

Supporting Information

Design, Synthesis, Antibacterial, and Antifungal Evaluation of Phenylthiazole Derivatives Containing a 1,3,4-Thiadiazole Thione Moiety

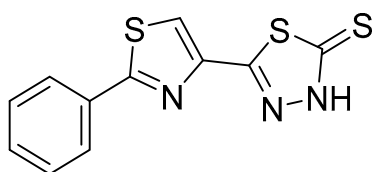
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† These two authors contributed equally to this work.

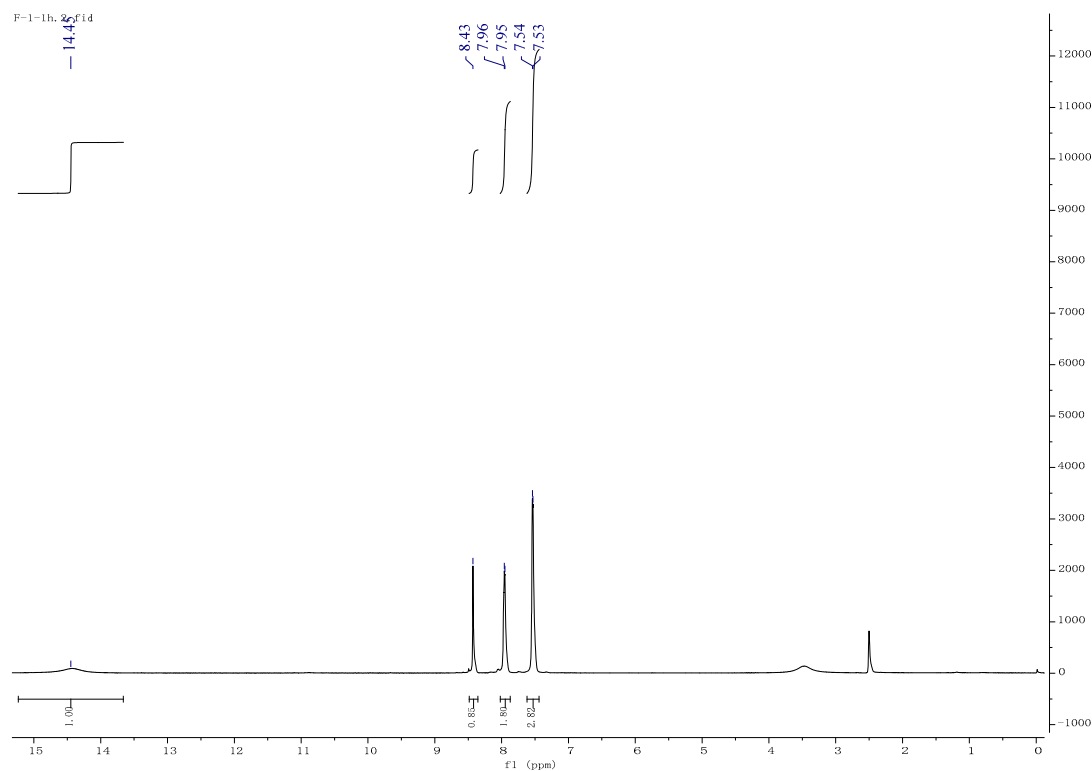
Table of Contents

1. The structure and data of target compounds (5a-5p)	2
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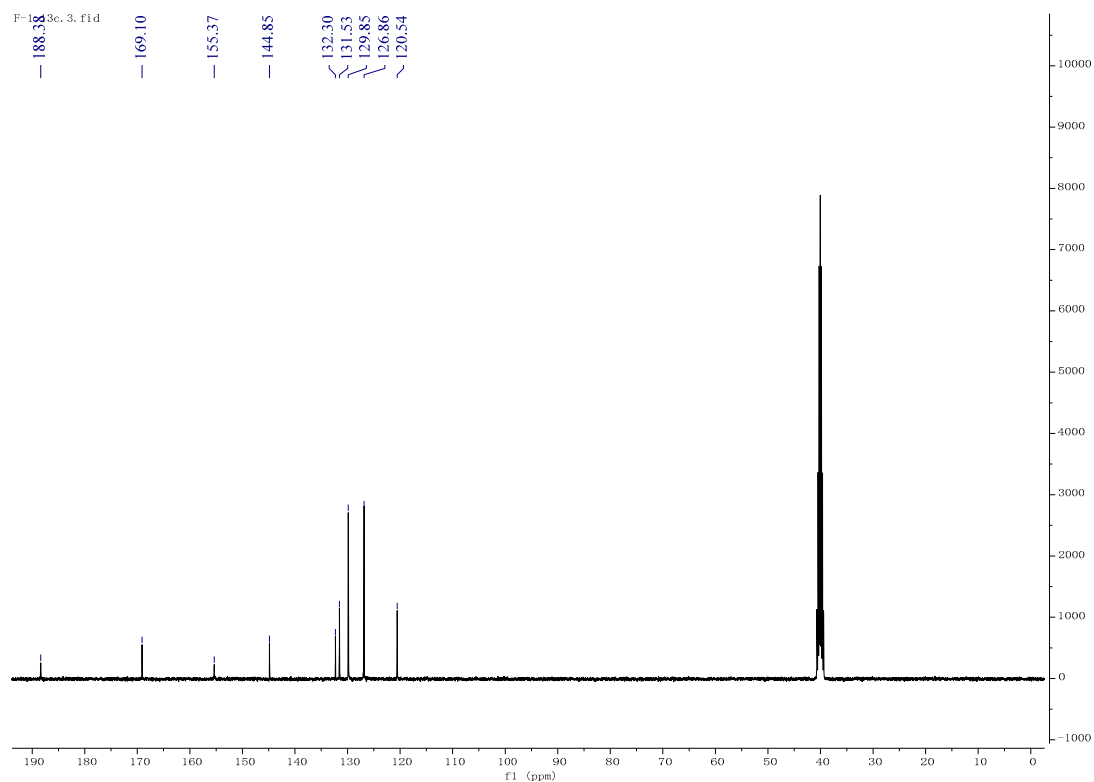
Compound **5a**, 5-(2-phenylthiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



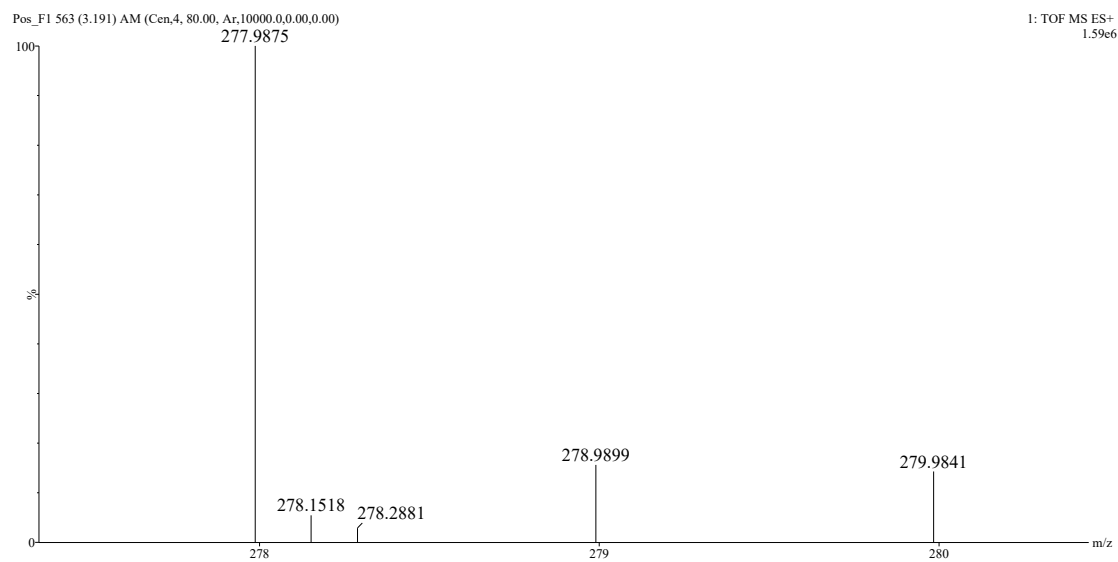
white solid, yield 83.2 %, m. p. >250°C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ : 14.45 (s, 1H), 8.43 (s, 1H), 8.02 – 7.87 (m, 2H), 7.62 – 7.44 (m, 3H). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ : 188.38, 169.10, 155.37, 144.85, 132.30, 131.53, 129.85 (2C), 126.86 (2C), 120.54. HRMS (ESI): calcd for $\text{C}_{11}\text{H}_7\text{N}_3\text{S}_3$ $[\text{M}+\text{H}]^+$: 277.9875, found, 277.9875.



The ^1H NMR spectrogram of compound **5a**

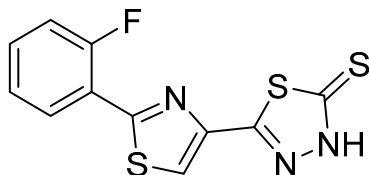


The ^{13}C NMR spectrogram of compound **5a**

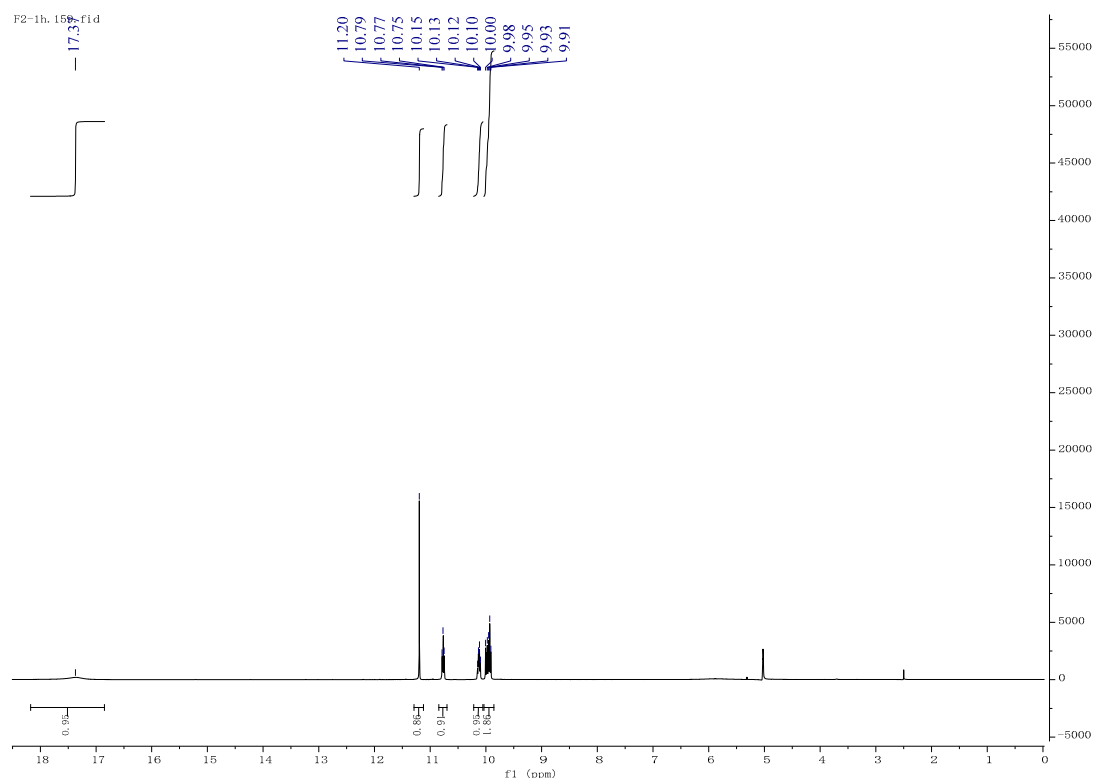


The HRMS spectrogram of compound **5a**

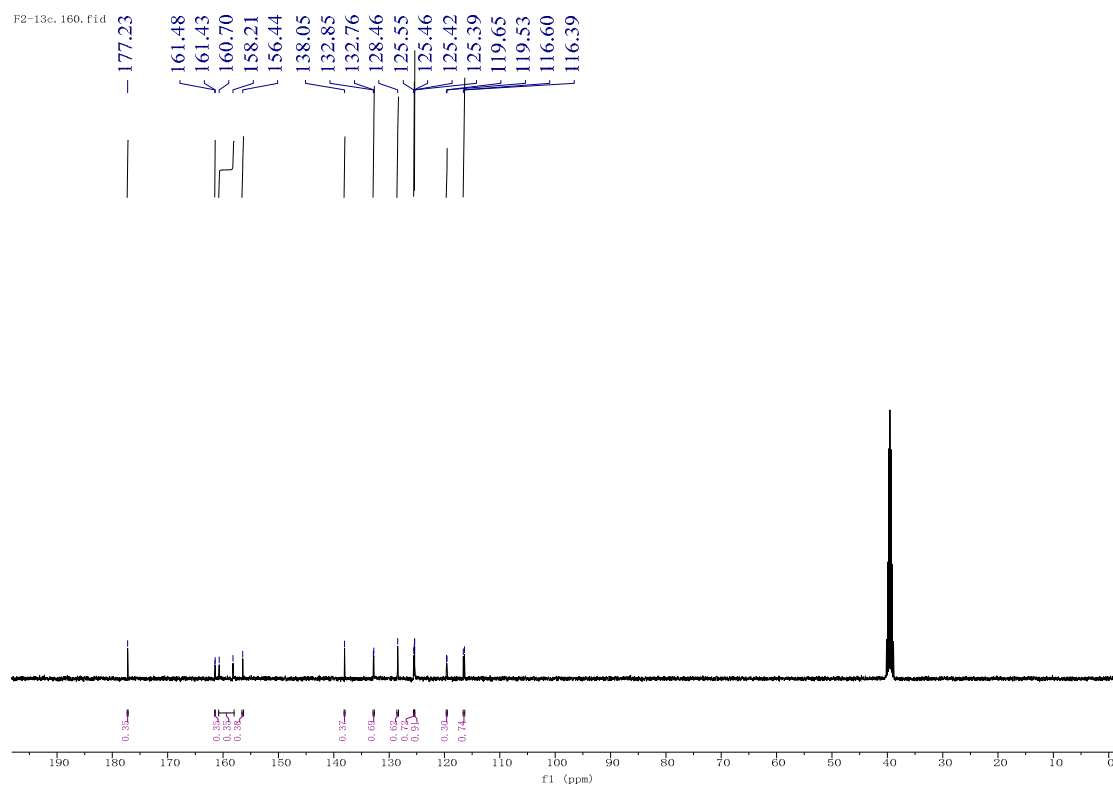
Compound **5b**, 5-(2-(2-fluorophenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



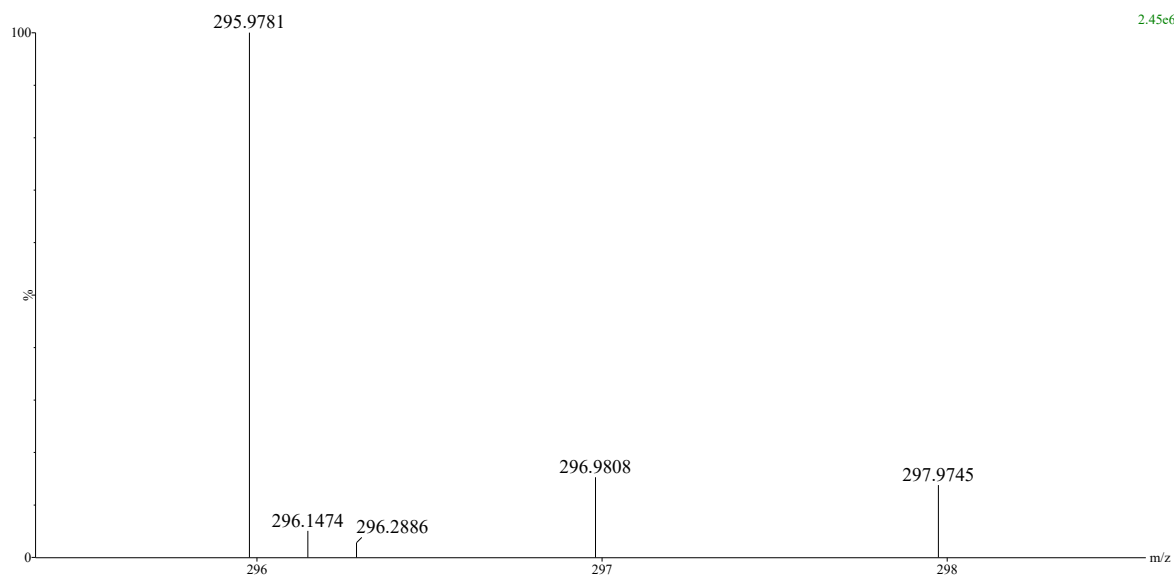
white solid, yield 84.7 %, m. p. 238.5-239.5°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 17.37 (s, 1H), 11.20 (s, 1H), 10.77 (t, $J = 7.8$ Hz, 1H), 10.12 (q, $J = 7.0$ Hz, 1H), 10.03 – 9.86 (m, 2H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 177.23, 161.46 (d, $J = 5.0$ Hz), 159.46 (d, $J = 250.8$ Hz), 156.44, 138.05, 132.81 (d, $J = 8.8$ Hz), 128.46, 125.51 (d, $J = 9.1$ Hz), 125.41 (d, $J = 3.2$ Hz), 119.59 (d, $J = 11.4$ Hz), 116.50 (d, $J = 21.3$ Hz). HRMS (ESI): calcd for $\text{C}_{11}\text{H}_6\text{FN}_3\text{S}_3$ $[\text{M}+\text{H}]^+$: 295.9781, found, 295.9781.



