A photo-induced three-component reaction of N-aryl piperidines, sulfur dioxide, and cycloketone oxime esters

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Supporting Information

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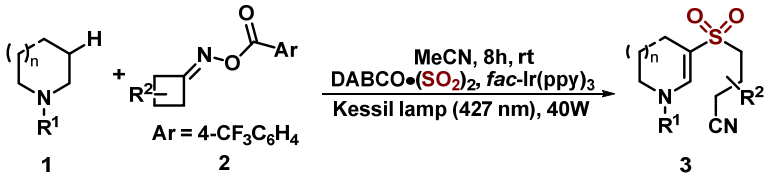
1. General Information

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32-63 μm, standard grade). Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr at 25-35 °C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. ^{1}H, and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values were quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF II Instrument.

2. General procedure for the synthesis of desired products 3



To a reaction tube equipped with a magnetic stir bar, *N*-aryl amines **1** (0.2 mmol), DABCO•$(SO_2)_2$ (0.3 mmol), cycloketone oxime esters **2** (0.5 mmol) *fac*-Ir$(ppy)_3$ (3 mmol%), and MeCN (2.0 mL) were added under N_2 atmosphere. The reaction mixture was stirred at room temperature under irradiation with a Kessil lamp (427 nm) for 8h. After completion of the reaction as monitored by TLC analysis, the mixture was evaporated, and the residue was washed with saturated $NaHCO_3$ aqueous solution (2.0 mL). The aqueous phase was extracted with EtOAc (2.0mL X 3). The combined organic phase was evaporated, and the residue was purified directly by flash column chromatography (PE/EtOAc (v/v): 2/1) to provide the corresponding product **3**.

3. Devices for the photocatalytic reactions

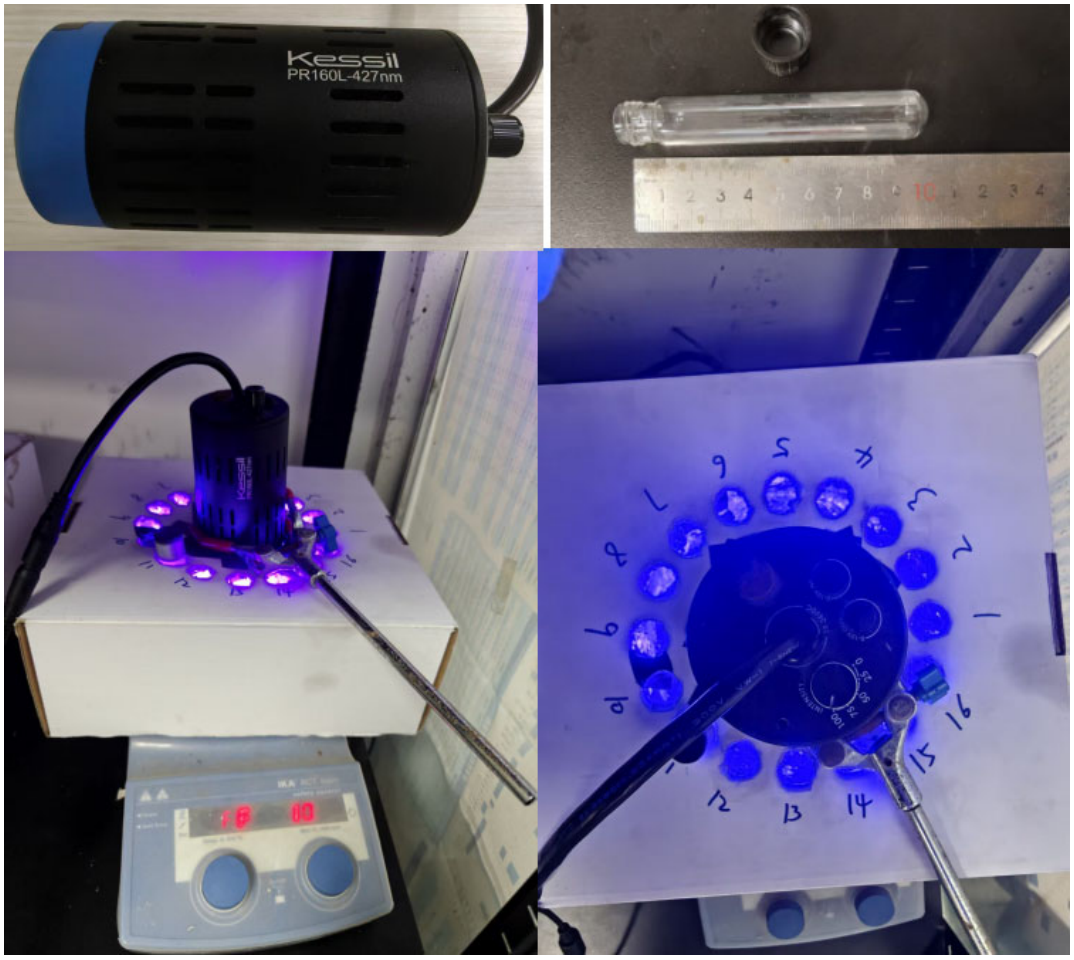


Figure S1. Devices for the photocatalytic reactions

Irradiation of visible light was performed with a 40 W 427 nm lamp. All photocatalyzed reactions were carried out at room temperature. The distance between tube and lamp was approximately 5 cm, and the light intensity value was 100.

Manufacture of the light source: LED lamp

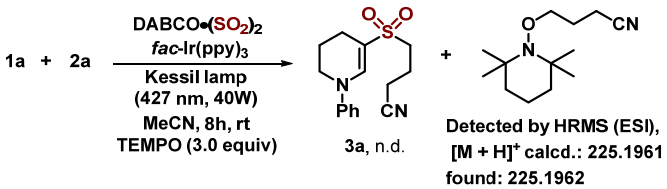
Manufacturer: Kessil

Model: PR160L-427 nm

Material of the irradiation vessel: borosilicate glass

4. Mechanistic Studies

4.1 Radical trapped experiment using TEMPO as radical scavenger



To a reaction tube equipped with a magnetic stir bar, *N*-aryl piparidine **1a** (0.2 mmol), DABCO•$(SO_2)_2$ (0.3 mmol), cycloketone oxime ester **2a** (0.5 mmol), *fac*-Ir$(ppy)_3$ (3 mmol%), TEMPO (0.6 mmol, 3.0 equiv), and MeCN (2.0 mL) were added under N_2 atmosphere. The reaction mixture was stirred at room temperature under irradiation with a Kessil lamp (427 nm) for 8h. Target product **3a** was not detected. In addition, the corresponding TEMPO adducts were detected in the reaction mixture by high resolution mass spectrum (HRMS).

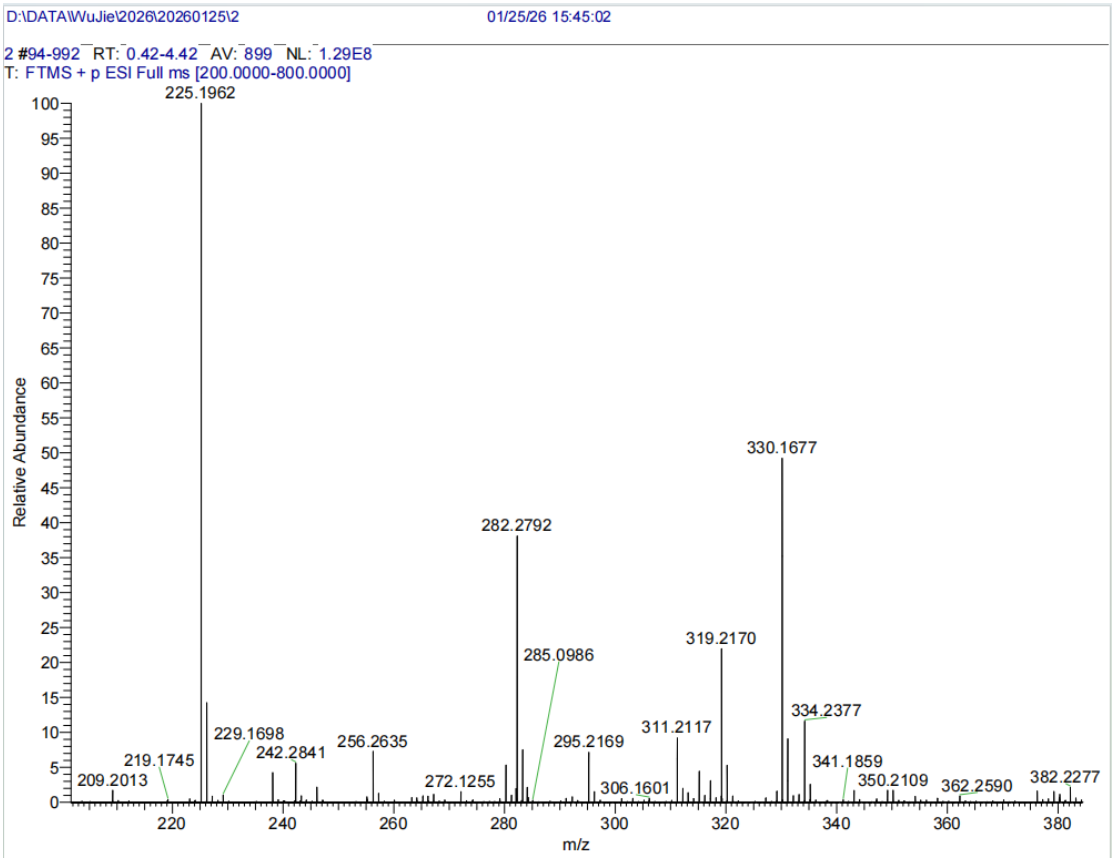
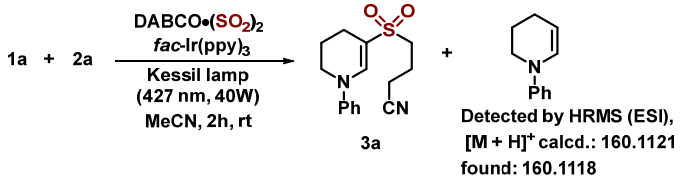


Figure S2. The HRMS of TEMPO adduct carbon radical.

4.2 Enamine intermediate detected by HRMS under standard conditions



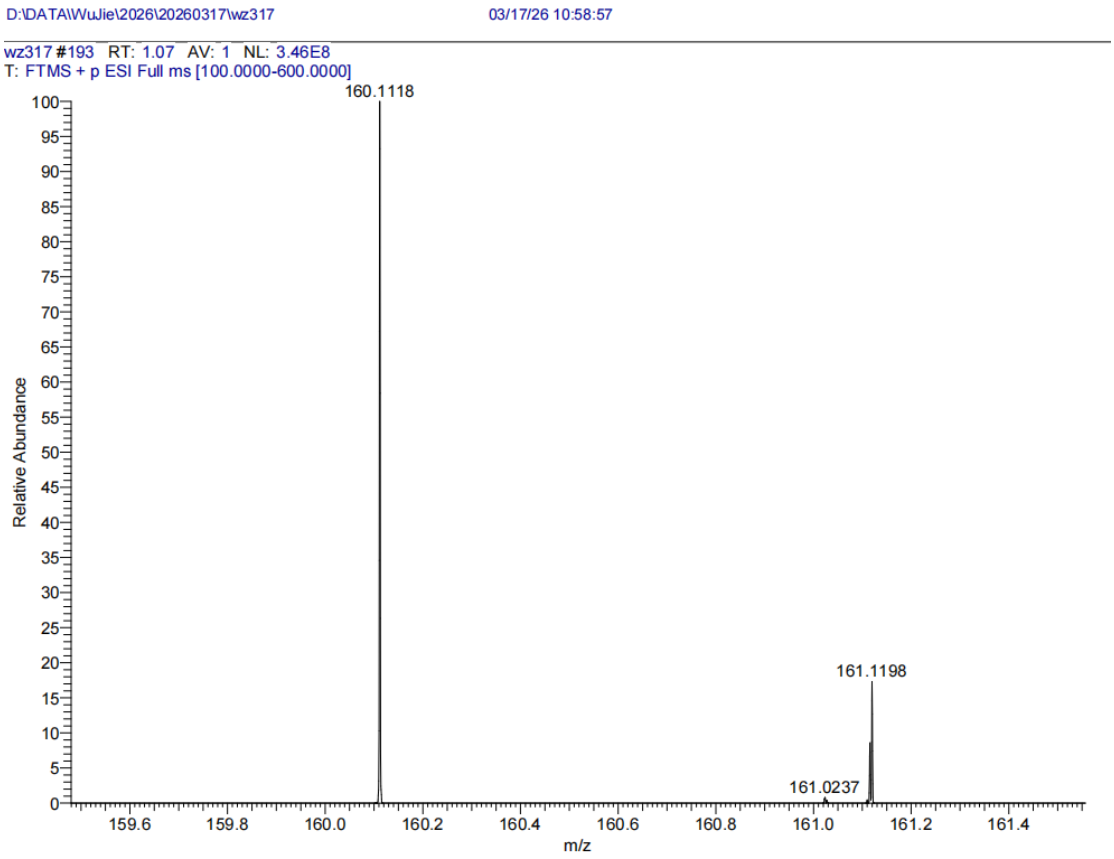


Figure S3. The intermediate enamine was detected by HRMS

4.3 Light on/off experiments.

To a reaction tube equipped with a magnetic stir bar, *N*-aryl piparidine **1a** (0.2 mmol), DABCO•$(SO_2)_2$ (0.3 mmol), cycloketone oxime ester **2a** (0.5 mmol), *fac*-Ir$(ppy)_3$ (3 mmol%), 1,3,5-Trimethoxybenzene (0.2 mmol) and MeCN (2.0 mL) were added under N_2 atmosphere.The reaction mixture was placed 5 cm away from a 40 W Kessil lamp (427 nm) and irradiated at room temperature for 12 hours under nitrogen atmosphere with the light turned on and off at intervals and the yields of product **3a** were determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as the internal standard (Figure S4).

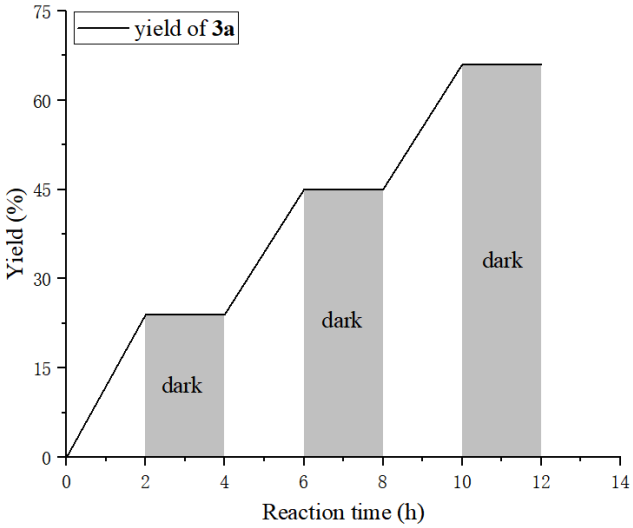


Figure S4. Light on/off experiments.

4.4 EPR experiments.

1) Procedure for EPR investigation of cycloketone oxime ester **2a**, *fac*-Ir(ppy)$_3$ and DABCO•$(SO_2)_2$ in MeCN.

To a reaction tube equipped with a magnetic stir bar, DABCO•$(SO_2)_2$ (0.3 mmol), cycloketone oxime ester **2a** (0.5 mmol), *fac*-Ir(ppy)$_3$ (3 mmol%), DMPO (5,5-dimethyl-1-pyrroline N-oxide) (0.1 mmol) and MeCN (2.0 mL) were added under N_2 atmosphere.The reaction mixture was stirred and irradiated with a 40 W Kessil lamp (427 nm) for 15 min. Subsequently, the solution sample was taken out into a small tube, and then analyzed by EPR. As shown in Figure S5, a distinct signal of a trapped radical was observed.

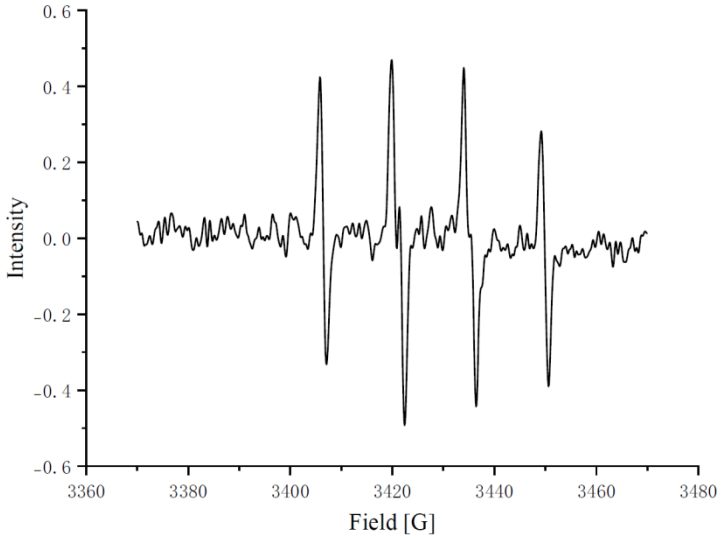


Figure S5. EPR investigation.

2) Procedure for EPR investigation of *N*-aryl piparidine **1a** (0.2 mmol), cycloketone oxime ester **2a**, *fac*-Ir(ppy)$_3$ and DABCO•(SO$_2$)$_2$ in MeCN.

To a reaction tube equipped with a magnetic stir bar, *N*-aryl piparidine **1a** (0.2 mmol), DABCO•(SO$_2$)$_2$ (0.3 mmol), cycloketone oxime ester **2a** (0.5 mmol), *fac*-Ir(ppy)$_3$ (3 mmol%), DMPO (5,5-dimethyl-1-pyrroline N-oxide) (0.1 mmol) and MeCN (2.0 mL) were added under N_2 atmosphere.The reaction mixture was stirred and irradiated with a 40 W Kessil lamp (427 nm) for 15 min. Subsequently, the solution sample was taken out into a small tube, and then analyzed by EPR. As shown in Figure S6, a distinct signal of a trapped radical was observed.

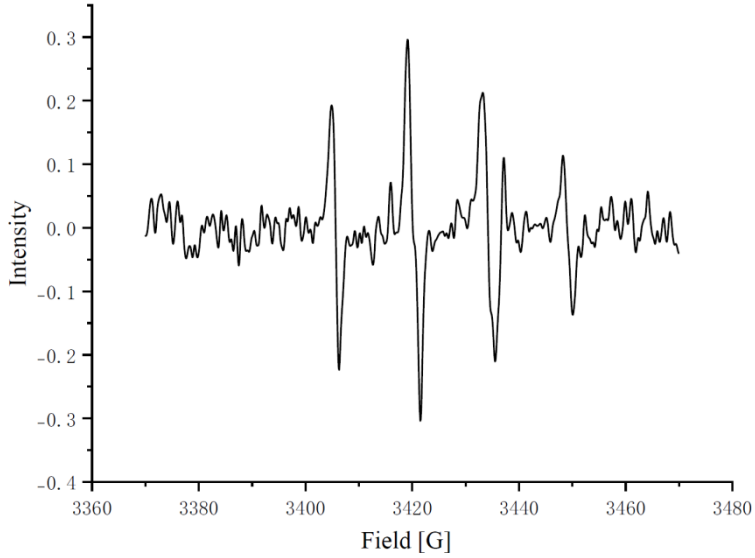
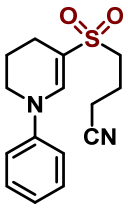


Figure S6. EPR investigation.

5. Characterization Data for Products

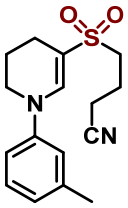


4-((1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3a)

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.65 (s, 1H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.12 - 7.06 (m, 3H), 3.65 - 3.62 (m, 2H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 2.44 (t, *J* = 6.2 Hz, 2H), 2.17 - 2.04 (m, 4H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 145.2, 141.0, 129.6, 123.8, 118.8, 118., 104.6, 51.4, 46.0, 21.0, 20.4, 19.5, 16.2.

HRMS (ESI) for $C_{15}H_{19}N_2O_2S$ $[M + H]^+$ calcd. 291.1162, found 291.1161.

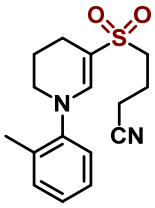


4-((1-(m-tolyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile(3b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 6.94 - 6.86 (m, 3H), 3.65 - 3.63 (m, 2H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.62 (t, *J* = 7.0 Hz, 2H), 2.46 (t, *J* = 6.2 Hz, 2H), 2.36 (s, 3H), 2.20 - 2.14 (m, 2H), 2.13 - 2.04 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 141.3, 139.6, 129.4, 124.7, 118.8, 118.6, 115.2, 104.3, 51.5, 46.1, 21.6, 21.1, 20.5, 19.5, 16.3.

HRMS (ESI) for $C_{16}H_{21}N_2O_2S$ $[M + H]^+$ calcd. 305.1318, found 305.1317.

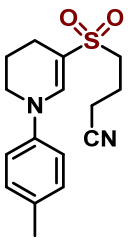


4-((1-(o-tolyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile(3c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 - 7.17 (m, 4H), 7.07 - 7,05 (m, Hz, 1H), 3.49 - 3.45 (m, 2H), 3.09 (t, *J* = 7.2 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.47 (t, *J* = 6.2 Hz, 2H), 2.28 (s, 3H), 2.17 - 2.05 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 144.7, 133.5, 131.6, 127.2, 127.2, 125.8, 118.7, 101.1, 51.5, 48.4, 21.3, 20.3, 19.6, 18.2, 16.3.

HRMS (ESI) for $C_{15}H_{21}N_2O_2S$ $[M + H]^+$ calcd. 305.1318, found 305.1316.

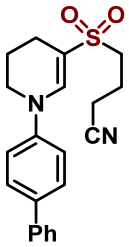


4-((1-(p-tolyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.98 - 6.96 (m, 2H), 3.64 - 3.61 (m, 2H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.45 (t, *J* = 6.2 Hz, 2H), 2.32 (s, 3H), 2.17 - 2.05 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 141.4, 133.7, 130.1, 118.7, 118.2, 103.7, 51.5, 46.3, 21.1, 20.7, 20.4, 19.5, 16.3.

HRMS (ESI) for $C_{16}H_{21}N_2O_2S$ $[M + H]^+$ calcd.305.1318, found 305.1317.

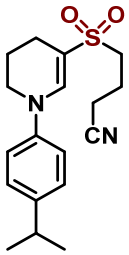


4-((1-([1,1'-biphenyl]-4-yl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3e)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.62 - 7.52 (m, 4H), 7.44 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.37 - 7.31 (m, 1H), 7.18 - 7.12 (m, 2H), 3.68 (t, *J* = 5.6 Hz, 2H), 3.12 (t, *J* = 7.3 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 2.48 (t, *J* = 6.2 Hz, 2H), 2.20 - 2.08 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.3, 140.8, 140.0, 136.7, 128.9, 128.1, 127.3, 126.8, 118.6, 118.2, 105.1, 51.5, 46.1, 21.1, 20.4, 19.5, 16.3.

HRMS (ESI) for $C_{21}H_{23}N_2O_2S$ $[M + H]^+$ calcd.367.1475, found 367.1476.

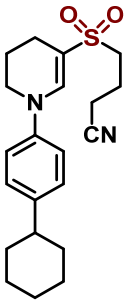


4-((1-(4-isopropylphenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.23 - 7.20 (m, 2H), 7.03 - 6.99 (m, 2H), 3.65 - 3.62 (m, 2H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.90 (t, *J* = 6.9 Hz, 1H), 2.62 (t, *J* = 7.0 Hz, 2H), 2.45 (t, *J* = 6.2 Hz, 2H), 2.19 - 2.06 (m, 4H), 1.25 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$ δ 144.8, 143.2, 141.4, 127.5, 118.6, 118.2, 103.8, 51.5, 46.2, 33.5, 24.0, 21.1, 20.4, 19.5, 16.3.

