

Supporting Information

A Rapid Synthesis of 2,5-Disubstituted-2,3-dihydrobenzofurans

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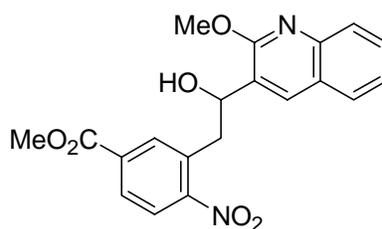
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Melting points are uncorrected. All solvents and reagents were used as received from commercial sources. Analytical samples were obtained by chromatography on silica gel using an ethyl acetate-hexanes mixture as the eluent unless specified otherwise.

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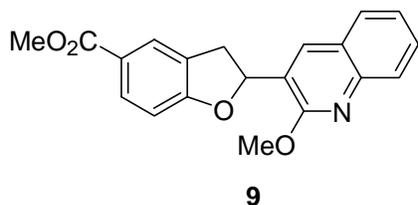
Preparation of Methyl 3-[2-hydroxy-2-(2-methoxyquinolin-3-yl)ethyl]-4-nitrobenzoate (8). To a mixture of 1.64 g (6.13 mmol) of **6**¹ and 1.38 g (7.37 mmol) of 2-methoxy-3-quinolinecarboxaldehyde **7** in 25 mL of THF was added dropwise 600 μ L of TBAF (1.00 M in THF). The mixture was stirred at rt for 30 min and quenched with

15 mL of sat. NH_4Cl . The layers were separated and the organic layer was washed with 15 mL of water. The organic layer was dried over MgSO_4 and the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography to give 1.85 g (75%) of **8** as a pale yellow solid: mp 130–131 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 2.85 (m, 1H), 3.50 (m, 2H), 3.94 (s, 3H), 4.17 (s, 3H), 5.19 (br s, 1H), 7.40 (m, 1H), 7.63 (m, 1H), 7.73 (d, 1H, $J = 8.8$ Hz), 7.89 (m, 2H), 8.04 (m, 2H), 8.11 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 39.4, 52.6, 53.4, 70.0, 124.2, 125.0, 126.7, 127.1, 127.4, 128.5, 129.3, 133.1, 133.2, 134.3, 134.7, 135.4, 145.6, 152.7, 159.1, 165.2; Anal. Calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_6$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.82; H, 4.62; N, 7.30.

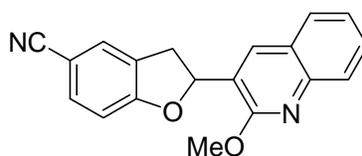
General Procedure for the preparation of 5-Substituted-2-Aryl-2,3-dihydro-1-benzofurans. Procedure A. To a mixture containing 1.00 g (5.12 mmol, 1.00 equiv) of methyl 3-methyl-4-nitrobenzoate (**11**) and 6.14 mmol (1.20 equiv) of the appropriately substituted aldehyde was added 7.68 ml (7.68 mmol) of TBAF (1.00 M in THF) followed by 1.32 g (10.24 mmol) of diisopropylethylamine. The resulting mixture was heated at reflux (3-20 h) and the reaction was monitored for the disappearance of starting materials and intermediates by TLC. The reaction mixture was cooled to rt and the residue was purified by silica gel chromatography or recrystallized from MeOH.

Procedure B. To a mixture containing 1.00 g (5.12 mmol, 1.2 equiv) of methyl 3-methyl-4-nitrobenzoate (**11**) and 4.27 mmol (1.00 equiv) of the appropriately substituted aldehyde was added 7.68 ml (7.68 mmol) of TBAF (1.00 M in THF) followed by 1.32 g (10.24 mmol) of diisopropylethylamine. The resulting mixture was heated at reflux (3-20 h) and the reaction was monitored for the disappearance of starting materials and

intermediates by TLC. The reaction mixture was cooled to rt and the residue was purified by silica gel chromatography or recrystallized from MeOH.



