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Preparation and use of MeO-PEG-supported chiral diphosphine ligands: soluble polymer-supported catalysts for asymmetric hydrogenation

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Abstract—Two new chiral MeO-PEG-supported (*R*)-BINAP and (3*R*,4*R*)-Pyrphos ligands were synthesized and employed in the Ru(II)- and Rh(I)-catalyzed asymmetric hydrogenation of 2-(6′-methoxy-2′-naphthyl)propenoic acid **5** and prochiral enamides **10**. The results showed that these new soluble polymeric catalysts exhibited high catalytic activity and enantioselectivity. Enantiomeric excesses (e.e.s) in the ranges 90–96% and 86–96% were achieved in the hydrogenation of **5** and **10**, respectively. Furthermore, these catalysts could be recovered easily and the recycled catalysts were shown to maintain their efficiency in subsequent reactions. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Asymmetric hydrogenation reactions catalyzed by chiral transition-metal complexes is one of the fundamental strategies for the synthesis of optically active organic compounds. Tremendous success has been achieved in the use of chiral arylphosphine ligands in Rh- and Ru-catalyzed asymmetric hydrogenation reactions.[1] As an example, the asymmetric hydrogenation of (*Z*)-2-acetamido-3-(3-methoxy-4-acetoxyphenyl)acrylic acid with Rh(DIPAMP)$^+$ catalyst was successfully developed by Knowles et al. as a commercial process for the production of L-Dopa.[2] However, a major problem associated with this homogeneous catalytic system is the separation and recycling of the expensive chiral catalyst. A common solution to this problem has been to 'heterogenize' a homogeneous catalyst by anchoring the catalyst onto an insoluble polymer support.[3] Unfortunately, despite the advantage of facile catalyst separation with this method, the use of such insoluble polymer-supported catalysts often suffers from lowered catalytic activity and/or stereoselectivity due to the restrictions of the polymer matrix, which results in limited mobility and accessibility of the active sites. Recently, another type of polymeric chiral catalyst, using a soluble linear polymer support has attracted much attention.[4] Such polymer-supported catalysts faithfully mimic the activity and stereoselectivity of the corresponding homogeneous catalysts since they are in the solution phase during the catalytic reactions. The recovery of the polymer-supported catalyst from the reaction mixture can be readily achieved by taking advantage of the solubility properties of the polymer and separation can thus be achieved using microporous filtration and precipitation methods. Most recently, we have developed a soluble chiral polyester-supported Ru(BINAP) catalyst which offered a better rate of reaction compared to the corresponding monomeric homogeneous catalyst while retaining high stereoselectivity.[5] This approach combines the advantages and/or minimizes disadvantages of homogeneous and heterogeneous catalysis. The use of soluble polymer-supported catalysts has also found success in other asymmetric transformations such as dihydroxylation,[6,7] epoxidation,[8] alkylation,[9] the Mukaiyama reaction,[10] ketone reduction[11,12] and cyclopropanation.[13] In order to establish more generality and versatility of this methodology, we aimed to use other readily available soluble polymers as supports in combination with other phosphine ligands.

Herein we report the preparation of a new class of soluble polymer-supported BINAP and (3*R*,4*R*)-3,4-bis(diphenylphosphino)-pyrrolidine (Pyrphos) ligands

