



Supporting Information

for

New efficient synthesis of polysubstituted 3,4-dihydroquinazolines and 4*H*-3,1-benzothiazines through a Passerini/Staudinger/aza-Wittig/addition/nucleophilic substitution sequence

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Experimental section and copies of NMR spectra

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1 Experimental section

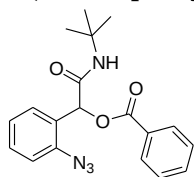
1.1 General information

Melting points were determined using an X-4 model apparatus and were uncorrected. ^1H NMR were recorded in CDCl_3 on a Varian Mercury 600 spectrometer and resonances were relative to TMS. $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded in CDCl_3 on a Varian Mercury 600 (150 MHz) with complete proton decoupling spectrophotometers (CDCl_3 : 77.0 ppm). HRMS was measured on an Agilent 6224 TOF LC/MS spectrometer. Amines, CS_2 and isocyanides were purchased from commercial suppliers and used without further purification. CH_2Cl_2 , toluene and CH_3CN were used after drying and distillation. Column chromatography purifications were performed using 400-630 mesh silica gel. Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F_{254} plates, which were visualized by exposure to ultraviolet light.

1.2 General procedure for preparation of azides **4** via Passerini reaction

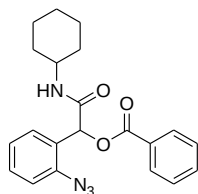
To a solution of 2-azidobenzaldehydes **1** (1 mmol) in CH_2Cl_2 (5 mL) was added sequentially benzoic acid (**2**) (0.122 g, 1 mmol) and isocyanides **3** (1 mmol) at room temperature. After the reaction mixture was stirred for 48 hours at ambient temperature, the solvent was removed under reduced pressure and the residue was recrystallized from ether/petroleum ether to give azide **4**.

1-(2-Azidophenyl)-2-(*tert*-butylamino)-2-oxoethyl benzoate (**4a**)



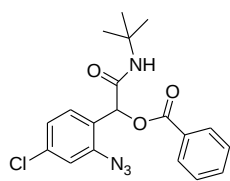
White solid (0.306 g, yield 87%), m.p. 134-136 °C, lit^[1] m.p. 136-137 °C. ^1H NMR (CDCl_3 , 600 MHz): δ (ppm) 8.10 (d, J = 7.6 Hz, 2H, Ar-H), 7.60-7.18 (m, 7H, Ar-H), 6.41 (s, 1H, CH), 6.11 (s, 1H, NH), 1.37 (s, 9H, 3CH₃).

1-(2-Azidophenyl)-2-(cyclohexylamino)-2-oxoethyl benzoate (**4b**)



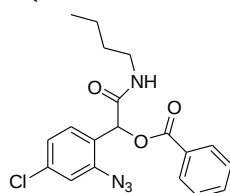
White solid (0.283 g, yield 75%), m.p. 151-153 °C; ^1H NMR (CDCl_3 , 600 MHz): δ (ppm) 8.10 (d, J = 7.2 Hz, 2H, Ar-H), 7.61-7.18 (m, 7H, Ar-H), 6.46 (s, 1H, CH), 6.13 (d, J = 7.2 Hz, 1H, NH), 3.84-3.79 (m, 1H, NCH), 2.00-1.13 (m, 10H, 5CH₂); ^{13}C NMR (CDCl_3 , 150 MHz): δ (ppm) 166.8, 165.0, 137.9, 133.5, 130.1, 129.7, 129.4, 129.1, 128.5, 126.9, 125.1, 118.3, 71.2, 48.2, 32.8, 32.6, 25.3, 24.6. HRMS (ESI-TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{23}\text{N}_4\text{O}_3^+$ 379.1765; Found 379.1771.

1-(2-Azido-4-chlorophenyl)-2-(*tert*-butylamino)-2-oxoethyl benzoate (**4c**)



White solid (yield 0.309 g, 80%), mp 168-169 °C; ^1H NMR (CDCl_3 , 600 MHz) δ (ppm) 8.07 (d, J = 7.2 Hz, 2H, Ar-H), 7.61 (t, J = 7.2 Hz, 1H, Ar-H), 7.52 (d, J = 8.4 Hz, 1H, Ar-H), 7.48 (t, J = 7.8 Hz, 2H, Ar-H), 7.19 (s, 1H, Ar-H), 7.16 (d, J = 7.8 Hz, 1H, Ar-H), 6.35 (s, 1H, CH), 6.11 (s, 1H, NH), 1.37 (s, 9H, 3CH₃); ^{13}C NMR (CDCl_3 , 150 MHz) δ (ppm) 166.5, 164.9, 139.4, 135.8, 133.7, 130.6, 129.8, 129.1, 128.6, 125.9, 125.5, 118.6, 70.9, 51.7, 28.6. HRMS (ESI-TOF) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{20}\text{ClN}_4\text{O}_3^+$ 387.1218; Found 387.1217.

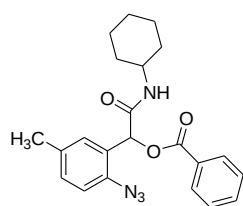
1-(2-Azido-4-chlorophenyl)-2-(butylamino)-2-oxoethyl benzoate (**4d**)



White solid (yield 0.289 g, 75%), mp 127-128 °C; ^1H NMR (CDCl_3 , 600 MHz) δ (ppm) 8.08 (d, J = 7.8 Hz, 2H, Ar-H), 7.61 (t, J = 7.2 Hz, 1H, Ar-H), 7.53 (d, J = 7.8 Hz, 1H, Ar-H), 7.48 (t, J = 7.8 Hz, 2H, Ar-H), 7.18 (s, 1H, Ar-H), 7.16 (t, J = 9.0 Hz, 1H, Ar-H), 6.43 (s, 1H, CH), 6.27 (s, 1H, NH), 3.37-3.27 (m, 2H, NCH₂), 1.54-1.49

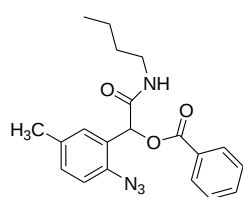
(m, 2H, CH₂), 1.37-1.31 (m, 2H, CH₂), 0.92 (t, *J* = 7.2 Hz, 3H, CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 167.3, 165.0, 139.3, 135.9, 133.7, 130.6, 129.8, 129.0, 128.6, 125.5, 125.4, 118.5, 70.8, 39.3, 31.5, 19.9, 13.7. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₁₉H₂₀ClN₄O₃⁺ 387.1218; Found 387.1219.