The ^1H NMR spectrogram of compound **5b**

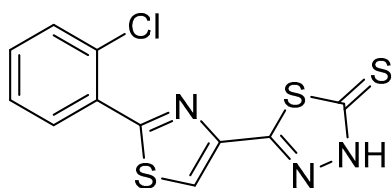


The ^{13}C NMR spectrogram of compound **5b**

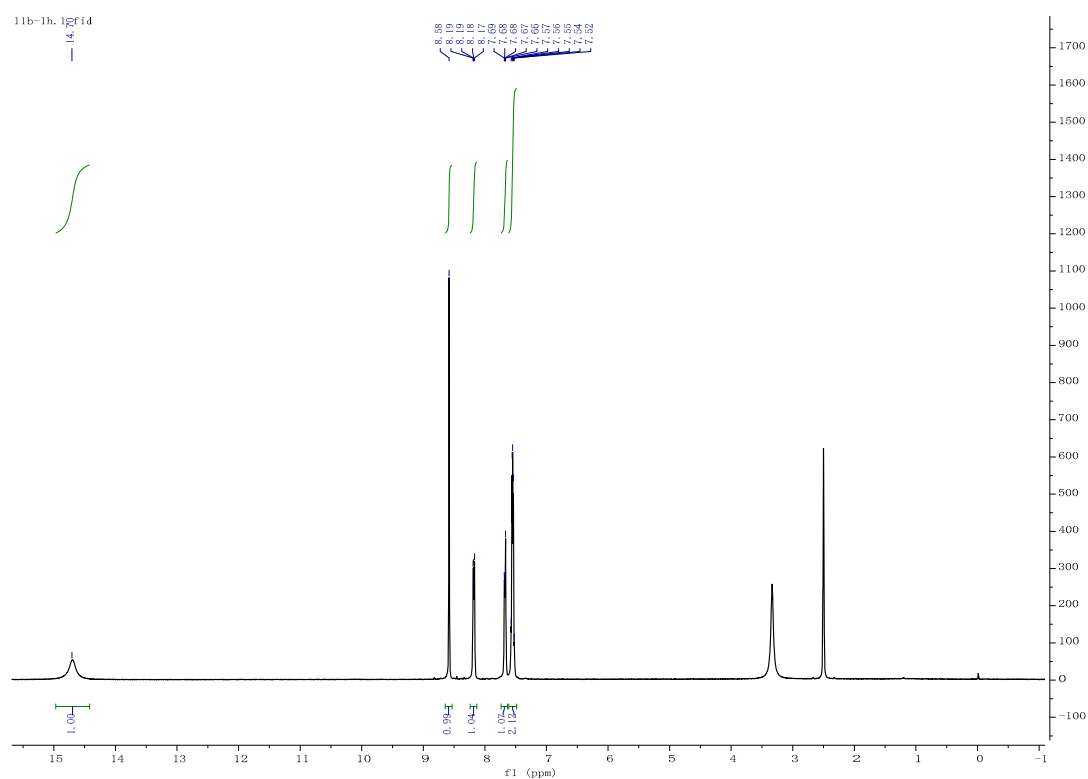


The HRMS spectrogram of compound **5b**

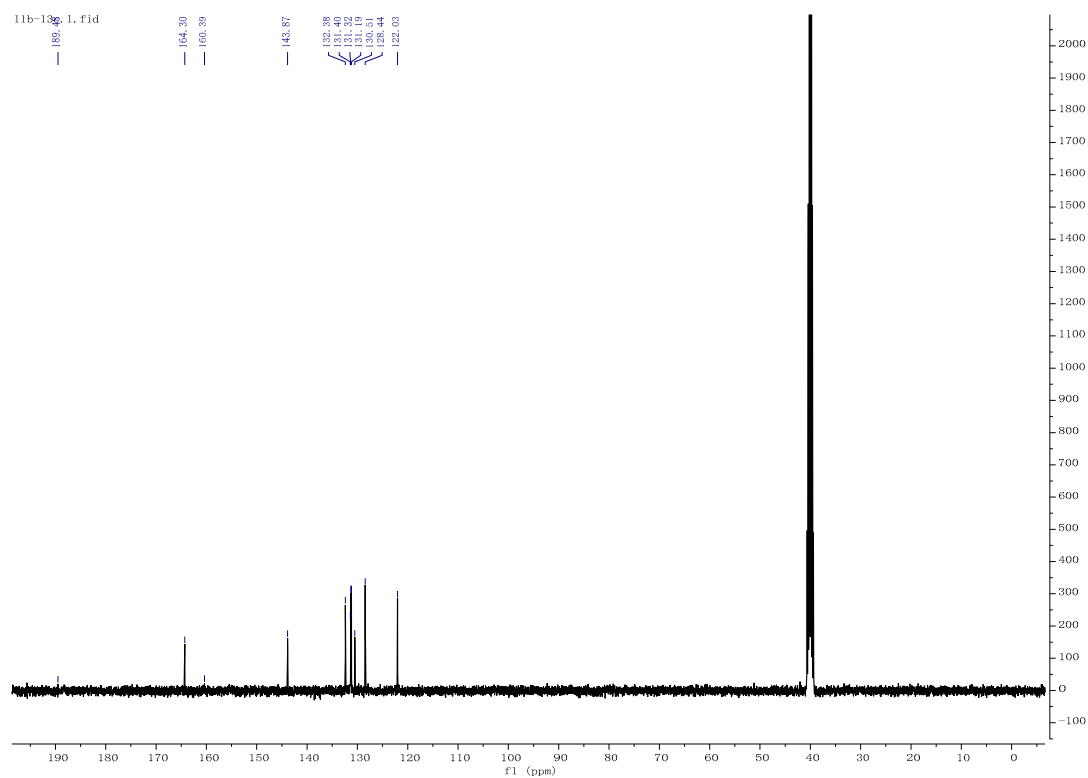
Compound **5c**, 5-(2-(2-chlorophenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



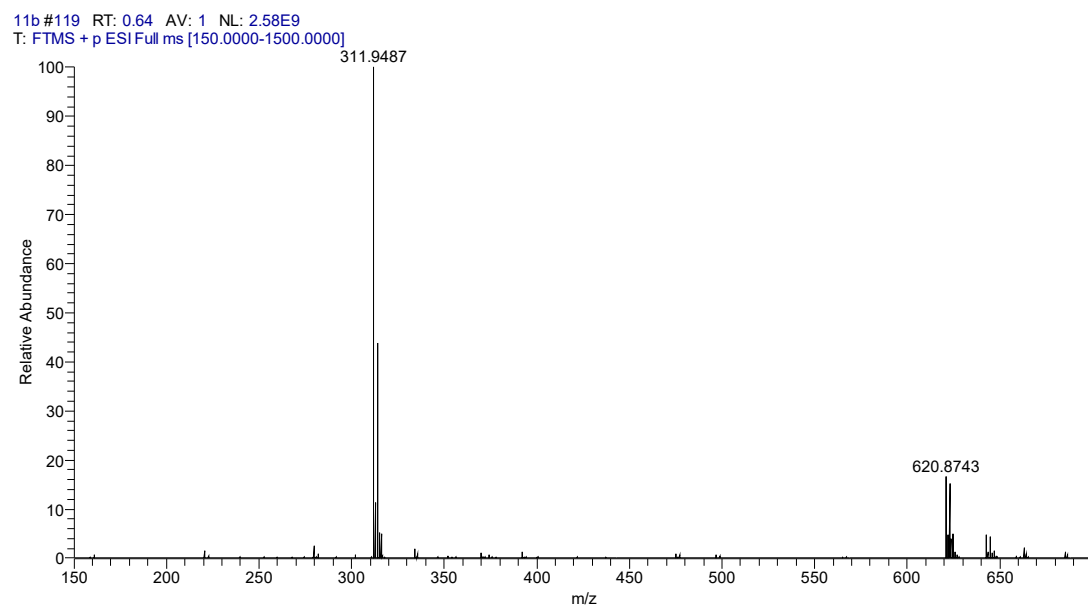
white solid, yield 80.1 %, m. p. 234.6-234.9°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.70 (s, 1H), 8.58 (s, 1H), 8.18 (dd, J = 6.0, 3.6 Hz, 1H), 7.74 – 7.63 (m, 1H), 7.55 (p, J = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 189.48, 164.30, 160.39, 143.87, 132.38, 131.40, 131.32, 131.19, 130.51, 128.44, 122.03. HRMS (ESI): calcd for $\text{C}_{11}\text{H}_6\text{ClN}_3\text{S}_3$ $[\text{M}+\text{H}]^+$: 311.9485; found, 311.9487.



The ^1H NMR spectrogram of compound **5c**

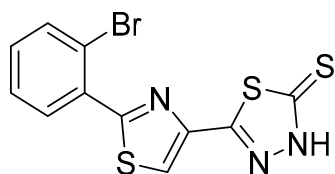


The ^{13}C NMR spectrogram of compound **5c**

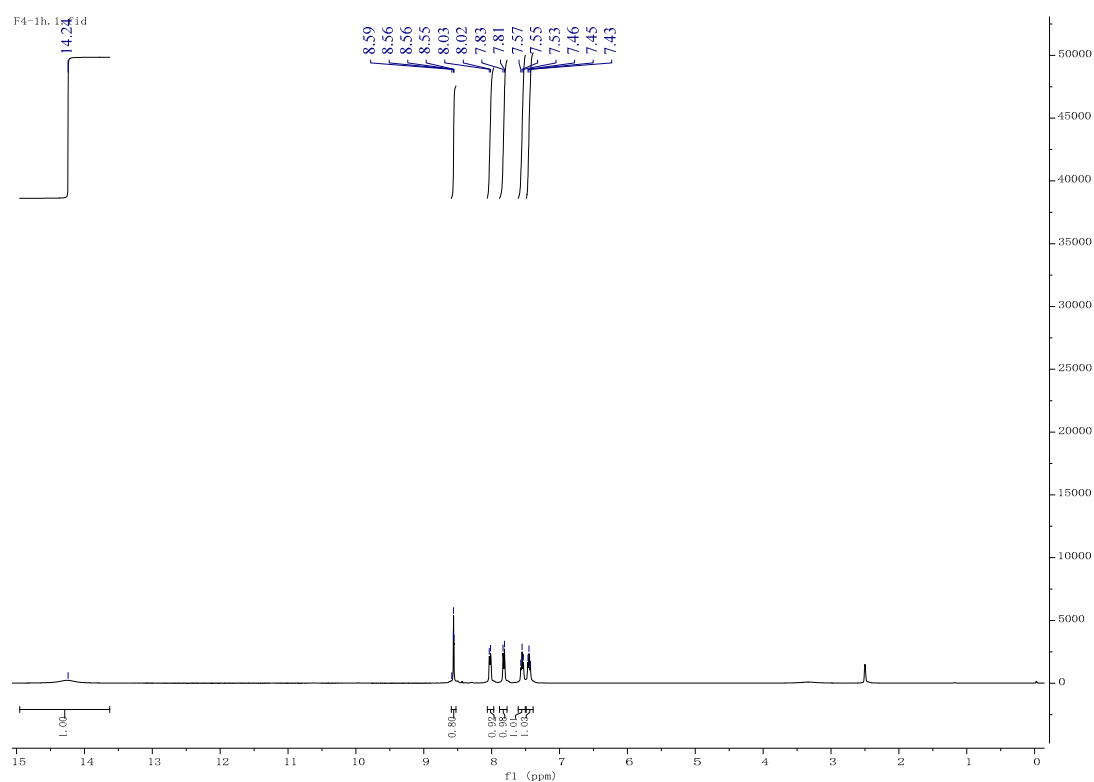


The HRMS spectrogram of compound **5c**

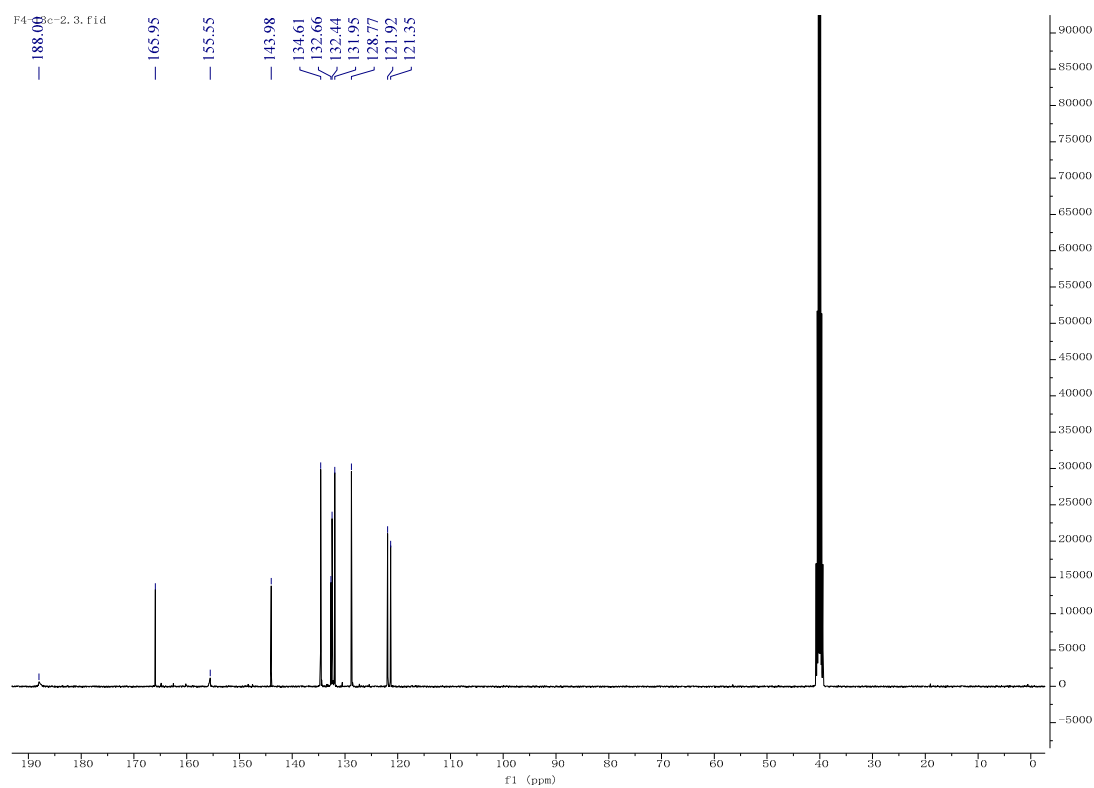
Compound **5d**, 5-(2-(2-bromophenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



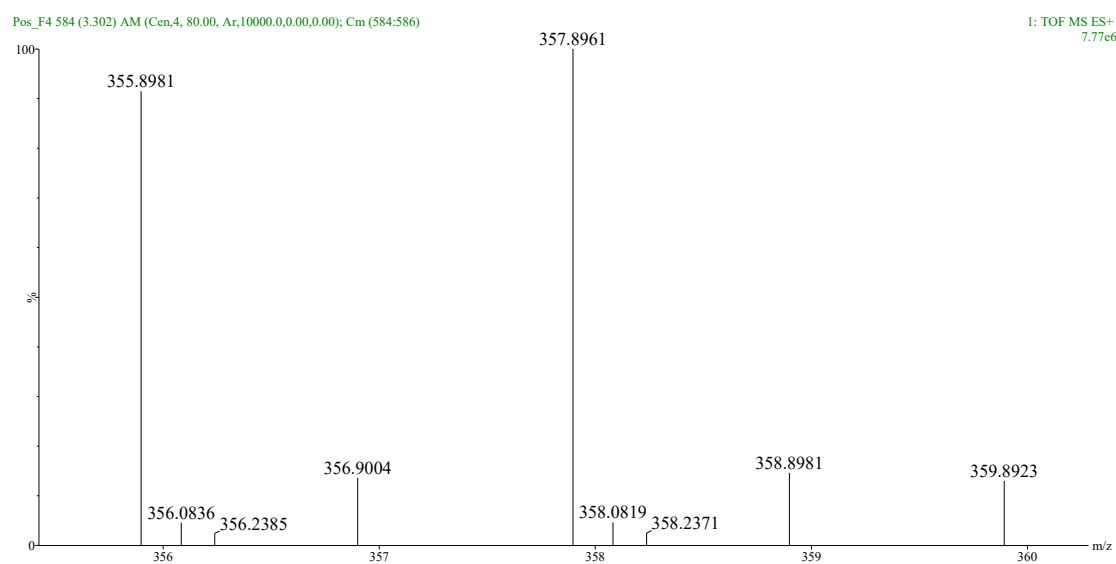
yellow solid, yield 84.3%, m. p. 222.7-223.7°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.24 (s, 1H), 8.56 (d, $J = 2.5$ Hz, 1H), 8.03 (d, $J = 7.8$ Hz, 1H), 7.82 (d, $J = 7.9$ Hz, 1H), 7.55 (t, $J = 7.5$ Hz, 1H), 7.45 (t, $J = 7.6$ Hz, 1H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 188.00, 165.95, 155.55, 143.98, 134.61, 132.66, 132.44, 131.95, 128.77, 121.92, 121.35. HRMS (ESI): calcd for $\text{C}_{11}\text{H}_6\text{BrN}_3\text{S}_3$ $[\text{M}+\text{H}]^+$: 355.8980, found, 355.8981.



