

Supporting Information

Synthesis and Structure-Activity Relationships of *N*-{3-[2-(4-Alkoxyphenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-carboxy Derivatives as Selective Acetyl-CoA Carboxylase 2 Inhibitors

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General Spectroscopic and Experimental Data. The NMR spectra were obtained on Bruker ARX-300 and Varian Inova-500 magnetic resonance spectrometer with internal standard as indicated for individual compounds. The chemical shifts are given in delta (δ) values and the coupling constants (J) in Hertz (Hz). Mass spectral analyses were accomplished using different techniques, including desorption chemical ionization (DCI), atmospheric pressure chemical ionization (APCI), and electrospray ionization (ESI), as specified for individual compounds. Elemental analysis was performed by Robertson Microlit Laboratories, Inc., Madison, New Jersey. All manipulations were performed under nitrogen atmosphere unless otherwise mentioned. All solvents and reagents were purified when necessary using standard procedures. Flash column chromatography was performed on silica gel 60 (Merck, 230-400 mesh) using the indicated solvent, or on Isco Companion system. Preparative HPLC was performed on an automated Gilson HPLC system. Mobile phase A: 0.1% TFA in H₂O. Mobile phase B: 0.1% TFA in CH₃CN.

hACC1 and hACC2 Assays. The ACC2 enzymatic assay has been developed using purified recombinant human ACC1 and ACC2 expressed in HEK293 and baculovirus/Sf9 system, respectively. In order to increase the expression and solubility of the protein, a chimeric version of ACC2 (“mito-minus”), in which the N-terminal transmembrane domain (1-275 amino acids of ACC2) was replaced with the corresponding ACC1 sequence (1-133 amino acids). The enzymatic assay measures ACC mediated incorporation of [¹⁴C] CO₂ into [¹⁴C]-Malonyl CoA. The assay was performed in 40 μ L reaction in a 96-well plate format. The assay buffer contains 50 mM Hepes/NaOH, pH 7.5, 10 mM citrate, 20 mM MgCl₂, 2 mM DTT, and 0.075% BSA. First, 20 μ L of test compounds was dissolved in 1% DMSO in assay buffer was dispensed into 96-well. Then, 10 μ L of enzyme in assay buffer was dispensed. The reaction was initiated by adding the following substrate mixture in assay buffer: 0.5 mM ATP, 0.25 mM acetyl-CoA, and 4 mM NaHCO₃ (0.6 mCi). The reaction was carried out at room temperature for 35 minutes and terminated by adding 100 μ L of 1N HCl. The plate was air-dried in a fume hood at room temperature overnight. 30 μ L of distilled water was added followed by adding 150 μ L of SuperMix liquid scintillation fluid (PerkinElmer). The radioactivity was determined in PerkinElmer microbeta after vigorous shaking. The IC₅₀ value was calculated from eight-point dose response curve of test compounds in duplicates.

Malonyl CoA extraction and Mass spec analysis. Tissues were rapidly excised from euthanized animals and flash frozen in liquid nitrogen. Frozen aliquots were weighed rapidly, being careful to prevent defrosting, and stored on dry ice. A 10x w/v aliquot of 5% sulfosalicylic acid, 50 μ M dithioerythritol was added and the tissue rapidly disrupted with a tissuemizer. 200 μ L aliquots of tissue homogenate were filtered through Millipore MAGVNOB filter plates. Supernatants were subject to LC/MS on Phenomenex Aqua C18 column.

Synthesis of N-{3-[2-(4-Isopropoxy-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide (9c)

4-Isopropoxy-phenol (4c). To a solution of hydroquinone (55.7 g, 0.5 mol) and 2-iodopropane (57.5 g, 0.33 mol) in ethanol was added a solution of potassium hydroxide (78.5 g, 0.5 mol) in water (100 mL). The dark brown solution was then refluxed for 16 hours. The solution was concentrated and the remaining aqueous phase was acidified

with 2N HCl and extracted with ethyl acetate (3 x 200 mL). The combined organic layers were washed with brine, dried over magnesium sulfate and filtered. The filtrate was concentrated to give over 70 g of crude material, which was triturated with methylene chloride and filtered. The filtrate was concentrated and purified on silica gel (5~35% ethyl acetate in hexane) to give 23.0 g of the title compound (46% yield). ¹H NMR (300 MHz, CDCl₃) δ ppm 1.30 (d, *J*=5.88 Hz, 6 H) 4.30 - 4.50 (m, 1 H) 4.78 (s, 1 H) 6.66 - 6.86 (m, 4 H); MS (ESI): *m/z* 151 (M-H).

5-Bromo-2-(4-isopropoxy-phenoxy)-thiazole (6c). A mixture of **4c** (0.95 g, 0.0062 mol), 2,5-dibromothiazole **5** (1.51 g, 0.0062 mol) and potassium carbonate (1.0 g, 0.007 mol) in 15 mL of dimethylformamide was stirred at 135°C for 4 h. The brown suspension was cooled to room temperature and poured into water. The aqueous phase was then extracted with ethyl acetate and the organic layer was washed with brine, dried over magnesium sulfate and filtered. The filtrate was concentrated and the crude was purified on silica gel (ethyl acetate in hexane, 10~30%) to give 1.35 g of pure product as a light yellow oil, which solidified upon standing (70% yield). ¹H NMR (300 MHz, DMSO-d₆) δ ppm 1.27 (d, *J*=5.88 Hz, 6 H) 4.52 - 4.69 (m, 1 H) 6.91 - 7.08 (m, 2 H) 7.23 - 7.34 (m, 2 H) 7.42 (s, 1 H); MS (ESI), *m/z* 315.96 (M+H)⁺.

