Novel and Selective Palladium-Catalyzed Annulation of 2-Alkynylphenols to Form 2-Substituted 3-Halobenzo[*b*]furans

Liang Yun, Shi Tang, Xu-Dong Zhang, Li-Qiu Mao, Ye-Xiang Xie and Jin-Heng Li*

*Key Laboratory of Chemical Biology & Traditional Chinese Medicine Research,
College of Chemistry and Chemical Engineering, Hunan Normal University,
Changsha 410081, China*

jhli@hunnu.edu.cn

Supporting Information

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(A) Materials:

2-Alkynylphenols **1a–g** were prepared from the reaction of the corresponding 2-iodophenols with terminal alkynes by known procedures.¹

(B) Typical experimental procedure

(1) Typical experimental procedure for the palladium-catalyzed annulation of 2-(2-*n*-octylethynyl)phenol (1a**) to form 2-octylbenzofuran (**2a**).** A mixture of 2-alkynylphenol **1a** (0.3 mmol), PdX₂ (5 mol %) and DCE (5 mL) was stirred at room temperature for the indicated time until complete consumption of starting material as judged by TLC and GC analysis. Then the mixture was filtered and evaporated, the residue was purified by flash column chromatography to afford **2a** (hexane/ethyl acetate).

(2) Typical experimental procedure for the synthesis of 2-substituted 3-halobenzo[*b*]furans **3 and **4**.** A mixture of 2-alkynylphenol **1** (0.3 mmol), PdX₂ (5 – 10 mol %), CuX₂ (3 equiv), HEt₃NX (0.2 equiv) and DCE (5 mL) was stirred at the indicated reaction temperature for 6-24 h until complete consumption of starting material as judged by TLC and GC analysis. Then the mixture was filtered and evaporated, the residue was purified by flash column chromatography to afford **3** or **4** (hexane/ethyl acetate).

(C) Analytical data for **2, **3** and **4****

2-octylbenzofuran (2a): Colorless oil; ^1H NMR (400 MHz) δ : 7.48 (d, $J = 8.0$ Hz, 1H), 7.41 (d, $J = 8.4$ Hz, 1H), 7.22 – 7.15 (m, 2H), 6.37 (s, 1H), 2.76 (t, $J = 7.6$ Hz, 2H), 1.77 – 1.70 (m, 2H), 1.41 – 1.27 (m, 10H), 0.88 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz) δ : 159.8, 154.6, 129.0, 123.0, 122.3, 120.1, 110.7, 101.7, 31.8, 29.3, 29.2, 28.4, 27.7, 22.7, 14.1; LRMS (EI, 20 eV) m/z (%): 230 (M^+ , 64), 187 (11), 173 (8), 145 (13), 131 (100); HRMS (EI) for $\text{C}_{16}\text{H}_{22}\text{O}$ (M^+): calcd. 230.1680, found 230.1678.

2-phenylbenzofuran (2b)¹: White solid, mp 118-121 °C (uncorrected); ^1H NMR (400 MHz) δ : 7.87 (d, $J = 7.2$ Hz, 2H), 7.58 (d, $J = 7.6$ Hz, 1H), 7.52 (d, $J = 8.0$ Hz, 1H), 7.45 (t, $J = 7.2$ Hz, 2H), 7.33 (t, $J = 7.2$ Hz, 1H), 7.28 (t, $J = 7.2$ Hz, 1H), 7.23 (t, $J = 7.2$ Hz, 1H), 7.03 (s, 1H); ^{13}C NMR (100 MHz) δ : 155.9, 154.9, 130.4, 129.2, 128.8, 128.5, 124.9, 124.2, 122.9, 120.9, 111.2, 101.3; LRMS (EI, 20 eV) m/z (%): 194 (M^+ , 100);

2-*p*-tolylbenzofuran (2c)²: White solid, mp 129-132 °C (uncorrected); ^1H NMR (400 MHz) δ : 7.76 (d, $J = 8.0$ Hz, 2H), 7.57 (d, $J = 8.4$ Hz, 1H), 7.51 (d, $J = 7.6$ Hz, 1H), 7.26 – 7.22 (m, 4H), 6.97 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz) δ : 156.2, 154.8, 138.6, 129.5, 129.4, 127.8, 124.9, 124.0, 122.9, 120.8, 111.1, 100.6, 21.4; LRMS (EI, 20 eV) m/z (%): 208 (M^+ , 100).

