

Supplementary Information for:

Design, synthesis, and synergistic activities of 2-aminothiazolyl compounds as colistin potent adjuvants against *Acinetobacter baumannii*

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Table of Contents

1. Materials and Methods	S2
2. Characterization data of Products C1-C19	S5
3. ¹HNMR and ¹³C NMR spectra of all target compounds	S11
4. Table S1. Dose-response of compounds C1-C19 for colistin potentiation against ACCT19606	S30

1 Materials and Methods

1.1 chemistry

All solvents and reagents were obtained from commercial suppliers and used without further purification. ^1H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were obtained on Bruker AM-400 spectrometer with CDCl_3 or $\text{DMSO}-d_6$ as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the ^1H NMR spectra as 0.00 ppm (CDCl_3 , $\delta = 7.26$ ppm. $\text{DMSO}-d_6$, $\delta = 2.54$ ppm). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet and m = multiplet), coupling constant (J values) in Hz and integration. Chemical shifts for ^{13}C NMR spectra were recorded in ppm from tetramethylsilane using the central peak of CDCl_3 ($\delta = 77.0$ ppm), $\text{DMSO}-d_6$ ($\delta = 40.45$ ppm) as the internal standard. High Resolution Mass Spectrometry (HRMS) were recorded under electron impact (70 eV) condition using a MicroMass GCT CA 055 instrument. Melting points were determined using a Büchi B540 melting point apparatus. Analytical thin layer chromatography (TLC) was carried out on precoated plates (silica gel 60 F254), and spots were visualized with ultraviolet (UV) light. The yields reported are the isolated yields.

The target compounds **C1-C19** were synthesized through a two-step reaction. Firstly, the 1-(4-hydroxyphenyl)ethan-1-one analogues **a1-a19** (1.0 eq.) were dissolved in ethyl acetate (EA) and cooled to 0 °C in an ice bath. *N*-bromosuccinimide (NBS, 1.2 eq.) and triethylamine (TEA, 1.5 eq.) were then added sequentially. The progress of the reaction was monitored by thin-layer chromatography (TLC) until the raw material had been completely consumed. Upon completion of the reaction, the reaction solution was extracted with water (H_2O) and EA. The organic phases were then combined, washed with saturated brine, dried over anhydrous magnesium sulphate (MgSO_4), and concentrated under reduced pressure to produce the crude products. Crude products were purified by silica gel column chromatography with a gradient of petroleum ether (PE) / EA (100:0 to 90:10, v/v), affording the key intermediates **b1-b19** (Yield: 55%-89%). Secondly, intermediates **b1-b19** (1.0 eq.) were dissolved in ethanol (EtOH) and reacted with thiourea compounds (1.0 eq.) under reflux for 1 hour, with the reaction progress monitored by TLC. Upon completion, the reaction mixture was extracted with an equal volume of H_2O / EA, and the organic layer was combined. After washing with saturated brine, the mixture was dried over anhydrous MgSO_4 and concentrated under reduced pressure to obtain the crude product. The crude product was then purified by silica gel column chromatography with a gradient of PE / EA (100:0 to 95:5, v/v), yielding the target compounds **C1-C19** (22%-77%). Purity testing of the final product **C1-C19** was conducted using Ultra-Performance Liquid Chromatography (UPLC, Waters, USA). The separation process was carried out on a BEH C18 column (3×100 mm, 2.5 μm), with the column temperature maintained at 40 °C. The mobile phase A was ultrapure water, and the mobile phase B was analytical-grade acetonitrile. The following gradient programme was employed: 0-2.0 min, holding 10% B; 2.0-12.0 min, 10% B to 100% B; 12.0-14.0 min, holding 100% B; 14.0-15.0 min, returning to 10% B. The flow rate was set at 0.40 mL/min, with detection occurring at 254 nm. Samples were dissolved in acetonitrile to yield solutions with a concentration of approximately 1 mg/mL. These solutions were then filtered through 0.22 μm membranes and injected at a volume of 2.0 μL . The calculation of compound purity was performed using peak area normalisation.

1.2 Antibacterial tests

The minimum inhibitory concentrations (MICs) of colistin and the target compounds were

determined using broth microdilution in Mueller-Hinton Broth (MHB), following the guidelines of the Clinical and Laboratory Standards Institute (CLSI, M07-A9, 2012a). The combined effects of the target compounds and colistin were assessed using the checkerboard method. In the checkerboard assay, colistin was serially diluted along the horizontal axis, while the target compounds were serially diluted along the vertical axis. A 96-well plate was inoculated with ATCC19606 at a concentration of $0.5\text{--}1.0 \times 10^6$ CFU/mL. After incubation for 16 hours at 37°C under aerobic conditions, the optical density (OD) values were measured to determine whether the wells were sterilized. The antibacterial activity was calculated using the fractional inhibitory concentration index (FICI) formula:

$$\text{FICI} = \text{MICAB}/\text{MICA} + \text{MICBA}/\text{MICB} = \text{FICA} + \text{FICB}.$$

Where MICA was the MIC of compound A alone, MICAB was the MIC of compound A in combination with compound B, MICB was the MIC of compound B alone, MICBA was the MIC of compound B in combination with compound A, FICA was the FIC of compound A, and FICB was the FIC of compound B. Synergy was defined as a FIC index ≤ 0.5 .

The procedure for testing the bactericidal activity of the target compounds against Gram-positive bacteria was as follows. First, a stock solution of the drug at a concentration of 10 mg/mL was prepared using dimethyl sulfoxide (DMSO), and then diluted to a working concentration of 512 µg/mL using LB medium. 200 µL of the diluted solution was added to the first column of a 96-well plate. Subsequently, 100 µL of blank LB medium was added to the remaining wells, and serial dilution was performed using a multichannel pipette to achieve drug concentrations of 512, 256, 128, 64, 32, 16, 8, 4, 2, 1, 0.5, and 0 µg/mL in each row. A single colony of the target bacterial strain was picked from an LB agar plate and inoculated into 5 mL of Mueller-Hinton Broth (MHB), followed by overnight incubation at 37°C with shaking at 220 rpm. The bacterial suspension was then diluted with fresh LB medium to approximately 1×10^6 CFU/mL, and 100 µL of the diluted suspension was added to each well. This resulted in a final drug concentration halved in each well. The 96-well plate was incubated overnight at 37°C, and the minimum inhibitory concentration (MIC) was determined by visually inspecting the wells for the lowest concentration of the drug that did not exhibit visible bacterial growth.

1.3 Time-kill assays

Overnight cultures of *A. baumannii* ATCC 19606 were diluted 1:1000 into 2 mL of fresh CAMHB and incubated at 37°C with aeration. Bacteria were exposed to colistin and/or candidate compounds at varying concentrations. A saline-only control was used as a blank. Samples (100 µL) were withdrawn at 0, 2, 4, 6, 8, and 24 hours, serially diluted, plated on cation-adjusted Mueller-Hinton agar (CAMHA), and incubated overnight at 37°C. Colony counts were used to calculate CFU/mL. Experiments were conducted with biological replicates. The experimental groups included the following treatments: blank control (CK), compound **C17** at 16 µg/mL alone, compound **C17** at 4 µg/mL alone, colistin at 0.25 µg/mL alone, and 4 µg/mL of compound **C17** combined with 0.25 µg/mL of colistin.

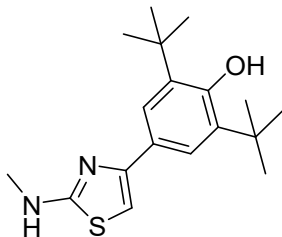
1.4 *In vivo* assay

All animal procedures were conducted in strict accordance with the guidelines approved by the Animal Care and Use Committee of Shanghai JiaoTong University. Six-week-old female Balb/c mice (n = 5 per group) were acclimatized for one week prior to the experiment. To establish a lethal peritonitis model, ATCC19606 was cultured to the mid-logarithmic phase, washed, and resuspended in a 5% (w/v) glucose solution. The bacterial suspension was then mixed at a 1:1 volume ratio with

a 10% (w/v) sterile porcine mucin solution (prepared in saline) to enhance virulence. Mice were challenged via intraperitoneal (i.p.) injection with 0.5 mL of this mixture, corresponding to a final inoculum of 7.2×10^7 CFU/mouse.

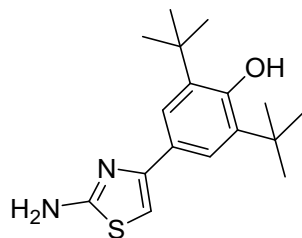
2. ¹H NMR and ¹³C NMR spectra of target compounds.

2.1 2-,6-di-tert-butyl-4-(2-(methylamino)thiazol-4-yl)phenol (C1).



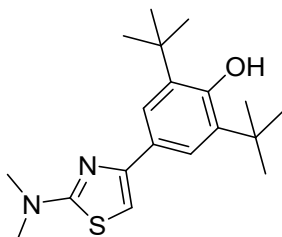
Yield: 103 mg, (55%); Yellow solid; m.p. 161.3-162.5 °C; Purity: 98.1%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.56 (s, 2H), 7.53 (q, *J* = 4.2 Hz, 1H), 6.98 (s, 1H), 6.78 (s, 1H), 2.84 (d, *J* = 4.2 Hz, 3H), 1.41 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 169.94, 154.00, 152.08, 139.47 (2C), 127.43, 122.79 (2C), 98.58, 35.07 (2C), 31.67, 30.89 (6C). HRMS (EI): *m/z* calcd for C₁₈H₂₆N₂OS [M]⁺: 318.1766; found: 318.1768.

2.2 4-(2-aminothiazol-4-yl)-2,6-di-tert-butylphenol (C2).



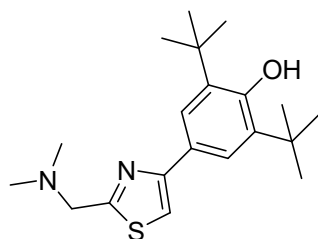
Yield: 120 mg, (47%); White solid; m.p. 173.4-174.8 °C; Purity: 97.6%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.56 (s, 2H), 7.02 (s, 2H), 7.00 (s, 1H), 6.74 (s, 1H), 1.43 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 168.43, 153.90, 151.51, 139.48 (2C), 127.36, 122.66 (2C), 99.22, 35.06 (2C), 30.90 (6C). HRMS (EI): *m/z* calcd for C₁₇H₂₄N₂OS [M]⁺: 304.1609; found: 304.1606.

2.3 2,6-di-tert-butyl-4-(2-(dimethylamino)thiazol-4-yl)phenol (C3).



Yield: 300 mg, (65%); Yellow solid; m.p. 127.1-128.3 °C; Purity: 98.0%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.62 (s, 2H), 7.02 (s, 1H), 6.90 (s, 1H), 3.08 (s, 6H), 1.44 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 170.42, 154.10, 152.63, 139.45 (2C), 127.31, 122.87 (2C), 99.72, 35.06 (2C), 30.87 (6C). HRMS (EI): *m/z* calcd for C₁₉H₂₈N₂OS [M]⁺: 332.1922; found: 332.1924.

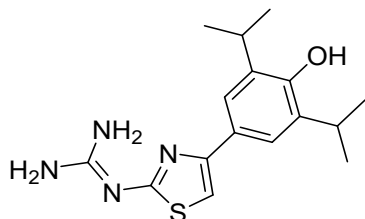
2.4 2,6-di-tert-butyl-4-(2-((dimethylamino)methyl)thiazol-4-yl)phenol (C4).



Yield: 83 mg, (42%); Yellow solid; m.p. 115.4-116.5 °C; Purity: 98.2%. ¹H NMR (400 MHz,

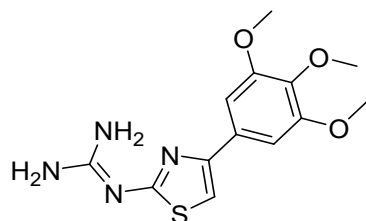
DMSO-*d*₆) δ 7.80 (s, 1H), 7.68 (s, 2H), 7.10 (s, 1H), 3.80 (s, 2H), 2.31 (s, 6H), 1.45 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 170.65, 155.42, 154.45, 139.77 (2C), 126.69, 123.05 (2C), 112.44, 60.91, 45.73 (2C), 35.11 (2C), 30.87 (6C). HRMS (EI): *m/z* calcd for C₂₀H₃₀N₂OS [M]⁺: 346.2079; found: 346.2082.

