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Synthesis of MeO-PEG$_{2000}$-supported chiral ferrocenyl oxazoline carbinol ligand and its application in asymmetric catalysis

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ABSTRACT

A simple method for the synthesis of a MeO-PEG-supported chiral ferrocenyl oxazoline carbinol ligand has been developed. The chiral ligand was successfully applied to the catalytic asymmetric addition of diethylzinc to aryl aldehydes, affording secondary alcohols in high yields and with excellent enantioselectivities (up to 94% ee). The chiral ligand can be recovered and reused twice with no apparent loss of catalyst efficiency.

1. Introduction

The development of more efficient and environmentally friendly methodologies in asymmetric catalysis is a very important area of research in organic chemistry. One area that has attracted a great deal of interest in recent years is combining asymmetric catalysis and polymer-supported transition metals.[1–3] Chiral catalyst immobilization can overcome problems that traditionally plague chiral catalysts, such as difficult separation and recycling.[2] However, immobilized ligands and catalysts often exhibit lower enantioselectivities and efficiencies than their non-immobilized counterparts. Therefore, one of the main challenges of immobilized chiral ligands is to maintain their activities and selectivities while facilitating their recovery and recyclability.

Recently, expensive chiral catalysts have been recovered and recycled by utilizing soluble PEG polymers as supports. These PEG-supported catalysts have higher catalytic activities and better enantioselectivities than those immobilized on other solid materials. PEG-supported catalysts can be easily separated from the reaction mixture by filtration, extraction or precipitation.[3]

In addition to its unique sandwich structure, ferrocene has many ideal properties such as low cost, thermal stability, planar chirality, rigid bulkiness, and ease of derivatization.[4] These characteristics make ferrocene suitable for its use as a scaffold for chiral ligands,[5] and it may also be beneficial for the new chiral ligand design. Recently, ferrocene and its derivatives with planar chiral ferrocenyl oxazoline ligands being the most widely used in asymmetric catalysis have been the subject of increasing interest in organometallic chemistry, materials science, and catalysis.[6] Among them, the ferrocenyl-oxazoline carbinols[7] and ferrocenyl-oxazoline silanol[8] developed by Bolm et al. were proven to be efficient catalysts for asymmetric arylation reaction of benzaldehydes. However, only a few reports on soluble polymer supported ferrocenyl oxazoline have been reported.[9]

The monomethyl ether of PEG (MeO-PEG) has been successfully used to support chiral ligands in some asymmetric reactions.[10] Recently, Zhou et al. reported a simple synthesis and application of MeO-PEG-supported chiral *N*,*P*-ligands and *N*,*S*-ligands containing a ferrocenyl oxazoline moiety.[9b] Although these results are important, further investigations are still needed and new applications remain to be explored. Herein, we report the synthesis of a MeO-PEG-supported chiral ferrocenyl oxazoline carbinol ligand and its preliminary application in catalytic asymmetric additions of diethylzinc to aldehydes, affording secondary alcohols in high yields and with excellent enantioselectivities. The chiral ligand can be recovered and reused twice without apparent loss of catalyst efficiency (see Fig. 1).

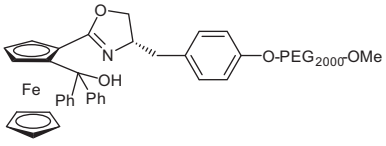

Figure 1. MeO-PEG-supported chiral ferrocenyl-oxazoline carbinol ligand.

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2. Results and discussion

MeO-PEG-supported chiral ferrocenyl oxazoline carbinol ligand **12** was synthesized from the chiral amino alcohol **6**, which was prepared from inexpensive and readily available L-tyrosine **1**. As shown in Figure 2, the steps for the synthesis of **6** include esterification, protection of the amino group, phenolic hydroxyl protection, reduction, and removal of the Boc-protecting group.[11]

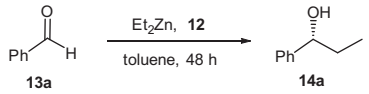
Figure 3 shows the synthetic steps for converting amino alcohol **6** into MeO-PEG-supported chiral ligand **12**. First, amino alcohol **6** reacted with ferrocene carboxylic acid to form oxazoline **9** according to the known procedure.[6a,12] Compound **10** was then formed in moderate yield by *ortho*-lithiation of ferrocenyl oxazoline **9** by using *s*-BuLi at −78 °C in THF, followed by the addition of Ph_2CO. The absolute configuration of **10** was assigned as (*Rp*,*S*) by X-ray crystallographic analysis.[13] Compound **10** was then converted into chiral ferrocenyl oxazoline ligand **11** by removal of the TBS protecting group. Finally, ligand **11** was reacted with poly(ethylene glycol) 2000 monomethyl ether mesylate with Cs_2CO_3 as the base in DMF to afford the desired MeO-PEG-supported chiral ligand **12** in 90% yield.[14]