The ^1H NMR spectrogram of compound **5d**

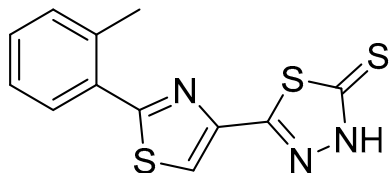


The ^{13}C NMR spectrogram of compound **5d**

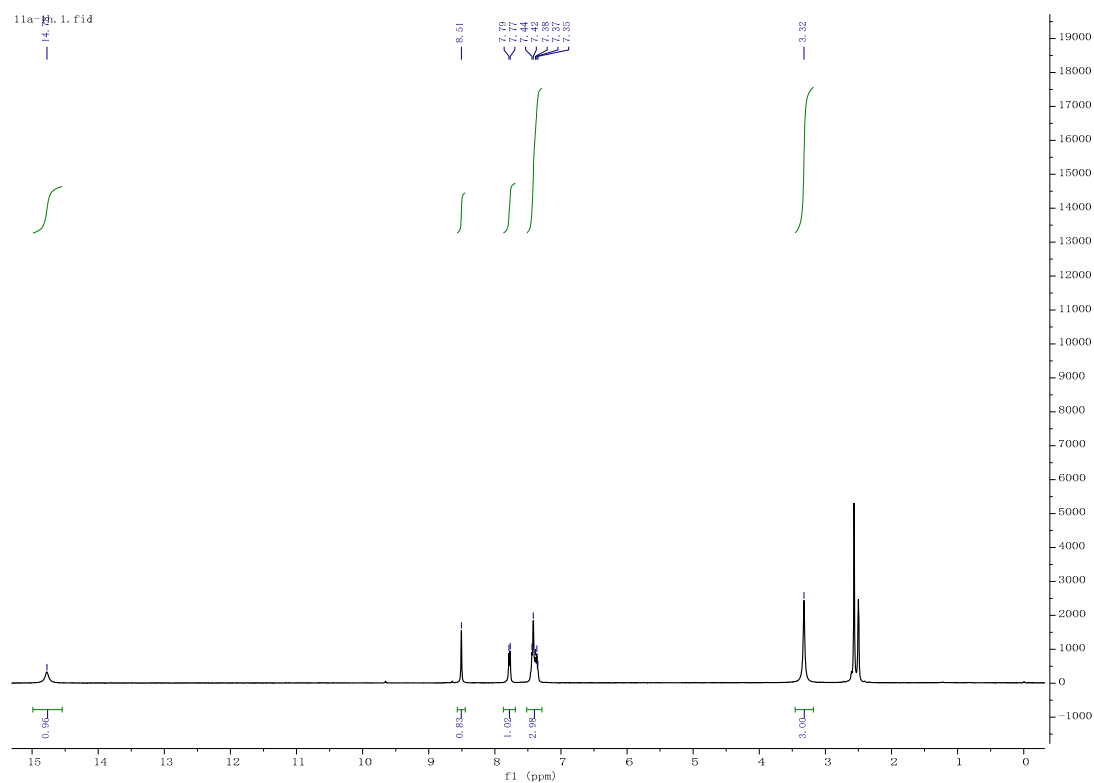


The HRMS spectrogram of compound **5d**

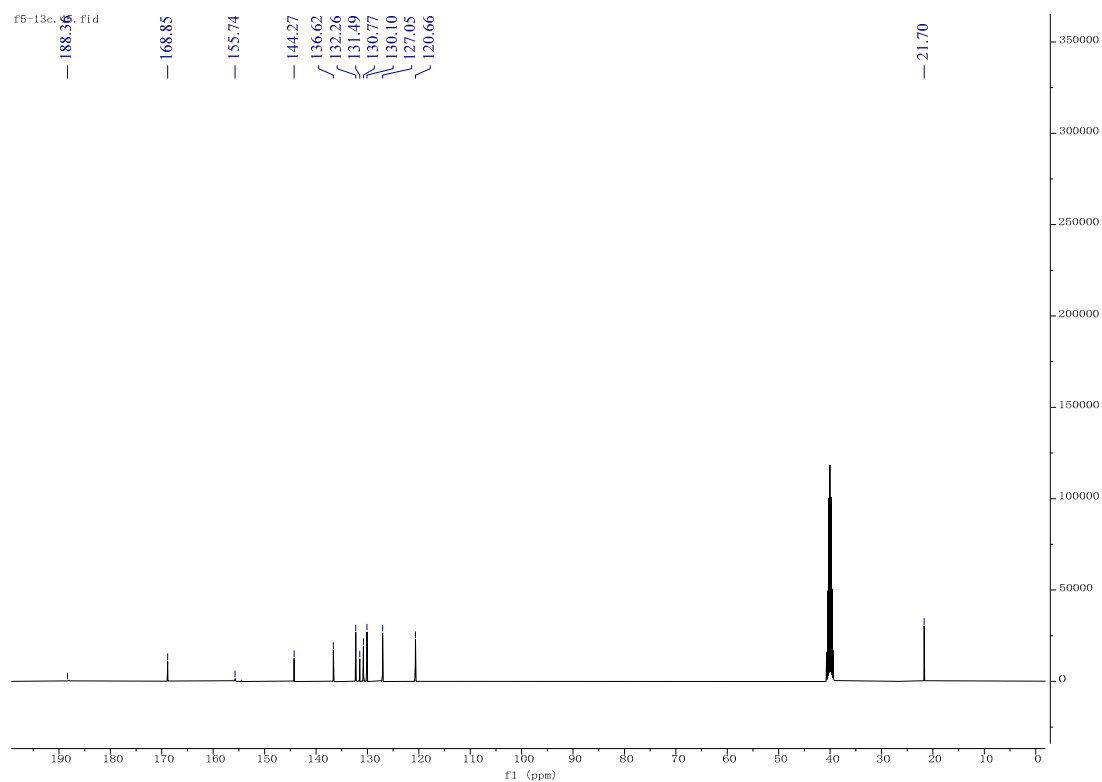
Compound **5e**, 5-(2-(o-tolyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



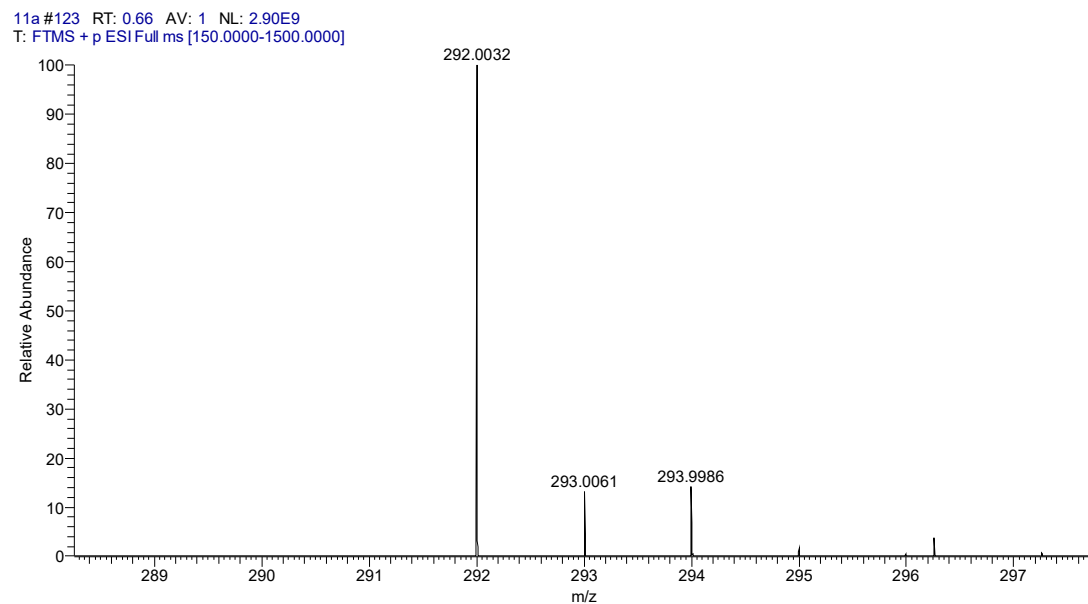
white solid, yield 83.2%, m. p. 229.3-230.1°C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ : 14.78 (s, 1H), 8.51 (s, 1H), 7.78 (d, $J = 7.2$ Hz, 1H), 7.52 – 7.29 (m, 3H), 3.32 (s, 3H). ^{13}C NMR (101 MHz, $\text{DMSO-}d_6$) δ : 188.36, 168.85, 155.74, 144.27, 136.62, 132.26, 131.49, 130.77, 130.10, 127.05, 120.66, 21.70. HRMS (ESI): calcd for $\text{C}_{12}\text{H}_9\text{N}_3\text{S}_3$ $[\text{M}+\text{H}]^+$: 292.0031, found, 292.0032.



The ^1H NMR spectrogram of compound **5e**

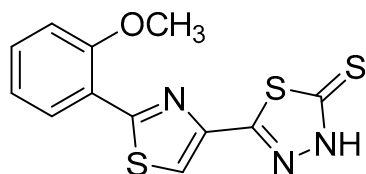


The ^{13}C NMR spectrogram of compound **5e**

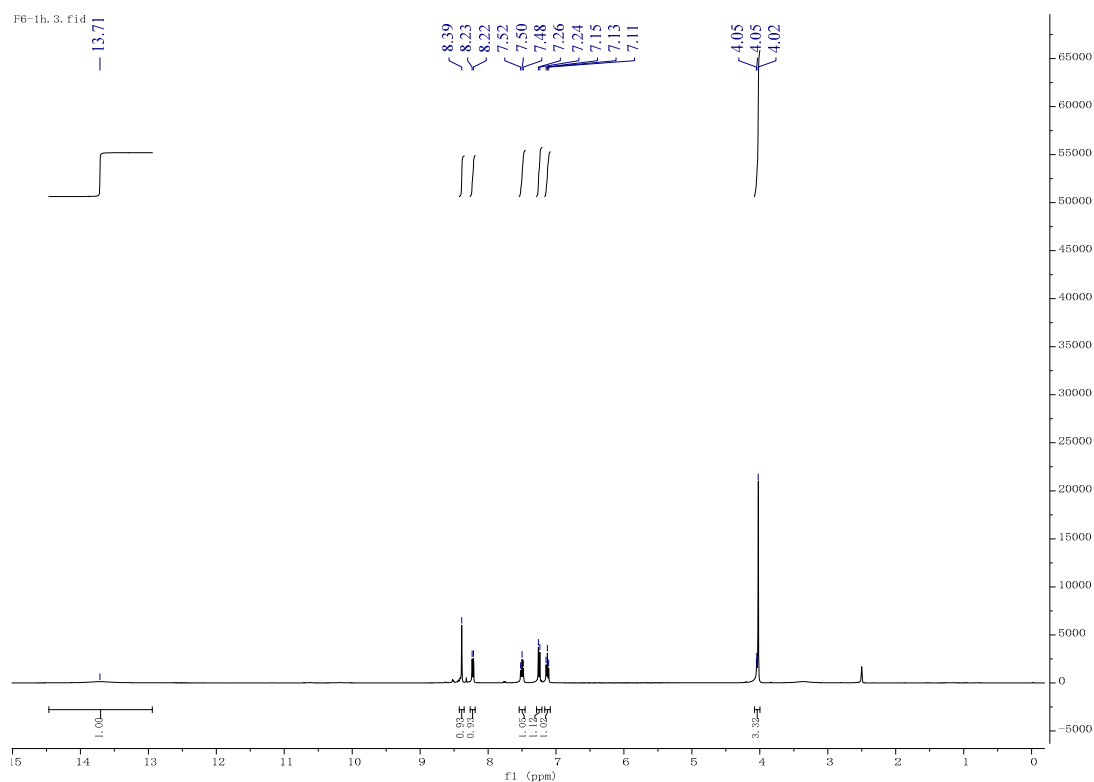


The HRMS spectrogram of compound **5e**

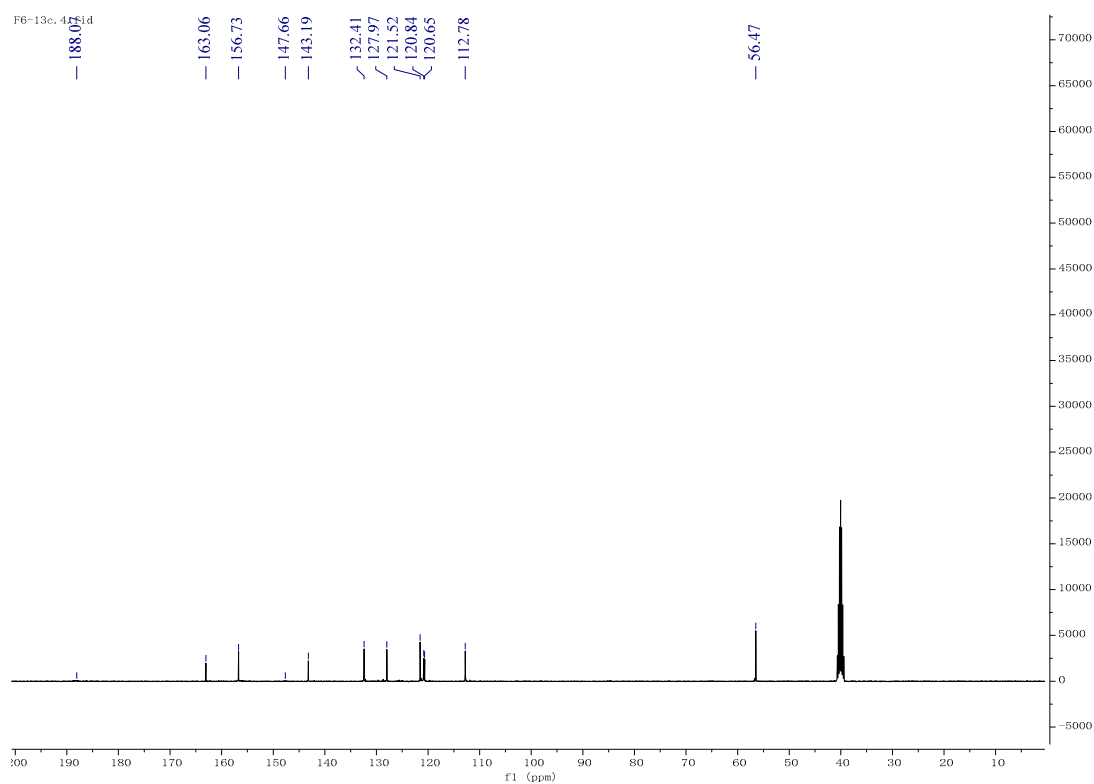
Compound **5f**, 5-(2-(2-methoxyphenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



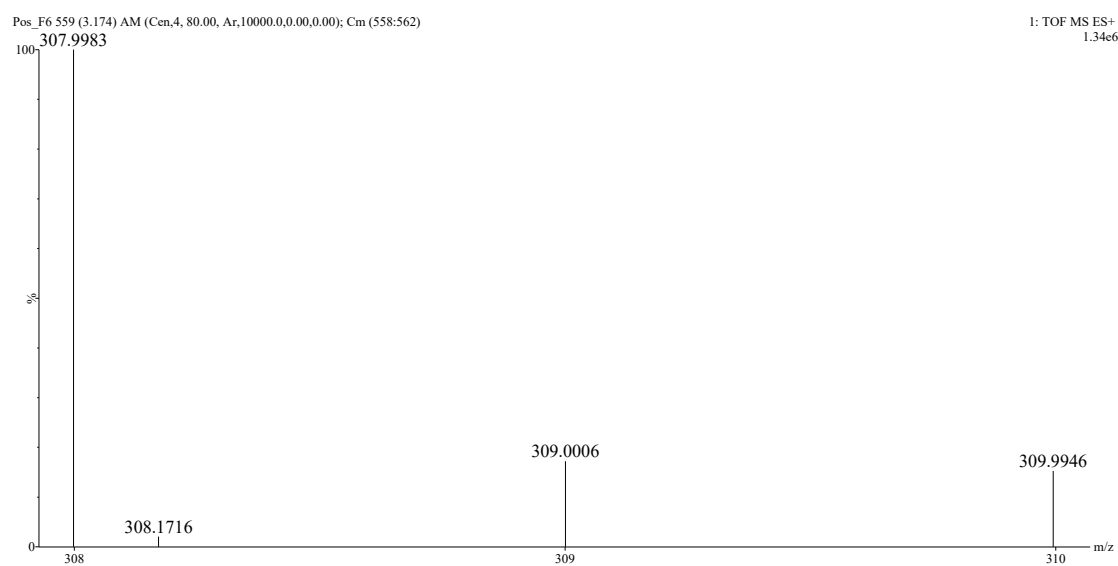
white solid, yield 82.7%, m. p.235.6-236.7C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ : 13.71 (s, 1H), 8.39 (s, 1H), 8.23 (d, $J = 7.8$ Hz, 1H), 7.50 (t, $J = 7.8$ Hz, 1H), 7.25 (d, $J = 8.4$ Hz, 1H), 7.13 (t, $J = 7.6$ Hz, 1H), 4.02 (s, 3H). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ : 188.07, 163.06, 156.73, 147.66, 143.19, 132.41, 127.97, 121.52, 120.84, 120.65, 112.78, 56.47. HRMS (ESI): calcd for $\text{C}_{12}\text{H}_9\text{N}_3\text{OS}_3$ $[\text{M}+\text{H}]^+$: 307.9981, found, 307.9983.



