Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

For

Oxidant-Controlled Divergent Transformations of 3-Aminoindazoles for the Synthesis of Pyrimido[1,2-b]-indazoles and Aromatic Nitrile-derived Dithioacetals

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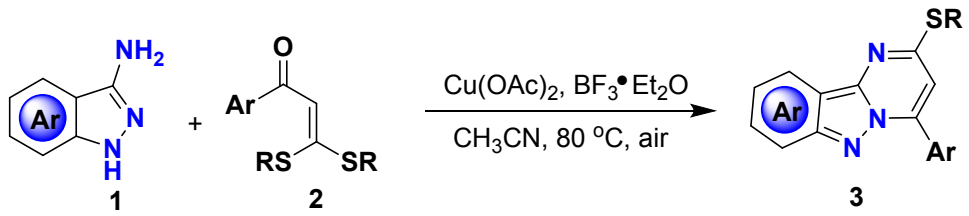
1. General information

All chemicals were purchased from Adamas Reagent, Ltd, Energy chemical company, J&K Scientific Ltd, Alfa Aesa chemical company and so forth. CH_3CN was dried by CaH prior to use. Unless otherwise stated, all experiments were conducted in a seal tube under air atmosphere. Reactions were monitored by TLC or GC-MS analysis. Flash column chromatography was performed over silica gel (200-300 mesh).

^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 500 spectrometer (500 MHz ^{1}H, 125 MHz ^{13}C) at room temperature. Chemical shifts were reported in ppm on the scale relative to $CDCl_3$ (δ = 7.26 for ^{1}H-NMR , δ = 77.00 for ^{13}C-NMR) or DMSO-d_6 (δ = 2.50 for ^{1}H-NMR, δ = 39.60 for ^{13}C-NMR) as an internal reference. High resolution mass spectra were recorded using Q-TOF time-of-flight mass spectrometer. Coupling constants (*J*) were reported in Hertz (Hz). The starting materials 1*H*-indazol-3-amine and 4-chloro-1*H*-indazol-3-amine, 5-bromo-1*H*-indazol-3-amine were purchased from Bide Pharmatech Ltd. Other 1*H*-indazol-3-amines were synthetized according to methods reported by previous literatures.[1]

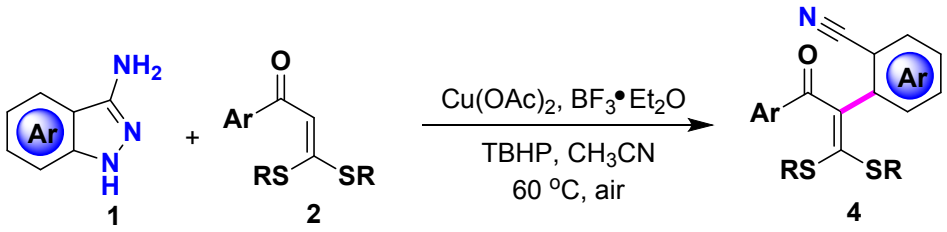
[1] (a) S. Antonysamy, G. Hirst, F. Park, P. Sprengeler, F. Stappenbeck, P. Steensma, M. Wilson, M. Wong, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 279. (b) W. Kong, Y. Zhou, Q. Song, *Adv. Synth. Catal.* **2018**, *360*, 1943.

2. General procedure for the synthesis of 3



In a sealed tube were placed **1** (0.3 mmol, 1 equiv), **2** (0.2 mmol, 1 equiv) and $Cu(OAc)_2$ (10 mol%) in CH_3CN (1 mL). Then $BF_3{\cdot}Et_2O$ (28.4 mg, 0.2 mmol, 1.0 equiv) was added to the tube. The resulting mixture was stirred at 80 °C for overnight. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 40:1, v/v) to give the desired product **3**.

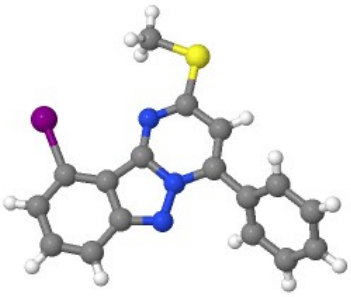
3. General procedure for the synthesis of 4



In a sealed tube were placed **1** (0.3 mmol, 1 equiv), **2** (0.2 mmol, 1 equiv) and $Cu(OAc)_2$ (10 mol%) in CH_3CN (1 mL). Then $BF_3{\cdot}Et_2O$ (28.4 mg, 0.2 mmol, 1.0 equiv) and TBHP (0.4 mmol, 2 equiv) were added to the tube. The resulting mixture was stirred at 60 °C for 18 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 80:1, v/v) to give the desired product **4**.

4. Crystal data of 3s and 4m

Crystallographic data for compound **3s** (CCDC-1906431) has been deposited with the Cambridge Crystallographic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email:deposit@ccdc.cam.ac.uk).



Displacement ellipsoids are drawn at 30% probability level

Bond precision: C-C = 0.0082 A Wavelength=0.71073

Cell: a=4.1200(5) b=14.2279(12) c=26.763(2)
alpha=90 beta=94.268(8) gamma=90

Temperature: 295 K

	Calculated	Reported
Volume	1564.5(3)	1564.5(3)
Space group	P 21/n	P 21/n
Hall group	-P 2yn	-P 2yn
Moiety formula	C17 H12 I N3 S	C17 H12 I N3 S
Sum formula	C17 H12 I N3 S	C17 H12 I N3 S
Mr	417.26	417.26
Dx,g cm-3	1.771	1.772
Z	4	4
Mu (mm-1)	2.179	2.179
F000	816.0	816.0
F000'	814.82	
h,k,lmax	5,17,32	5,17,32
Nref	3067	3060
Tmin,Tmax	0.599,0.706	0.462,1.000
Tmin'	0.587	

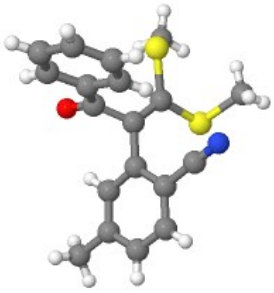
Correction method= # Reported T Limits: Tmin=0.462
Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.998 Theta(max)= 25.998

R(reflections)= 0.0463(2798) wR2(reflections)= 0.0989(3060)

S = 1.124 Npar= 201

Crystallographic data for compound **4m** (CCDC-1874924) has been deposited with the Cambridge Crystallographic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email:deposit@ccdc.cam.ac.uk).



Displacement ellipsoids are drawn at 30% probability level

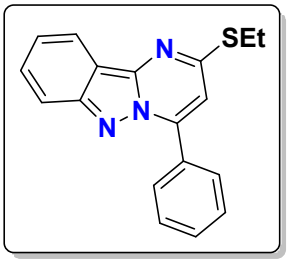
Bond precision: C-C = 0.0054 A Wavelength=0.71073
Cell: a=10.1327(10) b=12.0719(14) c=28.967(3)
alpha=90 beta=90 gamma=90
Temperature: 298 K

	Calculated	Reported
Volume	3543.3(7)	3543.3(7)
Space group	P b c a	P b c a
Hall group	-P 2ac 2ab	-P 2ac 2ab
Moiety formula	C19 H17 N O S2	C19 H17 N O S2
Sum formula	C19 H17 N O S2	C19 H17 N O S2
Mr	339.46	339.49
Dx,g cm-3	1.273	1.273
Z	8	8
Mu (mm-1)	0.304	0.304
F000	1424.0	1426.5
F000'	1426.45	
h,k,lmax	12,14,34	12,14,34
Nref	3117	3111
Tmin,Tmax		0.097,1.000
Tmin'		

Correction method= # Reported T Limits: Tmin=0.097 Tmax=1.000
AbsCorr = MULTI-SCAN
Data completeness= 0.998 Theta(max)= 25.000
R(reflections)= 0.0631(1790) wR2(reflections)= 0.1421(3111)
S = 0.951 Npar= 210

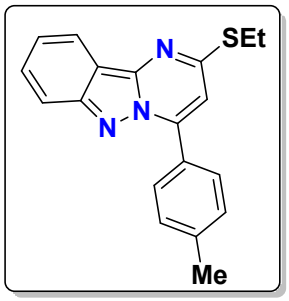
5. Characterization data for products

2-(ethylthio)-4-phenylpyrimido[1,2-b]indazole (3a)



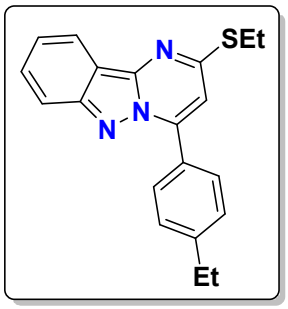
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (52.5 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1H), 8.17 – 8.07 (m, 2H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.61 – 7.51 (m, 4H), 7.25 – 7.19 (m, 1H), 7.06 (s, 1H), 3.43 (q, *J* = 7.4 Hz, 2H), 1.53 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.0, 151.0, 144.7, 144.3, 131.1, 130.9, 129.5, 129.4, 128.7, 120.8, 120.1, 116.4, 112.4, 110.5, 24.6, 14.4. HRMS (ESI, m/z) calcd for $C_{18}H_{16}N_3$ $[M+H]^+$: 306.1059; found: 306.1060.

2-(ethylthio)-4-(p-tolyl)pyrimido[1,2-b]indazole (3b)



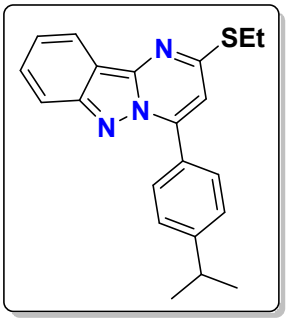
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (56.1 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 2H), 7.80 (d, *J* = 8.7 Hz, 1H), 7.60 – 7.54 (m, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.08 (s, 1H), 3.45 (q, *J* = 7.4 Hz, 2H), 2.49 (s, 3H), 1.55 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.9, 150.9, 144.7, 144.5, 141.4, 129.5, 129.4, 129.3, 128.2, 120.8, 120.0, 116.4, 112.4, 110.1, 24.6, 21.5, 14.4. HRMS (ESI, m/z) calcd for $C_{19}H_{18}N_3S$$[M+H]^+$: 320.1216; found: 320.1219.

4-(4-ethylphenyl)-2-(ethylthio)pyrimido[1,2-b]indazole (3c)



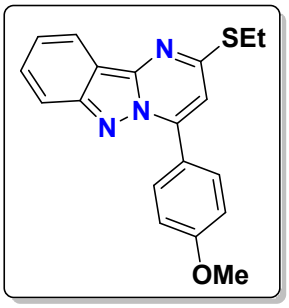
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (54.6 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.58 – 7.52 (m, 1H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.22 (dd, *J* = 10.9, 3.9 Hz, 1H), 7.06 (s, 1H), 3.42 (q, *J* = 7.4 Hz, 2H), 2.77 (q, *J* = 7.6 Hz, 2H), 1.53 (t, *J* = 7.4 Hz, 3H), 1.32 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.0, 151.0, 147.6, 144.7, 144.5, 129.5, 129.4, 128.4, 128.25, 120.8, 120.0, 116.4, 112.4, 110.2, 28.9, 24.6, 15.3, 14.4. HRMS (ESI, m/z) calcd for $C_{20}H_{20}N_3S$ $[M+H]^+$: 334.1372; found: 334.1375.

2-(ethylthio)-4-(4-isopropylphenyl)pyrimido[1,2-b]indazole (3d)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (52.1 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.54 (ddd, *J* = 8.6, 6.6, 1.1 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.24 – 7.18 (m, 1H), 7.06 (s, 1H), 3.42 (q, *J* = 7.4 Hz, 2H), 3.02 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.53 (t, *J* = 7.4 Hz, 3H), 1.33 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.0, 152.2, 151.0, 144.7, 144.5, 129.5, 129.4, 128.6, 126.9, 120.9, 120.1, 116.4, 112.4, 110.2, 34.2, 24.6, 23.8, 14.4. HRMS (ESI, m/z) calcd for $C_{21}H_{22}N_3S$ $[M+H]^+$: 348.1529; found: 348.1531.

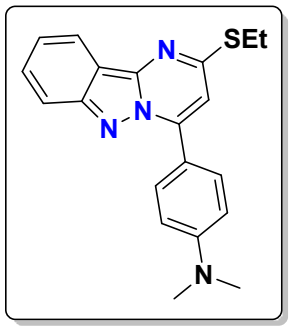
2-(ethylthio)-4-(4-methoxyphenyl)pyrimido[1,2-b]indazole (3e)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (60.3 mg, 90%).^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.3 Hz, 1H), 8.17 – 8.09 (m, 2H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.59 – 7.50 (m, 1H), 7.23 – 7.17 (m, 1H), 7.08 (d, *J* = 8.9 Hz, 2H), 7.04 (s, 1H), 3.90 (s, 3H), 3.42 (q, *J* = 7.4 Hz, 2H), 1.52 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.7, 156.9, 150.9, 144.7, 144.1, 131.1, 129.4, 123.2, 120.9, 12.0, 116.3, 114.1, 112.3, 109.6, 55.4, 24.6, 14.4.

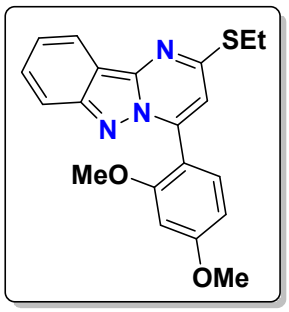
HRMS (ESI, m/z) calcd for $C_{19}H_{18}N_3OS$ $[M+H]^+$: 336.1165; found: 336.1165.

4-(2-(ethylthio)pyrimido[1,2-b]indazol-4-yl)-N,N-dimethylaniline (3f)



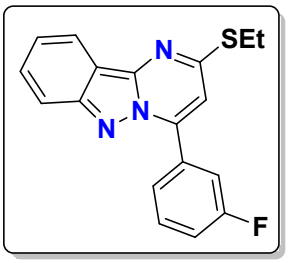
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (53.6 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.3 Hz, 1H), 8.20 – 8.13 (m, 2H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.60 – 7.49 (m, 1H), 7.22 – 7.15 (m, 1H), 7.06 (s, 1H), 6.84 (d, *J* = 9.0 Hz, 2H), 3.41 (q, *J* = 7.4 Hz, 2H), 3.07 (s, 6H), 1.52 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.6, 152.0, 150.8, 144.9, 144.8, 130.8, 129.2, 120.9, 119.7, 117.7, 116.3, 112.3, 111.5, 108.4, 40.1, 24.6, 14.5. HRMS (ESI, m/z) calcd for $C_{20}H_{21}N_4S$ $[M+H]^+$: 349.1481; found: 349.1487.

4-(2,4-dimethoxyphenyl)-2-(ethylthio)pyrimido[1,2-b]indazole (3g)



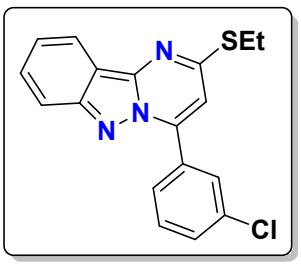
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow oil (58.9 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1H), 7.75 (d, *J* = 8.7 Hz, 1H), 7.58 – 7.46 (m, 1H), 7.24 – 7.17 (m, 2H), 7.10 – 7.01 (m, 3H), 3.81 (s, 3H), 3.74 (s, 3H), 3.42 (q, *J* = 7.4 Hz, 2H), 1.53 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4, 153.5, 151.6, 150.8, 144.2, 142.2, 129.2, 121.0, 120.8, 119.9, 117.4, 116.5, 116.0, 113.3, 112.4, 112.2, 56.4, 55.8, 24.6, 14.4. HRMS (ESI, m/z) calcd for $C_{20}H_{20}O_2N_3S$ $[M+H]^+$: 366.1271; found: 366.1271.

2-(ethylthio)-4-(3-fluorophenyl)pyrimido[1,2-b]indazole (3h)



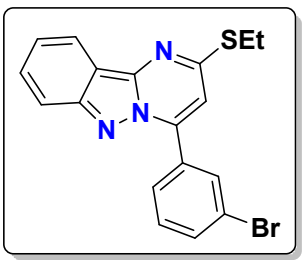
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (54.9 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.3 Hz, 1H), 7.97 – 7.91 (m, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.60 – 7.51 (m, 2H), 7.31 – 7.26 (m, 1H), 7.25 – 7.20 (m, 1H), 7.07 (s, 1H), 3.43 (q, *J* = 7.4 Hz, 2H), 1.53 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.5 (d, *J* = 247.6 Hz), 157.0, 151.0, 144.7, 142.8, 133.0 (d, *J* = 8.4 Hz), 130.4 (d, *J* = 8.3 Hz), 129.7, 125.1 (d, *J* = 3.1 Hz), 120.8, 120.4, 118.0 (d, *J* = 21.0 Hz), 116.7 (d, *J* = 23.9 Hz), 116.4, 112.4, 110.6, 24.7, 14.3. HRMS (ESI, m/z) calcd for $C_{18}H_{15}FN_3S$ $[M+H]^+$: 324.0965; found: 324.0969.

4-(3-chlorophenyl)-2-(ethylthio)pyrimido[1,2-b]indazole (3i)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (47.5 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.3 Hz, 1H), 8.11 (t, *J* = 1.6 Hz, 1H), 8.00 (dt, *J* = 7.4, 1.4 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.59 – 7.49 (m, 3H), 7.25 – 7.20 (m, 1H), 7.04 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.0, 151.0, 144.7, 142.7, 134.7, 132.8, 131.0, 130.0, 129.7, 129.4, 127.6, 120.8, 120.4, 116.4, 112.4, 110.6, 24.7, 14.3. HRMS (ESI, m/z) calcd for $C_{18}H_{15}ClN_3S$ $[M+H]^+$: 340.0670; found: 340.0672.

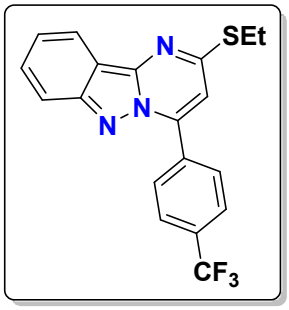
4-(3-bromophenyl)-2-(ethylthio)pyrimido[1,2-b]indazole (3j)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (45.2 mg, 59%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 – 8.23 (m, 2H), 8.09 (dd, *J* = 6.7, 1.1 Hz, 1H), 7.80 (d, *J* = 8.7 Hz, 1H), 7.73

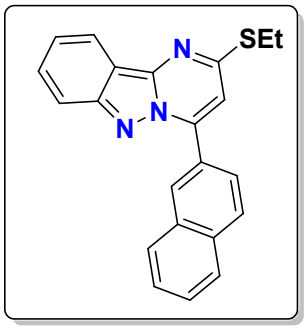
(ddd, J = 8.0, 1.8, 0.9 Hz, 1H), 7.62 – 7.55 (m, 1H), 7.49 (t, J = 7.9 Hz, 1H), 7.26 (dd, J = 7.7, 6.9 Hz, 1H), 7.07 (s, 1H), 3.45 (q, J = 7.4 Hz, 2H), 1.55 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.1, 151.0, 144.7, 142.6, 134.0, 133.1, 132.2, 130.2, 129.7, 128.1, 122.8, 120.8, 120.4, 116.4, 112.4, 110.6, 24.7, 14.3. HRMS (ESI, m/z) calcd for $C_{18}H_{15}BrN_3S$ $[M+H]^+$: 384.0165; found: 384.0170.

2-(ethylthio)-4-(4-(trifluoromethyl)phenyl)pyrimido[1,2-b]indazole (3k)



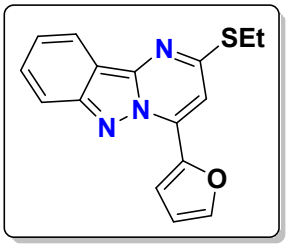
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (38.8 mg, 52%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (t, J = 7.9 Hz, 3H), 7.85 (d, J = 8.3 Hz, 2H), 7.76 (d, J = 8.7 Hz, 1H), 7.60 – 7.51 (m, 1H), 7.26 – 7.19 (m, 1H), 7.06 (s, 1H), 3.43 (q, J = 7.4 Hz, 2H), 1.53 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2, 151.1, 144.7, 142.7, 134.6, 132.7 (q, J = 32.9 Hz), 130.0, 129.9, 125.7 (q, J = 3.7 Hz), 124.8 (t, J = 272.9 Hz), 120.9, 120.5, 116.4, 112.4, 110.8, 24.7, 14.3. HRMS (ESI, m/z) calcd for $C_{19}H_{15}F_3N_3S$ $[M+H]^+$: 374.0933; found: 374.0935.

2-(ethylthio)-4-(naphthalen-2-yl)pyrimido[1,2-b]indazole (3l)



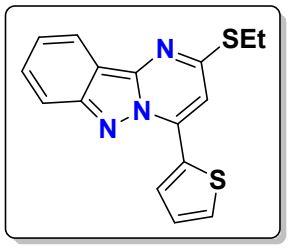
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (47.6 mg, 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.28 (d, J = 8.3 Hz, 1H), 8.16 (dd, J = 8.6, 1.7 Hz, 1H), 8.01 (dd, J = 20.1, 8.2 Hz, 2H), 7.93 (d, J = 7.9 Hz, 1H), 7.80 (d, J = 8.7 Hz, 1H), 7.58 (dddd, J = 12.0, 8.5, 6.7, 1.2 Hz, 3H), 7.26 – 7.21 (m, 1H), 7.18 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.0, 151.0, 144.8, 144.3, 134.4, 132.9, 130.0, 129.6, 128.9, 128.5, 128.3, 127.7, 127.7, 126.7, 125.7, 120.9, 120.2, 116.4, 112.4, 110.7, 24.7, 14.4. HRMS (ESI, m/z) calcd for $C_{22}H_{18}N_3S$ $[M+H]^+$: 356.1216; found: 356.1220.

2-(ethylthio)-4-(furan-2-yl)pyrimido[1,2-b]indazole (3m)



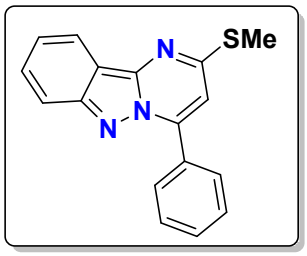
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (41.3 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (d, J = 3.5 Hz, 1H), 8.27 (d, J = 8.3 Hz, 1H), 7.86 (d, J = 8.7 Hz, 1H), 7.73 (d, J = 1.0 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.26 (dd, J = 7.7, 7.2 Hz, 1H), 6.77 (dd, J = 3.5, 1.7 Hz, 1H), 3.44 (q, J = 7.4 Hz, 2H), 1.54 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.1, 151.2, 145.4, 144.7, 144.0, 133.6, 129.7, 121.0, 120.2, 119.9, 116.2, 113.0, 112.3, 105.2, 24.7, 14.4. HRMS (ESI, m/z) calcd for $C_{16}H_{14}N_3SO$ $[M+H]^+$: 296.0852; found: 296.0852.

2-(ethylthio)-4-(thiophen-2-yl)pyrimido[1,2-b]indazole (3n)



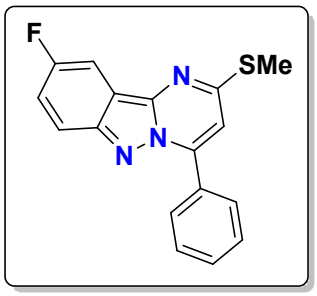
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (46.0 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 3.9, 1.1 Hz, 1H), 8.25 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.74 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.42 (s, 1H), 7.29 (dd, *J* = 5.0, 3.9 Hz, 1H), 7.23 (dd, *J* = 7.8, 7.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2, 150.9, 144.9, 137.8, 132.2, 131.4, 131.3, 129.8, 127.6, 121.0, 120.3, 116.4, 112.5, 106.6, 24.8, 14.5. HRMS (ESI, m/z) calcd for $C_{16}H_{14}N_3S_2$ $[M+H]^+$: 312.0624; found: 312.0626.

2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3o)



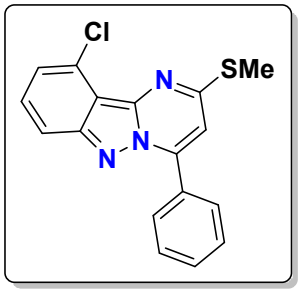
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (51.8 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.3 Hz, 1H), 8.17 – 8.11 (m, 2H), 7.80 (d, *J* = 8.7 Hz, 1H), 7.65 – 7.60 (m, 3H), 7.59 – 7.55 (m, 1H), 7.27 – 7.22 (m, 1H), 7.12 (s, 1H), 2.81 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.4, 151.0, 144.7, 144.2, 131.1, 131.0, 129.5, 129.4, 128.7, 120.9, 120.2, 116.4, 112.4, 110.2, 13.1. HRMS (ESI, m/z) calcd for $C_{17}H_{14}N_3S$ $[M+H]^+$: 292.0903; found: 292.0906.

9-fluoro-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3p)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow oil (46.9 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.05 (m, 2H), 7.82 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.74 (dd, *J* = 9.3, 4.4 Hz, 1H), 7.63 – 7.56 (m, 3H), 7.33 (td, *J* = 9.2, 2.5 Hz, 1H), 7.07 (s, 1H), 2.77 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2 (d, *J* = 240.7 Hz), 157.3, 148.1, 144.8 (d, *J* = 8.0 Hz), 144.4, 131.1, 130.9, 129.4, 128.8, 120.5 (d, *J* = 27.7 Hz), 118.4 (d, *J* = 9.0 Hz), 111.6 (d, *J* = 11.3 Hz), 110.3, 103.8 (d, *J* = 25.2 Hz), 13.1. HRMS (ESI, m/z) calcd for $C_{17}H_{13}FN_3S$ $[M+H]^+$: 310.0809; found: 310.0814.

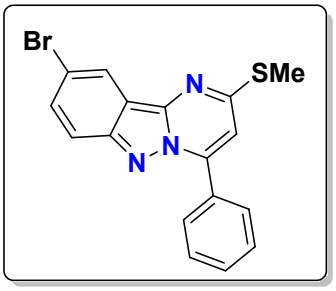
10-chloro-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3q)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (41.6 mg, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.04 (m, 2H), 7.65 (d, *J* = 8.6 Hz, 1H), 7.62 – 7.56 (m, 3H), 7.44 – 7.39 (m, 1H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.14 (s, 1H), 2.82 (s, 3H). ^{13}C

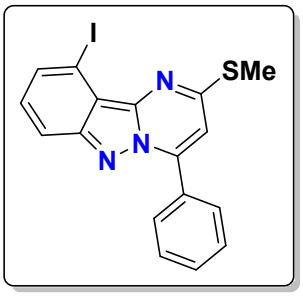
NMR (126 MHz, $CDCl_3$) δ 158.5, 151.7, 144.3, 144.1, 131.2, 130.9, 129.5, 129.5, 128.8, 127.8, 120.5, 115.1, 110.6, 110.1, 13.2. HRMS (ESI, m/z) calcd for $C_{17}H_{13}ClN_3S$ $[M+H]^+$: 326.0513; found: 326.0516.

9-bromo-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3r)



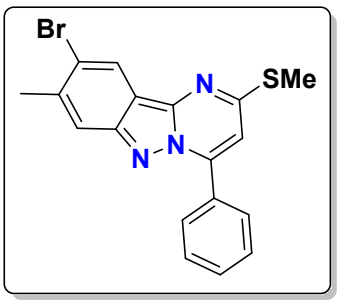
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (50.9 mg, 69%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, J = 1.3 Hz, 1H), 8.14 – 8.07 (m, 2H), 7.68 – 7.64 (m, 1H), 7.63 – 7.58 (m, 4H), 7.12 (s, 1H), 2.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3, 149.3, 144.4, 143.9, 132.9, 131.2, 130.8, 129.5, 128.8, 123.2, 118.2, 113.6, 113.1, 110.7, 13.2. HRMS (ESI, m/z) calcd for $C_{17}H_{13}BrN_3S$ $[M+H]^+$: 370.0008; found: 370.0008.

10-iodo-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3s)



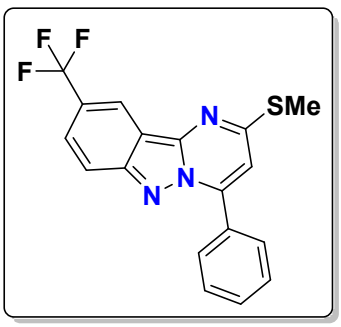
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (59.1 mg, 71%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 – 8.03 (m, 2H), 7.74 (d, J = 8.6 Hz, 1H), 7.70 (d, J = 7.0 Hz, 1H), 7.62 – 7.56 (m, 3H), 7.21 (dd, J = 8.6, 7.1 Hz, 1H), 7.17 (s, 1H), 2.89 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 151.3, 144.5, 144.3, 131.1, 130.9, 130.3, 129.4, 128.7, 116.4, 113.5, 110.8, 84.9, 13.9. HRMS (ESI, m/z) calcd for $C_{17}H_{13}IN_3S$ $[M+H]^+$: 417.9869; found: 417.9871.

9-bromo-8-methyl-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3t)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (55.9 mg, 73%). ^{11}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.06 (m, 2H), 8.05 (s, 1H), 8.02 (s, 1H), 7.61 – 7.55 (m, 3H), 7.07 (s, 1H), 2.76 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 150.4, 144.3, 144.2, 131.1, 130.9, 129.5, 129.4, 128.8, 127.9, 120.7, 119.6, 111.7, 110.3, 23.4, 13.2. HRMS (ESI, m/z) calcd for $C_{18}H_{15}BrN_3S$ $[M+H]^+$: 384.0165; found: 384.0170.

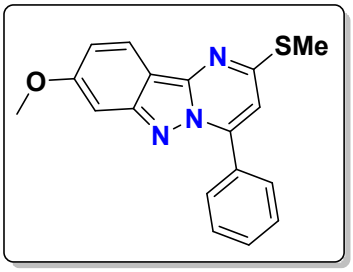
2-(methylthio)-4-phenyl-9-(trifluoromethyl)pyrimido[1,2-b]indazole (3u)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (89.3 mg, 83%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.09 (dd, J = 6.7, 3.0 Hz, 2H), 7.82 (d, J = 9.1 Hz, 1H), 7.68 (dd, J = 9.1, 1.6 Hz, 1H), 7.62 – 7.57 (m, 3H), 7.15 (s,

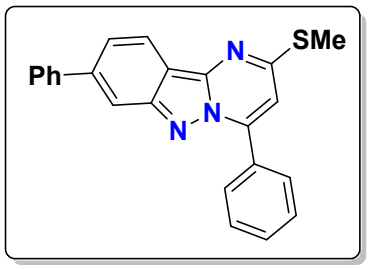
1H), 2.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6, 151.2, 145.6, 144.7, 131.3, 130.6, 129.5, 128.8, 125.5 (q, J = 2.9 Hz), 124.9 (q, J = 272.5 Hz), 122.0 (q, J = 32.4 Hz), 119.8 (q, J = 4.8 Hz), 117.3, 111.2, 111.0, 13.2. HRMS (ESI, m/z) calcd for $C_{18}H_{13}F_3N_3S$ $[M+H]^+$: 360.0777; found: 360.0777.

8-methoxy-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3v)



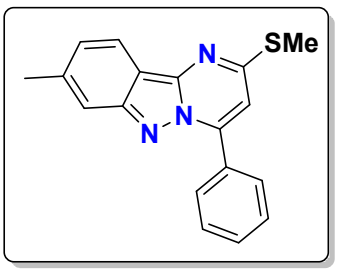
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (43.0 mg, 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.05 (m, 3H), 7.57 (dd, J = 5.0, 1.7 Hz, 3H), 7.03 (d, J = 1.8 Hz, 1H), 6.99 (s, 1H), 6.88 (dd, J = 9.0, 2.1 Hz, 1H), 3.90 (s, 3H), 2.76 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.6, 157.7, 152.6, 144.6, 144.1, 131.3, 130.9, 129.4, 128.7, 121.7, 114.7, 108.9, 107.3, 94.0, 55.3, 13.1. HRMS (ESI, m/z) calcd for $C_{18}H_{16}N_3OS$ $[M+H]^+$: 322.1009; found: 322.1013.

2-(methylthio)-4,8-diphenylpyrimido[1,2-b]indazole (3w)



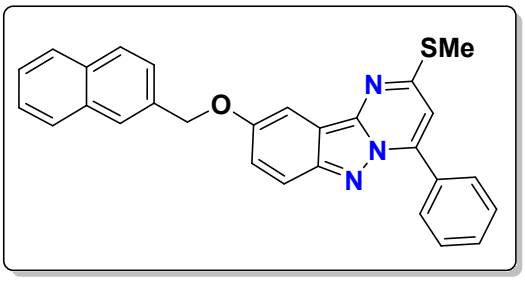
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 50:1, v/v) to give the product as a yellow solid (65.1 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (dd, J = 8.6, 0.5 Hz, 1H), 8.17 – 8.09 (m, 2H), 7.99 (s, 1H), 7.77 – 7.73 (m, 2H), 7.60 (dd, J = 5.1, 1.9 Hz, 3H), 7.52 – 7.46 (m, 3H), 7.39 (t, J = 7.4 Hz, 1H), 7.09 (s, 1H), 2.80 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 151.5, 144.7, 144.2, 142.6, 141.6, 131.1, 131.0, 129.4, 128.8, 128.7, 127.6, 127.5, 121.2, 120.7, 114.1, 111.6, 110.1, 13.1. HRMS (ESI, m/z) calcd for $C_{23}H_{18}N_3S$ $[M+H]^+$: 368.1216; found: 368.1216.

8-methyl-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3t)



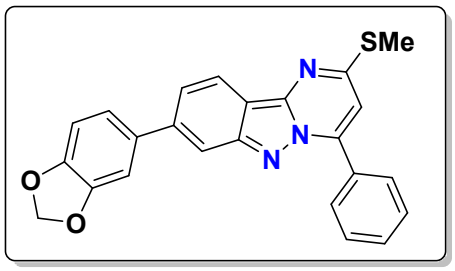
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 40:1, v/v) to give the product as a yellow solid (45.8 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 – 8.09 (m, 3H), 7.61 (dd, J = 5.1, 1.9 Hz, 3H), 7.56 (s, 1H), 7.08 (s, 2H), 2.80 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2, 151.7, 144.7, 144.2, 139.9, 131.3, 130.9, 129.4, 128.7, 123.0, 120.3, 115.0, 110.5, 109.7, 22.6, 13.1. HRMS (ESI, m/z) calcd for $C_{18}H_{16}N_3S$ $[M+H]^+$: 306.1059; found: 306.1059.

2-(methylthio)-9-(naphthalen-2-ylmethoxy)-4-phenylpyrimido[1,2-b]indazole (3y)



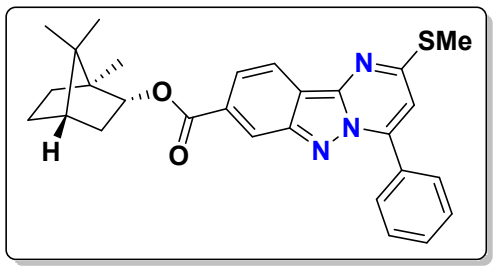
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 5:1, v/v) to give the product as a yellow solid (44.7 mg, 50%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.9 Hz, 1H), 8.09 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.96 (s, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.87 (dd, *J* = 4.7, 2.2 Hz, 2H), 7.64 – 7.57 (m, 4H), 7.54 – 7.48 (m, 2H), 7.18 (d, *J* = 1.9 Hz, 1H), 7.06 (s, 1H), 7.02 (s, 1H), 5.35 (s, 2H), 2.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6, 157.8, 152.58, 144.68, 144.18, 134.2, 133.3, 133.1, 131.2, 130.9, 129.4, 128.7, 128.4, 127.9, 127.7, 126.4, 126.2, 126.1, 125.3, 121.9, 115.0, 109.0, 107.5, 95.4, 70.1, 13.1.HRMS (ESI, m/z) calcd for $C_{28}H_{22}N_3OS$ $[M+H]^+$: 448.1478; found: 448.1479.

8-(benzo[d][1,3]dioxol-5-yl)-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3z)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 20:1, v/v) to give the product as a yellow solid (57.5 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.6 Hz, 1H), 8.16 – 8.08 (m, 2H), 7.88 (s, 1H), 7.64 – 7.56 (m, 3H), 7.42 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.09 (s, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 6.02 (s, 2H), 2.80 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 151.6, 148.2, 147.3, 144.8, 144.3, 142.3, 136.0, 131.2, 131.1, 129.5, 128.8, 121.2, 121.2, 120.7, 113.6, 111.4, 110.1, 108.6, 108.1, 101.2, 13.2. HRMS (ESI, m/z) calcd for $C_{24}H_{18}N_3O_2S$ $[M+H]^+$: 412.1114; found: 412.117.

