



Supporting Information

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Interrupted Carbonyl-Alkyne Metathesis

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Supporting Information

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1. General Information

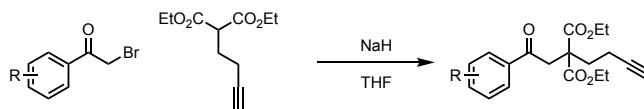
General Laboratory Procedures. All moisture-sensitive reactions were performed under an atmosphere of nitrogen in flame-dried round bottom flasks or glass vials fitted with rubber septa and/or septa equipped screw caps. Stainless steel syringes were used to transfer air or moisture-sensitive liquids. Flash chromatography was performed using silica gel Silia Flash[®] 40-63 micron (230-400 mesh) from Silicycle.

Materials and Instrumentation. All chemicals were purchased from commercial suppliers and were used as received unless otherwise stated. Proton Nuclear Magnetic Resonance NMR (¹H NMR) spectra and carbon nuclear magnetic resonance (¹³C NMR) spectra were recorded on a Varian Unity Plus 400, Varian MR400, Varian vnmrs 500, Varian Inova 500, Varian Mercury 500, and Varian vnmrs 700 spectrometers. Chemical shifts for protons are reported in parts per million and are referenced to the NMR solvent peak (CDCl₃: δ 7.26). Chemical shifts for carbons are reported in parts per million and are referenced to the carbon resonances of the NMR solvent (CDCl₃: δ 77.16). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants in Hertz (Hz). Mass spectroscopic (MS) data was recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Michigan in Ann Arbor, MI on an Agilent Q-TOF HPLC-MS with ESI high resolution mass spectrometer. Infrared (IR) spectra were obtained using either an Avatar 360 FT-IR or Perkin Elmer Spectrum BX FT-IR spectrometer. IR data are represented as frequency of absorption (cm⁻¹).

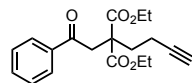
Abbreviations used: Et₃N = triethylamine, DMF = dimethylformamide, DCM = dichloromethane, NaH = sodium hydride, K₂CO₃ = potassium carbonate, THF = tetrahydrofuran, Na₂SO₄ = sodium sulfate, MgSO₄ = magnesium sulfate, TEBAC = benzyltriethylammonium chloride, GaCl₃ = gallium trichloride, AgSbF₆ = silver hexafluoroantimonate, CuI = copper iodide, Pd(PPh₃)₄ = palladium tetrakis(triphenylphosphine), NaOH = sodium hydroxide, KI = potassium iodide

2. Synthesis of Substrates and Intermediates

General alkylation procedure for the synthesis of intermediates:

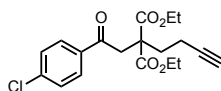


To a solution of diethyl 2-(but-3-yn-1-yl)malonate (1 eq.) in THF (0.3 M) at 0 °C was added NaH (60% dispersion in mineral oil, 1.1 eq.). Subsequently the reaction flask was warmed to room temperature, and appropriate bromoketone (1.1 eq.) was added. The resulting solution was refluxed for five hours. Ultimately the reaction was quenched with saturated aqueous ammonium chloride and extracted with diethyl ether (x3). The resulting organic phase was washed with saturated sodium chloride, dried over MgSO₄, and concentrated under reduced pressure to remove all volatile components. The crude material was purified using column chromatography to afford the desired intermediate compound.



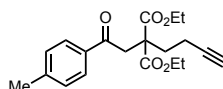
17

Diethyl 2-(but-3-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (I7): The alkylation reaction was performed on 1.41 mmol scale. Purification by flash column chromatography provided 0.46 g (99% yield) of **I7**. ¹H NMR (500 MHz; CDCl₃) δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 4.22 (q, *J* = 7.0 Hz, 4H), 3.77 (s, 2H), 2.42 (t, *J* = 7.6 Hz, 2H), 2.24 (t, *J* = 6.8 Hz, 2H), 1.84 (s, 1H), 1.25 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (125 MHz; CDCl₃) δ 196.5, 170.6, 136.7, 133.5, 128.8, 128.2, 83.4, 69.2, 61.9, 55.1, 41.7, 31.8, 14.6, 14.1; IR (Neat) 3280, 2981, 1727, 1686, 1597, 1581, 1448, 1409, 1356, 1270, 1225, 1181, 1067, 1019, 1002, 955, 895, 861, 755, 689, 639; HRMS: calcd for C₁₉H₂₃O₅⁺: 331.1540 found: 331.1545.



110

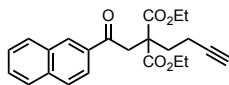
Diethyl 2-(but-3-yn-1-yl)-2-(2-(4-chlorophenyl)-2-oxoethyl)malonate (I10): The alkylation reaction was performed on 0.90 mmol scale. Purification by flash column chromatography provided 0.19 g (57% yield) of **I10**. ¹H NMR (500 MHz; CDCl₃) δ 7.89 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 4H), 3.72 (s, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 2.21 (td, *J* = 7.5, 2.6 Hz, 2H), 1.82 (t, *J* = 2.6 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (125 MHz; CDCl₃) δ 195.4, 170.5, 140.0, 135.0, 129.6, 129.1, 83.4, 69.3, 61.9, 55.1, 41.6, 31.7, 14.6, 14.1; IR (Neat) 3304, 2918, 2850, 2713, 1730, 1689, 1590, 1572, 1490, 1446, 1401, 1367, 1272, 1236, 1187, 1092, 1014, 957, 862, 821, 631; HRMS: calcd for C₁₉H₂₂ClO₅⁺: 365.1150 found: 365.1153.



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Diethyl 2-(but-3-yn-1-yl)-2-(2-oxo-2-(*p*-tolyl)ethyl)malonate (I12): The alkylation reaction was performed on 0.90 mmol scale. Purification by flash column chromatography provided 0.19 g (62% yield) of **I12**. ¹H NMR (500 MHz; CDCl₃) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 4H), 3.71 (s, 2H), 2.38 (d, *J* = 5.5 Hz, 5H), 2.20 (td, *J* = 7.6, 2.5 Hz, 2H),

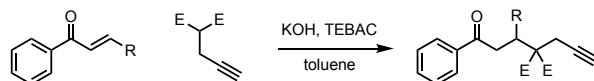
1.83 (t, $J = 2.6$ Hz, 1H), 1.21 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (125 MHz; CDCl_3) δ 196.1, 170.7, 144.4, 134.2, 129.5, 128.3, 83.4, 69.2, 61.8, 55.0, 41.5, 31.8, 21.8, 14.6, 14.1; IR (Neat) 3305, 2927, 1729, 1684, 1607, 1446, 1368, 1265, 1238, 1182, 1069, 1021, 863, 811, 733, 703, 637; HRMS: calcd for $\text{C}_{20}\text{H}_{25}\text{O}_5^+$: 345.1697 found: 345.1702.