HRMS (ESI) for $C_{18}H_{25}N_2O_2S$ $[M + H]^+$ calcd.333.1631, found 333.1635.

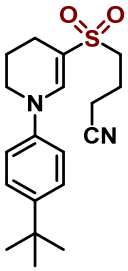


4-((1-(4-cyclohexylphenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3g)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.20 - 7.18 (m, 2H), 7.01 - 6.99 (m, 2H), 3.63 (t, *J* = 5.5 Hz, 2H), 3.09 (t, *J* = 7.3 Hz, 2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.48 - 2.43 (m, 6.2 Hz, 3H), 2.18 - 2.03 (m, 4H), 1.89 - 1.79 (m, 4H), 1.78 - 1.71 (m, 1H), 1.47 - 1.28 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 143.1, 141.4, 127.8, 118.7, 118.2, 103.7, 51.5, 46.2, 43.8, 34.5, 26.8, 26.1, 21.1, 20.4, 19.5, 16.3.

HRMS (ESI) for $C_{21}H_{29}N_2O_2S$ $[M + H]^+$ calcd.373.1944, found 373.1947.

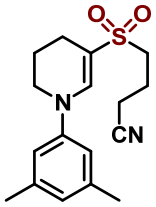


4-((1-(4-(tert-butyl)phenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3h)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.39 - 7.35 (m, 2H), 7.03 - 7.00 (m, 2H), 3.65 - 3.62 (m, 2H), 3.09 (dd, *J* = 7.8, 6.7 Hz, 2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.45 (t, *J* = 6.2 Hz, 2H), 2.18 - 2.04 (m, 4H), 1.31 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 142.8, 141.3, 126.4, 118.7, 117.8, 103.9, 51.5, 46.1, 34.3, 31.4, 21.1, 20.4, 19.5, 16.3.

HRMS (ESI) for $C_{19}H_{27}N_2O_2S$ $[M + H]^+$ calcd.347.1788, found 347.1788.

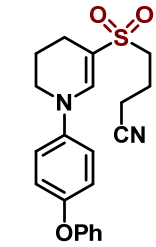


4-((1-(3,5-dimethylphenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3i)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 6.75 (s, 1H), 6.69 (s, 2H), 3.64 - 3.61 (m, 2H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.44 (t, *J* = 6.2 Hz, 2H), 2.31 (s, 6H), 2.15 (t, *J* = 7.2 Hz, 2H), 2.08 - 2.03 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 141.3, 139.3, 125.7, 118.7, 116.0, 103.9, 51.5, 46.2, 21.4, 21.1, 20.5, 19.5, 16.3.

HRMS (ESI) for $C_{17}H_{23}N_2O_2S$ $[M + H]^+$ calcd.319.1475, found 319.1478.

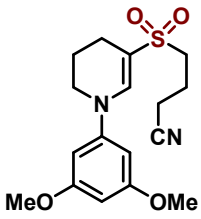


4-((1-(4-phenoxyphenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3j)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.36 - 7.32 (m, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.06 - 6.97 (m, 6H), 3.63 (t, *J* = 5.5 Hz, 2H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.62 (t, *J* = 7.0 Hz, 2H), 2.46 (t, *J* = 6.2 Hz, 2H), 2.20 - 2.06 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 153.6, 141.4, 141.1, 129.8, 123.3, 120.1, 119.9, 118.6, 118.5, 104.2, 51.5, 46.6, 21.1, 20.4, 19.5, 16.3.

HRMS (ESI) for $C_{21}H_{23}N_2O_3S$ $[M + H]^+$ calcd.383.1424, found 383.1472.

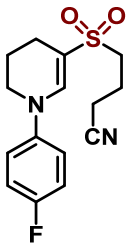


4-((1-(3,5-dimethoxyphenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3k)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 6.23 - 6.20 (m, 3H), 3.80 (s, 6H), 3.61 (dd, *J* = 6.9, 4.2 Hz, 2H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.62 (t, *J* = 7.0 Hz, 2H), 2.45 (t, *J* = 6.2 Hz, 2H), 2.20 - 2.05 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 147.1, 141.0, 118.6, 105.0, 97.0, 95.5, 55.5, 51.4, 46.12, 21.1, 20.5, 19.4, 16.3.

HRMS (ESI) for $C_{17}H_{23}N_2O_4S$ $[M + H]^+$ calcd.351.1373, found 351.1374.

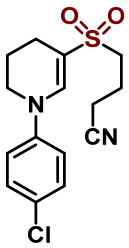


4-((1-(4-fluorophenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3l)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.08 - 7.01 (m, 4H), 3.63 - 3.60 (m, 2H), 3.10 (t, *J* = 7.3 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.45 (t, *J* = 6.2 Hz, 2H), 2.19 - 2.06 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (d, *J* = 241.0 Hz), 141.7 (d, *J* = 3.0 Hz), 141.3, 120.0 (d, *J* = 8.0 Hz), 118.7, 116.3 (d, *J* = 22.0 Hz), 104.6, 51.4, 46.6, 21.0, 20.3, 19.4, 16.3.

HRMS (ESI) for $C_{15}H_{18}O_4FS$ $[M + H]^+$ calcd. 309.1068, found 309.1066.

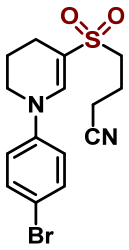


4-((1-(4-chlorophenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3m)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.33 - 7.30 (m, 2H), 7.02 - 6.98 (m, 2H), 3.63 - 3.60 (m, 2H), 3.11 (t, *J* = 7.3 Hz, 2H), 2.62 (t, *J* = 7.0 Hz, 2H), 2.46 (t, *J* = 6.2 Hz, 2H), 2.20 - 2.07 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 140.6, 129.6, 129.1, 119.2, 118.6, 105.8, 51.4, 46.1, 21.0, 20.3, 19.4, 16.3.

HRMS (ESI) for $C_{15}H_{18}N_2O_2ClS$ $[M + H]^+$ calcd.325.0772, found 325.0771.

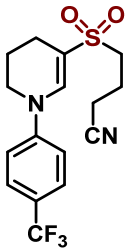


4-((1-(4-bromophenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3n)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.47 - 7.44 (m, 2H), 6.96 - 6.93 (m, 2H), 3.61 (t, *J* = 5.6 Hz, 2H), 3.11 (t, *J* = 7.2 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 2.46 (t, *J* = 6.3 Hz, 2H), 2.20 - 2.07 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 140.4, 132.5, 119.5, 118.5, 116.6, 106.0, 51.4, 46.1, 21.0, 20.4, 19.4, 16.3.

HRMS (ESI) for $C_{15}H_{18}N_2O_2BrS$ $[M + H]^+$ calcd.369.0267, found 369.0270.

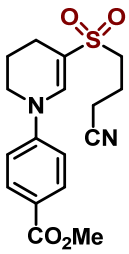


4-((1-(4-(trifluoromethyl)phenyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3o)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 3.69 - 3.66 (m, 2H), 3.12 (t, *J* = 7.3 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 2.49 (t, *J* = 6.2 Hz, 2H), 2.21 - 2.10 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 139.8, 126.9 (q, *J* = 3.8 Hz), 125.37 (q, *J* = 33.0 Hz), 124.1(q, *J* =269.0 Hz),118.5, 117.2, 107.8, 51.4, 45.8, 21.1, 20.4, 19.3, 16.3.

HRMS (ESI) for $C_{16}H_{18}N_2O_2F_3S$ $[M + H]^+$ calcd.359.1036, found 359.1035.

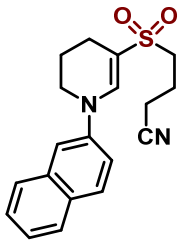


methyl 4-(5-((3-cyanopropyl)sulfonyl)-3,4-dihydropyridin-1(2H)-yl)benzoate (3p)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 - 8.01 (m, 2H), 7.73 (s, 1H), 7.12 - 7.08 (m, 2H), 3.90 (s, 3H), 3.68 (t, *J* = 5.6 Hz, 2H), 3.13 (dd, *J* = 8.0, 6.6 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 2.48 (t, *J* = 6.2 Hz, 2H), 2.20 - 2.09 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 148.3, 139.6, 131.3, 124.8, 118.6, 116.5, 107.9, 52.1, 51.4, 45.6, 21.0, 20.4, 19.3, 16.3.

HRMS (ESI) for $C_{17}H_{21}N_2O_4S$ $[M + H]^+$ calcd.349.1217, found 349.1218.

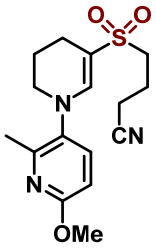


4-((1-(naphthalen-2-yl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile(3q)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 - 7.75 (m, 4H), 7.50 - 7.42 (m, 1H), 7.40 - 7.27 (m, 2H), 7.25 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.74 - 3.72 (m, 2H), 3.11 (dd, *J* = 8.0, 6.6 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 2.48 (t, *J* = 6.2 Hz, 2H), 2.20 - 2.08 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 141.1, 133.8, 130.2, 129.6, 127.7, 127.3, 127.1, 125.2, 118.7, 118.1, 114.5, 105.2, 51.5, 46.3, 21.1, 20.5, 19.5, 16.3.

HRMS (ESI) for $C_{19}H_{21}N_2O_2S$ $[M + H]^+$ calcd.341.1318, found 341.1317.

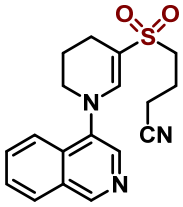


4-((6'-methoxy-2'-methyl-3,4-dihydro-2H-[1,3'-bipyridin]-5-yl)sulfonyl)butanenitrile (3r)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.6 Hz, 1H), 7.15 (s, 1H), 6.58 (d, *J* = 8.5 Hz, 1H), 3.92 (s, 3H), 3.42 m 3.39 (m, 2H), 3.09 (t, *J* = 7.3 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 2.46 (t, *J* = 6.2 Hz, 2H), 2.38 (s, 3H), 2.19 - 2.06 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 152.4, 144.6, 136.9, 134.6, 118.7, 108.7, 101.6, 53.7, 51.5, 48.6, 21.3, 20.7, 20.2, 19.5, 16.3.

HRMS (ESI) for $C_{16}H_{22}N_3O_3S$ $[M + H]^+$ calcd.336.1376, found 336.1372.

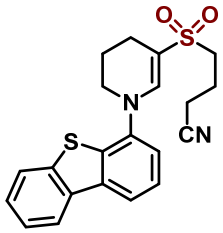


4-((1-(isoquinolin-4-yl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.37 (s, 1H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.90 - 7.78 (m, 2H), 7.72 - 7.68 (m, 1H), 7.46 (s, 1H), 3.71 (dd, *J* = 6.5, 4.4 Hz, 2H), 3.15 (t, *J* = 7.3 Hz, 2H), 2.65 (t, *J* = 7.0 Hz, 2H), 2.59 (t, *J* = 6.2 Hz, 2H), 2.25 - 2.16 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 144.4, 139.3, 137.7, 131.8, 131.5, 129.4, 128.4, 128.1, 121.5, 118.6, 104.3, 51.5, 49.5, 21.4, 20.5, 19.4, 16.3.

HRMS (ESI) for $C_{18}H_{20}N_3O_2S$ $[M + H]^+$ calcd.342.1271, found 342.1270.

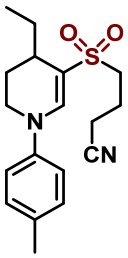


4-((1-(dibenzo[b,d]thiophen-4-yl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3t)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 - 8.12 (m, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.90 - 7.85 (m, 1H), 7.64 (s, 1H), 7.50 - 7,45 (m, 3H), 7.18 (d, *J* = 7.6 Hz, 1H), 3.75 (t, *J* = 5.4 Hz, 2H), 3.14 (t, *J* = 7.2 Hz, 2H), 2.65 (t, *J* = 7.1 Hz, 2H), 2.54 (t, *J* = 6.2 Hz, 2H), 2.25 - 2.14 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 140.9, 138.8, 137.8, 135.5, 133.8, 128.0, 127.5, 125.7, 124.9, 122.9, 122.0, 121.2, 119.4, 118.7, 104.0, 51.4, 47.3, 21.5, 20.6, 19.7, 16.3.

HRMS (ESI) for $C_{21}H_{21}N_2O_2S_2$ $[M + H]^+$ calcd.397.1039, found 397.1039.

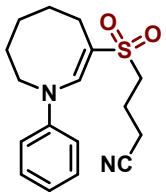


4-((4-ethyl-1-(p-tolyl)-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)butanenitrile (3u)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 3.67 - 3.46 (m, 2H), 3.11 (t, *J* = 7.3 Hz, 2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.51 (dd, *J* = 9.0, 5.3 Hz, 1H), 2.32 (s, 3H), 2.19 - 2.10 (m, 3H), 2.04 - 1.94 (m, 1H), 1.84 - 1.75 (m, 1H), 1.37 - 1.24 (m, 1H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 141.5, 133.8, 130.1, 118.7, 118.2, 108.2, 53.5, 42.3, 32.3, 27.5, 23.6, 20.7, 19.6, 16.3, 11.3.

HRMS (ESI) for $C_{18}H_{25}N_2O_2S$ $[M + H]^+$ calcd.333.1631, found 333.1628.

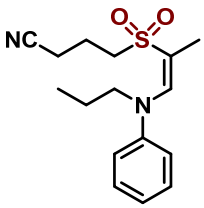


(E)-4-((1-phenyl-1,4,5,6,7,8-hexahydroazocin-3-yl)sulfonyl)butanenitrile (3v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.35 (dd, *J* = 8.9, 7.0 Hz, 2H), 7.17 - 7.13 (m, 3H), 4.07 (t, *J* = 6.5 Hz, 2H), 3.07 (t, *J* = 7.3 Hz, 2H), 2.89 (t, *J* = 6.9 Hz, 2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.14 (t, *J* = 7.2 Hz, 2H), 1.98 - 1.95 (m, 4H),1.92 - 1.69 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 146.7, 129.6, 124.9, 120.9, 118.7, 105.2, 51.8, 48.9, 29.9, 29.1, 23.9, 21.2, 19.6, 16.3.

HRMS (ESI) for $C_{17}H_{23}N_2O_2S$ $[M + H]^+$ calcd.319.1475, found 319.1477.

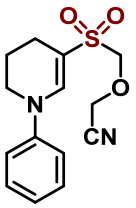


(Z)-4-((1-(propyl(p-tolyl)amino)prop-1-en-2-yl)sulfonyl)butanenitrile (3w)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (t, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 1.2 Hz, 1H), 7.26 - 7.21 (m, 1H), 7.16 - 7.11 (m, 2H), 3.58 - 3.54 (m, 2H), 3.03 (t, *J* = 7.3 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.13 (t, *J* = 7.2 Hz, 2H), 1.66 - 1.59 (m, 2H), 1.42 (s, 3H), 0.93 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 143.7, 129.2, 126.3, 125.6, 118.7, 101.4, 58.9, 50.8, 22.4, 19.5, 16.3, 11.7, 10.9.

HRMS (ESI) for $C_{16}H_{23}N_2O_2S$ $[M + H]^+$ calcd.307.1475, found 307.1472.

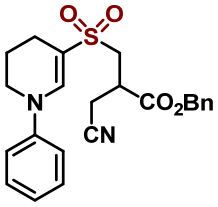


2-(((1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)methoxy)acetonitrile (3x)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.12 (dd, *J* = 18.9, 7.7 Hz, 3H), 4.69 (s, 2H), 4.50 (s, 2H), 3.67 (t, *J* = 5.6 Hz, 2H), 2.47 (t, *J* = 6.2 Hz, 2H), 2.12 - 2.06 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 143.1, 129.6, 124.3, 118.4, 115.0, 101.9, 82.4, 57.0, 46.3, 21.1, 20.5.

HRMS (ESI) for $C_{14}H_{17}N_2O_3S$ $[M + H]^+$ calcd.293,0954, found 293.0955.

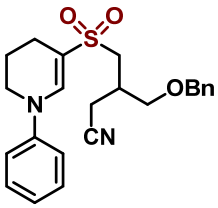


Benzyl3-cyano-2-(((1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)methyl)propanoate (3y)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.33 (d, *J* = 6.2 Hz, 7H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 5.18 (t, *J* = 12.1 Hz, 2H), 3.63 - 3.56 (m, 3H), 3.35 - 3.27 (m, 1H), 3.21 (dd, *J* = 14.1, 7.8 Hz, 1H), 3.04 - 2.92 (t, 2H), 2.43 (t, *J* = 6.6 Hz, 2H), 2.05 (dd, *J* = 6.7, 4.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 145.1, 141.6, 134.7, 129.6, 128.8, 128.7, 128.6, 124.1, 118.2, 116.9, 104.4, 68.2, 52.4, 46.1, 37.2, 21.0, 20.2, 19.4.

HRMS (ESI) for $C_{23}H_{25}N_2O_4S$ $[M + H]^+$ calcd.425.1530, found 425.1527.



4-(benzyloxy)-3-(((1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)sulfonyl)methyl)butanenitrile (3z)

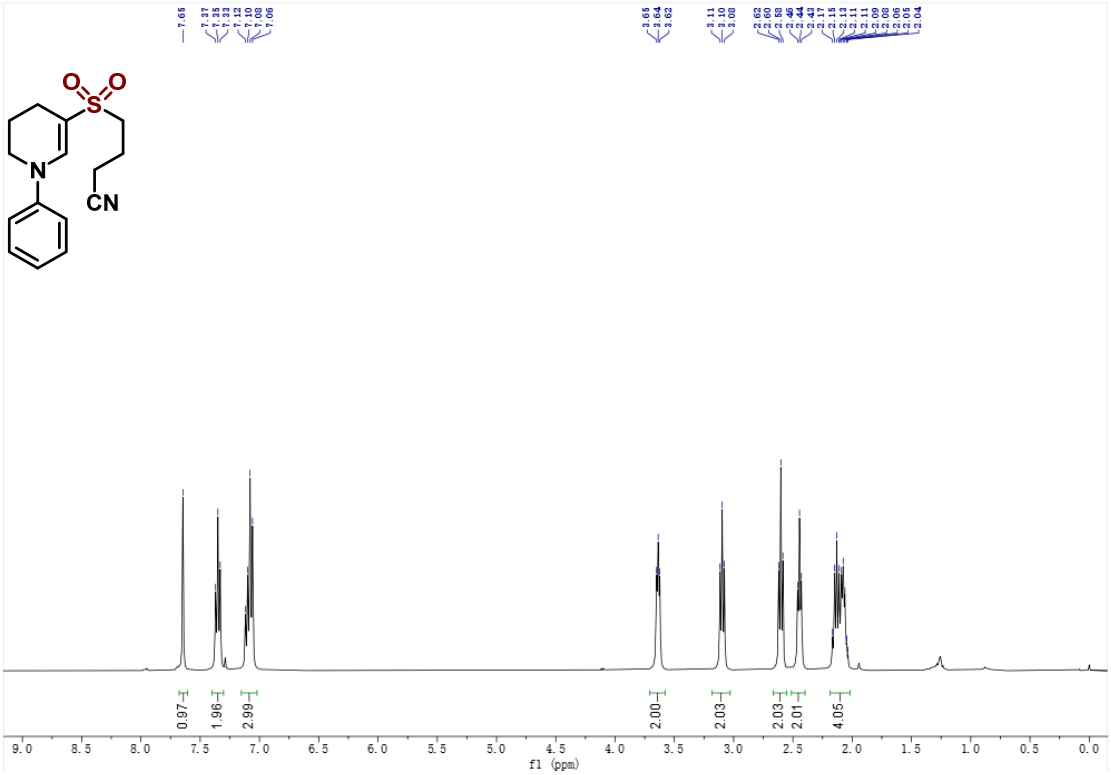
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.39 - 7.28 (m, 7H), 7.14 - 7.06 (m, 3H), 4.53 (s, 2H), 3.67 - 3.57 (m, 4H), 3.16 (dd, *J* = 14.4, 4.7 Hz, 1H), 3.01 (dd, *J* = 14.4, 7.6 Hz, 1H), 2.80 (d, *J* = 6.0 Hz, 2H), 2.64 (dd, *J* = 7.5, 5.4 Hz, 1H), 2.44 (t, *J* = 6.2 Hz, 2H), 2.11 - 2.00 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 141.0, 137.5, 129.6, 128.5, 128.0, 127.8, 123.9, 118.1, 117.9, 105.1, 73.5, 70.5, 53.2, 46.1, 31.9, 21.0, 20.4, 19.4.

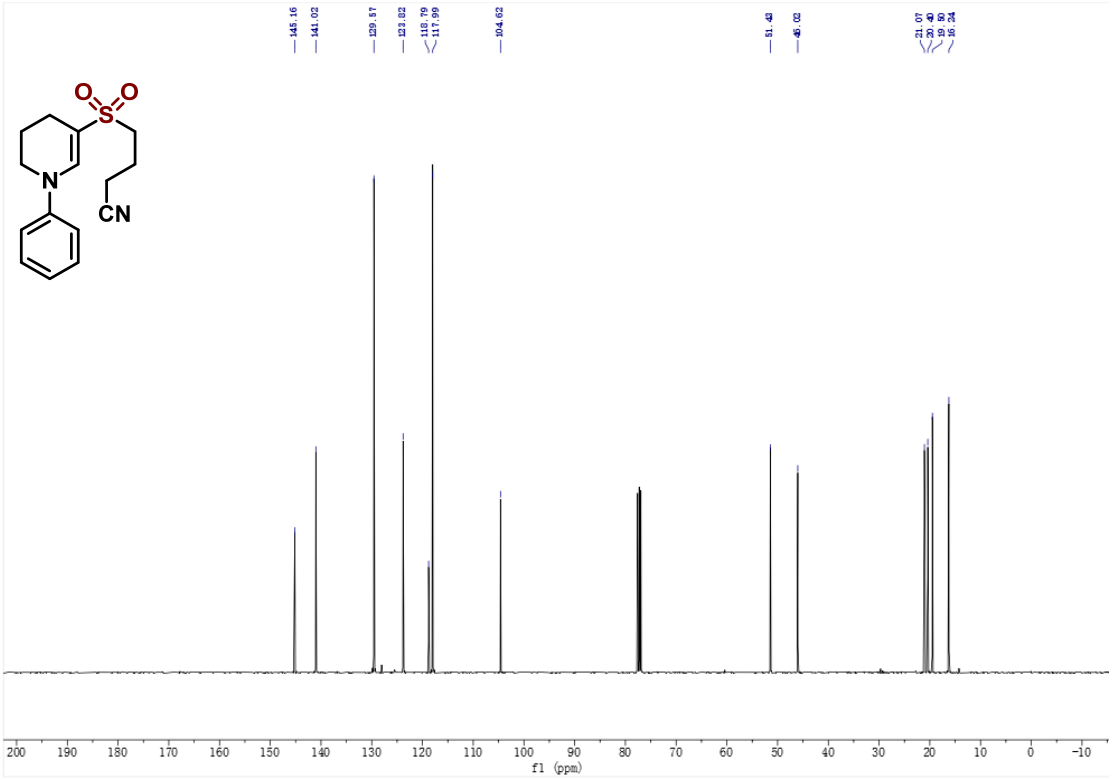
HRMS (ESI) for $C_{23}H_{27}N_2O_3S$ $[M + H]^+$ calcd.411.1737, found 411.1733.

