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Supporting Information

Synthesis of Benzo[*b*]azocin-2-ones by Aryl Amination and Ring-Expansion of α -(Iodophenyl)- β -oxoesters

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Ethyl 1-(2-iodophenyl)-2-oxocyclohexane-1-carboxylate (20b).^[25] According to GPA, TFAA (630 mg, 3.00 mmol), PIFA (1.12 g, 2.60 mmol) and β -oxoester **21b** (340 mg, 2.00 mmol) were converted in TFA (4 mL) and MeCN (4 mL) to furnish the title compound **20b** (468 mg, 1.26 mmol, 63%) after chromatography (SiO_2 , hexanes/MTBE 5:1, $R_f = 0.29$) as a colorless oil. $^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 1.27$ (t, $J = 7.1$ Hz, 3H), 1.75–1.91 (m, 2H), 1.97–2.07 (m, 2H), 2.58–2.85 (m, 4H), 4.20–4.37 (m, 2H), 6.96 (t, $J = 7.5$ Hz, 1H), 7.05 (d, $J = 7.9$ Hz, 1H), 7.32 (t, $J = 7.6$ Hz, 1H), 7.96 (d, $J = 7.8$ Hz, 1H) ppm. All spectroscopic data are in accordance with the literature.^[25] $\text{C}_{15}\text{H}_{17}\text{IO}_3$ (372.20 g mol $^{-1}$).

Methyl 1-(2-iodophenyl)-2-oxocycloheptane-1-carboxylate (20c).^[25] According to GPA, TFAA (315 mg, 1.50 mmol), PIFA (559 mg, 1.30 mmol) and β -oxoester **21c** (170 mg, 1.00 mmol) were converted in TFA (2 mL) and MeCN (2 mL) to furnish the the title compound **20c** (173 mg, 465 μmol , 47%) after chromatography (SiO_2 , hexanes/MTBE 2:1, $R_f = 0.43$) as a colorless oil. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.47–1.58 (m, 1H), 1.68–1.80 (m, 5H), 2.11–2.19 (m, 1H), 2.73–2.81 (m, 1H), 2.96–3.03 (m, 1H), 3.16–3.24 (m, 1H), 3.73 (s, 3H), 6.96 (t, $J = 7.6$ Hz, 1H), 7.02 (d, $J = 7.7$ Hz, 1H), 7.32 (t, $J = 7.7$ Hz, 1H), 7.94 (d, $J = 7.8$ Hz, 1H) ppm. All spectroscopic data are in accordance with the literature.^[25] $\text{C}_{15}\text{H}_{17}\text{IO}_3$ (372.20 g mol $^{-1}$).

Conversion of β -oxoester 20a with *n*-butylamine. According to GPB, β -oxoester **20a** (179 mg, 500 μ mol), K_3PO_4 (212 mg, 1.00 mmol) and CuI (14 mg, 75 μ mol) were converted with *n*-butylamine (0.5 mL). The crude product was purified by column chromatography (SiO_2 , hexanes/MTBE 1:1) to yield the benzazocinone **18b** (78 mg, 0.26 mmol, 51%, $R_f = 0.33$) as a colorless solid, mp 78 °C. As a second fraction, the acyclic amide **25b** (33 mg, 77 μ mol, 15%, $R_f = 0.17$) was obtained as a colorless oil.

Ethyl 1-butyl-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylate (18b).

1H -NMR (500 MHz, $CDCl_3$): $\delta = 0.87$ (t, $J = 7.3$ Hz, 3H), 1.16 (t, $J = 7.1$ Hz, 3H), 1.24–1.37 (m, 2H), 1.40–1.49 (m, 1H), 1.50–1.65 (m, 2H), 1.76–1.85 (m, 2H), 1.89–1.94 (m, 1H), 2.23 (dd, $J = 11.0$ Hz, $J = 7.8$ Hz, 1H), 2.44 (dd, $J = 13.4$ Hz, $J = 4.5$ Hz, 1H), 3.26 (ddd, $J = 13.3$ Hz, $J = 10.4$ Hz, $J = 5.0$ Hz, 1H), 3.55 (d, $J = 11.0$ Hz, 1H), 4.08 (dq, $J = 10.8$ Hz, $J = 7.1$ Hz, 1H), 4.16 (dq, $J = 10.8$ Hz, $J = 7.1$ Hz, 1H), 4.38 (ddd, $J = 13.3$ Hz, $J = 10.4$ Hz, $J = 5.9$ Hz, 1H), 7.21–7.24 (m, 1H), 7.28–7.32 (m, 2H), 7.33–7.35 (m, 1H) ppm. $^{13}C\{^1H\}$ -NMR (125 MHz, $CDCl_3$): $\delta = 13.85$ (CH_3), 13.98 (CH_3), 20.43 (CH_2), 24.27 (CH_2), 29.22 (CH_2), 31.95 (CH_2), 33.16 (CH_2), 44.78 (CH), 48.98 (CH_2), 61.88 (CH_2), 125.83 (CH), 126.87 (CH), 128.08 (CH), 128.41 (CH), 139.16 (C), 140.72 (C), 173.87 (C), 173.88 (C) ppm. IR (ATR): $\nu(\tilde{)} = 2960$ (w), 2937 (w), 2869 (w), 1734 (s), 1653 (vs), 1495 (m), 1456 (m), 1397 (m), 1302 (m), 1226 (m), 1187 (s), 1154 (m), 1102 (m), 1047 (m), 1028 (m), 767 (m), 741 (m) cm^{-1} . HR-MS (ESI): calcd. 310.1989 (for $C_{18}H_{25}LiNO_3^+$), found 310.1996 [$M + Li^+$]. $C_{18}H_{25}NO_3$ (303.40 $g\ mol^{-1}$).

