Diastereoselective and Enantioselective Rh(I)-Catalyzed Additions of Arylboronic Acids to *N*-*tert*-Butanesulfinyl and *N*-Diphenylphosphinoyl Aldimines

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General methods. Phenylboronic acid was purchased from Lancaster Synthesis and used as received. 3-Acetylphenylboronic acid was purchased from Frontier Scientific, Inc. and recrystallized from water before use. All other arylboronic acids were purchased from Aldrich and recrystallized from water before use. Acetylacetonatobis(cyclooctene)rhodium, 1,2-bis(diphenylphosphino)benzene, titanium (IV) ethoxide (containing 5-15% isopropanol), titanium (IV) isopropoxide, and all commercially available chiral ligands except DIPAMP were purchased from Strem and used without purification. DIPAMP and 4 M HCl (solution in 1,4-dioxane) were purchased from Aldrich. Benzaldehyde and 3-phenylpropionaldehyde were purchased from Acros and distilled prior to use. 1,4-Dioxane was either distilled from sodium-benzophenone ketyl under nitrogen and stored over MS 3 Å or extra dry dioxane (Acros, <50 ppm water) was passed through a column of dry, activated basic alumina under nitrogen and stored over MS 3 Å in an nitrogen filled glove box. Tetrahydrofuran was distilled from sodium-benzophenone ketyl under nitrogen directly before use. Methanol and Et₃N were distilled from calcium hydride under nitrogen directly before use. *tert*-Butanesulfinamide,¹ bis(acetonitrile)cyclooctadienerhodum tetrafluoroborate,² bis(cyclooctadiene)rhodium hexafluoroantimonate,³ bis(norbornadiene)rhodium tetrafluoroborate,³ *N-tert*-butanesulfinyl-3-phenylpropionaldimine,⁴ *N-tert*-butanesulfinyl benzaldimine,⁵ and *N*-diphenylphosphinoyl benzaldimine (**4**)⁶ were synthesized according to the literature procedures. Bis(acetonitrile)cyclooctadienerhodum hexafluoroantimonate was made by analogy to bis(acetonitrile)cyclooctadienerhodum tetrafluoroborate and used without purification.

Arylboronic acid addition reactions were performed in Kimble 5 mL microvials (Kimble product number 60700-5) equipped with PTFE stir-vanes (Kimble product number 749060-0003) and capped either with mini-inert seals (Kimble product number 749110-0022) and blue nylon caps (Kimble product number 410119-2015) or PTFE faced silicone septum (Kimble product number 774161-0020) and black phenolic caps (Kimble product number 410116-2000). The reactions in vials were heated in a custom made aluminum heating blocks drilled to fit the vials (UC machine shop) and the temperature was maintained by either placing a block on an IKA stirrer/hotplate (RCT basic model) with a thermistor controller (ETS-D4 fuzzy) or by placing three blocks in a Pierce heating/stirring module (Reacti-Therm III). Syringe pump additions were done using a digital syringe pump from New Era Pump Systems, Inc. (NE-1600 six syringe version).

Dr determinations were performed using an Agilent 1100 series LC equipped with either a silica normal phase column (Microsorb Si 100 Å packing) with a multiwavelength detector or a C-8 reverse phase column with a diode array detector and an MS. Enantiomeric excess determinations were performed on an Agilent 1100 series LC equipped with a Daicel AD or OD column and a multiwavelength detector. IR spectra were recorded on a Nicolet Avatar 360 FTIR spectrometer equipped with an attenuated total reflectance accessory, and only partial data are listed. Unless otherwise noted, ¹H and ¹³C NMR spectra were obtained in CDCl₃. Chemical shifts are reported in ppm and referenced to either the residual solvent peak (¹H, ¹³C) or TMS (¹H) as an internal standard, or trimethylphosphate as an external standard (³¹P). Elemental analyses and mass spectra were obtained from the Microanalytical Laboratory at the University of California, Berkeley.

***N-tert*-butanesulfinyl 4-methylbenzaldimine.** To a round bottom flask containing a magnetic stir bar, (*R_S*)-*tert*-butanesulfinamide (6.36 g, 52.5 mmol, 1.05 equiv), and 100 mL of THF was added 4-methylbenzaldehyde (5.90 mL, 50.0 mmol, 1.00 equiv) followed by 20 mL of Ti(OEt)₄ (97.1 mmol, 1.94 equiv). The reaction solution was stirred overnight at rt (16 h), and then the reaction was quenched by the slow addition of sat. aq NaHCO₃. The resulting mixture was diluted with EtOAc, filtered through a pad of celite, and the pad of celite was washed with EtOAc (100 mL). The organic layers were separated, dried over Na₂SO₄, filtered, and the solvent was removed under reduced pressure on a rotary evaporator. The imine was purified by chromatography (SiO₂, 90:10 EtOAc:hexanes) to provide 9.79 g (87% yield) of a white, crystalline solid. mp 63.1-64.4 °C. [α]_D²⁵ -89 ° (c 1.3, CHCl₃). ¹H NMR (500 MHz): δ 1.26 (9H, s), 2.42 (3H, s), 7.28 (2H, d, *J*=7.9 Hz), 7.75 (2H, d, *J*=8.0 Hz), 8.56 (1H, s). ¹³C NMR (126 MHz): δ 21.7, 22.5, 57.6, 129.3, 129.6, 131.5, 143.1, 162.4. IR: 1595, 1076, 823, 728 cm⁻¹. HRMS (FAB+) *m/z*: Calcd

for C₁₂H₁₈NOS: 224.110911. Found: 224.111570. Anal. calcd for C₁₂H₁₇NOS: C, 64.53; H, 7.67; N, 6.27. Found: C, 64.51; H, 7.81; N, 6.23.

