Electronic Supplementary Information

DBU-catalyzed annulation strategy for modular assembly of 2,3-

difunctionalized dihydrobenzofurans

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1. General information

Experimental: Unless otherwise noted, all the reactions were carried out using standard roundbottom flasks under air atmosphere. Reactions were monitored using thin-layer chromatography (TLC) on precoated silica gel 60 F_{254} plates. Visualization of the developed plates was performed under UV light (245 or 365 nm) stain. Silica-gel flash column chromatography was performed using 200–300 mesh silica gel.

Materials: Unless otherwise indicated, starting catalysts and materials were obtained from Energy Chemicals, Bidepharm. Moreover, commercially available reagents were used without additional purification

Instrumentation: Melting points were recorded on an uncorrected Melting Point instrument. The ¹H NMR spectra were recorded on a 300 MHz and 500 MHz NMR spectrometers. Spectra were referenced internally to the residual proton resonance in CDCl₃ (δ 7.26 ppm), or with TMS (δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ¹³C NMR spectra were recorded on a 75 or 125 MHz spectrometer and the spectra were referenced to CDCl₃ (δ = 77.16 ppm, the middle peak), and all ¹³C NMR were recorded with proton broadband decoupling and indicated as ¹³C{¹H} NMR. Coupling constants (*J*) were reported in Hertz (Hz). Multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet), and the coupling constants (*J*) are reported in Hertz (Hz). HRMS analysis with a quadrupole time-of-flight mass spectrometer yielded ion mass/charge (m/z) ratios in atomic mass units.

2. General procedure for the synthesis of 2-(2-nitrovinyl)phenols 1



To a 100 mL round-bottomed flask equipped with a stirring bar were added nitromethane (5.0 mL), NH₄OAc (77 mg, 1.0 mmol), and acetic acid (2.0 mL). The mixture was stirred at 90 °C for 15 min before addition of salicylaldehydes (5.0 mmol). The reaction mixture was heated at 135 °C for 3 h. After cooling to ambient temperature, the reaction was worked up with Et_2O (50 mL) and brine (50 mL). Purification by column chromatography on silica gel (200-300 mesh), using ethyl acetate and petroleum ether (1:8, v/v) as the elution solvent to give desired 2-(2-nitrovinyl)phenols **1** as a yellow solid. All the substrates are known compounds.

3. General procedure for the synthesis of 2,3-dihydrobenzofuran derivatives 3 and 5



To a solution of DBU (0.4 mmol) in DCM, 2-(2-nitrovinyl)phenols 1 (1 mmol) and α bromoacetophenones 2 (1 mmol) were added and the resulting mixture was stirred at room temperature for about 6 h. Upon the completion of this reaction, the mixture diluted with DCM (3×10 mL), and washed with water. Organic layers were combined, dried over Na₂SO₄, filtered, and evaporated under vacuum. The residue was purified using flash column chromatography with a silica gel (200-300 mesh), using ethyl acetate and petroleum ether (1:10-1:8, v/v) as the elution solvent to give desired products 3 and 5.

4. Procedure for the synthesis of compound 6.



A mixture of **3aa** (0.2 mmol), iron powder and HCl (1.0 equiv.) were added under air atmosphere to a resealable screw-capped Schlenk tube. EtOH (2.0 mL) was then added. The tube sealed with a Teflon-coated cap and the resulting mixture was stirred in an oil bath preheated to 80 °C for 12 h (monitored by TLC). Upon the completion of this reaction, the mixture was cooled to room temperature, extracted with DCM (3×10 mL), and washed with water. Organic layers were combined, dried over Na₂SO₄, filtered, and evaporated under vacuum. The residue was purified using flash column chromatography with a silica gel (200-300 mesh), using ethyl acetate and petroleum ether (1:10-1:8, v/v) as the elution solvent to give desired products **6** as a white solid in 73% yield.

