Synthesis of ynones by palladium-catalyzed acylation of terminal alkynes with acid chlorides

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Supporting Information

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2. Typical experimental procedures and analytical and spectral data for synthesized compounds.

1. General experimental methods:

All the reagents and solvents were obtained from commercial sources and used without purification unless otherwise stated. When necessary, TEA was dried prior to use by standard methods.¹ Gas chromatographic analyses were performed on an instrument equipped with a fused silica capillary column using decane as internal standard. Mass spectra (MS) were obtained at 70 eV on a GC system with a mass selective detector, fragment ions in m/z with relative intensities (%) in parenthesis. IR data were collected on a FT-IR spectrometer. ¹H NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts are reported in ppm using tetramethylsilane (TMS,

0.00 ppm) as internal standard. ^{13}C NMR spectra were recorded at 75 MHz with CDCl_3 as the internal reference. The catalysts were weighed out in an electronic microscale apparatus with a precision of 1 μg . When mentioned, the reactions were set up with the aid of a 12 place carousel reaction station equipped with gas-tight threaded caps with a valve, cooling reflux head system, and digital temperature controller. Reactions under microwave irradiation were conducted using microwave apparatus with a continuous focused microwave power delivery system with operator-selectable power output from 0 to 300 W. Reactions were performed in glass vessels (capacity 10 mL) sealed with a septum. The pressure is controlled by a load cell connected to the vessel via a 14-gauge needle, which penetrates just below the septum surface. The temperature of the contents of the vessel was monitored using a calibrated infrared temperature control mounted under the reaction vessel. All experiments were performed using a stirring option whereby the contents of the vessel are stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a Teflon-coated magnetic stir bar in the vessel.

2. Typical experimental procedures and analytical and spectral data for all synthesized compounds:

Compounds **3a**, **3c** and **3k**, are commercially available and were characterized by comparison of their IR, NMR and GC/MS spectra. Compounds **3b**,² **3d**,³ **3e**,³ **3f**,³ **3g**,⁴ **3h**,³ **3i**,³ **3j**,⁴ **3l**,⁵ **3m**⁶ and **3n**,² have been previously reported and were characterized by comparison of their IR, NMR and GC/MS spectra.

Typical experimental procedure for the palladium–catalyzed acylation coupling of 1-alkynes and acid chlorides. A reaction tube of the carousel reaction equipment, was charged with phenylacetylene (56 μL , 0.5 mmol), decane (97 μL , 0.5 mmol), benzoyl chloride (116 μL , 1 mmol), TEA (212 μL , 1.5 mmol), **2** (0.408 mg, 0.0005 mmol, 0.2 mol% Pd) or $\text{Pd}(\text{OAc})_2$ (0.240 mg, 0.001 mmol, 0.2 mol% Pd) and toluene (2 mL). The mixture was stirred at 110 $^\circ\text{C}$ or at rt (see Tables 1 and 2) in air or under Ar atmosphere and the reaction progress was analyzed by GLC. After completion, the crude reaction mixture was extracted with water and EtOAc (3 $\times$ 15 mL). The organic phases were dried, evaporated (15 mmHg) and the resulting crude material was purified by florisil chromatography (hexane/EtOAc) affording pure **diphenylpropynone (3a)**; yield: 76.9 mg (73%); R_f : 0.31 (hexane/EtOAc: 9/1); IR (film): ν (cm^{-1}) = 2199 ($\text{C}\equiv\text{C}$), 1642 ($\text{C}=\text{O}$); ^1H NMR: δ = 7.40-7.71 (m, 8H), 8.21-8.24 (m, 2H); ^{13}C NMR: δ = 86.9, 93.1, 120.2, 128.6, 128.7, 129.6, 130.8, 133.0, 134.1, 136.9, 178.0; MS: m/z (rel. Int.) = 206 (M^+ , 43), 179 (13), 178 (85), 176 (15), 130 (10), 129 (100), 105 (28), 101 (11), 89 (12), 77 (32), 76 (17), 75 (25), 74 (11) and 51 (31).