6. Copies of ^{1}H and ^{13}C NMR Spectra

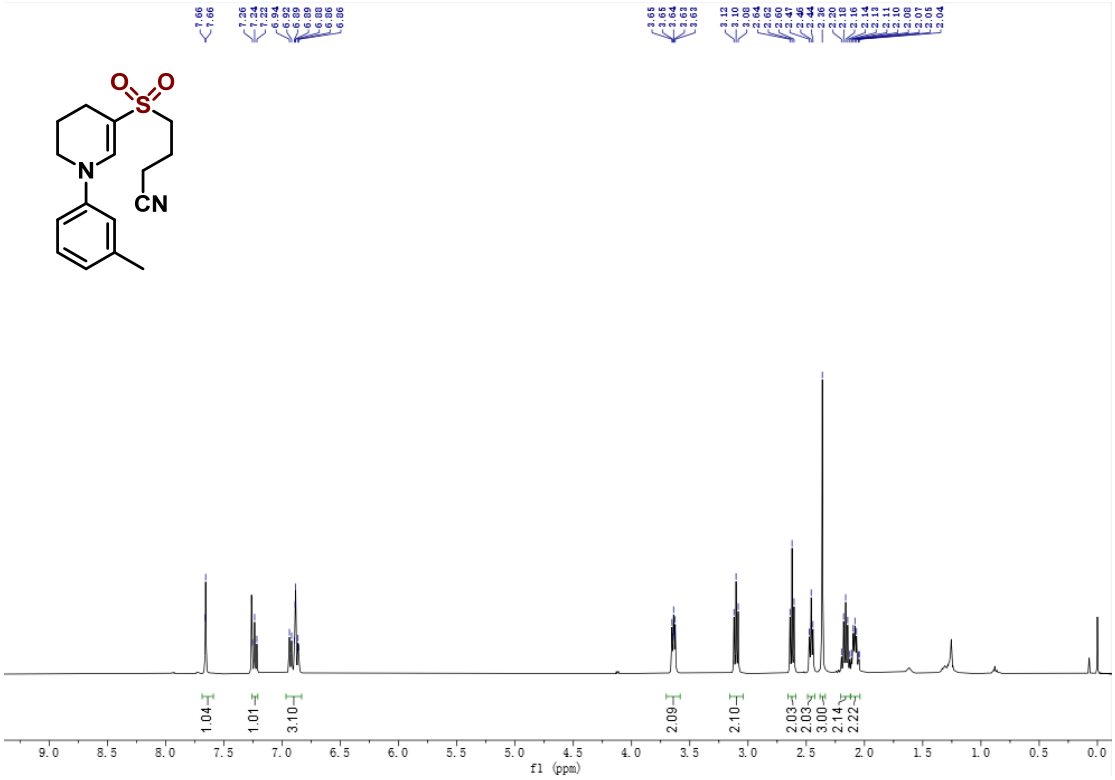
^{1}H NMR spectra of compound **3a** (400MHz, $CDCl_3$)



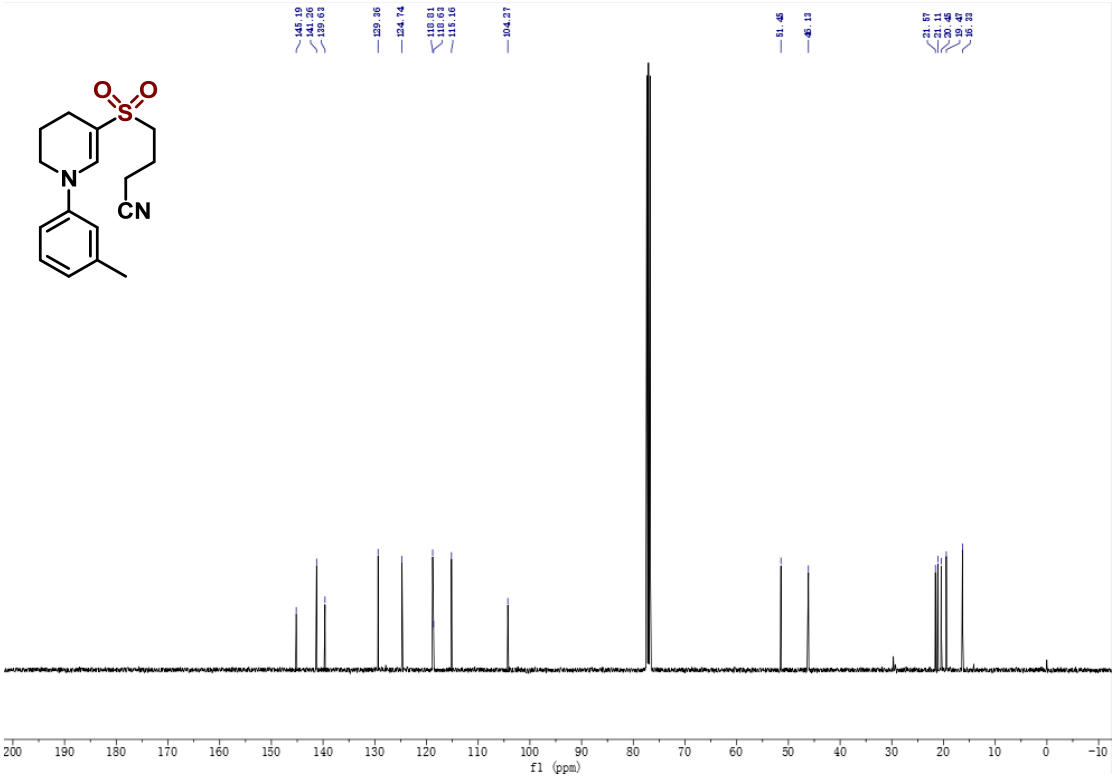
^{13}C NMR spectrum of compound **3a** (100 MHz, $CDCl_3$)



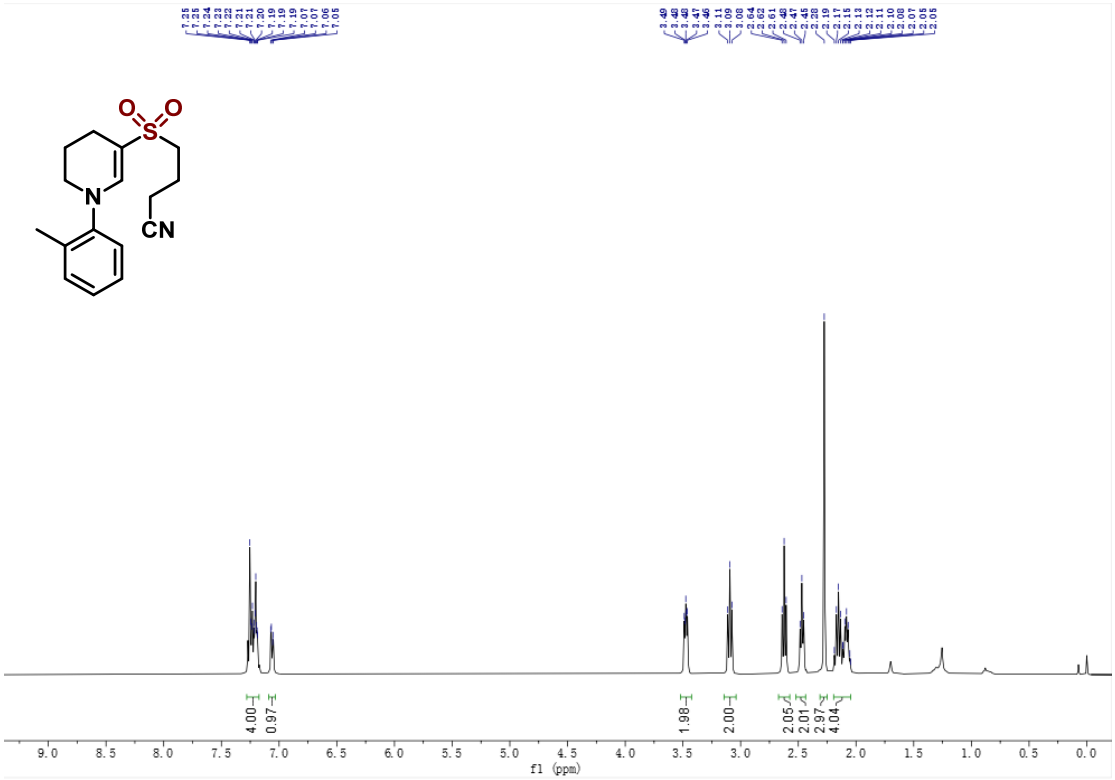
^{1}H NMR spectra of compound **3b** (400MHz, $CDCl_3$)



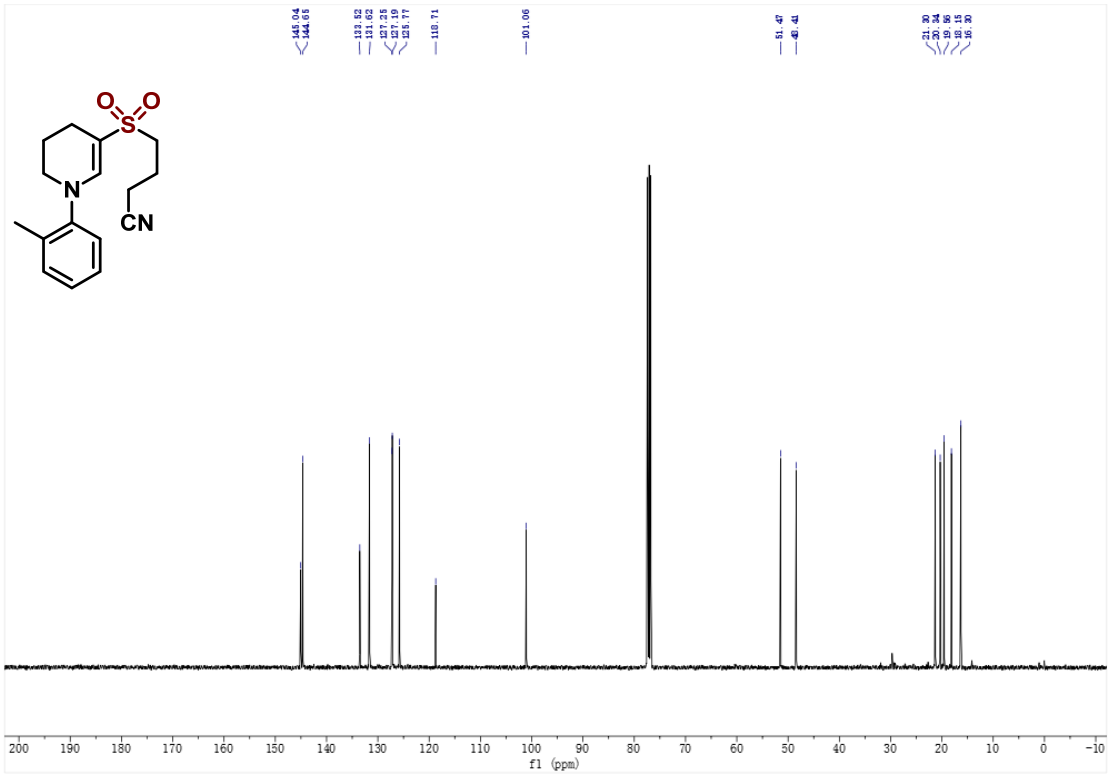
^{13}C NMR spectrum of compound **3b** (100 MHz, $CDCl_3$)



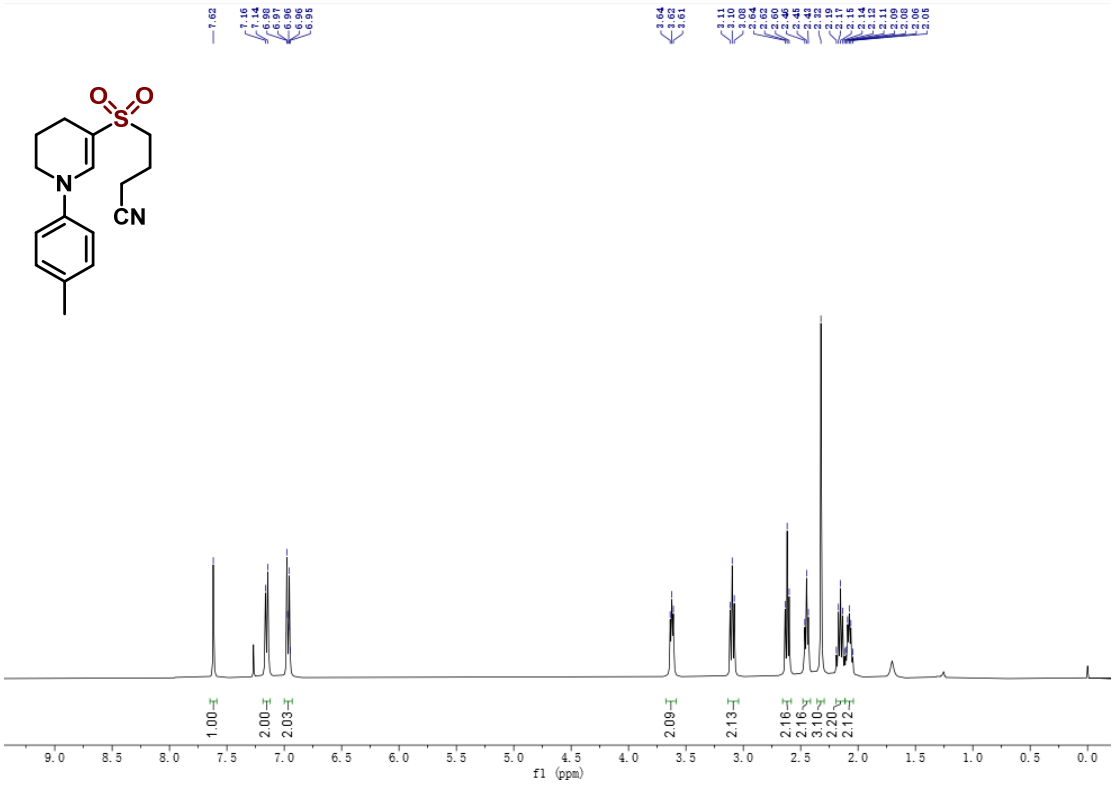
^{1}H NMR spectra of compound **3c** (400MHz, $CDCl_3$)



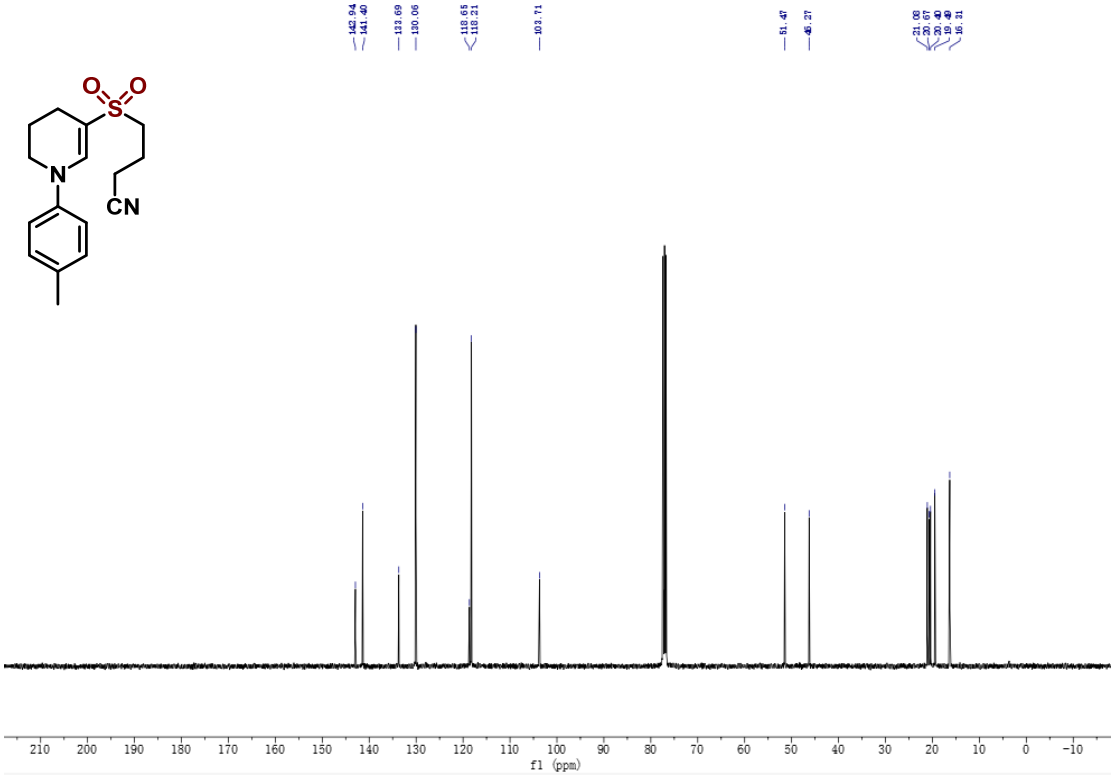
^{13}C NMR spectrum of compound **3c** (100 MHz, $CDCl_3$)



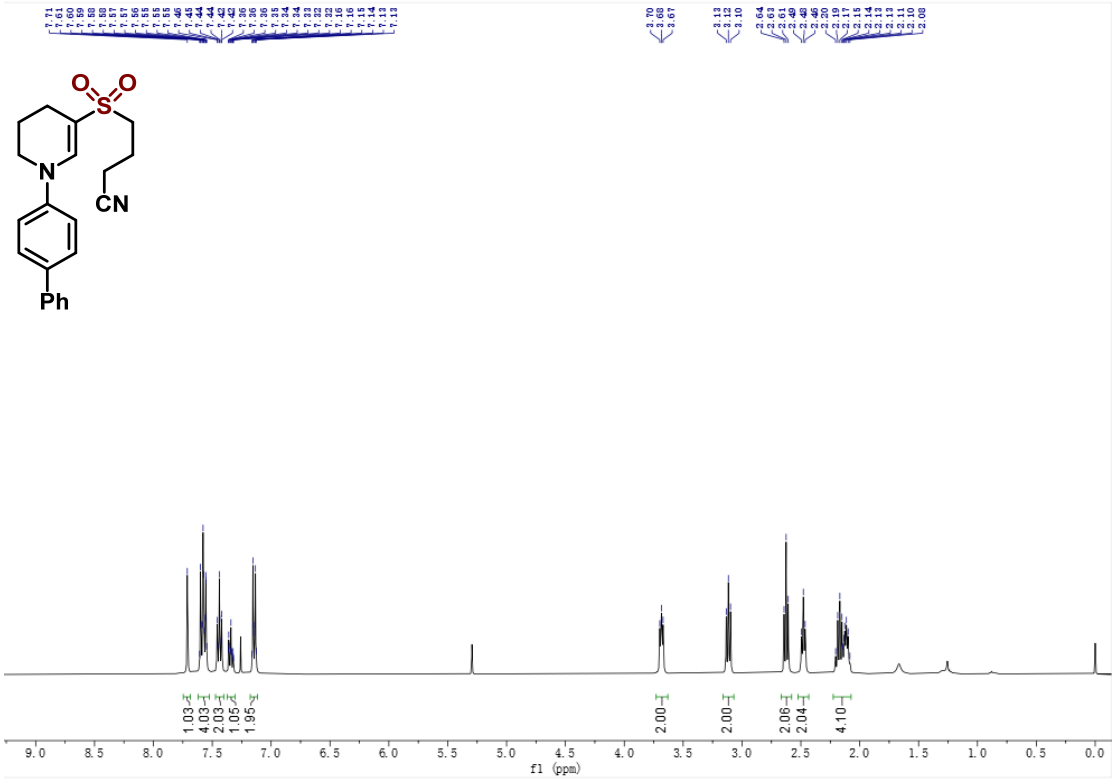
^{1}H NMR spectra of compound **3d** (400MHz, $CDCl_3$)



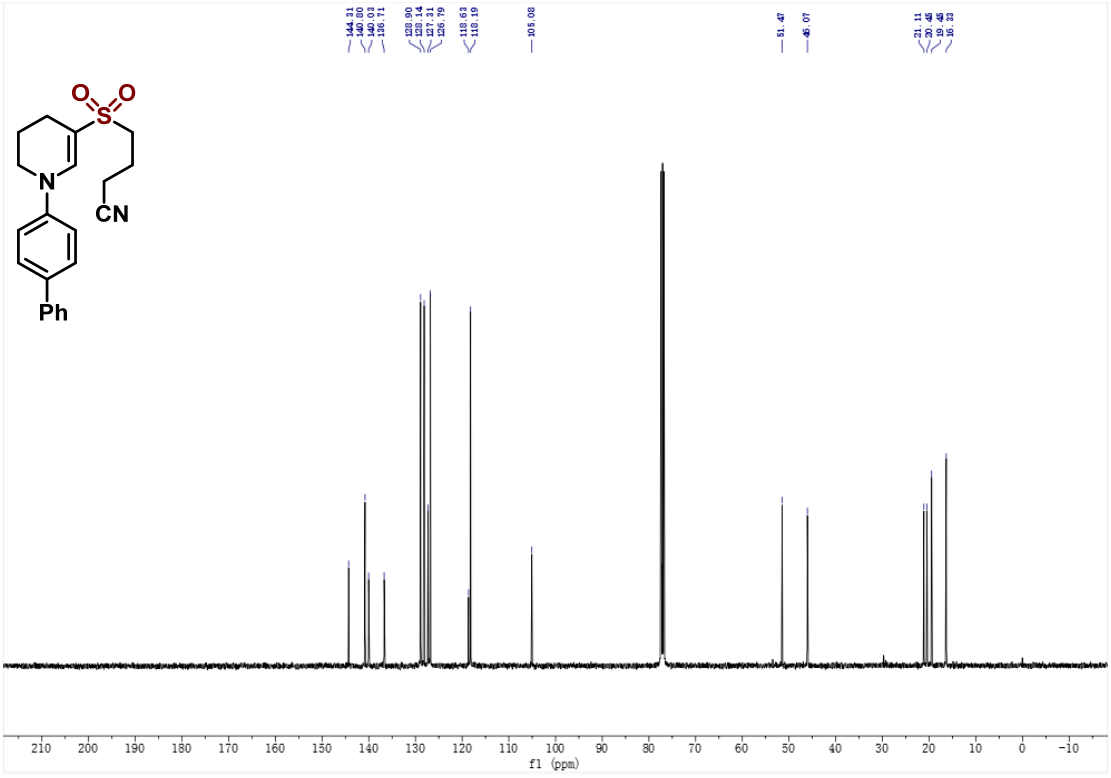
^{13}C NMR spectrum of compound **3d** (100 MHz, $CDCl_3$)



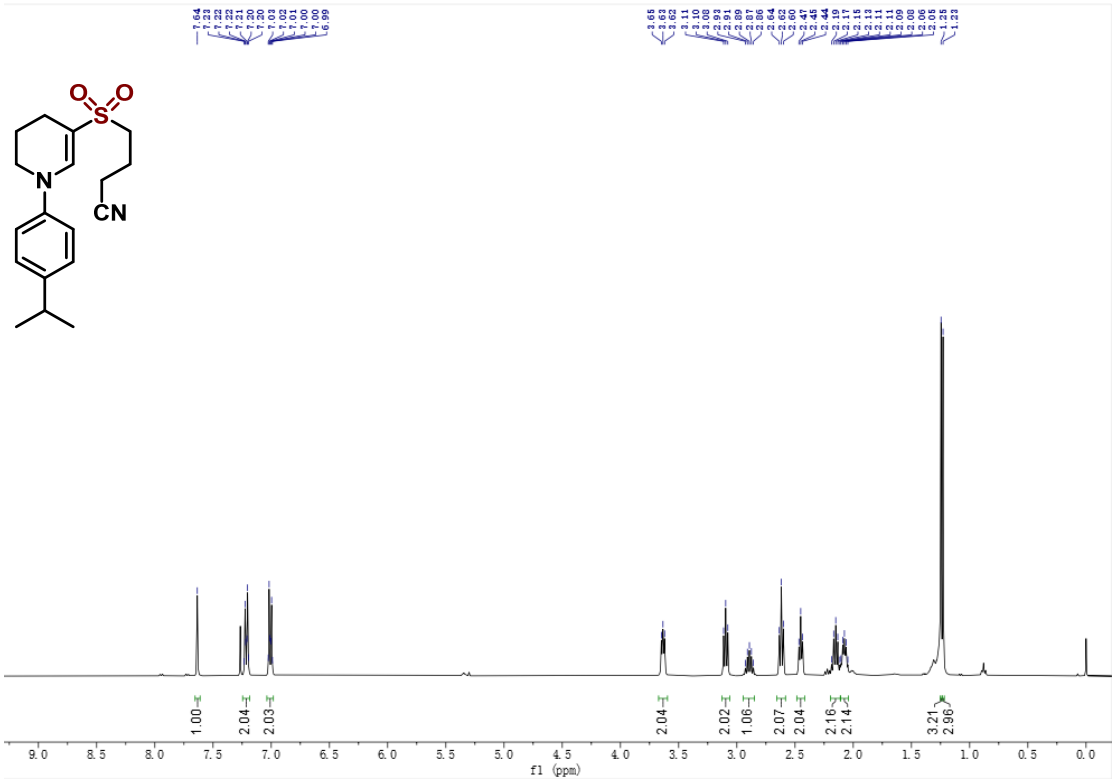
^{1}H NMR spectra of compound **3e** (400MHz, $CDCl_3$)



