Nickel-Catalyzed Asymmetric Hydroarylation of Vinylarenes: Direct Enantioselective Synthesis of Chiral 1,1-Diarylethanes

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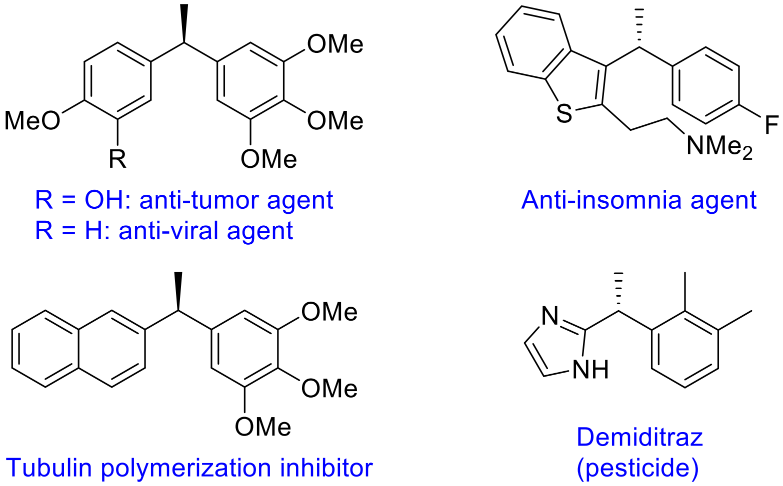
Abstract

The enantioselective hydroarylation of vinylarenes catalyzed by a chiral, non-racemic nickel catalyst is presented as a facile method to generate chiral 1,1-diarylethanes. These reactions proceed via formation of a chiral, non-racemic nickel benzyl intermediate. Transmetalation with arylboron nucleophiles and subsequent reductive elimination enables the formation of a variety of chiral 1,1-diarylethanes. The 1,1-diarylethane products from reactions of arylboronic acids containing electron-donating substituents are formed with typically greater than 90% ee, while the 1,1-diarylethanes generated from reactions of arylboronic acids containing electron-withdrawing groups are generated with typically less than 80% ee. These results are consistent with the rate of transmetalation with an arylboron nucleophile playing a key role in the enantioselectivity of these hydroarylation reactions. This mechanistic insight has led to the development of reactions of *neo*-pentylglycolate esters of arylboronic acids with vinylarenes that occur with higher enantioselectivities based on increased rates of transmetalation.

Keywords: hydroarylation, bisoxazoline ligand, enantioselective synthesis, 1,1-diarylethanes, nickel catalyst.

INTRODUCTION

Chiral 1,1-diarylethanes comprise a structural motif that has been widely studied due to the biological activity of these compounds and their potential as pharmaceuticals (Figure 1).[1] While numerous enantioselective syntheses have been reported to generate chiral, non-racemic 1,1-diarylethanes over the past decades,[2,3,4,6] catalytic and enantioselective formal hydroarylations of vinylarenes have emerged as simple and direct methods to form 1,1-diarylethanes from simple starting materials.[4,6]



R = OH: anti-tumor agent
R = H: anti-viral agent

Anti-insomnia agent

Tubulin polymerization inhibitor

Demiditraz
(pesticide)

Figure 1. Typical examples of 1,1-diarylethanes

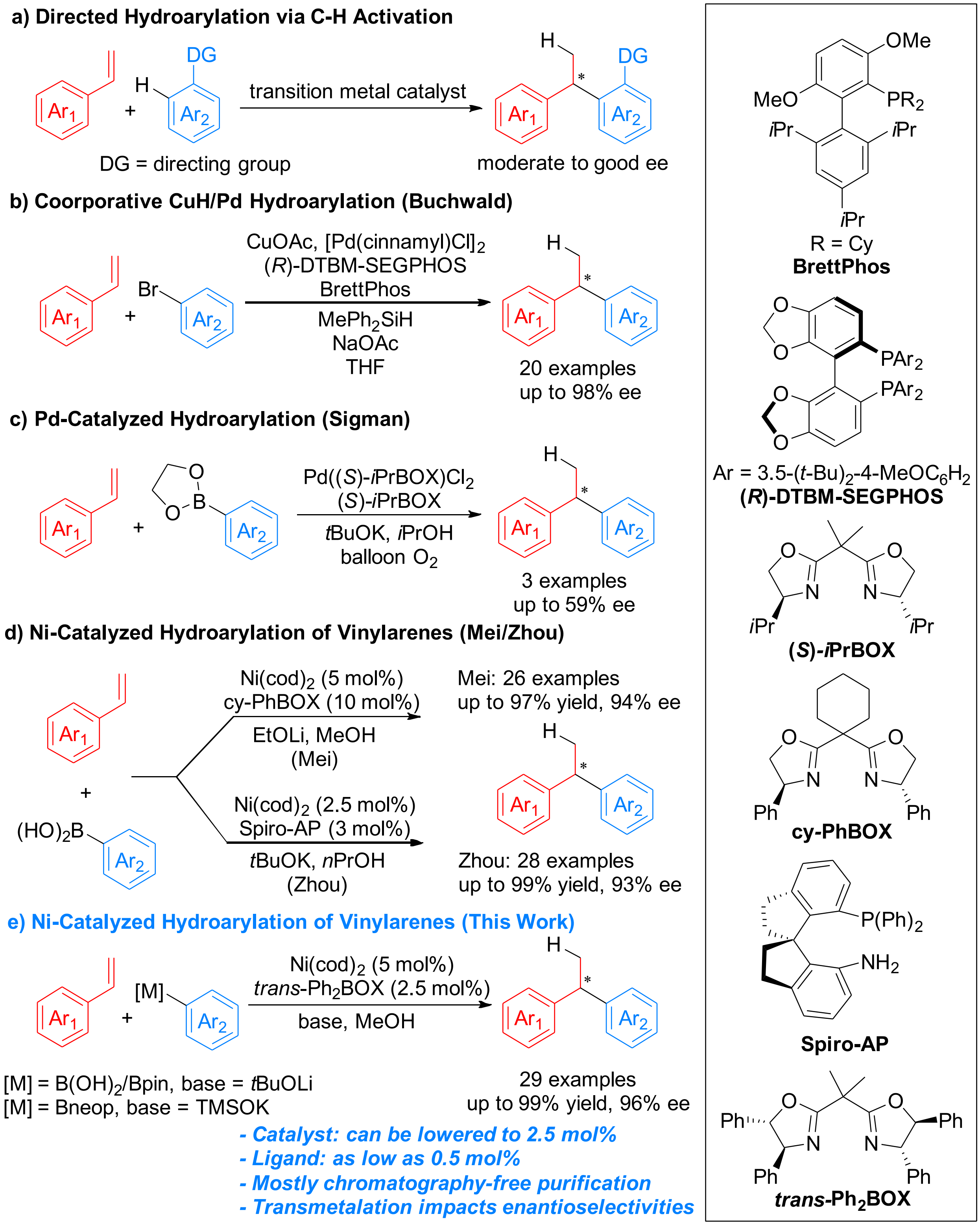
An attractive approach to catalytic, enantioselective hydroarylations of vinylarenes involves activation of an aryl C-H bond (Scheme 1a).[4] Generally, these reactions require arene substrates with functional groups capable of directing activation of an *ortho* C-H bond. Recently, catalytic, enantioselective hydroarylations of vinylarenes have been reported that do not require directed activation of an arene C-H bond. Unlike direct hydroarylations that rely on generation of a metal hydride by activation of an arene C-H bond, these hydroarylation reactions occur via generation of a metal hydride intermediate from an additional reagent, such as a protic solvent or a silane.[5,6]

In 2016, Buchwald and co-workers reported enantioselective formal hydroarylations of vinylarenes with aryl bromides that occur in the presence of cooperative palladium and copper catalysts (Scheme 1b).[6a] This approach to vinylarene hydroarylation generates 1,1-diarylethanes with high enantioselectivities. Unfortunately, these reactions rely on costly phosphine ligands for the palladium and copper catalysts and require a silane to form the key copper hydride intermediate. The ability to perform catalytic, enantioselective hydroarylations with Earth-abundant metal catalysts containing cheap chiral ligands[7] and to eliminate the need for silanes as the hydride source has the potential to render these reactions even more attractive to the synthetic chemistry community.

In 2011, Sigman and co-workers reported the first enantioselective hydroarylations of vinylarenes with arylboron nucleophiles to generate 1,1-diarylethanes in modest yields and enantioselectivities (Scheme 1c).[6b] These reactions occur in the presence of a palladium catalyst and a readily accessible bisoxazoline ligand (*i*PrBOX) and leverage *i*PrOH as the hydride source to form the key palladium hydride intermediate. Although only three examples were reported, this study provided the platform for recent advances in catalytic, enantioselective hydroarylation of vinylarenes. In 2018, Zhou and co-workers reported the first achiral Ni-catalyzed hydroarylations of styrenes and 1,3-dienes, employing MeOH as a formal hydride source and organoboron compounds as aryl nucleophiles to generate the racemic 1,1-diarylethanes in good to high yields.[5d] This study showed that a combination of a cheap, Earth-abundant nickel catalyst and MeOH enables highly efficient hydroarylations of vinylarenes.

Inspired by Zhou and co-workers' early study on hydroarylation of vinylarenes, we sought to develop an enantioselective nickel-catalyzed hydroarylation of vinylarenes. During our early efforts, Mei and co-workers reported enantioselective hydroarylation of styrenes in the presence of a nickel complex of a modified PhBOX ligand (Scheme 1d, top).[6c] Subsequently, Zhou and co-workers reported the nickel-catalyzed enantioselective hydroarylation of styrenes using a spiro-aminophosphine ligand (Scheme 1d, bottom).[6d] We now report catalytic, enantioselective hydroarylations of vinylarenes in the presence of a nickel complex of the *trans*-Ph_2BOX ligand (Scheme 1e). These reactions occur with high enantioselectivity with as low as 2.5 mol% nickel precatalyst and 0.5 mol% of a readily accessible chiral bisoxazoline ligand. The hydroarylation reactions encompass arylboronic acids and arylboronate esters as nucleophiles and, in many cases, do not require column chromatography to purify the 1,1-diarylethane products. In addition, we have gained data that suggest that the rate of transmetalation can significantly impact the enantioselectivity of the reaction.

