-pot approach by Claisen rearrangement of allyl vinyl ethers followed by rhodium-catalyzed “hydroacylation” (Scheme 13). Under optimized conditions, yields of 95% were obtained, and the catalyst could be reused with no loss of activity.

Scheme 13. One-Pot Synthesis of Cyclopentanones Catalyzed by PS-Supported Rh Complex 2.7



Jun²⁵ has reported the use of a PS-supported rhodium complex as a catalyst during the reaction of benzyl alcohols with terminal alkenes to give ketones (Scheme 14). The catalyst was generated in

Scheme 14. Ketone Synthesis Catalyzed by in Situ Generated Rh Catalyst

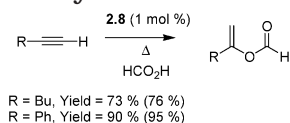


situ from PS-supported diphenylphosphine, RhCl₃·xH₂O and PPh₃. Yields were in the range 48–

77%. The catalyst formed was reused three times for each substrate with no decrease in activity.

The PS-supported arene ruthenium complex **2.8** has been reported to be a reusable catalyst for both enol formate synthesis and olefin cyclopropanation reactions.²⁶ The regioselective addition of formic acid to a range of terminal alkynes and diynes in the presence of **2.8** was investigated and compared to the nonsupported analogue (Scheme 15). Conversion to the corresponding enol formates was achieved in good yield. Similar results were observed for the olefin cyclopropanation of styrene, 4-methylstyrene, and α -methylstyrene with ethyl diazoacetate in the presence of **2.8**. The catalyst was reused five times with no loss of activity.

Scheme 15. Enol Formate Synthesis Catalyzed by PS-Arene Ru Catalyst **2.8**^a

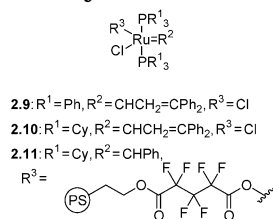


^a Yield using monomeric analogue in brackets.

2.3 Resin-Supported Olefin Metathesis

A number of PS-supported ruthenium complexes have been reported to catalyze olefin metathesis reactions. Grubbs²⁷ reported the preparation of a series of PS-supported ruthenium vinyl-carbene catalysts, which were based on the soluble complexes **2.9** and **2.10** (Scheme 16). These are known to catalyze the ring-opening metathesis polymerization (ROMP) of cyclic olefins and the metathesis of acyclic olefins.^{28,29} The complexes were tethered to the solid support by phosphine exchange with phosphine-functionalized PS resins in a manner analogous to the immobilization of Pd(0). The supported complexes have been found to exhibit similar catalytic properties to their homogeneous analogues, but reaction times are somewhat increased. Reuse showed a loss of catalytic activity of approximately 20% per cycle.

Scheme 16. Ru Catalysts **2.9**–**2.11**



In a slightly different approach, Mol³⁰ described the immobilization of a related ruthenium complex, **2.11**. Improved catalytic activity was observed for metathesis of internal alkenes. Recycling of the catalyst was investigated using the ring closing metathesis (RCM) of diethyl diallylmalonate as a model reaction, but a similar loss in activity to that reported by Grubbs was observed.

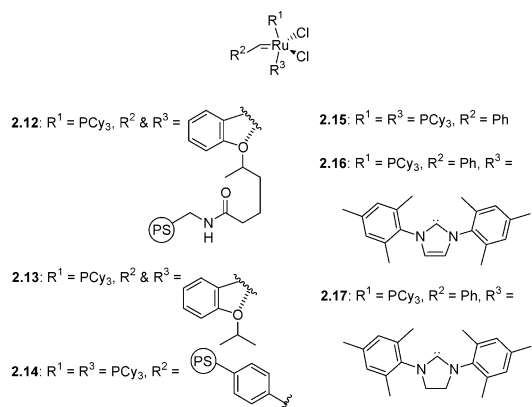
Dowden³¹ has reported the preparation and use of a particularly stable PS-supported ruthenium complex **2.12** in both RCM and cross metathesis reactions. The polymer was based on the homogeneous complex **2.13**.^{32,33} In a series of RCM reactions in the presence of **2.12**, good to quantitative yields were

obtained, with reactions carried out in air. Good yields were obtained over five runs using recycled catalyst, without the use of stabilizing additives.

Barrett³⁴ has described the use of the PS-supported precatalyst **2.14** in olefin metathesis. The so-called “boomerang” catalyst becomes homogeneous for the course of the reaction and is recaptured by the resin once the reaction is complete. Comparison with the homogeneous catalyst **2.15** for the RCM reaction of a number of diene substrates gave near identical results. Studies into the levels of ruthenium contamination in the RCM products revealed an approximate 10-fold decrease when compared to the homogeneous catalyst. Limited reuse of the PS-supported catalyst was possible with the addition of 1-hexene to the reaction mixture to reduce deactivation of the “carbene” species. A second-generation “boomerang” ruthenium catalyst has since been reported that catalyzed four consecutive RCM reactions with very little loss of activity.³⁵ The catalyst was based on the significantly more stable imidazolylidene-ruthenium complex **2.16**.^{36,37}

Nolan³⁸ immobilized RCM precursors **2.15**–**2.17** (Scheme 17) onto macroporous PS via impregnation.

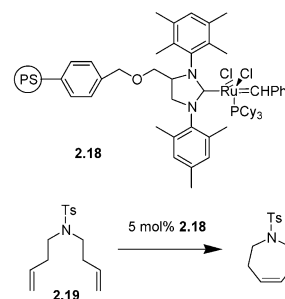
Scheme 17. Ru Catalysts **2.12**–**2.17**



All three polymer-supported catalysts were found to be efficient “boomerang” catalysts for the RCM of diethyl diallylmalonate with activity similar to that of the unsupported analogues and could be recycled four times without significant loss of activity. Catalyst **2.17** was found to be the most active for unhindered substrates, but the relative activity was found to be substrate dependent.

Blechert³⁹ reported the synthesis of the permanently immobilized olefin metathesis catalyst **2.18** (Scheme 18). This was used to catalyze olefin me-

Scheme 18. PS-Supported Catalyst **2.18** and Diene **2.19**



tathesis reactions including the formation of 7- and 15-membered rings and the generation of bicyclic structures. The complete cyclization of **2.19** (Scheme 18) was achieved by recycling the catalyst four times.

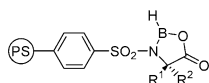
2.4 Resin-Mediated Cycloaddition Reactions

2.4.1 Diels–Alder Cycloadditions

With the formation of two new carbon–carbon bonds and four stereogenic centers, the Diels–Alder cycloaddition reaction is widely used in organic synthesis. Asymmetric Diels–Alder reactions using chiral catalysts have been extensively studied, and a number of highly efficient solution-phase catalysts have been reported.⁴⁰ Significant effort has also been applied to the immobilization of these catalysts onto a variety of supports.⁴¹

Itsuno⁴² investigated the use of both copolymerization and grafting methodologies for the preparation of a small number of PS-bound chiral oxazaborolidinone catalysts. Immobilized catalysts **2.20–2.23** (Scheme 19) were prepared, derived from the amino acids L-valine, L-isoleucine, D-phenylglycine, and L-threonine, respectively, and the model reaction between methacrolein and cyclopentadiene investigated (Scheme 20). The reaction, which essentially does not occur in the absence of catalyst, proceeded smoothly at $-78\text{ }^{\circ}\text{C}$ in the presence of all four catalysts. The best results were observed with **2.20**, which gave >99% of the exo product in 65% e.e. (Table 8, entry 1). Identical results were reported for recycled **2.20** (Table 8, entry 2).

Scheme 19. PS-Supported Catalysts **2.20–2.21**



2.20: $R^1 = \text{H}$, $R^2 = \text{CH}(\text{CH}_3)_2$
2.21: $R^1 = \text{H}$, $R^2 = \text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$
2.22: $R^1 = \text{Ph}$, $R^2 = \text{H}$
2.23: $R^1 = \text{H}$, $R^2 = \text{CH}(\text{OH})\text{CH}_3$

Scheme 20. Model Diels–Alder Cycloaddition of Methacrolein with Cyclopentadiene

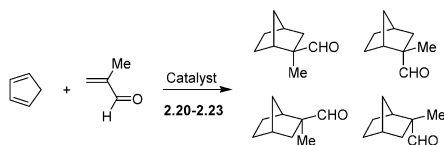


Table 8. Reaction between Methacrolein and Cyclopentadiene in the Presence of Oxazaborolidinone Catalysts **2.20–2.23**

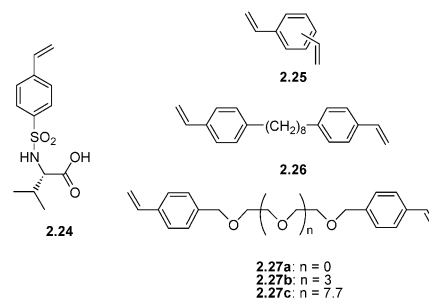
entry	catalyst	yield (%)	endo:exo	e.e. (%)
1	2.20	87	< 1:99	65
2	2.20 ^a	93	< 1:99	65
3	2.21	99	3:97	49
4	2.22	99	4:96	49
5	2.23	65	8:92	10

^a Recycled catalyst.

This study was later extended when the effect of the degree of resin cross-linking on catalytic properties was investigated.⁴³ A series of chiral oxazaborolidinone containing polymers were prepared and

evaluated. The copolymerization of monomer **2.24** with styrene and the cross-linking agents **2.25**, **2.26**, and **2.27a–c** (Scheme 21) furnished a series of

Scheme 21. Monomer **2.24** and Cross-Linking Agents **2.25**, **2.26**, and **2.27a–c**^a



^a Used in the Preparation of PS-Based Chiral Oxazaborolidinones

sulfonamide amino acid polymers. Treatment of these polymers with equimolar amounts of borane–methyl sulfide generated the corresponding chiral oxazaborolidinones which were assessed (Table 9). Yields were

Table 9. Reaction between Methacrolein and Cyclopentadiene in the Presence of Oxazaborolidinone Catalysts Derived from Monomer **2.24 and Cross-Linking Agents **2.25**, **2.26**, and **2.27a–c****

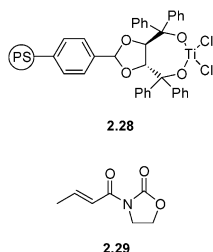
entry	catalyst derived		yield (%)	endo:exo	e.e. (%)
	from 2.24	and			
1	2.25		87	1:99	65
2	2.26		86	8:92	84
3	2.27a		85	5:95	77
4	2.27b		93	1:99	92
5	2.27b ^a		95	7:93	71
6	2.27c		88	4:96	95

^a Used in a continuous flow reactor.

found to be good (85–95%), and the ratio of exo to endo addition was greater than 9:1 for all the polymers. Percentages of e.e.'s were in the range 65–95%, with the *R* configuration favored for all. The highest e.e.'s were achieved with polymers incorporating the most flexible cross-linking agent (Table 9, entry 6), while the e.e.'s observed (95%) compared favorably with the solution-phase catalysts (86%). The polymer-supported catalysts were recovered and reused many times and the polymer derived from **2.27b** used in a flow reactor, although the use of such a highly swelling resin is not really to be recommended for continuous flow processes. Results were comparable with those obtained with the batch process (Table 9, entry 5).

The use of PS-supported Ti (IV)-TADDOLate **2.28** (Scheme 22) as an asymmetric catalyst for the Diels–Alder cycloaddition of cyclopentadiene with 3-crotonoyl-1,3-oxazolidin-2-one (**2.29**) has been reported.⁴⁴ The catalyst was prepared in four steps from 2% DVB cross-linked chloromethylated PS resin. The catalyst yielded, predominantly, the endo product in high overall yield and with an e.e. of 45–51%. Over five cycles, direct recycling of the catalyst led to a slight decrease in the level of the endo product (82 to 74%), while there was a significant decrease in enantioselectivity (48% e.e. to 11% e.e.). These findings were attributed to the gradual leaching of metal from the

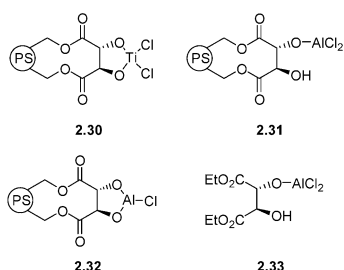
Scheme 22. PS-Supported Ti(IV)-TADDOLate **2.28, Catalyst for the Asymmetric Diels–Alder Addition of Cyclopentadiene to **2.29****



catalyst. Attempts at regenerating the titanium complex on the polymer were unsuccessful.