Typical procedure for optimization screens. Reactions were set up in a nitrogen filled glove box. To a vial containing a stir-vane and phenylboronic acid (1.00 mol, 2 equiv) was added the appropriate *N-tert*-butanesulfinyl imine (0.500 mmol, 1 equiv) and the catalyst components: ligand (if used) (0.0250-0.0275 mmol for bidentate ligands and 0.0250 to 0.0375 mmol for monodentate ligands) in 1 mL of dioxane followed by rhodium (0.0250 mmol, 0.0500 equiv) in 1 mL of dioxane. The vial was then sealed using a mini-inert seal and a blue nylon cap, and the vial was removed from the glove box. The vial was then placed in a heating block with stirring and heated to 70-100 °C (aluminum block temperature) for 15-18 h. The reaction mixtures were allowed to cool to rt, and they were transferred to a large test-tube. The reaction vessel was rinsed with 10 mL of benzene and the combined organic layers were washed with brine (1 mL). The organic layer was dried with MgSO₄ and filtered. A sample (50 µL of solution diluted with 1.0 mL of a mixture of 98:2 hexanes:EtOH which was 5 µM in benzonitrile as an external standard) was then analyzed by HPLC to determine the dr and conversion. Conversions were compared to the estimated yield from the external standard as a check for decomposition. Selected cases were isolated by chromatography (40:60 EtOAc:hexanes to 50:50 EtOAc:hexanes) and isolated yields in all cases mirrored conversion data obtained from the HPLC method.

For the reaction of *N-tert*-butanesulfinyl 4-methylbenzaldehyde with phenylboronic acid: silica column, 98:2 hexanes:EtOH, 1 mL/min, *r_t* benzonitrile = 4.9 min, *r_t* *N-tert*-butanesulfinyl 4-methylbenzaldehyde = 5.9 min, *r_t* (*R_S,R*)-**2a** = 11.0 min, *r_t* (*R_S,S*)-**2a** = 11.6 min.

For the reaction of *N-tert*-butanesulfinyl 3-phenylpropionaldehyde with phenylboronic acid: silica column, 98:2 Hexanes:EtOH, 1 mL/min, *r_t* benzonitrile = 4.9 min, *r_t* *N-tert*-butanesulfinyl 3-phenylpropionaldehyde = 7.2 min, *r_t* (*R_S,S*)-**2b** = 12.7 min, *r_t* (*R_S,R*)-**2b** = 14.0 min.

Table 1S. Full results of catalyst optimization screen.

entry	R ¹	[Rh]	L	conv. (%) ^d	dr ^b
1 ^c	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	-	25 ^d	91:9
2 ^c	2-phenylethyl	[Rh(cod)(MeCN) ₂]BF ₄	-	5 ^d	91:9
3	phenyl	[Rh(cod)(MeCN) ₂]SbF ₆	-	5	93:7
4	phenyl	[Rh(nbd) ₂]BF ₄	-	1	nd
5	phenyl	[Rh(cod) ₂]SbF ₆	-	11	92:8
6	phenyl	[Rh(cod)Cl] ₂	-	-	-
7	phenyl	Rh(acac)(cod) ₂	-	1	nd
8 ^c	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	-	18 ^d	88:12
9	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	P(Bu) ₃	10	92:8
10	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	P(Cy) ₃	27	90:10
11	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	P(<i>t</i> -Bu) ₃	30	93:7
12	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	P(Ph) ₃	12	91:9
13	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	P(<i>o</i> -tol) ₃	23	91:9
14	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	<i>t</i> -BuBOX	30	91:9
15	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	dppf	30	91:9
16	phenyl	Rh(acac)(coe) ₂	P(Bu) ₃	5	90:10
17	phenyl	Rh(acac)(coe) ₂	P(Cy) ₃	13	89:11
18	phenyl	Rh(acac)(coe) ₂	P(<i>t</i> -Bu) ₃	2	87:13
19	phenyl	Rh(acac)(coe) ₂	P(Ph) ₃	1	nd
20	phenyl	Rh(acac)(coe) ₂	P(<i>o</i> -tol) ₃	-	-
21	phenyl	Rh(acac)(coe) ₂	dppm	11	92:8
22	phenyl	Rh(acac)(coe) ₂	dppe	42	96:4
23	phenyl	Rh(acac)(coe) ₂	dppp	18	98:2
24	phenyl	Rh(acac)(coe) ₂	dppb	7	96:4
25	phenyl	Rh(acac)(coe) ₂	<i>t</i> -BuBOX	-	-
26	phenyl	Rh(acac)(coe) ₂	dppf	2	96:4
27	phenyl	Rh(acac)(coe) ₂	dppbenz	65	96:4
28	phenyl	[Rh(cod)Cl] ₂	dppbenz	-	-
29	phenyl	[Rh(cod)OH] ₂	dppbenz	29	93:7
30	phenyl	[Rh(cod)(MeCN) ₂]BF ₄	dppbenz	34	90:10
31	2-phenylethyl	Rh(acac)(coe) ₂	dppbenz	70	96:4
32 ^f	phenyl	Rh(acac)(coe) ₂	dppbenz	58	97:3

33 ^g	phenyl	Rh(acac)(coe) ₂	dppbenz	45	96:4
34 ^h	phenyl	Rh(acac)(coe) ₂	dppbenz	69	96:4
35 ⁱ	phenyl	Rh(acac)(coe) ₂	dppbenz	65	97:3

^a Conversion determined by HPLC ^b dr determined by HPLC ^c Reactions performed with 3 mol% rhodium ^d Isolated yield of pure material. ^e Reaction run at 120 °C. ^f Reaction run at 0.5 M in imine. ^g Reaction run at 1.0 M in imine. ^h Reaction run at 0.13 M in imine. ⁱ Reaction run with 5 equiv phenylboronic acid.

