

Supporting Information

Design, Synthesis, and Fungicidal Activities of Novel Piperidyl Thiazole Derivatives Containing Oxime Ether or Oxime Ester Moieties

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1. The Synthetic Procedure and Spectroscopic Data

Synthesis of *tert*-butyl 4-carbamoylpiperidine-1-carboxylate (2)¹

To a solution of piperidine-4-carboxamide **1** (12.00 g, 93.63 mmol) in acetonitrile (220 mL), (Boc)₂O (22.48 g, 102.99 mmol) and DMAP (1.20 g, 9.82 mmol) were added under mechanical stirring, and then stirred at room temperature for 10 h. The reaction solution gradually changed from clear to white turbidity. When the reaction was complete detected by TLC, the solvent was removed under vacuum condition and dichloromethane (150 mL) was added for re-dissolution. The organic phase was washed with saturated NaHCO₃ solution (80 mL), saturated NH₄Cl solution (80 mL), water (80 mL), brine (80 mL), dried over anhydrous MgSO₄, and concentrated in vacuum to afford white solid 17.54 g, 82.1 % yield, mp: 153 - 155 °C (Ref.²: 154 – 156 °C). ¹H NMR (400 MHz, CDCl₃) δ 5.54 (s, 2H, CNH₂), 4.13 (s, 2H, CH₂), 2.75 (s, 2H, CH₂), 2.25 - 2.33 (m, 1H, CH), 1.84 (d, *J* = 15.8 Hz, 2H, CH₂), 1.60 - 1.67 (m, 2H, CH₂), 1.44 (s, 9H, *t*-Bu-H).

Synthesis of *tert*-butyl 4-carbamothioylpiperidine-1-carboxylate (3)³

To a solution of *tert*-butyl 4-carbamoylpiperidine-1-carboxylate ((1.00 g, 4.38 mmol) in toluene (20 mL) was added Lawson reagent (1.06 g, 2.63 mmol), and the mixture was stirred mechanically at room temperature for 12 h, when the reaction was complete detected by TLC, the solvent was removed under vacuum condition and ethyl acetate (20 mL) was added for re-dissolution. The organic phase was washed

with 10% citric acid (15 mL*2), saturated NaHCO₃ solution (15 mL*2), and water (15 mL), dried over anhydrous MgSO₄, and concentrated in vacumm to afford white solid 0.88 g, 82.2 % yield, mp: 126 - 129 °C (Ref.⁴: 129 - 131 °C). ¹H NMR (400 MHz, CDCl₃) δ 7.45 (s, 1H, NH₂), 6.90 (s, 1H, NH₂), 4.22 (s, 2H, CH₂), 2.65 - 2.82 (m, 3H, CH + CH₂), 1.85 - 1.91 (m, 2H, CH₂), 1.66 - 1.77 (m, 2H, CH₂), 1.46 (s, 9H, *t*-Bu-H).

Synthesis of *tert*-butyl 4-(7-oxo-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidine-1-carboxylate (5)⁵

To a solution of *tert*-butyl 4-carbamothioylpiperidine-1-carboxylate (1.00 g, 4.09 mmol) in *tert*-butyl alcohol (20 mL), 2-bromocyclohexane-1,3-dione (0.78 g, 4.09 mmol) was added in six batches, 0.26 g was add each time, interval 15 min, after 15 min of stirring at room temperature, the mixture was heated to 85 °C, the reaction mixture was refluxed for 3 h. When the reaction was complete detected by TLC, the solvent was removed under vacuum condition and dichloromethane (20 mL) was added for redissolution. The organic phase was washed with saturated NaHCO₃ solution (15 mL*2) and water (15 mL), dried over anhydrous MgSO₄, and concentrated in vacumm to afford yellow solid 0.35 g, 25.4 % yield, mp: 77 - 79 °C.

¹H NMR (400 MHz, CDCl₃) δ 4.21 (s, 2H, CH₂), 3.09 - 3.16 (m, 1H, CH), 3.02 (d, *J* = 5.8 Hz, 2H, CH₂), 2.85 (s, 2H, CH₂), 2.61 (d, *J* = 5.6 Hz, 2H, CH₂), 2.18 - 2.24 (m, 2H, CH₂), 2.04 - 2.09 (m, 2H, CH₂), 1.67 - 1.77 (m, 2H, CH₂), 1.46 (s, 9H, *t*-Bu-H).

Synthesis of 2-(piperidin-4-yl)-5,6-dihydrobenzo[*d*]thiazol-7(4*H*)-one (6)⁶

The mixture of *tert*-butyl 4-(7-oxo-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidine-1-carboxylate (3.00 g, 8.92 mmol), 20% of dilute hydrochloric acid (30 mL), and dichloromethane (30 mL) was heat up to 40 °C and reflux for 10 h. When the reaction was complete detected by TLC, sodium hydroxide solution was add to adjust the pH of water layer to 9 ~ 10, the aqueous phase was extracted with dichloromethane (30 mL*5), the combined organic phase was dried over anhydrous MgSO₄, and concentrated in vacumm to afford yellow oil 2.01 g, 95.4 % yield. ¹H NMR (400 MHz, CDCl₃) δ 3.57 (d, *J* = 11.8 Hz, 2H, CH₂), 3.29 - 3.33 (m, 1H, CH), 3.13 (t, *J* = 9.8 Hz, 2H, CH₂), 3.02 (t, *J* = 5.6 Hz, 2H, CH₂), 2.63 (t, *J* = 5.6 Hz, 2H, CH₂), 2.41 (d, *J* = 15.6 Hz, 2H, CH₂), 2.19 - 2.33 (m, 4H, CH₂ + CH₂).

Synthesis of 2-(1-(2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)acetyl)piperidin-4-yl)-5,6-dihydrobenzo[*d*]thiazol-7(4*H*)-one (8)⁷

To a solution of 2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)acetic acid 7 (1.94 g, 9.32 mmol) in tetrahydrofuran (20 mL), *N,N*'-carbonyl diimidazole (CDI) (1.66 g, 10.25 mmol) was added in three batches under ice bath condition, 0.55 g was added each time, and stirred at room temperature for another 1 h. Then, triethylamine (1.41 g, 13.97 mmol) and 4-dimethylaminopyridine (DMAP) (0.23 g, 1.88 mmol)

were added respectively. Then, 2-(piperidin-4-yl)-5,6-dihydrobenzo[*d*]thiazol-7(4*H*)-one **7** (2.42 g, 10.25 mmol) were dissolved in THF (20 mL) and slowly dropped into the reaction solution. The reaction mixture continue reacting for 10 h at room temperature, When the reaction was complete detected by TLC, dilute hydrochloric acid was added to adjust the pH of water layer to 1, the aqueous phase extraction with ethyl acetate (30 mL*5), the combined organic phase was dried over anhydrous MgSO₄, and concentrated in vacumm and isolated by column chromatography (eluent, EA : PE=1:2; R_f=0.21) to afford white solid 3.56 g, 89.6 % yield, mp: 150 - 152 °C. ¹H NMR (400 MHz, CDCl₃) δ 6.35 (s, 1H, Pyrazolyl-**H**), 5.02 (d, *J* = 3.4 Hz, 2H, CH₂), 4.62 (d, *J* = 15.8 Hz, 1H, CH₂), 3.25 - 3.33 (m, 2H, CH₂), 3.04 (t, *J* = 5.6 Hz, 2H, CH₂), 2.87 (t, *J* = 13.2 Hz, 1H, CH), 2.64 (t, *J* = 7.2 Hz, 2H, CH₂), 2.33 (s, 3H, Pyrazolyl-CH₃), 2.16 - 2.27 (m, 4H, CH₂ + CH₂), 1.73 - 1.85 (m, 2H, CH₂).

Synthesis of 1-(4-(7-(hydroxyimino)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)ethanone (9)⁸

To a solution of 2-(1-(2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)acetyl)piperidin-4-yl)-5,6-dihydrobenzo[*d*]thiazol-7(4*H*)-one **8** (4.00 g, 9.38 mmol) in mathanol (80 mL), then hydroxylamine hydrochloride (0.98 g, 14.08 mmol) and K₂CO₃ (1.95 g, 14.08 mmol) were added, the reaction mixture was refluxed for 10 h. When the reaction was

complete detected by TLC, concentrated in vacumm to afford yellow solid 5.43 g, dichloromethane (70 mL) was added for redissolution. The organic phase was washed with water (40 mL*3), dried over anhydrous MgSO_4 , and concentrated in vacumm and isolated by column chromatography (eluent, EA : PE=1:2; R_f =0.32) to afford white solid 3.33 g, 80.8 % yield, mp: 120 - 122 $^{\circ}\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 9.45 (s, 1H, NOH), 6.33 (s, 1H, Pyrazolyl-H), 4.95 - 5.05 (m, 2H, CH_2), 4.61 (d, J = 13.6 Hz, 1H, CH_2), 3.23 - 3.31 (m, 2H, CH_2), 2.99 (t, J = 5.8 Hz, 2H, CH_2), 2.80 - 2.89 (m, 1H, CH), 2.65 (t, J = 5.4 Hz, 2H, CH_2), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.19 (t, J = 13.6 Hz, 2H, CH_2), 2.04 - 2.10 (m, 2H, CH_2), 1.74 - 1.82 (m, 2H, CH_2).

Synthesis of **1-(4-(7-((benzyloxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone (11a)⁹**

Under ice salt bath, the sodium hydride (0.06 g, 1.50 mmol) was added to anhydrous N, N - dimethyl formamide (15 mL), then, 1-(4-(7-(hydroxyimino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone (0.60 g, 1.36 mmol) was added in three batches, 0.20 g was added each time, interval of 10 min, and after that, the mixture was stirred for 1 h. Then, benzyl bromide (0.24 g, 1.50 mmol) was added slowly in 5 min. After the addition was finished, the mixture was stirred at room temperature for 2 h. When the reaction was complete detected by TLC, a small amount of saturated ammonium chloride solution was added to quench the reaction.

Water (50 mL) was added, and the mixture was extracted with ethyl acetate (30 mL*3), the combined organic phase was dried over anhydrous MgSO_4 , and concentrated in vacumm and isolated by column chromatography (Eluent, EA : PE=1:1; R_f =0.34) to afford white solid 0.6 g, 71.9 % yield, mp: 110 - 112 $^{\circ}\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.32 - 7.42(m, 5H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.24 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.59 (d, J = 13.2 Hz, 1H, CH_2), 4.02 (d, J = 14.0 Hz, 1H, CH_2), 3.22 -3.30 (m, 2H, CH_2), 2.96(t, J = 6.2 Hz, 2H, CH_2), 2.81 - 2.87 (m, 1H, CH), 2.62 (t, J = 6.2 Hz, 2H, CH_2), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.11 - 2.19 (m, 2H, CH_2), 2.03 - 2.06 (m, 2H, CH_2), 1.75 - 1.81 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.7, 163.8, 159.1, 148.4, 141.9, 137.6, 128.4, 128.3, 128.0, 127.9, 118.3, 104.3, 76.3, 51.6, 45.1, 42.2, 40.2, 32.4, 31.8, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{28}\text{F}_3\text{N}_5\text{O}_2\text{SNa}^+$ $[\text{M}+\text{Na}]^+$ 554.1808, found 554.1812.

11b-11s were synthesized using the similar procedure as **11a**, the relevant data obtained are as follows:

*2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-1-(4-(7-(((2-methylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidin-1-yl)ethanone 11b.* White solid, mp: 103 - 105 $^{\circ}\text{C}$, 43.8 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.31 - 7.39 (m, 1H, Ar-**H**), 7.18 - 7.24 (m, 3H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.25 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.59 (d, J = 13.2 Hz, 1H, CH_2), 4.02 (d, J = 14.0 Hz, 1H, CH_2), 3.17 - 3.28 (m, 2H, CH_2), 2.95 (t, J = 6.2 Hz, 2H, CH_2), 2.83 - 2.86 (m, 1H, CH), 2.63 (t, J = 6.2 Hz, 2H, CH_2), 2.41 (s, 3H, Ar- CH_3), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.02 -

2.17 (m, 4H, $\text{CH}_2 + \text{CH}_2$), 1.71 - 1.80 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.6, 163.8, 159.1, 148.0, 141.8, 136.9, 135.3, 130.3, 129.2, 128.2, 125.9, 118.2, 104.3, 74.8, 51.6, 45.1, 42.2, 40.1, 32.3, 31.7, 29.5, 28.2, 22.7, 19.1, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{27}\text{H}_{30}\text{F}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 568.1965, found 568.1967.

1-(4-((7-(((2-chlorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pyridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11c. White solid, mp: 101 - 103 °C, 31.2 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.35 - 7.45 (m, 2H, Ar-**H**), 7.24 - 7.27 (m, 2H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.35 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.59 (d, $J = 13.6$ Hz, 1H, CH_2), 4.02 (d, $J = 13.6$ Hz, 1H, CH_2), 3.17 - 3.30 (m, 2H, CH_2), 2.96 (t, $J = 6.2$ Hz, 2H, CH_2), 2.84 - 2.89 (m, 1H, CH), 2.63 (t, $J = 6.2$ Hz, 2H, CH_2), 2.30 (s, 3H, Pyrazolyl- CH_3), 2.11 - 2.23 (m, 2H, CH_2), 2.05 - 2.08 (m, 2H, CH_2), 1.75 - 1.81 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.9, 163.8, 159.3, 154.65, 148.6, 141.8, 135.4, 133.2, 129.6, 129.4, 129.0, 126.8, 121.4 (q, $J = 262.6$ Hz, CF_3), 118.2, 104.3, 73.4, 51.6, 45.1, 42.2, 40.1, 32.3, 31.7, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{ClF}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 588.1418, found 588.1422.

1-(4-((7-(((2-fluorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pyridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11d. White solid, mp: 109 - 111 °C, 36.1 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.42 - 7.46 (m, 1H, Ar-**H**), 7.29 - 7.34 (m, 1H, Ar-**H**), 7.13 - 7.17 (m, 1H, Ar-**H**), 7.06 - 7.10 (m, 1H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.31 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.59 (d, $J =$

13.2 Hz, 1H, CH_2), 4.02 (d, J = 13.6 Hz, 1H, CH_2), 3.18 - 3.30 (m, 2H, CH_2), 2.95 (t, J = 6.2 Hz, 2H, CH_2), 2.81 - 2.88 (m, 1H, CH), 2.62 (t, J = 6.4 Hz, 2H, CH_2), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.11 - 2.19 (m, 2H, CH_2), 2.02 - 2.08 (m, 2H, CH_2), 1.72 - 1.84 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.8, 163.8, 159.2, 148.6, 141.9, 130.5, 129.7, 124.8, 124.7, 124.0, 118.2, 115.5, 115.3, 104.3, 69.8, 51.6, 45.1, 42.2, 40.1, 32.3, 31.7, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{F}_4\text{N}_5\text{O}_2\text{S Na}^+$ $[\text{M}+\text{Na}]^+$ 572.1714, found 572.1717.

I-(4-((2-bromobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11e. White solid, mp: 99- 101 °C, 40.2 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.57 - 7.59 (m, 1H, Ar- H), 7.42 - 7.44 (m, 1H, Ar- H), 7.30 - 7.34 (m, 1H, Ar- H), 7.16 - 7.21 (m, 1H, Ar- H), 6.33 (s, 1H, Pyrazolyl- H), 5.33 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.59 (d, J = 13.2 Hz, 1H, CH_2), 4.03 (d, J = 13.6 Hz, 1H, CH_2), 3.21 - 3.31 (m, 2H, CH_2), 2.97 (t, J = 6.2 Hz, 2H, CH_2), 2.82 - 2.88 (m, 1H, CH), 2.64 (t, J = 6.2 Hz, 2H, CH_2), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.13 - 2.21 (m, 2H, CH_2), 2.03 - 2.09 (m, 2H, CH_2), 1.76 - 1.82 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.9, 163.8, 159.3, 148.7, 142.1, 141.8, 137.1, 132.7, 129.6, 129.3, 127.4, 122.9, 118.2, 104.3, 75.7, 51.6, 45.1, 42.2, 40.1, 32.4, 31.7, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{BrF}_3\text{N}_5\text{O}_2\text{S Na}^+$ $[\text{M}+\text{Na}]^+$ 632.0913, found 632.0916.

2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-1-(4-((3-methylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone 11f. White

solid, mp: 101 - 103 °C, 79.3 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.25 - 7.29 (m, 1H, Ar-**H**), 7.20 - 7.22 (m, 2H, Ar-**H**), 7.12 - 7.14 (m, 1H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.20 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.58 (d, J = 13.2 Hz, 1H, CH_2), 4.02 (d, J = 14.0 Hz, 1H, CH_2), 3.18 - 3.30 (m, 2H, CH_2), 2.95 (t, J = 6.2 Hz, 2H, CH_2), 2.81 - 2.87 (m, 1H, CH), 2.62 (t, J = 6.4 Hz, 2H, CH_2), 2.36 (s, 3H, Ar- CH_3), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.11 - 2.19 (m, 2H, CH_2), 2.01 - 2.08 (m, 2H, CH_2), 1.75 - 1.81 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.7, 173.7, 163.8, 159.1, 148.3, 141.9, 138.0, 137.5, 128.8, 128.7, 128.3, 125.4, 121.3 (q, J = 262.6 Hz, CF_3), 117.7, 104.3, 76.3, 51.6, 45.1, 42.2, 40.1, 32.4, 31.7, 29.4, 28.2, 22.7, 21.5, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{27}\text{H}_{30}\text{F}_3\text{N}_5\text{O}_2\text{S}$ Na^+ $[\text{M}+\text{Na}]^+$ 568.1965, found 568.1968.

1-(4-((7-((3-chlorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pyperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11g. White solid, mp: 95 - 97 °C, 22.9 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.40 (s, 1H, Ar-**H**), 7.27 - 7.30 (m, 3H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.20 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.59 (d, J = 13.6 Hz, 1H, CH_2), 4.03 (d, J = 14.0 Hz, 1H, CH_2), 3.19 - 3.31 (m, 2H, CH_2), 2.96 (t, J = 6.0 Hz, 2H, CH_2), 2.82 - 2.88 (m, 1H, CH), 2.61 (t, J = 6.2 Hz, 2H, CH_2), 2.30 (s, 3H, PyraZolyl- CH_3), 2.12 - 2.21 (m, 2H, CH_2), 2.02 - 2.08 (m, 2H, CH_2), 1.72 - 1.85 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.9, 172.0, 163.8, 159.3, 148.7, 141.9, 139.8, 134.3, 129.7, 128.0, 126.0, 122.6, 118.1, 104.3, 75.3, 51.6, 45.1, 42.2, 40.1, 32.4, 31.8, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI)

m/z Calcd for $C_{26}H_{27}ClF_3N_5O_2S$ $Na^+ [M+Na]^+$ 588.1418, found 588.1422.

*1-(4-((7-(((3-fluorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pipe
ridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11h.* White
solid, mp: 89 - 91 °C, 35.9 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 7.29 - 7.36 (m, 1H,
Ar-**H**), 7.10 - 7.17 (m, 2H, Ar-**H**), 6.98 - 7.03 (m, 1H, Ar-**H**), 6.33 (s, 1H,
Pyrazolyl-**H**), 5.23 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.58 (d, J = 13.6 Hz, 1H, CH_2),
4.03 (d, J = 13.6 Hz, 1H, CH_2), 3.21 - 3.31 (m, 2H, CH_2), 2.96 (t, J = 5.4 Hz, 2H,
 CH_2), 2.82 - 2.88 (m, 1H, CH), 2.62 (t, J = 5.2 Hz, 2H, CH_2), 2.31 (s, 3H,
Pyrazolyl- CH_3), 2.12 - 2.20 (m, 2H, CH_2), 2.03 - 2.07 (m, 2H, CH_2), 1.73 - 1.85 (m,
2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 173.9, 163.8, 159.3, 151.9, 148.7,
141.9, 140.3, 129.9, 123.3, 118.2, 114.8, 114.6, 104.3, 75.4, 51.6, 45.1, 42.2, 40.2,
32.4, 31.8, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $C_{26}H_{27}F_4N_5O_2S$ $Na^+ [M+Na]^+$ 572.1714, found 572.1718.

*1-(4-((7-(((3-bromobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pip
eridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11i.* White
solid, mp: 88 - 90 °C, 48.2 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 7.57 - 7.58 (m, 1H,
Ar-**H**), 7.43 - 7.46 (m, 1H, Ar-**H**), 7.31 - 7.34 (m, 1H, Ar-**H**), 7.20 - 7.24 (m, 1H,
Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.20 (s, 2H, CH_2), 4.99 (s, 2H, CH_2), 4.59 (d, J =
13.4 Hz, 1H, CH_2), 4.03 (d, J = 13.6 Hz, 1H, CH_2), 3.20 - 3.32 (m, 2H, CH_2), 2.96 (t,
 J = 6.0 Hz, 2H, CH_2), 2.83 - 2.90 (m, 1H, CH), 2.60 - 2.64 (m, 2H, CH_2), 2.31 (s, 3H,
Pyrazolyl- CH_3), 2.17 (t, J = 16.0 Hz, 2H, CH_2), 2.02 - 2.08 (m, 2H, CH_2), 1.73 - 1.86

(m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.9, 173.9, 163.8, 159.3, 148.8, 141.9, 140.0, 131.0, 130.0, 126.5, 122.5, 121.3 (q, $J = 262.6$ Hz, CF_3), 118.1, 104.3, 75.3, 51.6, 45.1, 42.2, 40.1, 32.3, 31.8, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{BrF}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 632.0913, found 632.0917.

2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-1-(4-(7-(((4-methylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone 11j. White solid, mp: 150 - 152 °C, 66.5 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.25 - 7.32 (m, 2H, Ar-**H**), 7.14 - 7.19 (m, 2H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.20 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.59 (d, $J = 13.2$ Hz, 1H, CH_2), 4.01 (d, $J = 13.6$ Hz, 1H, CH_2), 3.18 - 3.29 (m, 2H, CH_2), 2.95 (t, $J = 6.2$ Hz, 2H, CH_2), 2.80 - 2.88 (m, 1H, CH), 2.62 (t, $J = 6.2$ Hz, 2H, CH_2), 2.36 (s, 3H, PH-**H**), 2.32 (s, 3H, Pyrazolyl- CH_3), 2.10 - 2.18 (m, 2H, CH_2), 2.01 - 2.07 (m, 2H, CH_2), 1.74 - 1.83 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.6, 171.2, 163.8, 159.0, 148.2, 141.9, 137.7, 134.5, 129.1, 128.2, 118.3, 104.3, 76.2, 51.6, 45.1, 42.2, 40.1, 32.4, 31.7, 29.4, 28.2, 22.7, 21.2, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{27}\text{H}_{30}\text{F}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 568.1964, found 568.1969.

1-(4-(7-(((4-chlorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11k. White solid, mp: 106 - 108 °C, 68.6 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.28 - 7.33 (m, 4H, Ar-**H**) 6.32 (s, 1H, Pyrazolyl-**H**), 5.18 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.58 (d, $J = 13.6$ Hz, 1H, CH_2), 4.01 (d, $J = 13.6$ Hz, 1H, CH_2), 3.19 - 3.29 (m, 2H, CH_2), 2.94

(t, $J = 6.0$ Hz, 2H, CH_2), 2.79 - 2.86 (m, 1H, CH), 2.60 (t, $J = 6.2$ Hz, 2H, CH_2), 2.29 (s, 3H, Pyrazolyl- CH_3), 2.10 - 2.18 (m, 2H, CH_2), 2.00 - 2.06 (m, 2H, CH_2), 1.71 - 1.84 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.8, 173.9, 163.8, 159.3, 148.6, 141.9, 136.2, 133.7, 129.4, 128.6, 121.3 (q, $J = 262.6$ Hz, CF_3), 118.2, 104.3, 75.4, 51.6, 45.1, 42.2, 40.2, 32.4, 31.8, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{ClF}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 588.1418, found 588.1423.

1-(4-((4-fluorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11l. White solid, mp: 109 - 111 °C, 61.0 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.36 - 7.40 (m, 2H, Ar-**H**), 7.03 - 7.08 (m, 2H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.19 (s, 2H, CH_2), 4.98 (d, $J = 3.2$ Hz, 2**H**), 4.60 (d, $J = 13.2$ Hz, 1H, CH_2), 4.04 (d, $J = 13.6$ Hz, 1H, CH_2), 3.18 - 3.30 (m, 2H, CH_2), 2.95 (t, $J = 6.0$ Hz, 2H, CH_2), 2.80 - 2.87 (m, 1H, CH), 2.60 - 2.63 (m, 2H, CH_2), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.11 - 2.19 (m, 2H, CH_2), 2.01 - 2.08 (m, 2H, CH_2), 1.71 - 1.84 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.8, 172.1, 163.8, 159.2, 148.5, 141.9, 133.4, 129.9, 121.3 (q, $J = 262.6$ Hz, CF_3), 118.2, 115.4, 115.2, 104.3, 75.5, 51.6, 45.1, 42.2, 40.2, 32.4, 31.8, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{F}_4\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 572.1714, found 572.1717.

1-(4-((4-bromobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11m. White solid, mp: 113 - 115 °C, 46.8 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.45 - 7.51 (m,

2H, Ar-**H**), 7.24 - 7.32 (m, 2H, Ar-**H**), 6.35 (s, 1H, Pyrazolyl-**H**), 5.20 (s, 2H, **CH**₂), 5.01 (s, 2H, **CH**₂), 4.62 (d, *J* = 14.0 Hz, 1H, **CH**₂), 4.05 (d, *J* = 13.6 Hz, 1H, **CH**₂), 3.18 - 3.33 (m, 2H, **CH**₂), 2.98 (t, *J* = 6.0 Hz, 2H, **CH**₂), 2.83 - 2.90 (m, 1H, **CH**), 2.63 (t, *J* = 6.2 Hz, 2H, **CH**₂), 2.33 (s, 3H, Pyrazolyl-**CH**₃), 2.14 - 2.22 (m, 2H, **CH**₂), 2.03 - 2.10 (m, 2H, **CH**₂), 1.74 - 1.87 (m, 2H, **CH**₂). ¹³C NMR (100 MHz, CDCl₃) δ 176.8, 173.9, 163.8, 159.3, 148.6, 141.9, 136.7, 131.5, 129.7, 121.8, 121.4 (q, *J* = 272.7 Hz, CF₃), 118.1, 104.2, 75.4, 51.5, 45.0, 42.1, 40.1, 32.3, 31.8, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for C₂₆H₂₇BrF₃N₅O₂S Na⁺ [M+Na]⁺ 632.0913, found 632.0918.

1-(4-((7-(((3-bromo-2-fluorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11n.
 Yellow solid, mp: 120 - 122 °C, 32.8 % yield. ¹H NMR (400 MHz, CDCl₃) δ 7.47 - 7.53 (m, 1H, Ar-**H**), 7.34 - 7.39 (m, 1H, Ar-**H**), 7.00 - 7.05 (m, 1H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.30 (s, 2H, **CH**₂), 4.98 (s, 2H, **CH**₂), 4.59 (d, *J* = 13.6 Hz, 1H, **CH**₂), 4.02 (d, *J* = 13.6 Hz, 1H, **CH**₂), 3.18 - 3.31 (m, 2H, **CH**₂), 2.95 (t, *J* = 6.2 Hz, 2H, **CH**₂), 2.81 - 2.89 (m, 1H, **CH**), 2.61 (t, *J* = 6.2 Hz, 2H, **CH**₂), 2.31 (s, 3H, Pyrazolyl-**CH**₃), 2.12 - 2.20 (m, 2H, **CH**₂), 2.00 - 2.07 (m, 2H, **CH**₂), 1.72 - 1.85 (m, 2H, **CH**₂). ¹³C NMR (100 MHz, CDCl₃) δ 177.0, 174.0, 163.8, 159.4, 148.9, 141.9, 133.2, 129.4, 126.5, 125.0, 124.6, 121.4 (q, *J* = 272.7 Hz, CF₃), 118.1, 104.2, 69.6, 51.6, 45.0, 42.1, 40.1, 32.3, 31.7, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for C₂₆H₂₆BrF₄N₅O₂S Na⁺ [M+Na]⁺ 650.0819, found 650.0823.

1-(4-(7-(((2-bromo-6-fluorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11o.

White solid, mp: 128 - 130 °C, 62.0 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.20 - 7.33 (m, 2H, Ar-**H**), 7.01 - 7.08 (m, 1H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.38 (d, J = 2.0 Hz, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.58 (d, J = 13.6 Hz, 1H, CH_2), 3.99 (d, J = 13.6 Hz, 1H, CH_2), 3.16 - 3.28 (m, 2H, CH_2), 2.88 - 2.95 (m, 2H, CH_2), 2.79 - 2.86 (m, 1H, CH), 2.61 (t, J = 6.4 Hz, 2H, CH_2), 2.30 (s, 3H, Pyrazolyl- CH_3), 1.99 - 2.16 (m, 4H, $\text{CH}_2 + \text{CH}_2$), 1.68 - 1.80 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.8, 172.1, 163.8, 159.1, 148.6, 141.8, 136.7, 130.5, 125.4, 123.0, 121.3 (q, J = 262.6 Hz, CF_3), 118.2, 114.1, 104.3, 66.5, 51.6, 45.0, 42.2, 40.1, 32.3, 31.7, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{26}\text{ClF}_4\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 606.1324, found 606.1324.

1-(4-(7-(((2-bromo-5-fluorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11p.

White solid, mp: 99- 100 °C, 43.8 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.48 - 7.53 (m, 1H, Ar-**H**), 7.11 - 7.15 (m, 1H, Ar-**H**), 6.86 - 6.93 (m, 1H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.28 (s, 2H, CH_2), 4.99 (s, 2H, CH_2), 4.60 (d, J = 14.0 Hz, 1H, CH_2), 4.03 (d, J = 13.6 Hz, 1H, CH_2), 3.19 - 3.32 (m, 2H, CH_2), 2.98 (t, J = 6.2 Hz, 2H, CH_2), 2.86 - 2.90 (m, 1H, CH), 2.64 (t, J = 6.4 Hz, 2H, CH_2), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.15 - 2.22 (m, 2H, CH_2), 2.02 - 2.10 (m, 2H, CH_2), 1.74 - 1.87 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 177.1, 174.1, 163.8, 159.6, 149.1, 141.8,

139.6, 133.7, 121.3 (q, $J = 262.6$ Hz, CF_3), 118.0, 116.4, 116.2, 116.1, 116.0, 104.3, 77.4, 77.0, 76.7, 75.1, 51.6, 45.0, 42.1, 40.2, 32.3, 31.7, 29.4, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{26}\text{BrF}_4\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 650.0819, found 650.0824.

1-(4-((2,6-dibromobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11q. White solid, mp: 126 - 128 °C, 41.9 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.33 - 7.38 (m, 2H, Ar-**H**), 7.20 - 7.25 (m, 1H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.50 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.58 (d, $J = 13.6$ Hz, 1H, CH_2), 4.00 (d, $J = 13.6$ Hz, 1H, CH_2), 3.15 - 3.28 (m, 2H, CH_2), 2.93 (t, $J = 6.0$ Hz, 2H, CH_2), 2.80 - 2.86 (m, 1H, CH), 2.63 (t, $J = 6.2$ Hz, 2H, CH_2), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.01 - 2.16 (m, 4H, CH_2 + CH_2), 1.69 - 1.79 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.8, 171.0, 163.8, 159.1, 148.6, 141.9, 137.2, 132.5, 130.3, 128.4, 118.2, 104.3, 70.5, 51.6, 45.0, 42.2, 40.1, 32.3, 31.6, 29.5, 28.2, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{26}\text{Cl}_2\text{F}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 622.1028, found 622.1031.

1-(4-((2,6-dimethylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11r. White solid, mp: 98 - 100 °C, 56.0 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.03 - 7.18 (m, 3H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.28 (s, 2H, CH_2), 4.97 (s, 2H, CH_2), 4.57 (d, $J = 13.6$ Hz, 1H, CH_2), 4.00 (d, $J = 13.6$ Hz, 1H, CH_2), 3.17 - 3.27 (m, 2H, CH_2), 2.93 (t, $J = 6.0$ Hz, 2H, CH_2), 2.81 - 2.84 (m, 1H, CH), 2.63 (t, $J = 6.2$ Hz, 2H, CH_2), 2.43 - 2.47 (m, 6H, CH_3 + CH_3), 2.30 (s, 3H, Pyrazolyl- CH_3), 2.01 - 2.16 (m, 4H, CH_2 + CH_2).

CH_2), 1.67 - 1.77 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.4, 174.3, 163.8, 158.8, 151.3, 147.7, 141.8, 138.5, 133.2, 128.4, 128.1, 118.2, 104.3, 70.7, 51.6, 15.1, 42.2, 40.1, 32.3, 31.7, 29.5, 28.2, 22.7, 19.9, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{28}\text{H}_{32}\text{F}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 582.2121, found 582.1762.

1-(4-(7-(((2,6-difluorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 11s. White solid, mp: 139 - 141 °C, 18.1 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.27 - 7.35 (m, 1H, Ar-**H**), 6.88 - 6.96 (m, 2H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.30 (s, 2H, CH_2), 4.98 (s, 2H, CH_2), 4.58 (d, J = 13.2 Hz, 1H, CH_2), 4.00 (d, J = 13.6 Hz, 1H, CH_2), 3.16 - 3.30 (m, 2H, CH_2), 2.92 (t, J = 6.2 Hz, 2H, CH_2), 2.85 - 2.88 (m, 1H, CH), 2.60 (t, J = 6.2 Hz, 2H, CH_2), 2.30 (s, 3H, Pyrazolyl- CH_3), 2.08 - 2.16 (m, 2H, CH_2), 1.99 - 2.05 (m, 2H, CH_2), 1.72 - 1.81 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 176.8, 173.9, 163.8, 159.2, 148.7, 141.9, 130.6, 121.3 (q, J = 262.6 Hz, CF_3), 118.3, 113.2, 111.4, 111.2, 104.2, 63.3, 51.6, 45.0, 42.2, 40.1, 32.3, 31.7, 29.4, 28.1, 22.7, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{26}\text{F}_5\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 590.1619, found 590.1625.

Synthesis of
1-(4-(benzoyloxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl
)**-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone (13a)**

Under ice salt bath, the sodium hydride (0.07 g, 1.75 mmol) was added to

anhydrous *N,N*-dimethyl formamide (15 mL), then, 1-(4-(7-(hydroxyimino)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)ethanone (1.59 g, 0.70 mmol) was added in three batches, 0.23 g was added each time, interval of 10 min, and after that, the mixture was stirred for 1 h. Then, benzoyl chloride (0.23 g, 1.67 mmol) was added slowly in 5 min. After the addition was finished, the mixture was stirred at room temperature for 2 h. When the reaction was completed monitored by TLC, a small amount of saturated ammonium chloride solution was added to quench the reaction. Water (75 mL) was added, and the mixture was extracted with ethyl acetate (50 mL*3). The combined organic phase was dried over anhydrous MgSO₄, and concentrated in vacumm and isolated by column chromatography (eluent, EA : PE=1:3; R_f=0.46) to afford white solid 0.73 g, 84.7 % yield, mp: 220 - 222 °C. ¹H NMR (400MHz, CDCl₃) δ 8.19 - 8.21 (m, 2H, Ar-**H**), 7.65 - 7.69 (m, 1H, Ar-**H**), 7.54 - 7.58 (m, 2H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 4.99 (d, *J* = 4.4 Hz, 2H, CH₂), 4.62 (d, *J* = 13.6 Hz, 1H, CH₂), 4.06 (d, *J* = 13.6 Hz, 1H, CH₂), 3.24 - 3.32 (m, 2H, CH₂), 3.04 (t, *J* = 6.2 Hz, 2H, CH₂), 2.83 - 2.91 (m, 3H, CH₂ + CH), 2.31 (s, 3H, Pyrazolyl-CH₃), 2.14 - 2.18 (m, 4H, CH₂ + CH₂), 1.77 - 1.81 (m, 2H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 178.8, 172.4, 164.2, 163.9, 162.3, 155.7, 141.9, 133.6, 130.1, 129.6, 128.7, 121.3 (q, *J* = 272.7 Hz, CF₃), 117.6, 104.3, 51.5, 45.0, 42.0, 40.3, 32.2, 31.5, 29.9, 28.3, 22.5, 11.3. HRMS (MALDI) m/z Calcd for C₂₆H₂₆F₃N₅O₃S Na⁺ [M+Na]⁺ 568.1600, found 568.1606.

13b-13p were synthesized using the similar procedure as **13a**, the relevant data obtained are as follows:

2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-1-(4-(7-(((2-methylbenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone 13b. Yellow solid, mp 93 - 95 °C, 72.5 % yield. ¹H NMR (400 MHz, CDCl₃) δ 7.90 - 7.98 (m, 1H, Ar-**H**), 7.43 - 7.52 (m, 1H, Ar-**H**), 7.28 - 7.36 (m, 2H, Ar-**H**), 6.33 (d, *J* = 9.2 Hz, 1H, Pyrazolyl-**H**), 4.97 - 5.00 (m, 2H, CH₂), 4.59 (d, *J* = 13.2 Hz, 1H, CH₂), 4.03 (d, *J* = 13.6 Hz, 1H, CH₂), 3.18 - 3.29 (m, 2H, CH₂), 3.03 (t, *J* = 6.2 Hz, 2H, CH₂), 2.93 - 2.98 (m, 1H, CH), 2.86 - 2.90 (m, 2H, CH₂), 2.64 (s, 3H, Ar-CH₃), 2.30 (s, 3H, Pyrazolyl-CH₃), 2.07 - 2.23 (m, 4H, CH₂ + CH₂), 1.72 - 1.80 (m, 2H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 178.9, 176.5, 164.7, 163.8, 162.1, 155.4, 141.9, 140.7, 132.4, 131.9, 130.2, 128.4, 125.8, 121.3 (q, *J* = 272.7 Hz, CF₃), 117.7, 104.2, 51.5, 44.9, 42.0, 40.2, 32.2, 31.5, 29.9, 28.3, 22.5, 21.2, 11.3. HRMS (MALDI) m/z Calcd for C₂₇H₂₈F₃N₅O₃S Na⁺ [M+Na]⁺ 582.1757, found 582.1762.

1-(4-(7-(((2-fluorobenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 13c. White solid, mp: 188 - 190 °C, 80.8 % yield. ¹H NMR (400 MHz, CDCl₃) δ 7.99 - 8.03 (m, 1H, Ar-**H**), 7.59 - 7.65 (m, 1H, Ar-**H**), 7.22 - 7.33 (m, 2H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 4.92 - 5.02 (m, 2H, CH₂), 4.59 (d, *J* = 13.6 Hz, 1H, CH₂), 4.03 (d, *J* = 13.6 Hz, 1H, CH₂), 3.20 - 3.30 (m, 2H, CH₂), 3.02 (t, *J* = 6.2 Hz, 2H, CH₂), 2.84 - 2.89 (m, 3H, CH + CH₂), 2.31 (s, 3H, Pyrazolyl-CH₃), 2.10 - 2.19 (m, 4H, CH₂ +

CH_2), 1.70 - 1.80 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 179.2, 174.3, 163.9, 162.4, 160.2, 155.9, 141.9, 135.1, 135.0, 132.2, 124.3, 121.3 (q, $J = 272.7$ Hz, CF_3), 117.7, 117.3, 117.0, 104.2, 51.5, 45.0, 42.0, 40.3, 32.2, 31.5, 29.9, 28.2, 22.5, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{25}\text{F}_4\text{N}_5\text{O}_3\text{S Na}^+ [\text{M}+\text{Na}]^+$ 586.1506, found 586.1511.

*2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-1-(4-(7-(((3-methylbenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidin-1-yl)ethanone 13d.* White solid, mp: 143 - 145 °C, 48.6 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.87 - 8.02 (m, 2H, Ar-**H**), 7.35 - 7.48 (m, 2H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 4.93 - 5.02 (m, 2H, CH_2), 4.59 (d, $J = 13.2$ Hz, 1H, CH_2), 4.02 (d, $J = 14.0$ Hz, 1H, CH_2), 3.23 - 3.32 (m, 2H, CH_2), 3.03 (t, $J = 6.2$ Hz, 2H, CH_2), 2.94 - 3.00 (m, 1H, **H**), 2.87 - 2.90 ((m, 2H, CH_2), 2.44 (d, $J = 7.2$ Hz, 3H, Ar- CH_3), 2.32 (d, $J = 4.8$ Hz, 3H, Pyrazolyl- CH_3), 2.07 - 2.22 (m, 4H, $\text{CH}_2 + \text{CH}_2$), 1.75 - 1.85 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 178.8, 177.7, 164.4, 163.9, 162.3, 155.6, 141.9, 138.6, 134.4, 130.8, 128.7, 128.6, 127.1, 121.3 (q, $J = 272.7$ Hz, CF_3), 117.6, 104.3, 51.5, 44.9, 42.0, 40.3, 32.2, 31.5, 29.9, 28.3, 22.6, 21.4, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{27}\text{H}_{28}\text{F}_3\text{N}_5\text{O}_3\text{S Na}^+ [\text{M}+\text{Na}]^+$ 582.1757, found 582.1763.

*1-(4-(7-(((3-chlorobenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)ethanone 13e.* White solid, mp: 160 - 162 °C, 62.2 % yield. ^1H NMR (400 MHz, CDCl_3) δ 8.20 (t, $J = 1.8$ Hz, 1H, Ar-**H**), 8.05 - 8.08 (m, 1H, Ar-**H**), 7.60 - 7.63 (m, 1H, Ar-**H**), 7.49 (t, $J = 8.0$

Hz, 1H, Ar-**H**), 6.31 (s, 1H, Pyrazolyl-**H**), 4.98 (s, 2H, **CH**₂), 4.59 (d, *J* = 13.6 Hz, 1H, **CH**₂), 4.03 (d, *J* = 13.6 Hz, 1H, **CH**₂), 3.24 - 3.33 (m, 2H, **CH**₂), 3.03 (t, *J* = 6.0 Hz, 2H, **CH**₂), 2.90 - 2.99 (m, 1H, **CH**), 2.84 - 2.88 (m, 2H, **CH**₂), 2.30 (s, 3H, Pyrazolyl-**CH**₃), 2.08 - 2.23 (m, 4H, **CH**₂ + **CH**₂), 1.74 - 1.87 (m, 2H, **CH**₂). ¹³C NMR (100 MHz, CDCl₃) δ 179.0, 173.8, 163.9, 163.0, 162.6, 156.0, 141.9, 134.8, 133.6, 130.5, 130.2, 130.1, 128.2, 121.3 (q, *J* = 272.7 Hz, CF₃), 117.4, 104.3, 51.5, 44.9, 42.0, 40.3, 32.2, 31.5, 29.9, 28.2, 22.6, 11.3. HRMS (MALDI) m/z Calcd for C₂₆H₂₅ClF₃N₅O₃S Na⁺ [M+Na]⁺ 602.1211, found 602.1215.

1-(4-((3-fluorobenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 13f. White solid, mp: 155 - 157 °C, 48.3 % yield. ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, *J* = 8.0 Hz, 1H, Ar-**H**), 7.86 - 7.90 (m, 1H, Ar-**H**), 7.50 - 7.56 (m, 1H, Ar-**H**), 7.33 - 7.38 (m, 1H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 4.98 (s, 2H, **CH**₂), 4.61 (d, *J* = 13.6 Hz, 1H, **CH**₂), 4.06 (d, *J* = 14.0 Hz, 1H, **CH**₂), 3.21 - 3.33 (m, 2H, **CH**₂), 3.03 (t, *J* = 6.2 Hz, 2H, **CH**₂), 2.82 - 2.89 (m, 3H, **CH** + **CH**₂), 2.30 (s, 3H, Pyrazolyl-**CH**₃), 2.09 - 2.22 (m, 4H, **CH**₂ + **CH**₂), 1.73 - 1.86 (m, 2H, **CH**₂). ¹³C NMR (100 MHz, CDCl₃) δ 179.0, 170.3, 163.9, 163.1, 162.6, 161.4, 156.0, 141.9, 130.9, 130.4, 125.8, 121.3 (q, *J* = 272.7 Hz, CF₃), 120.7, 117.4, 117.0, 104.2, 51.5, 44.9, 42.0, 40.3, 32.2, 31.5, 29.9, 28.3, 22.5, 11.3. HRMS (MALDI) m/z Calcd for C₂₆H₂₅F₄N₅O₃S Na⁺ [M+Na]⁺ 586.1506, found 586.1510.

1-(4-((3-bromobenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pi

*peridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)ethanone 13g.* White solid, mp: 159 - 161 °C, 52.4 % yield. ¹H NMR (400 MHz, CDCl₃) δ 8.38 (t, *J* = 1.8 Hz, 1H, Ar-**H**), 8.10 - 8.13 (m, 1H, Ar-**H**), 7.76 - 7.79 (m, 1H, Ar-**H**), 7.43 (t, *J* = 8.0 Hz, 1H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 4.98 (s, 2H, CH₂), 4.59 (d, *J* = 13.2 Hz, 1H, CH₂), 4.04 (d, *J* = 13.6 Hz, 1H, CH₂), 3.24 - 3.34 (m, 2H, CH₂), 3.04 (t, *J* = 6.2 Hz, 2H, CH₂), 2.86 - 2.99 (m, 3H, CH + CH₂), 2.30 (s, 3H, Pyrazolyl-CH₃), 2.09 - 2.25 (m, 4H, CH₂ + CH₂), 1.77 - 1.88 (m, 2H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 179.1, 172.7, 163.8, 162.9, 162.6, 156.0, 141.9, 136.4, 133.1, 130.7, 130.4, 128.7, 122.7, 121.3 (q, *J* = 272.7 Hz, CF₃), 117.4, 104.3, 51.5, 44.9, 42.0, 40.3, 32.2, 31.5, 29.9, 28.2, 22.6, 11.3. HRMS (MALDI) m/z Calcd for C₂₆H₂₅BrF₃N₅O₃S Na⁺ [M+Na]⁺ 646.0706, found 646.0710.

*2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-1-(4-(7-(((4-methylbenzoyl)oxyimino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone 13h.* White solid, mp: 207 - 209 °C, 53.0 % yield. ¹H NMR (400 MHz, CDCl₃) δ 8.06 - 8.08 (m, 2H, Ar-**H**), 7.34 (d, *J* = 10.4 Hz, 2H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 4.94 - 5.03 (m, 2H, CH₂), 4.61 (d, *J* = 14.0 Hz, 1H, CH₂), 4.04 (d, *J* = 14.0 Hz, 1H, CH₂), 3.22 - 3.31 (m, 2H, CH₂), 3.02 (t, *J* = 6.0 Hz, 2H, CH₂), 2.81 - 2.97 (m, 3H, CH + CH₂), 2.46 (s, 3H, Ar-CH₃), 2.30 (s, 3H, Pyrazolyl-CH₃), 2.08 - 2.21 (m, 4H, CH₂ + CH₂), 1.73 - 1.83 (m, 2H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 178.8, 176.5, 164.3, 163.9, 162.2, 155.4, 144.5, 141.9, 130.1, 129.5, 126.0, 121.3 (q, *J* = 272.7 Hz, CF₃), 117.7, 104.3, 51.5, 45.0, 42.0, 40.3, 32.3, 31.5, 30.0, 28.3, 22.6, 21.8, 11.3. HRMS (MALDI)

m/z Calcd for $C_{27}H_{28}F_3N_5O_3S$ $Na^+ [M+Na]^+$ 582.1757, found 582.1763.

I-(4-(7-(((4-chlorobenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 13i. White solid, mp: 210 - 212 °C, 79.6 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 8.11 - 8.14 (m, 2H, Ar-**H**), 7.51 - 7.54 (m, 2H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 4.98 (d, J = 6.0 Hz, 2H, CH_2), 4.62 (d, J = 14.0 Hz, 1H, CH_2), 4.07 (d, J = 13.6 Hz, 1H, CH_2), 3.23 - 3.32 (m, 2H, CH_2), 3.03 (t, J = 6.2 Hz, 2H, CH_2), 2.85 - 2.89 (m, 3H, $CH + CH_2$), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.10 - 2.21 (m, 4H, $CH_2 + CH_2$), 1.73 - 1.86 (m, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 176.7, 163.9, 163.4, 162.5, 155.9, 141.9, 140.1, 131.4, 129.1, 127.3, 121.3 (q, J = 272.7 Hz, CF_3), 117.4, 104.3, 51.5, 45.0, 42.0, 40.3, 32.2, 31.5, 29.9, 28.3, 22.5, 11.3. HRMS (MALDI) m/z Calcd for $C_{26}H_{25}ClF_3N_5O_3S$ $Na^+ [M+Na]^+$ 602.1211, found 602.1215.

I-(4-(7-(((4-fluorobenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 13j. White solid, mp: 195 - 197 °C, 58.4 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 8.20 - 8.23 (m, 2H, Ar-**H**), 7.21 - 7.25 (m, 2H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 4.98 (d, J = 7.6 Hz, 2H, CH_2), 4.62 (d, J = 14.0 Hz, 1H, CH_2), 4.08 (d, J = 14.0 Hz, 1H, CH_2), 3.23 - 3.32 (m, 2H, CH_2), 3.04 (t, J = 6.2 Hz, 2H, CH_2), 2.94 - 3.00 (m, 1H, CH), 2.87 - 2.90 (m, 2H, CH_2), 2.32 (s, 3H, Pyrazolyl - CH_3), 2.07 - 2.20 (m, 4H, $CH_2 + CH_2$), 175 - 1.85 (m, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 176.7, 166.1, 163.9, 163.3, 162.5, 155.8, 141.9, 132.7, 125.0, 121.3 (q, J = 272.7 Hz, CF_3), 117.5, 116.0, 104.3,

51.5, 45.0, 42.0, 40.3, 32.2, 31.5, 29.9, 28.3, 22.5, 11.3. HRMS (MALDI) m/z Calcd for $C_{26}H_{25}F_4N_5O_3S$ $Na^+ [M+Na]^+$ 586.1506, found 586.1511.

1-(4-(7-(((4-bromobenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 13k. White solid, mp: 205 - 207 °C, 73.0 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 8.02 - 8.05 (m, 2H, CH_2), 7.67 - 7.70 (m, 2H, CH_2), 6.31 (s, 1H, Pyrazolyl-**H**), 4.98 (d, J = 4.8 Hz, 2H, CH_2), 4.61 (d, J = 13.2 Hz, 1H, CH_2), 4.05 (d, J = 16.0 Hz, 1H, CH_2), 3.22 - 3.31 (m, 2H, CH_2), 3.02 (t, J = 6.2 Hz, 2H, CH_2), 2.84 - 2.87 (m, 3H, $CH + CH_2$), 2.30 (s, 3H, Pyrazolyl- CH_3), 2.09 - 2.20 (m, 4H, $CH_2 + CH_2$), 1.72 - 1.85 (m, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 173.0, 163.9, 163.6, 162.5, 156.0, 141.9, 132.1, 131.5, 128.8, 127.7, 121.3 (q, J = 262.6 Hz, CF_3), 117.5, 104.3, 51.5, 45.0, 42.0, 40.3, 32.2, 31.5, 29.9, 28.3, 22.5, 11.3. HRMS (MALDI) m/z Calcd for $C_{26}H_{25}BrF_3N_5O_3S$ $Na^+ [M+Na]^+$ 646.0706, found 646.0710.

2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-1-(4-(7-(((4-(trifluoromethyl)benzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone 13l. White solid, mp: 195 - 197 °C, 32.0 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.4 Hz, 2H, CH_2), 7.82 (d, J = 8.4 Hz, 2H, CH_2), 6.32 (s, 1H, Pyrazolyl-**H**), 4.93 - 5.03 (m, 2H, CH_2), 4.63 (d, J = 14.0 Hz, 1H, CH_2), 4.09 (d, J = 13.2 Hz, 1H, CH_2), 3.25 - 3.32 (m, 2H, CH_2), 3.05 (t, J = 6.0 Hz, 2H, CH_2), 2.82 - 2.91 (m, 3H, $CH + CH_2$), 2.31 (s, 3H, Pyrazolyl - CH_3), 2.14 - 2.21 (m, 4H, $CH_2 + CH_2$), 1.75 - 1.86 (m, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.0, 172.7, 163.9, 163.1, 162.7,

156.2, 141.9, 135.2, 132.2, 130.4, 125.8, 117.4, 104.3, 51.5, 45.0, 42.0, 40.3, 32.2, 31.5, 30.0, 28.3, 22.5, 11.3. HRMS (MALDI) m/z Calcd for $C_{27}H_{25}F_6N_5O_3S$ Na^+ $[M+Na]^+$ 636.1474, found 636.1478.

