Synthesis of Isocoumarins and α -Pyrones via Electrophilic Cyclization

Tuanli Yao and Richard C. Larock*

Department of Chemistry, Iowa State University, Ames, Iowa 50011

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General. The ^1H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates, and visualization was effected with short wavelength UV light (254 nm). All melting points are uncorrected. All reagents were used directly as obtained commercially unless otherwise noted. The following starting materials were made according to literature procedures: methyl 4,5-dimethoxy-2-iodobenzoate,¹ *tert*-butyl 2-iodobenzoate,¹ methyl (Z)-3-iodo-2-propenoate,¹ methyl 2-trifluoromethanesulfonyloxy-1-cyclohexenecarboxylate,² ethyl 2-trifluoromethanesulfonyloxy-1-cyclopentenecarboxylate,³ ethyl (Z)-3-iodo-3-phenyl-2-propenoate,¹ methyl (Z)-3-iodo-2-methyl-3-phenyl-2-propenoate,¹ methyl (Z)-3-iodo-2,3-diphenyl-2-propenoate,¹ ethyl 3-iodoindole-2-carboxylate,³ methyl 2-ethynylbenzoate,⁴ and dimethyl 2,2'-(1,3-butadiyne-1,4-diyl)bisbenzoate.⁴

General procedure for preparation of the ester alkynes. To a solution of the corresponding aryl or vinylic iodide or triflate (1.0 mmol) and the terminal alkyne (1.2 mmol, 1.2 equiv) in Et_3N (4 mL) were added $\text{PdCl}_2(\text{PPh}_3)_2$ (1.4 mg, 2 mol %) and CuI (2.0 mg, 1 mol %). The resulting mixture was heated under an N_2 atm at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding ester alkyne.

Methyl 2-(phenylethynyl)benzoate (1). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 235 mg (99%) of the product as a yellow liquid with spectral properties identical to those previously reported.⁵

Methyl 2-(1-octynyl)benzoate (6). Purification by flash chromatography (15:1 hexane/EtOAc) afforded 168.4 mg (69%) of the product as a clear liquid: ¹H NMR (CDCl₃) δ 0.88-0.93 (m, 3H), 1.30-1.34 (m, 4H), 1.47-1.50 (m, 2H), 1.58-1.66 (m, 1H), 2.47 (t, *J* = 6.9 Hz, 2H), 3.91 (s, 3H), 7.30 (dt, *J* = 1.5, 7.8 Hz, 1H), 7.41 (dt, *J* = 1.5, 7.5 Hz, 1H), 7.51 (dd, *J* = 1.2, 7.8 Hz, 1H), 7.88 (dd, *J* = 1.2, 7.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.3, 16.6, 20.0, 22.8, 28.8, 28.9, 31.6, 52.2, 79.4, 96.2, 124.7, 127.3, 130.3, 131.7, 132.1, 134.4, 167.2; IR (neat, cm⁻¹) 2953, 2933, 2857, 1734, 1717; HRMS Calcd for C₁₆H₂₀O₂: 244.1463. Found: 244.1467.

Methyl 2-(1-cyclohexenylethynyl)benzoate (8). Purification by flash chromatography (20:1 hexane/EtOAc) afforded 221.7 mg (92%) of the product as a clear liquid with spectral properties identical to those previously reported.⁶

Methyl 2-(5-hydroxy-1-pentynyl)benzoate (11). Purification by flash chromatography (1:1.5 hexane/EtOAc) afforded 186.1 mg (85%) of the product as a clear liquid with spectral properties identical to those previously reported:⁹ ¹³C NMR (CDCl₃) δ 16.7, 31.2, 52.4, 61.7, 80.0, 95.4, 124.5, 127.5, 130.4, 131.8, 131.9, 134.3, 167.1.

Methyl 2-[tris(1-methylethyl)silylethynyl]benzoate (15). Purification by flash chromatography (20:1 hexane/EtOAc) afforded 307.9 mg (97%) of the product as a light yellow liquid: ¹H NMR (CDCl₃) δ 1.14 (d, *J* = 4.5 Hz, 21H), 3.91 (s, 3H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 6.6 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 11.5, 18.3, 52.3, 96.5, 105.3, 123.6, 128.2, 130.3, 131.5, 132.8, 135.1,

167.3; IR (neat, cm^{-1}) 2944, 2865, 1736, 1720; HRMS Calcd for $\text{C}_{19}\text{H}_{28}\text{O}_2\text{Si}$:

316.1858. Found: 316.1864.

Methyl 4,5-dimethoxy-2-(phenylethynyl)benzoate (17). Purification by flash chromatography (6:1 hexane/EtOAc) afforded 151 mg (51%) of the product as a white solid: mp 115-117 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 3.95 and 3.96 (9H), 7.08 (s, 1H), 7.34-7.36 (m, 3H), 7.51 (s, 1H), 7.56-7.59 (m, 2H); ^{13}C NMR (CDCl_3) δ 52.3, 56.3, 56.4, 88.8, 93.2, 113.1, 115.9, 117.7, 123.7, 124.7, 128.5, 128.6, 131.8, 148.8, 151.8, 166.5; IR (neat, cm^{-1}) 2950, 2850, 1724, 1701; HRMS Calcd for $\text{C}_{18}\text{H}_{16}\text{O}_4$: 296.1048. Found: 296.1054.

