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Electrochemical enaminone C-H thiolation/C-N amination cascade for thiazole synthesis and their diastereoselective dearomatization

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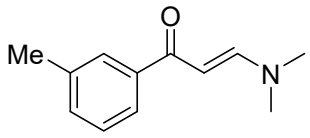
General experimental information

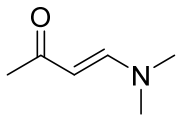
Enaminones **1** were synthesized following literature process.[1] All other chemicals and solvents used in the experiments were obtained from commercial sources and used directly without further purification. The organic solvents were treated following standard procedures before use. The NMR spectra were recorded in 400 MHz apparatus, and the frequencies for ^{1}H NMR and ^{13}C NMR test are 400 MHz and 100 MHz, respectively. The chemical shifts were reported in ppm with TMS as internal standard. HMRS data for new compounds were acquired in the mass spectrometer equipped with TOF analyzer. Melting points were rested in an X-4A apparatus without correcting temperature.

Characterization of enaminones 1

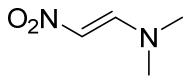
Compounds **1a, 1b, 1c, 1d, 1e, 1g, 1k, 1l, 1n, 1o, 1p, 1q, 1r, 1s, 1t, 1u, 1v, 1w, 1x, 1aa**;[1a] **1f**;[1b] **1h, 1i**;[1c] **1m**;[1d] and **1y**[1e] have been synthesized using literature method and characterized in the corresponding literatures. Other enaminones have been characterized with proper analytic methods.



(*E*)-3-(Dimethylamino)-1-(m-tolyl)prop-2-en-1-one (**1j**).[2] Yellow solid; mp 32-34 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 12.4 Hz, 1H), 7.71 (s, 1H), 7.68 (d, *J* = 7.4 Hz, 1H), 7.32-7.24 (m, 2H), 5.70 (d, *J* = 12.4 Hz, 1H), 3.11 (s, 3H), 2.90 (s, 3H), 2.39 (s, 3H).



(*E*)-4-(Dimethylamino)but-3-en-2-one (**1z**).[3] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 12.8 Hz, 1H), 5.05 (d, *J* = 12.8 Hz, 1H), 3.07 (s, 3H), 2.83 (s, 3H), 2.10 (s, 3H).



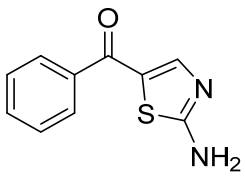
(*E*)-*N,N*-Dimethyl-2-nitroethen-1-amine (**1ab**).[4] Yellow solid; mp 95-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 10.7 Hz, 1H), 6.63 (d, *J* = 10.7 Hz, 1H), 3.22 (s, 3H), 2.89 (s, 3H).

General procedure for the synthesis of thiazoles 3

To a 25 mL three-neck bottle were added enaminone **1** (0.3 mmol, 1.0 equiv), **2** (0.6 mmol, 2.0 equiv), HCl(aq) (0.3 mmol, 1.0 equiv), and MeOH (10 mL). The bottle was then equipped with a graphite rod (ϕ 4 mm, about 15 mm immersion depth in solution) as the anode and a platinum plate (15 mm × 15 mm × 0.1 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA at room temperature for 1.5 h. After completion of the reaction, the mixture was concentrated and subjected to flash chromatography on silica gel with mixed petroleum ether, ethyl acetate and methanol ($V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4 ~ 10:10:1) as eluent to afford pure product.

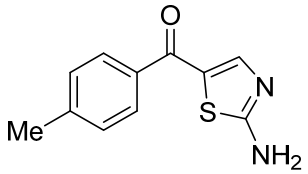
Procedure for the 10 mmol scale reaction for of 3a synthesis

To a 100 mL round-bottom flask were added enaminone **1a** (10 mmol, 1.0 equiv), **2a** (20 mmol, 2.0 equiv), HCl(aq) (10 mmol, 1.0 equiv), and MeOH (50 mL). The bottle was then equipped with a graphite rod (ϕ 4 mm, about 15 mm immersion depth in solution) as the anode and a platinum plate (15 mm × 15 mm × 0.1 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 30 mA at room temperature for 20 h. After the completion, the mixture was concentrated and water (80 mL) was added dropwise into the mixture at stirring. The precipitates formed thereby were collected by filtration. Washing the solid consequently with water and petroleum ether provided pure product **3a** (1.71 g, 84%).

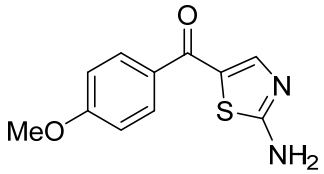


(2-Aminothiazol-5-yl)(phenyl)methanone (**3a**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (58.7 mg, 96% yield); mp 185-187 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.19 (s, 2H), 7.74 (d, *J* = 6.8 Hz, 2H), 7.64 (s, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* =

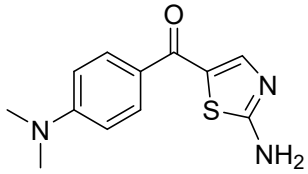
7.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.9, 175.2, 151.4, 138.8, 132.1, 129.0, 128.6, 127.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_9N_2OS$ 205.0430; Found 205.0444.



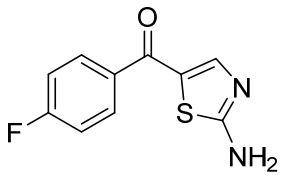
(2-Aminothiazol-5-yl)(p-tolyl)methanone (**3b**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (61.5 mg, 94% yield); mp 210-212 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.18 (s, 2H), 7.65 (d, J = 7.5 Hz, 3H), 7.33 (d, J = 7.9 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.6, 175.0, 150.9, 142.3, 136.0, 129.6, 128.8, 127.5, 21.5.



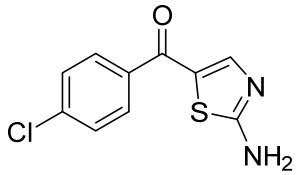
(2-Aminothiazol-5-yl)(4-methoxyphenyl)methanone (**3c**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (66.7 mg, 95% yield); mp 205-207 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (s, 2H), 7.76 (d, J = 8.8 Hz, 2H), 7.65 (s, 1H), 7.06 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.6, 174.7, 162.6, 150.3, 131.1, 130.9, 127.6, 114.3, 55.9.



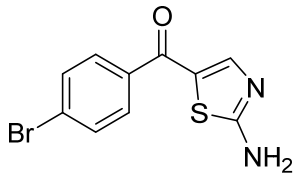
(2-Aminothiazol-5-yl)(4-(dimethylamino)phenyl)methanone (**3d**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (66.7 mg, 90% yield); mp 252-254 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.99 (s, 2H), 7.74 (d, J = 8.9 Hz, 2H), 7.67 (s, 1H), 6.81 (d, J = 9.0 Hz, 2H), 3.07 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.0, 174.0, 153.2, 148.5, 130.8, 128.1, 125.5, 111.4, 40.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}N_3OS$ 248.0852; Found 248.0853.



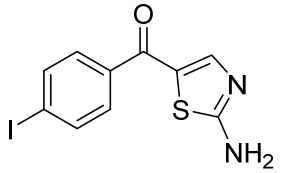
(2-Aminothiazol-5-yl)(4-fluorophenyl)methanone (**3e**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (57.9 mg, 87% yield); mp 199-201 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.24 (s, 2H), 7.86-7.80 (m, 2H), 7.67 (s, 1H), 7.35 (t, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.4, 175.3, 164.5 (d, J = 247.9 Hz), 151.6, 135.2, 135.2, 131.4 (d, J = 9.0 Hz), 127.2, 116.0 (d, J = 21.7 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ -108.30.



(2-Aminothiazol-5-yl)(4-chlorophenyl)methanone (**3f**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (60.0 mg, 84% yield); mp 217-219 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.27 (s, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.68 (s, 1H), 7.58 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.5, 175.4, 151.9, 137.4, 136.9, 130.6, 129.1, 127.1.

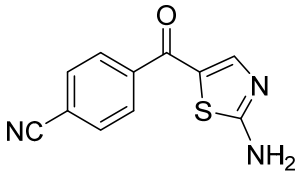


(2-Aminothiazol-5-yl)(4-bromophenyl)methanone (**3g**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (66.8 mg, 79% yield); mp 212-214 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.28 (s, 2H), 7.74-7.67 (m, 5H);^{13}C NMR (100 MHz, DMSO-d_6) δ 184.6, 175.4, 151.9, 137.7, 132.1, 130.7, 127.0, 125.8.

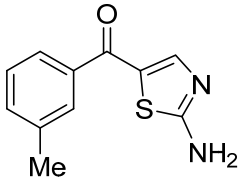


(2-Aminothiazol-5-yl)(4-iodophenyl)methanone (**3h**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ =

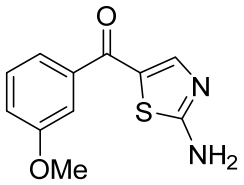
75:25:4; yellow solid (76.2 mg, 77% yield); mp 194-196 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.26 (s, 2H), 7.90 (d, J = 8.4 Hz, 2H), 7.67 (s, 1H), 7.52 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.9, 175.4, 151.8, 138.0, 137.9, 130.6, 127.0, 99.9.



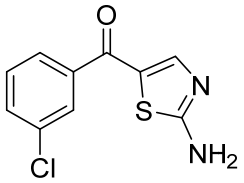
4-(2-Aminothiazole-5-carbonyl)benzonitrile (**3i**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (57.7 mg, 84% yield); mp 244-246 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.37 (s, 2H), 7.98 (d, J = 8.3 Hz, 2H), 7.87 (d, J = 8.3 Hz, 2H), 7.66 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.4, 175.8, 152.9, 142.5, 133.1, 129.4, 126.8, 118.8, 114.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_8N_3OS$ 230.0383; Found 230.0371.



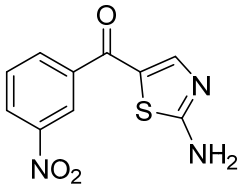
(2-Aminothiazol-5-yl)(m-tolyl)methanone (**3j**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (55.6 mg, 85% yield); mp 206-208 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (s, 2H), 7.65 (s, 1H), 7.56-7.49 (m, 2H), 7.44-7.38 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 186.0, 175.1, 151.4, 138.8, 138.5, 132.7, 129.1, 128.9, 127.5, 125.9, 21.4.



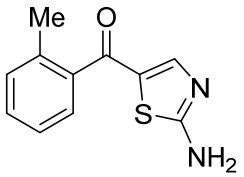
(2-Aminothiazol-5-yl)(3-methoxyphenyl)methanone (**3k**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (63.2 mg, 90% yield); mp 165-167 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23 (s, 2H), 7.67 (s, 1H), 7.44 (t, J = 7.8 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.22 (s, 1H), 7.19-7.15 (m, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.6, 175.2, 159.7, 151.5, 140.1, 130.2, 127.3, 121.0, 118.1, 113.4, 55.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}N_2O_2S$ 235.0536; Found 235.0542.



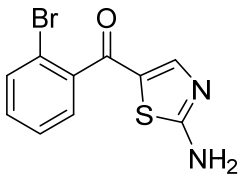
(2-Aminothiazol-5-yl)(3-chlorophenyl)methanone (**3l**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (59.3 mg, 83% yield); mp 210-212 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.31 (s, 2H), 7.72-7.65 (m, 4H), 7.55 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.2, 175.6, 152.3, 140.6, 133.9, 131.8, 131.0, 128.2, 127.4, 126.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_8ClN_2OS$ 239.0040; Found 239.0048.



(2-Aminothiazol-5-yl)(3-nitrophenyl)methanone (**3m**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (58.3 mg, 78% yield); mp 190-192 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.46-8.36 (m, 4H), 8.17 (d, J = 7.7 Hz, 1H), 7.85-7.76 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 183.4, 175.9, 153.0, 148.2, 139.8, 134.8, 130.8, 126.6, 126.4, 123.3.

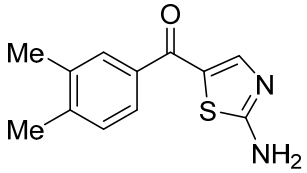


(2-Aminothiazol-5-yl)(o-tolyl)methanone (**3n**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (58.2 mg, 89% yield); mp 198-200 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.26 (s, 2H), 7.43-7.36 (m, 2H), 7.33-7.27 (m, 2H), 7.26 (s, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.1, 175.7, 152.2, 139.1, 135.6, 131.2, 130.2, 128.2, 127.9, 125.9, 19.5.

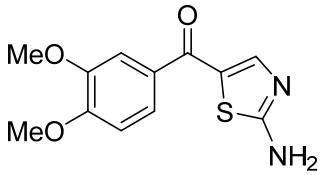


(2-Aminothiazol-5-yl)(2-bromophenyl)methanone (**3o**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ =

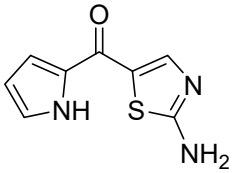
75:25:4; yellow solid (60.1 mg, 71% yield); mp 174-176 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (s, 2H), 7.72 (d, J = 7.8 Hz, 1H), 7.52-7.40 (m, 3H), 7.26 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.3, 176.1, 153.3, 140.7, 133.4, 131.8, 129.3, 128.1, 126.7, 119.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_8BrN_2OS$ 282.9535; Found 282.9539.



(2-Aminothiazol-5-yl)(3,4-dimethylphenyl)methanone (**3p**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (55.7 mg, 80% yield); mp 246-248 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.15 (s, 2H), 7.63 (s, 1H), 7.51 (s, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.27 (d, J = 7.7 Hz, 1H), 2.29 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.7, 174.9, 150.9, 141.1, 137.1, 136.4, 130.0, 129.6, 127.6, 126.4, 19.9, 19.8.

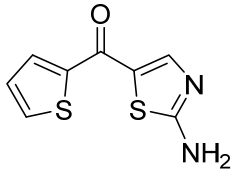


(2-Aminothiazol-5-yl)(3,4-dimethoxyphenyl)methanone (**3q**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (66.5 mg, 84% yield); mp 206-208 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (s, 2H), 7.71 (s, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.29 (s, 1H), 7.07 (d, J = 8.4 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.7, 174.7, 152.4, 150.4, 149.0, 131.1, 127.6, 122.7, 111.7, 111.4, 56.1, 56.0.

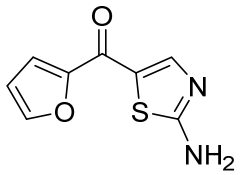


(2-Aminothiazol-5-yl)(1H-pyrrol-2-yl)methanone (**3r**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (44.0 mg, 76% yield); mp 270-272 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.77 (s, 1H), 7.94 (s, 1H), 7.91 (s, 2H), 7.08 (s, 1H), 7.03 (s, 1H), 6.22 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.1, 173.6, 147.1, 130.5, 127.0, 125.0,

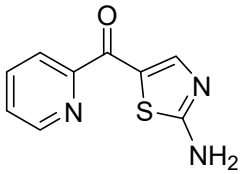
115.5, 110.4.



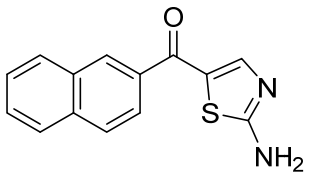
(2-Aminothiazol-5-yl)(thiophen-2-yl)methanone (**3s**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (47.9 mg, 76% yield); mp 178-180 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23 (s, 2H), 8.08 (s, 1H), 7.98-7.95 (m, 2H), 7.25 (t, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.5, 174.8, 149.7, 143.0, 133.4, 132.0, 128.9, 126.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_8H_7N_2OS_2$ 210.9994; Found 210.9993.



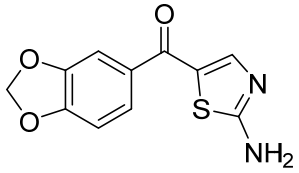
(2-Aminothiazol-5-yl)(furan-2-yl)methanone (**3t**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (32.0 mg, 55% yield); mp 247-249 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25-8.19 (m, 3H), 8.00 (s, 1H), 7.36 (d, J = 3.6 Hz, 1H), 6.76-6.72 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.9, 171.4, 152.1, 150.0, 147.3, 126.3, 117.4, 112.8.



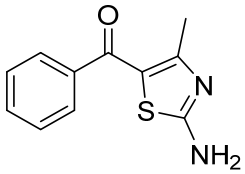
(2-Aminothiazol-5-yl)(pyridin-2-yl)methanone (**3u**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (41.8 mg, 68% yield); mp 251-253 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.74 (d, J = 4.7 Hz, 1H), 8.46 (s, 1H), 8.21 (s, 2H), 8.07-8.00 (m, 2H), 7.69-7.63 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.6, 176.7, 154.1, 153.5, 149.0, 138.2, 127.4, 123.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_9H_8N_3OS$ 206.0383; Found 206.0384.



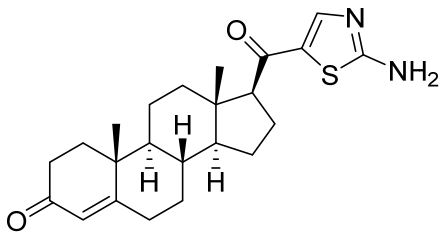
(2-Aminothiazol-5-yl)(naphthalen-2-yl)methanone (**3v**).[5] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (69.3 mg, 91% yield); mp 216-218 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.42 (s, 1H), 8.27 (s, 2H), 8.15 (d, *J* = 7.6 Hz, 1H), 8.07-7.99 (m, 2H), 7.83-7.78 (m, 2H), 7.68-7.60 (m, 2H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 185.8, 175.2, 151.7, 135.9, 134.8, 132.6, 129.8, 129.4, 128.8, 128.4, 128.1, 127.5, 127.3, 125.3.



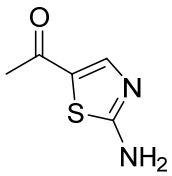
(2-Aminothiazol-5-yl)(benzo[d][1,3]dioxol-5-yl)methanone (**3w**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (61.8 mg, 83% yield); mp 280-282 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.15 (s, 2H), 7.66 (s, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.25 (s, 1H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.14 (s, 2H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 184.2, 174.9, 150.8, 150.6, 148.0, 132.8, 127.3, 124.4, 108.6, 108.5, 102.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_9N_2O_3S$ 249.0328; Found 249.0338.



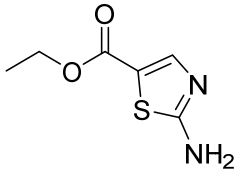
(2-Amino-4-methylthiazol-5-yl)(phenyl)methanone (**3x**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (56.9 mg, 87% yield); mp 131-133 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.98 (s, 2H), 7.61 (d, *J* = 6.9 Hz, 2H), 7.58-7.52 (m, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 187.1, 172.1, 160.6, 141.4, 131.6, 128.8, 128.0, 119.2, 19.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}N_2OS$ 219.0587; Found 219.0596.



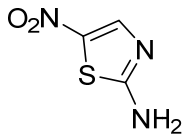
(8S,9S,10R,13S,14S,17S)-17-(2-Aminothiazole-5-carbonyl)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3H-cyclopenta[a]phenanthren-3-one (**3y**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:3; yellow solid (80.0 mg, 67% yield); mp 152-154 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (s, 2H), 7.83 (s, 1H), 5.63 (s, 1H), 3.20 (t, J = 7.7 Hz, 1H), 2.39 (t, J = 15.0 Hz, 2H), 2.27-2.11 (m, 3H), 1.95 (d, J = 12.6 Hz, 1H), 1.81 (d, J = 11.8 Hz, 1H), 1.69-1.44 (m, 7H), 1.34-1.21 (m, 3H), 1.12 (s, 3H), 1.03-0.90 (m, 2H), 0.58 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 198.4, 191.4, 174.7, 171.3, 148.8, 129.9, 123.7, 56.9, 55.8, 53.7, 44.7, 38.6, 38.4, 35.6, 35.5, 34.1, 32.5, 32.2, 24.8, 23.8, 21.0, 17.3, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{31}N_2O_2S$ 399.2101; Found 399.2101.



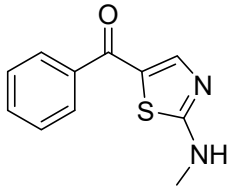
1-(2-Aminothiazol-5-yl)ethan-1-one (**3z**).[6] Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 25:25:2; yellow solid (37.1 mg, 87% yield); mp 169-171 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.03 (s, 2H), 7.93 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.0, 175.0, 149.9, 128.1, 26.1.



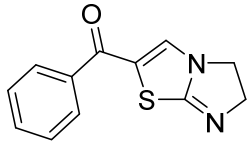
Ethyl 2-aminothiazole-5-carboxylate (**3aa**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (33.0 mg, 64% yield); mp 150-152 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (s, 2H), 7.68 (s, 1H), 4.18 (q, J = 7.1 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.9, 161.8, 148.3, 115.0, 60.6, 14.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_6H_9N_2O_2S$ 173.0379; Found 173.0382.



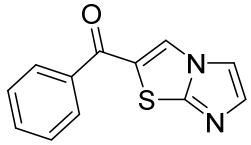
5-Nitrothiazol-2-amine (**3ab**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:3; yellow solid (13.5 mg, 31% yield); mp 204-206 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.81 (s, 2H), 8.25 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.9, 147.9, 135.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_3H_4N_3O_2S$ 146.0019; Found 146.0019.



(2-(Methylamino)thiazol-5-yl)(phenyl)methanone (**3ac**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (29.4 mg, 45% yield); mp 165-167 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.19 (s, 1H), 6.06 (s, 1H), 3.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.4, 163.7, 139.9, 137.7, 131.9, 128.7, 128.2, 116.5, 33.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}N_2OS$ 219.0587; Found 219.0590.

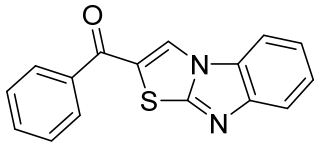


(5,6-Dihydroimidazo[2,1-b]thiazol-2-yl)(phenyl)methanone (**3ad**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 10:10:1; yellow liquid (55.2 mg, 80% yield); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (s, 1H), 7.70 (d, *J* = 7.0 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 2H), 4.16 (t, *J* = 8.9 Hz, 2H), 3.93 (t, *J* = 8.9 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.8, 164.8, 138.2, 138.0, 132.1, 129.1, 128.4, 118.3, 60.7, 45.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}N_2OS$ 231.0587; Found 231.0593.

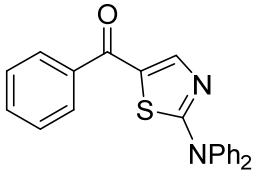


Imidazo[2,1-*b*]thiazol-2-yl(phenyl)methanone (**3ae**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 10:10:1; yellow liquid (59.5 mg, 87% yield); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.80 (s,

1H), 7.97 (d, J = 7.4 Hz, 2H), 7.88 (s, 1H), 7.79 (t, J = 7.4 Hz, 1H), 7.67 (t, J = 7.6 Hz, 2H), 7.46 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.9, 149.3, 136.9, 136.4, 133.5, 130.5, 130.2, 129.4, 129.2, 115.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_9N_2OS$ 229.0430; Found 229.0437.



Benzo[4,5]imidazo[2,1-b]thiazol-2-yl(phenyl)methanone (**3af**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 75:25:4; yellow solid (70.1 mg, 84% yield); mp 166-168 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.28 (s, 1H), 8.18 (d, J = 7.8 Hz, 1H), 7.98 (d, J = 7.1 Hz, 2H), 7.79-7.63 (m, 4H), 7.41 (t, J = 7.7 Hz, 1H), 7.33 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.5, 156.1, 148.5, 136.9, 133.5, 130.5, 130.1, 129.5, 129.4, 128.7, 125.1, 122.1, 119.1, 113.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{11}N_2OS$ 279.0587; Found 279.0594.

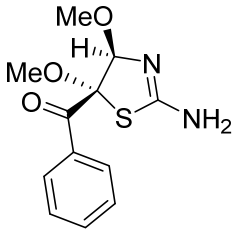


(2-(Diphenylamino)thiazol-5-yl)(phenyl)methanone (**3ag**). Eluent: V_{PET}/V_{EA} = 15:1; yellow solid (54.5 mg, 51% yield); mp 170-172 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83-7.74 (m, 3H), 7.54 (t, J = 7.4 Hz, 1H), 7.49-7.37 (m, 10H), 7.34-7.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0, 174.7, 149.4, 144.1, 138.2, 132.1, 130.5, 129.9, 128.7, 128.5, 127.4, 126.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{17}N_2OS$ 357.1056; Found 357.1072.

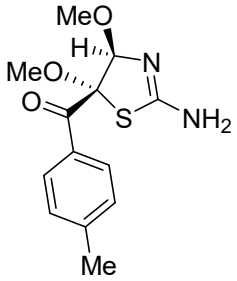
General procedure for the synthesis and characterization data of 4

To a 25 mL three-neck bottle were added enaminone **1** (0.3 mmol, 1.0 equiv), **2a** (0.36 mmol, 1.2 equiv), TfOH (0.6 mmol, 2.0 equiv), and alcohol (10 mL). The bottle was then equipped with a graphite rod (ϕ 4 mm, about 15 mm immersion depth in solution) as the anode and a platinum plate (15 mm × 15 mm × 0.1 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA at

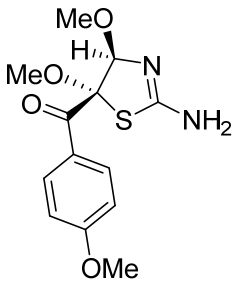
room temperature for 6.5 h. After completion, the mixture was concentrated and subjected to flash chromatography on silica gel eluting with the eluction of mixted petroleum ether, ethyl acetate and methanol($V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2 ~ 2:5:0) to afford pure product.



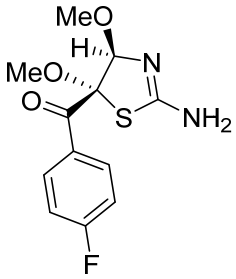
(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(phenyl)methanone (**4a**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (71.8 mg, 90% yield); mp 130-132 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.05 (d, J = 7.8 Hz, 2H), 7.66 (t, J = 7.3 Hz, 1H), 7.55 (t, J = 7.6 Hz, 2H), 7.12 (s, 2H), 5.50 (s, 1H), 3.17 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.7, 162.7, 134.7, 133.8, 129.5, 129.1, 118.5, 106.6, 55.1, 53.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{15}N_2O_3S$ 267.0798; Found 267.0804.



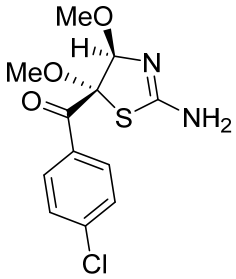
(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(p-tolyl)methanone (**4b**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (75.6 mg, 90% yield); mp 140-142 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (d, J = 6.8 Hz, 2H), 7.35 (d, J = 6.8 Hz, 2H), 7.09 (s, 2H), 5.48 (s, 1H), 3.14 (s, 3H), 3.03 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.1, 162.7, 144.2, 132.2, 129.7, 129.6, 118.8, 106.6, 55.1, 53.5, 21.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}N_2O_3S$ 281.0954; Found 281.0956.



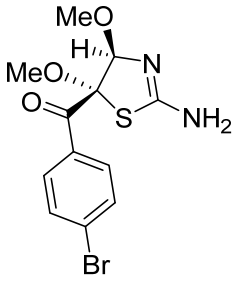
(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(4-methoxyphenyl)methanone (**4c**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (82.6 mg, 93% yield); mp 142-144 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.64 (s, 2H), 8.11 (d, J = 8.9 Hz, 2H), 7.12 (d, J = 9.0 Hz, 2H), 5.78 (s, 1H), 3.90 (s, 3H), 3.29 (s, 3H), 3.15 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.4, 170.8, 164.7, 132.2, 125.4, 116.0, 115.0, 94.9, 56.4, 56.2, 54.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}N_2O_4S$ 297.0904; Found 297.0895.



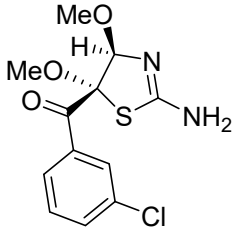
(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(4-fluorophenyl)methanone (**4d**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (65.6 mg, 77% yield); mp 132-134 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.14 (dd, J = 8.4, 5.7 Hz, 2H), 7.36 (t, J = 8.8 Hz, 2H), 7.13 (s, 2H), 5.51 (s, 1H), 3.16 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.3, 165.3 (d, J = 251.0 Hz), 162.7, 132.6 (d, J = 9.3 Hz), 131.4, 118.3, 116.2 (d, J = 21.7 Hz), 106.6, 55.1, 53.5; ^{19}F NMR (376 MHz, DMSO-d_6) δ -105.44; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}FN_2O_3S$ 285.0704; Found 285.0708.



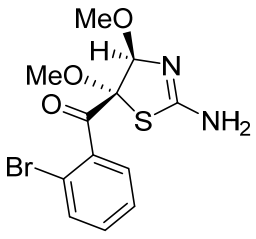
(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(4-chlorophenyl)methanone (4e). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (62.1 mg, 69% yield); mp 138-140 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.06 (d, J = 8.7 Hz, 2H), 7.61 (d, J = 8.7 Hz, 2H), 7.07 (s, 2H), 5.49 (s, 1H), 3.17 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.8, 162.6, 138.7, 133.4, 131.4, 129.3, 118.1, 106.7, 55.1, 53.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}ClN_2O_3S$ 301.0408; Found 301.0413.



(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(4-bromophenyl)methanone (**4f**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (79.5 mg, 77% yield); mp 140-142 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (d, J = 8.6 Hz, 2H), 7.76 (d, J = 8.6 Hz, 2H), 7.09 (s, 2H), 5.49 (s, 1H), 3.17 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.0, 162.6, 133.8, 132.3, 131.5, 127.9, 118.1, 106.7, 55.1, 53.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}BrN_2O_3S$ 344.9903; Found 344.9904.

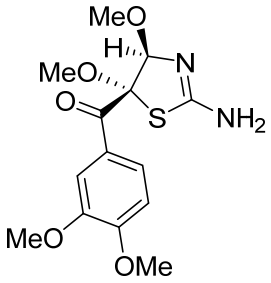


(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(3-chlorophenyl)methanone (**4g**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (66.6 mg, 74% yield); mp 128-130 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.04 (d, J = 7.8 Hz, 1H), 7.94 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.59 (t, J = 7.9 Hz, 1H), 7.09 (s, 2H), 5.49 (s, 1H), 3.19 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.7, 162.5, 136.6, 133.9, 133.5, 131.3, 128.7, 128.2, 117.9, 106.8, 55.1, 53.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}ClN_2O_3S$ 301.0408; Found 301.0418.

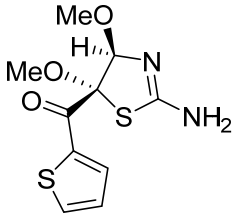


(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(2-bromophenyl)methanone (**4h**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (45.4 mg, 44% yield); mp 150-152 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (t, J = 7.4 Hz, 2H), 7.49 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.12 (s, 2H), 5.28 (s, 1H), 3.25 (s, 3H), 3.20 (s, 3H); ^{13}C

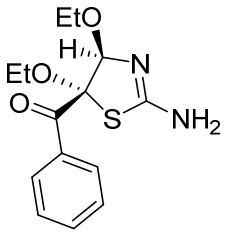
NMR (100 MHz, DMSO-d_6) δ 196.0, 161.9, 138.9, 134.1, 132.4, 128.8, 127.7, 120.2, 114.9, 108.4, 55.5, 53.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}BrN_2O_3S$ 344.9903; Found 344.9904.



(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(3,4-dimethoxyphenyl)methanone (**4i**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (51.8 mg, 53% yield); mp 164-166 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, J = 7.0 Hz, 1H), 7.51 (s, 1H), 7.09 (d, J = 8.6 Hz, 1H), 7.04 (s, 2H), 5.45 (s, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 3.16 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.9, 162.8, 153.7, 148.8, 127.3, 124.3, 119.1, 111.9, 111.4, 106.7, 56.2, 56.0, 55.2, 53.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{19}N_2O_5S$ 327.1009; Found 327.1016.

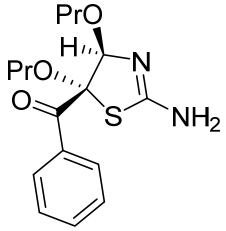


(2-Amino-4,5-dimethoxy-4,5-dihydrothiazol-5-yl)(thiophen-2-yl)methanone (**4j**). Eluent: V_{PET}/V_{EA} = 2:5; yellow solid (47.3 mg, 58% yield); mp 176-178 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.06 (t, J = 4.1 Hz, 2H), 7.28 (s, 1H), 7.21 (d, J = 44.9 Hz, 2H), 5.41 (s, 1H), 3.21 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.6, 162.8, 140.2, 135.8, 134.6, 129.2, 117.3, 106.7, 55.2, 53.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{13}N_2O_3S_2$ 273.0362; Found 273.0359.

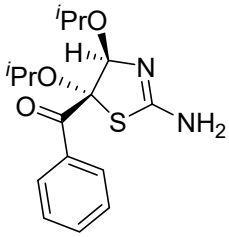


(2-Amino-4,5-diethoxy-4,5-dihydrothiazol-5-yl)(phenyl)methanone (**4k**). Eluent:

$V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; white solid (54.7 mg, 62% yield); mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.4 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 6.66 (s, 2H), 5.51 (s, 1H), 3.90-3.80 (m, 1H), 3.66-3.56 (m, 1H), 3.44-3.35 (m, 1H), 3.23-3.12 (m, 1H), 1.23 (t, *J* = 6.9 Hz, 3H), 0.74 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3, 171.3, 134.2, 133.6, 129.0, 128.7, 116.0, 95.7, 65.4, 63.4, 14.8, 14.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{19}N_2O_3S$ 295.1111; Found 295.1109.



(2-Amino-4,5-dipropoxy-4,5-dihydrothiazol-5-yl)(phenyl)methanone (**4l**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; yellow solid (53.1 mg, 55% yield); mp 83-85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 5.56 (s, 1H), 4.88 (s, 2H), 3.72-3.63 (m, 1H), 3.59-3.49 (m, 1H), 3.25-3.16 (m, 1H), 3.10-3.00 (m, 1H), 1.63-1.50 (m, 2H), 1.21-1.09 (m, 2H), 0.83 (t, *J* = 7.4 Hz, 3H), 0.42 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 164.1, 134.7, 133.2, 129.2, 128.4, 119.1, 104.8, 70.3, 68.4, 22.7, 22.4, 10.4, 10.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{23}N_2O_3S$ 323.1424; Found 323.1420.

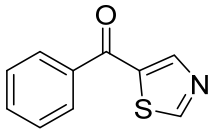


(2-Amino-4,5-diisopropoxy-4,5-dihydrothiazol-5-yl)(phenyl)methanone (**4m**). Eluent: $V_{PET}/V_{EA}/V_{MeOH}$ = 50:25:2; yellow solid (21.3 mg, 22% yield); mp 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.6 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 5.50 (s, 1H), 4.44 (s, 2H), 4.13-4.01 (m, 1H), 3.56-3.47 (m, 1H), 1.27 (d, *J* = 6.0 Hz, 3H), 1.02-0.89 (m, 6H), 0.49 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.0, 163.6, 135.5, 132.9, 129.5, 128.2, 118.8, 102.7, 71.7, 70.9, 24.4, 23.4, 23.0, 20.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{23}N_2O_3S$ 323.1424;

Found 323.1419.

Procedure for the synthesis and characterization data of 5

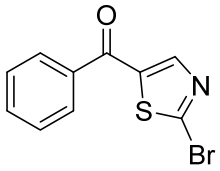
In a 15 mL sealed tube were charged with **3a** (0.2 mmol, 1.0 equiv), $NaNO_2$ (0.4 mmol, 2.0 equiv), $BF_3{\cdot}Et_2O$ (0.6 mmol, 3.0 equiv) and DMF (2 mL). The vessel was then sealed with Teflon cap and stirred at 100 °C for 12 h. Upon completion, the vessel was allowed to cool down to room temperature, and 10 mL water was added. The heterogeneous mixture was extracted with ethyl acetate (3×10 mL). The combined organic phase was dried over Na_2SO_4. After filtration, the acquired solution was collected and the solvent was removed at reduced pressure. The residue obtained therein was subjected to silica gel column chromatography to give pure product by using mixed petroleum ether and ethyl acetate (v/v = 10:1) as eluent.



Phenyl(thiazol-5-yl)methanone (**5**). Yellow solid (26.8 mg, 71% yield); mp 87-89 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.37 (s, 1H), 7.90 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.3, 159.2, 149.1, 139.4, 137.6, 133.2, 129.2, 128.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_8NOS$ 190.0321; Found 190.0323.

Procedure for the synthesis and characterization data of 6

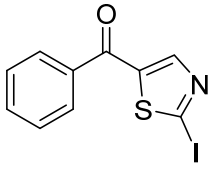
In a 15 mL sealed tube were charged with **3a** (0.2 mmol, 1.0 equiv), $NaNO_2$ (0.4 mmol, 2.0 equiv), NBS (0.6 mmol, 3.0 equiv) and DMF (2 mL). The vessel was then sealed with Teflon cap and stirred at room temperature for 12 h. Upon completion, water (10 mL) was added and the resulting suspension was extracted with ethyl acetate (3 × 10 mL). The combined organic phase was dried over Na_2SO_4. After filtration, the acquired solution was collected and the solvent was removed at reduced pressure. The residue was subjected to silica gel column chromatography to give pure product by using mixed petroleum ether and ethyl acetate (v/v = 20:1) as eluent.



(2-Bromothiazol-5-yl)(phenyl)methanone (**6**). Yellow solid (20.3 mg, 38% yield); mp 79-81 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.86 (d, *J* = 7.5 Hz, 2H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.2, 148.1, 143.9, 143.1, 136.9, 133.4, 129.1, 128.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_7BrNOS$ 267.9426; Found 267.9433.

Procedure for the synthesis and characterization data of 7

In a 15 mL sealed tube were charged with **3a** (0.2 mmol, 1.0 equiv), $NaNO_2$ (0.4 mmol, 2.0 equiv), NIS (0.6 mmol, 3.0 equiv) and DMF (2 mL). The vessel was then sealed with Teflon cap and stirred at 100 °C for 12 h. Upon completion, the vessel was allowed to cool down to room temperature, and 10 mL water was added. The heterogeneous mixture was extracted with ethyl acetate (3×10 mL). The combined organic phase was dried over Na_2SO_4. After filtration, the acquired solution was collected and the solvent was removed at reduced pressure. The residue was subjected to silica gel column chromatography to give pure product by using mixed petroleum ether and ethyl acetate (v/v = 20:1) as eluent.



(2-Iodothiazol-5-yl)(phenyl)methanone (**7**). Eluent: V_{PET}/V_{EA} = 20:1; yellow solid (31.5 mg, 50% yield); mp 85-87 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.86 (d, *J* = 7.3 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.8, 149.5, 145.2, 137.1, 133.4, 129.1, 128.9, 110.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_7INOS$ 315.9288; Found 315.9292.

