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Highly Enantioselective Addition of In Situ Prepared Arylzinc to Aldehydes Catalyzed by a Series of Atropisomeric Binaphthyl-Derived Amino Alcohols

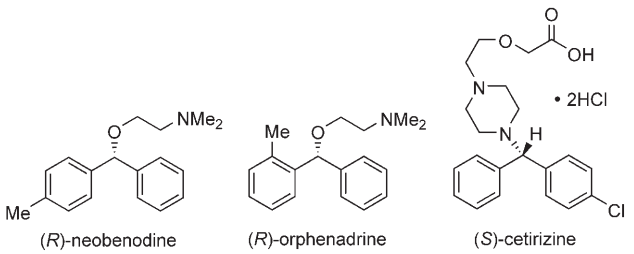
Gui Lu,[a, b] Fuk Yee Kwong,[a] Ji-Wu Ruan,[a] Yue-Ming Li,[a] and Albert S. C. Chan*[a]

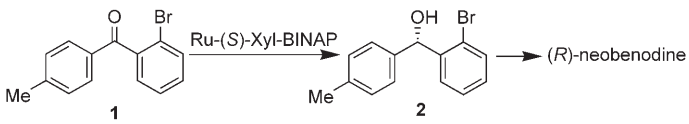
Abstract: The direct addition of in situ prepared arylzinc to aldehydes with chiral binaphthyl-derived amino alcohols as catalysts can afford optically active diarylmethanols in high yields and with excellent enantioselectivities (up to 99% *ee*, *ee* = enantiomeric excess). By using a single catalyst, both enantiomers of many pharmaceutically interesting diarylmethanols can be obtained by the proper combination of various arylzinc reagents with different aldehydes; this catalytic system also works well for the phenylation of aliphatic aldehydes to give up to 96% *ee*.

Keywords: amino alcohols · arylation · arylzinc · binaphthyl · enantioselectivity

Introduction

Chiral diarylmethanols are important precursors to many biologically active compounds, such as (*R*)-neobenodine, (*R*)-orphenadrine, and (*S*)-cetirizine.[1–8] Two scientifically important protocols for their enantioselective syntheses have been reported: (1) the asymmetric reduction of prochiral diaryl ketones and (2) the enantioselective aryl transfer to aromatic aldehydes. The successful examples of the former, such as Corey's CBS reduction[9–11] and Noyori's Ru-(*S*)-BINAP-catalyzed ketone hydrogenation (BINAP = 2,2′-diphenylphosphino-1,1′-binaphthyl),[12,13] required certain substrate attributes, such as *ortho*-substitution of one of the aryl groups or the presence of electronically differentiated aryl groups. Thus, precursors not possessing these structural features had to be synthesized through indirect protocols. For example, in the asymmetric synthesis of (*R*)-neobenodine, compound **2** was synthesized by the asymmetric hydrogenation of intermediate ketone **1**, in which the *ortho*-bromo group acted as an enantiodirective functional substituent and subsequently had to be removed (Scheme 1).[12]





Scheme 1.

The chiral induction in the asymmetric addition of aryl groups to aromatic aldehydes seems easy to realize because of the significant difference between the hydrogen atom and the aryl group of the aldehydes, yet successful examples of this reaction are mostly limited to the addition of diphenylzinc to aldehydes.[14–27] Altering the structure of diarylzinc and aldehydes can provide an array of optically active diarylmethanols and is of high interest. However, the prepara-

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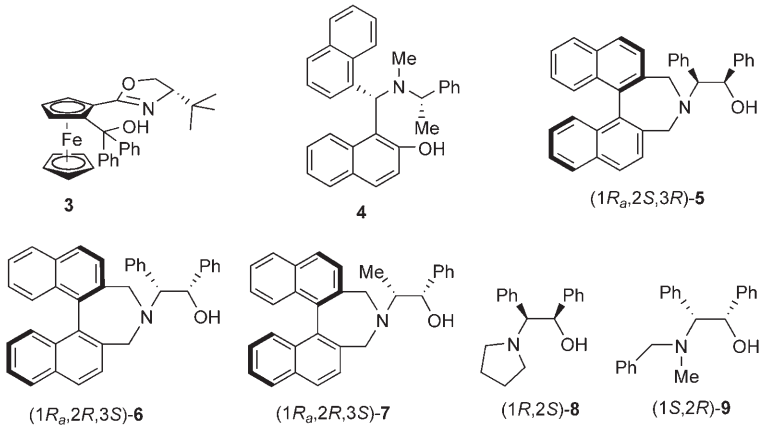
tion of diarylzinc reagents (usually from transmetalation with lithium or Grignard reagents) is tedious and difficult as salt-free reagents are required for achieving high enantioselectivity. Furthermore, many functionalized diarylzincs remain inaccessible due to the high reactivity of the organolithium or -magnesium intermediates.

