Hypervalent Iodine-Mediated Regioselective Cyclization of Acetylenic Malonates: Facile Synthesis of 1-Diiodomethylene Indane and Cyclopentane Derivatives

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Supporting Information

1. General experimental methods (S2)
2. General experimental procedure and characterization data. (S2-S7)
3. The NOE spectrum of compound 2a (S8)
4. Copies of $^1$H, $^{13}$C NMR spectra of products (S9-S40)
General experimental methods:

All reactions were performed in Schlenk tubes under nitrogen atmosphere. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63 µm, standard grade). Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr (house vacuum) at 25–35 °C. Commercial reagents and solvents were used as received. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale.

General Experimental procedure:

The mixture of acetylenic malonate (0.2 mmol) with Bu₄NI (221 mg, 0.6 mmol) in CF₃CH₂OH (2 mL) was treated with PhIO (132 mg, 0.6 mmol) at 25 °C, and the reaction mixture was allowed to stir at 25 °C for 24 hr. Upon completion by TLC, the reaction was quenched with saturated Na₂S₂O₃, and extracted by ethyl acetate (50 mL x 3). The organic layer was dried over anhydrous Na₂SO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (15% ethyl acetate in hexanes) to give the corresponding product 4.

Diethyl 1-(diiodomethylene)-1H-indene-2,2(3H)-dicarboxylate 4a:
colorless solid; m.p. 143-145 °C; ¹HNMR (400 MHz, CDCl₃): δ 8.64 (d, J = 7.6 Hz, 1 H), 7.21-7.33 (m, 3 H), 4.23-4.31 (m, 4 H), 3.64 (s, 2 H), 1.32 (t, J = 7.2 Hz, 6 H); ¹³C NMR (100 MHz, CDCl₃): δ 168.6, 151.0, 144.7, 139.3, 130.2, 126.6, 126.4, 125.1, 71.8, 62.7, 42.3, 14.2, 2.4; IR (KBr) 2981, 2927, 1736, 1716, 1458, 1438 cm⁻¹; HRMS m/z calcd for C₁₆H₁₆I₂NaO₄ ([M+Na⁺): 548.9036, found 548.9025.
Diethyl 1-(diiodomethylene)-5-methyl-1H-indene-2,2(3H)-dicarboxylate 4b: colorless solid; m.p. 147-149 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.50 (d, $J = 8.4$ Hz, 1 H), 7.08 (d, $J = 8.4$ Hz, 1 H), 7.03 (s, 1 H), 4.21-4.30 (m, 4 H), 3.59 (s, 2 H), 2.31 (s, 3 H), 1.31 (t, $J$ = 7.2 Hz, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.6, 150.9, 144.8, 140.6, 136.7, 127.2, 126.2, 125.4, 71.7, 62.5, 42.0, 21.6, 14.0, 0.7; IR (KBr) 2980, 2921, 1734, 1720, 1610, 1443 cm$^{-1}$; HRMS m/z calcd for C$_{17}$H$_{18}$I$_2$NaO$_4$ ([M+Na]$^+$): 562.9192, found 562.9154.

Diethyl 1-(diiodomethylene)-6-methoxy-1H-indene-2,2(3H)-dicarboxylate 4c: yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.20 (s, 1 H), 7.11 (d, $J = 8.4$ Hz, 1 H), 6.92 (d, $J = 8.4$ Hz, 1 H), 4.23-4.31 (m, 4 H), 3.82 (s, 3 H), 3.57 (s, 2 H), 1.32 (t, $J = 7.2$ Hz, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.7, 158.4, 151.1, 140.4, 137.1, 125.7, 117.3, 111.3, 72.5, 62.8, 55.9, 41.8, 14.3, 2.4; IR (KBr) 2926, 2853, 1735, 1605, 1481, 1463 cm$^{-1}$; HRMS m/z calcd for C$_{17}$H$_{18}$I$_2$NaO$_5$ ([M+Na]$^+$): 578.9141, found 578.9101.

Diethyl 1-(diiodomethylene)-5,6-dimethoxy-1H-indene-2,2(3H)-dicarboxylate 4d: yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.19 (s, 1 H), 6.69 (s, 1 H), 4.22-4.32 (m, 4 H), 3.90 (s, 3 H), 3.89 (s, 3 H), 3.57 (s, 2 H), 1.33 (t, $J = 7.2$ Hz, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.7, 151.1, 150.7, 147.4, 138.4, 131.5, 109.1, 106.7, 71.7, 62.6, 56.2, 56.1, 41.9, 14.0, -2.1; IR (KBr) 2930, 2854, 1735, 1604, 1502, 1465 cm$^{-1}$; HRMS m/z calcd for C$_{18}$H$_{20}$I$_2$NaO$_6$ ([M+Na]$^+$): 608.9247, found 608.9223.
Diethyl 5-chloro-1-(diiodomethylene)-1H-indene-2,2(3H)-dicarboxylate 4e: colorless solid; m.p. 122-124 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.56 (d, \(J = 8.8\) Hz, 1 H), 7.20-7.26 (m, 2 H), 4.22-4.32 (m, 4 H), 3.60 (s, 2 H), 1.32 (t, \(J = 7.2\) Hz, 6 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.4, 150.0, 146.4, 137.9, 135.9, 127.6, 126.8, 125.2, 71.8, 62.9, 41.7, 14.2, 3.4; IR (KBr) 2979, 2925, 1718, 1593, 1463, 1366 cm\(^{-1}\); HRMS m/z calcd for C\(_{16}\)H\(_{15}\)Cl\(_2\)NaO\(_4\) ([M+Na\(^+\)]: 582.8646, found 582.8620.