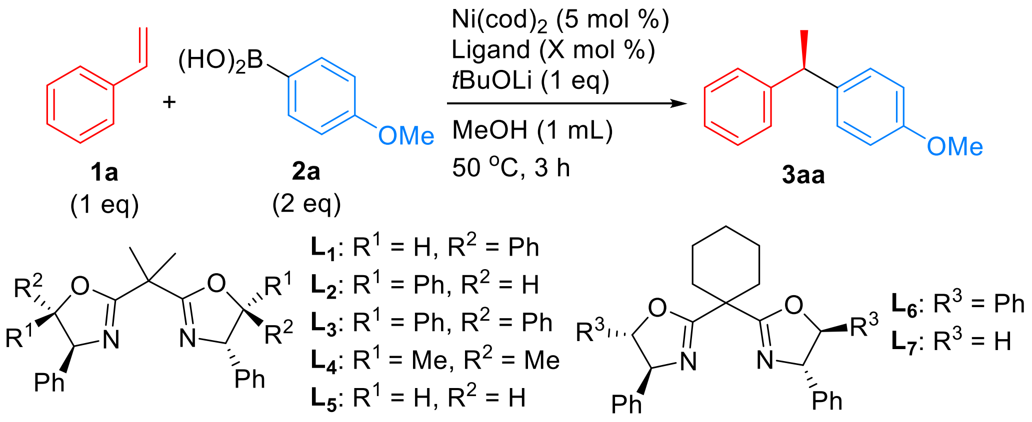
Scheme 1. Direct enantioselective hydroarylation of vinylarenes



RESULT AND DISCUSSION

Initially, the reaction of styrene **1a** and 4-methoxyphenylboronic acid **2a** in the presence of MeOH as a hydride source was evaluated to identify suitable reaction conditions.[5d] Reactions promoted by Ni(0) complexes of a variety of chiral bisoxazoline (BOX) ligands were studied to identify active and enantioselective catalysts (Table 1, entries 1-7). We found the nickel complex of *trans*-Ph_2BOX ligand **L1** provided the best combination of catalytic activity and enantioselectivity, furnishing the 1,1-diarylethane **3aa** in 99% yield with 82% ee (entry 1). The presence of base is critical to achieve high enantioselectivites. When the model reaction was run in the absence of base, the reaction formed 1,1-diarylethane **3aa** with significantly lower enantioselectivity (55% ee, compare entry 8 with entry 1). Notably, we found that the loading of ligand **L1** could be reduced to 1 mol% without lowering the yield or enantioselectivity of the reaction (entries 9-11). In fact, reducing the ligand loading in the reaction led to improved enantioselectivities. The ability to decrease the loading of ligand **L1** without detriment to the yield or enantioselectivity led us to reevaluate the Ni(0) complex of **L7**, which has previously been reported by Mei and co-workers (entries 12-14). Lowering the loading of ligand **L7** in our model reaction does not significantly impact the enantioselectivity of the reaction (compare entry 7 with entries 12-14), but the results clearly show the catalyst generated from Ni(cod)$_2$ and **L7** is less active than the corresponding nickel complex of **L1**. We chose to continue our studies by conducting reactions with catalyst generated from 5 mol% Ni(cod)$_2$ and 2.5 mol% **L1**. In the most closely related study,[6c] the use of EtOLi as a base in the hydroarylation reaction led to the highest enantioselectivities, but the use of EtOLi as a base in our model reaction led to slightly lower yield and enantioselectivity (entry 15).

Table 1. Reaction optimization[a]



Entry	Ligand	X	Yield (%)[b]	ee (%)[c]
1	**L1**	10	99	82
2	**L2**	10	31	81
3	**L3**	10	70	70
4	**L4**	10	47	67
5	**L5**	10	6	77
6	**L6**	10	64	88
7	**L7**	10	77	85
8[d]	**L1**	10	99	55
9	**L1**	5	96	86
10	**L1**	2.5	96 (93)[e]	92
11	**L1**	1	88	92
12	**L7**	5	72	87
13	**L7**	2.5	80	85
14	**L7**	1	29	80
15[f]	**L1**	2.5	87	88

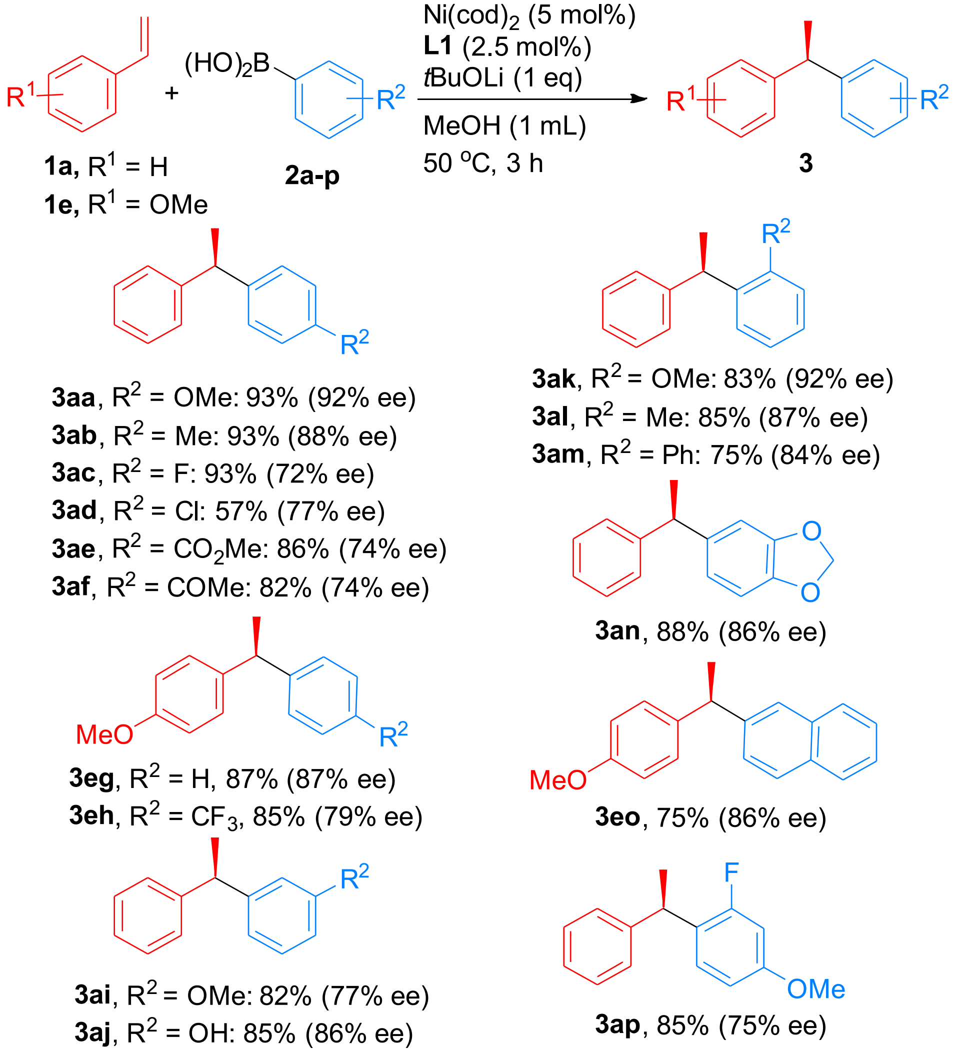
[a] Reaction condition: **1a** (0.25 mmol), **2a** (0.5 mmol), $Ni(cod)_2$ (5 mol%), *t*BuOLi (0.25 mmol). [b] Yields were determined by ^1H NMR spectroscopy of the crude reaction mixture using dibromomethane as an internal standard. [c] Enantioselectivities were determined by chiral HPLC. [d] Without *t*BuOLi. [e] Isolated yield. [f] 0.25 mmol EtOLi used instead of *t*BuOLi.

With reactions conditions identified that lead to high yields and enantioselectivities in our model reaction, we sought to establish the scope of the reaction by evaluating a variety of arylboronic acids (Scheme 2). At this stage, we found that the yield of the reaction is significantly impacted by the identity of the arylboronic acid. In many cases, the catalyst rapidly decomposes when the solid catalyst precursors are exposed to the solid arylboronic acid, especially in the presence of acidic arylboronic acids such as 4-fluorophenylboronic acid and 4-trifluoromethylphenylboronic acid.[8] To mitigate this issue, we performed these reactions by adding a stock solution of an arylboronic acid in MeOH to a mixture of the Ni(0) precatalyst, ligand **L1**, *t*BuOLi, and the vinylarene substrate.

The scope of the enantioselective hydroarylation reaction with respect to arylboronic acids is illustrated in Scheme 2. Reactions of styrene **1a** or 4-methoxystyrene **1e** with an array of substituted arylboronic acids generate 1,1-diarylethanes in good-to-high yields (57-93%) with good-to-excellent enantioselectivities (72-92%). The scope of these hydroarylation reactions encompasses a variety of *para*-, *meta*-, *ortho*-, and disubstituted arylboronic acids. Notably, arylboronic acids containing fluorides, chlorides, alcohols, esters, ketones, and acetals are suitable substrates for the nickel-catalyzed hydroarylation reaction. Reactions of arylboronic acids containing electron-donating substituents generally occur with high enantioselectivities. However, lower enantioselectivities are observed for 1,1-diarylethanes derived from reactions of arylboronic acids with electron-withdrawing substituents.

Reactions of vinylarenes with several arylboronic acid pinacol esters also occur to generate 1,1-diarylethanes in good-to-high yields (Scheme 3). These hydroarylation reactions occur in the highest yields and enantioselectivities when the catalyst is generated from 5 mol% Ni(cod)$_2$ and 5 mol% **L1**. Generally, the hydroarylations of vinylarenes with arylboronic acid pinacol esters occur

Scheme 2. Arylboronic acid substrate scope[a,b,c]



1a, R^1 = H
1e, R^1 = OMe

3aa, R^2 = OMe: 93% (92% ee)
3ab, R^2 = Me: 93% (88% ee)
3ac, R^2 = F: 93% (72% ee)
3ad, R^2 = Cl: 57% (77% ee)
3ae, R^2 = CO_2Me: 86% (74% ee)
3af, R^2 = COMe: 82% (74% ee)

3ak, R^2 = OMe: 83% (92% ee)
3al, R^2 = Me: 85% (87% ee)
3am, R^2 = Ph: 75% (84% ee)

3an, 88% (86% ee)

3eg, R^2 = H, 87% (87% ee)
3eh, R^2 = CF_3, 85% (79% ee)

3eo, 75% (86% ee)

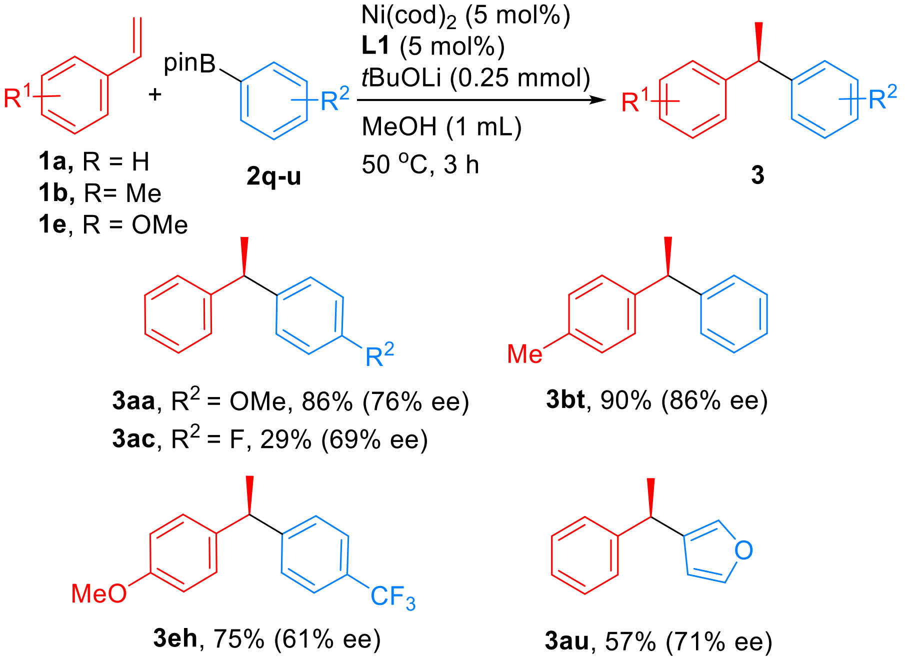
3ai, R^2 = OMe: 82% (77% ee)
3aj, R^2 = OH: 85% (86% ee)

3ap, 85% (75% ee)

[a]Reaction condition: **1a**/**1e** (0.25 mmol), **2a-p** (0.5 mmol), $Ni(cod)_2$ (0.0125 mmol), **L1** (0.0063 mmol), *t*BuOLi (0.25 mmol), MeOH (1 mL). [b]Isolated yields. [c]Enantioselectivities were determined by chiral HPLC.

with lower enantioselectivities than the analogous reactions of arylboronic acids. However, the increased stability of the boronate esters enables formal hydroheteroarylations of vinylarenes. For instance, the reaction of furan-3-boronic acid pinacol ester **2u** with styrene **1a** furnished **3au** in 57% yield, while the reaction of furan-3-boronic acid with styrene did not occur to form the hydroheteroarylation product.

