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Supporting Information

Pd-catalyzed cross-coupling of terminal alkynes with ene-yne-ketones: access to conjugated enynes *via* metal carbene migratory insertion

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1. General

All the palladium-catalyzed reactions were performed under nitrogen atmosphere in a flame-dried reaction tube. All solvents were distilled under nitrogen atmosphere prior to use. Toluene, dioxane and THF were dried over Na with benzophenone-ketyl intermediate as indicator. MeCN, MeOH were dried over CaH₂. For chromatography, 200-300 mesh silica gel (Qingdao, China) was employed. ¹H and ¹³C NMR spectra were recorded at 400 MHz and 100 MHz with Brucker ARX 400 spectrometer. Chemical shifts are reported in ppm using tetramethylsilane as internal standard when using CDCl₃ as solvent. IR spectra were recorded with a Thermo Electron Corporation Nicolet AVATAR 330 FT-IR spectrometer. MS data were obtained on an Agilent 5975C inert 350 EI mass spectrometer (GC-MS). HRMS data were obtained on a VG ZAB-HS mass spectrometer, Brucker Apex IV FTMS spectrometer. PE = petroleum ether, EA = ethyl acetate.

2. General procedure for the preparation of the ene-yne-ketones

The conjugated environmes 1a-m were synthesized by the procedure described in our recent report.¹ A typical procedure for the synthesis of environe 1c is as follows:



1-Heptyne (10 mmol) was dissolved in dry THF (15 mL) and the solution was cooled to -40 °C under nitrogen, *n*-butyllithium (1.6 M in hexanes, 6.8 mL, 11 mmol) was added dropwise over ca. 2 minutes while maintaining the temperature between -35 and -40 °C. After completion of the addition, anhydrous DMF (1.55 mL, 20mmol) was added in one portion and the cold bath was removed. The reaction mixture was allowed to warm to room temperature and aged for 30 minutes. The THF solution was poured into a vigorously stirred biphasic solution prepared from aqueous solution of KH₂PO₄ (50 mL, 30 mmol) and Et₂O (30 mL) cooled over ice to ca. +5 °C. Layers were separated and the organic extract was washed with water (2 x 30 mL). Combined aqueous layers were back extracted with Et₂O (30 mL). Combined organic layers were dried over Na₂SO₄ and filtered. Then solvent was removed in *vacuo* carefully under 0 °C to leave a crude acetylenicaldehyde.²

The crude aldehyde was then dissolved in THF (8 mL), and 1,3-dicarbonyl compound, acetoacetone, (10 mmol) was added into the solution. Then AcOH (2 mmol) and MgSO₄ (2 mmol) was added to the reaction mixture. The mixture was stirred at room temperature for about one hour. When the reaction was completed as monitored by TLC, filtration through *Celite* and removal of the solvent by rotary evaporation gave the crude product. The enynone **1c** was purified by chromatography on silica gel with the appropriate mixture of PE and EA (PE:EA=50:1) with about 70% yield (two steps).³ The unsymmetric1,3-dicarbonyl compounds would afford enynones (**1a**, **b**, **d**, **e**, **g**, **i**, **j**, **l**) as a mixture of *E*- and *Z*-isomer (about 1:1) (Scheme S1). The enynones need to be kept in refrigerator below 0 °C.¹

The spectral data for enynone **1c**: ¹ ¹H NMR (400 MHz, CDCl₃) δ 6.70 (t, J = 2.4 Hz, 1H), 2.47 (s, 3H), 2.44 (dt, J = 2.4, 7.1 Hz, 2H), 2.32 (s, 3H), 1.61-1.53 (m, 2H), 1.41-1.30 (m, 4H), 0.91 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 201.31, 195.76, 149.47, 123.24, 110.51, 76.83, 30.98, 30.91, 27.73, 27.19, 22.07, 20.15, 13.87.



Scheme S1. The structure of enynones used in this work.

3. General procedure for Pd-catalyzed alkyne-alkyne cross-coupling

Under an nitrogen atmosphere, $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 5 mol%), $P(2-furyl)_3$ (7.0 mg, 0.03 mmol, 15 mol%), and 1,4-benzoquinone (26 mg, 0.24 mmol) were successively added to a flame-dried 10 mL Schlenk tube. The reaction flask was degassed three times with nitrogen and dry dioxane (2.0 mL) was added using a syringe. Then iPr_2NH (0.60 mmol, 61 mg), terminal alkynes (2, 0.22 mmol) and enynone (1, 0.20 mmol) was added by syringe successively. Note that the terminal alkyne in a solid form was added to the reaction tube before the solvent. The reaction was heated at 90 °C with stirring for 1 h, then cooled to room temperature and filtered through a short plug of silica gel (PE:EA=5:1, 15 mL) as eluents. Solvent was then removed in vacuo to leave a crude mixture, which was purified by silica gel column chromatography to afford pure product conjugated enynes 3 or 4. (*Notice: The conjugated enynes are unstable even stored in nitrogen atmosphere in refrigerator at -40 °C, thus the measurement of the data for these products should be conducted as soon as possible when they were isolated.*)

