Highly Regio- and Stereoselective Synthesis of Indene Derivatives via Electrophilic Cyclization

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General Remarks:
Column chromatography was carried out on silica gel. $^1$H NMR spectra were recorded on 300 MHz or 400 MHz in CDCl$_3$ and $^{13}$C NMR spectra were recorded on 75 MHz or 100 MHz in CDCl$_3$ using TMS as internal standard. IR spectra were recorded on a FT-IR spectrometer and only major peaks are reported in cm$^{-1}$. Melting points were determined on a microscopic apparatus and were uncorrected. All new compounds were further characterized by element analysis; copies of their $^1$H NMR and $^{13}$C NMR spectra are provided. Commercially available reagents and solvents were used without further purification. THF was distilled immediately before use from Na/benzophenone.

Starting Materials:

**Dimethyl 2-(2-iodobenzyl)malonate:** To a solution of 1-(bromomethyl)-2-iodobenzene (1.48 g, 5.0 mmol) in 20 mL of dimethyl malonate was added NaH (0.48 g, 20.0 mmol). The resulting mixture was then allowed to stir at room temperature for 2 h. The mixture was poured into 20 mL of satd NH$_4$Cl (aq) and extracted with 3 × 30 mL of CH$_2$Cl$_2$. The extract was dried (Na$_2$SO$_4$) and filtered. The solvent was evaporated under reduced pressure, and the mixture was chromatographed using 10:1 hexanes/EtOAc to afford dimethyl 2-(2-iodobenzyl)malonate (1.69 g, 97%) as an oil: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.83-7.81 (d, $J$ = 8.1 Hz, 1H), 7.27-7.23 (m, 2H), 6.95-6.92 (m, 1H), 3.89-3.84 (t, $J$ = 8.1 Hz, 1H), 3.71 (s, 6H), 3.35-3.32 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.9, 140.0, 139.7, 130.5, 128.7, 128.3, 100.3, 52.6, 51.4, 39.3; IR (neat, cm$^{-1}$) 1752, 1737, 1437, 1292, 1230, 1154, 1017, 754.

**Diethyl 2-(2-iodobenzyl)malonate:** Diethyl 2-(2-iodobenzyl)malonate was prepared by the same method. But employing diethyl malonate (20 mL) afforded diethyl 2-(2-iodobenzyl)malonate 1.82 g (97%) as an oil: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.82-7.80 (m, 1H), 7.24-7.21 (m, 2H), 6.93-6.88 (m, 1H), 4.20-4.12 (m, 4H), 3.85-3.78 (m, 1H), 3.34-3.29 (m, 2H), 1.26-1.17 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.4, 140.2, 139.6, 130.5, 128.6, 128.2, 100.3, 61.4, 51.6, 39.2, 13.9; IR (neat, cm$^{-1}$) 2981, 2958, 2927, 1745, 1732, 1294, 1226, 1152, 753.

**Methyl 2-(2-iodobenzyl)-3-oxobutanoate:** Methyl 2-(2-iodobenzyl)-3-oxobutanoate was prepared by the same method. But employing methyl 3-oxobutanoate (20 mL) afforded methyl 2-(2-iodobenzyl)-3-oxobutanoate 1.59 g (96%) as an oil: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.38-7.37 (d, $J$ = 7.2 Hz, 1H), 7.25-7.13 (m, 2H), 6.94-6.88 (m, 1H), 4.00-3.95 (t, $J$ = 7.8 Hz, 1H), 3.69 (s, 3H), 3.27-3.24 (d, $J$ = 7.8 Hz, 2H), 2.24 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 202.0, 169.1, 140.5, 139.6, 130.8, 128.6, 128.4, 100.3, 58.8, 52.4, 38.5, 29.8; IR (neat, cm$^{-1}$) 2952, 1745, 1718, 1437, 1252, 1217, 1149, 1012, 753.

**3-(2-Iodobenzyl) pentane-2,4-dione:** 3-(2-Iodobenzyl)pentane-2,4-dione was prepared by the same method. But employing pentane-2,4-dione (20 mL) afforded 3-(2-Iodobenzyl)pentane-2,4-dione 1.52 g (96%) as a solid: mp 32-34 ℃; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 16.86 (s, 1H), 7.89-6.90 (m, 4H), 3.59 (s, 2H), 2.02 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 192.1, 141.2, 139.5, 128.5, 128.3, 127.4, 107.6, 101.2, 38.5, 23.1; IR (KBr, cm$^{-1}$) 3400, 1603, 1432, 1012, 747.

