

Supporting Information

for

Controlling alkyne reactivity by means of a copper-catalyzed radical reaction system for the synthesis of functionalized quaternary carbons

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Experimental procedures, compound characterization data, and NMR spectra

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1. General information.

All reactions were carried out under nitrogen (99.95%) atmosphere. For TLC analyses precoated Kieselgel 60 F254 plates (Merck, 0.25 mm thick) were used; for column chromatography silica gel 60 (Kanto chemical, 63–210 µm) was used. Visualization was accomplished by UV light (254 nm), ¹H and ¹³C NMR spectra were obtained using a JEOL 500 MHz NMR spectrometer. ¹H NMR and ¹³C NMR spectra were obtained in CDCl₃ by using CHCl₃ (for ¹H, δ = 7.26 ppm) and CDCl₃ (for ¹³C, δ = 77.16 ppm) as an internal standard. High resolution mass analyses were obtained using a ACQUITY UPLC/ TOF-MS for EI. Anhydrous toluene and THF were purchased from Kanto Chemical Co., Ltd. Other chemicals obtained from TCI, Sigma-Aldrich and Wako and Copper salts obtained from Sigma-Aldrich and Wako were used directly as supplied.



Table S1. Substrates

2. Synthesis and analytical data of 3

General Procedure for the reaction: CuBr (0.050 mmol), 1,10-Phen (0.10 mmol), NaI (1.0 mmol) and Cs_2CO_3 (2.0 mmol) were sequentially added to the dram vial equipped with a stir bar and a screw cap. MeCN (1.0 mL), **1** (1.5 mmol) and **2** (0.50 mmol) were added to a dram vial. The resulting mixture vigorously stirred under nitrogen atmosphere (purity 99.95%) for 24 h at 80 °C. After this time, the contents of the flask were filtered through the plug of silica gel with EtOAc as an eluent, and then concentrated by rotary evaporation. The crude residue was purified by flash chromatography and GPC, eluting with EtOAc/hexane to afford the product. The yield was checked by ¹H NMR analysis. **3a**, **3d**, **3f** and **3i** are reported compounds¹.



Following the general procedure above, using**2a** (97 mg, 0.5 mmol), **1a** (152 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3a** with inseparable side products. The yield was determined by ¹H NMR analysis (66%) and purified by GPC (52%); ¹H NMR (500 MHz, CDCl₃) δ 7.41-7.39 (m, 2H), 7.34-7.27 (m, 8H), 6.26 (s, 1H), 3.60 (q, *J* = 7.0 Hz, 2H), 1.31 (s, 6H), 1.08 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.6, 143.3, 137.5, 131.6, 128.8, 128.3, 128.19, 128.12, 127.8, 124.2, 123.3, 91.8, 88.0, 60.7, 44.3, 27.7, 13.9. This compound is a reported compound.¹



Following the general procedure above, using **2b** (111 mg, 0.5 mmol), **1a** (152 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3b** with inseparable side products. The yield was determined by ¹H NMR analysis and purified by GPC (52%); ¹H NMR (500 MHz, CDCl₃) δ 7.42-7.25 (m, 10H), 6.29 (s, 1H), 1.29 (s, 9H), 1.22 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 175.1, 143.2,

138.0, 131.6, 128.8, 128.3, 128.2, 128.1, 127.8, 92.3, 87.6, 80.6, 45.1, 27.8, 27.5; FT-IR (neat, cm⁻¹) 2974, 2930, 2869, 1722, 1488, 1366, 1132; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₂₄H₂₇O₂ 347.2011, found 347.2011.



Following the general procedure above, using **2c** (111 mg, 0.5 mmol), **1a** (152 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3c** with inseparable side products. The yield was determined by ¹H NMR analysis and purified by GPC (46%); ¹H NMR (500 MHz, CDCl₃) δ 7.41-7.39 (m, 2H), 7.34-7.26 (m, 8H), 6.33 (s, 1H), 3.74 (q, *J* = 7.1 Hz, 2H), 1.74-1.66 (m, 4H), 1.12 (t, *J* = 7.1 Hz, 3H), 0.82 (t, *J* = 7.5 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 174.8, 141.4, 137.9, 131.6, 128.5, 128.3, 128.1, 127.8, 124.8, 123.4, 92.3, 87.6, 60.5, 52.4, 29.2, 14.1, 8.8; FT-IR (neat, cm⁻¹) 2968, 2935, 2876, 1724, 1488, 1441, 1222, 1131; HRMS (EI-MS) *m*/*z* [M+H⁺] Calcd for C₂₄H₂₇O₂ 347.2011, found 347.2011.