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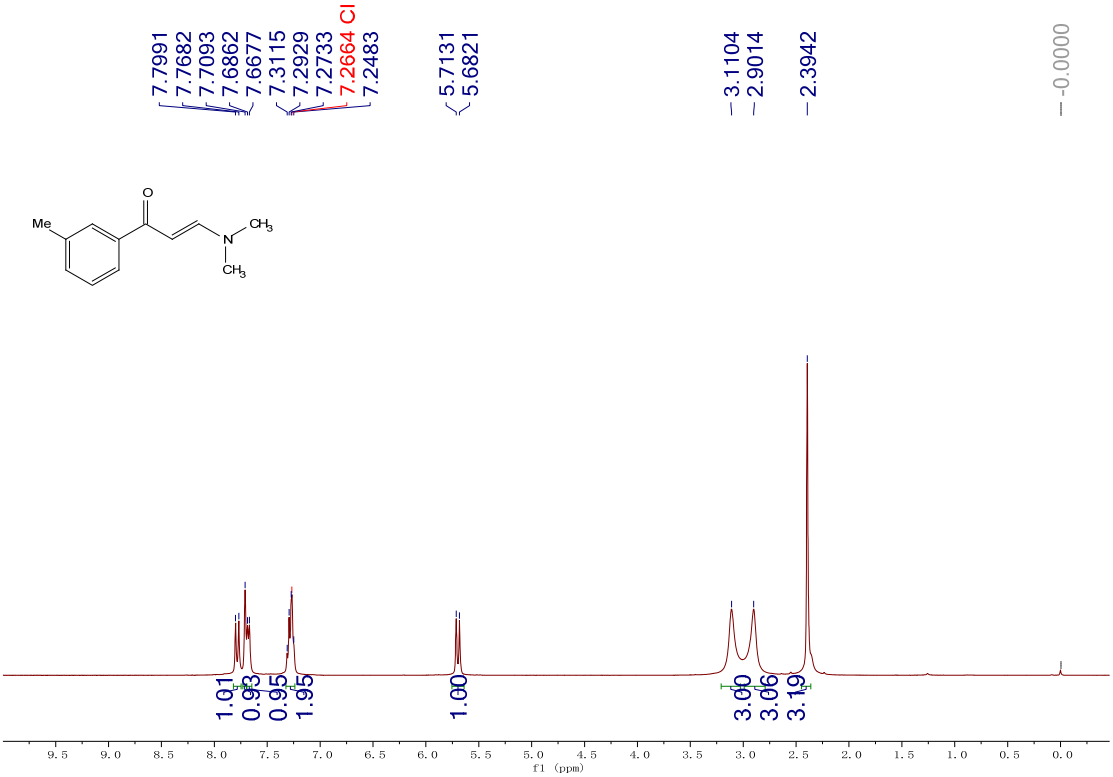
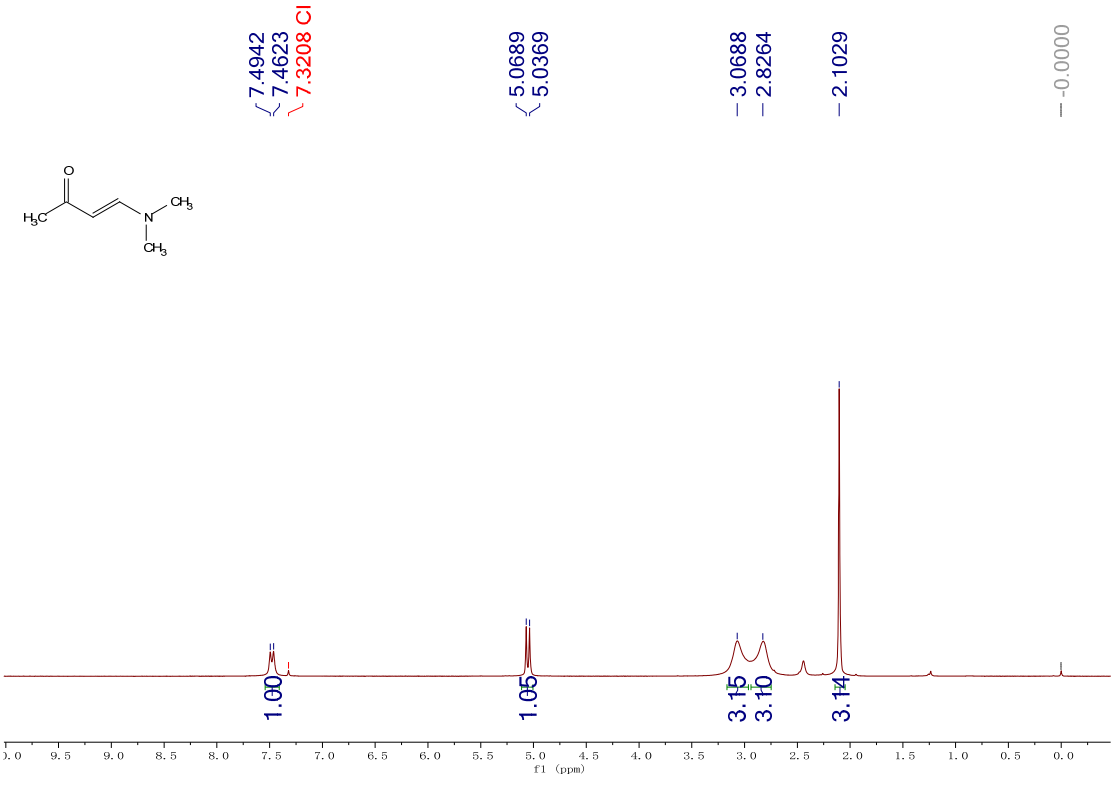
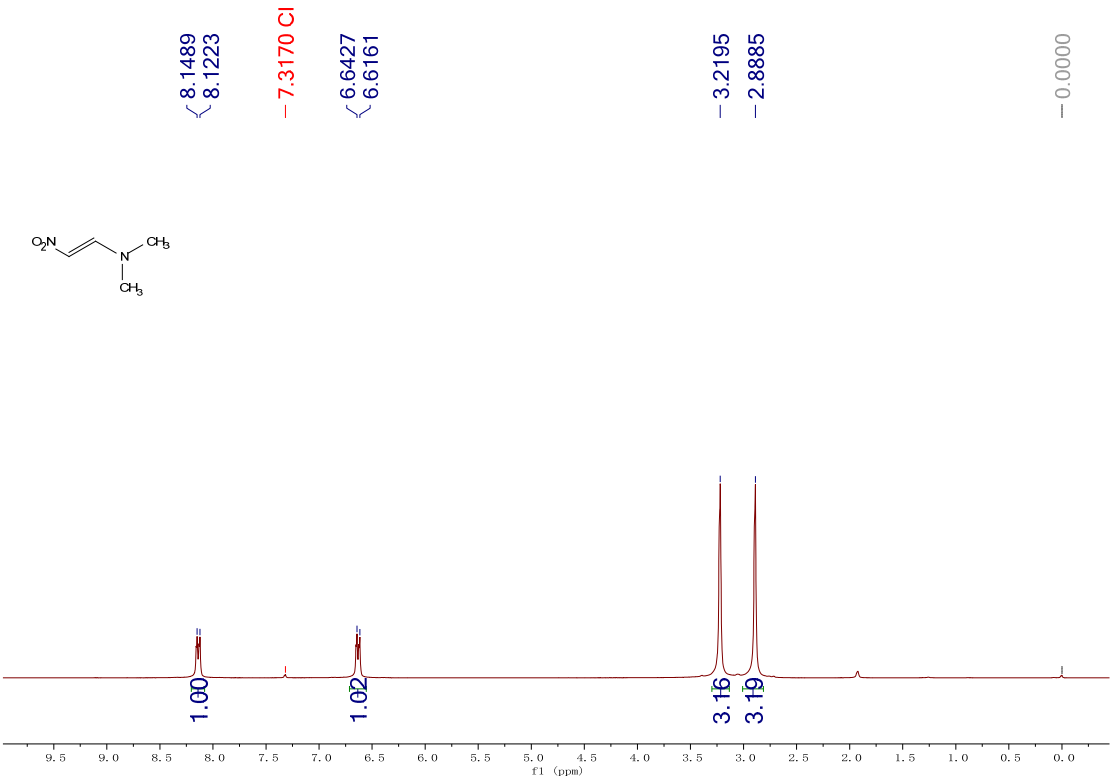
The ^{1}H and ^{13}C NMR spectra



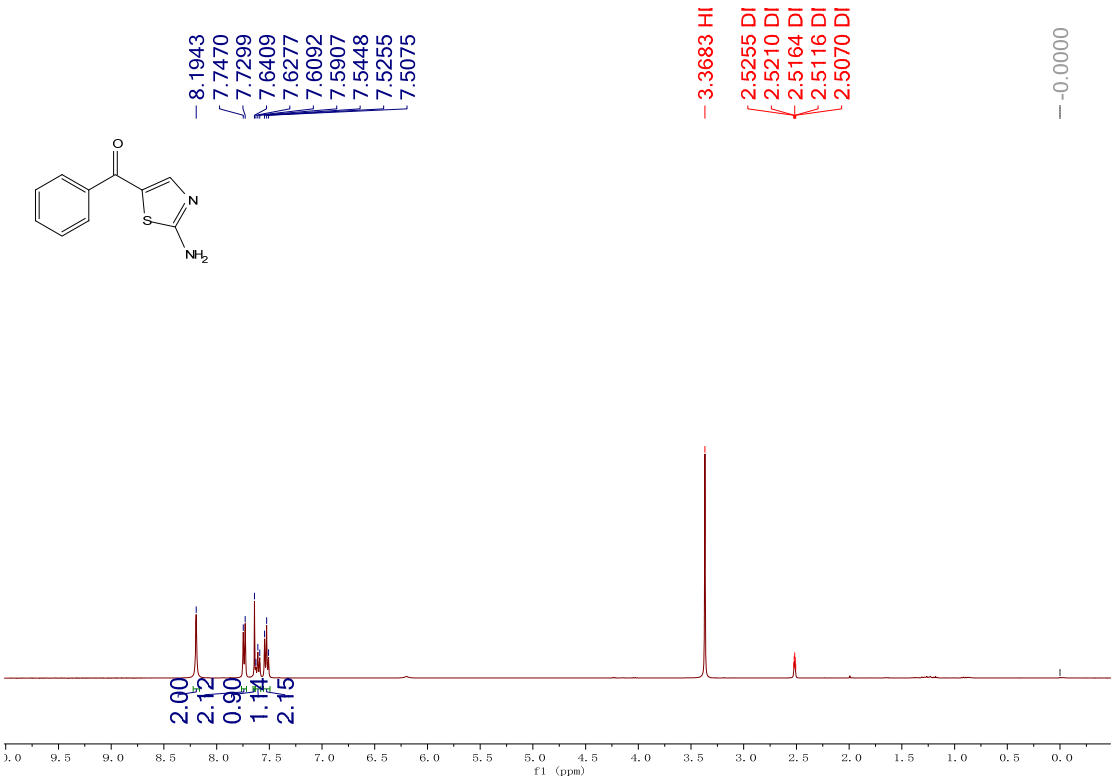
^{1}H NMR spectrum of **1j** (400 MHz, $CDCl_3$)



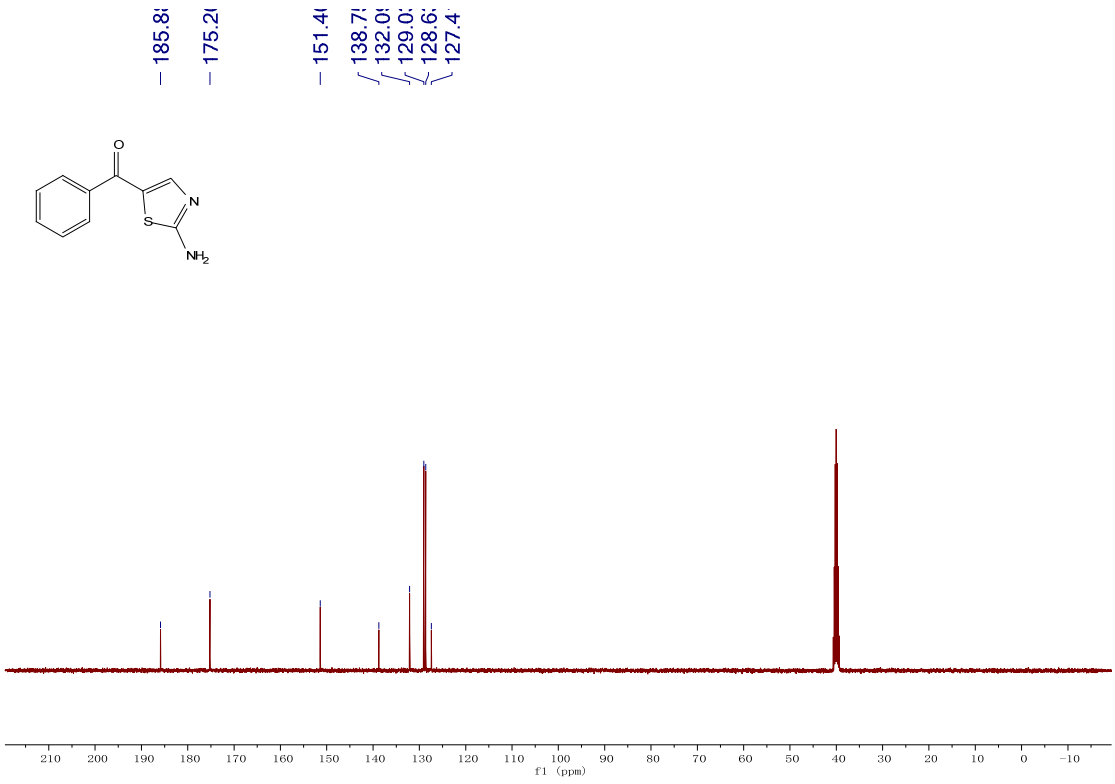
^{1}H NMR spectrum of **1z** (400 MHz, $CDCl_3$)



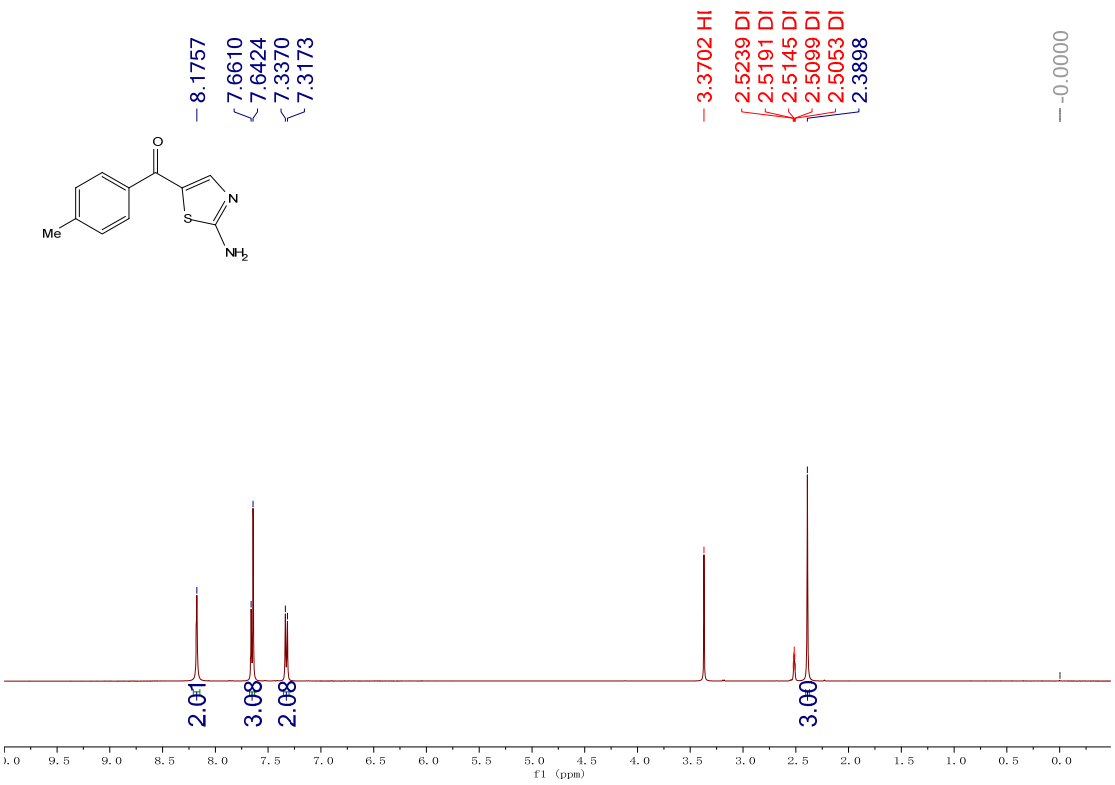
^{1}H NMR spectrum of **1ab** (400 MHz, $CDCl_3$)



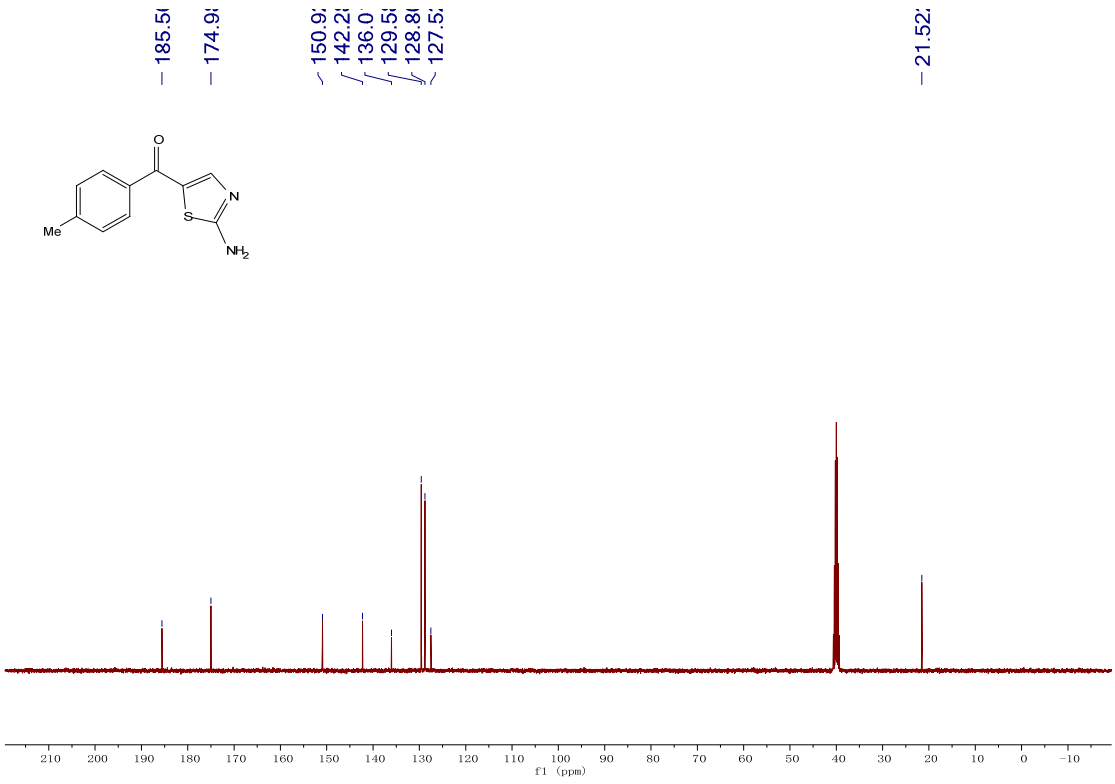
^{1}H NMR spectrum of **3a** (400 MHz, DMSO-d_6)



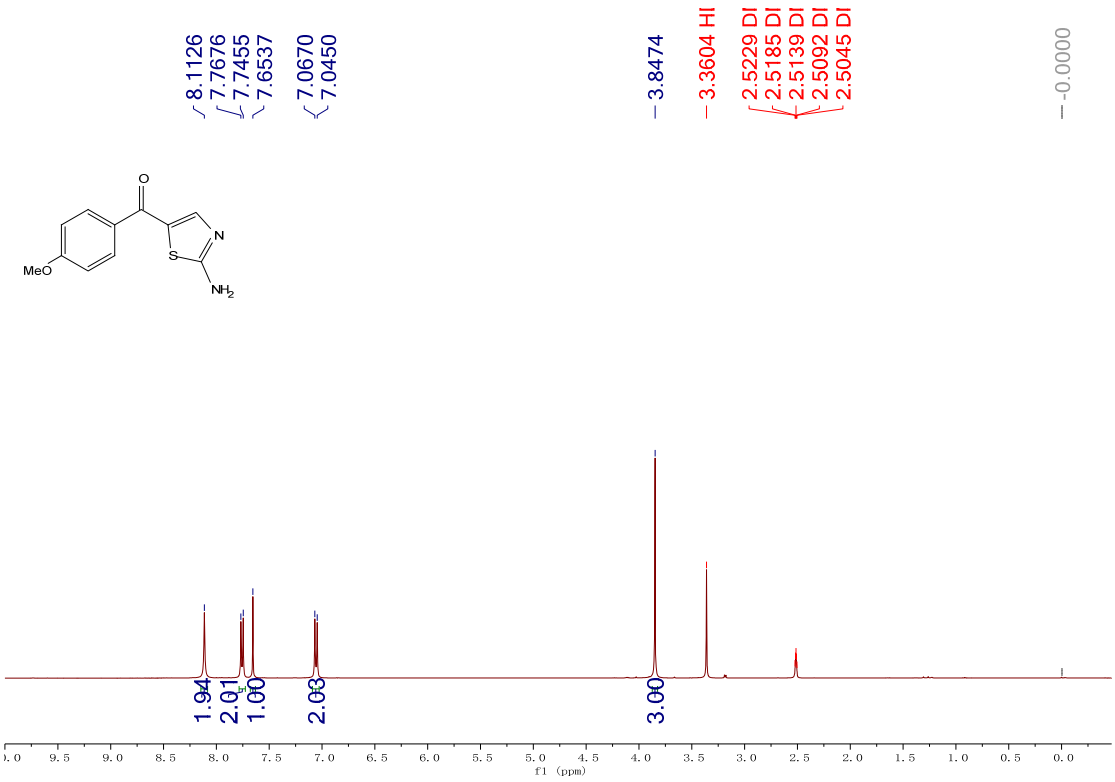
^{13}C NMR spectrum of **3a** (100 MHz, DMSO-d_6)



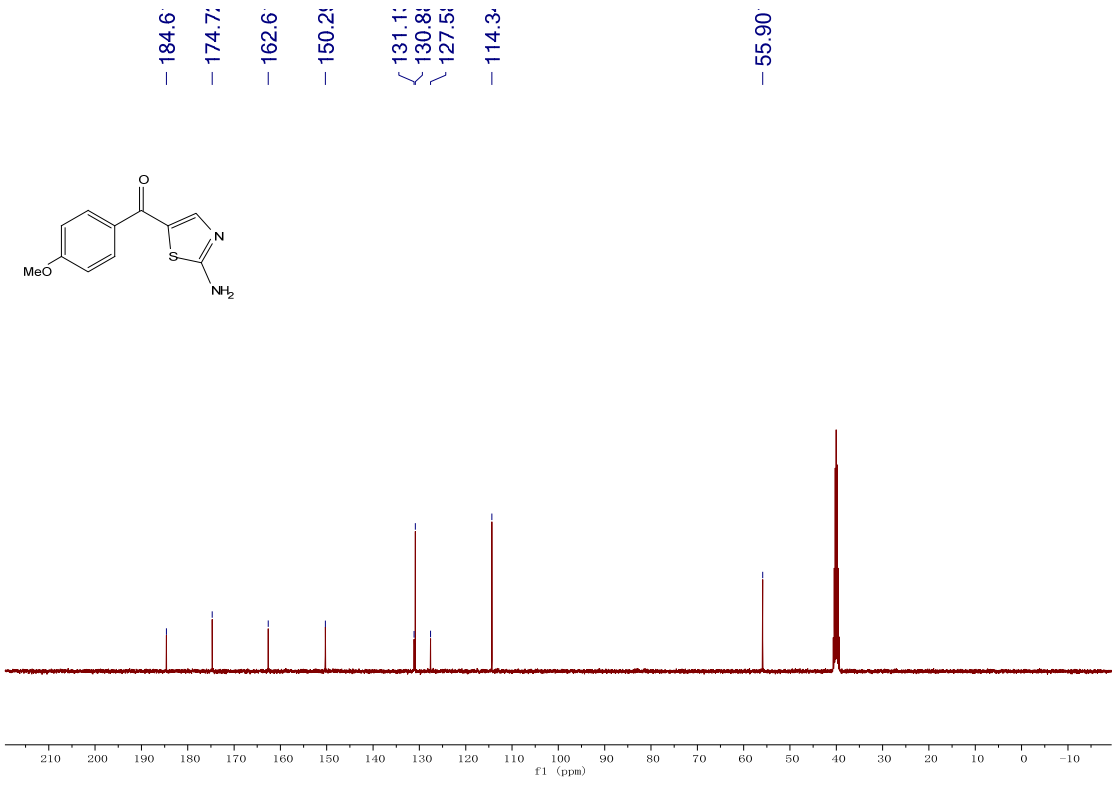
^{1}H NMR spectrum of **3b** (400 MHz, DMSO-d_6)



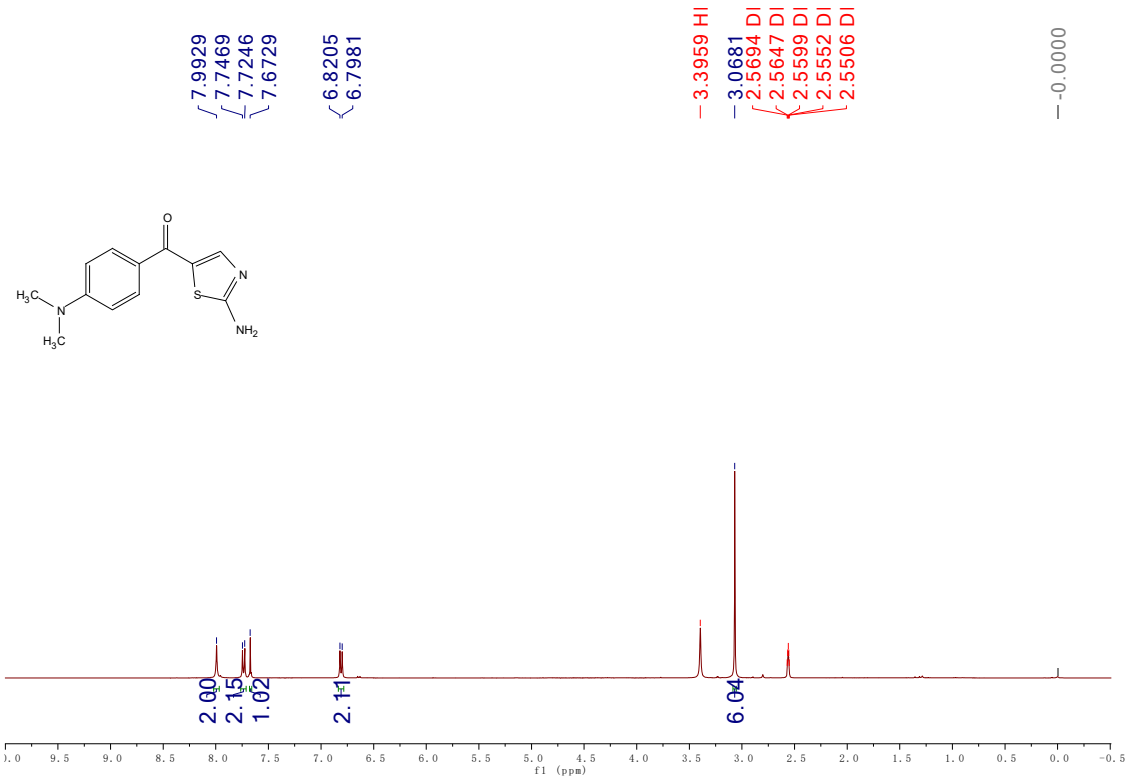
^{13}C NMR spectrum of **3b** (100 MHz, DMSO-d_6)



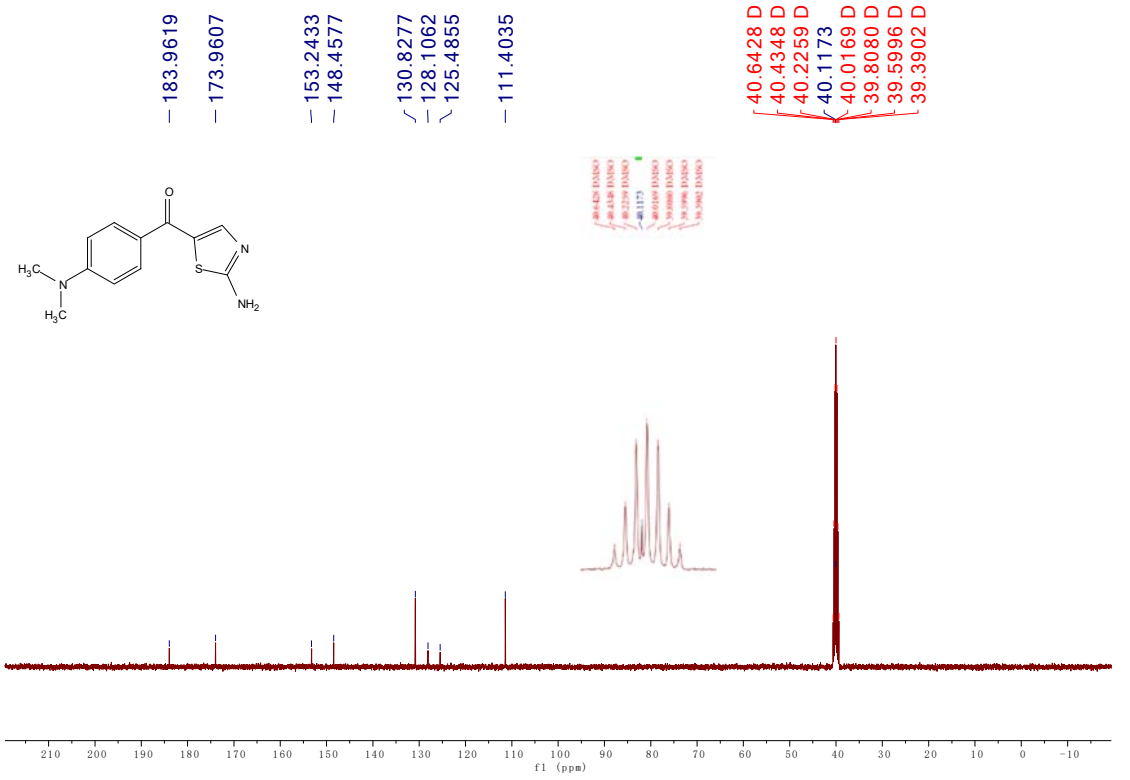
^{1}H NMR spectrum of **3c** (400 MHz, DMSO-d_6)



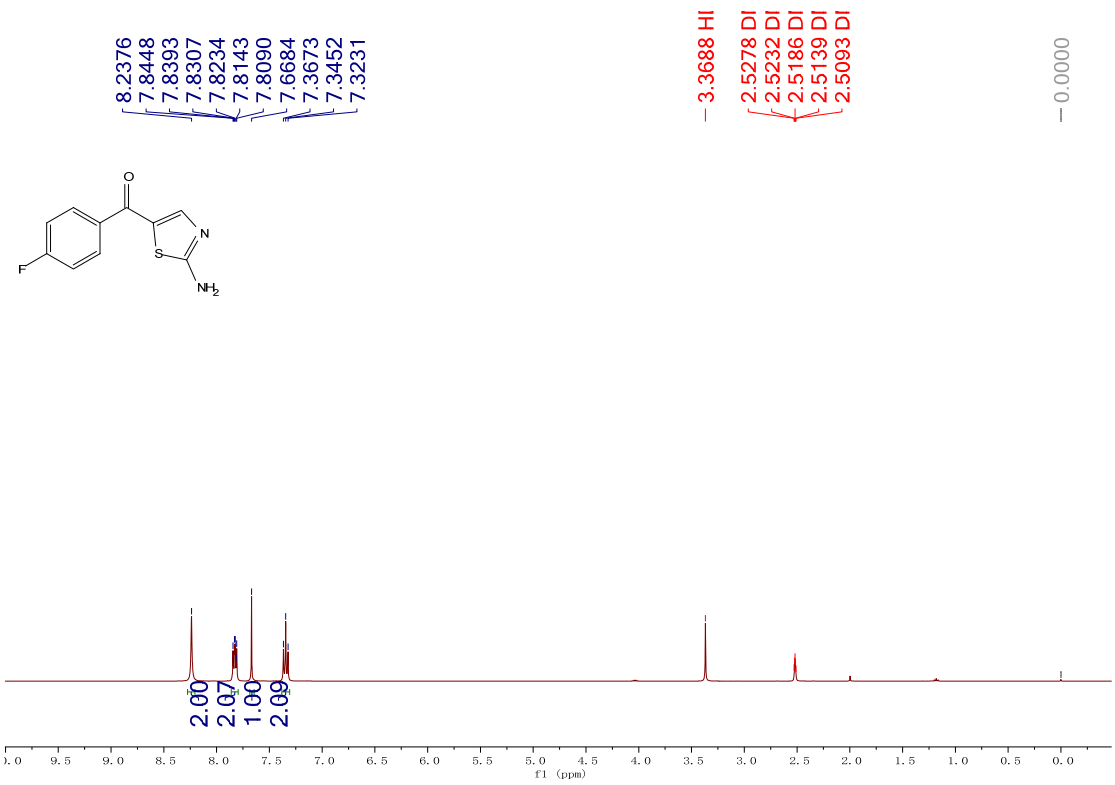
^{13}C NMR spectrum of **3c** (100 MHz, DMSO-d_6)



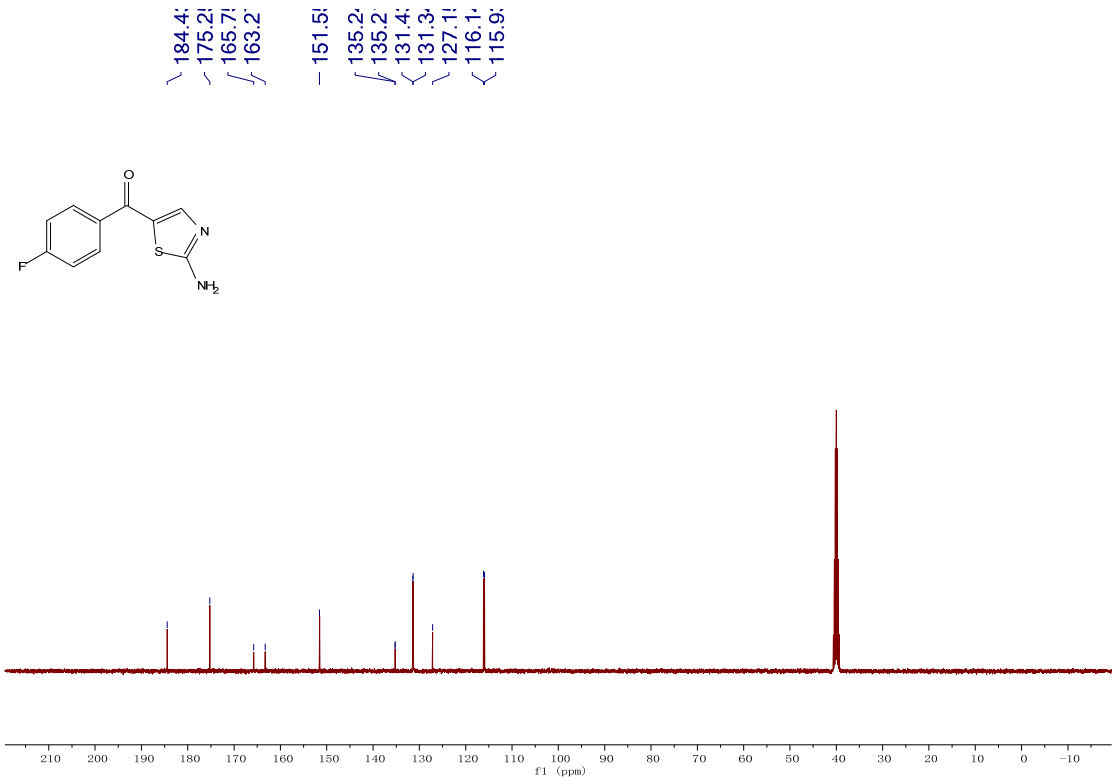
^{1}H NMR spectrum of **3d** (400 MHz, DMSO-d_6)



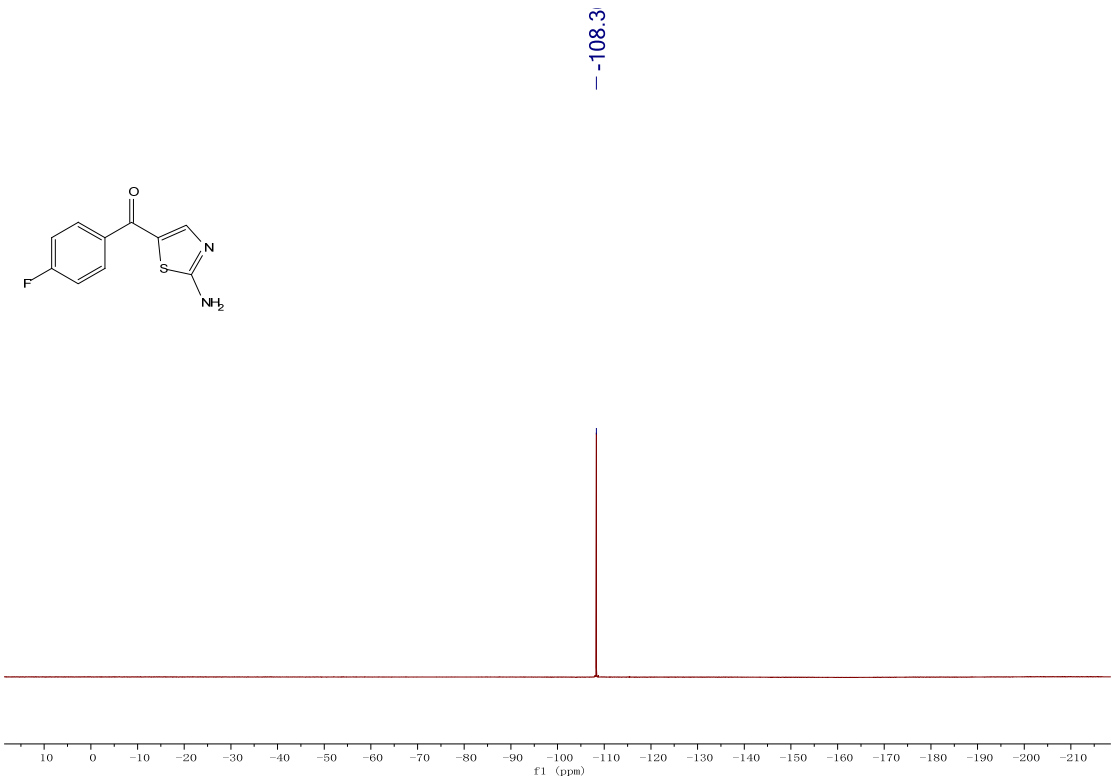
^{13}C NMR spectrum of **3d** (100 MHz, DMSO-d_6)



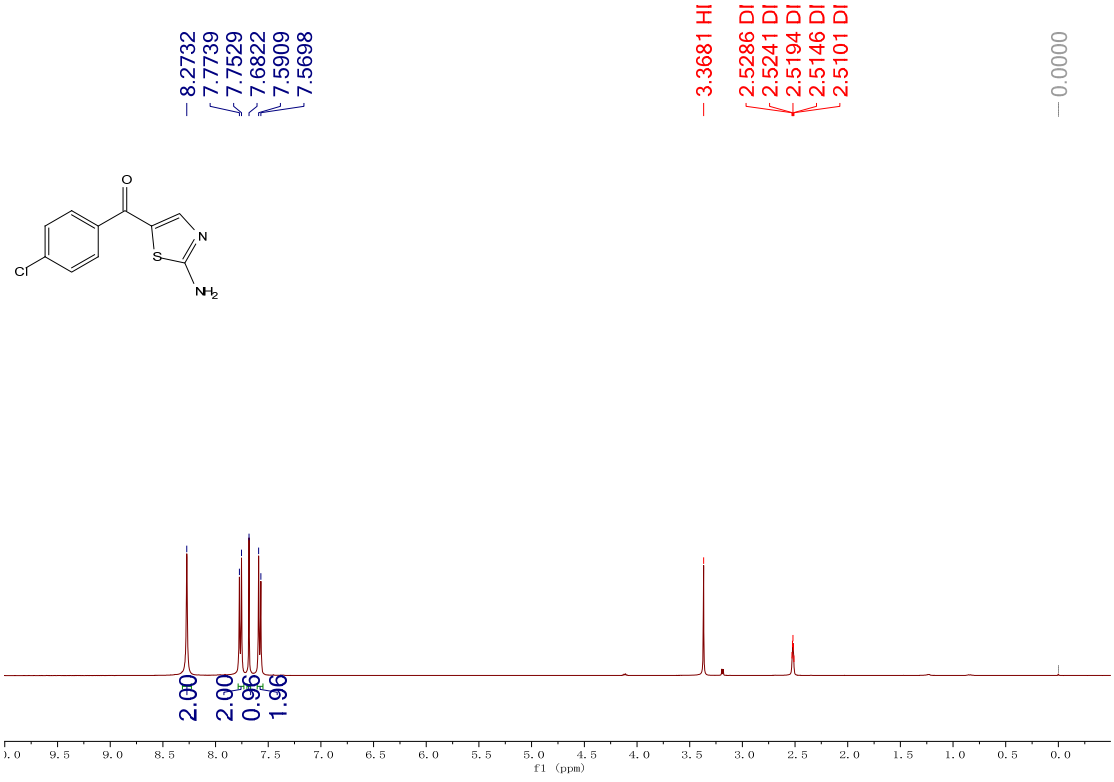
^{1}H NMR spectrum of **3e** (400 MHz, DMSO-d_6)



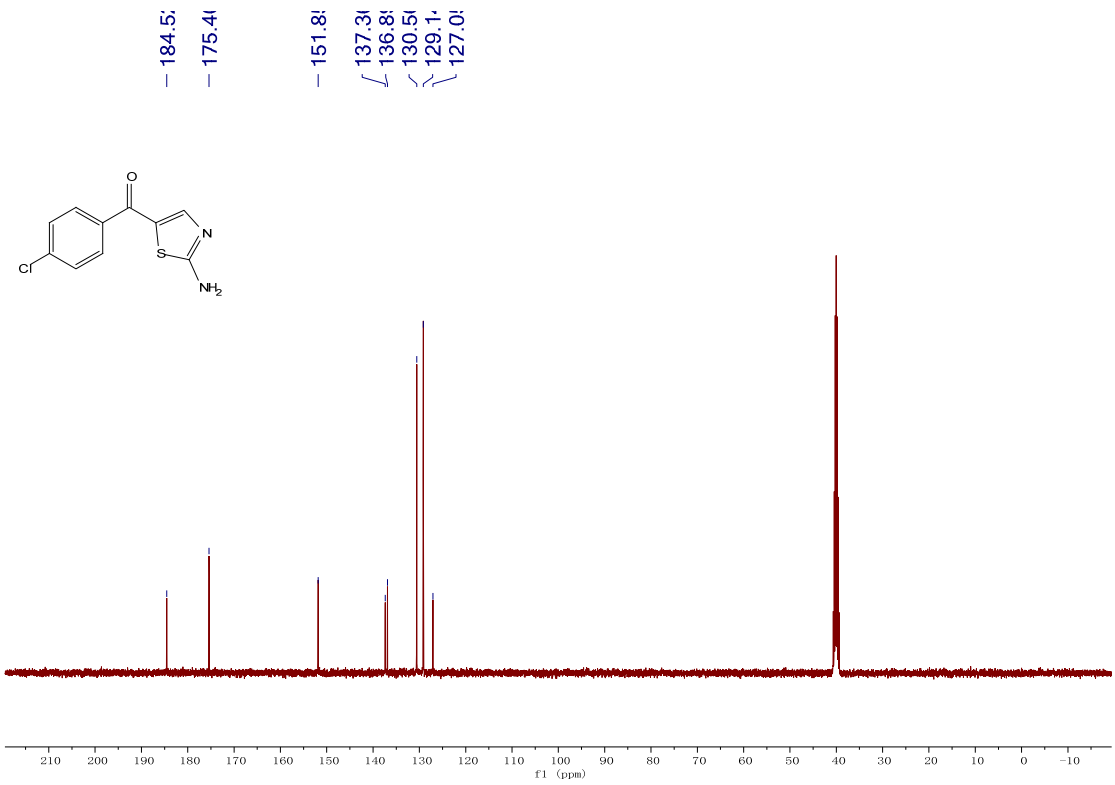
^{13}C NMR spectrum of **3e** (100 MHz, DMSO-d_6)