Typical procedure for the preparation of acetylenic malonates and ketones.

**Dimethyl 2-(2-(2-phenylethynyl)benzyl)malonate (1a):** To a solution of dimethyl 2-(2-iodobenzyl)malonate (0.35 g, 1.0 mmol) and 1-ethynylbenzene (0.12 g, 1.2 mmol) in Et$_3$N (4.0 mL) was added PdCl$_2$(PPh$_3$)$_2$ (14 mg, 2 mol %). The mixture was stirred for 5 min and CuI (2 mg, 1 mol %) was added. The resulting mixture was then stirred under an
argon atmosphere at room temperature for 12 h. The ammonium salt was removed by filtration, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to afford 1a 0.30 g (93 %) as an oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.58-7.50 (m, 3H), 7.37-7.33 (m, 3H), 7.28-7.21 (m, 3H), 4.04-3.99 (m, 1H), 3.69-3.68 (m, 6H), 3.49-3.46 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 169.3, 139.5, 132.3, 131.5, 129.9, 128.4, 128.3, 126.9, 123.1, 122.9, 94.2, 87.2, 52.4, 52.1, 33.9; IR (neat, cm$^{-1}$) 2953, 1756, 1737, 1438, 1231, 1153, 759; Anal.Calcd for C$_{20}$H$_{18}$O$_4$: C, 74.52; H, 5.63. Found: C, 74.63; H, 5.66.

**Diethyl 2-(2-(phenylethynyl)benzyl)malonate (1b):** The 1b was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and 1-ethynylbenzene (0.12 g, 1.2 mmol) at 60 °C for 6 h afforded 1b 0.33 g (93 %) as an oil: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.57-7.51 (m, 3H), 7.37-7.23 (m, 6H), 4.19-4.11 (m, 4H), 4.02-3.98 (t, $J$ = 8.0 Hz, 1H), 3.47-3.45 (d, $J$ = 7.6 Hz, 2H), 1.20-1.17 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.9, 139.7, 132.2, 131.5, 130.0, 128.3, 126.8, 123.1, 122.9, 94.1, 87.3, 61.3, 52.3, 33.9, 13.9; IR (neat, cm$^{-1}$) 2983, 1747, 1733, 1298, 1227, 1150, 759, 692; Anal.Calcd for C$_{22}$H$_{22}$O$_4$: C, 75.41; H, 6.33. Found: C, 75.40; H, 6.43.

**Diethyl 2-(2-(hept-1-ynyl)benzyl)malonate (1c):** The 1c was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and hept-1-yne (0.12 g, 1.2 mmol) at 60 °C for 6 h afforded 1c 0.31 g (89 %) as an oil: 1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.38-7.36 (m, 1H), 7.20-7.14 (m, 3H), 4.19-4.10 (m, 4H), 3.95-3.91 (t, $J$ = 7.6 Hz, 1H), 3.35-3.33 (d, $J$ = 8.0 Hz, 2H), 2.46-2.42 (t, $J$ = 6.8 Hz, 2H), 1.66-1.58 (m, 2H), 1.47-1.33 (m, 4H), 1.22-1.17 (m, 6H), 0.94-0.90 (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.9, 139.4, 132.1, 129.7, 127.4, 126.6, 123.7, 95.3, 78.4, 61.2, 52.0, 33.8, 31.1, 28.4, 22.1, 19.4, 13.9; IR (neat, cm$^{-1}$) 2959, 2934, 1734, 1226, 1151, 759; Anal.Calcd for C$_{21}$H$_{28}$O$_4$: C, 73.23; H, 8.19. Found: C, 73.37; H, 8.02.

