Synthesis of 3,4-Disubstituted 2*H*-1-Benzopyrans Through C-C Bond Formation via Electrophilic Cyclization

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General. The ^1H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. Thin layer chromatography was performed using 60 mesh silica gel plates, and visualization was effected with short wavelength UV light (254 nm). All melting points are uncorrected. All high resolution mass spectra were recorded using EI at 70 eV. All reagents were used directly as obtained commercially unless otherwise noted.

Preparation of starting materials.

General procedure for the palladium/copper-catalyzed reaction of phenyl propargyl ether with aryl halides. To a solution of 2.5 mmol of the aryl halide in Et_3N (15 ml) was added $\text{PdCl}_2(\text{PPh}_3)_2$ (2 mol %), which was then stirred for 5 min. CuI (1.5 mol %) was then added and the flask was sealed and flushed with Ar. The reaction was stirred for 20 min. A solution of 3.0 mmol of phenyl propargyl ether in 2 mL of Et_3N was then added dropwise and the reaction mixture was allowed to stir at room temperature for the desired time. After the reaction was over, the resulting solution was diluted with H_2O (10 ml) and extracted with diethyl ether (3 x 15 mL). The combined ether fractions were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by flash chromatography on silica gel using ethyl acetate/hexanes as the eluent.

Phenyl 3-*p*-tolylprop-2-yn-1-yl ether (4). This compound was obtained as a white solid: mp 71-72 °C; ^1H NMR (300 MHz, CDCl_3) δ 2.30 (s, 3H), 4.86 (s, 2H), 6.94-7.08 (m, 5H), 7.18-7.33 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.7, 56.9, 83.5, 87.5, 115.2,

119.5, 121.6, 129.3, 129.7, 132.0, 139.0, 158.1; IR (neat, cm^{-1}) 3032, 2914, 1598, 1490, 1214, 1029; HRMS m/z 222.10477 (calcd $\text{C}_{16}\text{H}_{14}\text{O}$, 222.10447).

3-(4-Methoxyphenyl)prop-2-yn-1-yl phenyl ether (5). This compound was obtained as a light brown solid: mp 61-62 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 3.77 (s, 3H), 4.88 (s, 2H), 6.81 (d, $J = 8.8$ Hz, 2H), 6.95-7.03 (m, 3H), 7.27-7.38 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 55.4, 56.8, 82.7, 87.2, 114.0, 114.5, 115.1, 121.5, 129.6, 133.5, 158.0, 160.0; IR (neat, cm^{-1}) 3042, 2919, 1598, 1506, 1239, 1024; HRMS m/z 238.09979 (calcd $\text{C}_{16}\text{H}_{14}\text{O}_2$, 238.09938).

3-(2-Methoxyphenyl)prop-2-yn-1-yl phenyl ether (6). This compound was obtained as a yellow oil: ^1H NMR (300 MHz, CDCl_3) δ 3.77 (s, 3H), 4.90 (s, 2H), 6.77-6.86 (m, 2H), 6.95 (t, $J = 7.3$ Hz, 1H), 7.02 (d, $J = 7.8$ Hz, 2H), 7.20-7.30 (m, 3H), 7.36 (dd, $J = 7.6, 1.6$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 55.7, 56.9, 83.6, 88.1, 110.6, 111.4, 115.1, 120.4, 121.3, 129.4, 130.2, 133.8, 157.9, 160.2; IR (neat, cm^{-1}) 3057, 3032, 2934, 2243, 1603, 1270, 1024; HRMS m/z 238.09968 (calcd $\text{C}_{16}\text{H}_{14}\text{O}_2$, 238.09938).

Substituted propargyl ether **7** was prepared according to a literature procedure.¹

3,5-Di-*tert*-butylphenyl propargyl ether (8). To a solution of 2.06 g of 3,5-di-*tert*-butylphenol (10.0 mmol) in dry acetone (50 ml) was added propargyl bromide (11.0 mmol) and anhydrous K_2CO_3 (11.0 mmol). The resulting mixture was refluxed for 24 h. The reaction mixture was diluted with H_2O (20 ml) and extracted with diethyl ether (3 x 20 ml). The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (7:1 hexane/EtOAc) to afford 1.68 g of the indicated compound **7** (69% yield) as a yellow oil: ^1H NMR (300 MHz, CDCl_3) δ 1.30 (s, 18H), 2.42 (t, $J = 2.5$ Hz, 1H), 4.63 (d, $J = 2.4$