The ^1H NMR spectrogram of compound **5f**



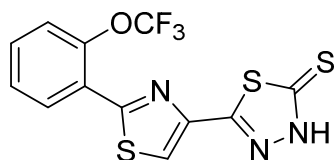
The ^{13}C NMR spectrogram of compound **5f**



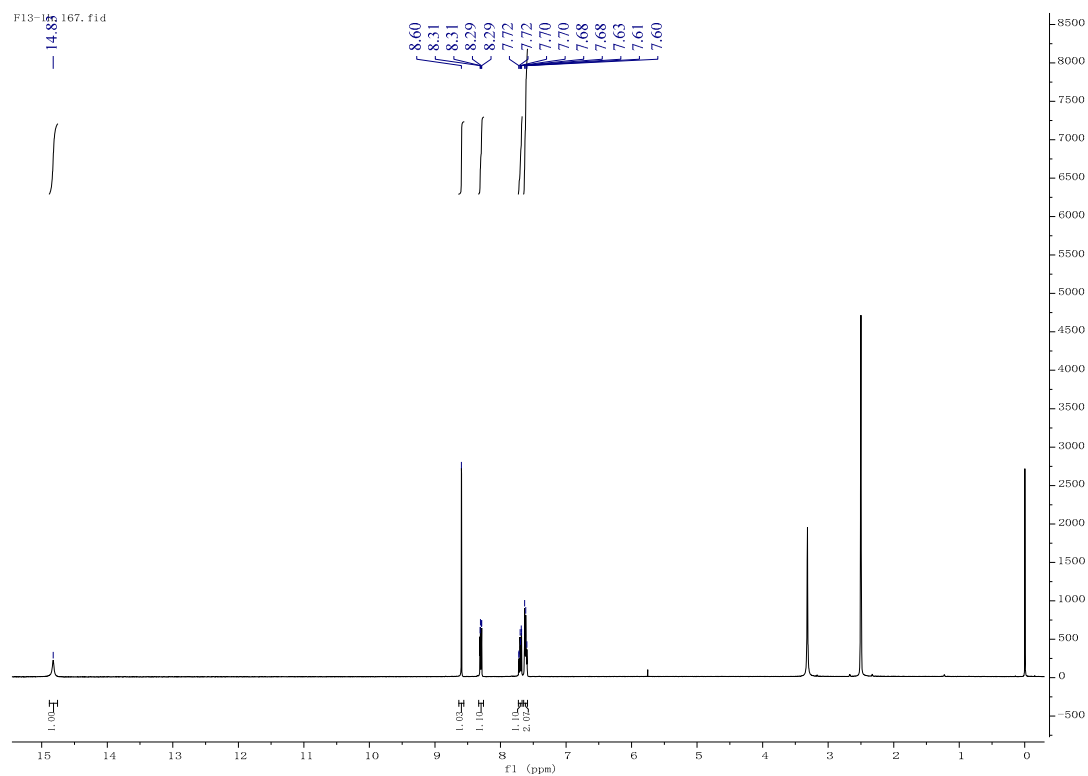
The HRMS spectrogram of compound **5f**

Compound **5g**, 5-(2-(2-(trifluoromethoxy)phenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)

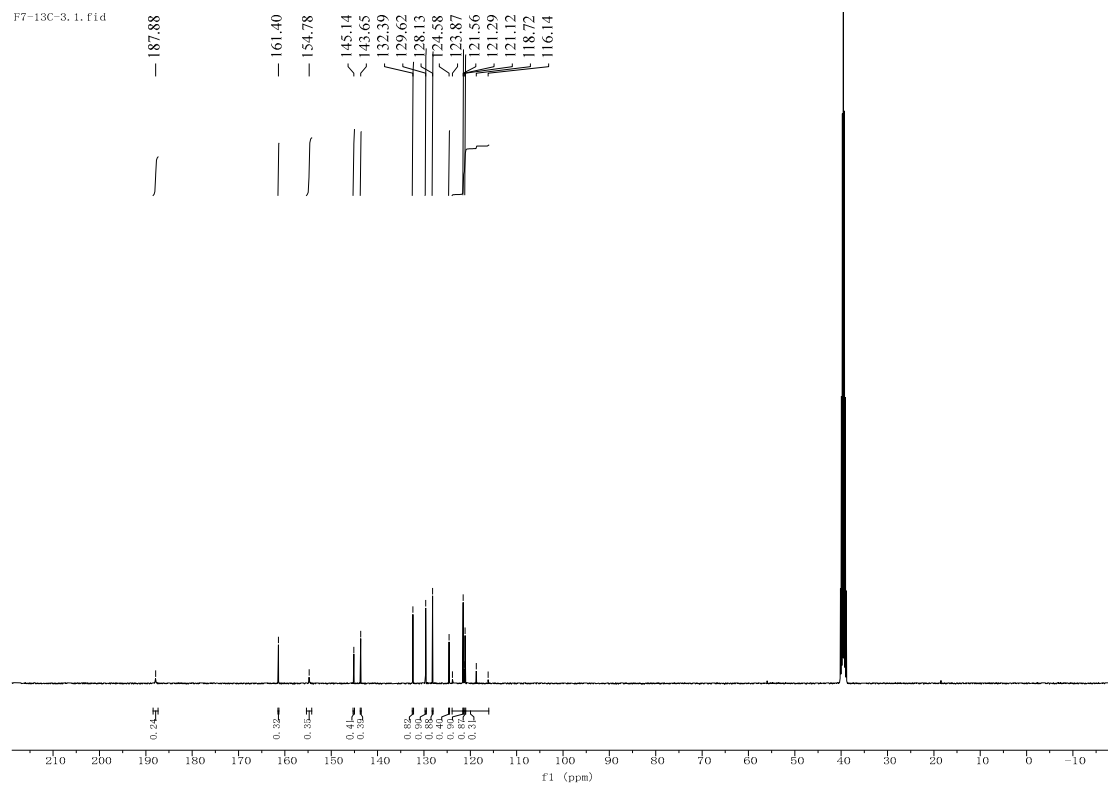
-thione:



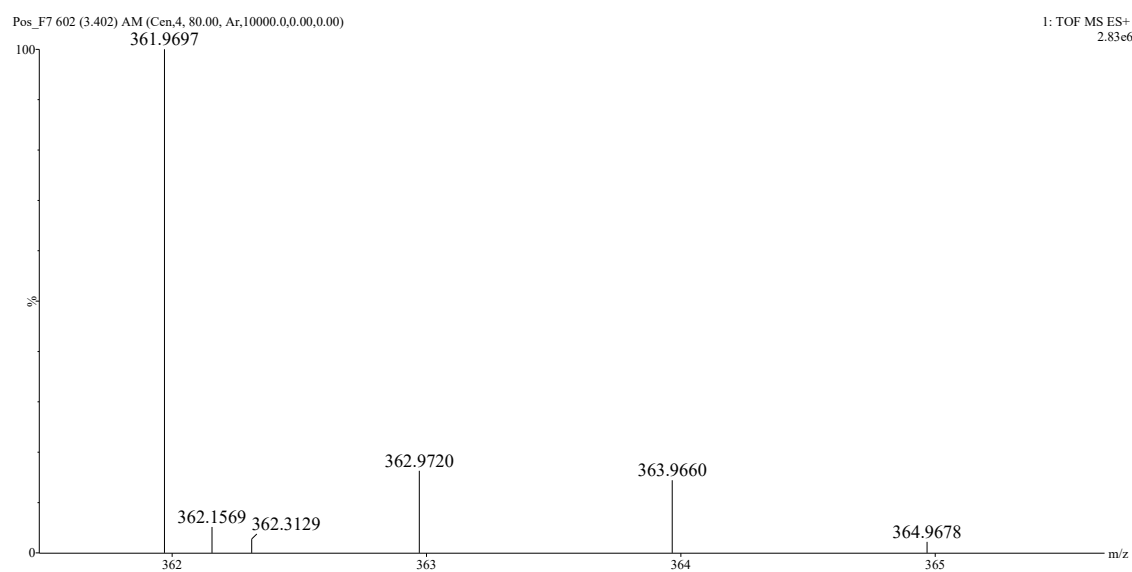
white solid, yield 85.6%, m. p. 230.2-230.7°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.83 (s, 1H), 8.60 (s, 1H), 8.30 (dd, $J = 8.1, 1.7$ Hz, 1H), 7.73 – 7.67 (m, 1H), 7.65 – 7.59 (m, 2H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 187.88, 161.40, 154.78, 145.14, 143.65, 132.39, 129.62, 128.13, 124.58, 121.56, 121.12, 120.01 (q, $J = 259.1$ Hz). HRMS (ESI): calcd for $\text{C}_{12}\text{H}_6\text{F}_3\text{N}_3\text{OS}_3$ $[\text{M}+\text{H}]^+$: 361.9698, found, 361.9697.



The ^1H NMR spectrogram of compound **5g**

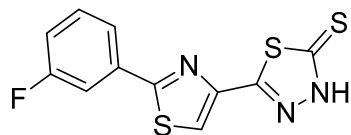


The ^{13}C NMR spectrogram of compound **5g**

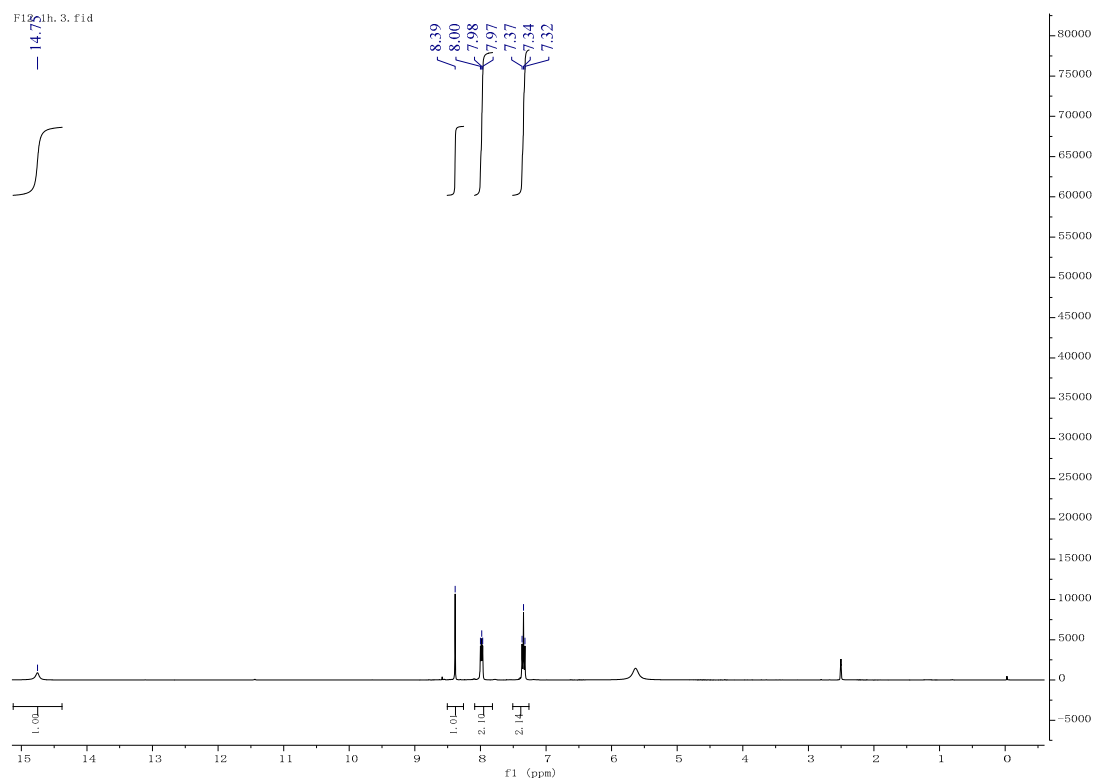


The HRMS spectrogram of compound **5g**

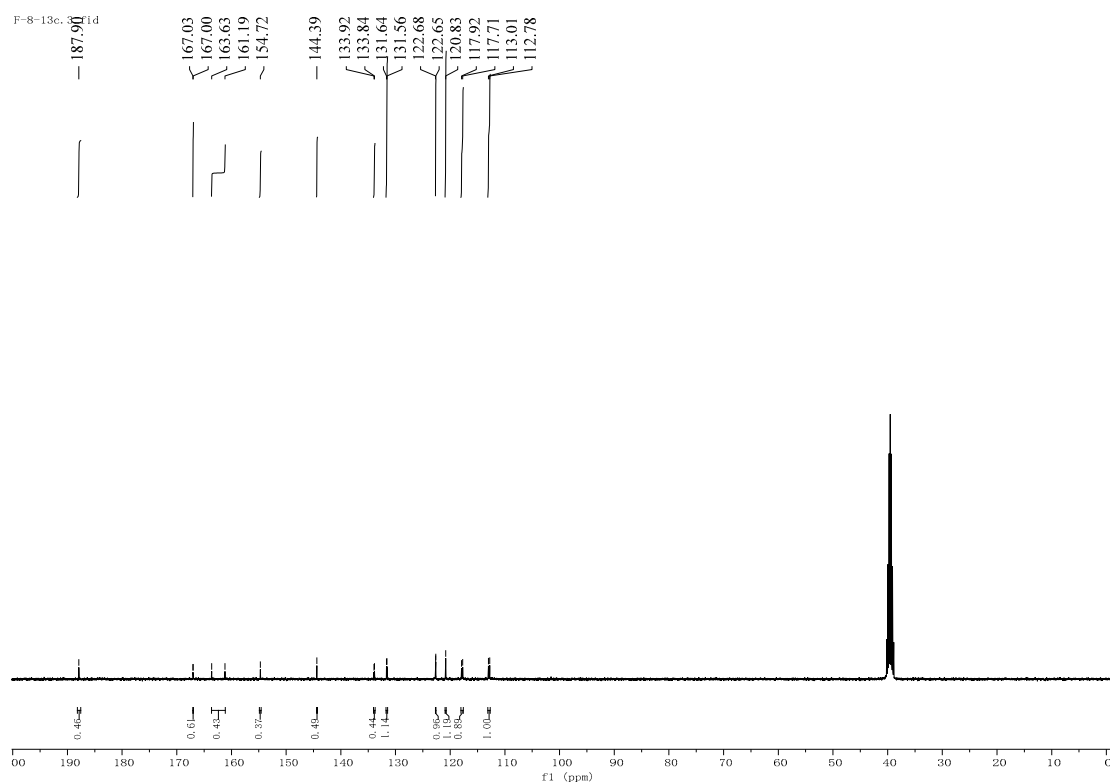
Compound **5h**, 5-(2-(3-fluorophenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



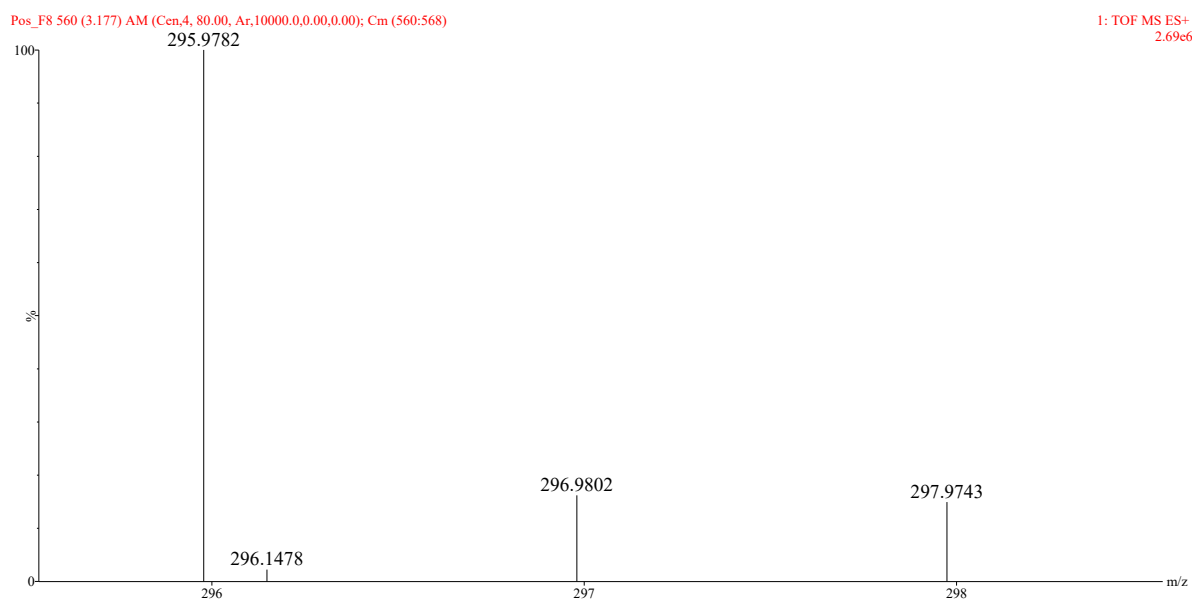
white solid, yield 84.5%, m. p. 219.1-220.0°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.74 (s, 1H), 8.47 (s, 1H), 7.78 (dd, J = 17.5, 8.7 Hz, 2H), 7.68 – 7.52 (m, 1H), 7.39 (t, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 187.90, 167.02 (d, J = 3.1 Hz), 162.41 (d, J = 245.1 Hz), 154.72, 144.39, 133.88 (d, J = 8.0 Hz), 131.60 (d, J = 8.5 Hz), 122.66 (d, J = 2.6 Hz), 120.83, 117.82 (d, J = 21.1 Hz), 112.89 (d, J = 23.6 Hz). HRMS (ESI): calcd for $\text{C}_{11}\text{H}_6\text{FN}_3\text{S}_3$ $[\text{M}+\text{H}]^+$: 295.9781, found, 295.9782.



