Electronic Supplementary Material (ESI) for Green Chemistry.

Synthesis of α cyanato-α'-carbonyl Sulfoxonium Ylides in Water

Qingyao Zhang,† Cankun Luo,† Ruizhi Lai, Zhiqian Lin, Pengfei Jia, Shuran Xu, Li Guo and Yong Wu*

Key Laboratory of Drug-Targeting and Drug Delivery System of the Education Ministry, Sichuan Engineering Laboratory for Plant-Sourced Drug and Sichuan Research Center for Drug Precision Industrial Technology, West China School of Pharmacy, Sichuan University, Chengdu, 610041 (P. R. China)

†These authors contributed equally.

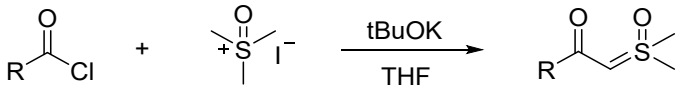
Table of Contents

1 General Information

Unless noted, all reactions were carried out in single necked flask with magnetic stirring under an atmosphere of air. Solvents used were of analytical purity. All the reactions were monitored by thin-layer chromatography (TLC) and were visualized using UV light and Iodine. The product purification was done using silica gel column chromatography. Thin-layer chromatography (TLC) characterization was performed with precoated silica gel GF254 (0.2mm), while column chromatography characterization was performed with silica gel (200-300 mesh). NMR spectra were recorded on a Varian spectrometer (400 or 600 MHz for ^{1}H, 100 or 150 MHz for ^{13}C and 376 MHz for ^{19}F). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^{1}H NMR and chloroform-*d* (δ 77.1) or DMSO-d_6 (δ 39.5) for ^{13}C NMR. Coupling constants were given in Hz. HRMS spectra were recorded on a Waters Q-TOF Premier. Melting points were measured with YRT-3 melting point apparatus (Shantou Keyi Instrument &Equipment Co., Ltd., Shantou, China).

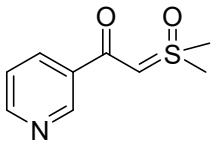
2 Experimental section

2.1 Preparation of sulfoxonium ylides 1a-28a[1, 2]



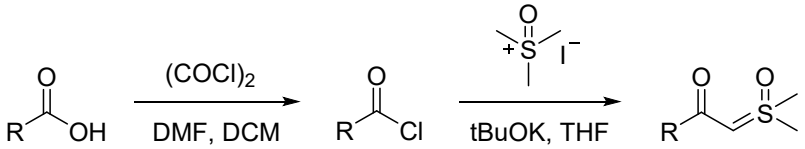
To a stirred solution of potassium tert-butoxide (1.0 g, 9.1 mmol) in THF (10 mL) was added trimethylsulfoxonium iodide (1.5 g, 6.9 mmol) at room temperature. The resulting mixture was refluxed for 3 h under argon. Then the reaction mixture was cooled to 0 °C, followed by addition of acylchlorides (2.3 mmol) in THF (2 mL). The reaction allowed to warm to room temperature and stirred for 3 h. After the solvent was evaporated, water (20 mL) and ethyl acetate (20 mL) were added to the residual crude product. The aqueous layer was separated and washed with ethyl acetate (3 × 20 mL) and the organic layers were combined. The organic solution was dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by column chromatography on silica gel. Sulfoxonium ylides **1a-21a, 23a-28a** were afforded in 65-98% yields according to this method.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1-(pyridin-3-yl)ethan-1-one (22a)



To a mixture of potassium tert-butoxide (3.03 g, 27 mmol) and anhydrous THF (55 mL) was added dried trimethylsulfoxonium chloride (3.47 g, 27 mmol) and the resulting mixture refluxed for 3 h under argon. The resulting mixture was cooled to 0 °C and to the mixture was added dropwise a solution of nicotinoyl chloride hydrochloride (1.6 g, 9 mmol), NEt_3 (1.26 mL, 9 mmol), and anhydrous THF (10 mL) which had been pre-stirred for 1 h at ambient temperature. The resulting mixture was warmed to ambient temperature and stirred for 72 h under argon. The resulting mixture was filtered through Celite and concentrated under reduced pressure to give an orange oil (3.3 g). The resulting residue was purified by automated flash column chromatography. The appropriate fractions were combined and concentrated to give **22a** as a off-white solid (460 mg) of sufficient purity to be used in the subsequent reactions without purification.

2.2 Preparation of sulfoxonium ylides 29a-32a[3]

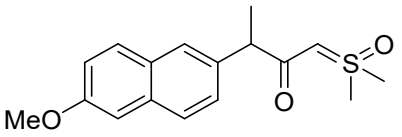


Step-I: To a stirred solution of a carboxylic acid (10 mmol) and DMF (2 drops) in CH_2Cl_2 (40 mL), $(COCl)_2$ (20 mmol, 1.8 mL) was added dropwise. The reaction was allowed to stir at room temperature overnight. Evaporation of the reaction mixture gave a residue which was dissolved in THF (20 mL). The resulting solution was used as acid chloride solution in subsequent reactions.

Step-II: To a stirred solution of potassium tert-butoxide (40 mmol, 4.5 g) in dry THF (40 mL), trimethylsulfoxonium iodide (30 mmol, 6.6 g) was added and the reaction was allowed to reflux for 3 h under argon. The reaction mixture was cooled to 0 °C and the solution of the acid chloride (obtained by **step-I**) was added dropwise to it. Then, the reaction was allowed to stir at room temperature for additional 3 h. After completion, 20 mL of water was added to the reaction mixture and the organic part was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with brine (20 mL) and water (10 mL). The organic solution was dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified on silica gel column

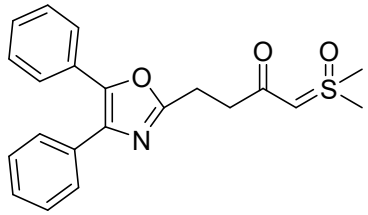
chromatography to afford sulfoxonium ylides **29a, 31a, 32a**. Sulfoxonium ylide **30a** does not require purification for the next step of synthesis .

1-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(6-methoxynaphthalen-2-yl)butan-2-one (29a)



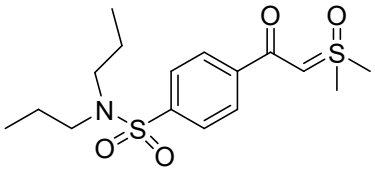
Yield: 85% (2.6 g). Yellow solid, m.p.: 115.1-116.7 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.71 – 7.63 (m, 3H), 7.40 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.14 – 7.09 (m, 2H), 4.31 (s, 1H), 3.89 (s, 3H), 3.64 (q, *J* = 7.1 Hz, 1H), 3.27 (d, *J* = 18.4 Hz, 6H), 1.51 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 192.1, 157.3, 138.4, 133.4, 129.2, 129.0, 126.8, 126.8, 125.8, 118.6, 105.6, 69.4, 55.3, 50.3, 42.0, 41.9, 18.3.

1-(dimethyl(oxo)-λ^6-sulfaneylidene)-4-(4,5-diphenyloxazol-2-yl)butan-2-one (31a)



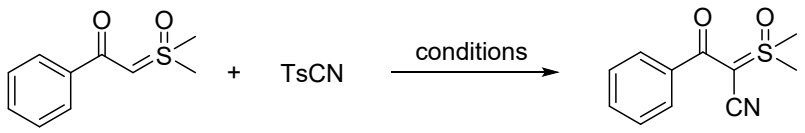
Yield: 72% (2.63 g). Yellow solid, m.p.: 137.1-139.0 °C. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 7.0 Hz, 2H), 7.55 (d, *J* = 7.0 Hz, 2H), 7.36 – 7.27 (m, 6H), 4.45 (s, 1H), 3.34 (s, 6H), 3.13 (t, *J* = 7.8 Hz, 2H), 2.72 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 188.0, 163.0, 145.1, 135.0, 132.6, 129.1, 128.6, 128.5, 128.3, 128.0, 127.9, 126.4, 69.5, 42.1, 37.2, 24.2.

4-(2-(dimethyl(oxo)-λ^6-sulfaneylidene)acetyl)-*N*,*N*-dipropylbenzenesulfonamide (32a)



Yield: 75% (2.71 g). Yellow solid, m.p.: 110.5-112.0 °C. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 5.05 (s, 1H), 3.49 (s, 6H), 3.05 – 2.96 (m, 4H), 1.51 – 1.41 (m, 4H), 0.84 – 0.74 (m, 6H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 180.3, 142.5, 141.6, 127.2, 126.8, 70.5, 49.9, 42.0, 21.9, 11.1.

2.3 Optimization of the reaction conditions[a]



1a **1b**

entry	catalyst	solvent	t (h)	eq of TsCN	yield (%)[b]
1	$B(C_6F_5)_3$	Tol	12	2	64
2	-	Tol	12	2	40
3	-	Tol	24	2	50
4	-	THF	24	2	57
5	-	iPrOH	24	2	47
6	-	MeCN	24	2	28
7	-	$CHCl_3$	24	2	90
8	-	EA	24	2	49
9	-	DMF	24	2	56
10	-	Acetone	24	2	88
11	-	DMSO	24	2	90
12	-	EtOH	24	2	30
13	-	DCE	24	2	51
14	-	H_2O	24	2	93
15	-	H_2O	24	1.1	83
16	-	H_2O	24	1.2	84
17	-	H_2O	24	1.5	92

[a] Reaction conditions: **1a** (0.2 mmol), TsCN, catalyst (5 mol%) in 2 mL of solvent at 60 °C under air.

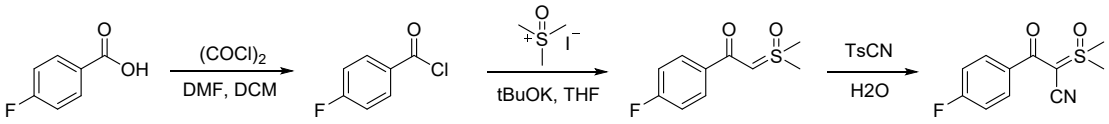
[b] Isolated yields after chromatography on silica gel.

2.4 Typical procedure for the reaction

To a 10 mL glass vial equipped with a magnetic stir bar was added the sulfoxonium ylide **1a** (0.2 mmol), TsCN (0.3 mmol). Then 2 mL H_2O was added and the mixture was stirred at 60 °C for 24 h determined by TLC. Afterwards, it was extracted with EA, and the organic layers were combined.

The organic solution was dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by silica gel chromatography using PE/EA.

2.5 Convertion from Carboxylic Acid to α-cyanato-α'-carbonyl Sulfoxonium Ylide 8b.



Step-I: To a stirred solution of a carboxylic acid (10 mol) and DMF (2 drops) in CH_2Cl_2 (40 mL), $(COCl)_2$ (20 mmol, 1.8 mL) was added dropwise. The reaction was allowed to stir at room temperature overnight. Evaporation of the reaction mixture gave a residue which was dissolved in THF (20 mL). The resulting solution was used as acid chloride solution in subsequent reactions.

Step-II: To a stirred solution of potassium tert-butoxide (40 mmol, 4.5 g) in dry THF (40 mL), trimethylsulfoxonium iodide (30 mmol, 6.6 g) was added and the reaction was allowed to reflux for 3 h under argon. The reaction mixture was cooled to 0 °C and the solution of the acid chloride (obtained by **step-I**) was added dropwise to it. Then, the reaction was allowed to stir at room temperature for additional 3 h. After completion, the mixture was filtered through a plug of celite (elution EA). Evaporation of the filtrate gave the crude product and no further purification was required for the next step of synthesis .

Step-III: To a 150 mL flask equipped with a magnetic stir bar was added the sulfoxonium ylide (obtained by **step-II**), TsCN (15 mmol, 2.72 g). Then 75 mL H_2O was added and the mixture was stirred at 60 °C for 24 h determined by TLC. Afterwards, it was extracted with EA, and the organic layers were combined. The organic solution was dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by silica gel chromatography using PE/EA to give the desired product **8b** in 81% (1.93 g, white solid).

2.6 Reference

1 J. Li, H. He, M. Huang, Y. Chen, Y. Luo, K. Yan, Q. Wang and Y. Wu, *Org. Lett.*, 2019, **21**, 9005-9008.

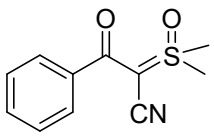
2 S. Hassell-Hart, E. Speranzini, S. Srikwanjai, E. Hossack, S. M. Roe, D. Fearon, D. Akinbosede, S. Hare and J. Spencer, *Org. Lett.*, 2022, **24**, 7924-7927.

3 S. Saha, B. Debnath, K. Talukdar, P. Karjee, S. Mandal and T. Punniyamurthy, *Org. Lett.*, 2023,

25, 3352-3357.

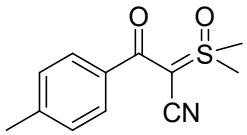
3 Characterization data for the products

2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxo-3-phenylpropanenitrile (1b)



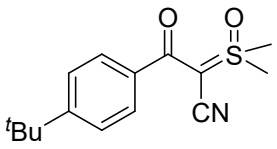
Yield: 92% (40.5 mg). White solid, m.p.: 159.1-161.0 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.79 – 7.71 (m, 2H), 7.57 – 7.51 (m, 1H), 7.51 – 7.45 (m, 2H), 3.83 (s, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 185.0, 138.1, 131.4, 128.2, 127.3, 117.0, 71.8, 40.4. **HRMS (ESI)** calculated for $C_{11}H_{12}NO_2S$ $[M+H]^+$ 222.0583, Found 222.0584.

2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxo-3-(*p*-tolyl)propanenitrile (2b)



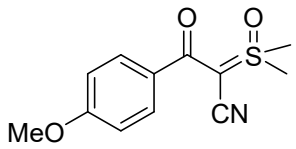
Yield: 88% (41.5 mg). White solid, m.p.: 153.1-154.5 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 3.63 (s, 6H), 2.36 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 186.3, 142.7, 134.6, 129.0, 127.9, 116.5, 70.1, 42.1, 21.6. **HRMS (ESI)** calculated for $C_{12}H_{14}NO_2S$ $[M+H]^+$ 236.0740, Found 236.0741.

3-(4-(*tert*-butyl)phenyl)-2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxopropanenitrile (3b)



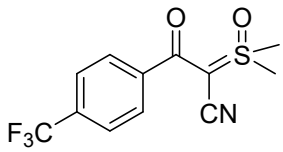
Yield: 92% (50.8 mg). Light yellow solid, m.p.: 148.4-150.2 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 3.63 (s, 6H), 1.30 (s, 9H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 186.2, 155.7, 134.5, 127.8, 125.3, 116.6, 70.0, 42.2, 35.0, 31.1. **HRMS (ESI)** calculated for $C_{15}H_{20}NO_2S$ $[M+H]^+$ 278.1209, Found 278.1207.

2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-(4-methoxyphenyl)-3-oxopropanenitrile (4b)



Yield: 90% (45 mg). White solid, m.p.: 145.1-147.0 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.84 (s, 3H), 3.65 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 185.3, 162.7, 130.0, 129.7, 116.5, 113.6, 69.4, 55.4, 42.4. **HRMS (ESI)** calculated for $C_{12}H_{14}NO_3S$ $[M+H]^+$ 252.0689, Found 252.0690.

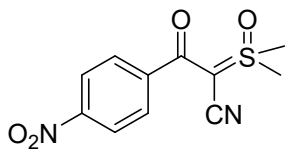
2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxo-3-(4-(trifluoromethyl)phenyl)propanenitrile (5b)



Yield: 88% (50.8 mg). White solid, m.p.: 153.7-155.2 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 3.61 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 185.0, 140.3, 133.4

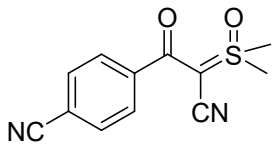
(q, *J* = 32.8 Hz), 128.3, 125.4 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 270.7 Hz), 115.7, 70.9, 42.1. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -62.98. **HRMS (ESI)** calculated for $C_{12}H_{11}F_3NO_2S$ $[M+H]^+$ 290.0457, Found 290.0456.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(4-nitrophenyl)-3-oxopropanenitrile (6b)



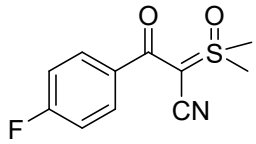
Yield: 96% (51.1 mg). Yellow solid, m.p.: 207.2-209.0 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.32 (d, *J* = 8.8 Hz, 2H), 7.93 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 183.2, 148.8, 143.6, 128.7, 123.6, 116.4, 72.9, 40.3. **HRMS (ESI)** calculated for $C_{11}H_{11}N_2O_4S$ $[M+H]^+$ 267.0434, Found 267.0437.

4-(2-cyano-2-(dimethyl(oxo)-λ^6-sulfaneylidene)acetyl)benzonitrile (7b)



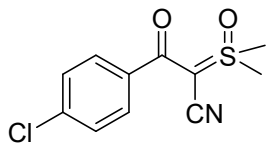
Yield: 97% (47.7 mg). White solid, m.p.: 203.4-204.8 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.97 (d, *J* = 7.9 Hz, 2H), 7.85 (d, *J* = 8.0 Hz, 2H), 3.85 (s, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 183.4, 142.0, 132.4, 128.0, 118.2, 116.4, 113.6, 72.6, 40.3. **HRMS (ESI)** calculated for $C_{12}H_{11}N_2O_2S$ $[M+H]^+$ 247.0536, Found 247.0537.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(4-fluorophenyl)-3-oxopropanenitrile (8b)



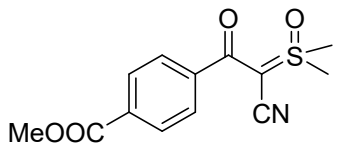
Yield: 95% (45.2 mg). White solid, m.p.: 160.0-161.2 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ7.98 – 7.90 (m, 2H), 7.15 – 7.06 (m, 2H), 3.67 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 184.9, 165.0 (d, *J* = 253.2 Hz), 133.33 (d, *J* = 3.1 Hz), 130.4 (d, *J* = 9.1 Hz), 116.1, 115.5 (d, *J* = 21.9 Hz), 70.0, 42.3. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -106.59. **HRMS (ESI)** calculated for $C_{11}H_{11}FNO_2S$ $[M+H]^+$ 240.0489, Found 240.0487.

3-(4-chlorophenyl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (9b)



Yield: 75% (38 mg). White solid, m.p.: 146.7-148.5 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 3.66 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 185.0, 138.3, 135.5, 129.3, 128.6, 116.0, 70.3, 42.2. **HRMS (ESI)** calculated for $C_{11}H_{11}ClNO_2S$ $[M+H]^+$ 256.0194, Found 256.0191.

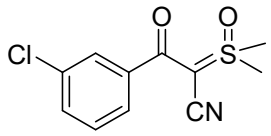
methyl 4-(2-cyano-2-(dimethyl(oxo)-λ^6-sulfaneylidene)acetyl)benzoate (10b)



Yield: 83% (46.1 mg). White solid, m.p.: 154.0-155.7 °C. **^{1}H NMR**

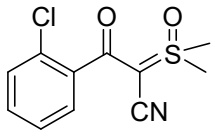
(400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.1 Hz, 2H), 3.92 (s, 3H), 3.68 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 185.5, 166.3, 140.9, 133.0, 129.6, 127.8, 115.7, 70.9, 52.4, 42.1. **HRMS (ESI)** calculated for $C_{13}H_{14}NO_4S$ $[M+H]^+$ 280.0638, Found 280.0640.

3-(3-chlorophenyl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (11b)



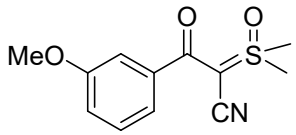
Yield: 78% (39.8 mg). White solid, m.p.: 134.3-136.1 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.83 – 7.73 (m, 2H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 3.65 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 184.8, 138.9, 134.5, 132.0, 129.7, 127.9, 126.0, 115.9, 70.7, 42.0. **HRMS (ESI)** calculated for $C_{11}H_{11}ClNO_2S$ $[M+H]^+$ 256.0194, Found 256.0192.

3-(2-chlorophenyl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (12b)



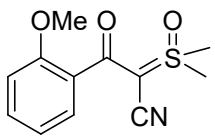
Yield: 90% (45.9 mg). White solid, m.p.: 126.5-127.8 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.41 (ddd, *J* = 7.2, 4.9, 1.8 Hz, 2H), 7.33 (dtd, *J* = 17.6, 7.3, 1.7 Hz, 2H), 3.65 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 186.1, 138.0, 131.2, 130.5, 130.1, 128.3, 127.0, 115.0, 72.3, 41.8. **HRMS (ESI)** calculated for $C_{11}H_{11}ClNO_2S$ $[M+H]^+$ 256.0194, Found 256.0195.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(3-methoxyphenyl)-3-oxopropanenitrile (13b)



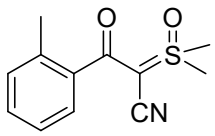
Yield: 96% (48 mg). White solid, m.p.: 77.1-78.9 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 7.7 Hz, 1H), 7.36 (t, *J* = 2.1 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.02 (dd, *J* = 8.3, 2.7 Hz, 1H), 3.81 (s, 3H), 3.63 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 186.2, 159.5, 138.5, 129.4, 120.3, 118.5, 116.3, 112.5, 70.5, 55.5, 42.1. **HRMS (ESI)** calculated for $C_{12}H_{14}NO_3S$ $[M+H]^+$ 252.0689, Found 252.0685.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(2-methoxyphenyl)-3-oxopropanenitrile (14b)



Yield: 97% (48.8 mg). White solid, m.p.: 150.0-152.6 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.44 – 7.36 (m, 2H), 7.01 – 6.92 (m, 2H), 3.88 (s, 3H), 3.65 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 187.0, 156.7, 132.1, 128.9, 128.1, 120.5, 115.5, 111.5, 72.0, 55.7, 42.1. **HRMS (ESI)** calculated for $C_{12}H_{14}NO_3S$ $[M+H]^+$ 252.0689, Found 252.0688.

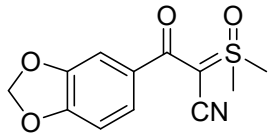
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-3-(o-tolyl)propanenitrile (15b)



Yield: 97% (45.7 mg). White solid, m.p.: 158.2-159.1 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.44 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.32 (td, *J* = 7.5, 1.5 Hz, 1H),

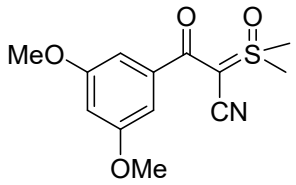
7.25 – 7.19 (m, 2H), 3.66 (s, 6H), 2.41 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 189.9, 138.1, 135.4, 131.0, 130.3, 127.2, 125.6, 115.5, 71.7, 42.0, 19.4. **HRMS (ESI)** calculated for $C_{12}H_{14}NO_2S$ $[M+H]^+$ 236.0740, Found 236.0739.

3-(benzo[*d*][1,3]dioxol-5-yl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (16b)



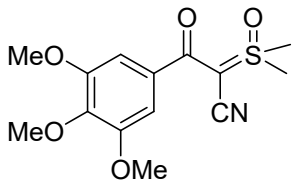
Yield: 91% (48.2 mg). White solid, m.p.: 95.1-97.0 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.39 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.24 (d, *J* = 1.7 Hz, 1H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.11 (s, 2H), 3.80 (s, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 183.5, 149.9, 147.1, 132.0, 122.7, 117.2, 107.8, 107.5, 101.7, 71.2, 40.5. **HRMS (ESI)** calculated for $C_{12}H_{12}NO_4S$ $[M+H]^+$ 266.0482, Found 266.0483.

3-(3,5-dimethoxyphenyl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (17b)



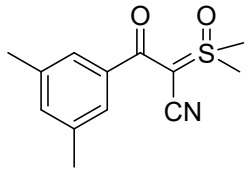
Yield: 95% (53.2 mg). White solid, m.p.: 156.0-157.5 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.00 (d, *J* = 2.3 Hz, 2H), 6.56 (t, *J* = 2.3 Hz, 1H), 3.78 (s, 6H), 3.63 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 186.0, 160.6, 139.0, 116.2, 105.6, 104.7, 70.6, 55.6, 42.0. **HRMS (ESI)** calculated for $C_{13}H_{16}NO_4S$ $[M+H]^+$ 282.0795, Found 282.0796.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-3-(3,4,5-trimethoxyphenyl)propanenitrile (18b)



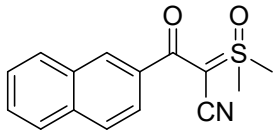
Yield: 94% (58.3 mg). White solid, m.p.: 126.1-127.5 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.17 (s, 2H), 3.85 (s, 6H), 3.84 (s, 3H), 3.63 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 185.2, 152.7, 141.2, 132.0, 116.3, 105.4, 70.1, 60.8, 56.2, 42.1. **HRMS (ESI)** calculated for $C_{14}H_{18}NO_5S$ $[M+H]^+$ 312.0900, Found 312.0901.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(3,5-dimethylphenyl)-3-oxopropanenitrile (19b)



Yield: 97% (48.4 mg). White solid, m.p.: 152.3-154.1 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.45 (s, 2H), 7.11 (s, 1H), 3.61 (s, 6H), 2.32 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 186.9, 137.9, 137.3, 133.6, 125.5, 116.3, 70.2, 42.0, 21.2. **HRMS (ESI)** calculated for $C_{13}H_{16}NO_2S$ $[M+H]^+$ 250.0896, Found 250.0894.

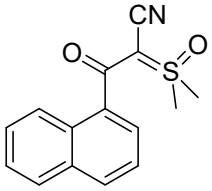
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(naphthalen-2-yl)-3-oxopropanenitrile (20b)



Yield: 96% (52.2 mg). White solid, m.p.: 138.0-140.0 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.46 (s, 1H), 7.96 – 7.81 (m, 4H), 7.59 – 7.47 (m,

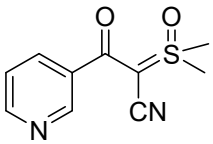
2H), 3.64 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 186.3, 134.9, 134.5, 132.3, 129.3, 128.8, 128.2, 128.0, 127.7, 126.7, 124.1, 116.4, 70.5, 42.1. **HRMS (ESI)** calculated for $C_{15}H_{14}NO_2S$ $[M+H]^+$ 272.0740, Found 272.0739.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(naphthalen-1-yl)-3-oxopropanenitrile (21b)



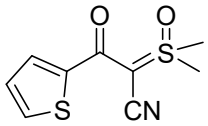
Yield: 89% (48.2 mg). White solid, m.p.: 139.1-141.0 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.21 – 8.13 (m, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.87 (dd, *J* = 7.0, 2.4 Hz, 1H), 7.76 (dd, *J* = 7.1, 1.2 Hz, 1H), 7.57 – 7.45 (m, 3H), 3.64 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 188.9, 135.4, 133.8, 131.2, 129.9, 128.5, 127.2, 126.4, 126.2, 125.1, 124.6, 115.7, 72.6, 42.0. **HRMS (ESI)** calculated for $C_{15}H_{14}NO_2S$ $[M+H]^+$ 272.0740, Found 272.0737.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-3-(pyridin-3-yl)propanenitrile (22b)



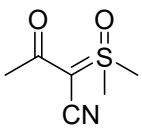
Yield: 92% (40.8 mg). White solid, m.p.: 148.0-149.5 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.90 (d, *J* = 2.2 Hz, 1H), 8.71 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.09 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.53 (dd, *J* = 8.0, 4.8 Hz, 1H), 3.85 (s, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 183.0, 151.8, 148.0, 135.1, 133.7, 123.5, 116.7, 72.5, 40.3. **HRMS (ESI)** calculated for $C_{10}H_{11}N_2O_2S$ $[M+H]^+$ 223.0536, Found 223.0537.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-3-(thiophen-2-yl)propanenitrile (23b)



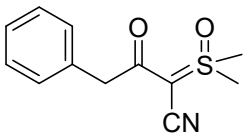
Yield: 94% (42.7 mg). White solid, m.p.: 213.1-215.0 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.90 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.86 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.20 (dd, *J* = 5.0, 3.8 Hz, 1H), 3.82 (s, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 175.6, 143.2, 132.3, 130.0, 128.2, 116.8, 70.3, 40.6. **HRMS (ESI)** calculated for $C_9H_{10}NO_2S_2$ $[M+H]^+$ 228.0147, Found 228.0148.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxobutanenitrile (24b)



Yield: 53% (16.9 mg). Light yellow solid, m.p.: 151.2-152.7 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 3.69 (s, 6H), 2.07 (s, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 188.4, 117.0, 71.1, 40.2, 26.9. **HRMS (ESI)** calculated for $C_6H_{10}NO_2S$ $[M+H]^+$ 160.0427, Found 160.0429.