With chiral ligand **12** in hand, the asymmetric addition of diethylzinc to aryl aldehydes was carried out to check its catalytic properties under various reaction conditions and the results are summarized in Table 1.

Initially, benzaldehyde and diethylzinc (Et_2Zn) were chosen as the model system,[16] and the effect of the catalyst loading was next examined. In the presence of 5 mol % of chiral ligand **12** at 0 °C the reaction preceded well to give the desired product with 87% ee and in 99% yield (Table 1, entry 1). When the catalyst loading was reduced to 3 mol %, (*R*)-1-phenylpropan-1-ol was obtained without a significant increase in the ee value (Table 1, entry 2). When the catalyst loading was further reduced to 1 mol %, the ee increased slightly to 89% (Table 1, entry 3). The yield and the ee of the product decreased significantly when the catalyst loading was reduced to 0.1 mol % (Table 1, entry 4). In view of the reactivity and enantioselectivity, these results demonstrate that the optimum amount of chiral ligand **12** was 1 mol %. Next, the effect of temperature was examined. The product was obtained with 84% ee and in 90% yield at −10 °C (Table 1, entry 5). When the temperature was increased to 20 °C, the ee decreased to 26% (Table 1, entry 6). In addition, the reaction of the ligand **10** was also carried out under the same reaction conditions. Compared with ligand **12**, the product was obtained in 99% yield, while the ee value did not change significantly (Table 1, entry 7). Thus, the optimal conditions for the model system were established as 1 mol % ferrocene **12** as the catalyst and 0 °C.

After optimizing the reaction conditions, the reactions of diethylzinc with aryl aldehydes with various steric and electronic properties were explored and the results are shown in Table 2. As shown previously, the reaction of benzaldehyde with diethylz-

Table 1
Optimization of the reaction conditions[a]



13a 14a

Entry	**12** (mol %)	Temp (°C)	Yield (%)[b]	ee (%)[c]	Config[d]
1	5	0	>99	87	(*R*)
2	3	0	>99	88	(*R*)
3	1	0	>99	89	(*R*)
4	0.1	0	69	40	(*R*)
5	1	−10	90	84	(*R*)
6	1	20	60	26	(*R*)
7[e]	1	0	99	91	(*R*)

[a] Conditions: benzaldehyde (0.5 mmol), Et_2Zn (2 mmol), ligand **12** (0.005 mmol) in toluene at 0 °C for 48 h.
[b] Isolated yields.
[c] Determined by chiral HPLC.
[d] The configuration of the major products is (*R*).[15]
[e] Ligand **10** was used instead of ligand **12**.

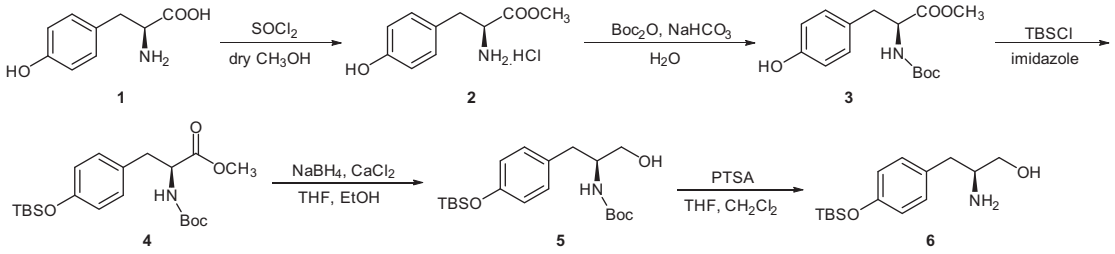


Figure 2. Synthesis of chiral amino alcohol **6**.