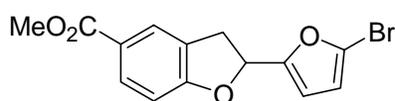
Preparation of 3-(Methyl 2,3-dihydro-1-benzofuran-5-carboxylate)-2-methoxyquinoline (9). According to General Procedure B, reaction of 1.00 g (5.12 mmol) methyl 3-methyl-4-nitrobenzoate **11** and 800 mg (4.30 mmol) of 2-methoxyquinoline-3-carbaldehyde **7** with 6.40 mL of TBAF (1.00 M in THF, 6.40 mmol) and 1.10 g (8.50 mmol) of diisopropylethylamine gave 990 mg (69%) of **9** as an analytically pure colorless solid by direct crystallization of the crude residue from MeOH: m.p 139-140 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.12 (dd, 1H, *J* = 16.2 and 7.2 Hz), 3.82 (dd, 1H, *J* = 16.1 and 9.6 Hz), 3.89 (s, 3H), 4.14 (s, 3H), 6.10 (dd, 1H, *J* = 10.4, 7.6, and 1.2 Hz), 7.00 (d, 1H, *J* = 8.4 Hz), 7.38 (ddd, 1H, *J* = 8.0, 6.8, and 1.2 Hz), 7.62 (ddd, 1H, *J* = 1.4, 7.0 and 8.2 Hz), 7.71 (dd, 1H, *J* = 8.0 and 1.2 Hz), 7.86 (d, 1H, *J* = 9.6 Hz), 7.88 (s, 1H), 7.97 (dd, 1H, *J* = 8.4 and 2.0 Hz), 8.06 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 36.7, 51.9, 53.7, 80.6, 109.2, 123.3, 124.4, 125.0, 125.7, 126.9, 126.9, 126.9, 127.7, 129.5, 131.3, 133.7, 146.0, 159.1, 163.6, 166.6; Anal. Calcd For C₂₀H₁₇NO₄: C, 71.63, H, 5.11; N, 4.18. Found: C, 71.63; H, 5.02; 4.12.



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Preparation of 3-(5-Cyano-2,3-dihydro-1-benzofuran)-2-methoxyquinoline (10)

According to General Procedure A, reaction of 1.00 g (6.20 mmol) of 3-methyl-4-nitrobenzotrile **12** and 1.39 g (7.40 mmol) of 2-methoxy-3-quinolinecarboxaldehyde **7** with 12.3 mL (12.3 mmol) of TBAF (1.00 M in THF) and 2.00 g (15.4 mmol) of diisopropylethylamine afforded 1.67 g (81%) of **10** as an analytically pure fluffy white solid by direct crystallization of the crude residue from MeOH: mp: 162-163 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.14 (dd, 1H, *J* = 16.3 and 7.4 Hz), 3.82 (dd, 1H, *J* = 16.1 and 10.0 Hz), 4.14 (s, 3H), 6.10 (t, 1H, *J* = 8.4 Hz), 7.03 (d, 1H, *J* = 8.4 Hz), 7.39 (t, 1H, *J* = 7.2 Hz), 7.44 (s, 1H), 7.33 (d, 1H, *J* = 8.4 Hz), 7.63 (d, 1H, *J* = 7.6 Hz), 7.72 (d, 1H, *J* = 8.0 Hz), 7.87 (d, 1H, *J* = 8.0 Hz), 8.03 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 36.4, 53.7, 80.8, 104.2, 110.3, 119.5, 124.5, 124.8, 125.0, 126.9, 127.6, 128.2, 129.0, 129.6, 133.7, 133.7, 146.0, 158.8, 163.1; Anal. Calcd for C₁₉H₁₄N₂O₂: C, 75.48; H, 4.67; N, 9.27. Found: C, 75.22; H, 4.62; N, 9.18.

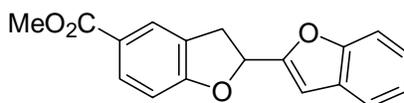


15

Methyl 2-(5-Bromo-2-furyl)-2,3-dihydro-1-benzofuran-5-carboxylate (15).

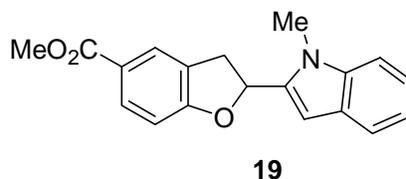
According to General Procedure A, reaction of 730 mg (3.74 mmol) of methyl 3-methyl-4-nitrobenzoate **11** and 785 mg (4.50 mmol) of 5-bromo-2-furaldehyde **14** with 5.61 mL

of TBAF (1.00 M in THF, 5.61 mmol) and 967 mg (7.48 mmol) of diisopropylethylamine gave 955 mg (79%) of **15** as a colorless solid: mp 92-93 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.51 (d, 2H, *J* = 9.7 Hz), 3.89 (s, 3H), 5.76 (t, 1H, *J* = 9.7 Hz), 6.30 (d, 1H, *J* = 3.3 Hz), 6.41 (d, 1H, *J* = 3.3 Hz), 6.81 (d, 1H, *J* = 8.4 Hz), 7.89 (d, 1H, *J* = 8.4 Hz), 7.91 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.1, 51.9, 77.8, 109.4, 111.5, 112.3, 123.1, 123.3, 126.5, 128.1, 131.4, 154.3, 162.8, 166.9; Anal. Calcd. For C₁₄H₁₁BrO₄: C, 52.04; H, 3.43. Found: C, 51.91; H, 3.20.