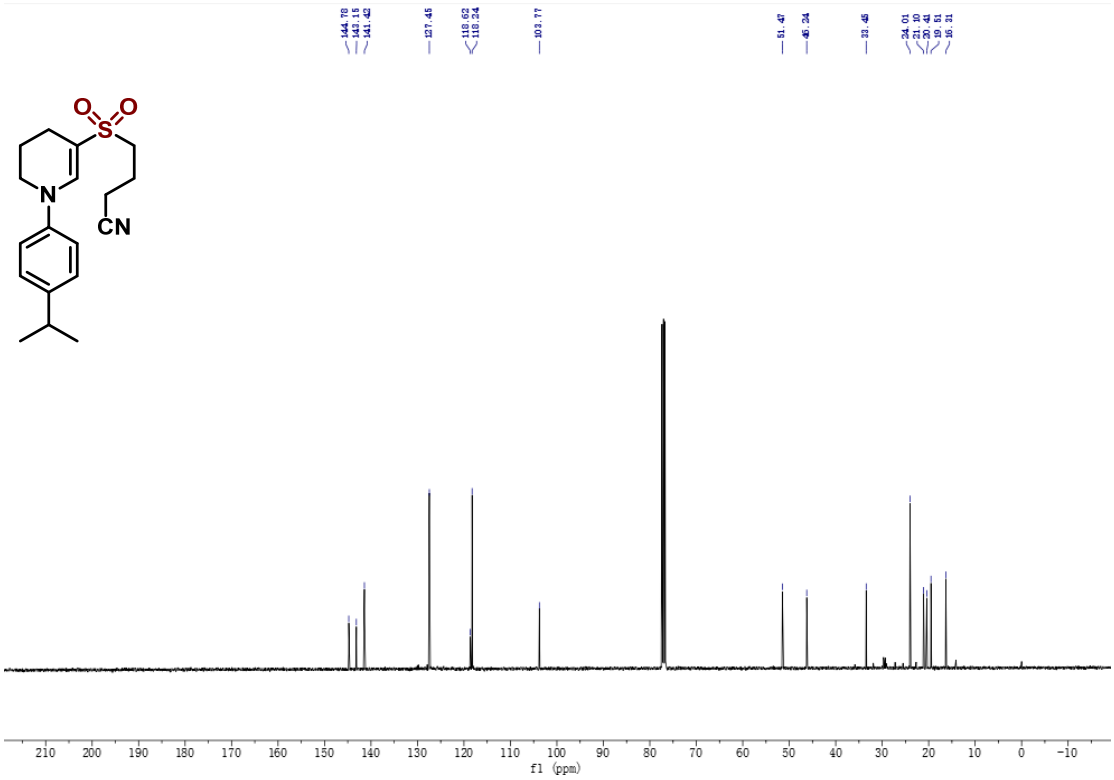
^{13}C NMR spectrum of compound **3e** (100 MHz, $CDCl_3$)



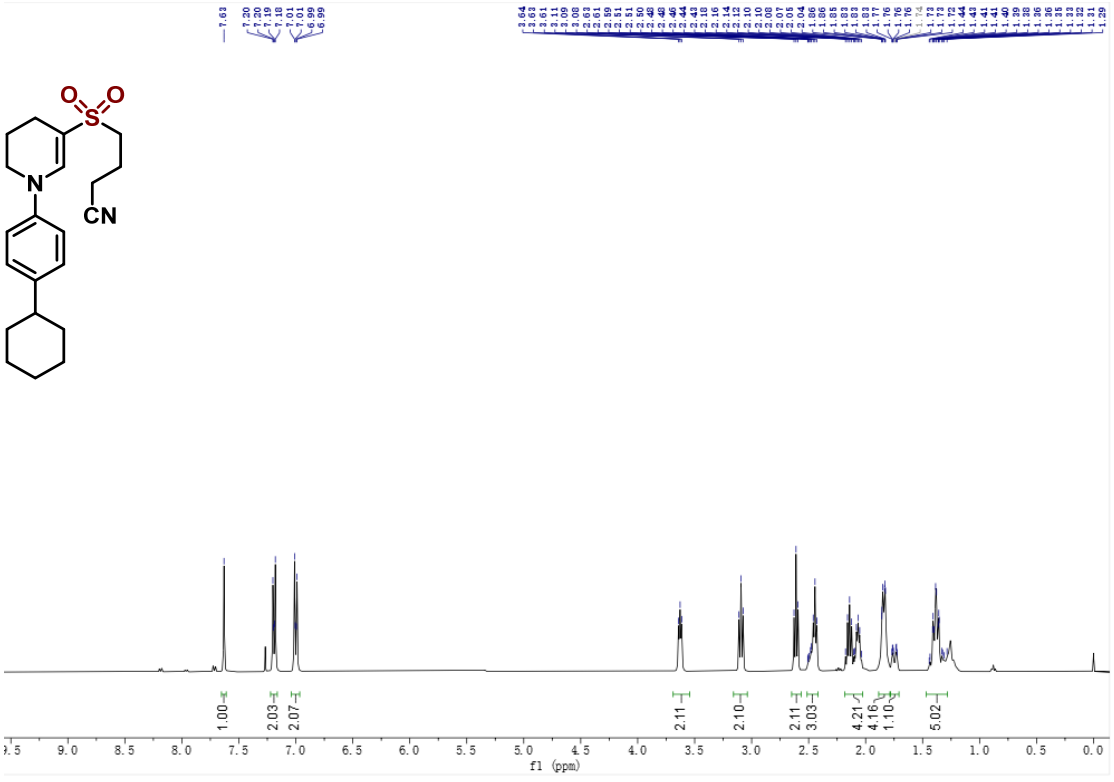
^{1}H NMR spectra of compound **3f** (400MHz, $CDCl_3$)



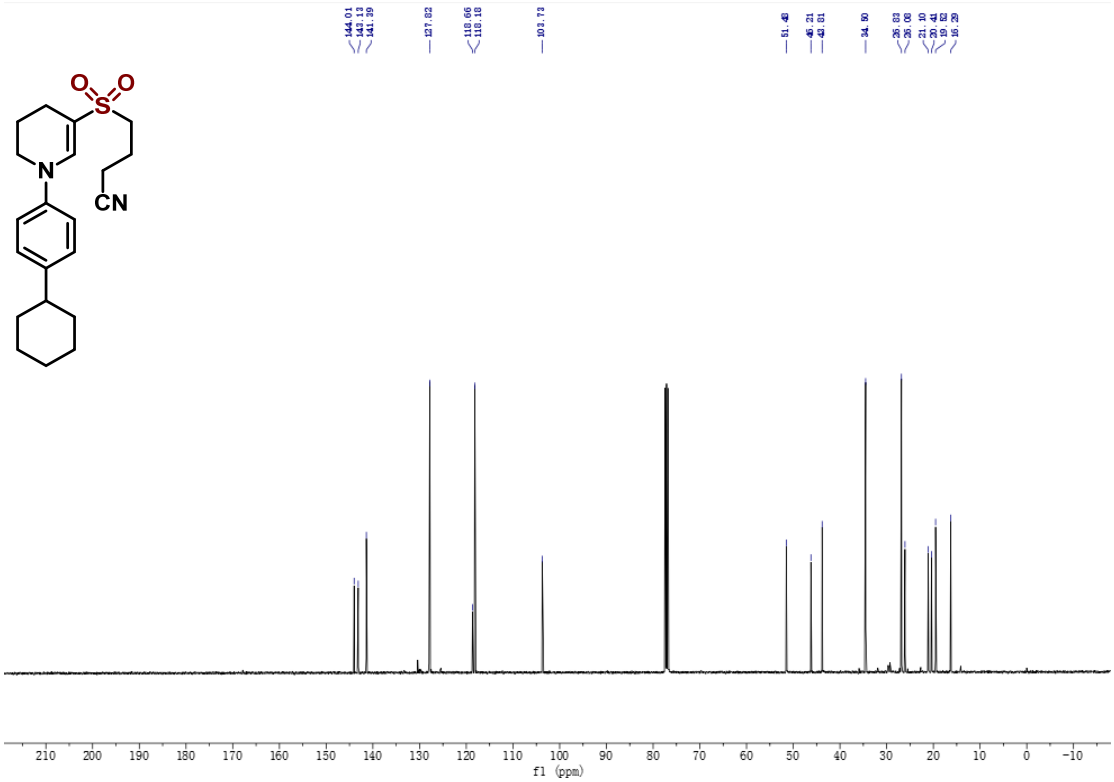
^{13}C NMR spectrum of compound **3f** (100 MHz, $CDCl_3$)



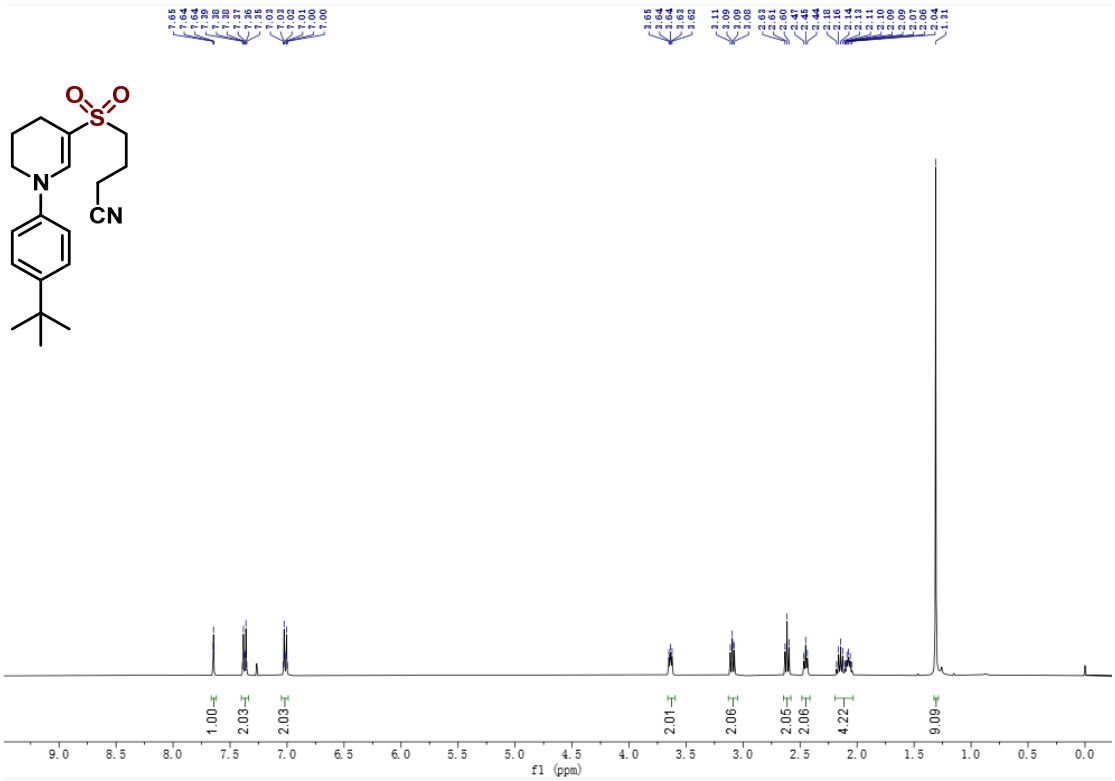
^{1}H NMR spectra of compound **3g** (400MHz, $CDCl_3$)



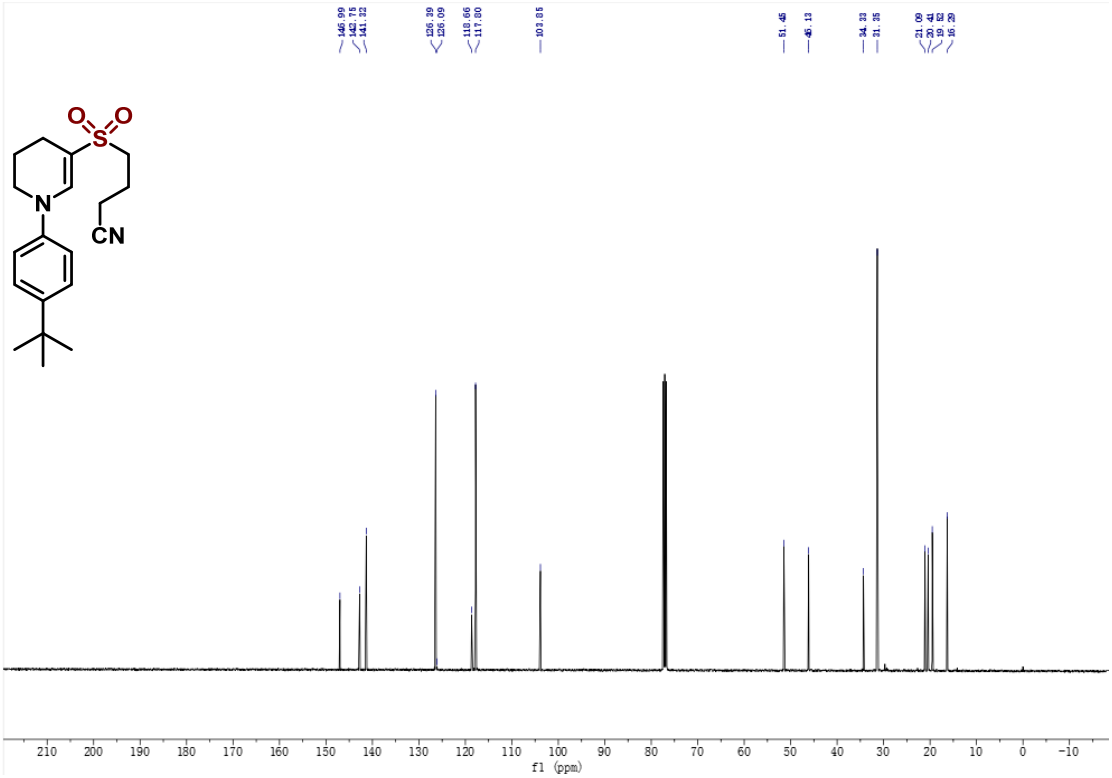
^{13}C NMR spectrum of compound **3g** (100 MHz, $CDCl_3$)



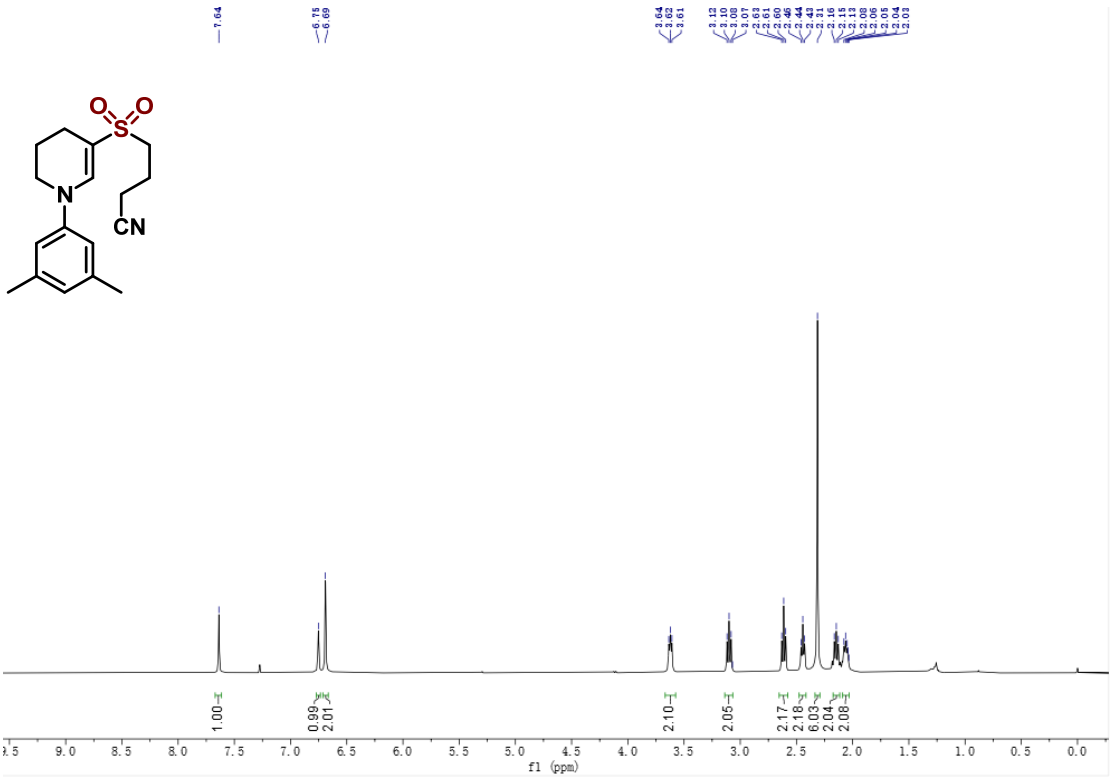
^{1}H NMR spectra of compound **3h** (400MHz, $CDCl_3$)



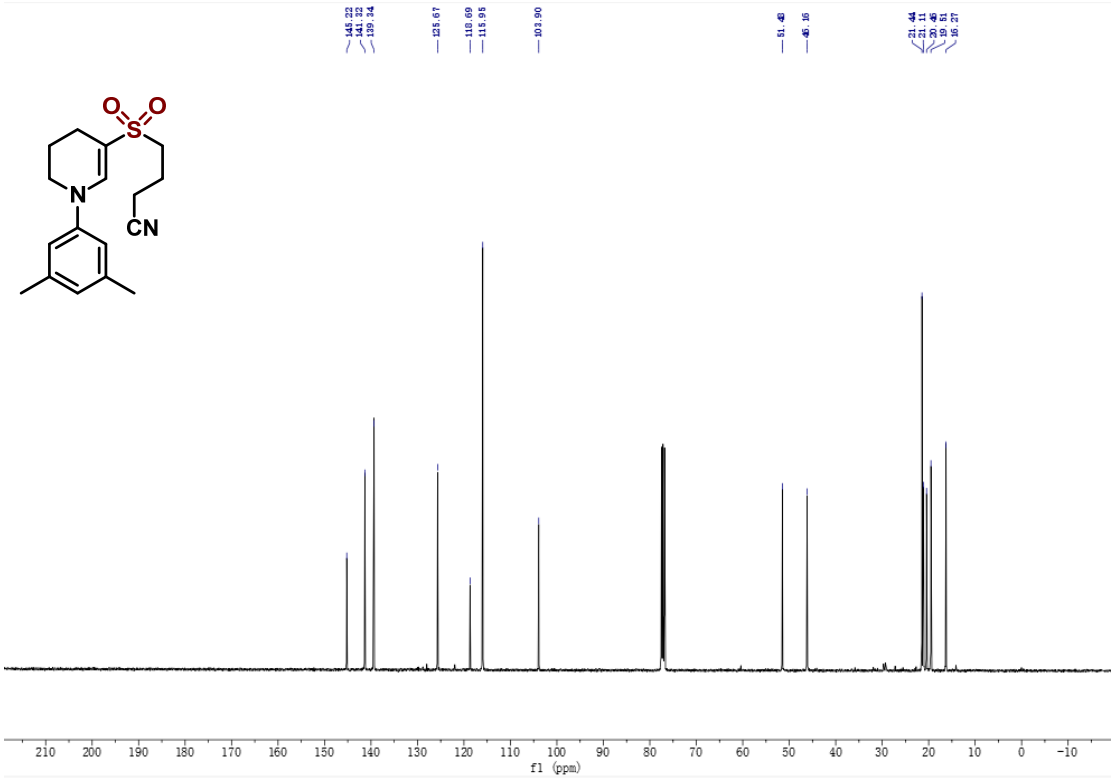
^{13}C NMR spectrum of compound **3h** (100 MHz, $CDCl_3$)



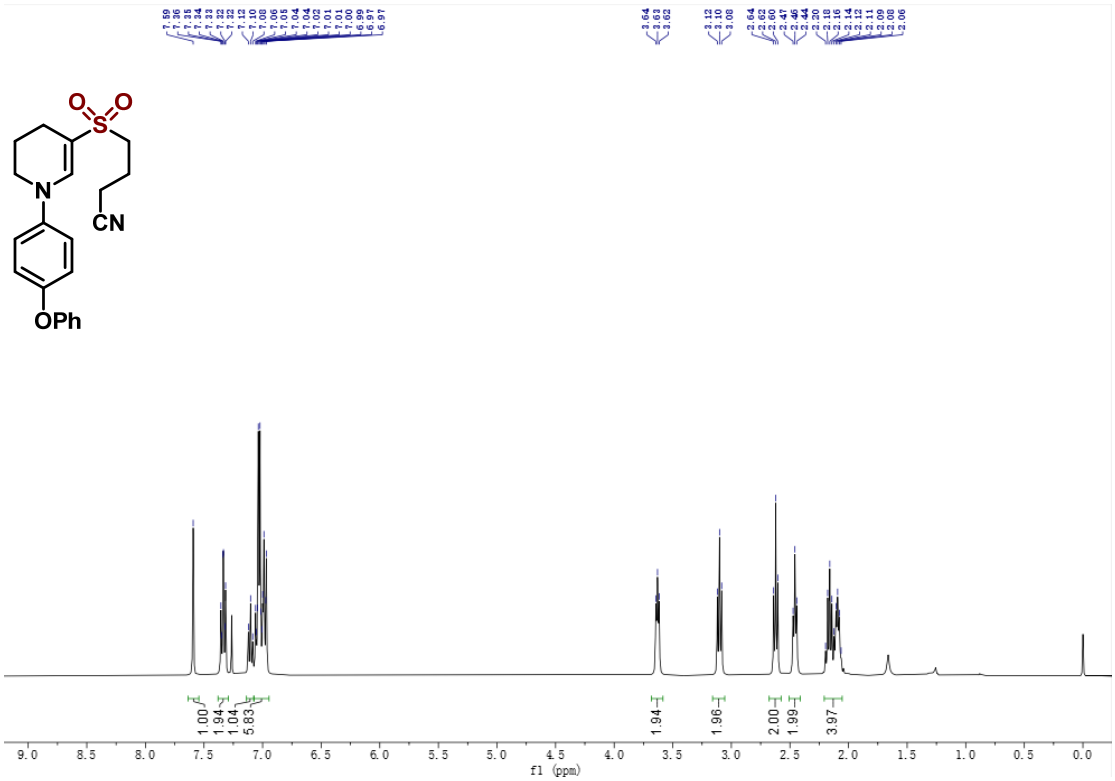
^{1}H NMR spectra of compound **3i** (400MHz, $CDCl_3$)