2-*tert*-butylbenzofuran (2d)³: Colorless oil; ^1H NMR (400 MHz) δ : 7.48 (d, $J = 8.8$ Hz, 1H), 7.41 (d, $J = 7.6$ Hz, 1H), 7.23 – 7.14 (m, 2H), 6.35 (s, 1H), 1.38 (s, 9H);

^{13}C NMR (100 MHz) δ : 167.4, 154.5, 128.8, 123.0, 122.2, 120.3, 110.7, 98.9, 31.6, 28.8; LRMS (EI, 20 eV) m/z (%): 174 (M^+ , 23), 159 (100).

6-methyl-2-phenylbenzofuran (2e)^{3,4}: White solid, mp 143-144 °C (uncorrected); ^1H NMR (400 MHz) δ : 7.84 (d, J = 7.6 Hz, 2H), 7.44 (t, J = 8.0 Hz, 3H), 7.33 (t, J = 7.2 Hz, 2H), 7.06 (d, J = 8.0 Hz, 1H), 6.97 (s, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz) δ : 155.3, 155.2, 134.5, 130.6, 128.7, 128.2, 126.6, 124.7, 124.3, 120.3, 111.4, 101.2, 21.8; LRMS (EI, 20 eV) m/z (%): 208 (M^+ , 100).

5,7-dichloro-2-phenylbenzofuran (2f)^{3,4}: White solid, mp 127-128 °C (uncorrected); ^1H NMR (400 MHz) δ : 7.86 (d, J = 7.6 Hz, 2H), 7.46 – 7.42 (m, 4H), 7.26 (s, 1H), 6.96 (s, 1H); ^{13}C NMR (100 MHz) δ : 158.1, 149.2, 131.4, 129.4, 129.3, 128.9, 128.6, 125.2, 124.2, 119.0, 117.1, 101.1; LRMS (EI, 20 eV) m/z (%): 262 (M^+ , 100).

5-nitro-2-phenylbenzofuran (2g)^{3,4}: Yellow solid, mp 152-153 °C (uncorrected); ^1H NMR (400 MHz) δ : 8.51 (s, 1H), 8.22 (d, J = 8.8 Hz, 1H), 7.88 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 8.8 Hz, 1H), 7.50 (t, J = 7.2 Hz, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.14 (s, 1H); ^{13}C NMR (100 MHz) δ : 159.2, 157.6, 144.3, 129.7, 129.6, 129.1, 129.0, 125.2, 120.1, 117.3, 111.4, 101.6; LRMS (EI, 20 eV) m/z (%): 239 (M^+ , 100).

2-octyl-3-bromobenzofuran (3a): Colorless oil; ^1H NMR (400 MHz) δ : 7.44 – 7.40 (m, 2H), 7.28 – 7.25 (m, 2H), 2.87 – 2.80 (m, 2H), 1.76 – 1.72 (m, 2H), 1.33–1.26 (m, 10H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz) δ : 155.9, 128.3, 124.3, 123.1, 120.7, 119.1, 111.0, 94.1, 31.8, 29.2, 27.9, 27.8, 27.5, 26.6, 22.6, 14.1; LRMS (EI, 20 eV) m/z (%): 310 ($\text{M}^+ + 2$, 60), 308 (M^+ , 58), 229 ($\text{M}^+ - \text{Br}$, 100); HRMS (EI) for $\text{C}_{16}\text{H}_{21}^{79}\text{BrO}$ (M^+): calcd. 308.0782, found 308.0781.

2-phenyl-3-bromobenzofuran (3b): White solid, 62–63 °C; ^1H NMR (400 MHz) δ : 8.17 (d, J = 8.4 Hz, 2H), 7.57 – 7.30 (m, 7H); ^{13}C NMR (100 MHz) δ : 153.1, 150.3, 129.6, 129.5, 129.0, 128.6, 126.7, 125.6, 123.5, 119.9, 111.3, 93.8; LRMS (EI, 20 eV) m/z (%): 274 ($\text{M}^+ + 2$, 98), 272 (M^+ , 100), 195 ($\text{M}^+ - \text{Br}$, 19); HRMS (EI) for $\text{C}_{14}\text{H}_9^{79}\text{BrO}$ (M^+): calcd. 271.9842, found 271.9842.

