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Supplementary Material - I

Benzothiazole carbamates and amides as antiproliferative species

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HPLC purity determination. Compounds were analyzed for purity (HPLC) using Agilent 1200 HPLC system equipped with a Quat Pump (G1311B), an injector (G1329B) 1260 ALS, TCC 1260 (G1316A) and a detector 1260 DAD VL+ (G1315C). Compounds were dissolved in methanol, final concentrations were ~ 1mg/mL. HPLC analysis was performed in two diverse systems for each compound.

Method A. Zorbax Eclipse Plus C18 4.6 × 150mm, 1.8 μ , S.N. USWKY01594 was used as the stationary phase. Eluent was made of the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). The analysis were performed at 280 nm for compounds **24 – 26** and **29 – 31**; at 290 nm for compounds **28, 33, 34** and **41** and at 320 nm for compounds **42 – 46**. Flow rate was 0.5 mL/min.

Compounds **24 – 26** and **29 – 31** were eluted using gradient protocol: 0–0.5 min 95% A, 0.5–3 min 95% A→ 5% A, 3–13 min 5% A, 13–14 min 5% A→ 95% A, 14–16 min 95% A.

Compound **28** was eluted using gradient protocol: 0–1.5 min 95% A, 1.5–5 min 95% A→ 5% A, 5–16 min 5% A, 16–18 min 5% A→ 95% A, 18–21 min 95% A.

Compounds **33** and **34** were eluted using gradient protocol: 0–1.5 min 95% A, 1.5–5 min 95% A→ 5% A, 5–16 min 5% A, 16–18 min 5% A→ 95% A, 18–20 min 95% A.

Compound **41** was eluted using gradient protocol: 0–1.5 min 95% A, 1.5–5 min 95% A→ 5% A, 5–16 min 5% A, 16–18 min 5% A→ 95% A.

Compounds **42 – 46** were eluted using gradient protocol: 0–1 min 95% A, 1–5 min 95% A→ 5% A, 5–16 min 5% A, 16–18 min 5% A→ 95% A.

Method B. Zorbax Eclipse Plus C18 4.6 × 150mm, 1.8 μ , S.N. USWKY01594 was used as the stationary phase. Eluent was made of the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis were performed at 280 nm for compounds **24 – 26** and **29 – 31**; at 290 nm for compounds **28, 34** and **41** and at 320 nm for compounds **32** and **42 – 46**. Flow rate was 0.5 mL/min.

Compounds **24 – 26** and **29 – 31** were eluted using gradient protocol: 0–0.5 min 95% A, 0.5–3 min 95% A→ 5% A, 3–13 min 5% A, 13–14 min 5% A→ 95% A, 14–16 min 95% A.

Compound **28** was eluted using gradient protocol: 0–1.5 min 95% A, 1.5–5 min 95% A→ 5% A, 5–16 min 5% A, 16–18 min 5% A→ 95% A, 18–21 min 95% A.

Compound **32** was eluted using gradient protocol: 0–1 min 95% A, 1–5 min 95% A→ 5% A, 5–14 min 5% A, 14–15 min 5% A→ 95% A, 15–16 min 95% A.

Compound **34** was eluted using gradient protocol: 0–1.5 min 95% A, 1.5–5 min 95% A→ 5% A, 5–16 min 5% A, 16–18 min 5% A→ 95% A, 18–20 min 95% A.

Compounds **41** – **46** were eluted using gradient protocol: 0–1 min 95% A, 1–5 min 95% A→ 5% A, 5–16 min 5% A, 16–18 min 5% A→ 95% A.

Method C. Zorbax Eclipse Plus C18 2.1 × 100mm, 1.8μ, S.N. USUXU04444 was used as the stationary phase. Eluent was made of the following solvents: water (A) and methanol (B). The analysis were performed at 320 nm for compound **32**. Flow rate was 0.5 mL/min.

Compound **32** was eluted using gradient protocol: 0–1 min 95% A, 1–5 min 95% A→ 5% A, 5–14 min 5% A, 14–15 min 5% A→ 95% A, 15–16 min 95% A.

Method D. Poroshell 120 EC-C18, 4.6 × 50mm, 2.7μ, S.N. USCFU07797 was used as the stationary phase. Eluent was made of the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). The analysis were performed at 290 nm for compound **33** and 280 nm for compounds **27** and **38**. Flow rate was 1 mL/min.

Compound **33** was eluted using gradient protocol: 0–0.5 min 95% A, 0.5–3 min 95% A→ 5% A, 3–13 min 5% A, 13–14 min 5% A→ 95% A, 14–15 min 95% A.

Compounds **27** and **38** were eluted using gradient protocol: 0–0.5 min 95% A, 0.5–1.5 min 95% A→ 5% A, 1.5–8 min 5% A, 8–9 min 5% A→ 95% A, 9–10 min 95% A.

Method E. Zorbax Eclipse Plus C18 4.6 × 150mm, 1.8μ, S.N. USWKY01594 was used as the stationary phase. Eluent was made of the following solvents: water (A) and acetonitrile (B). The analysis were performed at 280 nm for compound **37** and at 290 nm for compounds **35** and **36**. Flow rate was 0.5 mL/min.

Compounds **35** and **36** were eluted using gradient protocol: 0–1 min 95% A, 1–6 min 95% A→ 5% A, 6–13 min 5% A, 13–14 min 5% A→ 95% A, 14–17 min 95% A.

Compound **37** was eluted using gradient protocol: 0–1 min 95% A, 1–5 min 95% A→ 5% A, 5–16 min 5% A, 16–17 min 5% A→ 95% A, 17–18 min 95% A.

Method F. Zorbax Eclipse Plus C18 4.6 × 150mm, 1.8μ, S.N. USWKY01594 was used as the stationary phase. Eluent was made of the following solvents: water (A) and methanol (B). The analysis were performed at 290 nm for compounds **35** and **36** and at 280 nm for compound **37**. Flow rate was 0.5 mL/min.

Compounds **35** and **36** were eluted using gradient protocol: 0–1 min 95% A, 1–6 min 95% A→ 5% A, 6–13 min 5% A, 13–14 min 5% A→ 95% A, 14–17 min 95% A.

Compound **37** was eluted using gradient protocol: 0–1 min 95% A, 1–5 min 95% A→ 5% A, 5–16 min 5% A, 16–17 min 5% A→ 95% A, 17–18 min 95% A.

Method G. Zorbax Eclipse Plus C18 2.1 × 100mm, 1.8μ, S.N. USUXU04444 was used as the stationary phase. Eluent was made of the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis were performed at 295 nm for compounds **39** and **40**. Flow rate was 0.5 mL/min.

Compounds **39** and **40** were eluted using gradient protocol: 0–1 min 95% A→ 5% A, 1–7 min 5% A, 7–8 min 5% A→ 95% A, 8–10 min 95% A.

Method H. Zorbax Eclipse Plus C18 2.1 × 100mm, 1.8μ, S.N. USUXU04444 was used as the stationary phase. Eluent was made of the following solvents: 0.2% formic acid in water (A) and acetonitrile (B). The analysis were performed at 295 nm for compound **39**. Flow rate was 0.5 mL/min.

Compound **39** was eluted using gradient protocol: 0–1 min 95% A→ 5% A, 1–7 min 5% A, 7–8 min 5% A→ 95% A, 8–10 min 95% A.

Method I. Poroshell 120 EC-C18, 4.6 × 50mm, 2.7μ, S.N. USCFU07797 was used as the stationary phase. Eluent was made of the following solvents: 0.2% formic acid in water (A) and methanol (B). The analysis were performed at 280 nm for compounds **27** and **38** and at 295 nm for compound **37**. Flow rate was 0.5 mL/min.

Compounds **27** and **38** were eluted using protocol: 0–0.5 min 95%A, 0.5–1.5 min 95% A→ 5% A, 1.5–8 min 5% A, 8–9 5% A→ 95% A, 9–10 min 95% A.

Compound **40** was eluted using protocol: 0–1 min 95%A, 1–2 min 95% A→ 5% A, 2–10 min 5% A, 10–11 5% A→ 95% A, 11–12 min 95% A.

General procedure A for synthesis of 4-(alkylthio)anilines 13 – 16¹

The appropriate alkylthiol (1.5 eq) was added to the mixture containing 1-chloro-4-nitrobenzene (1 eq), potassium hydroxide (3 eq) and PEG as a solvent. The reaction mixture was stirred at 100 °C for 3.5 h and then poured onto the water. After the extraction with ethyl acetate, combined organic layers were dried over anhydrous Na₂SO₄, filtered and evaporated to dryness. The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent to afford the final product.

General procedure B for synthesis of 6-(alkylsulfanyl)-1,3-benzothiazol-2-amines 19 – 22: A solution of bromine (1.25 eq) in acetic acid was added to a stirring mixture of an appropriate 4-(alkylthio)aniline (1 eq), ammonium thiocyanate (4 eq), acetic acid and water at 10 °C. The reaction mixture was stirred at room temperature for 18 h, and then at 80 °C for 3 h. After cooling to room temperature, the reaction mixture was poured onto water and Na₂CO₃ was added in order to adjust pH to 5-6. The reaction mixture was extracted with

ethyl acetate, layers were separated and organic layer was washed with brine. Organic layer was dried over anhydrous Na₂SO₄, filtered and evaporated to dryness. The crude product was subjected to silica gel column chromatography using CH₂Cl₂/CH₃OH (or hexane/EtOAc for **22**) as eluent and reversed-phase flash chromatography, Biotage SP1, using CH₃OH/H₂O as eluent to afford the final product.

General procedure C for synthesis of (6-substituted-1,3-benzo[d]thiazol-2-yl)carbamates **24 – 26, 29, 31 and 32:** A solution of bromine (1.25 eq) in glacial acetic acid was added to a stirring mixture of an appropriate 4-substituted aniline (1 eq), ammonium thiocyanate (4 eq), acetic acid and water at 10 °C. The reaction mixture was stirred at room temperature for 18 h, and then at 80 °C for 3 h. After cooling to room temperature, the reaction mixture was poured onto water and Na₂CO₃ was added in order to adjust pH to 5-6. The reaction mixture was extracted with ethyl acetate, layers were separated and organic layer was washed with brine. Organic layer was dried over anhydrous Na₂SO₄, filtered and evaporated to dryness. The crude product 6-substituted benzothiazolamine was used in the next reaction step. An appropriate alkyl chloroformate (1.1 eq) and triethylamine (1.8 eq) were added to a solution of 6-substituted benzothiazolamine in benzene. The reaction mixture was stirred at 80°C for 3 h, and then poured onto cold water and extracted with ethyl acetate. Combined organic layers were dried over anhydrous Na₂SO₄, filtered and evaporated to dryness. The crude product was further purified in a manner provided for each compound.