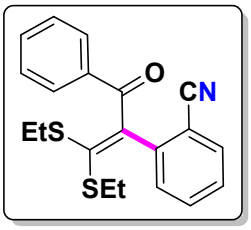
(1S,2R,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole-8-carboxylate (3β)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (64.5 mg, 69%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.29 (d, *J* = 8.6 Hz, 1H), 8.11 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.88 (dd, *J* = 8.6, 1.2 Hz, 1H), 7.63 (dd, *J* = 5.0, 1.7 Hz, 3H), 7.15 (s, 1H), 5.25 – 5.16 (m, 1H), 2.81 (s, 3H), 2.58 – 2.50 (m, 1H), 2.31 – 2.20 (m, 1H), 1.88 – 1.81 (m, 1H), 1.78 (t, *J* = 4.4 Hz, 1H), 1.47 (ddd, *J* = 12.2, 4.3, 2.1 Hz, 1H), 1.39 – 1.34 (m, 1H), 1.21 (dd, *J* = 13.8, 3.4 Hz, 1H), 1.01 (s, 3H), 0.97 (d, *J* = 8.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 158.4, 150.1, 144.5, 144.5, 131.8, 131.2, 130.9, 129.5, 128.9, 121.0, 120.0, 119.7, 114.5, 111.0, 80.8, 77.3, 77.1, 49.2, 47.9, 45.1, 37.0,

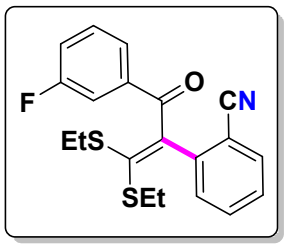
28.1, 27.5, 19.8, 19.0, 13.7, 13.2. HRMS (ESI, m/z) calcd for $C_{28}H_{30}N_3O_2S$ $[M+H]^+$: 472.2053; found: 472.2059.

2-(1,1-bis(ethylthio)-3-oxo-3-phenylprop-1-en-2-yl)benzonitrile (4a)



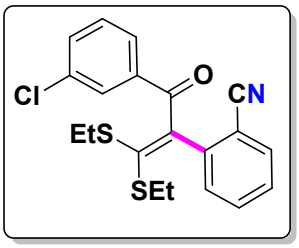
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow oil (40.9 mg, 58%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 – 8.09 (m, 2H), 7.73 – 7.67 (m, 1H), 7.60 – 7.53 (m, 3H), 7.51 – 7.46 (m, 2H), 7.41 – 7.36 (m, 1H), 2.86 (q, *J* = 7.4 Hz, 2H), 2.79 (q, *J* = 7.4 Hz, 2H), 1.22 (t, *J* = 7.4 Hz, 3H), 1.19 (t, *J* = 7.4 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 194.1, 142.6, 141.1, 140.1, 136.3, 133.5, 133.0, 132.5, 129.6, 129.6, 128.7, 128.2, 118.6, 113.4, 28.8, 28.2, 14.6, 14.6. HRMS (ESI, m/z) calcd for $C_{20}H_{20}NOS_2$ $[M+H]^+$: 354.0981; found: 354.0982.

2-(1,1-bis(ethylthio)-3-(4-fluorophenyl)-3-oxoprop-1-en-2-yl)benzonitrile (4b)



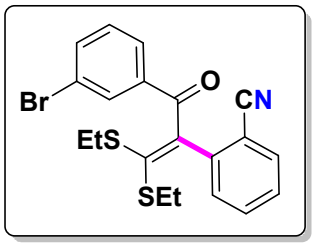
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow oil (39.3 mg, 53%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 1H), 7.83 – 7.77 (m, 1H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.58 (dd, *J* = 4.9, 1.2 Hz, 2H), 7.49 (td, *J* = 8.0, 5.5 Hz, 1H), 7.42 (ddd, *J* = 7.9, 5.2, 3.6 Hz, 1H), 7.30 – 7.25 (m, 1H), 2.88 (q, *J* = 7.4 Hz, 2H), 2.82 (q, *J* = 7.4 Hz, 2H), 1.24 (t, *J* = 7.4 Hz, 3H), 1.21 (t, *J* = 7.4 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 192.9, 162.9 (d, *J* = 248.3 Hz), 142.6, 141.7, 140.1, 138.7 (d, *J* = 6.5 Hz), 133.1, 132.6, 130.4 (d, *J* = 7.6 Hz), 129.8, 128.4, 125.5 (d, *J* = 2.9 Hz), 120.5 (d, *J* = 21.6 Hz), 118.5, 115.8 (d, *J* = 22.5 Hz), 113.5, 29.0, 28.3, 14.6, 14.5. HRMS (ESI, m/z) calcd for $C_{20}H_{19}NOFS_2$ $[M+H]^+$: 372.0887; found: 372.0890.

2-(3-(3-chlorophenyl)-1,1-bis(ethylthio)-3-oxoprop-1-en-2-yl)benzonitrile (4c)



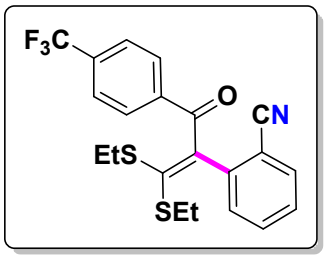
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow oil (42.6 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (t, *J* = 1.8 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.57 – 7.51 (m, 3H), 7.45 – 7.38 (m, 2H), 2.88 – 2.83 (m, 2H), 2.80 (q, *J* = 7.4 Hz, 2H), 1.22 (t, *J* = 6.7 Hz, 3H), 1.19 (t, *J* = 6.7 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 192.8, 142.8, 141.6, 140.1, 138.1, 135.0, 133.3, 133.0, 132.6, 130.0, 129.7, 129.2, 128.4, 127.7, 118.5, 113.5, 29.0, 28.3, 14.6, 14.5. HRMS (ESI, m/z) calcd for $C_{20}H_{19}NOClS_2$ $[M+H]^+$: 388.0591; found: 388.0597.

2-(3-(3-bromophenyl)-1,1-bis(ethylthio)-3-oxoprop-1-en-2-yl)benzonitrile (4d)



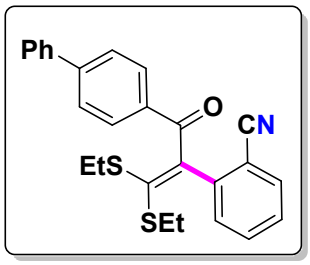
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow solid (41.3 mg, 48%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (t, *J* = 1.8 Hz, 1H), 8.11 – 8.06 (m, 1H), 7.75 – 7.68 (m, 2H), 7.61 – 7.55 (m, 2H), 7.45 – 7.41 (m, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 2.91 – 2.85 (m, 2H), 2.82 (t, *J* = 7.4 Hz, 2H), 1.24 (t, *J* = 5.6 Hz, 3H), 1.21 (t, *J* = 5.6 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 192.7, 142.8, 141.5, 140.1, 138.3, 136.2, 133.1, 132.6, 132.2, 130.3, 129.8, 128.4, 128.2, 123.1, 118.5, 113.5, 29.0, 28.4, 14.6, 14.6. HRMS (ESI, m/z) calcd for $C_{20}H_{19}NOBrS_2$ $[M+H]^+$: 432.0086; found: 432.0089.

2-(1,1-bis(ethylthio)-3-oxo-3-(4-(trifluoromethyl)phenyl)prop-1-en-2-yl)benzonitrile (4e)



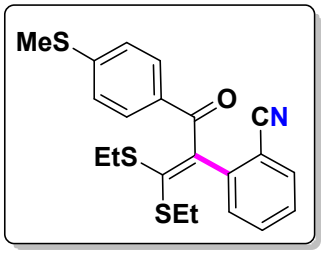
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow oil (37.0 mg, 44%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.43 – 7.40 (m, 1H), 2.85 (q, *J* = 7.4 Hz, 2H), 2.79 (q, *J* = 7.4 Hz, 2H), 1.22 (t, *J* = 7.4 Hz, 3H), 1.16 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.1, 143.6, 141.3, 140.1, 139.5, 134.5 (q, *J* = 32.8 Hz), 133.1, 132.7, 129.9, 129.8, 128.5, 125.8 (q, *J* = 3.8 Hz), 123.6 (q, *J* = 273.4 Hz), 118.6, 113.4, 29.1, 28.4, 14.7, 14.5. HRMS (ESI, m/z) calcd for $C_{21}H_{19}NOF_3S_2$ $[M+H]^+$: 422.0855; found: 422.0855.

2-(3-([1,1'-biphenyl]-4-yl)-1,1-bis(ethylthio)-3-oxoprop-1-en-2-yl)benzonitrile (4f)



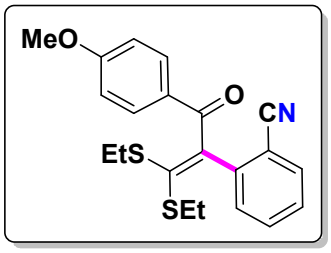
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow solid (50.6 mg, 59%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 – 8.18 (m, 2H), 7.77 – 7.69 (m, 3H), 7.66 – 7.59 (m, 3H), 7.55 (td, *J* = 7.7, 1.3 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.42 – 7.35 (m, 2H), 2.89 (q, *J* = 7.4 Hz, 2H), 2.83 (q, *J* = 7.4 Hz, 2H), 1.26 – 1.24 (m, 3H), 1.24 – 1.21 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.7, 146.2, 142.7, 140.7, 140.1, 139.8, 134.9, 133.0, 132.5, 130.2, 129.6, 128.9, 128.3, 127.4, 127.2, 118.7, 113.4, 28.8, 28.2, 14.7, 14.6. HRMS (ESI, m/z) calcd for $C_{26}H_{24}NOS_2$ $[M+H]^+$: 430.1294; found: 430.1298.

2-(1,1-bis(ethylthio)-3-(4-(methylthio)phenyl)-3-oxoprop-1-en-2-yl)benzonitrile (4g)



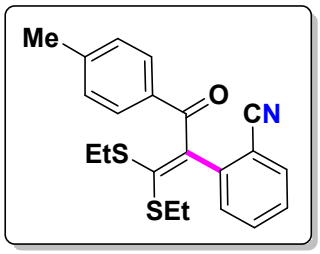
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow oil (45.5 mg, 57%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.5 Hz, 2H), 7.71 – 7.65 (m, 1H), 7.60 – 7.56 (m, 1H), 7.53 (td, *J* = 7.7, 1.2 Hz, 1H), 7.41 – 7.34 (m, 1H), 7.28 (d, *J* = 8.5 Hz, 2H), 2.83 (dq, *J* = 28.1, 7.4 Hz, 4H), 2.50 (s, 3H), 1.22 (td, *J* = 7.4, 2.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.2, 146.9, 142.8, 140.3, 140.1, 133.0, 132.5, 132.4, 130.1, 129.6, 128.3, 125.1, 118.7, 113.3, 28.8, 28.2, 14.8, 14.7, 14.6. HRMS (ESI, m/z) calcd for $C_{21}H_{22}NOS_3$ $[M+H]^+$: 400.0858; found: 400.0859.

2-(1,1-bis(ethylthio)-3-(4-methoxyphenyl)-3-oxoprop-1-en-2-yl)benzonitrile (4h)



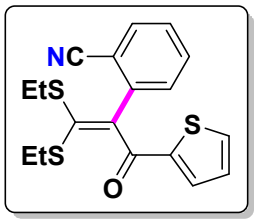
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 60:1, v/v) to give the product as a yellow oil (49.8 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.58 – 7.52 (m, 1H), 7.43 – 7.36 (m, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H), 2.86 (dq, *J* = 28.7, 7.4 Hz, 4H), 1.25 (dt, *J* = 14.5, 6.3 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.8, 164.1, 143.2, 140.2, 139.5, 133.0, 132.5, 132.1, 129.6, 129.0, 128.2, 118.8, 114.1, 113.2, 55.5, 28.7, 28.1, 14.8, 14.6. HRMS (ESI, m/z) calcd for $C_{21}H_{22}NO_2S_2$ $[M+H]^+$: 384.1086; found: 384.1090.

2-(1,1-bis(ethylthio)-3-oxo-3-(p-tolyl)prop-1-en-2-yl)benzonitrile (4i)



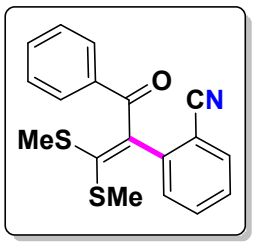
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow oil (44.0 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 6.9 Hz, 1H), 7.57 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.52 (td, *J* = 7.7, 1.3 Hz, 1H), 7.37 (td, *J* = 7.6, 1.4 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.86 (q, *J* = 7.4 Hz, 2H), 2.80 (q, *J* = 7.4 Hz, 2H), 2.40 (s, 3H), 1.22 (td, *J* = 7.4, 3.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.7, 144.6, 142.9, 140.1, 140.1, 133.6, 133.0, 132.4, 129.8, 129.5, 129.5, 128.2, 118.6, 113.3, 28.7, 28.1, 21.7, 14.7, 14.6. HRMS (ESI, m/z) calcd for $C_{21}H_{22}NOS_2$ $[M+H]^+$: 368.1137; found: 368.1137.

2-(1,1-bis(ethylthio)-3-oxo-3-(thiophen-2-yl)prop-1-en-2-yl)benzonitrile (4j)



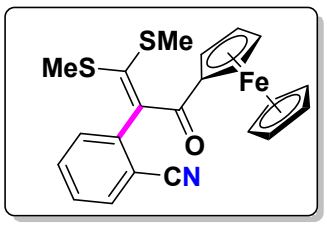
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 80:1, v/v) to give the product as a yellow oil (35.1 mg, 49%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 3.8, 0.7 Hz, 1H), 7.69 (t, *J* = 5.2 Hz, 2H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.55 (td, *J* = 7.7, 1.0 Hz, 1H), 7.39 (td, *J* = 7.5, 1.0 Hz, 1H), 7.14 (dd, *J* = 4.6, 4.1 Hz, 1H), 2.89 – 2.84 (m, 2H), 2.84 – 2.79 (m, 2H), 1.24 (d, *J* = 7.4 Hz, 3H), 1.21 (t, *J* = 6.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.3, 143.7, 142.3, 141.1, 139.7, 135.2, 134.8, 132.9, 132.6, 129.6, 128.5, 128.3, 118.6, 113.3, 28.8, 28.1, 14.7, 14.6. HRMS (ESI, m/z) calcd for $C_{18}H_{18}NOS_3$ $[M+H]^+$: 360.0545; found: 360.0548.

2-(1,1-bis(methylthio)-3-oxo-3-phenylprop-1-en-2-yl)benzonitrile (4k)



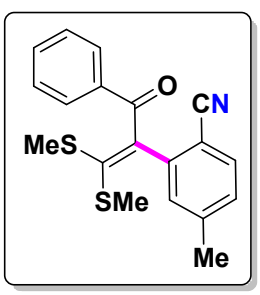
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 70:1, v/v) to give the product as a yellow oil (36.4 mg, 56%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.04 (m, 2H), 7.73 – 7.68 (m, 1H), 7.59 – 7.47 (m, 5H), 7.40 – 7.35 (m, 1H), 2.42 (s, 3H), 2.25 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 193.9, 144.2, 140.4, 140.0, 136.5 , 133.4, 133.2, 132.6, 129.6, 129.5, 128.8, 128.2, 118.6, 113.1, 17.5, 16.6. HRMS (ESI, m/z) calcd for $C_{18}H_{16}NOS_2$ $[M+H]^+$: 326.0668; found: 326.0670.

2-(1,1-bis(methylthio)-3-oxoferrocen-1-en-2-yl)benzonitrile (4l)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 70:1, v/v) to give the product as a rufous solid (43.4 mg, 50%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.68 (td, *J* = 7.8, 1.2 Hz, 1H), 7.47 (td, *J* = 7.6, 1.1 Hz, 1H), 4.98 (d, *J* = 29.5 Hz, 2H), 4.61 (d, *J* = 33.2 Hz, 2H), 3.79 (s, 5H), 2.39 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.5, 142.0, 140.9, 140.8, 132.6, 132.5, 128.9, 128.3, 118.9, 112.9, 79.0, 73.2, 72.9, 71.7, 69.9, 68.4, 17.3, 16.4. HRMS (ESI, m/z) calcd for $C_{22}H_{20}FeNOS_2$ $[M+H]^+$: 434.0030; found: 434.0034.

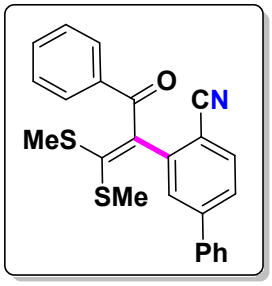
2-(1,1-bis(methylthio)-3-oxo-3-phenylprop-1-en-2-yl)-4-methylbenzonitrile (4m)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 70:1, v/v) to give the product as a white solid (42.7 mg, 63%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 – 8.06 (m, 2H), 7.60 – 7.54 (m, 2H), 7.53 – 7.47 (m, 2H), 7.31 (s, 1H), 7.19 – 7.15 (m, 1H), 2.42 (s, 3H), 2.36 (s, 3H), 2.25 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 194.0, 143.7, 143.6, 140.4, 140.1, 136.5, 133.4, 133.1, 130.2, 129.5, 129.1,

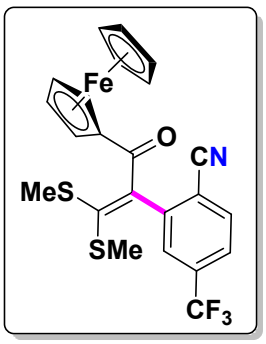
128.8, 118.8, 110.0, 21.8, 17.5, 16.6. HRMS (ESI, m/z) calcd for $C_{19}H_{18}NOS_2$ $[M+H]^+$: 340.0824; found: 340.0825.

2-(1,1-bis(methylthio)-3-oxo-3-phenylprop-1-en-2-yl)-[1,1'-biphenyl]-4-carbonitrile (4n)



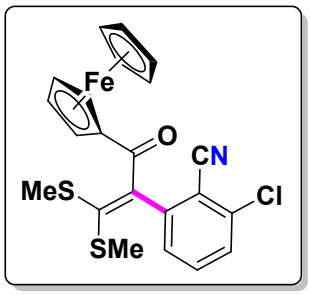
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 70:1, v/v) to give the product as a yellow solid (48.1 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 – 8.10 (m, 2H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 1.7 Hz, 1H), 7.62 – 7.54 (m, 4H), 7.53 – 7.48 (m, 2H), 7.47 – 7.42 (m, 2H), 7.42 – 7.37 (m, 1H), 2.45 (s, 3H), 2.28 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 193.9, 145.5, 144.2, 140.7, 140.1, 138.7, 136.5, 133.6, 133.5, 129.5, 129.0, 128.8, 128.7, 128.2, 127.3, 126.8, 118.7, 111.4, 17.5, 16.6. HRMS (ESI, m/z) calcd for $C_{24}H_{20}NOS_2$ $[M+H]^+$: 402.0981; found: 402.0984.

2-(1,1-bis(methylthio)-3-oxoferrocen-1-en-2-yl)-4-(trifluoromethyl)benzonitrile (4o)



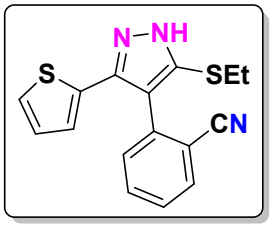
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 70:1, v/v) to give the product as a rufous solid (38.1 mg, 38%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 1.2, 0.4 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.89 (dd, *J* = 8.3, 1.4 Hz, 1H), 4.96 – 4.91 (m, 2H), 4.62 (d, *J* = 43.1 Hz, 2H), 3.78 (s, 5H), 2.39 (s, 3H), 2.28 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 144.2, 143.1, 140.2, 130.6 (q, *J* = 34.0 Hz), 129.8, 129.4 (q, *J* = 3.8 Hz), 129.2 (q, *J* = 3.8 Hz), 122.8 (q, *J* = 273.4 Hz), 117.7, 113.8, 79.1, 73.5, 73.2, 71.7, 70.0, 68.6, 17.4, 16.4.HRMS (ESI, m/z) calcd for $C_{23}H_{19}F_3FeNOS_2$ $[M+H]^+$: 502.0204; found: 502.0206.

2-(1,1-bis(methylthio)-3-oxoferrocen-1-en-2-yl)-6-chlorobenzonitrile (4p)



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 70:1, v/v) to give the product as a rufous solid (38.2 mg, 41%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 4.96 (d, *J* = 37.8 Hz, 2H), 4.61 (d, *J* = 38.2 Hz, 2H), 3.79 (s, 5H), 2.39 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 143.0, 142.0, 141.0, 137.2, 133.1, 128.9, 127.1, 116.1, 113.6, 79.0, 73.4, 73.1, 72.0, 70.0, 68.4, 17.4, 16.4. HRMS (ESI, m/z) calcd for $C_{22}H_{18}ClFeNNaOS_2$ $[M+Na]^+$: 489.9760; found: 489.9765.

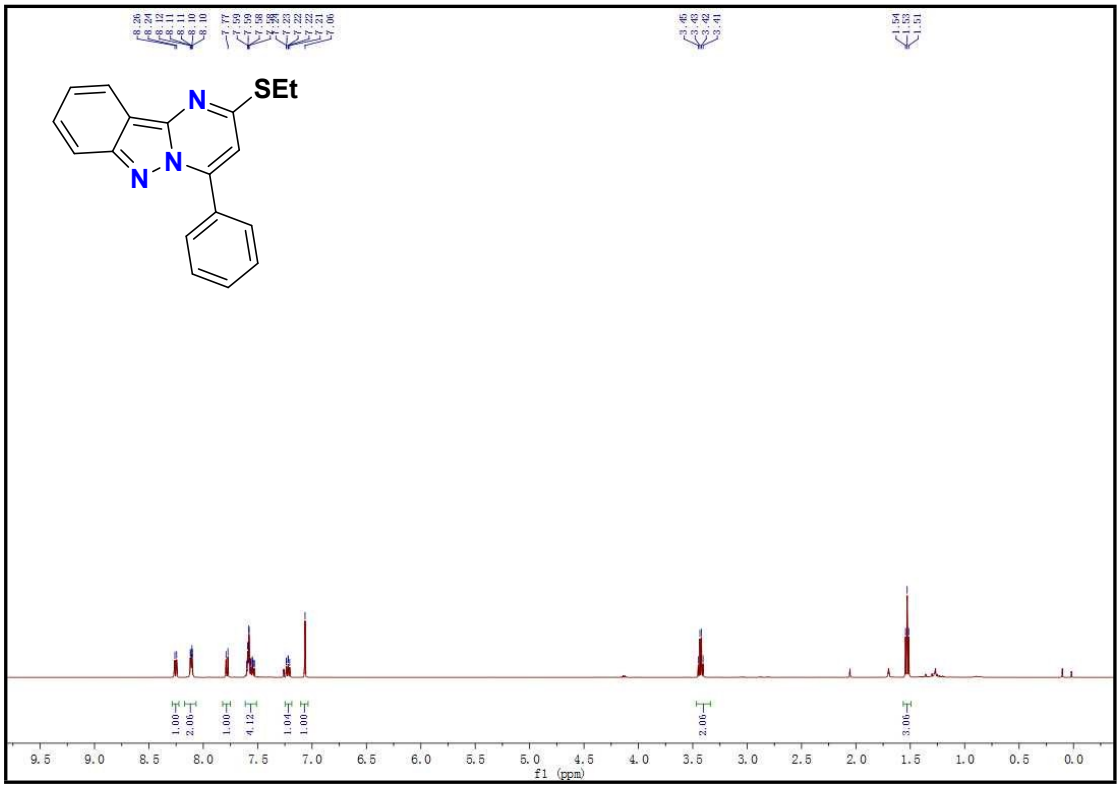
2-(5-(ethylthio)-3-(thiophen-2-yl)-1H-pyrazol-4-yl)benzonitrile (5)

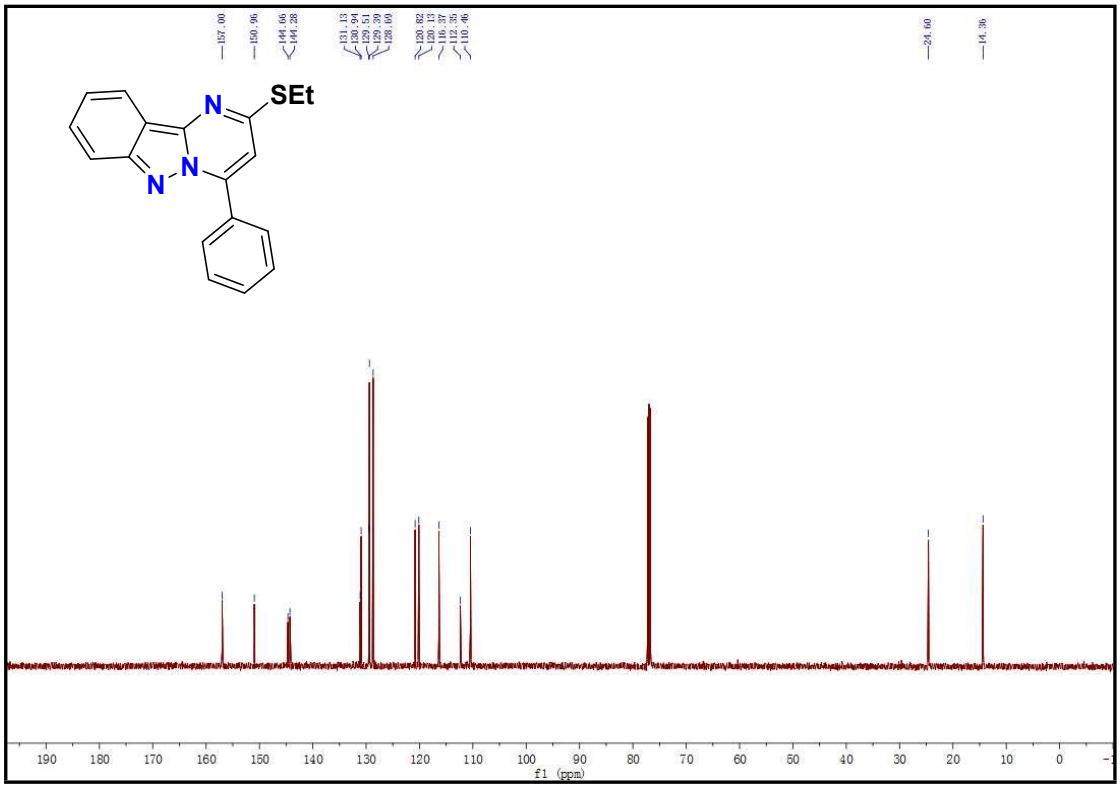


In a sealed tube were placed **4j** (0.15 mmol, 1 equiv), hydrazine hydrate (0.45 mmol, 3 equiv) in EtOH (1 mL). The resulting mixture was stirred at refulx for overnight. Upon completion of the reaction. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 2:1, v/v) to give the product as a yellow solid (42.4 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.22 (brs, 1H), 7.77 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.66 (td, *J* = 7.7, 1.4 Hz, 1H), 7.52 (td, *J* = 7.7, 1.2 Hz, 1H), 7.48 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.22 (dd, *J* = 5.1, 1.1 Hz, 1H), 6.92 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.86 (d, *J* = 3.0 Hz, 1H), 2.77 (qd, *J* = 7.2, 2.9 Hz, 2H), 1.20 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.3, 133.3, 132.7, 132.5, 128.5, 127.4, 125.9, 125.5, 117.8, 114.6, 29.5, 15.1.HRMS (ESI, m/z) calcd for $C_{16}H_{14}N_3S_2$ $[M+Na]^+$: 312.0624; found: 324.0626.

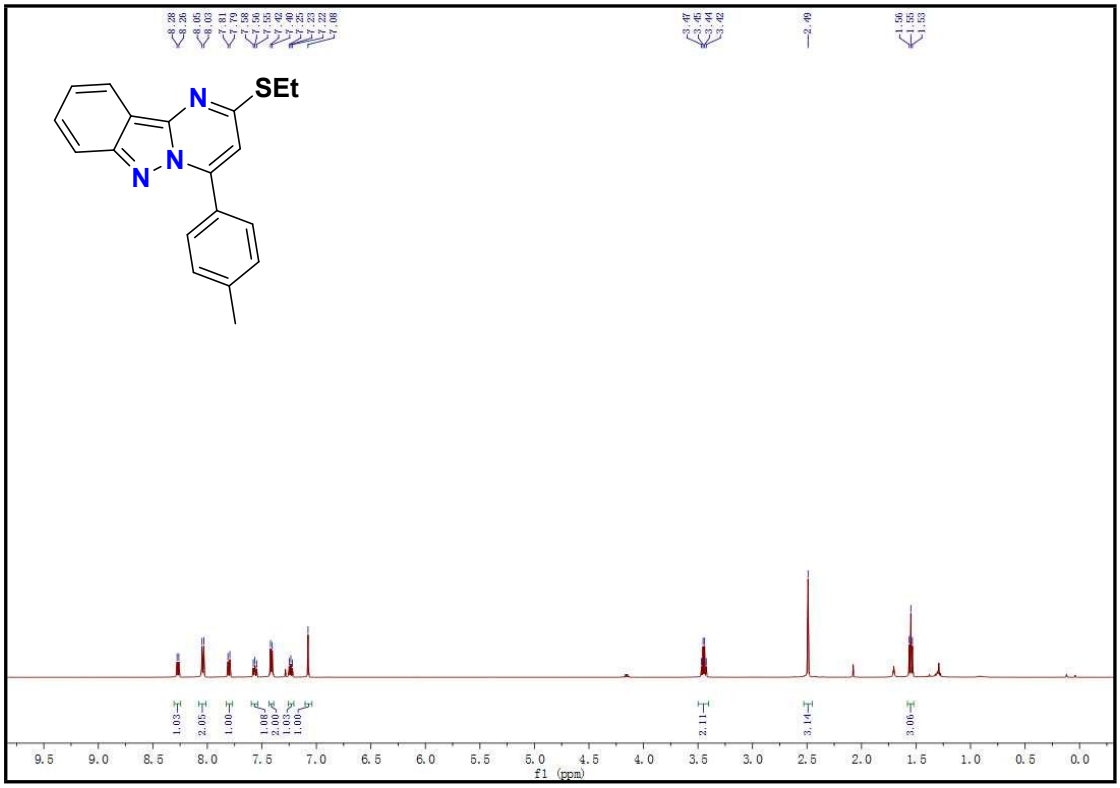
6. NMR spectroscopic data

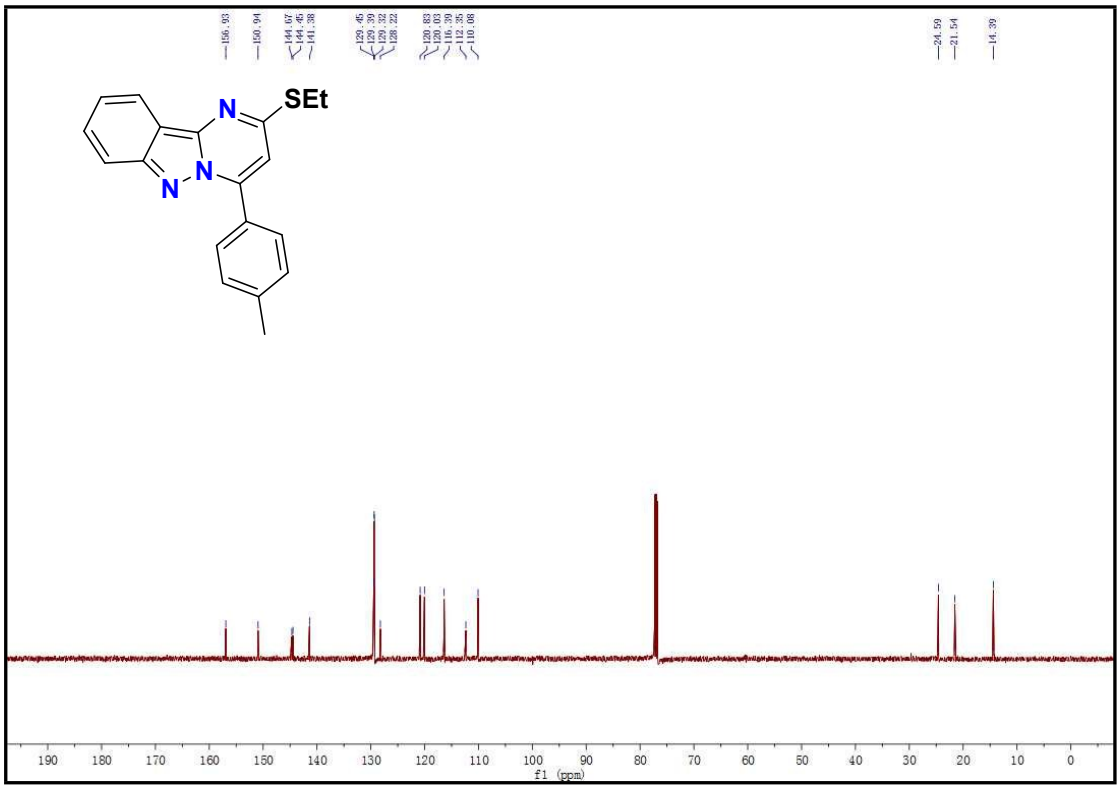
2-(ethylthio)-4-phenylpyrimido[1,2-b]indazole (3a)