Recently, the metal exchange between organoboron[28–30] or organoboronic derivatives[31–34] and diethylzinc has been proposed as an alternative for the synthesis of salt-free organozinc reagents. A notable example of an asymmetric aryl transfer reaction to aldehydes that involved an arylzinc species prepared in situ by an aryl boronic acid/diethylzinc exchange[31] has been described by Bolm and coworkers. By using chiral ferrocenyl oxazoline **3** as a ligand, the catalytic reaction was easy to perform and a broad range of products were prepared in high yields and with high enantioselectivities.[31] We also found that easily accessible chiral tertiary aminonaphthol **4** could serve as an efficient ligand for this asymmetric phenyl transfer reaction.[35]

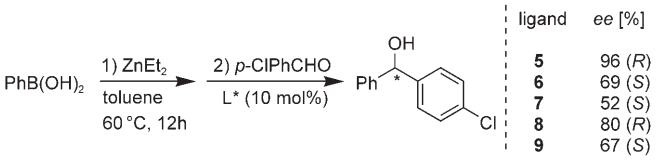
We have reported the application of binaphthyl-derived amino alcohol ligands **5–9** in the asymmetric alkyl- and alkynylzinc additions with high stereoselectivities.[36] The salient features of these chiral amino alcohol ligands include their ease of preparation and the flexibility of modifications on both the binaphthyl moiety and the amino alcohol backbone. Their unique rigidity and fine-tuning capability are expected to play a crucial role in catalytic asymmetric reactions. Herein, we report the application of these ligands to the asymmetric addition of different arylzinc reagents (prepared in situ) to various aldehydes with high stereoselectivity and broad substrate tolerance.



Results and Discussion

The enantioselective arylation of aromatic aldehydes was achieved by differentiation between the aryl group and the hydrogen atom of the aldehydes. A suitable chiral ligand with hindered geometry may specifically favor one enantiopathway in the transition states and lead to highly enantioselective outcomes. The sterically congested chiral binaphthyl-derived amino alcohol, which also has a great potential for fine-tuning, seems to be a good candidate for this reaction.

First we examined the chiral amino alcohols **5–9** on their catalytic performance in the asymmetric phenylation addition of 4-chlorobenzaldehyde, for which the arylzinc reagents were prepared in situ by the transmetalation of phenylboronic acid with diethylzinc (Scheme 2). All catalysts gave good yields with *ee* values ranging from 52 to 96%. The best result was obtained with (1R_a,2S,3R)-**5**, giving a chiral alcohol with 96% *ee*, while ligand (1R,2S)-**8** bearing a smaller backbone gave significantly lower *ee* (80% *ee*). The match of the configurations between the binaphthyl backbone and the phenyl substituent alpha to the amino moiety was quite important for obtaining high enantioselectivity in the product. In contrast, the unmatched configuration (1R_a,2R,3S)-**6** was detrimental to the enantioselectivity (69% *ee*). Amino alcohol ligands containing phenyl substituents at the α-position were found to be more effective than those containing a methyl substituent. In most cases, the configuration of the alcohol product could be correlated with the chirality of the amino alcohol moiety of the ligand.



Scheme 2.

Further investigations into the optimization of the reaction conditions, such as solvent, reaction temperature, and catalyst loading for the asymmetric phenylation of 4-chlorobenzaldehyde with (1R_a,2S,3R)-**5** as catalyst are listed in Table 1. When the reactions were carried out in mixed

Table 1. Optimization of the phenylation of 4-chlorobenzaldehyde in the presence of (1R_a,2S,3R)-**5**.[a]

Entry	T [°C]	Catalyst [mol%]	Yield [%]	*ee* [%][b]
1	−20	10	93	97(*R*)
2	0	10	96	96(*R*)
3	0	5	74	87(*R*)
4	25	10	83	95(*R*)

[a] Aldehyde/phenylboronic acid/diethylzinc = 0.5:1.2:3.6 (molar ratio), toluene as solvent, 12 h. [b] The *ee* values were determined by HPLC analysis with a 25 cm × 4.6 mm Chiralcel OB-H column (Daicel Chemical Industries). Absolute configuration was determined by comparison of the order of peak elution from HPLC analysis with literature values.