2.5 2-(4-(4-hydroxy-3,5-diisopropylphenyl)thiazol-2-yl)guanidine (C5).



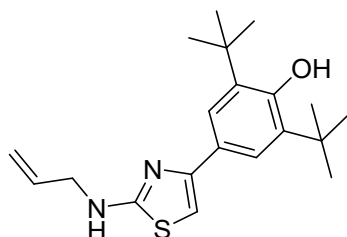
Yield: 120 mg, (77%); White solid; m.p. 124.6-125.7 °C; Purity: 97.0%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.33 (s, 1H), 8.26 (s, 4H), 7.54 (s, 1H), 7.48 (s, 2H), 1.22 (d, *J* = 6.9 Hz, 12H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 161.10, 154.80, 151.71, 136.02 (2C), 125.63, 121.56 (2C), 105.53, 26.82 (2C), 23.43 (4C). HRMS (EI): *m/z* calcd for C₁₆H₂₂N₄OS [M]⁺: 318.1514; found: 318.1518.

2.6 2-(4-(3,4,5-trimethoxyphenyl)thiazol-2-yl)guanidine (C6).



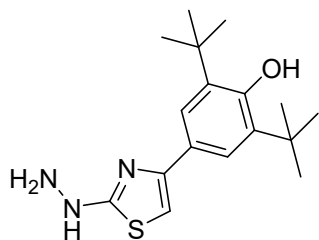
Yield: 120 mg, (47%); White solid; m.p. 181.4-182.8 °C; Purity: 97.8%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.20 (s, 4H), 7.79 (s, 1H), 7.19 (s, 2H), 3.87 (s, 6H), 3.70 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 160.92, 154.54, 153.63 (2C), 150.28, 138.33, 129.37, 108.27, 104.22 (2C), 60.62, 56.64 (2C). HRMS (EI): *m/z* calcd for C₁₇H₂₄N₂OS [M]⁺: 304.1609; found: 304.1606.

2.7 4-(2-(allylamino)thiazol-4-yl)-2,6-di-tert-butylphenol (C7).



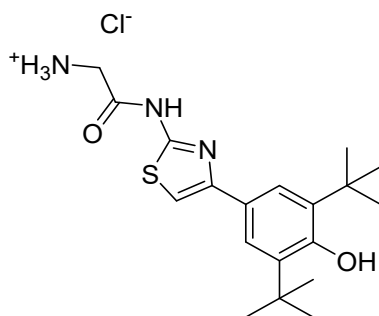
Yield: 50 mg, (45%); White solid; m.p. 124.8-125.6 °C; Purity: 98.5%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.37 (s, 2H), 7.00 (s, 1H), 5.95 – 5.86 (m, 1H), 5.36 (dd, *J* = 17.3, 1.5 Hz, 1H), 5.26 (dd, *J* = 10.3, 1.5 Hz, 1H), 4.07 (d, *J* = 5.6 Hz, 2H), 1.41 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 169.68, 155.60, 139.88 (2C), 138.85, 132.92, 125.82, 123.82 (2C), 118.14, 100.72, 48.22, 35.15 (2C), 30.65 (6C). HRMS (EI): *m/z* calcd for C₂₀H₂₈N₂OS [M]⁺: 344.1922; found: 344.1924.

2.8 2,6-di-tert-butyl-4-(2-hydrazineylthiazol-4-yl)phenol (C8).



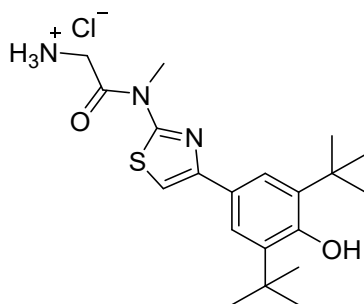
Yield: 50 mg, (42%); Green solid; m.p. 106.3-107.2 °C; Purity: 97.3%. ¹H NMR (400 MHz, CDCl₃) δ 7.52 (s, 2H), 6.51 (s, 1H), 5.59 (d, *J* = 5.3 Hz, 1H), 1.52 (s, 18H). ¹³C NMR (101 MHz, CDCl₃) δ 169.43, 159.26, 155.84, 141.56 (2C), 137.12, 122.95 (2C), 97.61, 34.59 (2C), 30.19 (6C). HRMS (EI): *m/z* calcd for C₁₇H₂₅N₃OS [M]⁺: 329.1718; found: 329.1715.

2.9 2-Amino-N-(4-(3,5-di-tert-butyl-4-hydroxyphenyl)thiazol-2-yl)acetamide hydrochloride (C9).



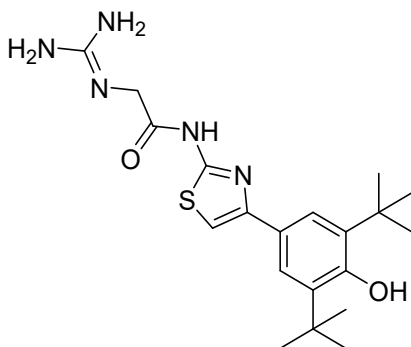
Yield: 50 mg, (36%); Yellow solid; m.p. 167.8-169.7 °C; Purity: 97.4%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.32 (s, 3H), 7.61 (s, 2H), 7.45 (s, 1H), 7.13 (s, 1H), 3.91 (s, 2H), 1.41 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.79, 157.14, 154.55, 150.74, 139.86 (2C), 126.36, 122.83 (2C), 106.57, 41.12, 35.10 (2C), 30.84 (6C). HRMS (EI): *m/z* calcd for C₁₉H₂₇N₃O₂S [M]⁺: 361.1824; found: 361.1821.

2.10 4-(2-(Allylamino)thiazol-4-yl)-2,6-di-tert-butylphenol hydrochloride (C10).



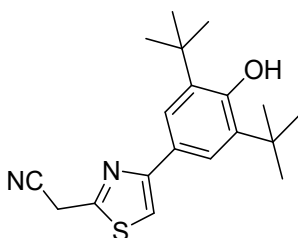
Yield: 63 mg, (35%); Yellow solid; m.p. 175.5-176.6 °C; Purity: 98.7%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.36 (s, 3H), 7.63 (s, 2H), 7.46 (s, 1H), 7.14 (s, 1H), 3.92 (s, 2H), 3.44 (s, 3H), 1.42 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.79, 157.16, 154.56, 150.74, 139.87 (2C), 126.37, 122.84 (2C), 106.56, 60.24, 41.12, 35.10 (2C), 30.84 (6C). HRMS (EI): *m/z* calcd for C₂₀H₂₉N₃O₂S [M]⁺: 375.1980; found: 375.1978.

2.11 N-(4-(3,5-di-tert-butyl-4-hydroxyphenyl)thiazol-2-yl)-2-((diaminomethylene)amino)acetamide (C11).



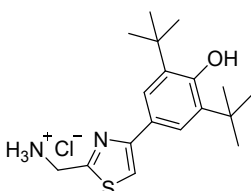
Yield: 37 mg, (22%); Yellow solid; m.p. 125.8-126.9 °C; Purity: 97.8%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.74 (t, *J* = 6.4 Hz, 1H), 7.62 (s, 2H), 7.47 (s, 4H), 7.40 (s, 1H), 7.11 (s, 1H), 4.19 (d, *J* = 6.4 Hz, 2H), 1.42 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.38, 158.45, 157.76, 154.49, 150.62, 139.88 (2C), 126.56, 122.83 (2C), 106.22, 44.05, 35.13 (2C), 30.89 (6C). HRMS (EI): *m/z* calcd for C₂₀H₂₉N₅O₂S [M]⁺: 403.2042; found: 403.2040.

2.12 2-(4-(3,5-di-tert-butyl-4-hydroxyphenyl)thiazol-2-yl)acetonitrile (C12).



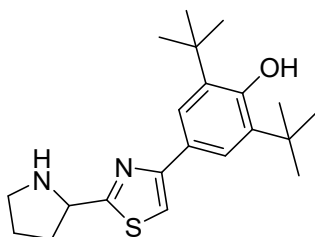
Yield: 130 mg, 28%; White solid; m.p. 149.7-150.9 °C; Purity: 98.8%. ¹H NMR (400 MHz, CDCl₃) δ 7.83 (s, 2H), 7.47 (s, 1H), 5.51 (s, 1H), 4.33 (s, 2H), 1.65 (s, 18H). ¹³C NMR (101 MHz, CDCl₃) δ 157.35, 156.94, 154.55, 136.41 (2C), 125.44, 123.58 (2C), 115.69, 111.97, 34.54 (2C), 30.37 (6C), 22.60. HRMS (EI): *m/z* calcd for C₁₉H₂₄N₂OS [M]⁺: 328.1609; found: 328.1611.

2.13 4-(2-(aminomethyl)thiazol-4-yl)-2,6-di-tert-butylphenol (C13).



Yield: 45 mg, (46%); Yellow solid; m.p. 110.3-111.4 °C; Purity: 97.3%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.63 (s, 2H), 7.97 (s, 1H), 7.73 (s, 2H), 4.51 (s, 2H), 1.45 (s, 18H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 161.85, 155.81, 154.76, 139.86 (2C), 125.98, 123.29 (2C), 113.94, 35.12 (2C), 30.85 (6C). HRMS (EI): *m/z* calcd for C₁₈H₂₆N₂OS [M]⁺: 318.1766; found: 318.1769.

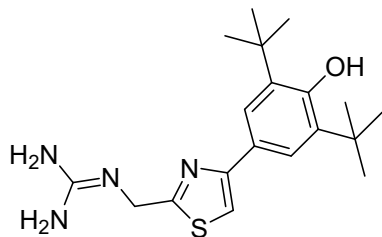
2.14 2,6-di-tert-butyl-4-(2-(pyrrolidin-2-yl)thiazol-4-yl)phenol (C14).



Yield: 52 mg, (41%); White solid; m.p. 130.5-131.2 °C; Purity: 98.4%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.03 (s, 1H), 7.73 (s, 2H), 5.14 (m, 1H), 4.40 (s, 1H), 3.51 – 3.34 (m, 2H), 2.56 (m, 1H), 2.27

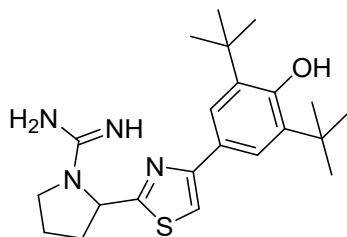
– 2.03 (m, 3H), 1.46 (s, 18H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 164.20, 156.09, 154.87, 139.89, 125.91 (2C), 123.39 (2C), 114.07, 59.09, 45.53, 35.12, 31.25 (2C), 30.82 (6C), 23.60. HRMS (EI): m/z calcd for $\text{C}_{21}\text{H}_{30}\text{N}_2\text{OS}$ $[\text{M}]^+$: 358.2079; found: 358.2080.

2.15 1-((4-(3,5-di-tert-butyl-4-hydroxyphenyl)thiazol-2-yl)methyl)guanidine (C15).



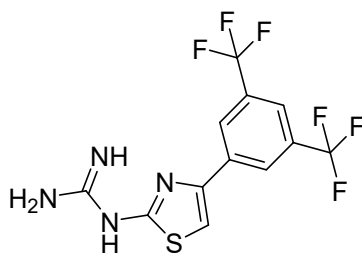
Yield: 283 mg, (29%); White solid; m.p. 240.7-241.8 °C; Purity: 98.2%. ^1H NMR (400 MHz, DMSO- d_6) δ 7.84 (s, 1H), 7.67 (s, 3H), 7.56 (s, 2H), 4.79 (s, 2H), 1.42 (s, 18H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 167.50, 157.90, 156.17, 154.70, 139.88 (2C), 126.26, 123.16 (2C), 112.29, 42.84, 35.13 (2C), 30.87 (6C). HRMS (EI): m/z calcd for $\text{C}_{19}\text{H}_{28}\text{N}_4\text{OS}$ $[\text{M}]^+$: 360.1984; found: 360.1987.

2.16 2-(4-(3,5-di-tert-butyl-4-hydroxyphenyl)thiazol-2-yl)pyrrolidine-1-carboximidamide (C16).