4. Characterization data for the products

(E)-Ethyl 2-methyl-5-(1-phenyloct-3-en-1-yn-3-yl)furan-3-carboxylate (3a)



¹H NMR (400 MHz, CDCl₃) δ 7.53-7.51 (m, 2H), 7.35-7.34 (m, 3H), 6.68 (s, 1H), 6.49 (t, *J* = 7.8 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.60 (s, 3H), 2.55-2.49 (m, 2H), 1.55-1.48 (m, 2H), 1.46-1.39 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H) , 0.95 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.02, 158.55, 150.23, 136.16, 131.56, 128.37, 128.32, 123.09, 115.06, 113.60, 107.18, 93.75, 83.85, 60.11, 31.15, 30.23, 22.34, 14.35, 13.90, 13.86; HRMS (ESI, *m/z*): calcd

for $C_{22}H_{25}O_3$ [M+H]⁺ 337.1798, found 337.1803; LRMS (EI, *m*/*z*): 336 (M⁺, 85), 293 (100), 280 (38), 247 (49), 205 (46); IR (film): 690, 755, 1086, 1220, 1716 cm⁻¹.

(E)-tert-Butyl 2-methyl-5-(1-phenyloct-3-en-1-yn-3-yl)furan-3-carboxylate (3b)



¹H NMR (400 MHz, CDCl₃) δ 7.52-7.50 (m, 2H), 7.36-7.33 (m, 3H), 6.63 (s, 1H), 6.47 (t, *J* = 7.8 Hz, 1H), 2.58 (s, 3H), 2.54-2.49 (m, 2H), 1.56 (s, 9H), 1.53-1.50 (m, 2H), 1.42-1.40 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.41, 157.83, 149.94, 135.93, 131.54, 128.32, 123.14, 116.49, 113.67, 107.52, 93.70, 83.96, 80.55, 31.16, 30.22, 28.30, 22.34, 13.90; HRMS (ESI, m/z): calcd for C₂₄H₂₉O₃ [M+H]⁺ 365.2111, found 365.2118; LRMS (EI, m/z): 364 (M⁺, 32), 281 (34), 265 (58), 252 (34), 207 (100); IR (film): 734, 755, 1088, 1170, 1711 cm⁻¹.

(E)-1-(2-Methyl-5-(1-phenyloct-3-en-1-yn-3-yl)furan-3-yl)ethanone (3c)



¹H NMR (400 MHz, CDCl₃) δ 7.54-7.52 (m, 2H), 7.36-7.35 (m, 3H), 6.63 (s, 1H), 6.52 (t, *J* = 7.8 Hz, 1H), 2.61 (s, 3H), 2.53 (q, *J* = 7.4 Hz, 2H), 2.42 (s, 3H), 1.56-1.49 (m, 2H), 1.47-1.38 (m, 2H), 0.95 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 194.15, 157.90, 150.17, 136.56, 131.54, 128.46, 128.36, 123.00, 122.79, 113.42, 106.83, 93.81,

83.77, 31.11, 30.24, 29.11, 22.33, 14.43, 13.88; HRMS (ESI, m/z): calcd for C₂₁H₂₃O₂ [M+H]⁺ 307.1693, found 307.1688; LRMS (EI, m/z): 306 (M⁺, 86), 263 (100), 250 (37), 235 (42), 178 (43); IR (film): 690, 755, 949, 1580, 1679 cm⁻¹.

(E)-Methyl 2-ethyl-5-(1-phenyloct-3-en-1-yn-3-yl)furan-3-carboxylate (3d)



¹H NMR (400 MHz, CDCl₃) δ 7.53-7.51 (m, 2H), 7.35-7.34 (m, 3H), 6.67 (s, 1H), 6.49 (t, *J* = 7.8 Hz, 1H), 3.82 (s, 3H), 3.02 (q, *J* = 7.5 Hz, 2H), 2.52 (q, *J* = 7.4 Hz, 2H), 1.54-1.49 (m, 2H), 1.47-1.39 (m, 2H), 1.28 (t, *J* = 7.5 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.35, 163.67, 150.25, 136.17, 131.55, 128.38, 128.32, 123.10, 113.80, 113.65, 107.17, 93.77, 83.85, 51.25, 31.17, 30.26,

22.37, 21.27, 13.90, 12.34; HRMS (ESI, m/z): calcd for C₂₂H₂₅O₃ [M+H]⁺ 337.1798, found 337.1803; LRMS (EI, m/z): 336 (M⁺, 74), 293 (100), 280 (31), 265 (24), 205 (48); IR (film): 690, 755, 1096, 1220, 1720 cm⁻¹.

