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Catalytic asymmetric aryl transfer: highly enantioselective preparation of (*R*)- and (*S*)-diarylmethanols catalyzed by the same chiral ferrocenyl aziridino alcohol

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Abstract

Highly enantioselective arylations of arylaldehydes using arylboronic acids as aryl resource were realized in the presence of a catalytic amount of (2*S*)-1-ferrocenylmethylaziridin-2-yl(diphenyl)methanol. In addition, the *R* or *S* enantiomers of a series of given diarylmethanols can be easily obtained in high yields with excellent enantioselectivities simply by the reverse combinations of both reaction partners. A possible transition state for the catalytic asymmetric addition has been proposed on the basis of previous studies.

1. Introduction

The efficient and highly enantioselective synthesis of chiral diarylmethanols is of primary importance because some of them are important intermediates for preparation of pharmacologically and biologically active compounds.[1] The catalytic enantioselective aryl transfer to arylaldehydes is seemingly the most efficient approach to chiral diarylmethanols because of the large steric and electronic differences between an aryl group and a hydrogen atom on an aldehyde substrate,[2] as compared with the asymmetric reduction of corresponding unsymmetrical ketones.[3] The asymmetric addition of diethylzinc to aldehydes shows a great success in the presence of a catalytic amount of various chiral amino alcohols,[4] and the asymmetric addition of diphenylzinc to aldehydes also seems to be a promising method for the synthesis of chiral diarylmethanols. However, the enantioselective phenylation of arylaldehydes using diphenylzinc itself as aryl resource achieved only limited success due to the presence of the competitive background reaction of diphenylzinc with aldehydes.[5–7] Although modification was later made to suppress the undesired background by using less reactive ethylphenylzinc that is readily available by mixing diphenylzinc with diethylzinc in a 1/2 ratio,[8,9] this approach still had some disadvantages: (1) diphenylzinc is an air-sensitive and expensive compound, (2) its use limits the reaction scope to the transfer of simple phenyl group, and (3) only one enantiomer of a given product was prepared in the presence of the same chiral ligand. Recent studies in this field have revealed that the catalytic enantioselective aryl transfer using arylboronic acids as aryl resources could overcome the above-mentioned drawbacks.[10–16] Unfortunately, ligands that effectively catalyze the asymmetric arylation of aldehydes using arylboronic acids as aryl resource with high ee values are relatively rare. In great contrast to the catalytic asymmetric alkylation of aldehydes with diethylzinc reagents, which becomes a very effective and general method,[4] the corresponding arylations are still in their infancy in the presence of a catalytic amount of chiral ligands in spite of their great potentials in organic synthesis.

β-Amino alcohols should be the first candidate ligands for catalytic asymmetric aryl transfer because of their easy availability and simple preparation conditions. More recently, we reported the synthesis of a series of chiral ferrocenyl aziridino alcohols,[17] azetidino alcohol,[18] and pyrrolidino alcohols[19] and their application in the catalytic asymmetric alkylation of aldehydes. In order to extend further the scope of our chiral

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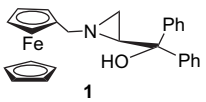
ferrocenyl aziridino alcohols, in this paper, we present our results on highly enantioselective preparation of (*R*)- and (*S*)-diarylmethanols in the presence of a catalytic amount of chiral ferrocenyl aziridino alcohol **1**.



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2. Results and discussion

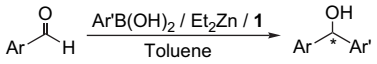
The chiral ferrocenyl aziridino alcohol **1** was easily synthesized from commercially available L-serine according to our previously reported procedure.[17c,d]

We initiated our studies by choosing *p*-methylbenzaldehyde as a model substrate to examine the efficiency of the asymmetric arylation of arylaldehyde in the presence of the chiral ligand **1** using phenylboronic acid as an aryl resource. The results are summarized in Table 1. The phenylzinc reagent was prepared in situ by heating a mixture of diethylzinc and phenylboronic acid in hexanes to 60 °C for 12 h. The phenyl transfer was conducted at 0 °C in the presence of 10 mol % of the chiral ligand **1**. The reactions afforded the corresponding addition product in excellent yield (90%) with high enantiomeric excess (88.5%).