1-(4-((7-(((2-methoxybenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 13m. White solid, mp: 133 - 135 °C, 35.2 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 7.80 - 7.84 (m, 1H, Ar-**H**), 7.49 - 7.57 (m, 1H, Ar-**H**), 6.99 - 7.07 (m, 2H, Ar-**H**), 6.31 (s, 1H, Pyrazolyl-**H**), 4.91 - 5.01 (m, 2H, CH_2), 4.58 (d, J = 13.6 Hz, 1H, CH_2), 4.01 (d, J = 13.6 Hz, 1H, CH_2), 3.89 (s, 3H, OCH_3), 3.16 - 3.31 (m, 2H, CH_2), 3.00 (t, J = 6.0 Hz, 2H, CH_2), 2.78 - 2.87 (m, 3H, CH + CH_2), 2.29 (s, 3H, Pyrazolyl - CH_3), 2.06 - 2.17 (m, 4H, CH_2 + CH_2), 1.69 - 1.75 (m, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 176.4, 163.9, 161.9, 158.9, 155.2, 141.9, 133.9, 131.8, 131.5, 120.2, 119.2, 118.0, 112.0, 104.2, 55.9, 51.5, 45.0, 42.0, 40.3, 32.2, 31.5, 29.8, 28.3, 22.5, 11.3. HRMS (MALDI) m/z Calcd for $C_{27}H_{28}F_3N_5O_4S$ Na^+ $[M+Na]^+$ 598.1706, found 598.1710.

2,2-dimethyl-1-(((2-(1-(2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)acetyl)piperidin-4-yl)-5,6-dihydrobenzo[d]thiazol-7(4H)-ylidene)amino)oxy)propan-1-one 13n. White solid, mp: 141 - 143 °C, 53.8 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 6.34 (s, 1H, Pyrazolyl-**H**), 4.93 - 5.06 (m, 2H, CH_2), 4.65 (d, J = 13.6 Hz, 1H, CH_2), 4.09 (d, J = 13.6 Hz, 1H, CH_2), 3.25 - 3.33 (m, 2H, CH_2), 3.00 (t, J = 6.2 Hz, 2H, CH_2), 2.79 - 2.93 (m, 3H, CH + CH_2), 2.32 (s, 3H, Pyrazolyl - CH_3), 2.08 - 2.24 (m, 4H,

$\text{CH}_2 + \text{CH}_2$), 1.75 - 1.84 (m, 2H, CH_2), 1.39 (s, 9H, *t*-Bu-**H**). ^{13}C NMR (100 MHz, CDCl_3) δ 178.5, 176.4, 175.3, 163.9, 161.9, 154.0, 141.9, 121.3 (q, $J = 262.6$ Hz, CF_3), 117.6, 104.2, 51.5, 45.0, 42.1, 40.4, 32.3, 31.6, 30.1, 28.2, 27.3, 22.5, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{24}\text{H}_{30}\text{F}_3\text{N}_5\text{O}_3\text{S Na}^+ [\text{M}+\text{Na}]^+$ 548.1913, found 548.1918.

Then, we synthesized compounds with the nitrogen of oxime ether (ester) and thiazolidine are on the same side.

Synthesis of *tert*-butyl 4-(4-oxo-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidine-1-carboxylate (15)²¹

To a solution of *tert*-butyl 4-carbamothioylpiperidine-1-carboxylate (1.00 g, 4.09 mmol) in *tert*-butyl alcohol (20 mL), 3-bromocyclohexane-1,2-dione (0.86 g, 4.50 mmol) was added in six batches, 0.29 g was add each time, interval 15 min, after 15 min of stirring at room temperature, the mixture was heated to 85 °C, the reaction mixture was refluxed for 4 h. When the reaction was complete detected by TLC, the solvent was removed under vacuum condition and dichloromethane (20 mL) was added for re-dissolution. The organic phase was washed with saturated NaHCO_3 solution (15 mL*2) and water (15 mL), dried over anhydrous MgSO_4 , and concentrated in vacumm and isolated by column chromatography (eluent, EA : PE=1:3; R_f =0.38) to afford yellow oil 0.64 g, 46.5 % yield. ^1H NMR (400 MHz, CDCl_3) δ 4.20 (s, 2H, CH_2), 3.14 - 3.21 (m, 1H, CH), 3.08 (t, $J = 6.2$ Hz, 2H, CH_2),

2.84 (t, $J = 13.6$ Hz, 2H, CH_2), 2.66 (t, $J = 6.6$ Hz, 2H, CH_2), 2.22 - 2.28 (m, 2H, CH_2), 2.06 - 2.10 (m, 2H, CH_2), 1.67 - 1.77 (m, 2H, CH_2), 1.47 (s, 9H, *t*-Bu- H).

Synthesis of 2-(piperidin-4-yl)-6,7-dihydrobenzo[*d*]thiazol-4(5*H*)-one (16)

The mixture of *tert*-butyl 4-(4-oxo-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidine-1-carboxylate (7.62 g, 22.67 mmol), 20% of dilute hydrochloric acid (75 mL), and dichloromethane (75 mL) was heated up to 40 C and reflux for 10 h. When the reaction was complete detected by TLC, sodium hydroxide solution was add to adjust the pH of water layer to 9 ~ 10, the aqueous phase extraction with dichloromethane (60 mL*4), the combined organic phase was dried over anhydrous MgSO_4 , and concentrated in vacumm to afford yellow oil 1.46 g, 53.3 % yield. ^1H NMR (400 MHz, CDCl_3) δ 3.17 - 3.19 (m, 1H, CH), 3.12 - 3.16 (m, 2H, CH_2), 3.06 (t, $J = 6.2$ Hz, 2H, CH_2), 2.68 - 2.75 (m, 2H, CH_2), 2.63 (t, $J = 6.6$ Hz, 2H, CH_2), 2.19 - 2.26 (m, 2H, CH_2), 2.08 - 2.11 (m, 2H, CH_2), 2.05 - 2.07 (m, 1H, NH), 1.64 - 1.74 (m, 2H, CH_2).

Synthesis of 2-(1-(2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)acetyl)piperidin-4-yl)-6,7-dihydrobenzo[*d*]thiazol-4(5*H*)-one (17)

To a solution of 2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)acetic acid 7 (2.56 g, 12.32 mmol) in tetrahydrofuran (25 mL), *N,N'*-carbonyl diimidazole (CDI) (2.20 g, 13.55 mmol) was added in three batches under ice bath conditions, 0.73 g was

added each time, and stirred at room temperature for another 1 h. Then, triethylamine (1.87 g, 18.48 mmol) and 4-dimethylaminopyridine (DMAP) (0.32 g, 2.62 mmol) were added respectively. Then, 2-(piperidin-4-yl)-6,7-dihydrobenzo[*d*]thiazol-4(5*H*)-one **16** (3.20 g, 13.55 mmol) were dissolved in 25 mL THF and slowly dropped into the reaction solution. The reaction mixture continue reacting for 10 h at room temperature, When the reaction was complete detected by TLC, dilute hydrochloric acid was add to adjust the pH to 1, the aqueous phase was extracted with ethyl acetate (40 mL*3), the combined organic phase was dried over anhydrous MgSO₄, and concentrated in vacumm to afford yellow solid 3.89 g, 74.1 % yield, mp: 145 - 147 °C. ¹H NMR (400 MHz, CDCl₃) δ 6.33 (s, 1H, Pyrazolyl-**H**), 4.98 (d, *J* = 6.4 Hz, 2H, CH₂), 4.58 (d, *J* = 13.6 Hz, 1H, CH₂), 3.22 - 3.33 (m, 2H, CH₂), 3.09 (t, *J* = 6.2 Hz, 2H, CH₂), 2.79 - 2.86 (m, 1H, CH), 2.65 (t, *J* = 6.4 Hz, 2H, CH₂), 2.31 (s, 3H, Pyrazolyl-CH₃), 2.22 - 2.28 (m, 2H, CH₂), 2.12 - 2.19 (m, 2H, CH₂), 1.68 - 1.84 (m, 2H, CH₂).

Synthesis of 1-(4-(4-(hydroxyimino)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)ethanone (18)

To a solution of 2-(1-(2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)acetyl)piperidin-4-yl)-6,7-dihydrobenzo[*d*]thiazol-4(5*H*)-one **17** (0.6 g, 1.41 mmol) in mathanol (15 mL), then hydroxylamine hydrochloride (0.15 g, 2.11 mmol) and K₂CO₃ (0.29 g, 2.11 mmol)

were added, the reaction mixture was refluxed for 10 h. When the reaction was complete detected by TLC, concentrated in vacumm to afford yellow solid, dichloromethane (15 mL) was added for re-dissolution. The organic phase was washed with water (10 mL*3), dried over anhydrous MgSO₄, and concentrated in vacumm and isolated by column chromatography (eluent, EA : PE=2:3; R_f=0.41) to afford white solid 0.42 g, 67.7 % yield, mp: 116 - 118 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.71 (s, 1H, NOH), 6.31 (s, 1H, Pyrazolyl-H), 4.99 (s, 2H, CH₂), 4.54 (d, *J* = 13.8 Hz, 1H, CH₂), 3.21 - 3.29 (m, 2H, CH₂), 2.79 - 2.88 (m, 5H, CH₂ + CH + CH₂), 2.29 (s, 3H, Pyrazolyl-CH₃), 2.11 - 1.20 (m, 2H, CH₂), 1.96 - 2.02 (m, 2H, CH₂), 1.68 - 1.81 (m, 2H, CH₂).

**Synthesis of
2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-1-(4-((2-methylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone (20a)**

Under ice salt bath, the sodium hydride (0.06 g, 1.50 mmol) was added to anhydrous N, N - dimethyl formamide (15 mL), then, 1-(4-(4-(hydroxyimino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-2-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone **18** (0.60 g, 1.36 mmol) was added in three batches, 0.20 g was added each time, interval of 10 min, and after that, the mixture was stirred for 1 h. Then, 1-(bromomethyl)-2-methylbenzene (0.26 g, 1.43 mmol) was added slowly in 5 min. After the addition was finished, the mixture was stirred at room temperature for 2 h. When the reaction was completed monitored by

TLC, a small amount of saturated ammonium chloride solution was added to quench the reaction. Water (50 mL) was added, and the mixture was extracted with ethyl acetate (30 mL*3). the combined organic phase was dried over anhydrous MgSO₄, and concentrated in vacumm and isolated by column chromatography (eluent, EA : PE=1:2; Rf=0.43) to afford white solid 0.6 g, 80.9 % yield, mp: 150 - 152 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.36 - 7.38 (m, 1H, Ar-**H**), 7.16 - 7.24 (q, *J* = 21.2, 3H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.32 (s, 2H, CH₂), 4.98 (m, 2H, CH₂), 4.64 (d, *J* = 13.6 Hz, 1H, CH₂), 4.02 (d, *J* = 14.0 Hz, 1H, CH₂), 3.34 - 3.42 (m, 1H, CH), 3.19 - 3.26 (m, 1H, CH₂), 2.86 (t, *J* = 6.0 Hz, 2H, CH₂), 2.81 (t, *J* = 6.4 Hz, 2H, CH₂), 2.72 - 2.76 (m, 1H, CH₂), 2.37 (s, 3H, Ar-CH₃), 2.31 (s, 3H, Pyrazolyl-CH₃), 2.14 - 2.24 (m, 2H, CH₂), 1.93 - 1.20 (m, 2H, CH₂), 1.63 - 1.77 (m, 2H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 172.0, 163.8, 151.1, 144.5, 142.0, 141.9, 141.6, 137.2, 135.4, 130.2, 129.1, 128.1, 125.8, 121.4 (q, *J* = 272.7 Hz, CF₃), 104.3, 75.0, 51.5, 45.2, 42.3, 40.8, 32.8, 32.2, 23.5, 23.3, 22.2, 19.1, 11.3. HRMS (MALDI) m/z Calcd for C₂₇H₃₀F₃N₅O₂S Na⁺ [M+Na]⁺ 568.1964, found 568.1968.

20b-20j and **21** were synthesized using the similar procedure as **20a**, the relevant data obtained are as follows:

1-(4-((4-(2-fluorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pyridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 20b. White solid, mp: 159 - 161 °C, 77.6 % yield. ¹H NMR (400 MHz, CDCl₃) δ 7.42 - 7.46 (m, 1H, Ar-**H**), 7.25 - 7.30 (m, 1H, Ar-**H**), 7.10 - 7.14 (m, 1H, Ar-**H**), 7.01 - 7.06 (m, 1H,

Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.36 (s, 1H, **CH**), 4.98 (q, $J = 20.4$ Hz, 2H, **CH₂**), 4.64 (d, $J = 13.6$ Hz, 1H, **CH₂**), 4.02 (d, $J = 13.6$ Hz, 1H, **CH₂**), 3.34 - 3.40 (m, 1H, **CH**), 3.23 (t, $J = 11.8$ Hz, 1H, **CH₂**), 2.81 - 2.88 (m, 4H, **CH₂** + **CH₂**), 2.74 - 2.76 (m, 1H, **CH₂**), 2.31 (s, 3H, Pyrazolyl-**CH₃**), 2.14 - 2.24 (m, 2H, **CH₂**), 1.94 - 2.01 (m, 2H, **CH₂**), 1.63 - 1.76 (m, 2H, **CH₂**). ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 163.8, 151.4, 144.4, 142.0, 141.9, 141.6, 137.5, 130.4, 129.5, 124.8, 124.0, 121.4 (q, $J = 272.7$ Hz, **CF₃**), 115.3, 104.2, 70.1, 51.5, 45.2, 42.3, 40.8, 32.8, 32.1, 23.5, 23.3, 22.2, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{F}_4\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 572.1714, found 572.1718.

1-(4-(((2-chlorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pyridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 20c. White solid, mp: 168 - 170 °C, 70.2 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.44 - 7.47 (m, 1H, Ar-**H**), 7.34 - 7.36 (m, 1H, Ar-**H**), 7.21 - 7.25 (m, 2H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.41 (s, 1H, **CH**), 4.97 (q, $J = 22.0$ Hz, 2H, **CH₂**), 4.63 (d, $J = 13.6$ Hz, 1H, **CH₂**), 4.00 (d, $J = 13.6$ Hz, 1H, **CH₂**), 3.32 - 3.40 (m, 1H, **CH**), 3.21 (t, $J = 11.6$ Hz, 1H, **CH₂**), 2.85 - 2.88 (m, 4H, **CH₂** + **CH₂**), 2.72 - 2.78 (m, 1H, **CH₂**), 2.30 (s, 3H, Pyrazolyl-**CH₃**), 2.12 - 2.22 (m, 2H, **CH₂**), 1.96 - 2.02 (m, 2H, **CH₂**), 1.61 - 1.74 (m, 2H, **CH₂**). ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 163.8, 151.6, 144.3, 142.0, 141.9, 141.6, 137.6, 135.6, 133.1, 129.3, 128.8, 126.7, 121.3 (q, $J = 262.6$ Hz, **CF₃**), 104.2, 73.5, 51.5, 45.2, 42.3, 40.8, 32.8, 32.1, 23.5, 23.4, 22.2, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{ClF}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 588.1418, found 588.1422.

*1-(4-((2-bromobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pirenidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)ethanone 20d. White solid, mp: 156 - 158 °C, 74.5 % yield. ¹H NMR (400 MHz, CDCl₃) δ 7.54 - 7.56 (m, 1H, Ar-**H**), 7.44 - 7.46 (m, 1H, Ar-**H**), 7.28 - 7.32 (m, 1H, Ar-**H**), 7.13 - 7.17 (m, 1H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.38 (s, 2H, CH₂), 4.91 - 5.05 (m, 2H, CH₂), 4.64 (d, *J* = 13.8 Hz, 1H, CH₂), 4.03 (d, *J* = 14.0 Hz, 1H, CH₂), 3.34 - 3.41 (m, 1H, CH), 3.22 (t, *J* = 13.0 Hz, 1H, CH₂), 2.88 (t, *J* = 6.4 Hz, 4H, CH₂ + CH₂), 2.76 (t, *J* = 12.8 Hz, 1H, CH₂), 2.31 (s, 3H, Pyrazolyl -CH₃), 2.13 - 2.23 (m, 2H, CH₂), 1.97 - 2.03 (m, 2H, CH₂), 1.66 - 1.75 (m, 2H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 172.0, 163.8, 151.7, 144.3, 142.0, 141.9, 141.6, 137.5, 132.6, 129.4, 129.0, 127.3, 122.9, 121.4 (q, *J* = 272.7 Hz, CF₃), 104.3, 75.7, 51.5, 45.2, 42.3, 40.8, 32.8, 32.1, 23.5, 23.4, 22.2, 11.3. HRMS (MALDI) m/z Calcd for C₂₆H₂₇BrF₃N₅O₂S Na⁺ [M+Na]⁺ 632.0913, found 632.0917.*

*2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-1-(4-((3-methylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone 20e. Yellow oil, 73.6 % yield. ¹H NMR (400 MHz, CDCl₃) δ 7.20 - 7.25 (m, 3H, Ar-**H**), 7.11 - 7.14 (m, 1H, Ar-**H**), 6.34 (s, 1H, Pyrazolyl-**H**), 5.27 (s, 2H, CH₂), 4.92 - 5.05 (m, 2H, CH₂), 4.64 (d, *J* = 13.4 Hz, 1H, CH₂), 3.34 - 3.42 (m, 1H, CH), 3.20 - 3.27 (m, 1H, CH₂), 2.81 - 2.88 (m, 4H, CH₂ + CH₂), 2.73 - 2.80 (m, 1H, CH₂), 2.36 (s, 3H, Ar-CH₃), 2.32 (s, 3H, Pyrazolyl -CH₃), 2.14 - 2.24 (m, 2H, CH₂), 1.94 - 2.01 (m, 2H, CH₂), 1.67 - 1.73 (m, 2H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 171.9, 163.8, 151.1,*

144.5, 142.1, 141.9, 141.7, 138.0, 137.3, 129.0, 128.6, 128.3, 125.3, 121.3 (q, $J = 262.6$ Hz, \mathbf{CF}_3), 104.2, 76.6, 51.5, 45.2, 42.3, 40.8, 32.8, 32.1, 23.5, 23.4, 22.2, 21.4, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{27}\text{H}_{30}\text{F}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 568.1964, found 568.1968.

1-(4-(((3-chlorobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pyridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 20f. Yellow oil, 65.5 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.39 - 7.40 (m, 1H, Ar-**H**), 7.27 - 7.28 (m, 3H, Ar-**H**), 6.34 (s, 1H, Pyrazolyl-**H**), 5.28 (s, 2H, CH_2), 4.92 - 5.05 (m, 2H, CH_2), 4.64 (d, $J = 13.2$ Hz, 1H, CH_2), 4.04 (d, $J = 13.6$ Hz, 1H, CH_2), 3.33 - 3.41 (m, 1H, CH), 3.20 - 3.27 (m, 1H, CH_2), 2.82 - 2.90 (m, 4H, $\text{CH}_2 + \text{CH}_2$), 2.73 - 2.81 (m, 1H, CH_2), 2.32 (s, 3H, Pyrazolyl- CH_3), 2.14 - 2.24 (m, 2H, CH_2), 1.96 - 2.03 (m, 2H, CH_2), 1.63 - 1.76 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 163.8, 151.5, 144.3, 142.0, 141.9, 141.6, 139.9, 137.6, 134.2, 129.6, 127.8, 126.0, 121.4 (q, $J = 272.7$ Hz, \mathbf{CF}_3), 104.2, 75.5, 51.5, 45.1, 42.2, 40.7, 32.8, 32.1, 23.5, 23.4, 22.2, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{ClF}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 588.1418, found 588.1423.

1-(4-(((3-bromobenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)pyridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 20g. Yellow oil, 68.7 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.53 (s, 1H, Ar-**H**), 7.41 (d, $J = 8.0$ Hz, 1H, Ar-**H**), 7.30 (d, $J = 7.6$ Hz, 1H, Ar-**H**), 7.21 (t, $J = 7.8$, 1H, Ar-**H**), 6.32 (s, 1H, Pyrazolyl-**H**), 5.25 (s, 2H, CH_2), 4.90 - 5.03 (m, 2H, CH_2), 4.62 (d, $J = 13.2$ Hz,

1H, CH_2), 4.01 (d, $J = 14.4$ Hz, 1H, CH_2), 3.31 - 3.39 (m, 1H, CH), 3.22 (t, $J = 12.8$ Hz, 1H, CH_2), 2.80 - 2.88 (m, 4H, $\text{CH}_2 + \text{CH}_2$), 2.75 (t, $J = 11.6$ Hz, 1H, CH_2), 2.30 (s, 3H, Pyrazolyl- CH_3), 2.12 - 2.22 (m, 2H, CH_2), 1.94 - 2.01 (m, 2H, CH_2), 1.63 - 1.74 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 163.8, 151.5, 144.3, 142.0, 141.9, 141.6, 140.1, 137.6, 130.9, 129.9, 126.5, 122.4, 121.4 (q, $J = 272.7$ Hz, CF_3), 104.2, 75.5, 51.5, 45.2, 42.3, 40.8, 32.8, 32.1, 23.5, 23.4, 22.2, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{BrF}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 632.0913, found 632.0917.

2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-1-(4-(((4-methylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone 20h. Yellow solid, mp:117 - 119 °C, 97.1 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.30 (d, $J = 7.6$ Hz, 2H, Ar- H), 7.16 (d, $J = 7.6$ Hz, 2H, Ar- H), 6.33 (s, 1H, Pyrazolyl- H), 5.25 (s, 2H, CH_2), 4.91 - 5.04 (m, 2H, CH_2), 4.63 (d, $J = 13.6$ Hz, 1H, CH_2), 4.01 (d, $J = 13.6$ Hz, 1H, CH_2), 3.33 - 3.40 (m, 1H, CH), 3.19 - 3.26 (m, 1H, CH_2), 2.85 (t, $J = 6.2$ Hz, 2H, CH_2), 2.80 (t, $J = 6.6$ Hz, 2H, CH_2), 2.73 - 2.76 (m, 1H, CH_2), 2.34 (s, 3H, CH_3), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.13 - 2.23 (m, 2H, CH_2), 1.92 - 1.98 (m, 2H, CH_2), 1.62 - 1.75 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 171.9, 163.8, 151.1, 144.5, 142.0, 141.9, 141.6, 137.4, 134.5, 129.0, 128.4, 121.3 (q, $J = 262.6$ Hz, CF_3), 104.2, 76.5, 51.5, 45.2, 42.3, 40.8, 32.8, 32.1, 23.5, 22.2, 21.2, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{27}\text{H}_{30}\text{F}_3\text{N}_5\text{O}_2\text{S Na}^+ [\text{M}+\text{Na}]^+$ 568.1964, found 568.1967.

2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-1-(4-(((4-methylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)ethanone 20i. White

solid, mp: 143 - 145 °C, 65.0 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.47 (d, J = 8.4 Hz, 2H, Ar-**H**), 7.27 (d, J = 6.4 Hz, 2H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 5.24 (s, 2H, CH_2), 4.91 - 5.05 (m, 2H, CH_2), 4.63 (d, J = 13.6 Hz, 1H, CH_2), 4.02 (d, J = 13.6 Hz, 1H, CH_2), 3.32 - 3.40 (m, 1H, **H**), 3.19 - 3.26 (m, 1H, CH_2), 2.86 (t, J = 6.2 Hz, 2H, CH_2), 2.80 (t, J = 6.4 Hz, 2H, CH_2), 2.72 - 2.75 (m, 1H, CH_2), 2.31 (s, 3H, Pyrazolyl- CH_3), 2.13 - 2.22 (m, 2H, CH_2), 1.94 - 2.00 (m, 2H, CH_2), 1.62 - 1.75 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 163.8, 151.4, 144.3, 142.0, 141.9, 141.7, 137.2, 131.5, 129.8, 121.7, 121.3 (q, J = 262.6 Hz, CF_3), 104.2, 75.6, 51.5, 45.2, 42.3, 40.8, 32.8, 32.1, 23.5, 23.4, 22.2, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{BrF}_3\text{N}_5\text{O}_2\text{S Na}^+$ [M+Na]⁺ 632.0913, found 632.0918.

1-(4-(((2,6-dimethylbenzyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)piperidin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 20j. White solid, mp: 89 - 91 °C, 33.9 % yield. ^1H NMR (400 MHz, CDCl_3) δ 7.12 - 7.16 (m, 1H, Ar-**H**), 7.04 - 7.06 (m, 2H, Ar-**H**), 6.34 (s, 1H, Pyrazolyl-**H**), 5.36 (s, 2H, CH_2), 4.92 - 5.06 (m, 2H, CH_2), 4.64 (d, J = 13.2 Hz, 1H, CH_2), 4.03 (d, J = 13.6 Hz, 1H, CH_2), 3.35 - 3.43 (m, 1H, **H**), 3.21 - 3.27 (m, 1H, CH_2), 2.85 (t, J = 6.0 Hz, 2H, CH_2), 2.78 - 2.81 (m, 1H, CH_2), 2.74 (t, J = 6.4 Hz, 2H, CH_2), 2.43 (s, 6H, $\text{CH}_3 + \text{CH}_3$), 2.32 (s, 3H, Pyrazolyl- CH_3), 2.16 - 2.25 (m, 2H, CH_2), 1.90 - 1.97 (m, 2H, CH_2), 1.64 - 1.77 (m, 2H, CH_2). ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 163.8, 151.0, 144.6, 141.9, 141.7, 138.7, 137.2, 133.0, 128.4, 128.1, 104.3, 71.0, 51.5, 45.2, 42.3, 40.8, 32.8, 32.1, 23.5, 23.2, 22.2, 19.8, 11.3. HRMS (MALDI) m/z Calcd for $\text{C}_{28}\text{H}_{32}\text{F}_3\text{N}_5\text{O}_2\text{S Na}^+$

$[M+Na]^+$ 582.2121, found 582.2125.

1-(4-((4-((2-fluorobenzoyl)oxy)imino)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)peridin-1-yl)-2-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)ethanone 21. White solid, mp: 109 - 111 °C, 63.4 % yield. 1H NMR (400 MHz, $CDCl_3$) δ 8.02 - 8.06 (m, 1H, Ar-**H**), 7.54 - 7.59 (m, 1H, Ar-**H**), 7.24 - 7.28 (m, 1H, Ar-**H**), 7.15 - 7.19 (m, 1H, Ar-**H**), 6.33 (s, 1H, Pyrazolyl-**H**), 4.96 - 5.05 (m, 2H, **CH**₂), 4.60 (d, J = 13.6 Hz, 1H, **CH**₂), 4.03 (d, J = 14.0 Hz, 1H, **CH**₂), 3.32 - 3.36 (m, 1H, **CH**), 3.24 - 3.30 (m, 1H, **CH**₂), 3.02 (t, J = 6.4 Hz, 2H, **CH**₂), 2.96 (t, J = 6.2 Hz, 2H, **CH**₂), 2.80 - 2.87 (m, 1H, **CH**₂), 2.31 (s, 3H, Pyrazolyl-**CH**₃), 2.15 - 2.27 (m, 2H, **CH**₂), 2.05 - 2.11 (m, 2H, **CH**₂), 1.68 - 1.86 (m, 2H, **CH**₂). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 163.9, 162.9, 162.0, 160.4, 158.5, 143.1, 142.0, 134.8, 132.6, 124.3, 121.4 (q, J = 272.7 Hz, **CF**₃), 117.1, 116.9, 104.2, 51.5, 45.0, 42.1, 40.5, 32.3, 31.9, 24.9, 23.6, 22.2, 11.3. HRMS (MALDI) m/z Calcd for $C_{26}H_{25}F_4N_5O_3S$ Na^+ $[M+Na]^+$ 586.1506, found 586.1510.

2. Fungicidal activity against *phytophthora capsici* (*in vitro*)

Plating Method: The oomycetes were inoculated into a petri dish containing 50 μ g/mL medical solution and incubated in a 25 °C biochemical incubator in dark. The fungicidal effect was investigated 3 days later. Each process is repeated 3 times. The control group was treated with sterile water. Activity results were estimated according to a percentage scale of 0-100 (0, no activity; 100, total kill).

$$\text{Control effect}(\%) = \frac{\text{blank colony diameter} - \text{colony diameter after liquid treatment}}{\text{blank colony diameter} - 4} \times 100$$

3.Fungicidal activity against *phytophthora capsici* (*in vivo*)

Plants infected with *P. capsici* were collected from pepper fields in Tianjin, China, in 2012. The pathogenic fungal isolates of *P. capsici* were grown on V8 juice agar medium at room temperature for 7 days. To simulate the formation of sporangium, the cultures were maintained under light at 24 °C for seven days. When abundant sporangia had formed, the sterile solution was replaced with sterile distilled water and the plates were maintained at 4 °C for 30 min and then left at room temperature (20–24 °C) for 1 h to enhance the release of zoospores from the sporangia. The flooding water, which contained zoospores and mycelium, was filtered using two layers of cheesecloth, and the concentration of the zoospore suspension was subsequently adjusted to approximately 1×10^6 zoospores mL⁻¹ using a hemocytometer. The inoculum was then used immediately.

The inoculation tests were conducted under greenhouse and growth chamber conditions. The pepper plants (*Capsicum annuum L.*) were grown in plastic trays (50 × 30 × 5 cm) in a greenhouse at 25 ± 2 °C in a sterilized mixture of vermiculite and worm cast (5:1 – v/v). The commercial fungicide dimethomorph was used as a positive control to compare its antifungal activity with those of the synthesized compounds. The title compounds and these controls were dissolved separately in DMF, and the resulting solutions were diluted to give concentrations of 3.125, 6.25, 12.5, 25, 50.0 and 100 µg mL⁻¹. When the plants had six leaves, each pepper root was treated with 1 mL of a solution of each chemical by making 1 cm long incisions in the

pepper plant 1 day prior to the inoculation with *P. capsici*. The zoospore inoculation of the pepper roots was performed by inoculating 1 mL of zoospore inoculum of *P. capsici* according to the same procedure used for the chemical treatment process. Six seedlings at the four-leaf stage were transplanted into a plastic pot (5×30×5 cm) containing the soil mix described previously. Seedlings that had been drenched with sterile distilled water instead of the zoospore inoculum were used as a negative control. Disease severity was evaluated after 7 days using a 0–5 scale (0 = no visible disease symptoms; 1 = leaves slightly wilted with brownish lesions beginning to appear on their stems; 2 = 30–50% of the entire plant diseased; 3 = 50–70% of the entire plant diseased; 4 = 70–90% of the entire plant diseased; 5 = dead plant).

4. Fungicidal activity against *pseudoperonospora cubensis* (*in vivo*).

Cucumber plants, which were cultivated by Shandong Mici with one fully expanded true leaf, were maintained in a greenhouse. The commercial fungicide dimethomorph was used as a positive control and its antifungal activity compared with those of the synthesized compounds. The synthesized compounds and the controls dissolved separately in DMF, and the resulting solutions were diluted to give the concentrations of 3.125, 6.25, 12.5, 25, and 50 $\mu\text{g mL}^{-1}$. The plants were then sprayed with these different fungicide solutions and allowed to dry in air for approximately 2 h. Cultures of *P. cubensis* were maintained on the cucumber plants and the spores were collected by shaking the leaves in water. The lower surfaces of the treated cucumber leaves were then sprayed with a spore suspension of ca. 100000

spores mL⁻¹. The plants were transferred to a thermo-hygrostat and held at 20 °C and >90% humidity for 5 days to allow for infection. The plants were then held in the greenhouse for 5 more days before being examined for their disease control score.

5. Fungicidal activity against *phytophthora infestans* (*in vivo*)

The plants (3-4 leaves) were sprayed with these different fungicide solutions and allowed to dry in air for approximately 2 h. Fresh potato phytophthora blight was cultured with rye medium for 10 days to produce potato phytophthora spores, which were mixed with sterile water into a spore suspension (1×10⁶), and the prepared spore suspension was uniformly inoculated on potato leaves. The plants were transferred to a thermo-hygrostat and held at 20 °C and >90% humidity for 5 days to allow for infection. The plants were then held in the greenhouse for 5 more days before being examined for their disease control score.

6. Scanning Electron Microscopy (SEM) Observations

SEM observations on the hyphae of *P. capsici* were conducted according to the method of previous work. 5 mm diameter of mycelial disks were cut from the periphery of the colony grown on PDA containing EC50 (0.0940 µg/mL) of compound **11b** and 0.5% DMSO (blank control) respectively. The samples were fixed in 2.5% glutaraldehyde at room temperature for 24 h, and were washed with 0.1 M phosphate buffer for 15 min, repeated three times, followed another 1 h fixation in 1% OsO₄ solution. Then the specimens were dehydrated in a gradient ethanol series (20%, 50%,

80%, and 100% respectively, 5 min for each alcohol dilution). After drying at critical point and gold coating, SEM observations were carried out with a scanning electron microscope (Hitachi, S-3400N, Japan) at an accelerating voltage of 15.0 kV.

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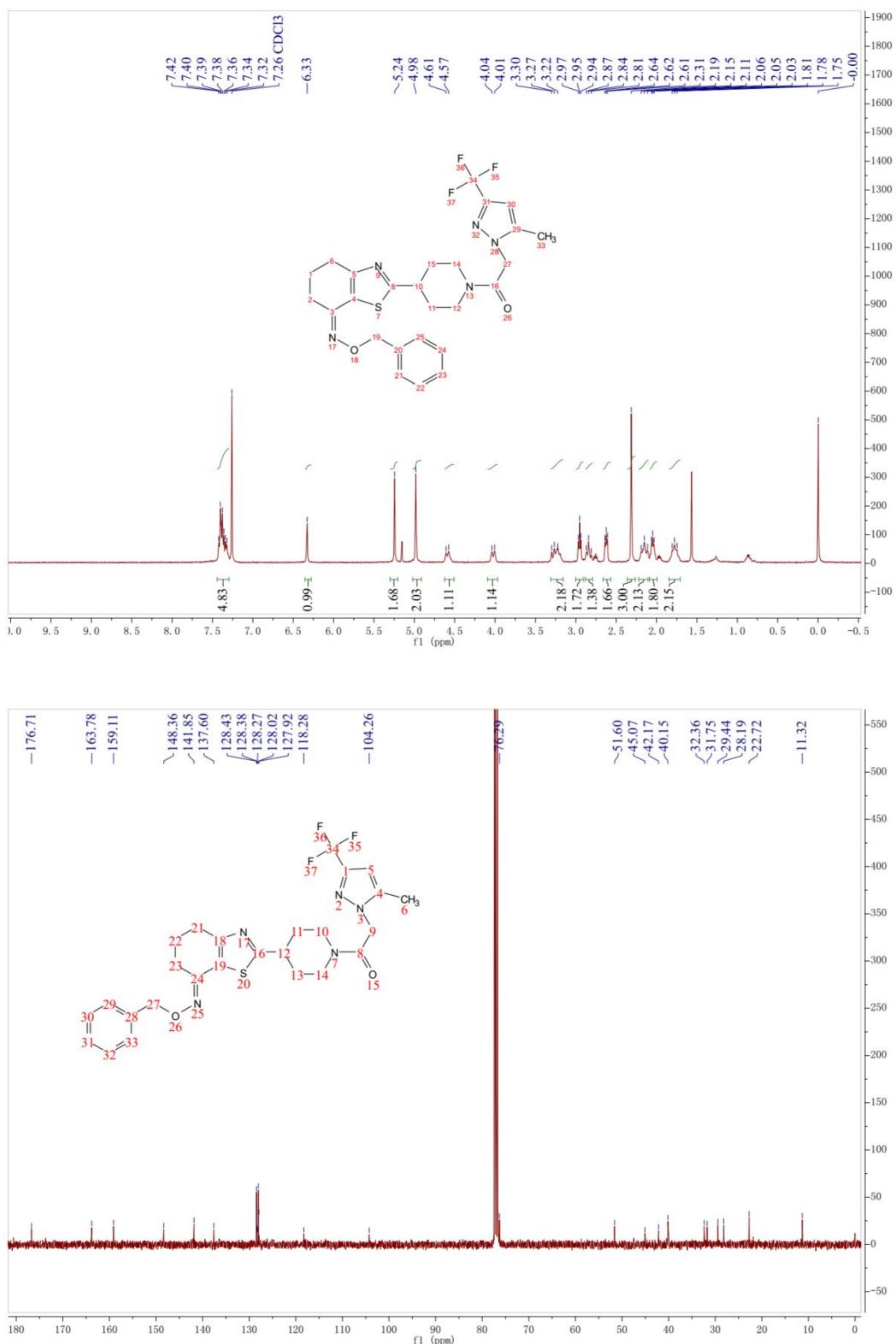
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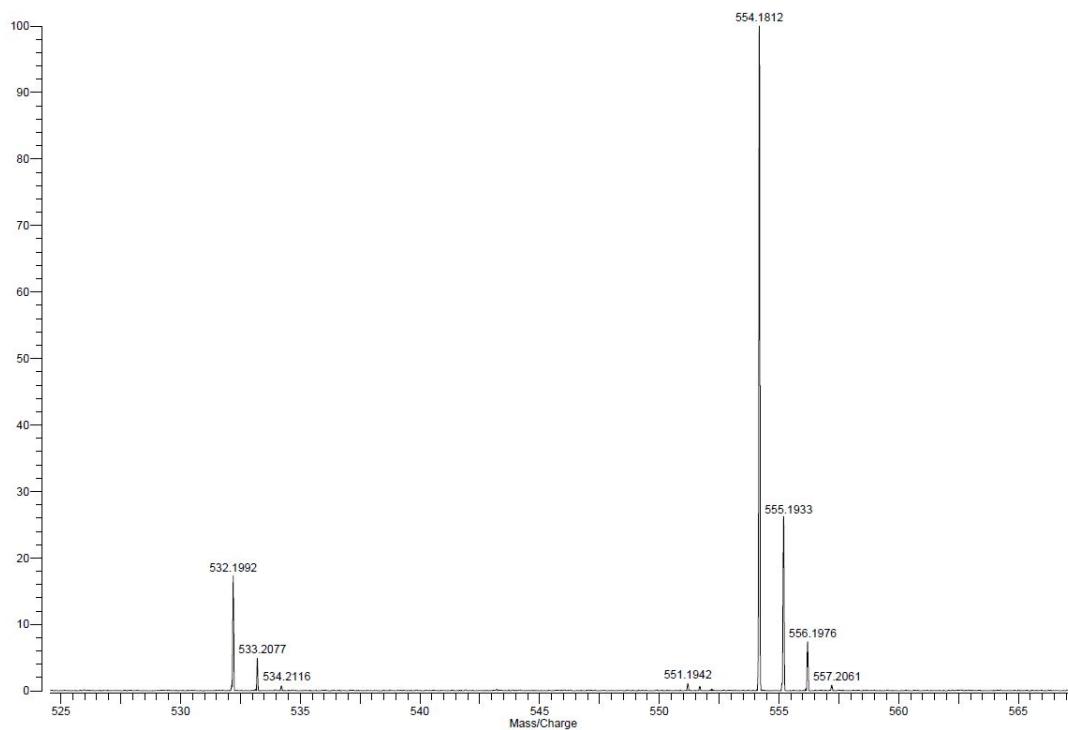
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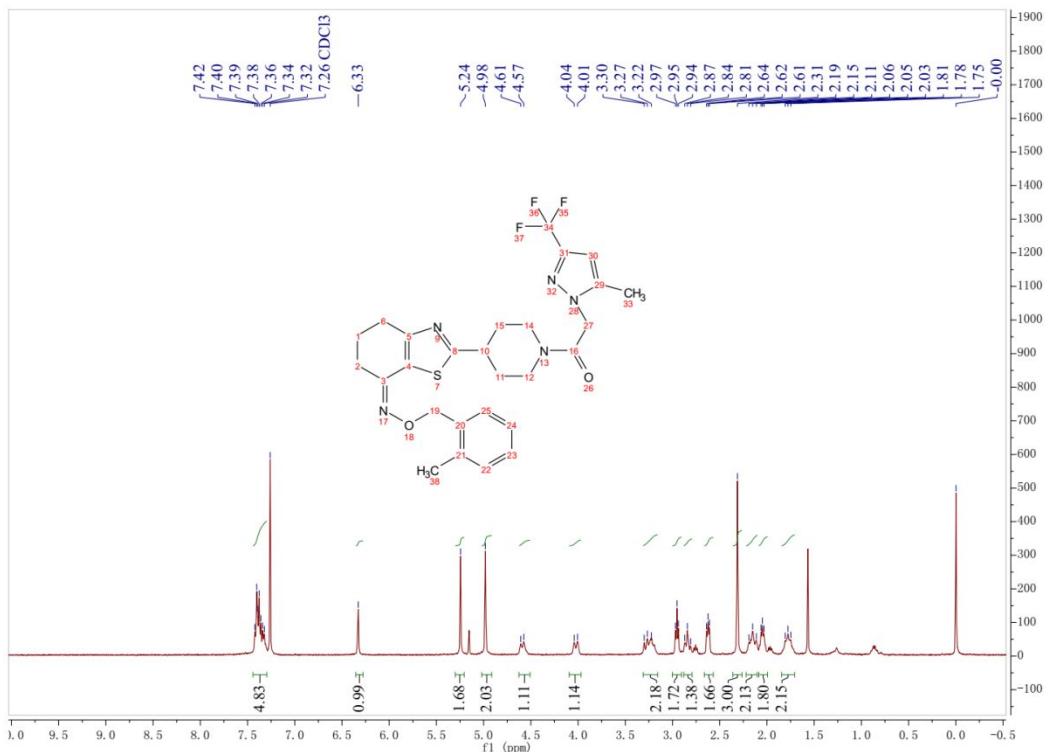
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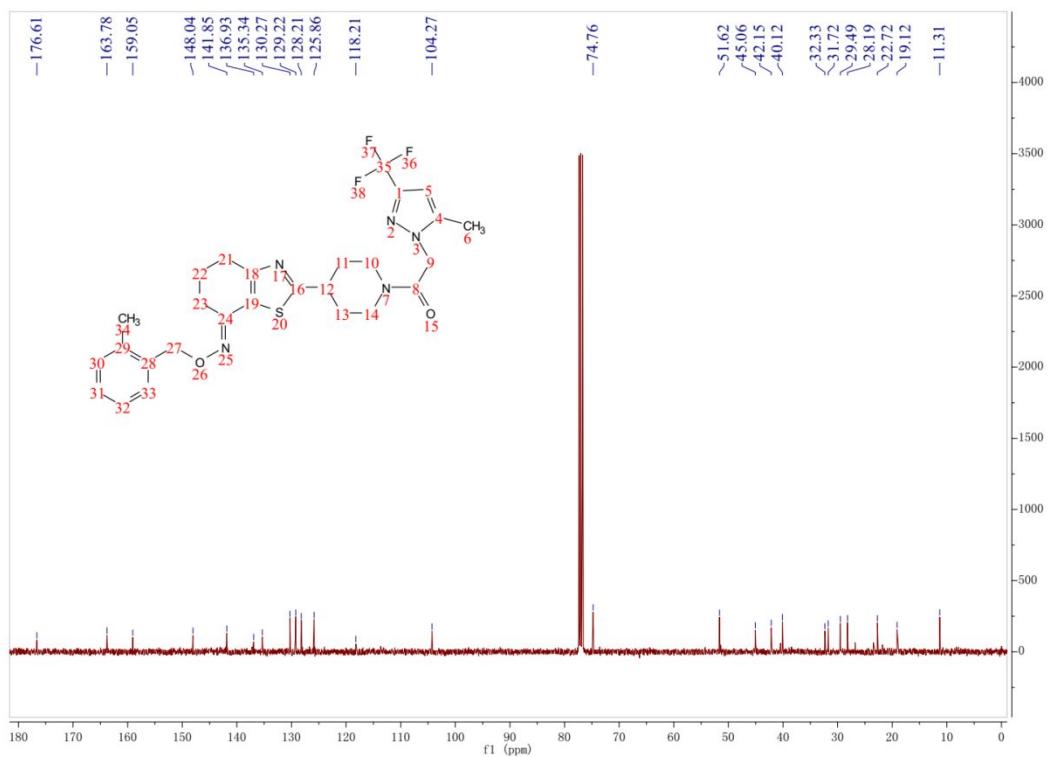
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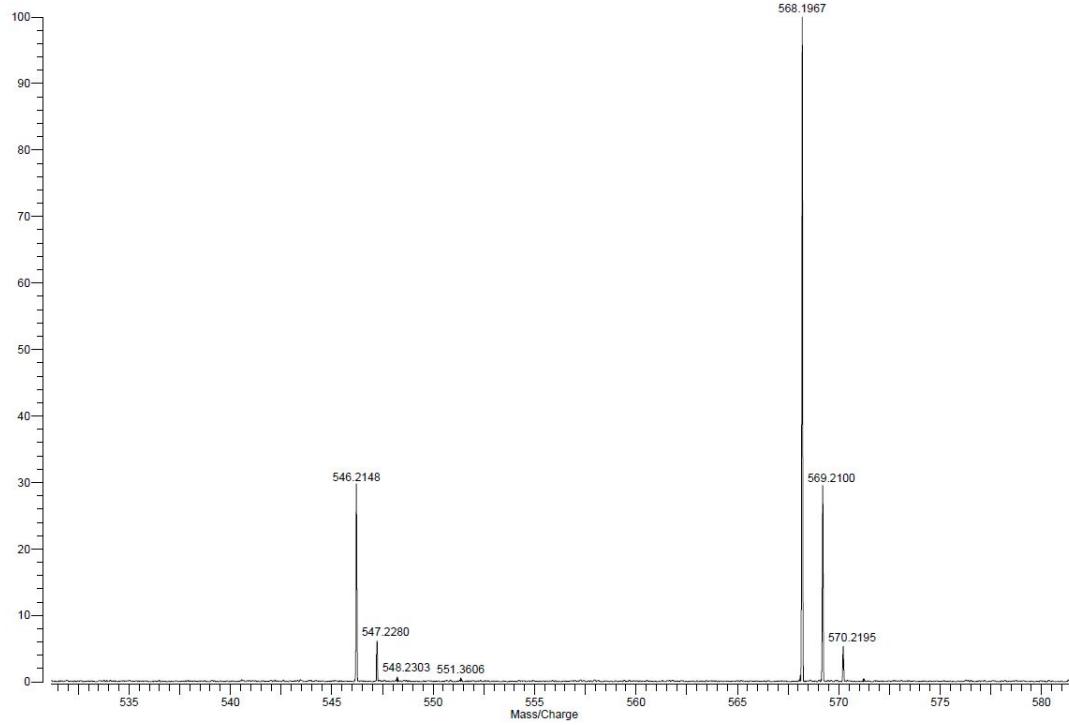
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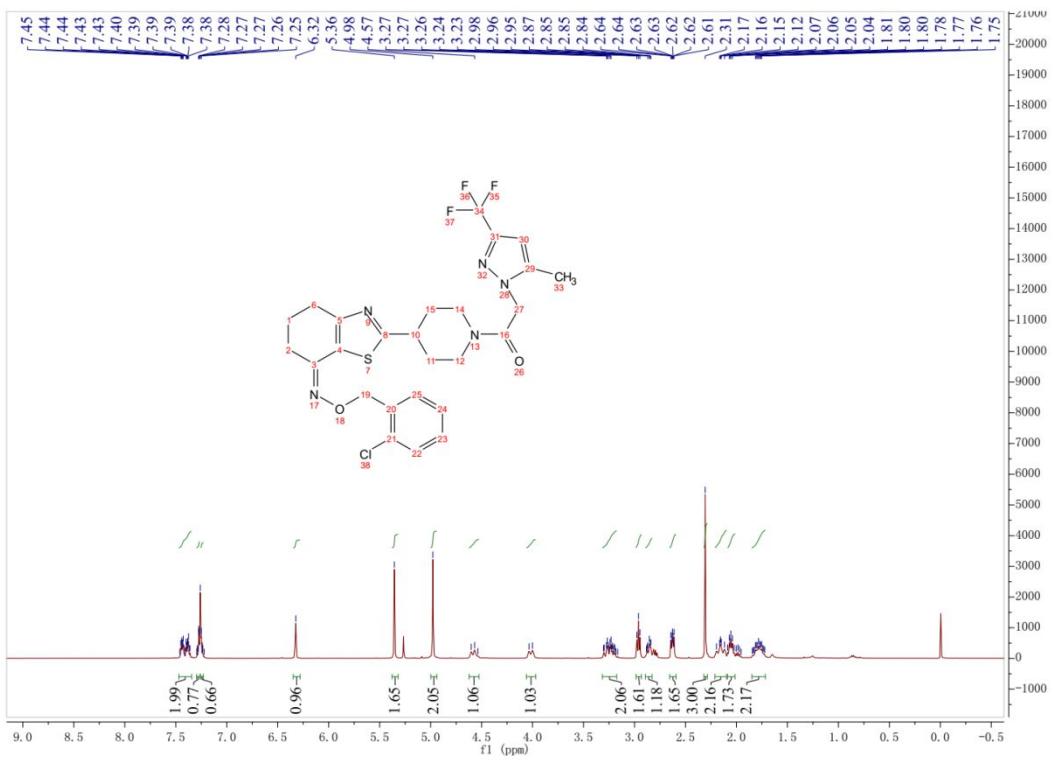