2-(1-Methyl-prop-2-ynyl)-isoindole-1, 3-dione (7, R₂ = Me). To a solution of 3-butyn-2-ol (2.5 g, 0.035 mol, Aldrich), phthalimide (5.4 g, 0.037 mol) and triphenylphosphine (14.1 g, 0.055 mol) in tetrahydrofuran was added dropwise a solution of diethyl azodicarboxylate (24.9 mL of 40% wt solution in toluene, 0.055 mol) at 0°C. Then the reaction mixture was stirred at room temperature for 3 h. Solvent was removed and the residue was triturated with ether to precipitate out triphenylphosphine oxide. The white solid was filtered off and the filtrate was concentrated and purified on silica gel (ethyl acetate in hexane, 5~30%) to give 4.15 g of product as a white crystal (60% yield). ¹H NMR (500 MHz, CDCl₃) δ ppm 1.72 (d, *J*=7.32 Hz, 6 H), 2.35 (d, *J*=2.44 Hz, 1 H), 5.18 - 5.25 (m, 1 H), 7.70 - 7.75 (m, 2 H), 7.83 - 7.89 (m, 2 H); MS (ESI), *m/z*: 200.0 (M+H)⁺.

2-{3-[2-(4-Isopropoxy-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-isoindole-1, 3-dione (8c). To a degassed solution of **6c** (16.0 g, 0.051 mol), **7** (12.2 g, 0.061 mol) and triethylamine (36.0 mL, 0.255 mol) in 250 mL of dry tetrahydrofuran was added dichlorobis(triphenylphosphine)palladium (1.8 g, 0.0026 mol) and copper iodide (0.25 g, 0.0013 mol) and the mixture was then refluxed under nitrogen for 3 h. After the removal of solvent, the residue was diluted with methylene chloride and filtered. The filtrate was concentrated and purified by chromatography on silica gel (ethyl acetate in hexane, 10~30%) to give 16.4 g of the desired product as a light yellow solid (74% yield). ¹H NMR (300 MHz, CDCl₃) δ ppm 1.34 (d, *J*=6.25 Hz, 6 H), 1.75 (d, *J*=7.35 Hz, 3 H), 4.43 - 4.59 (m, 1 H), 5.40 (q, *J*=6.99 Hz, 1 H), 6.82 - 6.95 (m, 2 H), 7.10 - 7.20 (m, 2 H), 7.31 (s, 1 H), 7.68 - 7.78 (m, 2 H), 7.82 - 7.92 (m, 2 H); MS (ESI), *m/z*: 433.6 (M+H)⁺.

N-{3-[2-(4-Isopropoxy-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide (9c). To a solution of **8c** (16.4 g, 0.038 mol) in a mixture of methylene chloride and ethanol (10:1, 275 mL) was added hydrazine monohydrate (19.0 g, 0.38 mol) and the reaction mixture was refluxed for 3 h. The reaction mixture was cooled and filtered. The filtrate was concentrated and dissolved in methylene chloride. The suspension was filtered again and the filtrate was evaporated under vacuum. The brown oil was used without further

purification. To a solution of the aforementioned crude in methylene chloride (300 mL) was added excess triethylamine (100 mL) and acetic anhydride (50 mL). The mixture was stirred at room temperature for 3 h. Methanol (100 mL) was added and the mixture was stirred overnight. Solvent was removed and the residue was treated with saturated NaHCO₃ and extracted with ethyl acetate. Organic layer was washed with brine, dried over magnesium sulfate and filtered. The filtrate was concentrated to give 16.4 g of crude as a brown liquid, which was purified by chromatography on silica gel (ethyl acetate in hexane, 50~75%) to give 10.3 g of the desired product as an off-white solid (35% overall yield). ¹H NMR (300 MHz, CDCl₃) δ ppm 1.34 (d, *J*=5.88 Hz, 6 H), 1.45 (d, *J*=6.62 Hz, 3 H), 1.99 (s, 3 H), 4.38 - 4.61 (m, 1 H), 4.96 - 5.09 (m, 1 H), 5.66 (s, 1 H), 6.83 - 6.97 (m, 2 H), 7.10 - 7.21 (m, 2 H), 7.29 (s, 1 H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ ppm 21.45, 21.67, 22.32, 36.22, 40.00, 69.74, 70.62, 96.72, 111.25, 116.72, 121.59, 142.31, 147.94, 155.66, 168.10, 173.08; MS (ESI), *m/z*: 345.0 (M+H)⁺; Anal. Calcd for C₁₈H₂₀N₂O₃S: C, 62.77; H, 5.85; N, 8.13; S, 9.31. Found: C, 62.82; H, 5.93; N, 8.14; S, 9.23.

N-{3-[2-(4-Isopropylsulfanyl-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide (9d)

4-Isopropylsulfanyl-phenol. A solution of 4-mercaptophenol (250 mg, 1.98 mmol) in acetone (2.5 mL) was treated with K₂CO₃ (290 mg, 2.1 mmol) and 2-iodopropane (316.9 μL, 3.17 mmol). The reaction was stirred at 25°C for 18 h and filtered. The filtrate was diluted with diethyl ether (60 mL) and washed with 1N NaOH (2 x 20 mL). The combined aqueous layers were acidified to pH 1 with 6N HCl and the resulting mixture was extracted with ethyl ether (40 mL). The organic layer was washed with brine (15 mL), dried over Na₂SO₄, and concentrated. The crude product was purified by flash chromatography on silica gel eluting with 10% ethyl acetate/hexanes to provide 299 mg (90%) of the desired product as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ ppm 1.24 (d, *J*=6.62 Hz, 6 H), 3.03 - 3.30 (m, 1 H), 4.83 (s, 1 H), 6.78 (d, *J*=8.82 Hz, 2 H), 7.35 (d, *J*=8.82 Hz, 2 H); MS (DCI) *m/z*: 169.0 (M + H)⁺.

(9d) ¹H NMR (300 MHz, DMSO-*d*₆) δ ppm 1.24 (d, *J*=6.62 Hz, 6 H), 1.33 (d, *J*=6.99 Hz, 3 H), 1.81 (s, 3 H), 3.42 - 3.57 (m, 1 H), 4.71 - 4.91 (m, 1 H), 7.35 (d, *J*=8.82 Hz, 2 H), 7.47 (d, *J*=8.82 Hz, 2 H), 7.50 (s, 1 H), 8.42 (d, *J*=7.72 Hz, 1 H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ ppm 21.4, 22.3, 22.7, 36.2, 37.3, 70.5, 97.0, 111.8, 120.8, 132.5, 133.1, 142.2, 153.2, 168.1, 171.6; MS (ESI) *m/z*: 361.1 (M + H)⁺. Anal. Calcd for C₁₈H₂₀N₂O₂S₂: C, 59.97, H, 5.59, N, 7.77. Found: C, 59.72, H, 5.74, N, 7.57.