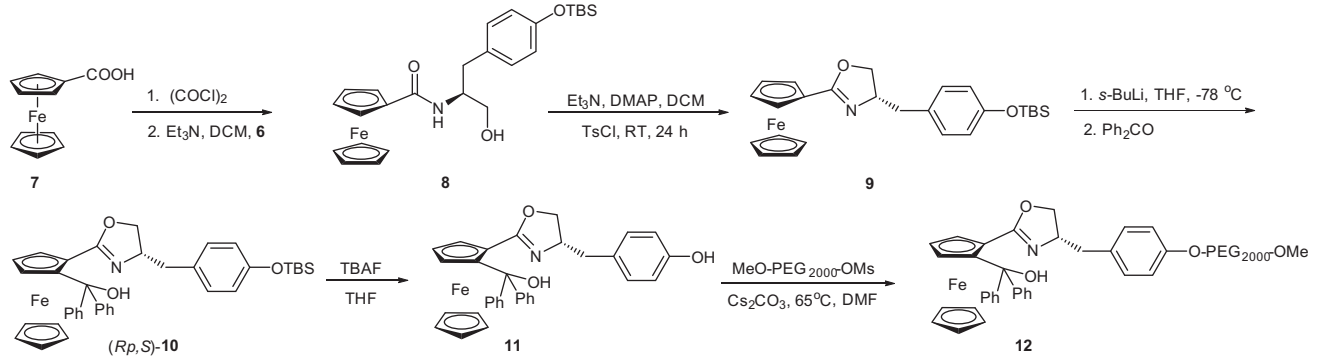
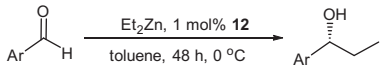
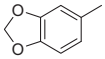


Figure 3. Synthesis of MeO-PEG-supported chiral ligand **12**.

Table 2
Asymmetric alkyl transfer reaction to substituted benzaldehydes **13** using chiral ligand **12** and Et_2Zn[a]



13 14

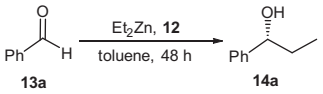
Entry	Ar	Yield (%)[b]	ee (%)[c]	Config[d]
1	Ph	99 **14a**	88	(*R*)
2	4-CH_3Ph	97 **14b**	84	(*R*)
3	4-CH_3OPh	95 **14c**	81	(*R*)
4	3-CH_3OPh	61 **14d**	70	(*R*)
5	2-CH_3OPh	66 **14e**	62	(*R*)
6		>99 **14f**	82	(*R*)
7		>99 **14g**	59	(*R*)
8		>99 **14h**	87	(*R*)
9	Fc	>99 **14i**	94	(*R*)
10	2-ClPh	68 **14j**	52	(*R*)
11	4-ClPh	69 **14k**	61	(*R*)

[a] Conditions: aldehyde (0.5 mmol), Et_2Zn (2 mmol), ligand **12** (0.005 mmol) in toluene at 0 °C for 48 h.
[b] Isolated yields.
[c] Determined by chiral HPLC.
[d] The major product had an (*R*)-configuration.

inc proceeded smoothly to give the corresponding products **14a** with 88% ee in 99% yield (Table 2, entry 1). *p*-Tolualdehyde also reacted with diethylzinc to give the desired product **14b** with 84% ee in 97% yield (Table 2, entry 2). *p*-Anisaldehyde showed good enantioselectivity (Table 2, entry 3). However, when a MeO group was at the *meta*- or *ortho*-positions, the ee of the reaction product decreased dramatically to 70% or 62%, respectively (Table 2, entries 4 and 5). These results suggest that the steric effect of the aldehyde is a key factor for controlling the reactivity. β-Naphthaldehyde also exhibited excellent reactivity and gave the desired products **14f** with 82% ee in 99% yield (Table 2, entry 6). The reaction of α-naphthaldehyde with diethylzinc led to products with lower ee values (Table 2, entry 7), indicating that the reaction was very sensitive to the steric hindrance of the aldehyde substrate. Benzo[*d*][1,3]dioxole-5-carbaldehyde also reacted with diethylzinc to give the desired product **14h** with 87% ee in 99% yield (Table 2, entry 8). The product for the addition of diethylzinc to ferrocenecarboxaldehyde gave the best ee (94%) with an isolated yield of 99% (Table 2, entry 9). When a benzaldehyde with a halide substituent was used as the substrate, the activity of the catalyst significantly decreased. For example, benzaldehyde with a Cl substituent at the 2- or 4-position reacted with diethylzinc to give **14j** and **14k** with 52% and 61% ee in 68% and 69% yields, respectively (Table 2, entries 10 and 11). This indicates that the electronic effect also plays an important role in this reaction.