Following the general procedure above, using **2d** (126 mg, 0.5 mmol), **1a** (152 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3d** with inseparable side products. The yield was determined by ¹H NMR analysis and purified by GPC (40%); ¹H NMR (500 MHz, CDCl₃) δ 7.41-7.39 (m, 2H), 7.35-7.27 (m, 8H), 6.74 (s, 1H), 3.99-3.92 (m, 2H), 3.89-3.83 (m, 2H), 1.55 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 170.5, 136.8, 136.1, 131.6, 128.8, 128.3, 128.16, 128.13, 126.1, 123.2, 91.5, 89.0, 61.7, 55.7, 23.3, 13.9. This compound is a reported compound.¹



Following the general procedure above, using **2e** (90 mg, 0.5 mmol), **1a** (152 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3e** with inseparable side products. The yield was determined by ¹H NMR analysis and purified by GPC (53%); ¹H NMR (500 MHz, CDCl₃) δ 7.40-7.34 (m, 7H), 7.29-7.27 (m, 3H), 6.59 (s, 1H), 4.09-4.02 (m, 2H), 2.08-2.02 (m, 1H), 1.66-1.62 (m, 1H), 1.41 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 180.0, 139.4, 137.7, 131.6, 128.7, 128.5, 128.4, 128.3, 128.2, 126.3, 123.1, 91.0, 89.5, 65.2, 44.7, 35.3, 24.7; FT-IR (neat, cm⁻¹) 2970, 2910, 2870, 1764, 1487, 1442, 1088, 1027; HRMS (EI-MS) *m*/*z* [M+H⁺] Calcd for C₂₁H₁₉O₂ 303.1385, found 303.1388.



Following the general procedure above, using **2f** (82 mg, 0.5 mmol), **1a** (152 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3f** with inseparable side products. The yield was determined by ¹H NMR analysis and purified by GPC (52%); ¹H NMR (500 MHz, CDCl₃) δ 7.42-7.40 (m, 2H), 7.35-7.25 (m, 6H), 6.34 (s, 1H), 1.93 (s, 2H), 1.22 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 210.2, 143.3, 137.1, 131.6, 128.8, 128.39, 128.35, 128.2, 91.7, 88.42, 50.8, 26.5, 26.3. This compound is a reported compound.¹



Following the general procedure above, using **2a** (97 mg, 0.5 mmol), **1b** (174 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3g** with inseparable side products. The yield was determined by ¹H NMR analysis and purified by GPC (53%); ¹H NMR (500 MHz, CDCl₃) δ 7.30 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 7.08 (d, J = 7.9 Hz, 2H), 6.23 (s, 1H), 3.65 (q, J = 7.1 Hz, 2H), 2.34 (s, 3H), 2.33 (s, 3H), 1.31 (s, 6H), 1.10 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.8, 142.7, 138.2, 137.5, 134.7, 131.5, 129.0, 128.7, 128.6, 124.4, 120.3, 91.4, 88.0, 60.6, 44.2, 27.7, 21.5, 21.3, 13.9; FT-IR (neat, cm⁻¹) 2975, 2921, 2868, 1727, 1507, 1133; HRMS (EI-MS) m/z [M+H⁺] Calcd for C₂₄H₂₇O₂ 347.2011, found 347.2011.



Following the general procedure above, using **2a** (97 mg, 0.5 mmol), **1c** (174 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3h** with inseparable side products. The yield was determined by ¹H NMR analysis and purified by GPC (58%); ¹H NMR (500 MHz, CDCl₃) δ 7.26-7.15 (m, 4H), 7.09-7.04 (m, 4H), 6.22 (s, 1H), 3.61 (q, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 2.30 (s, 3H), 1.30 (m, 2H), 1.09 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.7, 143.1, 137.9, 137.6, 137.4, 132.2, 129.4, 129.0, 128.6, 128.5, 128.2, 128.0, 125.8, 124.4, 123.2, 91.6, 88.1, 60.6, 44.3, 27.7, 21.5,

21.2, 13.9; FT-IR (neat, cm⁻¹) 2975, 2922, 2868, 1727, 1443, 1133; HRMS (EI-MS) *m*/*z* [M+H⁺] Calcd for C₂₄H₂₇O₂ 347.2011, found 347.2011.