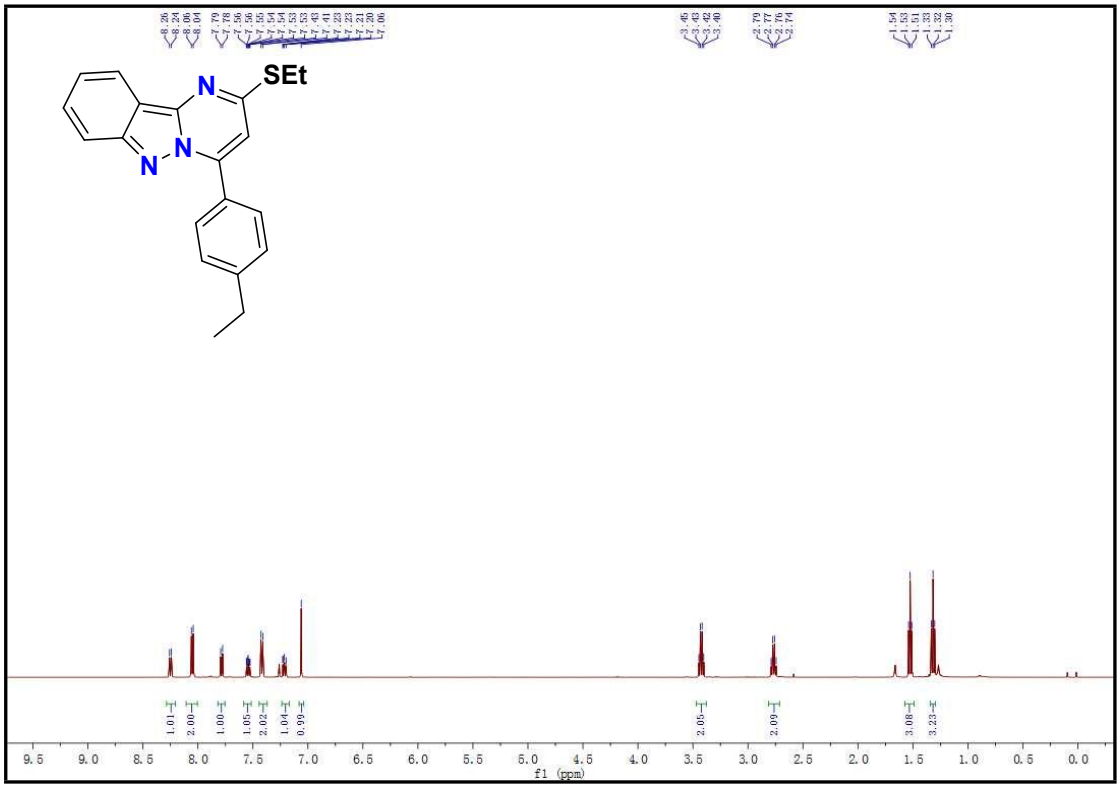


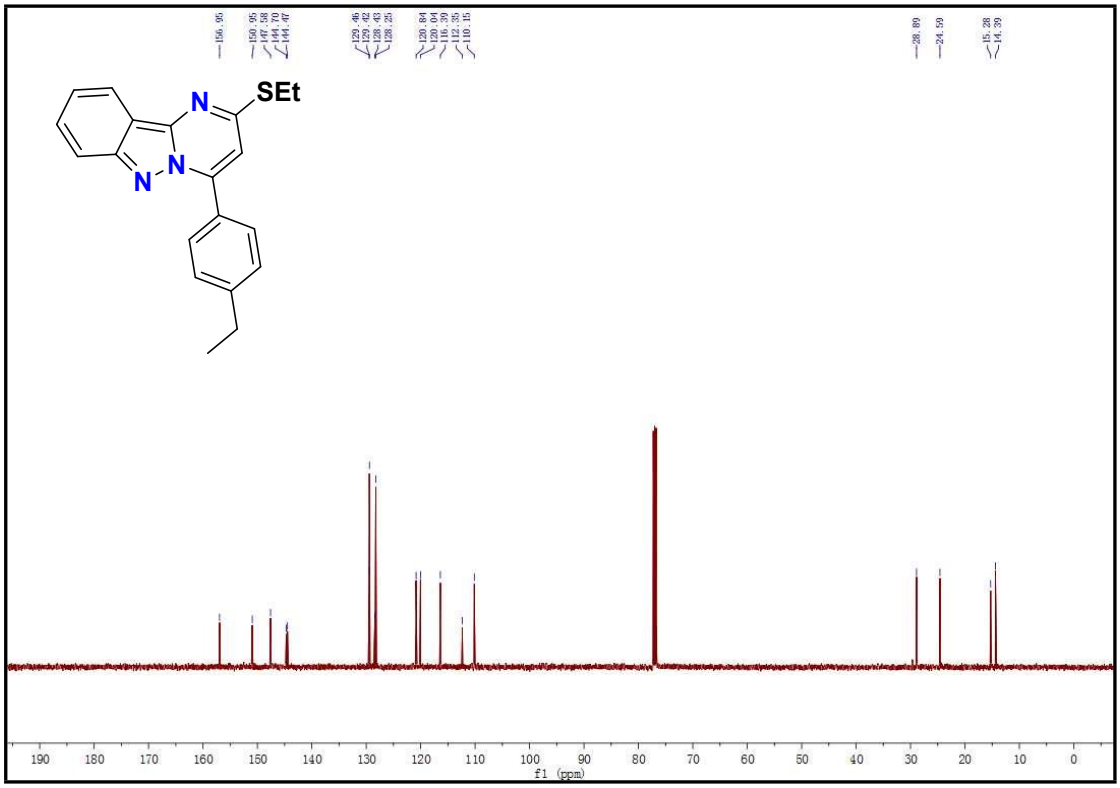
2-(ethylthio)-4-(p-tolyl)pyrimido[1,2-b]indazole (3b)



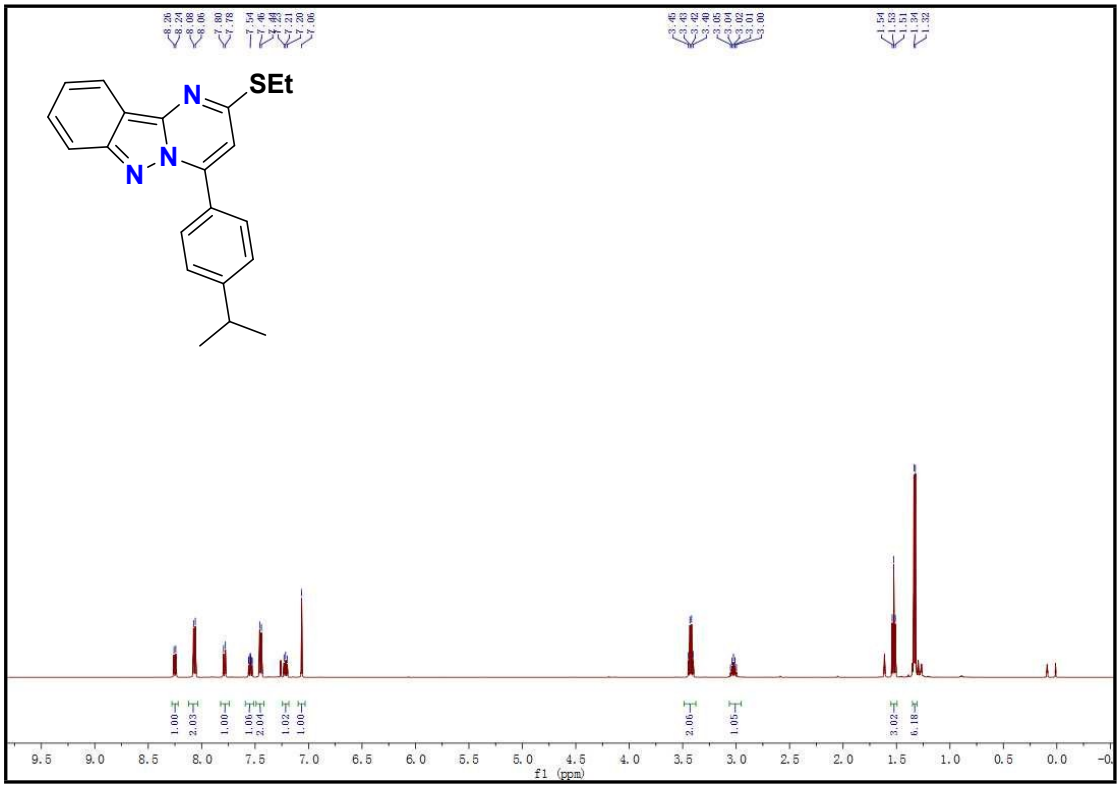


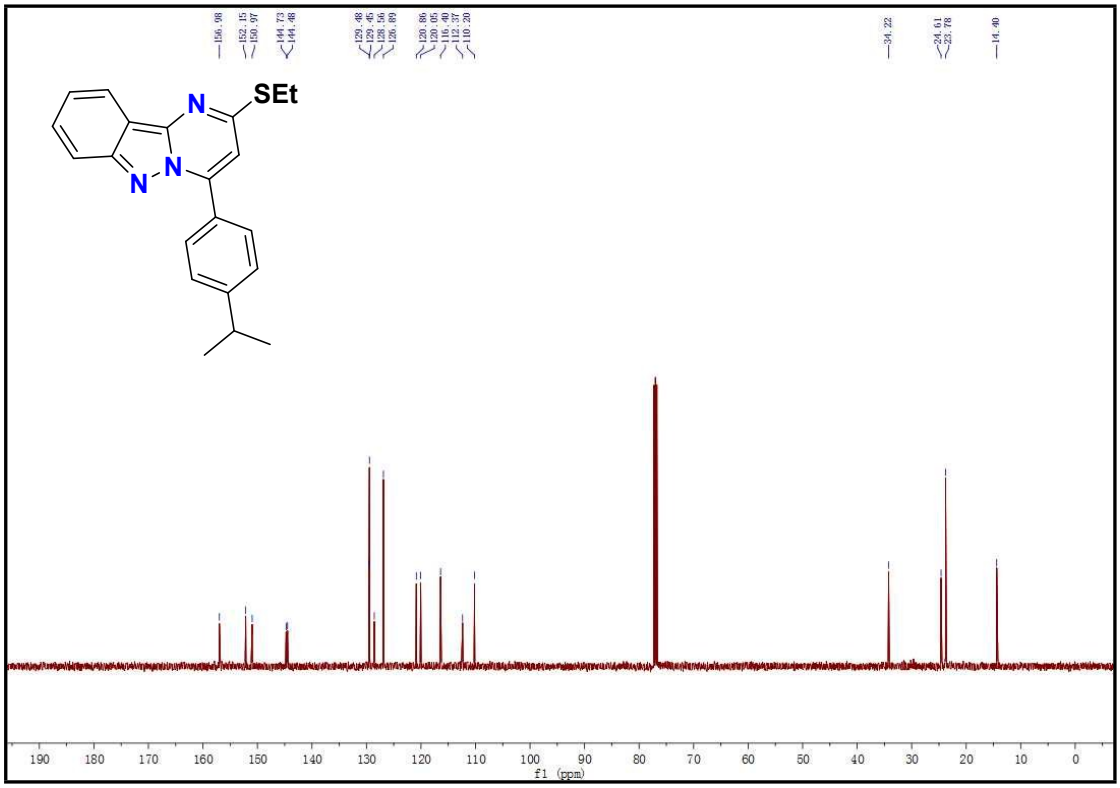
4-(4-ethylphenyl)-2-(ethylthio)pyrimido[1,2-b]indazole (3c)



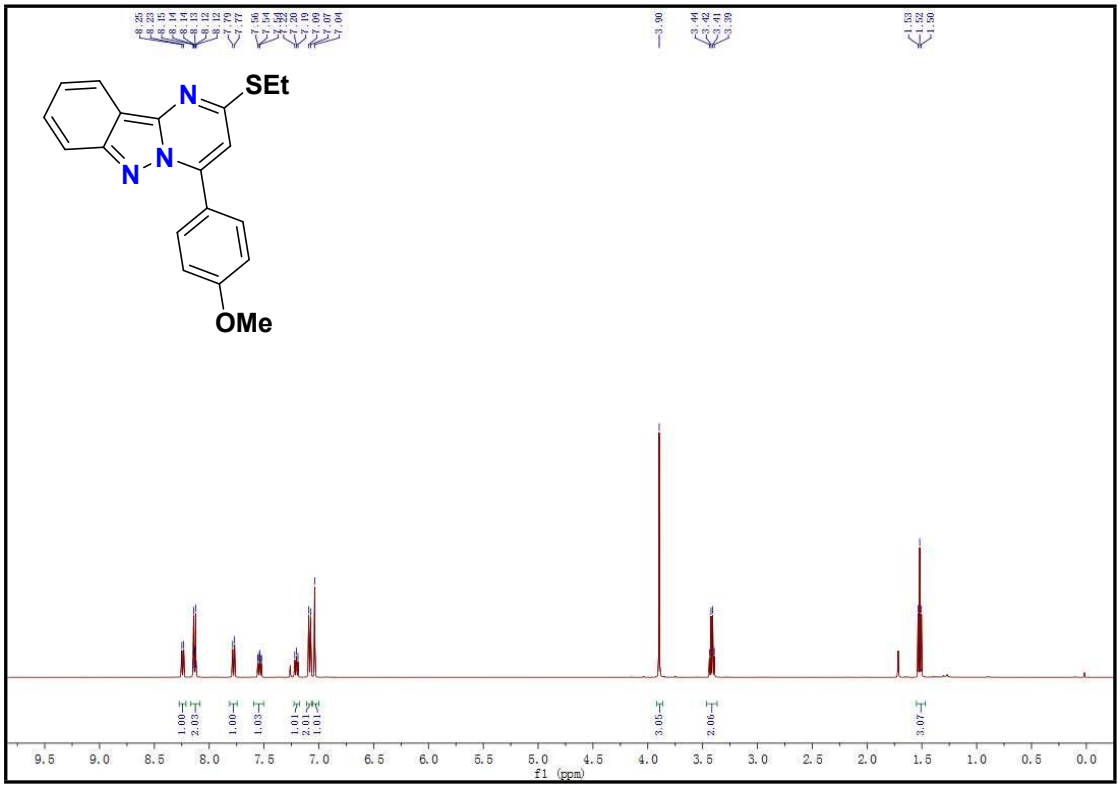


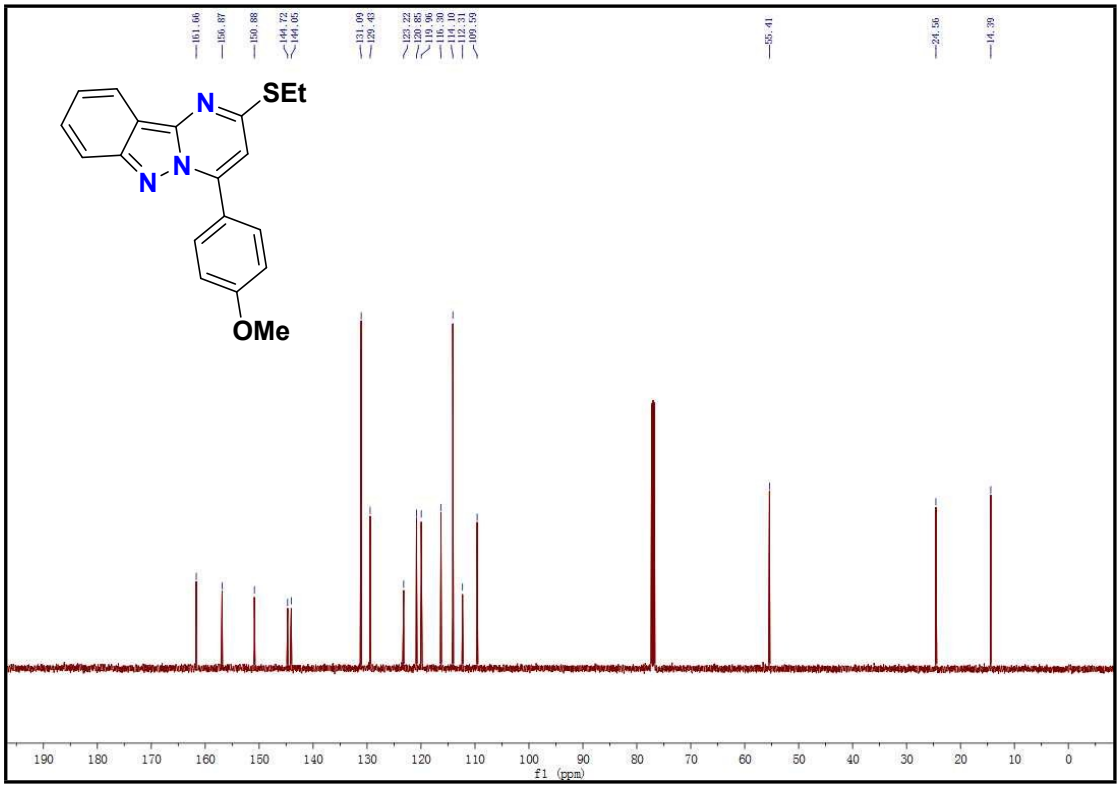
2-(ethylthio)-4-(4-isopropylphenyl)pyrimido[1,2-b]indazole (3d)



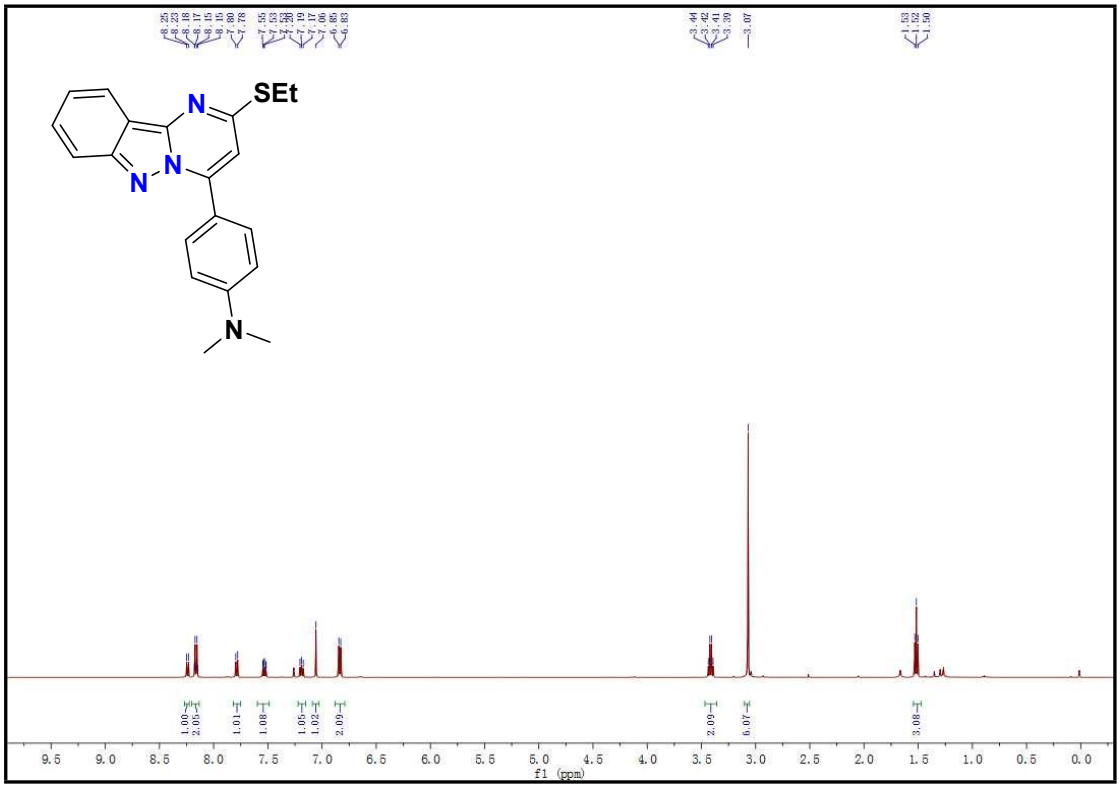


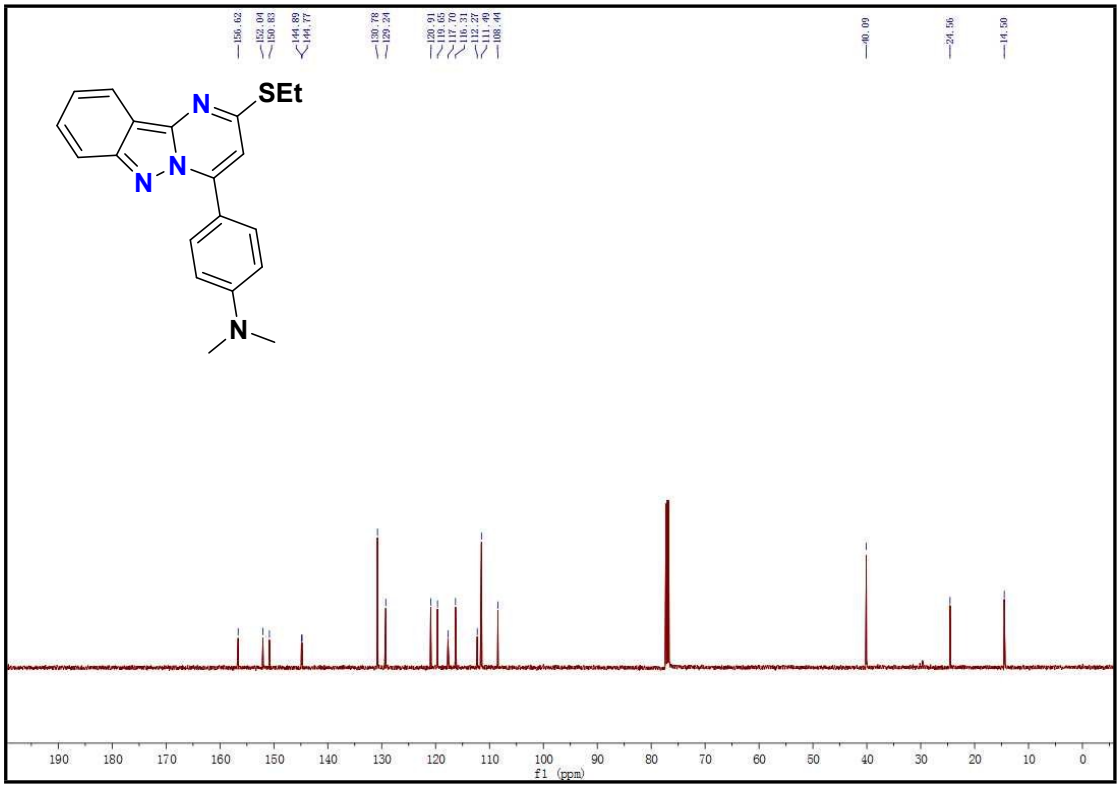
2-(ethylthio)-4-(4-methoxyphenyl)pyrimido[1,2-b]indazole (3e)



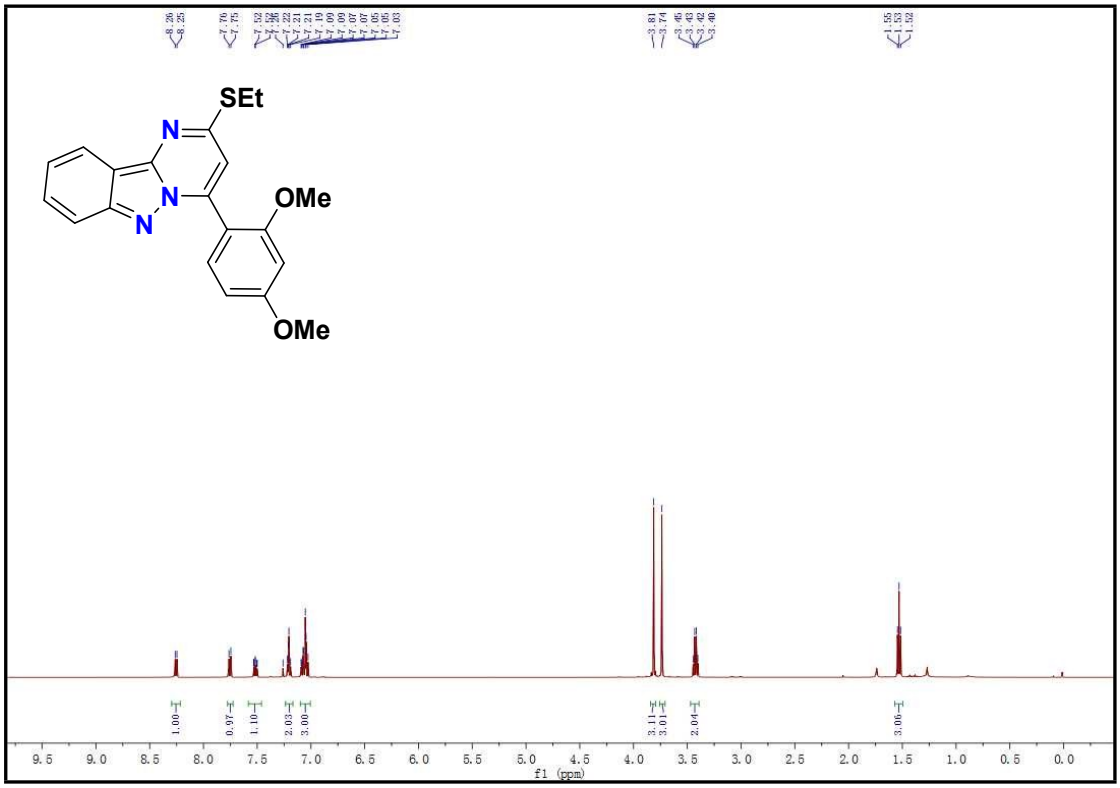


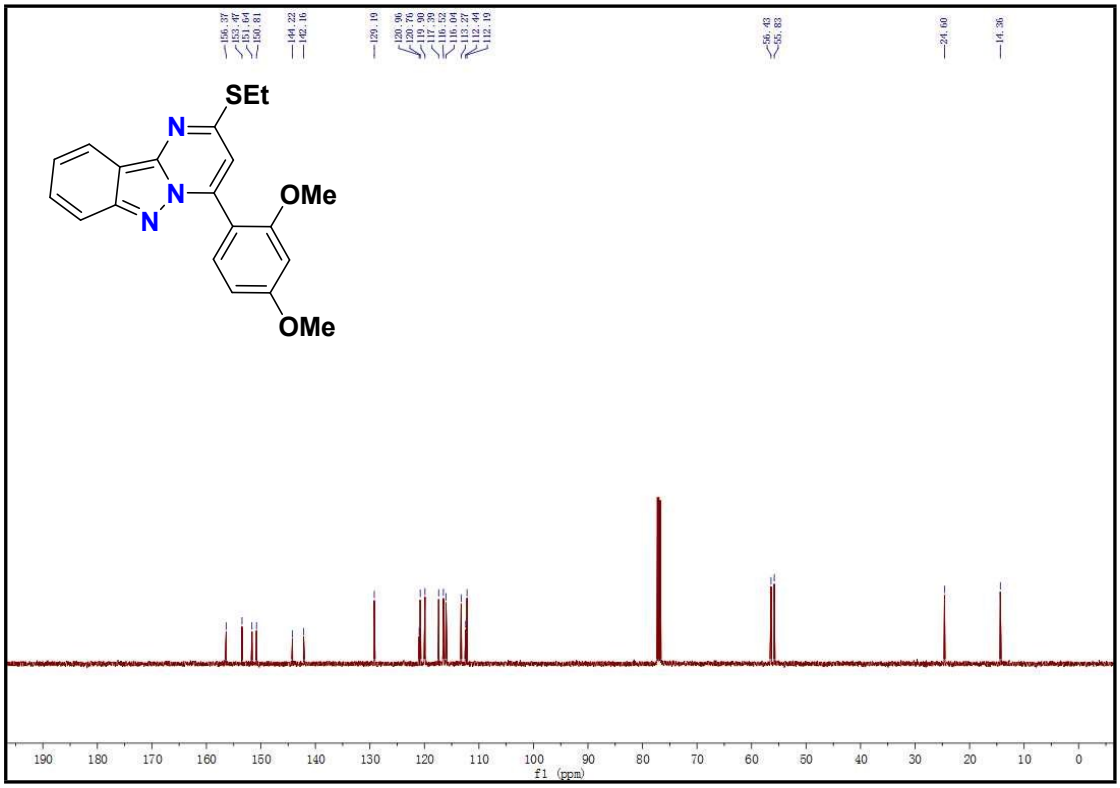
4-(2-(ethylthio)pyrimido[1,2-b]indazol-4-yl)-N,N-dimethylaniline (3f)



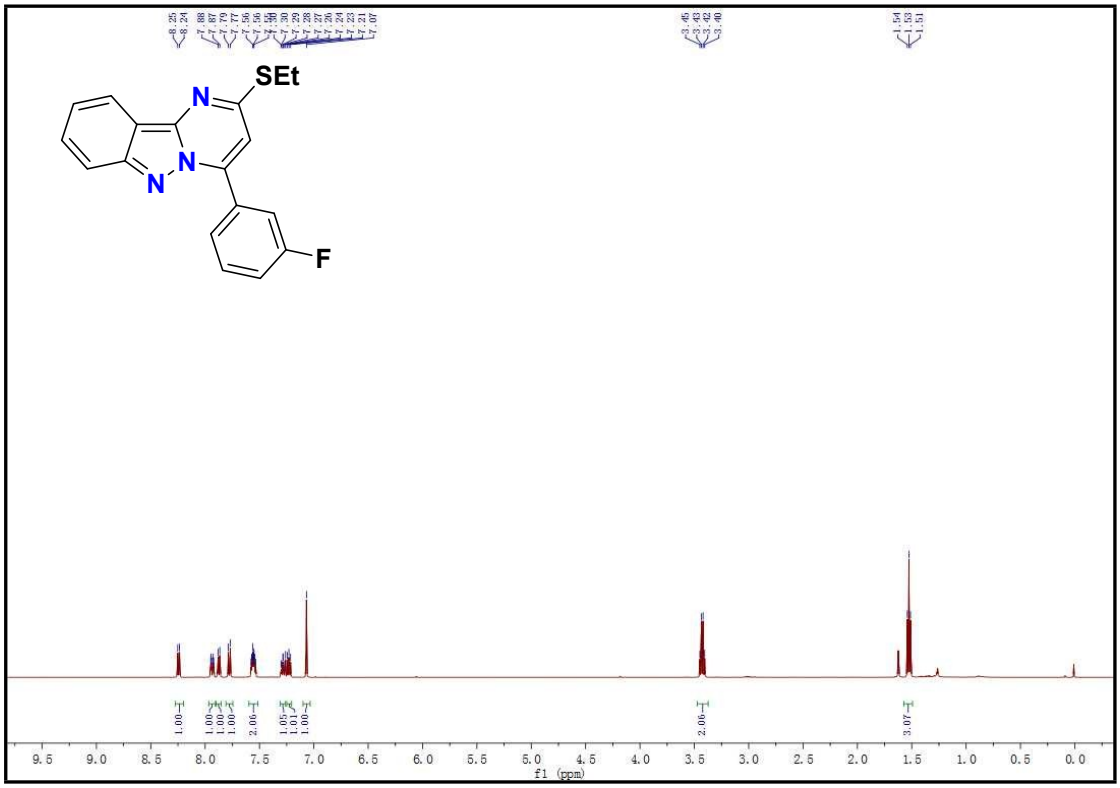


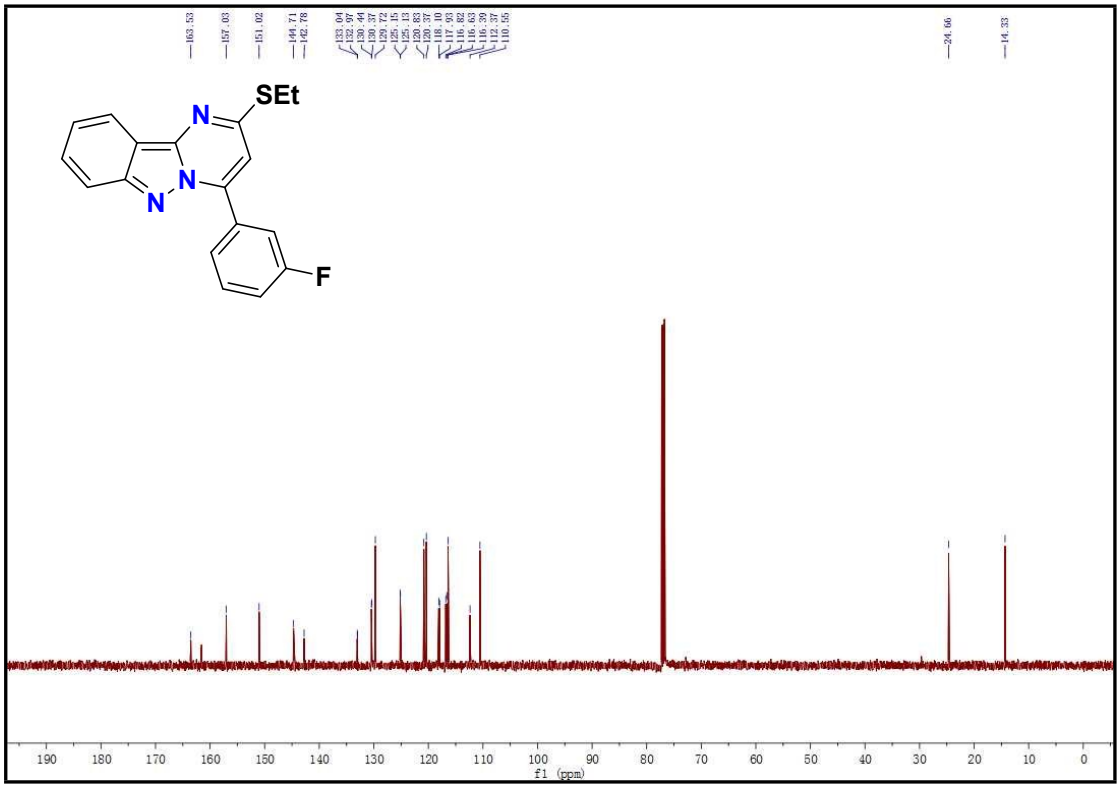
4-(2,4-dimethoxyphenyl)-2-(ethylthio)pyrimido[1,2-b]indazole (3g)



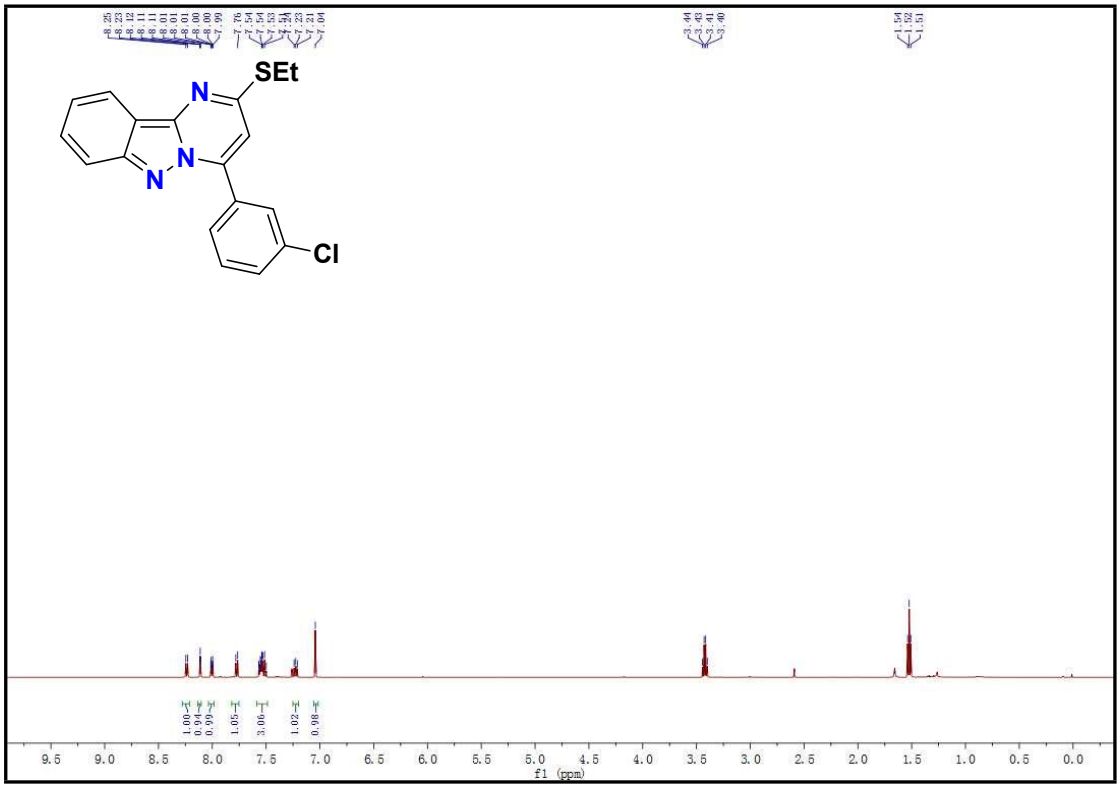


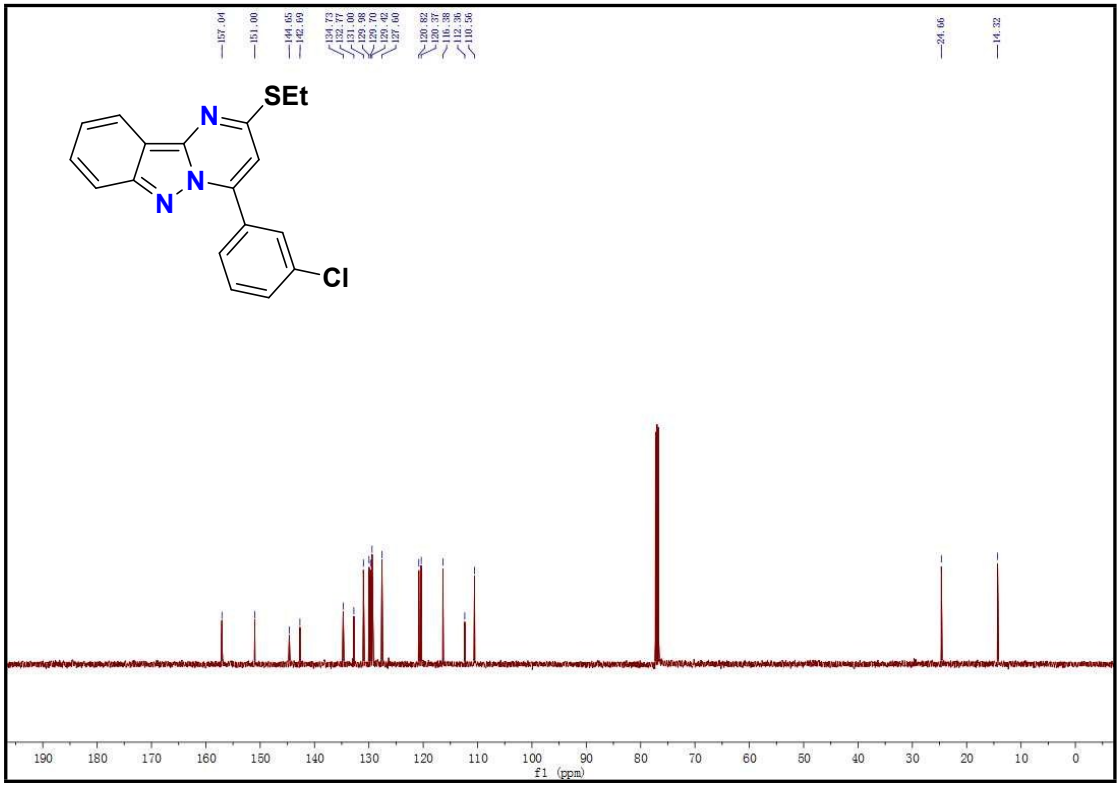
2-(ethylthio)-4-(3-fluorophenyl)pyrimido[1,2-b]indazole (3h)



