

Supplementary data for

Design, Synthesis and Biological Activity of Novel Aromatic Amide Derivatives Containing Sulfide and Sulfone Substructures

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1. Synthetic procedures of target compounds

1.1. Synthetic procedure for intermediate 3

To a mixture of substituted aromatic formic acid (70.0 mmol) in anhydrous toluene (200 mL), thionyl chloride (150.0 mmol) was added dropwise at room temperature. The reaction was heated to reflux for 12 h. The excess thionyl chloride and a little toluene were distilled to remove, followed by the addition of 2-chloroethylamine hydrochloride (70.0 mmol). The mixture was cooled to 0 °C in ice bath and triethylamine (150.0 mmol) was added dropwise. After completion of the reaction, the solution was concentrated in vacuum to remove toluene. The obtained residue was dissolved in ethyl acetate/water (v/v 1:1). The organic layer was extracted, dried by anhydrous magnesium sulfate, filtered and concentrated to be purified through chromatograph on silica gel using ethyl acetate/ether petroleum as eluent to give white solid 3.

N-(2-chloroethyl)-2-(trifluoromethyl)benzamide(3a)

White granular, yield 78%, m.p. 96–98 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 7.5 Hz, 1H, Ph-H), 7.64–7.49 (m, 3H, Ph-H), 6.31 (s, 1H, CONH), 3.81–3.74 (m, 2H, CH₂), 3.74–3.67 (m, 2H, CH₂).

N-(2-chloroethyl)-2-chloro-4-(methylsulfonyl)benzamide(3b)

White granular, yield 82%, m.p. 163–165 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.95 (s, 1H, Ph-H), 7.82 (s, 1H, Ph-H), 7.78 (s, 1H, Ph-H), 6.70 (s, 1H, CONH), 3.81 (s, 2H, CH₂), 3.74 (s, 2H, CH₂), 3.04 (s, 3H, CH₃).

N-(2-chloroethyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide(3c)

Yellow granular, yield 86%, m.p. 198–200 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.98 (s, 1H, pyrazole-H), 6.89 (t, *J* = 54.4 Hz, 1H, CHF₂), 6.84 (s, 1H, CONH), 3.94 (s, 3H, CH₃), 3.76 (dd, *J* = 11.0, 5.2 Hz, 2H, CH₂), 3.70 (t, *J* = 5.4 Hz, 2H, CH₂).

1.2. Synthetic procedure for intermediate 4a

To a solution of 2,3-dichloro-5-(trifluoromethyl)pyridine (10.0 mmol) in ethanol (20 mL), sodium hydrosulfide (mass fraction: 70%, 12.0 mmol) was added in batches. The reaction was stirred for 8 h at room temperature, followed by concentration in vacuum. The residue was dissolved in ethyl acetate/water (v/v 1:1). The organic layer was extracted, dried by anhydrous magnesium sulfate, filtered and concentrated to be purified through chromatograph on silica gel using *n*-hexane as eluent to give yellow solid 4a (yield 80%).

3-chloro-5-(trifluoromethyl)pyridine-2-thiol (4a)

Yellow granular, m.p. 143–145 °C. ¹H NMR (400 MHz, CDCl₃) δ 12.76 (s, 1H, SH), 7.91 (d, *J* = 0.8 Hz, 1H, pyridine-H), 7.82 (d, *J* = 1.8 Hz, 1H, pyridine-H).

1.3. Synthetic procedure for target compounds I-1 ~ I-12

A mixture of intermediate 4 (1.1mmol), potassium carbonate (1.3 mmol) in *N,N*-dimethylformamide (DMF) (5 mL) was heated to 80 °C and stirred for 10 min, followed by addition of material 3 (1.0 mmol). The reaction was continued to stir for 3 h at 80 °C. After reaction

completion, the solution was poured into ice-water (100 mL). The resulting precipitate was obtained through filtration, and purified by chromatograph on silica gel using petroleum ether/ethyl acetate as eluent to give white solid **I-1 ~ I-12**.

1.4. Synthetic procedure for target compounds **II-1 ~ II-12**

To a solution of compound **I-1** (1.0 mmol) in dichloromethane (15 mL) was added 85% *m*-chloroperoxybenzoic acid (2.1 mmol) in portions. After stirring for 5 h, the mixture was diluted with 200 mL of CH₂Cl₂ and extracted with saturated NaHCO₃ solution. The organic layer was dried by anhydrous magnesium sulfate, filtered and concentrated to be purified through chromatograph on silica gel using petroleum ether/ethyl acetate as eluent to give white solid **II-1**. Products **II-2 ~ II-12** were prepared similarly.

2. Structural characterization data of target compounds

***N*-(2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)thio)ethyl)-2-(trifluoromethyl) benzamide (I-1)**

White granular, yield 78%, m.p. 126–127 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.84 (s, 1H, pyridine-H), 8.79 (t, *J* = 5.2 Hz, 1H, CONH), 8.38 (s, 1H, pyridine-H), 7.79 (d, *J* = 7.8 Hz, 1H, Ph-H), 7.73 (t, *J* = 7.4 Hz, 1H, Ph-H), 7.66 (d, *J* = 7.6 Hz, 1H, Ph-H), 7.51 (d, *J* = 7.4 Hz, 1H, Ph-H), 3.57 (dd, *J* = 12.0, 6.1 Hz, 2H, CH₂), 3.44 (t, *J* = 6.3 Hz, 2H, CH₂). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 167.72, 162.19, 144.6 (q, *J* = 4.0 Hz), 136.72 (q, *J* = 2.0 Hz), 133.78 (q, *J* = 4.0 Hz), 132.87, 130.24, 128.93, 128.83, 126.7 (q, *J* = 5.0 Hz), 126.37 (q, *J* = 31.0 Hz), 124.18 (q, *J* = 271.0 Hz), 123.75 (q, *J* = 239.0 Hz), 122.23, 38.57, 29.83. HRMS, *m/z* (ESI) calculated for C₁₆H₁₂ClF₆N₂OS⁺ [M+H]⁺: 429.0258; found: 429.0259.

***N*-(2-((4-(trifluoromethyl)pyrimidin-2-yl)thio)ethyl)-2-(trifluoromethyl) benzamide (I-2)**

White granular, yield 82%, m.p. 102–103 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.72 (d, *J* = 4.9 Hz, 1H, pyrimidine-H), 7.66 (d, *J* = 7.5 Hz, 1H, Ph-H), 7.57–7.48 (m, 2H, Ph-H), 7.45 (d, *J* = 7.0 Hz, 1H, Ph-H), 7.27 (d, *J* = 4.9 Hz, 1H, pyrimidine-H), 6.48 (s, 1H, CONH), 3.79 (q, *J* = 6.1 Hz, 2H, CH₂), 3.42 (t, *J* = 6.2 Hz, 2H, CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 173.36, 168.04, 159.61, 155.78 (q, *J* = 36.5 Hz), 135.55, 131.95, 129.84, 128.39, 127.14 (q, *J* = 31.7 Hz), 126.31 (q, *J* = 4.9 Hz), 123.53 (q, *J* = 272.0 Hz), 120.01 (q, *J* = 273.7 Hz), 112.09 (q, *J* = 2.4 Hz), 39.42, 30.44. HRMS, *m/z* (ESI) calculated for C₁₅H₁₂F₆N₃OS⁺ [M+H]⁺: 396.0600; found: 396.0598.

***N*-(2-((5-methoxy-3H-imidazo[4,5-*b*]pyridin-2-yl)thio)ethyl)-2-(trifluoromethyl) benzamide (I-3)**

White granular, yield 86%, m.p. 146–148 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.06 and 12.70 (s, 1H, imidazole-H), 8.85 (q, *J* = 6.6 Hz, 1H, CONH), 7.84–7.61 (m, 4H, Ph-H), 7.52 (t, *J* = 6.3 Hz, 1H, pyridine-H), 6.60 (t, *J* = 8.7 Hz, 1H, pyridine-H), 3.86 (s, 3H, OCH₃), 3.62 (dt, *J* = 20.7, 6.0 Hz, 2H, CH₂), 3.44 (dt, *J* = 13.0, 6.4 Hz, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.70, 160.32, 136.69 (q, *J* = 2.1 Hz), 132.80, 130.19, 128.95, 126.65 (q, *J* = 4.9 Hz), 126.34 (q, *J* = 31.2 Hz), 124.17 (q, *J* = 272.1 Hz), 104.87, 53.64, 39.66, 30.77. HRMS, *m/z* (ESI) calculated for C₁₇H₁₆F₃N₄O₂S⁺ [M+H]⁺: 397.0941; found: 397.0940.

***N*-(2-((4-(pyridin-4-yl)thiazol-2-yl)thio)ethyl)-2-(trifluoromethyl)benzamide (I-4)**

White granular, yield 90%, m.p. 136–137 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.86 (s, 1H, CONH), 8.63 (s, 2H, pyridine-H), 8.40 (s, 1H, thiazole-H), 7.93 (s, 2H, pyridine-H), 7.79 (d, *J* = 6.1 Hz, 1H, Ph-H), 7.70 (d, *J* = 6.2 Hz, 1H, Ph-H), 7.66 (d, *J* = 6.5 Hz, 1H, Ph-H), 7.52 (d, *J* = 5.2 Hz, 1H, Ph-H), 3.68 (s, 2H, CH₂), 3.50 (s, 2H, CH₂). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 167.75, 165.41, 152.14, 150.77, 140.66, 136.67, 132.87, 130.28, 128.96, 126.7 (q, *J* = 4.0 Hz), 126.4 (q, *J* = 31.0 Hz), 124.2 (q, *J* = 272.0 Hz), 120.68, 118.87, 39.06, 33.29. HRMS, *m/z* (ESI) calculated for C₁₈H₁₅F₃N₃OS₂⁺ [M+H]⁺: 410.0603; found: 410.0604.

***N*-(2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)thio)ethyl)-2-chloro-4-(methylsulfonyl)benzamide (I-5)**

White granular, yield 84%, m.p. 181–182 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.94 (t, *J* = 5.5 Hz, 1H, CONH), 8.86 (s, 1H, pyridine-H), 8.40 (d, *J* = 1.5 Hz, 1H, pyridine-H), 8.06 (d, *J* = 1.5 Hz, 1H, Ph-H), 7.95 (dd, *J* = 8.0, 1.6 Hz, 1H, Ph-H), 7.68 (d, *J* = 8.0 Hz, 1H, Ph-H), 3.61 (q, *J* = 6.1 Hz, 2H, CH₂), 3.47 (t, *J* = 6.3 Hz, 2H, CH₂), 3.33 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ

170.53, 166.82, 149.45, 147.89, 146.41, 138.65, 136.06, 134.95, 133.55, 133.25, 130.94, 128.32 (q, $J = 270.6$ Hz), 127.30, 48.29, 43.26, 34.62. HRMS, m/z (ESI) calculated for $C_{16}H_{14}Cl_2F_3N_2O_3S_2^+$ $[M+H]^+$: 472.9770; found: 472.9769.

***N*-(2-((4-(trifluoromethyl)pyrimidin-2-yl)thio)ethyl)-2-chloro-4-(methylsulfonyl) benzamide (I-6)**

White granular, yield 87%, m.p. 167–168 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, $J = 4.9$ Hz, 1H, pyrimidine-H), 7.98 (d, $J = 1.4$ Hz, 1H, Ph-H), 7.87 (dd, $J = 8.0, 1.5$ Hz, 1H, Ph-H), 7.77 (d, $J = 8.0$ Hz, 1H, Ph-H), 7.38 (d, $J = 4.9$ Hz, 1H, pyrimidine-H), 6.96 (s, 1H, CONH), 3.93 (q, $J = 6.0$ Hz, 2H, CH_2), 3.54 (t, $J = 6.1$ Hz, 2H, CH_2), 3.11 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.28, 165.32, 159.71, 155.80 (q, $J = 36.5$ Hz), 142.83, 140.24, 132.08, 130.71, 129.04, 125.83, 120.02 (q, $J = 273.7$ Hz), 112.24 (q, $J = 2.3$ Hz), 44.35, 39.64, 30.54. HRMS, m/z (ESI) calculated for $C_{15}H_{14}ClF_3N_3O_3S_2^+$ $[M+H]^+$: 440.0112; found: 440.0110.

***N*-(2-((5-methoxy-3H-imidazo[4,5-b]pyridin-2-yl)thio)ethyl)-2-chloro-4-(methylsulfonyl)benzamide (I-7)**

White granular, yield 91%, m.p. 180–181 °C. ^1H NMR (400 MHz, $DMSO-d_6$) δ 13.05 and 12.70 (s, 1H, imidazole-H), 8.99 (s, 1H, CONH), 8.05 (d, $J = 1.6$ Hz, 1H, Ph-H), 7.92 (dd, $J = 8.0, 1.7$ Hz, 1H, Ph-H), 7.79 (s, 1H, pyridine-H), 7.70 (d, $J = 7.9$ Hz, 1H, Ph-H), 6.60 (d, $J = 8.5$ Hz, 1H, pyridine-H), 3.85 (s, 3H), 3.65 (s, 2H, CH_2), 3.47 (s, 2H, CH_2), 3.32 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $DMSO-d_6$) δ 165.76, 160.32, 143.14, 141.65, 131.34, 130.25, 128.45, 126.12, 104.89, 53.71, 43.55, 39.63, 30.86. HRMS, m/z (ESI) calculated for $C_{17}H_{18}ClN_4O_4S_2^+$ $[M+H]^+$: 441.0453; found: 441.0455.

***N*-(2-((4-(pyridin-4-yl)thiazol-2-yl)thio)ethyl)-2-chloro-4-(methylsulfonyl) benzamide (I-8)**

White granular, yield 90%, m.p. 142–143 °C. ^1H NMR (400 MHz, $DMSO-d_6$) δ 9.03 (t, $J = 5.6$ Hz, 1H, CONH), 8.65 (d, $J = 1.5$ Hz, 1H, pyridine-H), 8.64 (d, $J = 1.5$ Hz, 1H, pyridine-H), 8.41 (s, 1H, thiazole-H), 8.08 (d, $J = 1.6$ Hz, 1H, Ph-H), 7.97 – 7.93 (m, 2H, Ph-H and pyridine-H), 7.92 (d, $J = 1.5$ Hz, 1H, pyridine-H), 7.71 (d, $J = 8.0$ Hz, 1H, Ph-H), 3.73 (dd, $J = 12.4, 6.3$ Hz, 2H, CH_2), 3.54 (t, $J = 6.6$ Hz, 2H, CH_2), 3.34 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $DMSO-d_6$) δ 165.85, 165.38, 152.12, 150.79, 143.20, 141.65, 140.65, 131.40, 130.26, 128.54, 126.21, 120.68, 118.90, 43.57, 39.02, 33.42. HRMS, m/z (ESI) calculated for $C_{18}H_{17}ClN_3O_3S_3^+$ $[M+H]^+$: 454.0115; found: 454.0118.

***N*-(2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)thio)ethyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (I-9)**

White granular, yield 85%, m.p. 97–99 °C. ^1H NMR (400 MHz, $DMSO-d_6$) δ 8.78 (d, $J = 0.8$ Hz, 1H, pyridine-H), 8.51 (t, $J = 5.4$ Hz, 1H, CONH), 8.33 (d, $J = 1.5$ Hz, 1H, pyridine-H), 8.23 (s, 1H, pyrazole-H), 7.33 (t, $J = 54.2$ Hz, 1H, CHF_2), 3.92 (s, 3H, CH_3), 3.53 (dd, $J = 12.0, 6.1$ Hz, 2H, CH_2), 3.42 (t, $J = 6.5$ Hz, 2H, CH_2). ^{13}C NMR (101 MHz, $DMSO-d_6$) δ 162.13, 161.75, 145.07 (t, $J = 23.0$ Hz), 144.44 (q, $J = 4.1$ Hz), 133.67 (q, $J = 3.4$ Hz), 132.62, 128.77, 123.52 (q, $J = 273.4$ Hz), 122.32 (q, $J = 33.3$ Hz), 116.34 (t, $J = 3.6$ Hz), 110.02 (t, $J = 235.2$ Hz), 39.77, 38.25, 29.99. HRMS, m/z (ESI) calculated for $C_{14}H_{13}ClF_5N_4OS^+$ $[M+H]^+$: 415.0413; found: 415.0416.

***N*-(2-((4-(trifluoromethyl)pyrimidin-2-yl)thio)ethyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (I-10)**

Yellow sticky liquid, yield 81%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, $J = 4.9$ Hz, 1H, pyrimidine-H), 7.95 (s, 1H, pyrazole-H), 7.30 (d, $J = 4.9$ Hz, 1H, pyrimidine-H), 7.03 (s, 1H, CONH), 6.97 (t, $J = 54.2$ Hz, 1H, CHF_2), 3.92 (s, 3H, CH_3), 3.77 (q, $J = 6.2$ Hz, 2H, CH_2), 3.42 (t, $J = 6.3$ Hz, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.18, 161.73, 159.61, 155.64 (q, $J = 36.3$ Hz), 143.57 (t, $J = 26.9$ Hz), 134.14, 120.06 (q, $J = 273.7$ Hz), 116.16, 112.04 (q, $J = 2.5$ Hz), 110.98 (t, $J = 232.4$ Hz), 39.42, 38.70, 30.72. HRMS, m/z (ESI) calculated for $C_{13}H_{13}F_5N_5OS^+$ $[M+H]^+$: 382.0755; found: 382.0758.

***N*-(2-((5-methoxy-3H-imidazo[4,5-b]pyridin-2-yl)thio)ethyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (I-11)**

White granular, yield 88%, m.p. 200–201 °C. ^1H NMR (400 MHz, $DMSO-d_6$) δ 13.08 and 12.74 (s, 1H, imidazole-H), 8.63 (s, 1H, CONH), 8.24 (s, 1H, pyridine-H), 7.80 (s, 1H, pyrazole-H), 7.37 (t, $J = 54.2$ Hz, 1H, CHF_2), 6.62 (d, $J = 8.5$ Hz, 1H, pyridine-H), 3.93 (s, 3H, OCH_3), 3.88

(s, 3H, pyrazole-CH₃), 3.62 (d, *J* = 5.2 Hz, 2H, CH₂), 3.44 (t, *J* = 6.1 Hz, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 161.74, 160.32, 145.06 (t, *J* = 22.7 Hz), 132.62, 128.25, 116.34 (t, *J* = 3.9 Hz), 110.05 (t, *J* = 232.9 Hz), 104.86, 53.65, 39.78, 39.31, 31.00. HRMS, *m/z* (ESI) calculated for C₁₅H₁₇F₂N₆O₂S⁺ [M+H]⁺: 383.1096; found: 383.1098.

***N*-(2-((4-(pyridin-4-yl)thiazol-2-yl)thio)ethyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (I-12)**

Yellow granular, yield 87%, m.p. 153–154 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.61 (d, *J* = 5.8 Hz, 2H, pyridine-H), 8.54 (t, *J* = 5.5 Hz, 1H, CONH), 8.34 (s, 1H, thiazole-H), 8.18 (s, 1H, pyrazole-H), 7.87 (d, *J* = 6.0 Hz, 2H, pyridine-H), 7.31 (t, *J* = 54.2 Hz, 1H, CHF₂), 3.86 (s, 3H, CH₃), 3.62 (q, *J* = 6.2 Hz, 2H, CH₂), 3.45 (t, *J* = 6.5 Hz, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.42, 161.78, 152.08, 150.72, 145.07 (t, *J* = 22.7 Hz), 140.59, 132.66, 120.62, 118.77, 116.30, 110.05 (t, *J* = 233.0 Hz), 39.75, 38.74, 33.71. HRMS, *m/z* (ESI) calculated for C₁₆H₁₆F₂N₅OS₂⁺ [M+H]⁺: 396.0759; found: 396.0764.

***N*-(2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)sulfonyl)ethyl)-2-(trifluoromethyl)benzamide (II-1)**

White granular, yield 88%, m.p. 125–126 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.15 (s, 1H, pyridine-H), 8.90 (s, 1H, pyridine-H), 8.83 (t, *J* = 5.1 Hz, 1H, CONH), 7.79 (d, *J* = 7.7 Hz, 1H, Ph-H), 7.74 (t, *J* = 7.3 Hz, 1H, Ph-H), 7.66 (t, *J* = 7.5 Hz, 1H, Ph-H), 7.52 (d, *J* = 7.4 Hz, 1H, Ph-H), 3.98 (t, *J* = 6.7 Hz, 2H, CH₂), 3.74 (dd, *J* = 12.6, 6.4 Hz, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.65, 156.53 (q, *J* = 1.2 Hz), 144.75 (q, *J* = 4.0 Hz), 139.78 (q, *J* = 3.4 Hz), 136.17 (q, *J* = 2.1 Hz), 132.85, 130.43, 129.82 (q, *J* = 33.5 Hz), 129.61, 128.95, 126.72 (q, *J* = 4.9 Hz), 126.36 (q, *J* = 31.2 Hz), 124.11 (q, *J* = 272.0 Hz), 122.44 (q, *J* = 272.1 Hz), 51.14, 33.77. HRMS, *m/z* (ESI) calculated for C₁₆H₁₂ClF₆N₂O₃S⁺ [M+H]⁺: 461.0156; found: 461.0153.

***N*-(2-((4-(trifluoromethyl)pyrimidin-2-yl)sulfonyl)ethyl)-2-(trifluoromethyl)benzamide (II-2)**

White granular, yield 91%, m.p. 109–111 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.52 (d, *J* = 5.0 Hz, 1H, pyrimidine-H), 8.84 (s, 1H, CONH), 8.44 (d, *J* = 5.1 Hz, 1H, pyrimidine-H), 7.79 (d, *J* = 7.8 Hz, 1H, Ph-H), 7.74 (t, *J* = 7.4 Hz, 1H, Ph-H), 7.66 (t, *J* = 7.6 Hz, 1H, Ph-H), 7.54 (d, *J* = 7.5 Hz, 1H, Ph-H), 3.95 (s, 2H, CH₂), 3.77 (s, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.72, 165.57, 163.59, 155.57 (q, *J* = 36.8 Hz), 136.23, 132.83, 130.42, 128.98, 126.71 (q, *J* = 4.8 Hz), 126.46 (q, *J* = 31.6 Hz), 124.14 (q, *J* = 272.0 Hz), 121.56, 120.45 (q, *J* = 273.7 Hz), 50.39, 33.43. HRMS, *m/z* (ESI) calculated for C₁₅H₁₂F₆N₃O₃S⁺ [M+H]⁺: 428.0498; found: 428.0499.

***N*-(2-((5-methoxy-3H-imidazo[4,5-*b*]pyridin-2-yl)sulfonyl)ethyl)-2-(trifluoromethyl)benzamide (II-3)**

White granular, yield 87%, m.p. 183–184 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 14.48 (s, 1H, imidazole-H), 8.74 (t, *J* = 5.2 Hz, 1H, CONH), 8.13 (s, 1H, pyridine-H), 7.78–7.76 (m, 1H, Ph-H), 7.68–7.63 (m, 2H, Ph-H), 7.44–7.42 (m, 1H, Ph-H), 6.93 (d, *J* = 8.8 Hz, 1H, pyridine-H), 3.94 (s, 3H, CH₃), 3.85 (t, *J* = 6.3 Hz, 2H, CH₂), 3.68 (d, *J* = 5.6 Hz, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.65, 162.99, 136.13, 132.75, 130.42, 128.94, 126.71 (q, *J* = 4.9 Hz), 126.40 (q, *J* = 31.3 Hz), 124.11 (q, *J* = 271.9 Hz), 109.90, 54.13, 53.43, 33.81. HRMS, *m/z* (ESI) calculated for C₁₇H₁₆F₃N₄O₄S⁺ [M+H]⁺: 429.0839; found: 429.0840.

***N*-(2-((1-oxido-4-(pyridin-4-yl)thiazol-2-yl)sulfonyl)ethyl)-2-(trifluoromethyl)benzamide (II-4)**

White granular, yield 88%, m.p. 227–228 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.88 (s, 1H, thiazole-H), 8.79 (t, *J* = 5.4 Hz, 1H, CONH), 8.32 (d, *J* = 7.2 Hz, 2H, pyridine-H), 8.02 (d, *J* = 7.2 Hz, 2H, pyridine-H), 7.76 (d, *J* = 7.2 Hz, 1H, Ph-H), 7.69–7.62 (m, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 3.91 (t, *J* = 6.5 Hz, 2H, CH₂), 3.72 (q, *J* = 6.3 Hz, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.61, 165.89, 153.33, 139.70, 136.04, 132.75, 130.46, 129.20, 128.89, 126.73 (q, *J* = 4.9 Hz), 126.40 (q, *J* = 31.2 Hz), 124.85, 124.07 (q, *J* = 272.1 Hz), 123.99, 53.41, 33.79. HRMS, *m/z* (ESI) calculated for C₁₈H₁₅F₃N₃O₄S₂⁺ [M+H]⁺: 458.0451; found: 458.0449.

***N*-(2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)sulfonyl)ethyl)-2-chloro-4-(methylsulfonyl)benzamide (II-5)**

White granular, yield 90%, m.p. 182–183 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.15 (s, 1H,

pyridine-H), 8.97 (t, $J = 5.5$ Hz, 1H, CONH), 8.90 (s, 1H, pyridine-H), 8.05 (d, $J = 1.6$ Hz, 1H, Ph-H), 7.95 (dd, $J = 8.0, 1.7$ Hz, 1H, Ph-H), 7.69 (d, $J = 8.0$ Hz, 1H, Ph-H), 4.02 (t, $J = 6.7$ Hz, 2H, CH₂), 3.77 (dd, $J = 12.5, 6.3$ Hz, 2H, CH₂), 3.33 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 170.49, 161.26, 149.50 (q, $J = 3.8$ Hz), 148.04, 145.86, 144.55 (q, $J = 3.6$ Hz), 136.12, 135.04, 134.56 (q, $J = 33.5$ Hz), 134.36, 133.24 (q, $J = 5.1$ Hz), 130.90, 127.19 (q, $J = 272.2$ Hz), 55.97, 48.26, 38.57. HRMS, m/z (ESI) calculated for C₁₆H₁₄Cl₂F₃N₂O₅S₂⁺ [M+H]⁺: 504.9668; found: 504.9665.

***N*-(2-((4-(trifluoromethyl)pyrimidin-2-yl)sulfonyl)ethyl)-2-chloro-4-(methylsulfonyl)benzamide (II-6)**

White granular, yield 89%, m.p. 144–145 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.50 (d, $J = 4.9$ Hz, 1H, pyrimidine-H), 8.98 (t, $J = 5.1$ Hz, 1H, CONH), 8.44 (d, $J = 4.8$ Hz, 1H, pyrimidine-H), 8.04 (s, 1H, Ph-H), 7.95 (d, $J = 8.0$ Hz, 1H, Ph-H), 7.68 (d, $J = 7.8$ Hz, 1H, Ph-H), 3.96 (t, $J = 6.6$ Hz, 2H, CH₂), 3.78 (dd, $J = 12.3, 6.2$ Hz, 2H, CH₂), 3.32 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.28, 165.01, 163.10, 155.02 (q, $J = 36.7$ Hz), 142.84, 140.65, 130.90, 129.82, 128.01, 125.68, 121.11 (q, $J = 2.0$ Hz), 119.96 (q, $J = 273.7$ Hz), 49.93, 43.05, 32.96. HRMS, m/z (ESI) calculated for C₁₅H₁₄ClF₃N₃O₅S₂⁺ [M+H]⁺: 472.0010; found: 472.0015.