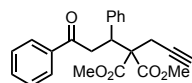
I17

Diethyl 2-(but-3-yn-1-yl)-2-(2-(naphthalen-2-yl)-2-oxoethyl)malonate (I17): The alkylation reaction was performed on 0.61 mmol scale. Purification by flash column chromatography provided 0.21 g (92% yield) of **I17**. ^1H NMR (500 MHz; CDCl_3) δ 8.51 (s, 1H), 8.02 (d, $J = 8.6$ Hz, 1H), 7.97 (d, $J = 8.0$ Hz, 1H), 7.88 (t, $J = 8.8$ Hz, 2H), 7.58 (dt, $J = 23.1, 7.2$ Hz, 2H), 4.24 (q, $J = 7.1$ Hz, 4H), 3.92 (s, 2H), 2.47 (t, $J = 7.6$ Hz, 2H), 2.27 (t, $J = 7.4$ Hz, 2H), 1.84 (s, 1H), 1.26 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (125 MHz; CDCl_3) δ 196.4, 170.6, 135.8, 133.9, 132.5, 129.9, 129.7, 128.7, 128.6, 127.9, 127.0, 123.7, 83.4, 69.3, 61.8, 55.1, 41.6, 31.8, 14.6, 14.1; IR (Neat) 3289, 2980, 2927, 1726, 1680, 1627, 1596, 1469, 1445, 1388, 1366, 1273, 1234, 1185, 1124, 1066, 1019, 942, 858, 820, 748, 633; HRMS: calcd for $\text{C}_{23}\text{H}_{25}\text{O}_5^+$: 381.1697 found: 381.1704.

General Michael addition procedure for the synthesis of intermediates:

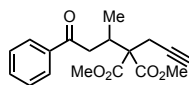


To a solution of appropriate enone (1 eq.) in toluene (1 M) was added KOH (0.06 eq.), TEBAC (0.06 eq.), and the corresponding alkyne (3 eq.). The resulting mixture was stirred at room temperature overnight. The reaction was subsequently quenched with water and extracted with dichloromethane (x3). The resulting organic phase was washed with saturated sodium chloride, dried over Na_2SO_4 , and concentrated under reduced pressure to remove all volatile components. The crude material was purified using column chromatography to afford the desired intermediate compound.



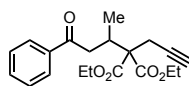
I13

Dimethyl 2-(3-oxo-1,3-diphenylpropyl)-2-(prop-2-yn-1-yl)malonate (I13): The Michael reaction was performed on 1.01 mmol scale. Purification by flash column chromatography provided 76 mg (20% yield) of **I13**. ^1H NMR (700 MHz; CDCl_3) δ 7.92 (d, $J = 7.7$ Hz, 2H), 7.51 (t, $J = 7.4$ Hz, 1H), 7.41 (t, $J = 7.7$ Hz, 2H), 7.22 (tt, $J = 13.7, 7.4$ Hz, 5H), 4.43 (dd, $J = 10.9, 2.4$ Hz, 1H), 3.87 – 3.80 (m, 4H), 3.80 – 3.73 (m, 4H), 2.77 (dd, $J = 17.2, 2.6$ Hz, 1H), 2.52 (dd, $J = 17.2, 2.6$ Hz, 1H), 2.17 (t, $J = 2.5$ Hz, 1H); ^{13}C NMR (175 MHz; CDCl_3) δ 197.8, 170.11, 170.05, 138.6, 137.1, 133.0, 129.1, 128.6, 128.5, 128.2, 127.7, 79.4, 72.5, 61.1, 53.0, 52.8, 43.6, 41.6, 24.3; IR (Neat) 3285, 3031, 2953, 1731, 1685, 1597, 1581, 1496, 1448, 1434, 1367, 1326, 1267, 1204, 1178, 1085, 1053, 1002, 968, 916, 868, 816, 746, 701, 689, 659; HRMS: calcd for $\text{C}_{23}\text{H}_{23}\text{O}_5^+$: 379.1540 found: 379.1546.



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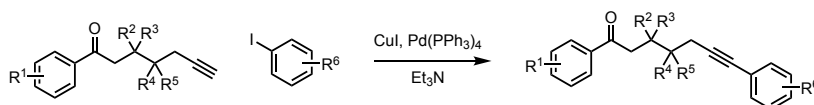
Dimethyl 2-(4-oxo-4-phenylbutan-2-yl)-2-(prop-2-yn-1-yl)malonate (I15): The Michael reaction was performed on 1.07 mmol scale. Purification by flash column chromatography provided 0.33 g (97% yield) of **I15**. $^1\text{H NMR}$ (700 MHz; CDCl_3) δ 8.01 (d, $J = 7.2$ Hz, 2H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.46 (t, $J = 7.7$ Hz, 2H), 3.79 (s, 3H), 3.76 (s, 3H), 3.50 (d, $J = 14.9$ Hz, 1H), 3.26 – 3.16 (m, 1H), 3.01 – 2.80 (m, 3H), 2.07 (t, $J = 2.7$ Hz, 1H), 0.98 (d, $J = 6.8$ Hz, 3H); $^{13}\text{C NMR}$ (175 MHz; CDCl_3) δ 198.9, 170.5, 170.1, 137.1, 133.2, 128.7, 128.4, 79.4, 71.8, 60.7, 52.9, 52.7, 42.5, 32.6, 23.0, 15.7; **IR** (Neat) 3288, 2954, 1730, 1686, 1598, 1581, 1448, 1435, 1367, 1271, 1231, 1204, 1157, 1097, 1051, 992, 952, 856, 755, 691, 659, 602; **HRMS**: calcd for $\text{C}_{18}\text{H}_{21}\text{O}_5^+$: 317.1384 found: 317.1392.



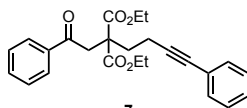
116

Diethyl 2-(4-oxo-4-phenylbutan-2-yl)-2-(prop-2-yn-1-yl)malonate (I16): The Michael reaction was performed on 1.08 mmol scale. Purification by flash column chromatography provided 0.33 g (89% yield) of **I16**. $^1\text{H NMR}$ (400 MHz; CDCl_3) δ 8.00 (d, $J = 7.3$ Hz, 2H), 7.53 (t, $J = 7.3$ Hz, 1H), 7.44 (t, $J = 7.6$ Hz, 2H), 4.35 – 4.14 (m, 4H), 3.52 (d, $J = 16.5$ Hz, 1H), 3.29 – 3.11 (m, 1H), 3.04 – 2.76 (m, 3H), 2.05 (t, $J = 2.7$ Hz, 1H), 1.26 (dt, $J = 15.7, 7.1$ Hz, 6H), 0.97 (d, $J = 6.8$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz; CDCl_3) δ 198.9, 170.0, 169.5, 137.1, 133.1, 128.6, 128.2, 79.5, 71.7, 61.7, 61.6, 60.3, 42.5, 32.2, 22.8, 15.5, 14.2, 14.1; **IR** (Neat) 3282, 2981, 1727, 1688, 1598, 1581, 1448, 1367, 1268, 1228, 1194, 1096, 1049, 1019, 1002, 943, 856, 754, 691, 657, 621; **HRMS**: calcd for $\text{C}_{20}\text{H}_{25}\text{O}_5^+$: 345.1697 found: 345.1705.

General Sonogashira procedure for the synthesis of substrates:



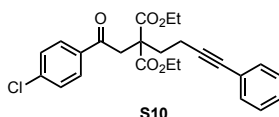
To a flame-dried flask was charged the appropriate alkyne (1 eq.), $\text{Pd}(\text{PPh}_3)_4$ (0.005 eq.), CuI (0.01 eq.), Et_3N (7.5 eq.), and the corresponding iodobenzene (1 eq.) under a nitrogen atmosphere. The resulting mixture was stirred at room temperature overnight. The reaction was subsequently diluted with DCM and filtered through silica. The resulting organic phase was washed with water, saturated ammonium chloride, and saturated sodium chloride, dried over Na_2SO_4 , and concentrated under reduced pressure to remove all volatile components. The crude material was purified using column chromatography to afford the desired substrate.