**Diethyl 2-(2-(3-(tetrahydro-2$^H$-pyran-2-yloxy)prop-1-ynyl)benzyl) malonate (1d):** The 1d was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and tetrahydro-2-(prop-2-ynyloxy)-2$^H$-pyran (0.17 g, 1.2 mmol) at 60 °C for 6 h afforded 1d 0.33 g (88 %) as an oil: 1H NMR (300 MHz, CDCl$_3$) $\delta$ 7.45-7.42 (m, 1H), 7.23-7.14 (m, 3H), 4.92-4.90 (t, $J$ = 3.3 Hz, 1H), 4.59-4.48 (m, 2H), 4.20-4.09 (m, 4H), 3.95-3.91 (t, $J$ = 7.6 Hz, 1H), 3.35-3.33 (d, $J$ = 8.0 Hz, 2H), 2.46-2.42 (t, $J$ = 6.8 Hz, 2H), 1.66-1.58 (m, 2H), 1.47-1.33 (m, 4H), 1.22-1.17 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.9, 139.4, 132.1, 129.7, 127.4, 126.6, 123.7, 95.3, 78.4, 61.2, 52.0, 33.8, 31.1, 28.4, 22.1, 19.4, 13.9; IR (neat, cm$^{-1}$) 2942, 1733, 1028, 761; Anal.Calcd for C$_{21}$H$_{26}$O$_6$: C, 67.36; H, 7.00. Found: C, 67.22; H, 6.88.

**Diethyl 2-(2-(2-(4-chlorophenyl)ethynyl)benzyl)malonate (1e):** The 1e was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and 1-chloro-4-ethynylbenzene (0.16 g, 1.2 mmol) for 12 h afforded 1e 0.35 g (91 %) as an oil: 1H NMR (300 MHz, CDCl$_3$) $\delta$ 7.52-7.47 (m, 3H), 7.35-7.22 (m, 5H), 4.92-4.90 (t, $J$ = 3.3 Hz, 1H), 4.59-4.48 (m, 2H), 4.20-4.09 (m, 4H), 3.95-3.85 (m, 2H), 3.59-3.53 (m, 1H), 3.37-3.34 (d, $J$ = 8.1 Hz, 2H), 1.87-1.72 (m, 2H), 1.67-1.54 (m, 4H), 1.22-1.17 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 169.8, 139.8, 132.5, 129.7, 128.4, 126.7, 122.4, 96.8, 90.0, 83.6, 62.0, 61.3, 54.6, 52.1, 33.6, 30.3, 25.3, 19.1, 13.9; IR (neat, cm$^{-1}$) 2942, 1733, 1028, 761; Anal.Calcd for C$_{22}$H$_{21}$ClO$_4$: C, 67.63; H, 7.00. Found: C, 67.22; H, 6.88.

**Methyl 2-(2-(phenylethynyl)benzyl)-3-oxobutanoate (1f):** The 1f was prepared by the
same method. But employing methyl 2-(2-iodobenzyl)-3-oxobutanoate (0.33 g, 1.0 mmol) and 1-ethynylbenzene (0.12 g, 1.2 mmol) for 12 h afforded 1f 0.28 g (90%) as an oil: 1H NMR (300 MHz, CDCl3) δ 7.55-7.50 (m, 3H), 7.39-7.34 (m, 3H), 7.26-7.21 (m, 3H), 4.13-4.08 (t, J = 6.9 Hz, 1H), 3.68-3.67 (m, 3H), 3.49-3.33 (m, 2H), 2.19 (m, 3H); 13C NMR (75 MHz, CDCl3) δ 202.4, 169.6, 140.0, 132.4, 131.5, 130.0, 128.5, 128.4, 126.8, 123.0, 122.7, 94.1, 87.4, 59.6, 52.3, 33.1, 29.7; IR (neat, cm⁻¹) 3422, 1743, 1717, 1150, 758; Anal. Calcd for C20H18O3: C, 78.41; H, 5.92. Found: C, 78.37; H, 6.08.

3-(2-(2-Phenylethynyl)benzyl)pentane-2,4-dione (1g): The 1g was prepared by the same method. But employing 3-(2-iodobenzyl)pentane-2,4-dione (0.32 g, 1.0 mmol) and 1-ethynylbenzene (0.12 g, 1.2 mmol) for 12 h afforded 1g 0.27 g (93%) as a solid: mp 106-108 °C; 1H NMR (400 MHz, CDCl3) δ 16.86 (s, 1H), 7.57-7.55 (m, 3H), 7.39-7.37 (m, 3H), 7.31-7.21 (m, 2H), 7.09-7.07 (d, J = 8.0 Hz, 1H), 3.89 (s, 2H), 2.08 (s, 6H); 13C NMR (75 MHz, CDCl3) δ 192.1, 141.3, 132.4, 131.5, 128.8, 128.4, 126.4, 126.3, 123.1, 122.7, 107.7, 94.7, 87.5, 31.4, 23.2; IR (KBr, cm⁻¹) 3408, 1596, 1493, 1441, 755; Anal. Calcd for C20H18O2: C, 82.73; H, 6.25. Found: C, 82.88; H, 6.23.

