Diversity-Oriented Synthesis of Tamoxifen-type Tetrasubstituted Olefins

Kenichiro Itami,* Toshiyuki Kamei, and Jun-ichi Yoshida*

*Department of Synthetic Chemistry & Biological Chemistry, Graduate School of Engineering,
Kyoto University, Nishikyo-ku, Kyoto 615-8510, Japan*

General. ^1H and ^{13}C NMR spectra were recorded on Varian GEMINI-2000 (^1H 300 MHz, ^{13}C 75 MHz) and JEOL A-500 (^1H 500 MHz, ^{13}C 125 MHz) spectrometers in CDCl_3 . EI mass spectra were recorded on JMS-SX102A spectrometer. FAB mass spectra were recorded on JMS-HX110A spectrometer. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. $\text{Pd}[\text{P}(t\text{-Bu})_3]_2$ was purchased from Strem Chemicals, Inc. and used as received.

1-Butynyldimethyl(2-pyridyl)silane (1).

To a solution of dichlorodimethylsilane (25.9 g, 200 mmol) in dry Et_2O (200 mL) was added a solution of 1-butyne(magnesium chloride) (100 mmol, 1.18 M) in THF at 0 $^\circ\text{C}$. After stirring the mixture at room temperature for 12 h, dry hexane (100 mL) was added to the mixture. Filtration, removal of solvents, and subsequent distillation afforded 1-butyne-(chloro)dimethylsilane (7.53 g, 51%) as colorless liquid. Bp 67–68 $^\circ\text{C}/55$ mmHg. ^1H NMR (300 MHz, CDCl_3) δ 0.53 (s, 6H), 1.15 (t, $J = 7.2$ Hz, 3H), 2.27 (q, $J = 7.2$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 3.8, 13.2, 13.5, 80.0, 111.6. IR (neat) 2979, 2180, 1314, 1256, 1044 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_6\text{H}_{11}\text{ClSi}$: 146.0319, found 146.0316.

To a solution of 2-bromopyridine (15.8 g, 100 mmol) in dry THF (100 mL) was added a solution of *i*-propylmagnesium chloride (100 mmol, 1.88 M) in THF at room temperature, and the mixture was stirred for 3 h. The resultant solution of 2-pyridylmagnesium chloride was added to a solution of 1-butyne-(chloro)dimethylsilane (15.1 g, 103 mmol) in THF (100 mL) at 0 $^\circ\text{C}$. After stirring the mixture at room temperature for 15 h, saturated aq NaHCO_3 (50 mL) was added to the mixture. Organic phase was separated and aqueous phase was extracted by Et_2O (100 mL $\times$ 3). The combined organic phase was

dried over MgSO_4 . Removal of solvents under reduced pressure and subsequent distillation afforded **1** (11.6 g, 61%) as colorless liquid. Bp 101–104 °C/7.0 mmHg. ^1H NMR (300 MHz, CDCl_3) δ 0.41 (s, 6H), 1.15 (t, J = 7.5 Hz, 3H), 2.27 (q, J = 7.5 Hz, 2H), 7.17 (ddd, J = 7.5, 4.8, 1.5 Hz, 1H), 7.57 (td, J = 7.5, 1.5 Hz, 1H), 7.72 (dt, J = 7.5, 1.2 Hz, 1H), 8.73 (ddd, J = 4.8, 1.5, 1.2 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ -1.5, 13.6 (two carbons), 80.8, 111.2, 122.9, 129.4, 134.1, 150.0, 165.4. IR (neat) 2979, 2176, 1576, 1417 cm^{-1} . HRMS (FAB) m/z calcd for $\text{C}_{11}\text{H}_{16}\text{NSi}$ (MH^+): 190.1052, found 190.1051.

1-Butynyldimethyl(3-pyridyl)silane. The title compound was prepared according to the procedure used for the preparation of **1**. Yield: 69%. Bp 130–132 °C/6.4 mmHg. ^1H NMR (300 MHz, CDCl_3) δ 0.42 (s, 6H), 1.19 (t, J = 7.5 Hz, 3H), 2.30 (q, J = 7.5 Hz, 2H), 7.28 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H), 7.91 (dt, J = 7.5, 1.8 Hz, 1H), 8.61 (dd, J = 4.8, 1.8 Hz, 1H), 8.80 (dd, J = 1.8, 1.2 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ -0.9, 13.5, 13.6, 80.2, 111.8, 123.1, 132.5, 141.3, 150.2, 154.1. IR (neat) 2979, 2176, 1574, 1559, 1395 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{11}\text{H}_{15}\text{NSi}$: 189.0974, found 189.0974.

1-Butynyldimethyl(4-pyridyl)silane. The title compound was prepared according to the procedure used for the preparation of **1**. Yield: 16%. Bp 103–105 °C/2.4 mmHg. ^1H NMR (300 MHz, CDCl_3) δ 0.39 (s, 6H), 1.18 (t, J = 7.5 Hz, 3H), 2.29 (q, J = 7.5 Hz, 2H), 7.49 (dm, J = 4.8 Hz, 2H), 8.58 (dm, J = 4.8 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ -1.3, 13.58, 13.61, 79.8, 112.0, 128.3, 147.6, 148.7. IR (neat) 3054, 2178, 1578, 1404 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{11}\text{H}_{15}\text{NSi}$: 189.0974, found 189.0976.