***N*-(2-((5-methoxy-3H-imidazo[4,5-*b*]pyridin-2-yl)sulfonyl)ethyl)-2-chloro-4-(methylsulfonyl)benzamide (II-7)**

White granular, yield 91%, m.p. 178–180 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 14.46 (s, 1H, imidazole-H), 8.87 (t, $J = 5.1$ Hz, 1H, CONH), 8.13 (s, 1H, pyridine-H), 8.03 (s, 1H, Ph-H), 7.90 (d, $J = 7.9$ Hz, 1H, Ph-H), 7.60 (d, $J = 8.0$ Hz, 1H, Ph-H), 6.92 (d, $J = 8.7$ Hz, 1H, pyridine-H), 3.94 (s, 3H, OCH₃), 3.88 (s, 2H, CH₂), 3.71 (s, 2H, CH₂), 3.32 (s, 3H, SO₂CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.69, 163.07, 143.36, 141.07, 131.43, 130.31, 128.53, 126.04, 109.74, 54.14, 53.45, 43.55, 33.81. HRMS, m/z (ESI) calculated for C₁₇H₁₈ClN₄O₆S₂⁺ [M+H]⁺: 473.0351; found: 473.0348.

***N*-(2-((1-oxido-4-(pyridin-4-yl)thiazol-2-yl)sulfonyl)ethyl)-2-chloro-4-(methylsulfonyl)benzamide (II-8)**

White granular, yield 90%, m.p. 236–237 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.99 (t, $J = 5.1$ Hz, 1H, CONH), 8.90 (s, 1H, thiazole-H), 8.32 (d, $J = 7.0$ Hz, 2H, pyridine-H), 8.03 (d, $J = 6.4$ Hz, 3H, pyridine-H and Ph-H), 7.91 (d, $J = 8.0$ Hz, 1H, Ph-H), 7.61 (d, $J = 8.0$ Hz, 1H, Ph-H), 3.96 (t, $J = 6.5$ Hz, 2H, CH₂), 3.76 (dd, $J = 11.8, 5.9$ Hz, 2H, CH₂), 3.31 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.84, 165.68, 153.31, 143.32, 140.94, 139.70, 131.43, 130.27, 129.23, 128.47, 126.05, 124.92, 124.01, 53.45, 43.51, 33.78. HRMS, m/z (ESI) calculated for C₁₈H₁₇ClN₃O₆S₃⁺ [M+H]⁺: 501.9963; found: 501.9966.

***N*-(2-((3-chloro-5-(trifluoromethyl)pyridin-2-yl)sulfonyl)ethyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (II-9)**

White granular, yield 86%, m.p. 138–139 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.99 (s, 1H, pyridine-H), 8.74 (s, 1H, pyridine-H), 8.41 (t, $J = 5.2$ Hz, 1H, NH), 8.08 (s, 1H, pyrazole-H), 7.28 (t, $J = 54.2$ Hz, 1H, CHF₂), 4.02 (t, $J = 6.2$ Hz, 2H, CH₂), 3.90 (s, 3H, CH₃), 3.69 (q, $J = 5.9$ Hz, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 161.73, 156.58, 145.02 (t, $J = 23.0$ Hz), 144.48 (q, $J = 3.8$ Hz), 139.45 (q, $J = 3.0$ Hz), 132.51, 129.75, 129.60 (q, $J = 33.4$ Hz), 122.29 (q, $J = 272.2$ Hz), 115.81 (t, $J = 3.4$ Hz), 109.92 (t, $J = 233.1$ Hz), 51.36, 39.72, 33.82. HRMS, m/z (ESI) calculated for C₁₄H₁₃ClF₅N₄O₃S⁺ [M+H]⁺: 447.0312; found: 447.0312.

***N*-(2-((4-(trifluoromethyl)pyrimidin-2-yl)sulfonyl)ethyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (II-10)**

White granular, yield 88%, m.p. 145–146 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.40 (d, $J = 5.0$ Hz, 1H, pyrimidine-H), 8.46 (t, $J = 4.8$ Hz, 1H, CONH), 8.32 (d, $J = 5.0$ Hz, 1H, pyrimidine-H), 8.06 (s, 1H, pyrazole-H), 7.24 (t, $J = 54.1$ Hz, 1H, CHF₂), 3.96 (t, $J = 6.2$ Hz, 2H, CH₂), 3.90 (s, 3H, CH₃), 3.67 (dd, $J = 11.4, 5.6$ Hz, 2H, CH₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.70, 163.41, 161.71, 155.46 (q, $J = 36.9$ Hz), 145.08 (t, $J = 23.1$ Hz), 132.60, 121.19, 120.38 (q, $J = 273.9$ Hz), 115.75 (t, $J = 3.4$ Hz), 109.91 (t, $J = 233.1$ Hz), 50.57, 39.78, 33.51. HRMS, m/z (ESI) calculated for C₁₃H₁₃F₅N₅O₃S⁺ [M+H]⁺: 414.0654; found: 414.0657.

***N*-(2-((5-methoxy-3H-imidazo[4,5-*b*]pyridin-2-yl)sulfonyl)ethyl)-3-(difluoro methyl)-1-**

methyl-1H-pyrazole-4-carboxamide (II-11)

White granular, yield 90%, m.p. 246–247 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 14.39 (s, 1H, imidazole-H), 8.25 (t, $J = 5.3$ Hz, 1H, CONH), 8.03 (s, 1H, pyridine-H), 7.82 (s, 1H, pyrazole-H), 7.24 (t, $J = 54.2$ Hz, 1H, CHF_2), 6.86 (d, $J = 8.8$ Hz, 1H, pyridine-H), 3.91 (s, 3H, OCH_3), 3.87 (d, $J = 6.3$ Hz, 2H, CH_2), 3.83 (s, 3H, CH_3), 3.63 (d, $J = 5.3$ Hz, 2H, CH_2). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 162.84, 161.51, 146.79, 144.94 (t, $J = 22.8$ Hz), 132.33, 115.72 (t, $J = 3.4$ Hz), 109.91 (t, $J = 233.2$ Hz), 54.03, 53.51, 40.55, 33.71. HRMS, m/z (ESI) calculated for $\text{C}_{15}\text{H}_{17}\text{F}_2\text{N}_6\text{O}_4\text{S}^+$ $[\text{M}+\text{H}]^+$: 415.0995; found: 415.1000.

N-(2-((1-oxido-4-(pyridin-4-yl)thiazol-2-yl)sulfonyl)ethyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (II-12)

White granular, yield 87%, m.p. 268–270 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.69 (s, 1H, thiazole-H), 8.33 (s, 1H, CONH), 8.26 (d, $J = 5.3$ Hz, 2H, pyridine-H), 7.91 (s, 1H, pyrazole-H), 7.86 (d, $J = 5.2$ Hz, 2H, pyridine-H), 7.15 (t, $J = 54.1$ Hz, 1H, CH), 3.95 (s, 2H, CH_2), 3.79 (s, 3H, CH_3), 3.65 (s, 2H, CH_2). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 170.95, 166.23, 157.81, 149.66 (t, $J = 23.0$ Hz), 144.24, 137.15, 133.77, 128.96, 128.42, 120.35, 114.53 (t, $J = 233.3$ Hz), 58.01, 44.35, 38.51. HRMS, m/z (ESI) calculated for $\text{C}_{16}\text{H}_{16}\text{F}_2\text{N}_5\text{O}_4\text{S}_2^+$ $[\text{M}+\text{H}]^+$: 444.0606; found: 444.0609.

3. Structure spectra of target compounds

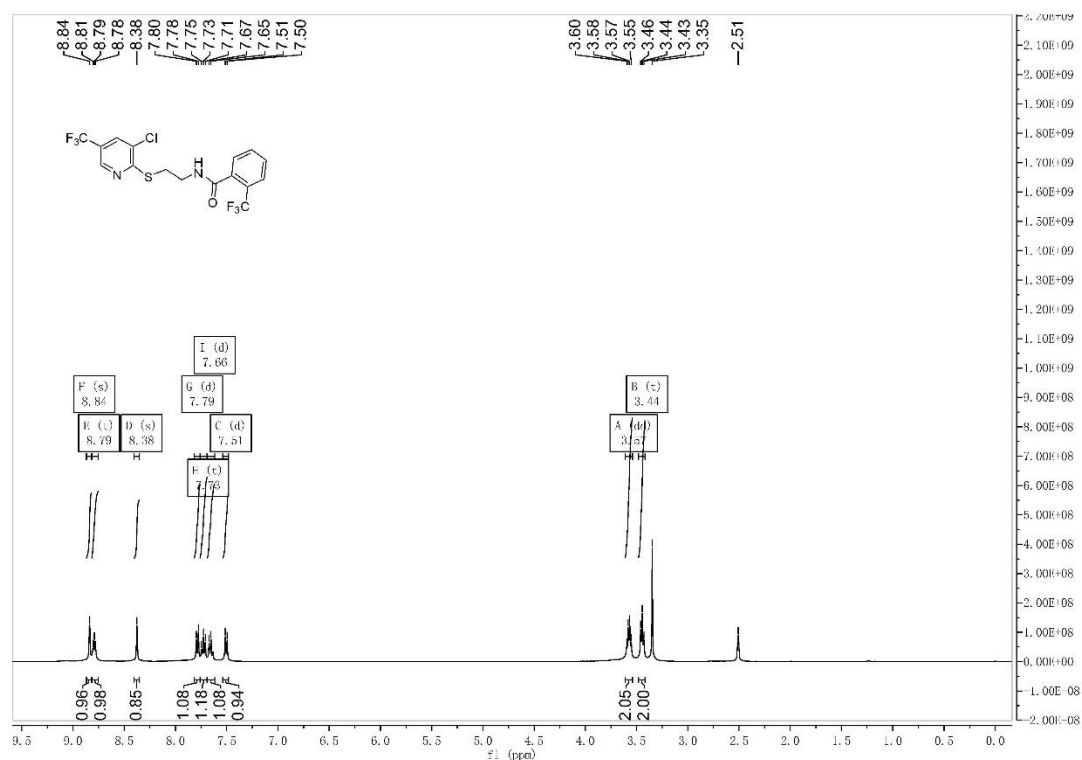


Fig. S1-1. ^1H -NMR of the target compound I-1.

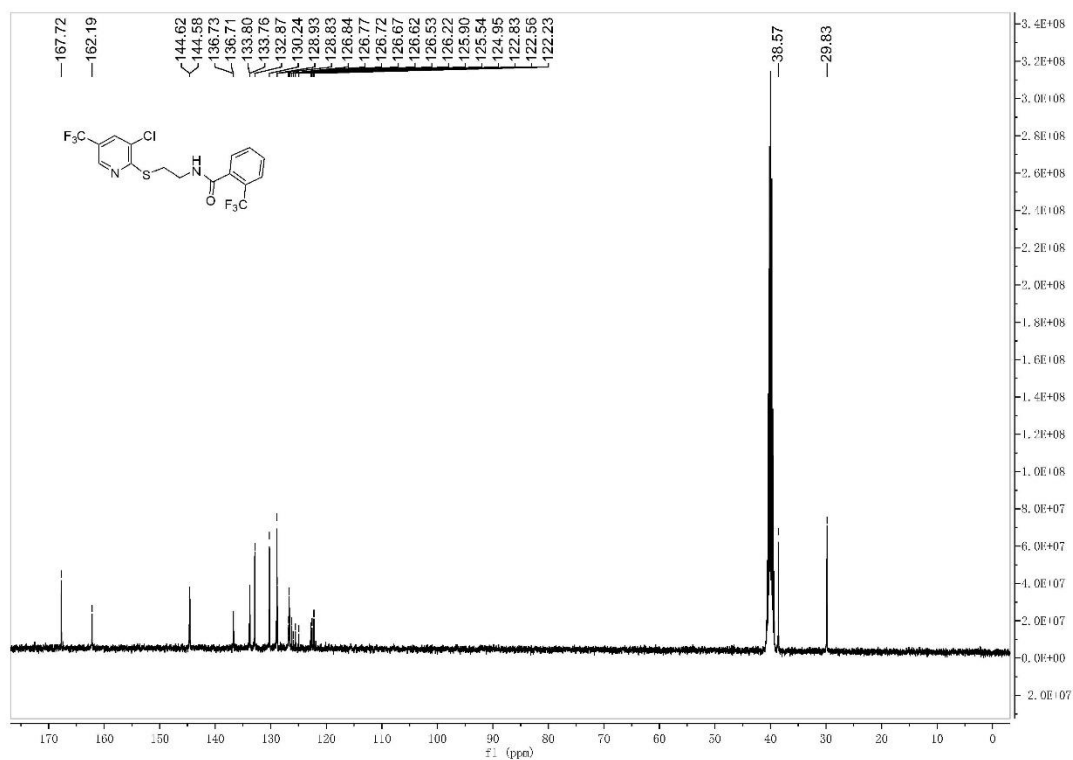


Fig. S1-2. ¹³C-NMR of the target compound I-1.

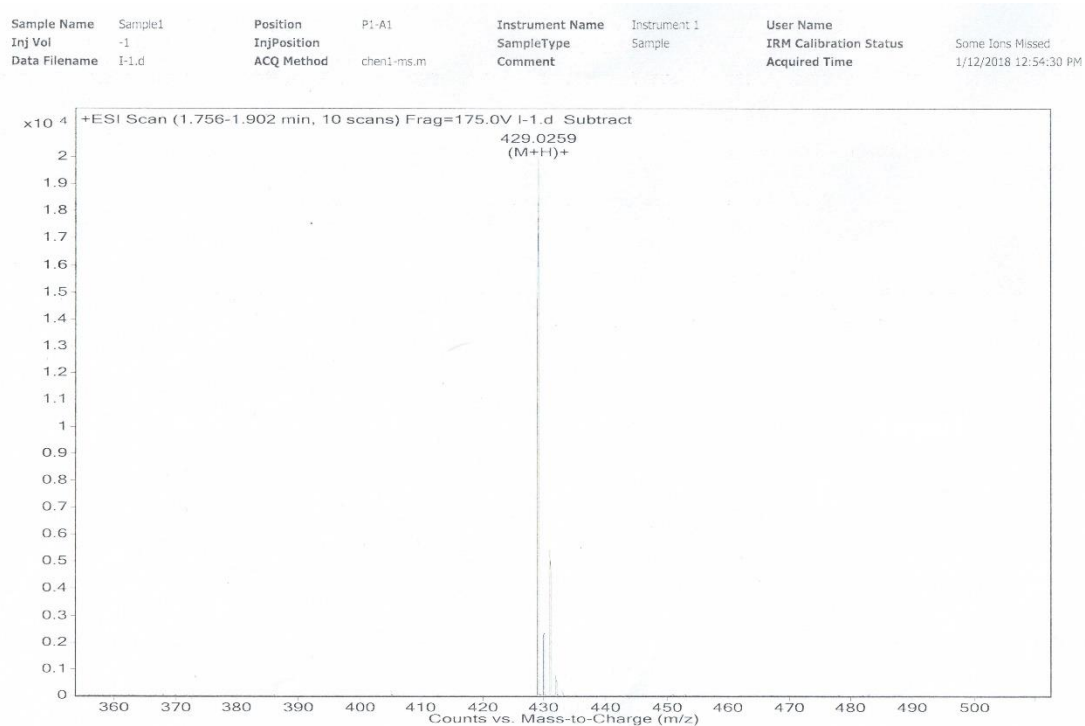


Fig. S1-3. HRMS of the target compound I-1.

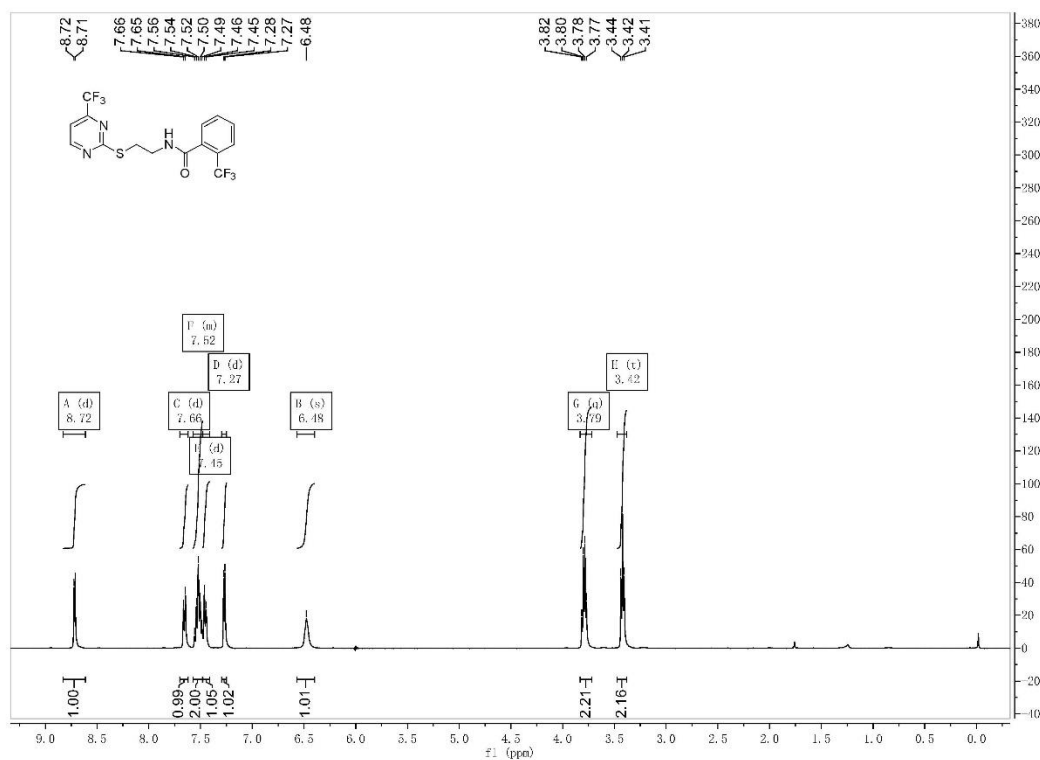


Fig. S2-1. ¹H-NMR of the target compound I-2.

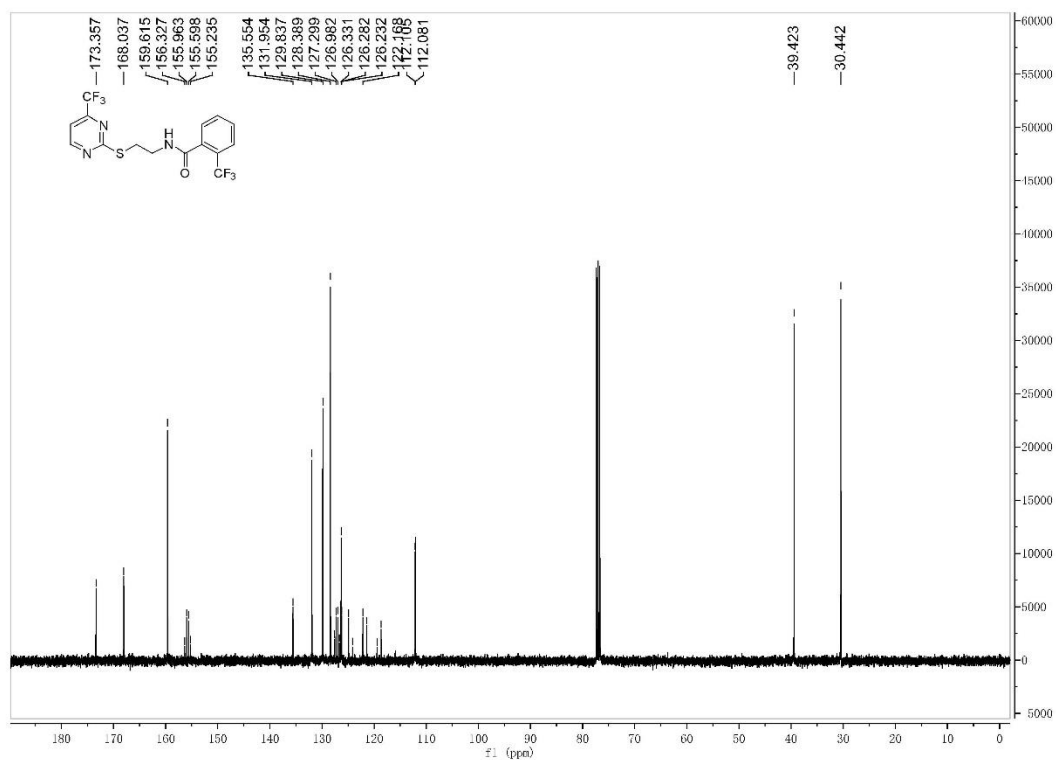


Fig. S2-2. ¹³C-NMR of the target compound I-2.

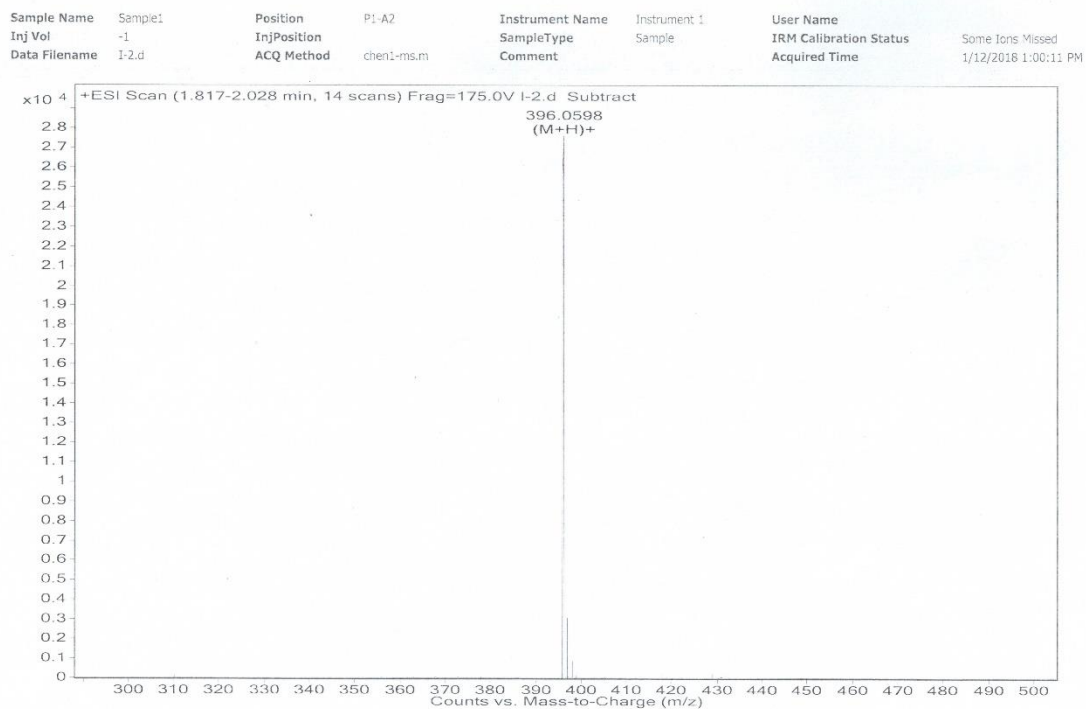


Fig. S2-3. HRMS of the target compound **I-2**.

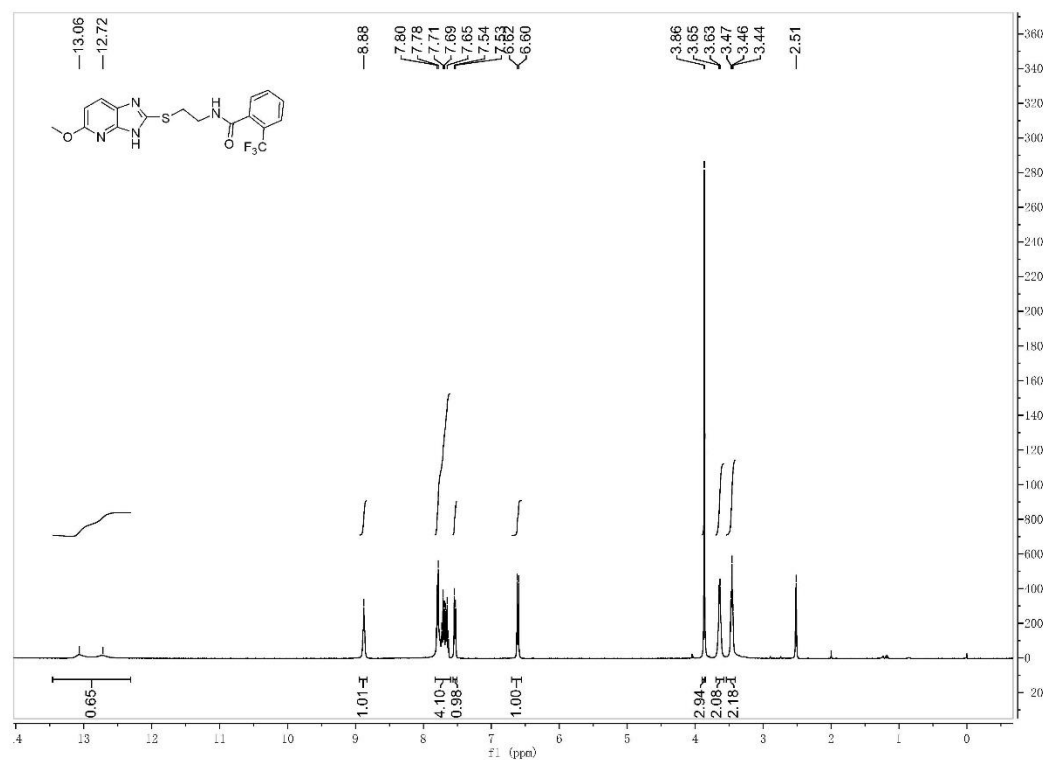


Fig. S3-1. ^1H -NMR of the target compound **I-3**.