Scheme 3. Arylboronic acid pinacol ester substrate scope[a,b,c]



1a, R = H
1b, R= Me
1e, R = OMe

2q-u

3

3aa, R^2 = OMe, 86% (76% ee)
3ac, R^2 = F, 29% (69% ee)

3bt, 90% (86% ee)

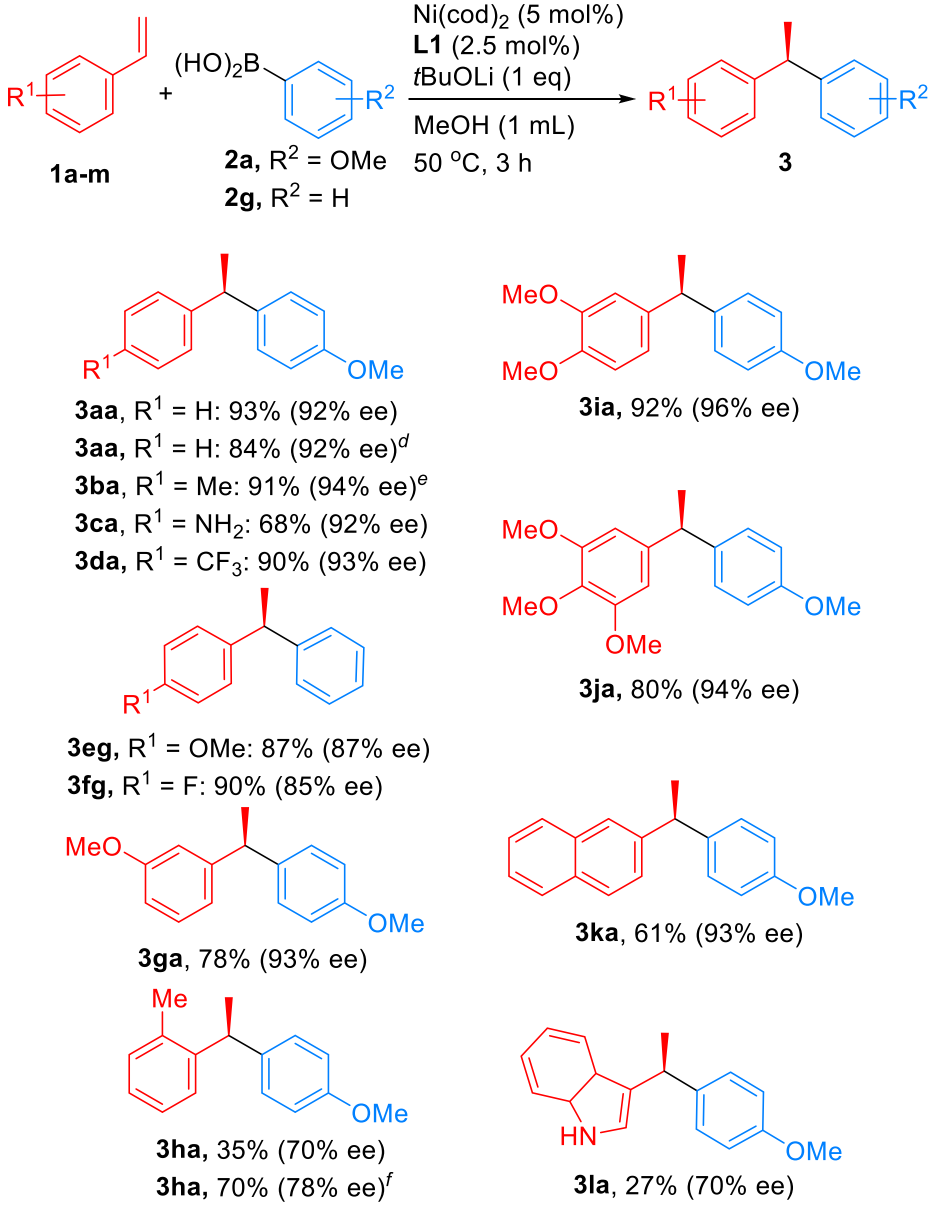
3eh, 75% (61% ee)

3au, 57% (71% ee)

[a]Reaction condition: **1a**/**1b**/**1e** (0.25 mmol), **2q-u** (0.5 mmol), Ni(cod)$_2$ (0.0125 mmol), **L1** (0.0125 mmol), *t*BuOLi (0.25 mmol), MeOH (1 mL). [b]Isolated yields. [c]Enantioselectivities were determined by chiral HPLC.

The scope of the enantioselective hydroarylation reaction with respect to vinylarene substrates is shown in Scheme 4. Reactions of 4-substituted styrenes containing either electron-donating groups (**1b**, **1e**) or electron-withdrawing groups (**1d**, **1f**) furnished the corresponding 1,1-diarylethanes in good-to-high yields (84-93%) and good-to-high enantioselectivities (84-94% ee). The loadings of Ni(cod)$_2$ and ligand **L1** can be reduced to as low as 2.5 mol% and 0.5 mol%, respectively, without significantly impacting the yield or enantioselectivity of the reaction. Notably, 4-aminostyrene **1c** is a suitable substrate for the alkene hydroarylation reaction and leads to the formation of 1,1-diarylethane **3ca** in 68% yield and 92% ee. Reactions of 2-methylstyrene **1h** produced the corresponding hydroarylation product with lower yield and enantioselectivity. Polysubstituted styrenes **1i**-**1j** and 2-vinylnaphthalene **1k** react to form 1,1-diarylethanes **3ia**-**3ka** in good-to-high yields (61-92%) with excellent enantioselectivities (93-96% ee). Additionally, the

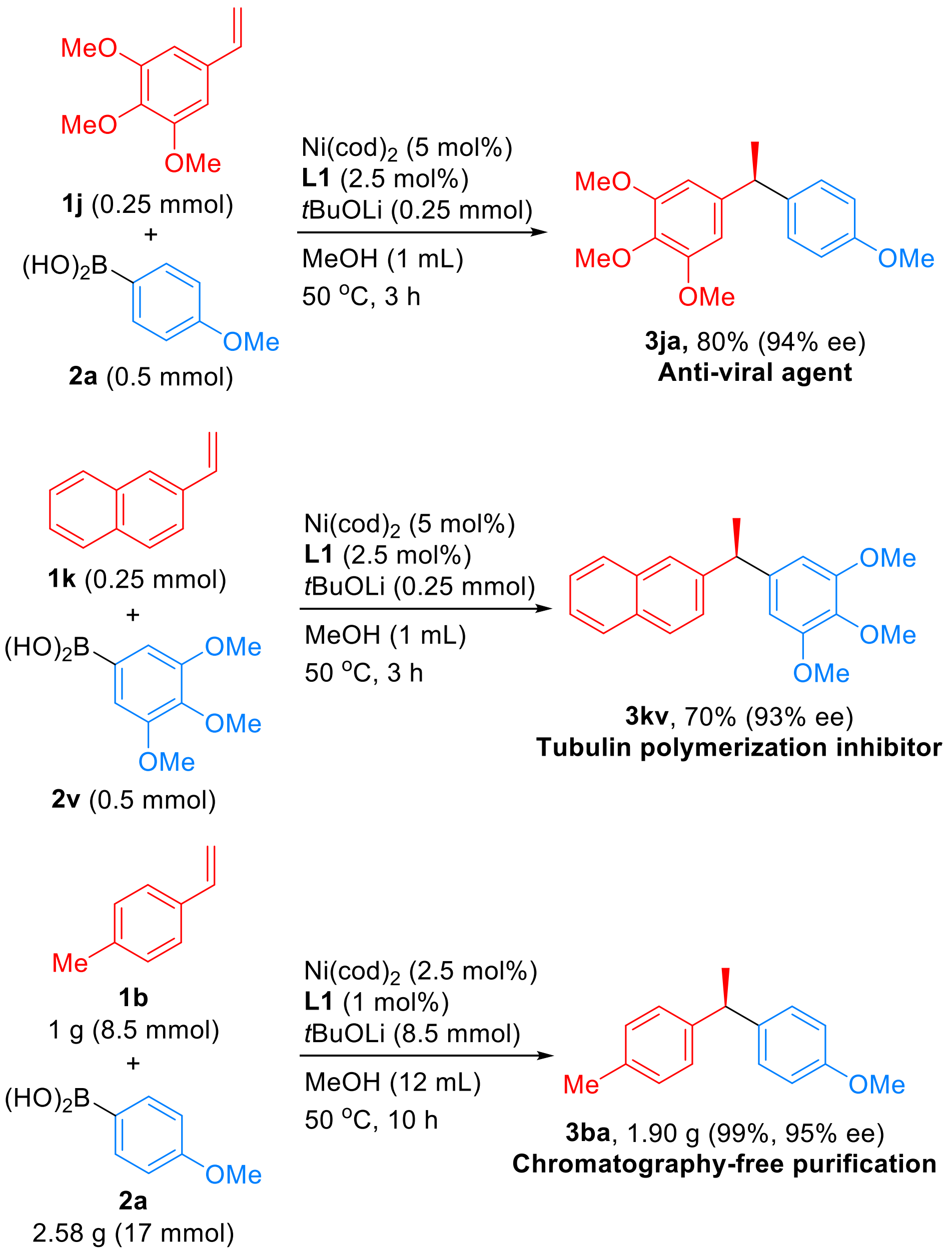
Scheme 4. Alkene substrate scope^{a,b,c}



^{a}Reaction condition: **1a**-**m** (0.25 mmol), **2a**/**2g** (0.5 mmol), Ni(cod)$_2$ (0.0125 mmol), **L1** (0.0063 mmol), *t*BuOLi (0.25 mmol), MeOH (1 mL). ^{b}Isolated yields. ^{c}Enantioselectivities were determined by chiral HPLC. ^{d}2.5 mol% Ni(cod)$_2$ and 0.5 mol% **L1** used. ^{e}1 mol% **L1** used. ^{f}10 mol% Ni(cod)$_2$ and 5 mol% **L1** used.