The ^1H NMR spectrogram of compound **5h**

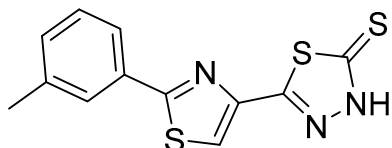


The ^{13}C NMR spectrogram of compound **5h**

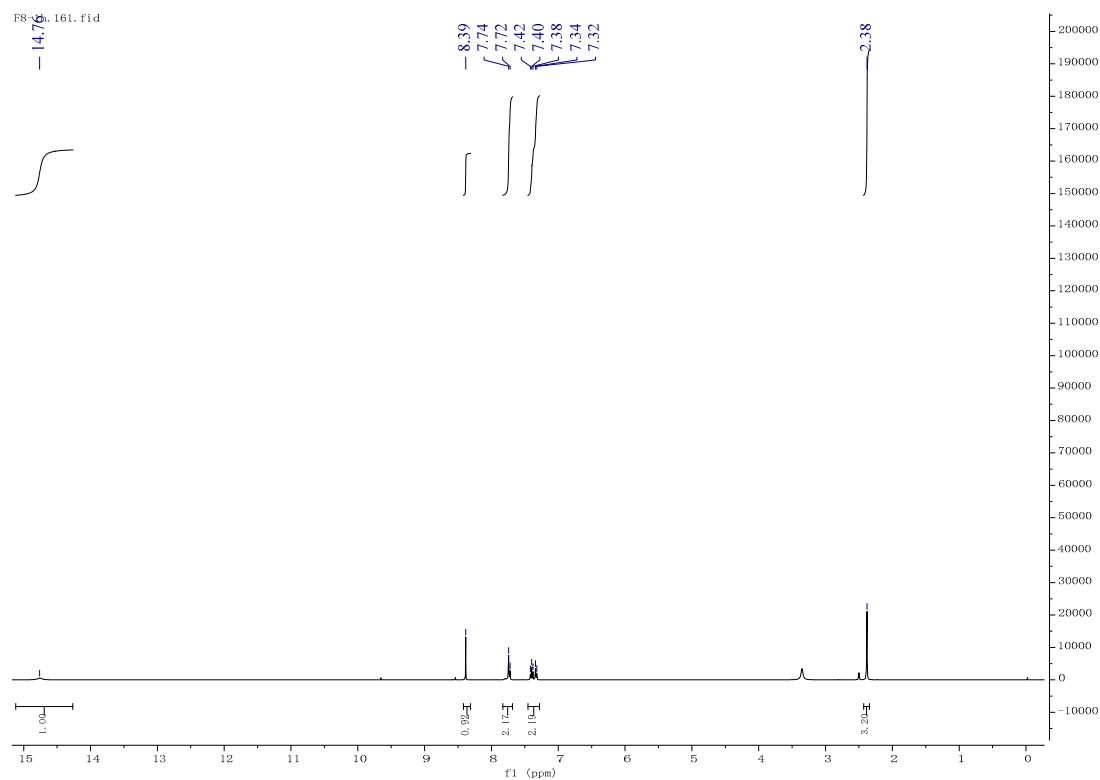


The HRMS spectrogram of compound **5h**

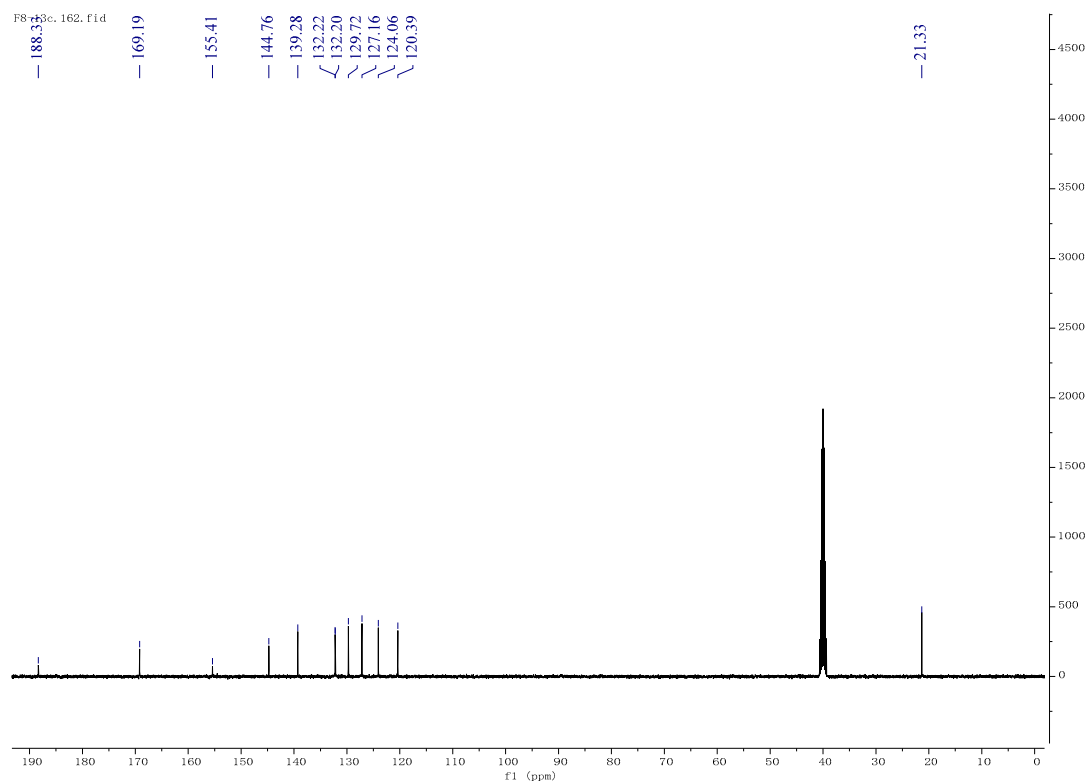
Compound **5i**, 5-(2-(m-tolyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3*H*)-thione:



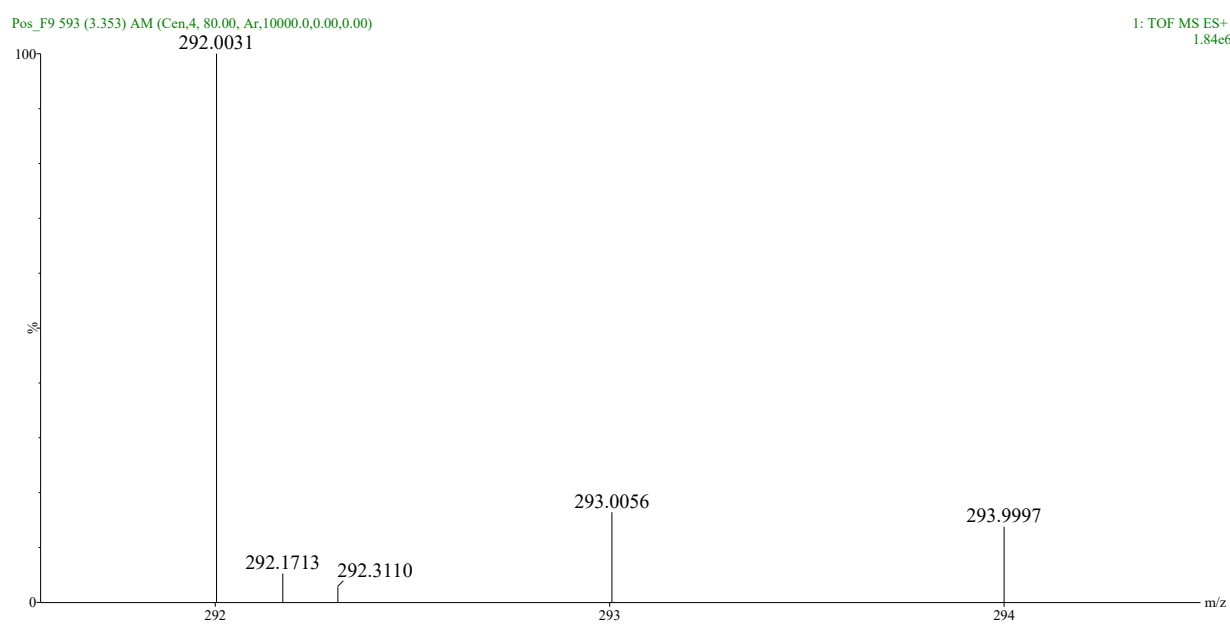
white solid, yield 84.8%, m. p. 224.9-225.4°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.76 (s, 1H), 8.39 (s, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.45 – 7.28 (m, 2H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 188.33, 169.19, 155.41, 144.76, 139.28, 132.22, 132.20, 129.72, 127.16, 124.06, 120.39, 21.33. HRMS (ESI): calcd for $\text{C}_{12}\text{H}_9\text{N}_3\text{S}_3$ $[\text{M}+\text{H}]^+$: 292.0032, found, 292.0031.



The ^1H NMR spectrogram of compound **5i**

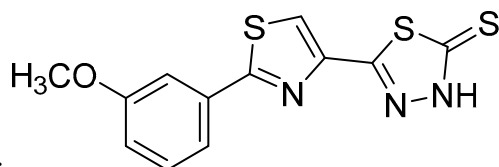


The ^{13}C NMR spectrogram of compound **5i**



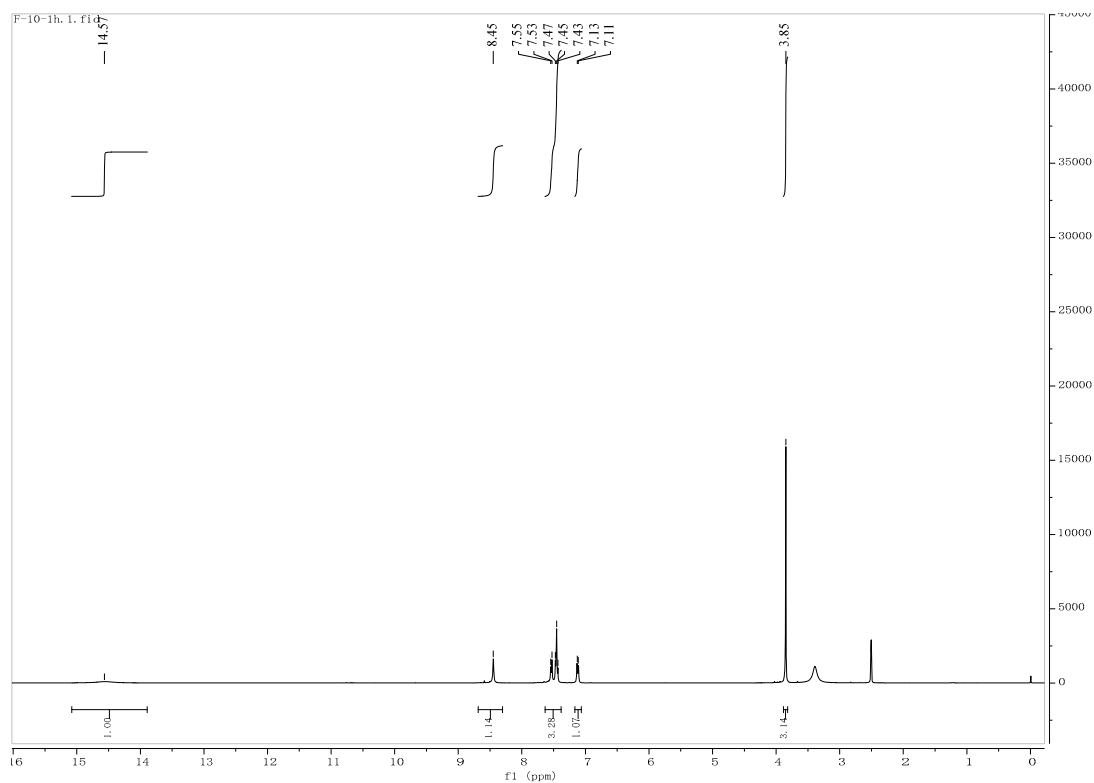
The HRMS spectrogram of compound **5i**

Compound **5j**, 5-(2-(3-methoxyphenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-

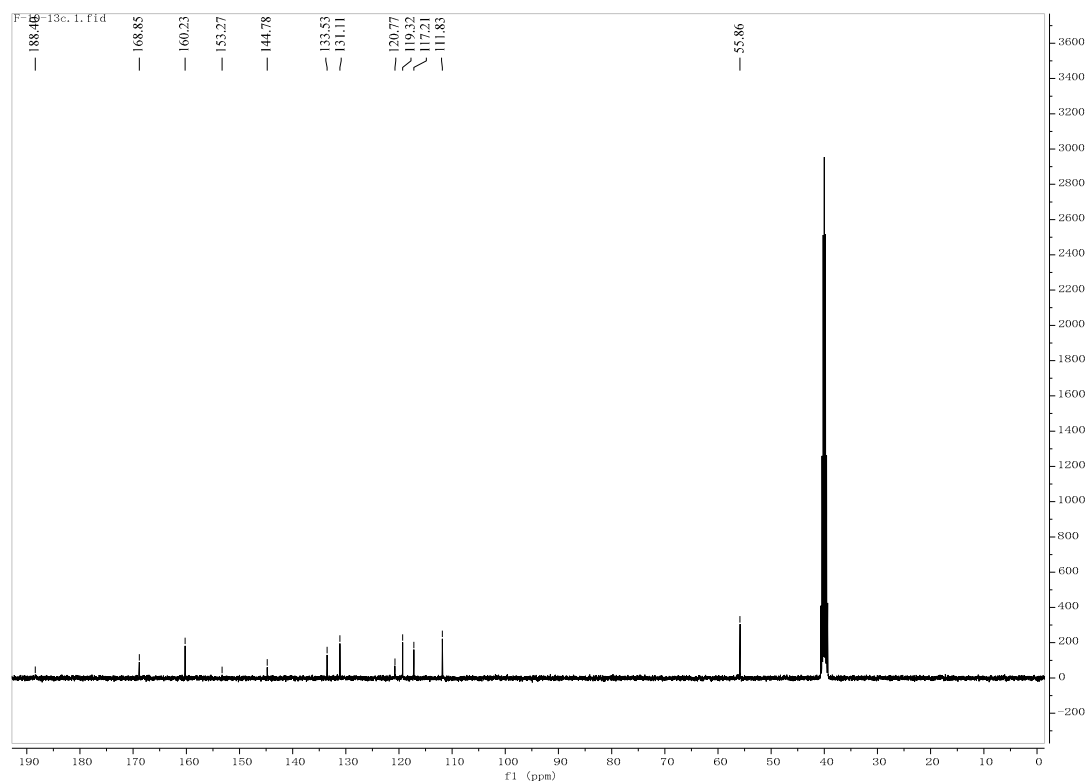


thione:

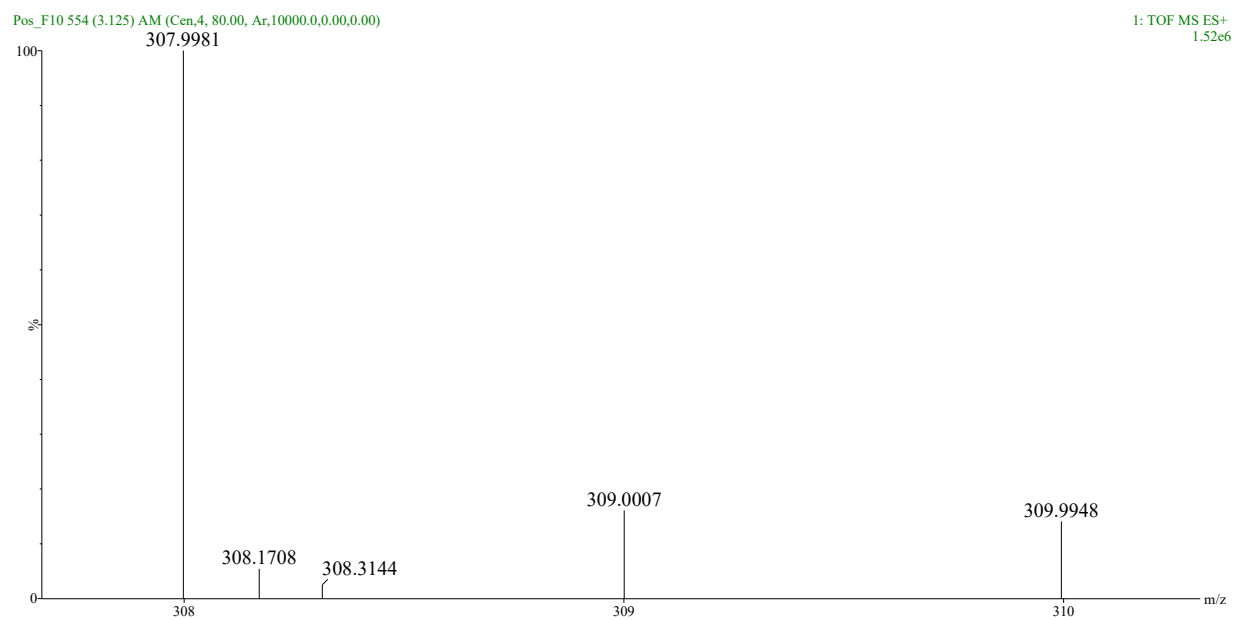
white solid, yield 83.1%, m. p. 228.9-230.1°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.57 (s, 1H), 8.45 (s, 1H), 7.63 – 7.38 (m, 3H), 7.12 (d, J = 6.5 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 188.40, 168.85, 160.23, 153.27, 144.78, 133.53, 131.11, 120.77, 119.32, 117.21, 111.83, 55.86. HRMS (ESI): calcd for $\text{C}_{12}\text{H}_9\text{N}_3\text{OS}_3$ $[\text{M}+\text{H}]^+$: 307.9981, found, 307.9981.



