Carbonylative Sonogashira Coupling of Terminal Alkynes with Aqueous Ammonia

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Supporting Information

Experimental

General procedure for the carbonylative coupling of phenylethyne (1) with an aryl iodide (2) summarized in Table 1: To a 25 mL of Schlenk tube equipped with a magnetic stirring bar under argon were added $\text{PdCl}_2(\text{PPh}_3)_2$ (3.5 mg, 0.005 mmol) and THF (3 mL). Phenylethyne (66 μL , 0.6 mmol) and **2** (0.5 mmol) were added successively to the mixture to form a pale yellow solution. Then, aqueous ammonia (0.5 M, 2 mL, 1.0 mmol) was added dropwise via syringe. The atmosphere was replaced with carbon monoxide with a balloon and stirring was continued at room temperature. After the period shown in Table 1, the mixture was passed through a Celite pad and the filtrate was washed with brine. The aqueous layer was extracted with diethyl ether (3×15 mL) and the combined organic layers were dried over anhydrous MgSO_4 , and concentrated in vacuo. The residue was purified by flash chromatography using hexanes-ethyl acetate to afford the corresponding α,β -alkynyl ketones **3**.

1-(4-Methoxyphenyl)-3-phenyl-2-propynone (3a)¹: Reaction time: 41 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 72% yield (85 mg) as a colorless solid. Mp 98 °C, Lit. mp 100 °C. IR (KBr): $\nu = 2201, 1630 \text{ cm}^{-1}$. ¹H NMR (300 MHz, CDCl_3): δ 3.90 ppm (s, 3H), 6.99 (d, $J = 8.7$ Hz, 2H), 7.38-7.50 (m, 3H), 7.67 (dd, $J = 8.1, 1.5$ Hz, 2H), 8.20 (d, $J = 8.7$ Hz, 2H). ¹³C NMR (300 MHz, CDCl_3): δ 55.54, 86.85, 92.27, 113.83, 120.26, 128.60, 130.22, 130.55, 131.93, 132.90, 164.43, 176.63.

1-(2-Methoxyphenyl)-3-phenyl-2-propynone (3b)²: Reaction time: 24 h. Purification by flash chromatography (50:1 hexanes:ethyl acetate) afforded the product in 76% yield (90 mg) as a colorless oil. IR (neat): $\nu = 2199, 1641, 1620, 1597 \text{ cm}^{-1}$. ¹H NMR (300 MHz, CDCl_3): δ 3.97 (s, 3H), 7.01-7.10 (m, 2H), 7.36-7.76 (m, 6H), 8.10 (dd, $J = 7.5, 1.5$ Hz, 2H). ¹³C NMR (300 MHz, CDCl_3): 55.88, 89.12, 91.55, 112.14, 120.26, 120.63, 126.64, 128.54, 130.41, 132.65, 132.92, 135.00, 159.77, 176.73.

1-(3-Methoxyphenyl)-3-phenyl-2-propynone (3c): Reaction time: 51 h. Purification by flash chromatography (50:1 hexanes:ethyl acetate) afforded the product in 81% yield (95 mg) as a colorless oil. IR (neat): $\nu = 2205, 1642, 1597, 1582 \text{ cm}^{-1}$. ¹H NMR (300 MHz, CDCl_3): δ 3.90 (s, 3H), 7.18 (ddd, $J = 8.1, 1.7, 1.2$ Hz, 1H), 7.40-7.53 (m, 4H), 7.67-7.72

¹ Johnston, K. M.; Shotter, R. G. *J. Chem. Soc., C*. **1967**, 23, 2476.

² Larock, R. C.; Harrison, L. W. *J. Am. Chem. Soc.* **1984**, 106, 4218.

(m, 3H), 7.87 (ddd, $J = 7.8, 1.5, 1.2$ Hz, 1H). ^{13}C NMR (300 MHz, CDCl_3): 55.44, 86.90, 92.97, 112.72, 120.03, 120.94, 122.85, 128.65, 129.61, 130.79, 133.05, 138.17, 159.74., 177.75. HRMS (EI) m/z calcd for $\text{C}_{16}\text{H}_{16}\text{O}_2 = 236.0837$, found 236.0845.