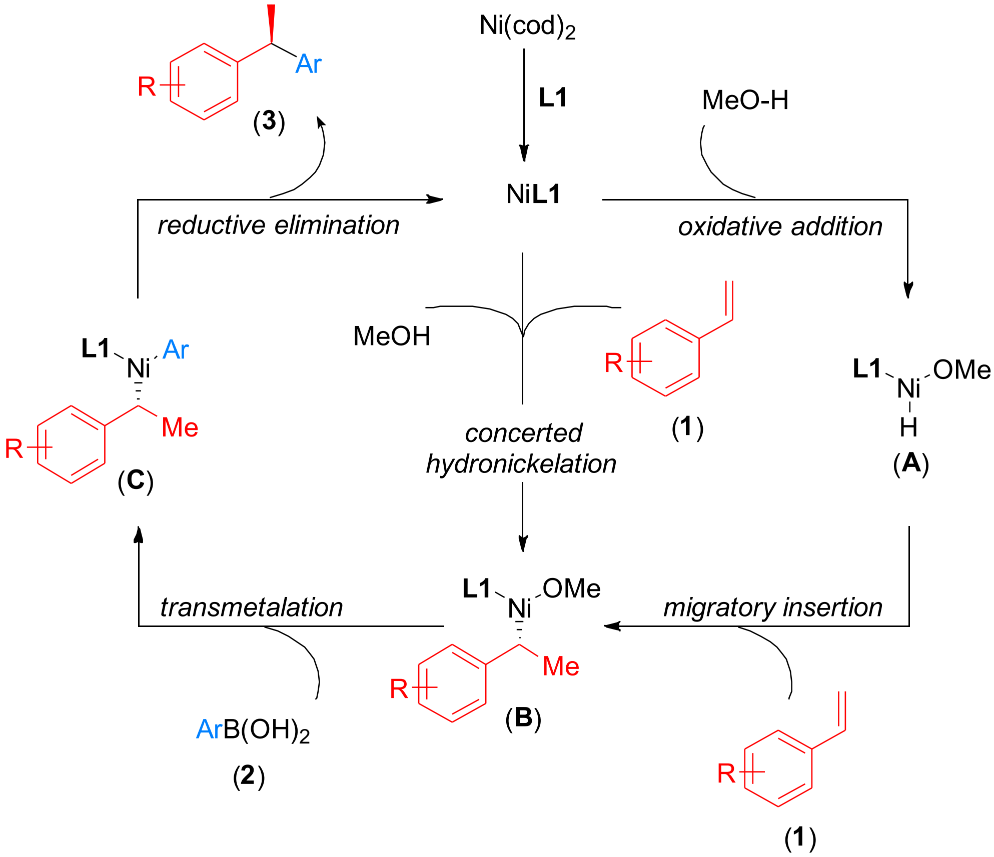
hydroarylation of 3-vinylindole **1l** formed the corresponding hydroarylation product in 27% yield with 70% ee. Reactions of α- or β-substituted styrenes (e.g. α-methylstyrene or indalin) and unactivated alkenes (e.g. 1-octene) did not occur under our reaction conditions.

Scheme 5. Synthetic utility and scalability



The synthetic utility of the enantioselective hydroarylation reaction was demonstrated in the syntheses of biologically active 1,1-diarylethanes (Scheme 5). The reaction of 3,4,5-trimethoxystyrene **1j** with 4-methoxyphenylboronic acid **2a** formed the anti-viral 1,1-diarylethane **3ja** in 80% yield and 93% ee. The reaction of 2-vinylnaphthalene **1k** with 3,4,5-trimethoxyphenylboronic acid **2v** generated the tubulin polymerization inhibitor **3kv** in 70% yield and 93% ee. These enantioselective hydroarylation reactions represent a straightforward synthetic approach to the valuable 1,1-diarylethane pharmacophore.[9] Furthermore, these hydroarylation reactions scale readily to the gram scale. The gram-scale reaction of 4-methylstyrene **1b** (8.5 mmol) with 4-methoxyphenylboronic acid **2a** (17 mmol) occurs to form **3ba** in 99% yield with 95% ee in the presence of a catalyst generated from 2.5 mol% Ni(cod)$_2$ and 1 mol% **L1**. Notably, a simple filtration through a short plug of silica enables isolation of pure **3ba** without column chromatography.

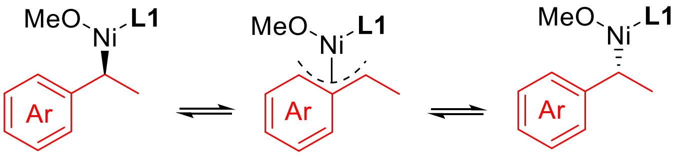
Scheme 6. Proposed mechanism



The catalytic cycle for Ni-catalyzed hydroarylation of this type was originally proposed by Zhou and co-workers[5d] and supported by studies from Mei and co-workers (Scheme 6).[6c] These studies propose oxidative addition of the alcohol O-H bond across the nickel catalyst. Subsequent migratory insertion of a vinylarene into the nickel-hydride, transmetalation with an arylboron nucleophile, and reductive elimination are proposed to be involved in the catalytic cycle. More recently, computational studies of hydroarylations of this type catalyzed by nickel complexes of phosphine and aminophosphine ligands have shown concerted hydronickelation of the vinylarene to be the more kinetically favorable step to initiate the formal hydroarylation reactions.[10a,10b] After concerted hydronickelation, transmetalation with an arylboron nucleophile and reductive elimination are calculated to form the 1,1-diarylethane product. These computational studies point to either concerted hydronickelation or transmetalation with an arylboron reagent as the turnover-limiting step. In a related study, Liu and Engle showed that concerted hydronickelation is energentically favorable in hydroarylations of carboxylic acids catalyzed by a nickel complex of a pyridine-oxazoline ligand.[10c]

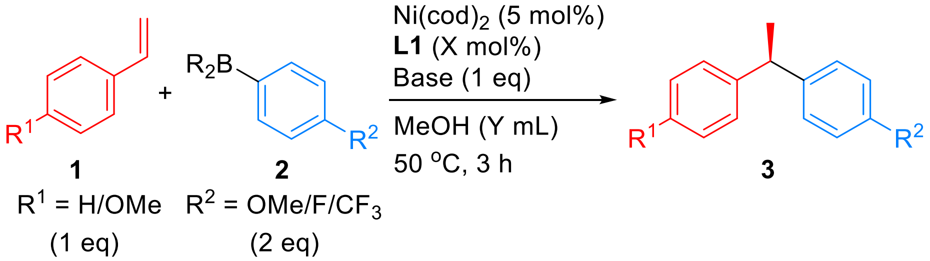
These computational studies add insight into the mechanism of the formal hydroarylation reaction and provide a model for facial selectivity during the concerted hydronickelation step. However, these studies do not address the fact that the identity of the arylboron nucleophile significantly impacts the enantioselectivity of the reaction. The enantioselectivity of the hydroarylation reaction is significantly higher when the reaction is run in the presence of *t*BuOLi versus the absence of *t*BuOLi (Table 1, compare entries 1 and 8). In addition, reactions of arylboronic acids containing electron-donating substituents occur with higher enantioselectivity than reactions of arylboronic acids containing electron-withdrawing substituents. Furthermore, reactions of arylboronate pinacol esters generally occur with lower enantioselectivity than reactions of the corresponding arylboronic acids (compare Schemes 2 and 3). These observations are consistent with the data reported by Mei and co-workers and suggest that the rate of transmetalation plays a key role in determining the enantioselectivity of the hydroarylation reaction. We hypothesize that the benzylic nickel species can undergo isomerization via interconversion between the η^1- and η^3-nickel benzyl complexes (Scheme 7).[11] In reactions of electron-rich arylboronic acids, the rate of transmetalation is likely faster than the rate of isomerization of the nickel benzyl species and the enantioselectivity of the migratory insertion is primarily responsible for the ratio of enantiomers isolated from the reaction. However, transmetalation in the absence of a base,[12] or with electron-deficient arylboronic acids[13] and arylboronate pinacol esters[14] is likely significantly slower, and the rates of transmetalation and isomerization of the benzylic nickel intermediates may become competitive. If the rates of transmetalation and isomerization are competitive, transmetalation with diastereomeric nickel complexes and subsequent reductive elimination can lead to lower enantioselectivities.

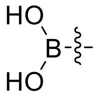
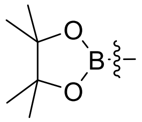
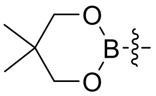
Scheme 7. Isomerization of benzylic nickel species



The ability to perform these formal hydroarylation reactions with arylboron nucleophiles and reaction conditions that lead to high rates of transmetalation should result in high enantioselectivities for the 1,1-diarylethane products. Recently, Denmark and co-workers illustrated that the use of potassium trimethylsilanoate (TMSOK) enabled rapid transmetalation of *neo*-pentylglycolate esters of arylboronic acids in palladium-catalyzed Suzuki-Miyaura coupling reactions.[13] Several *neo*-pentylglycolate esters of arylboronic acids were tested in our hydroarylation reaction (Table 2, entry 3). Although the yields of corresponding products were slightly lower than the reactions of arylboronic acids, the enantioselectivities of products derived from electron-deficient nucleophiles were improved (Table 2).

Table 2. Comparison of yields and enantioselectivities of products generated from different arylboron nucleophiles



Entry	Type of BR_2 **2**	Yields of products **3**[d,f]		
		R^1 = H R^2 = OMe	R^1 = H R^2 = F	R^1 = OMe R^2 = CF_3
1[a]	 (B(OH)$_2$)	93% (92% ee)	93% (72% ee)	85% (79% ee)
2[b]	 (Bpin)	86% (76% ee)	29% (69% ee)	75% (61% ee)
3[c]	 (Bneop)	93% (89% ee)	62% (87% ee)	79% (83% ee)

[a] X = 2.5, Y = 1, *t*BuOLi as base. [b] X = 5, Y = 1, *t*BuOLi as base. [c] X = 2.5, Y = 0.5, TMSOK as base. [d] Isolated yields. [e] Enantioselectivities were determined by chiral HPLC.

CONCLUSION

We have developed the enantioselective hydroarylation of vinylarenes catalyzed by a nickel catalyst prepared in situ from Ni(cod)$_2$ and *trans*-Ph$_2$BOX ligand **L1** to generate chiral 1,1-diarylethanes. These reactions proceed under mild reaction conditions and occur with as low as 2.5 mol% of the nickel precatalyst and 0.5 mol% of the chiral, non-racemic bisoxazoline ligand. Furthermore, the majority of the 1,1-diarylethane products were isolated in high purity without column chromatography. High enantioselectivities can be achieved by ensuring that the rate of transmetalation of arylboron nucleophiles is fast relative to the rate of isomerization of the key benzylic nickel intermediate. Studies to expand the reach of enantioselective, nickel-catalyzed alkene hydroarylation beyond vinylarenes are ongoing in our laboratory.

EXPERIMENTAL SECTION

General Information and Method. Unless otherwise noted, all reactions were conducted under inert atmosphere in a nitrogen-filled dry box or by standard Schlenk techniques. All glassware used for reactions were dried at 140 °C in an oven overnight.

The majority of hydroarylation products were isolated in high purities without column chromatography. If further purification was required, flash column chromatography was performed on SiliFlash® P60 silica gel (40-63μm, 60Å) using hexanes/ethyl acetate or hexanes/diethyl ether mixtures as eluents. Reaction products were visualized on TLC by UV light.

HRMS analysis was performed at the Iowa State University Chemical Instrumentation Facility on an Agilent 6540 QTOF spectrometer (ESI) or Agilent 7250 GC/Q-TOF (EI). NMR spectra were acquired on Varian MR-400 at the Iowa State University Chemical Instrumentation Facility.

