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Supplementary Material

Nickel-Catalyzed Cyclizations of Alkynyl Enones with Concomitant Stereoselective Tri- or Tetrasubstituted Alkene Introduction

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Experimental procedures.

Unless otherwise indicated, reagents were commercially available and were used without purification. All organolithium reagents were freshly titrated with 2,5-dimethoxybenzyl alcohol. Ni(COD)₂ was prepared from Ni(acac)₂ and 1,5-cyclooctadiene.¹ Alkynyl enone **6** was prepared by a Swern / Wittig sequence from 5-hexyn-1-ol. 1-Oxo-1,8-diphenyl-(2*E*)-octen-7-yne was prepared by a Sonogashira coupling² of alkynyl enone **6** with PhI in the presence of catalytic Pd(PPh₃)₄ and CuI. 1-Oxo-1-phenyl-(2*E*)-dodecen-7-yne was prepared from 5-hexyn-1-ol by hydroxyl group silylation, alkylation, deprotection, Swern oxidation, and Wittig olefination. 3-(4-Pentynyl)-2-cyclohexen-1-one (**3**) was synthesized by the literature method.³ Zinc chloride was dried at 150 °C at 0.1 mm and was stored in a glove box. All reactions were conducted in flame-dried glassware under a nitrogen or argon atmosphere.

General Procedure for Cyclizations with Alkylation: A 0.3-0.8 M solution of ZnCl₂ (2.2 equiv.) in THF was stirred at 0 °C, and the organolithium or Grignard reagent (3.3 equiv.) was added by syringe followed by stirring for 1 h at 0 °C. A 0.02-0.04 M THF solution of Ni(COD)₂ (0.04-0.10 equiv.) was added and resulting mixture was immediately transferred by cannula to a 0.2-0.6 M 0 °C THF solution of alkynyl-enone (1.0 equiv.). After stirring for 0.5-2.0 h at 0 °C, the reaction mixture was subjected to extractive work-up (NaHCO₃/EtOAc) followed by flash chromatography on silica gel to afford pure products. Although the above procedure was typically used, pure salt-free organozincs performed comparably.

General Procedure for Reductive Cyclizations: A 0.3-0.5 M solution of ZnCl₂ (2.5 equiv.) in THF was stirred at 0 °C, and *n*-BuLi (3.75 equiv.) was added by syringe followed by stirring at 0 °C for 1 h. (Commercial Et₂Zn (2.25 equiv.) may be used in place of the above mixture.) A 0.15 M solution of triphenylphosphine (0.2-0.5 equiv.) in THF was added to Ni(COD)₂ (0.04-0.10 equiv) at 25 °C. After 3 min, the nickel solution was transferred to the organozinc reagent, and the

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resulting mixture was immediately transferred by cannula to a 0.2-0.5 M 0 °C THF solution of alkynyl-enone (1.0 equiv.). After stirring for 0.5-4.0 h at 0 °C the reaction mixture was subjected to extractive work-up (NaHCO₃/EtOAc) followed by flash chromatography on silica gel to afford pure products.

2-(2-Oxo-2-phenylethyl)-Z-1-ethylidenecyclopentane (1a): Following the general procedure, 1-oxo-1-phenyl-(2*E*)-octen-7-yne (60 mg, 0.30 mmol), MeLi (0.92 mL, 1.10 mmol of a 1.2 M ethyl ether solution), zinc chloride (99 mg, 0.73 mmol) and Ni(COD)₂ (7 mg, 0.025 mmol) were employed to produce, after flash chromatography (35:1 hexanes:EtOAc), 53 mg (82%) of **1a** as a colorless oil that was homogeneous by TLC analysis. ¹H NMR (300 MHz, CDCl₃) δ 7.96 (m, 2H), 7.40-7.60 (m, 3H), 5.35 (m, 1H), 3.26 (s, 1H), 3.09 (dd, *J* = 3.9, 16.5 Hz, 1H), 2.92 (dd, *J* = 10.2, 16.2 Hz, 1H), 2.15-2.45 (m, 2H), 1.93 (m, 1H), 1.62 (d, *J* = 6.6 Hz, 3H), 1.42-1.75 (m, 3H); ¹³C NMR (75 MHz) δ 199.7, 146.7, 137.3, 132.9, 128.5, 128.0, 115.5, 43.1, 35.9, 33.3, 32.8, 24.1, 14.6; IR (film) 1687, 1597 cm⁻¹; MS (EI) *m/e* calcd for C₁₅H₁₈O 214.1358, found 214.1358 (M⁺).