Dimethyl (phenylethynyl)terephthalate (19). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 265 mg (90%) of the product as a white solid: mp 91-93 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 3.96 (s, 3H), 3.99 (s, 3H), 7.35-7.39 (m, 3H), 7.55-7.61 (m, 2H), 8.01-8.02 (m, 2H), 8.30 (t, $J = 1.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 52.71, 52.81, 87.6, 95.5, 123.2, 124.3, 128.6, 128.8, 129.1, 130.8, 132.0, 133.2, 135.2, 135.6, 165.9, 166.3; IR (neat, cm^{-1}) 1727; HRMS Calcd for $\text{C}_{18}\text{H}_{14}\text{O}_4$: 294.0892. Found: 294.0900.

***tert*-Butyl 2-(phenylethynyl)benzoate (22).** Purification by flash chromatography (30:1 hexane/EtOAc) afforded 272.1 mg (98%) of the product as a light yellow liquid: ^1H NMR (CDCl_3) δ 1.62 (s, 12H), 7.34-7.39 (m, 4H), 7.45 (t, $J = 7.5$ Hz, 1H), 7.55-7.58 (m, 2H), 7.62 (d, $J = 7.5$ Hz, 1H), 7.88 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 28.4, 81.9, 88.7, 93.9, 123.20, 123.21, 123.7, 128.1, 128.6, 130.2, 131.2, 131.8, 134.1, 134.3, 166.1; IR (neat, cm^{-1}) 3062, 2979, 2931, 1706; HRMS Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_2$: 278.1306. Found: 278.1309.

Methyl (Z)-5-phenyl-2-penten-4-ynoate (23). Purification by flash chromatography (15:1 hexane/EtOAc) afforded 165 mg (89%) of the product as a yellow liquid with spectral properties identical to those previously reported:⁵ ¹³C NMR (CDCl₃) δ 51.7, 86.5, 101.6, 122.8, 123.4, 127.9, 128.6, 129.4, 132.3, 165.4.

Methyl (Z)-2-nonen-4-ynoate (27). Purification by flash chromatography (15:1 hexane/EtOAc) afforded 134.5 mg (81%) of the product as a yellow liquid with spectral properties identical to those previously reported:⁵ ¹³C NMR (CDCl₃) δ 13.8, 19.9, 22.1, 30.6, 51.5, 77.8, 104.6, 124.5, 127.1, 165.5.

Ethyl (Z)-2-methyl-5-phenyl-2-penten-4-ynoate (29). Purification by flash chromatography (15:1 hexane/EtOAc) afforded 207 mg (97%) of the product as a yellow liquid: ¹H NMR (CDCl₃) δ 1.30 (t, *J* = 7.2 Hz, 3H), 2.13 (d, *J* = 1.2 Hz, 3H), 4.23 (q, *J* = 7.2 Hz, 2H), 6.03 (d, *J* = 1.8 Hz, 1H), 7.32-7.36 (m, 3H), 7.50-7.56 (m, 2H); ¹³C NMR (CDCl₃) δ 14.6, 25.5, 60.3, 88.6, 100.4, 123.0, 124.6, 128.6, 129.4, 132.2, 134.8, 165.3; IR (neat, cm⁻¹) 1721; HRMS Calcd for C₁₄H₁₄O₂: 214.0994. Found: 214.0998.

Ethyl (Z)-3,5-biphenyl-2-penten-4-ynoate (31). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 241 mg (92%) of the product as a yellow liquid: ¹H NMR (CDCl₃) δ 1.36 (t, *J* = 7.2 Hz, 3H), 4.31 (q, *J* = 7.2 Hz, 2H), 6.60 (s, 1H), 7.35-7.45 (m, 6H), 7.62-7.65 (m, 2H), 7.78-7.82 (m, 2H); ¹³C NMR (CDCl₃) δ 14.6, 60.6, 87.1, 102.3, 122.9, 123.0, 127.4, 128.6, 128.9, 129.5, 130.1, 132.3, 136.6, 137.4, 165.6; IR (neat, cm⁻¹) 1717; HRMS Calcd for C₁₉H₁₆O₂: 276.1150. Found: 276.1157.

Methyl (Z)-2-methyl-3,5-biphenyl-2-penten-4-ynoate (33). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 256 mg (93%) of the product as a yellow liquid: ¹H NMR (CDCl₃) δ 2.02 (s, 3H), 3.89 (s, 3H), 7.28-7.49 (m, 10H); ¹³C NMR

(CDCl₃) δ 17.5, 52.2, 89.8, 97.7, 123.5, 128.3, 128.5, 128.6, 128.8, 128.9, 130.0, 131.9, 134.6, 138.8, 169.0; IR (neat, cm⁻¹) 1707, 1720; HRMS Calcd for C₁₉H₁₆O₂: 276.1150. Found: 276.1157.

Methyl (Z)-2,3,5-triphenyl-2-penten-4-ynoate (36). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 249 mg (74%) of the product as a yellow liquid: ¹H NMR (CDCl₃) δ 3.90 (s, 3H), 7.13-7.23 (m, 8H), 7.26-7.38 (m, 5H), 7.48-7.54 (m, 2H); ¹³C NMR (CDCl₃) δ 52.7, 89.5, 97.8, 123.1, 128.0, 128.2, 128.28, 128.34, 128.4, 128.6, 129.1, 129.9, 130.0, 132.0, 135.5, 137.4, 139.6, 169.1; IR (neat, cm⁻¹) 1724; HRMS Calcd for C₂₄H₁₈O₂: 338.1307. Found: 338.1312.

Ethyl 2-(phenylethynyl)cyclohex-1-enecarboxylate (41). Purification by flash chromatography (15:1 hexane/EtOAc) afforded 252 mg (99%) of the product as a yellow liquid: ¹H NMR (CDCl₃) δ 1.29-1.34 (m, 3H), 1.66 (d, *J* = 2.7 Hz, 4H), 2.42 (d, *J* = 2.7 Hz, 4H), 4.20-4.29 (m, 2H), 7.29-7.36 (m, 3H), 7.44-7.47 (m, 2H); ¹³C NMR (CDCl₃) δ 14.6, 21.9, 22.1, 26.6, 32.6, 60.7, 89.7, 96.3, 123.7, 128.3, 128.5, 128.6, 131.8, 134.7, 167.7; IR (neat, cm⁻¹) 1698; HRMS Calcd for C₁₇H₁₈O₂: 254.1307. Found: 254.1310.