Chemical shifts are reported in ppm relative to a residual solvent peak ($CDCl_3$ = 7.26 ppm for ^1H and 77.16 ppm for ^{13}C). Coupling constants are reported in hertz. HPLC analyses were carried out on a Water Alliance HPLC system with an e2695 Separations Module and a 2489 (UV/Vis) dual wavelength detector. Optical rotations were measured on an Atago AP-300 automatic polarimeter.

Materials. All chemicals obtained from commercial sources were used directly without further purification. Bis(1,5-cyclooctadiene)nickel(0) was purchased from Strem Chemicals. Thionyl chloride was purchased from Sigma-Aldrich. Dimethylmalonic acid was purchased from Oakwood. (1*R*,2*S*)-2-amino-1,2-diphenylethanol, (*S*)-(+)-2-phenylglycinol and potassium trimethylsilanoate were purchased from AK Scientific. Anhydrous methanol was purchased from Sigma Aldrich.

The following boron compounds were purchased from AK Scientific: 4-methoxylphenylboronic acid; 4-methylphenylboronic acid; phenylboronic acid; 4-fluorophenylboronic acid; 3-methoxyphenylboronic acid; 3-fluorophenylboronic acid; 4-methoxycarrbonylphenylboronic acid; 4-acetylphenylboronic acid; 4-phenylboronic acid pinacol ester; and furan-3-boronic acid pinacol ester. The following arylboronic acid were purchased from Frontier: 4-chlorophenylboronic acid; 4-(trifluoromethyl)phenylboronic acid; 2-methoxyphenylboronic acid; and 3-methoxyphenylboronic acid. The following boron compounds were purchased from Combi Block: 2-methylphenylboronic acid; 3-hydroxyphenylboronic acid; 2-naphthaleneboronic acid; 3,4-(methylenedioxy)phenylboronic acid; 2-fluoro-4-methoxyphenylboronic acid; 4-methoxyphenylboronic acid pinacol ester; 4-methylphenylboronic acid pinacol ester; and 4-(trifluoromethyl)phenylboronic acid pinacol ester. 2-Biphenylboronic acid was obtained from Oakwood. Neopentylglycol esters were synthesized according to a reported literature procedure.[15]

Styrene and 4-fluorostyrene were purchased from Sigma-Aldrich. 4-Methoxystyrene, 4-methylstyrene and 2-methylstyrene were purchased from Alfa Aesar. The following vinylarenes were synthesized by Wittig reactions according to a reported literature procedure:[16] 4-trifluoromethylstyrene; 3-methoxystyrene; 3,4-dimethoxystyrene; 3,4,5-trimethoxystyrene; and 2-vinylnaphthalene. 3-Vinylindole was prepared according to a previous report.[17] Characterization for data of 4-trifluoromethylstyrene,[18] 3-methoxystyrene,[19] 3,4-dimethoxystyrene,[20] 3,4,5-trimethoxystyrene,[21] 2-vinylnaphthalene,[22] and 3-vinylindole[17] were in accordance with the reported data.

Ligand Synthesis. Ligands **L2**,[23] **L3**,[24] **L4**,[25] and **L5**[26] were synthesized according to reported literature procedures.

Ligand L1. A mixture of dimethylmalonic acid (5.0 mmol) in $SOCl_2$ (20 mL) was refluxed in an oil bath for 5 hours. After cooling to room temperature, the solvent was removed under reduced pressure to afford the corresponding crude acid chloride, which was directly used for the next step without further purification.

(1*R*,2*S*)-2-amino-1,2-diphenylethanol (10 mmol, 2 equiv.) was dissolved in DCM (20 mL) under nitrogen. The solution was cooled to 0 °C using an ice bath, and triethylamine (25 mmol, 5 equiv.) was added to the mixture. Next, a solution of crude dimethylmalonyl dichloride in DCM (10 mL) was added dropwise to the flask. The ice bath was removed, and the resulting mixture was stirred overnight at room temperature. The reaction mixture was washed with 1N HCl and then saturated aqueous $NaHCO_3$. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The resultant *bis*-amide residue was directly used for the final step without further purification.

To a solution of the *bis*-amide (1 mmol, 1 equiv.) in DCM (20 mL) was added 4-(dimethylamino)pyridine (5 mmol, 5 equiv.) and triethylamine (5 mmol, 5 equiv.). Then, a solution of *p*-toluenesulfonyl chloride (2.5 mmol, 2.5 equiv.) in DCM (12 mL) was added at room temperature. The resulting mixture was stirred at room temperature for three days. Upon completion of the reaction, the solution was washed with NH_4Cl and then $NaHCO_3$. The resulting organic layer was concentrated under reduced pressure and purified by silica gel column chromatography (Hexane:EtOAc = 80:20) to afford the desired BOX ligand **L1** (0.40 g, 82%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 10H), 5.33 (d, *J* = 7.6 Hz, 2H), 5.12 (d, *J* = 7.6 Hz, 2H), 1.90 (s, 6H). The NMR spectrum was in accordance with the reported data.[27]

Ligand L6. (1*R*,2*S*)-2-amino-1,2-diphenylethanol (10 mmol, 2 equiv.) was dissolved in DCM (20 mL) under nitrogen. The solution was cooled to 0 °C using an ice bath, and triethylamine (25 mmol, 5 equiv.) was added to the mixture. Next, a solution of cyclohexane-1,1-dicarbonyl chloride[28] (5 mmol, 1 equiv.) in DCM (10 mL) was added dropwise to the flask. The ice bath was removed and the resulting mixture was stirred overnight at room temperature. The reaction mixture was washed with 1N HCl and then saturated aqueous $NaHCO_3$. The organic layer was dried over Na_2SO_4 and the organic layer was concentrated in vacuo. The resultant *bis*-amide residue was directly used for the next step without purification.

To a solution of the *bis*-amide (1 mmol) in DCM (20 mL) was added 4-(dimethylamino)pyridine (5 mmol, 5 equiv.) and triethylamine (5 mmol, 5 equiv.). Then, a solution of *p*-toluenesulfonyl chloride (2.5 equiv.) in DCM (12 mL) was added at room temperature. The resulting mixture was stirred at room temperature for three days. Upon completion of the reaction, the solution was washed with saturated aqueous NH_4Cl and then saturated aqueous $NaHCO_3$. The resulting organic layer was concentrated in vacuo and purified by silica gel column chromatography (Hexane:EtOAc = 80:20) to afford the desired BOX ligand **L6** (0.38 g, 72%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 20H), 5.30 (d, *J* = 7.8 Hz, 2H), 5.16 (d, *J* = 7.9 Hz, 2H), 2.43 – 2.39 (m, 4H), 1.83 – 1.79 (m, 4H), 1.65 – 1.59 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 168.6, 142.1, 140.4, 128.9, 128.8, 128.4, 127.7, 126.8, 126.0, 89.4, 78.8, 44.3, 32.7, 25.4, 22.9. **HRMS** (ESI): Calcd. for $C_{36}H_{35}N_2O_2^+$ ([M+H]$^+$): 527.2693, Found: 527.2738.

Ligand L7. Ligand **L7** was synthesized using an analogous procedure to that for the synthesis of ligand **L6** with (*S*)-(+)-2-phenylglycinol used in place of (1*R*,2*S*)-2-amino-1,2-diphenylethanol. The crude product was purified by silica gel column chromatography (Hexane:EtOAc = 80:20) to afford the desired BOX ligand **L7** (0.29 g, 78%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 10H), 5.26 (dd, *J* = 10.2, 7.8 Hz, 2H), 4.65 (dd, *J* = 10.2, 8.4 Hz, 2H), 4.12 (t, *J* = 8.3 Hz, 2H), 2.27 – 2.16 (m, 4H), 1.71 – 1.65 (m, 4H), 1.54 – 1.50 (m, 2H). The NMR spectrum was in accordance with the reported data.[29]

General Procedure for Ni-Catalyzed Hydroarylation of Vinylarenes with Arylboronic Acids. In a nitrogen-filled glovebox, an oven dried 1-dram vial was charged with an appropriate arylboronic acid **2** (0.5 mmol) and MeOH (1 mL). The resulting mixture was gently stirred at room temperature until it was clear and was used immediately.

In a second oven dried 1-dram vial, Ni(cod)$_2$ (0.0125 mmol), ligand **L1** (0.0063 mmol), *t*BuOLi (0.25 mmol), and styrene **1a** or 4-methoxystyrene **1e** (0.25 mmol) were sequentially added. Then, the vial was charged with the as-prepared solution of the arylboronic acid in MeOH from the first vial, sealed and taken out of the glovebox. The reaction mixture was stirred at 50 °C in an aluminium reaction block (for 1-dram vials) for 3 hours. Upon completion, the reaction was cooled to room temperature and was diluted with 20 mL DCM. The solvent was removed under vacuum. The resulting residue was re-dissolved with DCM, filtered through a short plug of silica gel eluting with DCM and concentrated under vacuum. Unless otherwise stated, the hydroarylation products were isolated in high purity after concentration under vacuum. The racemic products were synthesized either by the same procedure with racemic ligand **L7**, or by a previously reported procedure.[5d] The absolute configuration of the chiral product **3aa** was assigned by comparison to the optical rotation reported in the literature.[6c] Absolute configurations of additional 1,1-diarylethanes were assigned based on the sense of absolute configuration observed for compound **3aa**.

*(R)-1-methoxy-4-(1-phenylethyl)benzene (**3aa**)*:[6c] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol). **3aa** was isolated in high purity without further purification as a colorless oil in 93% yield (49.4 mg, 0.22 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 18.0 min (minor); t_R 19.4 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 92% ee. $[\alpha]_D^{24}$ = -1.49° (c 0.74, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 2H), 7.25 – 7.15 (m, 5H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.13 (d, *J* = 7.2 Hz, 1H), 3.80 (s, 3H), 1.64 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.8, 146.8, 138.6, 128.5, 128.3, 127.5, 125.9, 113.1, 55.2, 43.9, 22.1.

*(R)-1-methyl-4-(1-phenylethyl)benzene (**3ab**)*:[3d] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-methylphenylboronic acid **2b** (68.0 mg, 0.5 mmol). **3ab** was isolated in high purity without further purification as a colorless oil in 93% yield (49.3 mg, 0.23 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 11.5 min (minor); t_R 12.6 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 88% ee. $[\alpha]_D^{24}$ = -1.60° (c 0.6, $CHCl_3$). **^{1}H NMR** (400 MHz, $CHCl_3$) δ 7.34 – 7.30 (m, 2H), 7.28 – 7.26 (m, 2H), 7.24 – 7.19 (m, 1H), 7.18 – 7.13 (m, 4H), 4.17 (q, *J* = 7.2 Hz, 1H), 2.36 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 146.6, 143.4, 135.5, 129.1, 128.4, 127.6, 127.5, 126.0, 44.4, 22.0, 21.0.

*(R)-1-fluoro-4-(1-phenylethyl)benzene (**3ac**)*:[3e] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-fluorophenylboronic acid **2c** (70.0 mg, 0.5 mmol). **3ac** was isolated in high purity without further purification as a colorless oil in 93% yield (46.6 mg, 0.23 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 8.7 min (minor); t_R 10.3 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 72% ee. $[\alpha]_D^{24}$ = -1.30° (c 0.74, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.22 – 7.16 (m, 5H), 6.98 (t, *J* = 8.7 Hz, 2H), 4.15 (q, *J* = 7.2 Hz, 1H), 1.64 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 161.3 (d, C-F, $^1J_{C\text{-}F}$ = 243.9 Hz), 146.2, 142.0 (d, C-F, $^4J_{C\text{-}F}$ = 3.4 Hz), 129.0 (d, C-F, $^3J_{C\text{-}F}$ = 7.7 Hz), 128.4, 127.5, 126.2, 115.1 (d, C-F, $^2J_{C\text{-}F}$ = 21.1 Hz), 44.0, 22.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.5.