Diethyl 1-(diiodomethylene)-5-fluoro-1H-indene-2,2(3H)-dicarboxylate 4f: colorless solid; m.p. 105-107 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.61 (dd, \(J = 8.8, 5.2\) Hz, 1 H), 6.98 (td, \(J = 8.8, 2.4\) Hz, 1 H), 6.91 (d, \(J = 8.0\) Hz, 1 H), 4.21-4.35 (m, 4 H), 3.61 (s, 2 H), 1.33 (t, \(J = 7.2\) Hz, 6 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.3, 164.8, 162.3, 149.7, 147.3, 147.2, 135.3, 128.3, 128.2, 113.8, 113.6, 112.0, 111.7, 71.8, 62.7, 41.6, 14.0, 1.6; IR (KBr) 2981, 2925, 1736, 1605, 1479, 1439, 1366 cm\(^{-1}\); HRMS m/z calcd for C\(_{16}\)H\(_{15}\)F\(_2\)NaO\(_4\) ([M+Na\(^+\)]: 566.8941, found 566.8901.

Diethyl 1-(diiodomethylene)-6-fluoro-1H-indene-2,2(3H)-dicarboxylate 4g: pale yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.37 (d, \(J = 11.2\) Hz, 1 H), 7.16 (t, \(J = 6.0\) Hz, 1 H), 7.05 (t, \(J = 8.4\) Hz, 1 H), 4.19-4.35 (m, 4 H), 3.59 (s, 2 H), 1.32 (t, \(J = 7.2\) Hz, 6 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.2, 162.4, 160.0, 150.0, 140.9, 140.8, 140.0, 125.9, 125.8, 117.3,
117.1, 113.5, 113.2, 72.2, 62.7, 41.5, 14.0, 4.4; IR (KBr) 2979, 2927, 2854, 1731, 1610, 1588, 1477, 1439 cm\(^{-1}\); HRMS m/z calcd for C\(_{16}\)H\(_{15}\)F\(_2\)NaO\(_4\) ([M+Na]\(^+\)): 566.8941, found 566.8903.

Dimethyl 1-(diiodomethylene)-1H-indene-2,2(3H)-dicarboxylate 4h: colorless solid; 155-157 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.64 (d, \(J = 8.0\) Hz, 1 H), 7.21-7.34 (m, 2 H), 7.22 (d, \(J = 7.2\) Hz, 1 H), 3.80 (s, 6 H), 3.65 (s, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 169.2, 151.0, 144.6, 139.2, 130.4, 126.6, 126.5, 125.2, 71.8, 53.7, 42.4, 2.7; IR (KBr) 3054, 2987, 1735, 1433, 1265 cm\(^{-1}\); HRMS m/z calcd for C\(_{14}\)H\(_{12}\)I\(_2\)NaO\(_4\) ([M+Na]\(^+\)): 520.8723, found 520.8705.

Dibenzyl 1-(diiodomethylene)-1H-indene-2,2(3H)-dicarboxylate 4i: pale yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.62 (d, \(J = 7.6\) Hz, 1 H), 7.15-7.37 (m, 14 H), 5.22 (s, 4 H), 3.63 (s, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.2, 150.9, 144.5, 139.2, 135.1, 130.2, 128.6, 128.4, 128.3, 126.4, 125.0, 71.8, 68.1, 42.3, 2.6; IR (KBr) 3064, 3032, 2960, 2926, 1735, 1497, 1456 cm\(^{-1}\); HRMS m/z calcd for C\(_{26}\)H\(_{20}\)I\(_2\)NaO\(_4\) ([M+Na]\(^+\)): 672.9349, found 672.9349.