Ethyl 2-(phenylethynyl)cyclopent-1-enecarboxylate (44). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 238 mg (99%) of the product as a white solid: mp 69-71 °C; ¹H NMR (CDCl₃) δ 1.34 (t, *J* = 7.2 Hz, 3H), 1.96 (quintet, *J* = 7.5 Hz, 2H), 2.75 (t, *J* = 7.5 Hz, 4H), 4.26 (q, *J* = 7.2 Hz, 2H), 7.31-7.36 (m, 3H), 7.49-7.52 (m, 2H); ¹³C NMR (CDCl₃) δ 14.6, 22.5, 33.6, 39.6, 60.6, 86.0, 99.7, 123.3, 128.6, 129.0, 132.0, 134.4, 138.4, 164.9; IR (neat, cm⁻¹) 1687; HRMS Calcd for C₁₆H₁₆O₂: 240.1150. Found: 240.1156.

Ethyl 1-methyl-3-(phenylethynyl)indole-2-carboxylate (46). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 300 mg (99%) of the product as a white solid: mp 85-86 °C; ¹H NMR (CDCl₃) δ 1.50 (t, *J* = 7.2 Hz, 3H), 4.09 (s, 3H), 4.48 (q, *J* = 7.2 Hz, 2H), 7.21-7.45 (m, 6H), 7.56-7.63 (m, 2H), 7.90 (d, *J* = 8.1 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.7, 32.5, 61.3, 83.2, 95.6, 105.0, 110.6, 121.6, 121.9, 124.4, 126.1, 128.2, 128.3, 128.6, 129.2, 131.6, 138.6, 162.0; IR (neat, cm⁻¹) 1703; HRMS Calcd for C₂₀H₁₇O₂N: 303.1259. Found: 303.1265.

General procedure for the electrophilic cyclization of ester alkynes by ICl. The ester alkyne (0.30 mmol) in 3 ml of CH₂Cl₂ was placed in a 4 dram vial and flushed with N₂. The ICl (1.2 equiv) in 0.5 ml of CH₂Cl₂ was added dropwise to the vial by a syringe. The reaction was stirred at room temperature for 30 min unless otherwise indicated. The reaction mixture was then diluted with 50 ml of ether, washed with 25 ml of satd aq Na₂S₂O₃, dried (MgSO₄) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

4-Iodo-3-phenylisocoumarin (2). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 94.6 mg (90%) of the product as a white solid with spectral properties identical to those previously reported⁷: mp 137-138 °C (lit.⁷ mp 136-138 °C).

3-*n*-Hexyl-4-iodoisocoumarin (7). Purification by flash chromatography (15:1 hexane/EtOAc) afforded 91.1 mg (85%) of the product as a clear liquid: ¹H NMR (CDCl₃) δ 0.87-0.91 (m, 3H), 1.29-1.44 (m, 7H), 1.71-1.76 (m, 2H), 2.91 (t, *J* = 7.8 Hz, 2H), 7.47-7.53 (m, 1H), 7.71-7.76 (m, 2H), 8.22 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.2, 16.6, 22.7, 27.4, 29.0, 31.7, 37.5, 76.3, 120.1, 128.7, 129.8, 130.6, 135.8, 138.2,

158.4, 162.1; IR (neat, cm^{-1}) 2955, 2929, 2858, 1736; HRMS Calcd for $\text{C}_{15}\text{H}_{17}\text{O}_2\text{I}$:

356.0273. Found: 356.0277.

3-(1-Cyclohexenyl)-4-iodoisocoumarin (9). Purification by flash chromatography (20:1 hexane/EtOAc) afforded 103.1 mg (98%) of the product as a white solid: mp 87-88 °C; ^1H NMR (CDCl_3) δ 1.67-1.80 (m, 4H), 2.21-2.35 (m, 4H), 6.15-6.17 (m, 1H), 7.51 (t, $J = 8.1$ Hz, 1H), 7.76-7.82 (m, 2H), 8.24 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 21.7, 22.4, 25.2, 26.6, 75.2, 120.4, 128.9, 129.8, 131.5, 134.1, 135.2, 135.7, 138.5, 157.4, 162.1; IR (neat, cm^{-1}) 2932, 1735; HRMS Calcd for $\text{C}_{15}\text{H}_{13}\text{O}_2\text{I}$: 351.9960. Found: 351.9966.

3-(3-Hydroxy-1-propyl)-4-iodoisocoumarin (12). Purification by flash chromatography (1:1 hexane/EtOAc) afforded 50.1 mg (51%) of the product as a white solid: mp 86-88 °C; ^1H NMR (CDCl_3) δ 1.78 (s, 1H), 1.98-2.03 (m, 2H), 3.05 (t, $J = 8.1$ Hz, 2H), 3.76 (t, $J = 6.3$ Hz, 2H), 7.48-7.54 (m, 1H), 7.73-7.77 (m, 2H), 8.20 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 30.3, 34.1, 61.9, 120.1, 128.9, 129.9, 130.6, 135.9, 138.0, 145.3, 157.6, 162.0; IR (neat, cm^{-1}) 3428, 2933, 2877, 1734; HRMS Calcd for $\text{C}_{12}\text{H}_{11}\text{O}_3\text{I}$: 329.9753. Found: 329.9756.