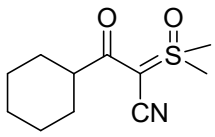
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-4-phenylbutanenitrile (25b)



Yield: 70% (33 mg). White solid, m.p.: 134.4-136.1 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.22 (m, 5H), 3.82 (s, 2H), 3.48 (s, 6H). **^{13}C NMR**

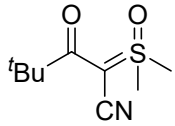
(100 MHz, Chloroform-*d*) δ 190.5, 134.6, 129.5, 128.6, 127.0, 115.8, 69.5, 46.2, 41.8. **HRMS (ESI)** calculated for $C_{12}H_{14}NO_2S$ $[M+H]^+$ 236.0740, Found 236.0741.

3-cyclohexyl-2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxopropanenitrile (26b)



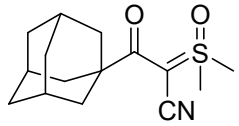
Yield: 83% (37.5 mg). White solid, m.p.: 138.6-140.0 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 3.53 (s, 6H), 2.65 (t, *J* = 11.3 Hz, 1H), 1.83 – 1.70 (m, 4H), 1.64 (d, *J* = 12.6 Hz, 1H), 1.43 – 1.08 (m, 5H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 196.9, 115.8, 68.6, 47.3, 42.0, 28.8, 25.7, 25.6. **HRMS (ESI)** calculated for $C_{11}H_{18}NO_2S$ $[M+H]^+$ 228.1053, Found 228.1054.

2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-4,4-dimethyl-3-oxopentanenitrile (27b)



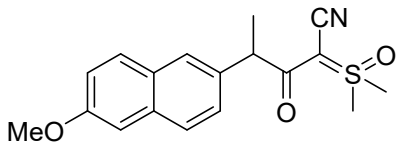
Yield: 84% (33.8 mg). White solid, m.p.: 122.0-124.0 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 3.53 (s, 6H), 1.24 (s, 9H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 199.7, 116.4, 68.8, 43.0, 42.2, 26.7. **HRMS (ESI)** calculated for $C_9H_{16}NO_2S$ $[M+H]^+$ 202.0896, Found 202.0895.

3-((3*r*,5*r*,7*r*)-adamantan-1-yl)-2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxopropanenitrile (28b)



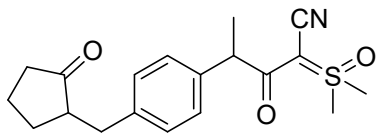
Yield: 96% (53.8 mg). White solid, m.p.: 166.1-167.5 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 3.52 (s, 6H), 2.01 (s, 3H), 1.94 (d, *J* = 3.0 Hz, 6H), 1.68 (d, *J* = 3.2 Hz, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 198.9, 116.4, 69.1, 45.2, 42.3, 37.8, 36.4, 28.2. **HRMS (ESI)** calculated for $C_{15}H_{22}NO_2S$ $[M+H]^+$ 280.1366, Found 280.1367.

2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-4-(6-methoxynaphthalen-2-yl)-3-oxopentanenitrile (29b)



Yield: 72% (47.3 mg). Light orange solid, m.p.: 72.5-74.0 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.75 – 7.64 (m, 3H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.17 – 7.06 (m, 2H), 4.26 (q, *J* = 7.0 Hz, 1H), 3.88 (s, 3H), 3.41 (s, 3H), 3.31 (s, 3H), 1.49 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 193.8, 157.6, 136.1, 133.7, 129.4, 129.0, 127.2, 126.5, 126.5, 119.0, 115.8, 105.6, 69.6, 55.3, 48.4, 41.8, 41.3, 18.2. **HRMS (ESI)** calculated for $C_{18}H_{20}NO_3S$ $[M+H]^+$ 330.1158, Found 330.1157.

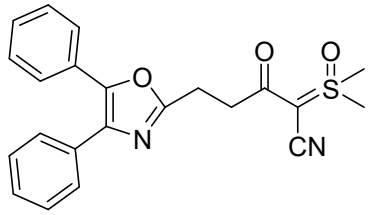
2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxo-4-(4-((2-oxocyclopentyl)methyl)phenyl)pentanenitrile (30b)



Yield: 60% (41.5 mg). White solid, m.p.: 78.1-79.5 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* =

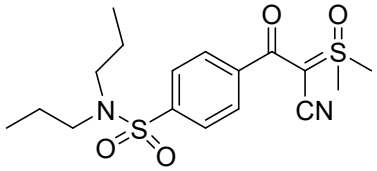
7.9 Hz, 2H), 4.15 – 4.08 (m, 1H), 3.49 (d, *J* = 29.8 Hz, 6H), 3.09 (dd, *J* = 13.9, 4.0 Hz, 1H), 2.52 – 2.42 (m, 1H), 2.37 – 2.26 (m, 2H), 2.15 – 2.05 (m, 2H), 1.99 – 1.90 (m, 1H), 1.78 – 1.65 (m, 1H), 1.59 – 1.48 (m, 1H), 1.41 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 220.4, 193.9, 138.8, 138.6, 129.2, 127.9, 115.6, 69.4, 51.0, 48.1, 42.0, 41.6, 38.2, 35.3, 29.4, 20.6, 18.3. **HRMS (ESI)** calculated for $C_{19}H_{24}NO_3S$ $[M+H]^+$ 346.1471, Found 346.1470.

2-(dimethyl(oxo)-λ^6-sulfaneylidene)-5-(4,5-diphenyloxazol-2-yl)-3-oxopentanenitrile (31b)



Yield: 70% (54.9 mg). White solid, m.p.: 137.1-139.0 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 7.3 Hz, 2H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.32 – 7.18 (m, 6H), 3.41 (s, 6H), 3.13 – 2.98 (m, 4H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 190.6, 162.1, 145.4, 134.9, 132.4, 128.9, 128.6, 128.6, 128.5, 128.1, 127.8, 126.5, 115.5, 69.6, 41.7, 35.8, 22.8. **HRMS (ESI)** calculated for $C_{22}H_{21}N_2O_3S$ $[M+H]^+$ 393.1267, Found 393.1265.

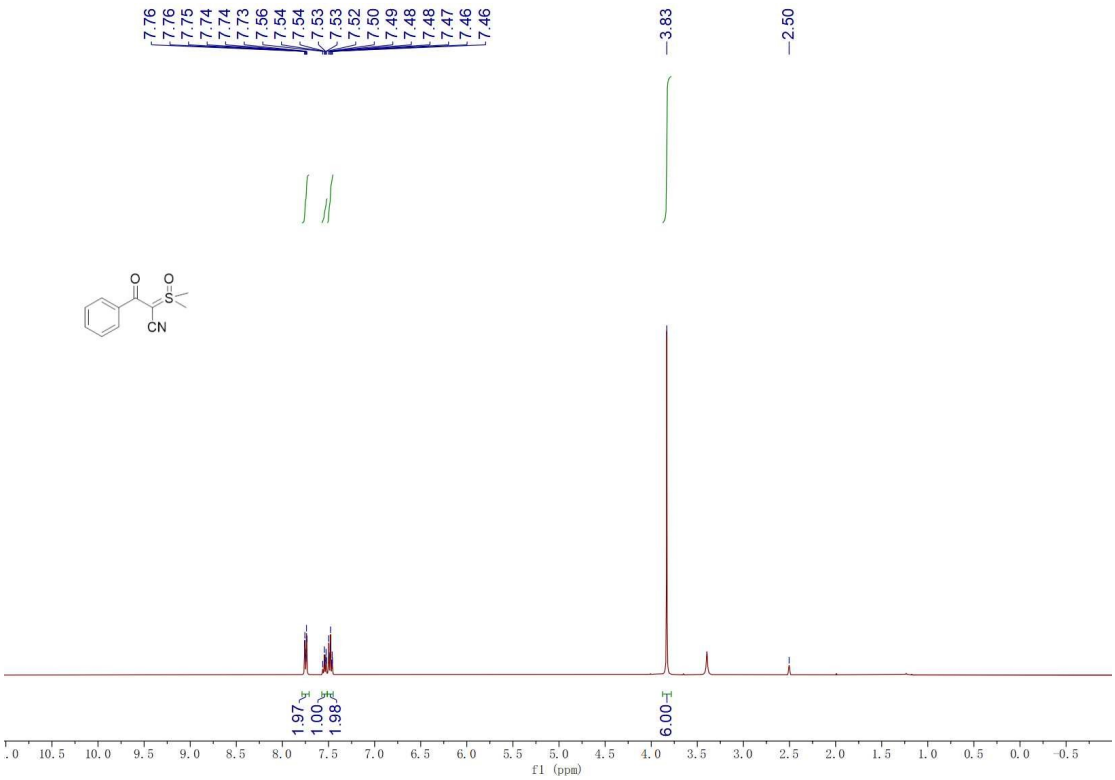
4-(2-cyano-2-(dimethyl(oxo)-λ^6-sulfaneylidene)acetyl)-*N*,*N*-dipropylbenzenesulfonamide (32b)

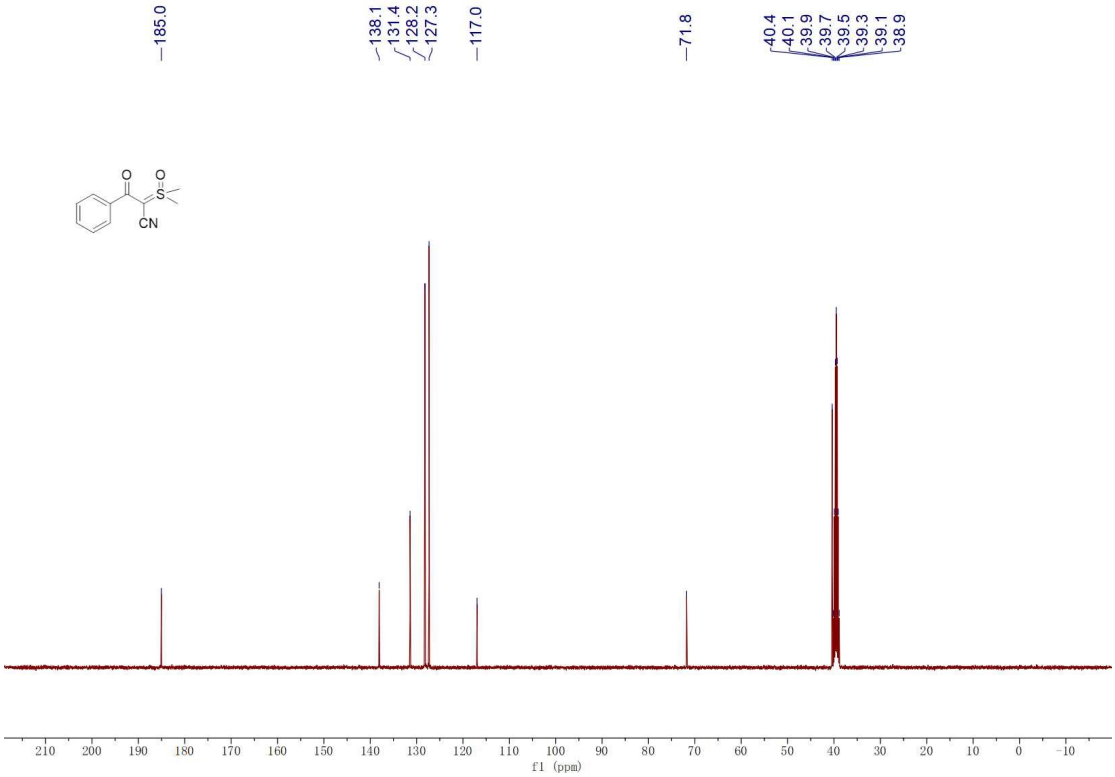


Yield: 80% (61.2 mg). White solid, m.p.: 176.1-178.0 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.1 Hz, 2H), 7.84 (d, *J* = 8.1 Hz, 2H), 3.69 (s, 6H), 3.07 (t, *J* = 7.4 Hz, 4H), 1.60 – 1.47 (m, 4H), 0.85 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 184.7, 143.0, 140.5, 128.6, 127.0, 115.6, 71.1, 50.1, 42.1, 22.1, 11.2. **HRMS (ESI)** calculated for $C_{17}H_{25}N_2O_4S_2$ $[M+H]^+$ 385.1250, Found 385.1251.

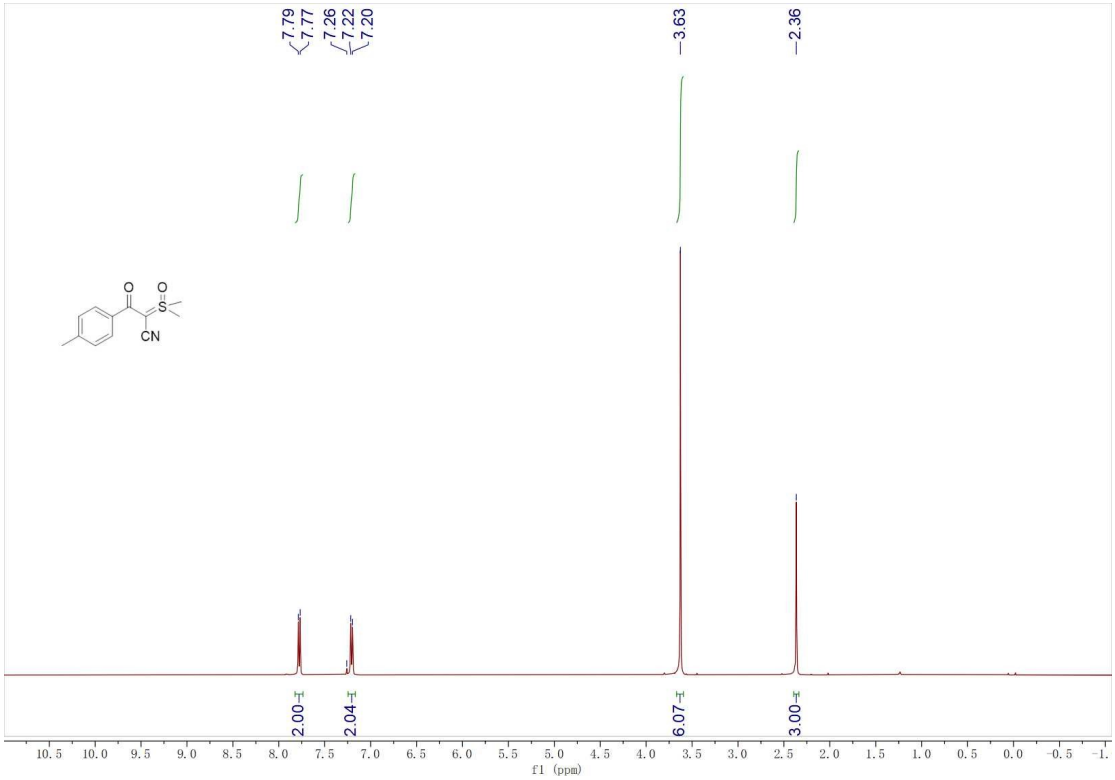
4 ^{1}H NMR and ^{13}C NMR Spectra of Products

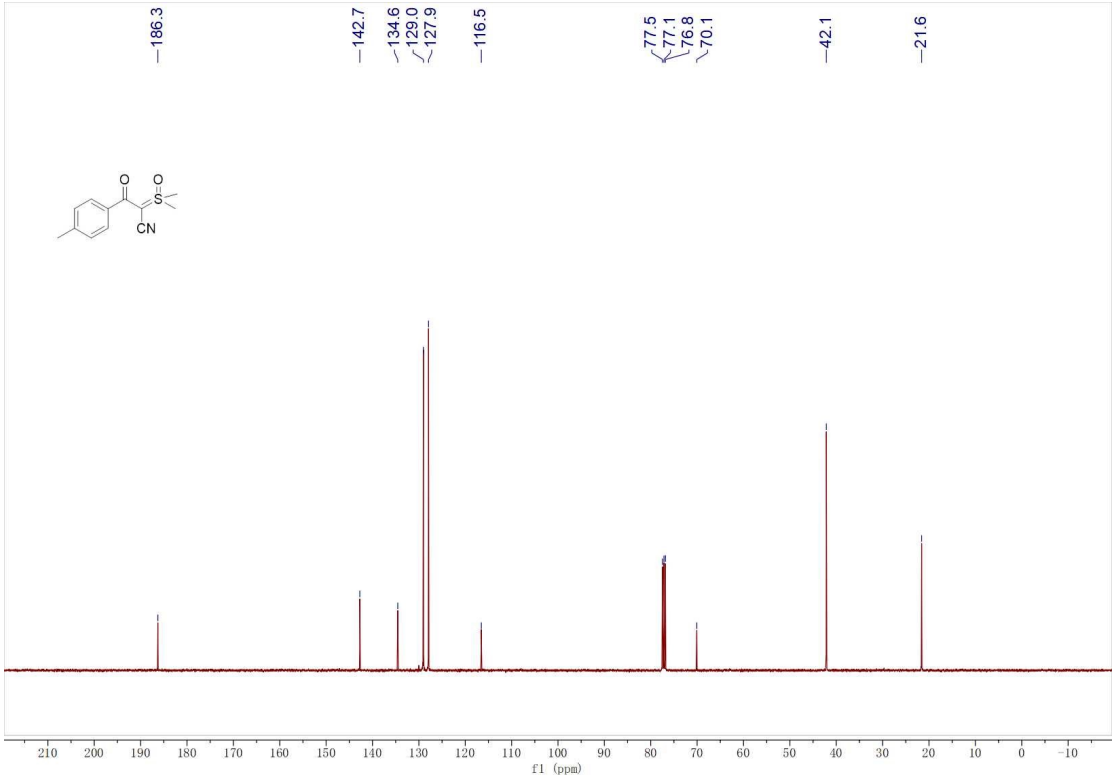
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-3-phenylpropanenitrile (1b)



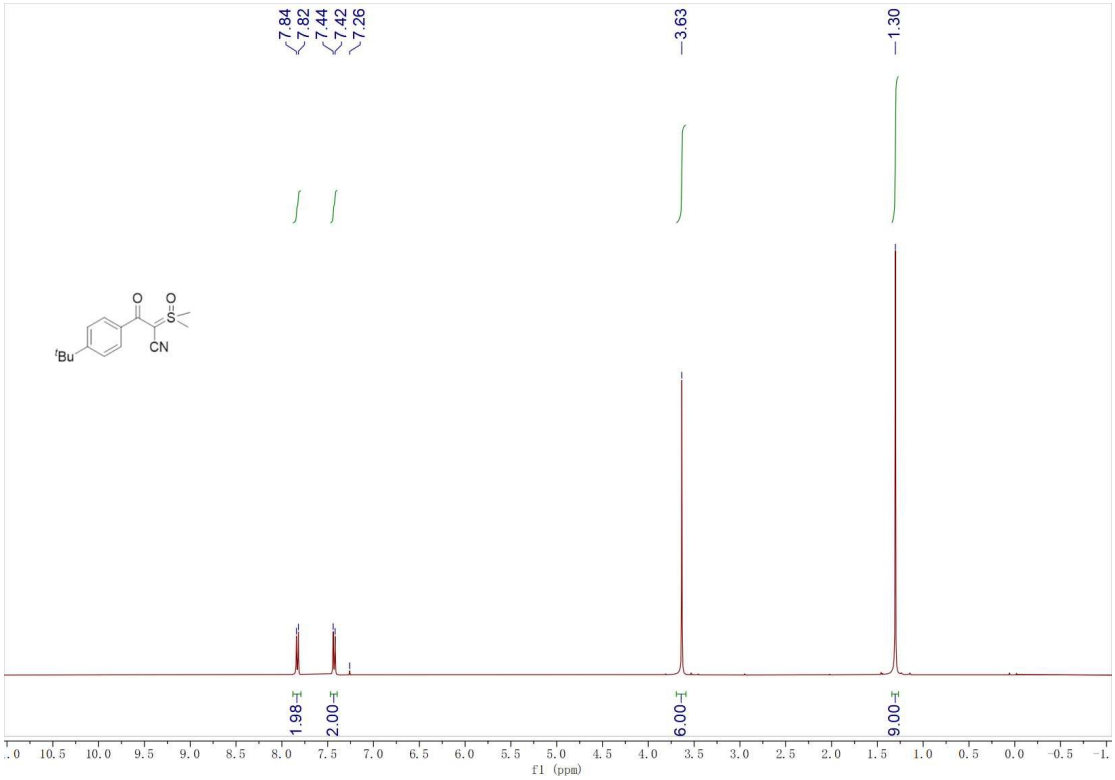


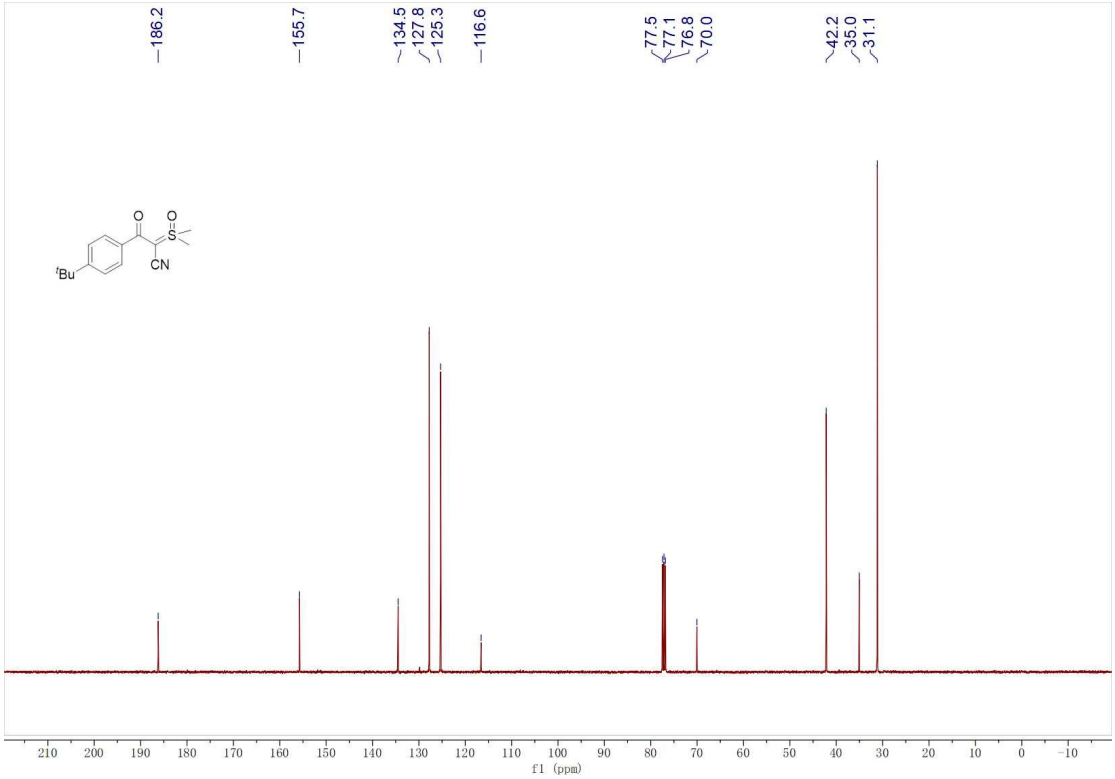
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-3-(*p*-tolyl)propanenitrile (2b)



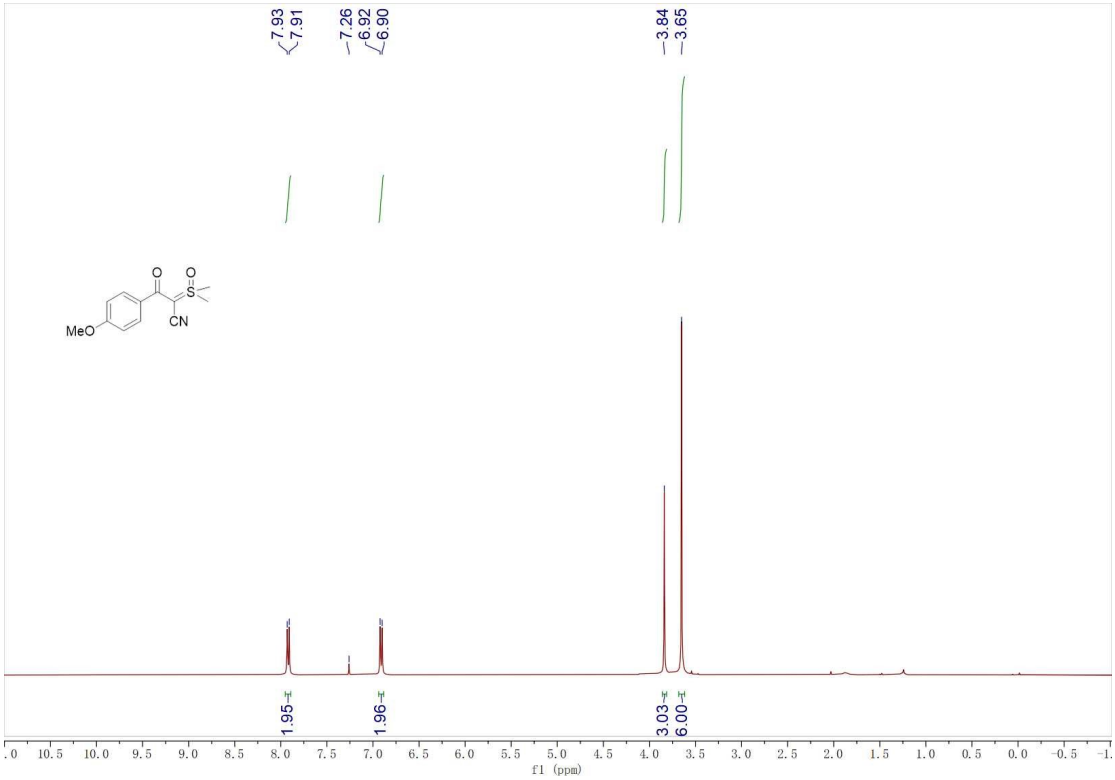


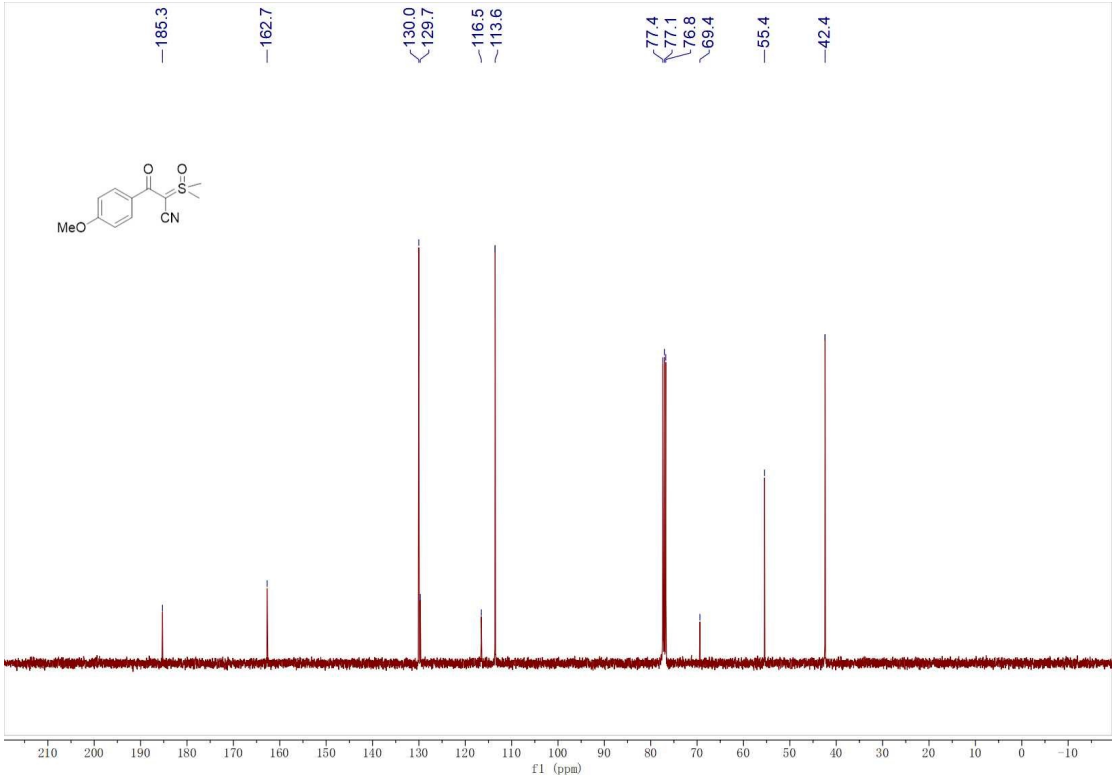
3-(4-(*tert*-butyl)phenyl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (3b)