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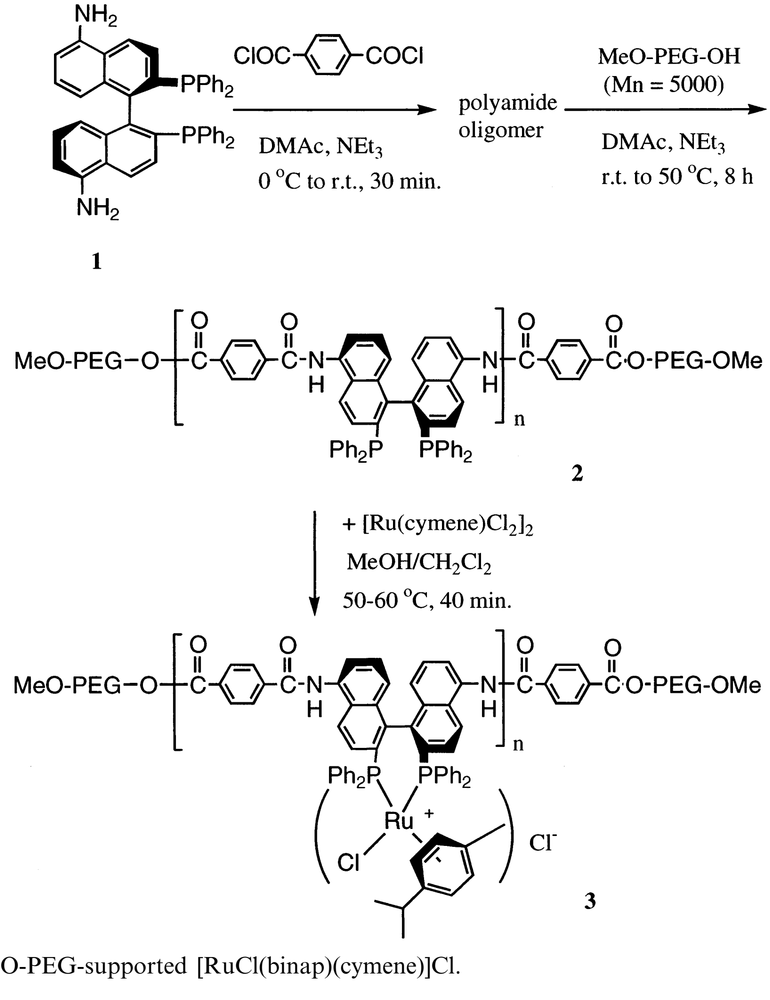
by using a commercially available polyethylene glycol monomethyl ether (MeO-PEG-OH) as support, and their applications in the asymmetric hydrogenation of 2-(6′-methoxy-2′-naphthyl)-propenoic acid and prochiral enamides, respectively.

2. Results and discussion

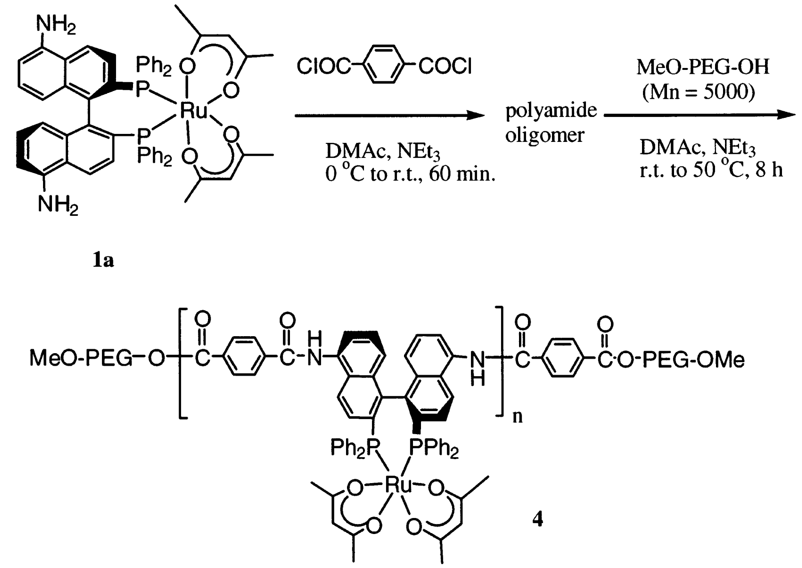
2.1. MeO-PEG-supported Ru(BINAP)

In our previous study,[5] BINAP was anchored onto a soluble chiral polyester via copolymerization of 5,5′-diamino (*R*)-BINAP, (2*S*,4*S*)-pentanediol, and terephthaloyl chloride. The chiral polyester-supported Ru(BINAP) catalyst showed higher catalytic activity in comparison to monomeric Ru(BINAP). However, the stereogenic centers on the polyester backbone did not significantly influence the asymmetric catalysis indicating that a stable catalyst conformation was not achieved. This was probably a result of the flexibility of the polyester chain. Our initial efforts in this study were therefore concentrated on the synthesis of the more rigid BINAP-containing polyamide polymer through the direct polycondensation of 5,5′-diamino (*R*)-BINAP **1** and terephthaloyl chloride. The reaction was easily completed in the presence of triethylamine or pyridine in *N*,*N*-dimethylacetamide (DMAc). Unfortunately, the BINAP-containing polyamide was insoluble in common organic solvents. This limited solubility restricted the preparation of the ruthenium(II) catalyst by the reaction of $[RuCl_2(cymene)]_2$ with the polyamide ligand. Thus, in order to improve the solubility of the polyamide-supported Ru(BINAP) catalyst, we chose polyethylene glycol monomethyl ether (MeO-PEG) as a co-support. This choice was based on the following advantages: firstly, MeO-PEG is commercially available and inexpensive and secondly, it has a broad solubility profile in organic solvents (soluble in methanol, THF, dichloromethane, toluene, DMF, acetonitrile and water, but insoluble in diethyl ether, *tert*-butyl methyl ether, *iso*-propyl alcohol and cold ethanol).