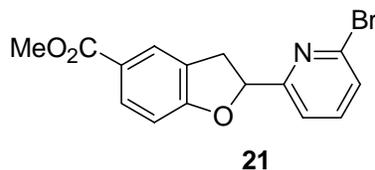
17

Methyl 2,3-Dihydro-2,2'-bi-1-benzofuran-5-carboxylate (17). According to General Procedure A, reaction of 800 mg (4.10 mmol) of methyl 3-methyl-4-nitrobenzoate **11** and 720 mg (4.92 mmol) of benzo[b]furan-2-carboxaldehyde **16** with 6.20 mL of TBAF (1.00 M in THF, 6.20 mmol) and 1.10 g (8.51 mmol) of diisopropylethylamine gave 992 mg (82%) of **17** as a colorless solid: mp 93-94 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.60 (d, 2H, *J* = 8.7 Hz), 3.91 (s, 3H), 5.95 (t, 1H, *J* = 8.7 Hz), 6.78 (s, 1H), 6.87 (d, 1H, *J* = 8.4 Hz), 7.31 (m, 2H), 7.48 (d, 1H, *J* = 8.1 Hz), 7.56 (d, 1H, *J* = 7.2 Hz), 7.94 (d, 1H, *J* = 8.4 Hz), 7.96 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 33.8, 52.0, 79.8, 105.1, 109.4, 111.6, 121.5, 123.1, 125.0, 126.6, 126.8, 127.8, 128.1, 131.4, 154.9, 155.4, 163.1, 166.9; Anal. Calcd. For C₁₈H₁₄O₄: C, 73.46; H, 4.79. Found: C, 73.73; H, 4.50.



Methyl 2-(1-Methyl-1H-indol-2-yl)-2,3-dihydro-1-benzofuran-5-carboxylate (19).

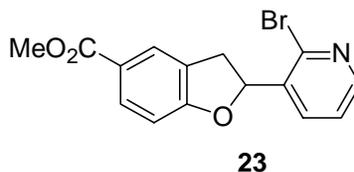
According to General Procedure B, reaction of 1.28 g (6.56 mmol) of methyl 3-methyl-4-nitrobenzoate **11** and 870 mg (5.46 mmol) of 1-methylindole-2-carboxaldehyde **18** with 9.84 mL of TBAF (1.00 M in THF, 9.84 mmol) and 1.70 g (13.12 mmol) of diisopropylethylamine gave 1.14 g (68%) of **19** as a colorless solid: mp 117-118 °C; ; ¹H NMR (CDCl₃, 400 MHz) δ 3.64 (d, 2H, *J* = 8.9 Hz), 3.84 (s, 3H), 3.92 (s, 3H), 6.08 (t, 1H, *J* = 8.9 Hz), 6.59 (s, 1H), 6.83 (d, 1H, *J* = 8.4 Hz), 7.13 (t, 1H, *J* = 7.1 Hz), 7.28 (t, 1H, *J* = 7.1 Hz), 7.36 (d, 1H, *J* = 8.3 Hz), 7.61 (d, 1H, *J* = 7.9 Hz), 7.93 (d, 1H, *J* = 8.4 Hz), 8.00 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 30.4, 34.0, 51.9, 78.4, 101.1, 109.3, 109.5, 119.9, 121.1, 122.6, 123.2, 126.7, 126.9, 131.4, 137.2, 137.8, 138.6, 163.0, 167.0; Anal. Calcd. For C₁₉H₁₇NO₃: C, 74.24; H, 5.58; N, 4.56. Found: C, 74.15; H, 5.45; N, 4.48.



Methyl 2-(6-Bromopyridin-2-yl)-2,3-dihydro-1-benzofuran-5-carboxylate (21).

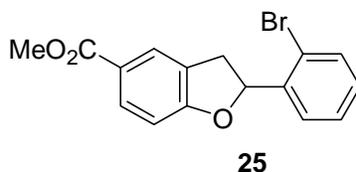
According to General Procedure B, reaction of 710 mg (3.64 mmol) of methyl 3-methyl-4-nitrobenzoate **11** and 564 mg (3.03 mmol) of 6-bromo-2-pyridinecarboxaldehyde **20** with 5.46 mL of TBAF (1.00 M in THF, 5.46 mmol) and 941 mg (7.28 mmol) of

diisopropylethylamine gave 780 mg (77%) of **21** as a colorless oil: ^1H NMR (CDCl_3 , 400 MHz) δ 3.37 (dd, 1H, $J = 16.0$ and 6.6 Hz), 3.73 (dd, 1H, $J = 16.0$ and 10.1 Hz), 3.83 (s, 3H), 5.85 (dd, 1H, $J = 10.1$ and 6.6 Hz), 6.87 (d, 1H, $J = 8.4$ Hz), 7.37 (m, 2H), 7.51 (m, 1H), 7.83 (s, 1H), 7.87 (d, 1H, $J = 8.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 36.1, 51.9, 84.2, 109.2, 118.8, 123.6, 126.4, 126.9, 127.3, 132.7, 139.3, 141.8, 162.1, 163.2, 166.7; Anal. Calcd. For $\text{C}_{15}\text{H}_{12}\text{BrNO}_3$: C, 53.91; H, 3.62; N, 4.19. Found: C, 53.88; H, 3.51; N, 4.06.