5. Characterization data for all products.



(3-(Nitromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3aa). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, $R_f = 0.5$) to afford a light yellow oil in 93% yield (263 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.08 (d, J = 7.5Hz, 2H), 7.62-7.67 (m, 1H), 7.50-7.55 (m, 2H) 7.21 (d, J = 7.5Hz, 2H) , 6.87-6.98 (m, 2H) 5.88 (d, J = 7.2Hz, 1H), 4.70-4.80 (m, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 193.50, 158.58, 134.11, 130.12, 129.54, 128.83, 124.68, 123.68, 121.94, 110.52, 85.16, 77.28, 41.89, 29.71; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₆H₁₃NO₄ + H]⁺ 284.0917, found 284.0920.



(3-(Nitromethyl)-2,3-dihydrobenzofuran-2-yl)(*p*-tolyl)methanone (3ab). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a light yellow oil in 81% yield (240 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.97 (d, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 8.1,Hz, 2H), 7.20 (d, *J* = 7.5Hz, 2H), 6.85-6.96 (m, 2H), 5.84 (d, *J* = 5.4 Hz, 1H) 4.69-4.79 (m, 3H), 2.44 (s,3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 193.05, 158.64, 145.21, 130.07, 129.64, 129.56, 124.69, 123.78, 121.86, 110.46, 85.07, 77.30, 41.92, 21.83; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₇H₁₅NO₄ + H]⁺ 298.1074, found 298.1078.



(4-Methoxyphenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3ac). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, $R_f = 0.5$) to afford a light yellow oil in 88% yield (275 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.08 (d, J = 9.0Hz, 2H), 7.19-7.26 (m, 2H), 6.86-7.01 (m, 4H), 5.83 (d, J = 7.5Hz, 1H), 4.69-4.81 (m, 3H), 3.90 (s, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 191.82, 164.28, 158.63, 131.97, 130.04, 127.27, 124.65, 123.84, 121.83, 114.07, 110.43, 85.09, 77.33, 55.60, 41.94; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₇H₁₅NO₅ + H]⁺ 314.1023, found 314.1018.



(4-Fluorophenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3ad). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 63% yield (190 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.21–8.09 (m, 2H), 7.25–7.16 (m, 4H), 7.01–6.92 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.82 (d, *J* = 5.0 Hz, 1H), 4.84 – 4.80 (m, 1H), 4.80 – 4.66 (m, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 192.1, 166.4 (d, *J*_{C-F} = 255.1 Hz), 158.5, 132.5 (d, *J*_{C-F} = 9.3 Hz), 130.9 (d, *J*_{C-F} = 2.7 Hz), 130.2, 124.8, 123.7, 122.1, 116.1 (d, *J*_{C-F} = 21.8 Hz), 110.6, 85.4, 77.3, 41.9; ¹⁹F NMR (471 MHz, CDCl₃) δ -102.99; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₆H₁₃FNO₄ 302.0823, found 302.0826.

(4-Chlorophenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3ae). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a yellow oil in 75% yield (237 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.03 (d, J = 8.7 Hz, 2H), 7.49 (d, J = 8.7 Hz, 2H), 7.21(d, J = 7.5 Hz, 2H), 6.93-6.98 (m, 1H), 6.86 (d, J = 8.1Hz, 1H), 5.81 (d, J = 4.8 Hz, 1H), 4.64-4.84 (m, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 192.27, 158.10, 140.37, 132.44, 130.78, 129.91, 128.90, 124.45, 123.31, 121.81, 110.25, 85.01, 76.92, 41.46; HRMS (ESI-TOF) m/z: [M + H]⁺ calcd for [C₁₆H₁₂ClNO₄ + H]⁺ 318.0528, found 318.0525.