Ethyl 6-(butylamino)-2-(2-iodophenyl)-6-oxohexanoate (25b).

1H -NMR (500 MHz, $CDCl_3$): $\delta = 0.91$ (t, $J = 7.3$ Hz, 3H), 1.20 (t, $J = 7.1$ Hz, 3H), 1.33 (sext, $J = 7.3$ Hz, 2H), 1.43–1.49 (m, 2H), 1.59–1.69 (m, 2H), 1.73–1.80 (m, 1H), 1.99–2.07 (m, 1H), 2.18 (t, $J = 7.5$ Hz, 2H), 3.23 (q, $J = 7.0$ Hz, 2H), 4.01 (t, $J = 7.4$ Hz, 1H), 4.07–4.18 (m, 2H), 5.53 (br s, 1H), 6.90–6.95 (m, 1H), 7.30–7.31 (m, 2H), 7.84 (d, $J = 7.9$ Hz, 1H) ppm. $^{13}C\{^1H\}$ -NMR (125 MHz, $CDCl_3$): $\delta = 13.73$ (CH_3), 14.09 (CH_3), 20.05 (CH_2), 23.53 (CH_2), 31.66 (CH_2), 32.93 (CH_2), 36.37 (CH_2), 39.21 (CH_2), 54.68 (CH), 60.99 (CH_2), 101.62 (C), 127.67 (CH), 128.65 (CH), 128.83 (CH), 139.75 (CH), 141.89 (C), 172.17 (C), 173.27 (C) ppm. IR (ATR): $\nu(\tilde{)} = 3300$ (w), 2938 (w), 1731 (vs), 1640 (vs), 1548 (s), 1465 (m), 1369 (m), 1178 (m), 1149 (s), 1010 (s), 746

(s) cm^{-1} . HR-MS (EI, 70 eV): calcd. 431.0952 (for $\text{C}_{18}\text{H}_{26}\text{INO}_3^+$), found 431.0952 [M^+]. $\text{C}_{18}\text{H}_{26}\text{INO}_3$ (431.31 g mol^{-1}).

Conversion of β -oxoester 20a with *n*-hexylamine. According to GPB, β -oxoester **20a** (179 mg, 500 μmol), K_3PO_4 (212 mg, 1.00 mmol) and CuI (14 mg, 75 μmol) were converted with *n*-hexylamine (0.5 mL). The crude mixture was separated by column chromatography (SiO_2 , hexanes/MTBE 1:2) to yield as the first fraction the benzofuran **23a** (4 mg, 0.02 mmol, 4%, $R_f = 0.65$) as a pale yellow oil. Secondly, the benzazocinone **18c** (83 mg, 0.25 mmol, 50%, $R_f = 0.34$) was eluted as a colorless oil. As third and fourth fractions, the acyclic amide **25c** (5 mg, 0.01 mmol, 2%, $R_f = 0.21$) and the acyclic amide **24c** (26 mg, 78 μmol , 16%, $R_f = 0.18$) were obtained, both as a colorless oils.

Ethyl 1-hexyl-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylate (18c).

$^1\text{H-NMR}$ (500 MHz, CDCl_3): $\delta = 0.80\text{--}0.82$ (m, 3H), 1.14 (t, $J = 7.1$ Hz, 3H), 1.21–1.23 (m, 5H), 1.26–1.32 (m, 1H), 1.39–1.64 (m, 3H), 1.74–1.85 (m, 2H), 1.87–1.92 (m, 1H), 2.21 (dd, $J = 11.0$ Hz, $J = 7.8$ Hz, 1H), 2.40–2.44 (m, 1H), 3.23 (ddd, $J = 13.2$ Hz, $J = 10.8$ Hz, $J = 4.9$ Hz, 1H), 3.53 (d, $J = 10.7$ Hz, 1H), 4.06 (dq, $J = 10.8$ Hz, $J = 7.1$ Hz, 1H), 4.13 (dq, $J = 10.8$ Hz, $J = 7.1$ Hz, 1H), 4.35 (ddd, $J = 13.2$ Hz, $J = 10.8$ Hz, $J = 5.8$ Hz, 1H), 7.19–7.22 (m, 1H), 7.26–7.33 (m, 3H) ppm. $^{13}\text{C}\{^1\text{H}\}\text{-NMR}$ (125 MHz, CDCl_3): $\delta = 13.92$ (2 CH_3), 22.36 (CH_2), 24.21 (CH_2), 26.70 (CH_2), 26.90 (CH_2), 31.51 (CH_2), 31.92 (CH_2), 33.09 (CH_2), 44.72 (CH), 49.17 (CH_2), 60.82 (CH_2), 125.81 (CH), 126.80 (CH), 128.03 (CH), 128.36 (CH), 139.10 (C), 140.65 (C), 173.74 (C), 173.83 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 2931$ (w), 2864 (w), 1733 (s), 1652 (vs), 1493 (m), 1454 (m), 1396 (m), 1300 (m), 1224 (m), 1183 (s), 1150 (m), 1098 (m), 1046 (m), 1025 (m), 765 (m), 738 (m) cm^{-1} . HR-MS (EI, 70 eV): calcd. 331.2142 (for $\text{C}_{20}\text{H}_{29}\text{NO}_3^+$), found 310.2140 [M^+]. $\text{C}_{20}\text{H}_{29}\text{NO}_3$ (331.46 g mol^{-1}).