3-Phenyl-1-(4-methylphenyl)-2-propynone (3d)³: Reaction time: 47 h. Purification by flash chromatography (50:1 hexanes:ethyl acetate) afforded the product in 64% yield (70 mg) as a colorless solid. Mp 70 °C, Lit. mp 71 °C. IR (KBr): $\nu = 2203, 1634, 1608, 1570$ cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 2.45 ppm (s, 3H), 7.30-7.45 (m, 5H), 7.68 (d, $J = 8.7$ Hz, 2H), 8.12 (d, $J = 8.7$ Hz, 2H). ^{13}C NMR (300 MHz, CDCl_3): δ 21.79, 86.91, 92.56, 120.17, 128.61, 129.31, 129.66, 130.64, 132.98, 134.53, 145.21, 177.68.

1,3-Diphenyl-2-propynone (3e)⁴: Reaction time: 25 h. Purification by flash chromatography (50:1 hexanes:ethyl acetate) afforded the product in 76% yield (78 mg) as a colorless solid. Mp 46-47 °C, Lit. mp 46-48 °C. IR (KBr): $\nu = 2201, 1651$ cm^{-1} . ^1H NMR (300 MHz, CDCl_3): 7.40-7.56 (m, 5H), 7.60 (m, 1H), 7.70 (m, 2H), 8.23 (ddd, $J = 8.4, 1.8, 1.2$ Hz, 2H). ^{13}C NMR (300 MHz, CDCl_3): 86.85, 93.11, 120.09, 128.61, 128.67, 129.57, 130.80, 133.06, 134.12, 136.84 178.03.

1-(1-Naphthyl)-3-phenyl-2-propynone (3f)⁵: Reaction time: 34 h. Purification by flash chromatography (50:1 hexanes:ethyl acetate) afforded the product in 50% yield (64 mg) as a colorless solid. Mp 95 °C, Lit. 95 °C. IR (KBr): $\nu = 2193, 1632, 1619$ cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 7.43-7.71 (m, 8H), 7.91 (d, $J = 8.7$ Hz, 1H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.65 (d, $J = 6.9$ Hz, 1H), 9.23 (d, $J = 8.4$ Hz, 1H). ^{13}C NMR (300 MHz, CDCl_3): 88.46, 91.68, 120.32, 124.45, 125.96, 126.74, 128.55, 128.64, 128.93, 130.58, 130.71, 132.92, 133.84, 134.50, 135.08, 179.71.

1-{4-(1-Oxoethyl)phenyl}-3-phenyl-2-propynone (3g): Reaction time: 25 h. Purification by flash chromatography (50:1 hexanes:ethyl acetate) afforded the product in 75% yield (93 mg) as a colorless solid. Mp 103-104 °C. IR (KBr): $\nu = 2199, 1686, 1632$ cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 2.67 ppm (s, 3H), 7.42-7.54 (m, 3H), 7.69-7.73 (m, 2H), 8.09 (d, $J = 8.7$ Hz, 2H), 8.31 (d, $J = 8.7$ Hz, 2H). ^{13}C NMR (300 MHz, CDCl_3): δ 26.95, 86.75, 94.28, 119.70, 128.42, 128.74, 129.67, 131.10, 133.15, 139.77, 140.75, 177.11, 197.42. HRMS (EI) m/z calcd for $\text{C}_{17}\text{H}_{12}\text{O}_2 = 248.0837$, found 248.0831.

1-(4-Chlorophenyl)-3-phenyl-2-propynone (3i)⁶: Reaction time: 12 h. Purification by flash chromatography (50:1 hexanes:ethyl acetate) afforded the product in 67% yield (80 mg) as a colorless solid. Mp 104-105 °C, Lit. mp 105 °C. IR (KBr): $\nu = 2201, 1655$ cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 7.43-7.51 ppm (m, 5H), 7.70 (d, $J = 8.4$ Hz, 2H), 8.16 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (300 MHz, CDCl_3): 86.52, 93.59, 119.80, 128.68, 128.94, 130.81, 130.93, 133.05, 135.21, 140.65, 176.59.

³ Baddar, F. G.; Al-Hajjar, F. H.; El-Rayyes, N. R. *J. Heterocyclic Chem.*, **1976**, *13*, 195.

⁴ Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.

⁵ Arcadi, A.; Cacchi, S.; Marinelli, F.; Pace, P.; Sanzi, G. *Synlett*, **1995**, 823.