Altava et al.² described the preparation of PS-supported Lewis acids **2.30–2.33** (Scheme 23) de-

Scheme 23. Lewis Acids **2.30–2.33**



rived by the complexation of TiCl_4 or AlEtCl_2 onto (2*R*,3*R*)-tartaric acid grafted onto chloromethyl-PS resin. The catalytic properties of the PS-supported Lewis acids in the Diels–Alder addition of methacrolein and cyclopentadiene (Scheme 20) were compared to those of the soluble analogue **2.33**. Upon immobilization, the exo/endo ratios were found to drop significantly (Table 10). Reuse of **2.30** was reported and showed a significant drop in yield (25%) after one cycle (Table 10, entry 2).

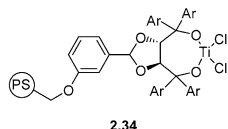
Table 10. Reaction between Methacrolein and Cyclopentadiene in the Presence of Lewis Acids **2.30–2.33**

entry	catalyst	yield (%)	exo/endo	e.e. (%)
1	2.30	86	7	0
2	2.30 ^a	60	6	0
3	2.31	93	8	3
4	2.32	43	8	0
5	2.33	80	24	18

^a Recycled catalyst.

The effect of the morphology of the polymeric support has been investigated with some surprising results reported.⁴⁵ The catalytic activity of **2.34** (Scheme 24), prepared by both copolymerization and

Scheme 24. PS-Supported Diels–Alder Catalyst **2.34**



grafting methodologies, on the addition of cyclopentadiene to 3-crotonyl-1,3-oxazolidin-2-one **2.29** was

explored. It was observed that the major isomer obtained was dependent on the method of preparation. The grafted polymer favored formation of the (2*R*,3*S*) isomer, whereas the monolithic polymer prepared by copolymerization favored the (2*S*,3*R*) isomer!

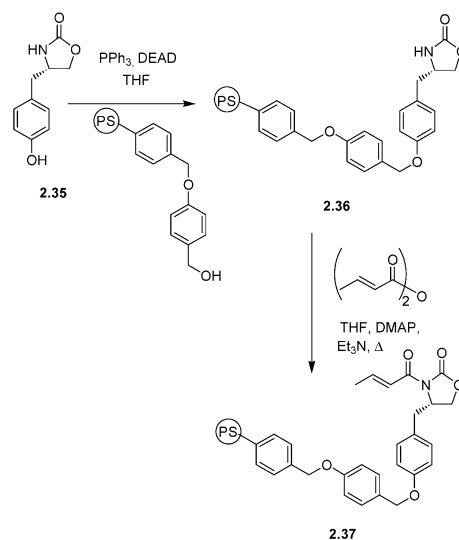
2.4.2 Resin-Based Catalysts for 1,3-Dipolar Cycloadditions

Pu et al.⁴⁶ described the use of polybinaphthyl Lewis acids as catalysts for the 1,3-dipolar cycloaddition of nitrones to alkenes. Excellent enantioselectivities were observed (up to 99% e.e.), and the catalysts were reused several times without significant loss of activity.

Allin and Shuttleworth⁴⁷ first described the immobilization of the “Evans” oxazolidinone onto Merrifield resin and its subsequent use as a chiral auxiliary in the preparation of a chiral α -alkyl carboxylic acid. The desired acid was formed in 42% yield with an e.e. of 96%.

Faita⁴⁸ described the use of the same chiral auxiliary during the 1,3-dipolar cyclo-addition of nitrile oxides and nitrones in the presence of Mg(II). **2.37** was prepared in two steps from (4*S*)-*p*-hydroxybenzyl-1,3-oxazolidin-2-one **2.35** and PS-resin derivatized with the Wang linker (Scheme 25). Following reaction

Scheme 25. Immobilization of the Oxazolidinone Chiral Auxiliary



of **2.37** with diphenylnitrone, the desired cycloadducts were cleaved from the chiral auxiliary with NaBH_4 and concurrent regeneration of **2.36**, which was transformed again to **2.37** and reused. Yields were generally poor, but good exo/endo and enantioselectivities were observed (Table 11).

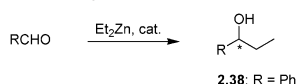
Table 11. 1,3-Dipolar Cycloaddition of **2.37 and Diphenylnitrone**

entry	use	yield (%)	exo:endo	e.e. (%)
1	1	28	5:95	78
2	2	30	5:95	73
3	3	25	7:93	73

2.5 Immobilized Chiral Ligands for Diethylzinc Additions to Aldehydes

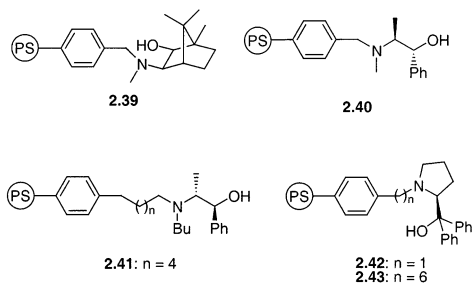
The asymmetric addition of dialkyl zinc species to aromatic and aliphatic aldehydes is a commonly used practice for the preparation of optically active secondary alcohols⁴⁹ with a number of high yielding, enantioselective solution-phase catalysts, based on β -amino alcohols, known. Accordingly, a number of polymer-supported catalysts have been reported and detailed mechanistic studies carried out,⁵⁰ allowing the most important factors necessary for successful polymer-supported catalysts to be investigated.⁵¹ The asymmetric addition of diethylzinc to benzaldehyde to give 1-phenylpropanol **2.38** is often used as a model reaction (Scheme 26).

Scheme 26. Catalytic Asymmetric Addition of Diethylzinc to Aldehydes



Itsuno and Frechét⁵⁰ have reported the use of a number of PS-supported chiral amino alcohols as catalysts for the reaction and have also carried out studies to elucidate the mechanism of the reaction. The most useful results were achieved with **2.39** (Scheme 27), which contains an amino-isoborneol

Scheme 27. PS-Supported Catalysts **2.39**–**2.43** for the Asymmetric Addition of Diethylzinc to Aldehydes



moiety bound to DVB cross-linked PS. This supported catalyst gave **2.38** in 91% yield with an e.e. of 92% (Table 12, entry 1). (1*R*, 2*S*)-(–)-ephedrine loaded

Table 12. Asymmetric Addition of Diethylzinc to Benzaldehyde in the Presence of PS-Supported Catalysts **2.39 and **2.40****

entry	catalyst	yield (%)	e.e. (%)
1	2.39	91	92
2	2.40	96	80
3	2.40 ^a	93	81

^a Recycled catalyst.

onto DVB cross-linked PS (**2.40**) was also investigated, and in the model reaction gave **2.38** in 96% yield and 80% e.e. (Table 12, entry 2). Reuse of **2.40** gave near identical results (Table 12, entry 3), although only one cycle of reuse was reported. Mechanistically, strong evidence for the existence of an initially formed PS-bound chiral zinc alkoxide has been established. It was observed that a polymer-

bound zinc alkoxide, formed by incubation of **2.40** with either diethyl, dibutyl, or diisobutyl zinc, catalyzed the subsequent reaction of diethylzinc to benzaldehyde and gave exclusively the ethylated product. The recovered polymer-bound chiral zinc alkoxides were found to be active over several cycles of reuse without requiring regeneration. These observations strongly suggest that the chiral alkoxide product of the reaction is not covalently bound to the polymeric zinc complex and that ethylation occurs from the excess free diethylzinc in solution. The polymer bound zinc presumably acts to activate the carbonyl group but does not participate in alkylation.

Soai et al.⁵² reported the use of **2.40** as an effective catalyst. In the model reaction, using 10 mol % catalyst, **2.38** was obtained in 83% yield and 89% e.e. (Table 13, entry 1). With straight-chain aliphatic

Table 13. Asymmetric Addition of Diethylzinc to Various Aldehydes in the Presence of PS-Bound (1*R*, 2*S*)-(–)-Ephedrine **2.40**

entry	RCHO	yield (%)	e.e. (%)
1	C ₆ H ₅	83	89
2	<i>p</i> -Cl-C ₆ H ₄	78	83
3	<i>p</i> -MeO-C ₆ H ₄	75	54
4	<i>o</i> -MeO-C ₆ H ₄	79	51
5	<i>o</i> -naphthyl	78	56
6	CH ₃ (CH ₂) ₅	71	21

aldehydes, much reduced enantioselectivity was observed (Table 13, entry 6). The recovered catalyst was reported to be effective.

Additional reports by these workers detailed an investigation into the effect of using a spacer moiety between the polymer backbone and the chiral catalyst, while comparing the solution-phase catalytic properties of various *N*-alkyl ephedrine monomers with the solid-phase variants.⁵³ Using this approach, it was found that PS-supported *N*-butylnorephridrine **2.41**, attached to the polymer support via a six-carbon spacer unit, gave better catalytic performance than the two-carbon spacer. Thus, nonanal gave undecan-3-ol in 75% yield and 69% e.e. (Table 14, entry 2).

Table 14. Asymmetric Addition of Diethylzinc to Various Aldehydes in the Presence of Catalysts **2.41, **2.42**, and **2.43****

entry	catalyst	RCHO	yield (%)	e.e. (%)
1	2.41	C ₆ H ₅	91	82
2	2.41	CH ₃ (CH ₂) ₇	75	69
3	2.41 ^a	CH ₃ (CH ₂) ₇	80	71
4	2.41	C ₆ H ₅ (CH ₂) ₂	77	75
5	2.41	(<i>E</i>)-C ₆ H ₅ CH=CH ₂	53	51
6	2.42	C ₆ H ₅	68	24
7	2.43	C ₆ H ₅	91	61

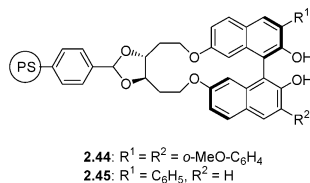
^a Recycled catalyst.

Reuse of the catalyst gave essentially identical results (Table 14, entry 3). The spacer effect was clearly demonstrated by comparison of PS-bound catalysts **2.42** and **2.43**, which contain the same bound chiral amino-alcohol moiety but differ in the presence or absence of the six-carbon spacer. Significant improvements in both the yield and enantio-

selectivity were observed for the long chain spacer (Table 14, entries 6 and 7).

Lipshutz⁵⁴ described the preparation and evaluation of a small series of symmetrical and unsymmetrical cyclo-BINOLs supported on 2% DVB/PS (Scheme 28). These catalyzed the addition of dieth-

Scheme 28. PS-Supported Cyclo-BINOLs **2.44** and **2.45**



ylzinc to a number of aromatic aldehydes in good yield and with high enantioselectivity (Table 15,

Table 15. Asymmetric Addition of Diethylzinc to Various Aldehydes in the Presence of PS-Supported BINOLs **2.44, **2.45**, and Ti(*i*-O-Pr)₄**

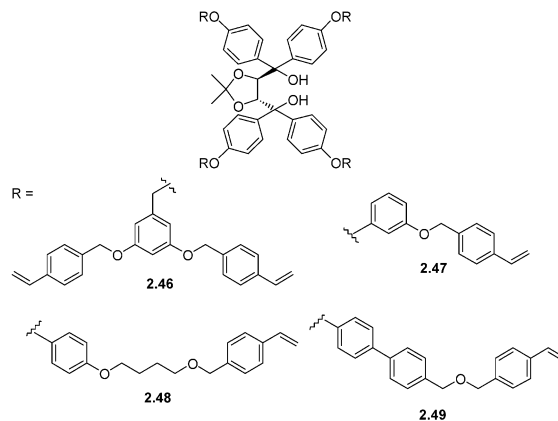
entry	catalyst	RCHO	yield (%)	e.e. (%)
1	2.44	C ₆ H ₅	89	96
2	2.44 ^a	C ₆ H ₅	92	92
3	2.44 ^b	C ₆ H ₅	90	90
4	2.44 ^c	C ₆ H ₅	83	93
5	2.44	<i>p</i> -MeO-C ₆ H ₄	90	95
6	2.44	<i>p</i> -Cl-C ₆ H ₄	84	98
7	2.44	C ₆ H ₅ (CH ₂) ₂	56	84
8	2.45	C ₆ H ₅	92	95
9	(<i>S</i>)-BINOL	C ₆ H ₅	92	92
10	2.45	<i>p</i> -MeO-C ₆ H ₄	95	96
11	(<i>S</i>)-BINOL	<i>p</i> -MeO-C ₆ H ₄	79	

^a First reuse. ^b Second reuse. ^c Third reuse.

entries 1, 5, and 6). During reuse of **2.44**, no loss in enantioselectivity over four cycles was observed (Table 15, entries 1–4). The potential of unsymmetrical PS-bound cyclo-BINOLs to increase enantioselectivity relative to the parent BINOL was demonstrated with **2.45**. In the presence of Ti(*i*-O-Pr)₄, **2.45** was found to catalyze the addition of diethylzinc to benzaldehyde with comparable results to the soluble parent (*S*)-BINOL (Table 15, entries 8 and 9). With *p*-anisaldehyde as substrate, a significant increase in enantioselectivity was observed (Table 15, entries 10 and 11).