MeO-PEG-supported BINAP ligand **2** was prepared by condensation of **1** with terephthaloyl chloride in the presence of triethylamine in DMAc followed by reaction with MeO-PEG-OH ($M_w = 5000$), which proceeded in excellent 98% yield. The ruthenium catalyst **3** was conveniently prepared in situ from ligand **2** and $[RuCl_2(cymene)]_2$ in a methanol–dichloromethane mixed solvent system (1:1 v/v) (as shown in Scheme 1). Another type of MeO-PEG-supported Ru(BINAP)-$(acac)_2$ catalyst **4** was also prepared by a similar



Scheme 1. Synthesis of MeO-PEG-supported [RuCl(binap)(cymene)]Cl.



Scheme 2. Synthesis of MeO-PEG-supported Ru(BINAP)(acac)$_2$.

method. Ru(BINAP)(acac)$_2$ **1a** was firstly synthesized according to the published method[14] and was reacted with terephthaloyl chloride to give a polyamide oligomer, and then further reacted with MeO-PEG-OH to afford the catalyst **4** in 98% yield (Scheme 2). It was interesting to note that the complexation of BINAP with ruthenium improved the solubility of the polyamide oligomer in organic solvents. Thus, high loading MeO-PEG-supported Ru(BINAP)(acac)$_2$ catalyst could be prepared in contrast to the first approach. The MeO-PEG-supported BINAP ligand and Ru(BINAP) catalysts were characterized by ^{1}H and ^{31}P NMR analysis. The molecular weight of each polymer was determined by gel permeation chromatography (GPC). (The detailed experimental data are summarized in Table 1.) The ^{31}P NMR spectra of the MeO-PEG-supported BINAP ligands and their ruthenium complexes were in close agreement to those of the parent systems.

In order to test the efficiency of these new MeO-PEG-supported Ru(BINAP) complexes in asymmetric catalysis, the hydrogenation of 2-(6′-methoxy-2′-naphthyl)-propenoic acid **5** was chosen as a standard reaction. The choice was based on the fact that Ru(BINAP)-type complexes are known to be effective catalysts in the asymmetric hydrogenation of 2-arylacrylic acids. Additionally, the reduced products represent an important class of anti-inflammatory drugs.

According to the previous studies on Ru(BINAP) type complex-catalyzed hydrogenation of 2-arylacrylic acids, the solvent markedly affects the catalytic activity and enantioselectivity. Because methanol is known to be the best solvent in terms of enantioselectivity and the prepared MeO-PEG-supported Ru(BINAP) catalysts were methanol soluble, the hydrogenation reactions were performed in methanol solvent (unless otherwise noted). The experimental results are summarized in Table 2. From the table several conclusions can be drawn: both MeO-PEG-supported Ru(BINAP) catalysts showed high catalytic activity and enantioselectivity and in comparison to the parent monomeric Ru(BINAP) catalysts, slightly higher enantioselectivities were obtained (entries 2 vs 7 and 8 vs 12). Lower reaction temperatures and higher hydrogen pressure afforded better e.e. in both cases (entries 1, 2 and 8–10). By comparing the catalytic efficiency of these two catalysts, it can be seen that the MeO-PEG-supported Ru(BINAP)(acac)$_2$ catalyst is the more active and