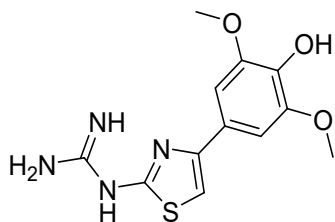
Yield: 67 mg, (30%); White solid; m.p. 140.9-141.8 °C; Purity: 97.6%. ^1H NMR (400 MHz, DMSO- d_6) δ 7.84 (s, 1H), 7.68 (s, 3H), 7.67 (s, 2H), 7.15 (s, 1H), 5.55 (m, 1H), 3.70 – 3.47 (m, 2H), 2.43 – 1.91 (m, 4H), 1.42 (s, 18H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 170.43, 156.42, 155.92, 154.71, 139.89 (2C), 126.26, 123.23 (2C), 112.22, 59.79, 48.13, 35.11 (2C), 33.90, 30.85 (6C), 22.96. HRMS (EI): m/z calcd for $\text{C}_{22}\text{H}_{32}\text{N}_4\text{OS}$ $[\text{M}]^+$: 400.2297; found: 400.2299.

2.17 1-(4-(3,5-bis(trifluoromethyl)phenyl)thiazol-2-yl)guanidine (C17).



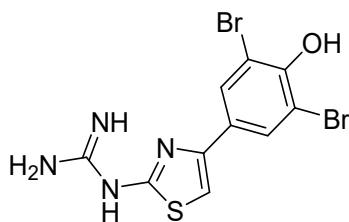
Yield: 203 mg, (48%); White solid; m.p. 196.8-197.9 °C; Purity: 96.2%. ^1H NMR (400 MHz, DMSO- d_6) δ 8.60 (s, 2H), 8.28 (s, 1H), 8.14 (s, 4H), 8.04 (s, 1H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 162.55, 154.58, 147.34, 136.25, 131.34 ((q, $^2J_{\text{CF}}$ = 32.32 Hz, 2C), 126.96 (q, $^3J_{\text{CF}}$ = 3.03 Hz, 2C), 123.81 (q, $^1J_{\text{CF}}$ = 271.69 Hz, 2C), 121.67 (q, $^3J_{\text{CF}}$ = 3.03 Hz), 112.56. HRMS (EI): m/z calcd for $\text{C}_{22}\text{H}_3\text{F}_6\text{N}_4\text{OS}$ $[\text{M}]^+$: 354.0374; found: 354.0375.

2.18 1-(4-(4-hydroxy-3,5-dimethoxyphenyl)thiazol-2-yl)guanidine (C18).



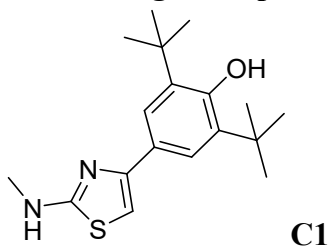
Yield: 108 mg, (25%); White solid; m.p. 219.5-220.7 °C; Purity: 97.6%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.62 (s, 1H), 8.07 (s, 4H), 7.58 (s, 1H), 7.15 (s, 2H), 3.85 (s, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 162.06, 154.82, 150.74, 148.64 (2C), 136.74, 124.44, 105.88, 104.51 (2C), 56.74. HRMS (EI): m/z calcd for C₁₂H₁₄N₄O₃S [M]⁺: 294.0787; found: 294.0789.

2.19 1-(4-(3,5-dibromo-4-hydroxyphenyl)thiazol-2-yl)guanidine (C19).

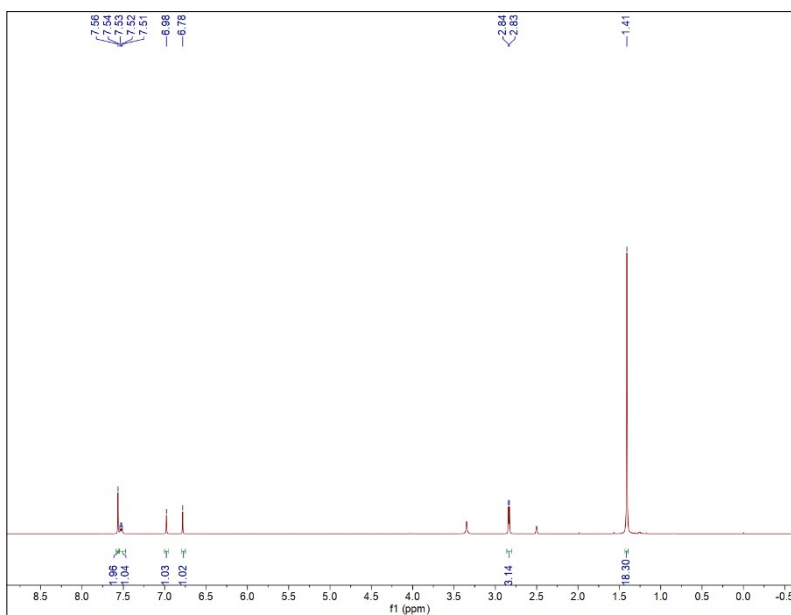


Yield: 108 mg, (25%); White solid; m.p. 295.6-296.3 °C; Purity: 98.3%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.22 (s, 4H), 8.16 (s, 2H), 7.85 (s, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.09, 158.87, 155.96, 152.51, 134.88 (2C), 133.02, 117.61 (2C), 113.70. HRMS (EI): m/z calcd for C₁₂H₁₄N₄O₃S [M]⁺: 294.0787; found: 294.0789.

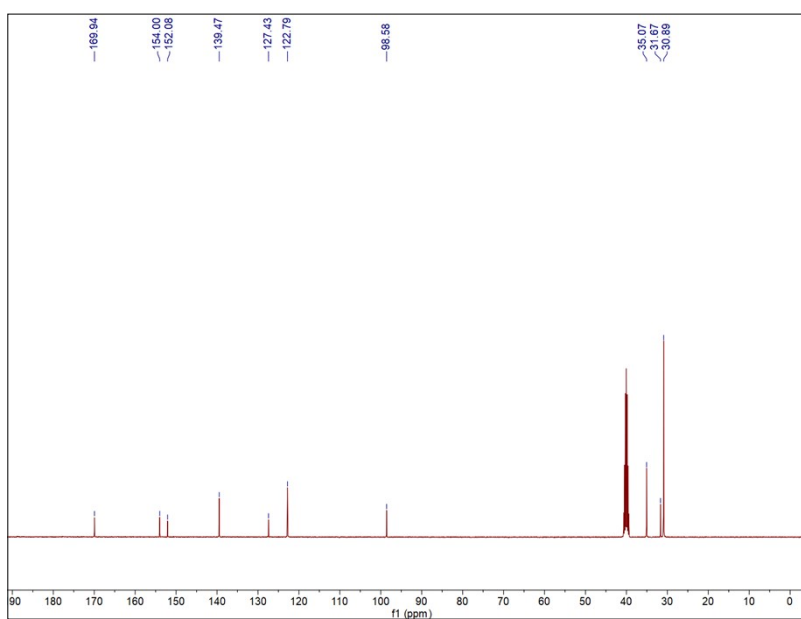
3. ^1H NMR and ^{13}C NMR spectra of target compounds.

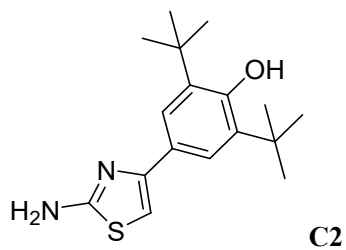


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO}-d_6$.

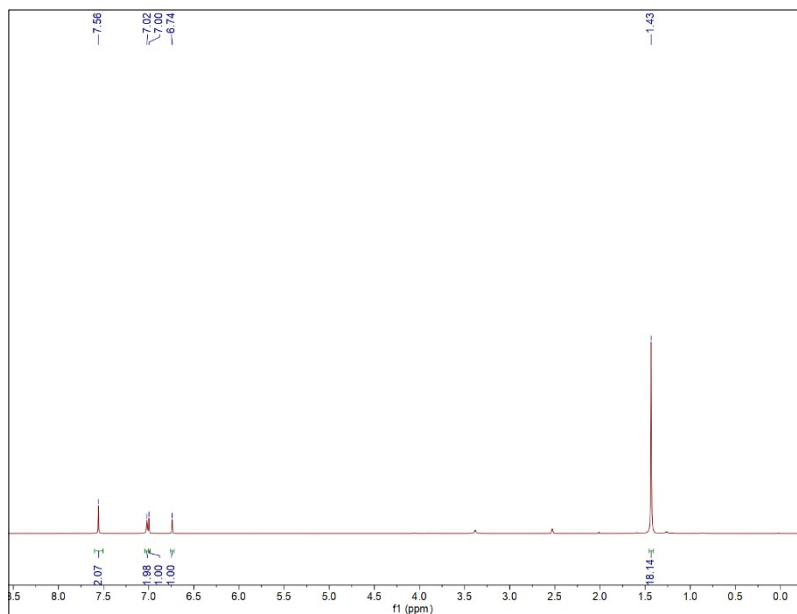


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO}-d_6$.

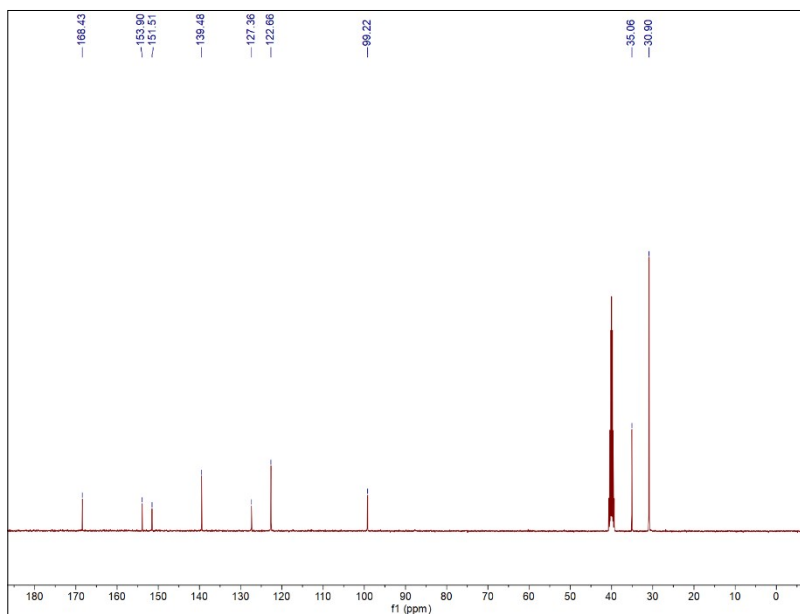


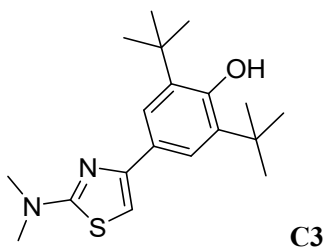


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.

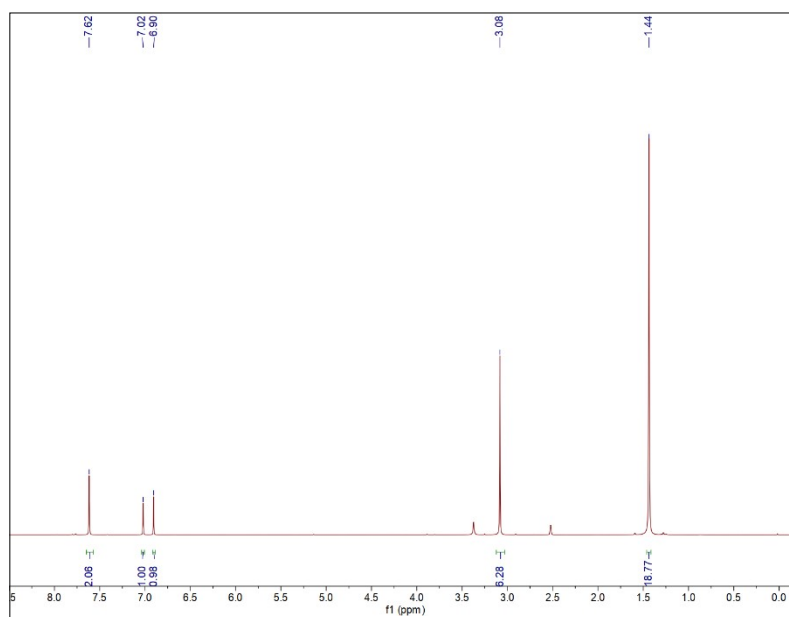


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.