2-*p*-tolyl-3-bromobenzofuran (3c): White solid, mp 72–74 °C; ^1H NMR (400 MHz) δ : 8.06 (d, J = 8.8 Hz, 2H), 7.54 (d, J = 8.8 Hz, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.36 – 7.24 (m, 4H), 2.41 (s, 3H); ^{13}C NMR (100 MHz) δ : 153.0, 150.6, 139.2, 129.5, 129.3, 126.7, 125.3, 123.4, 119.7, 111.2, 93.1, 21.5; LRMS (EI, 20 eV) m/z (%): 288 ($\text{M}^+ + 2$, 97), 286 (M^+ , 100), 207 ($\text{M}^+ - \text{Br}$, 17); HRMS (EI) for $\text{C}_{15}\text{H}_{11}^{79}\text{BrO}$ (M^+): calcd. 285.9999, found 285.9997.

2-*tert*-butyl-3-bromobenzofuran (3d): Colorless oil; ^1H NMR (400 MHz) δ : 7.46 (d, J = 8.8 Hz, 1H), 7.41 (d, J = 8.8 Hz, 1H), 7.28 – 7.25 (m, 2H), 1.51 (s, 9H); ^{13}C

NMR (100 MHz) δ : 160.0, 152.3, 129.5, 124.4, 122.9, 119.2, 110.9, 91.2, 34.3, 28.9; LRMS (EI, 20 eV) m/z (%): 254 ($M^+ + 2$, 21), 252 (M^+ , 23), 239 (100), 237 (90), 158 ($M^+ - CH_3 - Br$, 36); HRMS (EI) for $C_{12}H_{13}^{79}BrO$ (M^+): calcd. 252.0154, found 252.0150.

3-bromo-6-methyl-2-phenylbenzofuran (3e): White solid, mp 120-121 °C (uncorrected); 1H NMR (400 MHz) δ : 8.13 (d, $J = 8.0$ Hz, 2H), 7.46 (t, $J = 7.6$ Hz, 2H), 7.40 – 7.37 (m, 2H), 7.27 (s, 1H), 7.10 (d, $J = 7.6$ Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz) δ : 153.4, 149.5, 136.0, 129.6, 128.7, 128.5, 127.1, 126.5, 124.8, 119.3, 111.4, 93.7, 21.6; LRMS (EI, 20 eV) m/z (%): 288 ($M^+ + 2$, 100), 286 (M^+ , 98), 207 ($M^+ - Br$, 12), 178 (40), 103 (12), 89 (21), 76 (21); HRMS (EI) for $C_{15}H_{11}^{79}BrO$ (M^+): calcd. 285.9993, found 285.9991.

3-bromo-5,7-dichloro-2-phenylbenzofuran (3f): White solid, mp 133-134 °C (uncorrected); 1H NMR (400 MHz) δ : 8.17 (d, $J = 8.0$ Hz, 2H), 7.53 – 7.42 (m, 4H), 7.35 – 7.33 (m, 1H); ^{13}C NMR (100 MHz) δ : 152.7, 147.6, 131.9, 129.9, 129.4, 128.7, 128.5, 127.0, 125.6, 118.2, 117.4, 93.0; LRMS (EI, 20 eV) m/z (%): 344 ($M^+ + 4$, 44), 342 ($M^+ + 2$, 100), 340 (M^+ , 62), 233 (51), 263 (20), 261 ($M^+ - Br$, 32), 228 (8), 226 ($M^+ - Br - Cl$, 24), 163 (64), 116 (24), 98 (29), 81 (29); HRMS (EI) for $C_{14}H_7Cl_2^{79}BrO$ (M^+): calcd. 339.9057, found 339.9053.

