Supporting Information for

Design and Synthesis of 2,4-disubstituted Thiazole Amide Derivatives as Potential Anti-schizophrenia Agents

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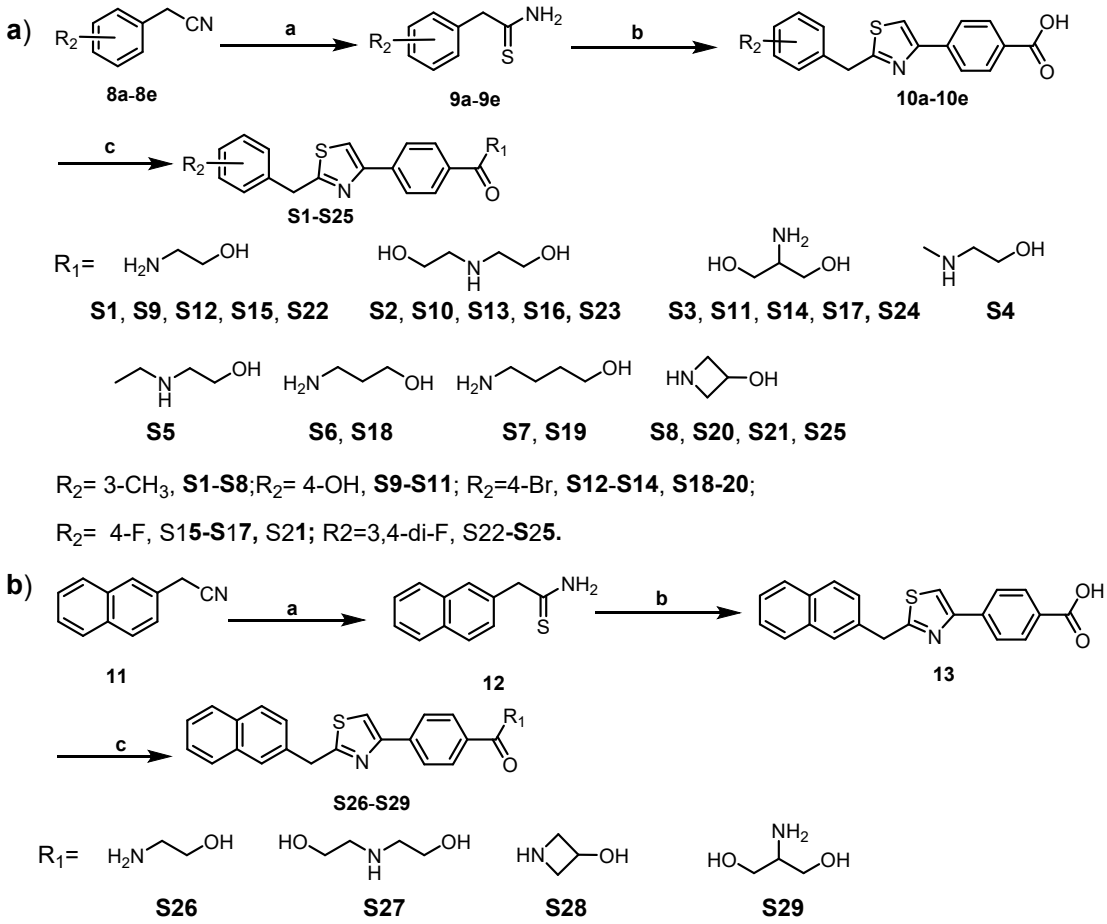
1. Synthesis of compounds S1-S29

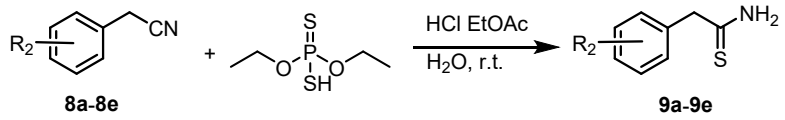
General procedures and materials

All starting compounds and solvents were obtained from commercial suppliers and were used as received unless otherwise indicated. Per-deuterated solvents for NMR spectroscopy were obtained from Cambridge Isotope Laboratories and were used as received. Anhydrous dichloromethane (CH_2Cl_2) was distilled over calcium hydride (CaH_2) under N_2. Column chromatography was carried out on flash grade silica gel, using 0–20 psig pressure. Analytical TLC was carried out by using tapered silica plates with a preadsorbent zone. NMR spectra were obtained with a Bruker spectrometer (500 MHz) with *d*-chloroform ($CDCl_3$) and d_6-DMSO as solvent. High resolution mass spectra were recorded on a SCIEX TripleTOF 5600+system.



Scheme S1. Synthesis of compounds **S1** – **S29**. Regents and conditions: a Diethylphosphorodithioate, HCl·EtOAc, H_2O, r.t.; (b) 4-(2-Bromo-acetyl)-benzoic acid, EtOH, 80 °C; (c) HR_1, HOBT, EDCI, DCM, r.t..

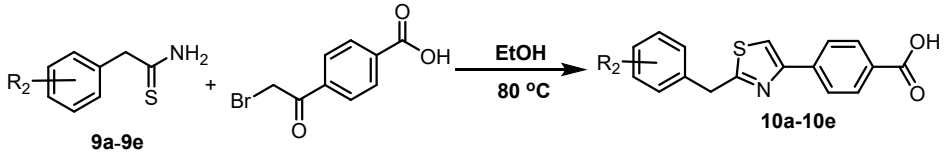
General procedures for the construction of compounds 9a-9e.



8a-8e 9a-9e

A solution of substituent phenyl acetonitrile (1 equiv.) in ethyl acetate in a 250 mL flask was added hydrogen chloride (HCl) solution in ethyl acetate, H2O and O,O'-diethyl dithiophosphate (1 equiv.). The reaction mixture was stirred at room temperature and monitored by TLC. After completion of the reaction, the excess solvent was removed under reduced pressure. The organic phase was washed with saturated $NaHCO_3$, followed by extraction with ethyl acetate. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was triturated with petroleum ether and used directly in the next step.

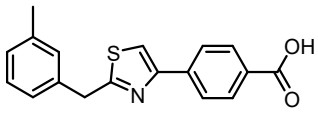
General procedures for the construction of compounds 10a-10e.



9a-9e 10a-10e

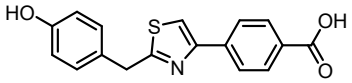
Into a 250 mL flask were added compound **9** (1 equiv.), 4-(bromoacetyl)benzoic acid (1.3 equiv.) and ethanol. The resulting mixture was heated to reflux at 110 °C for 0.5 hours. After completion of the reaction, the mixture was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The crude product was triturated with dichloromethane to yield compound **10a- 10e**.

Compound **10a**



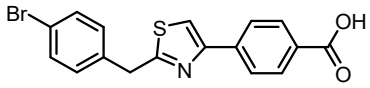
Compound **10a** was obtained by compound **9a** (3.7 g, 22mmol) and 4-(bromoacetyl)benzoic acid (1.3 equiv.) in 78% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (s, 1H), 8.09 – 8.05 (m, 2H), 8.02 – 7.98 (m, 2H), 7.24 (t, J = 7.5 Hz, 1H), 7.20 – 7.15 (m, 2H), 7.09 (t, J = 6.8 Hz, 1H), 4.36 (s, 2H), 2.28 (s, 3H).

Compound **10b**



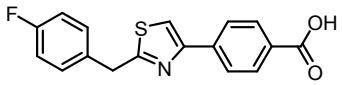
Compound **10b** was obtained by compound **9b** (3.7 g, 22mmol) and 4-(bromoacetyl)benzoic acid (1.3 equiv.) in 80% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.40 (s, 1H), 8.12 (s, 1H), 8.09 – 8.04 (m, 2H), 8.03 – 7.97 (m, 2H), 7.21 – 7.15 (m, 2H), 6.78 – 6.72 (m, 2H), 4.26 (s, 2H).

Compound **10c**



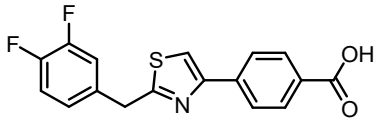
Compound **10c** was obtained by compound **9c** (3.7 g, 16mmol) and 4-(bromoacetyl)benzoic acid (1.3 equiv.) in 72% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.17 (s, 1H), 8.08 – 8.03 (m, 2H), 8.01 – 7.96 (m, 2H), 7.58 – 7.52 (m, 2H), 7.39 – 7.32 (m, 2H), 4.40 (s, 2H).

Compound **10d**



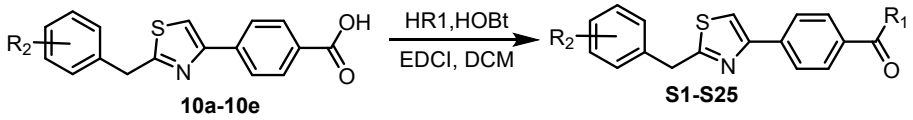
Compound **10d** was obtained by compound **9d** (3.7 g, 21.9mmol) and 4-(bromoacetyl)benzoic acid (1.3 equiv.) in 80% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.17 (s, 1H), 8.09 – 8.05 (m, 2H), 8.02 – 7.99 (m, 2H), 7.48 – 7.42 (m, 2H), 7.23 – 7.16 (m, 2H), 4.42 (s, 2H).

Compound **10e**



Compound **10e** was obtained by compound **9e** (3.7 g, 19.8mmol) and 4-(bromoacetyl)benzoic acid (1.3 equiv.) in 75% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.18 (s, 1H), 8.10 – 8.05 (m, 2H), 8.04 – 7.98 (m, 2H), 7.55 – 7.47 (m, 1H), 7.47 – 7.38 (m, 1H), 7.30 – 7.23 (m, 1H), 4.44 (s, 2H).

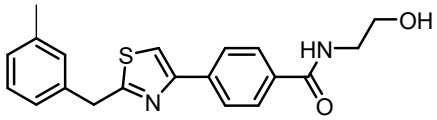
General procedures for the construction of compounds S1-S29.



10a-10e **S1-S25**

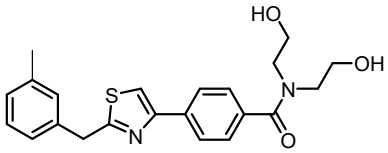
To a 100 mL flask were successively added compound **10**, HOBt, EDCI and the resulting mixture was stirred at r.t. for 1 h. then the corresponding amine compound was added the reaction was stirred for another 2-6 hs. After completion of the reaction, the mixture was washed with brine (saturated NaCl solution) and extracted with DCM. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (eluent: DCM/EtOH = 15:1, v/v) to afford the corresponding product.

Compound S1



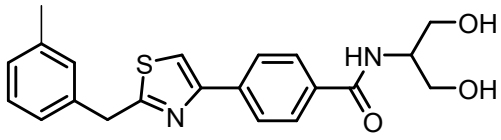
Compound **S1** was obtained by compound **10a** (309 mg, 1 mmol) and ethanolamine (72 mmol, 1.2 mmol) in 83% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 (t, J = 5.6 Hz, 1 H, C=O-NH), 8.11 (s, 1 H, Ar), 8.06 – 8.01 (m, 2 H, Ar), 7.96 – 7.92 (m, 2 H, Ar), 7.25 (t, J = 7.5 Hz, 1 H, Ar), 7.20 – 7.16 (m, 2 H, Ar), 7.10 (d, J = 7.4 Hz, 1 H, Ar), 4.76 (t, J = 5.6 Hz, 1 H, OH), 4.36 (s, 2 H, CH_2), 3.54 (q, J = 6.1 Hz, 2 H,CH_2), 3.36 (q, J = 6.0 Hz, 2 H,CH_2), 2.30 (s, 3 H,CH_3). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.8 (S-C=N), 170.3 (C=O), 153.3 (Ar), 138.0 (Ar), 137.8 (Ar), 136.5 (N-C), 134.5 (Ar), 129.6 (Ar), 128.6 (Ar), 127.6 (Ar), 127.4 (Ar), 126.1 (Ar), 125.7 (Ar), 115.1 (S-C), 58.6 (CH_2), 38.7 (CH_2), 21.0 (CH_3). HRAM-MS (ESI, m/z) calculated for $C_{20}H_{20}N_2O_2S$ $[M+H]^+$: 353.1318, found 353.1327.

Compound S2



Compound **S2** was obtained by compound **10a** (307 mg, 1 mmol) and 2,2'-azanediylbis(ethan-1-ol) (125.8 mg, 1.2 mmol) in 88% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.04 (s, 1 H, Ar), 8.01 – 7.96 (m, 2 H, Ar), 7.49 – 7.44 (m, 2 H, Ar), 7.25 (t, J = 7.5 Hz, 1 H, Ar), 7.21 – 7.14 (m, 2 H, Ar), 7.09 (d, J = 7.4 Hz, 1 H, Ar), 4.84 (t, J = 5.5 Hz, 1 H, Ar), 4.79 (t, J = 5.3 Hz, 1 H, Ar), 4.35 (s, 2 H, OH), 3.64 (q, J = 6.0 Hz, 2 H, CH_2), 3.55 (t, J = 6.1 Hz, 2 H, CH_2), 3.47 (q, J = 5.7 Hz, 2 H, CH_2), 3.37 – 3.32 (m, 2 H, CH_2), 2.29 (s, 3 H, CH_3). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.4 (C=O, S-C=N), 165.9 (Ar), 153.1 (Ar), 137.9 (Ar), 137.8 (Ar), 136.5 (N-C), 133.7 (Ar), 129.6 (Ar), 128.6 (Ar), 127.8 (Ar), 127.6 (Ar), 126.1 (Ar), 125.7 (Ar), 115.8 (S-C), 59.8 (CH_2), 42.2 (CH_2), 38.7 (CH_2), 21.0 (CH_3). HRAM-MS (ESI, m/z) calculated for $C_{22}H_{24}N_2O_3S$ $[M+H]^+$: 397.1580, found 397.1587.

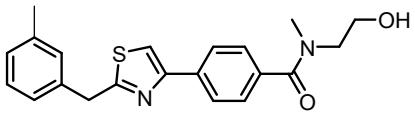
Compound S3



Compound **S3** was obtained by compound **10a** (312 mg, 1 mmol) and 2-aminopropane-1,3-diol (110 mg, 1.2 mmol) in 82% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (s, 1 H, C=O-NH), 8.05 - 8.02 (m, 2 H, Ar), 8.01 (d, J = 8.1 Hz, 1 H, Ar), 7.98 - 7.92 (m, 2 H, Ar), 7.25 (t, J = 7.5 Hz, 1 H, Ar), 7.22 - 7.15 (m, 2 H, Ar), 7.10 (d, J = 7.4 Hz, 1 H, Ar), 4.69 (t, J = 5.7 Hz, 2 H, CH_2), 4.36 (s, 2 H, OH), 4.05 - 3.95 (m, 1 H, CH), 3.55 (t, J = 5.9 Hz, 4 H, CH_2), 2.30 (s, 3 H, CH_3). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.5 (C=O, S-C=N), 165.8 (Ar), 153.1 (Ar), 137.9 (Ar), 137.9 (Ar), 136.4 (N-C), 133.9 (Ar), 129.6 (Ar), 128.6 (Ar), 127.9 (Ar), 127.7

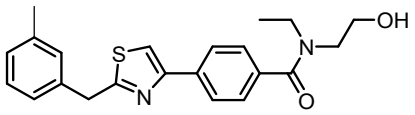
(Ar), 126.1 (Ar), 125.6 (Ar), 115.8 (S-C), 60.4 (CH_2), 53.9 (CH_2), 38.7 (CH_2), 21.0 (CH_3). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{22}N_2O_3S$ $[M+H]^+$: 383.1424, found 383.1434.

Compound S4



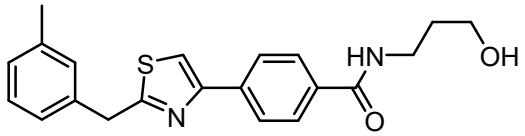
Compound **S4** was obtained by compound **10a** (308mg,1mmol) and 2-(methylamino)ethan-1-ol (106.7 mg, 1.2 mmol) in 81% yield as a white solid.^{1}H NMR (500 MHz, DMSO-d_6) δ 8.04 (s, 1 H, C=O-NH), 7.98 (t, J = 8.2 Hz, 2 H, Ar), 7.47 (d, J = 7.9 Hz, 2 H, Ar), 7.24 (t, J = 7.5 Hz, 1 H, Ar), 7.20 - 7.14 (m, 2 H, Ar), 7.09 (d, J = 7.4 Hz, 1 H, Ar), 4.82 (t, J = 5.5 Hz, 1 H, OH), 4.35 (s, 2 H, CH_2), 3.69 - 3.58 (m, 1 H, CH_2), 3.55 - 3.45 (m, 2 H, CH_2), 3.30 (t, J = 5.8 Hz, 1 H, CH_2), 3.01 - 2.94 (m, 3 H, CH_3), 2.29 (s, 3 H, CH_3). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.7 (S-C=N), 170.3 (C=O), 153.3 (Ar), 138.0 (Ar), 137.9 (Ar), 136.3 (N-C), 134.6 (Ar), 129.6 (Ar), 128.6 (Ar), 127.6 (Ar), 127.6 (Ar), 126.1 (Ar), 125.7 (Ar), 115.1 (S-C), 58.1 (CH_2), 49.7 (CH_2), 38.7 (CH_2), 32.6 (CH_3), 21.0 (CH_3). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{22}N_2O_2S$ $[M+H]^+$: 367.1475, found 367.1480.

Compound S5



Compound **S5** was obtained by compound **10a** (308 mg, 1 mmol) and 2-(ethylamino)ethan-1-ol (109 mg, 1.2 mmol) in 83% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.04 (s, 1 H, C=O-NH), 7.99 (s, 2 H, Ar), 7.43 (d, J = 7.7 Hz, 2 H, Ar), 7.24 (t, J = 7.5 Hz, 1 H, Ar), 7.21 - 7.15 (m, 2 H, Ar), 7.09 (d, J = 7.5 Hz, 1 H, Ar), 4.80 (s, 1 H, OH), 4.35 (s, 2 H, CH_2), 3.61 (s, 1 H, CH), 3.48 (s, 3 H, CH_3), 3.27 (s, 2 H, CH_2), 2.29 (s, 3 H, CH_3), 1.19 - 0.99 (m, 3 H, CH_3). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3 (C=O, S-C=N), 153.3 (Ar), 138.0 (Ar), 137.8 (Ar), 136.6 (N-C), 129.6 (Ar), 128.6 (Ar), 127.6 (Ar), 127.3 (Ar), 126.8 (Ar), 126.1 (Ar), 125.8 (Ar), 115.1 (S-C), 58.7 (CH_2), 46.9 (CH_2), 44.3 (CH_2), 38.7 (CH_2), 21.0 (CH_3), 13.9 (CH_3). HRAM-MS (ESI, *m/z*) calculated for $C_{22}H_{24}N_2O_2S$ $[M+Na]^+$: 403.1451, found 403.1456.

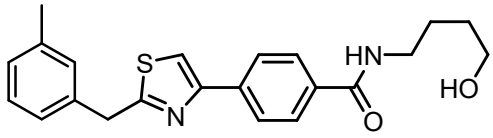
Compound S6



Compound **S6** was obtained by compound **10a** (308 mg, 1 mmol) and 3-aminopropan-1-ol (89.8 mg,1.2 mmol) in 77% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 (t, J = 5.6 Hz, 1 H, C=O-NH), 8.10 (s, 1 H, Ar), 8.06 - 8.01 (m, 2 H, Ar), 7.95 - 7.89 (m, 2 H, Ar), 7.25 (t, J = 7.5 Hz, 1 H, Ar), 7.21 - 7.15 (m, 2 H, Ar), 7.10

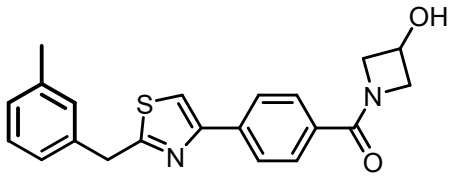
(d, J = 7.4 Hz, 1 H, Ar), 4.51 (t, J = 5.2 Hz, 1 H, OH), 4.36 (s, 2 H, CH_2), 3.49 (q, J = 6.0 Hz, 2 H, CH_2), 3.35 (q, 2 H, CH_2), 2.30 (s, 3 H, CH_3), 1.71 (p, J = 6.6 Hz, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.4 (C=O, S-C=N), 165.8 (Ar), 153.1 (Ar), 137.9 (Ar), 137.8 (Ar), 136.4 (N-C), 133.8 (Ar), 129.6 (Ar), 128.6 (Ar), 127.7 (Ar), 127.6 (Ar), 126.1 (Ar), 125.7 (Ar), 115.7 (S-C), 58.6 (CH_2), 38.7 (CH_2), 36.6 (CH_2), 32.5 (CH_2), 21.0 (CH_3). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{22}N_2O_2S$ $[M+H]^+$: 367.1475, found 367.1480.

Compound S7



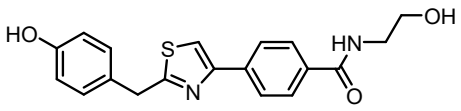
Compound **S7** was obtained by compound **10a** (308 mg, 1 mmol) and 4-aminobutan-1-ol (106.5 mg, 1.2 mmol) in 76% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (t, J = 5.7 Hz, 1H, C=O-NH), 8.10 (s, 1 H, Ar), 8.06 - 8.01 (m, 2 H, Ar), 7.95 - 7.89 (m, 2 H, Ar), 7.25 (t, J = 7.5 Hz, 1 H, Ar), 7.21 - 7.15 (m, 2 H, Ar), 7.10 (d, J = 7.5 Hz, 1 H, Ar), 4.43 (t, J = 5.1 Hz, 1 H, OH), 4.36 (s, 2 H, CH_2), 3.44 (q, J = 6.2 Hz, 2 H, CH_2), 3.29 (q, J = 6.6 Hz, 2 H, CH_2), 2.30 (s, 3 H, CH_3), 1.64 - 1.53 (m, 2 H, CH_2), 1.53 - 1.40 (m, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.4 (C=O, S-C=N), 165.6 (Ar), 153.1 (Ar), 137.9 (Ar), 137.8 (Ar), 136.4 (N-C), 133.8 (Ar), 129.6 (Ar), 128.6 (Ar), 127.7 (Ar), 127.6 (Ar), 126.1 (Ar), 125.7 (Ar), 115.7 (S-C), 60.5 (CH_2), 39.2 (CH_2), 38.7 (CH_2), 30.1 (CH_2), 25.9 (CH_2), 21.0 (CH_3). HRAM-MS (ESI, *m/z*) calculated for $C_{22}H_{24}N_2O_2S$ $[M+H]^+$: 381.1631, found 381.1632.

Compound S8



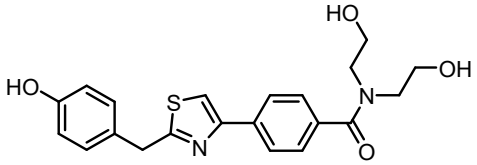
Compound **S8** was obtained by compound **10a** (309 mg, 1 mmol) and azetidin-3-ol (87.7 mg, 1.2 mmol) in 79% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.10 (s, 1 H, Ar), 8.05 - 7.99 (m, 2 H, Ar), 7.72 - 7.67 (m, 2 H, Ar), 7.25 (t, J = 7.5 Hz, 1 H, Ar), 7.21 - 7.15 (m, 2 H, Ar), 7.09 (d, J = 7.4 Hz, 1 H, Ar), 5.77 (d, J = 6.0 Hz, 1 H, OH), 4.56 - 4.45 (m, 2 H, CH_2), 4.36 (s, 2 H, CH_2), 4.26 (t, J = 8.2 Hz, 1 H, CH), 4.11 - 4.05 (m, 1 H, CH), 3.84 - 3.77 (m, 1 H, CH), 2.29 (s, 3 H, CH_3). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.4 (C=O, S-C=N), 168.6 (Ar), 153.1 (Ar), 137.9 (Ar), 137.8 (Ar), 136.3 (N-C), 132.4 (Ar), 129.6 (Ar), 128.6(Ar), 128.3 (Ar), 127.6 (Ar), 126.1 (Ar), 125.8 (Ar), 115.8 (S-C), 62.8 (CH), 60.5 (CH_2), 58.5 (CH_2), 38.7 (CH_2), 21.0 (CH_3). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{20}N_2O_2S$ $[M+H]^+$: 365.1318, found 365.1322.

Compound S9



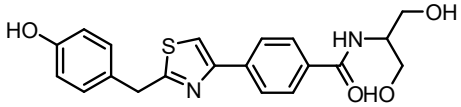
Compound **S9** was obtained by compound **10b** (310 mg, 1 mmol) and ethanolamine (73 mg, 1.2 mmol) in 80% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.38 (s, 1 H, C=O-NH), 8.48 (t, J = 5.6 Hz, 1 H, Ar), 8.08 (s, 1 H, Ar), 8.05 - 7.99 (m, 2 H, Ar), 7.94 - 7.90 (m, 2 H, Ar), 7.20 - 7.14 (m, 2 H, Ar), 6.77 - 6.71 (m, 2 H, Ar), 4.74 (t, J = 5.7 Hz, 1 H, OH), 4.26 (s, 2 H, CH_2), 3.53 (q, J = 5.5 Hz, 2 H, CH_2), 3.35 (q, J = 5.8 Hz, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.7 (C=O, S-C=N), 165.9 (Ar), 156.4 (Ar), 153.1 (Ar), 136.5 (N-C), 133.6 (Ar), 130.1 (Ar), 128.1 (Ar), 127.8 (Ar), 125.7 (Ar), 115.6 (Ar), 115.5 (S-C), 59.8 (CH_2), 42.2 (CH_2), 38.0 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{19}H_{18}N_2O_3S$ $[M+H]^+$: 355.1111; found 355.1108.

Compound S10



Compound **S10** was obtained by compound **10b** (310 mg, 1 mmol) and 2,2'-azanediylbis(ethan-1-ol) (125.8 mg, 1.2 mmol) in 74% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.38 (s, 1 H, Ar), 8.01 (s, 1 H, Ar), 7.98 (d, J = 8.0 Hz, 2 H, Ar), 7.46 (d, J = 8.1 Hz, 2 H, Ar), 7.20 - 7.14 (m, 2 H, Ar), 6.80 - 6.68 (m, 2 H, Ar), 4.84 (t, J = 5.6 Hz, 1 H, OH), 4.79 (t, J = 5.3 Hz, 1 H, OH), 4.26 (s, 2 H, CH_2), 3.63 (q, J = 5.9 Hz, 2 H, CH_2), 3.54 (t, J = 6.1 Hz, 2 H, CH_2), 3.47 (q, J = 5.6 Hz, 2 H, CH_2), 3.34 (d, J = 7.1 Hz, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.5 (S-C=N), 170.8 (C=O), 156.4 (Ar), 153.3 (Ar), 136.5 (N-C), 134.6 (Ar), 130.1 (Ar), 128.2 (Ar), 127.4 (Ar), 125.7 (Ar), 115.4 (S-C), 114.9 (Ar), 58.6 (CH_2), 51.7 (CH_2), 47.6 (CH_2), 38.0 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{22}N_2O_4S$ $[M+H]^+$: 399.1373; found 399.1372.

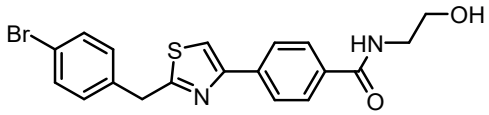
Compound S11



Compound **S11** was obtained by compound **10b** (310.9 mg, 1 mmol) and 2-aminopropane-1,3-diol (109 mg, 1.2 mmol) in 81% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.39 (s, 1 H, C=O-NH), 8.09 (s, 1 H, Ar), 8.07 - 7.98 (m, 3 H, Ar), 7.98 - 7.91 (m, 2 H, Ar), 7.18 (d, J = 8.0 Hz, 2 H, Ar), 6.75 (d, J = 8.0 Hz, 2 H, Ar), 4.69 (t, J = 5.2 Hz, 2 H, OH), 4.27 (s, 2 H, CH_2), 4.05 - 3.95 (m, 1 H, CH), 3.54 (t, J = 5.7 Hz, 4 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.7 (C=O, S-C=N), 165.8 (Ar), 156.4 (Ar), 153.1 (Ar), 136.5 (N-C), 133.8 (Ar), 130.1 (Ar), 128.1 (Ar), 127.9 (Ar), 125.6 (Ar), 115.6 (Ar), 115.5 (S-C), 60.4 (CH), 53.9 (CH_2), 38.0

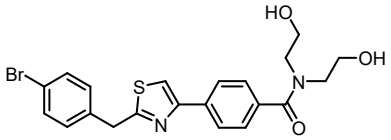
(CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{20}H_{20}N_2O_4S$ $[M+H]^+$: 385.1217, found 385.1216.

Compound S12



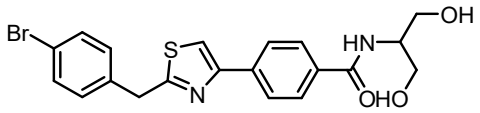
Compound **S12** was obtained by compound **10c** (372 mg, 1 mmol) and ethanolamine (60.7 mg, 1.2 mmol) in 79% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.49 (t, J = 5.6 Hz, 1 H, C=O-NH), 8.11 (s, 1 H, Ar), 8.04 - 8.00 (m, 2 H, Ar), 7.94 - 7.90 (m, 2 H, Ar), 7.57 - 7.53 (m, 2 H, Ar), 7.37 - 7.33 (m, 2 H, Ar), 4.77 (t, J = 5.6 Hz, 1 H, OH), 4.39 (s, 2 H, CH_2), 3.53 (q, J = 5.9 Hz, 2 H, CH_2), 3.35 (q, J = 6.0 Hz, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.6 (C=O, S-C=N), 166.0 (Ar), 153.3 (Ar), 137.5 (Ar), 136.4 (N-C), 133.7 (Ar), 131.6 (Ar), 131.3 (Ar), 127.8 (Ar), 125.7 (Ar), 120.2 (Ar), 115.9 (S-C), 59.8 (CH_2), 42.2 (CH_2), 37.9 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{19}H_{17}BrN_2O_2S$ $[M+H]^+$: 417.0267, found 417.0259.

Compound S13



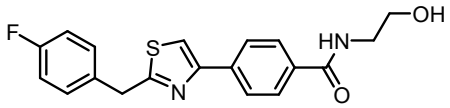
Compound **S13** was obtained by compound **10c** (373.9 mg, 1 mmol) and 2,2'-azanediylbis(ethan-1-ol) (126 mg, 1.2 mmol) in 82% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.06 (s, 1 H, Ar), 8.00 - 7.95 (m, 2 H, Ar), 7.59 - 7.52 (m, 2 H, Ar), 7.48 - 7.43 (m, 2 H, Ar), 7.39 - 7.32 (m, 2 H, Ar), 4.81 (dt, J = 25.1, 5.4 Hz, 2 H, OH), 4.39 (s, 2 H, CH_2), 3.63 (q, J = 5.9 Hz, 2 H, CH_2), 3.53 (t, J = 6.1 Hz, 2 H, CH_2), 3.46 (q, J = 6.0, 5.5 Hz, 2 H, CH_2), 3.33 (d, J = 9.1 Hz, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.8 (C=O, S-C=N), 169.4 (Ar), 153.5 (Ar), 137.5 (Ar), 136.6 (N-C), 134.4 (Ar), 131.6 (Ar), 131.3 (Ar), 127.4 (Ar), 125.7 (Ar), 120.2 (Ar), 115.2 (S-C), 58.6 (CH_2), 51.7 (CH_2), 47.5 (CH_2), 37.8 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{21}BrN_2O_3S$ $[M+H]^+$: 461.0529; found 461.0534.

Compound S14



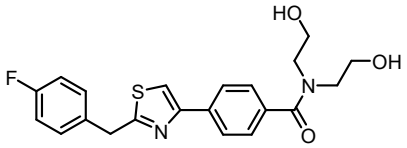
Compound **S14** was obtained by compound **10c** (37 3mg, 1 mmol) and 2-aminopropane-1,3-diol (108.9 mg, 1.2 mmol) in 85% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.13 (s, 1 H, C=O-NH), 8.06 - 7.97 (m, 3 H, Ar), 7.97 - 7.89 (m, 2 H, Ar), 7.60 - 7.51 (m, 2 H, Ar), 7.41 - 7.30 (m, 2 H, Ar), 4.68 (t, J = 5.8 Hz, 2 H, OH), 4.40 (s, 2 H, CH_2), 4.03 - 3.92 (m, 1 H, CH), 3.53 (t, J = 5.9 Hz, 4 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.7 (C=O, S-C=N), 165.8 (Ar), 153.3 (Ar), 137.5 (Ar), 136.3 (N-C), 133.9 (Ar), 131.6 (Ar), 131.3 (Ar), 127.8 (Ar), 125.6 (Ar), 120.2 (Ar), 115.9 (S-C), 60.4 (CH), 53.9 (CH_2), 37.9 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{20}H_{19}BrN_2O_3S$ $[M+H]^+$: 447.0373, found 447.0374.

Compound S15



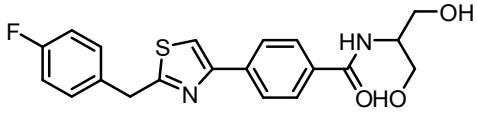
Compound **S15** was obtained by compound **10d** (313 mg, 1 mmol) and ethanolamine (73 mg, 1.2 mmol) in 80% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.48 (t, J = 5.7 Hz, 1 H, C=O-NH), 8.10 (s, 1 H, Ar), 8.02 (d, J = 8.4 Hz, 2 H, Ar), 7.92 (d, J = 8.3 Hz, 2 H, Ar), 7.44 (dd, J = 8.5, 5.7 Hz, 2 H, Ar), 7.19 (t, J = 8.8 Hz, 2 H, Ar), 4.77 (t, J = 5.6 Hz, 1 H, OH), 4.40 (s, 2 H, CH_2), 3.53 (q, J = 6.0 Hz, 2 H, CH_2), 3.35 (q, J = 6.0 Hz, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3 (C=O, S-C=N), 166.0 (Ar), 161.3 (d, J = 242.8 Hz, Ar), 153.3 (Ar), 136.5 (N-C), 134.3 (d, J = 3.0 Hz, Ar), 133.7 (Ar), 131.03 (d, J = 8.1 Hz, Ar), 127.8 (Ar), 125.7 (Ar), 115.8 (Ar), 115.5 (Ar) (d, J = 21.3 Hz, S-C), 59.5 (CH_2), 43.5 (CH_2), 37.8 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{19}H_{17}FN_2O_2S$ $[M+Na]^+$: 379.0892, found 379.0884.

Compound S16



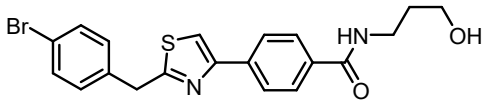
Compound **S16** was obtained by compound **10d** (312.9 mg, 1 mmol) and 2-aminopropane-1,3-diol (126 mg, 1.2 mmol) in 75% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.05 (s, 1 H, Ar), 7.99 (d, J = 8.1 Hz, 2 H, Ar), 7.49 - 7.41 (m, 4 H, Ar), 7.19 (t, J = 8.8 Hz, 2 H, Ar), 4.81 (dt, J = 24.8, 5.5 Hz, 2 H, OH), 4.41 (s, 2 H, CH_2), 3.63 (t, J = 6.0 Hz, 2 H, CH_2), 3.54 (t, J = 6.0 Hz, 2 H, CH_2), 3.47 (q, J = 6.0 Hz, 2 H, CH_2), 3.35 (d, J = 5.0 Hz, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.8 (C=O, S-C=N), 169.4 (Ar), 161.3 (d, J = 242.9 Hz, Ar), 154.0 (Ar), 137.2 (N-C), 134.5 (Ar), 134.3 (d, J = 3.1 Hz, Ar), 131.0 (d, J = 8.2 Hz, Ar), 127.4 (Ar), 125.7 (Ar), 115.4 (d, J = 21.3 Hz, Ar), 115.1 (S-C), 59.3 (CH_2), 37.7 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{21}FN_2O_3S$ $[M+H]^+$: 401.1330; found, 401.1339.

Compound S17



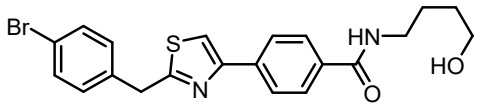
Compound **S17** was obtained by compound **10d** (312 mg, 1 mmol) and 2,2'-azanediylbis(ethan-1-ol) (108.8 mg, 1.2 mmol) in 79% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.12 (s, 1 H, C=O-NH), 8.05 - 7.98 (m, 3 H, Ar), 7.96 - 7.91 (m, 2 H, Ar), 7.48 - 7.40 (m, 2 H, Ar), 7.24 - 7.15 (m, 2 H, Ar), 4.68 (t, J = 5.7 Hz, 2 H, OH), 4.41 (s, 2 H, CH_2), 3.99 (dt, J = 7.8, 5.7 Hz, 1 H, CH), 3.53 (t, J = 5.8 Hz, 4 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3 (C=O, S-C=N), 165.8 (Ar), 161.3 (d, J = 243.0 Hz, Ar), 153.3 (Ar), 136.4 (N-C), 134.2 (d, J = 3.1 Hz, Ar), 133.9 (Ar), 131.0 (d, J = 8.2 Hz, Ar), 127.9 (Ar), 125.6 (Ar), 115.8 (Ar), 115.5 (d, J = 21.3 Hz, S-C), 60.4 (CH), 53.9 (CH_2), 37.7 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{20}H_{19}FN_2O_3S$ $[M+H]^+$: 387.1173, found 387.1177.