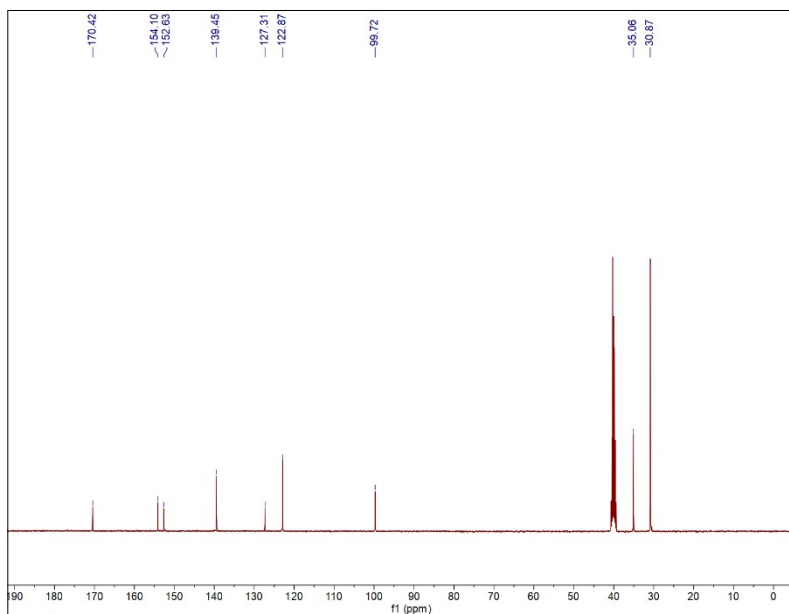


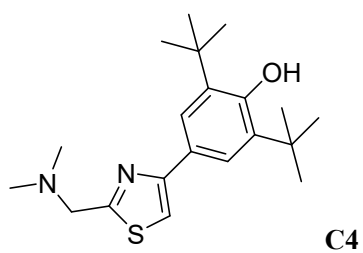


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO}-d_6$.

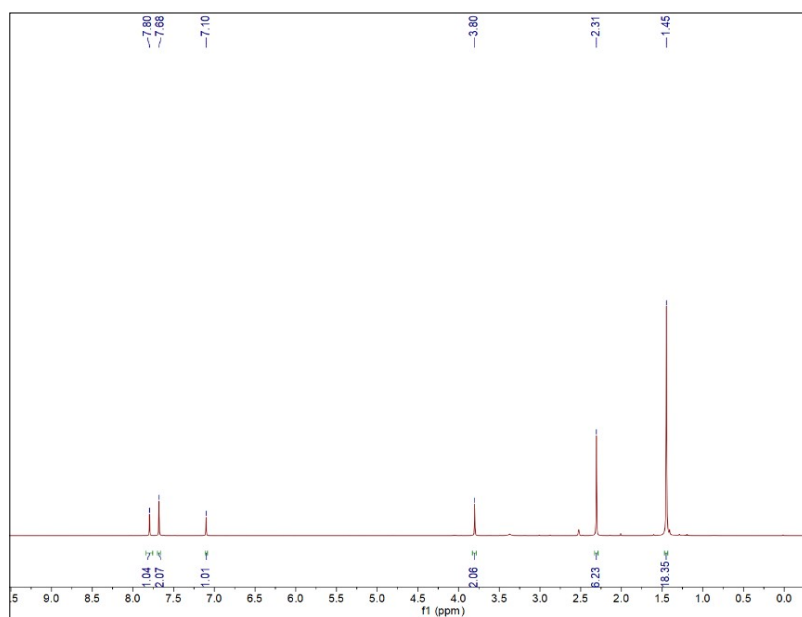


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO}-d_6$.

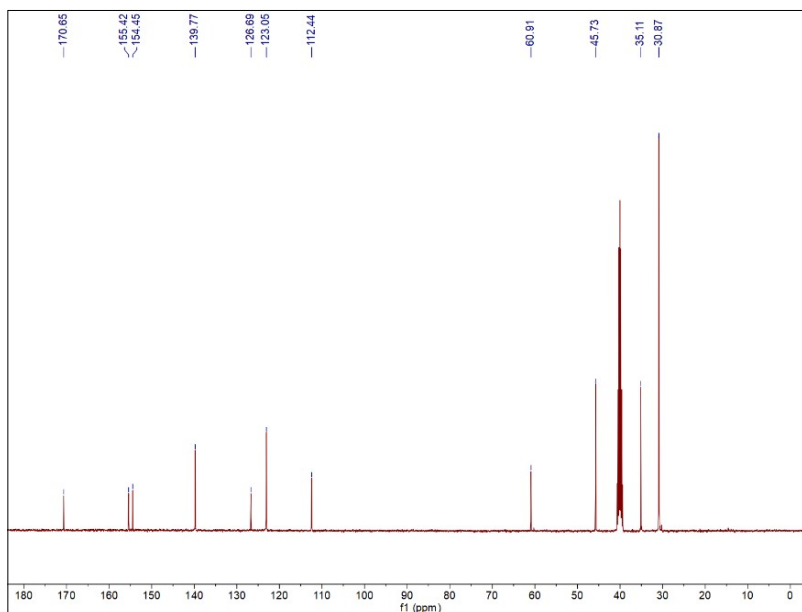


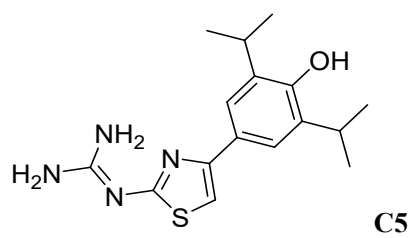


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO}-d_6$.

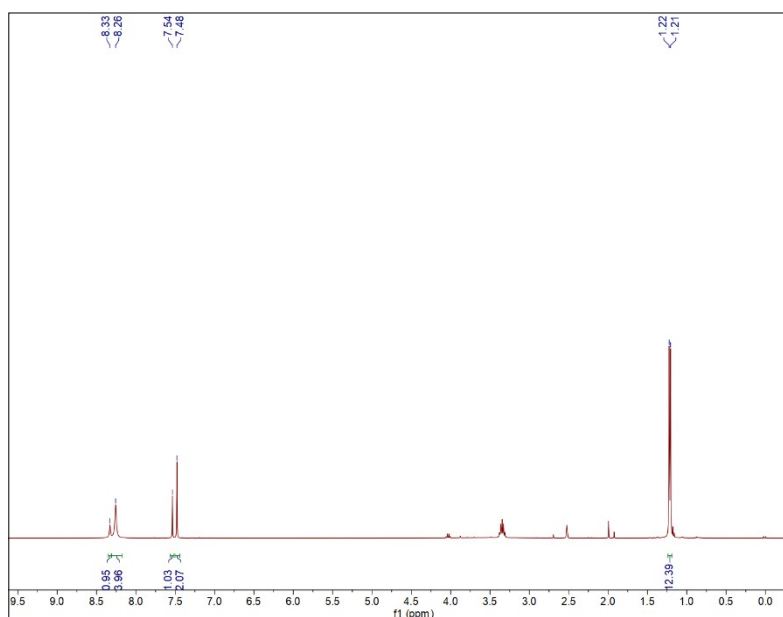


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO}-d_6$.

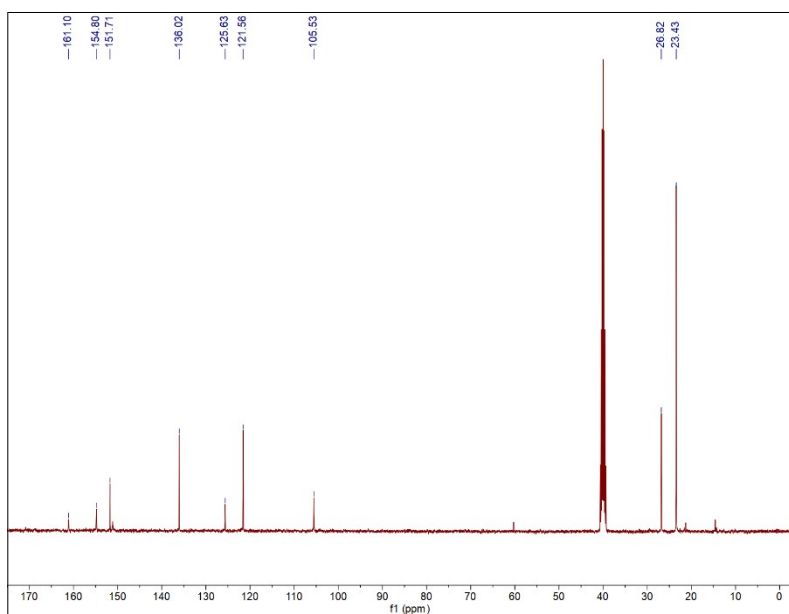


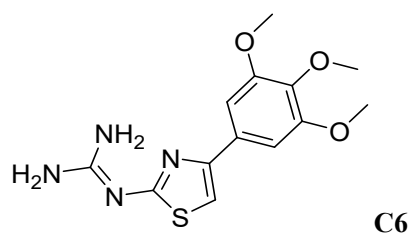


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO}-d_6$.

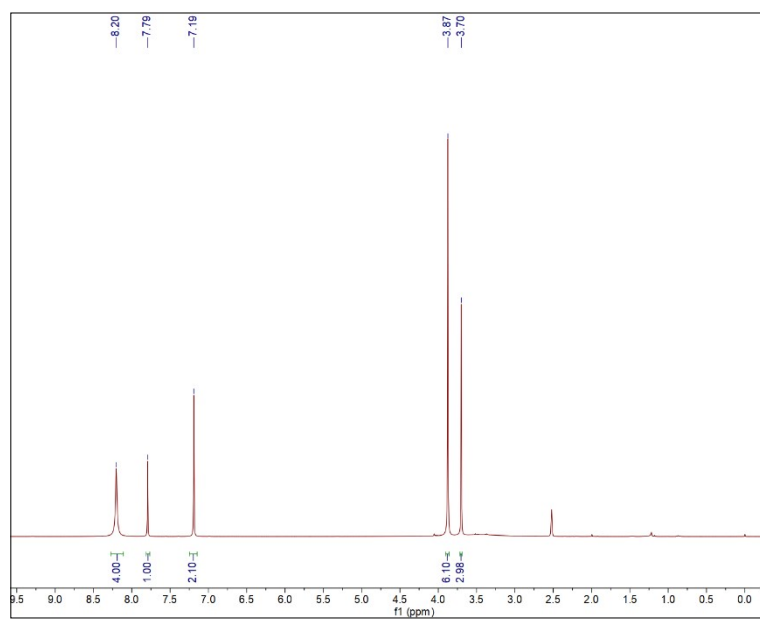


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO}-d_6$.

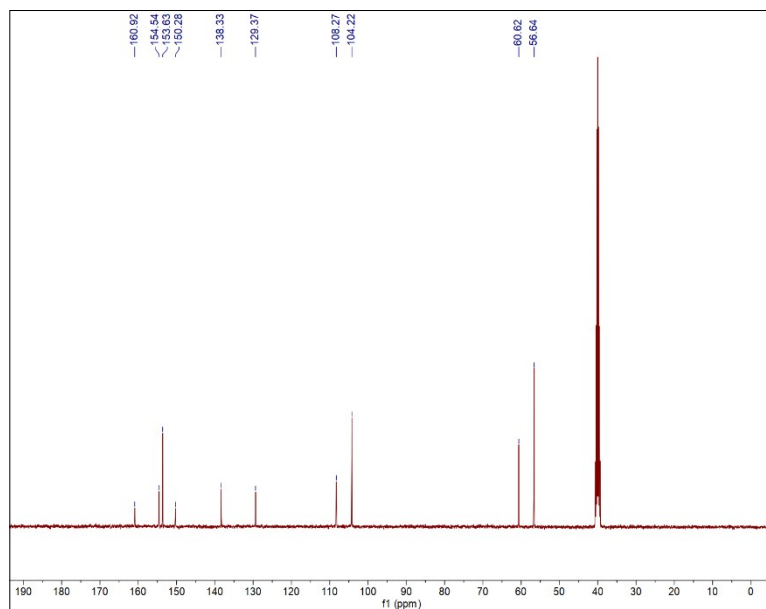


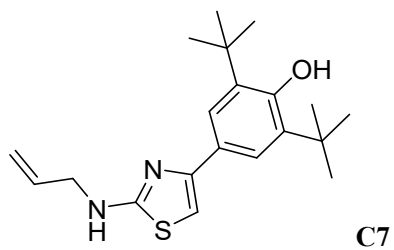


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.