1-Phenyl-3-(triisopropylsilyl)propyn-2-one (3b): R_f : 0.45 (hexane/EtOAc: 9/1); IR (film): ν (cm^{-1}) = 2149 ($\text{C}\equiv\text{C}$), 1646 ($\text{C}=\text{O}$); ^1H NMR: δ = 1.16-1.20 (m, 21H), 7.49 (t, 2H, J = 7.37 Hz), 7.61 (t, 1H, J = 7.41 Hz), 8.16-8.19 (m, 2H); ^{13}C NMR: δ = 11.1, 18.5, 97.9, 103.1, 128.6, 129.5, 134.0, 136.8, 177.4; MS: m/z (rel. Int.) = 244 (M^+ -42, 20), 243 (M^+ -43, 81), 215 (30), 201 (10), 188 (10), 187 (66), 173 (31), 161 (12), 159 (23), 155 (16), 145 (32), 141 (19), 129 (16), 115 (33), 105 (100), 77 (64), 75 (27), 53 (11) and 51 (11).

1-Phenylnon-2-yn-1-one (3c); yield: 32.7 mg (31%); R_f : 0.44 (hexane/EtOAc: 9/1); IR (film): ν (cm^{-1}) = 2235, 2201 ($\text{C}\equiv\text{C}$), 1645 ($\text{C}=\text{O}$); ^1H NMR: δ = 0.84-1.73 (m, 11H), 2.50 (t, 2H, J = 7.10 Hz), 7.45-7.50 (m, 2H), 7.57-7.62 (m, 1H), 8.13-8.16 (m, 2H); ^{13}C NMR: δ = 14.0, 19.2, 22.5, 27.7, 28.6, 31.2, 79.6, 96.9, 128.4, 129.5, 133.8, 136.9, 178.2; MS: m/z (rel. Int.) = 213 (M^+-1 , 5), 186 (11), 185 (12), 171 (14), 158 (12), 157 (27), 145 (16), 144 (14), 129 (12), 128 (13), 115 (29), 106 (10), 105 (100), 79 (13), 77 (42), 67 (11), 66 (14) and 51 (15).

1-(4-Chlorophenyl)-3-phenylpropynone (3d): R_f : 0.37 (hexane/EtOAc: 9/1); Mp 105-106 °C (Lit. 104-105 °C); IR (film, CH_2Cl_2): ν (cm^{-1}) = 2201 ($\text{C}\equiv\text{C}$), 1655 ($\text{C}=\text{O}$); ^1H NMR: δ = 7.40-7.52 (m, 5H), 7.66-7.70 (m, 2H), 8.15 (d, 2H, J = 8.58); ^{13}C NMR: δ = 86.6, 93.6, 119.9, 128.7, 129.0, 130.8, 130.9, 133.1, 135.3, 140.7, 176.6; MS: m/z (rel. Int.) = 242 (M^++2 , 8), 240 (M^+ , 26), 214 (17), 212 (54), 176 (19), 129 (100), 111 (10), 75 (31) and 51 (11).

1-(4-Methoxyphenyl)-3-phenylpropynone (3e): R_f : 0.13 (hexane/EtOAc: 9/1); Mp 99 °C (Lit. 98 °C); IR (film, CH_2Cl_2): ν (cm^{-1}) = 2201 ($\text{C}\equiv\text{C}$), 1630 ($\text{C}=\text{O}$); ^1H NMR: δ = 3.89 (s, 3H), 6.98 (d, 2H, J = 9.03 Hz), 7.38-7.50 (m, 3H), 7.65-7.68 (m, 2H), 8.19 (d, 2H, J = 8.91 Hz); ^{13}C NMR: δ = 55.5, 86.9, 92.2, 113.8, 120.3, 128.6, 130.3, 130.5, 131.9, 132.9, 164.5, 176.6; MS: m/z (rel. Int.) = 236 (M^+ , 79), 208 (100), 193 (82), 165 (67), 164 (19), 163 (11), 135 (19), 129 (98), 92 (16), 77 (25), 75 (27) and 63 (23).