1-(2-Azido-5-methylphenyl)-2-(cyclohexylamino)-2-oxoethyl benzoate (4e)



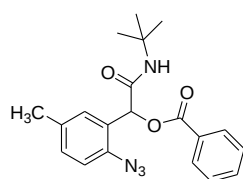
White solid (yield 0.309 g, 79%), mp 169-171 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 8.10 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.60 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.47 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.40 (s, 1H, Ar-H), 7.20 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.09 (t, *J* = 7.8 Hz, 1H, Ar-H), 6.41 (s, 1H, CH), 6.12 (d, *J* = 8.4 Hz, 1H, NH), 3.84-3.79 (m, 1H, NCH), 2.34 (s, 3H, CH₃), 2.00-1.12 (m, 10H, 5CH₂); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 166.9, 165.1, 135.1, 133.5, 130.9, 130.0, 129.8, 129.4, 128.5, 126.7, 118.3, 71.5, 48.2, 32.9, 32.7, 25.4, 24.6, 20.9. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₂H₂₅N₄O₃⁺ 393.1921; Found 393.1933.

1-(2-Azido-5-methylphenyl)-2-(butylamino)-2-oxoethyl benzoate (4f)



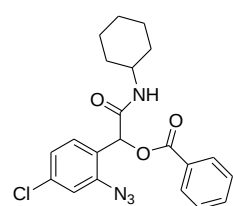
White solid (yield 0.319 g, 87%), mp 135-137 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 8.11 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.60 (t, *J* = 7.8 Hz, 1H, Ar-H), 7.47 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.40 (s, 1H, Ar-H), 7.20 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.09 (d, *J* = 7.8 Hz, 1H, Ar-H), 6.44 (s, 1H, CH), 6.22 (s, 1H, NH), 3.37-3.25 (m, 2H, NCH₂), 2.35 (s, 3H, CH₃), 1.54-1.50 (m, 2H, CH₂), 1.35-1.31 (m, 2H, CH₂), 0.91 (t, *J* = 7.2 Hz, 3H, CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 167.8, 165.2, 135.1, 133.5, 130.9, 130.5, 129.9, 129.3, 128.5, 126.6, 118.2, 71.3, 39.3, 31.5, 20.9, 19.9, 13.7. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₀H₂₃N₄O₃⁺ 367.1765; Found 367.1767.

1-(2-Azido-5-methylphenyl)-2-(tert-butylamino)-2-oxoethyl benzoate (4g)



White solid (yield 0.296 g, 81%), mp 145-147 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 8.10 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.59 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.47 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.39 (s, 1H, Ar-H), 7.20 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.09 (d, *J* = 7.8 Hz, 1H, Ar-H), 6.36 (s, 1H, CH), 6.09 (s, 1H, NH), 2.34 (s, 3H, CH₃), 1.37 (s, 9H, 3CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 167.0, 165.1, 135.1, 133.5, 130.8, 129.9, 129.8, 129.4, 128.5, 126.9, 118.3, 71.5, 51.6, 28.7, 20.9. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₀H₂₃N₄O₃⁺ 367.1765; Found 367.1770.

1-(2-Azido-4-chlorophenyl)-2-(cyclohexylamino)-2-oxoethyl benzoate (4h)



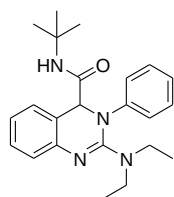
White solid (yield 0.347 g, 84%), mp 168-170 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 8.07 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.61 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.53-7.46 (m, 3H, Ar-H), 7.18 (s, 1H, Ar-H), 7.16 (d, *J* = 8.4 Hz, 1H, Ar-H), 6.40 (s, 1H, CH), 6.12 (d, *J* = 7.8 Hz, 1H, NH), 3.83-3.79 (m, 1H, NCH), 1.99-1.12 (m, 10H, 5CH₂); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 166.4, 165.0, 139.4, 135.9, 133.7, 130.7, 129.8, 129.1, 128.6, 125.7, 125.5, 118.6, 70.8, 48.3, 32.9, 32.7, 25.4, 24.6. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₁H₂₂ClN₄O₃⁺ 413.1375; Found 413.1382.

1.3 General procedure for preparation of 3,4-dihydroquinazolines 8

To a stirred solution of azide **4** (1 mmol) in toluene (5 mL) was added dropwise triphenylphosphine (0.26 g, 1 mmol) in toluene (5 mL) at room temperature. After the reaction mixture was stirred for 2–4 h at ambient temperature, isocyanate (1 mmol) was added and the reaction mixture was stirred for 2–8 h at room temperature (for aromatic isocyanate) or 60–80 °C (for aliphatic isocyanate). Then secondary amine (1 mmol) was added and the reaction mixture was stirred for 1–6 h at room temperature. After the addition reaction was completed, the solvent was removed and CH₃CN (5 mL) with K₂CO₃ (0.136 g, 1 mmol) was

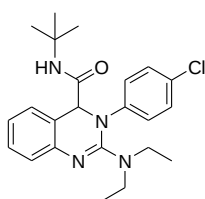
added and the mixture was left to stirred at 80 °C for 1–4 h. The solvent was removed under reduced pressure and the residual was purified by column chromatography with EtOAc/ petroleum ether to give 3,4-dihydroquinazolines **8**.

***N*-tert-Butyl-2-(diethylamino)-3,4-dihydro-3-phenylquinazoline-4-carboxamide (8a)**



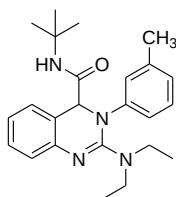
White solid (0.317 g, yield 84%), m.p. 118-121 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.31-6.96 (m, 9H, Ar-H), 5.46 (s, 1H, NH), 4.99 (s, 1H, CH), 3.57-3.55 (m, 2H, NCH₂), 3.14-3.08 (m, 2H, NCH₂), 1.23 (s, 9H, 3CH₃), 1.01 (t, *J* = 6.6 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.5, 153.2, 146.5, 144.4, 129.1, 128.9, 126.2, 124.2, 123.3, 123.2, 122.1, 67.3, 51.3, 41.6, 41.2, 28.5, 28.1, 12.5, 12.4. Anal. Calcd for C₂₃H₃₀N₄O: C, 72.98; H, 7.99; N, 14.80. Found: C, 72.75; H, 7.72; N, 14.67. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₃H₃₁N₄O⁺ 379.2492; Found 379.2494.