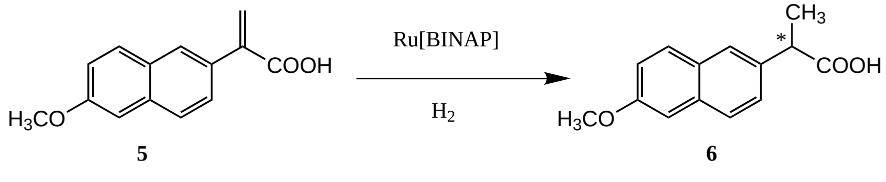


Table 1. MeO-PEG-supported BINAP ligand and Ru(BINAP) catalyst

Ligand or catalyst	Yield of Polym. (%)	^{31}P NMR (ppm)	BINAP or Ru(BINAP) (wt%)[a]	Molecular weight M_w (M_w/Mn)[b]
2	98.0	−16.80	5.6	11763 (1.24)
4	98.4	55.37, 55.15	16.0	18891 (3.10)

[a] The amounts of BINAP or Ru(BINAP) moieties in the polymer were determined by ^{1}H NMR.

[b] Determined by GPC on the basis of polystyrene calibration in THF.

Table 2. Asymmetric hydrogenation of **5** catalyzed by MeO-PEG-supported Ru(BINAP) catalysts[a]

Entry	Catalyst	Sub./cat.	Temp. (°C)	H_2 (psi)	Time	E.e.[b] (%)	Conv.[b] (%)
1	**3**	200	rt	1000	2 h	91.2	100
2	**3**	100	0–2	1800	8 h	96.0	100
3	**3**[c]	100	0–2	1800	8 h	95.8	100
4	**3**[d]	100	0–2	1800	8 h	96.3	100
5	Ru(BINAP)[e]	200	rt	1000	60 h	80.5	37.5
6	Ru(BINAP)[f]	200	rt	1000	4 h	87.7	95.4
7	Ru(BINAP)[g]	100	0–2	1800	8 h	94.4	100
8	**4**	1000	rt	1000	10 min	90.2	100
9	**4**[h]	1000	rt	1000	10 min	90.0	98.5
10	**4**	500	0–2	1800	30 min	95.8	100
11	**4**[i]	500	0–2	1800	30 min	95.6	100
12	Ru(BINAP)[j]	1000	rt	1000	15 min	89.0	98.2

[a] The hydrogenation reactions were carried out in methanol under the reaction conditions: NEt_3/sub. = 1:1 (mol/mol) except for entries 8–12 (no addition of NEt_3); catalyst (in entries 8–12) was aged before use. Catalysts with (*R*)-BINAP give (*R*)-enantiomeric product, which was determined by comparison of the optical rotation with the literature value.[16]

[b] Determined by HPLC analysis using a SUMICHIRAL OA-2500 chiral column.

[c] Recycled catalyst of entry 2 was used (the second catalytic cycle).

[d] Recycled catalyst of entry 3 was used (the third catalytic cycle).

[e] Ru(BINAP) = chiral polyester-supported [RuCl(binap)(cymene)]Cl reported in Ref. 5, using methanol–toluene (9:1, v/v) as solvent, in which the polymeric catalyst is insoluble.

[f] Ru(BINAP) = chiral polyester-supported [RuCl(binap)(cymene)]Cl, using methanol–toluene (2:3, v/v) as solvent, see: Ref. 5.

[g] The parent catalyst, [RuCl(binap)(cymene)]Cl.

[h] Recycled catalyst of entry 8 was used.

[i] Recycled catalyst of entry 10 was used.

[j] The parent catalyst, Ru(BINAP)$(acac)_2$.

maintains high enantioselectivity (entries 1 vs 8 and 2 vs 10), which agrees with the previous reports.[14,15]

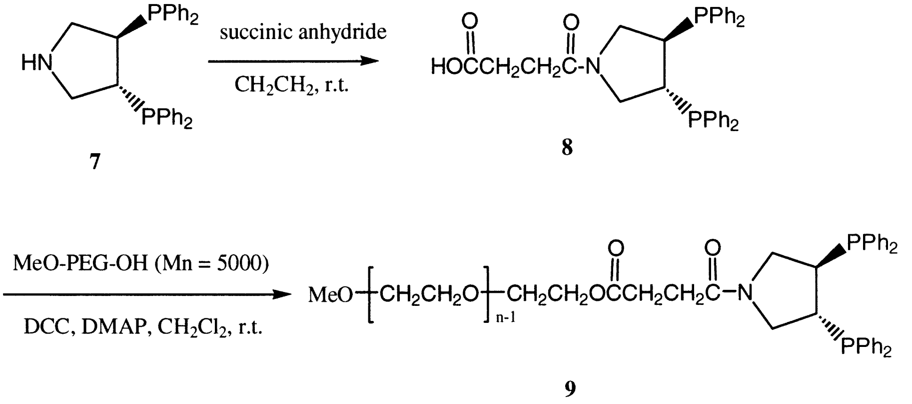
In contrast to the chiral polyester-supported [RuCl(binap)(cymene)]Cl catalyst,[5] the MeO-PEG-supported catalyst catalyzed the hydrogenation reaction in methanol in a completely homogeneous manner, had higher catalytic activity and induced higher enantioselectivity (entries 1–6).