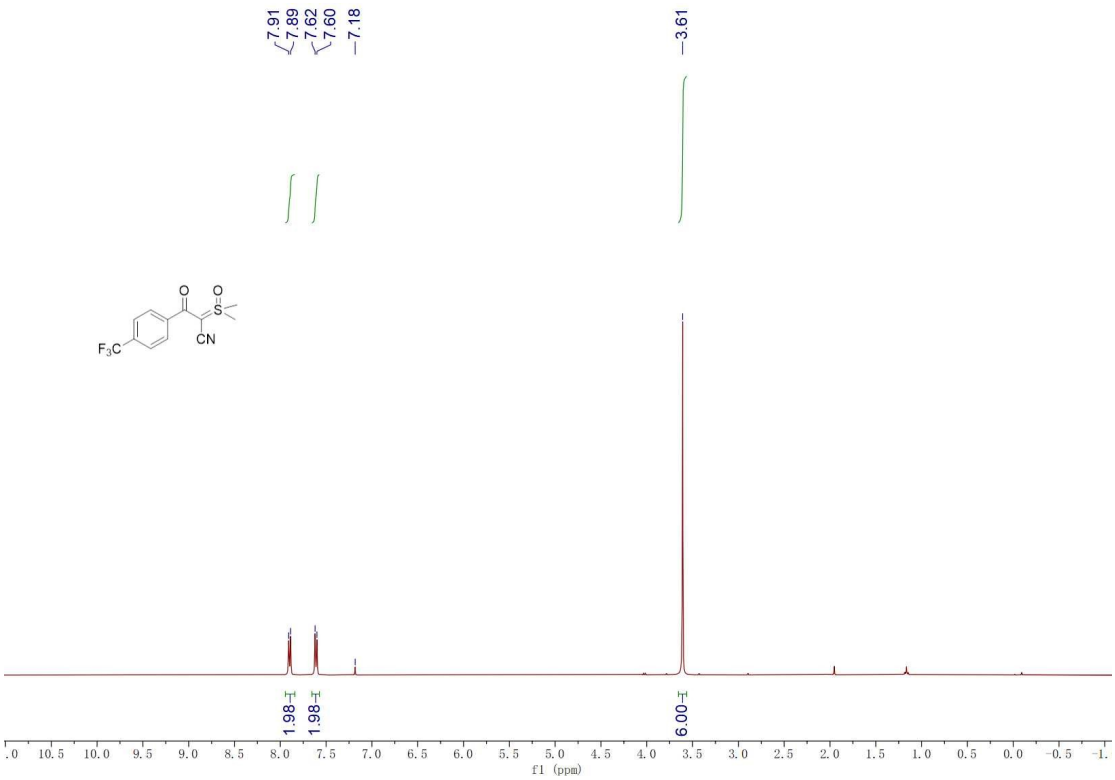


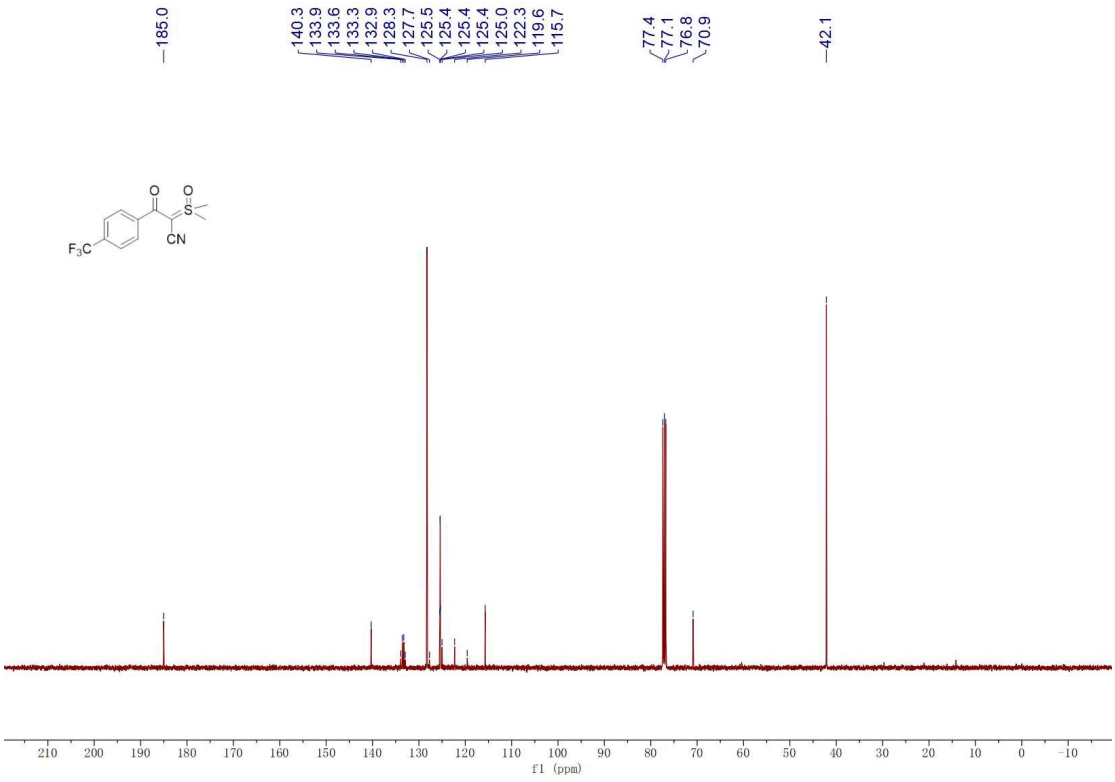
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(4-methoxyphenyl)-3-oxopropanenitrile (4b)

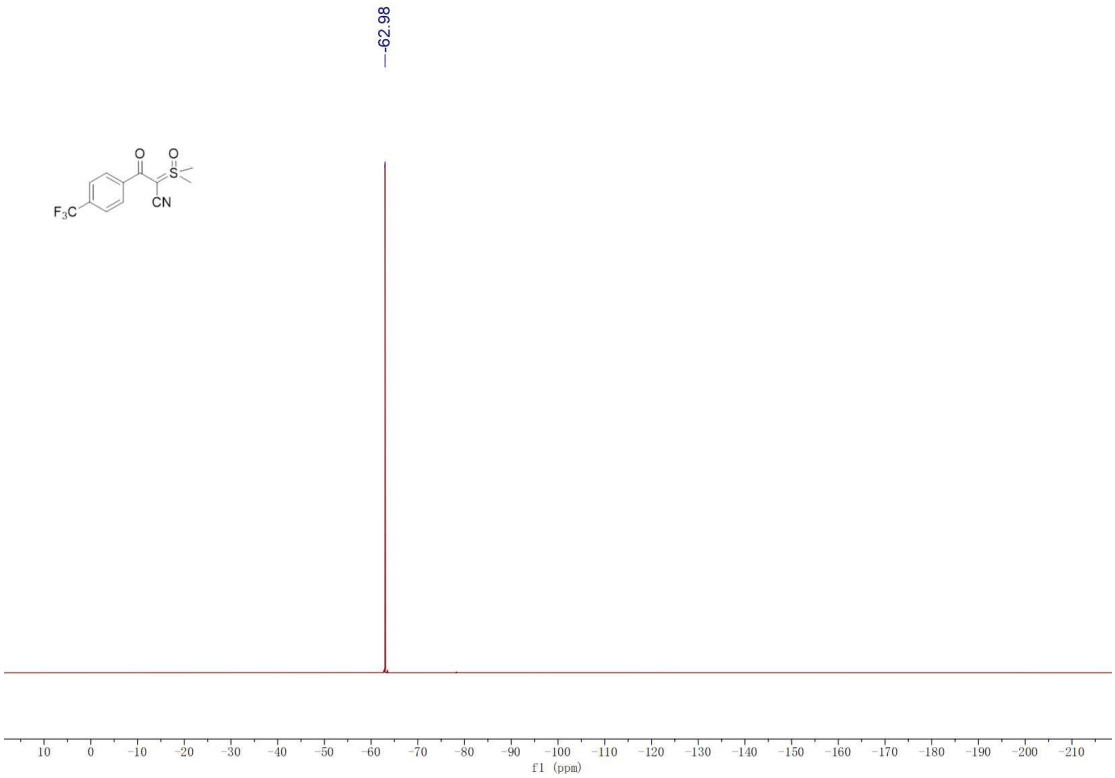




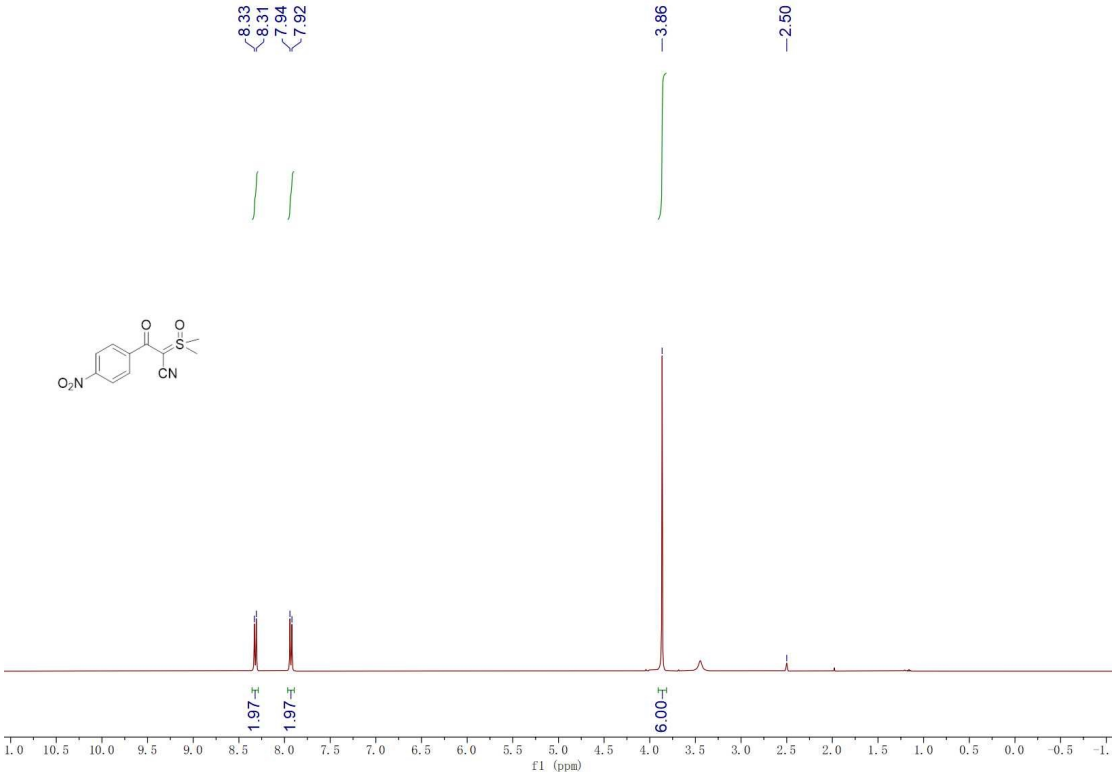
2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxo-3-(4-(trifluoromethyl)phenyl)propanenitrile (5b)

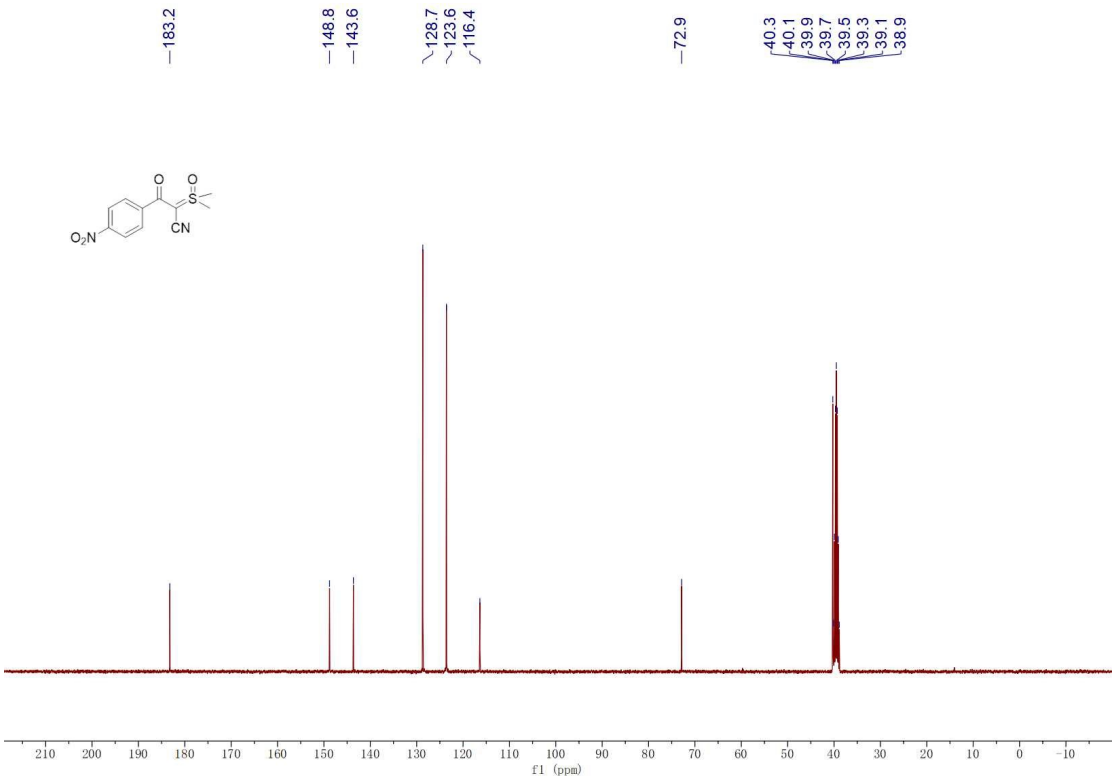

7.91
7.89
7.62
7.60
7.18
3.61
O
O
S
CN
F3C
1.98
1.98
6.00
f1 (ppm)


185.0
140.3
133.9
133.6
133.3
132.9
128.3
127.7
125.5
125.4
125.4
125.4
125.0
122.3
119.6
115.7
77.4
77.1
76.8
70.9
42.1
O
O
S
CN
F3C
f1 (ppm)

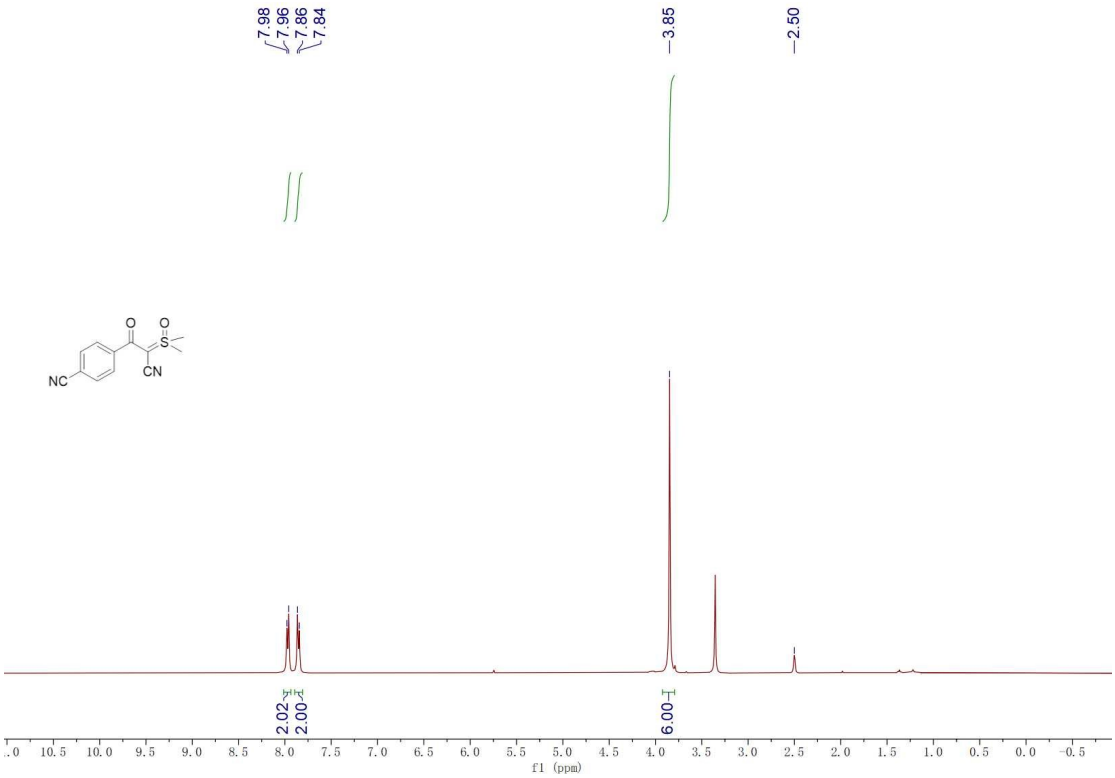


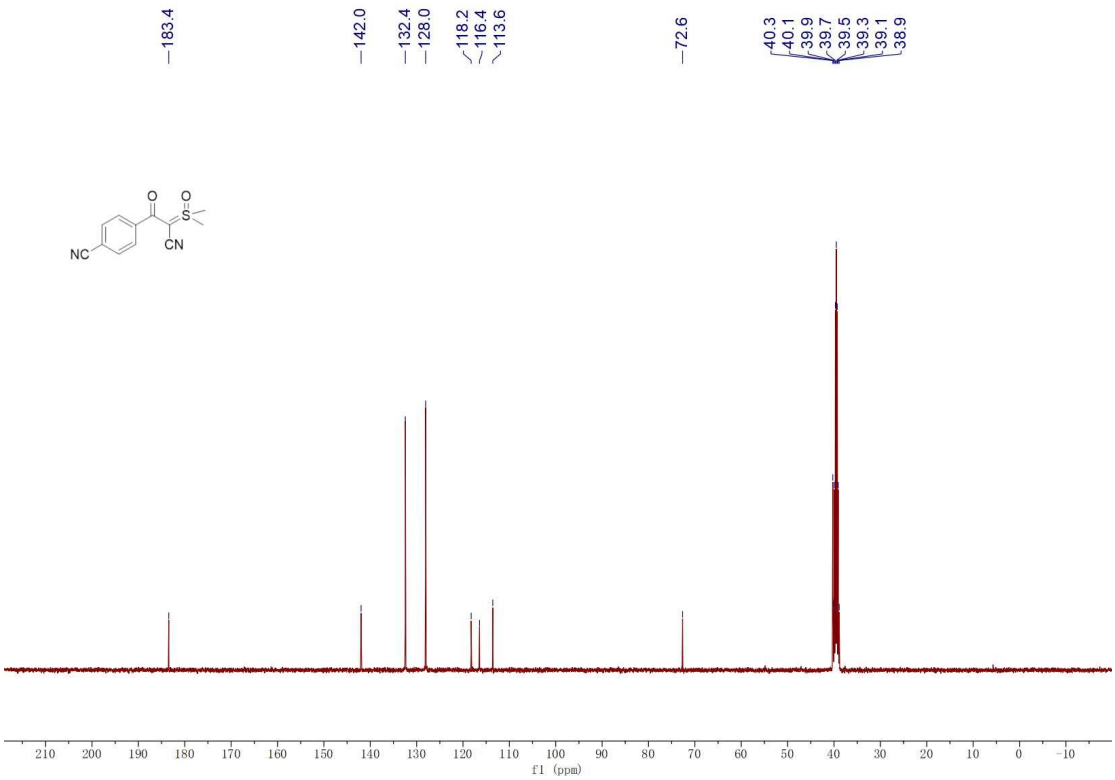
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(4-nitrophenyl)-3-oxopropanenitrile (6b)



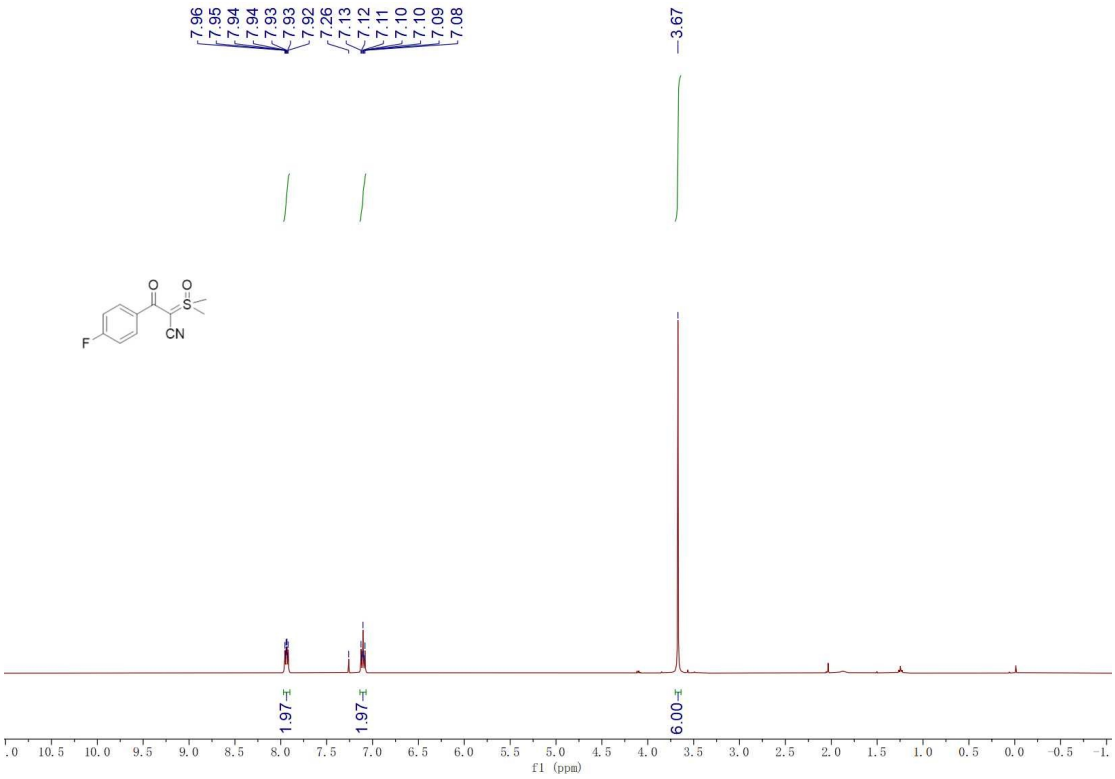


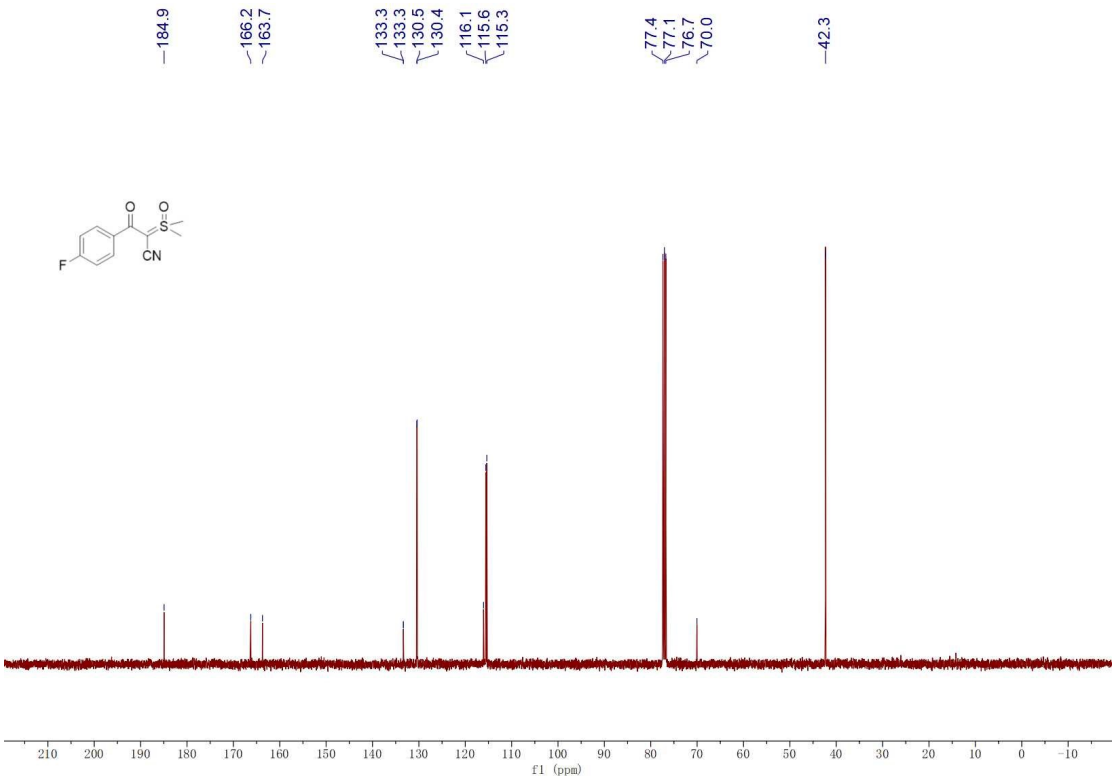
4-(2-cyano-2-(dimethyl(oxo)-λ⁶-sulfaneylidene)acetyl)benzonitrile (7b)