In an extensive study, Seebach^{55,56} investigated the catalytic properties of a small series of polymer-bound diisopropoxy-Ti-TADDOLate catalysts over 20 cycles of reuse with 0.2 equiv of catalyst at a loading of 0.1 mmol/g. Four polymer bound Ti complexes were prepared by copolymerization of styrene derivatized with the TADDOL monomers **2.46**–**2.49** (Scheme 29), followed by treatment with Ti(OCHMe₂)₄. Analysis of the Ti complex of the catalyst derived from monomer **2.46** showed that approximately 85% of the chiral diol moieties were complexed with Ti(IV). This catalyst gave the best results, with constant enantioselectivities of 96% e.e. over 20 runs. It was also noted that catalyst performance decreased with increased chain length of the cross-linker agents. The activity of **2.46** was investigated at various loadings

Scheme 29. TADDOL Derivatized Styrene Monomers **2.46**–**2.49**

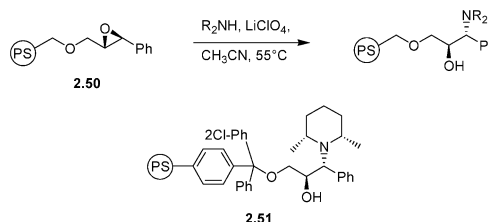


(0.14 and 0.25 mmol g⁻¹) with only a slight variation in enantioselectivity observed and very little loss of activity over 20 cycles.

Seebach⁵⁷ later reported the immobilization of several dendritic and nondendritic BINOL derivatives onto PS. Ti-BINOLates were found to be active in the addition of diethyl zinc and trimethylsilyl cyanide to aldehydes with similar selectivities to the unsupported analogues (up to 86% e.e.). The best polymers showed minor or no loss in selectivity after 20 cycles. PS Bound Al-BINOLates, prepared by the addition of AlMe₃ to a suspension of the PS-BINOL beads in toluene, were found to catalyze the 1,3-dipolar cycloaddition of diphenyl nitron to vinyl ethers. In all cases, the conversion was found to have gone to completion with *exo/endo* selectivities corresponding to those of the unsupported analogue. In contrast to the Ti-BINOLates the polymers could not be used in further catalytic cycles, neither directly or following reloading with fresh AlMe₃.

An extensive study by Vidal-Ferran⁵⁸ focused on a number of polymer-bound chiral-1,2 amino alcohols, synthesized by the regio- and stereospecific epoxide opening of PS-bound (*2S,3S*)-2,3-epoxy-3-phenylpropanol **2.50** with secondary amines (Scheme 30). The

Scheme 30. Preparation of PS-Supported Chiral-1,2-Amino Alcohols



resulting polymers showed good catalytic activity in the addition of diethylzinc to benzaldehyde. Improved catalytic activity was observed when the catalyst was attached via the 2-chlorotrityl linker to PS resin instead of directly to Merrifield resin. The addition of diethyl zinc to 14 aromatic aldehydes in the presence of **2.51** was investigated (Table 16). **2.38** was obtained in 98% yield and 94% e.e. (Table 16,

Table 16. Asymmetric Addition of Diethylzinc to Various Aldehydes in the Presence of 2.51

entry	RCHO	yield (%)	e.e. (%)
1	C ₆ H ₅	98	94
2	<i>p</i> -F-C ₆ H ₄	99	95
3	<i>o</i> -Me-C ₆ H ₄	94	94
4	<i>o</i> -MeO-C ₆ H ₄	98	94

entry 1). Reuse led to no decrease in enantioselectivity.

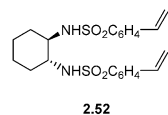
Hodge⁵⁹ described the use of PS-supported ephedrine and camphor derivatives as catalysts in a continuous flow reactor. Solutions of diethylzinc and benzaldehyde in toluene were continuously pumped through the bead bed and passed slowly up the column, with product continuously collected from the top. Under optimal conditions, using PS-bound (1*R*,2*S*)-ephedrine, **2.38** was obtained in 98% yield and 98% e.e. These results compared favorably with the soluble monomeric catalyst, which under typical conditions gave an e.e. of 81%. Hodge suggested several reasons for the better performance of the flow system: first, that the substrate effectively experiences a higher mol % of catalyst (concentration levels on the supports are usually high mM), and second, the continuous removal of the reaction product (the reaction product is itself a catalyst for the reaction that leads to racemic product). Using PS-camphor catalysts initial results over the first six runs were good (Table 17, entries 1, 2, and 3). However, after

Table 17. Asymmetric Addition of Diethylzinc to Benzaldehyde in a Continuous Flow Reactor Using the PS-Camphor Catalyst

entry	run	yield (%)	e.e. (%)
1	1	95	97
2	4	97	97
3	6	81	94
4	7	97	86
5	14	50	84
6	16	54	81

extended use, loss of catalytic activity was observed (Table 17, entries 4, 5, and 6), apparently due to the gradual degradation of the catalyst.

Kurth⁶⁰ investigated a supported catalyst strategy where the catalytic moiety was an integral part of the polymer cross-link. This was achieved by copolymerization of **2.52** (Scheme 31) with styrene. Dur-

Scheme 31. Chiral Cross-Linking Agent 2.52

ing the asymmetric addition of diethylzinc to aldehydes, good yields and high to moderate e.e.'s were obtained (Table 18).

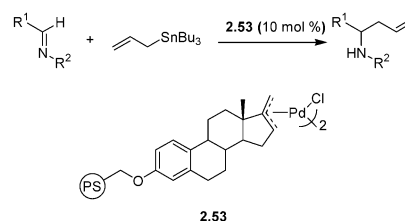
2.6 Miscellaneous: Other C–C Bond Forming Reactions

Yamamoto⁶¹ described the use of the PS-bound chiral π -allylpalladium catalyst **2.53** for asymmetric allylation of imines with allyltributylstannane. **2.53**

Table 18. Asymmetric Addition of Diethylzinc to Various Aldehydes in the Presence of the Resin Cross-Link Functionalized Catalyst from Co-Polymerization of 2.52 with Styrene

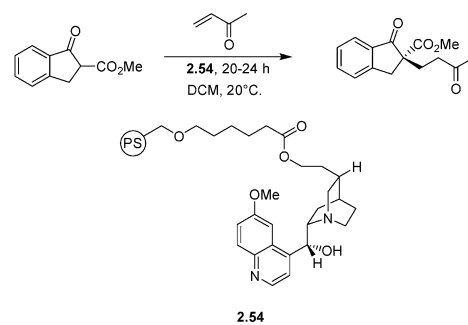
entry	RCHO	yield (%)	e.e. (%)
1	C ₆ H ₅	82	98
2	C ₆ H ₅ CH=CH ₂	80	63
3	<i>p</i> -Me-C ₆ H ₄	85	83
4	<i>p</i> -MeO-C ₆ H ₄	75	70
5	<i>o</i> -Cl-C ₆ H ₄	85	56
6	<i>p</i> -Me-C ₆ H ₄	71	56

was prepared in three steps from estrone and chloromethylated PS resin. The reaction of a series of imines with allyltributylstannane in the presence of **2.53** was investigated (Scheme 32). Yields ranged

Scheme 32. Reaction of Imines with Allyltributylstannane Catalyzed by PS-Supported Chiral π -Allylpalladium Catalyst 2.53

from 24% to near quantitative, but the observed enantioselectivities were only moderate. Reuse was demonstrated with no loss in activity or enantioselectivity observed over four cycles.

The use of polymer-supported catalysts derived from cinchona alkaloids in asymmetric Michael reactions has been disclosed.⁶² A series of catalysts derived from quinine and quinidine were prepared, either directly attached to chloromethylated resin or via a number of spacer moieties, and the efficiency of the catalysts to promote conjugate addition between the β -keto ester 2-carbomethoxy-indan-1-one and methyl vinyl ketone (Scheme 33) assessed. Good yields were observed for all catalysts, whereas enantioselectivity was found to be highly sensitive to both the nature of the alkaloid and the length of the spacer. The highest enantioselectivity (87%) was obtained with supported alkaloid **2.54**.

Scheme 33. Conjugate Addition of β -Keto Esters and Methyl Vinyl Ketones Catalyzed by PS-Supported Cinchona Alkaloids

Masaki⁶³ has reported catalysis of carbon–carbon bond formation between acetals and silylated nucleophiles (Scheme 34) with a polymer derived by copolymerization of functionalized styrene monomer **2.55**

Scheme 34. The Reaction of Silylated Nucleophiles with Acetals Catalyzed by Polymeric 2.55

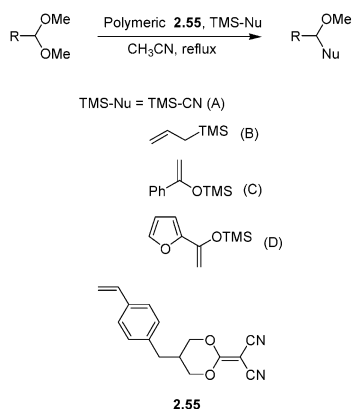


Table 19. Reaction of Acetals with Silylated Nucleophiles in the Presence of Polymeric 2.55

entry	R	TMS-Nu	time (h)	yield (%)
1	<i>p</i> -OMe-C ₆ H ₄	A	2	99
2	<i>p</i> -OMe-C ₆ H ₄	B	2	no reaction
3	<i>p</i> -OMe-C ₆ H ₄	C	6	96
4	<i>p</i> -OMe-C ₆ H ₄	D	5	74
5	C ₆ H ₅	A	2	95
6	C ₆ H ₅	B	24	trace
7	C ₆ H ₅	C	6.5	trace
8	C ₆ H ₅	D	21	63
9	(CH ₂) ₈ CH ₃	A	2	96
10	(CH ₂) ₈ CH ₃	B	24	16
11	(CH ₂) ₈ CH ₃	C	16	38
12	(CH ₂) ₈ CH ₃	D	17	no reaction

and ethylene glycol dimethacrylate (EGDMA) as a cross-linker. Yields obtained ranged from near quantitative (Table 19, entries 1, 3, 5, and 9) to 0% (Table 19, entries 2 and 12). The catalyst could be reused with no loss in activity.

3.0 Immobilized Oxidants

The oxidation of functional groups is one of the most fundamental reactions in organic chemistry but is often accompanied by complications. These include the use of malodorous materials such as thiols or toxic metal complexes which tend to contaminate products and complicate workup issues. Poor selectivities are often observed and harsh conditions to drive the reactions are frequently required.

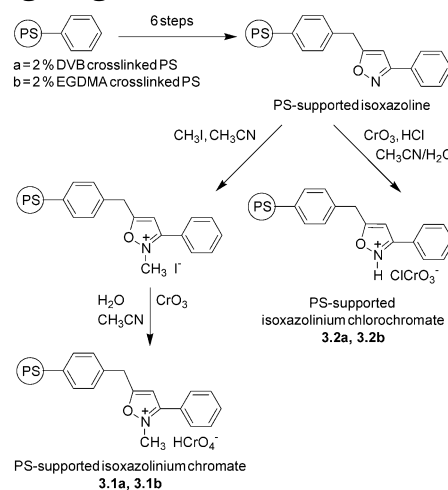
Several groups have addressed these issues, immobilizing various oxidizing agents upon a variety of supports, most being derived from common solution counterparts, while attempting to alleviate the aforementioned problems with the added advantage that the reagents can be easily reused or recycled.