2-(2-Oxo-2-phenylethyl)-Z-1-(*n*-pentylidene)cyclopentane (1b): Following the general procedure, 1-oxo-1-phenyl-(2*E*)-octen-7-yne (0.10 g, 0.50 mmol), *n*-BuLi (0.58 mL, 1.4 mmol of a 2.43 M hexane solution), zinc chloride (0.75 mL, 0.75 mmol of a 1.0 M ether solution), and Ni(COD)₂ (6.9 mg, 0.025 mmol) were employed to produce, after flash chromatography (24:1 to 9:1 hexanes : EtOAc), in order of elution, 65 mg (51 %) of **1b** and 11 mg (11%) of **2a**, both as colorless oils that were homogeneous by TLC analysis. For **1b**: ¹H NMR (300 MHz, CDCl₃) δ 7.97 (m, 2H), 7.40-7.60 (m, 3H), 5.27 (tq, *J* = 7.3, 1.9 Hz, 1H), 3.24 (m, 1H), 3.06 (dd, *J* = 3.8, 16.6 Hz, 1H), 2.94 (dd, *J* = 10.5, 16.6 Hz, 1H), 2.34 (m, 1H), 2.25 (m, 1H), 1.86-2.06 (m, 3H), 1.41-1.76 (m, 3H), 1.32 (m, 4H), 0.88 (m, 3H); ¹³C NMR (75 MHz) δ 199.7, 145.5, 137.3, 132.9, 128.5, 128.0, 121.8, 43.6, 36.1, 33.2, 32.8, 32.2, 29.0, 24.0, 22.4, 14.0; IR (film) 1684, 1596, 1579; cm⁻¹; MS (EI) *m/e* calcd for C₁₈H₂₄O 256.1827, found 256.1822 (M⁺). Anal. Calcd for C₁₈H₂₄O: C, 84.32; H, 9.44. Found: C, 84.16; H, 9.57. The alkene stereochemistry was assigned by observation of 1.3 % and 1.0 % NOE of the allylic ring methylene protons (δ 2.25 and 2.34) that are syn to the alkene proton upon irradiation of that alkene proton at δ 5.27. Assignments were confirmed by homonuclear decoupling experiments.

2-(2-Oxo-2-phenylethyl)-Z-1-benzylidenecyclopentane (1c): Following the general procedure, 1-oxo-1-phenyl-(2*E*)-octen-7-yne (43.5 mg, 0.22 mmol), PhMgBr (1.10 mL, 1.10 mmol of a 1.0 M THF solution), zinc chloride (98 mg, 0.72 mmol) and Ni(COD)₂ (5.5 mg, 0.020 mmol) were

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employed to produce, after flash chromatography (21:1 hexanes:EtOAc), 37 mg (61%) of **1c** as a white crystalline solid that was recrystallized from hexanes / ether: mp. 96-97 °C, ^1H NMR (500 MHz, CDCl_3) δ 7.80 (m, 2H), 7.55 (m, 1H), 7.38 (m, 2H), 7.28 (m, 4H), 7.15 (m, 1H), 6.44 (m, 1H), 3.76 (m, 1H), 3.07 (dd, J = 3.0, 17.0 Hz, 1H), 2.86 (dd, J = 11.5, 17.0 Hz, 1H), 2.59 (m, 1H), 2.53 (m, 1H), 2.05 (dq, J = 12.8, 7.8 Hz, 1H), 1.71 (m, 2H), 1.58 (m, 1H); ^{13}C NMR (125 MHz) δ 199.7, 149.8, 138.0, 137.1, 132.9, 128.5, 128.03, 128.01, 126.1, 121.6, 41.7, 36.5, 36.0, 33.5, 23.4; IR (KBr) 1673, 1593 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{20}\text{H}_{20}\text{O}$: 276.1514, found: 276.1510 (M^+). The alkene stereochemistry was assigned by observation of 1.4 % and 1.3 % NOE of the allylic ring methylene protons (δ 2.53 and 2.59) that are syn to the alkene proton upon irradiation of that alkene proton at δ 6.44. Assignments were confirmed by homonuclear decoupling experiments.