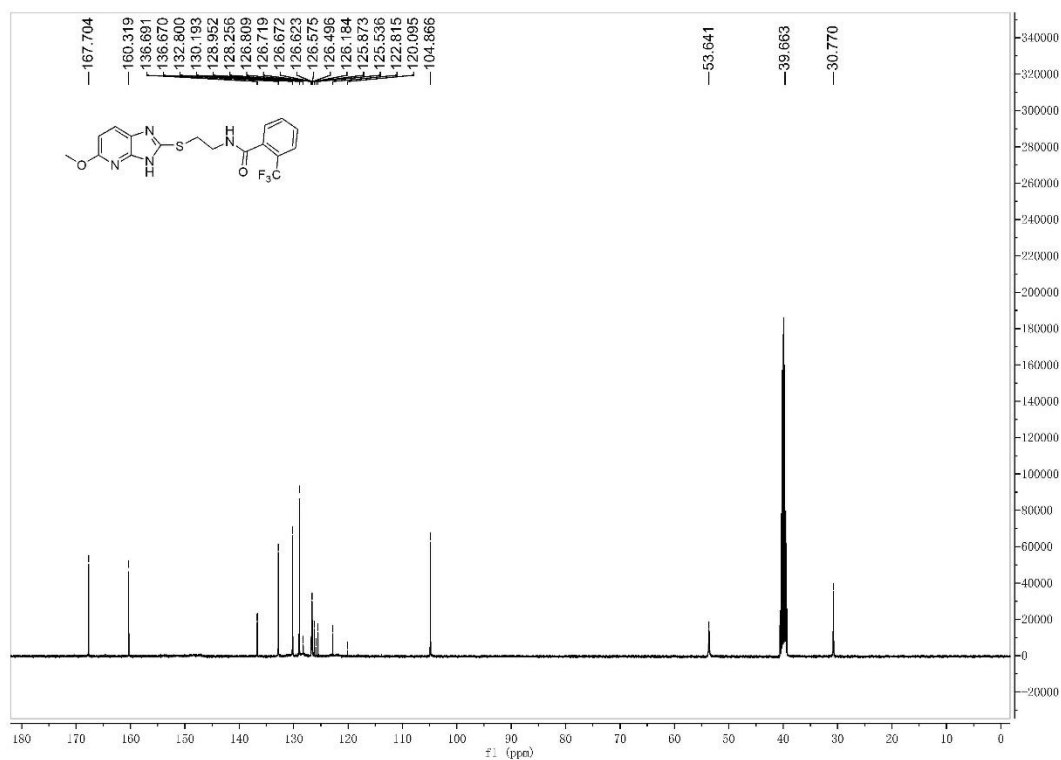


Fig. S3-2. ¹³C-NMR of the target compound I-3.

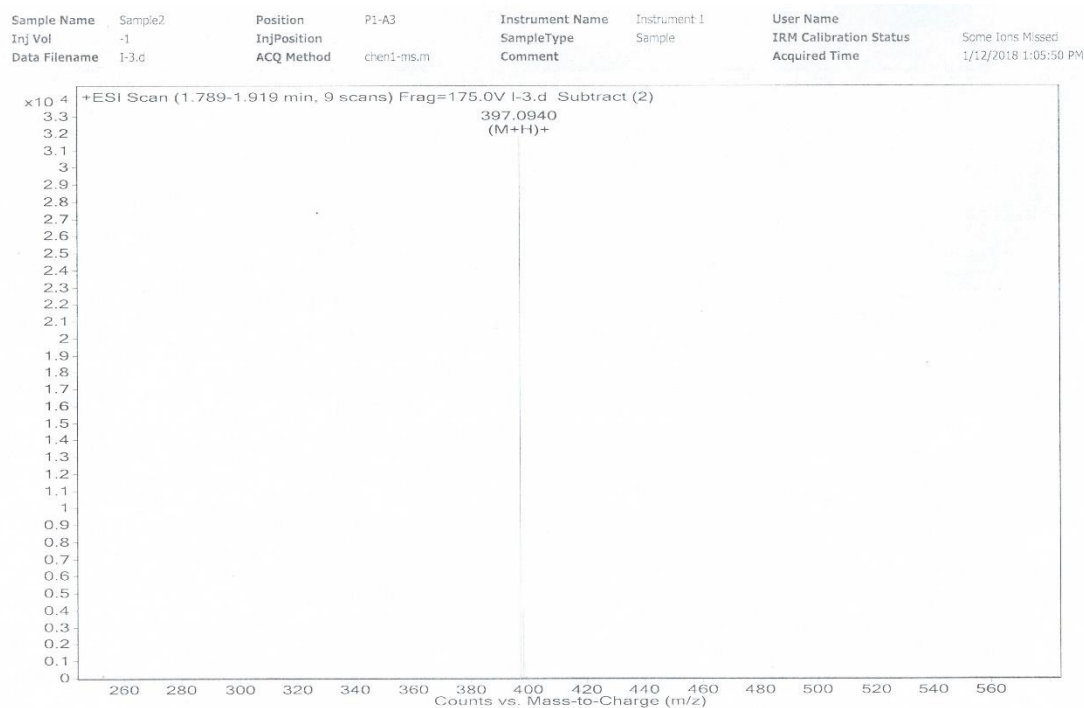


Fig. S3-3. HRMS of the target compound I-3.

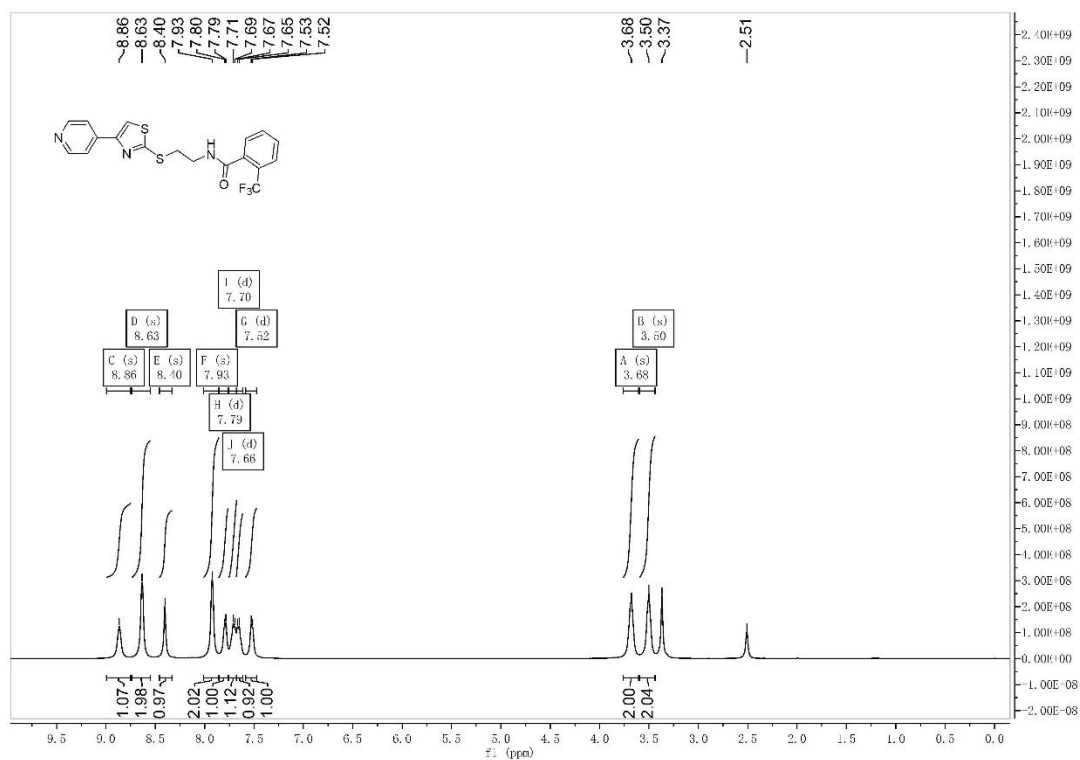


Fig. S4-1. ¹H-NMR of the target compound I-4.

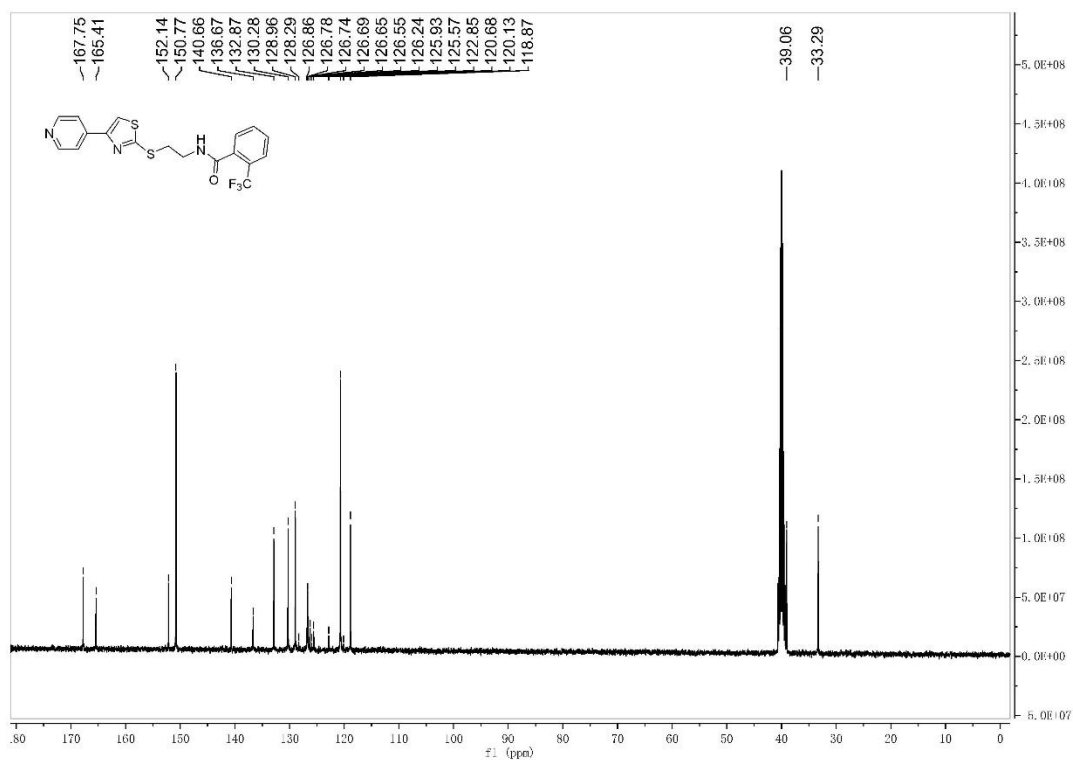


Fig. S4-2. ¹³C-NMR of the target compound I-4.

Sample Name	Sample2	Position	P1-A4	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	I-4.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 1:11:34 PM

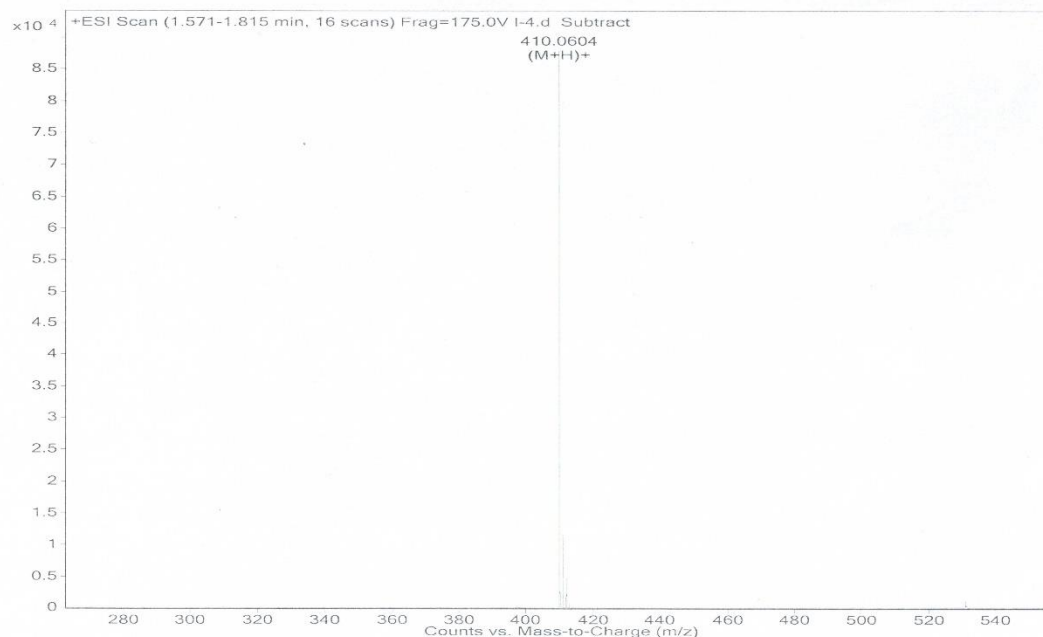


Fig. S4-3. HRMS of the target compound **I-4**.

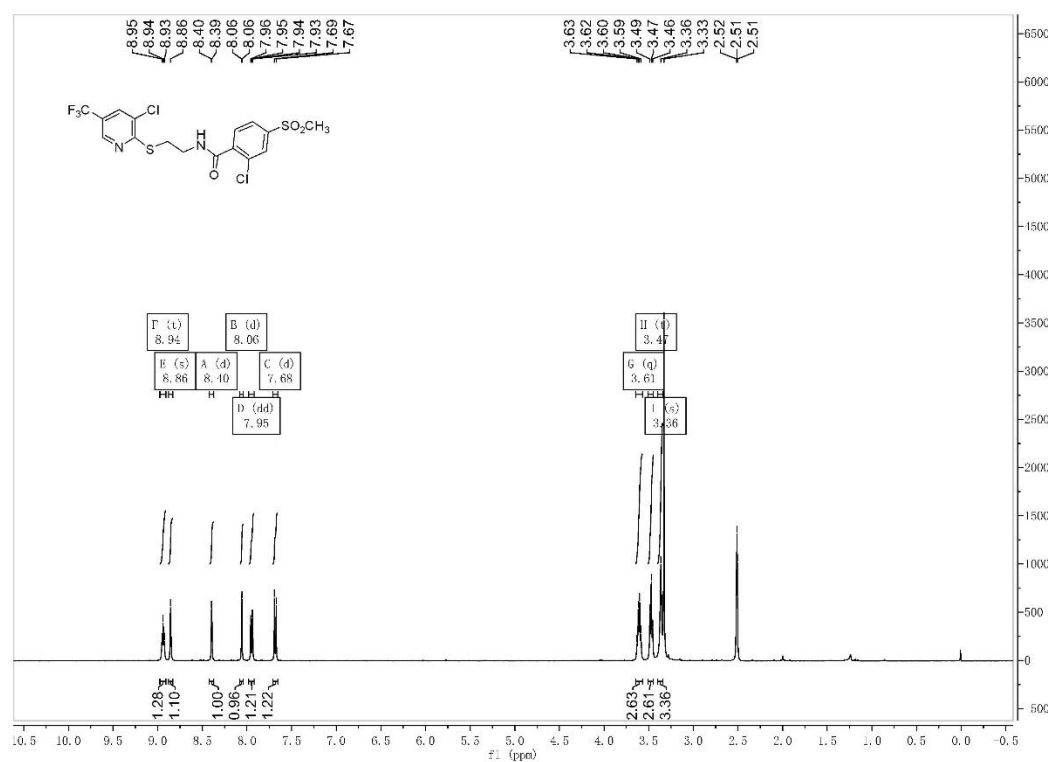


Fig. S5-1. ¹H-NMR of the target compound **I-5**.

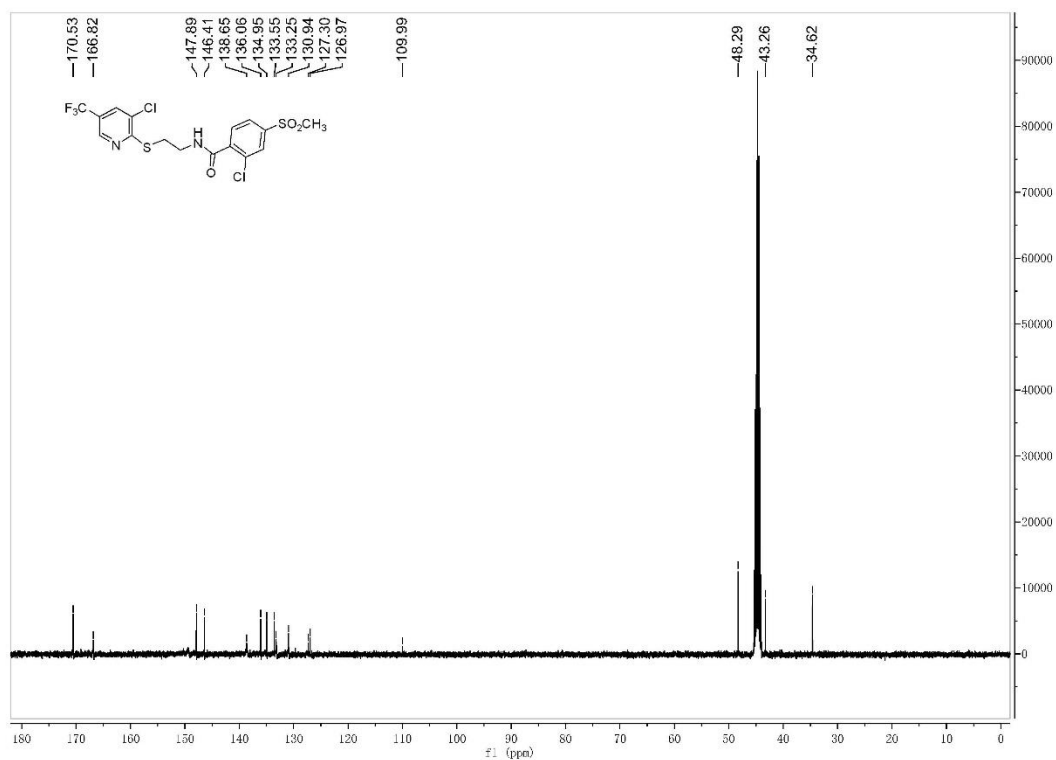


Fig. S5-2. ¹³C-NMR of the target compound I-5.

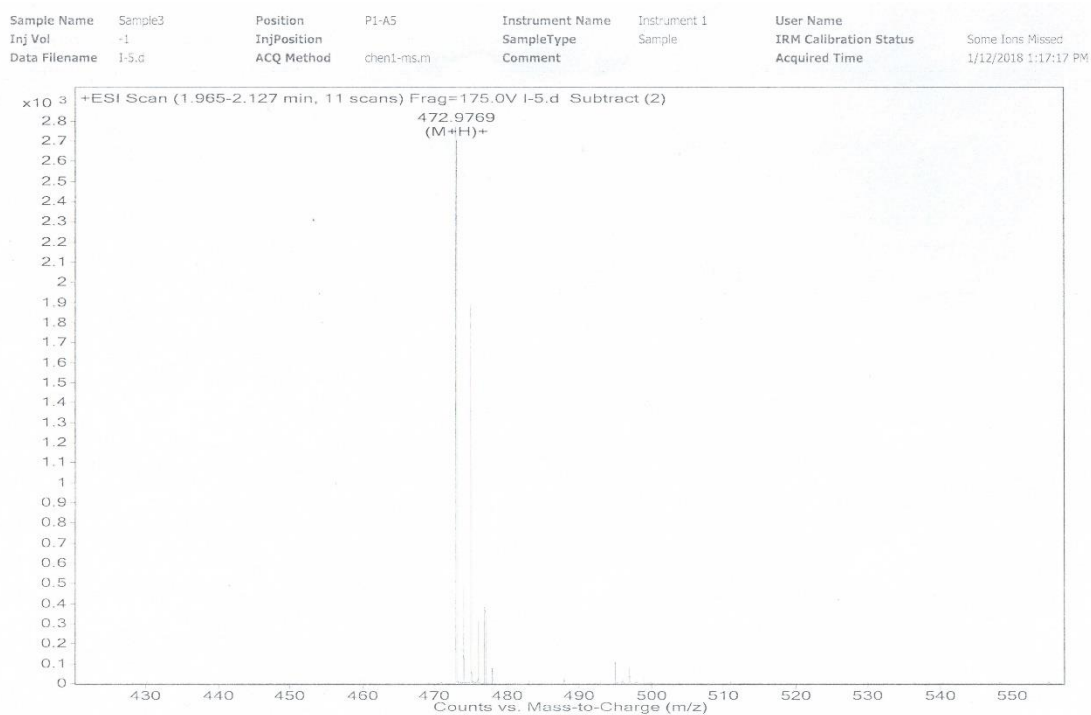


Fig. S5-3. HRMS of the target compound I-5.



Fig. S6-1. ^1H -NMR of the target compound I-6.

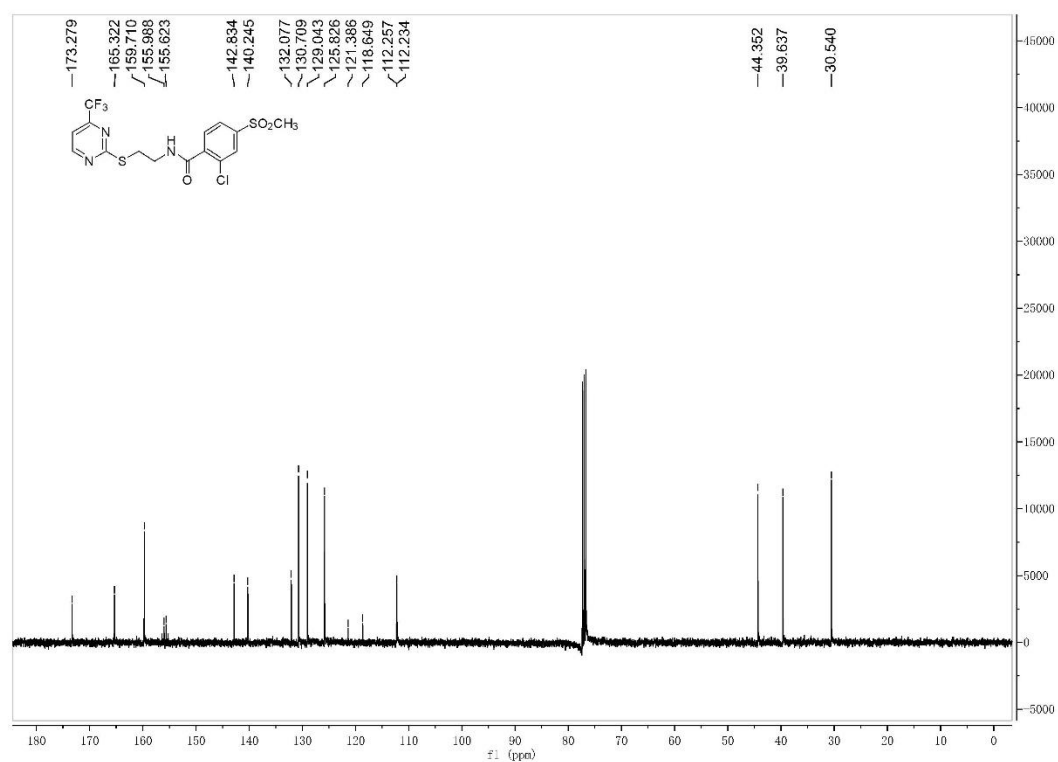


Fig. S6-2. ^{13}C -NMR of the target compound I-6.

Sample Name	Sample3	Position	P1-A6	Instrument Name	Instrument 1	User Name	
Inj Vol	~1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	I-6.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 1:23:00 PM

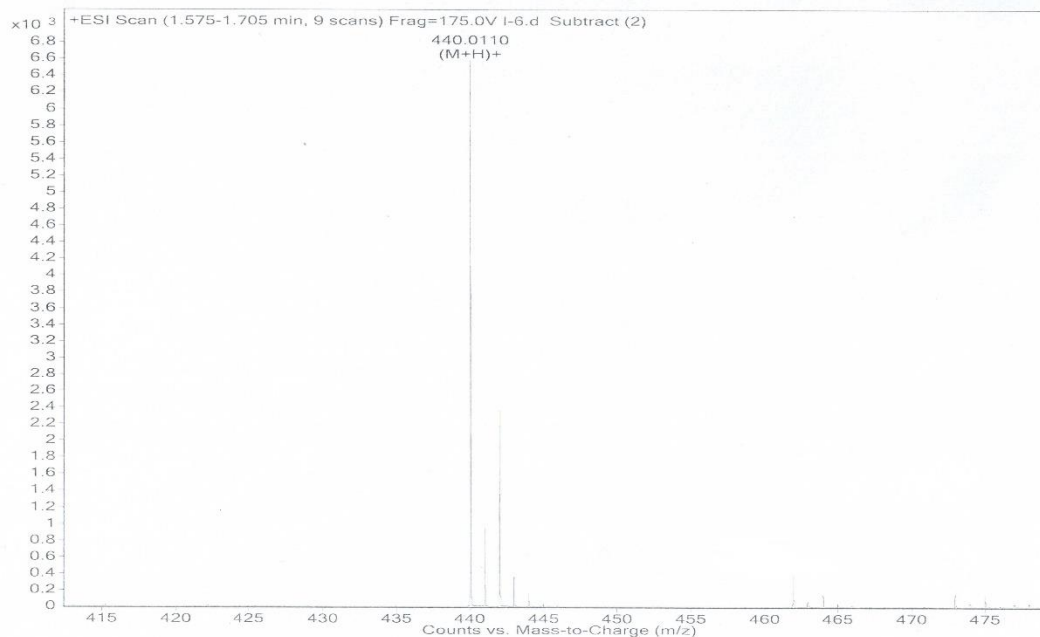


Fig. S6-3. HRMS of the target compound I-6.

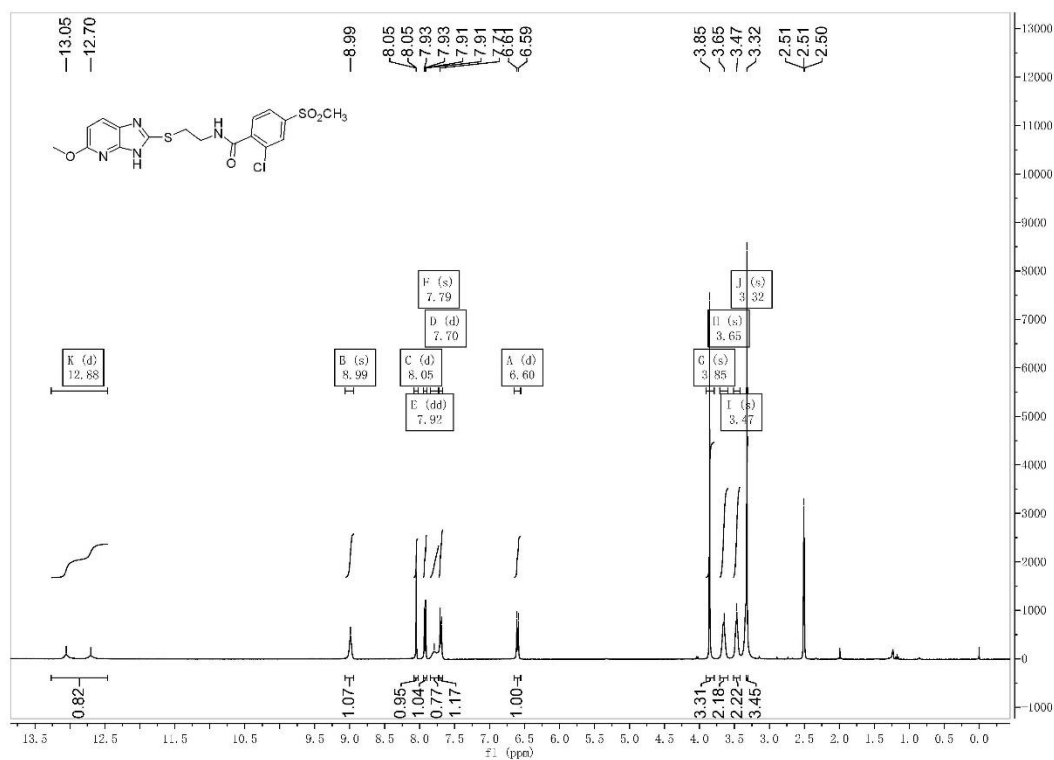


Fig. S7-1. ^1H -NMR of the target compound I-7.