Compound S18



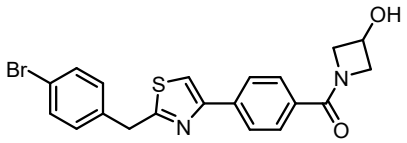
Compound **S18** was obtained by compound **10c** (372.8 mg, 1 mmol) and 3-aminopropan-1-ol (89.8 mg, 1.2 mmol) in 74% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.49 (t, J = 5.7 Hz, 1 H, C=O-NH), 8.12 (s, 1 H, Ar), 8.02 (d, J = 8.0 Hz, 2 H, Ar), 7.91 (d, J = 8.1 Hz, 2 H, Ar), 7.56 (d, J = 8.0 Hz, 2 H, Ar), 7.37 (d, J = 8.0 Hz, 2 H, Ar), 4.49 (t, J = 5.2 Hz, 1 H, OH), 4.41 (s, 2 H, CH_2), 3.48 (q, J = 6.0 Hz, 2 H, CH_2), 3.34 - 3.31 (m, 2 H, CH_2), 1.73 - 1.66 (m, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.6 (C=O, S-C=N), 165.8 (Ar), 153.3 (Ar), 137.5 (Ar), 136.4 (N-C), 133.8 (Ar), 131.6 (Ar), 131.3 (Ar), 127.8 (Ar), 125.7 (Ar), 120.2 (Ar), 115.9 (S-C), 58.7 (CH_2), 37.9 (CH_2), 36.6 (CH_2), 32.5 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{20}H_{19}BrN_2O_2S$ $[M+Na]^+$: 453.0248, found 453.0247.

Compound S19



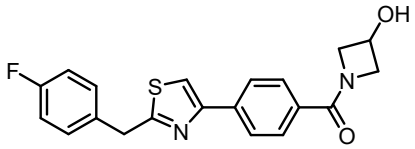
Compound **S19** was obtained by compound **10c** (373 mg, 1 mmol) and 4-aminobutan-1-ol(106.6 mg, 1.2 mmol) in 76% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 (t, J = 5.7 Hz, 1 H, C=O-NH), 8.12 (s, 1 H, Ar), 8.06 - 7.99 (m, 2 H, Ar), 7.94 - 7.86 (m, 2 H, Ar), 7.58 - 7.53 (m, 2 H, Ar), 7.38 - 7.33 (m, 2 H, Ar), 4.43 (t, J = 5.1 Hz, 1 H, OH), 4.40 (s, 2 H, CH_2), 3.42 (q, J = 6.0 Hz, 2 H, CH_2), 3.27 (q, J = 6.6 Hz, 2 H, CH_2), 1.60 - 1.52 (m, 2 H, CH_2), 1.51 - 1.42 (m, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.6 (C=O, S-C=N), 165.6 (Ar), 153.3 (Ar), 137.5 (Ar), 136.3 (N-C), 133.9 (Ar), 131.6 (Ar), 131.3 (Ar), 127.7 (Ar), 125.7 (Ar), 120.2 (Ar), 115.8 (S-C), 60.5 (CH_2), 41.4 (CH_2), 37.9 (CH_2), 30.0 (CH_2), 25.9 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{21}BrN_2O_2S$ $[M+H]^+$: 445.0580; found 445.0585.

Compound S20



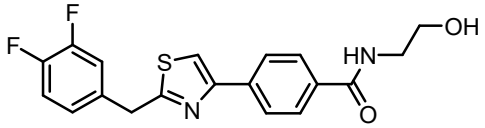
Compound **S20** was obtained by compound **10c** (373 mg, 1 mmol) and azetidin-3-ol (87.6 mg, 1.2 mmol) in 77% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (s, 1 H, Ar), 8.02 - 7.97 (m, 2 H, Ar), 7.70 - 7.65 (m, 2 H, Ar), 7.57 - 7.53 (m, 2 H, Ar), 7.38 - 7.33 (m, 2 H, Ar), 5.76 (d, J = 6.0 Hz, 1 H, OH), 4.54 - 4.44 (m, 2 H, CH_2), 4.39 (s, 2 H, CH_2), 4.29 - 4.22 (m, 1 H, CH), 4.09 - 4.04 (m, 1 H, CH_2), 3.83 - 3.76 (m, 1 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.6 (C=O, S-C=N), 168.6 (Ar), 153.2 (Ar), 137.5 (Ar), 136.2 (N-C), 132.4 (Ar), 131.6 (Ar), 131.3 (Ar), 128.4 (Ar), 125.8 (Ar), 120.2 (Ar), 115.9 (S-C), 62.8 (CH), 60.5 (CH_2), 58.5 (CH_2), 37.8 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{20}H_{17}BrN_2O_2S$ $[M+H]^+$: 429.0267, found 429.0273.

Compound S21



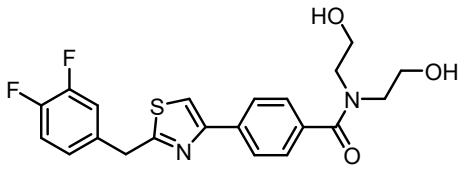
Compound **S21** was obtained by compound **10d** (312 mg, 1 mmol) and azetidin-3-ol(ethan-1-ol) (87.4 mg, 1.2 mmol) in 82% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (s, 1 H, Ar), 8.05 - 7.98 (m, 2 H, Ar), 7.72 - 7.67 (m, 2 H, Ar), 7.48 - 7.41 (m, 2 H, Ar), 7.23 - 7.16 (m, 2 H, Ar), 5.78 (d, J = 5.2 Hz, 1 H, OH), 4.58 - 4.44 (m, 2 H, CH_2), 4.41 (s, 2 H, CH_2), 4.27 (dd, J = 10.9, 6.4 Hz, 1 H, CH), 4.12 - 4.04 (m, 1 H, CH_2), 3.82 (dd, J = 10.8, 3.8 Hz, 1 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.2 (C=O, S-C=N), 168.6 (Ar), 161.3 (d, J = 242.9 Hz, Ar), 153.2 (Ar), 136.2 (N-C), 134.2 (d, J = 3.1 Hz, Ar), 132.4 (Ar), 131.0 (d, J = 8.2 Hz, Ar), 128.4 (Ar), 125.8 (Ar), 115.8 (Ar), 115.4 (d, J = 21.3 Hz, S-C), 62.8 (CH), 60.5 (CH_2), 58.5 (CH_2), 37.7 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{20}H_{17}FN_2O_2S$ $[M+H]^+$: 369.1068, found 369.1077.

Compound S22



Compound **S22** was obtained by compound **10e** (344 mg, 1 mmol) and ethanolamine (76 mg, 1.2 mmol) in 82% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 (t, J = 5.6 Hz, 1 H, C=O-NH), 8.14 (s, 1 H, Ar), 8.07 - 8.01 (m, 2 H, Ar), 7.98 - 7.92 (m, 2 H, Ar), 7.56 - 7.47 (m, 1 H, Ar), 7.47 - 7.39 (m, 1 H, Ar), 7.30 - 7.24 (m, 1 H, Ar), 4.77 (t, J = 5.6 Hz, 1 H, OH), 4.44 (s, 2 H, CH_2), 3.55 (q, J = 6.0 Hz, 2 H, CH_2), 3.40 - 3.33 (m, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.3 (C=O, S-C=N), 165.9 (Ar), 153.3 (Ar), 149.3 (dd, J = 245.9, 12.8 Hz, Ar), 148.6 (dd, J = 244.9, 12.5 Hz, Ar), 136.4 (N-C), 135.7 (dd, J = 6.1, 3.8 Hz, Ar), 133.7 (Ar), 127.8 (Ar), 126.0 (dd, J = 6.5, 3.4 Hz, Ar), 125.7 (Ar), 117.9 (dd, J = 52.4, 17.1 Hz, Ar), 115.9 (S-C), 59.8 (CH_2), 42.2 (CH_2), 37.3 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{19}H_{16}F_2N_2O_2S$ $[M+H]^+$: 375.0973, found 375.0974.

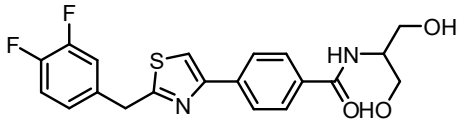
Compound S23



Compound **S23** was obtained by compound **10e** (330 mg, 1 mmol) and 2-aminopropane-1,3-diol (125.7 mg, 1.2 mmol) in 77% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.06 (s, 1 H, Ar), 8.00 - 7.95 (m, 2 H, Ar), 7.53 - 7.42 (m, 3 H, Ar), 7.44 - 7.37 (m, 1 H, Ar), 7.28 - 7.22 (m, 1 H, Ar), 4.86 (t, J = 5.5 Hz, 1 H, OH), 4.81 (d, J = 5.5 Hz, 1 H, OH), 4.41 (s, 2 H, CH_2), 3.63 (q, J = 6.0 Hz, 2 H,

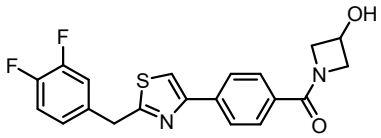
CH_2), 3.54 (t, J = 6.1 Hz, 2 H, CH_2), 3.46 (q, J = 6.0 Hz, 2 H, CH_2), 3.34 (t, J = 5.6 Hz, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.9 (C=O, S-C=N), 169.2 (Ar), 153.6 (Ar), 149.3 (dd, J = 245.8, 12.7 Hz, Ar), 148.6 (dd, J = 244.8, 12.4 Hz, Ar), 136.6 (N-C), 135.8 (dd, J = 6.0, 3.8 Hz, Ar), 134.5 (Ar), 127.4 (Ar), 126.0 (dd, J = 6.5, 3.3 Hz, Ar), 125.8 (Ar), 117.9 (dd, J = 49.9, 17.1 Hz, Ar), 115.2 (S-C), 58.6 (CH_2), 51.7 (CH_2), 47.6 (CH_2), 37.0 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{21}H_{20}F_2N_2O_3S$ $[M+H]^+$: 419.1235, found 419.1239.

Compound S24



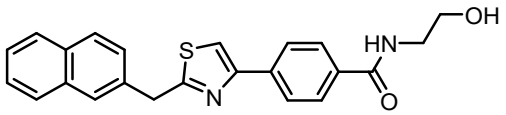
Compound **S24** was obtained by compound **10e** (331 mg, 1 mmol) and 2,2'-azanediylbis(ethan-1-ol) (109 mg, 1.2 mmol) in 85% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.14 (s, 1 H, C=O-NH), 8.05 - 8.00 (m, 2 H, Ar), 8.00 (d, J = 8.1 Hz, 1 H, Ar), 7.97 - 7.91 (m, 2 H, Ar), 7.55 - 7.47 (m, 1 H, Ar), 7.48 - 7.39 (m, 1 H, Ar), 7.30 - 7.23 (m, 1 H, Ar), 4.67 (t, J = 5.7 Hz, 2 H, OH), 4.43 (s, 2 H, CH_2), 4.03 - 3.94 (m, 1 H, CH), 3.53 (t, J = 5.7 Hz, 4 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.4 (C=O, S-C=N), 165.8(Ar), 153.3 (Ar), 149.3 (dd, J = 245.7, 12.7 Hz, Ar), 148.6 (dd, J = 244.9, 12.6 Hz, Ar), 136.3 (N-C), 135.7 (dd, J = 5.7, 4.2 Hz, Ar), 133.9 (Ar), 128.0 (Ar), 126.0 (dd, J = 6.5, 3.4 Hz, Ar), 125.6 (Ar), 117.9 (dd, J = 52.8, 17.2 Hz, Ar), 115.9 (S-C), 60.4 (CH_2), 53.9 (CH_2), 37.5 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{20}H_{18}F_2N_2O_3S$ $[M+H]^+$: 405.1079; found 405.1080.

Compound S25



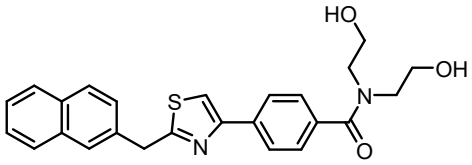
Compound **S25** was obtained by compound **10e** (283.6 mg, 1 mmol) and azetidin-3-ol (75 mg, 1.2mmol) in 78% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.12 (s, 1 H, Ar), 8.03 - 7.98 (m, 2 H, Ar), 7.71 - 7.65 (m, 2 H, Ar), 7.54 - 7.46 (m, 1 H, Ar), 7.47 - 7.38 (m, 1 H, Ar), 7.29 - 7.22 (m, 1 H, Ar), 5.77 (d, J = 5.9 Hz, 1 H, OH), 4.55 - 4.44 (m, 2 H, CH_2), 4.42 (s, 2 H, CH_2), 4.25 (t, J = 8.4 Hz, 1 H, CH), 4.09 - 4.04 (m, 1 H, CH_2), 3.82 - 3.76 (m, 1 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.3 (C=O, S-C=N), 168.6 (Ar), 153.3 (Ar), 149.3 (dd, J = 245.7, 12.7 Hz, Ar), 148.6 (dd, J = 244.8, 12.3 Hz, Ar), 136.2 (N-C), 135.7 (dd, J = 5.7, 4.2 Hz, Ar), 132.5 (Ar), 128.4 (Ar), 126.0 (dd, J = 6.5, 3.3 Hz, Ar), 125.8 (Ar), 117.9 (dd, J = 51.6, 17.1 Hz, Ar), 116.0 (S-C), 62.8 (CH), 60.5 (CH_2), 58.5 (CH_2), 37.4 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{20}H_{16}F_2N_2O_2S$ $[M+ Na]^+$: 409.0798; found 409.0800.

Compound S26



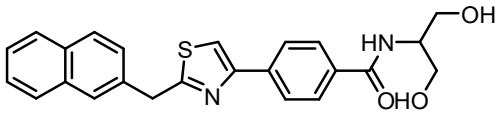
Compound **S26** was obtained by compound **13** (345 mg, 1mmol) ethanolamine (73 mg, 1.2 mmol) in 79% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (t, J = 5.6 Hz, 1 H, C=O-NH), 8.13 (s, 1 H, Ar), 8.06 (d, J = 8.1 Hz, 2 H, Ar), 7.98 - 7.88 (m, 6 H, Ar), 7.57 - 7.48 (m, 3 H, Ar), 4.77 (t, J = 5.7 Hz, 1 H, OH), 4.59 (s, 2 H, CH_2), 3.58 - 3.51 (m, 2 H, CH_2), 3.40 - 3.33 (m, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.7 (C=O, S-C=N), 166.4 (Ar), 153.7 (Ar), 136.9 (Ar), 136.1 (N-C), 134.2 (Ar), 133.6 (Ar), 132.5 (Ar), 128.8 (Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (Ar), 126.8 (Ar), 126.4 (Ar), 126.2 (Ar), 116.4 (S-C), 60.3 (CH_2), 42.7 (CH_2), 39.4 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{23}H_{20}N_2O_2S$ $[M+H]^+$: 389.1318, found 389.1327.

Compound S27



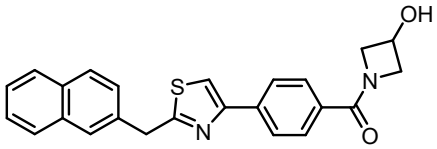
Compound **S27** was obtained by compound **13** (345 mg, 1 mmol) 2-aminopropane-1,3-diol (126 mg, 1.2 mmol) in 75% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.06 (s, 1 H, C=O-NH), 8.00 (d, J = 7.9 Hz, 2 H, Ar), 7.94 - 7.88 (m, 4 H, Ar), 7.57 - 7.48 (m, 3 H, Ar), 7.47 (d, J = 8.1 Hz, 2 H, Ar), 4.85 (t, J = 5.8 Hz, 1 H, OH), 4.79 (t, J = 5.5 Hz, 1 H, OH), 4.58 (s, 2 H, CH_2), 3.70 - 3.60 (m, 2 H, CH_2), 3.54 (t, J = 6.2 Hz, 2 H, CH_2), 3.51 - 3.44 (m, 2 H, CH_2), 3.36 - 3.31 (m, 2 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.8 (S-C=N), 170.1 (C=O), 153.4 (Ar), 136.6 (N-C), 135.7 (Ar), 134.5 (Ar), 133.1 (Ar), 132.0 (Ar), 128.3 (Ar), 127.6 (Ar), 127.4 (Ar), 127.4 (Ar), 126.3 (Ar), 125.9 (Ar), 125.7 (Ar), 115.2 (S-C), 58.6 (CH_2), 51.7 (CH_2), 47.6 (CH_2), 38.9 (CH_2). HRAM-MS (ESI, *m/z*) calculated for $C_{25}H_{24}N_2O_3S$ $[M+H]^+$: 433.1580, found 433.1588.

Compound S28



Compound **S28** was obtained by compound **13** (341 mg, 1 mmol) azetidin-3-ol (107.8 mg, 1.2 mmol) in 87% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.13 (s, 1 H, C=O-NH), 8.04 (d, J = 8.1 Hz, 2 H, Ar), 8.01 (d, J = 8.0 Hz, 1 H, Ar), 7.97 - 7.88 (m, 6 H, Ar), 7.56 - 7.47 (m, 3 H, Ar), 4.68 (t, J = 5.7 Hz, 2 H, OH), 4.59 (s, 2 H, CH_2), 4.04 - 3.96 (m, 1 H, CH), 3.54 (t, J = 5.8 Hz, 4 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.4 (C=O, S-C=N), 165.8 (Ar), 153.2 (Ar), 136.4 (N-C), 135.7 (Ar), 133.9 (Ar), 133.1 (Ar), 132.0 (Ar), 128.3 (Ar), 128.0 (Ar), 127.6 (Ar), 127.4 (Ar), 127.4 (Ar), 126.4 (Ar), 125.9 (Ar), 125.6 (Ar), 115.9 (S-C), 60.4 (CH), 53.9 (CH_2), 39.0 (CH_2). HRMS (ESI, m/z) calculated for $C_{24}H_{22}N_2O_3S$ $[M+H]^+$: 419.1424, found 419.1431.

Compound S29



Compound **S29** was obtained by compound **13** (345 mg, 1 mmol) azetidin-3-ol (87.6 mg, 1.2 mmol) in 79% yield as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (s, 1 H, Ar), 8.02 (d, J = 8.2 Hz, 2 H, Ar), 7.94 - 7.87 (m, 4 H, Ar), 7.69 (d, J = 8.3 Hz, 2 H, Ar), 7.56 - 7.48 (m, 3 H, Ar), 5.77 (s, 1 H, OH), 4.58 (s, 2 H, CH_2), 4.48 (h, J = 6.6, 6.1 Hz, 2 H, CH_2), 4.26 (t, J = 8.5 Hz, 1 H, CH), 4.10 - 4.03 (m, 1 H, CH_2), 3.84 - 3.76 (m, 1 H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3 (C=O, S-C=N), 168.6 (Ar), 153.1 (Ar), 136.3 (N-C), 135.7 (Ar), 133.1 (Ar), 132.4 (Ar), 132.0 (Ar), 128.4 (Ar), 128.3 (Ar), 127.6 (Ar), 127.4 (Ar), 127.4 (Ar), 126.3 (Ar), 125.9 (Ar), 125.8 (Ar), 116.0 (S-C), 62.8 (CH), 60.5 (CH_2), 58.5 (CH_2), 38.9 (CH_2). HRMS (ESI, m/z) calculated for C24H20N2O2S [M+H]+: 401.1318, found 401.1323.

2. MK-801-Induced Hyperlocomotion Test

Animals

Adult male and female ICR mice (22 ± 4 g) were purchased from Pizhou Oriental Breeding Co., Ltd. (Xuzhou, China) and housed under controlled conditions (21 ± 3 °C, 50 ± 20% humidity) with a 12-hour light/dark cycle (8 a.m. to 8 p.m.). The mice had free access to food and water and were randomly assigned to experimental groups (n = 6 per group) with individual cage housing. All procedures followed ethical guidelines to minimize animal suffering and reduce sample sizes, in compliance with the approved protocols (Project ID: 202300036) from the Ethics and Experimental Animal Committee of Jiangsu Ocean University.

Compounds:

MK-801 was dissolved in normal saline to prepare a 0.02 mg/ml working solution. Compounds FTBMT and **S1 – S29** were first prepared as 30 mg/ml stock solutions using a mixture of ethanol and Cremophor EL (polyoxyethylated castor oil) (1:1, v/v), which were subsequently diluted to desired concentrations with normal saline prior to administration.

Experimental procedures and statistical analysis [1]

The experiment was conducted in 20 × 20 cm^2 Plexiglas chambers under standardized environmental conditions. Male mice were grouped (6 mice in each group), weighed (20-25 g), labeled (solvent group, model group and drug administration group), and placed in a laboratory box in the field for an hour. Subsequently, the mice were orally given FTBMT (10, 30, 60 mg/kg), or targeted compounds (3, 10, 30 mg/kg) and settled into the open field. After 30 minutes, a 0.02 mg/ml of MK-801 (Dizocilpine) solution was intraperitoneally injected, and mice were immediately put back to the open field. Their activity of the mice was monitored after the injection for 60 minutes. After the recording, the recorded distance is analyzed using Prism 8.0. The total activity distance of mice within 60 minutes were calculated to calculate the inhibition rate of the compounds. The total activity distance of mice within 60 minutes were calculated to estimate the ED_{50} of the compounds. Data were presented as Mean ± SEM and statistically analyzed using one-way variance. When the P value is less than 0.05, it indicates statistical significance between groups.

$$\text{Inhibition rate} = \frac{total\ distance\ traveled\ in\ the\ drug\ administered\ group - \ total\ distance\ traveled\ in\ s}{total\ distance\ traveled\ in\ solvent\ group}$$

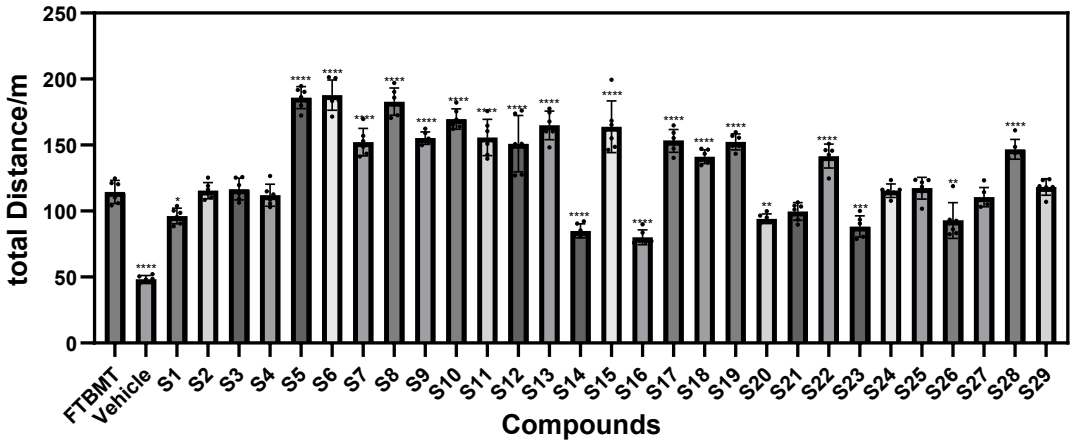


Fig. S1. The scatter plots of the mouse movement distance for S1-S29 at 30 mg/kg (compared with FTBMT: * $P < 0.05$, ** $P < 0.01$, *** $P<0.001$, **** $P<0.0001$).

3. Rotarod Test

Animals:

Adult male ICR mice (22 ± 4 g) were purchased from Pizhou Oriental Breeding Co., Ltd. (Xuzhou, China) and housed under controlled conditions (21 ± 3 °C, 50 ± 20% humidity) with a 12-hour light/dark cycle (8 a.m. to 8 p.m.). The mice had free access to food and water and were randomly assigned to experimental groups (n = 6 per group) with individual cage housing. All procedures followed ethical guidelines to minimize animal suffering and reduce sample sizes, in compliance with the approved protocols (Project ID: 202500039) from the Ethics and Experimental Animal Committee of Jiangsu Ocean University.

Compounds:

Compounds **S14**, **S16**, **S23** and **S29** were prepared as 30 mg/ml stock solutions using a mixture of ethanol and Cremophor EL (polyoxyethylated castor oil) (1:1, v/v), which were subsequently diluted to desired concentrations with normal saline prior to administration.

Experimental procedures and statistical analysis

The rotarod test equipment consisted of an accelerating rotating rod and was used to evaluate the motor coordination and balance of mice. All mice were randomly divided into groups of six and underwent training. The animals were gently placed on the stationary rod and allowed to acclimate to the environment for 2–3 minutes. The rod was then started at a very low rotation speed (e.g., 4–8 rpm) to allow the animals to learn to walk on it. Whenever an animal fell, it was immediately placed back on the rod. Each training session lasted 3–5 minutes, and 2–3 sessions could be conducted per day, with at least 1 hour between sessions. Over the next 1–2 days, the rotation speed was gradually increased or an acceleration mode was used for training until the animals' fall times stabilized (with small within-group variation), indicating that the animals had learned the task.

Thirty minutes before the formal experiment began, the mice were administered the treatment via gavage. Thirty minutes after administration, the qualified mice were placed on the rod at an initial speed of 12 rpm, and the acceleration mode was activated, gradually increasing the speed to 24 rpm. During the 180-second test period, the time from the start of the experiment until each mouse fell from the rotarod was recorded as the latency, in order to observe whether the animals exhibited impaired motor coordination. Each animal was tested 2–3 times, with at least 30 minutes between tests, and the average value was taken as the final score for that animal. Experimental data were statistically analyzed and graphed using GraphPad Prism 10 software. One-way ANOVA was used for intergroup comparisons, with a P value < 0.05 considered statistically.

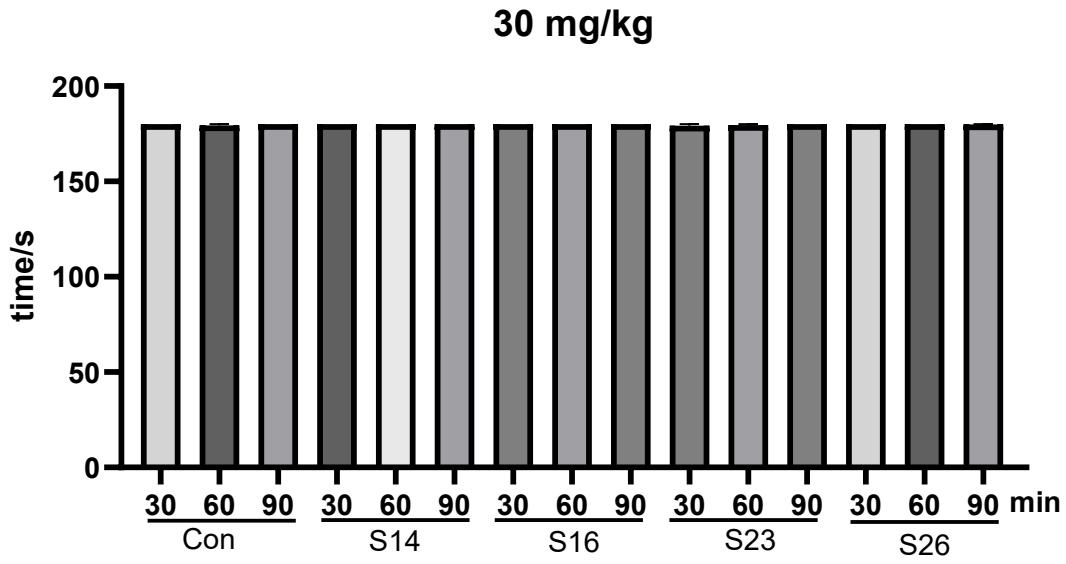


Fig. S2. Mean latency of six trials of staying on the rod of Comp. S14, S16, S23 and S26 at 30 mg/kg.

4. Evaluation of GPR52 Agonistic Activities.

Forskolin was used as the reference compound in this test and reported GPR52 agonist 4-(3-(3-fluoro-5-(trifluoromethyl)-benzyl)-5-methyl-1H-1,2,4-triazol-1-yl)-2-methylbenzamide (FTBMT) was synthesized and used as the positive control compound when screened in our assay in a 12-point concentration-response. After transfection for 48 h, CHO cells expressing human GPR52 were seeded at 12000 cells/well and were incubated with test compounds (0.0126 nM-50000 nM, DMSO) for 30 min at 37 °C in the stimulation buffer (HBSS with 5mM HEPES, 0.5mM IBMX and 0.1% BSA (pH 7.4)). Glosensor cAMP reagent was added and incubated 60 minutes at room temperature with a sealing film. Luminescence in light counts per second (lcps) was recorded and EC_{50} values were calculated by using nonlinear regression analysis with GraphPad Prism. EC_{50} is the concentration of the compounds that produces a response that is 50% of its maximal effect. Data were presented as Mean ± SEM and statistically analyzed using one-way variance. [2]

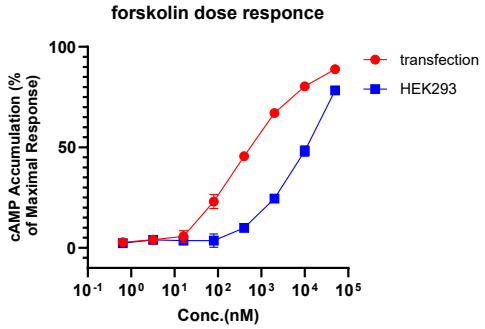


Fig. S3. Dose-Response Curve of the Reference Compound Forskolin

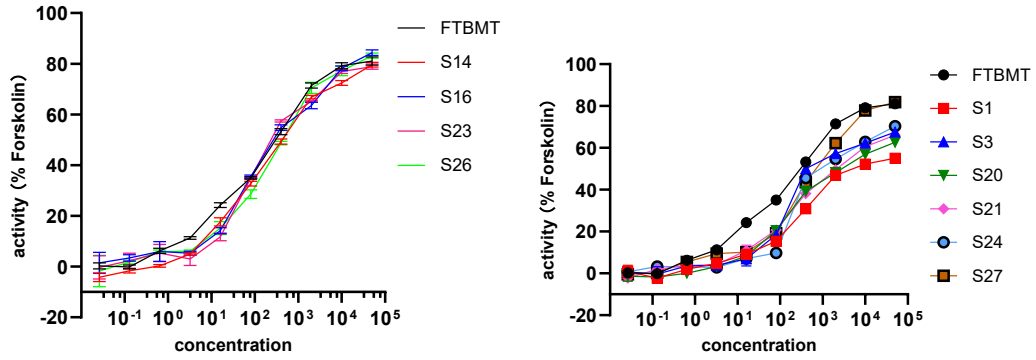


Fig. S4. Concentration–response curves for the selected compounds.

5. Molecular Docking

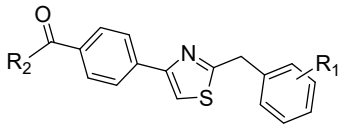
The CDOCKER module in Discovery Studio 2016 was adopted as the molecular docking program to analyze interaction patterns and binding conformations between the compounds and GPR52 protein in this study. The crystal structure of GPR52 (PDB ID: 6LI0) was retrieved from the RCSB Protein Data Bank(http://www.pdb.org), with Compounds **2** and **7** serving as positive controls to benchmark the binding performance of newly designed compounds. Protein preparation was performed using the Prepare Protein tool, involving structure import, atomic defect repair (adding missing atoms, correcting connectivity/termini), and protonation state optimization for ionizable residues. A spherical binding site (radius: 11.20 Å; center coordinates: X = 34.83, Y = 71.03, Z = 66.48) was defined around the native ligand (EN6). The native ligand was then redocked into this site. As shown in **Table S1**, the resulting RMSD value was less than 1.0 Å. This successful reproduction of the original binding mode confirms the rationality of the parameter settings used in Discovery Studio.

For ligand preparation, 2D structures of designed compounds were drawn in ChemBioDraw Ultra 12.0, converted to 3D conformations in ChemBio3D Ultra 12.0, and saved as .mol2 files. These ligands were then processed in Discovery Studio 2016 via the Prepare Ligand module (hydrogen addition, isomer generation, and 3D conformation optimization using Catalyst algorithms). Final docking simulations were executed with the CDOCKER protocol to predict binding poses within the defined active site. The docking results of the designed compounds and GPR52 protein are shown in **Table S2**[3] and the CDOCKER energy and Interaction Energy for **S14**, **S16**, **S23** and **S26**.

Table S1 The RMSD for the reference EN6.

Name	Reference	RMSD (Å)
EN6-1	EN6	0.4906
EN6-2	EN6	0.7201
EN6-3	EN6	0.6330
EN6-4	EN6	0.7357
EN6-5	EN6	0.7572
EN6-6	EN6	0.7187
EN6-7	EN6	1.0857
EN6-8	EN6	0.9246
EN6-9	EN6	0.9402
EN6-10	EN6	0.8486

Table S2. Molecular docking score of designed compound and control compound **2** and **7**



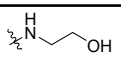
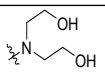
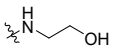
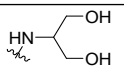
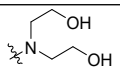
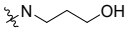
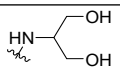
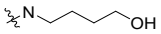
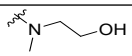
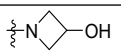
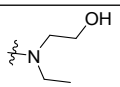
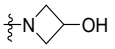
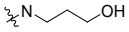
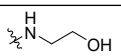
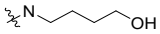
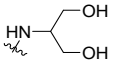
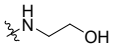
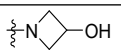
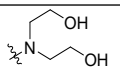
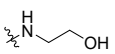
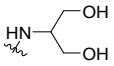
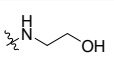
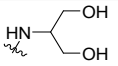
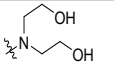
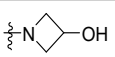
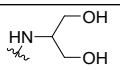
Comp.	R_1	R_2	Score	Comp.	R_1	R_2	Score
2	—	—	53.7	**S15**	4-F		60.1
7	—	—	54.9	**S16**	4-F		71.4
S1	4-CH_3		62.1	**S17**	4-F		63.0
S2	4-CH_3		68.1	**S18**	4-Br		67.5
S3	4-CH_3		64.4	**S19**	4-Br		64.0
S4	4-CH_3		62.3	**S20**	4-Br		63.5
S5	4-CH_3		62.8	**S21**	4-F		62.1
S6	4-CH_3		63.7	**S22**	3,4-di-F		61.8
S7	4-CH_3		60.9	**S23**	3,4-di-F		65.4
S8	4-CH_3		63.1	**S24**	3,4-di-F		65.5
S09	4-OH		61.2	**S25**	3,4-di-F		63.3
S10	4-OH		63.6	**S26**			70.0
S11	4-OH		65.5	**S27**			66.1
S12	4-Br		61.8	**S28**			66.4
S13	4-Br		65.1	**S29**			61.2
S14	4-Br		68.5				

Table S3 CDOCKER energy and Interaction Energy for **S14**, **S16**, **S23** and **S26**

Compounds	- CDOCKER energy±SD	- Interaction Energy±SD
S14	38.9756±7.0317	63.8954±5.0366
S16	31.2143±1.056	62.7666±2.3275
S23	28.6999±2.0879	63.2125±2.6203
S26	37.4107±2.1851	61.9668±2.5021
FTBMT	10.4247±7.4011	51.8056±6.2146

6. ADME Prediction

ADMET prediction was performed using the SwissADME online server (http://www.swissadme.ch/). [3] It is a network-based ADMET screening tool that predicts the drug-like properties of newly designed compounds, to reduce the cost and time associated with drug development. This study evaluates the newly designed compounds from multiple aspects, including drug properties, absorption, distribution, and toxicity. The ADMET Prediction results of the designed compounds are shown in **Table S2**.