Table 2S. Solvent screen.

entry	solvent	conv. (%) ^a	dr
1	DMF	-	-
2	toluene	10	96:4
3	THF	60	97:3
4	chlorobenzene	6	96:4
5	trifluorotoluene	-	-
6	butyl acetate	33	96:4
7	DME	49	96:4
8	DCE	-	-
9	propionitrile	-	-
10	diglyme	62	97:3
11	DMSO	-	-
12	dioxane	66	96:4
13	dioxane/H ₂ O (9/1)	58	96:4
14	dioxane/MeOH (9/1)	51	96:4

^a Conversion and dr determined by HPLC

General procedure for additions to *N*-*tert*-butanesulfinyl imines. Reactions were set up in a nitrogen filled glove box, capped, removed from the box and heated in a reaction block on the tabletop. To a vial containing a stir-vane and the appropriate *N*-*tert*-butanesulfinyl imine (0.500 mmol, 1 equiv) was added 1,2-bis(diphenylphosphino)benzene (12.3 mg, 0.0275 mmol, 0.0550 equiv) in 1 mL of dioxane followed by acetylacetonatobis(cyclooctene) rhodium (10.6 mg, 0.0250 mmol, 0.0500 equiv) in 1 mL of dioxane. This was sealed with a phenolic cap and a PTFE-faced silicone septum, removed from the glove box, and placed in a heating block with stirring. The reaction vessel was attached to a nitrogen line using a needle and the reaction mixture was heated to 70 °C (aluminum block temperature). Arylboronic acid (1.00 mmol, 2 equiv) was then added to the reaction mixture as a solution in dioxane (2 mL) by syringe over 6 to 10 h by the means of a syringe pump. The reaction mixture was stirred an additional period of time (4-6 h), then allowed to cool to rt. The reaction mixture was then diluted with EtOAc and washed with 2 mL of brine. The brine was back-extracted with EtOAc (2 x 2 mL) and the combined organic layers were dried over Na₂SO₄, filtered, and the solvent was removed under reduced pressure. The products were isolated by chromatography (SiO₂) using EtOAc/hexanes mixtures, and were visualized with UV and CMA stain (products are difficult to see by UV).

(*R_S,R*)-(1-(4-methylphenyl)-1-phenylmethyl)-2-methylpropanesulfinamide (2a). The general procedure was followed with the addition of 4-methylphenylboronic acid occurring over 6 h. The product was isolated by chromatography (50:50 EtOAc:hexanes) as an off-white solid (144 mg, 96% yield). mp 134.7-137.2 °C. 97:3 dr (HPLC, silica column, 98:2 hexanes:EtOH, 1.0 mL/min, λ = 254 nm, r_t(*R_S,R*) = 13.0 min, r_t(*R_S,S*) = 14.0 min)). [α]_D²⁵ -68.4 (c 0.77, CHCl₃). ¹H NMR (400Mhz): δ 1.26 (9H, s), 2.31 (3H, s), 3.66 (1H, br s), 5.61 (1H, br s), 7.12 (2H, d, *J*=7.9 Hz), 7.22-7.28 (3H, m), 7.32 (2H, m), 7.41 (2H, d, *J*=7.4 Hz). ¹³C NMR (101 Mhz): δ 21.0, 22.7, 55.8, 61.8, 127.1, 127.5, 127.8, 128.5, 129.5, 137.5, 139.8, 141.4. IR: 1030, 821, 702 cm⁻¹. HRMS (FAB+) *m/z*: Calcd for C₁₈H₂₄NOS: 302.157861. Found: 302.158120. Anal. calcd for C₁₈H₂₃NOS: C, 71.72; H, 7.69; N, 4.65; S, 10.64. Found: C, 71.37; H, 7.74; N, 4.63; S, 10.61.

(*R,S,S*)-(1,3-diphenylpropyl)-2-methylpropanesulfinamide (2b). The general procedure was followed with the addition of phenylboronic acid occurring over 10 h. The product was isolated by chromatography (50:50 EtOAc:hexanes) as an off-white solid (136 mg, 86% yield). mp 108.9-109.8 °C. 97:3 dr (HPLC, silica column, hexanes:EtOH 98:2, 1.0 mL/min, λ = 230 nm, $r_t(R,S,S)$ = 14.3 min, $r_t(R,S,R)$ = 15.5 min). $[\alpha]_D^{25}$ 81.8 ° (*c* 0.78, CHCl₃). ¹H NMR (400 MHz): δ 1.14 (9H, s), 2.13-2.17 (2H, m), 2.52-2.56 (2H, m), 3.39 (1H, br s), 4.43 (1H, m), 7.13-7.19 (3H, m), 7.26-7.36 (7H, m). ¹³C NMR (101 MHz): δ 22.5, 32.2, 40.2, 55.4, 59.0, 126.1, 127.7, 128.4, 128.48, 128.51, 141.1, 141.6. IR: 1055, 1047, 689 cm⁻¹. HRMS (FAB+) *m/z*: Calcd for C₁₉H₂₆NOS: 316.173511. Found: 316.173140. Anal. calcd for C₁₉H₂₅NOS: C, 72.34; H, 7.99; N, 4.44. Found: C, 72.30; H, 8.20; N, 4.45.