The recyclability of MeO-PEG-supported chiral ligand **12** was also studied and the results are presented in Table 3. After the reaction was completed, diethyl ether (Et_2O) was added to the reaction system. Since MeO-PEG supported ligand **12** does not dissolve in Et_2O, it precipitated from the reaction mixture. The catalyst was then recovered by filtration and the recovered chiral ligand **12** was used for another catalytic cycle. The catalyst maintained good enantioselectivity even after being recovered and reused twice. For the fourth run, the activity of the catalyst decreased a great deal. It should be noted that the reaction protocol as well as the separation and recycling method are simple and efficient.

Table 3
Recycling experiments[a]



13a 14a

Run	Ligand	Yield (%)[b]	ee (%)[c]	Config.[d]
1	**12**	>99	88	(*R*)
2	**12**	97	83	(*R*)
3	**12**	97	81	(*R*)
4	**12**	54	62	(*R*)

[a] Conditions: benzaldehyde (0.5 mmol), Et_2Zn (2 mmol), ligand **12** (0.005 mmol) in toluene at 0 °C for 48 h.
[b] Isolated yields.
[c] Determined by HPLC.
[d] The major product had an (*R*)-configuration.

3. Conclusion

In conclusion, the synthesis of MeO-PEG-supported chiral ferrocenyl-oxazoline carbinol ligand **12** has been described and its catalytic use in asymmetric alkyl-transfer reactions to substituted benzaldehydes has been demonstrated. High yields and good enantioselectivities were achieved in all of the reactions. Furthermore, the catalyst can be easily recovered and reused in successive catalytic additions, while maintaining its enantioselectivity even at the third cycle. We are currently exploring the potential use of this new class of ligands in other enantioselective reactions.

4. Experimental

4.1. General

Unless otherwise noted, all catalytic reactions were carried out under an atmosphere of dry N_2 with oven-dried glassware and anhydrous solvents. ^1H and ^{13}C NMR spectra were obtained on a Bruker 400 MHz spectrometer with $CDCl_3$ as the solvent. Chemical shifts were measured relative to tetramethylsilane as an internal reference. IR spectra were recorded on Nicolet-NEXUS 670 FT-IR spectrometer. Melting points were determined using a Beijing X-5 melting point apparatus and were uncorrected. Mass spectra were recorded on a Bruker esquire-3000. Enantiomeric excesses were determined by HPLC (Chiralcel-OD and Chiralcel-OB columns) with UV detection and an *i*-PrOH/hexane mobile phase. Toluene was distilled under an N_2 atmosphere after drying with sodium/benzophenone. Diethylzinc (1.0 M solution in hexane) was purchased from Aldrich, and used directly. (*S*)-2-Amino-3-[4-(*tert*-butyldimethylsilyloxy)-phenyl]-propan-1-ol **6** was prepared according to the procedure in the literature.[11] Other chemicals and reagents were obtained from commercial sources and used directly.

4.2. Typical procedure for the preparation of MeO-PEG-supported ligand 12

4.2.1. Synthesis of the compound 8

Oxalyl chloride (0.72 mL, 7.5 mmol) was added via syringe to a stirred suspension of ferrocenecarboxylic acid **7** (0.82 g, 3.56 mmol) in CH_2C1_2 (25 mL) at room temperature under nitrogen. This mixture was allowed to react for 2 h and then evaporated to dryness to give a purple solid. The resultant crude ferrocenyl chloride was dissolved in CH_2C1_2 and added dropwise to a solution of (*S*)-2-amino-3-[4-(*tert*-butyldimethylsilyloxy)-phenyl]-propan-1-ol **6** (1.8 g, 6.3 mmol) and triethylamine (1.1 mL, 7.2 mmol) in