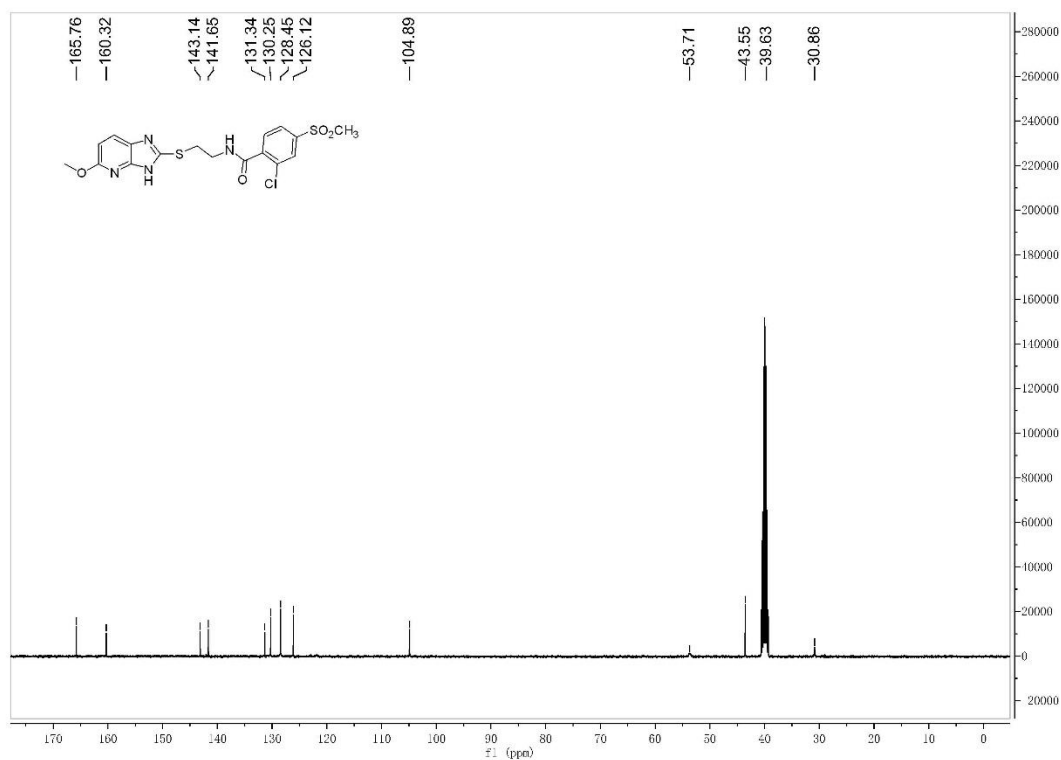


Fig. S7-2. ¹³C-NMR of the target compound I-7.

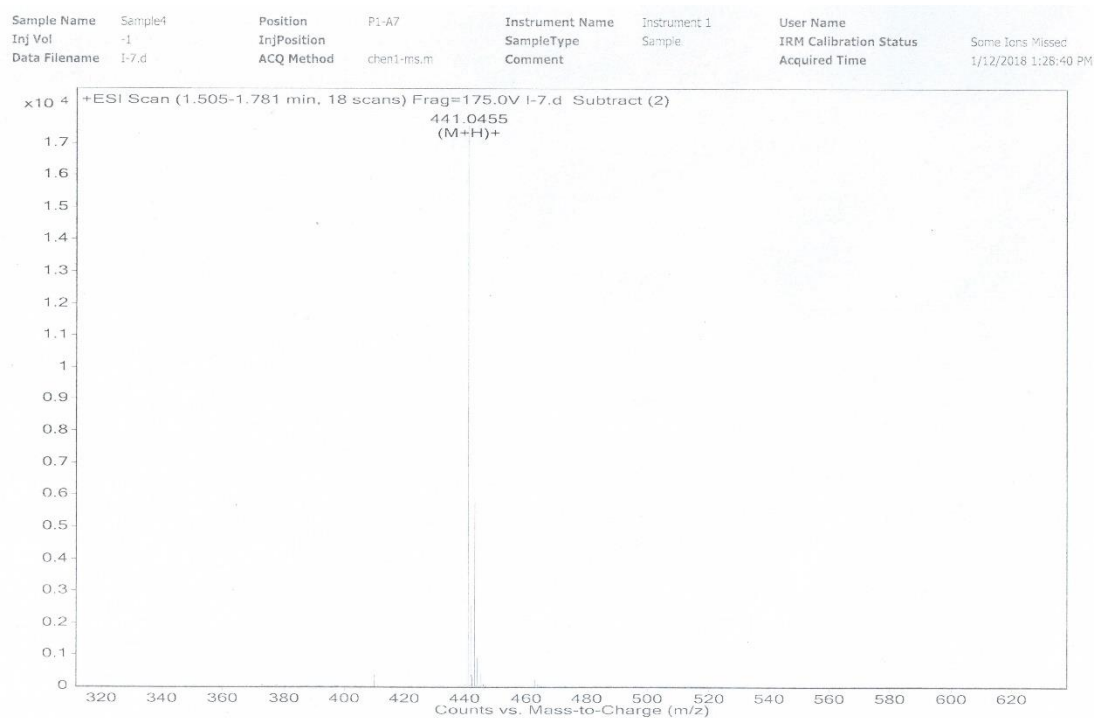


Fig. S7-3. HRMS of the target compound I-7.

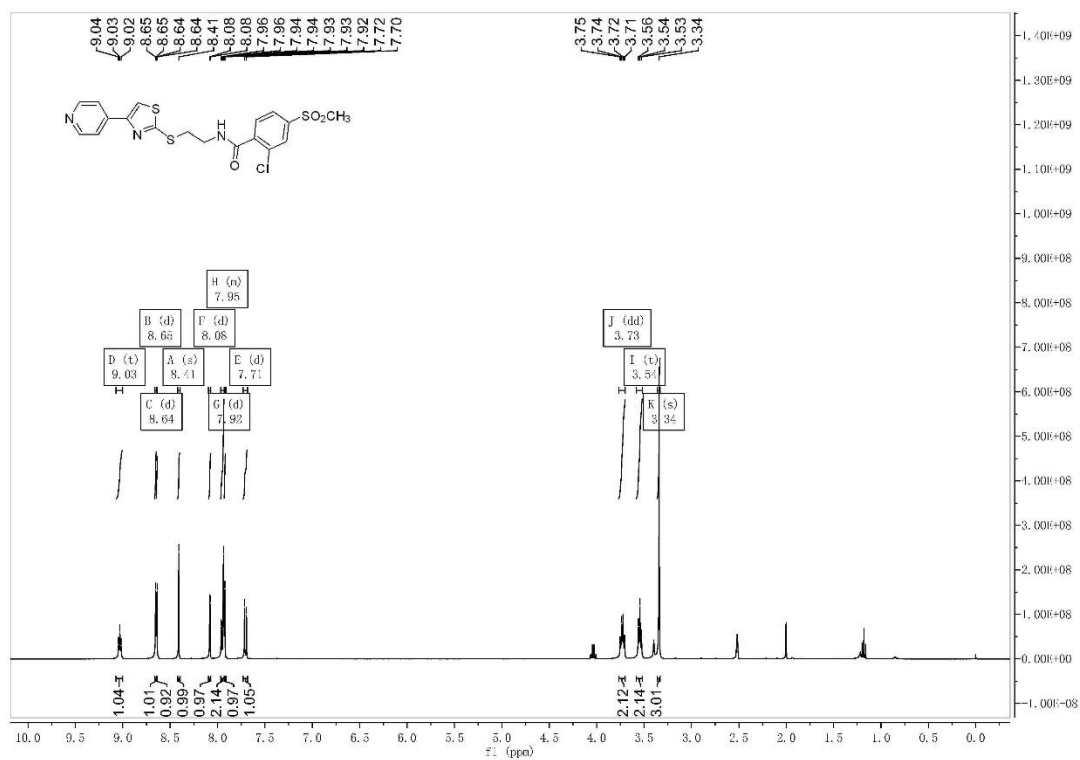


Fig. S8-1. ¹H-NMR of the target compound I-8.

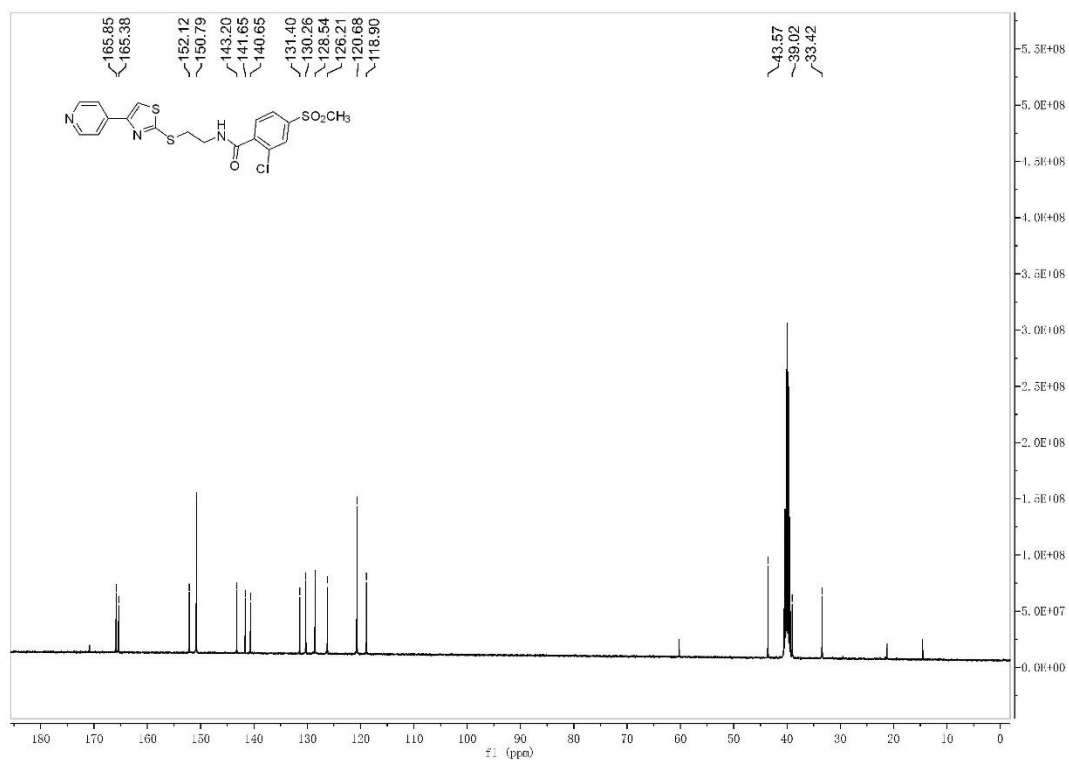


Fig. S8-2. ¹³C-NMR of the target compound I-8.

Sample Name	Sample4	Position	P1-AB	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	I-8.d	ACQ Method	chem1-ms.m	Comment		Acquired Time	1/12/2018 1:34:21 PM

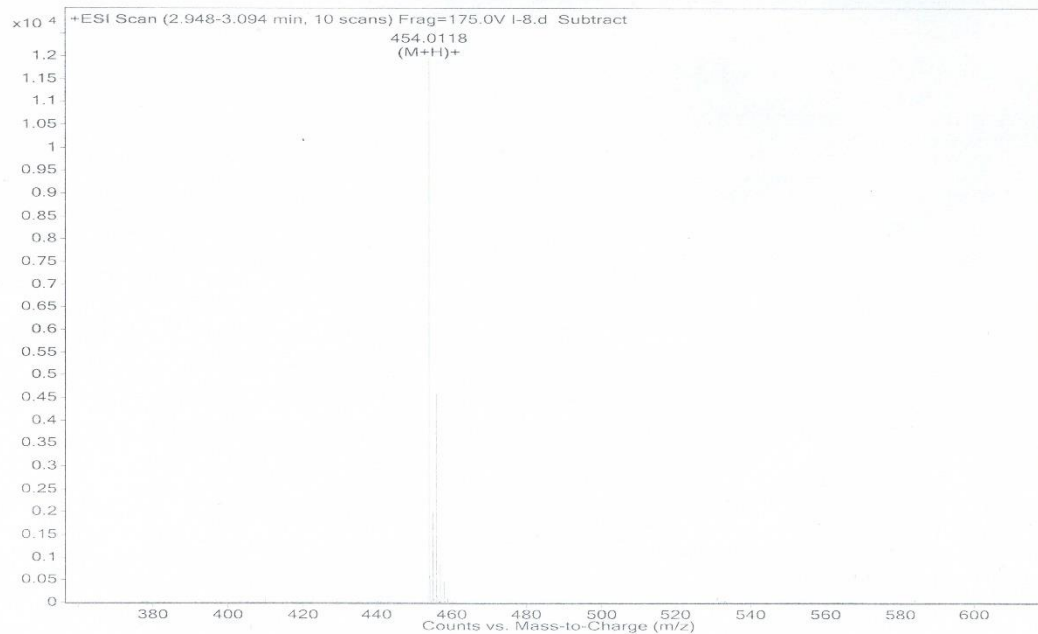


Fig. S8-3. HRMS of the target compound **I-8**.

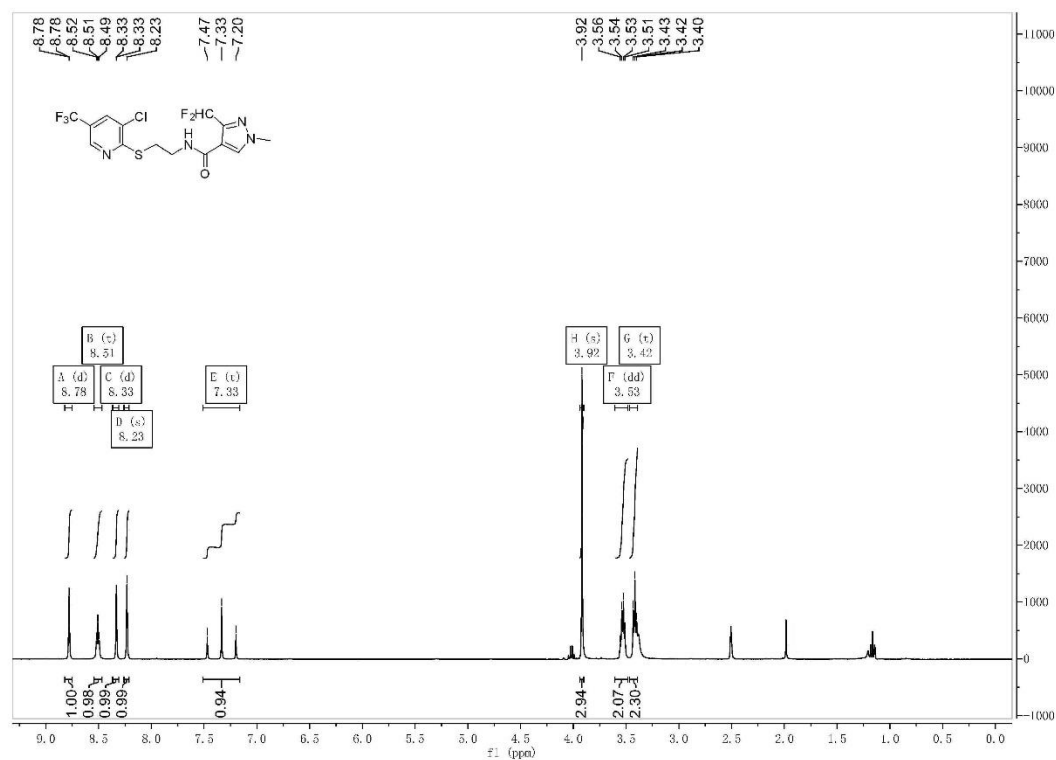


Fig. S9-1. ¹H-NMR of the target compound **I-9**.

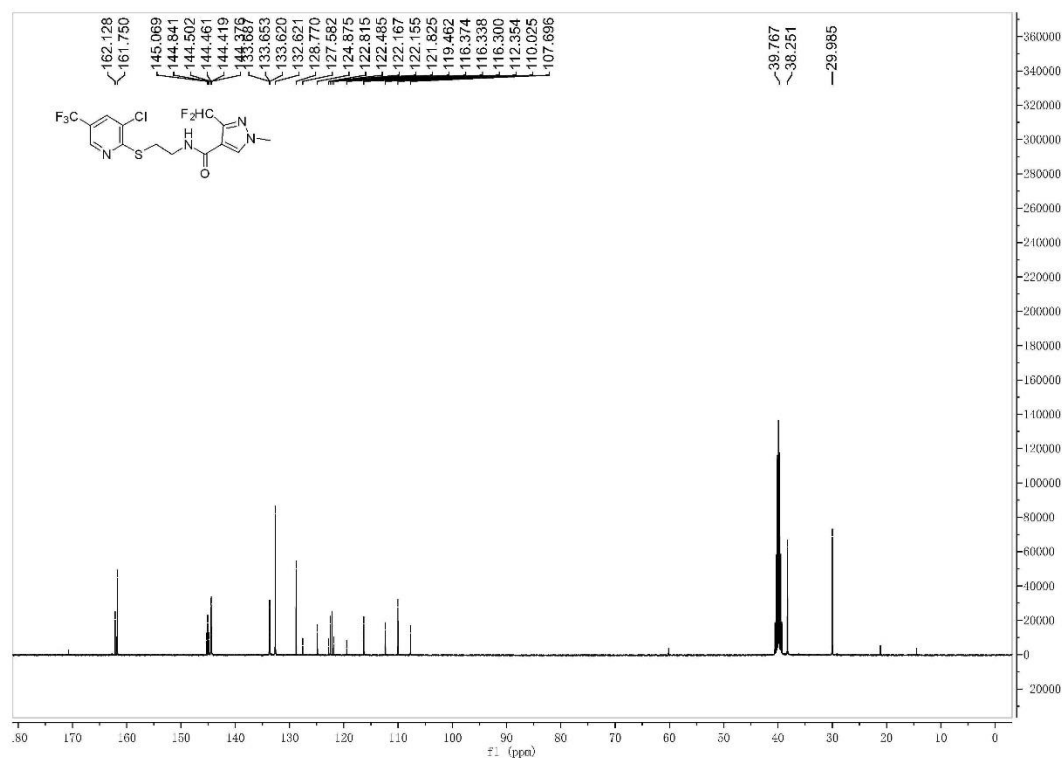


Fig. S9-2. ¹³C-NMR of the target compound I-9.

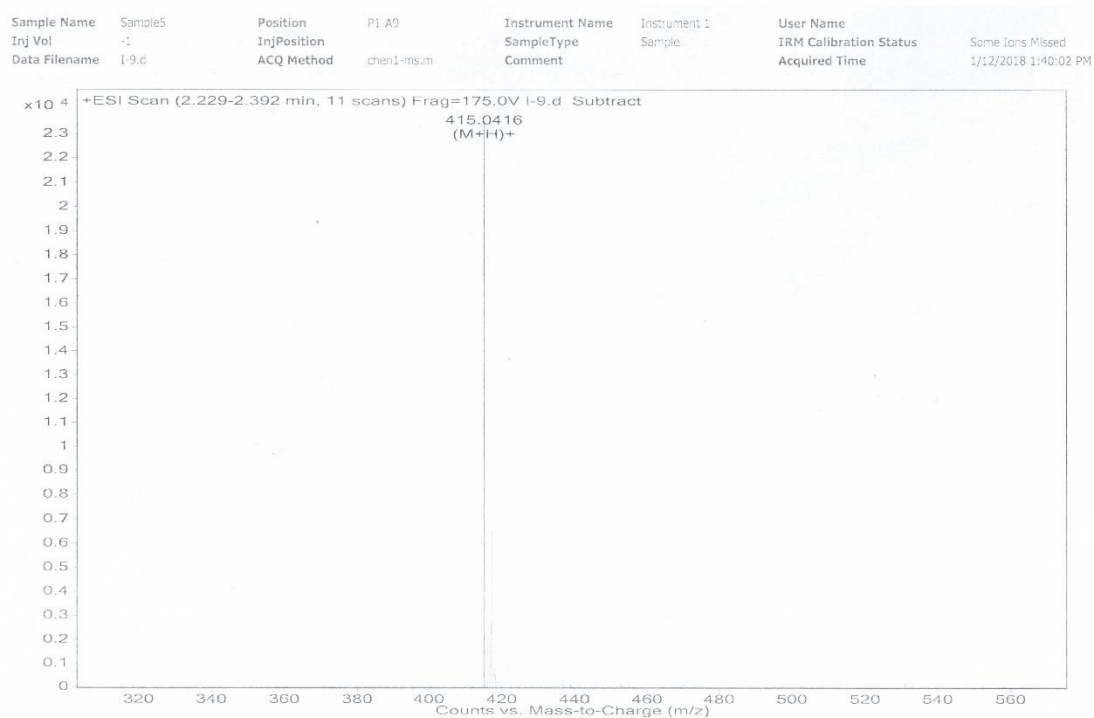


Fig. S9-3. HRMS of the target compound I-9.

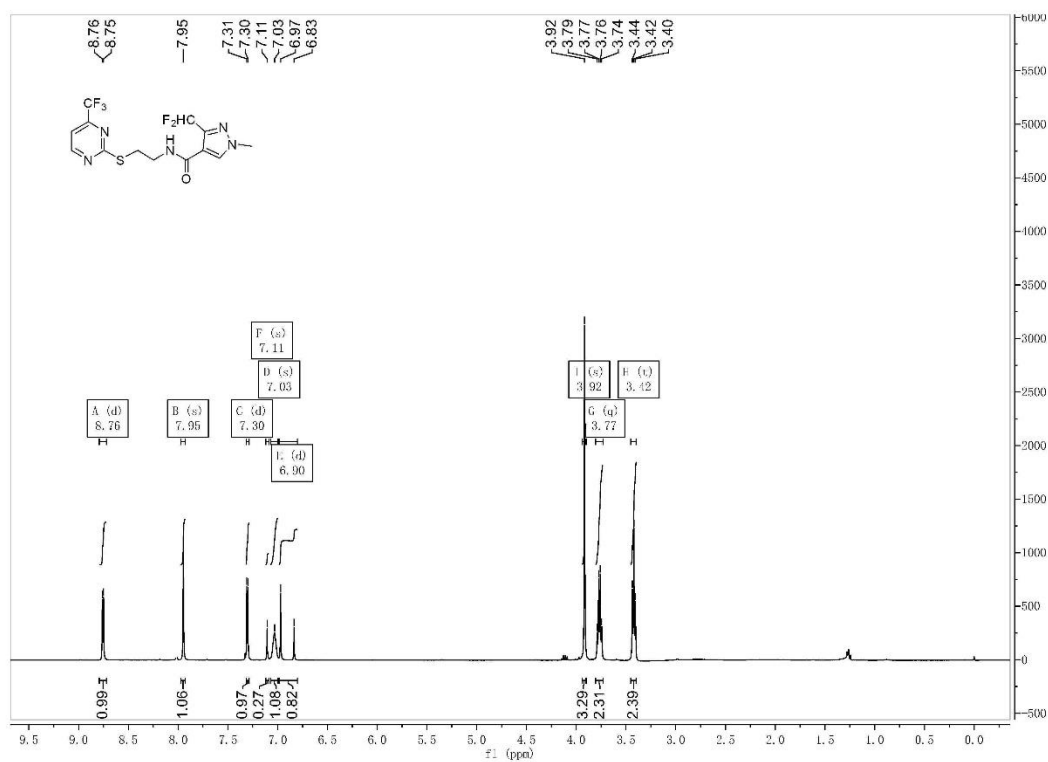


Fig. S10-1. ¹H-NMR of the target compound I-10.

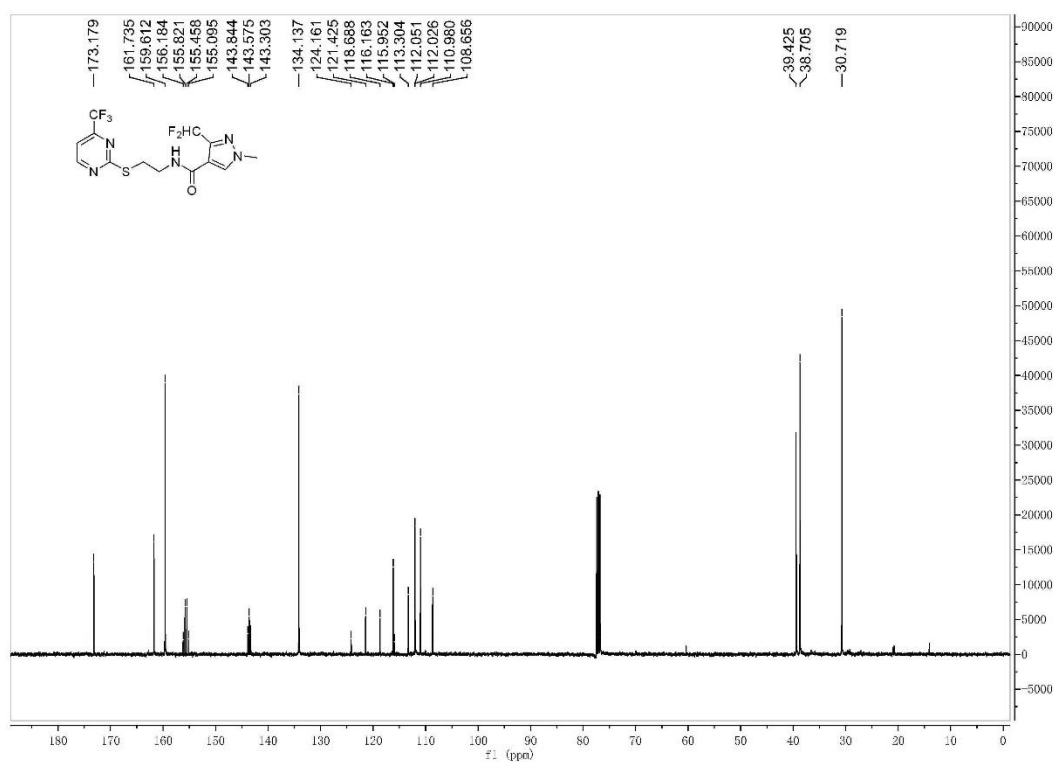


Fig. S10-2. ¹³C-NMR of the target compound I-10.