1-Butynyldimethylphenylsilane.¹ To a solution of chlorodimethylphenylsilane (5.1 g, 30 mmol) in dry THF (30 mL) was added a solution of 1-butylnylmagnesium chloride (33 mmol, 2.00 M) in THF at 0 °C. After stirring the mixture at room temperature for 17 h and then at 70 °C (reflux) for 7 h, H_2O (20 mL) was added to the mixture. Organic phase was separated and aqueous phase was extracted by EtOAc (20 mL $\times$ 3). The combined organic phase was dried over MgSO_4 . Removal of solvents under reduced pressure and subsequent distillation afforded the title compound (3.74 g, 66%) as colorless liquid. Bp 97–99 °C/6.5 mmHg. ^1H NMR (300 MHz, CDCl_3) δ 0.41 (s, 6H), 1.20 (t, J = 7.5 Hz, 3H), 2.31 (q, J = 7.5 Hz, 2H), 7.35–7.42 (m, 3H), 7.62–7.68 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ -0.6, 13.6, 13.8, 81.4, 110.9, 127.8, 129.2, 133.6, 137.6. IR (neat) 2979, 2176, 1429 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{12}\text{H}_{16}\text{Si}$: 188.1021, found 188.1020.

(1) Fleming, I.; Mwaniki, J. M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1237.

Typical Procedure of Cu-Catalyzed Carbomagnesation across **1** (Eq 1).

To a suspension of 1-butynyldimethyl(2-pyridyl)silane (**1**: 66.6 mg, 0.35 mmol) and CuI (17.2 mg, 0.09 mmol) in dry Et₂O (0.6 mL) was added a solution of phenylmagnesium iodide (0.30 mmol, 1.20 M) in Et₂O at 0 °C. After stirring the mixture at 0 °C for 6 h, H₂O (1 mL) and 28% *aq* NH₃ (1 mL) were added to the mixture. Organic phase was separated and aqueous phase was extracted by EtOAc (2 mL × 3). Removal of solvents under reduced pressure afforded the crude **2**. The yield was determined to be 90% by ¹H-NMR analysis using 1,2-dichloroethene as an internal standard. ¹H NMR (300 MHz, CDCl₃) δ 0.52 (s, 6H), 0.85 (t, *J* = 7.5 Hz, 3H), 2.60 (q, *J* = 7.5 Hz, 2H), 5.94 (s, 1H), 7.18–7.23 (m, 1H), 7.25–7.35 (m, 3H), 7.44 (dm, *J* = 8.1 Hz, 2H), 7.60 (dm, *J* = 3.6 Hz, 2H), 8.81 (ddd, *J* = 4.5, 1.5, 1.2 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ –1.6, 13.7, 28.4, 122.7, 123.9, 126.3, 127.4, 128.1, 129.4, 134.0, 142.8, 150.1, 161.1, 167.7. IR (neat) 2967, 1593, 1574, 1418, 1246 cm^{–1}. HRMS (EI) *m/z* calcd for C₁₇H₂₁NSi: 267.1443, found 267.1442.

Typical Procedure of Catalytic One-Pot Diarylation of **1** (Table 1).

To a suspension of 1-butynyldimethyl(2-pyridyl)silane (**1**: 190.5 mg, 1.01 mmol) and CuI (57.0 mg, 0.30 mmol) in dry Et₂O (2 mL) was added a solution of phenylmagnesium iodide (Ar¹MgI: 1.50 mmol, 1.93 M) in Et₂O at 0 °C. After stirring the mixture for 6 h, a solution of 4-[2-(*N,N*-dimethylamino)ethoxy]phenyl iodide (Ar²I: 435.8 mg, 1.50 mmol) and Pd[P(*t*-Bu)₃]₂ (25.2 mg, 0.05 mmol) in dry THF (2 mL) were added to the mixture. The resultant mixture was stirred at 40 °C for 16 h. After cooling the reaction mixture to room temperature, H₂O (ca. 10 mL) was added to the mixture. Organic phase was separated and aqueous phase was extracted by CHCl₃ (10 mL × 3). The combined organic phase was washed with H₂O (10 mL × 2) and dried over MgSO₄. Removal of solvents under

reduced pressure and subsequent silica gel chromatography (CHCl₃/MeOH/Et₃N = 100/10/1) afforded **3ac** (236.1 mg, 55%) as pale yellow oil. The stereochemistry was determined to be 88% *E* by ¹H-NMR analysis.

3aa: 80% yield, 92% *E*. ¹H NMR (300 MHz, CDCl₃) δ 0.37 (s, 6H), 0.70 (t, *J* = 7.5 Hz, 3H), 2.52 (q, *J* = 7.5 Hz, 2H), 6.83 (dm, *J* = 6.9 Hz, 2H), 6.88–6.95 (m, 3H), 6.98–7.09 (m, 5H), 7.21 (ddd, *J* = 7.5, 5.1, 1.5 Hz, 1H), 7.62 (td, *J* = 7.5, 1.5 Hz, 1H), 7.69 (td, *J* = 7.5, 1.5 Hz, 1H), 8.82 (ddd, *J* = 5.1, 1.8, 1.2 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ -1.0, 12.8, 31.7, 122.6, 124.5, 125.7, 127.2, 127.3, 128.7, 129.2, 129.4, 133.9, 137.3, 142.4, 144.1, 150.1, 157.3, 168.0. IR (KBr) 2973, 1574, 1248, 1143, 812, 700 cm⁻¹. HRMS (EI) *m/z* calcd for C₂₃H₂₅NSi: 343.1756, found 343.1755.