3.1 Oxidation with Immobilized Transition Metal Complexes

Sreekumar has extensively reported the development of a wide range of polymer-supported oxidants for the oxidation of a range of primary and secondary alcohols. The preparation, utility, regeneration, and reuse of these reagents is reviewed below. Polymer-supported isoxazolinium chromate (**3.1a**, **3.1b**) and chlorochromate (**3.2a**, **3.2b**) on both 2% DVB cross-

linked and 2% EGDMA cross-linked PS have been prepared (Scheme 35).⁶⁴

Scheme 35. Preparation of PS-Supported Isoxazolinium Chromate and Chlorochromate, Oxidizing Reagents (3.1a–3.2b)

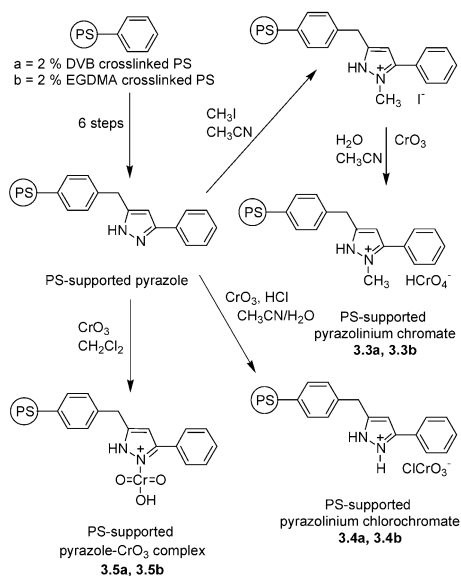


The immobilized reagents were capable of oxidizing primary alcohols to the corresponding carbonyl compounds in yields of 75%. Compared to the DVB cross-linked materials, EGDMA cross-linked reagents required slightly shorter reaction times, presumably because of their superior flexibility, improved solvation, and increased compatibility with polar reagents and solvents. Chlorochromate resins showed a slight increase in reactivity compared to the chromate resins, which was attributed to the less basic nature of the chlorochromate anion compared to the chromate anion. Reaction of the partially spent reagents with alcoholic potassium hydroxide removed the various chromium species from the resins. Treatment with CrO₃ in water/acetonitrile or CrO₃, conc. HCl in water/acetonitrile (Scheme 35) regenerated the reagents, which retained almost identical reactivity to the original resins after six cycles. The synthesis of the related pyrazolinium chromate (**3.3a**, **3.3b**), chlorochromate (**3.4a**, **3.4b**), and pyrazole-CrO₃ (**3.5a**, **3.5b**) complex resins from the corresponding pyrazole resin (Scheme 36) was also reported.⁶⁵

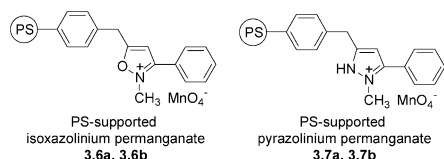
These resins were found to oxidize alcohols in slightly higher yields than the corresponding isoxazolinium materials. As previously observed, the EGDMA cross-linked reagents required shorter reaction times, while the chlorochromate resins were the most efficient. The partially spent reagents were regenerated as described above. After five regeneration/oxidation cycles the reagents showed reasonable recyclability with a reduction of only 5–7% isolated yield of the desired products. Permanganates immobilized upon DVB or EGDMA cross-linked isoxazolinium⁶⁶ (**3.6a**, **3.6b**) and pyrazolinium⁶⁷ (**3.7a**, **3.7b**) resins have also been developed (Scheme 37).

In contrast to traditional potassium permanganate methods, no overoxidation to the acid was observed with the resin bound reagent, even following extended reaction times and large excesses of reagent. Residual manganese and unreacted permanganate were removed from the polymers by washing with

Scheme 36. Preparation of PS-Supported Pyrazolinium Chromate, Chlorochromate, and Pyrazole-CrO₃ Complex Resins (3.3a–3.6b)



Scheme 37. PS-Supported Isoxazolinium and Pyrazolinium Permanganate Reagents (3.6a–3.7b)



ferrous ammonium sulfate and reloaded with potassium permanganate in acetone to regenerate the original resin bound oxidants which retained almost identical oxidizing abilities after five oxidation/regeneration cycles. Yields and reaction times for the oxidation of various substrates with the seven reagents on the different supports are shown in Table 20.

Table 20. Yields and Reaction Times for the Oxidation of Various Alcohols with the Seven Different PS-Supported Reagents^a

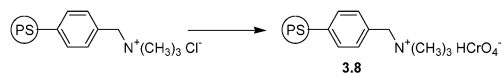
reagent/ substrate	3.1b	3.2b	3.3b	3.4b	3.5b	3.6b	3.7b
benzyl alcohol	78 (39)	80 (37)	80 (38)	82 (36)	75 (37)	83 (25)	83 (24)
<i>p</i> -nitrobenzyl alcohol	80 (31)	81 (29)	72 (40)	80 (38)	84 (41)	88 (27)	78 (27)
<i>n</i> -butanol	75 (37)	80 (35)	78 (36)	80 (34)	75 (75)	85 (22)	84 (27)
α -phenyl ethanol	75 (41)	81 (40)	80 (37)	84 (35)	77 (38)	85 (24)	87 (23)
<i>p</i> -methoxy α -phenyl ethanol	81 (36)	86 (35)	73 (35)	90 (34)	81 (34)	85 (22)	87 (21)

^a Yields (%) (reaction times) (h).

Oxidation of benzyl chloride to benzaldehyde using a chromate salt supported on Indion 810 resin (**3.8**) was reported by Yadav,⁶⁸ and up to 90% conversion was detected (Scheme 38).

A detailed investigation of the effects of a variety of factors and the kinetics of the reaction was undertaken. The resin was washed with 0.2 M

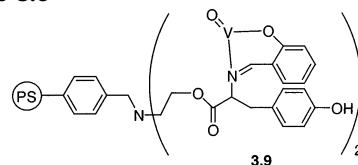
Scheme 38. Preparation of PS-Supported Chromate Salt on Indion 810 Resin



sodium hydroxide to remove chromium species and regenerated by further treatment with CrO₃. In the second use the conversion of benzyl chloride slightly decreased; hence, for the third use instead of treatment with NaOH the spent polymeric reagent was treated directly with CrO₃, and showed an increase in reactivity.

Kumar⁶⁹ described the preparation of a novel polymer bound vanadium ion complex (**3.9**) (Scheme 39). The reagent efficiently catalyzed the direct formation of phenol from benzene with hydrogen peroxide as an oxidant.

Scheme 39. PS-Bound Vanadium Complexed Schiff Base 3.9



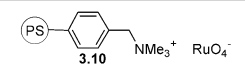
The main advantages of **3.9** compared to previously used vanadium complexes were that the materials could be used catalytically and did not decompose during the reaction. The hydroxylation of benzene was achieved in 30% yield with no byproducts. At the end of the reaction the macroporous polymer was easily recovered by filtration and could be recycled 10 times before the catalyst began to degrade.

3.2 Alcohol Oxidation

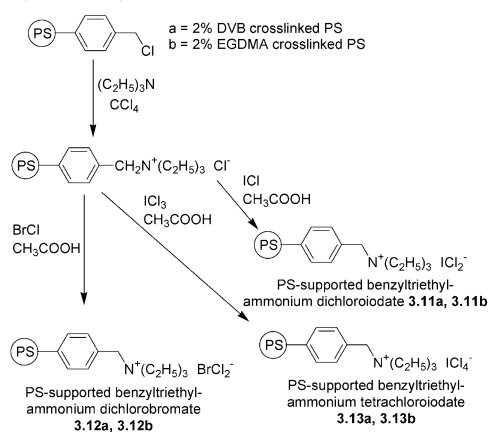
Ley and co-workers developed the use of tetra-*n*-propylammonium perruthenate (TPAP) for the oxidation of both primary and secondary alcohols in 1981 and reported an immobilized variant in 1997.⁷⁰ The method, which uses very mild conditions, only requires substoichiometric levels of the transition metal oxidant complex. The resin-bound analogue **3.10** was obtained by addition of Amberlyst ion-exchange resin (IR 27) to an aqueous solution of potassium perruthenate, followed by ultrasonification. The resulting PS-TPAP resin was used in a series of alcohol oxidation reactions. Yields and reaction times for a selection of these are shown in Table 21.

The spent reagent could be recovered by simple filtration and reused although with a decrease in yield, 95% (first run), 88% (second run), 72% (third run). The use of molecular oxygen as the co-oxidant was later reported.⁷¹ In most cases, oxidation yields were greater than 90% for a range of allylic, benzylic, and simple aliphatic alcohols although nonactivated substrates required longer reaction times. High selectivity for primary versus secondary alcohols was observed (Table 21, entry 5).

Oxidizing polyhalide derivatives of benzyltriethylammonium resins (**3.11–3.13**) have been prepared as shown in Scheme 40.⁷²

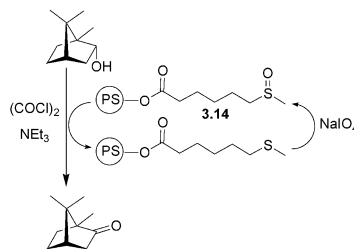
Table 21. PS-Supported TPAP (3.10) with Reaction Times and Yields for a Selection of Substrates


Entry	Alcohol	Product	Time (h)	Yield (%)
1			16	95
2			16	95
3			16	62
4			16	50
5			3	99
			3	<1

Scheme 40. Preparation of Polyhalide Derivatives of Benzyltriethylammonium Resins (3.11–3.13)

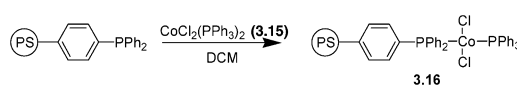
Using a 3-fold molar excess of the polymeric reagent, alcohols were oxidized under mild conditions (30 °C in chloroform). The most efficient reagent was found to be the dichlorobromate (**3.12a**, **3.12b**), and again the EGDMA cross-linked polymeric reagents required shorter reaction times. Treatment with dilute HCl and subsequent reaction with the corresponding halogen chlorides as shown in Scheme 40 easily regenerated the spent reagents. However, over five cycles the extent of oxidation was found to be slightly decreased.

Vedras developed a resin-based variant of the Swern oxidation using the readily available sulfoxide, 6-(methylsulfinyl)hexanoic acid as an efficient substitute for DMSO⁷³ to give the polymer-supported oxidant **3.14**. Under optimized conditions, use of a 2 molar excess of the immobilized reagent quantitatively oxidized *endo*-borneal to camphor (Scheme 41). However, although subsequent filtration of the reaction mixture easily separated the spent reagent, recycling was not completely successful. After regeneration with sodium metaperiodate, the oxidation capacity of the polymer was reduced (yields fell from 92 to 78%). This was attributed to possible cross-linking of the PS backbone by reaction with oxalyl chloride, although the poor solubility of the sodium metaperiodate and blockage of the beads was probably also an issue. Soluble PEG was therefore investigated as an alternative support.⁷⁴

Scheme 41. Oxidation of *endo*-Borneal with a PS-Supported DMSO Equivalent (3.14) in a Swern Type Oxidation, and Regeneration of the Reagent with Sodium *meta*-Periodate

A number of alcohols were tested under optimized conditions. In each case the soluble polymer was recovered by ether precipitation at –20 °C, although the filtrate was found to contain PEG impurities. Carbonyl compounds were afforded in greater than 95% yield and no loss of oxidation capability, after five oxidation/regeneration cycles was observed.

Leadbeater⁷⁵ prepared resin bound cobalt phosphine complex **3.16** by agitating commercially available diphenylphosphino-PS with a solution of **3.15** (Scheme 42).

Scheme 42. Preparation of PS-Supported Cobalt Phosphine Complex 3.16

Use of this catalyst (1 mol %) with 2 equiv of *tert*-butyl hydroperoxide oxidized benzylic and allylic alcohols to the corresponding carbonyl compounds. Simple aliphatic alcohols were unaffected. High yields were obtained for a variety of substrates, and better selectivities compared to the nonsupported reagent were observed (oxidation of benzyl alcohol with unbound **3.15** produced an equal amount of benzaldehyde and benzoic acid after 1.5 h). In the presence of **3.16**, the formation of the acid was greatly reduced (86% aldehyde, 9% acid) after the same reaction time. Recyclability and catalyst leaching were assessed by the consecutive oxidation of 1-phenylethanol using the same batch of supported catalyst for five consecutive runs; yields remained around 90%, while ³¹P NMR of the crude reaction mixtures and UV/Vis analysis showed no loss of catalyst. These results clearly demonstrate the recyclability and lack of significant leaching of the catalyst from this support.

Kessat reported the synthesis of 2-methyl-4-poly(styrylmethyl) thazolium hydrotribromide (**3.17**),^{76,77} and poly(4-methyl-5-vinylthazolium) hydrotribromide (**3.18**)⁷⁸ resins (Scheme 43).