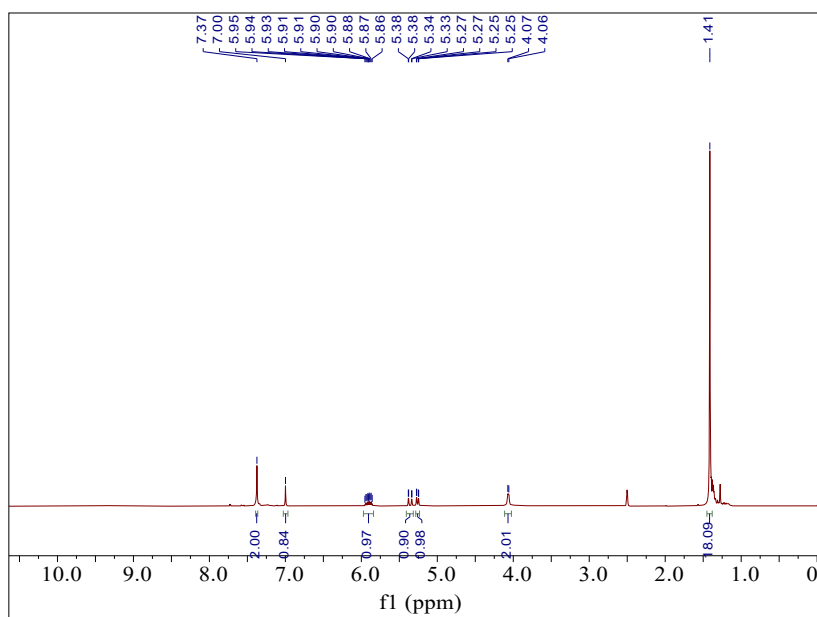


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.

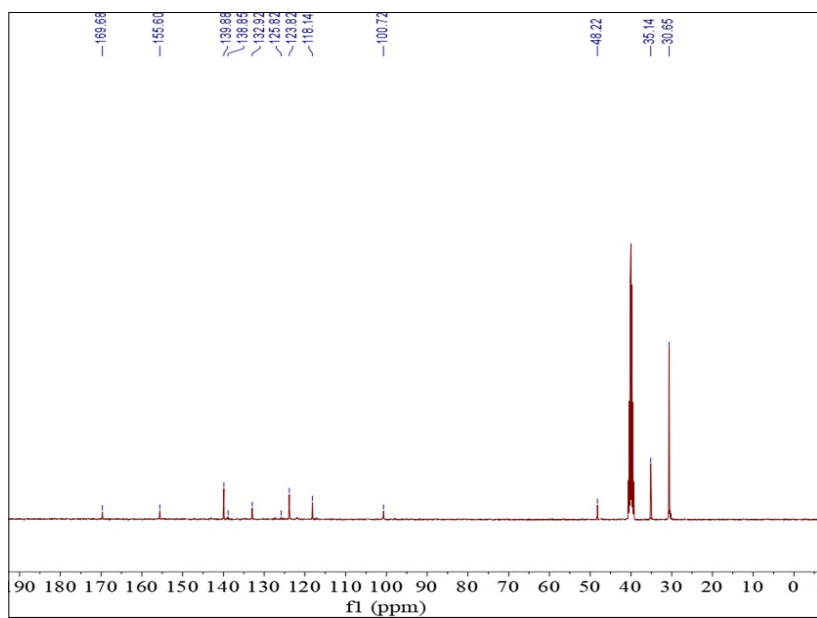


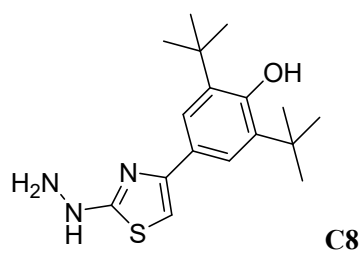


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.

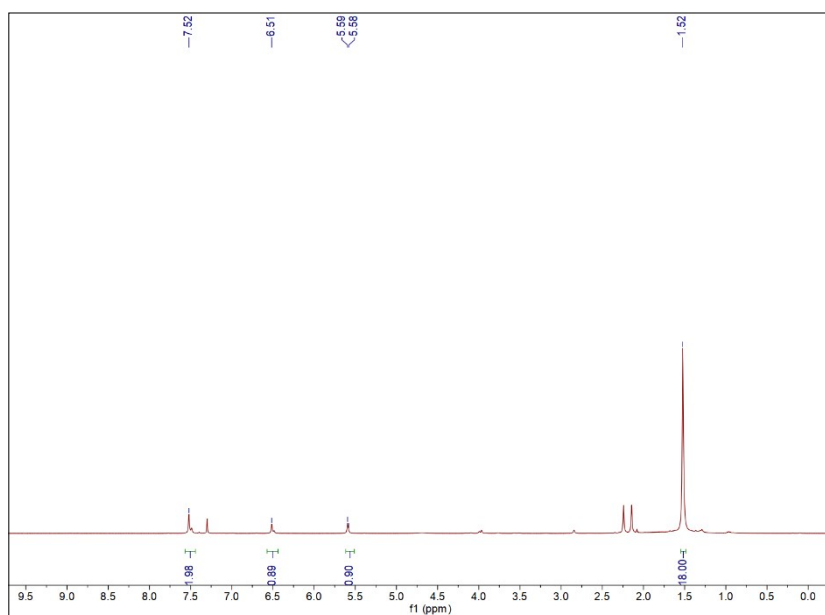


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.

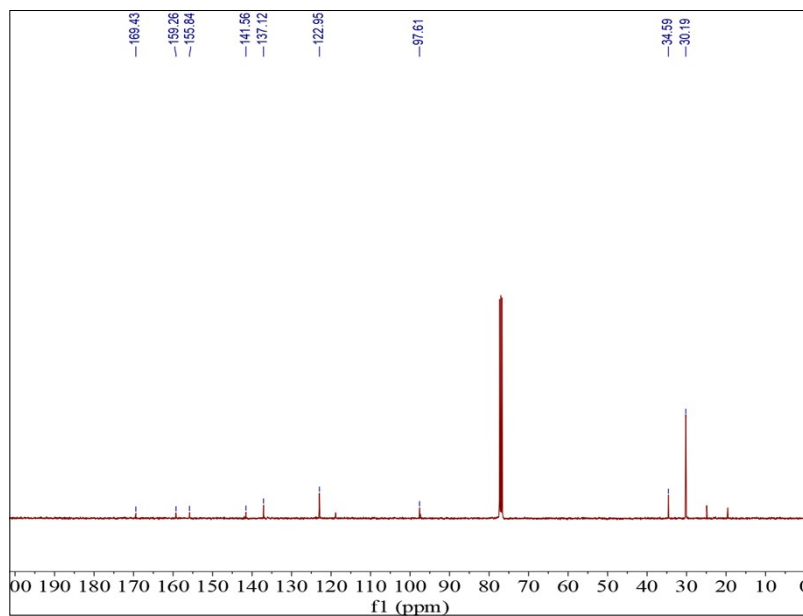


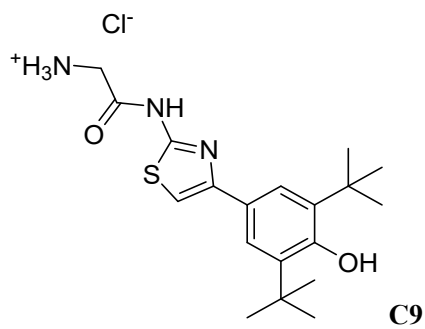


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was CDCl_3 .

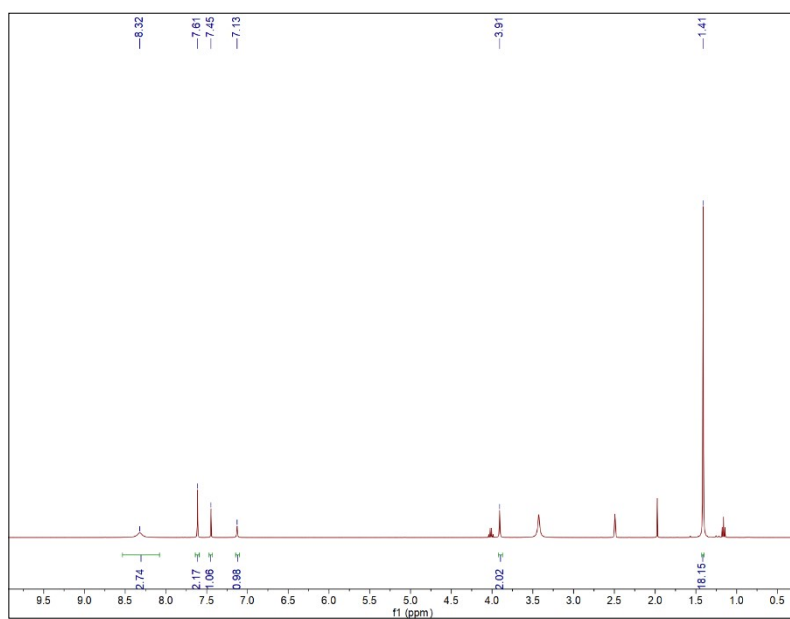


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was CDCl_3 .

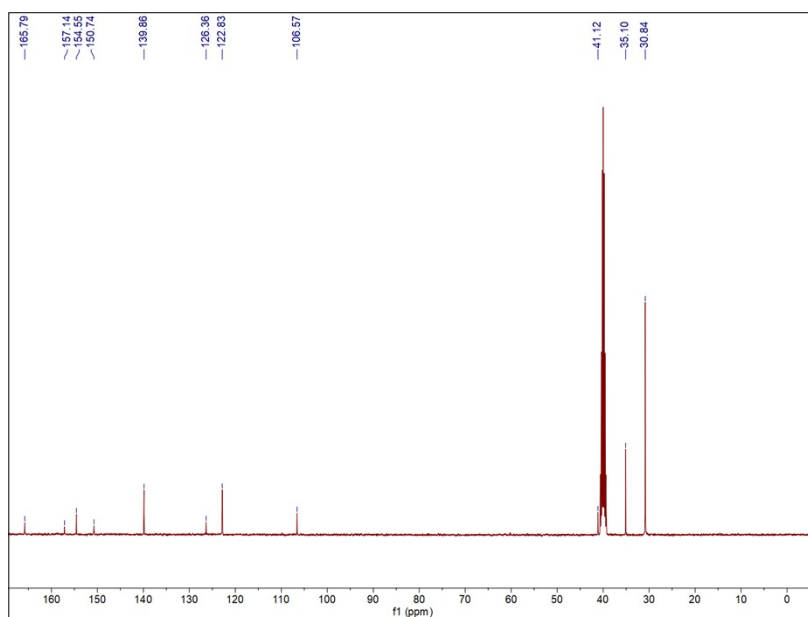


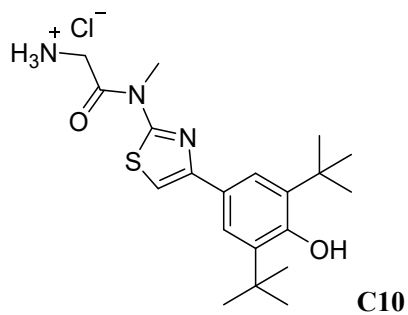


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.