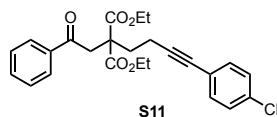
7

Diethyl 2-(2-oxo-2-phenylethyl)-2-(4-phenylbut-3-yn-1-yl)malonate (7): The Sonogashira reaction was performed on 1.36 mmol scale. Purification by flash column chromatography provided 0.26 g (47% yield) of **7**. $^1\text{H NMR}$ (500 MHz; CDCl_3) δ 7.97 (d, $J = 7.4$ Hz, 2H), 7.53 (t, $J = 7.4$ Hz, 1H), 7.41 (t, $J = 7.6$ Hz, 2H), 7.21 (q, $J = 6.0, 5.4$ Hz, 5H), 4.22 (q, $J = 6.9$ Hz, 4H),

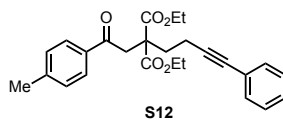
3.85 (s, 2H), 2.60 – 2.34 (m, 4H), 1.25 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (125 MHz; CDCl_3) δ 196.6, 170.7, 136.6, 133.5, 131.6, 128.7, 128.2 (two carbons observed by HSQC), 127.7, 123.7, 89.0, 81.5, 61.9, 55.2, 41.6, 31.9, 15.6, 14.1; IR (Neat) 2981, 1730, 1688, 1598, 1581, 1491, 1448, 1389, 1366, 1296, 1226, 1184, 1069, 1023, 1003, 862, 757, 691, 618; HRMS: calcd for $\text{C}_{25}\text{H}_{27}\text{O}_5^+$: 407.1853 found: 407.1856.



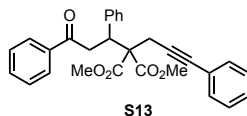
Diethyl 2-(2-(4-chlorophenyl)-2-oxoethyl)-2-(4-phenylbut-3-yn-1-yl)malonate (S10): The Sonogashira reaction was performed on 0.49 mmol scale. Purification by flash column chromatography provided 0.19 g (87% yield) of **S10**. ^1H NMR (500 MHz; CDCl_3) δ 7.86 (d, $J = 8.0$ Hz, 2H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.23 – 7.09 (m, 5H), 4.21 (q, $J = 7.0$ Hz, 4H), 3.83 (s, 2H), 2.47 (dd, $J = 16.0, 5.9$ Hz, 4H), 1.23 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (125 MHz; CDCl_3) δ 195.3, 170.5, 139.8, 134.8, 131.4, 129.5, 128.9, 128.1, 127.7, 123.4, 88.9, 81.5, 61.8, 55.1, 41.4, 31.5, 15.4, 14.0; IR (Neat) 2981, 1728, 1687, 1589, 1571, 1490, 1443, 1400, 1366, 1294, 1272, 1225, 1193, 1091, 1067, 1002, 958, 916, 861, 813, 756, 692; HRMS: calcd for $\text{C}_{25}\text{H}_{26}\text{ClO}_5^+$: 441.1463 found: 441.1470.



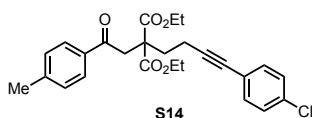
Diethyl 2-(4-(4-chlorophenyl)but-3-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (S11): The Sonogashira reaction was performed on 0.61 mmol scale. Purification by flash column chromatography provided 0.23 g (85% yield) of **S11**. ^1H NMR (400 MHz; CDCl_3) δ 7.96 (d, $J = 7.2$ Hz, 2H), 7.54 (t, $J = 7.4$ Hz, 1H), 7.41 (t, $J = 7.7$ Hz, 2H), 7.18 – 7.08 (m, 4H), 4.22 (q, $J = 7.1$ Hz, 4H), 3.85 (s, 2H), 2.61 – 2.36 (m, 4H), 1.25 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (100 MHz; CDCl_3) δ 196.5, 170.6, 136.6, 133.7, 133.5, 132.8, 128.8, 128.5, 128.2, 122.1, 90.1, 80.4, 61.9, 55.1, 41.6, 31.7, 15.6, 14.1; IR (Neat) 2981, 1727, 1687, 1597, 1581, 1489, 1448, 1397, 1355, 1294, 1225, 1180, 1089, 1066, 1013, 861, 828, 750, 688; HRMS: calcd for $\text{C}_{25}\text{H}_{26}\text{ClO}_5^+$: 441.1463 found: 441.1476.



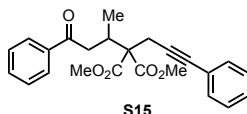
Diethyl 2-(2-oxo-2-(*p*-tolyl)ethyl)-2-(4-phenylbut-3-yn-1-yl)malonate (S12): The Sonogashira reaction was performed on 0.52 mmol scale. Purification by flash column chromatography provided 0.22 g (99% yield) of **S12**. ^1H NMR (400 MHz; CDCl_3) δ 7.86 (d, $J = 8.1$ Hz, 2H), 7.29 – 7.09 (m, 7H), 4.21 (q, $J = 7.1$ Hz, 4H), 3.83 (s, 2H), 2.48 (dd, $J = 14.9, 6.0$ Hz, 4H), 2.36 (s, 3H), 1.23 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (125 MHz; CDCl_3) δ 196.0, 170.6, 144.2, 134.0, 131.4, 129.3, 128.2, 128.1, 127.6, 123.5, 88.9, 81.3, 61.7, 55.0, 41.3, 31.7, 21.6, 15.4, 14.0; IR (Neat) 2982, 1728, 1683, 1607, 1490, 1443, 1408, 1367, 1353, 1295, 1229, 1180, 1067, 1022, 908, 861, 808, 756, 728, 691, 648; HRMS: calcd for $\text{C}_{26}\text{H}_{29}\text{O}_5^+$: 421.2010 found: 421.2020.



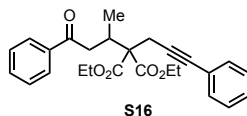
Dimethyl 2-(3-oxo-1,3-diphenylpropyl)-2-(3-phenylprop-2-yn-1-yl)malonate (S13): The Sonogashira reaction was performed on 0.12 mmol scale. Purification by flash column chromatography provided 47 mg (87% yield) of **S13**. $^1\text{H NMR}$ (500 MHz; CDCl_3) δ 7.94 (d, $J = 7.7$ Hz, 2H), 7.53 – 7.43 (m, 3H), 7.38 (t, $J = 7.5$ Hz, 2H), 7.34 (s, 3H), 7.24 (d, $J = 16.9$ Hz, 5H), 4.54 (d, $J = 11.0$ Hz, 1H), 3.97 (d, $J = 17.2$ Hz, 1H), 3.85 (s, 3H), 3.83 – 3.78 (m, 1H), 3.77 (s, 3H), 3.02 (d, $J = 17.4$ Hz, 1H), 2.78 (d, $J = 17.4$ Hz, 1H); $^{13}\text{C NMR}$ (125 MHz; CDCl_3) δ 197.9, 170.19, 170.15, 138.6, 137.1, 132.9, 131.7, 129.1, 128.5, 128.44, 128.39, 128.22, 128.18, 127.7, 123.3, 85.0, 84.7, 61.4, 52.9, 52.8, 43.9, 41.7, 25.0; **IR** (Neat) 2954, 1753, 1715, 1687, 1597, 1488, 1449, 1436, 1417, 1357, 1329, 1308, 1247, 1215, 1195, 1181, 1173, 1081, 1056, 1003, 989, 979, 956, 915, 882, 847, 816, 754, 741, 718, 703, 686, 659, 622, 607; **HRMS**: calcd for $\text{C}_{29}\text{H}_{27}\text{O}_5^+$: 455.1853 found: 455.1864.