Sample Name	Sample5	Position	P1-B1	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	I-10.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 1:45:42 PM

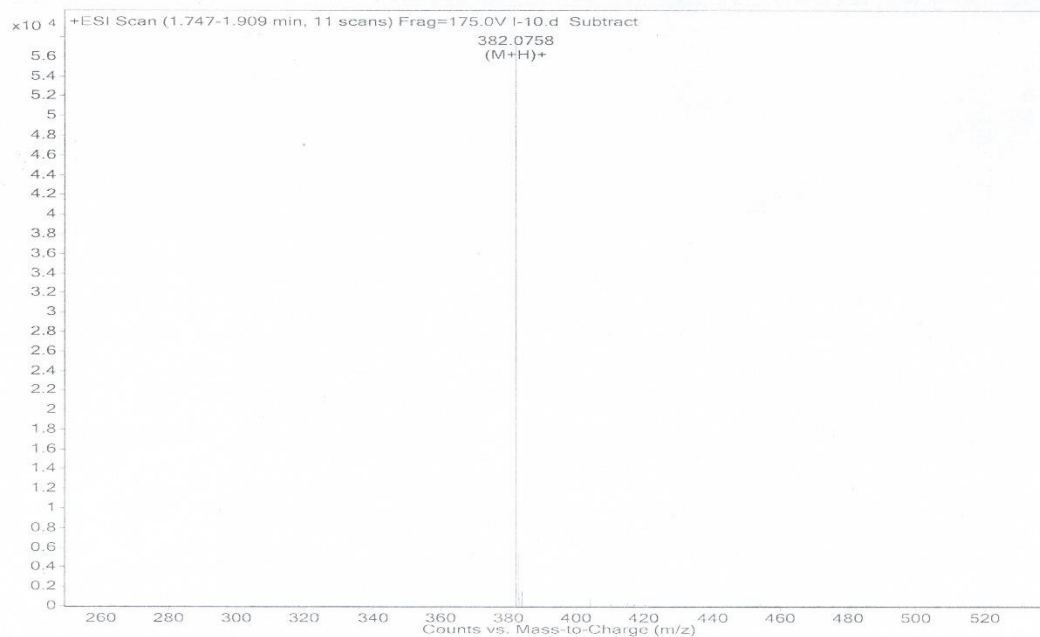


Fig. S10-3. HRMS of the target compound **I-10**.

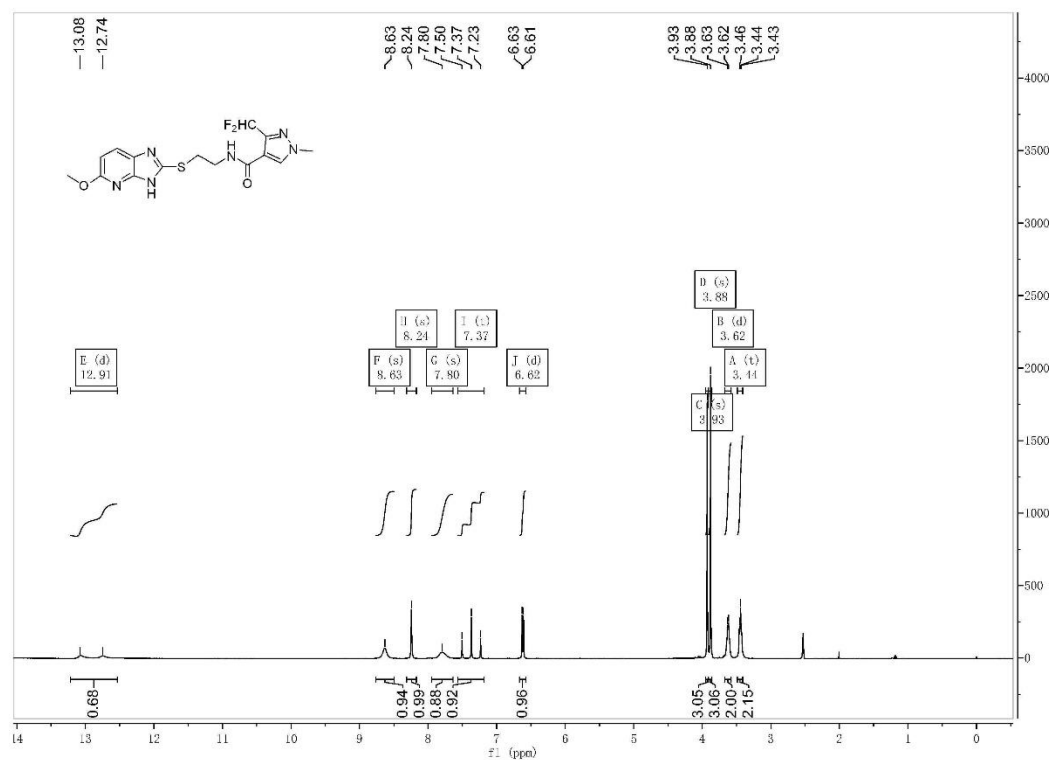


Fig. S11-1. ¹H-NMR of the target compound **I-11**.

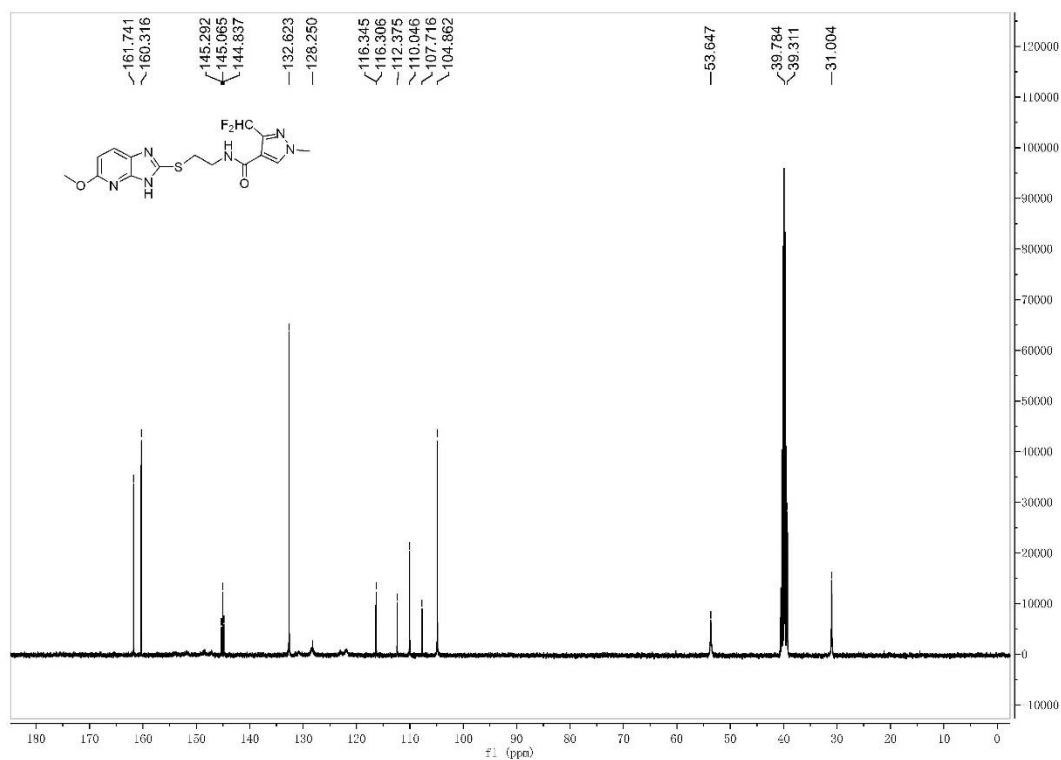


Fig. S11-2. ¹³C-NMR of the target compound I-11.



Fig. S11-3. HRMS of the target compound I-11.

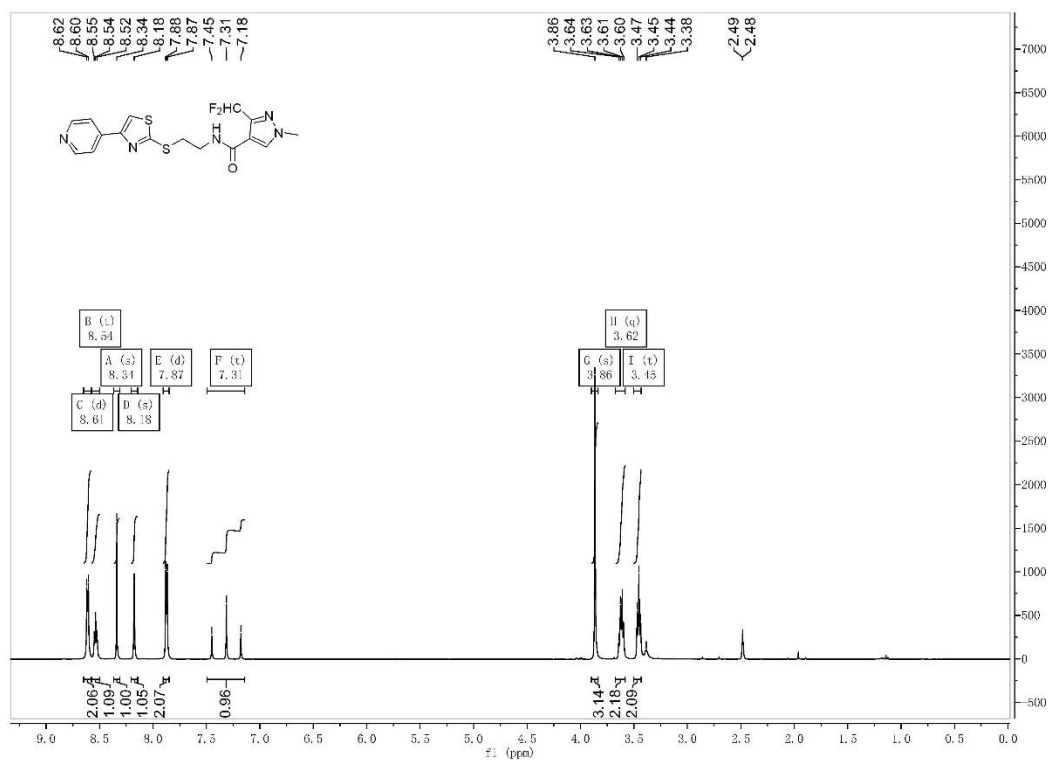


Fig. S12-1. ¹H-NMR of the target compound I-12.

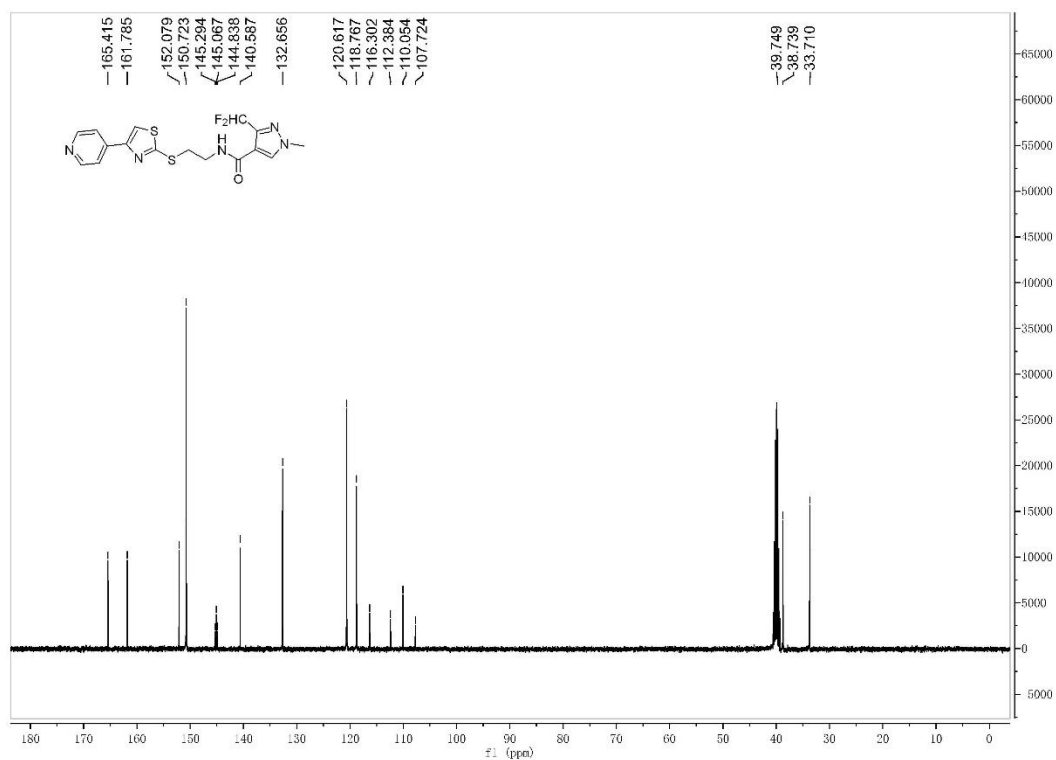


Fig. S12-2. ¹³C-NMR of the target compound I-12.

Sample Name	Sample6	Position	P1-B3	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	I-12.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 1:57:02 PM

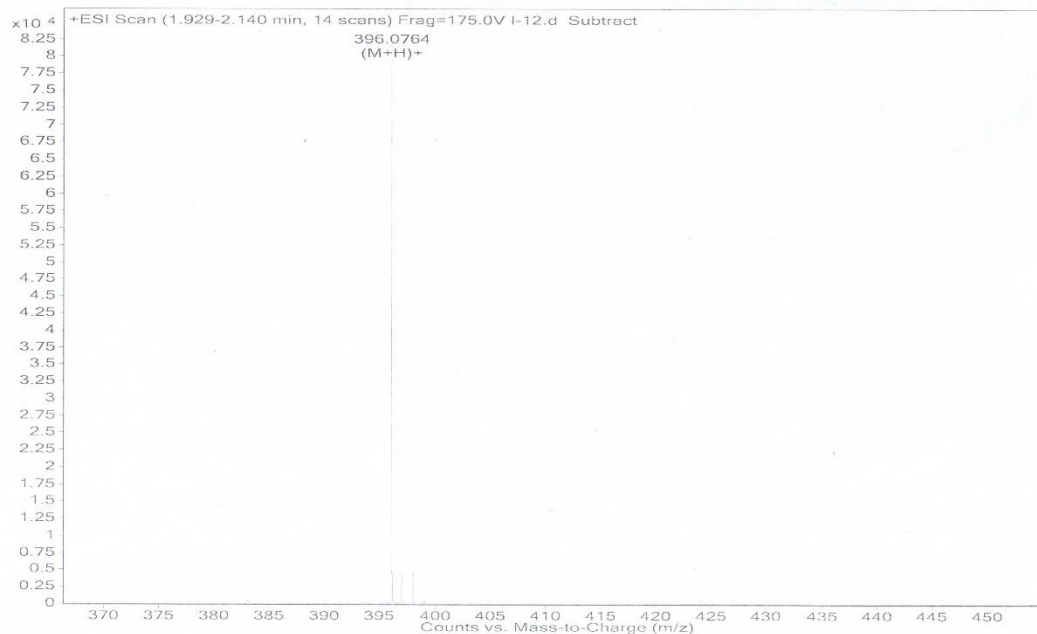


Fig. S12-3. HRMS of the target compound **I-12**.

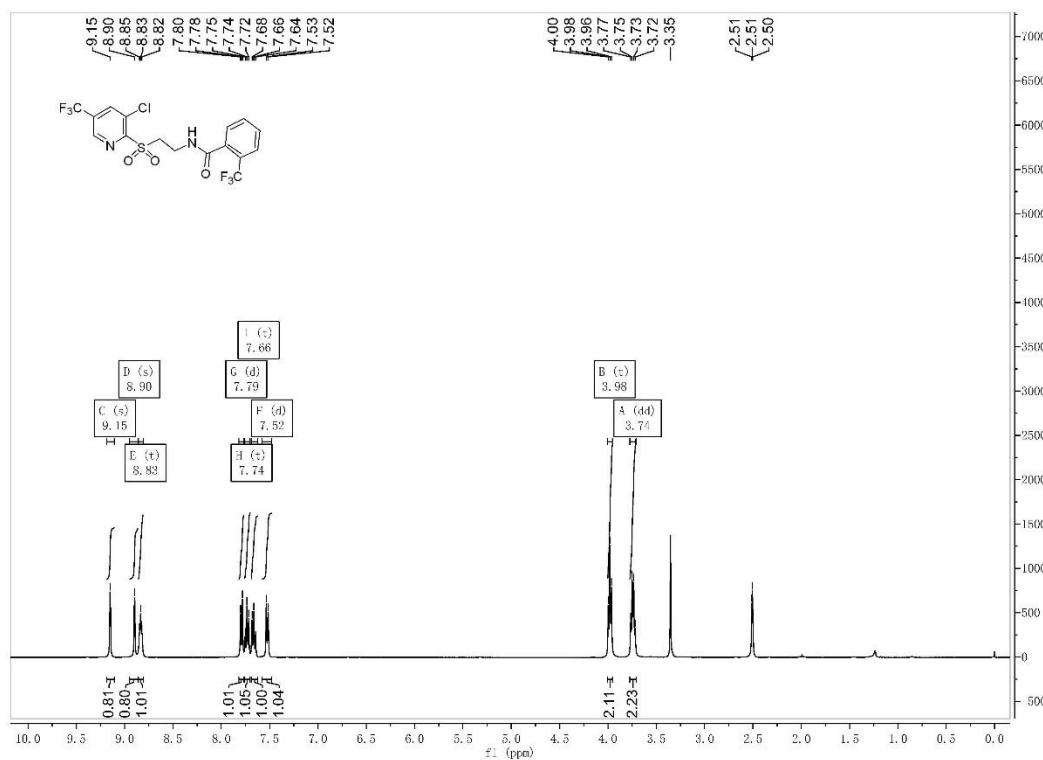


Fig. S13-1. ¹H-NMR of the target compound **II-1**.

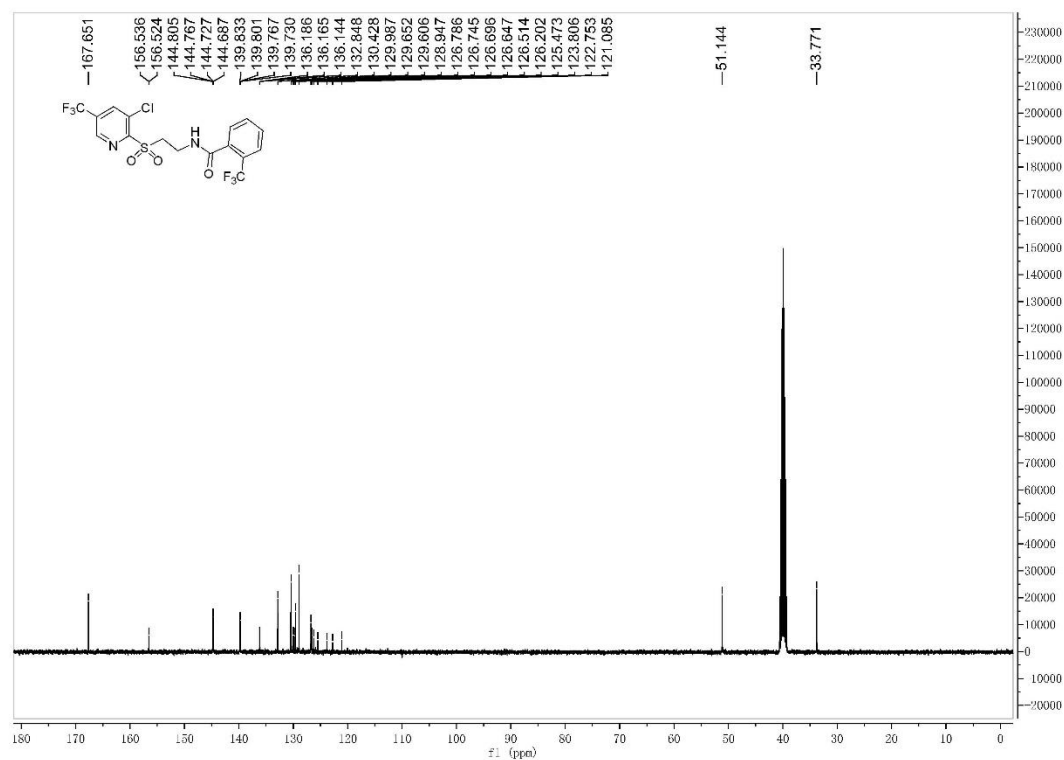


Fig. S13-2. ¹³C-NMR of the target compound **II-1**.

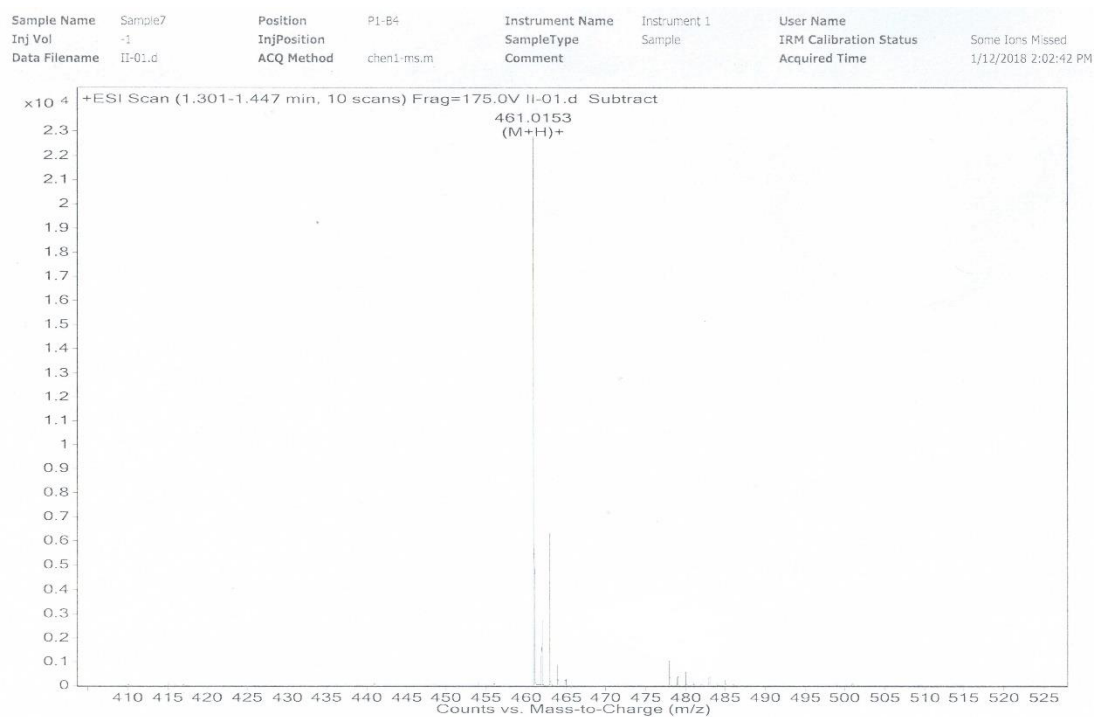


Fig. S13-3. HRMS of the target compound **II-1**.

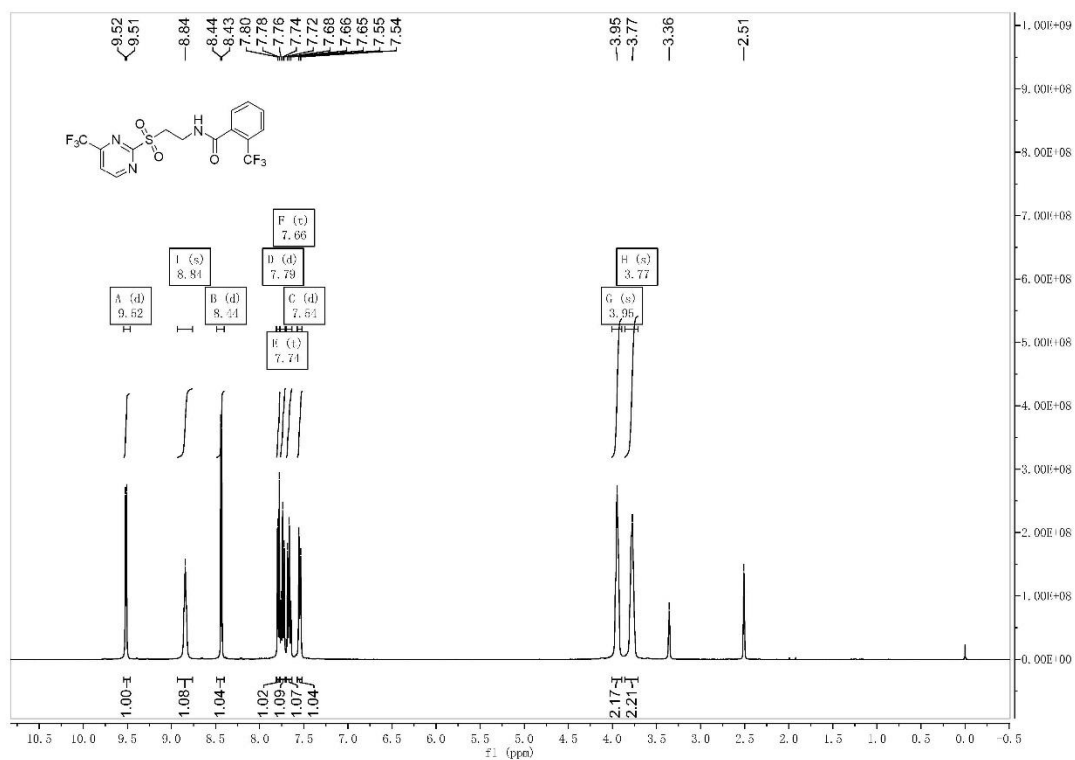


Fig. S14-1. ^1H -NMR of the target compound II-2.

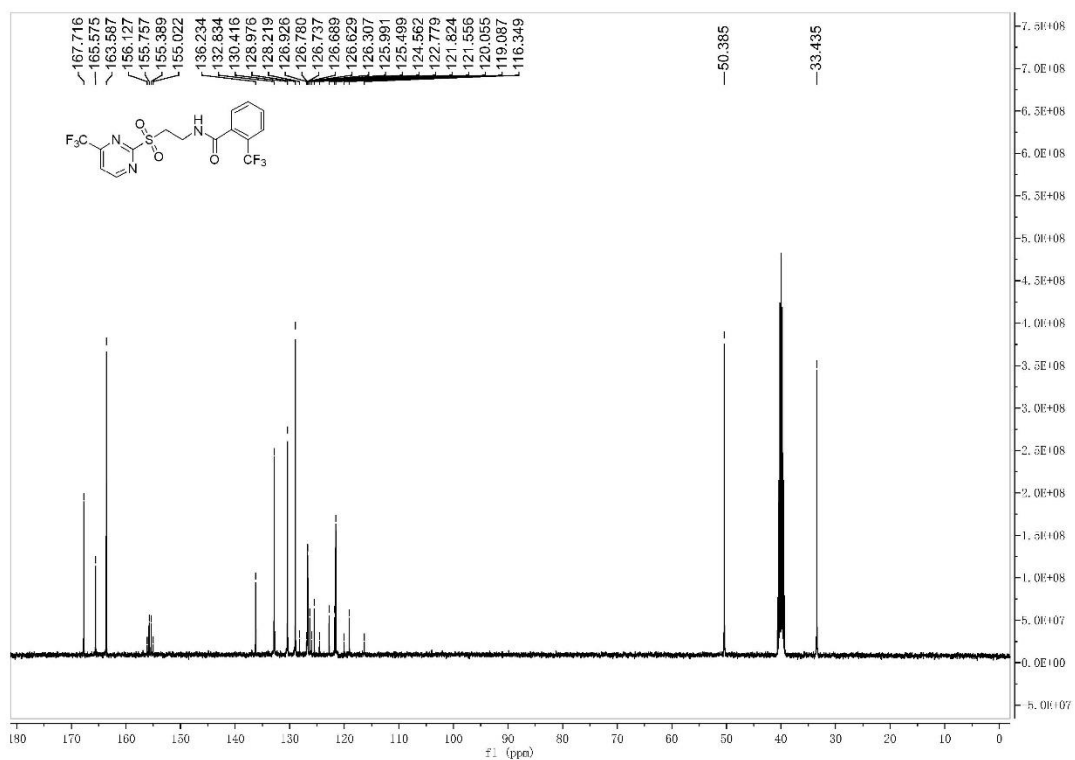


Fig. S14-2. ^{13}C -NMR of the target compound II-2.

