Supporting Information For

**Microwave-Promoted Three-Component Coupling of Aldehyde, Alkyne and
Amine via C-H Activation Catalyzed by Copper in Water**

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Context

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Experimental

General Information:

The materials were used as purchased (except for CuI) and water was distilled and deoxygenated by argon. All reactions under microwave conditions were monitored by thin-layer chromatography (TLC) on gel F₂₅₄ plates. The silica gel (200–300 meshes) for column chromatography was from the Qingdao Marine Chemical Factory in China, and the distillation range of petroleum is 60–90 °C.

¹H and ¹³C NMR spectra were recorded in CDCl₃ solution on the Varian Mercury-plus 300BB instruments, and spectral data are reported in *ppm* relative to tetramethylsilane (TMS) as internal standard. MS were measured on a HP-5988 spectrometer by direct inlet at 70 eV, and signals were given in *m/z* with relative intensity (%) in brackets. This A³ coupling reaction under microwave condition was performed on a 700 W LG microwave oven (model WD 700(MG-5082M)) set at a power setting of 40%.

Spectroscopic data for following A³ coupling adducts has been reported previously (see reference 3 and 4 in text). Details of compound characterization are provided hereinafter (pp 4–11).

Preparation of CuI:

Copper (I) Iodide

CuI = 190.45

To an aqueous solution of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (1 g, 0.4 mmol) was added with vigorously stirring the slightly excessive aqueous solution of NaHSO_3 (0.25 g, 0.21 mmol) filtered through filterable paper and the same amount of NaI (0.6 g, 0.4 mmol) under argon. The reaction mixture was stirred, and then a pinkish white precipitate was obtained. The precipitate was filtered in vacuo and successively washed with H_2O , anhydrous EtOH , and anhydrous $(\text{Et})_2\text{O}$. Handle the process as soon as possible. After drying in vacuo the pinkish white solid was obtained. (The above step should be operated under the artificial illumination)

Typical procedure for the A³-coupling reaction:

A 10 mL sealed tube was charged with CuI (0.15 mmol), aldehyde (1.0 mmol), amine (1.3 mmol), alkyne (1.6 mmol) and water (1.5 mL) under argon. The sealed tube was exposed to the microwave irradiation for 1 min using an unmodified microwave oven operating at its 40% power. The reaction mixture was cooled to lower temperature and was irradiated again for the same time. After some such successive irradiations and cooling sequences, the reaction was completed until the aldehyde had been consumed as judged by TLC analysis. After completion of the reaction, it was cooled to room temperature, put into ice water and stirred for 5 min. The solvent of Et₂O and the saturated NH₄Cl solution were added to the resulting mixture, and the organic layer was separated followed by the extraction of the aqueous layer with Et₂O. The combined organic extracts were washed with a saturated NaHCO₃ solution and brine, and dried over anhydrous Na₂SO₄. After removal of the solvent the residue was purified by the column chromatography on silica gel to furnish the expected product.

Spectroscopic data for following adducts:

¹H NMR (300 MHz, CDCl₃, *ppm*): δ 7.65–7.63 (m, 2H), 7.53–7.50 (m, 2H), 7.40–7.31 (m, 6H), 4.80 (s, 1H), 3.74 (brs, 4H), 2.64 (brs, 4H); ¹³C NMR (75 MHz, CDCl₃, *ppm*): δ 137.8, 131.8, 128.6, 128.2, 127.8, 123.0, 88.5, 85.0, 67.2, 62.0, 49.9; MS *m/z* (%) 277 (M⁺, 20), 200 (24), 191 (100), 115 (6), 86 (12), 56 (19).