General procedure D for synthesis of compounds **28, 30 and 33 – 37:** An appropriate alkyl chloroformate (1.1 eq) and triethylamine (1.8 eq) were added to a solution of corresponding 6-(alkylsulfanyl)-1,3-benzothiazol-2-amine (1 eq) in benzene. After 3 h of stirring at 80 °C the reaction mixture was poured onto water and extracted with ethyl acetate. Combined organic layers were dried over anhydrous Na₂SO₄, filtered and evaporated to dryness. The crude product was subjected to silica gel column chromatography and silica gel flash chromatography, Biotage SP1, using hexane/ethyl acetate as eluent to afford the final product.

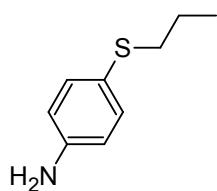
General procedure E for synthesis of *N*-[6-(propylsulfanyl)-1,3-benzothiazol-2-yl]alkanamides **41 – 46:** The alkanoyl chlorides were prepared according to known procedures using an appropriate commercially available acids and thionyl chloride as starting materials.² A solution of an appropriate alkanoyl chloride (1.3 eq) in benzene was added dropwise into the solution of corresponding benzothiazolamine (1 eq) (**19** or **20**) in CH₂Cl₂/benzene (1:1, v/v) at 0 °C. The reaction mixture was stirred at the same temperature until consumption of starting benzothiazolamine (TLC control). The reaction was quenched with cold water. The layers were separated and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and evaporated to dryness. The crude product was subjected to a multiple column chromatography to afford desired compound.

General procedure F for synthesis of compounds **27 and 38:**³

To a stirring solution of **24** (1 eq) in CH₂Cl₂, MCPBA (1 eq for **38** and 4 eq for **27**) was added. After stirring (4h in the dark for **38** and 16h for **27**) at room temperature, 10% aqueous Na₂S₂O₃ solution was added. The layers were separated, organic layer was washed with saturated aqueous NaHCO₃ solution, dried over anhydrous Na₂SO₄, filtered and evaporated to dryness. The crude product was further purified in a manner provided for each compound

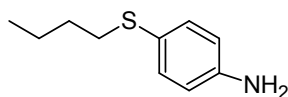
General procedure G for synthesis of compounds 39 and 40:⁴ To a solution of **28** (1 eq) in methanol, acetonitrile (1.5 eq) and K₂CO₃ (0.7 eq) were added. The mixture is cooled to 0 °C with vigorous stirring and hydrogen-peroxide (1.2 eq for **39** and 4 eq for **40**) was added dropwise as a solution in methanol over 30 minutes. The reaction was maintained at 0 °C four hours (for **39**) or at room temperature overnight (for **40**). After consumption of starting material, the mixture is poured onto brine and extracted with CH₂Cl₂. Organic layers were dried over anhydrous Na₂SO₄ and evaporated to dryness. The crude product was further purified in a manner provided for each compound.

4-(Propylthio)aniline (**13**)



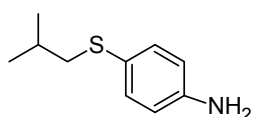
The general procedure A was followed using 1-propanethiol (471 mg, 6.18 mmol), 1-chloro-4-nitrobenzene (650 mg, 4.12 mmol), potassium-hydroxide (694 mg, 12.4 mmol) and PEG-600 (19 mL) to afford 433 mg of final product as brown oil. Yield 63%. IR (ATR): 3456m, 3349s, 3214m, 3026m, 2961s, 2928s, 2870m, 1620s, 1596s, 1494s, 1457m, 1377m, 1284s, 1236m, 1176m, 1146m, 1089m, 1011m, 821m, 734w, 629w, 515w cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 7.23 (d, *J* = 8.2 Hz, 2H), 6.62 (d, *J* = 8.6 Hz, 2H), 2.77 – 2.71 (m, 2H), 1.63 – 1.54 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 145.54, 133.69, 123.78, 115.52, 38.33, 22.62, 13.22.

4-(Butylthio)aniline (**14**)



The general procedure A was followed using 1-butanethiol (204 μL, 1.904 mmol), 1-chloro-4-nitrobenzene (200 mg, 1.27 mmol), potassium-hydroxide (214 mg, 3.81 mmol) and PEG-1000 (6 g) to afford 111.7 mg of final product as brown oil. Yield 49%. ¹H NMR (500 MHz, CDCl₃, δ): 7.23 (d, *J* = 8.5 Hz, 1H), 6.62 (d, *J* = 8.3 Hz, 1H), 3.72 (bs, 2H), 2.77 (t, *J* = 7.4 Hz, 2H), 1.58 – 1.52 (m, 2H), 1.44 – 1.36 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 145.61, 133.67, 123.92, 115.57, 36.05, 31.49, 21.79, 13.63.

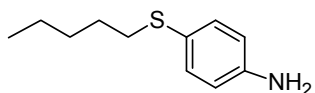
[4-(Isobutylthio)phenyl]amine (**15**)



The general procedure A was followed using 2-methyl-1-propanthiol (516 μL, 4.75 mmol), 1-chloro-4-nitrobenzene (500 mg, 3.17 mmol), potassium-hydroxide (534 mg,

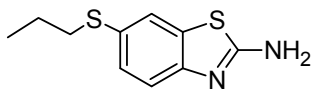
9.52 mmol) and PEG-600 (15 mL) to afford 110.1 mg of final product as a brown oil. Yield 19%. IR (ATR): 3462m, 3360m, 3217m, 3023m, 2956s, 2926m, 2868m, 1621s, 1598s, 1494s, 1462m, 1282m, 1245m, 1175m, 822m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 7.22 (d, $J = 8.7$ Hz, 2H), 6.61 (d, $J = 8.5$ Hz, 2H), 3.67 (bs, 2H), 2.66 (d, $J = 6.9$ Hz, 2H), 1.76 (sep, $J = 6.8$ Hz, 1H), 0.99 (d, $J = 6.6$ Hz, 6H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 145.54, 133.47, 124.42, 115.56, 45.52, 28.18, 21.89. (+)ESI-HRMS: m/z 182.09943 corresponds to molecular formula $\text{C}_{10}\text{H}_{15}\text{NSH}^+$ (error, -2.02 ppm).

4-(Pentylthio)aniline (16)



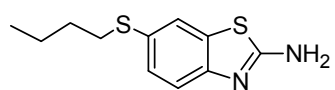
The general procedure A was followed using 1-pentanethiol (472 μL , 3.80 mmol), 1-chloro-4-nitrobenzene (400 mg, 2.54 mmol), potassium-hydroxide (428 mg, 7.63 mmol) and PEG-600 (12 mL) to afford 156 mg of final product as yellow oil. Yield 31%. IR (ATR): 3459m, 3362s, 3213m, 3026m, 2956s, 2927s, 2857s, 1621s, 1597s, 1495s, 1462m, 1378w, 1336m, 1283s, 1177m, 1111w, 1094w, 822m, 518m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 7.22 (d, $J = 8.6$ Hz, 2H), 6.62 (d, $J = 8.2$ Hz, 2H), 3.72 (bs, 2H), 2.76 (t, $J = 7.5$ Hz, 2H), 1.59 – 1.53 (m, 2H), 1.39 – 1.26 (m, 4H), 0.87 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 145.62, 133.65, 123.91, 115.56, 36.34, 30.86, 29.06, 22.24, 13.95. (+)ESI-HRMS: m/z 196.11548 corresponds to molecular formula $\text{C}_{11}\text{H}_{17}\text{NSH}^+$ (error, +0.15 ppm).

6-(Propylsulfanyl)-1,3-benzothiazol-2-amine (19)



The general procedure B was followed using solution of bromine (215 μL , 4.20 mmol) in acetic acid (1.4 mL), 4-(propylthio)aniline (562.7 mg, 3.364 mmol), ammonium thiocyanate (1.02 g, 13.4 mmol), acetic acid (5.6 mL) and water (0.3 mL) to afford 617.2 mg of final product as pale yellow solid. Yield 82%. M.p. = (115 – 117) $^{\circ}\text{C}$. IR (ATR): 3369s, 3290m, 3092s, 2962s, 2924s, 2863m, 2753m, 1641s, 1589m, 1532s, 1445s, 1300m, 1268m, 1117m, 1001w, 894w, 876w, 810m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 7.60 (d, $J = 1.8$ Hz, 1H), 7.45 (d, $J = 8.5$ Hz, 1H), 7.35 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.8$ Hz, 1H), 2.87 (t, $J = 7.3$ Hz, 2H), 1.68 – 1.60 (m, 2H), 1.01 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 166.69, 151.66, 131.89, 128.24, 126.78, 122.76, 117.93, 36.32, 22.04, 13.04. (+)ESI-HRMS: m/z 225.05194 corresponds to molecular formula $\text{C}_{10}\text{H}_{12}\text{N}_2\text{S}_2\text{H}^+$ (error, +2.10 ppm).