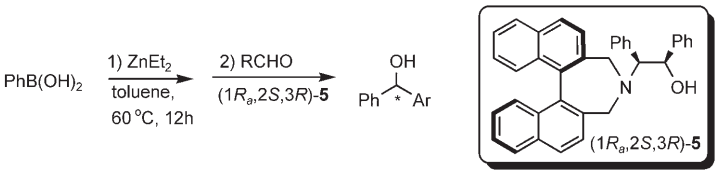
hexane-toluene (1:1) solvent, the enantioselectivity was about 5% lower than in toluene solvent. A slight increase in the *ee* was observed when the reaction temperature was lowered from 25 to −20°C (Table 1, entries 1, 2, and 4). A decrease of catalyst loading caused a significant drop in the *ee* of the product (Table 1, entries 2 and 3).

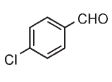
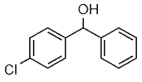
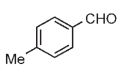
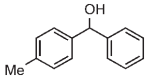
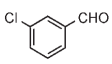
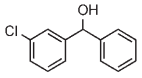
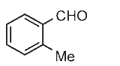
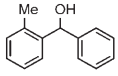
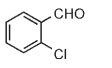
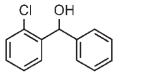
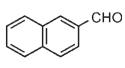
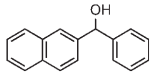
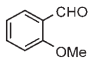
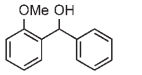
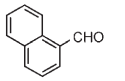
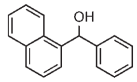
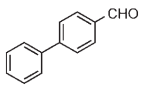
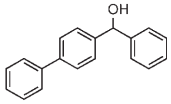
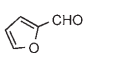
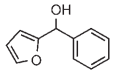
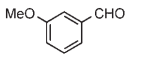
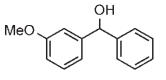
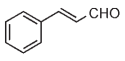
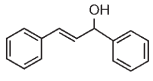
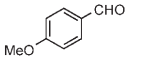
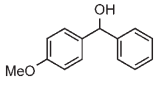
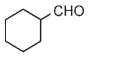
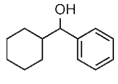
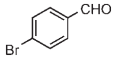
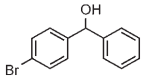
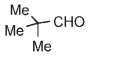
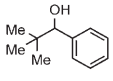
The preliminary optimized reaction conditions were then applied to the phenyl transfer reaction for a variety of aromatic aldehydes (Table 2). The reaction generally proceeded with excellent enantioselectivities (up to 99% *ee*). Under the newly developed protocol, the scope of substrates was not limited to *para*-substituted aromatic aldehydes, the *meta*- or even *ortho*-substituted substrates also afforded the corresponding products with good yields and excellent *ee*'s (Table 2, entries 2–4, 6 and 10).

Next we examined the reactivity of phenyl addition to *para*-tolualdehyde and *ortho*-tolualdehyde. The products of these reactions were highly-valued intermediates for antihistaminic neobenodine and orphenadrine. In this study, we found that not only the yields of the addition products, but also the enantioselectivities were uniformly high (>97% *ee*) (Table 2, entries 9 and 10). Aromatic aldehydes possessing steric hindrance, such as 1-naphthaldehyde and 2-naphthaldehyde, also proved to be suitable substrates for the asymmetric phenylation reaction (Table 2, entries 11 and 12). The in situ prepared phenylzinc reagent also worked well for the phenyl addition to other aldehydes, particularly aliphatic aldehydes, furaldehyde, and α,β-unsaturated *trans*-cinnamyl aldehydes, giving products with good to excellent *ee*'s in most cases.