Ethyl 6-(hexylamino)-2-(2-iodophenyl)-6-oxohexanoate (25c). $^1\text{H-NMR}$ (500 MHz, CDCl_3): $\delta = 0.88$ (t, $J = 7.0$ Hz, 3H), 1.21 (t, $J = 7.1$ Hz, 3H), 1.28–1.33 (m, 6H), 1.45–1.49 (m, 2H), 1.62–1.68 (m, 2H), 1.73–1.80 (m, 1H), 2.00–2.07 (m, 1H), 2.19 (t, $J = 7.5$ Hz, 2H), 3.22 (q, $J = 7.0$ Hz, 2H), 4.02 (dd, $J = 8.1$ Hz, $J = 6.7$ Hz, 1H), 4.08–4.19 (m, 2H), 5.49 (br s, 1H), 6.91–6.96 (m, 1H), 7.30–7.31 (m, 2H), 7.85 (d, $J = 7.9$ Hz, 1H) ppm. $^{13}\text{C}\{^1\text{H}\}\text{-NMR}$ (125 MHz, CDCl_3): $\delta = 14.02$ (CH_3), 14.10 (CH_3), 22.55

(CH₂), 23.55 (CH₂), 26.59 (CH₂), 29.58 (CH₂), 31.47 (CH₂), 32.94 (CH₂), 36.41 (CH₂), 39.53 (CH₂), 54.70 (CH), 61.01 (CH₂), 101.64 (C), 127.69 (CH), 128.67 (CH), 128.85 (CH), 139.77 (CH), 141.91 (C), 172.16 (C), 173.30 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3276 (w), 2929 (s), 2861 (m), 1733 (vs), 1642 (vs), 1549 (s), 1465 (s), 1437 (m), 1370 (m), 1178 (m), 1150 (s), 1010 (s), 747 (s) cm⁻¹. HR-MS (EI, 70 eV): calcd. 459.1265 (for C₂₀H₃₀INO₃⁺), found 459.1262 [M⁺]. C₂₀H₃₀INO₃ (459.37 g mol⁻¹).

Ethyl 6-(hexylamino)-6-oxo-2-phenylhexanoate (24c). ¹H-NMR (500 MHz, CDCl₃): δ = 0.86–0.88 (m, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.25–1.32 (m, 6H), 1.43–1.49 (m, 2H), 1.53–1.66 (m, 2H), 1.73–1.82 (m, 1H), 2.03–2.12 (m, 1H), 2.12–2.17 (m, 2H), 3.19–3.23 (m, 2H), 3.52 (t, *J* = 7.6 Hz, 1H), 4.07 (dq, *J* = 10.8 Hz, *J* = 7.1 Hz, 1H), 4.14 (dq, *J* = 10.8 Hz, *J* = 7.1 Hz, 1H), 5.48 (br s, 1H), 7.22–7.32 (m, 5H) ppm. ¹³C{¹H}-NMR (125 MHz, CDCl₃): δ = 13.99 (CH₃), 14.09 (CH₃), 22.52 (CH₂), 23.72 (CH₂), 26.56 (CH₂), 29.55 (CH₂), 31.44 (CH₂), 33.05 (CH₂), 36.39 (CH₂), 39.50 (CH₂), 51.55 (CH), 60.77 (CH₂), 127.20 (CH), 127.80 (2 CH), 128.59 (2 CH), 138.94 (C), 172.22 (C), 173.88 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3294 (w), 2954 (m), 2927 (m), 2857 (m), 1732 (vs), 1641 (vs), 1549 (m), 1455 (m), 1175 (m), 1148 (m), 1026 (m), 732 (m), 698 (s) cm⁻¹. HR-MS (EI, 70 eV): calcd. 333.2298 (for C₂₀H₃₁NO₃⁺), found 333.2297 [M⁺]. C₂₀H₃₁NO₃ (333.47 g mol⁻¹).

Conversion of β -oxoester 20a with cyclohexylamine. According to GPB, β -oxoester **20a** (179 mg, 500 μ mol), K₃PO₄ (212 mg, 1.00 mmol) and CuI (14 mg, 75 μ mol) were converted with cyclohexylamine (0.5 mL). The crude mixture was separated by column chromatography (SiO₂, hexanes/MTBE 1:2) to yield the benzofuran **23a** (13 mg, 56 μ mol, 11%, *R*_f = 0.65) as a pale yellow oil in the first fraction. Secondly, the benzazocinone **18d** (83 mg, 0.25 mmol, 50%, *R*_f = 0.31) was eluted as a colorless solid, mp 120–123 °C. As third fraction, the acyclic amide **24d** (22 mg, 66 μ mol, 13%, *R*_f = 0.19) was obtained as a colorless oil.