2-(2-Oxo-2-phenylethyl)-Z-1-(3-butenylidene)cyclopentane (1d): Following the general procedure, 1-oxo-1-phenyl-(2*E*)-octen-7-yne (60 mg, 0.30 mmol), vinylmagnesium bromide (1.05 ml, 1.05 mmol of a 1.0 M THF solution), zinc chloride (95 mg, 0.70 mmol) and $\text{Ni}(\text{COD})_2$ (6 mg, 0.021 mmol) were employed to produce, after flash chromatography (25:1 pentane:Et₂O), in order of elution, 10.5 mg of **1d** as a yellow oil and 35 mg of mixture of **1d** and **2a** (6:1 molar ratio based on ^1H NMR integration.) Total combined yield of **1d**: 41 mg, 59 %. For **1d**: ^1H NMR (500 MHz, CDCl_3) δ 7.96 (m, 2H), 7.56 (tt, J = 1.5, 7.5 Hz, 1H), 7.46 (m, 2H), 6.46 (dt, J = 10.5, 17.0 Hz, 1H), 5.99 (dd, J = 2.0, 11.0 Hz, 1H), 5.07 (dd, J = 1.0, 17.0 Hz, 1H), 4.97 (d, J = 10.0 Hz, 1H), 3.45 (m, 1H), 3.00-3.10 (m, 2H), 2.42-2.52 (m, 1H), 2.28-2.38 (m, 1H), 1.95 (m, 1H), 1.67 (m, 2H), 1.49-1.55 (m, 1H); ^{13}C NMR (125 MHz) δ 199.3, 150.7, 137.1, 133.9, 133.0, 128.6, 128.1, 122.0, 114.9, 43.9, 36.5, 33.6, 32.8, 23.8; IR (film) 1685, 1652, 1597, 1581 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{16}\text{H}_{18}\text{O}$ 226.1358, found 226.1354 (M^+).

2-(2-Oxo-2-phenylethyl)-E-1-(1-phenylpentylidene)cyclopentane (1e): Following the general procedure, 1-oxo-1,8-diphenyl-(2*E*)-octen-7-yne (53 mg, 0.19 mmol), *n*-BuLi (0.41 mL, 0.83 mmol of a 2.03 M hexane solution), zinc chloride (68 mg, 0.50 mmol), and $\text{Ni}(\text{COD})_2$ (6.9 mg, 0.025 mmol) were employed to produce, after flash chromatography (49:1 hexanes : EtOAc), in order of elution, 43 mg (68 %) of **1e** and 4.0 mg (8 %) of **2b**, both as colorless oils that were homogeneous by TLC analysis. For **1e**: ^1H NMR (300 MHz, CDCl_3) δ 8.00-8.20 (m, 2H), 7.57-7.60 (m, 1H), 7.48-7.51 (m, 2H), 7.30-7.33 (m, 2H), 7.19-7.23 (m, 1H), 7.13-7.14 (m, 2H), 3.46 (m, 1H), 3.13 (dd, J = 4.0, 16.5 Hz, 1H), 3.07 (dd, J = 10.0, 16.5 Hz, 1H), 2.38 (t, J = 7.0 Hz, 2H), 2.16-2.24 (m, 1H), 2.08-2.14 (m, 1H), 1.87-1.94 (m, 1H), 1.52-1.71 (m, 3H), 1.16-1.28 (m, 4H), 0.80 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz) δ 199.7, 143.6, 142.3,

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137.4, 133.7, 133.0, 128.6, 128.3, 128.1, 127.9, 125.9, 43.7, 37.7, 34.6, 32.4, 31.4, 30.8, 24.0, 22.8, 14.0; IR (film) 1686, 1598, 1580 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{24}\text{H}_{28}\text{O}$ 332.2140, found 332.2135 (M^+). The alkene stereochemistry was assigned by observation of 7.6 % NOE of the cyclopentyl ring methine proton (δ 3.46) and 2.9 % and 0.8 % NOE's of the two diastereotopic protons α to the carbonyl (δ 3.13 and 3.07, respectively) upon irradiation of the allylic protons in the butyl group (δ 2.38). Assignments were confirmed by homonuclear decoupling experiments.