Another significant advantage of this protocol was that various substituted arylzinc reagents could be easily transferred to aldehydes by using different arylboronic acids as aryl sources. We further explored the asymmetric arylzinc addition and the results indicated that various substituted aryl groups worked satisfactorily to afford the corresponding diarylmethanols in good yields and with high *ee*'s (Table 3). This reaction was rather sensitive to the electronic effect of arylboronic acids. The presence of an electron-donating group in the arylboronic acids greatly facilitated the addition process to give high *ee*'s (up to 99%; Table 3, entries 1, 2, 5, and 6), suggesting a mechanism that involves a nucleophilic attack by the aryl group onto the carbonyl carbon. Steric hindrance around the boron atom retarded the rate of reaction and lowered both product yield and enantioselectivity (Table 3, entries 8–10). The use of alkylboronic acid afforded the product in 67% yield and with 45% *ee*, while

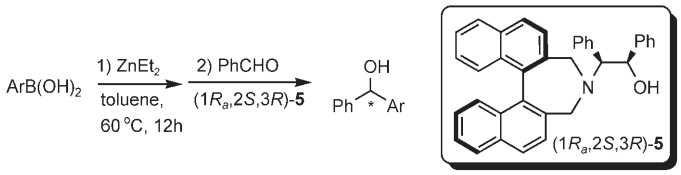
Table 2. Asymmetric phenyl transfer to various aldehydes.[a]

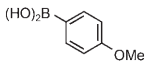
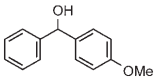
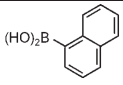
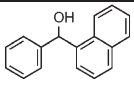
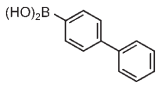
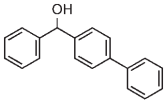
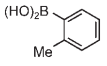
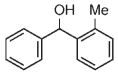
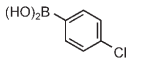
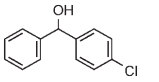
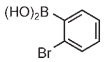
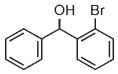
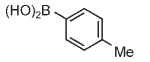
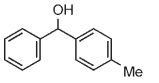
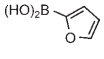
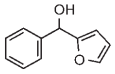
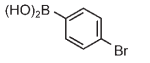
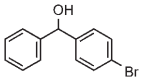
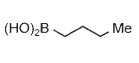
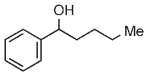
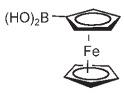
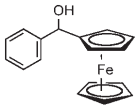


Entry	RCHO	Product	*T* [°C]	Yield [%]	*ee* [%][b]	Entry	RCHO	Product	*T* [°C]	Yield [%]	*ee* [%][b]
1			0	96	96(*R*)	9			−20	92	97(*R*)
2			0	95	94(*R*)	10			0	95	98(*R*)
3			−20	96	90(*R*)	11			−20	94	93(*R*)
4			0	96	93(*R*)	12			0	91	95(*R*)
5			−20	95	99(*R*)	13			−20	91	92(*R*)
6			0	95	97(*R*)	14			−20	96	79(*R*)
7			−20	93	98(*R*)	15			0	96	91(*R*)
8			−20	96	96(*R*)	16			0	88	96(*R*)

[a] Aldehyde/**5**/phenylboronic acid/diethylzinc = 0.5:0.05:1.2:3.6 (molar ratio), toluene as solvent, 60°C, 12 h. [b] The *ee*'s were determined by HPLC spectroscopic analyses. Absolute configurations were determined by comparison of the order of peak elution from HPLC analyses with literature values.

Table 3. Asymmetric aryl transfer to benzaldehyde.[a]



Entry	$ArB(OH)_2$	Product	T [°C]	Yield [%]	*ee* [%][b]	Entry	$ArB(OH)_2$	Product	T [°C]	Yield [%]	*ee* [%][b]
1			−20	96	97(*S*)	8			0	92	74(*S*)
2			−20	91	98(*S*)	9			0	89	*rac*
3			0	95	87(*S*)	10			0	85	*rac*
4			−20	91	73(*S*)						
5			0	95	93(*S*)	11			0	90	16(*S*)
6			−20	92	99(*S*)						
7			−20	90	71(*S*)	12			0	67	45(*R*)
						13			0	91	61(*S*)

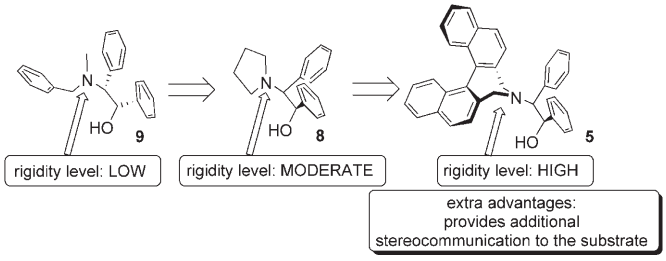
[a] Benzaldehyde/**5**/arylboronic acid/diethylzinc = 0.5:0.05:1.2:3.6 (molar ratio), toluene as solvent, 12 h. [b] The *ee*'s were determined by HPLC spectroscopic analyses. Absolute configurations were determined by comparison of the order of peak elution from HPLC analyses with literature values.

ferrocenylboronic acid produced the product in a 91 % yield and with 61 % *ee* (Table 3, entries 12–13).