Table S4. The ADMET Prediction results of the designed compounds

Comp.	MW	Log $P_{o/w}$ (<5)	Log *S*	Pharmacokinetics			Drug likeness
				HIA	BBB	CYP2D6	
S1	352.45	3.30	-4.29	High	No	Yes	Yes
S2	396.50	3.16	-4.16	High	No	Yes	Yes
S3	382.48	3.23	-3.98	High	No	Yes	Yes
S4	380.50	3.68	-4.71	High	No	Yes	Yes
S5	366.48	3.32	-4.47	High	No	Yes	Yes
S6	366.48	3.42	-4.52	High	No	Yes	Yes
S7	380.50	3.66	-4.74	High	No	Yes	Yes
S8	364.46	3.18	-4.49	High	No	Yes	Yes
S9	354.42	2.58	-3.85	High	No	Yes	Yes
S10	398.48	2.92	-3.62	High	No	Yes	Yes
S11	366.43	2.69	-4.05	High	No	Yes	Yes
S12	417.32	3.16	-4.90	High	No	Yes	Yes
S13	461.37	3.38	-4.67	High	No	Yes	Yes
S14	447.35	3.63	-4.59	High	No	Yes	Yes
S15	356.41	2.55	-4.15	High	No	Yes	Yes
S16	400.47	3.06	-3.92	High	No	Yes	Yes
S17	386.44	2.20	-3.84	High	No	Yes	Yes
S18	431.35	3.55	-5.82	High	No	Yes	Yes
S19	445.37	3.83	-5.35	High	No	Yes	Yes
S20	429.33	3.36	-5.10	High	No	Yes	Yes
S21	368.42	3.06	-4.35	High	No	Yes	Yes
S22	374.40	2.90	-4.31	High	No	Yes	Yes
S23	418.46	3.20	-4.08	High	No	Yes	Yes
S24	404.43	3.05	-4.00	High	No	Yes	Yes
S25	386.42	3.09	-4.51	High	No	Yes	Yes
S26	388.48	3.26	-5.12	High	No	Yes	Yes
S27	432.53	3.03	-4.89	High	No	Yes	Yes
S28	418.51	3.19	-4.82	High	No	Yes	Yes
S29	400.49	3.30	-5.33	High	No	Yes	Yes

Log *S* scale: Insoluble <-10<Poorly<-6<Moderately <-4<Soluble <-2 Very <0 <Highly.

HIA: Human intestinal absorption. BBB: Blood Brain Barrier penetration.

7. **Molecular Dynamics**

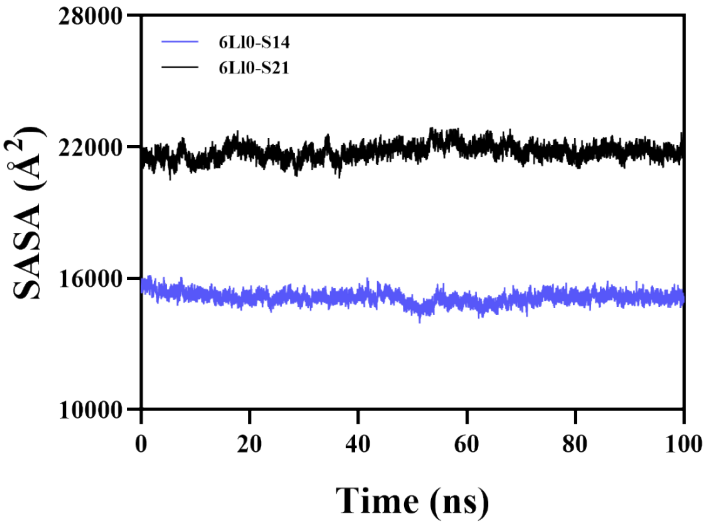
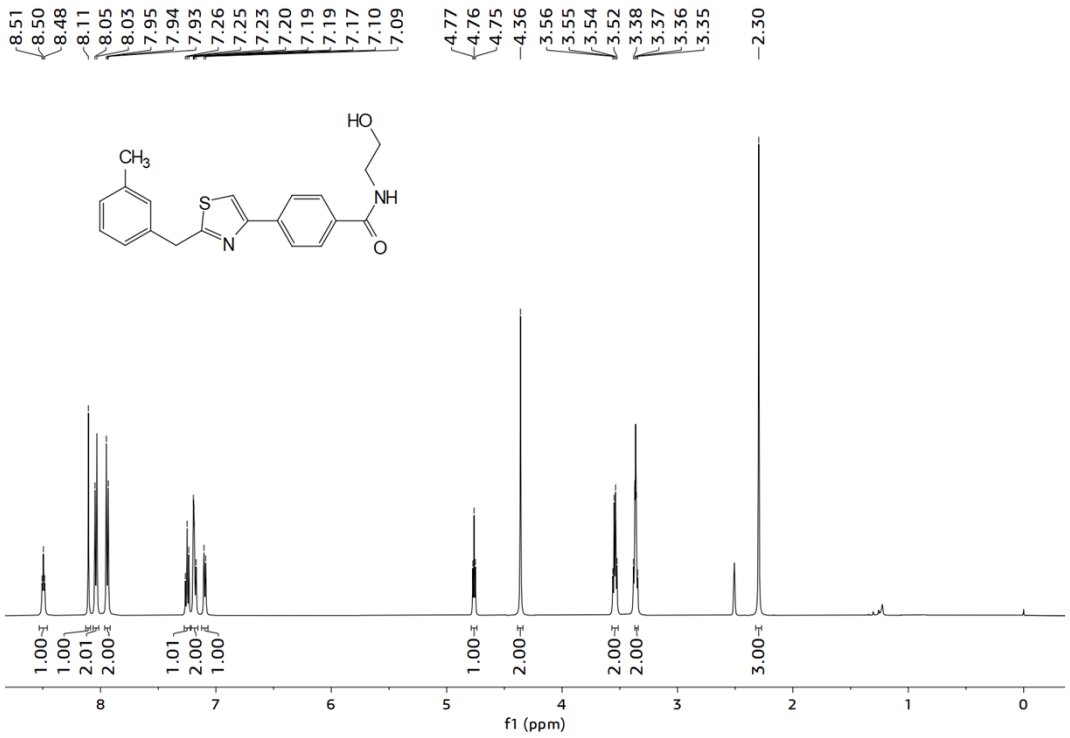


Fig. S5. Solvent-accessible surface area (SASA) fluctuations of S14-GPR52 and S21-GPR52 complexes during the simulation

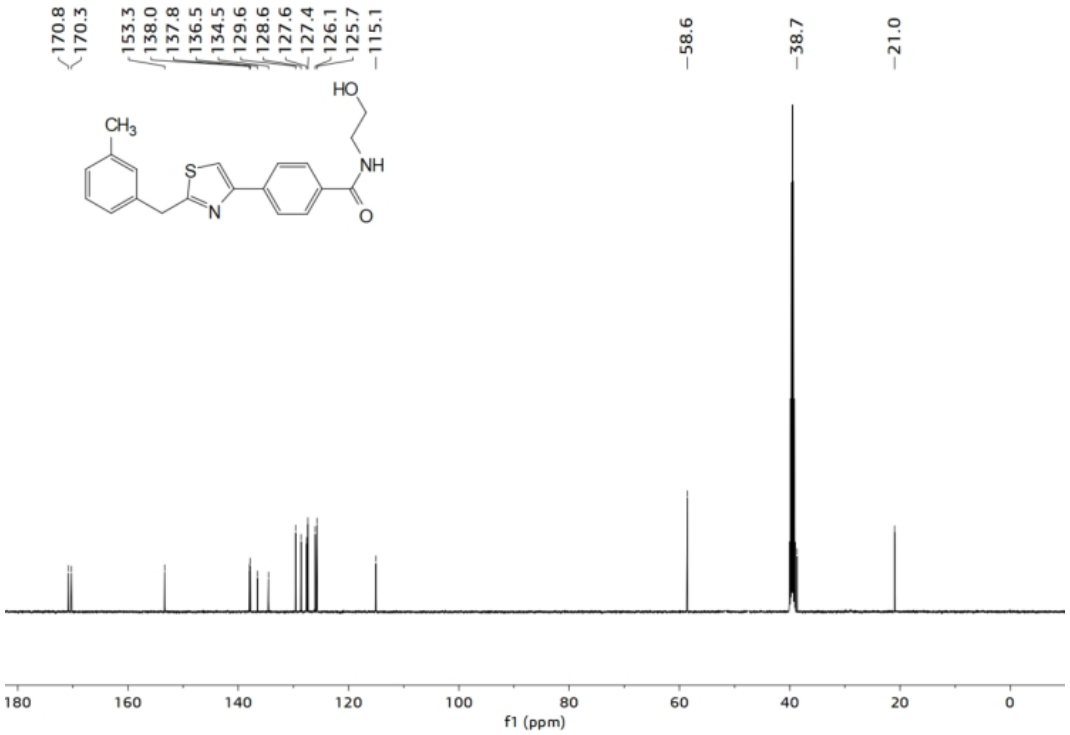
8. The ^{1}H NMR, ^{13}C NMR spectra and HRMS of the new compounds

Compound **S1**:

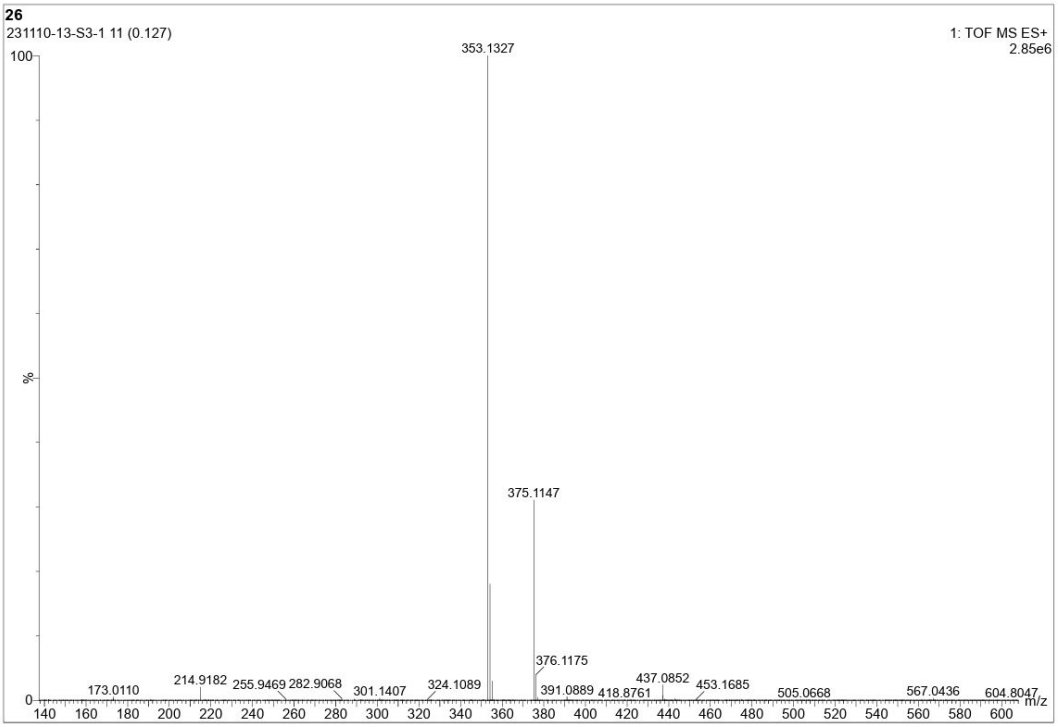
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

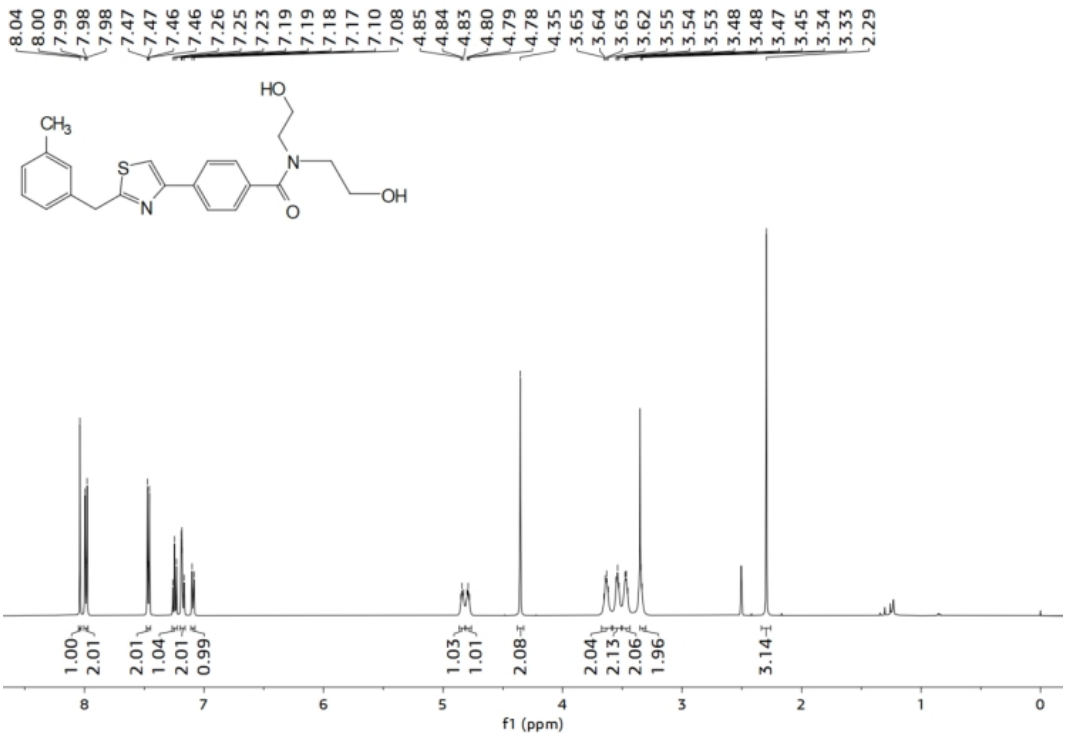


High resolution mass spectrum of **S1**

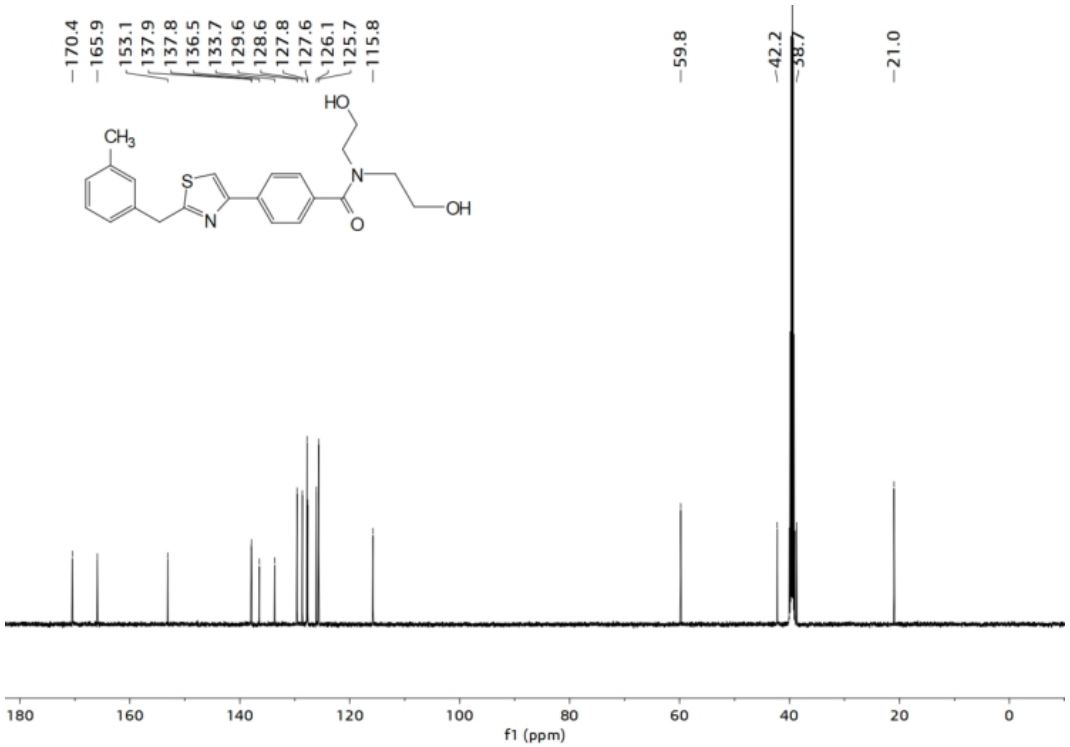


Compound **S2**:

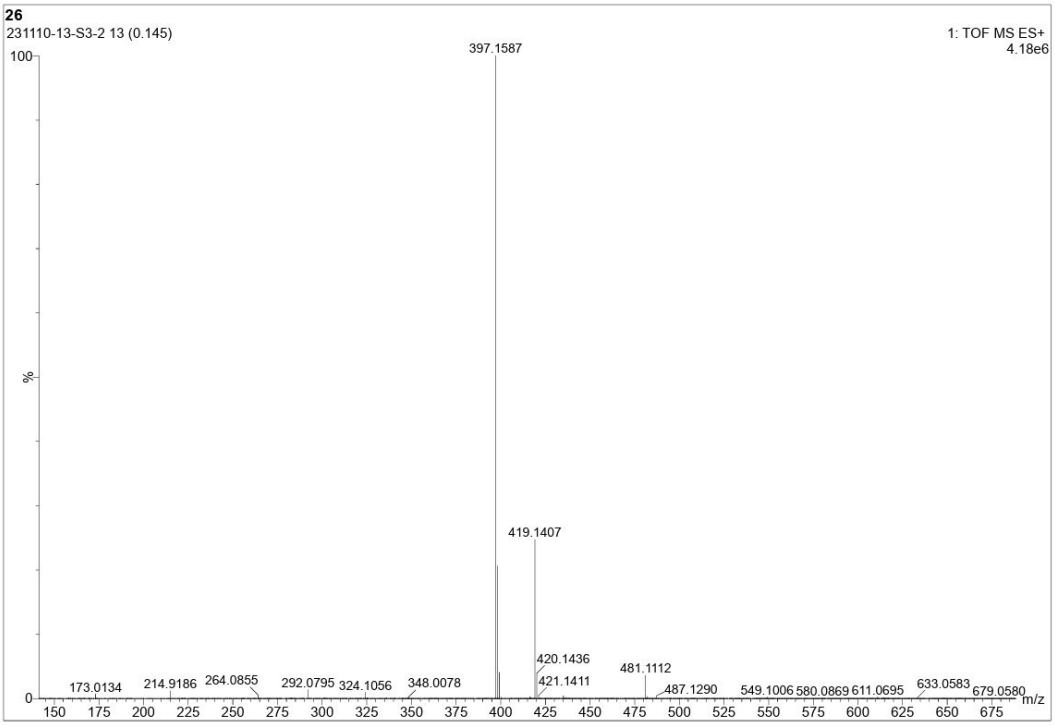
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

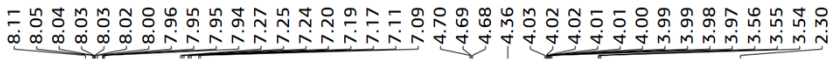


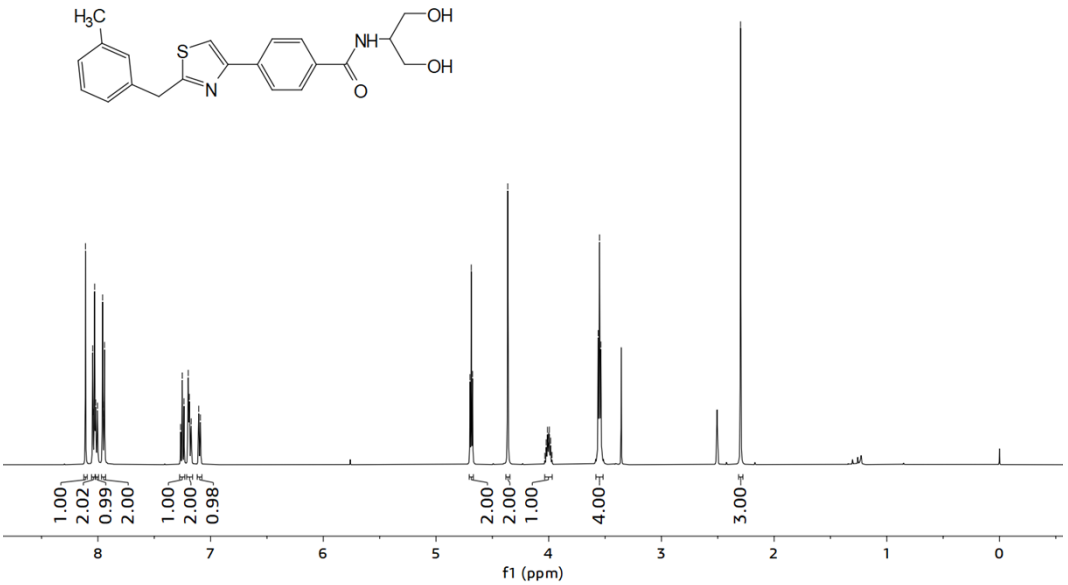
High resolution mass spectrum of **S2**



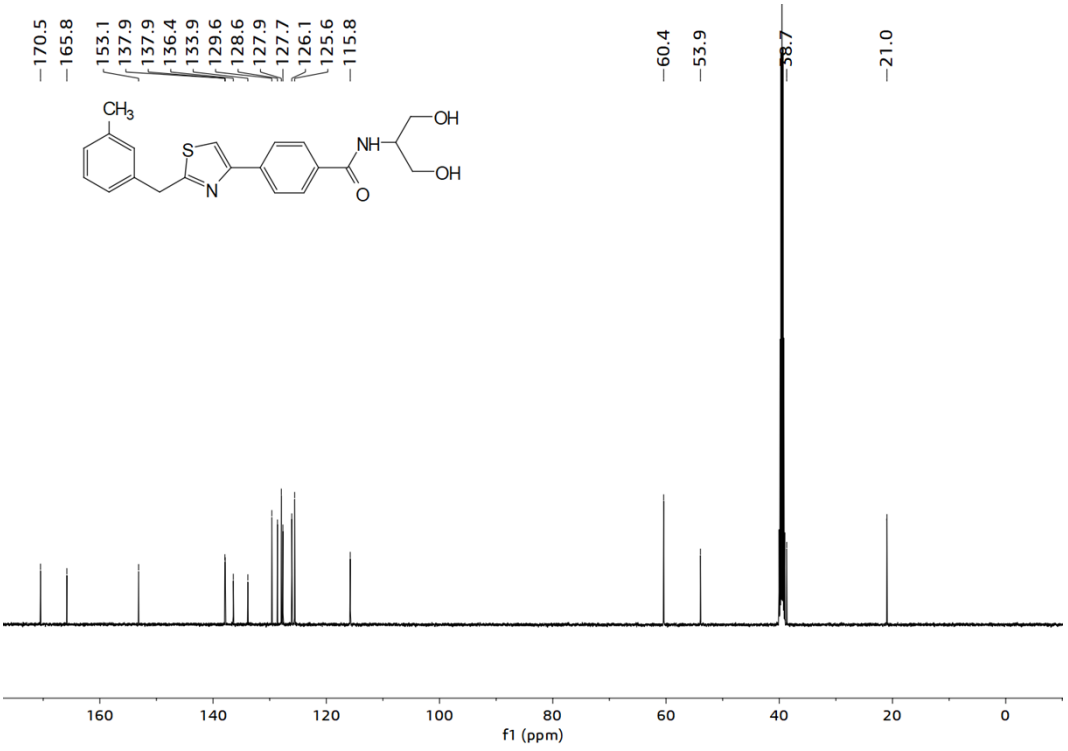
Compound **S3**:

^{1}H NMR (500 MHz, DMSO-d_6)

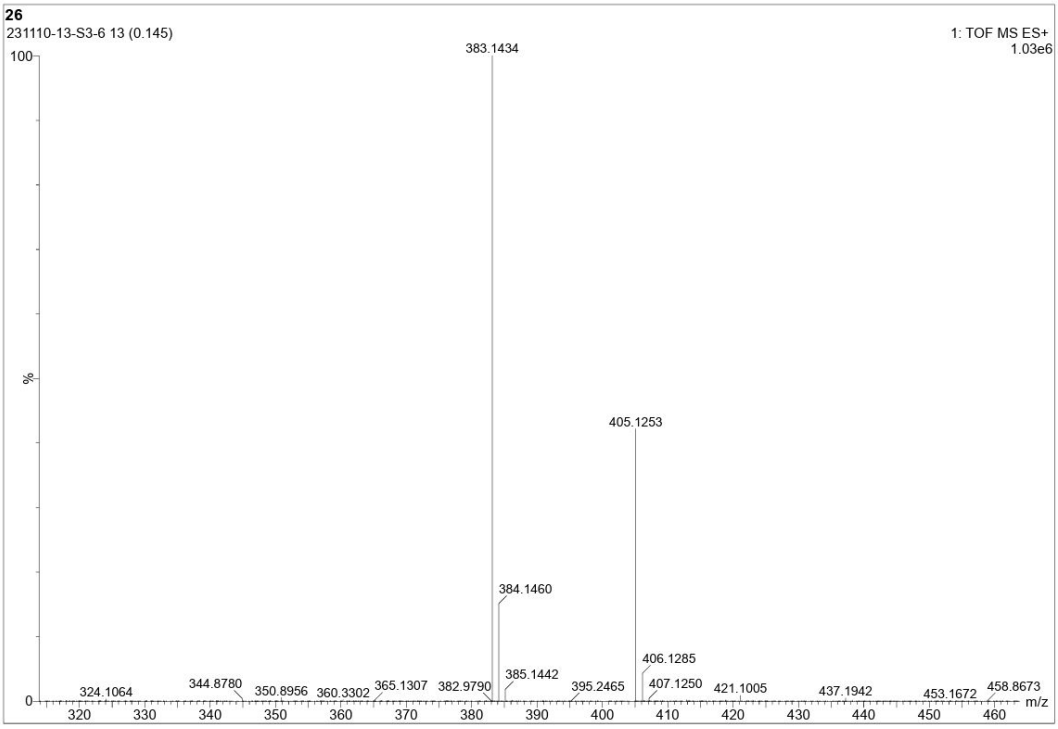




^{13}C NMR (125 MHz, DMSO-d_6)

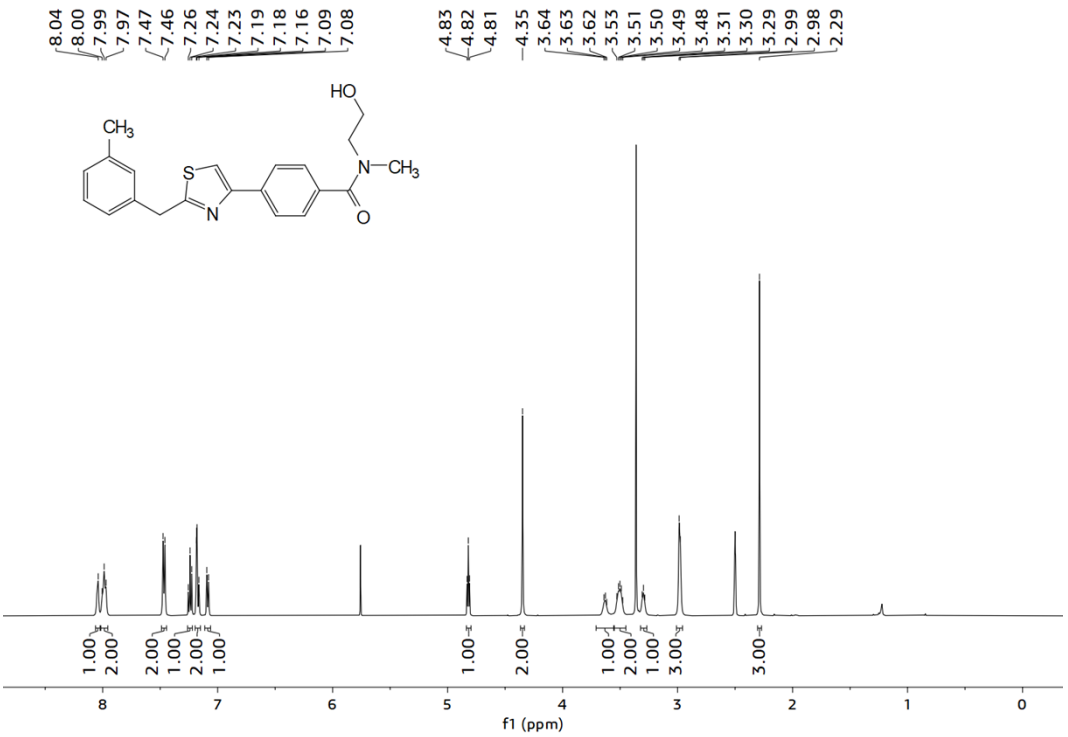


High resolution mass spectrum of **S3**

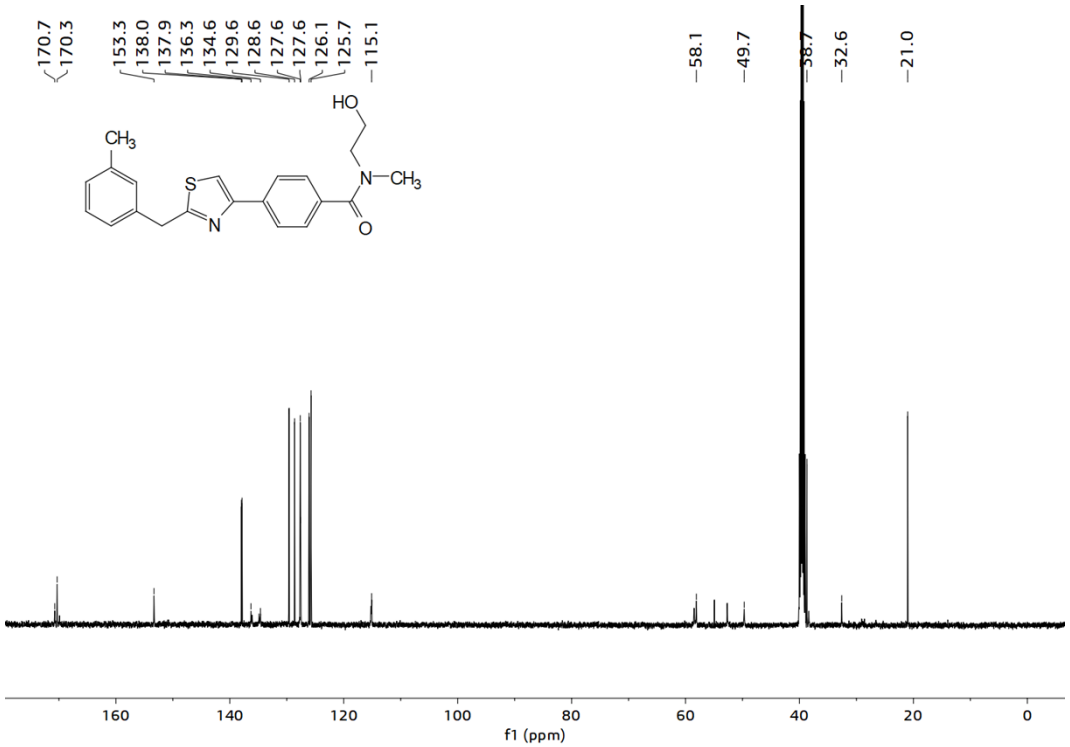


Compound **S4**:

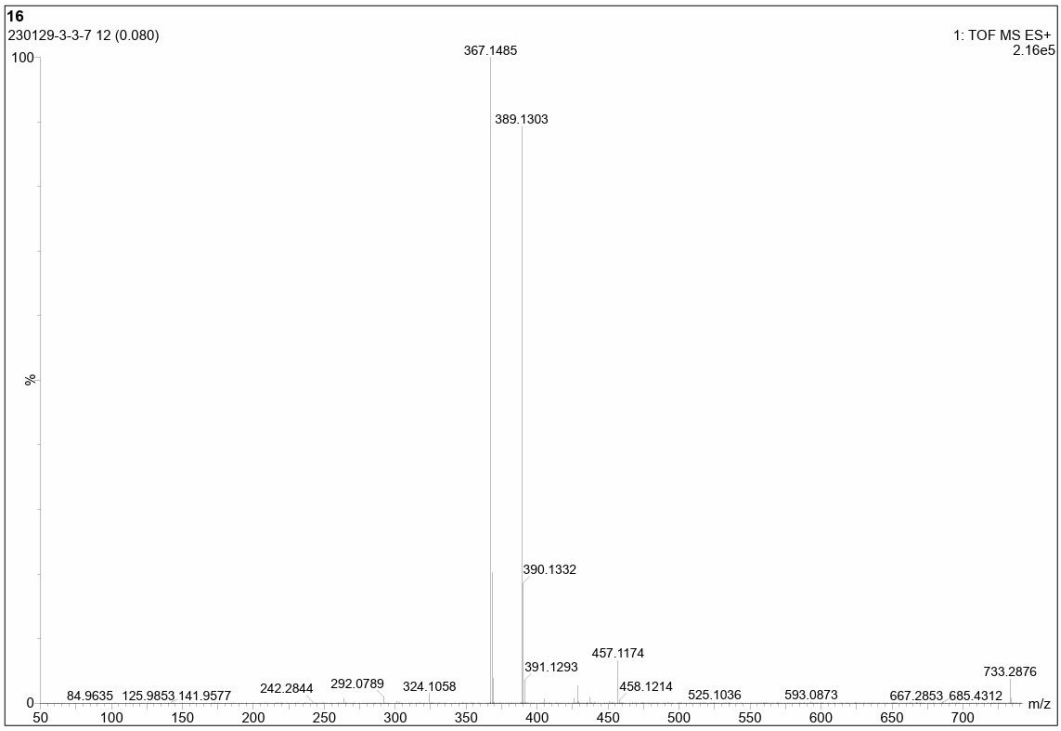
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

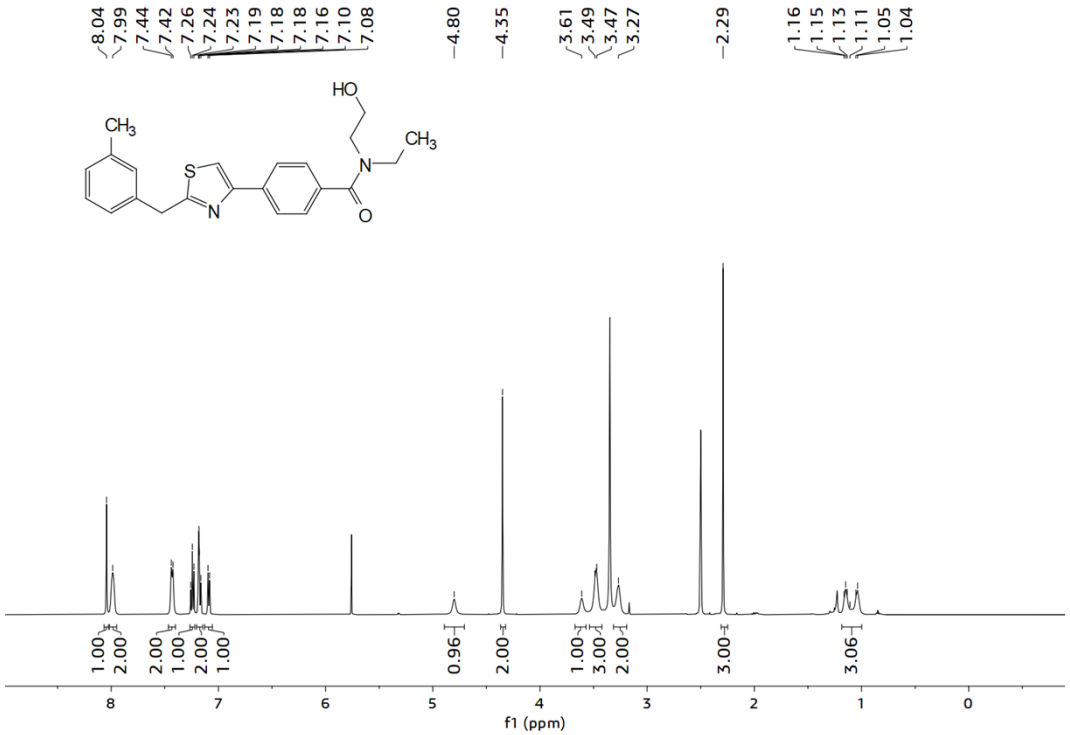


High resolution mass spectrum of **S4**

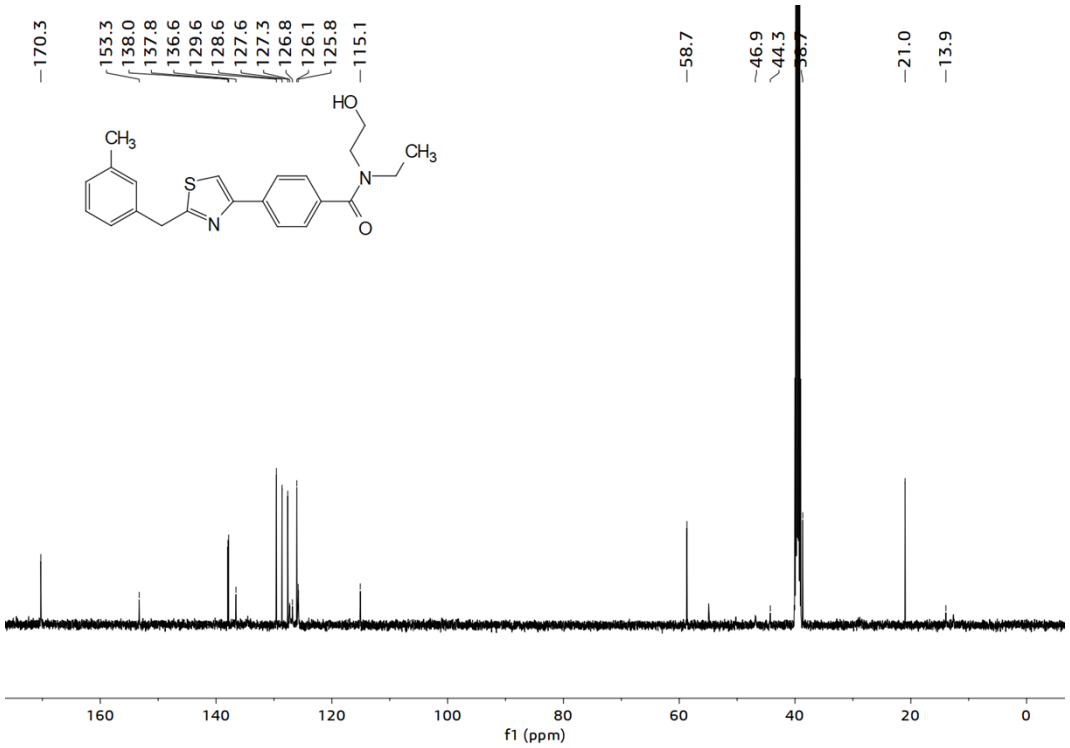


Compound **S5**:

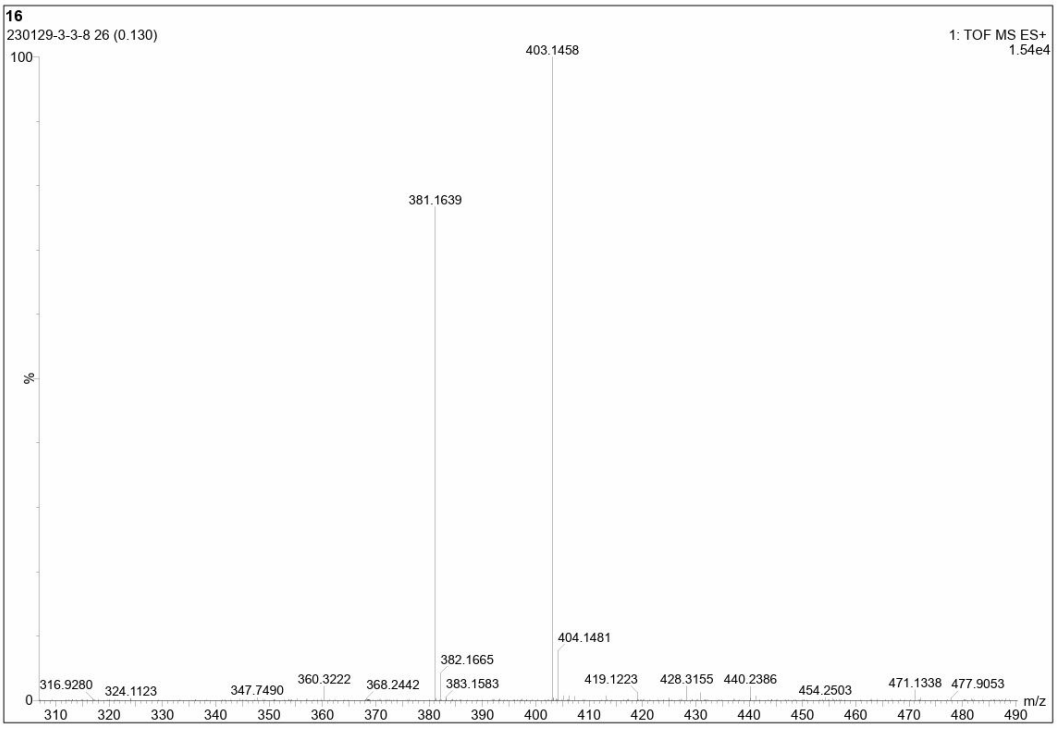
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

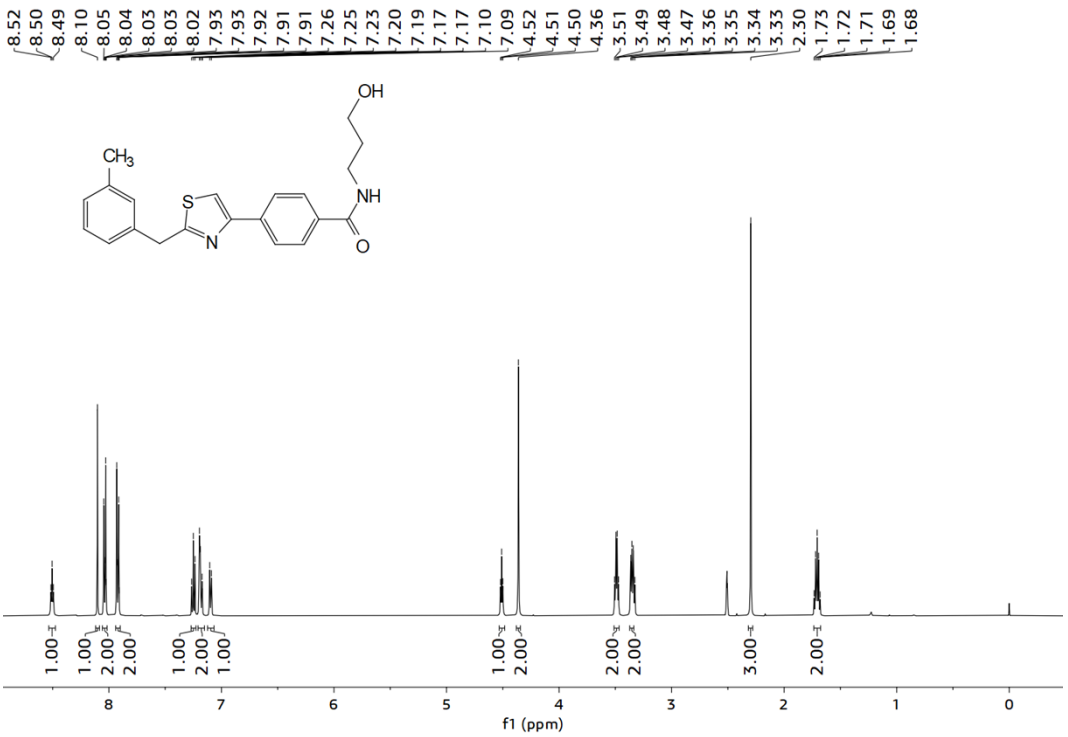


High resolution mass spectrum of **S5**

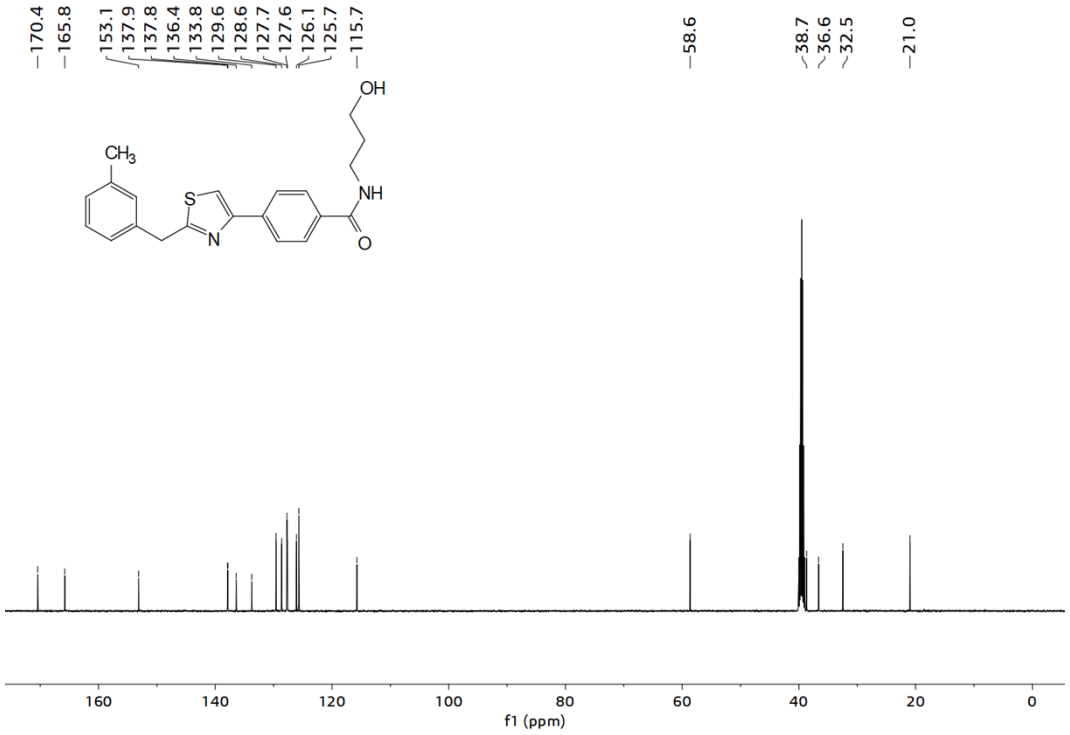


Compound **S6**:

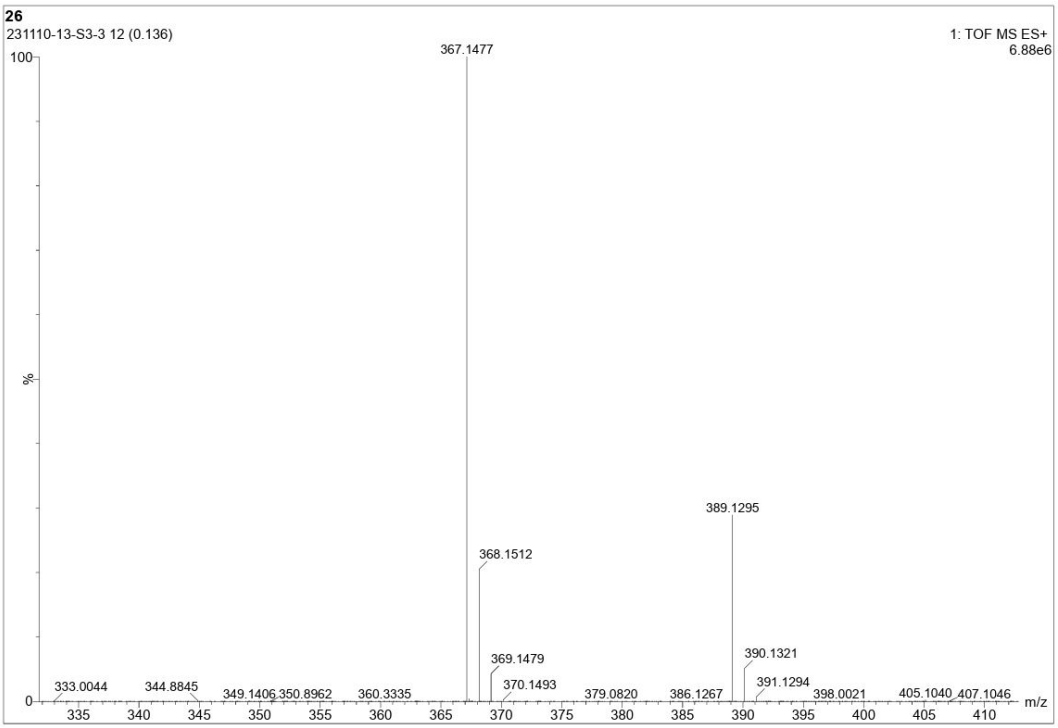
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

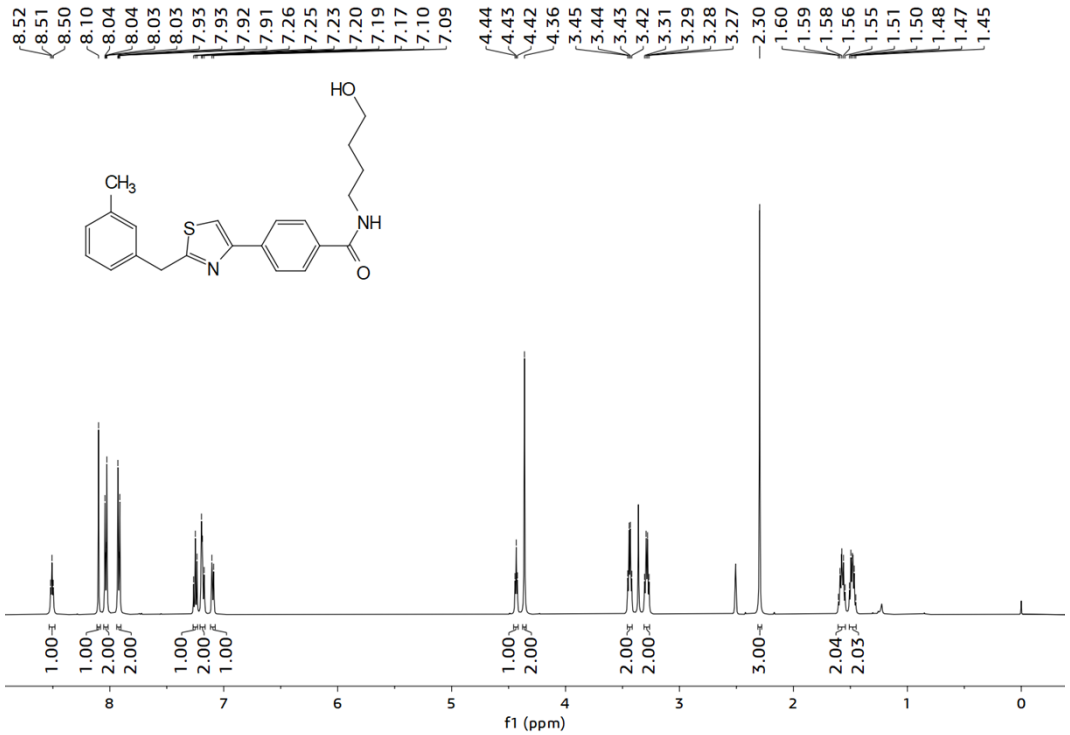


High resolution mass spectrum of **S6**

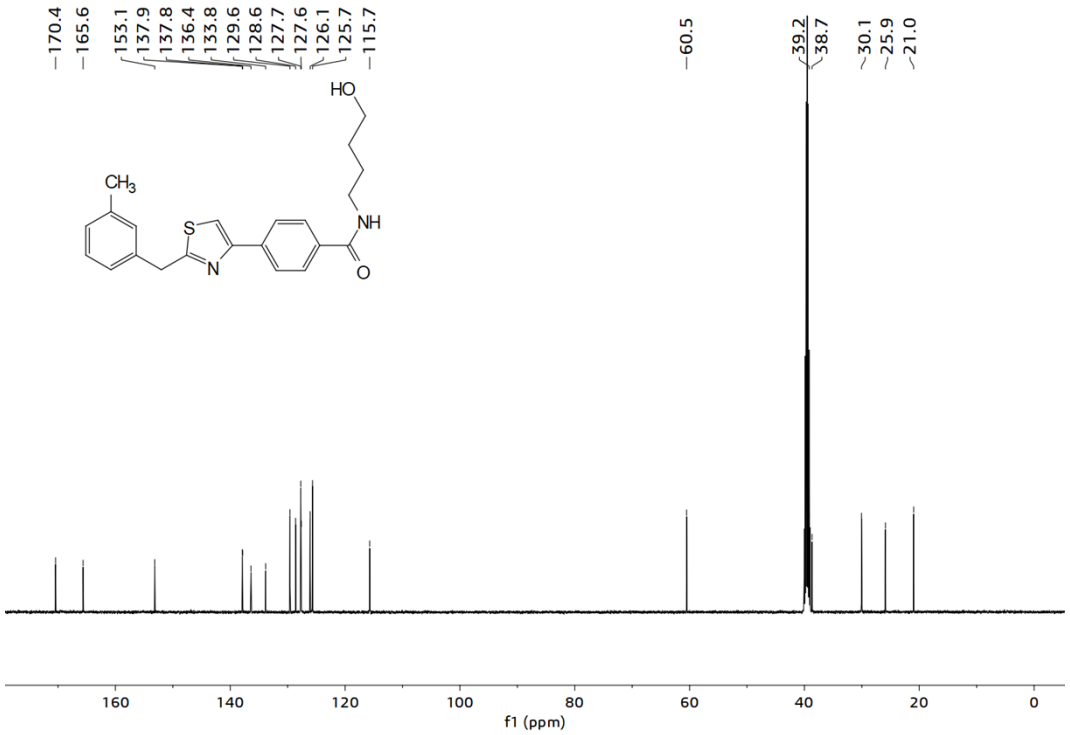


Compound **S7**:

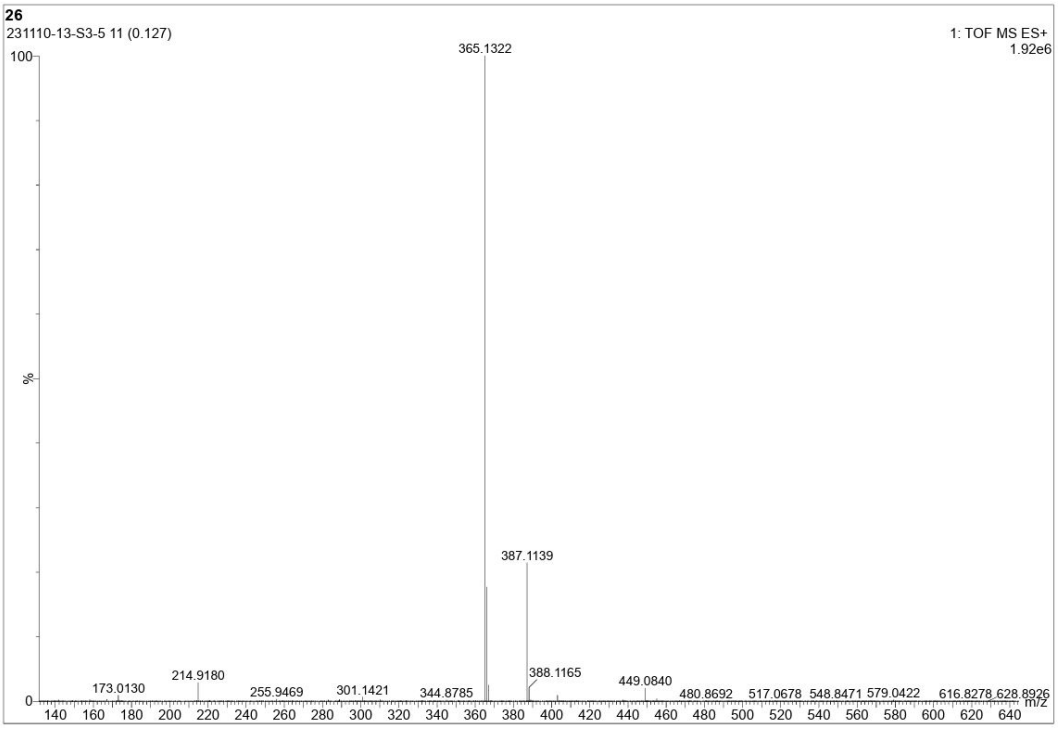
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

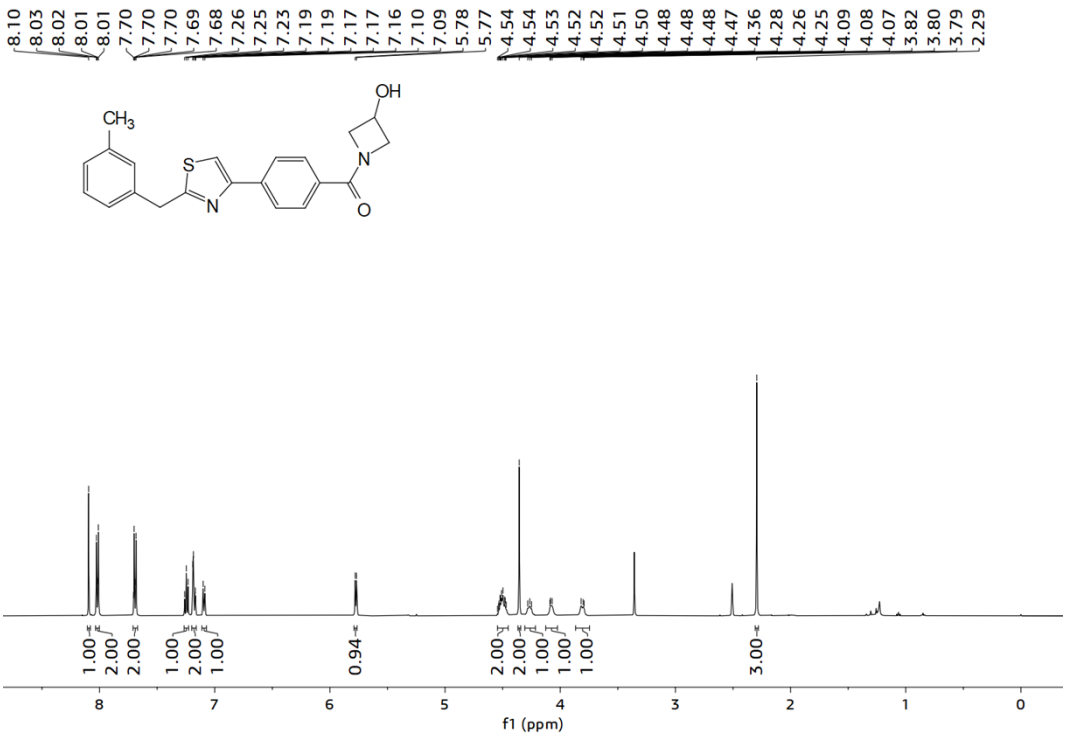


High resolution mass spectrum of **S7**

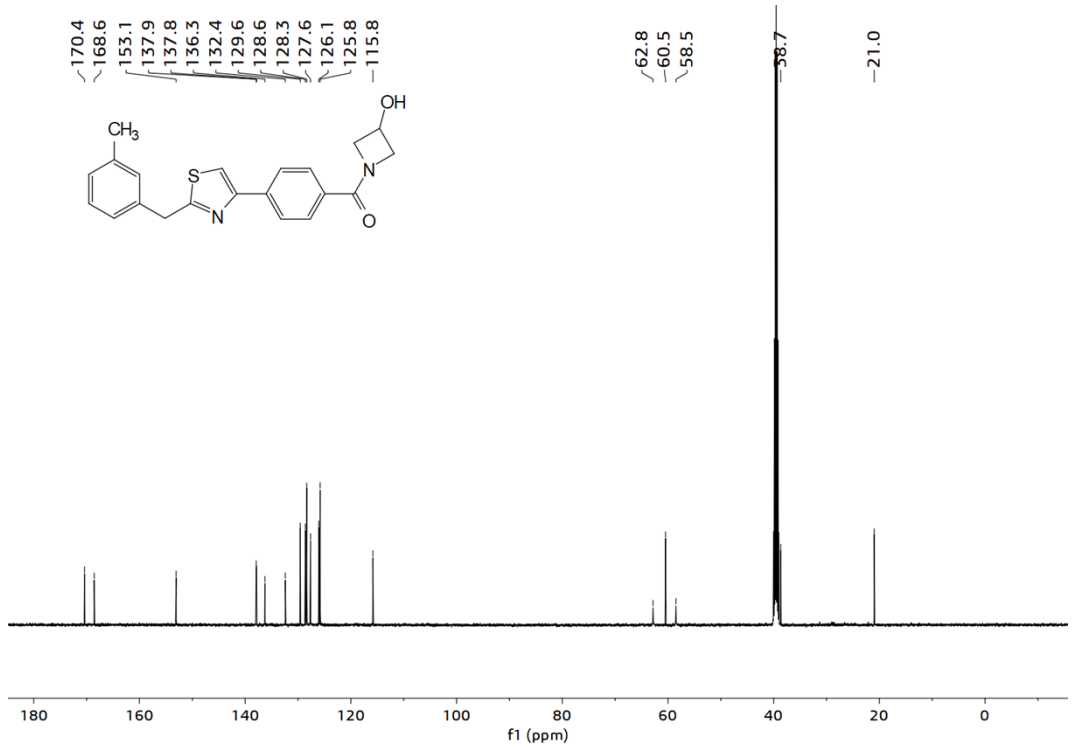


Compound **S8**:

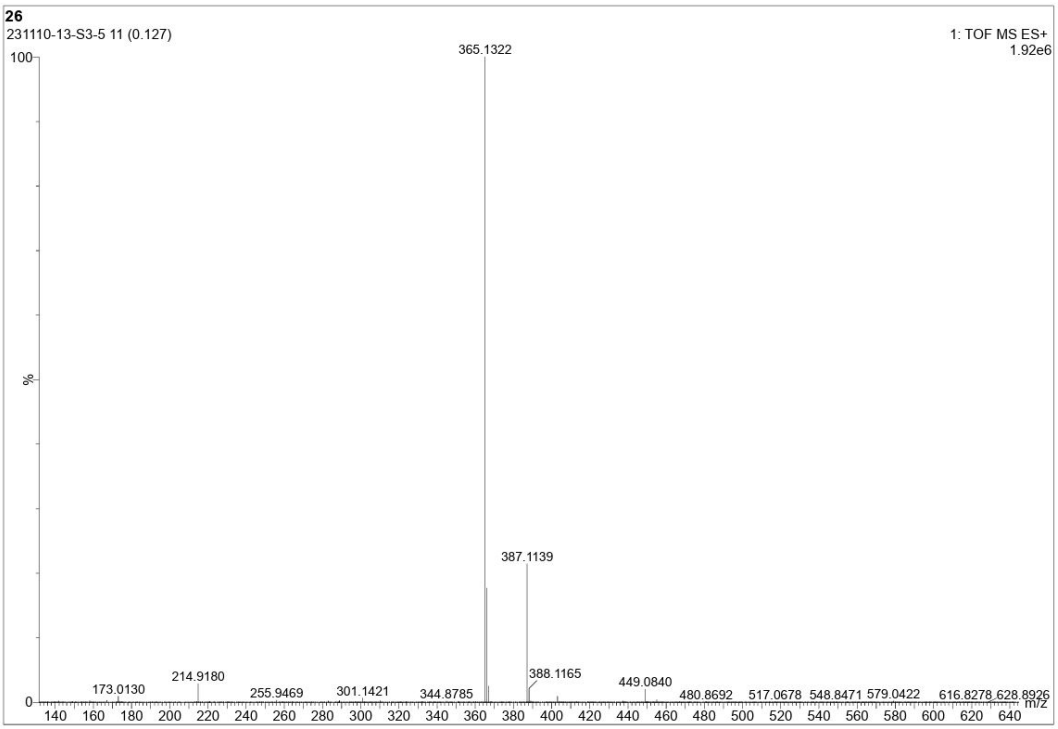
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

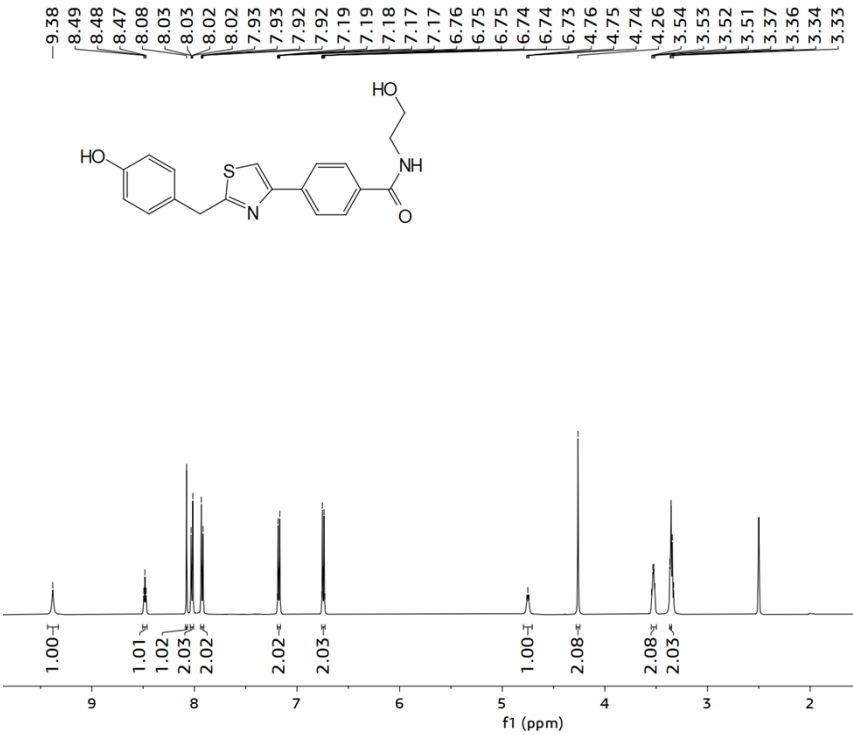


High resolution mass spectrum of **S8**

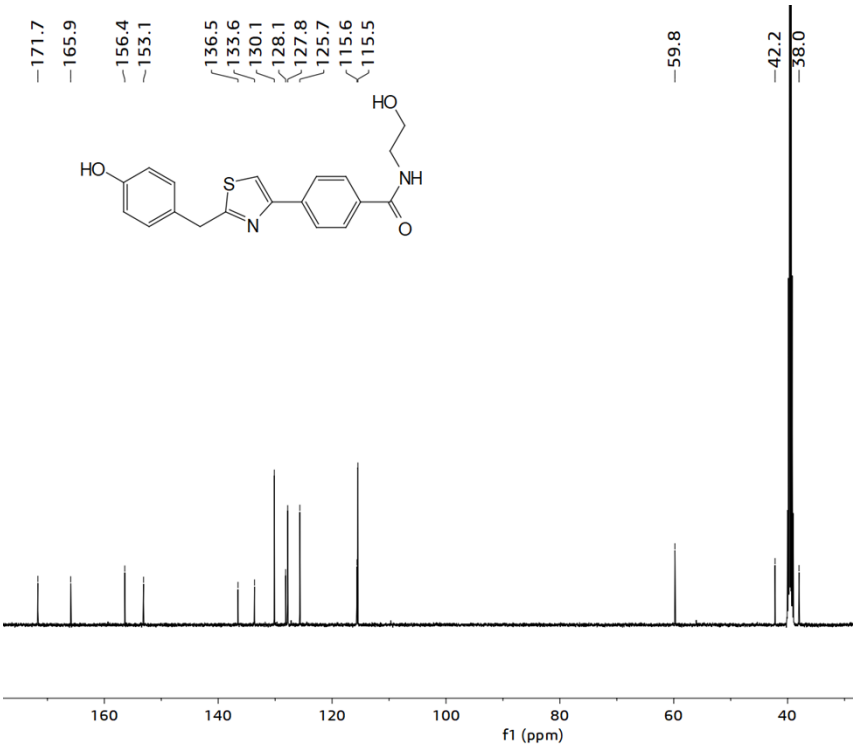


Compound **S9**:

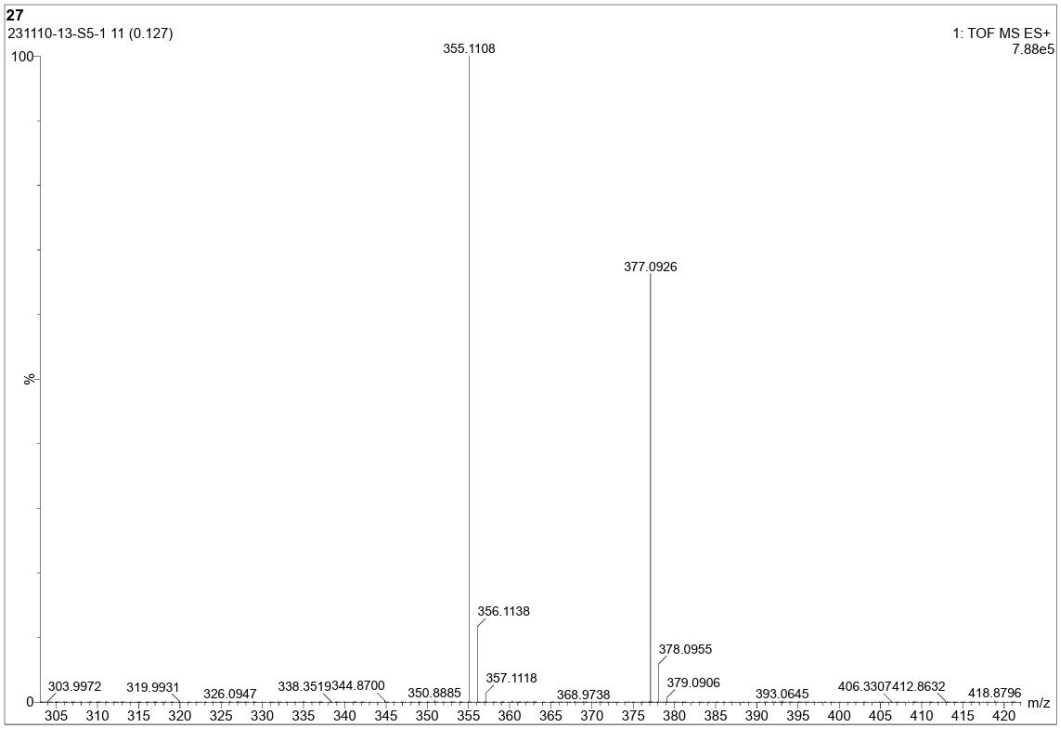
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

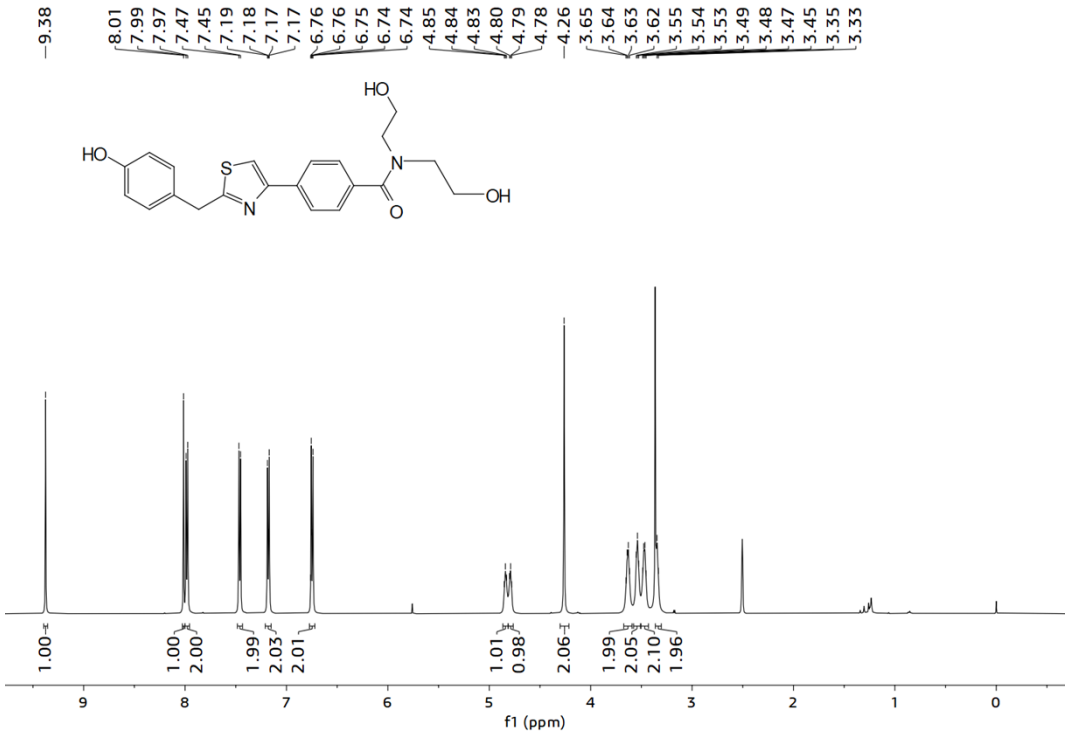


High resolution mass spectrum of **S9**

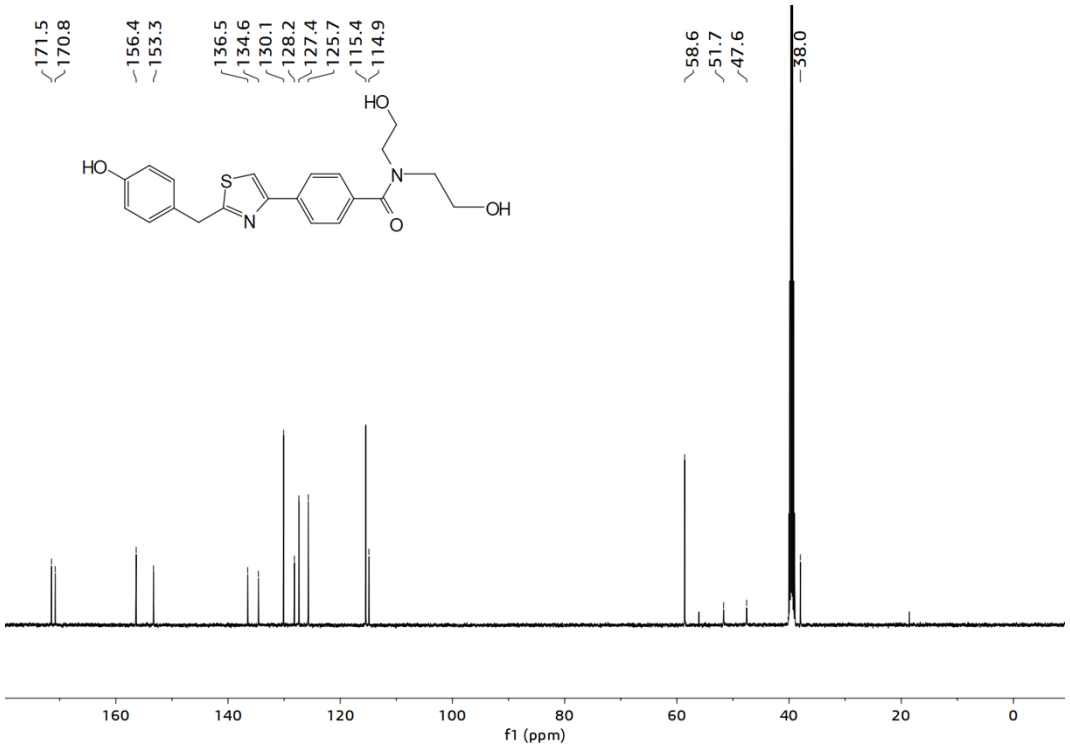


Compound **S10**:

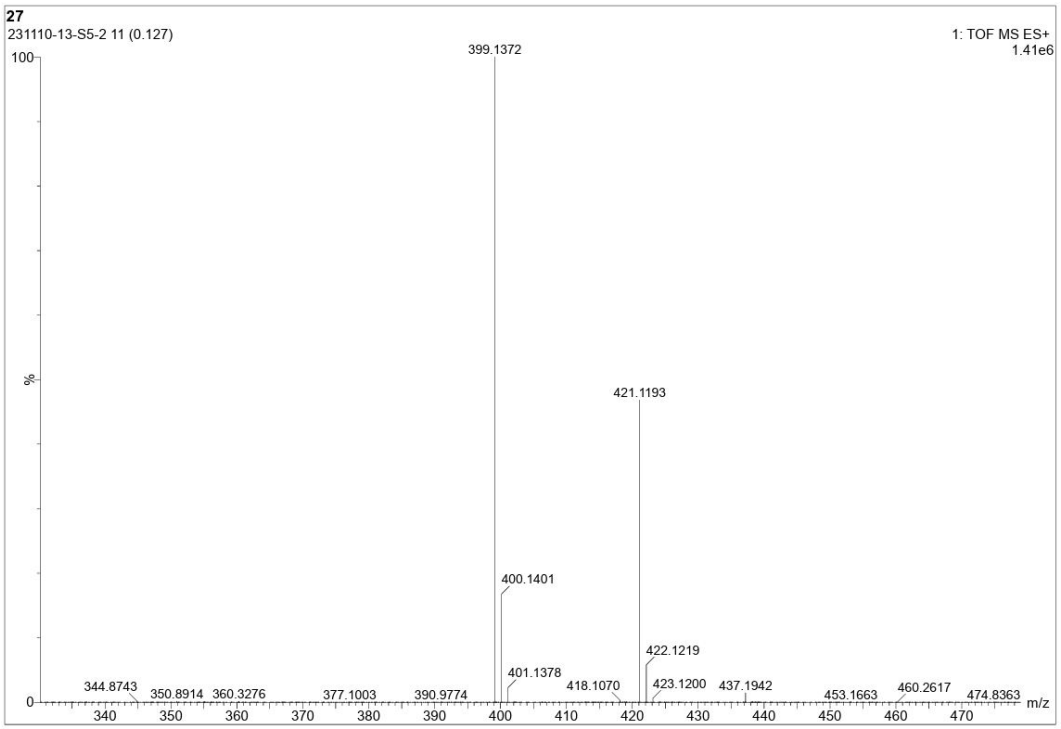
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

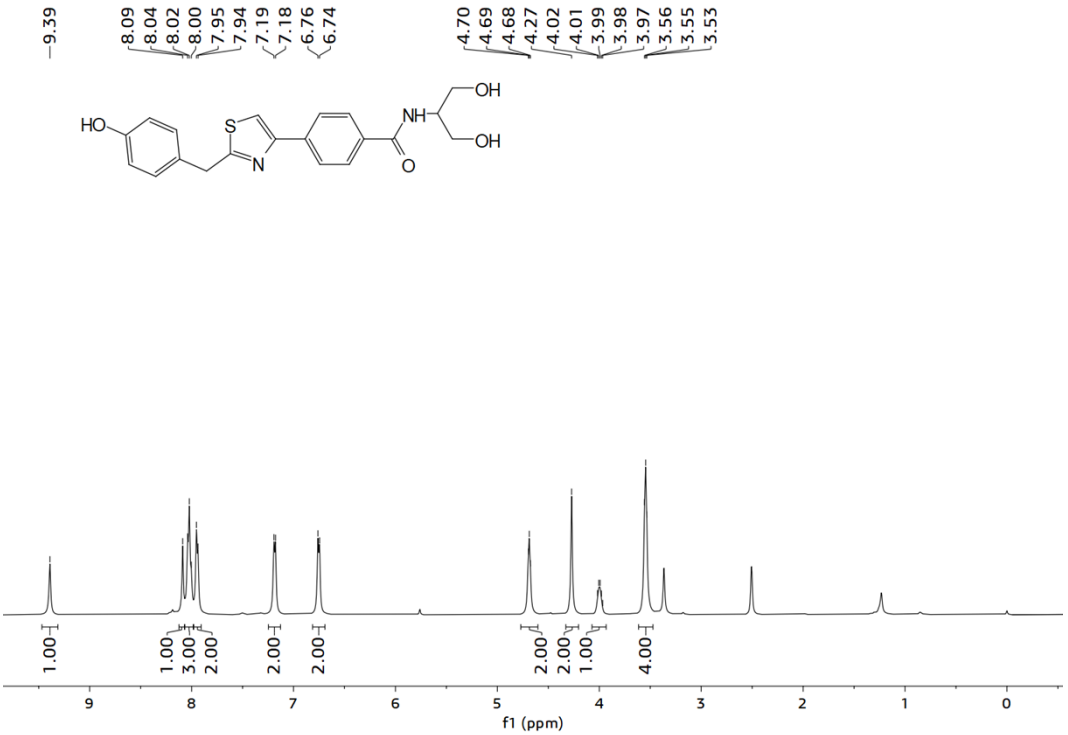


High resolution mass spectrum of **S10**

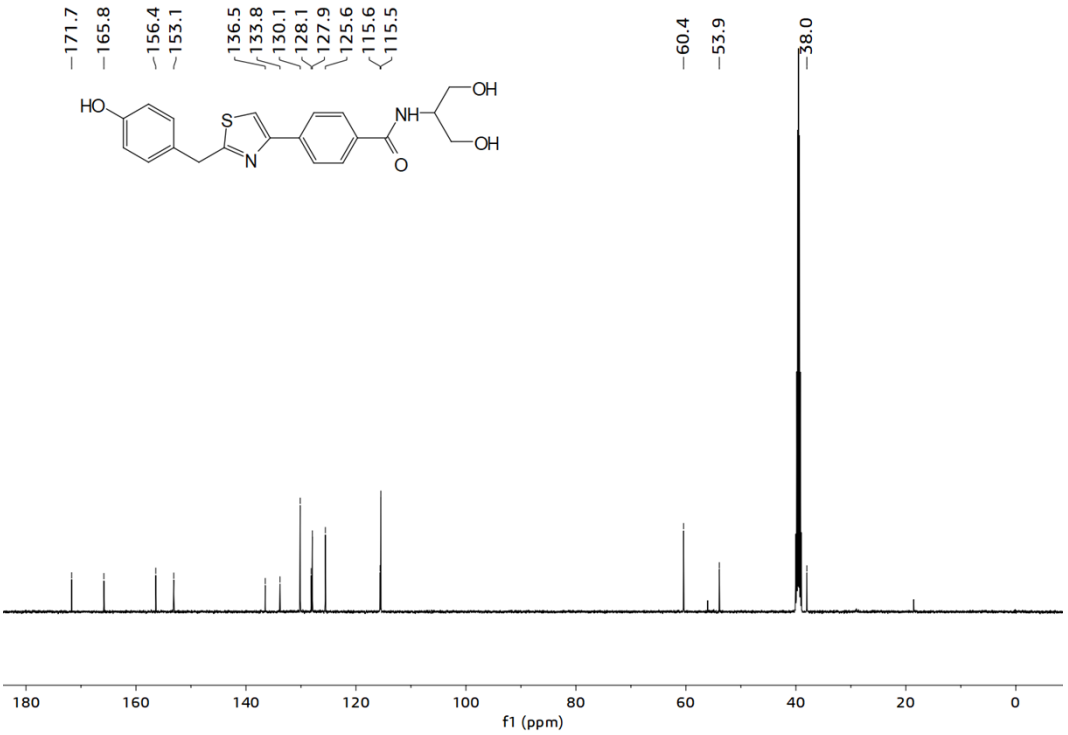


Compound **S11**:

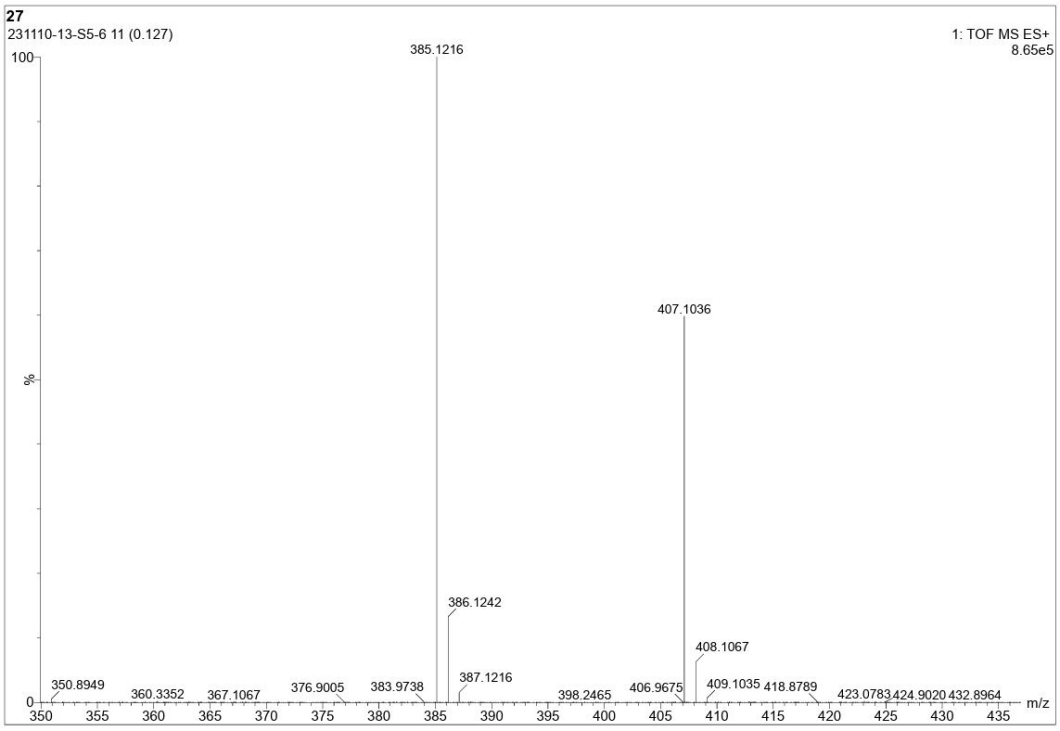
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

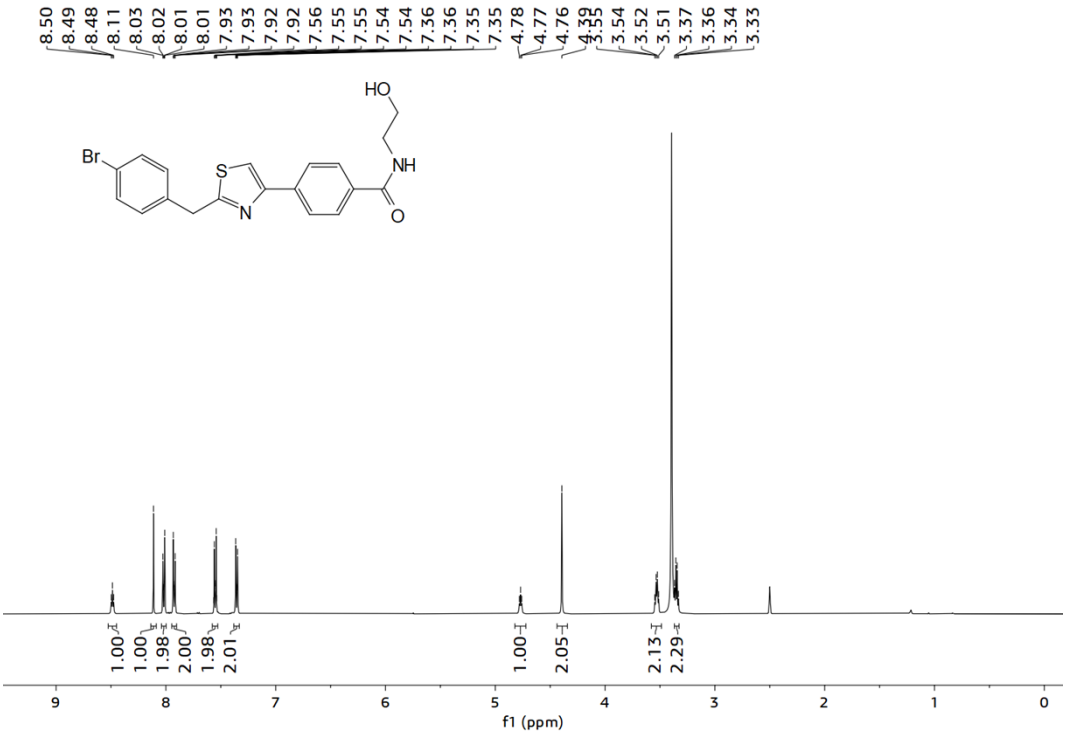


High resolution mass spectrum of **S11**

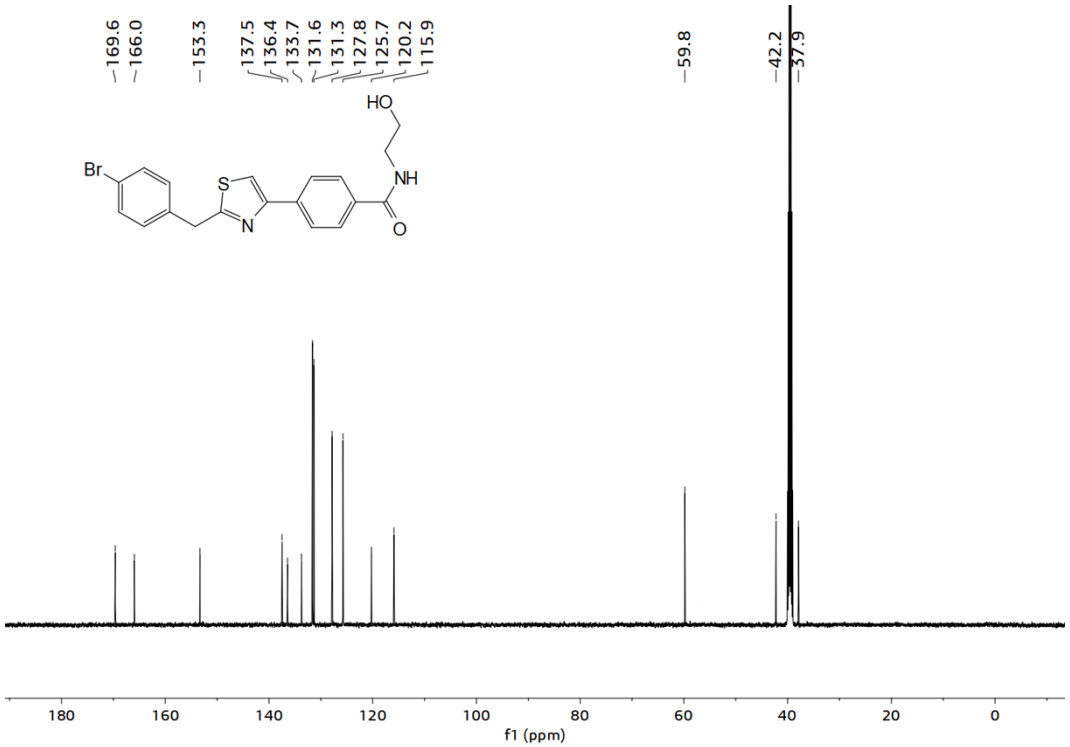


Compound **S12**:

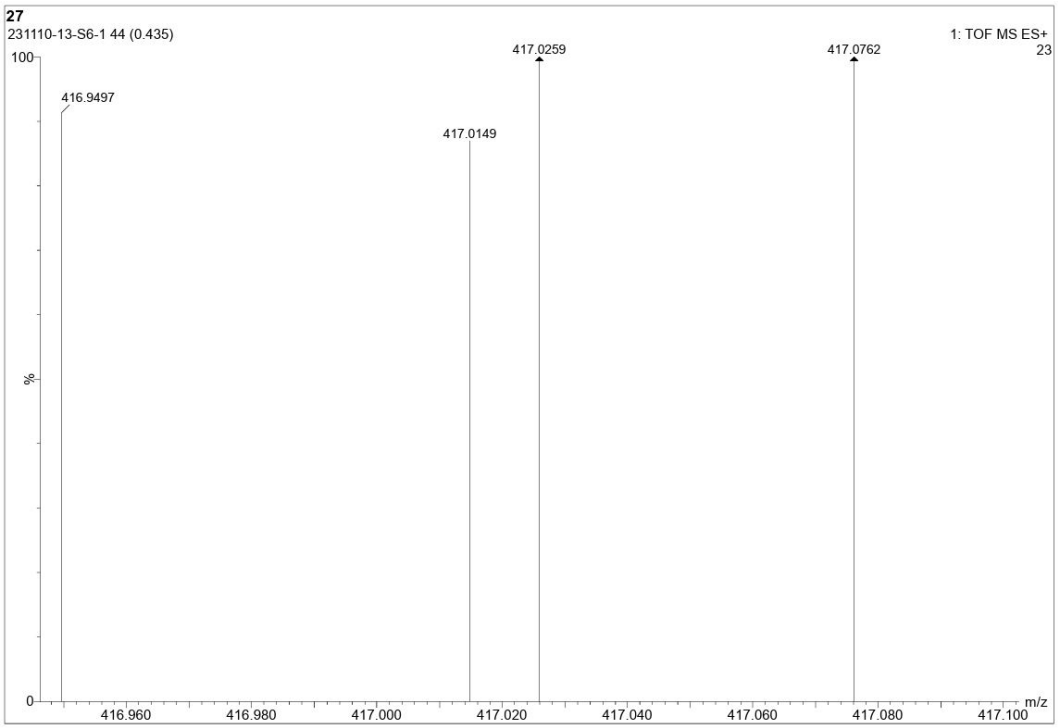
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

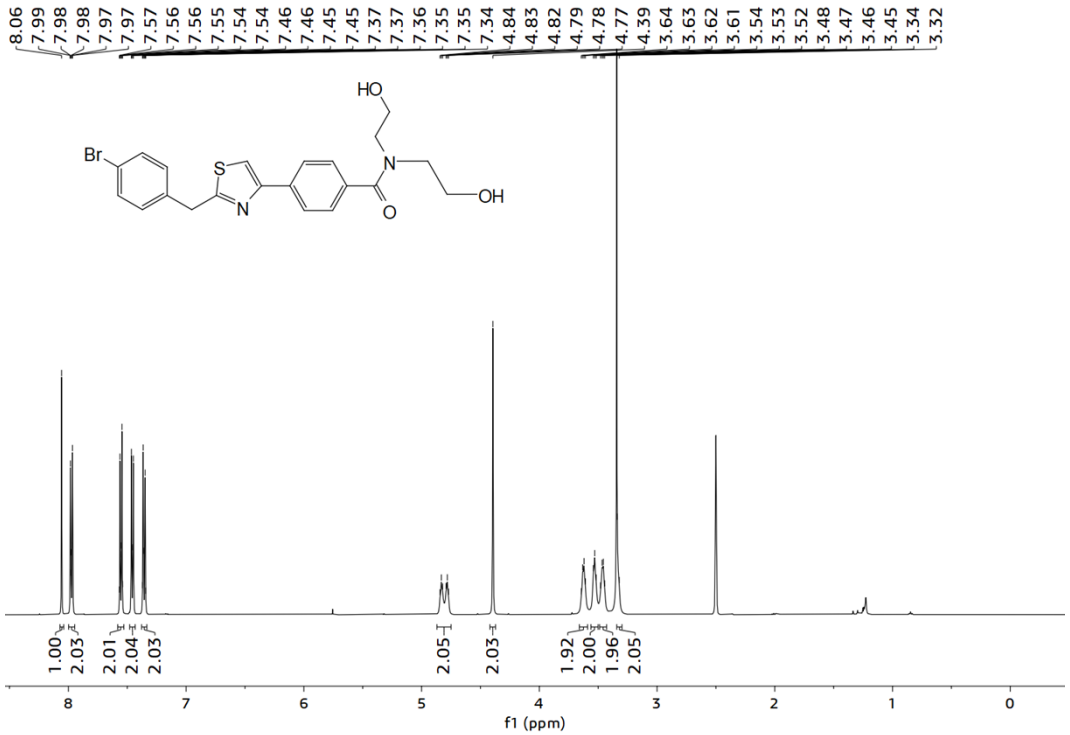


High resolution mass spectrum of **S12**

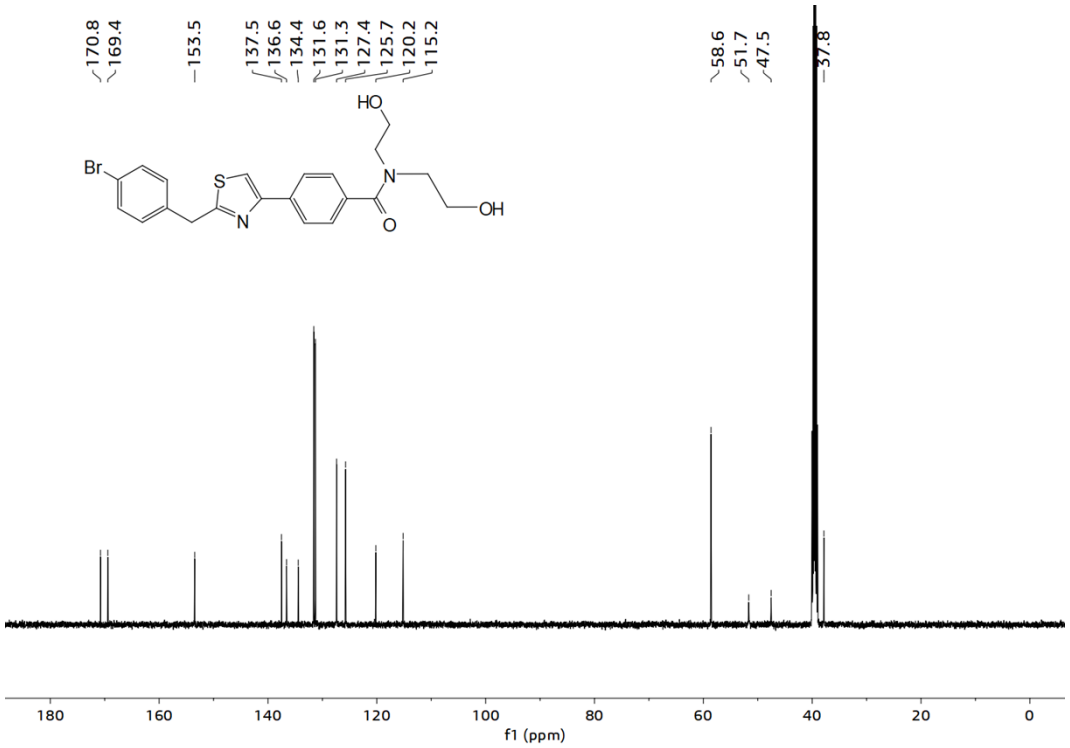


Compound **S13**:

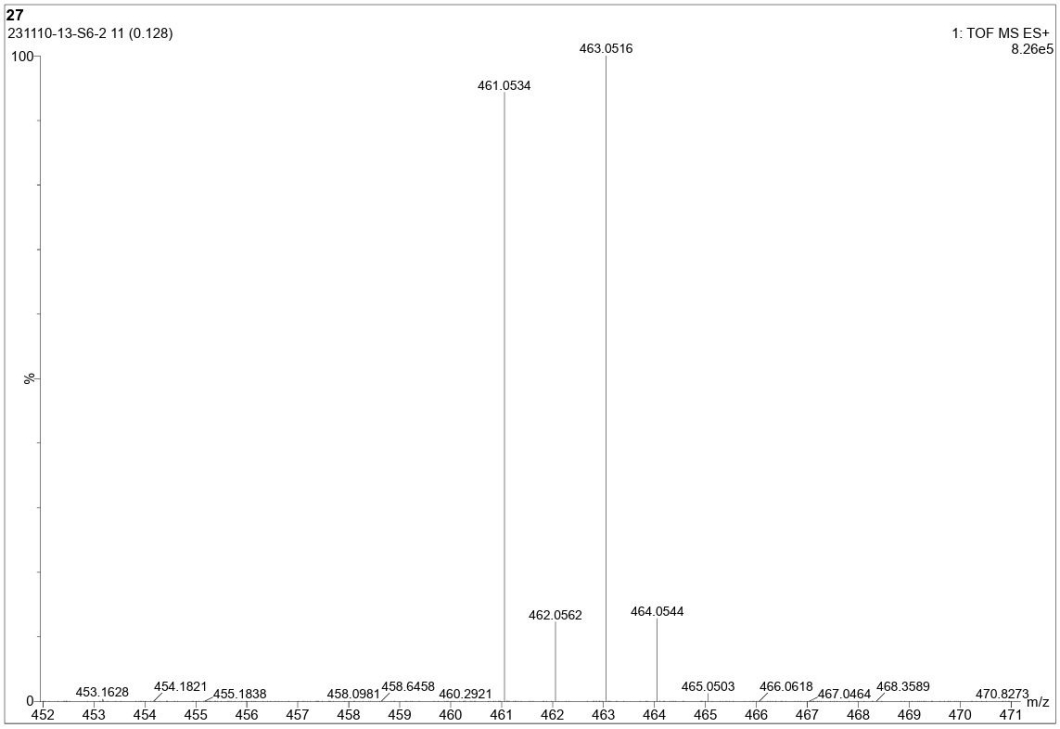
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

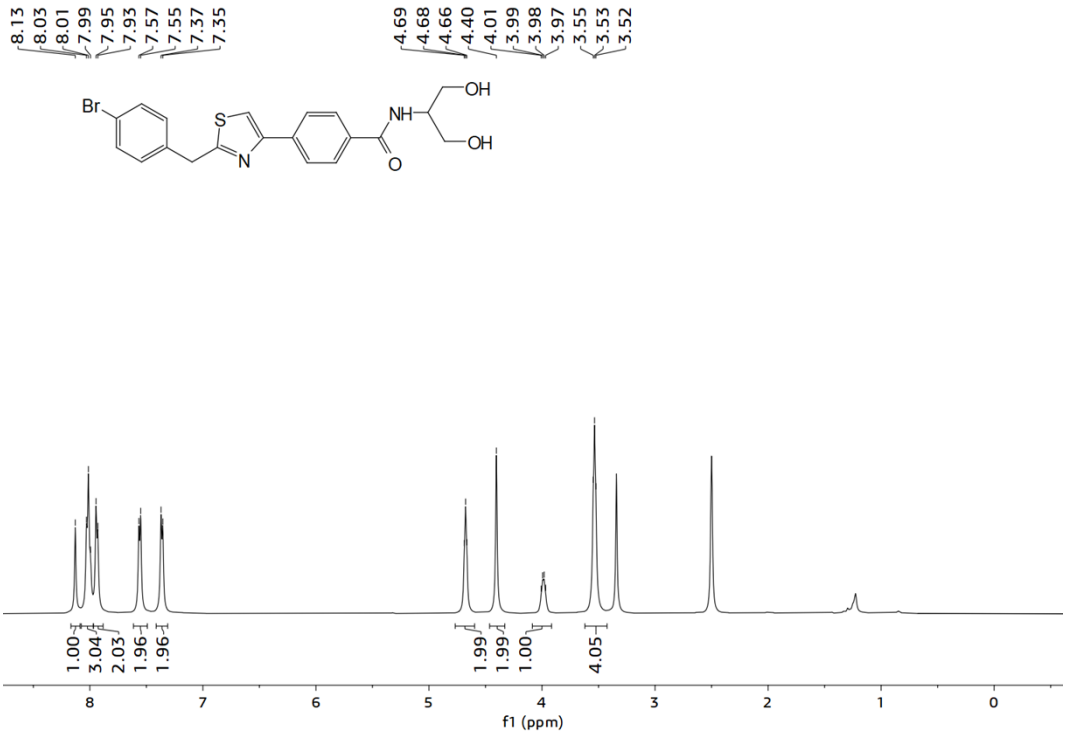


High resolution mass spectrum of **S13**

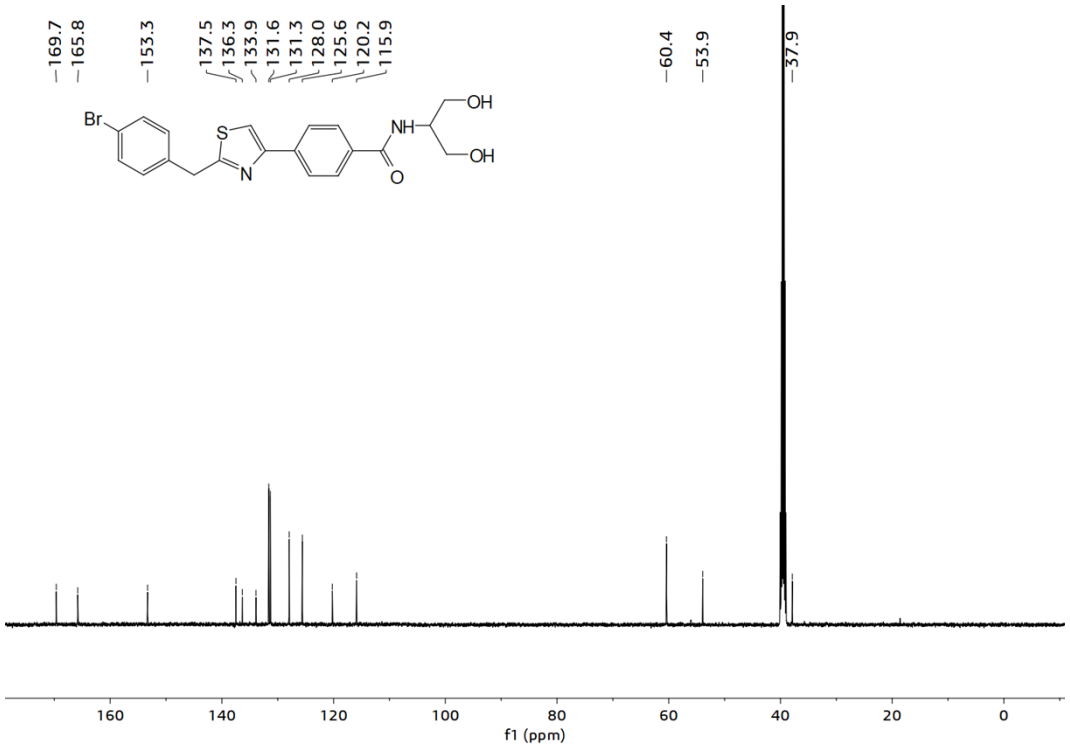


Compound **S14**:

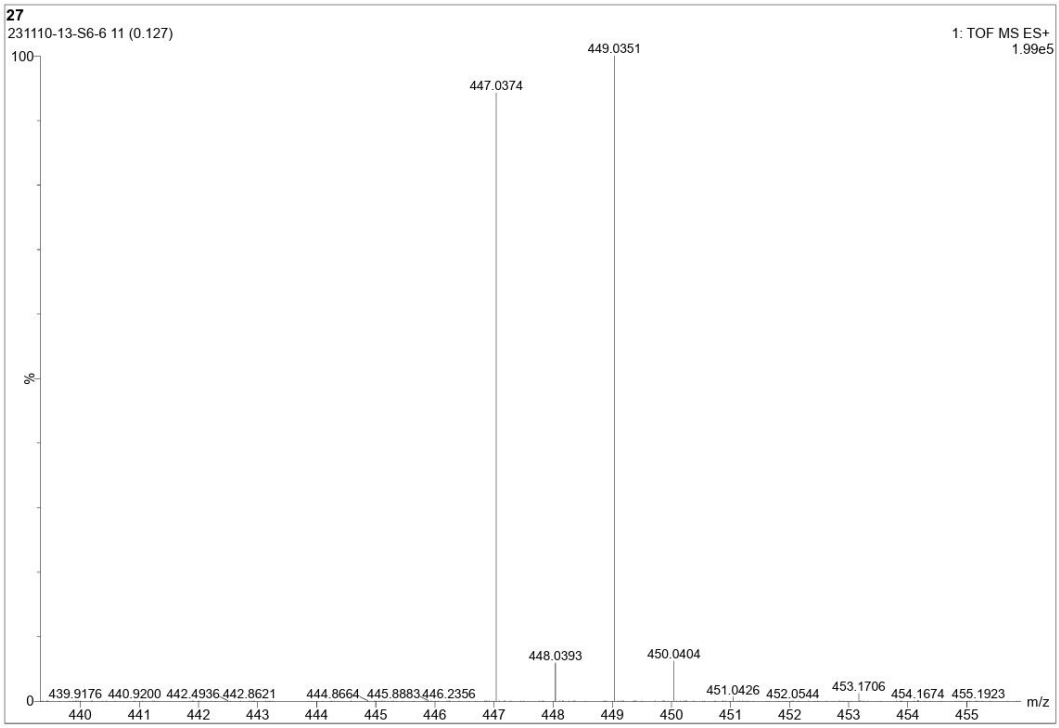
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