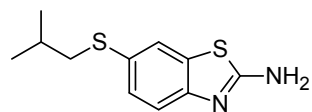
6-(Butylsulfanyl)-1,3-benzothiazol-2-amine (20)



The general procedure B was followed using solution of bromine (209 μL , 4.08 mmol) in acetic acid (2.1 mL), 4-(butylthio)aniline **14** (593 mg, 3.27 mmol), ammonium thiocyanate (995.6 mg, 13.08 mmol), acetic acid (8.5 mL) and water (0.45 mL) to afford 725 mg of final product as pale yellow solid. Yield 93%. M.p. = (96 – 98) $^{\circ}\text{C}$. IR (ATR): 3397s, 3277m, 3084m, 2962s, 2928s, 2871m, 2736w, 1635s, 1591m, 1529s, 1453s, 1299m, 1271m, 1110m, 809m, 766w cm^{-1} . ^1H NMR (500

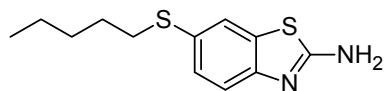
MHz, CDCl₃, δ): 7.61 (d, $J = 1.8$ Hz, 1H), 7.46 (d, $J = 8.3$ Hz, 1H), 7.34 (dd, $J_1 = 8.3$ Hz, $J_2 = 1.8$ Hz, 1H), 5.21 (bs, 2H), 2.89 (t, $J = 7.3$ Hz, 2H), 1.63 – 1.57 (m, 2H), 1.47 – 1.40 (m, 2H), 0.91 (t, $J = 7.3$ Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 165.77, 150.85, 132.32, 129.71, 129.18, 123.12, 119.36, 35.27, 31.35, 21.84, 13.61. (+)ESI-HRMS: m/z 239.06740 corresponds to molecular formula C₁₁H₁₄N₂S₂H⁺ (error, +1.18 ppm).

6-(Isobutylthio)-1,3-benzothiazol-2-amine (21)



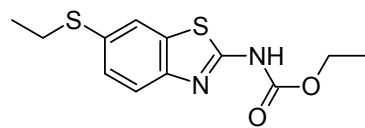
The general procedure B was followed using solution of bromine (36 μ L, 0.70 mmol) in acetic acid (0.4 mL), 4-(isobutylthio)aniline **15** (83 mg, 0.56 mmol), ammonium thiocyanate (170.3 mg, 2.237 mmol), acetic acid (1.5 mL) and water (70 μ L) to afford 72.2 mg of final product as yellow solid. Yield 54%. M.p. = (129 – 131) °C. IR (ATR): 3354m, 3290m, 3234m, 3080s, 2959s, 2748w, 1642s, 1588w, 1526s, 1440s, 1365w, 1332w, 1301m, 1269m, 1114m, 821m cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 7.61 (bs, 1H), 7.43 (d, $J = 8.3$ Hz, 1H), 7.3 – 7.32 (m, 1H), 5.47 (bs, 2H), 2.78 (d, $J = 6.9$ Hz, 2H), 1.82 (sep, $J = 6.7$ Hz, 1H), 1.02 (d, $J = 6.6$ Hz, 6H). ¹³C NMR (125 MHz, CDCl₃, δ): 165.83, 150.80, 132.31, 130.16, 129.10, 123.02, 119.35, 44.68, 28.24, 21.94. (+)ESI-HRMS m/z 239.06666 corresponds to molecular formula C₁₁H₁₄N₂S₂H⁺ (error, -1.89 ppm).

6-(Pentylsulfanyl)-1,3-benzothiazol-2-amine (22)



The general procedure B was followed using solution of bromine (42 μ L, 0.82 mmol) in acetic acid (0.5 mL), 4-(pentylthio)aniline **16** (129 mg, 0.660 mmol), ammonium thiocyanate (201 mg, 2.64 mmol), acetic acid (2 mL) and water (0.1 mL) to afford 68.8 mg of final product as yellow oil. Yield 56%. IR (ATR): 3429m, 3279m, 3075s, 2957s, 2927s, 2859s, 2730m, 1643s, 1588m, 1526s, 1452s, 1372m, 1338m, 1319m, 1298m, 1271m, 1106m, 1045w, 894w, 814m cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 7.61 (d, $J = 1.8$ Hz, 1H), 7.44 (d, $J = 8.5$ Hz, 1H), 7.33 (dd, $J_1 = 8.2$ Hz, $J_2 = 1.8$ Hz, 1H), 5.46 (s, 2H), 2.89 – 2.86 (m, 2H), 1.64 – 1.58 (m, 2H), 1.42 – 1.28 (m, 4H), 0.88 (t, $J = 7.2$ Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 165.85, 150.89, 132.32, 129.70, 129.17, 123.11, 119.35, 35.57, 30.88, 28.95, 22.21, 13.93. (+)ESI-HRMS: m/z 235.08255 corresponds to molecular formula C₁₂H₁₆N₂S₂H⁺ (error, -0.85 ppm).

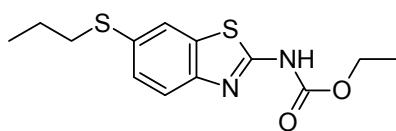
Ethyl [6-(ethylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (24)



The general procedure C was followed using a solution of bromine (101 μ L, 1.97 mmol) in glacial acetic acid (1 mL), 4-(ethylthio)aniline hydrochloride (300 mg, 1.58 mmol), ammonium thiocyanate (481 mg, 6.32 mmol), glacial acetic acid (4 mL) and water (0.15 mL). The crude product was dissolved in benzene (5 mL) and subjected to the next reaction step including ethyl chloroformate (165 μ L, 1.73 mmol) and triethylamine (395 μ L, 2.83 mmol). 179.4 mg of the final product was obtained after crystallization from benzene as pale yellow solid. Yield 40%. M.p. =

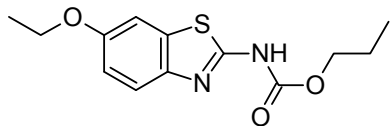
(162 – 165) °C. IR (ATR): 3432w, 3400w, 3162m, 3124m, 3079m, 3045m, 2973s, 2924s, 2776m, 1720s, 1599s, 1557s, 1444s, 1364m, 1290s, 1250s, 1119m, 1070m, 1048m, 1021w, 820m, 757m cm^{-1} . ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 7.96 (d, $J = 1.6$ Hz, 1H), 7.61 (d, $J = 8.4$ Hz, 1H), 7.36 (dd, $J_1 = 8.4$ Hz, $J_2 = 1.8$ Hz, 1H), 4.24 (q, $J = 7.1$ Hz, 2H), 2.98 (q, $J = 7.3$ Hz, 2H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.22 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 159.53, 153.88, 147.84; 132.61, 130.26, 127.58, 121.85, 120.52, 61.94, 27.48, 14.30. (+)ESI-HRMS: m/z 283.05655 corresponds to molecular formula $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, -1.38 ppm). HPLC purity, method A: $t_R = 8.695$, area 99.27%. Method B: $t_R = 9.906$, area 96.29%.

Ethyl [6-(propylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (25)



The general procedure C was followed using a solution of bromine (63 μL , 1.2 mmol) in glacial acetic acid (0.5 mL), 4-(propylthio)aniline hydrochloride (200 mg, 0.982 mmol), ammonium thiocyanate (299 mg, 3.93 mmol), glacial acetic acid (2.5 mL) and water (0.1 mL). The crude product was dissolved in benzene (5 mL) and subjected to the next reaction step including ethyl chloroformate (103 μL , 1.08 mmol) and triethylamine (246 μL , 1.76 mmol). The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent, to afford 60 mg of final product as pale yellow solid. Yield 21%. M.p. = (158 – 162) °C. IR (ATR): 3135w, 3076w, 2957m, 2909m, 2869m, 2782m, 1725s, 1597s, 1561s, 1453s, 1428m, 1270s, 1243s, 1110m, 1069m, 1045m, 1022m, 816m, 759m, 707m cm^{-1} . ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 12.00 (bs, 1H), 7.96 (d, $J = 1.4$ Hz, 1H), 7.60 (d, $J = 8.5$ Hz, 1H), 7.36 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.8$ Hz, 1H), 4.24 (q, $J = 7.1$ Hz, 2H), 2.94 (t, $J = 7.1$ Hz, 2H), 1.61 – 1.54 (m, 2H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.96 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (50 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 159.85, 154.23, 148.00, 132.89, 130.76, 127.84, 122.09, 120.78, 62.20, 35.57, 22.22, 14.52, 13.34. (+)ESI-HRMS: m/z 297.07191 corresponds to molecular formula $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, -2.30 ppm). HPLC purity, method A: $t_R = 9.194$, area 99.67%. Method B: $t_R = 10.528$, area 99.44%.

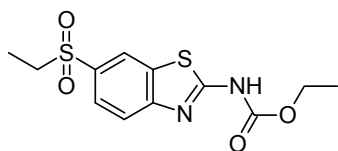
Propyl (6-ethoxy-1,3-benzothiazol-2-yl)carbamate (26)



The general procedure C was followed using a solution of bromine (93 μL , 1.8 mmol) in glacial acetic acid (0.5 mL), 4-ethoxyaniline (188 μL , 1.46 mmol), ammonium thiocyanate (444 mg, 5.83 mmol), glacial acetic acid (2.5 mL) and water (0.1 mL). The crude product was dissolved in benzene (5 mL) and subjected to the next reaction step including propyl chloroformate (180 μL , 1.6 mmol) and triethylamine (366 μL , 2.63 mmol). The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent. After the crystallization from benzene 100.7 mg of final product was obtained as pale yellow solid. Yield 25%. M.p. = (168 – 169) °C. IR (ATR): 3161w, 3081m, 2977s, 2933m, 2802m, 1718s, 1612s, 1562s, 1463s, 1391m, 1272s, 1242s, 1212s, 1113m, 1057s, 971w, 941m, 792m, 760m cm^{-1} . ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 11.83 (bs,

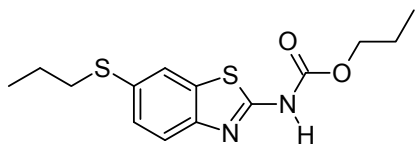
1H), 7.56 (d, $J = 8.9$ Hz, 1H), 7.51 (d, $J = 2.5$ Hz, 1H), 6.97 (dd, $J_1 = 8.7$ Hz, $J_2 = 2.5$ Hz, 1H), 4.14 (t, $J = 6.6$ Hz, 1H), 4.04 (q, $J = 7.0$ Hz, 2H), 1.69 – 1.62 (m, 2H), 1.33 (t, $J = 6.9$ Hz, 3H), 0.93 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 157.46, 155.12, 143.28, 132.76, 120.81, 114.97, 105.47, 67.16, 63.62, 21.73, 14.70, 10.13. (+)ESI-HRMS: m/z 281.09541 corresponds to molecular formula $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_3\text{SH}^+$ (error, -0.10 ppm). HPLC purity, method A: $t_{\text{R}} = 8.520$, area 99.48%. Method B: $t_{\text{R}} = 9.741$, area 96.69%.