***N*-tert-Butyl-3-(4-chlorophenyl)-2-(diethylamino)-3,4-dihydroquinazoline-4-carboxamide (8b)**



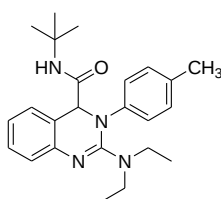
White solid (0.331 g, yield 80%), m.p. 169-171 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.32-6.99 (m, 8H, Ar-H), 5.37 (s, 1H, NH), 4.93 (s, 1H, CH), 3.61-3.53 (m, 2H, NCH₂), 3.09-3.05 (m, 2H, NCH₂), 1.21 (s, 9H, 3CH₃), 1.01 (t, *J* = 7.8 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.3, 152.9, 145.1, 144.3, 129.6, 129.4, 129.0, 126.1, 124.6, 123.4, 122.4, 122.0, 67.2, 51.4, 41.9, 28.3, 12.6. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₃H₃₀ClN₄O⁺ 413.2103; Found 413.2100.

***N*-tert-Butyl-2-(diethylamino)-3,4-dihydro-3-*m*-tolylquinazoline-4-carboxamide (8c)**



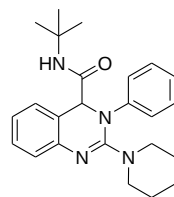
White solid (0.297 g, yield 76%), m.p. 106-108 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.30-6.95 (m, 7H, Ar-H), 6.89 (d, *J* = 7.2 Hz, 1H, Ar-H), 5.46 (s, 1H, NH), 4.99 (s, 1H, CH), 3.62-3.56 (m, 2H, NCH₂), 3.13-3.07 (m, 2H, NCH₂), 2.30 (s, 3H, CH₃), 1.23 (s, 9H, 3CH₃), 1.01 (t, *J* = 6.6 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.5, 153.2, 146.5, 144.5, 138.9, 129.1, 128.7, 126.2, 125.0, 123.8, 123.1, 122.2, 122.1, 120.3, 67.3, 51.3, 41.7, 28.4, 21.3, 12.5. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₄H₃₃N₄O⁺ 393.2649; Found 393.2650.

***N*-tert-Butyl-2-(diethylamino)-3,4-dihydro-3-*p*-tolylquinazoline-4-carboxamide (8d)**



White solid (0.309 g, yield 79%), m.p. 121-123 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.30-6.95 (m, 8H, Ar-H), 5.47 (s, 1H, NH), 4.95 (s, 1H, CH), 3.60-3.55 (m, 2H, NCH₂), 3.12-3.06 (m, 2H, NCH₂), 2.29 (s, 3H, CH₃), 1.23 (s, 9H, 3CH₃), 1.01 (t, *J* = 6.6 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.5, 153.3, 144.4, 144.0, 133.9, 129.4, 129.1, 126.1, 123.2, 123.1, 123.0, 122.0, 67.4, 51.2, 41.8, 28.7, 28.4, 28.1, 27.8, 21.1, 20.5, 12.7, 12.3. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₄H₃₃N₄O⁺ 393.2649; Found 393.2649.

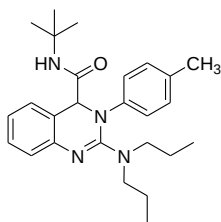
***N*-tert-Butyl-3,4-dihydro-3-phenyl-2-(piperidin-1-yl)quinazoline-4-carboxamide (8e)**



White solid (0.281 g, yield 72%), m.p. 177-179 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.28-6.97 (m, 9H, Ar-H), 5.45 (s, 1H, NH), 5.02 (s, 1H, CH), 3.38 (t, *J* = 7.2 Hz, 4H, 2NCH₂), 1.50-1.35 (m, 6H, 3CH₂), 1.24 (s, 9H, 3CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.5, 153.3, 146.1, 144.2, 129.1, 128.9, 126.1, 124.0, 123.1, 122.8, 122.5, 122.2, 66.8, 51.3, 47.4, 28.3, 25.2, 24.6. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₄H₃₁N₄O⁺ 391.2492; Found 391.2491.

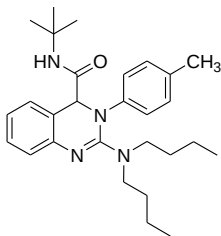
***N*-tert-Butyl-2-(dipropylamino)-3,4-dihydro-3-*p*-tolylquinazoline-4-carboxamide (8f)**

White solid (0.358 g, yield 85%), m.p. 108-109 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.30-6.94 (m, 8H, Ar-H), 5.40 (s, 1H, NH), 4.94 (s, 1H, CH), 3.56-3.49 (m, 2H, NCH₂), 2.87-2.83 (m, 2H, NCH₂), 2.29 (s, 3H,



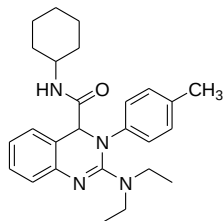
CH₃), 1.54-1.41 (m, 4H, 2CH₂), 1.21 (s, 9H, 3CH₃), 0.82 (t, *J* = 7.2 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.5, 154.0, 144.6, 144.3, 134.0, 129.5, 129.1, 126.2, 123.5, 123.1, 122.0, 121.9, 67.6, 51.2, 49.4, 28.3, 20.8, 20.6, 11.5. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₆H₃₇N₄O⁺ 421.2961; Found 421.2962.

N-tert-Butyl-2-(diethylamino)-3,4-dihydro-3-p-tolylquinazoline-4-carboxamide (8g)



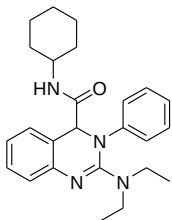
White solid (0.309 g, yield 69%), m.p. 114-116 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.30-6.95 (m, 8H, Ar-H), 5.40 (s, 1H, NH), 4.94 (s, 1H, CH), 3.62-3.58 (m, 2H, NCH₂), 2.90-2.86 (m, 2H, NCH₂), 2.29 (s, 3H, CH₃), 1.50-1.21 (m, 17H, 4CH₂ and 3CH₃), 0.87 (t, *J* = 7.2 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.5, 153.9, 144.6, 144.3, 134.0, 129.4, 129.1, 126.2, 123.6, 123.1, 122.0, 121.9, 67.6, 51.2, 47.4, 29.6, 28.3, 20.8, 20.3, 13.9. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₈H₄₁N₄O⁺ 449.3275; Found 449.3275.