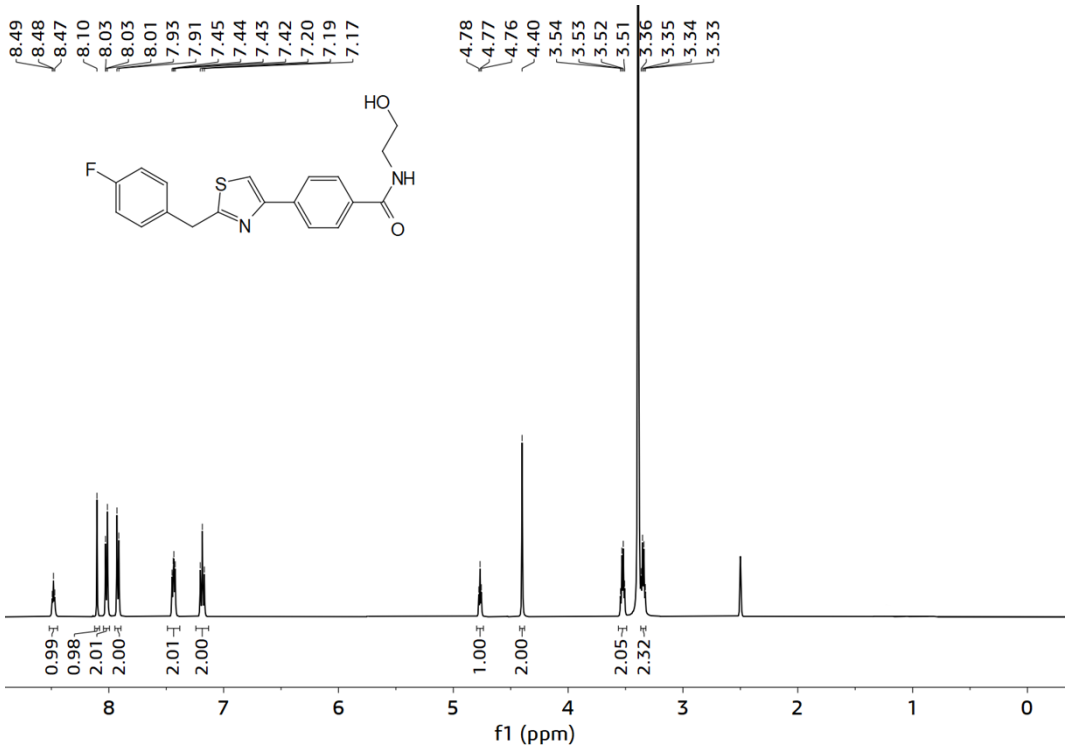


High resolution mass spectrum of **S14**

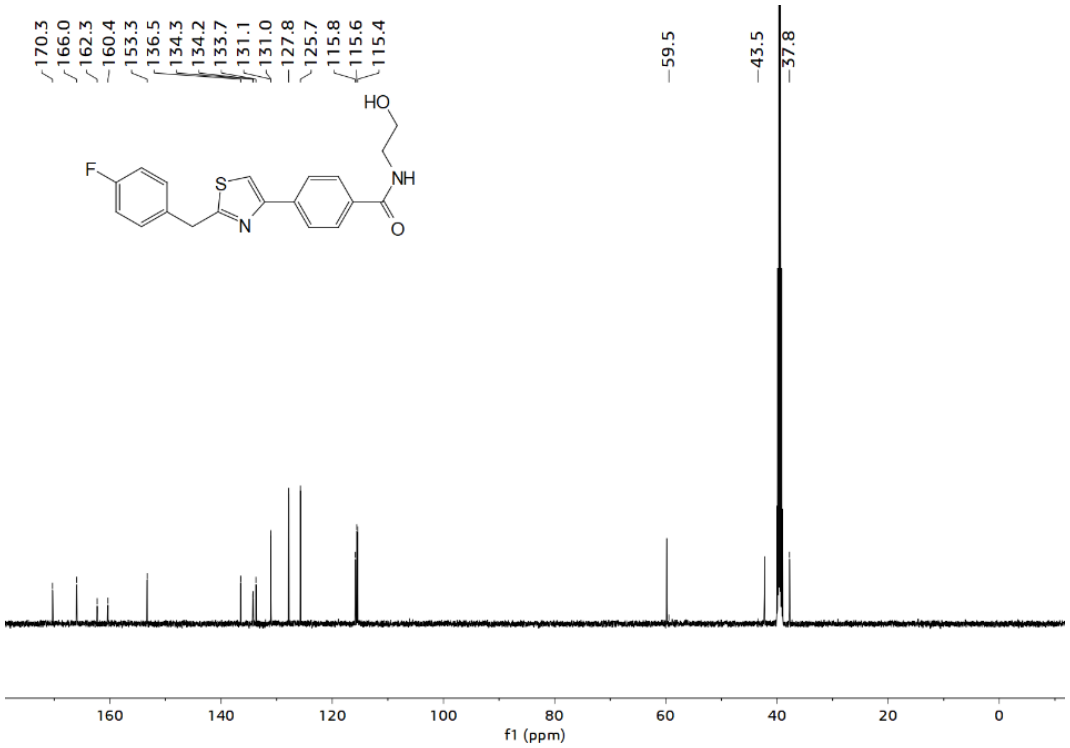


Compound **S15**:

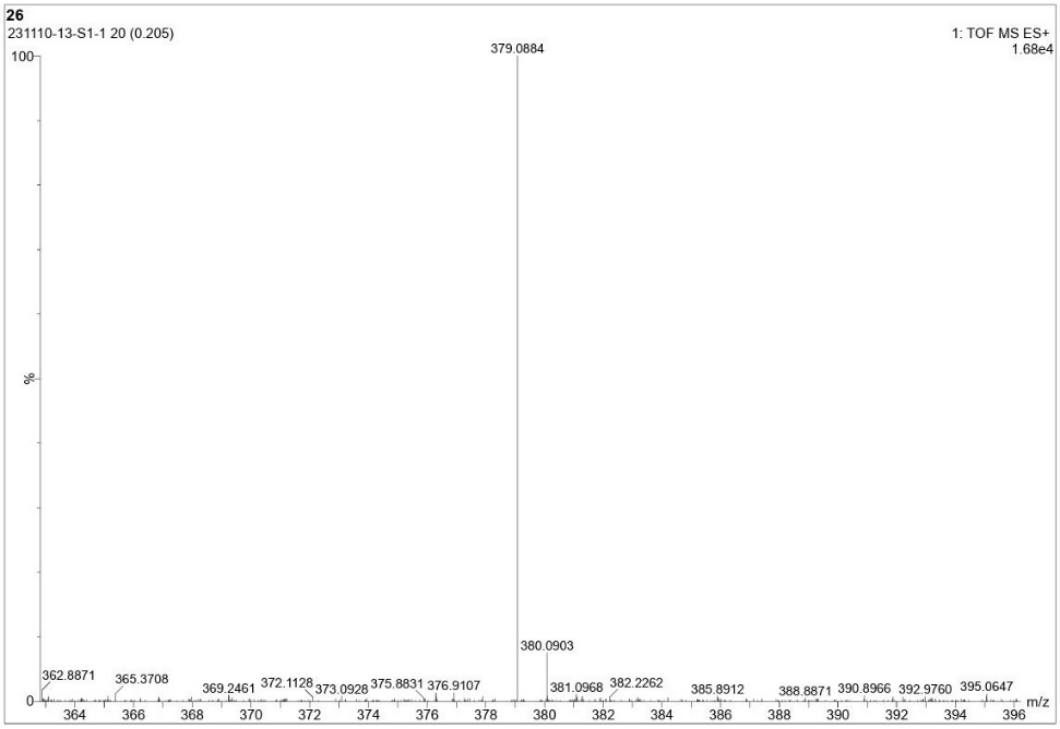
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

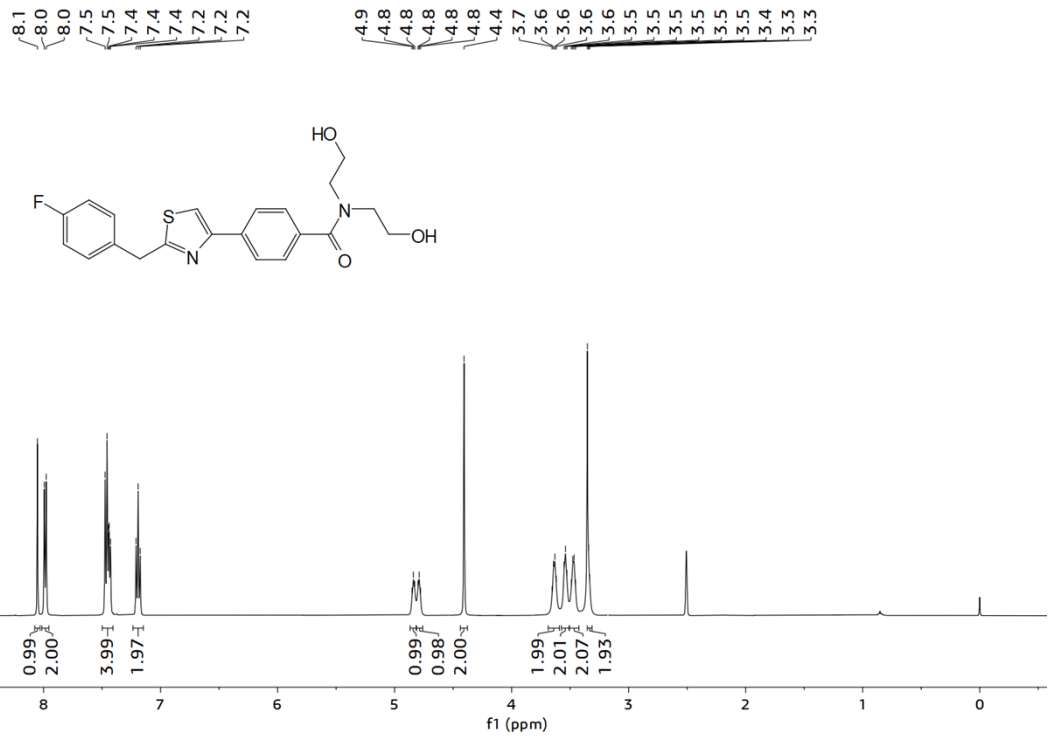


High resolution mass spectrum of **S15**

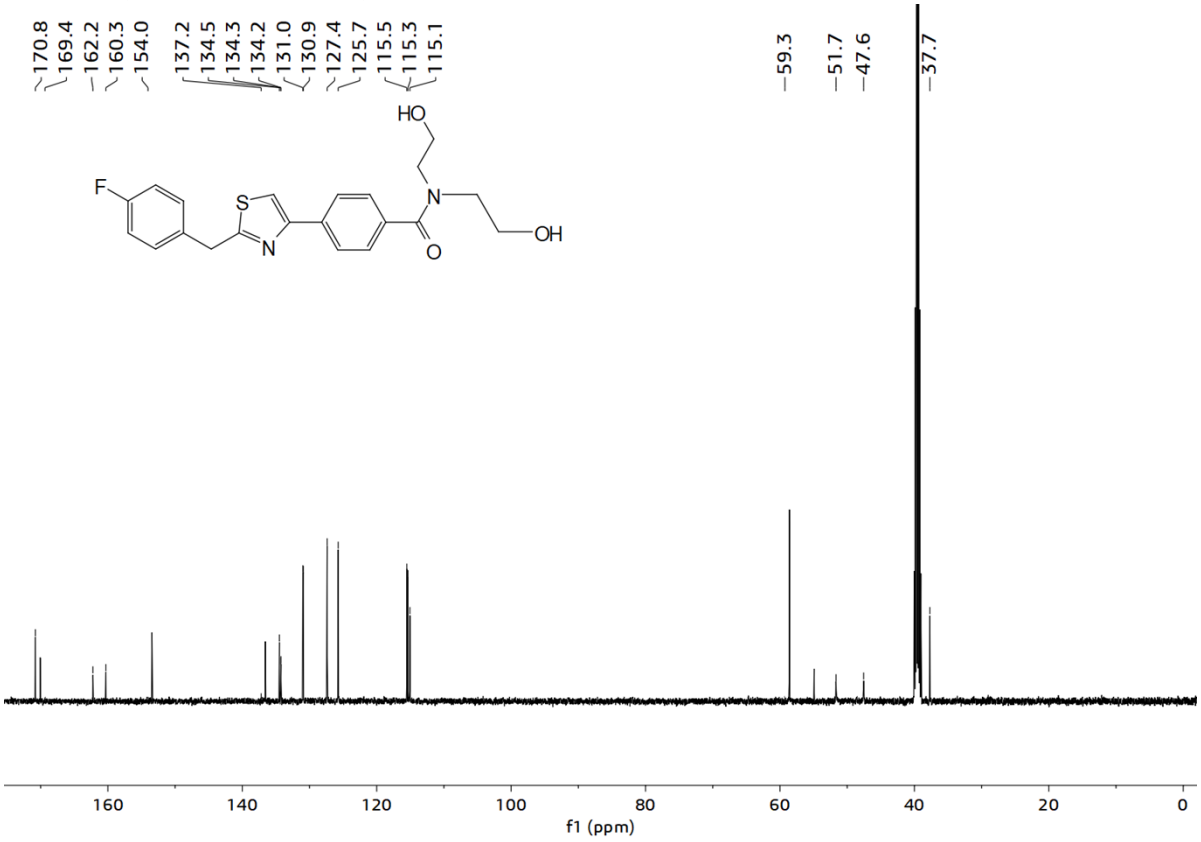


Compound **S16**:

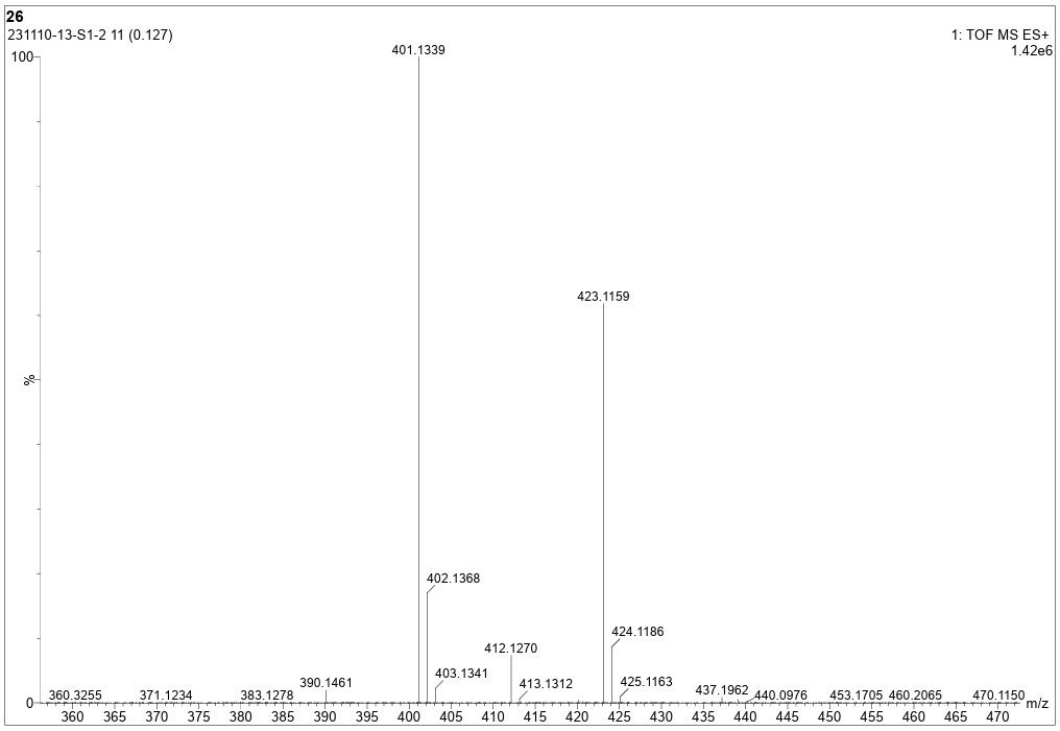
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

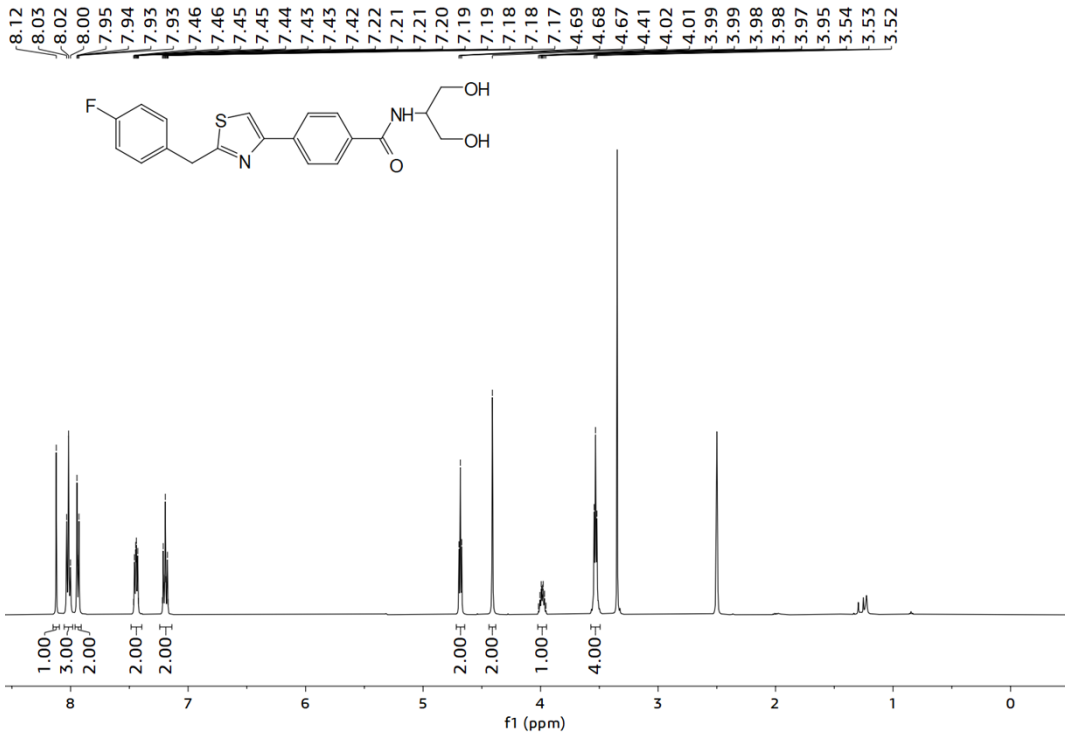


High resolution mass spectrum of **S16**

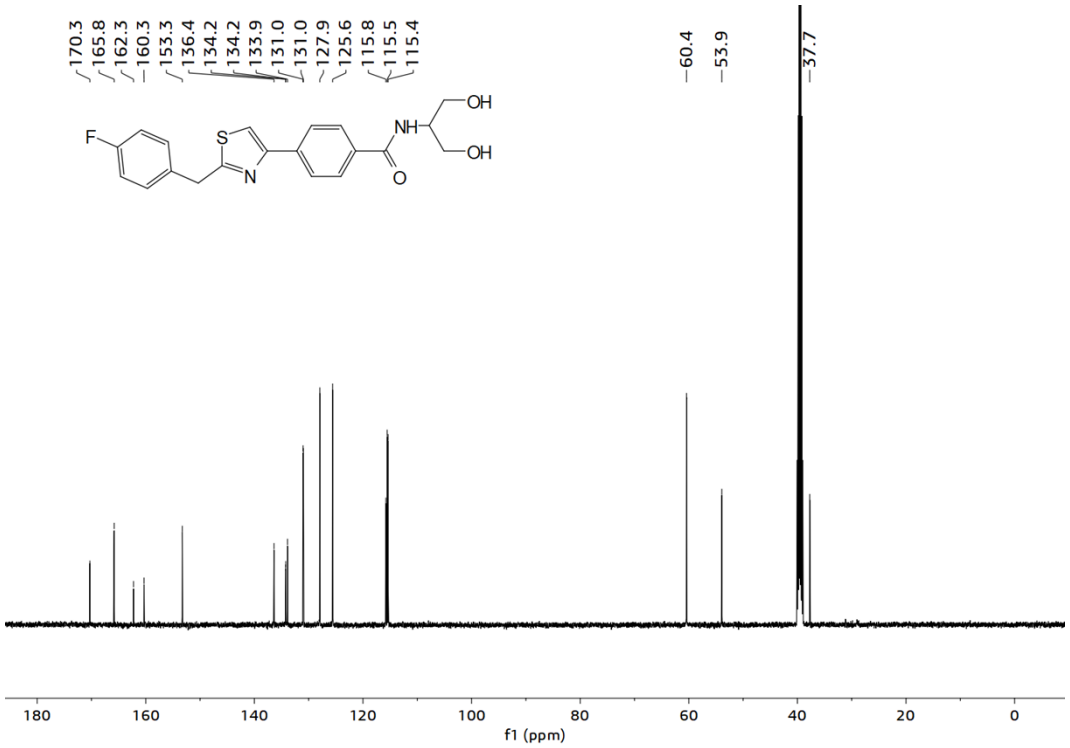


Compound **S17**:

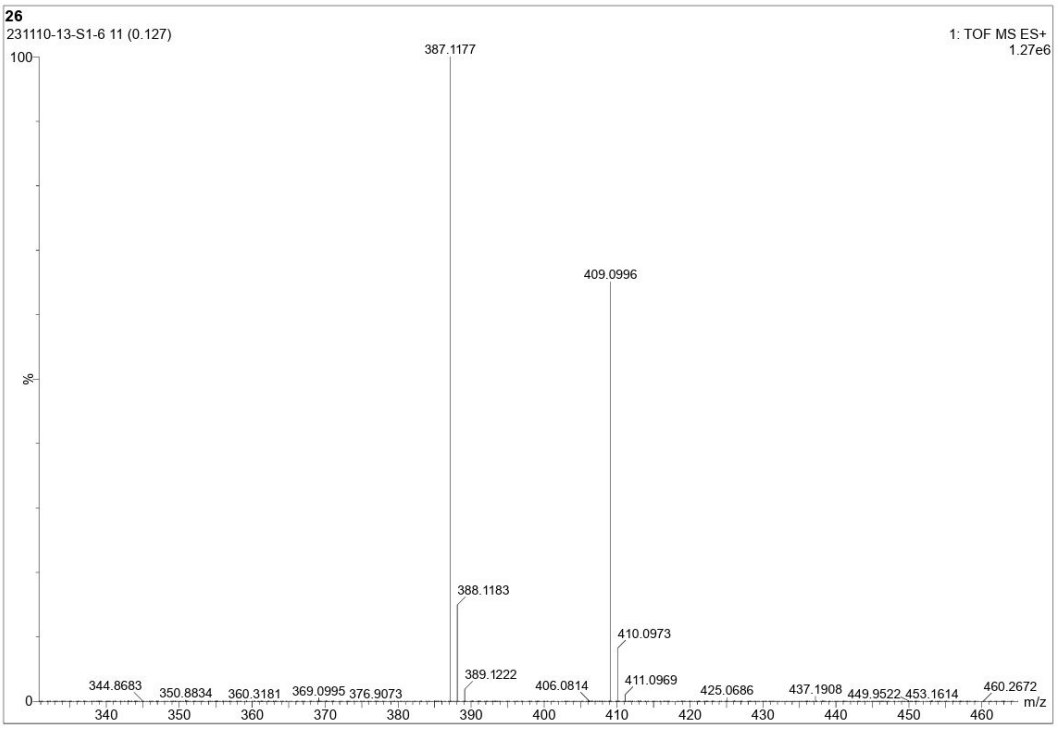
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

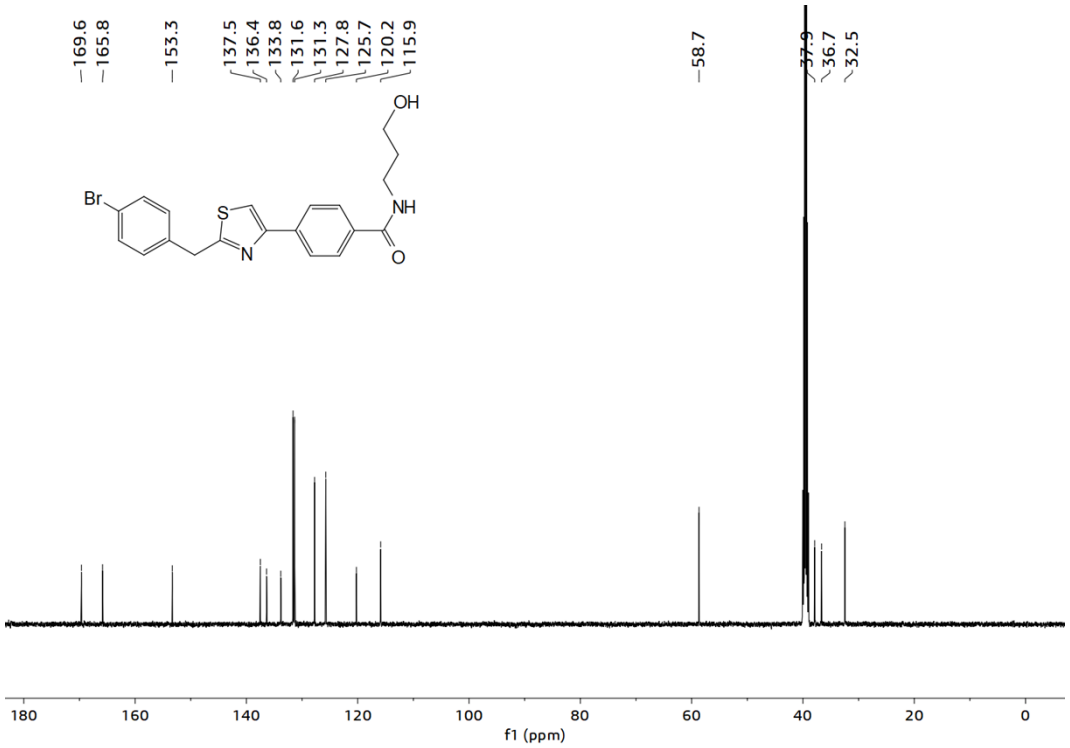


High resolution mass spectrum of **S17**

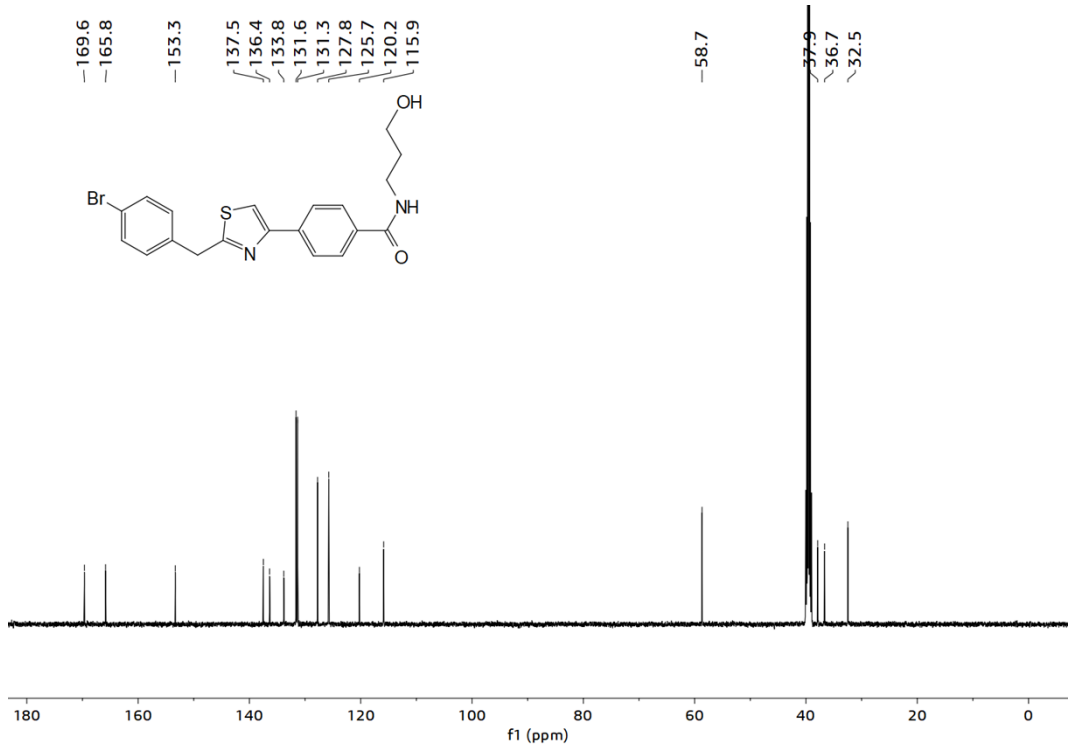


Compound **S18**:

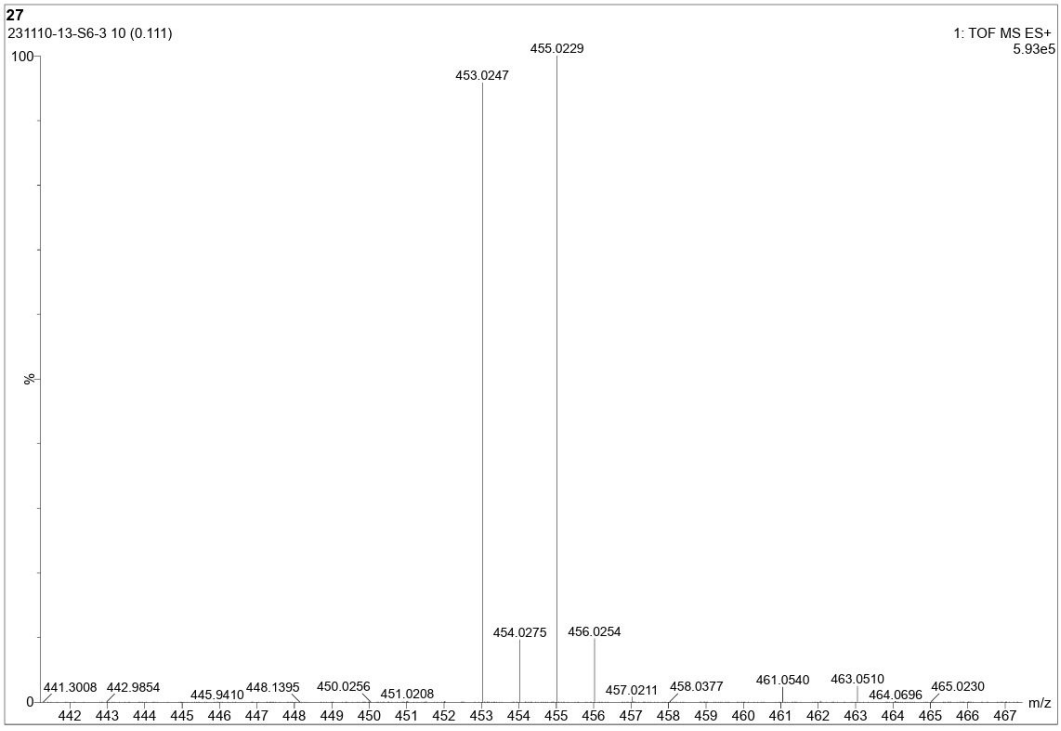
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

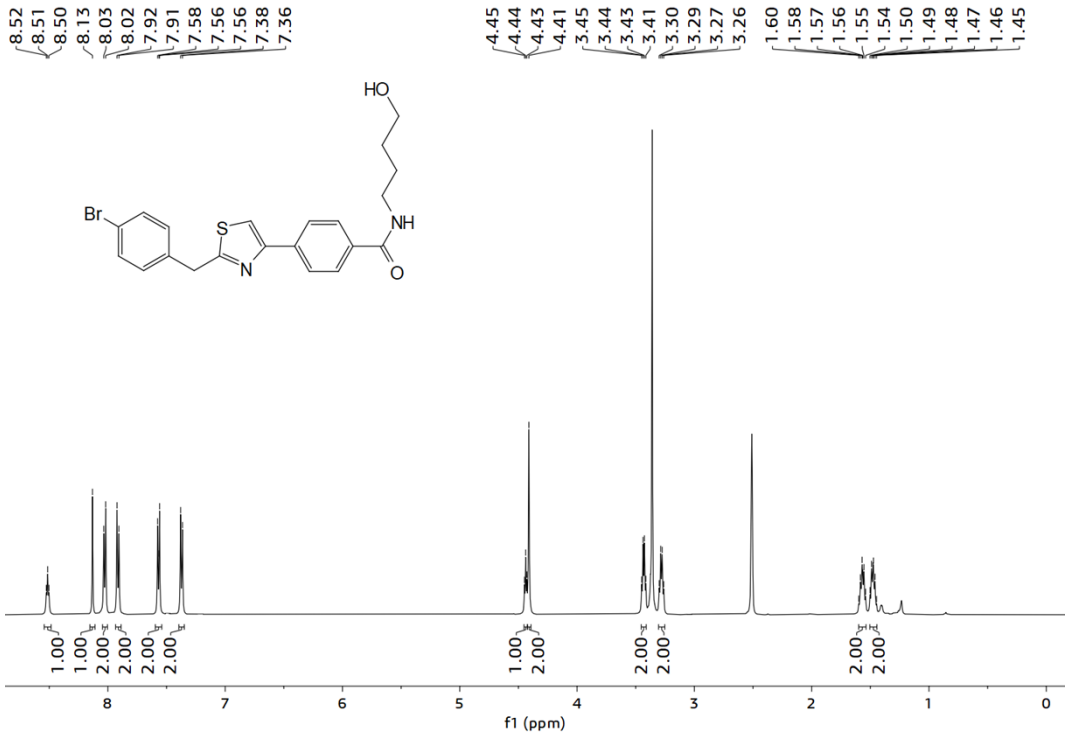


High resolution mass spectrum of **S18**

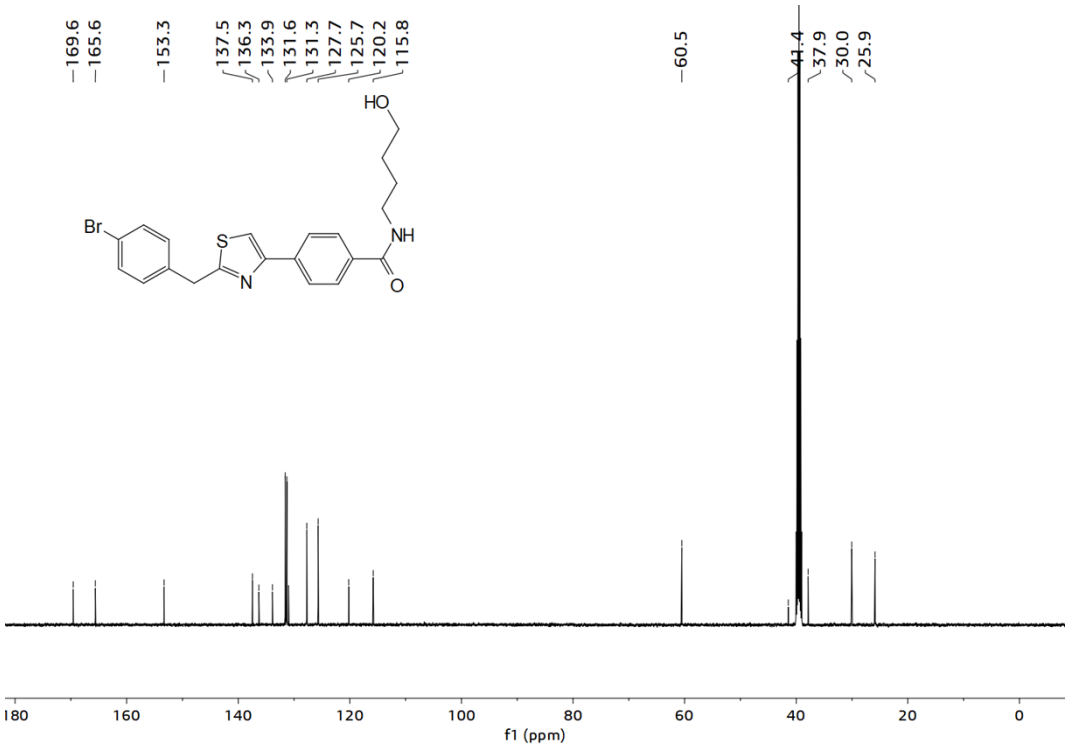


Compound **S19**:

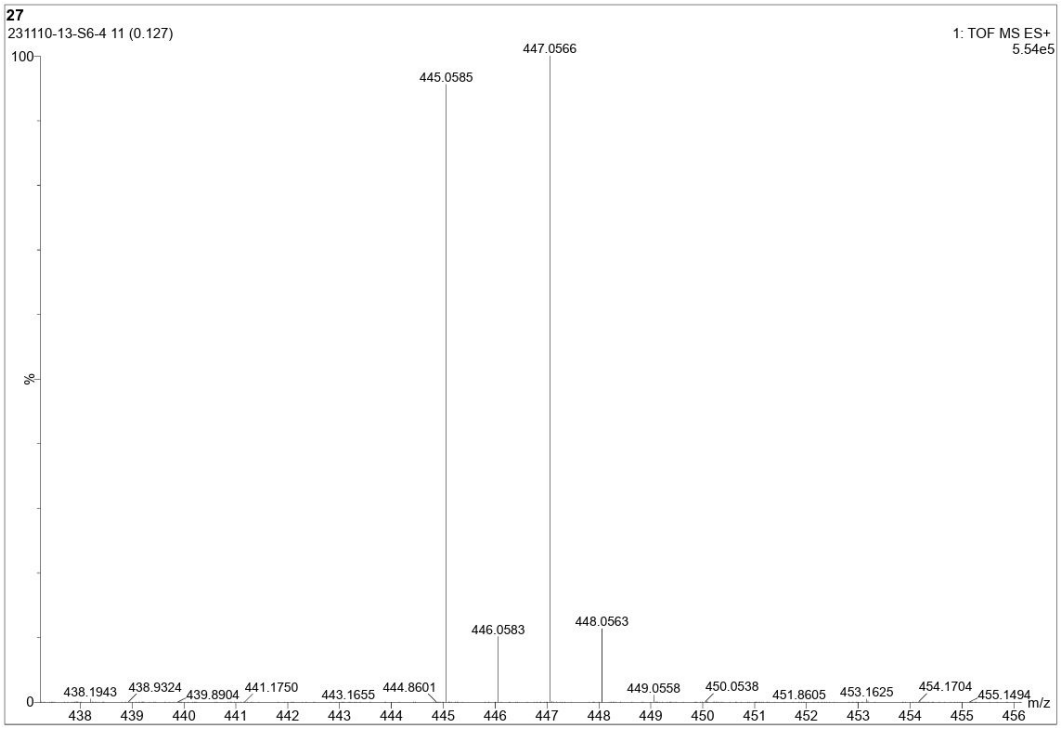
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