(*R,S,S*)-(1-(4-methoxyphenyl)-3-phenylpropyl)-2-methylpropanesulfinamide (2c). The general procedure was followed with the addition of 4-methoxyphenylboronic acid occurring over 6 h. The product was isolated by chromatography (40:60 EtOAc:hexanes to 50:50 EtOAc:hexanes) as an off-white solid (121 mg, 70% yield). mp 88.3-90.0 °C. 96:4 dr (LC/MS, C-8 reverse phase column, 70:30:0.01 MeOH:H₂O:TFA to 95:5:0.01 MeOH:H₂O:TFA over 10 min, 1.0 mL/min, λ = 254 nm, $r_t(R,S,S)$ = 5.9 min, $r_t(R,S,R)$ = 6.2 min). $[\alpha]_D^{25}$ -67.4 ° (*c* 0.82, CHCl₃). ¹H NMR (400 MHz): δ 1.14 (9H, s), 2.07-2.15 (2H, m), 2.50-2.55 (2H, m), 3.37 (1H, s), 3.82 (3H, s), 4.37 (1H, m), 6.89 (2H, d, *J*=8.5 Hz), 7.12-7.28 (7H, m). ¹³C NMR (101 MHz): δ 22.5, 32.2, 40.2, 55.2, 55.3, 58.3, 113.9, 126.0, 128.4, 128.5, 128.9, 133.4, 141.1, 159.0. IR: 1510, 1247, 1047, 1030, 702 cm⁻¹. HRMS (FAB+) *m/z*: Calcd for C₂₀H₂₈NO₂S: 346.184076. Found: 346.184510. Anal. calcd for C₂₀H₂₇NO₂S: C, 69.53; H, 7.88; N, 4.05; S, 9.28. Found: C, 69.22; H, 7.90; N, 4.19; S, 9.43.

(*R,S,S*)-(1-(4-trifluoromethylphenyl)-3-phenylpropyl)-2-methylpropanesulfinamide (2d). The general procedure was followed with the addition of 4-trifluoromethylphenylboronic acid occurring over 10 h. The product was isolated by chromatography (40:60 EtOAc:hexanes to 50:50 EtOAc:hexanes) as an off-white solid (140 mg, 73% yield). mp 116.0-117.0 °C. 97:3 dr (HPLC, silica column, 98:2 hexanes:EtOH, 1.0 mL/min, λ = 210 nm, $r_t(R,S,S)$ = 15.4 min, $r_t(R,S,R)$ = 13.9 min). $[\alpha]_D^{25}$ -74 ° (*c* 0.99, CHCl₃). ¹H NMR (500 MHz): δ 1.15 (9H, s), 2.10-2.22 (2H, m), 2.50-2.62 (2H, m), 3.44 (1H, br s), 4.50 (1H, t, *J*=5.7 Hz), 7.13 (2H, d, *J*=7.6 Hz), 7.18-7.20 (1H, m), 7.26-7.29 (2H, m), 7.43 (2H, d, *J*=8.0 Hz), 7.62 (2H, d, *J*=8.2 Hz). ¹³C NMR (126 MHz): δ 22.4, 32.1, 40.0, 55.6, 58.4, 124.0 (q, *J*=270 Hz), 125.5 (q, *J*=3.8 Hz), 126.3, 128.0, 128.4, 128.6, 129.9 (q, *J*=33 Hz), 140.5, 145.9. IR: 1328, 1126, 1046, 844, 698 cm⁻¹. HRMS (FAB+) *m/z*: Calcd for C₂₀H₂₅F₃NO₂S: 384.160896. Found: 384.161330. Anal. calcd for C₂₀H₂₄F₃NOS: C, 62.64; H, 6.31; N, 3.65. Found: C, 62.85; H, 6.53; N, 3.64.

(*R,S,S*)-(1-(3-acetylphenyl)-3-phenylpropyl)-2-methylpropanesulfinamide (2e). The general procedure was followed with the addition of 3-acetylphenylboronic acid as a solution in THF (due to low solubility in dioxane) occurring over 6 h. The product was isolated by chromatography (40:60 EtOAc:hexanes to 50:50