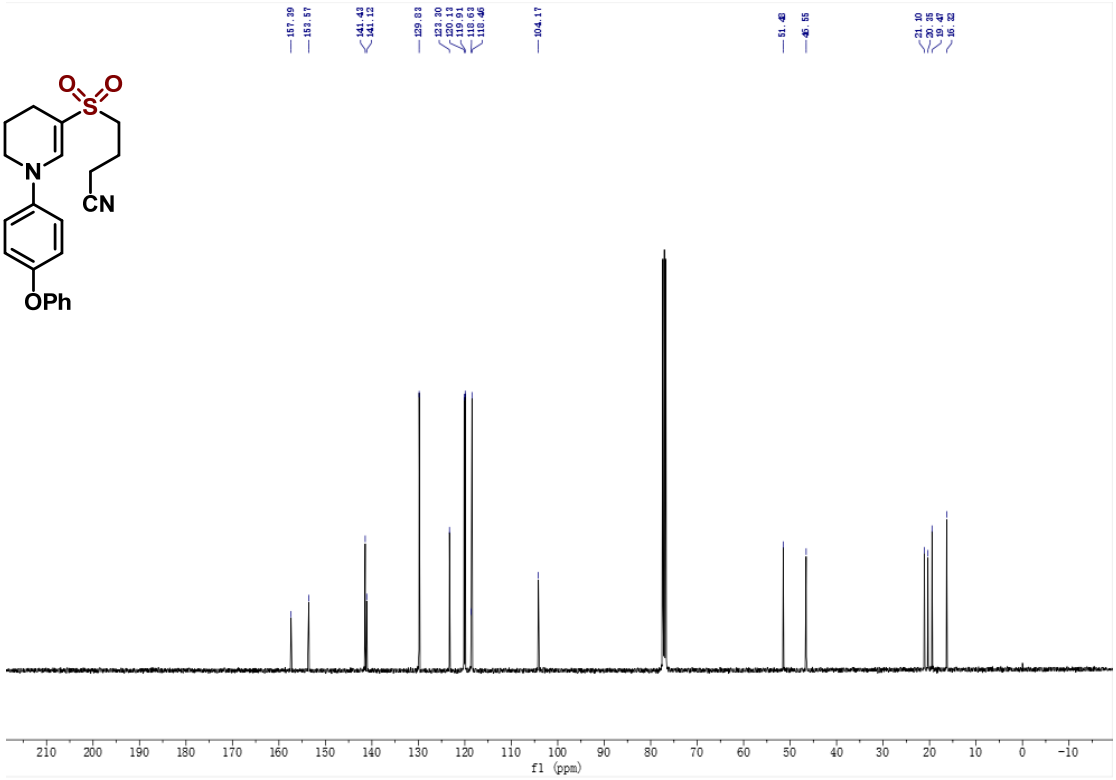
^{13}C NMR spectrum of compound **3i** (100 MHz, $CDCl_3$)



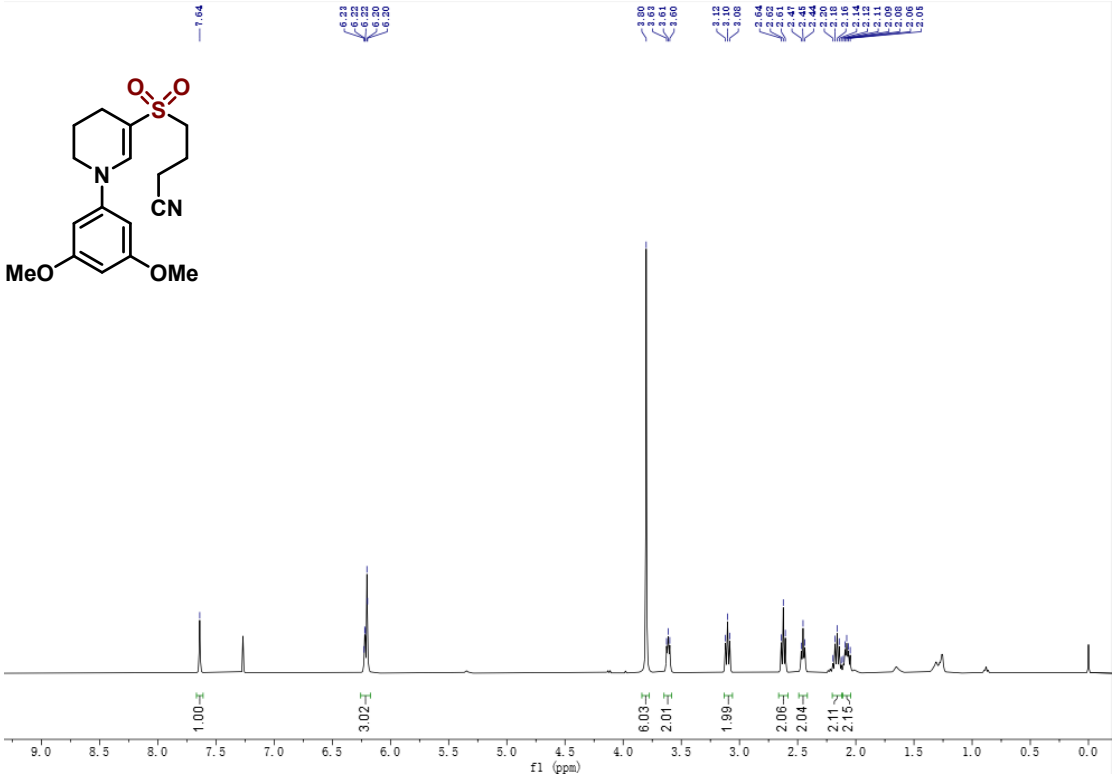
^{1}H NMR spectra of compound **3j** (400MHz, $CDCl_3$)



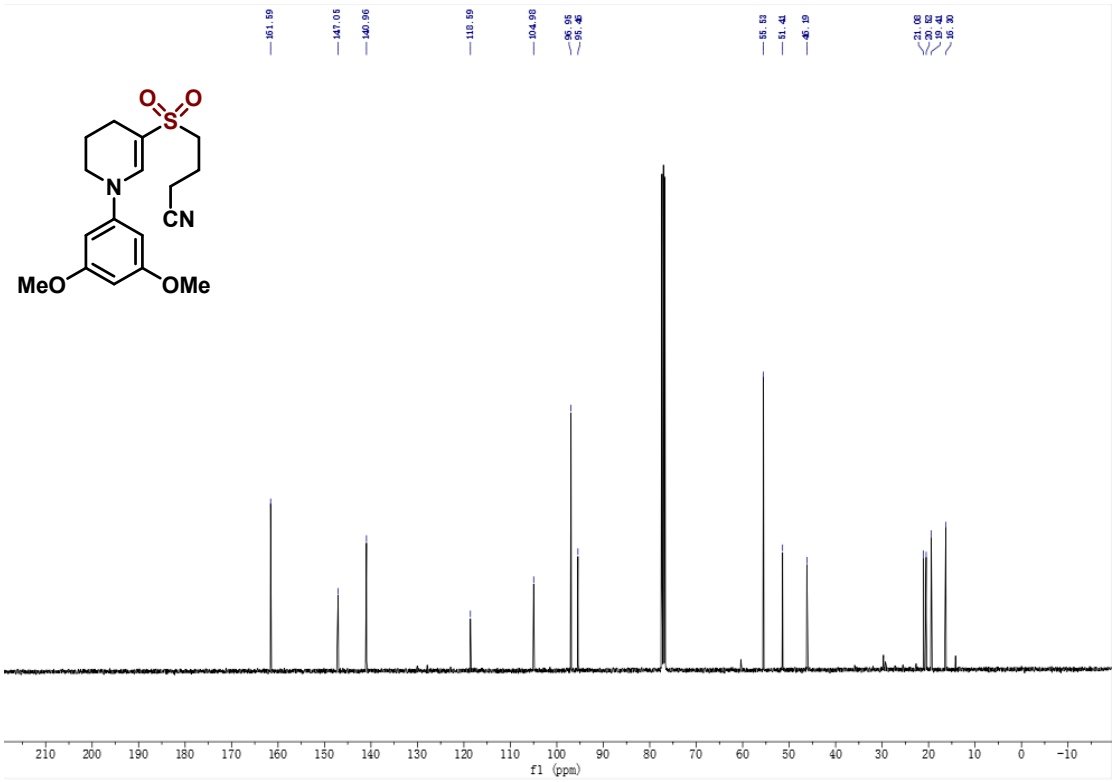
^{13}C NMR spectrum of compound **3j** (100 MHz, $CDCl_3$)



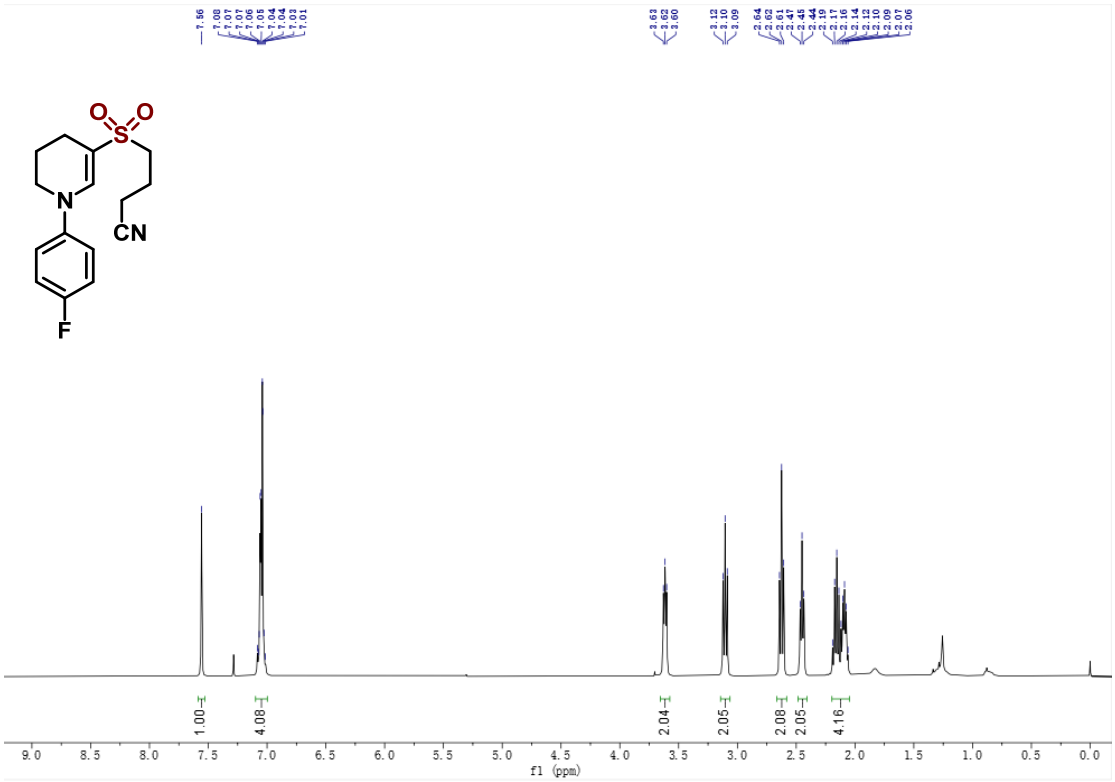
^{1}H NMR spectra of compound **3k** (400MHz, $CDCl_3$)



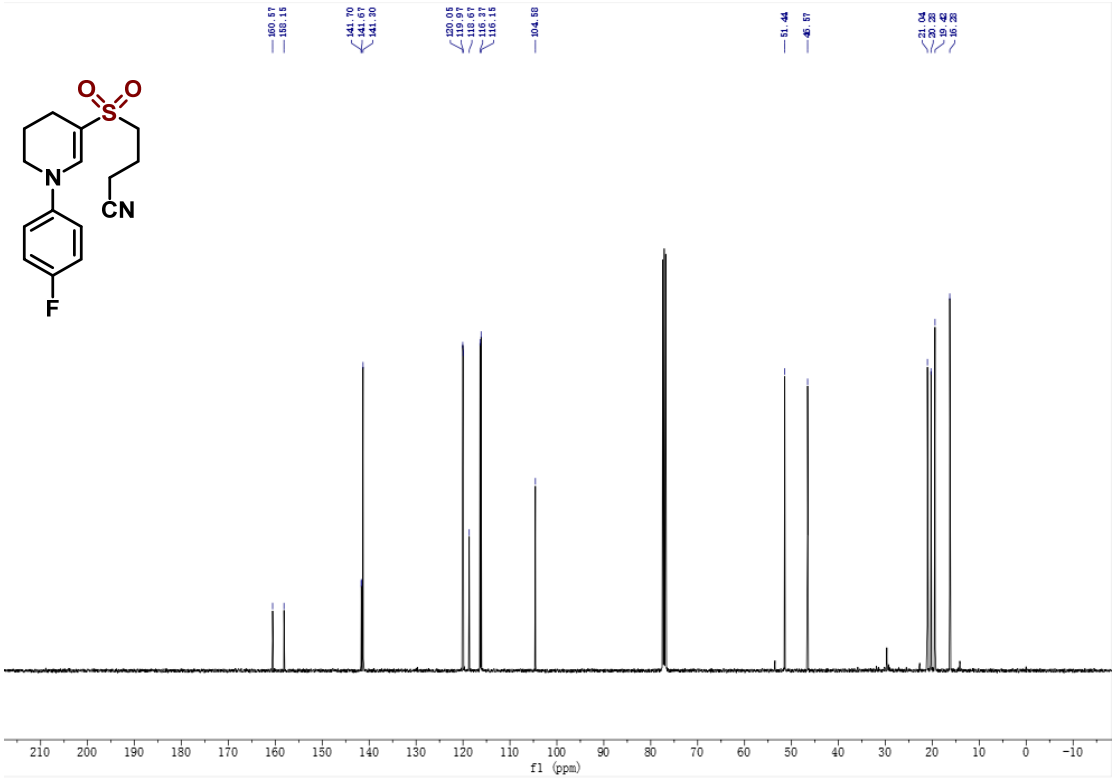
^{13}C NMR spectrum of compound **3k** (100 MHz, $CDCl_3$)



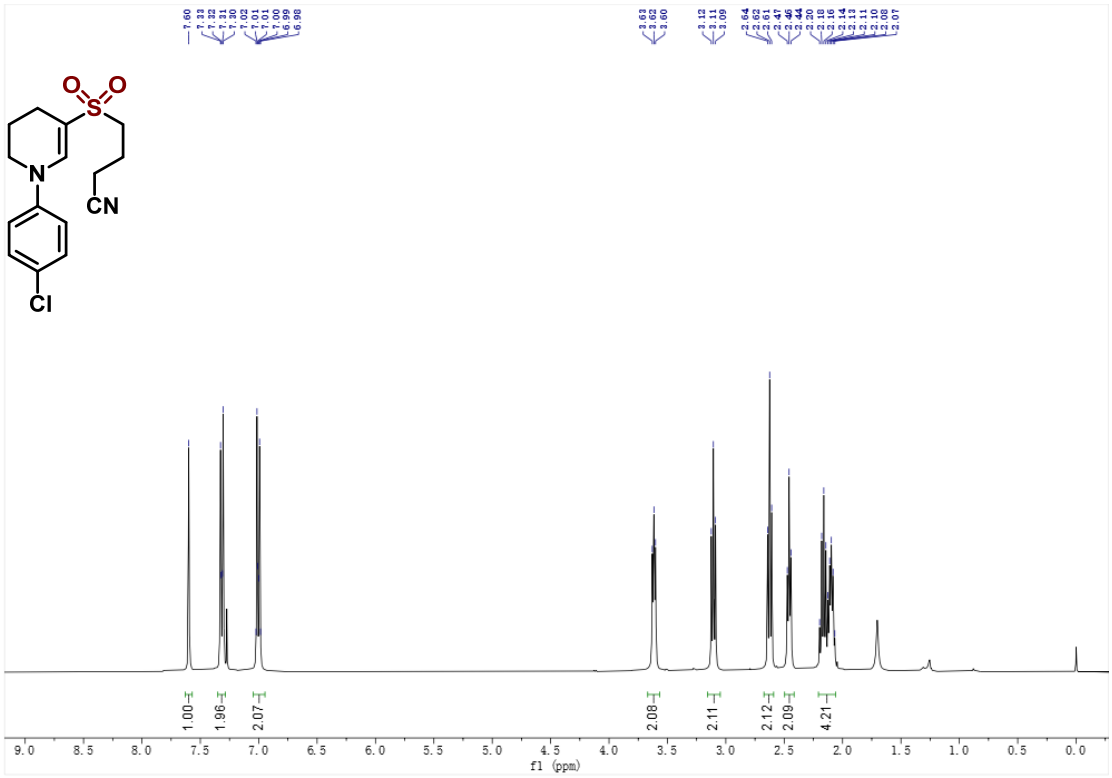
^{1}H NMR spectra of compound **3l** (400MHz, $CDCl_3$)



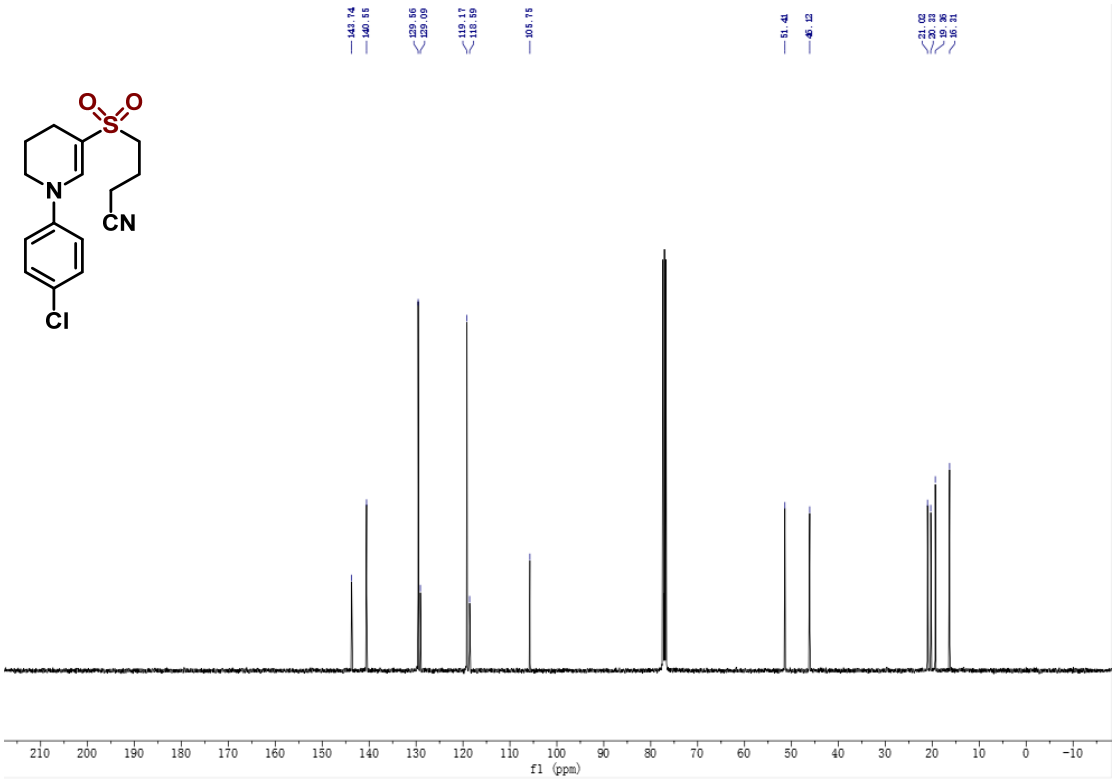
^{13}C NMR spectrum of compound **3l** (100 MHz, $CDCl_3$)



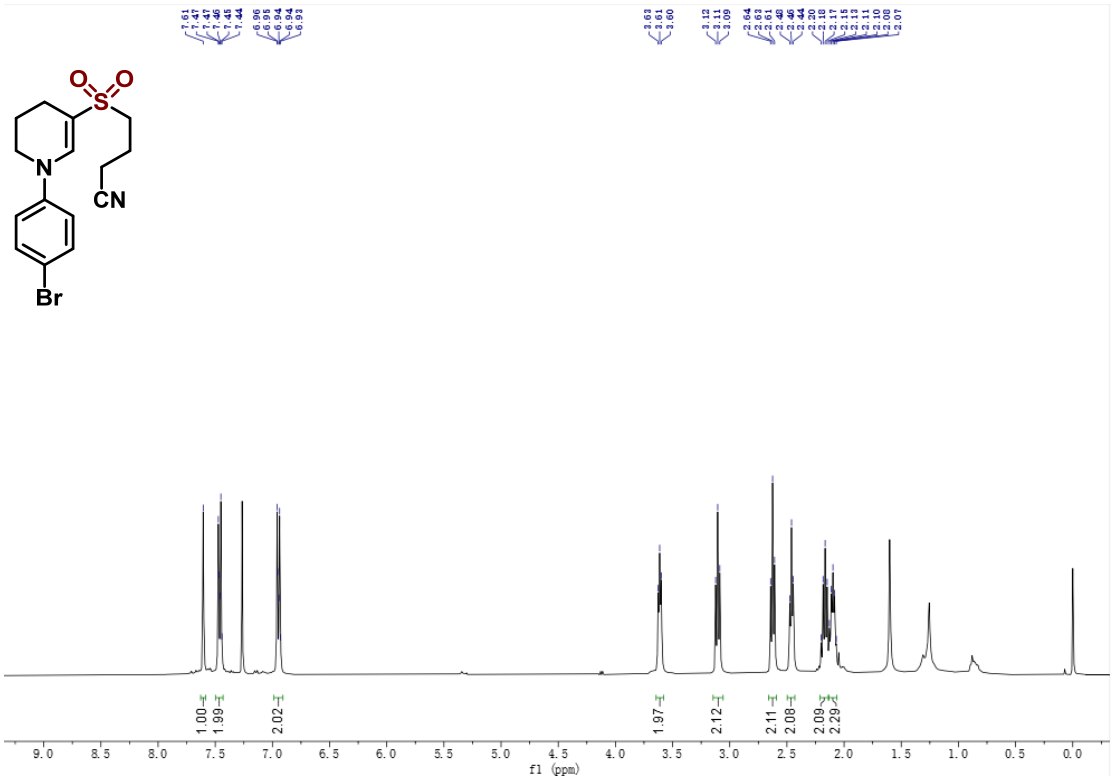
^{1}H NMR spectra of compound **3m** (400MHz, $CDCl_3$)



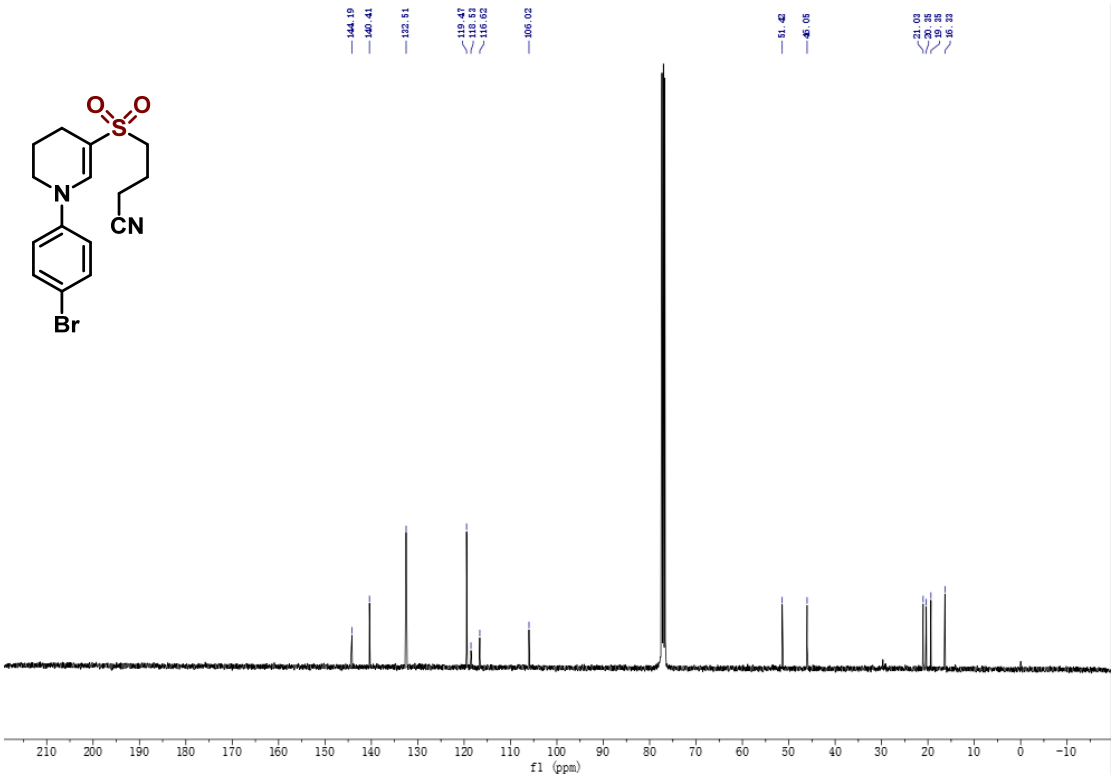
^{13}C NMR spectrum of compound **3m** (100 MHz, $CDCl_3$)