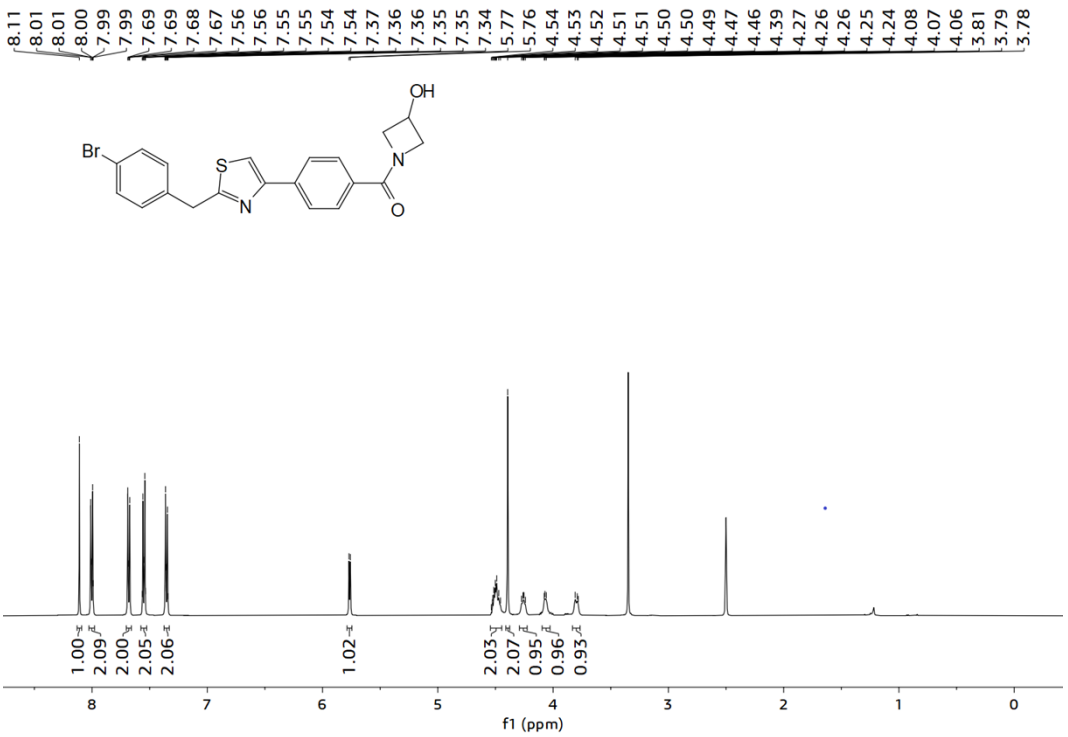


High resolution mass spectrum of **S19**

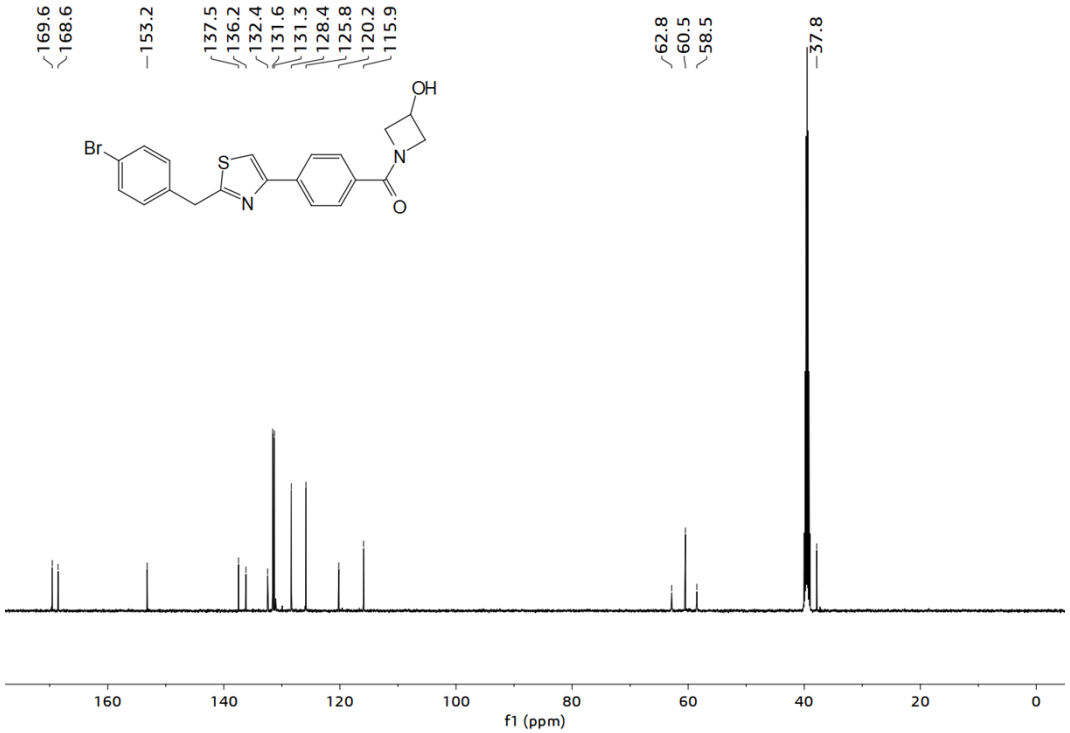


Compound **S20**:

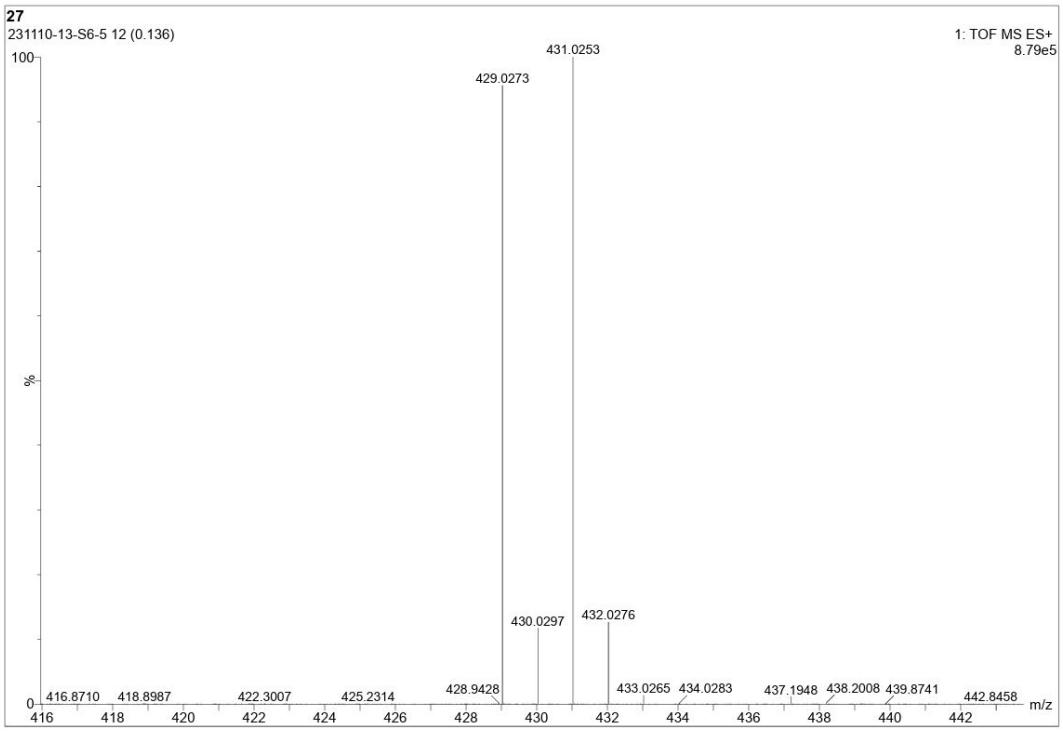
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

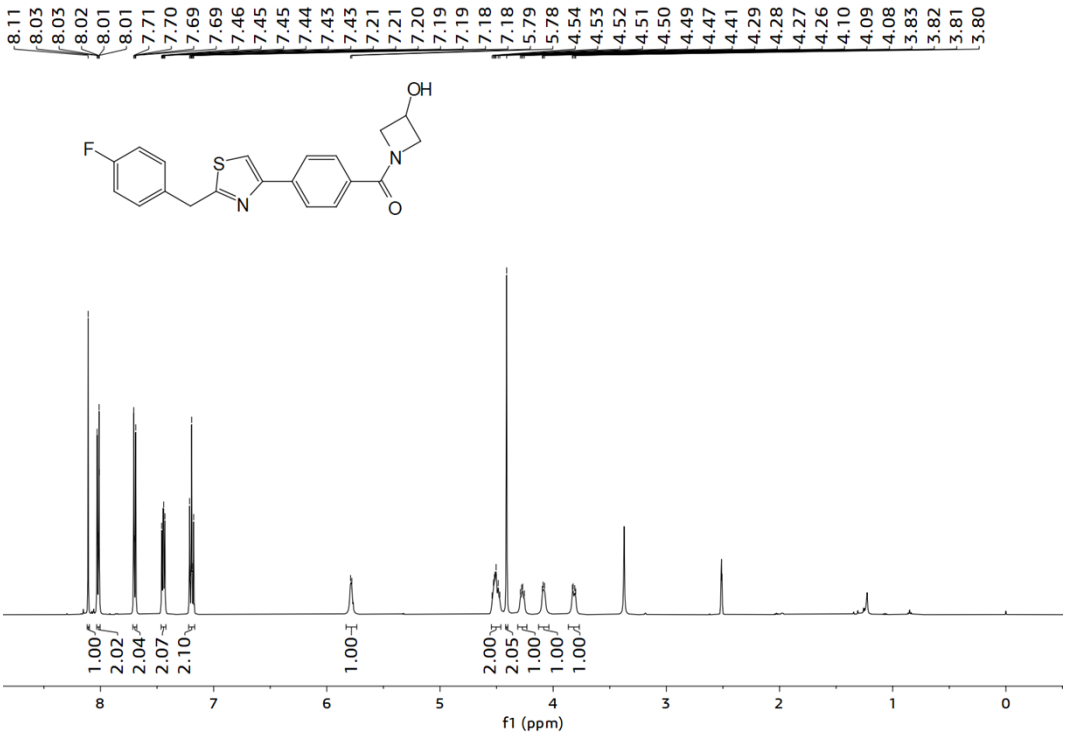


High resolution mass spectrum of **S20**

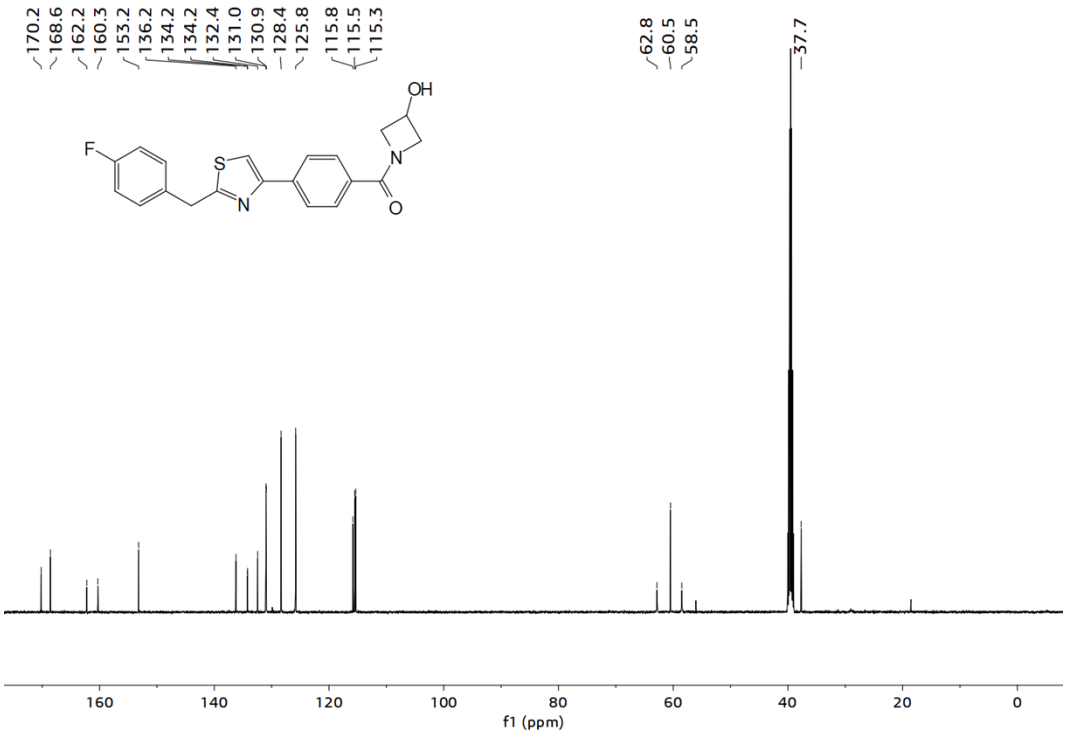


Compound **S21**:

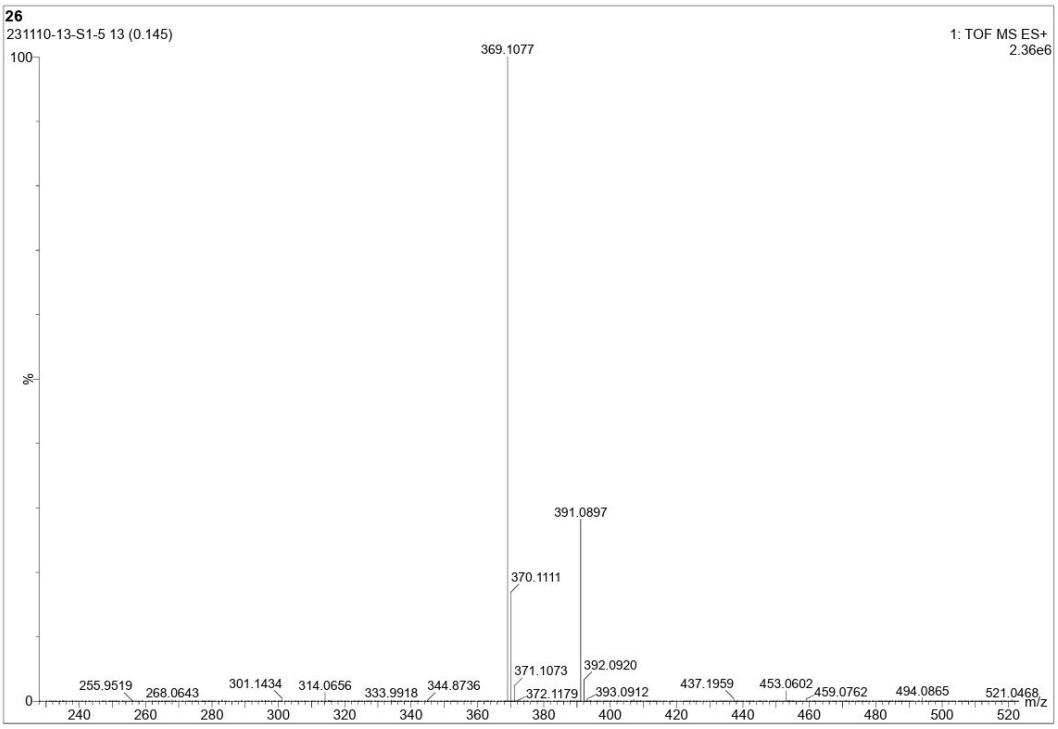
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

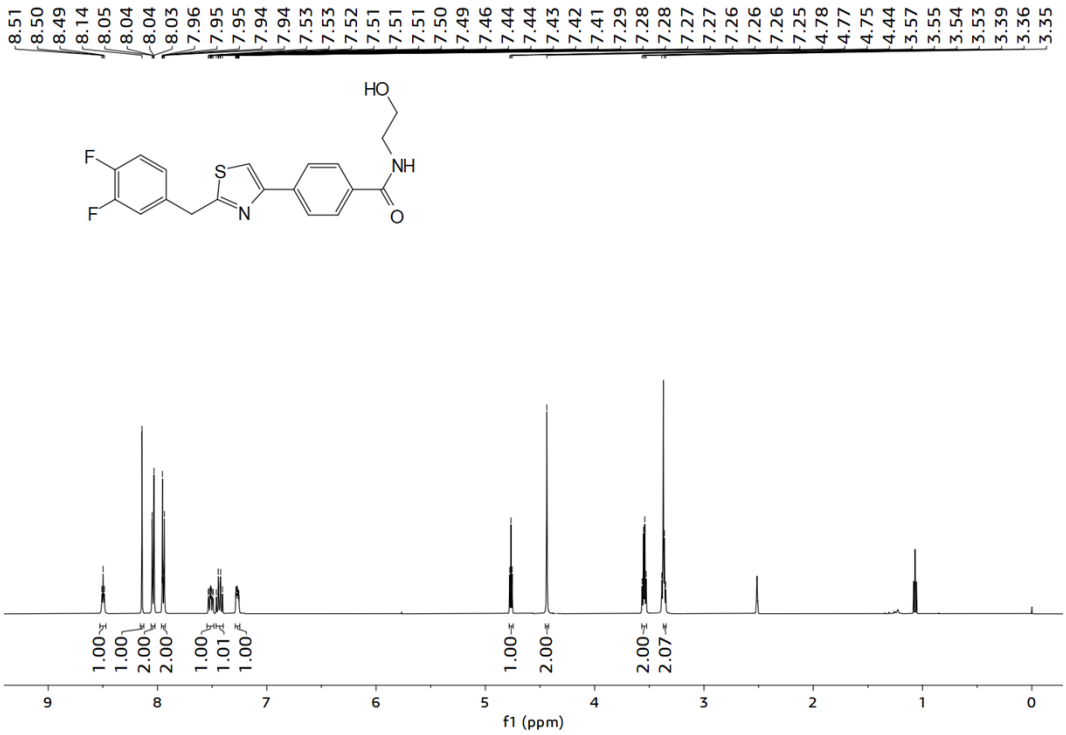


High resolution mass spectrum of **S21**

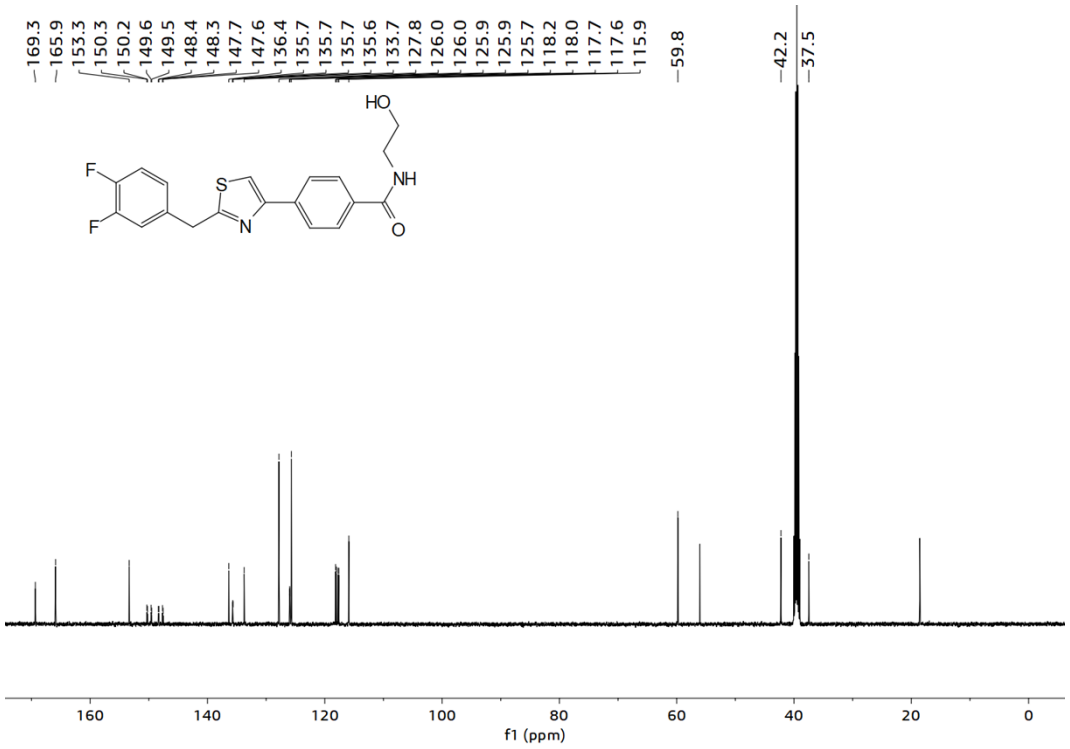


Compound **S22**:

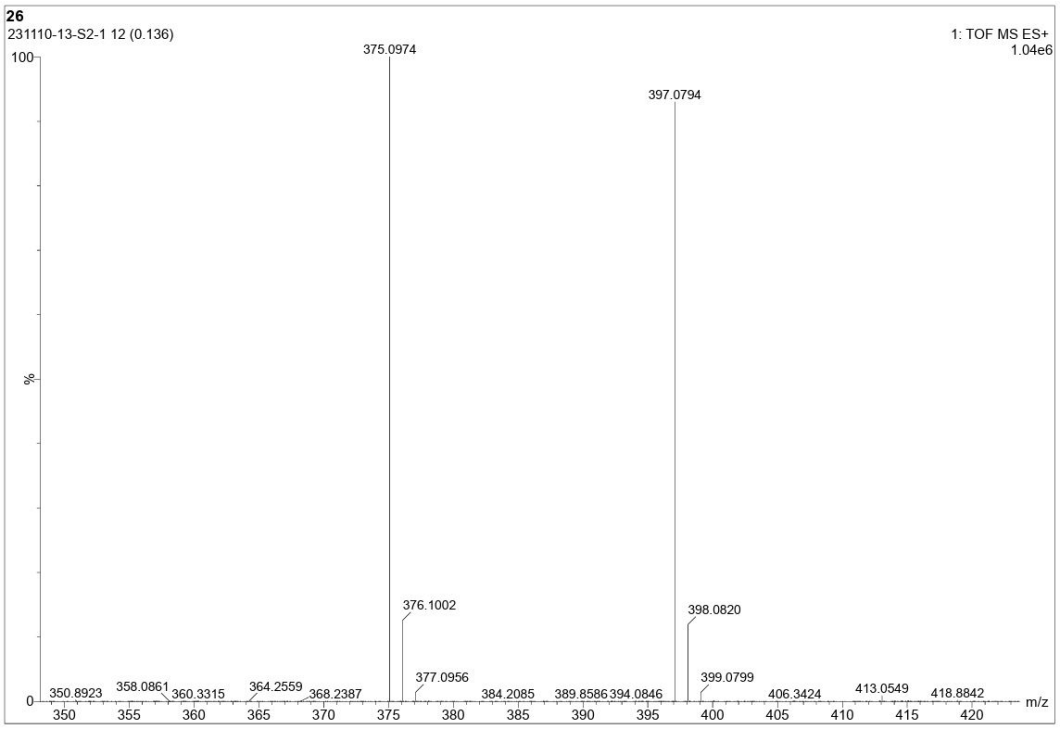
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

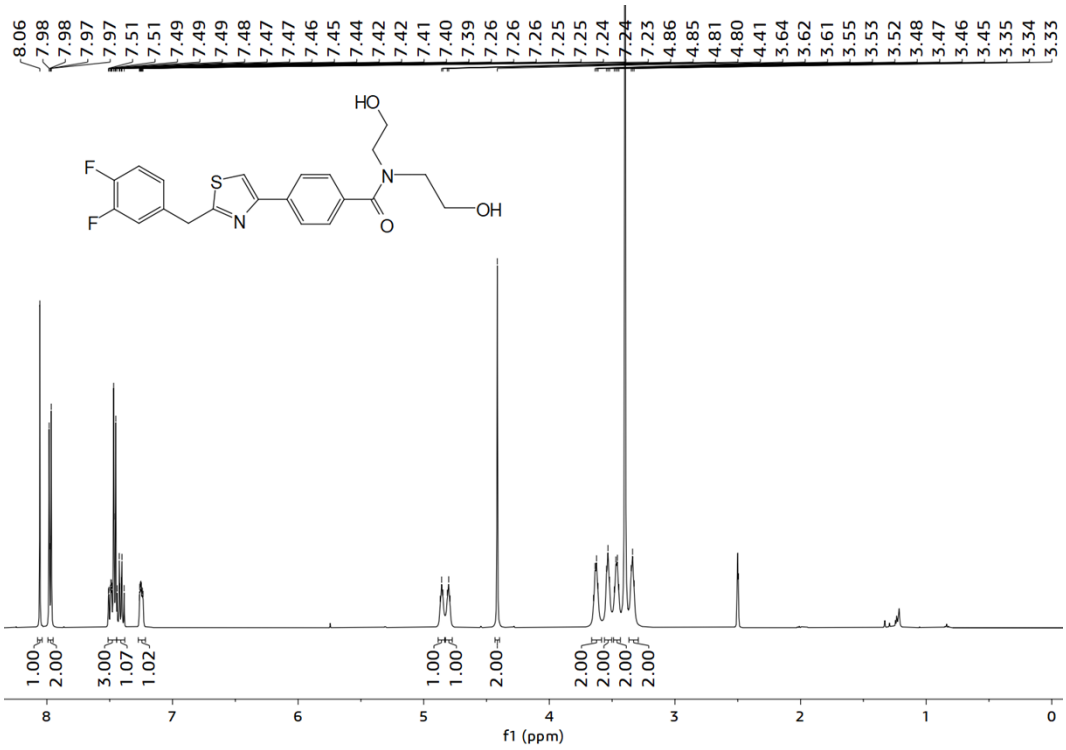


High resolution mass spectrum of **S22**

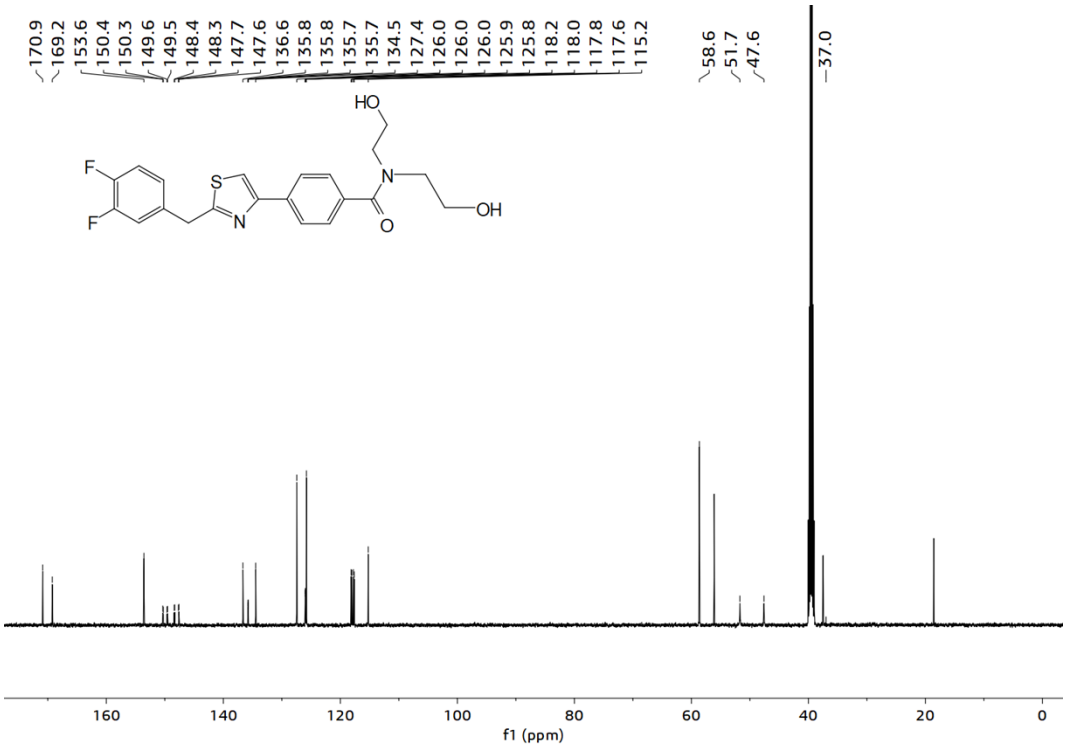


Compound **S23**:

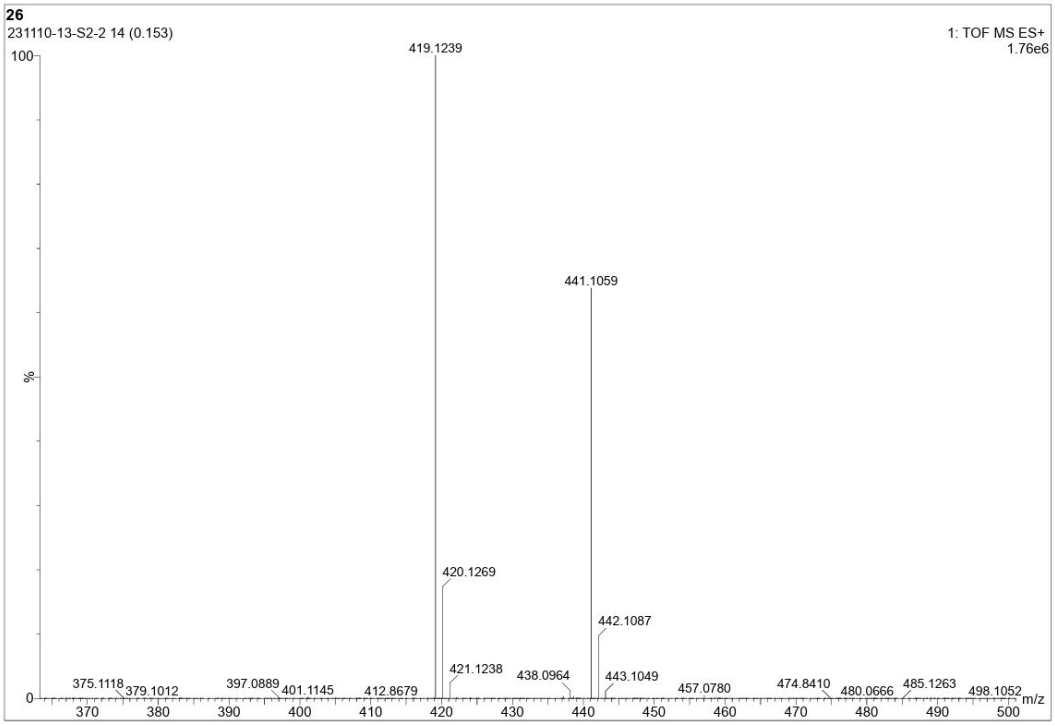
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

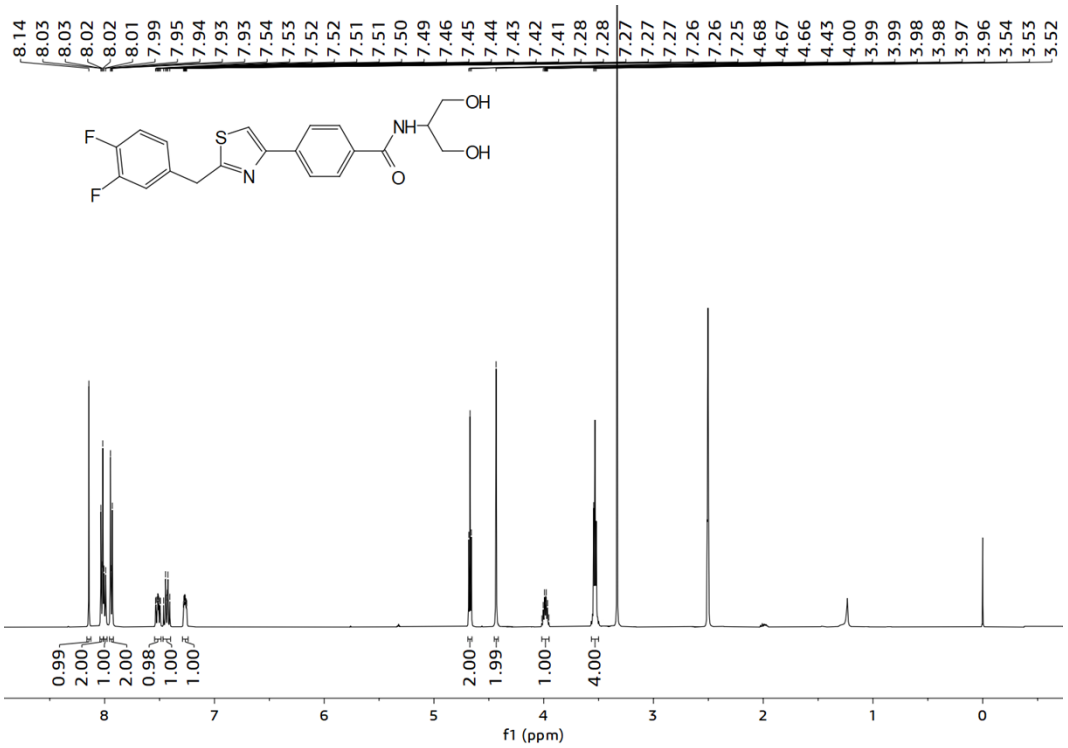


High resolution mass spectrum of **S23**

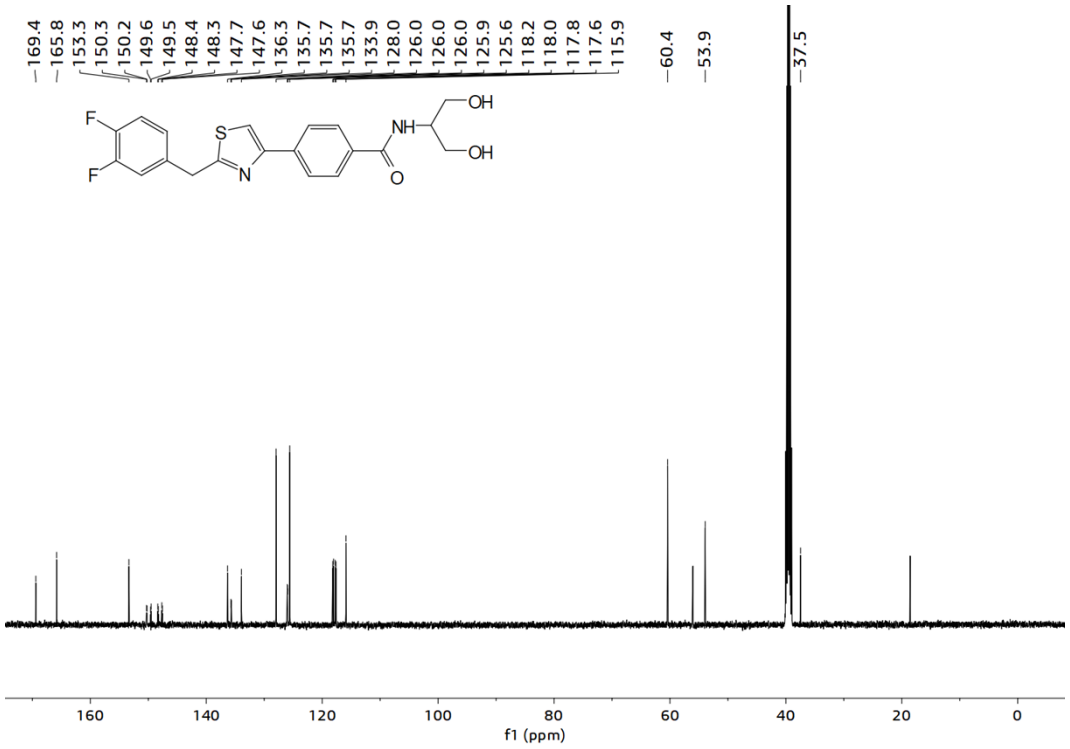


Compound **S24**:

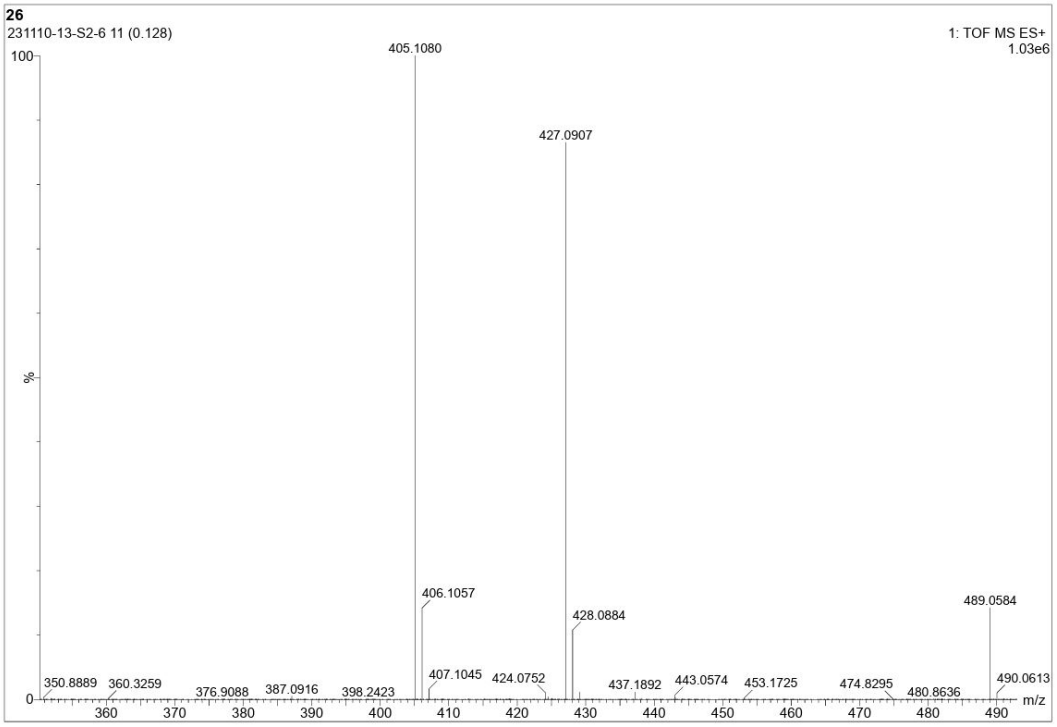
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