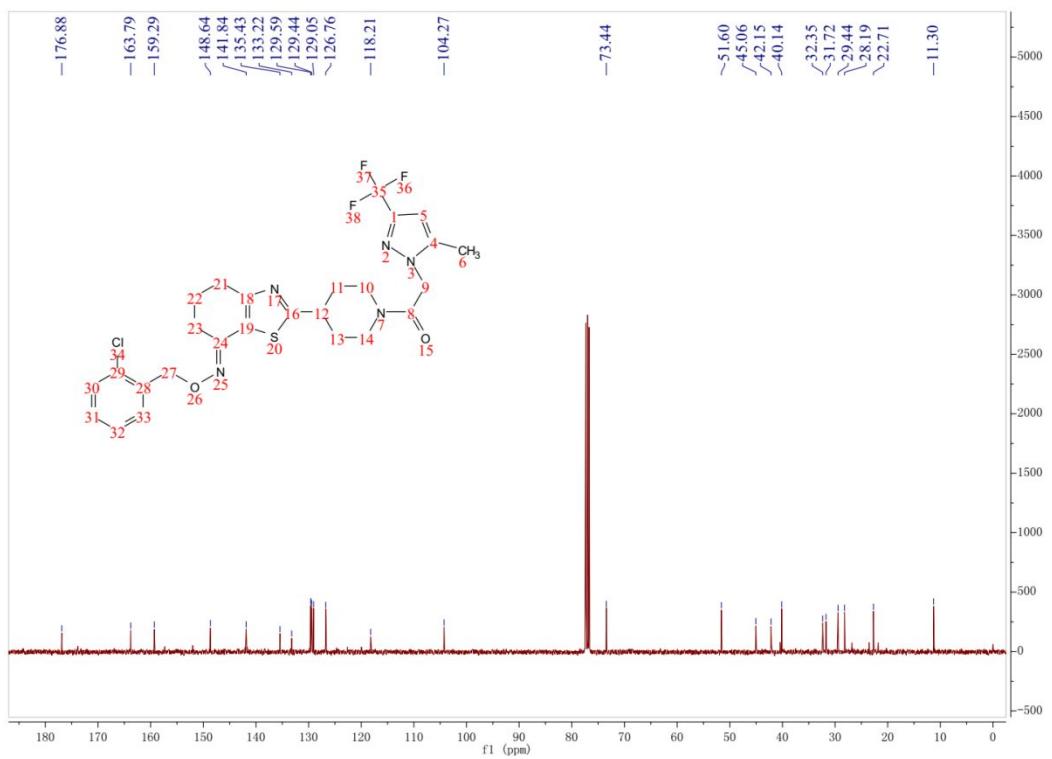
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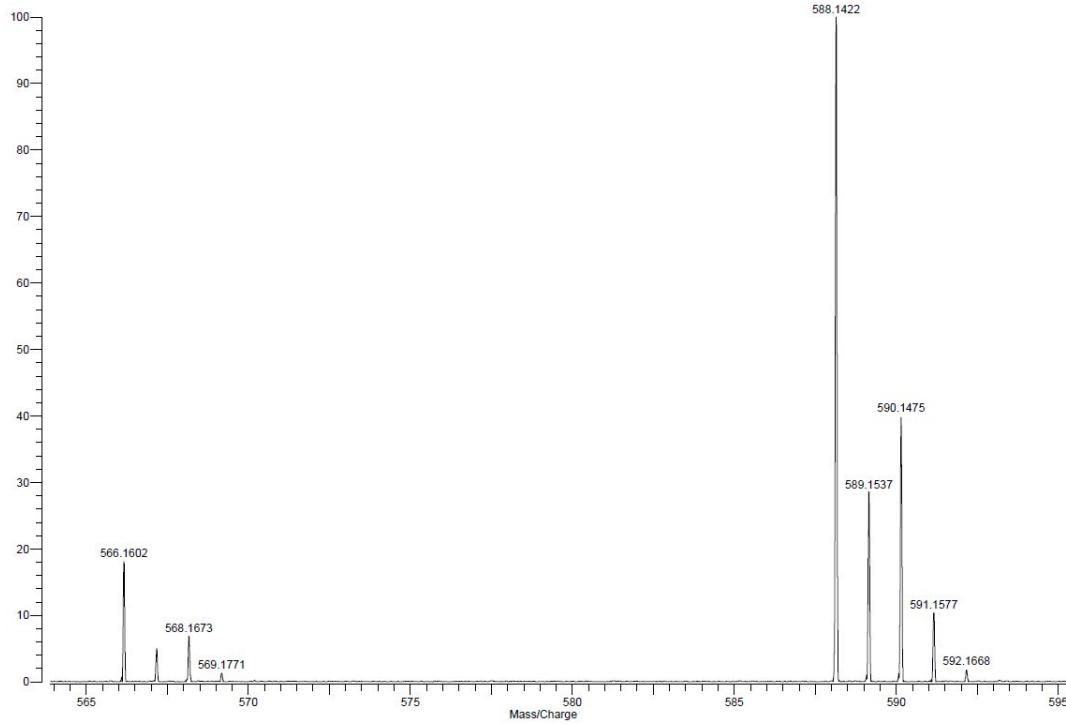
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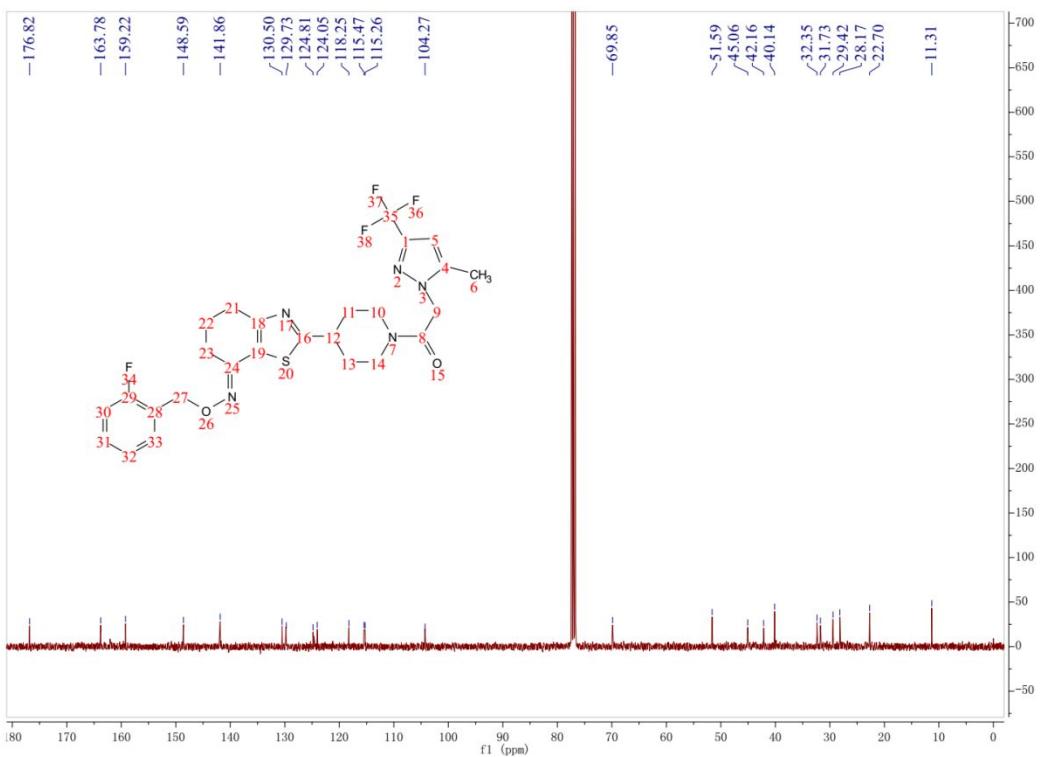
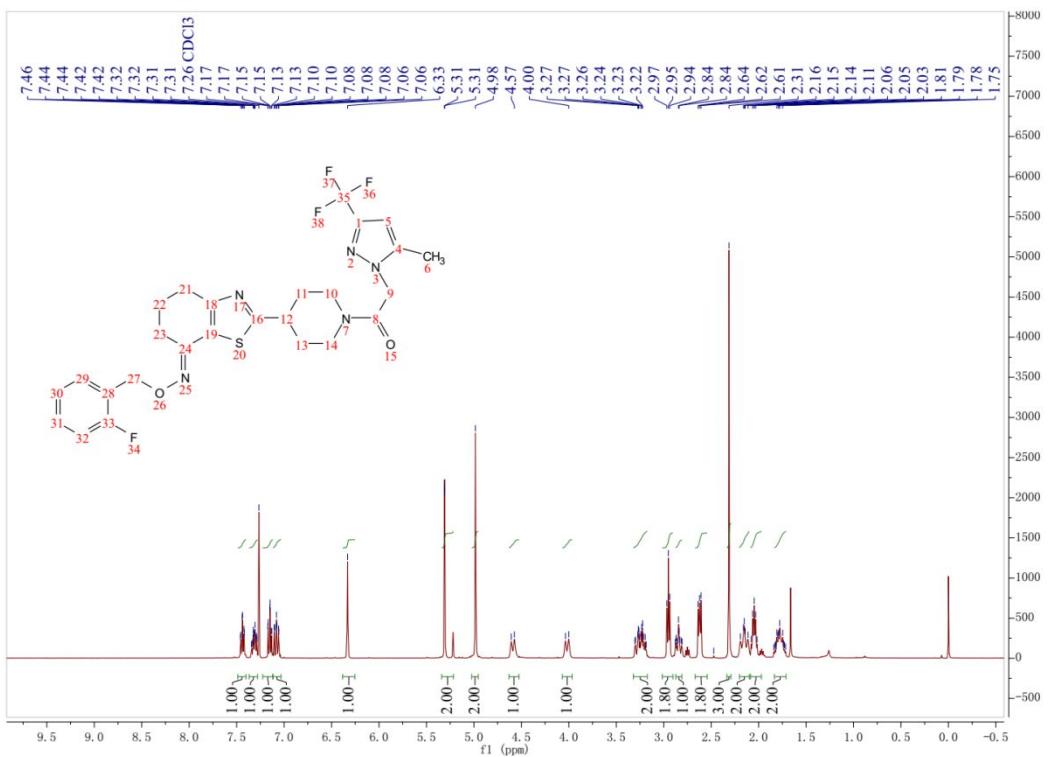


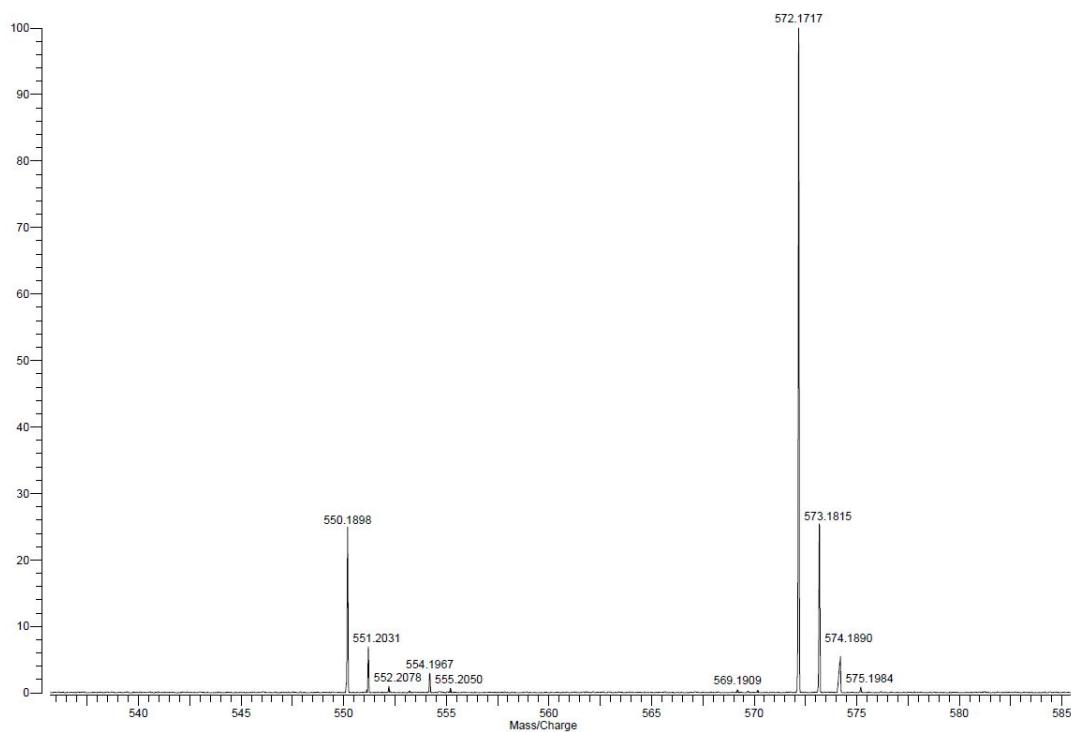
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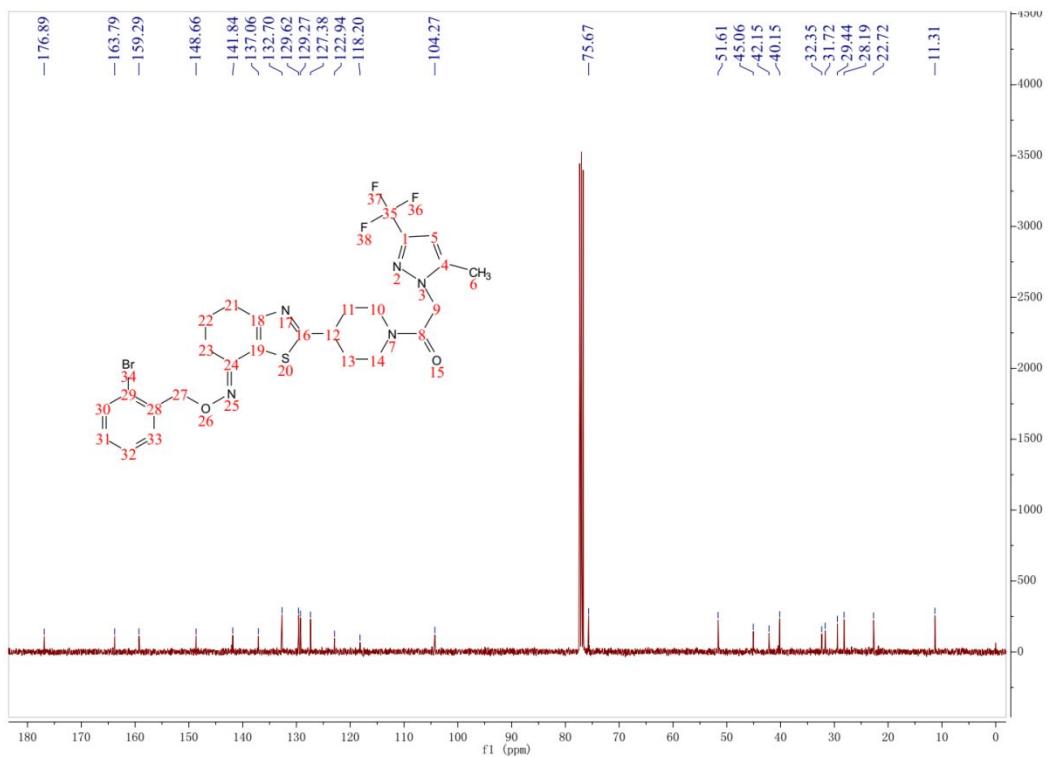
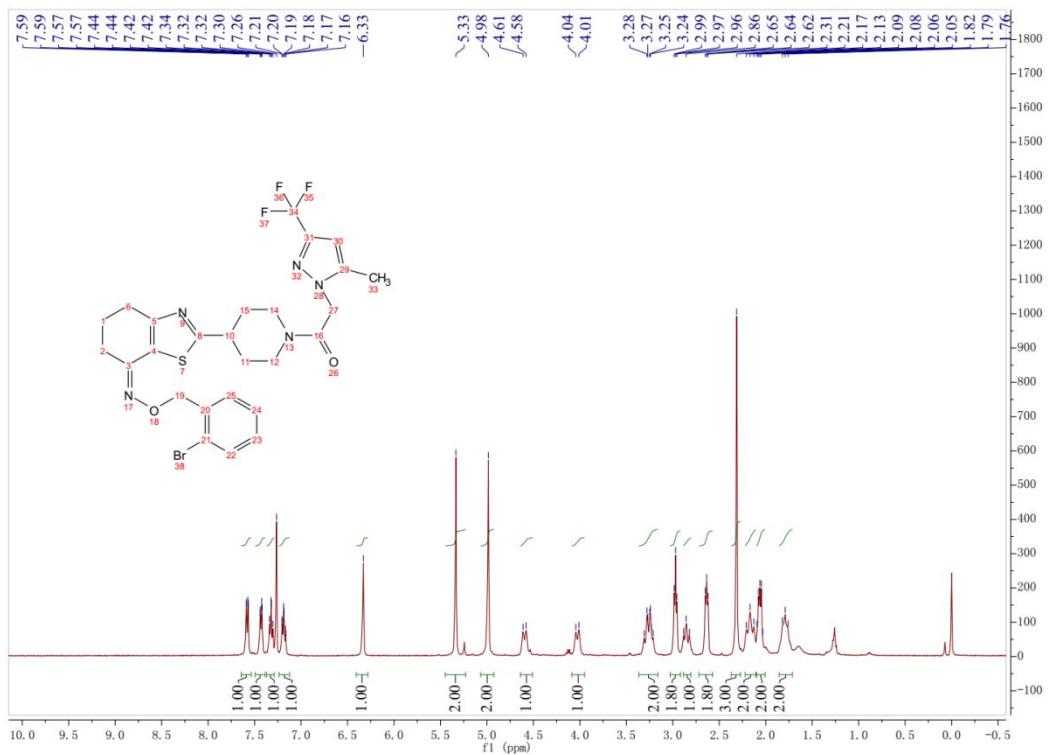


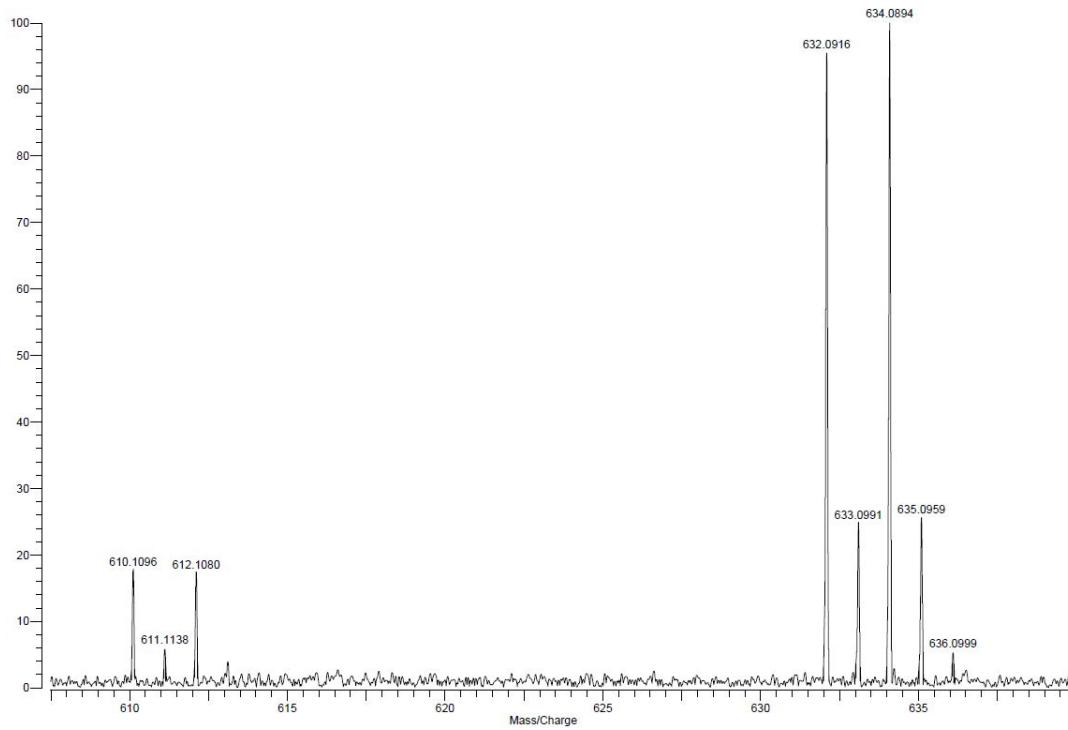
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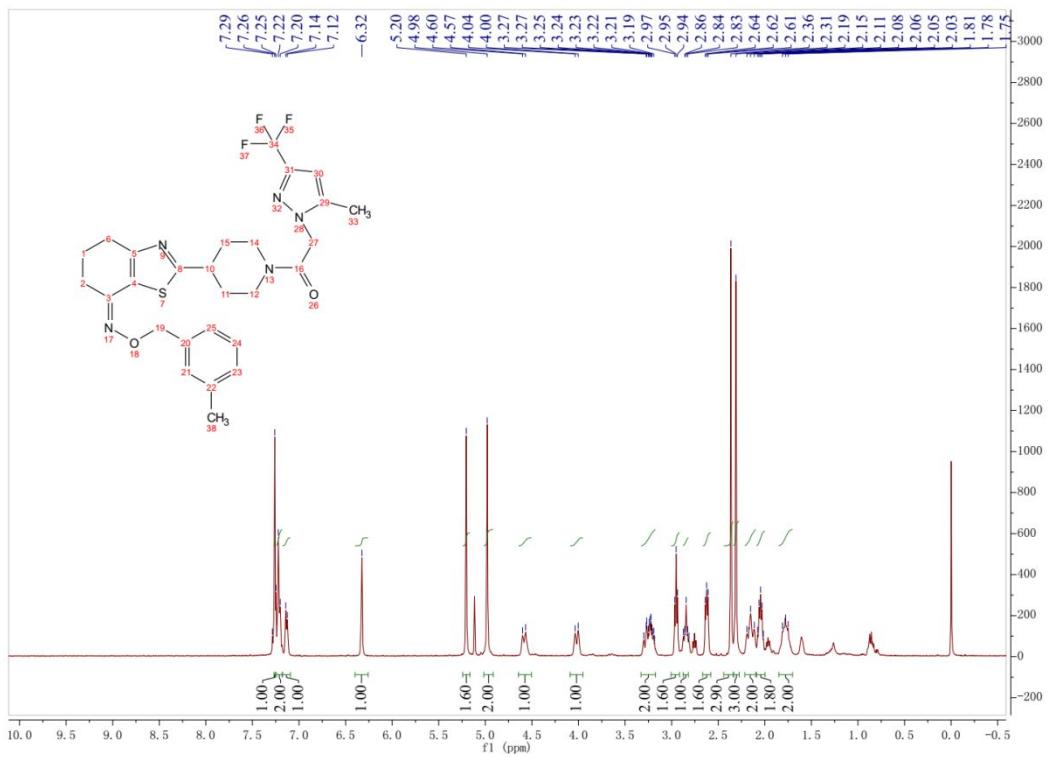


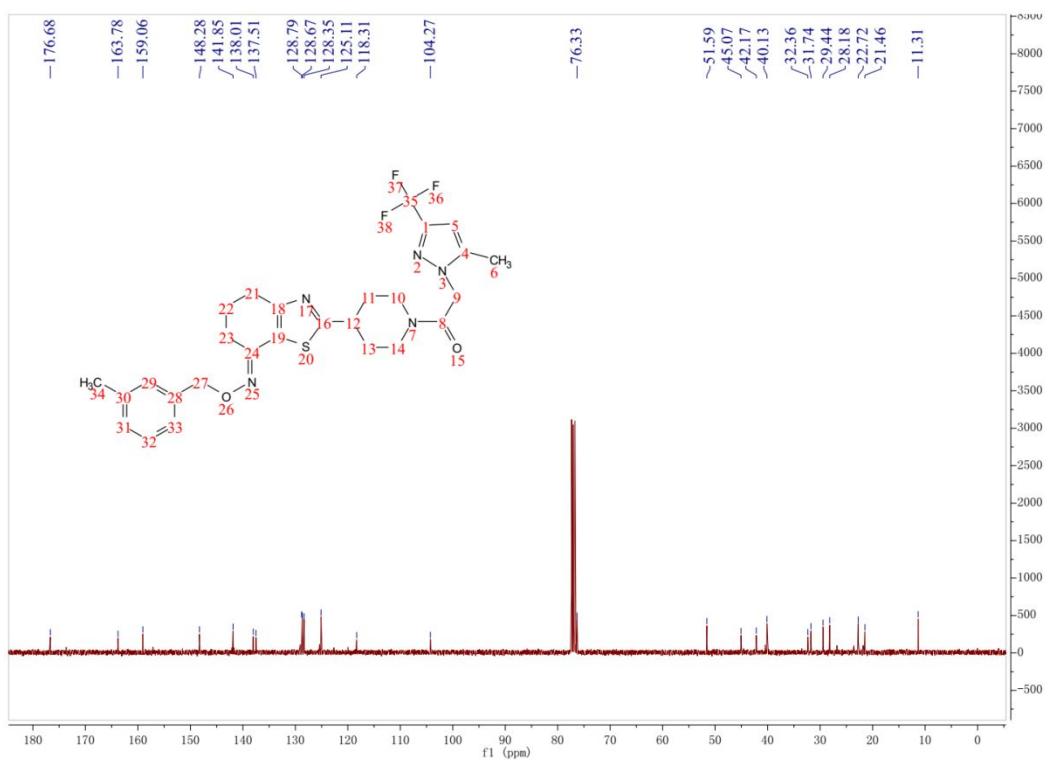
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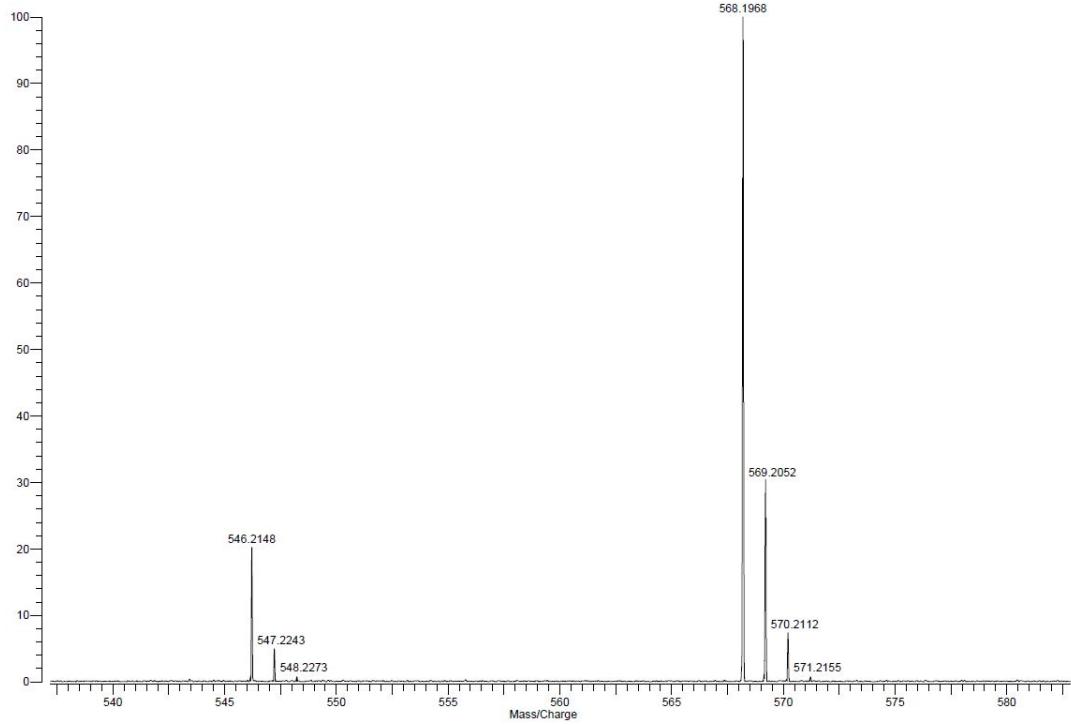
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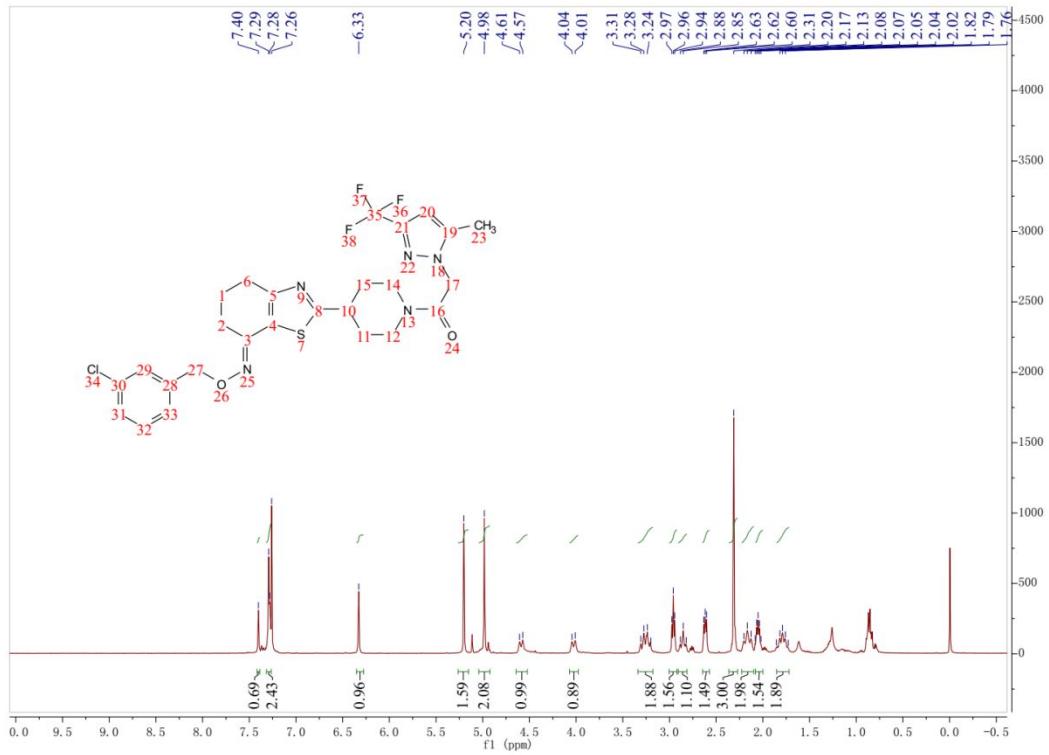


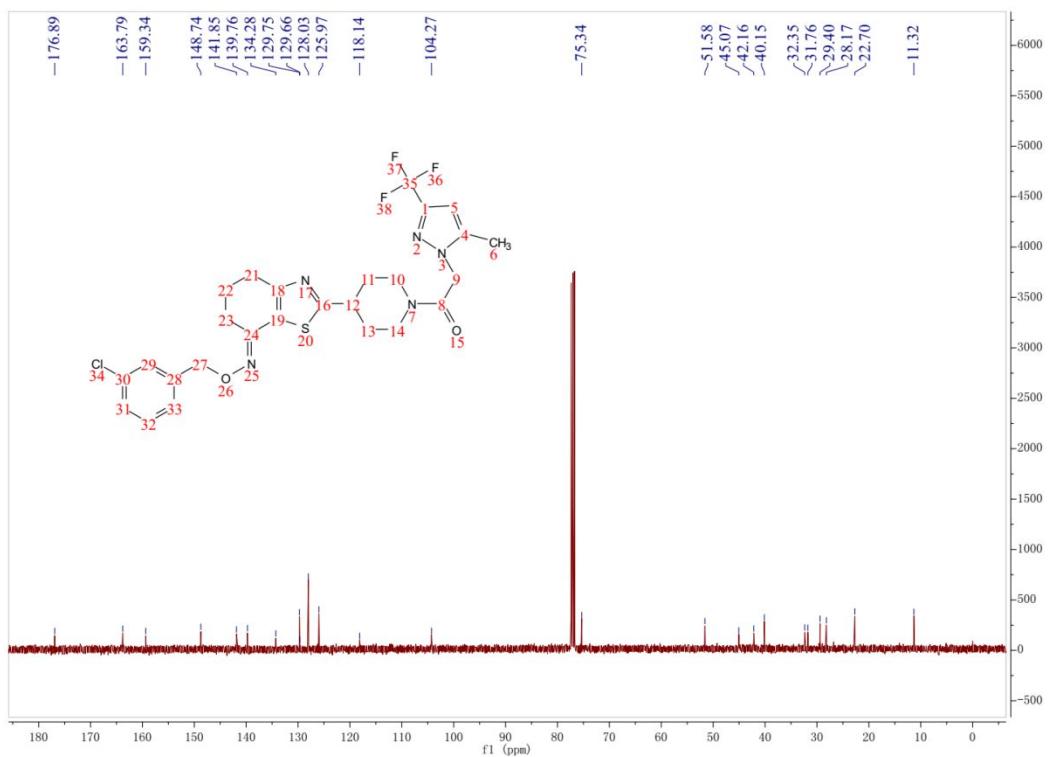
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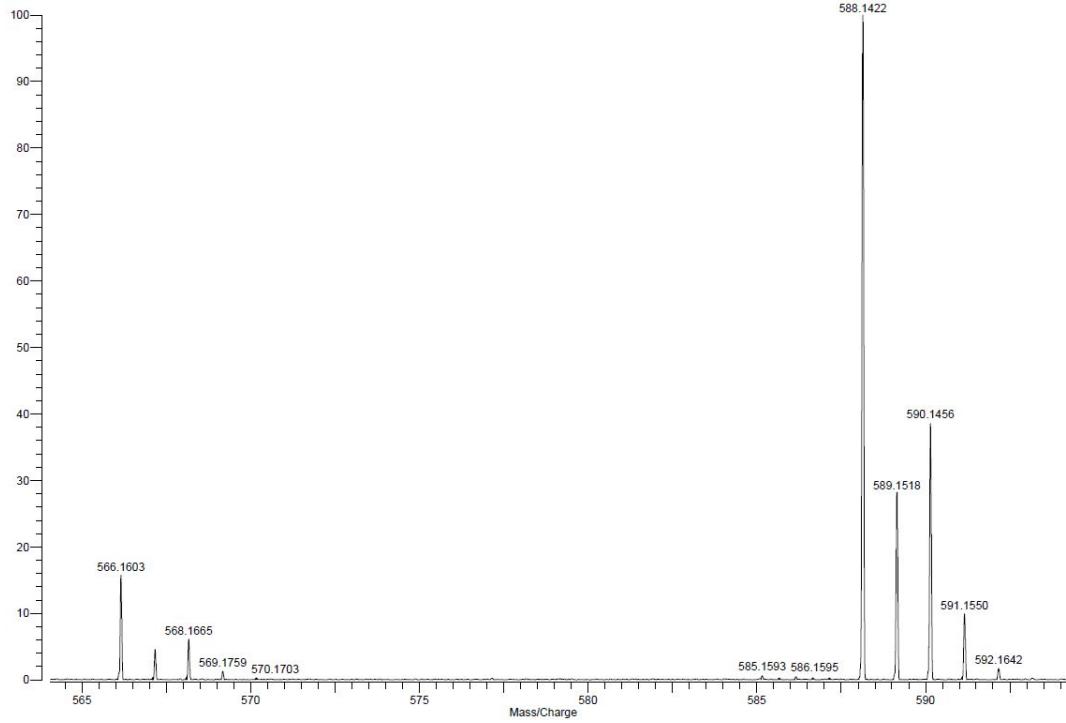
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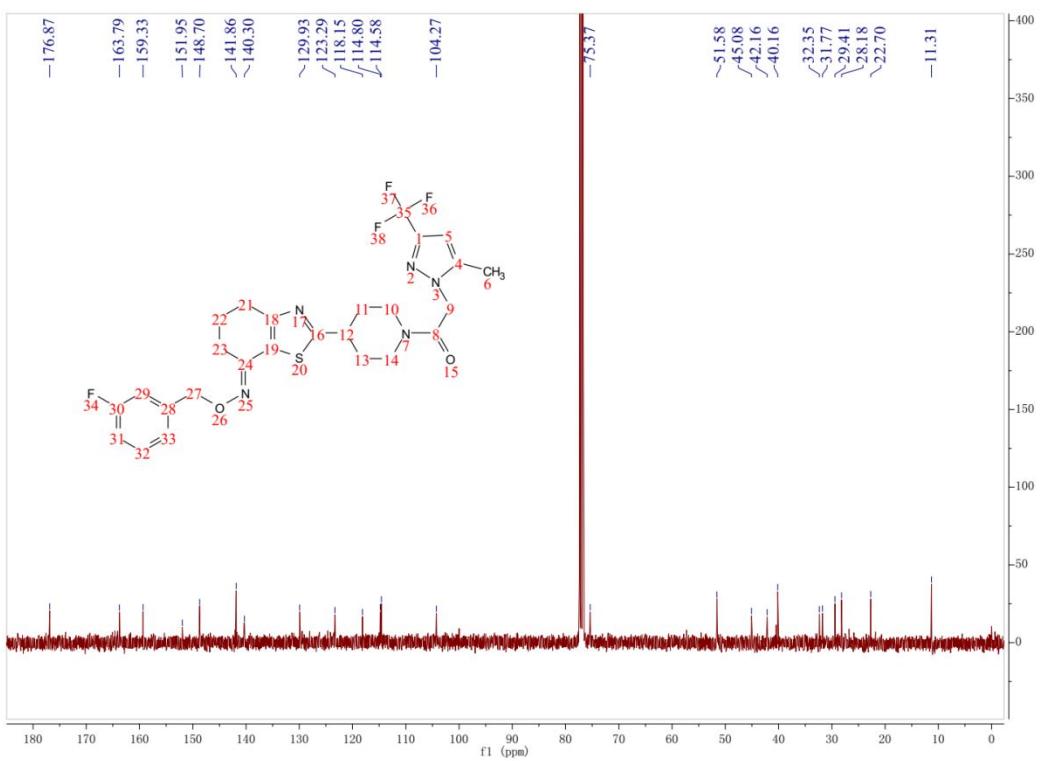
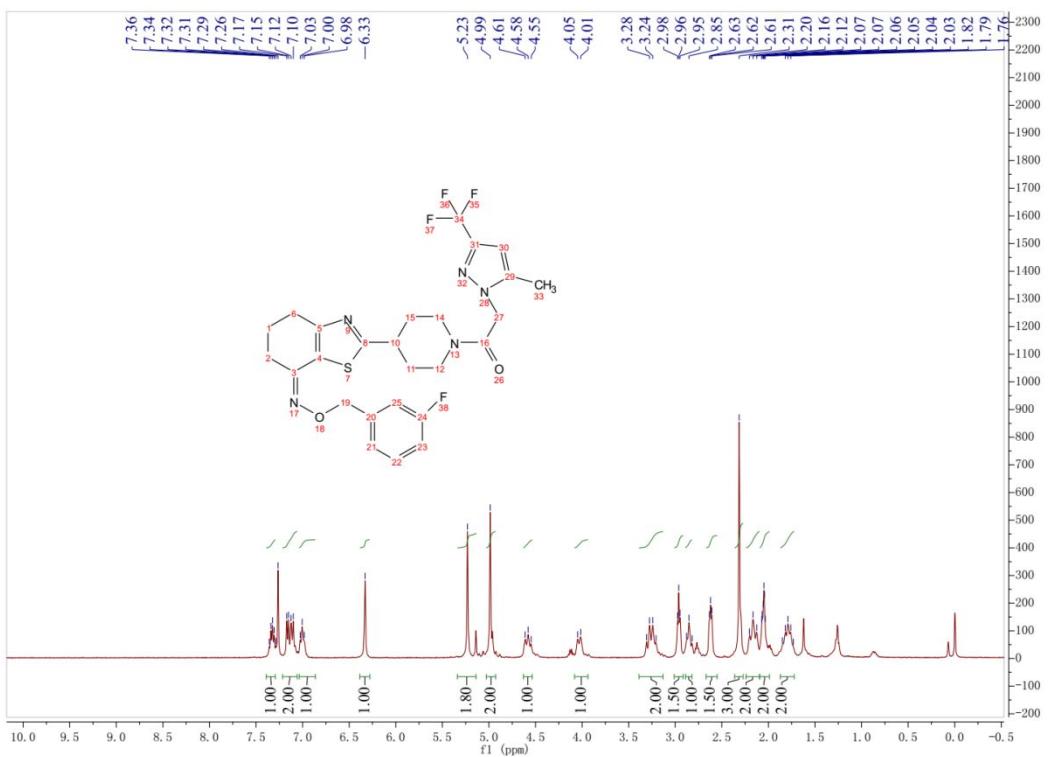


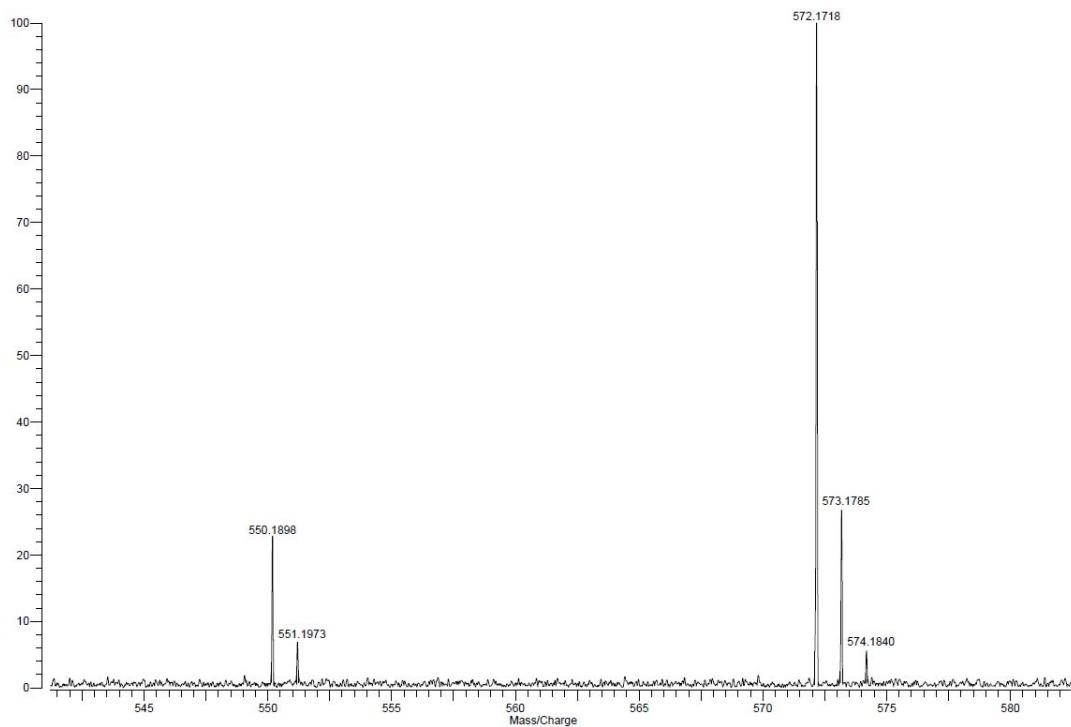
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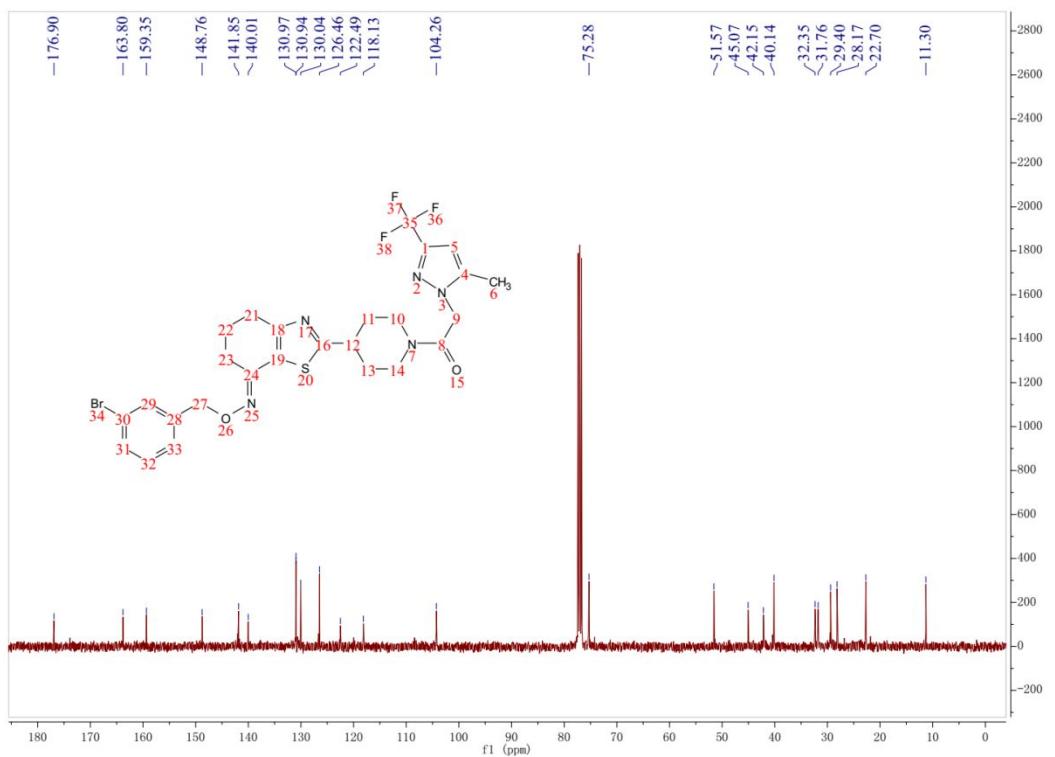
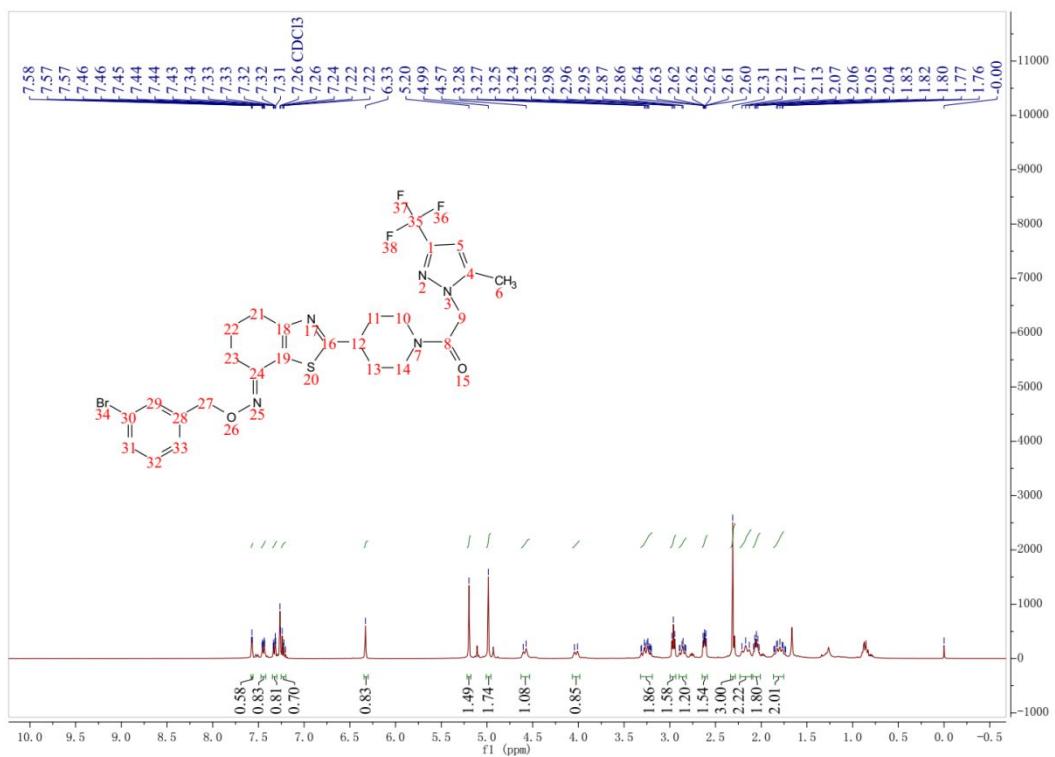


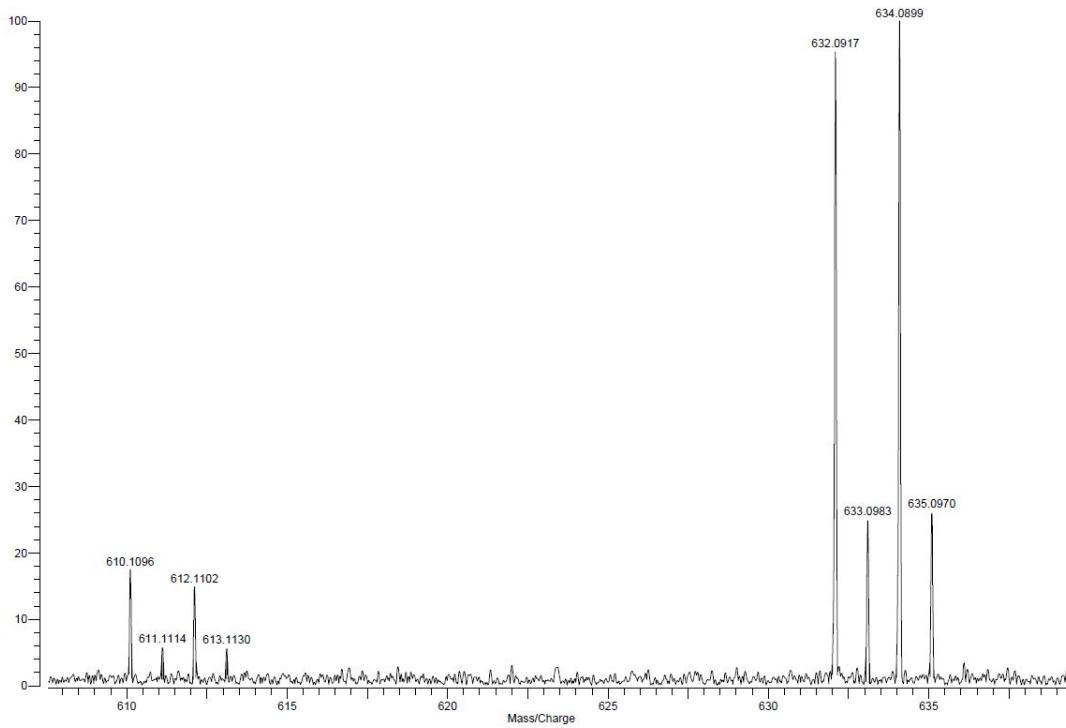
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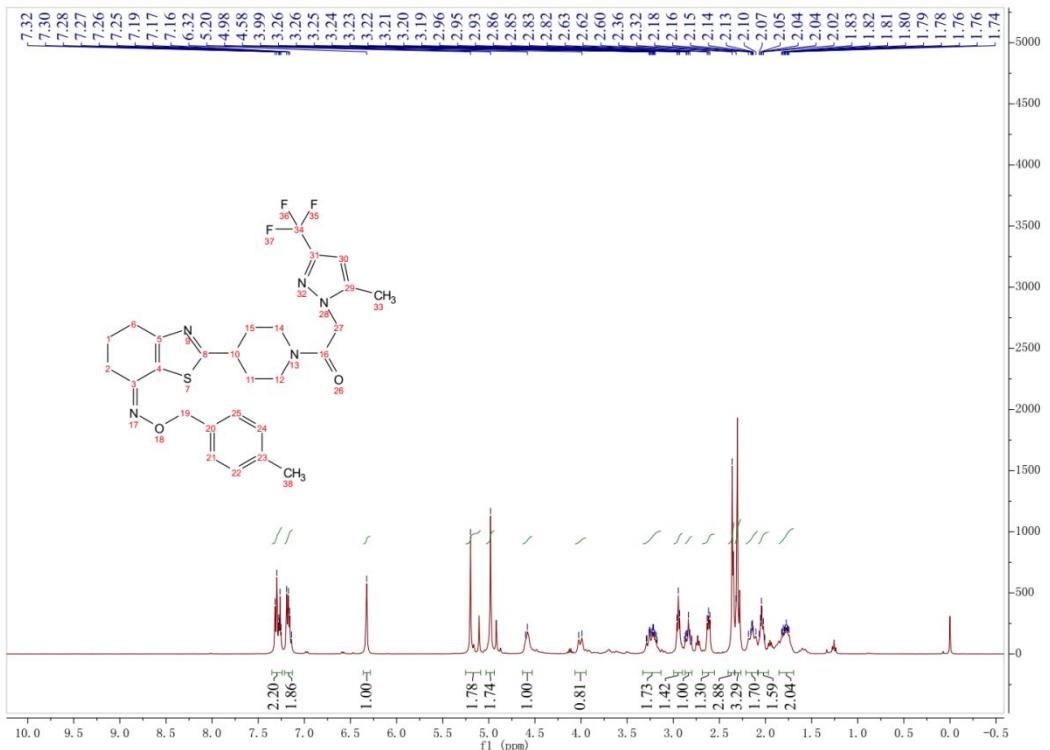