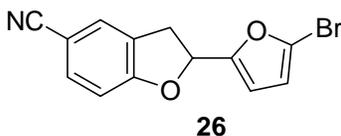


Methyl 2-(2-Bromopyridin-3-yl)-2,3-dihydro-1-benzofuran-5-carboxylate (23).

According to General Procedure A, reaction of 420 mg (2.15 mmol) of methyl 3-methyl-4-nitrobenzoate **11** and 478 mg (2.58 mmol) of 2-bromo-3-pyridinecarboxaldehyde **22** with 3.22 mL of TBAF (1.00 M in THF, 3.22 mmol) and 556 mg (4.30 mmol) of diisopropylethylamine gave 590 mg (85%) of **23** as a colorless solid: mp 96-97 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 3.04 (dd, 1H, $J = 16.0$ and 7.0 Hz), 3.85 (s, 3H), 3.90 (dd, 1H, $J = 16.0$ and 9.9 Hz), 6.01 (dd, 1H, $J = 9.9$ and 7.0 Hz), 6.91 (d, 1H, $J = 8.4$ Hz), 7.24 (m, 1H), 7.70 (dd, 1H, $J = 7.6$ and 1.9 Hz), 7.84 (s, 1H), 7.91 (d, 1H, $J = 8.4$ Hz), 8.28 (dd, 1H, $J = 4.7$ and 1.9 Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 36.9, 52.0, 82.6, 109.2, 123.1, 123.8, 126.0, 126.9, 127.1, 131.5, 134.9, 138.6, 140.6, 149.4, 163.2, 166.7; Anal. Calcd. For $\text{C}_{15}\text{H}_{12}\text{BrNO}_3$: C, 53.91; H, 3.62; N, 4.19. Found: C, 53.88; H, 3.46; N, 4.06.

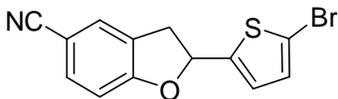


Methyl 2-(2-Bromophenyl)-2,3-dihydro-1-benzofuran-5-carboxylate (25). According to General Procedure B, reaction of 720 mg (3.69 mmol) of methyl 3-methyl-4-nitrobenzoate **11** and 560 mg (3.02 mmol) of 2-bromobenzaldehyde **24** with 5.53 mL of TBAF (1.00 M in THF, 5.53 mmol) and 954 mg (7.38 mmol) of diisopropylethylamine gave 800 mg (83%) of **25** as a colorless solid: mp 57-58 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.07 (dd, 1H, *J* = 15.9 and 7.2 Hz), 3.86 (dd, 1H, *J* = 15.9 and 9.3 Hz), 3.89 (s, 3H), 6.12 (dd, 1H, *J* = 9.3 and 7.2 Hz), 6.95 (d, 1H, *J* = 8.4 Hz), 7.18 (dt, 1H, *J* = 7.7 and 1.0 Hz), 7.31 (dt, 1H, *J* = 7.7 and 1.0 Hz), 7.46 (dd, 1H, *J* = 7.7 and 1.0 Hz), 7.59 (dd, 1H, *J* = 7.7 and 1.0 Hz), 7.88 (s, 1H), 7.95 (d, 1H, *J* = 8.4 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 37.1, 51.9, 84.0, 109.1, 120.9, 123.4, 126.5, 127.0, 127.8, 129.4, 131.4, 132.9, 141.1, 163.7, 166.9; Anal. Calcd. For C₁₆H₁₃BrO₃: C, 57.68; H, 3.93. Found: C, 57.66; H, 3.89.