The ^1H NMR spectrogram of compound **5j**

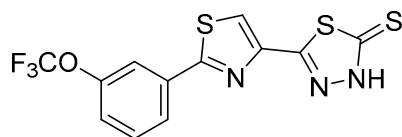


The ^{13}C NMR spectrogram of compound **5j**

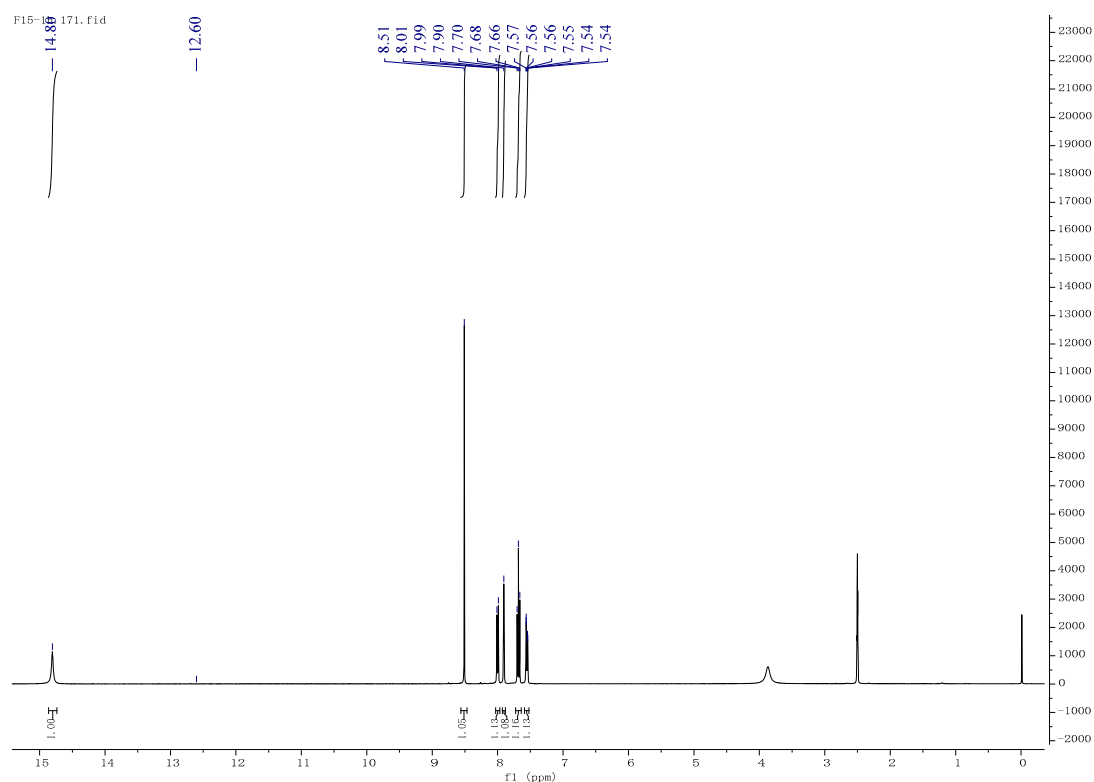


The HRMS spectrogram of compound **5j**

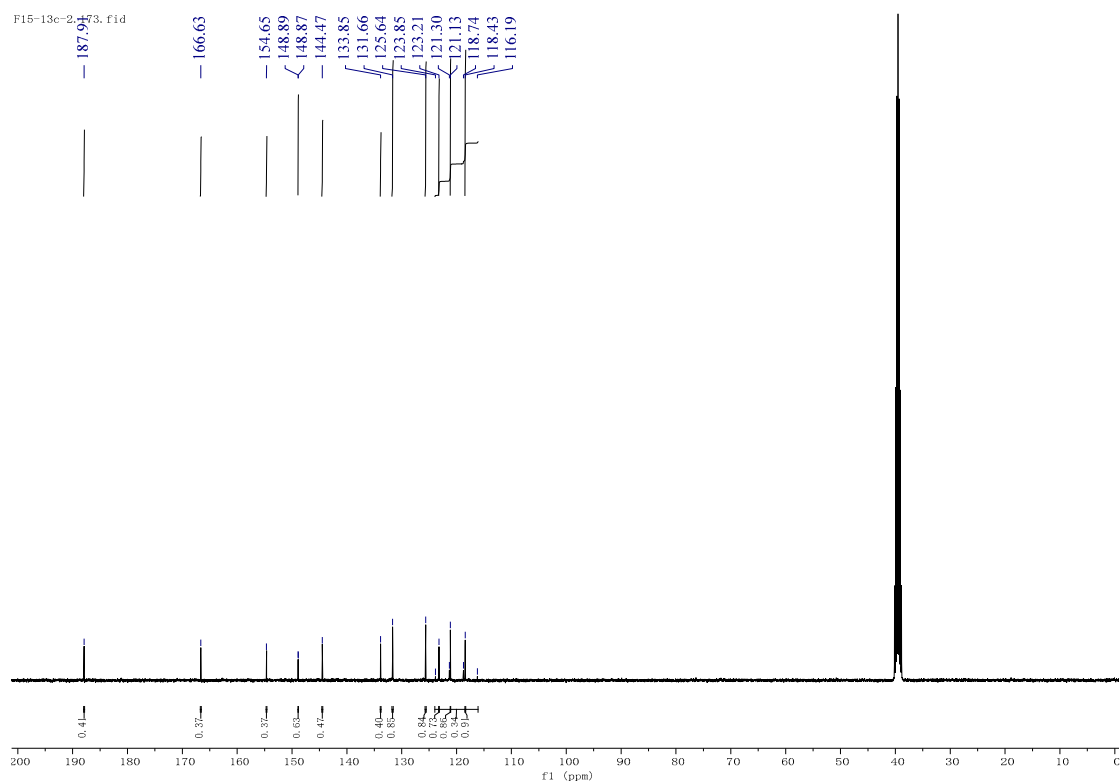
Compound **5k**, 5-(2-(3-(trifluoromethoxy)phenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



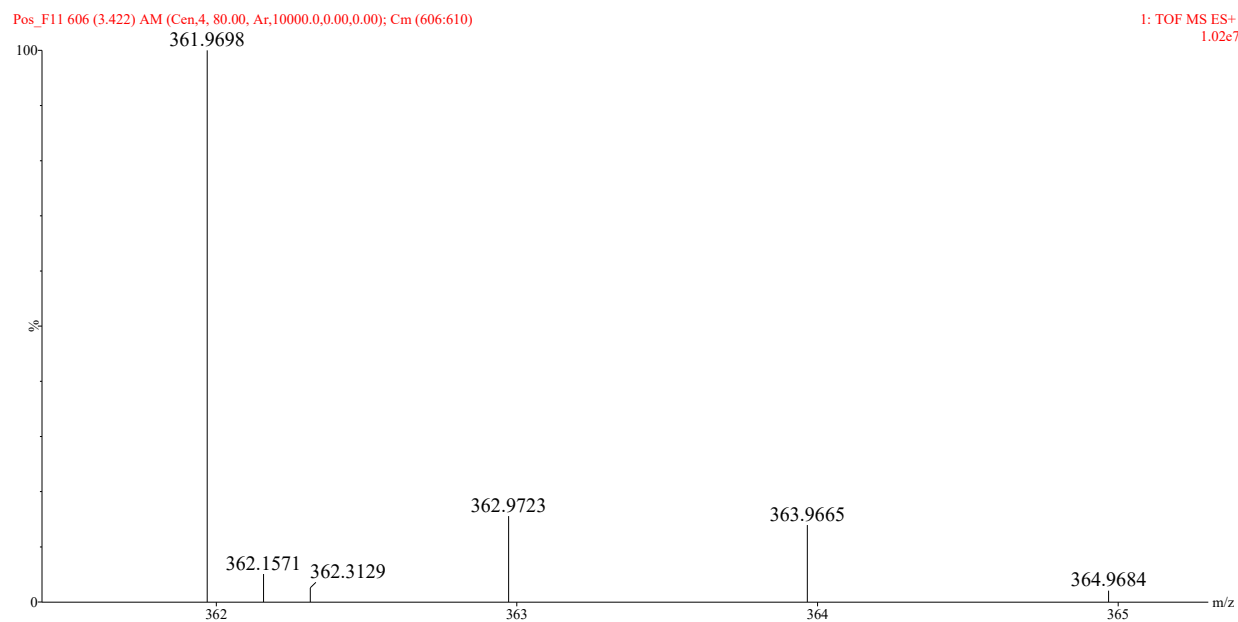
white solid, yield 82.6 %, m. p. 228.6-228.9°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.80 (s, 1H), 8.51 (s, 1H), 8.00 (d, J = 8.3 Hz, 1H), 7.90 (s, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.59 – 7.52 (m, 1H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 187.91, 166.63, 154.65, 148.88 (d, J = 2.0 Hz), 144.47, 133.85, 131.66, 125.64, 123.21, 121.13, 120.02 (q, J = 256.9 Hz), 118.43. HRMS (ESI): calcd for $\text{C}_{12}\text{H}_6\text{F}_3\text{N}_3\text{OS}_3[\text{M}+\text{H}]^+$: 361.9698, found, 361.9698.



The ^1H NMR spectrogram of compound **5k**

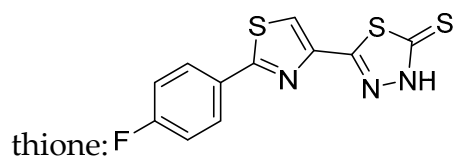


The ^{13}C NMR spectrogram of compound **5k**

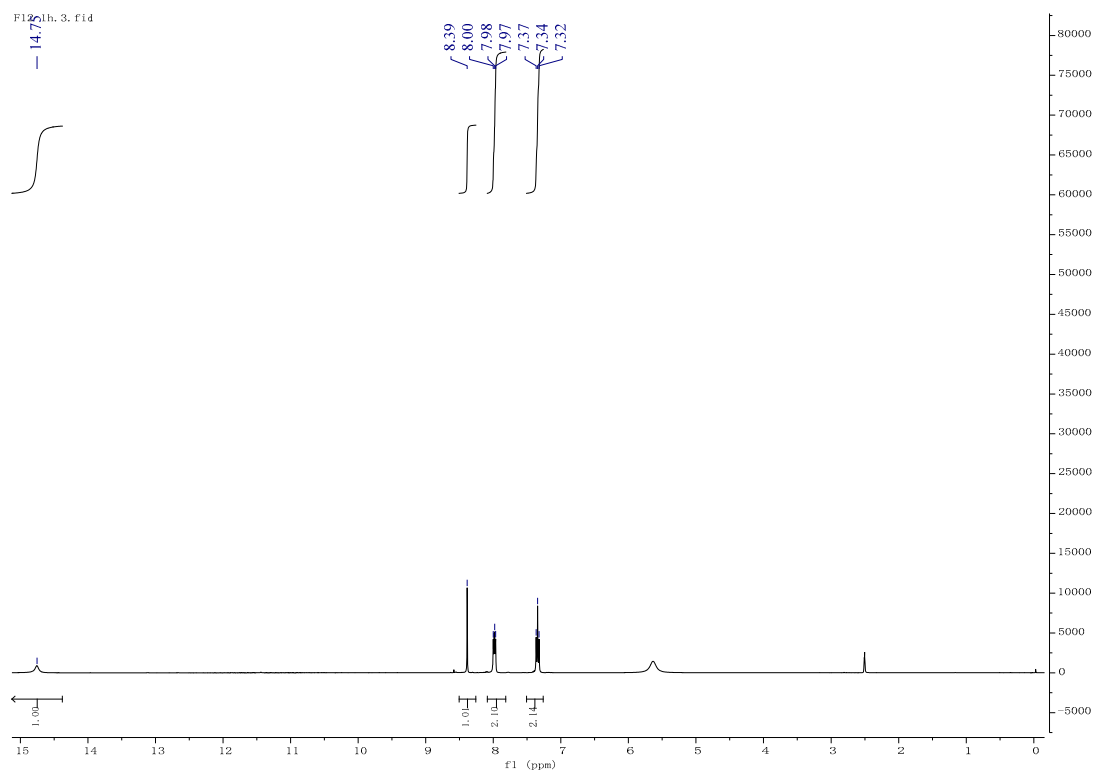


The HRMS spectrogram of compound **5k**

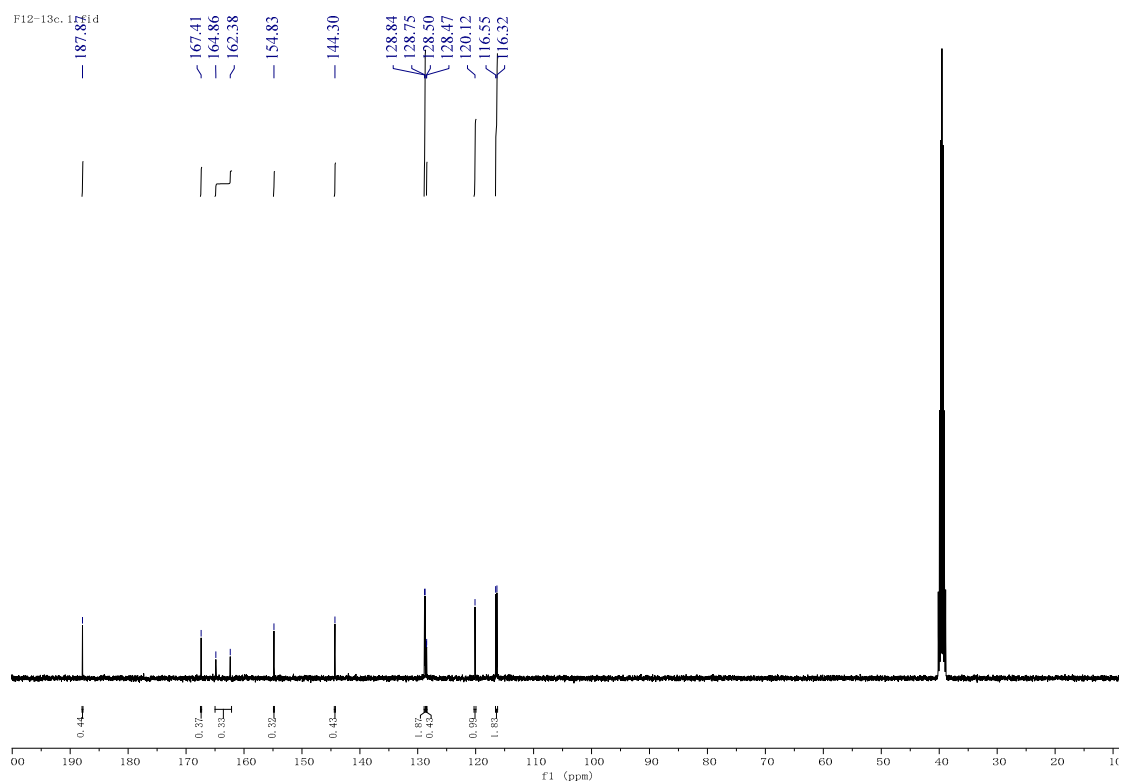
Compound **51**, 5-(2-(4-fluorophenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-



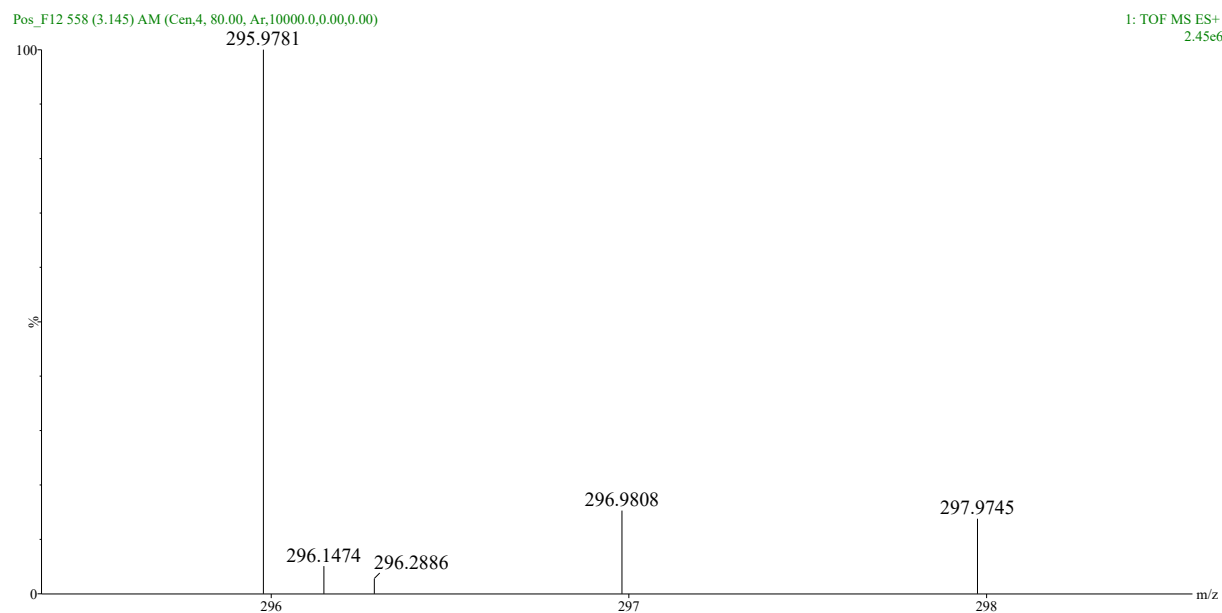
white solid, yield 81.8 %, m. p. >250°C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ : 14.75 (s, 1H), 8.39 (s, 1H), 8.09 – 7.82 (m, 2H), 7.34 (t, $J = 8.8$ Hz, 2H). ^{13}C NMR (101 MHz, $\text{DMSO-}d_6$) δ : 187.87, 167.41, 163.62 (d, $J = 249.3$ Hz), 154.83, 144.30, 128.79 (d, $J = 8.8$ Hz), 128.48 (2C) (d, $J = 3.0$ Hz), 120.12, 116.43 (2C) (d, $J = 22.3$ Hz). HRMS (ESI): calcd for $\text{C}_{11}\text{H}_6\text{FN}_3\text{S}_3$ $[\text{M}+\text{H}]^+$: 295.9781, found, 295.9781.



