A Remarkably Efficient Coupling of Acid Chlorides with Alkynes in Water

Liang Chen^a and Chao-Jun Li^{*a, b}

^a: Department of Chemistry, Tulane University, New Orleans, Louisiana 70118 USA; ^bDepartment of Chemistry, McGill University, 801 Sherbrooke St. West, Montreal, Quebec H3A 2K6, Canada.
Email: cj.li@mcgill.ca

Supporting information

Experimental:

¹H NMR, ¹³C NMR, GC-MS and IR were performed at the Department of Chemistry of Tulane University.

General Procedure. All reactions were carried out by the following general procedure except the synthesis of compound (5), 1-(4-nitrophenyl)-3-phenylprop-2-yn-1-one. 1 mmol of terminal alkynes, 2 mmol of acid chloride, 20 mg of sodium lauryl sulfate (7 mol%), 14 mg PdCl₂(PPh₃)₂ (2 mol%) and 10 mg CuI (5 mol%) were added in a small test tube (10 mL) that was cooled by ice-water bath then 1 mL ice-cold water that dissolved 414 mg K₂CO₃ (3 mmol) was added to the test tube in small portions while stirring. After the addition was completed, the reaction mixture was capped, then heated and stirred at 65°C for 4 hours. Then the reaction mixture was cooled and extracted with ethyl ether (3 × 10 mL) and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 10:1 or 20:1) to give the pure product.

Characteristic Data

1,3-diphenylprop-2-yn-1-one

1,3-diphenylprop-2-yn-1-one (1)¹ (202 mg, 98% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.19 (dd, *J* = 8.0 Hz, 1.6 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.48-7.34 (m, 5H); ¹³C NMR (400 MHz, CDCl₃): δ 178.2, 137.0, 134.4, 133.3, 131.1, 129.8, 129.0, 128.9, 120.2, 93.4, 87.2; IR (neat) cm⁻¹ 3057, 2199, 1640; GC-MS (Relative Intensity) 206 (M⁺, 70), 178 (100), 129 (78), 101 (12), 75 (22), 51 (19).

3-phenyl-1-*m*-tolylprop-2-yn-1-one

3-phenyl-1-*m*-tolylprop-2-yn-1-one (2)² (218 mg, 99% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.04-7.99 (m, 2H), 7.68-7.66 (m, 2H), 7.47-7.39 (m, 5H), 2.43 (s, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 178.5, 138.7, 137.1, 135.2, 133.3, 131.0, 130.0, 128.9, 128.7, 127.4, 120.4, 93.1, 87.2, 21.6; IR (neat) cm⁻¹ 3057, 2914, 2205, 1633; GC-MS (Relative Intensity) 220 (M⁺, 69), 192 (100), 129 (73), 101 (17), 91 (12), 75 (28), 65 (19), 51 (15).

3-phenyl-1-*p*-tolylprop-2-yn-1-one

3-phenyl-1-*p*-tolylprop-2-yn-1-one (3)¹ (215 mg, 98% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.42-7.35 (m, 3H), 7.25 (d, *J* = 8.4 Hz, 2H), 2.37 (s, 3H) ; ¹³C NMR (400 MHz, CDCl₃): δ 177.9, 145.5, 134.8, 133.3, 131.0, 129.9, 129.6, 128.9, 120.4, 92.9, 87.2, 22.1; IR (neat) cm⁻¹ 3057, 2914, 2192, 1640; GC-MS (Relative Intensity) 220 (M⁺, 77), 192 (100), 191 (54), 129 (50), 101 (8), 75 (12), 51 (5).

1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-one

1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-one (4)³ (193 mg, 82% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.09 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.32-7.28 (m, 3H), 6.87 (d, *J* = 8.8 Hz, 2H), 3.76 (s, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 176.6, 164.5, 132.9, 131.9, 130.6, 130.2, 128.6, 120.2, 113.8, 92.3, 86.9, 55.5; IR (neat) cm⁻¹ 3057, 2199, 1627; GC-MS (Relative Intensity) 236 (M⁺, 79), 208 (100), 193 (92), 165 (65), 129 (53), 101 (17), 75 (28), 63 (24), 51 (13).