Diethyl 2-(4-(4-chlorophenyl)but-3-yn-1-yl)-2-(2-oxo-2-(p-tolyl)ethyl)malonate (S14): The Sonogashira reaction was performed on 0.24 mmol scale. Purification by flash column chromatography provided 35 mg (32% yield) of **S14**. $^1\text{H NMR}$ (700 MHz; CDCl_3) δ 7.84 (d, $J = 8.2$ Hz, 2H), 7.18 (d, $J = 8.1$ Hz, 2H), 7.14 (d, $J = 8.5$ Hz, 2H), 7.09 (d, $J = 8.5$ Hz, 2H), 4.21 (qd, $J = 7.1, 2.7$ Hz, 4H), 3.82 (s, 2H), 2.49 (t, $J = 6.8$ Hz, 2H), 2.44 (t, $J = 6.9$ Hz, 2H), 2.38 (s, 3H), 1.24 (t, $J = 7.1$ Hz, 6H); $^{13}\text{C NMR}$ (175 MHz; CDCl_3) δ 196.1, 170.7, 144.4, 134.1, 133.6, 132.8, 129.4, 128.4, 128.3, 122.2, 90.2, 80.4, 61.8, 55.1, 41.4, 31.6, 21.8, 15.5, 14.1; **IR** (Neat) 2980, 2917, 1729, 1683, 1607, 1572, 1489, 1445, 1408, 1366, 1294, 1230, 1189, 1090, 1066, 1013, 861, 829, 809, 757; **HRMS**: calcd for $\text{C}_{26}\text{H}_{28}\text{ClO}_5^+$: 455.1620 found: 455.1633.

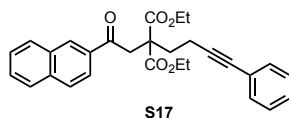


Dimethyl 2-(4-oxo-4-phenylbutan-2-yl)-2-(3-phenylprop-2-yn-1-yl)malonate (S15): The Sonogashira reaction was performed on 0.54 mmol scale. Purification by flash column chromatography provided 0.19 g (90% yield) of **S15**. $^1\text{H NMR}$ (400 MHz; CDCl_3) δ 7.98 (d, $J = 7.5$ Hz, 2H), 7.49 (t, $J = 7.4$ Hz, 1H), 7.40 – 7.32 (m, 4H), 7.29 – 7.17 (m, 3H), 3.76 (d, $J = 11.1$ Hz, 6H), 3.60 (d, $J = 15.5$ Hz, 1H), 3.37 – 3.20 (m, 1H), 3.20 – 2.99 (m, 2H), 2.85 (dd, $J = 16.3, 10.8$ Hz, 1H), 0.99 (d, $J = 6.8$ Hz, 3H); $^{13}\text{C NMR}$ (125 MHz; CDCl_3) δ 199.1, 170.6, 170.3, 137.1, 133.1, 131.7, 128.7, 128.4 (two carbons observed by HSQC), 128.2, 123.2, 85.1, 84.0, 61.1, 52.9, 52.8, 42.6, 32.8, 23.7, 15.8; **IR** (Neat) 2919, 2850, 1731, 1687, 1598, 1581, 1491, 1448, 1372, 1299, 1202, 1096, 1045, 1002, 914, 848, 755, 733, 691, 633, 607; **HRMS**: calcd for $\text{C}_{24}\text{H}_{25}\text{O}_5^+$: 393.1697 found: 393.1705.



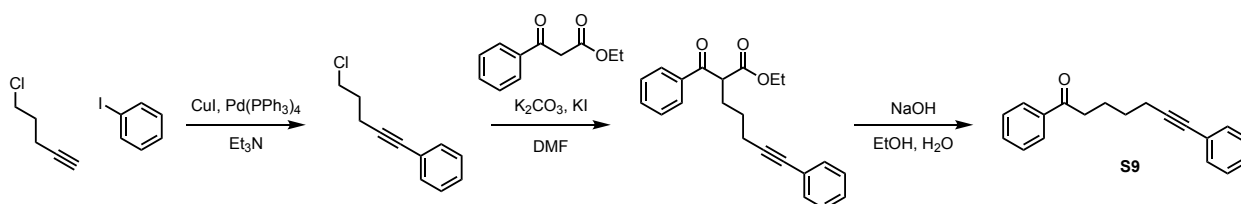
Diethyl 2-(4-oxo-4-phenylbutan-2-yl)-2-(3-phenylprop-2-yn-1-yl)malonate (S16): The Sonogashira reaction was performed on 0.58 mmol scale. Purification by flash column chromatography provided 0.24 g (98% yield) of **S16**. $^1\text{H NMR}$ (400 MHz; CDCl_3) δ 8.00 (d, $J = 7.6$ Hz, 2H), 7.48 (t, $J = 7.3$ Hz, 1H), 7.35 (t, $J = 7.0$ Hz, 4H), 7.28 – 7.23 (m, 3H), 4.33 – 4.15 (m, 4H), 3.65 (d, $J = 15.8$ Hz, 1H), 3.35 – 3.23 (m, 1H), 3.22 – 3.01 (m, 2H), 2.88 (dd, $J = 16.3, 10.9$ Hz, 1H), 1.26 (dt, $J = 14.3, 7.1$ Hz, 6H), 1.02 (d, $J = 6.8$ Hz, 3H); $^{13}\text{C NMR}$ (125 MHz; CDCl_3) δ

199.2, 170.2, 169.8, 137.2, 133.1, 131.7, 128.7, 128.4 (two carbons observed by HSQC), 128.1, 123.4, 85.4, 83.9, 61.8, 61.7, 60.9, 42.7, 32.6, 23.6, 15.8, 14.3, 14.2; **IR** (Neat) 2979, 2917, 1726, 1687, 1598, 1581, 1491, 1447, 1366, 1265, 1225, 1188, 1095, 1047, 1029, 1001, 914, 857, 754, 731, 690, 658, 616; **HRMS**: calcd for $C_{26}H_{29}O_5^+$: 421.2010 found: 421.2011.



Diethyl 2-(2-(naphthalen-2-yl)-2-oxoethyl)-2-(4-phenylbut-3-yn-1-yl)malonate (S17): The Sonogashira reaction was performed on 0.28 mmol scale. Purification by flash column chromatography provided 65 mg (51% yield) of **S17**. **¹H NMR** (400 MHz; $CDCl_3$) δ 8.50 (s, 1H), 8.01 (dd, $J = 8.6, 1.7$ Hz, 1H), 7.89 (d, $J = 8.1$ Hz, 1H), 7.84 (dd, $J = 8.3, 3.8$ Hz, 2H), 7.67 – 7.48 (m, 2H), 7.18 – 7.04 (m, 5H), 4.25 (q, $J = 6.8$ Hz, 4H), 4.02 (s, 2H), 2.60 – 2.45 (m, 4H), 1.27 (t, $J = 7.1$ Hz, 6H); **¹³C NMR** (125 MHz; $CDCl_3$) δ 196.5, 170.8, 135.8, 133.9, 132.6, 131.5, 130.1, 129.8, 128.7, 128.6, 128.1, 127.9, 127.7, 126.9, 123.8, 123.5, 89.0, 81.6, 61.9, 55.3, 41.6, 31.8, 15.6, 14.2; **IR** (Neat) 2979, 2917, 1727, 1680, 1627, 1597, 1490, 1468, 1442, 1388, 1366, 1274, 1233, 1181, 1123, 1066, 1020, 957, 943, 914, 857, 821, 754, 691, 634; **HRMS**: calcd for $C_{29}H_{28}O_5Na^+$: 479.1829 found: 479.1835.