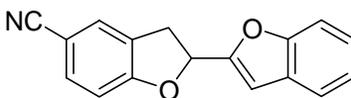
2-(5-Bromo-2-furyl)-2,3-dihydro-1-benzofuran-5-carboxylate (26). According to General Procedure B, reaction of 640 mg (3.95 mmol) of 3-methyl-4-nitrobenzonitrile **12** and 576 mg (3.29 mmol) of 5-bromo-2-furaldehyde **14** with 5.92 mL of TBAF (1.00 M in THF, 5.92 mmol) and 1.02 g (7.90 mmol) of diisopropylethylamine gave 840 mg (88%) of **26** as a colorless solid: mp 119 °C (decomp); ¹H NMR (CDCl₃, 400 MHz) δ 3.52 (d,

2H, $J = 8.9$ Hz), 5.78 (t, 1H, $J = 8.9$ Hz), 6.31 (d, 1H, $J = 3.3$ Hz), 6.43 (d, 1H, $J = 3.3$ Hz), 6.83 (d, 1H, $J = 8.2$ Hz), 7.46 (d, 1H, $J = 8.2$ Hz), 7.48 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 33.2, 77.9, 104.2, 110.6, 112.0, 112.4, 119.4, 123.5, 127.7, 128.8, 133.9, 135.6, 162.4; Anal. Calcd. For $\text{C}_{13}\text{H}_8\text{BrNO}_2$: C, 53.82; H, 2.78; N, 4.83. Found: C, 53.70; H, 2.57; N, 4.57.



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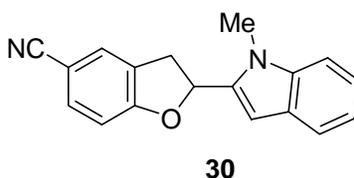
2-(5-Bromo-2-thiophene)-2,3-dihydro-1-benzofuran-5-carboxylate (28). According to General Procedure A, reaction of 500 mg (3.10 mmol) of 3-methyl-4-nitrobenzonitrile **12** and 710 mg (3.70 mmol) of 5-bromo-2-thiophenecarboxaldehyde **27** with 6.20 mL of TBAF (1.00 M in THF, 6.20 mmol) and 1.00 g (7.70 mmol) of diisopropylethylamine gave 770 mg (82%) of **28** as a colorless solid: mp 97-98 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 3.35 (dd, 1H, $J = 16.1$ and 7.2 Hz), 3.68 (dd, $J = 16.1$ and 5.2 Hz), 5.98 (dd, 1H, $J = 7.2$ and 5.2 Hz), 6.88 (m, 2H), 6.96 (d, 1H, $J = 3.6$ Hz), 7.49 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 37.2, 81.0, 104.6, 110.7, 113.3, 119.3, 126.1, 127.6, 128.9, 129.8, 134.0, 144.7, 162.2; Anal. Calcd for $\text{C}_{13}\text{H}_8\text{BrNOS}$: C, 51.00; H, 2.63; N, 4.57. Found: C, 50.98; H, 2.62; N, 4.50.



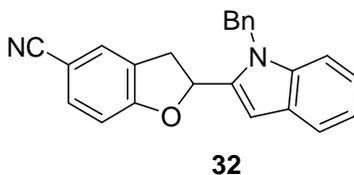
29

2,3-Dihydro-2,2'-bi-1-benzofuran-5-carbonitrile (29). According to General Procedure A, reaction of 700 mg (4.30 mmol) of 3-methyl-4-nitrobenzonitrile **12** and 760 mg (5.20 mmol) of benzo[b]furan-2-carboxaldehyde **16** with 6.50 mL of TBAF (1.00 M in THF, 6.50 mmol) and 1.10 g (8.50 mmol) of diisopropylethylamine gave 920 mg

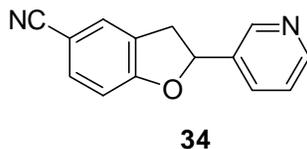
(82%) of **29** as a light yellow solid: mp 119-120 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.63 (d, 2H, *J* = 8.6 Hz), 5.99 (t, 1H, *J* = 8.6 Hz), 6.82 (s, 1H), 6.90 (d, 1H, *J* = 8.3 Hz), 7.27 (d, 1H, *J* = 7.1 Hz), 7.33 (t, 1H, *J* = 7.1 Hz), 7.52 (m, 3H), 7.58 (d, 1H, *J* = 8.3 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 33.7, 78.6, 104.4, 105.5, 110.6, 111.6, 119.4, 121.5, 123.2, 125.2, 127.6, 127.8, 128.9, 133.9, 154.1, 155.4, 162.6; Anal. Calcd. For C₁₇H₁₁NO₂: C, 78.15; H, 4.24; N, 5.36. Found: C, 77.77; H, 4.14; N, 5.22.