Ethyl 1-cyclohexyl-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylate (18d). ¹H-NMR (500 MHz, CDCl₃): δ = 0.97–1.05 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.33–1.39 (m, 1H), 1.43–1.53 (m, 3H), 1.55–1.60 (m, 1H), 1.68–1.70 (m, 2H), 1.77–1.84 (m, 3H), 1.86–1.92 (m, 1H), 2.14–2.23 (m, 2H), 2.40–2.44 (m, 1H), 3.63 (d, *J* = 11.1 Hz, 1H), 4.09 (dq, *J* = 10.7 Hz, *J* = 7.2 Hz, 1H), 4.16 (dq, *J* = 10.7 Hz, *J* = 7.2

Hz, 1H), 4.56 (tt, $J = 12.0$ Hz, $J = 3.5$ Hz, 1H), 7.20–7.21 (m, 1H), 7.27–7.30 (m, 1H), 7.32–7.37 (m, 2H) ppm. $^{13}\text{C}\{^1\text{H}\}$ -NMR (125 MHz, CDCl_3): $\delta = 13.89$ (CH_3), 24.43 (CH_2), 25.45 (CH_2), 25.80 (CH_2), 25.92 (CH_2), 29.97 (CH_2), 32.15 (CH_2), 32.78 (CH_2), 33.57 (CH_2), 44.86 (CH), 55.36 (CH), 60.77 (CH_2), 126.81 (CH), 127.30 (CH), 127.82 (CH), 128.85 (CH), 138.30 (C), 140.51 (C), 173.77 (C), 173.84 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 2930$ (m), 2856 (w), 1732 (vs), 1645 (vs), 1492 (m), 1446 (m), 1369 (m), 1302 (m), 1222 (m), 1186 (s), 1143 (m), 1024 (m), 769 (m), 745 (m) cm^{-1} . HR-MS (EI, 70 eV): calcd. 329.1985 (for $\text{C}_{20}\text{H}_{27}\text{NO}_3^+$), found 329.1985 [M^+]. $\text{C}_{20}\text{H}_{27}\text{NO}_3$ (329.44 g mol^{-1}).

Ethyl 6-(cyclohexylamino)-6-oxo-2-phenylhexanoate (24d). ^1H -NMR (500 MHz, CDCl_3): $\delta = 1.04$ – 1.15 (m, 3H), 1.19 (t, $J = 7.1$ Hz, 3H), 1.29– 1.39 (m, 2H), 1.55– 1.62 (m, 3H), 1.67– 1.70 (m, 2H), 1.74– 1.81 (m, 1H), 1.87– 1.89 (m, 2H), 2.03– 2.10 (m, 1H), 2.13 (t, $J = 7.9$ Hz, 2H), 3.52 (t, $J = 7.6$ Hz, 1H), 3.70– 3.77 (m, 1H), 4.07 (dq, $J = 10.8$ Hz, $J = 7.1$ Hz, 1H), 4.14 (dq, $J = 10.8$ Hz, $J = 7.1$ Hz, 1H), 5.35 (br d, $J = 7.6$ Hz, 1H), 7.22– 7.26 (m, 1H), 7.27– 7.32 (m, 4H) ppm. $^{13}\text{C}\{^1\text{H}\}$ -NMR (125 MHz, CDCl_3): $\delta = 14.08$ (CH_3), 23.75 (CH_2), 24.84 (2 CH_2), 25.49 (CH_2), 32.99 (CH_2), 33.18 (2 CH_2), 36.53 (CH_2), 48.08 (CH), 51.54 (CH), 60.76 (CH_2), 127.20 (CH), 127.80 (2 CH), 128.59 (2 CH), 138.95 (C), 171.36 (C), 173.88 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 3288$ (w), 2929 (s), 2853 (m), 1731 (vs), 1637 (vs), 1544 (s), 1451 (m), 1146 (s), 1027 (m), 733 (m), 698 (s) cm^{-1} . HR-MS (EI, 70 eV): calcd. 331.2142 (for $\text{C}_{20}\text{H}_{29}\text{NO}_3^+$), found 331.2135 [M^+]. $\text{C}_{20}\text{H}_{29}\text{NO}_3$ (331.46 g mol^{-1}).

Conversion of β -oxoester 20a with allylamine. According to GPB, β -oxoester **20a** (179 mg, 500 μmol), K_3PO_4 (212 mg, 1.00 mmol) and CuI (14 mg, 75 μmol) were converted with allylamine (0.5 mL). The crude product was purified by column chromatography (SiO_2 , hexanes/MTBE 1:2) to yield the benzazocinone **18e** (70 mg, 0.24 mmol, 49%, $R_f = 0.28$) as a colorless oil. As second fraction, the acyclic amide **24e** (30 mg, 0.10 mmol, 20%, $R_f = 0.12$) was obtained as a colorless oil.

Ethyl 1-allyl-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylate (18e). ^1H -NMR (500 MHz, CDCl_3): $\delta = 1.17$ (t, $J = 7.0$ Hz, 3H), 1.51– 1.60 (m, 1H), 1.77– 1.94 (m, 3H), 2.25– 2.29 (m, 1H), 2.42– 2.46 (m, 1H), 3.52 (d, $J = 11.2$ Hz, 1H), 4.05– 4.18 (m, 3H), 4.76 (dd, $J = 14.4$ Hz, $J = 6.3$ Hz, 1H), 5.10 (d, $J = 10.1$ Hz, 1H), 5.15

(d, $J = 17.1$ Hz, 1H), 5.86–5.94 (m, 1H), 7.20–7.33 (m, 4H) ppm. $^{13}\text{C}\{^1\text{H}\}$ -NMR (125 MHz, CDCl_3): $\delta = 13.96$ (CH_3), 24.28 (CH_2), 32.01 (CH_2), 33.06 (CH_2), 44.78 (CH), 51.74 (CH_2), 60.84 (CH_2), 118.78 (CH_2), 125.96 (CH), 126.95 (CH), 127.99 (CH), 128.57 (CH), 132.19 (CH), 139.04 (C), 140.48 (C), 173.81 (C), 173.82 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 2979$ (w), 2935 (w), 1731 (vs), 1651 (vs), 1493 (m), 1454 (m), 1389 (m), 1225 (m), 1185 (s), 1150 (m), 1098 (m), 765 (m), 739 (m) cm^{-1} . HR-MS (ESI): calcd. 287.1516 (for $\text{C}_{17}\text{H}_{21}\text{NO}_3^+$), found 287.1518 [M^+]. $\text{C}_{17}\text{H}_{21}\text{NO}_3$ (287.36 g mol^{-1}).

