Supplementary Information

Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

Kazuya Yamaguchi,¹ Junichiro Yamaguchi,*¹ Armido Studer,ᵇ and Kenichiro Itami*ᵃ

¹ Department of Chemistry, Graduate School of Science, Nagoya University, Chikusa, Nagoya 464-8602, Japan
ᵇ Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Corrensstrasse 40, 48149 Münster, Germany

E-mail: junichiro@chem.nagoya-u.ac.jp, itami.kenichiro@a.mbox.nagoya-u.ac.jp

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1. General

Unless otherwise noted, all materials including dry solvents were obtained from commercial suppliers and used as received. 4,5,6,7-Tetrahydrobenzo[5]thiophene (1f), 2-methylnaphthalen-1-ylboronic acid (2a)², 2-methoxynaphthalen-1-ylboronic acid (2b)³, and L²–L⁵ were synthesized according to procedures reported in the literature. Unless otherwise noted, all reactions were performed with dry solvents under an atmosphere of argon in flame-dried glassware using standard vacuum-line techniques. All C–H bond arylation reactions were performed in screw cap 20 mL glass vessel tubes and heated in an 8-well reaction block (heater + magnetic stirrer) unless otherwise noted. All work-up and purification procedures were carried out with reagent-grade solvents in air.

Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F₂₅₄ precoated plates (0.25 mm). The developed chromatogram was analyzed by UV lamp (254 nm). Flash column chromatography was performed with E. Merck silica gel 60 (230–400 mesh). Preparative thin-layer chromatography (PTLC) was performed using Wakogel B5-F silica coated plates (0.75 mm) prepared in our laboratory. Gas chromatography (GC) analysis was conducted on a Shimadzu GC-2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). GCMS analysis was conducted on a Shimadzu GCMS-QP2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). High-resolution mass spectra (HRMS) were obtained from JEOL JMS-T100GCV (EI), JMS-T100TD (DART) or JMS-700 (FAB) instruments. Chiral HPLC analysis was conducted on a Shimadzu Prominence 2000 instrument equipped with DAISO Chiracel OD-H (4.6 mm x 250 mm). Optical rotations were measured using a JASCO P-1010-GT digital polarimeter with CHCl₃ as the solvent.

Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECS-400 (¹H 400 MHz, $^{13}$C 100 MHz) spectrometer. Chemical shifts for $^1$H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm) or residual peak of DMSO (δ 2.50 ppm) and CD$_2$Cl$_2$ (5.32 ppm). Chemical shifts for $^{13}$C NMR are expressed in ppm relative to CDCl$_3$ (δ 77.0 ppm), CD$_2$Cl$_2$ (53.8 ppm) or DMSO (δ 39.5 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, sep = septet, m = multiplet, br = broad signal), coupling constant (Hz), and integration.

(1) S. Nomura, E. Kawanishi, K. Ueta, WO2005012326.
2. Preparation of Arylboronic Acid

**General Procedure**

**(2,4-Dimethylnaphthalen-1-yl)boronic acid (2c):** To a solution of 1,3-dimethylnaphthalene (2.11 g, 13.5 mmol) in CH$_3$CN (20 mL) was added N-bromosuccinimide (2.53 g, 14.2 mmol). The mixture was stirred at room temperature for 2 h and evaporated under reduced pressure. The resulting precipitate was filtered off and the filtrate was evaporated under reduced pressure. The residue was purified by short silica-gel column chromatography (hexane/EtOAc = 9:1) to give 1-bromo-2,4-dimethylnaphthalene as a colorless oil which was used for the next step without further purification. To a solution of 1-bromo-2,4-dimethylnaphthalene (3.16 g, 12.5 mmol) in THF (25 mL) was slowly added n-BuLi (1.6 M in hexane, 8.19 mL, 13.1 mmol) at −78 °C under argon atmosphere. After stirring at −78 °C for 1 h, trimethyl borate (4.18 mL, 37.5 mmol) was added, stirred at −78 °C for 30 min, then room temperature for 30 min. To the mixture was added 10% HCl (60 mL) and the resultant mixture was further stirred for 1 h. The mixture was extracted with EtOAc, and the organic layer was washed with water, brine, dried over anhydrous Na$_2$SO$_4$ and evaporated under reduced pressure. Hexane was added to the residue, and the resulting precipitate was collected to give 2c (2.01 g, 74%) as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.98–7.91 (m, 1H), 7.84–7.77 (m, 1H), 7.49–7.40 (m, 2H), 7.12 (s, 1H), 5.01 (s, 2H), 2.63 (s, 3H), 2.48 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 137.81, 135.20, 130.54, 129.09, 127.94, 125.96, 124.81, 124.30, 22.40, 19.36; HRMS (EI) $m/z$ calcd for C$_{12}$H$_{13}$BO$_2$ [M]$^+$ 200.1009, found 200.1013.

**(2-Ethynaphthalen-1-yl)boronic acid (2d):** Following the general procedure, 2d (5.32 g, 42%) was obtained as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.90–7.77 (m, 3H), 7.49–7.40 (m, 2H), 7.12 (s, 1H), 5.01 (s, 2H), 2.63 (s, 3H), 2.48 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 137.81, 135.20, 130.54, 129.09, 127.94, 125.96, 124.81, 124.30, 22.40, 19.36; HRMS (EI) $m/z$ calcd for C$_{12}$H$_{13}$BO$_2$ [M]$^+$ 200.1009, found 200.1013.
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CDCl₃ δ 144.69, 135.00, 131.43, 129.17, 128.28, 127.48, 126.82, 126.22, 125.04, 30.16, 16.87; HRMS (EI) m/z calcd for C₁₂H₁₃BO₂ [M⁺]: 200.1009, found: 200.1014.

B(OH)₂ i-Pr₂e (2-isopropynaphthalen-1-yl)boronic acid (2e): Following the general procedure, 2e (4.09 g, 57%) was obtained as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.86–7.74 (m, 3H), 7.50–7.36 (m, 3H), 4.89 (s, 2H), 3.21–3.06 (m, 1H), 1.34 (d, J = 6.7 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 148.55, 134.81, 131.68, 129.31, 128.23, 127.60, 126.20, 125.11, 123.29, 35.34, 24.42; HRMS (EI) m/z calcd for C₁₃H₁₅BO₂ [M⁺]: 214.1165, found: 214.1166.