Hz, 2H), 6.83 (d, $J = 1.6$ Hz, 2H), 7.05 (d, $J = 1.5$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.5, 35.0, 55.7, 75.4, 79.1, 109.4, 115.7, 152.2, 157.3; IR (neat, cm^{-1}) 3298, 2939, 1588, 1424, 1285, 1050; HRMS m/z 244.18311 (calcd $\text{C}_{17}\text{H}_{24}\text{O}$, 244.18272).

General procedure for the palladium/copper-catalyzed reaction of terminal alkynes with iodobenzene. To a solution of 4.5 mmol of iodobenzene in Et_3N (15 ml), was added $\text{PdCl}_2(\text{PPh}_3)_2$ (2 mol %), and CuI (1.5 mol %), and the mixture was stirred for 30 min under Ar. A solution of 3.0 mmol of the terminal alkyne in 2 mL of Et_3N was then added dropwise and the reaction mixture was allowed to stir at room temperature for the desired time. After the reaction was over, the resulting solution was diluted with H_2O (10 ml) and extracted with diethyl ether (3 x 15 mL). The combined ether fractions were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by flash chromatography on silica gel using ethyl acetate/hexanes as the eluent.

4-(3-Phenylprop-2-yn-1-yloxy)benzaldehyde (9). This compound was obtained as a brown solid: mp 86-87 $^\circ\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 5.00 (s, 2H), 7.14 (d, $J = 8.8$ Hz, 2H), 7.25-7.32 (m, 3H), 7.41-7.44 (m, 2H), 7.87 (d, $J = 8.8$ Hz, 2H), 9.90 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 57.0, 82.9, 88.1, 115.4, 122.0, 128.5, 129.1, 130.6, 132.0, 132.1, 162.8, 191.0; IR (neat, cm^{-1}) 3078, 2827, 1690, 1598, 1250, 1009; HRMS m/z 236.08409 (calcd $\text{C}_{16}\text{H}_{12}\text{O}_2$, 236.08373).

3,5-Di-*tert*-butylphenyl 3-phenylprop-2-yn-1-yl ether (10). This compound was obtained as a light yellow solid: mp 54-55 $^\circ\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 1.32 (s, 18H), 4.91 (s, 2H), 6.91 (d, $J = 1.6$ Hz, 2H), 7.06 (t, $J = 1.5$ Hz, 1H), 7.26-7.31 (m, 3H), 7.41-7.45 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.7, 35.2, 56.8, 84.5, 87.2, 109.6,

115.8, 122.6, 128.5, 128.8, 132.0, 152.4, 157.6; IR (neat, cm^{-1}) 3081, 2963, 1591, 1362, 1297, 1051; HRMS m/z 320.21446 (calcd $\text{C}_{23}\text{H}_{28}\text{O}$, 320.21402).

General procedure for the triphenylphosphine/diethyl azodicarboxylate-promoted formation of the substituted phenyl propargylic ethers. To a solution of 1.31 g of PPh_3 (5.0 mmol) in dry benzene (15 ml) was added the substituted propargylic alcohol (5.0 mmol) and the substituted phenol (5.0 mmol) under an inert atmosphere with stirring. Diethyl azodicarboxylate (0.87 g, 5.0 mmol) was then added slowly and the reaction mixture was stirred at r.t. for 18 to 36 h. After the reaction was complete, the solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography on silica gel using hexanes/ethyl acetate as the eluent.

3-*tert*-Butylphenyl 3-phenylprop-2-yn-1-yl ether (11). This compound was obtained as a yellow oil: ^1H NMR (300 MHz, CDCl_3) δ 1.30 (s, 9H), 4.86 (s, 2H), 6.83 (dd, $J = 8.0, 2.3$ Hz, 1H), 6.96-7.02 (m, 1H), 7.08 (t, $J = 1.9$ Hz, 1H), 7.19-7.25 (m, 4H), 7.39-7.42 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.4, 34.8, 56.6, 84.3, 87.2, 111.2, 113.1, 118.6, 122.4, 128.4, 128.7, 129.1, 131.9, 153.0, 157.7; IR (neat, cm^{-1}) 3067, 2955, 2868, 1588, 1485, 1270, 1029; HRMS m/z 264.15187 (calcd $\text{C}_{19}\text{H}_{20}\text{O}$, 264.15142).