This methodology was quite flexible for the asymmetric syntheses of diarylmethanols. By using the same chiral binaphthyl-derived amino alcohol (e.g., $(1R_a,2S,3R)$-**5**) as a catalyst, both enantiomers of the corresponding alcohols could be obtained in good yields and with high *ee*'s. Hence, with the aid of a proper combination of arylboronic acids and aromatic aldehydes, a diverse array of oppositely configured chiral diarylmethanols can be obtained.

In the structural evaluation of the ligand backbone of the chiral ferrocenyl oxazoline ligand **3**, binaphthyl-derived *N,O* ligand $(1R_a,2S,3R)$-**5** offers additional parameters (binaphthyl-moiety) for fine-tuning the ligand structure, which will have high potential and versatility in dealing with a board scope of reactants. In our experiments, ligand **5** did provide us comparable and sometimes even higher enantioselectivities for the arylation of both aromatic and aliphatic aldehydes when compared with ligand **3**.

The rational design of the ligand scaffold **5** was based on the rigidity level of the ligand architecture (Scheme 3). We speculated that the low rigidity of the amino-alcohol **9** (opposite configuration) afforded low enantioselectivity in the product (Schemes 2 and 3). In contrast, the relatively rigid structure of **8** produced better enantioselectivity. This rigid configuration presumably provided a better enantio-locking of the substrate. Thus, it prompted us to propose the incorporation of the azepine moiety in ligand **5** to provide a better stereooutcome. Notably, apart from the 7-membered azepine scaffold, we also introduced atropo-chirality into this ligand to provide a better match for stereocommunication to the orientation of the substrate on approach. The unique features of this ligand design are the chiral-wall (from binaphthyl-skeleton) moiety and the rigid ligand scaffold. These rational concepts will potentially provide us with a valuable direction for future ligand design in related asymmetric catalysis.



Scheme 3.

Conclusion

We have applied a series of structurally rigid chiral binaphthyl-derived amino alcohol ligands to the asymmetric

addition of arylzinc (prepared in situ) to various aldehydes. The *N,O* ligand ($1R_a,2S,3R$)-**5** produced excellent enantioselectivities (up to 99% *ee*) in the asymmetric arylation of both aromatic and aliphatic aldehydes. A diverse array of optically active diarylmethanols, which are of high interest in biological and pharmaceutical sciences, can be obtained in one step by altering the structures of nucleophiles and the aldehydes. Because of the simplicity of the ligand synthesis and the ease of ligand modification, these chiral amino alcohols may constitute a new set of versatile catalysts for the enantioselective arylation of various carbonyl compounds.

Experimental Section

All experiments were carried out under a nitrogen atmosphere. Unless otherwise stated, commercial reagents were used as received without further purification. The reactions were carried out in solvents distilled from standard drying agents. Toluene and THF were freshly distilled from sodium and sodium benzophenone ketyl under nitrogen, respectively.[37] Aldehydes were freshly distilled under reduced pressure before use. ^{1}H NMR spectra were recorded on a Varian (500 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ ($\delta = 7.26$ ppm) or with tetramethylsilane (TMS, $\delta = 0.00$ ppm) as the internal standard. Chemical shifts (δ) were reported as parts per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were recorded on a Varian 500 spectrometer and referenced to $CDCl_3$ ($\delta = 77.0$ ppm). TLC was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (Merck or MN, 230–400 mesh) was used for flash-column chromatography. HPLC analyses were conducted on a Waters™ 600 instrument by using Chiralcel® columns (0.46 cm diameter × 25 cm length). The absolute configurations of the products were determined based on the comparison of HPLC traces and/or the direction of optical rotation with known compounds.