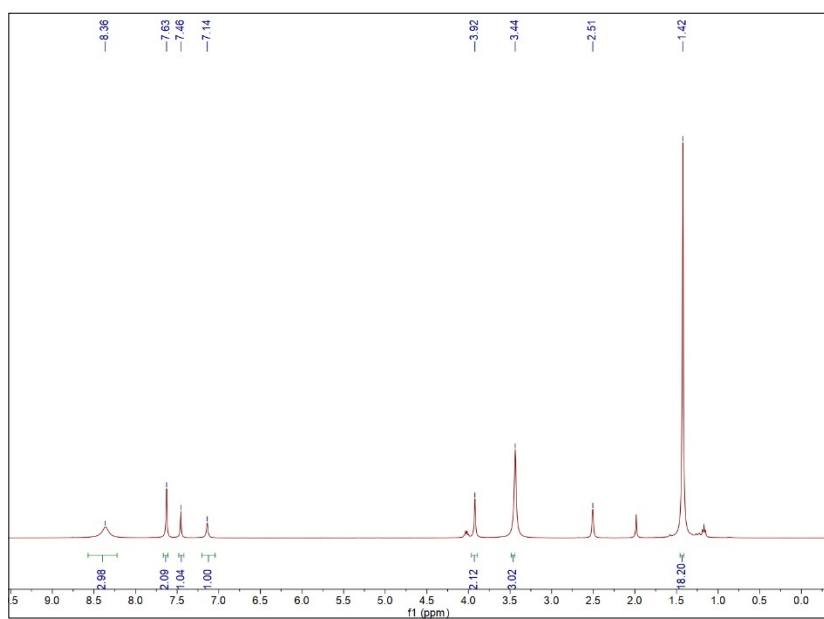


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.

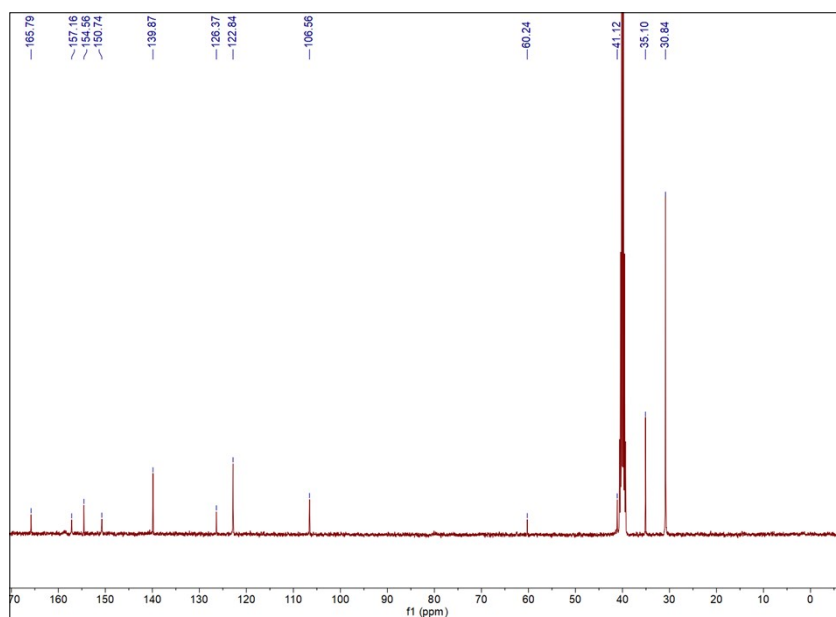


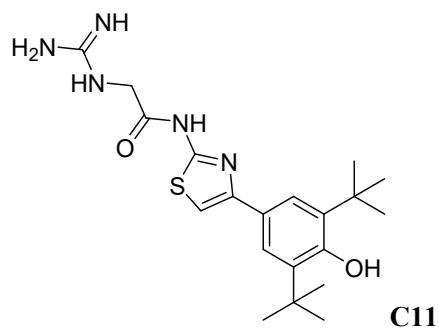


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.

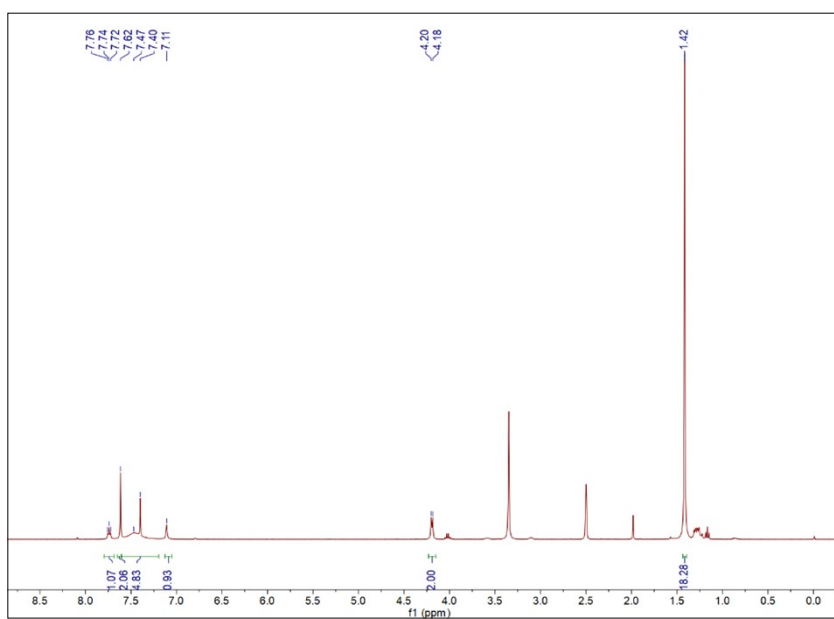


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.

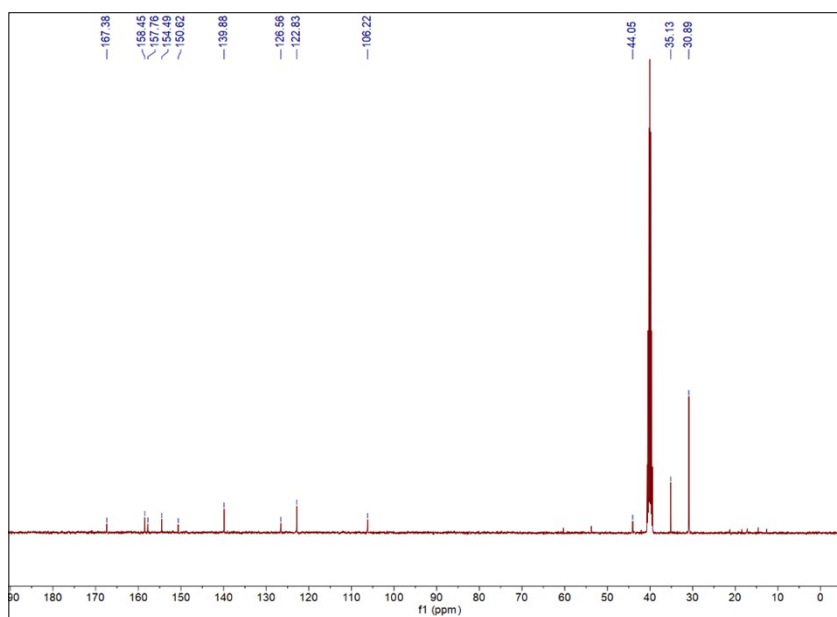


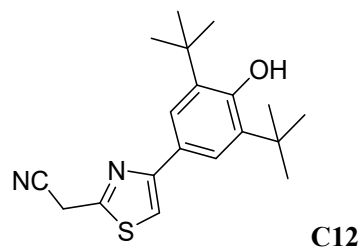


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.

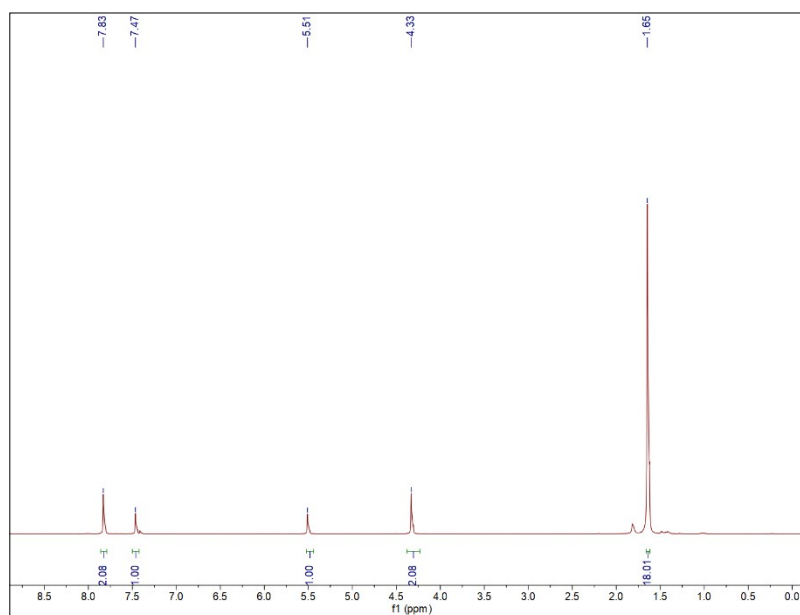


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.

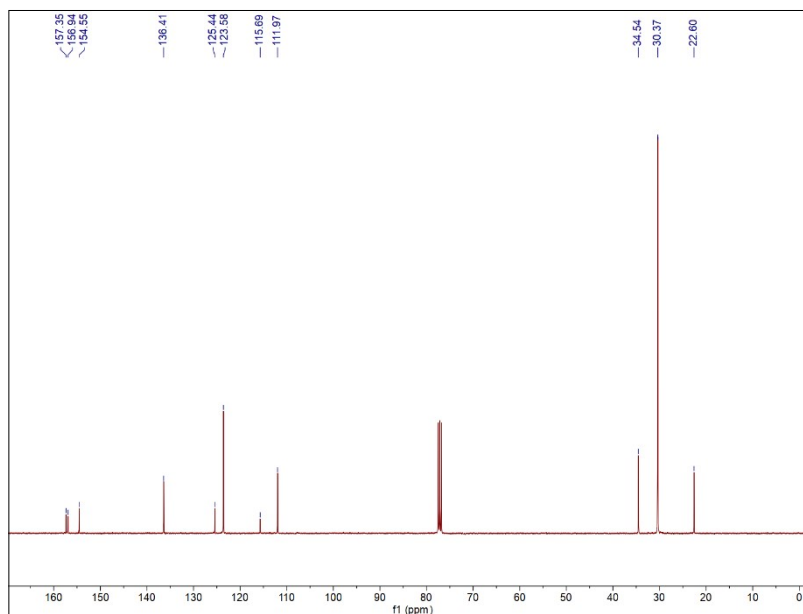


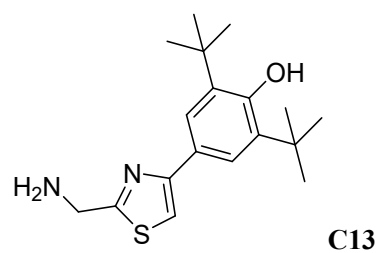


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was CDCl_3 .

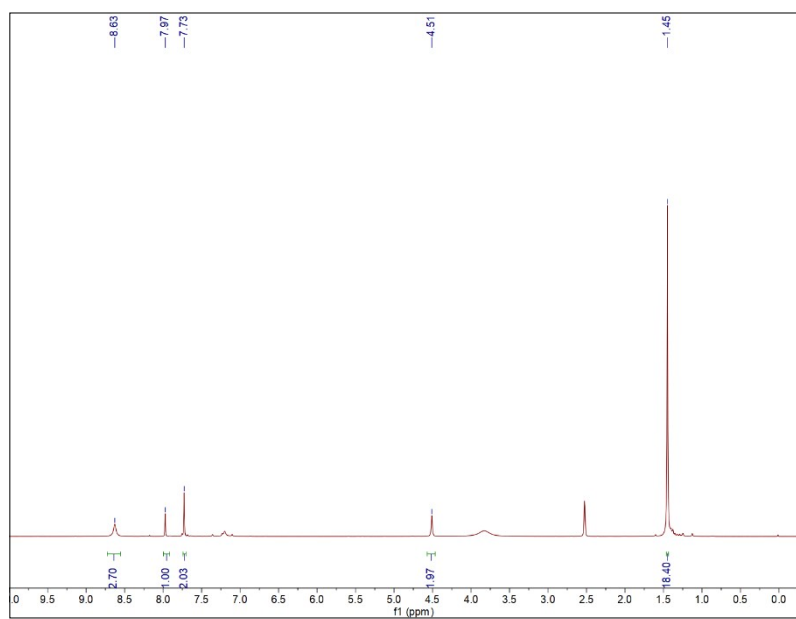


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was CDCl_3 .