To a 20-mL screw cap glass vessel containing a magnetic stirring bar were added Pd(OAc)₂ (5.6 mg, 0.025 mmol), L₅ (6.3 mg, 0.025 mmol), DMF (0.1 mL), and CF₃CO₂H (37 µL, 0.5 mmol). The mixture was stirred at 80 °C for 10 min and cooled to room temperature. To this mixture were added thiophene 1 (0.25 mmol), arylboronic acid 2 (1.0 mmol) and TEMPO (156 mg, 1.0 mmol), and the mixture was stirred at 80 °C for 12 h under air. After cooling the reaction mixture to room temperature, the mixture was passed through a short pad of silica gel (EtOAc) and the filtrate was evaporated under reduced pressure. The residue was purified by preparative thin-layer chromatography to give the arylated product 3. The C4/C5 regioselectivity of the reaction was determined by ¹H NMR.
Compound Data of Coupling Products

2,3-Dimethyl-4-(2-methylnaphthalen-1-yl)thiophene (3aa): Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3aa (53 mg, 84%, C4/C5 = 99:1) as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.81 (d, \(J = 7.6\) Hz, 1H), 7.76 (d, \(J = 8.3\) Hz, 1H), 7.43–7.27 (m, 4H), 6.84 (s, 1H), 2.46 (s, 3H), 2.22 (s, 3H), 1.71 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 140.57, 134.45, 133.85, 133.42, 133.21, 132.93, 131.87, 128.44, 127.70, 127.26, 125.91, 125.86, 124.74, 118.83, 20.43, 13.74, 12.19; HRMS (DART) \(m/z\) calcd for C\(_{17}\)H\(_{17}\)S [M+H]\(^+\): 253.1051, found: 253.1049.

3-Methyl-4-(2-methylnaphthalen-1-yl)thiophene (3ba): Following the general procedure with 3-methylthiophene (1b: 25 mg) and 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ba (40 mg, 68%, C4/C5 = 95:5) as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.83 (d, \(J = 8.1\) Hz, 1H), 7.78 (d, \(J = 8.1\) Hz, 1H), 7.43–7.31 (m, 4H), 7.15–7.11 (m, 1H), 7.09 (d, \(J = 3.1\) Hz, 1H), 2.22 (s, 3H), 1.86 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 140.32, 137.77, 134.55, 133.41, 132.89, 131.91, 128.45, 127.77, 127.43, 125.97, 125.77, 124.81, 123.32, 121.15, 20.40, 14.48; HRMS (DART) \(m/z\) calcd for C\(_{16}\)H\(_{15}\)S [M+H]\(^+\): 239.0894, found: 239.0890.
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3-Ethyl-4-(2-methylnaphthalen-1-yl)thiophene (3ca): Following the general procedure with 3-ethylthiophene (1c: 28 mg) and 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ca (40 mg, 64%, C4/C5 = 97:3) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 (d, $J$ = 8.1 Hz, 1H), 7.77 (d, $J$ = 8.5 Hz, 1H), 7.45–7.30 (m, 4H), 7.18–7.14 (m, 1H), 7.08 (d, $J$ = 3.1 Hz, 1H), 2.22 (s, 3H), 2.18 (q, $J$ = 7.6 Hz, 2H), 1.01 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.36, 139.79, 134.60, 133.49, 132.95, 131.88, 128.45, 127.74, 127.42, 125.92, 125.85, 124.79, 123.36, 119.86, 22.21, 20.49, 13.85; HRMS (DART) m/z calcd for C$_{17}$H$_{17}$S [M+H]$^+$: 253.1051, found: 253.1054.

2-Ethyl-4-(2-methylnaphthalen-1-yl)thiophene (3da): Following the general procedure with 2-ethylthiophene (1d: 28 mg) and 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg), the crude was purified by preparative thin-layer chromatography (hexane) to give 3da (42 mg, 66%, C4/C5 = 92:8) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.84–7.78 (m, 1H), 7.75 (d, $J$ = 8.6 Hz, 1H), 7.60 (d, $J$ = 8.2 Hz, 1H), 7.43–7.31 (m, 3H), 6.94 (d, $J$ = 1.0 Hz, 1H), 6.74 (d, $J$ = 1.4 Hz, 1H), 2.94 (q, $J$ = 7.7 Hz, 2H), 2.32 (s, 3H), 1.38 (t, $J$ = 7.7 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.19, 139.00, 134.02, 133.72, 133.33, 131.88, 128.52, 127.67, 127.19, 126.15, 126.09, 125.81, 124.74, 120.94, 23.46, 20.82, 15.93; HRMS (DART) m/z calcd for C$_{17}$H$_{17}$S [M+H]$^+$: 253.1051, found: 253.1048.
3-Methoxy-4-(2-methylnaphthalen-1-yl)-2-phenylthiophene (3ea): Following the general procedure with 3-methoxy-2-phenylthiophene (1e: 48 mg) and 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg), the crude product was purified by preparative thin-layer chromatography (hexane/EtOAc = 49:1) to give 3ea (56 mg, 68%, C4/C5 = 94:6) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.89–7.75 (m, 4H), 7.74–7.66 (m, 1H), 7.49–7.34 (m, 5H), 7.31–7.21 (m, 1H), 7.00 (s, 1H), 3.26 (s, 3H), 2.39 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.74, 134.97, 134.83, 133.30, 133.23, 131.95, 131.27, 128.66, 128.51, 127.84, 127.83, 127.10, 127.04, 126.74, 126.17, 125.81, 124.90, 121.12, 60.33, 20.70; HRMS (DART) $m/z$ calcd for C$_{22}$H$_{19}$OS [M+H]$^+$: 331.1157, found: 331.1163.