Ethyl [6-(ethanesulfonyl)-1,3-benzothiazol-2-yl]carbamate (27)



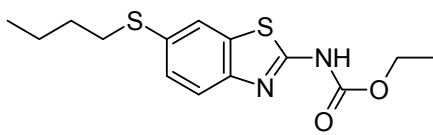
The general procedure F was followed using **24** (50 mg, 0.2 mmol), CH_2Cl_2 (15 mL) and MCPBA (122 mg, 0.707 mmol). The 30.5 mg of final product was obtained as pale yellow solid. Yield 55%. M.p. = (257 – 259) °C. IR: 3121m, 3072w, 2979m, 2944m, 2775w, 1721s, 1602m, 1556s, 1450m, 1307s, 1254m, 1150s, 1103w, 1044w, 1018w, 830w, 786w, 757w, 715w cm^{-1} . ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 12.37 (bs, 1H), 8.58 (d, $J = 0.9$ Hz, 1H), 7.89 – 7.85 (m, 2H), 4.28 (q, $J = 7.1$ Hz, 2H), 3.31 – 3.28 (m, 2H), 1.30 (t, $J = 7.1$ Hz, 3H), 1.12 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , $(\text{CD}_3)_2\text{SO}$, δ): 163.77, 153.80, 152.94, 132.42, 132.16, 125.29, 122.37, 120.27, 62.05, 49.76, 14.12, 7.18. (+)ESI-HRMS: m/z 315.04662 corresponds to molecular formula $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_4\text{S}_2\text{H}^+$ (error, -0.48 ppm). HPLC purity, method D: $t_{\text{R}} = 4.187$, area 95.46%. Method I: $t_{\text{R}} = 4.662$, area 95.51%.

Propyl [6-(propylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (28)



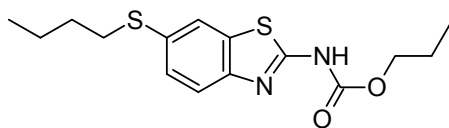
The general procedure D was followed using propyl chloroformate (854 μL , 7.60 mmol), triethylamine (1.75 mL, 12.4 mmol), **19** (1.55 g, 6.91 mmol) and benzene (18 mL). The final product was obtained as pale yellow solid. The yield was 778 mg (47%). M.p. = (138 – 140) °C. IR (ATR): 3167m, 3062m, 2960s, 2932m, 2876m, 1724s, 1598s, 1562s, 1449m, 1447s, 1308m, 1273s, 1244s, 1047m, 962w, 888w, 805m, 782m, 755m cm^{-1} . ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 12.01 (bs, 1H), 7.96 (d, $J = 1.7$ Hz, 1H), 7.60 (d, $J = 8.4$ Hz, 1H), 7.36 (dd, $J_1 = 8.4$ Hz, $J_2 = 1.9$ Hz, 1H), 4.15 (t, $J = 6.7$ Hz, 2H), 2.94 (t, $J = 7.2$ Hz, 2H), 1.70 – 1.63 (m, 2H), 1.61 – 1.54 (m, 2H), 0.98 – 0.92 (m, 6H). ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 159.54, 154.00, 147.74, 132.61, 130.49, 127.58, 121.82, 120.49, 67.28, 35.38, 21.99, 21.68, 13.09, 10.10. (+)ESI-HRMS: m/z 311.08810 corresponds to molecular formula $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, -0.47 ppm). HPLC purity, method A: $t_{\text{R}} = 11.532$, area 98.23%. Method B: $t_{\text{R}} = 13.159$, area 98.53%.

Ethyl [6-(butylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (**29**)



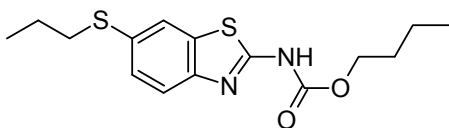
The general procedure C was followed using a solution of bromine (90 μL , 1.8 mmol) in glacial acetic acid (1 mL), 4-(butylthio)aniline (**14**) (253.9 mg, 1.400 mmol), ammonium thiocyanate (426 mg, 5.60 mmol), glacial acetic acid (4 mL) and water (0.15 mL). The crude product was dissolved in benzene (5 mL) and subjected to the next reaction step including ethyl chloroformate (147 μL , 1.54 mmol) and triethylamine (351 μL , 2.52 mmol). The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent. The final product was obtained after crystallization from benzene as 83.2 mg of pale yellow solid. Yield 19%. M.p. = (138 – 140) $^{\circ}\text{C}$. IR (ATR): 3139m, 3072s, 2983s, 2954s, 2931s, 2865s, 2794s, 1724s, 1603s, 1570s, 1452s, 1366m, 1340m, 1313m, 1293s, 1274s, 1250s, 1113m, 1070m, 1048m, 1022m, 816s, 781m, 760s, 708m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 11.90 (bs, 1H), 7.86 (d, $J = 8.6$ Hz, 1H), 7.78 (d, $J = 1.7$ Hz, 1H), 7.40 (dd, $J_1 = 8.4$ Hz, $J_2 = 1.8$ Hz, 1H), 4.41 (q, $J = 7.3$ Hz, 2H), 2.96 (t, $J = 7.5$ Hz, 2H), 1.67 – 1.61 (m, 2H), 1.50 – 1.41 (m, 5H), 0.93 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 161.39, 153.81, 147.21, 132.40, 131.82, 128.33, 122.21, 120.81, 62.88, 34.73, 31.28, 21.89, 14.46, 13.63. (+)ESI-HRMS: m/z 311.08801 corresponds to molecular formula $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, -0.76 ppm). HPLC purity, method A: $t_{\text{R}} = 9.757$, area 97.08%. Method B: $t_{\text{R}} = 11.594$, area 96.14%.

Propyl [6-(butylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (**30**)



The general procedure D was followed using propyl chloroformate (713 μL , 6.34 mmol), triethylamine (1.45 mL, 10.4 mmol), **20** (1.37 g, 5.77 mmol) and benzene (29 mL). The final product was obtained as yellow solid. The yield was 543 mg (29%). M.p. = 130 $^{\circ}\text{C}$. IR (ATR): 3169m, 3068m, 2960s, 2926s, 2785m, 1725s, 1601m, 1564m, 1451m, 1288m, 1247m, 1070w, 818w, 752w cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 11.35 (bs, 1H), 7.82 (d, $J = 8.5$ Hz, 1H), 7.78 (d, $J = 1.4$ Hz, 1H), 7.40 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.8$ Hz, 1H), 4.30 (t, $J = 6.8$ Hz, 2H), 2.96 (t, $J = 7.4$ Hz, 2H), 1.84 – 1.77 (m, 2H), 1.67 – 1.61 (m, 2H), 1.50 – 1.42 (m, 2H), 0.99 (t, $J = 7.5$ Hz, 3H), 0.92 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 161.06, 153.80, 147.35, 132.54, 131.83, 128.42, 122.29, 120.83, 68.53, 34.77, 31.31, 22.14, 21.91, 13.65, 10.32. (+)ESI-HRMS: m/z 325.10408 corresponds to molecular formula $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, +0.56 ppm). HPLC purity, method A: $t_{\text{R}} = 10.371$, area 96.76%. Method B: $t_{\text{R}} = 12.388$, area 98.58%.

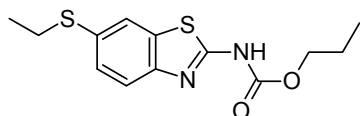
Butyl [6-(propylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (**31**)



The general procedure C was followed using a solution of bromine (94 μL , 1.8 mmol) in glacial acetic acid (1 mL), 4-(propylthio)aniline

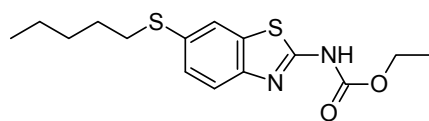
hydrochloride (300 mg, 1.47 mmol), ammonium thiocyanate (448 mg, 5.88 mmol), glacial acetic acid (4 mL) and water (0.15 mL). The crude product was dissolved in benzene (5 mL) and subjected to the next reaction step including butyl chloroformate (205 μ L, 1.61 mmol) and triethylamine (369 μ L, 2.65 mmol). The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent and then crystallized from benzene as pale yellow solid. The yield was 133 mg, 28%. M.p. = (74 – 80) °C. IR (ATR): 3170m, 3070m, 2961s, 2931s, 2872m, 1721s, 1602s, 1562s, 1456m, 1293s, 1248s, 1074w, 814w, 762w cm^{-1} . ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 7.94 (d, J = 1.6 Hz, 1H), 7.60 (d, J = 8.3 Hz, 1H), 7.35 (dd, J_1 = 8.5 Hz, J_2 = 1.8 Hz, 1H), 4.19 (t, J = 6.6 Hz, 2H), 2.94 (t, J = 7.1 Hz, 2H), 1.65 – 1.53 (m, 4H), 1.41 – 1.35 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 159.60, 154.04, 147.74, 132.63, 130.53, 127.60, 121.84, 120.51, 65.59, 35.43, 30.34, 22.02, 18.50, 13.55, 13.11. (+)ESI-HRMS: m/z 325.10391 corresponds to molecular formula $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, +0.05 ppm). HPLC purity, method A: t_R = 10.346, area 99.78%. Method B: t_R = 11.916, area 99.36%.

