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Synthesis of *P*-Chiral Dihydrobenzooxaphospholes Through Negishi Cross-Coupling

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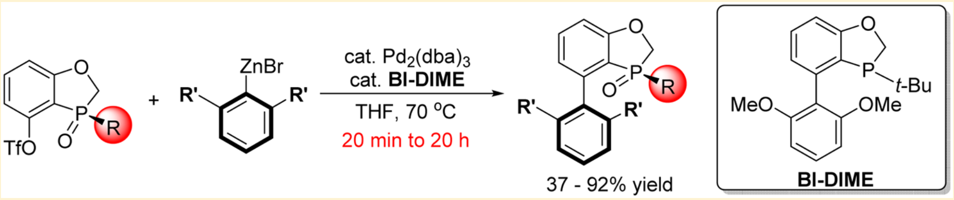
Supporting Information



ABSTRACT: An efficient Negishi cross-coupling was developed for the synthesis of the biaryl axes present in useful *P*-chiral dihydrobenzooxaphosphole ligands. This approach has allowed for the synthesis of new derivatives of these ligands that were not accessible by the previous route employing Suzuki–Miyaura cross-coupling. The use of $Pd_2(dba)_3$/**BI-DIME** as the catalyst system affords the desired biaryl compounds in good yields with excellent rates and with catalyst loadings as low as 0.25 mol %.

Ligand accelerated catalysis[1] is a valuable tool for the straightforward synthesis of complex molecular frameworks.[2] Over the years, many privileged ligand[3] structures have been developed and applied to useful reactions. In the continual effort to identify new ligand architectures for valuable organic transformations, our laboratories have recently reported a privileged class of *P*-chiral dihydrobenzooxaphosphole-derived ligands (**4**, Scheme 1), whereby this common core structure can be used for ligands suitable for both standard[4] and asymmetric[5] Suzuki–Miyaura[6] cross-coupling reactions, asymmetric hydrogenations of functionalized[7] and unfunctionalized[8] alkenes, Buchwald–Hartwig[9] amination[10] reactions, asymmetric propargylation[11] reactions, and asymmetric boronic acid addition reactions.[12] In particular, the monophosphine **BI-DIME** and derivatives are highly effective in Suzuki–Miyaura cross-coupling chemistry.[4,5] As such, the introduction of the biaryl axis found in this family of ligands is installed using a Suzuki–Miyaura cross-coupling reaction between triflate **1a** and boronic acid **2** employing Pd/**BI-DIME** as the catalyst.[4a] Because of the extreme utility of this family of ligands, we have been interested in preparing derivatives of this class of ligands by varying the substituent on phosphorus (**5**) to determine if these changes could have significant impact and utility on catalytic reactions. For example, the triflate containing a ferrocenyl (Fc) substituent on phosphorus (**1b**) was prepared to generate the *P*-Fc analogue of **BI-DIME**. However, under the standard Suzuki cross-coupling conditions used to install the biaryl axis, poor yield of the desired cross-coupling product **3b** was obtained, resulting in mostly hydrolysis of the triflate. A survey of other catalysts did not improve the yield of the desired coupling. At this point, we decided to attempt the biaryl synthesis employing a Negishi cross-coupling process.[13] The dimethoxyphenyl zinc bromide reagent **7** is easily prepared by deprotonation of 1,3-dimethoxybenzene followed by addition of $ZnBr_2$. Gratifyingly, the Negishi cross-coupling employing Pd/**BI-DIME** as the catalyst was highly effective in forming the desired biaryl moiety. In this note, we describe the generality of the Pd/**BI-DIME** catalyzed Negishi cross-coupling reaction for the synthesis of **BI-DIME** analogues.

The substrate scope for the Negishi cross-coupling reaction is given in Table 1. The coupling utilizing triflate **1a** can be employed to prepare the **BI-DIME** derivatives that were previously prepared using Suzuki–Miyaura cross-coupling chemistry (entries 1, 3, and 4). Notably, the Negishi coupling was superior to the Suzuki–Miyaura reaction for the synthesis of **3c** and **3e**; **3c** could not be prepared using a Suzuki reaction, and **3e** is achieved in only 30% yield under Suzuki conditions.[14] Additionally, reaction times were typically significantly reduced with many of the cross-coupling reactions complete in <1 h. When the *P*-*t*-Bu substituent of the triflate electrophile was replaced with smaller groups (i.e., R = Fc, **1b** or R = Ph, **1c**), catalyst loadings and reaction times could be reduced as compared with triflate **1a** (entries 6–13 vs entries 1–4). However, reactions of triflates **1b** or **1c** with more hindered aryl zinc reagents did require longer reaction times to reach completion at 1–2 mol % Pd-loadings (entries 9, 11, and 13).

Because the Negishi cross-coupling reaction with triflate **1a** to prepare **3a** was observed to be very fast employing only 1 mol % Pd loading (Table 1, entry 1), we examined the reaction rate for this process at reduced catalyst loadings (Scheme 2). Notably, the catalyst loading could be reduced to 0.25 mol % Pd loading

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Scheme 1. BI-DIME Ligand and Derivatives

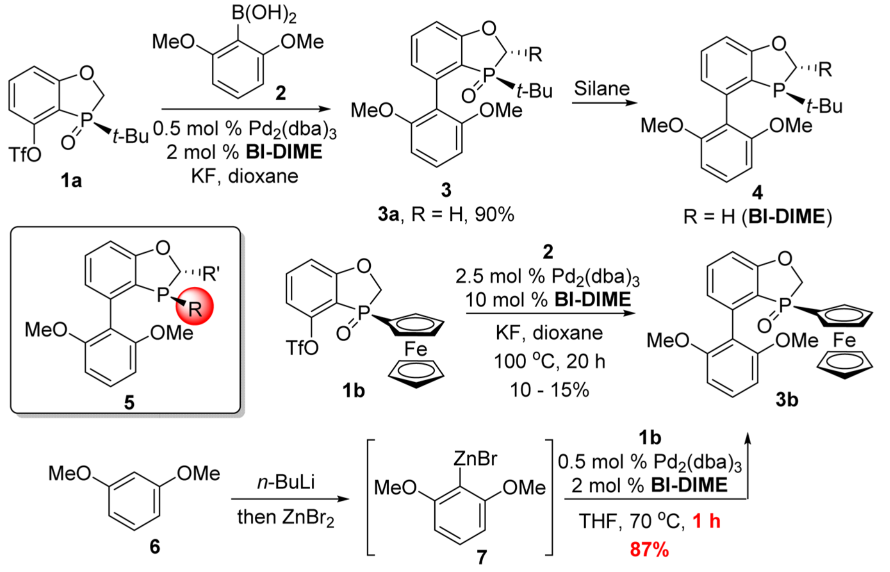
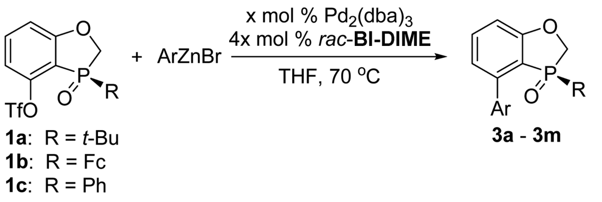


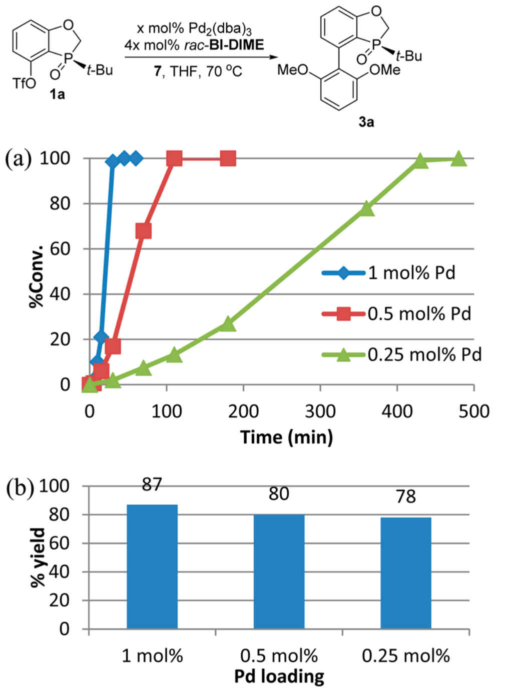
Table 1. Pd/BI-DIME Catalyzed Negishi Cross-Coupling[a]



entry	R	Ar	x	time	% yield
1[b]	^{t}Bu	2,6-(MeO)$_2$C$_6$H$_3$	0.5	1 h	**3a**, 87
2	^{t}Bu	2,6-(^{i}PrO)$_2$C$_6$H$_3$	2.0	5 h	**3c**, 75
			1.0	20 h	**3c**, 50
3	^{t}Bu	2,6-(PhO)$_2$C$_6$H$_3$	0.5	2 h	**3d**, 54
4[c]	^{t}Bu	9-anthracenyl	2.0	10 h	**3e**, 79
5[d]	^{t}Bu	mesityl	2.0	2 h	**3f**, 37
6	Fc	2,6-(MeO)$_2$C$_6$H$_3$	0.5	0.4 h	**3b**, 92
7	Fc	2,6-(^{i}PrO)$_2$C$_6$H$_3$	2.0	1.5 h	**3g**, 83
8	Fc	2,6-(PhO)$_2$C$_6$H$_3$	0.5	2 h	**3h**, 75
9[c]	Fc	9-anthracenyl	1.0	10 h	**3i**, 83
10	Ph	2,6-(MeO)$_2$C$_6$H$_3$	0.5	0.25 h	**3j**, 84
11	Ph	2,6-(^{i}PrO)$_2$C$_6$H$_3$	0.5	20 h	**3k**, 65
		2,6-(^{i}PrO)$_2$C$_6$H$_3$	2.0	0.4 h	**3k**, 78
12	Ph	2,6-(PhO)$_2$C$_6$H$_3$	0.5	0.4 h	**3l**, 73
13[c]	Ph	9-anthracenyl	0.5	20 h	**3m**, 74