(4-Bromophenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3af). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow liquid in 63% yield (227 mg); ¹H NMR (500 MHz, CDCl₃) δ 7.97–7.93 (m, 2H), 7.69–7.63 (m, 2H), 7.25–7.19 (m, 2H), 6.98–6.93 (m, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 5.81 (d, *J* = 5.0 Hz, 1H), 4.82–4.78 (m, 1H), 4.78–4.64 (m, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 192.8, 158.4, 133.2, 132.2, 131.2, 130.2, 129.6, 124.8, 123.6, 122.2, 110.6, 85.4, 77.2, 41.8; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₆H₁₃BrNO₄ 362.0022, found 362.0021.

[1,1'-Biphenyl]-4-yl(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3ag). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 71% yield (255 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.17 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 7.5 Hz, 2H), 7.49 (d, J = 7.5 Hz, 2H), 7.46–7.39 (m, 1H), 7.26–7.19 (m, 2H), 6.97 (d, J = 7.5 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 5.90 (d, J = 5.0 Hz, 1H), 4.86–4.81 (m, 1H), 4.81–4.68 (m, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 193.1, 158.7, 146.9, 139.8, 133.2, 130.29, 130.27, 129.2, 128.6, 127.6, 127.5, 124.8, 123.8, 122.1, 110.7, 85.4, 77.4, 42.0; HRMS (ESI-TOF) m/z: [M + H]⁺ calcd for C₂₂H₁₈NO₄ 360.1230, found 360.1232.

(3-(Nitromethyl)-2,3-dihydrobenzofuran-2-yl)(*m*-tolyl)methanone (3ah). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 70% yield (208 mg); ¹H NMR (500 MHz, CDCl₃) δ 7.91–7.83 (m, 2H), 7.47–7.38 (m, 2H), 7.25–7.18 (m, 2H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 5.87 (d, *J* = 4.5 Hz, 1H), 4.79–4.75 (m, 1H), 4.75–4.66 (m, 2H), 2.44 (s, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 193.7, 158.8, 138.9, 135.0, 134.5, 130.3, 130.1, 128.8, 126.8, 124.8, 123.8, 122.0, 110.7, 85.2, 77.5, 42.1, 21.5; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₇H₁₆NO₄ 298.1074, found 298.1073.

(3-Fluorophenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3ai). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 60% yield (180 mg); ¹H NMR (500 MHz, CDCl₃) δ 7.94–7.87 (m, 1H), 7.83–7.75 (m, 1H), 7.56–7.47 (m, 1H), 7.39–7.31 (m, 1H), 7.26–7.20 (m, 2H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 5.81 (d, *J* = 4.5 Hz, 1H), 4.85–4.80 (m, 1H), 4.80–4.66 (m, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 192.5, 162.9 (d, *J*_{C-F} = 247.0 Hz), 158.5, 136.5 (d, *J*_{C-F} = 6.8 Hz), 130.6 (d, *J*_{C-F} = 7.5 Hz), 130.3, 125.5 (d, *J*_{C-F} = 3.1 Hz), 124.8, 123.6, 122.2, 121.3 (d, *J*_{C-F} = 21.2 Hz), 116.5 (d, *J*_{C-F} = 22.6 Hz), 110.7, 85.5, 77.3, 41.9; ¹⁹F NMR (471 MHz, CDCl₃) δ -111.68; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₆H₁₃FNO₄ 302.0823, found 302.0815.

(3-Chlorophenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3aj). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 66% yield (209 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.06 (d, J = 2.0 Hz, 1H), 8.01–7.95 (m, 1H), 7.64–7.58 (m, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.25–7.19 (m, 2H), 7.01–6.92 (m, 1H), 6.87 (d, J = 8.0 Hz, 1H), 5.82 (d, J = 4.5 Hz, 1H), 4.84–4.79 (m, 1H), 4.79–4.65 (m, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 193.1, 158.4, 136.0, 135.2, 134.1, 130.3, 130.2, 129.7, 127.8, 124.8, 123.6, 122.2, 110.7, 85.4, 77.3, 41.8; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₆H₁₃ClNO₄ 318.0528, found 318.0525.