Propyl [6-(ethylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (32)



The general procedure C was followed using a solution of bromine (101 μ L, 1.80 mmol) in glacial acetic acid (1 mL), 4-(propylthio)aniline hydrochloride (300 mg, 1.58 mmol), ammonium thiocyanate (481 mg, 6.32 mmol), glacial acetic acid (4 mL) and water (0.15 mL). The crude product was dissolved in benzene (7 mL) and subjected to the next reaction step including propyl chloroformate (195 μ L, 1.73 mmol) and triethylamine (396 μ L, 2.84 mmol). The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent and reversed-phase flash chromatography, Biotage SP1, using $\text{CH}_3\text{OH}/\text{H}_2\text{O}$ as eluent to afford 125 mg of final product as pale yellow solid. Yield 27%. M.p. = (137 – 138) °C. IR (ATR): 3062m, 2968s, 2922s, 1717s, 1600m, 1562m, 1445m, 1396w, 1287m, 1248m, 1072w, 1044w, 759w, cm^{-1} . ^1H NMR (500 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 12.01 (bs, 1H), 7.95 (d, J = 1.8 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.36 (dd, J_1 = 8.5 Hz, J_2 = 1.8 Hz, 1H), 4.15 (t, J = 6.8 Hz, 1H), 2.98 (q, J = 7.3 Hz, 2H), 1.70 – 1.63 (m, 2H), 1.22 (t, J = 7.3 Hz, 3H), 0.93 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $(\text{CD}_3)_2\text{SO}$, δ): 160.13, 154.54, 148.24, 133.06, 130.67, 128.02, 122.27, 120.93, 67.73, 27.93, 22.12, 14.74, 10.56. (+)ESI-HRMS: m/z 297.07243 corresponds to molecular formula $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, -0.57 ppm). HPLC purity, method B: t_R = 12.996, area 95.61%. Method C: t_R = 14.178, area 95.09%.

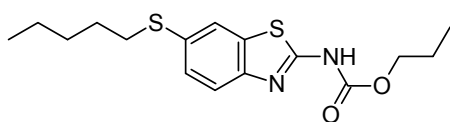
Ethyl [6-(pentylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (33)



The general procedure D was followed using ethyl chloroformate (78 μ L, 0.82 mmol), triethylamine (186 μ L, 1.33 mmol), **22** (188 mg, 0.745 mmol) and benzene (4 mL). The final product was obtained as pale yellow solid. The yield was 51.4 mg (21%). M.p. = (137 – 138) °C. IR (ATR): 3175m, 3152m, 3123m, 3058m, 2956s, 2924s,

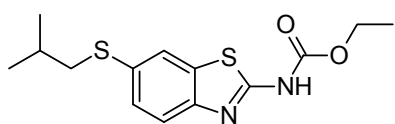
2854s, 1724s, 1597s, 1550s, 1460s, 1370m, 1296s, 1241s, 1069m, 818m, 766m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 11.60 (bs, 1H), 7.84 (d, $J = 8.5$ Hz, 1H), 7.78 (d, $J = 1.6$ Hz, 1H), 7.40 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.6$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 2.95 (t, $J = 7.5$ Hz, 2H), 1.69 – 1.63 (m, 2H), 1.45 – 1.39 (m, 5H), 1.37 – 1.29 (m, 2H), 0.89 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 161.19, 153.75, 147.25, 132.47, 131.85, 128.37, 122.22, 120.82, 62.90, 35.01, 30.93, 28.88, 22.23, 14.46, 13.94. (+)ESI-HRMS: m/z 325.10435 corresponds to molecular formula $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, +1.40 ppm). HPLC purity, method A: $t_R = 12.206$, area 98.52%. Method D: $t_R = 4.563$, area 98.28%.

Propyl [6-(pentylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (34)



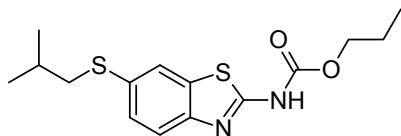
The general procedure D was followed using propyl chloroformate (92 μL , 0.82 mmol), triethylamine (186 μL , 1.33 mmol), **22** (188 mg, 0.745 mmol) and benzene (4 mL). The final product was obtained as yellow solid. The yield was 101.4 mg (40%). M.p. = (116 – 118) $^{\circ}\text{C}$. IR (ATR): 3170m, 3127m, 3062m, 2956s, 2923s, 2853s, 2784m, 1725s, 1601s, 1562s, 1451m, 1393m, 1309m, 1289s, 1248s, 1069m, 821m, 752m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 11.72 (bs, 1H), 7.84 (d, $J = 8.6$ Hz, 1H), 7.78 (d, $J = 1.5$ Hz, 1H), 7.40 (dd, $J_1 = 8.4$ Hz, $J_2 = 1.8$ Hz, 1H), 4.30 (t, $J = 6.8$ Hz, 2H), 2.94 (t, $J = 7.4$ Hz, 2H), 1.84 – 1.77 (m, 2H), 1.69 – 1.63 (m, 2H), 1.45 – 1.39 (m, 2H), 1.36 – 1.29 (m, 2H), 0.99 (t, $J = 7.5$ Hz, 3H), 0.89 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 161.31, 153.88, 147.26, 132.43, 131.80, 128.37, 122.23, 120.77, 68.50, 35.03, 30.92, 28.87, 22.22, 22.11, 13.93, 10.30. (+)ESI-HRMS: m/z 339.12006 corresponds to molecular formula $\text{C}_{16}\text{H}_{22}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, +1.51 ppm). HPLC purity, method A: $t_R = 13.079$, area 96.82%. Method B: $t_R = 14.812$, area 95.51%.

Ethyl {6-[(2-methylpropyl)sulfanyl]-1,3-benzothiazol-2-yl}carbamate (35)



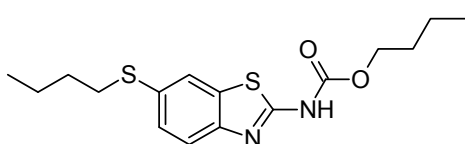
The general procedure D was followed using ethyl chloroformate (34 μL , 0.36 mmol), triethylamine (82 μL , 0.58 mmol), **21** (77 mg, 0.32 mmol) and benzene (1.8 mL) to afford 19.1 mg of final product as white solid. Yield 23%. M.p. = (159 – 160) $^{\circ}\text{C}$. IR (ATR): 3139m, 3081m, 2968s, 2914s, 2866m, 1722s, 1599s, 1560s, 1458m, 1275s, 1246s, 1111m, 1070m, 1049m, 1019m, 820m, 789m, 762m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 11.47 (bs, 1H), 7.84 (d, $J = 8.5$ Hz, 1H), 7.77 (d, $J = 1.6$ Hz, 1H), 7.40 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.8$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 2.85 (d, $J = 6.9$ Hz, 2H), 1.88 (sep, $J = 6.7$ Hz, 1H), 1.42 (t, $J = 7.1$ Hz, 3H), 1.05 (d, $J = 6.6$ Hz, 6H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 161.25, 153.77, 147.18, 132.44, 132.27, 128.30, 122.13, 62.88, 44.10, 28.32, 22.01, 14.46. (+)ESI-HRMS: m/z 311.08796 corresponds to molecular formula $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, -0.92 ppm). HPLC purity, method E: $t_R = 12.189$, area 99.00%. Method B: $t_R = 13.873$, area 99.59%.

Propyl {6-[(2-methylpropyl)sulfanyl]-1,3-benzothiazol-2-yl}carbamate (36)



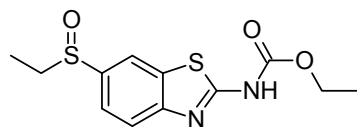
The general procedure D was followed using propyl chloroformate (33 μ L, 0.29 mmol), triethylamine (67 μ L, 0.29 mmol), **21** (63.9 mg, 0.268 mmol) and benzene (1.5 mL) to afford 53.7 mg of final product as pale yellow solid. Yield 62%. M.p. = (139 – 141) $^{\circ}$ C. IR (ATR): 3172m, 3131m, 3074m, 2919s, 2852m, 1722s, 1599m, 1565m, 1456m, 1282s, 1245s, 1074m, 818m, 760m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 11.60 – 11.58 (m, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 1.6 Hz, 1H), 7.40 (dd, J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H), 4.30 (t, J = 6.8 Hz, 2H), 2.85 (d, J = 6.8 Hz, 2H), 1.91 – 1.77 (m, 3H), 1.05 (d, J = 6.6 Hz, 6H), 0.99 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 161.18, 153.85, 147.23, 132.47, 132.25, 128.33, 122.16, 120.79, 68.49, 44.11, 28.31, 22.00, 10.30. (+)ESI-HRMS: m/z 325.10387 corresponds to formula $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, -0.08 ppm). HPLC purity, method E: t_R = 12.787, area 98.08%. Method F: t_R = 14.618, area 99.74%.

Butyl [6-(butylsulfanyl)-1,3-benzothiazol-2-yl]carbamate (37)



The general procedure D was followed using butyl chloroformate (175 μ L, 1.35 mmol), triethylamine (309 μ L, 2.21 mmol), **20** (293.7 mg, 1.232 mmol) and benzene (5 mL) to afford 131 mg of final product as yellow solid. Yield 32%. M.p. = (120 – 121) $^{\circ}$ C. IR (ATR): 3143m, 3077m, 2953s, 2928s, 2866m, 1727s, 1598s, 1452m, 1276m, 1246m, 1108w, 1074w, 820m, 782w, 756m cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 11.64 – 11.41 (m, 1H), 7.84 – 7.81 (m, 1H), 7.78 (d, J = 1.5 Hz, 1H), 7.40 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 4.35 (t, J = 6.7 Hz, 2H), 2.96 (t, J = 7.4 Hz, 2H), 1.79 – 1.73 (m, 2H), 1.67 – 1.61 (m, 2H), 1.50 – 1.38 (m, 4H), 0.97 – 0.91 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 161.50, 153.95, 147.22, 132.39, 131.77, 128.33, 122.25, 120.76, 66.76, 34.75, 31.28, 30.76, 21.88, 18.99, 13.66. (+)ESI-HRMS: m/z 339.12048 corresponds to molecular formula $\text{C}_{16}\text{H}_{22}\text{N}_2\text{O}_2\text{S}_2\text{H}^+$ (error, +2.77 ppm). HPLC purity, method E: t_R = 12.749, area 95.92%. Method F: t_R = 14.577, area 98.25%.