It was reported that the reaction conditions, such as temperature, loading of catalyst, and additive [DiMPEG, dimethoxy poly(ethylene glycol)], could influence the enantioselectivity. We first investigated the effect of reaction temperature on enantioselectivity in the presence of 10 mol % of the chiral ligand **1**. Lowering the reaction temperature from 0 to −20 °C led to an increase in the enatioselectivity from 88.5 to 92.7% (Table 1, entries 1 and 2). Further lowering the reaction temperature to −40 °C led to the decrease in both yield and ee (entry 3). Then, we examined the effects of the chiral ligand loading on enantioselectivity. Increasing the amount of ligand from 10 to 15% led to an improvement in both yield and enantioselectivity at 0 °C (entry 4 vs entry 1), but increasing the ligand loading from 10 to 15% did not result in the improvement of yield and enantioselectivity at −20 °C (entry 5 vs entry 2).

Bolm et al. and Chan et al. reported, respectively, that addition of the additive such as DiMPEG to the reaction system could improve the enantioselectivity of the products.[10] We also studied the effect of the additive (DiMPEG) on enantioselectivity. The addition of 10 mol % of DiMPEG 2000 to the present reaction system gave the corresponding diarylmethanol with 91.2% ee at room temperature (Table 1, entry 6). A slight improvement in ee but in a great decrease in chemical yield was observed when the reaction was carried out at −20 °C (entry 7). The deteriorated yield could be ascribed to the lower solubility of DiMPEG, because a suspension or

Table 1
Asymmetric arylation of arylaldehydes catalyzed by **1**[a]



Entry	Ar	Ar′	**1** (mol %)	Temperature (°C)	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	*p*-MeC_6H_4	C_6H_5	10	0	90	88.5	*S*
2	*p*-MeC_6H_4	C_6H_5	10	−20	92	92.7	*S*
3	*p*-MeC_6H_4	C_6H_5	10	−40	88	90.3	*S*
4	*p*-MeC_6H_4	C_6H_5	15	0	96	92.0	*S*
5	*p*-MeC_6H_4	C_6H_5	15	−20	92	92.8	*S*
6	*p*-MeC_6H_4	C_6H_5	10	25	89	91.2[e]	*S*
7	*p*-MeC_6H_4	C_6H_5	10	−20	53	92.6[e]	*S*
8	*o*-$MeOC_6H_4$	C_6H_5	10	−20	85	80.6	*S*
9	*m*-$MeOC_6H_4$	C_6H_5	10	−20	88	89.6	*S*
10	*p*-$MeOC_6H_4$	C_6H_5	10	−20	91	85.0	*S*
11	*m*-$PhOC_6H_4$	C_6H_5	10	−20	93	95.7	*S*
12	*o*-ClC_6H_4	C_6H_5	10	−20	90	93.2	*S*
13	*m*-ClC_6H_4	C_6H_5	10	−20	88	86.3	*S*
14	*p*-ClC_6H_4	C_6H_5	10	−20	90	87.6	*S*
15	*m*-BrC_6H_4	C_6H_5	10	−20	86	88.1	*S*
16	*o*-$CF_3C_6H_4$	C_6H_5	10	−20	87	87.9	*S*
17	3,4-$OCH_2OC_6H_3$	C_6H_5	10	−20	79	83.0	*S*
18	Ferrocenyl	C_6H_5	10	−20	95	92.9	*S*
19	C_6H_5	*p*-MeC_6H_4	10	−20	89	94.1	*R*
20	C_6H_5	*p*-$MeOC_6H_4$	10	−20	92	90.7	*R*
21	C_6H_5	*p*-ClC_6H_4	10	−20	83	92.7	*R*
22	*o*-MeC_6H_4	*p*-ClC_6H_4	10	−20	91	94.7	*S*