EtOAc:hexanes) as an oil (144 mg, 80% yield). 97:3 dr (LC/MS, C-8 reverse phase column, MeOH:H₂O:TFA 40:60:0.01 to 95:5:0.01 over 10 min, 1.0 mL/min, λ = 220 nm, $r_t(R_S,S)$ = 9.6 min, $r_t(R_S,R)$ = 9.9 min). $[\alpha]_D^{25}$ -81.8 (c 0.81, CHCl₃). ¹H NMR (400 MHz): δ 1.15 (9H, s), 2.13-2.22 (2H, m), 2.54-2.60 (2H, m), 2.61 (3H, s), 3.44 (1H, d, J =2.1 Hz), 4.50-4.53 (1H, m), 7.13 (2H, d, J =7.0 Hz), 7.19 (1H, t, J =7.4 Hz), 7.26-7.29 (2H, m), 7.46 (1H, t, J =7.6 Hz), 7.52 (2H, d, J =7.7 Hz), 7.89 (1H, dd, J = 1.3, 7.6 Hz), 7.92 (1H, s). ¹³C NMR (101 MHz): δ 22.4, 26.7, 32.2, 40.0, 55.6, 58.6, 126.2, 127.5, 127.8, 128.4, 128.6, 128.8, 132.5, 137.4, 140.6, 142.5, 197.9. IR: 1684, 1047, 699 cm⁻¹. HRMS (FAB+) m/z : Calcd for C₂₁H₂₈NO₂S: 358.184076. Found: 358.183430. Anal. calcd for C₂₁H₂₇NO₂S: C, 70.55; H, 7.61; N, 3.92. Found: C, 70.16; H, 7.59; N, 3.92.

(*R_{S,S}*)-(1-(4-methoxyphenyl)-1-phenylmethyl)-2-methylpropanesulfinamide (2f). The general procedure was followed with the addition of 4-methoxyphenylboronic acid occurring over 10 h. The product was isolated by chromatography (60:40 EtOAc:hexanes) as an oil (121 mg, 76% yield). 97:3 dr (HPLC, silica column, hexanes:*i*PrOH 97:3, 1.0 mL/min, λ = 210 nm, $r_t(R_S,S)$ = 19.2 min, $r_t(R_S,R)$ = 21.6 min). $[\alpha]_D^{25}$ -73.5 (c 0.75, CHCl₃). ¹H NMR (400 MHz): δ 1.25 (9H, s), 3.70 (1H, br s), 3.79 (3H, s), 5.60 (1H, br s), 6.86 (2H, d, J =8.6 Hz), 7.23-7.38 (7H, m). ¹³C NMR (101 MHz): δ 22.7, 55.2, 55.8, 61.5, 113.9, 127.1, 127.7, 128.8, 129.1, 133.2, 143.0, 159.1. IR: 1509, 1249, 1031, 698 cm⁻¹. HRMS (FAB+) m/z : Calcd for C₁₈H₂₄NO₂S: 318.152776. Found: 318.152050.

(*R_{S,S}*)-(1-phenyl-1-(4-trifluoromethylphenyl)methyl)-2-methylpropanesulfinamide (2g). The general procedure was followed with the addition of 4-trifluoromethylphenylboronic acid occurring over 6 h. The product was isolated by chromatography (75:25 EtOAc:hexanes to 50:50 EtOAc:hexanes) as an oil (136 mg, 71% yield). 98:2 dr (HPLC, silica column, hexanes:*i*PrOH 98:2, 1.0 mL/min, λ = 210 nm, $r_t(R_S,S)$ = 12.3 min, $r_t(R_S,R)$ = 10.4 min). $[\alpha]_D^{25}$ -51.1 (c 0.70, CHCl₃). ¹H NMR (400 MHz): δ 1.28 (9H, s), 3.72 (1H, br s), 5.70 (1H, br s), 7.26-7.35 (5H, m), 7.55 (2H, d, J =8.3 Hz), 7.60 (2H, d, J =8.4 Hz). IR: 1323, 1122, 1110, 1065, 698 cm⁻¹. HRMS (FAB+) m/z : Calcd for C₁₈H₂₁NOF₃S: 356.129596. Found: 356.130320. Anal. calcd for C₁₈H₂₀NOF₃S: C, 60.83; H, 5.67; N, 3.94; S, 9.02. Found: C, 60.65; H, 5.70; N, 4.08; S, 9.23.

(*R_{S,S}*)-(1-(4-chlorophenyl)-1-phenylmethyl)-2-methylpropanesulfinamide (2h). The general procedure was followed with the addition of 4-chlorophenylboronic acid occurring over 10 h. The product was isolated by chromatography (50:50 EtOAc:hexanes) as an off-white solid (151 mg, 94% yield). mp 141-144 °C dec. 99:1 dr (HPLC, silica column, hexanes:*i*PrOH 98:2, 1.0 mL/min, λ = 230 nm, $r_t(R_S,S)$ = 20.2 min, $r_t(R_S,R)$ = 26.5 min). $[\alpha]_D^{25}$ -74.5 ° (c 0.86, CHCl₃). ¹H NMR (400 MHz): δ 1.26 (9H, s), 3.69 (1H, s), 5.62 (1H, d, J =1.9 Hz), 7.28-7.37 (9H, m). ¹³C NMR (101 MHz): δ 22.7, 55.9, 61.4, 127.1, 128.0, 128.8, 129.0, 129.2, 133.5, 139.7, 142.1. IR: 1065, 812, 701 cm⁻¹. HRMS (FAB+) m/z : Calcd for C₁₇H₂₁NOSCl: 322.103239. Found: 322.103320. Anal. calcd for C₁₇H₂₀NOSCl: C, 63.44; H, 6.26; N, 4.35; S, 10.19. Found: C, 63.47; H, 6.41; N, 4.36; S, 10.19.