The ^1H NMR spectrogram of compound **51**

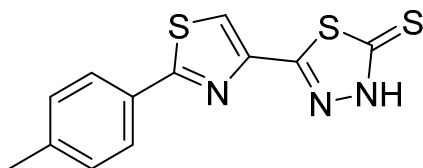


The ^{13}C NMR spectrum of compound **51**



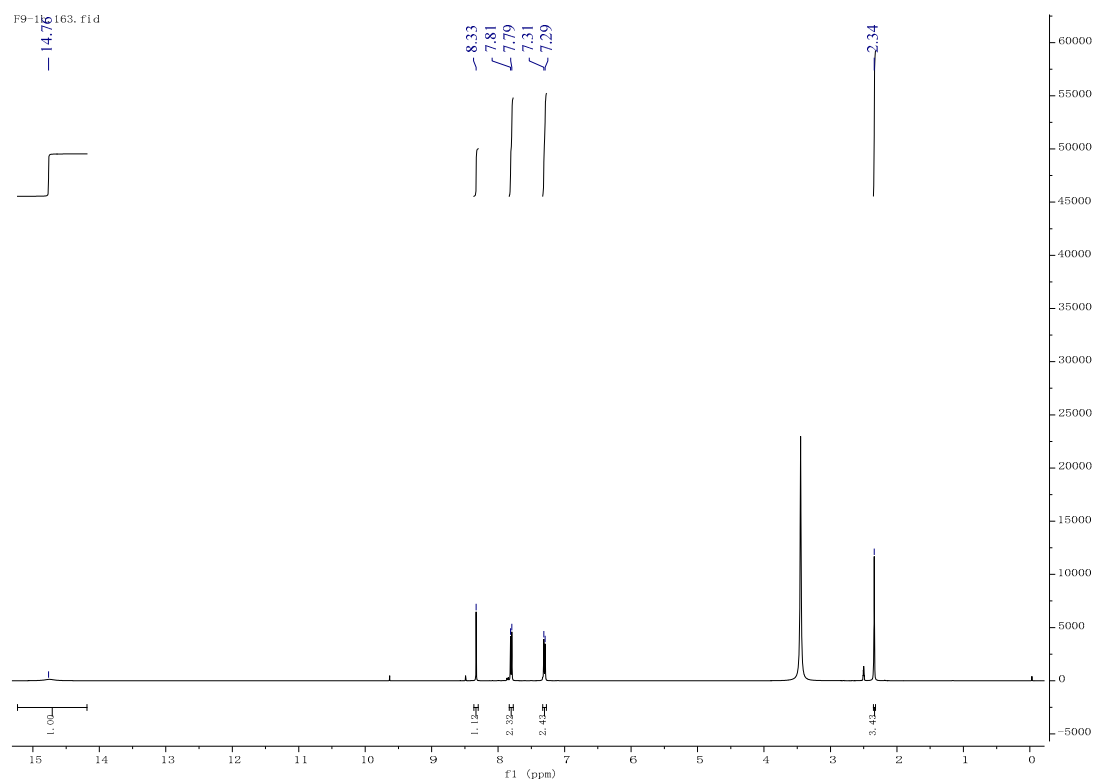
The HRMS spectrum of compound **51**

Compound **5m**, 5-(2-(p-tolyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:

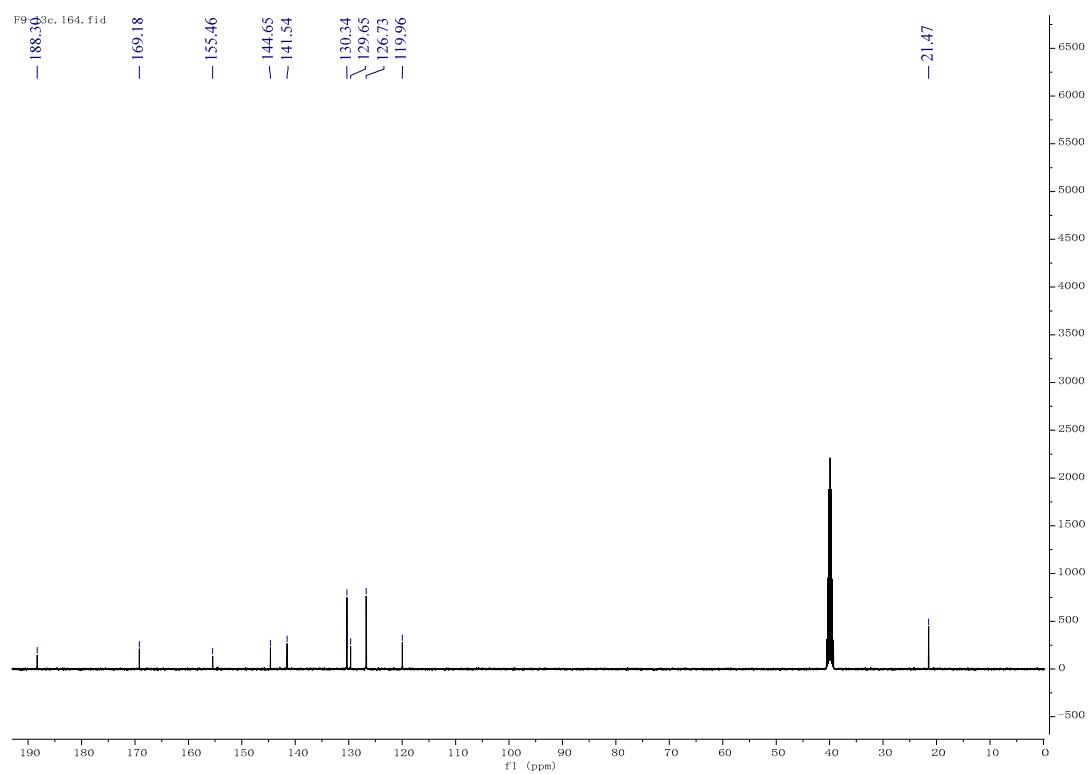


yellow solid, yield 85.2 %, m. p.247.7-248.6°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.76 (s, 1H), 8.33 (s, 1H), 7.80 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 188.30, 169.18, 155.46, 144.65, 141.54, 130.34 (2C), 129.65, 126.73 (2C), 119.96, 21.47. HRMS (ESI): calcd for $\text{C}_{12}\text{H}_9\text{N}_3\text{S}_3$

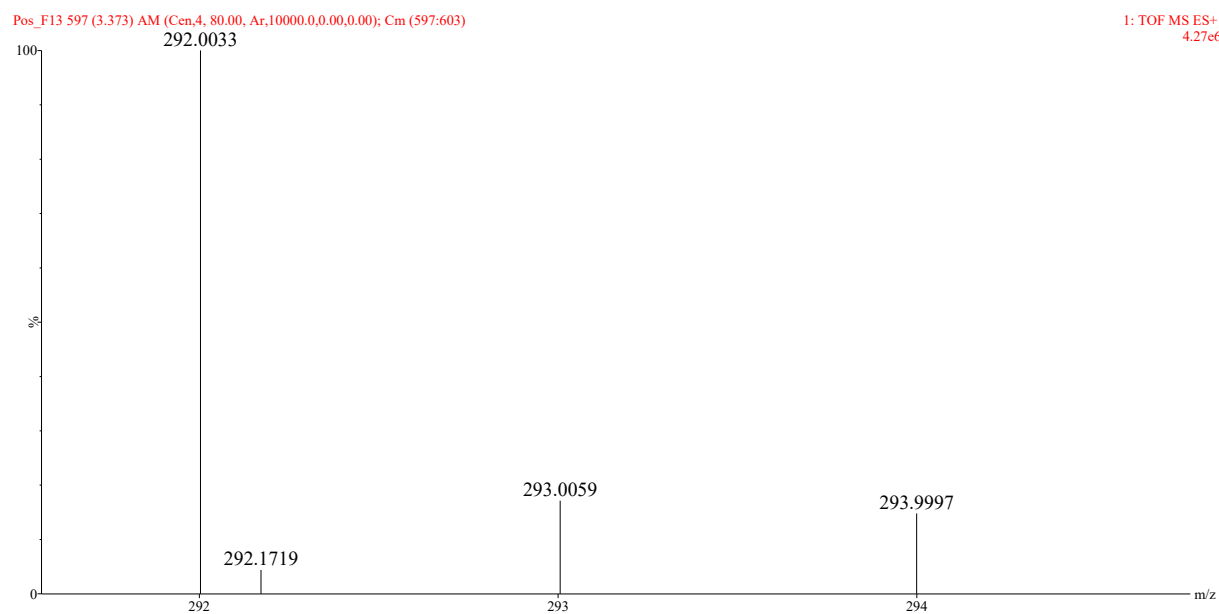
$[\text{M}+\text{H}]^+$: 292.0032, found, 292.0033.



The ^1H NMR spectrogram of compound **5m**

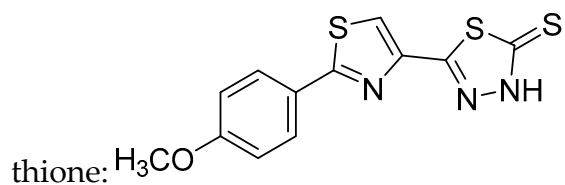


The ^{13}C NMR spectrogram of compound **5m**

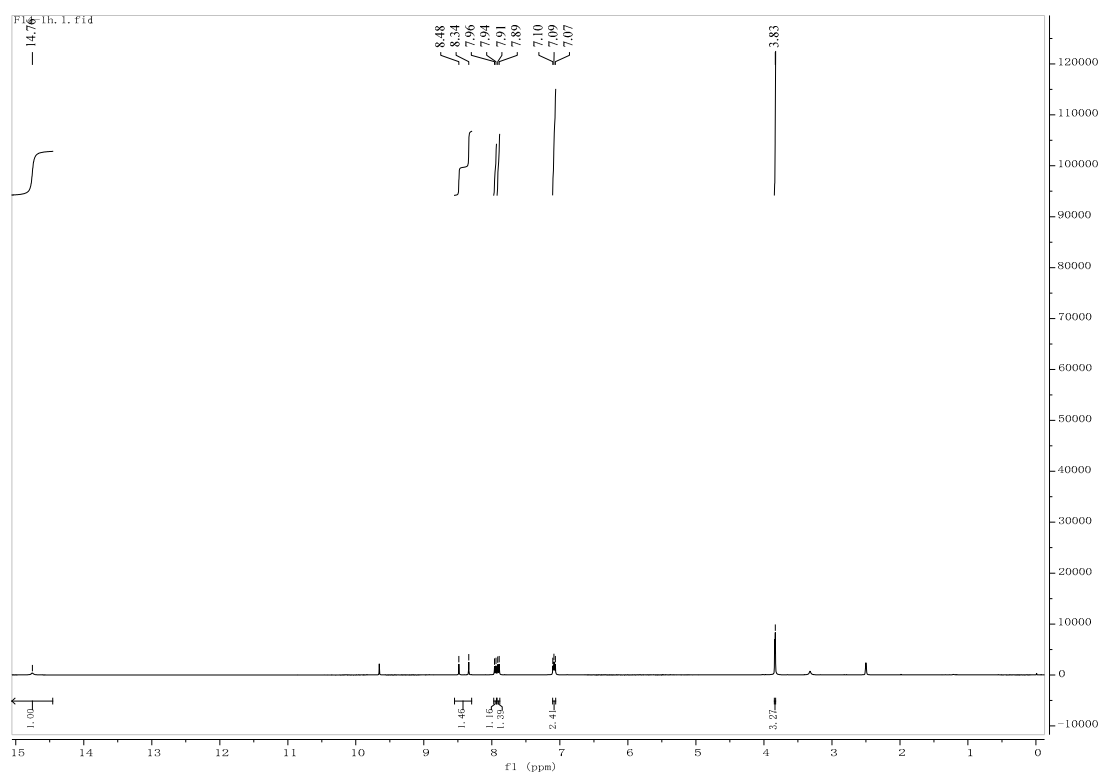


The HRMS spectrogram of compound **5m**

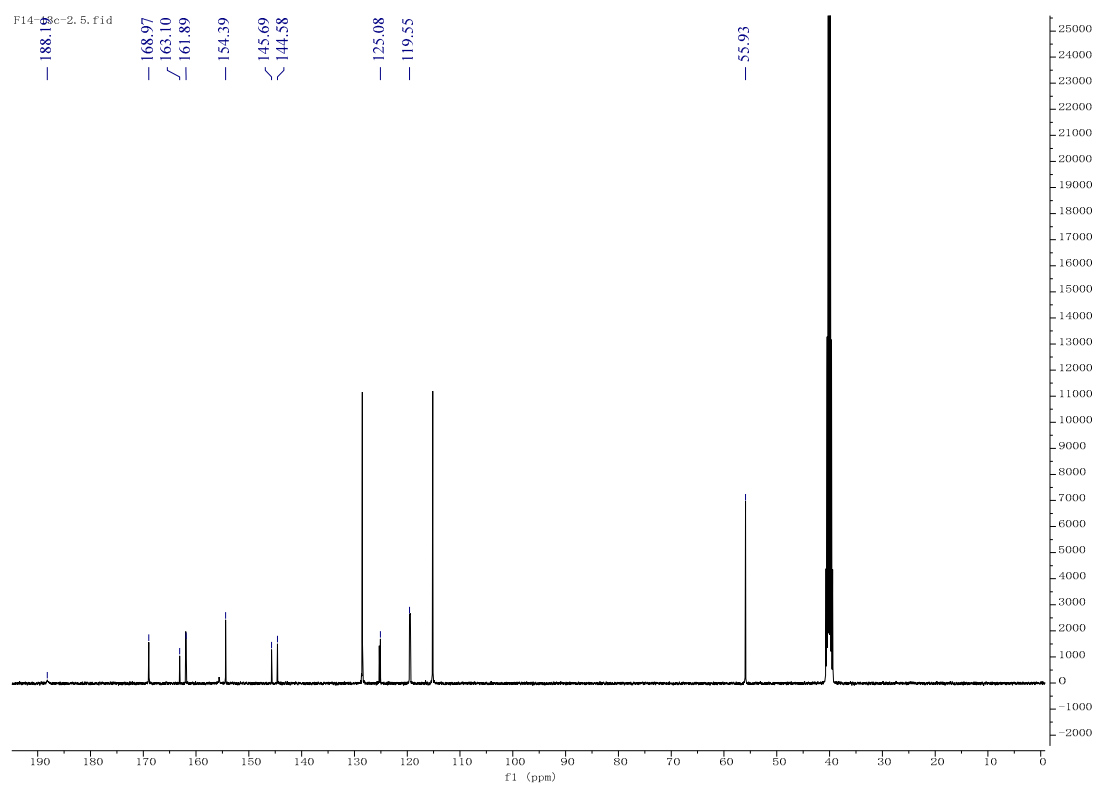
Compound **5n**, 5-(2-(4-methoxyphenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-



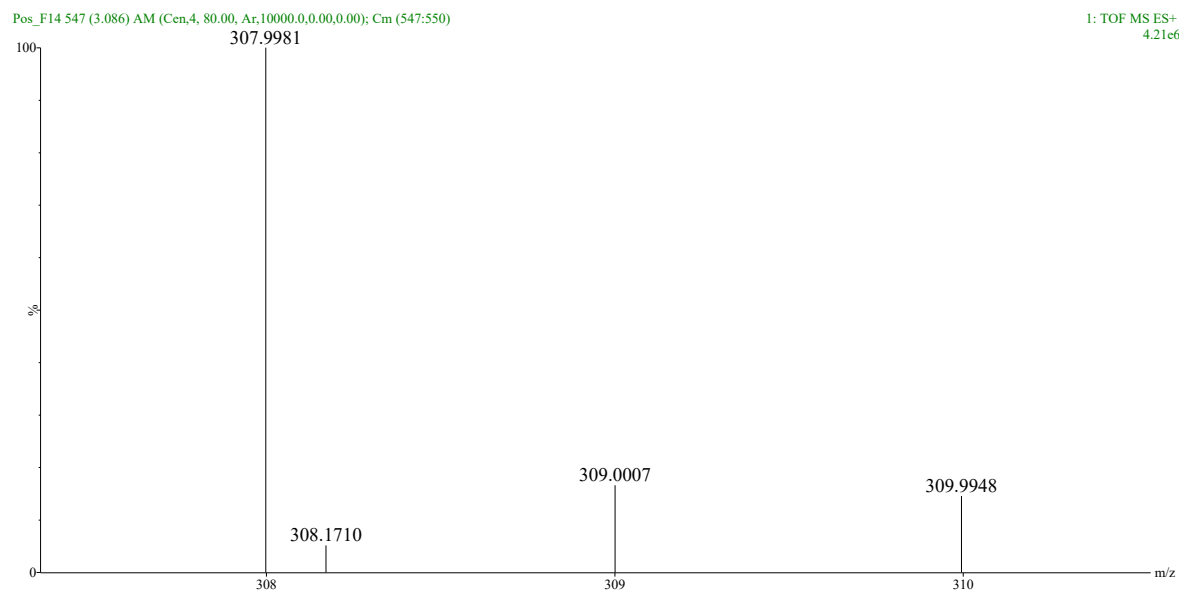
yellow solid, yield 82.1 %, m. p. 219.8-221.5°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.76 (s, 1H), 8.41 (d, $J = 57.9$ Hz, 1H), 7.95 (d, $J = 8.8$ Hz, 1H), 7.90 (d, $J = 8.8$ Hz, 1H), 7.11 – 7.06 (m, 2H), 3.83 (s, 3H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 188.19, 168.97, 163.10, 161.89, 154.39, 145.69, 144.58, 125.08 (2C), 119.55 (2C), 55.93. HRMS (ESI): calcd for $\text{C}_{12}\text{H}_9\text{N}_3\text{OS}_3$ $[\text{M}+\text{H}]^+$: 307.9981, found, 307.9981.