[a] Reaction conditions: triflate **1** (0.40−1.40 mmol), arene (2.1−2.2 equiv), *n*-BuLi (2.0 equiv), ZnBr$_2$ (2.4 equiv), Pd$_2$(dba)$_3$ (0.5−2.0 mol %), *rac*-**BI-DIME** (2−8 mol %), 70 °C. [b] (*S*)-**BI-DIME** was used as ligand to avoid potential contamination of the product with racemic **3a** derived from oxidation of *rac*-**BI-DIME** during the workup. A control experiment utilizing *rac*-**BI-DIME** as the ligand gave identical reaction rate and yields compared to (*S*)-**BI-DIME**, indicating no catalytic nonlinear effects in the cross-coupling. [c] Aryllithium prepared by Li-halogen exchange between 9-bromoanthracene (1.75−2.05 equiv) and *t*-BuLi (3.4−4.0 equiv). [d] Aryllithium prepared by Li-halogen exchange between 2-bromomesitylene (2.05 equiv) and *t*-BuLi (4.0 equiv).

Scheme 2. (a) Effect of Catalyst Loading in the Negishi Coupling with Triflate 1a[a] and (b) Reaction Yields

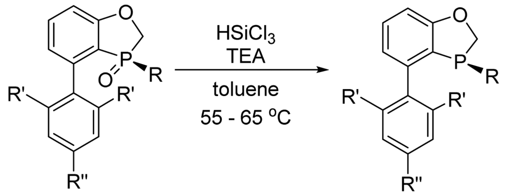


[a] Reaction conditions: triflate **1a** (0.500 g, 1.40 mmol), 1,3-dimethoxybenzne (0.38 mL g, 2.9 mmol), *n*-BuLi (2.55M, 1.1 mL, 2.8 mmol), ZnBr$_2$ (0.754 g, 3.35 mmol), Pd$_2$(dba)$_3$ (0.125−0.5 mol %), *rac*-**BI-DIME** (0.5−2 mol %), THF (4.7 mL), 70 °C. Conversion to the desired product was measured by UPLC at 220 nm.

giving full conversion in ~7 h. Reaction yield was slightly reduced at lower catalyst loadings due to increased amounts of byproduct formation at lower Pd loadings (see also Table 1, entry 2). Finally, initial rates demonstrated an increase in reaction rate with respect to time that is indicative of formation of the active catalyst that is generated in situ. Because Pd(0) is used as the precatalyst, the induction period observed for the formation of the catalytically active species is likely related to ligand exchange by the phosphine ligand.

Reduction of the **BI-DIME** derivatives containing *P*-Fc (**3b**) and *P*-Ph (**3j**) substituents was performed employing HSiCl$_3$/TEA (Scheme 3). Ligand **5c** containing bis(*ortho*-methyl) substitution on the lower aryl ring (i.e., mesityl) in place of bis(*ortho*-methoxy) substitution was also prepared for compar-

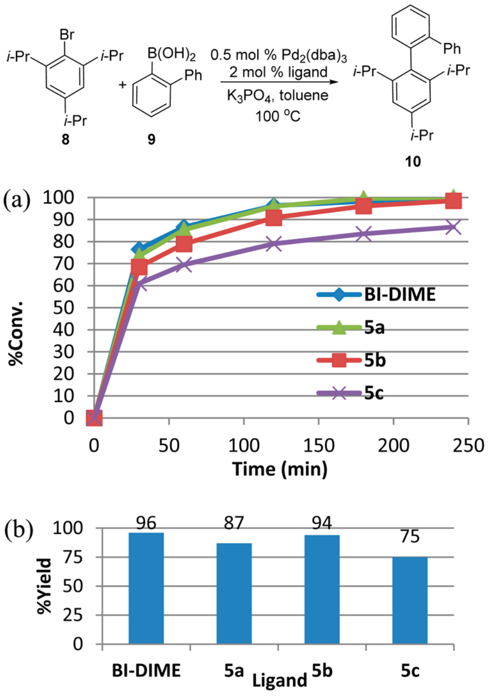
Scheme 3. Phosphine Oxide Reduction of New BI-DIME Analogues



5a, R = Fc, R' = OMe, R'' = H; 51%
5b, R = Ph, R' = OMe, R'' = H; 89%
5c, R = *t*-Bu, R' = R'' = Me; 88%

ison. These three new **BI-DIME** derivatives were then compared against **BI-DIME** in a standard Suzuki–Miyaura cross-coupling reaction to form hindered biaryls (Scheme 4).

Scheme 4. (a) Ligand Activity in Hindered Suzuki–Miyaura Cross-Coupling and (b) NMR Yields Determined Using Dimethyl Fumarate as Standard[a]



[a]Bromide **8** (127 μL, 0.500 mmol), boronic acid **9** (148 mg, 0.750 mmol), K_3PO_4 (318 mg, 1.50 mmol), $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol, 0.5 mol %), ligand (2 mol %), toluene (1.0 mL), 100 °C. Conversion to the desired product was measured by UPLC at 220 nm.

Interestingly, all three ligands containing bis(*ortho*-methoxy) substitution gave comparable reaction rates and yields in the cross-coupling to form **10** (Scheme 4, **BI-DIME** vs **5a** vs **5b**). It is surprising that the phosphorus substituent seems to have little impact on the coupling. This observation suggests that analogues of this family of ligand with *P*-substituents other than *t*-Bu may be useful in other reactions where **BI-DIME** and its derivatives have been applied.[4,5,7,8,10−12,14] Ligand **5c** was not as effective in the coupling studied. The better activity of Pd catalysts derived from similar ligands bearing bis(*ortho*-methoxyphenyl) substitution compared to those with bis(*ortho*-alkylphenyl) substitution for very hindered Suzuki–Miyaura cross coupling reactions has been previously noted by Buchwald.[15]

In summary, a convenient and efficient Negishi cross-coupling method employing Pd/**BI-DIME** as catalyst for the synthesis of **BI-DIME** analogues was disclosed. In many instances, the Negishi coupling enabled the synthesis of derivatives that were previously either inaccessible or provided in poor yields when employing a Suzuki–Miyaura coupling to install the desired biaryl axis. New **BI-DIME** analogues bearing alternate substitution on phosphorus were prepared and demonstrated to have similar effectiveness to **BI-DIME** in Suzuki–Miyaura cross-coupling to generate hindered biaryls. The ability to further tune the reactivity of catalysts derived from a transition metal and **BI-DIME** through the variation of the substitution on phosphorus may lead to catalysts with unique reactivity/selectivity in desirable catalytic transformations.

■ EXPERIMENTAL SECTION

General Methods. Unless otherwise stated, all reactions were carried out using oven- or flame-dried glassware under an inert atmosphere of N_2 or Ar. Anhydrous solvents (THF, toluene) were purchased from commercial vendors and degassed by Ar sparge before use. Triflates were prepared according to our previously published procedures.[4a,12] $ZnBr_2$ was dried under high vacuum (~1 Torr) at 135 °C overnight and then stored and dispensed in a N_2-filled glovebox. ^1H NMR spectra were recorded on 400 or 500 MHz spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as an internal standard ($CDCl_3$: 7.26 ppm, CD_2Cl_2: 5.32). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, h = hextet, hept = heptet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR was recorded using 125 or 100 MHz instruments with complete proton decoupling. Chemical shifts are reported in ppm with the solvent as the internal standard ($CDCl_3$: 77.0 ppm, CD_2Cl_2: 53.84). ^{31}P NMR spectra were recorded using 202 or 161 MHz instruments with complete proton decoupling. Chemical shifts are reported relative to 85% H_3PO_4. High-resolution mass spectroscopy was performed on a TOF instrument with ESI and positive and negative ionization modes. Flash chromatography was performed using columns packed with silica gel.