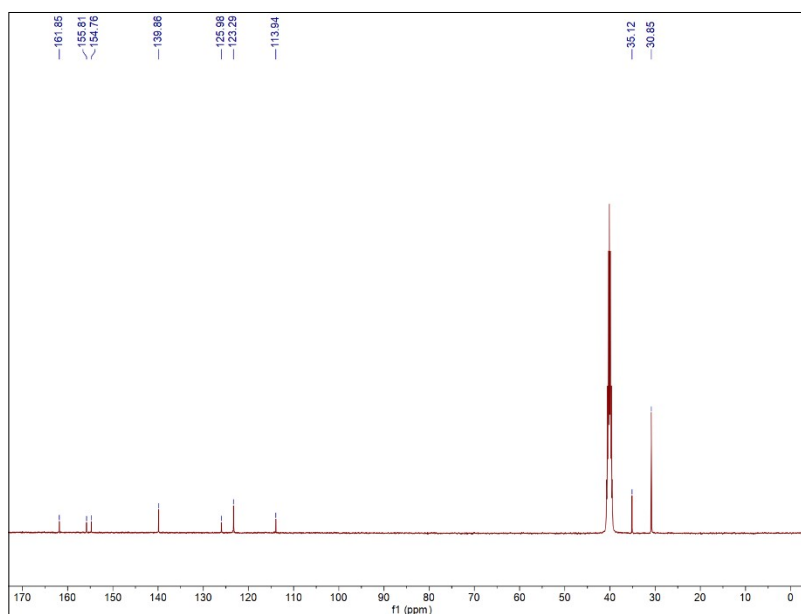


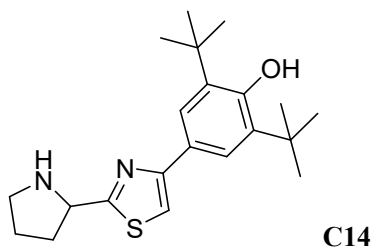


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO}-d_6$.

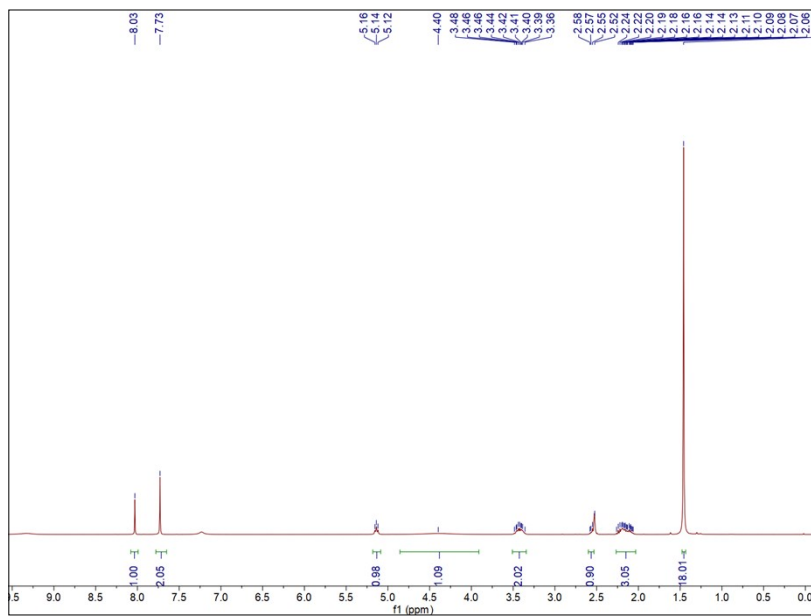


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO}-d_6$.

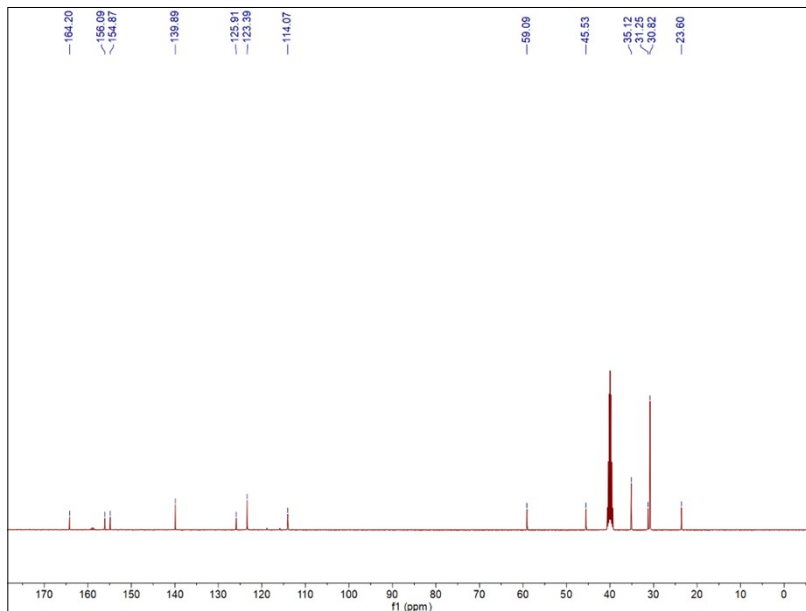


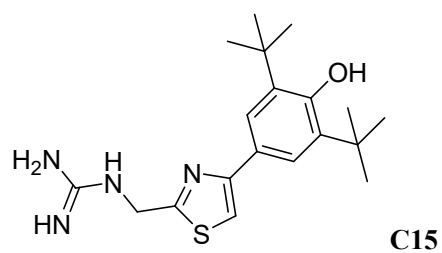


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.

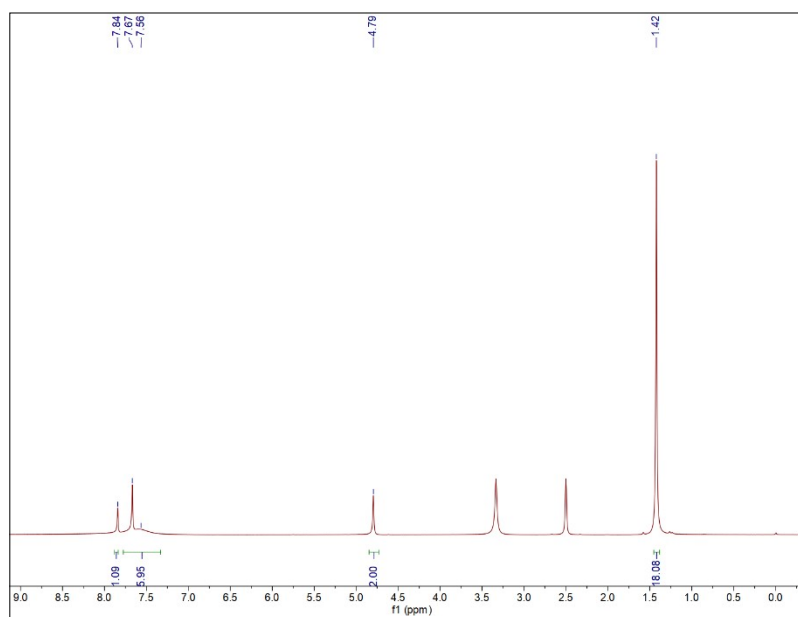


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.

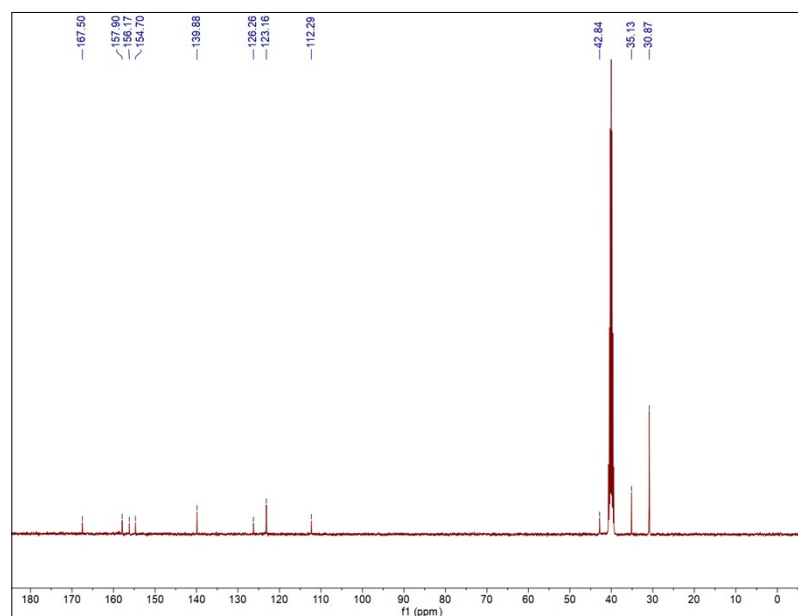


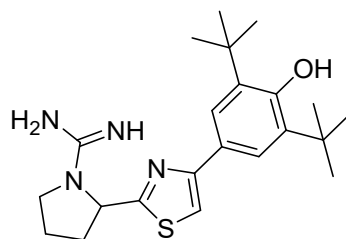


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.



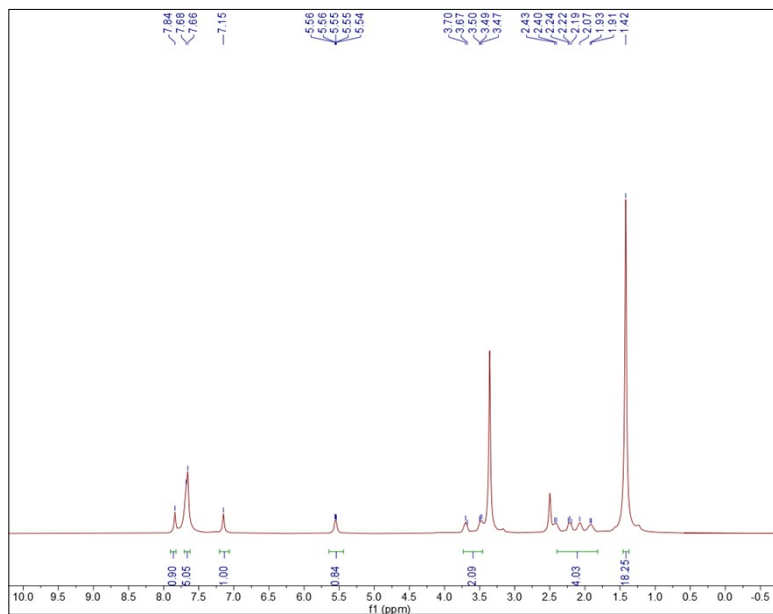
The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.



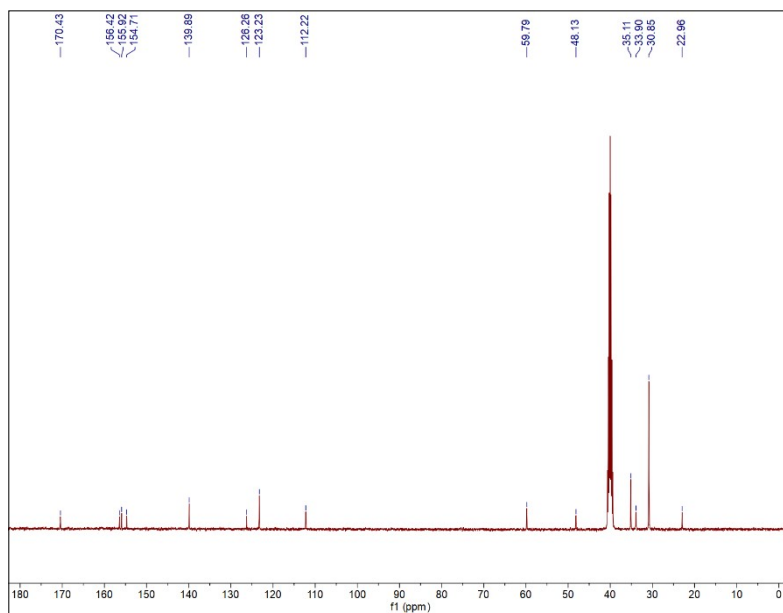


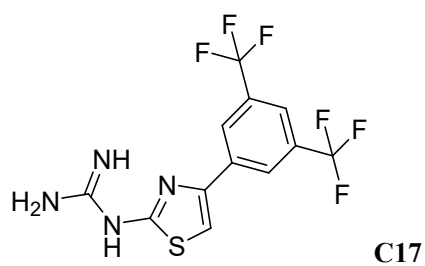
C16

The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO}-d_6$.