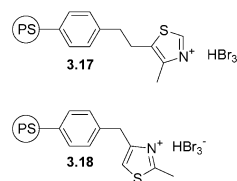
Scheme 43. PS-Supported Tribromide Reagents 3.17 and 3.18

Table 22. Oxidation of Alcohols with Supported Tribromide Reagents 3.17 and 3.18

entry	alcohol	product	yield (%)	
			3.17	3.18
1	CH ₃ CH ₂ CH ₂ OH	CH ₃ CH ₂ CHO	81	78
2	CH ₃ (CH ₂) ₁₂ CH ₂ OH	CH ₃ (CH ₂) ₁₂ CHO	100	99
3	benzyl alcohol	benzaldehyde	99	100
4	allyl alcohol	2-propenal	86	80
5	CH ₃ CHOH(CH ₂) ₂ OH	CH ₃ CO(CH ₂) ₂ OH	93	86
6	2-methyl-2-propanol	no reaction	0	0

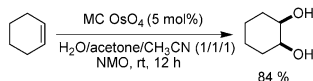
The reagents were found to efficiently oxidize alcohols, in the presence of aqueous sodium hydroxide, to the corresponding carbonyl compounds in good to excellent yields (Table 22). Interestingly, secondary alcohol oxidation was found to be preferred to primary (Table 22, entries 5 and 6). The reagents were found to be stable, safe to use, and easy to recover and regenerate. No loss in activity after several oxidation/regeneration cycles was observed.

3.3 Alkene Oxidation

3.3.1 Dihydroxylation

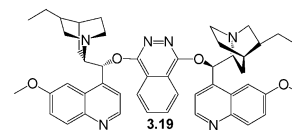
Osmium tetroxide is an efficient reagent for the conversion of alkenes into vicinal diols.⁷⁹ Although it is an expensive, volatile and highly toxic reagent, it is often used due to its generality and mildness. Two major advancements have contributed to its increased synthetic utility: (a) the use of cinchona alkaloid derivatives reported by Sharpless in 1980 to prepare diols stereoselectively⁸⁰ and (b) the use of NMO reported by Sharpless in 1988,⁷⁹ and later in 1990, potassium ferricyanide⁸¹ (further improved enantioselectivity) as co-oxidants which enabled the catalytic use of osmium tetroxide. Many attempts to immobilize both the metal oxidant and the chiral ligands have been reported.

Kobayashi⁸² reported the synthesis and use of a recoverable and recyclable osmium tetroxide catalyst in 1998. MC OsO₄ was prepared by cooling and adding methanol to a 40 °C solution of osmium tetroxide, to which had been added linear PS dissolved in hexane. The resultant hardened powder polymer was collected by filtration, dried, and used in the dihydroxylation of cyclohexene. The optimum solvent system and co-oxidant were then identified (Scheme 44).

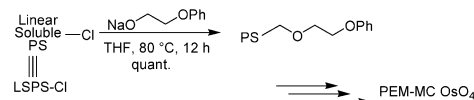
Scheme 44. Dihydroxylation of Cyclohexene with MC Osmium Tetroxide

A range of alkenes (cyclic, acyclic, exo, endo, and bulky alkenes) were subjected to the dihydroxylation conditions and were all found to be suitable substrates, reacting in good yield. The catalyst, which was recovered quantitatively (determined by weight) by simple filtration, could be reused and after five uses no loss of activity was observed, with yields remaining around 83% for cyclohexene. Quite remarkably, no contamination of the products with osmium tetroxide as determined by iodometric titra-

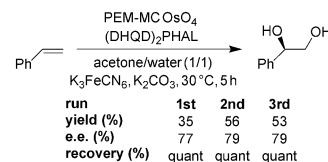
tion was observed. Recently, Kobayashi⁸³ improved the process further; catalytic asymmetric dihydroxylation was realized using the well-known bis-cinchona alkaloids such as 1,4-bis(9-*O*-dihydroquinidiny)phthalazine (**3.19**) as the chiral ligand (Scheme 45).

Scheme 45. Chiral bis-Cinchona Alkaloid Ligand 3.19 for Use in Asymmetric Dihydroxylations

The chiral catalyst requires reaction conditions different from those previously optimized. Because of the use of potassium ferricyanide as the co-oxidant the polymer used for microencapsulation had to be modified as poor yields and recovery were observed with the original PS material. Encapsulated phenoxyethoxymethyl-PS (PEM-PS), which was readily prepared by etherification of linear chloromethyl PS, was therefore developed (Scheme 46).

Scheme 46. Preparation of PEM-PS

Following the previously mentioned procedures (PEM-MC OsO₄) was prepared and tested in the asymmetric oxidation of styrene. In acetone/water (1/1) moderate chemical yields, good e.e., and high recovery of the catalyst were obtained (Scheme 47).

Scheme 47. Asymmetric Dihydroxylation of Styrene with Chiral Ligands and PEM-PS OsO₄

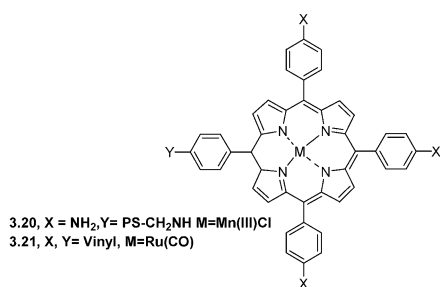
In each case quantitative recovery of the catalyst, with no leaching of osmium, was observed (determined by weight and fluorescence X-ray analysis).

3.3.2 Epoxidation

The epoxidation of alkenes is a transformation of significant importance in organic synthesis. The resultant epoxides are valuable templates in the construction of a wide range of compounds via regio- and stereocontrolled nucleophilic ring opening reactions. The reaction is commonly effected by an oxygen donor such as a peracid or NMO, but these reagents by themselves usually react slowly and give poor yields. Transition metal complexes have therefore been used to catalyze the transformation, and some of these have been immobilized upon a range of PS-based supports. Tangestaninejad⁸⁴ described the preparation and use of PS-bound manganese porphyrin catalyst **3.20** (Scheme 48), which in the presence of NaIO₄ and imidazole (functioning as an axial ligand) allowed the epoxidation of a variety of alkenes including unactivated substrates such as

cyclooctene and cyclohexene (95 and 75% yield, respectively).

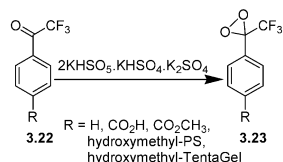
Scheme 48. PS-Bound Manganese Porphyrin Catalyst, 3.20 and PS-Bound Ruthenium Porphyrin Catalyst 3.21 for the Epoxidation of Alkenes



3.20 could be removed from the reaction mixture by simple filtration and displayed consistent reactivity and selectivity in eight repeated epoxidations of cyclooctene. Severin⁸⁵ reported the use of a related ruthenium porphyrin catalyst **3.21**. Co-polymerization of **3.21** with EGDMA (1:99) afforded macroporous, highly cross-linked polymeric catalysts, which in the presence of 2,6-dichloropyridine *N*-oxide catalyzed the epoxidation of alkenes (99 and 94% yield for styrene and cyclooctene, respectively). **3.21**, which could also be used in the catalytic oxidation of aromatic alkanes and secondary alcohols to the corresponding ketones, could be recycled after isolation by filtration from the reaction mixture but was found to have decreased activity in further epoxidations.

Prompted by work reported by Sreekumar, Marples⁸⁶ investigated the use of (trifluoromethyl)dioxirane derivatives to effect the epoxidation of alkenes. Methyl(trifluoromethyl)dioxirane is a more powerful oxidant than dimethyldioxirane, and derivatives (**3.23**) could be prepared by in situ treatment of the trifluoromethyl aryl ketones (**3.22**) with oxone (Scheme 49).

Scheme 49. Preparation of (Trifluoromethyl) Dioxirane Derivatives



Although the resin bound reagents were not as active as their solution-phase counterparts (Table 23), they could be reused many times.

Sherrington⁸⁷ grafted titanium tetraisopropoxide onto poly(*p*-hydroxystyrene) resins with different cross-linking levels and used this catalyst for the epoxidation of alkenes in the presence of *tert*-butyl hydroperoxide. The activity of the titanate was found to increase upon immobilization and decrease with higher levels of cross-linking. After the first cycle, the yield of the epoxidation of cyclohexene fell from 95 to 50% and remained at this level for a further three cycles. Sherrington observed that the titanium content of the polymer decreased between the first and

Table 23. Epoxidation of Olefins with (Trifluoro)methyl Dioxirane Derivatives 3.23

substrate	R	yield (%)	time (h)
<i>trans</i> -stilbene	CO ₂ CH ₃	98	24
<i>trans</i> -stilbene	tentagel	97	48
<i>trans</i> -stilbene	hydroxymethyl PS	64	36
<i>cis</i> -stilbene	CO ₂ CH ₃	99	24
<i>cis</i> -stilbene	tentagel	61	48
<i>cis</i> -stilbene	hydroxymethyl PS	51	38
cholesterol	CO ₂ CH ₃	100	24
cholesterol	tentagel	37	48
cholesterol	hydroxymethyl PS	76	48

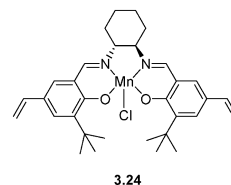
the fourth runs and suggested that titanium was released by an exchange reaction with *tert*-butyl hydroperoxide in the reaction medium. The catalyst was also active in the transesterification of methyl methacrylate with 2-ethylhexanol.

3.3.3 Asymmetric Epoxidation

A variety of complexes have been immobilized for the asymmetric epoxidation of alkenes, the most common of which is Jacobsen's Mn(Salen) complex. Some successes with this catalyst regarding yield and e.e. of the products obtained have been reported; however, in some cases recyclability has been shown to be limited.

One of the first successful, reusable, PS-supported Mn(Salen) complexes was reported by Salvadori in 1996.⁸⁸ Polymerization of the chiral Mn(II)Salen complex (**3.24**) (Scheme 50) which contains two

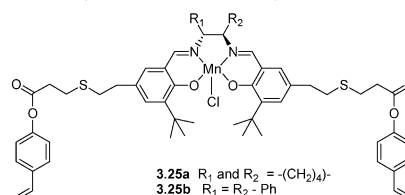
Scheme 50. Chiral Mn (II) Salen Complex 3.24 with 2 Polymerizable Vinyl Groups



polymerizable vinyl groups with styrene and DVB afforded the immobilized catalyst, which in the presence of *m*CPBA and NMO afforded the epoxides of styrene and *cis*-methylstyrene in 99% yield (15% e.e.) and 95% yield (41% e.e.), respectively. The catalyst, which could easily be recovered by filtration, retained its efficiency in terms of yield and e.e. after five recycles.

Salvadori⁸⁹ later reported the synthesis of polymers with longer spacer groups between the active metal center and the polymeric backbone (**3.25**, Scheme 51).

Scheme 51. Salvadori Mn (II) Salen Complex 3.25 with a Spacer Group between the Active Metal Centre and Polymerizable Vinyl Groups



The modification, which was intended to make the catalyst more like the corresponding homogeneous

counterpart, had the desired effect: e.e.'s improved to 26% for styrene oxide (catalyst **3.25b**) and to 62% for *cis*- β -methylstyrene oxide (catalyst **3.25a**, Scheme 51).

Three other alkenes were subjected to epoxidation with the three different polymeric catalysts (Table 24). It was concluded that immobilized catalysts

Table 24. Chiral Epoxidation of Olefins by Catalysts 3.24 and 3.25

substrate	catalyst	yield (%)	e.e. (%)
dihydronaphthalene	3.24	48	10
dihydronaphthalene	3.25a	40	21
dihydronaphthalene	3.25b	49	37
indene	3.24	96	27
indene	3.25a	97	27
indene	3.25b	96	46
1-phenylcyclohexene	3.24	39	21
1-phenylcyclohexene	3.25a	25	38
1-phenylcyclohexene	3.25b	46	42

containing a spacer group between the active metal center and the polymeric backbone afforded epoxides with higher e.e. than those without the spacer group. However, the influence of the chiral diamine could not be explained, in some cases **3.25a** gave products with better e.e., whereas in other cases it was **3.25b**.

Sherrington suggested that lower e.e.'s compared with the nonsupported catalyst were observed when two polymerizable double bonds were present in the active monomer as the ligands would be placed on cross-links inhibiting the formation of a nonplanar transition state which was thought to be essential for high e.e.'s.⁹⁰ This prompted him to synthesize and report the activity of the catalyst in a pendant fashion to PS and polymethacrylate supports.⁹¹ Although the latter was found to catalyze the epoxidation of 1-phenylcyclohex-1-ene in e.e.'s equivalent to that of the nonpolymeric counterpart the catalyst showed a steep decrease in activity and selectivity between the first and second recycles. Sherrington concluded that the stability of the manganese complex was too low to allow viable recycling.