3-(2-Methylnaphthalen-1-yl)-4,5,6,7-tetrahydrobenzo[b]thiophene (3fa): Following the general procedure with 4,5,6,7-tetrahydrobenzo[b]thiophene (1f: 35 mg) and 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3fa (43 mg, 61%, C4/C5 = >99:1) as a colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.80 (d, $J = 7.9$ Hz, 1H), 7.74 (d, $J = 8.5$ Hz, 1H), 7.47–7.28 (m, 4H), 6.87 (s, 1H), 2.95–2.82 (m, 2H), 2.23 (s, 3H), 2.12–1.97 (m, 2H), 1.91–1.80 (m, 2H), 1.73–1.60 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 139.01, 135.86, 135.47, 134.38, 133.38, 133.16, 131.87, 128.44, 127.74, 127.24, 125.90, 125.85, 124.73, 119.37, 25.42, 24.60, 23.53, 22.67, 20.48; HRMS (DART) $m/z$ calcd for C$_{19}$H$_{19}$S [M+H]$^+$: 279.1207, found: 279.1204.
3-(2-Methylnaphthalen-1-yl)benzo[b]thiophene (3ga): Following the general procedure with benzo[b]thiophene (3g; 34 mg) with 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ga (50 mg, 73%, C4/C5 = >99:1) as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.97 (d, \(J = 8.1\) Hz, 1H), 7.86 (d, \(J = 8.1\) Hz, 1H), 7.84 (d, \(J = 8.5\) Hz, 1H), 7.46 (d, \(J = 8.5\) Hz, 1H), 7.42–7.32 (m, 4H), 7.30–7.19 (m, 2H), 7.15 (d, \(J = 8.1\) Hz, 1H), 2.21 (s, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 139.99, 139.49, 135.26, 135.11, 133.53, 132.02, 131.31, 128.60, 127.93, 127.81, 126.06, 125.90, 124.94, 124.74, 124.41, 124.21, 123.17, 122.68, 20.55; HRMS (DART) \(m/z\) calcd for C\(_{19}\)H\(_{15}\)S [M+H]\(^+\): 275.0894, found: 275.0892.

2,3,5-Trimethyl-4-(2-methylnaphthalen-1-yl)thiophene (3ha): Following the general procedure with 2,3,5-trimethylthiophene (1h: 32 mg) and 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ha (47 mg, 70%) as a white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.83 (d, \(J = 7.6\) Hz, 1H), 7.76 (d, \(J = 8.5\) Hz, 1H), 7.44–7.30 (m, 4H), 2.39 (s, 3H), 2.18 (s, 3H), 1.98 (s, 3H), 1.63 (s, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 137.20, 134.73, 133.28, 133.11, 132.94, 132.03, 130.55, 128.87, 128.49, 127.83, 127.21, 125.95, 125.62, 124.74, 20.05, 13.42, 13.32, 12.68; HRMS (DART) \(m/z\) calcd for C\(_{18}\)H\(_{19}\)S [M+H]\(^+\): 267.1208, found: 267.1206.
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4-(2-Methoxynaphthalen-1-yl)-2,3-dimethylthiophene (3ab): Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2-methoxynaphthalen-1-ylboronic acid (2b: 202 mg), the crude product was purified by preparative thin-layer chromatography (hexane/EtOAc = 49:1) to give 3ab (51 mg, 76%, C4/C5 = >99:1) as a white solid. 1H NMR (400 MHz, CDCl3) δ 7.87 (d, J = 9.0 Hz, 1H), 7.83–7.77 (m, 1H), 7.49–7.43 (m, 1H), 7.37–7.29 (m, 3H), 6.93 (s, 1H), 3.85 (s, 3H), 2.46 (s, 3H), 1.79 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 154.51, 137.19, 134.26, 133.88, 132.43, 129.13, 128.95, 127.55, 126.32, 125.27, 123.49, 120.82, 119.81, 113.59, 56.62, 13.80, 12.36; HRMS (DART) m/z calcd for C17H17O5S [M+H]+: 269.1007, found: 269.1007.

4-(2,4-Dimethynaphthalen-1-yl)-2,3-dimethylthiophene (3ac): Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2,4-dimethynaphthalen-1-ylboronic acid (2c: 200 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ac (49 mg, 73%, C4/C5 = >99:1) as a white solid. 1H NMR (400 MHz, CD2Cl2) δ 7.98 (d, J = 8.1 Hz, 1H), 7.46–7.40 (m, 1H), 7.39–7.30 (m, 2H), 7.28 (s, 1H), 6.82 (s, 1H), 2.70 (s, 3H), 2.46 (s, 3H), 2.17 (s, 3H), 1.69 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 140.80, 134.04, 133.56, 133.40, 133.36, 132.78, 132.11, 131.01, 129.32, 126.49, 125.56, 124.58, 123.91, 118.92, 20.31, 19.33, 13.75, 12.22; HRMS (DART) m/z calcd for C18H19S [M+H]+: 267.1208, found: 267.1207.

4-(2-Ethynaphthalen-1-yl)-2,3-dimethylthiophene (3ad): Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2-ethynaphthalen-1-ylboronic acid (2d: 200 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ad (46 mg, 69%, C4/C5...
= 98:2) as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.81 (d, \(J = 7.6\) Hz, 1H), 7.80 (d, \(J = 8.5\) Hz, 1H), 7.44 (d, \(J = 8.5\) Hz, 1H), 7.42–7.29 (m, 3H), 6.86 (s, 1H), 2.64–2.41 (m, 5H), 1.70 (s, 3H), 1.13 (t, \(J = 7.6\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 140.63, 140.22, 133.46, 133.10, 132.67, 131.88, 127.69, 127.65, 127.02, 126.10, 125.85, 124.82, 119.07, 26.93, 15.73, 13.75, 12.31; HRMS (DART) \(m/z\) calcd for C\(_{18}\)H\(_{19}\)S \([\text{M+H}]^+\): 267.1207, found: 267.1203.