*(R)-3-(tert-Butyl)-4-(2,6-dimethoxyphenyl)-2H-benzo[d][1,3]-oxaphosphole 3-Oxide (**3a**).*[4a] A crimp-cap vial with a magnetic stir-bar was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). To the vial was charged 0.38 mL (2.9 mmol) of 1,3-dimethoxybenzene followed by 2.5 mL of THF. The mixture was cooled in an ice-bath, and 1.25 mL (2.2 M, 2.8 mmol) of *n*-BuLi was charged dropwise over 5 min. The mixture was then warmed to rt and allowed to stir for 2 h. In a second crimp-cap vial was prepared a slurry of $ZnBr_2$ (754 mg, 3.35 mmol) in 1.2 mL of THF. To the $ZnBr_2$ mixture cooled in an ice-bath was charged the aryllithium solution by canula transfer. The resulting mixture was then warmed to rt and allowed to stir for 15 min before use. In a third crimp-cap vial with stir-bar were charged triflate **1a** (500 mg, 1.40 mmol), $Pd_2(dba)_3$ (6.4 mg, 0.0070 mmol), and (*S*)-**BI-DIME** (9.2 mg, 0.028 mmol). The mixture was inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was allowed to stir for 10 min. The ArZnBr solution was then transferred to the catalyst/triflate solution using cannula transfer. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 8 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (10 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 10 mL). Combined organics were washed with 20% citric acid (2 × 8 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 50–100% EtOAc in hexanes to 3% MeOH in EtOAc) afforded 420 mg (87%) of **3a** as a white solid. Spectral data was in complete agreement with the published data.[4a] Mp 120–123 °C.

*(R)-4-(2,6-Dimethoxyphenyl)-3-(ferrocenyl)-2H-benzo[d][1,3]-oxaphosphole 3-Oxide (**3b**).* A crimp-cap vial with magnetic stir-bar

was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). To the vial was charged 0.11 mL (0.83 mmol) of 1,3-dimethoxybenzene followed by 1.0 mL of THF. The mixture was cooled in an ice-bath, and 0.31 mL (2.55 M, 0.79 mmol) of *n*-BuLi was charged dropwise over 5 min. The mixture was then warmed to rt and allowed to stir for 2 h. In a second crimp-cap vial with stir-bar was charged solid $ZnBr_2$ (214 mg, 0.952 mmol) under N_2. To the agitated $ZnBr_2$ in an ice-bath was charged the aryllithium solution by canula transfer. The resulting mixture was then warmed to rt and allowed to stir for 15 min before use. In a third crimp-cap vial with stir-bar were charged triflate **1b** (193 mg, 0.397 mmol), $Pd_2(dba)_3$ (1.8 mg, 0.0020 mmol), and *rac*-**BI-DIME** (2.6 mg, 0.0079 mmol). The mixture was inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was allowed to stir for 10 min. The ArZnBr solution was then transferred to the catalyst/triflate solution using cannula transfer. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). Combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 50−90% EtOAc in hexanes) afforded 173 mg (92%) of **3b** as an orange solid. Mp 230−233 °C; R_f = 0.22 (75% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (t, J = 7.8 Hz, 1H), 7.22 (t, J = 8.4 Hz, 1H), 6.95 (dd, J = 8.3 Hz, J = 3.8 Hz, 1H), 6.80 (dd, J = 7.2 Hz, J = 3.4 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.25 (d, J = 8.4 Hz, 1H), 4.66 (dd, J = 14 Hz, J = 11 Hz, 1H), 4.57 (dd, J = 14 Hz, J = 0.9 Hz, 1H), 4.34 (s, 1H), 4.30 (s, 1H), 4.23 (s, 5H), 4.05 (s, 1H), 3.98 (s, 1H), 3.79 (s, 3H), 3.14 (s, 3H); $^{31}P\{^1H\}$NMR (202 MHz, $CDCl_3$) δ 40.5 ppm; $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 164.0 (d, J_{C-P} = 22.1 Hz), 158.6, 157.1, 138.0 (d, J_{C-P} = 6.0 Hz), 134.5 (d, J_{C-P} = 1.5 Hz), 129.5, 123.9 (d, J_{C-P} = 8.4 Hz), 118.9 (d, J_{C-P} = 108 Hz), 116.1 (d, J_{C-P} = 3.0 Hz), 112.4 (d, J_{C-P} = 6.0 Hz), 104.1, 102.8, 73.05 (d, J_{C-P} = 11.6 Hz), 72.03 (d, J_{C-P} = 11.3 Hz), 71.22 (d, J_{C-P} = 11.1 Hz), 69.88 (d, J_{C-P} = 16.4 Hz), 69.39, 69.28 (d, J_{C-P} = 73 Hz), 69.17 (d, J_{C-P} = 190 Hz), 56.21, 55.03; HRMS(EI) *m*/*z* calcd for $C_{25}H_{24}FeO_4P$ [M + H]$^+$ 475.0762, found 475.0759.

*(R)-3-(tert-Butyl)-4-(2,6-diisopropoxyphenyl)-2H-benzo[d][1,3]-oxaphosphole 3-Oxide (**3c**).* A crimp-cap vial with magnetic stir-bar was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). The vial was sequentially charged with 0.62 mL (3.1 mmol) of 1,3-diisopropoxybenzene, 1.5 mL of hexanes, and 1.1 mL (2.55M, 2.8 mmol) of *n*-BuLi. The mixture was then immersed in an oil bath at 70 °C and allowed to stir for 2.5 h to afford a white slurry. The mixture was then cooled to rt, and 2.2 mL of THF was charged to afford a homogeneous solution. In a second crimp-cap vial with stir-bar was charged solid $ZnBr_2$ (754 mg, 3.35 mmol) under N_2. To the agitated $ZnBr_2$ at rt was charged the aryllithium solution by canula transfer. The resulting mixture was allowed to stir for 15 min before use. To a 1-dram vial with stir-bar were charged triflate **1a** (500 mg, 1.40 mmol), $Pd_2(dba)_3$ (25.6 mg, 0.0280 mmol), and *rac*-**BI-DIME** (36.9 mg, 0.112 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was allowed to stir for 10 min. The catalyst/triflate solution was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.4 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 8 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (10 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 10 mL). Combined organics were washed with 20% citric acid (2 × 8 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 30 to 70 to 90% EtOAc in hexanes) afforded 423 mg (75%) of **3c** as a white solid. Mp 77−80 °C; R_f = 0.33 (100% EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (t, J = 7.9 Hz, 1H), 7.20 (t, J = 8.4 Hz, 1H), 6.85 (dd, J = 8.3 Hz, J = 3.4 Hz, 1H), 6.83 (dd, J = 7.6 Hz, J = 3.3 Hz, 1H), 6.56 (d, J = 8.4 Hz, 1H), 6.47 (d, J = 8.4 Hz, 1H), 4.50 (sept, J = 6.1 Hz, 1H), 4.47 (sept, J = 6.1 Hz, 1H), 4.48 (d, J = 13 Hz, 1H), 4.30 (dd, J = 14 Hz, J = 11 Hz, 1H), 1.30 (d, J = 3.1 Hz, 3H), 1.22 (d, J = 6.1 Hz, 3H), 1.16 (d, J = 6.1 Hz, 6H), 0.92 (d, J = 16 Hz, 9H); $^{31}P\{^1H\}$NMR (162 MHz, $CDCl_3$) δ 62.5 ppm; $^{13}C\{^1H\}$-NMR (126 MHz, $CDCl_3$) δ 164.8 (d, J_{C-P} = 19.5 Hz), 157.7, 156.0, 139.4 (d, J_{C-P} = 5.62 Hz), 133.5 (d, J_{C-P} = 1.7 Hz), 129.4, 125.4 (d, J_{C-P} = 8.6 Hz), 118.6 (d, J_{C-P} = 2.4 Hz), 114.6 (d, J_{C-P} = 92.4 Hz), 111.7 (d, J_{C-P} = 5.6 Hz), 105.2, 103.8, 70.63, 69.38, 65.28 (d, J_{C-P} = 61.2 Hz), 33.68 (d, J_{C-P} = 71.8 Hz), 23.79, 23.32, 22.23, 22.02, 21.94; HRMS(EI) *m*/*z* calcd for $C_{23}H_{32}O_4P$ [M + H]$^+$ 403.2038, found 403.2047.

*(R)-3-(tert-Butyl)-4-(2,6-diphenoxyphenyl)-2H-benzo[d][1,3]-oxaphosphole 3-Oxide (**3d**).*[16] A crimp-cap vial with magnetic stir-bar was charged with 805 mg (3.07 mmol) of 1,3-diphenoxybenzene. The vial was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). To the vial was sequentially charged 1.5 mL of hexanes and 1.35 mL (2.1M, 2.8 mmol) of *n*-BuLi. The mixture then immersed in an oil bath at 70 °C and allowed to stir for 2.5 h to afford a white slurry. The mixture was then cooled to rt, and 2.2 mL of THF was charged to afford a homogeneous solution. In a second crimp-cap vial with stir-bar was charged solid $ZnBr_2$ (754 mg, 3.35 mmol) under N_2. To the agitated $ZnBr_2$ at rt was charged the aryllithium solution by canula transfer. The resulting mixture was allowed to stir for 15 min before use. To a 1-dram vial with stir-bar were charged triflate **1a** (500 mg, 1.40 mmol), $Pd_2(dba)_3$ (6.4 mg, 0.0070 mmol), and *rac*-**BI-DIME** (9.2 mg, 0.028 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was allowed to stir for 10 min. The catalyst/triflate solution was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.4 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 8 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (10 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 10 mL). Combined organics were washed with 20% citric acid (2 × 8 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 30 to 70 to 90% EtOAc in hexanes) afforded 357 mg (54%) of **3d** as a white solid. Spectral data was in complete agreement with the published data.[15] Mp 90−95 °C (lit.[16] mp 97−99 °C).