(E)-Methyl 5-(1,5-diphenylpent-3-en-1-yn-3-yl)-2-methylfuran-3-carboxylate (3e)



¹H NMR (400 MHz, CDCl₃) δ 7.56-7.54 (m, 2H), 7.37-7.35 (m, 3H), 7.32-7.30 (m, 4H), 7.25-7.21 (m, 1H), 6.74 (s, 1H), 6.62 (t, J = 7.9 Hz, 1H), 3.85 (d, J = 7.9 Hz, 2H), 3.83 (s, 3H), 2.57 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.35, 158.99, 150.02, 139.58, 133.57, 131.68, 128.62, 128.39, 126.36, 122.82, 114.84, 114.09, 107.95,

94.06, 83.65, 51.31, 36.86, 13.82; HRMS (ESI, m/z): calcd for C₂₄H₂₁O₃ [M+H]⁺ 357.1485, found 357.1494; LRMS (EI, m/z): 356 (M⁺, 100), 281 (37), 252 (58), 207 (25), 165 (28); IR (film): 691, 755, 1095, 1222, 1718 cm⁻¹.

(E)-1-(5-(1,5-Diphenylpent-3-en-1-yn-3-yl)-2-methylfuran-3-yl)ethanone (3f)



¹H NMR (400 MHz, CDCl₃) δ 7.57-7.54 (m, 2H), 7.38-7.35 (m, 3H), 7.34-7.28 (m, 4H), 7.24-7.21 (m, 1H), 6.70 (s, 1H), 6.64 (t, J = 7.9 Hz, 1H), 3.86 (d, J = 7.9 Hz, 2H), 2.58 (s, 3H), 2.42 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 194.05, 158.16, 149.87, 139.49, 133.94, 131.66, 128.67, 128.62, 128.42, 126.38, 122.85, 122.74, 113.93, 107.62, 94.08, 83.61, 36.86,

29.12, 14.42; HRMS (ESI, m/z): calcd for C₂₄H₂₁O₂ [M+H]⁺ 341.1536, found 341.1535; LRMS (EI, m/z): 340 (M⁺, 7), 281 (32), 253 (21), 207 (100), 91 (42); IR (film): 691, 755, 950, 1580, 1678 cm⁻¹.

(*E*)-Methyl 5-(5-(benzyloxy)-1-phenylpent-3-en-1-yn-3-yl)-2-methylfuran-3carboxylate (3g)



¹H NMR (400 MHz, CDCl₃) δ 7.47-7.44 (m, 2H), 7.39-7.25 (m, 8H), 6.78 (s, 1H), 6.61 (t, *J* = 6.9 Hz, 1H), 4.60 (s, 2H), 4.50 (d, *J* = 6.9 Hz, 2H), 3.83 (s, 3H), 2.60 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.21, 159.48, 149.49, 138.13, 131.64, 130.33, 128.77, 128.37, 128.35, 127.85, 127.63, 122.45, 115.62, 114.96, 108.99, 95.16, 82.64, 72.35, 68.09, 51.34, 13.87; HRMS (ESI, *m/z*): calcd

for $C_{25}H_{23}O_4 [M+H]^+ 387.1591$, found 387.1602; IR (film): 691, 756, 776, 1092, 1719 cm⁻¹.

(*E*)-1-(5-(5-(Benzyloxy)-1-phenylpent-3-en-1-yn-3-yl)-2-methylfuran-3-yl) ethanone (3h)



¹H NMR (400 MHz, CDCl₃) δ 7.48-7.45 (m, 2H), 7.39-7.31 (m, 8H), 6.74 (s, 1H), 6.63 (t, J = 6.9 Hz, 1H), 4.60 (s, 2H), 4.50 (d, J = 6.9 Hz, 2H), 2.62 (s, 3H), 2.42 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 193.94, 158.67, 149.35, 138.10, 131.63, 130.73, 128.85, 128.38, 127.85, 127.65, 122.95, 122.39, 115.44, 108.62, 95.19, 82.61, 72.38, 68.08, 29.12,

14.49; HRMS (ESI, m/z): calcd for C₂₅H₂₃O₃ [M+H]⁺ 371.1642, found 371.1650; IR (film): 692, 737, 755, 1072, 1679 cm⁻¹.

Ethyl 2-methyl-5-(4-methyl-1-phenylpent-3-en-1-yn-3-yl)furan-3-carboxylate (3i)



¹H NMR (400 MHz, CDCl₃) δ 7.50-7.47 (m, 2H), 7.34-7.29 (m, 3H), 6.64 (s, 1H), 6.61 (d, *J* = 7.1 Hz, 2H), 2.60 (s, 3H), 2.21 (s, 3H), 2.12 (s, 3H), 1.35 (t, J=7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.14, 157.88, 149.93, 144.69, 131.36, 128.23, 127.96, 123.60, 114.60, 109.44, 109.11, 92.18, 86.99, 60.09, 24.95, 22.01, 14.35, 13.90; HRMS (ESI, *m/z*): calcd for C₂₀H₂₁O₃ [M+H]⁺ 309.1485, found 309.1483; LRMS (EI,

m/*z*): 308 (M⁺, 100), 279 (30), 191 (23), 165 (26), 115 (19); IR (film): 690, 755, 1086, 1231, 1715 cm⁻¹.