¹H NMR (300 MHz, CDCl₃, *ppm*): δ 7.76–7.73 (m, 1H), 7.51–7.47 (m, 2H), 7.40–7.37 (m, 1H), 7.32–7.22 (m, 5H), 5.12 (s, 1H), 3.71–3.66 (m, 4H), 2.68–2.64 (m, 4H); ¹³C NMR (75 MHz, CDCl₃, *ppm*): δ 135.4, 134.5, 131.7, 130.4, 129.8, 129.0, 128.2, 126.2, 122.7, 88.2, 84.6, 67.0, 58.8, 49.7; MS *m/z* (%) 311 (M⁺, 14), 280 (6), 225 (100), 189 (54), 86 (84), 56 (61).

¹H NMR (300 MHz, CDCl₃, *ppm*): δ 7.64 (s, 1H), 7.53–7.50 (m, 3H), 7.33–7.27 (m, 5H), 4.75 (s, 1H), 3.74–3.72 (m, 4H), 2.62–2.60 (m, 4H); ¹³C NMR (75 MHz, CDCl₃, *ppm*): δ 140.0, 134.1, 131.8, 129.4, 128.5, 128.4, 128.3, 127.9, 126.6, 122.6, 89.0, 84.0, 67.0, 61.4, 49.7; MS *m/z* (%) 311 (M⁺, 18), 280 (7), 225 (100), 189 (38), 86 (32), 56 (47).

^1H NMR (300 MHz, CDCl_3 , ppm): δ 7.60–7.57 (m, 2H), 7.53–7.49 (m, 2H), 7.35–7.32 (m, 5H), 4.76 (s, 1H), 3.74–3.72 (m, 4H), 2.62–2.61 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 136.4, 133.5, 131.7, 129.8, 128.3, 122.6, 88.8, 84.3, 67.0, 61.2, 49.7; MS m/z (%) 311 (M^+ , 16), 225 (100), 135 (52), 86 (22), 77 (20), 56 (26).

^1H NMR (300 MHz, CDCl_3 , ppm): δ 7.70–7.65 (m, 1H), 7.51–7.47 (m, 2H), 7.35–7.27 (m, 4H), 7.18–7.04 (m, 2H), 5.08 (s, 1H), 3.75–3.71 (m, 4H), 2.68–2.65 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 162.3 (d, $J = 247\text{ Hz}$), 131.8, 130.6, 129.8 (d, $J = 8.0\text{ Hz}$), 128.3, 128.2, 124.7 (d, $J = 14\text{ Hz}$), 123.6 (d, $J = 3\text{ Hz}$), 122.7, 115.7 (d, $J = 22\text{ Hz}$), 87.6, 84.7, 67.0, 55.4, 49.8; MS m/z (%) 295 (M^+ , 14), 226 (14), 209 (100), 86 (27), 77 (28), 56 (47).

^1H NMR (300 MHz, CDCl_3 , ppm): δ 7.53–7.51 (m, 6H), 7.35–7.34 (m, 3H), 4.75 (s, 1H), 3.74–3.73 (m, 4H), 2.63–2.62 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 136.9, 131.7, 131.2, 130.1, 128.3, 122.6, 121.7, 88.9, 84.2, 67.0, 61.3, 49.7; MS m/z (%) 357 (M^+ , 20), 271 (99), 269 (100), 189 (97), 86 (51), 77 (15), 56 (81).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 8.25–8.21 (m, 2H), 7.88–7.84 (m, 2H), 7.54–7.51 (m, 2H), 7.38–7.36 (m, 3H), 4.88 (s, 1H), 3.76–3.73 (m, 4H), 2.64–2.63 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 147.3, 145.3, 131.7, 129.2, 128.5, 128.3, 123.3, 122.1, 89.2, 82.5, 66.8, 61.2, 49.6.