[a] The molar ratio of Ar′B(OH)$_2$/Et$_2$Zn/aldehyde was 1/3/1.
[b] Isolated yields.
[c] Determined by HPLC using chiral columns: Chiralcel OD, OB or Chiralpak AD, respectively. In all cases, the product chromatograms were compared against a known racemic mixture.
[d] Absolute configuration assigned by comparison with known elution order from Chiralcel OD, OB or Chiralpak AD columns according to the literature.[11–15]
[e] DiMPEG (10 mol%) was added.

turbid solution was observed at lower temperature. Therefore, the best reaction condition was using 10 mol % of the chiral ligand **1** in the absence of DiMPEG at −20 °C.

Encouraged by the results obtained for *p*-methylbenzaldehyde, we investigated a variety of other arylaldehydes to probe their behaviors under the optimized reaction conditions in this catalytic system. As can be seen from Table 1, good to excellent enantioselectivities could be achieved for various aromatic aldehydes, including *ortho*-, *para*- and *meta*-substituted benzaldehydes (entries 8–16), heliotropin (entry 17), and ferrocenecarboxaldehyde (entry 18). The presence of electron-donating (entries 8–11) or electron-withdrawing substituents (entries 12–16) on the benzene ring also furnished the corresponding products in good to outstanding levels of enantioselectivity. The best asymmetric induction (as high as 95.7% ee) was obtained by using *m*-phenoxybenzaldehyde as the substrate (entry 11).

The *S* absolute configuration for the diarylmethanols of addition products, the same as the addition of diethylzinc to arylaldehydes catalyzed by **1**,[17c,d] was noted in all the examples studied (Table 1, entries 1–18). Comparison of the absolute configuration of the addition products for the phenylation of arylaldehydes with the ethylation of arylaldehydes enabled us to ascertain that the present phenyl transfer process was mechanistically similar to ethyl transfer process.[8e,9] That is, the *si* face of arylaldehydes was attacked by an ethyl group or a phenyl group, respectively (Fig. 1).[17a]

In order to examine if substituted phenyl groups could be transferred to aldehydes with the same levels of enantioselectivity, the aryl transfer reaction of some substituted phenylboronic acids with benzaldehyde was investigated (Table 1, entries 19–21). The reaction of benzaldehyde with *p*-methylphenylboronic acid, which was a reverse combination of the reaction of *p*-methylbenzaldehyde with phenylboronic acid, gave a desired addition product possessing the *R* absolute configuration with an outstanding enantioselectivity (94.1%, entry 19). Thus, both the *R* and *S* enantiomers of phenyl *p*-methylphenylmethanol can be obtained by carrying out either phenyl transfer to *p*-methylbenzaldehyde or *p*-methylphenyl transfer to benzaldehyde in the presence of the same chiral ligand **1** (entry 19 vs entry 2). The reaction of benzaldehyde with *p*-methoxyphenylboronic acid, and *p*-chlorophenylboronic acid, respectively, also proceeded well with good to excellent enantioselectivities to afford *R* absolute configuration for corresponding diarylmethanols (entries 20 and 21). This is one of the most interesting features of the methodology used herein since both *R* and *S* enantiomers of a given product can be readily prepared in high yields with excellent enantioselectivities

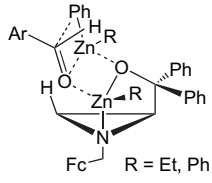
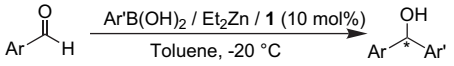


Figure 1. A possible transition state of the phenylation of arylaldehydes.