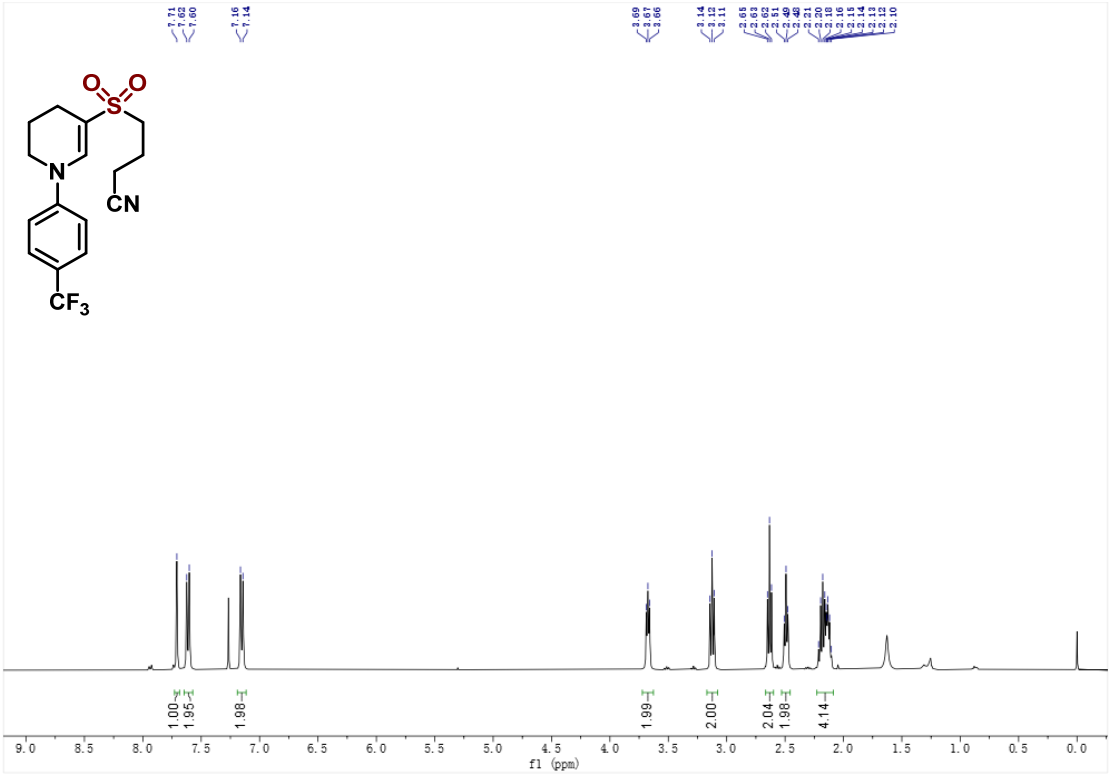
^{1}H NMR spectra of compound **3n** (400MHz, $CDCl_3$)



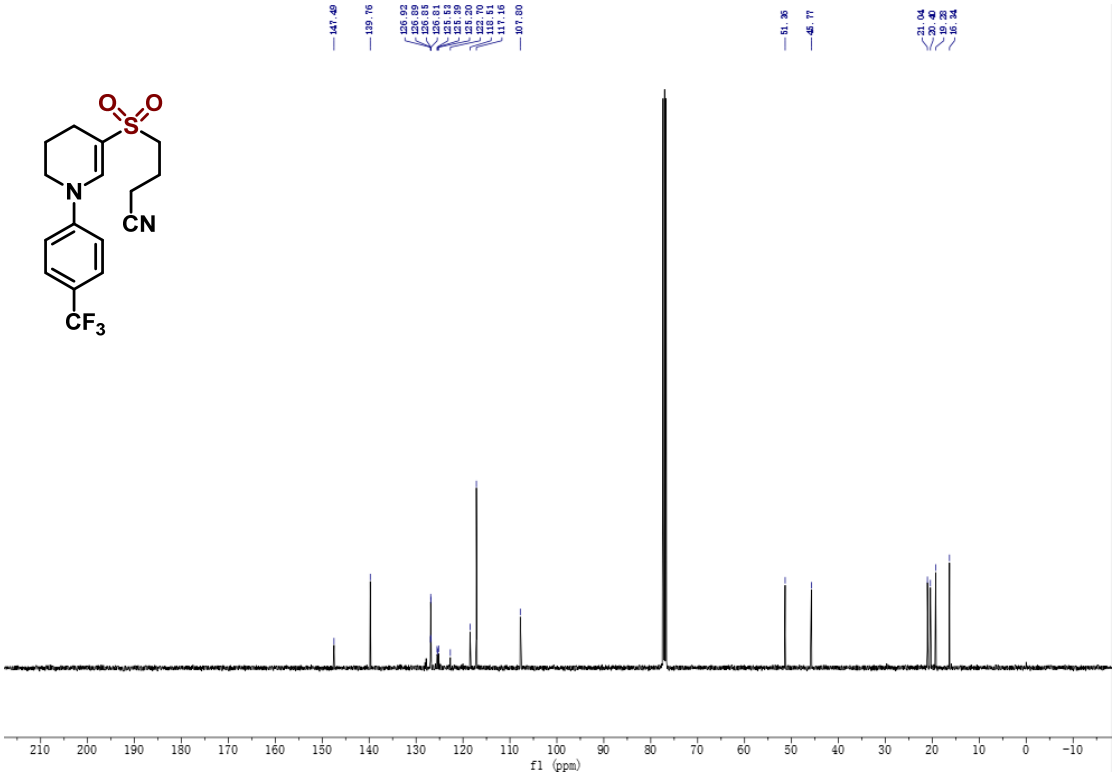
^{13}C NMR spectrum of compound **3n** (100 MHz, $CDCl_3$)



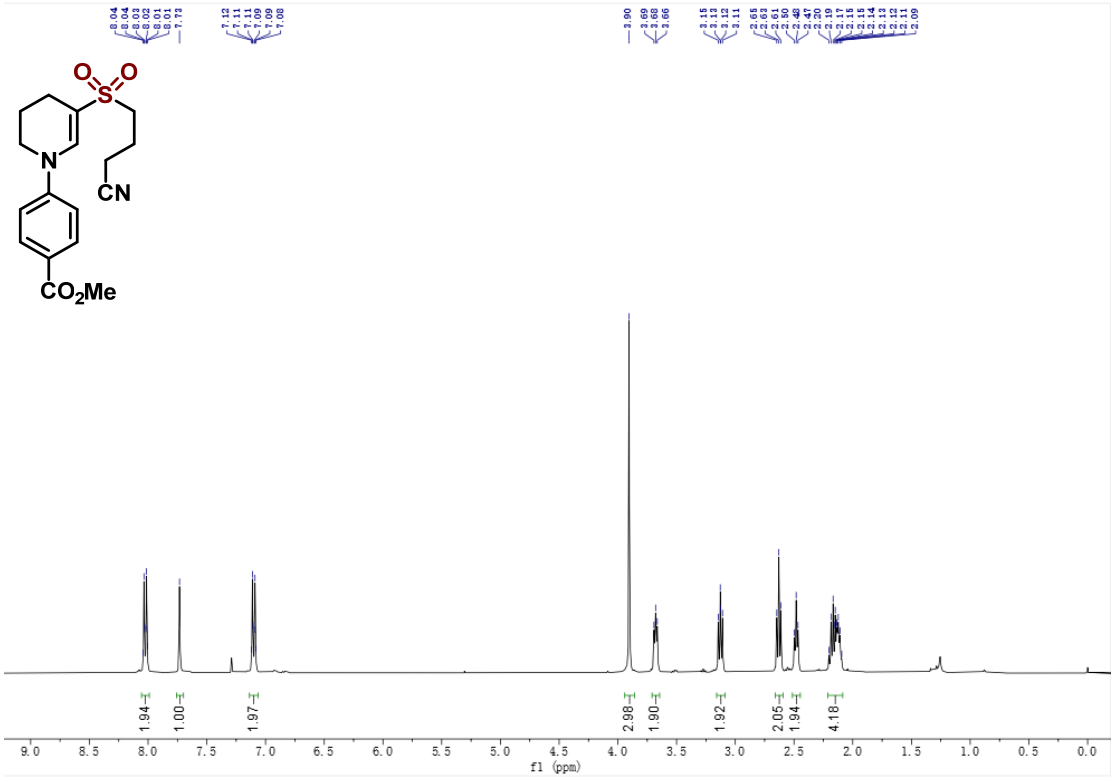
^{1}H NMR spectra of compound **3o** (400MHz, $CDCl_3$)



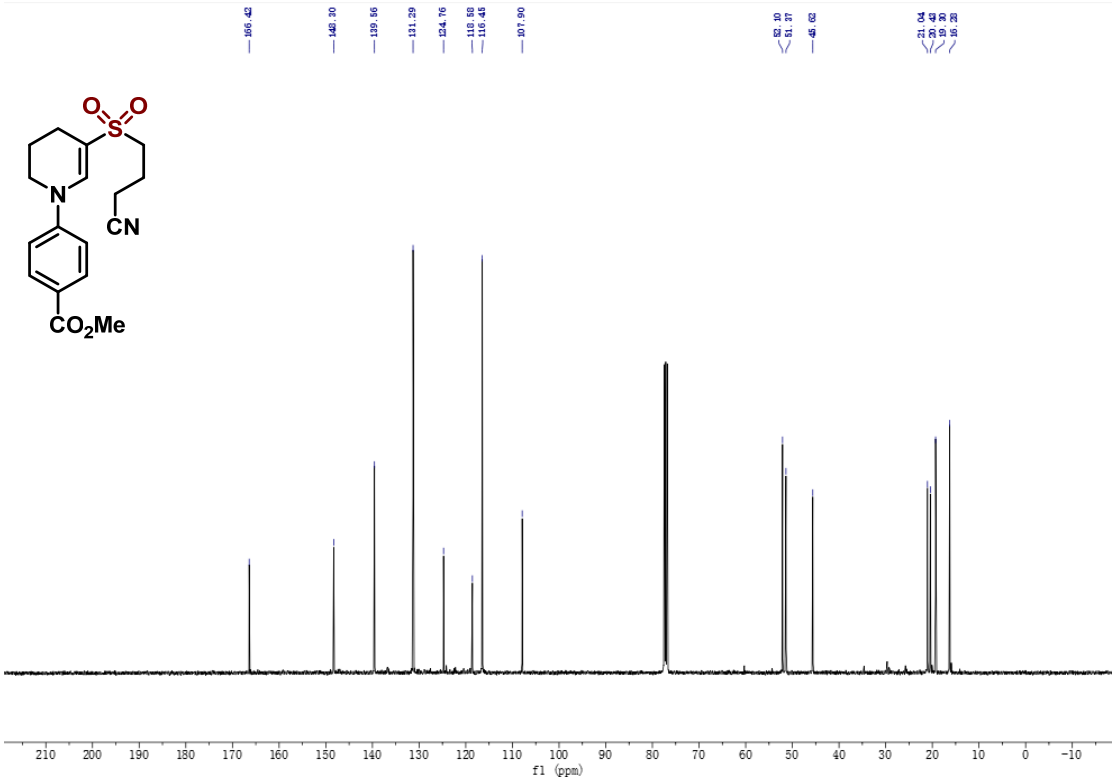
^{13}C NMR spectrum of compound **3o** (100 MHz, $CDCl_3$)



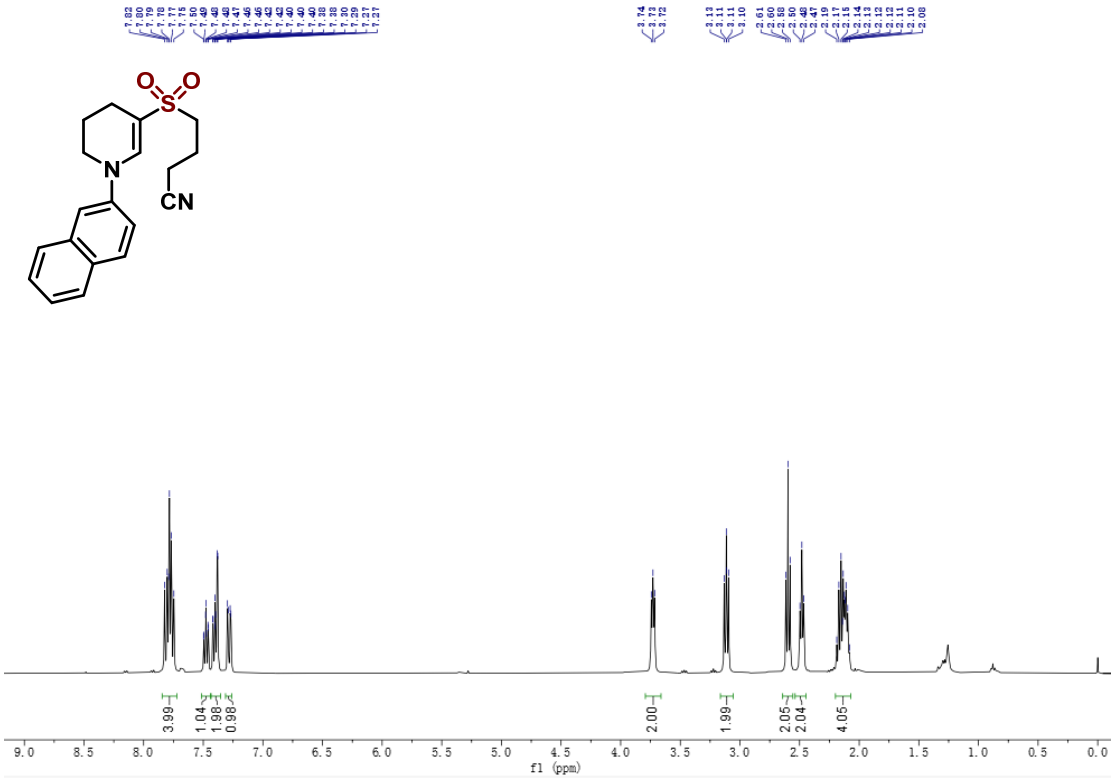
^{1}H NMR spectra of compound **3p** (400MHz, $CDCl_3$)



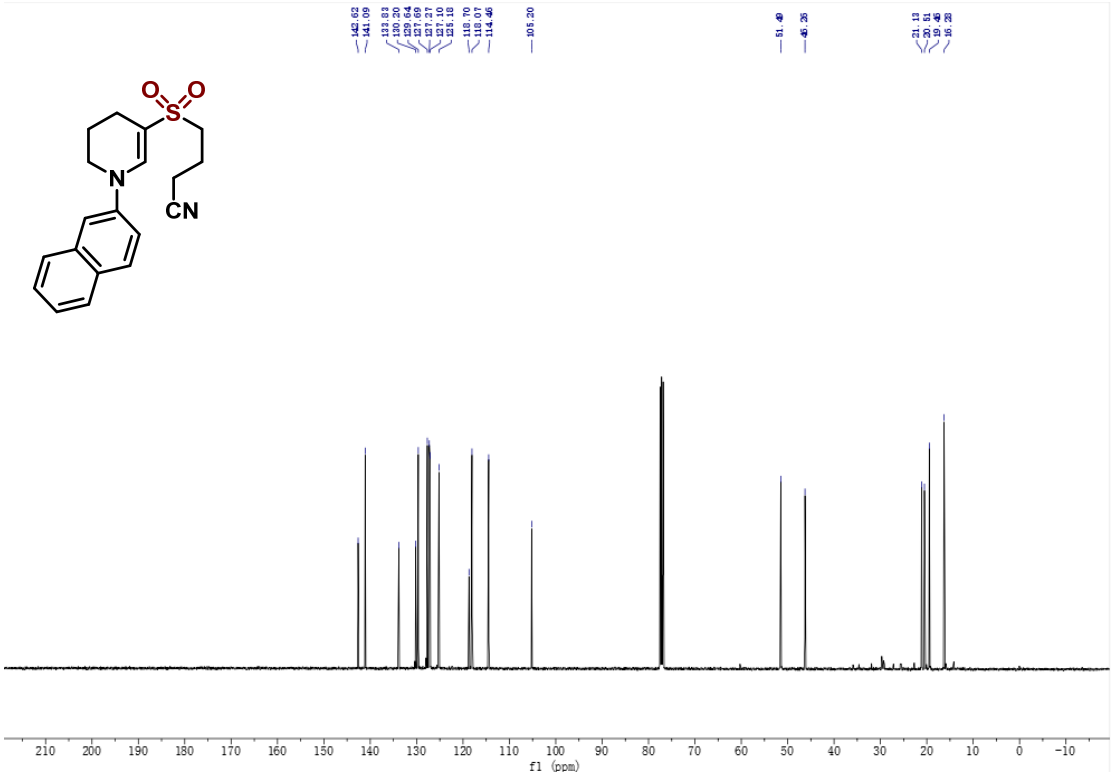
^{13}C NMR spectrum of compound **3p** (100 MHz, $CDCl_3$)



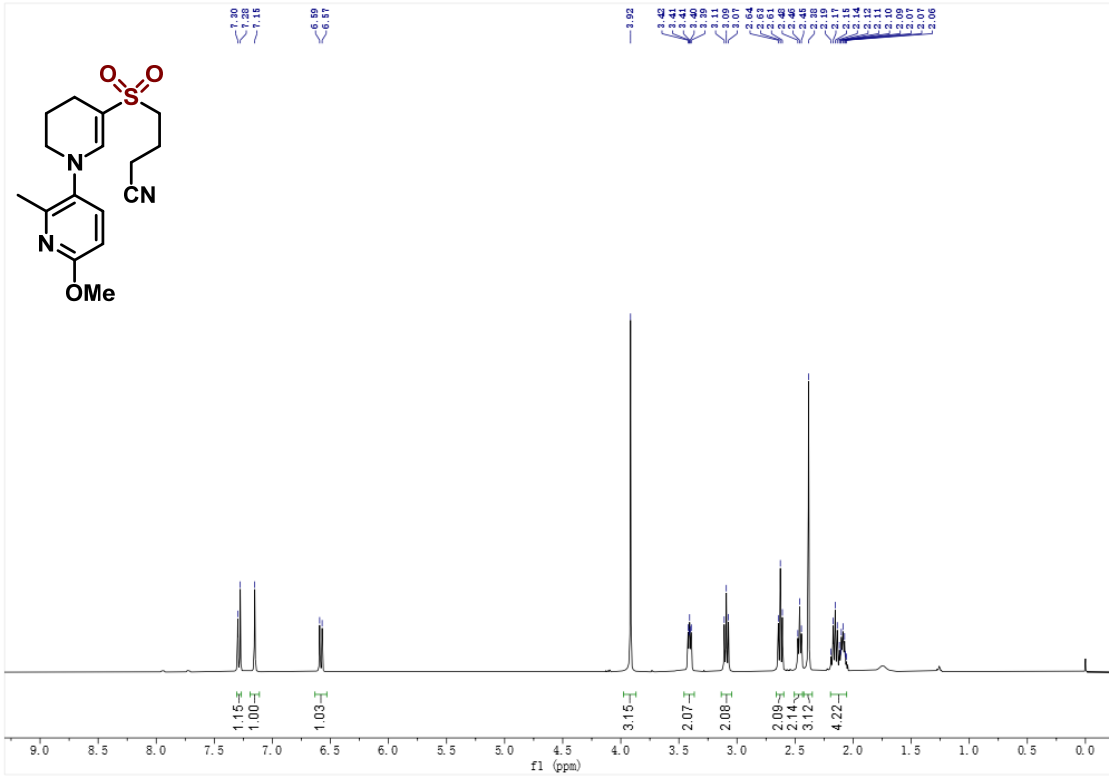
^{1}H NMR spectra of compound **3q** (400MHz, $CDCl_3$)



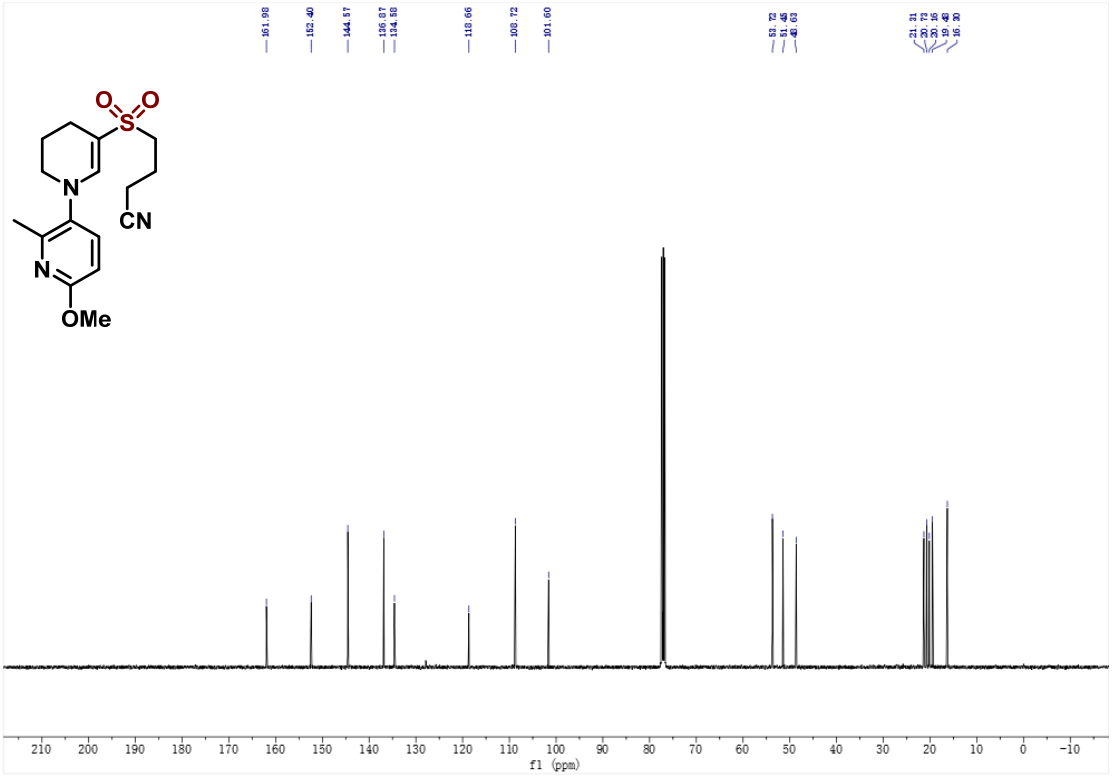
^{13}C NMR spectrum of compound **3q** (100 MHz, $CDCl_3$)