The two catalysts prepared in this study were easily separated from the reaction mixture by solvent precipitation, and the recovered catalysts showed no loss of enantioselectivity upon re-use (entries 2 vs 4 and 8 vs 11).

2.2. MeO-PEG-supported rhodium catalyst containing Pyrphos

Based on the successful use of MeO-PEG-supported Ru(BINAP) catalysts for asymmetric hydrogenation, we also designed and prepared MeO-PEG-supported Pyrphos–rhodium(I) catalyst. In order to introduce the chiral diphosphine ligand **7** into the polyethylene glycol monomethyl ether (MeO-PEG, $M_w = 5000$) chain, the carboxylic acid modified derivative **8** was first synthesized in high yield by the reaction of **7** with succinic anhydride in dichloromethane at room temperature. The coupling of acid **8** with polyethylene glycol monomethyl ether was carried out in the presence of dicyclohexylcarbodiimide (DCC) and 4-*N*,*N*-dimethylaminopyridine (DMAP) in dichloromethane at room temperature to afford MeO-PEG-supported Pyrphos ligand **9** in >98% yield (Scheme 3). Confirmation of ligand attachment was established by NMR spectroscopic analysis of **9**.

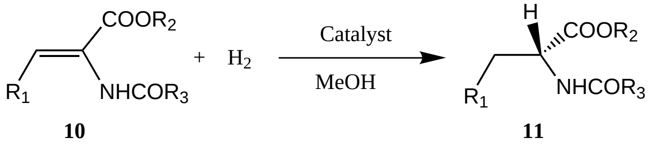
With the MeO-PEG-supported Pyrphos ligand in hand, we examined its asymmetric induction properties in the Rh(I)-catalyzed asymmetric hydrogenation of prochiral enamides **10**.



Scheme 3. Synthesis of Pyrphos-containing monomer and polymeric ligands.

The rhodium catalyst was prepared in situ from ligand **9** and $[Rh(COD)_2]^+BF_4^-$ in methanol at room temperature and used in the hydrogenation reactions without further purification. The monomeric catalyst $[Rh(8)(COD)]^+BF_4^-$ was also synthesized by the same method. The experimental results are shown in Table 3. Several prochiral enamide substrates were tested and complete conversions and high enantioselectivities were achieved in reactions catalyzed by the MeO-PEG-supported catalyst. For example, with 0.25 mol% $[Rh(9)(COD)]^+BF_4^-$, the hydrogenation of **10a** under 800 psi of hydrogen pressure at room temperature afforded product with 95.5% e.e. in 4 h. By comparing to the monomeric catalyst, the MeO-PEG-supported catalyst showed similar enantioselectivity with the exception of substrate **10d** (entry 7). The reason for the reduced enantioselectivity in the hydrogenation of **10d** is not clear.

In addition to the high catalytic efficiency, the value of designing such a soluble catalyst was further confirmed by the easy separation and recycling of this catalyst. Upon completion of the reaction, most of the solvent was removed under reduced pressure followed by addition of diethyl ether. The catalyst was precipitated and recovered quantitatively via filtration. The recovered catalyst was re-used in at least three cycles with the same enantioselectivity (entries 2–4). In contrast, the insoluble polyethylene glycol grafted polystyrene-supported Pyrphos-containing rhodium catalyst abruptly loses its catalytic activity in the second cycle.[17] Furthermore, the high selectivity observed in the hydrogenation of **10e** is particularly important because the reduced product is a valuable precursor for the synthesis of L-Dopa.[2] The facile separation and recycling of the catalyst may further improve the economics of this process.