Ethyl 6-(allylamino)-6-oxo-2-phenylhexanoate (24e). ^1H -NMR (500 MHz, CDCl_3): $\delta = 1.16$ (t, $J = 7.1$ Hz, 3H), 1.51–1.65 (m, 2H), 1.77 (dddd, $J = 13.3$ Hz, $J = 10.2$ Hz, $J = 7.3$ Hz, $J = 5.8$ Hz, 1H), 2.05 (dddd, $J = 13.3$ Hz, $J = 10.5$ Hz, $J = 7.9$ Hz, $J = 5.5$ Hz, 1H), 2.13–2.19 (m, 2H), 3.50 (t, $J = 7.6$ Hz, 1H), 3.82 (tt, $J = 5.7$ Hz, $J = 1.4$ Hz, 2H), 4.01–4.14 (m, 2H), 5.08 (dq, $J = 10.2$ Hz, $J = 1.4$ Hz, 1H), 5.12 (dq, $J = 17.2$ Hz, $J = 1.6$ Hz, 1H), 5.59 (br s, 1H), 5.78 (ddt, $J = 17.2$ Hz, $J = 10.2$ Hz, $J = 5.7$ Hz, 1H), 7.19–7.29 (m, 5H) ppm. $^{13}\text{C}\{^1\text{H}\}$ -NMR (125 MHz, CDCl_3): $\delta = 14.06$ (CH_3), 23.63 (CH_2), 33.01 (CH_2), 36.23 (CH_2), 41.86 (CH_2), 51.53 (CH), 60.75 (CH_2), 116.33 (CH_2), 127.20 (CH), 127.80 (2 CH), 128.58 (2 CH), 134.21 (CH), 138.89 (C), 172.16 (C), 173.83 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 3288$ (w), 2929 (w), 1731 (vs), 1642 (vs), 1547 (s), 1457 (m), 1372 (m), 1269 (m), 1174 (s), 1152 (vs), 1026 (m), 920 (m), 734 (m), 700 (vs) cm^{-1} . HR-MS (EI, 70 eV): calcd. 289.1672 (for $\text{C}_{17}\text{H}_{23}\text{NO}_3^+$), found 289.1669 [M^+]. $\text{C}_{17}\text{H}_{23}\text{NO}_3$ (289.38 g mol^{-1}).

Ethyl 1-(2-ethoxyethyl)-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylate (18f). According to GPB, β -oxoester **20a** (179 mg, 500 μmol), K_3PO_4 (212 mg, 1.00 mmol) and CuI (14 mg, 75 μmol) were converted with 2-ethoxyethylamine (0.5 mL). The crude product was purified by column chromatography (SiO_2 , hexanes/MTBE 5:1) to yield the benzazocinone **18f** (60 mg, 0.19 mmol, 38%, $R_f = 0.26$) as a colorless oil. ^1H -NMR (500 MHz, CDCl_3): $\delta = 1.12$ (t, $J = 7.0$ Hz, 3H), 1.17 (t, $J = 7.1$ Hz, 3H), 1.53 (dddd, $J = 14.3$ Hz, $J = 12.3$ Hz, $J = 11.1$ Hz, $J = 5.6$ Hz, 1H), 1.75–1.95 (m, 3H), 2.24 (dd, $J = 11.4$ Hz, $J = 8.1$ Hz, 1H), 2.44–2.48 (m, 1H), 3.41–3.47 (m, 2H), 3.50 (ddd, $J = 9.2$ Hz, $J = 5.9$ Hz, $J = 4.4$ Hz, 1H), 3.53–3.57 (m, 1H), 3.61 (ddd, $J = 9.2$ Hz, $J = 7.6$ Hz, $J = 5.5$ Hz, 1H), 3.67 (dd, $J = 11.1$ Hz, $J = 1.0$ Hz, 1H), 4.08–4.18 (m, 2H), 4.49 (ddd, $J = 13.4$ Hz, $J = 7.6$ Hz, $J = 5.9$ Hz, 1H), 7.29–7.31 (m, 3H), 7.31–7.35 (m, 1H) ppm. $^{13}\text{C}\{^1\text{H}\}$ -NMR (125 MHz, CDCl_3): $\delta = 14.02$ (CH_3), 15.01

(CH₃), 24.34 (CH₂), 32.14 (CH₂), 33.06 (CH₂), 44.54 (CH), 48.44 (CH₂), 60.84 (CH₂), 66.11 (CH₂), 66.68 (CH₂), 126.10 (CH), 127.05 (CH), 128.05 (CH), 128.47 (CH), 139.15 (C), 140.74 (C), 173.95 (C), 174.36 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 2972$ (w), 2942 (w), 2864 (w), 1730 (s), 1653 (vs), 1494 (m), 1454 (m), 1392 (m), 1300 (m), 1225 (m), 1186 (m), 1113 (s), 1045 (m), 1026 (m), 766 (m), 735 (m) cm⁻¹. HR-MS (EI, 70 eV): calcd. 319.1778 (for C₁₈H₂₅NO₄⁺), found 319.1772 [M⁺]. C₁₈H₂₅NO₄ (319.40 g mol⁻¹).