Miscellaneous procedures for the synthesis of all other substrates:



To a flame-dried flask was charged 5-chloropent-1-yne (1 eq.), $Pd(PPh_3)_4$ (0.005 eq.), CuI (0.01 eq.), Et_3N (7.5 eq.), and iodobenzene (1 eq.) under a nitrogen atmosphere. The resulting mixture was stirred at room temperature overnight. The reaction was subsequently diluted with DCM and filtered through silica. The resulting organic phase was washed with water, saturated ammonium chloride, and saturated sodium chloride, dried over Na_2SO_4 , and concentrated under reduced pressure to remove all volatile components. The crude material was used in the following step without further purification.

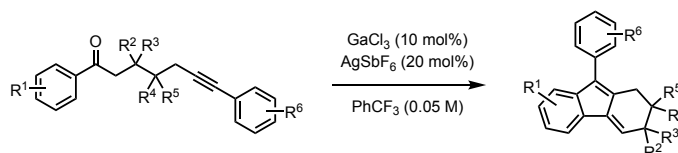
To a solution of alkyne (1.0 eq.) and DMF (0.25 M), KI (1.2 eq.) and K_2CO_3 (2.0 eq.) were added. Ethyl benzoylacetate (1.0 eq.) was added and the resulting mixture was stirred at 80 °C overnight. The reaction was subsequently quenched with water and extracted with ethyl acetate (x3). The resulting organic phase was washed with saturated sodium chloride, dried over Na_2SO_4 , and concentrated under reduced pressure to remove all volatile components. The crude material was used in the following step without further purification.

To a solution of aryl ketone (1.0 eq.) in ethanol and water (1:1; 0.2 M), $NaOH$ (4 eq.) was added. The resulting mixture was stirred at 80 °C for two hours. The reaction was subsequently quenched with water and extracted with ethyl acetate (x3). The resulting organic phase was washed with saturated sodium chloride, dried over Na_2SO_4 , and concentrated under reduced pressure to remove all volatile components. The crude material was purified using column chromatography to afford the desired substrate.

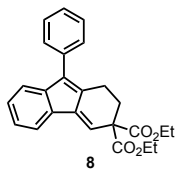
1,7-diphenylhept-6-yn-1-one (S9): The 3-step sequence was performed on 9.75 mmol scale. Purification by flash column chromatography provided 1.1 g (43% yield) of **S9**. $^1\text{H NMR}$ (700 MHz; CDCl_3) δ 7.97 (d, $J = 7.3$ Hz, 2H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.45 (t, $J = 7.7$ Hz, 2H), 7.40 – 7.36 (m, 2H), 7.30 – 7.25 (m, 3H), 3.05 (t, $J = 7.3$ Hz, 2H), 2.48 (t, $J = 7.0$ Hz, 2H), 1.94 (p, $J = 7.5$ Hz, 2H), 1.72 (p, $J = 7.2$ Hz, 2H); $^{13}\text{C NMR}$ (175 MHz; CDCl_3) δ 200.2, 137.1, 133.1, 131.7, 128.7, 128.3, 128.2, 127.7, 124.0, 89.9, 81.1, 38.2, 28.4, 23.7, 19.4; **IR** (Neat) 2936, 1682, 1597, 1580, 1489, 1448, 1355, 1282, 1222, 1196, 1179, 1157, 1070, 1001, 976, 914, 754, 736, 688, 654; **HRMS**: calcd for $\text{C}_{19}\text{H}_{19}\text{O}^+$: 263.1430 found: 263.1438.

3. Synthesis of Products

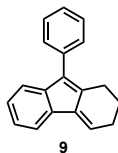
General procedure for the synthesis of products:



A flame-dried flask was charged with substrate (1.0 eq.), GaCl_3 (0.1 eq.), AgSbF_6 (0.2 eq.), and trifluorotoluene (0.05 M) under a nitrogen atmosphere. The resulting mixture was allowed to react at room temperature for 18-24 hours. The reaction was subsequently filtered through a plug of silica eluting with DCM. The filtrate was concentrated under reduced pressure to remove all volatile components. The crude material was purified using column chromatography to afford the desired product.

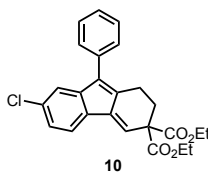


Diethyl 9-phenyl-1,2-dihydro-3H-fluorene-3,3-dicarboxylate (8): The cyclization of **7** was performed on 0.17 mmol scale. Purification by flash column chromatography provided 61 mg (92% yield) of **8**. $^1\text{H NMR}$ (400 MHz; CDCl_3) δ 7.65 (d, $J = 7.2$ Hz, 1H), 7.53 – 7.43 (m, 4H), 7.40 – 7.29 (m, 2H), 7.28 – 7.21 (m, 1H), 7.18 (t, $J = 7.3$ Hz, 1H), 6.96 (s, 1H), 4.48 – 4.05 (m, 4H), 2.94 (t, $J = 6.3$ Hz, 2H), 2.39 (t, $J = 6.3$ Hz, 2H), 1.30 (t, $J = 7.1$ Hz, 6H); $^{13}\text{C NMR}$ (100 MHz; CDCl_3) δ 170.1, 143.8, 141.7, 137.9, 134.9, 134.5, 132.1, 128.7, 128.6, 128.3, 127.7, 124.9, 123.2, 120.2, 119.6, 62.1, 56.1, 31.0, 20.9, 14.2; **IR** (Neat) 2979, 2925, 1728, 1603, 1445, 1366, 1234, 1178, 1158, 1095, 1054, 1017, 929, 856, 748, 700, 626; **HRMS**: calcd for $\text{C}_{25}\text{H}_{25}\text{O}_4^+$: 389.1747 found: 389.1751.

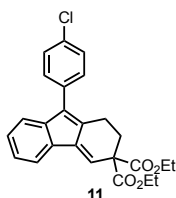


9-phenyl-2,3-dihydro-1H-fluorene (9): The cyclization of **S9** was performed on 1.77 mmol scale. Purification by flash column chromatography provided 250 mg (58% yield) of **9**. $^1\text{H NMR}$ (400 MHz; CDCl_3) δ 7.61 (d, $J = 7.3$ Hz, 1H), 7.51 (dt, $J = 15.3, 7.4$ Hz, 4H), 7.37 (t, $J = 8.0$ Hz, 2H), 7.30 – 7.22 (m, 1H), 7.18 (t, $J = 7.3$ Hz, 1H), 6.99 (t, $J = 4.5$ Hz, 1H), 2.87 – 2.77 (m, 2H), 2.55

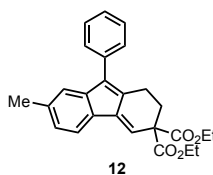
(q, $J = 5.7$ Hz, 2H), 1.92 (p, $J = 6.1$ Hz, 2H); ^{13}C NMR (100 MHz; CDCl_3) δ 143.3, 140.4, 135.4, 135.2, 135.0, 134.6, 129.8, 128.9, 128.5, 127.3, 127.2, 124.3, 119.19, 119.18, 26.4, 24.6, 24.1; **IR** (Neat) 2934, 2860, 1648, 1604, 1493, 1461, 1450, 1335, 1323, 1282, 1246, 1170, 1152, 1075, 1029, 965, 931, 883, 847, 773, 745, 700, 653; **HRMS**: calcd for $\text{C}_{19}\text{H}_{17}^+$: 245.1325 found: 245.1325.