3ab: 60% yield, 92% *E*. ¹H NMR (300 MHz, CDCl₃) δ 0.37 (s, 6H), 0.68 (t, *J* = 7.5 Hz, 3H), 2.50 (q, *J* = 7.5 Hz, 2H), 3.67 (s, 3H), 6.58 (d, *J* = 9.0 Hz, 2H), 6.73 (d, *J* = 9.0 Hz, 2H), 6.89–7.15 (m, 5H), 7.20 (ddd, *J* = 7.5, 4.8, 1.5 Hz, 1H), 7.57–7.70 (m, 2H), 8.81 (dm, *J* = 4.8 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ -1.0, 12.7, 31.7, 54.9, 112.7, 122.5, 125.6, 127.2, 128.7, 129.4, 130.1, 134.0, 136.3, 136.5, 142.5, 150.1, 156.6, 157.4, 168.1. IR (KBr) 1574, 1506, 1242 cm⁻¹. HRMS (EI) *m/z* calcd for C₂₄H₂₇NOSi: 373.1862, found 373.1855.

3ac: 55% yield, 88% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.36 (s, 6H), 0.68 (t, J = 7.5 Hz, 3H), 2.29 (s, 6H), 2.49 (q, J = 7.5 Hz, 2H), 2.63 (t, J = 5.7 Hz, 2H), 3.91 (t, J = 5.7 Hz, 2H), 6.58 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.4 Hz, 2H), 6.90–7.25 (m, 6H), 7.60 (td, J = 7.5, 1.2 Hz, 1H), 7.66 (d, J = 7.5 Hz, 1H), 8.80 (dm, J = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ -1.0, 12.7, 31.7, 45.9, 58.3, 65.6, 113.4, 122.5, 125.6, 127.2, 128.7, 129.4, 130.0, 133.9, 136.4, 136.6, 142.5, 150.1, 155.9, 157.4, 168.2. IR (neat) 2971, 1505, 1242 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{27}\text{H}_{34}\text{N}_2\text{OSi}$: 430.2440, found 430.2440.

The stereochemistry of major product (**3ac**) was determined by the NOE experiments. Representative results are shown below.

3ad: 75% yield, 95% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.39 (s, 6H), 0.71 (t, J = 7.2 Hz, 3H), 2.54 (q, J = 7.2 Hz, 2H), 6.86–6.96 (m, 4H), 6.96–7.10 (m, 3H), 7.15–7.30 (m, 3H), 7.55–7.65 (m, 2H), 8.80 (dd, J = 4.8, 1.5 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ -1.1, 12.7, 31.8, 122.7, 124.2 (q, $J_{\text{C-F}}$ = 3.8 Hz), 124.4 (q, $J_{\text{C-F}}$ = 271.6 Hz), 126.1, 126.7 (q, $J_{\text{C-F}}$ = 32.0 Hz), 127.4, 128.5, 129.3, 129.4, 134.0, 136.5, 141.9, 148.2, 150.2, 158.3, 167.4. IR (neat) 2973, 1612, 1325 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{24}\text{H}_{24}\text{F}_3\text{NSi}$: 411.1630, found 411.1631.

The stereochemistry of major product (**3ad**) was determined by the NOE experiments. Representative results are shown below.

3ae: 58% yield, 94% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.37 (s, 6H), 0.70 (t, $J = 7.2$ Hz, 3H), 1.33 (t, $J = 7.2$ Hz, 3H), 2.52 (q, $J = 7.2$ Hz, 2H), 4.28 (q, $J = 7.2$ Hz, 2H), 6.85–6.95 (m, 4H), 7.00–7.07 (m, 3H), 7.10–7.25 (m, 1H), 7.55–7.68 (m, 2H), 7.72 (d, $J = 8.1$ Hz, 2H), 8.82 (dm, $J = 5.1$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ -1.1, 12.7, 14.3, 31.8, 60.6, 122.7, 126.1, 126.6, 127.4, 128.5, 128.7, 129.2, 129.4, 134.0, 136.9, 142.0, 149.7, 150.2, 157.9, 166.8, 167.5. IR (KBr) 2945, 1715, 1605, 1271 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{26}\text{H}_{29}\text{NO}_2\text{Si}$: 415.1968, found 415.1971.

3af: 69% yield, 94% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.38 (s, 6H), 0.69 (t, $J = 7.5$ Hz, 3H), 2.51 (q, $J = 7.5$ Hz, 2H), 6.75 (d, $J = 8.0$ Hz, 2H), 6.89 (d, $J = 8.0$ Hz, 2H), 6.97–7.10 (m, 5H), 7.19–7.24 (m, 1H), 7.58–7.65 (m, 2H), 8.81 (dm, $J = 5.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ -1.0, 12.7, 31.8, 122.6, 122.7, 126.0, 127.4, 127.5, 128.6, 129.4, 130.3, 130.5, 134.0, 134.1, 136.2, 150.2, 158.1, 167.6. IR (neat) 2967, 1574, 1485, 1248 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{23}\text{H}_{24}\text{ClNSi}$: 377.1367, found 377.1371.