2-(2-Oxo-2-phenylethyl)-Z-1-(1-phenylpentylidene)cyclopentane (1f): Following the general procedure, 1-oxo-1-phenyl-(2*E*)-dodecen-7-yne (69 mg, 0.27 mmol), PhMgBr (1.05 ml, 1.05 mmol of a 1.0 M THF solution), zinc chloride (95 mg, 0.70 mmol) and Ni(COD)_2 (6 mg, 0.021 mmol) were employed to produce, after flash chromatography (50:1 pentane: Et_2O) 34 mg (38%) of **1f** as colorless glass that was homogeneous by TLC analysis. ^1H NMR (500 MHz, CDCl_3) δ 7.18-7.46 (m, 10H), 3.09 (m, 1H), 2.83 (dd, J = 4.0, 14.5 Hz, 1H), 2.45-2.54 (m, 1H), 2.35-2.45 (m, 2H), 2.33 (dd, J = 12.0, 14.0 Hz, 1H), 2.26 (m, 1H), 1.76-1.87 (m, 1H), 1.62-1.76 (m, 2H), 1.49-1.57 (m, 1H), 1.22-1.35 (m, 4H), 0.86 (m, 3H); ^{13}C NMR (125 MHz) δ 200.1, 143.6, 142.2, 136.4, 134.3, 132.5, 128.8, 128.6, 128.4, 128.2, 126.2, 42.8, 39.0, 36.1, 31.1, 30.2, 29.8, 23.6, 22.6, 14.1; IR (film) 1678, 1597, 1580 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{24}\text{H}_{28}\text{O}$ 332.2140, found 332.2139 (M^+).

2-(2-Oxo-2-phenylethyl)methylidenecyclopentane (2a): Following the general procedure, 1-oxo-1-phenyl-(2*E*)-octen-7-yne (51 mg, 0.26 mmol), Et_2Zn (74 mg, 0.061 ml, 0.60 mmol), zinc chloride (27 mg, 0.20 mmol), PPh_3 (37 mg, 0.14 mmol) and Ni(COD)_2 (6 mg, 0.021 mmol) were employed to produce, after flash chromatography (20:1 pentane: Et_2O), 48 mg (92%) of **2a** as a colorless oil that was homogeneous by TLC analysis. ^1H NMR (500 MHz, CDCl_3) δ 7.97 (m, 2H), 7.56 (m, 1H), 7.47 (m, 2H), 4.93 (d, J = 2.0 Hz, 1H), 4.82 (d, J = 2.0 Hz, 1H), 3.24 (dd, J = 3.5, 15.5 Hz, 1H), 2.93-3.04 (m, 2H), 2.30-2.47 (m, 2H), 2.05 (dq, J = 4.5, 12.0 Hz, 1H), 1.73 (m, 1H), 1.61 (m, 1H), 1.31 (m, 1H); ^{13}C NMR (125 MHz) δ 199.8, 155.9, 137.2, 133.0, 128.6, 128.1, 104.7, 43.6, 39.8, 33.4, 33.0, 24.1; IR (film) 1686, 1652, 1595, 1580 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{14}\text{H}_{16}\text{O}$: 200.1201, found: 200.1207 (M^+).

2-(2-Oxo-2-phenylethyl)-E-1-benzylidenecyclopentane (2b): Following the general procedure, 1-oxo-1,8-diphenyl-(2*E*)-octen-1-yne (49 mg, 0.18 mmol), $n\text{-BuLi}$ (0.40 mL, 0.80 mmol of a 2.00 M hexane solution), zinc chloride (68 mg, 0.50 mmol), Ni(COD)_2 (6.9 mg, 0.025 mmol), and triphenylphosphine (52 mg, 0.20 mmol) were employed to produce, after flash chromatography (49:1 hexanes : EtOAc), in order of elution, 23 mg (47 %) of **2b** and 11 mg (19 %) of **1e**, both as