*(R)-1-chloro-4-(1-phenylethyl)benzene (**3ad**)*:[3d] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-chlorophenylboronic acid **2d** (78.2 mg, 0.5 mmol). **3ad** was isolated in high purity without further purification as a colorless oil in 57% yield (30.9 mg, 0.14 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 7.7 min (minor); t_R 8.4 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 77% ee. $[\alpha]_D^{24}$ = -1.5° (c 0.64, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.16 (m, 9H), 4.15 (q, *J* = 7.2 Hz, 1H), 1.64 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 145.8, 144.9, 131.8, 129.0, 128.5, 128.5, 127.5, 126.3, 44.2, 21.8.

*Methyl (R)-4-(1-phenylethyl)benzoate (**3ae**)*:[6c] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-(methoxycarbonyl)phenyl)boronic acid **2e** (90.0 mg, 0.5 mmol). **3ae** was isolated in high purity without further purification as a colorless oil in 86% yield (52.9 mg, 0.22 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25

°C) t_R 6.0 min (major); t_R 6.8 min (minor) [Chiracel ASH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 74% ee. $[\alpha]_D^{24}$ = -0.82° (c 0.78, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.33 – 7.29 (m, 4H), 7.23 – 7.20 (m, 3H), 4.22 (q, *J* = 7.2 Hz, 1H), 3.91 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.0, 151.7, 145.4, 129.8, 128.5, 128.0, 127.7, 127.6, 126.3, 52.0, 44.8, 21.6.

*(R)-1-(4-(1-phenylethyl)phenyl)ethan-1-one (**3af**)*:[30] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-acetylphenylboronic acid **2f** (82.0 mg, 0.5 mmol). **3af** was isolated in high purity without further purification as a colorless oil in 82% yield (45.9 mg, 0.20 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 10.9 min (minor); t_R 11.4 min (major) [Chiracel ASH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 98:2, 1.0 mL/min] to be 74% ee. $[\alpha]_D^{24}$ = -1.1° (c 0.86, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.34 – 7.29 (m, 4H), 7.23 – 7.19 (m, 3H), 4.22 (q, *J* = 7.2 Hz, 1H), 2.58 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 197.8, 152.0, 145.3, 135.2, 128.6, 128.5, 127.8, 127.6, 126.4, 44.8, 26.6, 21.6.

*(S)-1-methoxy-4-(1-phenylethyl)benzene (**3eg**)*:[6a] Prepared according to the general procedure from 4-methoxystyrene **1e** (33.5 mg, 0.25 mmol) and phenylboronic acid **2g** (61.0 mg, 0.5 mmol). **3eg** was isolated in high purity without further purification as a colorless oil in 87% yield (46.2 mg, 0.22 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 17.6 min (major); t_R 19.0 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 87% ee. $[\alpha]_D^{24}$ = +1.55° (c 0.58, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 2H), 7.25 – 7.15 (m, 5H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.13 (d, *J* = 7.2 Hz, 1H), 3.80 (s, 3H), 1.64 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.8, 146.8, 138.6, 128.5, 128.3, 127.5, 125.9, 113.1, 55.2, 43.9, 22.1.

(S)-1-methoxy-4-(1-(4-(trifluoromethyl)phenyl)ethyl)benzene (3eh):[2c] Prepared according to the general procedure from 4-methoxystyrene **1e** (33.5 mg, 0.25 mmol) and 4-(trifluoromethyl)phenylboronic acid **2h** (95.0 mg, 0.5 mmol). **3eh** was isolated in high purity without further purification as a colorless oil in 85% yield (59.6 mg, 0.21 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 7.0 min (major); t_R 9.7 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 79% ee. $[\alpha]_D^{24} = +1.74°$ (c 0.54, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.18 (d, *J* = 7.2 Hz, 1H), 3.80 (s, 3H), 1.65 (d, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 158.1, 150.9, 137.4, 128.5, 128.3 (d, C-F, $^2J_{C-F}$ = 32.3 Hz), 127.9, 125.3 (q, C-F, $^3J_{C-F}$ = 3.8 Hz), 124.3 (d, C-F, $^1J_{C-F}$ = 272.7 Hz), 113.9, 55.2, 43.9, 21.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.3.

(R)-1-methoxyl-3-(1-phenylethyl)benzene (3ai):[31] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 3-methoxyphenylboronic acid **2i** (76.0 mg, 0.5 mmol). **3ai** was isolated in high purity without further purification as a colorless oil in 82% yield (43.5 mg, 0.20 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 7.2 min (minor); t_R 7.7 min (major) [Chiracel ODH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 77% ee. $[\alpha]_D^{24} = -1.21°$ (c 0.76, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.30 (m, 2H), 7.27 – 7.19 (m, 4H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.82 (t, *J* = 2.4 Hz, 1H), 6.76 (dd, *J* = 8.2, 2.6 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 1H), 3.80 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 159.6, 148.1, 146.2, 129.3, 128.4, 127.6, 126.1, 120.1, 113.8, 111.0, 55.1, 44.8, 21.8.

(R)-3-(1-phenylethyl)phenol (3aj):[9a] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 3-hydroxyphenylboronic acid **2j** (69.0 mg, 0.5 mmol). **3aj** was

isolated in high purity without further purification as a colorless oil in 85% yield (42.1 mg, 0.21 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 28.4 min (major); t_R 38.4 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 86% ee. $[\alpha]_D^{24}$ = -1.11° (c 0.54, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H), 7.26 – 7.15 (m, 4H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.69 – 6.65 (m, 2H), 4.79 (s, 1H), 4.12 (q, *J* = 7.2 Hz, 1H), 1.64 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 155.4, 148.4, 146.1, 129.6, 128.4, 127.6, 126.1, 120.2, 114.6, 113.0, 44.6, 21.7.

(R)-1-methoxy-2-(1-phenylethyl)benzene (***3ak***):[32] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 2-methoxyphenylboronic acid **2g** (76.0 mg, 0.5 mmol). **3ak** was isolated in high purity without further purification as a colorless oil in 83% yield (44.1 mg, 0.21 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 9.0 min (major); t_R 14.1 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 92% ee. $[\alpha]_D^{24}$ = -1.45° (c 0.62, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 4H), 7.26 – 7.19 (m, 3H), 6.97 (td, *J* = 7.5, 1.2 Hz, 1H), 6.90 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 4.65 (q, *J* = 7.3 Hz, 1H), 3.82 (s, 3H), 1.65 (d, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 156.9, 146.4, 134.9, 128.1, 127.8, 127.7, 127.1, 125.7, 120.6, 110.6, 55.4, 37.4, 21.0.

(R)-1-methyl-2-(1-phenylethyl)benzene ***(3al)***:[32] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 2-methylphenylboronic acid **2l** (68.0 mg, 0.5 mmol). **3al** was isolated in high purity without further purification as a colorless oil in 85% yield (41.7 mg, 0.21 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 10.5 min (major); t_R 14.7 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 87% ee. $[\alpha]_D^{24}$ = -1.20° (c 0.78, $CHCl_3$). **^{1}H**

NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 3H), 7.28 – 7.25 (m, 1H), 7.24 – 7.18 (m, 5H), 4.38 (q, *J* = 7.2 Hz, 1H), 2.29 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H). **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 146.3, 144.0, 136.1, 130.4, 128.4, 127.7, 126.7, 126.1, 126.1, 125.9, 41.0, 22.2, 19.8.

(R)-2-(1-phenylethyl)-1,1'-biphenyl ***(3am)***: Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 2-biphenylboronic acid **2m** (99.0 mg, 0.5 mmol). The crude reaction mixture was purified by flash column chromatography (hexane:EtOAc = 90:10) to give **3am** as colorless oil in 75% yield (48.4 mg, 0.19 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 6.3 min (minor); t_R 8.3 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 84% ee. $[\alpha]_D^{24}$ = -0.87° (c 0.90, $CHCl_3$). **^1H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 5H), 7.34 – 7.28 (m, 6H), 7.23 – 7.19 (m, 1H), 7.17 – 7.14 (m, 2H), 4.39 (q, *J* = 7.2 Hz, 1H), 1.63 (d, *J* = 7.2 Hz, 3H). **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 146.6, 144.1, 141.9, 141.8, 130.1, 129.4, 128.2, 128.1, 127.7, 127.6, 127.6, 126.9, 125.8, 125.8, 40.2, 22.4. **HRMS** (EI): Calcd. for $C_{20}H_{18}^+$ ($[M]^+$): 258.1403, Found: 258.1404.

(R)-5-(1-Phenylethyl)-1,3-benzodioxole ***(3an)***:[9a] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 3,4-methylenedioxyphenylboronic acid **2n** (83.0 mg, 0.5 mmol). **3an** was isolated in high purity without further purification as a colorless oil in 88% yield (49.8 mg, 0.22 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 19.6 min (major); t_R 20.9 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 86% ee. $[\alpha]_D^{24}$ = -0.94° (c 0.68, $CHCl_3$). **^1H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.30 (m, 2H), 7.26 – 7.19 (m, 3H), 6.78 – 6.72 (m, 3H), 5.92 (s, 2H), 4.11 (q, *J* = 7.2 Hz, 1H), 1.63 (d, *J* = 7.2 Hz, 3H). **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 147.6, 146.4, 145.7, 140.5, 128.4, 127.5, 126.1, 120.4, 108.2, 108.0, 100.8, 44.5, 22.0.

(R)-2-(1-(4-methoxyphenyl)ethyl)naphthalene (3eo):[33] Prepared according to the general procedure from 4-methoxystyrene **1e** (33.5 mg, 0.25 mmol) and 2-naphthaleneboronic acid **2o** (86.0 mg, 0.5 mmol). The crude reaction mixture was purified by flash column chromatography (hexane:EtOAc = 90:10) to give **3eo** as colorless oil in 75% yield (49.2 mg, 0.19 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 23.7 min (major); t_R 30.4 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 86% ee. $[\alpha]_D^{24}$ = +1.50° (c 0.77, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.82 (m, 2H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.73 (s, 1H), 7.52 – 7.44 (m, 2H), 7.35 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 4.32 (q, *J* = 7.2 Hz, 1H), 3.82 (s, 3H), 1.76 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 158.0, 144.2, 138.4, 133.6, 132.1, 128.7, 128.0, 127.8, 127.6, 126.9, 126.0, 125.4, 125.2, 113.8, 55.3, 44.1, 22.0.