General procedure for the catalytic addition of arylzinc to benzaldehyde: A solution of phenylboronic acid (1.2 mmol, 146.3 mg) in toluene (1.5 mL) was mixed with a diethylzinc solution (1.1 M in toluene, 3.6 mmol, 3.27 mL) in a sealed vessel under a nitrogen atmosphere. After the reaction mixture had been stirred for 12 h at 60 °C, the vessel was cooled to 0 °C and a solution of chiral amino alcohol **5** (0.05 mmol) in toluene was added with continued stirring for 15 min. 4-Chlorobenzaldehyde (0.50 mmol, 70.3 mg) was subsequently added and the mixture was allowed to stir at 0 °C overnight. The reaction was then quenched with aqueous HCl solution (5%, ~6 mL), extracted with EtOAc (3 × 5 mL), and dried with Na_2SO_4. The crude product diarylmethanol was purified by flash- column chromatography (silica gel, 10% EtOAc/hexane) to give the product in 96% yield and with 96% *ee*. The *ee* was determined by HPLC analysis with a 25 cm × 4.6 mm Chiralcel OB-H column (Daicel Chemical Industries) (eluent: 10% 2-propanol in hexane; flow rate: 0.5 mL min^{-1}; UV lamp = 270 nm): $t_R(R) = 27.4$ min, $t_R(S) = 42.5$ min.

(*R*)-(4-Chlorophenyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.37$–7.26 (m, 9H; ArH), 5.72 (s, 1H; CH), 2.90 ppm (d, $J = 3.5$ Hz, 1H; OH); HPLC (Daicel Chiralcel OB-H; hexane/*i*PrOH 90:10; 0.5 mL min^{-1}; $\lambda = 270$ nm): $t_R(R) = 27.4$ min, $t_R(S) = 42.5$ min.

(*R*)-(3-Chlorophenyl)phenylmethanol:[21] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.40$ (m, 1H; ArH), 7.37–7.33 (m, 4H; ArH), 7.32–7.29 (m, 1H; ArH), 7.26–7.23 (m, 3H; ArH), 5.74 (d, $J = 3.0$ Hz, 1H; CH), 2.69 ppm (d, $J = 3.0$ Hz, 1H; OH); HPLC (Daicel Chiralcel OB-H; hexane/*i*PrOH 95:5; 1.0 mL min^{-1}; $\lambda = 254$ nm): $t_R(R) = 28.5$ min, $t_R(S) = 44.5$ min.

(*R*)-(2-Chlorophenyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.63$ (m, 1H; ArH), 7.41–7.28 (m, 7H; ArH), 7.25–7.22 (m, 1H; ArH), 6.21 (d, $J = 3.5$ Hz, 1H; CH), 2.72 ppm (d, $J = 4.0$ Hz, 1H; OH); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 95:5; 1.0 mL min^{-1}; $\lambda = 254$ nm): $t_R(R) = 12.9$ min, $t_R(S) = 16.7$ min.

(*R*)-(2-Methoxyphenyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.47$–7.26 (m, 7H; ArH), 7.03–7.00 (m, 1H; ArH), 6.94–6.92 (m, 1H; ArH), 6.12 (s, 1H; CH), 3.81 (s, 3H; CH_3), 3.32 ppm (s, 1H; OH); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 97:3; 0.8 mL min^{-1}; $\lambda = 254$ nm): $t_R(S) = 38.9$ min, $t_R(R) = 43.9$ min.

(*R*)-(4-Biphenyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta) =$ 7.59–7.57 (m, 4H; ArH), 7.47–7.42 (m, 6H; ArH), 7.38–7.33 (m, 3H; ArH), 7.31–7.26 (m, 1H; ArH), 5.91 (d, $J = 3.0$ Hz, 1H; CH), 2.26 ppm (d, $J = 3.5$ Hz, 1H; OH); HPLC (Daicel Chiralcel OB-H; hexane/*i*PrOH 95:5; 1.0 mL min^{-1}; $\lambda = 254$ nm): $t_R(R) = 42.2$ min, $t_R(S) = 66.3$ min.

(*R*)-(3-Methoxyphenyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.41$–7.27 (m, 6H; ArH), 6.98–6.96 (m, 2H; ArH), 6.85–6.82 (m, 1H; ArH), 5.78 (d, $J = 15.5$ Hz, 1H; CH), 3.79 (s, 3H; CH_3), 2.67 (d, $J =$ 3.5 Hz, 1H; OH); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 95:5; 0.8 mL min^{-1}; $\lambda = 254$ nm): $t_R(S) = 30.9$ min, $t_R(R) = 47.0$ min.