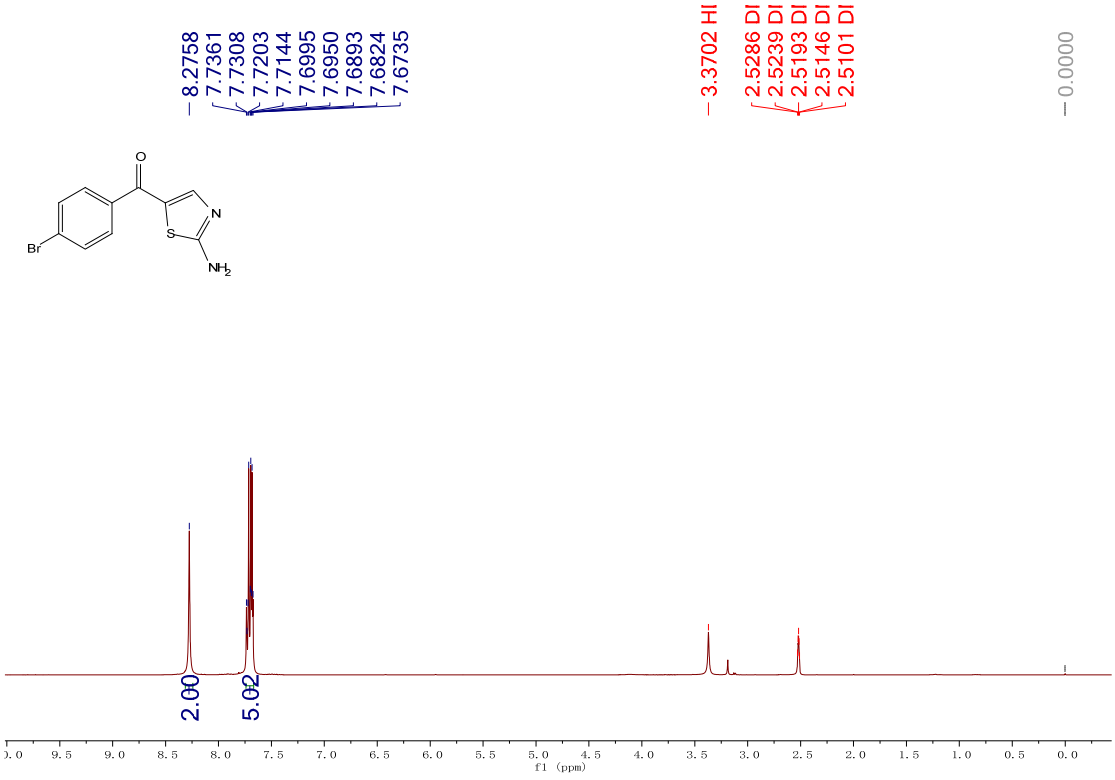
^{19}F NMR spectrum of **3e** (376 MHz, DMSO-d_6)



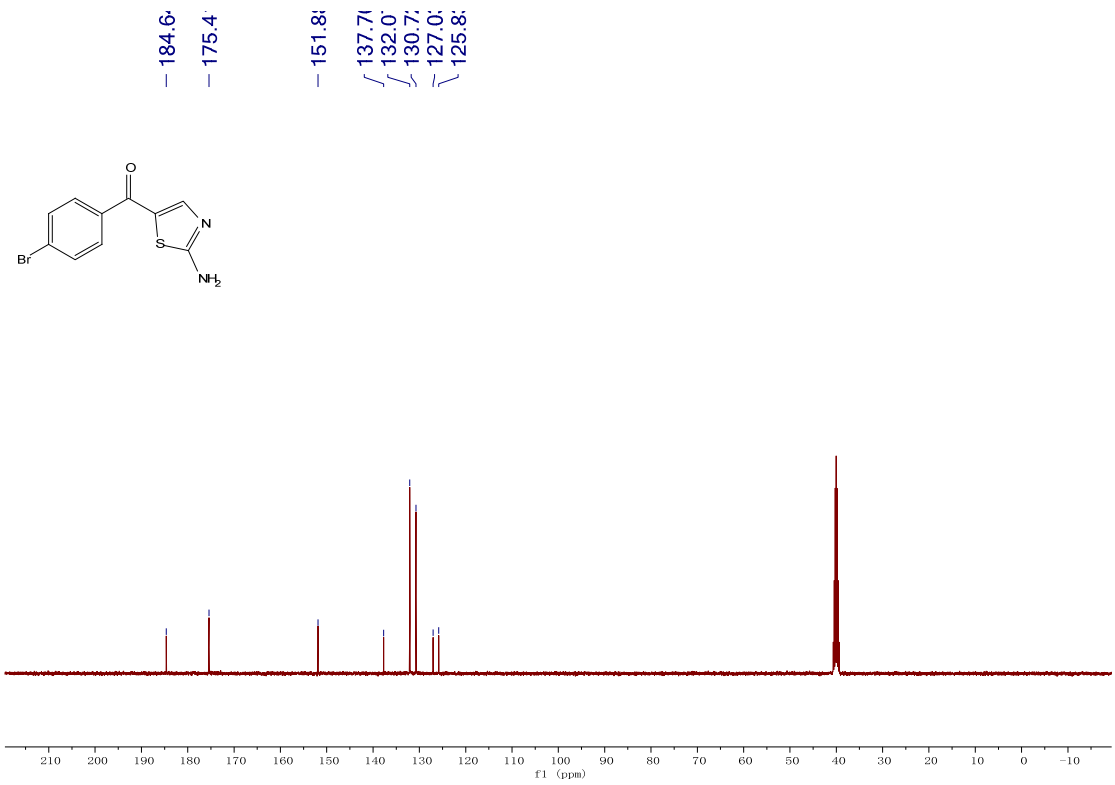
^{1}H NMR spectrum of **3f** (400 MHz, DMSO-d_6)



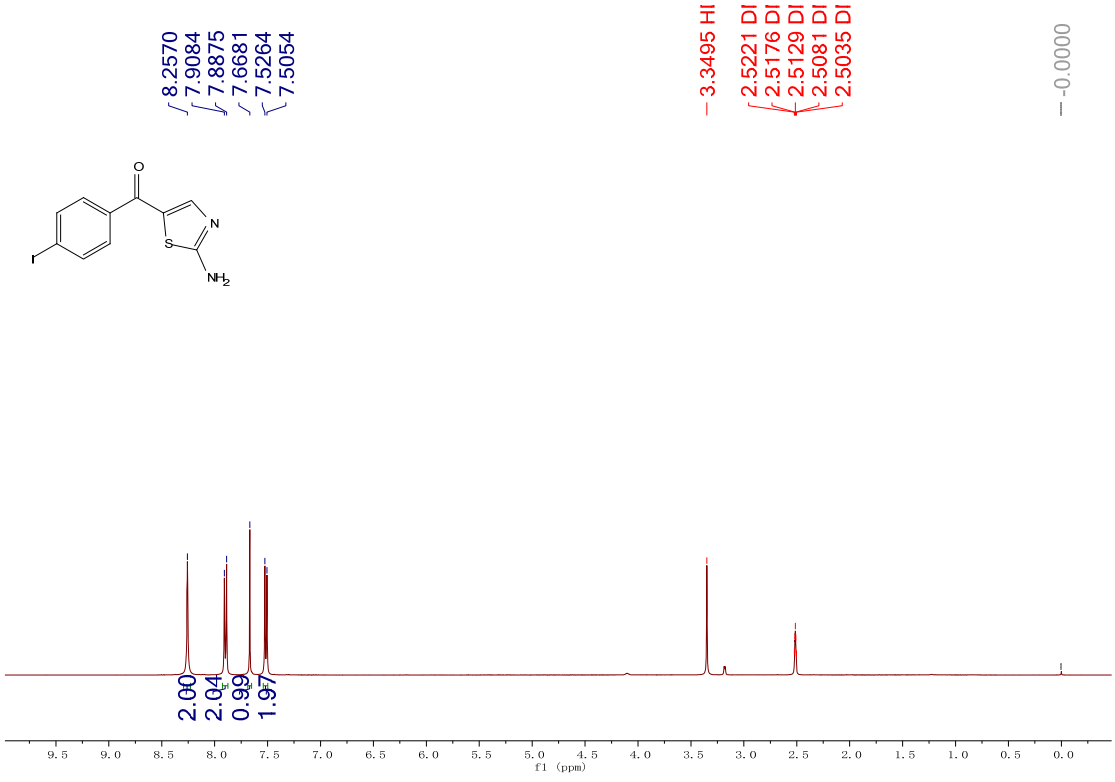
^{13}C NMR spectrum of **3f** (100 MHz, DMSO-d_6)



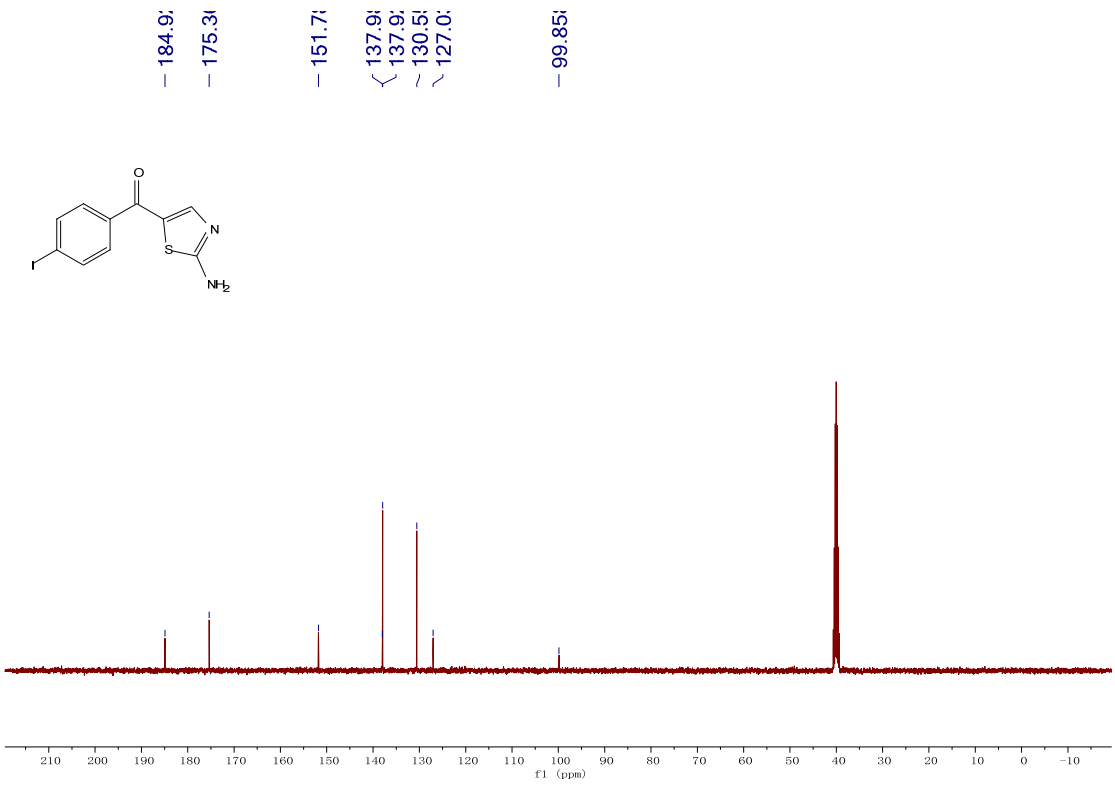
^{1}H NMR spectrum of **3g** (400 MHz, DMSO-d_6)



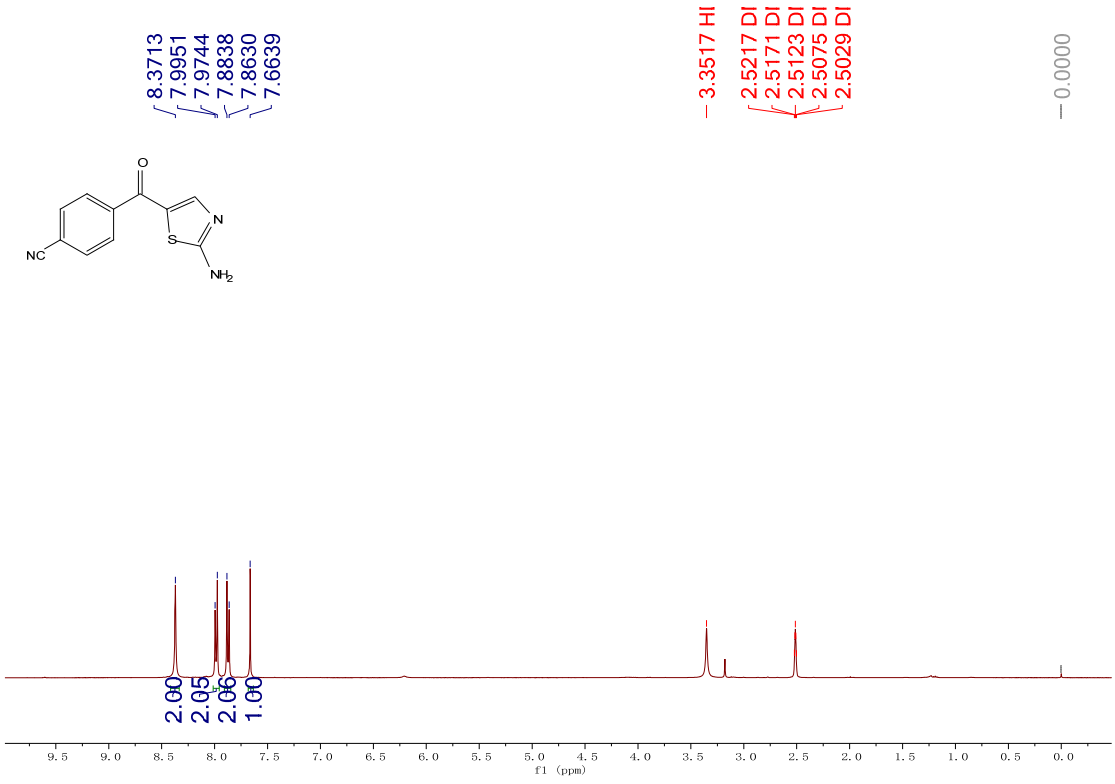
^{13}C NMR spectrum of **3g** (100 MHz, DMSO-d_6)



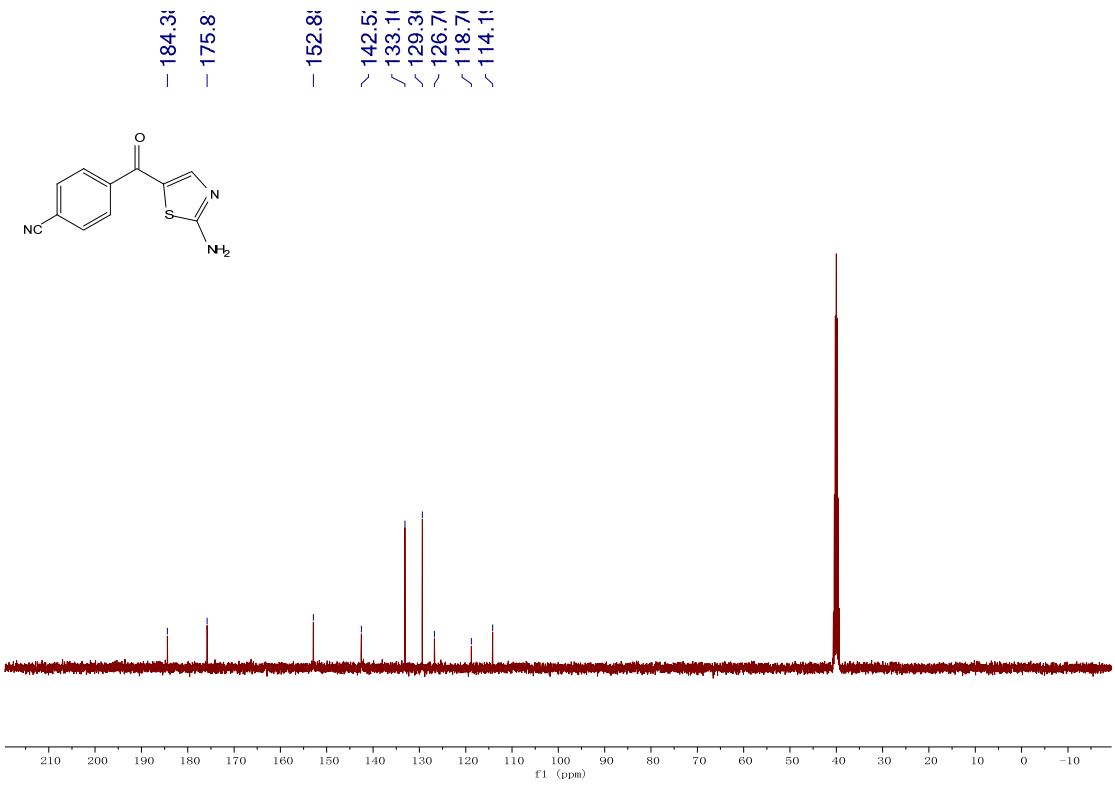
^{1}H NMR spectrum of **3h** (400 MHz, DMSO-d_6)



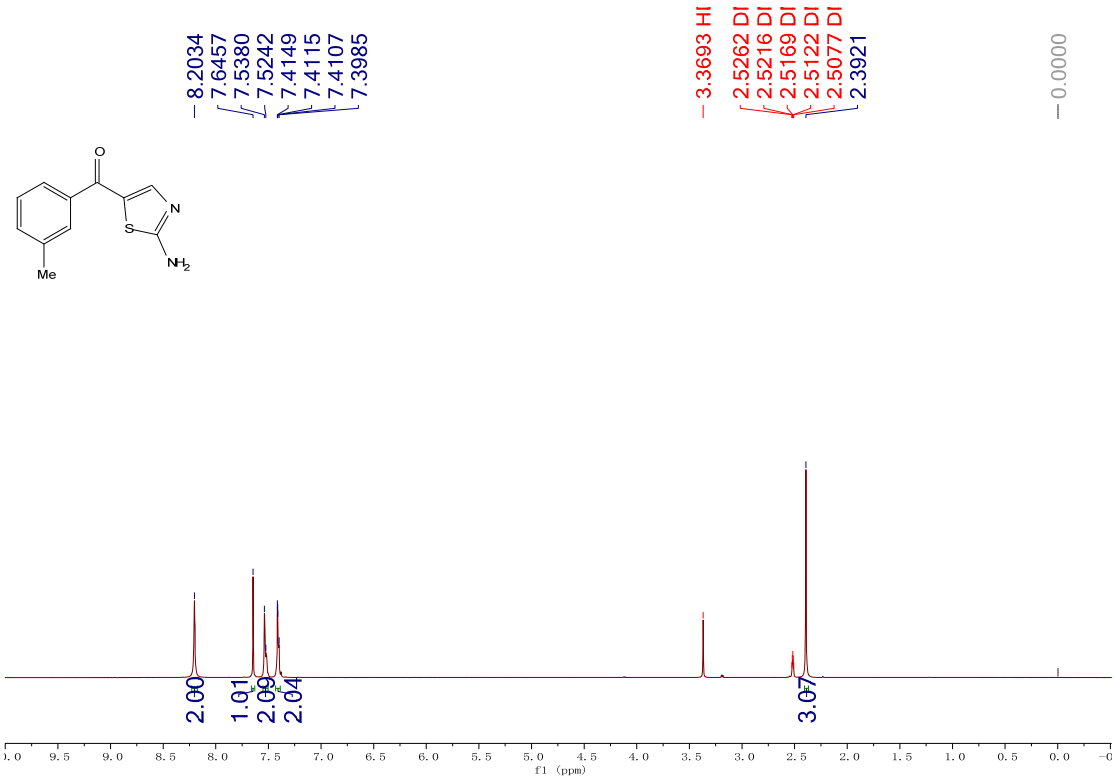
^{13}C NMR spectrum of **3h** (100 MHz, DMSO-d_6)



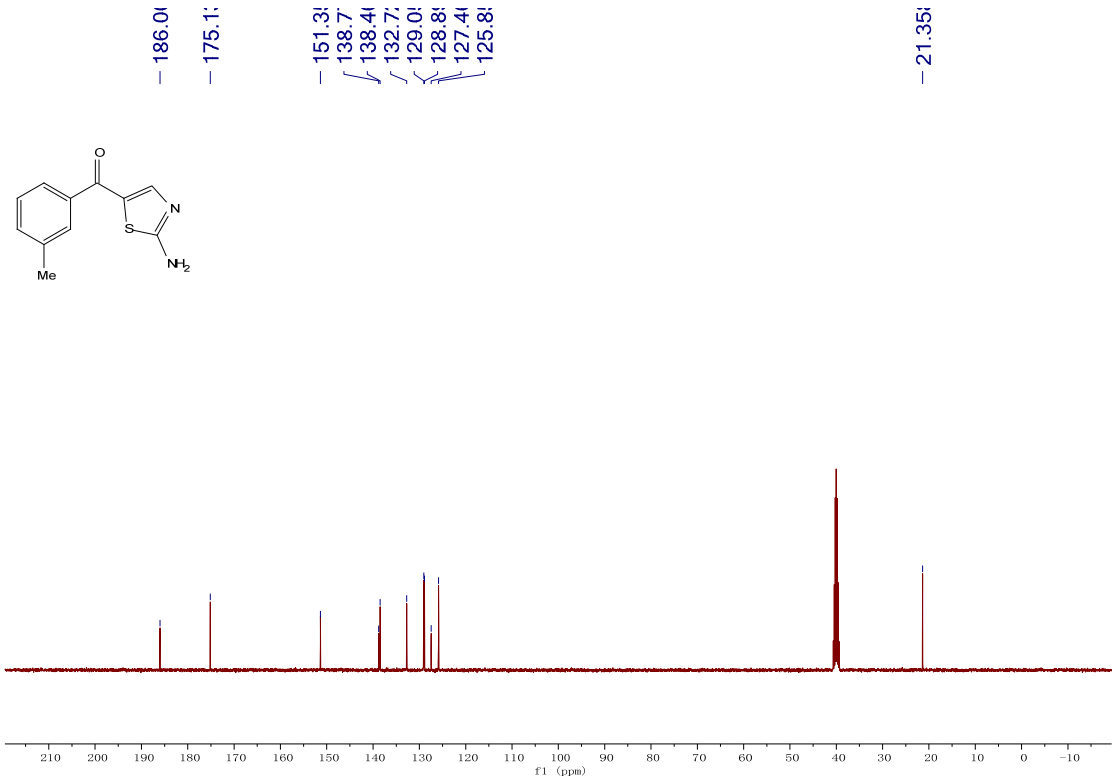
^{1}H NMR spectrum of **3i** (400 MHz, DMSO-d_6)



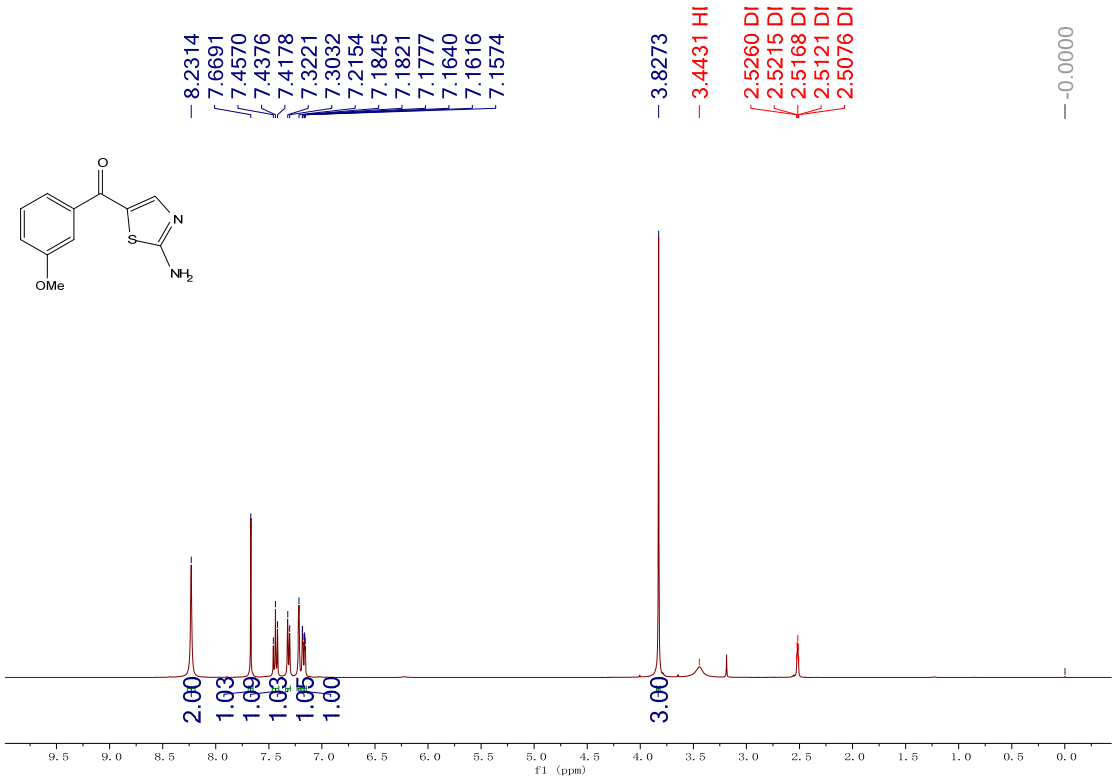
^{13}C NMR spectrum of **3i** (100 MHz, DMSO-d_6)



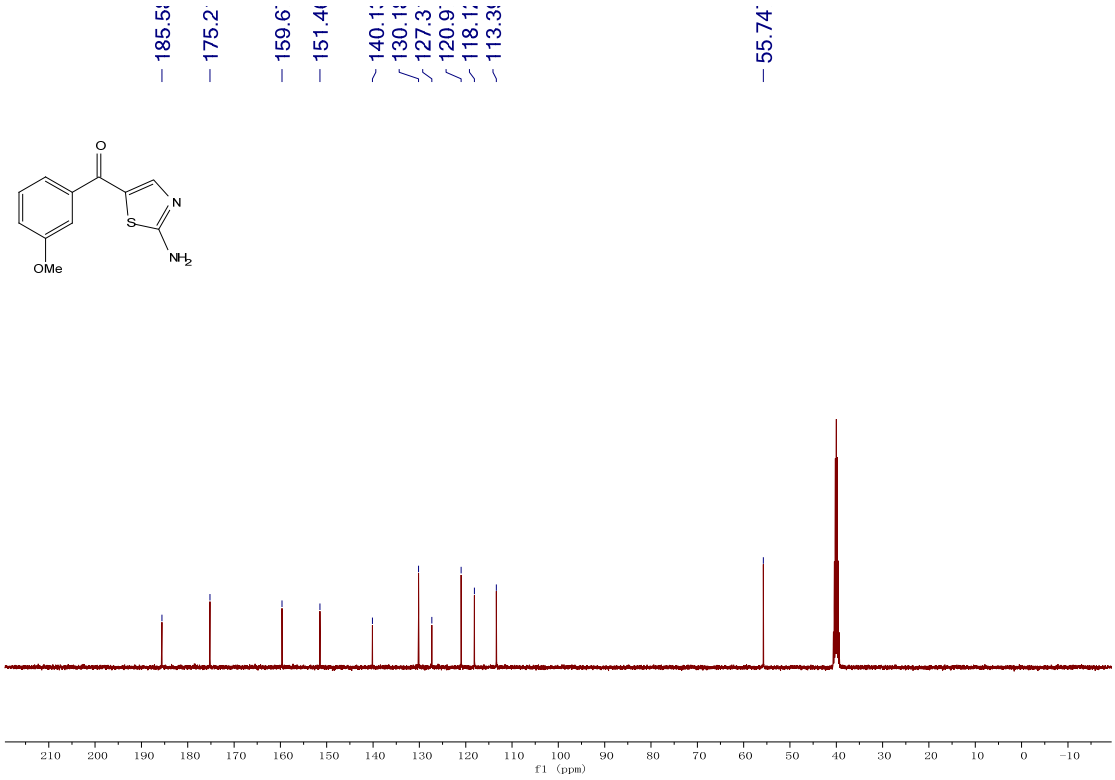
^{1}H NMR spectrum of **3j** (400 MHz, DMSO-d_6)



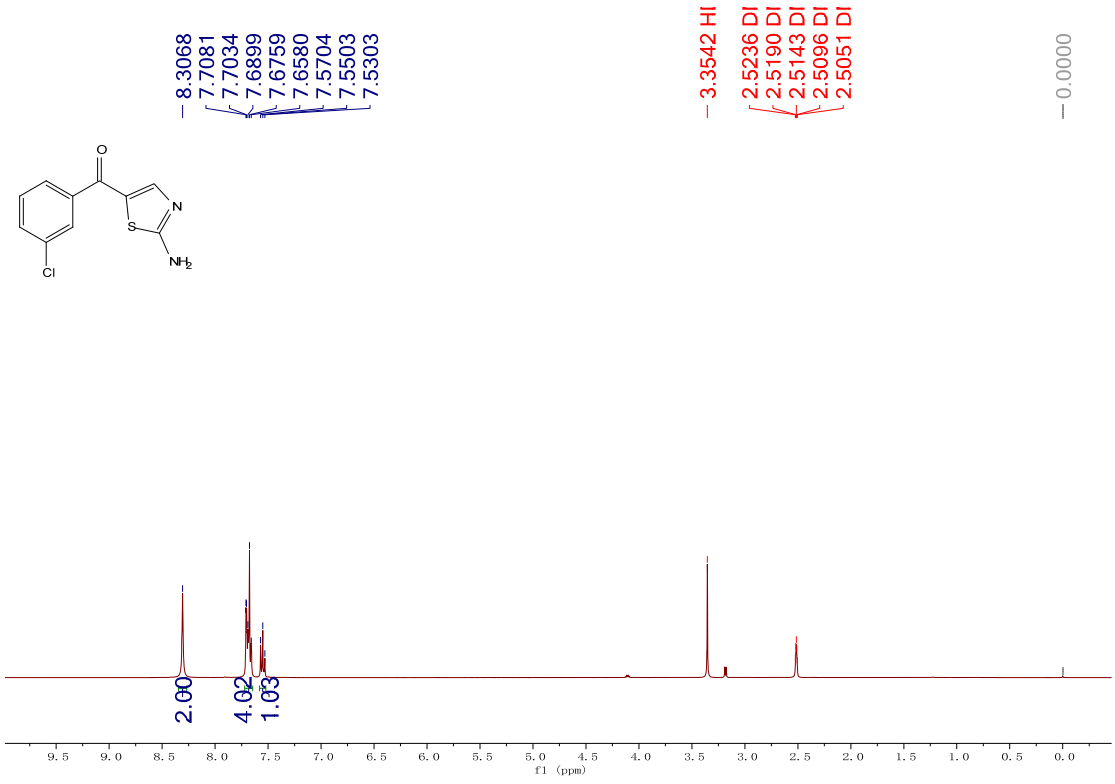
^{13}C NMR spectrum of **3j** (100 MHz, DMSO-d_6)



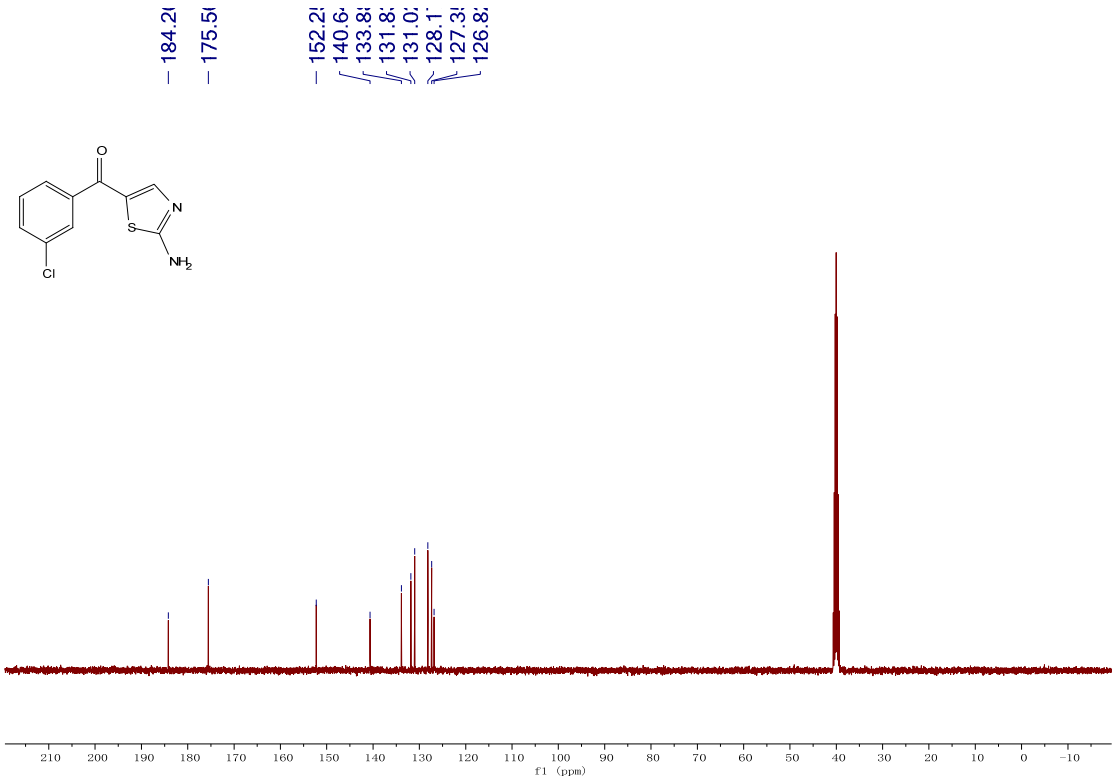
^{1}H NMR spectrum of **3k** (400 MHz, DMSO-d_6)



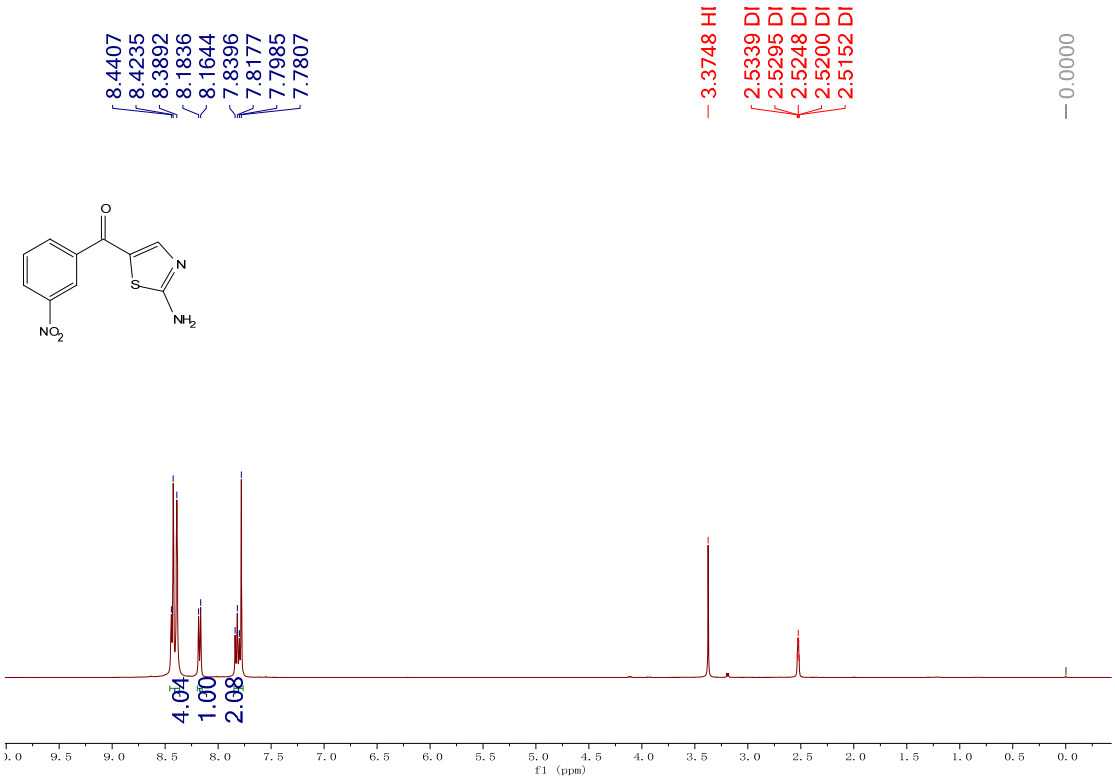
^{13}C NMR spectrum of **3k** (100 MHz, DMSO-d_6)



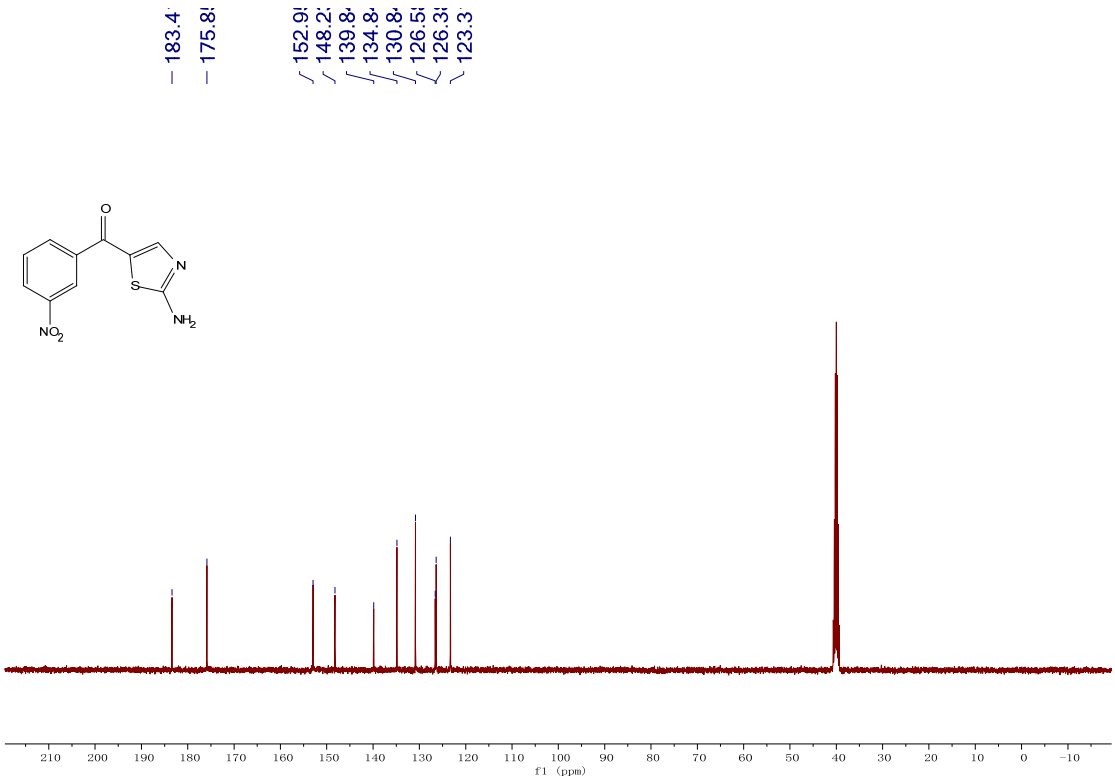
^{1}H NMR spectrum of **3l** (400 MHz, DMSO-d_6)