*(R)-4-(Anthracen-9-yl)-3-(tert-butyl)-2H-benzo[d][1,3]-oxaphosphole 3-Oxide (**3e**).*[14] To a 25 mL 2-neck round-bottom flask with magnetic stir-bar and fitted with a reflux condenser with a short-path distillation head at the top of the condenser was charged 527 mg (2.05 mmol) of 9-bromoanthracene. The second neck of the flask was capped with a septum, and the system was inerted with N_2 using vacuum-purge cycles (3×). THF (2.5 mL) was then charged, and the solution was cooled to −78 °C in a dry ice acetone bath. *t*-BuLi (1.5 M in pentane, 2.67 mL, 4.0 mmol) was then added dropwise over 10 min. The resulting yellow slurry was stirred at −78 °C for 5 min and then allowed to warm to rt and stirred for an additional 10 min before use. In a separate flask was prepared a solution of $ZnBr_2$ (540 mg, 2.4 mmol) in 1.8 mL of THF. This solution was then transferred by cannula to the aryllithium reagent at rt, and the mixture was allowed to stir for an additional 15 min. To a 1-dram vial with stir-bar were charged triflate **1a** (358 mg, 1.00 mmol), $Pd_2(dba)_3$ (18.3 mg, 0.0200 mmol), and *rac*-**BI-DIME** (26.4 mg, 0.0800 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was allowed to stir for 10 min. The catalyst/triflate solution was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.25 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. Note that during the reaction pentane was distilled off via the short-path distillation head. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). Combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture

by flash chromatography (gradient, 50% to 100% EtOAc in hexanes) afforded 304 mg (75%) of **3e** as a white solid. Spectral data was in complete agreement with the published data.[14] Mp 217−219 °C.

*(R)-3-(tert-Butyl)-4-mesityl-2H-benzo[d][1,3]oxaphosphole 3-Oxide (**3f**).* To a 25 mL 2-neck round-bottom flask with magnetic stir-bar and fitted with a reflux condenser with a short-path distillation head at the top of the condenser under N_2 was charged 0.31 mL (408 mg, 2.05 mmol) of 2-bromomesitylene. THF (2.5 mL) was then charged, and the solution was cooled to −78 °C in a dry ice acetone bath. *t*-BuLi (1.5 M in pentane, 2.67 mL, 4.0 mmol) was then added dropwise over 10 min. The resulting yellow slurry was stirred at −78 °C for 5 min and then allowed to warm to rt and stirred for an additional 10 min before use. In a separate flask was prepared a solution of $ZnBr_2$ (540 mg, 2.4 mmol) in 1.8 mL of THF. This solution was then transferred by cannula to the aryllithium reagent at rt, and the mixture was allowed to stir for an additional 15 min. To a 1-dram vial with stir-bar were charged triflate **1a** (358 mg, 1.00 mmol), $Pd_2(dba)_3$ (18.3 mg, 0.0200 mmol), and *rac*-**BI-DIME** (26.4 mg, 0.0800 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was allowed to stir for 10 min. The catalyst/triflate solution was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.25 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. Note that during the reaction pentane was distilled off via the short-path distillation head. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). Combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 30 to 70 to 90% EtOAc in hexanes) afforded 122 mg (37%) of **3f** as an off-white solid. Mp 135−138 °C; R_f = 0.22 (70% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (t, J = 8.0 Hz, 1H), 6.97 (s, 1H), 6.94 (dd, J = 8.2 Hz, J = 3.3 Hz, 1H), 6.88 (s, 1H), 6.80 (dd, J = 7.1 Hz, J = 3.3 Hz, 1H), 4.51 (dd, J = 14 Hz, J = 2.7 Hz, 1H), 4.38 (dd, J = 14 Hz, J = 11 Hz, 1H), 2.29 (s, 3H), 2.21 (s, 3H), 2.05 (s, 3H), 0.90 (d, J = 16 Hz, 9H); ^{31}P{^{1}H}NMR (162 MHz, $CDCl_3$) δ 62.6 ppm; ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 166.1 (d, J_{C-P} = 19.3 Hz), 144.3 (d, J_{C-P} = 6.5 Hz), 137.7, 137.6, 136.7 (d, J_{C-P} = 1.9 Hz), 135.1, 134.6 (d, J_{C-P} = 1.7 Hz), 128.9, 127.9, 124.2 (d, J_{C-P} = 8.5 Hz), 113.7 (d, J_{C-P} = 89.4 Hz), 112.6 (d, J_{C-P} = 5.3 Hz), 65.73 (d, J_{C-P} = 61.0 Hz), 33.41 (d, J_{C-P} = 71.9 Hz), 23.94, 21.08, 21.01, 20.94; HRMS(EI) m/z calcd for $C_{20}H_{26}O_2P$ $[M + H]^+$ 329.1670, found 329.1670.

*(R)-4-(2,6-Diisopropoxyphenyl)-3-(ferrocenyl)-2H-benzo[d][1,3]oxaphosphole 3-Oxide (**3g**).* A crimp-cap vial with magnetic stir-bar was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). The vial was sequentially charged with 0.18 mL (0.87 mmol) of 1,3-diisopropoxybenzene, 0.45 mL of hexanes, and 0.31 mL (2.55M, 0.79 mmol) of *n*-BuLi. The mixture then immersed in an oil bath at 70 °C and allowed to stir for 2.5 h to afford a white slurry. The mixture was then cooled to rt, and 0.6 mL of THF was charged to afford a homogeneous solution. In a second crimp-cap vial with stir-bar was charged solid $ZnBr_2$ (214 mg, 0.952 mmol) under N_2. To the agitated $ZnBr_2$ at rt was charged the aryllithium solution by canula transfer. The resulting mixture was allowed to stir for 15 min before use. To a 1-dram vial with stir-bar were charged triflate **1b** (193 mg, 0.397 mmol), $Pd_2(dba)_3$ (7.3 mg, 0.0080 mmol), and *rac*-**BI-DIME** (10.5 mg, 0.0318 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was sonicated for 2 min and then allowed to stir for 10 min. The catalyst/triflate slurry was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.5 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). Combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 20−50% EtOAc in hexanes) afforded 174 mg (83%) of **3g** as an orange solid. Mp 140−143 °C; R_f = 0.21 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, J = 8.0 Hz, 1H), 7.137 (t, J = 8.5 Hz, 1H), 6.90 (dd, J = 8.3 Hz, J = 3.9 Hz, 1H), 6.75 (dd, J = 7.2 Hz, J = 3.3 Hz, 1H), 6.58 (d, J = 8.3 Hz, 1H), 6.22 (d, J = 8.3 Hz, 1H), 4.63 (dd, J = 14 Hz, J = 11 Hz, 1H), 4.55 (d, J = 14 Hz, 1H), 4.47 (sept, J = 6.1 Hz, 1H), 4.29 (m, 1H), 4.26 (m, 1H), 4.22 (s, 5H), 4.09 (m, 1H), 3.98 (m, 1H), 3.89 (sept, J = 6.1 Hz, 1H), 1.23 (d, J = 6.1 Hz, 3H), 1.18 (d, J = 6.1 Hz, 3H), 0.95 (d, J = 6.1 Hz, 3H), 0.75 (d, J = 3H); ^{31}P{^{1}H}NMR (202 MHz, $CDCl_3$) δ 40.1 ppm; ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 163.6 (d, J_{C-P} = 22.1 Hz), 157.6, 156.0, 139.0 (d, J_{C-P} = 6.0 Hz), 133.8 (d, J_{C-P} = 1.2 Hz), 128.9, 124.2 (d, J_{C-P} = 8.7 Hz), 118.9 (d, J_{C-P} = 108 Hz), 118.6 (d, J_{C-P} = 3.2 Hz), 111.7 (d, J_{C-P} = 6.2 Hz), 106.0, 105.3, 73.16 (d, J_{C-P} = 12.1 Hz), 71.80 (d, J_{C-P} = 11.1 Hz), 71.24, 71.18 (d, J_{C-P} = 13.1 Hz), 70.05 (d, J_{C-P} = 17.1 Hz), 69.68, 69.42 (d, J_{C-P} = 123 Hz), 69.31, 69.12 (d, J_{C-P} = 73 Hz), 22.57, 22.54, 22.16, 21.52; HRMS(EI) m/z calcd for $C_{29}H_{32}FeO_4P$ $[M + H]^+$ 531.1388, found 531.1388.