4-(2-Isopropynaphthalen-1-yl)-2,3-dimethylthiophene (3ae): Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2-isopropynaphthalen-1-ylboronic acid (2e: 214 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ae (44 mg, 62%, C4/C5 = 98:2) as a white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.85 (d, \(J = 8.6\) Hz, 1H), 7.81 (d, \(J = 8.6\) Hz, 1H), 7.52 (d, \(J = 8.6\) Hz, 1H), 7.42–7.37 (m, 1H), 7.36–7.29 (m, 2H), 6.85 (s, 1H), 2.92 (sep, \(J = 6.8\) Hz, 1H), 2.47 (s, 3H), 1.72 (s, 3H), 1.20 (d, \(J = 6.8\) Hz, 3H), 1.18 (d, \(J = 6.8\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 144.89, 140.33, 133.58, 133.40, 132.66, 132.26, 131.85, 127.95, 127.64, 126.38, 125.84, 124.89, 123.65, 118.98, 30.52, 24.54, 23.20, 13.77, 12.35; HRMS (DART) \(m/z\) calcd for C\(_{19}\)H\(_{21}\)S \([\text{M+H}]^+\): 281.1364, found: 281.1369.

4-(2,6-Dimethoxyphenyl)-2,3-dimethylthiophene (3af): Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2,6-dimethoxyphenylboronic acid (2f: 182 mg), the crude product was purified by preparative thin-layer chromatography (hexane/EtOAc = 49/1) to give 3af (47 mg, 76%, C4/C5 = >99:1) as a white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.27 (t, \(J = 8.4\) Hz, 1H), 6.88 (s, 1H), 6.62 (d, \(J = 8.5\) Hz, 2H), 3.73 (s, 6H), 2.39 (s, 3H), 1.86 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 158.35, 134.64,
133.64, 131.60, 128.67, 119.70, 115.09, 103.93, 55.84, 13.80, 12.44; HRMS (DART) m/z calcd for C_{14}H_{17}O_{2}S [M+H]^+: 249.0953, found: 239.0949.

**4-(2,6-Dimethylphenyl)-2,3-dimethylthiophene (3ag):** Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2,6-dimethylphenylboronic acid (2g: 150 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ag (36 mg, 67%, C4/C5 = >99:1) as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.18–7.11 (m, 1H), 7.07 (d, \(J = 7.9\) Hz, 2H), 6.69 (s, 1H), 2.41 (s, 3H), 2.01 (s, 6H), 1.76 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.95, 137.50, 137.28, 132.91, 132.08, 127.08, 126.99, 117.18, 20.36, 13.69, 12.04; HRMS (DART) m/z calcd for C_{14}H_{17}S [M+H]^+: 217.0501, found: 217.0503.

**4-Mesityl-2,3-dimethylthiophene (3ah):** Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2,4,6-trimethylphenylboronic acid (2h: 164 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ah (41 mg, 72%, C4/C5 = >99:1) as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.91 (s, 2H), 6.68 (s, 1H), 2.40 (s, 3H), 2.31 (s, 3H), 1.97 (s, 6H), 1.76 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.95, 137.14, 136.60, 134.53, 132.75, 132.26, 127.81, 117.34, 21.05, 20.26, 13.72, 12.09; HRMS (DART) m/z calcd for C_{15}H_{19}S [M+H]^+: 231.1207, found: 231.1209.
2,3-Dimethyl-4-(2-(trifluoromethyl)phenyl)thiophene (3ai): Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and 2-(trifluoromethyl)phenylboronic acid (2i: 190 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3ai (48 mg, 75%, C4/C5 = 91:9) as a colorless oil. $^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.75 (d, $J$ = 7.6 Hz, 1H), 7.58 (t, $J$ = 7.6 Hz, 1H), 7.48 (t, $J$ = 7.6 Hz, 1H), 7.26 (d, $J$ = 7.6 Hz, 1H), 6.89 (s, 1H), 2.40 (s, 3H), 1.84 (s, 3H); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 140.16, 137.43, 133.12, 132.77, 132.73, 131.72, 129.69 (q, $J$ = 29.1 Hz), 127.92, 126.30 (q, $J$ = 4.7 Hz), 124.60 (q, $J$ = 274.4 Hz), 119.93, 13.70, 12.62; HRMS (DART) m/z calcd for C$_{13}$H$_{12}$F$_3$S [M+H]$^+$: 257.0612, found: 257.0615.

3-(4,5-Dimethylthiophen-3-yl)-2,6-dimethoxypyridine (3aj): Following the general procedure with 2,3-dimethylthiophene (1a: 28 mg) and (2,6-dimethoxypyridin-3-yl)boronic acid (2j: 183 mg), the crude product was purified by preparative thin-layer chromatography (hexane/EtOAc = 6:1) to give 3aj (31 mg, 50%, C4/C5 = >99:1) as a pale yellow solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39 (d, $J$ = 8.1 Hz, 1H), 6.89 (s, 1H), 6.34 (d, $J$ = 7.9 Hz, 1H), 3.95 (s, 3H), 3.93 (s, 3H), 2.39 (s, 3H), 1.96 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.35, 159.75, 142.29, 138.40, 133.05, 132.73, 119.11, 111.95, 100.35, 53.55, 53.34, 13.6, 12.67; HRMS (DART) m/z calcd for C$_{13}$H$_{16}$NO$_2$S [M+H]$^+$: 250.0902, found: 250.0907.
Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

3-(2,6-Dimethoxyphenyl)-2,4,5-trimethylthiophene (3hf): Following the general procedure with 2,3,5-dimethylthiophene (1h: 32 mg) and (2,6-dimethoxyphenyl)boronic acid (2f: 182 mg), the crude product was purified by preparative thin-layer chromatography (hexane/EtOAc = 10:1) to give 3hf (46 mg, 70%) as a white solid. 

1H NMR (400 MHz, CDCl₃) δ 7.31–7.24 (m, 1H), 6.63 (d, J = 8.5 Hz, 2H), 3.74 (s, 6H), 2.33 (s, 3H), 2.12 (s, 3H), 1.79 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 158.36, 133.45, 131.51, 128.72, 127.74, 114.23, 103.85, 55.76, 13.80, 13.40, 12.79; HRMS (DART) m/z calcd for C₁₅H₁₉O₂S [M+H]^+: 263.1106, found: 263.1104.

3-(2,6-Dimethylphenyl)-2,4,5-trimethylthiophene (3hg): Following the general procedure with 2,3,5-dimethylthiophene (1h: 32 mg) and (2,6-dimethylphenyl)boronic acid (2g: 150 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3hg (28 mg, 48%) as a colorless oil. 