Janda⁹² compared insoluble and soluble polymers as supports for the immobilization of the Mn(Salen) ligand. Yields and e.e.'s for the asymmetric epoxidation of *cis*- β -methylstyrene catalyzed by the four different polymers are shown in Table 25 and essentially show that all four polymers performed equally well.

Table 25. Yields and e.e.'s for the Asymmetric Epoxidation of *cis*- β -Methylstyrene by 3.26–3.29 and Comparison with the Nonimmobilized Catalyst

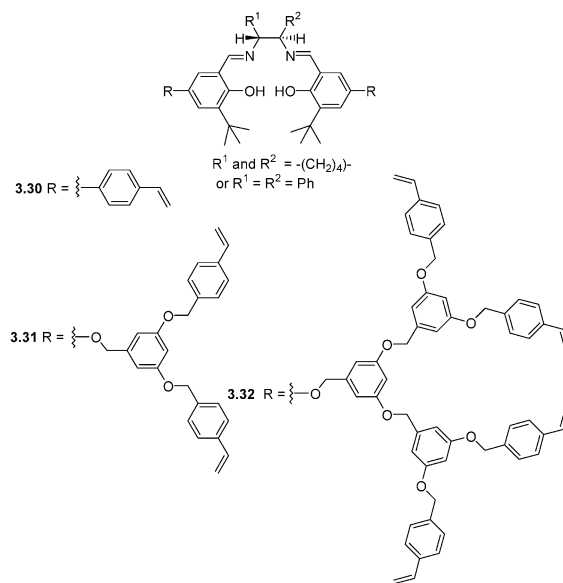
catalyst	yield (%)	e.e. (%)
nonimmobilized	88	82
MeO-PEG (3.26)	88	79
non-cross-linked PS (3.27)	90	79
JandaJel (3.28)	88	77
Merrifield (3.29)	86	75

In all cases, e.e.'s compared with the nonimmobilized catalyst. However, resins **3.26** and **3.27**, which had to be recovered by ether or methanol precipitation, only retained their initial activity for one

recycling run. Further attempts to isolate and reuse these catalysts gave poor results. Recovery of **3.28** and **3.29** was achieved by simple filtration, but **3.28** could only be successfully used three times after which poor conversion and e.e. were observed. The authors concluded that under the reaction conditions the ligand underwent decomposition.

Seebach⁹³ prepared dendritic and nondendritic Salen derivatives **3.30–3.32** (Scheme 52).

Scheme 52. Dendritic and Non-Dendritic Salen Derivatives for the Asymmetric Epoxidation of Alkenes



Copolymerization of the styryl Salen ligands with styrene afforded the immobilized derivatives which upon loading with Mn were found to be active catalysts for the epoxidation of phenyl-substituted alkenes in the presence of NMO and *m*CPBA. Conversions and e.e.'s for the most active polymeric catalysts for each substrate are shown in Table 26.

Table 26. Conversion and e.e.'s of the Epoxidation of Various Alkenes Catalyzed by Ligands 3.30–3.31

alkene	polymer	conversion (%)	e.e. (%)
styrene	3.30	quant	62
3-methyl styrene	3.30	quant	54
1-phenyl cyclohexene	3.31	75	84
dihydronaphthalene	3.31	88	62
trans-stilbene	3.31	9	22

Polymers derived from **3.30** were reused 10 times and showed no drop in e.e. or conversion; however, the dendritically cross-linked polymers **3.31** and **3.32** showed a major drop in both selectivity and conversion upon attempted reuse. As attempts at reloading the polymers with Mn did not restore the initial activity and no Salen derived complexes were detected by NMR spectroscopy of the crude reaction mixtures it was concluded that leaching of the Salen or Mn was not responsible for the drop in activity.

Suresh⁹⁴ reported the preparation of tartrate-functionalized polymers, which were prepared by grafting tartaric acid onto 1 and 2% DVB and tetraethyleneglycol diacrylate (TEGDA) cross-linked

PS or by employing diallyl tartarate (DAT) as a cross-linker. These polymers functioned as alternatives for the diethyl tartarate (DET) ligand, which is employed in the Sharpless epoxidation of allylic alcohols, where it is normally necessary to remove the DET by alkaline hydrolysis or chromatography. Yields and e.e.'s achieved for the five catalysts are shown in Table 27. Thus, the lower cross-linked and more

Table 27. Epoxidation of *trans*-Cinnamate by Tartrate Functionalized Polymers

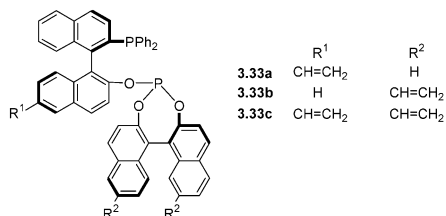
resin	time (min)	yield (%)	e.e. (%)
homogeneous	180	85	97
1 % DVB	460	81	90
2 % DVB	465	78	66
1 % TEGDA	380	66	91
2 % TEGDA	390	72	72
DAT cross-linked	435	74	61

flexible polymers afforded higher e.e.'s, i.e., TEGDA polymers were more active than the corresponding DVB cross-linked polymers, presumably attributable to the enhanced swelling of the former. The resins could be successfully used three times under the same reaction conditions.

3.3.4 Other Alkene Oxidation Reactions

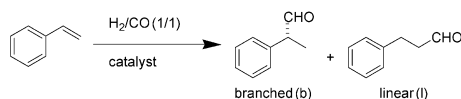
Nozaki⁹⁵ reported the preparation of vinyl BINAPHOS (**3.33a**–**3.33c**) (Scheme 53) that contained one,

Scheme 53. Vinyl BINAPHOS with Differing Numbers of Polymerizable Vinyl Groups Used to Prepare PS Derivatives for Hydroformylation



two, or three polymerizable vinyl groups. Copolymerization of these (3%) with various percentages of styrene (0 or 10%) and DVB (87 or 97%) followed by treatment with Rh(acac)₂(CO)₂ afforded highly cross-linked polymers which in the presence of hydrogen and carbon monoxide efficiently catalyzed the asymmetric hydroformylation of styrene (Scheme 54).

Scheme 54. Hydroformylation of Styrene Catalyzed by 3.33



Yields obtained with immobilized catalysts **3.33a** and **3.33b** were higher than those obtained for **3.33c**, the reduction in cross-linking was found to have no significant effect on the selectivities (Table 28, which also demonstrates reuse).

The asymmetric hydroformylation of vinyl acetate was also studied. Similar results to those obtained with styrene were obtained.

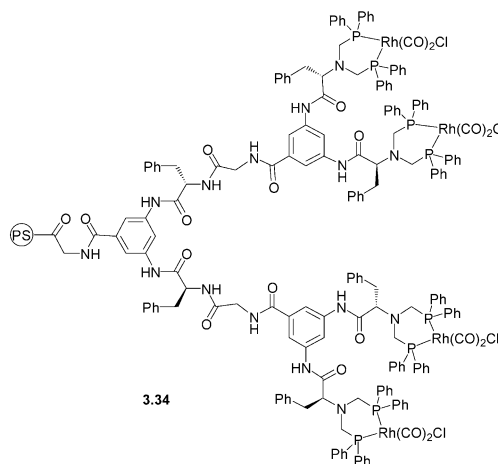
Table 28. Yields and e.e.'s Obtained for the Hydroformylation of Styrene with PS-Bound BINAPHOS Derivatives 3.33

BINAPHOS	b:l ^a	e.e.
3.33a	64:16	89
3.33a^b	83:17	89
3.33a^c	79:21	86
3.33b	89:11	89
3.33c	88:12	68

^a Branched:linear ratio of products. ^b Monomer composition of 10% styrene, 87% DVB, and 3% **3.28**. ^c Reuse of the catalyst.

Arya⁹⁶ complexed [Rh(CO)₂Cl]₂ with dendritic phosphine ligands anchored onto a PS support (**3.34**, Scheme 55). The ligands were found to be efficient catalysts for the hydroformylation of several alkenes.

Scheme 55. Generation 3.0 Octavalent Dendritic Phosphine Ligand Complexed with [Rh(CO)₂Cl]₂



In some cases (mostly second generation dendrimers) the catalysts were found to be reactive for several cycles (Table 29). The authors suggested that the

Table 29. Hydroformylation of Styrene with Dendritic Phosphine Ligand 3.34

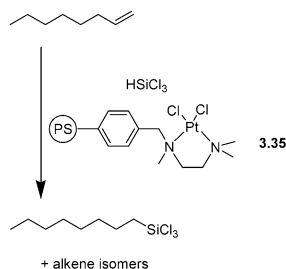
generation	cycle	time (h)	conversion (%)	b:l ^a
1	1	5	42	13:1
1	3	23	85	10:1
1	6	24	8	10:1
2	1	16	>99	16:1
2	3	22	>99	12:1
2	6	22	88	12:1
3	1	22	99	10:1
3	3	22	99	12:1
3	6	22	47	12:1

^a Branched:linear ratio of products.

high reactivity of the polymeric catalyst was due to the cooperativity of the dendritic ligands.

Sherrington⁹⁷ developed both macroporous and collapsed macroporous PS resins (and polymethacrylate) supported platinum-based catalysts (**3.35**) bearing trimethyl-ethylenediamine as a ligand for the metal (loaded with platinum by treatment with K₂PtCl₄). These efficiently catalyzed the hydrosilylation of oct-1-ene with trichlorosilane at room temperature in solventless conditions (Scheme 56). Of all supported catalysts macroporous PS was the most active yielding 70% of the desired product after 2 h

Scheme 56. Hydrosilylation of Oct-1-ene at Room Temperature in Solventless Conditions by PS-Supported Pt Catalyst 3.35

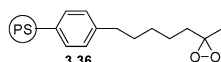


with a final yield of 90%. All data reported were for the fifth use of the sample catalyst demonstrating the recyclability of the catalyst.

3.4 Potpourri: Other Immobilized Oxidants

Sreekumar⁹⁸ developed PS bound dioxirane (**3.36**), which was found to oxidize a variety of organic substrates including alkenes to epoxides, pyridines to *N*-oxides, and amines to nitro compounds in yields between 73 and 85% (Table 30).

Table 30. Use of PS-Bound Dioxirane 3.36 to Oxidize Organic Substrates

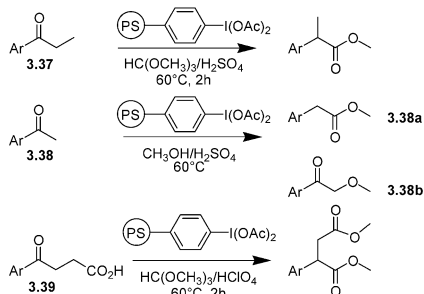


substrate	product	time (h)	yield (%)
aniline	nitrobenzene	43	83
<i>p</i> -toluidine	<i>p</i> -nitrotoluene	32	88
pyridine	pyridine- <i>N</i> -oxide	35	83
2,3-lutidine	2,3-lutidine- <i>N</i> -oxide	31	80
styrene	styrene oxide	40	82
cyclohexene	cyclohexene oxide	60	73

The polymer, which was prepared via a six-step procedure, was recovered by filtration. Treatment with potassium peroxymonosulfate regenerated the reagent, which was employed in consecutive oxidative reactions of aniline. After five cycles only a minor decrease in the isolated yield (86% (first run) to 83% (fifth run)) was observed.

Yokoyama⁹⁹ reported the synthesis and use of poly(styrene(iodosodiacetate)) to promote the oxidative 1,2-aryl migration of alkyl aryl ketones (Scheme 57).

Scheme 57. Oxidative 1,2-Aryl Migration of Alkyl Aryl Ketones Mediated by PS-I(OAc)₂



Good yields for a variety of substrates were obtained (Table 31), while spent reagents were recovered by simple filtration and regenerated by treatment with

Table 31. Yields of Aryl Migration Mediated by PS-I(OAc)₂ and the Nonimmobilized Counterpart PhI(OAc)₂

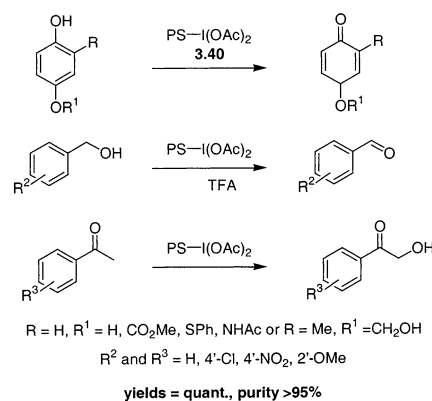
ketone	Ar	PS-I(OAc) ₂	PhI(OAc) ₂
3.37	C ₆ H ₅	81	85
3.37	<i>p</i> -CH ₃ C ₆ H ₄	89	91
3.37	<i>p</i> -CH ₃ C ₆ H ₄	84 ^a	
3.38^b	C ₆ H ₅	41/14	56/21
3.38^b	<i>p</i> -CH ₃ C ₆ H ₄	41/10	67/11
3.39	C ₆ H ₅	95	88

^a Reaction with regenerated PSI(OAc)₂. ^b Yield of **3.38a/3.38b**.

peracetic acid. The reagent was also found to catalyze the iodination of a variety of aromatic compounds, again with good yield and recyclability.