Diethyl 2-(2-(3-hydroxyprop-1-ynyl)benzyl)malonate (1h): The 1h was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and but-3-yn-2-ol (0.07 g, 1.2 mmol) for 12 h afforded 1h 0.29 g (94%) as an oil: 1H NMR (300 MHz, CDCl3) δ 7.40-7.38 (m, 1H), 7.30-7.15 (m, 3H), 4.51 (s, 2H), 4.23-4.12 (m, 4H), 3.89-3.84 (m, 1H), 3.37-3.35 (d, J = 7.2 Hz, 2H), 2.84 (s, 1H) 1.26-1.19 (m, 6H); 13C NMR (75 MHz, CDCl3) δ 169.2, 140.1, 131.8, 130.0, 128.4, 126.8, 122.3, 93.0, 81.8, 61.6, 52.5, 51.4, 33.8, 13.9; IR (neat, cm⁻¹) 3462, 2983, 1732, 1300, 1228, 1154, 1029, 762; Anal. Calcd for C17H20O5: C, 67.09; H, 6.62. Found: C, 67.23; H, 6.68.

Diethyl 2-(2-(3-hydroxybut-1-ynyl)benzyl)malonate (1i): The 1i was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and prop-2-yn-1-ol (0.08 g, 1.2 mmol) for 12 h afforded 1i 0.31 g (96%) as an oil: 1H NMR (300 MHz, CDCl3) δ 7.39-7.37 (m, 1H), 7.28-7.14 (m, 3H), 4.79-4.73 (q, J = 6.9 Hz, 1H), 4.22-4.11 (m, 4H), 3.87-3.82 (m, 1H), 3.35-3.33 (d, J = 6.9 Hz, 2H), 2.92 (s, 1H), 1.56-1.53 (m, 3H), 1.25-1.18 (m, 6H); 13C NMR (75 MHz, CDCl3) δ 169.2, 140.1, 131.8, 130.0, 128.4, 126.8, 122.3, 96.7, 81.8, 61.6, 58.6, 52.5, 33.9, 24.2, 13.9; IR (neat, cm⁻¹) 3437, 2982, 1732, 1450, 1371, 1301, 1228, 1154, 1029, 762; Anal. Calcd for C18H22O5: C, 67.91; H, 6.97. Found: C, 68.01; H, 6.88.

Diethyl 2-(2-(3-hydroxy-3-phenylprop-1-ynyl)benzyl)malonate (1j): The 1j was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and 1-phenylprop-2-yn-1-ol (0.16 g, 1.2 mmol) for 12 h afforded 1j 0.34 g (90%) as an oil: 1H NMR (300 MHz, CDCl3) δ 7.62-7.60 (m, 2H), 7.43-7.15 (m, 7H), 5.70 (s, 1H), 4.15-4.08 (m, 4H), 3.88-3.83 (t, J = 7.8 Hz, 1H), 3.61 (s, 1H), 3.39-3.37 (d, J = 6.0 Hz, 2H), 1.20-1.15 (t, J = 7.8 Hz, 6H); 13C NMR (75 MHz, CDCl3) δ 169.2, 169.1, 140.8, 140.1, 131.9, 130.0, 128.6, 128.5, 128.1, 126.8, 126.6, 122.2, 94.5, 84.3, 64.8, 61.6, 52.5, 33.9, 13.9; IR (neat, cm⁻¹) 3465, 2981, 1732, 1450, 1370, 1302, 1229, 1154, 1029, 761; Anal. Calcd for C23H24O5: C, 72.61; H, 6.36. Found: C, 72.47; H, 6.48.