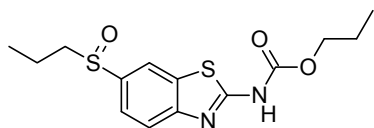
Ethyl [6-(ethanesulfinyl)-1,3-benzothiazol-2-yl]carbamate (38)



The general procedure F was followed using **24** (42.5 mg, 0.151 mmol), CH_2Cl_2 (20 mL) and MCPBA (26.0 mg, 0.151 mmol). Na_2SO_4 . The crude product was purified by reversed-phase flash chromatography, Biotage SP1, using $\text{CH}_3\text{OH}/\text{H}_2\text{O}$ as eluent affording 12.6 mg of white solid. Yield 28%. M.p. = 195 $^{\circ}$ C. IR (ATR): 3359m, 3175m, 3056m, 2924s, 2853s, 1713s, 1658m, 1634m, 1602s, 1564s, 1448m, 1366m, 1301s, 1276m, 1250s, 1103m, 1072m, 1044m, 891w, 827w, 794m, 761m, 708w cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , δ): 10.94 (bs, 1H), 8.13 (d, J = 1.4 Hz, 1H), 8.02 (d, J = 8.5 Hz, 1H), 7.59 (dd, J_1 = 8.5 Hz, J_2 = 1.6 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 3.00 –

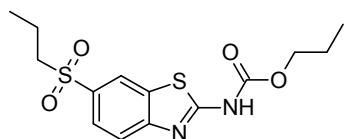
2.93 (m, 1H), 2.88 – 2.81 (m, 1H), 1.43 (t, $J = 7.2$ Hz, 3H), 1.23 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , δ): 163.04, 153.58, 150.90, 138.24, 132.77, 121.84, 121.18, 117.98, 63.26, 50.76, 14.47, 6.14. (+)ESI-HRMS: m/z 299.05162 corresponds to molecular formula $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_3\text{S}_2\text{H}^+$ (error, -0.81 ppm). HPLC purity, method D: $t_{\text{R}} = 4.087$, area 95.52%. Method I: $t_{\text{R}} = 4.668$, area 95.14%.

Propyl [6-(propane-1-sulfinyl)-1,3-benzothiazol-2-yl]carbamate (39)

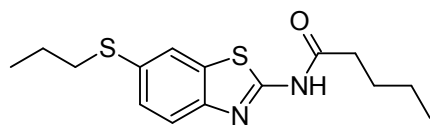


The general procedure G was followed using **28** (30.3 mg, 0.098 mmol), methanol (0.5 mL), acetonitrile (8 μL , 0.1 mmol), K_2CO_3 (10 mg, 0.07 mmol) and solution of hydrogen-peroxide (12 μL , 0.12 eq) in methanol (0.5 mL). The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent to afford 8.4 mg of final product as white solid. Yield 26%. IR (ATR): 3165m, 3127m, 3057m, 2964s, 2933s, 2876s, 2780m, 1724s, 1601s, 1557s, 1449s, 1404m, 1292s, 1274s, 1249s, 1066s, 1032m, 966m, 890m, 829m, 784m, 754m, 708w cm^{-1} . ^1H NMR (500 MHz, CD_3OD , δ): 12.21 (bs, N-H), 8.28 – 8.26 (m, 1H), 7.84 – 7.83 (m, 1H), 7.66 – 7.64 (m, 1H), 4.17 (t, $J = 6.6$ Hz, 2H), 2.95 – 2.77 (m, 2H), 1.70 – 1.47 (m, 4H), 0.97 – 0.92 (m, 6H). ^{13}C NMR (125 MHz, CD_3OD , δ): 161.76, 154.08, 151.19, 138.54, 132.39, 121.86, 120.73, 118.13, 67.47, 57.75, 21.63, 15.32, 12.91, 10.09. (+)ESI-HRMS: m/z 327.08293 correspond to molecular formula $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_3\text{S}_2\text{H}^+$ (error, -0.72 ppm). HPLC purity, method G: $t_{\text{R}} = 5.365$, area 97.49%. Method H: $t_{\text{R}} = 3.559$, area 96.03%.

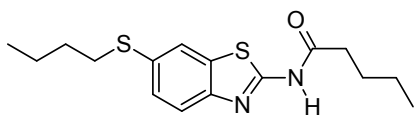
Propyl [6-(propane-1-sulfonyl)-1,3-benzothiazol-2-yl]carbamate (40)



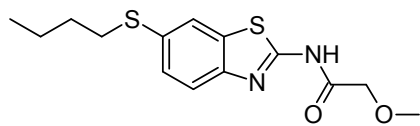
The general procedure G was followed using **28** (42.2 mg, 0.136 mmol), methanol (0.5 mL), acetonitrile (10 μL , 0.2 mmol), K_2CO_3 (13 mg, 0.095 mmol) and solution of hydrogen-peroxide (54 μL , 0.54 mmol) in methanol (0.5 mL). The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as an eluent and reversed-phase flash chromatography using $\text{CH}_3\text{OH}/\text{H}_2\text{O}$ as an eluent to afford 22.5 mg of final product as white solid. Yield 48%. M.p. = 270 $^\circ\text{C}$. IR (ATR): 3169m, 3125m, 2971s, 2936m, 2880m, 2771w, 1730s, 1598m, 1550s, 1454m, 1405w, 1346w, 1306s, 1279s, 1231s, 1147s, 1103m, 1072m, 942w, 825w, 784m, 757m, 710w cm^{-1} . ^1H NMR (500 MHz, CD_3OD , δ): 12.37 (bs, N-H), 8.57 – 8.56 (m, 2H), 7.88 – 7.84 (m, 2H), 4.18 (t, $J = 6.6$ Hz, 2H), 3.30 – 3.26 (m, 2H), 1.72 – 1.66 (m, 2H), 1.60 – 1.53 (m, 2H), 0.96 – 0.89 (m, 6H). ^{13}C NMR (125 MHz, CD_3OD , δ): 164.40, 154.55, 153.40, 133.75, 132.65, 125.91, 123.03, 120.99, 68.09, 57.20, 22.11, 16.76, 12.99, 10.57. (+)ESI-HRMS: m/z 343.07768 corresponds to molecular formula $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_4\text{S}_2\text{H}^+$ (error, -1.16 ppm). HPLC purity, method G: $t_{\text{R}} = 5.253$, area 98.21%. Method I: $t_{\text{R}} = 5.480$, area 97.67%.

***N*-[6-(propylsulfanyl)-1,3-benzothiazol-2-yl]pentanamide (41)**

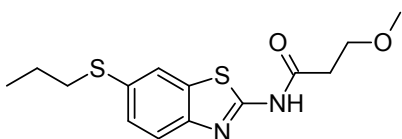
The general procedure E was followed using a solution of pentanoyl chloride (87.2 mg, 0.723 mmol) in benzene (1.5 mL) and a solution of **19** (124.8 mg, 0.556 mmol) in CH₂Cl₂/benzene (2 mL, 1:1, v/v). The reaction mixture was stirred for 4 h and worked up according to general procedure. The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate and reversed-phase flash chromatography, Biotage SP1, using methanol/water as eluent to afford 35.3 mg of final product as pale yellow solid. Yield 21%. M.p. = 113 °C. IR (ATR): 3276m, 3178m, 3128m, 3064m, 2960s, 2930m, 2870m, 1660s, 1594s, 1538s, 1439m, 1374w, 1345m, 1295m, 1266m, 1192w, 1087w, 815w, 774w cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 10.66 (bs, 1H), 7.81 (d, *J* = 1.6 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.44 (dd, *J*₁ = 8.5 Hz, *J*₂ = 1.8 Hz, 1H), 2.94 (t, *J* = 7.3 Hz, 2H), 2.46 (t, *J* = 7.6 Hz, 2H), 1.73 – 1.66 (m, 4H), 1.37 – 1.30 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 171.64, 158.91, 146.43, 132.89, 132.38, 128.68, 122.46, 120.58, 36.91, 36.26, 26.97, 22.54, 22.19, 13.64, 13.38. (+)ESI-HRMS: *m/z* 309.10813 corresponds to molecular formula C₁₅H₂₀N₂OS₂H⁺ (error, -2.76 ppm). HPLC purity, method A: *t*_R = 11.671, area 97.05%. Method B: *t*_R = 13.245, area 98.01%.

***N*-[6-(butylsulfanyl)-1,3-benzothiazol-2-yl]pentanamide (42)**

The general procedure E was followed using a solution of pentanoyl chloride (69.6 mg, 0.58 mmol) in benzene (1 mL) and a solution of **20** (86 mg, 0.36 mmol) in CH₂Cl₂/benzene (2.2 mL, 1:1, v/v). The reaction mixture was stirred for 3 h at 0°C, then 13 h at room temperature and worked up according to general procedure. The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate and reversed-phase flash chromatography, Biotage SP1, using methanol/water as eluent to afford 32.6 mg of final product as white solid. Yield 28%. M.p. = 117 °C. IR (ATR): 3144m, 3116m, 3036m, 2958s, 2927s, 2870s, 1694s, 1590s, 1542s, 1443m, 1380m, 1349m, 1306w, 1269s, 1172m, 1099w, 1052w, 976w, 892w, 810m, 769w cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 10.15 (bs, 1H), 7.80 (d, *J* = 1.6 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.43 (dd, *J*₁ = 8.5 Hz, *J*₂ = 1.8 Hz, 1H), 2.98 – 2.95 (m, 2H), 2.49 – 2.46 (m, 2H), 1.74 – 1.68 (m, 2H), 1.67 – 1.61 (m, 2H), 1.50 – 1.34 (m, 4H), 0.94 – 0.89 (m, 6H). ¹³C NMR (125 MHz, CDCl₃, δ): 171.61, 158.86, 146.39, 132.87, 132.45, 128.53, 122.31, 120.55, 36.22, 34.53, 31.21, 26.94, 22.16, 21.86, 13.61, 13.59. (+) ESI-HRMS: *m/z* 323.12407 corresponds to molecular formula C₁₆H₂₂N₂OS₂H⁺ (error, -1.73 ppm). HPLC purity, method A: *t*_R = 12.200, area 96.72%. Method B: *t*_R = 13.409, area 98.18%.