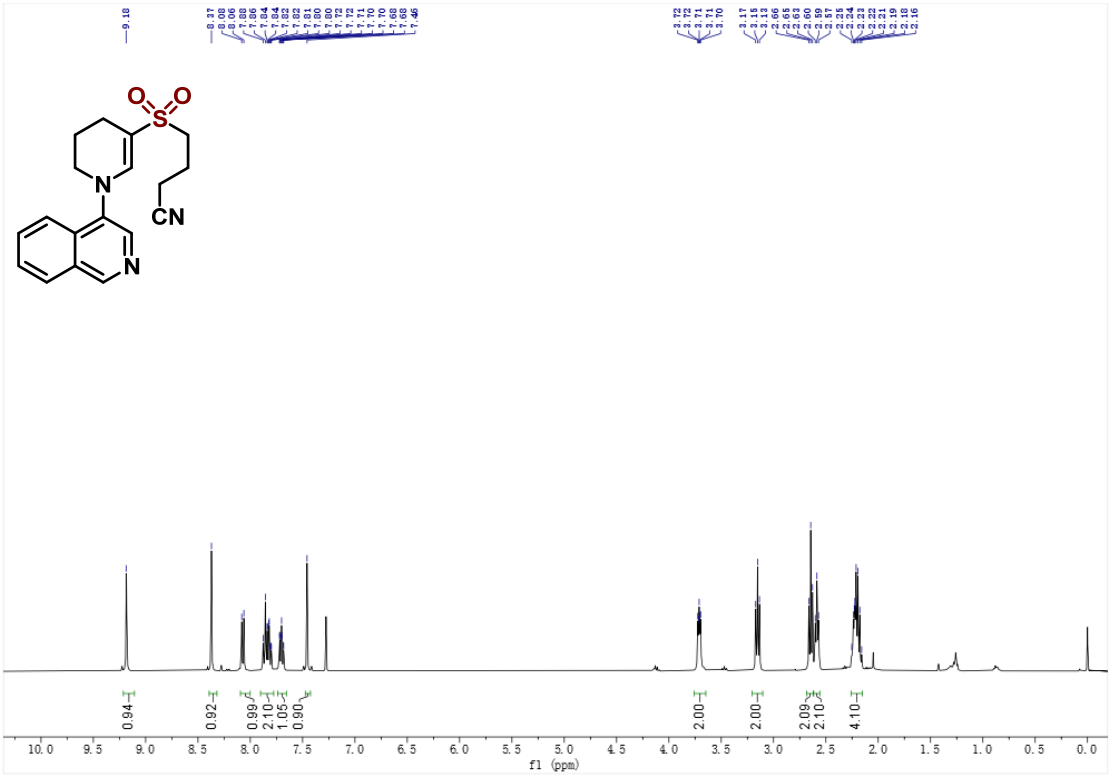
^{1}H NMR spectra of compound **3r** (400MHz, $CDCl_3$)



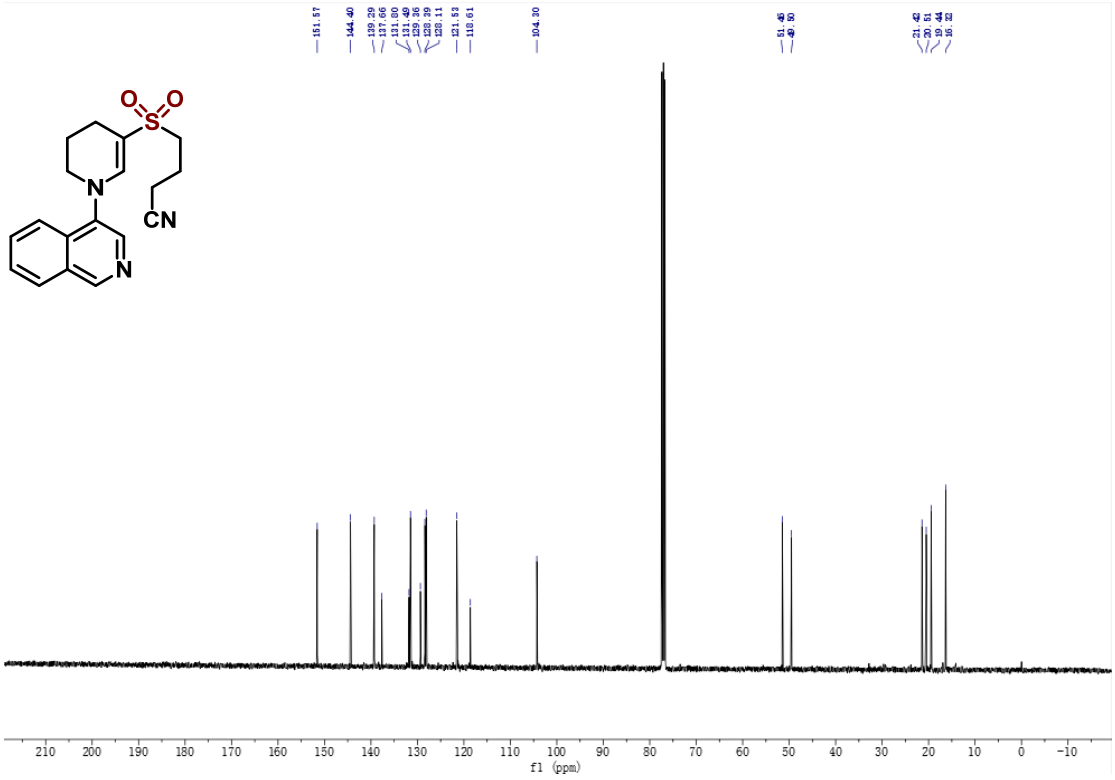
^{13}C NMR spectrum of compound **3r** (100 MHz, $CDCl_3$)



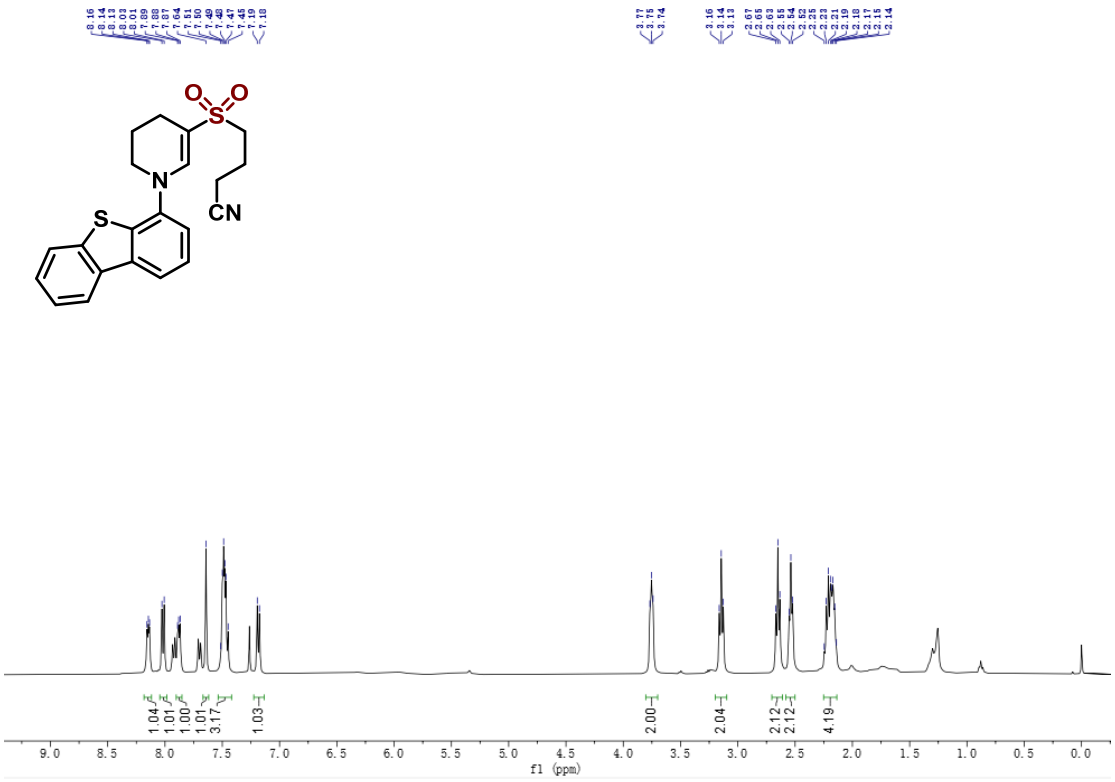
^{1}H NMR spectra of compound **3s** (400MHz, $CDCl_3$)



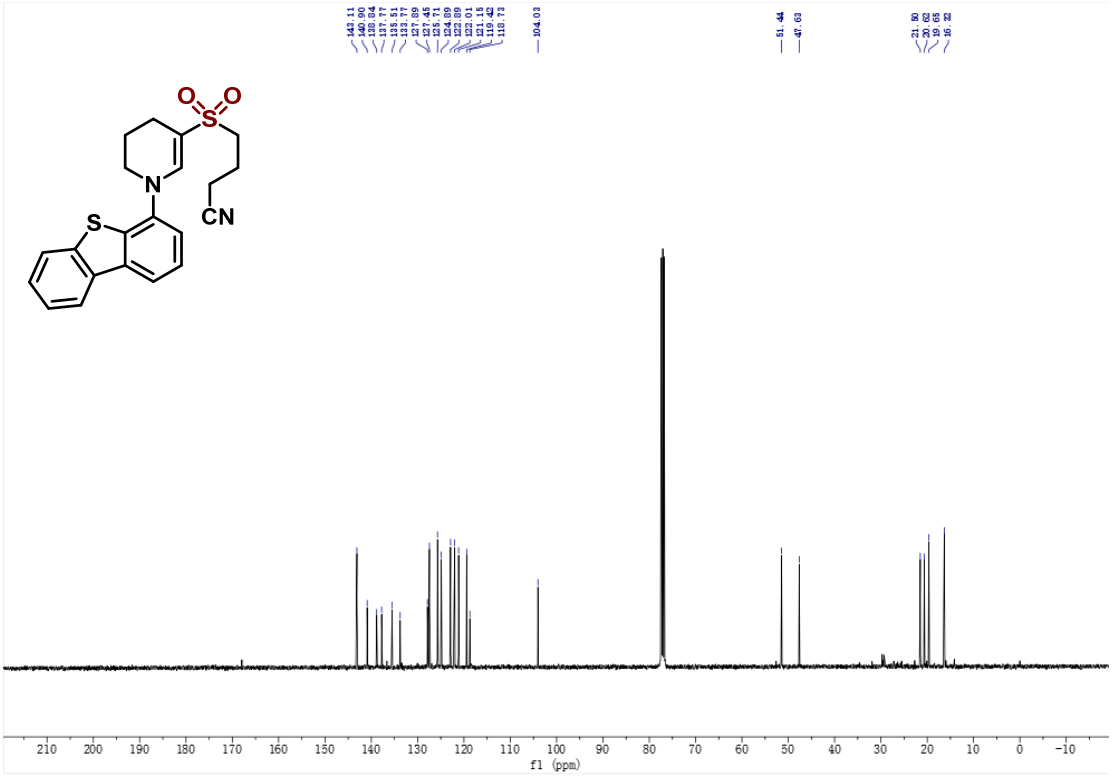
^{13}C NMR spectrum of compound **3s** (100 MHz, $CDCl_3$)



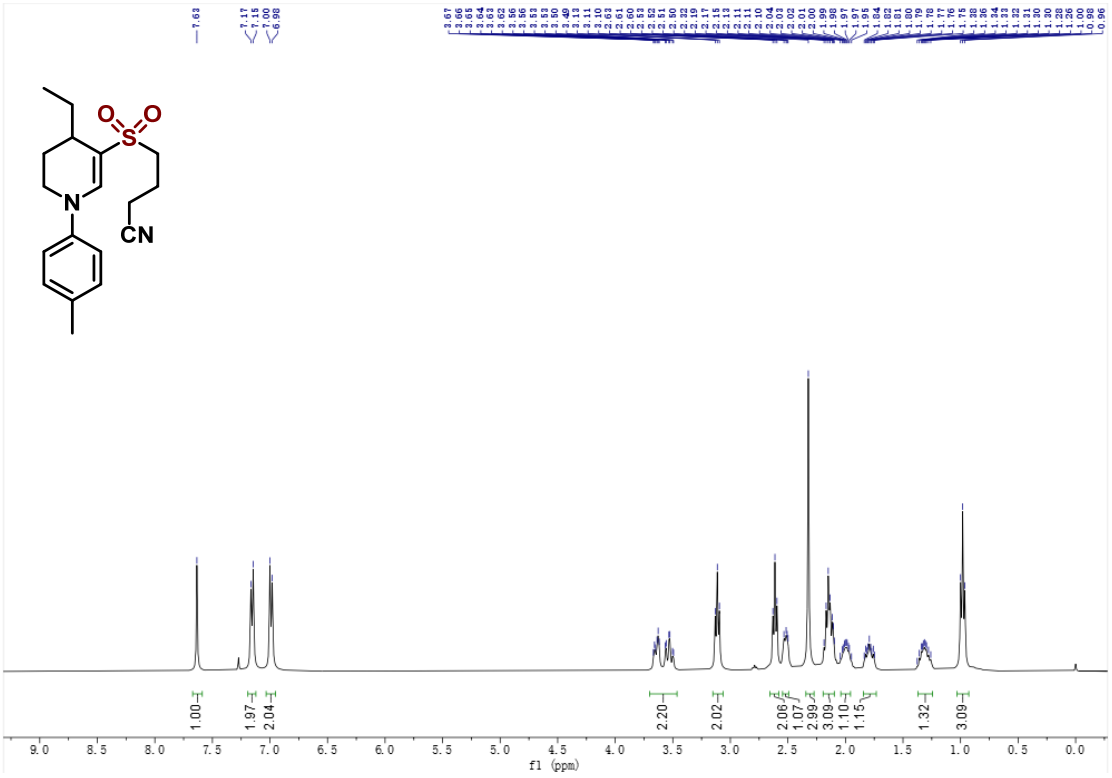
^{1}H NMR spectra of compound **3t** (400MHz, $CDCl_3$)



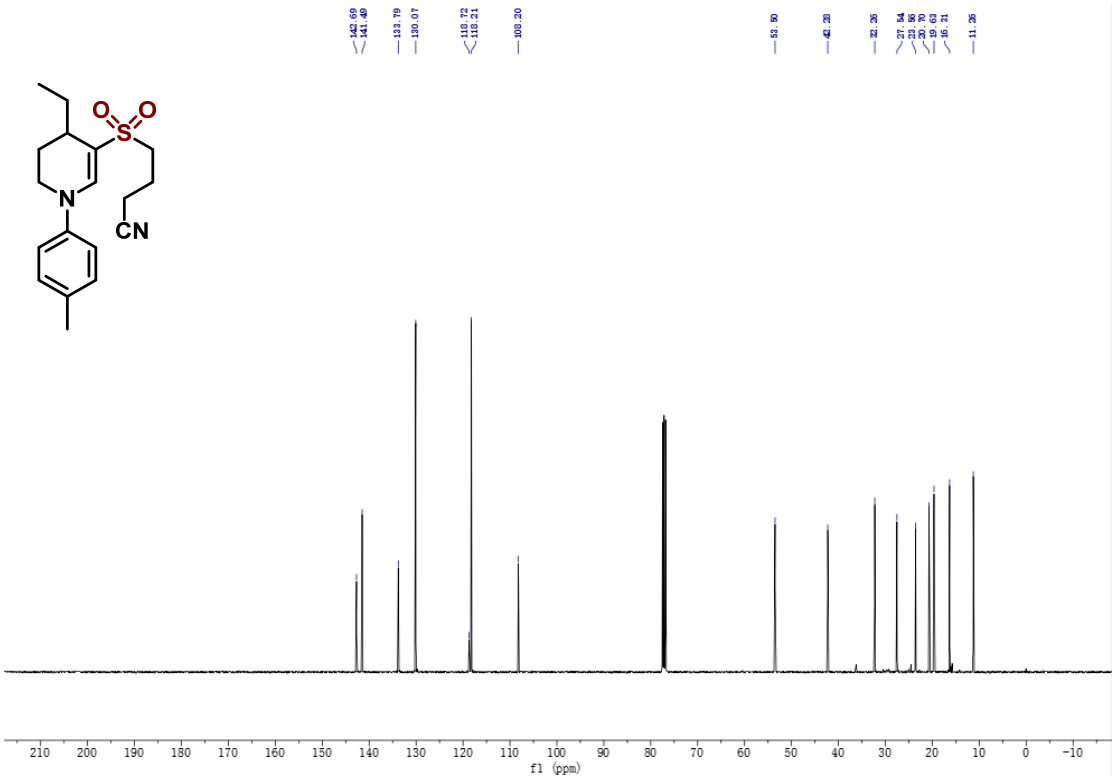
^{13}C NMR spectrum of compound **3t** (100 MHz, $CDCl_3$)



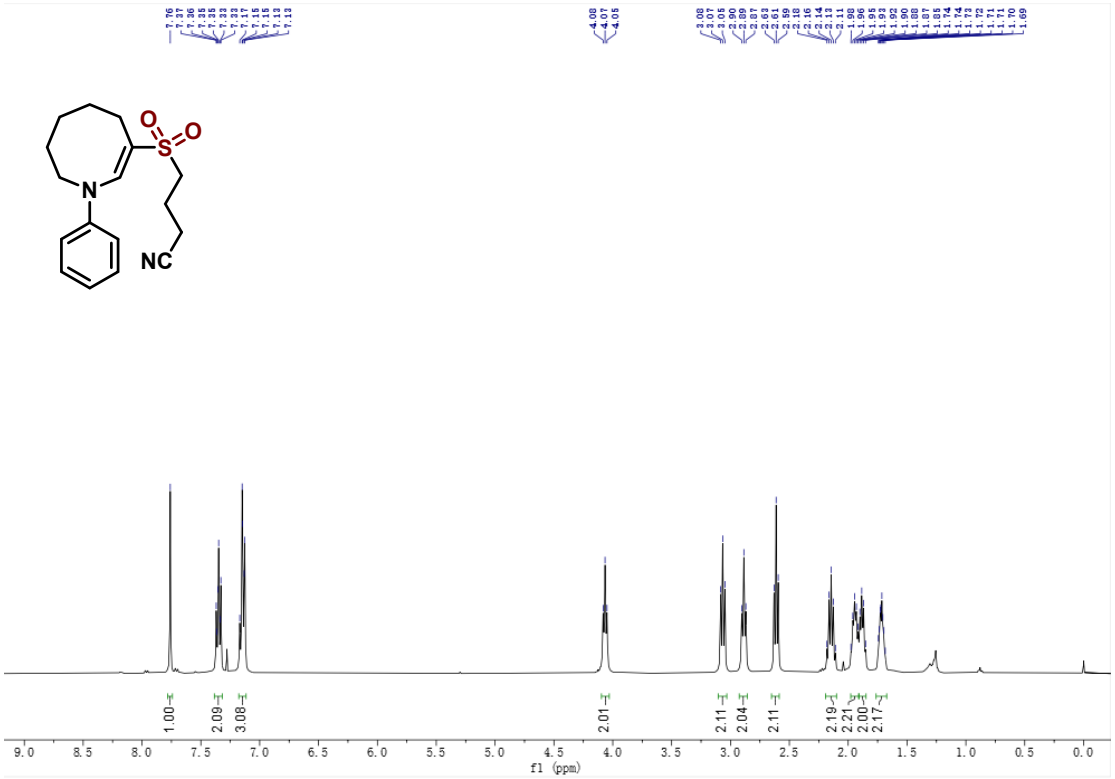
^{1}H NMR spectra of compound **3u** (400MHz, $CDCl_3$)



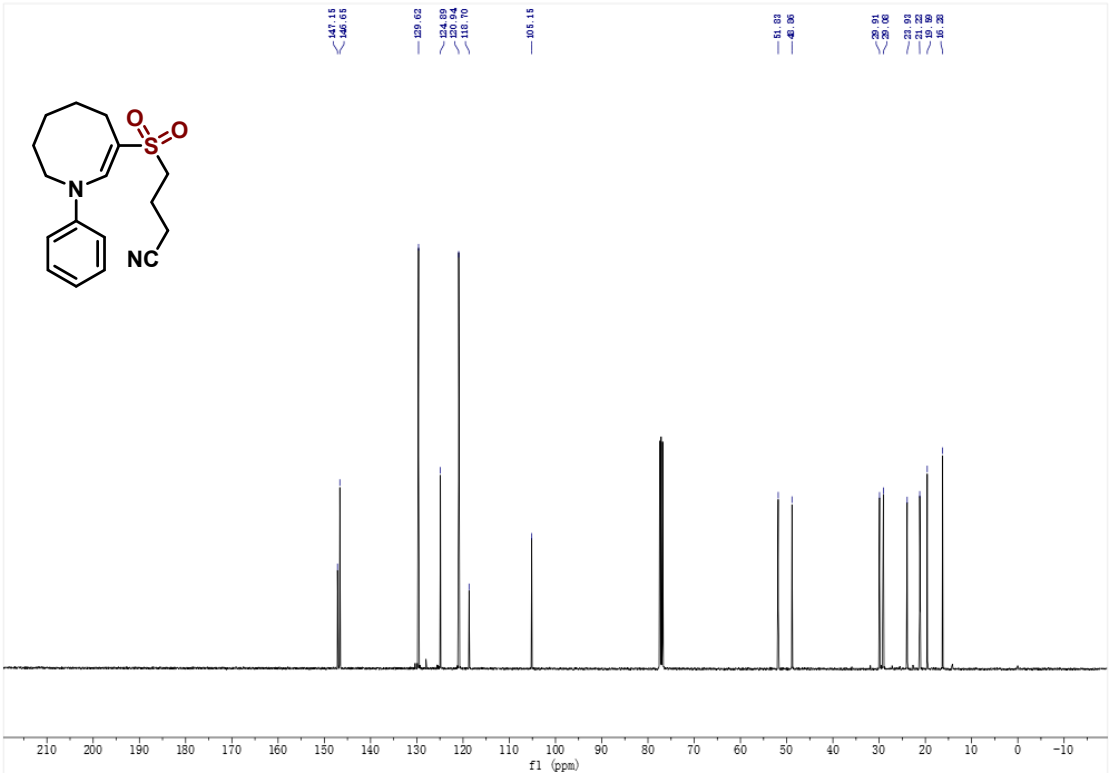
^{13}C NMR spectrum of compound **3u** (100 MHz, $CDCl_3$)



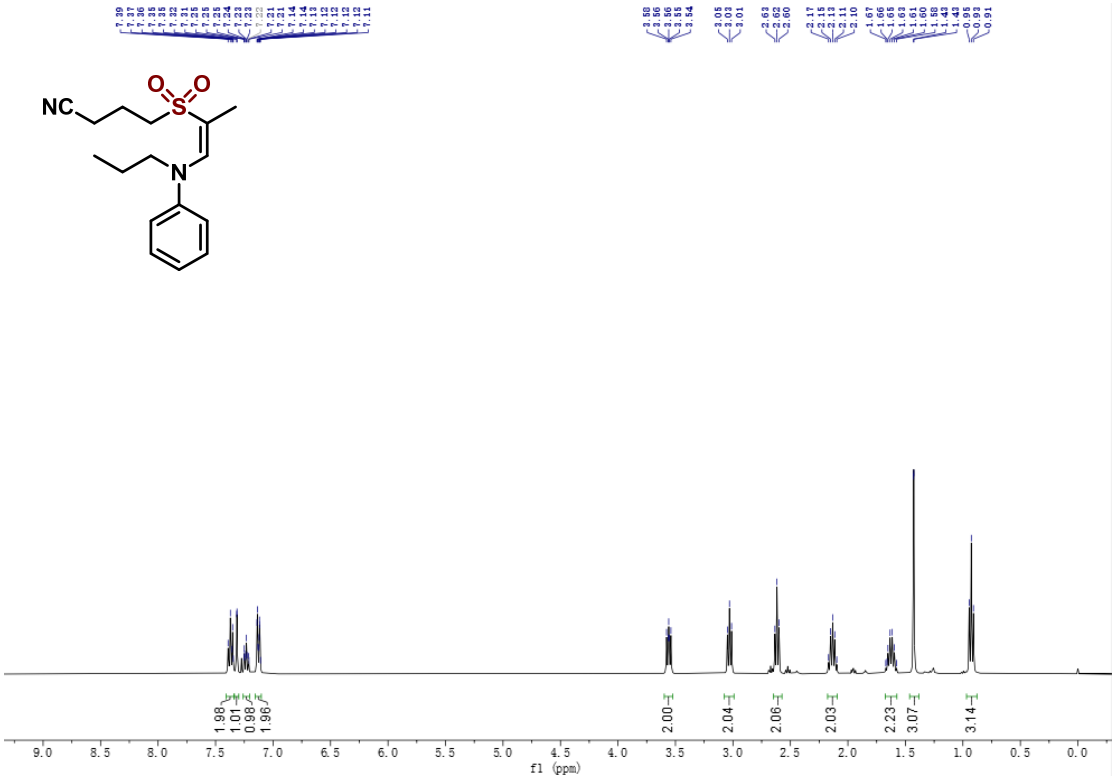
^{1}H NMR spectra of compound **3v** (400MHz, $CDCl_3$)