⁶ Delaude, L.; Masdue, A. M.; Alper, H. *Synthesis*, **1994**, 1149.

General procedure for the carbonylative coupling of alkylalkynes **5 with aryl halides **2** summarized in Table 2:** To a solution of an alkylalkyne (**5**, 0.6 mmol), **2** (0.5 mmol), PdCl₂(PPh₃)₂ (17.5 mg, 0.025 mmol) and CuI (1.9 mg, 0.01 mmol) in THF (3 mL) was added aqueous ammonia (0.5 M, 2 mL, 1.0 mmol). The atmosphere was replaced with carbon monoxide with a balloon and stirring was continued at room temperature for the period shown in Table 2. The resulting mixture was passed through a Celite pad and the filtrate was washed with brine. The aqueous layer was extracted with diethyl ether (3 × 15 mL) and the combined organic layers were dried over MgSO₄, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel.

1-(4-Methoxyphenyl)-2-nonyn-1-one (6aa): Reaction time: 24 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 74% yield (90 mg) as a colorless oil. IR (neat): ν = 2932, 2858, 2199, 1638, 1597 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 0.93 ppm (t, J = 6.6 Hz, 3H), 1.31-1.68 (m, 8H), 2.48 (t, J = 6.9 Hz, 2H), 3.88 (s, 3H), 6.94 (d, J = 8.4 Hz, 2H), 8.11 (d, J = 6.6 Hz, 2H). ¹³C NMR (300 MHz, CDCl₃): 13.98, 19.15, 22.45, 27.78, 28.60, 31.19, 55.51, 79.59, 95.97, 113.65, 130.29, 131.86, 164.21, 176.95. HRMS (EI) m/z calcd for C₁₆H₂₀O₂ = 244.1463, found 244.1461.

1-(4-Methylphenyl)-2-nonyn-1-one (6ad): Reaction time: 24 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 78% yield (89 mg) as a colorless oil. IR (neat): ν = 2955, 2936, 2859, 2199, 1646, 1605 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 0.91 ppm (t, J = 7.2 Hz, 3H), 1.20-1.75 (m, 8H), 2.49 (t, J = 7.2 Hz, 2H), 7.27 (d, J = 8.7 Hz, 2H), 8.03 (d, J = 7.2 Hz, 2H). ¹³C NMR (300 MHz, CDCl₃): δ 13.94, 19.13, 21.69, 22.42, 27.73, 28.56, 31.16, 79.67, 96.27, 129.12, 129.60, 134.60, 144.81, 177.90. HRMS (EI) m/z calcd for C₁₆H₂₀O = 228.1514, found 228.1511.

1-(1-Naphthyl)-2-nonyn-1-one (6af): Reaction time: 25 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 60% yield (79 mg) as a colorless oil. IR (neat): ν = 3050, 2955, 2936, 2859, 2209, 1638 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 0.91 ppm (t, J = 6.9 Hz, 3H), 1.32-1.69 (m, 8H), 2.51 (t, J = 7.2 Hz, 2H), 7.54-7.66 (m, 3H), 7.89 (d, J = 7.2 Hz, 1H), 8.06 (d, J = 8.1 Hz, 1H), 8.54 (dd, J = 7.5, 1.5 Hz, 1H), 9.18 (d, J = 8.7 Hz, 1H). ¹³C NMR (300 MHz, CDCl₃): δ 13.99, 19.18, 22.46, 27.74, 28.63, 31.19, 81.25, 95.37, 124.34, 125.95, 126.58, 128.44, 128.73, 130.63, 132.94, 133.75, 134.41, 134.76, 180.00. HRMS (EI) m/z calcd for C₁₉H₂₀O = 264.1514, found 264.1518.

1-{4-(1-Oxoethyl)phenyl}-2-nonyn-1-one (6ag): Reaction time: 30 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 47% yield (60 mg) as a colorless oil. IR (neat): ν = 2967, 2930, 2859, 2238, 2203, 1691, 1649 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 0.91 ppm (t, J = 6.9 Hz, 3H), 1.20-1.75 (m, 8H), 2.53 (t, J = 7.8 Hz, 2H), 2.66 (s, 3H), 8.04 (d, J = 6.6 Hz, 2H), 8.22 (d, J = 6.6 Hz, 2H). ¹³C NMR (300 MHz, CDCl₃): δ 13.99, 19.23, 22.44, 26.95, 27.65, 28.60, 31.16, 79.57, 98.27, 128.29, 129.64, 139.82, 140.56, 177.33, 197.51. HRMS (EI) m/z calcd for C₁₇H₂₀O₂ = 256.1463, found 256.1474.