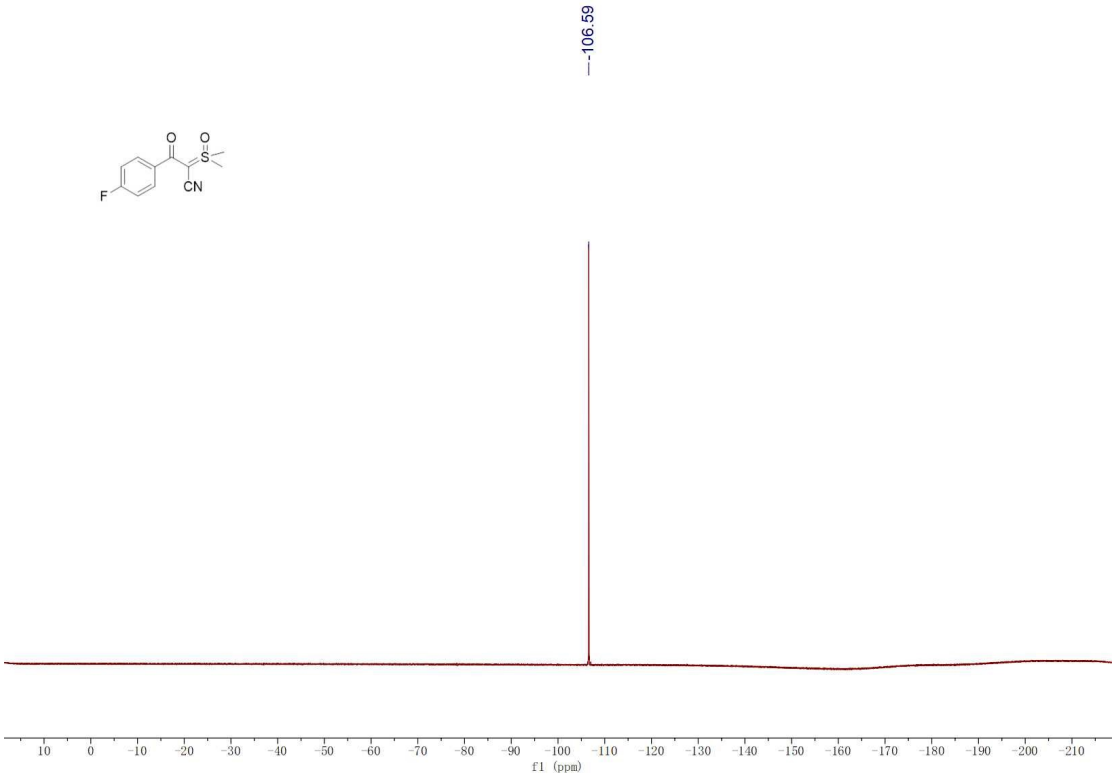




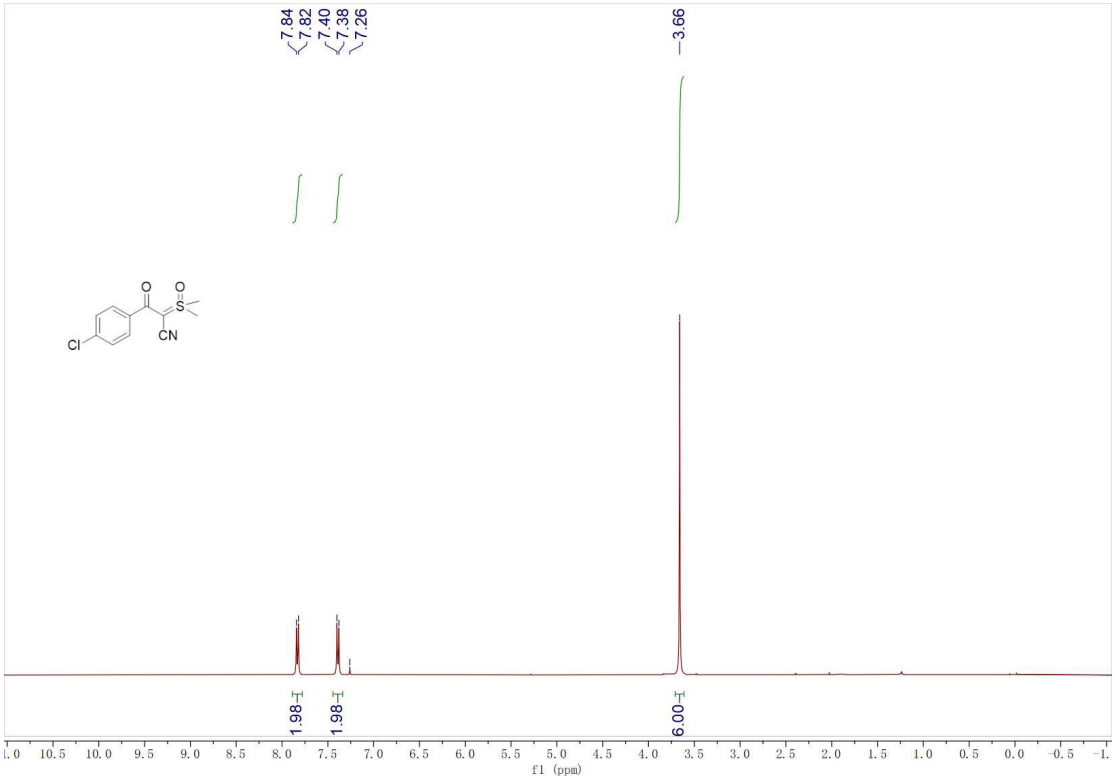
2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-(4-fluorophenyl)-3-oxopropanenitrile (8b)

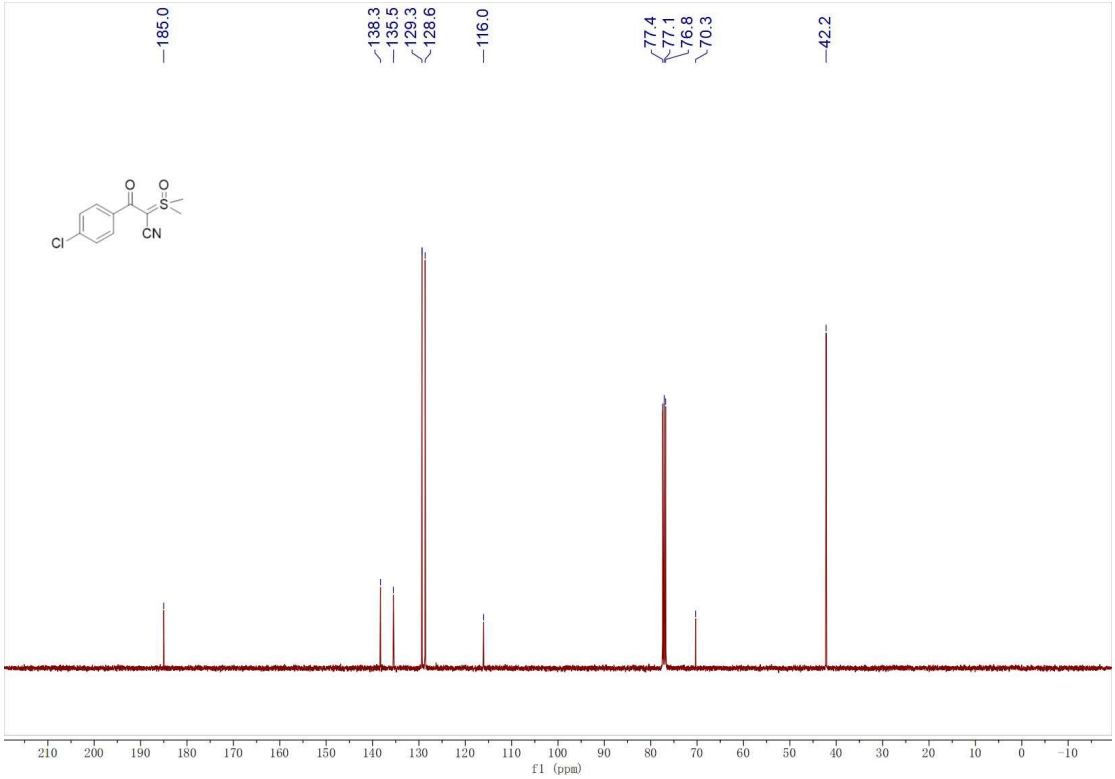




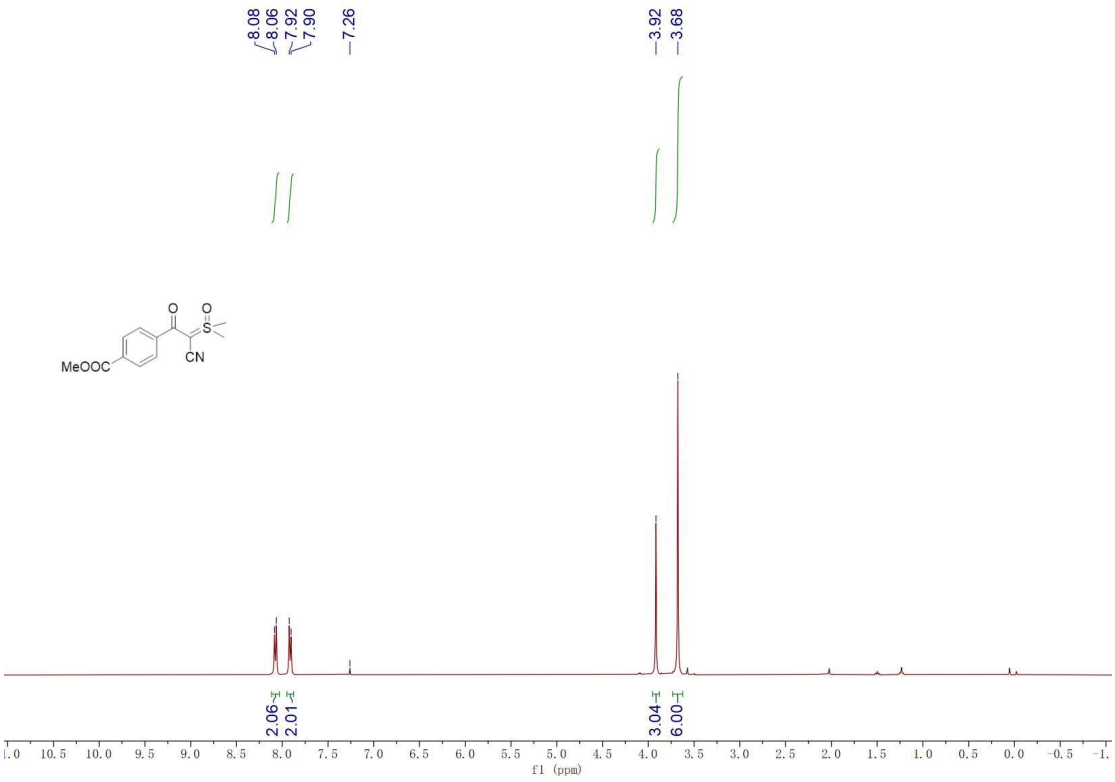


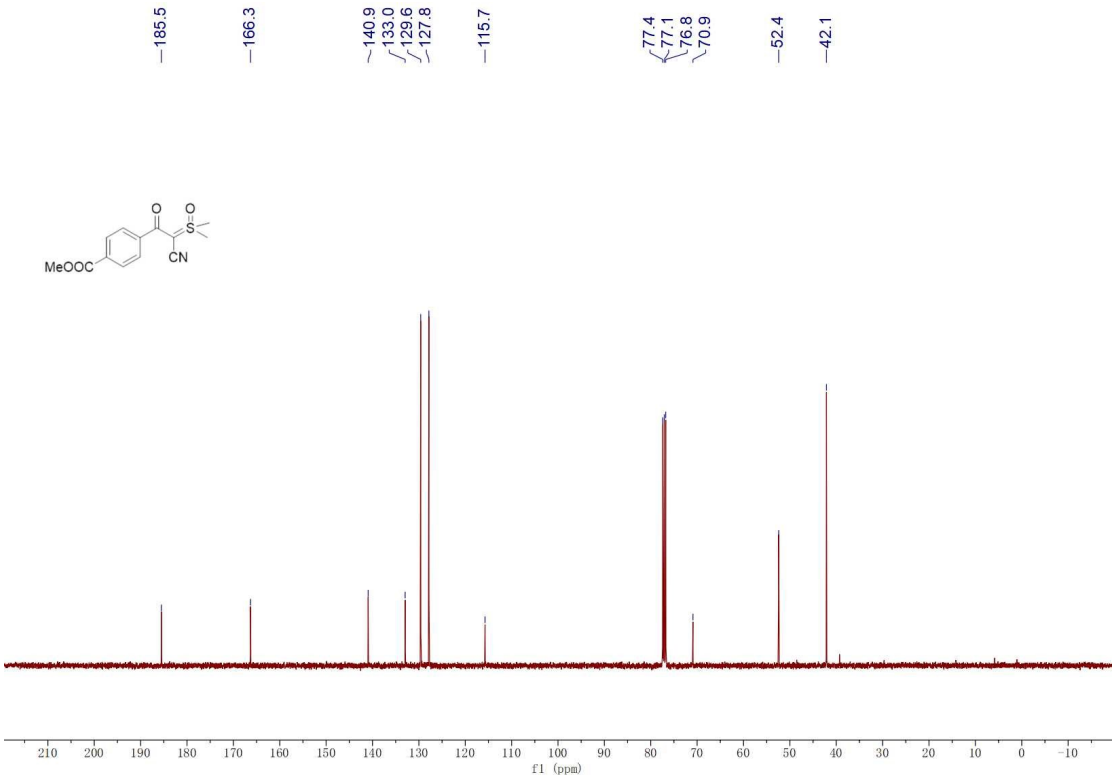
3-(4-chlorophenyl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (9b)



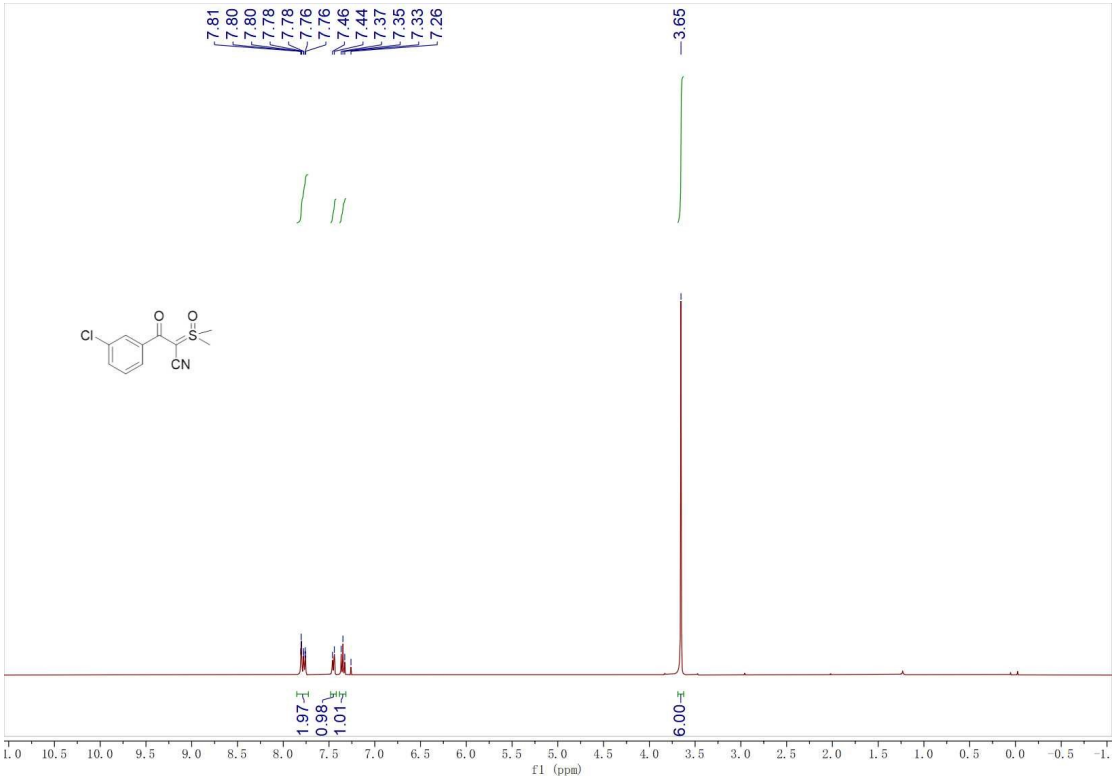


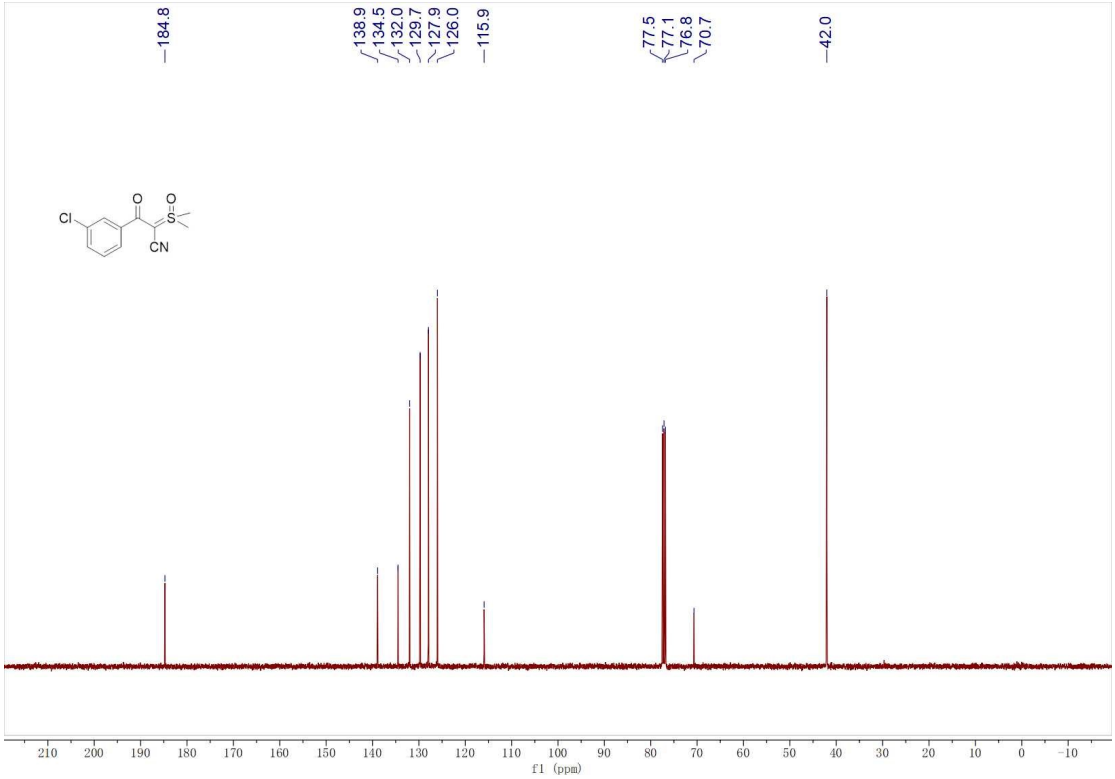
methyl 4-(2-cyano-2-(dimethyl(oxo)-λ^6-sulfaneylidene)acetyl)benzoate (10b)



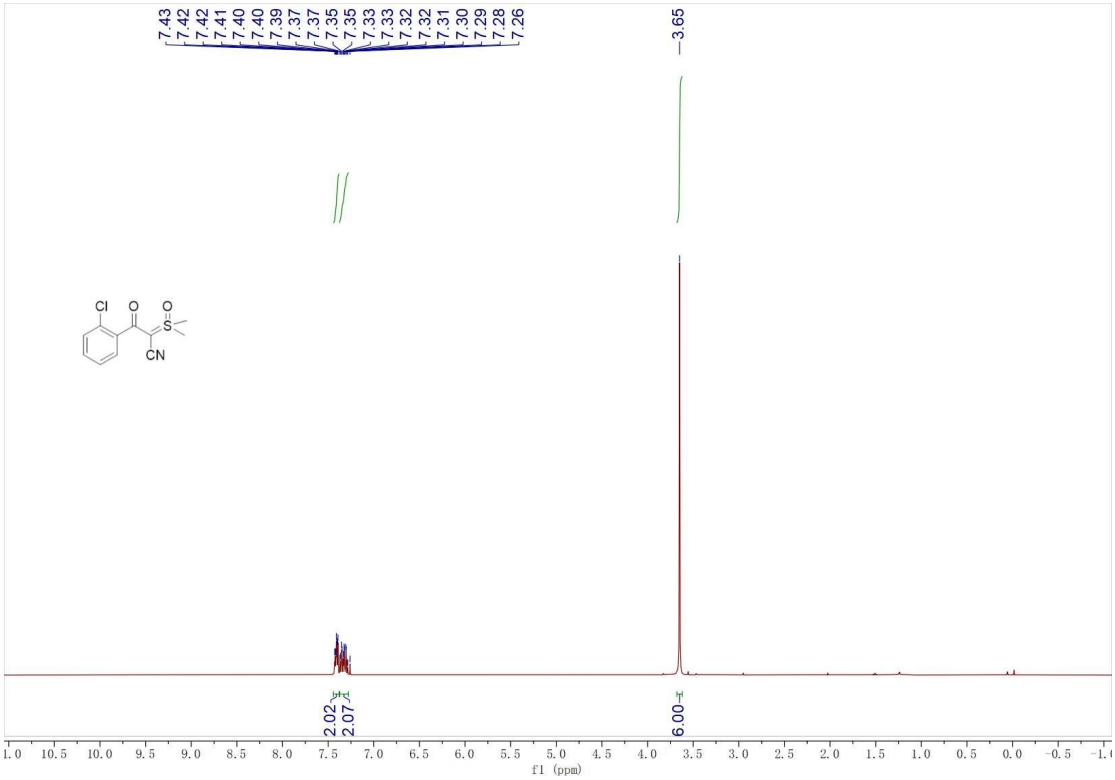


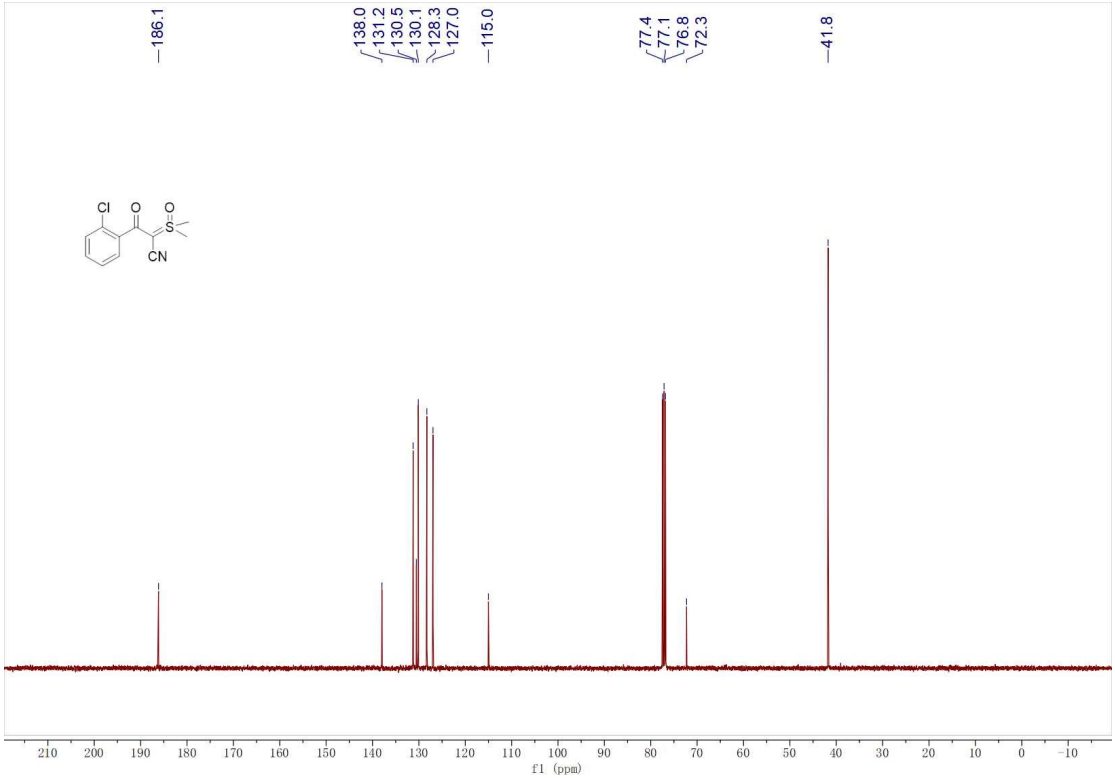
3-(3-chlorophenyl)-2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxopropanenitrile (11b)



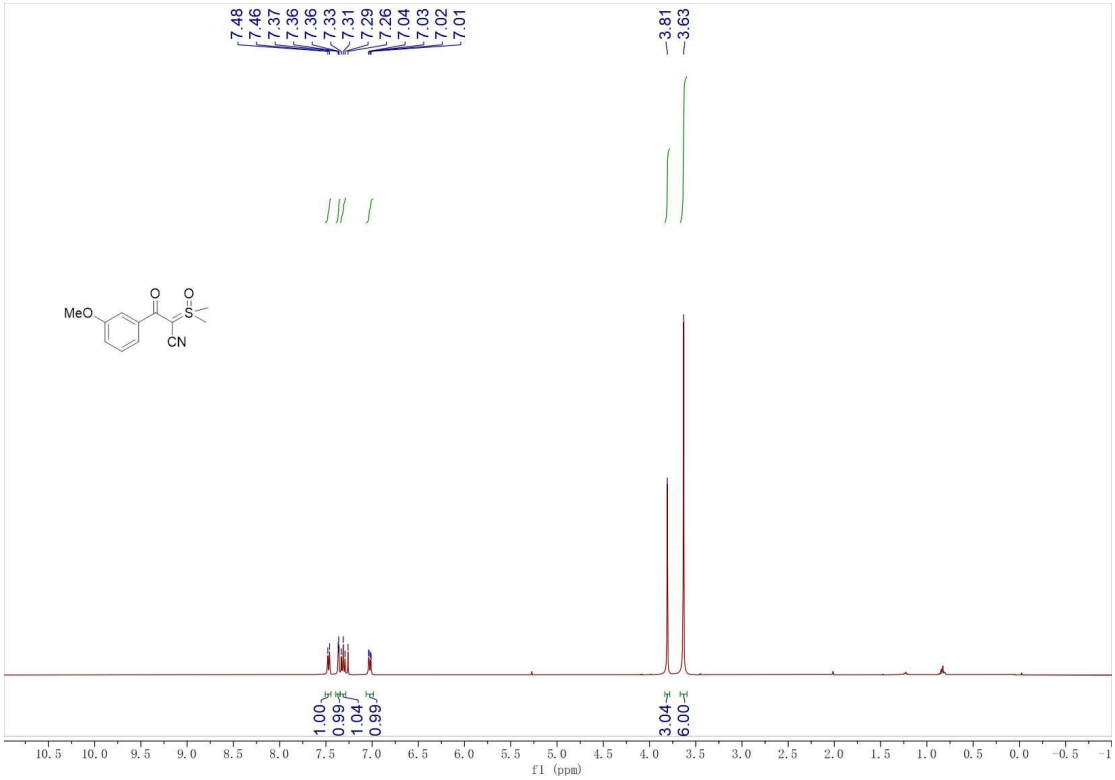


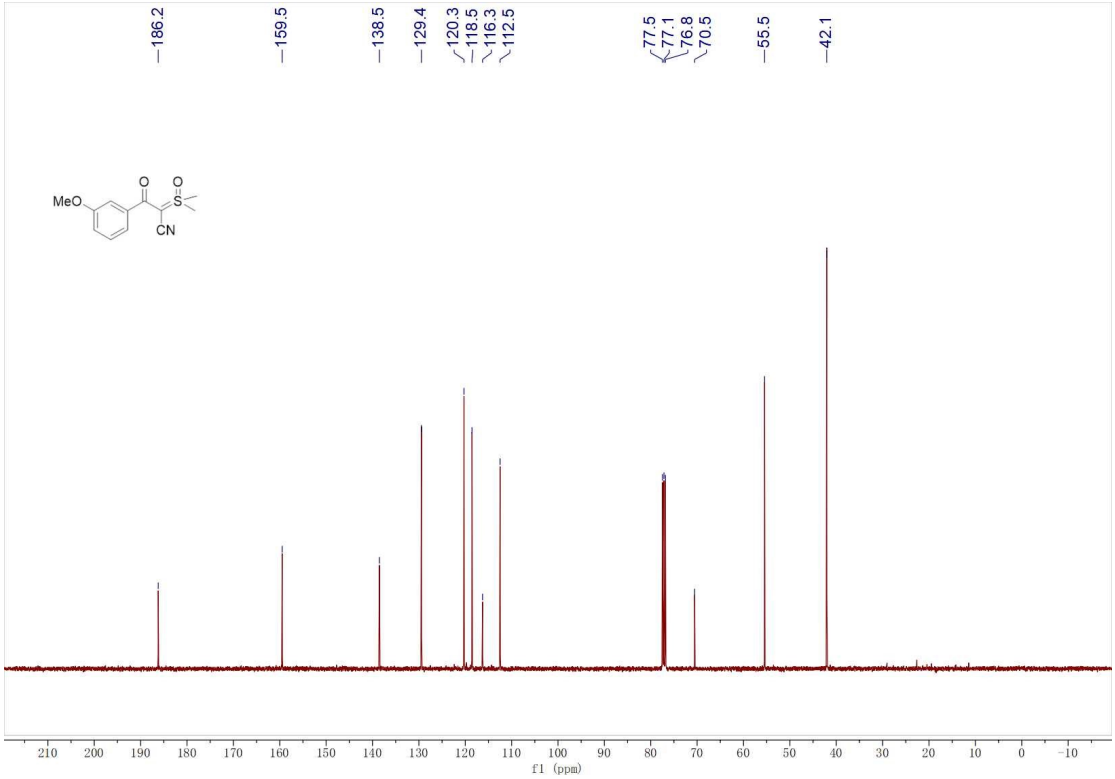
3-(2-chlorophenyl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (12b)