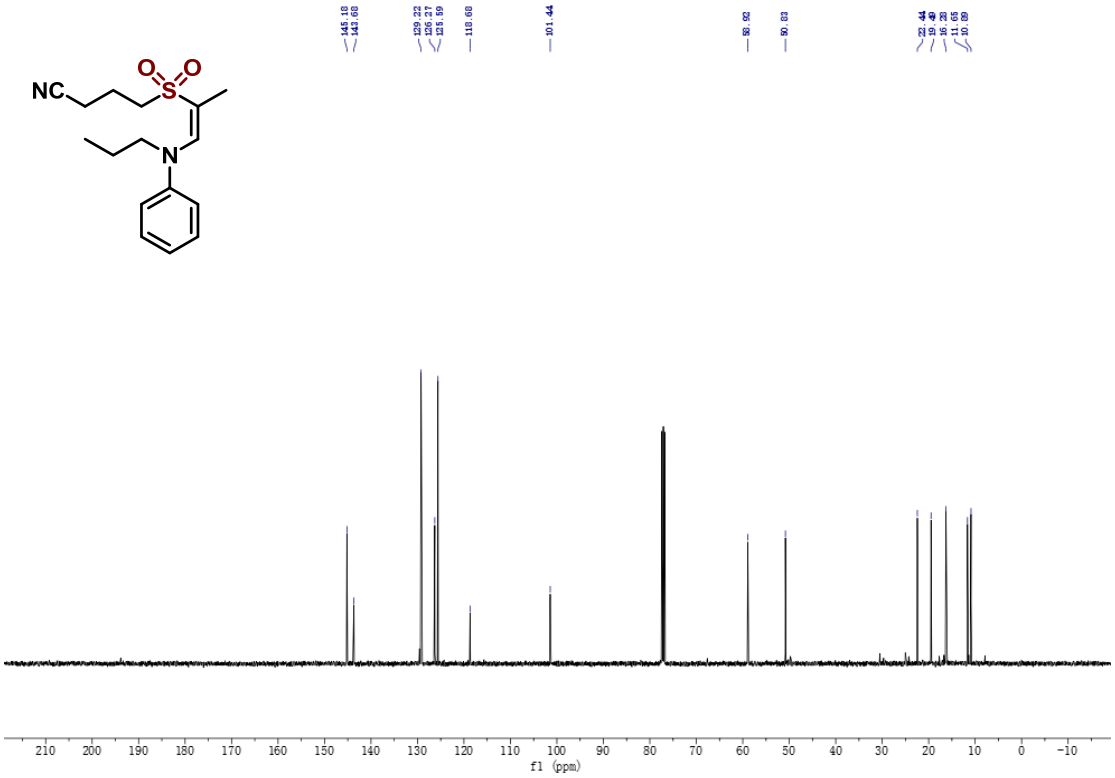
^{13}C NMR spectrum of compound **3v** (100 MHz, $CDCl_3$)



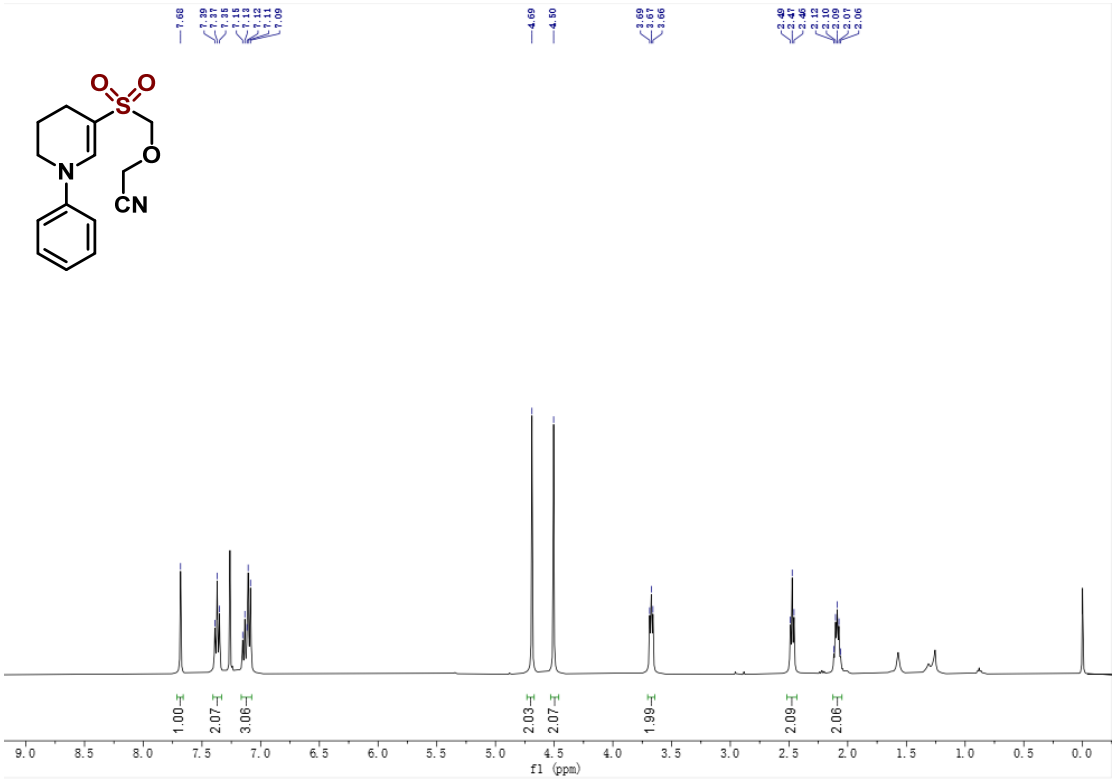
^{1}H NMR spectra of compound **3w** (400MHz, $CDCl_3$)



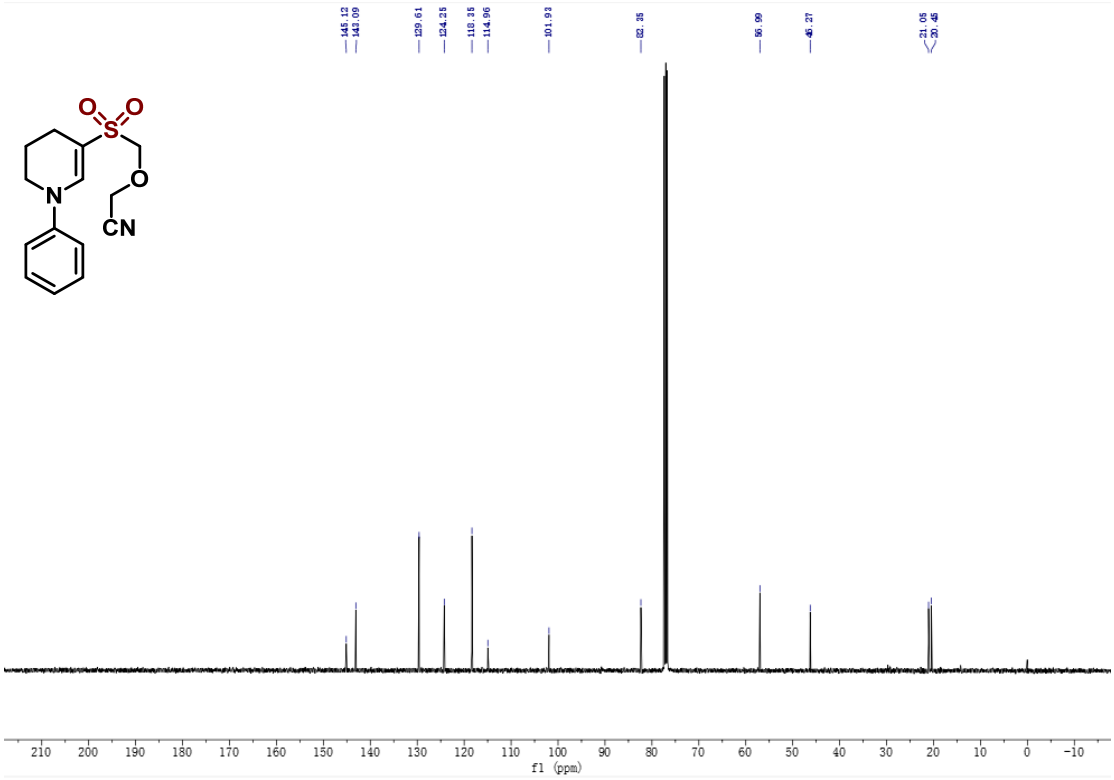
^{13}C NMR spectrum of compound **3w** (100 MHz, $CDCl_3$)



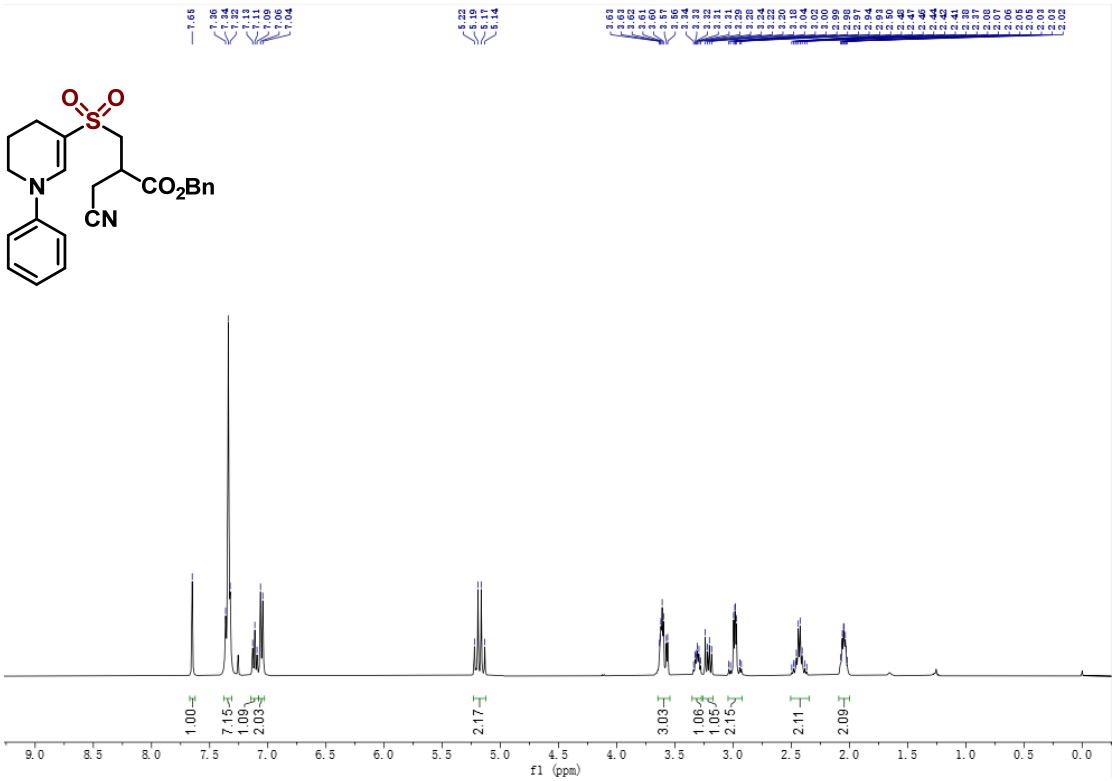
^{1}H NMR spectra of compound **3x** (400MHz, $CDCl_3$)



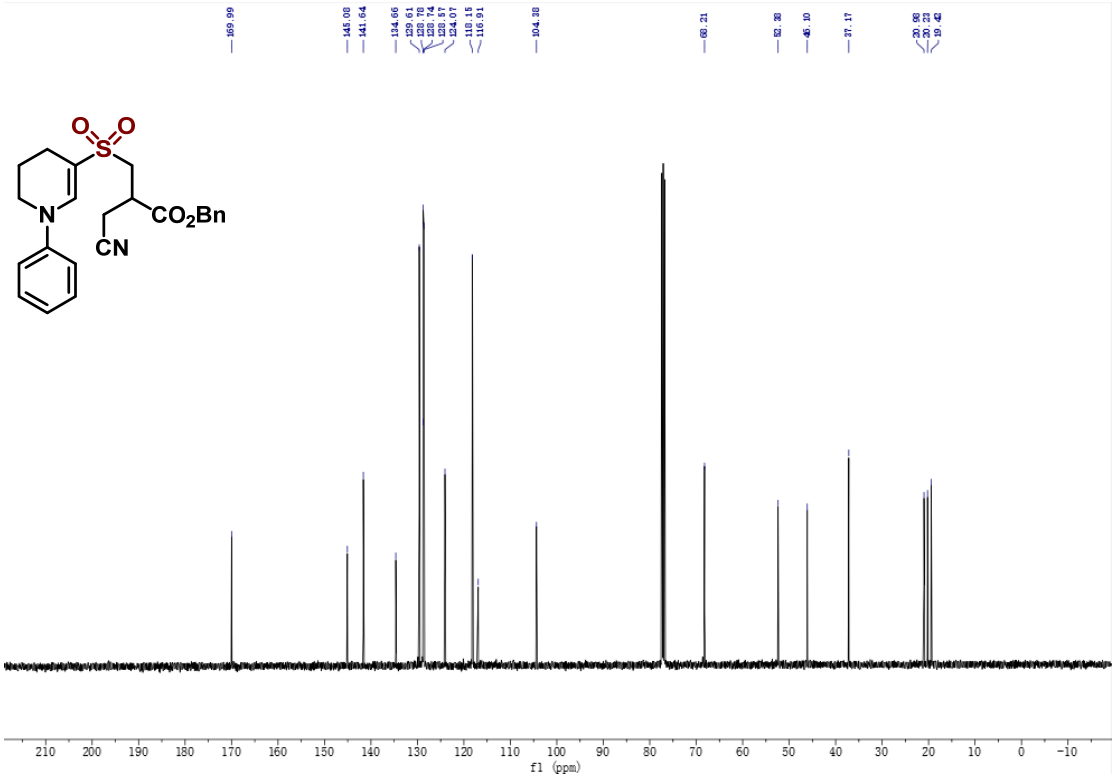
^{13}C NMR spectrum of compound **3x** (100 MHz, $CDCl_3$)



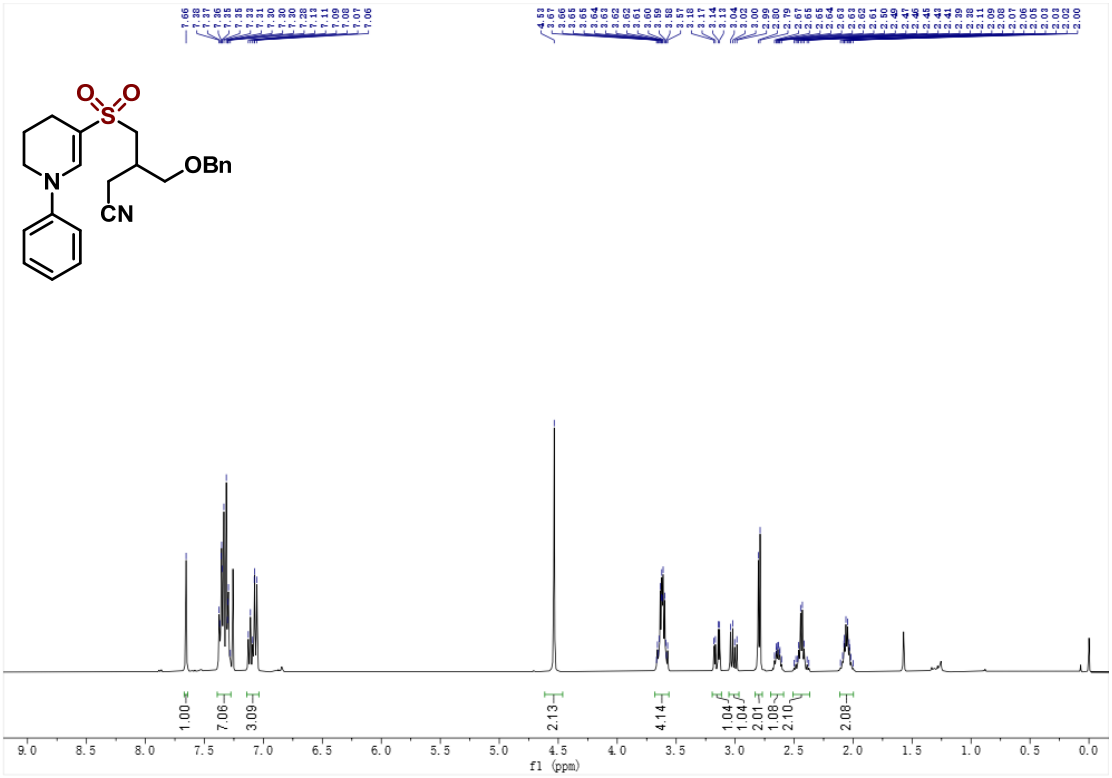
^{1}H NMR spectra of compound **3y** (400MHz, $CDCl_3$)



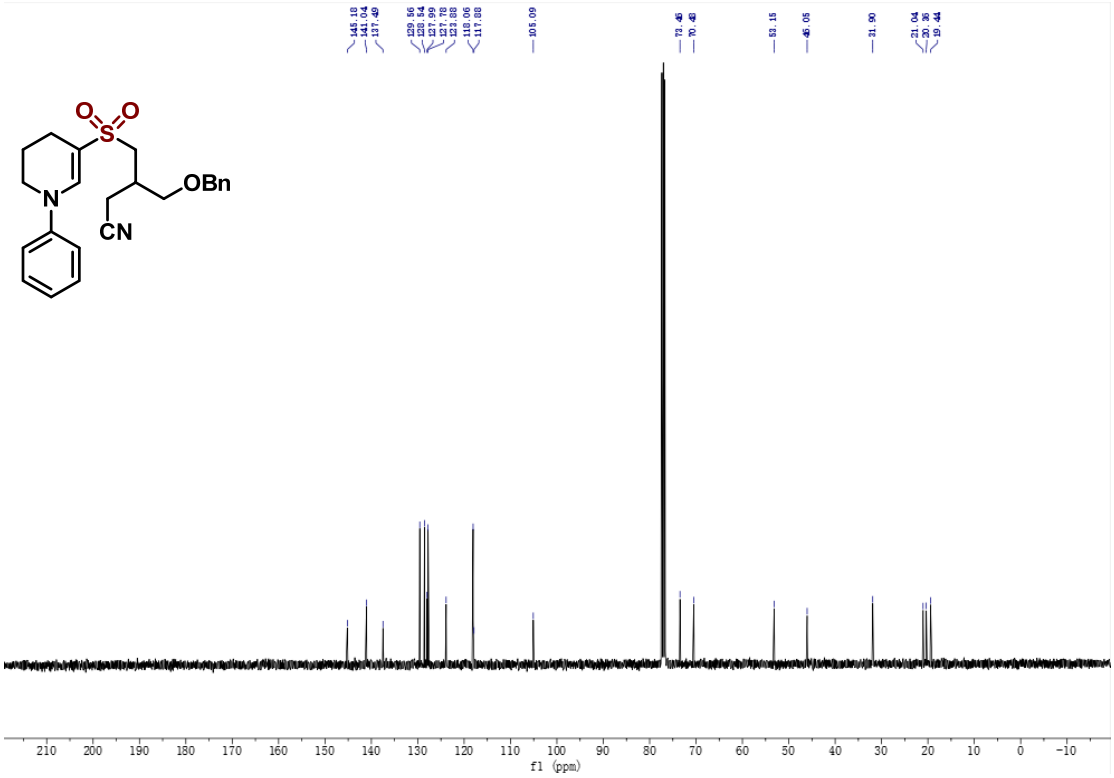
^{13}C NMR spectrum of compound **3y** (100 MHz, $CDCl_3$)



^{1}H NMR spectra of compound **3z** (400MHz, $CDCl_3$)



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



7. Crystallographic details of 3u

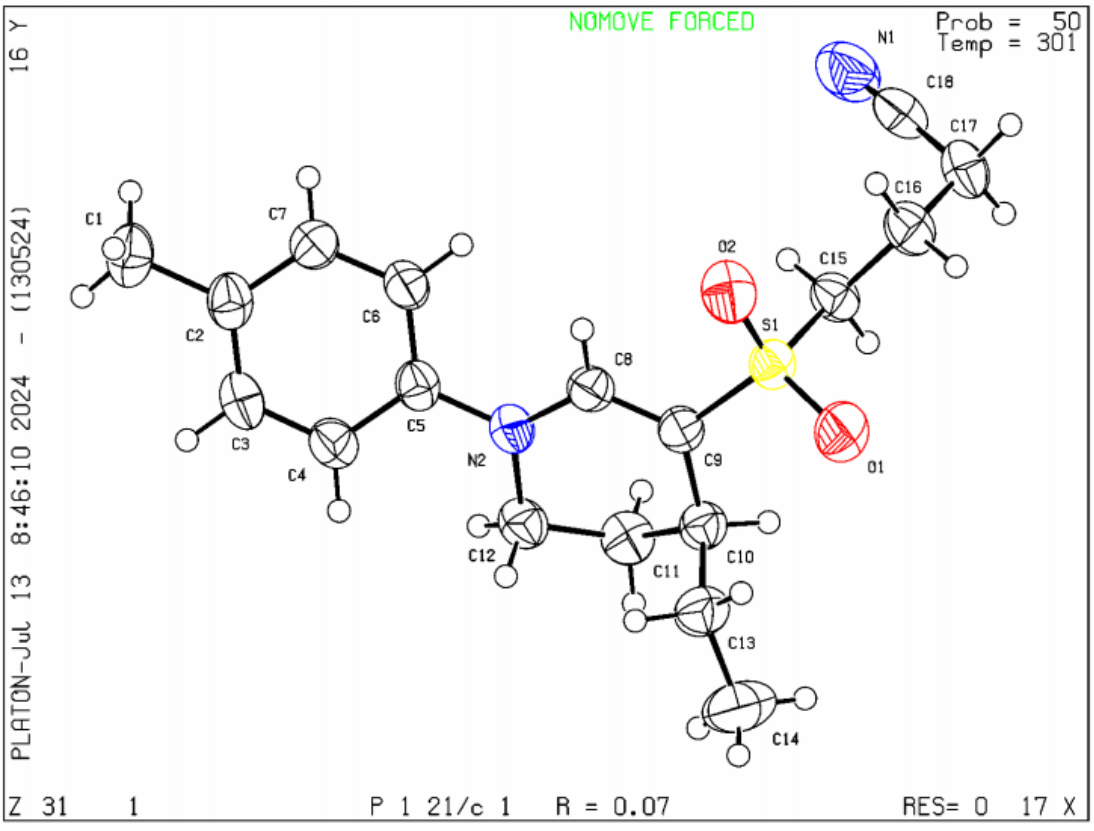


Table S1 Crystal data and structure refinement for 3u.

Bond precision:	C-C = 0.0042 A	Wavelength = 0.71073	
Cell:	a = 16.2169(15)	b = 10.9188(10)	c = 10.4535(10)
	alpha = 90	beta = 107.393(3)	gamma = 90
Temperature	301 K		
	Calculated	Reported	
Volume	1766.4(3)	1766.4(3)	
Space group	P 21/c	P 1 21/c 1	
Hall group	-P 2ybc	-P 2ybc	
Sum formula	C18 H24 N2 O2 S	C18 H24 N2 O2 S	
Mr	332.45	332.45	
Dx, g cm-3	1.250	1.250	
Z	4	4	
Mu (mm-1)	0.194	0.194	
F000	712.0	712.0	
F000’	712.76		
h, k, 1max	21,14,13	21,14,13	
Nref	4404	4377	
Tmin, Tmax	0.956,0.960	0.616,0.746	
Tmin’	0.956		

Correction method = # Reported T Limits: Tmin=0.616 Tmax=0.746

Data completeness = 0.994 Theta (max) = 28.336

R (reflections) 0.0737(3231) wR2 (reflections) = 0.2125(4377)

S = 1.069 Npar = 210