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.55–7.52 (m, 4H), 7.35–7.33 (m, 3H), 7.21–7.18 (m, 2H), 4.77 (s, 1H), 3.75–3.74 (m, 4H), 2.67–2.63 (m, 4H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 137.4, 134.8, 131.8, 128.9, 128.5, 128.2, 128.1, 123.0, 88.2, 85.3, 67.1, 61.7, 49.8, 21.1; MS *m/z* (%) 291 (M^+ , 15), 260 (21), 205 (100), 77 (4), 56 (12).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.56–7.50 (m, 4H), 7.35–7.26 (m, 3H), 6.93–6.89 (m, 2H), 4.74 (s, 1H), 3.82 (m, 3H), 3.78–3.74 (m, 4H), 2.68–2.63 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 159.4, 132.0, 130.1, 130.0, 128.5, 128.4, 123.3, 113.8, 88.5, 85.6, 67.4, 61.7, 55.5, 50.1; MS *m/z* (%) 307 (M^+ , 4), 221 (38), 135 (30), 87 (100), 77 (26), 43 (73).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 8.38–8.36 (m, 1H), 7.90–7.79 (m, 3H), 7.54–7.41 (m, 5H), 7.32–7.31 (m, 3H), 5.42 (s, 1H), 3.72–3.60 (m, 4H), 2.70–2.69 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 134.0, 133.1, 131.8, 128.9, 128.5, 128.3, 128.2, 127.1, 125.9, 124.7, 123.0, 89.0, 85.0, 67.2, 60.1, 49.8; MS *m/z* (%) 327 (M^+ ,

16), 258 (8), 241 (100), 200 (26), 115 (14), 86 (16), 56 (18).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.50–7.49 (m, 2H), 7.49–7.48 (m, 1H), 7.43–7.32 (m, 3H), 6.51–6.50 (m, 1H), 6.36–6.35 (m, 1H), 4.87 (s, 1H), 3.80–3.76 (m, 4H), 2.66–2.65 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 150.7, 142.8, 131.8, 128.4, 128.3, 122.5, 110.1, 109.7, 87.0, 82.8, 66.9, 56.1, 49.6; MS *m/z* (%) 267 (M^+ , 6), 181 (100), 152 (33), 86 (13), 77 (10), 56 (21).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.46–7.40 (m, 2H), 7.30–7.26 (m, 3H), 3.81–3.70 (m, 4H), 3.51 (t, $J = 8.4$ Hz, 1H), 2.77–2.71 (m, 2H), 2.60–2.53 (m, 2H), 1.74–1.48 (m, 4H), 1.00–0.95 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 131.6, 128.1, 127.8, 123.1, 87.0, 86.1, 67.0, 57.7, 49.6, 34.9, 19.7, 13.8; MS *m/z* (%) 243 (M^+ , 5), 200 (100), 128 (12), 115 (43), 77 (6), 41 (9).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.45–7.44 (m, 2H), 7.29–7.28 (m, 3H), 3.79–3.74 (m, 4H), 3.13 (d, $J = 9.9$ Hz, 1H), 2.70–2.69 (m, 2H), 2.53–2.50 (m, 2H), 2.14–2.04 (m, 2H), 1.77–1.59 (m, 4H), 1.32–0.96 (m, 5H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 131.6, 128.1, 127.7, 123.3, 86.7, 86.5, 67.0, 63.8, 49.8, 38.9, 30.9, 30.2, 26.6, 26.1, 25.9; MS *m/z* (%) 283 (M^+ , 2), 200 (100), 115 (20), 77 (2), 55 (9), 41 (10).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.66–7.64 (m, 2H), 7.54–7.51 (m, 2H), 7.39–7.33 (m, 6H), 4.92 (s, 1H), 2.73 (m, 4H), 1.83 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 138.4, 131.7, 128.2, 128.0, 127.5, 123.1, 86.8, 86.6, 59.0, 50.2, 23.4;

MS m/z (%) 261 (M^+ , 18), 191 (100), 184 (61), 115 (13), 77 (5).