(3E)-3-(Iodomethylene)-2-benzofuran-1(3H)-one (14). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 51 mg (63%) of the product as a white solid: mp 80-82 °C; ^1H NMR (CDCl_3) δ 6.56 (s, 1H), 7.67 (t, $J = 7.5$ Hz, 1H), 7.80 (t, $J = 7.8$ Hz, 1H), 7.95 (d, $J = 7.8$ Hz, 1H), 8.71 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 57.9, 124.4, 126.1, 126.7, 131.4, 134.7, 138.0, 149.2, 165.8; IR (neat, cm^{-1}) 1777; HRMS Calcd for $\text{C}_9\text{H}_5\text{O}_2\text{I}$: 271.9334. Found: 271.9341.

(3E)-3-[Iodo(triisopropylsilyl)methylene]-2-benzofuran-1(3H)-one (16).

Purification by flash chromatography (20:1 hexane/EtOAc) afforded 123.6 mg (96%) of the product as a white solid: mp 117-120 °C; ¹H NMR (CDCl₃) δ 1.17 (d, *J* = 7.5 Hz, 18H), 1.64-1.74 (m, 3H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.79 (t, *J* = 7.2 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 1H), 9.18 (d, *J* = 8.1 Hz, 1H); ¹³C NMR (CDCl₃) δ 13.6, 18.9, 84.8, 125.8, 126.5, 127.1, 131.1, 134.3, 139.2, 153.1, 165.9; IR (neat, cm⁻¹) 2946, 2866, 1784; HRMS Calcd for C₁₈H₂₅O₂ISi: 428.0668. Found: 428.0676.

4-Iodo-6,7-dimethoxy-3-phenylisocoumarin (18). Purification by flash

chromatography (2:1 hexane/EtOAc) afforded 124.2 mg (100%) of the product as a white solid: mp 178-179 °C; ¹H NMR (CDCl₃) δ 4.01 (s, 3H), 4.07 (s, 3H), 7.30 (s, 1H), 7.45-7.47 (m, 3H), 7.67-7.70 (m, 3H); ¹³C NMR (CDCl₃) δ 56.6, 56.8, 76.4, 109.7, 113.1, 113.2, 128.2, 130.2, 130.3, 134.1, 135.5, 150.5, 154.1, 155.8, 161.7; IR (neat, cm⁻¹) 2963, 1733; HRMS Calcd for C₁₇H₁₃O₄I: 407.9858. Found: 407.9865. Anal. Calcd for C₁₇H₁₃O₄I: C, 50.00; H, 3.21. Found: C, 50.12; H, 2.79.

Methyl 4-iodo-3-phenyl-6-isocoumarincarboxylate (20). Purification by flash

chromatography (4:1 hexane/EtOAc) afforded 107 mg (88%) of the product as a white solid: mp 164-166 °C; ¹H NMR (CDCl₃) δ 4.03 (s, 3H), 7.48-7.50 (m, 3H), 7.69-7.72 (m, 2H), 8.18 (d, *J* = 8.1 Hz, 1H), 8.38 (d, *J* = 8.1 Hz, 1H), 8.56 (d, *J* = 1.2 Hz, 1H); ¹³C NMR (CDCl₃) δ 53.1, 76.0, 123.4, 128.4, 129.7, 130.2, 130.4, 130.7, 133.3, 135.2, 136.8, 138.7, 155.7, 161.1, 165.7; IR (neat, cm⁻¹) 1727; HRMS Calcd for C₁₇H₁₁O₄I: 405.9702. Found: 405.9710. Anal. Calcd for C₁₇H₁₁O₄I: C, 50.27; H, 2.73. Found: C, 50.11; H, 2.34.

5-Iodo-6-phenyl-2(2*H*)-pyranone (24). Purification by flash chromatography (6:1 hexane/EtOAc) afforded 83.6 mg (94%) of the product as a white solid with spectral properties identical to those previously reported:⁸ mp 100-101 °C (lit.⁸ mp 101-103 °C).

6-*n*-Butyl-5-iodo-2(2*H*)-pyranone (28). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 66.6 mg (80%) of the product as a clear liquid with spectral properties identical to those previously reported:⁸ ¹³C NMR (CDCl₃) δ 13.9, 22.4, 29.2, 36.6, 67.8, 114.9, 152.0, 161.6, 166.0.

5-Iodo-4,6-diphenyl-2(2*H*)-pyranone (32). Purification by flash chromatography (6:1 hexane/EtOAc) afforded 94 mg (84%) of the product as a white solid: mp 185-186 °C; ¹H NMR (CDCl₃) δ 6.30 (s, 1H), 7.20-7.39 (m, 2H), 7.42-7.51 (m, 6H), 7.69-7.78 (m, 2H); ¹³C NMR (CDCl₃) δ 113.2, 128.3, 128.4, 128.5, 129.7, 129.9, 130.9, 135.1, 140.5, 161.3, 161.4, 162.0; IR (neat, cm⁻¹) 1709; HRMS Calcd for C₁₇H₁₁O₂I: 373.9804. Found: 373.9812.

5-Iodo-3,4,6-triphenyl-2(2*H*)-pyranone (37). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 23 mg (17%) of the product as a yellow solid: mp 180-182 °C; ¹H NMR (CDCl₃) δ 7.04-7.18 (m, 7H), 7.23-7.28 (m, 3H), 7.46-7.51 (m, 3H), 7.76-7.81 (m, 2H); ¹³C NMR (CDCl₃) δ 125.7, 127.97, 127.99, 128.1, 128.4, 128.6, 129.1, 130.1, 130.5, 130.8, 134.1, 135.2, 140.7, 157.1, 160.1, 161.8; IR (neat, cm⁻¹) 1718; HRMS Calcd for C₂₃H₁₅O₂I: 450.0117. Found: 450.0124.