N-{3-[2-(4-Isopropylamino-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide (9e)

[4-(5-Bromo-thiazol-2-yloxy)-phenyl]-carbamic acid, *tert*-butyl ester. (4-Hydroxy-phenyl)-carbamic acid *tert*-butyl ester (6.0 g, 0.014 mol), 2,5-dibromo-thiazole (6.8 g, 0.014 mol) and K₂CO₃ (4.4 g, 0.015 mol) were combined in DMSO (46 mL). The reaction was heated in an oil bath at 130 °C for 3 h. Upon completion, the reaction was cooled, poured into 300 ml water and diluted with EtOAc. The layers were separated and the aqueous layer was extracted several times with EtOAc. The organics were combined, dried (Na₂SO₄), filtered and concentrated. The residue was purified by flash column

chromatography (0 - 75% EtOAc in hexanes) to give the desired product (3.4 g, 9.1 mmol, 65%) as a off-white solid: $^1\text{H NMR}$ (300 MHz, DMSO- d_6) δ ppm 1.48 (s, 9 H), 7.28 (d, $J=9.19$ Hz, 2 H), 7.42 (s, 1 H), 7.54 (d, $J=8.82$ Hz, 2 H), 9.52 (s, 1 H); MS (ESI) m/z 371.0 (M + H) $^+$.

tert-Butyl 4-((5-[3-(acetylamino)but-1-ynyl]-1,3-thiazol-2-yl)oxy)phenylcarbamate. [4-(5-Bromo-thiazol-2-yloxy)-phenyl]-carbamic acid tert-butyl ester (1.0 g, 2.7 mmol), N-(1-methyl-prop-2-ynyl)-acetamide (390 mg, 3.51 mmol, Gardner, J. N. *Can. J. Chem.*, **1973**, *51*, 1416-1418), CuI (20.0 mg, 0.11 mmol), Et₃N (1.2 mL) and THF (6.0 mL) were combined in a pressure tube and degassed for 2 min with N₂. PdCl₂(PPh₃)₂ (94.0 mg, 0.14 mmol) was added, the reaction was capped and heated to 80 °C for 30 min. The reaction was cooled, poured into saturated aqueous NH₄Cl and diluted with EtOAc. The layers were separated, the aqueous layer extracted with EtOAc and the combined organics were dried (Na₂SO₄), filtered and concentrated. The residue was passed through a pad of silica gel eluting first with CH₂Cl₂ (by-products and starting materials) and then 3% MeOH in CH₂Cl₂ to provide the desired product (880 mg, 2.2 mmol, 81%) as a white solid. $^1\text{H NMR}$ (300 MHz, DMSO- d_6) δ ppm 1.32 (d, $J=6.99$ Hz, 3 H), 1.44 - 1.52 (m, 9 H), 1.81 (s, 3 H), 4.74 - 4.87 (m, 1 H), 7.27 (d, $J = 9.0$ Hz, 2 H), 7.48 (s, 1 H), 7.53 (d, $J = 9.0$ Hz, 2 H), 8.41 (d, $J=7.72$ Hz, 1 H), 9.52 (s, 1 H); MS (ESI) m/z 402.0 (M + H) $^+$.

(9e) tert-Butyl 4-((5-[3-(acetylamino)but-1-ynyl]-1,3-thiazol-2-yl)oxy)phenylcarbamate (2.85g, 7.0 mmol) was dissolved in CH₂Cl₂ (35 ml) and TFA (8.75 ml, 25% v/v) was added via syringe. After 4 h of stirring at rt, the reaction solution was concentrated by rotary evaporation and then placed on high vacuum for 2h to give a light yellow solid which was used in the next step without further purification. A portion of the crude product from above (500 mg, 1.7 mmol) was dissolved in a buffer solution prepared from NaOAc / HOAc in MeOH (6 ml). To this solution was added acetone (0.374 ml, 5.1 mmol) followed by NaCNBH₃ (320 mg, 5.1 mmol). The reaction was heated to 70°C in a water bath for 1 h. The reaction solution was cooled and MeOH was evaporated. The residue was taken up in EtOAc and quenched with water. The layers were separated and the aqueous layer was extracted once with EtOAc. The combined organics was dried (Na₂SO₄), filtered and concentrated. The residue was purified by flash column chromatography to give **9e** (340 mg, 66%) as a hygroscopic white solid. $^1\text{H NMR}$ (300 MHz, DMSO- d_6) δ ppm 1.06 - 1.20 (d, $J = 6.0$ Hz, 6 H), 1.31 (d, $J=6.99$ Hz, 3 H), 1.80 (s, 3 H), 3.52 (m, 1 H), 4.70 - 4.88 (m, 1 H), 5.64 (d, $J=7.72$ Hz, 1 H), 6.52 - 6.65 (d, $J = 9.0$ Hz, 2 H), 7.00 - 7.13 (d, $J = 9.0$ Hz, 2 H), 7.46 (s, 1 H), 8.39 (d, $J=7.72$ Hz, 1 H); $^{13}\text{C NMR}$ (75 MHz, DMSO- d_6) δ 21.5, 22.3, 36.2, 43.2, 70.8, 96.4, 110.8, 112.7, 121.2, 142.5, 144.9, 147.0, 168.1, 174.6; HRMS (TOF) calc for C₁₈H₂₁N₃O₂S: 344.13545 [(M + H) $^+$]; found: 344.14285; calcd for C₁₈H₁₉N₃O₂S: C, 62.95; H, 6.16; N, 12.23; found: C, 62.45, H, 5.67, N, 11.97.