3-(Cyclohex-1-enyl)prop-2-yn-1-yl phenyl ether (12). This compound was obtained as a dark brown oil: ^1H NMR (300 MHz, CDCl_3) δ 1.53-1.62 (m, 4H), 2.04-2.10 (m, 4H), 4.77 (s, 2H), 6.10-6.13 (m, 1H), 6.93-6.98 (m, 2H), 7.24-7.30 (m, 2H), 7.40-7.70 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.5, 22.3, 25.7, 29.0, 56.7, 81.3, 89.1, 115.0, 120.0, 121.3, 129.5, 136.1, 157.9; IR (neat, cm^{-1}) 3032, 2919, 2217, 1593, 1485, 1219; HRMS m/z 212.12047 (calcd $\text{C}_{15}\text{H}_{16}\text{O}$, 212.12012).

1-Naphthyl 3-phenylprop-2-yn-1-yl ether (13). This compound was obtained as a light brown solid: mp 50-51 °C; ¹H NMR (300 MHz, CDCl₃) δ 5.08 (s, 2H), 6.99 (d, *J* = 7.4 Hz, 1H), 7.26-7.49 (m, 9H), 7.77-7.80 (m, 1H), 8.30-8.33 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 57.2, 84.2, 87.5, 105.9, 121.2, 122.4, 122.6, 125.6, 125.9, 126.0, 126.7, 127.7, 128.5, 128.9, 132.0, 134.8, 153.8; IR (neat, cm⁻¹) 3057, 2914, 1577, 1398, 1229, 1091; HRMS *m/z* 258.10497 (calcd C₁₉H₁₄O, 258.10447).

General procedure for iodocyclization. To a solution of 0.25 mmol of the ether and 3 mL of CH₃NO₂, 2.0 equiv of NaHCO₃ and 3.0 equiv of I₂ dissolved in 2 mL of CH₃NO₂ was added gradually. The reaction mixture was allowed to stir at room temperature for the desired time. Alternatively, to a solution of 0.25 mmol of the ether and 3 mL of CH₃NO₂ at -25 to -30 °C, 1.5 equiv of ICl dissolved in 2 mL of CH₃NO₂ was added gradually. The reaction mixture was allowed to stir at -25 to -30 °C for the desired time. The excess I₂ or ICl was removed by washing with satd aq Na₂S₂O₃. The mixture was then extracted by diethyl ether (3 x 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/ethyl acetate as the eluent.

3-Iodo-4-phenyl-2*H*-benzopyran (2). This compound was obtained as a pale yellow solid: mp 99-100 °C; ¹H NMR (300 MHz, CDCl₃) δ 5.06 (s, 2H), 6.61 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.76 (dt, *J* = 7.7, 1.1 Hz, 1H), 6.85 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.14 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.18-7.22 (m, 2H), 7.39-7.46 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 75.1, 91.2, 116.1, 121.7, 124.2, 126.5, 128.3, 128.7, 129.5, 129.7, 140.0, 142.0, 153.3; IR (neat, cm⁻¹) 3062, 2904, 1475, 1219, 1029, 994; HRMS *m/z* 333.98600 (calcd C₁₅H₁₁IO, 333.98547).

Figure 1. X-ray structure of compound **2**

3-Iodo-4-(4-methylphenyl)-2H-benzopyran (24). This compound was obtained as a pale brown solid: mp 68-69 °C; ^1H NMR (300 MHz, CDCl_3) δ 2.23 (s, 3H), 4.87 (s, 2H), 6.46 (dd, $J = 7.7, 1.6$ Hz, 1H), 6.58 (t, $J = 7.5$ Hz, 1H), 6.66 (d, $J = 8.0$ Hz, 1H), 6.89-6.98 (m, 3H), 7.07 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.6, 75.2, 91.1, 116.1, 121.7, 124.4, 126.6, 129.4, 129.5, 129.7, 137.1, 138.1, 142.0, 153.5; IR (neat, cm^{-1}) 3032, 2914, 2842, 1475, 1219, 999; HRMS m/z 348.00051 (calcd $\text{C}_{16}\text{H}_{13}\text{IO}$, 348.00112).