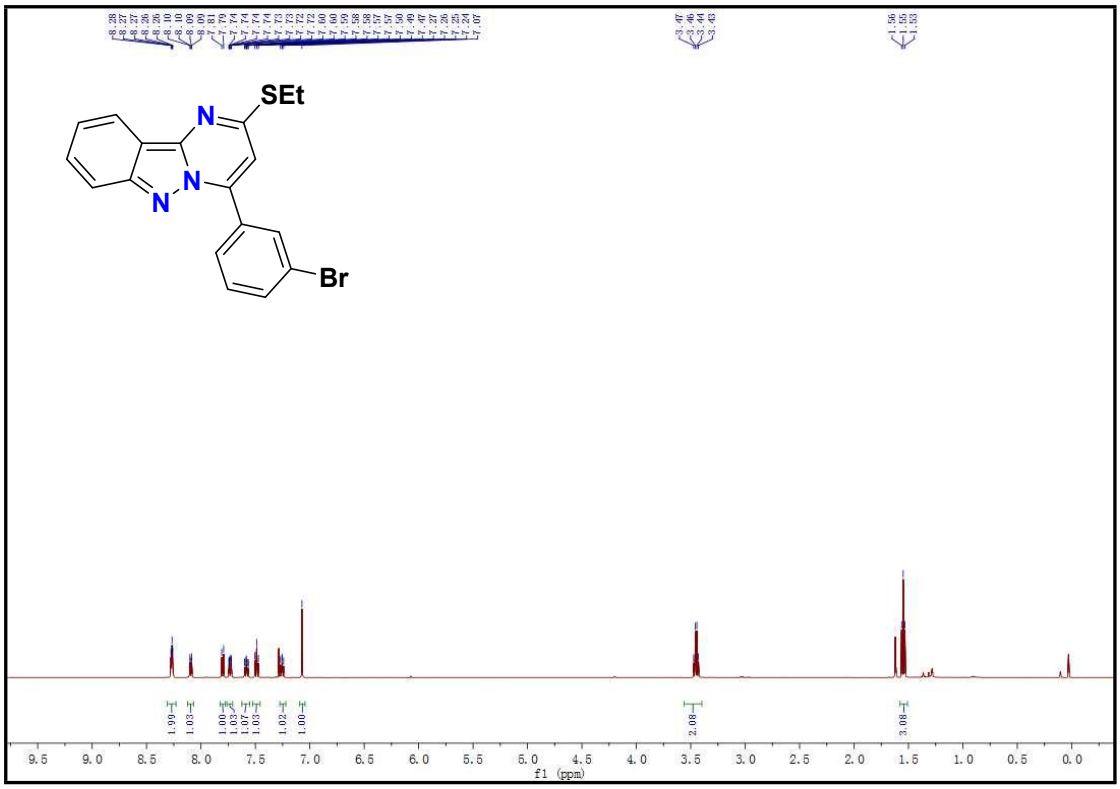


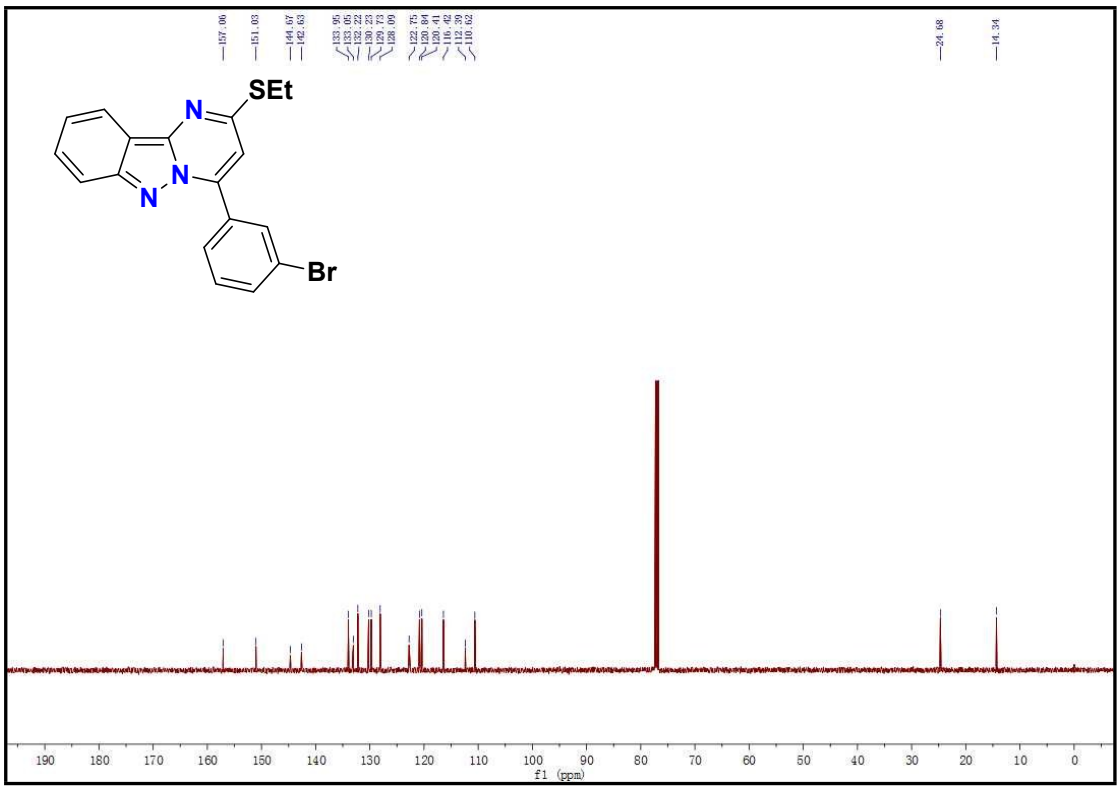
4-(3-chlorophenyl)-2-(ethylthio)pyrimido[1,2-b]indazole (3i)



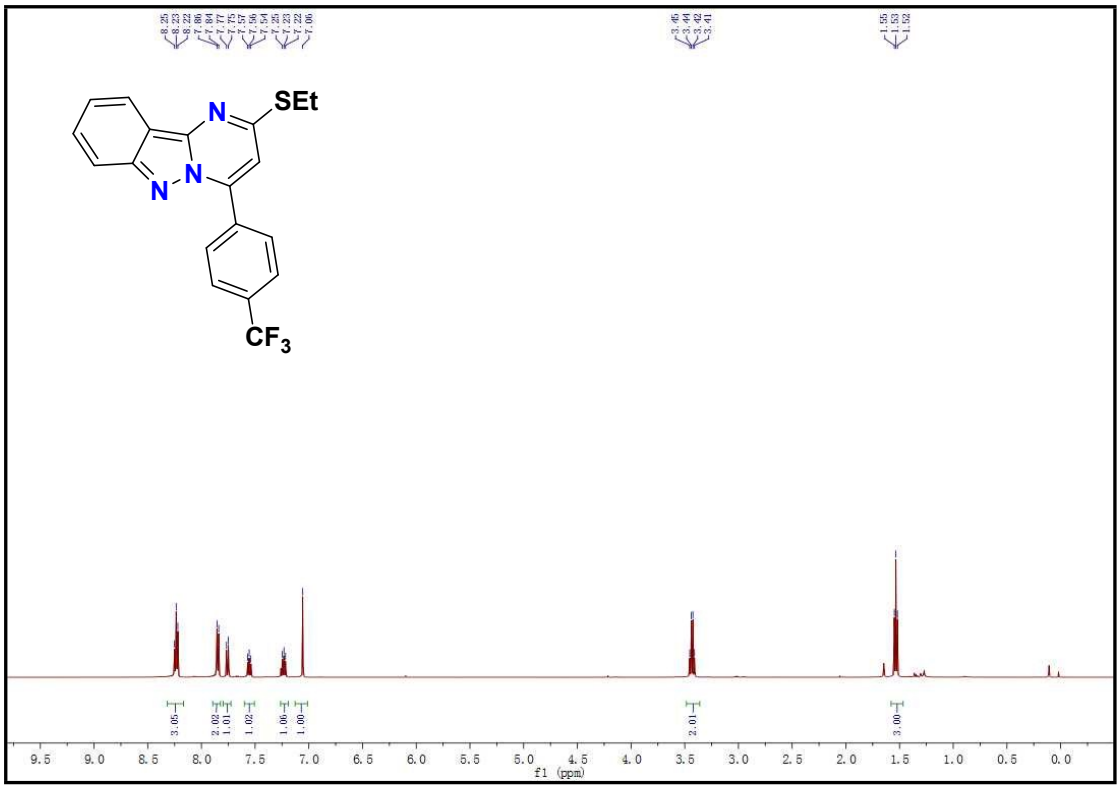


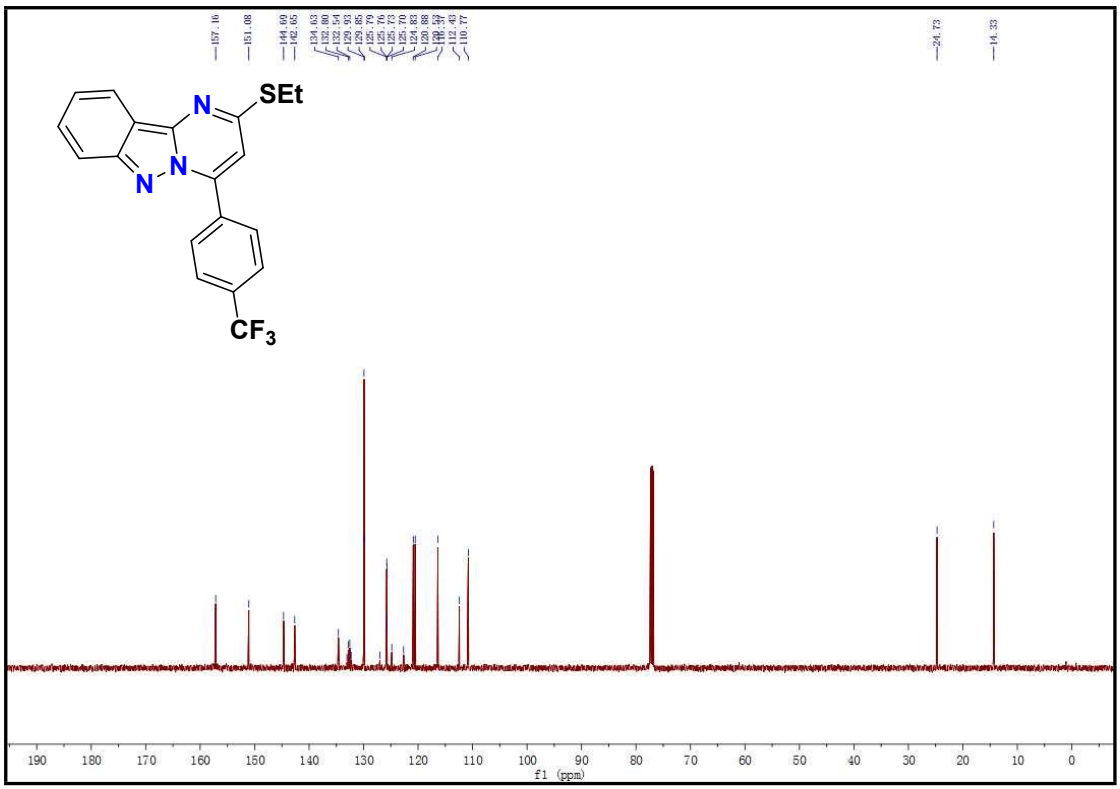
4-(3-bromophenyl)-2-(ethylthio)pyrimido[1,2-b]indazole (3j)



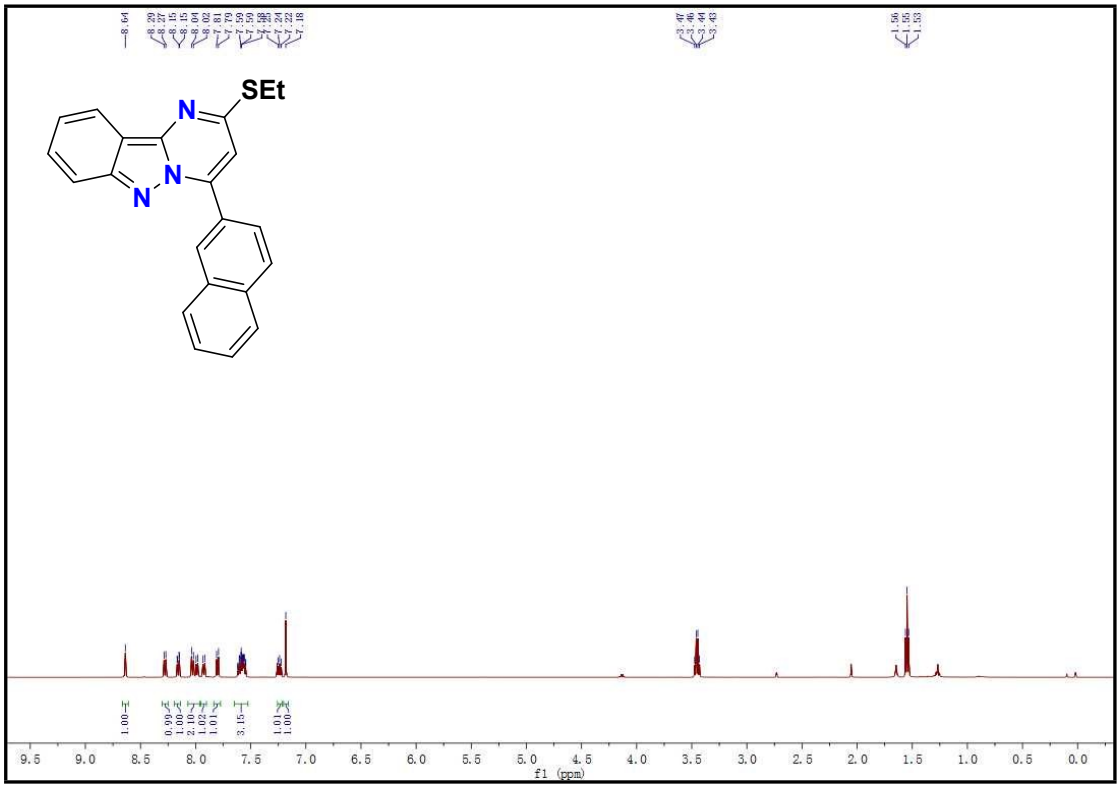


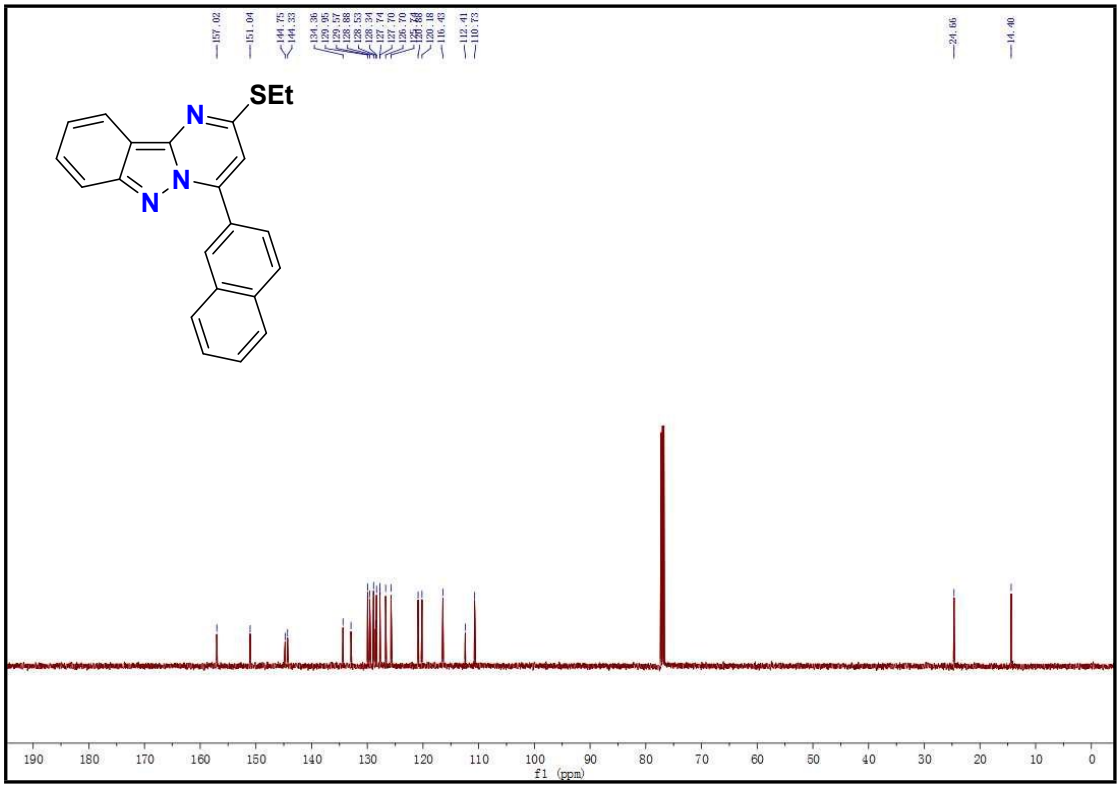
2-(ethylthio)-4-(4-(trifluoromethyl)phenyl)pyrimido[1,2-b]indazole (3k)



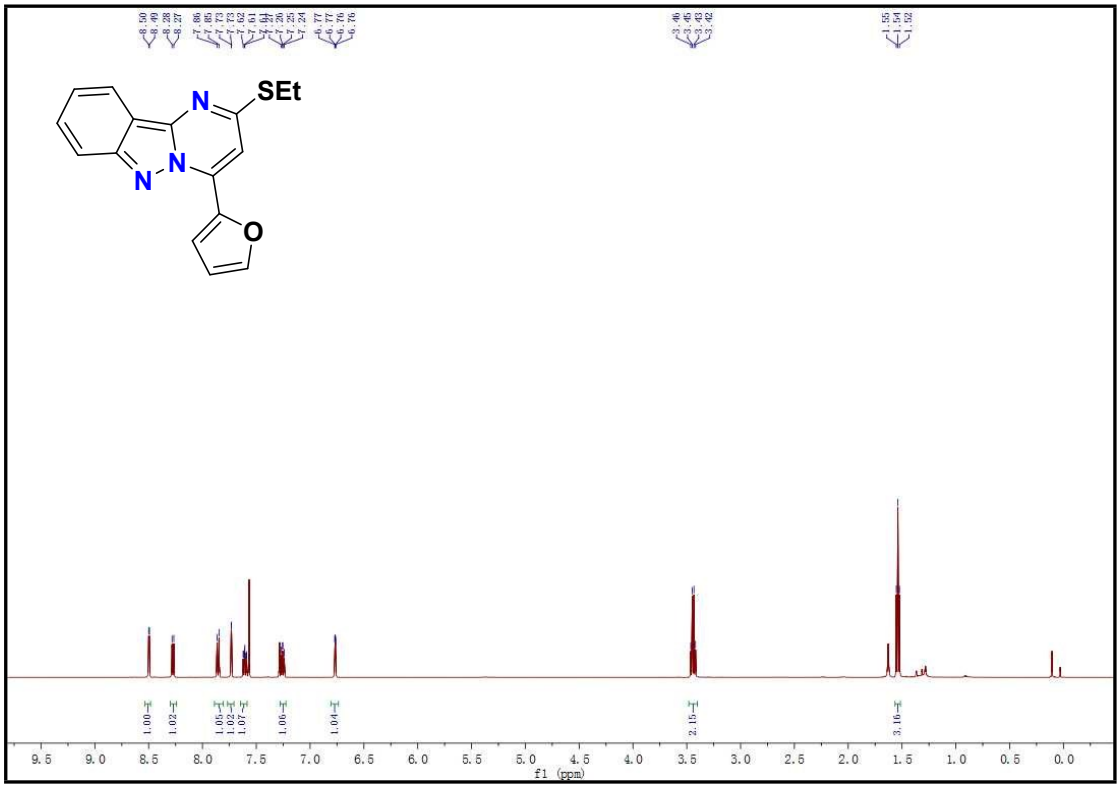


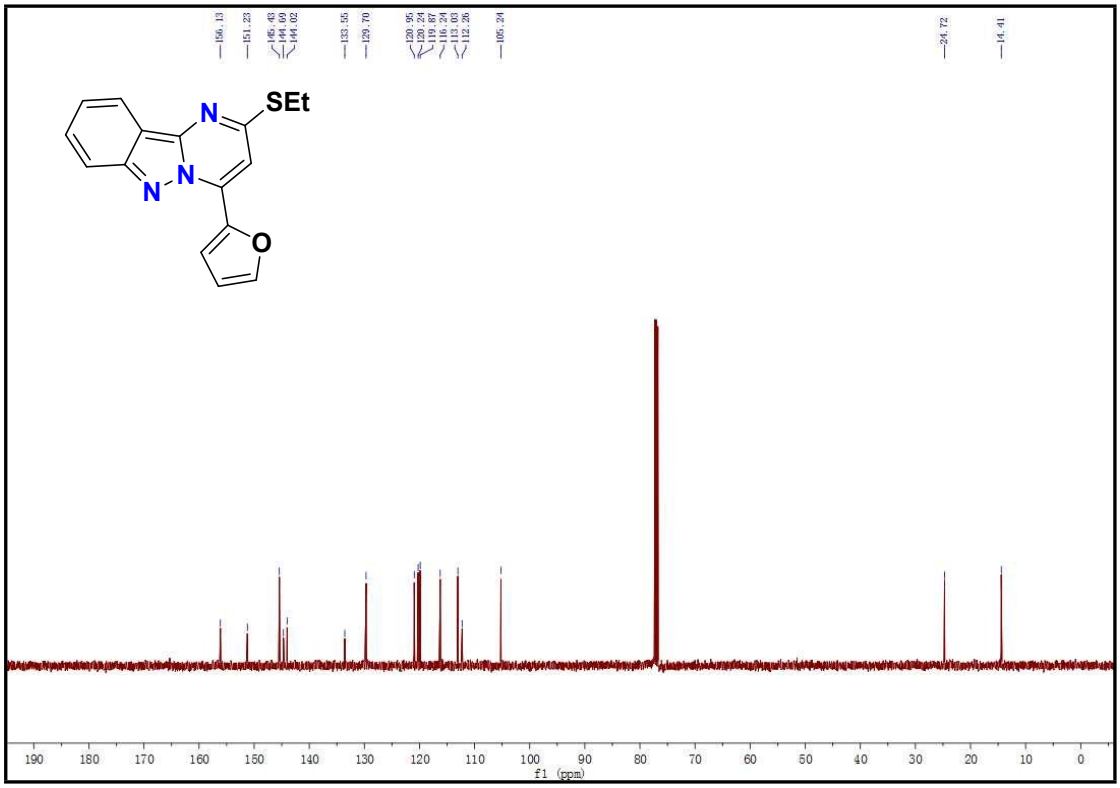
2-(ethylthio)-4-(naphthalen-2-yl)pyrimido[1,2-b]indazole (3l)



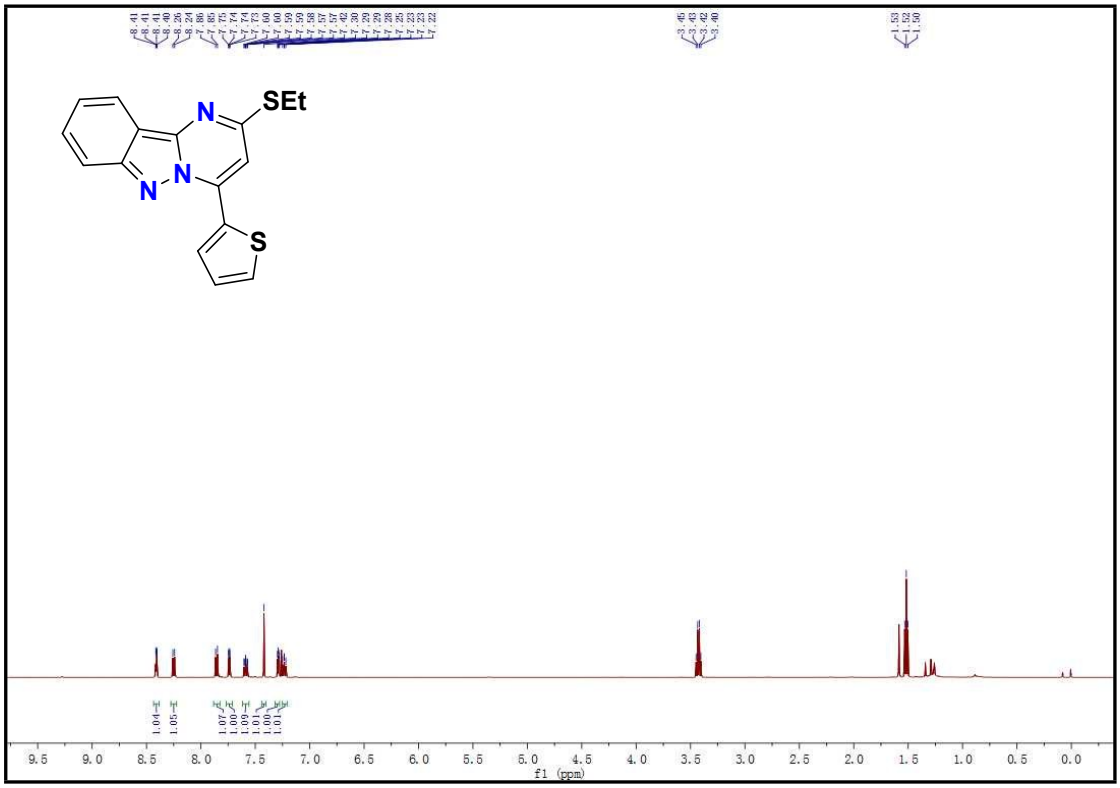


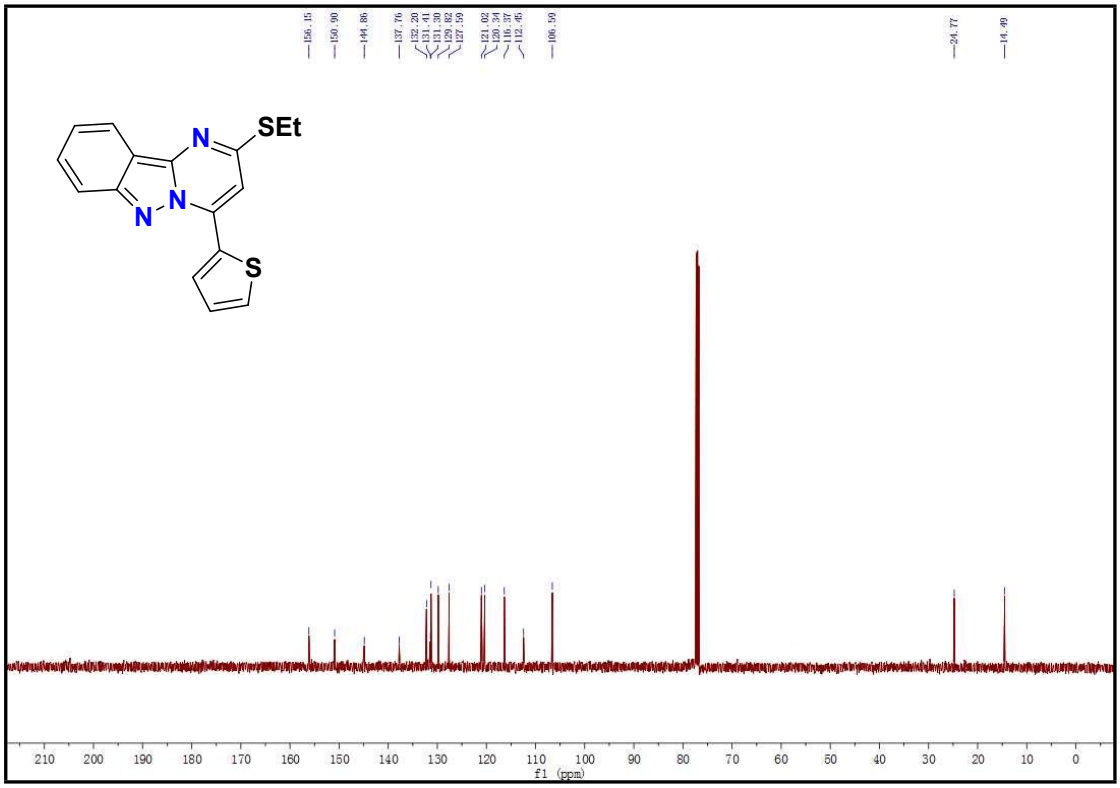
2-(ethylthio)-4-(furan-2-yl)pyrimido[1,2-b]indazole (3m)



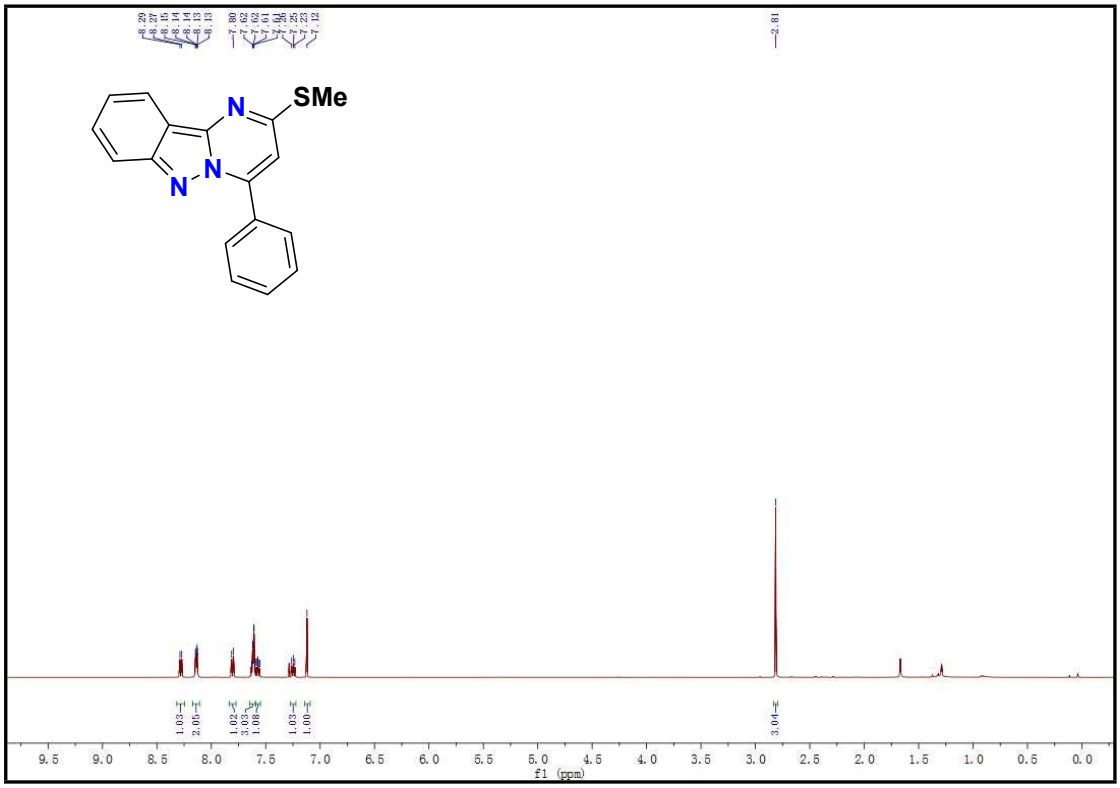


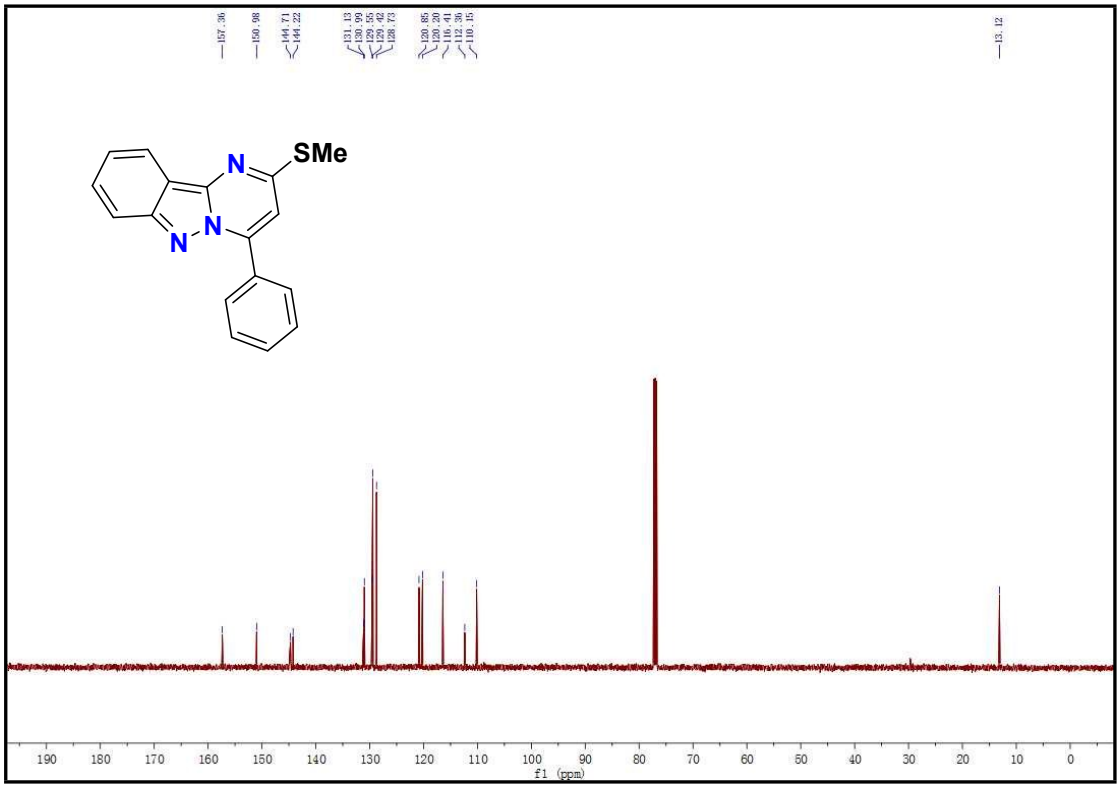
2-(ethylthio)-4-(thiophen-2-yl)pyrimido[1,2-b]indazole (3n)