N-{3-[2-(4-Isopropyl-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide (9f)

5-Bromo-2-(4-isopropyl-phenoxy)-thiazole. 4-isopropyl-phenol (184 mg, 1.35 mmol), 2,5-dibromothiazole (300 mg, 1.2 mmol) and K₂CO₃ (187 mg, 1.35 mmol) were combined in DMSO (3.5 ml). The reaction was heated in the microwave for 30 min at 130 °C. Upon completion the reaction was poured into water and diluted with EtOAc. The layers were separated and the organics were washed with 15% NaOH and then with

water again. The organics were combined, dried (Na_2SO_4), filtered and concentrated to provide a crude product, which was used without further purification.

(9f) ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ ppm 1.21 (d, $J = 7.0$, 6H), 1.32 (d, $J = 7.0$, 3H), 1.81 (s, 3H), 2.87-3.0 (m, 1H), 4.76-4.86 (m, 1H), 7.27 (d, $J = 8.82$ Hz, 2H), 7.36 (d, $J = 8.45$ Hz, 2H), 7.48 (s, 1H), 8.41 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR (75 MHz, $\text{Methanol-}d_4$) δ 21.8, 22.4, 24.4, 34.9, 38.5, 72.2, 96.4, 113.6, 121.2, 129.2, 142.9, 148.9, 154.6, 172.1, 175.4; MS (ESI) m/z 329.0 ($\text{M} + \text{H}^+$); HRMS (TOF) calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$ [$\text{M} + \text{H}^+$], 329.12455; found: 329.13206.

N-{3-[2-(6-Isopropoxy-pyridin-3-yloxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide (9g)

5-Bromo-2-isopropoxy-pyridine. To isopropanol (11 mL, 143 mmol) under nitrogen at 25°C was added sodium hydride (95%, 1.94 g, 76.7 mmol) portion-wise over 5 min. The reaction was stirred for 16 h and a solution of 2-fluoro-5-bromopyridine (9 g, 51 mmol) in DMF (250 mL) was added over 10 min. The resulting mixture was heated at 130°C for 4 h and cooled to 25°C . The mixture was diluted with ether (500 mL) and washed with water (600 mL) and brine (300mL). The organics were dried (MgSO_4), filtered, and concentrated to provide 10.1g of the desired product (92%). ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ ppm 1.28 (d, $J=6.25$ Hz, 6 H) 5.08 - 5.28 (m, 1 H) 6.75 (d, $J=8.82$ Hz, 1 H) 7.86 (dd, $J=8.82$, 2.57 Hz, 1 H) 8.26 (d, $J=2.57$ Hz, 1 H); MS (ESI) m/z 217.9 ($\text{M} + \text{H}^+$).

6-Isopropoxy-pyridin-3-ol. To a solution of 5-bromo-2-isopropoxy-pyridine (7.9 g, 36.6 mmol) in THF (100 mL) cooled at -78°C under nitrogen was added butyllithium (1.6M in hexanes, 37 mL, 59.2 mmol) dropwise over 10 min. The reaction was stirred for 20 min and trimethyl borate (6.7 mL, 59.2 mmol) was added. The resulting mixture was stirred for 2 h at -78°C and peracetic acid (32% in acetic acid, 13 mL, 59.2 mmol) was added. After 10 min at -78°C , the reaction was warmed to 0°C and stirred for 1 h. The reaction was cooled to -10°C and treated with 10% aqueous sodium bisulfite (30 mL). The mixture was concentrated to 1/3 volume and extracted with ether (300 mL). The organics were washed with water (300 mL) and brine (200 mL), dried (MgSO_4), filtered, and concentrated to provide 5.2 g of the desired compound (92%). ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ ppm 1.23 (d, $J=6.25$ Hz, 6 H), 4.95 - 5.17 (m, 1 H), 6.57 (d, $J=8.82$ Hz, 1 H), 7.14 (dd, $J=8.82$, 2.94 Hz, 1 H), 7.65 (d, $J=2.94$ Hz, 1 H), 9.21 (s, 1 H); MS (DCI) m/z 154.0 ($\text{M} + \text{H}^+$).

(9g) ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ ppm 1.22 - 1.42 (m, 9 H), 1.81 (s, 3 H), 4.68 - 4.92 (m, 1 H), 5.12 - 5.30 (m, 1 H), 6.85 (d, $J=9.19$ Hz, 1 H), 7.48 (s, 1 H), 7.81 (dd, $J=9.01$, 3.13 Hz, 1 H), 8.24 (d, $J=2.94$ Hz, 1 H), 8.42 (d, $J=7.72$ Hz, 1 H); MS (ESI) m/z 346 ($\text{M} + \text{H}^+$); ^{13}C NMR (126 MHz, CDCl_3) δ ppm 21.98, 22.17, 23.20, 37.64, 68.74, 72.13, 95.14, 112.18, 112.23, 131.59, 138.67, 142.16, 145.84, 161.29, 168.74, 173.27.

N-{3-[2-(4-Isopropoxy-phenylsulfanyl)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide (9h)

4-(5-Bromo-thiazol-2-ylsulfanyl)-phenol. A solution of 4-mercaptophenol (300 mg, 2.38 mmol) and 2,5-dibromothiazole (635 mg, 2.61 mmol) in DMF (5 mL) was treated with K_2CO_3 (290 mg, 2.1 mmol) and the resulting mixture was heated at 90°C for 20 min. The reaction was cooled to 25°C , diluted with water (20 mL) and extracted with 1:1

EtOAc/Et₂O (100 mL). The organic layer was washed with water (3 x 25 mL), and brine (25 mL), dried (Na₂SO₄), filtered, and evaporated. The crude product was purified by flash chromatography on silica gel eluting with a solvent gradient from 10 to 25% EtOAc in hexanes to provide 586 mg (85 %) of the desired compound as a white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ ppm 6.91 (d, *J*=8.82 Hz, 2 H), 7.54 (d, *J*=8.82 Hz, 2 H), 7.75 (s, 1 H), 10.23 (br.s, 1 H); MS (ESI) *m/z* 289.8 (M + H)⁺.

N-{3-[2-(4-Hydroxy-phenylsulfanyl)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide.