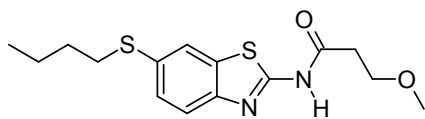
***N*-[6-(butylsulfanyl)-1,3-benzothiazol-2-yl]-2-methoxyacetamide (43).**

The general procedure E was followed using a solution of methoxyacetyl chloride (51.5 mg, 0.474 mmol) in benzene (1 mL) and a solution of **20** (70.7 mg, 0.296 mmol) in CH₂Cl₂/benzene (2.2 mL, 1:1, v/v). The reaction mixture was stirred for 4 h at 0°C, then 13 h at room temperature and worked up according to general procedure. The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent to afford 41.3 mg of final product as pale yellow solid. Yield 45 %. M.p. = 62 °C. IR (ATR): 3382w, 3207w, 2956m, 2929m, 2871w, 1703m, 1594m, 1537s, 1448m, 1272m, 1196w, 1119m, 994w, 817w, 745w cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 9.86 (bs, 1H), 7.79 – 7.78 (m, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.43 (dd, *J*₁ = 8.5 Hz, *J*₂ = 1.8 Hz, 1H), 4.16 (s, 2H), 3.52 (s, 3H), 2.97 – 2.94 (m, 2H), 1.67 – 1.61 (m, 2H), 1.49 – 1.42 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 168.07, 156.52, 146.85, 133.03, 132.65, 128.58, 122.18, 121.26, 71.25, 59.57, 34.55, 31.24, 21.89, 13.61. (+)ESI-HRMS: *m/z* 311.08743 corresponds to molecular formula C₁₄H₁₈N₂O₂S₂H⁺ (error, -2.62 ppm). HPLC purity, method A: *t*_R = 10.999, area 98.02%. Method B: *t*_R = 12.336, area 98.37%.

***N*-[6-(propylsulfanyl)-1,3-benzothiazol-2-yl]propanamide (44)**

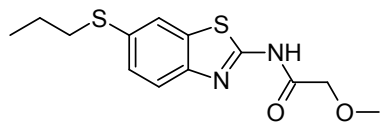
The general procedure E was followed using a solution of 3-methoxypropionyl chloride (106 mg, 0.869 mmol) in benzene (1.5 mL) and a solution of **19** (150 mg, 0.67 mmol) in CH₂Cl₂/benzene (2 mL, 1:1, v/v). The reaction mixture was stirred for 18 h and worked up according to general procedure. The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent, reversed-phase flash chromatography, Biotage SP1, using ethanol/water as eluent and NH flash chromatography, Biotage SP1, using hexane/ethyl acetate as eluent to afford 63.2 mg of final product as white solid. Yield 30%. M.p. = 111 °C. IR (ATR): 3270w, 3118m, 3038m, 2962s, 2922s, 2811m, 1704m, 1591s, 1544s, 1447m, 1394m, 1270s, 1174m, 1120m, 1067m, 810m cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 10.26 (bs, 1H), 7.79 (d, *J* = 1.8 Hz, 1H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.43 (dd, *J*₁ = 8.5 Hz, *J*₂ = 1.8 Hz, 1H), 3.76 (t, *J* = 5.5 Hz, 2H), 3.48 (s, 1H), 2.93 (t, *J* = 7.3 Hz, 2H), 2.77 (t, *J* = 5.5 Hz, 2H), 1.71 – 1.64 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 169.86, 157.57, 146.97, 133.08, 132.12, 128.67, 122.39, 121.02, 67.67, 59.20, 36.96, 36.90, 22.56, 13.37. (+)ESI-HRMS: *m/z* 311.08741 corresponds to molecular formula C₁₄H₁₈N₂O₂S₂H⁺ (error, -2.67 ppm). HPLC purity, method A: *t*_R = 10.325, area 98.09%. Method B: *t*_R = 11.326, area 99.00%.

N-[6-(butylsulfanyl)-1,3-benzothiazol-2-yl]-3-methoxypropanamide (**45**)



The general procedure E was followed using a solution of 3-methoxypropionyl chloride (163.8 mg, 1.342 mmol) in benzene (2 mL) and a solution of **20** (200 mg, 0.839 mmol) in CH₂Cl₂/benzene (4.4 mL, 1:1, v/v). The reaction mixture was stirred for 6 h at 0°C, then 16 h at room temperature and worked up according to general procedure. The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate and multiple reversed-phase column chromatography using methanol/water as eluent to afford 86.9 mg of final product as pale yellow solid. Yield 32 %. M.p. = 99 °C. IR (ATR): 3147s, 3046m, 2953s, 2924s, 2875s, 2814m, 1703s, 1592s, 1536s, 1451m, 1417m, 1395m, 1332m, 1267s, 1160s, 1116s, 1068m, 988w, 960m, 808m, 793m, 757m cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 10.33 (bs, 1H), 7.78 (d, *J* = 1.6 Hz, 1H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.42 (dd, *J*₁ = 8.5 Hz, *J*₂ = 1.8 Hz, 1H), 3.77 – 3.74 (m, 2H), 3.47 (s, 3H), 2.97 – 2.94 (m, 2H), 2.78 – 2.75 (m, 2H), 1.67 – 1.61 (m, 2H), 1.50 – 1.42 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 169.88, 157.62, 146.90, 133.07, 132.24, 128.55, 122.24, 121.00, 67.67, 59.18, 36.90, 34.60, 31.26, 21.89, 13.62. (+) ESI-HRMS: *m/z* 325.10332 corresponds to molecular formula C₁₅H₂₀N₂O₂S₂H⁺ (error, -1.77 ppm). HPLC purity, method A: *t*_R = 10.636, area 96.78%. Method B: *t*_R = 12.682, area 98.30%.

2-Methoxy-*N*-[6-(propylsulfanyl)-1,3-benzothiazol-2-yl]acetamide (**46**)



The general procedure E was followed using a solution of methoxyacetyl chloride (60.9 mg, 0.561 mmol) in benzene (1 mL) and a solution of **19** (96.8 mg, 0.431 mmol) in CH₂Cl₂/benzene (2 mL, 1:1, v/v). The reaction mixture was stirred for 2 h at 0°C and worked up according to general procedure. The crude product was subjected to silica gel column chromatography using hexane/ethyl acetate as eluent to afford 28.9 mg of final product as pale yellow solid. Yield 23 %. M.p. = 62 °C. IR (ATR): 3170m, 3062m, 2966m, 2938m, 2829w, 1688m, 1590m, 1534s, 1453m, 1273s, 1197m, 1119m, 992w, 809w, 772w, 744w cm⁻¹. ¹H NMR (500 MHz, CDCl₃, δ): 9.80 (bs, 1H), 7.79 (d, *J* = 1.4 Hz, 1H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.44 (dd, *J*₁ = 8.5 Hz, *J*₂ = 1.4 Hz, 1H), 4.16 (s, 2H), 3.52 (s, 3H), 2.93 (t, *J* = 7.2 Hz, 2H), 1.71 – 1.64 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, δ): 168.01, 156.40, 146.99, 133.09, 132.48, 128.67, 122.32, 121.32, 71.22, 59.54, 36.90, 22.53, 13.35. (+)ESI-HRMS: *m/z* 297.07173 corresponds to molecular formula C₁₃H₁₆N₂O₂S₂H⁺ (error, -2.91 ppm). HPLC purity, method A: *t*_R = 10.423, area 97.81%. Method B: *t*_R = 11.602, area 98.30%.

Table S1. In vitro antiproliferative activity (GI₅₀, μ M) against a panel of 60 cell lines^a

Panel/Cell line	24	25	26	28	29	30	33
Leukemia							
CCRF-CEM	26.8	3.33	>100	2.98	0.66	0.39	0.63
HL-60 (TB)	22.4	1.17	>100	0.26	0.27	0.31	0.35
K-562	2.48	0.39	>100	0.40	0.29	0.28	0.39
MOLT-4	3.07	3.26	>100	0.94	0.60	0.47	0.85
RPMI-8226	32.4	2.91	>100	1.56	1.29	0.50	1.04
SR	10.9	0.54	>100	0.43	0.27	0.19	0.27
Non-Small Cell Lung Cancer							
A549/ATCC	17.1	0.83	>100	0.98	0.67	0.64	2.37
EKVX	N.T.	N.T.	N.T.	N.T.	N.T.	1.27	0.56
HOP-62	20.8	3.80	>100	35.5	4.72	0.82	0.49
HOP-92	N.T.	N.T.	N.T.	0.39	1.04	0.41	1.44
NCI-H226	32.2	15.2	>100	>100	1.53	1.03	1.95
NCI-H23	53.7	6.92	>100	>100	4.48	0.90	1.15
NCI-H322M	24.1	6.37	>100	1.97	2.06	0.95	5.10
NCI-H460	18.7	2.44	>100	0.46	0.42	0.40	0.52
NCI-H522	14.0	0.31	>100	1.00	0.93	0.32	0.24
Colon Cancer							
COLO 205	38.5	1.75	>100	0.80	0.38	0.26	0.53
HCC-2998	35.8	8.33	>100	>100	37.8	6.80	4.88
HCT-116	22.0	0.79	>100	0.47	0.43	0.37	0.47
HCT-15	20.1	0.67	>100	0.50	0.41	0.44	0.38
HT29	11.5	0.38	>100	0.40	0.38	0.34	0.35
KM12	16.3	0.76	>100	0.41	0.38	0.37	0.41
SW-620	11.7	0.55	>100	0.41	0.37	0.37	0.45
CNS Cancer							
SF-268	29.4	4.60	>100	18.5	1.45	15.8	0.87
SF-295	17.8	1.53	>100	0.64	0.34	0.39	0.39
SF-539	31.2	1.99	>100	0.56	0.27	0.33	0.40
SNB-19	24.9	5.12	>100	1.57	0.62	0.61	0.78
SNB-75	18.6	2.07	34.8	1.65	0.12	0.23	0.41
U251	19.6	1.62	>100	0.68	0.49	0.46	0.41
Melanoma							
LOXIMVI	N.T.	N.T.	N.T.	1.13	0.63	0.56	0.46
MALME-3M	24.6	2.70	>100	0.52	N.T.	6.06	0.51
M14	28.6	0.62	>100	0.56	0.32	0.34	0.45
MDA-MB-435	1.48	0.20	17.5	0.17	0.12	0.07	0.19
SK-MEL-2	N.T.	N.T.	N.T.	0.63	0.44	0.31	0.43
SK-MEL-28	27.4	5.46	>100	2.72	0.96	2.81	66.2
SK-MEL-5	30.9	1.81	>100	1.25	0.39	0.37	0.66
UACC-257	39.0	2.70	>100	>100	0.87		>100
UACC-62	20.0	1.32	>100	0.42	0.55	0.44	0.32
Ovarian Cancer							
IGROV1	23.8	3.19	>100	0.62	1.46	1.30	0.94
OVCAR-3	20.4	1.87	>100	0.44	0.35	0.37	0.35
OVCAR-4	30.6	6.94	>100	>100	2.45	0.87	
OVCAR-5	43.7	6.75	>100	18.4	6.84	1.81	2.73
OVCAR-8	28.2	4.16	>100	>100	1.76	1.78	4.85
NCI/ADR-RES	23.1	0.95	>100	0.61	0.45	0.40	0.36
SK-OV-3	22.7	5.32	>100	2.47	0.64	0.40	0.54