1H NMR (400 MHz, CDCl₃) δ 7.17–7.06 (m, 3H), 2.34 (s, 3H), 2.02 (s, 3H), 1.97 (s, 6H), 1.69 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 138.71, 137.34, 136.74, 131.77, 128.88, 128.81, 127.01, 19.99, 13.28, 13.21, 12.56; HRMS (DART) m/z calcd for C₁₅H₁₉S [M+H]^+: 231.1208, found: 231.1207.

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**3-Mesityl-2,4,5-trimethylthiophene (3hh):** Following the general procedure with 2,3,5-dimethylthiophene (1h: 32 mg) and mesitylboronic acid (2h: 164 mg), the crude product was purified by preparative thin-layer chromatography (hexane) to give 3hh (35 mg, 58%) as a colorless oil. 

\[ \text{H NMR (400 MHz, CDCl}_3 \text{): } \delta 6.91 (s, 2H), 2.34 (s, 3H), 2.32 (s, 3H), 2.02 (s, 3H), 1.93 (s, 6H), 1.69 (s, 3H). \]

\[ \text{13C NMR (100 MHz, CDCl}_3 \text{): } \delta 138.71, 137.16, 136.42, 133.72, 131.98, 128.90, 128.65, 127.84, 21.11, 19.91, 13.30, 13.25, 12.62. \]

HRMS (DART) m/z calcd for C\(_{16}\)H\(_{21}\)S [M+H\(^+\)]: 245.1364, found: 245.1363.

**2-Mesityl-3-methylbenzofuran (3ih):** Following the general procedure with 3-methylbenzofuran (1i: 33 mg) and mesitylboronic acid (2h: 164 mg), the crude product was purified by preparative thin-layer chromatography (hexane/EtOAc = 99:1) to give 3ih (42 mg, 67%) as a colorless oil. 

\[ \text{H NMR (400 MHz, CDCl}_2 \text{Cl}_2 \text{): } \delta 7.61–7.55 (m, 1H), 7.50–7.43 (m, 1H), 7.33–7.25 (m, 2H), 7.00 (s, 2H), 2.36 (s, 3H), 2.13 (s, 6H), 2.08 (s, 3H); \]

\[ \text{13C NMR (100 MHz, CDCl}_2 \text{Cl}_2 \text{): } \delta 154.88, 151.62, 139.54, 139.26, 130.51, 128.41, 127.25, 123.96, 122.44, 119.52, 113.13, 111.21, 21.33, 19.97, 8.39; \]

HRMS (DART) m/z calcd for C\(_{18}\)H\(_{19}\)O [M+H\(^+\)]: 251.1436, found: 251.1434.

**2-Mesitylbenzofuran (3jh):** Following the general procedure with benzofuran (1j: 30 mg) and mesitylboronic acid (2h: 164 mg), the crude product was purified by preparative thin-layer chromatography (hexane/EtOAc = 99:1) to give 3jh (52 mg, 87%) as a colorless oil. 

\[ \text{H NMR (400 MHz, CDCl}_3 \text{): } \delta 7.63–7.58 (m, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.32–7.22 (m, 2H), 6.96 (s, 2H), 6.64 (s, 1H), 2.33 (s, 3H), 2.22 (s, 6H); \]

\[ \text{13C NMR (100 MHz, CDCl}_3 \text{): } \delta 155.02, 154.71, 139.01, 138.38, 128.83, 127.69, 123.64, 122.55, 120.67, 111.14, 106.04, 21.18, 20.49; \]

HRMS (DART) m/z calcd for C\(_{17}\)H\(_{17}\)O [M+H\(^+\)]: 237.1279, found: 237.1279.
2-Mesityl-1,3-dimethyl-1H-indole (3kh): Following the general procedure with 1,3-dimethyl-1H-indole (1k: 36 mg) and mesitylboronic acid (2h: 164 mg), the crude product was purified by preparative thin-layer chromatography (hexane/EtOAc = 20:1) to give 3kh (16 mg, 24%) as a white solid. \( ^1 \text{H NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 7.68–7.58 (m, 1H), 7.33 (d, \( J = 8.2 \text{ Hz} \), 1H), 7.25–7.20 (m, 1H), 7.17–7.12 (m, 1H), 6.98 (s, 2H), 3.39 (s, 3H), 2.36 (s, 3H), 2.06 (s, 3H), 1.97 (s, 6H); \( ^{13} \text{C NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 138.84, 138.17, 136.78, 136.15, 128.49, 128.30, 127.94, 120.74, 118.53, 118.51, 108.96, 107.61, 29.65, 21.21, 19.99, 8.86; HRMS (DART) \( m/z \) calcd for C\(_{19}\)H\(_{22}\)N [M+H]\(^+\): 264.1752, found: 264.1752.

4. Enantioselective C–H Coupling

To a 20-mL screw cap glass vessel containing a magnetic stirring bar were added Pd(OAc)\(_2\) (5.6 mg, 0.025 mmol), L4 (5.6 mg, 0.025 mmol) and \( n \)-PrOH (0.1 mL). The mixture was stirred at 70 °C for 10 min and cooled to room temperature. To the mixture were added 2,3-dimethylthiophene (1a: 28 mg, 0.25 mmol), 2-methylnaphthalen-1-ylboronic acid (2a: 186 mg, 1.00 mmol) and TEMPO (156 mg, 1.00 mmol), and the mixture was stirred at 70 °C for 12 h under air. After cooling the reaction mixture to room temperature, the mixture was passed through a short pad of silica gel (EtOAc) and the filtrate was evaporated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane) to give (S)-3aa (40 mg, 63% yield, C4/C5 = 95:5, 41% ee) as a colorless oil. The enantiomeric
excess was determined by HPLC with a Chiracel OD-H column, UV detected at 254 nm, flow rate 1.0 mL/min (hexane). Retention times ($t_r$): major enantiomer $t_r = 11.0$ min, minor enantiomer $t_r = 9.5$ min (HPLC chart is shown in p. S81).