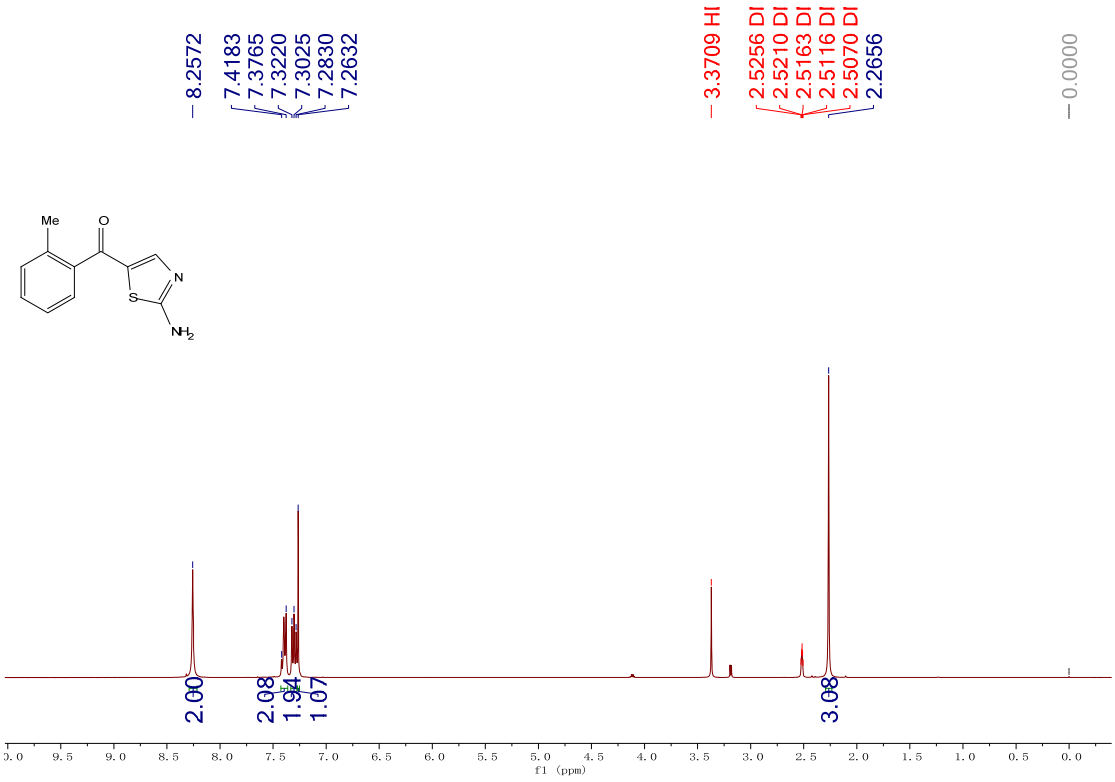
^{13}C NMR spectrum of **3l** (100 MHz, DMSO-d_6)



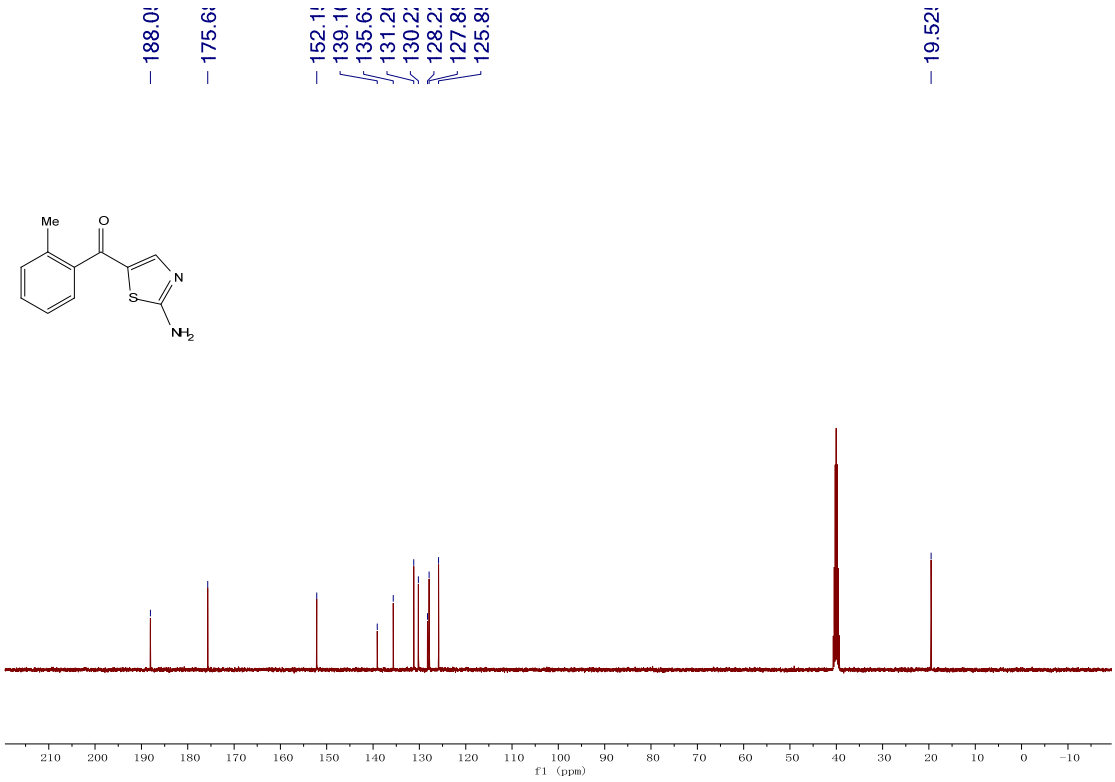
^{1}H NMR spectrum of **3m** (400 MHz, DMSO-d_6)



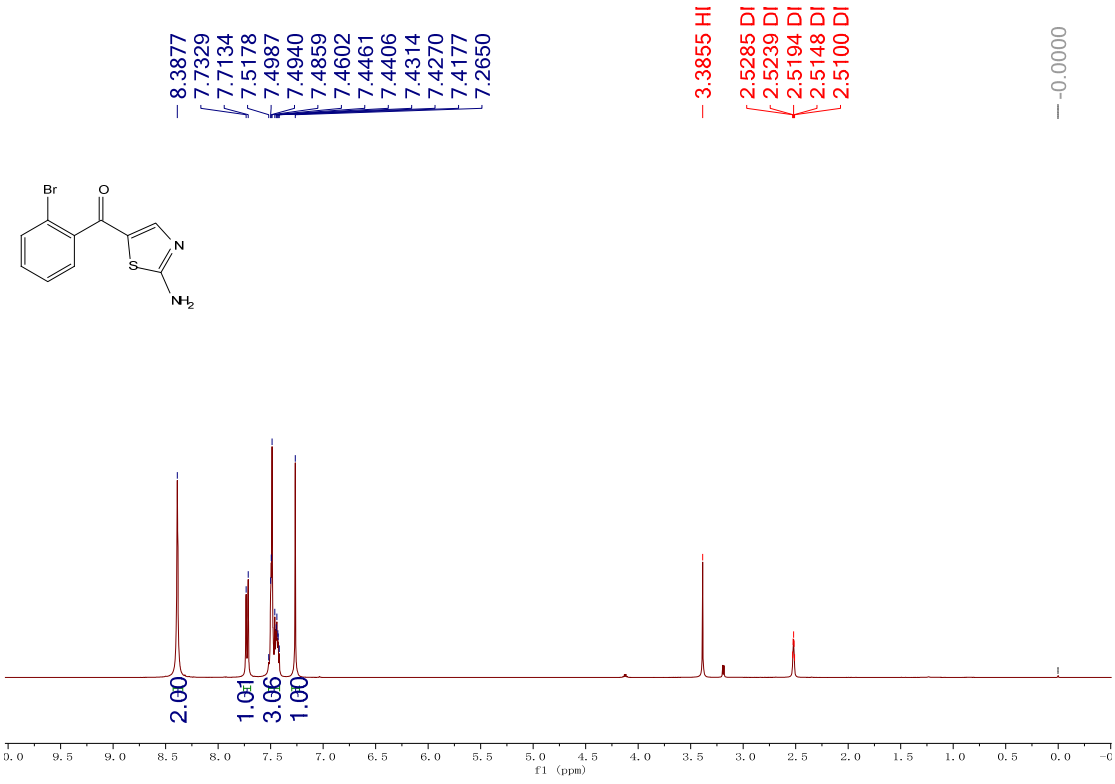
^{13}C NMR spectrum of **3m** (100 MHz, DMSO-d_6)



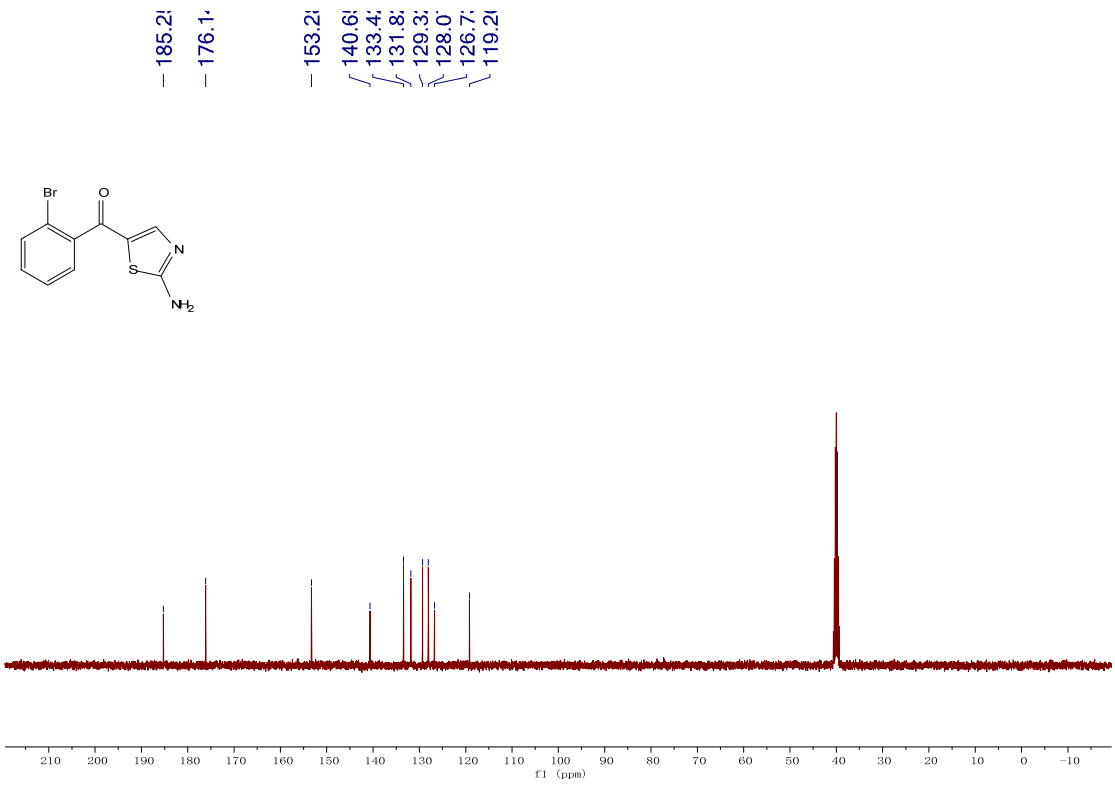
^{1}H NMR spectrum of **3n** (400 MHz, DMSO-d_6)



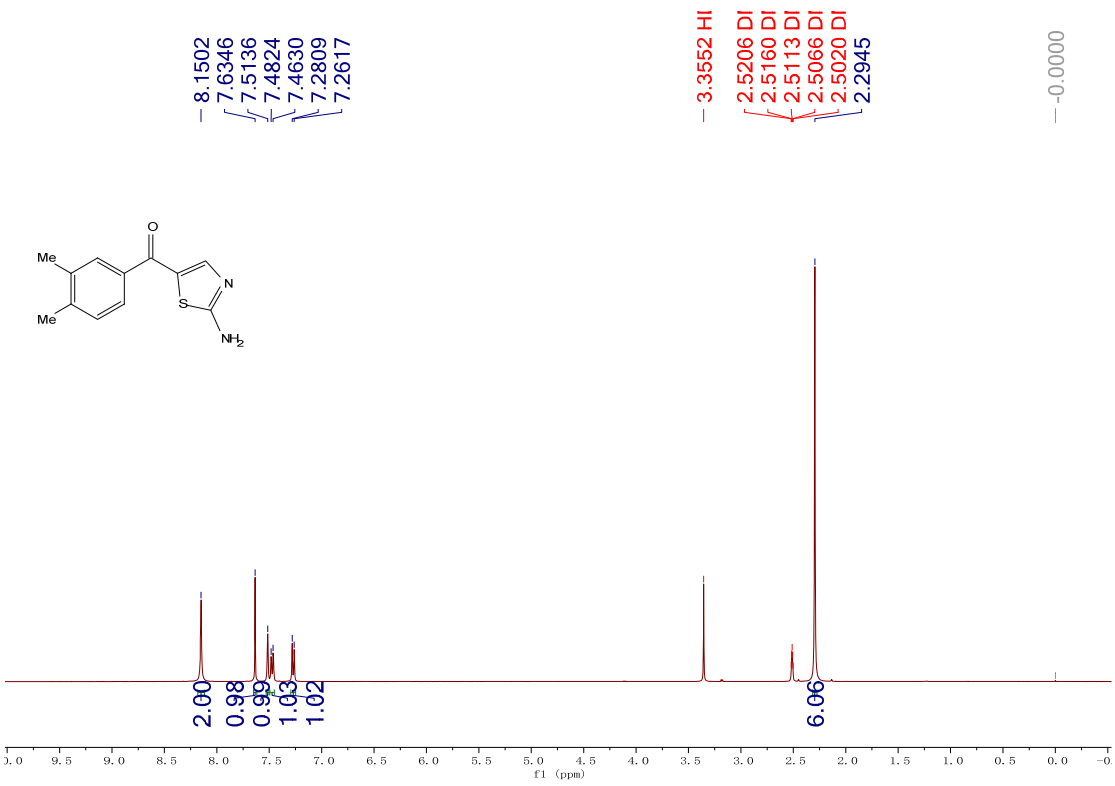
^{13}C NMR spectrum of **3n** (100 MHz, DMSO-d_6)



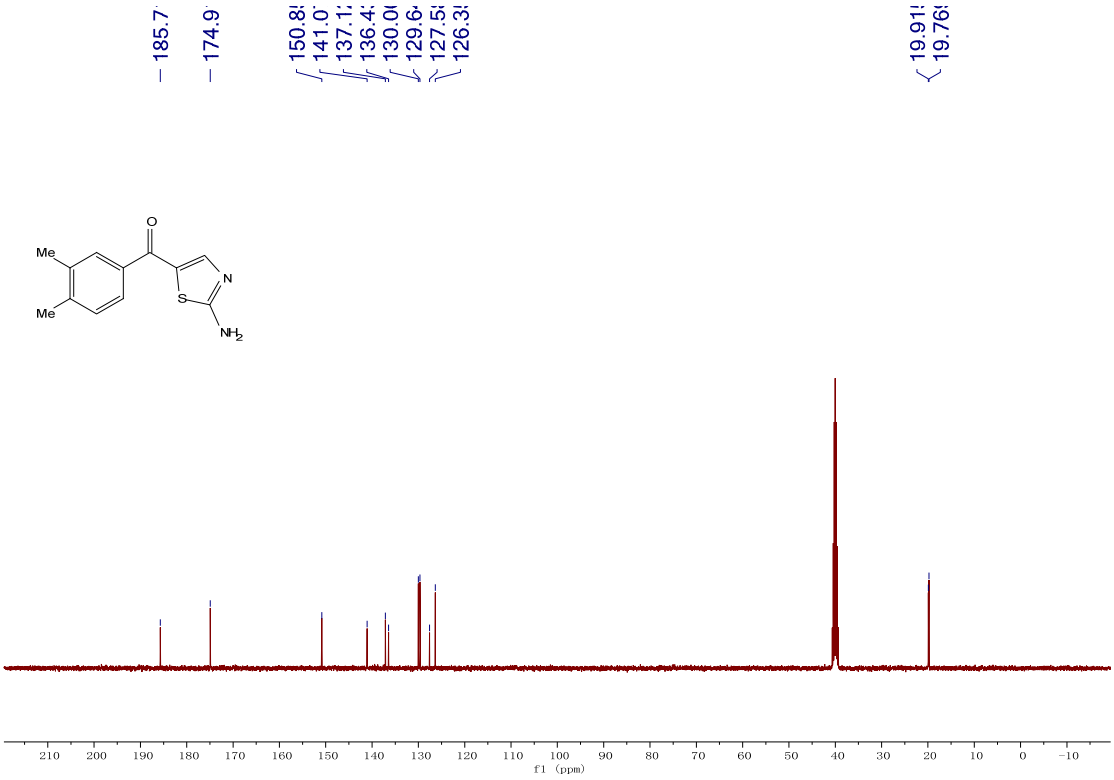
^{1}H NMR spectrum of **3o** (400 MHz, DMSO-d_6)



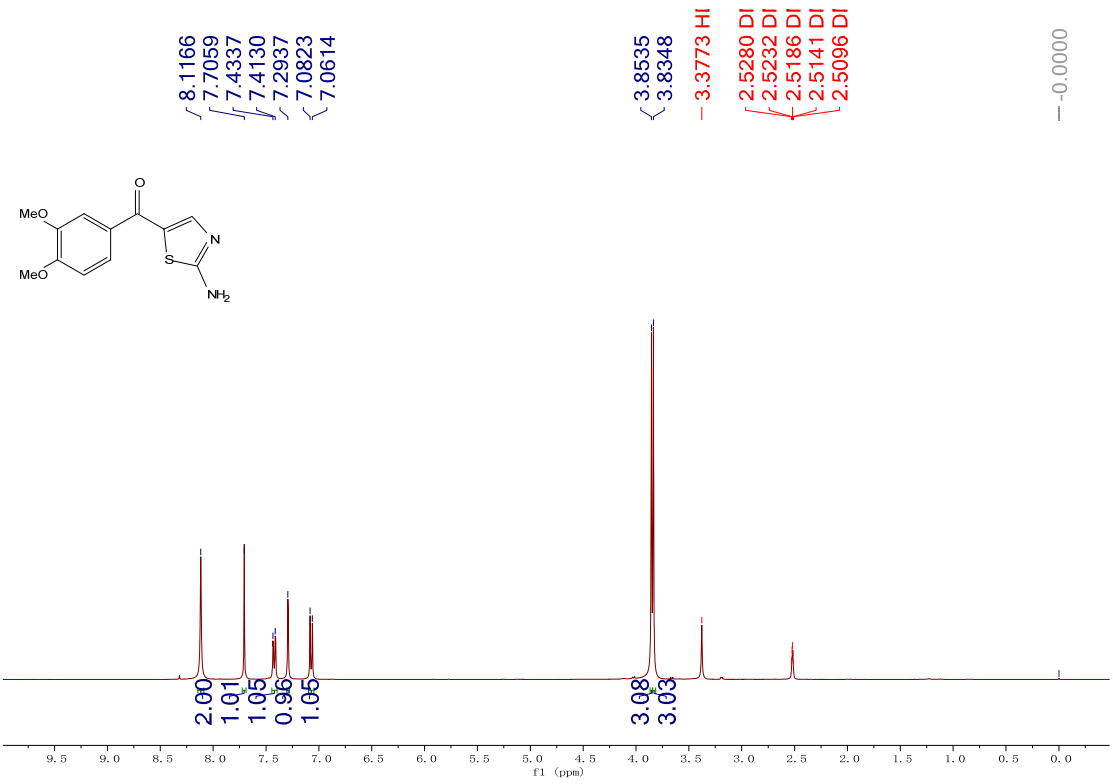
^{13}C NMR spectrum of **3o** (100 MHz, DMSO-d_6)



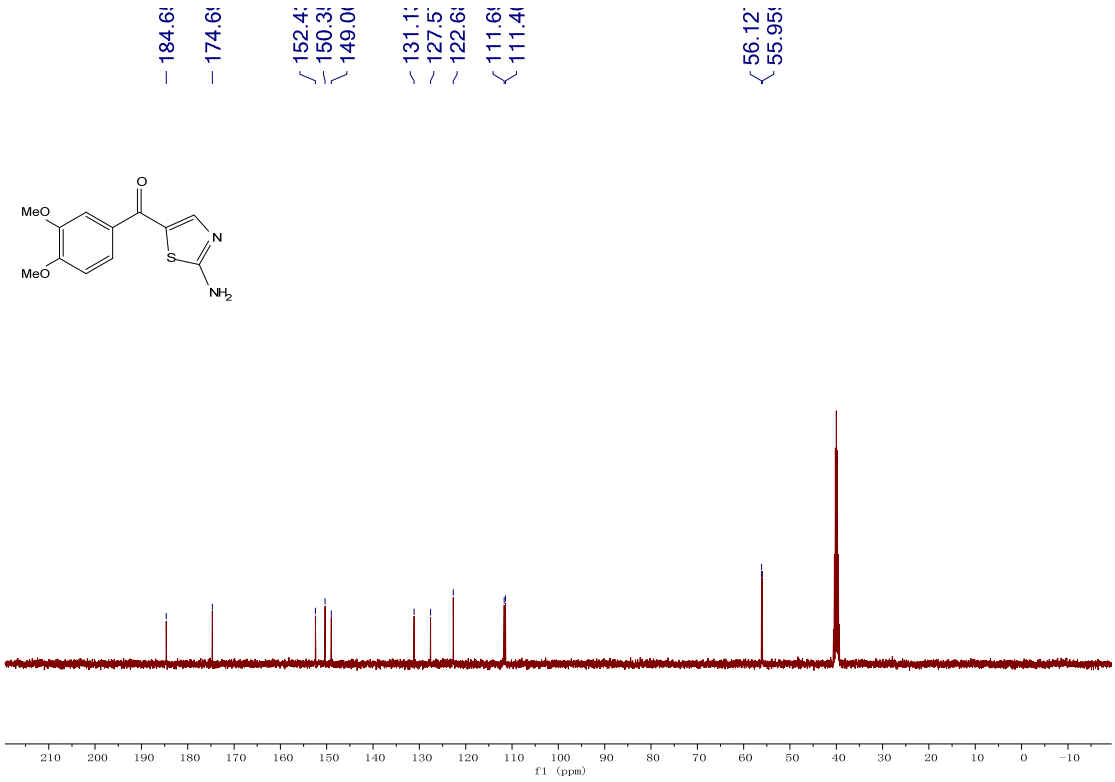
^{1}H NMR spectrum of **3p** (400 MHz, DMSO-d_6)



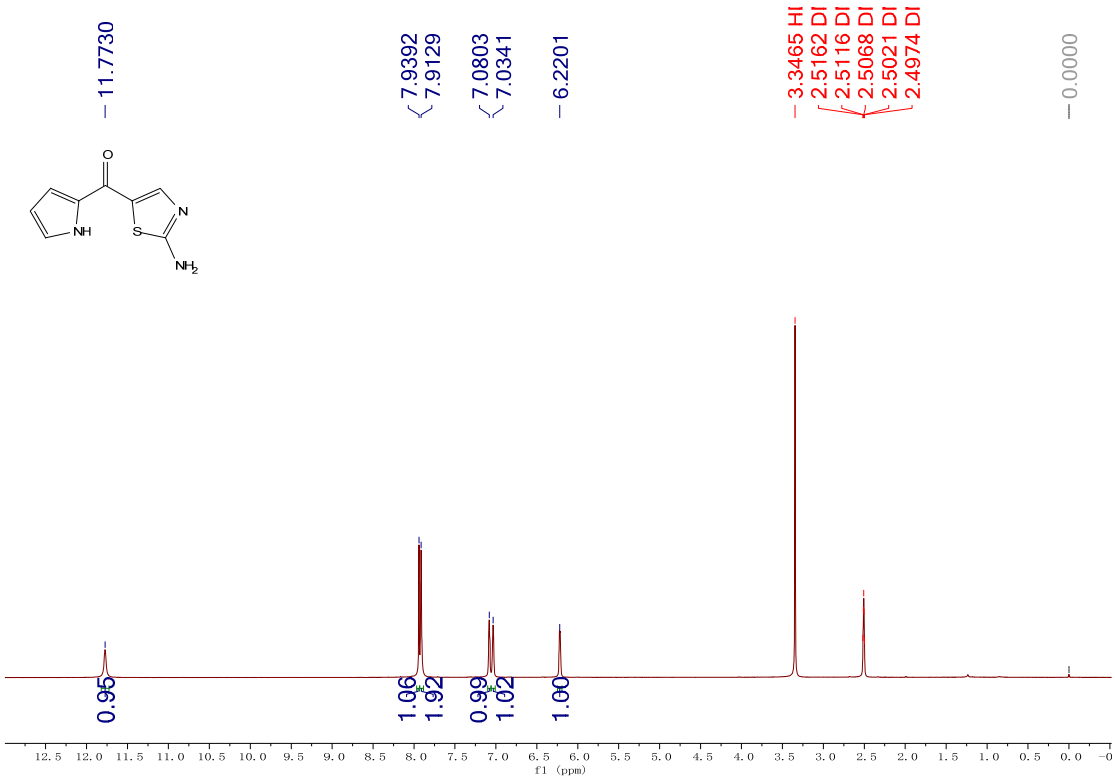
^{13}C NMR spectrum of **3p** (100 MHz, DMSO-d_6)



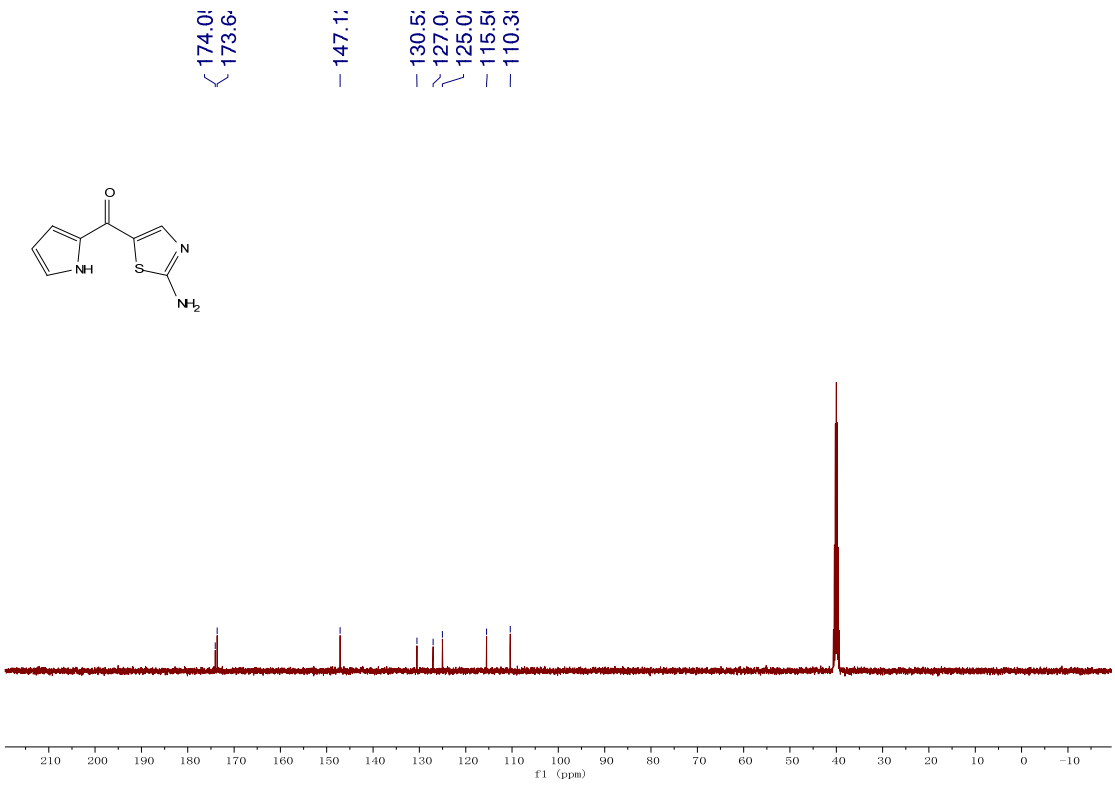
^{1}H NMR spectrum of **3q** (400 MHz, DMSO-d_6)



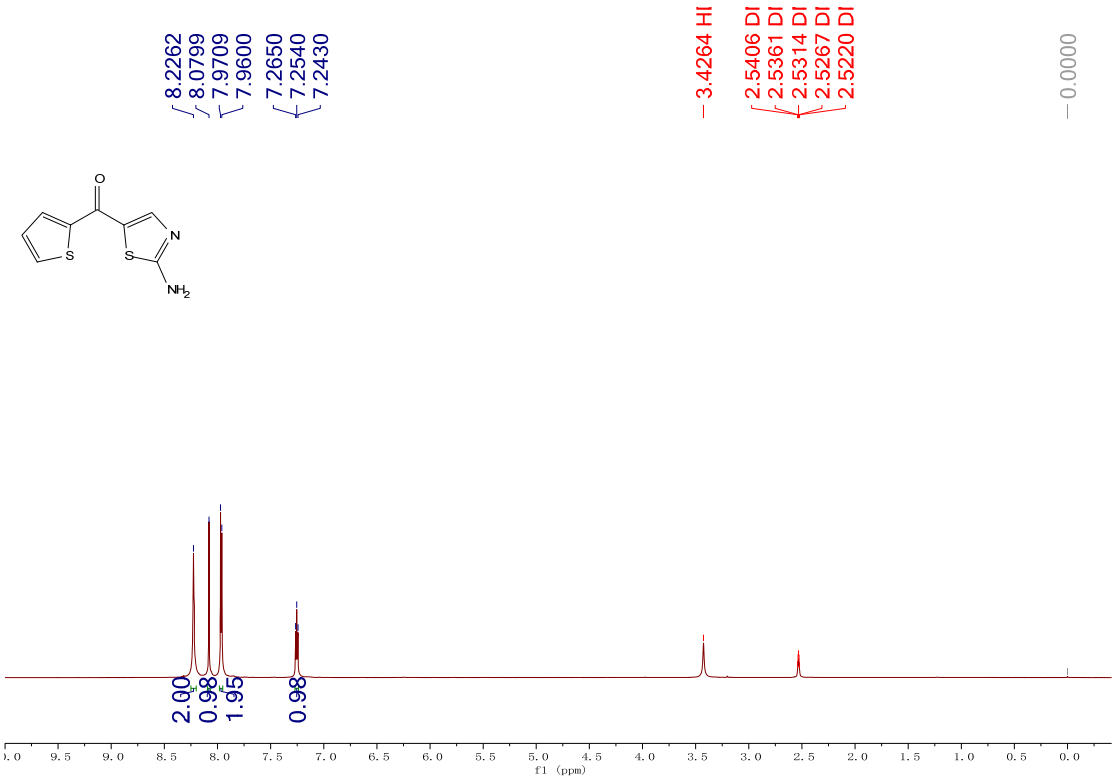
^{13}C NMR spectrum of **3q** (100 MHz, DMSO-d_6)



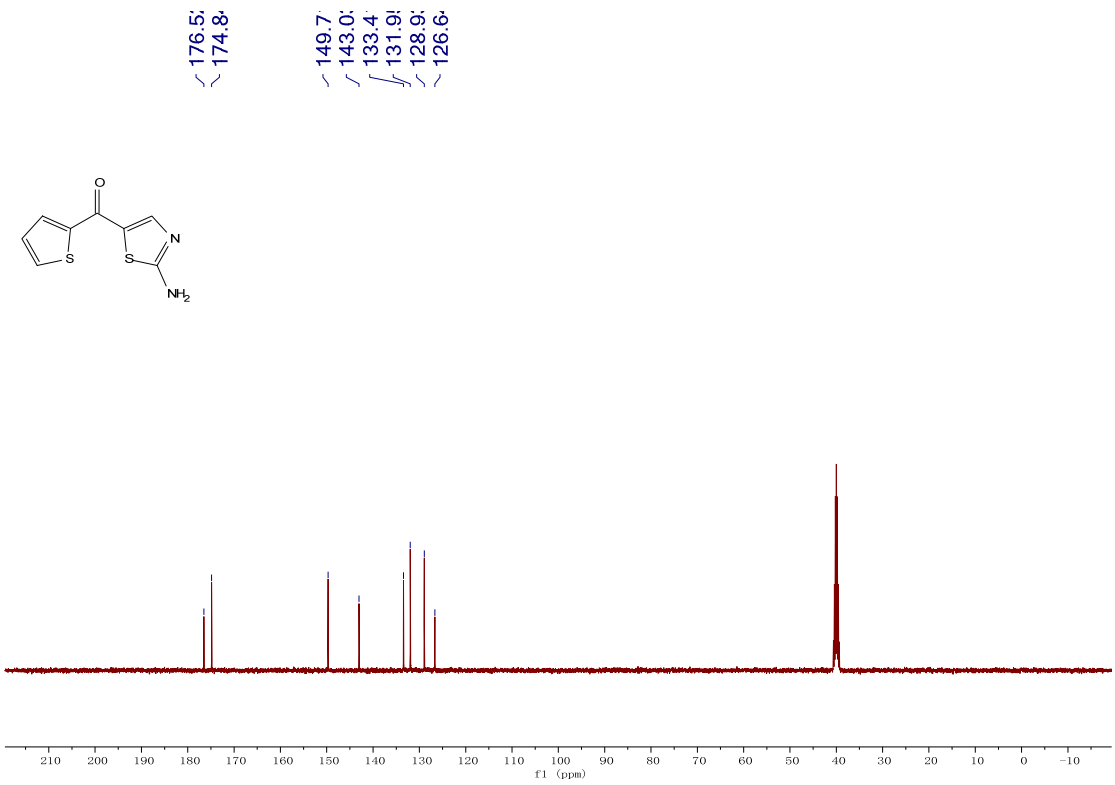
^{1}H NMR spectrum of **3r** (400 MHz, DMSO-d_6)



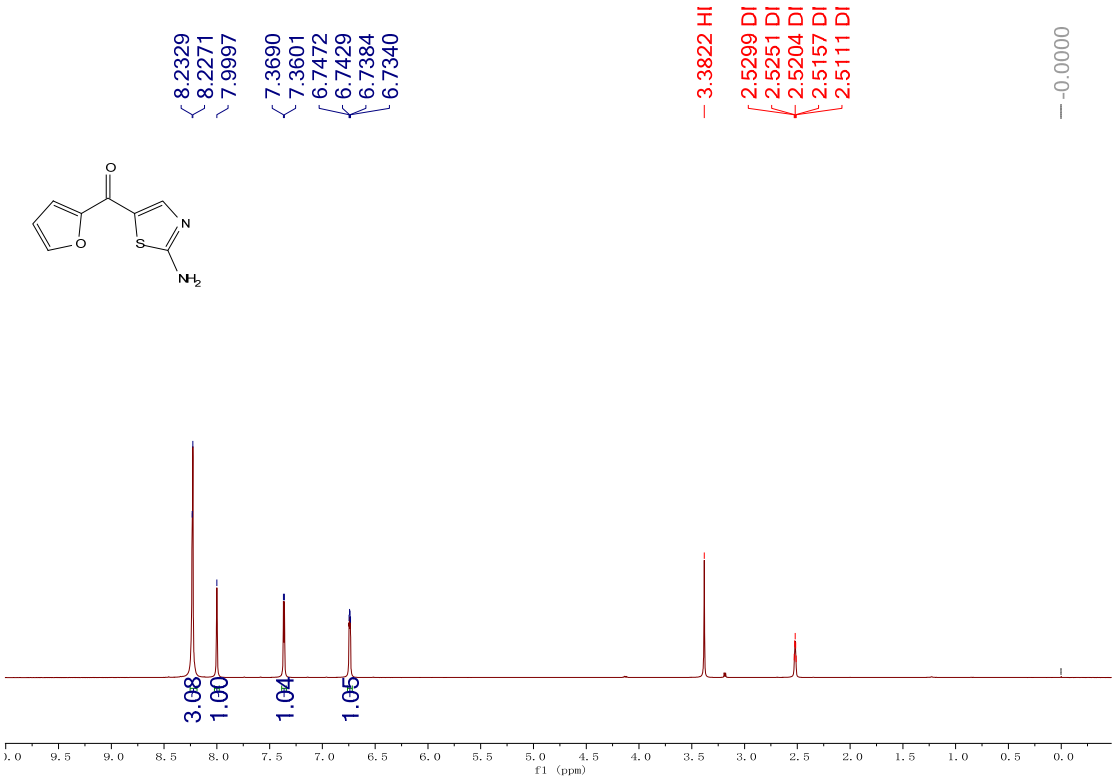
^{13}C NMR spectrum of **3r** (100 MHz, DMSO-d_6)



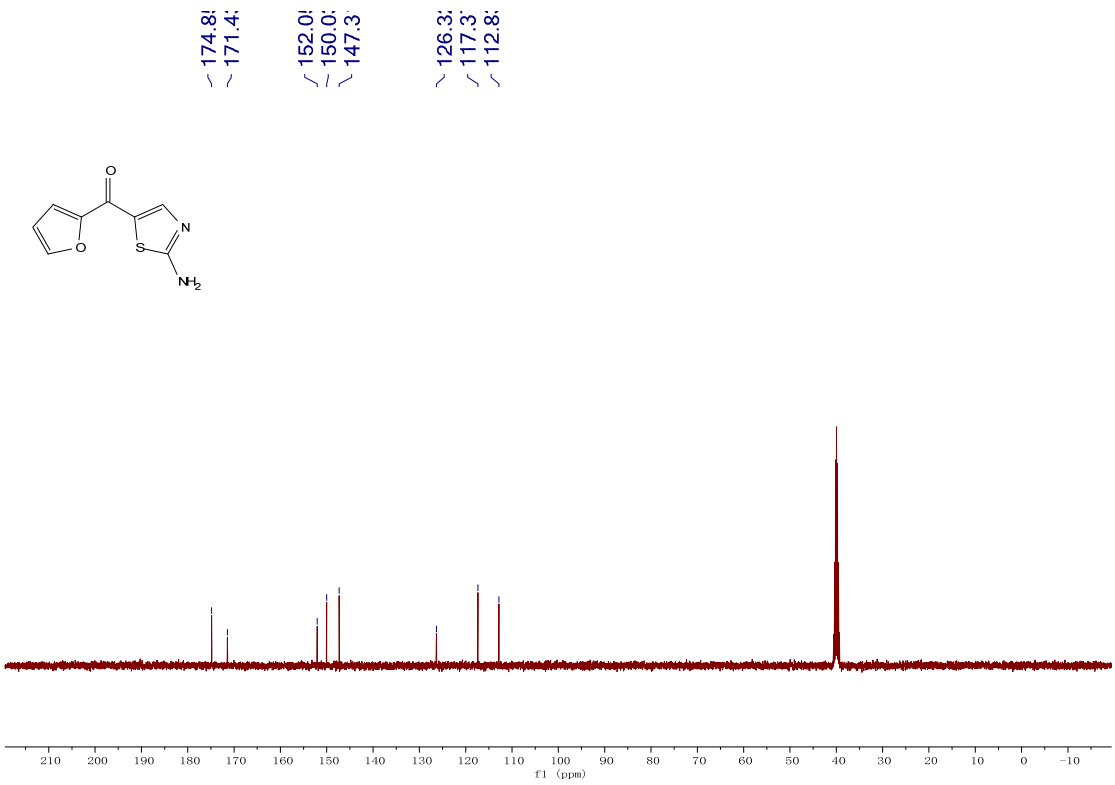
^{1}H NMR spectrum of **3s** (400 MHz, DMSO-d_6)



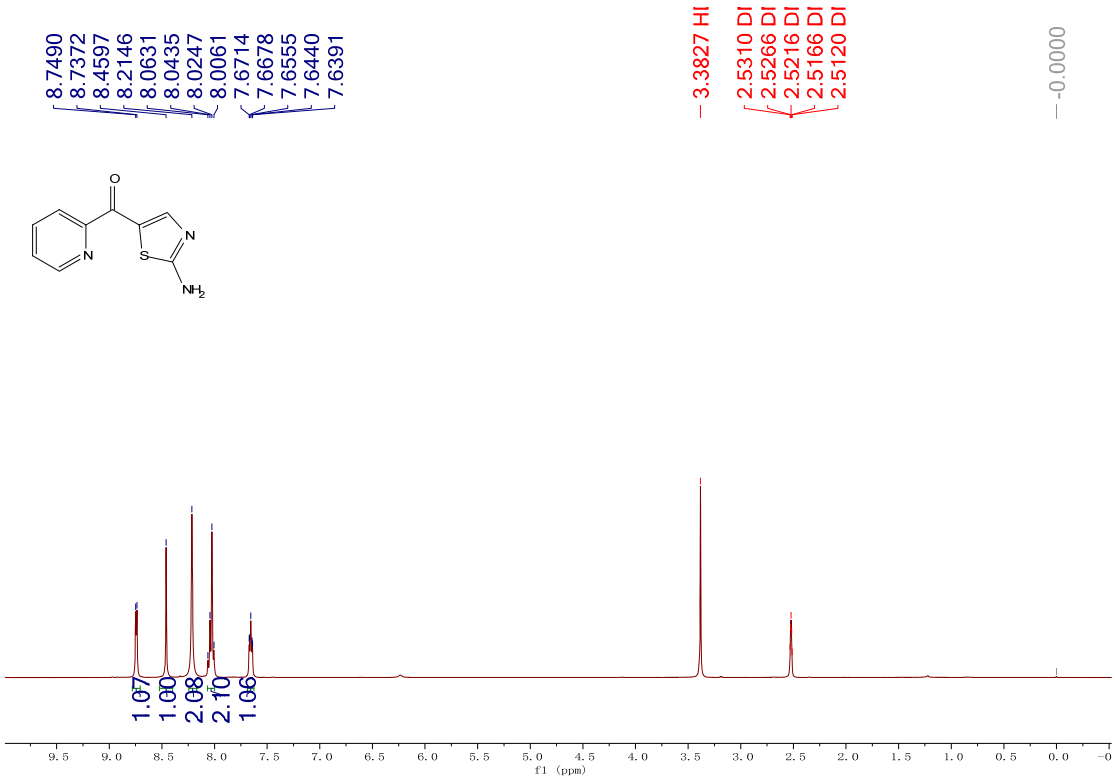
^{13}C NMR spectrum of **3s** (100 MHz, DMSO-d_6)