(R)-2-fluoro-4-methoxy-1-(1-phenylethyl)benzene (3ap):[34] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 3,4-methylenedioxyphenylboronic acid **2p** (85.0 mg, 0.5 mmol). **3ap** was isolated in high purity without further purification as a colorless oil in 85% yield (48.9 mg, 0.21 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 19.8 min (major); t_R 20.9 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 75% ee. $[\alpha]_D^{24}$ = -0.92° (c 0.98, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 4H), 7.24 – 7.19 (m, 1H), 7.13 (t, *J* = 8.7 Hz, 1H), 6.67 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.61 (dd, *J* = 12.0, 2.5 Hz, 1H), 4.43 (q, *J* = 7.3 Hz, 1H), 3.79 (s, 3H), 1.64 (d, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 161.0 (d, C-F, $^1J_{C-F}$ = 245.3 Hz), 159.2 (d, C-F, $^3J_{C-F}$ = 11.0 Hz), 145.5, 128.8 (d, C-F, $^3J_{C-F}$ = 7.0 Hz), 128.4, 127.4, 126.1, 125.2 (d, C-F, $^2J_{C-F}$ = 19.8 Hz), 109.6 (d, C-F, $^4J_{C-F}$ = 3.0 Hz), 101.6 (d, C-F, $^2J_{C-F}$ = 28.4 Hz), 55.5, 37.1, 20.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.7.

*(R)-1-methoxy-4-(1-(p-tolyl)ethyl)benzene (**3ba**)*:[35] Prepared according to the general procedure from 4-methylstyrene **1b** (29.5 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol), with 0.0025 mmol **L1** used. **3ba** was isolated in high purity without further purification as a colorless oil in 91% yield (51.5 mg, 0.23 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 18.8 min (minor); t_R 21.4 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 94% ee. $[\alpha]_D^{24}$ = -1.45° (c 0.66, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.18 – 7.11 (m, 6H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.11 (q, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 2.35 (d, *J* = 1.2 Hz, 3H), 1.64 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.8, 143.8, 138.8, 135.4, 129.0, 128.5, 127.4, 113.7, 55.2, 43.6, 22.2, 21.0.

*(R)-4-(1-(4-methoxyphenyl)ethyl)aniline (**3ca**)*:[36] Prepared according to the general procedure from 4-vinylaniline **1d** (29.8 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol). **3ca** was isolated in high purity without further purification as a white solid in 68% yield (38.6 mg, 0.17 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.6 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.65 (d, *J* = 8.4 Hz, 2H), 4.02 (q, *J* = 7.2 Hz, 1H), 3.78 (s, 5H), 1.58 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.7, 143.8, 139.2, 137.3, 128.4, 128.3, 115.4, 113.6, 55.2, 43.1, 22.2. Next, **3ca** (15.00 mg, 0.066 mmol, 1 equiv.), benzoyl chloride (13.86 mg, 0.099 mmol, 1.5 equiv.), triethylamine (33.33 mg, 0.33 mmol, 5 equiv.) and DCM (2 mL) were combined in a 1-dram vial under air and stirred overnight at room temperature. The reaction mixture was washed successively with 1N HCl and brine. The organic layer was separated, dried over anhydrous sodium sulfate and concentrated under reduced pressure to afford the amide derivative of **3ca** as a white solid which was used directly to determine the enantiomeric excess without further purification. The enantiomeric excess was determined by HPLC analysis

(220 nm, 25 °C) t_R 27.9 min (major); t_R 40.1 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 92% ee. $[\alpha]_D^{24}$ = -1.70° (c 0.65, $CHCl_3$).

*(R)-1-methoxy-4-(1-(4-(trifluoromethyl)phenyl)ethyl)benzene (**3da**)*:[6c] Prepared according to the general procedure from 4-(trifluoromethyl)styrene **1e** (43.0 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol). **3da** was isolated in high purity without further purification as a colorless oil in 90% yield (63.1 mg, 0.23 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 7.0 min (minor); t_R 9.6 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 93% ee. $[\alpha]_D^{24}$ = -1.67° (c 0.72, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 4.18 (d, J = 7.2 Hz, 1H), 3.80 (s, 3H), 1.65 (d, J = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 158.1, 150.9, 137.4, 128.5, 128.3 (d, C-F, $^2J_{C\text{-}F}$ = 32.3 Hz), 127.8, 125.3 (q, C-F, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.3 (d, C-F, $^1J_{C\text{-}F}$ = 272.7 Hz), 113.9, 55.2, 43.8, 21.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.3.

*(S)-1-fluoro-4-(1-phenylethyl)benzene (**3fg**)*:[9a] Prepared according to the general procedure from 4-fluorostyrene **1f** (30.5 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol). **3fg** was isolated in high purity without further purification as a colorless oil in 90% yield (40.1 mg, 0.23 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 8.7 min (major); t_R 10.3 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 85% ee. $[\alpha]_D^{24}$ = +1.45° (c 0.58, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.22 – 7.16 (m, 5H), 6.98 (t, J = 8.7 Hz, 2H), 4.15 (q, J = 7.2 Hz, 1H), 1.64 (d, J = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 161.3 (d, C-F, $^1J_{C\text{-}F}$ = 243.9 Hz), 146.2, 142.0 (d, C-F, $^4J_{C\text{-}F}$ = 3.4 Hz), 129.0 (d, C-F, $^3J_{C\text{-}F}$ = 7.7

Hz), 128.4, 127.5, 126.2, 115.1 (d, C-F, ${}^{2}J_{C\text{-}F}$ = 21.1 Hz), 44.0, 22.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.5.

*(S)-1-methoxy-3-(1-(4-methoxyphenyl)ethyl)benzene (**3ga**)*:[6c] Prepared according to the general procedure from 3-methoxystyrene **1g** (33.5 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol). **3ha** was isolated in high purity without further purification as a colorless oil in 78% yield (43.5 mg, 0.20 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 25.8 min (minor); t_R 33.7 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 93% ee. $[\alpha]_D^{24}$ = -1.83° (c 0.76, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (t, *J* = 7.9 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 2H), 6.87 – 6.84 (m, 3H), 6.81 – 6.80 (m, 1H), 6.76 (dd, *J* = 8.1, 2.6 Hz, 1H), 4.11 (q, *J* = 7.2 Hz, 1H), 3.80 (d, 6H, 2 x OMe), 1.64 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 159.6, 157.9, 148.5, 138.4, 129.3, 128.5, 120.1, 113.8, 113.7, 110.9, 55.2, 55.1, 44.0, 22.0.

*(S)-1-(1-(4-methoxyphenyl)ethyl)-2-methylbenzene (**3ha**)*:[6c] Prepared according to the general procedure from 2-methylstyrene **1h** (29.5 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol), with 0.025 mmol Ni(cod)$_2$ and 0.013 mmol **L1** used. **3ga** was isolated in high purity without further purification as a colorless oil in 70% yield (39.6 mg, 0.18 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 11.0 min (minor); t_R 13.7 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 77% ee. $[\alpha]_D^{24}$ = -1.16° (c 0.74, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 1H), 7.24 – 7.18 (m, 1H), 7.15 – 7.14 (m, 2H), 7.09 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.30 (q, *J* = 7.2 Hz, 1H), 3.79 (s, 3H), 2.26 (s, 3H), 1.61 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.7, 144.3, 138.4, 136.0, 130.4, 128.6, 126.6, 126.0, 126.0, 113.7, 55.2, 40.1, 22.2, 19.7.

*(S)-1,2-dimethoxy-4-(1-(4-methoxyphenyl)ethyl)benzene (**3ia**)*:[37] Prepared according to the general procedure from 3,4-dimethoxystyrene **1i** (41.1 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol). **3ia** was isolated in high purity without further purification as a colorless oil in 92% yield (62.6 mg, 0.23 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 27.5 min (minor); t_R 38.3 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 96% ee. $[\alpha]_D^{24}$ = -1.02° (c 0.88, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.6 Hz, 2H), 6.88 – 6.76 (m, 4H), 6.72 (d, *J* = 1.6 Hz, 1H), 4.07 (q, *J* = 7.2 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 3.79 (s, 3H), 1.61 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.8, 148.8, 147.2, 139.4, 138.8, 128.4, 119.2, 113.7, 111.1, 111.0, 55.9, 55.8, 55.2, 43.5, 22.3.

*(S)-2-(1-(4-methoxyphenyl)ethyl)naphthalene (**3ka**)*:[3b] Prepared according to the general procedure from 2-vinylnaphthalene **1k** (38.5 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol). The crude reaction mixture was purified by flash column chromatography (hexane:Et_2O = 100:1) to give **3ka** as a colorless oil in 61% yield (40.0 mg, 0.15 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 24.5 min (minor); t_R 31.2 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 93% ee. $[\alpha]_D^{24}$ = -1.38° (c 0.64, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.82 (m, 2H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.73 (s, 1H), 7.52 – 7.44 (m, 2H), 7.35 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 4.32 (q, *J* = 7.2 Hz, 1H), 3.82 (s, 3H), 1.76 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.9, 144.2, 138.4, 133.6, 132.1, 128.7, 128.0, 127.8, 127.6, 126.9, 126.0, 125.4, 125.2, 113.8, 55.3, 44.1, 22.0.

*(S)-3-(1-(4-methoxyphenyl)ethyl)-1H-indole (**3la**)*:[2g] Prepared according to the general procedure from 3-vinylindole **1l** (35.6 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0

mg, 0.5 mmol). The crude reaction mixture was purified by flash column chromatography (hexane:EtOAc = 90:10) to give **3la** as a while solid in 27% yield (40.0 mg, 0.07 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 11.8 min (minor); t_R 13.3 min (major) [Chiracel ODH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 70% ee. $[\alpha]_D^{24} = -1.50°$ (c 0.52, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.36 (dd, *J* = 14.3, 8.0 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 7.2 Hz, 1H), 7.03 – 6.99 (m, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.34 (q, *J* = 7.2 Hz, 1H), 3.78 (s, 3H), 1.69 (d, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.7, 139.0, 136.6, 128.3, 126.9, 121.9, 121.8, 121.0, 119.8, 119.2, 113.7, 111.0, 55.2, 36.1, 22.6.

General Procedure for Ni-Catalyzed Hydroarylation of Vinylarenes with Arylboronic Acid Pinacol Esters. In a nitrogen-filled glovebox, an oven dried 1-dram vial was charged with an appropriate arylboronic acid pinacol ester **2** (0.5 mmol) and MeOH (1 mL). The resulting mixture was gently stirred at room temperature until it was clear and was used immediately.

In a second oven dried 1-dram vial, $Ni(cod)_2$ (0.0125 mmol), ligand **L1** (0.0125 mmol), *t*BuOLi (0.25 mmol), and an appropriate vinylarene **1** (0.25 mmol) were sequentially added. Then, the vial was charged with the as-prepared solution of the arylboronic acid pinacol ester in MeOH from the first vial, sealed and taken out of the glovebox. The reaction mixture was stirred at 50 °C in an aluminium reaction block (for 1-dram vials) for 3 hours. Upon completion, the reaction was cooled to room temperature and was diluted with 20 mL DCM. The solvent was removed under vacuum. The resulting residue was re-dissolved with DCM, filtered through a short plug of silica gel eluting with DCM and concentrated under vacuum. The crude product was purified by flash column chromatography (hexane:Et_2O = 100:1). The racemic products were synthesized either by the same procedure with racemic ligand **L7**, or by a previously reported method.[5d]

*(R)-1-methoxy-4-(1-phenylethyl)benzene (**3aa**)*:[6c] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-methoxyphenylboronic acid pinacol ester **2q** (117.0 mg, 0.5 mmol). **3aa** was isolated as a colorless oil in 86% yield (45.6 mg, 0.22 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 17.7 min (minor); t_R 19.1 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 76% ee. $[\alpha]_D^{24}$ = -1.40° (c 0.60, $CHCl_3$). The NMR spectra were in agreement with product **3aa** derived from 4-methoxyphenylboronic acid **2a**.