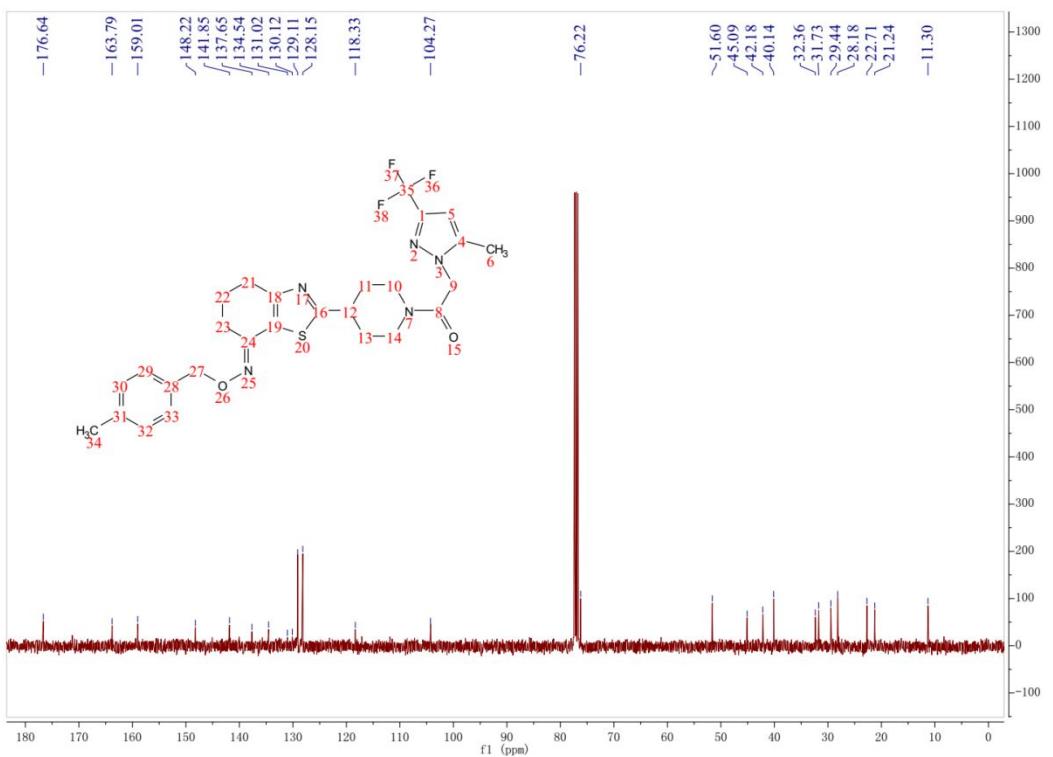
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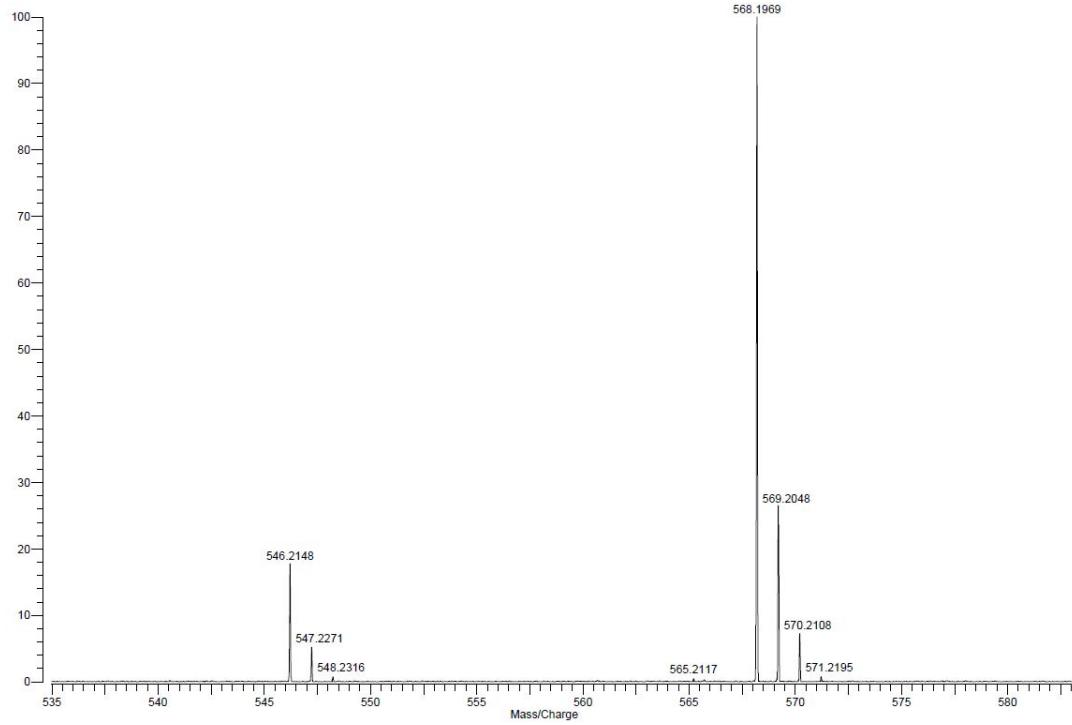
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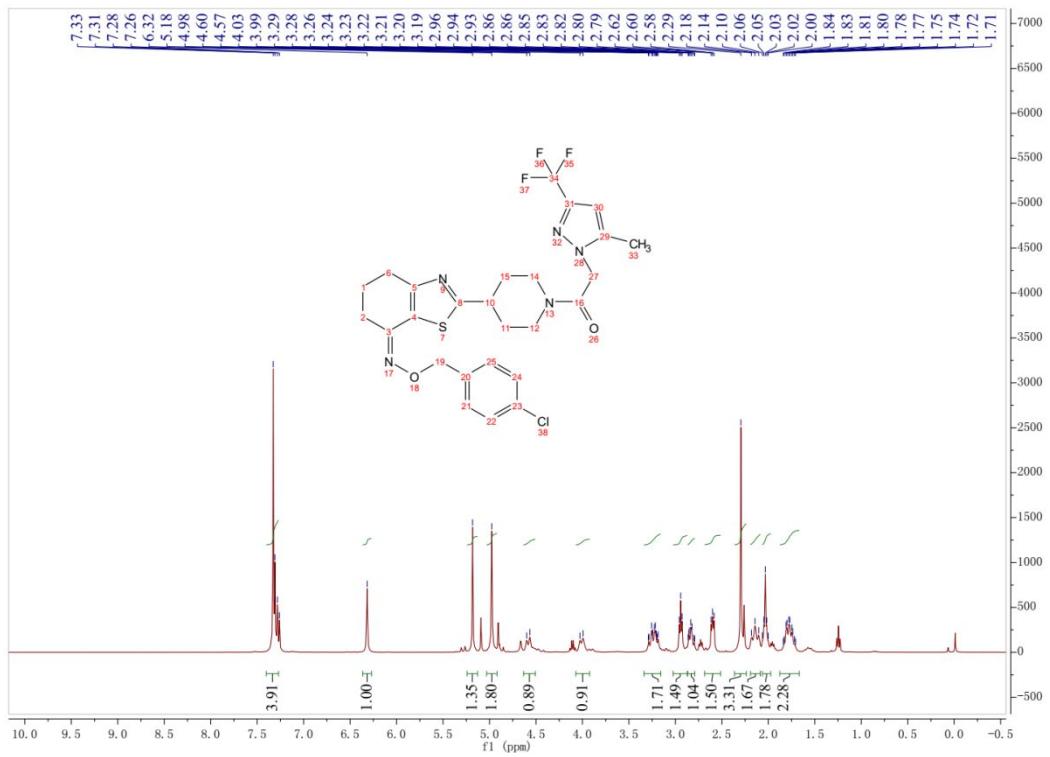


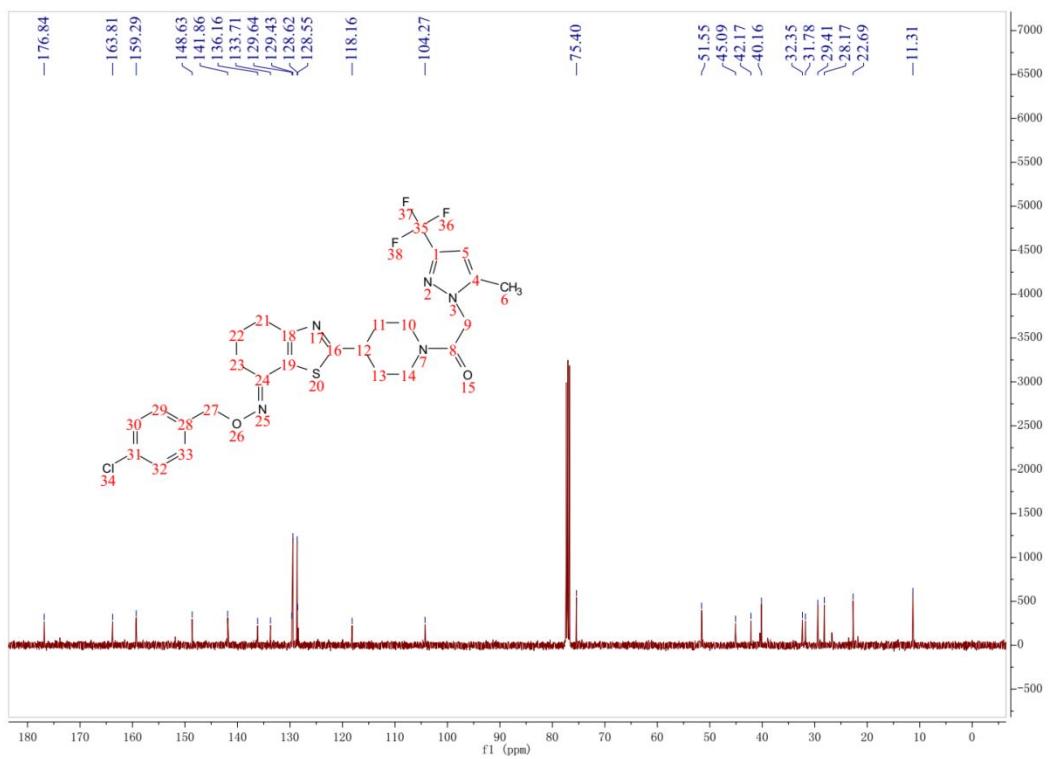
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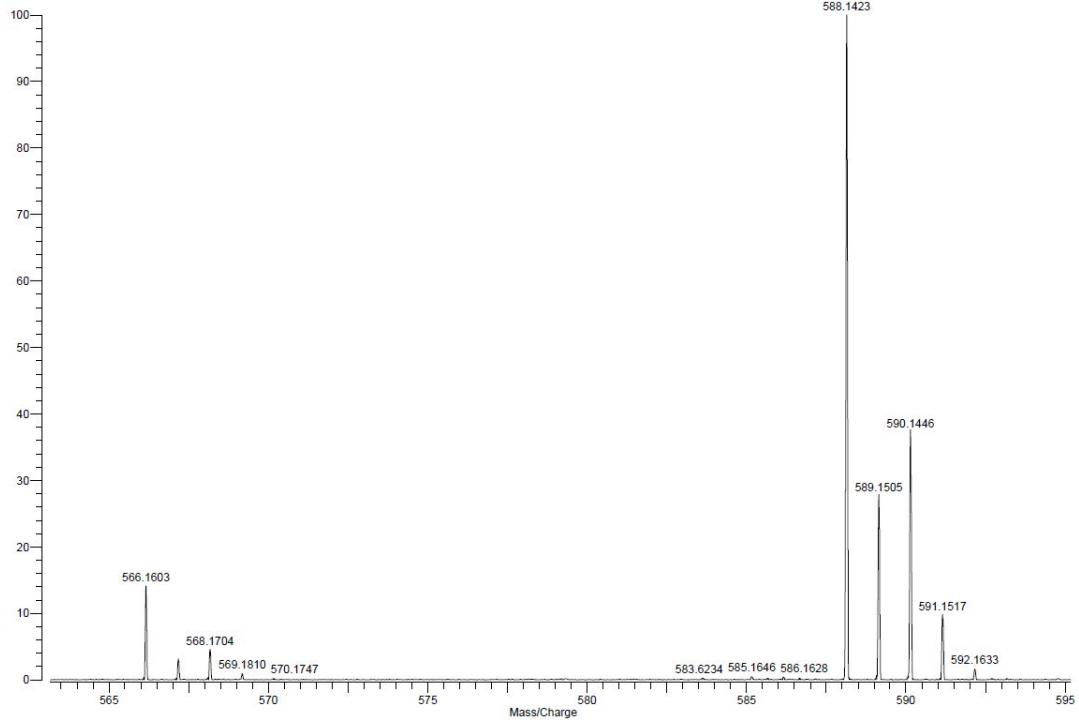
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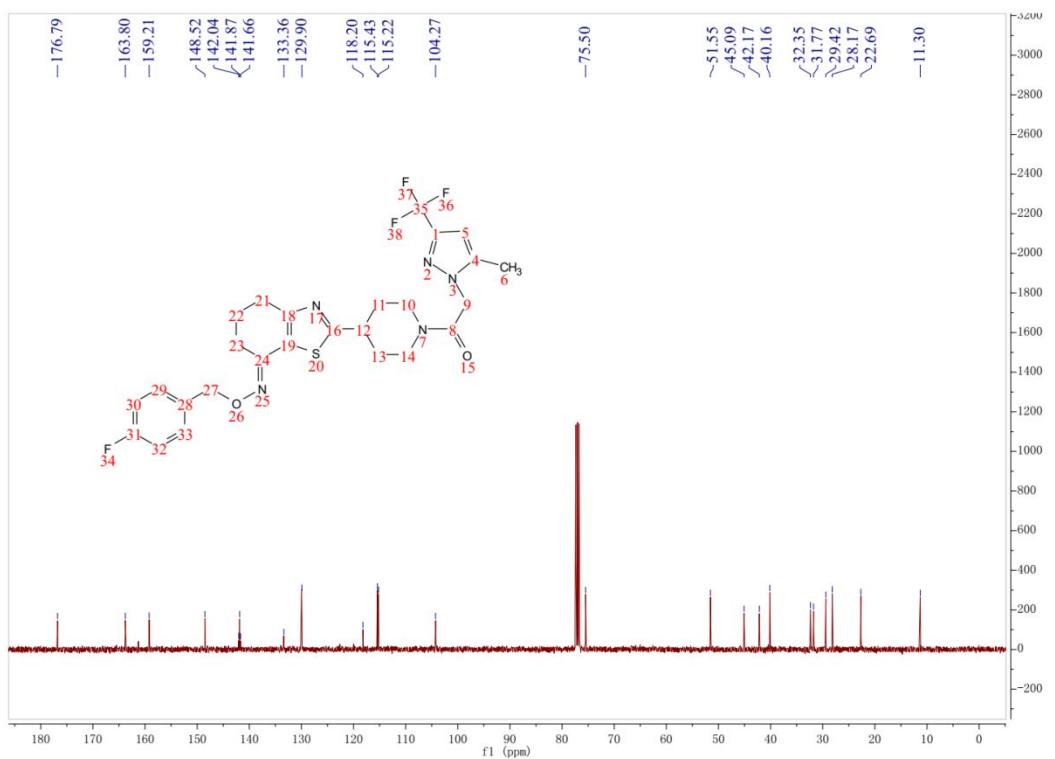
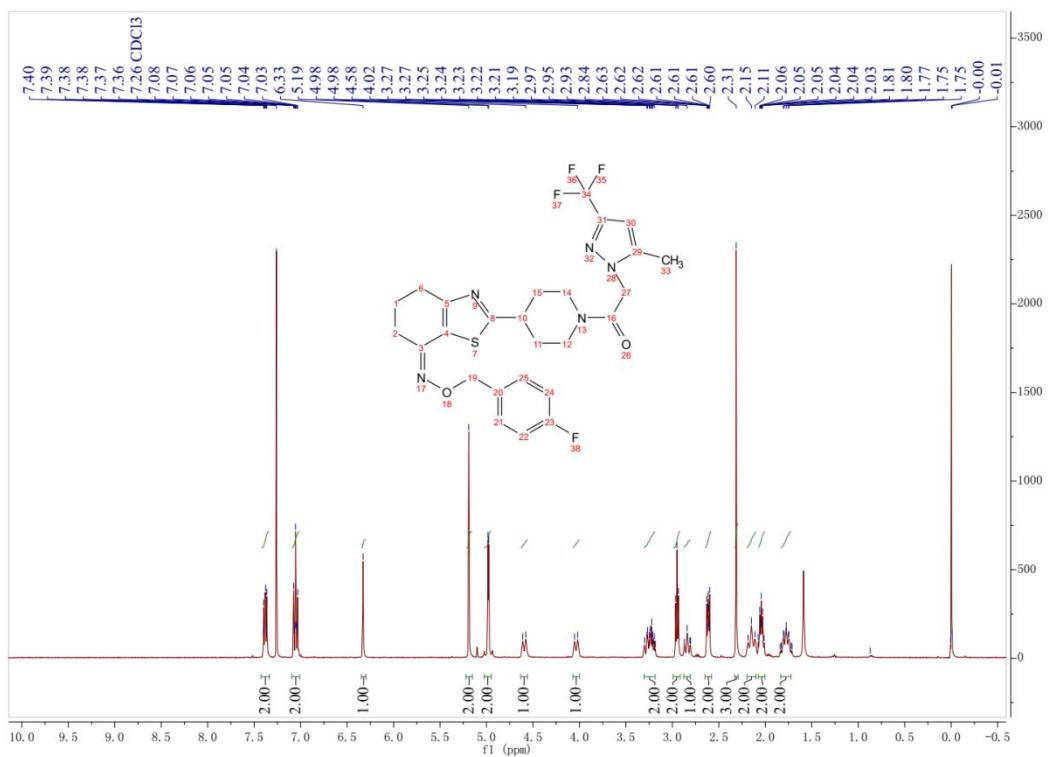
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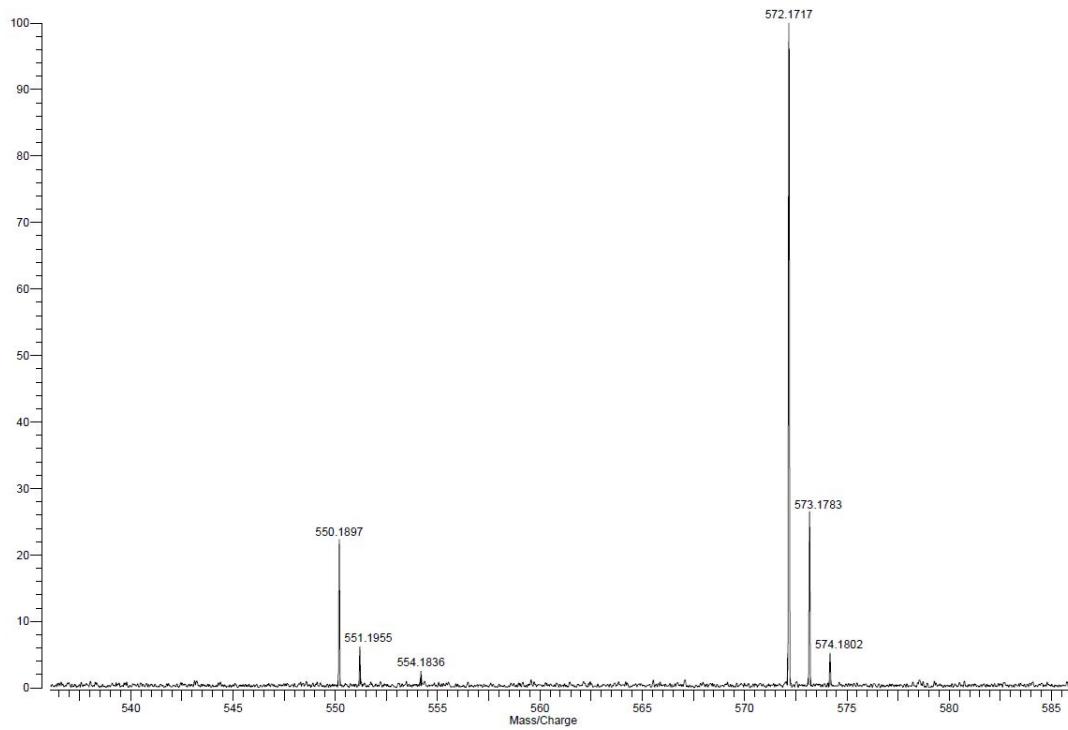
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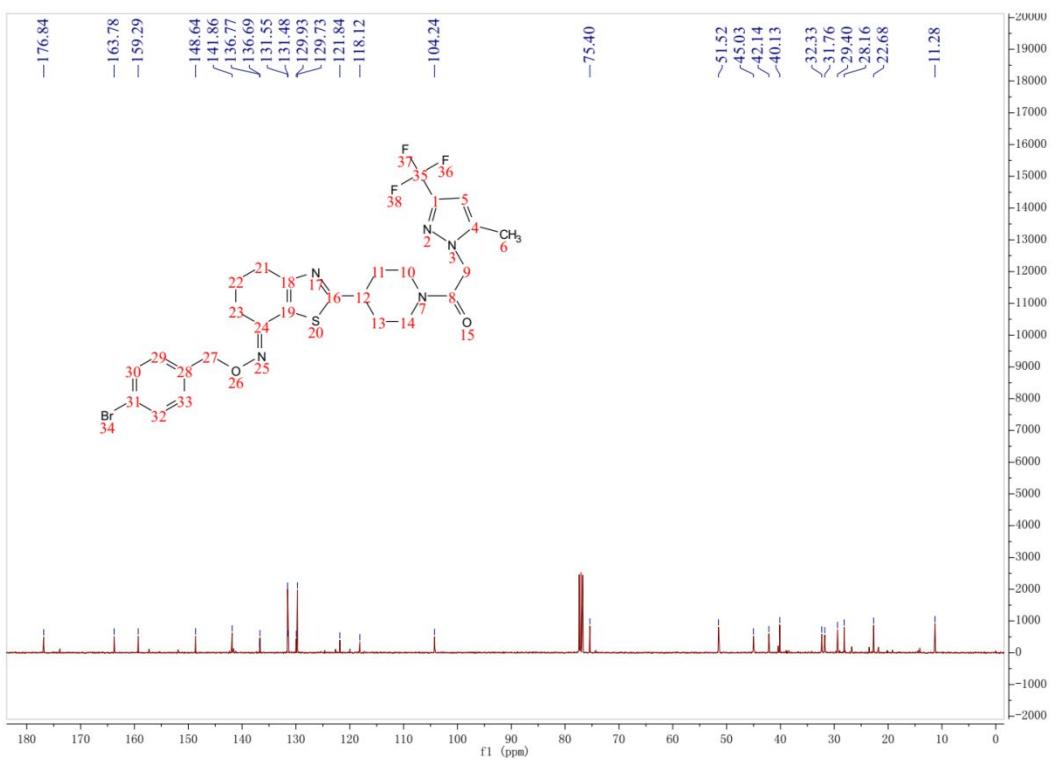
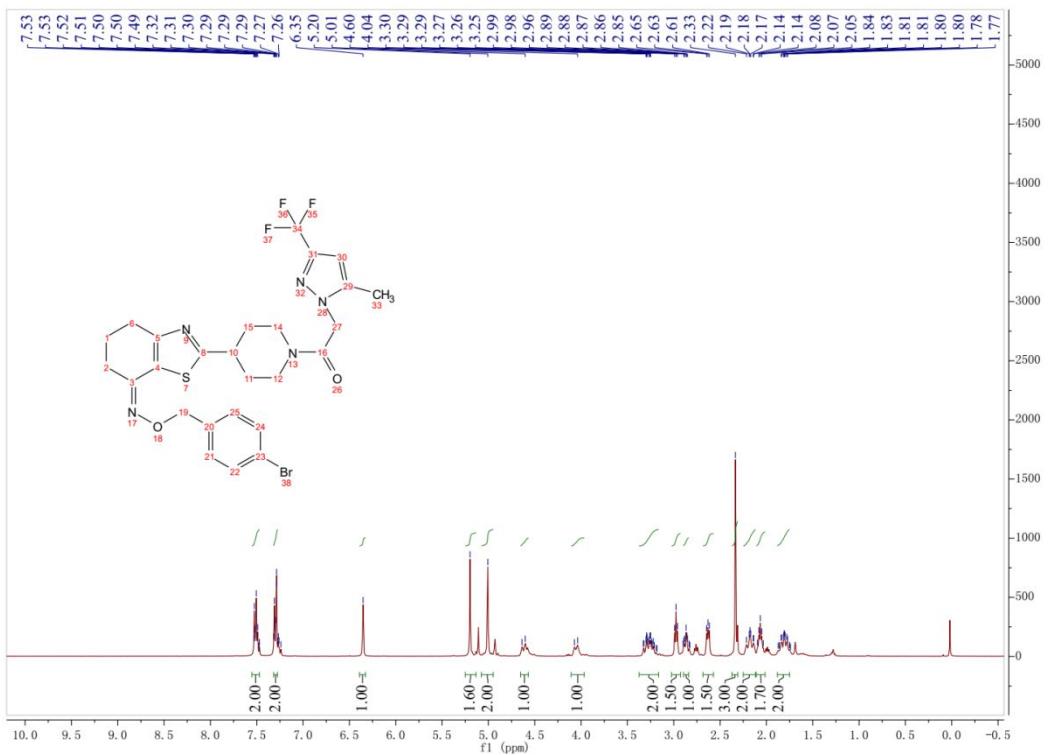
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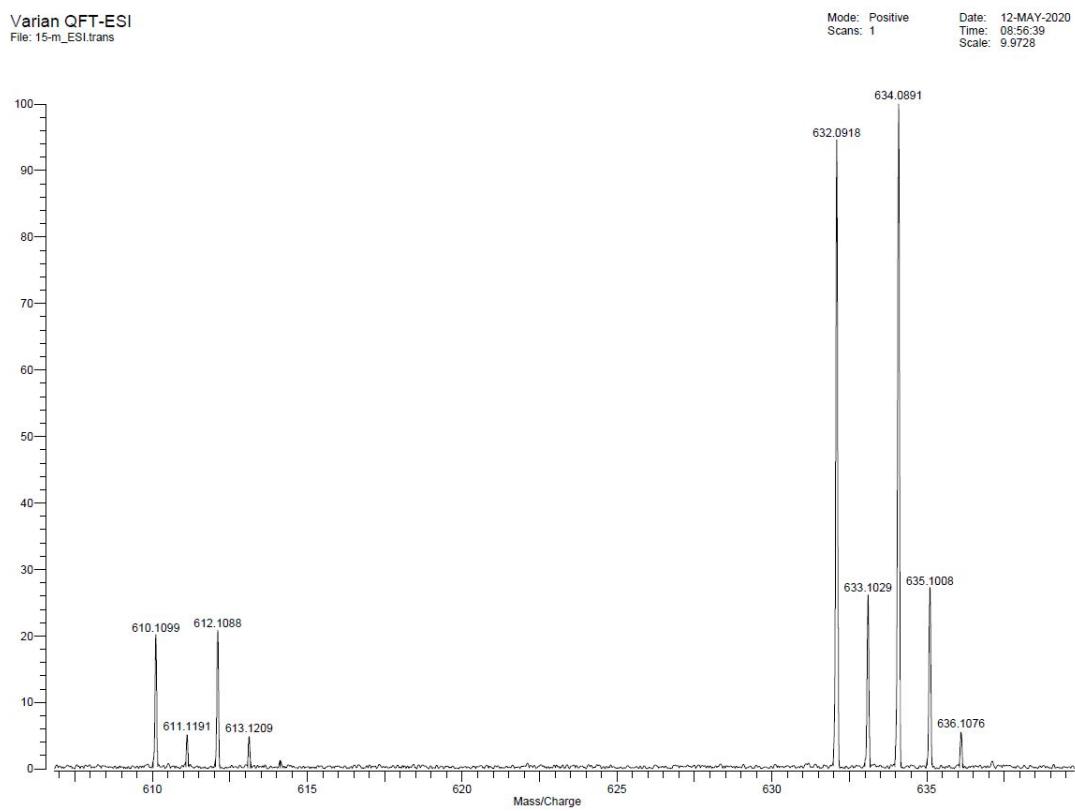
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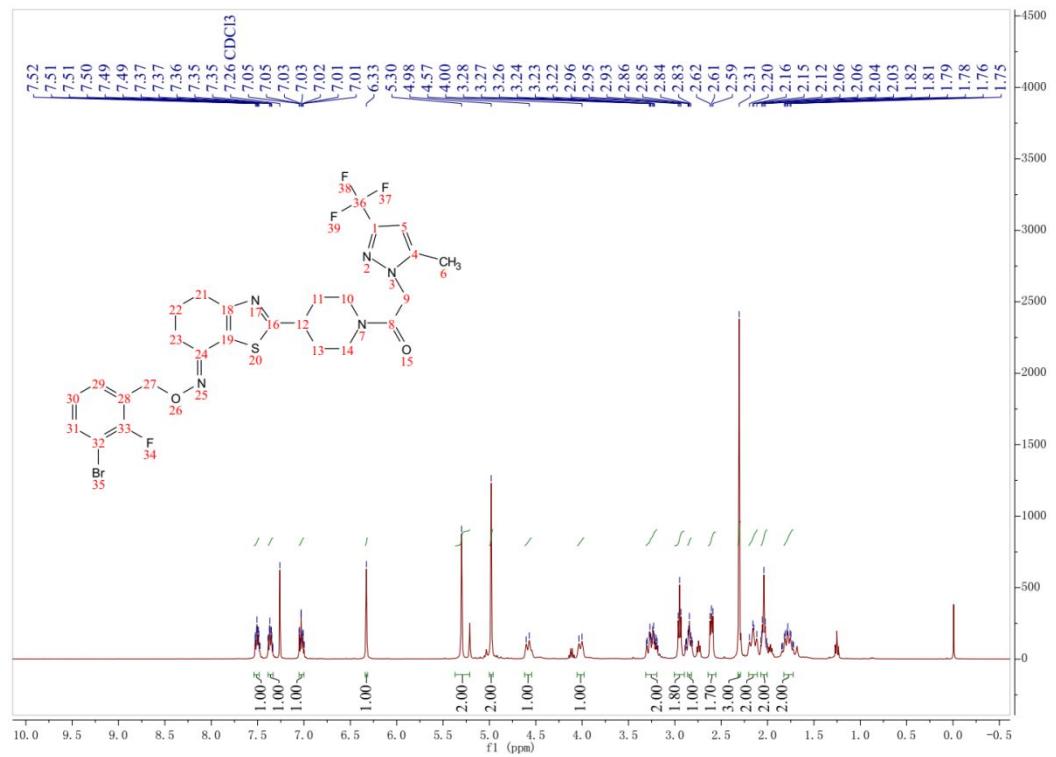


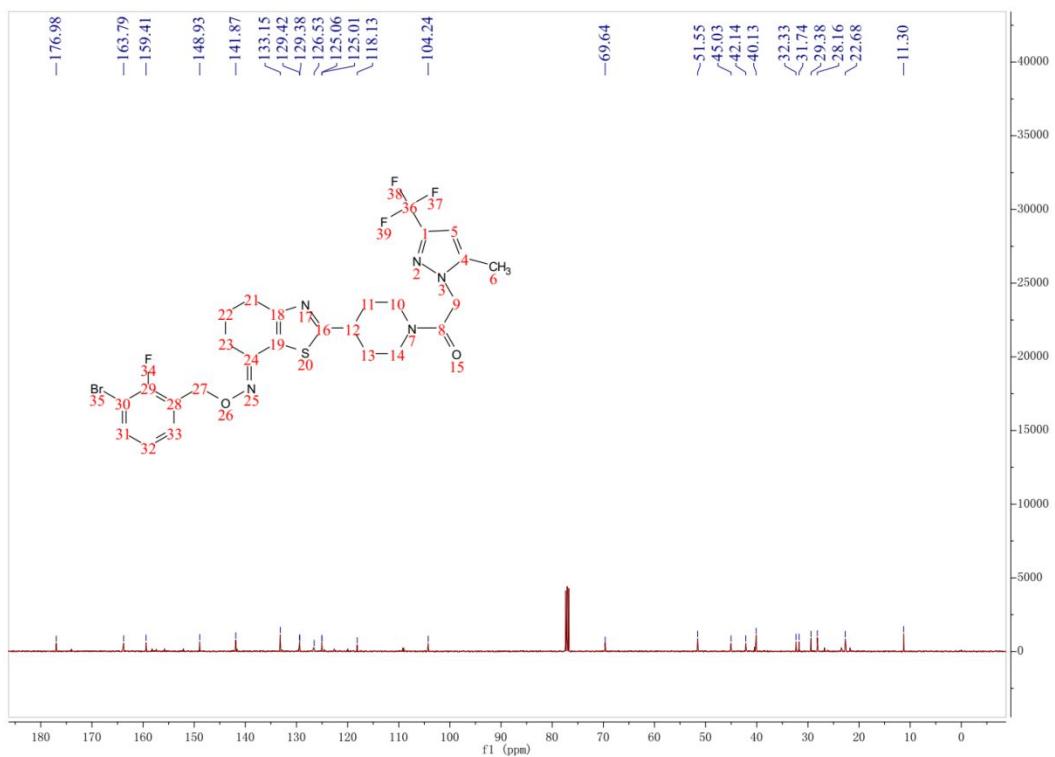
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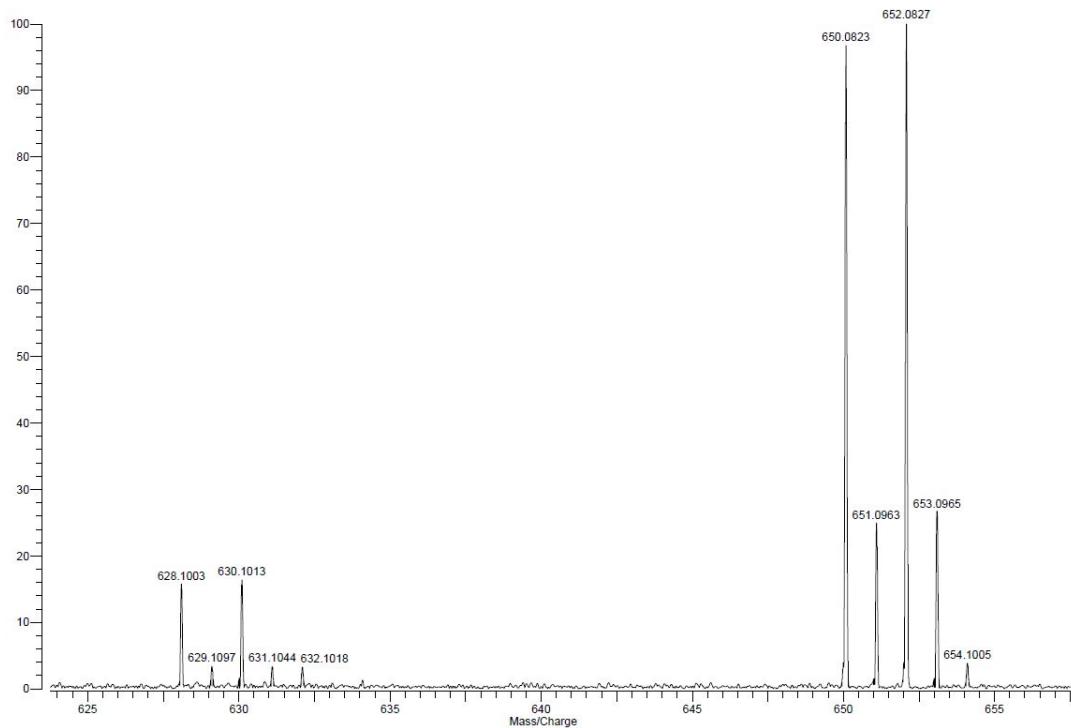
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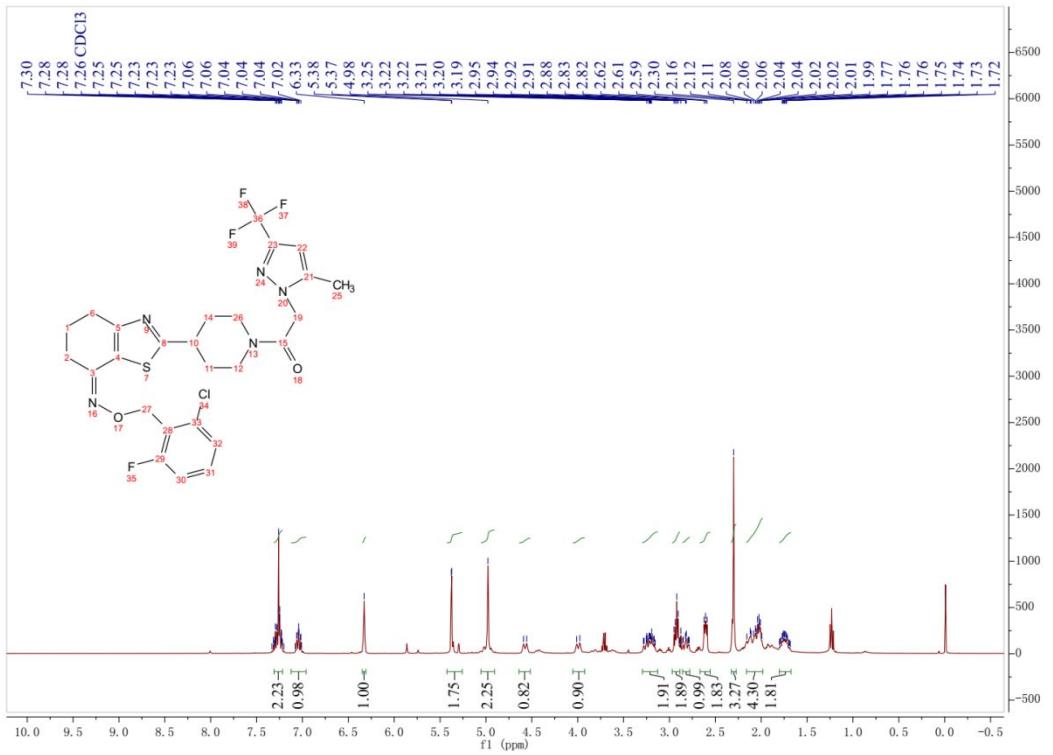


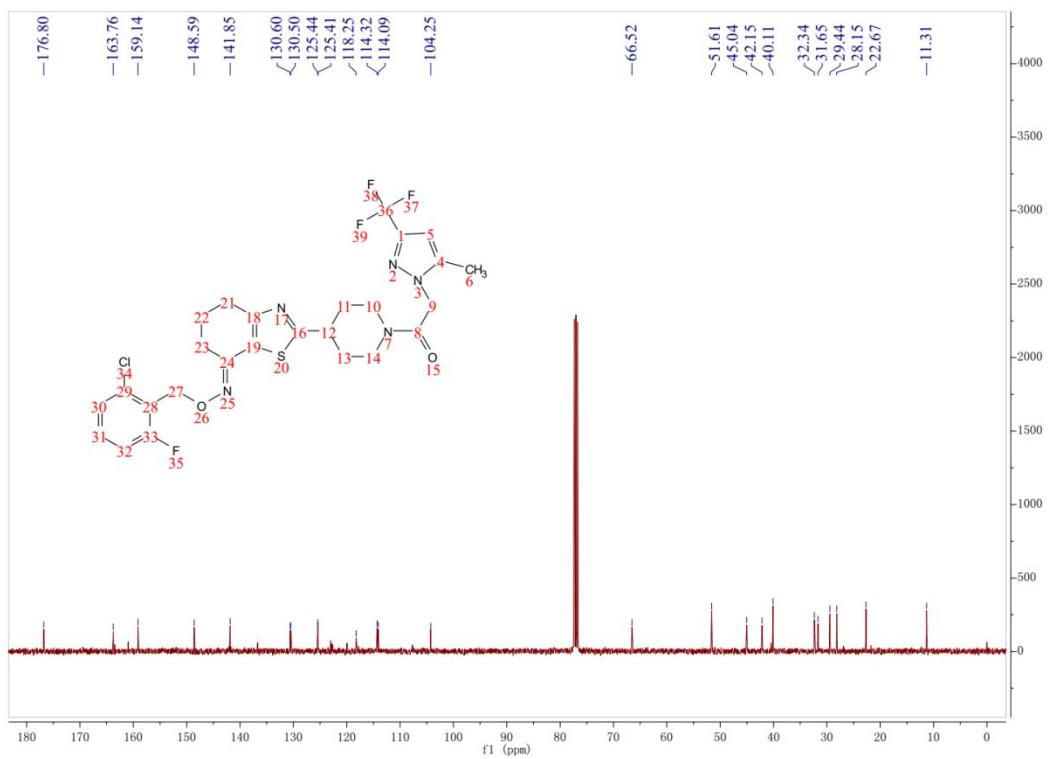
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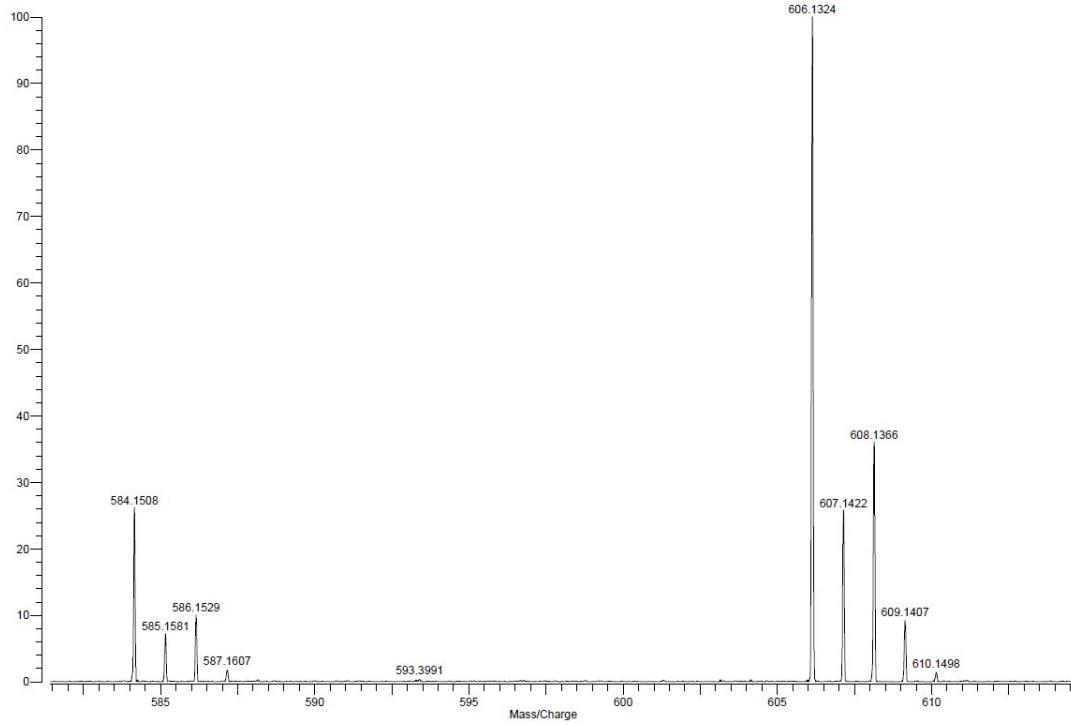
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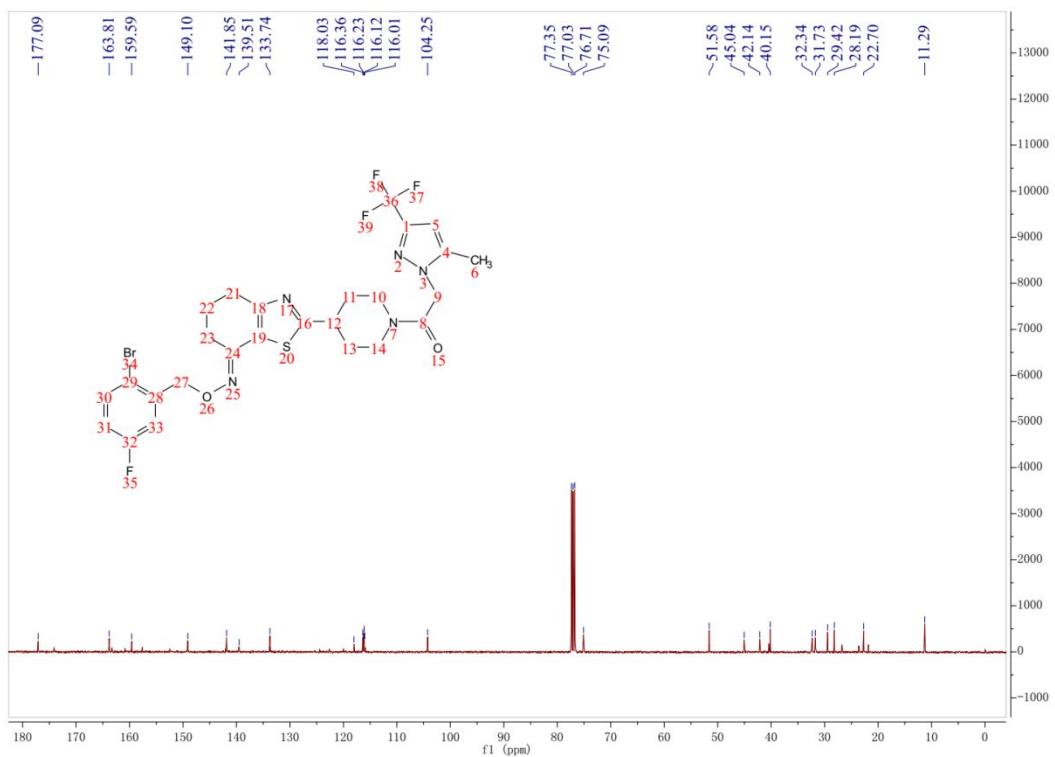
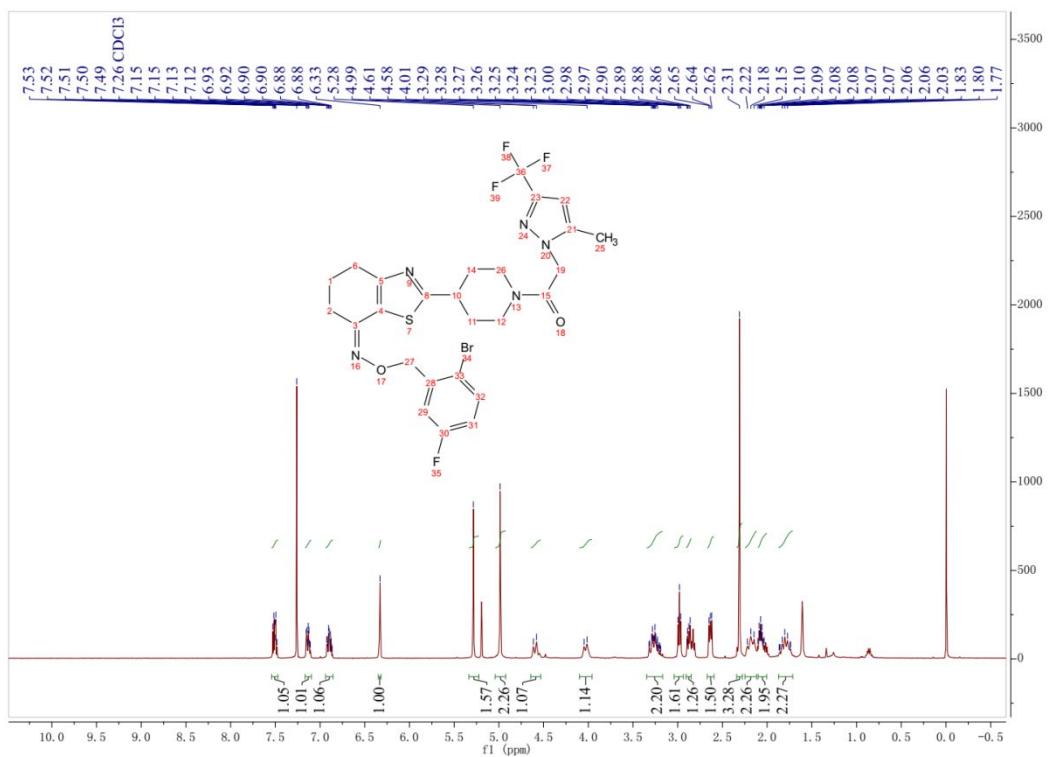
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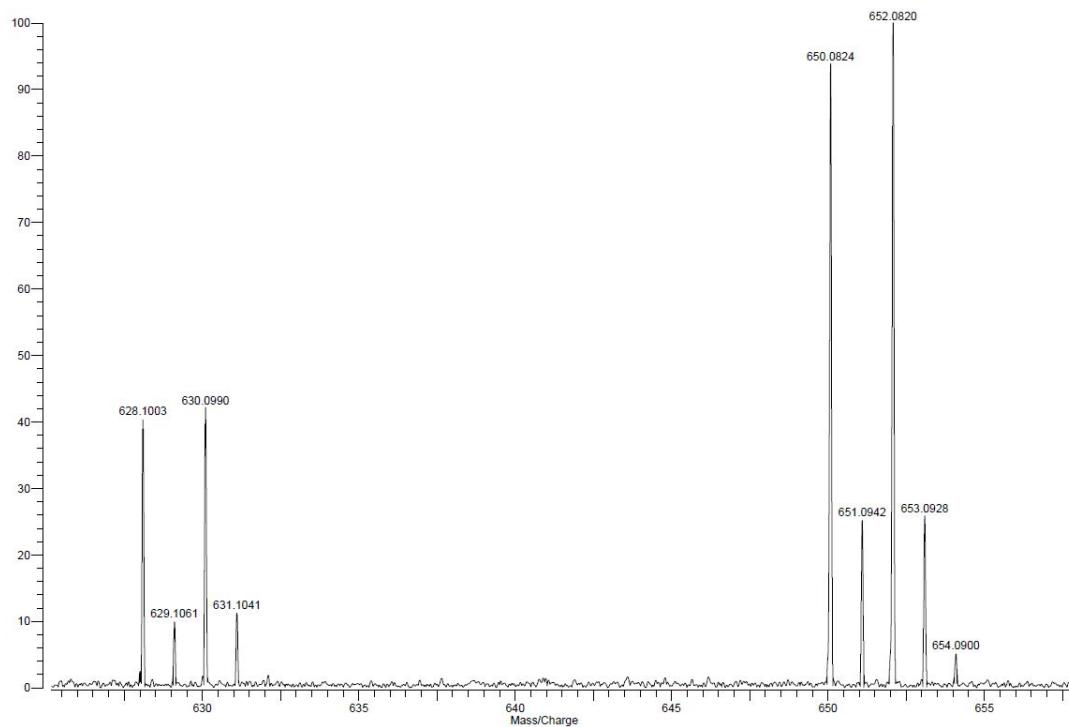
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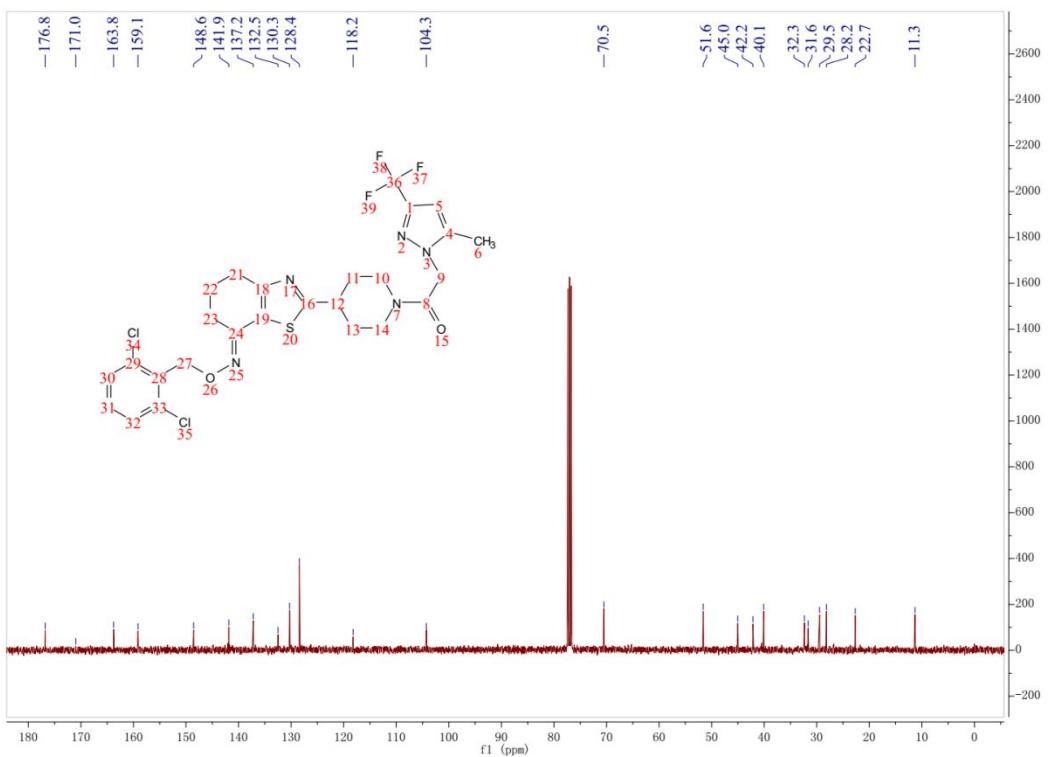
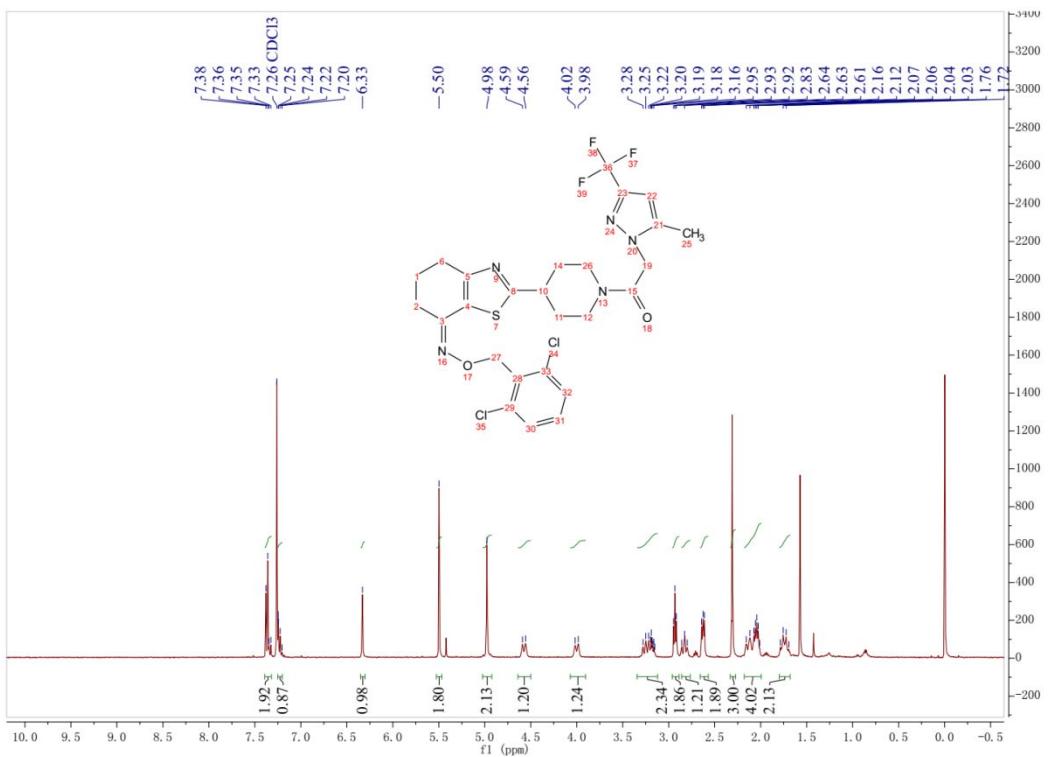