3-Iodo-4-(4-methoxyphenyl)-2H-benzopyran (25). This compound was obtained as a pale brown solid: mp 110-111 °C; ^1H NMR (300 MHz, CDCl_3) δ 3.85 (s, 3H), 5.05 (s, 2H), 6.66 (dd, $J = 7.7, 1.2$ Hz, 1H), 6.77 (t, $J = 7.4$ Hz, 1H), 6.84 (d, $J = 8.0$ Hz, 1H), 6.96 (d, $J = 8.6$ Hz, 2H), 7.11-7.17 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 55.5, 75.2, 91.4, 114.1, 116.1, 121.7, 124.6, 126.6, 129.7, 130.8, 132.3, 141.7, 153.5, 159.5; IR (neat, cm^{-1}) 2955, 2918, 2833, 1505, 1244, 1171, 1037; HRMS m/z 363.99640 (calcd $\text{C}_{16}\text{H}_{13}\text{IO}_2$, 363.99603).

3-Iodo-4-(4-nitrophenyl)-2H-benzopyran (26). This compound was obtained as a yellow solid: mp 140-142 °C (decomp.); ^1H NMR (300 MHz, CDCl_3) δ 5.07 (s, 2H), 6.50 (dd, $J = 7.7, 1.4$ Hz, 1H), 6.79 (dt, $J = 7.8, 0.9$ Hz, 1H), 6.88 (dd, $J = 8.2, 0.9$ Hz, 1H),

7.19 (dt, $J = 8.0, 1.4$ Hz, 1H), 7.41 (dd, $J = 6.9, 1.9$ Hz, 2H), 8.32 (dd, $J = 6.9, 1.8$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 75.0, 91.8, 116.5, 122.0, 123.4, 124.1, 125.9, 130.4, 130.8, 140.4, 146.6, 147.8, 153.2; IR (neat, cm^{-1}) 3093, 2837, 1926, 1593, 1516, 1337, 1219; HRMS m/z 378.97119 (calcd $\text{C}_{15}\text{H}_{10}\text{INO}_3$, 378.97055).

3-Iodo-4-(2-methoxyphenyl)-2H-benzopyran (27). This compound was obtained as a light brown solid: mp 111-113 °C; ^1H NMR (300 MHz, CDCl_3) δ 3.75 (s, 3H), 5.01-5.13 (m, 2H), 6.57 (dd, $J = 7.8, 1.5$ Hz, 1H), 6.74 (dt, $J = 7.6, 1.1$ Hz, 1H), 6.83 (dd, $J = 7.1, 1.0$ Hz, 1H), 6.96-7.14 (m, 4H), 7.37-7.42 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 55.9, 74.9, 92.7, 111.6, 116.0, 121.0, 121.7, 123.8, 126.1, 129.0, 129.5, 130.0, 131.0, 139.5, 153.2, 156.9; IR (neat, cm^{-1}) 2955, 2918, 1505, 1244, 1171, 1037; HRMS m/z 363.99644 (calcd $\text{C}_{16}\text{H}_{13}\text{IO}_2$, 363.99603).

3-Iodo-6-methyl-4-phenyl-2H-benzopyran (28). This compound was obtained as a brown oil: ^1H NMR (300 MHz, CDCl_3) δ 2.10 (s, 3H), 5.01 (s, 2H), 6.41 (s, 1H), 6.75 (d, $J = 8.2$, Hz, 1H), 6.94 (d, $J = 8.2$, Hz, 1H), 7.17-7.20 (m, 2H), 7.40-7.46 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 20.8, 75.1, 91.4, 115.8, 124.1, 126.8, 128.2, 128.6, 129.5, 130.2, 131.0, 140.1, 142.1, 151.1; IR (neat, cm^{-1}) 3052, 2914, 1741, 1485, 1229, 999; HRMS m/z 348.00155 (calcd $\text{C}_{16}\text{H}_{13}\text{IO}$, 348.00112).