1-[(4-*tert*-Butyl)phenyl]-3-phenylpropynone (3f): R_f : 0.32 (hexane/EtOAc: 9/1); IR (film): ν (cm^{-1}) = 2199 ($\text{C}\equiv\text{C}$), 1643 ($\text{C}=\text{O}$); ^1H NMR: δ = 1.36 (s, 9H), 7.38-7.48 (m,

3H), 7.54 (d, 2H, $J = 8.43$ Hz), 7.66-7.70 (m, 2H), 8.16 (d, 2H, $J = 8.58$ Hz); ^{13}C NMR: $\delta = 31.0, 35.3, 87.0, 92.6, 120.3, 125.6, 128.6, 129.5, 130.6, 133.0, 134.5, 158.1, 177.7$; MS: m/z (rel. Int.) = 262 (M^+ , 17), 248 (12), 247 (60), 191 (10) and 129 (100).

1-(4-Nitrophenyl)-3-phenylpropynone (3g): R_f : 0.40 (hexane/EtOAc: 9/1); mp 162-163 °C; IR (KBr): ν (cm^{-1}) = 2200 ($\text{C}\equiv\text{C}$), 1650 ($\text{C}=\text{O}$); ^1H NMR: $\delta = 7.49$ -7.86 (m, 5H), 8.49 (s, 4H); ^{13}C NMR: $\delta = 86.4, 95.4, 119.3, 123.8, 128.8, 130.4, 131.4, 133.2, 140.9, 150.8, 175.9$; MS: m/z (rel. Int.) = 251 (M^+ , 18), 176 (12), 129 (100) and 75 (18).

1-(3-Methoxyphenyl)-3-phenylpropynone (3h): R_f : 0.30 (hexane/EtOAc: 9/1); IR (film): ν (cm^{-1}) = 2205 ($\text{C}\equiv\text{C}$), 1642 ($\text{C}=\text{O}$); ^1H NMR: $\delta = 3.97$ (s, 3H), 7.01-7.11 (m, 2H), 7.36-7.76 (m, 6H), 8.12 (dd, $J = 7.7, 1.5$, 2H); ^{13}C NMR: $\delta = 55.9, 89.1, 91.6, 112.1, 120.3, 120.6, 126.6, 128.5, 130.5, 132.7, 132.9, 135.0, 159.8, 176.7$; MS: m/z (rel. Int.) = 236 (M^+ , 46), 208 (40), 178 (19), 164 (23), 129 (100), 77 (11), 75 (18), 63 (12) and 51 (10).

1-(2-Methoxyphenyl)-3-phenylpropynone (3i): R_f : 0.25 (hexane/EtOAc: 9/1); IR (film): ν (cm^{-1}) = 2199 ($\text{C}\equiv\text{C}$), 1641 ($\text{C}=\text{O}$); ^1H NMR: $\delta = 73.90$ (s, 3H), 7.18 (dd, $J = 8.1, 1.7$, 1H), 7.40-7.53 (m, 4H), 7.68-7.72 (m, 3H), 7.87 (dd, $J = 8.0, 1.7$ Hz, 1H); ^{13}C NMR: $\delta = 55.4, 86.9, 93.0, 112.7, 120.0, 120.9, 122.9, 128.7, 129.6, 130.8, 133.1, 138.2, 159.7, 177.8$; MS: m/z (rel. Int.) = 236 (M^+ , 19), 235 (37), 207 (35), 178 (18), 165 (32), 131 (39), 129 (100), 121 (78), 115 (52), 105 (41), 92 (28), 77 (49), 75 (40), 63 (25) and 51 (34).

3-Phenyl-1-[4-(3-phenylpropynoyl)phenyl]propynone (3j): R_f : 0.20 (hexane/EtOAc : 9/1); IR (film, CH_2Cl_2): ν (cm^{-1}) = 2200 ($\text{C}\equiv\text{C}$), 1630 ($\text{C}=\text{O}$); ^1H NMR: δ = 7.43-7.52 (m, 6H), 7.72 (d, 4H, J = 6.87 Hz), 8.36 (s, 4H); ^{13}C NMR: δ = 86.8, 94.5, 119.8, 128.8, 129.6, 131.2, 133.2, 140.5, 177.1; MS: m/z (rel. Int.) = 334 (M^+ , 100), 278 (16), 130 (10), 129 (100) and 75 (12).