2-(1-Methyl-1H-indol-2-yl)-2,3-dihydro-1-benzofuran-5-carboxylate (30). According to General Procedure B, reaction of 660 mg (4.07 mmol) of **12** and 540 mg (3.39 mmol) of *N*-methyl-2-indolecarboxaldehyde (**18**) with 6.10 mL of TBAF (1.00 M in THF, 6.10 mmol) and 1.05 g (8.14 mmol) of diisopropylethylamine gave 690 mg (79%) of **30** as a colorless solid: mp 169-170 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.65 (d, 2H, *J* = 8.8 Hz), 3.85 (s, 3H), 6.10 (t, 1H, *J* = 8.8 Hz), 6.59 (s, 1H), 6.85 (d, 1H, *J* = 8.4 Hz), 7.15 (t, 1H, *J* = 7.2 Hz), 7.30 (m, 1H), 7.37 (d, 1H, *J* = 8.2 Hz), 7.48 (dd, 1H, *J* = 8.2 and 1.3 Hz), 7.53 (s, 1H), 7.62 (d, 1H, *J* = 8.4 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 30.4, 33.7, 78.4, 101.1, 102.8, 104.0, 109.3, 110.6, 120.0, 121.2, 122.7, 126.8, 128.1, 128.8, 133.9, 136.5, 138.6, 162.4; Anal. Calcd. For C₁₈H₁₄N₂O: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.44; H, 5.05; N, 10.11.

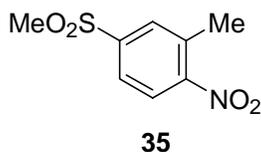


2-(1-Benzyl-1H-indol-2-yl)-2,3-dihydro-1-benzofuran-5-carbonitrile (32). According to the General Procedure A, reaction of 530 mg (3.26 mmol) of **12** and 920 mg (3.91 mmol) of *N*-benzyl-2-indolecarboxaldehyde (**31**) with 4.90 mL of TBAF (1.00 M in THF, 4.90 mmol) and 845 mg (6.54 mmol) of diisopropylethylamine gave 851 mg (79%) of **32** as a colorless foam: ^1H NMR (CDCl_3 , 400 MHz) δ 3.56 (m, 2H), 5.54 (s, 2H), 5.99 (t, 1H, $J = 9.1$ Hz), 6.68 (s, 1H), 6.76 (d, 1H, $J = 8.3$ Hz), 7.03 (m, 2H), 7.16 (t, 1H, $J = 7.3$ Hz), 7.29 (m, 5H), 7.46 (d, 1H, $J = 8.3$ Hz), 7.49 (s, 1H), 7.66 (d, 1H, $J = 7.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 33.8, 47.3, 78.2, 101.8, 104.1, 109.9, 110.6, 119.4, 120.3, 121.3, 123.0, 126.0, 127.0, 127.5, 128.1, 128.7, 128.8, 133.8, 136.8, 137.6, 138.4, 162.3; Anal. Calcd. For $\text{C}_{24}\text{H}_{18}\text{N}_2\text{O}$: C, 82.26; H, 5.18; N, 7.99. Found: C, 82.60, H, 5.21; N, 8.01.

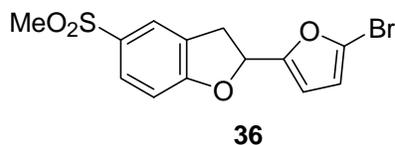


2-(Pyridin-3-yl)-2,3-dihydro-1-benzofuran-5-carbonitrile (34). According General Procedure A, reaction of 530 mg (3.27 mmol) of **12** and 421 mg (3.92 mmol) of 3-pyridinecarboxaldehyde (**33**) with 4.91 mL of TBAF (1.00 M in THF, 4.91 mmol) and 845 mg (6.54 mmol) of diisopropylethylamine gave 680 mg (93%) of **34** as a colorless

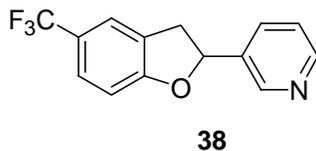
oil: ^1H NMR (CDCl_3 , 400 MHz) δ 3.19 (dd, 1H, $J = 16.0$ and 8.0 Hz), 3.69 (dd, 1H, $J = 16.0$ and 9.7 Hz), 5.85 (dd, 1H, $J = 9.7$ and 8.0 Hz), 6.87 (d, 1H, $J = 8.4$ Hz), 7.27 (m, 1H), 7.43 (m, 2H), 7.64 (m, 1H), 8.53 (dd, 1H, $J = 4.8$ and 1.5 Hz), 8.58 (d, 1H, $J = 2.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 37.2, 82.9, 104.3, 110.4, 119.3, 123.7, 127.7, 128.9, 133.3, 133.9, 136.2, 147.4, 150.0, 162.8; Anal. Calcd. For $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}$: C, 75.66, 4.54; N, 12.60. Found: C, 75.32; H, 4.41; N, 12.58.