The synthesis of a soluble polymer supported analogue of the reagent (**3.40**) has also been reported and was used to carryout a variety of organic transformations including the oxidation of quinols and primary alcohols and the α -hydroxylation of ketones (Scheme 58).¹⁰⁰

Scheme 58. Catalysis of Oxidative Transformations with Soluble PS-(IOAc)₂



The use of PS-supported bromate (PS-Br(v)) and cross-linked poly(4-vinylpyridinium) bromate supported (PVP-Br(v)) have been reported by Tamami.¹⁰¹ The reagents were prepared by exchanging Cl⁻ on Amberlite ion-exchange resins or poly(4-vinylpyridinium). HCl resins with BrO₃⁻ (NaBrO₃ source) and used in a variety of oxidations, examples of which are shown in Table 32.

Table 32. Oxidative Transformations with PVP and PS-Supported Bromate Reagents

substrate	product	reagent ^a	time (mins)	yield (%)
benzyl alcohol	benzoic acid	PVP-Br(v)	60	95
benzyl alcohol	benzaldehyde	PS-Br(v)	120	87
toluene	benzoic acid	PVP-Br(v)	240	5
2-octanol	2-octanone	PVP-Br(v)	120	70
2-octano	2-octanone	PS-Br(v)	480	0
(CH ₃ (CH ₂) ₃ S) ₂	(CH ₃ (CH ₂) ₃ S) ₂	PVP-Br(v)	10	93
(CH ₃ (CH ₂) ₃ S) ₂	(CH ₃ (CH ₂) ₃ S) ₂	PS-Br(v)	90	81

^a PS = polystyrene, PVP = polyvinylpyridine.

The oxidizing ability of PVP-Br(v) was found to be higher than that of PS-Br(v). Regeneration of the spent polymer was reported by repeated exchange with NaBrO₃.

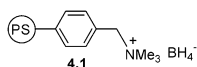
4.0 Immobilized Resin-Based Reductants

Most published syntheses contain a reduction step at some stage in the synthetic process. However, reducing agents, like oxidizing agents, can often be unselective, can contaminate the required products, and can be air-sensitive. Immobilization can, in some cases, relieve some of these difficulties, and in ideal instances no purification of the crude reaction mixture, other than simple filtration, is required. Various groups have reported asymmetric reduction processes using immobilized reagents/catalysts; in these cases, the main advantage offered by immobilization is often recycling of the expensive ligands.

4.1 General Reduction Processes

One of the first examples of utilizing a polymer bound reducing agent was reported in 1977 by Gibson,¹⁰² who described the preparation of anion-exchange resin-supported borohydride. This resin was simply prepared by treating 2–3 equiv. of aqueous NaBH₄ with quaternary ammonium chloride resins of various porosities to yield **4.1** (Scheme 59).

Scheme 59. Borohydride Supported upon an Anion Exchange Resin



These reagents were found to rapidly reduce aldehydes: the more porous resins being the most reactive.

The following year Hutchins¹⁰³ successfully incorporated cyanoborohydride onto Amberlyst 26 ion-exchange resins. The reagent, which was found to be essentially indefinitely stable in a closed container at room temperature, was effective in a variety of reductive transformations, including reductive amination, amine dimethylation, reduction of conjugated enones to allylic alcohols, dehalogenations, and the conversion of pyridinium ions into their tetrahydro derivatives (Table 33). Importantly, cyanide residues

Table 33. Reductive Transformations Mediated by PS-Supported Cyanoborohydride

substrate	product	time (h)	yield (%) ^a
cyclooctanone	cyclooctylamine	48	49 (48)
PhCH(Me)NH ₂	PhCH(Me)NMe ₂	20	84 (81)
α-ionone	α-ionol	3	70 (72)
Me(CH ₂) ₁₁ I	Me(CH ₂) ₁₀ CH ₃	5	89 (89)
4-cyano- <i>N</i> -(<i>p</i> -nitrobenzyl)-pyridinium bromide	4-cyano- <i>N</i> -(<i>p</i> -nitrobenzyl)-1,2,4,5-tetrahydropyridine	15	71 (75)

^a Yields in parentheses denote those obtained for unsupported NaBH₃CN.

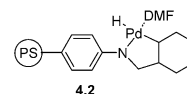
were retained on the polymer and not extracted into either the organic or aqueous phases. The spent reagent, which was recovered by simple filtration, was washed with dilute acid (HCN generated) and regenerated with NaBH₃CN.

Tamami¹⁰⁴ later reported the immobilization of the unstable chloroaluminum borohydride onto a poly-

vinylpyridine support. The reagent was found to reduce a variety of functional groups including aldehydes, ketones, acid chlorides, epoxides and azides in high yields, while esters, amides, oximes, and nitro compounds were unaffected. The reagent could be regenerated and showed no loss in reduction capacity.

Islam¹⁰⁵ reported the use of PS bound Pd(II) complex (**4.2**, Scheme 60) as a catalyst for the reduction

Scheme 60. PS-Supported Pd Complex 4.2



of nitroalkanes, nitriles, and ketones in 1997. The catalyst, which was prepared from macroporous PS (5% DVB), was found to be stable under the high temperature and pressure reaction conditions employed. Table 34 summarizes some of the results

Table 34. Reductions with PS–Pd Complex 4.2

substrate	product	catalyst	yield (%) ⁱ
nitromethane	methylamine	4.2	98
benzophenone	diphenylmethanol	4.2	96
acetone	2-propanol	4.2	92
acetonitrile	diethylamine	4.2	90
	ethylamine		8
1-hexane	hexane	4.2	96
phenylacetylene	ethylbenzene	4.2	97
cyclohexane	Cyclohexane	4.2	98

obtained. The same catalyst could be used repeatedly and reactions were later extended to include alkenes and alkynes (Table 34),^{106,107} while the catalyst could be stored for more than a year and showed consistent activity even after the tenth recycle.

Rajasree¹⁰⁸ found that polymer-bound ethylenediamine-borane reagents (**4.3a**, **4.3b**, Scheme 61) efficiently converted aldehydes to primary alcohols and quantitatively reduced aryl and allylic aldehydes (Table 35). The reagents were found to be selective

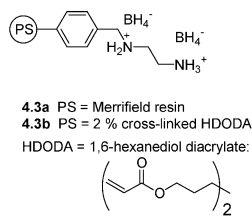
Table 35. Reduction of Aromatic and Allylic Alcohols with PS-Supported Borane Reagent 4.3b

entry	substrate	product	time (h)	yield (%) ^a
1	benzaldehyde	benzyl alcohol	6	100
2	<i>p</i> -cyano-benzaldehyde	4-cyanobenzyl alcohol	4	100
3	<i>o</i> -nitro-benzaldehyde	2-nitrobenzyl alcohol	3	100
4	benzaldehyde and acetophenone	benzyl alcohol and diphenyl methanol	6 6	100 0

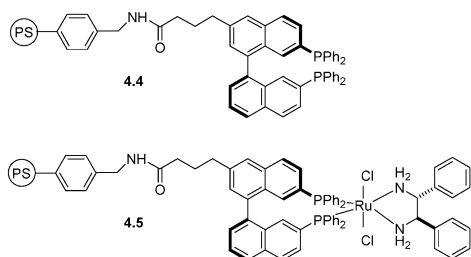
^a Yields reported for use of reagent **4.3b**.

for the reduction of aldehydes over ketones (Table 35, entry 4).

The reagent derived from the HDODA cross-linked PS was found to be more effective than the DVB counterpart, both in preparation of the reagent and reactivity. The spent resin/reagent was treated with HCl and subsequently reacted with NaBH₄. The regenerated resin maintained its initial catalytic activity.

Scheme 61. PS-Supported Ethylene Diamine-Borohydride Reagents 4.3

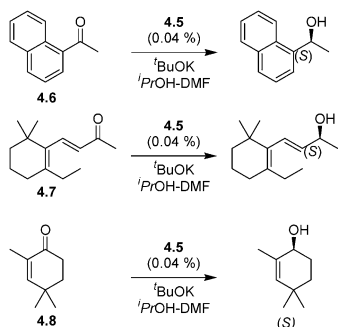
Ruthenium complexes of BINAP have become widely used due to their high catalytic activity in a range of asymmetric organic transformations with a variety of substrates. Bayston¹⁰⁹ described the preparation of PS-supported BINAP derivative **4.4** (Scheme 62).

Scheme 62. PS-Supported BINAP Derivatives 4.4 and 4.5

Activation of the catalyst with (cod)Ru(bis-methyl) and HBr in acetone afforded the active hydrogenation catalyst, which was found to be effective in the enantioselective reduction of olefins and β -keto esters. It was postulated that the reactive intermediate was a ruthenium dibromide species. A drop of only 2% in e.e. was observed on going to a heterogeneous system for the reduction of ethyl acetoacetate; most importantly the catalyst could be reused with only a minor loss in activity.

4.2 Asymmetric Reduction of Ketones

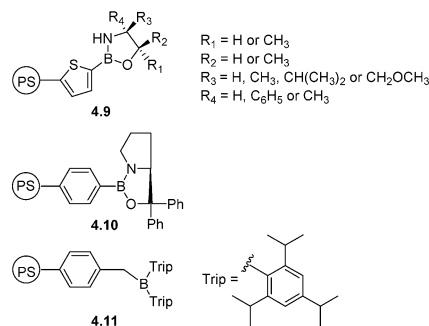
Noyori¹¹⁰ published the synthesis of both enantiomers of BINAP in 1981. He subsequently developed their use in asymmetric transformations, which included a polymer bound derivative (**4.5**, Scheme 62).¹¹¹ **4.5** was observed to be an excellent catalyst for the asymmetric hydrogenation of aromatic and allylic ketones (Scheme 63). Excellent conversions and high e.e.'s were observed for all substrates tested (Table 36). While the catalyst retained activity fol-

Scheme 63. Asymmetric Reduction of Ketones Catalyzed by PS-Supported BINAP Derivative 4.5**Table 36. Asymmetric Reduction with PS-Supported BINAP 4.5**

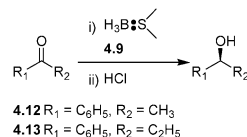
entry	substrate	reuse no.	time (h)	conversion (%)	e.e. (%)
1	4.6	1	26	99	98
2	4.6	9	30	99	98
3	4.6	13	48	96	97
4	4.7	1	15	100	84
5	4.7	6	30	100	83
6	4.7	11	72	100	87
7	4.8	1	22	99	93
8	4.8	8	48	94	94

lowing reuse, reaction times had to be increased (Table 36, entries 3, 6, and 8), but high conversions and e.e.'s were still obtained.

Various groups have reported the immobilization of chiral or sterically hindered organo-boron reagents **4.9–4.11** onto PS (Scheme 64).

Scheme 64. PS-Supported Chiral Organo-Boron Reagents

Hodge¹¹² prepared the polymer bound boronic acid precursor to **4.9** by metalation of the polymeric support followed by reaction with borane and subsequent hydrolysis. Thiophene is more readily lithiated than benzene; hence, a variety of polymers containing the heterocycle were prepared which included: (1) linear poly (2-vinylthiophene), (2) copolymers of 2-vinylthiophene (VT) and DVB, and (3) various copolymers of styrene, VT, and DVB. These resins were functionalized with oxazaborolidine and tested in the reduction of ketones **4.12** and **4.13** with borane-dimethyl sulfide complex (Scheme 65).

Scheme 65. Enantioselective Reduction of Prochiral Ketones with Boron-Dimethyl Sulfide Complex and Immobilized Chiral Borane Reagent 4.9

The results obtained suggested that of the gel type polymers (2% cross-linked), the best catalysts in terms of yield and e.e. were those with higher percentages of VT (51% and 73%) in the polymer matrix; increased cross-linking of the gel type polymers (1 to 2 to 5%) decreased the e.e.'s obtained, whereas macroporous PS catalysts behaved similarly to 2% cross-linked gel-type polymers. The best results were obtained with (1*R*, 2*S*)-(–)-norephedrine as the

β -amino alcohol (R_1 and $R_4 = H$, $R_2 = C_6H_5$, $R_3 = CH_3$) (**4.9**). One of the most effective catalysts (2% DVB, 51% VT, 0.95 mmol/g loading of oxazaborolidine residue) was successfully used four times in the reduction of propiophenone, with e.e.'s of 61, 58, 63, and 60%.