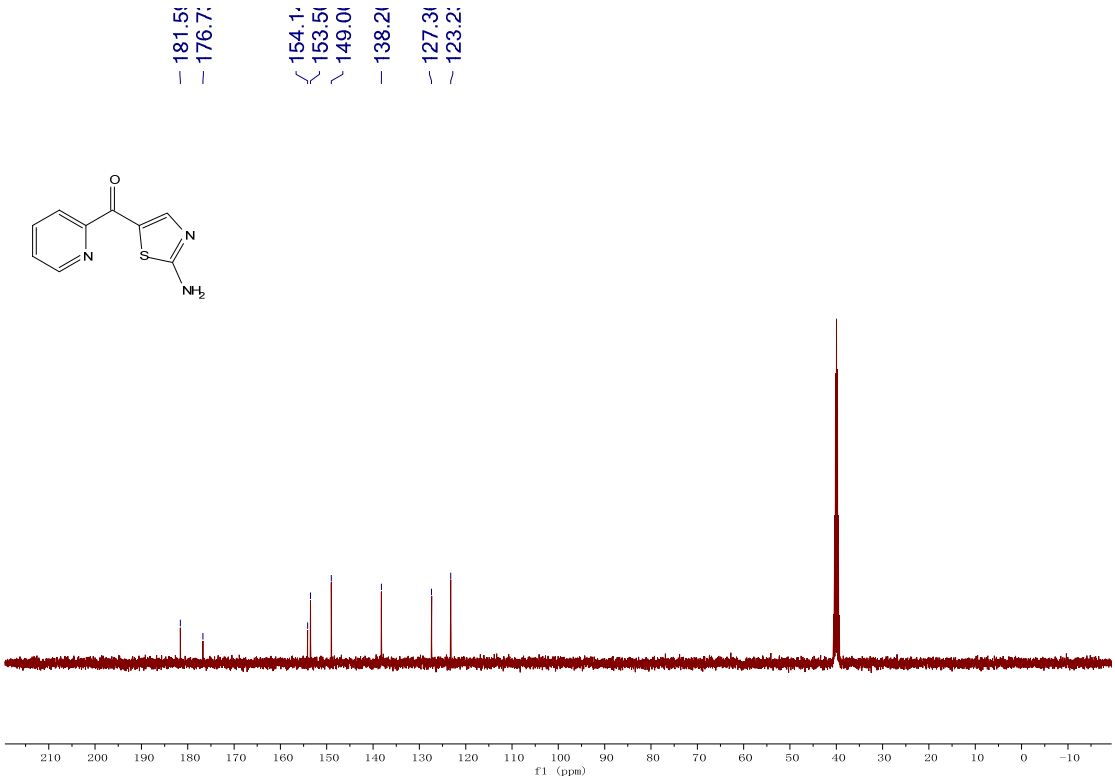
^{1}H NMR spectrum of **3t** (400 MHz, DMSO-d_6)



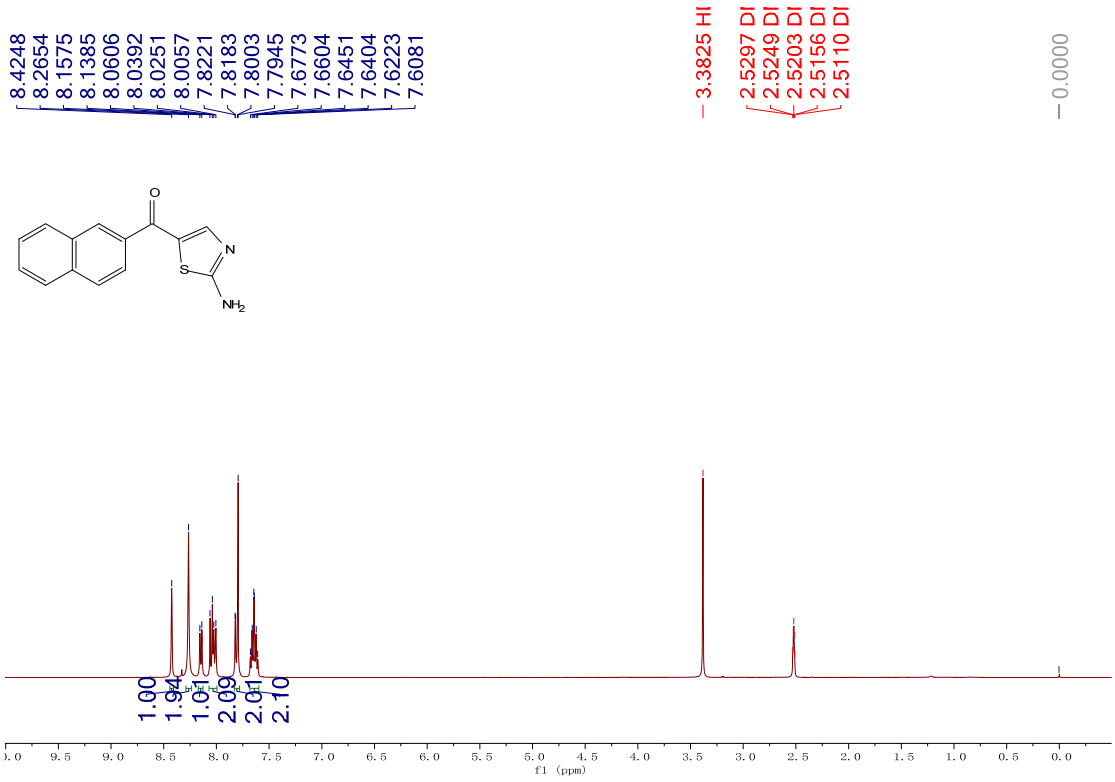
^{13}C NMR spectrum of **3t** (100 MHz, DMSO-d_6)



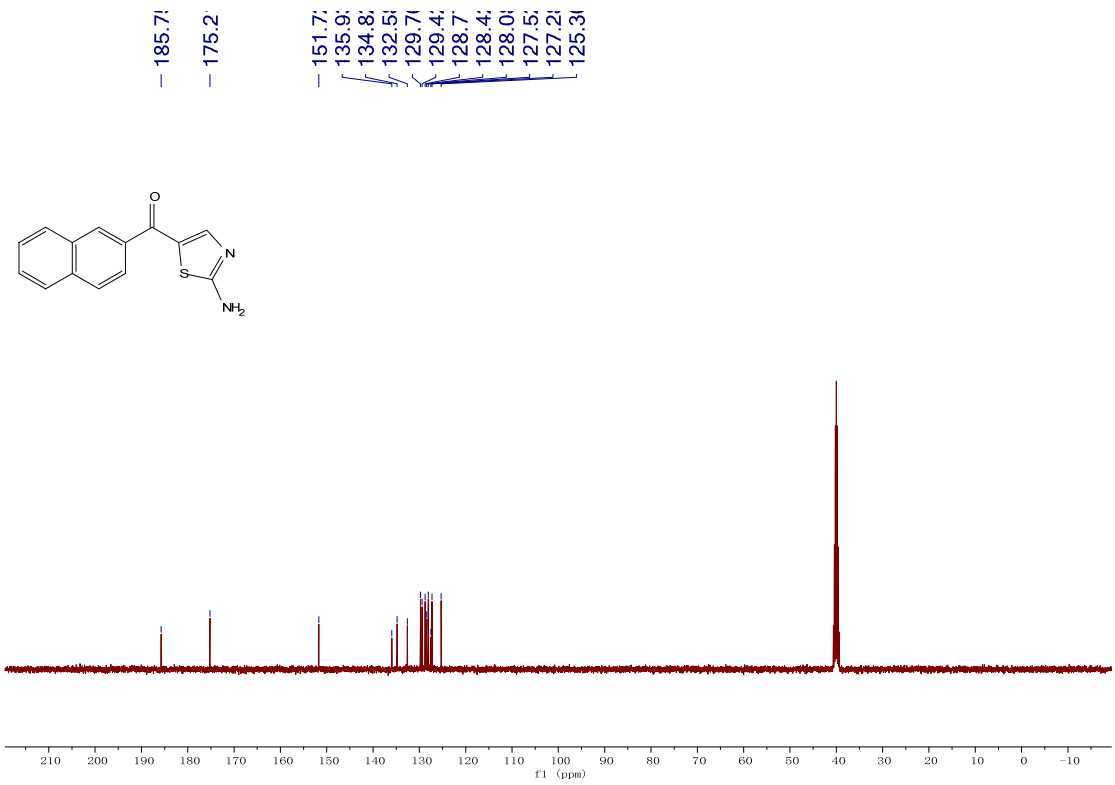
^{1}H NMR spectrum of **3u** (400 MHz, DMSO-d_6)



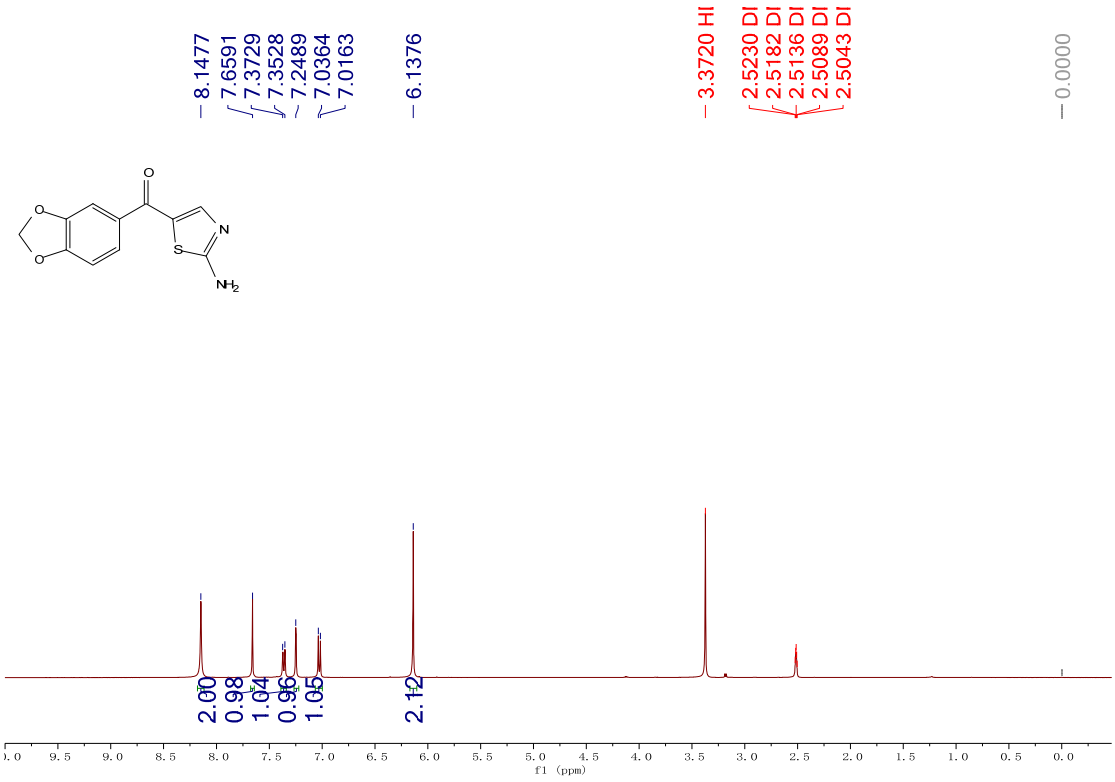
^{13}C NMR spectrum of **3u** (100 MHz, DMSO-d_6)



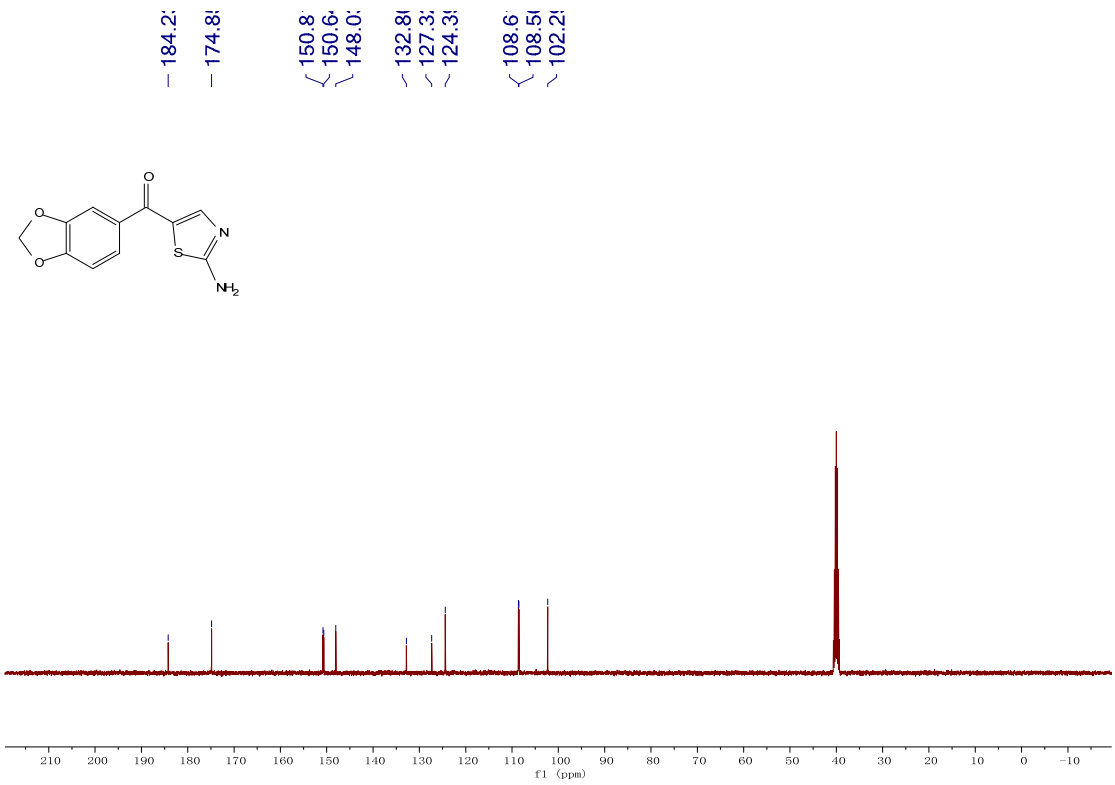
^{1}H NMR spectrum of **3v** (400 MHz, DMSO-d_6)



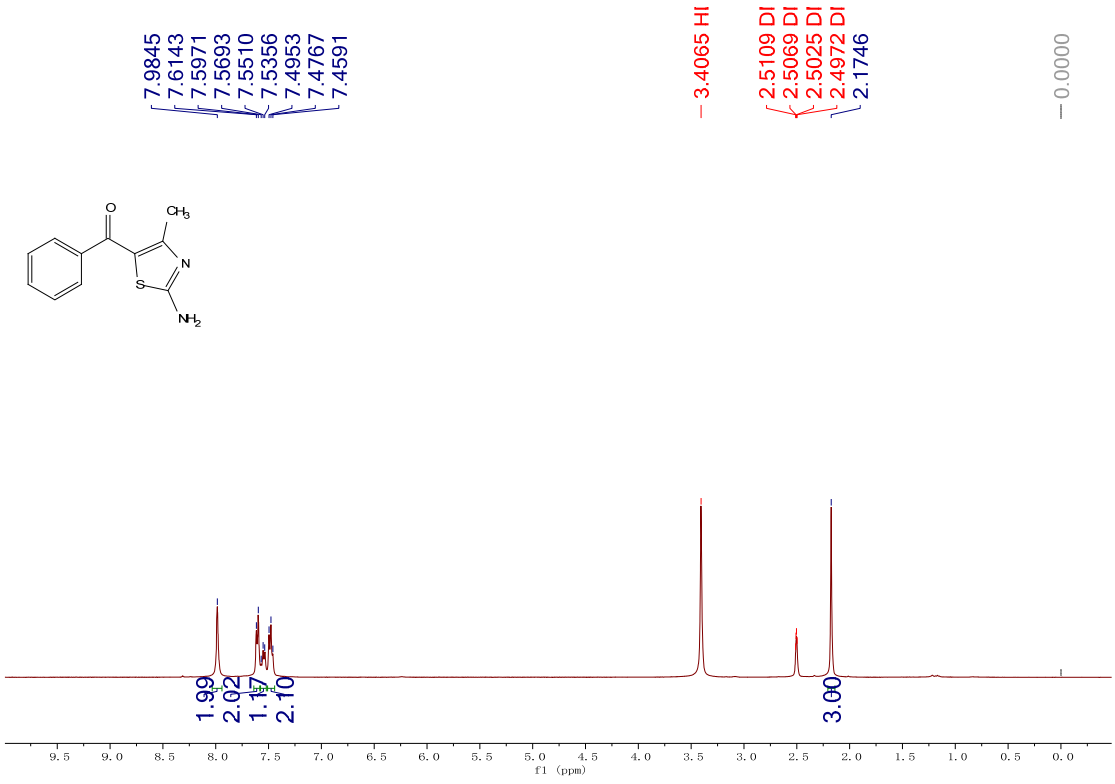
^{13}C NMR spectrum of **3v** (100 MHz, DMSO-d_6)



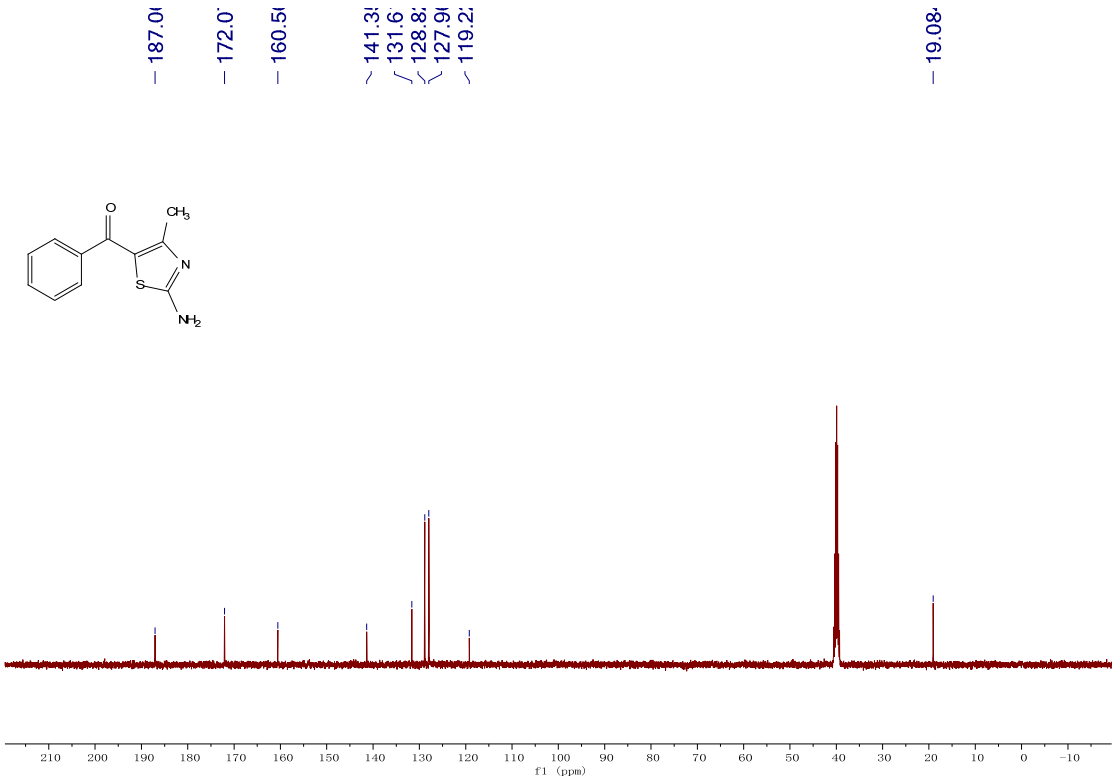
^{1}H NMR spectrum of **3w** (400 MHz, DMSO-d_6)



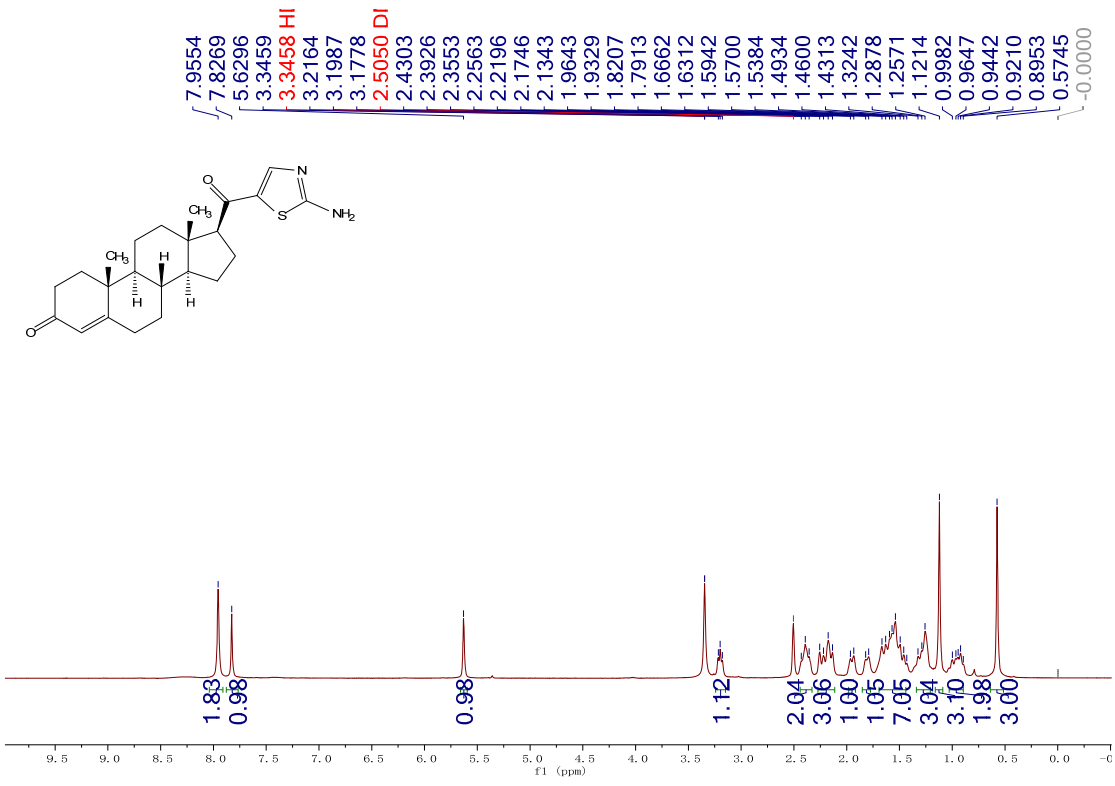
^{13}C NMR spectrum of **3w** (100 MHz, DMSO-d_6)



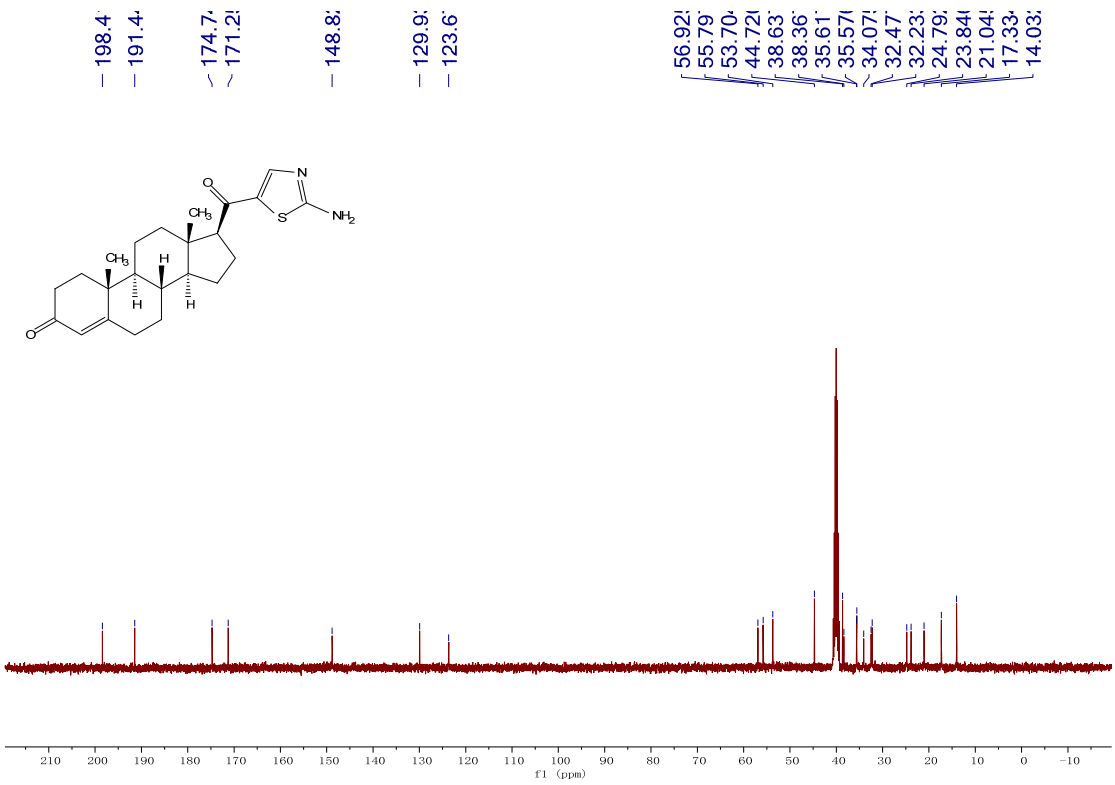
^{1}H NMR spectrum of **3x** (400 MHz, DMSO-d_6)



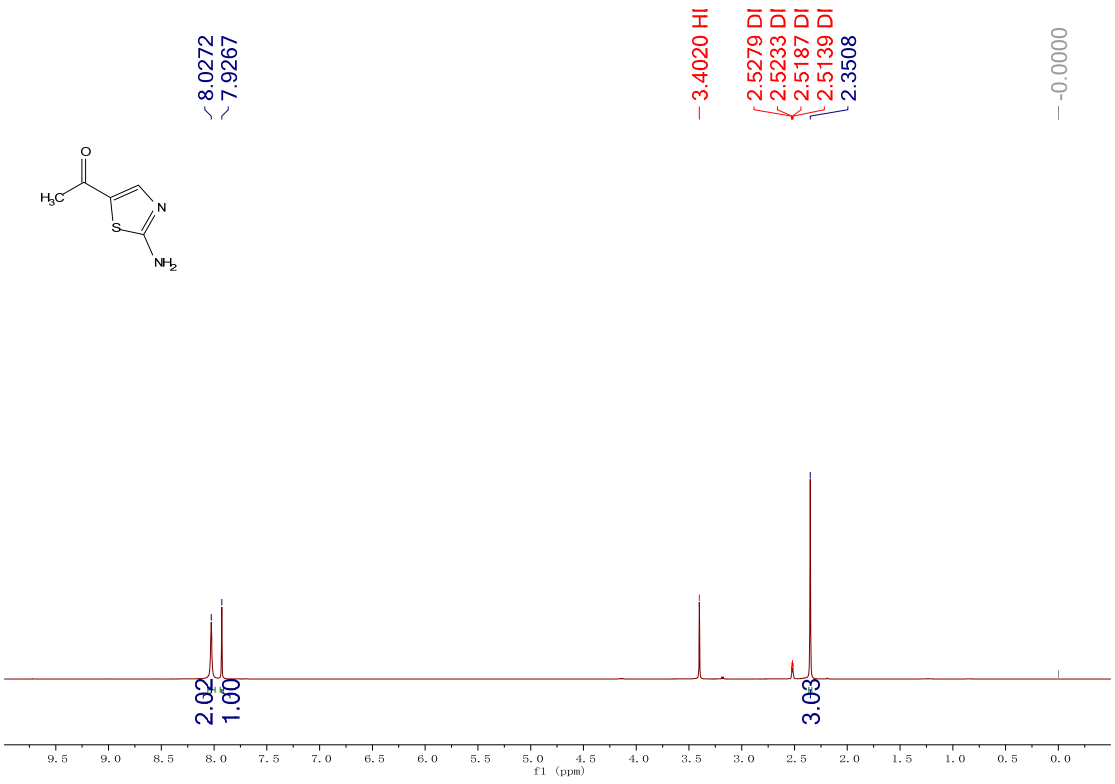
^{13}C NMR spectrum of **3x** (100 MHz, DMSO-d_6)



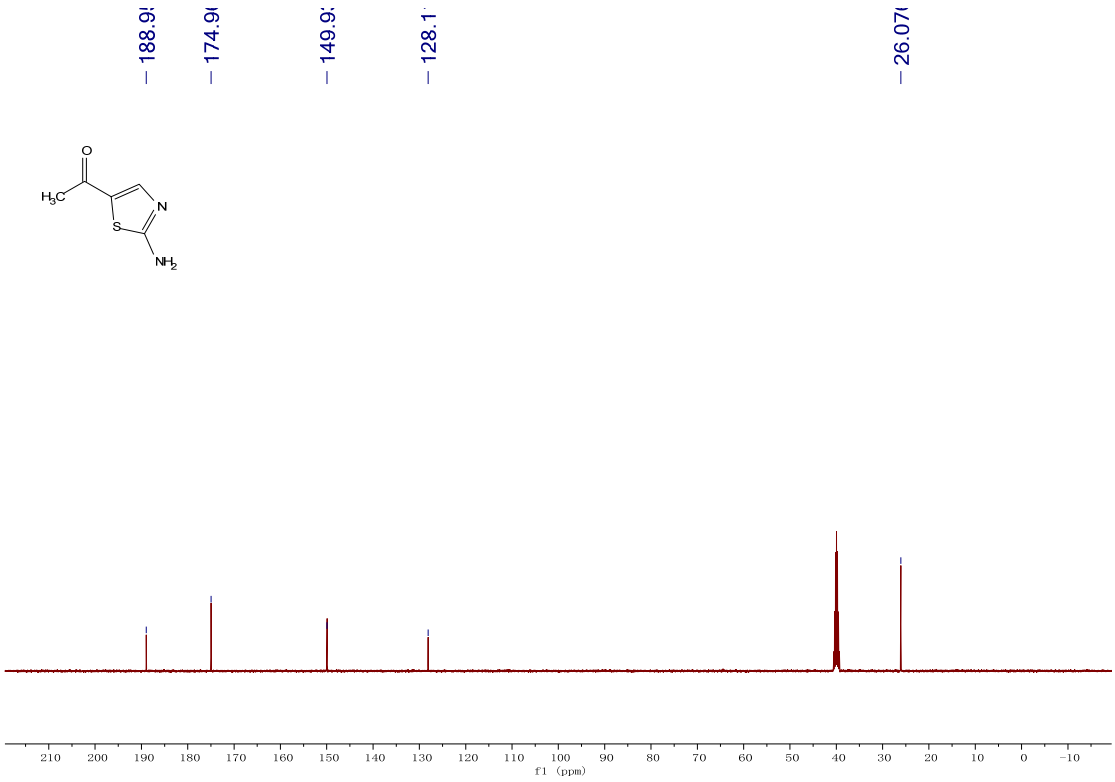
^{1}H NMR spectrum of **3y** (400 MHz, DMSO-d_6)



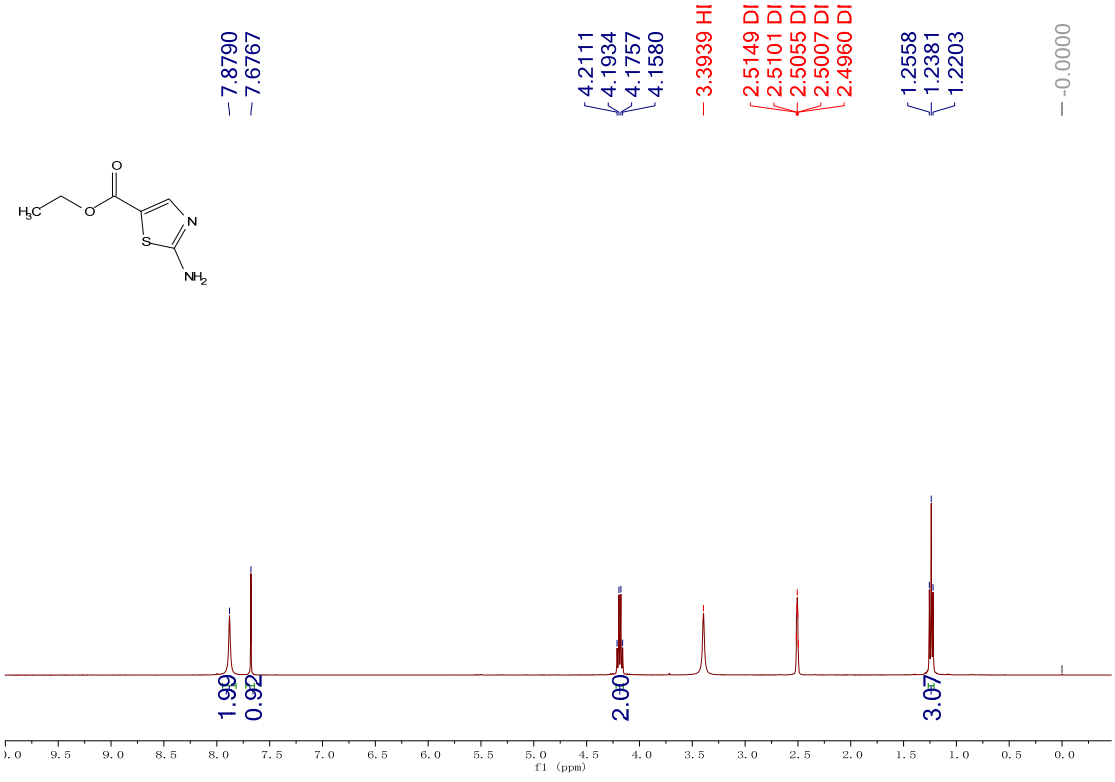
^{13}C NMR spectrum of **3y** (100 MHz, DMSO-d_6)



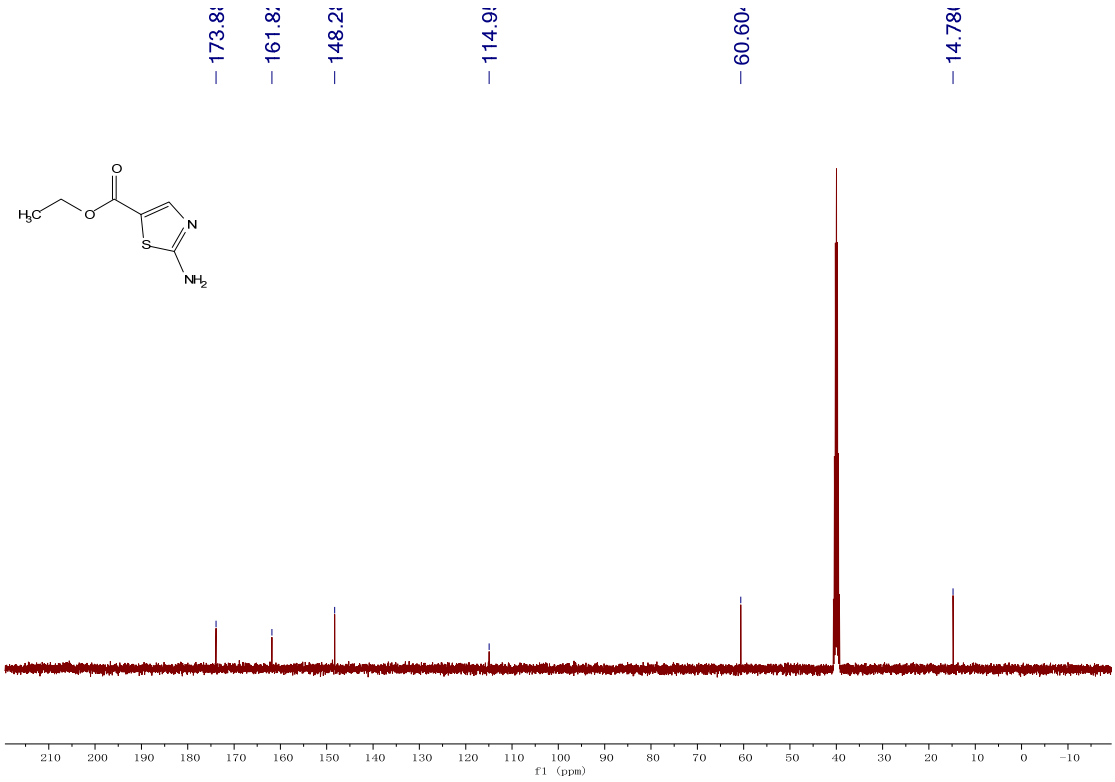
^{1}H NMR spectrum of **3z** (400 MHz, DMSO-d_6)



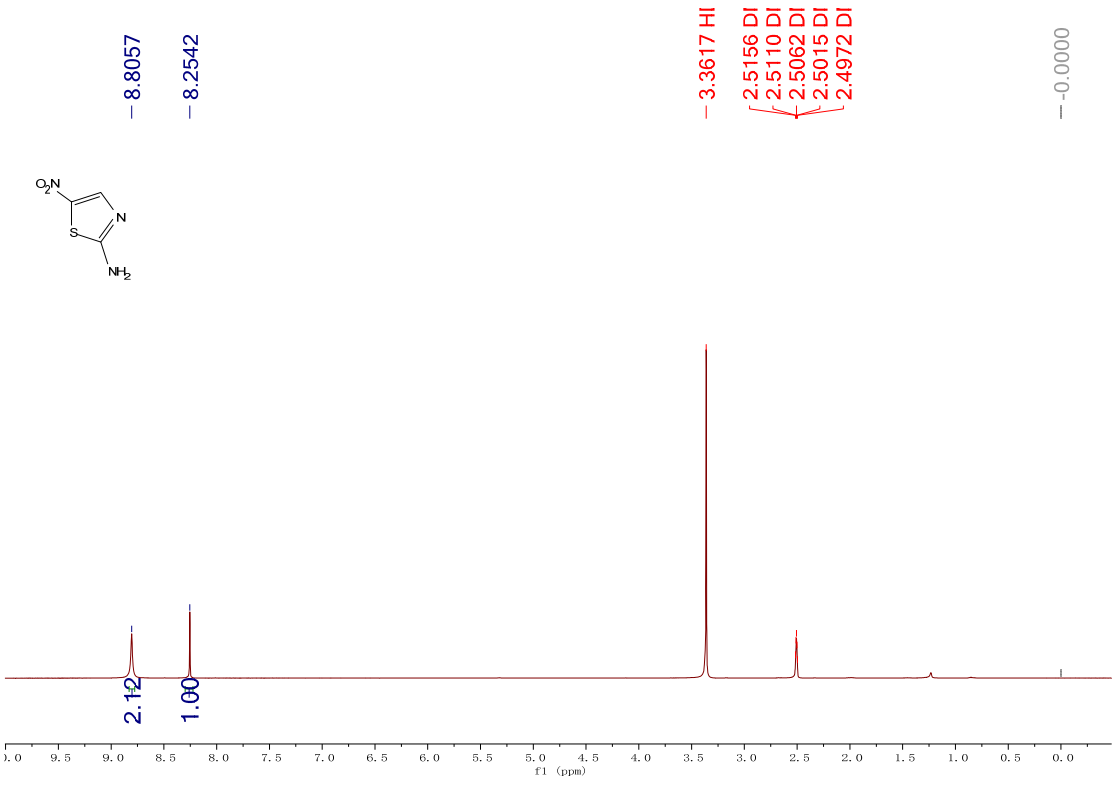
^{13}C NMR spectrum of **3z** (100 MHz, DMSO-d_6)



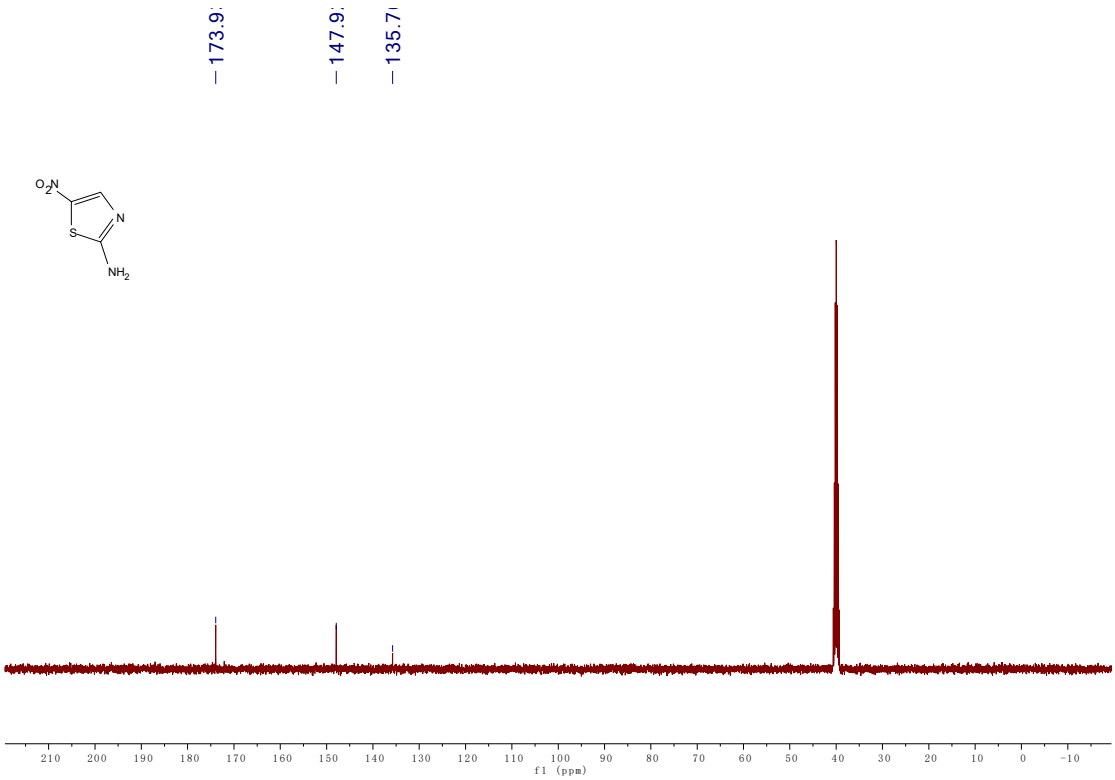
^{1}H NMR spectrum of **3aa** (400 MHz, DMSO-d_6)