Diethyl 2-(2-(3-hydroxy-3-p-tolylprop-1-ynyl)benzyl)malonate (1k): The 1k was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and 1-p-tolylprop-2-yn-1-ol (0.18 g, 1.2 mmol) for 12 h afforded 1k 0.37 g (93%) as an oil: 1H NMR (300 MHz, CDCl3) δ 7.51-7.16 (m, 8H), 5.68-5.66 (d, J = 5.4 Hz, 1H), 4.19-4.09 (m, 4H), 3.89-3.85 (t, J = 6.9 Hz, 1H), 3.48-3.46 (d, J = 6.6 Hz, 1H),
3.39-3.37 (d, J = 6.9 Hz, 2H), 2.36 (s, 3H), 1.22-1.17 (t, J = 6.3 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 169.3, 169.2, 140.2, 137.9, 131.9, 130.0, 129.2, 128.5, 126.8, 126.6, 122.2, 94.7, 84.1, 64.7, 61.6, 52.5, 33.9, 21.1, 13.9; IR (neat, cm⁻¹) 3474, 1732, 1301, 1228, 1154, 1030, 762; Anal. Calcd for C₂₄H₂₆O₅: C, 73.08; H, 6.64. Found: C, 73.22; H, 6.50.

Diethyl 2-(2-(3-(furan-2-yl)-3-hydroxyprop-1-ynyl)benzyl)malonate (1l): The 1l was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and 1-(furan-2-yl)prop-2-yn-1-ol (0.15 g, 1.2 mmol) for 12 h afforded 1l 0.32 g (87 %) as an oil: ¹H NMR (300 MHz, CDCl₃) δ 7.45-7.42 (m, 2H), 7.31-7.17 (m, 3H), 6.50-6.49 (m, 1H), 6.37-6.36 (m, 1H) 5.70-5.68 (d, J = 6.0 Hz, 1H), 4.21-4.10 (m, 4H), 3.91-3.87 (m, 1H), 3.63-3.60 (d, J = 6.9 Hz, 1H), 3.41-3.38 (d, J = 7.2 Hz, 2H), 1.22-1.17 (t, J = 6.9 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 169.2, 169.1, 153.0, 142.8, 140.3, 132.0, 130.0, 128.7, 126.8, 121.9, 110.3, 107.5, 91.9, 83.6, 61.6, 58.5, 52.4, 33.8, 13.9; IR (neat, cm⁻¹) 3467, 2984, 1733, 1229, 1153, 1015, 762; Anal. Calcd for C₂₁H₂₂O₆: C, 68.10; H, 5.99. Found: C, 68.22; H, 6.00.

Diethyl 2-(2-(3-hydroxy-3-methylbut-1-ynyl)benzyl)malonate (1m): The 1m was prepared by the same method. But employing diethyl 2-(2-iodobenzyl)malonate (0.38 g, 1.0 mmol) and 2-methylbut-3-yn-2-ol (0.10 g, 1.2 mmol) for 12 h afforded 1m 0.32 g (96 %) as an oil: ¹H NMR (300 MHz, CDCl₃) δ 7.38-7.35 (m, 1H), 7.27-7.13 (m, 3H), 4.24-4.07 (m, 4H), 3.87-3.82 (t, J = 7.5 Hz, 1H), 3.35-3.32 (d, J = 7.2 Hz, 2H), 3.04 (s, 1H), 1.61 (s, 6H) 1.24-1.18 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 169.2, 140.0, 131.7, 130.1, 128.2, 126.8, 122.4, 99.5, 79.9, 65.3, 61.5, 52.5, 34.0, 31.3, 14.0; IR (neat, cm⁻¹) 3439, 2982, 1732, 1370, 1301, 1229, 1157, 1032, 761; Anal. Calcd for C₁₉H₂₄O₅: C, 68.66; H, 7.28. Found: C, 68.71; H, 7.14.

General procedure for electrophilic cyclization of acetylenic malonates and ketones.

To a solution of 0.30 mmol of the alkyne, 2.0 equiv of t-BuOK and 1.5 mL of THF was added gradually 2.0 equiv of electrophile dissolved in 1.5 mL of THF. The reaction mixture was flushed with argon and allowed to stir at room temperature for the desired time. The excess I₂ was removed by washing with a saturated aq solution of Na₂S₂O₃. The aq solution was then extracted with diethyl ether (2×10 mL). The combined ether layers were dried over anhydrous Na₂SO₄ and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel using hexanes/EtOAc as the eluent.

CO₂Me  CO₂Me
Ph  I

2a: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 125.0 mg (93%) of the indicated compound as a solid: mp 117-118 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.57-8.55 (d, J = 6.0 Hz, 1H), 7.49-7.47 (m, 2H), 7.35-7.13 (m, 3H), 4.24-4.07 (m, 4H), 3.87-3.82 (t, J = 7.5 Hz, 1H), 3.35-3.32 (d, J = 7.2 Hz, 2H), 3.04 (s, 1H), 1.61 (s, 6H) 1.24-1.18 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 170.1, 144.7, 143.4, 143.2, 139.4, 129.6, 129.3, 128.2, 127.6, 126.3, 126.0, 124.4, 93.6, 68.9, 52.7, 43.1; IR (KBr, cm⁻¹) 2952, 1733, 1436, 1272, 1173, 1058, 910, 764, 732, 699; Anal. Calcd for C₂₀H₁₇IO₄: C, 53.59; H, 3.82. Found: C, 53.41; H, 3.83.