^1H NMR (300 MHz, CDCl_3 , ppm): δ 7.77–7.74 (m, 2H), 7.64–7.61 (m, 2H), 7.48–7.35 (m, 6H), 4.90 (s, 1H), 2.69–2.66 (m, 4H), 1.74–1.67 (m, 4H), 1.58–1.52 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 138.5, 131.7, 128.4, 128.2, 127.9, 127.3, 123.2, 87.8, 86.0, 62.3, 50.6, 26.1, 24.3; MS m/z (%) 275 (M^+ , 20), 198 (81), 191 (100), 115 (14), 84 (24), 77 (6).

^1H NMR (300 MHz, CDCl_3 , ppm): δ 7.72–7.70 (m, 2H), 7.54–7.52 (m, 2H), 7.38–7.32 (m, 6H), 5.08 (s, 1H), 2.66–2.58 (m, 4H), 1.09 (t, $J = 3.3$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 139.8, 131.8, 128.3, 128.2, 128.0, 127.2, 123.4, 87.4, 86.1, 57.0, 44.5, 13.6; MS m/z (%) 263 (M^+ , 7), 248 (9), 191 (100), 186 (31), 77 (5).

^1H NMR (300 MHz, CDCl_3 , ppm): δ 7.88–7.86 (m, 2H), 7.61–7.55 (m, 2H), 7.47–7.26 (m, 6H), 5.14 (s, 1H), 3.38–3.28 (m, 4H), 1.41 (d, $J = 6.3$ Hz, 6H), 1.17 (d, $J = 6.3$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 142.1, 131.3, 128.5, 128.3, 127.8, 127.7, 126.8, 123.9, 91.6, 85.9, 50.4, 46.6, 23.8, 20.7; MS m/z (%) 291 (M^+ , 3), 276 (11), 214 (4), 191 (100), 165 (5), 77 (4).

^1H NMR (300 MHz, CDCl_3 , ppm): δ 7.75–7.73 (m, 2H), 7.47–7.45 (m, 2H), 7.32–7.22 (m, 6H), 5.03 (s, 1H), 2.75–2.67 (m, 2H), 2.34–2.30 (m, 2H), 1.79–0.84 (m, 18H); ^{13}C NMR (75 MHz, CDCl_3 , ppm): δ 142.3, 131.3, 128.3, 127.9, 127.7, 126.7, 124.0, 92.0, 85.2, 56.0, 51.4, 34.3, 32.4, 26.7, 26.5, 26.1; MS m/z (%) 371 (M^+ , 7), 315 (19), 238 (15), 191 (100), 55 (25), 41 (17).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.75–7.73 (m, 2H), 7.64–7.62 (m, 2H), 7.59–7.33 (m, 11H), 4.98 (s, 1H), 3.74 (dd, $J = 12.3, 28.5\text{Hz}$, 2H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 139.2, 139.0, 131.9, 129.0, 128.3, 128.1, 127.5, 127.0, 123.2, 88.6, 84.6, 59.5, 58.9, 38.0; MS m/z (%) 311 (M^+ , 13), 234 (34), 191 (100), 91 (57), 77 (9).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.70–7.64 (m, 2H), 7.45–7.22 (m, 10H), 6.82–6.79 (m, 3H), 5.53 (s, 1H), 4.19 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 146.5, 139.7, 131.7, 129.1, 128.8, 128.3, 128.2, 127.3, 122.7, 118.5, 114.0, 88.4, 85.0, 50.6; MS m/z (%) 283 (M^+ , 7), 206 (4), 191 (100), 91 (13), 77 (19).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.66–7.64 (m, 2H), 7.60–7.31 (m, 8H), 4.89 (s, 1H), 1.32 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 142.6, 131.4, 128.5, 128.1, 127.9, 127.3, 123.4, 92.4, 84.2, 51.8, 48.7, 29.8; MS m/z (%) 263 (M^+ , 2), 248 (17), 191 (100), 77 (11).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.56–7.55 (m, 2H), 7.36–7.26 (m, 3H), 4.53 (s, 1H), 3.71–3.69 (m, 4H), 2.55–2.52 (m, 4H), 2.30 (t, $J = 7.2\text{Hz}$, 2H), 1.61–1.54 (m, 2H), 1.45–1.32 (m, 4H), 0.91 (t, $J = 7.2\text{Hz}$, 3H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 138.3, 128.6, 128.1, 127.5, 88.8, 75.3, 67.1, 61.6, 49.7, 31.1, 28.7, 22.2, 18.7, 14.0; MS m/z (%) 271 (M^+ , 17), 194 (100), 128 (55), 91 (70), 86 (69), 56 (65), 41 (41).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.57–7.55 (m, 2H), 7.37–7.26 (m, 3H), 4.58 (s, 1H), 3.72–3.70 (m, 4H), 2.54–2.51 (m, 4H), 0.24 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 137.4, 128.5, 128.1, 127.7, 100.9, 93.0, 67.1, 62.0, 49.6, 0.13; MS *m/z* (%) 273 (M^+ , 21), 196 (100), 187 (28), 159 (68), 86 (67), 73 (21), 56 (59), 43 (18).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.58–7.57 (m, 2H), 7.37–7.33 (m, 2H), 7.31–7.27 (m, 1H), 4.59 (s, 1H), 4.48 (s, 2H), 3.73–3.69 (m, 4H), 2.58–2.54 (m, 4H), 0.97 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 137.6, 128.4, 128.0, 127.6, 86.8, 80.2, 67.0, 61.4, 51.7, 49.7, 25.7, 18.2, -5.2; MS *m/z* (%) 345 (M^+ , 8), 268 (26), 176 (31), 128 (26), 86 (44), 75 (53), 73 (100), 56 (24).