One-pot method for synthesis of 2e. To a vial with a stir-vane was added *tert*-butanesulfonamide (65.4 mg, 0.540 mmol, 1.09 equiv), 3-phenylpropionaldehyde (66.4 mg, 0.495 mmol, 1.00 equiv), and dioxane (1 mL). Titanium isopropoxide (0.298 mL, 1.00 mmol, 2.02 equiv) was then added by syringe. The vial was sealed using a PTFE faced silicone septum and a phenolic cap, and the sealed vial was removed from the glove box. The vial was attached to a nitrogen line and heated in a heating block to 40 °C for 3 h. At this time, TLC analysis showed the reaction to be complete (75:25 hexanes:EtOAc, CMA stain and UV). A solution of the pre-mixed catalyst (10.6 mg acetylacetonatobis(cyclooctene)rhodium and 12.3 mg of 1,2-bis(diphenylphosphino)benzene mixed in 1 mL of dioxane) was added by syringe followed by a solution of 3-acetylphenylboronic acid (164 mg, 1.00 mmol, 2.02 equiv) in 2 mL of dioxane and 0.33 mL of THF (to solubilize the boronic acid) over 10 h. After 18.5 h, the vial was removed from the block and allowed to cool to rt. The usual workup procedure was followed (see general procedure for additions to *N-tert*-butanesulfinyl imines). The crude NMR showed 74–78% conversion of imine to **2e**. Analysis by LC/MS (C-8 reverse phase column, MeOH:H₂O:TFA 40:60:0.01 to 95:5:0.01 over 10 min, 1.0 mL/min, λ = 254 nm, $r_t(R_{S,S})$ = 4.57 min, $r_t(R_{S,R})$ = 5.03 min) showed the crude product had a 97:3 dr. After chromatography, 126 mg (71% yield) of pure **2e** was isolated. Spectral data matched those reported above for **2e**.

Determination of Sulfinyl Aldimine Addition Stereochemistry. The absolute configurations of **2a–d** and **2f–h** were assigned by comparison to samples prepared by addition of the appropriate Grignard reagent or organolithium reagent to the *N-tert*-butanesulfinyl aldimines for which the sense of induction has been well established.⁷ The samples were compared by HPLC retention times as well as ¹H NMR. In all cases examined, the sense of induction for the Rh(I) catalyzed addition was opposite to that observed for addition of Grignard reagents. The configuration of **2e** was assigned by analogy to the other results. Additionally, the *N-tert*-butanesulfinyl group was cleaved from **2h**, the resulting amine hydrochloride **5** was converted to the free-base, and the configuration was confirmed by comparison of the optical rotation of the free amine to the literature value (vide infra).

(R)-(+)-(1-(4-chlorophenyl)-1-phenylmethyl)-diphenylphosphoramidate (5e). *N*-Diphenylphosphinoyl benzaldehyde (76.3 mg, 0.250 mmol) was weighed into a vial with a stir-vane. The ligand (7.3 mg, 0.01375 mmol, 0.055 equiv) was added as a solution in 0.5 mL of dioxane followed by a dioxane solution (0.5 mL) of acetylacetonatobis(cyclooctene)rhodium (5.3 mg, 0.0125 mmol, 0.05 equiv). The solution was stirred until it was homogeneous (1 min), and powdered, activated 3 Å MS were added. The reaction vial was capped with a PTFE faced silicone septum and cap, and the sealed vial was removed from the glove box. The vial was connected to a nitrogen line and freshly distilled Et₃N (0.035 mL, 0.250 mmol, 1 equiv) was added by syringe. The vial was heated to 70 °C in a heating block and a dioxane (1 mL) solution of 4-chlorophenylboronic acid was then added over 10 h. After 16 h, the reaction was removed from the block, allowed to cool to rt, opened, and the contents were transferred to a 25 mL test-tube. The vial was washed with EtOAc (2 x 5 mL) and the combined organic layers were washed with brine (2 mL). The aqueous layer was then washed with EtOAc (2 x 2 mL) and the combined organic layers were dried over Na₂SO₄. The organic layers were then filtered, and the solvent was removed under reduced pressure. The crude material was then purified by chromatography (98:2 CH₂Cl₂:MeOH) to afford the phosphoramidate as an off-white solid which was contaminated with a small amount of 4-chlorophenylboroxime as determined by NMR analysis. The material was treated with PS-DEAM resin (Argonaut) in THF for 6 h with gentle shaking, and the product solution was filtered off.⁸ The resin was washed with THF (10 x 2 mL) and the organic layers were concentrated to afford the product as an off-white solid (101 mg, 97%). mp 190.2–191.2 °C. 94% ee (Chiral HPLC analysis, Daicel AD column, hexanes:*i*-PrOH 90:10, 1.0 mL/min, λ = 250 nm, $r_t(S)$ = 27.4 min, $r_t(R)$ = 30.8 min). $[\alpha]_D^{25}$ = +8.8 ° (*c* 0.55, CHCl₃). ¹H NMR (500 MHz): δ 3.63 (1H,

dd, $J=6.5$, 10 Hz), 5.42 (1H, t, $J=10.5$ Hz), 7.20-7.27 (7H, m), 7.29-7.34 (2H, m), 7.38 (4H, dt, $J=3.2$, 7.6 Hz), 7.46-7.49 (2H, m), 7.80-7.84 (4H, m). ^{13}C NMR (101 MHz): δ 58.0, 127.4, 127.5, 128.4, 128.5, 128.56, 128.65, 129.0, 131.3, 131.5, 132.00, 132.02, 132.04, 132.1, 132.16, 132.22, 132.3, 132.33, 132.5, 133.0, 135.7, 141.76, 141.79, 142.75, 142.79.⁹ ^{31}P NMR (162 MHz): δ 23.5. IR: 1108, 723, 691 cm^{-1} . HRMS (FAB+) m/z : Calcd for $\text{C}_{25}\text{H}_{22}\text{ClNOP}$: 418.113350. Found: 418.112756. The configuration of **4** was assigned by comparison of the optical rotation of the unprotected amine to the known literature (vide infra).