6-tert-Butyl-3-iodo-4-phenyl-2H-benzopyran (29). This compound was obtained as a pale yellow solid: mp 84-86 °C; ^1H NMR (300 MHz, CDCl_3) δ 1.11 (s, 9H), 5.03 (s, 2H), 6.63 (d, $J = 2.4$ Hz, 1H), 6.79 (d, $J = 8.4$ Hz, 1H), 7.16 (d, $J = 2.4$ Hz, 1H), 7.18-7.22 (m, 2H), 7.37-7.48 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.4, 34.3, 75.2, 90.9, 115.4, 123.5, 123.8, 126.6, 128.3, 128.6, 129.5, 140.1, 142.4, 144.5, 151.1; IR (neat, cm^{-1}) 3052, 2950, 1485, 1357, 1229, 1004; HRMS m/z 390.04856 (calcd $\text{C}_{19}\text{H}_{19}\text{IO}$, 390.04807).

3-Iodo-6-methoxy-4-phenyl-2H-benzopyran (30). This compound was obtained as a pale brown solid: mp 81-82 °C; ^1H NMR (300 MHz, CDCl_3) δ 3.59 (s, 3H), 4.99 (s, 2H), 6.19 (d, J = 2.9 Hz, 1H), 6.69 (dd, J = 8.7, 2.9 Hz, 1H), 6.79 (d, J = 8.7 Hz, 1H), 7.18-7.23 (m, 2H), 7.38-7.46 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 55.8, 75.3, 92.4, 112.5, 114.4, 116.6, 125.1, 128.4, 128.8, 129.5, 140.0, 142.1, 147.4, 154.3; IR (neat, cm^{-1}) 2991, 2924, 2822, 1572, 1480, 1301, 1198; HRMS m/z 363.99663 (calcd $\text{C}_{16}\text{H}_{13}\text{IO}_2$, 363.99603).

6-Chloro-3-iodo-4-phenyl-2H-benzopyran (31). This compound was obtained as a brown solid: mp 89-90 °C; ^1H NMR (300 MHz, CDCl_3) δ 5.07 (s, 2H), 6.59 (d, J = 2.6 Hz, 1H), 6.79 (d, J = 8.6 Hz, 1H), 7.09 (dd, J = 8.6, 2.5 Hz, 1H), 7.19 (dd, J = 7.8, 1.9 Hz, 2H), 7.43-7.48 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 75.3, 93.0, 117.4, 125.3, 126.1, 126.7, 128.6, 129.0, 129.4, 129.5, 139.4, 141.2, 151.9; IR (neat, cm^{-1}) 2919, 2848, 1477, 1403, 1093, 638; HRMS m/z 367.94723 (calcd $\text{C}_{15}\text{H}_{10}\text{ClIO}$, 367.94649).

3-Iodo-4-phenyl-2H-benzopyran-6-carbaldehyde (32) and 3-(iodophenylmethylene)-2,3-dihydrobenzofuran-5-carbaldehyde (33). These compounds were obtained as a light brown solid as a 2:1 mixture: ^1H NMR (300 MHz, CDCl_3) δ 5.07 (s, 2H), 5.19 (s, 1H), 6.95 (d, J = 8.3 Hz, 1H), 7.11 (d, J = 8.5 Hz, 3H), 7.19-7.23 (m, 3H), 7.31-7.40 (m, 4H), 7.47-7.49 (m, 2H), 7.70 (dd, J = 8.3, 1.9 Hz, 1H), 7.90 (d, J = 8.7 Hz, 2H), 9.68 (s, 1H), 9.92 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 75.5, 80.1, 92.7, 98.49, 99.4, 115.9, 116.9, 123.8, 128.1, 128.5, 128.7, 128.8, 129.0, 129.1, 129.3, 130.7, 130.9, 131.8, 132.2, 139.2, 141.0, 147.2, 158.6, 162.7, 190.7, 190.9; IR (neat, cm^{-1}) 3057, 2827, 1690, 1598, 1234, 1157; HRMS m/z 361.98090 (calcd $\text{C}_{16}\text{H}_{11}\text{IO}_2$, 361.98038).