1-(2-Aminophenyl)-2-nonyn-1-one (6ah): Reaction time: 40 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 71% yield (81 mg) as a pale yellow oil. IR (neat): $\nu = 3449, 3341, 2955, 2930, 2859, 2226, 1622, 1586 \text{ cm}^{-1}$. ^1H NMR (300 MHz, CDCl_3): δ 0.90 ppm (t, $J = 6.9 \text{ Hz}$, 3H), 1.25-1.72 (m, 8H), 2.48 (t, $J = 7.8 \text{ Hz}$, 2H), 6.29 (brs, 2H), 6.61-6.71 (m, 2H), 7.29-7.31 (m, 1H), 8.06-8.09 (m, 1H). ^{13}C NMR (300 MHz, CDCl_3): δ 13.93, 19.08, 22.40, 27.73, 28.53, 31.13, 79.75, 95.77, 115.80, 116.58, 118.68, 134.53, 134.92, 150.89, 179.83. HRMS (EI) m/z calcd for $\text{C}_{15}\text{H}_{19}\text{ON} = 229.1467$, found 229.1474. Anal. Calcd for $\text{C}_{15}\text{H}_{19}\text{ON}$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.76; H, 8.28; N, 5.99.

1-(4-Chlorophenyl)-2-nonyn-1-one (6ai): Reaction time: 26 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 70% yield (87 mg) as a colorless oil. IR (neat): $\nu = 2930, 2859, 2238, 2201, 1637, 1597, 1576 \text{ cm}^{-1}$. ^1H NMR (300 MHz, CDCl_3): δ 0.91 (s, 3H), 1.20-1.75 (m, 8H), 2.50 (t, $J = 7.2 \text{ Hz}$, 2H), 7.44 (d, $J = 8.1 \text{ Hz}$, 2H), 8.05 (d, $J = 8.1 \text{ Hz}$, 2H). ^{13}C NMR (300 MHz, CDCl_3): 13.95, 19.16, 22.42, 27.66, 28.58, 31.14, 79.33, 97.45, 128.77, 130.78, 135.27, 140.37, 176.81. HRMS (EI) m/z calcd for $\text{C}_{15}\text{H}_{17}\text{ClO} = 248.0968$, found 248.0967.

1,4-Di(1-oxo-2-nonyn-1-yl)benzene (8): Reaction time: 27 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 53% yield (93 mg) as a colorless oil. IR (neat): $\nu = 2957, 2930, 2859, 2236, 2199, 1657 \text{ cm}^{-1}$. ^1H NMR (300 MHz, CDCl_3): δ 0.91 ppm (t, $J = 7.2 \text{ Hz}$, 6H), 1.30-1.76 (m, 16H), 2.53 (t, $J = 6.9 \text{ Hz}$, 4H), 8.22 (s, 4H). ^{13}C NMR (300 MHz, CDCl_3): δ 13.99, 19.25, 22.45, 27.66, 28.62, 31.17, 79.63, 98.40, 129.47, 140.33, 177.33. HRMS (EI) m/z calcd for $\text{C}_{24}\text{H}_{30}\text{O}_2 = 350.2246$, found 350.2237.

1-(1-Octyn-1-yl)-4-(1-oxo-2-nonyn-1-yl)benzene (9): Reaction time: 27 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 37% yield (60 mg) as a colorless oil. IR (neat): $\nu = 2957, 2932, 2859, 2234, 2201, 1647, 1601 \text{ cm}^{-1}$. ^1H NMR (300 MHz, CDCl_3): δ 0.90 ppm (t, $J = 6.9 \text{ Hz}$, 6H), 1.25-1.70 (m, 16H), 2.40-2.55 (m, 4H), 7.46 (d, $J = 8.7 \text{ Hz}$, 2H), 8.04 (d, $J = 8.7 \text{ Hz}$, 2H). ^{13}C NMR (300 MHz, CDCl_3): δ 14.00, 14.03, 19.21, 19.55, 22.47, 22.52, 27.72, 28.46, 28.59, 28.62, 31.19, 31.30, 79.59, 80.18, 95.15, 97.13, 129.34, 129.96, 131.52, 135.51, 177.43. HRMS (EI) m/z calcd for $\text{C}_{23}\text{H}_{30}\text{O} = 322.2297$, found 322.2288.