3gc: 55% yield, 92% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.36 (s, 6H), 0.66 (t, $J = 7.5$ Hz, 3H), 2.30 (s, 6H), 2.46 (q, $J = 7.5$ Hz, 2H), 2.65 (t, $J = 5.7$ Hz, 2H), 3.93 (t, $J = 5.7$ Hz, 2H), 6.61 (d, $J = 9.0$ Hz, 2H), 6.69 (d, $J = 9.0$ Hz, 2H), 6.73–6.78 (m, 1H), 6.90–7.00 (m, 3H), 7.15–7.22 (m, 1H), 7.56–7.65 (m, 2H), 8.80 (dm, $J = 5.1$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ -1.1, 12.7, 31.4, 45.9, 58.3, 65.6, 113.6, 122.59, 122.65, 125.8, 127.2, 128.5, 129.4, 129.9, 133.1, 133.9, 136.0, 137.9, 144.5, 150.2, 155.8, 156.1, 167.9. IR (neat) 2969, 1505, 1277, 1244 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{27}\text{H}_{33}\text{ClN}_2\text{OSi}$: 464.2051, found 464.2052.

The stereochemistry of major product (**3gc**) was determined by the NOE experiments. Representative results are shown below.

3gh: 79% yield, 92% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.36 (s, 6H), 0.67 (t, $J = 7.5$ Hz, 3H), 2.18 (s, 3H), 2.47 (q, $J = 7.5$ Hz, 2H), 6.70 (d, $J = 7.8$ Hz, 2H), 6.75–6.80 (m, 1H), 6.86 (d, $J = 7.8$ Hz, 2H), 6.94–7.00 (m, 3H), 7.17–7.24 (m, 1H), 7.61 (td, $J = 7.5, 1.8$ Hz, 1H), 7.66 (dm, $J = 7.5$ Hz, 1H), 8.81 (dm, $J = 5.1$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ -1.1, 12.7, 21.0, 31.5, 122.6, 125.8, 127.2, 128.2, 128.47, 128.55, 128.8, 129.4, 133.1, 134.0, 134.1, 138.4, 140.4, 144.5, 150.2, 155.4, 167.9. IR (neat) 2963, 1583, 1574, 1559, 1248 cm^{-1} .

HRMS (EI) m/z calcd for $C_{24}H_{24}ClNSi$: 391.1522, found 391.1523.

The stereochemistry of major product (**3gh**) was determined by the NOE experiments. Representative results are shown below.

Typical Procedure of Borodesilylation of **3** (Table 2, Runs 1, 3, 4, and 6).

To a solution of **3aa** (68.8 mg, 0.20 mmol, 94% *E*) in dry CH_2Cl_2 (0.5 mL) was added a solution of BCl_3 (0.44 mmol, 1.0 M) in CH_2Cl_2 at $-41^\circ C$. After stirring the mixture at $-41^\circ C$ for 5 h, a solution of pinacol (136.9 mg, 1.16 mmol) and Et_3N (0.5 mL) in dry CH_2Cl_2 (0.5 mL) was added to the mixture. After stirring the mixture at room temperature for 14 h, saturated *aq* $NaHCO_3$ (ca. 2 mL) was added to the mixture. Organic phase was separated and aqueous phase was extracted by CH_2Cl_2 (2 mL $\times$ 3). The combined organic phase was dried over $MgSO_4$. Removal of solvents under reduced pressure and subsequent silica gel chromatography (hexane/ $EtOAc$ = 20/1) afforded **4aa** (54.8 mg, 82%) as white solid. The stereochemistry was determined to be 98% *Z* by 1H -NMR analysis.

Typical Procedure of Borodesilylation of **3** Bearing Aminoethoxy Side Chain (Table 2, Runs 2 and 5).

To a solution of **3ac** (1.26 g, 2.93 mmol, 88% *E*) in dry CH₂Cl₂ (10 mL) was added a solution of BCl₃ (9.90 mmol, 1.0 M) in CH₂Cl₂ at –41 °C. After stirring the mixture at –41 °C for 5 h, a solution of pinacol (3.65 g, 30.9 mmol) and Et₃N (5 mL) in dry CH₂Cl₂ (5 mL) was added to the mixture. After stirring the mixture at room temperature for 3 h, Cs₂CO₃ (5.90 g, 18.1 mmol) and dry toluene (6 mL) were added to the mixture. The resultant mixture was stirred at 80 °C for 13 h. After cooling the mixture to room temperature, saturated *aq* NaHCO₃ (ca. 20 mL) was added to the mixture. Organic phase was separated and aqueous phase was extracted by CH₂Cl₂ (20 mL × 3). The combined organic phase was dried over MgSO₄. Removal of solvents under reduced pressure and subsequent silica gel chromatography (CHCl₃/MeOH/Et₃N = 100/10/1) afforded **4ac** (800.7 mg, 65%) as pale yellow oil. The stereochemistry was determined to be 94% *Z* by ¹H-NMR analysis.