Table 2
Enantioselective preparation of (*R*)- and (*S*)-diarylmethanols catalyzed by **1**[a]



Entry	Ar	Ar′	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	*p*-MeC_6H_4	*p*-$MeOC_6H_4$	84	92.9	*R*
2	*p*-$MeOC_6H_4$	*p*-MeC_6H_4	89	98.0	*S*
3	*p*-MeC_6H_4	*p*-ClC_6H_4	85	90.3	*R*
4	*p*-ClC_6H_4	*p*-MeC_6H_4	84	96.5	*S*
5	*p*-$MeOC_6H_4$	*p*-ClC_6H_4	83	92.9	*R*
6	*p*-ClC_6H_4	*p*-$MeOC_6H_4$	86	96.4	*S*
7	*p*-MeC_6H_4	*o*-MeC_6H_4	81	88.6	*R*
8	*o*-MeC_6H_4	*p*-MeC_6H_4	87	97.0	*S*
9	*p*-$MeOC_6H_4$	*o*-MeC_6H_4	87	83.1	*R*
10	*o*-MeC_6H_4	*p*-$MeOC_6H_4$	83	97.5	*S*
11	C_6H_5	*o*-MeC_6H_4	87	88.9	*R*
12	*o*-MeC_6H_4	C_6H_5	89	95.9	*S*

[a] The molar ratio of Ar′$B(OH)_2$/Et_2Zn/aldehyde was 1/3/1.
[b] Isolated yields.
[c] Determined by HPLC using chiral columns: Chiralcel OD, OB or Chiralpak AD, respectively. In all cases, the product chromatograms were compared against a known racemic mixture.
[d] Absolute configuration assigned by considering the similarity in the stereochemical reaction pathway (Fig. 1).

in the presence of the identical catalyst, only by the reverse combination of both reaction partners (arylboronic acid and aromatic aldehydes).

The aryl transfer reaction of substituted phenylboronic acid (*p*-chlorophenylboronic acid) with substituted benzaldehyde (*o*-methylbenzaldehyde) afforded also the corresponding product with enantioselectivity up to 94.7% (Table 1, entry 22).

So far the assessed substrate scope of the aryl transfer reaction seems to be rather limited.[10–16] That is, phenyl transferred to aromatic aldehydes (substituted benzaldehydes) or aryl transferred to benzaldehyde has usually been investigated, affording aryl*phenyl*methanols. To the best of our knowledge, only one example has just been reported about the synthesis of diarylmethanols with two differently substituted aryl groups by organozinc reagents.[20]

In order to further examine the generality of this methodology and the applicability of the approach to more functionalized diarylmethanols, a series of reverse combinations of the reaction of arylaldehydes with arylboronic acid were tested and the results are summarized in Table 2. As seen in Table 2, just by appropriate choice of both reaction partners, both the enantiomers of a given diarylmethanol can be easily obtained in good yields with high enantioselectivities by the means of the same catalyst **1** (entries 1–12). Probably due to the steric effects of the *ortho* substituents, arylboronic acid with *ortho*-methyl group gave the corresponding products with a slightly lower ee values (entries 7, 9, and 11).

3. Conclusion

We have shown that chiral ferrocenyl aziridino alcohol **1** is a very effective ligand for enantioselective aryl transfer to

arylaldehydes using arylboronic acids as aryl resources. The main advantages of this process are high yields and enantioselectivities as well as configuration-controlled synthesis of *R* or *S* enantiomers of a given diarylmethanol by means of the same catalyst. Further application of chiral ferrocenyl aziridino alcohol **1** for asymmetric synthesis is under investigation in our laboratory.