20 mL of CH_2C1_2 in an ice-water bath under a nitrogen atmosphere. The reaction mixture was stirred at room temperature overnight. The reaction mixture was washed with H_2O and saturated aqueous NaCl, dried over $MgSO_4$, filtered and evaporated in vacuo. The crude product was purified by column chromatography (1:1 EtOAc/petroleum ether) to give product **8** as an orange solid (1.17 g, 66.5%). $[\alpha]_D = -1.2$ (*c* 1.03, $CHCl_3$); mp 120–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.15 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 5.88 (d, J = 6.6 Hz, 1H), 4.62 (s, 1H), 4.49 (s, 1H), 4.32 (d, J = 6.4 Hz, 2H), 4.26 (t, J = 10.6 Hz, 1H), 4.08 (s, 5H), 3.77 (d, J = 10.6 Hz, 1H), 3.68 (s, 1H), 3.50 (s, 1H), 2.95 (dd, J = 14.0, 6.3 Hz, 1H), 2.79 (dd, J = 14.0, 8.4 Hz, 1H), 1.06–0.92 (m, 9H), 0.17 (d, J = 2.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.69, 154.61, 130.08, 120.42, 75.31, 70.64, 69.81, 68.54, 67.68, 65.49, 53.40, 36.33, 30.96, 25.66, 18.18, −4.41; HRMS (ESI) *m*/*z*: Calcd for $C_{26}H_{35}FeNO_3Si$ $[M+H]^+$: 494.1814; found: 494.1816.

4.2.2. Synthesis of compound 9

The above product **8** (2.3 g, 4.6 mmol) was dissolved in 50 mL CH_2C1_2 and then 1.3 mL (2 equiv) Et_3N was added. After stirring for 2 h, TsCl (0.98 g, 1.1 equiv) and a catalytic amount DMAP were added and the solution was stirred at room temperature under nitrogen overnight. Next, 50 mL of CH_2C1_2 were added, and the resulting solution was washed with saturated ammonium chloride solution and saturated aqueous $NaHCO_3$. After extracting with CH_2C1_2, the organics were dried over $MgSO_4$, filtered and concentrated. The residue was purified using silica gel column chromatography (1:3 EtOAc/petroleum ether) to afford the pure product **9** (2.0 g, 91%) as a yellow solid. $[\alpha]_D = -1.5$ (*c* 0.67, $CHCl_3$); mp 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.10 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.4 Hz, 2H), 4.75 (t, J = 1.8 Hz, 2H), 4.44–4.37 (m, 1H), 4.36–4.33 (m, 2H), 4.31 (d, J = 6.9 Hz, 1H), 4.23 (t, J = 8.7 Hz, 1H), 4.18 (s, 5H), 4.10–4.00 (m, 1H), 3.17 (dd, J = 13.9, 4.5 Hz, 1H), 2.60 (dd, J = 13.7, 9.3 Hz, 1H), 0.98 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.18, 130.61, 130.14, 120.05, 71.36, 70.27, 69.62, 68.93, 67.89, 40.97, 25.63, −4.46; HRMS (ESI) *m*/*z*: Calcd for $C_{26}H_{33}FeNO_2Si$ $[M+H]^+$: 476.1708; found: 476.1693.

4.2.3. Synthesis of compound 10

A yellow/orange stirred solution of **9** (0.998 g, 2.1 mmol) in THF (20 mL) under nitrogen was cooled to −78 °C in a Schlenk tube. Next, *s*-BuLi (2.52 mL, 1.2 equiv, 1 M in hexane) was added dropwise to the solution. After stirring at −78 °C for 2 h, the Schlenk tube was heated to −60 °C and stirring was maintained for another 15 min. Next Ph_2CO (574 mg, 3 mmol) was added and the reaction mixture was allowed to warm to room temperature. Finally the reaction mixture was quenched with saturated ammonium chloride and diluted with ether. The two layers were separated and the aqueous phase was extracted with Et_2O. The organics were combined, dried over $MgSO_4$, filtered and evaporated. The crude product was purified by column chromatography to afford **10** as a red crystalline solid. Recrystallisation from hexane and CH_2C1_2 gave pure **10** as a single diastereo-isomer. Mp 192–194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.06 (s, 1H), 7.52 (d, J = 7.3 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.28–7.22 (m, 2H), 7.20–7.04 (m, 7H), 6.83–6.75 (m, 2H), 4.72 (dd, J = 2.5, 1.6 Hz, 1H), 4.25 (d, J = 2.8 Hz, 1H), 4.22 (s, 5H), 4.12–4.03 (m, 2H), 4.00–3.92 (m, 1H), 3.70 (dd, J = 2.5, 1.6 Hz, 1H), 3.05 (dd, J = 13.6, 4.0 Hz, 1H), 2.66 (dd, J = 13.6, 7.2 Hz, 1H), 0.97 (d, J = 2.9 Hz, 9H), 0.17 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.24, 154.32, 149.33, 146.56, 130.58–130.41, 130.26, 127.89, 127.53, 127.14, 126.58, 126.30, 120.16, 100.42, 75.15, 71.20, 70.85, 70.46, 68.12, 66.80, 65.70, 40.47, 25.70, 18.19, −4.39; HRMS (ESI) *m*/*z*: Calcd for $C_{39}H_{43}FeNO_3Si$ $[M+H]^+$: 658.2440; found: 658.2436.