Sample Name	Sample7	Position	PI-85	Instrument Name	Instrument 1	User Name	
Inj Vol	~1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	II-02.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 2:08:22 PM

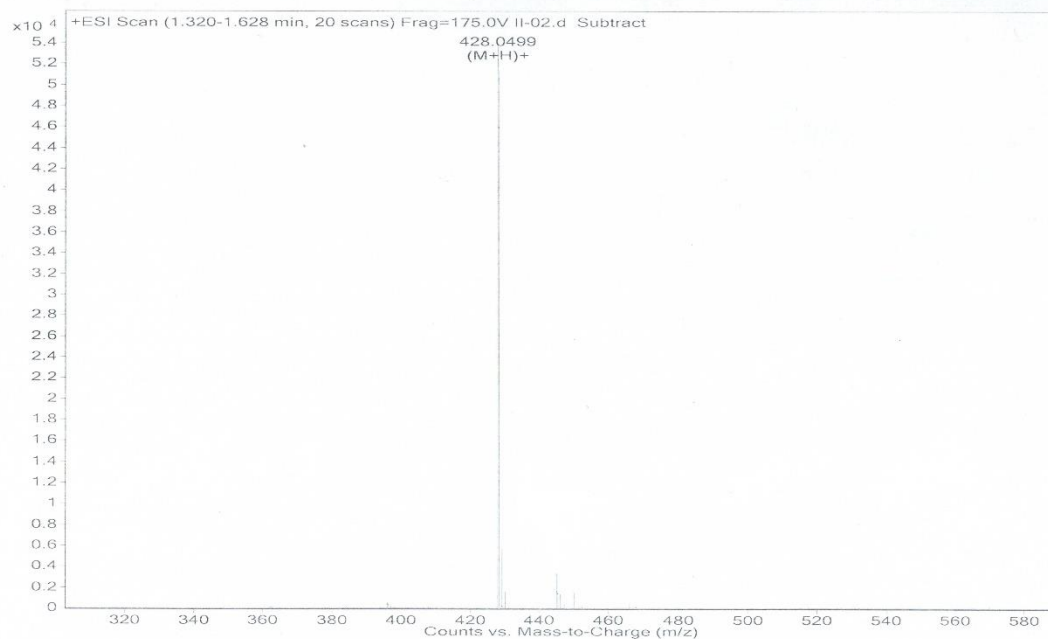


Fig. S14-3. HRMS of the target compound **II-2**.

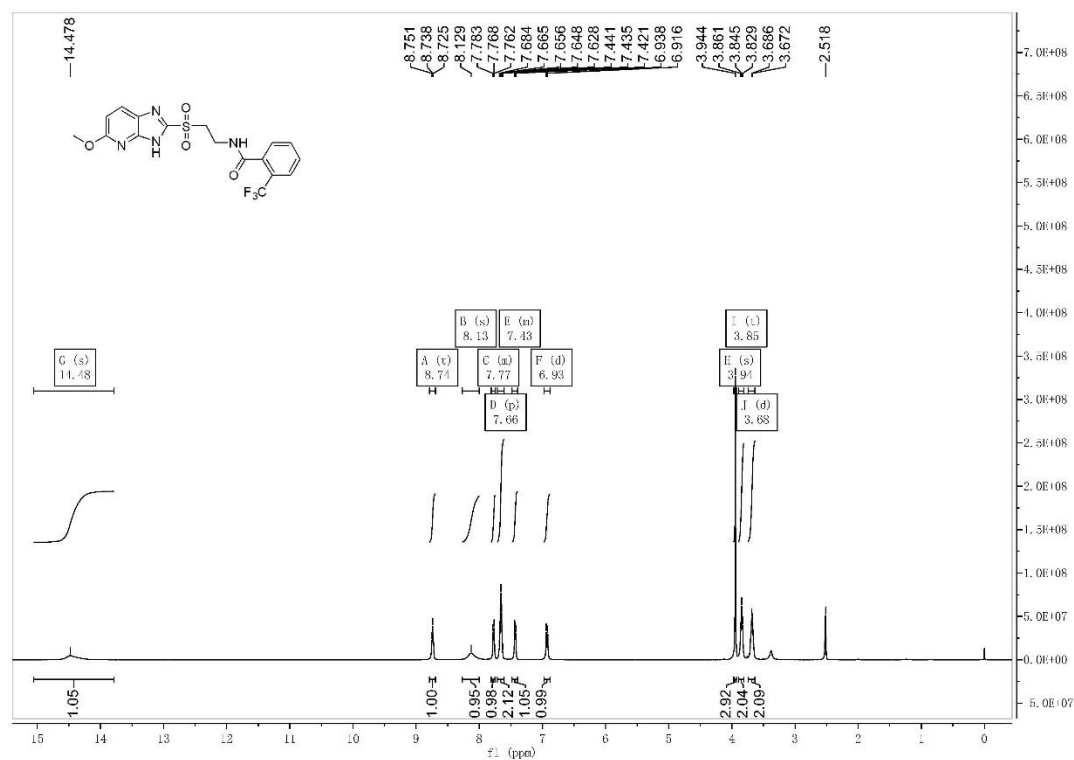


Fig. S15-1. ^1H -NMR of the target compound **II-3**.

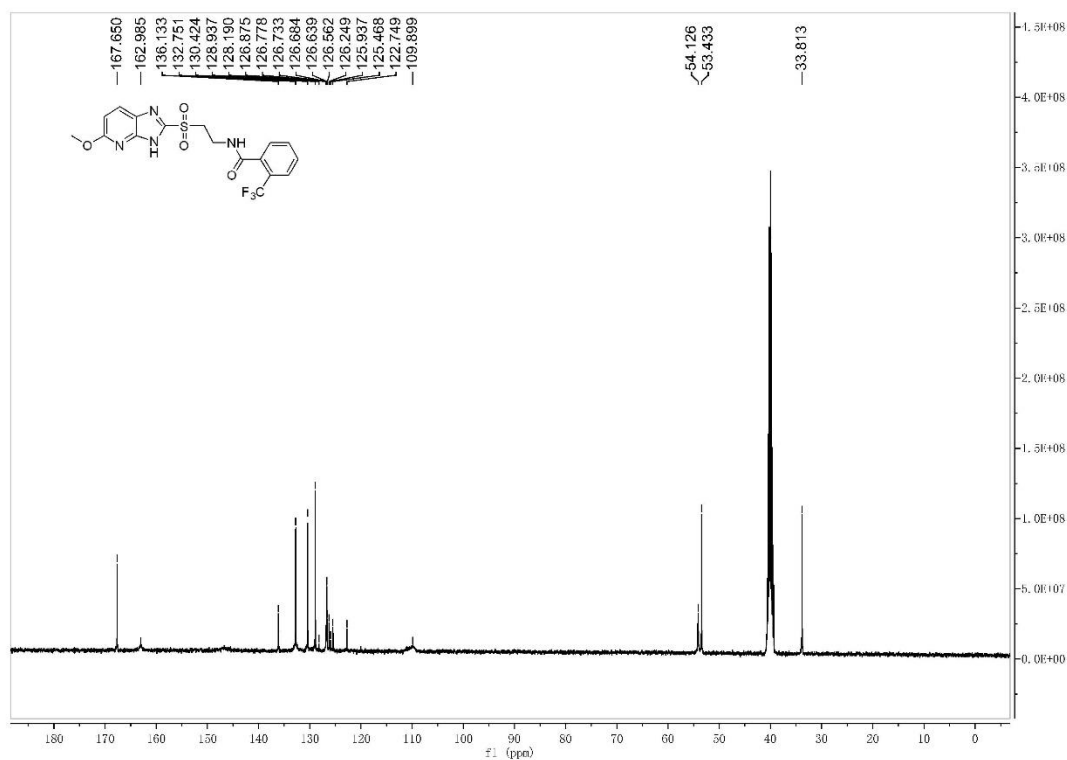


Fig. S15-2. ¹³C-NMR of the target compound **II-3**.

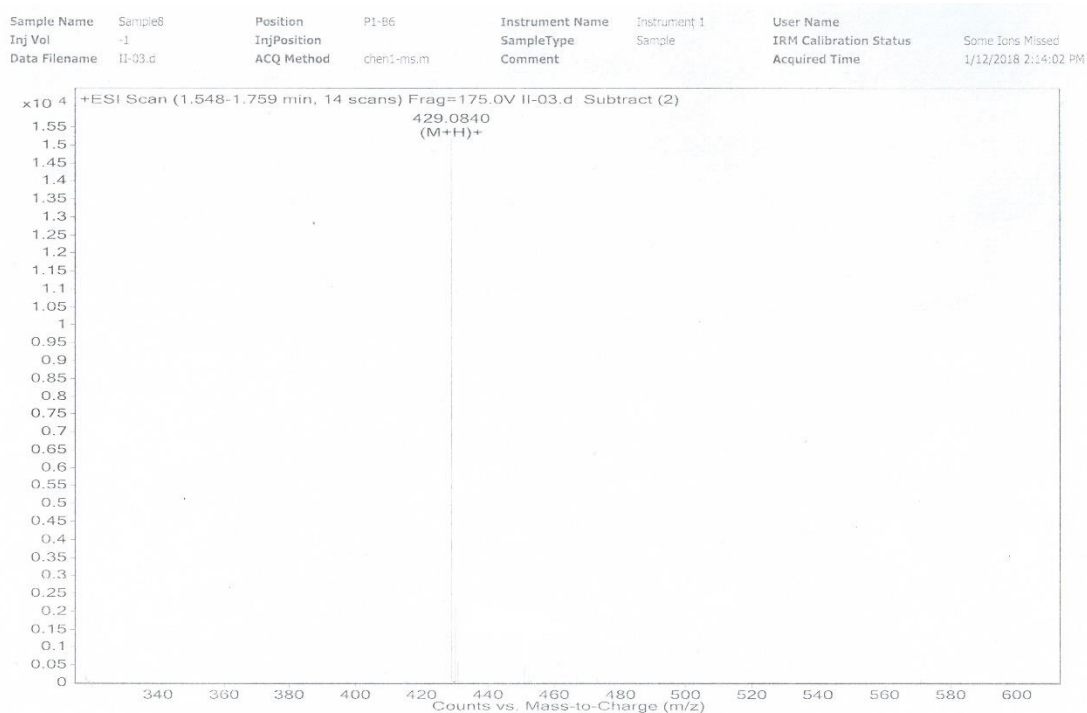


Fig. S15-3. HRMS of the target compound **II-3**.

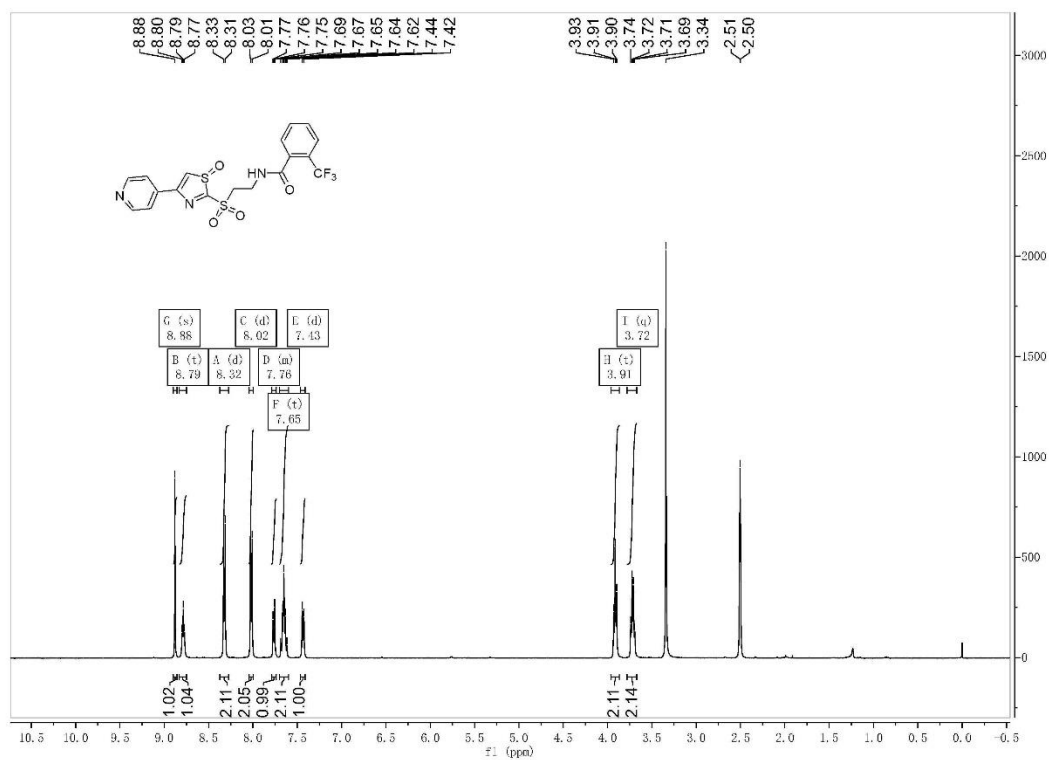


Fig. S16-1. ¹H-NMR of the target compound II-4.

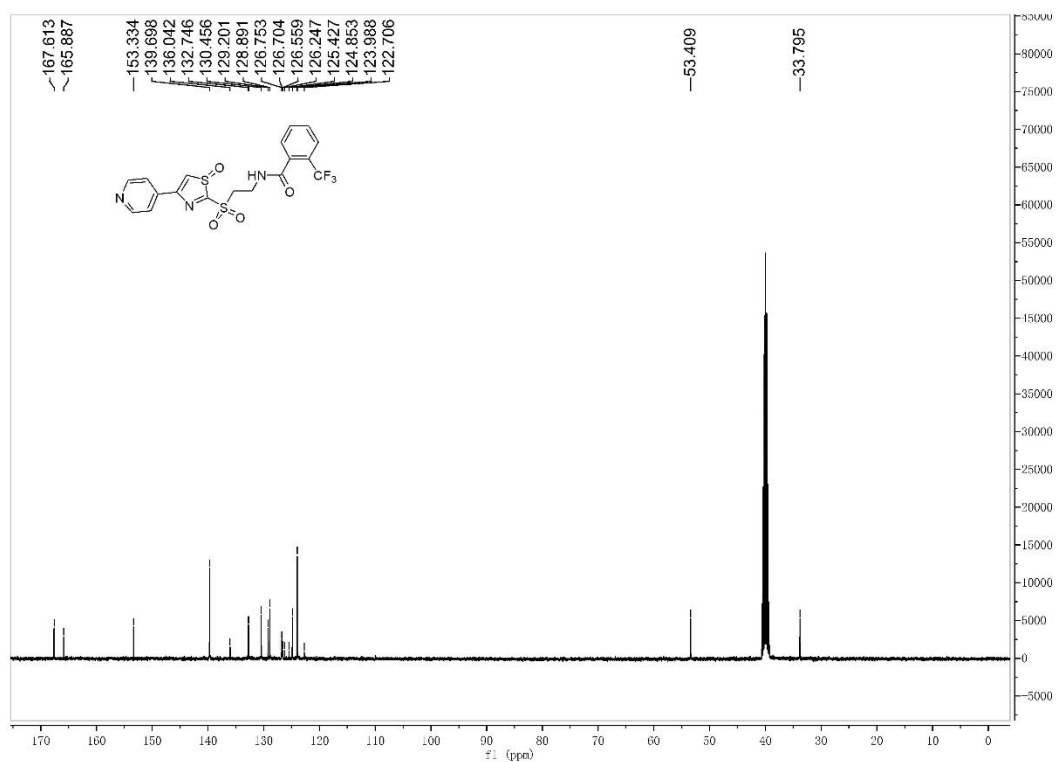


Fig. S16-2. ¹³C-NMR of the target compound II-4.

Sample Name	Sample8	Position	P1-B7	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	II-04.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 2:19:42 PM

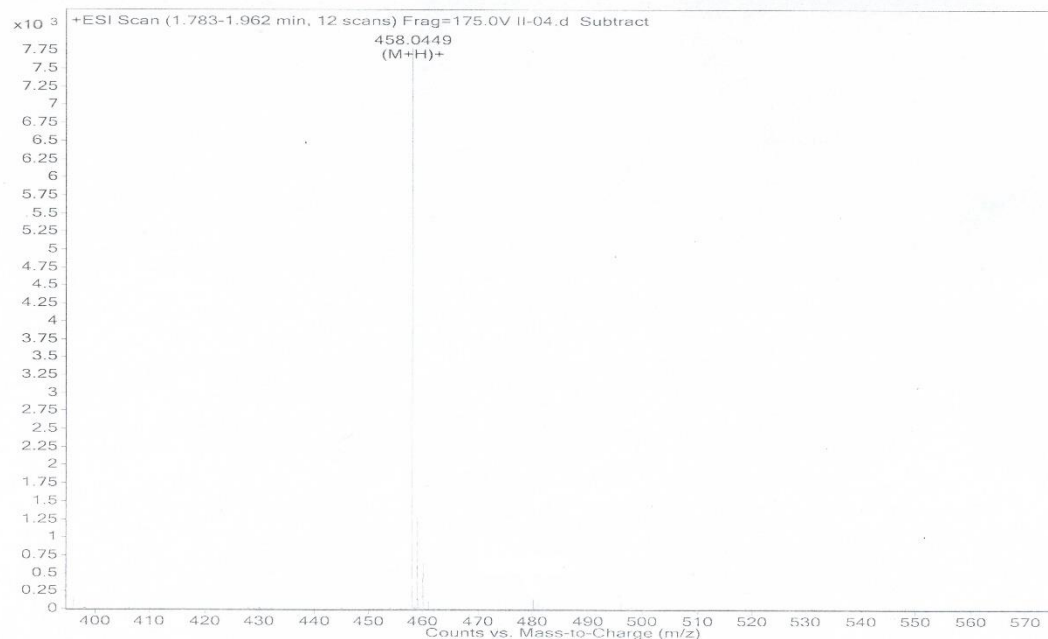


Fig. S16-3. HRMS of the target compound **II-4**.

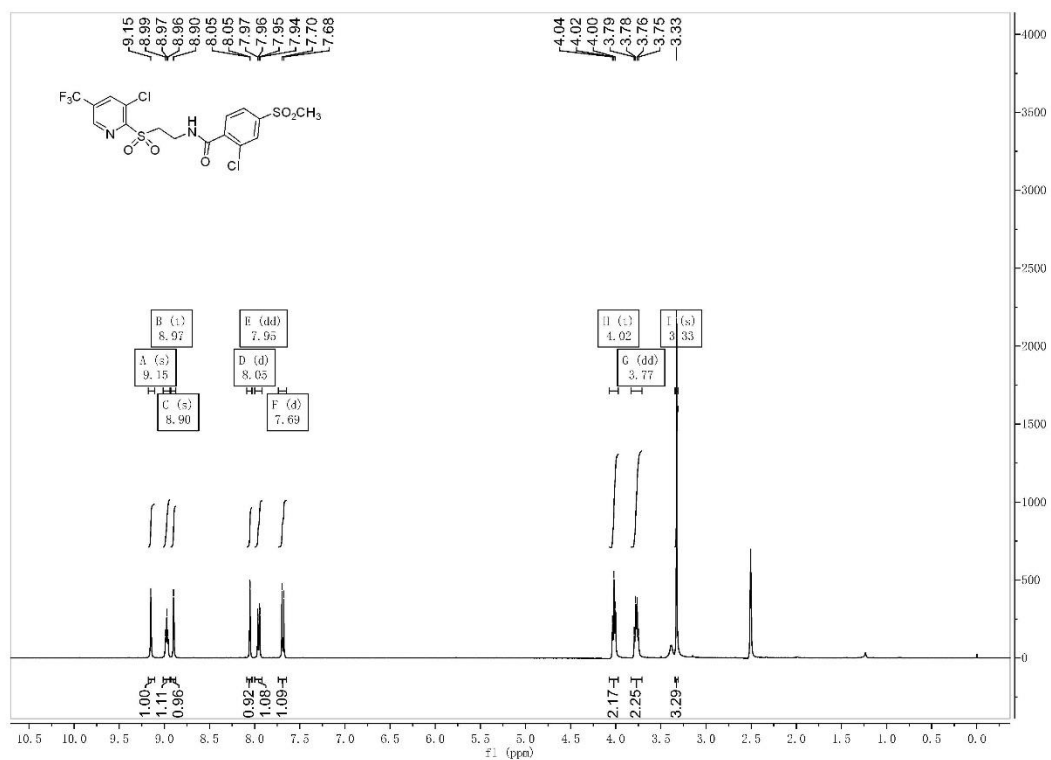


Fig. S17-1. ^1H -NMR of the target compound **II-5**.

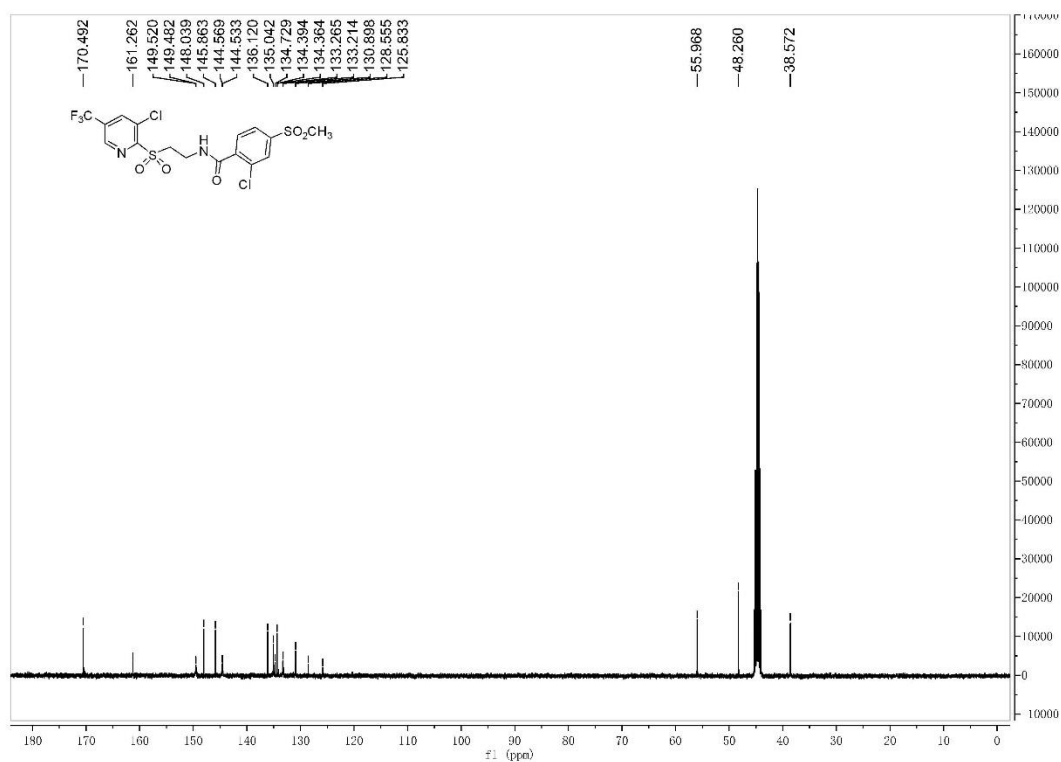


Fig. S17-2. ¹³C-NMR of the target compound II-5.