(S)-3ae (19 mg, 27% yield, C4/C5 = 93:7, 72% ee) was obtained by the reaction of 1a and 2-isopropynaphthalen-1-ylboronic acid (2e: 214 mg) as a colorless oil. Analytically pure compound was obtained by using GPC system. The enantiomeric excess was determined by HPLC with a Chiracel OD-H column, UV detected at 254 nm, flow rate 1.0 mL/min (hexane). Retention times ($t_r$): major enantiomer $t_r = 8.5$ min, minor enantiomer $t_r = 7.6$ min (HPLC chart is shown in p. S82). $[\alpha]_{D}^{21} +35.5 \ (c \ 1.00, \text{CHCl}_3)$

5. Effect of Reaction Parameters

The effect of reaction parameters (additive, equivalents of CF$_3$CO$_2$H, catalytic amount of Pd(OAc)$_2$, ligand, equivalents of TEMPO, and atmosphere) was investigated. The arylation of 2,3-dimethylthiophene (1a) with 2-methylnaphthalen-1-ylboronic acid (2a) was used as the model reaction.
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Supplementary Information (Yamaguchi, Yamaguchi, Studer, Itami)
Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

Table S1. Effect of additive.\textsuperscript{a}

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\textsuperscript{a} Conditions: 1a (0.25 mmol), 2a (1.0 mmol), Pd(OAc)\textsubscript{2} (0.025 mmol), L4 (0.025 mmol), TEMPO (1.0 mmol), additive (0.25 mmol), DMF (0.1 mL), 60 \textdegree C, 12 h, under air.
\textsuperscript{b} Isolated yield.
\textsuperscript{c} Determined by \textsuperscript{1}H NMR.

Table S2. Effect of CF\textsubscript{3}CO\textsubscript{2}H.\textsuperscript{a}

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\textsuperscript{a} Conditions: 1a (0.25 mmol), 2a (1.0 mmol), Pd(OAc)\textsubscript{2} (0.025 mmol), L5 (0.025 mmol), TEMPO (1.0 mmol), CF\textsubscript{3}CO\textsubscript{2}H (x mmol), DMF (0.1 mL), 80 \textdegree C, 12 h, under air.
\textsuperscript{b} Isolated yield.
\textsuperscript{c} Determined by \textsuperscript{1}H NMR.
Table S3. Investigation of reaction conditions.  

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<th>L5 (mol %)</th>
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$^a$: Conditions: 1a (0.25 mmol), 2a (1.0 mmol), Pd(OAc)$_2$ (0.025 mmol), L5 (0.025 mmol), TEMPO (1.0 mmol), CF$_3$CO$_2$H (0.75 mmol), DMF (0.1 mL), 80 °C, under air or oxygen atmosphere.  
$^b$: Isolated yield.  
$^c$: Determined by $^1$H NMR.

6. Determination of Absolute Stereochemistry

The absolute stereochemistry of coupling product 3ae was determined by X-ray crystallography after derivatization of both racemic (Scheme S1) and enantiomerically enriched 3ae (Scheme S2). Racemic coupling product (±)-3ae was converted into carboxylic acid (±)-5 in 3 steps (Scheme S1). Condensation of (±)-5 and (S)-1-phenethylamine gave a mixture of diastereomers 6a and 6b (ratio of 6a/6b = 1:1 by $^1$H NMR analysis, shown on p. S77). Finally, 6b was separated from the mixture of 6a and 6b by crystallization, and the absolute stereochemistry of 6b was determined to be R configuration by X-ray analysis. Therefore, compound 6a was determined to have S configuration.

The application of the above-mentioned procedure to enantiomerically enriched 3ae (63% ee) led to the formation of a mixture of 6a and 6b (ratio of 6a/6b = 4:1 by $^1$H NMR analysis, shown on p. S78) as shown in Scheme S2. According to these results, the enantioselective C–H arylation of thiophene 1a with arylboronic acid 2e using ligand L4 was found to selectively afford the S configuration of heterobiaryl 3ae.
**Supplementary Information** (Yamaguchi, Yamaguchi, Studer, Itami)

**Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling**

Scheme S1. Transformation for determination of absolute configuration.

Scheme S2. Transformation from enantiomerically enriched 3ae.

---

2-Bromo-3-(2-isopropynaphthalen-1-yl)-4,5-dimethylthiophene (4): To a solution of 3ae (194 mg, 0.69 mmol) in DMF (3.0 mL) was added N-bromosuccinimide (185 mg, 1.04 mmol). After stirring the mixture for 24 h at room temperature, the residue was purified by preparative thin-layer chromatography (hexane) to give brominated compound 4 (196 mg, 79%) as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ
under reduced pressure. The residue was purified by preparative thin layer chromatography (hexane/EtOAc = 1:1) to give the carboxylic acid 5: To a solution of 4 (234 mg, 0.65 mmol) in THF (5.0 mL) was slowly added n-BuLi (1.6 M in hexane, 447 µL, 0.72 mmol) at –78 °C. After stirring at –78 °C for 30 min, the solution of DMF (76 µL, 0.98 mmol) in THF (1.0 mL) was added and stirred at –78 °C for 1 h and room temperature for 1 h. The mixture was poured into saturated aqueous NaHCO₃, and then extracted with EtOAc. The organic layer was washed with water, brine, dried over anhydrous Na₂SO₄, and evaporated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/EtOAc = 5:1) to give a formyletad product (105 mg, 52%) as a yellow oil. To the resulting compound (49 mg, 0.16 mmol) in aqueous acetone (2.0 mL) was added NaClO₂ (29 mg, 0.32 mmol), NaH₂PO₄•H₂O (38 mg, 0.32 mmol) and 2-methyl-2-butene (39 mg, 0.56 mmol) and the mixture was stirred at room temperature for 2 days. The mixture was diluted with EtOAc and water, and then extracted with EtOAc. The organic layer was washed with brine, water, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. The residue was purified by preparative thin-layer chromatography (hexane/EtOAc = 1:1) to give the carboxylic acid 5 (49 mg, 96%) as a white solid. 