(*R*)-(4-Methoxyphenyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.39$–7.26 (m, 7H; ArH), 6.89–6.87 (m, 2H; ArH), 5.78 (s, 1H; CH), 3.79 (s, 3H; CH_3), 2.54 ppm (s, 1H; OH); HPLC (Daicel Chiralcel AD; hexane/*i*PrOH 97:3; 0.5 mL min^{-1}; $\lambda = 254$ nm): $t_R(R) = 64.6$ min, $t_R(S) =$ 70.0 min; HPLC (Daicel Chiralcel OJ; hexane/*i*PrOH 90:10; 1.0 mL min^{-1}; $\lambda = 254$ nm): $t_R(R) = 30.7$ min, $t_R(S) = 34.1$ min.

(*R*)-(4-Bromophenyl)phenylmethanol:[31] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.47$–7.44 (m, 2H; ArH), 7.37–7.29 (m, 5H; ArH), 7.21–7.19 (m, 2H; ArH), 5.67 (d, $J = 3.0$ Hz, 1H; CH), 3.16 (d, $J = 3.0$ Hz, 1H; OH); HPLC (Daicel Chiralcel OB-H; hexane/*i*PrOH 90:10; 0.5 mL min^{-1}; $\lambda = 254$ nm): $t_R(R) = 26.3$ min, $t_R(S) = 35.2$ min.

(*R*)-(4-Tolyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.40$–7.34 (m, 4H; ArH), 7.29–7.26 (m, 3H; ArH), 7.18–7.16 (m, 2H; ArH), 5.81 (d, $J = 3.5$ Hz, 1H; CH), 2.36 (s, 3H; CH_3), 2.32 ppm (d, $J = 3.0$ Hz, 1H; OH); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 98:2; 0.9 mL min^{-1}; $\lambda = 254$ nm): $t_R(S) = 28.5$ min, $t_R(R) = 33.7$ min.

(*R*)-(2-Tolyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.55$ (d, $J = 7.0$ Hz, 1H; ArH), 7.38–7.24 (m, 7H; ArH), 7.19 (m, 1H; ArH), 6.00 (d, $J = 3.5$ Hz, 1H; CH), 2.35 (d, $J = 3.5$ Hz, 1H; OH), 2.27 ppm (s, 3H; CH_3); HPLC (Daicel Chiralcel OB-H; hexane/*i*PrOH 96:4; 0.8 mL min^{-1}; $\lambda = 254$ nm): $t_R(R) = 24.9$ min, $t_R(S) = 32.4$ min.

(*R*)-(2-Naphthyl)phenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.90 (m, 1H; ArH), 7.87–7.84 (m, 2H; ArH), 7.82–7.80 (d, $J = 9.0$ Hz, 1H; ArH), 7.54–7.49 (m, 2H; ArH), 7.45–7.43 (m, 3H; ArH), 7.39–7.35 (m, 2H; ArH), 7.33–7.30 (m, 1H; ArH), 5.96 (s, 1H; CH), 2.73 ppm (d, $J = 3.5$ Hz, 1H; OH); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 95:5; 1.0 mL min^{-1}; $\lambda = 254$ nm): $t_R(S) = 28.2$ min, $t_R(R) = 34.8$ min.

(*R*)-(1-Naphthyl)phenylmethanol:[31] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 8.07 (d, $J = 8.5$ Hz, 1H; ArH), 7.96 (d, $J = 7.0$ Hz, 1H; ArH), 7.90 (d, $J =$ 8.5 Hz, 1H; ArH), 7.66 (d, $J = 7.0$ Hz, 1H; ArH), 7.57–7.48 (m, 3H; ArH), 7.45–7.34 (m, 5H; ArH), 6.43 (s, 1H; CH), 3.47 (d, $J = 4.5$ Hz, 1H; OH); HPLC: Daicel Chiralcel OD-H; hexane:*i*PrOH = 90:10; 1.0 mL min^{-1}; $\lambda = 254$ nm; $t_R(S) = 13.2$ min, $t_R(R) = 28.3$ min.