4aa: 82% yield, 98% *Z*. ¹H NMR (300 MHz, CDCl₃) δ 1.00 (t, *J* = 7.5 Hz, 3H), 1.33 (s, 12H), 2.71 (q, *J* = 7.5 Hz, 2H), 6.90–7.15 (m, 10H). ¹³C NMR (125 MHz, CDCl₃) δ 13.7, 24.7, 31.9, 83.6, 125.1, 126.2, 127.4, 127.5, 129.2, 129.5, 141.4, 141.9, 154.7. IR (KBr) 2977, 1595, 1489, 1348, 1144 cm^{–1}. HRMS (EI) *m/z* calcd for C₂₂H₂₇BO₂: 334.2104, found 334.2106.

4ac: 65% yield, 94% *Z*. ¹H NMR (300 MHz, CDCl₃) δ 0.97 (t, *J* = 7.5 Hz, 3H), 1.32 (s, 12H), 2.30 (s, 6H), 2.666 (t, *J* = 5.7 Hz, 2H), 2.668 (q, *J* = 7.5 Hz, 2H), 3.95 (q, *J* = 5.7 Hz, 2H), 6.59 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 6.98 (dd, *J* = 7.5, 1.5 Hz, 2H), 7.04–7.16 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 13.7, 24.7, 31.9, 45.8, 58.2, 65.5, 83.5, 113.6, 126.1, 127.6, 129.2, 130.5, 133.8, 142.1, 153.6, 156.4. IR (neat) 2977, 1509, 1144 cm^{–1}. HRMS (EI) *m/z* calcd for C₂₆H₃₆BNO₃: 421.2788, found 421.2790.

4ad: 80% yield, 99% Z. ^1H NMR (300 MHz, CDCl_3) δ 1.00 (t, J = 7.5 Hz, 3H), 1.33 (s, 12H), 2.76 (q, J = 7.5 Hz, 2H), 6.93–6.98 (m, 2H), 7.03 (d, J = 8.1 Hz, 2H), 7.08–7.17 (m, 3H), 7.29 (d, J = 8.1 Hz, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.7, 24.7, 31.9, 83.8, 124.3 (q, $J_{\text{C-F}}$ = 3.9 Hz), 124.4 (q, $J_{\text{C-F}}$ = 270.3 Hz), 126.6, 127.0 (q, $J_{\text{C-F}}$ = 32.0 Hz), 127.8, 129.0, 129.8, 141.4, 145.6, 157.3. IR (KBr) 2936, 1595, 1275 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{23}\text{H}_{26}\text{BF}_3\text{O}_2$: 402.1978, found 402.1978.

4ae: 64% yield, >99% Z. ^1H NMR (300 MHz, CDCl_3) δ 1.00 (t, J = 7.5 Hz, 3H), 1.32 (s, 12H), 1.33 (t, J = 7.2 Hz, 3H), 2.73 (q, J = 7.5 Hz, 2H), 4.29 (q, J = 7.2 Hz, 2H), 6.90–7.05 (m, 4H), 7.09–7.15 (m, 3H), 7.73 (d, J = 8.4 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 13.7, 14.3, 24.6, 31.9, 60.6, 83.7, 126.5, 127.0, 127.7, 128.8, 129.0, 129.5, 141.5, 146.9, 156.8, 166.8. IR (KBr) 2982, 1709, 1345, 1271 cm^{-1} . HRMS (FAB) m/z calcd for $\text{C}_{25}\text{H}_{31}\text{BO}_4$: 406.2315, found 406.2323.

4gc: 77% yield, 95% Z. ^1H NMR (300 MHz, CDCl_3) δ 0.96 (t, J = 7.5 Hz, 3H), 1.32 (s, 12H), 2.30 (s, 6H), 2.64 (q, J = 7.5 Hz, 2H), 2.66 (t, J = 5.7 Hz, 2H), 3.96 (t, J = 5.7 Hz, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.77–6.83 (m, 3H), 6.98–7.10 (m, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.7, 24.7, 31.7, 45.8, 58.3, 65.6, 83.7, 113.8,

126.2, 127.7, 128.85, 128.89, 130.4, 133.2, 133.5, 144.1, 152.1, 156.6. IR (neat) 2977, 1607, 1507, 1348 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{26}\text{H}_{35}\text{BCINO}_3$: 455.2399, found 455.2399.

4gh: 73% yield, 97% Z. ^1H NMR (300 MHz, CDCl_3) δ 0.98 (t, J = 7.2 Hz, 3H), 1.32 (s, 12H), 2.21 (s, 3H), 2.66 (q, J = 7.2 Hz, 2H), 6.75–6.82 (m, 3H), 6.87 (d, J = 8.4 Hz, 2H), 7.00–7.10 (m, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.7, 21.0, 24.7, 31.8, 83.7, 126.3, 127.7, 128.4, 128.8, 128.9, 129.3, 133.5, 134.9, 137.8, 144.1, 152.3. IR (KBr) 2977, 1605, 1590, 1561, 1361 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{BClO}_2$: 382.1871, found 382.1870.

Typical Procedure of Suzuki–Miyaura Coupling of **4** with Aryl Iodide (Table 3).