Following the general procedure above, using **2a** (97 mg, 0.5 mmol), **1d** (240 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **3i** with inseparable side products. The yield was determined by ¹H NMR analysis and purified by GPC (63%); ¹H NMR (500 MHz, CDCl₃) δ 8.02 (d, J = 7.9 Hz, 2H), 7.96 (d, J = 7.9 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 6.36 (s, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.66 (q, J = 7.1 Hz, 2H), 1.31 (s, 6H), (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.2, 166.7, 166.5, 145.1, 141.8, 131.4, 129.6, 129.53, 129.52, 128.8, 127.8, 123.1, 93.9, 87.9, 60.8, 52.3, 52.2, 44.4, 27.5, 13.9; FT-IR (neat, cm⁻¹) 2973, 2951, 1717, 1603, 1434, 1270, 1102; HRMS (EI-MS) m/z [M+H⁺] Calcd for C₂₆H₂₇O₆ 435.1808, found 435.1808. This compound is a reported compound.¹



Following the general procedure above, using 2a (97 mg, 0.5 mmol), 1e (270 mg, 1.5 mmol), CuBr (10.8 mg, 0.075 mmol), Cs₂CO₃ (656 mg, 2.00 mmol), 1,10-Phen (27.1 mg, 0.15 mmol), NaI (150 mg, 1.0 mmol) and toluene (1.0 mL), the crude residue was purified by flash Chromatography on silica gel

with EtOAc/hexane to afford the desired compound **3j** in 53% yield (87 mg).; ¹H NMR (500 MHz, CDCl₃) δ 7.41 (dd, J = 1.2 and 2.9 Hz, 1H), 7.27-7.24 (m, 2H), 7.18 (dd, J = 1.3 and 2.9 Hz, 1H), 7.09 (dd, J = 1.2 and 5.0 Hz, 1H), 6.20 (s, 1H), 3.73 (q, J = 7.1 Hz, 2H), 1.34 (s, 6H), 1.09 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.8, 143.7, 137.1, 129.9, 128.5, 125.3, 125.1, 124.1, 122.3, 119.1, 90.7, 82.7, 60.8, 44.2, 27.6, 14.0; FT-IR (neat, cm⁻¹) 3104, 2975, 2932, 2868, 1723, 1466, 1132; HRMS (EI-MS) m/z [M+H⁺] Calcd for C₁₈H₁₉O₂S₂ 331.0826, found 331.0822.

3. Synthesis and analytical data of 5

General Procedure for the reaction: CuI (10 mol %), 1,10-Phen (10 mol %), Cy₂NMe (1.0 equiv), **2** (1.0 equiv) and **4** (3.0 equiv) were sequentially added to the dram vial equipped with a stir bar and a screw cap. 1,4-dioxane (1.0 mL) was added to a dram vial. The resulting mixture vigorously stirred under nitrogen atmosphere (purity 99.95%) for 20 h at 100 °C. After this time, the contents of the flask were filtered through the plug of silica gel with EtOAc as an eluent, and then concentrated by rotary evaporation. The crude residue was purified by flash chromatography and GPC, eluting with EtOAc/hexane to afford the product. The yield was checked by ¹H NMR analysis.



Following the general procedure above, using **2a** (97 mg, 0.5 mmol), **4a** (238.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **5a** with isomers (95 mg, 70%). The desired product yield was determined by ¹H NMR analysis (69%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.30 (d, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.04 (s, 1H), 6.99 (t, *J* = 7.7 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 3.23 (s, 3H), 1.56 (s, 6H), 1.06 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.0, 168.4, 144.6, 144.2, 129.5, 128.1, 125.2, 122.2, 120.6, 108.1, 61.4, 43.4, 26.3, 26.2, 14.0; FT-IR (neat, cm⁻¹) 2976, 1707, 1607, 1467, 1229, 1137; HRMS (EI-MS) *m*/*z* [M+H⁺] Calcd for C₁₆H₂₀O₃N 274.1443, found 274.1443.