tert-Butyl 2-methyl-5-(4-methyl-1-phenylpent-3-en-1-yn-3-yl)furan-3-carboxy late (3j)



¹H NMR (400 MHz, CDCl₃) δ 7.49-7.46 (m, 2H), 7.32-7.30 (m, 3H), 6.60 (s, 1H), 2.57 (s, 3H), 2.20 (s, 3H), 2.11 (s, 3H), 1.56 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 163.52, 157.14, 149.61, 144.56, 131.35, 128.23, 127.92, 123.66, 116.05, 109.78, 109.19, 92.13, 87.10, 80.50, 28.31, 24.91, 21.99, 13.96; HRMS (ESI, *m/z*): calcd for C₂₂H₂₅O₃ [M+H]⁺ 337.1798, found 337.1808; LRMS (EI, *m/z*): 336 (M⁺, 46),

280 (100), 265 (34), 191 (32), 57 (37); IR (film): 690, 755, 1089, 1170, 1710 cm⁻¹.

1-(5-(1-Cyclopentylidene-3-phenylprop-2-yn-1-yl)-2-methylfuran-3-yl)ethanone (3k)



¹H NMR (400 MHz, CDCl₃) δ 7.51-7.49 (m, 2H), 7.35-7.26 (m, 3H), 6.62 (s, 1H), 2.75 (t, *J* = 7.1 Hz, 4H), 2.62 (s, 3H), 2.42 (s, 3H), 1.87-1.72 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 194.26, 157.19, 156.03, 150.62, 131.36, 128.26, 128.01, 123.53, 122.51, 107.46, 105.26, 92.29, 86.41, 35.68, 33.37, 29.12, 27.30, 25.68, 14.51; HRMS (ESI, *m/z*): calcd for C₂₁H₂₁O₂ [M+H]⁺ 305.1536, found 305.1531; LRMS (EI,

m/*z*): 304 (M⁺, 100), 263 (28), 207 (19), 189 (19), 135 (23); IR (film): 690, 756, 946, 1233, 1677 cm⁻¹.

Methyl 5-(1-cyclopentylidene-3-phenylprop-2-yn-1-yl)-2-methylfuran-3carboxylate (3l)



¹H NMR (400 MHz, CDCl₃) δ 7.51-7.49 (m, 2H), 7.34-7.30 (m, 3H), 6.65 (s, 1H), 3.83 (s, 3H), 2.76-2.71 (m, 4H), 2.60 (s, 3H), 1.85-1.74 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 164.59, 158.04, 155.80, 150.68, 131.40, 128.25, 127.96, 123.63, 114.44, 107.80, 105.43, 92.30, 86.44, 51.25, 35.65, 33.39, 27.32, 25.73, 13.90; HRMS (ESI, *m*/*z*): calcd for C₂₁H₂₁O₃ [M+H]⁺ 321.1485, found 321.1486; LRMS (EI,

m/*z*): 320 (M⁺, 100), 279 (30), 253 (19), 202 (37), 189 (22); IR (film): 691, 755, 1091, 1234, 1718 cm⁻¹.

(*E*)-2-(1,5-Diphenylpent-3-en-1-yn-3-yl)-5-methylfuran (3m)



¹H NMR (400 MHz, CDCl₃) δ 7.54-7.52 (m, 2H), 7.35-7.34 (m, 3H), 7.30 (d, *J* = 4.4 Hz, 4H), 7.24-7.20 (m, 1H), 6.56 (t, *J* = 7.9 Hz, 1H), 6.42 (d, *J* = 3.1 Hz, 1H), 6.00 (dd, *J* = 0.9, 3.1 Hz, 1H), 3.85 (d, *J* = 7.9 Hz, 2H), 2.28 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 152.13, 150.63, 140.03, 131.73, 131.62, 128.67, 128.54, 128.39, 128.36, 126.21, 123.16, 114.79, 108.63, 107.38, 93.45, 84.50, 36.83, 13.66; HRMS (ESI, *m/z*): calcd for C₂₂H₁₉O

[M+H]⁺ 299.1430, found 299.1434; LRMS (EI, *m/z*): 298 (M⁺, 100), 255 (42), 194 (46), 179 (50), 152 (34); IR (film): 690, 698, 755, 784, 1016 cm⁻¹.

(E)-1-(2-Methyl-5-(1-(trimethylsilyl)oct-3-en-1-yn-3-yl)furan-3-yl)ethanone (3n)



¹H NMR (400 MHz, CDCl₃) δ 6.54 (s, 1H), 6.47 (t, *J* = 7.8 Hz, 1H), 2.58 (s, 3H), 2.44 (q, *J* = 7.4 Hz, 2H), 2.41 (s, 3H), 1.50-1.43 (m, 2H), 1.41-1.36 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H), 0.26 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 194.18, 157.90, 150.05, 137.53, 122.74, 113.58, 106.88, 99.37, 99.32, 30.95, 30.13, 29.08, 22.27, 14.42, 13.83, -0.06; HRMS (ESI, *m/z*): calcd for C₁₈H₂₇O₂Si [M+H]⁺ 303.1775, found 303.1771;

LRMS (EI, *m/z*): 302 (M⁺, 77), 259 (100), 246 (70), 231 (46), 73 (54); IR (film): 760, 843, 1231, 1250, 1682 cm⁻¹.