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.62–7.31 (m, 30H), 4.70 (s, 1H), 4.49 (s, 1H), 4.40 (q, $J = 6.6\text{Hz}$, 1H), 3.95 (q, $J = 6.6\text{Hz}$, 1H), 1.77 (brs, 2H), 1.45 (d, $J = 6.6\text{Hz}$, 3H), 1.40 (d, $J = 6.6\text{Hz}$, 3H). Assignments were made by comparing the relative areas of proton signals at δ 4.70 and 4.49, respectively.

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.87–7.27 (m, 40H), 5.11 (s, 1H), 5.03 (s, 1H), 4.23–3.60 (m, 6H), 1.82 (d, $J = 7.2\text{Hz}$, 3H), 1.31 (d, $J = 7.2\text{Hz}$, 3H). Assignments were made by comparing the relative areas of proton signals at δ 5.11 and 5.03, respectively.

^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.69–7.67 (m, 2H), 7.51–7.50 (m, 2H), 7.39–7.29 (m, 6H), 5.24 (s, 1H), 3.78 (s, 3H), 3.78–3.74 (m, 1H), 2.76–2.70 (m, 2H), 2.20–2.04 (m, 2H), 1.83–1.78 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3 , *ppm*): δ 174.6, 138.9, 131.8, 128.3, 127.6, 122.9, 87.9, 85.1, 63.1, 57.3, 51.9, 47.4, 29.7, 23.2; MS *m/z* (%) 319 (M^+ , <1), 260 (21), 191 (100), 85 (18), 57 (38), 43 (26).

Copies of ^1H NMR of these Compounds:

¹H NMR of 1a

¹H NMR of 1b

5.128
5.120

3.709
3.695
3.678
3.662

2.675
2.667
2.660
2.644

¹H NMR of 1c

^1H NMR of 1d

¹H NMR of 1f

^1H NMR of **1j**

^1H NMR of 1k

¹H NMR of 11

¹H NMR of 1m

¹H NMR of 2a

¹H NMR of 2c

¹H NMR of 2d

5.034

^1H NMR of 2e

¹H NMR of 2g

¹H NMR of 2h

^1H NMR of **2i**

^1H NMR of 3b

¹H NMR of 3c

¹H NMR of 4b

¹H NMR of 4c