1-(Methylsulfonyl)-3-methyl-4-nitrobenzene (35). To a stirred solution of 6.00 g (29.8 mmol) of 4-nitro-1-(methylsulfonyl)benzene² in 50 mL of THF at -10 °C was added dropwise 12.0 mL (35.04 mmol) of a 3M solution of methylmagnesium chloride. The resulting dark solution was stirred for 30 min at 0 °C and then quenched with 30 mL of 1N aqueous iodine solution. The mixture was extracted with 150 mL of EtOAc, dried over MgSO_4 , and concentrated under reduced pressure. The residue was purified by silica gel chromatography to afford 2.57 g (40%) of **35** as a yellow solid: mp 111-112 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 2.66 (s, 3H), 3.10 (s, 3H), 7.92 (d, 1H, $J = 8.4$ Hz), 7.95 (s, 1H), 8.06 (d, 1H, $J = 8.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 20.0, 44.3, 125.5, 126.1, 131.9, 134.9, 144.0, 152.3; Anal. Calcd. For $\text{C}_8\text{H}_9\text{NO}_4\text{S}$: C, 44.64; H, 4.21; N, 6.51. Found: C, 44.82; H, 4.11; N, 6.55.

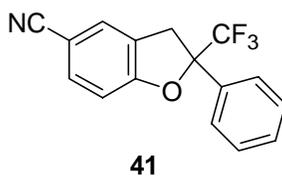


2-(5-Bromo-2-furyl)-5-methylsulfonyl-2,3-dihydro-1-benzofuran (36). According to General Procedure A, reaction of 594 mg (2.76 mmol) of **35** and 580 mg (3.31 mmol) of 5-bromo-2-furaldehyde **14** with 4.14 mL of TBAF (1.00 M in THF, 4.14 mmol) and 713 mg (5.52 mmol) of diisopropylethylamine gave 445 mg (47%) of **36** as a yellow solid: mp 115 °C (decomp); ¹H NMR (CDCl₃, 400 MHz) δ 3.04 (s, 3H), 3.55 (d, 2H, *J* = 9.4 Hz), 5.82 (t, 1H, *J* = 9.4 Hz), 6.31 (d, 1H, *J* = 3.3 Hz), 6.43 (d, 1H, *J* = 3.3 Hz), 6.90 (d, 1H, *J* = 8.4 Hz), 7.76 (d, 1H, *J* = 8.4 Hz), 7.78 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 33.3, 45.0, 110.1, 112.0, 112.4, 123.4, 124.6, 127.8, 129.4, 133.0, 153.6, 163.2; Anal. Calcd. For C₁₃H₁₁BrO₄S: C, 45.50; H, 3.23. Found: C, 45.23; H, 3.14.



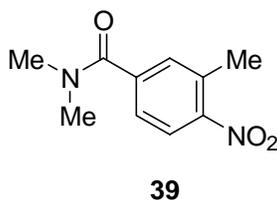
2-(3-Pyridin-3-yl)-5-trifluoromethyl-2,3-dihydro-1-benzofuran (38). According to General Procedure A, reaction of 500 mg (3.10 mmol) of **37**³ and 400 mg (3.72 mmol) of 3-pyridinecarboxaldehyde **33** with 4.65 mL of TBAF (1.00 M in THF, 4.65 mmol) and 800 mg (6.20 mmol) of diisopropylethylamine gave 270 mg (33%) of **38** as a yellow oil: ¹H NMR (CDCl₃, 400 MHz) δ 3.26 (dd, 1H, *J* = 16.1 and 7.6 Hz) 3.75 (dd, 1H, *J* = 16.1 and 9.4 Hz), 5.89 (dd, 1H, *J* = 9.4 and 7.6 Hz), 6.95 (d, 1H, *J* = 8.8 Hz) 7.33 (dd, 1H, *J* = 7.8 and 4.8 Hz), 7.47 (s, 1H), 7.48 (d, 1H, *J* = 7.6 Hz), 7.73 (dt, 1H, *J* = 8.0 and 2.0 Hz), 8.61 (d, 1H, *J* = 1.4 and 4.8 Hz), 8.66 (d, 1H, *J* = 2.0 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ

37.6, 82.7, 109.5, 122.4 (q, $J = 4.0$ Hz), 123.6 (q, $J = 32.4$ Hz), 123.8, 124.4 (q, $J = 271.4$ Hz), 126.5 (q, $J = 4.0$ Hz), 126.9, 133.3, 136.7, 147.6, 149.8, 162.0; ^{19}F NMR (CDCl_3 , 376 MHz) δ -61.6; Anal. Calcd for $\text{C}_{14}\text{H}_{10}\text{F}_3\text{NO}$: C, 63.40; H, 3.80; N, 5.28. Found: C, 63.02; H, 3.63; N, 5.31.