4.2.4. Synthesis of compound 11

A solution of TBAF (1.8 mL of 1.0 M solution in THF solution) in 10 mL of THF was added to a round bottom flask. Compound **10** (0.6 g, 0.91 mmol) in THF (10 mL) was then added dropwise, and the mixture was stirred until the reaction was complete. The solvents were removed under reduced pressure after which water was added to the residue. The aqueous layer was extracted twice with EtOAc, and the combined organics were dried with $MgSO_4$, filtered, and concentrated. The residue was purified on silica gel to give the desired product **11** (0.47 g, yield 95%). $[\alpha]_D = -1.4$ (*c* 0.1, $CHCl_3$); mp 179–181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.22 (s, 1H), 7.51–7.49 (m, 2H), 7.30 (t, J = 6.4 Hz, 2H), 7.25–7.22 (m, 1H), 7.20–7.04 (m, 7H), 6.87–6.76 (m, 2H), 5.36 (s, 1H), 4.73 (dd, J = 2.6, 1.6 Hz, 1H), 4.25 (t, J = 2.6 Hz, 1H), 4.22 (s, 5H), 4.18–4.01 (m, 2H), 3.97 (d, J = 2.9 Hz, 1H), 3.68 (dd, J = 2.6, 1.6 Hz, 1H), 3.03–2.92 (m, 1H), 2.77–2.66 (m, 1H); HRMS (ESI) *m*/*z*: Calcd for $C_{33}H_{29}FeNO_3$ $[M+H]^+$: 544.1575; found: 544.1562.

4.2.5. Synthesis of compound 12

Nitrogen gas was bubbled through a solution of the above product **11** (0.4 g) in DMF (20 mL). Next, Cs_2CO_3 (0.6 g) and MeO-PEG-OMs (1.55 g) were added to the solution. The mixture was heated to 65 °C until the reaction was complete. After removal of DMF in vacuo, HCl (2 M) was added and the mixture was extracted with CH_2C1_2. The combined organics were washed with saturated NaCl solution, dried with $MgSO_4$, filtered, and concentrated. Next, Et_2O (25 mL) was added slowly with vigorous stirring at 0 °C. The precipitate formed was isolated by filtration and then dried in vacuo to give the MeO-PEG derivatives **12** (yield 90%). $[\alpha]_D = -17.2$ (*c* 0.53, $CHCl_3$); mp 43–45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.08 (s, 1H), 7.51 (d, J = 7.5 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.25–7.23 (m, 1H), 7.19–7.08 (m, 7H), 6.89 (d, J = 8.6 Hz, 2H), 4.73–4.70 (m, 1H), 4.25 (dd, J = 4.8, 2.2 Hz, 1H), 4.21 (s, 5H), 4.11–4.07 (m, 4H), 4.01–3.92 (m, 1H), 3.82 (dd, J = 9.1, 4.3 Hz, 3H), 3.72–3.68 (m, 4H), 3.68–3.57 (m, 171H), 3.55 (dd, J = 5.7, 3.6 Hz, 2H), 3.49–3.44 (m, 2H), 3.38 (s, 3H), 3.05 (dd, J = 16.8, 6.8 Hz, 1H), 2.70 (dd, J = 14.0, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.27, 157.53, 149.28, 146.53, 130.45, 129.67, 127.21, 127.08, 126.59, 126.32, 114.80, 100.35, 75.13, 71.95, 70.82, 70.79, 70.67, 70.66, 70.58–70.44, 69.74, 68.13, 67.45, 66.73, 65.66, 59.04, 40.24.