Ethyl [1-(methoxycarbonyl)methyl]-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylate (18j). According to GPC, benzazocinone **18g** (124 mg, 500 μ mol), *n*BuLi (0.21 mL, 2.5 mol L⁻¹ in hexanes, 0.53 mmol) and *i*Pr₂NH (54 mg, 0.53 mmol) were converted with methyl bromoacetate (81 mg, 0.53 mmol) to yield the title compound **18j** (126 mg, 395 μ mol, 79%) after chromatography (SiO₂, hexanes/MTBE 1:5, *R*_f = 0.28) as a colorless solid, mp 100–104 °C. ¹H-NMR (500 MHz, CDCl₃): $\delta = 1.16$ (t, *J* = 7.1 Hz, 3H), 1.53 (dddd, *J* = 14.3 Hz, *J* = 12.9 Hz, *J* = 11.1 Hz, *J* = 5.4 Hz, 1H), 1.80 (td, *J* = 12.9 Hz, *J* = 5.4 Hz, 1H), 1.88–1.95 (m, 2H), 2.27 (dd, *J* = 12.3 Hz, *J* = 8.2 Hz, 1H), 2.47 (dd, *J* = 14.3 Hz, *J* = 5.4 Hz, 1H), 3.71 (s, 3H), 4.01 (dd, *J* = 11.1 Hz, *J* = 0.9 Hz, 1H), 4.06–4.17 (m, 2H), 4.35 (d, *J* = 17.0 Hz, 1H), 4.58 (d, *J* = 17.0 Hz, 1H), 7.24–7.30 (m, 3H), 7.33–7.35 (m, 1H) ppm. ¹³C{¹H}-NMR (125 MHz, CDCl₃): $\delta = 13.94$ (CH₃), 24.19 (CH₂), 32.15 (CH₂), 32.53 (CH₂), 44.44 (CH), 50.98 (CH₂), 52.07 (CH₃), 60.78 (CH₂), 125.28 (CH), 127.49 (CH), 128.12 (CH), 128.68 (CH), 138.71 (C), 140.83 (C), 169.28 (C), 173.87 (C), 174.31 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 2973$ (w), 2952 (w), 1757 (s), 1716 (vs), 1649 (vs), 1496 (m), 1441 (m), 1384 (m), 1220 (s), 1196 (vs), 1095 (m), 1025 (m), 977 (m), 781 (m), 742 (m), 722 (m) cm⁻¹. HR-MS (EI, 70 eV): calcd. 319.1414 (for C₁₇H₂₁NO₅⁺), found 319.1426 [M⁺]. C₁₇H₂₁NO₅ (319.36 g mol⁻¹).

Ethyl 1-[1-(ethoxycarbonyl)ethyl]-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylate (18k). According to GPC, benzazocinone **18g** (124 mg, 500 μ mol) in abs. THF (1 mL), *n*BuLi (0.21 mL, 2.5 mol L⁻¹ in hexanes, 0.53 mmol) and *i*Pr₂NH (54 mg, 0.53 mmol) were converted with ethyl 2-bromopropionate (96 mg, 0.53 mmol) to yield in a first fraction the title compound **18k** (59 mg, 0.17 mmol, 34%, *R*_f = 0.32) after chromatography (SiO₂, hexanes/EtOAc 1:1) as a colorless oil. The product **18k** was isolated as a mixture of two diastereomers (ratio 87:13 by ¹H-NMR). In the se-

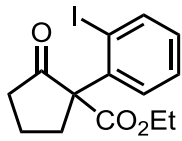
cond fraction, starting material **18g** (45 mg, 0.18 mmol, 36%, $R_f = 0.11$) was recovered. $^1\text{H-NMR}$ (500 MHz, CDCl_3), major diastereomer: $\delta = 1.06\text{--}1.11$ (m, 3H), 1.19–1.25 (m, 6H), 1.42–1.53 (m, 1H), 1.65–1.77 (m, 1H), 1.80–1.89 (m, 2H), 2.18–2.23 (m, 1H), 2.35–2.39 (m, 1H), 3.64 (dd, $J = 11.1$ Hz, $J = 6.5$ Hz, 1H), 4.00–4.09 (m, 2H), 4.13–4.23 (m, 2H), 4.96–5.02 (m, 1H), 7.17–7.22 (m, 1H), 7.23–7.28 (m, 2H), 7.38–7.41 (m, 1H) ppm; minor diastereomer: $\delta = 1.06\text{--}1.11$ (m, 3H), 1.19–1.25 (m, 3H), 1.42–1.53 (m, 4H), 1.65–1.89 (m, 3H), 2.11–2.17 (m, 1H), 2.35–2.39 (m, 1H), 3.74 (dd, $J = 11.0$ Hz, $J = 6.7$ Hz, 1H), 4.00–4.09 (m, 2H), 4.13–4.23 (m, 3H), 7.17–7.22 (m, 1H), 7.23–7.28 (m, 3H) ppm. $^{13}\text{C}\{^1\text{H}\}\text{-NMR}$ (125 MHz, CDCl_3), major diastereomer: $\delta = 13.96$ (CH_3), 14.15 (CH_3), 15.02 (CH_3), 24.31 (CH_2), 32.01 (CH_2), 33.13 (CH_2), 44.69 (CH), 54.86 (CH), 60.87 (CH_2), 61.28 (CH_2), 126.90 (2 CH), 127.81 (CH), 129.11 (CH), 138.45 (C), 139.88 (C), 172.20 (C), 173.76 (C), 174.26 (C) ppm; minor diastereomer: $\delta = 13.96$ (CH_3), 14.30 (CH_3), 14.91 (CH_3), 24.13 (CH_2), 32.05 (CH_2), 33.06 (CH_2), 44.80 (CH), 59.64 (CH), 60.91 (CH_2), 61.20 (CH_2), 126.53 (CH), 126.96 (CH), 128.21 (CH), 128.85 (CH), 139.27 (C), 140.46 (C), 171.01 (C), 173.41 (C), 173.82 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 2978$ (w), 2941 (w), 1731 (vs), 1656 (vs), 1494 (m), 1452 (m), 1371 (m), 1303 (m), 1226 (m), 1186 (s), 1090 (m), 1049 (m), 1022 (m), 768 (m), 738 (m) cm^{-1} . HR-MS (EI, 70 eV): calcd. 347.1727 (for $\text{C}_{19}\text{H}_{25}\text{NO}_5^+$), found 347.1734 [M^+]. $\text{C}_{19}\text{H}_{25}\text{NO}_5$ (347.41 g mol^{-1}).