1-(4-nitrophenyl)-3-phenylprop-2-yn-1-one

1-(4-nitrophenyl)-3-phenylprop-2-yn-1-one (5)³ (128 mg, 51% yield) 4-nitrobenzoyl chloride (370 mg, 2 mmol, 2 equiv) was dissolved in 200 mg toluene in a small test tube (10 mL) that was cooled by ice-water bath, then phenylacetylene (102 mg, 1 mmol, 1

equiv), sodium lauryl sulfate (20 mg, 7 mol %), PdCl₂(PPh₃)₂ (14 mg, 2 mol%) and CuI (10 mg, 5 mol%) were added into the test tube. After that, 1 mL ice-cold water that dissolved K₂CO₃ (414 mg, 3 mmol) was added to the test tube in small portions while stirring. After completing the addition, the reaction mixture was capped, then heated and stirred at 65°C for 4 hours. Then the reaction mixture was cooled and extracted with ethyl ether (3 × 10mL) and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 10:1) to give 128 mg of pure product 1-(4-nitrophenyl)-3-phenylprop-2-yn-1-one (51% yield). ¹H NMR (400 MHz, CDCl₃): δ 8.36 (s, 4H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.52-7.42 (m, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 176.1, 151.1, 141.2, 133.5, 131.7, 130.7, 129.1, 124.1, 119.6, 95.7, 86.7; IR (neat) cm⁻¹ 3057, 2186, 1646; GC-MS (Relative Intensity) 252 (M⁺, 25), 223 (27), 129 (100).

3-(naphthalen-1-yl)-1-phenylprop-2-yn-1-one

3-(naphthalen-1-yl)-1-phenylprop-2-yn-1-one (6)⁴ (205 mg, 80% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.40 (d, *J* = 8.0 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 2H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 3H), 7.41 (t, *J* = 8.0 Hz, 1H); ¹³C NMR (400 MHz, CDCl₃): δ 178.2, 137.3, 134.5, 133.9, 133.6, 133.3, 131.9, 129.9, 129.0, 128.9, 128.1, 127.3, 126.0, 125.5, 117.8, 92.0, 91.8; IR (neat) cm⁻¹ 3057, 2186, 1640; GC-MS (Relative Intensity) 256 (M⁺, 96), 227 (100), 179 (63), 150 (46), 77 (28), 51 (27).

3-(naphthalen-1-yl)-1-*p*-tolylprop-2-yn-1-one

3-(naphthalen-1-yl)-1-*p*-tolylprop-2-yn-1-one (7)⁵ (262 mg, 97% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.40 (d, *J* = 8.4 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 2H), 7.93-7.90 (m, 2H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 177.9, 145.5, 135.0, 133.9, 133.4, 133.3, 131.7, 130.0, 129.7, 128.8, 128.0, 127.2, 126.0, 125.5, 118.0, 92.0, 91.3, 22.1; IR (neat) cm⁻¹ 3058, 2917, 2186, 1635; GC-MS (Relative Intensity) 270 (M⁺, 100), 242 (88), 179 (43), 150 (28), 121 (15), 91 (9).

1-phenylnon-2-yn-1-one

1-phenylnon-2-yn-1-one (8)⁶ (141 mg, 66% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.09 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 2H), 2.44 (t, *J* = 6.8 Hz, 2H), 1.64-1.58 (m, 2H), 1.46-1.40 (m, 2H), 1.29-1.25 (m, 4H), 0.85 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 178.4, 137.1, 134.1, 129.7, 128.7, 97.1, 79.9, 31.4, 28.8, 28.0, 22.7, 19.4, 14.2; IR (neat) cm⁻¹ 3057, 2927, 2856, 2192, 1640; GC-MS (Relative Intensity) 214 (M⁺, 5), 199 (10), 186 (26), 171 (23), 157 (48), 145 (19), 129 (19), 115 (52), 105 (100), 77 (73), 51 (30).

1-*p*-tolynon-2-yn-1-one

1-*p*-tolynon-2-yn-1-one (9)¹ (176 mg, 77% yield) ¹H NMR (400 MHz, CDCl₃): δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 2.43 (t, *J* = 7.2 Hz, 2H), 2.36 (s, 3H), 1.65-1.57 (m, 2H), 1.46-1.38 (m, 2H), 1.29-1.25 (m, 4H), 0.86 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 178.1, 145.1, 134.8, 129.9, 129.4, 96.5, 79.9, 31.4, 28.8, 28.0, 22.7, 22.0, 19.4, 14.2; IR (neat) cm⁻¹ 3025, 2934, 2856, 2186, 1640; GC-MS (Relative Intensity) 228 (M⁺, 6), 213 (25), 185 (63), 171 (42), 158 (20), 145 (19), 129 (26), 119 (100), 91 (39), 79 (11), 65 (10).