1-(2-Furyl)-3-phenylpropynone (3k): R_f : 0.15 (hexane/EtOAc: 9/1); IR (film): ν (cm^{-1}) = 2201 ($\text{C}\equiv\text{C}$), 1633 ($\text{C}=\text{O}$); ^1H NMR: δ = 6.61 (dd, 1H, J = 6.6, 1.7 Hz), 7.38-7.51 (m, 4H), 7.64-7.80 (m, 3H); ^{13}C NMR: δ = 86.2, 91.9, 112.6, 119.8, 120.9, 128.6, 130.8, 133.0, 148.0, 153.2, 164.7; MS: m/z (rel. Int.) = 196 (M^+ , 55), 168 (58), 140 (25), 139 (100), 129 (91), 114 (13), 101 (11), 75 (30), 74 (12) and 51 (16).

(E)-1,5-Diphenyl-1-penten-4-yn-3-one (3l): R_f : 0.19 (hexane/EtOAc: 9/1); Mp 71-72 °C (Lit 73-74 °C); IR (film, CH_2Cl_2): ν (cm^{-1}) = 2205 ($\text{C}\equiv\text{C}$), 1630 ($\text{C}=\text{O}$); ^1H NMR: δ = 6.87 (d, 1H, J = 16.05 Hz), 7.35-7.51 (m, 6H), 7.59-7.67 (m, 4H), 7.92 (d, 1H, J = 16.05 Hz); ^{13}C NMR: δ = 86.6, 91.5, 120.2, 128.5, 128.6, 128.7, 129.0, 130.6, 131.1, 132.9, 134.0, 148.3, 178.2; MS: m/z (rel. Int.) = 232 (M^+ , 36), 231 (M^+-1 , 100), 204 (20), 203 (52), 202 (59), 129 (66), 103 (11), 102 (55), 101 (32), 89 (12), 77 (29), 76 (17), 75 (24) and 51 (26).

1-Cyclohexyl-3-phenylpropynone (3m): R_f : 0.37 (hexane/EtOAc: 9/1); IR (film): ν (cm^{-1}) = 2199 ($\text{C}\equiv\text{C}$), 1665 ($\text{C}=\text{O}$); ^1H NMR: δ = 1.17-2.16 (m, 10H), 2.46-2.56 (m, 1H), 7.35-7.47 (m, 3H), 7.56-7.59 (m, 2H); ^{13}C NMR: δ = 25.4, 25.8, 28.3, 52.3, 87.2,

91.3, 120.2, 128.5, 130.5, 132.9, 191.4; MS: m/z (rel. Int.) = 212 (M^+ , 2), 130 (16), 129 (100), 102 (23), 75 (10) and 55 (16).

4,4-Dimethyl-1-phenylpent-1-yn-3-one (3n): IR (film): ν (cm^{-1}) = 2199 ($\text{C}\equiv\text{C}$), 1663 ($\text{C}=\text{O}$); ^1H NMR: δ = 1.28 (s, 9H), 7.35-7.47 (m, 3H), 7.56-7.59 (m, 2H); ^{13}C NMR: δ = 26.0, 44.8, 85.9, 92.1, 120.2, 128.5, 130.5, 132.8, 194.1; MS: m/z (rel. Int.) = 186 (M^+ , 1), 158 (17), 143 (18), 130 (12), 129 (100), 75 (11) and 57 (20).

Typical experimental procedure for the palladium–catalyzed acylation coupling of 1-alkynes and acid chlorides under microwave irradiation. A reaction tube of the microwave reaction equipment, was charged with phenylacetylene (56 μL , 0.5 mmol), decane (97 μL , 0.5 mmol), benzoyl chloride (116 μL , 1 mmol), TEA (212 μL , 1.5 mmol), **2** (0.408 mg, 0.0005 mmol, 0.2 mol% Pd) and toluene (2 mL). The mixture was stirred at 80 °C under microwave irradiation (120 W) (see Table 2) in air. After completion, the crude reaction mixture was extracted with water and EtOAc (3×15 mL). The organic phases were dried, evaporated (15 mmHg) and the resulting crude material was purified by florisil chromatography (hexane/EtOAc)

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