5,7-Di-*tert*-butyl-3-iodo-4-phenyl-2*H*-benzopyran (34). This compound was obtained as a yellow solid: mp 142-143 °C; ¹H NMR (300 MHz, CDCl₃) δ 0.89 (s, 9H), 1.31 (s, 9H), 4.81 (s, 2H), 6.89 (d, *J* = 1.9 Hz, 1H), 7.12 (d, *J* = 2.1 Hz, 2H), 7.24-7.27 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 31.3, 32.1, 35.2, 36.8, 7.8, 85.0, 109.5, 119.9, 122.7, 127.6, 128.0, 131.1, 143.7, 143.9, 149.8, 152.5, 157.2; IR (neat, cm⁻¹) 2955, 2893, 1593, 1444, 1403, 1004; HRMS *m/z* 446.11117 (calcd C₂₃H₂₇IO, 446.11067).

7-*tert*-Butyl-3-iodo-4-phenyl-2*H*-benzopyran (35). This compound was obtained as a light brown solid: mp 97-98 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.30 (s, 9H), 5.09 (s, 2H), 6.59 (d, *J* = 4.3 Hz, 1H), 6.83 (dd, *J* = 8.1, 1.8 Hz, 1H), 6.93 (d, *J* = 1.7 Hz, 1H), 7.21-7.25 (m, 2H), 7.40-7.44 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 31.3, 35.0, 75.3, 90.1, 113.3, 118.7, 121.8, 126.1, 128.3, 128.7, 129.5, 140.2, 142.0, 153.1, 153.8; IR (neat, cm⁻¹) 2965, 2904, 2356, 1603, 1485, 1004; HRMS *m/z* 390.04856 (calcd C₁₉H₁₉IO, 390.04807).

7-Chloro-3-iodo-4-phenyl-2*H*-benzopyran (36). This compound was obtained as a light brown solid: mp 90-91 °C; ¹H NMR (300 MHz, CDCl₃) δ 5.06 (s, 2H), 6.52 (d, *J* = 8.3 Hz, 1H), 6.72 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.85 (d, *J* = 2.1 Hz, 1H), 7.16-7.19 (m, 2H), 7.41-7.48 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 75.3, 91.2, 116.5, 121.9, 122.7, 127.4, 128.5, 128.8, 129.4, 134.7, 139.6, 141.3, 154.0; IR (neat, cm⁻¹) 2837, 1588, 1475, 1413, 1219, 999; HRMS *m/z* 367.94720 (calcd C₁₅H₁₀ClIO, 367.94649).

5-Chloro-3-iodo-4-phenyl-2*H*-benzopyran (37). This compound was obtained as a light brown solid: mp 73-74 °C; ¹H NMR (300 MHz, CDCl₃) δ 4.94 (s, 2H), 6.88-6.91 (m, 2H), 7.10 (t, *J* = 8.0 Hz, 1H), 7.17-7.20 (m, 2H), 7.34-7.38 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 76.0, 92.8, 115.2, 123.3, 125.0, 128.0, 128.1, 129.7, 129.9, 131.7, 140.4,

141.3, 156.6; IR (neat, cm^{-1}) 3052, 2937, 1588, 1444, 1239, 999; HRMS m/z 367.94725 (calcd $\text{C}_{15}\text{H}_{10}\text{ClIO}$, 367.94649).

3-Iodo-7-methoxy-4-phenyl-2*H*-benzopyran (38) and 3-iodo-5-methoxy-4-phenyl-2*H*-benzopyran (39). These compounds were obtained as a light brown solid as a 2:3 mixture: ^1H NMR (300 MHz, CDCl_3) δ 3.22 (s, 3H), 3.76 (s, 2H), 4.93 (s, 2H), 5.04 (s, 1H), 6.31 (dd, $J = 8.6, 2.5$ Hz, 1H), 6.37-6.47 (m, 2H), 6.50-6.62 (m, 2H), 7.12-7.21 (m, 4H), 7.28-7.47 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 55.6, 55.8, 75.3, 75.8, 87.0, 89.0, 101.7, 106.1, 107.4, 109.2, 115.1, 117.8, 127.0, 127.6, 127.7, 128.2, 128.5, 128.6, 129.5, 130.2, 140.2, 140.5, 141.8, 143.4, 154.7, 156.0, 156.1, 161.0; IR (neat, cm^{-1}) 3016, 2934, 2827, 1608, 1465, 1270; HRMS m/z 363.99664 (calcd $\text{C}_{16}\text{H}_{13}\text{IO}_2$, 363.99603).