*(R)-4-(2,6-Diphenoxyphenyl)-3-(ferrocenyl)-2H-benzo[d][1,3]oxaphosphole 3-Oxide (**3h**).* A crimp-cap vial with magnetic stir-bar was charged with 237 mg (0.905 mmol) of 1,3-diphenoxybenzene. The vial was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). To the vial was sequentially charged 0.45 mL of hexanes and 0.32 mL (2.55M, 0.82 mmol) of *n*-BuLi. The mixture then immersed in an oil bath at 70 °C and allowed to stir for 2.5 h to afford a white slurry. The mixture was then cooled to rt, and 0.6 mL of THF was charged to afford a homogeneous solution. In a second crimp-cap vial with stir-bar was charged solid $ZnBr_2$ (222 mg, 0.987 mmol) under N_2. To the agitated $ZnBr_2$ at rt was charged the aryllithium solution by canula transfer. The resulting mixture was allowed to stir for 15 min before use. To a 1-dram vial with stir-bar were charged triflate **1b** (200 mg, 0.411 mmol), $Pd_2(dba)_3$ (1.9 mg, 0.0020 mmol), and *rac*-**BI-DIME** (2.7 mg, 0.0080 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was sonicated for 2 min and then allowed to stir for 10 min. The catalyst/triflate slurry was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.5 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). Combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 20−50% EtOAc in hexanes) afforded 186 mg (75%) of **3h** as an orange solid. Mp 225−228 °C; R_f = 0.23 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29−7.35 (m, 3H), 7.22−7.27 (m, 2H), 7.15 (t, J = 8.1 Hz, 2H), 7.05−7.12 (m, 2H), 6.96 (t, J = 7.3 Hz, 1H), 6.90 (dd, J = 8.3 Hz, J = 3.5 Hz, 1H), 6.80 (dd, J = 7.6 Hz, J = 3.7 Hz, 1H), 6.58 (d, J = 7.8 Hz, 2H), 6.52 (d, J = 8.1 Hz, 1H), 6.30 (d, J = 8.2 Hz, 1H), 4.72 (dd, J = 14 Hz, J = 11 Hz, 1H), 4.66 (d, J = 14 Hz, 1H), 4.49 (m, 1H), 4.42 (m, 1H), 4.30 (m, 1H), 4.29 (s, 5H), 4.16 (m, 1H); ^{31}P{^{1}H}NMR (202 MHz, $CDCl_3$) δ 40.6 ppm; ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 163.9 (d, J_{C-P} = 22.1 Hz), 157.9, 156.9, 156.3, 155.6, 136.2 (d, J_{C-P} = 5.8 Hz), 134.2 (d, J_{C-P} = 1.2 Hz), 129.6, 129.3, 129.2, 123.94, 123.93 (d, J_{C-P} = 8.2 Hz), 123.0, 121.2, 120.9 (d, J_{C-P} = 3.2 Hz), 119.1, 119.0 (d, J_{C-P} = 107 Hz), 113.0 (d, J_{C-P} = 6.0 Hz), 111.5, 110.9, 73.47 (d, J_{C-P} = 11.7 Hz), 72.39 (d, J_{C-P} = 11.4 Hz), 71.57 (d, J_{C-P} = 11.1 Hz), 70.31 (d, J_{C-P} = 16.3 Hz), 69.46, 69.41 (d, J_{C-P} = 73 Hz), 69.28 (d, J_{C-P} = 122 Hz); HRMS(EI) m/z calcd for $C_{35}H_{28}FeO_4P$ $[M + H]^+$ 599.1075, found 599.1077.

*(R)-4-(Anthracen-9-yl)-3-(ferrocenyl)-2H-benzo[d][1,3]oxaphosphole 3-Oxide (**3i**).* To a 15 mL 2-neck round-bottom flask with magnetic stir-bar fitted with a reflux condenser with a short-path distillation head at the top of the condenser was charged 209 mg (0.813 mmol) of 9-bromoanthracene. The second neck of the flask was capped with a septum, and the system was inerted with N_2 using vacuum-purge

cycles (3×). THF (1.0 mL) was then charged, and the solution was cooled to −78 °C in a dry ice acetone bath. *t*-BuLi (1.5 M in pentane, 1.1 mL, 1.6 mmol) was then added dropwise over 10 min. The resulting yellow slurry was stirred at −78 °C for 5 min and then allowed to warm to rt and stirred for an additional 10 min before use. In a separate flask was prepared a solution of $ZnBr_2$ (214 mg, 0.952 mmol) in 0.72 mL of THF. This solution was then transferred by cannula to the aryllithium reagent at rt, and the mixture was allowed to stir for an additional 15 min. To a 1-dram vial with stir-bar were charged triflate **1b** (193 mg, 0.397 mmol), $Pd_2(dba)_3$ (3.6 mg, 0.0039 mmol), and *rac*-**BI-DIME** (5.2 mg, 0.016 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (1.0 mL) was then added, and the mixture was sonicated for 2 min and then allowed to stir for 10 min. The catalyst/triflate slurry was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.5 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. Note that during the reaction pentane was distilled off via the short-path distillation head. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). Combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 20−50% EtOAc in hexanes) afforded 130 mg (64%) of **3i** as an orange solid. Mp > 300 °C; R_f = 0.35 (75% EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.5 Hz, 1H), 7.61−7.67 (m, 2H), 7.38−7.49 (m, 2H), 7.17−7.22 (m, 1H), 7.16 (dd, J = 8.2 Hz, J = 3.6 Hz, 1H), 6.99 (dd, J = 7.2 Hz, J = 3.5 Hz, 1H), 6.77−6.86 (m, 2H), 4.64 (dd, J = 14 Hz, J = 12 Hz, 1H), 4.53 (dd, J = 14 Hz, J = 1.7 Hz, 1H), 4.04 (s, 5H), 4.03 (m, 1H), 3.83 (m, 1H), 3.69 (m, 1H), 2.94 (m, 1H); $^{31}P\{^1H\}$NMR (202 MHz, $CDCl_3$) δ 39.8 ppm; $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 164.0 (d, J_{C-P} = 21.9 Hz), 141.6 (d, J_{C-P} = 6.3 Hz), 134.8 (d, J_{C-P} = 1.2 Hz), 132.4 (d, J_{C-P} = 3.1 Hz), 131.1, 130.7, 129.7, 128.0, 127.8, 127.2, 127.1, 126.1, 125.7, 125.6, 125.0, 124.6 (d, J_{C-P} = 8.3 Hz), 124.5, 119.9 (d, J_{C-P} = 106 Hz), 113.3 (d, J_{C-P} = 5.8 Hz), 72.06 (d, J_{C-P} = 11.8 Hz), 71.95 (d, J_{C-P} = 11.8 Hz), 71.63 (d, J_{C-P} = 11.3 Hz), 69.40 (d, J_{C-P} = 16.7 Hz), 69.08, 69.03 (d, J_{C-P} = 73 Hz), 67.41 (d, J_{C-P} = 124 Hz); HRMS(EI) *m/z* calcd for $C_{31}H_{24}FeO_2P$ $[M + H]^+$ 515.0863, found 515.0864.

(R)-4-(2,6-Dimethoxyphenyl)-3-(phenyl)-2H-benzo[d][1,3]-oxaphosphole 3-Oxide ***(3j)***. A crimp-cap vial with magnetic stir-bar was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). To the vial was charged 0.28 mL (2.1 mmol) of 1,3-dimethoxybenzene followed by 1.8 mL of THF. The mixture was cooled in an ice-bath, and 0.78 mL (2.55 M, 2.0 mmol) of *n*-BuLi was charged dropwise over 5 min. The mixture was then warmed to rt and allowed to stir for 2 h. In a second crimp-cap vial was prepared a slurry of $ZnBr_2$ (540 mg, 2.40 mmol) in 0.89 mL of THF. To the $ZnBr_2$ mixture cooled in an ice-bath was charged the aryllithium solution by canula transfer. The resulting mixture was then warmed to rt and allowed to stir for 15 min before use. In a third crimp-cap vial with stir-bar were charged triflate **1c** (378 mg, 1.00 mmol), $Pd_2(dba)_3$ (4.6 mg, 0.0050 mmol), and *rac*-**BI-DIME** (6.6 mg, 0.020 mmol). The mixture was inerted with N_2 using vacuum-purge cycles (3×). THF (0.71 mL) was then added, and the mixture was allowed to stir for 10 min. The ArZnBr solution was then transferred to the catalyst/triflate solution using cannula transfer. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). Combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 50−80% EtOAc in hexanes) afforded 308 mg (84%) of **3j** as a white solid. Mp 175−177 °C; R_f = 0.20 (80% EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (t, J = 7.9 Hz, 1H), 7.42 (t, J = 7.1 Hz, 1H), 7.27−7.39 (m, 4H), 7.16 (t, J = 8.4 Hz, 1H), 7.03 (dd, J = 8.5 Hz, J = 3.8 Hz, 1H), 6.86 (dd, J = 7.2 Hz, J = 3.5 Hz, 1H), 6.61 (d, J = 8.4 Hz, 1H), 6.08 (d, J = 8.4 Hz, 1H), 4.66 (dd, J = 14 Hz, J = 11 Hz, 1H), 4.48 (d, J = 14 Hz, 1H), 3.80 (s, 3H), 2.99 (s, 3H); $^{31}P\{^1H\}$NMR (202 MHz, $CDCl_3$) δ 38.4 ppm; $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 165.6 (d, J_{C-P} = 21.7 Hz), 158.5, 156.6, 138.7 (d, J_{C-P} = 6.2 Hz), 135.1 (d, J_{C-P} = 1.4 Hz), 131.4 (d, J_{C-P} = 3.0 Hz), 131.2 (d, J_{C-P} = 107 Hz), 131.1 (d, J_{C-P} = 10.8 Hz), 129.7, 128.0 (d, J_{C-P} = 13.0 Hz), 124.5 (d, J_{C-P} = 8.6 Hz), 116.8 (d, J_{C-P} = 106 Hz), 112.4 (d, J_{C-P} = 6.2 Hz), 104.0, 102.3, 70.24 (d, J_{C-P} = 69 Hz), 56.17, 54.64; HRMS(EI) *m/z* calcd for $C_{21}H_{20}O_4P$ $[M + H]^+$ 367.1099, found 367.1101.