(E)-Ethyl 2-methyl-5-(1-(p-tolyl)oct-3-en-1-yn-3-yl)furan-3-carboxylate (4a)



¹H NMR (400 MHz, CDCl₃) δ 7.41 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 6.67 (s, 1H), 6.47 (t, J = 7.8 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 2.59 (s, 3H), 2.51 (q, J = 7.4Hz, 2H), 2.37 (s, 3H), 1.55-1.48 (m, 2H), 1.46-1.38 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.05, 158.52, 150.34, 138.54, 135.79, 131.44, 129.08, 120.02, 115.04, 113.70, 107.14, 93.92, 83.19, 60.10, 31.16, 30.19, 22.34, 21.46,

14.35, 13.90, 13.86; HRMS (ESI, m/z): calcd for C₂₃H₂₇O₃ [M+H]⁺ 351.1955, found 351.1958; LRMS (EI, m/z): 350 (M⁺, 72), 307 (100), 294 (26), 261 (38), 219 (32); IR (film): 776, 816, 1086, 1221, 1716 cm⁻¹.

(*E*)-Ethyl 5-(1-(4-(dimethylamino)phenyl)oct-3-en-1-yn-3-yl)-2-methylfuran-3carboxylate (4b)



¹H NMR (400 MHz, CDCl₃) δ 7.39 (d, J = 7.0 Hz, 2H), 6.67-6.65 (m, 3H), 6.41 (t, J = 7.7 Hz, 1H), 4.29 (q, J =7.1 Hz, 2H), 2.99 (s, 6H), 2.59 (s, 3H), 2.50 (q, J = 7.4Hz, 2H), 1.53-1.47 (m, 2H), 1.44-1.38 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.14, 158.40, 150.73, 150.20, 134.55, 132.66, 115.00, 114.09, 111.81, 109.96, 107.04, 94.98, 81.79, 60.06, 40.19, 31.23, 30.14, 22.37, 14.37, 13.93, 13.87; HRMS (ESI, *m*/z): calcd for C₂₄H₃₀NO₃

[M+H]⁺380.2220, found 380.2227; IR (film): 776, 816, 1086, 1221, 1716 cm⁻¹.

(*E*)-Ethyl 2-methyl-5-(1-(4-(trifluoromethyl)phenyl)oct-3-en-1-yn-3-yl)furan-3carboxylate (4c)



¹H NMR (400 MHz, CDCl₃) δ 7.61 (s, 4H), 6.66 (s, 1H), 6.55 (t, *J* = 7.8 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.60 (s, 3H), 2.52 (q, *J* = 7.4 Hz, 2H), 1.56-1.49 (m, 2H), 1.45-1.39 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.95, 158.71, 149.80, 137.33, 131.78, 130.10 (q, *J* = 32.7 Hz), 126.87, 125.28 (q, *J* = 3.8 Hz), 123.89 (q, *J* = 272.4 Hz), 115.12, 113.23, 107.28, 92.29, 86.25, 60.19, 31.09, 30.34, 22.34,

14.35, 13.87; HRMS (ESI, m/z): calcd for C₂₃H₂₄F₃O₃ [M+H]⁺ 405.1672, found 405.1680; LRMS (EI, m/z): 404 (M⁺, 100), 361 (96), 348 (67), 319 (58), 273 (66); IR

(film): 841, 1067, 1087, 1128, 1322 cm⁻¹.

(E)-Ethyl 5-(1-(4-fluorophenyl)oct-3-en-1-yn-3-yl)-2-methylfuran-3-carboxylate



(**4d**)

¹H NMR (400 MHz, CDCl₃) δ 7.51-7.48 (m, 2H), 7.04 (t, J = 8.7 Hz, 2H), 6.66 (s, 1H), 6.49 (t, J = 7.8 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 2.60 (s, 3H), 2.50 (q, J = 7.4 Hz, 2H), 1.55-1.48 (m, 2H), 1.46-1.38 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H), 0.95 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.97, 162.57 (d, J = 250.0 Hz), 158.56, 150.14, 136.26, 133.43 (d, J = 8.2 Hz), 119.18 (d, J = 3.5 Hz), 115.73,

115.62 (d, J = 22.1 Hz), 113.47, 107.17, 92.65, 83.56, 60.12, 31.12, 30.22, 22.33, 14.34, 13.87, 13.84; HRMS (ESI, m/z): calcd for C₂₂H₂₄FO₃ [M+H]⁺ 355.1704, found 355.1702; LRMS (EI, m/z): 354 (M⁺, 72), 311 (100), 298 (39), 265 (52), 223 (53); IR (film): 835, 1086, 1227, 1507, 1716 cm⁻¹.