4. Experimental

4.1. General

Melting points were determined using YRT-3 melting point apparatus and were uncorrected. Optical rotations were measured with Perkin–Elmer, model 341 Polarimeter at 20 °C in $CHCl_3$. The ee value was determined by HPLC using a chiral column with hexane/2-propanol (ratio as indicated) as the eluent. The chiral HPLC methods were calibrated with the corresponding racemic mixtures. The chromatographic system consisted of a JASCO model PU-1580 intelligent HPLC pump and a JASCO model UV-1575 intelligent UV/Vis detector (254 nm). The injection loop had a 20 μL capacity. The column used was a Chiralcel OD or a Chiralpak AD (250 × 4.6 mm) from Daicel Chemical Ind., Ltd (Japan). The column was operated at ambient temperature. NMR spectra (^1H and ^{13}C) were performed on a Bruker DPX 400 (400 MHz) spectrometer using solutions in $CDCl_3$ (referenced internally to Me_4Si); *J* values are given in hertz. IR spectra were determined on a Therme Nicolet IR 200 spectrophotometer. TLC was performed on dry silica gel plates developed with hexane/ethyl acetate. Mass spectra were obtained using a Waters Q-Tof Micro™ instrument with an electrospray ionization source (ESIMS). All the ESIMS spectra were performed using MeOH as the solvent.

4.2. Reagents and solvents

Except for diethylzinc purchased from Aldrich, all other reagents were purchased in China. Toluene was pre-dried over calcium chloride and then distilled from sodium before use. Ether was distilled from sodium benzophenone ketyl. All other reagents were commercially available and were used as received.

4.3. General procedure for the asymmetric arylation of arylaldehydes catalyzed by *1*

A dried Schlenk tube containing toluene (2 mL), arylboronic acid (122 mg, 1 mmol), and diethylzinc (3 mmol, 1.0 M solution in hexanes) was heated at 60 °C for 12 h. After the mixture was cooled to room temperature, the chiral amino alcohol ligand **1** (42.3 mg, 0.1 mmol) was added. The mixture was stirred for another 15 min, cooled to −20 °C, and the aldehyde (1 mmol) was subsequently added under nitrogen atmosphere. After 48 h at −20 °C, the reaction was quenched by the addition of saturated aqueous NH_4Cl (8 mL). The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. Purification of the residue by the preparative silica gel TLC plate (hexane/EtOAc) afforded the pure diarylmethanol. The ee value was determined by HPLC analyses using a chiral column: OB, OD and AD, respectively. In all cases, the product chromatograms were compared against a known racemic mixture.

4.3.1. (R)-(4-Methoxyphenyl)-(4′-methylphenyl)methanol (entry 1, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.13 (br, 1H, OH), 2.33 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 5.78 (s, 1H, CH), 6.85–6.87 (m, 2H, ArH), 7.12–7.15 (m, 2H, ArH), 7.22–7.29 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1 (CH_3), 55.3 (OCH_3), 75.7 (ArCHOHAr′), 113.8 (2CH), 126.3 (2CH), 127.8 (2CH), 129.1 (2CH), 136.3 (C), 137.1 (C), 141.1 (C), 158.9 (C). Enantiomeric excess: 92.9%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=2/98, 1 mL/min, t_R=32.7 min, t_S=36.7 min.

4.3.2. (S)-(4-Methoxyphenyl)-(4′-methylphenyl)methanol (entry 2, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.17 (br, 1H, OH), 2.32 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 5.77 (s, 1H, CH), 6.84–6.87 (m, 2H, ArH), 7.13–7.15 (m, 2H, ArH), 7.24–7.29 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1 (CH_3), 55.2 (OCH_3), 75.6 (ArCHOHAr′), 113.8 (2CH), 126.3 (2CH), 127.8 (2CH), 129.1 (2CH), 136.3 (C), 137.1 (C), 141.1 (C), 158.9 (C). IR (KBr pellets): 3337, 3006, 2898, 2831, 1611, 1511, 1459, 1407, 1326, 1252, 1172, 1113, 1032, 812, 771, 551 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{16}O_2$: 251.1048 (M^++Na), found: 251.1041. Enantiomeric excess: 98.0%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=2/98, 1 mL/min, t_R=33.3 min, t_S=36.9 min.