1-Benzyl-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylic acid *N*-[2-(ethoxycarbonyl)ethyl]amide (27b). According to GPD, HATU (209 mg, 550 μmol), DIPEA (142 mg, 1.10 mmol) and β -alanine ethyl ester-hydrochloride (115 mg, 749 μmol) were converted with benzazocinone **26** (154 mg, 500 μmol) to yield the title compound **27b** (173 mg, 424 μmol , 85%) after chromatography (SiO_2 , hexanes/EtOAc 1:3, $R_f = 0.33$) as a colorless oil. $^1\text{H-NMR}$ (500 MHz, CDCl_3): $\delta = 1.20$ (t, $J = 7.1$ Hz, 3H), 1.37 (dddd, $J = 14.3$ Hz, $J = 12.6$ Hz, $J = 10.9$ Hz, $J = 5.5$ Hz, 1H), 1.73 (dtdd, $J = 14.6$ Hz, $J = 12.7$ Hz, $J = 5.5$ Hz, $J = 1.8$ Hz, 1H), 1.83–1.93 (m, 2H), 2.26–2.32 (m, 4H), 2.57 (dd, $J = 10.9$ Hz, $J = 0.9$ Hz, 1H), 2.98 (dq, $J = 13.1$ Hz, $J = 7.0$ Hz, 1H), 3.18 (dq, $J = 13.1$ Hz, $J = 6.6$ Hz, 1H), 3.62 (br t, $J = 5.8$ Hz, 1H), 3.99–4.09 (m, 2H), 4.13 (d, $J = 13.7$ Hz, 1H), 6.00 (d, $J = 13.7$ Hz, 1H), 7.22–7.27 (m, 4H), 7.28–7.31 (m, 3H), 7.31–7.36 (m, 2H) ppm. $^{13}\text{C}\{^1\text{H}\}\text{-NMR}$ (125 MHz, CDCl_3): $\delta = 14.14$ (CH_3), 24.42 (CH_2), 31.54 (CH_2), 33.11 (CH_2), 33.70 (CH_2), 35.11 (CH_2), 45.19 (CH), 51.93 (CH_2), 60.38 (CH_2), 125.76 (CH), 127.20 (CH), 127.77 (CH), 128.09

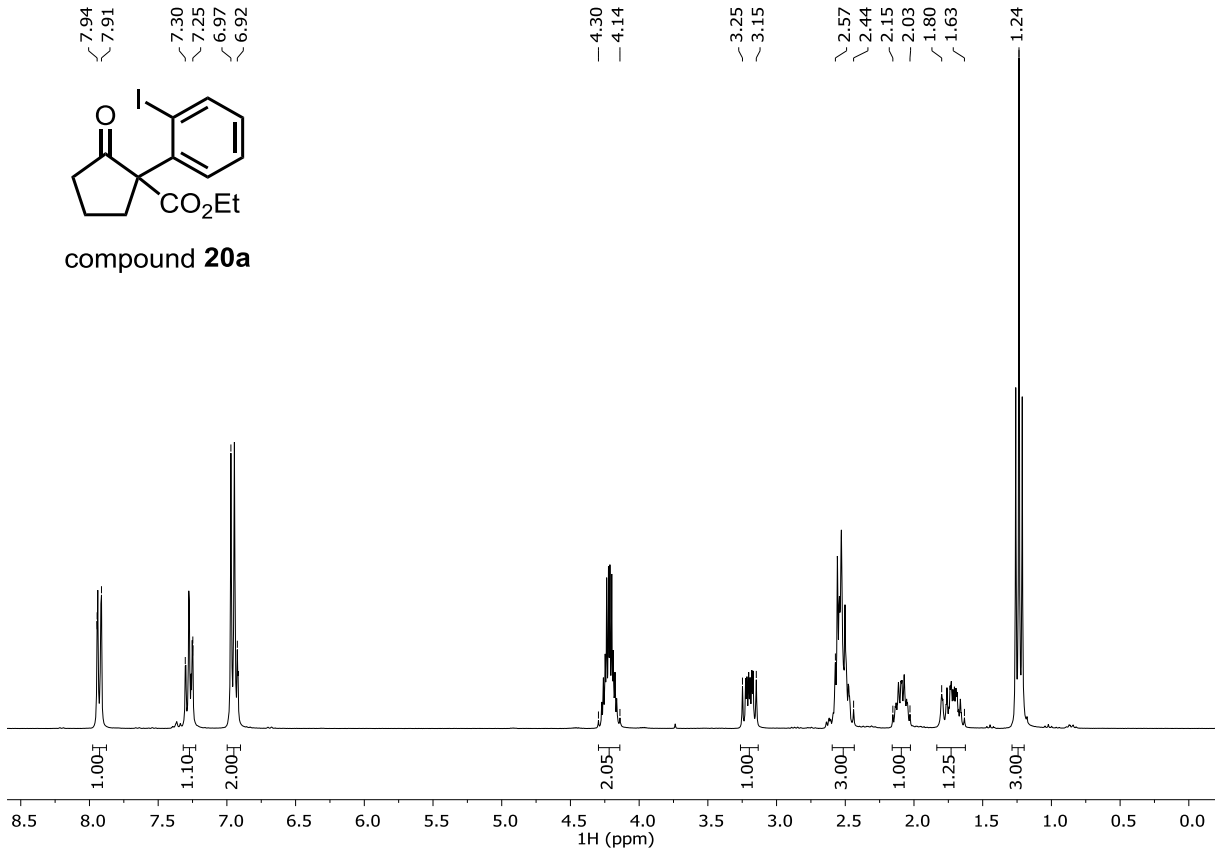
(CH), 128.76 (CH), 128.83 (2 CH), 129.99 (2 CH), 136.79 (C), 139.22 (C), 140.20 (C), 171.43 (C), 172.98 (C), 173.79 (C) ppm. IR (ATR): $\nu(\text{tilde}) = 3412$ (w), 3031 (w), 2939 (w), 2865 (w), 1731 (s), 1675 (s), 1650 (vs), 1513 (m), 1492 (m), 1452 (m), 1393 (m), 1181 (s), 1152 (m), 844 (m), 759 (m), 735 (m), 705 (s), 634 (m) cm^{-1} . HR-MS (EI, 70 eV): calcd. 408.2044 (for $\text{C}_{24}\text{H}_{28}\text{N}_2\text{O}_4^+$), found 408.2039 [M^+]. $\text{C}_{24}\text{H}_{28}\text{N}_2\text{O}_4$ (408.50 g mol^{-1}).