4.2.6. Typical procedure for the addition of diethylzinc to aldehydes using MeO-PEG-supported ferrocene 12

Chiral ligand **12** (0.005 mmol) was placed in a dried Schlenk tube under a nitrogen atmosphere. Freshly distilled toluene (2.0 mL) was then added followed by diethylzinc (2.0 mL, 1 M in hexane). The resulting solution was cooled to 0 °C and stirred for approximately 30 min. The aldehyde (0.5 mmol) was then added and the reaction mixture was stirred for 48 h. The reaction was quenched with saturated ammonium chloride solution (4.0 mL). The mixture was then extracted with diethyl ether, and the organic portion was washed with saturated aqueous NaCl. The combined organics were then dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude compound was purified by flash chromatography to give the final product.

4.2.7. 1-Phenylpropan-1-ol 14a

99% yield, 88% ee, $[\alpha]_D^{20} = +27.7$ (*c* 2.2, $CHCl_3$), [Determined by HPLC analysis Chiralcel OD-H column, Hexane/*i*-PrOH = 100/2, Flow rate: 1 mL/min, UV detection at 254 nm, Retention time: t_{major} = 13.31 min, t_{minor} = 17.24 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, 3H), 1.71–1.92 (m, 2H), 1.96 (br, 1H), 4.51–4.72 (m, 1H), 7.25–7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 128.4, 127.4, 126.2, 75.9, 31.9, 10.2.

4.2.8. 1-(*p*-Tolyl)propan-1-ol 14b

97% yield, 84% ee, $[\alpha]_D^{20}$ = +33.9 (*c* 5.0, $CHCl_3$), [Determined by HPLC analysis Chiralcel OB-H column, Hexane/*i*-PrOH = 95/5, Flow rate: 0.5 mL/min, UV detection at 254 nm, Retention time: t_{major} = 7.92 min, t_{minor} = 5.95 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.3 Hz, 3H), 1.63–1.92 (m, 2H), 2.31 (s, 3H), 2.49 (br s, 1H), 4.45 (t, *J* = 6.8 Hz, 1H), 7.10 (d, *J* = 8.6 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 137.8, 129.9, 127.1, 76.6, 32.8, 22.1, 10.8.

4.2.9. 1-(4-Methoxyphenyl)propan-1-ol 14c

95% yield, 81% ee, $[\alpha]_D^{20}$ = +30.5 (*c* 2.6, $CHCl_3$), [Determined by HPLC analysis Chiralcel OD-H column, Hexane/*i*-PrOH = 100/1, Flow rate: 1 mL/min, UV detection at 254 nm, Retention time: t_{major} = 33.05 min, t_{minor} = 38.07 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.3 Hz, 3H), 1.56–1.87 (m, 2H), 1.99 (br s, 1H), 3.73 (s, 3H), 4.44 (t, *J* = 6.8 Hz, 1H), 6.79 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 135.8, 126.7, 112.7, 74.9, 54.7, 31.2, 9.6.

4.2.10. 1-(3-Methoxyphenyl)propan-1-ol 14d

61% yield, 70% ee, $[\alpha]_D^{20}$ = +19.9 (*c* 0.5, $CHCl_3$), [Determined by HPLC analysis Chiralcel OD-H column, Hexane/*i*-PrOH = 100/2, Flow rate: 1 mL/min, UV detection at 254 nm, Retention time: t_{major} = 28.16 min, t_{minor} = 33.43 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.3 Hz, 3H), 1.61–1.79 (m, 2H), 2.58 (br s, 1H), 3.75 (s, 3H), 4.50 (t, *J* = 6.6 Hz, 1H), 6.76 (dd, *J* = 8.3 Hz, 2.4 Hz, 1H), 6.85–6.87 (m, 2H), 7.21 (dd, *J* = 8.3 Hz, 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 146.9, 130.0, 118.9, 113.7, 112.2, 15.8, 55.8, 32.6, 10.7.

4.2.11. 1-(2-Methoxyphenyl)propan-1-ol 14e

66% yield, 62% ee, $[\alpha]_D^{20}$ = +12.6 (*c* 4.1, $CHCl_3$), [Determined by HPLC analysis Chiralcel OD-H column, Hexane/*i*-PrOH = 100/1, Flow rate: 1 mL/min, UV detection at 254 nm, Retention time: t_{major} = 21.74 min, t_{minor} = 20.71 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.4 Hz, 3H), 1.80–1.87 (m, 2H), 2.82 (d, *J* = 6.1 Hz, 1H), 3.86 (s, 3H), 4.80–4.85 (m, 1H), 6.89–7.35 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 132.4, 128.0, 126.9, 120.5, 110.4, 71.9, 55.1, 30.1, 10.3.