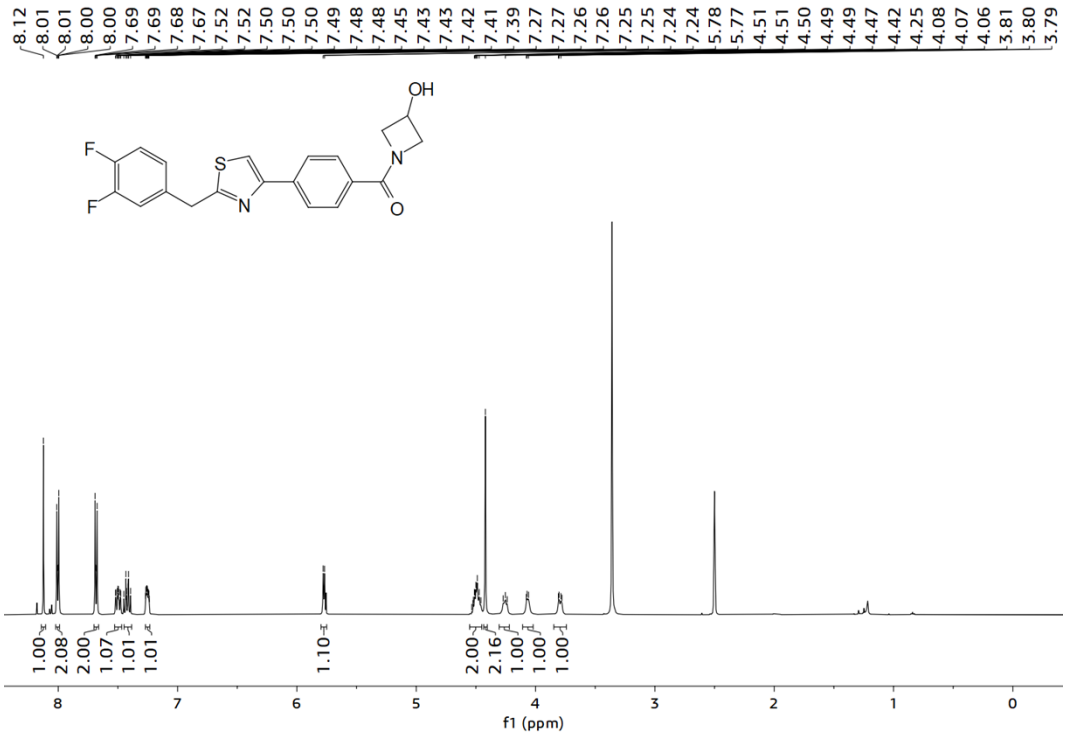


High resolution mass spectrum of **S24**

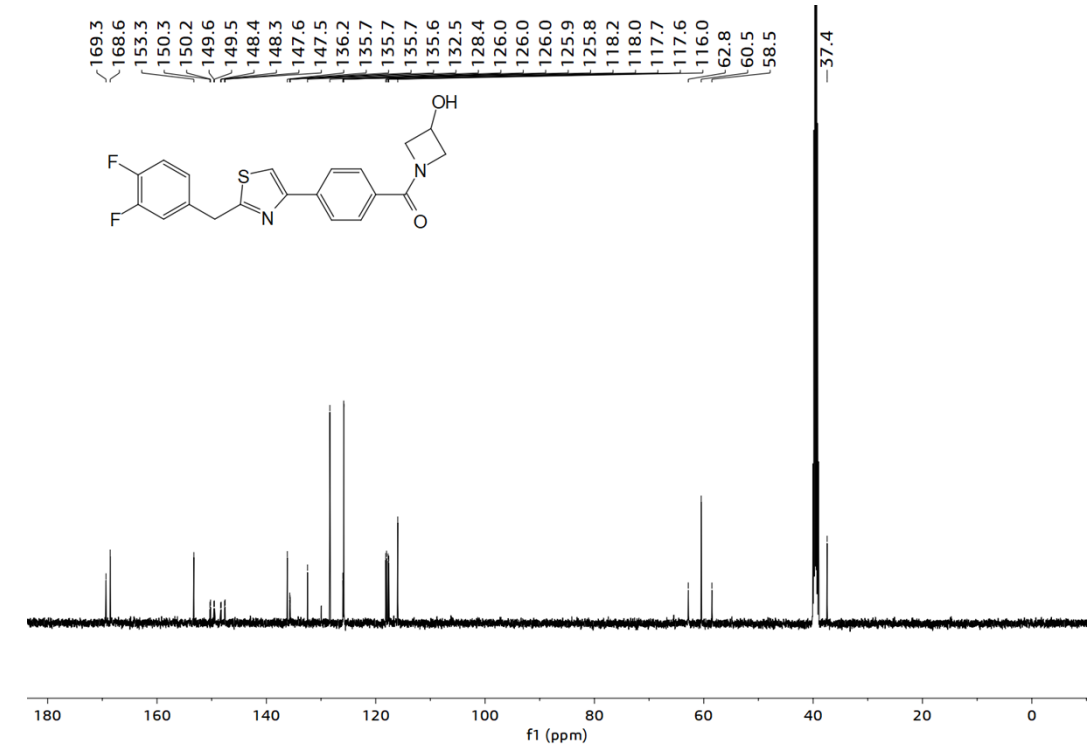


Compound **S25**:

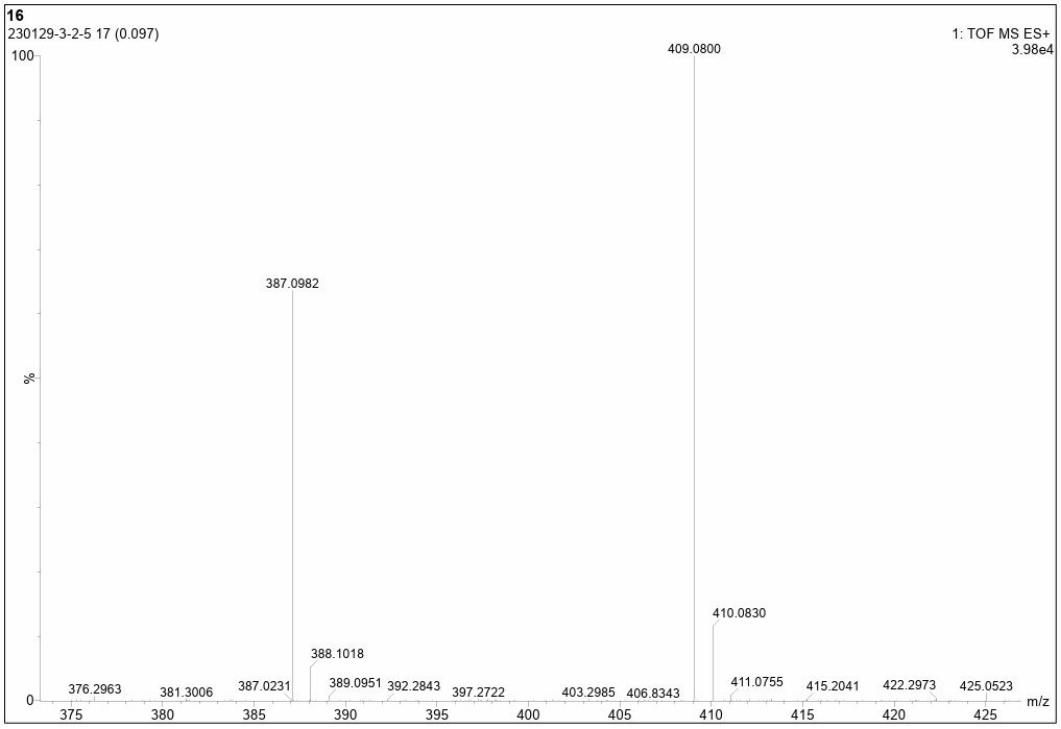
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

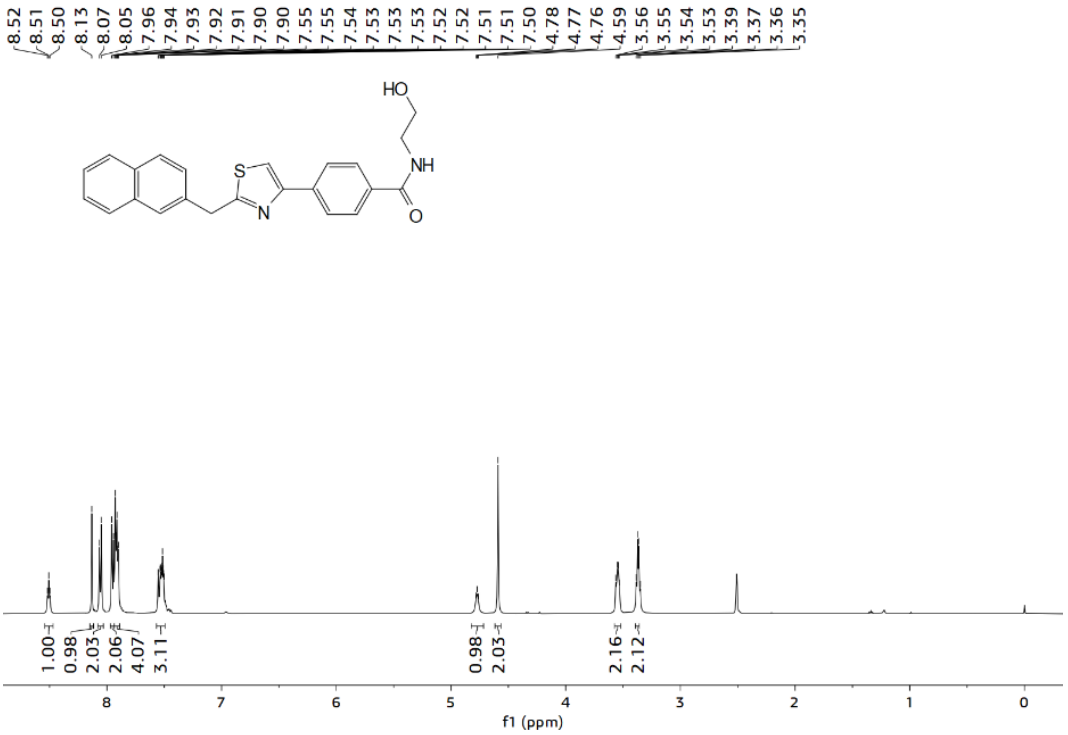


High resolution mass spectrum of **S25**

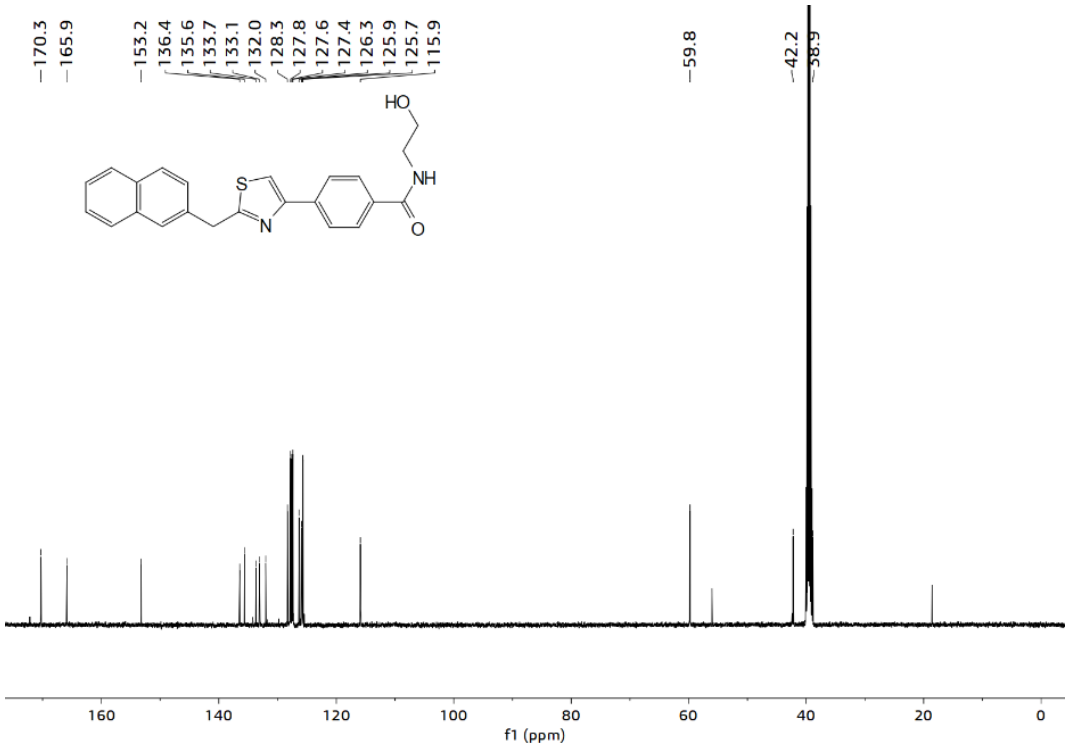


Compound **S26**:

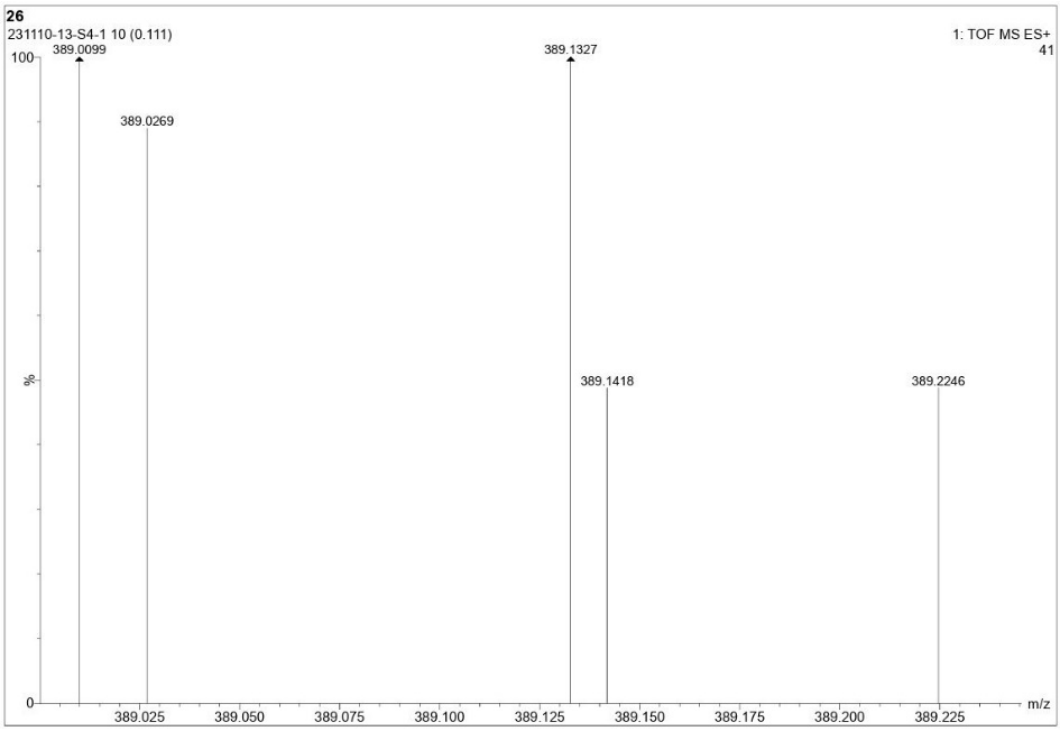
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

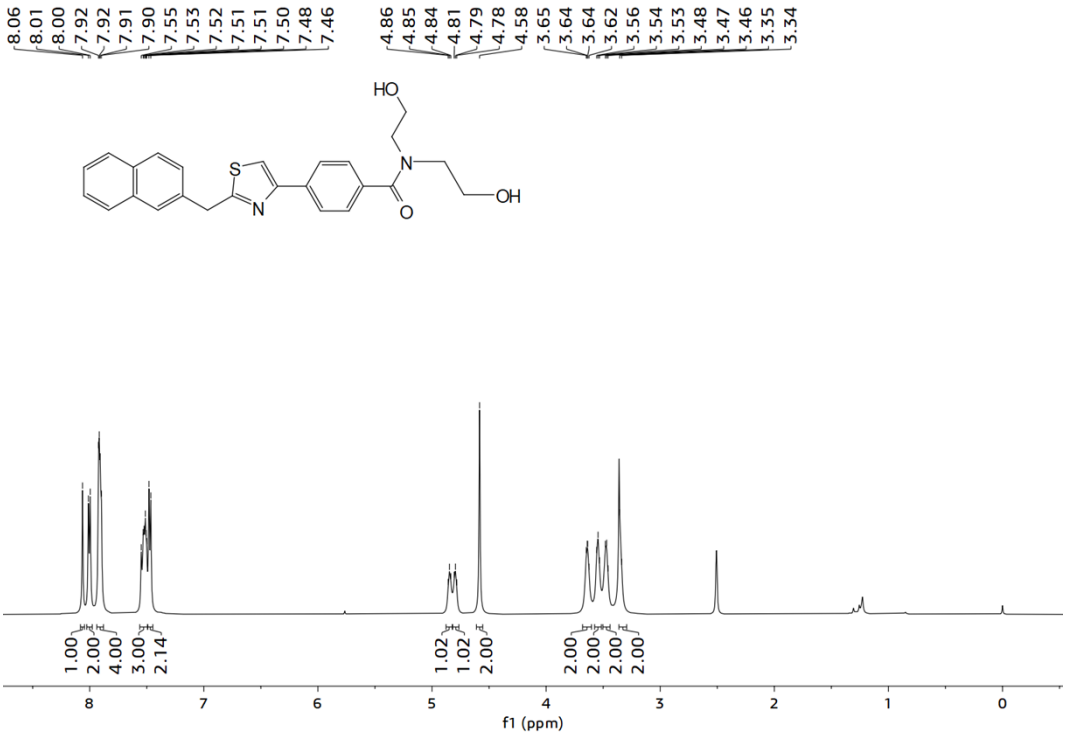


High resolution mass spectrum of **S26**

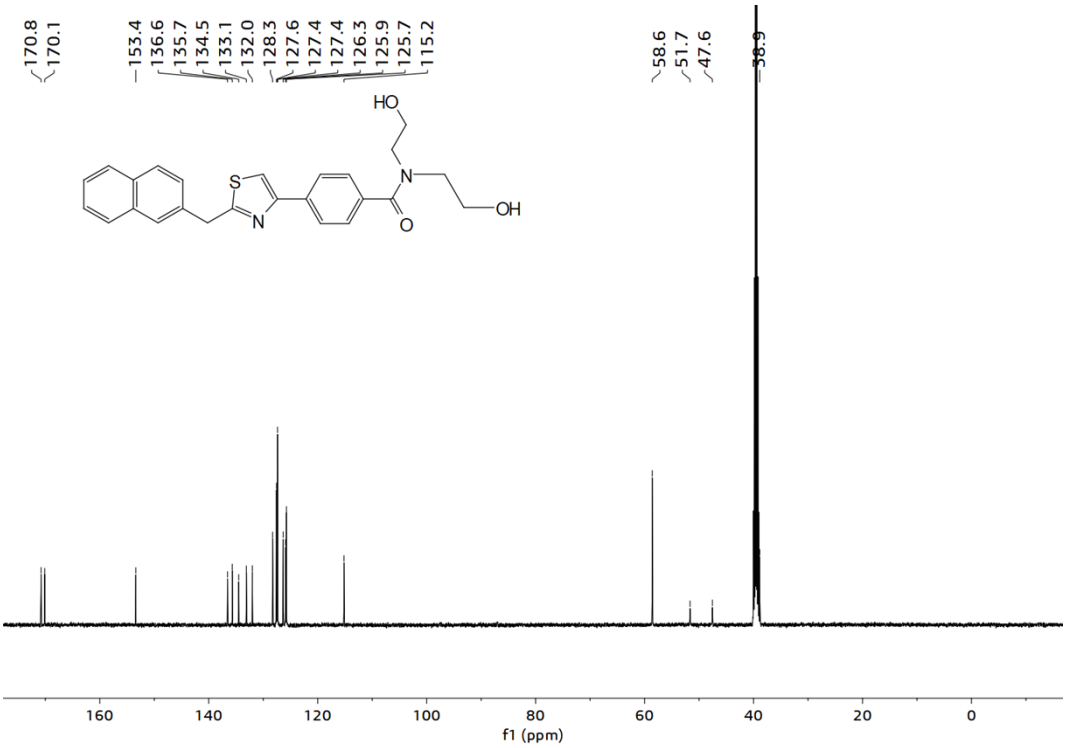


Compound **S27**:

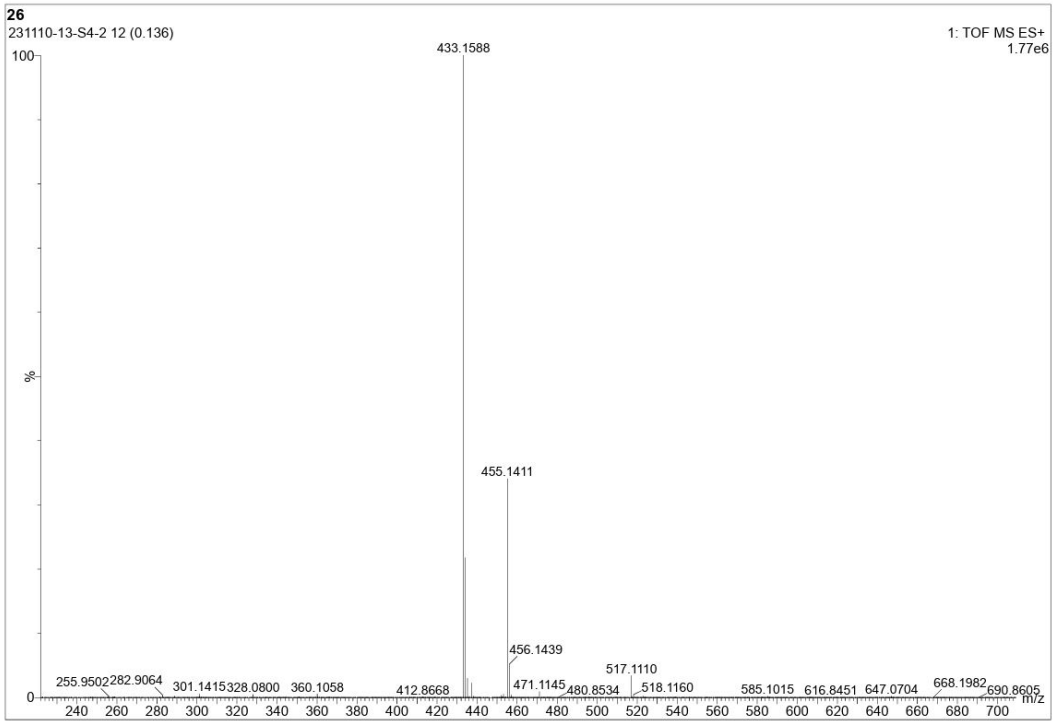
^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)

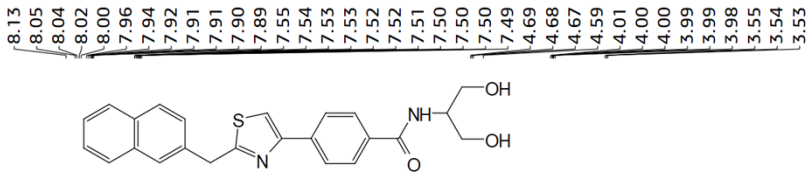


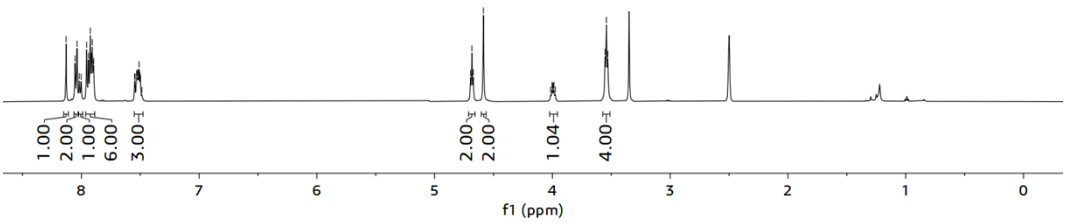
High resolution mass spectrum of **S27**



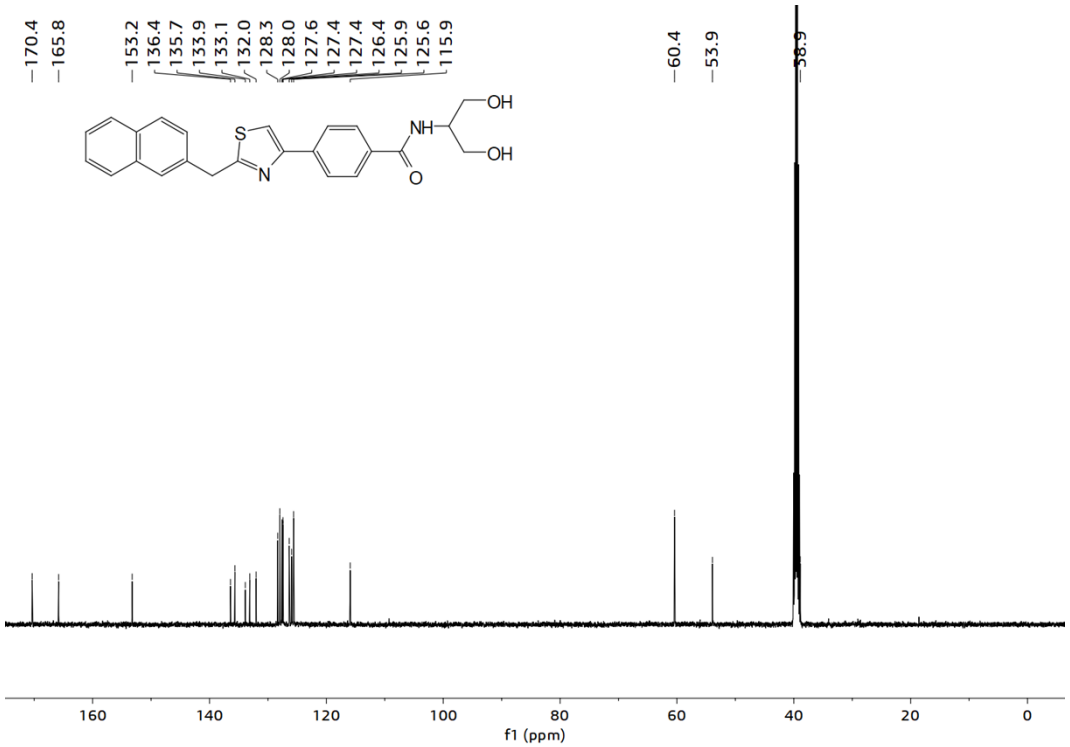
Compound **S28**:

^{1}H NMR (500 MHz, DMSO-d_6)

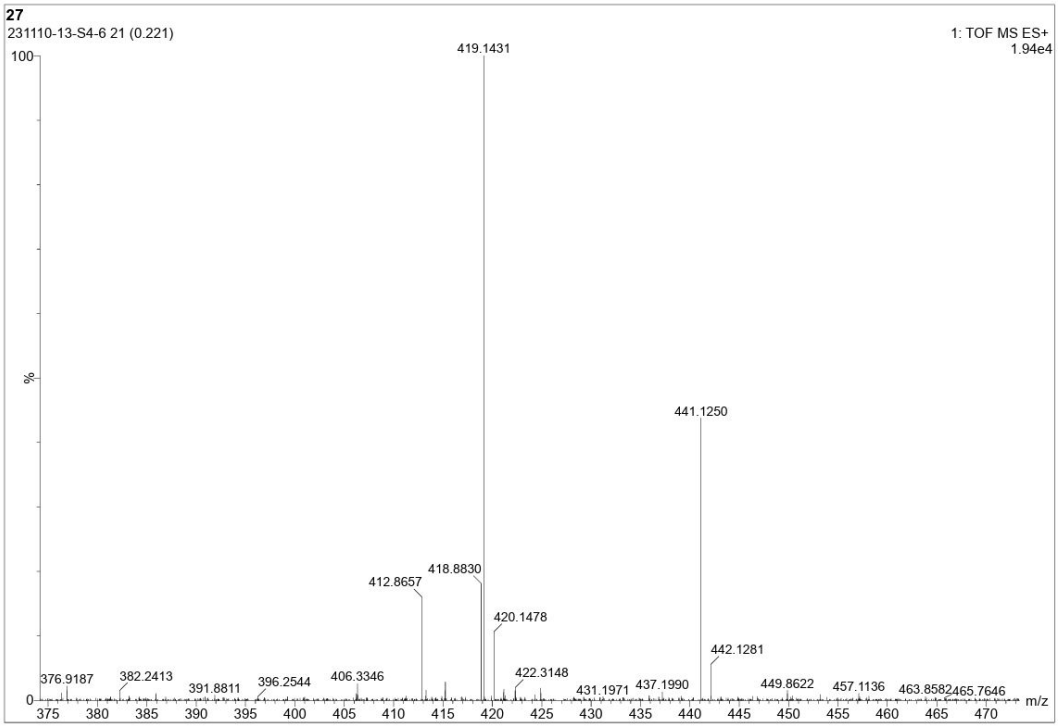




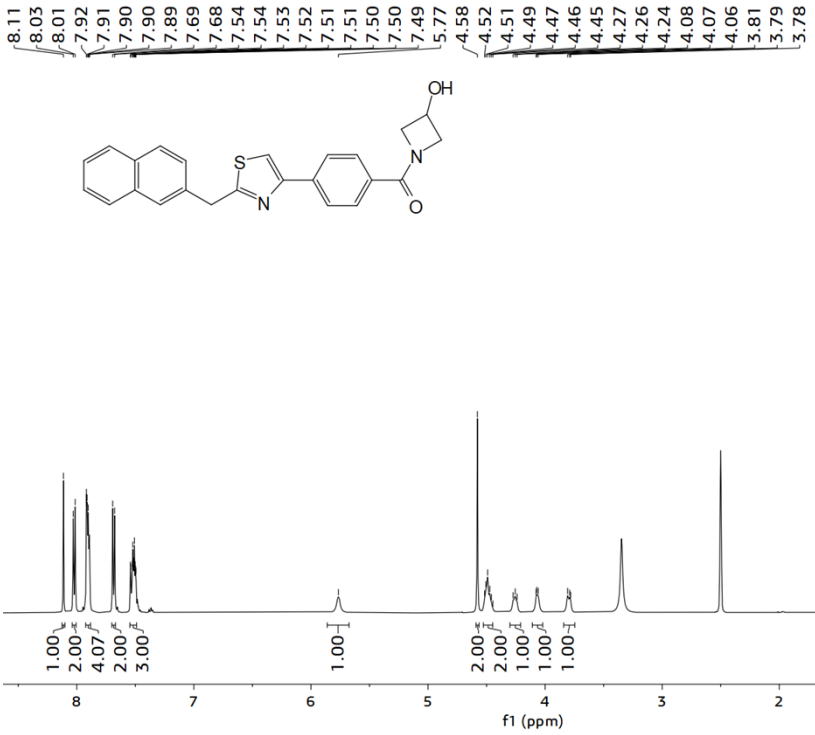
^{13}C NMR (125 MHz, DMSO-d_6)



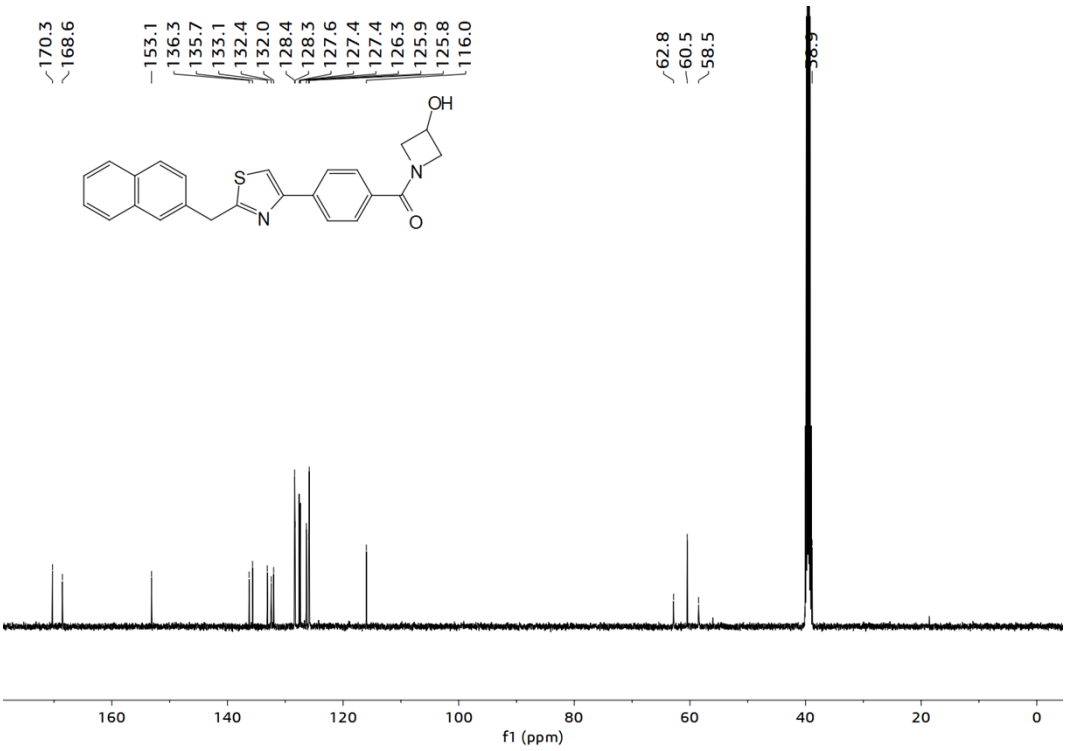
High resolution mass spectrum of **S28**



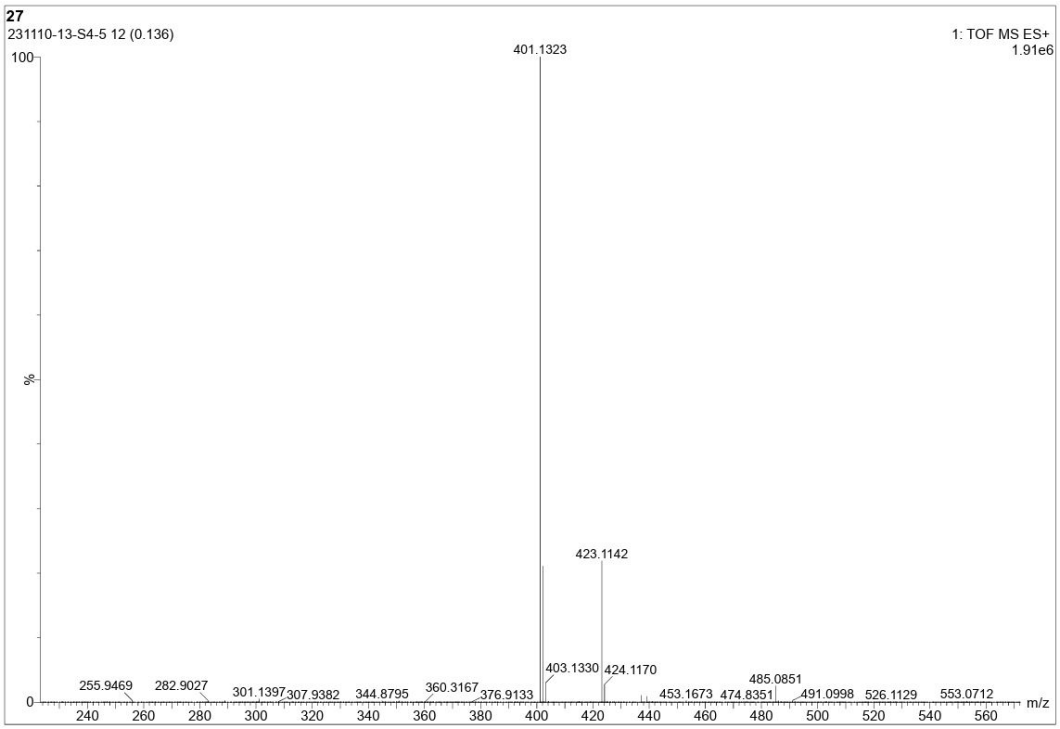
Compound **S29**: ^{1}H NMR (500 MHz, DMSO-d_6)



^{13}C NMR (125 MHz, DMSO-d_6)



High resolution mass spectrum of **S29**



9. Reference

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