Renal Cancer							
786-0	29.1	4.56	>100	2.32	0.53	0.39	0.54
A498	13.7	0.67	>100	0.27	0.13	0.12	1.22
ACHN	42.3	7.19	>100	36.0	0.91	0.82	0.91
CAKI-1	40.2	3.54	>100	N.T.	0.59	0.59	0.63
RXF 393	0.21	N.T.	23.0	>100	0.90	0.88	1.03
SN12C	23.7	3.10	>100	0.91	0.65	0.73	0.96
TK-10	22.8	4.48	>100	>100	8.44	2.91	2.25
UO-31	27.3	4.28	>100	2.22	1.05	0.60	1.39
Prostate Cancer							
PC-3	26.9	4.64	>100	0.96	0.73	0.55	0.80
DU-145	28.4	5.75	>100	>100	2.37	1.27	1.72
Breast Cancer							
MCF-7	15.7	0.88	27.6	0.47	0.35	0.31	0.30
MDA-MB-231/ATCC	14.8	2.37	>100	0.94	1.28	0.58	0.95
HS 578T	19.4	2.17	>100	1.38	0.45	0.52	0.94
BT-549	29.9	2.23	>100	0.72	0.76	0.42	0.49
T-47D	33.3	3.55	>100	17.6	1.68	0.24	0.58
MDA-MB-468	16.4	1.26	0.20	0.55	0.30	0.49	0.56
MID^b	19.9	2.13	81.2	2.14	0.74	0.58	0.83

^a Five dose assay was performed against 60 cancer cell lines treated with selected compounds for 48 hours using SRB procedure

^bMID = Mean GI₅₀ values for each compound against full 60-cell panel

N.T. – not tested

Table S2. IC₅₀ values calculated for **25, 26, 28 – 30, 32, 33 – 37** and **41 – 46** using MTT assay^c

Comp.	Structure	MCF-7 (IC ₅₀ , μM)	A375 (IC ₅₀ , μM)	K562 (IC ₅₀ , μM)	NT2/D1 (IC ₅₀ , μM)	MRC-5 (IC ₅₀ , μM)
25		61.4±4.2	85.0±5.6	>100	>1	-
26		>100	>100	>100	-	-
28		24.2±3.1	>100	>100	0.2±0.03	> 300
29		>100	91.6±6.0	>100	>1	-
30		>100	45.2±3.4	>100	0.1±0.01	>300
32		>100	-	-	>1	-
34		>100	-	-	>1	-
35		>100	-	-	>1	-
36		>100	>100	7.7±2.0	>1	-
37		>100	-	-	>1	-
39		> 100	-	-	-	-
40		> 100	-	-	-	-
41		30.5±2.5	77.5±4.5	53.2±4.0	>1	> 300
42		>100	>100	>100	>1	-
43		>100	>100	>100	>1	-
44		95.5±5.5	>100	66.3±4.2	>1	-
45		92.5±5.0	>100	44.2±3.3	>1	-
46		>100	>100	>100	>1	-
Doxorubicin		0.4	-	2	-	-
Cisplatin		-	-	-	1.11±0.17	-

^cIC₅₀ values were calculated after 48 h treatment of selected cell lines with five concentrations of investigated compounds using MTT assay. The measurements were performed in triplicate.

Evaluation of antiproliferative effects of compounds **28** and **30** on NT2/D1 cell line

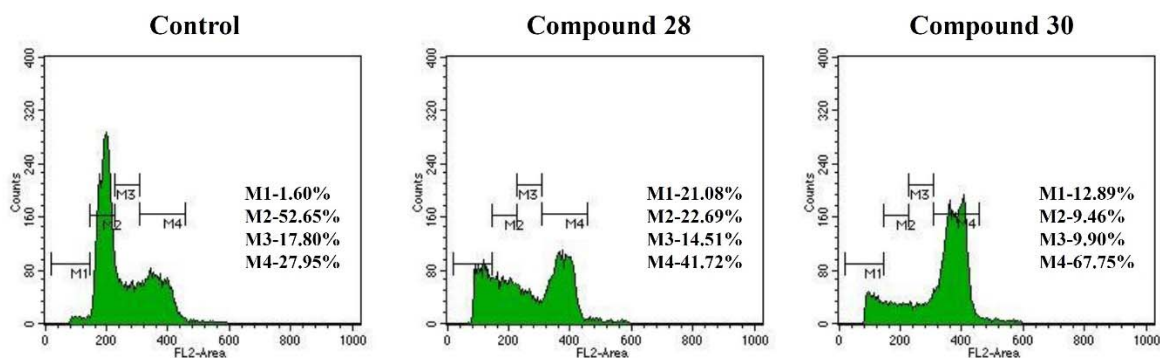


Figure S1. Cell cycle phase distribution after 24 h treatment of NT2/D1 cells with compounds **28** and **30** (M1 – sub G1, M2 – G0/G1, M3 – S, M4 – G2/M).

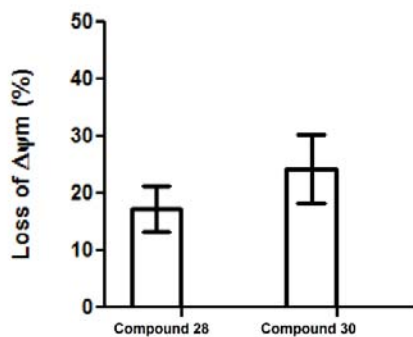


Figure S2. Mitochondrial membrane potential (MMP) in NT2/D1 cells after 48 h treatment with **28** and **30** compared to control cells' MMP

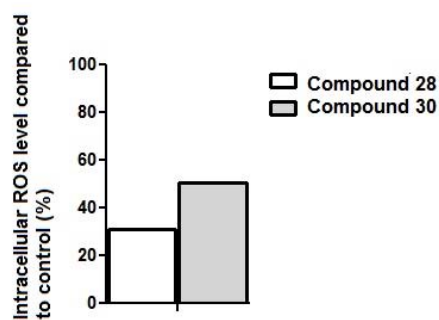


Figure S3. Intracellular ROS level in NT2/D1 cells after 48 h treatment with compounds **28** and **30** at 1 μM compared to control cells.

Table S3. Non-tumored animal toxicity assay for compound 28**Nontumored Animal Toxicity Assay for S775033**

Report generated on 04-Nov-2014

EXPERIMENT: AAZ-844 / 0 / 8B		TUMOR: NO CELLS		HOST: Athymic Nudes		IMPLANT DATE: 07-OCT-2014	
MEMO NO:		SOURCE/LINE: 0		SOURCE: BTB		STAGING DATE: 07-OCT-2014	
BOOK NO:		IMPLANT SITE: 0		SEX: F		EVALUATION DATE: 21-OCT-2014	
TREATMENT							
Grp	NSC	Dose/Units	Rt.	Schedule	Death Days	Surv/Total Day 14	
7	D-S775033	50.00 mg/kg/dose	IP	QD X 1, Day 0	--	1/1	
8	D-S775033	100.00 mg/kg/dose	IP	QD X 1, Day 0	--	1/1	
9	D-S775033	200.00 mg/kg/dose	IP	QD X 1, Day 0	--	1/1	

VEHICLES								
Grp		NSC #	Dose	Vehicle	Vehicle Description	Concentration	Inj. Vol.	
7	->	S775033 / 2	(Dose = 50.00)	:	in 100% DMSO	(Soluble - no visible particles)	50.0 mg/ml	Inj. Vol.: 1 ul/gm body wt
8	->	S775033 / 2	(Dose = 100.00)	:	in 100% DMSO	(Soluble - no visible particles)	50.0 mg/ml	Inj. Vol.: 2 ul/gm body wt
9	->	S775033 / 2	(Dose = 200.00)	:	in 100% DMSO	(Soluble - no visible particles)	50.0 mg/ml	Inj. Vol.: 4 ul/gm body wt

NOTE: All treatment was administered according to exact body weight.

Table S4. Non-tumored animal toxicity assay for compound 30**Nontumored Animal Toxicity Assay for S779403**

Report generated on 20-Jan-2015

EXPERIMENT: AAZ-858 / 0 / 8B		TUMOR: NO CELLS		HOST: Athymic Nudes		IMPLANT DATE: 29-DEC-2014	
MEMO NO:		SOURCE/LINE: 0		SOURCE: BTB		STAGING DATE: 29-DEC-2014	
BOOK NO:		IMPLANT SITE: 0		SEX: F		EVALUATION DATE: 12-JAN-2015	
TREATMENT							
Grp	NSC	Dose/Units	Rt.	Schedule	Death Days	Surv/Total Day 14	
4	D-S779403	100.00 mg/kg/dose	IP	QD X 1, Day 0	--	1/1	
5	D-S779403	200.00 mg/kg/dose	IP	QD X 1, Day 0	--	1/1	
6	D-S779403	400.00 mg/kg/dose	IP	QD X 1, Day 0	--	1/1	

VEHICLES								
Grp		NSC #	Dose	Vehicle	Vehicle Description	Concentration	Inj. Vol.	
4	->	S779403 / 2	(Dose = 100.00)	:	in 100% DMSO	(Soluble - no visible particles)	200.0 mg/ml	Inj. Vol.: 1 ul/gm body wt
5	->	S779403 / 2	(Dose = 200.00)	:	in 100% DMSO	(Soluble - no visible particles)	200.0 mg/ml	Inj. Vol.: 2 ul/gm body wt
6	->	S779403 / 2	(Dose = 400.00)	:	in 100% DMSO	(Soluble - no visible particles)	200.0 mg/ml	Inj. Vol.: 4 ul/gm body wt

NOTE: All treatment was administered according to exact body weight.

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