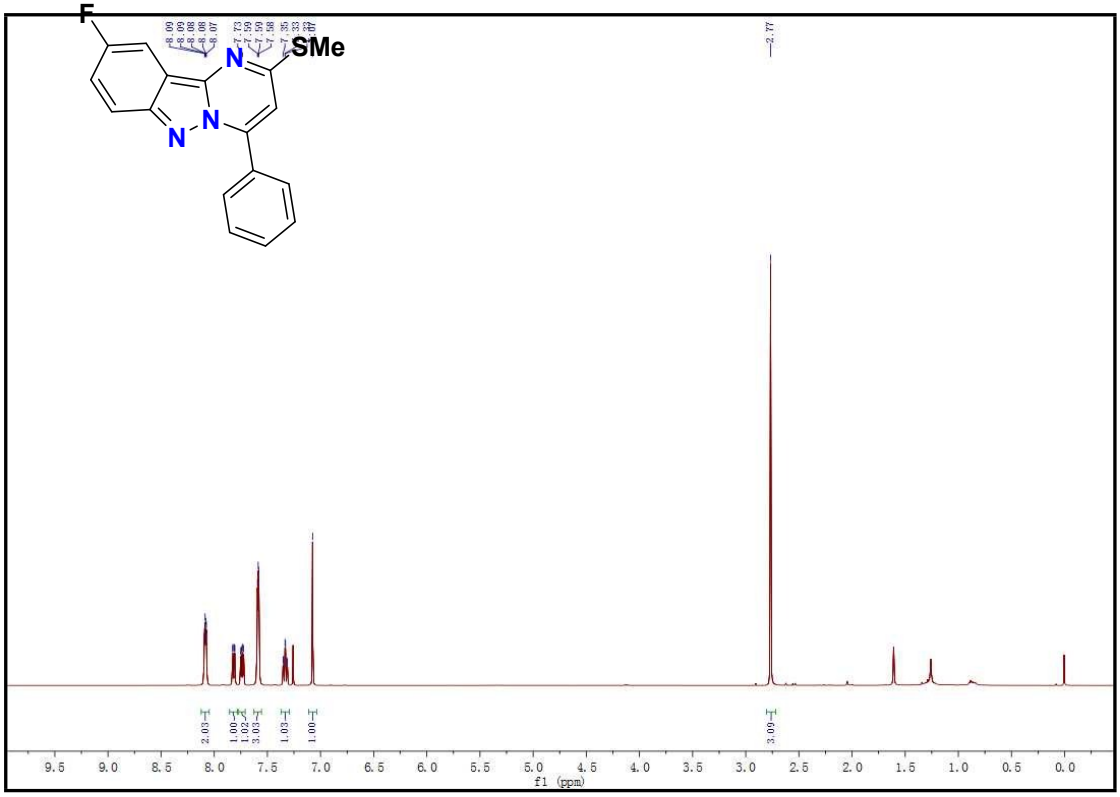


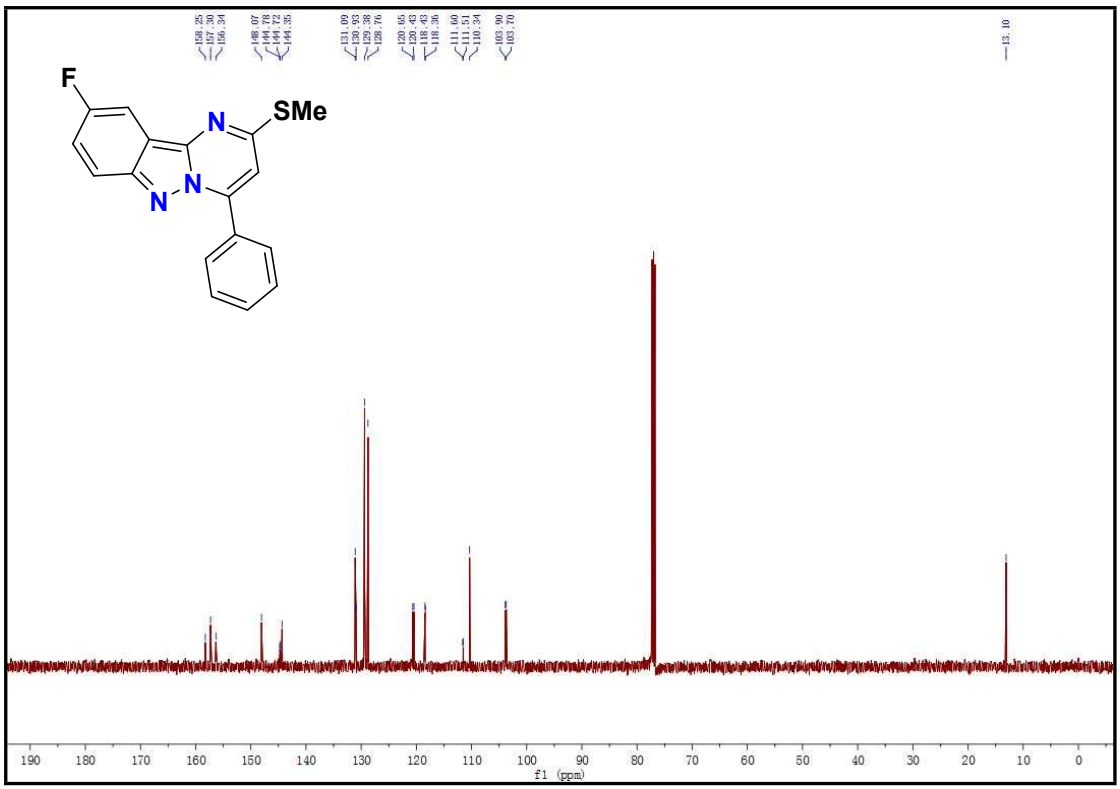
2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3o)



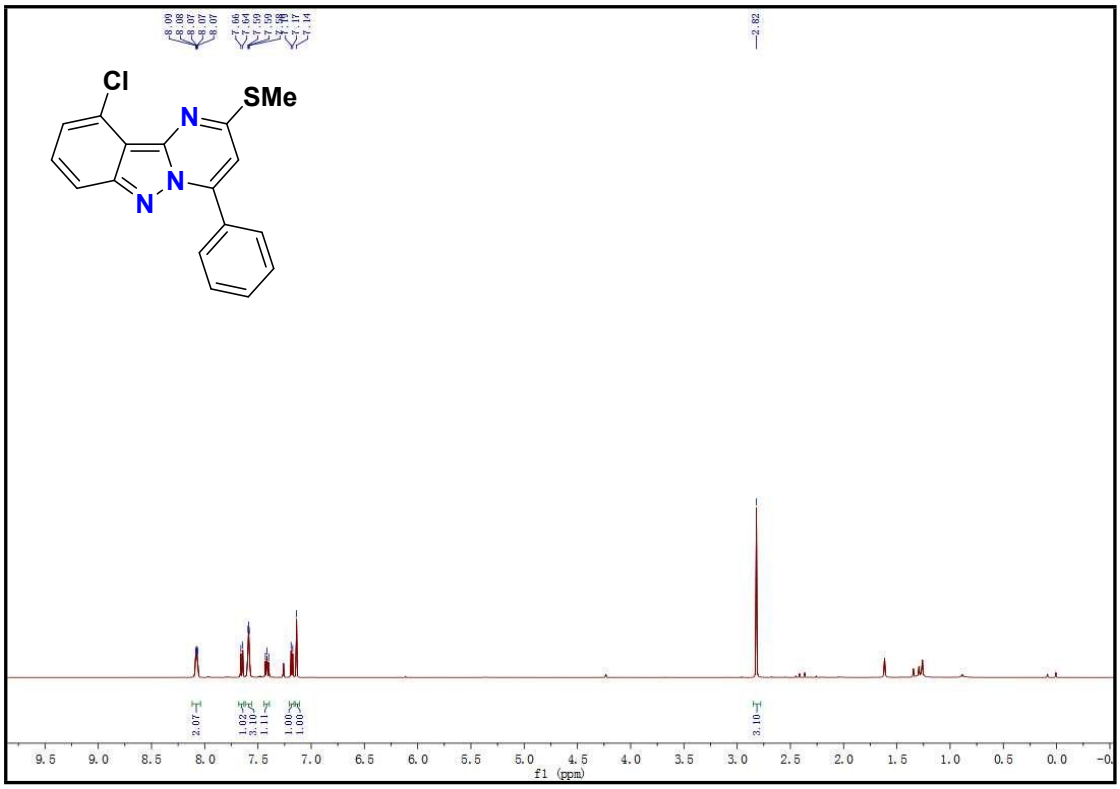


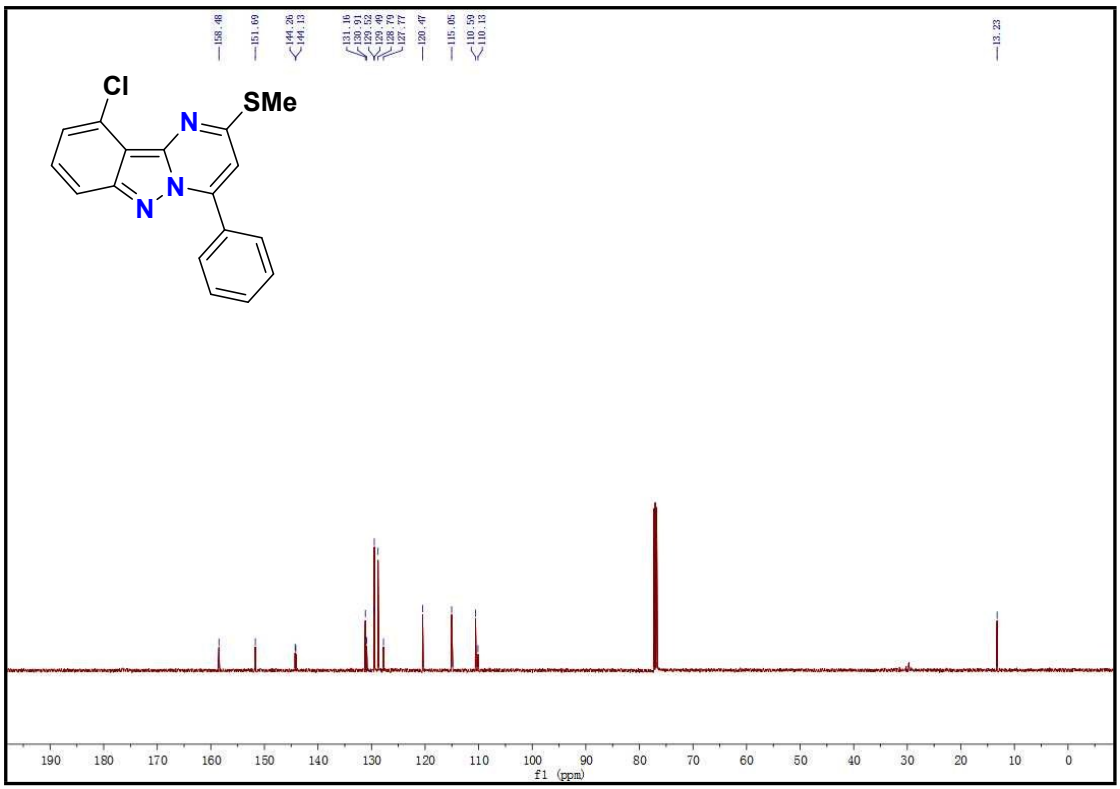
9-fluoro-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3p)



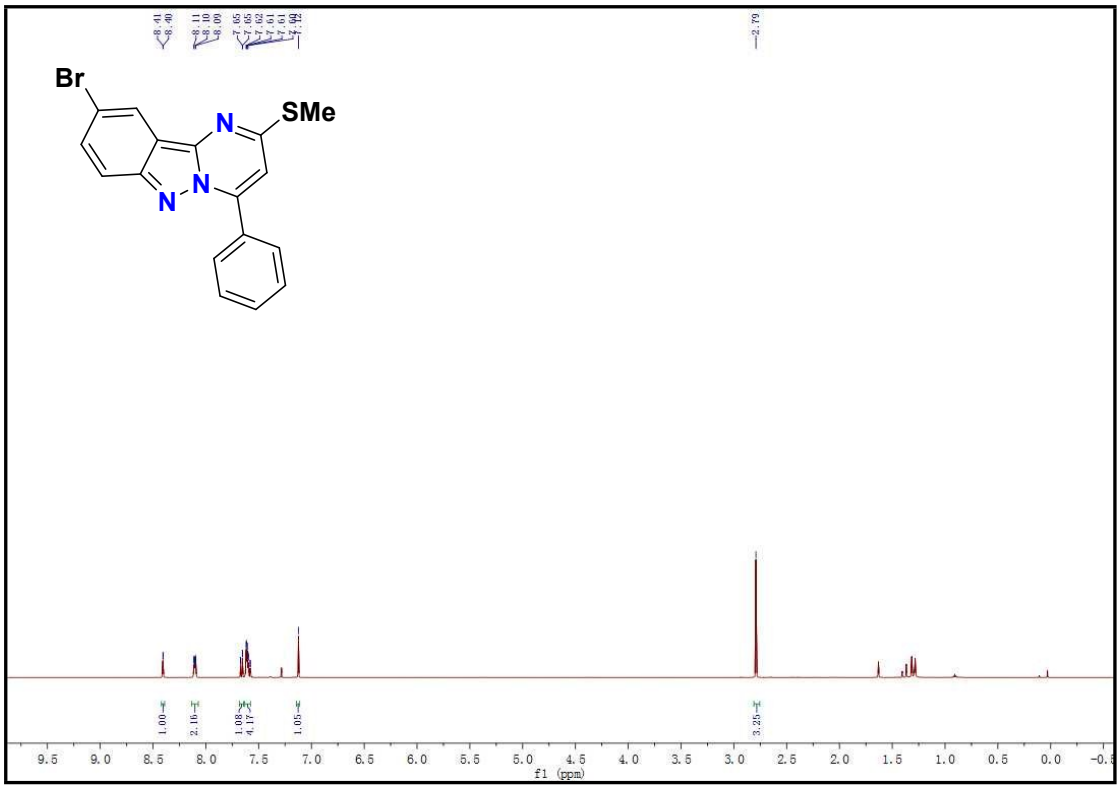


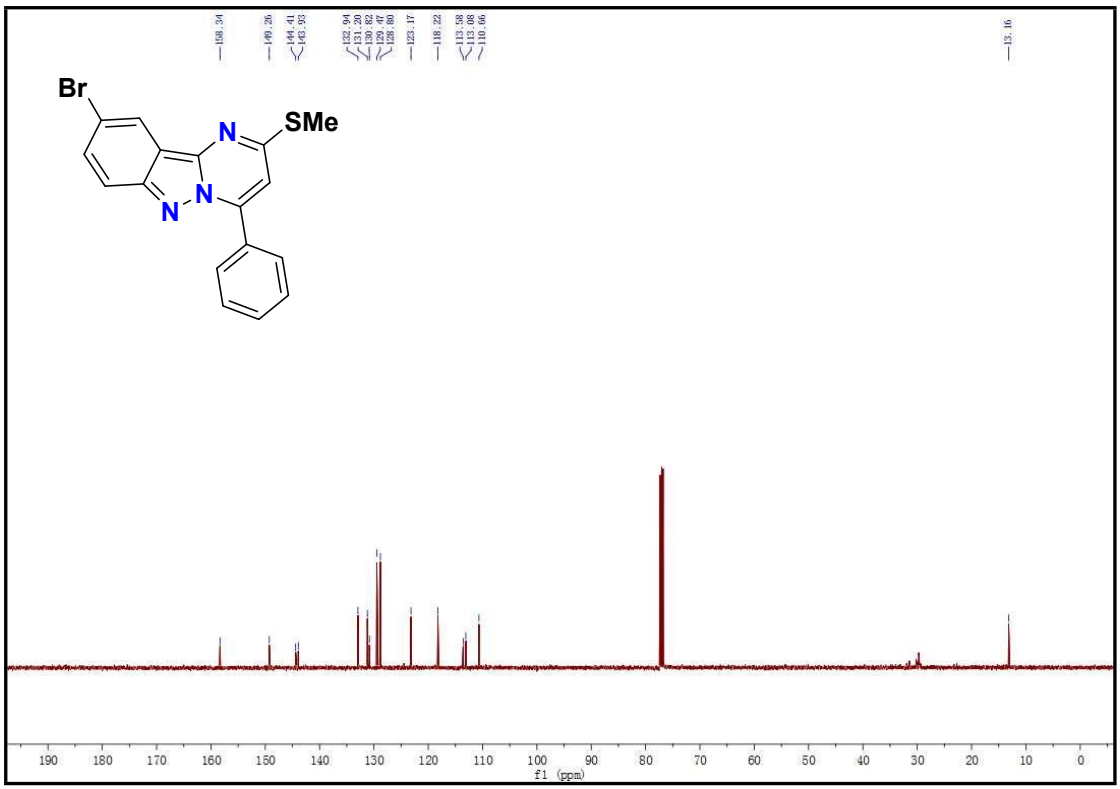
10-chloro-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3q)



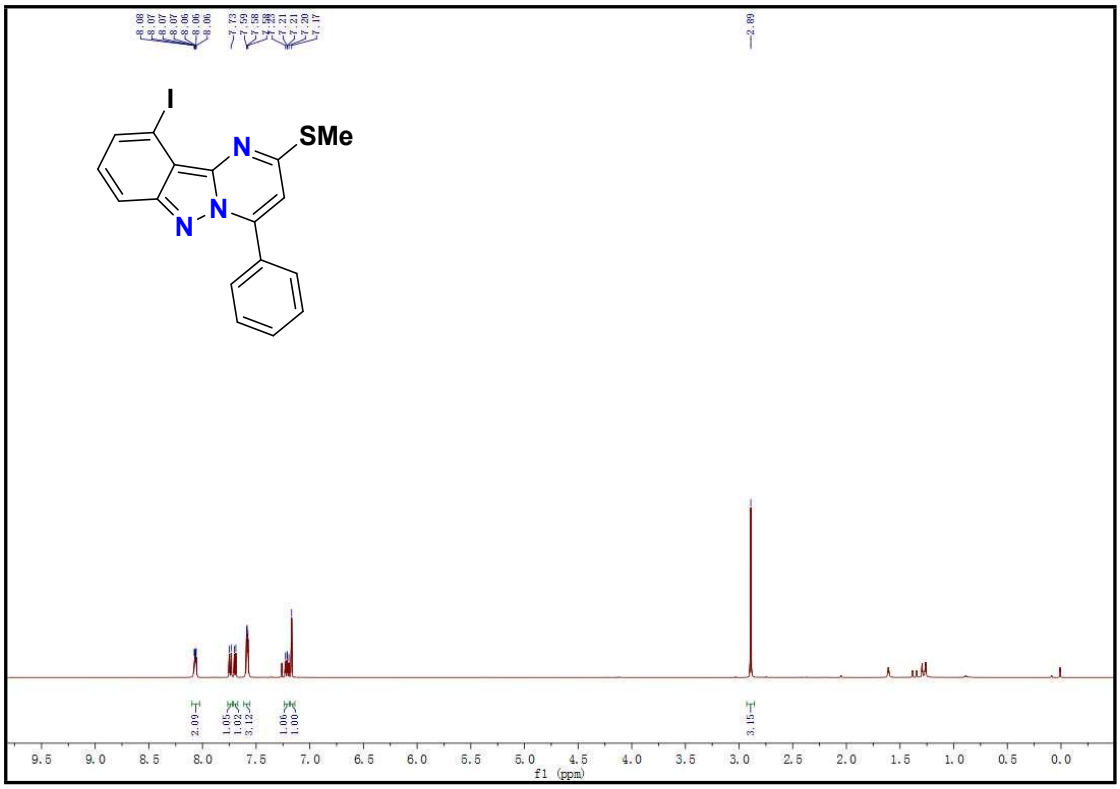


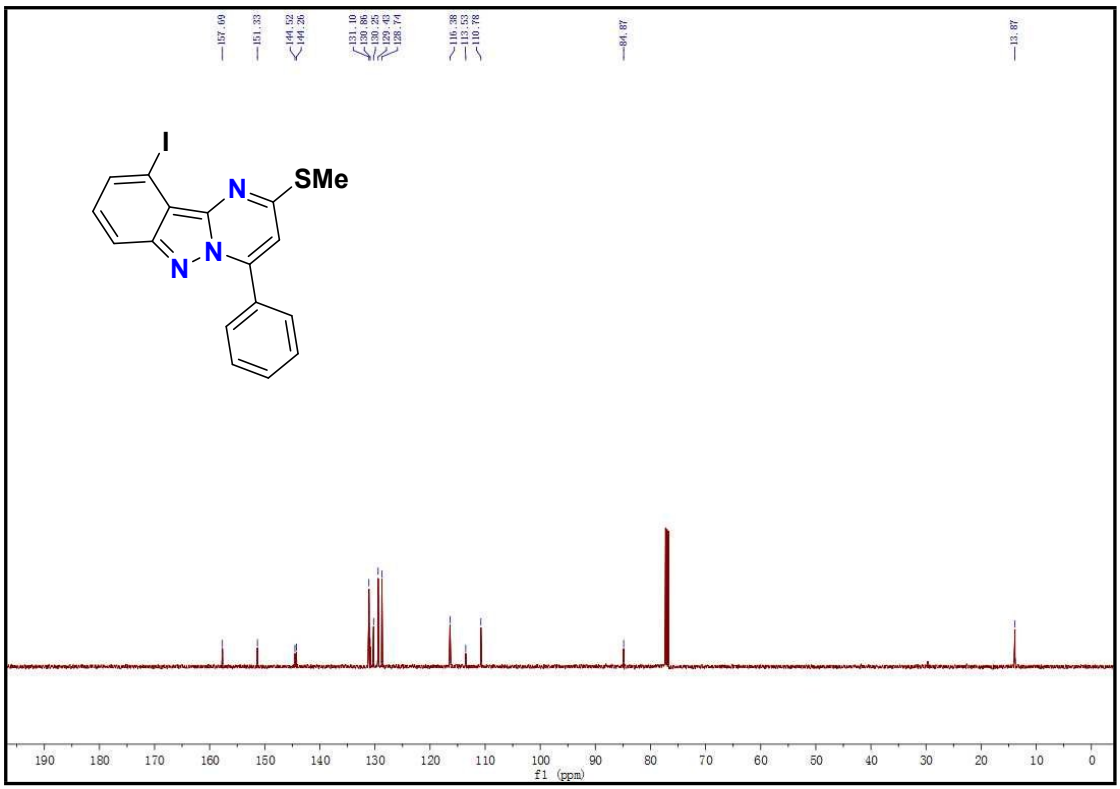
9-bromo-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3r)



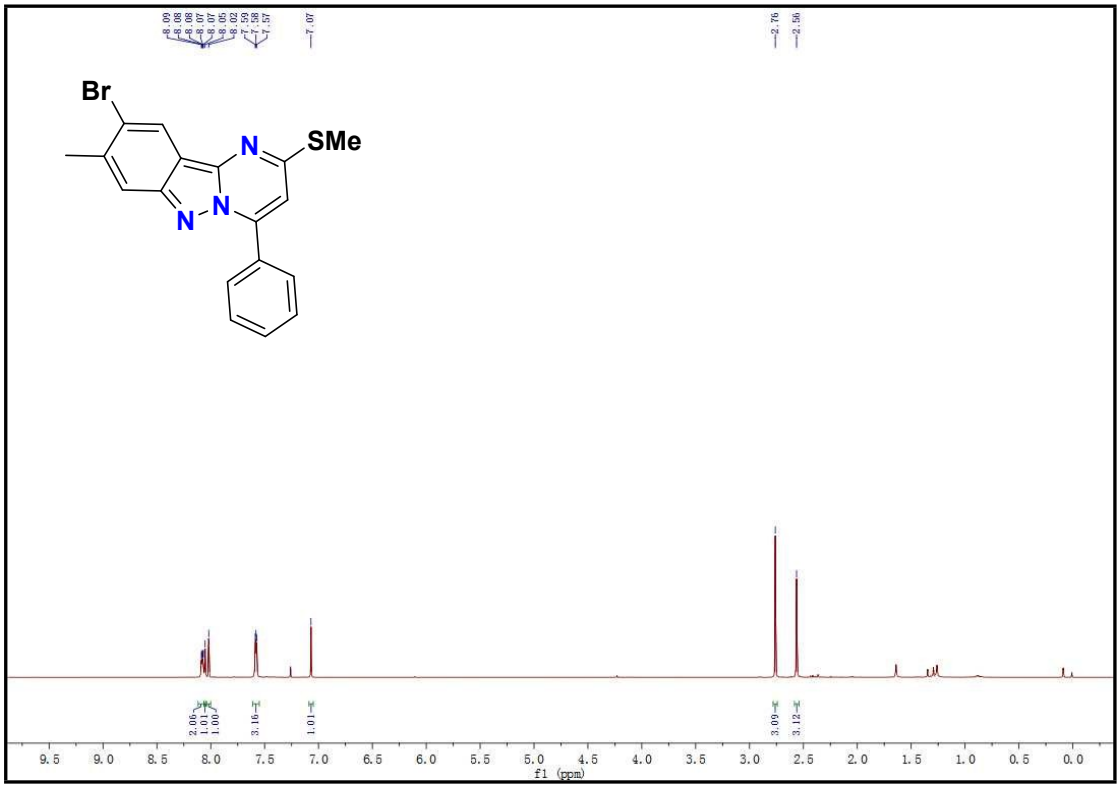


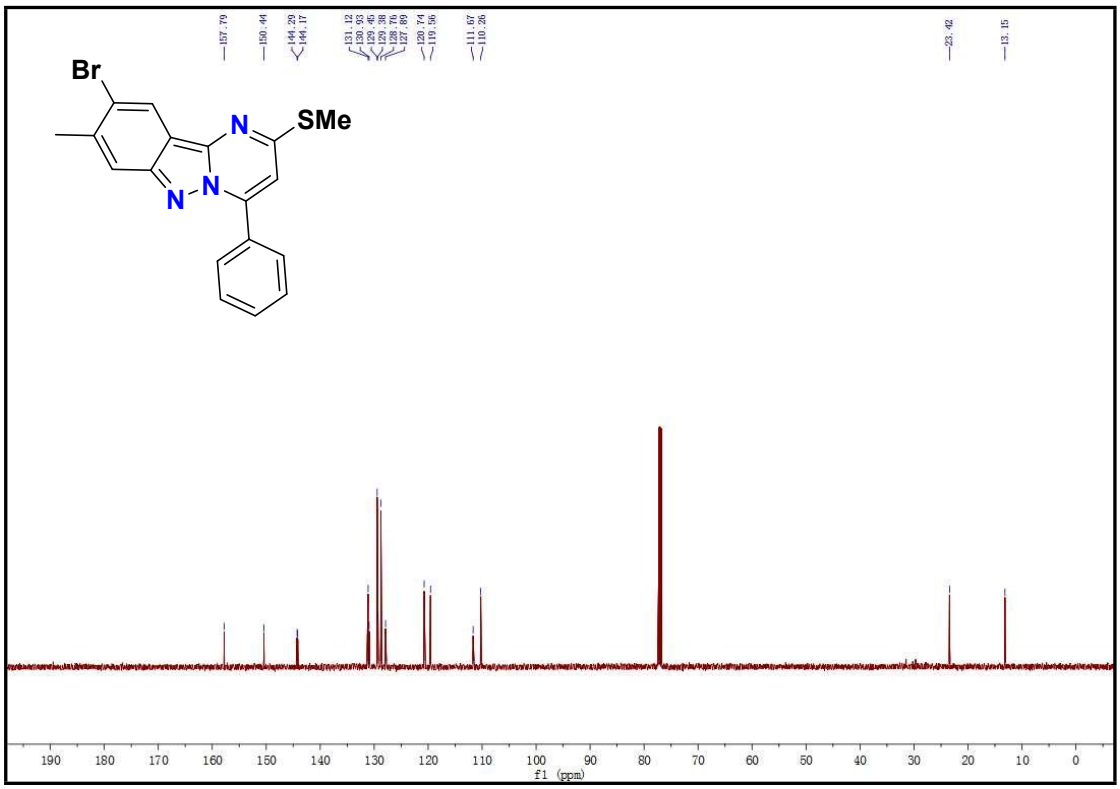
10-iodo-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3s)



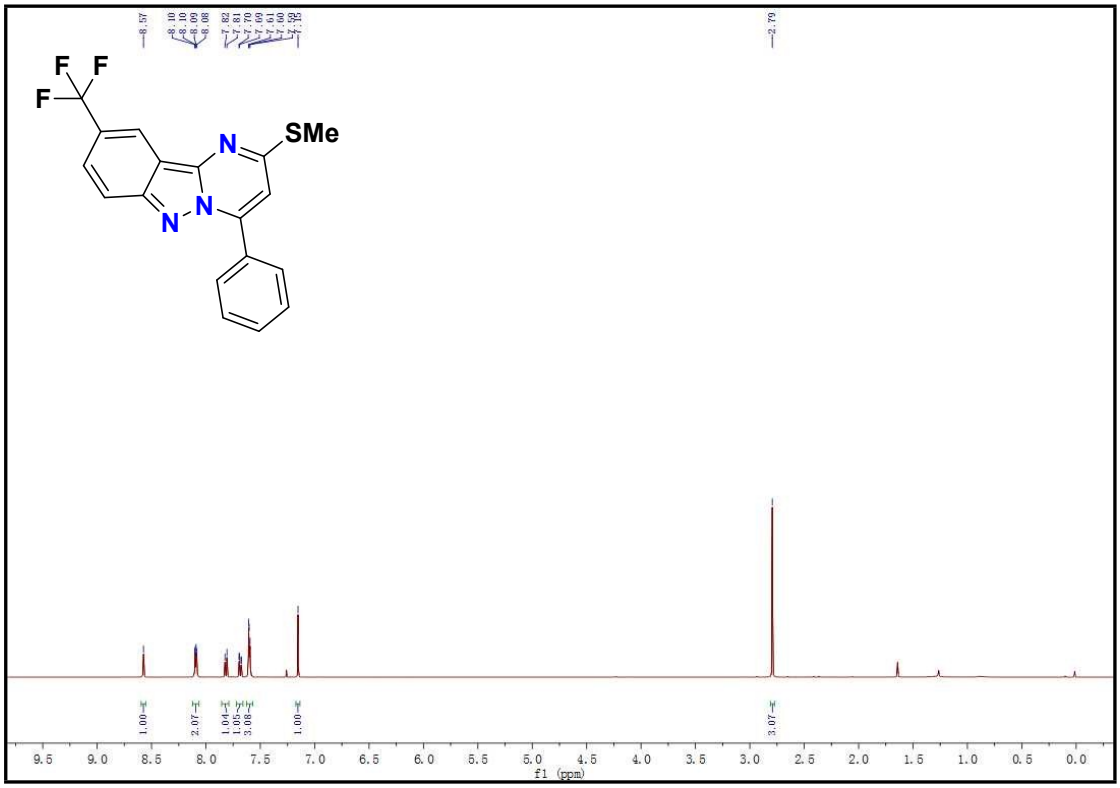


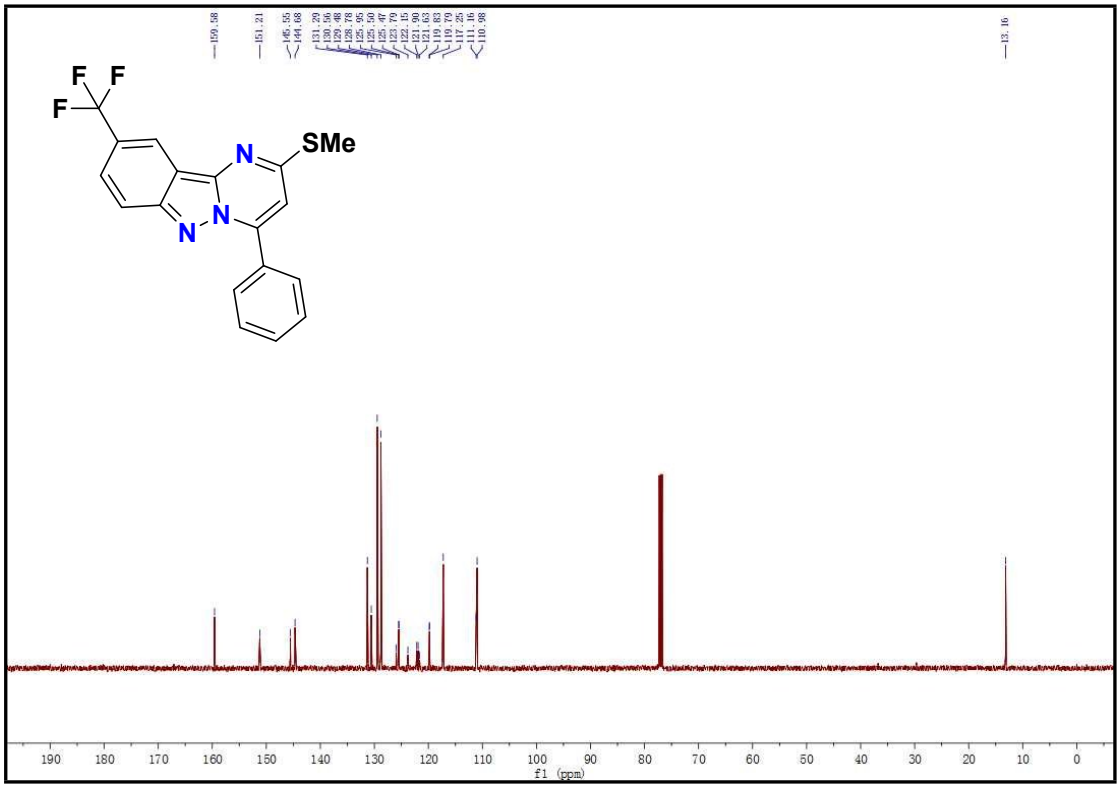
9-bromo-8-methyl-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3t)



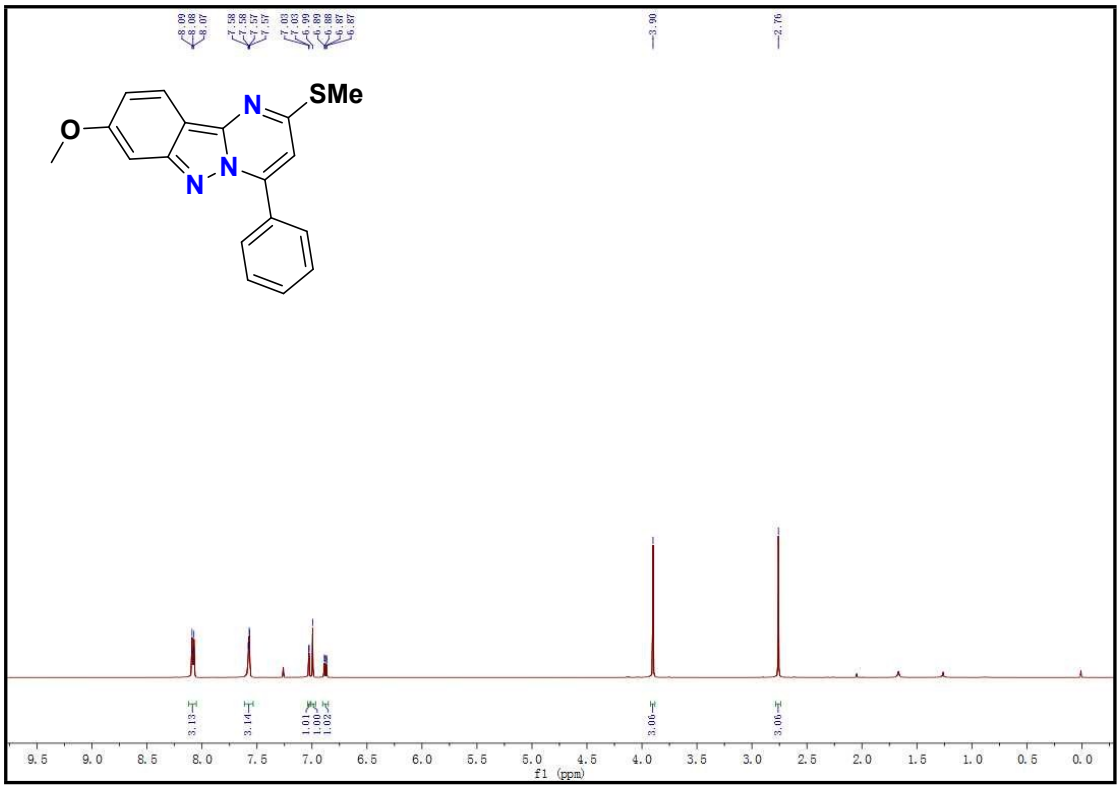


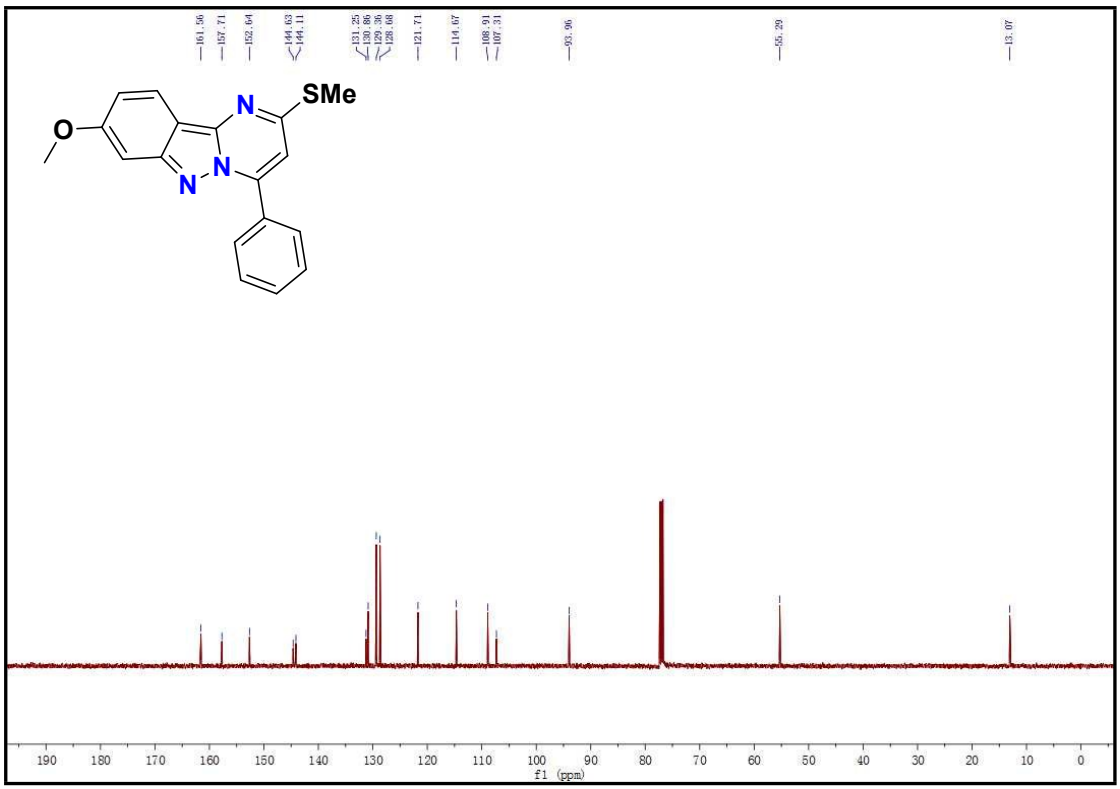
2-(methylthio)-4-phenyl-9-(trifluoromethyl)pyrimido[1,2-b]indazole (3u)