The ^1H NMR spectrogram of compound **5n**

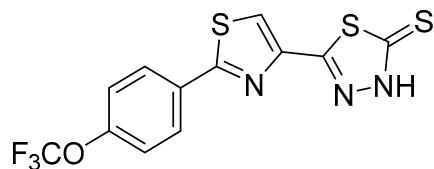


The ^{13}C NMR spectrogram of compound **5n**

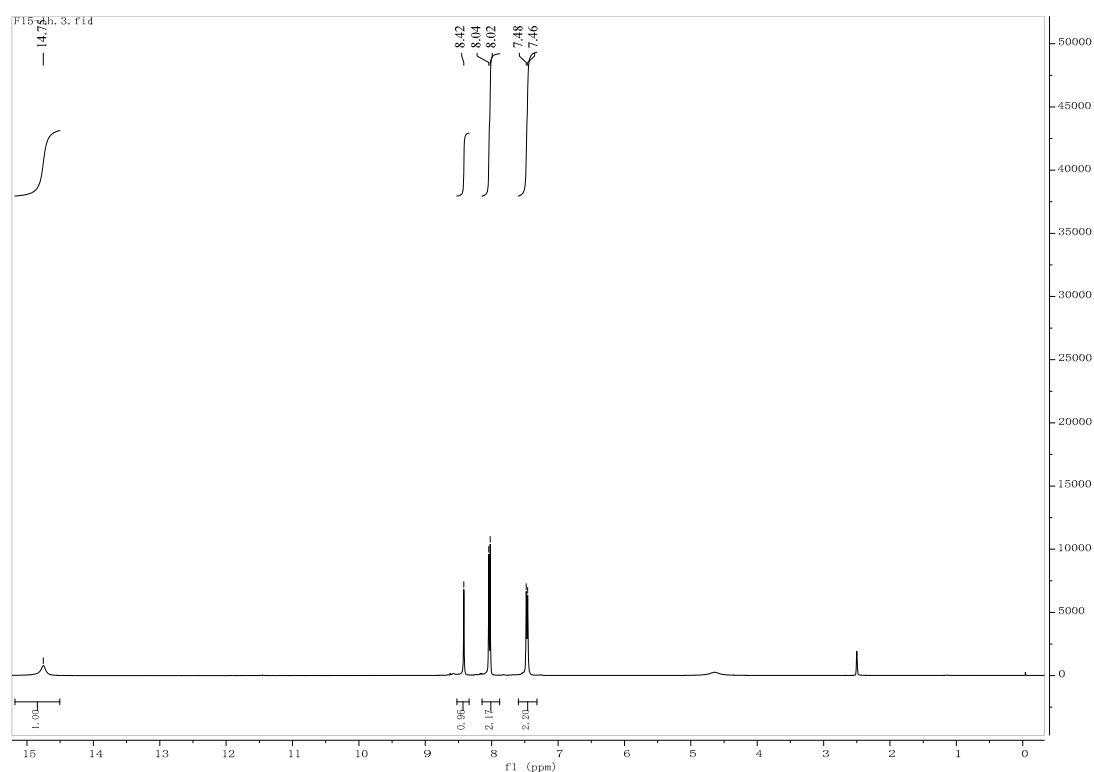


The HRMS spectrogram of compound **5n**

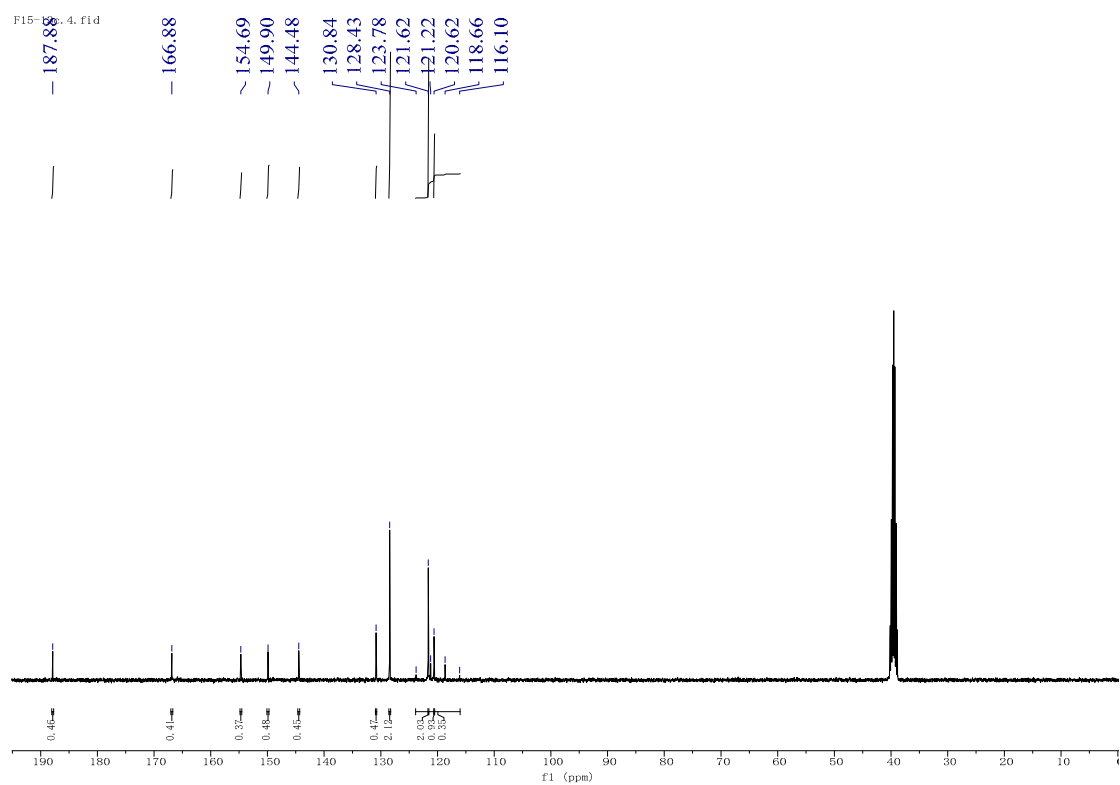
Compound **5o**, 5-(2-(4-(trifluoromethoxy)phenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



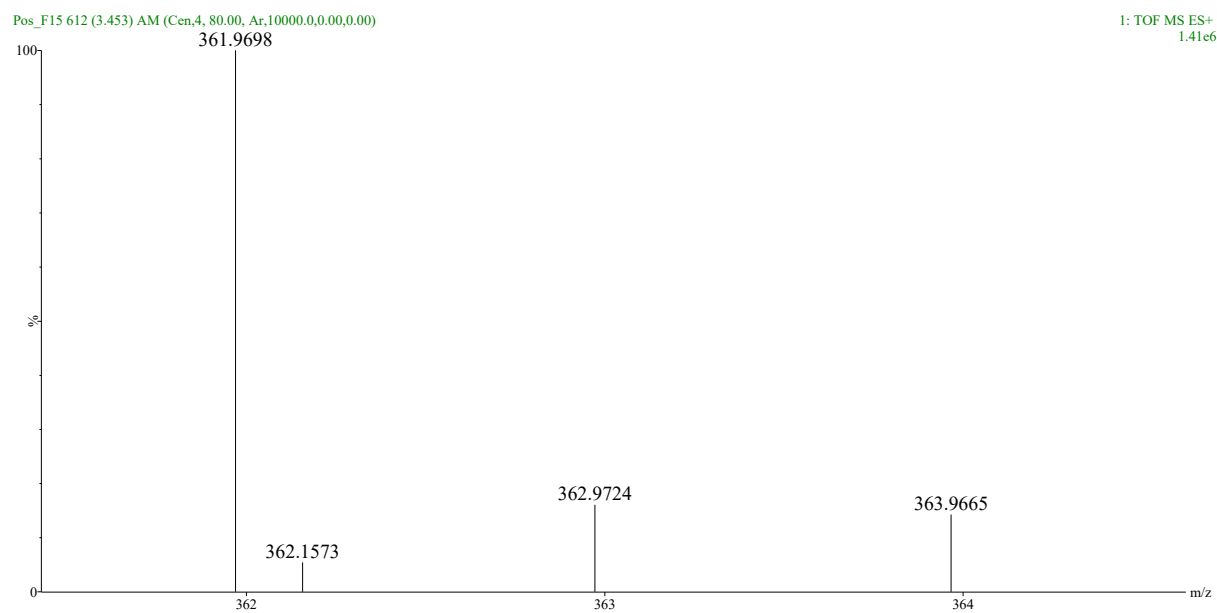
white solid, yield 83.5 %, m. p. 246.8-247.6°C; ^1H NMR (400 MHz, DMSO- d_6) δ : 14.75 (s, 1H), 8.42 (s, 1H), 8.03 (d, J = 8.7 Hz, 2H), 7.47 (d, J = 8.3 Hz, 2H). ^{13}C NMR (101 MHz, DMSO- d_6) δ : 187.88, 166.88, 154.69, 149.90, 144.48, 130.84, 128.43 (2C), 121.62 (2C), 120.62, 119.94 (q, J = 257.4 Hz). HRMS (ESI): calcd for $\text{C}_{12}\text{H}_6\text{F}_3\text{N}_3\text{OS}_3$ $[\text{M}+\text{H}]^+$: 361.9698, found, 361.9698.



The ^1H NMR spectrogram of compound **5o**

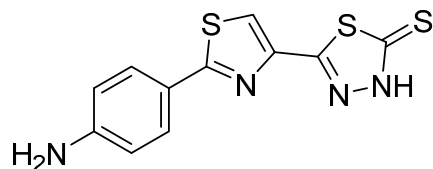


The ^{13}C NMR spectrogram of compound **50**

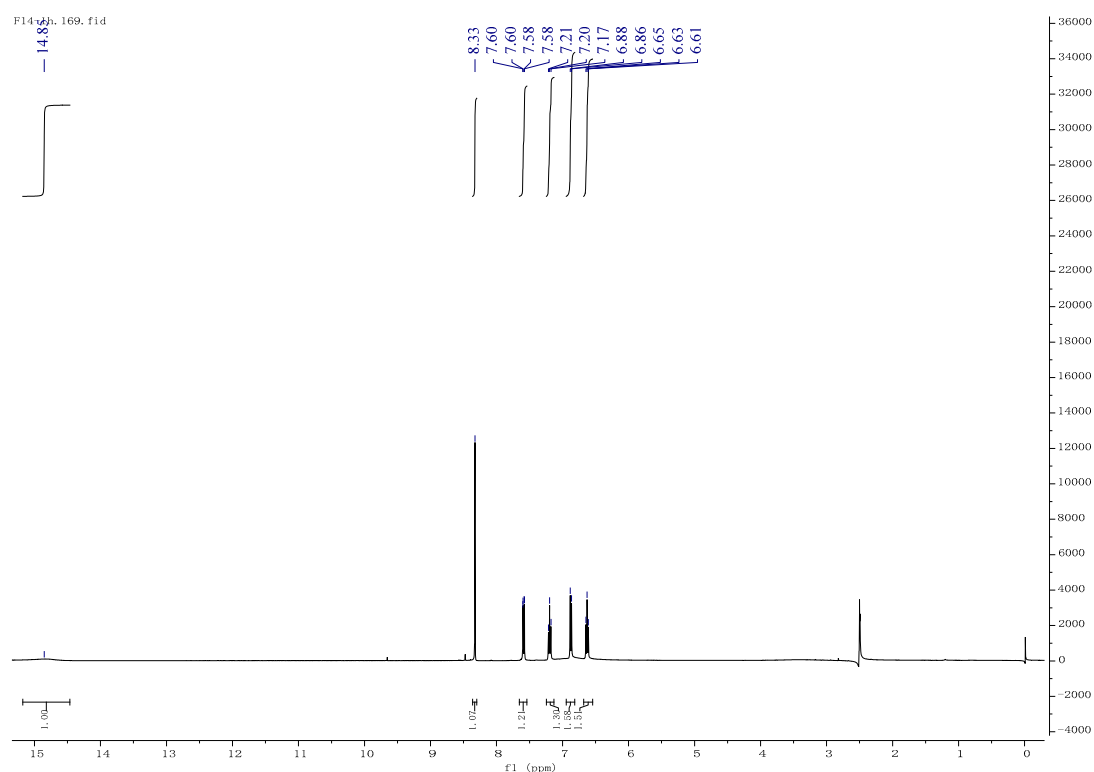


The HRMS spectrogram of compound **50**

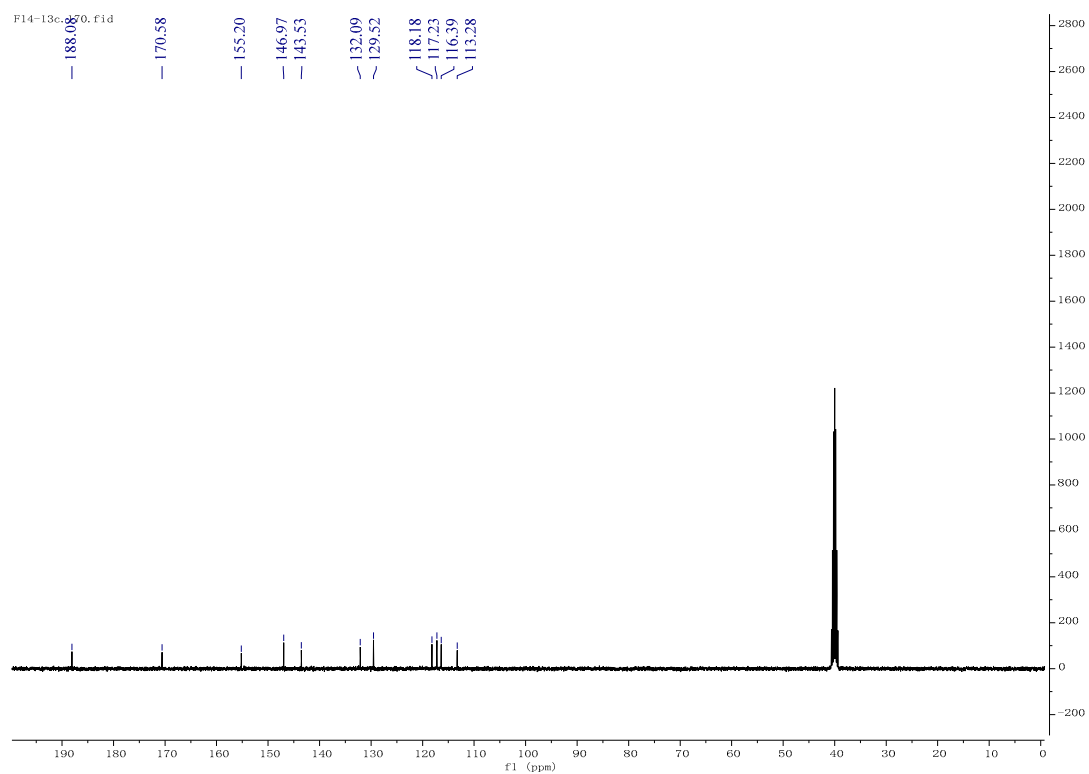
Compound **5p**, 5-(2-(4-aminophenyl)thiazol-4-yl)-1,3,4-thiadiazole-2(3H)-thione:



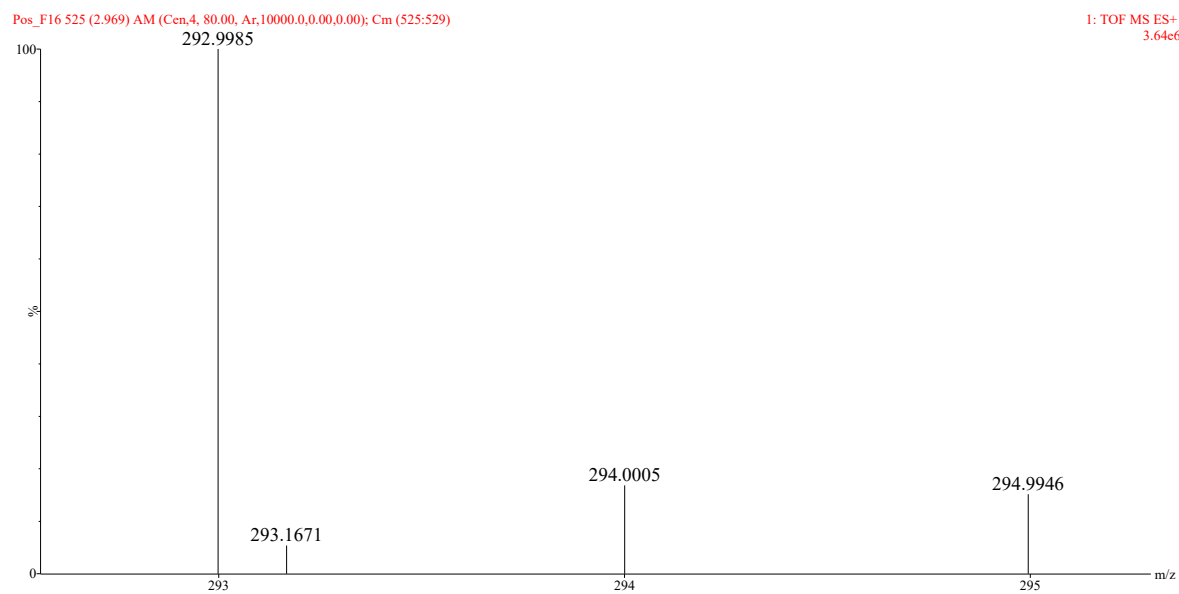
gray solid, yield 86.4 %, m. p. >250°C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ : 14.85 (s, 1H), 8.33 (s, 1H), 7.59 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.19 (t, $J = 7.7$ Hz, 1H), 6.87 (d, $J = 8.3$ Hz, 2H), 6.63 (t, $J = 7.5$ Hz, 2H). ^{13}C NMR (101 MHz, $\text{DMSO-}d_6$) δ : 188.08, 170.58, 155.20, 146.97, 143.53, 132.09, 129.52, 118.18, 117.23, 116.39, 113.28. HRMS (ESI): calcd for $\text{C}_{11}\text{H}_8\text{N}_4\text{S}_3$ $[\text{M}+\text{H}]^+$: 292.9984, found, 292.9985.



The ^1H NMR spectrogram of compound **5p**



The ^{13}C NMR spectrogram of compound **5p**



The HRMS spectrogram of compound **5p**