(5*E*)-5-[Iodo(phenyl)methylene]-3,4-diphenylfuran-2(5*H*)-one (38). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 74 mg (55%) of the product as a yellow solid: mp 138-140 °C; ¹H NMR (CDCl₃) δ 7.22-7.27 (m, 3H), 7.28-7.33 (m, 1H), 7.33-7.42 (m, 6H), 7.45-7.53 (m, 5H); ¹³C NMR (CDCl₃) δ 84.9, 128.2, 128.4, 129.3,

129.36, 129.4, 129.5, 129.7, 130.1, 130.2, 130.7, 132.0, 141.5, 146.2, 149.9, 167.4; IR (neat, cm^{-1}) 1764; HRMS Calcd for $\text{C}_{23}\text{H}_{15}\text{O}_2\text{I}$: 450.0117. Found: 450.0123. Anal. Calcd for $\text{C}_{23}\text{H}_{15}\text{O}_2\text{I}$: C, 61.35; H, 3.36. Found: C, 61.20; H, 2.97.

(3E)-3-[Iodo(phenyl)methylene]-4,5,6,7-tetrahydro-2-benzofuran-1(3H)-one (42).

Purification by flash chromatography (10:1 hexane/EtOAc) afforded 58 mg (55%) of the product as a pale pink solid: mp 134-135 °C; ^1H NMR (CDCl_3) δ 1.71-1.87 (m, 4H), 2.28-2.32 (m, 2H), 2.94-3.00 (m, 2H), 7.26-7.37 (m, 3H), 7.45-7.48 (m, 2H); ^{13}C NMR (CDCl_3) δ 21.0, 21.4, 22.6, 27.8, 81.0, 128.2, 129.2, 130.3, 131.8, 140.5, 148.1, 151.3, 168.5; IR (neat, cm^{-1}) 1763; HRMS Calcd for $\text{C}_{16}\text{H}_{16}\text{O}_2$: 240.1150. Found: 240.1156.

4,4'-Diiodo-1H,1H'-3,3'-biisocoumarin (49). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 147 mg (90%) of the product as a yellow solid: mp >260 °C; ^1H NMR (CDCl_3) δ 7.67-7.71 (m, 2H), 7.82-7.91 (m, 4H), 8.35 (dd, J = 0.9, 8.1 Hz, 2H); ^{13}C NMR (CDCl_3) δ 82.3, 121.5, 130.4, 131.0, 131.8, 136.2, 136.7, 148.9, 160.6; IR (neat, cm^{-1}) 1723; HRMS Calcd for $\text{C}_{18}\text{H}_8\text{O}_4\text{I}_2$: 541.8512. Found: 541.8525.

General procedure for the electrophilic cyclization of ester alkynes by I_2 . The ester alkyne (0.30 mmol), I_2 (1.2 equiv) and CH_2Cl_2 (3 ml) were placed in a 4 dram vial and flushed with N_2 . The reaction mixture was stirred at room temperature for 1 h unless otherwise indicated. The reaction mixture was then diluted with 50 ml of ether, washed with 25 ml of satd aq $\text{Na}_2\text{S}_2\text{O}_3$, dried (MgSO_4) and filtered. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

5-Iodo-3-methyl-6-phenyl-2(2H)-pyranone (30). Purification by flash chromatography (6:1 hexane/EtOAc) afforded 79 mg (84%) of the product as a white

solid: mp 116-118 °C; ^1H NMR (CDCl_3) δ 2.37 (d, $J = 0.9$ Hz, 3H), 6.26 (d, $J = 0.9$ Hz, 1H), 7.44-7.48 (m, 3H), 7.62-7.68 (m, 2H); ^{13}C NMR (CDCl_3) δ 29.2, 112.4, 128.4, 129.8, 130.8, 134.8, 158.6, 161.1, 161.3; IR (neat, cm^{-1}) 1726; HRMS Calcd for $\text{C}_{12}\text{H}_9\text{O}_2\text{I}$: 311.9647. Found: 311.9651.

5-Iodo-3-methyl-4,6-diphenyl-2(2H)-pyranone (34). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 19 mg (17%) of the product as a white solid: ^1H NMR (CDCl_3) δ 1.97 (s, 3H), 7.13-7.16 (m, 2H), 7.42-7.53 (m, 6H), 7.68-7.72 (m, 2H); IR (neat, cm^{-1}) 1721; HRMS Calcd for $\text{C}_{18}\text{H}_{13}\text{O}_2\text{I}$: 387.9960. Found: 387.9964.

(5E)-5-[Iodo(phenyl)methylene]-3-methyl-4-phenylfuran-2-(5H)-one (35). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 88 mg (76%) of the product as a yellow solid: mp 120-121 °C; ^1H NMR (CDCl_3) δ 1.83 (s, 3H), 7.23-7.38 (m, 5H), 7.44-7.55 (m, 5H); ^{13}C NMR (CDCl_3) δ 10.2, 82.9, 128.2, 129.1, 129.2, 129.5, 130.3, 131.1, 132.0, 141.0, 146.4, 151.8, 169.1; IR (neat, cm^{-1}) 1762; HRMS Calcd for $\text{C}_{18}\text{H}_{13}\text{O}_2\text{I}$: 387.9960. Found: 387.9970.