4,4-Dimethyl-1-(4-methoxyphenyl)-2-pentyn-1-one (6ba): Reaction time: 20 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 87% yield (94 mg) as a colorless oil. IR (neat): $\nu = 2993, 2932, 2903, 2842, 2211, 1647, 1597, 1576 \text{ cm}^{-1}$. ^1H NMR (300 MHz, CDCl_3): δ 1.37 (s, 9H), 3.88 (s, 3H), 6.95 (d, $J = 8.4 \text{ Hz}$, 2H), 8.10 (d, $J = 8.4 \text{ Hz}$, 2H). ^{13}C NMR (300 MHz, CDCl_3): 27.95, 30.18, 55.50, 78.02, 103.05, 113.66, 130.41, 131.83, 164.17, 177.06. HRMS (EI) m/z calcd for $\text{C}_{14}\text{H}_{16}\text{O}_2 = 216.1150$, found 216.1158.

4,4-Dimethyl-1-phenyl-2-pentyn-1-one (6be)⁷: Reaction time: 24 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 77% yield (71

⁷ Smith III, A. B.; Levenberg, P. A.; Suits, J. Z. *Synthesis*, **1986**, 184.

mg) as a colorless oil. IR (neat): ν = 3065, 2973, 2932, 2870, 2212, 1647, 1619, 1599, 1582 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 1.39 (s, 9H), 7.48-7.623 (m, 3H), 8.12 (dd, J = 8.1, 1.2 Hz, 2H). ^{13}C NMR (300 MHz, CDCl_3): 28.01, 30.14, 78.06, 103.96, 128.44, 129.47, 133.79, 136.97, 178.36.

4,4-Dimethyl-1-(1-naphthyl)-2-pentyn-1-one (6bf): Reaction time: 19 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 69% yield (82 mg) as a colorless oil. IR (neat): ν = 2973, 2930, 2869, 2207, 1637, 1619, 1591, 1574 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 1.40 (s, 9H), 7.53-7.65 (m, 3H), 7.88 (d, J = 7.2 Hz, 1H), 8.06 (d, J = 8.1 Hz, 1H), 8.50 (d, J = 7.2 Hz, 1H), 9.15 (d, J = 8.7 Hz, 1H). ^{13}C NMR (300 MHz, CDCl_3): 27.96, 30.14, 79.79, 102.31, 124.35, 125.96, 126.57, 128.43, 128.67, 130.64, 133.19, 133.76, 134.13, 134.66, 180.13. HRMS (EI) m/z calcd for $\text{C}_{17}\text{H}_{16}\text{O}$ = 236.1201, found 236.1208.

4-Hydroxy-1-(4-methoxyphenyl)-4-methyl-2-pentyn-1-one (6ca): Reaction time: 46 h. Purification by flash chromatography (30:1 hexanes:ethyl acetate) afforded the product in 55% yield based on ^1H NMR. Calculation was based on signals of methoxy groups at 3.89 (s, 3H for **6ca**) and 3.78 (s, 3H for **2a**).

5-Hydroxy-1-(4-methoxyphenyl)-2-pentyn-1-one (6da): Reaction time: 48 h. Purification by flash chromatography (3:1 hexanes:ethyl acetate) afforded the product in 56% yield (57 mg) as a colorless solid. Mp 104 $^{\circ}\text{C}$. IR (KBr): ν = 3420, 2204, 1635 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 2.44 (brs, 1H), 2.76(t, J = 6.3 Hz, 2H), 3.88 (s, 3H), 3.89 (t, J = 6.3 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 8.11 (d, J = 9.0 Hz, 2H). ^{13}C NMR (300 MHz, CDCl_3): 23.52, 55.54, 60.27, 80.65, 92.62, 113.78, 129.93, 132.03, 164.48, 176.90. HRMS (EI) m/z calcd for $\text{C}_{12}\text{H}_{12}\text{O}_3$ = 204.0786, found 204.0794.

3g

3g

6aa

6ad

6ad

6ag

6ag

6ai

6ai

6ba

6ba

6ca

8

8

6

6