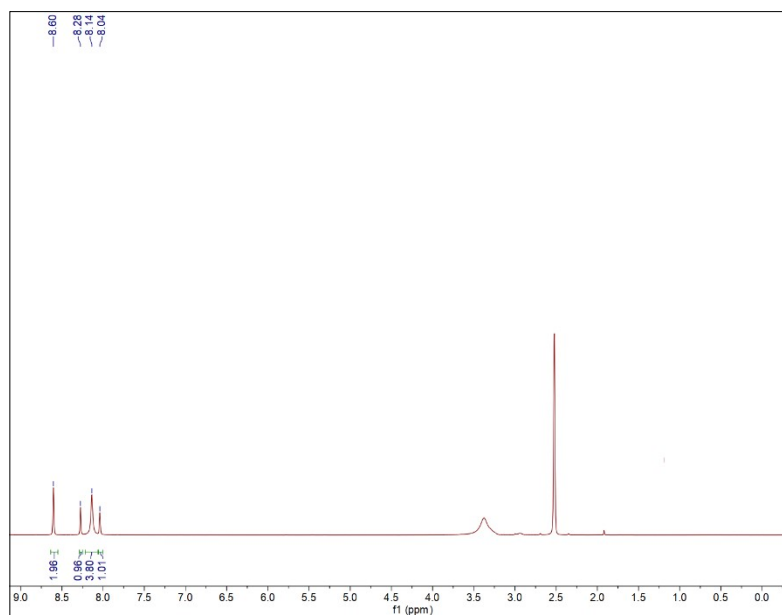


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO}-d_6$.

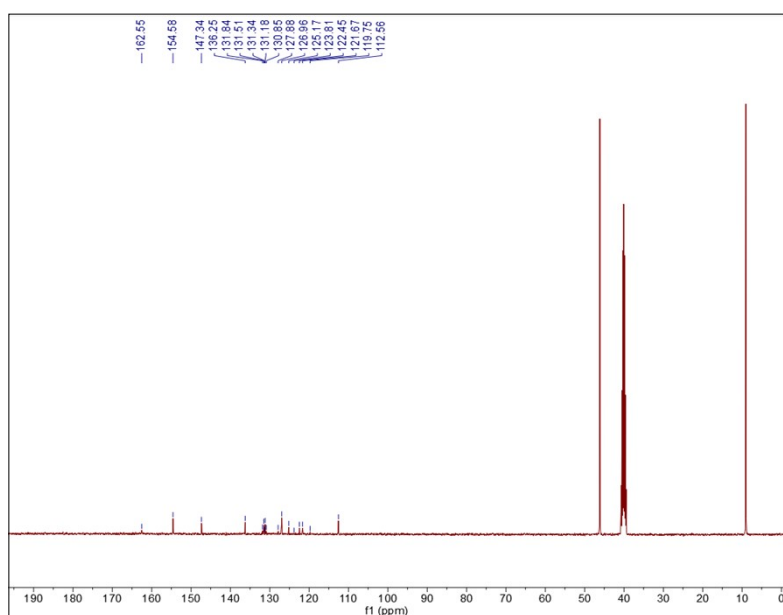


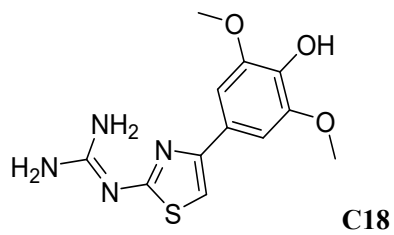


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO}-d_6$.

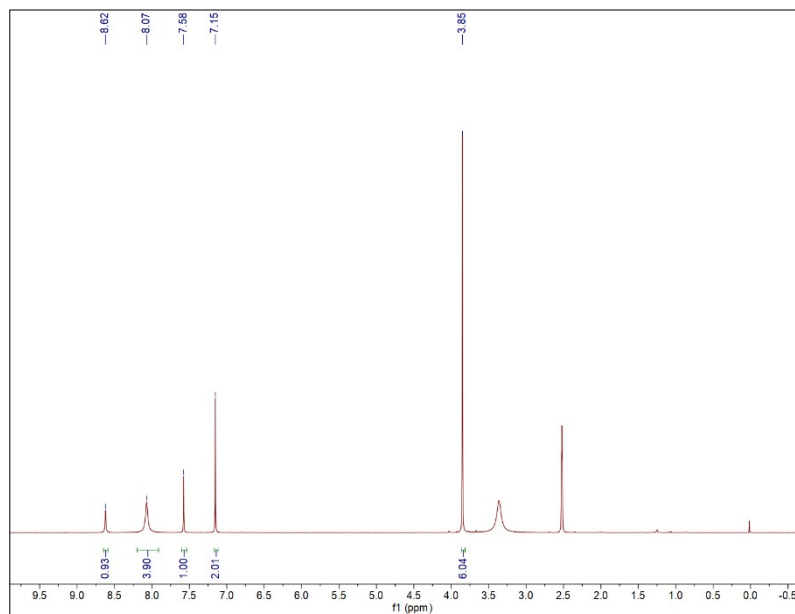


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO}-d_6$.

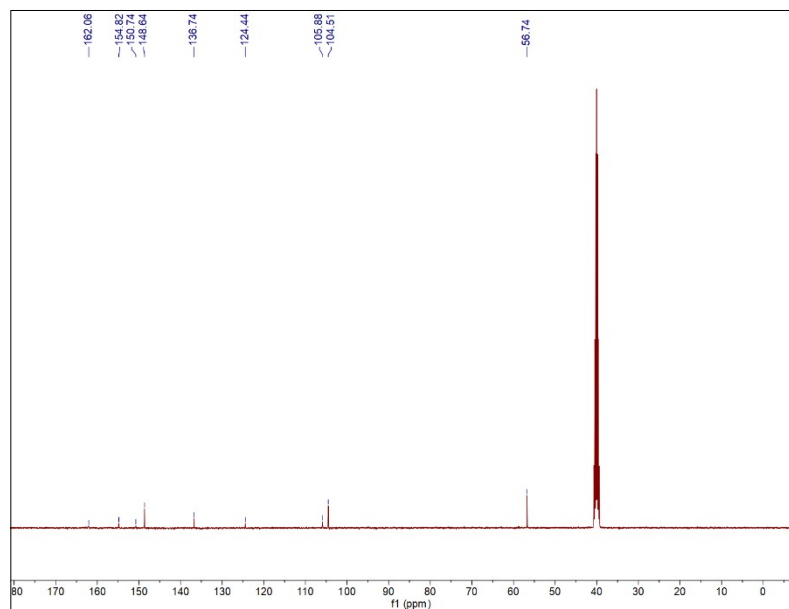


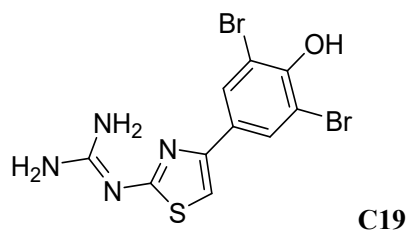


The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO}-d_6$.

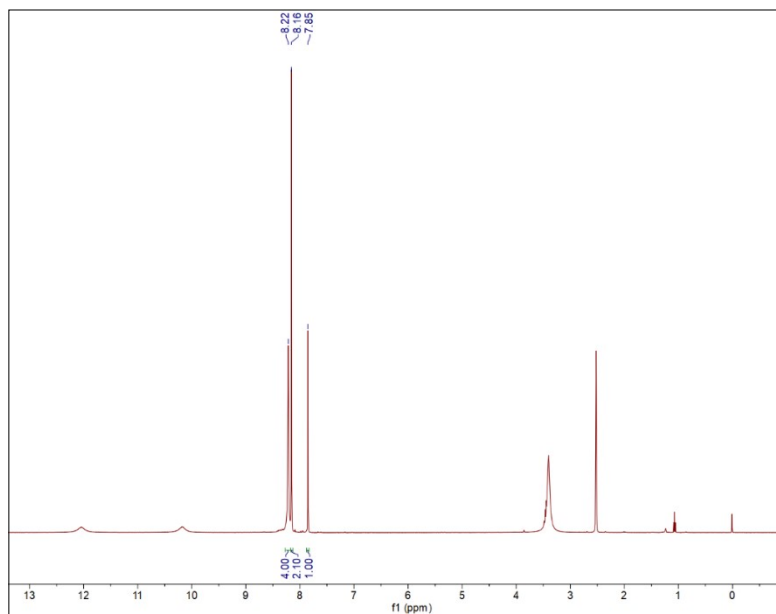


The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO}-d_6$.





The ^1H NMR frequency (MHz) was 400 MHz and the solvent was $\text{DMSO-}d_6$.



The ^{13}C NMR frequency (MHz) was 101 MHz and the solvent was $\text{DMSO-}d_6$.

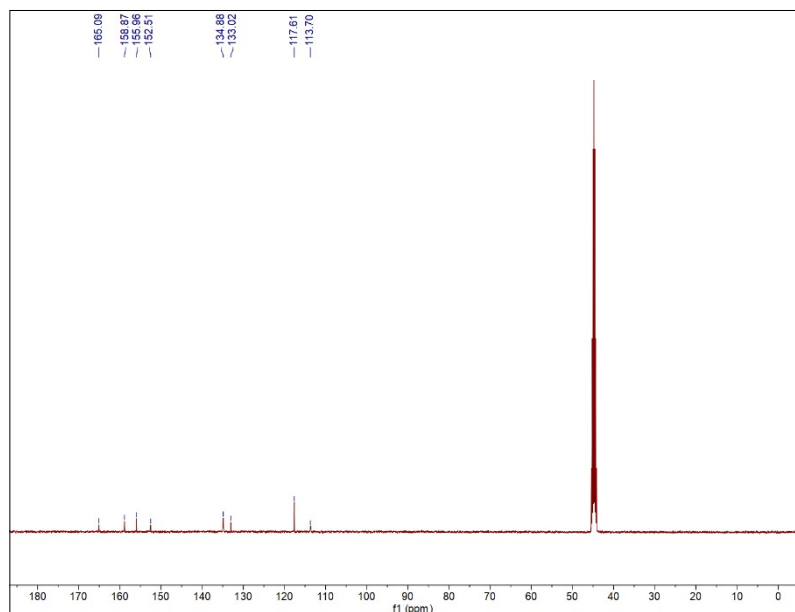


Table S1. Dose-response of compounds **C1-C19** for colistin potentiation against ACCT19606

Compound	MIC (μg/mL)	Concentration Tested (μg/mL)	Colistin MIC (μg/mL)
C1	>256	32	>4
		8	0.06
		4	0.25
C2	>256	32	>4
		8	>4
		4	0.25
C3	>256	32	1
		8	0.5
		4	0.5
C4	>256	32	>4
		8	0.125
		4	0.25
C5	>256	32	>4
		8	0.125
		4	0.25
C6	>256	32	1
		8	1
		4	1
C7	>256	32	>4
		8	0.125
		4	0.125
C8	>256	32	>4
		8	0.25
		4	0.5
C9	>256	32	0.03
		8	0.25
		4	0.5
C10	>256	32	0.25
		8	0.25
		4	0.25
C11	>256	32	>4
		8	0.5
		4	0.25
C12	>256	32	1
		8	1
		4	1
C13	>256	32	0.5
		8	0.5
		4	1
C14	>256	32	0.06

		8	0.125
		4	0.25
		32	0.5
C15	>256	8	0.5
		4	1
		32	0.015
C16	>256	8	0.125
		4	0.25
		32	0.03
C17	256	8	0.125
		4	0.25
		32	1
C18	>256	8	1
		4	1
		32	0.25
C19	>256	8	0.5
		4	0.5