CO₂Et  CO₂Et
Ph

2b: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 128.5 mg (90%) of the indicated compound as an oil: ¹H NMR (400 MHz, CDCl₃) δ 8.56-8.54
(m, 1H), 7.55-7.53 (m, 2H), 7.33-7.22 (m, 6H), 3.86-3.65 (m, 6H), 1.12-1.09 (t, J = 7.2 Hz, 6H); 13C NMR (100 MHz, CDCl3) δ 169.6, 144.7, 143.5, 143.3, 139.5, 129.4, 128.0, 127.4, 126.3, 125.8, 124.3, 93.5, 69.1, 61.7, 42.9, 13.6; IR (neat, cm⁻¹) 2982, 1730, 1466, 1442, 1263, 1184, 1080, 1056, 764, 732, 698; Anal.Calcd for C22H21IO4: C, 55.48; H, 4.44. Found: C, 55.52; H, 4.42.

2c: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 124.1 mg (88%) of the indicated compound as an oil: 1H NMR (300 MHz, CDCl3) δ 8.65-8.63 (m, 1H), 7.28-7.19 (m, 3H), 4.24-4.17 (q, J = 6.9 Hz, 4H), 3.60 (s, 2H), 2.67-2.62 (m, 2H), 1.71-1.66 (m, 2H), 1.39-1.32 (m, 4H), 1.30-1.23(m, 6H), 0.95-0.90 (t, J = 7.2 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 170.2, 144.1, 140.1, 139.1, 129.1, 126.1, 125.7, 124.3, 105.6, 66.7, 62.0, 45.6, 42.0, 31.3, 30.6, 22.6, 14.1, 13.9; IR (neat, cm⁻¹) 2958, 2933, 1730, 1465, 1253, 1235, 1186, 1058, 762; Anal.Calcd for C21H27IO4: C, 53.63; H, 5.79. Found: C, 53.80; H, 5.68.

3e: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 96.4 mg (63%) of the indicated compound as an oil: 1H NMR (400 MHz, CDCl3) δ 7.41-7.37 (m, 2H), 7.29-7.26 (m, 2H), 7.17-7.11 (m, 2H), 6.86-6.82 (m, 1H), 6.19-6.17 (d, J = 8.0 Hz, 1H), 4.37-4.26 (m, 4H), 3.75 (s, 2H), 1.38-1.34 (m, 6H); 13C NMR (100 MHz, CDCl3) δ 169.1, 146.7, 144.7, 143.2, 137.9, 134.2, 129.4, 129.3, 128.8, 126.8, 125.2, 124.7, 95.5, 68.9, 62.3, 42.5, 14.0; IR (neat, cm⁻¹) 3435, 1733, 1710, 1248, 1079, 1028; Anal.Calcd for C22H20ClIO4: C, 51.73; H, 3.95. Found: C, 51.90; H, 4.01.

2f: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 81.6 mg (63%) of the indicated compound as a solid: mp 112-114 °C; 1H NMR (300 MHz, CDCl3) δ 8.70-8.68 (d, J = 7.5 Hz, 1H), 7.36-7.20 (m, 8H), 3.68-3.36 (q, J = 15.9 Hz, 2H), 3.37 (s, 3H), 2.08 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 203.5, 171.1, 145.2, 144.6, 143.0, 139.7, 129.7, 129.1, 128.3, 127.8, 126.2, 126.0, 124.4, 92.0, 73.5, 52.4, 41.2, 28.0; IR (KBr, cm⁻¹) 3424, 1733, 1710, 1253, 1128, 1079, 1028; Anal.Calcd for C20H17IO3: C, 55.57; H, 3.96. Found: C, 55.68; H, 4.03.