4-(1-Cyclohexenyl)-3-iodo-2*H*-benzopyran (40). This compound was obtained as a light brown oil: ^1H NMR (300 MHz, CDCl_3) δ 1.65-1.76 (m, 4H), 2.05 (m, 2H), 2.18-2.20 (m, 2H), 4.93 (s, 2H), 5.60-5.62 (m, 1H), 6.79 (dd, $J = 8.0, 0.9$ Hz, 1H), 6.86 (dt, $J = 7.6, 1.1$ Hz, 1H), 7.06 (dd, $J = 7.7, 1.5$ Hz, 1H), 7.13 (dt, $J = 7.7, 1.7$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.2, 22.8, 25.3, 27.6, 74.7, 89.2, 116.1, 121.7, 122.8, 125.6, 129.3, 129.5, 137.5, 143.5, 153.6; IR (neat, cm^{-1}) 3027, 2914, 1598, 1475, 1209, 1034; HRMS m/z 338.01726 (calcd $\text{C}_{15}\text{H}_{15}\text{IO}$, 338.01677).

4-Hydroxymethyl-3-iodo-2*H*-benzopyran (42). This compound was obtained as a yellow solid: mp 62-63 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 2.06 (s, 1H), 4.64 (s, 2H), 4.86 (s, 2H), 6.82 (d, $J = 8.0$ Hz, 1H), 6.92-6.98 (m, 1H), 7.18 (dt, $J = 8.0, 1.3$ Hz, 1H), 7.41 (dd, $J = 7.7, 1.1$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 66.0, 75.0, 93.8, 116.4, 121.8, 122.1, 124.3, 129.9, 137.3, 153.7; IR (neat, cm^{-1}) 3334, 2934, 1480, 1444, 1219, 1009; HRMS m/z 287.96514 (calcd $\text{C}_{10}\text{H}_9\text{IO}_2$, 287.96473).

3-Iodo-4-phenyl-2H-benzo[h]chromene (43). This compound was obtained as a light brown solid: mp 104-105 °C; ^1H NMR (300 MHz, CDCl_3) δ 5.25 (s, 2H), 6.77 (d, J = 8.5 Hz, 1H), 7.21-7.25 (m, 3H), 7.42-7.50 (m, 5H), 7.68-7.71 (m, 1H), 8.17-8.20 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 75.6, 88.1, 118.8, 120.8, 122.2, 124.0, 124.3, 126.0, 127.1, 127.7, 128.3, 128.7, 129.6, 134.3, 140.2, 142.7, 149.4; IR (neat, cm^{-1}) 3055, 2923, 2847, 1562, 1400, 1341; HRMS m/z 384.00158 (calcd $\text{C}_{19}\text{H}_{13}\text{IO}$, 384.00112).

General procedure for the PhSeBr cyclizations. To a solution of 0.25 mmol of the substituted phenyl propargylic ether and CH_2Cl_2 (3 mL), 0.375 mmol of PhSeBr dissolved in 2 mL of CH_2Cl_2 was added dropwise. The mixture was allowed to stir at room temperature for the desired time. The reaction mixture was washed with 20 mL of water and extracted with diethyl ether (3 x 10 mL). The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product, which was further purified by flash chromatography on silica gel using hexanes/ethyl acetate as the eluent.

4-Phenyl-3-phenylselenenyl-2H-benzopyran (23). This compound was obtained as a brown oil: ^1H NMR (300 MHz, CDCl_3) δ 4.84 (s, 2H), 6.84-6.87 (m, 2H), 6.94 (t, J = 7.4 Hz, 1H), 7.12-7.25 (m, 5H), 7.27-7.34 (m, 4H), 7.40-7.44 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 29.9, 71.1, 115.3, 121.4, 124.0, 128.2, 128.4, 128.8, 129.1, 129.2, 129.2, 129.3, 129.6, 134.6, 141.0, 158.4; IR (neat, cm^{-1}) 3052, 2919, 1582, 1480, 1224, 1024; HRMS m/z 364.03707 (calcd $\text{C}_{21}\text{H}_{16}\text{OSe}$, 364.03664).