Following the general procedure above, using **2l** (142 mg, 0.5 mmol), **4b** (283.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **5b** with isomers (121 mg, 62%). The desired product yield was determined by ¹H NMR analysis (63%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.19 (t, *J* = 7.5 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.08 (s, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 6.94 (d, *J* = 6.9 Hz, 2H), 6.82 (dd, *J* = 2.4 and 8.5 Hz, 1H), 6.69 (d, *J* = 8.5 Hz, 1H), 4.04 (q, *J* = 6.3 Hz, 2H), 3.71 (s, 3H), 3.20 (s, 3H), 2.41 (t, *J* = 8.0 Hz, 2H), 1.80-1.74 (m, 2H), 1.59 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 176.1, 168.1, 155.7, 144.7, 141.0, 138.0, 128.6, 128.4, 128.3, 126.0, 121.3, 114.9, 111.7, 108.5, 64.7, 55.9, 43.5, 31.9, 30.0, 26.36, 26.34; FT-IR (neat, cm⁻¹) 2935, 1703, 1592, 1469, 1222, 1129; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₂₄H₂₈O₄N 394.2018, found 394.2017.



Following the general procedure above, using **2a** (97 mg, 0.5 mmol), **4c** (259.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **5c** with isomers (91 mg, 63%). The desired product yield was determined by ¹H NMR analysis (64%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.05 (s, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 6.94 (s, 1H), 6.62 (d, *J* = 7.9 Hz, 1H), 4.01 (q, *J* = 7.1 Hz, 2H), 3.15 (s, 3H), 2.25 (s, 3H), 1.50 (s, 6H), 1.02 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.0, 168.4, 144.3, 142.0, 131.5, 129.7, 128.3, 126.0, 120.7, 107.8, 61.4, 43.5, 26.4, 26.3, 21.3, 14.1; FT-IR (neat, cm⁻¹) 2977, 1706, 1616, 1488, 1365, 1338, 1255, 1133; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₁₇H₂₂O₃N 288.1600, found 288.1600.



Following the general procedure above, using **2a** (97 mg, 0.5 mmol), **4d** (265.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **5d** with isomers (84 mg, 58%). The desired product yield was determined by ¹H NMR analysis (54%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.09 (dd, *J* = 2.5 and 8.9 Hz, 1H), 7.08 (s, 1H), 6.96 (dt, *J* = 2.5 and 8.8 Hz, 1H), 6.70 (dd, *J* = 4.3 and 8.6 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.21 (s, 3H), 1.55 (s, 6H), 1.10 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.5, 168.1, 158 (d, *J* = 239 Hz), 140.3, 127 (d, *J* = 2.8 Hz), 121 (d, *J* = 8.9 Hz), 115 (d, *J* = 23.7 Hz), 113 (d, *J* = 27 Hz), 108 (d, *J* = 8.3 Hz), 61.5, 43.5, 26.3, 26.2, 14.0; FT-IR (neat, cm⁻¹) 2978, 1708, 1618, 1467, 1138; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₁₆H₁₉O₃NF 292.1349, found 292.1349.



Following the general procedure above, using **2h** (103 mg, 0.5 mmol), **4a** (238.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **5e** (47% pure *E*-compound). The yield was determined by ¹H NMR analysis (60%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.31 (d, *J* = 7.5 Hz, 1H), 7.27 (dt, *J* = 1.1 and 7.8 Hz, 1H), 7.25 (s, 1H), 7.00 (dt, *J* = 0.9 and 7.6 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.25 (s, 3H), 2.95-2.90 (m, 2H), 2.45-2.40 (m, 2H), 2.08-1.97 (m, 2H), 1.13 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 173.7, 168.1, 144.0, 142.7, 129.5, 129.1, 125.0, 122.2, 120.3, 108.0, 61.4, 48.1, 33.1, 26.2, 16.2, 14.1; FT-IR (neat, cm⁻¹) 2939, 1706, 1607, 1467, 1377, 1336, 1215, 1094; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₁₇H₂₀O₃N 286.1443, found 286.1443.



Following the general procedure above, using **2i** (110 mg, 0.5 mmol), **4a** (238.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **5f** with isomers (92 mg, 62%). The desired product yield was determined by ¹H NMR analysis (60%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.38 (d, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 7.7 Hz, 1H), 7.15 (s, 1H), 7.01 (t, *J* = 7.7 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 3.57 (s, 3H), 3.24 (s, 3H), 2.10-2.00 (m, 4H), 1.68-1.52 (m, 5H), 0.97-0.88 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 176.0, 168.2, 144.3, 143.0, 129.4, 128.2, 125.3, 122.3, 120.6, 108.1, 52.5, 47.4, 34.0, 26.2, 25.3, 22.3; FT-IR (neat, cm⁻¹) 2931, 1701, 1605, 1464, 1239, 1069; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₁₈H₂₂O₃N 300.1600, found 300.1602.