\[
\begin{align*}
\text{C NMR (100 MHz, DMSO-}\text{d}_6) & \delta 12.3 (\text{br s, 1H}), 7.97–7.83 (\text{m, 2H}), 7.58 (d, J = 8.5 \text{ Hz, 1H}), 7.48–7.29 (\text{m, 2H}), 7.05 (d, J = 8.5 \text{ Hz, 1H}), 2.72–2.60 (\text{m, 1H}), 2.47 (s, 3H), 1.56 (s, 3H), 1.15 (d, J = 6.7 \text{ Hz, 3H}), 1.11 (d, J = 6.7 \text{ Hz, 3H});
\end{align*}
\]

\[\text{13C NMR (100 MHz, DMSO-}\text{d}_6) \delta 162.46, 145.47, 142.95, 139.67, 135.29, 131.65, 131.50, 131.26, 127.84, 127.77, 126.27, 126.08, 124.88, 123.62, 30.70, 23.31, 23.08, 13.76, 12.19; \]

HRMS (FAB) \(m/z\) calcd for \(\text{C}_{20}\text{H}_{20}\text{O}_2\text{S} [\text{M}+]\): 325.1184, found: 324.1175.

\((R)-3-(2\text{-Isopropynaphthalen-1-yl})-4,5\text{-dimethylthiophene-2-carboxamide (6b):}\) To a solution of carboxylic acid 5 (36 mg, 0.11 mmol) and (S)-1-phenylethylamine (17 µL, 0.13 mmol) in DMF (1.0 mL) were added 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (25 mg, 0.13 mmol) and 1-hydroxybenzotriazole (15 mg, 0.11 mmol). After stirring the mixture at room temperature for 12 h, the mixture was poured into saturated aqueous NaHCO₃, and then extracted with EtOAc. The organic layer was washed with water, brine, dried over anhydrous Na₂SO₄, and evaporated under reduced pressure. The residue was purified by preparative thin-layer chromatography.
(hexane/EtOAc = 5:1) to give a mixture of 6a and 6b (39 mg, 83%) as a pale yellow oil. To the residue was added hexane (1.0 mL) and the resulting precipitate was collected by filtration to give the single isomer product 6b (11 mg) as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.95 (d, $J = 8.5$ Hz, 1H), 7.86 (d, $J = 8.1$ Hz, 1H), 7.60 (d, $J = 8.5$ Hz, 1H), 7.52–7.43 (m, 1H), 7.39–7.31 (m, 1H), 7.29–7.20 (m, 1H), 7.03–6.95 (m, 1H), 6.94–6.84 (m, 2H), 6.20 (d, $J = 7.6$ Hz, 2H), 5.36 (d, $J = 7.6$ Hz, 1H), 4.85–4.75 (m, 1H), 2.87 (sep, $J = 6.7$ Hz, 1H), 2.48 (s, 3H), 1.71 (s, 3H), 1.24 (d, $J = 6.7$ Hz, 3H), 1.23 (d, $J = 6.7$ Hz, 3H), 0.90 (d, $J = 6.7$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 160.76, 145.47, 143.01, 139.56, 138.78, 134.87, 132.36, 132.33, 132.08, 129.93, 129.52, 128.12, 128.02, 127.19, 126.45, 125.97, 125.62, 124.99, 123.98, 48.41, 30.91, 23.81, 23.49, 22.61, 14.09, 12.58; HRMS (DART) $m/z$ calcd for C$_{28}$H$_{30}$NOS [M+H]$^+$: 428.2048, found: 428.2052.
7. X-ray Crystal Structure Analysis of 6b

A suitable crystal was mounted with mineral oil on a glass fiber and transferred to the goniometer of a Rigaku Saturn CCD diffractometer. Graphite-monochromated Mo Kα radiation (λ = 0.71070 Å) was used. The structures were solved by direct methods with (SIR-97)\(^6\) and refined by full-matrix least-squares techniques against \(F^2\) (SHELXL-97).\(^7\) The intensities were corrected for Lorentz and polarization effects. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed using AFIX instructions. Details of the crystal data and a summary of the intensity data collection parameters for 6b are listed in Table S4.

<table>
<thead>
<tr>
<th>Table S4. Crystallographic data and structure refinement details for 6b.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6b</strong></td>
</tr>
<tr>
<td>formula</td>
</tr>
<tr>
<td>fw</td>
</tr>
<tr>
<td>(T) (K)</td>
</tr>
<tr>
<td>(\lambda) (Å)</td>
</tr>
<tr>
<td>cryst syst</td>
</tr>
<tr>
<td>space group</td>
</tr>
<tr>
<td>(a), (Å)</td>
</tr>
<tr>
<td>(b), (Å)</td>
</tr>
<tr>
<td>(c), (Å)</td>
</tr>
<tr>
<td>(\alpha), (deg)</td>
</tr>
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<tr>
<td>(\gamma), (deg)</td>
</tr>
<tr>
<td>(V), (Å(^3))</td>
</tr>
<tr>
<td>(Z)</td>
</tr>
<tr>
<td>(D_{\text{calc}}), (g / cm(^3))</td>
</tr>
<tr>
<td>(m), (mm(^{-1}))</td>
</tr>
<tr>
<td>(F(000))</td>
</tr>
<tr>
<td>cryst size (mm)</td>
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<tr>
<td>2θ range, (deg)</td>
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<tr>
<td>reflns collected</td>
</tr>
<tr>
<td>indep reflns/R(_{int})</td>
</tr>
<tr>
<td>params</td>
</tr>
<tr>
<td>GOF on (F^2)</td>
</tr>
<tr>
<td>(R_1), wR(_2) [I&gt;2σ(I)]</td>
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<tr>
<td>(R_1), wR(_2) (all data)</td>
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<tr>
<td>abs struct param</td>
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</table>


\(^7\) G. M. Sheldrick, University of Göttingen: Göttingen, Germany, 1997.
**Figure S1.** ORTEP drawing of 6b with 50% thermal ellipsoid. All hydrogen atoms except N–H and C*–H are omitted for clarity.
8. Computational Study

The Gaussian 03 program running on a SGI Altix4700 system was used for optimization (B3LYP/6-31G(d)). All structures were optimized without any symmetry assumptions. Zero-point energy, enthalpy, and Gibbs free energy at 298.15 K and 1 atm were estimated from the gas-phase studies unless otherwise noted. Harmonic vibration frequency calculations at the same level were performed to verify all stationary points as local minima (with no imaginary frequency) or transition states (with one imaginary frequency). IRC calculations were also performed to check transition states. Visualization of the results was performed by use of POV-Ray for Windows v3.5 software.