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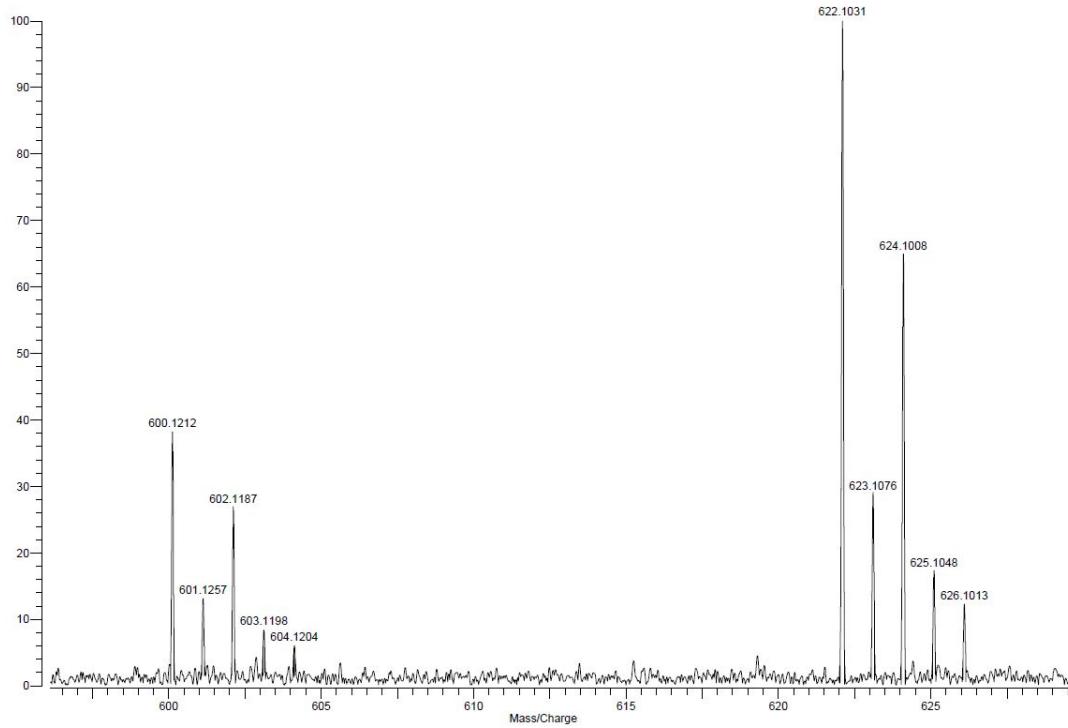


11q

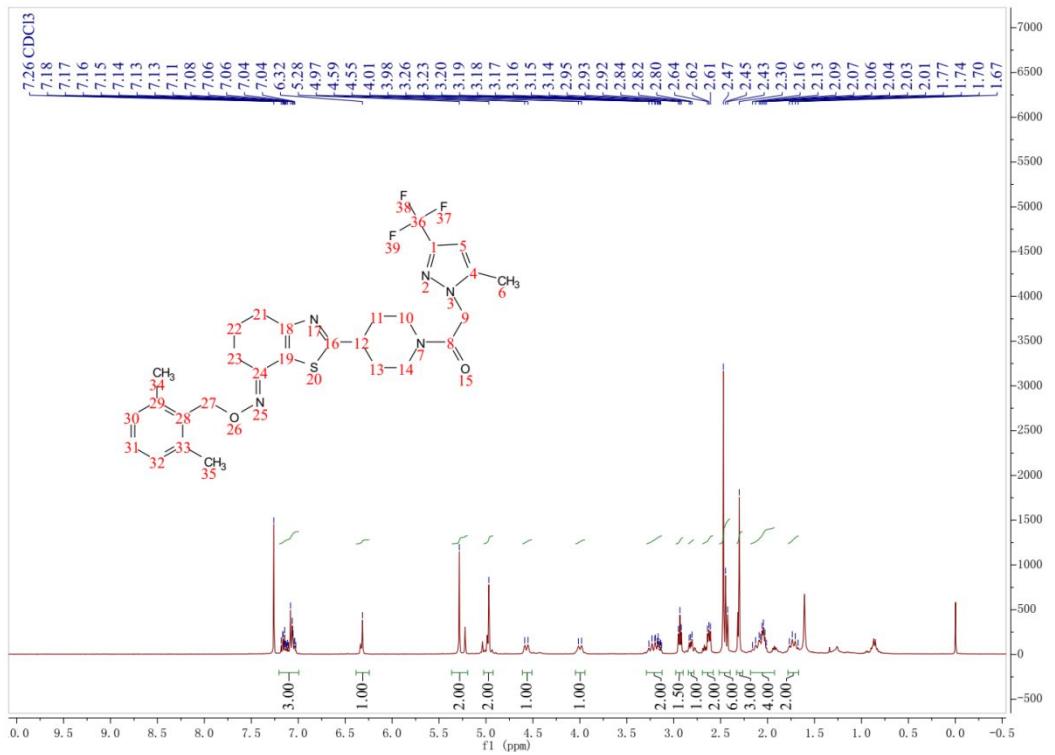


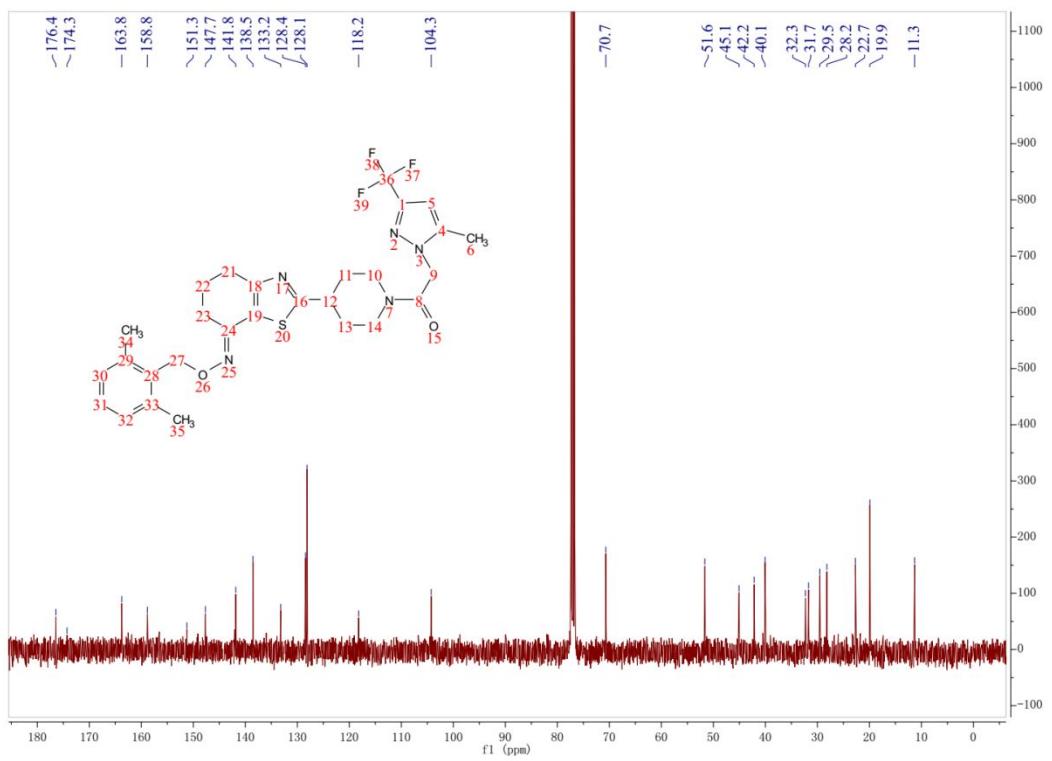
Varian QFT-ESI
File: 15-q_ESI.trans

Mode: Positive Date: 12-MAY-2020
Scans: 1 Time: 15:50:14
Scale: 38.6486



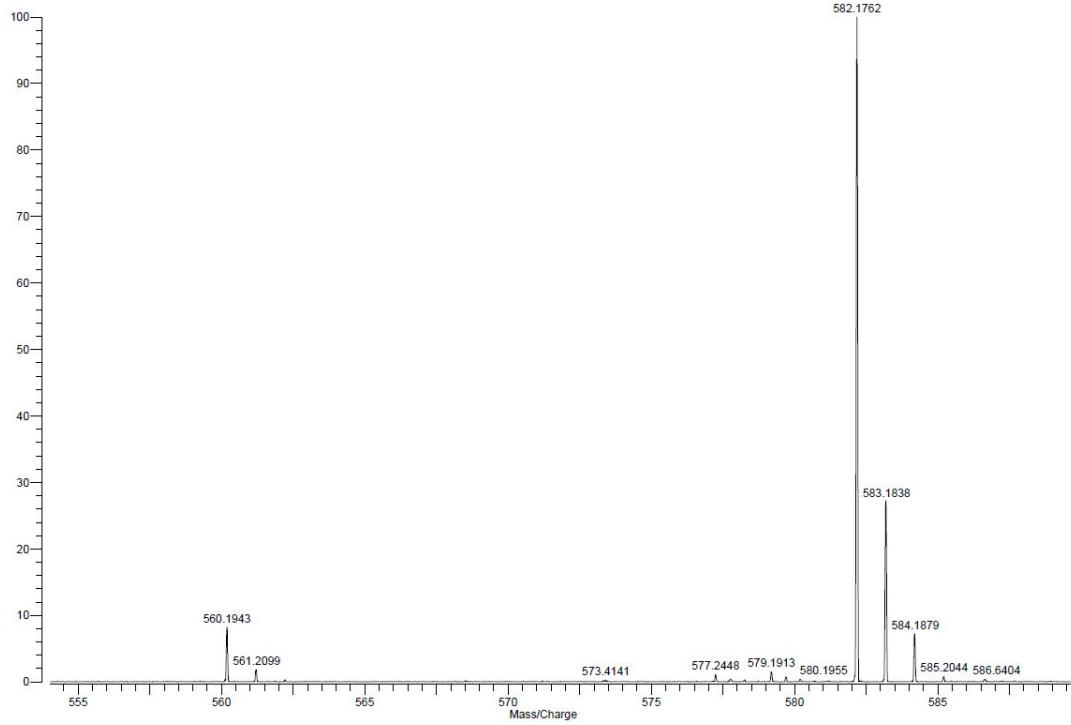
11r



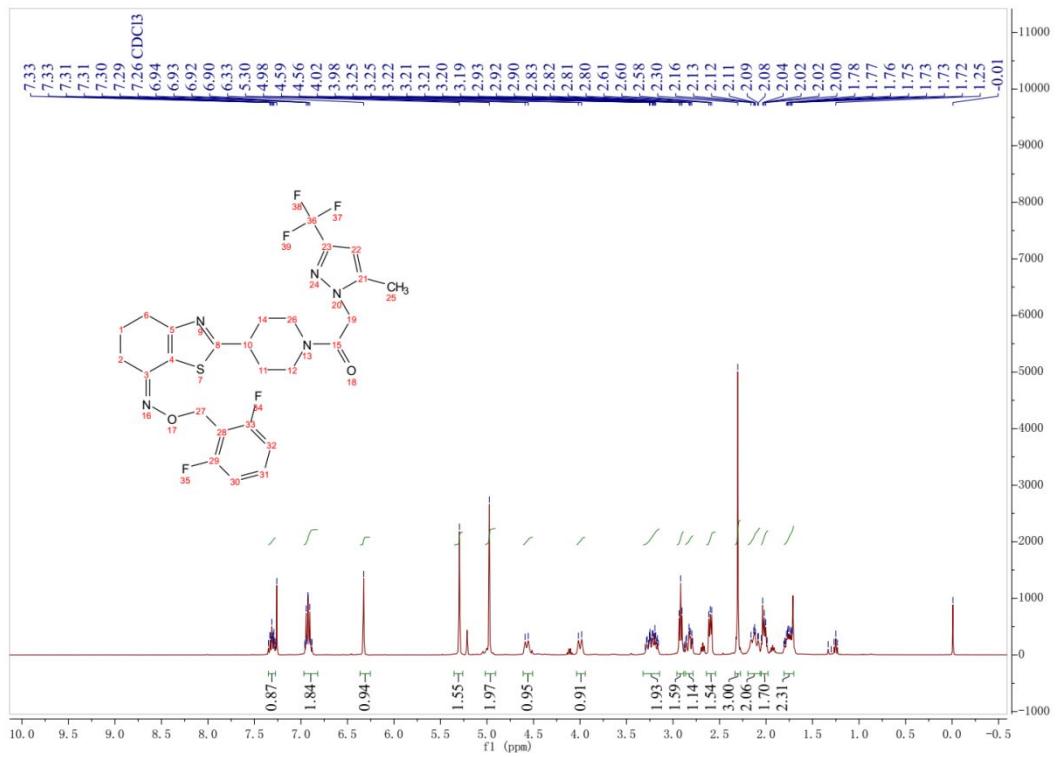


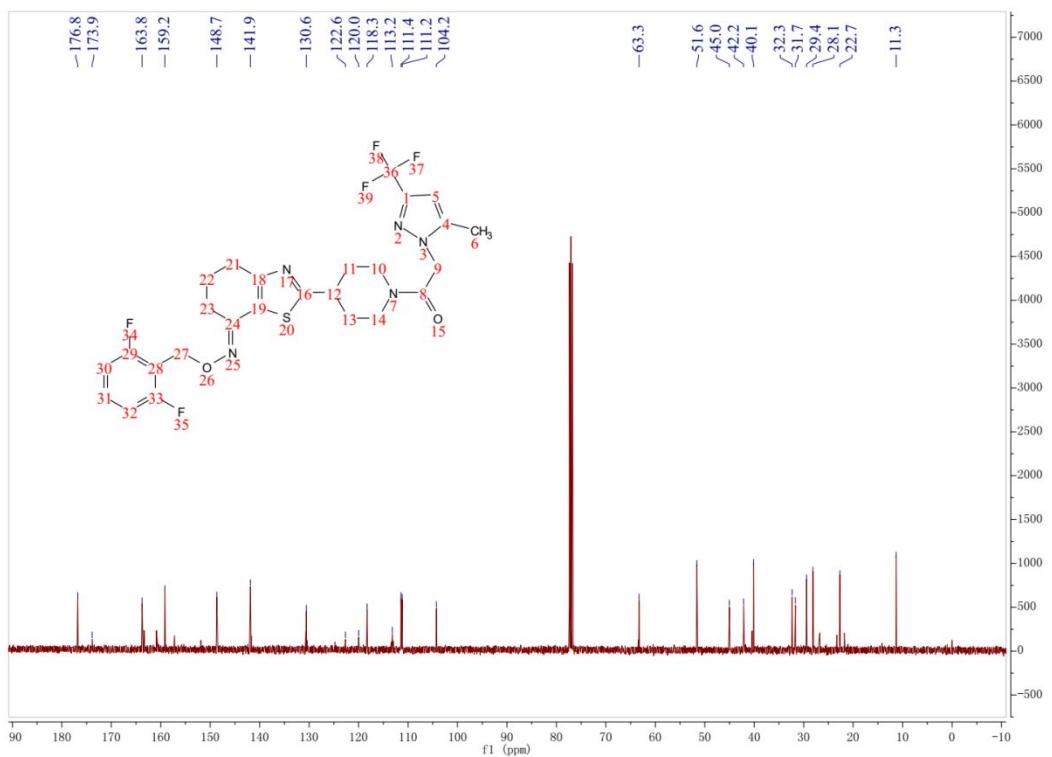
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File: 15-r_ESI.trans

Mode: Positive
Scans: 1
Date: 12-MAY-2020
Time: 12:14:41
Scale: 1.1398



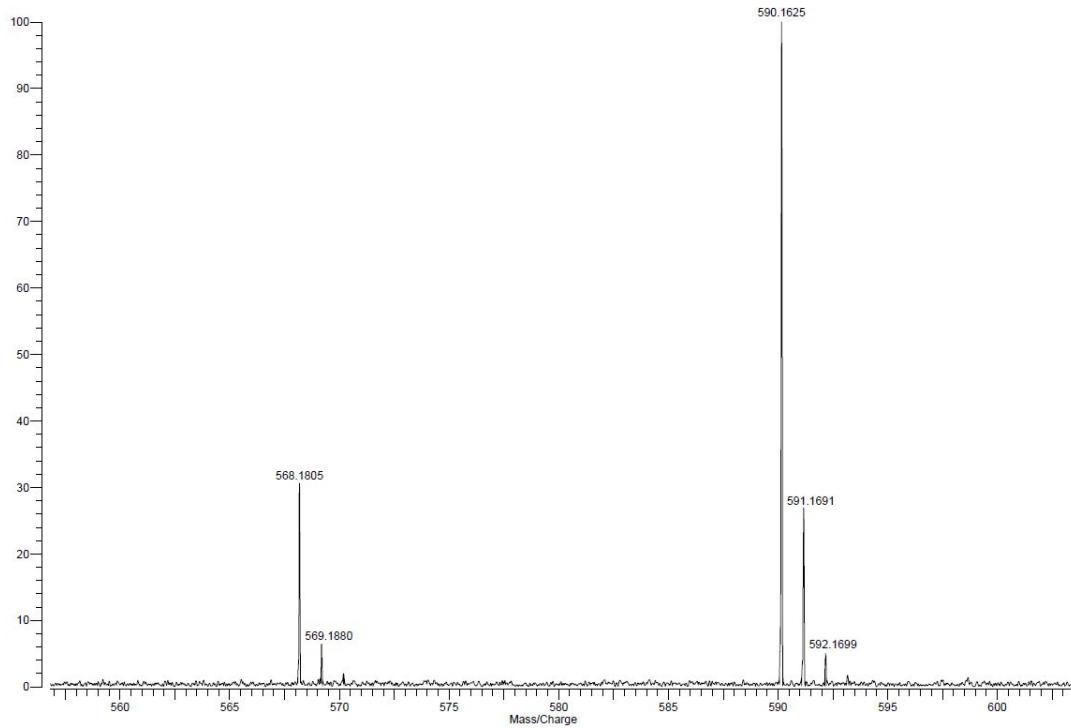
11s





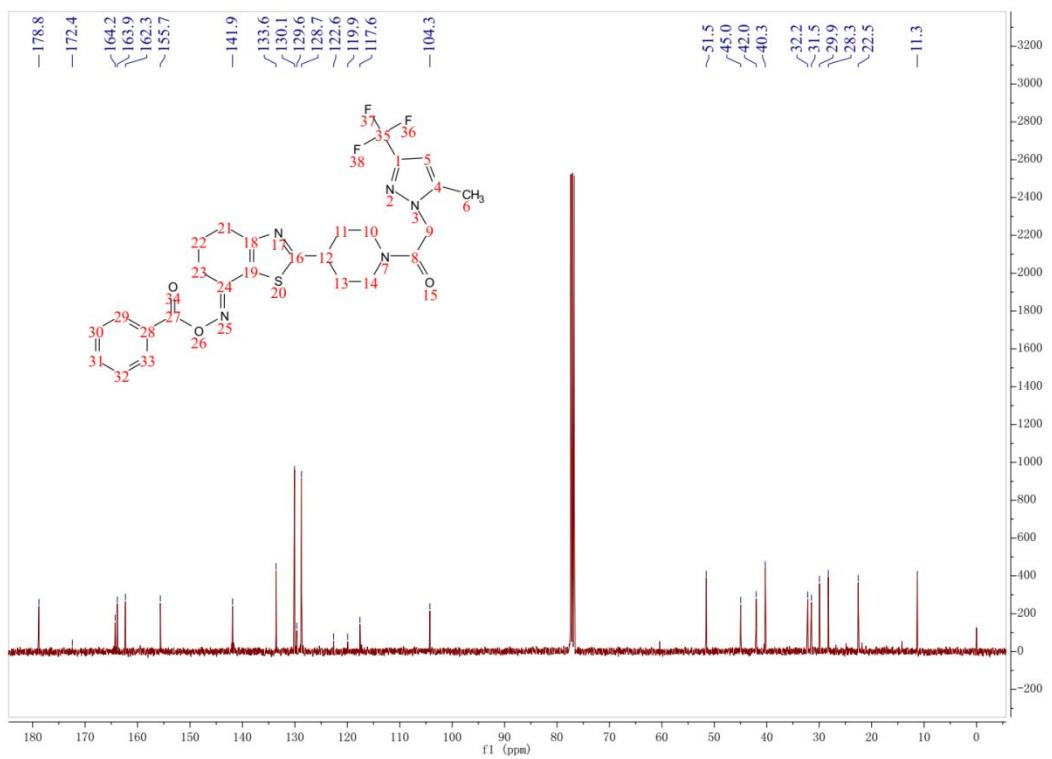
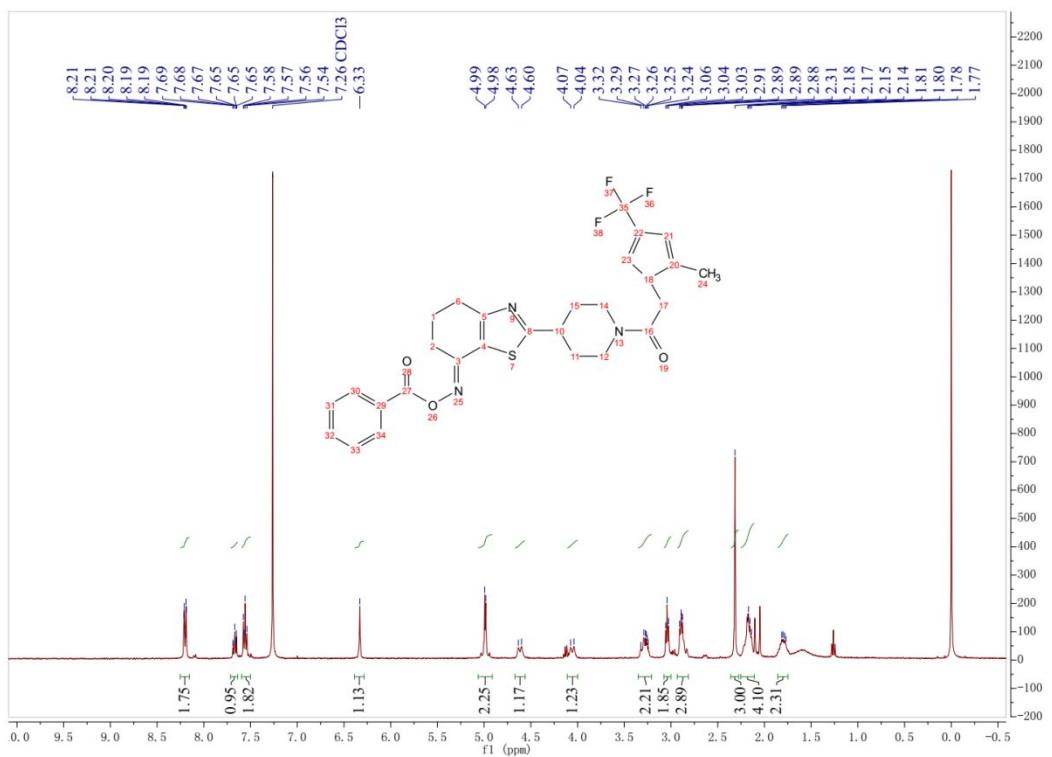
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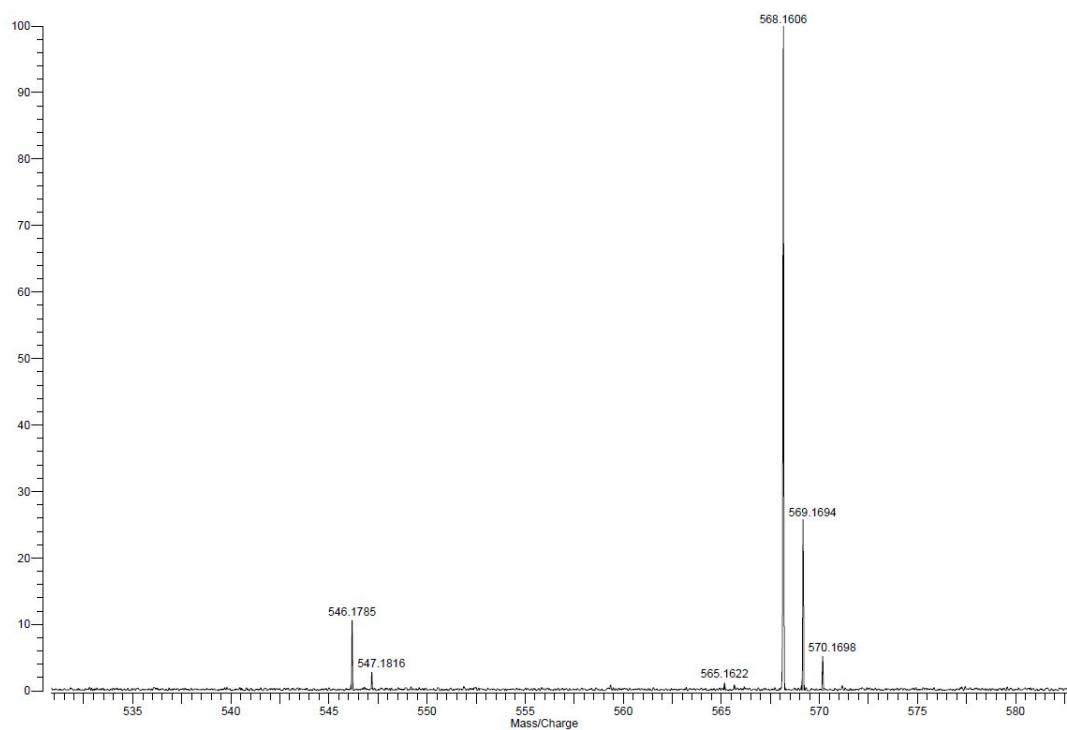
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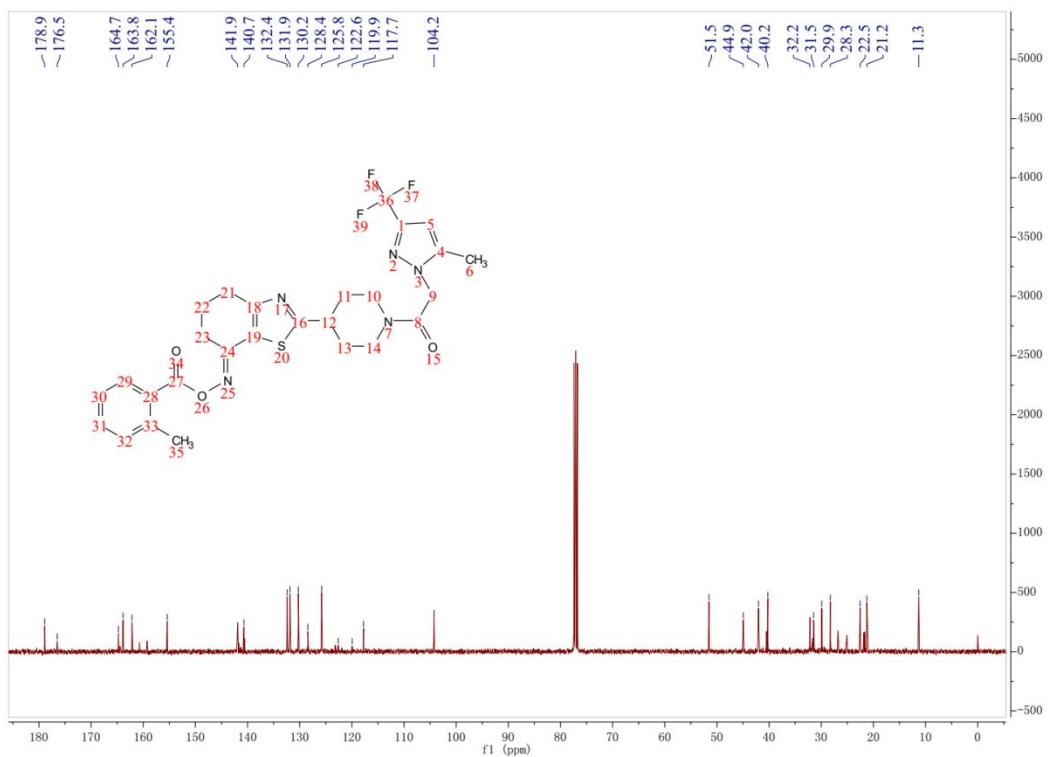
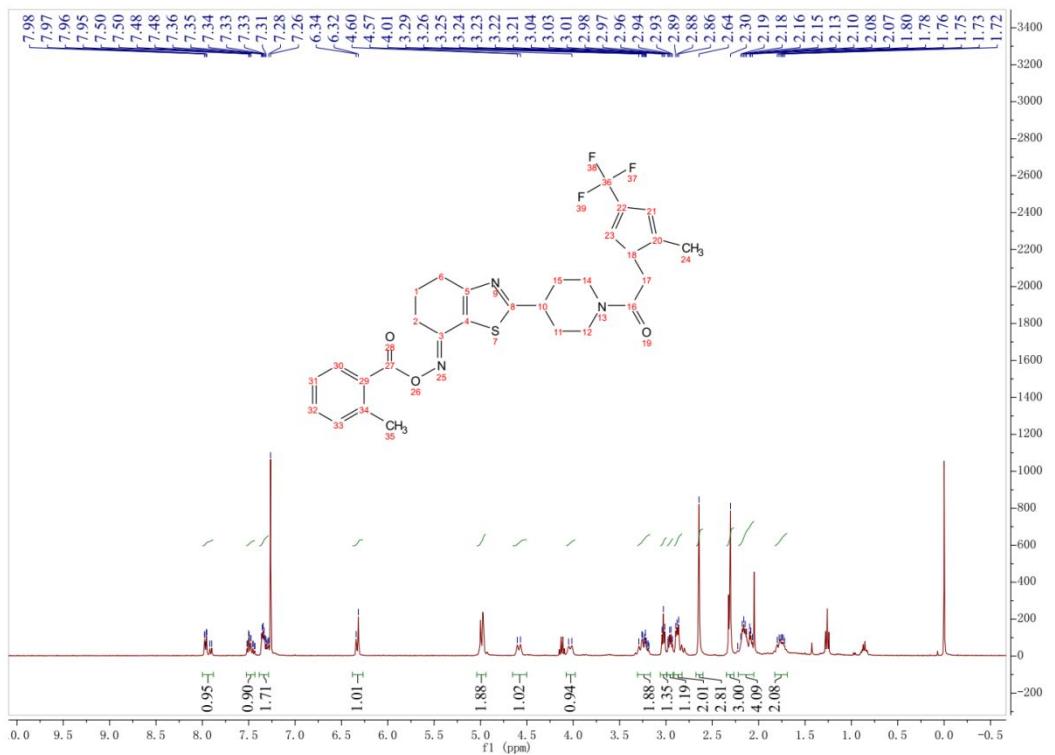
13a

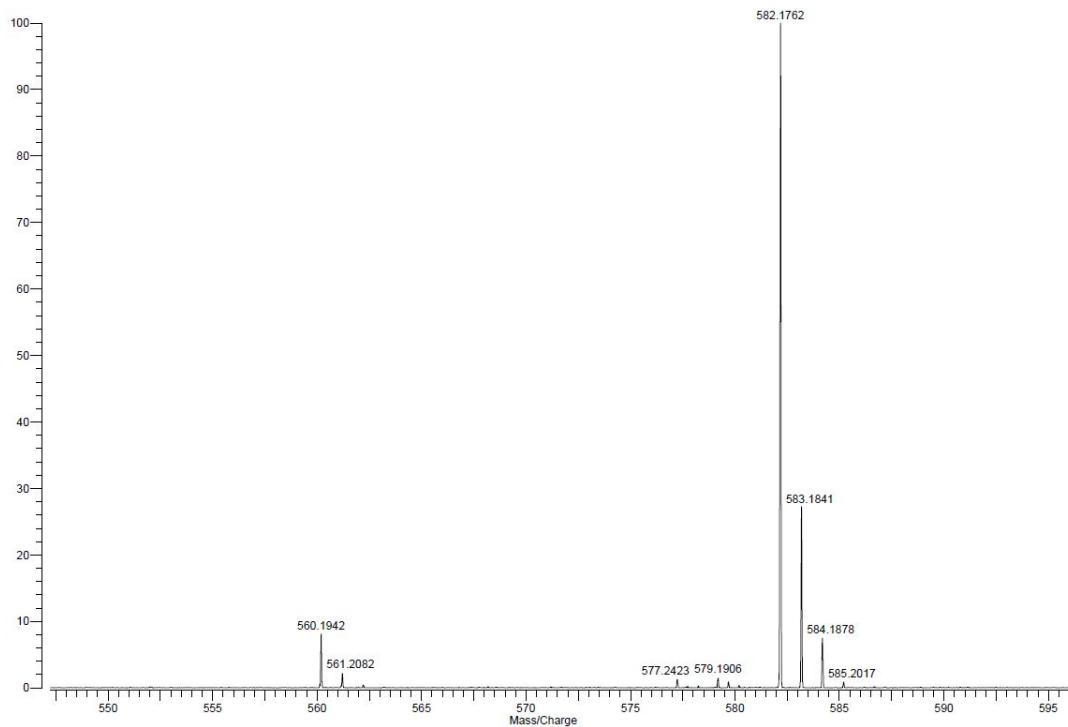
S75



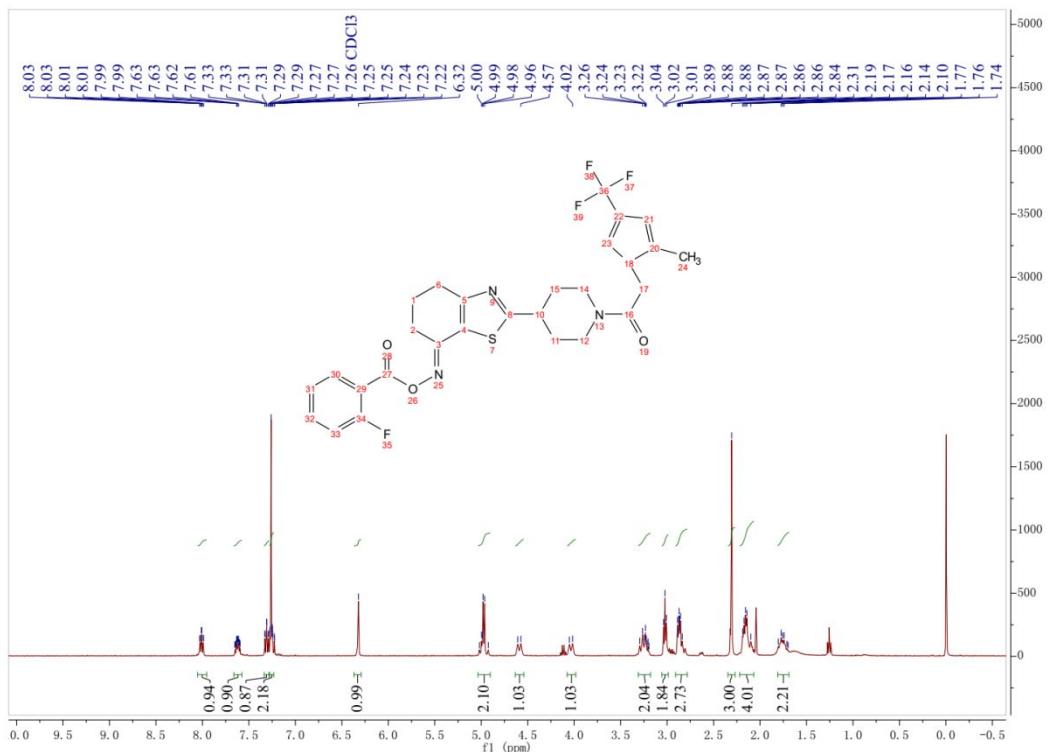


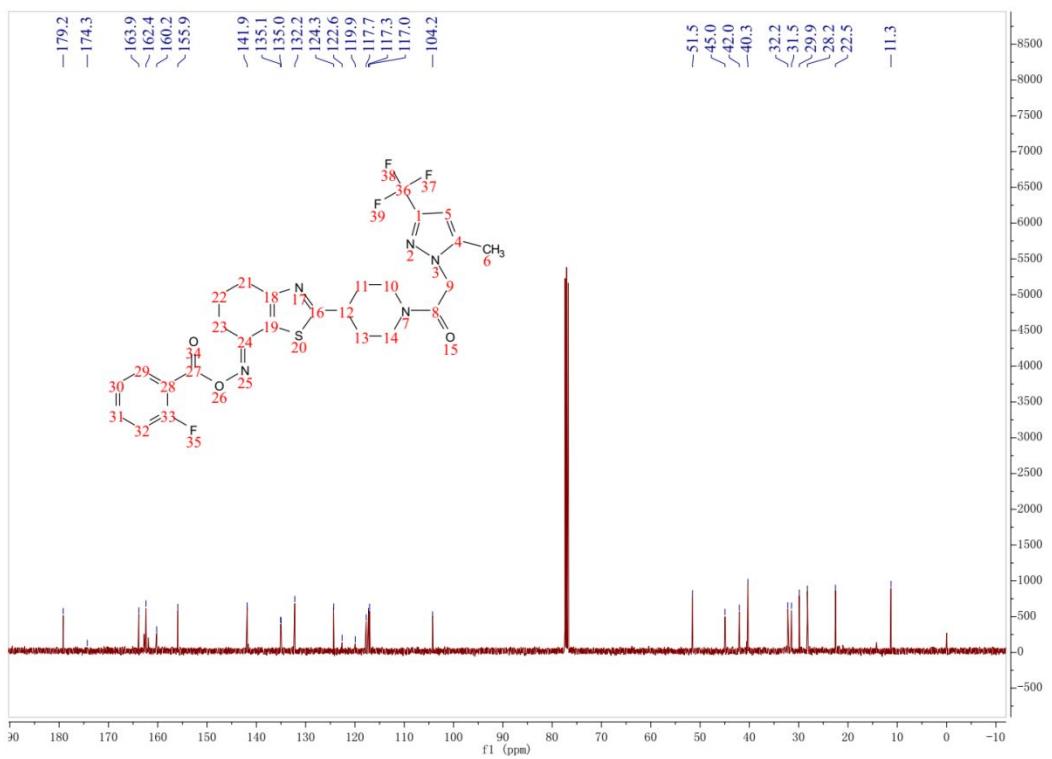
13b





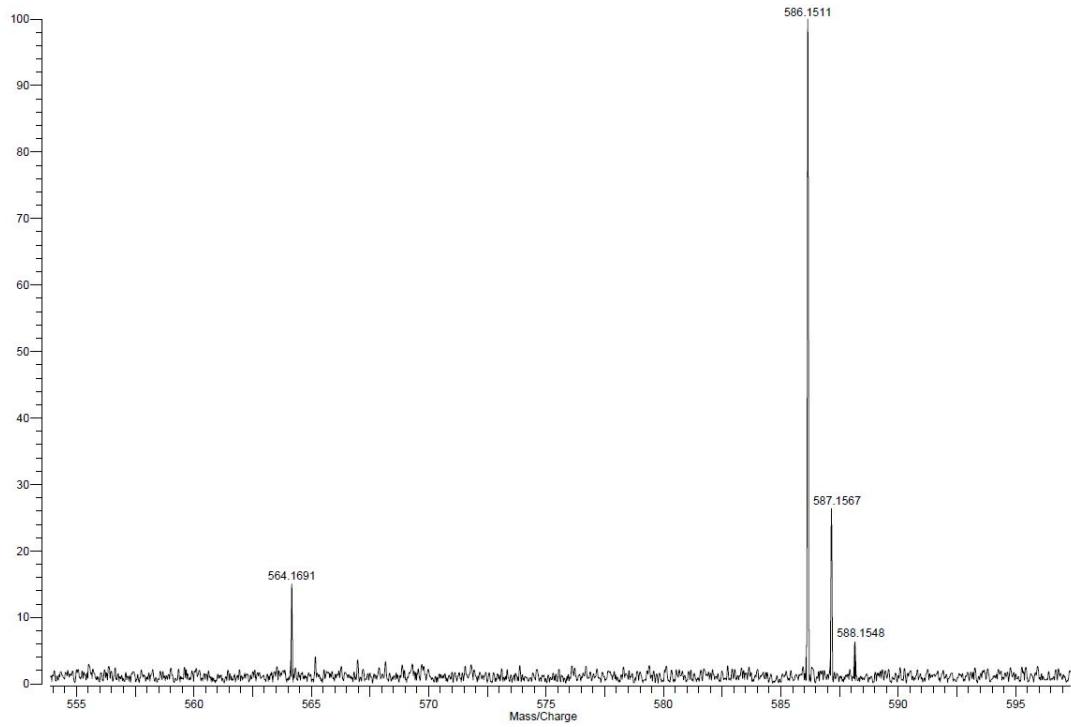
13c



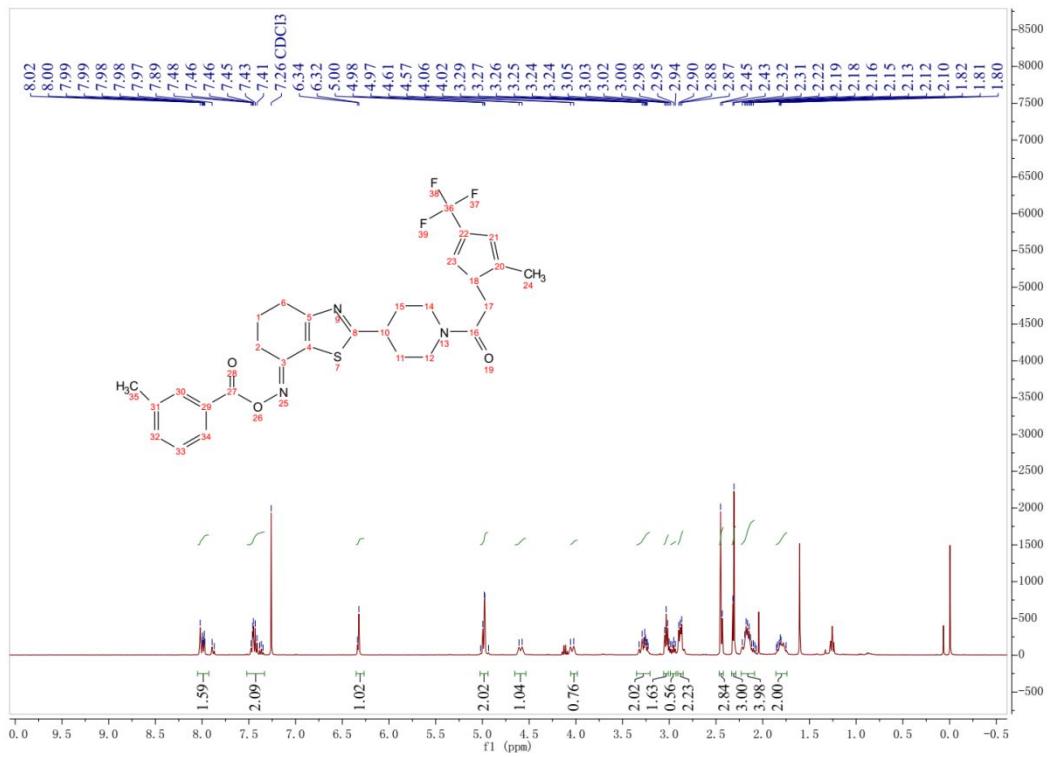


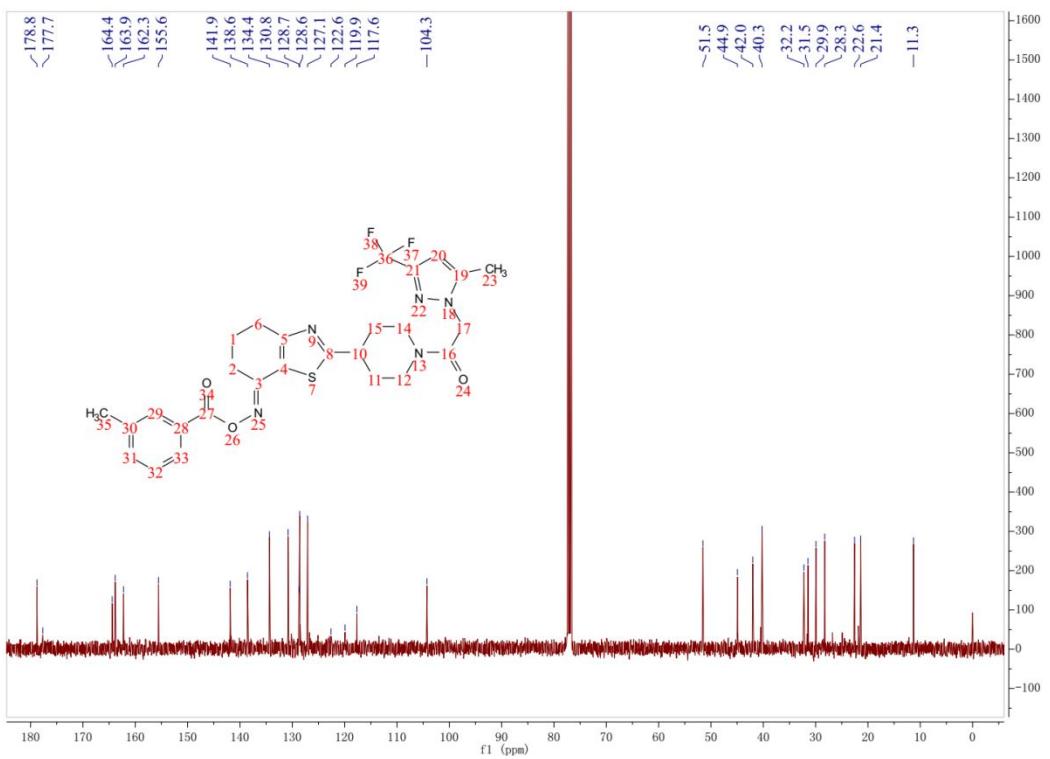
Varian QFT-ESI
File: 17-d_ESI.trans

Mode: Positive
Scans: 1
Date: 12-MAY-2020
Time: 15:31:04
Scale: 36.1713



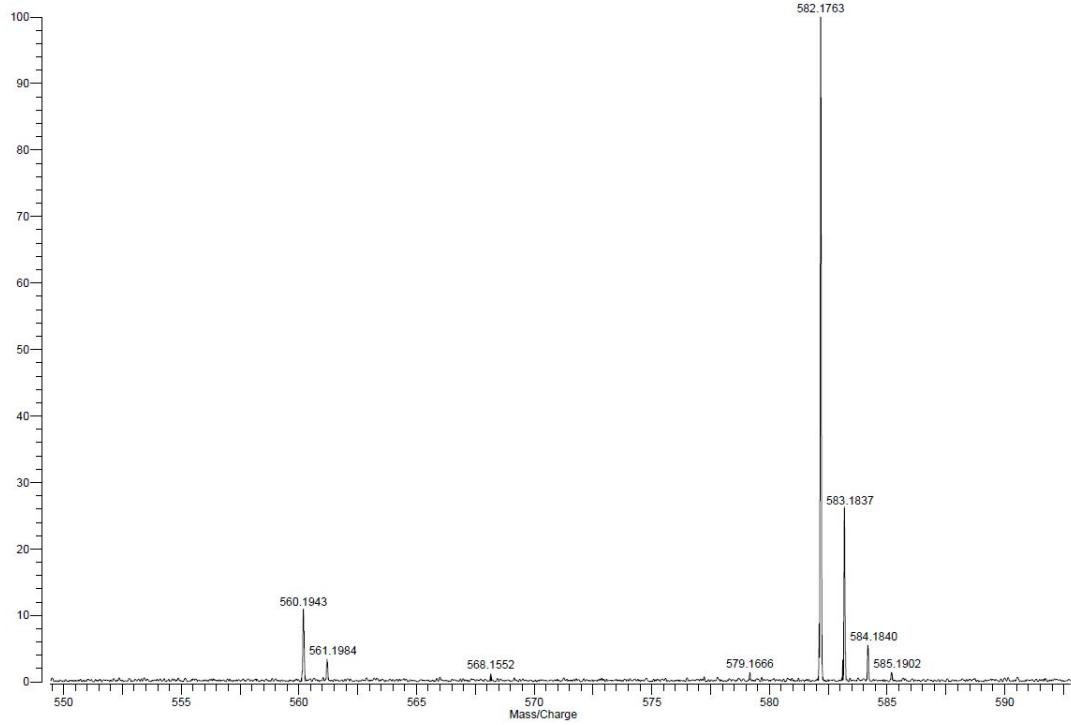
13d





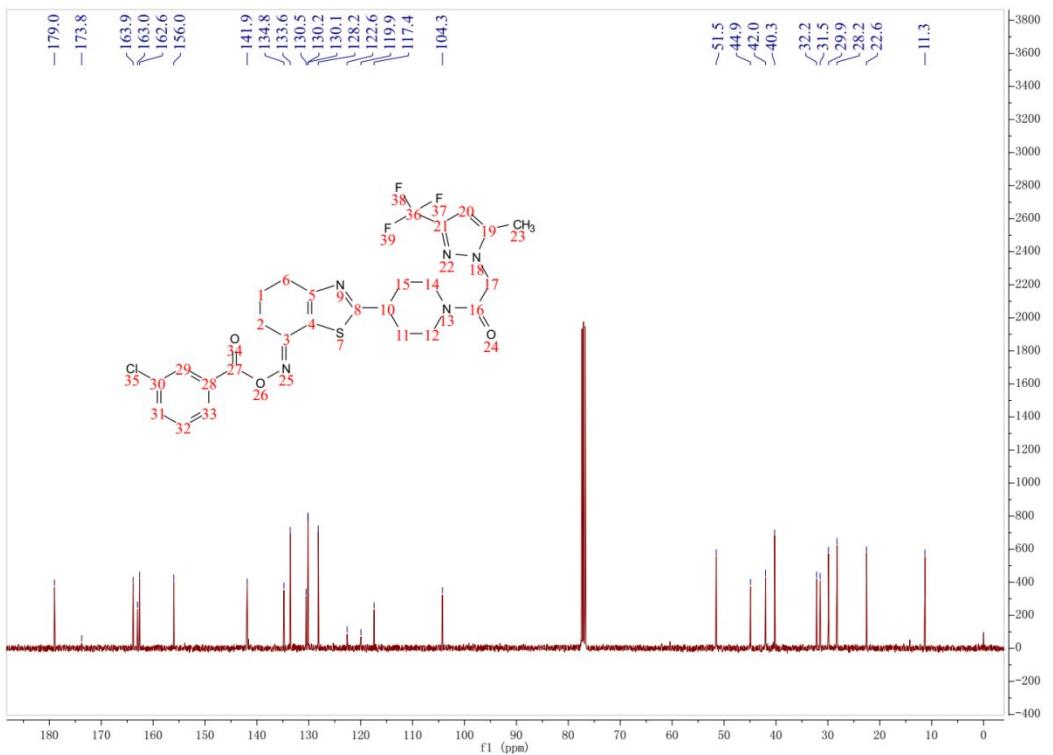
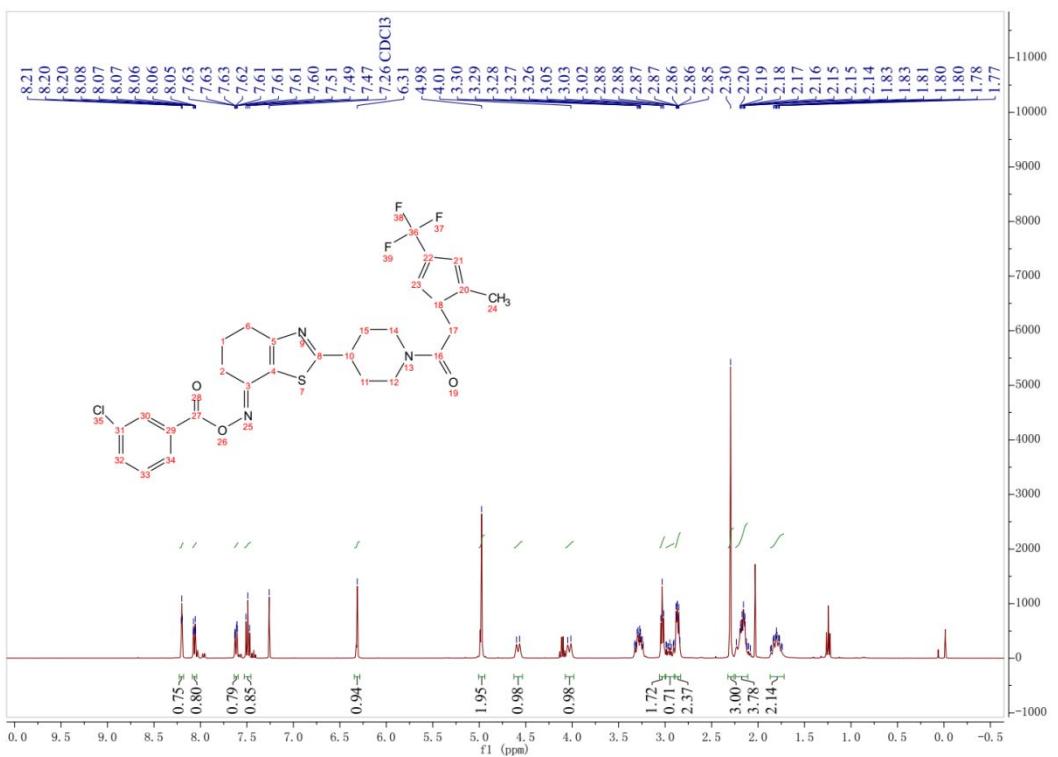
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File: 17-f_ESI.trans