Following the general procedure above, using **2j** (156 mg, 0.5 mmol), **4a** (238.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **5g** with isomers (118 mg, 60%). The desired product yield was determined by ¹H NMR analysis (59%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.25-7.22 (m, 4H), 7.06 (d, *J* = 8.2 Hz, 2H), 7.04 (s, 1H), 6.89 (t, *J* = 7.7 Hz, 1H), 6.79 (d, *J* = 7.7

Hz, 1H),5.02 (s, 2H), 3.23 (s, 3H), 1.59 (s, 6H), 1.28 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 175.9, 168.3, 151.2, 144.3, 144.2, 132.5, 129.4, 128.2, 128.0, 125.4, 125.1, 122.3, 120.5, 108.1, 67.1, 43.6, 34.6, 31.3, 26.3, 26.2; FT-IR (neat, cm⁻¹) 2959, 1708, 1608, 1466, 1255, 1134; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₂₅H₃₀O₃N 392.2226, found 392.2226.



Following the general procedure above, using **4a** (153 mg, 0.5 mmol), **2k** (238.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to afford the desired compound **5h** with isomers (121 mg, 62%). The desired product yield was determined by ¹H NMR analysis (64%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.76-7.74 (m, 1H), 7.67-7.63 (m, 2H), 7.57 (s, 1H), 7.46-7.42 (m, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.11 (t, *J* = 7.7 Hz, 1H), 7.06 (s, 1H), 6.74 (t, *J* = 7.6 Hz, 1H), 6.70 (d, *J* = 7.6 Hz, 1H), 5.21 (s, 2H), 3.21 (s, 3H), 1.60 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 175.8, 144.1, 144.0, 133.08, 133.04, 132.84, 129.37, 128.3, 128.1, 128.0, 127.6, 127.5, 126.2, 126.1, 125.8, 125.0, 122.1, 120.4, 107.9, 67.3, 43.5, 25.3, 26.2; FT-IR (neat, cm⁻¹) 3053, 2973, 1703, 1607, 1466, 1123; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₂₆H₂₄O₃N 386.1756, found 386.1756.



Following the general procedure above, using 4e (97 mg, 0.5 mmol), 2a (259.5 mg, 1.5 mmol), CuI (9.5 mg, 0.05 mmol), 1,10-Phen (9 mg, 0.05 mmol), Cy₂NMe (97.6 mg, 0.1 mmol) and 1,4-dioxane (1.0 mL), the crude residue was purified by flash Chromatography on silica gel with EtOAc/hexane to

afford the desired compound **5i** with isomers (105 mg, 73%). The desired product yield was determined by ¹H NMR analysis (65%) and purified by GPC (*E*-isomer).; ¹H NMR (500 MHz, CDCl₃) δ 7.31 (d, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.04 (s, 1H), 6.98 (t, *J* = 7.7 Hz, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.79 (q, *J* = 7.2 Hz, 2H), 1.57 (s, 6H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.0, 167.9, 144.4, 143.3, 129.4, 128.2, 125.3, 122.0, 120.8, 108.2, 61.4, 43.4, 34.7, 26.3, 14.1, 12.8; FT-IR (neat, cm⁻¹) 2976, 1704, 1606, 1466, 1344, 1221, 1138; HRMS (ESI-MS) *m*/*z* [M+H⁺] Calcd for C₁₇H₂₂O₃N 288.1600, found 288.1600.

4. Reference

1 C. Che, H. Zheng, G. Zhu, Org. Lett. 2015, 17, 1617-1620.

5. Spectral charts for new compounds

¹³C NMR(CDCl₃)









M

7.5

7.0

0.0 9.5

9.0

8.5 8.0

F-96.0

5.0 4.5 f1 (ppm) 4.0

3.5

3.0 2.5 2.0

6.5 6.0 5.5

0.0 -0

9.18 6.05 4

1.0 0.5

1.5















M

2.094 8.354

7.5

7.0

0.0 9.5

9.0 8.5 8.0

1:04

6.5

6.0 5.5

5.0 4.5 f1 (ppm)

4.0

3.5

3.0 2.5

¹³C NMR(CDCl₃)

F60.9

1.0 0.5

0.0 -0

1.5

I-96.2

2.0































5b

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[∼]Ph

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7.5 7.0 6.5

6.0 5.5

5.0 f1 (ppm) 4.5



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