(3-Bromophenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3ak). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 64% yield (231 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.25–8.19 (m, 1H), 8.06–7.98 (m, 1H), 7.79–7.73 (m, 1H), 7.44–7.37 (m, 1H), 7.26–7.19 (m, 2H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 5.81 (d, *J* = 4.5 Hz, 1H), 4.84–4.79 (m, 1H), 4.79–4.65 (m, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 192.4, 158.4, 137.0, 136.2, 132.6, 130.5, 130.3, 128.2, 124.8, 123.5, 123.2, 122.2, 110.7, 85.4, 77.27, 41.8; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₆H₁₃BrNO₄ 362.0022, found 362.0019.

(3-(Nitromethyl)-2,3-dihydrobenzofuran-2-yl)(3-(trifluoromethyl)phenyl)methanone (3a). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 55% yield (193 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.36 (s, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.26–7.20 (m, 2H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 9.0 Hz, 1H), 5.86 (d, *J* = 4.5 Hz, 1H), 4.89–4.83 (m, 1H), 4.82–4.67 (m, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 192.6, 158.3, 135.1, 132.9, 131.5 (d, *J*_{C-F} = 33.0 Hz), 130.5 (d, *J*_{C-F} = 3.8 Hz), 130.4, 129.6, 126.6 (q, *J*_{C-F} = 3.9 Hz), 124.8, 123.5, 122.3, 110.6, 85.6, 77.3, 41.8; ¹⁹F NMR (471 MHz, CDCl₃) δ -62.83; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₇H₁₃F₃NO₄ 352.0791, found 352.0789.

(3-(Nitromethyl)-2,3-dihydrobenzofuran-2-yl)(*o*-tolyl)methanone (3am). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 74% yield (220 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.49–7.41 (m, 1H), 7.37–7.27 (m, 2H), 7.26–7.17 (m, 2H), 6.99–6.92 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.79–5.72 (m, 1H), 4.77–4.71 (m, 1H), 4.71–4.61 (m, 2H), 2.46 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 197.8, 158.8, 139.8, 134.7, 132.4, 132.3, 130.3, 129.5, 125.8, 124.7, 123.6, 122.0, 110.7, 86.3, 77.6, 42.3, 21.3; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₇H₁₆NO₄ 298.1074, found 298.1072.

Naphthalen-2-yl(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3an). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 10, R_f = 0.5) to afford a light yellow oil in 69% yield (229 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.72–8.63 (m,

1H), 8.13–8.00 (m, 2H), 7.98–7.87 (m, 2H), 7.71–7.55 (m, 2H), 7.26–7.19 (m, 2H), 6.97 (d, J = 7.5 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 6.04 (d, J = 4.5 Hz, 1H), 4.90–4.84 (m, 1H), 4.84–4.68 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 193.5, 158.8, 136.1, 132.6, 132.1, 131.8, 130.3, 130.1, 129.3, 128.9, 128.0, 127.2, 124.8, 124.7, 123.8, 122.1, 110.7, 85.4, 77.4, 42.2; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₂₂H₁₈NO₄ 334.1074, found 334.1079.

(5-Methyl-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3ba). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow oil in 75% yield (222 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.03 (d, J = 6.9 Hz, 2H), 7.57-7.63 (m, 1H), 7.45-7.50 (m, 2H), 6.97 (d, J = 7.2 Hz, 2H), 6.72 (d, J = 8.7 Hz, 1H), 5.80 (d, J = 3.6 Hz, 1H), 4.63-4.72(m, 3H), 2.25 (s,3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 193.68, 156.51, 134.37, 134.04, 131.44, 130.58, 129.51, 128.80, 125.06, 123.63, 110.05, 85.27, 77.32, 42.00, 20.79; HRMS (ESI) m/z: [M + H]⁺ calcd for [C₁₇H₁₅NO₄ + H]⁺ 298.1074, found 298.1076.