3-bromo-5-nitro-2-phenylbenzofuran (3g): Pale yellow solid, mp 143-144 °C (uncorrected); ^1H NMR (400 MHz) δ : 8.44 (s, 1H), 8.25 (d, J = 8.8 Hz, 1H), 8.14 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 9.2 Hz, 1H), 7.53 – 7.47 (m, 3H); ^{13}C NMR (100 MHz) δ : 155.8, 153.6, 144.6, 130.2, 130.1, 128.8, 128.3, 126.9, 121.2, 116.5, 111.8, 93.8; LRMS (EI, 20 eV) m/z (%): 319 ($\text{M}^+ + 2$, 97), 317 (M^+ , 100), 238 ($\text{M}^+ - \text{Br}$, 16); HRMS (EI) for $\text{C}_{14}\text{H}_8^{79}\text{BrNO}_3$ (M^+): calcd. 316.9688, found 316.9687.

2-octyl-3-chlorobenzofuran (4a): Colorless oil; ^1H NMR (400 MHz) δ : 7.38 (d, J = 8.0 Hz, 1H), 7.34 – 7.31 (m, 1H), 7.28 – 7.25 (m, 2H), 2.85 (t, J = 7.6 Hz, 2H), 1.76 – 1.72 (m, 2H), 1.34– 1.26 (m, 10H), 0.88 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz) δ : 159.2, 154.2, 131.0, 124.4, 124.2, 123.1, 120.7, 110.9, 31.8, 29.3, 29.2, 29.0, 27.9, 27.8, 22.7, 14.1; LRMS (EI, 20 eV) m/z (%): 266 ($\text{M}^+ + 2$, 17), 264 (M^+ , 48), 229 ($\text{M}^+ - \text{Cl}$, 27), 165 (100); HRMS (EI) for $\text{C}_{16}\text{H}_{21}^{35}\text{ClO}$ (M^+): calcd. 264.1287, found 264.1285.

2-phenyl-3-chlorobenzofuran (4b): White solid, mp 68-70 °C; ^1H NMR (400 MHz) δ : 8.20 (d, J = 8.8 Hz, 2H), 7.28 – 7.25 (m, 5H), 7.40 – 7.31 (m, 2H); ^{13}C NMR (100 MHz) δ : 153.9, 153.0, 132.4, 130.0, 129.2, 128.5, 127.6, 125.7, 123.5, 121.8, 111.2; LRMS (EI, 20 eV) m/z (%): 230 ($\text{M}^+ + 2$, 43), 228 (M^+ , 100), 193 ($\text{M}^+ - \text{Cl}$, 28); HRMS (EI) for $\text{C}_{14}\text{H}_9^{35}\text{ClO}$ (M^+): calcd. 228.0347, found 228.0346.

2-*p*-tolyl-3-chlorobenzofuran (4c): White solid, m.p. 79-80 °C; ^1H NMR (400 MHz) δ : 8.07 (d, J = 8.8 Hz, 2H), 7.49 – 7.43 (m, 2H), 7.37 – 7.30 (m, 4H), 2.43 (s,

3H); ^{13}C NMR (100 MHz) δ : 153.8, 153.3, 139.4, 132.5, 129.2, 127.4, 127.2, 125.4, 123.4, 121.7, 111.1, 21.5; LRMS (EI, 20 eV) m/z (%): 244 ($\text{M}^+ + 2$, 41), 242 (M^+ , 100), 207 ($\text{M}^+ - \text{Cl}$, 32); HRMS (EI) for $\text{C}_{15}\text{H}_{11}^{35}\text{ClO}$ (M^+): calcd. 242.0504, found 242.0504.

2-*tert*-butyl-3-chlorobenzofuran (4d): Colorless oil; ^1H NMR (400 MHz) δ : 7.50 (d, $J = 8.8$ Hz, 1H), 7.40 – 7.38 (m, 1H), 7.28 – 7.25 (m, 2H), 1.49 (s, 9H); ^{13}C NMR (100 MHz) δ : 158.8, 151.9, 128.1, 124.3, 122.8, 118.3, 111.0, 110.7, 34.1, 28.7; LRMS (EI, 20 eV) m/z (%): 210 ($\text{M}^+ + 2$, 8), 208 (M^+ , 25), 193 (100), 158 ($\text{M}^+ - \text{CH}_3 - \text{Cl}$, 20); HRMS (EI) for $\text{C}_{12}\text{H}_{13}^{35}\text{ClO}$ (M^+): calcd. 208.0659, found 208.0654.