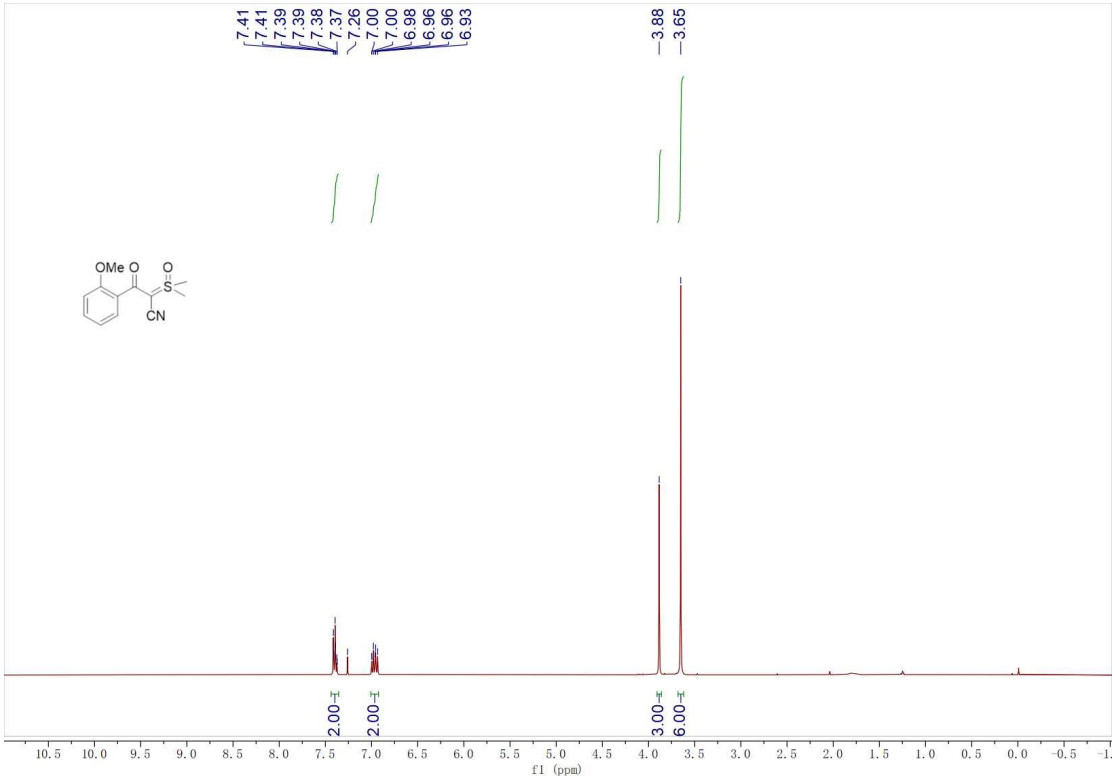


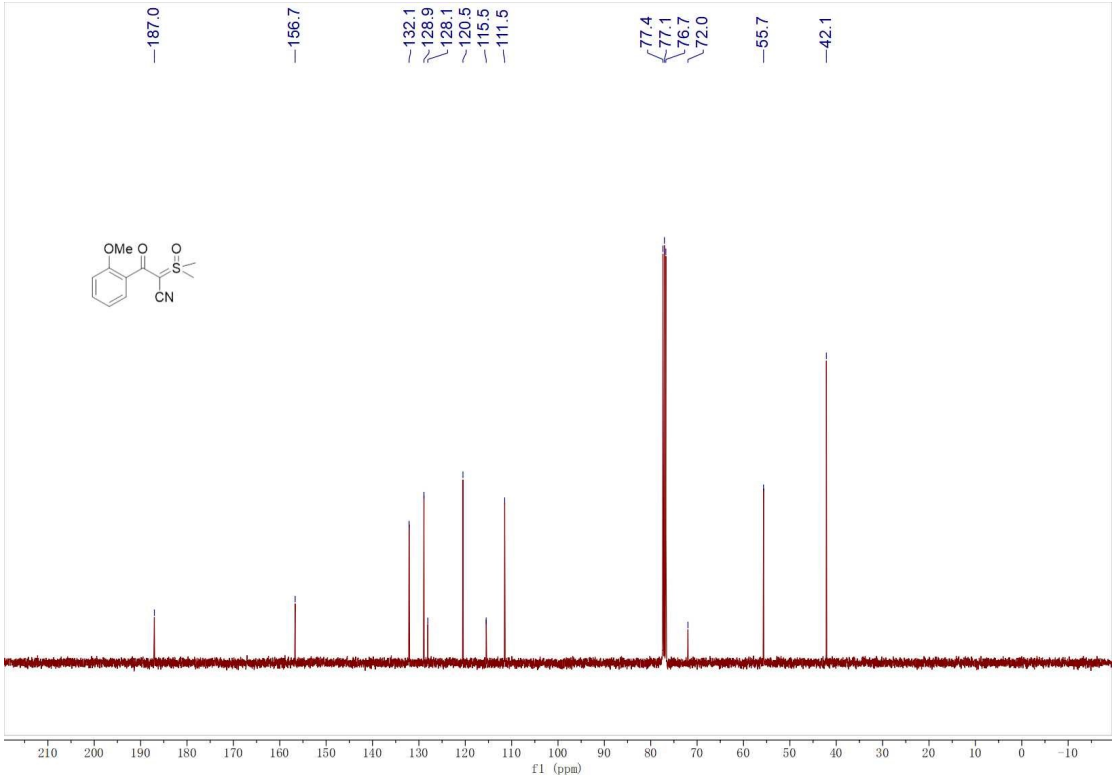
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(3-methoxyphenyl)-3-oxopropanenitrile (13b)



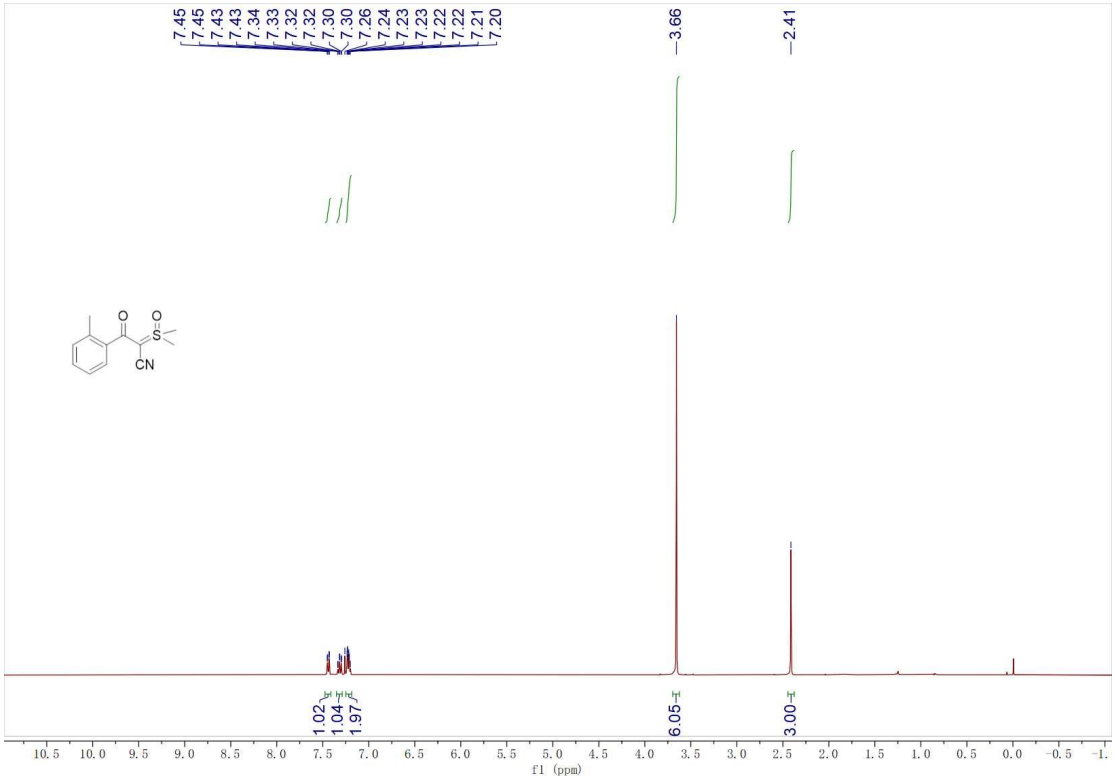


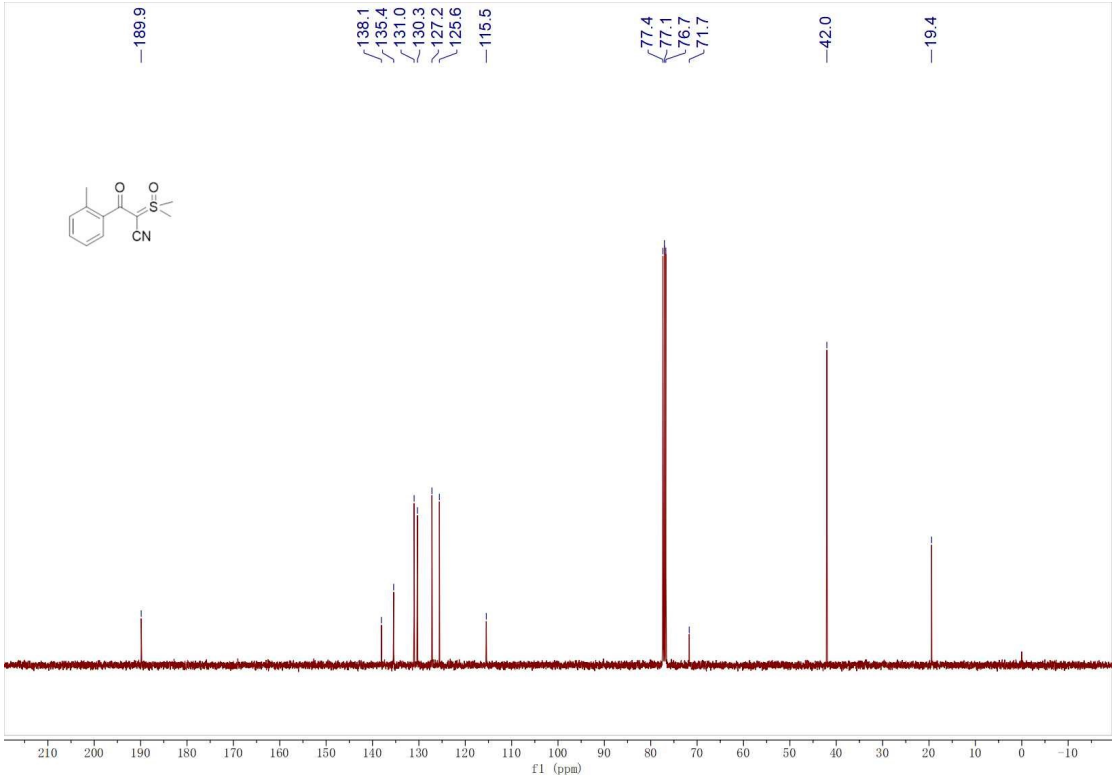
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(2-methoxyphenyl)-3-oxopropanenitrile (14b)



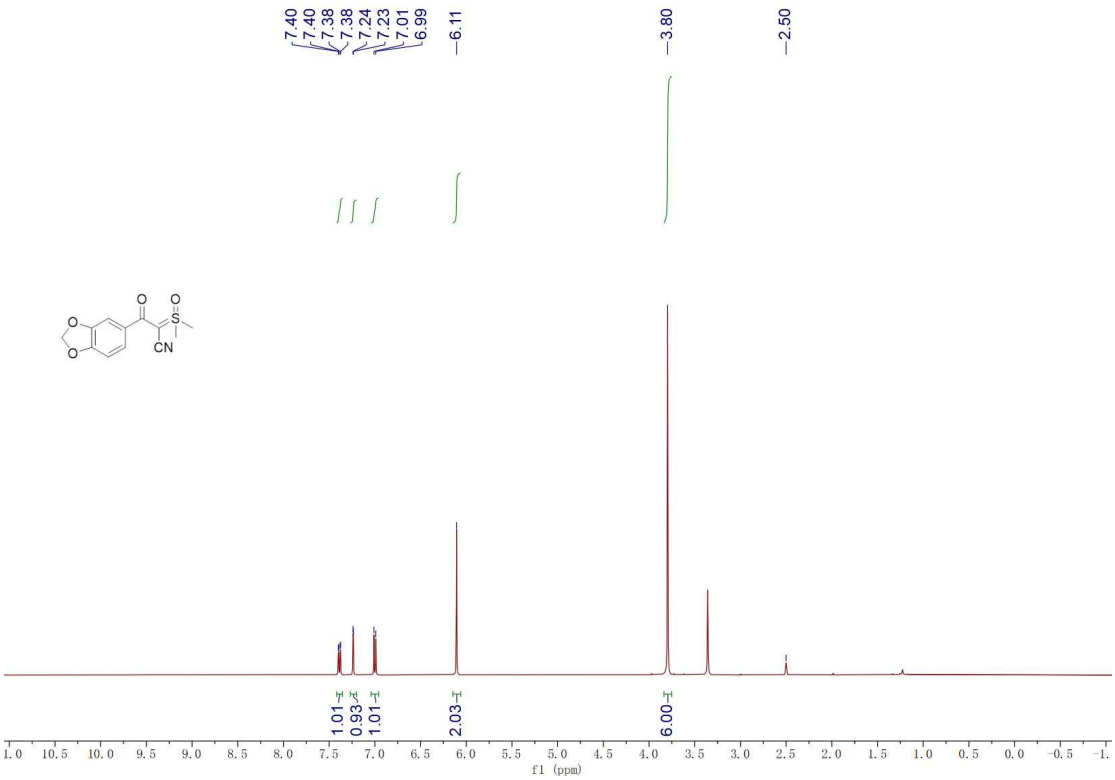


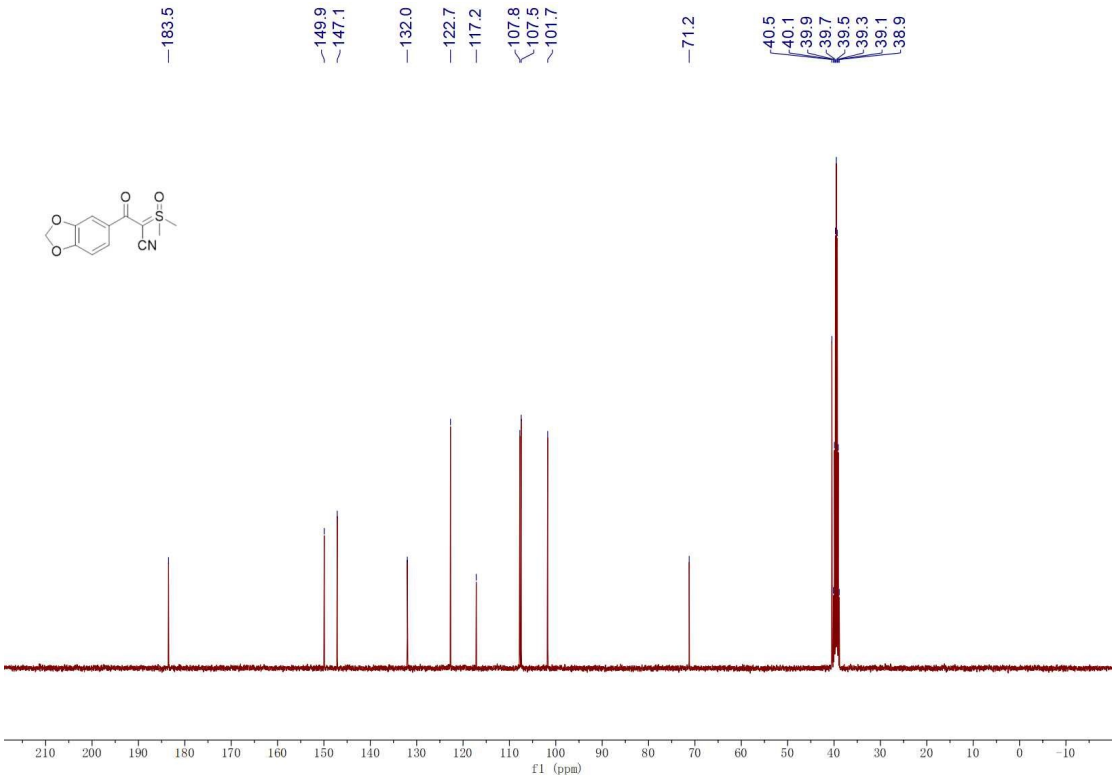
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-3-(o-tolyl)propanenitrile (15b)



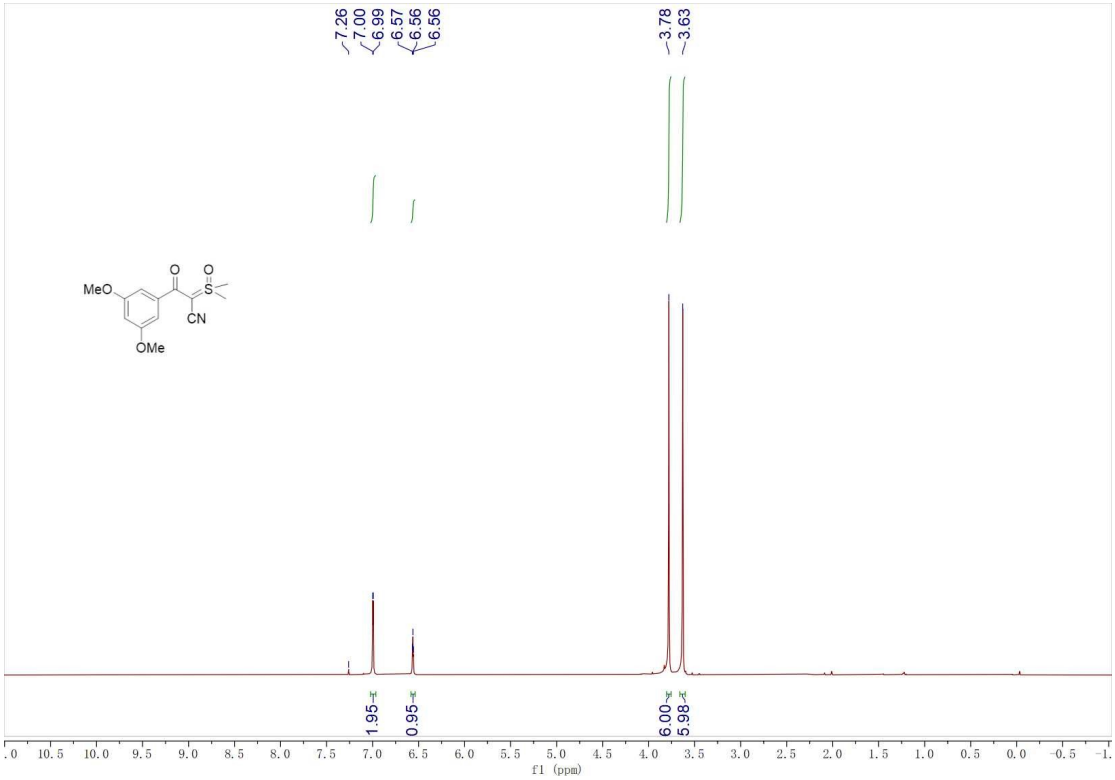


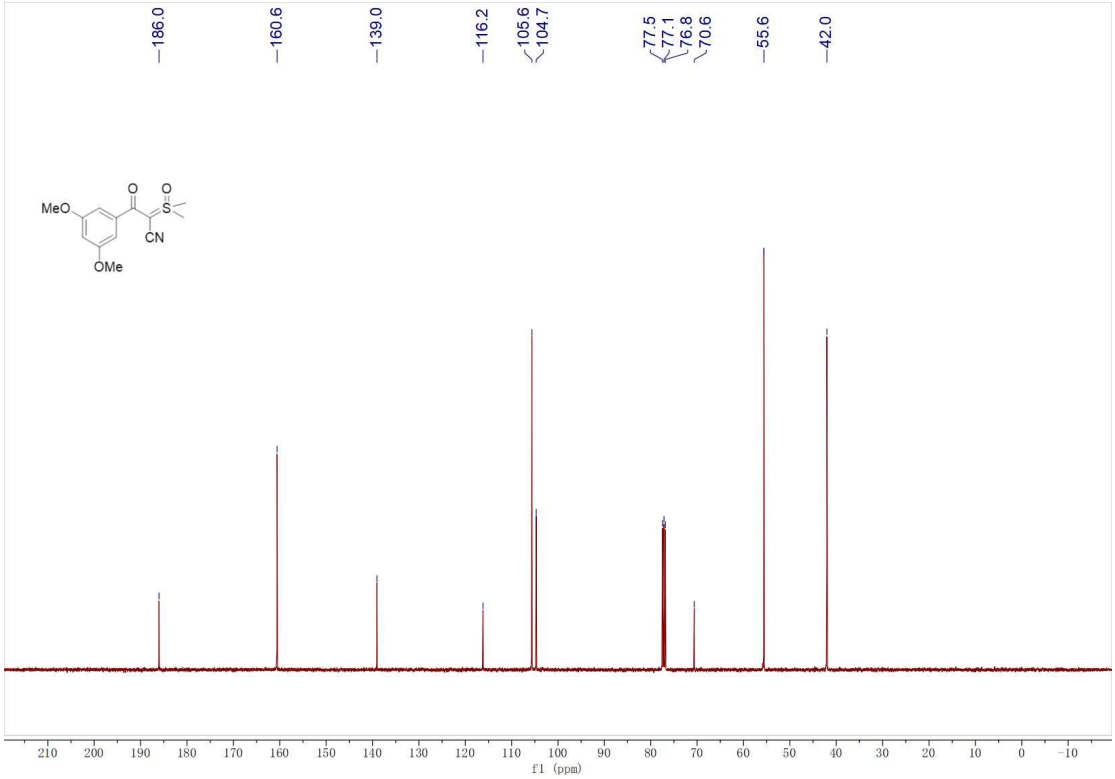
3-(benzo[*d*][1,3]dioxol-5-yl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (16b)



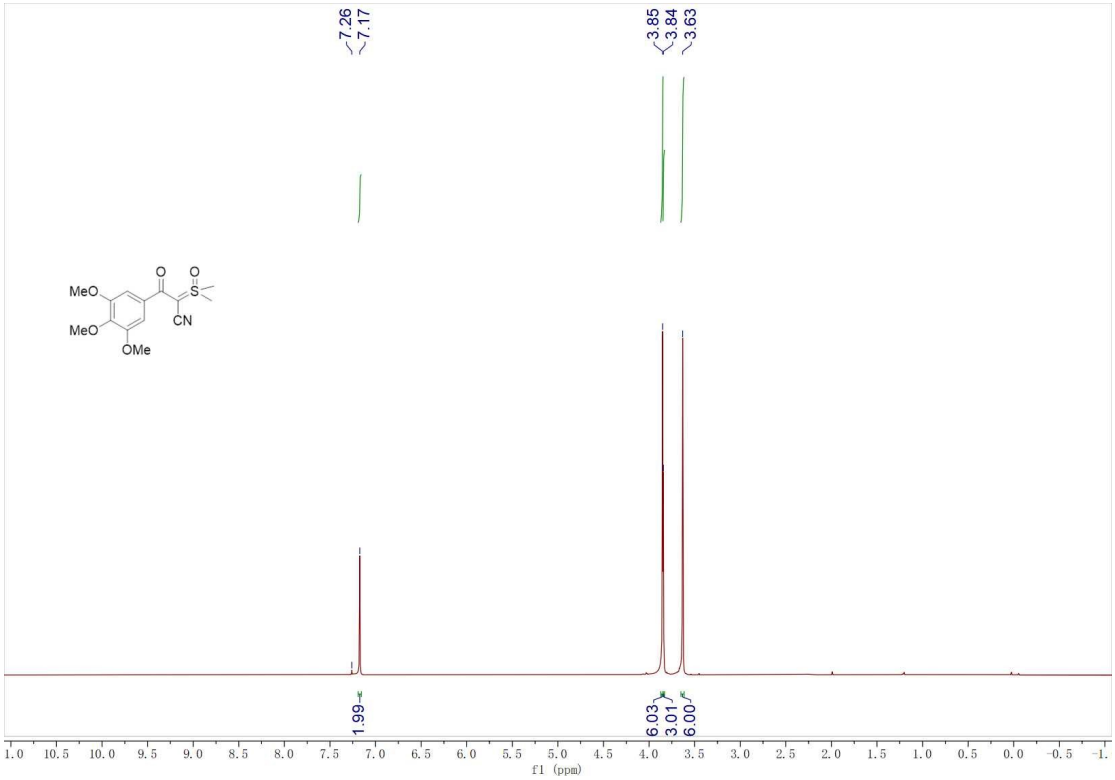


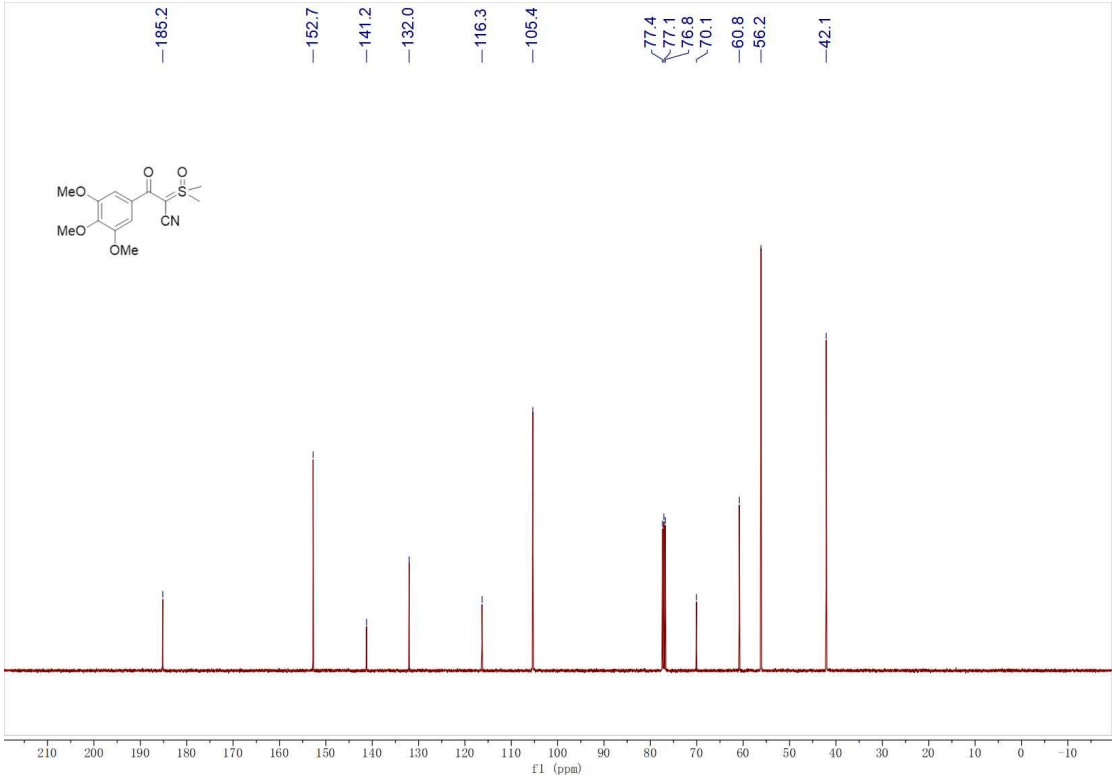
3-(3,5-dimethoxyphenyl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (17b)