10a: R_1=Ph, R_2=H, R_3=CH_3;

10b: R_1=Ph, R_2= R_3=CH_3;

10c: R_1=R_3=Ph, R_2=H;

10d: R_1=R_2=H, R_3=CH_3;

10e: R_1=3,4-(-OCH_2O-)C_6H_3, R_2=H, R_3=CH_3.

Table 3. The $[Rh(\mathbf{9}\text{ or }\mathbf{8})(COD)]^+BF_4^-$-catalyzed asymmetric hydrogenation of prochiral enamides **10**[a]

Entry	Substrate	E.e. % (ligand **9**)[b]	E.e. % (ligand **8**)[b]
1	**10a**	95.5	94.9
2	**10a** (cycle 1)[c]	96.0	–
3	**10a** (cycle 2)[c]	95.6	–
4	**10a** (cycle 3)[c]	94.0	–
5	**10b**	90.0	89.8
6	**10c**	96.0	95.8
7	**10d**	86.9	89.0
8	**10e**	93.0	93.5

[a] The hydrogenation reactions were carried out in methanol with a sub./cat. = 400 (mol/mol) under 800 psi H_2 pressure at room temperature. All catalytic reactions reached 100% conversion in 4 h to give (*R*)-enantiomeric products, which were determined by comparison of the optical rotation with the literature value.[18]

[b] The e.e.s were determined by gas chromatography using a 25 m Chiralsil L-Val capillary column.

[c] Recovered catalyst was used.

In conclusion, two new chiral MeO-PEG-supported (*R*)-BINAP and (3*R*,4*R*)-Pyrphos ligands were synthesized and employed in the Ru(II)- and Rh(I)-catalyzed asymmetric hydrogenations of 2-(6′-methoxy-2′-naphthyl)propenoic acid **5** and prochiral enamides **10**. The results showed that these new soluble polymeric catalysts exhibited high catalytic activity and enantioselectivity. E.e.s in the ranges 90–96% and 86–96% were achieved in the hydrogenation of **5** and **10**, respectively. Furthermore, these catalysts could be recovered easily and the recycled catalyst was shown to maintain similar efficiency as compared with the freshly prepared one. We believe this new technique has the potential not only for laboratory-scale research but also for industrial applications.

3. Experimental

3.1. Materials and equipment

Unless otherwise noted, all experiments were carried out under a nitrogen atmosphere by using standard Schlenk-type techniques, or performed in a glovebox. All solvents were dried using standard, published methods and were distilled under a nitrogen atmosphere before use. Polyethylene glycol monomethyl ether (MeO-PEG, $M_w = 5000$) was purchased from Aldrich and was dried over P_2O_5 under vacuum before use. Other chemicals were obtained from commercial sources, and were used without further purification, unless otherwise stated. (*R*)-5,5′-Diamino-2,2′-bis-(diphenylphosphino)-1,1′-binaphthyls (5,5′-diamino (*R*)-BINAP) **1** was synthesized according to the published method.[19] (3*R*,4*R*)-3,4-Bis(diphenylphosphino)–pyrrolidine (Pyrphos) **7** was previously synthesized.[20]

NMR spectra were obtained on a Bruker Model Advance DPX 400 spectrometer (400 MHz ^1H and 162 Hz ^{31}P) using tetramethylsilane for ^1H as an internal standard, 85% of H_3PO_4 in D_2O for ^{31}P as an external standard, and coupling constants are given in hertz. All signals are reported in ppm units. For high-pressure hydrogenation, a 50 mL stainless autoclave equipped with a glass liner was used.

3.2. MeO-PEG-supported BINAP 2

To a cooled solution of terephthaloyl chloride (62 mg, 0.305 mmol) and dried DMAc (3 mL), 5,5′-diamino (*R*)-BINAP **1** (150 mg, 0.23 mmol) and NEt_3 (60 μL, 0.75 mmol) in dried DMAc (2 mL) was added dropwise with stirring. The reaction mixture was stirred at rt for another 60 min under a nitrogen atmosphere. A solution of MeO-PEG-OH (Mn = 5000, 800 mg, 0.16 mmol