3-chloro-6-methyl-2-phenylbenzofuran (4e): White solid, mp 122-123 °C (uncorrected); ^1H NMR (400 MHz) δ : 8.16 (d, $J = 7.6$ Hz, 1H), 8.11 (d, $J = 8.0$ Hz, 1H), 7.50 – 7.29 (m, 5H), 7.11 (d, $J = 8.0$ Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz) δ : 153.1, 148.3, 136.0, 129.5, 128.7, 128.6, 126.4, 126.2, 126.1, 124.8, 118.4, 111.6, 21.8; LRMS (EI, 20 eV) m/z (%): 244 ($\text{M}^+ + 2$, 34), 242 (M^+ , 100), 207 ($\text{M}^+ - \text{Cl}$, 12), 178 (61), 152 (20), 103 (43), 89 (42), 76 (65); HRMS (EI) for $\text{C}_{15}\text{H}_{11}^{35}\text{ClO}$ (M^+): calcd. 242.0498, found 242.0495.

3,5,7-trichloro-2-phenylbenzofuran (4f): White solid, mp 128-130 °C (uncorrected); ^1H NMR (400 MHz) δ : 8.19 (d, $J = 8.4$ Hz, 2H), 7.55 – 7.45 (m, 4H), 7.36 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR (100 MHz) δ : 155.4, 148.2, 134.8, 130.0, 128.9, 128.6, 127.7,

125.5, 125.2, 120.2, 119.0, 101.2; LRMS (EI, 20 eV) m/z (%): 298 ($M^+ + 2$, 7), 296 (M^+ , 8), 263 (46), 261 ($M^+ - Cl$, 71), 233 (74), 226 ($M^+ - 2Cl$, 38), 194 ($M^+ - 3Cl$, 20), 163 (100), 81 (46); HRMS (EI) for $C_{14}H_7^{35}Cl_3O$ (M^+): calcd. 295.9563, found 295.9561.

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(D) Spectra

2-octylbenzofuran (2a)

2-octylbenzofuran (2a)

2-phenylbenzofuran (2b)

2-phenylbenzofuran (2b)

2-*p*-tolylbenzofuran (2c)

2-*tert*-butylbenzofuran (2d)

2-*tert*-butylbenzofuran (2d)

6-methyl-2-phenylbenzofuran (2e)

6-methyl-2-phenylbenzofuran (2e)

5,7-dichloro-2-phenylbenzofuran (2f)

5,7-dichloro-2-phenylbenzofuran (2f)

5-nitro-2-phenylbenzofuran (2g)

5-nitro-2-phenylbenzofuran (2g)

2-octyl-3-bromobenzofuran (3a)

2-octyl-3-bromobenzofuran (3a)

2-phenyl-3-bromobenzofuran (3b)

2-phenyl-3-bromobenzofuran (3b)

2-*p*-tolyl-3-bromobenzofuran (3c)

2-*p*-tolyl-3-bromobenzofuran (3c)

2-*tert*-butyl-3-bromobenzofuran (3d)

2-*tert*-butyl-3-bromobenzofuran (3d)

3-bromo-6-methyl-2-phenylbenzofuran (3e)

3-bromo-6-methyl-2-phenylbenzofuran (3e)

3-bromo-5,7-dichloro-2-phenylbenzofuran (3f)

3-bromo-5,7-dichloro-2-phenylbenzofuran (3f)

3-bromo-5-nitro-2-phenylbenzofuran (3g)

3-bromo-5-nitro-2-phenylbenzofuran (3g)

2-octyl-3-chlorobenzofuran (4a)

2-octyl-3-chlorobenzofuran (4a)

2-phenyl-3-chlorobenzofuran (4b)

2-phenyl-3-chlorobenzofuran (4b)

2-*p*-tolyl-3-chlorobenzofuran (4c)

2-*p*-tolyl-3-chlorobenzofuran (4c)

2-*tert*-butyl-3-chlorobenzofuran (4d)

2-*tert*-butyl-3-chlorobenzofuran (4d)

3-chloro-6-methyl-2-phenylbenzofuran (4e)

3,5,7-trichloro-2-phenylbenzofuran (4f)

3,5,7-trichloro-2-phenylbenzofuran (4f)