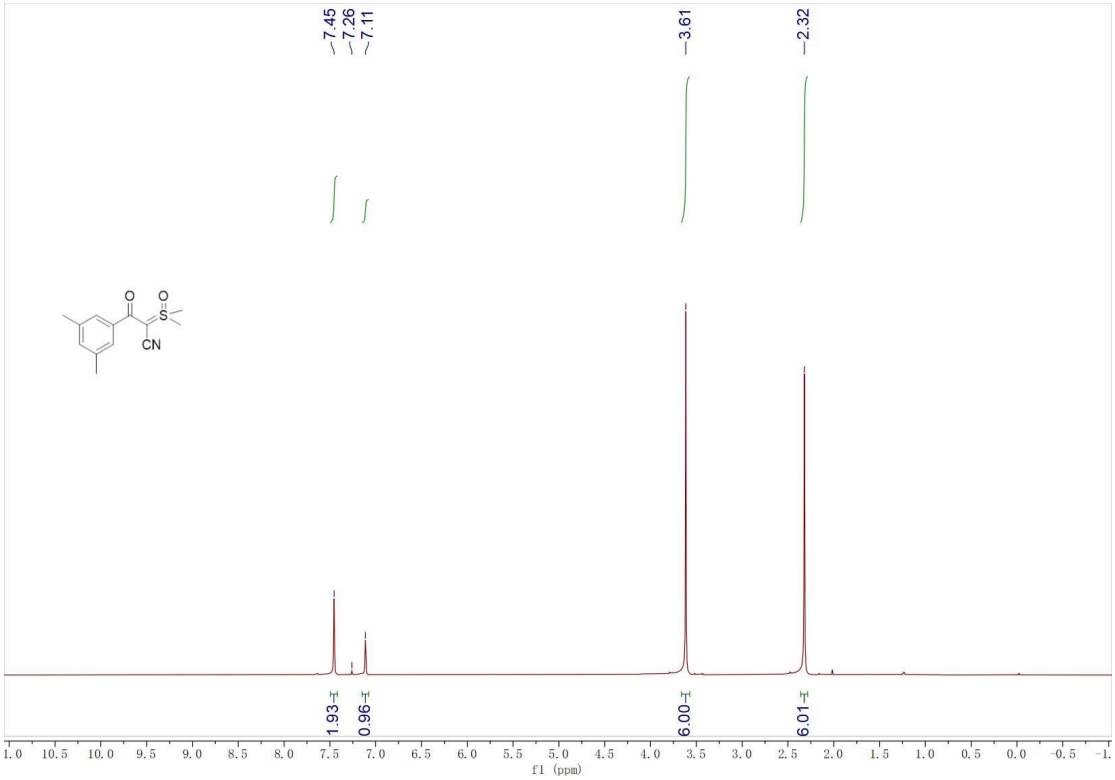


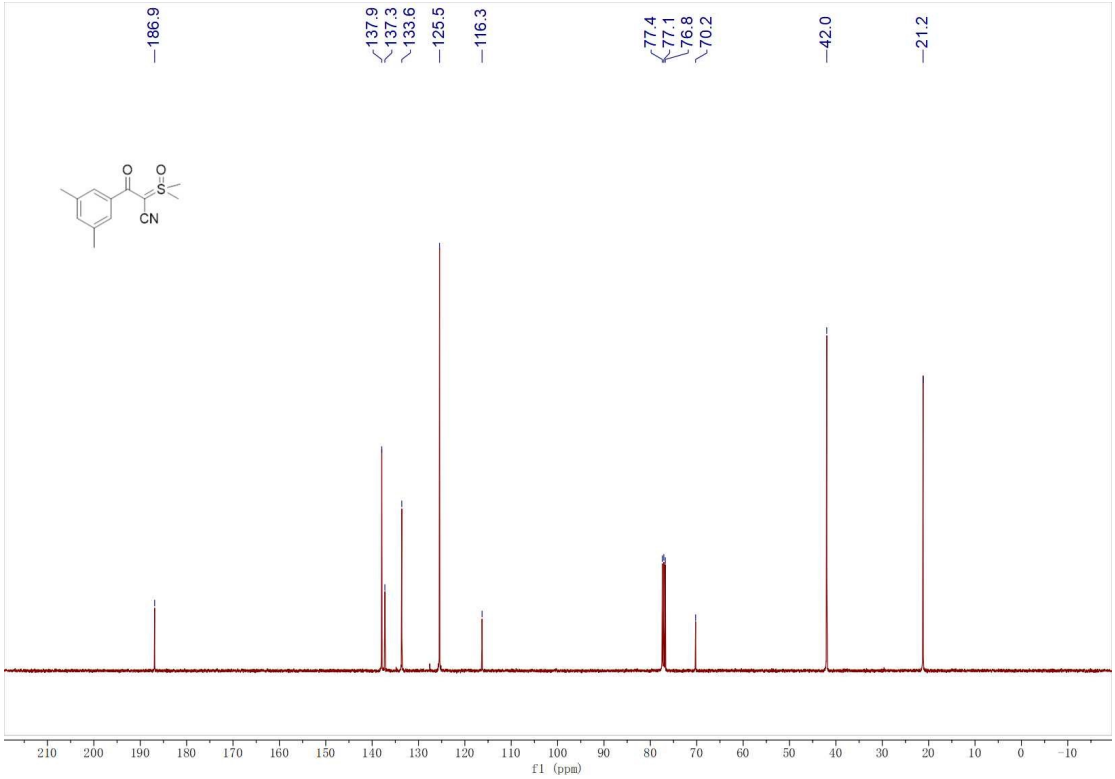
2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxo-3-(3,4,5-trimethoxyphenyl)propanenitrile (18b)



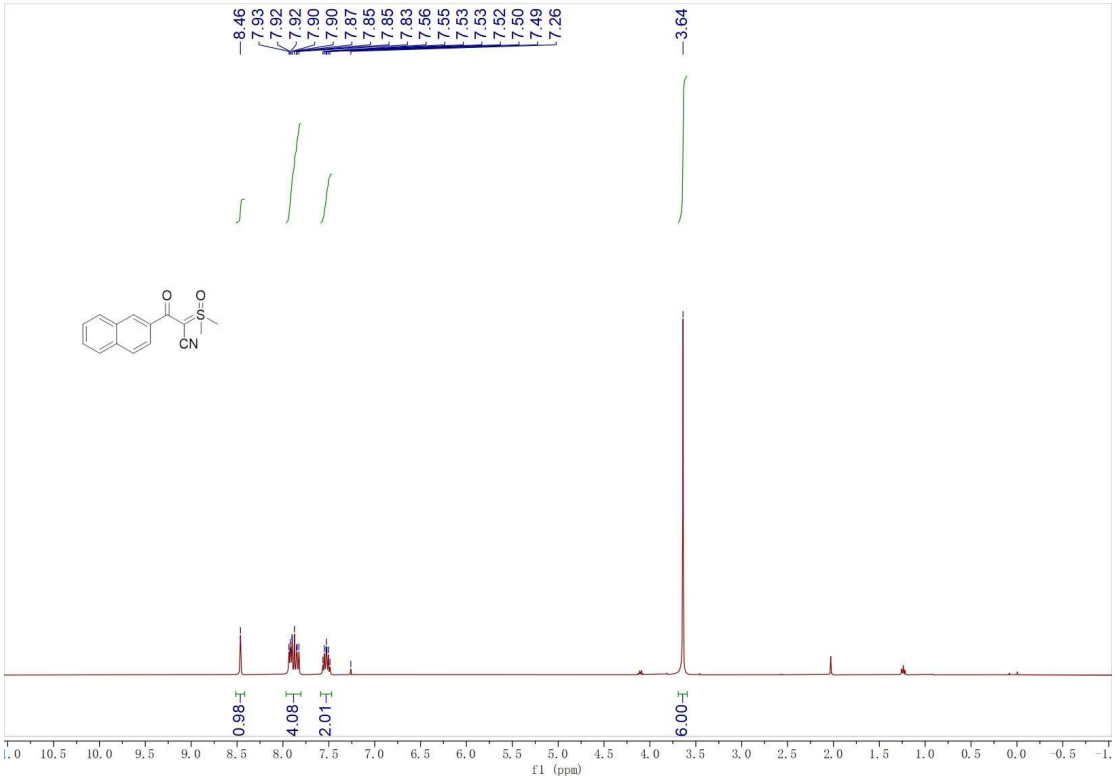


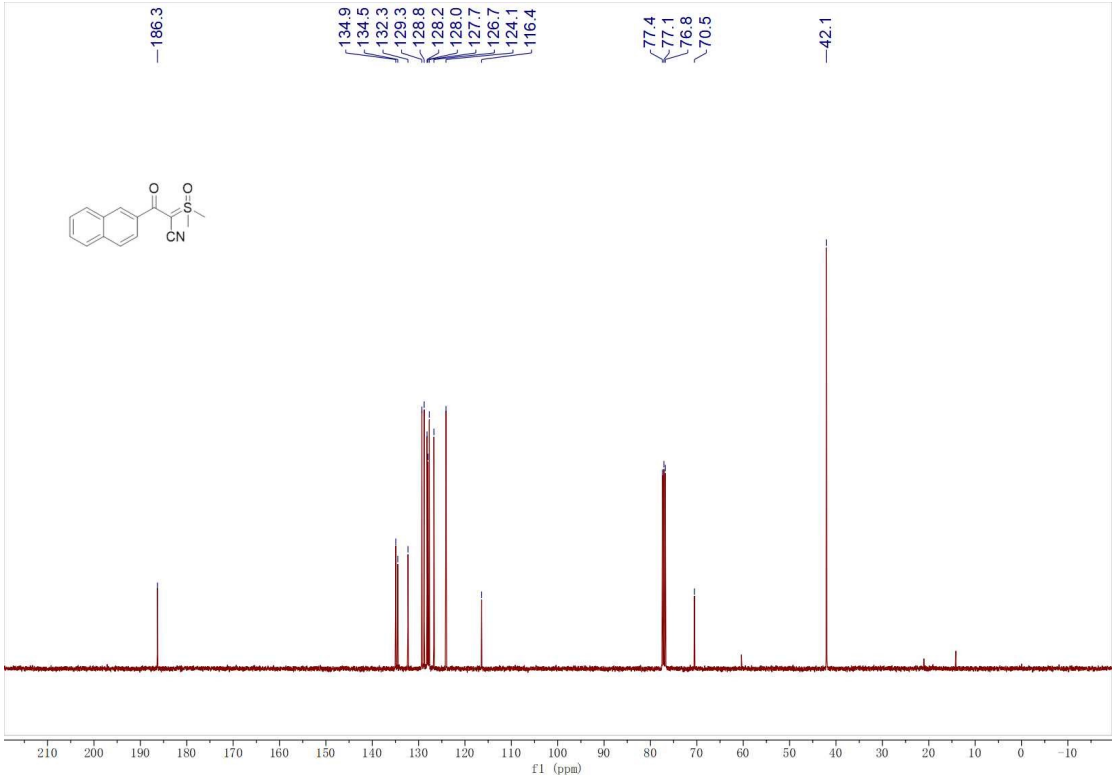
2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-(3,5-dimethylphenyl)-3-oxopropanenitrile (19b)



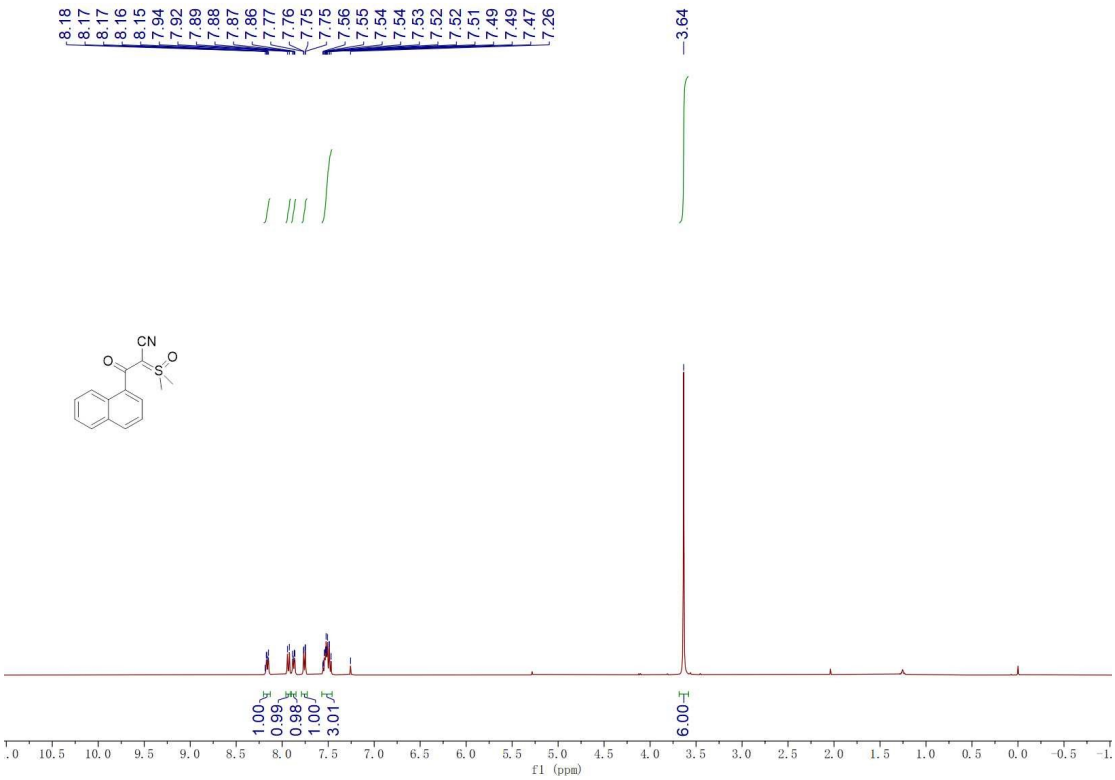


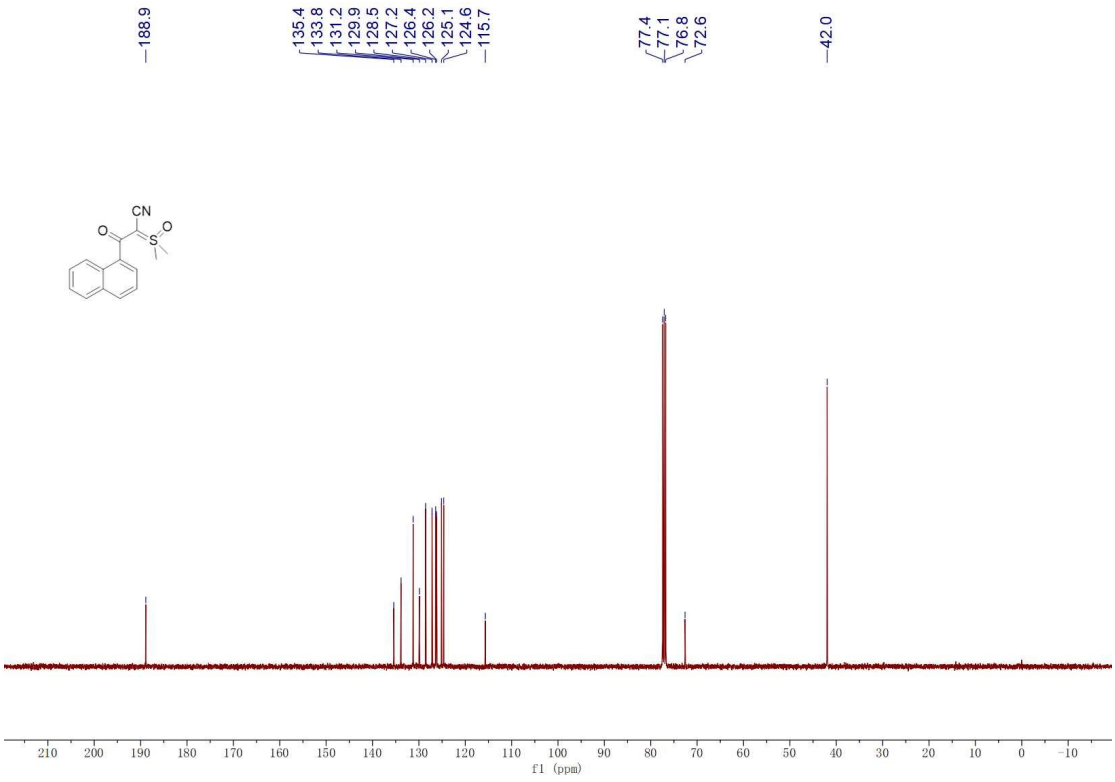
2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-(naphthalen-2-yl)-3-oxopropanenitrile (20b)



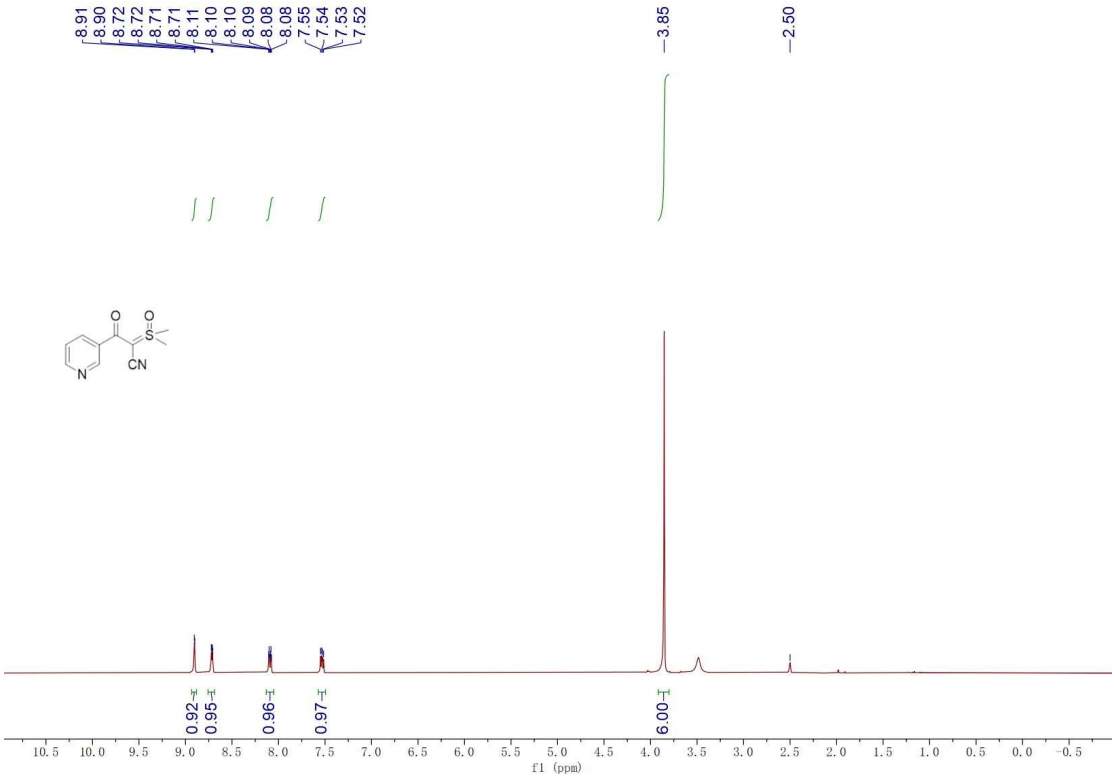


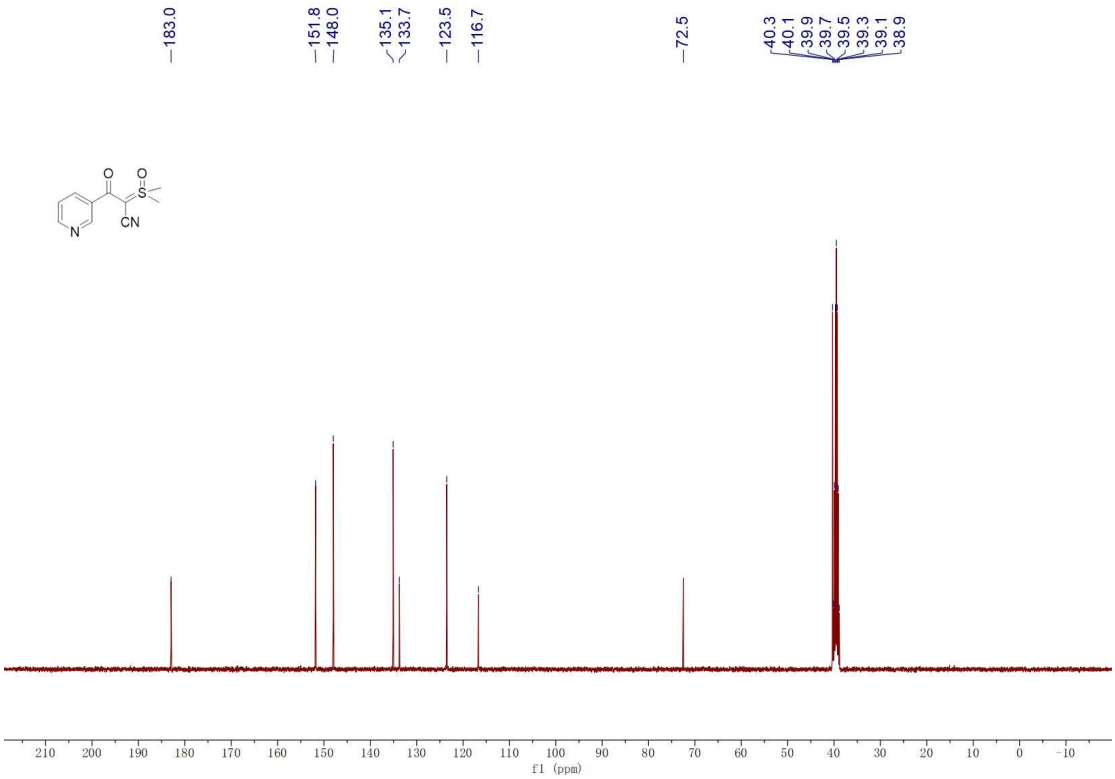
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-(naphthalen-1-yl)-3-oxopropanenitrile (21b)



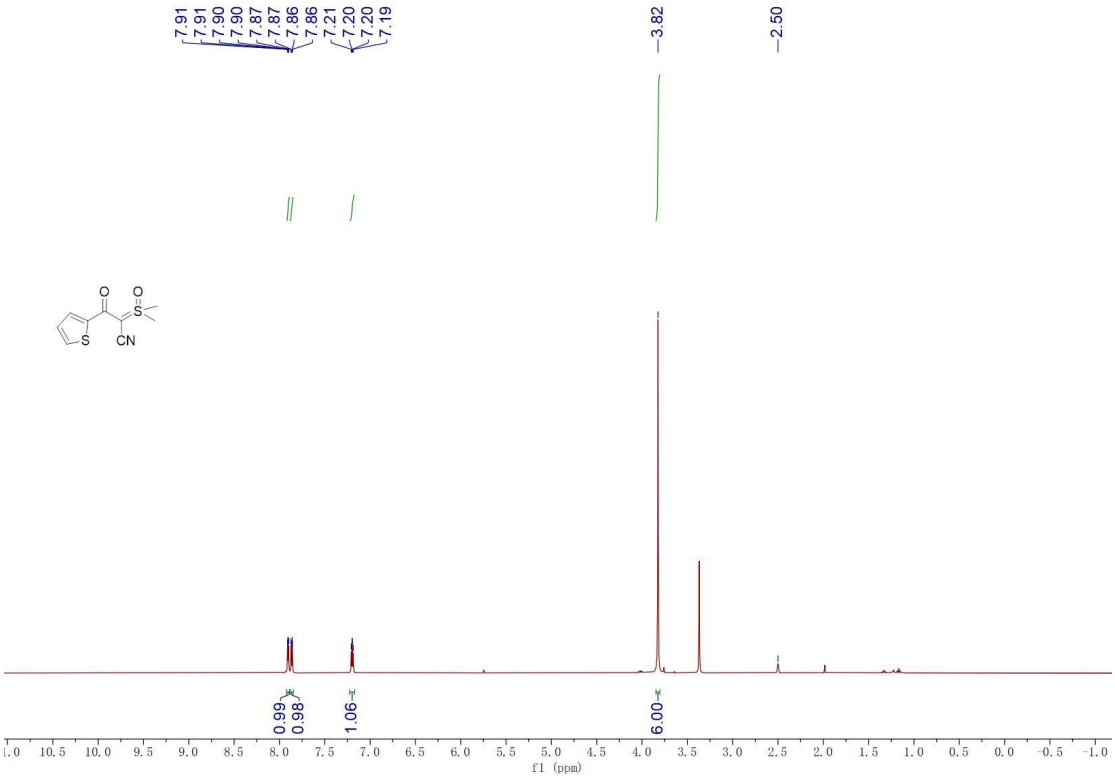


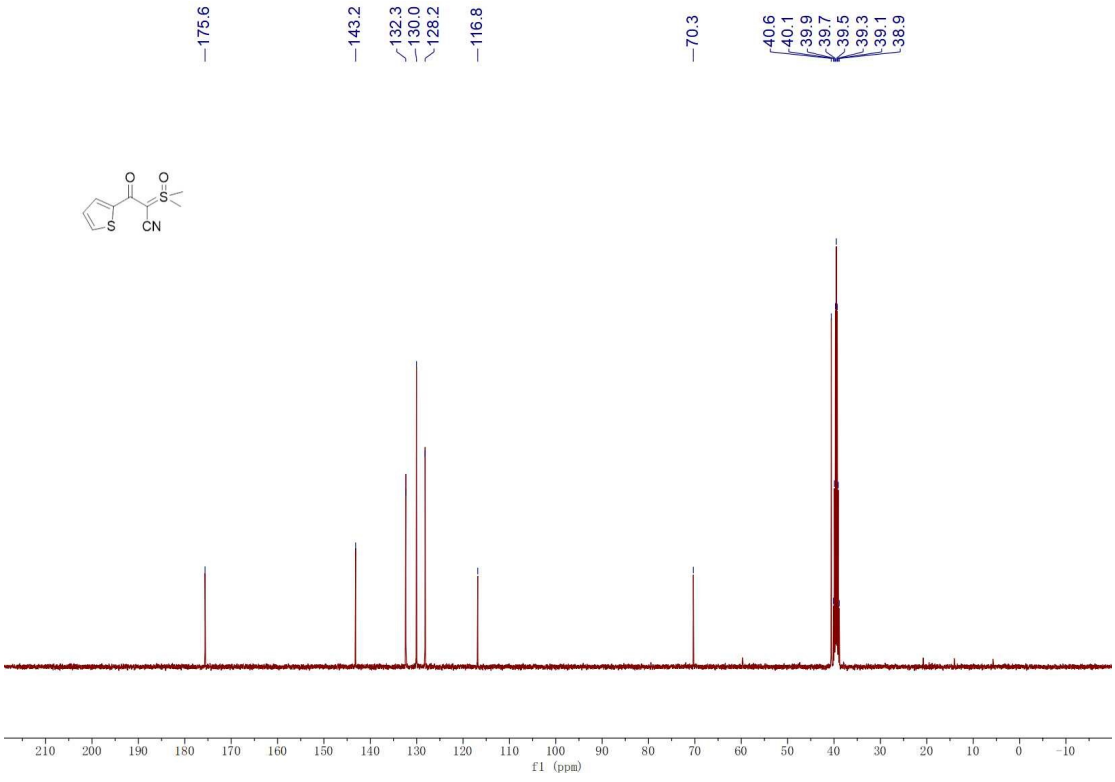
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-3-(pyridin-3-yl)propanenitrile (22b)