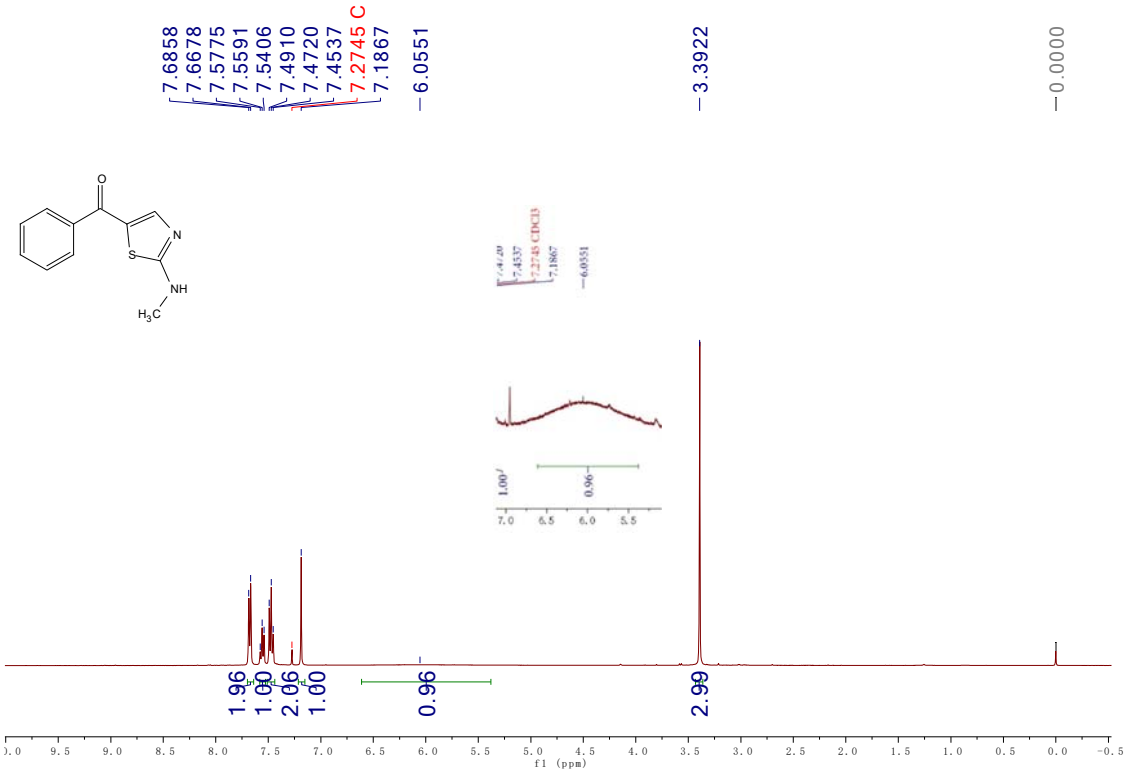
^{13}C NMR spectrum of **3aa** (100 MHz, DMSO-d_6)



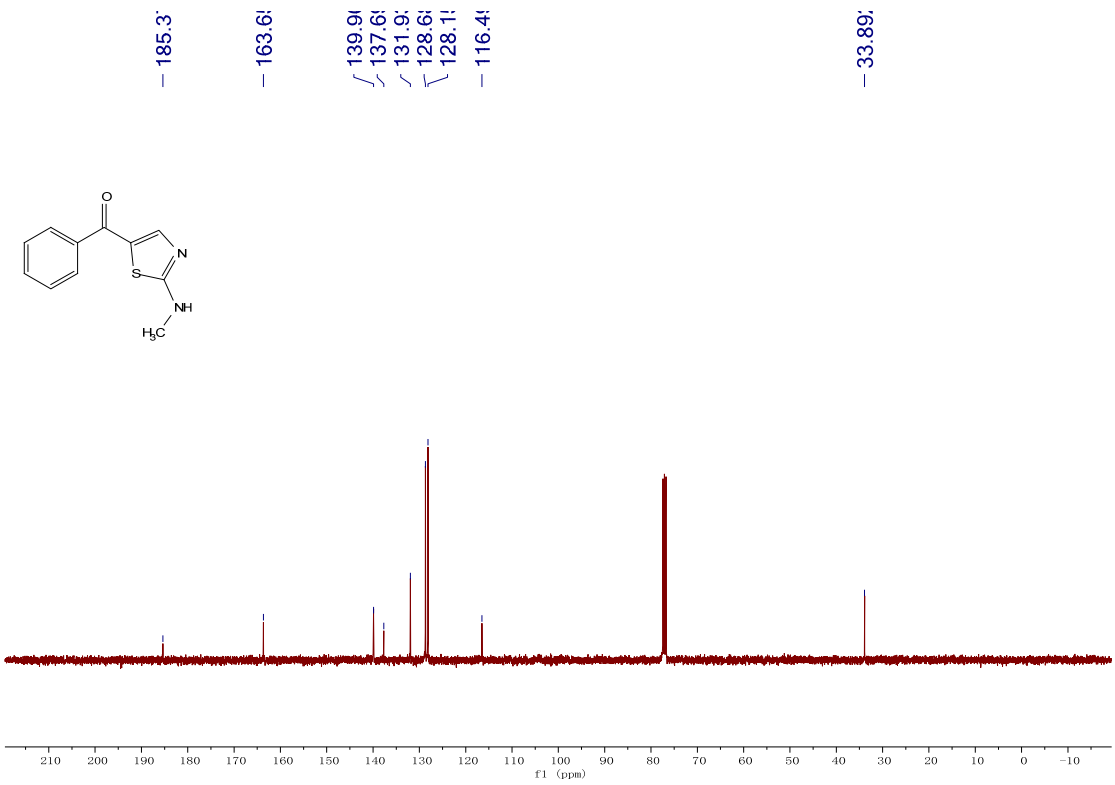
^{1}H NMR spectrum of **3ab** (400 MHz, DMSO-d_6)



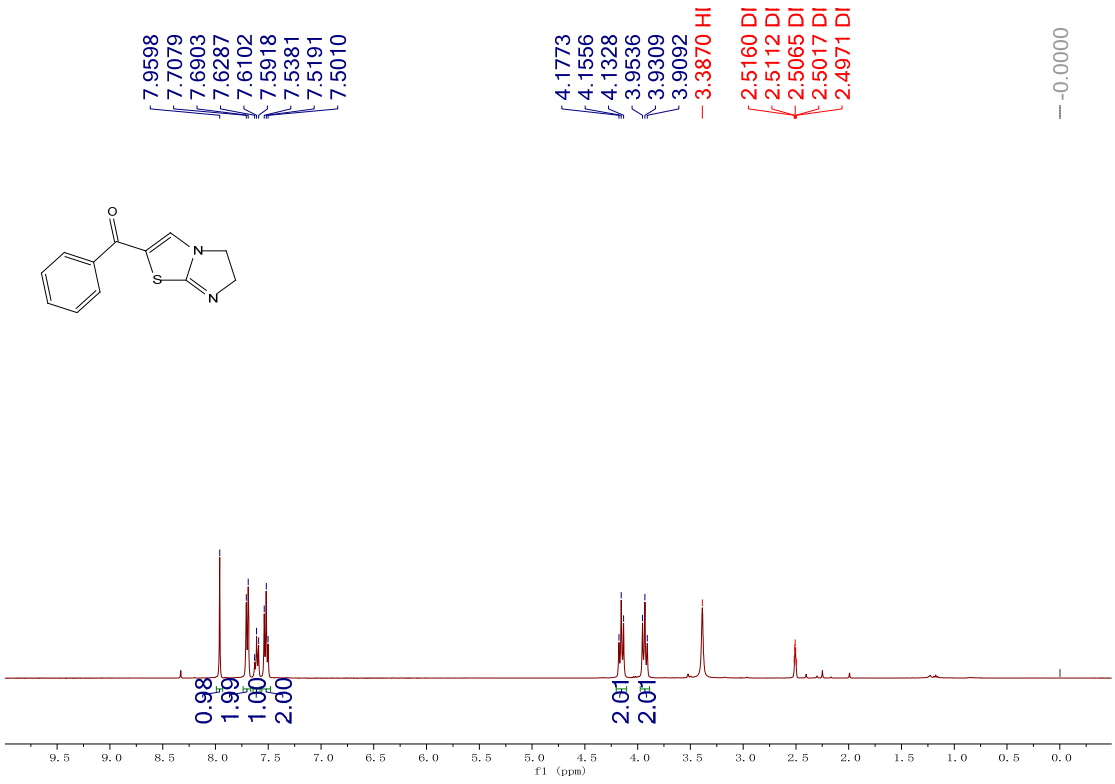
^{13}C NMR spectrum of **3ab** (100 MHz, DMSO-d_6)



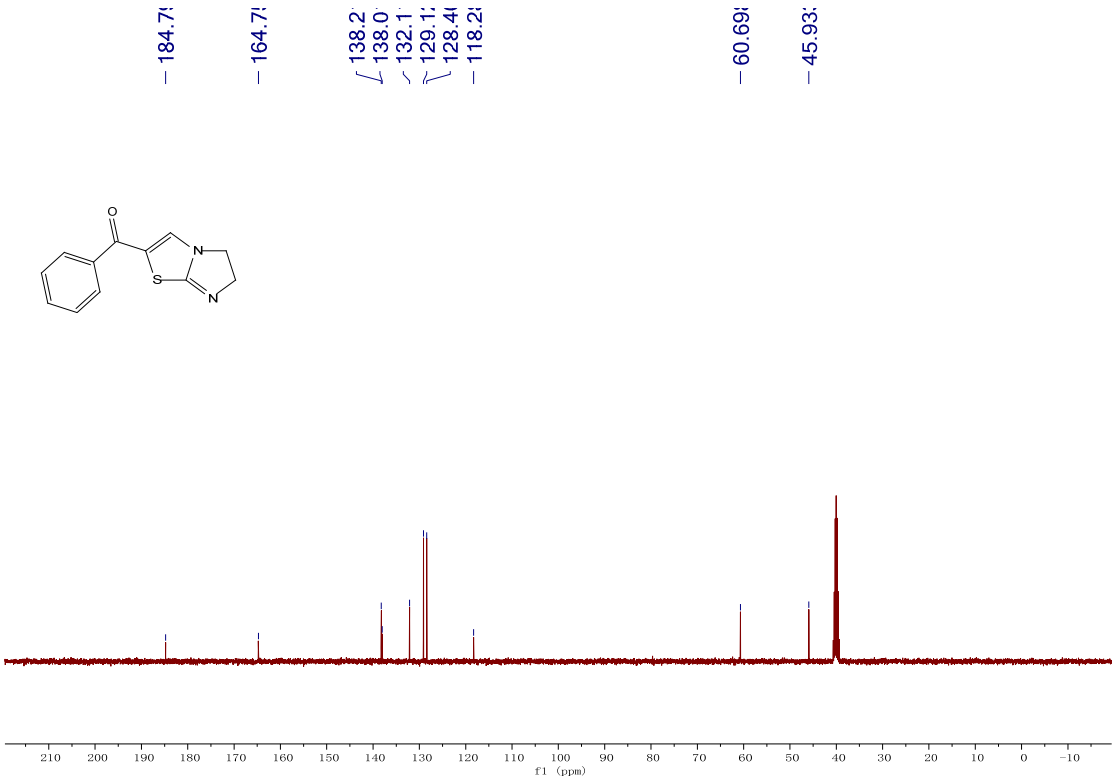
^{1}H NMR spectrum of **3ac** (400 MHz, $CDCl_3$)



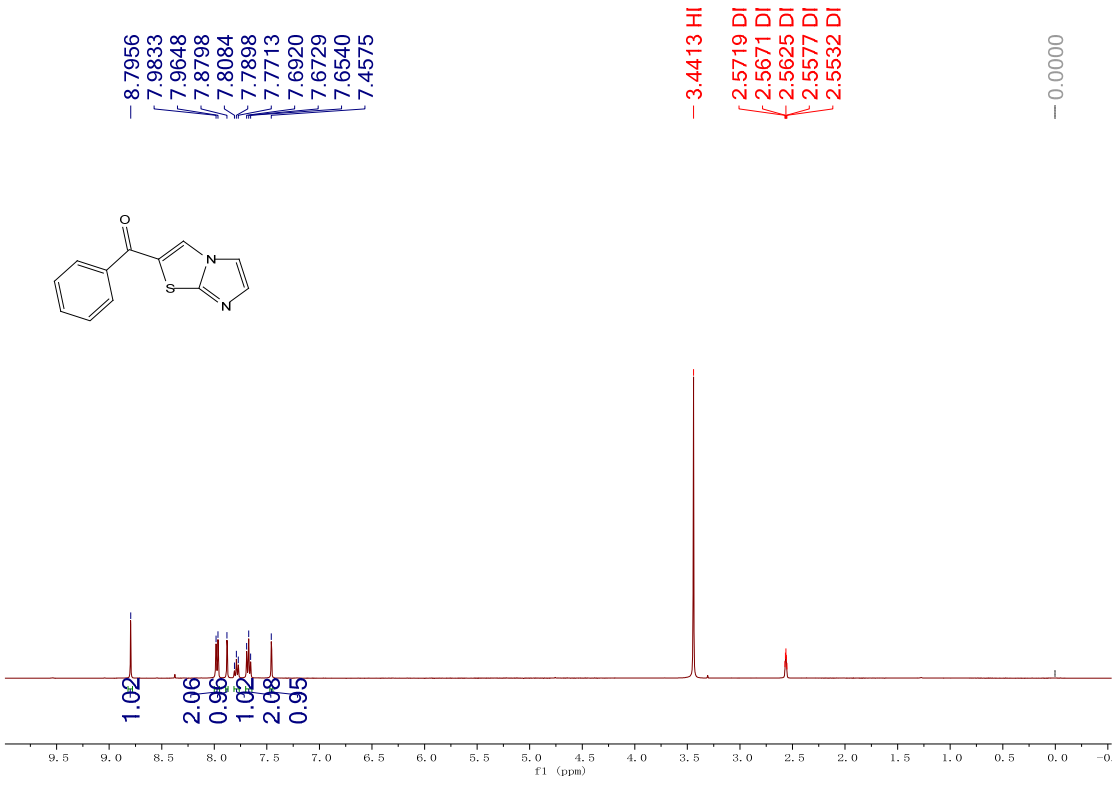
^{13}C NMR spectrum of **3ac** (100 MHz, $CDCl_3$)\



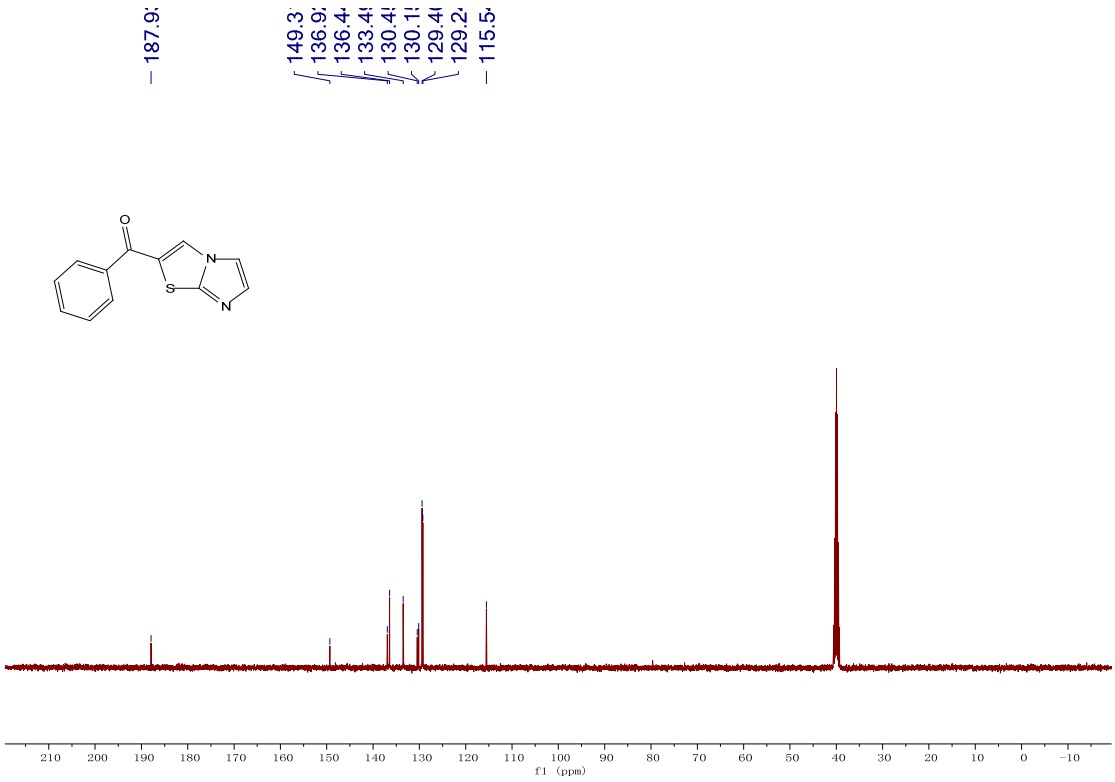
^{1}H NMR spectrum of **3ad** (400 MHz, DMSO-d_6)



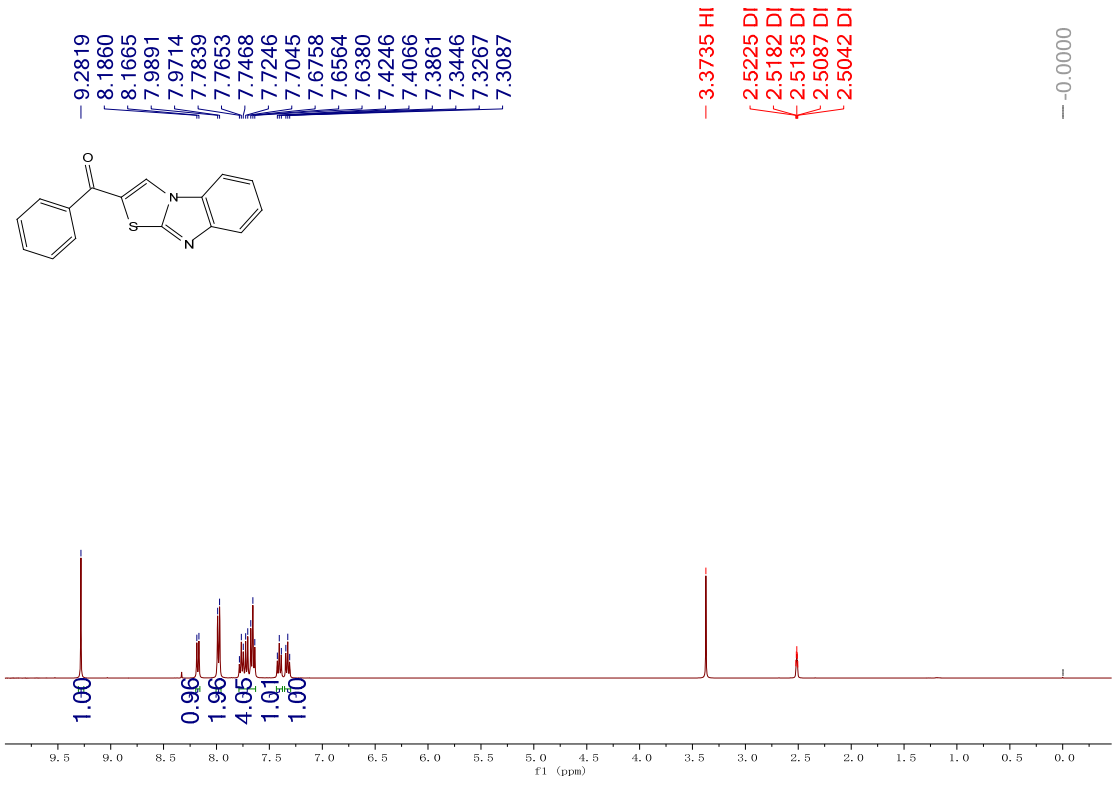
^{13}C NMR spectrum of **3ad** (100 MHz, DMSO-d_6)



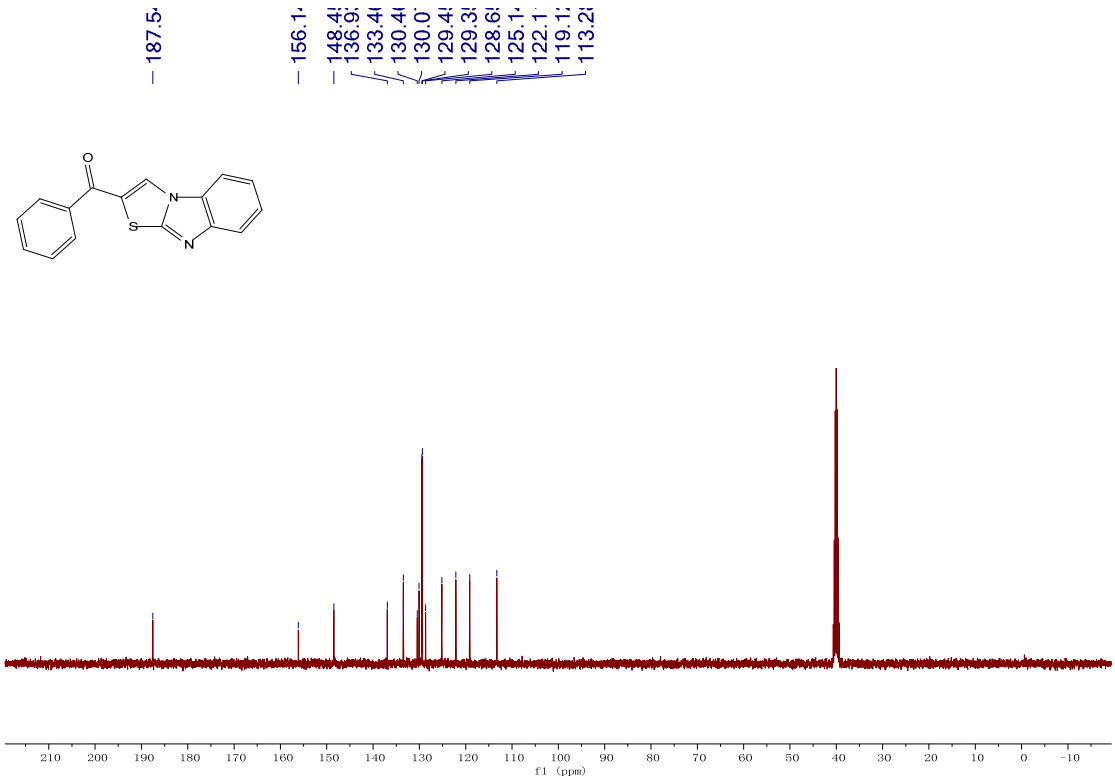
^{1}H NMR spectrum of **3ae** (400 MHz, DMSO-d_6)



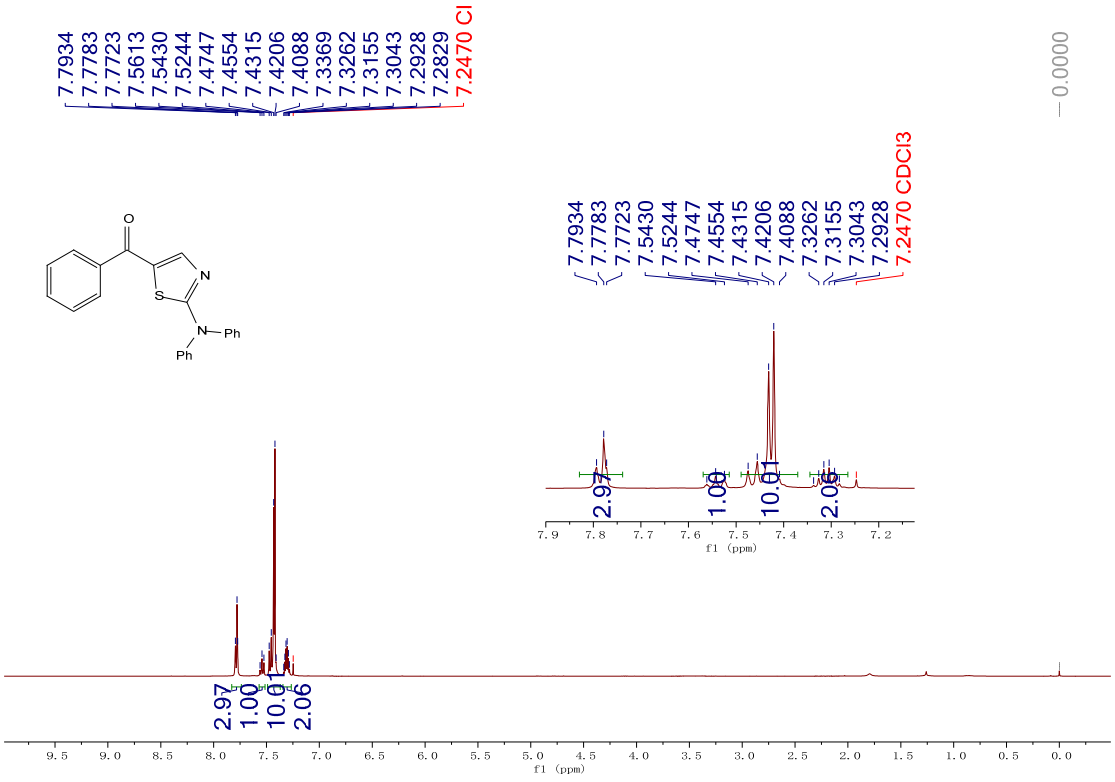
^{13}C NMR spectrum of **3ae** (100 MHz, DMSO-d_6)



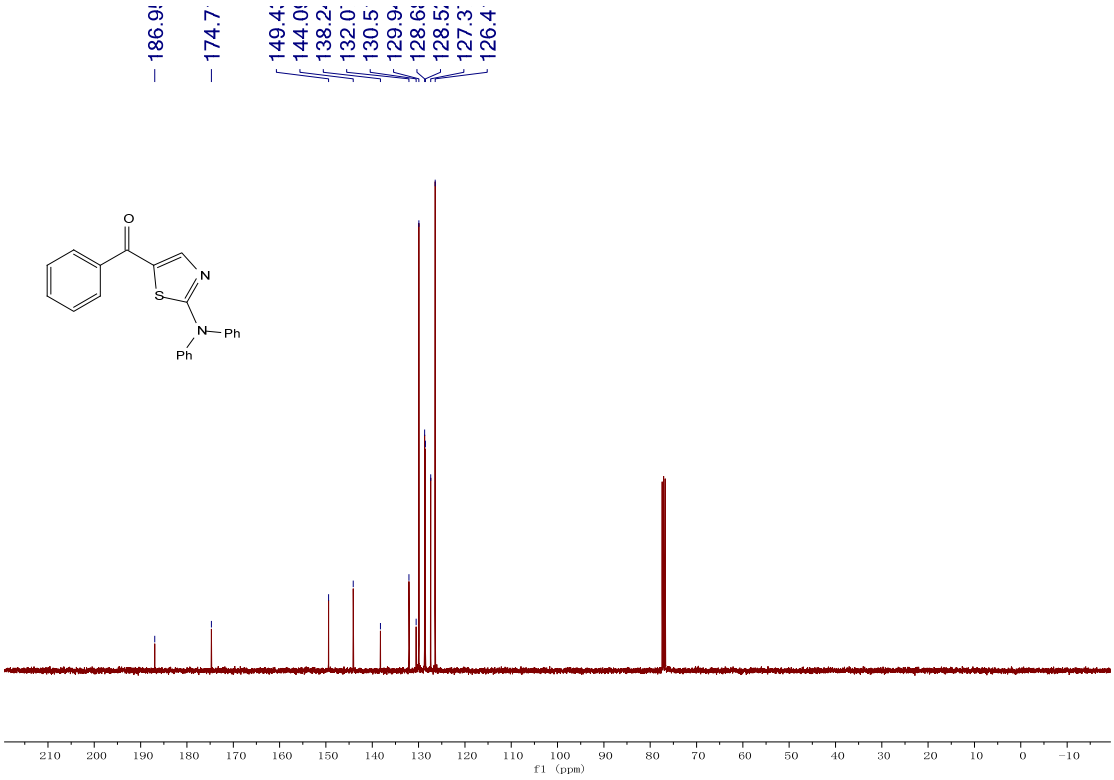
^{1}H NMR spectrum of **3af** (400 MHz, DMSO-d_6)



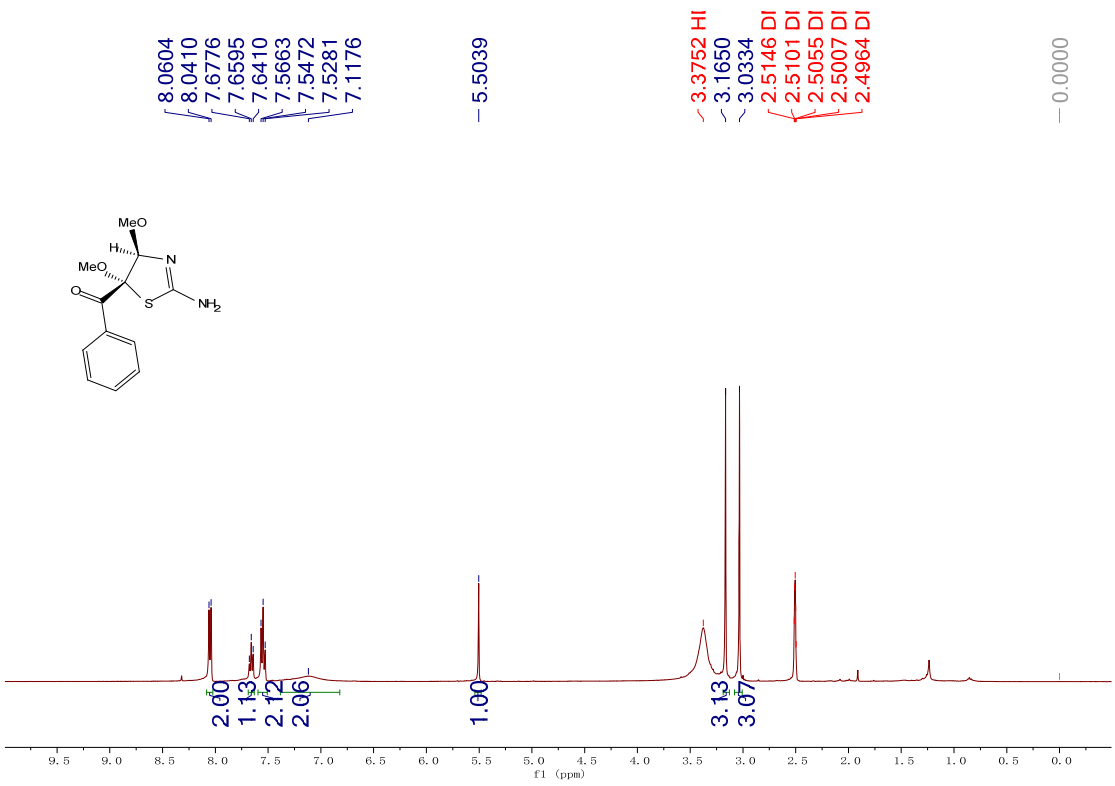
^{13}C NMR spectrum of **3af** (100 MHz, DMSO-d_6)



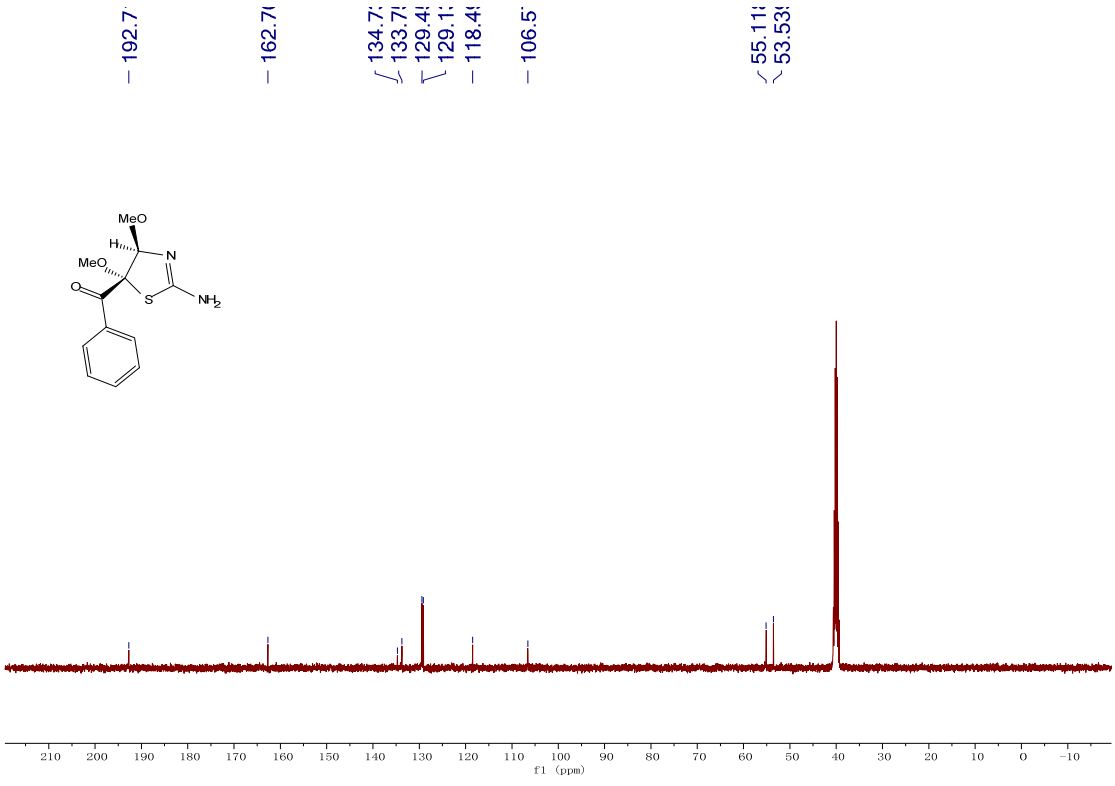
^{1}H NMR spectrum of **3ag** (400 MHz, $CDCl_3$)



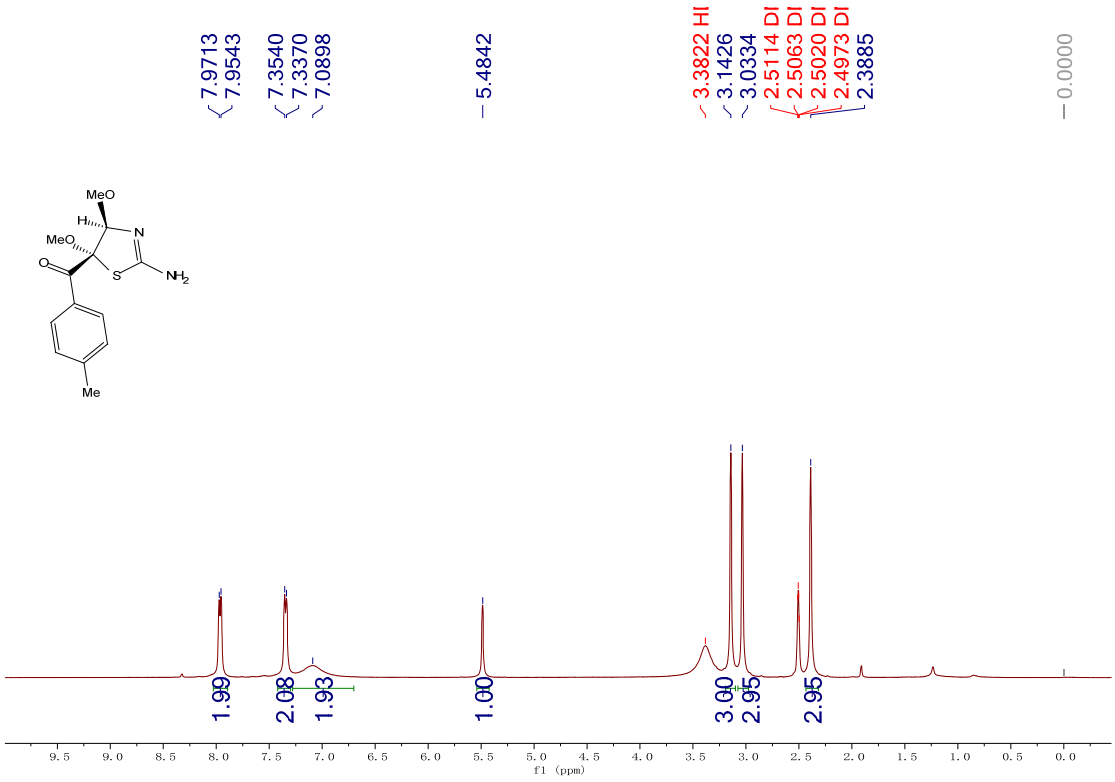
^{13}C NMR spectrum of **3ag** (100 MHz, $CDCl_3$)



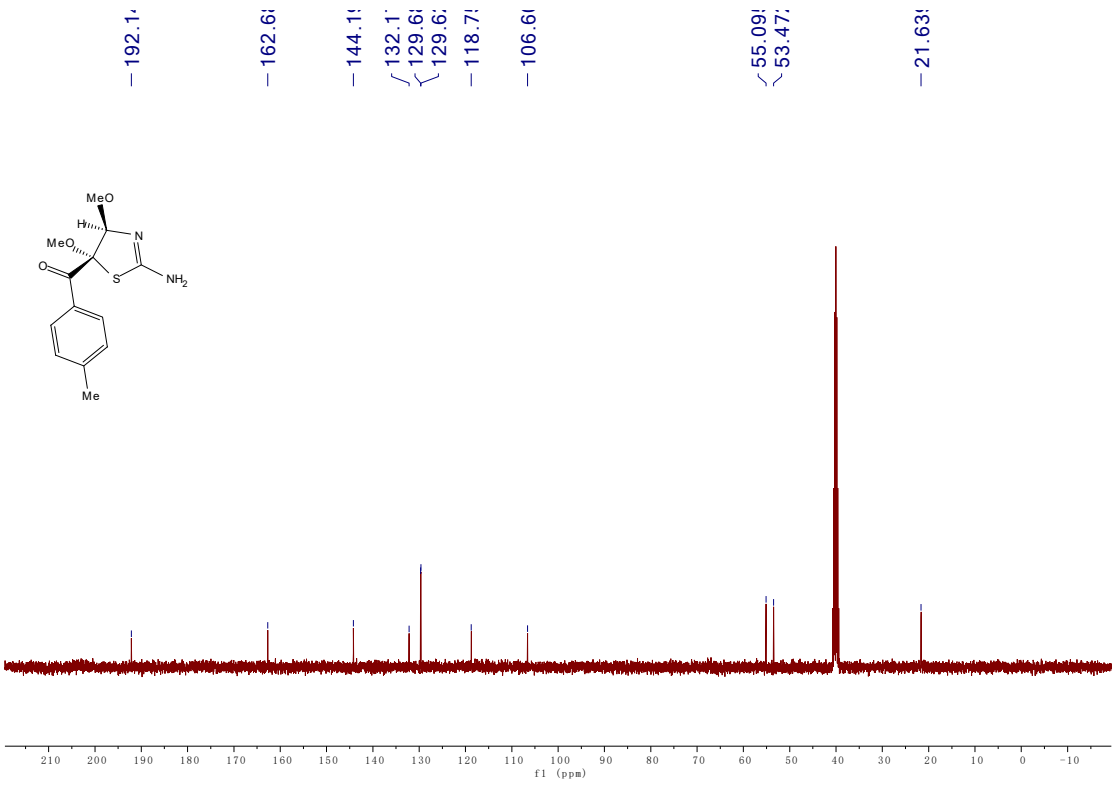
^{1}H NMR spectrum of **4a** (400 MHz, DMSO-d_6)