Table S5. Uncorrected and thermal-corrected (298K) energies of stationary points (Hartree).

<table>
<thead>
<tr>
<th>compound</th>
<th>E</th>
<th>E + ZPE</th>
<th>H</th>
<th>G</th>
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<tr>
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<td>-1016.084792</td>
<td>-1016.068980</td>
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<tr>
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a) E: electronic energy; ZPE: zero-point energy; H (=E+ZPE+E\text{vib}+E\text{rot}+E\text{trans}+RT): sum of electronic and thermal enthalpies; G (=H–TS): sum of electronic and thermal free energies.

Table S6. Cartesian coordinates of optimized species.

**3ba**

<table>
<thead>
<tr>
<th>Atom</th>
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<th>y</th>
<th>z</th>
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</thead>
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**TS-1**

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**TS-2**

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<td>H</td>
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<td>-0.968604</td>
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9. Racemization Study

A preliminary racemization study was examined using enantiomerically enriched (R)-3aa, which was obtained by chiral HPLC separation (Table S7). When (R)-3aa was heated at 80 °C, any racemization was not observed. When (R)-3aa was heated at 120 °C, obvious erosion of ee was observed.

Table S7. Racemization examination.

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>80 °C (hexane)</td>
<td>95% ee</td>
</tr>
<tr>
<td>120 °C (DMF)</td>
<td>13% ee</td>
</tr>
</tbody>
</table>
10. $^1$H and $^{13}$C NMR Spectra

$^1$H NMR (400 MHz, CDCl$_3$) of 3aa:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3aa:
Supplementary Information (Yamaguchi, Yamaguchi, Studer, Itami)

Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

\(^1\)H NMR (400 MHz, CDCl\(_3\)) of 3ba:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ba:
\(^1\)H NMR (400 MHz, CDCl\(_3\)) of 3ca:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ca:
$^1$H NMR (400 MHz, CDCl$_3$) of 3da:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3da:
1H NMR (400 MHz, CDCl₃) of 3ea:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ea:
1H NMR (400 MHz, CDCl3) of 3fa:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3fa:
$^1$H NMR (400 MHz, CDCl$_3$) of 3ga:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ga:
^{1}H NMR (400 MHz, CDCl\textsubscript{3}) of 3ha:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ha:
\(^1\)H NMR (400 MHz, CDCl\(_3\)) of 3ab:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ab:
Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

\(^1\)H NMR (400 MHz, CD\(_2\)Cl\(_2\)) of 3ac:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ac:
Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

$^1$H NMR (400 MHz, CDCl$_3$) of 3ad:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ad:
$^1$H NMR (400 MHz, CDCl$_3$) of 3ae:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ae:
$^1$H NMR (400 MHz, CDCl$_3$) of 3af:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3af:
$^1$H NMR (400 MHz, CDCl$_3$) of 3ag:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ag:
Supplementary Information (Yamaguchi, Yamaguchi, Studer, Itami)

Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

1H NMR (400 MHz, CDCl₃) of 3ah:
Supplementary Information (Yamaguchi, Yamaguchi, Studer, Itami)

Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

$^{13}$C NMR (100 MHz, CDCl$_3$) of 3ah:
Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) of 3ai:
$^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) of 3ai:
$^1$H NMR (400 MHz, CDCl$_3$) of 3aj:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3aj:
\(^1\)H NMR (400 MHz, CDCl\(_3\)) of 3hf:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3hf:
Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

$^1$H NMR (400 MHz, CDCl$_3$) of 3hg:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3hg:
$^1$H NMR (400 MHz, CDCl$_3$) of 3hh:
Supplementary Information (Yamaguchi, Yamaguchi, Studer, Itami)

Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

$^{13}$C NMR (100 MHz, CDCl$_3$) of 3hh:
1H NMR (400 MHz, CD2Cl2) of 3ih:
$\text{Hindered Biaryls by } \text{C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling}$

$^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) of 3ih:

![NMR spectrum of 3ih](image)
Supplementary Information (Yamaguchi, Yamaguchi, Studer, Itami)

Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

$^1$H NMR (400 MHz, CDCl$_3$) of 3jh:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3jh:
$^1$H NMR (400 MHz, CDCl$_3$) of 3kh:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 3kh:
1H NMR (400 MHz, CD2Cl2) of 4:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 4:
Supplementary Information (Yamaguchi, Yamaguchi, Studer, Itami)
Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)) of 5:
Supplementary Information (Yamaguchi, Yamaguchi, Studer, Itami)

Hindered Biaryls by C–H Coupling: Bisoxazoline-Pd Catalysis Leading to Enantioselective C–H Coupling

$^{13}$C NMR (100 MHz, DMSO-$d_6$) of 5:
$^1$H NMR (400 MHz, CDCl$_3$) of 6a+6b from racemate 3ae:
*H NMR (400 MHz, CDCl₃) of 6a+6b from enantiomerically enriched 3ae:
$^1$H NMR (400 MHz, CDCl$_3$) of 6b:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 6b:
11. HPLC Chart

HPLC chart of 3aa

racemate

\[ \text{OD-H} \circledast \]
254 nm
hexane
1.0 mL/min

Enantiomerically enriched

\[ \text{OD-H} \circledast \]
254 nm
hexane
1.0 mL/min
HPLC chart of 3ae:

racemate

OD-H @
254 nm
hexane
1.0 mL/min

retention time  area
7.057 13491841
7.819 946765
8.312 15780
8.600 13263610

Enantiomerically enriched with L4

OD-H @
254 nm
hexane
1.0 mL/min

retention time  area
7.624 695918
8.522 4196117

Enantiomerically enriched with ent-L4

OD-H @
254 nm
hexane
1.0 mL/min

retention time  area
7.047 43634169
8.159 9127
8.489 3349
8.757 6132047

L4

ent-L4