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colorless oils that were homogeneous by TLC analysis. For **2b**: ^1H NMR (300 MHz, CDCl_3) δ 8.01 (m, 2H), 7.59 (m, 1H), 7.48 (m, 2H), 7.32 (m, 4H), 7.19 (m, 1H), 6.31 (q, $J = 2.5$ Hz, 1H), 3.34 (dd, $J = 4.8, 16.3$ Hz, 1H), 3.24 (m, 1H), 3.08 (dd, $J = 8.75, 16.3$ Hz, 1H), 2.58-2.74 (m, 2H), 2.05 (m, 1H), 1.88 (m, 1H), 1.71 (m, 1H), 1.37 (m, 1H); ^{13}C NMR (75 MHz) δ 199.7, 149.4, 138.5, 137.3, 133.0, 128.6, 128.20, 128.17, 128.14, 126.0, 121.1, 44.1, 42.0, 32.5, 31.5, 24.9; IR (KBr) 1681, 1644, 1594, 1578 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{20}\text{H}_{20}\text{O}$ 276.1514, found 276.1517 (M^+).

2-(2-Oxo-2-phenylethyl)-E-1-(n-pentalidene)cyclopentane (2c): Following the general procedure, 1-oxo-1-phenyl-(2*E*)-dodecen-7-yne (70 mg, 0.28 mmol), *n*-BuLi (0.42 ml, 1.05 mmol of a 2.5 M hexanes solution), zinc chloride (95 mg, 0.70 mmol), PPh_3 (34 mg, 0.13 mmol) and $\text{Ni}(\text{COD})_2$ (6 mg, 0.021 mmol) were employed to produce, after flash chromatography (42:1 pentane: Et_2O), in order of elution, 14 mg (16%) of **1g** and 41 mg (58%) of **2c**, both as colorless oils that were homogeneous by TLC analysis. For **2c**: ^1H NMR (500 MHz, CDCl_3) δ 7.97 (m, 2H), 7.55 (tt, $J = 1.5, 7.5$ Hz, 1H), 7.46 (m, 2H), 5.18 (m, 1H), 3.19 (dd, $J = 4.5, 16.0$ Hz, 1H), 2.94 (m, 1H), 2.88 (dd, $J = 9.0, 15.5$ Hz, 1H), 2.16-2.36 (m, 2H), 1.92-2.02 (m, 3H), 1.75 (m, 1H), 1.53-1.63 (m, 1H), 1.20-1.35 (m, 5H), 0.89 (m, 3H); ^{13}C NMR (125 MHz) δ 200.2, 145.3, 137.4, 132.9, 128.5, 128.1, 120.6, 43.9, 40.2, 33.3, 31.8, 29.2, 28.9, 24.0, 22.4, 14.0; IR (film) 1688, 1597, 1581 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{18}\text{H}_{24}\text{O}$ 256.1827, found 256.1823 (M^+).

2-(2-Oxo-2-phenylethyl)-1-(1-butylpentalidene)cyclopentane (1g): ^1H NMR (500 MHz, CDCl_3) δ 7.95 (m, 2H), 7.55 (tt, $J = 1.5, 7.5$ Hz, 1H), 7.46 (m, 2H), 3.28 (app q, $J = 7.0$ Hz, 1H), 2.92 (m, 2H), 2.32 (m, 1H), 2.23 (m, 1H), 2.05 (m, 1H), 1.97 (m, 3H), 1.69 (m, 3H), 1.51-1.56 (m, 1H), 1.20-1.40 (m, 8H), 0.91 (m, 3H), 0.87 (m, 3H); ^{13}C NMR (125 MHz) δ 200.0, 139.3, 137.4, 132.9, 131.8, 128.5, 128.1, 43.3, 37.5, 32.3, 32.1, 30.8, 30.3, 29.3, 23.5, 23.04, 22.95, 14.15, 14.11; IR (film) 1687, 1597, 1581 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{22}\text{H}_{32}\text{O}$ 312.2453, found 312.2458 (M^+).