4-Methyl-3-phenylselenenyl-2H-benzopyran (41). This compound was obtained as a brown solid: mp 54-55 °C; ^1H NMR (300 MHz, CDCl_3) δ 2.66 (s, 3H), 4.80 (s, 2H), 6.83 (d, J = 7.9 Hz, 2H), 6.92 (t, J = 7.3 Hz, 1H), 7.20-7.26 (m, 4H), 7.42-7.44 (m, 2H); ^{13}C

NMR (75 MHz, CDCl₃) δ 30.1, 72.1, 115.2, 121.3, 125.4, 127.6, 128.4, 129.5 (2C), 129.7, 130.2, 132.5, 158.5; IR (neat, cm⁻¹) 3057, 2914, 2847, 1593, 1485, 1229; HRMS *m/z* 302.02154 (calcd C₁₆H₁₄OSe, 302.02099).

3-(4-Fluoro-3-methylphenylethynyl)-4-phenyl-2*H*-benzopyran (44). To a solution of 0.17 g of 3-iodo-4-phenyl-2*H*-benzopyran (**2**) (0.5 mmol) in Et₃N (5 ml), was added PdCl₂(PPh₃)₂ (2 mol %) and CuI (1.5 mol %), and the mixture was stirred for 30 min under Ar. 0.6 Mmol of 5-ethynyl-2-fluorotoluene dissolved in 1 mL of Et₃N was then added dropwise and the reaction mixture was allowed to stir at room temperature for 24 h. The reaction was monitored by TLC and an additional 0.4 mmol of the 5-ethynyl-2-fluorotoluene dissolved in 1 mL of Et₃N was added slowly under an inert atmosphere and the reaction mixture was further allowed to stir at room temperature for another 24 h. After the reaction was over, the resulting solution was diluted with H₂O (5 ml) and extracted with diethyl ether (3 x 10 mL). The combined ether fractions 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/ethyl acetate as the eluent to obtain the desired compound **44** in an 87% yield as a pale yellow solid: mp 79-80 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.18 (d, *J* = 1.6 Hz, 3H), 4.88 (s, 2H), 6.81-6.93 (m, 4H), 6.97-7.05 (m, 2H), 7.10-7.21 (m, 1H), 7.39-7.45 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 14.6 (d, *J* = 3.4 Hz), 68.0, 86.7 (d, *J* = 1.9 Hz), 95.1 (d, *J* = 0.8 Hz), 112.4, 115.3 (d, *J* = 9.4 Hz), 116.4, 118.9 (d, *J* = 3.8 Hz), 121.8, 124.3, 125.3 (d, *J* = 18.2 Hz), 126.8, 128.2 (d, *J* = 10.2 Hz), 129.8, 130.2, 130.8 (d, *J* = 8.4 Hz), 134.7 (d, *J* = 5.7 Hz), 136.6, 140.8, 154.6, 160.1, 162.6; IR (neat, cm⁻¹) 3047, 2919, 2192, 1480, 1224, 1106; HRMS *m/z* 340.12694 (calcd C₂₄H₁₇FO, 340.12634).

1,4-Dihydro-2,5-dioxacyclopenta[*a*]naphthalen-3-one (45). To a solution of 0.14 g of 4-hydroxymethyl-3-iodo-2*H*-benzopyran (**42**) (0.5 mmol) in DMF (5 ml) was added PdCl₂(PPh₃)₂ (5 mol %) and K₂CO₃ (2 equiv), and the mixture was stirred for 6 h under an atmosphere of CO at 60 °C. The reaction was monitored by TLC and, after completion of the reaction, the resulting solution was cooled to room temperature, diluted with ether (15 ml), and washed with brine (15 ml). The aqueous layer was extracted with diethyl ether (3 x 15 mL). The combined ether fractions 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/ethyl acetate as the eluent to obtain the desired compound **45** in an 72% yield as a brown solid: mp 151-152 °C; ¹H NMR (400 MHz, CDCl₃) 5.13-5.15 (m, 4H), 6.92-6.99 (m, 2H), 7.07 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.34 (dt, *J* = 8.2, 0.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 63.3, 68.8, 116.4, 117.2, 118.3, 122.0, 124.2, 133.8, 154.1, 154.8, 170.7; IR (neat, cm⁻¹) 2361, 1744, 1666, 1449, 1336, 1181, 1052; HRMS *m/z* 188.04776 (calcd C₁₁H₈O₃, 188.04743).

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