*(R)-1-fluoro-4-(1-phenylethyl)benzene (**3ac**)*:[3e] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-fluorophenylboronic acid pinacol ester **2r** (111.0 mg, 0.5 mmol). **3ac** was isolated in high purity without further purification as a colorless oil in 29% yield (14.5 mg, 0.073 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 8.5 min (minor); t_R 10.1 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 69% ee. $[\alpha]_D^{24}$ = -1.38° (c 0.70, $CHCl_3$). The NMR spectra were in agreement with product **3ac** derived from 4-fluorophenylboronic acid **2c**.

*(S)-1-methoxy-4-(1-(4-(trifluoromethyl)phenyl)ethyl)benzene (**3eh**)*:[2c] Prepared according to the general procedure from 4-methoxystyrene **1e** (33.5 mg, 0.25 mmol) and 4-(trifluoromethyl)phenylboronic acid pinacol ester **2s** (136.0 mg, 0.5 mmol). **3eh** was isolated as a colorless oil in 75% yield (52.5 mg, 0.19 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 7.3 min (major); t_R 10.7 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 61% ee. $[\alpha]_D^{24}$ = +1.70° (c 0.70, $CHCl_3$). The NMR spectra were in agreement with product **3eh** derived from 4-trifluoromethylphenylboronic acid **2h**.

*(S)-1-methyl-4-(1-phenylethyl)benzene (**3bt**)*:[9a] Prepared according to the general procedure from 4-methylstyrene **1b** (29.5 mg, 0.25 mmol) and phenylboronic acid pinacol ester **2t** (102.0 mg, 0.5 mmol). **3bt** was isolated as a colorless oil in 90% yield (44.2 mg, 0.23 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 11.4 min (major); t_R 12.5 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 86% ee. $[\alpha]_D^{24}$ = +1.50° (c 0.76, $CHCl_3$). **^{1}H NMR** (400 MHz, $CHCl_3$) δ 7.34 – 7.30 (m, 2H), 7.28 – 7.26 (m, 2H), 7.24 – 7.19 (m, 1H), 7.18 – 7.13 (m, 4H), 4.17 (q, *J* = 7.2 Hz, 1H), 2.36 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 146.6, 143.4, 135.5, 129.1, 128.4, 127.6, 127.5, 126.0, 44.4, 22.0, 21.0.

*(R)-3-(1-phenylethyl)furan (**3au**)*: Prepared according to the general procedure from styrene **1b** (26.0 mg, 0.25 mmol) and furan-3-boronic acid pinacol ester **2u** (97.0 mg, 0.5 mmol). **3au** was isolated as a colorless oil in 57% yield (24.5 mg, 0.14 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 13.9 min (major); t_R 15.9 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 95:5, 1.0 mL/min] to be 71% ee. $[\alpha]_D^{24}$ = -1.30 (c 0.76, $CHCl_3$). **^{1}H NMR** (400 MHz, $CHCl_3$) 7.35 (t, *J* = 1.7 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.24 – 7.19 (m, 4H), 6.22 – 6.21 (m, 1H), 3.97 (q, *J* = 6.9 Hz, 1H), 1.56 (d, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 146.0, 142.9, 138.8, 130.3, 128.4, 127.3, 126.2, 110.5, 36.4, 22.0. **HRMS** (EI): Calcd. for $C_{12}H_{12}O^+$ ($[M]^+$): 172.0883, Found: 172.0881.

General Procedure for Ni-Catalyzed Hydroarylation of Vinylarenes with Arylboronic Acid Neopentylglycol Esters. In an oven dried 1-dram vial, $Ni(cod)_2$ (0.0125 mmol), ligand **L1** (0.0063 mmol), potassium trimethylsilanoate (TMSOK, 0.25 mmol), arylboronic acid neopentylglycol ester **2**, an appropriate vinylarene **1** (0.25 mmol), and MeOH (0.5 mL). Then, the vial was sealed and taken out of the glovebox. The reaction mixture was stirred at 50 °C in an aluminium reaction block (for 1-dram vials) for 3 hours. Upon completion, the reaction was cooled to room temperature and was diluted with 20 mL DCM. The solvent was removed under vacuum. The resulting residue was re-dissolved with DCM, filtered through a short plug of silica gel eluting with DCM and concentrated under vacuum. The crude product was purified by flash column chromatography (hexane:Et_2O = 100:1). The racemic products were synthesized either by the same procedure with racemic ligand **L7**, or by a previously reported method.[5d]

*(R)-1-methoxy-4-(1-phenylethyl)benzene (**3aa**)*:[6c] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-methoxyphenylboronic acid neopentylglycol ester **2w** (110.0 mg, 0.5 mmol). **3aa** was isolated as a colorless oil in 93% yield (45.6 mg, 0.22 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 17.6 min (minor); t_R 18.8 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 88% ee. $[\alpha]_D^{24}$ = -1.42° (c 0.62, $CHCl_3$). The NMR spectra were in agreement with product **3aa** derived from 4-methoxyphenylboronic acid **2a**.

*(R)-1-fluoro-4-(1-phenylethyl)benzene (**3ac**)*:[3e] Prepared according to the general procedure from styrene **1a** (26.0 mg, 0.25 mmol) and 4-fluorophenylboronic acid neopentylglycol ester **2x** (104.0 mg, 0.5 mmol). **3ac** was isolated in high purity without further purification as a colorless oil in 63% yield (31.5 mg, 0.16 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 8.9 min (minor); t_R 10.5 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 88% ee. $[\alpha]_D^{24}$ = -1.38° (c 0.70, $CHCl_3$). The NMR spectra were in agreement with product **3ac** derived from 4-fluorophenylboronic acid **2c**.

*(S)-1-methoxy-4-(1-(4-(trifluoromethyl)phenyl)ethyl)benzene (**3eh**)*:[2c] Prepared according to the general procedure from 4-methoxystyrene **1e** (33.5 mg, 0.25 mmol) and 4-

(trifluoromethyl)phenylboronic acid neopentylglycol ester **2y** (129.0 mg, 0.5 mmol). **3eh** was isolated as a colorless oil in 79% yield (55.4 mg, 0.20 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 7.3 min (major); t_R 10.1 min (minor) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 83% ee. $[\alpha]_D^{24}$ = +1.74° (c 0.54, $CHCl_3$). The NMR spectra were in agreement with product **3eh** derived from 4-trifluoromethylphenylboronic acid **2h**.

Synthetic Utility. The anti-viral agent **3ja** and the tubulin polymerization inhibitor **3kv** were synthesized follow the general procedure for Ni-catalyzed hydroarylation of vinylarenes with arylboronic acids.

*(S)-1,2,3-trimethoxy-5-(1-(4-methoxyphenyl)ethyl)benzene (**3ja**)*:[9a] Prepared according to the general procedure from 3,4,5-trimethoxystyrene **1j** (48.6 mg, 0.25 mmol) and 4-methoxyphenylboronic acid **2a** (76.0 mg, 0.5 mmol). **3ja** was isolated in high purity without further purification as a colorless oil in 80% yield (60.5 mg, 0.20 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 28.7 min (minor); t_R 38.2 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 94% ee. $[\alpha]_D^{24}$ = +1.59° (c 0.58, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.43 (s, 2H), 4.04 (q, *J* = 7.2 Hz, 1H), 3.82 (s, 3H), 3.82 (s, 6H), 3.79 (s, 3H), 1.60 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 157.9, 153.0, 142.5, 138.3, 136.2, 128.4, 113.7, 104.6, 60.8, 56.0, 55.2, 44.2, 22.2.

*(R)-2-(1-(3,4,5-trimethoxyphenyl)ethyl)naphthalene (**3kv**)*:[9d] Prepared according to the general procedure (see section 5) from 2-vinylnaphthalene **1k** (48.6 mg, 0.25 mmol) and 3,4,5-trimethoxyphenylboronic acid **2v** (106.0 mg, 0.5 mmol). The crude reaction mixture was purified by flash column chromatography (hexane:Et_2O = 100:1) to give **3kv** as a colorless oil in 70% yield

(56.42 mg, 0.18 mmol). The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 10.7 min (minor); t_R 11.3 min (major) [Chiracel ODH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 93% ee. $[\alpha]_D^{24}$ = +1.80° (c 0.54, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.79 (m, 2H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.69 (s, 1H), 7.49 – 7.42 (m, 2H), 7.33 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.48 (s, 2H), 4.26 (q, *J* = 7.2 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 6H), 1.73 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 153.1, 143.6, 141.9, 136.3, 133.5, 132.1, 128.0, 127.7, 127.6, 126.7, 126.0, 125.4, 125.2, 104.9, 60.8, 56.1, 45.1, 21.9.

Gram-Scale Reaction. In a nitrogen-filled glovebox, an oven-dried 20-mL scintillation vial was charged with 4-methoxyphenylboronic acid **2a** (2.58 g, 17 mmol) and MeOH (10 mL). The resulting mixture was gently stirred at room temperature until it was clear. Next, *t*BuOLi (0.680 g, 8.5 mmol), 4-methylstyrene **1b** (1.00 g, 8.5 mmol), ligand **L1** (41.31 g, 0.085 mmol) and Ni(cod)$_2$ (58.65 g, 0.212 mmol) were sequentially added. Then, the vial was sealed, gently stirred for two minutes at room temperature before being taken out of the glovebox. The reaction mixture was stirred at 50 °C in an aluminium reaction block (for 20-mL scintillation vials) for 10 hours. Upon completion, the reaction was cooled to room temperature and was diluted with 20 mL DCM. The solvent was removed under vacuum. The resulting residue was re-dissolved with hexane:DCM = 70:30, filtered through a short plug of silica gel eluting with hexane:DCM = 70:30 and concentrated under vacuum to obtain 1.90 g **4b** (99% yield, 95% ee) as a clear liquid. The product was isolated in high purity without column chromatography. The enantiomeric excess was determined by HPLC analysis (220 nm, 25 °C) t_R 18.4 min (minor); t_R 20.9 min (major) [Chiracel OJH (0.46 cm x 25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*PrOH, 90:10, 1.0 mL/min] to be 95% ee. $[\alpha]_D^{24} = -1.45°$ (c 0.76, $CHCl_3$). The NMR spectra were in agreement with product **3ba** derived from the small-scale reaction.

ASSOCIATED CONTENT

The following Supporting Information is available free of charge on the ACS Publications website at DOI: xxxxx/xxxx

NMR spectra and HPLC traces (PDF)

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Notes

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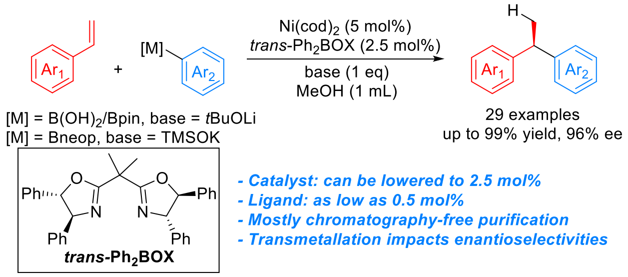

- ***Catalyst: can be lowered to 2.5 mol%***
- ***Ligand: as low as 0.5 mol%***
- ***Mostly chromatography-free purification***
- ***Transmetallation impacts enantioselectivities***