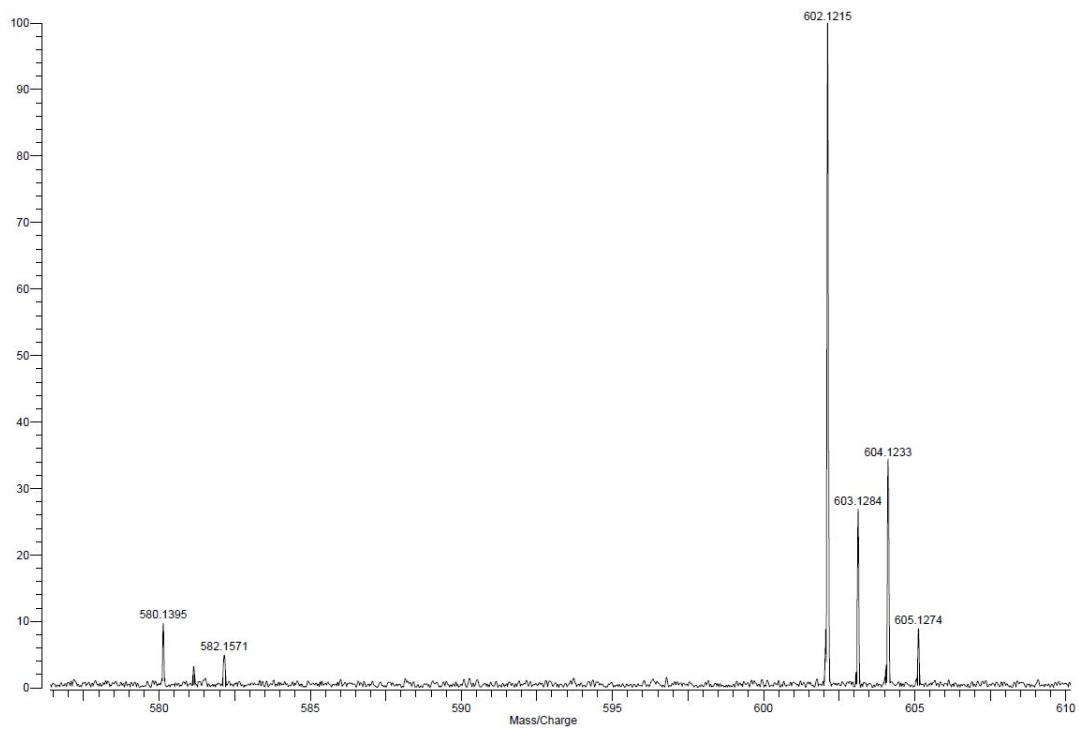
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Scans: 1
Date: 12-MAY-2020
Time: 12:17:13
Scale: 7.6477



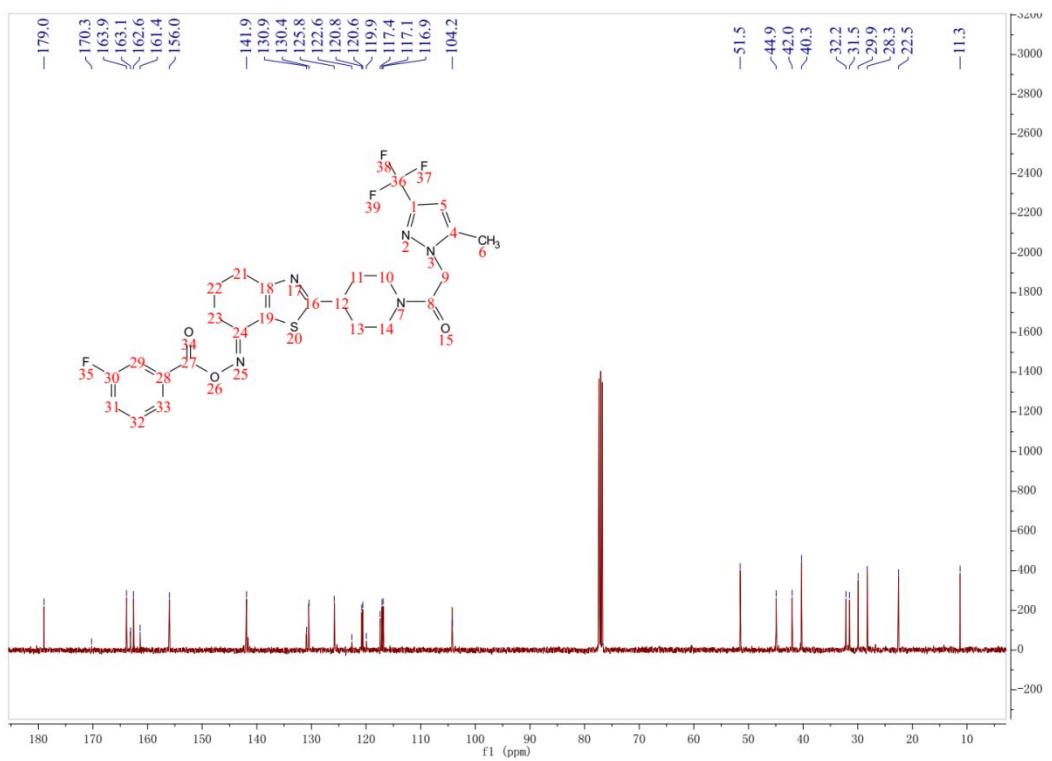
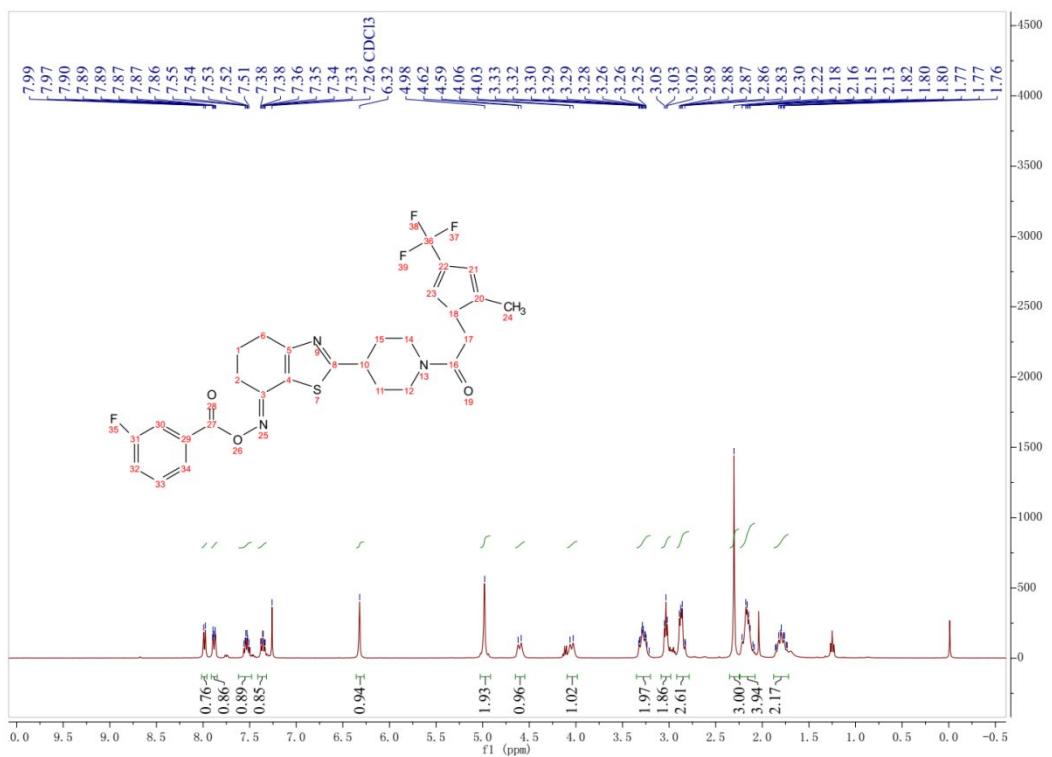
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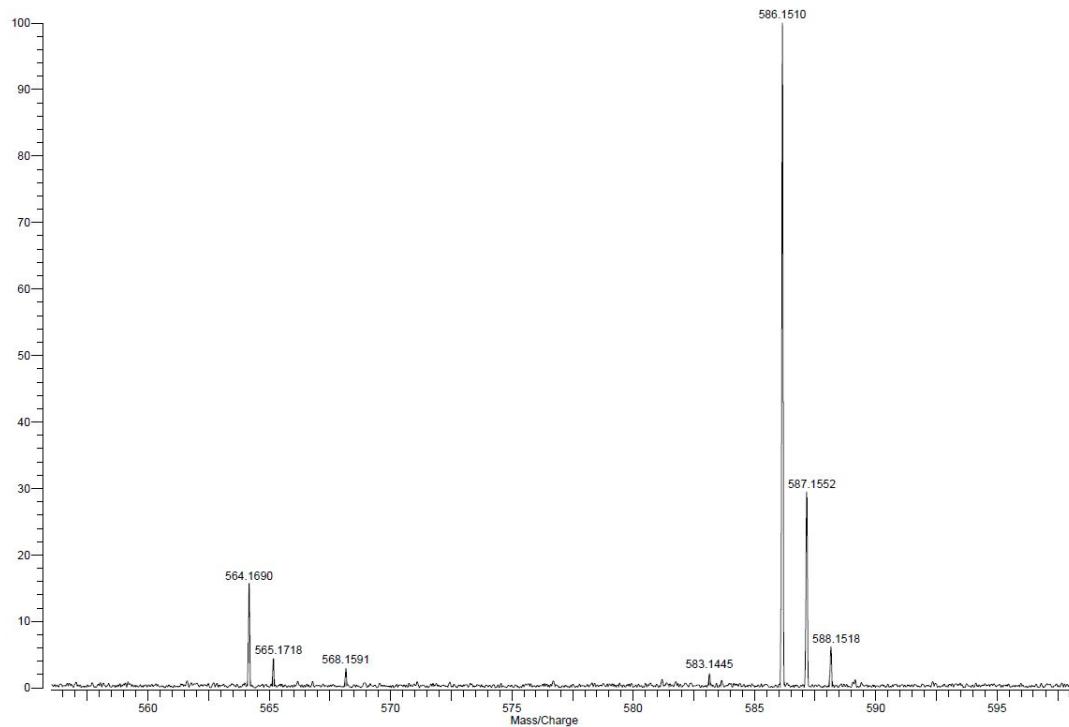
S82



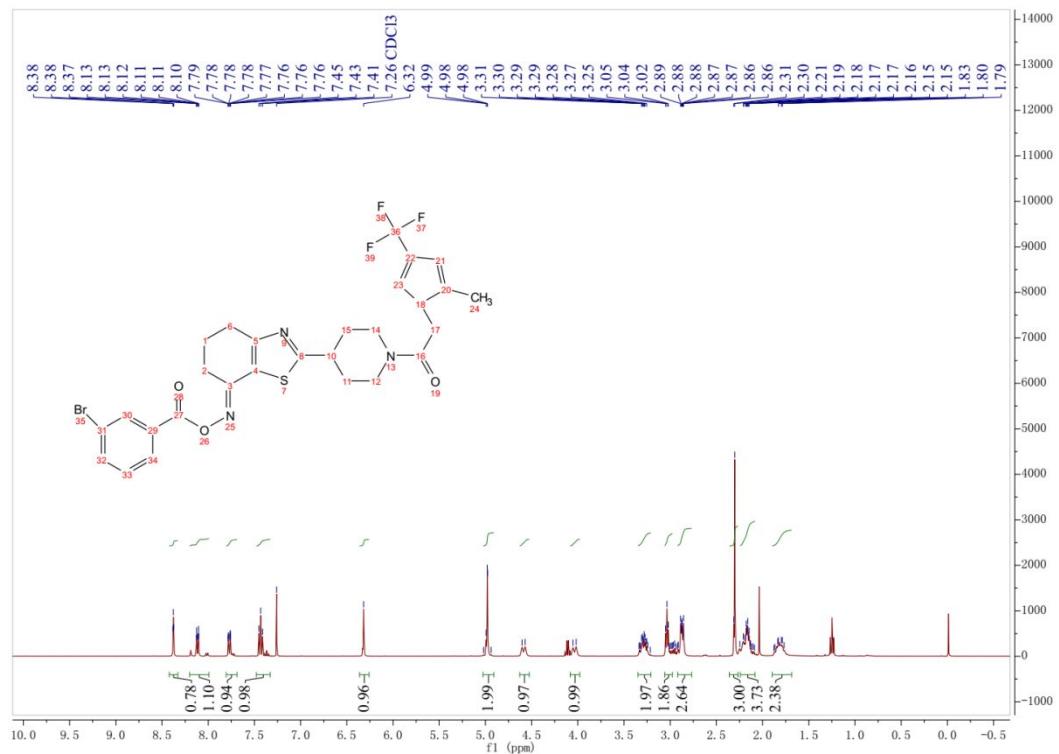


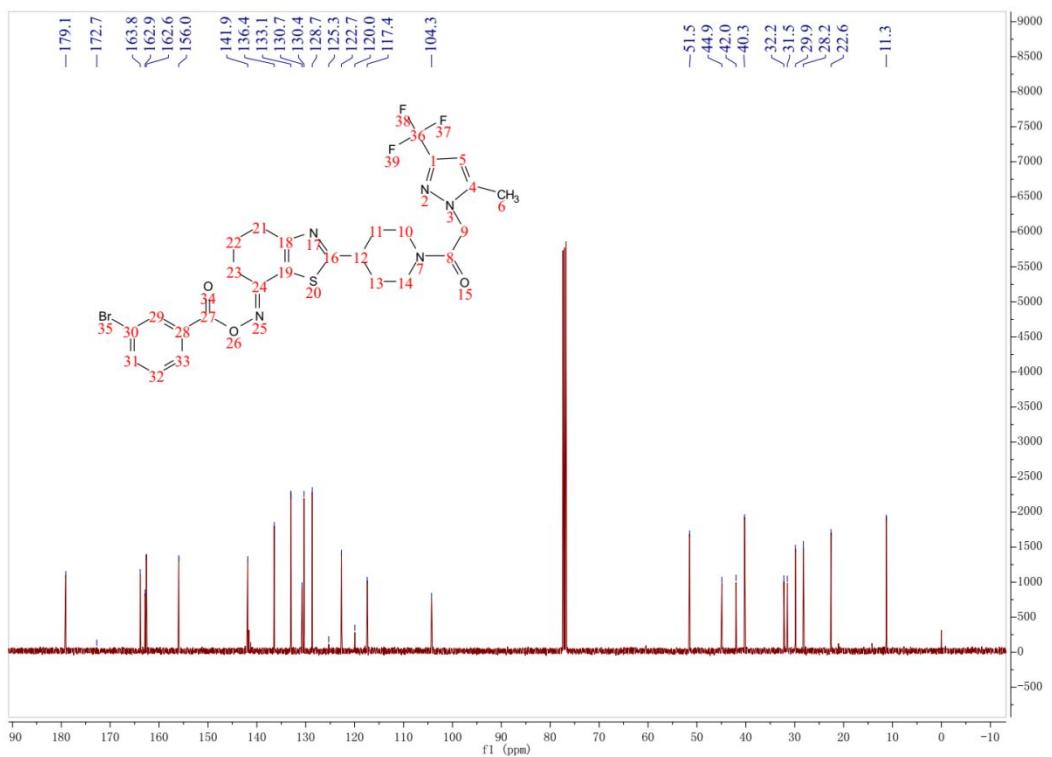
13f





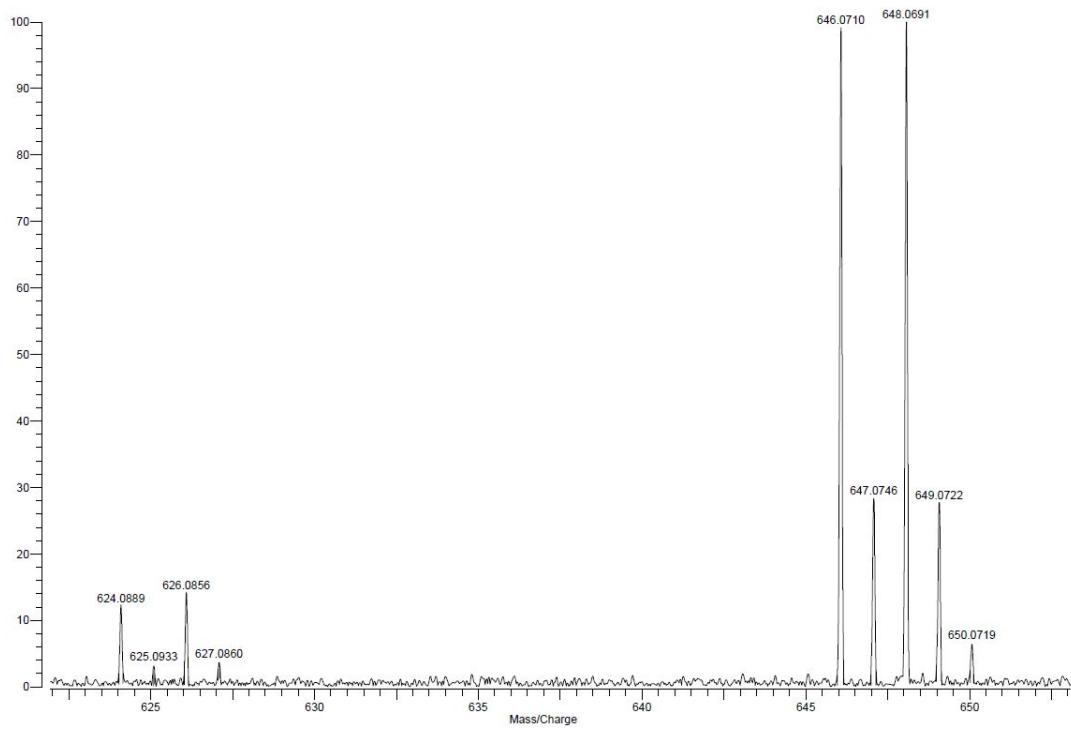
13g



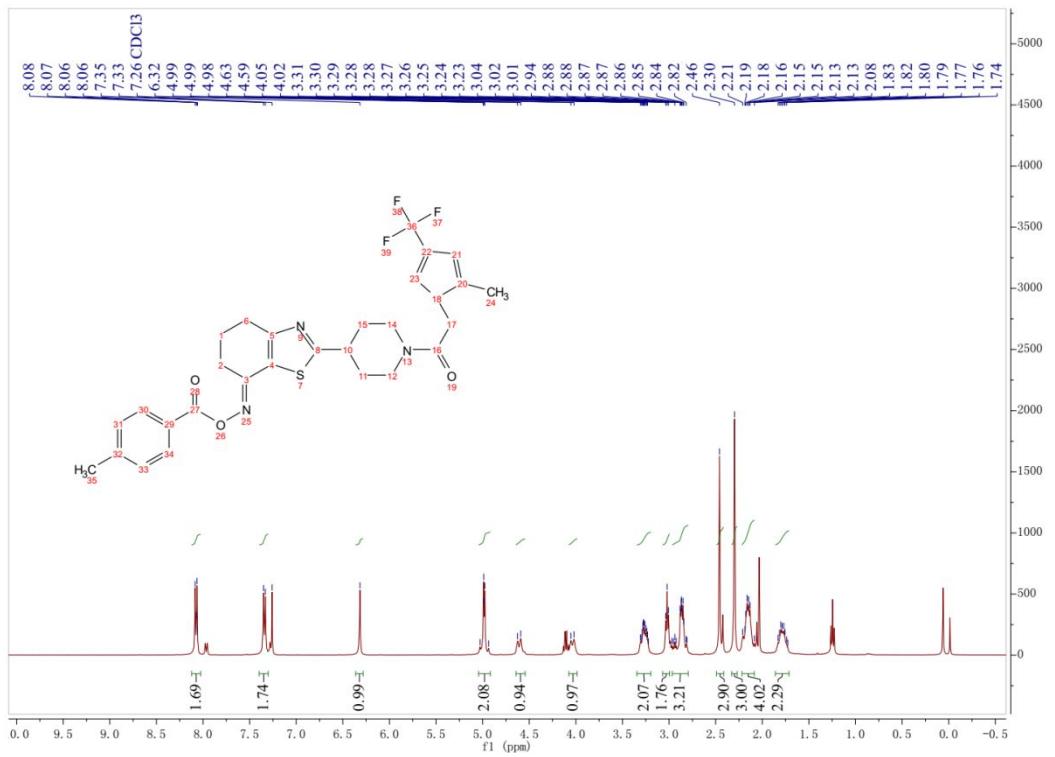


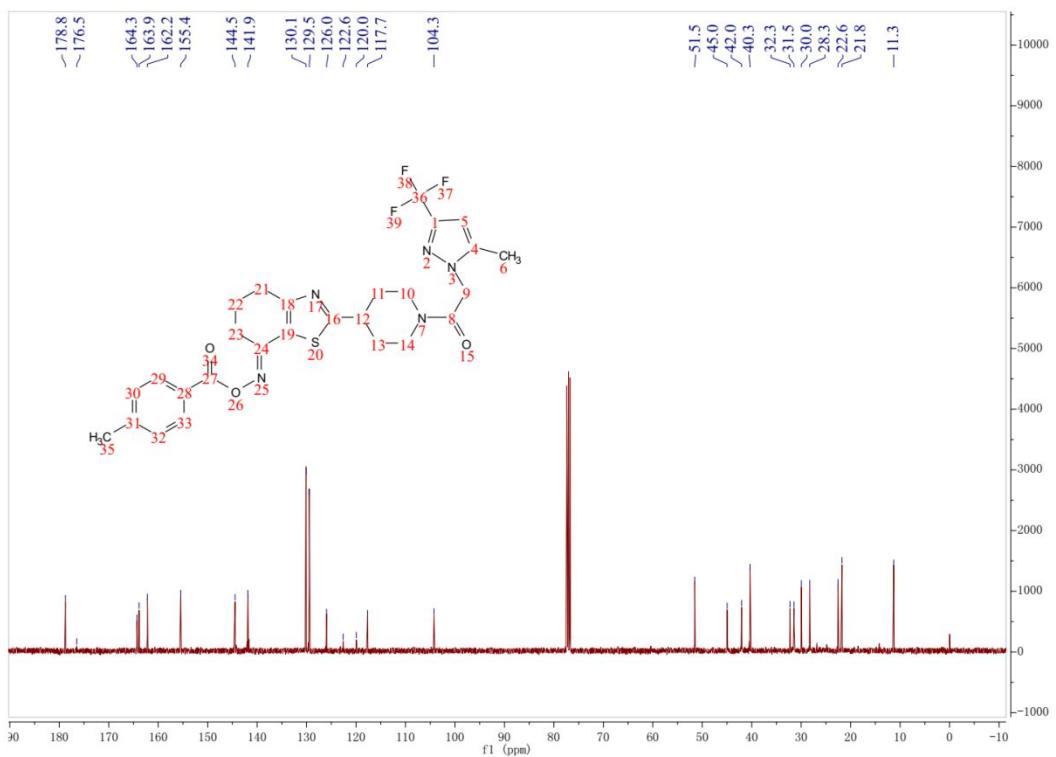
Varian QFT-ESI

Mode: Positive Date: 12-MAY-2020
Scans: 1 Time: 12:27:53
Scale: 20.9420



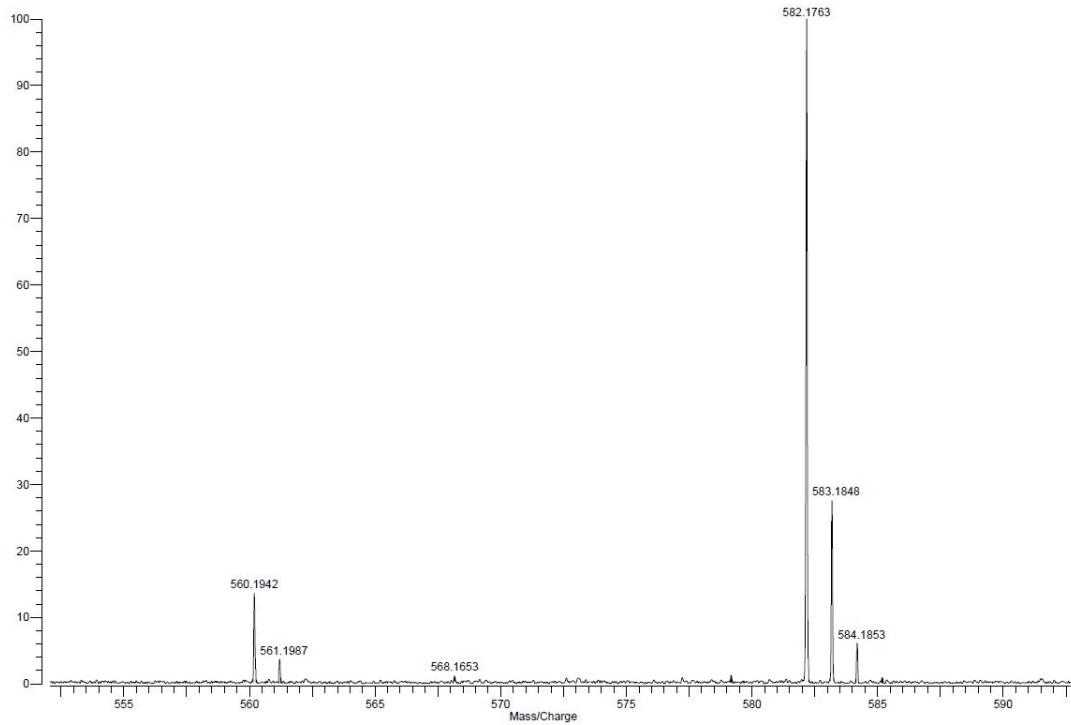
13h





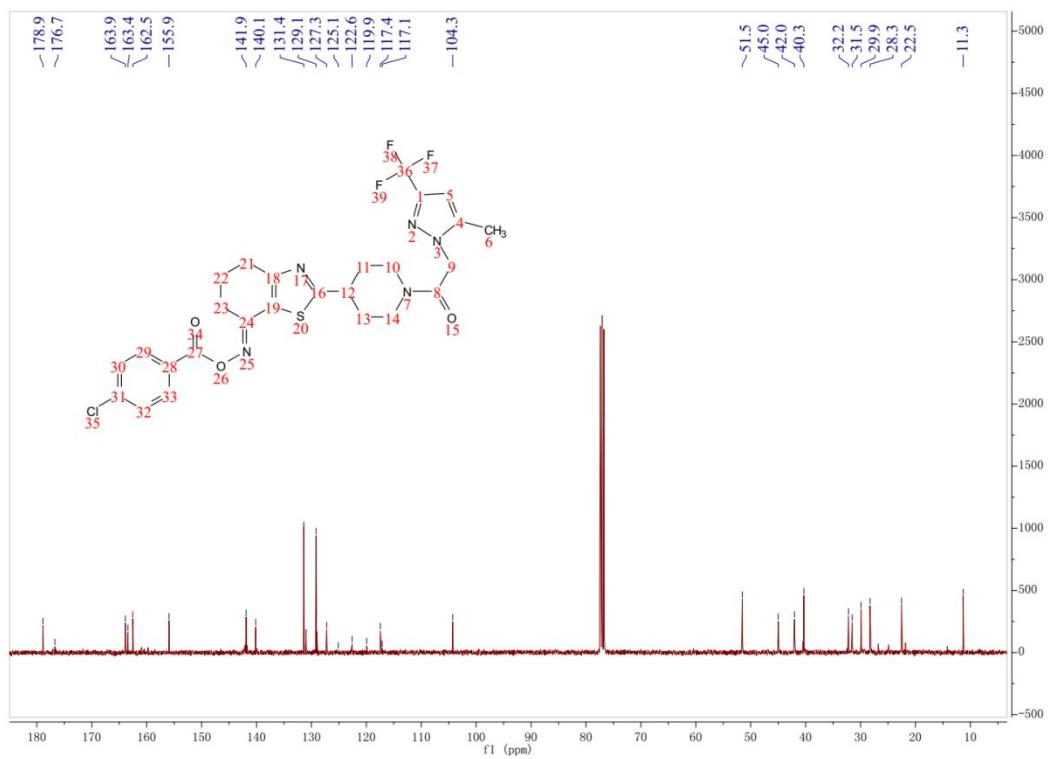
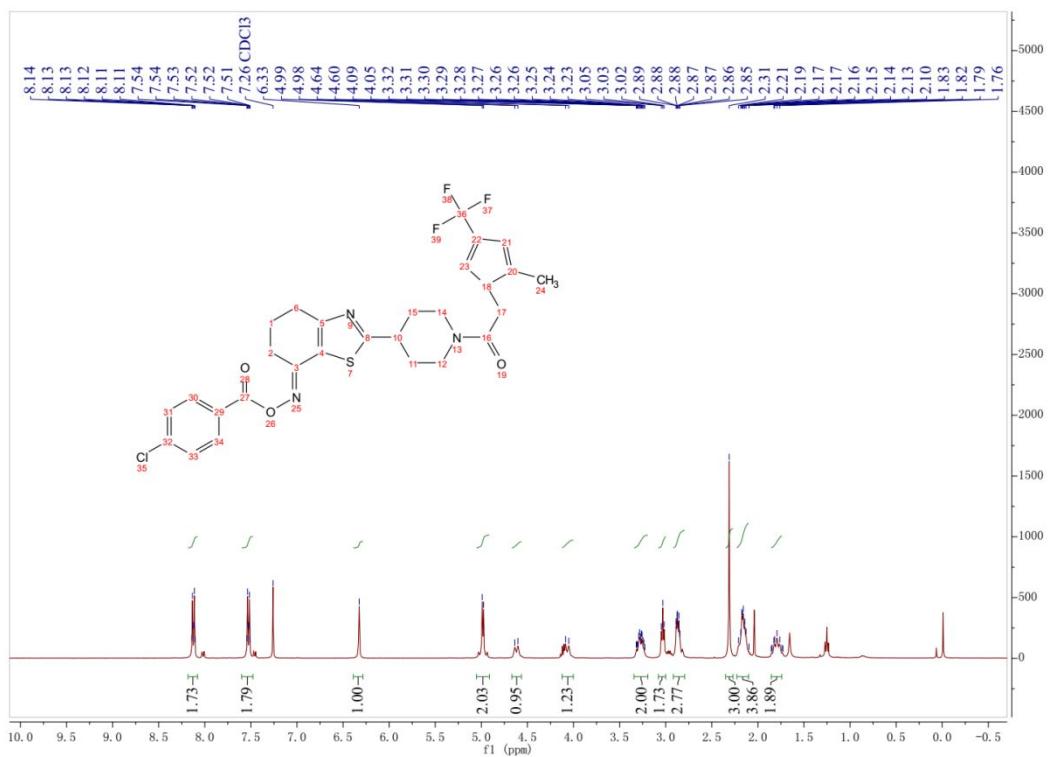
Varian QFT-ESI
File: 17-j_ESI.trans

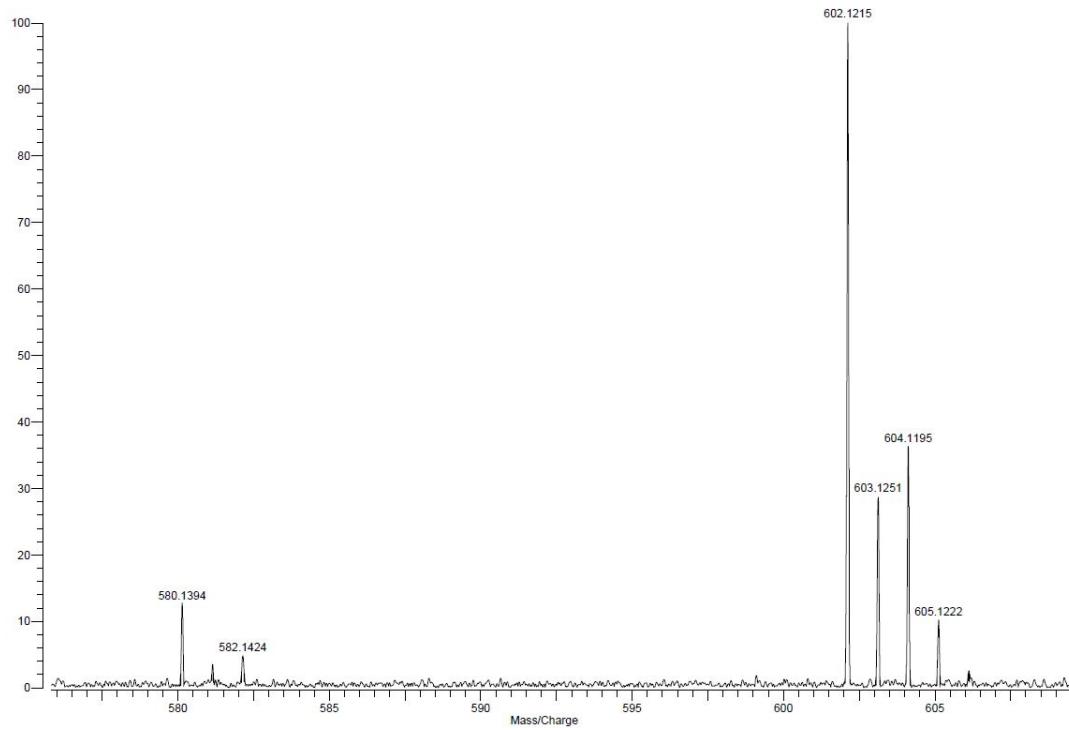
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Scans: 1
Date: 12-MAY-2020
Time: 12:19:07
Scale: 7.7166



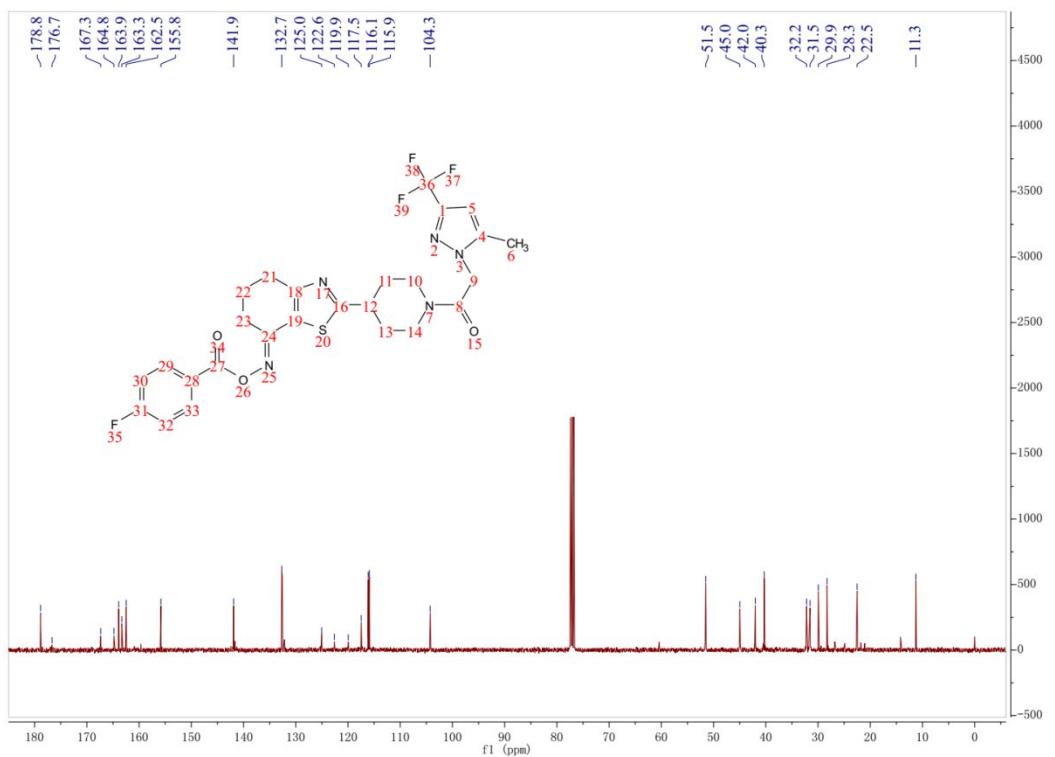
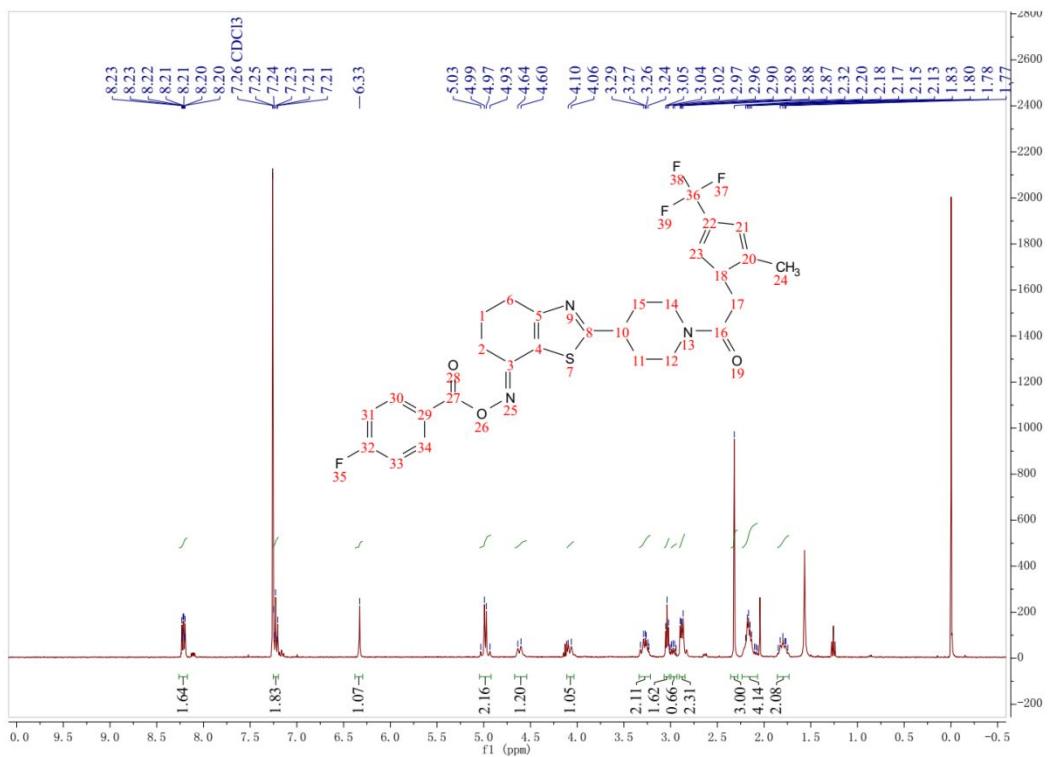
13i