OH) in DMAc (5 mL) was then added. The mixture was stirred at 40–50°C for a further 8 h. To this solution was slowly added diethyl ether (50 mL) with vigorous stirring. The precipitated polymer was filtered and washed with cold methanol and diethyl ether, then dried under vacuum to give MeO-PEG-supported BINAP ligand **2** (0.97 g, 98%). ^{1}H NMR (400 MHz, CD_2Cl_2): 3.27–3.80 (polyethylene glycol peaks), 6.79 (t, *J* = 7.80 Hz, 2H), 7.02–7.20 (m, 19.2H), 7.45 (t, 2H) 7.60 (s, 2H), 8.09–8.16 (m, 6); ^{31}P NMR (160 MHz, CD_2Cl_2): −16.82. Molecular weight (M_w) = 10540 (on the basis of polystyrene calibration); amount of BINAP moieties = 5.65 g per 100 g polymer (determined by ^{1}H NMR).

3.3. MeO-PEG-supported [RuCl(binap)(cymene)]Cl 3

A mixture of MeO-PEG-supported BINAP **2** (500 mg, 28 mg, 0.045 mmol BINAP) and $[RuCl_2(cymene)]_2$ (13.5 mg, 0.022 mmol) in dichloromethane/MeOH (1/1, v/v, 10 mL) was magnetically stirred under a nitrogen atmosphere at 50–60°C for 40 min. After cooling to room temperature, the solvent was removed under reduced pressure to give pale yellow catalyst **3**. This catalyst was used in the asymmetric hydrogenation reactions without further purification. ^{31}P NMR (160 MHz, $CDCl_3$): 25.1 (d, *J* = 61.4 Hz), 38.8 (d, *J* = 62.9 Hz).

3.4. Ru(5,5′-Diamino BINAP)(acac)$_2$ 1a

A 50 mL flask equipped with a condenser and a stirring bar was charged with of 5,5′-diamino (*R*)-BINAP **1** (0.5 g, 0.767 mmol), $Ru(acac)_3$ (0.30 g, 0.754 mmol), Zn dust (1 g) and degassed EtOH (20 mL) under a nitrogen atmosphere. The mixture was heated under reflux overnight. Most of the solvent was removed under reduced pressure and the evaporation residue was extracted with CH_2Cl_2 (three times) the combined brownish–yellow organic extract was concentrated under reduced pressure to give **1a** (695 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): 1.27 (s, 3H), 1.54 (d, *J* = 5.62 Hz, 6H), 1.84 (s, 3H), 3.90 (s, 4H), 4.79 (s, 1H), 5.04 (s, 1H), 6.06 (d, *J* = 8.61 Hz, 1H), 6.13 (d, *J* = 8.58 Hz, 1H), 6.36–7.70 (m, 28H); ^{31}P NMR (160 MHz, $CDCl_3$): 55.4(s), 55.1(s).

3.5. MeO-PEG-supported Ru(BINAP)(acac)$_2$ 4

To a cooled solution of terephthaloyl chloride (30 mg, 0.148 mmol) and dried DMAc (2 mL), a solution of **1a** (100 mg, 0.104 mmol) in dried DMAc (2 mL) containing NEt_3 (50 μL, 0.35 mmol) was added dropwise with stirring. The reaction mixture was stirred at rt for another 60 min under a nitrogen atmosphere. A solution of MeO-PEG-OH (Mn = 5000, 430 mg, 0.086 mmol) in DMAc (4 mL) was then added. The solution was stirred at rt for 30 min, then heated to 40–50°C and stirred for a further 8 h. To this solution was slowly added diethyl ether (25 mL) with vigorous stirring. The precipitated polymer was filtered and washed with cold methanol and diethyl ether, then dried in vacuo to give yellow product **4** (540 mg, 98%). ^{31}P NMR (160 MHz, CD_2Cl_2): 55.15, 55.37. Molecular weight (M_w) = 10540 (on the basis of polystyrene calibration); amount of $Ru(BINAP)(acac)_2$ moieties = 16.0 g per 100 g polymer (determined by ^{1}H NMR).