(E)-Ethyl 5-(1-(6-methoxynaphthalen-2-yl)oct-3-en-1-yn-3-yl)-2-methylfuran-3-



carboxylate (4e)

¹H NMR (400 MHz, CDCl₃) δ 7.96 (s, 1H), 7.73-7.68 (m, 2H), 7.53 (dd, J = 1.6, 8.5 Hz, 1H), 7.16 (dd, J = 2.5, 8.9 Hz, 1H), 7.12-7.11 (m, 1H), 6.72 (s, 1H), 6.50 (t, J = 7.8 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 3.92 (s, 3H), 2.60 (s, 3H), 2.59-2.53 (m, 2H), 1.56-1.50 (m, 2H), 1.47-1.41 (m, 2H), 1.36 (t, J = 7.1 Hz, 3H), 0.96 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.06, 158.53, 158.37, 150.36, 135.96, 134.20,

131.19, 129.31, 128.93, 128.46, 126.82, 119.44, 117.97, 115.09, 113.75, 107.20, 105.84, 94.38, 83.52, 60.12, 55.30, 31.20, 30.28, 22.38, 14.37, 13.94, 13.89; HRMS (ESI, m/z): calcd for C₂₇H₂₉O₄ [M+H]⁺ 417.2060, found 417.2080; LRMS (EI, m/z): 416 (M⁺, 78), 373 (100), 327 (23), 285 (22), 195 (19); IR (film): 776, 1086, 1228, 1269, 1715 cm⁻¹.

$(E) - Ethyl \ 2-methyl - 5-(1-(thiophen - 3-yl)oct - 3-en - 1-yn - 3-yl) furan - 3-carboxylate$



(**4f**)

¹H NMR (400 MHz, CDCl₃) δ 7.51 (dd, J = 1.1, 3.0 Hz, 1H), 7.31-7.29 (m, 1H), 7.18 (dd, J = 1.1, 5.0 Hz, 1H), 6.66 (s, 1H), 6.48 (t, J = 7.8 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 2.59 (s, 3H), 2.50 (q, J = 7.4 Hz, 2H), 1.54-1.47 (m, 2H), 1.44-1.38 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H) , 0.94 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.00, 158.55, 150.17, 136.09, 129.82, 128.65, 125.37, 122.08, 115.03, 113.52, 107.17, 88.78, 83.35, 60.10, 31.12, 30.19, 22.32, 14.34, 13.89, 13.85; HRMS (ESI, m/z): calcd for C₂₀H₂₃O₃S [M+H]⁺ 343.1362, found 343.1367; LRMS (EI, m/z): 342 (M⁺, 90), 299 (100), 286 (36), 253 (63), 211 (49); IR (film): 776, 1086, 1221, 1233, 1716 cm⁻¹.

(*E*)-Ethyl 2-methyl-5-(1-(thiophen-2-yl)oct-3-en-1-yn-3-yl)furan-3-carboxylate (4g)



¹H NMR (400 MHz, CDCl₃) δ 7.30-7.26 (m, 2H), 7.02-7.00 (m, 1H), 6.65 (s, 1H), 6.49 (t, J = 7.8 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 2.59 (s, 3H), 2.49 (q, J = 7.4 Hz, 2H), 1.54-1.47 (m, 2H), 1.45-1.38 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H) , 0.95 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.99, 158.60, 149.87, 136.51, 131.96, 127.39, 127.07, 123.02, 115.08, 113.46, 107.24, 87.57, 86.83, 60.13, 31.12, 30.26, 22.32, 14.35, 13.88, 13.85; HRMS (ESI, m/z): calcd

for C₂₀H₂₃O₃S [M+H]⁺ 343.1362, found 343.1367; LRMS (EI, m/z): 342 (M⁺, 72), 299 (100), 286 (34), 253 (47), 211 (44); IR (film): 700, 776, 1086, 1225, 1716 cm⁻¹.

(E)-Ethyl 5-(dodec-5-en-7-yn-6-yl)-2-methylfuran-3-carboxylate (4h)



¹H NMR (400 MHz, CDCl₃) δ 6.57 (s, 1H), 6.35 (t, *J* = 7.7 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.57 (s, 3H), 2.44-2.38 (m, 4H), 1.63-1.33 (m, 11H), 0.97-0.91 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 164.11, 158.32, 151.00, 134.67, 114.92, 113.81, 106.91, 94.95, 74.97, 60.05, 31.17, 30.81, 29.96, 22.35, 21.95, 19.12, 14.33, 13.88, 13.83, 13.55; HRMS (ESI, *m*/*z*): calcd for C₂₀H₂₉O₃ [M+H]⁺ 317.2111,

found 317.2110; LRMS (EI, *m/z*): 316 (M⁺, 61), 273 (100), 260 (28), 227 (38), 128 (23); IR (film): 776, 821, 1083, 1230, 1717 cm⁻¹.