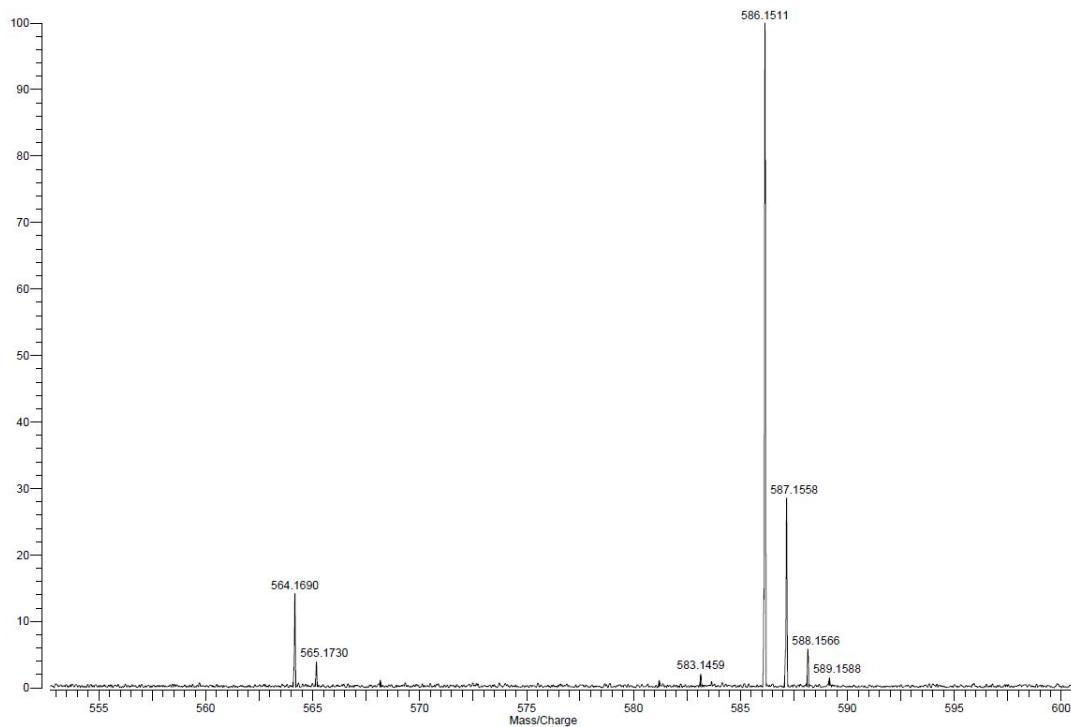
S89



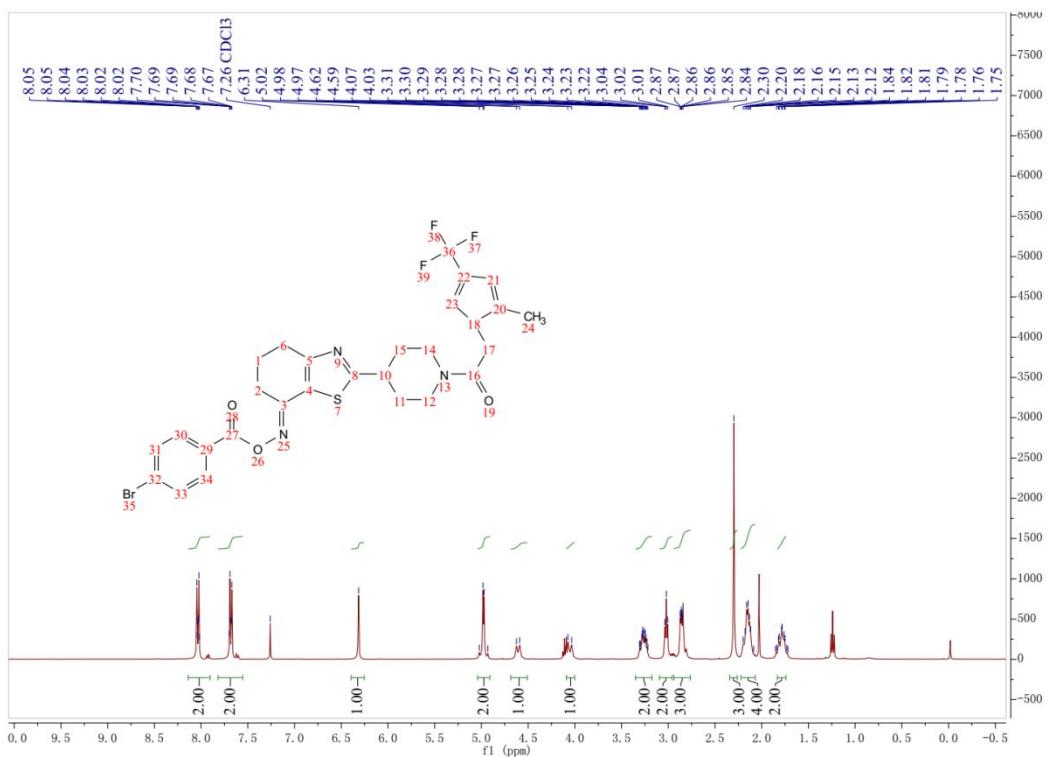


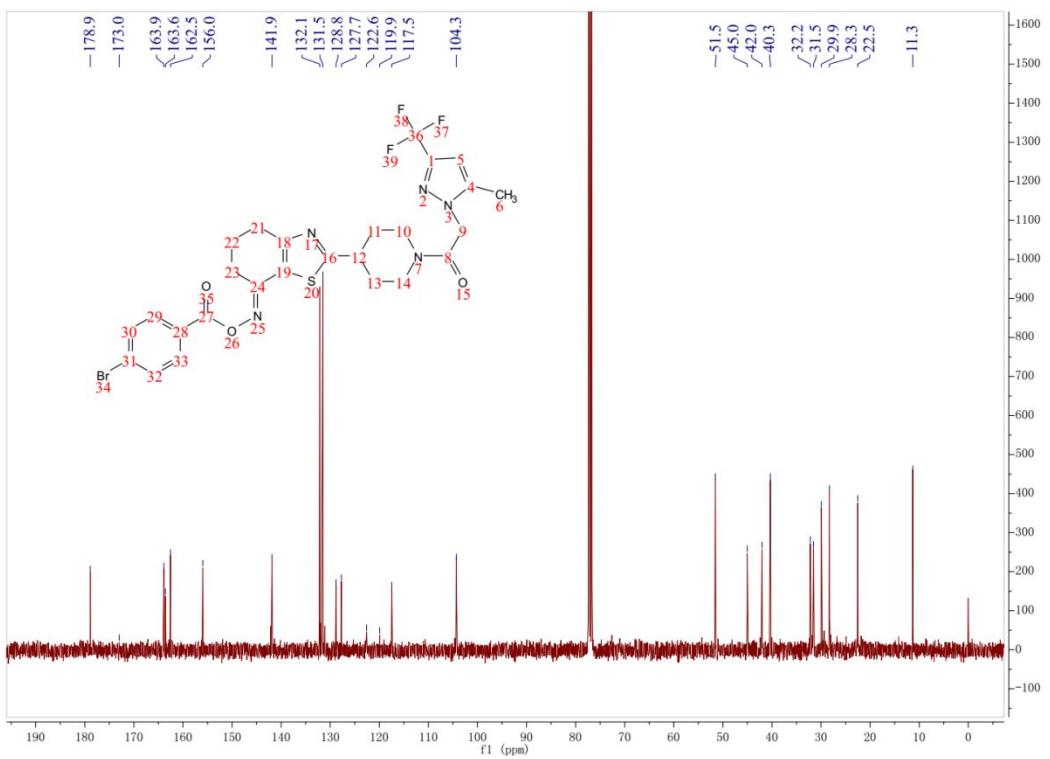
13j





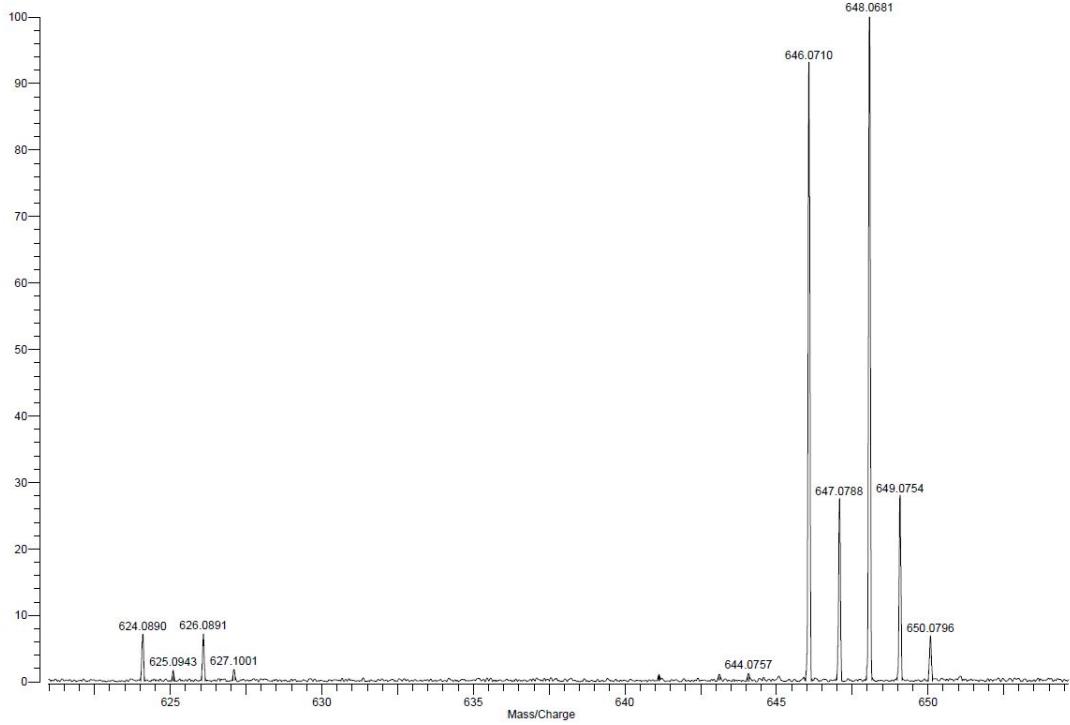
13k



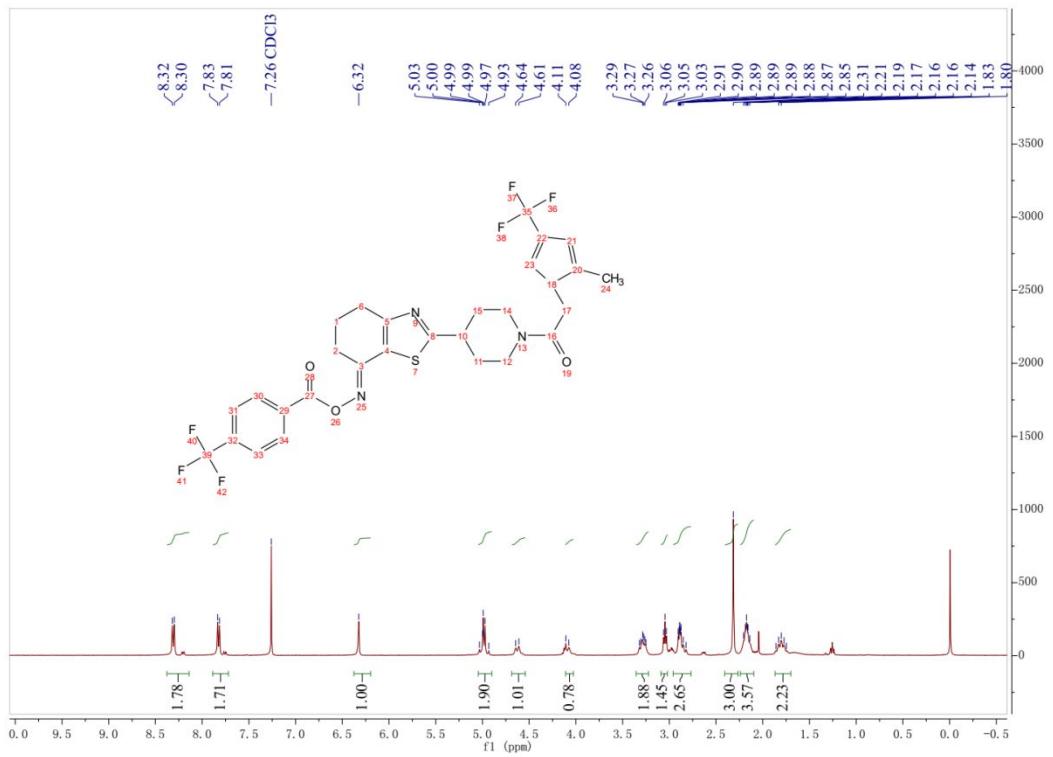


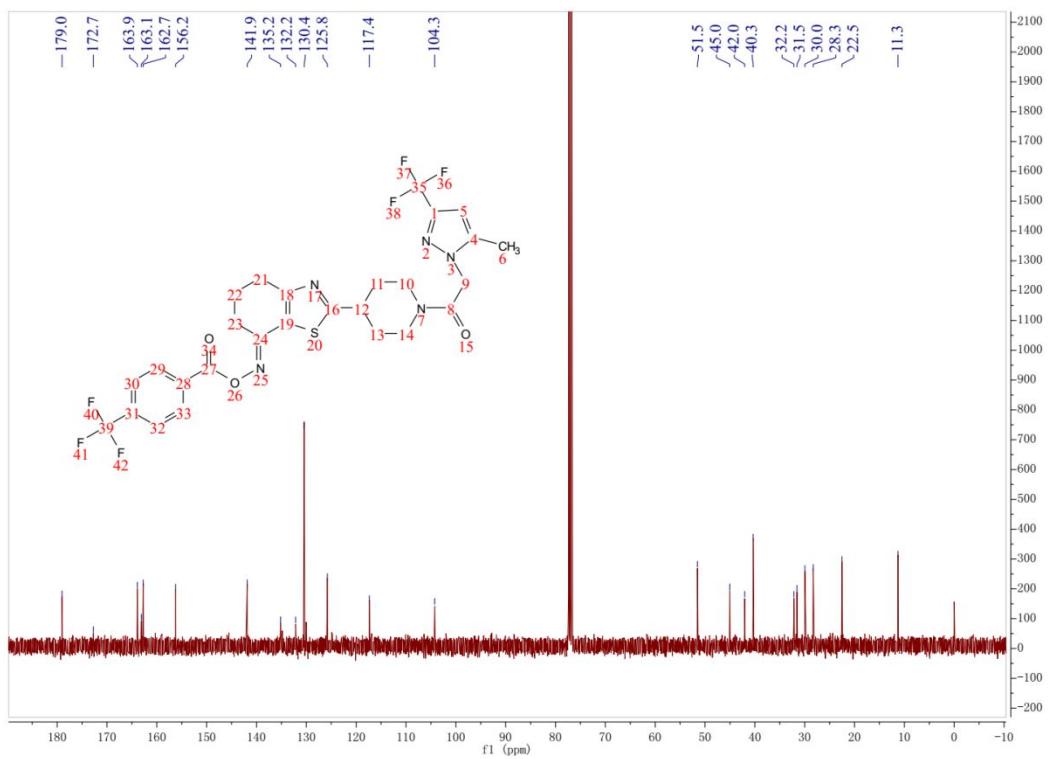
Varian QFT-ESI
File: 17-m_ESI.trans

Mode: Positive
Scans: 1
Date: 13-MAY-2020
Time: 11:48:22
Scale: 7.9422



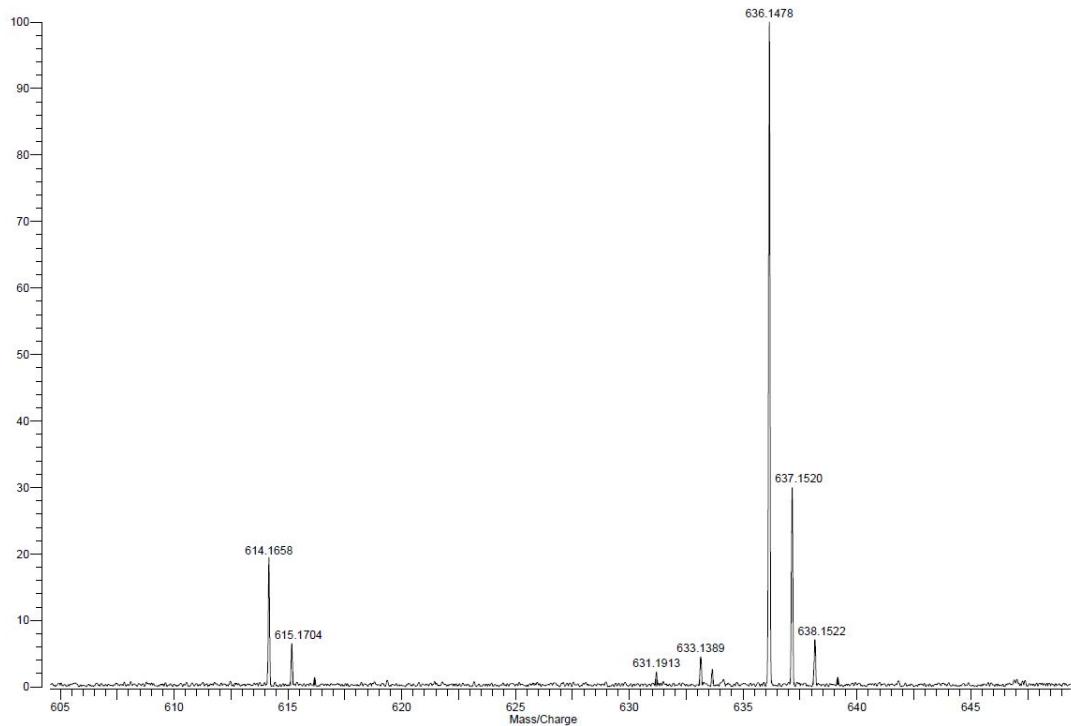
13l



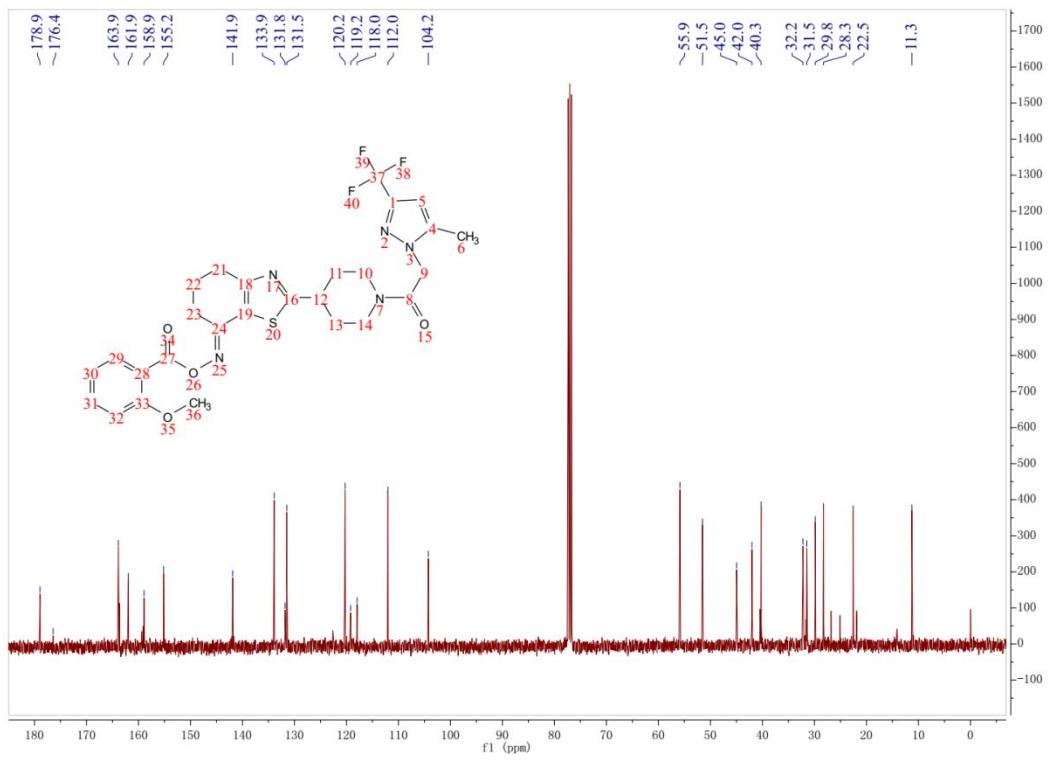
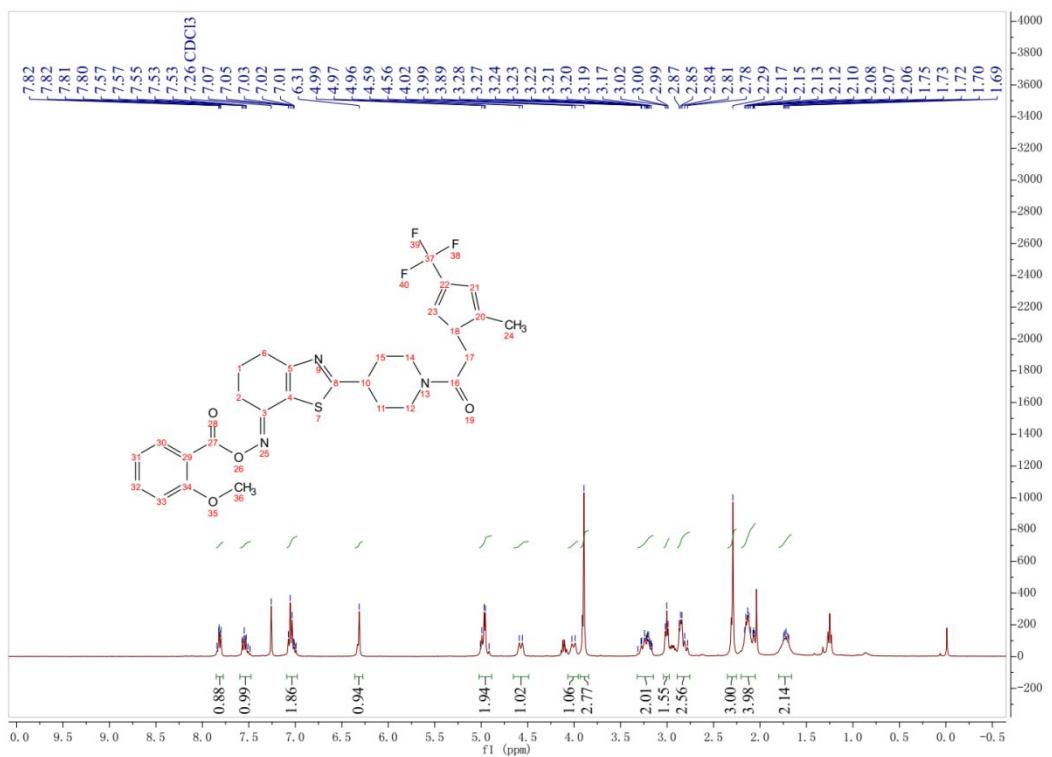


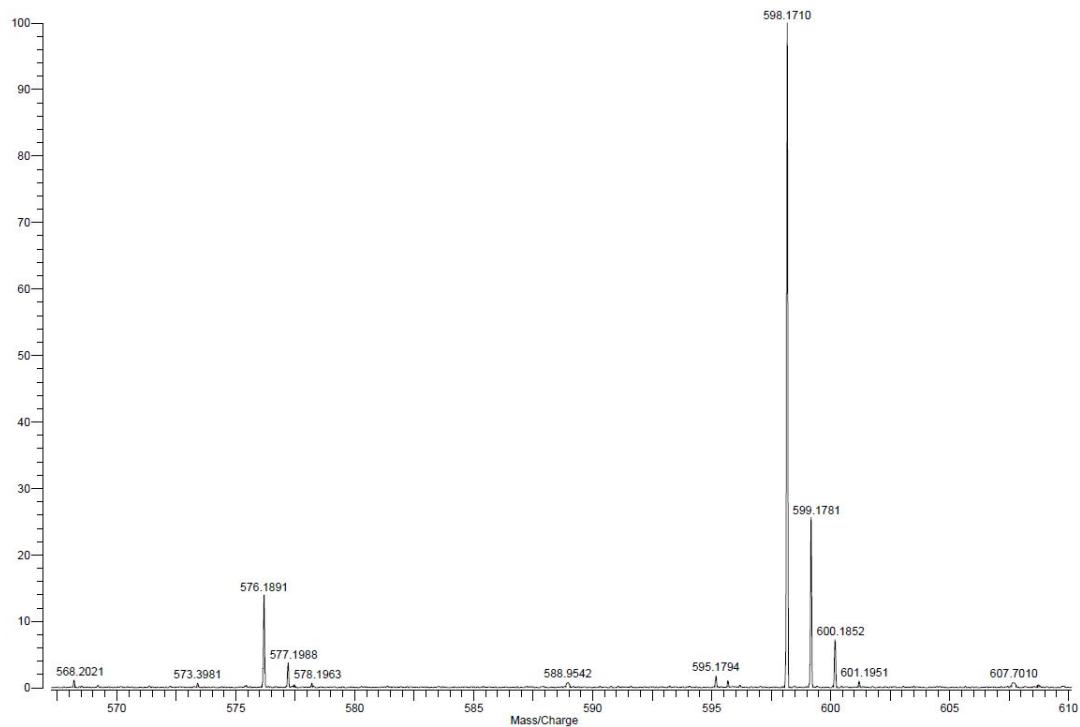
Varian QFT-ESI
File: 17-n_ESI.trans

Mode: Positive
Scans: 1
Date: 13-MAY-2020
Time: 15:35:35
Scale: 10.3080

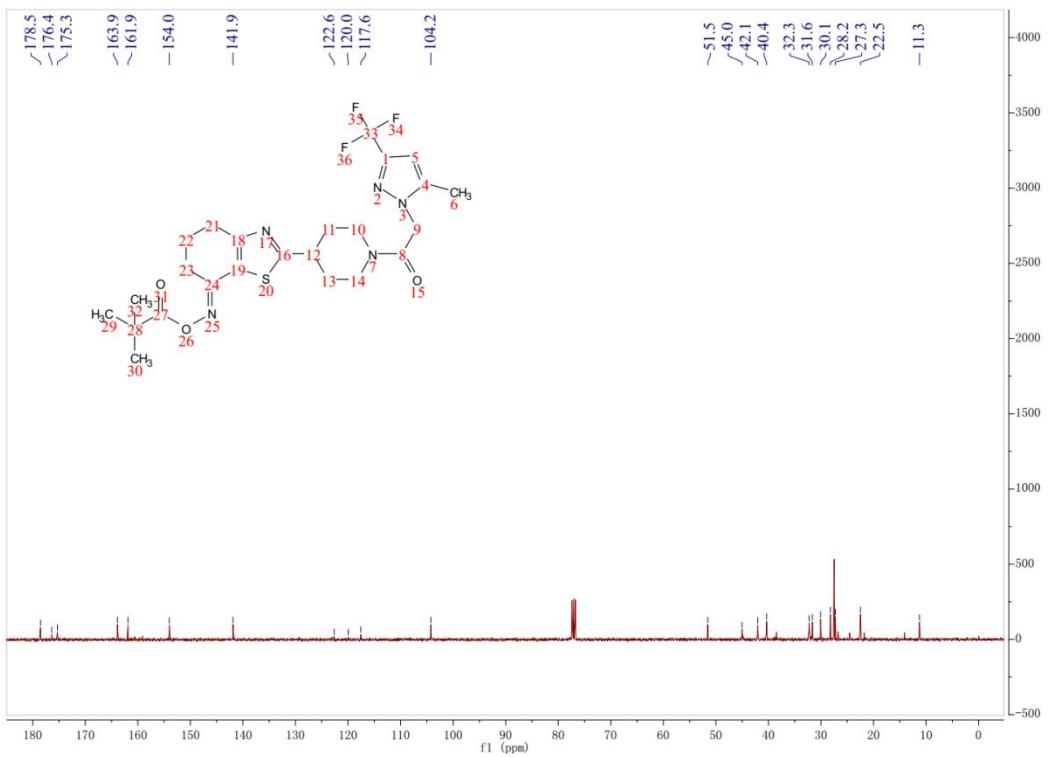
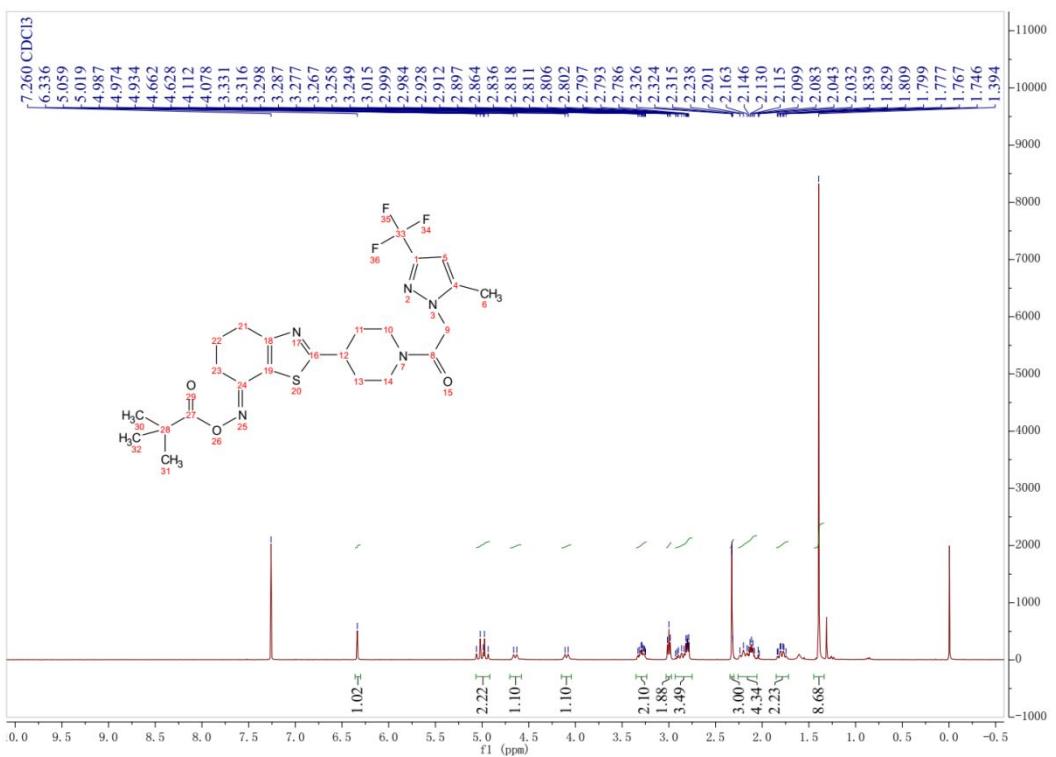


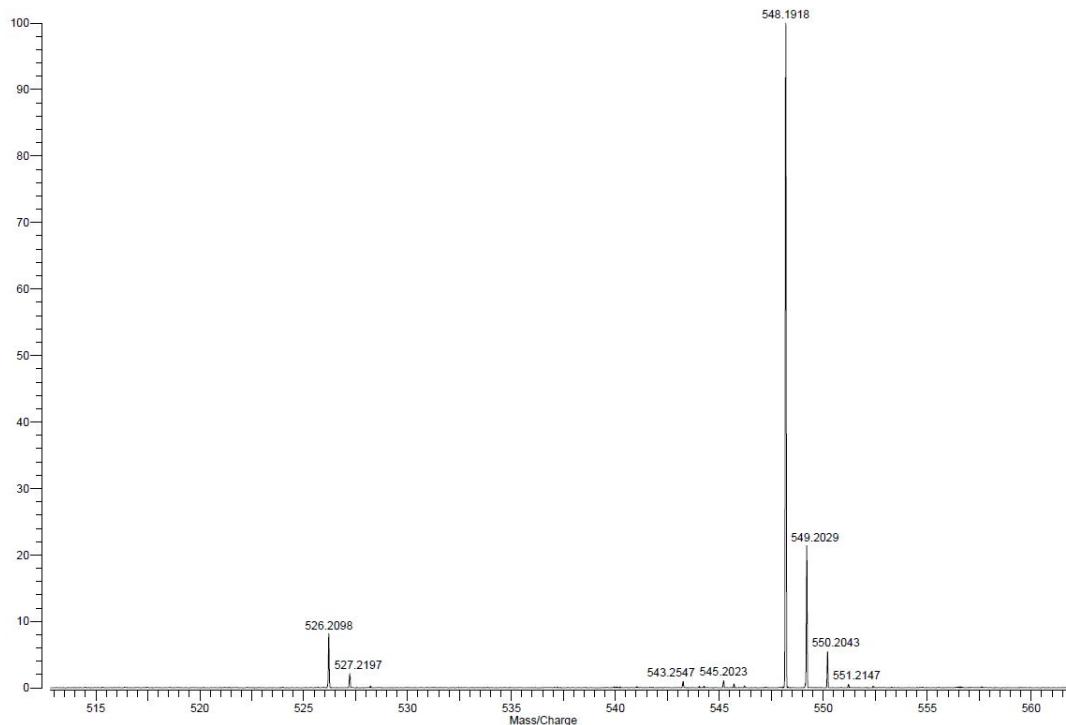
13m



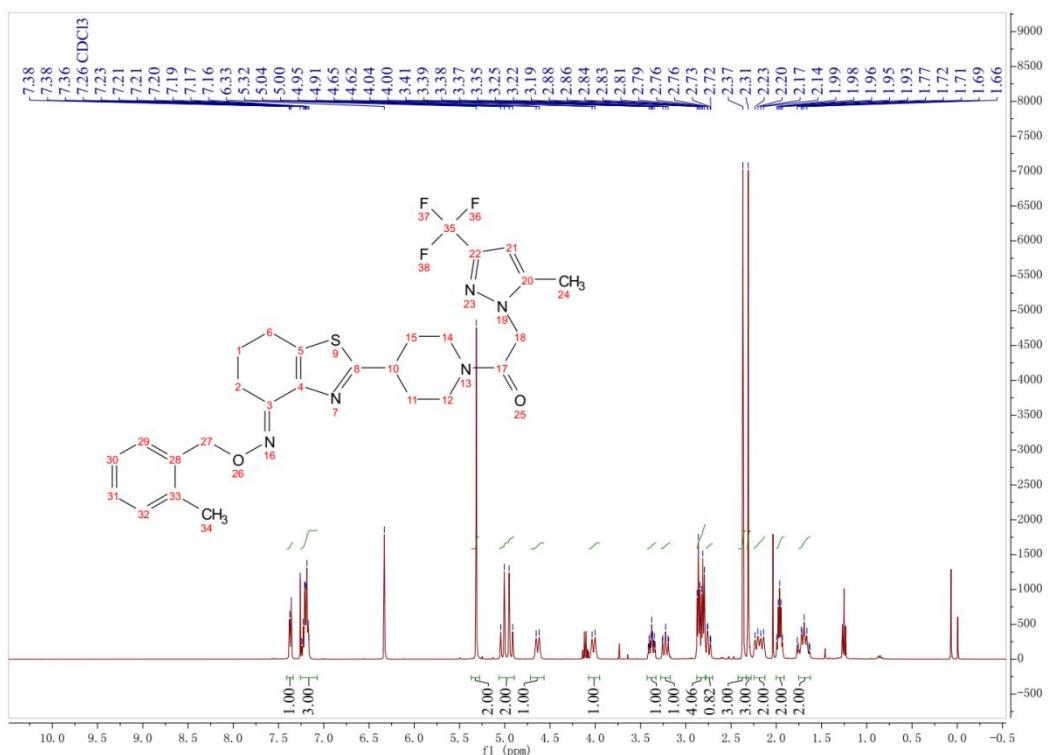


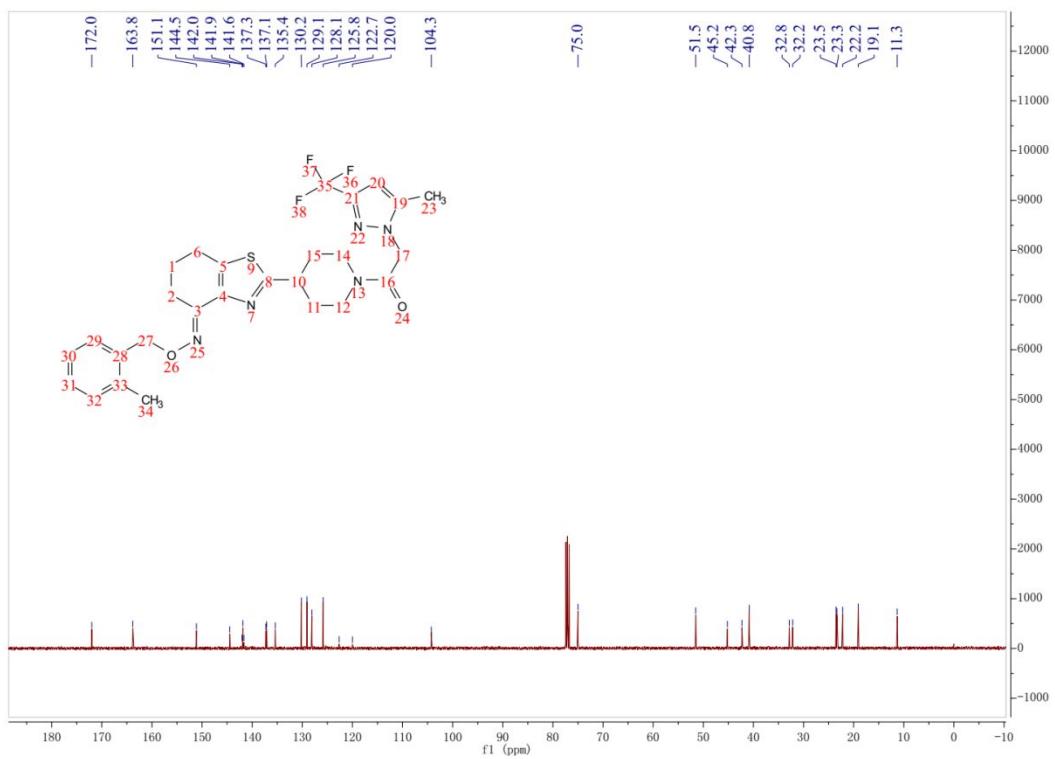
13n





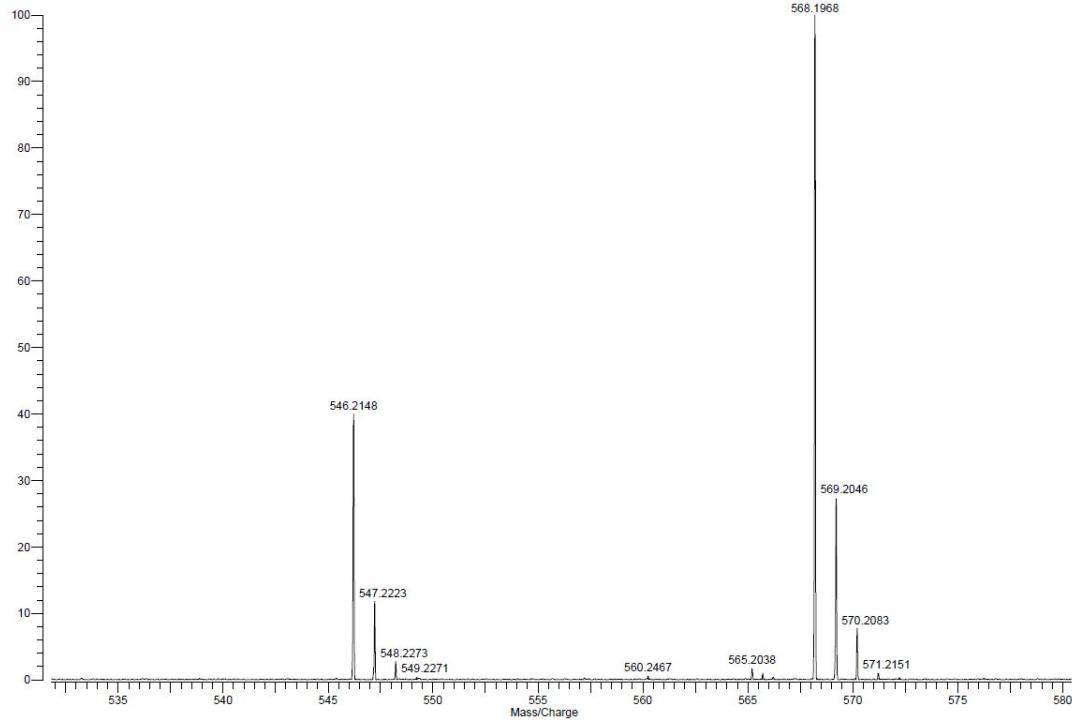
20a



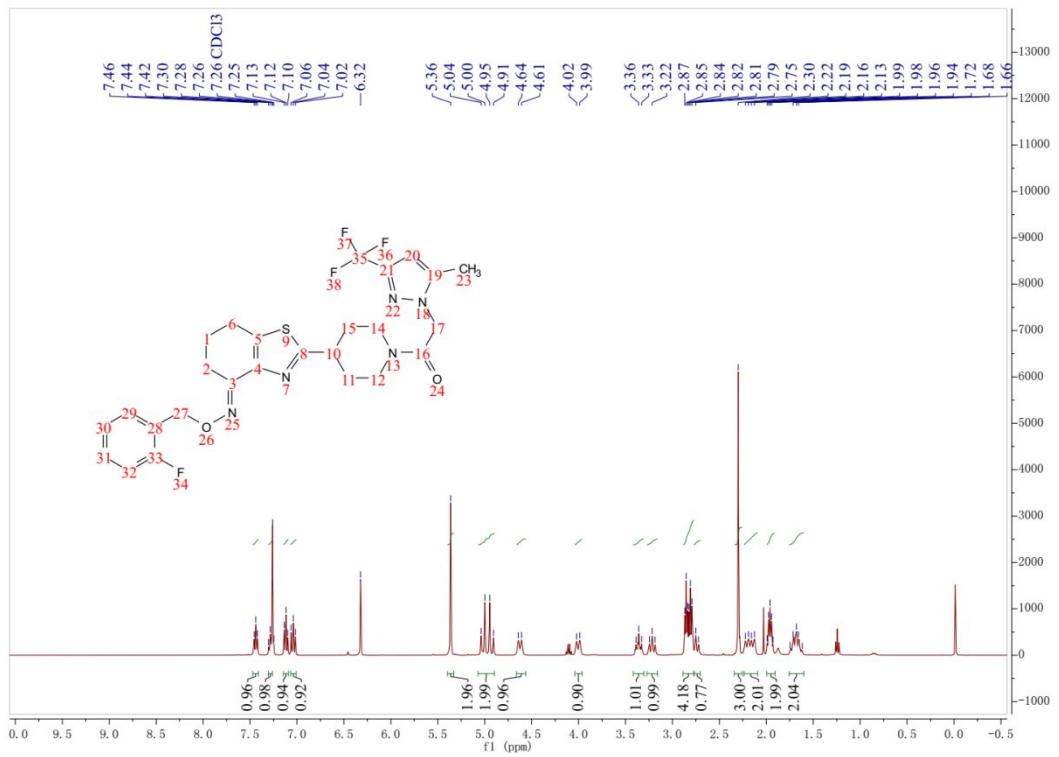


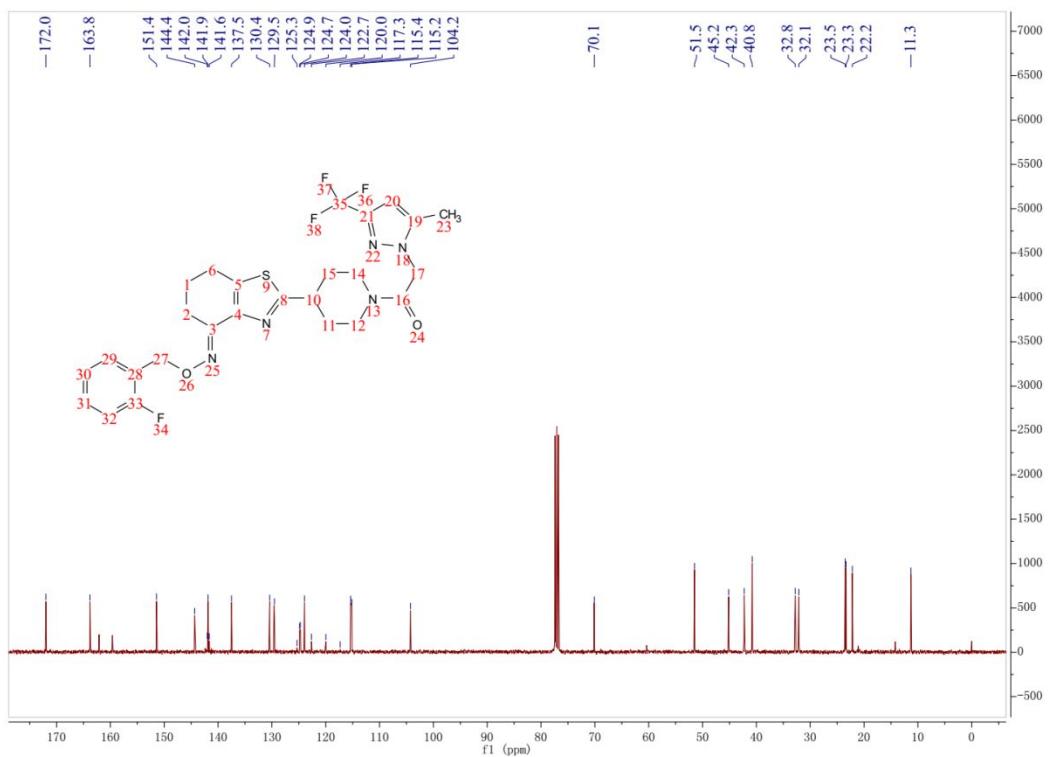
Varian QFT-ESI
File: 26a_ESI.trans

Mode: Positive
Scans: 1
Date: 13-MAY-2020
Time: 11:40:28
Scale: 2.5430



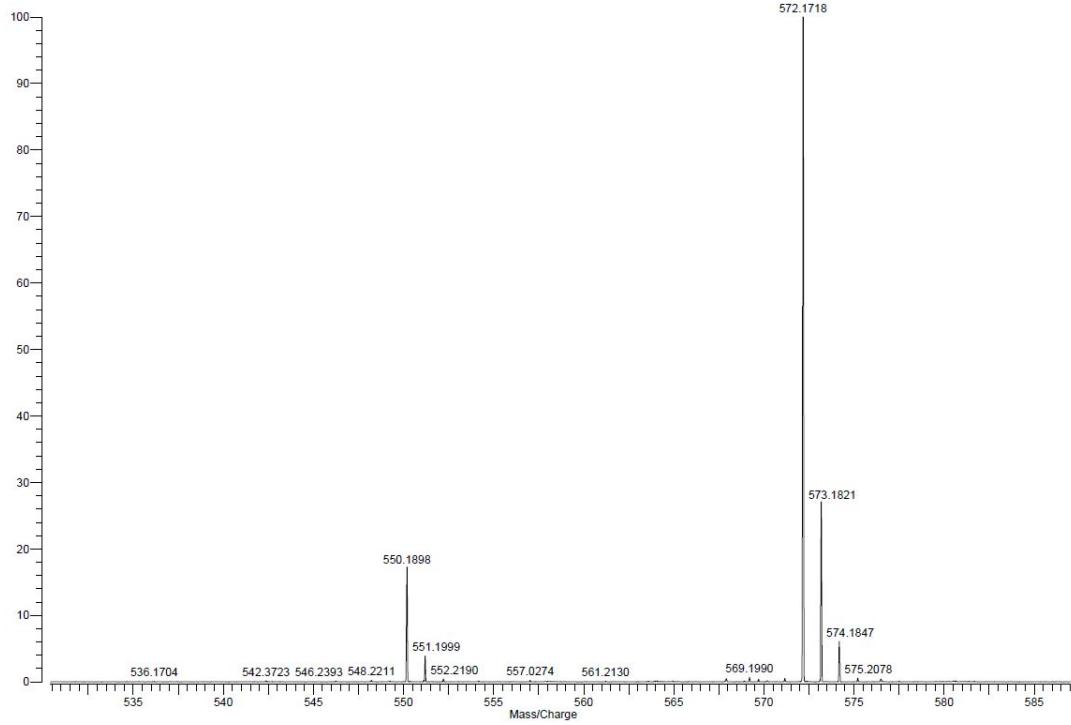
20b





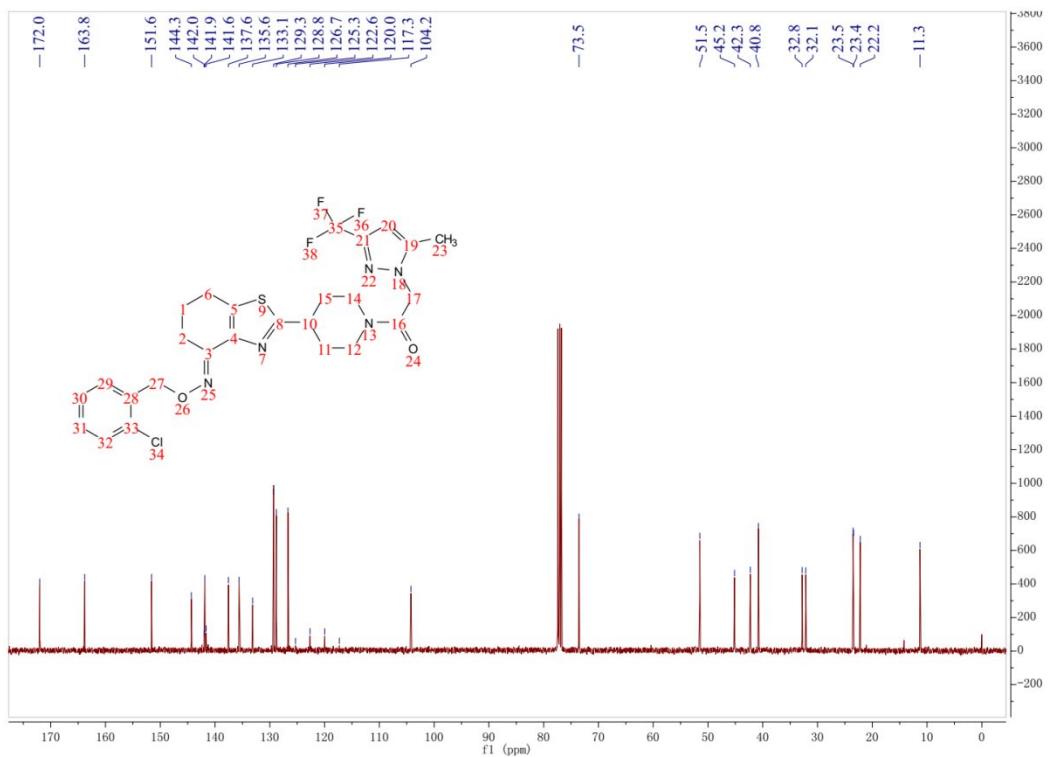
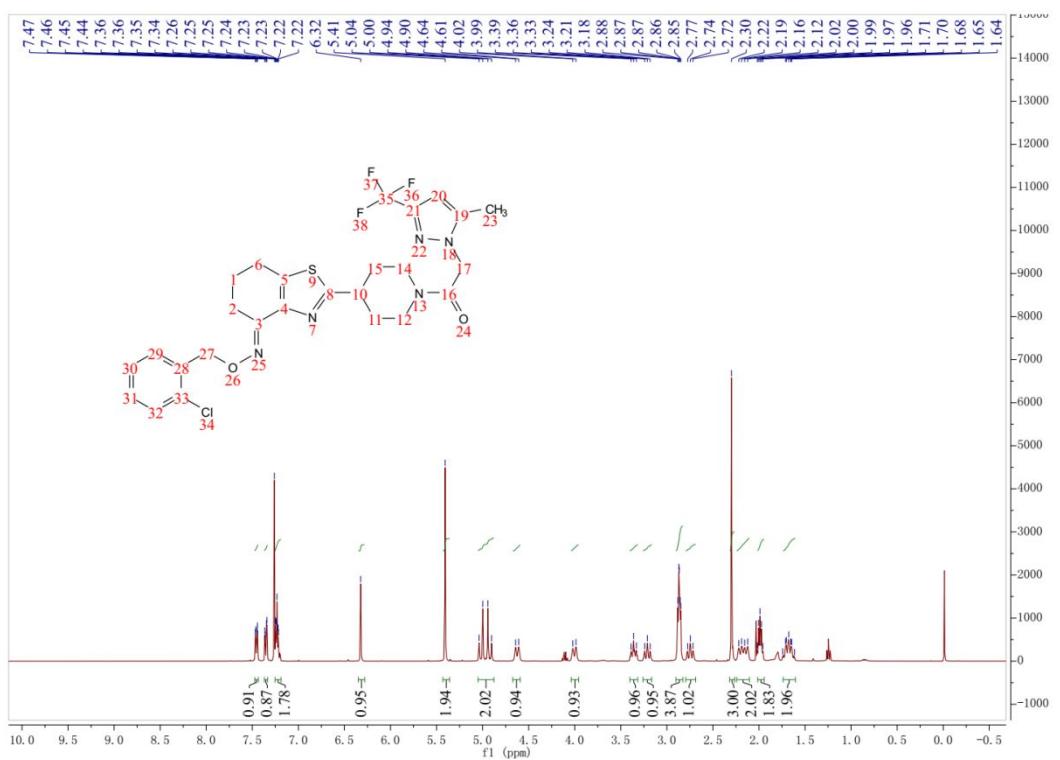
Varian QFT-ESI
File: 26b_ESI.trans

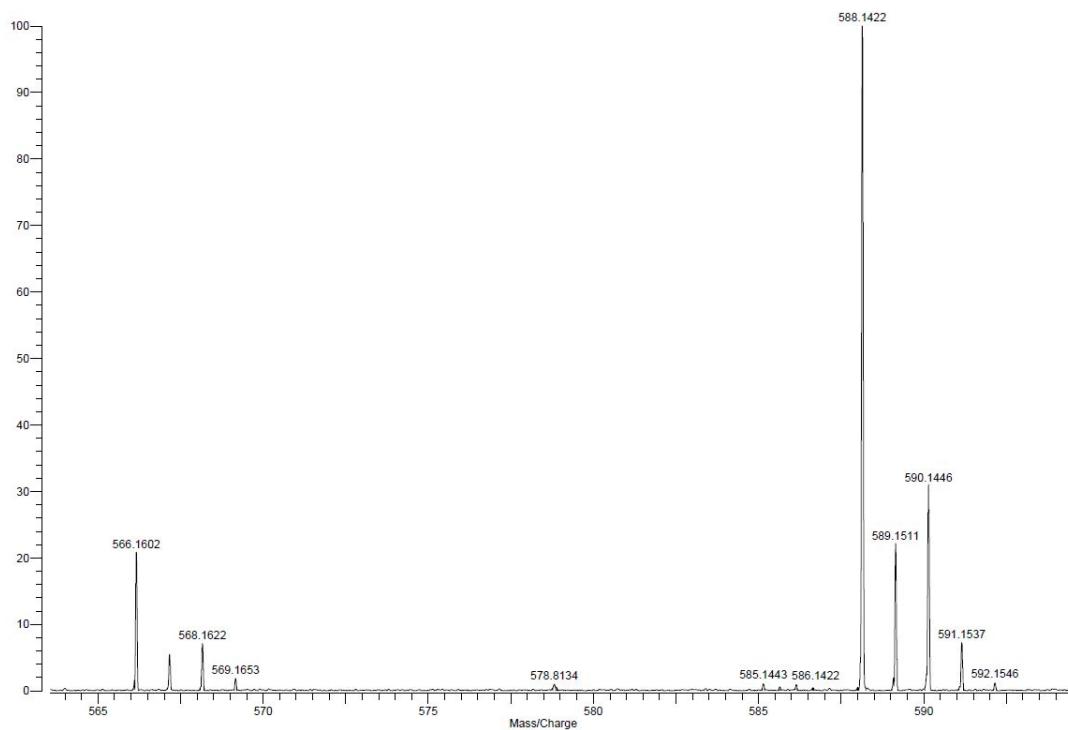
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Scans: 1
Date: 13-MAY-2020
Time: 15:42:51
Scale: 0.6066



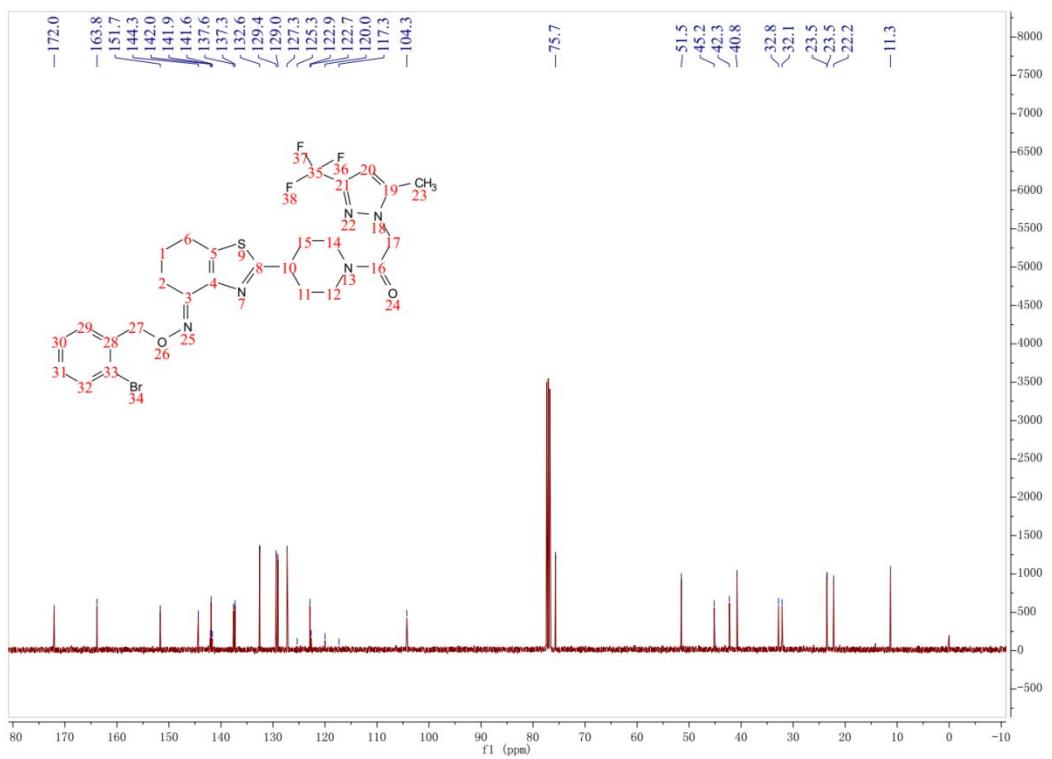
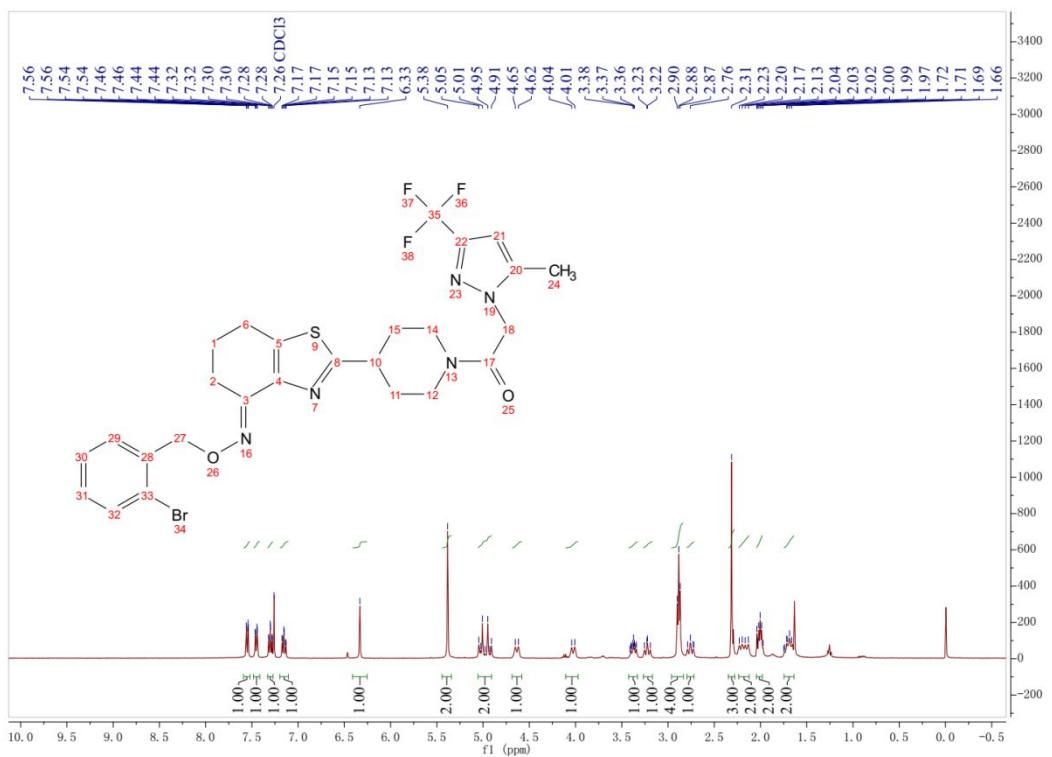
20c