N-Cyclohexyl-2-(diethylamino)-3,4-dihydro-3-p-tolylquinazoline-4-carboxamide (8h)



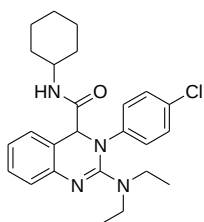
White solid (0.296 g, yield 71%), m.p. 125-127 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.30-6.95 (m, 8H, Ar-H), 5.51 (d, *J* = 7.2 Hz, 1H, NH), 5.01 (s, 1H, CH), 3.70-3.65 (m, 1H, NCH), 3.57-3.54 (m, 2H, NCH₂), 3.14-3.08 (m, 2H, NCH₂), 2.30 (s, 3H, CH₃), 1.79-1.08 (m, 10H, 5CH₂), 0.99 (t, *J* = 6.6 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.3, 153.3, 144.5, 144.0, 133.9, 129.4, 129.0, 126.0, 123.3, 123.0, 121.9, 121.7, 66.9, 48.3, 41.8, 32.3, 25.2, 24.3, 20.7, 12.5. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₆H₃₅N₄O⁺ 419.2805; Found 419.2804.

N-Cyclohexyl-2-(diethylamino)-3,4-dihydro-3-phenylquinazoline-4-carboxamide (8i)



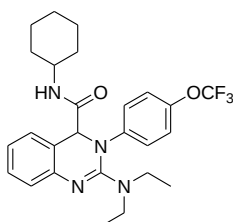
White solid (0.347 g, yield 86%), m.p. 145-147 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.29-6.96 (m, 9H, Ar-H), 5.50 (d, *J* = 7.8 Hz, 1H, NH), 5.06 (s, 1H, CH), 3.71-3.66 (m, 1H, NCH), 3.57-3.52 (m, 2H, NCH₂), 3.16-3.10 (m, 2H, NCH₂), 1.80-1.10 (m, 10H, 5CH₂), 1.00 (t, *J* = 6.6 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.3, 153.2, 146.5, 144.5, 129.1, 128.9, 126.0, 124.3, 123.3, 123.2, 122.1, 121.9, 66.8, 48.4, 41.9, 32.4, 32.3, 25.3, 24.4, 12.5. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₅H₃₃N₄O⁺ 405.2649; Found 405.2647.

3-(4-Chlorophenyl)-N-cyclohexyl-2-(diethylamino)-3,4-dihydroquinazoline-4-carboxamide (8j)



White solid (0.343 g, yield 78%), m.p. 136-138 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.32-6.98 (m, 8H, Ar-H), 5.43 (d, *J* = 7.2 Hz, 1H, NH), 5.00 (s, 1H, CH), 3.69-3.64 (m, 1H, NCH), 3.55-3.51 (m, 2H, NCH₂), 3.13-3.07 (m, 2H, NCH₂), 1.80-1.07 (m, 10H, 5CH₂), 1.01 (t, *J* = 7.2 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.1, 152.9, 145.0, 144.4, 129.6, 129.3, 128.9, 126.0, 124.6, 123.3, 122.4, 121.7, 66.6, 48.5, 42.0, 32.8, 32.3, 24.4, 13.0, 12.2. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₅H₃₂ClN₄O⁺ 439.2259; Found 439.2254.

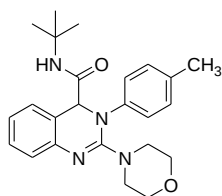
N-Cyclohexyl-2-(diethylamino)-3,4-dihydro-3-(4-(trifluoromethoxy)phenyl)quinazoline-4-carboxamide (8k)



White solid (0.391 g, yield 80%), m.p. 140-142 °C; ¹H NMR (CDCl₃, 600 MHz): δ (ppm) 7.35-7.00 (m, 8H, Ar-H), 5.43 (d, *J* = 7.2 Hz, 1H, NH), 5.02 (s, 1H, CH), 3.70-3.65 (m, 1H, NCH), 3.56-3.49 (m, 2H, NCH₂), 3.15-3.09 (m, 2H, NCH₂), 1.78-1.00 (m, 16H, 5CH₂ and 2CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ (ppm) 169.0, 152.9, 145.4, 145.0, 144.4, 129.3, 125.9, 124.4, 123.4, 122.4, 122.0 (q, ¹*J*_{F-C} = 255.1

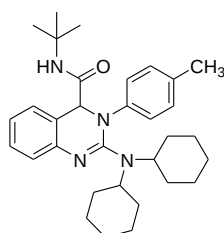
Hz), 121.6, 121.5, 66.6, 48.4, 42.0, 32.7, 32.3, 25.3, 24.4, 12.8. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{26}H_{32}F_3N_4O_2^+$ 489.2472; Found 489.2470.

***N*-tert-butyl-3,4-dihydro-2-morpholino-3-*p*-tolylquinazoline-4-carboxamide (8l)**



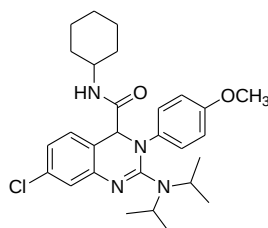
White solid (0.284 g, yield 70%), m.p. 138-139 °C; 1H NMR ($CDCl_3$, 600 MHz): δ (ppm) 7.32-7.00 (m, 8H, Ar-H), 5.45 (s, 1H, NH), 4.99 (s, 1H, CH), 3.55-3.36 (m, 8H, 2CH₂O and 2CH₂N), 2.31 (s, 3H, CH₃), 1.24 (s, 9H, 3CH₃); ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) 169.5, 153.2, 143.8, 143.1, 134.1, 129.6, 129.4, 129.2, 126.0, 123.3, 122.7, 122.6, 66.7, 66.3, 51.3, 46.7, 28.3, 20.7. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{24}H_{31}N_4O_2^+$ 407.2442; Found 407.2440.

***N*-tert-Butyl-2-(dicyclohexylamino)-3,4-dihydro-3-*p*-tolylquinazoline-4-carboxamide (8m)**



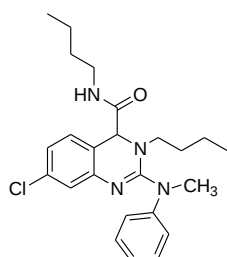
White solid (0.232 g, yield 57%), m.p. 112-115 °C; 1H NMR ($CDCl_3$, 600 MHz): δ (ppm) 7.59-6.91 (m, 8H, Ar-H), 5.88 (s, 0.25H, 0.25NH), 5.67 (s, 0.75H, 0.75NH), 4.82 and 4.79 (ss, 1H, CH), 2.38-2.27 (m, 5H, 2CHN and CH₃), 1.77-0.94 (m, 29H, 10CH₂ and 3CH₃); ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) 173.7 (minor), 169.7, 152.9, 145.4 (minor), 144.7, 143.4 (minor), 136.3 (minor), 134.6, 132.2 (minor), 130.5, (minor), 129.4, 128.8, 127.8 (minor), 126.6, 124.8, 123.4, 123.2 (minor), 122.9, 122.2, 121.7 (minor), 118.9 (minor), 71.0 (minor), 68.3, 59.7 (minor), 57.8, 51.2, 51.3, 33.8, 28.7, 28.5, 26.8, 25.7, 20.9. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{32}H_{45}N_4O^+$ 501.3588; Found 501.3586.