To a solution of $\text{Pd}[\text{P}(t\text{-Bu})_3]_2$ (5.2 mg, 0.01 mmol) in dry THF (0.2 mL) were added iodobenzene (Ar^3I : 49.0 mg, 0.24 mmol), a solution of **4ac** (84.3 mg, 0.20 mmol) in dry THF (0.4 mL), NaOH (24.5 mg, 0.61 mmol), H_2O (10.8 mg, 0.60 mmol), and dry THF (0.1 mL) at room temperature. The mixture was stirred at 60 $^\circ\text{C}$ for 24 h. After cooling the reaction mixture to room temperature, H_2O (ca. 1 mL) was added to the mixture. Organic phase was separated and aqueous phase was extracted by CHCl_3 (2 mL $\times$ 3). The combined organic phase was dried over MgSO_4 . Removal of solvents under reduced pressure and subsequent silica gel chromatography ($\text{CHCl}_3/\text{MeOH}/\text{Et}_3\text{N}$ = 100/10/1) afforded **5aca** (72.3 mg, 98%) as white solid. The stereochemistry was determined to be 95% Z by ^1H -NMR analysis.

5aac:² 95% yield, 99% *E*. ¹H NMR (300 MHz, CDCl₃) δ 0.95 (t, *J* = 7.5 Hz, 3H), 2.36 (s, 6H), 2.51 (q, *J* = 7.5 Hz, 2H), 2.76 (t, *J* = 5.7 Hz, 2H), 4.09 (t, *J* = 5.7 Hz, 2H), 6.86–6.92 (m, 4H), 6.96–7.04 (m, 3H), 7.09–7.18 (m, 7H). ¹³C NMR (75 MHz, CDCl₃) δ 13.5, 28.9, 45.9, 58.3, 65.8, 114.0, 125.6, 125.9, 127.2, 127.7, 129.6, 130.5, 130.7, 136.0, 138.3, 141.8, 142.3, 143.3, 157.5.

5aah:³ 96% yield, 99% *E*. ¹H NMR (300 MHz, CDCl₃) δ 0.97 (t, *J* = 7.5 Hz, 3H), 2.39 (s, 3H), 2.52 (q, *J* = 7.5 Hz, 2H), 6.88–6.93 (m, 2H), 6.98–7.06 (m, 3H), 7.08–7.21 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 13.6, 21.2, 29.0, 125.6, 126.0, 127.3, 127.7, 128.8, 129.3, 129.7, 130.7, 136.2, 138.7, 140.6, 141.9, 142.3, 143.2.

5aca:² 98% yield, 95% *Z*. ¹H NMR (300 MHz, CDCl₃) δ 0.93 (t, *J* = 7.5 Hz, 3H), 2.31 (s, 6H), 2.46 (q, *J* = 7.5 Hz, 2H), 2.68 (t, *J* = 5.7 Hz, 2H), 3.95 (t, *J* = 5.7 Hz, 2H), 6.56 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 8.7 Hz, 2H), 7.10–7.40 (m, 10H). ¹³C NMR (125 MHz, CDCl₃) δ 13.6, 29.0, 45.7, 58.2, 65.5, 113.3, 125.9, 126.4, 127.8, 128.0, 129.4, 129.6, 131.8, 135.5, 138.2, 141.2, 142.3, 143.7, 156.7.

(2) Miller, R. B.; Al-Hassan, M. I. *J. Org. Chem.* **1985**, 50, 2121.

(3) Al-Hassan, M. I. *Synth. Commun.* **1987**, 17, 1413.

5acb: 95% yield, 95% *Z*. ^1H NMR (300 MHz, CDCl_3) δ 0.93 (t, J = 7.5 Hz, 3H), 2.28 (s, 6H), 2.48 (q, J = 7.5 Hz, 2H), 2.64 (t, J = 5.7 Hz, 2H), 3.83 (s, 3H), 3.92 (t, J = 5.7 Hz, 2H), 6.55 (d, J = 9.0 Hz, 2H), 6.76 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 7.07–7.20 (m, 7H). ^{13}C NMR (75 MHz, CDCl_3) δ 13.6, 29.0, 45.8, 55.2, 58.2, 65.7, 113.3, 113.4, 125.8, 127.8, 129.7, 130.5, 131.8, 135.8, 136.2, 137.8, 140.9, 142.6, 156.7, 158.2. IR (KBr) 2961, 1605, 1509, 1242 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{27}\text{H}_{31}\text{NO}_2$: 401.2355, found 401.2354.

5aci: 92% yield, 95% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.92 (t, J = 7.5 Hz, 3H), 2.30 (s, 6H), 2.46 (q, J = 7.5 Hz, 2H), 2.67 (t, J = 6.0 Hz, 2H), 3.80 (s, 3H), 3.94 (t, J = 6.0 Hz, 2H), 6.55 (d, J = 8.7 Hz, 2H), 6.75–6.86 (m, 3H), 6.77 (d, J = 8.7 Hz, 2H), 7.07–7.20 (m, 5H), 7.26 (t, J = 7.8 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 13.6, 29.0, 45.8, 55.2, 58.2, 65.6, 112.0, 113.3, 115.0, 122.0, 126.0, 127.8, 129.0, 129.7, 131.7, 135.2, 138.0, 141.3, 142.3, 145.2, 156.7, 159.3. IR (KBr) 1603, 1574, 1509, 1283, 1248 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{27}\text{H}_{31}\text{NO}_2$: 401.2355, found 401.2355.