3.6. General procedure for the hydrogenation of 2-(6′-methoxy-2′-naphthyl)propenoic acid 5 catalyzed by catalyst 3

In a glovebox under a nitrogen atmosphere, a 45 mL glass-lined stainless steel reactor with a magnetic stirring bar was charged with catalyst **3** (3.66 mg), substrate **5** (15 mg), NEt_3 (8 μL) and MeOH (2.5 mL). The reactor was closed and pressurized with H_2 to 1000 psi. The mixture was stirred with a magnetic stirrer under H_2 pressure at 25°C for 2 h. The H_2 gas pressure was vented and the products were analyzed by HPLC using a SUMICHIRAL OA-2500 column: 6×10^{-3} M NH_4OAc of MeOH solution; flow rate = 1.2 mL/min; t_R (*R*)-enantiomer = 14.63, t_R (*S*)-enantiomer = 17.33, and t_R **5** = 14.82 min.

3.7. Asymmetric hydrogenation of 5 catalyzed by catalyst 3 illustrating the recycle of the MeO-PEG-supported Ru(BINAP) catalysts

In a glovebox under a nitrogen atmosphere, a 45 mL glass-lined stainless steel reactor with a magnetic stirring bar was charged with catalyst **3** (7.32 mg), substrate **5** (30 mg), NEt_3 (16 μL) and MeOH (4 mL). The autoclave was pressurized with hydrogen to 1800 psi and the mixture was stirred at 0°C for 8 h. The autoclave was depressurized, and most of the methanol was then removed under reduced pressure. The residue was treated with diethyl ether (20 mL). The precipitated polymeric catalyst was collected by filtration for re-use in the next reaction. The filtrate was used for the determination of e.e. and conversion of the product.

3.8. (3*R*,4*R*)-*N*-(4-Carboxybutanoyl)-3,4-bis-(diphenylphosphino)-pyrrolidine 8

To a solution of **7** in CH_2Cl_2 was added succinic anhydride (2–3 equivalents) and the mixture was stirred overnight. After washing with water, the CH_2Cl_2 phase was dried over anhydrous $MgSO_4$. The crude product was further purified by column chromatography to give **8** (more than 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$): 2.42–2.45 (m, 2H), 2.61–2.65 (m, 2H), 2.89 (m, 1H), 1.98 (m, 1H), 3.34 (t, *J* = 11.89 Hz, 1H), 3.71 (t, *J* = 12.79 Hz, 1H), 3.86–3.89 (m, 2H), 7.16–7.18 (m, 4H), 7.24–7.26 (m, 4H), 7.31–7.38 (m, 12H); ^{31}P NMR (160 MHz, $CDCl_3$): −12.14, −12.69.

3.9. MeO-PEG-supported Pyrphos 9

DCC (55 mg, 0.267 mmol) was added to a mixture of MeO-PEG-OH (450 mg, 0.09 mmol), DMAP (10 mg, 0.082 mmol), and **8** (50 mg, 0.093 mmol) in CH_2Cl_2. The mixture was stirred overnight and the urea precipitate was removed by filtration through Celite. To this solution was slowly added cold dried diethyl ether (25 mL) with vigorous stirring. The precipitated polymer was filtered and washed with cold methanol and diethyl ether, then dried in vacuo to give pale yellow product **9** (488 mg, 98%). ^{1}H NMR (400 MHz, CD_2Cl_2): 3.65–3.71 (polyethylene glycol peaks), 7.14–7.17 (m, 4H), 7.20–7.22 (m, 4H), 7.30–7.38 (m, 12H), 1.5–3.5 (m, 10H); ^{31}P NMR (160 MHz, $CDCl_3$): −12.63, −12.85; amount of Pyrphos moieties = 4.0 g per 100 g polymer (determined by ^{1}H NMR).

3.10. General procedure for the hydrogenation of prochiral enamides 10

In situ MeO-PEG-supported rhodium catalyst was prepared by mixing of **10** (500 mg, 0.045 mmol of Pyrphos) and $[Rh(COD)_2]BF_4$ (20 mg, 0.043 mmol) in methanol for 60 min at ambient temperature. In a glovebox under a nitrogen atmosphere, a 45 mL glass-lined stainless steel reactor with a magnetic stirring bar was charged with the above in situ prepared catalyst (2.5×10^{-4} mmol Rh) and the substrate for hydrogenation (0.1 mmol). The mixture was diluted to 2.5 mL by further addition of methanol. The reactor was closed and pressurized to 800 psi H_2 pressure and stirred at ambient temperature. The conversion and e.e. of product was determined by gas chromatography using a 25 m Chiralsil L-Val capillary column. The separation and recycling of the catalyst was carried out as in the method described above.

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