1-Benzyl-2-oxo-1,2,3,4,5,6-hexahydrobenzo[*b*]azocine-6-carboxylic acid *N*-(2,2,2-trifluoroethyl)amide (27c). According to GPD, HATU (209 mg, 550 μmol), DIPEA (71 mg, 0.55 mmol) and 2,2,2-trifluoroethylamine (74 mg, 0.75 mmol) were converted with benzazocinone **26** (154 mg, 500 μmol) to yield the title compound **27c** (172 mg, 441 μmol , 88%) after chromatography (SiO_2 , hexanes/EtOAc 1:1, $R_f = 0.29$) as a colorless solid, mp 127–128 $^\circ\text{C}$. $^1\text{H-NMR}$ (500 MHz, CDCl_3): $\delta = 1.40$ (dddd, $J = 14.4$ Hz, $J = 12.8$ Hz, $J = 10.9$ Hz, $J = 5.5$ Hz, 1H), 1.70–1.79 (m, 1H), 1.85–1.94 (m, 2H), 2.30–2.34 (m, 2H), 2.65 (dd, $J = 10.9$ Hz, $J = 0.9$ Hz, 1H), 3.25 (dq, $J = 14.8$ Hz, $J = 9.0$ Hz, $J = 5.8$ Hz, 1H), 3.42 (br t, $J = 6.6$ Hz, 1H), 3.67 (dq, $J = 14.8$ Hz, $J = 9.1$ Hz, $J = 7.5$ Hz, 1H), 4.09 (d, $J = 13.7$ Hz, 1H), 6.08 (d, $J = 13.7$ Hz, 1H), 7.21 (dd, $J = 7.9$ Hz, $J = 1.1$ Hz, 1H), 7.25–7.28 (m, 6H), 7.35–7.40 (m, 2H) ppm. $^{13}\text{C}\{^1\text{H}\}$ -NMR (125 MHz, CDCl_3): $\delta = 24.31$ (CH_2), 31.45 (CH_2), 33.06 (CH_2), 40.20 (q, $^2J_{\text{CF}} = 34.8$ Hz, CH_2), 45.23 (CH), 51.79 (CH_2), 123.68 (q, $^1J_{\text{CF}} = 279.1$ Hz, C), 125.83 (CH), 127.16 (CH), 127.57 (CH), 128.47 (CH), 128.83 (2 CH), 128.92 (CH), 130.09 (2 CH), 136.87 (C), 139.08 (C), 139.30 (C), 173.08 (C), 173.64 (C) ppm. $^{19}\text{F}\{^1\text{H}\}$ -NMR (470 MHz, CDCl_3): $\delta = -72.10$ (s, CF_3) ppm. IR (ATR): $\nu(\text{tilde}) = 3410$ (m), 2969 (w), 2948 (w), 2865 (w), 1690 (s), 1644 (vs), 1598 (m), 1514 (m), 1493 (m), 1454 (m), 1438 (m), 1392 (s), 1276 (s), 1228 (m), 1195 (m), 1162 (s), 1144 (vs), 1083 (m), 989 (m), 833 (m), 780 (m), 764 (s), 733 (s), 711 (s), 664 (m), 633 (s) cm^{-1} . HR-MS (EI, 70 eV): calcd. 390.1550 (for $\text{C}_{21}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_2^+$), found 390.1541 [M^+]. $\text{C}_{21}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_2$ (390.41 g mol^{-1}).

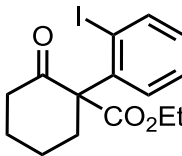
7.94
7.91
7.30
7.25
6.97
6.92



compound **20a**



7.97
7.95
7.33
7.06
7.04
6.96



compound **20b**