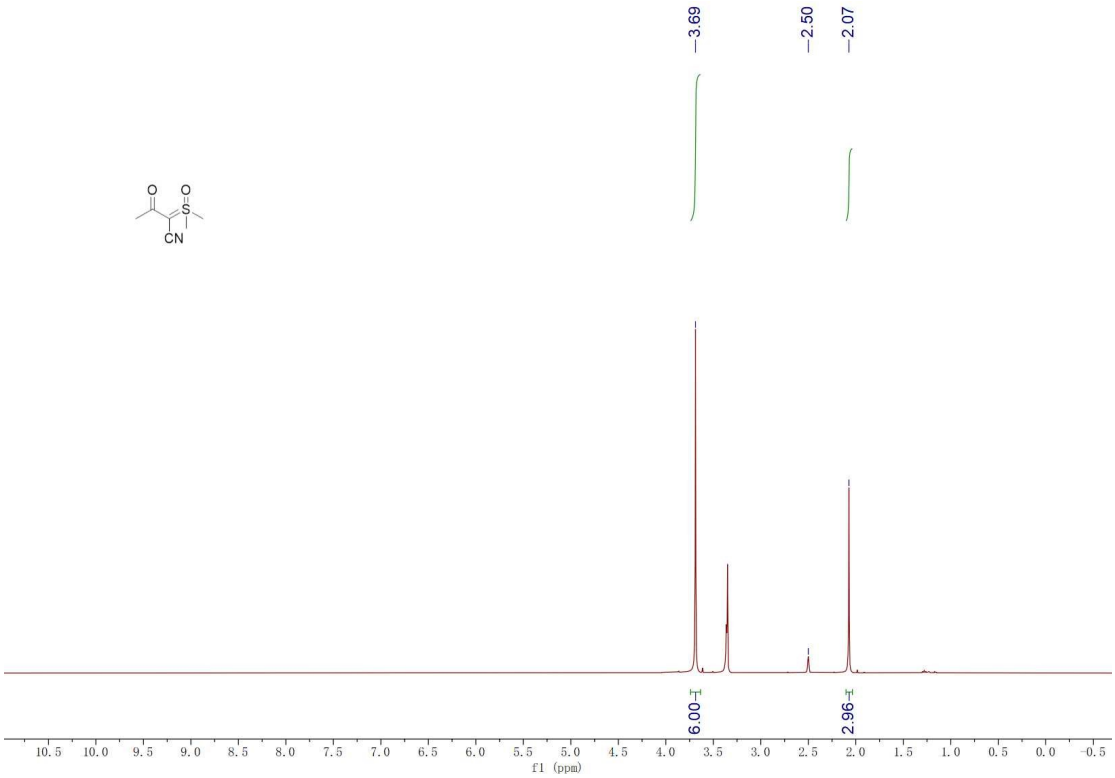


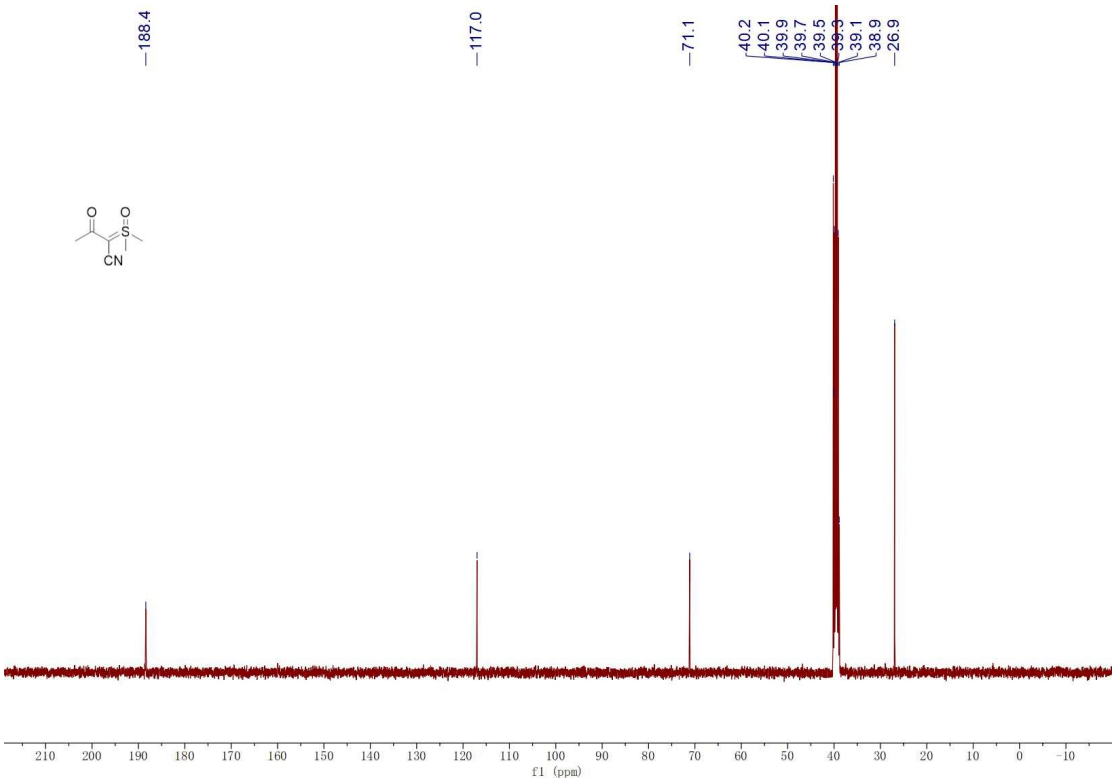
2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxo-3-(thiophen-2-yl)propanenitrile (23b)



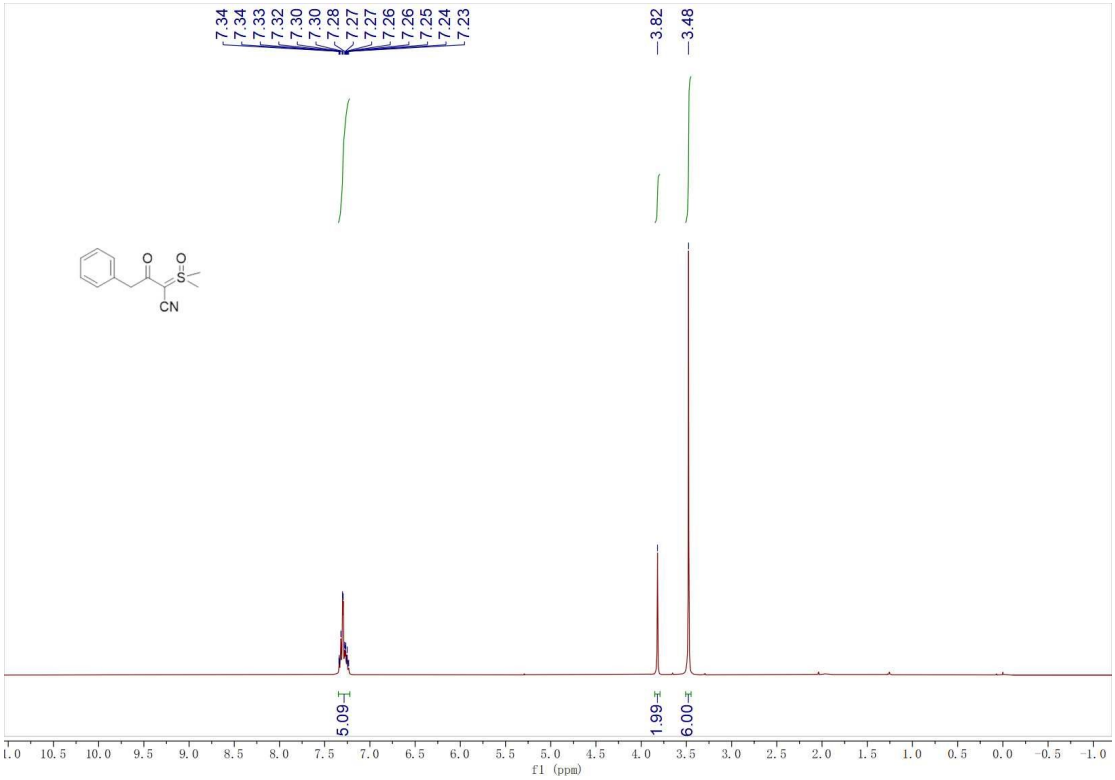


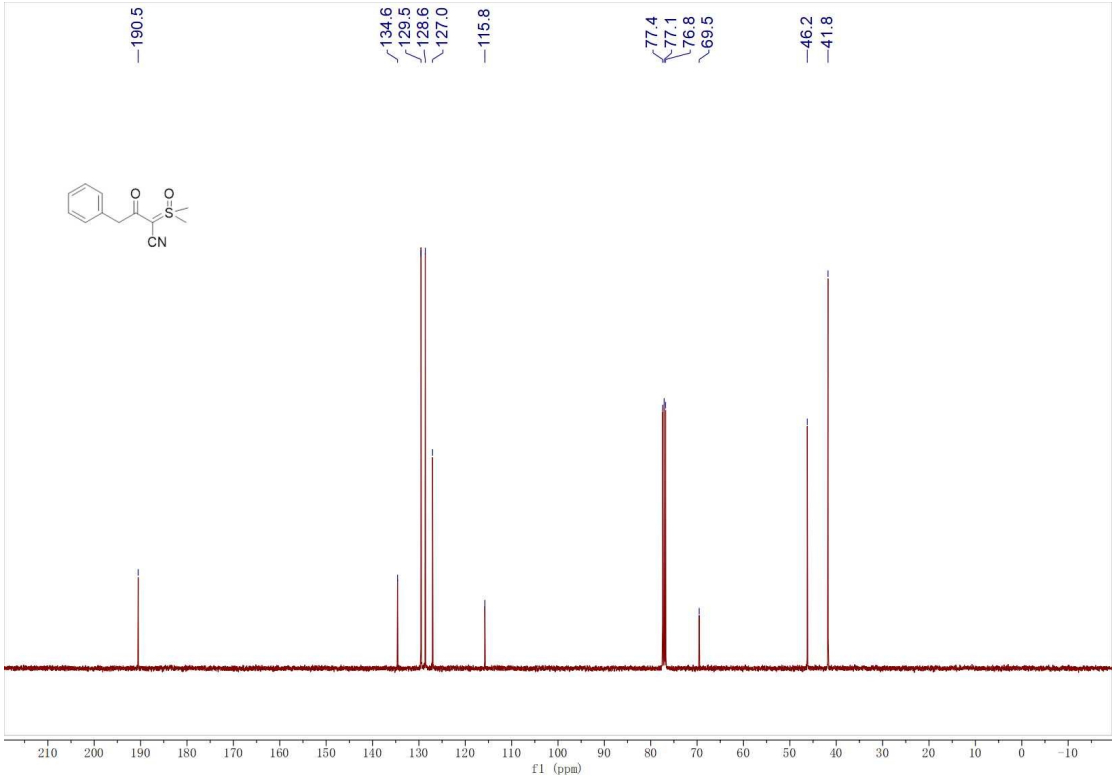
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxobutanenitrile (24b)



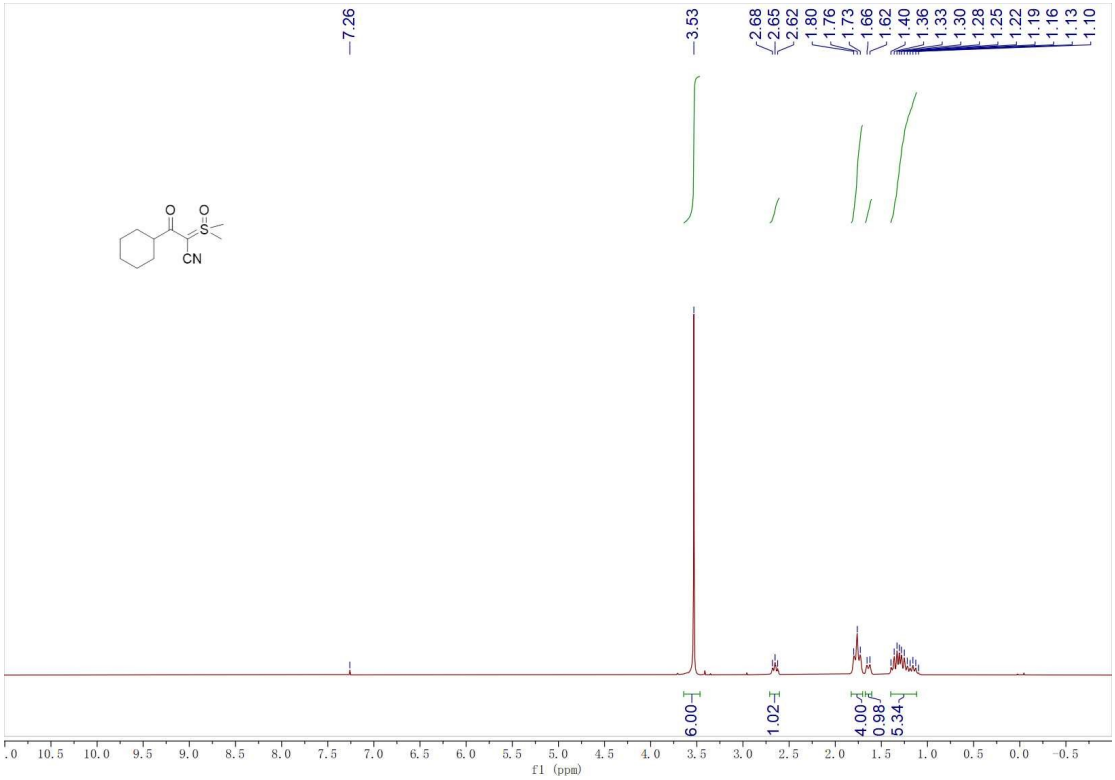


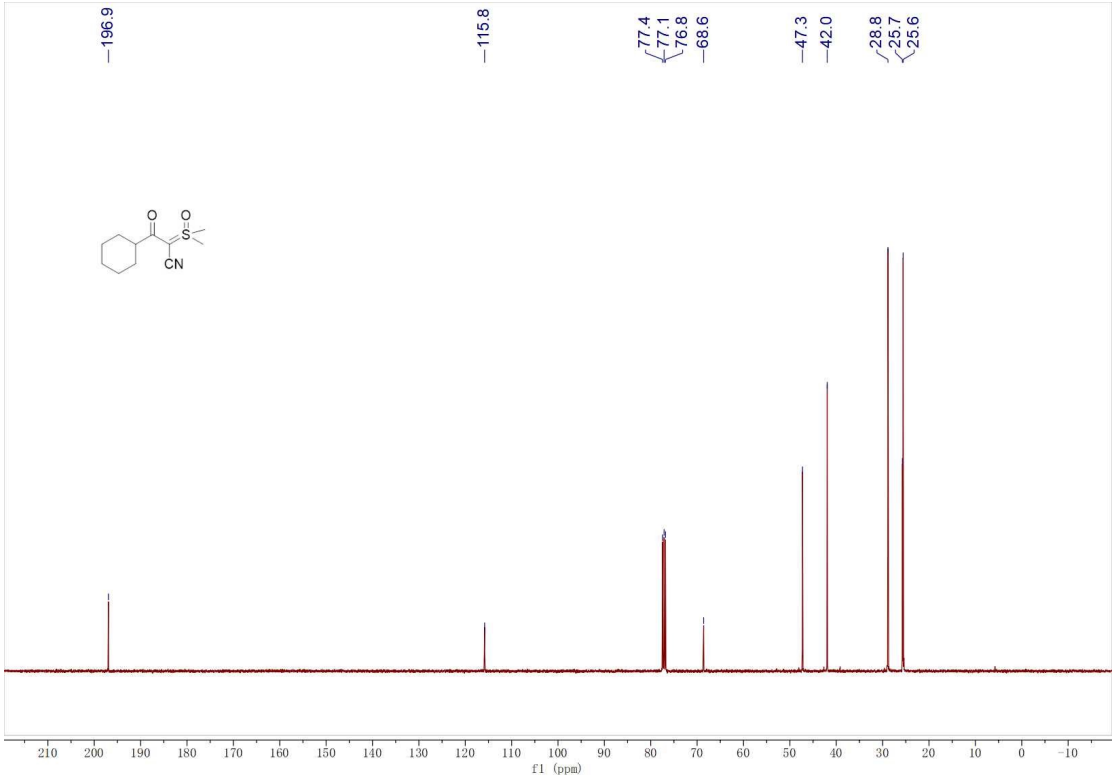
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-4-phenylbutanenitrile (25b)



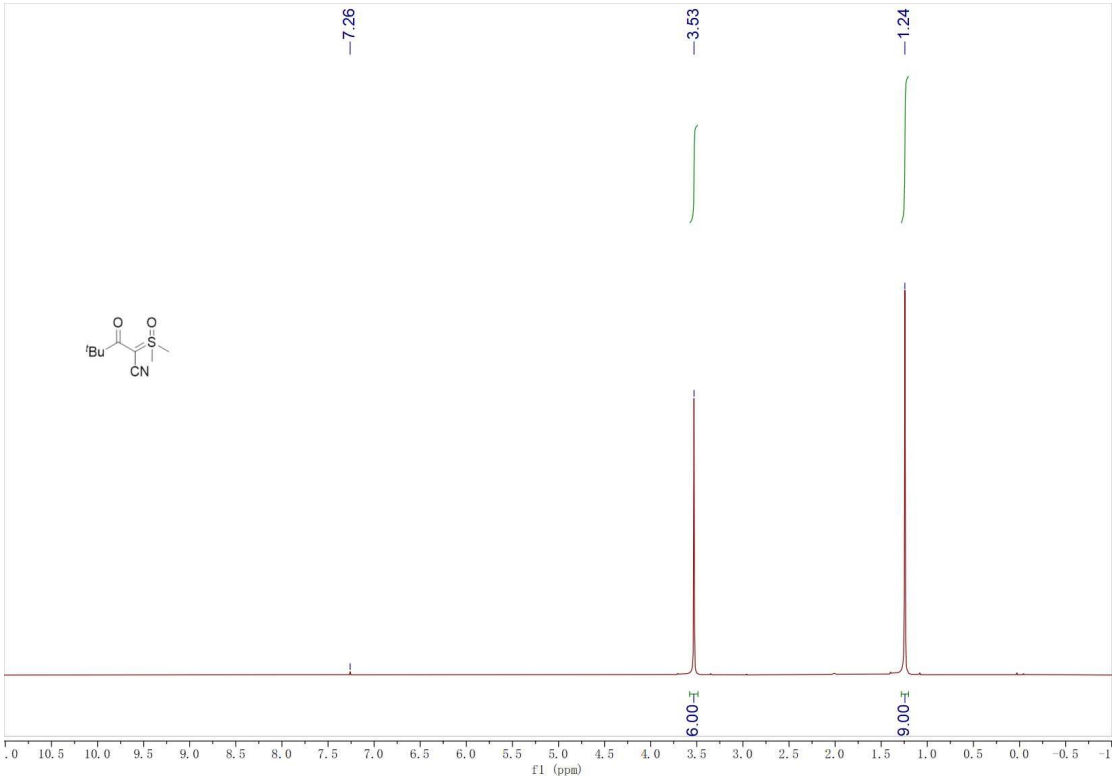


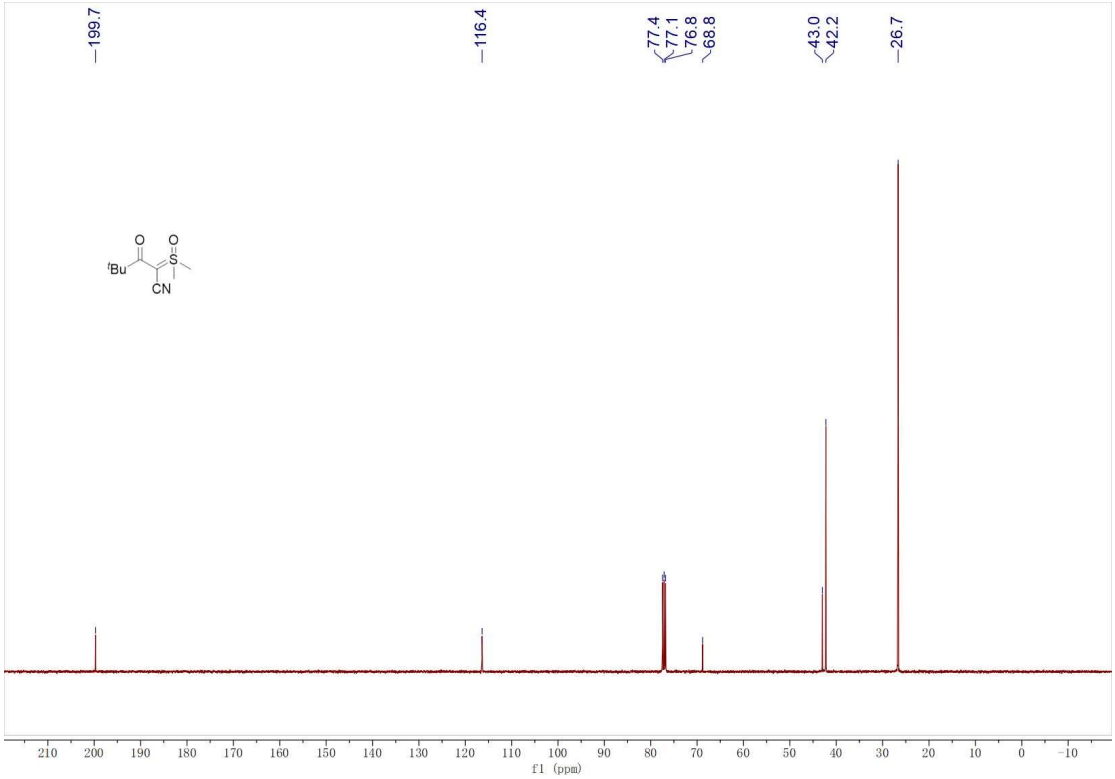
3-cyclohexyl-2-(dimethyl(oxo)-λ⁶-sulfaneylidene)-3-oxopropanenitrile (26b)



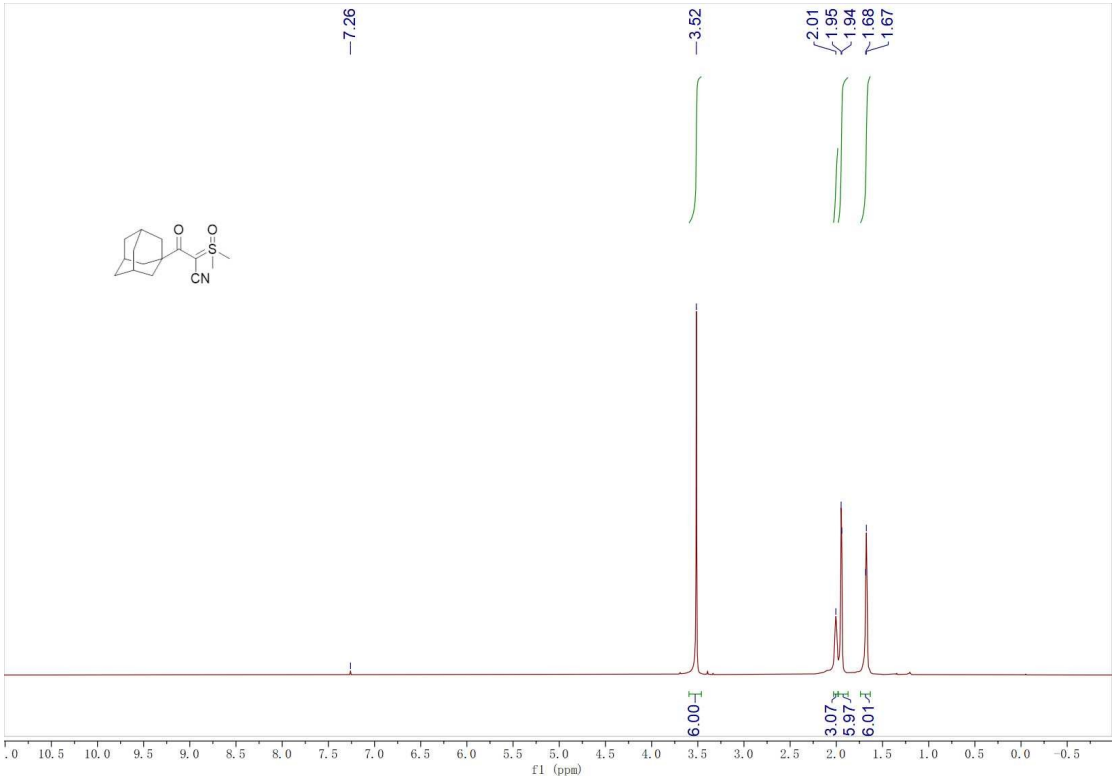


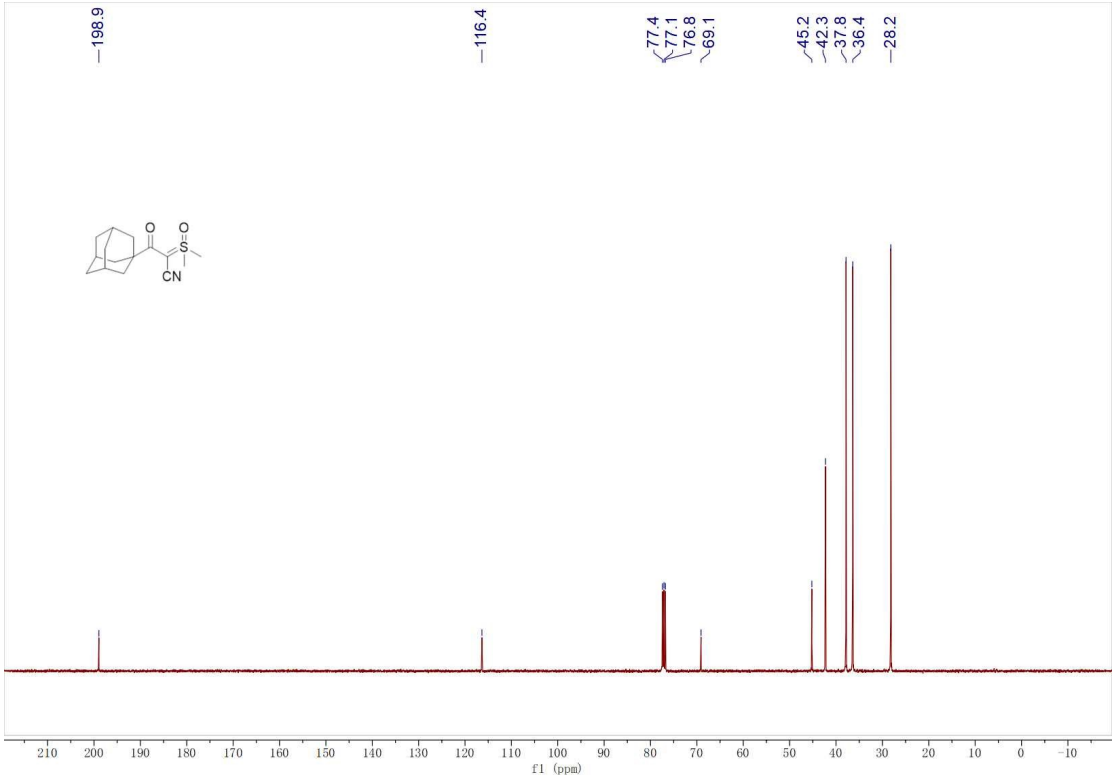
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-4,4-dimethyl-3-oxopentanenitrile (27b)