Sample Name	Sample9	Position	P1-B8	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	II-05.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 2:25:24 PM

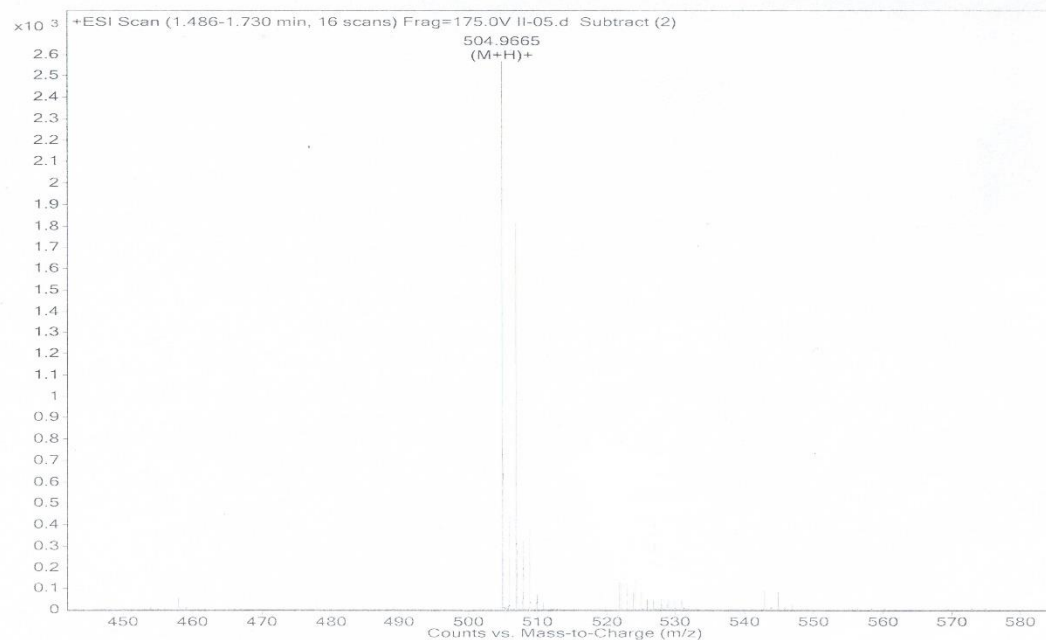
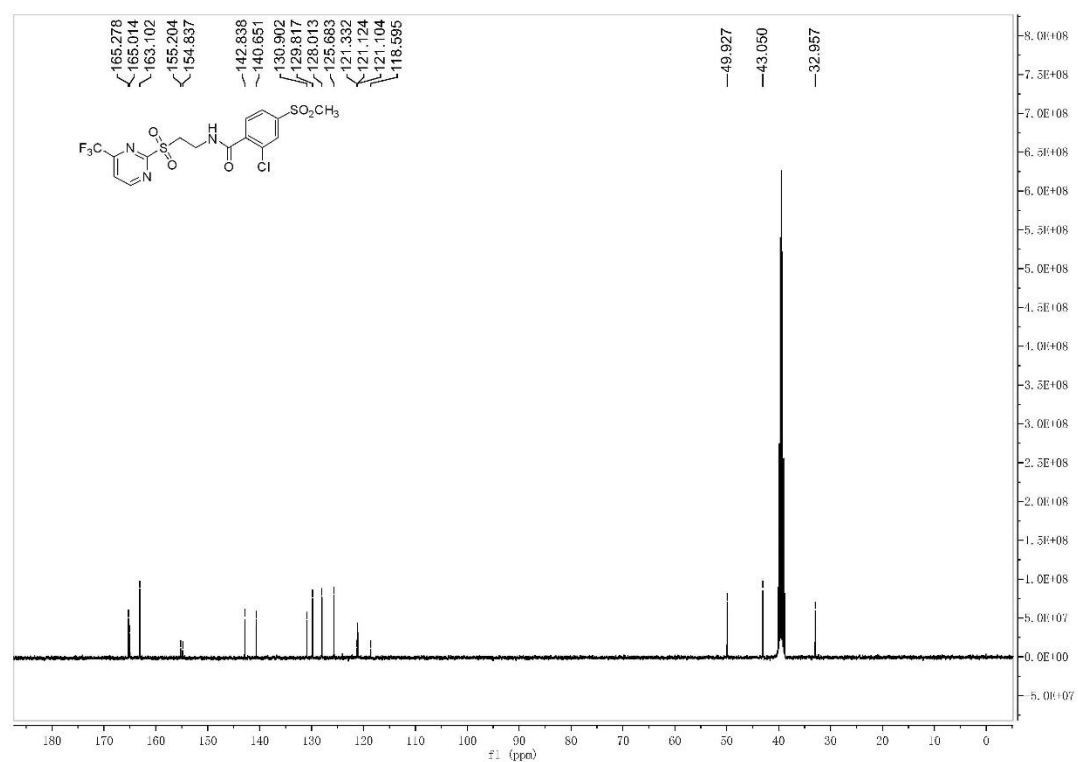
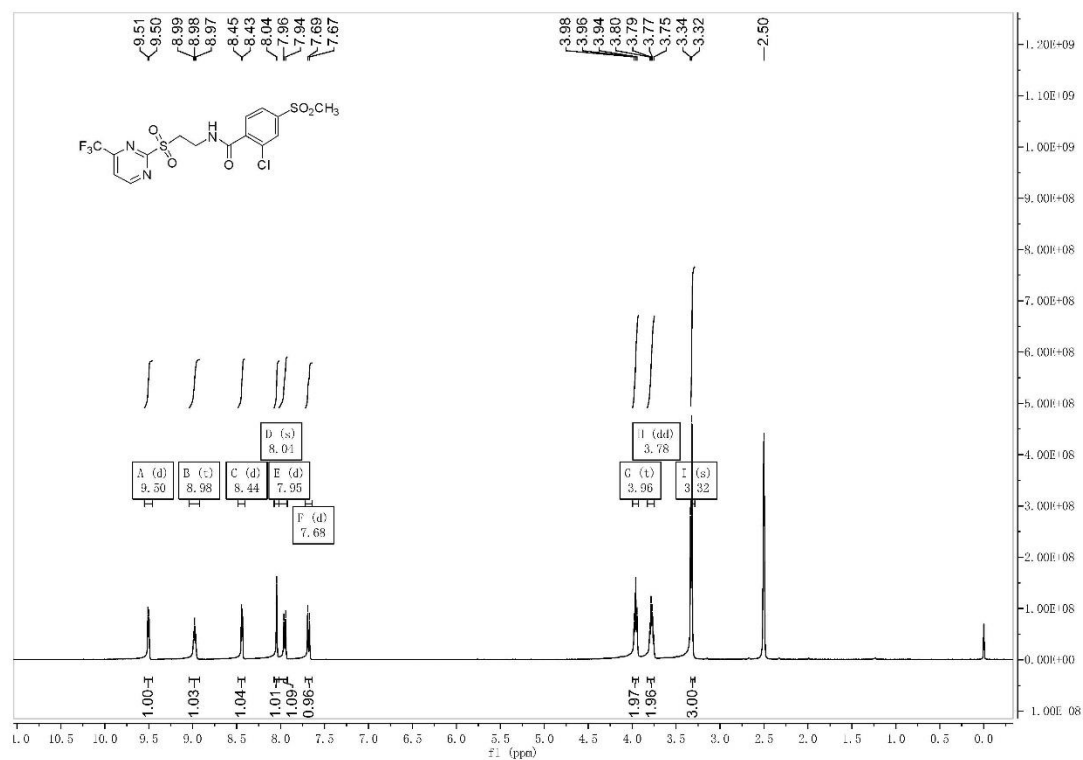


Fig. S17-3. HRMS of the target compound II-5.



Sample Name	Sample9	Position	P1-B9	Instrument Name	Instrument 1	User Name	
Inj Vol	~1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	II-06.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 2:31:07 PM

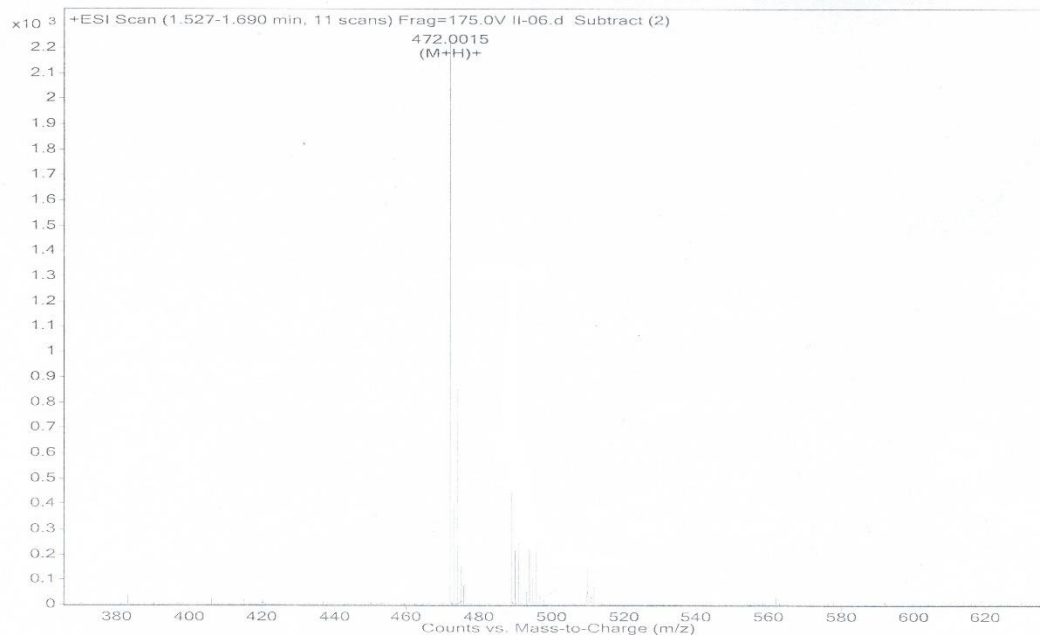


Fig. S18-3. HRMS of the target compound **II-6**.

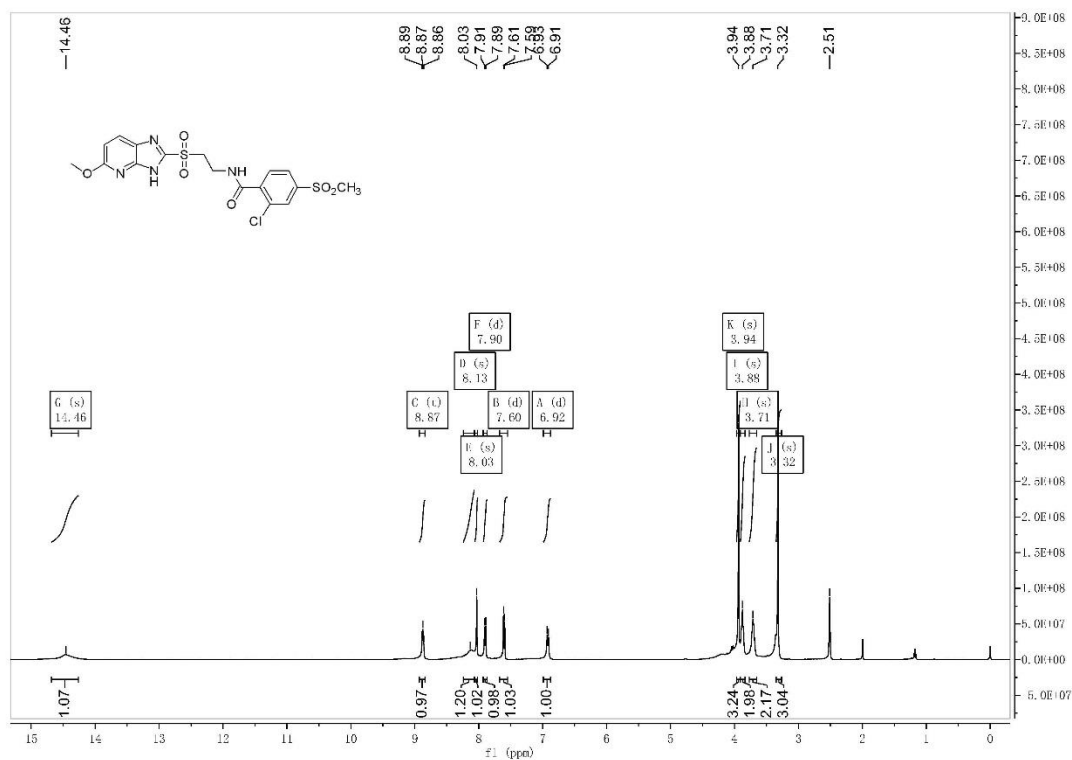


Fig. S19-1. ^1H -NMR of the target compound **II-7**.

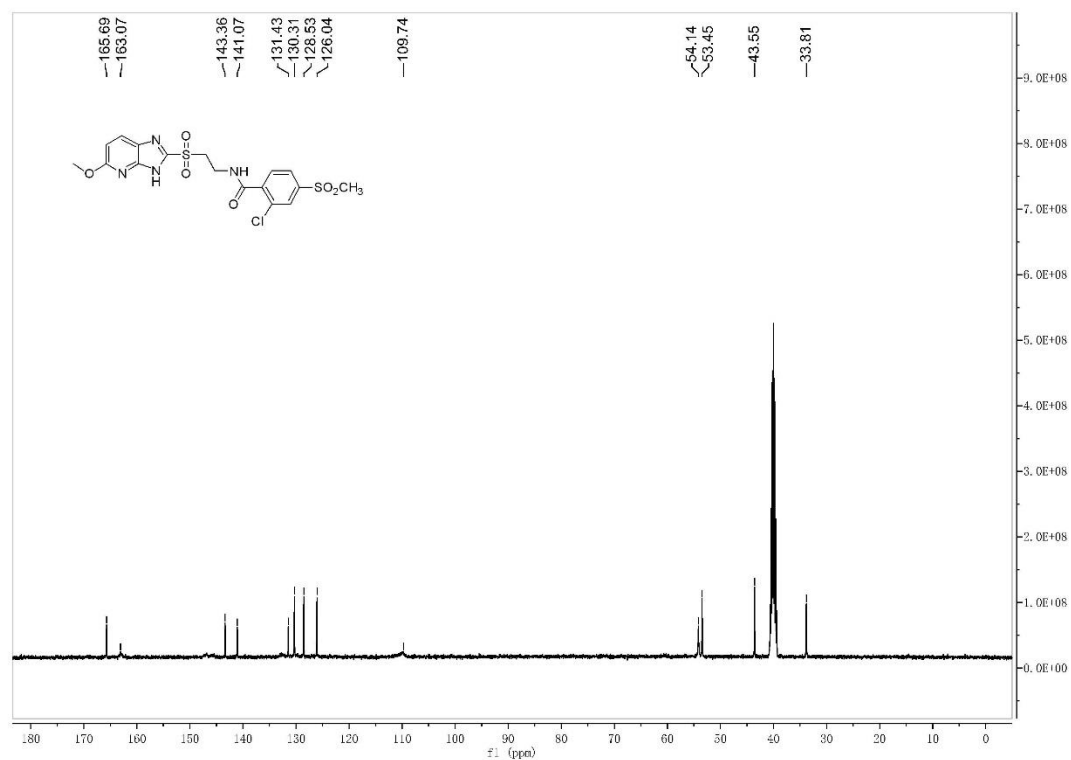


Fig. S19-2. ¹³C-NMR of the target compound **II-7**.

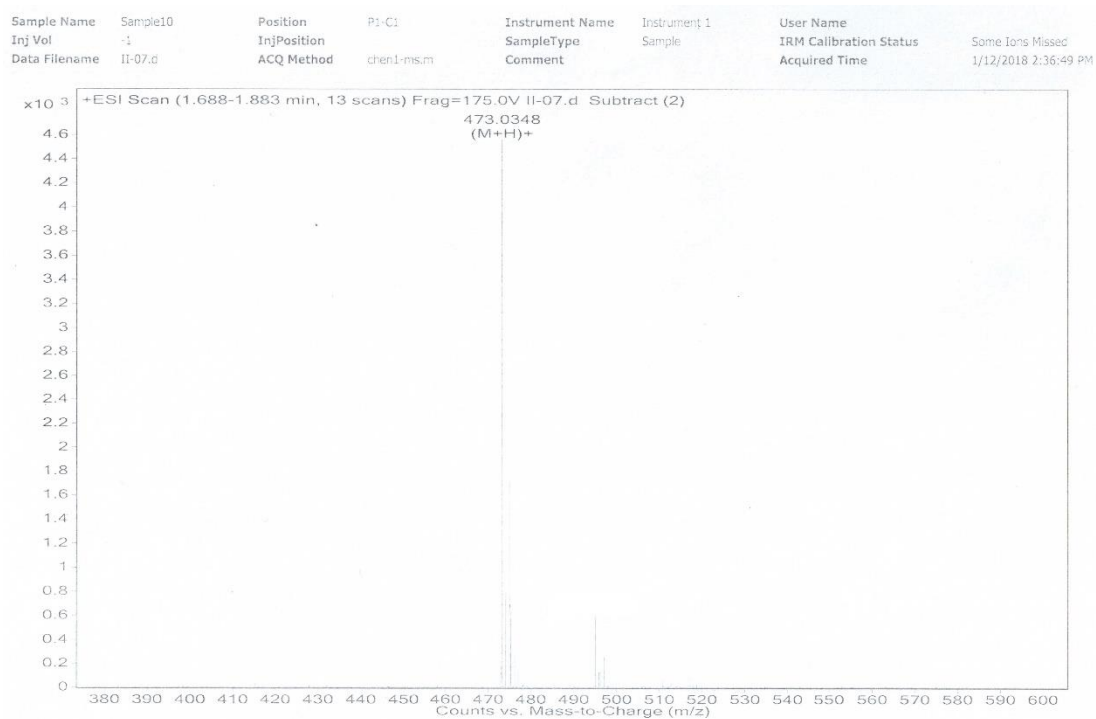


Fig. S19-3. HRMS of the target compound **II-7**.

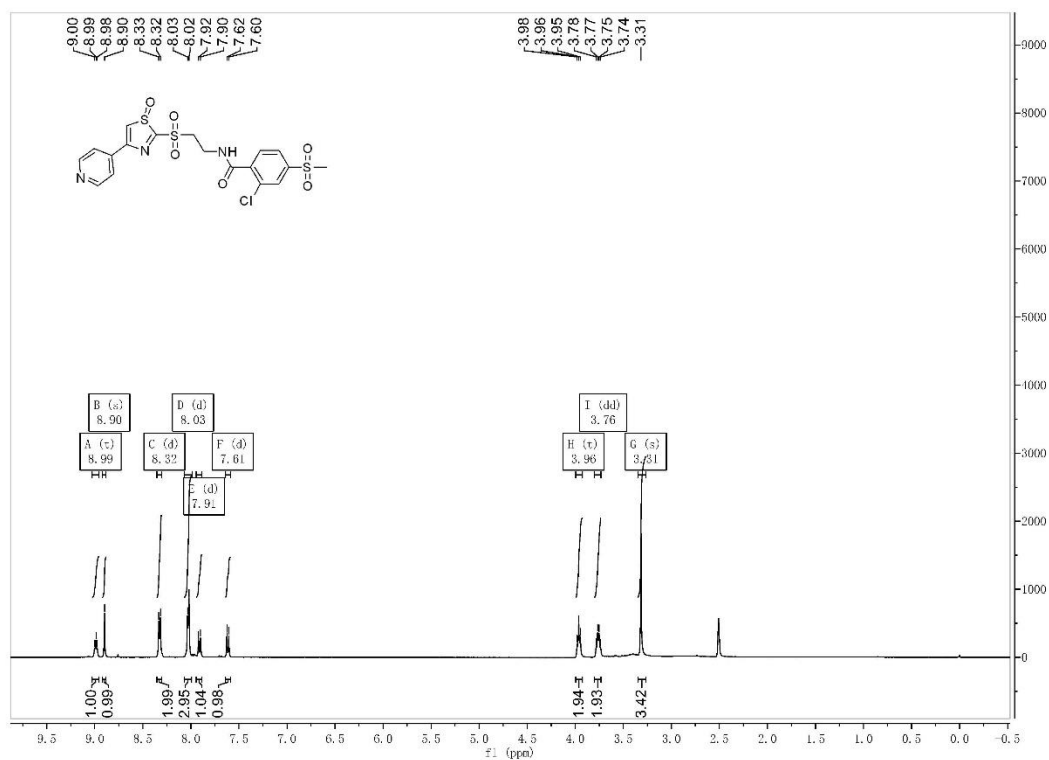


Fig. S20-1. ¹H-NMR of the target compound **II-8**.

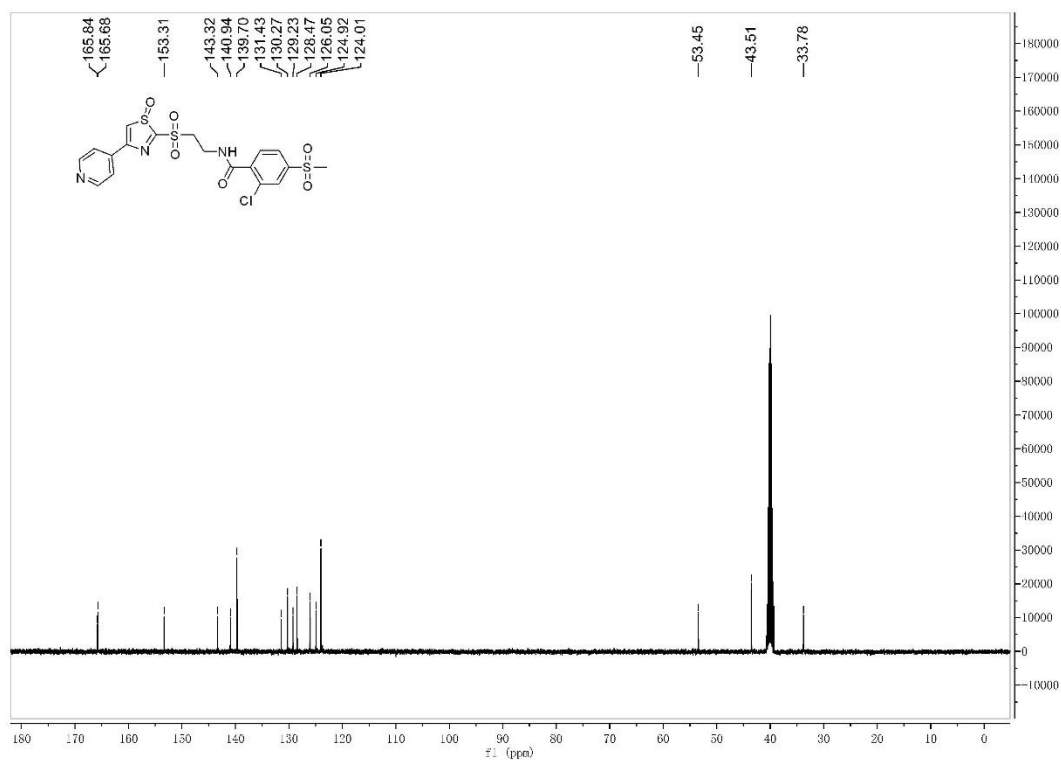


Fig. S20-2. ¹³C-NMR of the target compound **II-8**.

Sample Name	Sample10	Position	P1-C2	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	II-08.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 2:42:34 PM

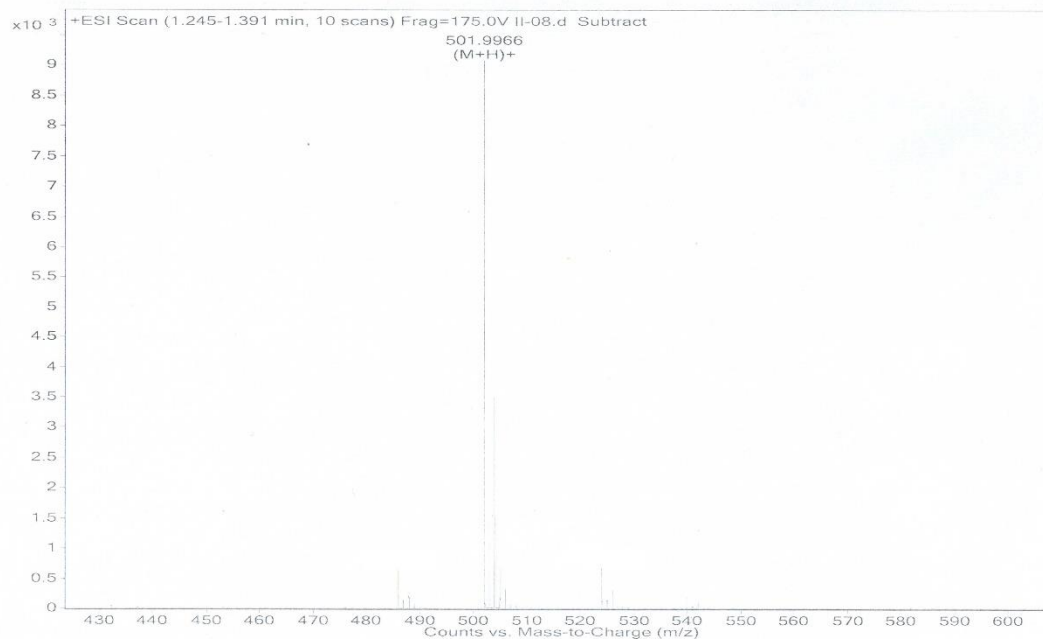


Fig. S20-3. HRMS of the target compound **II-8**.

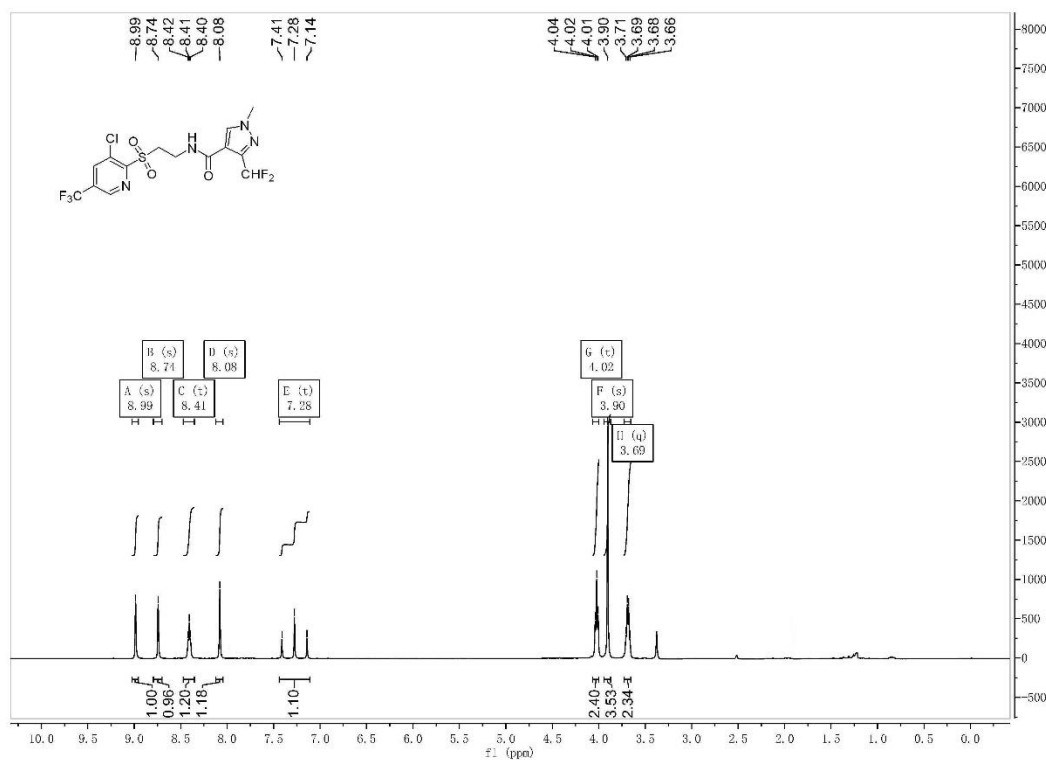


Fig. S21-1. ^1H -NMR of the target compound **II-9**.

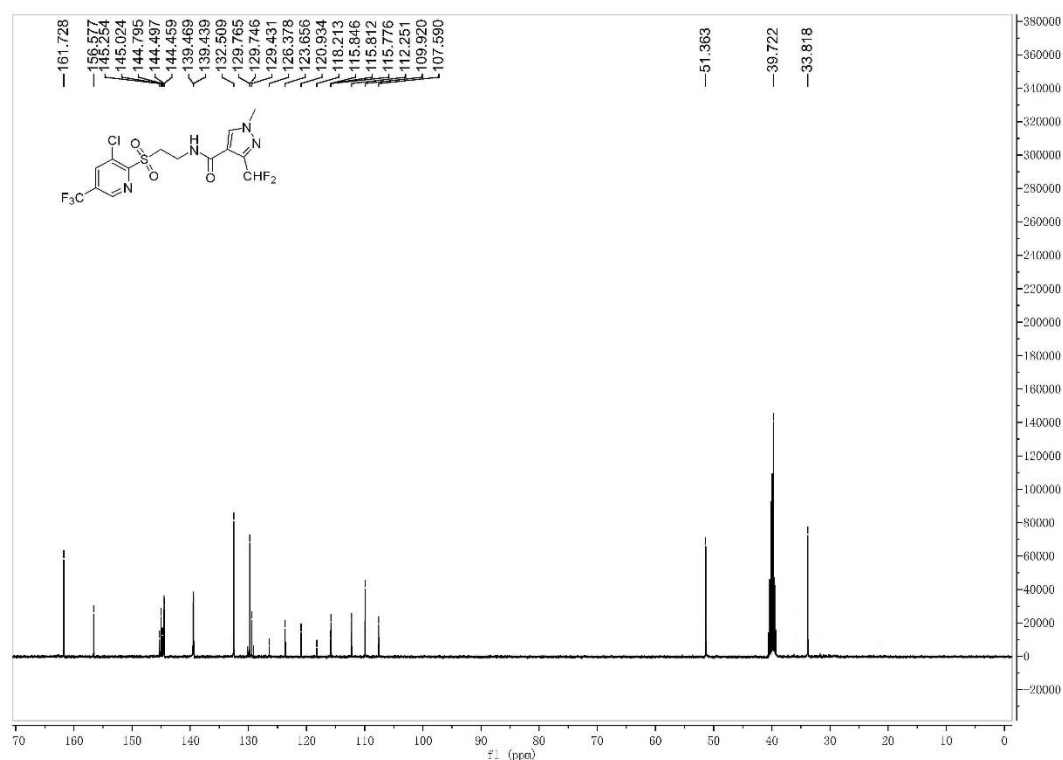


Fig. S21-2. ¹³C-NMR of the target compound **II-9**.