7-Chloro-*N*-cyclohexyl-2-(diisopropylamino)-3-(4-methoxyphenyl)-3,4-dihydroquinazoline-4-carboxamide (8n)



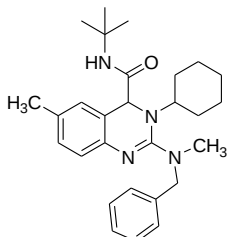
White solid (yield 0.269 g, 54%), mp 82-84 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.17 (s, 1H, Ar-H), 7.05 (d, J = 7.8 Hz, 2H, Ar-H), 6.92-6.88 (m, 2H, Ar-H), 6.78 (d, J = 8.4 Hz, 2H, Ar-H), 5.68 (d, J = 7.2 Hz, 1H, NH), 4.82-3.69 (m, 6H, OCH₃ and 3NCH), 1.82-1.02 (m, 22H, 5CH₂ and 4CH₃); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.1, 157.2, 153.0, 146.2, 139.9, 134.2, 127.5, 125.9, 122.9, 121.5, 120.2, 114.3, 67.6, 55.4, 48.5, 32.7, 32.6, 25.4, 24.6, 23.2, 19.0. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{28}H_{38}ClN_4O_2^+$ 497.2678; Found 497.2669.

***N*,3-Dibutyl-7-chloro-2-(methyl(phenyl)amino)-3,4-dihydroquinazoline-4-carboxamide (8o)**



White solid (yield 0.277 g, 65%), mp 127-129 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.23 (t, J = 7.2 Hz, 2H, Ar-H), 7.17 (d, J = 8.4 Hz, 1H, Ar-H), 7.13 (s, 1H, Ar-H), 7.05 (d, J = 7.8 Hz, 1H, Ar-H), 6.96 (d, J = 7.2 Hz, 2H, Ar-H), 6.84 (t, J = 6.6 Hz, 1H, Ar-H), 5.08 (s, 1H, CH), 3.98 (s, 1H, NH), 3.67-3.23 (m, 4H, 2NCH₂), 2.54 (s, 3H, NCH₃), 1.57-1.06 (m, 8H, 4CH₂), 0.98 (t, J = 7.2 Hz, 3H, CH₃), 0.76 (t, J = 7.2 Hz, 3H, CH₃); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.3, 149.6, 146.6, 146.1, 135.3, 130.8, 128.9, 124.9, 123.7, 123.5, 119.5, 116.9, 71.0, 46.6, 41.7, 38.4, 31.3, 29.8, 20.2, 19.7, 13.8, 13.6. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{24}H_{32}ClN_4O^+$ 427.2259; Found 427.2261.

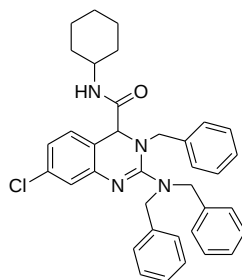
2-(Benzyl(methyl)amino)-*N*-(tert-butyl)-3-cyclohexyl-6-methyl-3,4-dihydroquinazoline-4-carboxamide (8p)



White solid (yield 0.329 g, 74%), mp 51-53 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.47-7.11 (m, 8H, Ar-H and NH), 7.03 (d, J = 7.8 Hz, 1H, Ar-H), 4.62 (s, 1H, CH), 3.59-3.47 (m, 3H, NCH₂ and NCH), 2.30 (s, 3H, NCH₃), 2.07 (s, 3H, CH₃), 2.00-1.24 (m, 19H, 5CH₂ and 3CH₃); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.9, 139.3, 137.5, 136.0, 133.9, 130.6, 129.4, 129.3, 128.5, 128.3, 127.0, 123.9, 69.0,

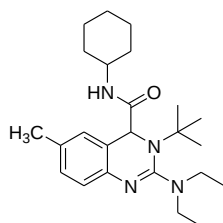
59.7, 56.7, 50.6, 39.3, 35.1, 28.8, 25.3, 24.4, 21.1. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{28}H_{39}N_4O^+$ 447.3118; Found 447.3115.

3-Benzyl-7-chloro-*N*-cyclohexyl-2-(dibenzylamino)-3,4-dihydroquinazoline-4-carboxamide (8q)



White solid (yield 0.385 g, 67%), mp 60-62 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.33-7.18 (m, 15H, Ar-H), 7.07 (d, J = 6.6 Hz, 2H, Ar-H), 6.76 (d, J = 7.8 Hz, 1H, NH), 6.52 (s, 1H, Ar-H), 4.78 (s, 1H, CH), 4.46 (d, J = 15.6 Hz, 1H, NCH_2^a), 4.28 (d, J = 15.6 Hz, 1H, NCH_2^b), 4.23-4.14 (m, 2H, NCH_2), 4.14 (t, J = 6.6 Hz, 1H, NCH), 3.82 (d, J = 13.8 Hz, 1H, NCH_2^a), 3.74-3.69 (m, 1H, NCH), 3.57 (d, J = 14.4 Hz, 1H, NCH_2^b), 1.86-1.02 (m, 10H, 5 CH_2); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 171.3, 155.0, 151.4, 139.1, 138.6, 137.9, 133.3, 130.7, 128.7, 128.6, 128.2, 127.7, 127.5, 127.4, 127.2, 126.8, 121.5, 120.8, 64.7, 54.8, 52.0, 48.8, 47.6, 33.2, 32.9, 25.5, 24.8. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{36}H_{38}ClN_4O^+$ 577.2729; Found 577.2725.

3-(*tert*-Butyl)-*N*-cyclohexyl-2-(diethylamino)-6-methyl-3,4-dihydroquinazoline-4-carboxamide (8r)

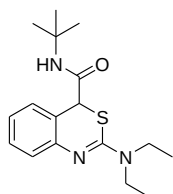


White solid (yield 0.168 g, 42%), mp 51-52 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.53 (d, J = 7.2 Hz, 1H, NH), 7.08 (d, J = 8.4 Hz, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 7.00 (d, J = 7.8 Hz, 1H, Ar-H), 4.80 (s, 1H, CH), 3.84-3.80 (m, 1H, NCH), 2.61-2.58 (m, 2H, NCH_2), 2.43-2.39 (m, 2H, NCH_2), 2.28 (s, 3H, CH_3), 1.90-1.26 (m, 19H, 5 CH_2 and 3 CH_3), 1.01 (t, J = 7.2 Hz, 5H, 5/6 $\times$ 2 CH_3), 0.88 (t, J = 6.6 Hz, 1H, 1/6 $\times$ 2 CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 171.6, 137.5, 136.4, 133.8, 130.7, 129.8, 129.2, 123.5, 64.8, 57.3 (minor), 47.2 (minor), 43.8, 33.2, 33.0, 31.6, 30.1 (minor), 29.7, 29.3 (minor), 25.6, 24.7, 22.7 (minor), 21.0, 14.1 (minor), 12.5. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{24}H_{39}N_4O^+$ 399.3118; Found 399.3110.