Diethyl 7-chloro-9-phenyl-1,2-dihydro-3H-fluorene-3,3-dicarboxylate (10): The cyclization of **S10** was performed on 0.04 mmol scale. Purification by flash column chromatography provided 11 mg (62% yield) of **10**. ^1H NMR (500 MHz; CDCl_3) δ 7.54 (d, $J = 7.9$ Hz, 1H), 7.47 (dt, $J = 12.3, 7.4$ Hz, 4H), 7.38 (t, $J = 7.0$ Hz, 1H), 7.27 (d, $J = 5.1$ Hz, 1H), 7.15 (d, $J = 7.9$ Hz, 1H), 6.94 (s, 1H), 4.38 – 4.13 (m, 4H), 2.93 (t, $J = 6.3$ Hz, 2H), 2.38 (t, $J = 6.3$ Hz, 2H), 1.29 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (175 MHz; CDCl_3) δ 170.0, 145.5, 140.7, 137.2, 134.2, 133.9, 133.7, 133.2, 128.8, 128.6, 128.0, 124.7, 124.3, 121.0, 120.1, 62.2, 56.1, 30.9, 21.0, 14.2; **IR** (Neat) 2979, 2925, 1729, 1601, 1571, 1492, 1444, 1366, 1276, 1232, 1178, 1160, 1137, 1108, 1094, 1068, 1054, 1014, 947, 858, 817, 746, 725, 702, 683, 642, 622; **HRMS**: calcd for $\text{C}_{25}\text{H}_{24}\text{ClO}_4^+$: 423.1358 found: 423.1365.

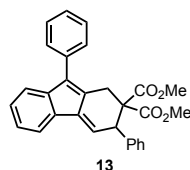


Diethyl 9-(4-chlorophenyl)-1,2-dihydro-3H-fluorene-3,3-dicarboxylate (11): The cyclization of **S11** was performed on 0.21 mmol scale. Purification by flash column chromatography provided 53 mg (59% yield) of **11**. ^1H NMR (500 MHz; CDCl_3) δ 7.66 (d, $J = 7.3$ Hz, 1H), 7.50 – 7.39 (m, 4H), 7.25 (d, $J = 5.8$ Hz, 2H), 7.19 (t, $J = 6.5$ Hz, 1H), 6.98 (s, 1H), 4.27 (qt, $J = 10.7, 5.4$ Hz, 4H), 2.91 (t, $J = 6.2$ Hz, 2H), 2.39 (t, $J = 6.2$ Hz, 2H), 1.30 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (125 MHz; CDCl_3) δ 170.0, 143.4, 141.5, 136.7, 134.8, 133.5, 133.0, 132.6, 130.0, 128.9, 128.4, 125.1, 123.8, 120.3, 119.4, 62.2, 56.1, 31.0, 20.9, 14.2; **IR** (Neat) 2980, 1731, 1490, 1453, 1366, 1288, 1269, 1236, 1178, 1160, 1136, 1090, 1069, 1055, 1014, 929, 857, 829, 751, 720, 705, 654; **HRMS**: calcd for $\text{C}_{25}\text{H}_{24}\text{ClO}_4^+$: 423.1358 found: 423.1362.

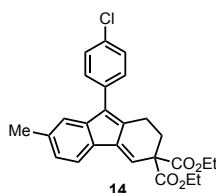


Diethyl 7-methyl-9-phenyl-1,2-dihydro-3H-fluorene-3,3-dicarboxylate (12): The cyclization of **S12** was performed on 0.15 mmol scale. Purification by flash column chromatography provided 52 mg (85% yield) of **12**. ^1H NMR (400 MHz; CDCl_3) δ 7.53 (d, $J = 7.5$ Hz, 1H), 7.50 – 7.44 (m, 4H), 7.42 – 7.32 (m, 1H), 7.12 (s, 1H), 6.99 (d, $J = 7.5$ Hz, 1H), 6.89 (s, 1H), 4.39 – 4.13 (m, 4H), 2.92 (t, $J = 6.4$ Hz, 2H), 2.46 – 2.25 (m, 5H), 1.30 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (100 MHz; CDCl_3) δ 170.2, 144.1, 141.5, 138.3, 137.8, 134.7, 132.4, 132.3, 128.7, 128.6, 127.6, 125.5, 122.4, 120.5, 120.0, 62.0, 56.1, 31.0, 22.0, 21.0, 14.2; **IR** (Neat) 2978, 2920, 1729, 1608, 1491, 1466, 1443,

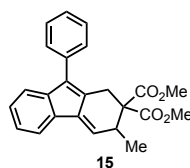
1365, 1285, 1269, 1230, 1174, 1140, 1112, 1094, 1068, 1053, 1016, 960, 937, 856, 817, 767, 739, 700, 649, 628; **HRMS**: calcd for $C_{26}H_{27}O_4^+$: 403.1904 found: 403.1910.



Dimethyl 3,9-diphenyl-1,3-dihydro-2H-fluorene-2,2-dicarboxylate (13): The cyclization of **S13** was performed on 0.08 mmol scale. Purification by flash column chromatography provided 30 mg (86% yield) of **13**. **¹H NMR** (500 MHz; $CDCl_3$) δ 7.59 (d, J = 7.3 Hz, 1H), 7.54 (d, J = 7.4 Hz, 2H), 7.49 (t, J = 7.5 Hz, 2H), 7.38 (dd, J = 13.9, 7.3 Hz, 2H), 7.33 – 7.16 (m, 7H), 6.92 (d, J = 6.0 Hz, 1H), 4.83 (d, J = 5.9 Hz, 1H), 3.66 (s, 3H), 3.55 (s, 3H), 3.50 (d, J = 17.1 Hz, 1H), 3.33 (d, J = 17.1 Hz, 1H); **¹³C NMR** (125 MHz; $CDCl_3$) δ 170.9, 169.8, 143.8, 139.5, 139.0, 136.2, 134.9, 134.4, 129.9, 129.5, 128.8, 128.74, 128.71, 128.1, 127.9, 127.8, 127.6, 125.1, 120.1, 119.8, 60.9, 53.2, 52.6, 47.0, 25.5; **IR** (Neat) 2994, 2947, 1744, 1727, 1650, 1601, 1491, 1446, 1427, 1377, 1296, 1253, 1236, 1199, 1176, 1123, 1079, 1058, 940, 881, 842, 819, 776, 760, 720, 700, 688, 628, 618; **HRMS**: calcd for $C_{29}H_{25}O_4^+$: 437.1747 found: 437.1736.

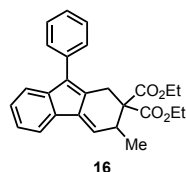


Diethyl 9-(4-chlorophenyl)-7-methyl-1,2-dihydro-3H-fluorene-3,3-dicarboxylate (14): The cyclization of **S14** was performed on 0.67 mmol scale. Purification by flash column chromatography provided 27 mg (91% yield) of **14**. **¹H NMR** (400 MHz; $CDCl_3$) δ 7.53 (d, J = 7.5 Hz, 1H), 7.48 – 7.37 (m, 4H), 7.06 (s, 1H), 6.99 (d, J = 7.5 Hz, 1H), 6.90 (s, 1H), 4.39 – 4.05 (m, 4H), 2.88 (t, J = 6.4 Hz, 2H), 2.49 – 2.25 (m, 5H), 1.29 (t, J = 7.1 Hz, 6H); **¹³C NMR** (100 MHz; $CDCl_3$) δ 170.1, 143.7, 141.4, 138.5, 136.6, 133.4, 133.1, 132.8, 132.2, 130.0, 128.9, 125.7, 122.9, 120.3, 120.1, 62.1, 56.0, 30.9, 22.0, 20.9, 14.2; **IR** (Neat) 2978, 2919, 1728, 1610, 1489, 1466, 1443, 1400, 1365, 1285, 1269, 1243, 1174, 1140, 1089, 1068, 1053, 1013, 961, 937, 901, 857, 838, 817, 753, 728, 631; **HRMS**: calcd for $C_{26}H_{26}ClO_4^+$: 437.1514 found: 437.1523.