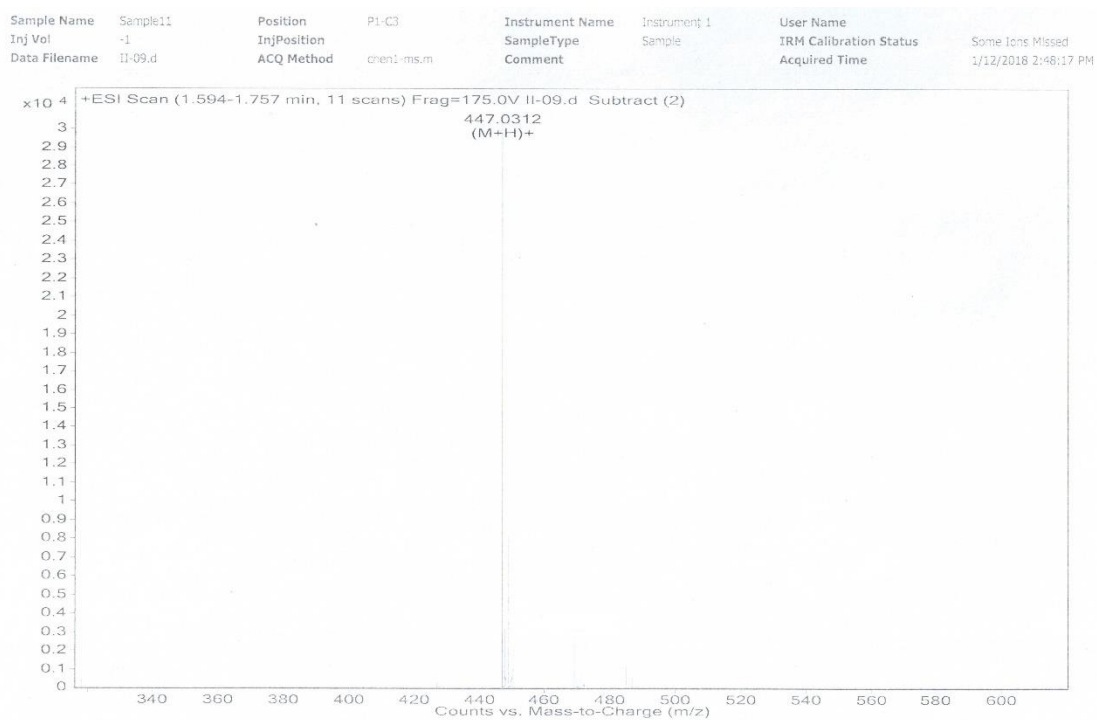


Fig. S21-3. HRMS of the target compound **II-9**.

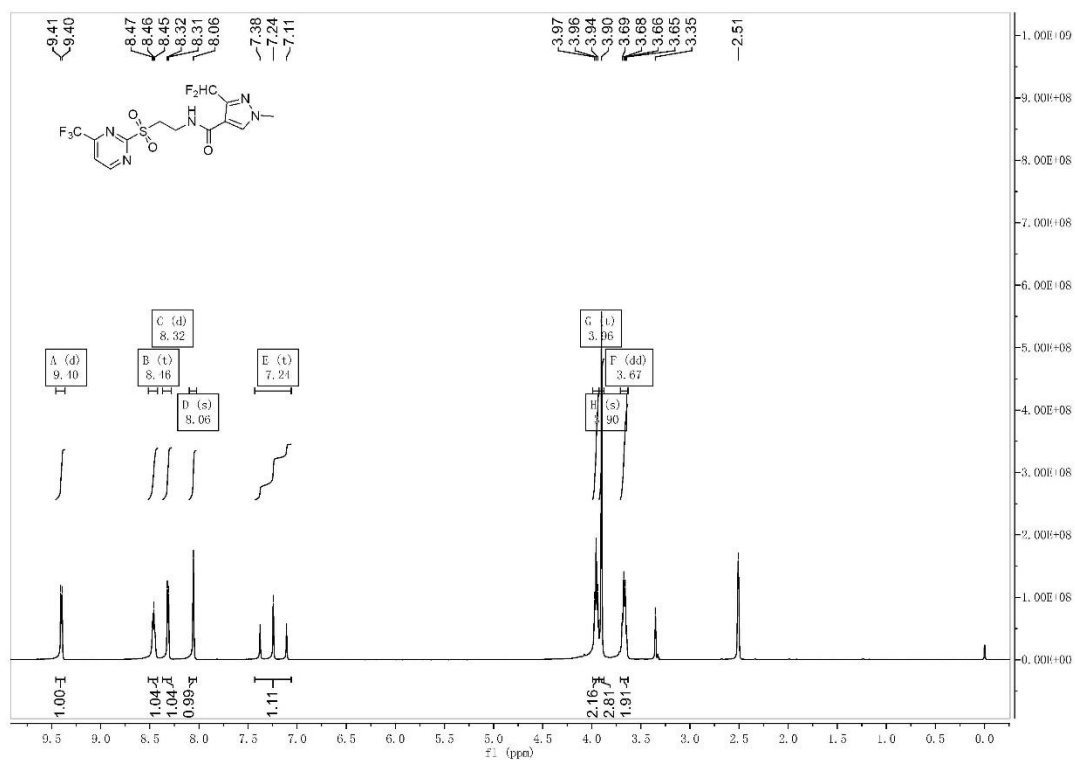


Fig. S22-1. ¹H-NMR of the target compound **II-10**.

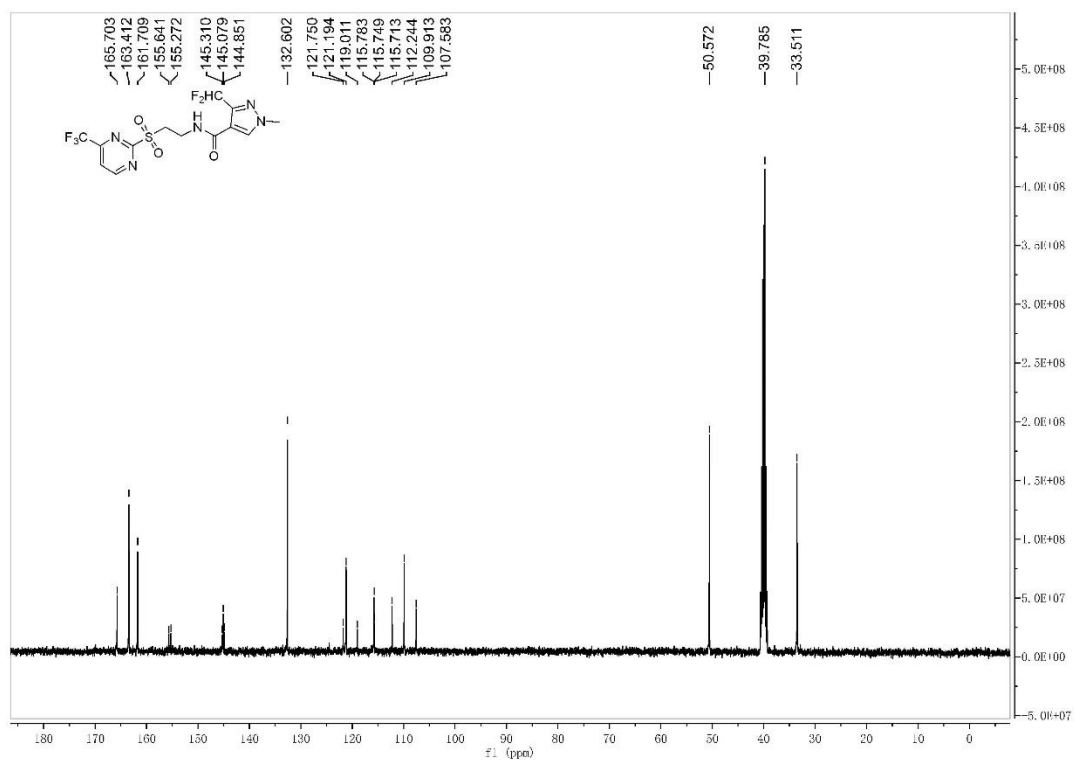


Fig. S22-2. ¹³C-NMR of the target compound **II-10**.

Sample Name	Sample11	Position	P1-C1	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	II-010.d	ACQ Method	cheni-ms.m	Comment		Acquired Time	1/12/2018 2:54:01 PM

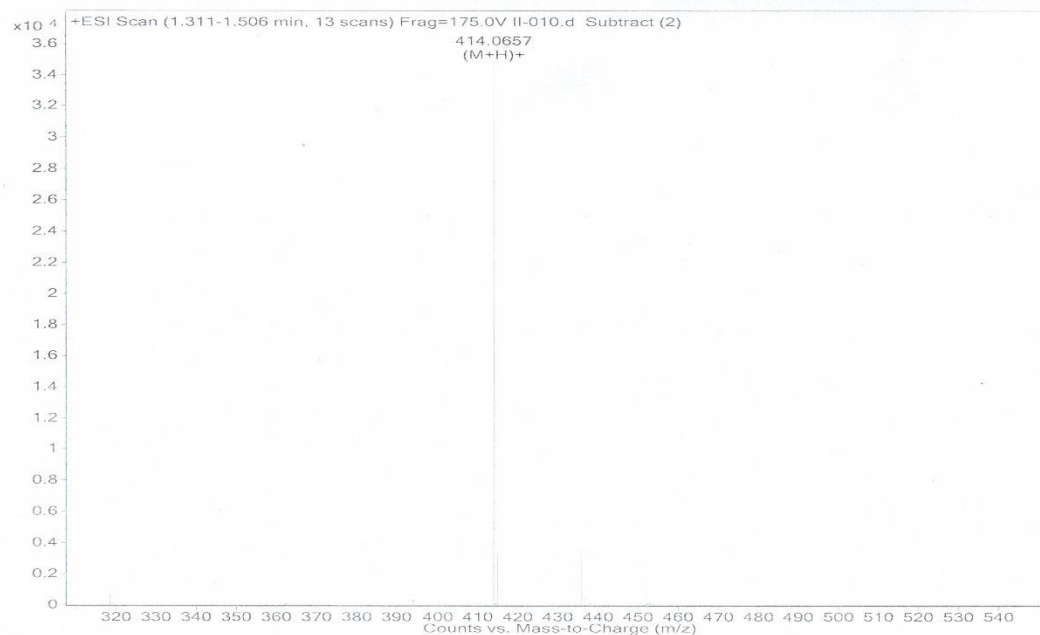


Fig. S22-3. HRMS of the target compound **II-10**.

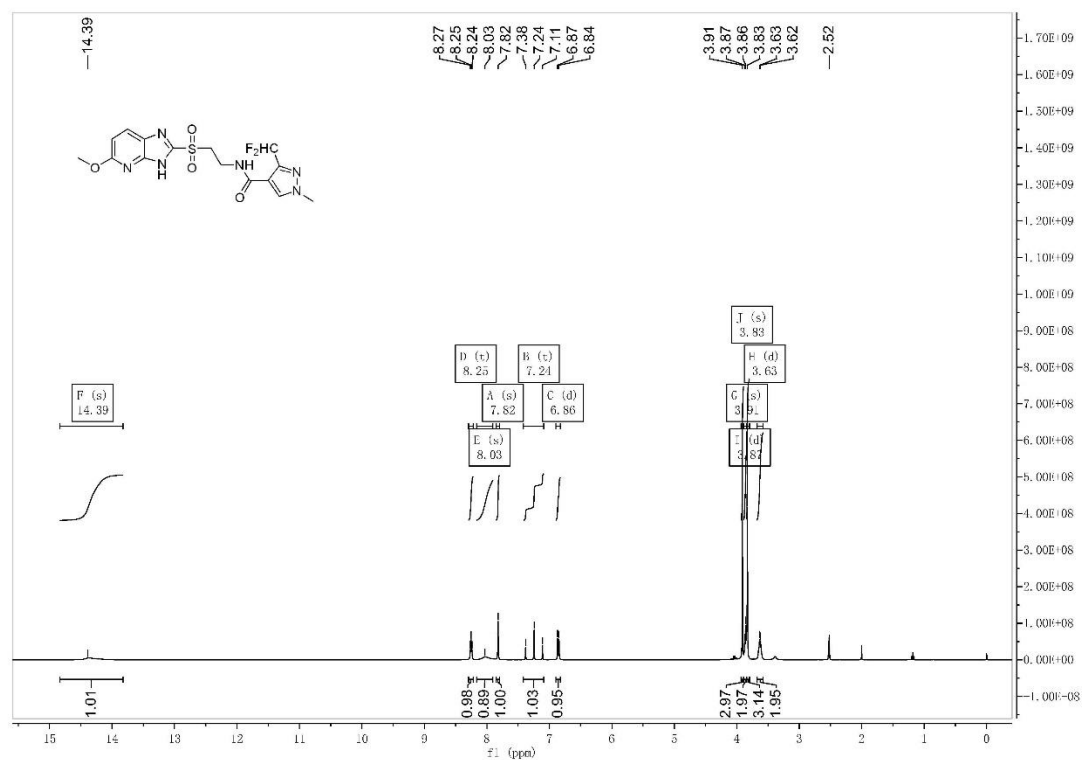


Fig. S23-1. ^1H -NMR of the target compound **II-11**.

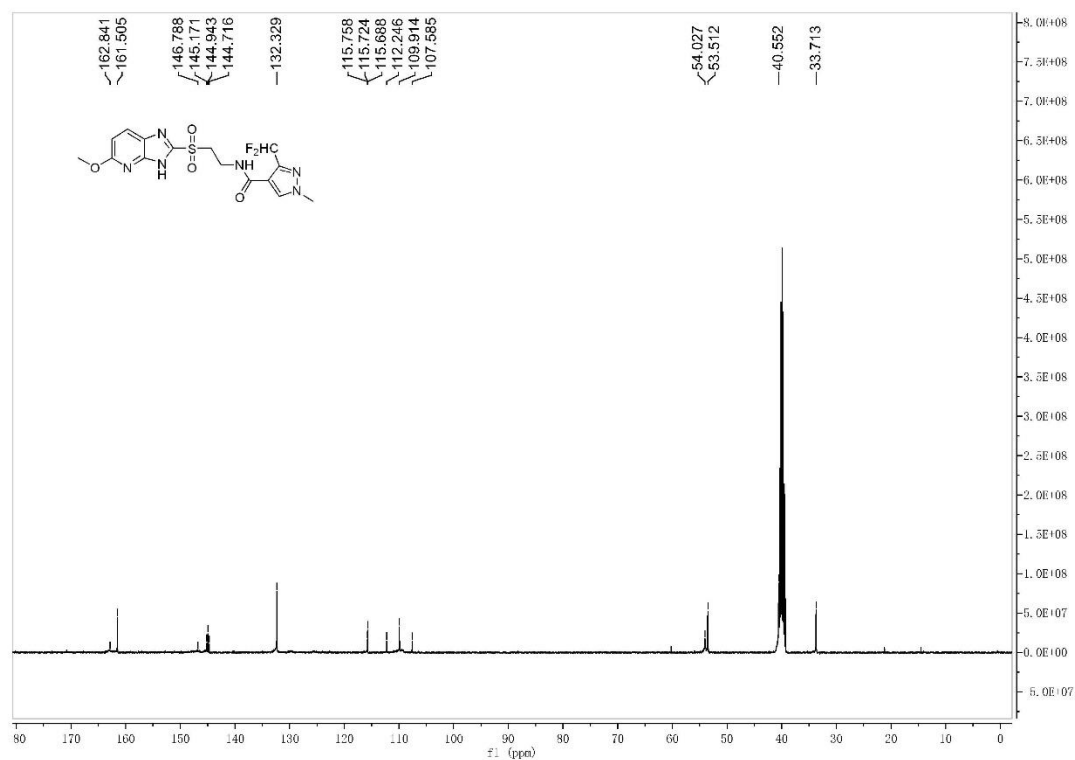


Fig. S23-2. ¹³C-NMR of the target compound II-11.

Sample Name	Sample12	Position	P1-CS	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	II-011.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 2:59:44 PM

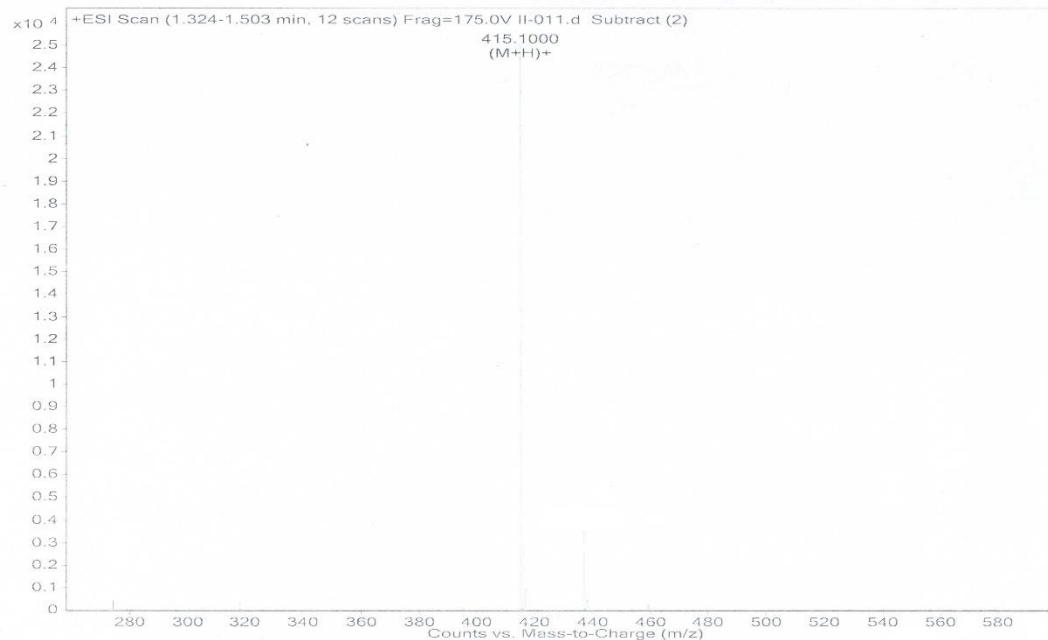


Fig. S23-3. HRMS of the target compound II-11.

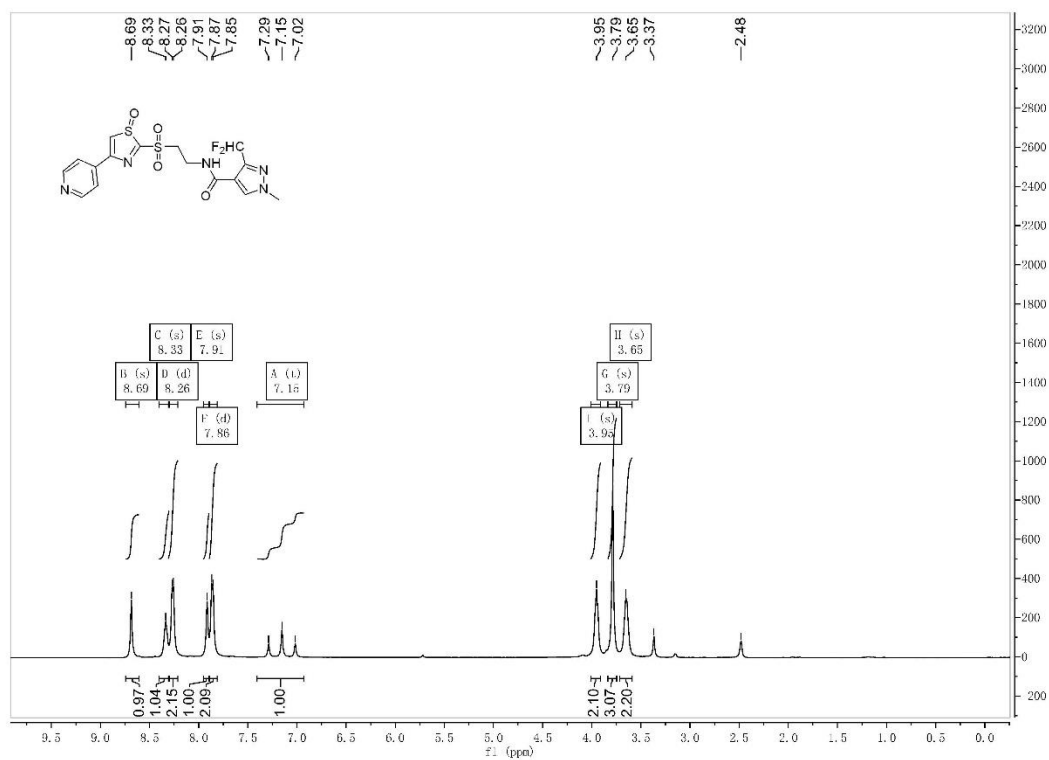


Fig. S24-1. ¹H-NMR of the target compound II-12.

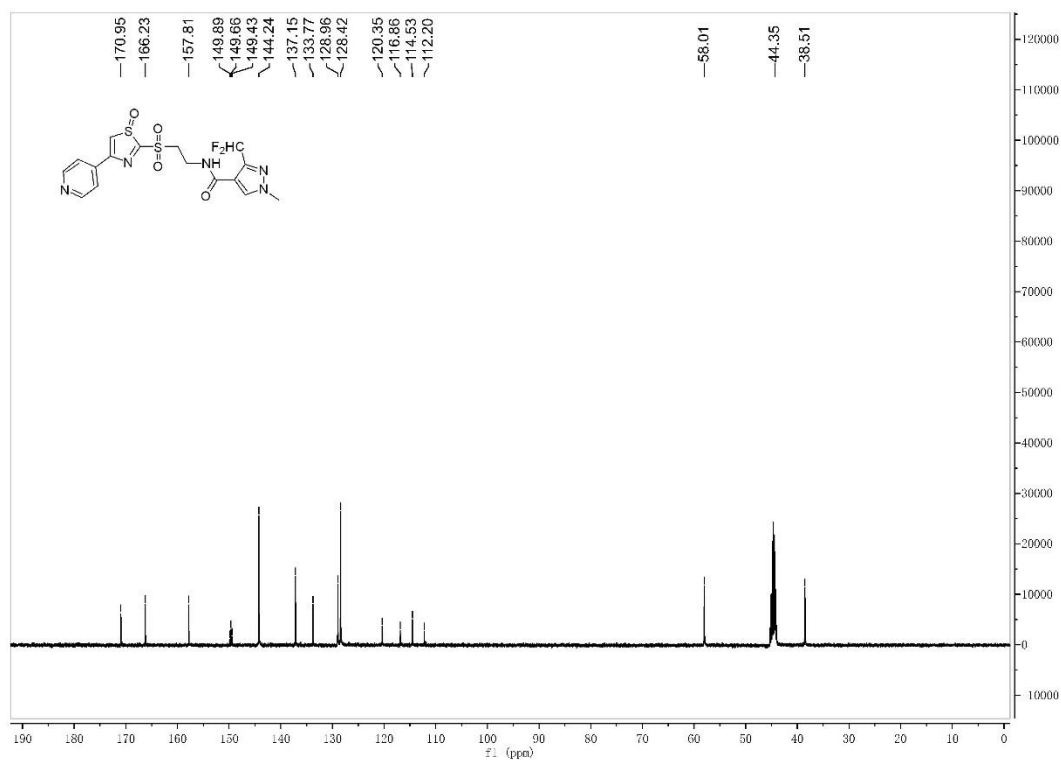


Fig. S24-2. ¹³C-NMR of the target compound II-12.

Sample Name	Sample12	Position	P1 C6	Instrument Name	Instrument 1	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	II-012.d	ACQ Method	chen1-ms.m	Comment		Acquired Time	1/12/2018 3:05:29 PM

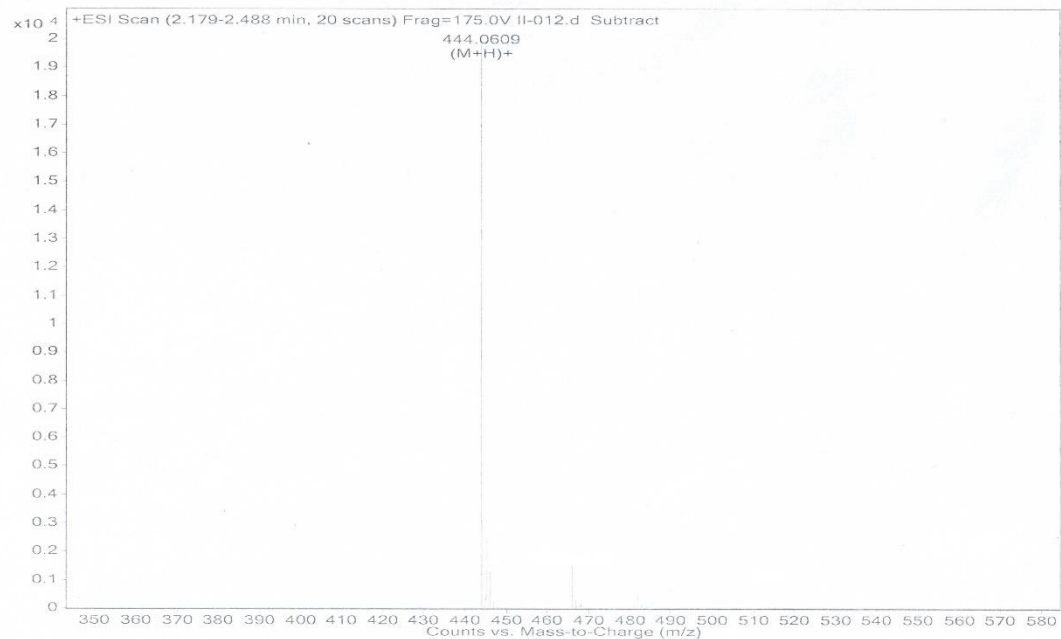


Fig. S24-3. HRMS of the target compound **II-12**.