Table 3S. Full Table of Chiral Ligands Screened.

entry ^d	chiral ligand	yield (%) ^b	ee (%) ^c	config.
1 ^d	dppbenz	99	-	+/-
2 ^d	(<i>R</i>)-BINAP	nd	22	<i>R</i>
3 ^d	(<i>R</i>)-tol-BINAP	89	32	<i>R</i>
4	(<i>S,S</i>)-CHIRAPHOS	nd	32	<i>S</i>
5	(<i>R</i>)-PROPHOS	35	65	<i>R</i>
6 ^d	(<i>R,R</i>)-Me-DUPHOS	52	48	<i>S</i>
7	(<i>R,R</i>)-Et-DUPHOS	nd	45	<i>S</i>
8 ^d	(<i>R,R</i>)- <i>i</i> -Pr-DUPHOS	86	60	<i>R</i>
9	(<i>S,S</i>)-NORPHOS	37	75	<i>S</i>
10	(<i>R,R</i>)-DIPAMP	50	32	<i>R</i>
11	(<i>R,R</i>)-Et-BPE	45	90	<i>S</i>
12	(<i>R,R</i>)-DegupHOS	46	96	<i>R</i>
13 ^d	(<i>R,R</i>)-DegupHOS	97	94	<i>R</i>

^a See above for reaction details. ^b Isolated yields after chromatography. ^c Ee determined by HPLC analysis, configuration assigned by comparison of the optical rotation of the free amine with the literature.¹⁰ ^d Reactions were run at 70 °C.

(1-(4-methoxyphenyl)-1-phenylmethyl)-diphenylphosphoramidate (5b). The general procedure was followed except that 3 equiv of 4-methoxyphenylboronic acid as a solution in 1.57 mL of dioxane were added over 20 h and the reaction mixture was allowed to stir for an additional 4 h before it was worked up according to the general procedure. Chromatography (SiO_2 , acetone: CH_2Cl_2 10:90) then afforded **5b** as an off-white solid (95.2 mg, 93% yield). mp 159.7-160.7 °C. 93% ee (Chiral HPLC analysis, Daicel OD column, hexanes:*i*-PrOH 90:10, 1.0 mL/min, λ = 250 nm, $r_t(S)$ = 13.0 min, $r_t(R)$ = 14.9 min). $[\alpha]_D^{25} = +14^\circ$ (c 0.55, CHCl_3). ^1H NMR (500 MHz): δ 3.56 (1H, dd, $J=6.6$, 10.2 Hz), 3.79 (3H, s), 5.42 (1H, t, $J=10.8$ Hz), 6.82 (2H, d, $J=9.0$ Hz), 7.18 (2H, d, $J=9.0$ Hz), 7.22-7.31 (5H, m), 7.34-7.40 (4H, m), 7.43-7.48 (2H, m), 7.81-7.86 (4H, m). ^{13}C NMR (101 MHz): δ 55.2, 58.0, 113.8, 127.1, 127.5, 128.3, 128.4, 128.8, 131.6, 131.7, 131.81, 131.84, 132.18, 132.22, 132.28, 132.32, 133.0, 135.6 (d, $J=4.4$ Hz), 143.5 (d, $J=5.1$ Hz), 158.6.¹¹ ^{31}P NMR (162 MHz): δ 23.3. IR: 1194, 1178, 1110, 718, 696 cm^{-1} . HRMS (FAB+) m/z : Calcd for $\text{C}_{26}\text{H}_{25}\text{NO}_2\text{P}$: 414.162293. Found: 414.161760. Anal. calcd for $\text{C}_{26}\text{H}_{24}\text{NO}_2\text{P}$: C, 75.53; H, 5.85; N, 3.39. Found: C, 75.22; H, 5.98; N, 3.37.

(1-(4-trifluoromethylphenyl)-1-phenylmethyl)-diphenylphosphoramidate (5c). The general procedure was followed except that 3 equiv of 4-(trifluoromethyl)phenylboronic acid as a solution in 1.57 mL of dioxane were added over 20 h and the reaction mixture was allowed to stir for an additional 4 h before it was worked up according to the general procedure. Chromatography (SiO₂, acetone:CH₂Cl₂ 5:95 to 1:15) afforded **5c** as an off-white solid (98.2 mg, 88% yield). mp 175.3-177.5 °C. 88% ee (Chiral HPLC analysis, Daicel AD column, hexanes:*i*-PrOH 90:10, 1.0 mL/min, λ = 250 nm, r_t(S) = 19.1 min, r_t(R) = 21.3 min). [α]²⁵_D = -1.7 ° (c 0.72, CHCl₃). ¹H NMR (500 MHz): δ 3.61 (1H, dd, *J*=6.8, 10 Hz), 5.52 (1H, t, *J*=10.8 Hz), 7.22-7.4 (11H, m), 7.42-7.55 (4H, m), 7.79-7.85 (4H, m). ¹³C NMR (125 MHz): δ 58.2, 124.1 (q, *J*=272 Hz), 125.3 (q, *J*=3.8 Hz), 127.5, 127.6, 128.0, 128.37, 128.41, 128.47, 128.51, 128.7, 129.3 (q, *J*=32 Hz), 131.3, 131.6, 131.95, 131.98, 132.00, 132.02, 132.1, 132.2, 132.30, 132.34, 132.6, 142.5 (d, *J*=5.2 Hz), 147.2 (m). ³¹P NMR (162 MHz): δ 23.4. ¹⁹F NMR (376 MHz): δ -61.7. IR: 1330, 1110, 1068, 718, 692 cm⁻¹. HRMS (FAB+) *m/z*: Calcd for C₂₆H₂₁F₃NOP: 452.139113. Found: 452.139280. Anal. calcd for C₂₆H₂₁F₃NOP: C, 69.18; H, 4.69; N, 3.10. Found: C, 69.01; H, 4.77; N, 2.91.