Franot and Stone¹¹³ prepared a similar catalyst (**4.10**) supported on 1% DVB cross-linked PS, functionalized with 8% of the oxazaborolidine moiety. The polymeric catalyst was used in the reduction of acetophenone and cyclohexylmethyl ketone in the presence of different complexes of borane as a reducing agent. Results obtained with the immobilized ligand compared favorably with those achieved with the heterogeneous analogue (Table 37). Recyclability

Table 37. Enantioselective Reduction of Ketones with Chiral Reagent 4.10 in the Presence of Various Borane Complexes as Reducing Agents

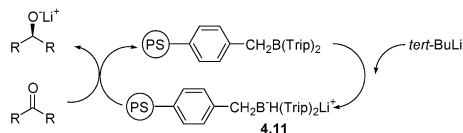
entry	ketone	borane ligand	e.e.
1 ^a	acetophenone	1,4-oxathiane	97
2	acetophenone	1,4-oxathiane	94
3	acetophenone	SMe ₂	98
4	cyclohexylmethyl ketone	1,4-oxathiane	80
5	cyclohexylmethyl ketone	1,4-oxathiane	82
6	cyclohexylmethyl ketone	SMe ₂	83

^a Results achieved with the homogeneous catalyst.

was tested by the reduction of acetophenone with the most active borane complex, borane dimethyl sulfide. The catalyst was successfully used a second time with little loss in selectivity, but during the third reaction the e.e. dropped to between 70 and 80%.

The use of (ditriptylborylmethyl)-PS (**4.11**, Scheme 64) in the presence of *tert*-butyl lithium (Scheme 66)

Scheme 66. Mechanism for the Reduction of Ketones by PS-Supported Chiral Borane 4.11 Reagent in the Presence of *tert*-BuLi



was reported by Smith¹¹⁴ affording secondary alcohols with excellent isomeric purity (Table 38); all reactions

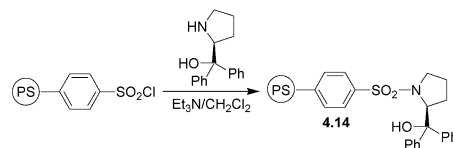
Table 38. Reduction of Ketones by PS-Supported Chiral Borane 4.11 in the Presence of *tert*-BuLi

ketone	% alcohol	yield (%)
2-methylcyclopentanone	>99 cis	85
2-methylcyclohexanone	>99 cis	90
3-methylcyclohexanone	>99 trans	89
4-methylcyclohexanone	99 cis	91
5- <i>tert</i> -butylcyclohexanone	>99 cis	96

were conveniently carried out at room temperature. **4.11** could be separated from the reaction mixture by simple filtration and behaved in the same way as the original reagent even after several reuses.

Zhao¹¹⁵ reported the synthesis of a novel polymer-supported sulfonamide **4.14** (Scheme 67). In the presence of diborane, (which was generated by treating NaBH₄ with Me₃SiCl or BF₃·OEt₂) and between 10 and 30 mol % of catalyst, β -acetophenone was

Scheme 67. Preparation of Chiral PS-Supported Sulfonamides



reduced to the corresponding secondary alcohol in excellent yield and e.e (99 and 95% for NaBH₄/BF₃·OEt₂ with 15 mol % of catalyst).

As had been previously observed by Hodge¹¹² the e.e. initially improved with increased levels of catalyst but leveled off at 25 mol %. To extend the scope of the reduction the catalyst was tested in the reduction of several other ketones (Table 39).

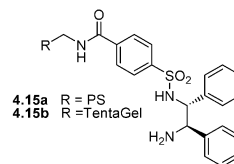
Table 39. Reduction of Ketones with Chiral PS-Supported Sulfonamide 4.14

ketone	NaBH ₄ /Me ₃ SiCl		NaBH ₄ /BF ₃ ·Et ₂	
	yield (%)	e.e. (%)	yield (%)	e.e. (%)
acetophenone	98	96	98	95
<i>p</i> -bromoacetophenone	97	96	98	94
<i>p</i> -methoxyacetophenone	97	84	97	84
benzylacetone	97	65	98	65
2-butanone	91	51	92	48

It can be seen that the chiral reducing system was efficient for the reduction of aryl ketones but less so for alkyl ketones. The polymer-supported catalysts were easily recovered by filtration and regenerated by refluxing with methanol and washing with hot water. Repeated oxidation of acetophenone showed that over three runs no loss of performance was observed.

Polywka¹¹⁶ developed PS and TentaGel-bound analogues (**4.15a** and **4.15b**, Scheme 68) of Noyori's

Scheme 68. PS-Supported Chiral Ligand for the Ruthenium-Catalyzed Reduction of Aryl Ketones



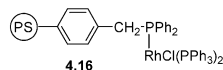
(1*S*,2*S*)-*N*-(*p*-tolylsulfonyl)-1,2-diphenylethylenediamine chiral ligand which was found to be an excellent chiral catalyst for the Ru-catalyzed transfer hydrogenation of ketones and imines. The active catalyst was formed in situ by treating **4.15a** and **4.15b** with [RuCl₂(*p*-cymene)]₂ and tested in the reduction of acetophenone. When 2-propanol was used as the hydrogen donor, **4.15a** gave the desired product in 88% conversion and 91% e.e., whereas **4.15b** gave only 9% conversion and poor e.e.; however, attempted reuse of **4.15a** failed, the reason for which was unclear. Use of formic acid:triethylamine as the hydrogen donor gave better results, **4.15a** was fairly inactive (only 21% conversion after 28 h), whereas **4.15b** gave the desired product in 96% conversion and 97% e.e. The catalyst could be reused once, and high enantioselectivity was maintained, but

the time to reach 96% conversion increased to 72 h. Use of a cosolvent (DCM or DMF) increased the activity of **4.15a** (71% conversion, >99% e.e. after 18 h) compared to **4.15b** (46% conversion, 88% e.e. after the same time scale). Subsequent use of the catalyst showed loss of activity.

4.3 Alkene Reduction

In 1971, Grubbs¹¹⁷ reported the first example of a polymer-supported catalyst for the hydrogenation of alkenes. The immobilized rhodium catalyst (**4.16**, Scheme 69) was used in the presence of hydrogen to

Scheme 69. Immobilized Rhodium Alkene Hydrogenation Catalyst **4.16**

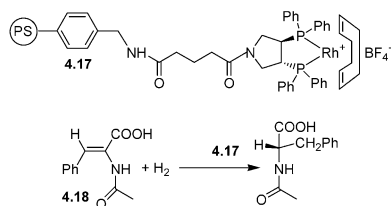


effect the quantitative hydrogenation of a variety of different sized alkenes.

On increasing ring size or going from an acyclic to cyclic alkene the reduction rate decreased suggesting that the majority of the reaction took place within the beads. The catalyst, which was easily recovered by filtration, could be reused. Over 10 runs, activity only varied by $\pm 5\%$.

Nagel¹¹⁸ reported the synthesis of the rhodium complex **4.17** on TentaGel resin. Under optimized conditions, the immobilized catalyst was found to hydrogenate α -(acetylamine)cinnamic acid **4.18** to form the *S*-enantiomer of *N*-acetylphenyl glycine with an activity and selectivity equal to that of the homogeneous catalyst (Scheme 70).

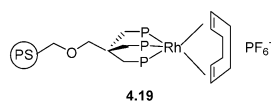
Scheme 70. Immobilized Rhodium Catalyst **4.17** and the Reduction of *N*-Acetyldihydrophenylglycine



The polymer bound catalyst was reused but subsequent attempts failed; the abrupt loss in activity observed could not be explained.

Bianchini¹¹⁹ described the synthesis of a tripodal triphosphine anchored to PS and its complex with $[\text{RhCl}(\text{cod})]_2$ (**4.19**, Scheme 71). Use of 0.5 mol % of the catalyst under harsh experimental conditions (160 °C, 30 bar H_2 in the presence of potassium *tert*-butoxide) converted benzothiophene to 2-ethylthiophenol (49%) with a trace of the desulfurized product ethylbenzene (3%) in 2 h. The catalyst could be recycled, in the second run, after the same time 48 and 4% of the reduced products were obtained.

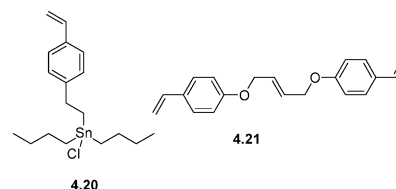
Scheme 71. PS-Supported Tripodal Triphosphine Complex with $[\text{RhCl}(\text{cod})]_2$ (Ph groups on P not shown for clarity)



4.4. Resin-Based Tin and Germanium Reductants

Deleuze¹²⁰ described the synthesis of the organotin monomer **4.20** (Scheme 72). Macroporous, catalytic

Scheme 72. Organotin Monomer **4.20** and Cross-Linker **4.21**

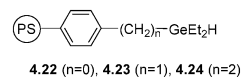


supports were prepared by co-polymerization of the monomer with styrene and DVB (20 and 45%) or bis-1,4-(4-vinylphenoxy) but-2-ene, **4.21** (15, and 30%) as cross-linkers.

The efficiency of the supports as reduction catalysts was examined by the reduction of bromoadamantane with NaBH_4 as the co-reductant. The initial reactivity for supports cross-linked with **4.21** (30 and 15%) showed high activity, and total conversion was obtained after 4 h, but this was only maintained for five successive runs. In contrast, the supports prepared with 20% DVB maintained total conversion over 10 successive cycles. The higher cross-linked network (45%) showed similar reactivity for six cycles but displayed reduced activity until the tenth.

The preparation of polymer-supported organogermanium hydrides (**4.22**, **4.23**, **4.24**, Scheme 73) were described by Mochida.¹²¹

Scheme 73. PS-Supported Organo-Germanium Hydride Reagents **4.22**–**4.24**



The reagents were capable of reducing alkylhalides in reasonable chemical yields by heating the polymer-supported reagent and substrate with free-radical initiators such as di-*tert*-butyl peroxide. The observed order of reactivity was **4.22** > **4.23** > **4.24** attributed to decreased steric hindrance around the germanium. The reactivity of the halogens was found to be $\text{I} > \text{Br} > \text{Cl}$. The spent polymer was recovered by filtration, washed with ether, and regenerated with LiAlH_4 . The extent of regeneration of germanium hydrides was reported as 90% several regeneration/reduction cycles later.

5.0 Conclusions

As this review shows, a variety of polystyrene-based supports are widely used as recyclable materials for both catalysis and reagents and cover a broad range of chemical transformations. Many of these supports, although polystyrene-based, use a variety of cross-linking agents. A theme that reoccurs throughout this review is that the use of the more flexible EGDMA cross-link appears to input beneficial properties into the efficiency of the desired chemical transformation. Clearly, the supports used as carriers for catalysts and reagents need to be further developed and optimized, not only for chemical stability

and reaction specificity but increasingly for sustained recyclability.

6.0 Abbreviations

BDOB	benzodioxaborole
BINAP	bis(diphenylphosphino)-1,1'-binaphthyl
BINAPHOS	2-(diphenylphosphino)-1,1'-binaphthalen-2'yl 1,1'-binaphthalene-2,2'-diyl phosphite
BINOL	2,2'-dihydroxy-1,1'-binaphthyl
mCPBA	meta-chloroperoxybenzoic acid
cod	cyclooctadiene
DAT	diallyl tartrate
DET	diethyl tartrate
DVB	divinylbenzene
EGDMA	ethylene glycol dimethylacrylate
HDODA	1,6-hexanediol diacrylate
MC	microencapsulated
NMO	4-methylmorpholine <i>N</i> -oxide
PEG	poly(ethylene glycol)
PEM	phenoxyethoxymethyl
PS	polystyrene
PVT	poly(2-vinylthiophene)
RCM	ring closing metathesis
ROMP	ring opening metathesis polymerization
TADDOL	$\alpha,\alpha,\alpha',\alpha'$ -tetraaryl-1,3-dioxolane-4,5-dimethanol
TPAP	tetrapropylammonium perruthenate
TPPTS	di(μ -chloro)bis(η^3 -allyl)dipalladium(II)
TEGDA	tetraethyleneglycol diacrylate
VT	2-vinylthiophene
XPS	X-ray photoelectron spectroscopy

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