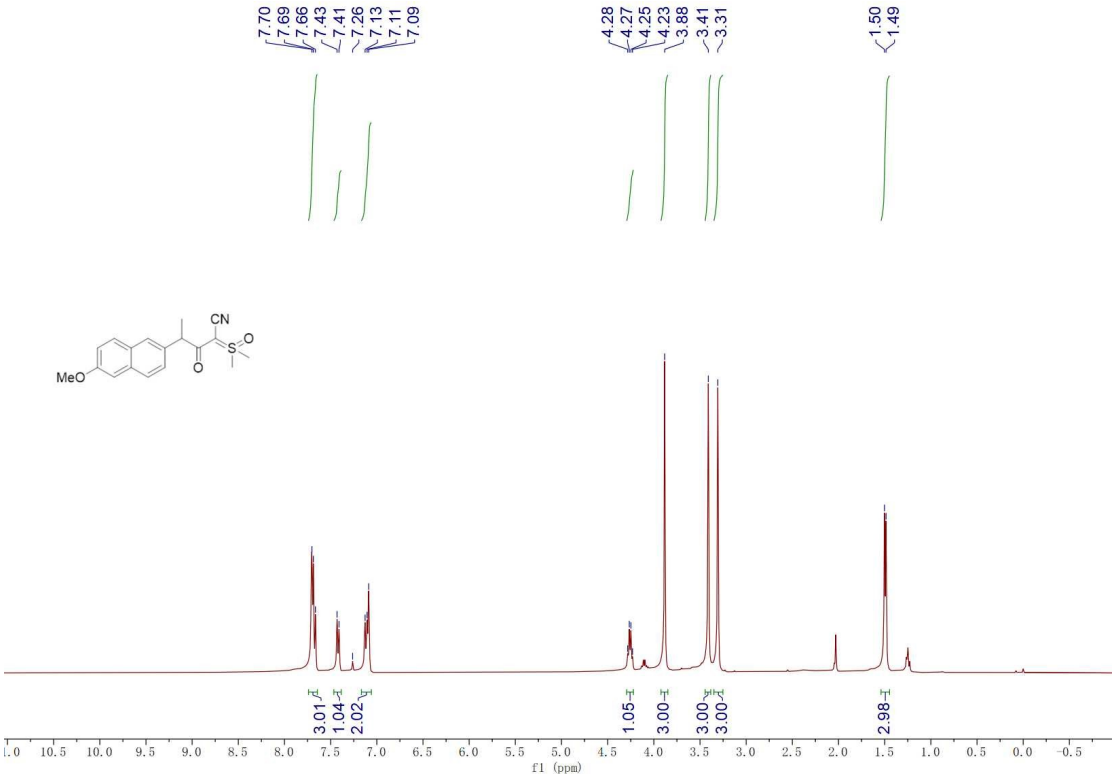


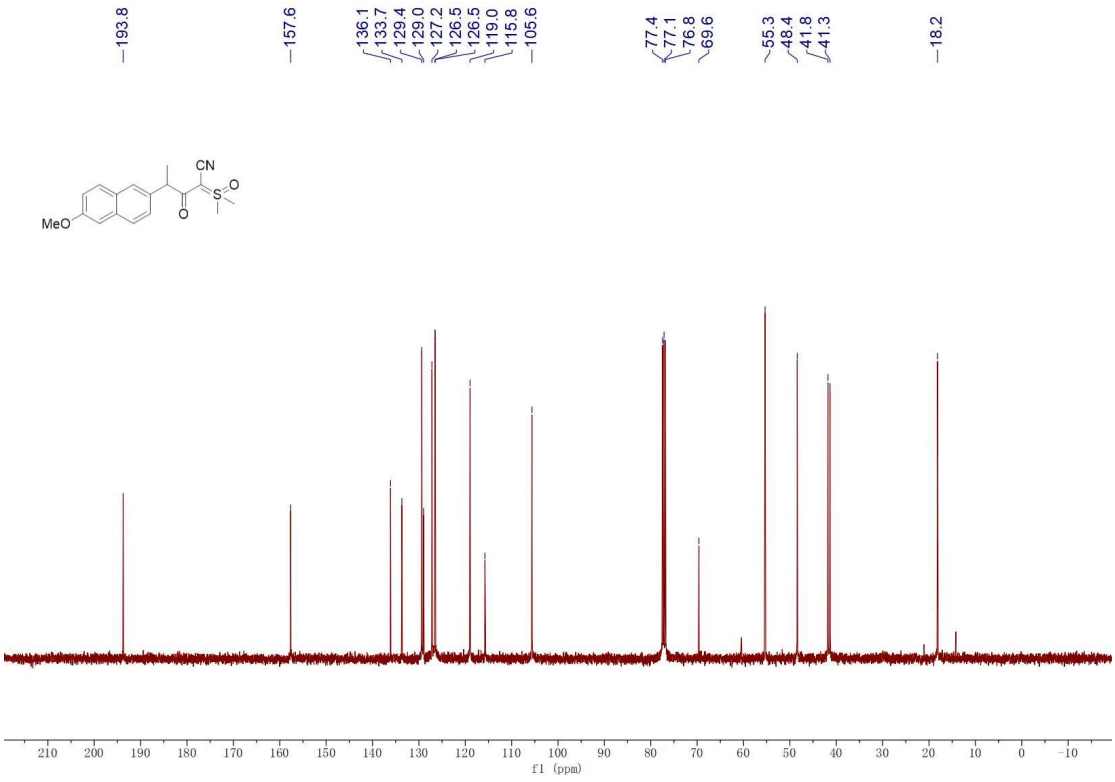
3-((3*r*,5*r*,7*r*)-adamantan-1-yl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxopropanenitrile (28b)



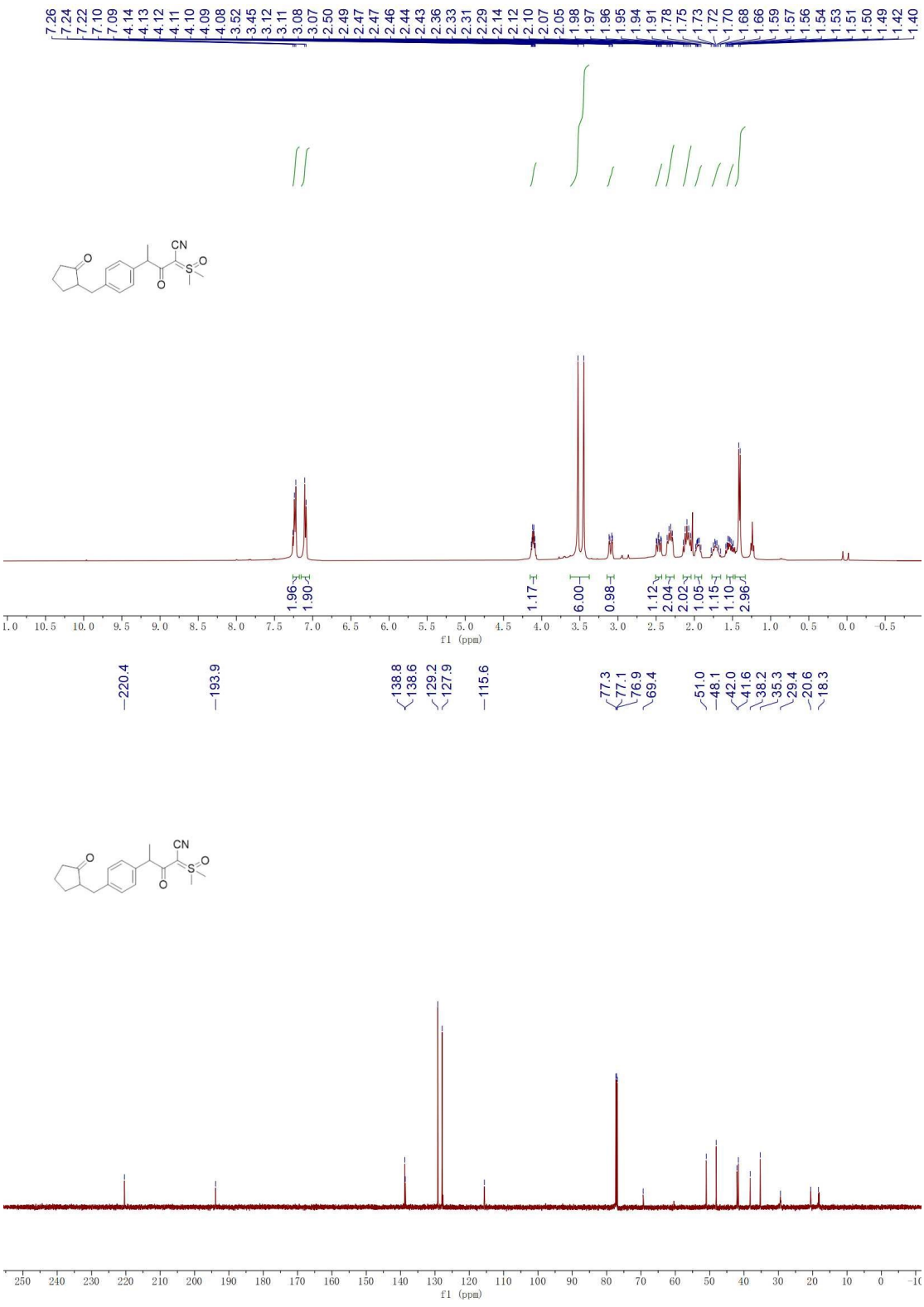


2-(dimethyl(oxo)-λ^6-sulfaneylidene)-4-(6-methoxynaphthalen-2-yl)-3-oxopentanenitrile (29b)

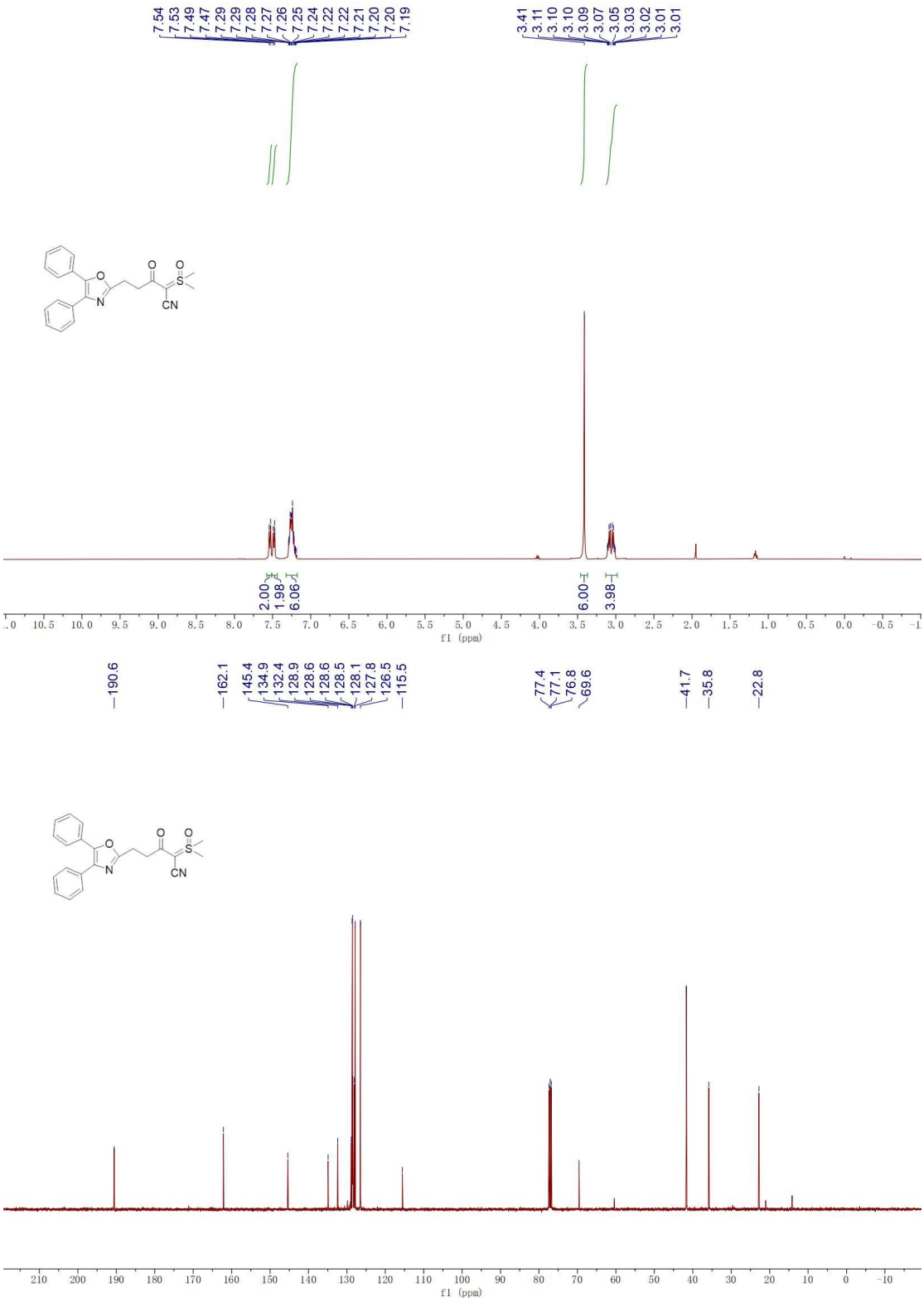




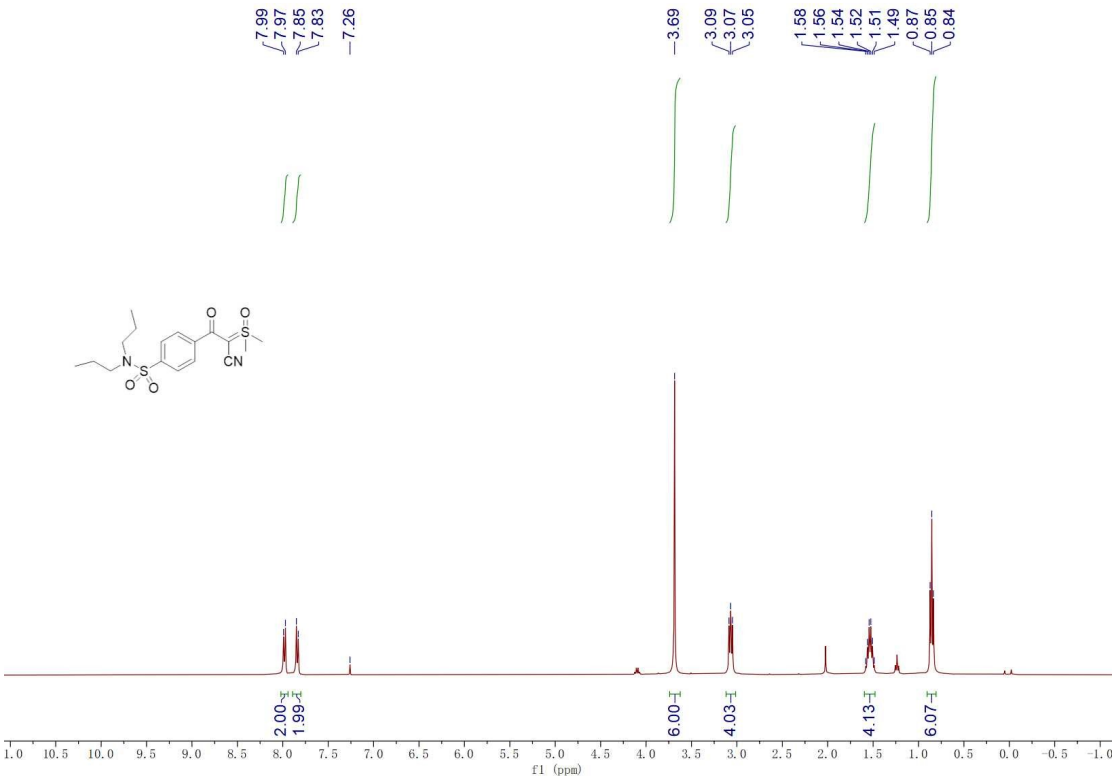
2-(dimethyl(oxo)-λ^6-sulfaneylidene)-3-oxo-4-(4-((2-oxocyclopentyl)methyl)phenyl)pentanenitrile (30b)

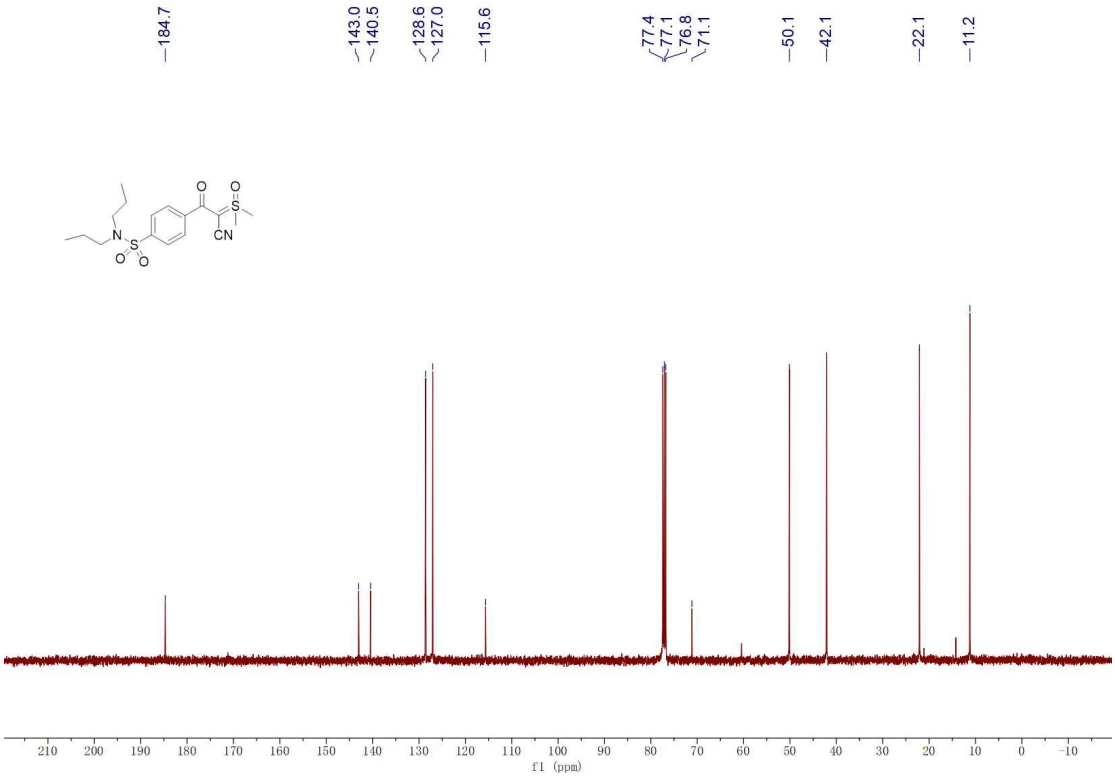


2-(dimethyl(oxo)-λ^6-sulfaneylidene)-5-(4,5-diphenyloxazol-2-yl)-3-oxopentanenitrile (31b)



4-(2-cyano-2-(dimethyl(oxo)-λ^6-sulfaneylidene)acetyl)-*N*,*N*-dipropylbenzenesulfonamide (32b)


7.99
7.97
7.85
7.83
7.26
3.69
3.09
3.07
3.05
1.58
1.56
1.54
1.52
1.51
1.49
0.87
0.85
0.84
2.00
1.99
6.00
4.03
4.13
6.07
f1 (ppm)


184.7
143.0
140.5
128.6
127.0
115.6
77.4
77.1
76.8
71.1
50.1
42.1
22.1
11.2
f1 (ppm)

5 LCMS, GCMS analysis of the reaction system and standard *p*-toluenesulfinic acid

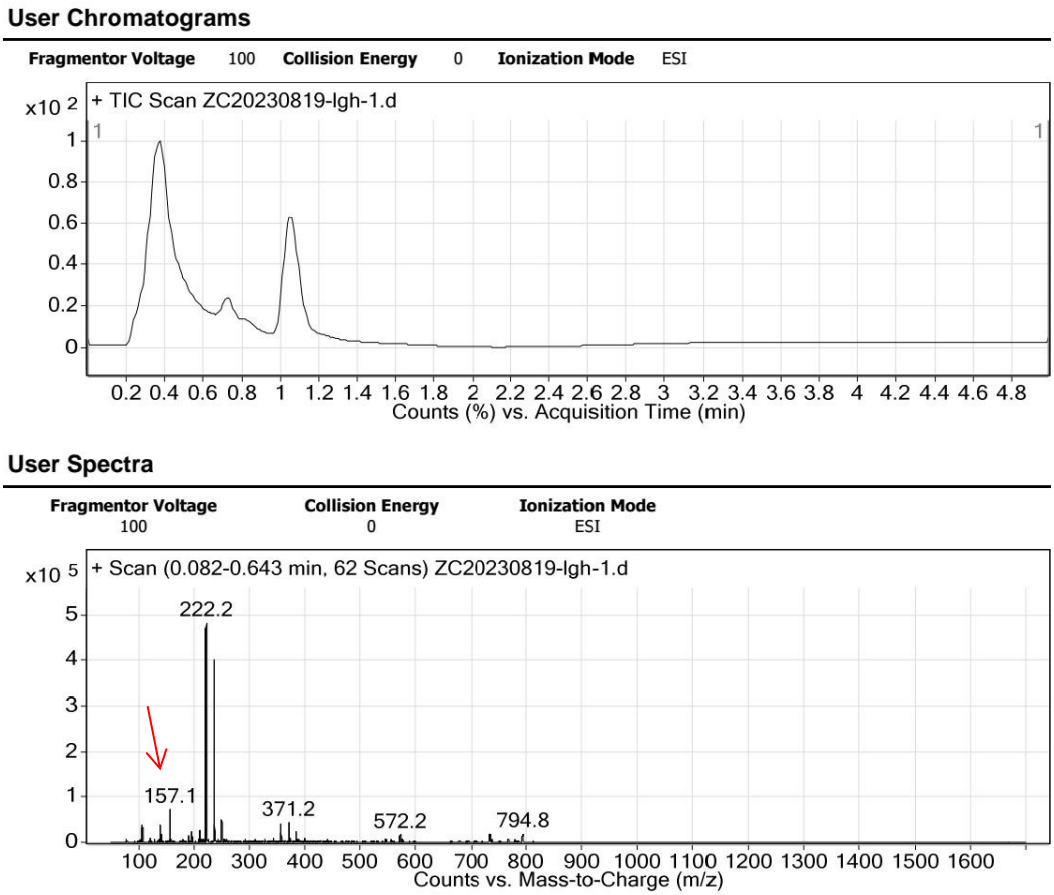


Figure 1 LCMS of the reaction system

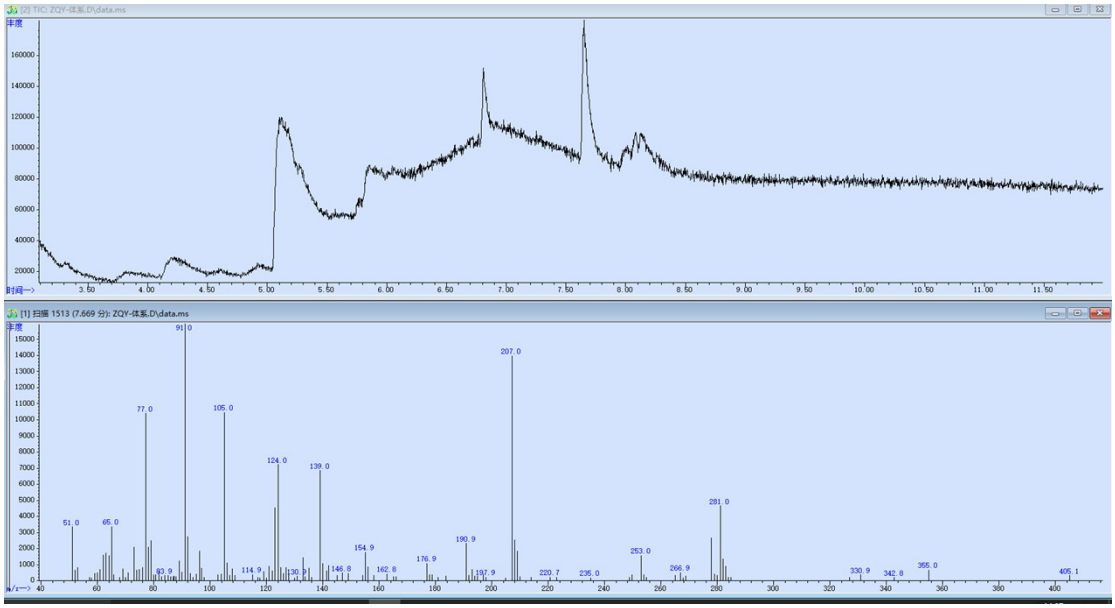


Figure 2 GCMS of the reaction system

t_R : retention time

t_R (the reaction system) = 7.669 min

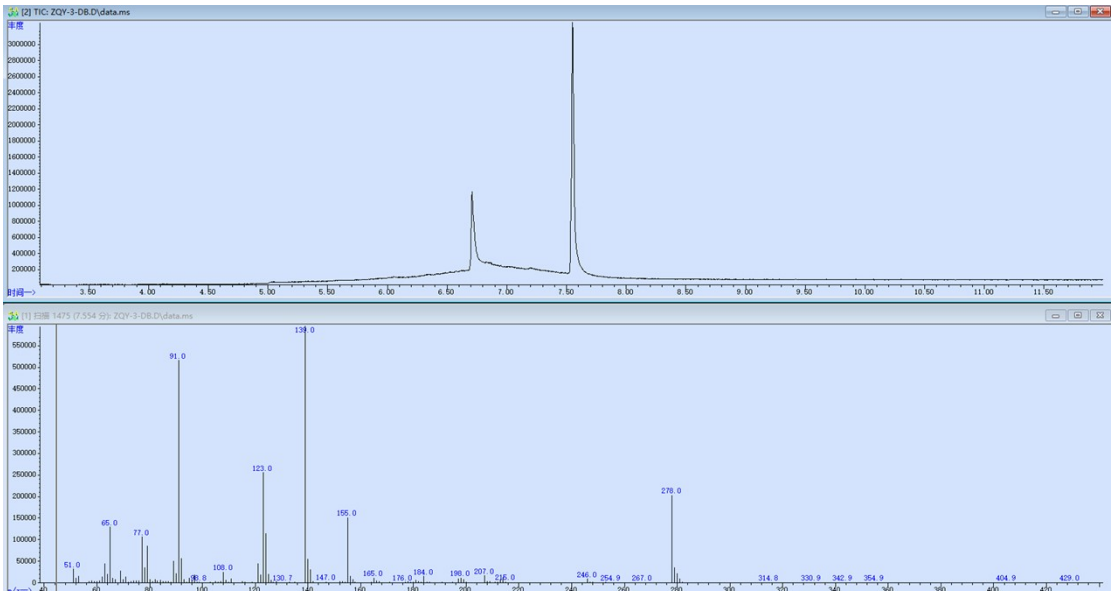


Figure 3 GCMS of the standard *p*-toluenesulfinic acid (purchased from bide pharm)

t_R (standard *p*-toluenesulfinic acid) = 7.554 min