4-Iodo-3-phenyl-6,7-dihydrocyclopenta[c]pyran-1-5(H)-one (45). Purification by flash chromatography (5:1 hexane/EtOAc) afforded 86 mg (85%) of the product as a white solid: mp 134-135 °C; ^1H NMR (CDCl_3) δ 2.07-2.18 (m, 2H), 2.92-3.05 (m, 4H), 7.42-7.47 (m, 3H), 7.68-7.72 (m, 2H); ^{13}C NMR (CDCl_3) δ 21.7, 31.7, 40.7, 70.3, 125.6, 128.3, 129.8, 130.6, 134.0, 159.8, 160.6, 163.1; IR (neat, cm^{-1}) 1723; HRMS Calcd for $\text{C}_{14}\text{H}_{11}\text{O}_2\text{I}$: 337.9804. Found: 337.9808. Anal. Calcd for $\text{C}_{14}\text{H}_{11}\text{O}_2\text{I}$: C, 49.73; H, 3.28. Found: C, 49.62; H, 2.81.

4-Iodo-9-methyl-3-phenylpyrano[3,4-*b*]indol-1(9H)-one (47). 3.0 Equiv of I_2 was used. Purification by flash chromatography (2:1 hexane/ CH_2Cl_2) afforded 101 mg (84%)

of the product as a white solid: mp 241-242 °C; ^1H NMR (CDCl_3) δ 4.27 (s, 3H), 7.36 (t, J = 8.1 Hz, 1H), 7.45-7.52 (m, 4H), 7.56-7.62 (m, 1H), 7.69-7.73 (m, 2H), 8.93 (d, J = 8.4 Hz, 1H); ^{13}C NMR (CDCl_3) δ 31.6, 65.9, 77.5, 110.8, 120.9, 121.2, 122.8, 122.9, 125.9, 128.2, 128.3, 130.0, 130.5, 135.0, 141.6, 152.5, 156.8; IR (neat, cm^{-1}) 1707; HRMS Calcd for $\text{C}_{18}\text{H}_{12}\text{O}_2\text{IN}$: 400.9913. Found: 400.9919.

General procedure for the electrophilic cyclization of ester alkynes by PhSeCl or *p*-O₂NC₆H₄SCl. The ester alkyne (0.30 mmol), PhSeCl or *p*-O₂NC₆H₄SCl (1.5 equiv) and CH_2Cl_2 (3 ml) were placed in a 4 dram vial and flushed with N_2 . The reaction mixture was stirred at room temperature for 1 h unless otherwise indicated. The solvent was evaporated under reduced pressure and the product was isolated by chromatography on a silica gel column.

4-(*p*-Nitrophenyl)sulfenyl-3-phenylisocoumarin (3). Purification by flash chromatography (3:1 hexane/EtOAc) afforded 101 mg (90%) of the product as a white solid: mp 220-221 °C; ^1H NMR (CDCl_3) δ 7.20-7.26 (m, 2H), 7.38-7.47 (m, 3H), 7.57-7.68 (m, 3H), 7.71-7.84 (m, 2H), 8.10 (d, J = 8.7 Hz, 2H), 8.41 (dd, J = 7.8, 0.6 Hz, 1H); ^{13}C NMR (CDCl_3) δ 104.7, 121.1, 124.7, 125.5, 125.7, 128.4, 129.4, 129.5, 130.5, 131.0, 132.5, 136.0, 137.2, 145.9, 146.6, 161.1, 161.5; IR (neat, cm^{-1}) 1739; $^1\text{HRMS}$ Calcd for $\text{C}_{21}\text{H}_{13}\text{O}_4\text{S}$: 375.0565. Found: 375.0569.

3-(1-Cyclohexenyl)-4-(*p*-nitrophenylsulfenyl)isocoumarin (10). Purification by flash chromatography (7:1 hexane/EtOAc) afforded 79.2 mg (70%) of the product as a white solid: mp 222-224 °C; ^1H NMR (CDCl_3) δ 1.60-1.76 (m, 4H), 2.13-2.18 (m, 2H), 2.31-2.36 (m, 2H), 6.15-6.18 (m, 1H), 7.18 (dt, J = 9.0, 2.7 Hz, 2H), 7.53 (t, J = 7.3 Hz, 1H), 7.65-7.75 (m, 2H), 8.07 (dt, J = 9.0, 2.4 Hz, 2H), 8.34 (d, J = 7.5 Hz, 1H); ^{13}C NMR

(CDCl₃) δ 21.6, 22.4, 25.6, 27.2, 103.3, 120.9, 124.6, 125.4, 125.6, 129.0, 130.3, 131.2, 135.0, 135.7, 137.4, 145.7, 147.2, 161.4, 164.1; IR (neat, cm⁻¹) 1741, 1517, 1338; HRMS Calcd for C₂₁H₁₇NO₄S: 379.0878. Found: 379.0886.

5-(*p*-Nitrophenyl)sulfenyl-6-phenyl-2(2*H*)-pyranone (25). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 77.6 mg (80%) of the product as a yellow solid: mp 158-159 °C; ¹H NMR (CDCl₃) δ 6.39 (d, *J* = 9.6 Hz, 1H), 7.23-7.28 (m, 2H), 7.36-7.51 (m, 4H), 7.70-7.74 (m, 2H), 8.13-8.18 (m, 2H); ¹³C NMR (CDCl₃) δ 105.7, 115.9, 124.8, 126.5, 128.6, 129.2, 131.3, 131.7, 145.8, 146.2, 150.1, 160.3, 166.3; IR (neat, cm⁻¹) 1744, 1513, 1339; HRMS Calcd for C₁₇H₁₁NO₄S: 325.0409. Found: 325.0416.