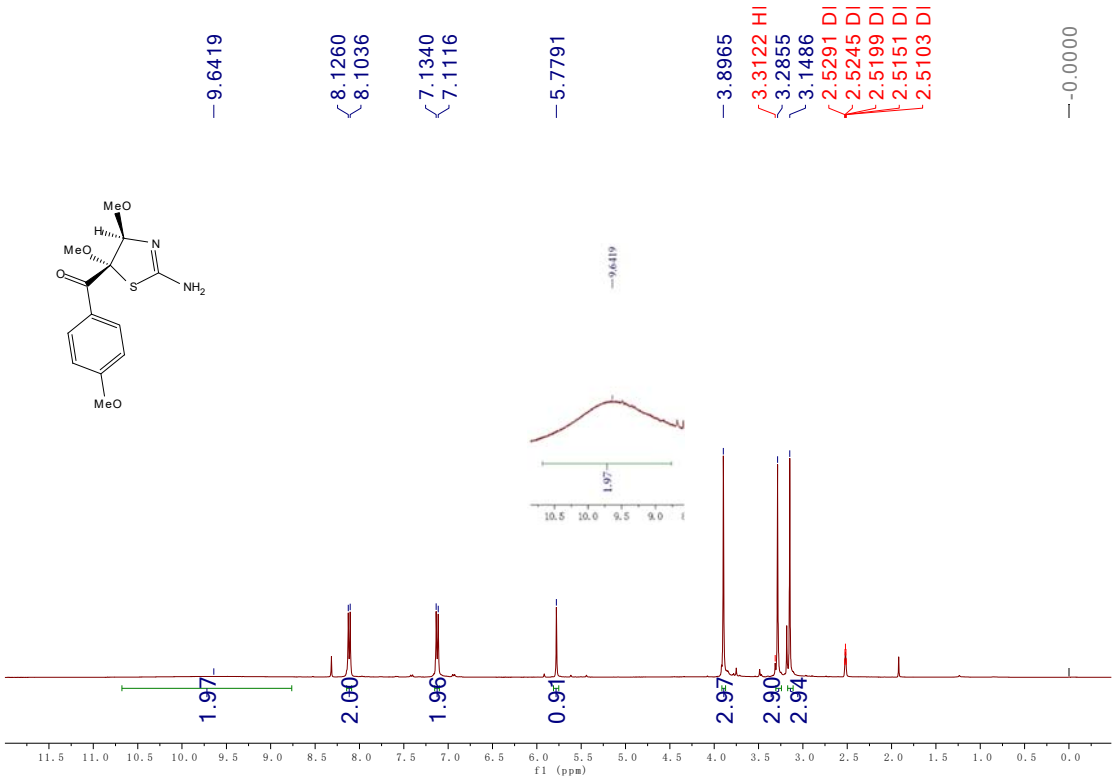
^{13}C NMR spectrum of **4a** (100 MHz, DMSO-d_6)



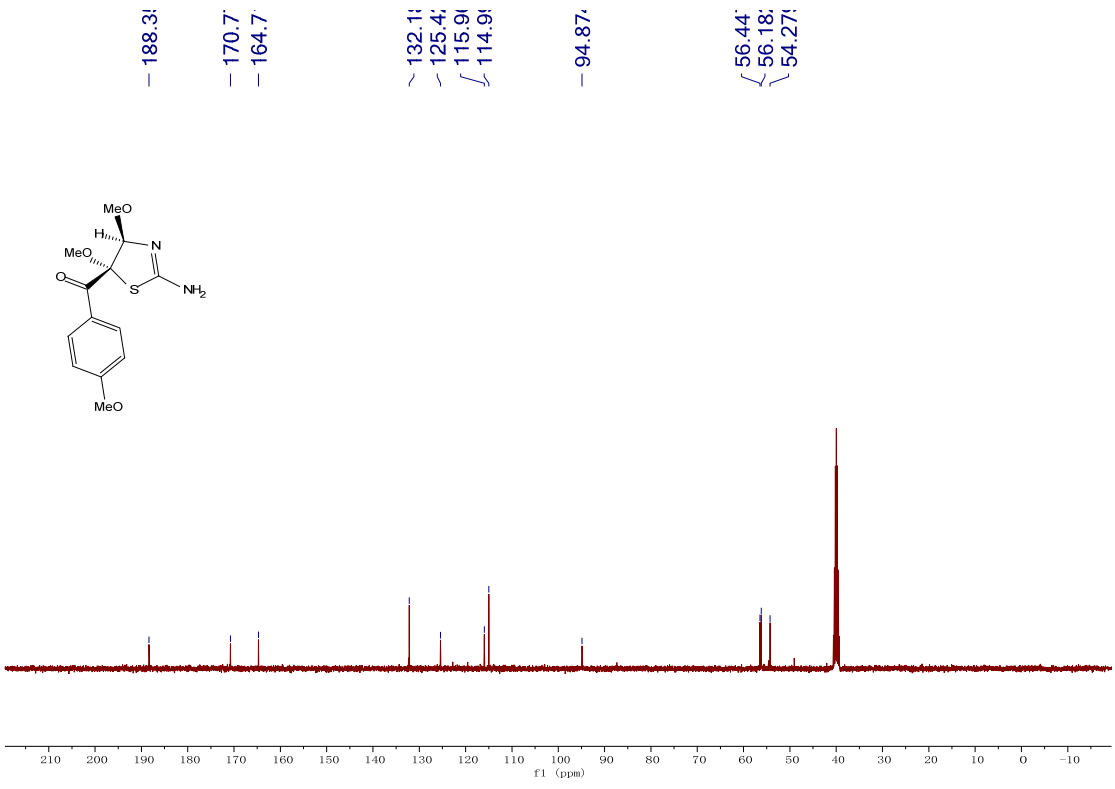
^{1}H NMR spectrum of **4b** (400 MHz, DMSO-d_6)



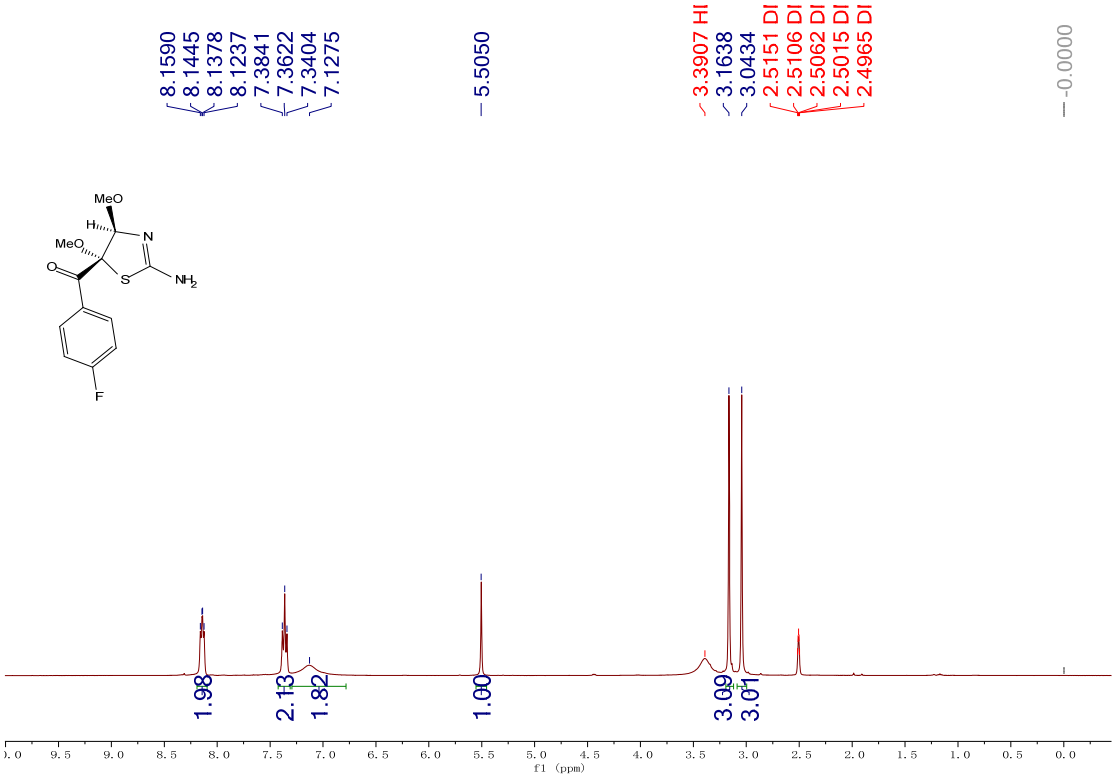
^{13}C NMR spectrum of **4b** (100 MHz, DMSO-d_6)



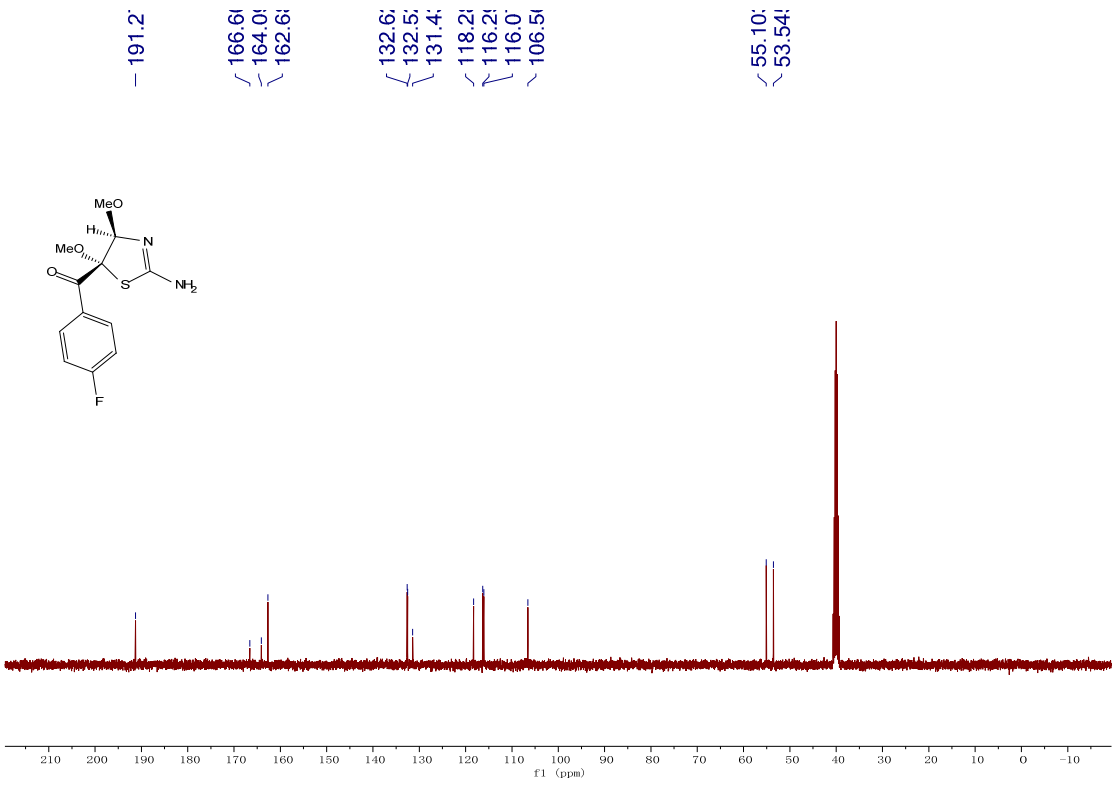
^{1}H NMR spectrum of **4c** (400 MHz, DMSO-d_6)



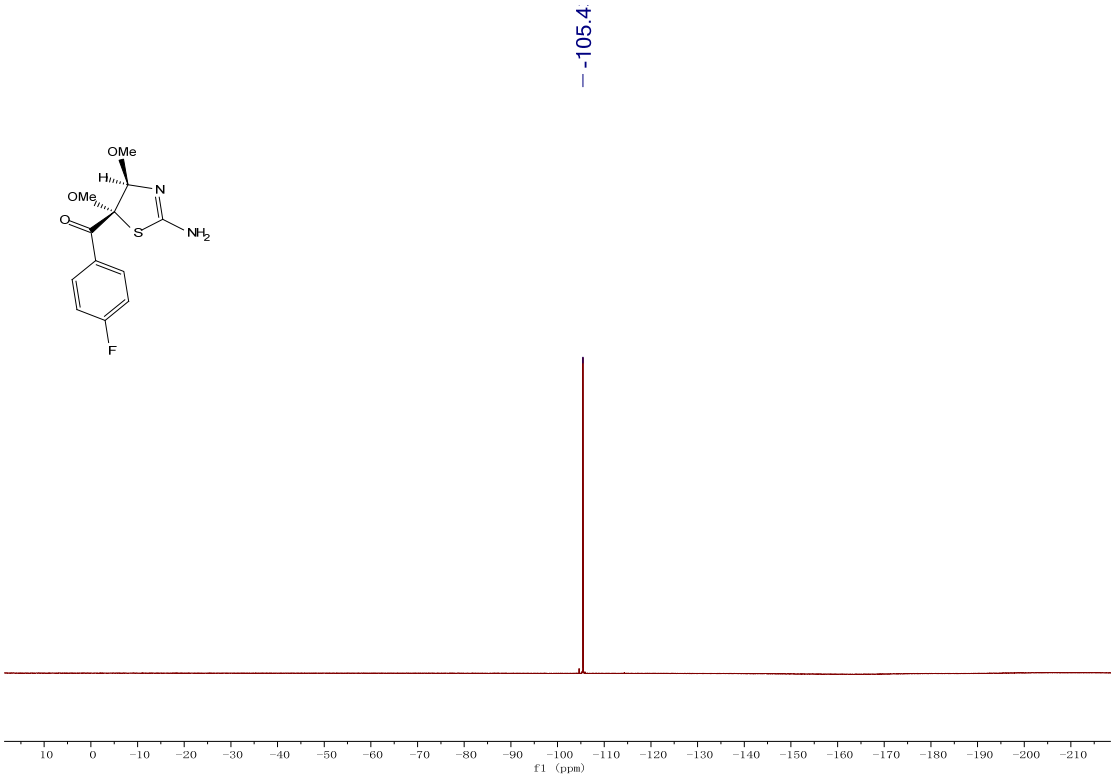
^{13}C NMR spectrum of **4c** (100 MHz, DMSO-d_6)



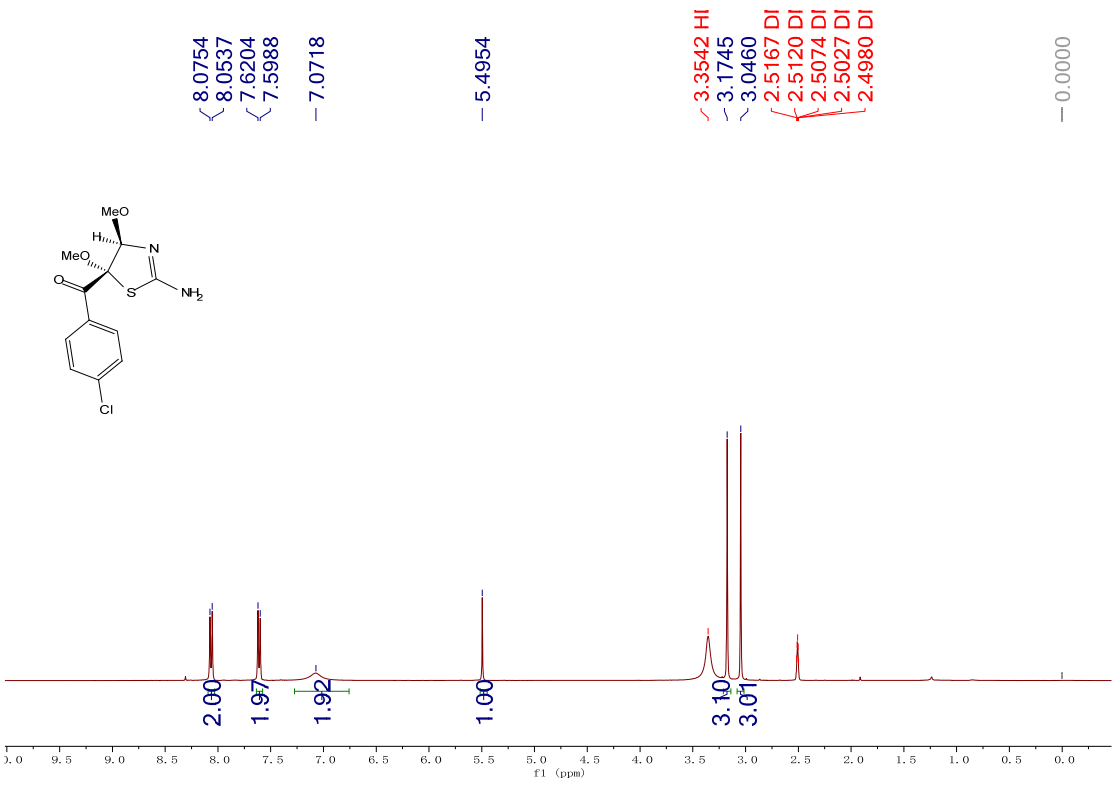
^{1}H NMR spectrum of **4d** (400 MHz, DMSO-d_6)



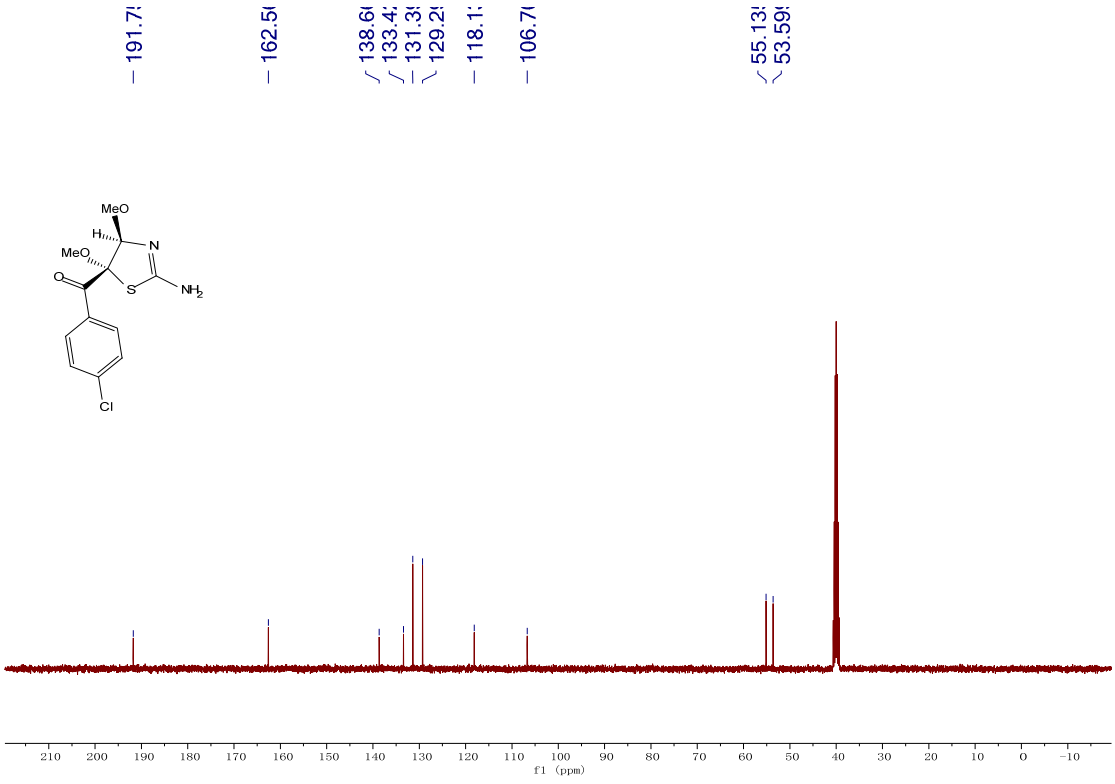
^{13}C NMR spectrum of **4d** (100 MHz, DMSO-d_6)



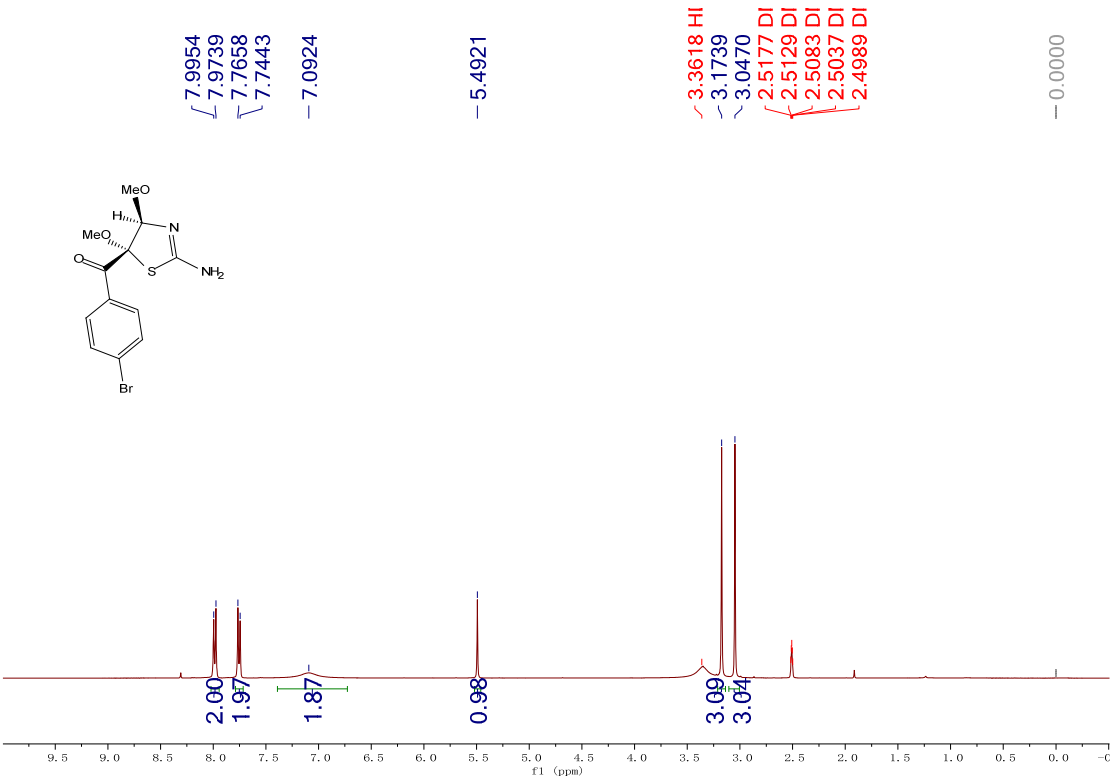
^{19}F NMR spectrum of **4d** (376 MHz, DMSO-d_6)



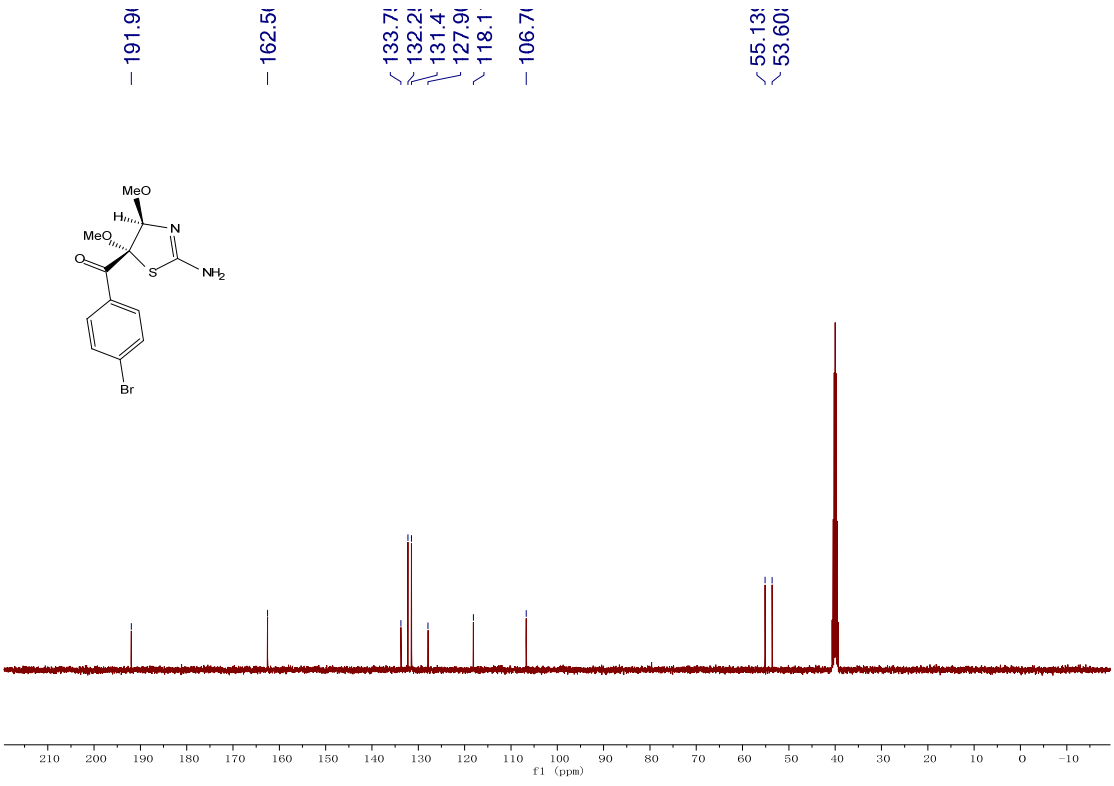
^{1}H NMR spectrum of **4e** (400 MHz, DMSO-d_6)



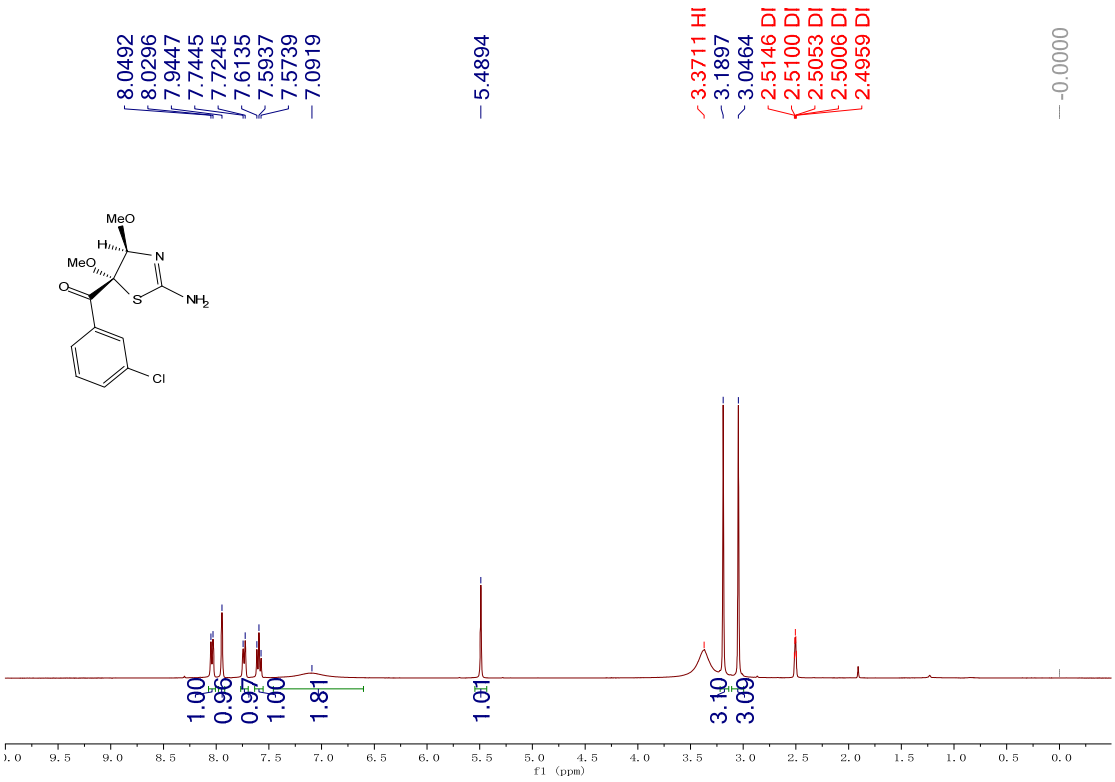
^{13}C NMR spectrum of **4e** (100 MHz, DMSO-d_6)



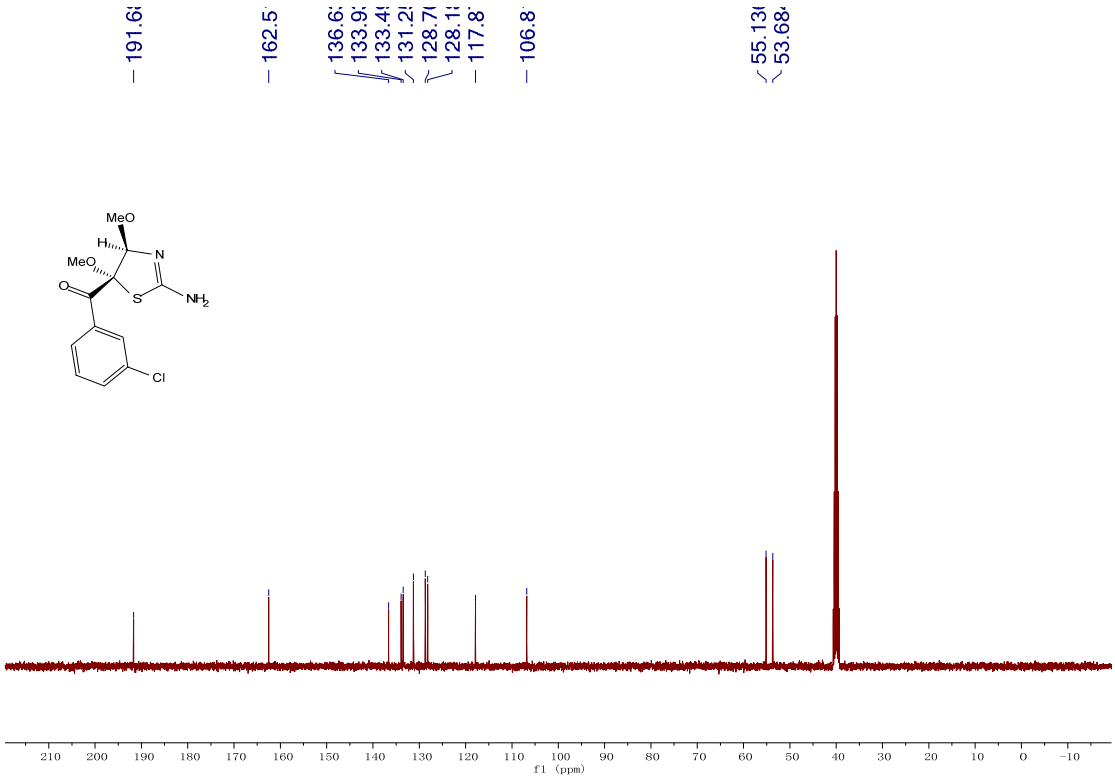
^{1}H NMR spectrum of **4f** (400 MHz, DMSO-d_6)



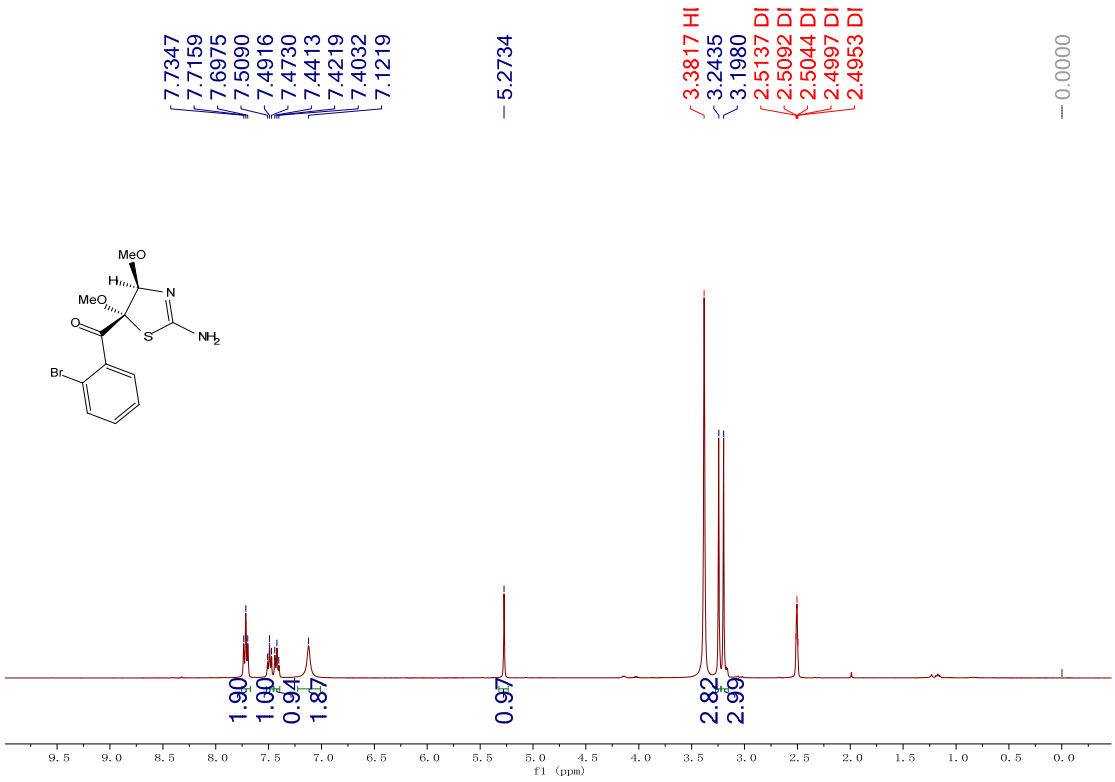
^{13}C NMR spectrum of **4f** (100 MHz, DMSO-d_6)



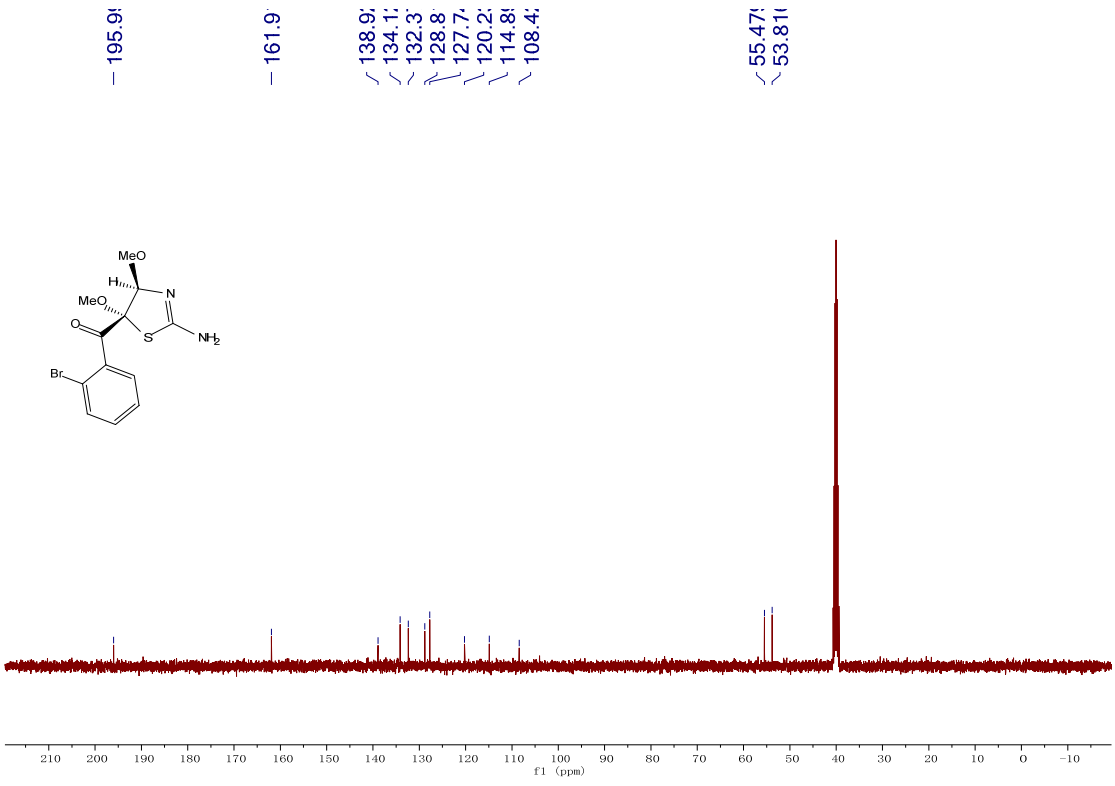
^{1}H NMR spectrum of **4g** (400 MHz, DMSO-d_6)



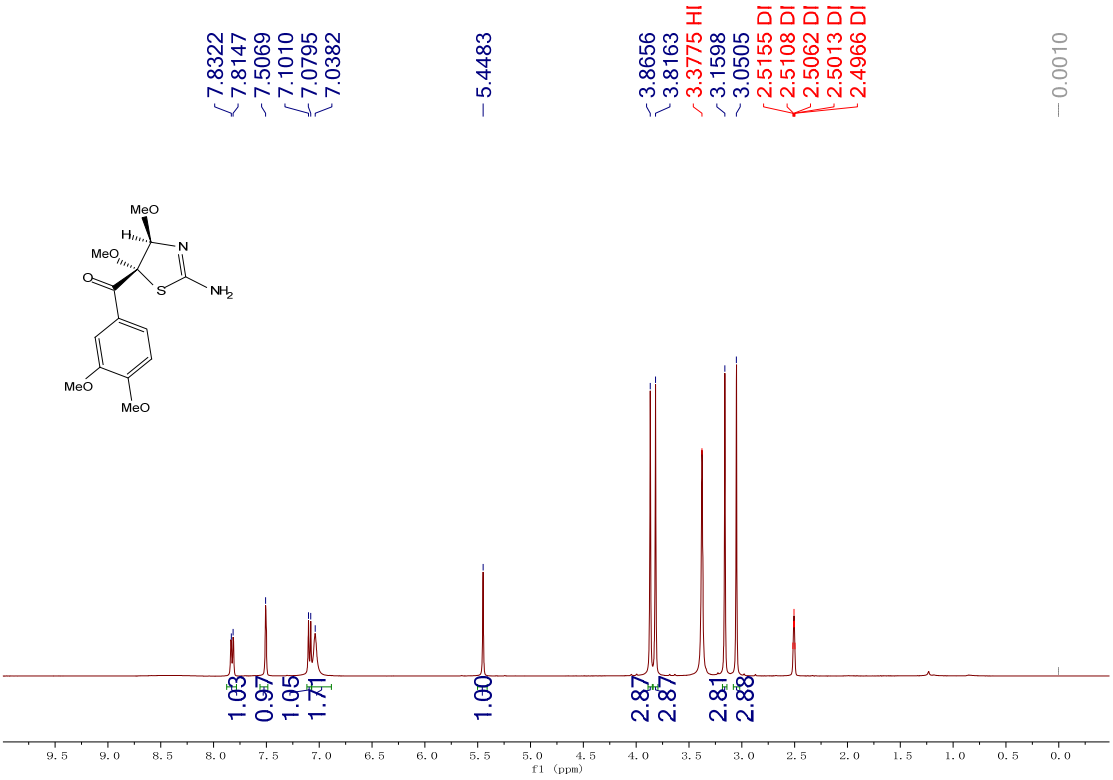
^{13}C NMR spectrum of **4g** (100 MHz, DMSO-d_6)



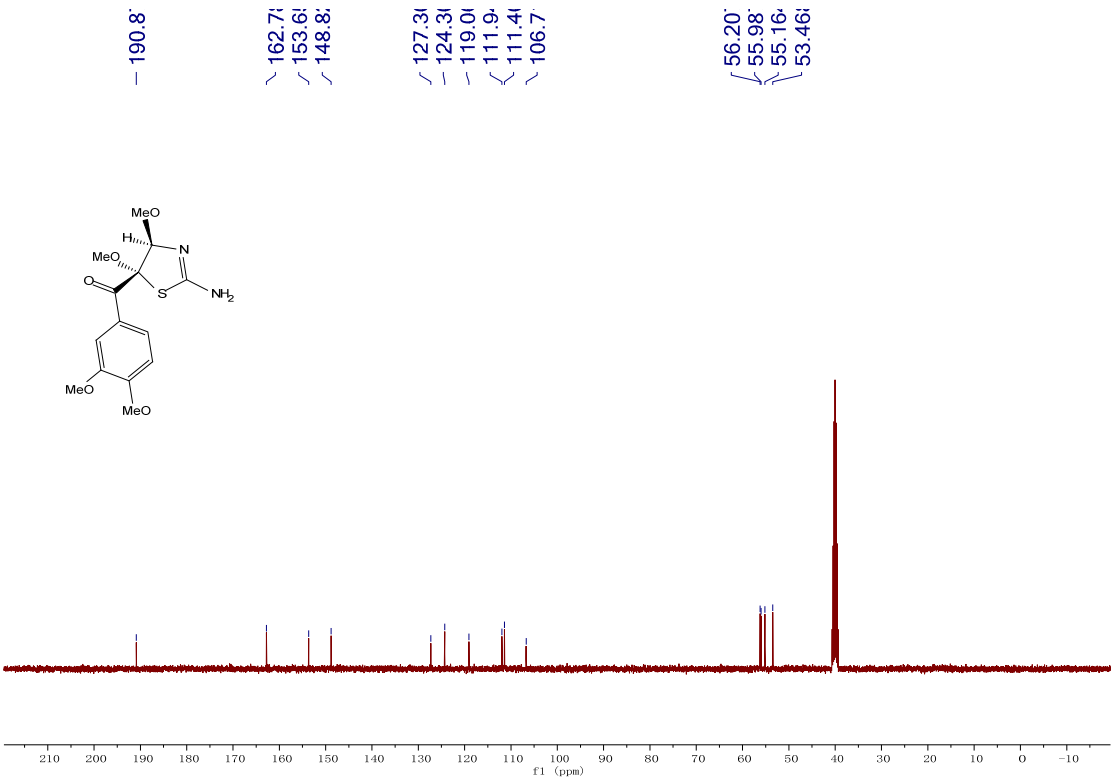
^{1}H NMR spectrum of **4h** (400 MHz, DMSO-d_6)