3-cyclohexenyl-1-phenylprop-2-yn-1-one

3-cyclohexenyl-1-phenylprop-2-yn-1-one (10)⁷ (174 mg, 83% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.04 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 2H), 6.46 (m, 1H), 2.18-2.06 (m, 4H), 1.59-1.50 (m, 4H); ¹³C NMR (400 MHz, CDCl₃): δ 178.4, 143.0, 137.2, 134.1, 129.6, 128.7, 119.3, 96.0, 85.4, 28.6, 26.4, 22.1, 21.3; IR (neat) cm⁻¹ 3063, 2927, 2186, 1633; GC-MS (Relative Intensity) 210 (M⁺, 82), 195 (5), 181 (19), 167 (34), 153 (29), 133 (19), 115 (19), 105 (99), 77 (100), 51 (39).

3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-one

3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-one (11)⁸ (234 mg, 99% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.08 (d, *J* = 8.0 Hz, 2H), 7.50-7.47 (m, 3H), 7.37 (t, *J* = 7.2 Hz, 2H), 6.78 (d, *J* = 8.8 Hz, 2H), 3.68 (s, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 178.2, 162.0, 137.2, 135.4, 134.2, 129.7, 128.8, 114.7, 112.0, 94.7, 87.1, 55.6; IR (neat) cm⁻¹ 3057, 2956, 2192, 1635; GC-MS (Relative Intensity) 236 (M⁺, 100), 208 (52), 193 (64), 165 (55), 159 (91), 144 (20), 116 (25), 77 (50), 51 (41).

3-(4-bromophenyl)-1-phenylprop-2-yn-1-one

3-(4-bromophenyl)-1-phenylprop-2-yn-1-one (12)⁹ (251 mg, 88% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.06-8.03 (m, 2H), 7.47-7.37 (m, 7H); ¹³C NMR (400 MHz, CDCl₃): δ 177.9, 136.8, 134.6, 134.5, 132.3, 129.8, 128.9, 125.8, 119.2, 91.9, 87.9; IR (neat) cm⁻¹ 3051, 2192, 1628; GC-MS (Relative Intensity) 286 (M⁺⁺², 45), 284 (M⁺, 46), 258 (100), 256 (83), 206 (54), 176 (76), 151 (21), 128 (48), 101 (18), 77 (63), 51 (62).

1-phenyl-3-p-tolylprop-2-yn-1-one

1-phenyl-3-p-tolylprop-2-yn-1-one (13)¹⁰ (202 mg, 92% yield) ¹H NMR (400 MHz, CDCl₃): δ 8.18 (dd, *J* = 8.4 Hz, 1.2 Hz, 2H), 7.57-7.44 (m, 5H), 7.16 (d, *J* = 8.0 Hz, 2H), 2.33 (s, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 178.2, 141.8, 137.1, 134.3, 133.4, 129.7, 129.7, 128.8, 117.1, 94.1, 87.0, 22.0; IR (neat) cm⁻¹ 3063, 2921, 2199, 1633; GC-MS

(Relative Intensity) 220 (M^+ , 79), 192 (93), 191 (53), 143 (100), 115 (24), 89 (21), 77 (24), 63 (14), 51 (21).

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1. Ahmed, M. S. M.; Mori, A. *Org. Lett.* **2003**, *5*, 3057.
 2. Zanina, A. S.; Shergina, S. I.; Sokolov, I. E.; Kotlyarevskii, I. L. *Seriya Khimicheskaya* **1981**, *5*, 1158.
 3. Alonso, D. A.; Najera, C.; Pacheco, M. C. *J. Org. Chem.* **2003**, *69*, 1615.
 4. Delaude, L.; Masdeu, A. M.; Alper, H. *Synthesis* **1994**, *11*, 1149.
 5. Kundu, N. G.; Pal, M.; Chowdhury, C. *J. Chem. Res., Synop.* **1995**, *1*, 4.
 6. Parker, K. A.; Ledebor, M. W. *J. Org. Chem* **1996**, *61*, 3214.
 7. Marvell, E. N.; Gosink, T.; Churchley, P.; Li, T. *J. Org. Chem.* **1972**, *37*, 2989.
 8. Fetter, J.; Nagy, I.; Giang, L. T.; Kajtar-Peredy, M.; Rockenbauer, A.; Korecz, L.; Czira, G. *J. Chem. Soc., Perkin Trans. 1* **2001**, *9*, 1131.
 9. Qian, H.; Shao, L.-X.; Huang, X. *Synlett* **2001**, *10*, 1571.
 10. Kakusawa, N.; Tobiyasu, Y.; Yasuike, S.; Yamaguchi, K.; Seki, H.; Kurita, J. *Tetrahedron Lett.* **2003**, *44*, 8589.