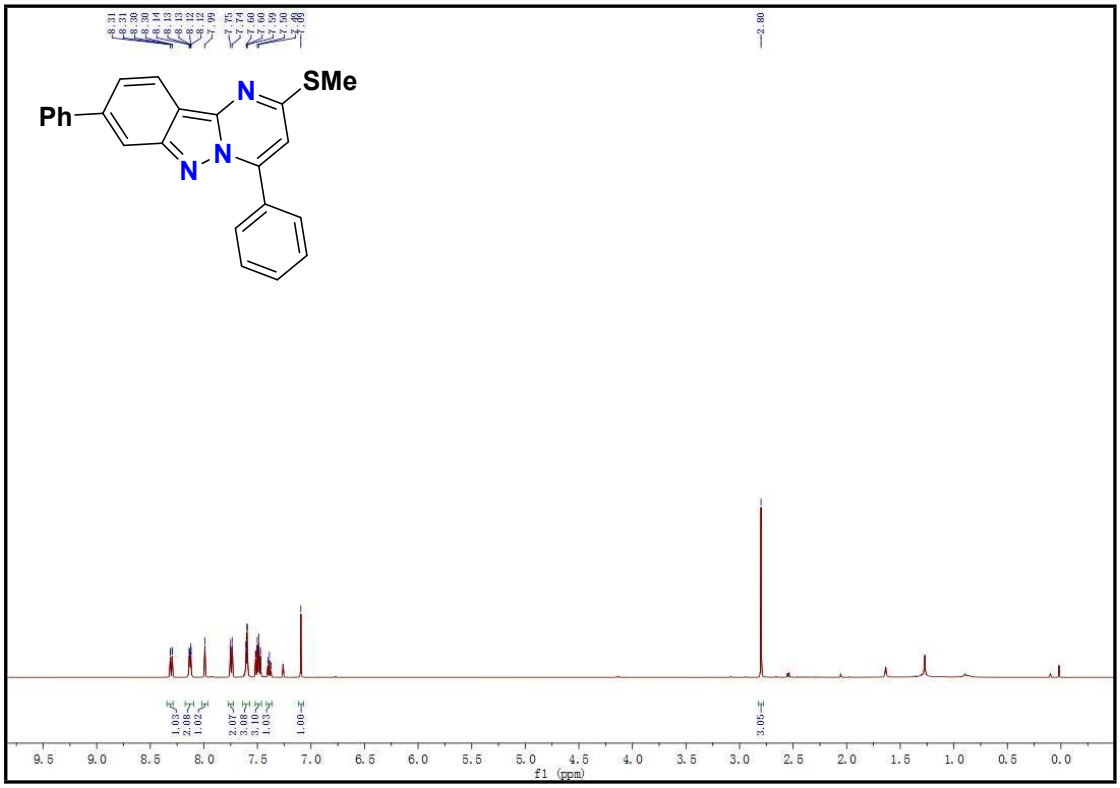


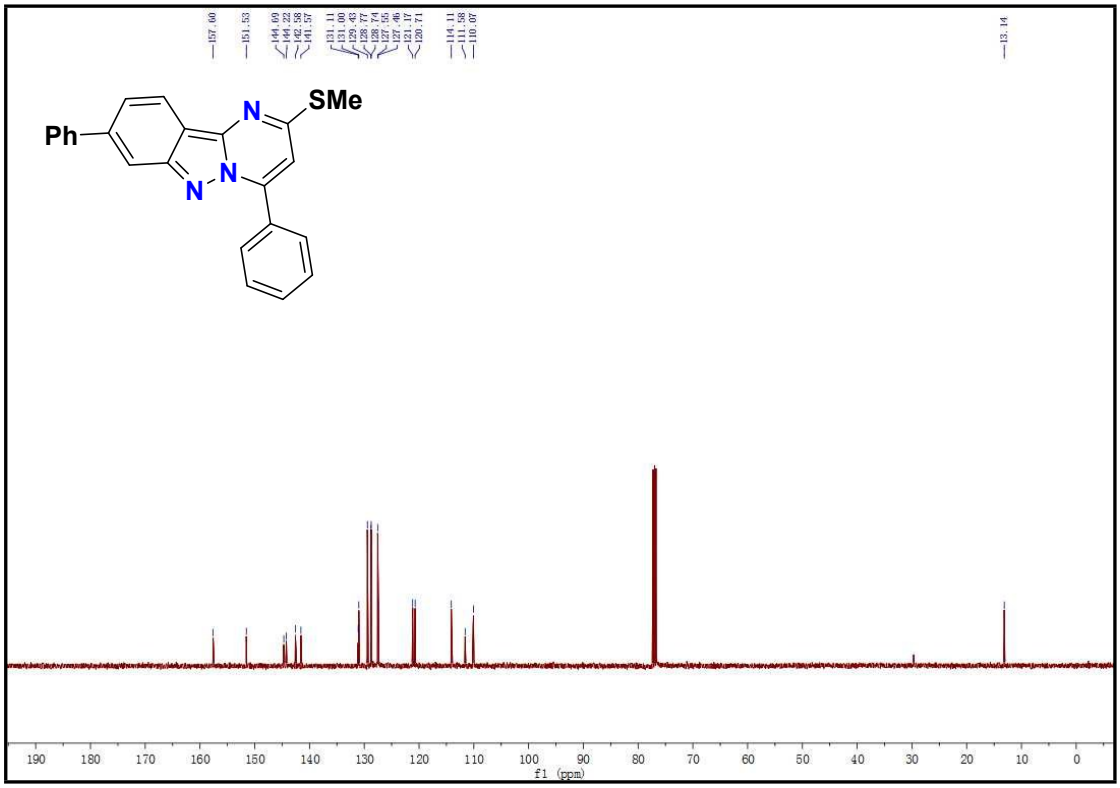
8-methoxy-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3v)



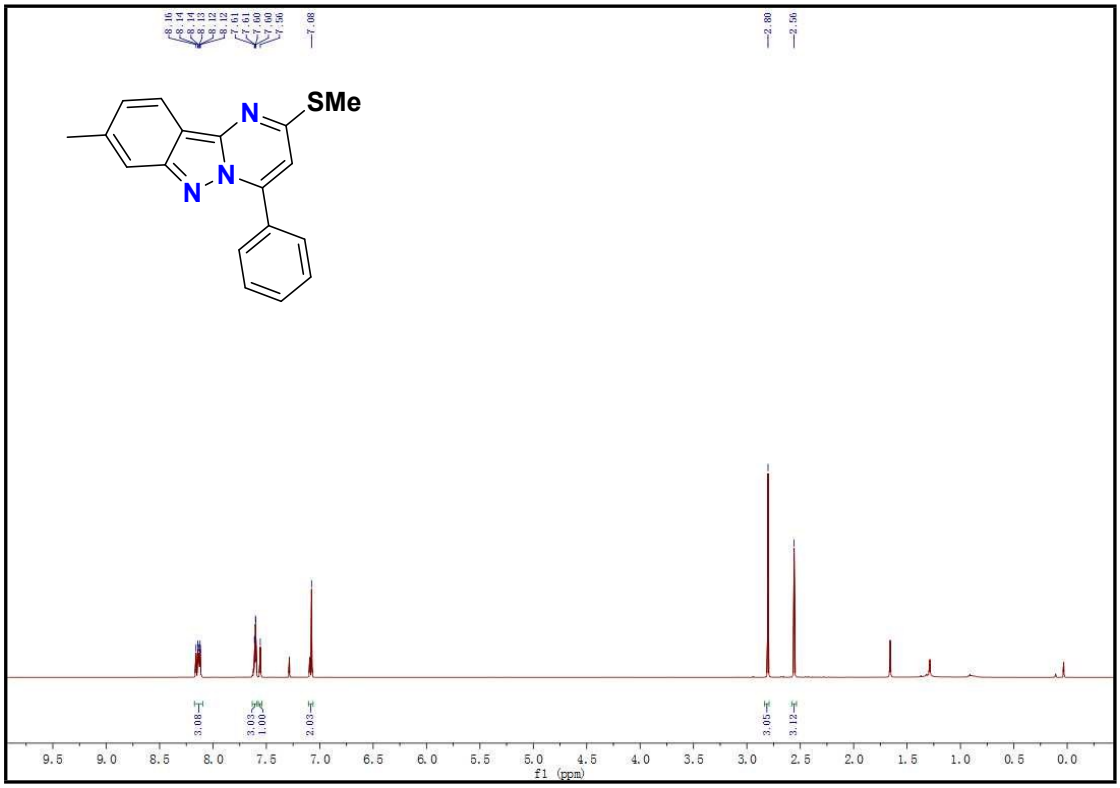


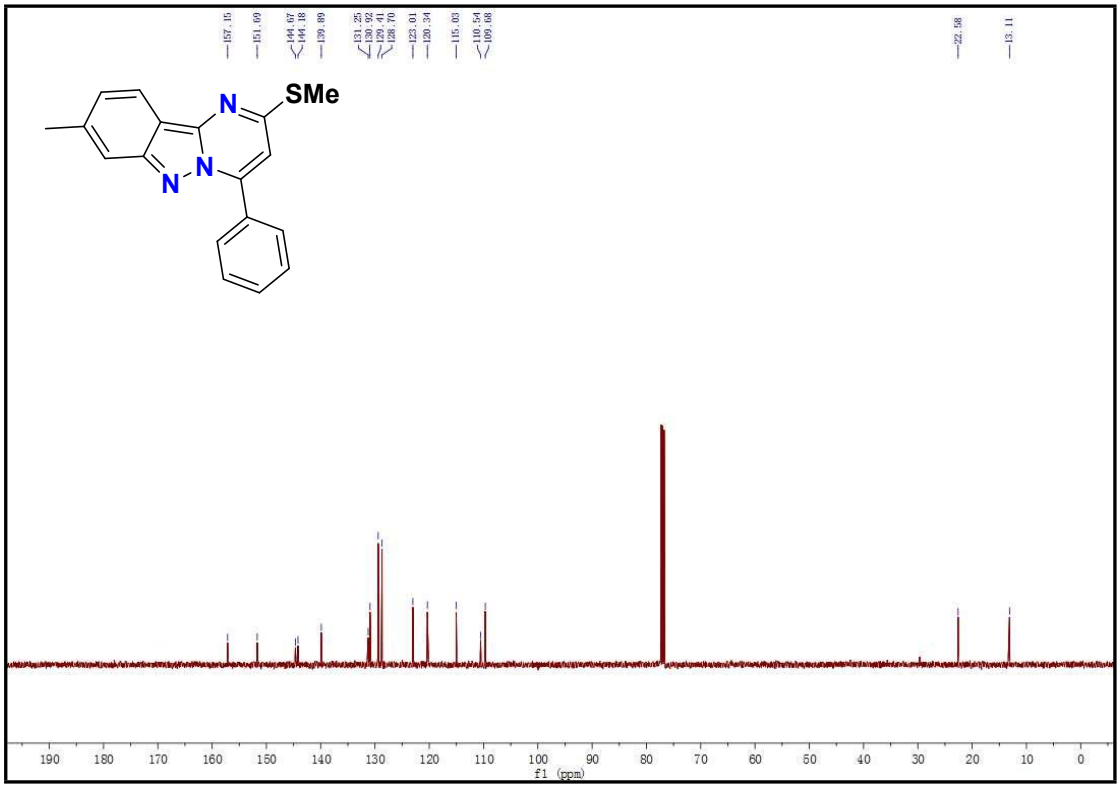
2-(methylthio)-4,8-diphenylpyrimido[1,2-b]indazole (3w)



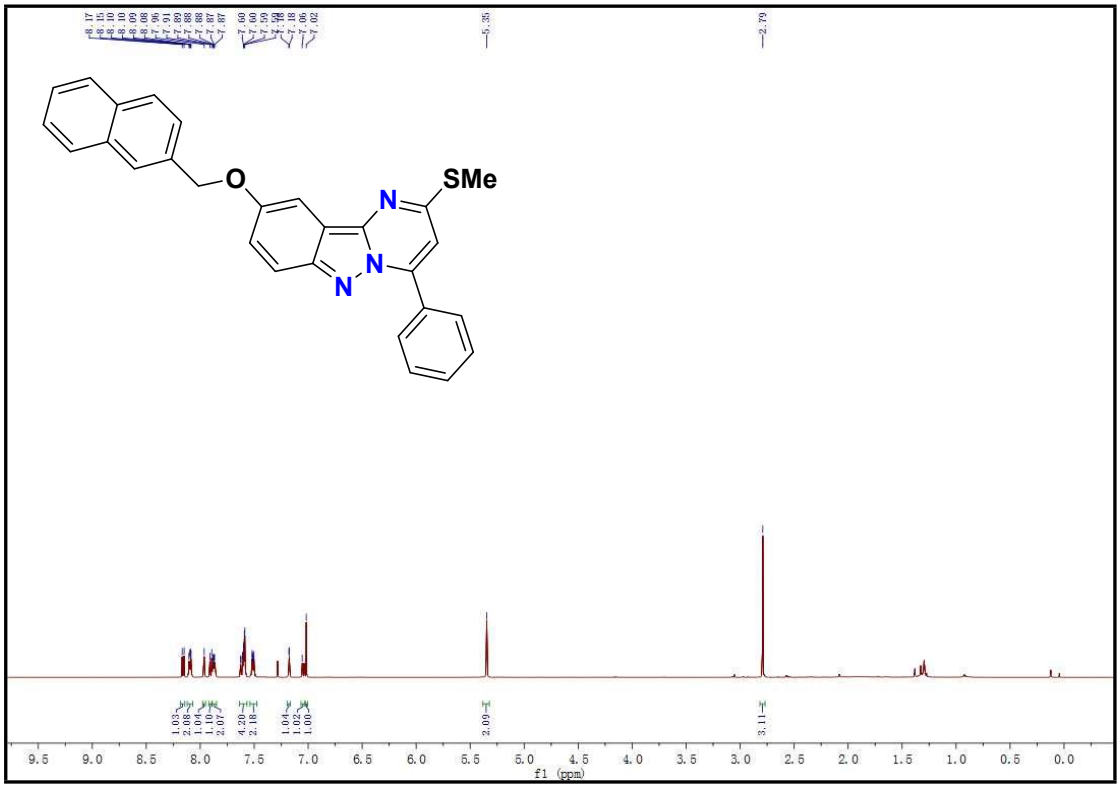


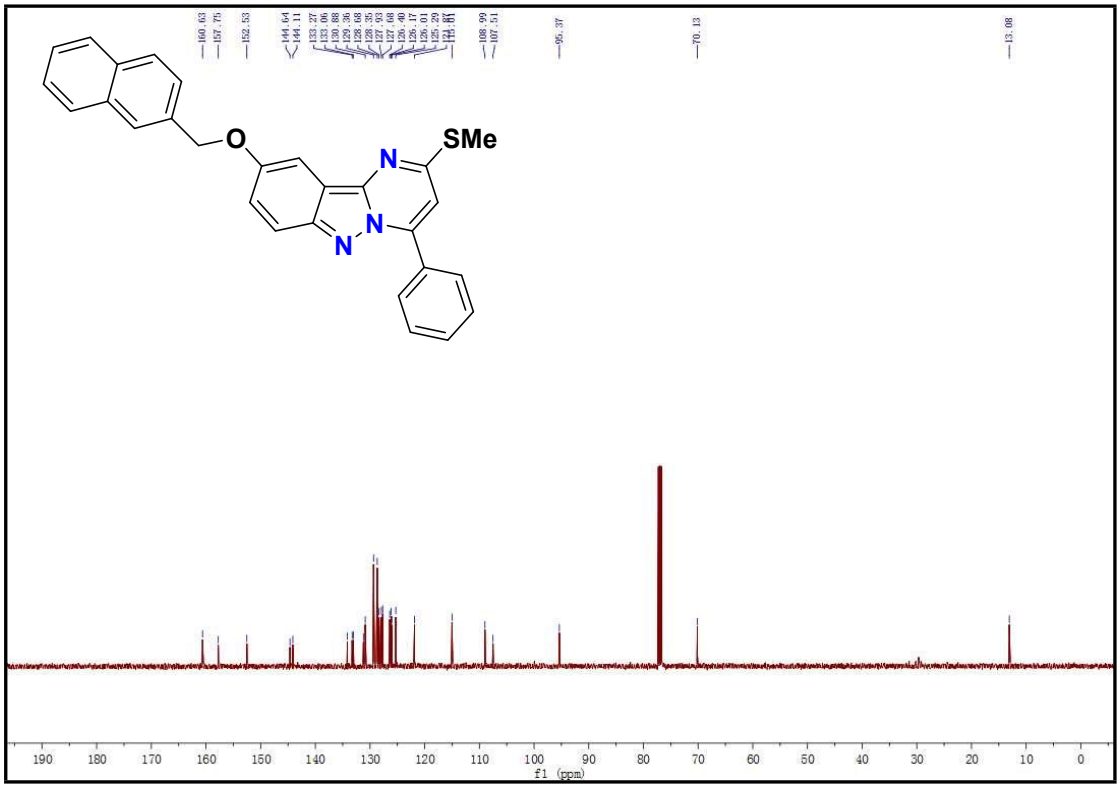
8-methyl-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3x)



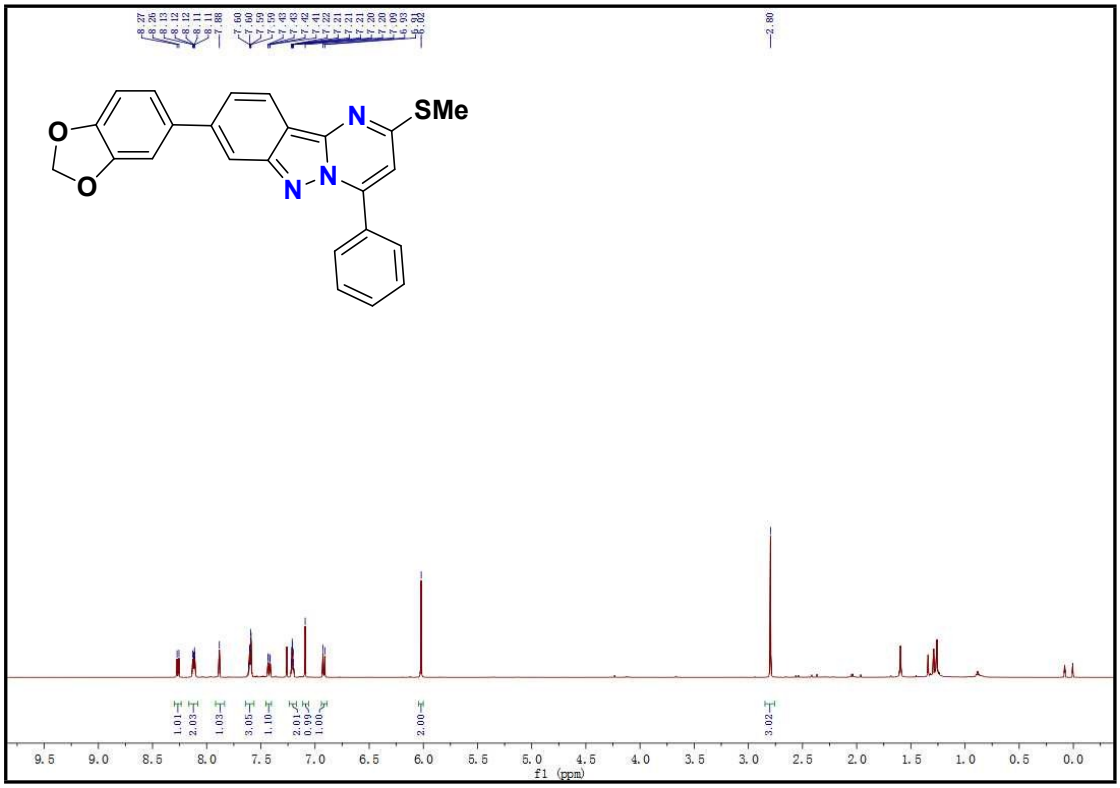


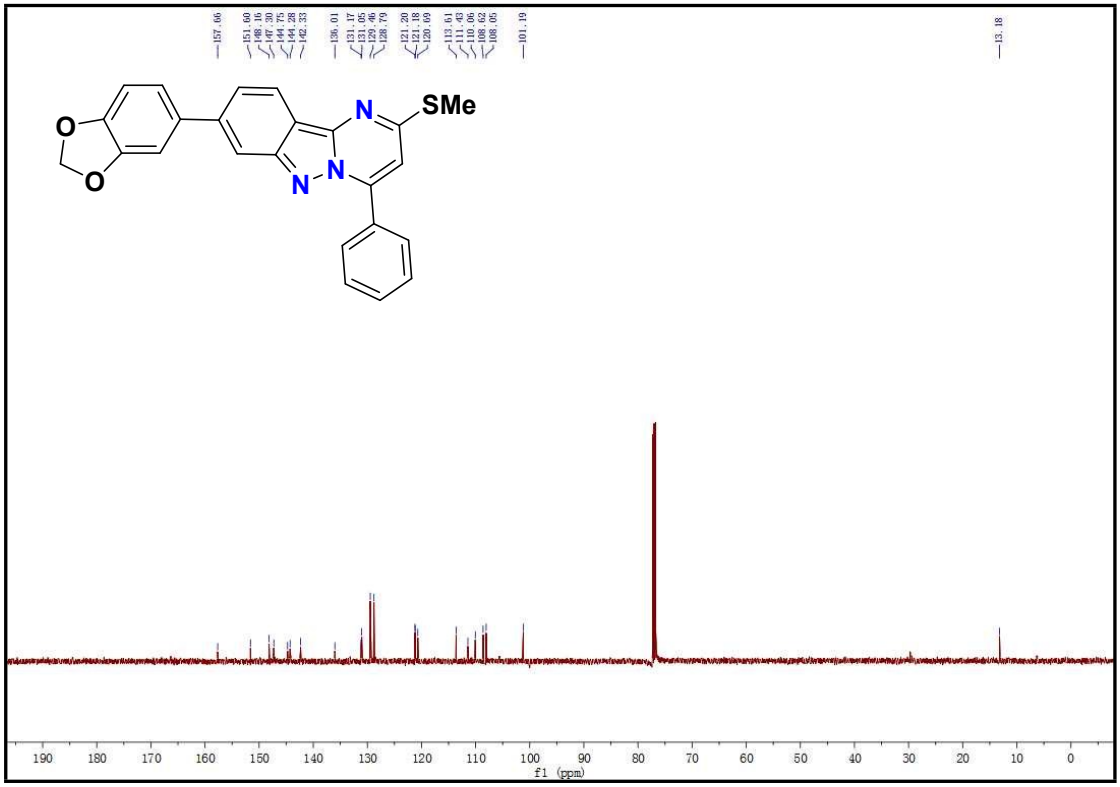
2-(methylthio)-9-(naphthalen-2-ylmethoxy)-4-phenylpyrimido[1,2-b]indazole (3y)



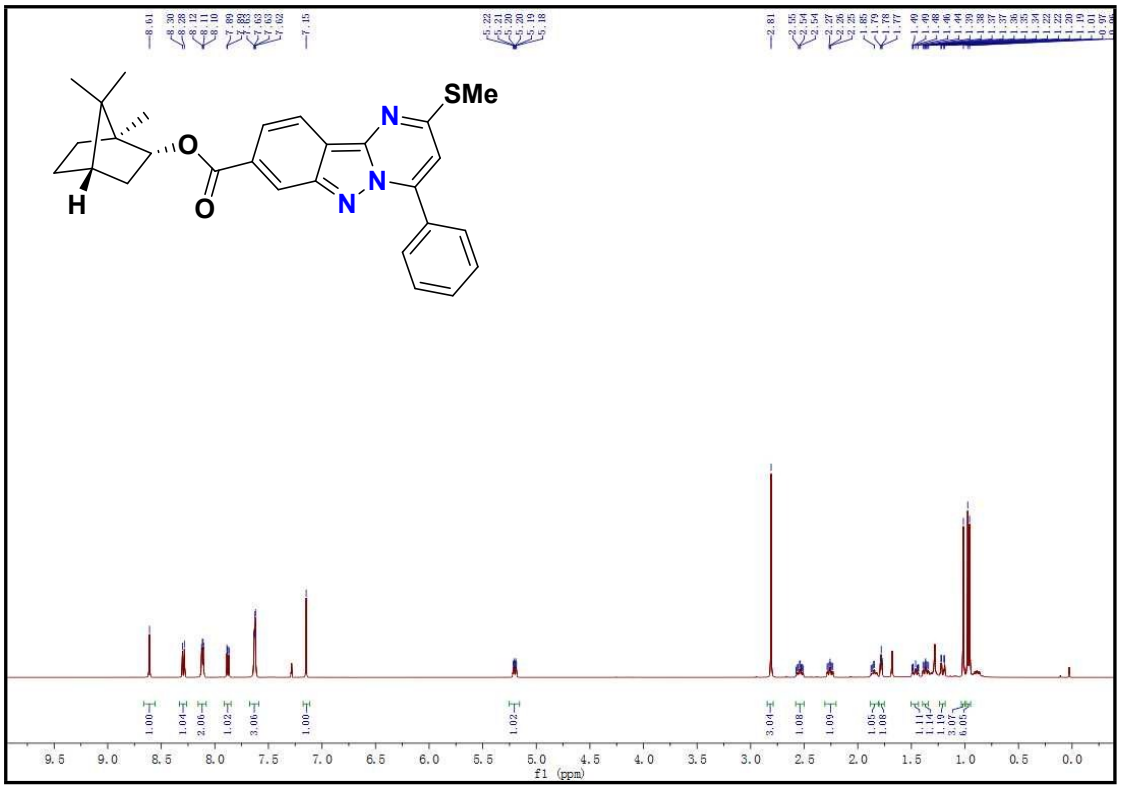


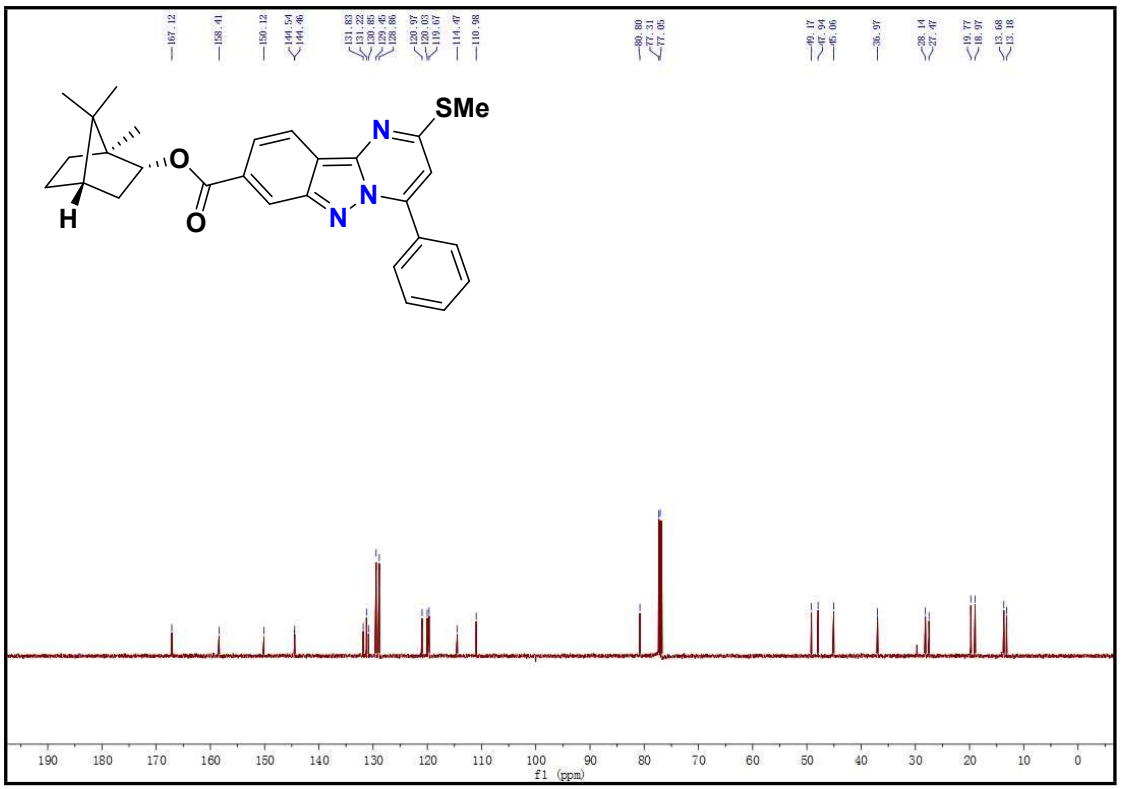
8-(benzo[d][1,3]dioxol-5-yl)-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole (3z)



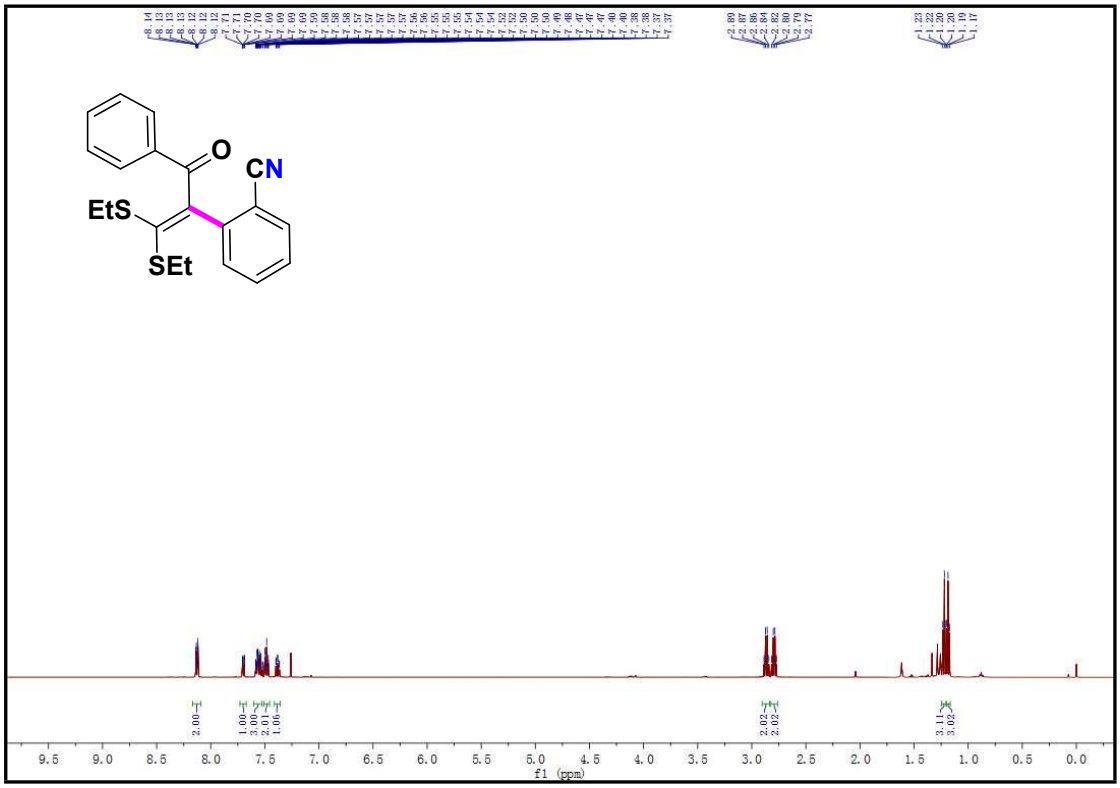


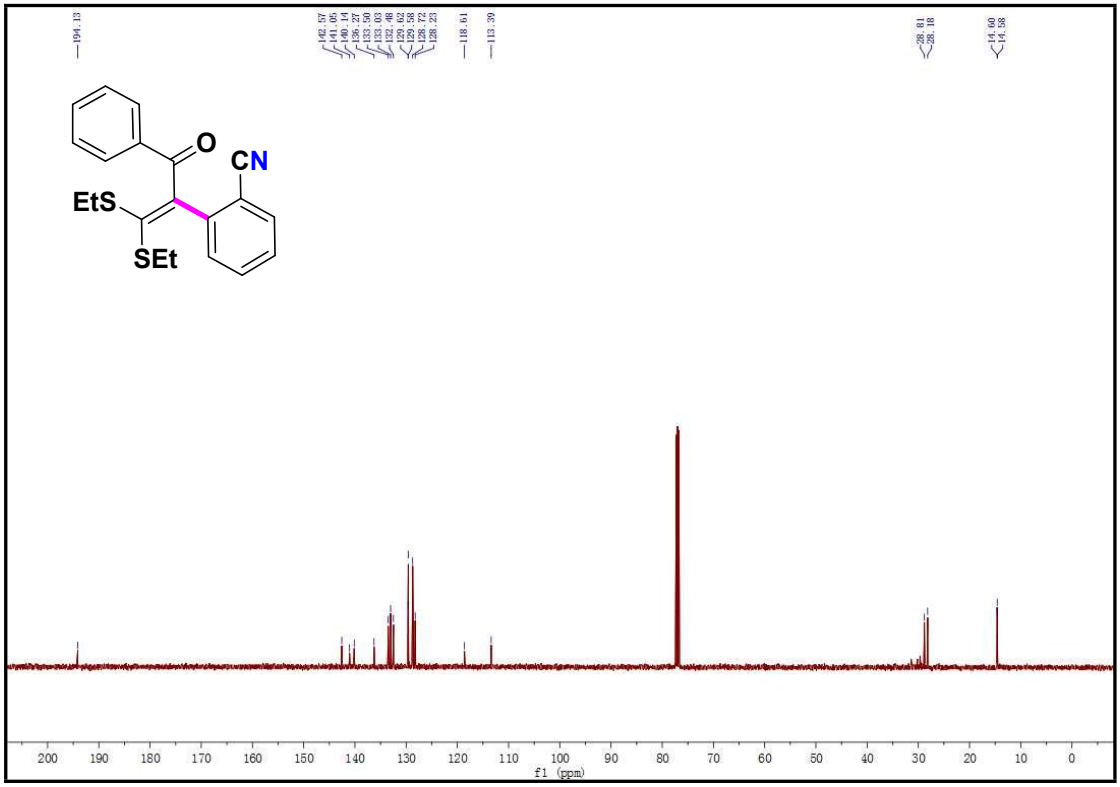
(1S,2R,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl-2-(methylthio)-4-phenylpyrimido[1,2-b]indazole-8-carboxylate (3β)