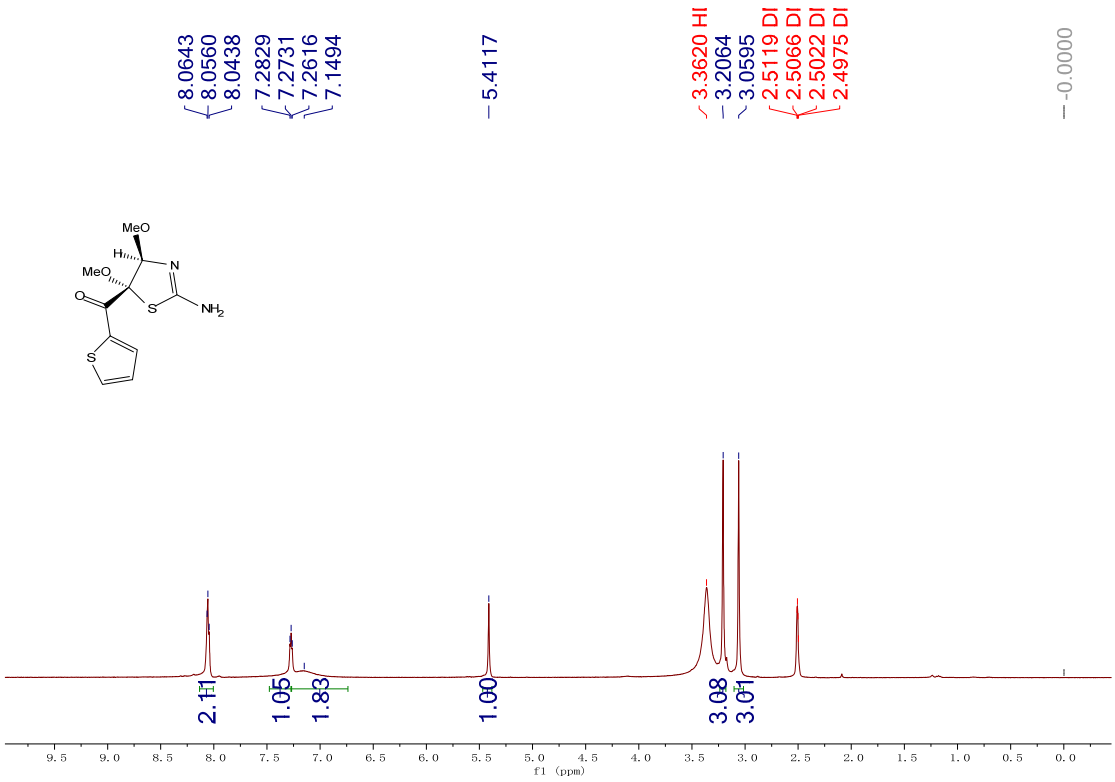
^{13}C NMR spectrum of **4h** (100 MHz, DMSO-d_6)



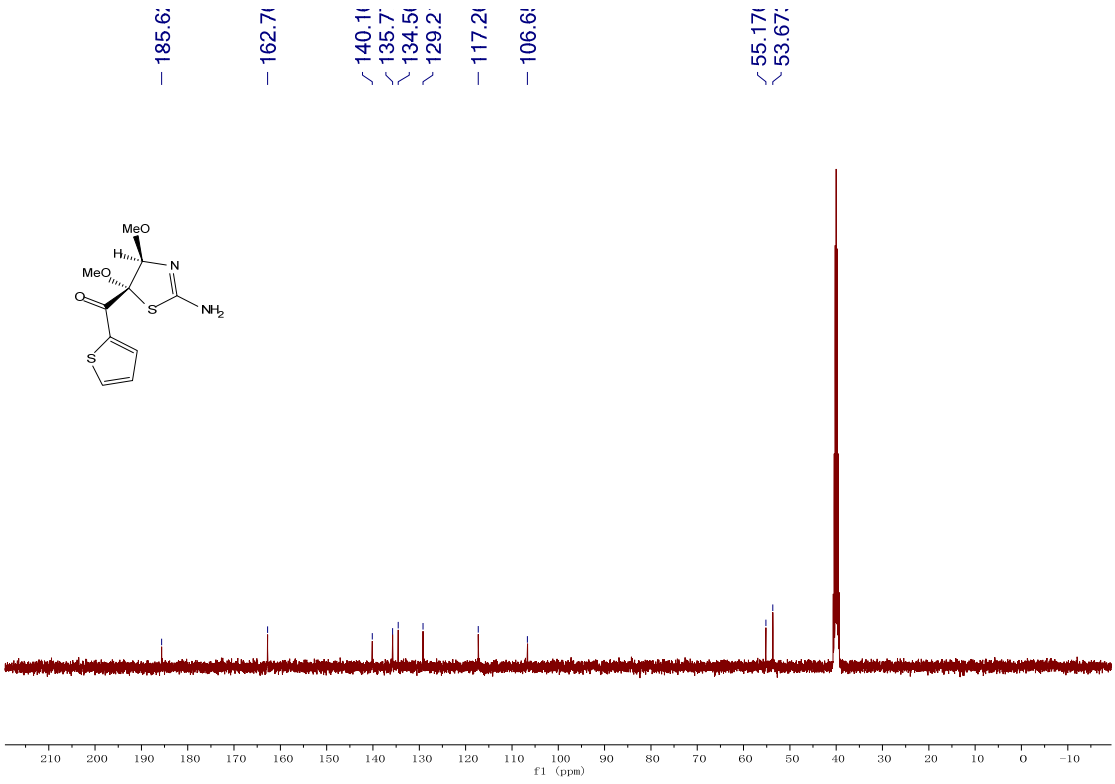
^{1}H NMR spectrum of **4i** (400 MHz, DMSO-d_6)



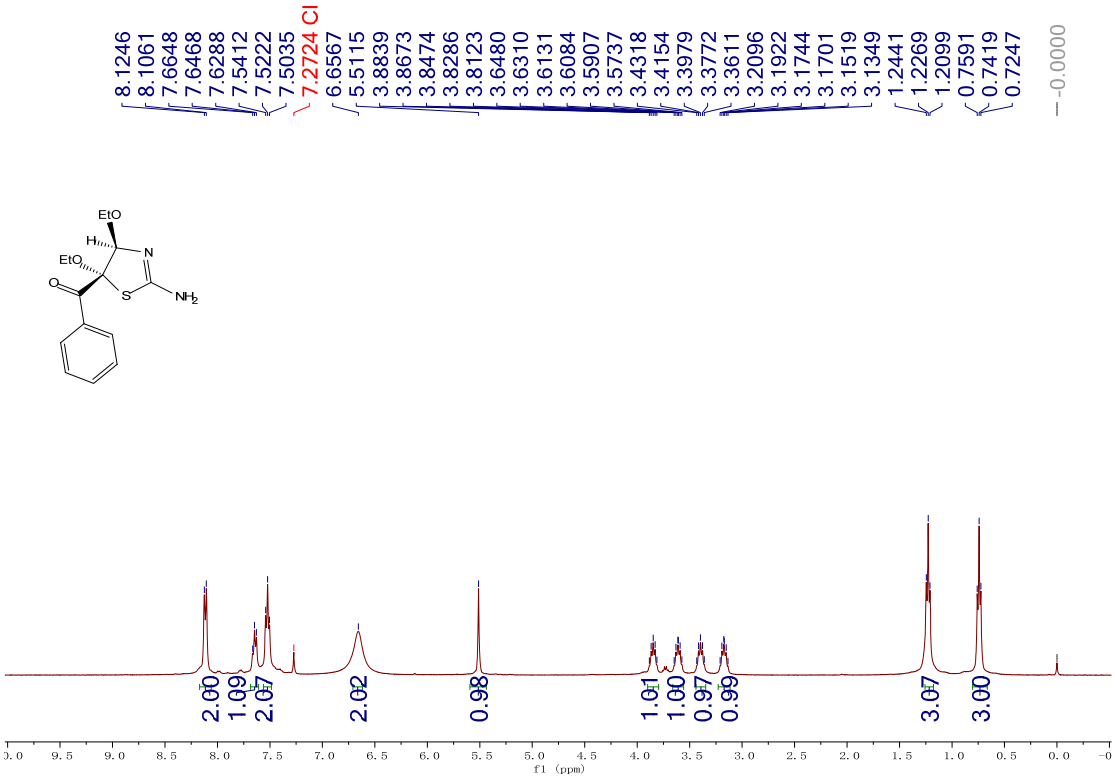
^{13}C NMR spectrum of **4i** (100 MHz, DMSO-d_6)



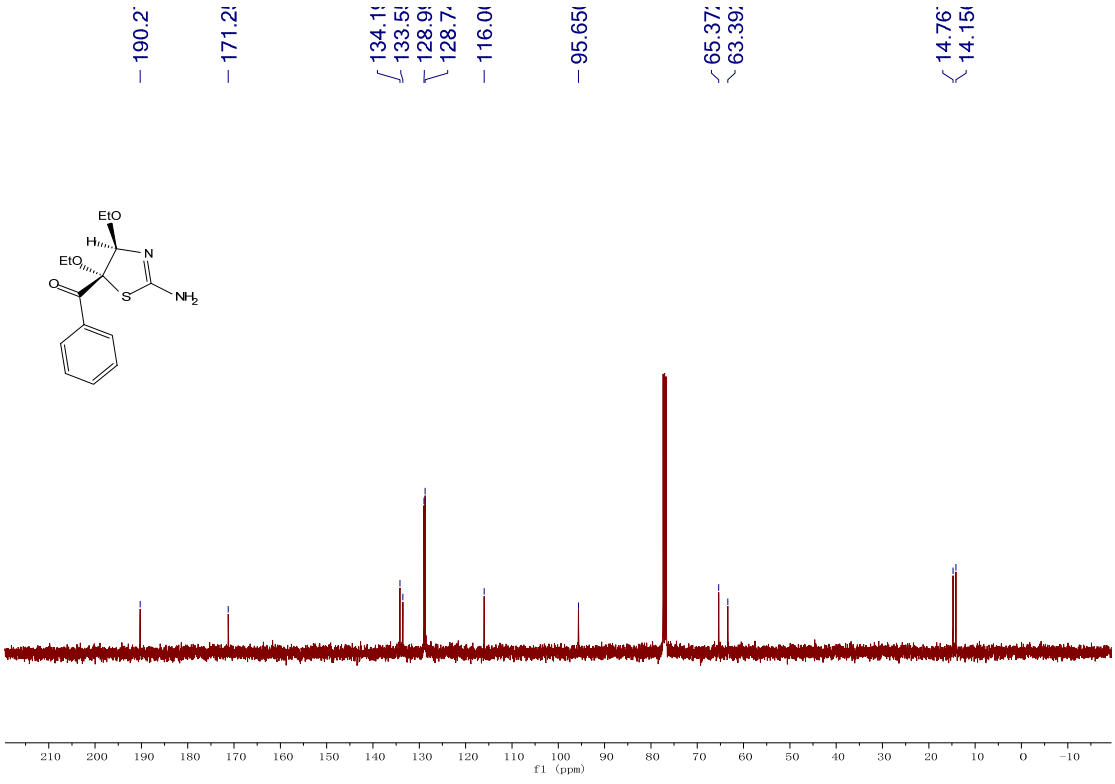
^{1}H NMR spectrum of **4j** (400 MHz, DMSO-d_6)



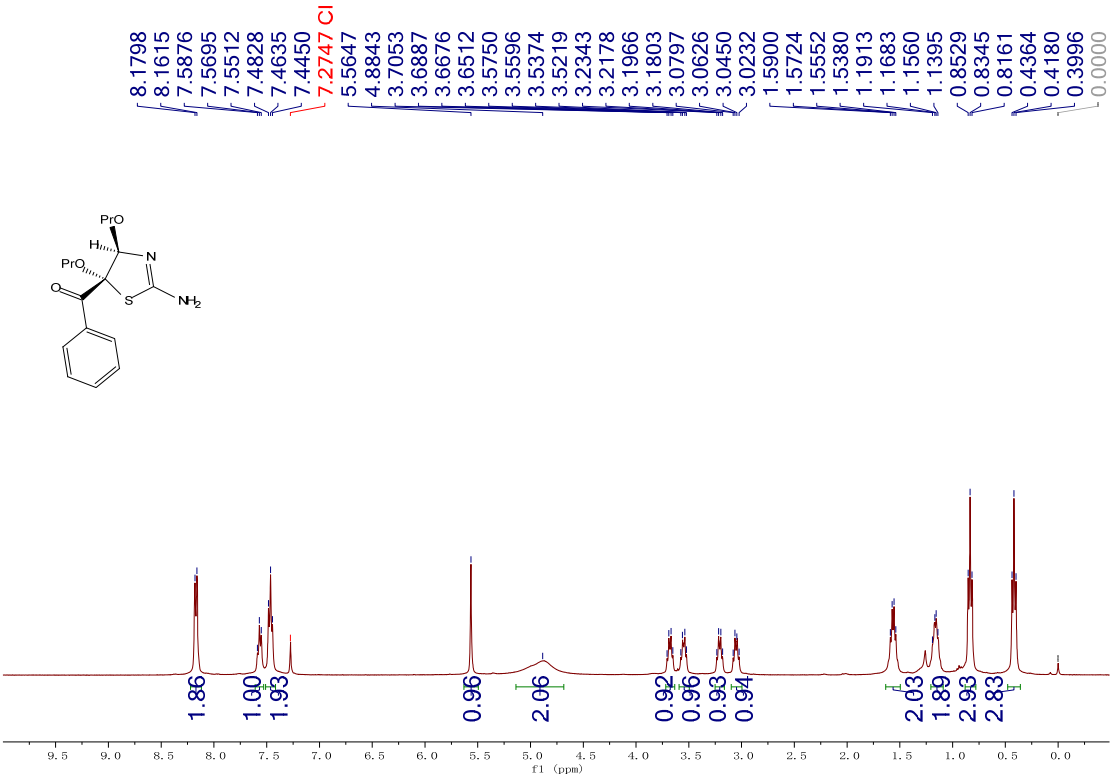
^{13}C NMR spectrum of **4j** (100 MHz, DMSO-d_6)



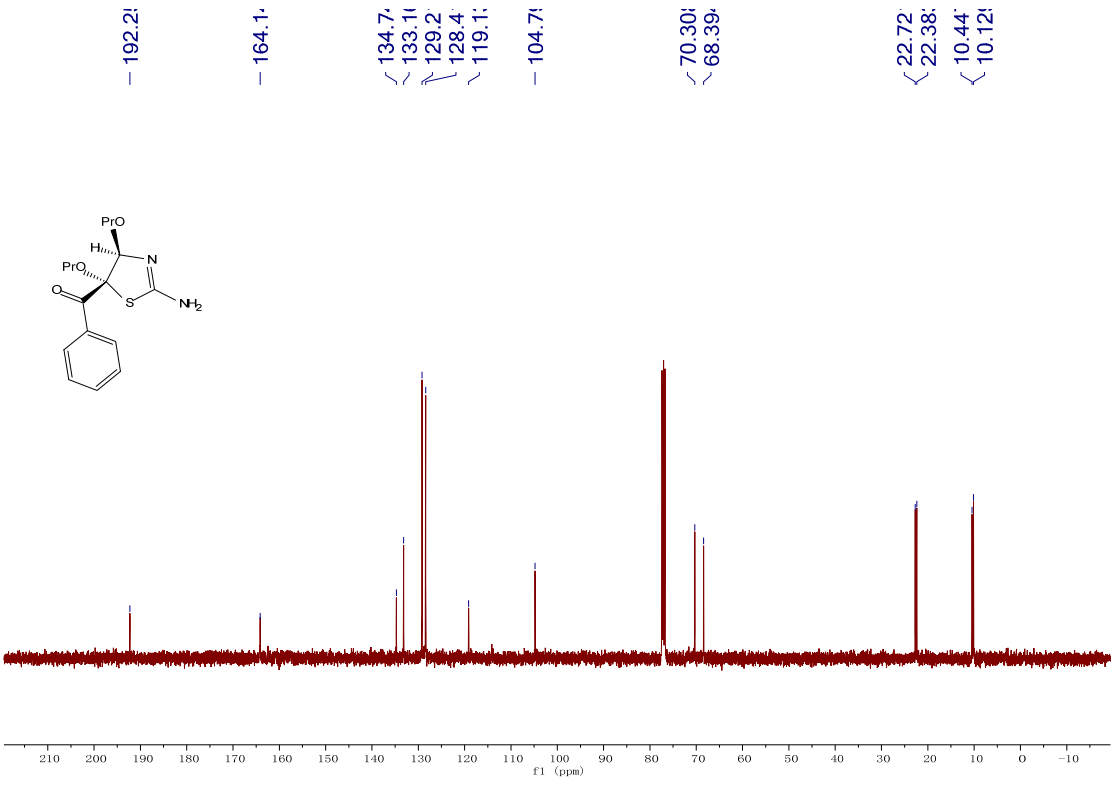
^{1}H NMR spectrum of **4k** (400 MHz, $CDCl_3$)



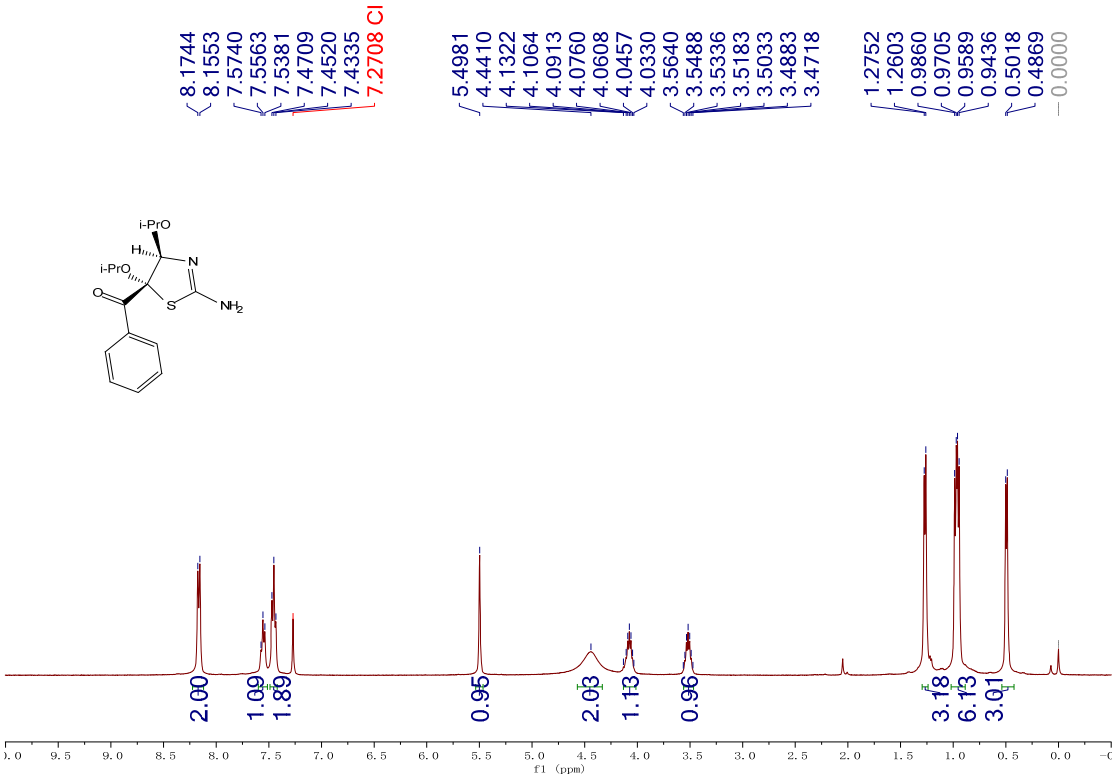
^{13}C NMR spectrum of **4k** (100 MHz, $CDCl_3$)



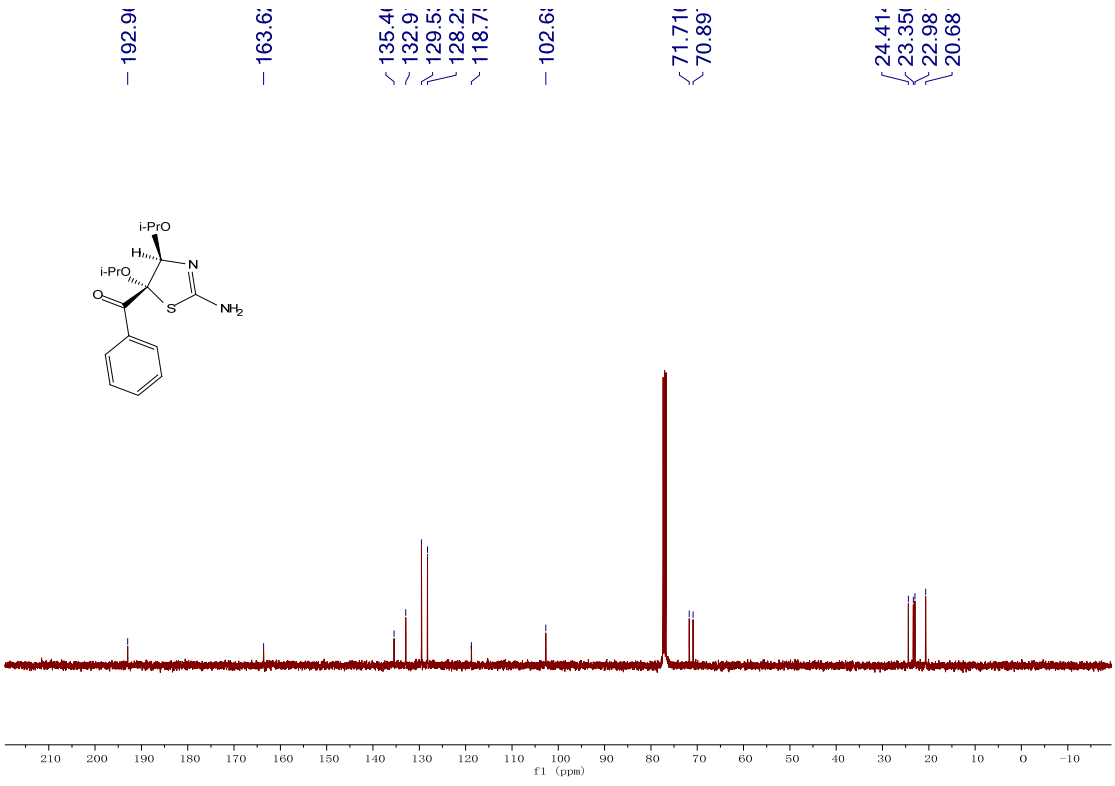
^{1}H NMR spectrum of **4l** (400 MHz, $CDCl_3$)



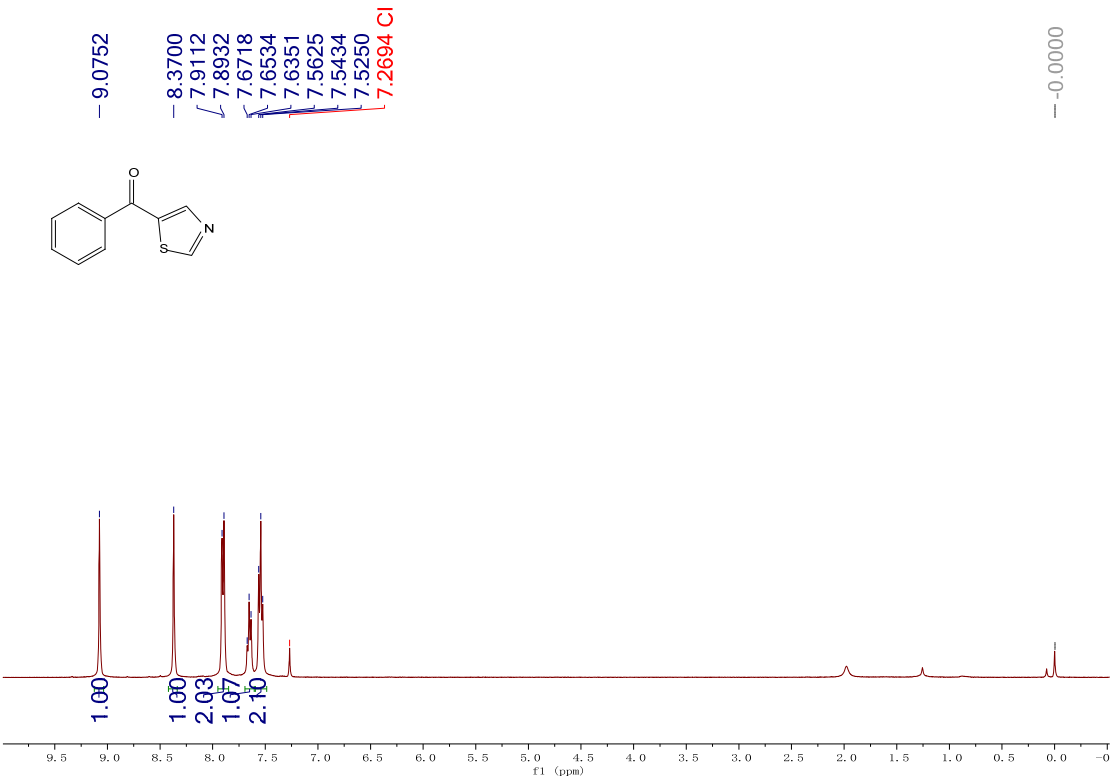
^{13}C NMR spectrum of **4l** (100 MHz, $CDCl_3$)



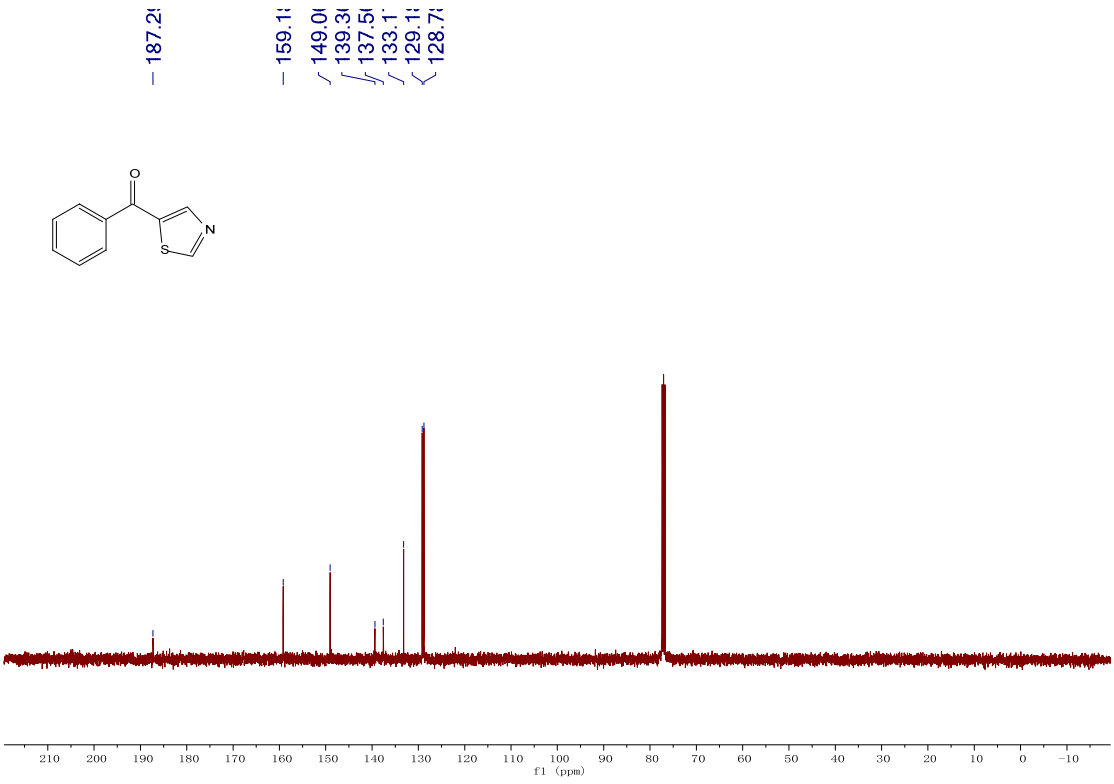
^{1}H NMR spectrum of **4m** (400 MHz, $CDCl_3$)



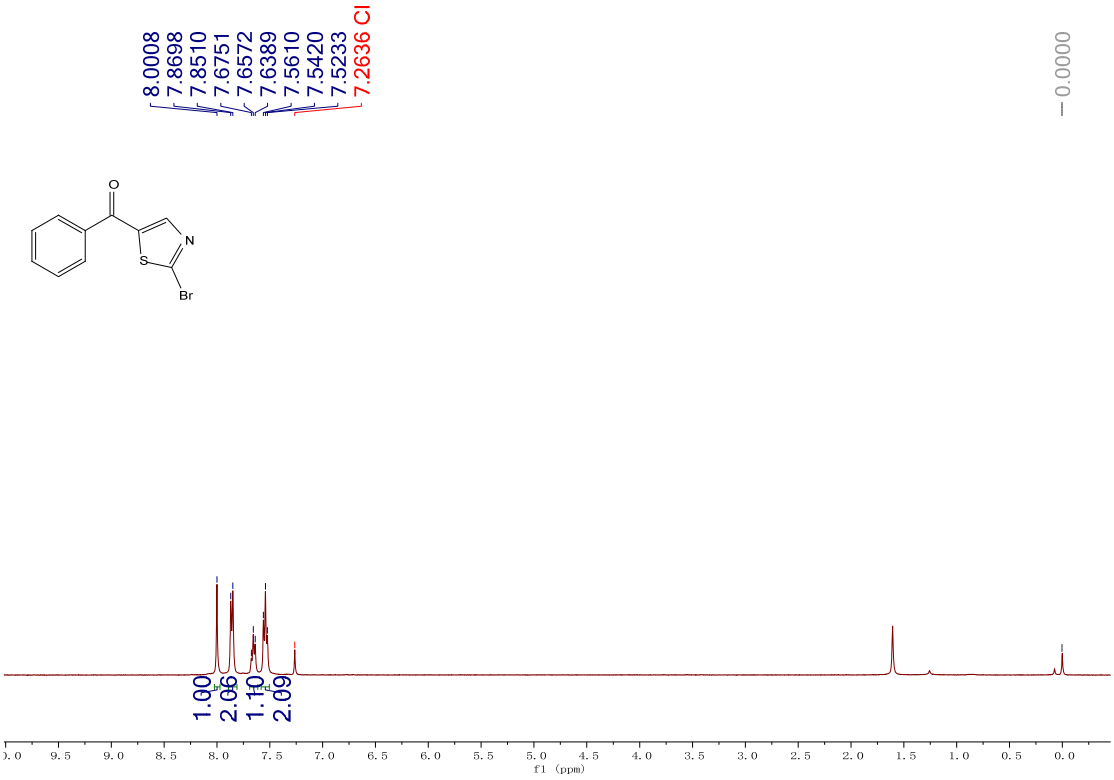
^{13}C NMR spectrum of **4m** (100 MHz, $CDCl_3$)



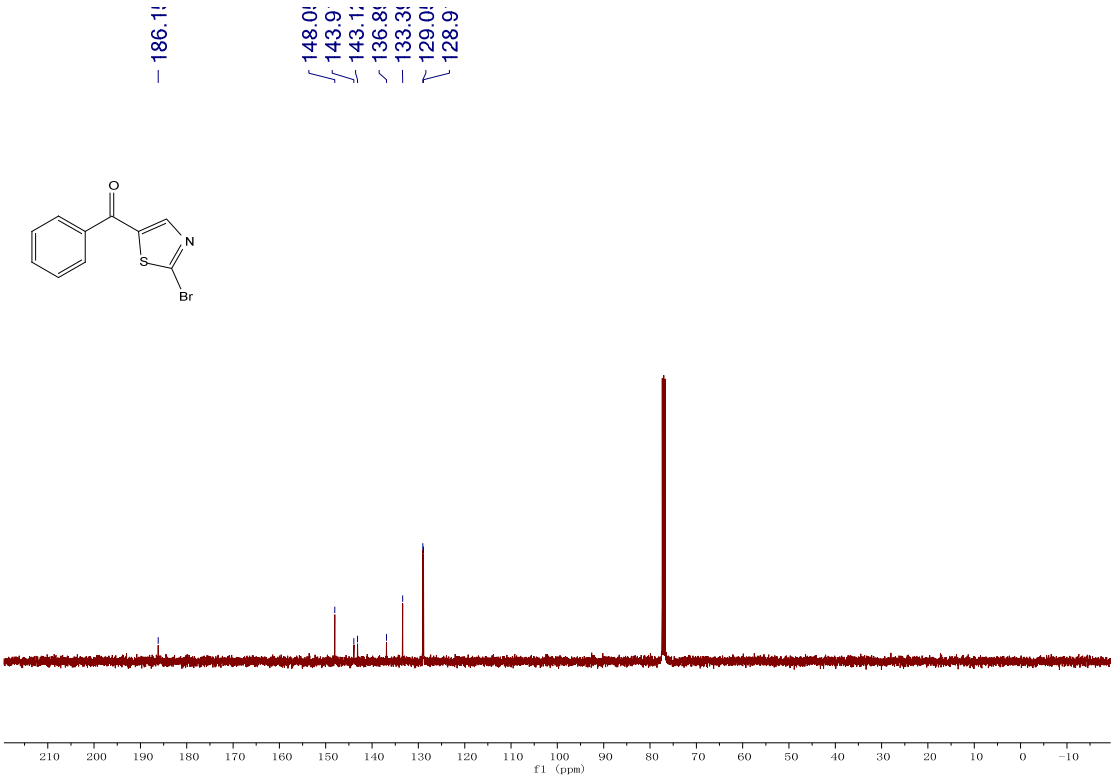
^{1}H NMR spectrum of **5** (400 MHz, $CDCl_3$)



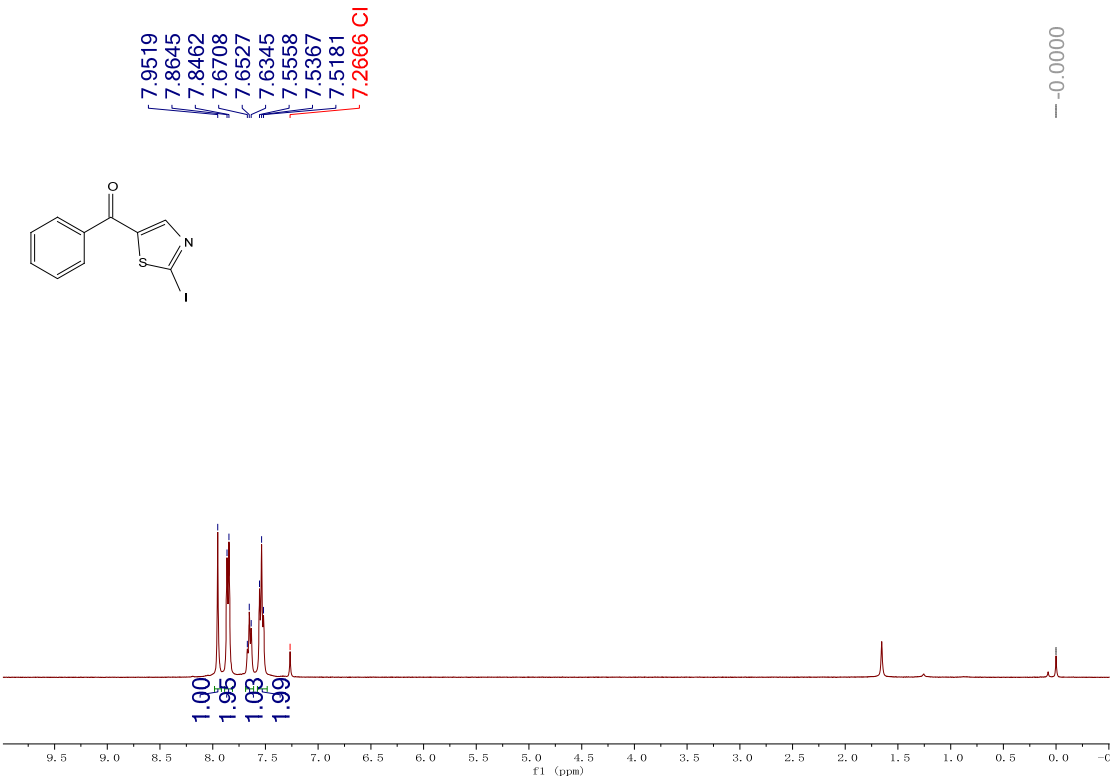
^{13}C NMR spectrum of **5** (100 MHz, $CDCl_3$)



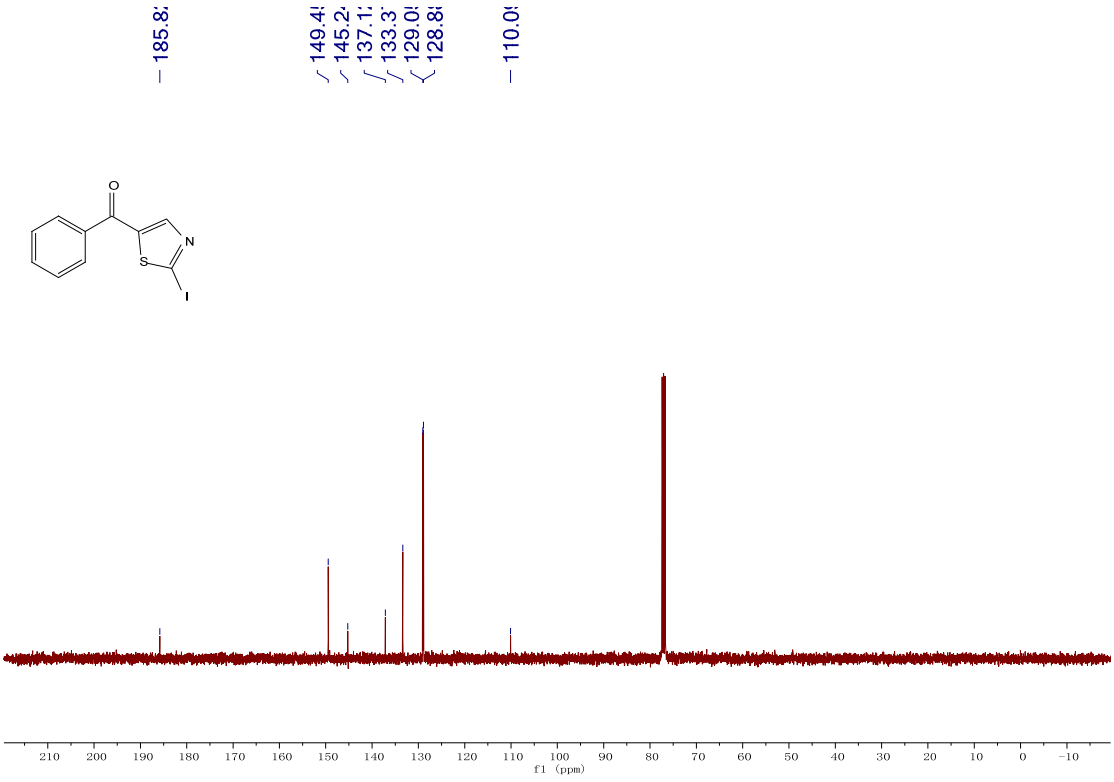
^{1}H NMR spectrum of **6** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **6** (100 MHz, $CDCl_3$)



^{1}H NMR spectrum of **7** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **7** (100 MHz, $CDCl_3$)

Crystallographic information

Procedure for the crystal preparation

Pure sample **4d** (30 mg) was solved in trichloromethane (3 mL) in a 15 mL test tube. methanol (0.5mL) and petroleum ether (0.5 mL) were then added. The tube was then sealed with plastic membrane. Some holes were pricked in the membrane with needle. The tube was then located at quiet atmosphere. The slow evaporation of the solvent led to the successful preparation of single crystal.

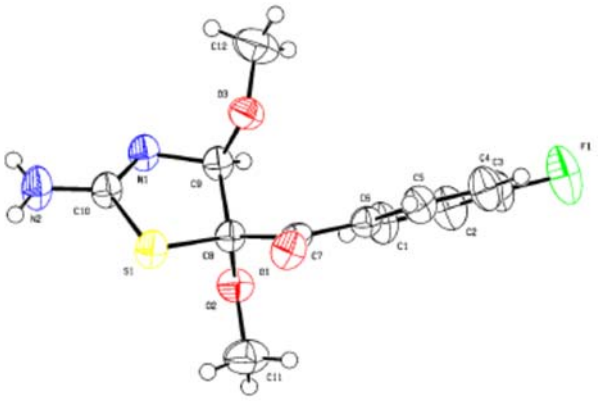


Figure S1 The X-ray crystal structure of **4d**