1.4 General procedure for preparation of 4*H*-3,1-benzothiazines 11

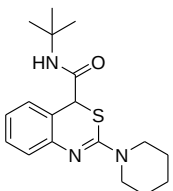
To a stirred solution of azide **4** (1 mmol) in CH_2Cl_2 (3 mL) was added dropwise triphenylphosphine (0.26 g, 1 mmol) in CH_2Cl_2 (2 mL) at room temperature. After the reaction mixture was stirred for 2–4 h at ambient temperature, CS_2 (0.76 g, 10 mmol) was added and the reaction mixture was stirred at 40 °C for 24 h. The solvent and excess CS_2 was completely removed and CH_3CN (5 mL) was added. Then secondary amine (1 mmol) was added and the reaction mixture was stirred for 1–6 h at room temperature. After the addition reaction was completed, K_2CO_3 (0.136 g, 1 mmol) was added and the mixture was left to stirred at 80 °C for 1–4 h. the solvent was removed under reduced pressure and the residual was purified by column chromatography with EtOAc/ petroleum ether to give 4*H*-3,1-benzothiazines **11**.

N-(*tert*-Butyl)-2-(diethylamino)- 4*H*-3,1-benzothiazine-4-carboxamide (11a)



White solid (yield 0.262 g, 82%), mp 136-138 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.29 (t, J = 7.2 Hz, 1H, Ar-H), 7.14 (d, J = 7.2 Hz, 2H, Ar-H), 7.01 (t, J = 6.6 Hz, 1H, Ar-H), 5.49 (s, 1H, NH), 4.46 (s, 1H, CH), 3.80-3.50 (m, 4H, 2 $\times$ NCH_2), 1.23 (t, J = 7.2 Hz, 6H, 2 CH_3), 1.20 (s, 9H, 3 CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.4, 152.7, 145.7, 129.3, 127.5, 125.2, 122.9, 118.0, 51.4, 48.5, 43.7, 28.3, 14.1. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{26}N_3OS^+$ 320.1791; Found 320.1785.

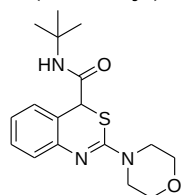
N-(*tert*-Butyl)-2-(piperidin-1-yl)-4*H*-3,1-benzothiazine-4-carboxamide (11b)



White solid (yield 0.274 g, 83%), mp 141-142 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.30 (t, J = 7.8 Hz, 1H, Ar-H), 7.14 (d, J = 7.8 Hz, 2H, Ar-H), 7.04 (t, J = 7.8 Hz, 1H, Ar-H), 5.51 (s, 1H, NH), 4.50 (s, 1H, CH), 3.83-3.73 (m, 4H, 2 $\times$ NCH_2), 1.71-1.59 (m, 6H, 3 CH_2), 1.22 (s, 9H, 3 CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.3, 153.7, 145.4,

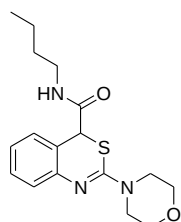
129.3, 127.5, 125.3, 123.3, 118.1, 51.4, 48.5, 48.0, 28.3, 26.0, 24.9. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{18}H_{26}N_3OS^+$ 332.1791; Found 332.1788.

***N*-(*tert*-Butyl)-2-morpholino-4*H*-3,1-benzothiazine-4-carboxamide (11c)**



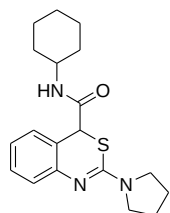
White solid (yield 0.279 g, 84%), mp 157-159 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.32 (t, J = 7.8 Hz, 1H, Ar-H), 7.16 (d, J = 7.8 Hz, 2H, Ar-H), 7.09 (t, J = 7.8 Hz, 1H, Ar-H), 5.43 (s, 1H, NH), 4.52 (s, 1H, CH), 3.83-3.73 (m, 8H, 4CH₂), 1.22 (s, 9H, 3CH₃); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.9, 154.4, 144.8, 129.5, 127.5, 125.5, 124.0, 118.3, 66.7, 51.5, 48.4, 47.4, 28.3. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{24}N_3O_2S^+$ 334.1584; Found 334.1582.

***N*-Butyl-2-morpholino-4*H*-3,1-benzothiazine-4-carboxamide (11d)**



White solid (yield 0.259 g, 78%), mp 123-125 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.34 (t, J = 7.2 Hz, 1H, Ar-H), 7.18-7.15 (m, 2H, Ar-H), 7.10 (t, J = 7.2 Hz, 1H, Ar-H), 5.50 (s, 1H, NH), 4.63 (s, 1H, CH), 3.84-3.73 (m, 8H, 4CH₂), 3.20-3.03 (m, 2H, NCH₂), 1.36-1.32 (m, 2H, CH₂), 1.24-1.19 (m, 2H, CH₂), 0.86 (t, J = 7.8 Hz, 3H, CH₃); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.0, 154.6, 144.9, 129.7, 127.7, 125.6, 124.1, 117.5, 66.6, 47.4, 47.2, 39.6, 31.3, 19.7, 13.7. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{17}H_{24}N_3O_2S^+$ 334.1584; Found 334.1581.

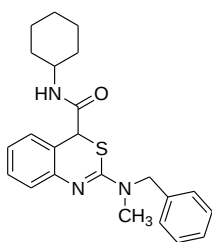
***N*-Cyclohexyl-2-(pyrrolidin-1-yl)-4*H*-3,1-benzothiazine-4-carboxamide (11e)**



White solid (yield 0.265 g, 77%), mp 148-150 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.30 (t, J = 7.8 Hz, 1H, Ar-H), 7.16 (d, J = 7.8 Hz, 1H, Ar-H), 7.12 (d, J = 7.2 Hz, 1H, Ar-H), 7.01 (t, J = 7.8 Hz, 1H, Ar-H), 5.55 (d, J = 6.6 Hz, 1H, NH), 4.53 (s, 1H, CH), 3.76-3.56 (m, 5H, 2×NCH₂ and NCH), 1.98-1.94 (m, 4H, 2CH₂), 1.71-0.96 (m, 10H, 5CH₂); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.5, 151.9, 145.7, 129.5, 127.7, 125.3, 122.9, 117.2, 48.1, 48.0, 47.6, 32.2, 25.3, 25.0, 24.1. HRMS (ESI-TOF) m/z $[M+H]^+$

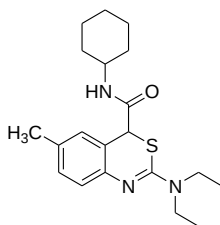
Calcd for $C_{19}H_{26}N_3OS^+$ 344.1791; Found 344.1785.