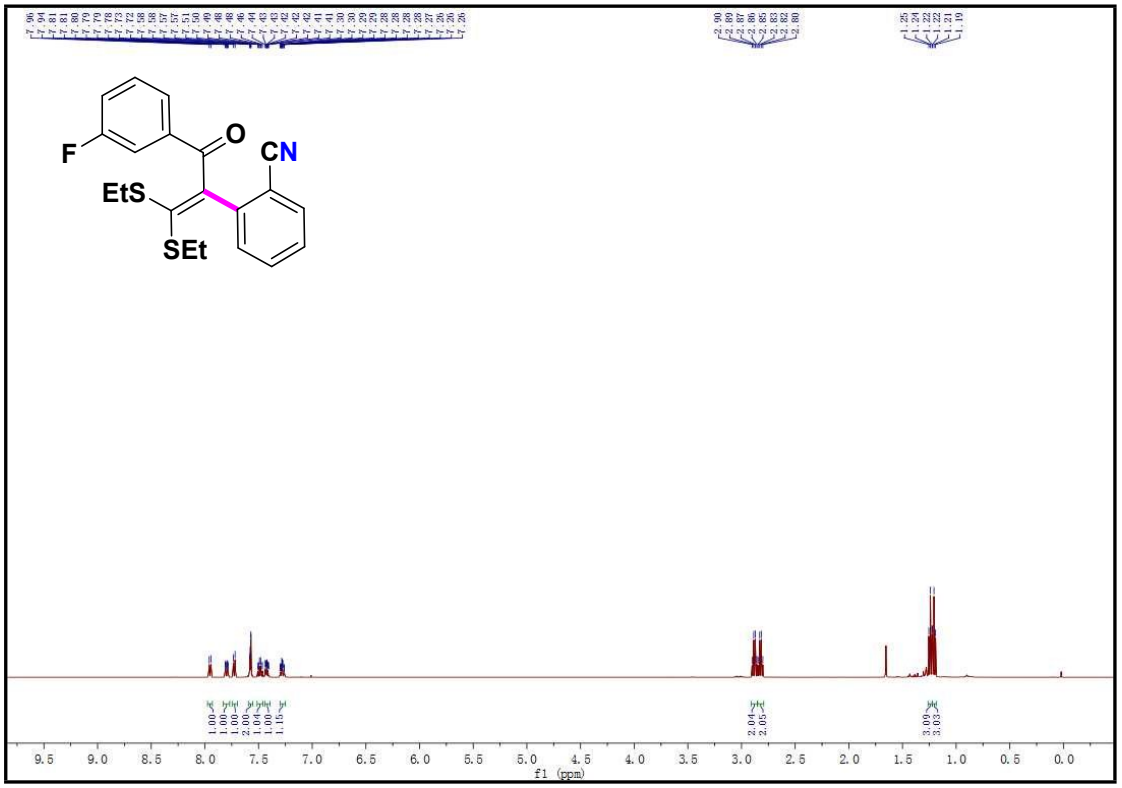


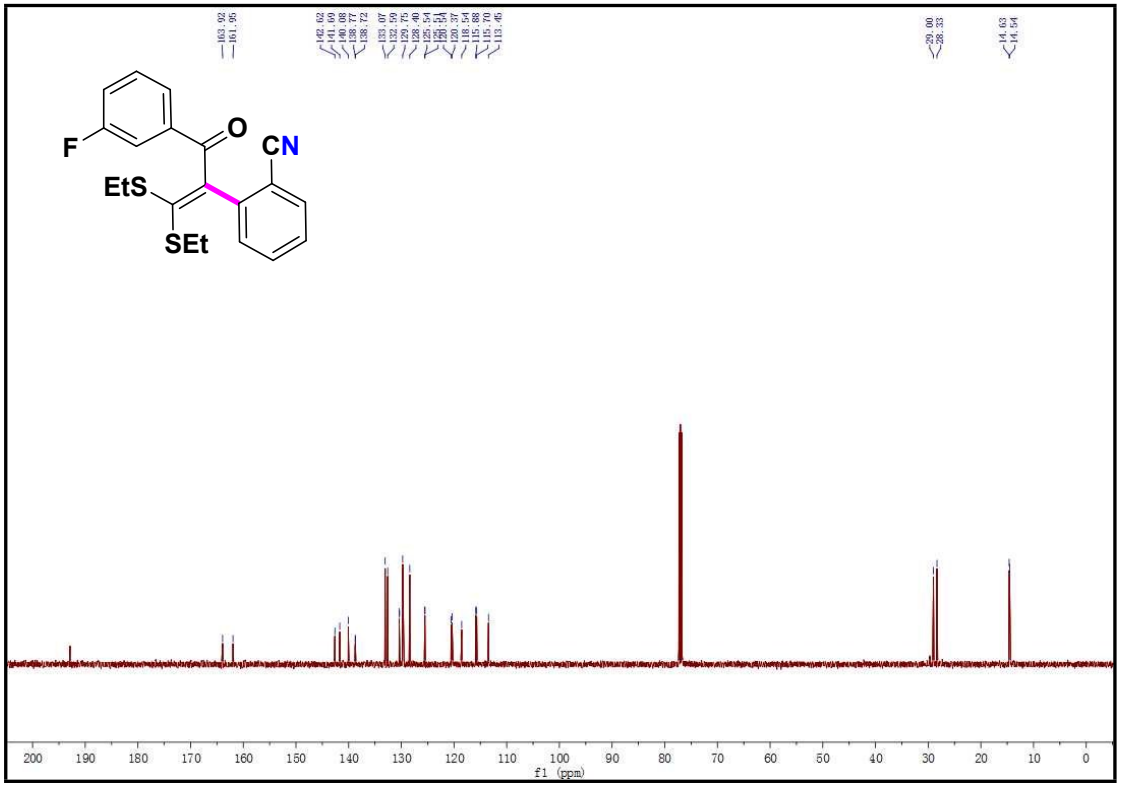
2-(1,1-bis(ethylthio)-3-oxo-3-phenylprop-1-en-2-yl)benzonitrile (4a)



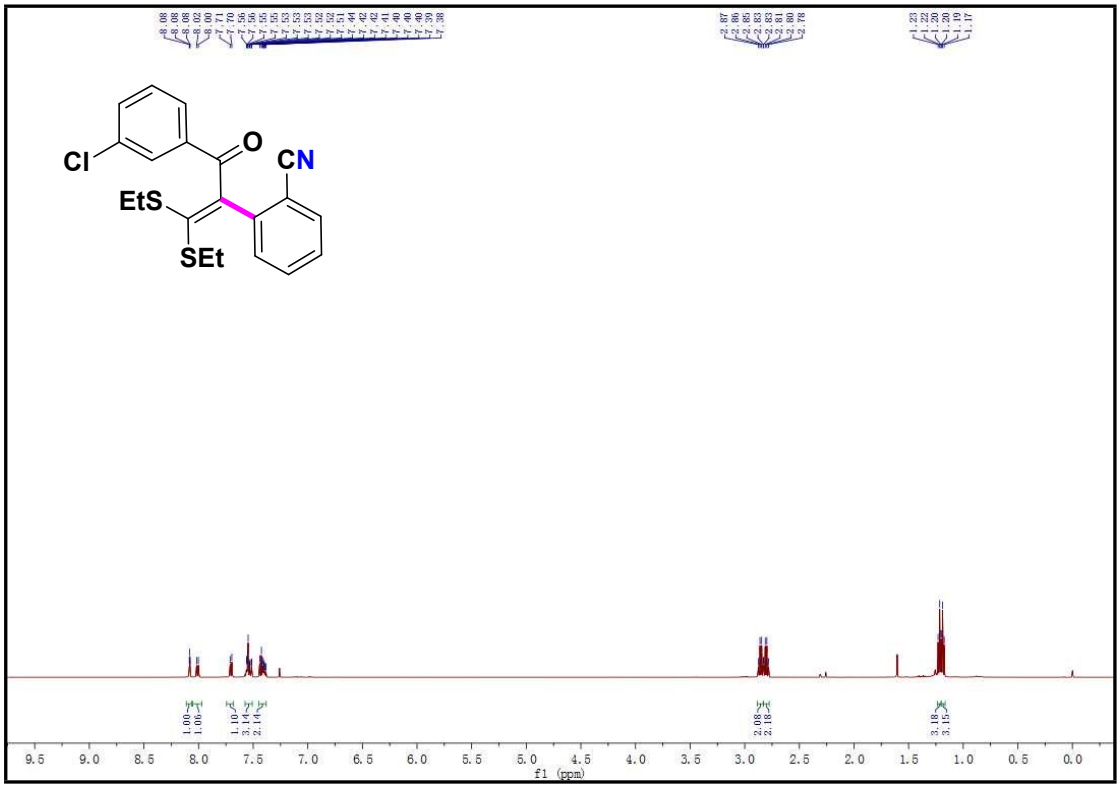


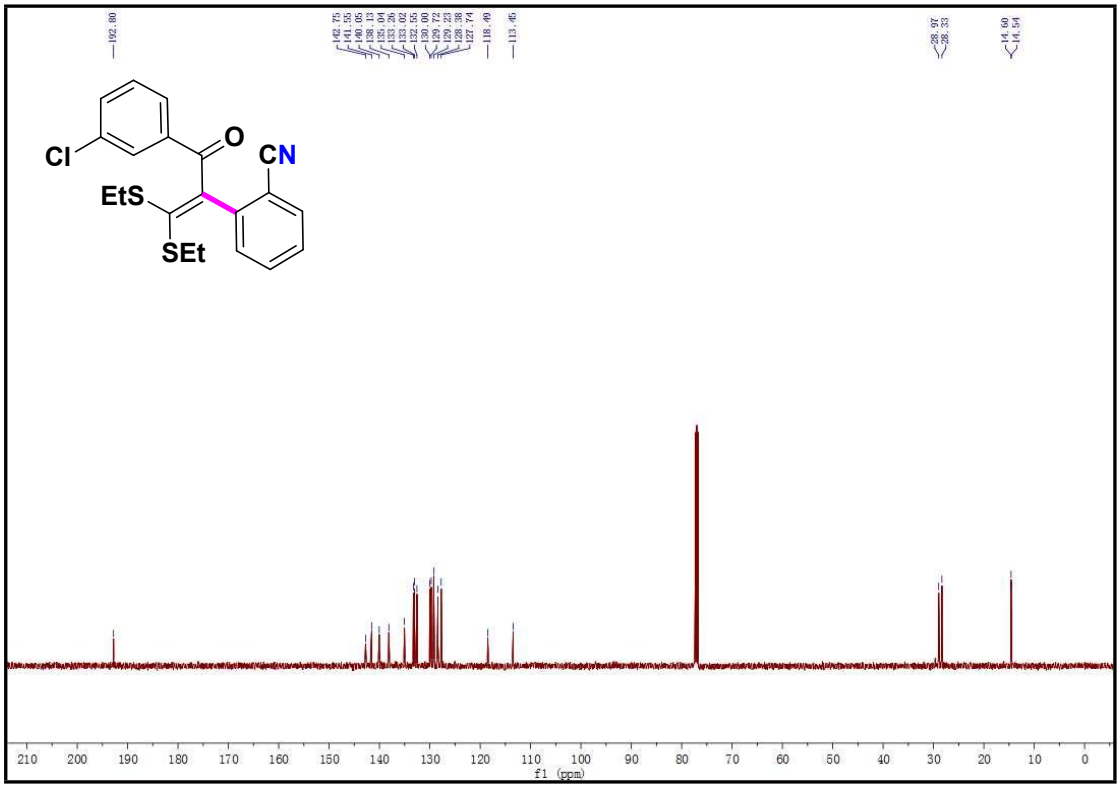
2-(1,1-bis(ethylthio)-3-(4-fluorophenyl)-3-oxoprop-1-en-2-yl)benzonitrile (4b)



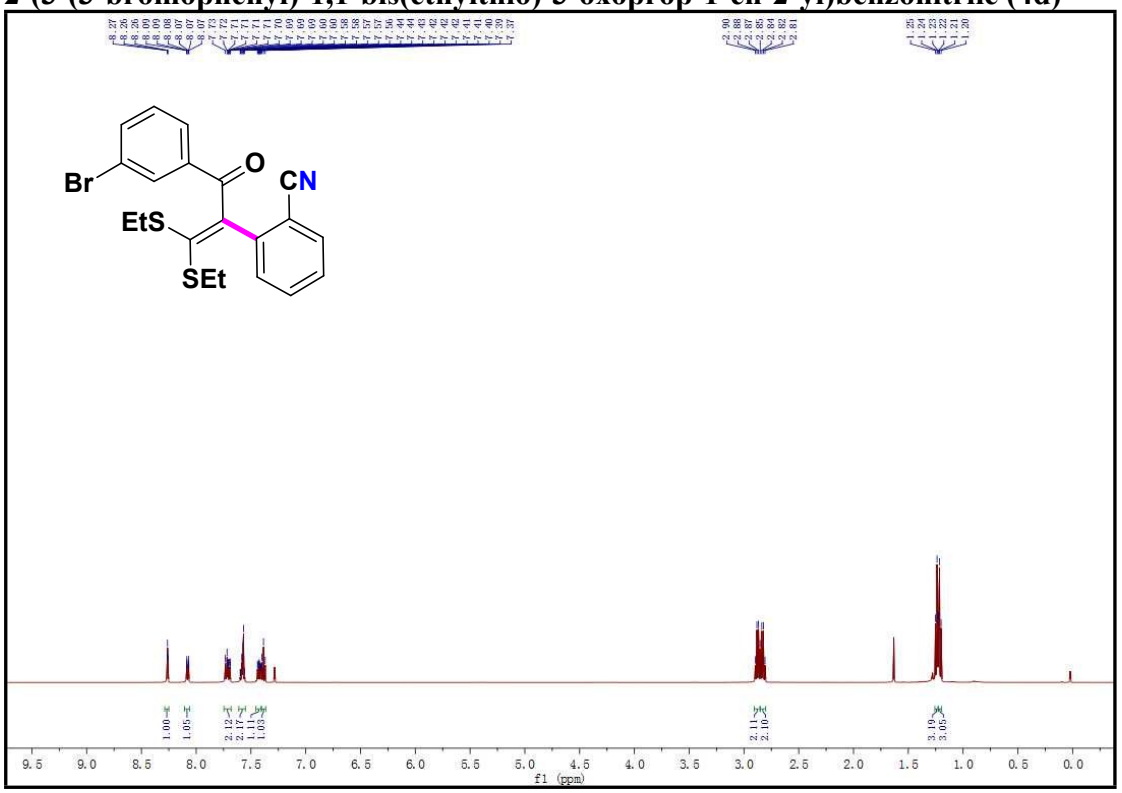


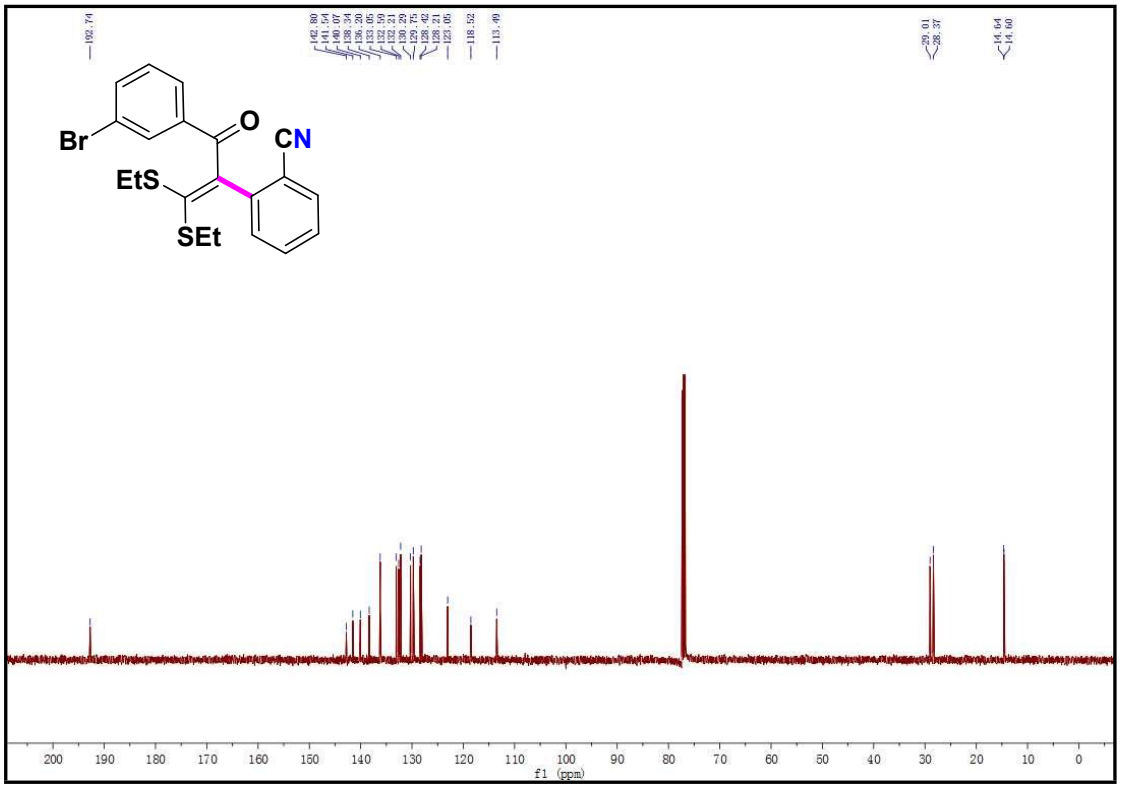
2-(3-(3-chlorophenyl)-1,1-bis(ethylthio)-3-oxoprop-1-en-2-yl)benzonitrile (4c)



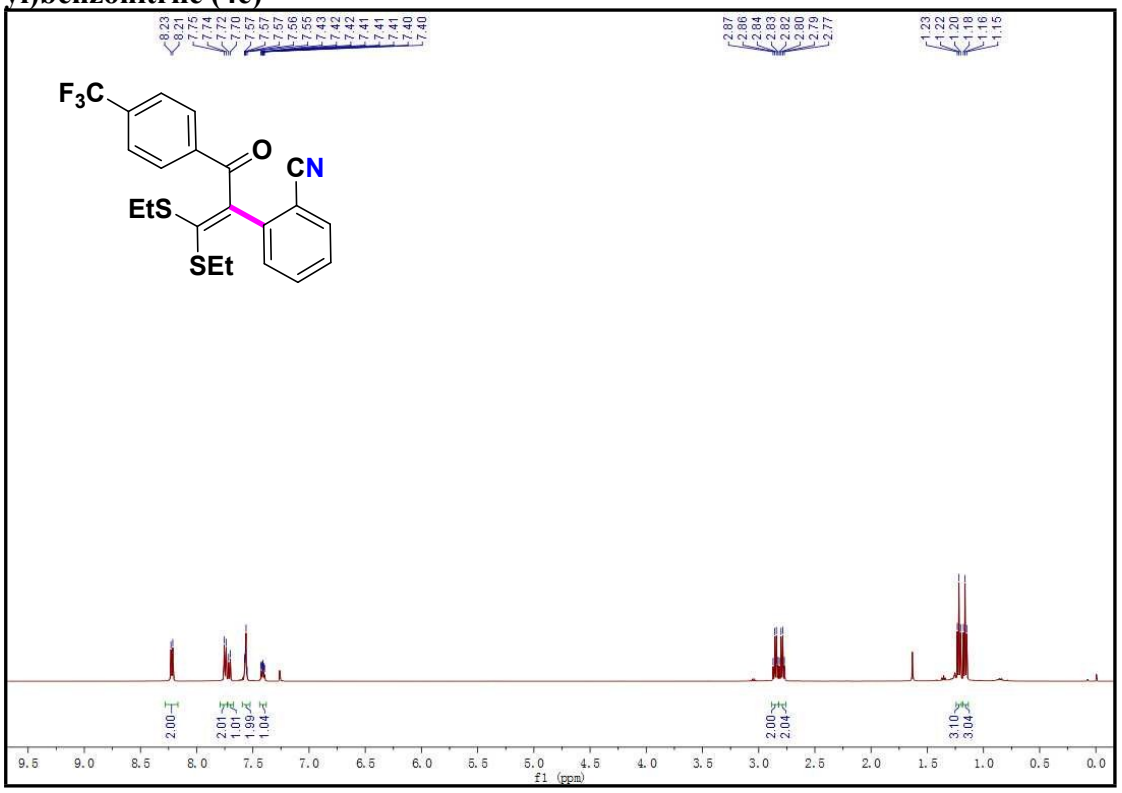


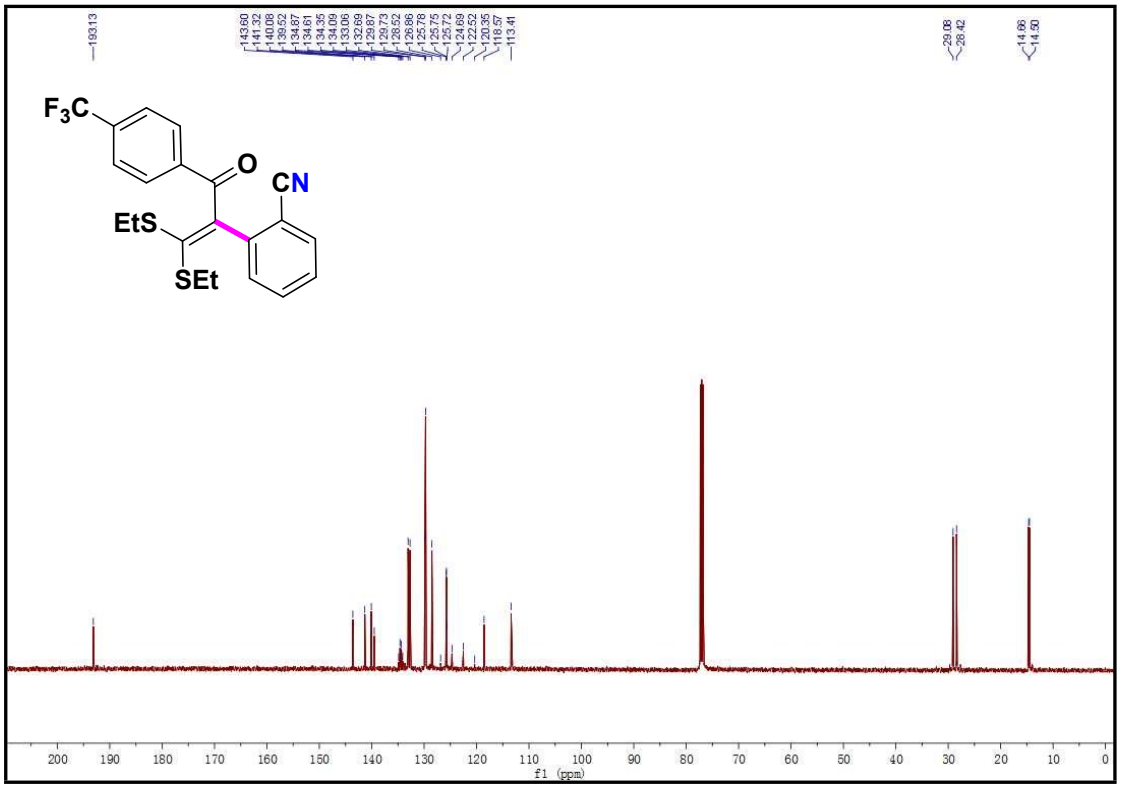
2-(3-(3-bromophenyl)-1,1-bis(ethylthio)-3-oxoprop-1-en-2-yl)benzonitrile (4d)



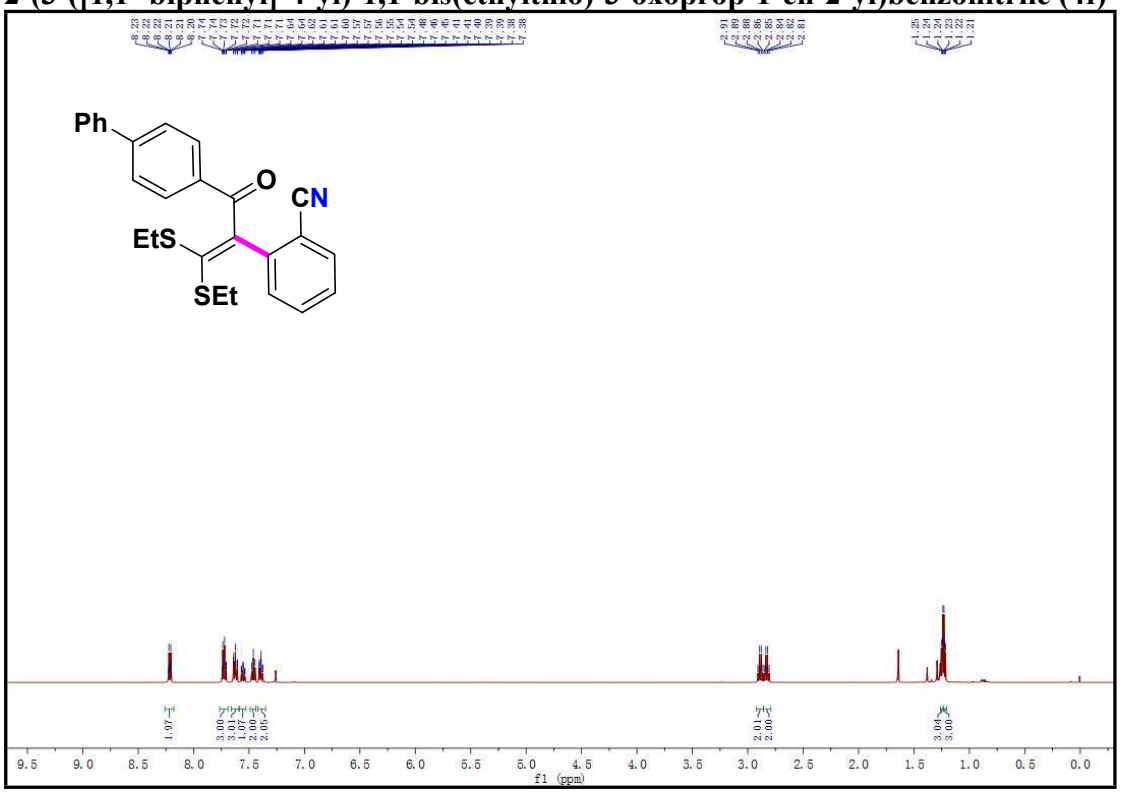


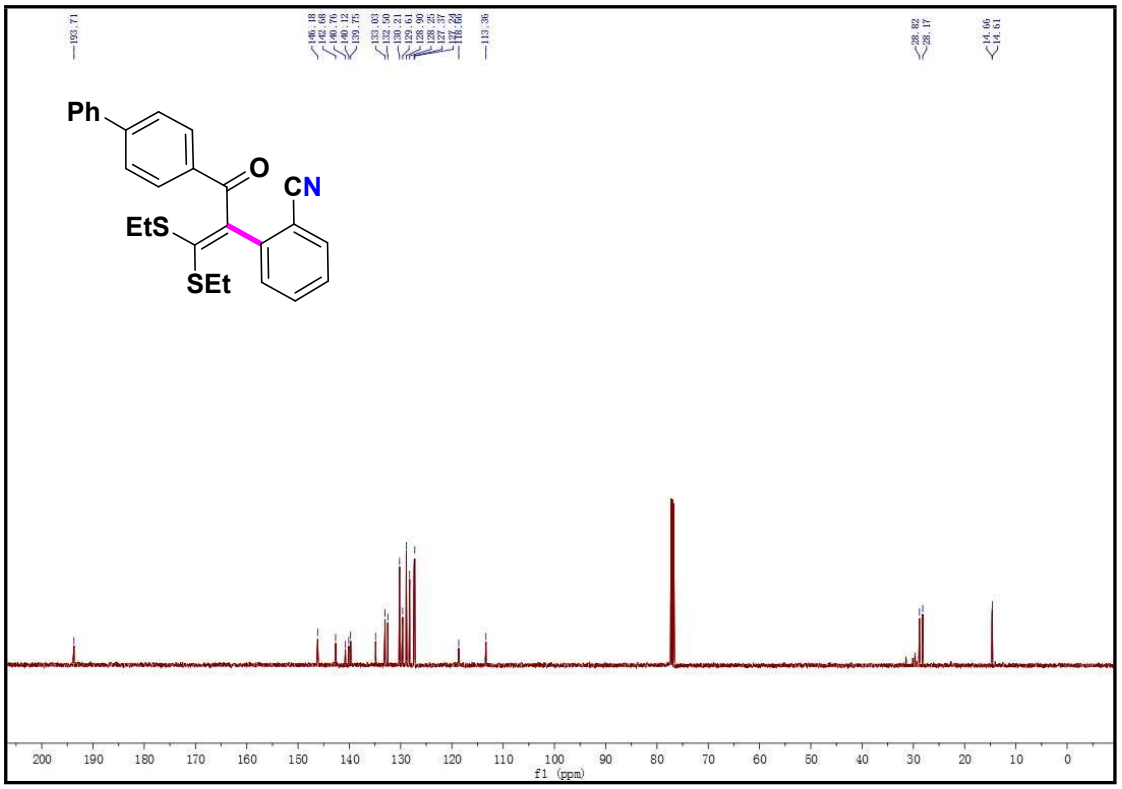
2-(1,1-bis(ethylthio)-3-oxo-3-(4-(trifluoromethyl)phenyl)prop-1-en-2-yl)benzonitrile (4e)



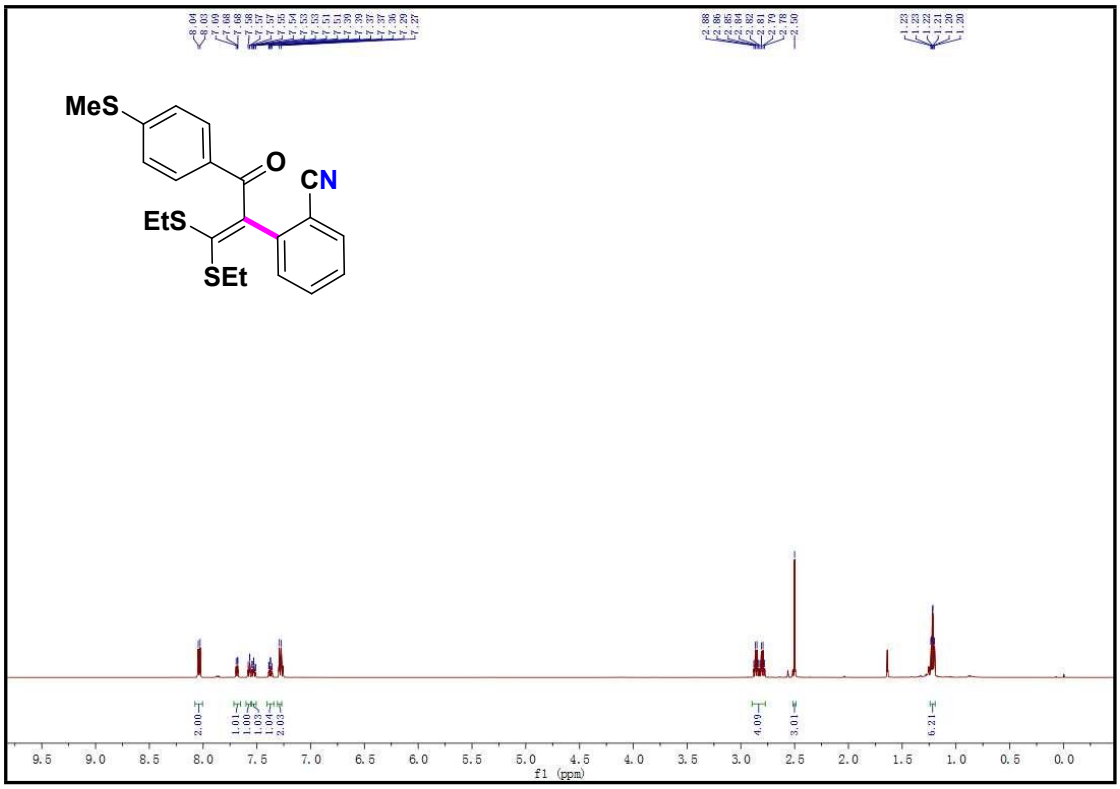


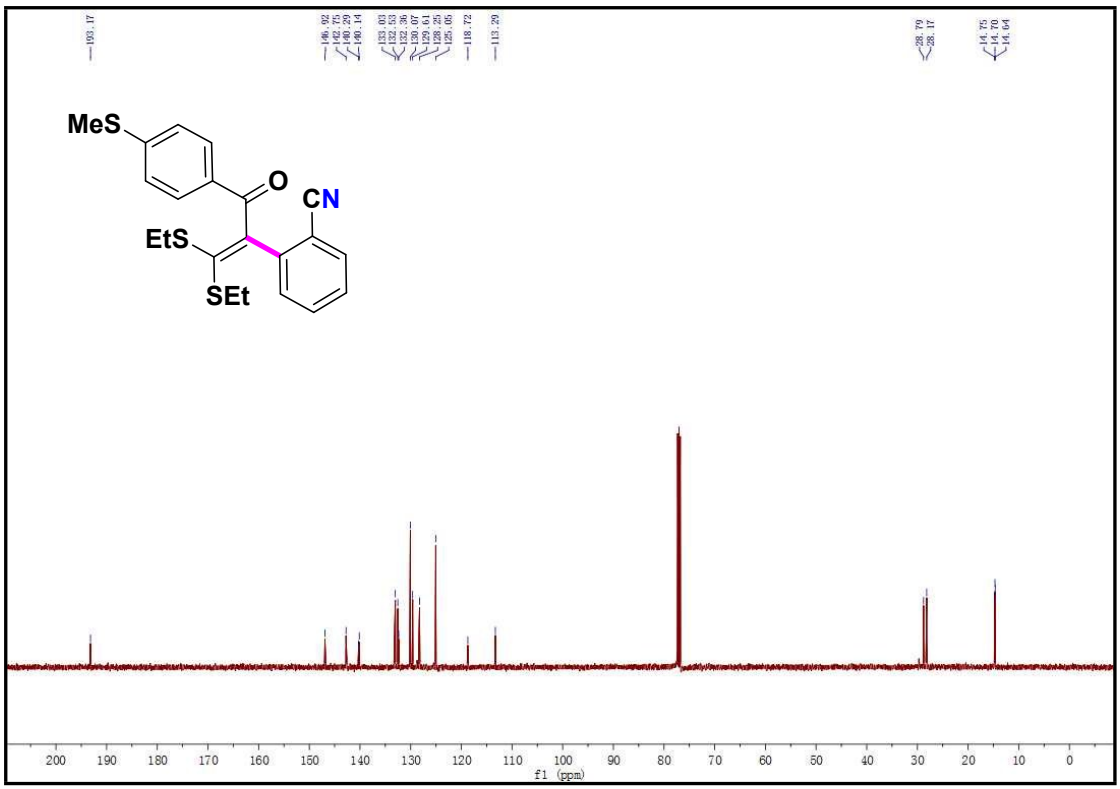
2-(3-([1,1'-biphenyl]-4-yl)-1,1-bis(ethylthio)-3-oxoprop-1-en-2-yl)benzonitrile (4f)