¹H NMR (300 MHz, DMSO- *d*₆) δ ppm 1.30 (d, *J*=6.99 Hz, 3 H), 1.79 (s, 3 H), 4.57 - 4.91 (m, 1 H), 6.91 (d, *J*=8.46 Hz, 2 H), 7.54 (d, *J*=8.46 Hz, 2 H), 7.80 (s, 1 H), 8.37 (d, *J*=7.72 Hz, 1 H), 10.23 (br. s, 1 H); MS (ESI) *m/z* 319.0 (M + H)⁺.

(9h) A solution of N-{3-[2-(4-hydroxy-phenylsulfanyl)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-acetamide (50 mg, 0.157 mmol), Ph₃P (57.5 mg, 0.22 mmol), and 2-propanol (17.25 μL, 0.252 mmol) in THF (0.5 mL) was treated with diethyl azodicarboxylate (40 μL, 0.22 mmol) dropwise over 2 min. The reaction was stirred at 25°C for 12 h and concentrated. The crude product was purified by reverse-phase HPLC on an Atlantis C18 column (1.9 x 10 cm, 5 μm particle size) using a gradient of 5 to 100% acetonitrile in 0.1% aqueous TFA to provide 10 mg (18%) of **9h** as a pale yellow oil. ¹H NMR (300 MHz, DMSO- *d*₆) δ ppm 1.30 (d, *J*=6.25 Hz, 9 H), 1.79 (s, 3 H), 4.64 - 4.76 (m, 1 H), 4.74 - 4.92 (m, 1 H), 7.07 (d, *J*=8.82 Hz, 2 H), 7.63 (d, *J*=8.82 Hz, 2 H), 7.82 (s, 1 H), 8.37 (d, *J*=7.72 Hz, 1 H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ ppm 21.37, 21.60, 22.31, 36.27, 69.66, 69.98, 98.87, 117.16, 117.64, 118.88, 136.89, 147.06, 159.63, 168.10, 169.50; MS (ESI) *m/z* 361.0 (M + H)⁺. Anal. Calcd for C₁₈H₂₀N₂O₂S₂ · ¼ H₂O: C, 59.23; H, 5.66; N, 7.67. Found: C, 59.31; H, 5.37; N, 7.36.

N-{3-[2-(4-Isopropoxy-phenoxy)-thiazol-5-yl]-prop-2-ynyl}-acetamide (9i)

MS (DCI): 331 (M+H)⁺; ¹H NMR (300 MHz, CDCl₃) δ ppm 1.34 (d, *J*=5.88 Hz, 6 H), 2.02 (s, 3 H), 4.26 (d, *J*=5.52 Hz, 2 H), 4.41 - 4.62 (m, 1 H), 5.64 (br. s, 1 H), 6.81 - 7.01 (m, 2 H), 7.09 - 7.22 (m, 2 H), 7.30 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ ppm 21.09, 22.87, 29.94, 70.43, 73.21, 90.59, 111.54, 116.81, 121.44, 142.45, 148.22, 156.09, 169.85, 174.32. Analysis C₁₇H₁₈N₂O₃S.0.1CH₂Cl₂: Calcd C, 60.60; H, 5.41; N, 8.27; Found C, 60.70; H, 5.23; N, 7.89.

N-{1-Cyclopropyl-3-[2-(4-isopropoxy-phenoxy)-thiazol-5-yl]-prop-2-ynyl}-acetamide (9j)

1-Cyclopropyl-3-trimethylsilanyl-prop-2-yn-1-ol. To a solution of ethynyl-trimethylsilane (2g, 20.36 mmole) in tetrahydrofuran (45 mL) at -78°C was added a solution of 2.5M n-BuLi in hexane (8.14 mL, 21.25 mmole), and the mixture was stirred at room temperature for 20 minutes. The cyclopropanecarbaldehyde (1.7 g, 24.25 mmole) was added and the reaction mixture was allowed to warm up to room temperature. After an hour the reaction mixture was quenched with saturated aqueous ammonium chloride and most of tetrahydrofuran was evaporated. The mixture was extracted with ethyl acetate (100 mL). The ethyl acetate phase was washed with water (x2) and brine, dried over magnesium sulfate, filtered and evaporated. The desired compound (3.36g, 98%) was

obtained as light yellow oil. $^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 0.17 (s, 9 H), 0.37 - 0.64 (m, 4 H), 1.14 - 1.33 (m, 1 H), 1.79 (s, 1 H), 4.25 (d, $J=6.35$ Hz, 1 H); MS (DCI), m/z : 168 ($\text{M}+\text{NH}_4\text{-H}_2\text{O}$) $^+$.

2-(1-Cyclopropyl-3-trimethylsilanyl-prop-2-ynyl)-isoindole-1, 3-dione. To a solution of 1-cyclopropyl-3-trimethylsilanyl-prop-2-yn-1-ol (1.09 g, 0.0065 mol), phthalimide (972 mg, 0.0066 mol) and triphenylphosphine (2.54 g, 0.0097 mol) in tetrahydrofuran (50 mL) at 0°C was added a solution of 40% wt of diethyl azodicarboxylate in toluene (1.53 mL, 0.0098 mol) drop-wise. The reaction mixture was stirred at room temperature overnight. Solvent was removed in vacuum and the residue was dissolved with ether. After 4 hours the triphenylphosphine oxide was removed by filtration. The product (0.65 g, 37%) was separated from silica gel column by using a gradient of 5 to 10% ethyl acetate in hexane as a white solid. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ ppm 0.16 (s, 9 H), 0.29 - 0.41 (m, 1 H), 0.42 - 0.55 (m, 1 H), 0.58 - 0.78 (m, 2 H), 1.61 - 1.77 (m, 1 H), 4.46 (d, $J=8.82$ Hz, 1 H), 7.65 - 7.78 (m, 2 H), 7.82 - 7.94 (m, 2 H); MS (DCI), m/z : 298 ($\text{M}+\text{H}$) $^+$.