(*R*)-(2-Furyl)phenylmethanol:[16] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.45$–7.43 (m, 2H; 1 ArH, 1=C*H*–O), 7.40–7.37 (m, 3H; ArH), 7.35–7.32 (m, 1H; ArH), 6.33 (m, 1H; =C*H*–), 6.12 (d, $J = 3.0$ Hz, 1H; =C*H*–), 5.81 (s, 1H; C*H*(OH)), 2.69 ppm (s, 1H; OH); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 97:3; 1.0 mL min^{-1}; $\lambda = 254$ nm): $t_R(S) = 21.2$ min, $t_R(R) =$ 25.1 min.

(*S*)-(*E*)-1,3-Diphenyl-2-propenol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.47–7.45 (m, 2H; ArH), 7.42–7.38 (m, 4H; ArH), 7.35–7.31 (m, 3H; ArH), 7.29–7.26 (m, 1H; ArH), 6.72–6.69 (d, $J = 15.5$ Hz, 1H; CH= C*H*CH(OH)(Ph)), 6.43–6.38 (m, 1H; PhC*H*=CH), 5.39 (d, $J = 6.5$ Hz, 1H; CH), 2.41 ppm (s, 1H; OH); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 80:20; 0.8 mL min^{-1}; $\lambda = 254$ nm): $t_R(S) = 10.6$ min, $t_R(R) =$ 12.9 min.

(*S*)-Cyclohexylphenylmethanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.36$–7.33 (m, 2H; ArH), 7.31–7.27 (m, 3H; ArH), 4.37–4.36 (m, 1H; C*H*OH), 1.97–2.05 (m, 2H; 1CH, 1OH), 1.78–1.75 (m, 1H; CH_2), 1.70–1.59 (m, 3H; CH_2), 1.40–1.37 (m, 1H; CH_2), 1.25–0.92 ppm (m, 5H; CH_2); HPLC (Daicel Chiralcel AD; hexane/*i*PrOH 97:3; 0.5 mL min^{-1}; $\lambda = 254$ nm): $t_R(S) = 22.0$ min, $t_R(R) = 24.1$ min.

(*S*)-2,2-Dimethyl-1-phenylpropanol:[26] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.34–7.25 (m, 5H; ArH), 4.39 (d, $J = 3.0$ Hz, 1H; CH), 1.93 (s, 1H; OH); 0.93 ppm (s, 9H; CH_3); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 98:2; 0.9 mL min^{-1}; $\lambda = 254$ nm): $t_R(S) = 11.7$ min, $t_R(R) = 13.4$ min.

(*S*)-(2-Bromophenyl)phenylmethanol:[31] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.60–7.54 (m, 2H; ArH), 7.42–7.29 (m, 6H; ArH), 7.17–7.14 (m, 1H; ArH), 6.19 (d, $J = 4.0$ Hz, 1H; CH), 2.52 ppm (d, $J = 3.5$ Hz, 1H; OH); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 90:10; 1.0 mL min^{-1}; $\lambda =$ 254 nm): $t_R(R) = 8.8$ min, $t_R(S) = 11.9$ min.

(*R*)-1-Phenylpentanol:[38] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.28$–7.23 (m, 4H; ArH), 7.21–7.17 (m, 1H; ArH), 4.49 (t, $J = 6.5$ Hz, 1H; CH), 2.01 (s, 1H; OH), 1.78–1.62 (m, 3H; CH_2), 0.83 ppm (m, 4H; $3CH_3$, $1CH_2$); HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 99:1; 1.0 mL min^{-1}; $\lambda =$ 254 nm): $t_R(R) = 24.3$ min, $t_R(S) = 31.5$ min.

(*S*)-(Ferrocenyl)phenylmethanol:[31] ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.31–7.30 (m, 2H; ArH), 7.24 (t, $J = 7.5$ Hz, 2H; ArH), 7.18–7.15 (m, 1H; ArH), 5.38 (s, 1H; CH), 4.14 (s, 5H; CH=CH), 4.14–4.00 (m, 4H; CH=CH), 2.45 ppm (s, 1H; OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 143.3$, 128.3, 127.5, 126.3, 94.3, 73.8, 72.4, 72.1, 68.8, 68.6, 68.2, 68.2, 67.5, 66.1 ppm; HPLC (Daicel Chiralcel OD-H; hexane/*i*PrOH 93:7; 1.0 mL min^{-1}; $\lambda = 254$ nm): $t_R(R) = 14.8$ min, $t_R(S) = 24.3$ min.

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