3-Phenyl-4-(phenylselenyl)isocoumarin (4). Purification by flash chromatography (7:1 hexane/EtOAc) to afford 124 mg (95%) of the product as a white solid: mp 137-139 °C; ¹H NMR (CDCl₃) δ 7.12-7.22 (m, 5H), 7.38-7.48 (m, 3H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.65-7.74 (m, 3H), 8.05 (d, *J* = 8.1 Hz, 1H), 8.37 (dd, *J* = 8.1, 1.2 Hz, 1H); ¹³C NMR (CDCl₃) δ 105.0, 121.1, 126.7, 128.1, 128.5, 129.0, 129.1, 129.7, 129.9, 130.0, 130.4, 132.1, 134.3, 135.6, 138.7, 159.8, 162.0; IR (neat, cm⁻¹) 1739; ¹HRMS Calcd for C₂₁H₁₄O₂Se: 378.0160. Found: 378.0167.

Methyl 3-phenyl-4-phenylselenyl-6-isocoumarincarboxylate (21). Purification by flash chromatography (4:1 hexane/EtOAc) afforded 95 mg (73%) of the product as a white solid: mp 137-139 °C; ¹H NMR (CDCl₃) δ 3.93 (s, 3H), 7.16-7.26 (m, 5H), 7.39-7.47 (m, 3H), 7.66 (dd, *J* = 7.5, 1.5 Hz, 2H), 8.13 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.41 (d, *J* = 8.1 Hz, 1H), 8.75 (d, *J* = 0.9 Hz, 1H); ¹³C NMR (CDCl₃) δ 53.0, 105.4, 124.0, 127.1, 128.1, 129.2, 129.8, 129.9, 130.0, 13.1, 130.3, 130.6, 131.5, 133.9, 136.4, 139.0, 160.2,

161.3, 165.9; IR (neat, cm^{-1}) 1728, 1739; HRMS Calcd for $\text{C}_{23}\text{H}_{16}\text{O}_2\text{Se}$: 436.0214.

Found: 436.0220.

6-Phenyl-5-(phenylselenyl)-2(2H)-pyranone (26). Purification by flash chromatography (6:1 hexane/EtOAc) afforded 95.3 mg (97%) of the product as a yellow oil: ^1H NMR (CDCl_3) δ 6.20 (d, $J = 9.6$ Hz, 1H), 7.28-7.32 (m, 3H), 7.33-7.40 (m, 3H), 7.43-7.49 (m, 3H), 7.68-7.71 (m, 2H); ^{13}C NMR (CDCl_3) δ 105.2, 115.2, 128.2, 128.4, 129.4, 130.0, 130.2, 131.0, 132.5, 132.8, 150.3, 161.4, 162.0; IR (neat, cm^{-1}) 1738; HRMS Calcd for $\text{C}_{16}\text{H}_{12}\text{O}_2\text{Se}$: 328.0003. Found: 328.0009.

3,4,6-Triphenyl-5-phenylselenyl-2(2H)-pyranone (39). Purification by flash chromatography (8:1 hexane/EtOAc) and recrystallization (hexane/EtOAc) afforded 44 mg (30%) of the product as a yellow solid: mp 140-141 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 6.79-6.82 (m, 2H), 6.86-6.89 (m, 2H), 6.98-7.26 (m, 11H), 7.34-7.46 (m, 3H), 7.73-7.78 (m, 2H); ^{13}C NMR (CDCl_3) δ 108.6, 126.2, 127.0, 127.3, 127.8, 127.9, 128.1, 129.1, 129.4, 130.0, 130.7, 131.1, 132.2, 134.0, 134.1, 137.6, 158.0, 162.0, 163.9; IR (neat, cm^{-1}) 1718; HRMS Calcd for $\text{C}_{29}\text{H}_{20}\text{O}_2\text{Se}$: 480.0630. Found: 480.0642.

(5E)-5-[Phenyl(phenylselenyl)methylene]-3,4-diphenylfuran-2(5H)-one (40). Purification by flash chromatography (8:1 hexane/EtOAc) afforded 60.0 mg (41%) of the product as a yellow solid: mp 192-193 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 6.57-6.61 (m, 2H), 6.62-6.73 (m, 5H), 6.83 (t, $J = 7.6$ Hz, 2H), 6.90-6.97 (m, 3H), 7.06 (t, $J = 7.2$ Hz, 1H), 7.16-7.23 (m, 5H), 7.23-7.25 (m, 2H); ^{13}C NMR (CDCl_3) δ 126.8, 127.1, 127.5, 127.8, 127.9, 128.1, 128.3, 128.4, 128.6, 128.8, 129.3, 129.4, 129.6, 130.8, 131.1, 132.9, 136.6, 142.8, 147.6, 167.9; IR (neat, cm^{-1}) 1756, 1724; HRMS Calcd for $\text{C}_{29}\text{H}_{20}\text{O}_2\text{Se}$: 480.0631. Found: 480.0639.

(3E)-3-[Phenyl(phenylselenenyl)methylene]-4,5,6,7-tetrahydro-2-benzofuran-1(3H)-one (43). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 68.2 mg (60%) of the product as a pale yellow solid: mp 172-173 °C; ¹H NMR (CDCl₃) δ 1.41-1.47 (m, 2H), 1.56-1.64 (m, 4H), 2.25-2.30 (m, 2H), 6.97-7.04 (m, 4H), 7.07-7.15 (m, 4H), 7.25-7.28 (m, 2H); ¹³C NMR (CDCl₃) δ 20.8, 21.4, 22.1, 24.2, 122.3, 126.9, 127.9, 128.4, 128.6, 128.7, 128.8, 130.5, 134.5, 137.0, 144.2, 149.7, 169.2; IR (neat, cm⁻¹) 1760, 1717; HRMS Calcd for C₂₉H₂₀O₂Se: 382.0473. Found: 382.0481.