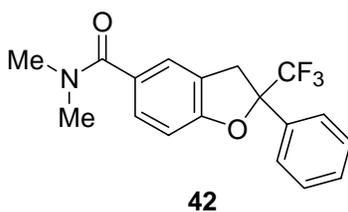


2-Phenyl-2-trifluoromethyl-2,3-dihydro-1-benzofuran-5-carbonitrile (41).

According to General Procedure A, reaction of 370 mg (2.28 mmol) of **12** and 476 mg (2.73 mmol) of 2,2,2-trifluoroacetophenone **40** with 3.42 mL of TBAF (1.00 M in THF, 3.42 mmol) and 589 mg (4.56 mmol) of diisopropylethylamine gave 640 mg (97%) of **41** as a colorless oil: ^1H NMR (CDCl_3 , 400 MHz) δ 3.69 (d, 1H, $J = 16.5$ Hz), 4.02 (d, 1H, $J = 16.5$ Hz), 7.05 (d, 1H, $J = 8.4$ Hz), 7.44 (m, 4H), 7.53 (d, 1H, $J = 8.4$ Hz), 7.61 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 38.3, 89.8 (q, $J = 30$ Hz), 105.6, 110.9, 119.0, 124.4 (q, $J = 284$ Hz), 126.4, 128.7, 128.8, 129.6, 134.1, 135.9, 161.6; ^{19}F NMR (CDCl_3 , 376 MHz) δ -81.3; Anal. Calcd. For $\text{C}_{16}\text{H}_{10}\text{F}_3\text{NO}$: C, 66.44; H, 3.48; N, 4.84. Found: C, 66.12; H, 3.22; N, 4.83.



***N,N*-Dimethyl-3-methyl-4-nitrobenzamide (39).** To slurry of 5.00 g (27.6 mmol) of 3-methyl-4-nitrobenzoic acid in 100 mL of CH₂Cl₂ was added 4.20 g (33.12 mmol) of oxalyl chloride followed by one drop of DMF. The resulting mixture became homogeneous after stirring for 4 h at rt and was concentrated under reduced pressure. The residue was redissolved in 50 mL of CH₂Cl₂ and added dropwise to an excess of aqueous dimethylamine. After 30 min the reaction mixture was extracted with 100 mL of CH₂Cl₂, washed with 100 mL of 10% aqueous HCl, and 100 mL of brine. After drying over MgSO₄, the solvent was removed under reduced pressure and the residual solid was recrystallized from an EtOAc/hexane mixture to provide 5.31 g (100%) of **39** as a light yellow solid: mp 68-69 °C; ¹H NMR (CDCl₃, 400 MHz) δ 2.58 (s, 3H); 2.94 (s, 3H), 3.09 (s, 3H), 7.33 (d, 1H, *J* = 8.3 Hz), 7.37 (s, 1H), 7.95 (d, 1H, *J* = 8.3 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 20.3, 35.3, 39.4, 124.8, 125.4, 131.4, 134.1, 141.0, 149.4, 169.4; Anal. Calcd. For C₁₀H₁₂N₂O₃: C, 57.68; H, 5.81; N, 13.45. Found: C, 57.51; H, 5.69; N, 13.33.



***N,N*-Dimethyl 2-phenyl-2-trifluoromethyl-2,3-dihydro-1-benzofuran-5-carbamide (42).** According to General Procedure A, reaction of 380 mg (1.97 mmol) of **39** and 413 mg (2.37 mmol) of 2,2,2-trifluoroacetophenone **40** with 2.96 mL of TBAF (1.00 M in THF, 2.96 mmol) and 510 mg (3.94 mmol) of diisopropylethylamine gave 570 mg (86%)

of **42** as a light yellow solid: mp 114-115 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.03 (br s, 6H), 3.64 (d, 1H, *J* = 16.0 Hz), 3.99 (d, 1H, *J* = 16.0 Hz), 6.96 (d, 1H, *J* = 8.4 Hz), 7.31 (m, 2H), 7.40 (m, 3H), 7.61 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 38.8, 89.1 (q, *J* = 30 Hz), 109.4, 124.4, 124.5 (q, *J* = 284 Hz), 126.4, 126.9, 128.4, 128.6, 129.3, 130.1, 136.8, 159.3, 171.3; ¹⁹F NMR (CDCl₃, 376 MHz) δ -81.1; Anal. Calcd. For C₁₈H₁₆F₃NO₂: C, 64.47; H, 4.81; N, 4.18. Found: C, 64.13; H, 4.67; N, 4.11.

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3. Zumstein sen, F.; Assmann, E.; Koenigsferger, R.; Holzbauer, R.; Zumstein jun, F. German Patent, DE2750170, 1978.