Z-1-Ethylidenespiro[4.5]decane-7-one (4a): Following the general procedure, 3-(4-pentynyl)-2-cyclohexen-1-one (70 mg, 0.43 mmol), MeLi (1.72 ml, 1.5 mmol of a 0.87 M ethyl ether solution), zinc chloride (0.136 g, 1.0 mmol) and $\text{Ni}(\text{COD})_2$ (11.5 mg, 0.042 mmol) were employed to produce, after flash chromatography (4:1 hexanes: EtOAc), 55.5 mg (72%) of **4a** as a pale-yellow liquid that was homogeneous by TLC analysis. ^1H NMR (500 MHz, CDCl_3) δ 5.39 (tq, $J = 2.0, 7.5$ Hz, 1H), 2.78 (d, $J = 14.0$ Hz, 1H), 2.25-2.38 (m, 5H), 2.17 (dt, $J = 14.0, 2.0$ Hz, 1H), 1.95-2.03 (m, 1H), 1.76 (dt, $J = 7.5, 2.0$ Hz, 3H), 1.70-1.80 (m, 1H), 1.44-1.64 (m, 5H); ^{13}C NMR (125 MHz) δ 211.7, 148.0, 116.5, 50.1, 48.6, 41.3, 39.5, 36.3, 34.2, 23.3,

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23.2, 13.9; IR (film) 1713, 1435 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{12}\text{H}_{18}\text{O}$ 178.1358, found 178.1354 (M^+).

Z-1-Benzylidenespiro[4.5]decane-7-one (4b): Following the general procedure, 3-(4-pentynyl)-2-cyclohexen-1-one (74 mg, 0.46 mmol), PhMgBr (1.8 ml, 1.8 mmol of a 1.0 M THF solution), zinc chloride (0.163 g, 1.20 mmol) and Ni(COD)_2 (11 mg, 0.040 mmol) were employed to produce, after flash chromatography (10:1 hexanes:EtOAc), in order of elution, 8 mg (7%) of compound **5b** as a white solid and 83 mg (76%) of **4b** as a colorless oil that were homogeneous by TLC analysis. For **4b**: ^1H NMR (500 MHz, CDCl_3) δ 7.15-7.32 (m, 5H), 6.58 (s, 1H), 2.53 (m, 2H), 2.46 (d, $J = 14.0$ Hz, 1H), 2.18 (doublet of sextet, $J = 14.0, 2.2$ Hz, 1H), 2.10 (dt, $J = 13.5, 2.5$ Hz, 1H), 1.90-2.00 (m, 1H), 1.78-1.90 (m, 2H), 1.50-1.70 (m, 6H); ^{13}C NMR (125 MHz) δ 211.5, 150.6, 138.3, 129.2, 127.9, 126.4, 123.1, 51.5, 49.7, 41.0, 38.4, 35.9, 35.2, 22.9, 22.5; IR (film) 1714, 1492, 1445 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{17}\text{H}_{20}\text{O}$ 240.1514, found 240.1506 (M^+). The alkene stereochemistry was assigned by observation of 7.0% NOE of the allylic methylene protons (δ 2.53) upon irradiation of the alkene proton (δ 6.58) and 1.2% NOE of the axial proton α to carbonyl group and spirocenter (δ 2.46) upon irradiation of the phenyl ring ortho-protons (δ 7.17). Assignments were confirmed by homonuclear decoupling experiments. *Compound 5b*: ^1H NMR (500 MHz, CDCl_3) δ 7.18 (tt, $J = 1.0, 7.5$ Hz, 1H), 7.10 (dt, $J = 1.5, 7.5$ Hz, 1H), 7.05 (dd, $J = 1.5, 7.5$ Hz, 1H), 6.80 (d, $J = 7.5$ Hz, 1H), 6.28 (t, $J = 2.0$ Hz, 1H), 3.47 (s, 1H), 2.66 (dt, $J = 7.5, 13.5$ Hz, 1H), 2.52-2.61 (m, 1H), 2.41-2.50 (m, 1H), 2.34 (doublet of sextets, $J = 14.0, 2.0$ Hz, 1H), 1.97 (ddd, $J = 3.5, 6.5, 13.0$ Hz, 1H), 1.73-1.89 (m, 4H), 1.64 (ddt, $J = 1.5, 4.5, 13.5$ Hz, 1H), 1.52 (m, 1H), 1.43 (m, 1H); ^{13}C NMR (125 MHz) δ 214.0, 152.0, 134.2, 131.3, 127.4, 126.8, 126.6, 126.0, 118.2, 62.0, 49.8, 38.6, 35.4, 29.5, 27.3, 23.0, 22.5; IR (KBr) 1704, 1656, 1479 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{17}\text{H}_{18}\text{O}$ 238.1358, found 238.1359 (M^+).