3-Phenylisocoumarin (5). The ester alkyne (0.30 mmol), 40% HI (2.0 equiv) and CH₂Cl₂ (3 ml) were placed in a 4 dram vial and flushed with N₂. The reaction mixture was stirred at room temperature for 96 h. The reaction mixture was then diluted with 50 ml of ether, washed with 25 mL of satd aq NaHCO₃, 25 mL of H₂O, dried (MgSO₄) and filtered. The solvent was evaporated under reduced pressure and isolated by chromatography on silica gel (10:1 hexane/EtOAc) to afford 63 mg (92%) of the product as a white solid with spectral properties identical to those previously reported:⁹ mp 87-89 °C (lit.⁹ mp 90-91 °C).

3-Phenyl-4-(phenylethynyl)isocoumarin (50). This compound was prepared using the same procedure used for the preparation of the earlier ester alkynes. Purification by flash chromatography (10:1 hexane/EtOAc) afforded 238 mg (73%) of the product as a white solid: mp 145-146 °C; ¹H NMR (CDCl₃) δ 7.38-7.40 (m, 3H), 7.48-7.62 (m, 6H), 7.83-7.89 (m, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 8.22-8.25 (m, 2H), 8.35 (d, *J* = 7.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 82.9, 97.7, 99.9, 119.9, 123.0, 125.6, 128.4, 128.7, 128.92, 128.97, 129.0, 129.7, 130.6, 131.5, 132.6, 135.4, 137.2, 156.9, 161.2; IR (neat, cm⁻¹) 1743; HRMS Calcd for C₂₃H₁₄O₂: 322.0993. Found: 322.0997.

Ethyl (*E*)-3-(3-phenylisocoumarin-4-yl)-2-propenoate (51). To a solution of 4-iodo-3-phenylisocoumarin (0.25 mmol) and ethyl acrylate (1.0 mmol, 4.0 equiv) in DMF (1 ml) were added Pd(OAc)₂ (2.8 mg, 5 mol %), *n*-Bu₄NCl (0.25 mmol, 1 equiv) and Na₂CO₃ (0.625 mmol, 2.5 equiv). The resulting mixture was heated under an N₂ atmosphere at 85 °C for 30 h. The mixture was cooled to room temperature and diluted with 70 ml of ether, washed with 25 mL of satd aq NaCl, dried (MgSO₄) and filtered. The solvent was evaporated under reduced pressure. The reaction mixture was chromatographed using 5:1 hexane/EtOAc to afford 47.2 mg (60 %) of the product as a white solid: mp 106-109 °C; ¹H NMR (CDCl₃) δ 1.32 (t, *J* = 7.2 Hz, 3H), 4.26 (q, *J* = 7.2 Hz, 2H), 6.25 (d, *J* = 16.5 Hz, 1H), 7.45-7.47 (m, 3H), 7.59-7.70 (m, 4H), 7.80-7.85 (m, 2H), 8.41 (d, *J* = 7.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.5, 61.0, 111.1, 120.7, 124.3, 126.0, 128.6, 128.8, 129.9, 130.4, 130.5, 132.5, 135.2, 136.2, 138.3, 153.8, 161.5, 166.3; IR (neat, cm⁻¹) 1740, 1716; HRMS Calcd for C₂₀H₁₆O₄: 320.1048. Found: 320.1053.

3,4-Diphenylisocoumarin (52). To a solution of 4-iodo-3-phenylisocoumarin (0.25 mmol) and NaBPh₄ (0.3 mmol, 1.2 equiv) in DMF (1 ml) were added Pd(OAc)₂ (2.8 mg, 5 mol %) and LiCl (0.25 mmol, 1 equiv). The resulting mixture was heated under an N₂ atmosphere at 85 °C for 20 h. The mixture was cooled to room temperature and diluted with 70 ml of ether, washed with 25 ml of satd aq NaCl, dried (MgSO₄) and filtered. The solvent was evaporated under reduced pressure. The reaction mixture was chromatographed using 12:1 hexane/EtOAc and recrystallized from hexane/EtOAc to afford 44.0 mg (58 %) of the product as a white solid with spectral properties identical to those previously reported:¹ mp 170-171 °C (lit.¹ mp 169-171 °C).

3-Methyl-5,6-diphenyl-2(2H)-pyranone (53). To a solution of 5-iodo-3-methyl-6-phenyl-2(2H)-pyranone (0.25 mmol) and phenylboronic acid (0.5 mmol, 2.0 equiv) in 10 mL of DMF/H₂O (V/V = 4/1) were added PdCl₂(PhCN)₂ (1.9 mg, 2 mol %) and KF (0.5 mmol, 2.0 equiv). The resulting mixture was heated under an N₂ atmosphere at 100 °C for 2 h. The mixture was cooled to room temperature and diluted with 70 ml of ether, washed with 25 ml of satd aq NaCl, dried (MgSO₄) and filtered. The solvent was evaporated under reduced pressure. The reaction mixture was chromatographed using 4:1 hexane/EtOAc to afford 41 mg (90 %) of the product as a white solid: mp 122-124 °C; ¹H NMR (CDCl₃) δ 1.96 (d, *J* = 1.2 Hz, 3H), 6.25 (d, *J* = 0.9 Hz, 1H), 7.12-7.18 (m, 4H), 7.20-7.28 (m, 3H), 7.32-7.37 (m, 3H); ¹³C NMR (CDCl₃) δ 22.1, 112.8, 119.9, 128.1, 128.3, 129.2, 129.4, 129.7, 130.8, 132.6, 134.9, 157.3, 157.4, 162.2; IR (neat, cm⁻¹) 1727; HRMS Calcd for C₁₈H₁₄O₂: 262.0994. Found: 262.0996.

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Table 1, compound 4

0.003