4.3.3. (R)-(4-Chlorophenyl)-(4′-methylphenyl)methanol (entry 3, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 3H, CH_3), 5.78 (s, 1H, CH), 7.14–7.16 (m, 2H, ArH), 7.22–7.25 (m, 2H, ArH), 7.29–7.30 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1 (CH_3), 75.5 (ArCHOHAr′), 126.5 (2CH), 127.8 (2CH), 128.6 (2CH), 129.4 (2CH), 133.2 (C), 137.7 (C), 140.6 (C), 142.4 (C). IR (KBr pellets): 3358, 3025, 2918, 2924, 1903, 1595, 1511, 1484, 1405, 1328, 1245, 1192, 1116, 1087, 1038, 1013, 918, 858, 802, 765, 694, 656, 502, 549 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{13}ClO$: 215.0628 (M^+−OH), found: 215.0636. Enantiomeric excess: 90.3%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=2/98, 0.5 mL/min, t_R=54.6 min, t_S=60.7 min.

4.3.4. (S)-(4-Chlorophenyl)-(4′-methylphenyl)methanol (entry 4, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.19 (br, 1H, OH), 2.33 (s, 3H, CH_3), 5.78 (s, 1H, CH), 7.14–7.16 (m, 2H, ArH), 7.22–7.26 (m, 2H, ArH), 7.29–7.32 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2 (CH_3), 75.4 (ArCHOHAr′), 126.5 (2CH), 127.8 (2CH), 128.6 (2CH), 129.4 (2CH), 133.1 (C), 137.6 (C), 140.6 (C), 142.4 (C). IR (KBr pellets): 3358, 3025, 2918, 2924, 1903, 1595, 1511, 1484, 1405, 1328, 1245, 1192, 1116, 1087, 1038, 1013, 918, 858, 802, 765, 694, 656, 502,

549 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{13}ClO$: 215.0628 (M^+-OH), found: 215.0636. Enantiomeric excess: 96.5%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=2/98, 0.5 mL/min, t_R=54.8 min, t_S=60.8 min.

4.3.5. (R)-(4-Chlorophenyl)-(4′-methoxyphenyl)methanol (entry 5, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H, OCH_3), 5.76 (s, 1H, CH), 6.85–6.89 (m, 2H, ArH), 7.23–7.25 (m, 2H, ArH), 7.26–7.29 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.3 (OCH_3), 75.2 (ArCHOHAr′), 114.0 (2CH), 127.8 (2CH), 127.9 (2CH), 128.5 (2CH), 133.1 (C), 135.8 (C), 142.5 (C), 159.2 (C). IR (KBr pellets): 3374, 2958, 2831, 1609, 1511, 1487, 1461, 1403, 1249, 1172, 1089, 1032, 857, 805, 769, 554 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{13}ClO_2$: 231.0577 (M^+-OH), found: 231.0585. Enantiomeric excess: 93.2%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=2/100, 0.5 mL/min, t_R=96.0 min, t_S=88.1 min.

4.3.6. (S)-(4-Chlorophenyl)-(4′-methoxyphenyl)methanol (entry 6, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.28 (br, 1H, OH), 3.78 (s, 3H, OCH_3), 5.75 (s, 1H, CH), 6.84–6.87 (m, 2H, ArH), 7.22–7.25 (m, 2H, ArH), 7.29 (s, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.3 (OCH_3), 75.2 (ArCHOHAr′), 114.0 (2CH), 127.8 (2CH), 127.9 (2CH), 128.5 (2CH), 133.1 (C), 135.8 (C), 142.4 (C), 159.2 (C). IR (KBr pellets): 3374, 2958, 2831, 1609, 1511, 1487, 1461, 1403, 1249, 1172, 1089, 1032, 857, 805, 769, 554 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{13}ClO_2$: 231.0577 (M^+-OH), found: 231.0585. Enantiomeric excess: 96.3%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=2/100, 0.5 mL/min, t_R=94.7 min, t_S=86.3 min.