(R)-4-(2,6-Diisopropoxyphenyl)-3-(phenyl)-2H-benzo[d][1,3]-oxaphosphole 3-Oxide ***(3k)***. A crimp-cap vial with magnetic stir-bar was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). The vial was sequentially charged with 0.44 mL (2.2 mmol) of 1,3-diisopropoxybenzene, 1.1 mL of hexanes, and 0.78 mL (2.55M, 2.0 mmol) of *n*-BuLi. The mixture was then immersed in an oil bath at 70 °C and allowed to stir for 2.5 h to afford a white slurry. The mixture was then cooled to rt, and 1.6 mL of THF was charged to afford a homogeneous solution. In a second crimp-cap vial with stir-bar was charged solid $ZnBr_2$ (540 mg, 2.40 mmol) under N_2. To the agitated $ZnBr_2$ at rt was charged the aryllithium solution by canula transfer. The resulting mixture was allowed to stir for 15 min before use. To a 1-dram vial with stir-bar were charged triflate **1c** (378 mg, 1.00 mmol), $Pd_2(dba)_3$ (18.3 mg, 0.0200 mmol), and *rac*-**BI-DIME** (26.4 mg, 0.0800 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (0.71 mL) was then added, and the mixture was allowed to stir for 10 min. The catalyst/triflate solution was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.3 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). The combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 20−50% EtOAc in hexanes) afforded 330 mg (78%) of **3k** as a clear glass. R_f = 0.20 (50% EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (t, J = 7.9 Hz, 1H), 7.31−7.41 (m, 3H), 7.24−7.29 (m, 2H), 7.07 (t, J = 8.4 Hz, 1H), 6.98 (dd, J = 8.4 Hz, J = 3.8 Hz, 1H), 6.81 (dd, J = 7.4 Hz, J = 3.6 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 6.07 (d, J = 8.4 Hz, 1H), 4.61 (dd, J = 14 Hz, J = 11 Hz, 1H), 4.47 (sept, J = 6.1 Hz, 1H) 4.46 (d, J = 14 Hz, 1H), 3.88 (sept, J = 6.1 Hz, 1H), 1.30 (d, J = 6.1 Hz, 3H), 1.19 (d, J = 6.1 Hz, 3H), 0.95 (d, J = 6.1 Hz, 3H), 0.71 (d, J = 6.1 Hz, 3H); $^{31}P\{^1H\}$NMR (202 MHz, $CDCl_3$) δ 37.9 ppm; $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 165.1 (d, J_{C-P} = 21.7 Hz), 157.4, 155.7, 139.8 (d, J_{C-P} = 6.1 Hz), 134.4 (d, J_{C-P} = 1.4 Hz), 131.6 (d, J_{C-P} = 74.1 Hz), 131.4 (d, J_{C-P} = 3.0 Hz), 131.0 (d, J_{C-P} = 10.7 Hz), 129.1, 127.9 (d, J_{C-P} = 12.9 Hz), 124.8 (d, J_{C-P} = 8.7 Hz), 118.2 (d, J_{C-P} = 3.2 Hz), 116.7 (d, J_{C-P} = 107 Hz), 111.7 (d, J_{C-P} = 6.2 Hz), 105.8, 104.9, 77.16, 69.95 (d, J_{C-P} = 69 Hz), 69.64, 22.30, 22.18, 22.13, 21.60; HRMS(EI) *m/z* calcd for $C_{25}H_{28}O_4P$ $[M + H]^+$ 423.1725, found 423.1722.

(R)-4-(2,6-Diphenoxyphenyl)-3-(phenyl)-2H-benzo[d][1,3]-oxaphosphole 3-Oxide ***(3l)***. A crimp-cap vial with magnetic stir-bar was charged with 577 mg (2.20 mmol) of 1,3-diphenoxybenzene. The vial was sealed with a crimp-cap septum and inerted with N_2 using vacuum-purge cycles (3×). To the vial were sequentially charged 1.1 mL of hexanes and 0.78 mL (2.55M, 2.0 mmol) of *n*-BuLi. The mixture then immersed in an oil bath at 70 °C and allowed to stir for 2.5 h to afford a white slurry. The mixture was then cooled to rt, and 1.6 mL of THF was charged to afford a homogeneous solution. In a second crimp-cap vial with stir-bar was charged solid $ZnBr_2$ (754 mg, 3.35 mmol) under N_2. To the agitated $ZnBr_2$ at rt was charged the aryllithium solution by canula transfer. The resulting mixture was allowed to stir for 15 min before use. To a 1-dram vial with stir-bar were charged triflate **1c** (378 mg, 1.00 mmol), $Pd_2(dba)_3$ (4.6 mg, 0.0050 mmol), and *rac*-**BI-DIME** (6.6 mg, 0.020 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (0.71 mL) was then added, and the mixture was allowed to

stir for 10 min. The catalyst/triflate solution was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.3 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). The combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 20−50% EtOAc in hexanes) afforded 357 mg (73%) of **3l** as a white solid. Mp 215−225 °C; R_f = 0.27 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47−7.57 (m, 3H), 7.44 (t, J = 7.9 Hz, 1H), 7.38 (td, J = 7.7 Hz, J = 3.2 Hz, 2H), 7.29−7.35 (m, 4H), 7.08−7.17 (m, 3H), 6.94−7.05 (m, 3H), 6.90 (dd, J = 7.2 Hz, J = 3.4 Hz, 1H), 6.49 (dd, J = 8.9 Hz, J = 0.7 Hz, 1H), 6.41 (d, J = 8.3 Hz, 2H), 6.14 (dd, J = 8.2 Hz, J = 0.6 Hz, 1H), 4.69 (dd, J = 14 Hz, J = 11 Hz, 1H), 4.53 (dd, J = 14 Hz, J = 0.7 Hz, 1H); ^{31}P{^{1}H}NMR (202 MHz, $CDCl_3$) δ 38.7 ppm; ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 165.5 (d, J_{C-P} = 21.6 Hz), 157.9, 156.7, 156.2, 155.3, 137.2 (d, J_{C-P} = 6.0 Hz), 134.9 (d, J_{C-P} = 1.3 Hz), 131.9 (d, J_{C-P} = 2.9 Hz), 131.5 (d, J_{C-P} = 106 Hz), 131.3 (d, J_{C-P} = 10.8 Hz), 129.6, 129.4, 129.3, 128.4 (d, J_{C-P} = 13.0 Hz), 124.5 (d, J_{C-P} = 8.5 Hz), 124.1, 123.1, 121.4, 120.3 (d, J_{C-P} = 3.2 Hz), 119.0, 116.5 (d, J_{C-P} = 105 Hz), 113.0 (d, J_{C-P} = 6.1 Hz), 111.0, 110.6, 70.14 (d, J_{C-P} = 69 Hz); HRMS(EI) m/z calcd for $C_{31}H_{24}O_4P$ [M + H]$^+$ 491.1412, found 491.1417.