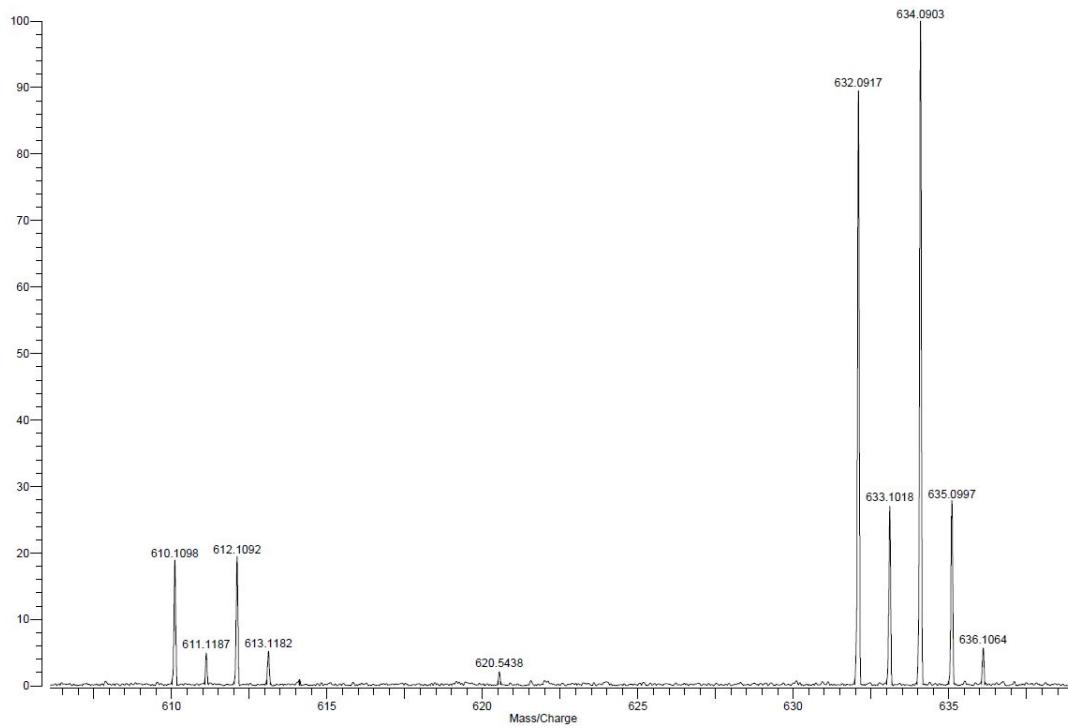
S103



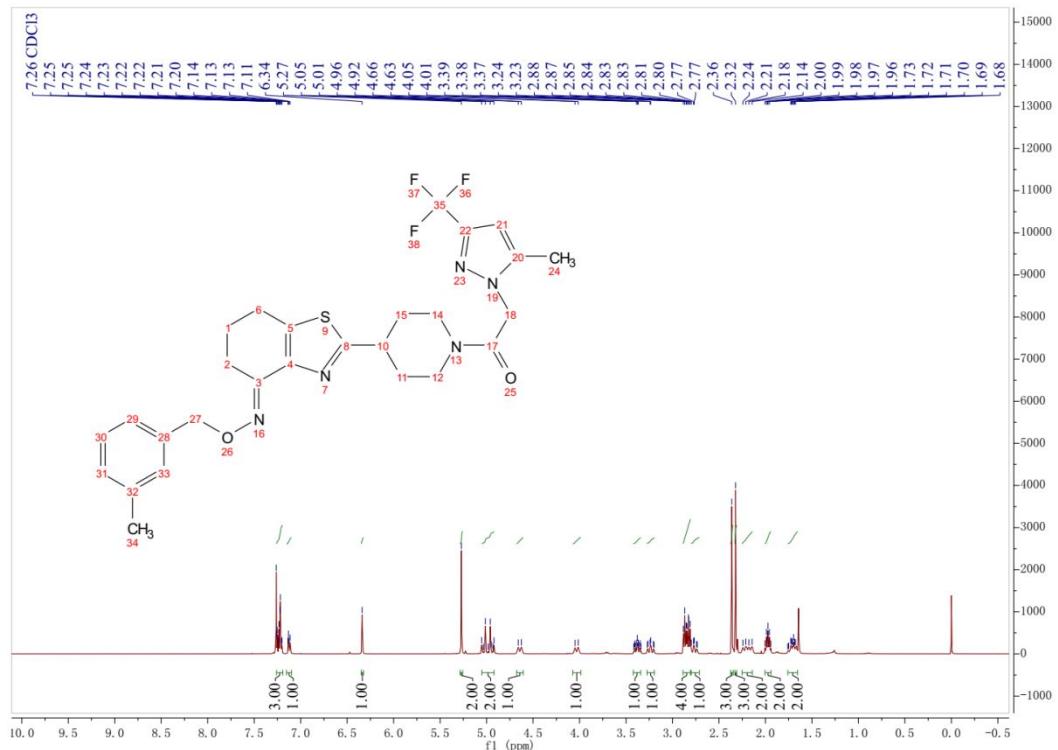


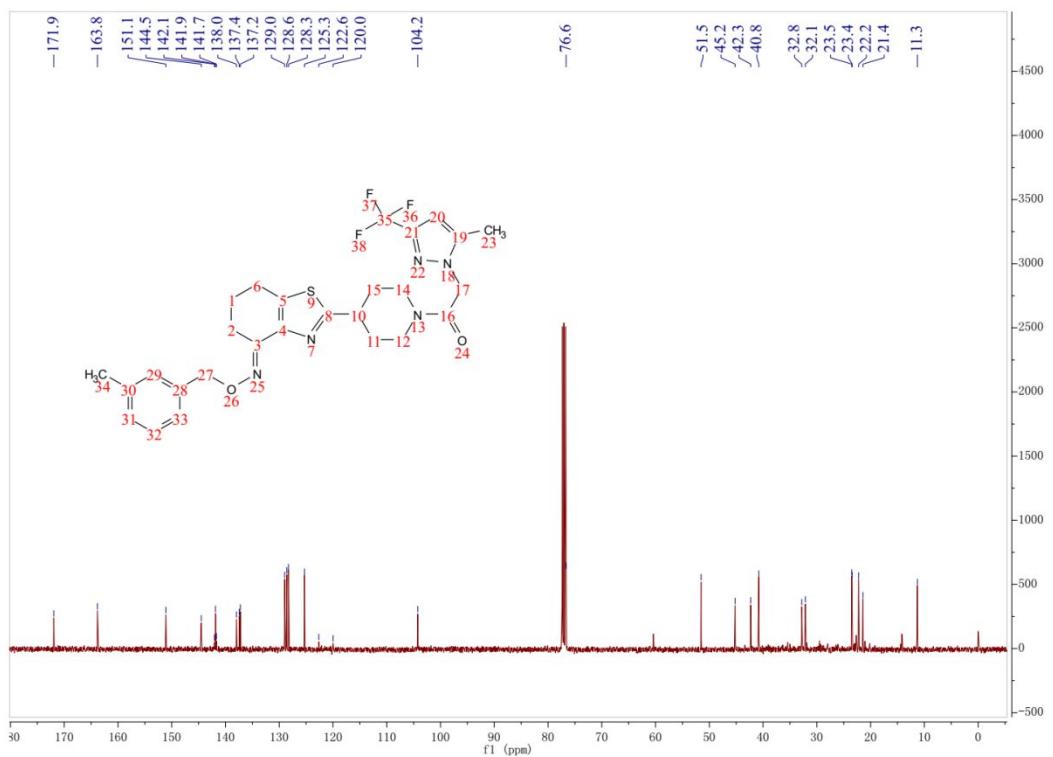
20d





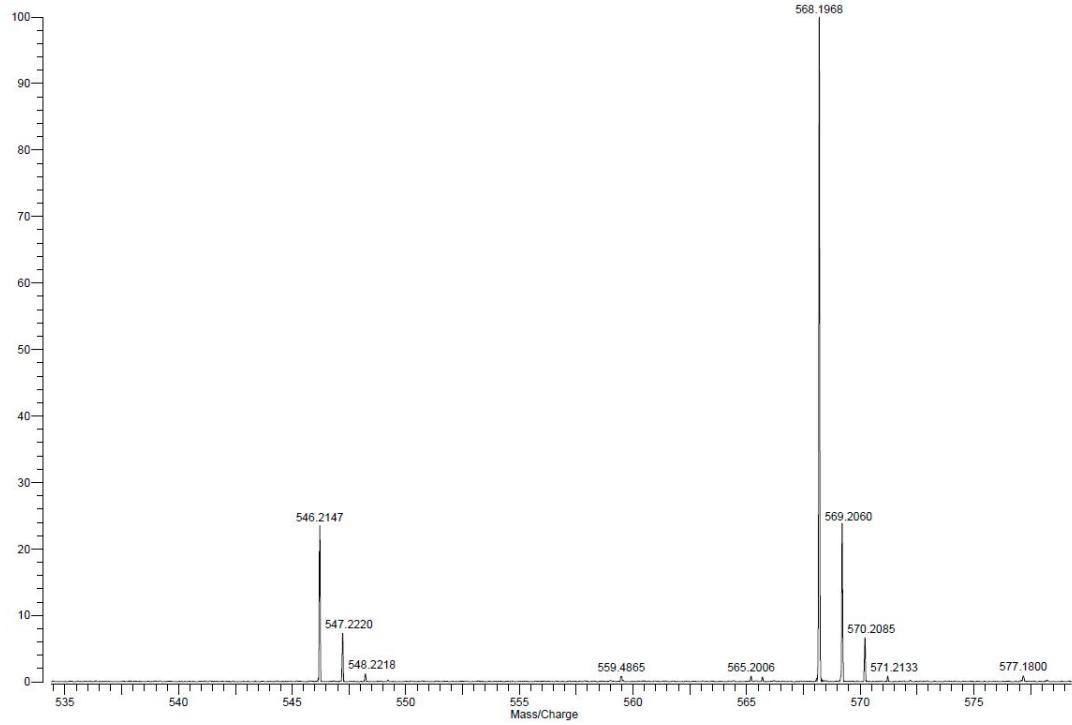
20e



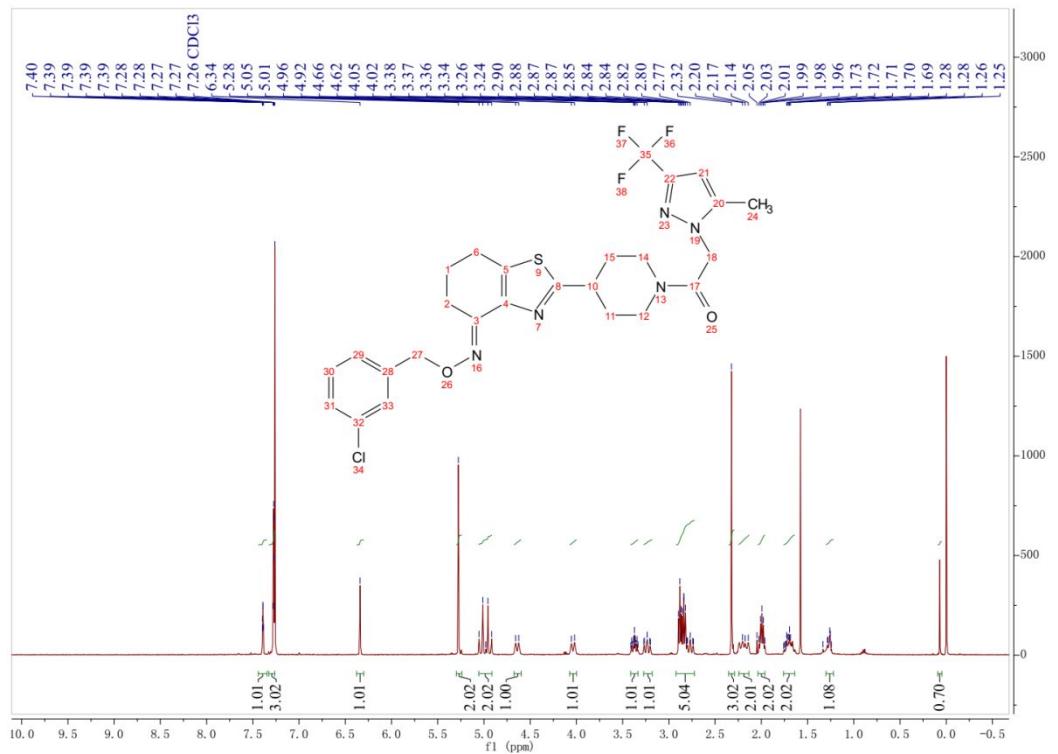


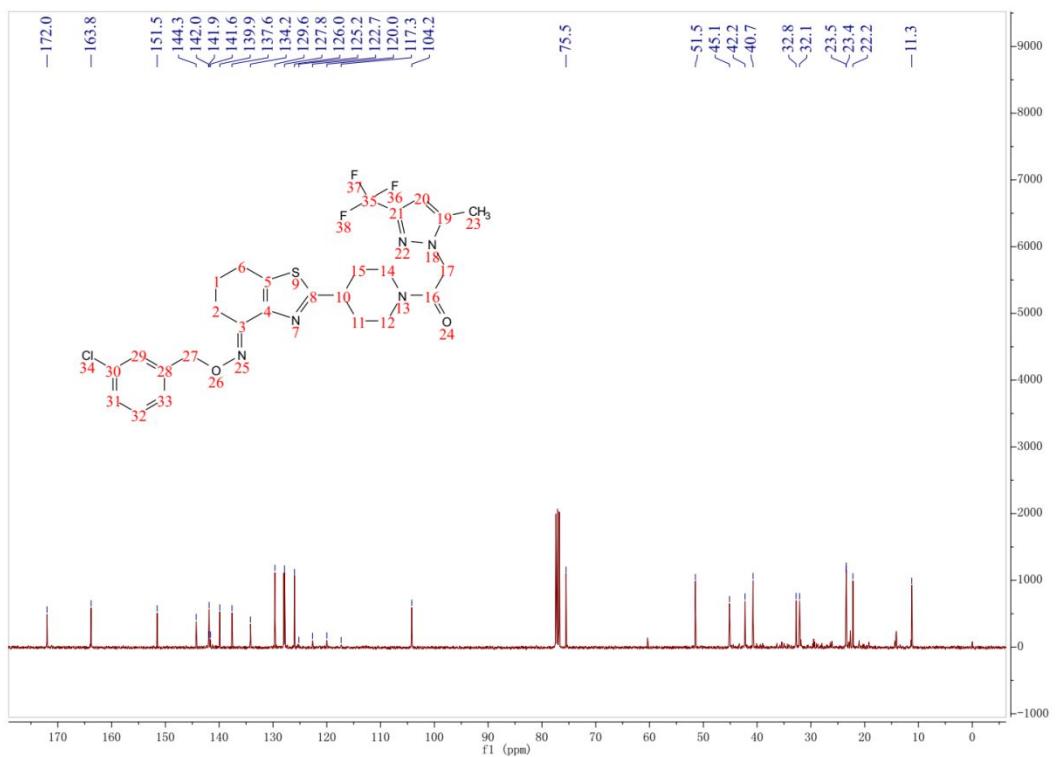
Varian QFT-ESI
File: 26e_ESI.trans

Mode: Positive
Scans: 1
Date: 13-MAY-2020
Time: 11:42:55
Scale: 2.4240



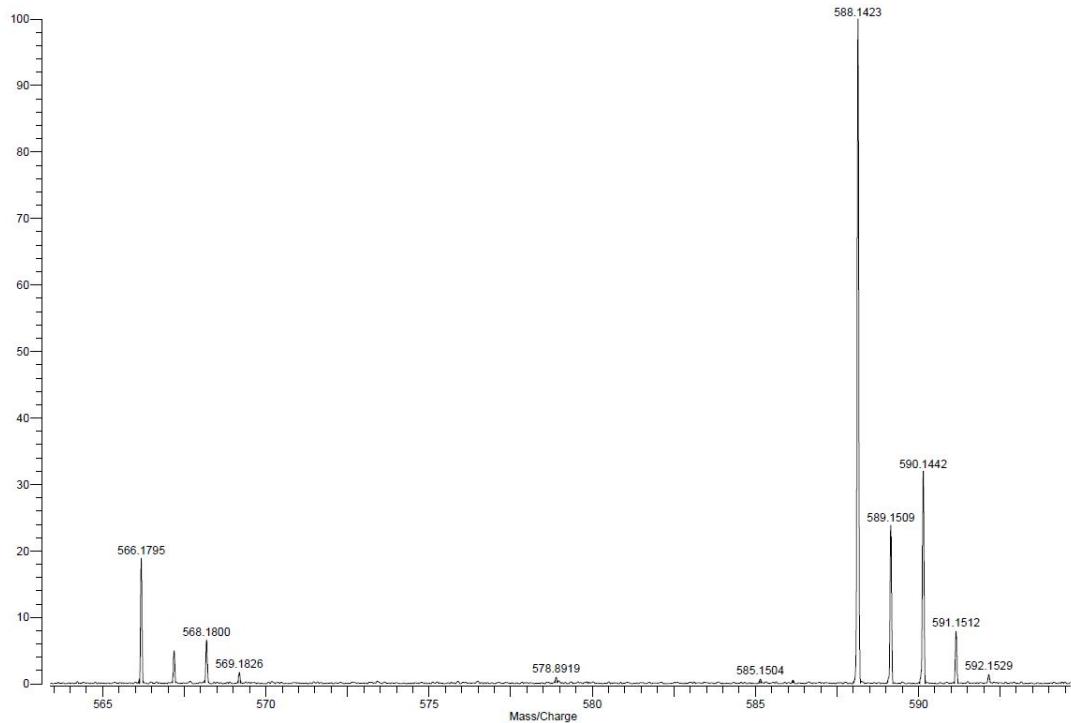
20f





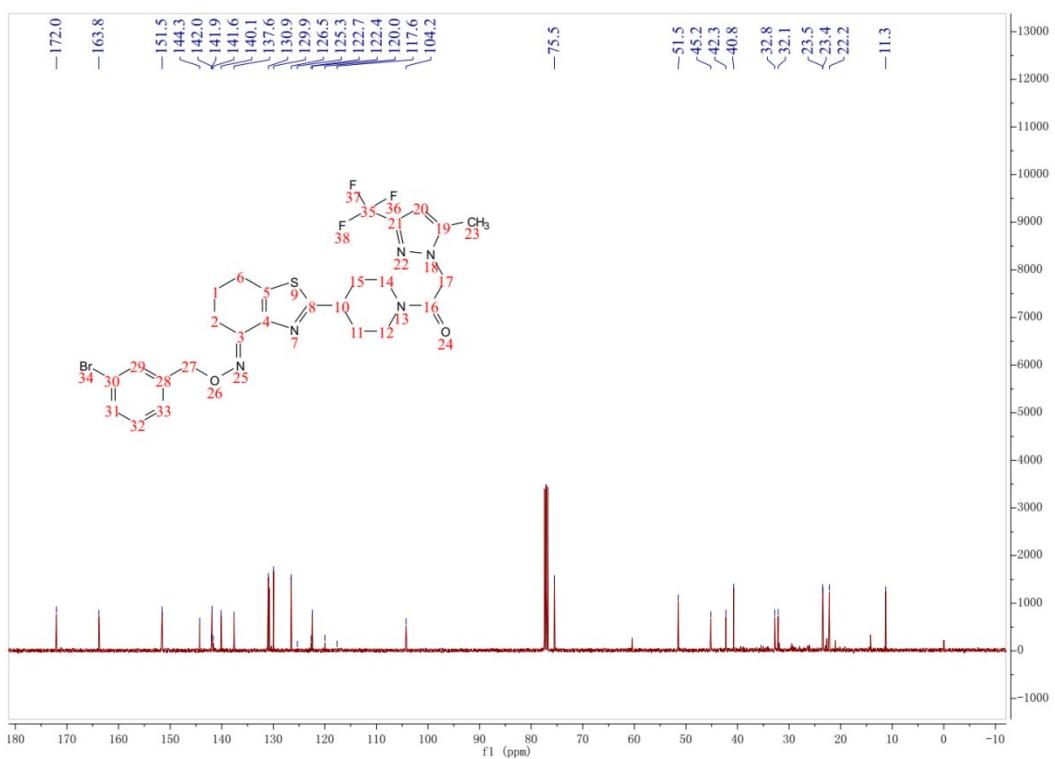
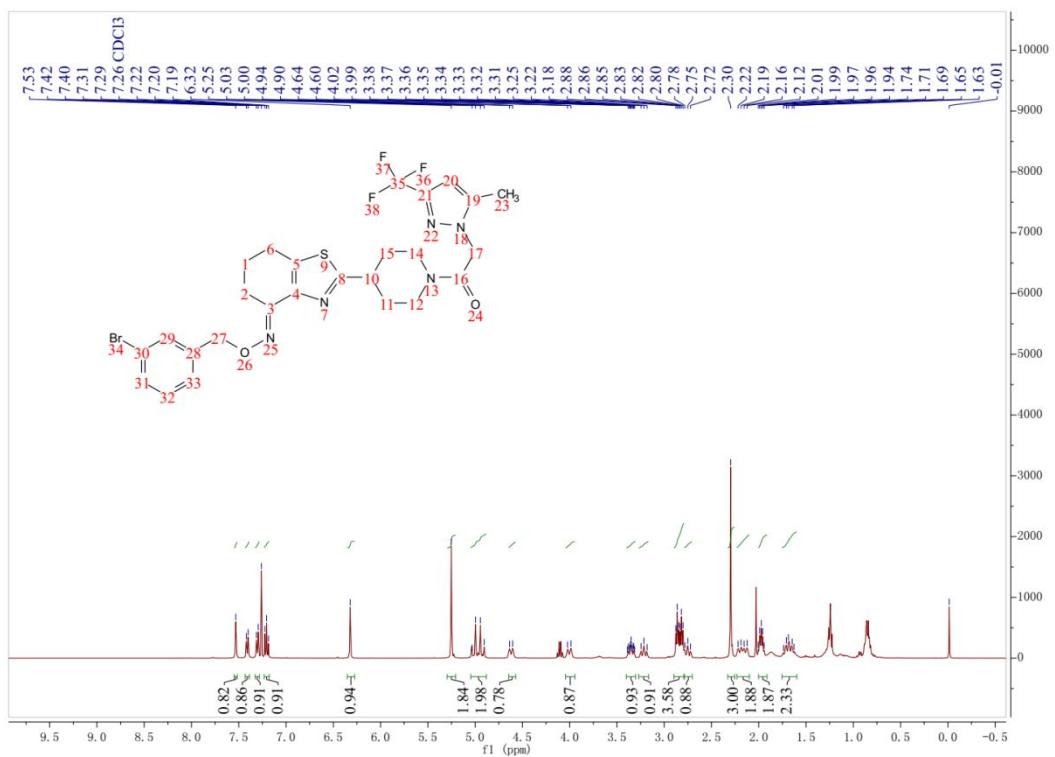
Varian QFT-ESI
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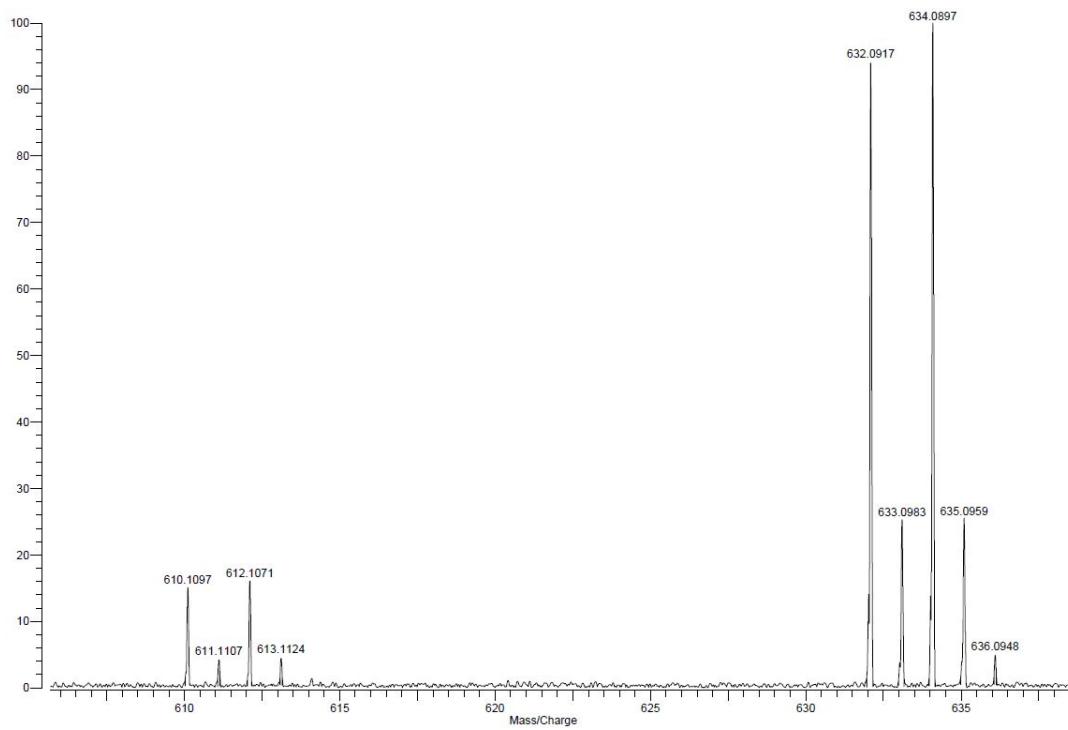
Mode: Positive
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Date: 13-MAY-2020
Time: 12:09:18
Scale: 4.2307



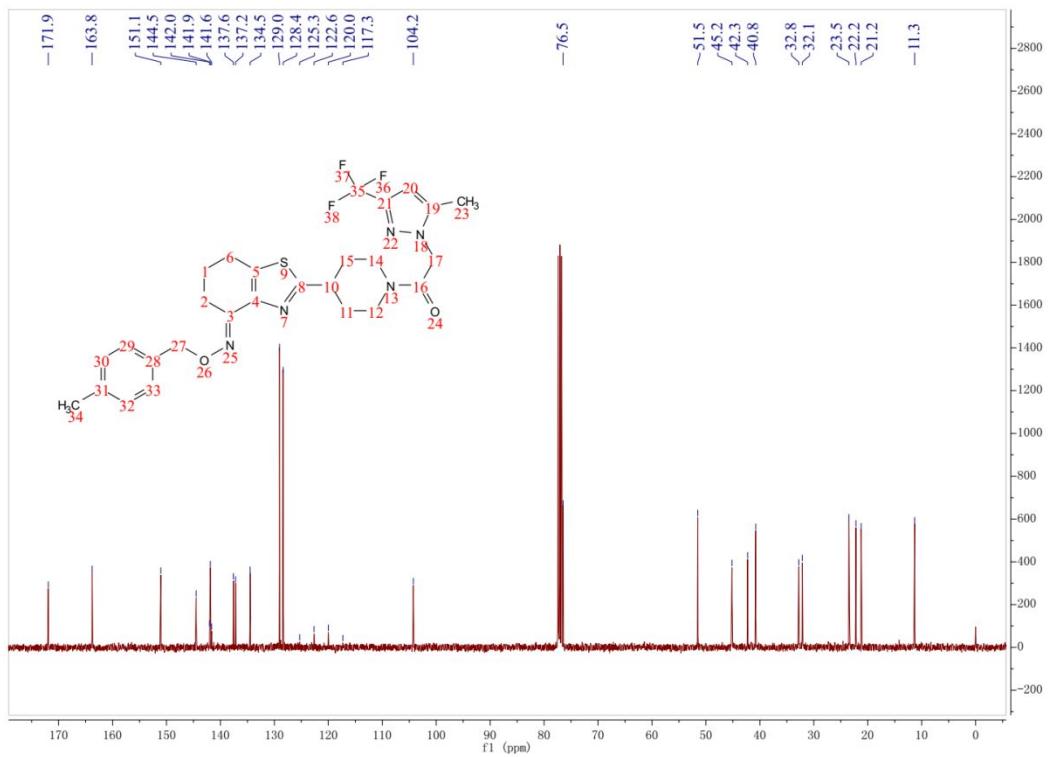
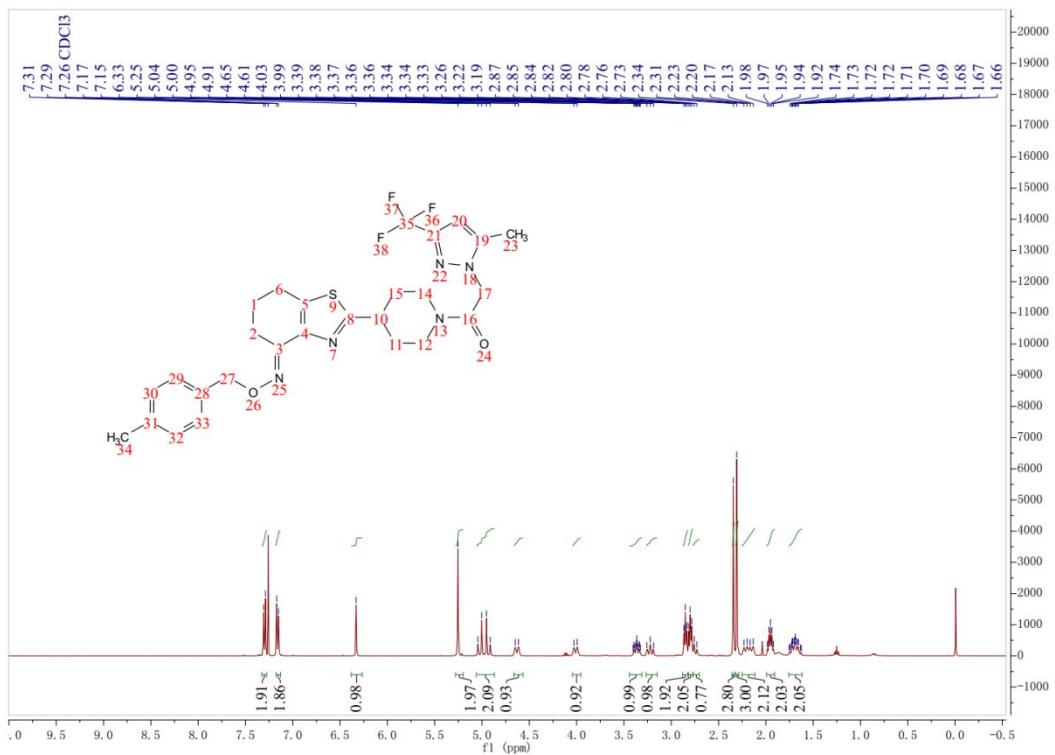
20g

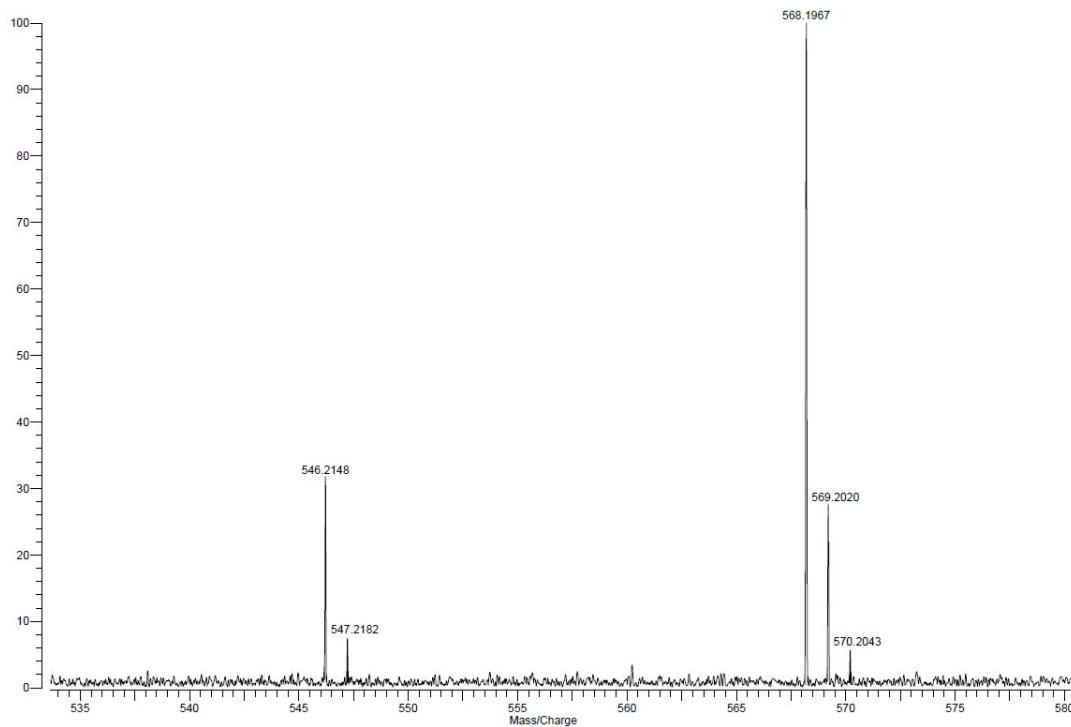
S110



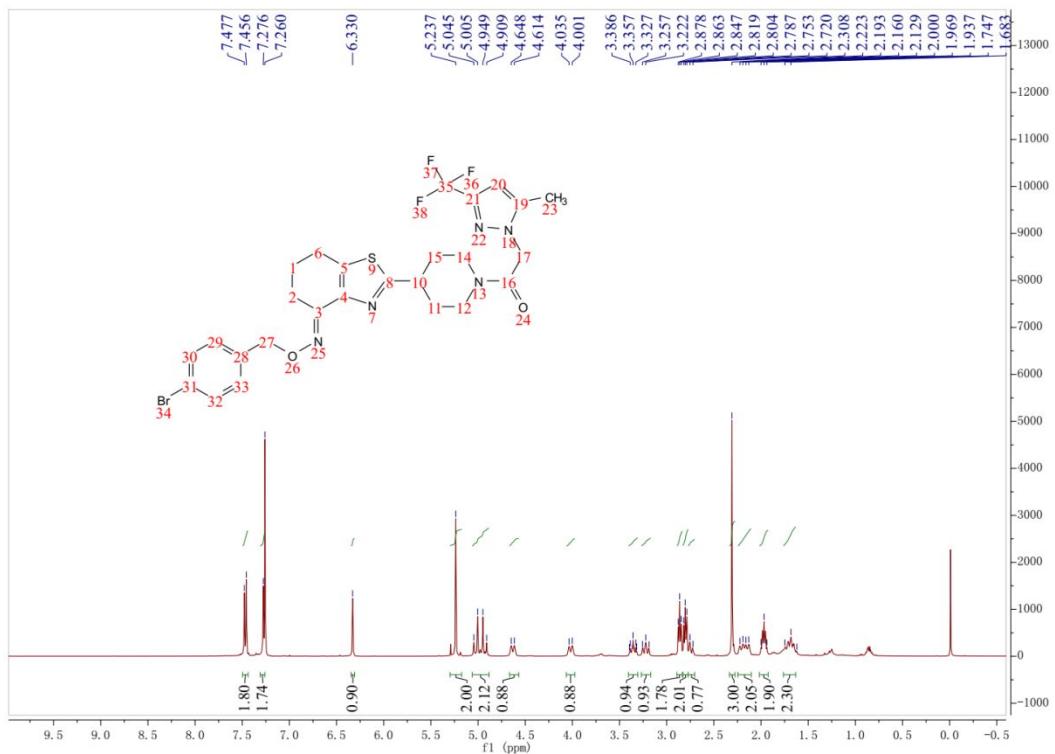


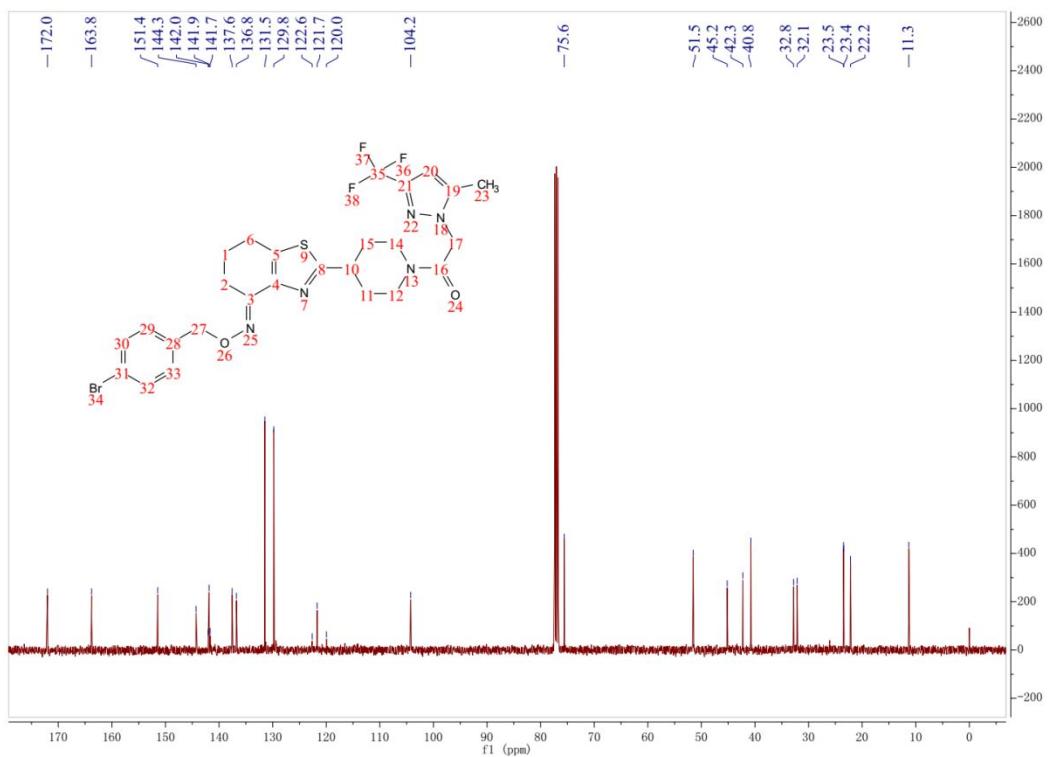
20h





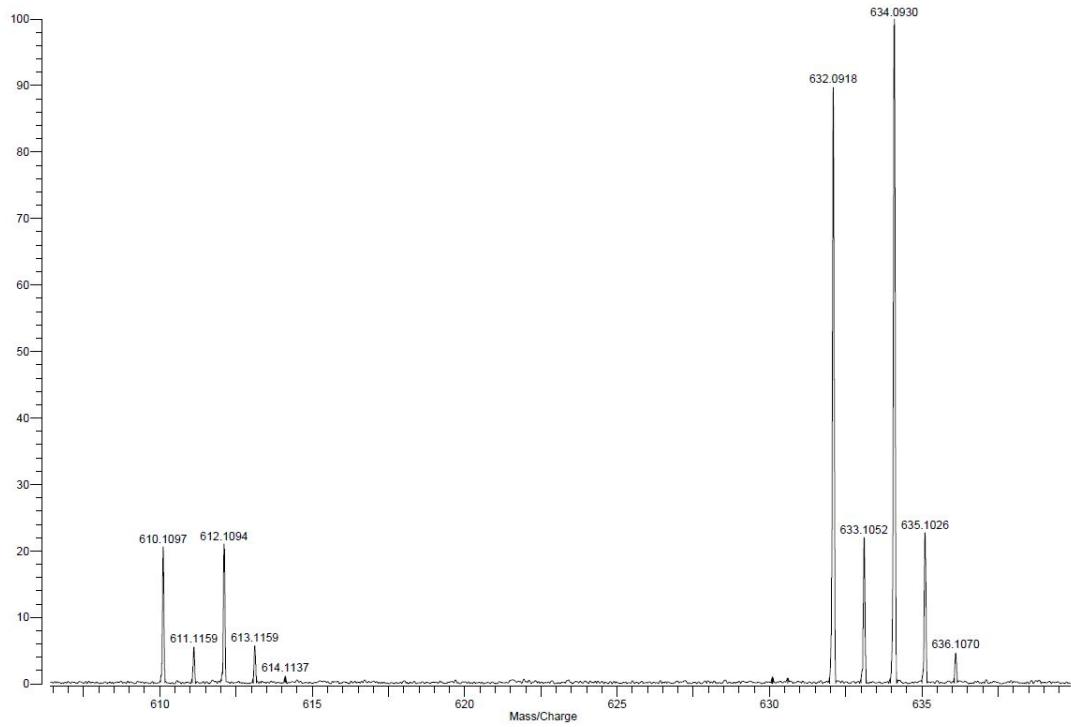
20i



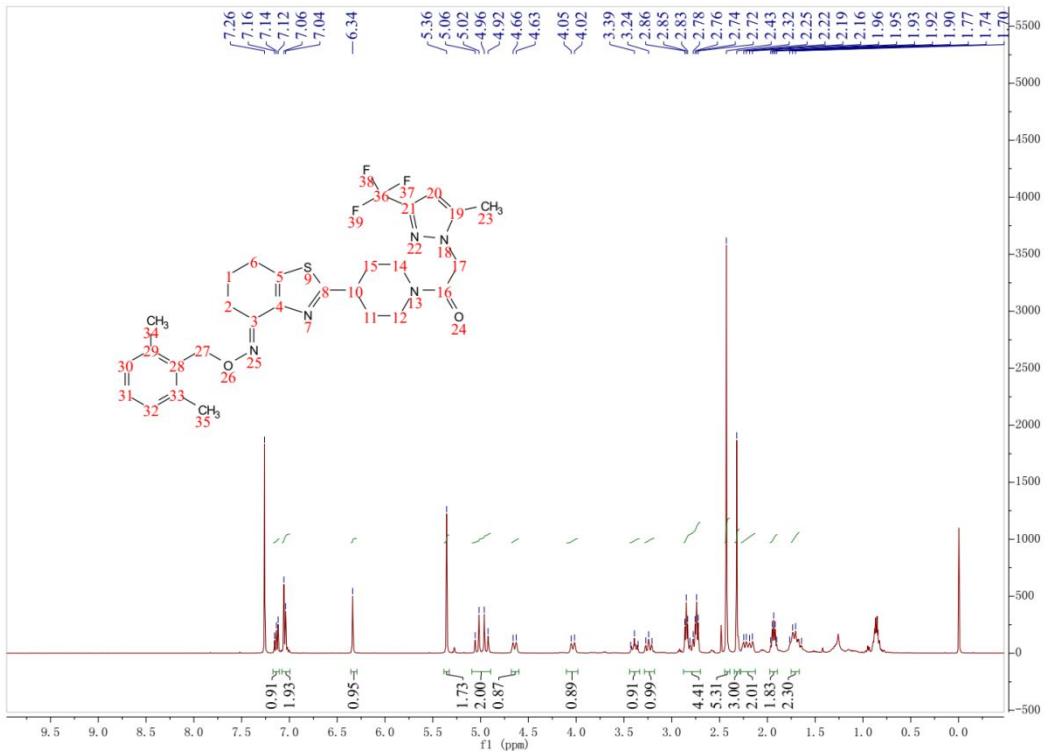


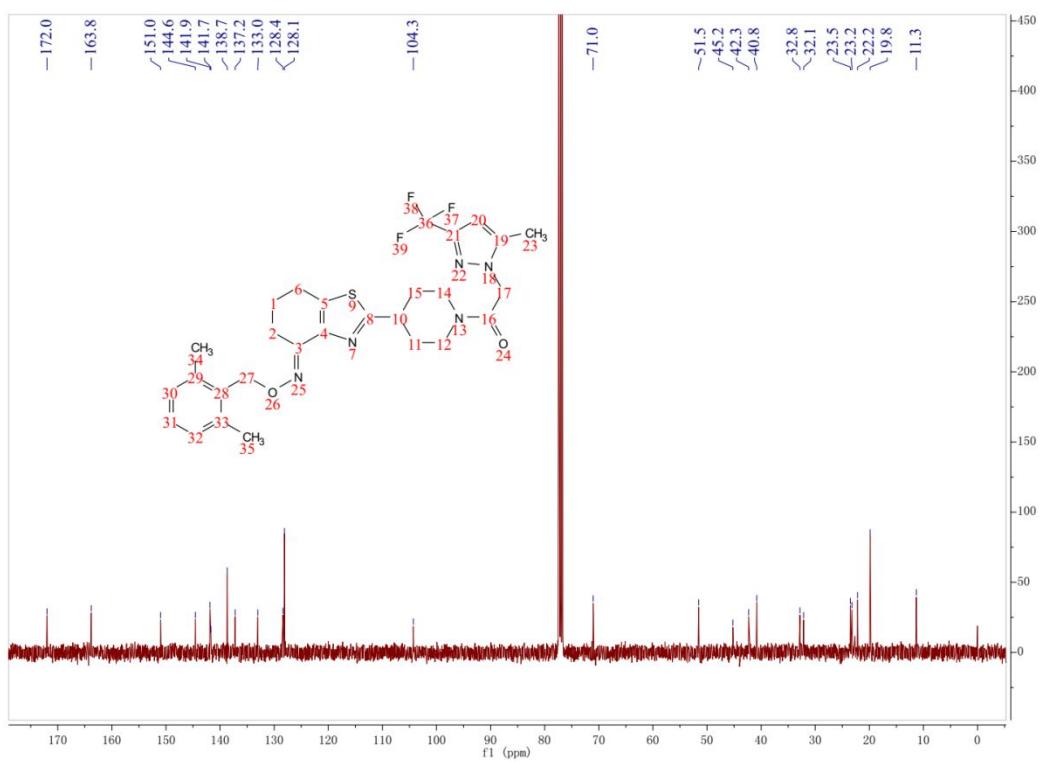
Varian QFT-ESI
File: 26i_ESI.trans

Mode: Positive Date: 13-MAY-2020
Scans: 1 Time: 12:04:14
Scale: 7.0319



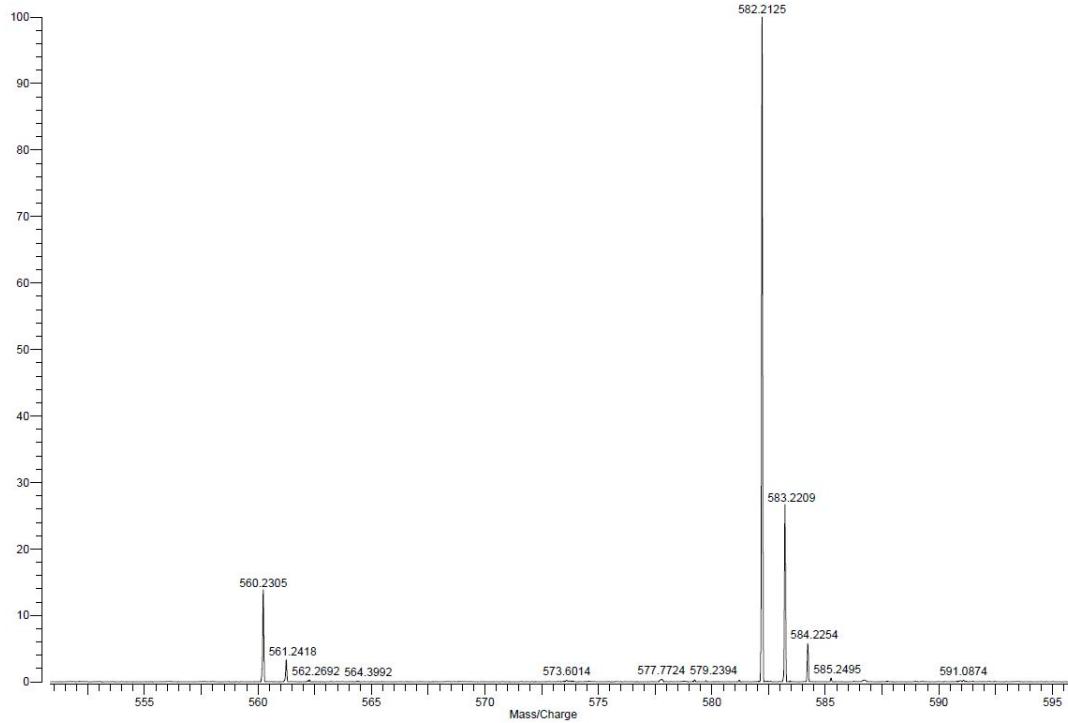
20j





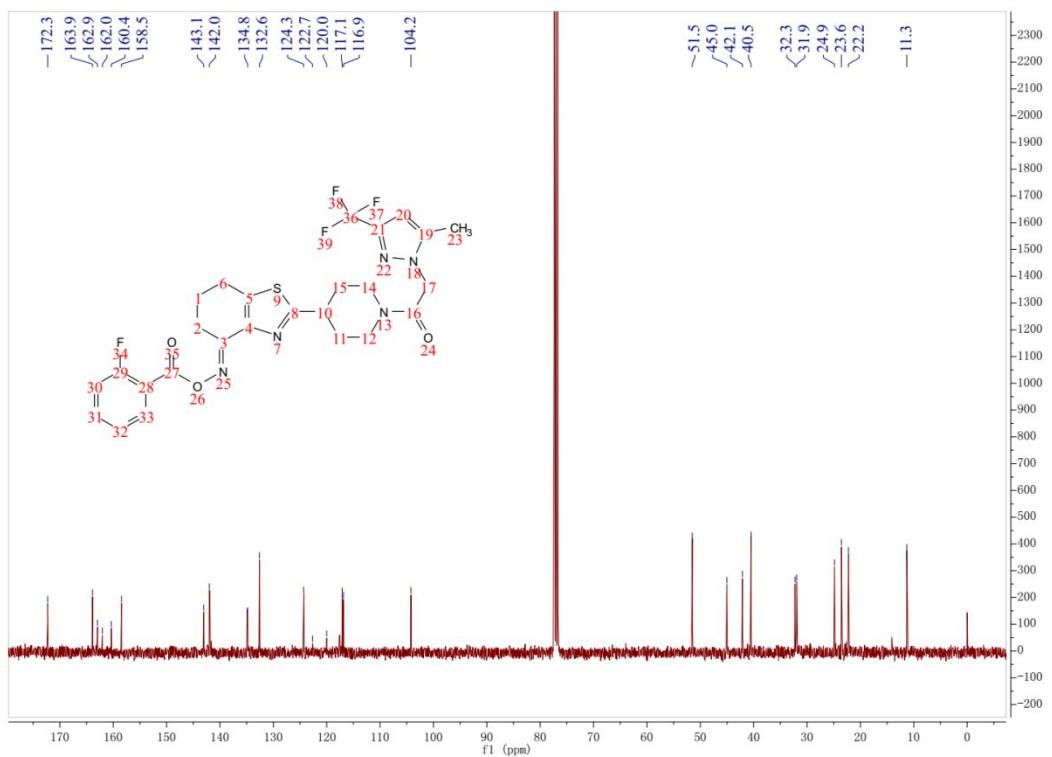
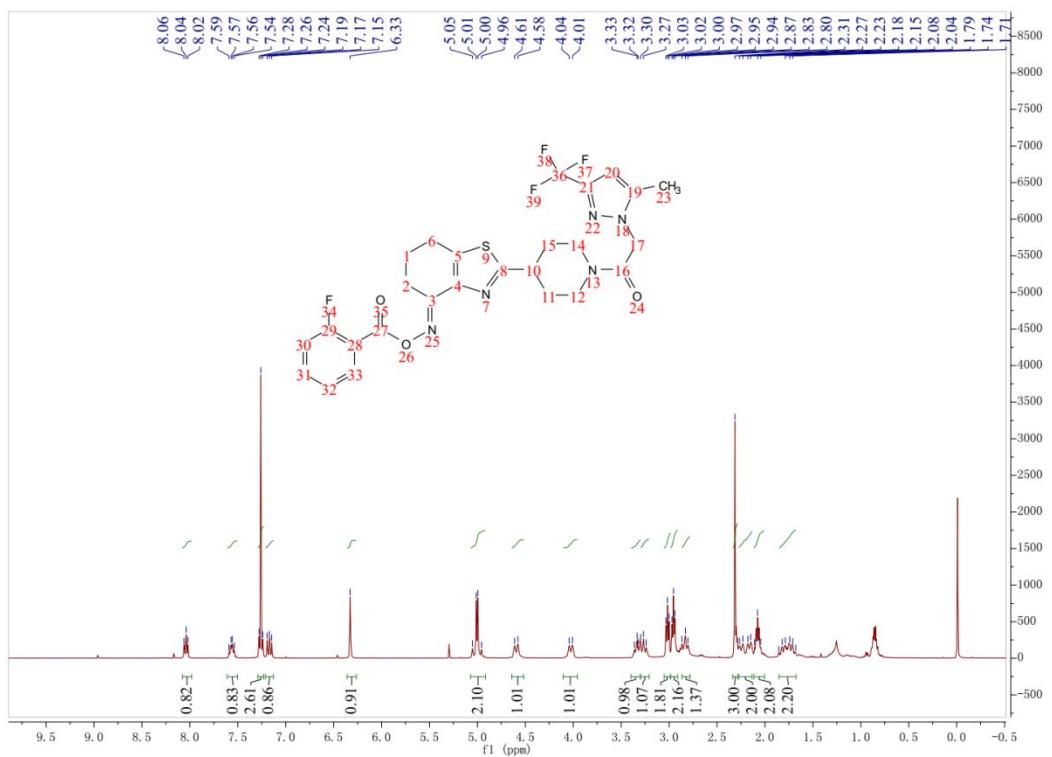
Varian QFT-ESI
File: 26_ESI.trans

Mode: Positive
Scans: 1
Date: 13-MAY-2020
Time: 15:50:58
Scale: 0.8281



21

S117



Varian QFT-ESI
File: 27_ESI.trans

Mode: Positive
Scans: 1
Date: 13-MAY-2020
Time: 15:23:16
Scale: 0.7798