4.2.12. 1-(Naphthalen-2-yl)propan-1-ol 14f

99% yield, 82% ee, $[\alpha]_D^{20}$ = +31.1 (*c* 2.4, $CHCl_3$), [Determined by HPLC analysis Chiralcel OD-H column, Hexane/*i*-PrOH = 90/10, Flow rate: 0.5 mL/min, UV detection at 254 nm, Retention time: t_{major} = 22.42 min, t_{minor} = 19.54 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.3 Hz, 3H), 1.62–1.93 (m, 2H), 2.47 (br s, 1H), 4.65 (t, *J* = 6.6 Hz, 1H), 7.35–7.43 (m, 3H), 7.67 (s, 1H), 7.71–7.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 133.9, 133.6, 128.9, 128.6, 128.4, 126.9, 126.7, 125.7, 125.0, 76.9, 32.5, 10.9.

4.2.13. 1-(Naphthalen-1-yl)propan-1-ol 14g

99% yield, 59% ee, $[\alpha]_D^{20}$ = +32.8 (*c* 2.5, $CHCl_3$), [Determined by HPLC analysis Chiralcel OD-H column, Hexane/*i*-PrOH = 95/5, Flow rate: 1 mL/min, UV detection at 254 nm, Retention time: t_{major} = 27.53 min, t_{minor} = 13.38 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (t, *J* = 7.4 Hz, 3H), 1.87–2.02 (m, 2H), 2.94 (br, 1H), 5.32 (t, *J* = 6.2 Hz, 1H), 7.46–8.11 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 134.9, 131.7, 129.8, 128.6, 126.7, 126.3, 126.1, 124.3, 123.8, 73.5, 32.1, 11.4.

4.2.14. 1-(Benzo[*d*][1,3]dioxol-5-yl)propan-1-ol 14h

99% yield, 87% ee, $[\alpha]_D^{20}$ = +23.7 (*c* 1.5, $CHCl_3$), [Determined by HPLC analysis Chiralcel OD-H column, Hexane/*i*-PrOH = 98/2, Flow rate: 1 mL/min, UV detection at 254 nm, Retention time: t_{major} = 26.18 min, t_{minor} = 34.46 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.4 Hz, 3H), 1.79–2.01 (m, 2H), 1.89 (s, 1H), 4.57 (t, *J* = 6.5 Hz, 1H), 5.98 (s, 2H), 6.73–6.80 (m, 2H), 6.85 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 147.5, 139.5, 120.1, 108.7, 106.8, 101.6, 76.8, 32.3, 10.7.

4.2.15. (1-Hydroxypropyl)ferrocene 14i

99% yield, 94% ee, [Determined by HPLC analysis Chiralcel OD-H column, Hexane/*i*-PrOH = 100/2, Flow rate: 1.0 mL/min, UV detection at 254 nm, Retention time: t_{major} = 12.93 min, t_{minor} = 14.02 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.4 Hz, 3H), 1.55–1.65 (m, 2H), 1.93 (d, *J* = 3.2 Hz, 1H), 4.05–4.18 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 94.6, 71.6, 68.8, 68.4, 68.1, 67.5, 65.8, 31.6, 10.9.

4.2.16. 1-(2-Chlorophenyl)propan-1-ol 14j

68% yield, 52% ee, $[\alpha]_D^{20}$ = +28.9 (*c* 0.69, $CHCl_3$), [Determined by HPLC analysis Chiralcel OB-H column, Hexane/*i*-PrOH = 95/5, Flow rate: 0.5 mL/min, UV detection at 254 nm, Retention time: t_{major} = 13.22 min, t_{minor} = 10.25 min].

4.2.17. 1-(4-Chlorophenyl)propan-1-ol 14k

69% yield, 61% ee, $[\alpha]_D^{20}$ = +27.8 (*c* 3.2, $CHCl_3$), [Determined by HPLC analysis Chiralcel OB-H column, Hexane/*i*-PrOH = 95/5, Flow rate: 0.5 mL/min, UV detection at 254 nm, Retention time: t_{major} = 14.67 min, t_{minor} = 12.66 min]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.3 Hz, 3H), 1.63–1.92 (m, 2H), 2.37 (d, *J* = 2.6 Hz, 1H), 4.50 (t, *J* = 6.6 Hz, 1H), 7.21–7.32 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 133.8, 129.5, 128.3, 76.1, 32.7, 10.9.

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A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetasy.2016.08.018.

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