*(R)-4-(Anthracen-9-yl)-3-(phenyl)-2H-benzo[d][1,3]oxaphosphole 3-Oxide (**3m**).* To a 25 mL 2-neck round-bottom flask with magnetic stir-bar fitted with a reflux condenser with a short-path distillation head at the top of the condenser was charged 450 mg (1.75 mmol) of 9-bromoanthracene. The second neck of the flask was capped with a septum, and the system was inerted with N_2 using vacuum-purge cycles (3×). THF (1.6 mL) was then charged, and the solution was cooled to −78 °C in a dry ice acetone bath. *t*-BuLi (1.5 M in pentane, 2.27 mL, 3.4 mmol) was then added dropwise over 10 min. The resulting yellow slurry was stirred at −78 °C for 5 min and then allowed to warm to rt and stirred for an additional 10 min before use. In a separate flask was prepared a solution of $ZnBr_2$ (450 mg, 2.0 mmol) in 1.5 mL of THF. This solution was then transferred by cannula to the aryllithium reagent at rt, and the mixture was allowed to stir for an additional 15 min. To a 1-dram vial with stir-bar were charged triflate **1c** (378 mg, 1.00 mmol), $Pd_2(dba)_3$ (4.6 mg, 0.0050 mmol), and *rac*-**BI-DIME** (6.6 mg, 0.020 mmol). The vial was capped with a septum cap and inerted with N_2 using vacuum-purge cycles (3×). THF (0.5 mL) was then added, and the mixture was allowed to stir for 10 min. The catalyst/triflate solution was then transferred to the ArZnBr solution using cannula transfer. The residue in the vial was rinsed with an additional 0.25 mL of THF. The final mixture was then immersed in an oil bath at 70 °C and monitored by UPLC. Note that during the reaction pentane was distilled off via the short-path distillation head. After the time given in Table 1, the reaction was cooled to rt and quenched with 5 mL of 2 M HCl. THF was removed in vacuo, and CH_2Cl_2 (5 mL) was then added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (1 × 5 mL). Combined organics were washed with 20% citric acid (2 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by flash chromatography (gradient, 20−50% EtOAc in hexanes) afforded 300 mg (74%) of **3m** as an off-white solid. Mp 205−208 °C; R_f = 0.31 (75% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.00 (d, J = 7.8 Hz, 1H), 7.78 (d, J = 8.5 Hz, 1H), 7.70 (t, J = 8.1 Hz, 1H), 7.66 (d, J = 8.6 Hz, 1H), 7.42−7.51 (m, 2H), 7.22−7.26 (m, 1H), 7.00−7.16 (m, 3H), 6.79−6.90 (m, 4H), 6.71−6.77 (m, 2H), 4.68 (dd, J = 14 Hz, J = 11 Hz, 1H), 4.60 (dd, J = 14 Hz, J = 2.0 Hz, 1H); ^{31}P{^{1}H}NMR (202 MHz, $CDCl_3$) δ 37.4 ppm; ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 165.3 (d, J_{C-P} = 21.4 Hz), 142.2 (d, J_{C-P} = 6.6 Hz), 135.3 (d, J_{C-P} = 1.2 Hz), 132.0 (d, J_{C-P} = 3.1 Hz), 131.4 (d, J_{C-P} = 3.1 Hz), 131.73 (d, J_{C-P} = 56 Hz), 131.70, 130.2 (d, J_{C-P} = 10.7 Hz), 130.1, 129.1 (d, J_{C-P} = 8.1 Hz), 128.0 (d, J_{C-P} = 8.3 Hz), 127.82, 127.80, 127.4, 127.1, 125.8, 125.52, 125.48, 125.0 (d, J_{C-P} = 8.4 Hz), 124.9, 124.3, 118.3 (d, J_{C-P} = 104 Hz), 113.3 (d, J_{C-P} = 5.9 Hz), 69.74 (d, J_{C-P} = 69 Hz); HRMS(EI) m/z calcd for $C_{27}H_{20}O_2P$ [M + H]$^+$ 407.1201, found 407.1205.

*(S)-4-(2,6-Dimethoxyphenyl)-3-(ferrocenyl)-2,3-dihydrobenzo[d]-[1,3]oxaphosphole (**5a**).* To a 5 mL Schlenk flask with magnetic stir-bar was charged 275 mg (0.580 mmol) of oxide **3b**. A reflux condenser was added, and the reaction was inerted with Ar using vacuum-purge cycles. Toluene (1.6 mL) was charged followed by triethylamine (0.16 mL, 1.2 mmol) and $HSiCl_3$ (0.088 mL, 0.87 mmol). The mixture was then immersed in an oil bath at 55 °C and monitored by ^{31}P NMR spectroscopy. After 2 h, the reaction was cooled to rt and quenched with 2 mL of degassed (Ar sparge) 30% NaOH. The mixture was then allowed to vigorously stir at rt for 1 h. The aqueous layer was removed and subsequently extracted under Ar with MeTHF (2 × 2 mL) followed by CH_2Cl_2 (2 × 2 mL). The combined organics were dried with $MgSO_4$, filtered quickly through a pad of Celite, and immediately concentrated in vacuo. The crude residue was chromatographed on the bench by dissolving the crude solid in CH_2Cl_2 and loading the mixture onto a short pad of silica gel and eluting with degassed (Ar sparge) hexanes/EtOAc (10−50%) using Ar to pressurize the flash column. The product fractions were immediately collected and concentrated in vacuo to afford 135 mg (51%) of **5a** as a yellow-orange solid. Mp 195−197 °C; R_f = 0.34 (20% EtOAc/hexanes); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.33 (t, J = 8.4 Hz, 1H), 7.24 (t, J = 7.7 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 6.67 (dd, J = 7.3 Hz, J = 3.2 Hz, 1H), 6.54 (d, J = 8.4 Hz, 1H), 5.19 (dd, J = 12 Hz, J = 3.1 Hz, 1H), 4.79 (dd, J = 31 Hz, J = 12 Hz, 1H), 4.20 (s, 1H), 4.16 (s, 1H), 4.13 (s, 1H), 4.08 (s, 5H), 3.79 (s, 3H), 3.68 (s, 1H), 3.35 (s, 3H); ^{31}P{^{1}H}NMR (202 MHz, CD_2Cl_2) δ −42.4 ppm; ^{13}C{^{1}H}NMR (126 MHz, CD_2Cl_2) δ 162.8, 158.8, 158.1, 138.7 (d, J_{C-P} = 19.2 Hz), 131.1, 129.9, 129.4 (d, J_{C-P} = 6.8 Hz), 123.8 (d, J_{C-P} = 3.7 Hz), 119.7, 110.7 (d, J_{C-P} = 1.0 Hz), 104.7, 104.4, 78.44 (d, J_{C-P} = 22.4 Hz), 74.97 (d, J_{C-P} = 31.8 Hz), 74.77 (d, J_{C-P} = 20.6 Hz), 71.32, 70.73 (d, J_{C-P} = 7.2 Hz), 69.72 (d, J_{C-P} = 2.8 Hz), 69.42 (d, J_{C-P} = 0.9 Hz), 56.67 (d, J_{C-P} = 1.0 Hz), 56.09; HRMS(EI) m/z calcd for $C_{25}H_{24}FeO_4P$ [M + O + H]$^+$ 475.0762, found 475.0785.

*(S)-4-(2,6-Dimethoxyphenyl)-3-(phenyl)-2,3-dihydrobenzo[d]-[1,3]oxaphosphole (**5b**).* To a 5 mL Schlenk flask with magnetic stir-bar was charged 200 mg (0.546 mmol) of oxide **3i**. A reflux condenser was added, and the reaction was inerted with Ar using vacuum-purge cycles. Toluene (1.5 mL) was charged followed by triethylamine (0.15 mL, 1.1 mmol) and $HSiCl_3$ (0.083 mL, 0.82 mmol). The mixture was then immersed in an oil bath at 55 °C and monitored by ^{31}P NMR spectroscopy. After 2 h, the reaction was cooled to rt and quenched with 2 mL of degassed (Ar sparge) 30% NaOH. The mixture was then allowed to vigorously stir at rt for 30 min. The aqueous layer was removed and subsequently extracted under Ar with MTBE (3 × 2 mL). The combined organics were dried with $MgSO_4$, filtered quickly through a pad of Celite, and immediately concentrated in vacuo. The crude residue was chromatographed on the bench by dissolving the crude solid in CH_2Cl_2 and loading the mixture onto a short pad of silica gel and eluting with degassed (Ar sparge) hexanes/EtOAc (10% to 30%) using Ar to pressurize the flash column. The product fractions were immediately collected and concentrated in vacuo to afford 171 mg (89%) of **5b** as a white solid. Mp 80−82 °C; R_f = 0.56 (30% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (t, J = 7.9 Hz, 1H), 7.13−7.26 (m, 6H), 7.02 (d, J = 31 Hz, 1H), 6.87 (dd, J = 7.0 Hz, J = 3.2 Hz, 1H), 6.64 (d, J = 8.3 Hz, 1H), 6.37 (d, J = 8.4 Hz, 1H), 4.65−4.78 (m, 2H), 3.79 (s, 3H), 3.02 (s, 3H); ^{31}P{^{1}H}NMR (202 MHz, $CDCl_3$) δ −33.7 ppm; ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 163.2, 157.6, 157.3, 139.0 (d, J_{C-P} = 19.7 Hz), 138.3 (d, J_{C-P} = 23.0 Hz), 132.3 (d, J_{C-P} = 20.0 Hz), 131.2, 129.2, 128.8, 128.0 (d, J_{C-P} = 7.1 Hz), 125.4 (d, J_{C-P} = 3.6 Hz), 123.7 (d, J_{C-P} = 4.1 Hz), 118.9 (d, J_{C-P} = 2.2 Hz), 110.1, 104.0, 103.4, 75.46 (d, J_{C-P} = 22.3 Hz), 56.06, 54.67; HRMS(EI) m/z calcd for $C_{21}H_{20}O_3P$ [M + H]$^+$ 351.1150, found 351.1141.