2-(1-Cyclopropyl-prop-2-ynyl)-isoindole-1, 3-dione. To a solution of 2-(1-cyclopropyl-3-trimethylsilanyl-prop-2-ynyl)-isoindole-1, 3-dione (0.6 g, 0.002 mol) in tetrahydrofuran (25 mL) at room temperature was added a solution of 1N tetrabutylammonium fluoride in tetrahydrofuran (5 mL, 0.005 mol) and the mixture was stirred for 10 minutes. The reaction mixture was concentrated and purified on silica gel column using 10% ethyl acetate in hexane as eluent. The desired compound was obtained as a white solid (290mg, 63.8%). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ ppm 0.31 - 0.45 (m, 1 H), 0.45 - 0.58 (m, 1 H), 0.58 - 0.84 (m, 2 H), 1.66 - 1.87 (m, 1 H), 2.37 (d, $J=2.57$ Hz, 1 H), 4.41 (dd, $J=9.01, 2.39$ Hz, 1 H), 7.64 - 7.80 (m, 2 H), 7.82 - 7.97 (m, 2 H); MS (DCI), m/z : 226 ($\text{M}+\text{H}$) $^+$.

(9j) $^1\text{H NMR}$ (300 MHz, CDCl_3) δ ppm 0.39 - 0.61 (m, 4 H), 1.08 - 1.25 (m, 1 H), 1.34 (d, $J=5.88$ Hz, 6 H), 2.02 (s, 3 H), 4.51 (heptet, $J=6.25$ Hz, 1 H), 4.88 (dd, $J=8.64, 6.43$ Hz, 1 H), 5.75 (d, $J=8.09$ Hz, 1 H), 6.85 - 6.98 (m, 2 H), 7.11 - 7.21 (m, 2 H), 7.28 (s, 1 H); $^{13}\text{C NMR}$ (75 MHz, CHLOROFORM-D) δ ppm 2.01, 3.01, 15.32, 21.95, 23.21, 44.85, 70.45, 72.99, 91.82, 111.47, 116.80, 121.48, 142.44, 148.29, 156.09, 168.90, 174.24; MS (DCI), m/z : 371 ($\text{M}+\text{H}$) $^+$; HRMS (TOF) calcd for $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_3\text{S}$ [($\text{M} + \text{H}^+$)] 371.14239; found: 371.14289.

4-[2-(4-Phenoxy-phenoxy)-thiazol-5-yl]-but-3-yn-2-ol (9k)

2-(4-Phenoxy-phenoxy)-thiazole. To a solution of 4-phenoxy-phenol (11.11 g) in DMSO (60 mL) were added 2-bromo-thiazole (9.8 g, 0.06 mol) and potassium carbonate (8.25 g, 0.06 mol), and the mixture was heated at 100°C overnight. The reaction mixture was extracted with methylene chloride (180 mL), washed with water (3 x 100 mL) and brine, dried over magnesium sulfate, filtered and evaporated. The product was purified on silica gel column using a gradient of 3 to 10% ethyl acetate in hexane and yielded the desired product as light yellow oil (8.9 g, 55%). MS (ESI) m/z 270 ($\text{M}+\text{H}$) $^+$; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ ppm 6.81 (d, $J=4.04$ Hz, 1 H), 6.99 - 7.08 (m, 4 H), 7.08 - 7.16 (m, 1 H), 7.19 - 7.30 (m, 3 H), 7.30 - 7.40 (m, 2 H).

5-Iodo-2-(4-phenoxy-phenoxy)-thiazole. To a solution of 2-(4-phenoxy-phenoxy)-thiazole (2.34 g, 0.087 mol) in tetrahydrofuran (75 mL) at -78°C was added a solution of

2.5M BuLi in hexane (3.74 mL, 0.087 mol). The mixture was stirred for two hour before adding iodine (2.2 g, 0.087 mol). The reaction mixture was allowed to warm up to room temperature. Ethyl acetate (100 mL) was added and the mixture was washed with an aqueous solution of 10% NaHSO₃ (1x), water (2x), brine (1x), dried over magnesium sulfate and concentrated. The crude product was purified on silica gel column using a gradient of 2 to 10% ethyl acetate in hexane to give the desired product as yellowish oil (3.1 g, 90%). MS (ESI) m/z 396 (M + H)⁺; ¹H NMR (300 MHz, CDCl₃) δ ppm 6.98 - 7.08 (m, 4 H), 7.09 - 7.17 (m, 1 H), 7.18 - 7.25 (m, 2 H), 7.30 (s, 1 H), 7.31 - 7.40 (m, 2 H). δ ppm 6.98 - 7.08 (m, 4 H), 7.09 - 7.17 (m, 1 H), 7.18 - 7.25 (m, 2 H), 7.30 (s, 1 H), 7.31 - 7.40 (m, 2 H).

(9k) To a mixture of 5-Iodo-2-(4-phenoxy-phenoxy)-thiazole (200 mg, 0.506 mmol), 3-butyn-2-ol (80 μ L, 2.0 mmol, 2.0 eq.) and triethylamine (0.5 mL, 3.59 mmol, 7.1 eq.) in THF (2 mL) was added CuI (3 mg, 0.016 mmol, 3.1% eq.), Pd(PPh₃)₂Cl₂ (20 mg, 0.028mmol, 5.6% eq.) consecutively at room temperature. The mixture was stirred at room temperature overnight. Ethyl acetate was added and the mixture was washed with water (1x), brine (1x), dried over MgSO₄ and concentrated. The residue was purified on silica gel column eluting with ethyl acetate and hexane with the maximal ethyl acetate being 50% to give the desired product as yellowish viscous oil (154 mg, 90%). MS (DCI): 338 (M+H)⁺; ¹H NMR (300 MHz, CDCl₃) δ ppm 1.53 (d, J =6.62 Hz, 3 H), 4.73 (q, J =6.62 Hz, 1 H), 6.98 - 7.08 (m, 4 H), 7.09 - 7.18 (m, 1 H), 7.21 - 7.25 (m, 2 H), 7.31 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ ppm 23.96, 58.61, 73.80, 96.62, 111.92, 119.01, 119.77, 121.65, 129.82, 142.16, 150.10, 155.29, 156.75, 173.59. Analysis C₁₉H₁₅NO₃S.0.05CH₂Cl₂: Calcd C 66.97, H 4.45, N 4.10; Found C 66.67, H 4.40, N 4.00.