2-(Benzyl(methyl)amino)-*N*-cyclohexyl-4*H*-3,1-benzothiazine-4-carboxamide (11f)



White solid (yield 0.311 g, 79%), mp 120-121 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.31-7.15 (m, 8H, Ar-H), 7.06 (t, J = 7.2 Hz, 1H, Ar-H), 5.48 (d, J = 6.6 Hz, 1H, NH), 5.00 (d, J = 15.0 Hz, 1H, NCH₂^a), 4.73 (d, J = 15.6 Hz, 1H, NCH₂^b), 4.60 (s, 1H, CH), 3.69-3.64 (m, 1H, NCH), 3.16 (s, 3H, NCH₃), 1.73-0.92 (m, 10H, 5CH₂); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.2, 154.4, 145.6, 137.3, 129.5, 128.6, 127.5, 127.4, 125.5, 123.4, 117.4, 54.2, 48.4, 47.8, 36.5, 32.3, 25.3, 24.3. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{23}H_{28}N_3OS^+$ 394.1948; Found 394.1945.

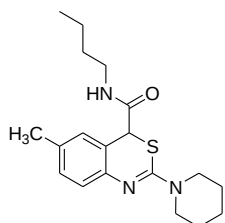
***N*-Cyclohexyl-2-(diethylamino)-6-methyl-4*H*-3,1-benzothiazine-4-carboxamide (11g)**



White solid (yield 0.258 g, 72%), mp 142-143 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.10 (d, J = 7.8 Hz, 1H, Ar-H), 7.04 (d, J = 8.4 Hz, 1H, Ar-H), 6.94 (s, 1H, Ar-H), 5.52 (d, J = 6.0 Hz, 1H, NH), 4.49 (s, 1H, CH), 3.75-3.48 (m, 5H, 2×NCH₂ and NCH), 2.31 (s, 3H, CH₃), 1.73-1.26 (m, 7H, 7/10×5CH₂), 1.20 (t, J = 7.2 Hz, 6H, 2CH₃), 1.11-0.93 (m, 3H, 3/10×5CH₂); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.6, 152.2, 143.4, 132.6, 130.2, 127.9, 125.1, 117.3, 48.2, 47.7, 43.6, 32.4, 32.3, 25.4, 24.3, 20.8, 14.1. HRMS (ESI-TOF) m/z $[M+H]^+$ Calcd for $C_{20}H_{29}N_3OS^+$ 360.2104; Found 360.2098.

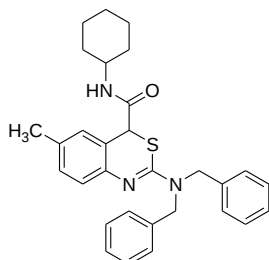
***N*-Butyl-6-methyl-2-(piperidin-1-yl)-4*H*-3,1-benzothiazine-4-carboxamide (11h)**

White solid (yield 0.279 g, 81%), mp 135-136 °C; 1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.12 (d, J = 7.8 Hz, 1H, Ar-H), 7.05 (d, J = 8.4 Hz, 1H, Ar-H), 6.94 (s, 1H, Ar-H), 5.59 (s, 1H, NH), 4.55 (s, 1H, CH), 3.77-3.71 (m, 4H, 2×NCH₂), 3.27-2.98 (m, 2H, NCH₂), 2.32 (s, 3H, CH₃), 1.68-1.58 (m, 6H, 3CH₂),



1.37-1.18 (m, 4H, 2CH₂), 0.85 (t, J = 7.2 Hz, 3H, CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 169.5, 153.4, 143.1, 133.1, 130.2, 128.1, 125.3, 117.1, 47.8, 47.6, 39.5, 31.3, 25.9, 24.9, 20.8, 19.7, 13.7. HRMS (ESI-TOF) m/z [M+H]⁺ Calcd for C₁₉H₂₈N₃OS⁺ 346.1948; Found 346.1945.

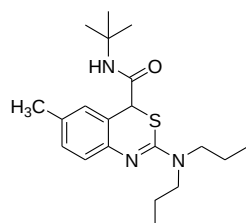
N-Cyclohexyl-2-(dibenzylamino)-6-methyl-4H-3,1-benzothiazine-4-carboxamide (11i)



White solid (yield 0.377 g, 78%), mp 156-158 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.32-7.25 (m, 10H, Ar-H), 7.14 (d, J = 7.8 Hz, 1H, Ar-H), 7.10 (d, J = 8.4 Hz, 1H, Ar-H), 6.98 (s, 1H, Ar-H), 5.47 (d, J = 7.8 Hz, 1H, NH), 5.10 (s, 2H, NCH₂), 4.57 (s, 1H, CH), 4.54 (d, J = 16.2 Hz, 2H, NCH₂), 3.69-3.65 (m, 1H, NCH), 2.34 (s, 3H, CH₃), 1.78-0.92 (m, 10H, 5CH₂); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 168.4, 154.0, 143.1, 137.5, 133.3, 130.3, 128.5, 128.0, 127.7, 127.3, 125.5, 117.3, 51.1, 48.6, 48.0, 32.5, 32.4, 25.3, 24.5, 20.9. HRMS

(ESI-TOF) m/z [M+H]⁺ Calcd for C₃₀H₃₄N₃OS⁺ 484.2417; Found 484.2411.

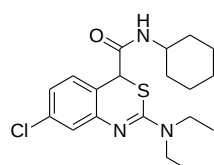
N-(tert-Butyl)-2-(dipropylamino)-6-methyl-4H-3,1-benzothiazine-4-carboxamide (11j)



White solid (yield 0.271 g, 75%), mp 156-157 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.09 (d, J = 7.8 Hz, 1H, Ar-H), 7.02 (d, J = 7.8 Hz, 1H, Ar-H), 6.93 (s, 1H, Ar-H), 5.50 (s, 1H, NH), 4.41 (s, 1H, CH), 3.67-3.62 (m, 2H, NCH₂), 3.40-3.36 (m, 2H, NCH₂), 2.31 (s, 3H, CH₃), 1.69-1.62 (m, 4H, 2CH₂), 1.20 (s, 9H, 3CH₃), 0.93 (t, J = 7.2 Hz, 6H, 2CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 168.6, 152.6, 143.2, 132.5, 130.0, 127.9, 125.1, 117.6, 51.3, 51.1, 48.6, 28.3, 22.0, 20.8, 11.3.