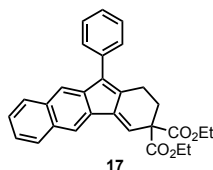


Dimethyl 3-methyl-9-phenyl-1,3-dihydro-2H-fluorene-2,2-dicarboxylate (15): The cyclization of **S15** was performed on 0.1 mmol scale. Purification by flash column chromatography provided 24 mg (67% yield) of **15**. **¹H NMR** (500 MHz; $CDCl_3$) δ 7.55 (d, J = 7.2 Hz, 1H), 7.48 (q, J = 7.6 Hz, 4H), 7.37 (t, J = 6.7 Hz, 1H), 7.29 (d, J = 7.4 Hz, 1H), 7.21 (t, J = 7.2 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 6.86 (d, J = 5.7 Hz, 1H), 3.75 (s, 3H), 3.61 (s, 3H), 3.60 – 3.55 (m, 1H), 3.48 (d, J = 16.8 Hz, 1H), 3.27 (d, J = 16.9 Hz, 1H), 1.16 (d, J = 7.2 Hz, 3H); **¹³C NMR** (100 MHz; $CDCl_3$) δ 171.0, 170.7, 143.7, 138.2, 138.0, 134.8, 134.5, 131.4, 129.6, 128.8, 128.7, 127.6, 127.6, 124.9, 119.8, 119.6, 60.2, 53.0, 52.9, 35.6, 25.8, 15.9; **IR** (Neat) 2954, 1745, 1721, 1650, 1601, 1494, 1444,

1434, 1379, 1338, 1267, 1249, 1200, 1178, 1153, 1085, 1046, 1029, 969, 958, 943, 923, 907, 884, 852, 818, 776, 759, 699, 680, 635, 607; **HRMS**: calcd for $C_{24}H_{23}O_4^+$: 375.1591 found: 375.1598.