(E)-Ethyl 2-methyl-5-(tridec-5-en-7-yn-6-yl)furan-3-carboxylate (4i)



¹H NMR (400 MHz, CDCl₃) δ 6.57 (s, 1H), 6.35 (t, J = 7.7 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.57 (s, 3H), 2.44-2.38 (m, 4H), 1.65-1.57 (m, 2H), 1.49-1.33 (m, 11H), 0.95-0.91 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 164.10, 158.34, 150.99, 134.66, 114.92, 113.81, 106.90, 94.98, 75.00, 60.03, 31.17, 31.06, 29.97, 28.41, 22.35, 22.18, 19.38, 14.32, 13.96, 13.88, 13.82; HRMS (ESI, m/z): calcd for C₂₁H₃₁O₃ [M+H]⁺

331.2268, found 331.2265; LRMS (EI, *m*/*z*): 330 (M⁺, 74), 287 (100), 274 (28), 128 (14), 115 (13); IR (film): 776, 1083, 1230, 1717, 2930 cm⁻¹.

(E)-Ethyl 5-(2,2-dimethyldec-5-en-3-yn-5-yl)-2-methylfuran-3-carboxylate (4j)



¹H NMR (400 MHz, CDCl₃) δ 6.53 (s, 1H), 6.34 (t, *J* = 7.7 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.56 (s, 3H), 2.39 (q, *J* = 7.3 Hz, 2H), 1.48-1.29 (m, 16H), 0.93 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.15, 158.27, 150.99, 134.50, 114.95, 113.83, 106.87, 103.19, 73.47, 60.07, 31.05, 31.02, 29.83, 28.15, 22.31, 14.35, 13.88, 13.87; HRMS (ESI, *m*/*z*): calcd for C₂₀H₂₉O₃ [M+H]⁺ 317.2111, found

317.2116; LRMS (EI, *m/z*): 316 (M⁺, 73), 273 (100), 260 (43), 227 (20), 128 (20); IR (film): 776, 1083, 1230, 1717, 2930 cm⁻¹.

(E)-Ethyl 2-methyl-5-(1-phenyldec-5-en-3-yn-5-yl)furan-3-carboxylate (4k)



¹H NMR (400 MHz, CDCl₃) δ 7.33-7.22 (m, 5H), 6.50 (s, 1H), 6.34 (t, *J* = 7.7 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.92 (t, *J* = 7.3 Hz, 2H), 2.73 (t, *J* = 7.3 Hz, 2H), 2.56 (s, 3H), 2.34 (q, *J* = 7.3 Hz, 2H), 1.44-1.34 (m, 7H), 0.91 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.07, 158.35, 150.80, 140.49, 135.12, 128.45, 128.36, 126.28, 114.92, 113.57, 106.93, 93.87, 75.71, 60.03, 35.01, 31.15, 29.93,

22.30, 21.54, 14.36, 13.91, 13.81; HRMS (ESI, m/z): calcd for C₂₄H₂₉O₃ [M+H]⁺ 365.2111, found 365.2112; LRMS (EI, m/z): 364 (M⁺, 61), 321 (25), 167 (40), 115 (15), 91 (100); IR (film): 776, 1083, 1230, 1717, 2930 cm⁻¹.

(E)-Ethyl 5-(1-(benzyloxy)dec-5-en-3-yn-5-yl)-2-methylfuran-3-carboxylate (41)



¹H NMR (400 MHz, CDCl₃) δ 7.37-7.26 (m, 5H), 6.58 (s, 1H), 6.37 (t, J = 7.7 Hz, 1H), 4.59 (s, 2H), 4.27 (q, J = 7.1 Hz, 2H), 3.68 (t, J = 7.0 Hz, 2H), 2.74 (t, J = 7.0 Hz, 2H), 2.57 (s, 3H), 2.40 (q, J = 7.3 Hz, 2H), 1.48-1.31 (m, 7H), 0.91 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.06, 158.40, 150.74, 138.06, 135.28, 128.37, 127.64, 114.93, 113.52, 107.00, 91.35, 73.03, 68.52, 60.05, 31.12,

29.99, 22.30, 20.92, 14.33, 13.89, 13.82; HRMS (ESI, m/z): calcd for C₂₅H₃₁O₄ [M+H]⁺ 395.2217, found 395.2227; IR (film): 776, 1083, 1230, 1717, 2930 cm⁻¹.