(5-Methyl-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(*p*-tolyl)methanone (3bb). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow solid in 83% yield (258 mg); mp 90-98 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 7.2 Hz, 2H), 6.72 (d, *J* = 9.0 Hz, 1H), 5.77 (d, *J* = 4.5 Hz, 1H), 4.62-4.71 (m, 3H), 2.40 (s, 3H), 2.24 (s, 3H); ¹³C {¹H} NMR (75 MHz, CDCl₃) δ 193.69 · 156.50 · 134.03, 130.58, 129.51, 128.79, 125.06, 110.04, 85.26, 77.31, 41.99, 20.77; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₈H₁₇NO₄ + H]⁺ 312.1230, found 312.1225.

(4-Methoxyphenyl)(5-methyl-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3bc). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow solid in 88% yield (287 mg); mp 75-77 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.10 (d, J = 9.0 Hz, 2H), 7.00-7.03 (m, 4H), 6.79 (d, J = 8.7 Hz, 1H), 5.83 (d, J = 3.9 Hz, 1H), 4.71-4.79 (m, 3H), 3.93 (s, 3H), 2.31 (s, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 192.40, 164.63, 156.96, 132.35, 131.73, 130.89, 127.71, 125.42, 124.17, 114.43, 110.38, 85.62, 55.98, 42.48, 21.19; HRMS (ESI-TOF) m/z: [M + H]⁺ calcd for [C₁₈H₁₇NO₅ + H]⁺ 328.1179, found 328.1172.

(4-Chlorophenyl)(5-methyl-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3be). This compound was purified by column chromatography (ethyl acetate/petroleum ether = $1: 8, R_f = 1: 8$

0.5) to afford a yellow solid in 71% yield (235 mg); mp 70-73 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.01 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 6.99 (s, 2H), 6.73 (d, J = 8.4 Hz, 1H), 5.77 (d, J = 4.2 Hz, 1H), 4.64-4.74 (m, 3H), 2.27 (s, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 192.68, 156.29, 140.47, 132.70, 131.59, 131.02, 130.63, 129.13, 125.08, 123.52, 85.37, 77.21, 41.80, 20.80; HRMS (ESI-TOF) m/z: [M + H]⁺ calcd for [C₁₇H₁₄ClNO₄ + H]⁺ 332.0684, found 332.0689.

(5-Chloro-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3ca). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow solid in 83% yield (263 mg); mp 85-89 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.07 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.21–7.14 (m, 2H), 6.80 (d, *J* = 9.2 Hz, 1H), 5.90 (d, *J* = 4.7 Hz, 1H), 4.81–4.76 (m, 1H), 4.76–4.64 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 193.04, 157.36, 134.40, 134.25, 130.27, 129.67, 129.01, 126.91, 125.70, 124.95, 111.68, 85.75, 41.81; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₆H₁₂ClNO₄ + H]⁺ 318.0528, found 318.0520.

(5-Chloro-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(4-chlorophenyl)methanone (3ce). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow oil in 75% yield (264 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.01 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 7.5 Hz, 2H), 6.78 (d, J = 9.0 Hz, 1H), 5.84 (d, J = 4.5 Hz, 1H) , 4.68-4.81 (m, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 192.31, 157.40, 141.26, 131.39, 129.61, 127.32, 125.85, 125.21, 11.93, 86.14, 77.12, 41.93; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₆H₁₁Cl₂NO₄ + H]⁺ 352.0138, found 352.0140.

(5-Bromo-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3da). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, $R_f = 0.5$) to afford a yellow oil in 80% yield (288 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.06 (d, J = 7.2 Hz, 2H), 7.62-7.67 (m, 1H), 7.50-7.55 (m, 2H), 7.30-7.33 (m, 2H), 6.75 (d, J = 8.7 Hz, 1H), 5.89 (d, J = 4.5 Hz, 1H), 4.69-4.76 (m, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 192.90, 157.76, 134.28, 134.11, 133.02, 129.54, 128.89, 127.71, 126.15, 113.73, 112.12, 85.55, 76.82, 41.60; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₆H₁₂BrNO₄ + H]⁺ 362.0022, found 362.0026.