HRMS (ESI-TOF) m/z [M+H]⁺ Calcd for C₂₀H₃₂N₃OS⁺ 362.2261; Found 362.2258.

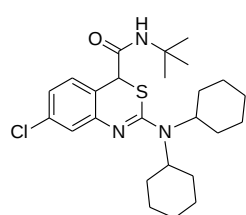
7-Chloro-N-cyclohexyl-2-(diethylamino)-4H-3,1-benzothiazine-4-carboxamide (11k)



White solid (yield 0.315 g, 83%), mp 162-164 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.15 (s, 1H, Ar-H), 7.06 (d, J = 8.4 Hz, 1H, Ar-H), 6.98 (d, J = 7.8 Hz, 1H, Ar-H), 5.49 (d, J = 6.0 Hz, 1H, NH), 4.53 (s, 1H, CH), 3.74-3.48 (m, 5H, 2×NCH₂ and NCH), 1.74-1.29 (m, 7H, 7/10×5CH₂), 1.21 (t, J = 7.2 Hz, 6H, 2CH₃), 1.12-0.94 (m, 3H, 3/10×5CH₂); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 168.0, 153.5, 147.1,

134.7, 128.4, 125.0, 122.7, 116.0, 48.4, 47.1, 43.9, 32.4, 32.3, 25.3, 24.3, 14.0. HRMS (ESI-TOF) m/z [M+H]⁺ Calcd for C₁₉H₂₇ClN₃OS⁺ 380.1558; Found 380.1554.

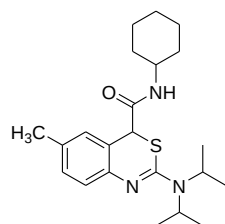
N-(tert-Butyl)-7-chloro-2-(dicyclohexylamino)-4H-3,1-benzothiazine-4-carboxamide (11l)



White solid (yield 0.249 g, 54%), mp 118-120 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.12 (s, 1H, Ar-H), 7.05 (d, J = 7.8 Hz, 1H, Ar-H), 6.97 (d, J = 7.8 Hz, 1H, Ar-H), 5.58 (s, 1H, NH), 4.41 (s, 1H, CH), 3.80-3.67 (m, 2H, 2CH), 2.21-1.15 (m, 29H, 10CH₂ and 3CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 168.2, 152.5, 146.6, 134.4, 128.4, 124.6, 122.6, 116.6, 59.1, 51.5, 48.3, 32.0, 30.7, 28.4, 26.3, 26.2, 25.4. HRMS (ESI-TOF) m/z [M+H]⁺ Calcd for C₂₅H₃₇ClN₃OS⁺ 462.2340; Found

462.2336.

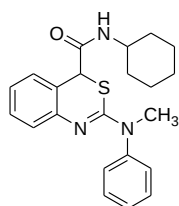
N-Cyclohexyl-2-(diisopropylamino)-6-methyl-4H-3,1-benzothiazine-4-carboxamide (11m)



White solid (yield 0.186 g, 48%), mp 168-169 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.09 (d, J = 7.8 Hz, 1H, Ar-H), 7.03 (d, J = 8.4 Hz, 1H, Ar-H), 6.92 (s, 1H, Ar-H), 5.61 (d, J = 6.6 Hz, 1H, NH), 4.48 (s, 1H, CH), 4.23-4.18 (m, 2H, 2NCH), 3.69-3.64 (m, 1H, NCH), 2.31 (s, 3H, CH₃), 1.78-0.94 (m, 22H, 5CH₂ and 4CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 168.8, 150.9, 143.0, 132.6, 130.0, 127.8, 125.0, 117.5, 49.0, 48.2, 48.0, 32.5, 32.3, 25.4, 24.3, 22.1, 20.8. HRMS (ESI-TOF)

m/z [M+H]⁺ Calcd for C₂₂H₃₄N₃OS⁺ 388.2417; Found 388.2412.

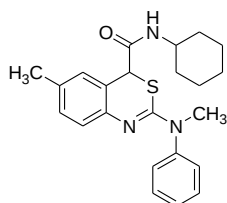
N-Cyclohexyl-2-(methyl(phenyl)amino)-4H-3,1-benzothiazine-4-carboxamide (11n)



White solid (yield 0.212 g, 56%), mp 194-196 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.41 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.34 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.25-7.10 (m, 3H, Ar-H), 7.17 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.09 (t, *J* = 7.2 Hz, 1H, Ar-H), 5.64 (d, *J* = 6.0 Hz, 1H, NH), 4.47 (s, 1H, CH), 3.70-3.66 (m, 1H, NCH), 3.56 (s, 3H, NCH₃), 1.81-0.99 (m, 10H, 5CH₂); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 167.9, 153.2, 144.9, 144.0, 129.3, 128.6, 127.8, 127.7, 127.6, 125.5, 123.9, 118.2, 48.3, 48.0, 39.7, 32.4, 25.4, 24.3. HRMS

(ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₂H₂₆N₃OS⁺ 380.1791; Found 380.1785.

N-Cyclohexyl-6-methyl-2-(methyl(phenyl)amino)-4H-3,1-benzothiazine-4-carboxamide (11o)



White solid (yield 0.201 g, 51%), mp 207-208 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.40 (t, *J* = 7.2 Hz, 2H, Ar-H), 7.32 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.22-7.14 (m, 4H, Ar-H), 6.97 (s, 1H, Ar-H), 5.69 (d, *J* = 5.4 Hz, 1H, NH), 4.41 (s, 1H, CH), 3.70-3.66 (m, 1H, NCH), 3.54 (s, 3H, NCH₃), 2.33 (s, 3H, CH₃), 1.81-1.01 (m, 10H, 5CH₂); ¹³C NMR (CDCl₃, 150 MHz) δ (ppm) 168.0, 152.5, 144.1, 142.5, 133.6, 130.1, 129.3, 128.3, 127.6, 127.4, 125.3, 117.9, 48.3, 48.1, 39.7, 32.4, 25.4, 24.3,

20.8. HRMS (ESI-TOF) *m/z* [M+H]⁺ Calcd for C₂₃H₂₈N₃OS⁺ 394.1948; Found 394.1942.

1.5 Reference

1. He, P.; Wu, J.; Nie, Y. B.; Ding, M. W. *Tetrahedron* **2009**, 65, 8563-8570.

2. Copies of ^1H and ^{13}C NMR spectrum of compound 4, 8 and 11