Diethyl 2-(diiodomethylene)cyclopentane-1,1-dicarboxylate 4l: pale yellow oil; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 4.20-4.37 (m, 4 H), 2.62 (t, \(J = 7.2\) Hz, 2 H), 2.53 (t, \(J = 7.2\) Hz, 2 H), 1.78-1.84 (m, 2 H), 1.33 (t, \(J = 7.2\) Hz, 6 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 168.4, 155.9, 68.3, 62.2, 44.4, 41.2, 24.1, 14.1, 8.4; IR (KBr) 2978, 1728, 1444, 1366, 1261 cm\(^{-1}\); HRMS m/z calcd for C\(_{12}\)H\(_{10}\)I\(_2\)NaO\(_4\) ([M+Na]\(^+\)): 500.9036, found 500.9009.
Dimethyl 2-(diiodomethylene)cyclopentane-1,1-dicarboxylate 4m: pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 3.80 (s, 6 H), 2.63 (t, $J$ = 6.8 Hz, 2 H), 2.53 (t, $J$ = 7.2 Hz, 2 H), 1.77-1.85 (m, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.0, 155.8, 68.2, 53.2, 44.3, 41.3, 24.2, 8.7; IR (KBr) 2919, 2850, 1735, 1432, 1264 cm$^{-1}$; HRMS m/z calcd for C$_{10}$H$_{12}$I$_2$NaO$_4$ ([M+Na]$^+$): 472.8723, found 472.8767.

Dibenzyl 2-(diiodomethylene)cyclopentane-1,1-dicarboxylate 4n: pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.20-7.40 (m, 10 H), 5.21 (s, 4 H), 2.63 (t, $J$ = 6.4 Hz, 2 H), 2.51 (t, $J$ = 7.2 Hz, 2 H), 1.70-1.80 (m, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.1, 155.9, 135.3, 128.6, 128.4, 128.1, 68.3, 67.9, 44.3, 41.5, 24.2, 8.8; IR (KBr) 2919, 2844, 1728, 1453, 1261 cm$^{-1}$; HRMS m/z calcd for C$_{22}$H$_{20}$I$_2$NaO$_4$ ([M+Na]$^+$): 624.9349, found 624.9377.

Diethyl 1-(diiodomethylene)-5-fluoro-1H-indene-2,2(3H)-dicarboxylate 2a:
pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.61 (d, $J$ = 7.2 Hz, 1 H), 7.26-7.36 (m, 3 H), 6.86 (s, 1 H), 4.22 (q, $J$ = 7.2 Hz, 4 H), 3.66 (s, 2 H), 1.26 (t, $J$ = 7.2 Hz, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.5, 144.8, 144.6, 138.0, 130.1, 126.4, 124.9, 124.8, 73.6, 67.1, 62.3, 39.8, 14.1; IR (KBr) 2980, 2930, 1734, 1471, 1366, 1247 cm$^{-1}$; HRMS m/z calcd for C$_{16}$H$_{17}$INaO$_4$ ([M+Na]$^+$): 423.0069, found 423.0035.
Diethyl 2-(2-(iodoethynyl)benzylidene)malonate 7: pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.16 (s, 1 H), 7.45-7.49 (m, 2 H), 7.27-7.32 (m, 2 H), 4.26-4.35 (m, 4 H), 1.36 (t, $J$ = 7.2 Hz, 3 H), 1.23 (t, $J$ = 7.2 Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.3, 164.0, 140.3, 136.0, 133.5, 129.9, 128.8, 128.0, 127.7, 124.6, 91.7, 61.8, 14.2, 13.9, 13.8; IR (KBr) 2984, 2928, 1725, 1705, 1625, 1467, 1445, 1374 cm$^{-1}$; HRMS m/z calcd for C$_{16}$H$_{15}$INaO$_4$ ([M+Na]$^+$): 420.9913, found 420.9955.

Diethyl 2-(2-(iodoethynyl)phenyl)malonate 9: pale yellow oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.42-7.47 (m, 2 H), 7.35 (t, $J$ = 7.6 Hz, 1 H), 7.25-7.29 (m, 1 H), 5.22 (s, 1 H), 4.22 (q, $J$ = 7.2 Hz, 4 H), 1.28 (t, $J$ = 7.0 Hz, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.0, 135.9, 133.0, 129.2, 128.7, 127.9, 123.9, 91.9, 62.0, 55.8, 14.2, 11.8; IR (KBr) 2979, 2926, 1735, 1488, 1467, 1445, 1367 cm$^{-1}$; HRMS m/z calcd for C$_{15}$H$_{15}$INaO$_4$ ([M+Na]$^+$): 408.9913, found 408.9877.

Diethyl 1-(1,5-bis(trimethylsilyl)penta-1,4-diyn-3-ylidene)-1H-indene-2,2(3H)-dicarboxylate 10: pale yellow oil; $^1$HNMR (400 MHz, CDCl$_3$): $\delta$ 8.64 (d, $J$ = 11.2 Hz, 1 H), 7.20-7.32 (m, 3 H), 4.20 (q, $J$ = 6.8 Hz, 4 H), 3.65 (s, 2 H), 1.27 (t, $J$ = 6.8 Hz, 6 H), 0.30 (s, 9 H), 0.22 (s, 9 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.1, 153.9, 144.6, 138.1, 130.4, 126.9, 125.9, 124.6, 102.5, 101.8, 101.2, 100.4, 66.0, 62.0, 41.8, 14.1, -0.2; HRMS m/z calcd for C$_{26}$H$_{34}$NaO$_4$Si$_2$ ([M+Na]$^+$): 489.1893, found 489.1915.
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