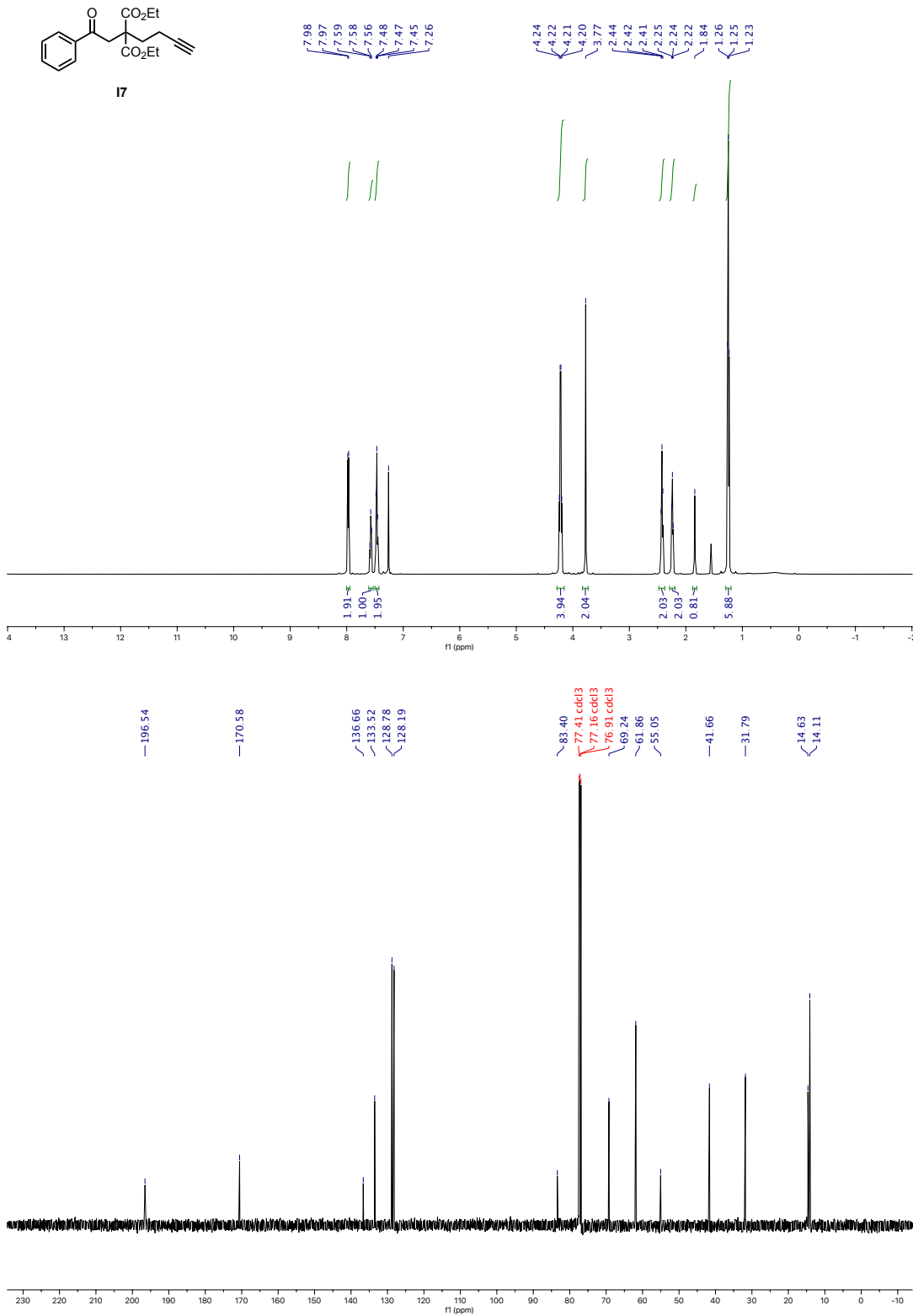


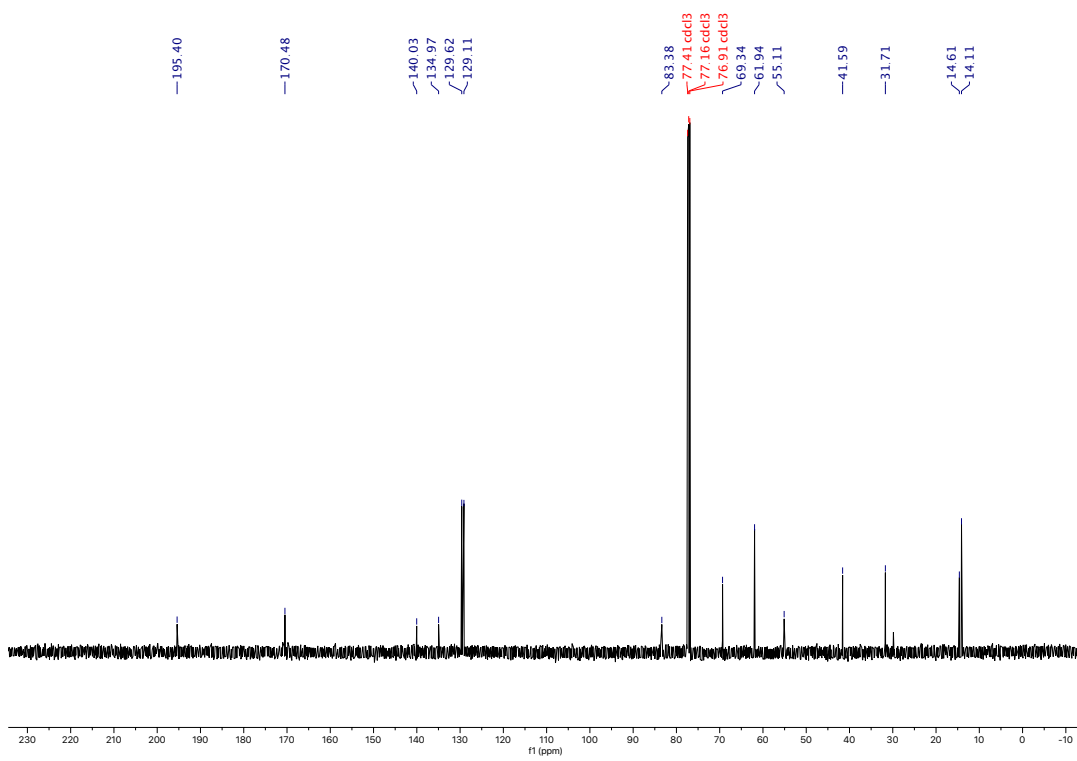
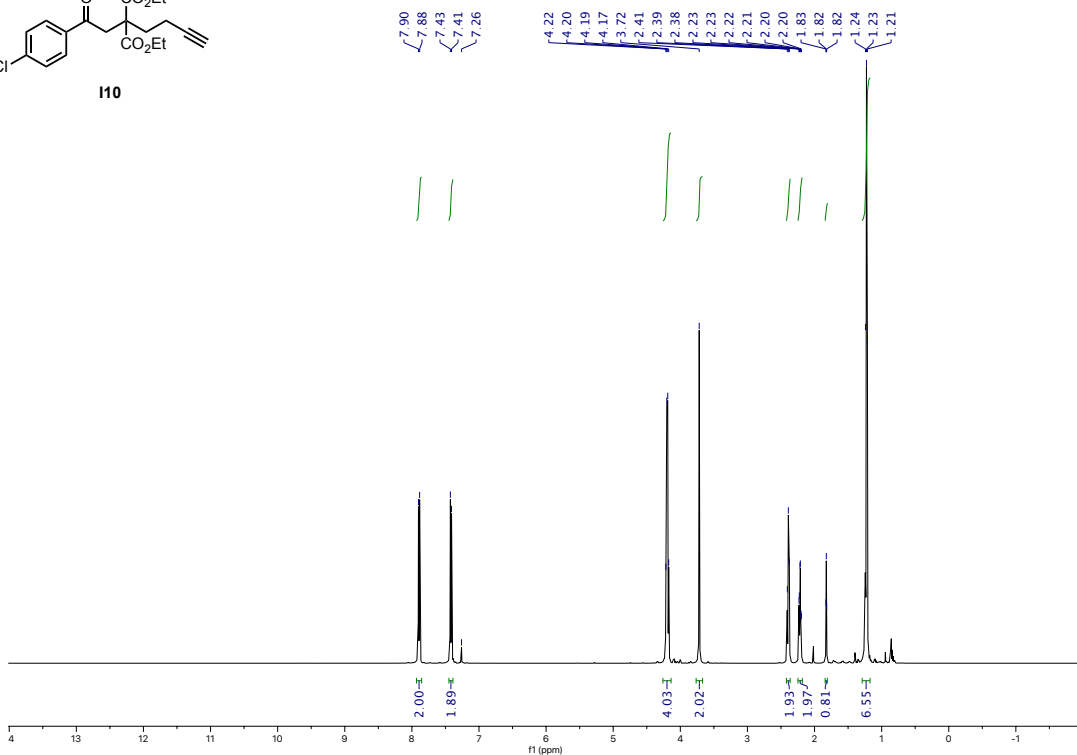
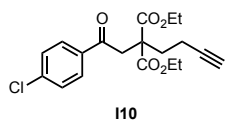
Diethyl 3-methyl-9-phenyl-1,3-dihydro-2H-fluorene-2,2-dicarboxylate (16): The cyclization of **S16** was performed on 0.1 mmol scale. Purification by flash column chromatography provided 28 mg (70% yield) of **16**. $^1\text{H NMR}$ (500 MHz; CDCl_3) δ 7.56 (d, $J = 7.2$ Hz, 1H), 7.49 (dt, $J = 15.1, 7.4$ Hz, 4H), 7.37 (t, $J = 7.1$ Hz, 1H), 7.30 (d, $J = 7.4$ Hz, 1H), 7.21 (t, $J = 7.3$ Hz, 1H), 7.16 (t, $J = 7.3$ Hz, 1H), 6.87 (d, $J = 5.8$ Hz, 1H), 4.29 – 4.16 (m, 2H), 4.14 – 3.98 (m, 2H), 3.57 (p, $J = 7.0$ Hz, 1H), 3.47 (d, $J = 16.8$ Hz, 1H), 3.26 (d, $J = 16.8$ Hz, 1H), 1.26 (t, $J = 7.1$ Hz, 3H), 1.18 (d, $J = 7.2$ Hz, 3H), 1.06 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz; CDCl_3) δ 170.5, 170.3, 143.6, 138.1, 137.9, 134.9, 134.5, 131.7, 129.9, 128.8, 128.7, 127.6, 127.5, 124.8, 119.7, 119.6, 61.72, 61.65, 60.2, 35.5, 25.7, 15.8, 14.2, 14.1; **IR** (Neat) 2976, 2931, 1729, 1652, 1603, 1492, 1462, 1444, 1366, 1338, 1296, 1259, 1229, 1178, 1150, 1089, 1045, 1030, 964, 931, 856, 774, 754, 701, 633, 604; **HRMS**: calcd for $C_{26}H_{27}O_4^+$: 403.1904 found: 403.1906.

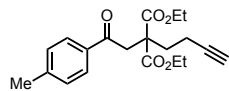


Diethyl 11-phenyl-1,2-dihydro-3H-benzo[b]fluorene-3,3-dicarboxylate (17): The cyclization of **S17** was performed on 0.14 mmol scale. Purification by flash column chromatography provided 29 mg (48% yield) of **17**. $^1\text{H NMR}$ (500 MHz; CDCl_3) δ 7.82 (d, $J = 7.5$ Hz, 2H), 7.68 (d, $J = 8.2$ Hz, 1H), 7.57 – 7.47 (m, 3H), 7.44 (t, $J = 8.3$ Hz, 3H), 7.32 (t, $J = 7.3$ Hz, 1H), 7.14 (d, $J = 6.5$ Hz, 2H), 4.41 – 4.12 (m, 4H), 2.75 (t, $J = 6.3$ Hz, 2H), 2.43 (t, $J = 6.3$ Hz, 2H), 1.31 (t, $J = 7.1$ Hz, 6H); $^{13}\text{C NMR}$ (125 MHz; CDCl_3) δ 170.0, 141.8, 139.9, 139.6, 137.3, 135.0, 132.8, 131.5, 129.4, 128.9, 128.5, 128.0, 127.7, 125.8, 125.4 (two carbons observed by HSQC), 125.2, 124.8, 118.5, 62.2, 56.4, 31.4, 20.3, 14.2; **IR** (Neat) 2978, 2917, 1728, 1650, 1557, 1520, 1491, 1441, 1386, 1365, 1325, 1297, 1282, 1260, 1231, 1178, 1161, 1068, 1054, 1028, 1017, 988, 922, 857, 816, 745, 700, 674, 631; **HRMS**: calcd for $C_{29}H_{27}O_4^+$: 439.1904 found: 439.1916.

4. NMR Spectra







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