4.3.7. (R)-(2-Methylphenyl)-(4′-methylphenyl)methanol (entry 7, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.22 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 5.94 (s, 1H, CH), 7.10–7.15 (m, 3H, ArH), 7.16–7.23 (m, 5H, ArH), 7.51–7.53 (m, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4 (CH_3), 21.1 (CH_3), 73.2 (ArCHOHAr′), 126.0 (2CH), 127.1 (3CH), 129.2 (3CH), 135.3 (C), 137.3 (C), 140.0 (C), 141.6 (C). IR (KBr pellets): 3369, 3022, 2920, 1511, 1486, 1459, 1380, 1310, 1174, 1111, 1017, 862, 815, 777, 745, 631, 573 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{16}O$: 235.1099 (M^++Na), found: 235.1095. Enantiomeric excess: 86.6%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=1/100, 0.5 mL/min, t_R=37.9 min, t_S=43.2 min.

4.3.8. (S)-(2-Methylphenyl)-(4′-methylphenyl)methanol (entry 8, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.22 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 5.95 (s, 1H, CH), 7.11–7.13 (m, 3H, ArH), 7.16–7.24 (m, 5H, ArH), 7.51–7.53 (m, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4 (CH_3), 21.1 (CH_3), 73.2 (ArCHOHAr′), 126.1 (2CH), 127.1 (3CH), 129.2 (3CH), 135.3 (C), 137.3 (C), 140.0 (C), 141.6 (C). IR (KBr pellets): 3369, 3022, 2920, 1511, 1486, 1459, 1380, 1310, 1174, 1111, 1017, 862, 815, 777, 745, 631, 573 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{16}O$: 235.1099 (M^++Na), found: 235.1095. Enantiomeric excess: 97.0%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=1/100, 0.5 mL/min, t_R=37.7 min, t_S=43.6 min.

4.3.9. (R)-(2-Methylphenyl)-(4′-methoxyphenyl)methanol (entry 9, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.19 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 5.92 (s, 1H, CH), 6.82–6.88 (m, 2H, ArH), 7.18–7.25 (m, 5H, ArH), 7.54–7.55 (m, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4 (CH_3), 55.3 (OCH_3), 72.9 (ArCHOHAr′), 113.9 (2CH), 126.0 (1CH), 127.2 (1CH), 127.3 (1CH), 128.5 (2CH), 130.5 (1CH), 135.1 (C), 136.8 (C), 141.7 (C), 159.0 (C). IR (KBr pellets): 3392, 3022, 2953, 2835, 1610, 1584, 1461, 1302, 1249, 1172, 1032, 861, 829, 777, 747, 646, 626, 580 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{16}O_2$: 251.1048 (M^++Na), found: 251.1053. Enantiomeric excess: 83.1%, Chiralcel OD: *i*-PrOH/hexane=1/100, 0.5 mL/min, t_R=135.9 min, t_S=144.8 min.

4.3.10. (S)-(2-Methylphenyl)-(4′-methoxyphenyl)methanol (entry 10, Table 2)

^1H NMR (400 MHz, $CDCl_3$): δ 2.11 (br, 1H, OH), 2.20 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 5.94 (s, 1H, CH), 6.83–6.85 (m, 2H, ArH), 7.11–7.24 (m, 5H, ArH), 7.55–7.57 (m, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.3 (CH_3), 55.3 (OCH_3), 73.0 (ArCHOHAr′), 113.9 (2CH), 125.9 (1CH), 126.1 (1CH), 127.4 (1CH), 128.5 (2CH), 130.5 (1CH), 135.1 (C), 135.2 (C), 141.6 (C), 159.1 (C). IR (KBr pellets): 3392, 3022, 2953, 2835, 1610, 1584, 1461, 1302, 1249, 1172, 1032, 861, 829, 777, 747, 646, 626, 580 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{16}O_2$: 251.1048 (M^++Na), found: 251.1053. Enantiomeric excess: 97.5%, Chiralcel OD, 216 nm, *i*-PrOH/hexane=1/100, 0.5 mL/min, t_R=136.5 min, t_S=144.0 min.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.01.040.

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