(5-Bromo-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(p-tolyl)methanone (3db). This

compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, $R_f = 0.5$) to afford a yellow solid in 83% yield (311 mg); mp 105-110 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.96 (d, J = 8.4 Hz, 2H), 7.31-7.34 (m, 4H), 6.75 (d, J = 9.3 Hz, 1H), 5.87 (d, J = 4.5 Hz, 1H), 4.68-4.79 (m, 3H), 2.45 (s, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 192.43, 157.82, 145.45, 132.96, 131.56, 129.63, 127.69, 126.22, 113.64, 112.07, 85.47, 77.08, 41.62, 21.86; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₇H₁₄BrNO₄ + H]⁺ 376.0179, found 376.0189.

(5-Bromo-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(4-methoxyphenyl)methanone (3dc). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow solid in 88% yield (344 mg); mp 120 -125 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.04 (d, J = 9.0 Hz, 2H), 7.29-7.31 (m, 2H), 6.98 (d, J = 8.7 Hz, 2H), 6.74 (d, J = 9.0 Hz, 1H), 5.84 (d, J = 4.8 Hz, 1H), 4.69-4.78 (m, 3H), 3.89 (s,3H); ¹³C {¹H} NMR (75 MHz, CDCl₃) δ 191.23, 164.42, 157.83, 132.91, 131.99, 127.68, 126.33, 114.13, 113.59, 112.02, 85.46, 76.86, 55.63, 41.63; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₇H₁₄BrNO₅ + H]⁺ 392.0128, found 392.0123.

(5-Bromo-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(4-chlorophenyl)methanone (3de). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow oil in 75% yield (295 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.02 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.31-7.34 (m, 2H), 6.74 (d, J = 9.0 Hz, 1H), 5.84 (d, J = 4.8 Hz, 1H), 4.68-4.82 (m, 3H); ¹³C {¹H} NMR (75 MHz, CDCl₃) δ 191.90, 157.53, 140.85, 131.01, 129.22, 127.71, 126.01, 113.86, 112.10, 85.65, 76.71, 41.39; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₆H₁₁ClBrNO₄ + H]⁺ 395.9633, found 395.9635.

(6-Methoxy-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3ea). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, $R_f = 0.5$) to afford a yellow oil in 70% yield (219 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.05 (d, J = 7.2Hz, 2H), 7.61-7.66 (m, 1H), 7.49-7.54 (m, 2H), 7.07 (d, J = 8.1 Hz, 1H), 6.45-6.50 (m, 2H), 5.88 (d, J = 3Hz, 1H), 4.64-4.70 (m, 3H), 3.74 (s, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 193.62, 161.77, 160.03, 134.09, 129.44, 128.84, 124.89, 115.43, 107.93, 96.76, 85.91, 77.48, 55.55, 41.60; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₇H₁₅NO₅ + H]⁺ 314.1023, found 314.1017.

(6-Methoxy-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(p-tolyl)methanone (3eb). This

compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, $R_f = 0.5$) to afford a yellow oil in 72% yield (235 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.95 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.07 (d, J = 8.1 Hz, 1H), 6.46-6.50 (m, 2H) , 5.87 (d, J = 3.6 Hz, 1H) 4.64-4.70 (m, 3H), 3.75 (s, 3H), 2.44 (s, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 193.14, 161.75, 160.10, 145.18, 131.76, 129.55, 124.86, 115.50, 107.85, 96.73, 85.84, 77.52, 55.54, 41.66, 21.81; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₈H₁₇NO₅ + H]⁺ 328.1179, found 328.1174.