Z-1-(n-Pentylidene)spiro[4.5]decane-7-one (4c): Following the general procedure, 3-(4-pentynyl)-2-cyclohexen-1-one (78 mg, 0.48 mmol), $n\text{-BuLi}$ (0.90 ml, 1.8 mmol of a 2.0 M hexanes solution), zinc chloride (0.163 g, 1.2 mmol) and Ni(COD)_2 (11 mg, 0.040 mmol) were employed to produce, after flash chromatography (10:1 hexanes:EtOAc), 64 mg (60%) of **4c** as a pale-yellow oil that was homogeneous by TLC analysis. ^1H NMR (500 MHz, CDCl_3) δ 5.28 (tt, $J = 2.0, 7.5$ Hz, 1H), 2.72 (d, $J = 14.0$ Hz, 1H), 2.26-2.39 (m, 4H), 2.13-2.23 (m, 4H), 1.98 (m, 1H), 1.75 (m, 1H), 1.45-1.65 (m, 5H), 1.33 (m, 4H), 0.90 (m, 3H); ^{13}C NMR (125 MHz) δ 211.7, 146.9, 123.2, 50.7, 48.6, 41.3, 39.5, 36.4, 34.8, 32.6, 28.0, 23.4, 23.3, 22.5, 14.1; IR (film) 1715, 1451 cm^{-1} ; MS (EI) m/e calcd for $\text{C}_{15}\text{H}_{24}\text{O}$ 220.1827, found 220.1824 (M^+).

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Cyclization of 1-oxo-1-phenyl-(2E)-octene-7-yne with Diethylzinc-d₁₀: *t*-BuLi (3.6 ml of a 1.39 M pentane solution, 5.0 mmol) was added over 15 minutes dropwise by syringe drive to a 4.5 ml -78 °C Et₂O solution of CD₃CD₂I (0.402 g, 0.200 ml, 2.50 mmol). After stirring for 15 minutes at -78 °C the mixture was allowed to warm to room temperature with stirring for 1 h. The organolithium solution was re-cooled to -78 °C, and a 2 ml THF solution of ZnCl₂ (0.205 g, 1.50 mmol) was added. The resulting solution was allowed to warm to 0 °C with stirring for 1 h. Ni(COD)₂ (4.5 mg, 0.016 mmol) was treated with a 1 ml THF solution of PPh₃ (22 mg, 0.084 mmol). After 3 minutes of stirring the brown-red solution was transferred to the organozinc reagent, and the resulting mixture was immediately transferred by cannula to a 0 °C, 0.5 ml THF solution of 1-oxo-1-phenyl -(2E)-octene-7-yne (74 mg, 0.37 mmol). After stirring for 5 h at 0 °C, the reaction mixture was quenched with 40 ml of saturated NaHCO₃, extracted with EtOAc (3x40 ml), dried with Na₂SO₄, filtered, and concentrated. Flash chromatography (silica gel, pentane/Et₂O 25:1) afforded 48 mg (65%) of **2d** as a colorless oil that was homogeneous by TLC analysis. In comparison to the spectral data of **2a**, in the ¹H NMR spectrum (500 MHz), the alkene proton signal at δ 4.82 displayed an integration corresponding to 32 % of one proton. This signal was assigned by observation of 1.6 % NOE of this alkene proton (δ 4.82) upon irradiation of the α proton to the carbonyl (δ 3.24) and 1.0 % NOE of the other alkene proton (δ 4.92) upon irradiation of the allylic ring methylene protons (δ 2.30-2.47) on an undeuterated sample of **2a**. In the ¹³C spectrum (125 MHz), a signal at δ 104.4 (t, J = 24 Hz) was apparent for the deuterated component **4d**. MS (EI) *m/e* (% rel inten): 199 (0.09), 200 (0.45), 201 (0.80), 202 (0.16).

References

- (1) Krysan, D. J.; Mackenzie, P. B. *J. Org. Chem.* **1990**, *55*, 4229.
- (2) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.
- (3) Sidduri, A.; Rozema, M. J.; Knochel, P. *J. Org. Chem.* **1993**, *58*, 2694.