*(S)-3-(tert-Butyl)-4-mesityl-2,3-dihydrobenzo[d][1,3]-oxaphosphole (**5c**).* To a 5 mL Schlenk flask with magnetic stir-bar was charged 128 mg (0.390 mmol) of oxide **3f**. A reflux condenser was added, and the reaction was inerted with Ar using vacuum-purge cycles. Toluene (1.5 mL) was charged followed by triethylamine (0.22 mL, 1.6 mmol) and $HSiCl_3$ (0.12 mL, 1.2 mmol). The mixture was then

immersed in an oil bath at 65 °C and monitored by ^{31}P NMR spectroscopy. After 3 h, the reaction was cooled to rt and quenched with 2 mL of degassed (Ar sparge) 30% NaOH. The mixture was then allowed to vigorously stir at rt for 1 h. The aqueous layer was removed and subsequently extracted under Ar with MTBE (3 × 2 mL). The combined organics were dried with $MgSO_4$, filtered quickly through a pad of Celite, and immediately concentrated in vacuo. The crude residue was chromatographed on the bench by dissolving the crude in hexanes and loading the mixture onto a short pad of silica gel and eluting with degassed (Ar sparge) hexanes/EtOAc (neat hexane to 10% EtOAc/hexanes) using Ar to pressurize the flash column. The product fractions were immediately collected and concentrated in vacuo to afford 108 mg (88%) of **5c** as an off-white solid. Mp 65−67 °C; R_f = 0.64 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.22 (t, J = 7.8 Hz, 1H), 6.84 (s, 1H), 6.81 (s, 1H), 6.79 (d, J = 8.5 Hz, 1H), 6.62 (dd, J = 7.5 Hz, J = 3.3 Hz, 1H), 4.77 (dd, J = 13 Hz, J = 2.1 Hz, 1H), 4.41 (dd, J = 26 Hz, J = 13 Hz, 1H), 2.22 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 0.67 (d, J = 12 Hz, 9H); $^{31}P\{^1H\}$NMR (202 MHz, CD_2Cl_2) δ −8.3 ppm; $^{13}C\{^1H\}$NMR (100 MHz, CD_2Cl_2) δ 164.2, 145.6 (d, J_{C-P} = 17.7 Hz), 138.5, 136.8, 135.8, 135.2, 130.9, 128.5, 128.3, 124.0 (d, J_{C-P} = 15.2 Hz), 123.0 (d, J_{C-P} = 4.2 Hz), 109.4, 70.36 (d, J_{C-P} = 26.0 Hz), 30.85 (d, J_{C-P} = 19.4 Hz), 26.74 (d, J_{C-P} = 14.2 Hz), 21.04, 20.75 (d, J_{C-P} = 11.3 Hz), 20.73; HRMS(EI) m/z calcd for $C_{20}H_{26}OP$ $[M + H]^+$ 313.1721, found 313.1715.

General Procedure for Suzuki−Miyaura Cross Coupling (Scheme 4). In a N_2-filled glovebox, to a microwave vial with magnetic stir-bar were charged 2.3 mg (0.0025 mmol) of $Pd_2(dba)_3$, 0.010 mmol of ligand, 318 mg (1.50 mmol) of K_3PO_4, and 149 mg (0.750 mmol) of 2-bipheny boronic acid **9**. The vial was sealed with a crimp-cap septum and removed from the glovebox. Degassed (Ar sparge) toluene (1.0 mL) and 0.127 mL (0.500 mmol) of bromide **8** were charged, and the vial was inserted into an oil bath at 100 °C. Aliquots were removed by syringe and quenched in MeOH and analyzed by UPLC. After complete consumption of the starting aryl bromide, the reaction was cooled to rt and partitioned between water and CH_2Cl_2. The organic layer was collected, dried with Na_2SO_4, and concentrated in vacuo. The yield of the crude mixture was determined by ^{1}HNMR spectroscopy using dimethylfumarate as the analytical standard.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02649.

Copies of ^{1}H and ^{13}C NMR spectra of the compounds (PDF)

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Notes

The authors declare no competing financial interest.

■ DEDICATION

This work is dedicated to the life and memory of Richard Joseph Sieber and Mary Marcella “Chumly” Sieber.

■ REFERENCES

(1) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059.

(2) (a) Trost, B. M. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5348−5355. (b) Farina, V.; Reeves, J. T.; Senanayake, C. H.; Song, J. J. *Chem. Rev.* **2006**, *106*, 2734.

(3) (a) Yoon, T. P.; Jacobsen, E. N. *Science* **2003**, *299*, 1691−1693. (b) Pfaltz, A.; Drury, W. J., III *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5723−5726.

(4) (a) Tang, W.; Capacci, A. G.; Wei, X.; Li, W.; White, A.; Patel, N. D.; Savoie, J.; Gao, J. J.; Rodriguez, S.; Qu, B.; Haddad, N.; Lu, B. Z.; Krishnamurthy, D.; Yee, N. K.; Senanayake, C. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 5879. (b) Zhao, Q.; Li, C.; Senanayake, C. H.; Tang, W. *Chem. - Eur. J.* **2013**, *19*, 2261−2265.

(5) (a) Tang, W.; Patel, N. D.; Xu, G.; Xu, X.; Savoie, J.; Ma, S.; Hao, M.-H.; Keshipeddy, S.; Capacci, A. G.; Wei, X.; Zhang, Y.; Gao, J.; Li, W.; Rodriguez, S.; Lu, B. Z.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2012**, *14*, 2258. (b) Xu, G.; Fu, W.; Liu, G.; Senanayake, C. H.; Tang, W. *J. Am. Chem. Soc.* **2014**, *136*, 570. (c) Fandrick, K. R.; Li, W.; Zhang, Y.; Tang, W.; Gao, J.; Rodriguez, S.; Patel, N. D.; Reeves, D. C.; Wu, J. − P.; Sanyal, S.; Gonnella, N.; Qu, B.; Haddad, N.; Lorenz, J. C.; Sidhu, K.; Wang, J.; Ma, S.; Grinberg, N.; Lee, H.; Tsantrizos, Y.; Poupart, M. − A.; Busacca, C. A.; Yee, N. K.; Lu, B. Z.; Senanayake, C. H. *Angew. Chem., Int. Ed.* **2015**, *54*, 7144.

(6) Reviews: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (b) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633−9695. (c) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417−1492.

(7) (a) Tang, W.; Qu, B.; Capacci, A. G.; Rodriguez, S.; Wei, X.; Haddad, N.; Narayanan, B.; Ma, S.; Grinberg, N.; Yee, N. K.; Krishnamurthy, D.; Senanayake, C. H. *Org. Lett.* **2010**, *12*, 176. (b) Tang, W.; Capacci, A. G.; White, A.; Ma, S.; Rodriguez, S.; Qu, B.; Savoie, J.; Patel, N. D.; Wei, X.; Haddad, N.; Grinberg, N.; Yee, N. K.; Krishnamurthy, D.; Senanayake, C. H. *Org. Lett.* **2010**, *12*, 1104.

(8) (a) Qu, B.; Samankumara, L. P.; Savoie, J.; Fandrick, D. R.; Haddad, N.; Wei, X.; Ma, S.; Lee, H.; Rodriguez, S.; Busacca, C. A.; Yee, N. K.; Song, J. J.; Senanayake, C. H. *J. Org. Chem.* **2014**, *79*, 993. (b) Qu, B.; Samankumara, L. P.; Ma, S.; Fandrick, K. R.; Desrosiers, J.-N.; Rodriguez, S.; Li, Z.; Haddad, N.; Han, Z. S.; McKellop, K.; Pennino, S.; Grinberg, N.; Gonnella, N. C.; Song, J. J.; Senanayake, C. H. *Angew. Chem., Int. Ed.* **2014**, *53*, 14428.

(9) Reviews: (a) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2011**, *2*, 27−50. (b) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338−6361. (c) Hartwig, J. F. *Acc. Chem. Res.* **1998**, *31*, 852−860. (d) Wolfe, J. P.; Wagaw, S.; Marcoux, J. − F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805−818.

(10) Rodriguez, S.; Qu, B.; Haddad, N.; Reeves, D.; Tang, W.; Krishnamurthy, D.; Senanayake, C. H. *Adv. Synth. Catal.* **2011**, *353*, 533.

(11) Fandrick, D. R.; Fandrick, K. R.; Reeves, J. T.; Tan, Z.; Tang, W.; Capacci, A. G.; Rodriguez, S.; Song, J. J.; Lee, H.; Yee, N. K.; Senanayake, C. H. *J. Am. Chem. Soc.* **2010**, *132*, 7600.

(12) Sieber, J. D.; Chennamadhavuni, D.; Fandrick, K. R.; Qu, B.; Han, Z. S.; Savoie, J.; Ma, S.; Samankumara, L. P.; Grinberg, N.; Lee, H.; Song, J. J.; Senanayake, C. H. *Org. Lett.* **2014**, *16*, 5494.

(13) (a) King, A. O.; Okukado, N.; Negishi, E. − I. *J. Chem. Soc., Chem. Commun.* **1977**, 683−684. (b) Erdik, E. *Tetrahedron* **1992**, *48*, 9577−9648. (c) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176−4211.

(14) Tang, W.; Keshipeddy, S.; Zhang, Y.; Wei, X.; Savoie, J.; Patel, N. D.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2011**, *13*, 1366−1369.

(15) (a) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461−1473. (b) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685−4696. (c) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 1871−1876.

(16) Li, K.; Hu, N.; Luo, R.; Yuan, W.; Tang, W. *J. Org. Chem.* **2013**, *78*, 6350−6355.