3f: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 31.1 mg (24%) of the indicated compound as an oil: 1H NMR (300 MHz, CDCl3) δ 7.42-7.33 (m, 5H), 7.17-7.09 (m, 2H), 6.83-6.78 (m, 1H), 6.16-6.13 (d, J = 8.1 Hz, 1H), 3.86-3.85 (m, 3H), 3.68-3.51 (q, J = 17.1 Hz, 2H), 2.60-2.59 (m, 3H); 13C NMR (75 MHz, CDCl3) δ 201.6, 170.6, 146.9, 145.7, 142.9, 138.4, 129.2, 128.7, 128.5, 127.6, 126.9, 125.2, 124.8, 97.7, 74.1, 52.9, 41.2, 28.7; IR (neat, cm⁻¹) 3433, 1733, 1708, 1253, 1161, 1064; Anal.Calcd for C20H17IO3: C, 55.57; H, 3.96. Found: C, 55.75; H, 4.05.
3g: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 112.3 mg (90%) of the indicated compound as a solid: mp 165-167 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.38-7.28 (m, 5H), 7.09-7.02 (m, 2H), 6.77-6.73 (m, 1H), 6.12-6.09 (d, $J = 7.8$ Hz, 1H), 3.33 (s, 2H), 2.42 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 203.0, 147.7, 145.5, 142.8, 138.8, 129.3, 129.0, 128.7, 127.5, 127.2, 125.2, 125.1, 98.2, 79.3, 39.6, 28.9; IR (KBr, cm$^{-1}$) 3388, 1704, 1354, 1154, 762, 734, 694; Anal.Calcd for C$_{20}$H$_{17}$I$_2$O$_2$: C, 57.71; H, 4.12. Found: C, 57.90; H, 4.30.

2h: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 97.9 mg (85%) of the indicated compound as a solid: mp 117-118 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ 8.32-8.29 (d, $J = 8.4$ Hz, 1H), 7.42-7.33 (m, 3H), 5.39-5.04 (m, 2H), 4.22-4.14 (m, 2H), 3.72-3.52 (q, $J = 16.5$ Hz, 2H), 1.25-1.20 (m, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 167.9, 166.9, 144.9, 142.1, 135.6, 130.8, 126.5, 125.0, 123.5, 78.3, 63.3, 62.9, 38.9, 13.9; IR (KBr, cm$^{-1}$) 1756, 1733, 1235, 1159, 1009; Anal.Calcd for C$_{15}$H$_{13}$I$_2$O$_4$: C, 46.90; H, 3.41. Found: C, 46.73; H, 3.38.

2i: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 66.9 mg (56%) of the indicated compound as a solid: mp 104-106 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ 8.31-8.28 (d, $J = 7.5$ Hz, 1H), 7.42-7.31 (m, 3H), 5.36-5.29 (q, $J = 6.9$ Hz, 1H), 4.19-4.12 (q, $J = 6.9$ Hz, 2H), 3.57 (s, 2H), 1.72-1.69 (d, $J = 6.9$ Hz, 3H), 1.23-1.18 (t, $J = 6.9$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 168.2, 167.3, 143.7, 140.0, 136.9, 130.6, 126.5, 124.9, 123.7, 86.8, 86.7, 62.9, 62.3, 40.1, 19.3, 13.7; IR (KBr, cm$^{-1}$) 1732, 1237, 1157, 761; Anal.Calcd for C$_{16}$H$_{15}$I$_2$O$_4$: C, 48.26; H, 3.80. Found: C, 48.43; H, 3.80.

2j: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 75.9 mg (55%) of the indicated compound as a solid: mp 168-170 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ 8.52-8.50 (d, $J = 6.9$ Hz, 1H), 7.53-7.33 (m, 8H), 6.34 (s, 1H), 3.77-3.38 (q, $J = 17.7$ Hz, 2H), 3.69-3.25 (m, 2H), 0.79-0.74 (m, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 167.8, 167.6, 144.4, 144.1, 137.0, 134.9, 131.0, 129.1, 128.6, 128.4, 126.5, 124.0, 89.5, 80.6, 62.7, 62.3, 40.9, 13.1; IR (KBr, cm$^{-1}$) 3435, 1732, 1239, 1157, 1409; Anal.Calcd for C$_{21}$H$_{17}$I$_2$O$_4$: C, 54.80; H, 3.72. Found: C, 54.91; H, 3.69.