(1-(3-acetylphenyl)-1-phenylmethyl)-diphenylphosphoramidate (5d). The general procedure was followed except that 3 equiv of 3-acetylphenylboronic acid (123 mg, 0.75 mmol), which is poorly soluble in dioxane, was added over 20 h as a solution in THF/dioxane (42:58 THF:dioxane, 1.57 mL). The reaction mixture was allowed to stir for an additional 4 h before it was worked up according to the general procedure. Chromatography (SiO₂, EtOAc:hexanes 50:50 to 70:30) afforded 101 mg (93% yield) of **5d** as a yellow solid. mp 139-141 °C. [α]²⁵_D = -1.8 ° (c 0.60, CHCl₃). ¹H NMR (400 MHz): δ 2.56 (3H, s), 3.66 (1H, dd, *J*=6.8, 10.1 Hz), 5.54 (1H, t, *J*=10.8 Hz), 7.25-7.51 (13H, m), 7.79-7.89 (6H, m). ¹³C NMR (125 MHz): δ 26.7, 58.3, 127.2, 127.36, 127.43, 127.5, 128.3, 128.39, 128.41, 128.5, 128.65, 128.70, 131.4, 131.6, 131.9, 132.0, 132.1, 132.15, 132.23, 132.4, 132.5, 132.6, 137.1, 142.7 (d, *J*=4.0 Hz), 143.9 (d, *J*=4.9 Hz), 198.0. ³¹P NMR (162 MHz): δ 23.3. IR: 1682, 1177, 1106, 1066, 726, 691 cm⁻¹. HRMS (FAB+) *m/z*: Calcd for C₂₇H₂₅NO₂P: 426.162293. Found: 426.163050. The ee of **5d** was determined by formation of the (*R*)- and (*S*)-MTPA amides and analysis by GC (vide infra) (100-300 °C, 5 °C/min ramp; (*R*)-MTPA derivative of (*R*)-amine *r*_t = 39.0 min, (*S*)-MTPA derivative of (*R*)-amine *r*_t = 39.3 min). The enantiopurity of the amine was determined to be 88% ee.

(S)-4-Chloro-α-phenyl-bezenemethanamine HCl salt 6 from 2h. Sulfinamide **2h** (49.3 mg, 0.153 mmol) was cleaved by the reported method¹³ to afford 35.5 mg (91% yield) of the white amine hydrochloride. mp 266-270 °C dec. (lit.¹⁰ 267-270 °C). ¹H NMR (MeOD-*d*₄, 400 MHz): δ 5.68 (1H, s), 7.38-7.48 (9H, m). Analytical data matched the reported data.¹⁰ The amine hydrochloride was converted to the free base and the optical rotation measured: [α]²⁵_D = +8.7 ° (c 1.5, EtOH). (lit.¹⁴ [α]²⁵_D = +10.8 ° (c 2.18, EtOH) for (*S*)).

(R)-4-Chloro-α-phenyl-bezenemethanamine HCl salt 6 from 5e. Diphenylphosphoramidate **5e** (63.8 mg, 0.153 mmol) was dissolved in MeOH (0.315 mL) and a solution of 4M HCl in dioxane was added (0.315 mL, 8.2 equiv). An additional 0.072 mL of CDCl₃ was added (for a deuterium lock) and the reaction mixture was allowed to stand at rt. Reaction progress was followed by ³¹P NMR. After standing at rt for 3.5 h, the reaction mixture was heated to 40 °C for an additional 5.5 h at which time the reaction was judged complete by ³¹P NMR. The reaction mixture was transferred to a vial and the solvent removed under reduced pressure. The crude material was then triturated with dry ether to afford 36.8 mg (95% yield) of the amine hydrochloride.¹⁵ mp 274-278 °C dec. (lit.¹⁰ 267-270 °C). ¹H NMR (MeOD-*d*₄, 400 MHz): δ 5.68 (1H, s), 7.39-7.49 (9H, m). Analytical data matched the reported data.¹⁰ The amine hydrochloride was converted to the free base and the optical rotation measured: [α]²⁵_D = -8.4 ° (c 0.83, EtOH). (lit.¹¹ (*S*)-10b: [α]²³_D = +10.8 ° (c = 2.18, ethanol). The optical purity of the amine hydrochloride was verified by formation of the (*R*)- and (*S*)-MTPA amides and analysis by GC according to the published

procedure¹⁶ (100-300 °C, 5 °C/min ramp; (*R*)-MTPA derivative of (*R*)-amine $r_t = 36.6$ min, (*S*)-MTPA derivative of (*R*)-amine $r_t = 36.8$ min). The enantiopurity of the amine was found to be 92% ee.

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