1-Methyl-3-[2-(4-phenoxy-phenoxy)-thiazol-5-yl]-prop-2-ynylamine (9l)

MS (DCI) m/z : 337 (M+H)⁺; ¹H NMR (300 MHz, CDCl₃) δ ppm 1.52 (d, J =6.99 Hz, 3 H), 4.06 (q, J =6.99 Hz, 1 H), 6.99 - 7.07 (m, 4 H), 7.09 - 7.18 (m, J =7.35, 7.35 Hz, 1 H), 7.20 - 7.25 (m, 2 H), 7.30 (s, 1 H), 7.32 - 7.45 (m, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ ppm 24.09, 39.47, 71.45, 99.36, 112.59, 118.99, 119.75, 121.61, 123.60, 129.80, 141.46, 150.15, 155.18, 156.80, 172.96. Analysis C₁₉H₁₆N₂O₂S.0.05CH₂Cl₂: Calcd C, 67.17; H, 4.76; N, 8.22; Found C, 66.94; H, 4.48; N, 8.02.

1-[3-[2-(4-Isopropoxy-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl]-3-methyl-urea (9m)

To a solution of the crude 3-[2-(4-isopropoxy-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynylamine (0.245 g, 0.00081 mol) in methylene chloride (3 mL) at room temperature was added methylisocyanate (100 mg, 0.0017 mol) and stirred for four hours. The reaction mixture was concentrated and the product 215 mg (73.8%) was isolated via silica column, using a gradient of 25% to 100% ethyl acetate in hexane, as a white solid. ¹H NMR (300 MHz, CDCl₃) δ ppm 1.34 (d, J =5.88 Hz, 6 H), 1.45 (d, J =6.62 Hz, 3 H), 2.79 (d, J =4.78 Hz, 3 H), 4.36 (d, J =4.04 Hz, 1 H), 4.42 - 4.62 (m, 2 H), 4.77 - 4.91 (m, 1 H), 6.80 - 6.96 (m, 2 H), 7.09 - 7.22 (m, 2 H), 7.28 (s, 1 H); MS (DCI), m/z : 360 (M+H)⁺. Anal Calcd for C₁₈H₂₁N₃O₃S: C, 60.15; H, 5.89; N, 11.69; S, 8.92. Found: C, 59.98; H, 5.98; N, 11.46; S, 8.77.

{3-[2-(4-Isopropoxy-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-carbamic acid methyl ester (9n)

A solution of **8c** (4.3 g, 0.01 mol) and hydrazine monohydrate (5.0 g, 0.1 mol) in a mixture of methylene chloride and ethanol (10:1) was refluxed for 1 h. Solvent was removed after filtration and the residue was treated with more methylene chloride. The solution was decanted and concentrated to give 3.0 g of crude product as yellow oil, which was used without further purification. The aforementioned crude was dissolved in tetrahydrofuran and treated with N, N-diisopropylethylamine, followed by methyl chloroformate. After stirring at room temperature for 30 min, the reaction was quenched with methanol. Solvent was removed and the residue was purified on silica gel (ethyl acetate/hexane, 10~50%) to give 3.3 g of product as a white solid (91% yield). ¹H NMR (300 MHz, DMSO-*d*₆) δ ppm 1.27 (d, *J*=6.25 Hz, 6 H), 1.34 (d, *J*=6.99 Hz, 3 H), 3.55 (s, 3 H), 4.48 - 4.72 (m, 2 H), 6.93 - 7.07 (m, 2 H), 7.24 - 7.34 (m, 2 H), 7.48 (s, 1 H), 7.75 (d, *J*=7.72 Hz, 1 H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ ppm 21.4, 21.67, 40.0, 51.43, 69.73, 70.83, 96.69, 111.22, 114.21, 116.72, 121.59, 142.31, 147.94, 155.66, 173.10; MS (ESI), *m/z*: 361.0 (M+1)⁺. Anal Calcd for C₁₈H₂₀N₂O₄S: C, 59.98; H, 5.59; N, 7.77; S, 8.90. Found C, 60.10; H, 5.22; N, 7.71; S, 8.95.

(R)-(+)-{3-[2-(4-Isopropoxy-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-carbamic acid methyl ester (9o)

The compound was prepared via the same route as described for **9n** by replacing 3-butyn-2-ol with (*S*)-(-)-3-butyn-2-ol. [α] = 114.11 (CHCl₃, *c* = 1, room temperature). MS (ESI), *m/z*: 361.0 (M+1)⁺. Anal. Calcd for C₁₈H₂₀N₂O₄S: C, 59.98; H, 5.59; N, 7.77; S, 8.90. Found: C, 59.72; H, 5.58; N, 7.75; S, 8.91.

(S)-(-)-{3-[2-(4-Isopropoxy-phenoxy)-thiazol-5-yl]-1-methyl-prop-2-ynyl}-carbamic acid methyl ester (9p)

The compound was prepared via the same route as described for **9n** by replacing 3-butyn-2-ol with (*R*)-(+)-3-butyn-2-ol. [α] = -116.9 (CHCl₃, *c* = 1, room temperature). MS (ESI), *m/z*: 361.0 (M+1)⁺. Anal Calcd for C₁₈H₂₀N₂O₄S: C, 59.98; H, 5.59; N, 7.77; S, 8.90. Found: C, 59.69; H, 5.33; N, 7.70; S, 9.04. Enantiomeric excess (98.7%) was determined by using chiral HPLC (Column: Chiralpak AD 4.6 mmID x 250 mm, Mobile Phase: Hex/EtOH/MeOH = 80/10/10, Flow Rate: 1.0 mL/min, Detector: UV 260 nm, Column Temp: 40°C).