5adb: 97% yield, >99% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.98 (t, J = 7.5 Hz, 3H), 2.55 (q, J = 7.5 Hz, 2H), 3.84 (s, 3H), 6.93 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 6.9 Hz, 2H), 7.08–7.23 (m, 7H), 7.27 (d, J = 6.9 Hz, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.5, 29.2, 55.2, 113.7, 124.2 (q, $J_{\text{C-F}}$ = 270.4 Hz), 124.3 (q, $J_{\text{C-F}}$ = 3.9 Hz), 126.5, 127.6 (q, $J_{\text{C-F}}$ = 20.4 Hz), 127.9, 129.6, 130.6, 130.7, 130.97, 131.02, 135.1, 137.1, 141.7, 143.7, 147.1, 158.5. IR (KBr) 1611, 1509, 1329, 1246 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{24}\text{H}_{21}\text{F}_3\text{O}$: 382.1544, found 382.1542.

5adf: 90% yield, >99% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.97 (t, J = 7.5 Hz, 3H), 2.51 (q, J = 7.5 Hz, 2H), 6.99 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 7.8 Hz, 2H), 7.15–7.22 (m, 5H), 7.28 (d, J = 8.1 Hz, 2H), 7.37 (d, J = 7.8 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 13.4, 29.1, 124.1 (q, $J_{\text{C-F}}$ = 269.9 Hz), 124.4 (q, $J_{\text{C-F}}$ = 3.5 Hz), 126.8, 127.9 (q, $J_{\text{C-F}}$ = 31.9 Hz), 128.1, 128.6, 129.5, 130.87, 130.93, 132.9, 136.4, 141.10, 141.15, 144.7, 146.3. IR (KBr) 1613, 1489, 1323 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{23}\text{H}_{18}\text{ClF}_3$: 386.1049, found 386.1049.

5adj: 95% yield, >99% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.86 (t, J = 7.5 Hz, 3H), 2.36 (q, J = 7.5 Hz, 2H), 3.69 (s, 3H), 6.92 (d, J = 8.4 Hz, 1H), 6.97–7.04 (m, 1H), 7.02 (d, J = 8.4 Hz, 2H), 7.10–7.35 (m, 9H). ^{13}C NMR (125 MHz, CDCl_3) δ 12.7, 29.4, 55.4, 111.3, 120.5, 124.0, 124.3 (q, $J_{\text{C-F}}$ = 270.4 Hz), 126.4, 127.4 (q, $J_{\text{C-F}}$ = 30.0 Hz), 127.9, 128.6, 129.6, 130.3, 130.8, 131.6, 133.7, 141.3, 144.3, 146.3, 156.8. IR (KBr) 1615, 1489, 1462, 1325 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{24}\text{H}_{21}\text{F}_3\text{O}$: 382.1544, found 382.1543.

5adk: 67% yield, >99% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.97 (t, J = 7.5 Hz, 3H), 2.49 (q, J = 7.5 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 7.06–7.12 (m, 2H), 7.15–7.22 (m, 3H), 7.27 (d, J = 8.7 Hz, 2H), 7.27–7.40 (m, 1H), 7.49 (d, J = 7.8 Hz, 1H), 8.60 (brs, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.5, 29.1, 123.4, 124.0 (q, $J_{\text{C-F}}$ = 270.4 Hz), 124.5 (q, $J_{\text{C-F}}$ = 3.9 Hz), 128.0 (q, $J_{\text{C-F}}$ = 32.0 Hz), 128.1, 129.3, 130.9 (q, $J_{\text{C-F}}$ = 2.8 Hz), 133.9, 136.9, 137.0, 138.4, 140.7, 145.8, 146.1, 148.2, 150.0. IR (KBr) 1615, 1408, 1325, 1165 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{22}\text{H}_{18}\text{F}_3\text{N}$: 353.1391, found 353.1390.

5gcb: 80% yield, 96% *Z*. ^1H NMR (300 MHz, CDCl_3) δ 0.93 (t, J = 7.5 Hz, 3H), 2.29 (s, 6H), 2.47 (q, J = 7.5 Hz, 2H), 2.65 (t, J = 6.0 Hz, 2H), 3.82 (s, 3H), 3.95 (t, J = 6.0 Hz, 2H), 6.59 (d, J = 8.7 Hz, 2H), 6.76 (d, J = 8.1 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 6.92–6.98 (m, 1H), 7.04–7.09 (m, 2H), 7.11–7.18 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 13.5, 28.8, 45.8, 55.1, 58.2, 65.7, 113.4, 113.5, 126.0, 128.2, 129.0, 129.3, 130.4, 131.8, 133.6, 135.3, 135.8, 138.9, 139.5, 144.7, 156.9, 158.3. IR (neat) 1607, 1592, 1500, 1464, 1244, 1173 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{27}\text{H}_{30}\text{ClNO}_2$: 435.1965, found 435.1965.