2k: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 83.9 mg (59%) of the indicated compound as a solid: mp 130-132 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ 8.51-8.48 (m, 1H), 7.44-7.31 (m, 5H), 7.19-7.17 (m, 2H), 6.30 (s, 1H), 3.76-3.68
(m, 2H), 3.44-3.32 (m, 2H), 2.35 (s, 3H), 0.80-0.75 (m, 3H); 13C NMR (75 MHz, CDCl3) δ 167.8, 167.7, 144.4, 143.8, 139.1, 137.1, 131.8, 130.9, 129.2, 128.4, 126.6, 125.1, 123.9, 89.6, 81.0, 62.6, 62.3, 40.8, 21.1, 13.1; IR (KBr, cm⁻¹) 1756, 1733, 1240, 1158, 763, 731; Anal. Calcd for C22H19IO4: C, 55.71; H, 4.04. Found: C, 55.90; H, 3.99.

2l: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 82.4 mg (61%) of the indicated compound as a solid: mp 115-117 °C; 1H NMR (300 MHz, CDCl3) δ 8.46-8.44 (m, 1H), 7.48-7.32 (m, 4H), 6.44-6.36 (m, 2H), 6.22 (s, 1H), 3.98-3.90 (m, 1H), 3.82-3.40 (m, 3H), 1.03-0.98 (t, J = 7.2 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 167.9, 167.4, 147.1, 144.4, 144.3, 144.1, 137.0, 131.1, 126.7, 125.1, 123.9, 111.7, 110.5, 83.8, 77.8, 62.5, 62.4, 40.9, 13.5; IR (KBr, cm⁻¹) 3437, 1732, 1240, 1256, 1047, 760; Anal. Calcd for C19H15IO5: C, 50.69; H, 3.36. Found: C, 50.77; H, 3.41.

2m: The reaction mixture was chromatographed using 10:1 hexanes/EtOAc to afford 64.3 mg (52%) of the indicated compound as a solid: mp 77-78 °C; 1H NMR (300 MHz, CDCl3) δ 8.47-8.45 (m, 1H), 7.39-7.31 (m, 3H), 4.17-4.10 (q, J = 7.5 Hz, 2H), 3.59-3.47 (q, J = 16.5 Hz, 2H), 1.87 (s, 3H), 1.72 (s, 3H), 1.21-1.17 (t, J = 7.2 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 168.0, 167.3, 143.9, 139.3, 137.7, 130.4, 126.2, 124.9, 124.6, 95.1, 88.6, 62.8, 61.6, 39.8, 33.0, 26.8, 13.7; IR (KBr, cm⁻¹) 1733, 1297, 1237, 1173, 1123; Anal. Calcd for C17H17IO4: C, 49.53; H, 4.16. Found: C, 49.69; H, 4.30.

4h: This indene derivative was prepared by the following procedure. To a solution of 2h (76.8 mg, 0.20 mmol) and 1-ethynyl-4-nitrobenzene (35.3 g, 0.24 mmol) in Et3N (2.0 mL) was added PdCl2(PPh3)2 (2.8 mg, 2 mol %). The mixture was stirred for 5 min and CuI (0.4 mg, 1 mol %) was added. The resulting mixture was then stirred under an argon atmosphere at 55 °C for 6 h. The ammonium salt was removed by filtration, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to afford 4h 66.1 mg (82%) as a solid: mp 138-140 °C; 1H NMR (300 MHz, CDCl3) δ 8.29-8.24 (m, 2H), 8.15-8.12 (d, J = 7.5 Hz, 1H), 7.71-7.67 (m, 2H), 7.43-7.36 (m, 3H), 5.38-4.97 (m, 2H), 4.28-4.17 (m, 2H), 3.76-3.60 (q, J = 16.8, 2H), 1.30-1.24 (m, 3H); 13C NMR (75 MHz, CDCl3) δ 168.4, 167.1, 147.4, 146.0, 145.0, 135.5, 132.2, 131.2, 129.0, 127.5, 125.2, 124.1, 123.8, 108.1, 96.4, 88.9, 70.7, 63.1, 60.7, 39.0, 13.9; IR (KBr, cm⁻¹) 1757, 1734, 1592, 1518, 1433, 1343, 1518, 1343, 1232, 1159, 855, 754, 731; Anal. Calcd for C23H17NO6: C, 68.48; H, 4.25; N, 3.47. Found: C, 68.68; H, 4.16; N, 3.44.
CO₂Et
Ph
1b
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\begin{align*}
\text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{OH} & \\
\text{i} & 
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2a
2a
4h