N-{3-[2-(4-Isopropoxy-phenoxy)-thiazol-4-yl]-1-methyl-prop-2-ynyl}-acetamide (10)

MS (DCI) *m/z*: 345 (M+H)⁺, 362 (M+NH₄)⁺; ¹H NMR (300 MHz, CDCl₃) δ ppm 1.34 (d, *J*=5.88 Hz, 6 H), 1.46 (d, *J*=6.99 Hz, 3 H), 1.98 (s, 3 H), 4.45 - 4.57 (m, 1 H), 4.94 - 5.07 (m, 1 H), 5.72 (d, *J*=8.09 Hz, 1 H), 6.86 - 6.95 (m, 3 H), 7.13 - 7.21 (m, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ ppm 21.90, 22.03, 23.08, 37.34, 70.42, 88.87, 116.73, 116.83, 121.39, 131.29, 132.06, 148.45, 155.92, 169.04, 173.49. Analysis C₁₈H₂₀N₂O₃S.0.1CH₂Cl₂: Calcd C, 61.60; H, 5.85; N, 7.94; Found C, 61.76; H, 5.58; N, 7.49.

N-{3-[4-(4-isopropoxyphenoxy)phenyl]-1-methylprop-2-ynyl}acetamide (12)

4-(4-Isopropoxyphenyl)phenyl bromide. To a mixture of 4-isopropoxyphenol (505 mg, 3.31 mmol), 1,4-dibromobenzene (2.34 g, 9.92 mmol.), K₂CO₃ (960 mg, 6.87 mmol) and pyridine (20 mL) at 80 °C was added Cu(II) oxide (650 mg, 8.17 mmol). After the addition, the mixture was refluxed vigorously for 20h. After cooling, methylene chloride was added and the mixture was filtered through celite. The filtrate was concentrated to dryness. The residue was dissolved in ether, which was washed with 10% HCl (2x), 1N NaOH (2x), brine (1x), dried over MgSO₄, and concentrated. The residue was purified on silica gel column eluting with hexane and ethyl acetate gradient to give the desired product as a white solid (477 mg, 47%). MS (DCI): *m/z* 307, 309 (M+H)⁺; ¹H NMR (300 MHz, CDCl₃) δ ppm 1.34 (d, *J*=6.25 Hz, 6 H), 4.41 - 4.55 (m, 1 H), 6.79 - 6.84 (m, 2 H), 6.84 - 6.90 (m, 2 H), 6.91 - 6.98 (m, 2 H), 7.34 - 7.43 (m, 2 H).

(12) MS (DCI): *m/z* 338 (M+H)⁺; ¹H NMR (300 MHz, CDCl₃) δ ppm 1.34 (d, *J*=5.88 Hz, 6 H), 1.48 (d, *J*=6.62 Hz, 3 H), 2.00 (s, 3 H), 4.42 - 4.56 (m, 1 H), 4.97 - 5.08 (m, 1 H), 6.82 - 6.91 (m, 4 H), 6.92 - 6.99 (m, 2 H), 7.30 - 7.37 (m, 2 H). ¹³C NMR (75 MHz, CDCl₃) δ ppm 22.01, 22.63, 23.26, 37.64, 70.50, 81.85, 88.40, 116.21, 117.08, 117.08, 121.07, 133.14, 149.07, 154.47, 158.73, 168.75; Analysis C₂₁H₂₃NO₃·0.1H₂O: Calcd C, 74.36; H, 6.89; N, 4.12; Found C, 74.17; H, 6.81; N, 4.17.

{1-Methyl-3-[2-(4-phenoxy-phenoxy)-thiazol-5-yl]-prop-2-ynyl}-urea (9a)

To a solution of **9l** (100mg, 0.3 mmol) in methylene chloride (4mL) was added trichloroacetyl isocyanate (50μL, 0.42mmol) at 0 °C. The reaction mixture was stirred for 15 min and concentrated. The resulting oil was dissolved in methanol (4 mL) and heated to reflux for 4 h. The crude product was purified by reverse-phase HPLC on an Atlantis C18 column (1.9 x 10 cm, 5 μm particle size) using a gradient of 5% to 100% acetonitrile:0.1% aqueous TFA to provide 72 mg of **9a** (63%). ¹H NMR (300 MHz, DMSO-*d*₆) δ ppm 1.32 (d, *J*=6.99 Hz, 3 H), 4.53 - 4.77 (m, 1 H), 5.54 (s, 2 H), 6.45 (d, *J*=8.46 Hz, 1 H), 6.97 - 7.26 (m, 5 H), 7.35 - 7.47 (m, 4 H), 7.48 (s, 1 H); MS (ESI) *m/z* 379.9 (M + H)⁺; Analysis C₂₁H₁₈N₂O₃S·0.2H₂O: Calcd C, 66.02; H, 4.85; N, 7.33; Found C, 66.15; H, 5.01; N, 7.12.

N-{1-Methyl-3-[2-(4-phenoxy-phenoxy)-thiazol-5-yl]-prop-2-ynyl}-acetamide (9b)

To a solution of **9l** (200 mg, 0.595 mmol) and triethylamine (250 uL, 1.78 mmol) in methylene chloride (3mL) was added acetic anhydride (68uL, 0.714 mmol) at ambient temperature. The reaction mixture was stirred for 15 min and concentrated. The residual was purified by flash chromatography on silica gel eluting with a solvent gradient from 30% to 70% ethyl acetate in hexanes to provide 218 mg (97%) of **9b** as a light yellow solid. MS (DCI) *m/z*: 379 (M+H)⁺; ¹H NMR (300 MHz, CDCl₃) δ ppm 1.46 (d, *J*=6.99 Hz, 3 H), 2.00 (s, 3 H), 4.96 - 5.11 (m, 1 H), 5.64 (br. s, 1 H), 6.99 - 7.08 (m, 4 H), 7.09 - 7.17 (m, 1 H), 7.20 - 7.25 (m, 2 H), 7.30 (s, 1 H), 7.31 - 7.42 (m, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ ppm 22.05, 23.07, 37.51, 72.05, 95.07, 111.92, 119.01, 119.72, 121.61, 123.65, 129.82, 129.82, 142.17, 150.05, 155.29, 156.70, 168.96, 173.39. Analysis C₂₁H₁₈N₂O₃S·0.1CH₂Cl₂: Calcd C, 65.50; H, 4.74; N, 7.24; Found C, 65.45; H, 4.56; N 7.04.