5gcl: 82% yield, 98% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.92 (t, $J = 7.5$ Hz, 3H), 2.33 (s, 6H), 2.34 (s, 3H), 2.43 (q, $J = 7.5$ Hz, 2H), 2.70 (t, $J = 5.7$ Hz, 2H), 3.97 (t, $J = 5.7$ Hz, 2H), 6.60 (d, $J = 8.1$ Hz, 2H), 6.78 (d, $J = 8.1$ Hz, 2H), 6.92–7.00 (m, 1H), 7.02–7.18 (m, 5H), 7.20–7.28 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.5, 21.5, 28.8, 45.7, 58.1, 65.4, 113.5, 126.1, 126.3, 127.5, 127.9, 128.0, 128.2, 129.1, 129.3, 129.4, 129.87, 129.93, 133.6, 135.0, 137.6, 139.3, 139.7, 143.2, 144.4, 156.8. IR (KBr) 1605, 1509, 1244, 1177 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{27}\text{H}_{30}\text{ClNO}$: 419.2016, found 419.2018.

5gcm: 87% yield, 99% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.97 (t, $J = 7.5$ Hz, 3H), 2.30 (s, 6H), 2.56 (q, $J = 7.5$ Hz, 2H), 2.67 (t, $J = 5.7$ Hz, 2H), 3.96 (t, $J = 5.7$ Hz, 2H), 6.60 (d, $J = 8.7$ Hz, 2H), 6.78 (d, $J = 8.7$ Hz, 2H), 6.87–6.95 (m, 2H), 7.04–7.09 (m, 2H), 7.11–7.14 (m, 2H), 7.25–7.28 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 13.6, 29.0, 45.8, 58.2, 65.7, 113.5, 122.9, 124.7, 126.1, 128.2, 129.0, 129.2, 129.3, 131.6, 133.6, 133.9, 134.7, 140.5, 143.4, 144.4, 157.1. IR (neat) 2971, 1605, 1592, 1561, 1509, 1470, 1242 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{24}\text{H}_{26}\text{ClNOS}$: 411.1424, found 411.1424.

5ghn: 93% yield, >99% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.87 (t, J = 7.5 Hz, 3H), 2.19 (s, 3H), 2.22 (s, 3H), 2.24–2.40 (m, 2H), 6.81 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 7.01–7.06 (m, 1H), 7.08–7.19 (m, 2H), 7.20–7.35 (m, 5H). ^{13}C NMR (125 MHz, CDCl_3) δ 12.8, 19.8, 21.0, 29.0, 125.6, 126.3, 127.0, 128.2, 128.3, 129.1, 129.3, 129.4, 130.1, 130.3, 133.7, 135.5, 135.9, 137.7, 138.6, 140.1, 142.2, 144.1. IR (KBr) 1593, 1561, 1510, 1453, 1325 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{24}\text{H}_{23}\text{Cl}$: 346.1488, found 346.1488.

5gho: 98% yield, >99% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.95 (t, J = 7.5 Hz, 3H), 2.23 (s, 3H), 2.46 (q, J = 7.5 Hz, 2H), 6.70–6.85 (m, 5H), 6.88 (s, 1H), 6.90 (s, 1H), 6.93–6.98 (m, 1H), 7.06–7.20 (m, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.3, 21.0, 28.9, 102.3 (t, $J_{\text{C-F}}$ = 25.1 Hz), 112.2 (d, $J_{\text{C-F}}$ = 19.4 Hz), 126.6, 128.0, 128.5, 129.15, 129.21, 130.3, 133.8, 136.2, 137.7, 138.2, 141.6, 143.5, 146.4 (t, $J_{\text{C-F}}$ = 8.8 Hz), 162.8 (dd, $J_{\text{C-F}}$ = 247.1, 12.5 Hz). IR (neat) 2973, 1620, 1590, 1429, 1334, 1117 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{23}\text{H}_{19}\text{ClF}_2$: 368.1143, found 368.1144.

5ghp: 99% yield, >99% *E*. ^1H NMR (300 MHz, CDCl_3) δ 0.78 (t, J = 7.5 Hz, 3H), 2.16 (s, 3H), 2.21 (q, J = 7.5 Hz, 2H), 6.79 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 7.07–7.18 (m, 3H), 7.28–7.32 (m, 1H), 7.40–7.55 (m, 4H), 7.78–7.88 (m, 2H), 8.02–8.08 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 12.9, 21.0, 29.4, 125.5, 125.7, 125.92, 125.95, 126.1, 126.5, 127.2, 127.3, 128.2, 129.2, 129.4, 129.5, 129.7, 131.8, 133.8, 133.9, 135.7, 137.2, 138.4, 140.4, 141.8, 144.0. IR (neat) 1592, 1563, 1507, 1472, 1393 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{27}\text{H}_{23}\text{Cl}$: 382.1488, found 382.1488.

^{13}C -NMR (75 MHz, CDCl_3)

^{13}C -NMR (75 MHz, CDCl_3)

^{13}C -NMR (75 MHz, CDCl_3)

^{13}C -NMR (75 MHz, CDCl_3)

Chemical structure of 1-phenyl-1-propyne: CC#CC1=CC=CC=C1

^{13}C -NMR (75 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (100 MHz, CDCl_3)

^{13}C -NMR (100 MHz, CDCl_3)

^{13}C -NMR (75 MHz, CDCl_3)

77.425
77.000
76.575

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (75 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

¹³C-NMR (75 MHz, CDCl₃)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (75 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)

^{13}C -NMR (125 MHz, CDCl_3)