(E)-Ethyl 5-(1-hydroxydec-5-en-3-yn-5-yl)-2-methylfuran-3-carboxylate (4m)



¹H NMR (400 MHz, CDCl₃) δ 6.57 (s, 1H), 6.39 (t, *J* = 7.7 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.82 (t, *J* = 6.3 Hz, 2H), 2.71 (t, *J* = 6.3 Hz, 2H), 2.57 (s, 3H), 2.40 (q, *J* = 7.4 Hz, 2H), 1.50-1.33 (m, 8H), 0.93 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.06, 158.47, 150.61, 135.63, 114.97, 113.38, 106.95, 91.00, 76.90, 61.19, 60.12, 31.09, 30.08, 23.87, 22.32, 14.34, 13.87, 13.83; HRMS (ESI, *m/z*):

calcd for C₁₈H₂₅O₄ [M+H]⁺ 305.1747, found 305.1742; LRMS (EI, *m/z*): 304 (M⁺, 78), 261 (100), 248 (58), 215 (66), 173 (43); IR (film): 776, 1083, 1230, 1717, 2930 cm⁻¹.

(*E*)-Ethyl 2-methyl-5-(1-(trimethylsilyl)oct-3-en-1-yn-3-yl)furan-3-carboxylate (4n)



¹H NMR (400 MHz, CDCl₃) δ 6.50 (s, 1H), 6.34 (t, J = 7.8 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 2.49 (s, 3H), 2.36 (q, J = 7.4 Hz, 2H), 1.43-1.25 (m, 7H), 0.85 (t, J = 7.1 Hz, 3H), 0.17 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 164.03, 158.48, 150.10, 137.12, 115.03, 113.76, 107.23, 99.31, 99.23, 60.09, 30.97, 30.10, 22.28, 14.33, 13.86, 13.83, -0.07; HRMS (ESI, m/z): calcd for C₁₉H₂₉O₃Si [M+H]⁺ 333.1880, found

333.1881; LRMS (EI, *m/z*): 332 (M⁺, 94), 289 (100), 276 (71), 261 (34), 243 (41); IR (film): 842, 1088, 1229, 1250, 1719 cm⁻¹.

(*E*)-Ethyl 2-methyl-5-(1-(triisopropylsilyl)oct-3-en-1-yn-3-yl)furan-3-carboxylate (40)



¹H NMR (400 MHz, CDCl₃) δ 6.60 (s, 1H), 6.46 (t, J = 7.8 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 2.57 (s, 3H), 2.47 (q, J = 7.4 Hz, 2H), 1.50-1.32 (m, 9H), 1.13 (s, 18H), 0.92 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.01, 158.40, 150.36, 136.67, 115.03, 114.06, 107.30, 101.09, 95.67, 60.04, 31.11, 30.33, 22.41, 18.62, 14.23, 13.86, 13.80, 11.27; HRMS (ESI, m/z): calcd for C₂₅H₄₁O₃Si [M+H]⁺

417.2820, found 417.2830; LRMS (EI, *m/z*): 416 (M⁺, 66), 373 (100), 345 (32), 331 (30), 303 (25); IR (film): 677, 776, 1091, 1230, 1720 cm⁻¹.

5. References

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6. ¹H and ¹³C NMR spectra of products





















S20



ppm (t1)











































S31





































S40













7. Control experiment



Under an nitrogen atmosphere, $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 5 mol%), P(2-furyl)₃ (7.0 mg, 0.03 mmol, 15 mol%), and 1,4-benzoquinone (26 mg, 0.24 mmol) were successively added to a flame-dried 10 mL Schlenk tube. The reaction flask was degassed three times with nitrogen and dry dioxane (2.0 mL) was added using a syringe. Then *i*Pr₂NH (0.60 mmol, 61 mg), terminal alkynes (**2a**, 0.22 mmol) and enynone (**1d**, E/Z = 1.5:1, 0.20 mmol) was added by syringe successively. The reaction was heated at 90 °C with stirring for 5 min or 10 min, then cooled to room temperature and filtered through a short plug of silica gel (PE:EA=5:1, 15 mL) as eluents. Solvent was then removed in *vacuo* to leave a crude mixture, which was analyzed by ¹H NMR [by adding mesitylene (0.1 mmol) as the internal standard].





	<i>E</i> -1d	Z-1d	3d	E/Z
0 min	60%	40%	0%	1.50:1
5 min	53%	35%	5%	1.51:1
10 min	32%	21%	32%	1.51:1

The results of these control experiments were summarized as follows:

Based on these results, it was obvious that the ratio of the E/Z isomers remained unchanged during the conversion of the starting material to the prodcut. According to the proposed mechanism and our previous report (ref. 6), only *E*-isomer can undergo cyclization to form furyl Pd-carbene species. The *Z*-isomer should be first isomerized to the *E*-isomer for undergoing further reaction with the terminal alkynes. Thus we can conclude that E/Z isomers undergo fast isomerization under the reaction conditions.

This conclusion is also in accordance with the previous work that cyclization to form furyl Pd-carbene species is a rate-limiting step (energy barrier = 22-26 kcal/mol, ref. 6) and thus needs a reaction temperature about 90 $^{\circ}$ C, while the isomerization of the ene-yne-ketones can even occur in room temperature over an extended period of time (ref. 5k).

8. NOESY spectrum of product 3n

500 M 1 H spectra of **3n**



S48

NOESY spectra of product **3n**