(6-Methoxy-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(4-methoxyphenyl)methanone (3ec). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow oil in 80% yield (274 mg); ¹H NMR (300 MHz, CDCl₃) δ 7.97 (d, J = 9.0 Hz, 2H), 6.99 (d, J = 8.1 Hz, 1H), 6.91 (d, J = 8.7 Hz, 2H), 6.38-6.43 (m, 2H), 5.77 (d, J = 1.5 Hz, 1H), 4.57-4.64 (m, 3H), 3.82 (s, 3H), 3.68 (s, 3H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 190.87, 163.20, 160.65, 159.03, 130.81, 123.79, 114.56, 113.01, 106.71, 95.65, 84.77, 76.48, 54.52, 40.61; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₈H₁₇NO₆ + H]⁺ 344.1129, found 344.1129.

MeO

(4-Chlorophenyl)(6-methoxy-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3ee). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow oil in 66% yield (229 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.01 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.1 Hz, 1H), 6.49 (d, J = 8.1 Hz, 1H), 6.44 (d, J = 8.1 Hz, 1H), 5.83 (d, J = 1.8 Hz, 1H), 4.64-4.73 (m, 3H), 3.75 (s, 3H); ¹³C {¹H} NMR (75 MHz, CDCl₃) δ 192.62, 161.78, 159.80, 140.57, 132.66, 130.94, 129.14, 124.89, 115.28, 108.02, 96.78, 86.05, 77.37, 55.56, 41.41; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₇H₁₄CINO₅ + H]⁺ 348.0633, found 348.0630.

(4-Chlorophenyl)(3-(nitromethyl)-2,3-dihydronaphtho[2,3-*b*]furan-2-yl)methanone (3fe). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow oil in 60% yield (220 mg); ¹H NMR (300 MHz, CDCl₃) δ 8.02 (d, *J* = 8.7 Hz, 2H), 7.70-7.85 (m, 3H), 7.49-7.56 (m, 3H), 7.36-7.41 (m, 1H), 7.14 (d, *J* = 9.0 Hz, 1H), 6.09 (d, *J* = 2.1 Hz, 1H), 5.15-5.20 (m, 1H), 4.99-5.05 (m, 1H), 4.63-4.71 (m, 1H); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 192.31, 156.62, 140.59, 130.02, 129.16, 121.42, 114.46, 112.16, 109.99, 86.12, 75.91, 41.75; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₂₀H₁₄ClNO₄ + H]⁺ 368.0684, found 368.0686.

3-(Nitromethyl)-3*H***-spiro[benzofuran-2,2'-inden]-1'(3'***H***)-one (5). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, R_f = 0.5) to afford a yellow oil in 65% yield (191 mg); ¹H NMR (300 MHz, CDCl₃) \delta 7.86 (d,** *J* **= 7.8 Hz, 1H), 7.66 (d,** *J* **= 7.5 Hz, 1H), 7.43-7.47 (m, 2H), 7.14-7.25 (m, 2H), 6.97 (d,** *J* **= 7.5 Hz, 1H), 6.81 (d,** *J* **= 8.1 Hz, 1H), 4.77-4.81 (m, 2H),4.58-4.62(m, 1H), 3.39 (s, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) \delta 200.21, 158.33, 150.55, 130.43, 128.91, 126.87, 125.91, 125.05, 124.53, 122.12, 110.72, 91.84, 75.71, 43.67, 35.85; HRMS (ESI-TOF)** *m/z***: [M + H]⁺ calcd for [C₁₇H₁₃NO₄ + H]⁺ 296.0917, found 296.0915.**

(*Z*)-2-benzylidene-3-(nitromethyl)-2,3-dihydrobenzofuran (6). This compound was purified by column chromatography (ethyl acetate/petroleum ether = 1: 8, $R_f = 0.5$) to afford a white solid in 73% yield (39 mg); mp 199-201 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.00-7.98 (m, 2H), 7.52-7.49 (m, 3H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 7.9 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.40 (d, *J* = 8.6 Hz, 1H), 4.52-4.63 (m, 1H), 4.29 (t, *J* = 8.1 Hz, 1H), 4.13 (d, *J* = 16.9 Hz, 1H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 169.84, 157.74, 132.82, 131.28, 130.41, 129.11, 129.01, 128.71, 125.48, 121.65, 109.95, 90.88, 68.19, 44.17; HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for [C₁₆H₁₄NO₃ + H]⁺ 268.0974, found 268.0978.

Figure S2. GC-MS spectra of possibly intermediate B

57. X-ray crystallographic data of compound 3q

Figure S1. ORTEP drawing of compound **3bb** (30% probability for the thermal ellipsoid).

The purified compound **3bb** is dissolved in a mixed solvent of dichloromethane and *n*-hexane, and placed in a dark cabinet to slowly evaporate. After several days, a colourless bulk crystal is obtained. The X-ray crystal-structure determinations were obtained on a Bruker Smart CCDC APEX-2 diffractometer (graphite-monochromated Mo $K\alpha$ radiation, λ =0.71073 nm) at 293.15 K.

| CCDC number | 2375967 | | |
|-------------------------------------|--|--|--|
| Identification code | 131202b_0m | | |
| Empirical formula | $C_{18}H_{17}NO_4$ | | |
| Formula weight | 311.32 | | |
| Temperature | 293.15(10) K | | |
| Wavelength | 0.71073 Å | | |
| Crystal system | monoclinic | | |
| Space group | C2/c | | |
| Unit cell dimensions | $a = 26.440(2) \text{ Å} \qquad \alpha = 90^{\circ}.$ | | |
| | $b = 7.9493(7) \text{ Å} \qquad \beta = 107.7360(10)^{\circ}.$ | | |
| | $c = 15.9676(13) \text{ Å} \gamma = 90^{\circ}.$ | | |
| Volume | 3196.5(5) Å ³ | | |
| Z | 8 | | |
| Density (calculated) | 1.294 Mg/m ³ | | |
| Absorption coefficient | 0.092 mm ⁻¹ | | |
| F(000) | 1312.0 | | |
| Crystal size | $0.14\times0.13\times0.11\ mm^3$ | | |
| 2Θ range for data collection | 3.234 to 55.284°. | | |
| Index ranges | $-34 \le h \le 33, -9 \le k \le 10, -20 \le l \le 20$ | | |
| Reflections collected | 13429 | | |
| Independent reflections | $3708 [R_{int} = 0.0248, R_{sigma} = 0.0212]$ | | |
| Data / restraints / parameters | 3708/0/209 | | |
| Goodness-of-fit on F ² | 1.052 | | |
| Final R indices [I>2sigma(I)] | $R_1 = 0.0471, wR_2 = 0.1350$ | | |
| R indices (all data) | $R_1 = 0.0584, wR_2 = 0.1464$ | | |
| Largest diff. peak and hole | 0.20 and -0.19 e.Å ⁻³ | | |

Table S1. Crystal data and structure refinement for compound 3bb.

8. ¹H and ¹³C NMR spectra for all compounds

(3-(Nitromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3aa)

(4-Methoxyphenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3ac)

S18

(4-bromophenyl)(3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3af)

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1 δ (ppm)

(5-Bromo-3-(nitromethyl)-2,3-dihydrobenzofuran-2-yl)(4-chlorophenyl)methanone (3de)

(4-Chlorophenyl)(3-(nitromethyl)-2,3-dihydronaphtho[2,3-b]furan-2-yl)methanone (3fe)

| 8.0391 8.0104 7.8538 7.8538 7.7842 7.7546 7.7546 7.7285 | 7.5820 7.5585 7.5139 7.5149 7.5149 7.5149 7.5149 7.4863 7.4863 7.3803 7.3803 7.3564 | 5.1535 5.1979 5.1979 5.1893 5.1893 5.1631 5.1631 5.1545 | 5.1459 5.0469 5.0368 5.0368 4.9928 4.7127 4.6776 4.6688 4.6688 |
|--|--|--|--|
| | THE TAXES THE COMPANY | | 10 |