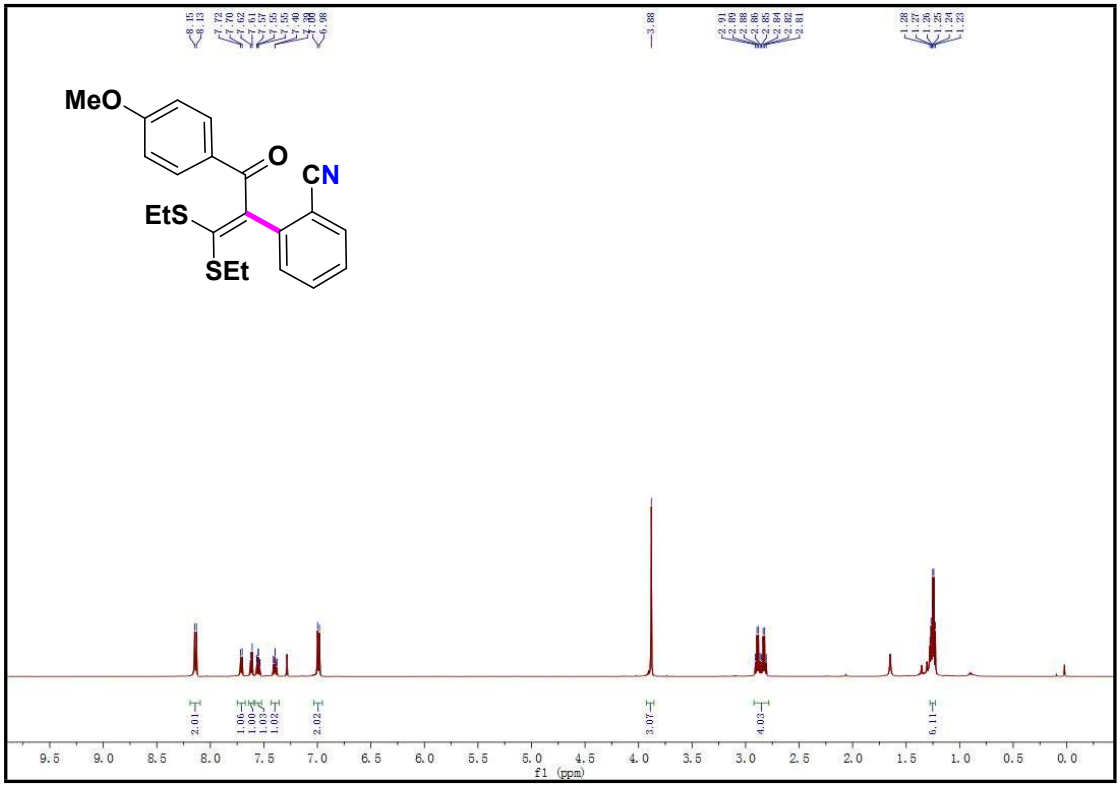


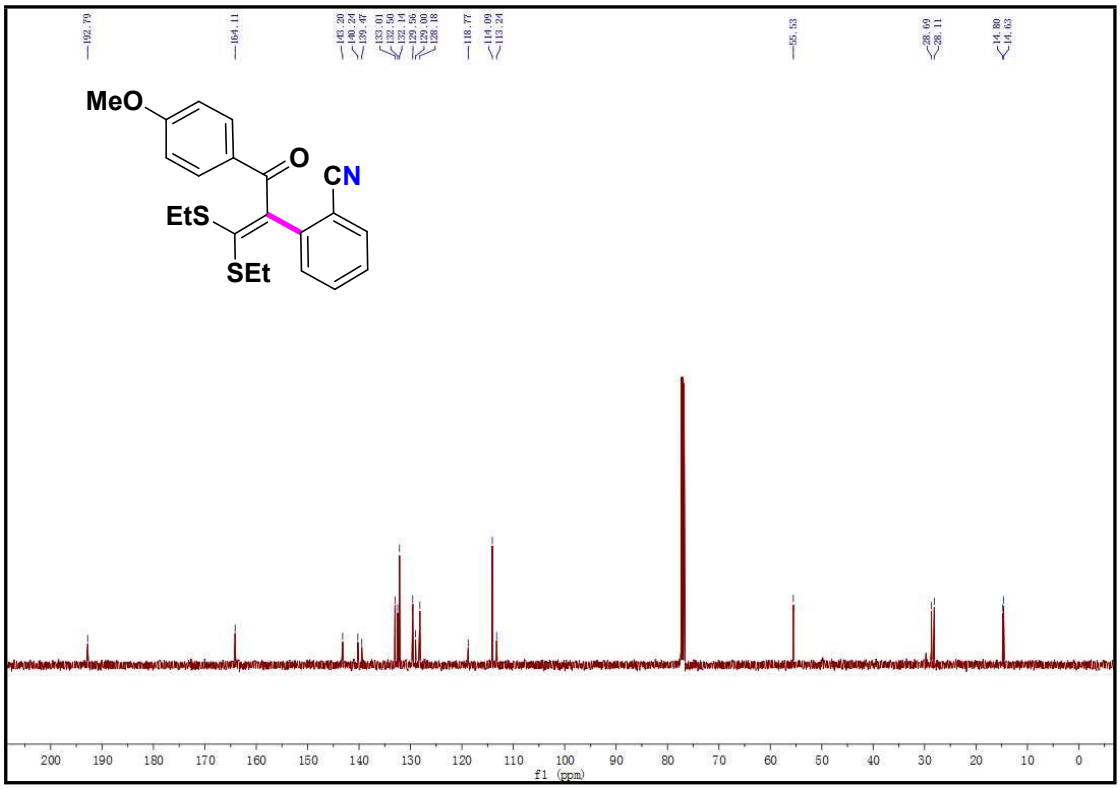
2-(1,1-bis(ethylthio)-3-(4-(methylthio)phenyl)-3-oxoprop-1-en-2-yl)benzonitrile (4g)



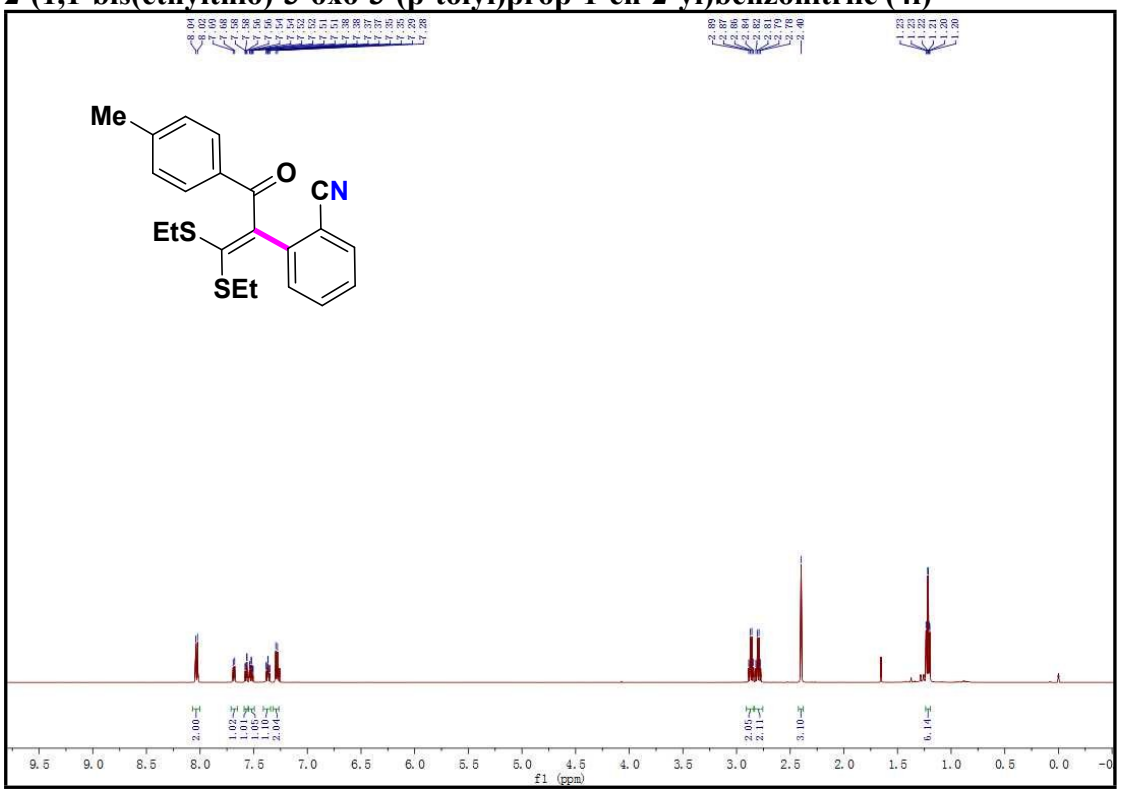


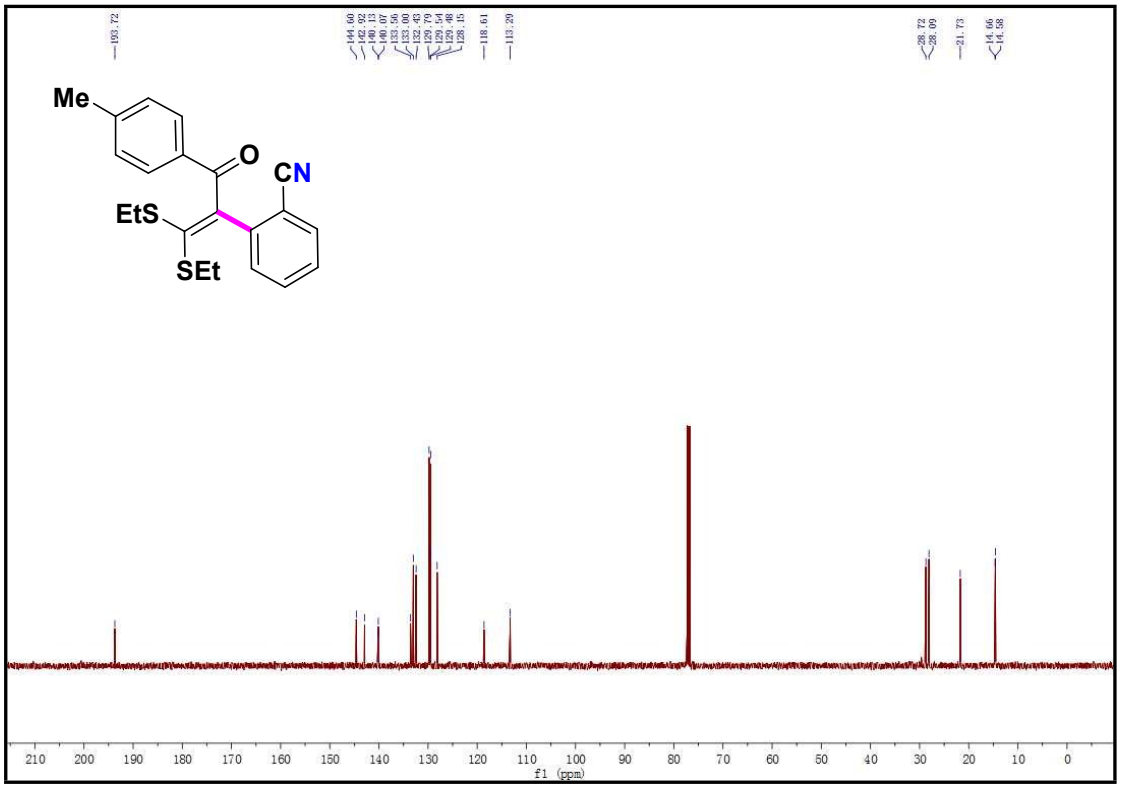
2-(1,1-bis(ethylthio)-3-(4-methoxyphenyl)-3-oxoprop-1-en-2-yl)benzonitrile (4h)



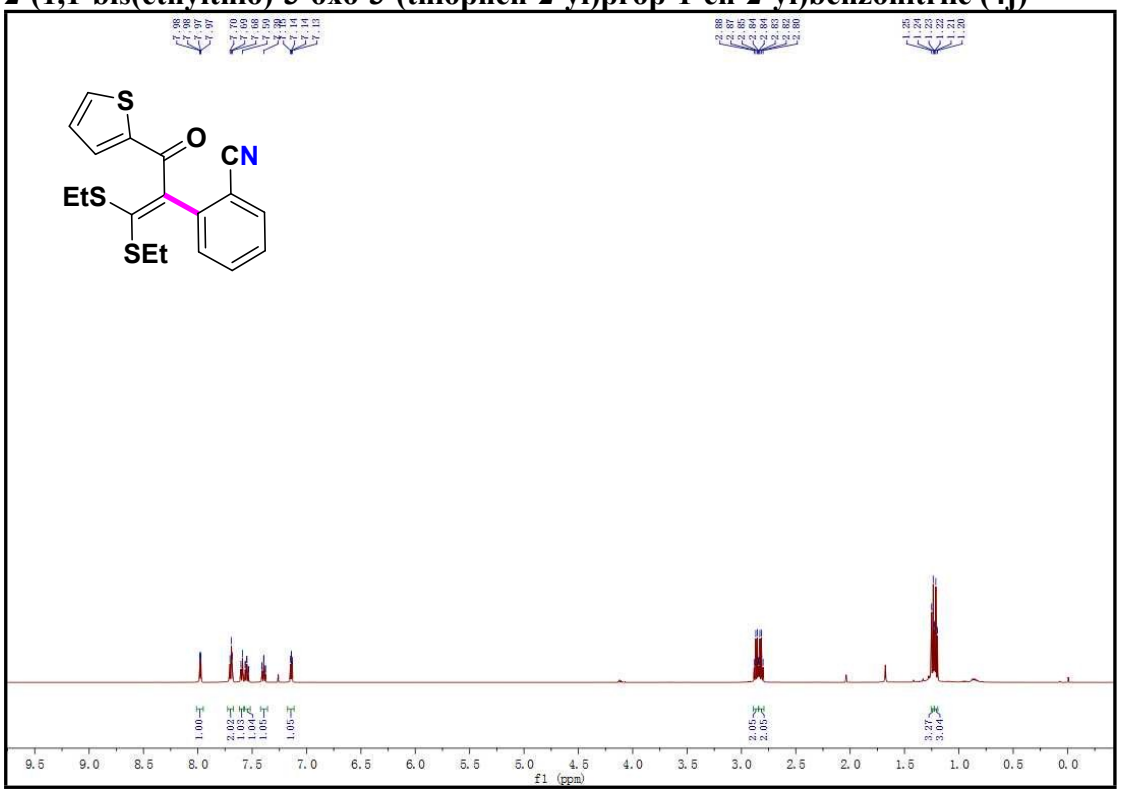


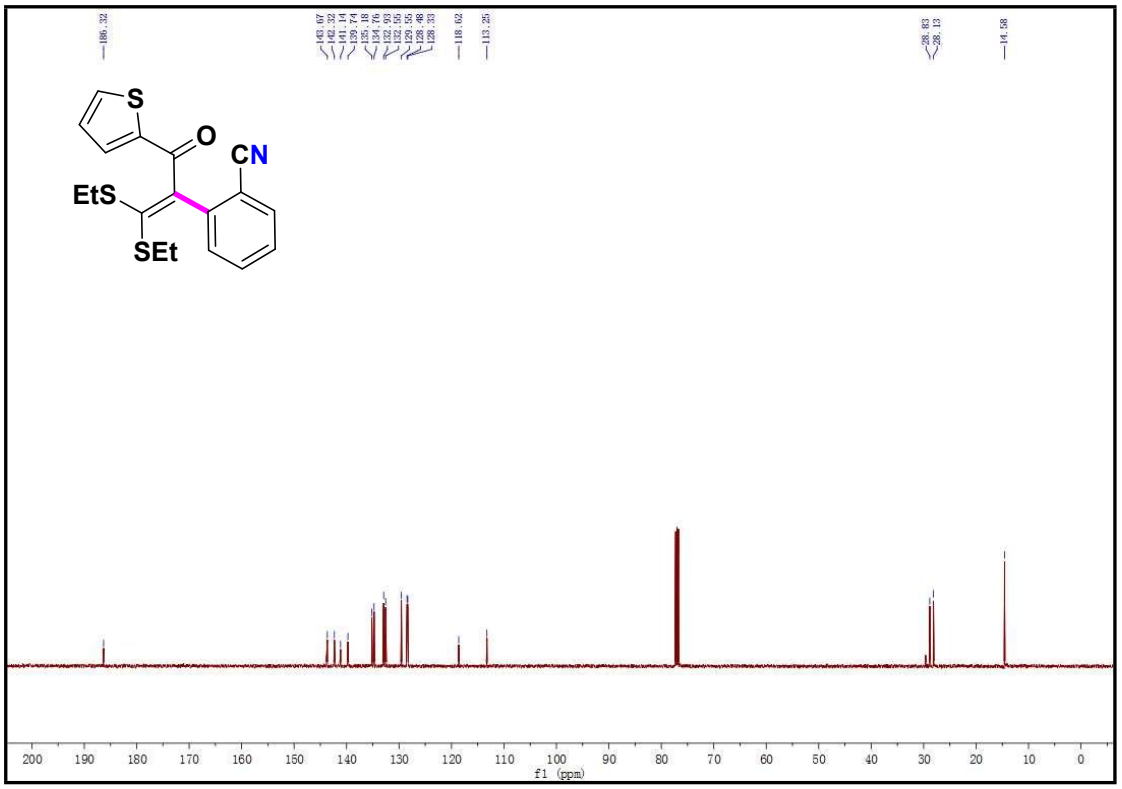
2-(1,1-bis(ethylthio)-3-oxo-3-(p-tolyl)prop-1-en-2-yl)benzonitrile (4i)



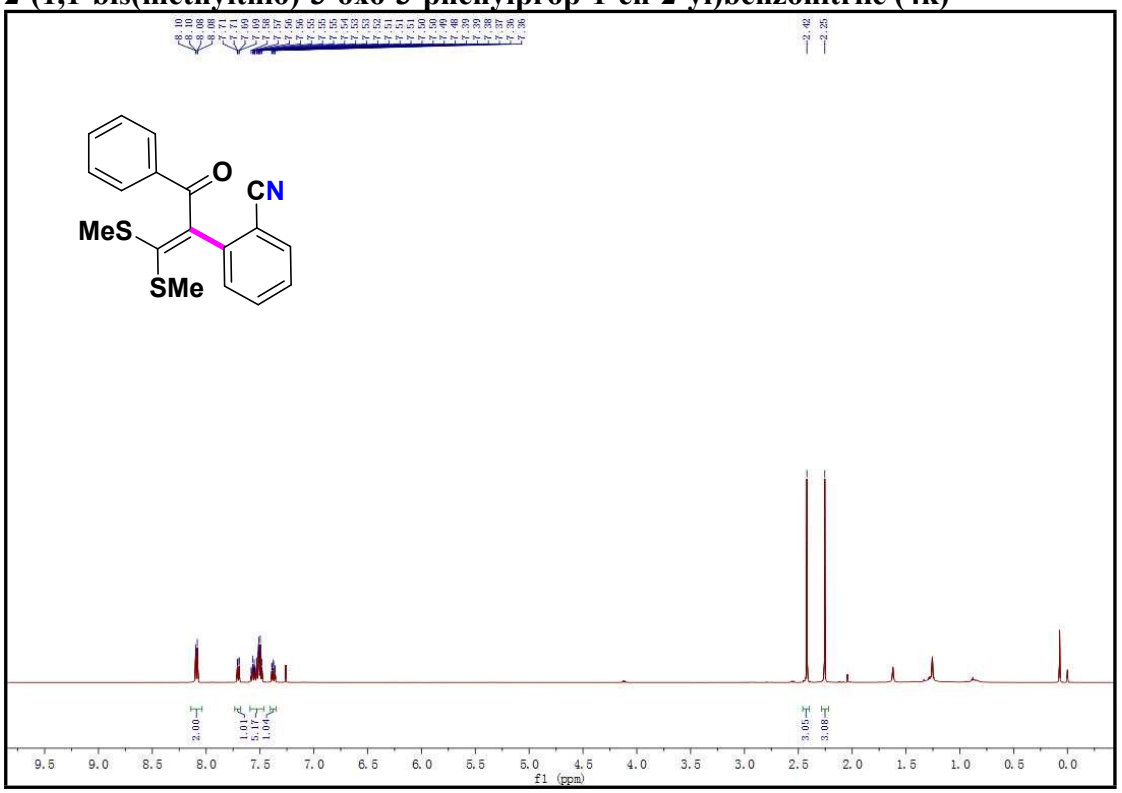


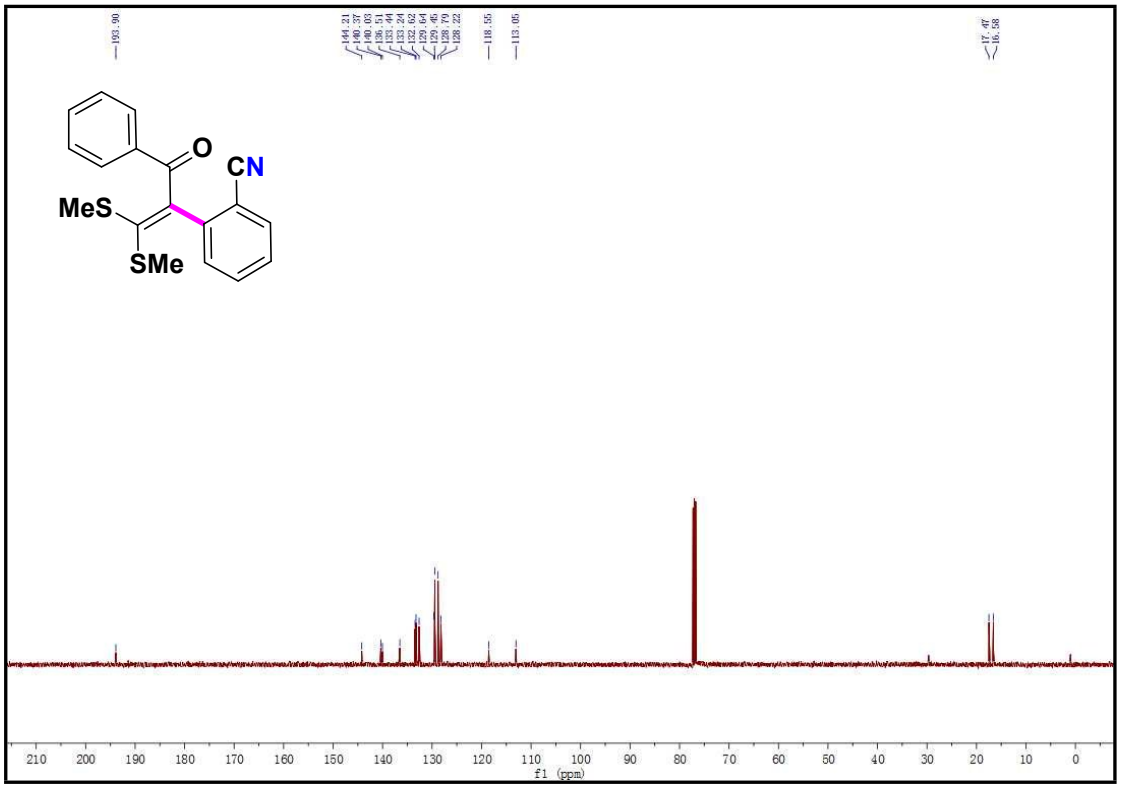
2-(1,1-bis(ethylthio)-3-oxo-3-(thiophen-2-yl)prop-1-en-2-yl)benzonitrile (4j)



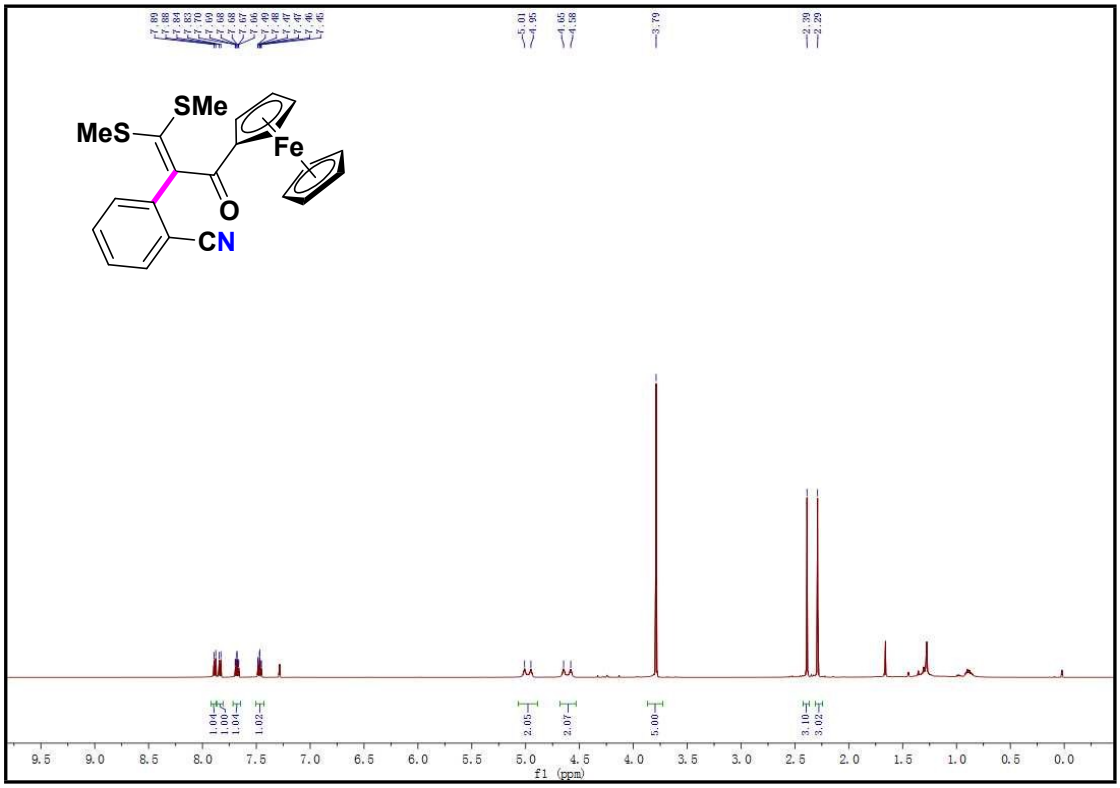


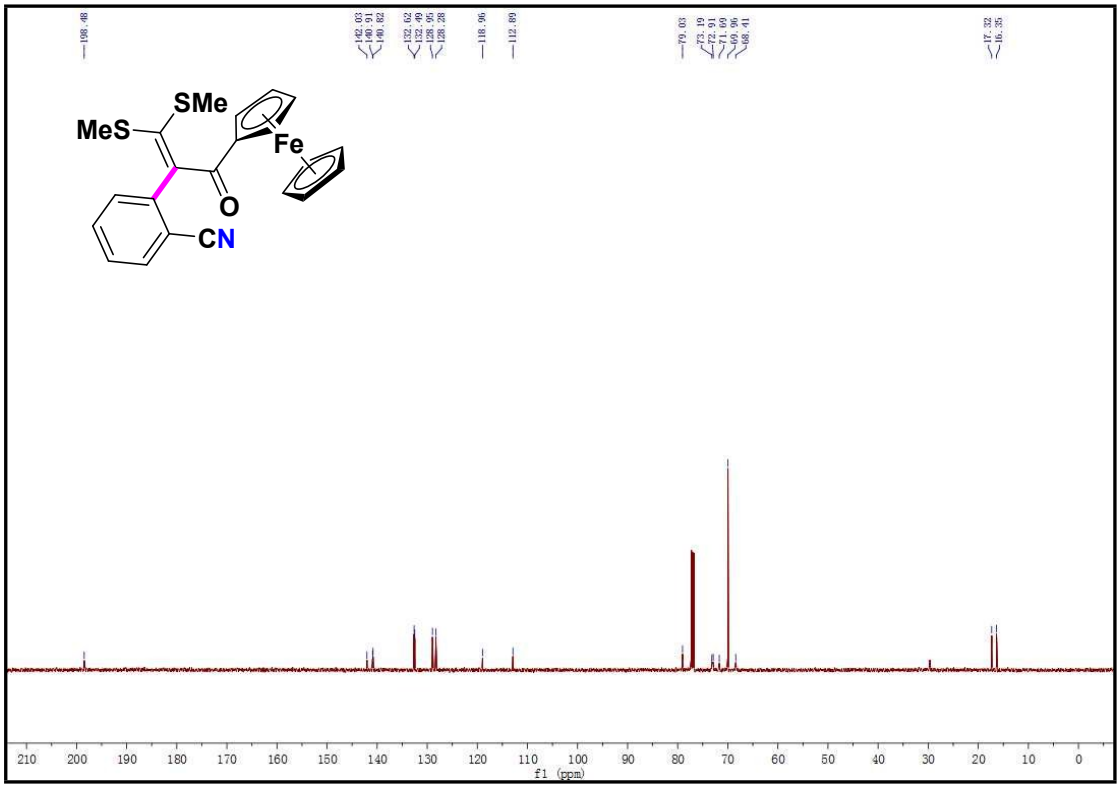
2-(1,1-bis(methylthio)-3-oxo-3-phenylprop-1-en-2-yl)benzonitrile (4k)



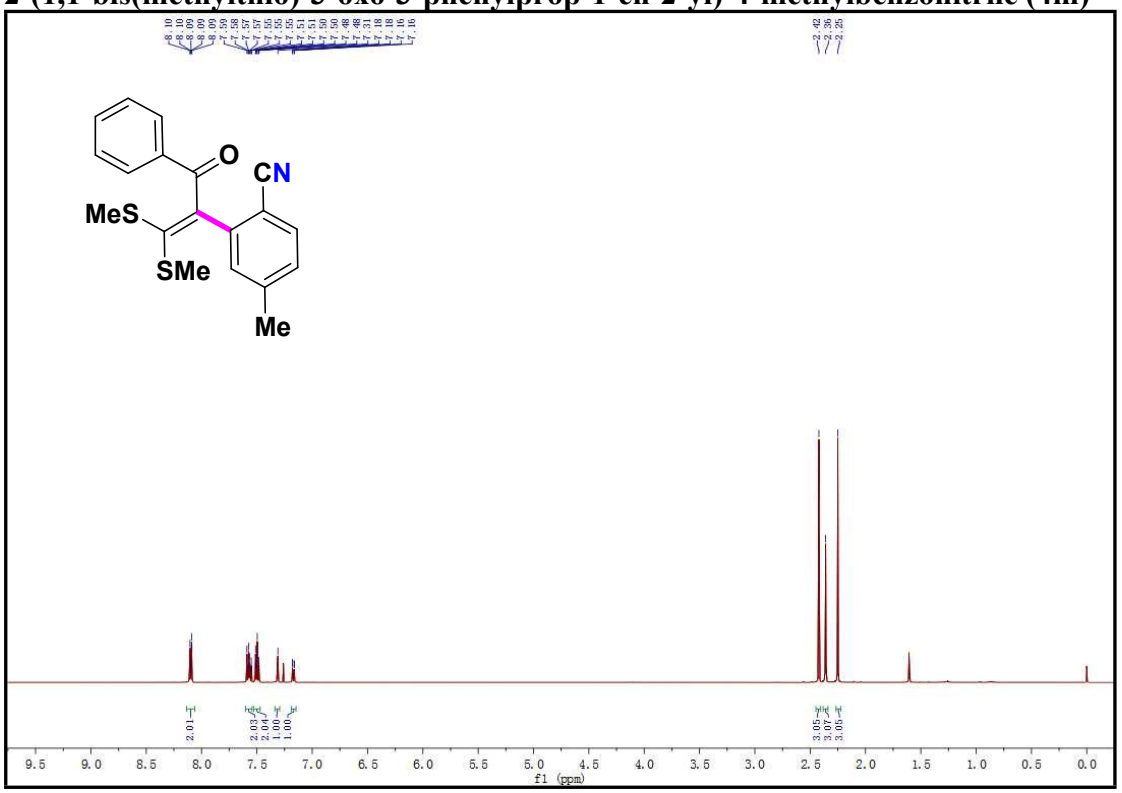


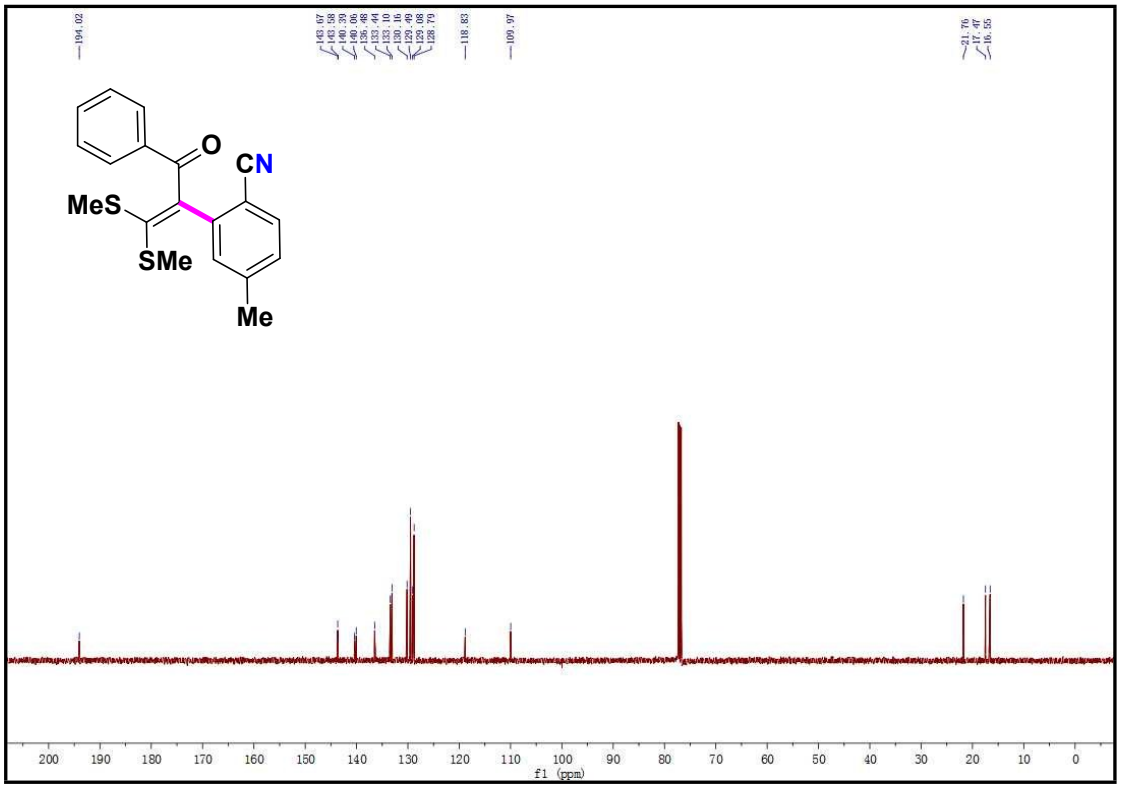
2-(1,1-bis(methylthio)-3-oxoferrocen-1-en-2-yl)benzonitrile (4l)



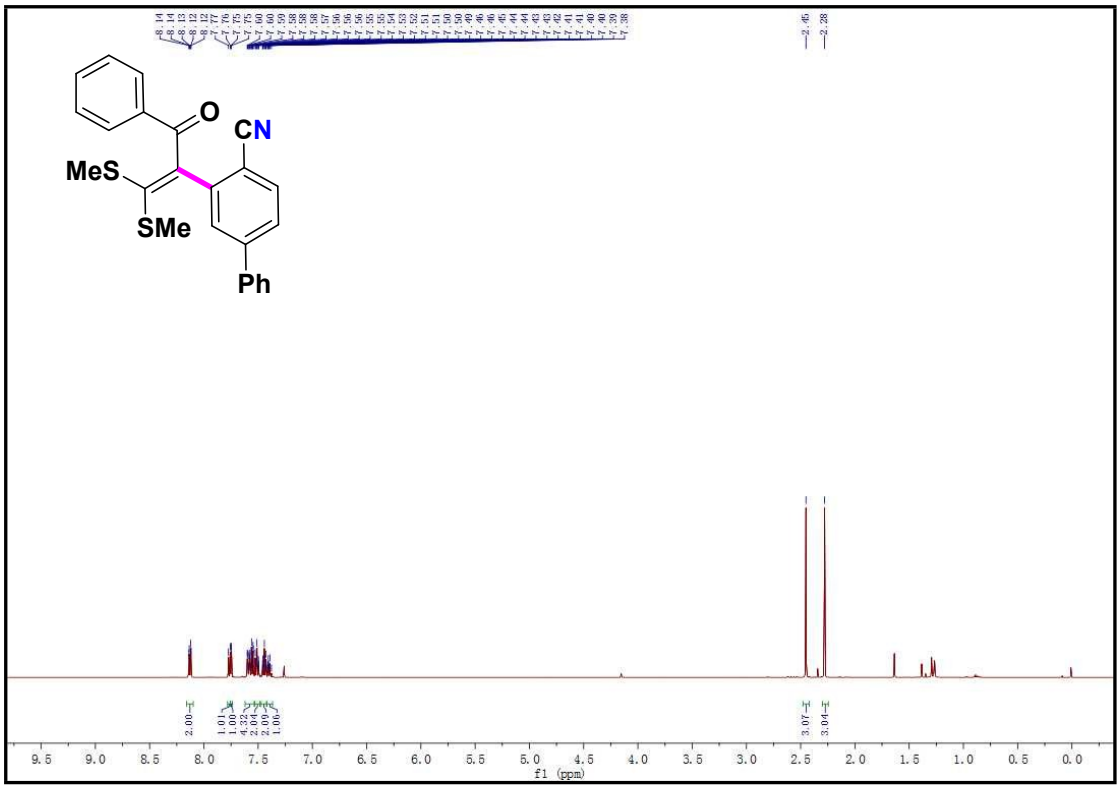


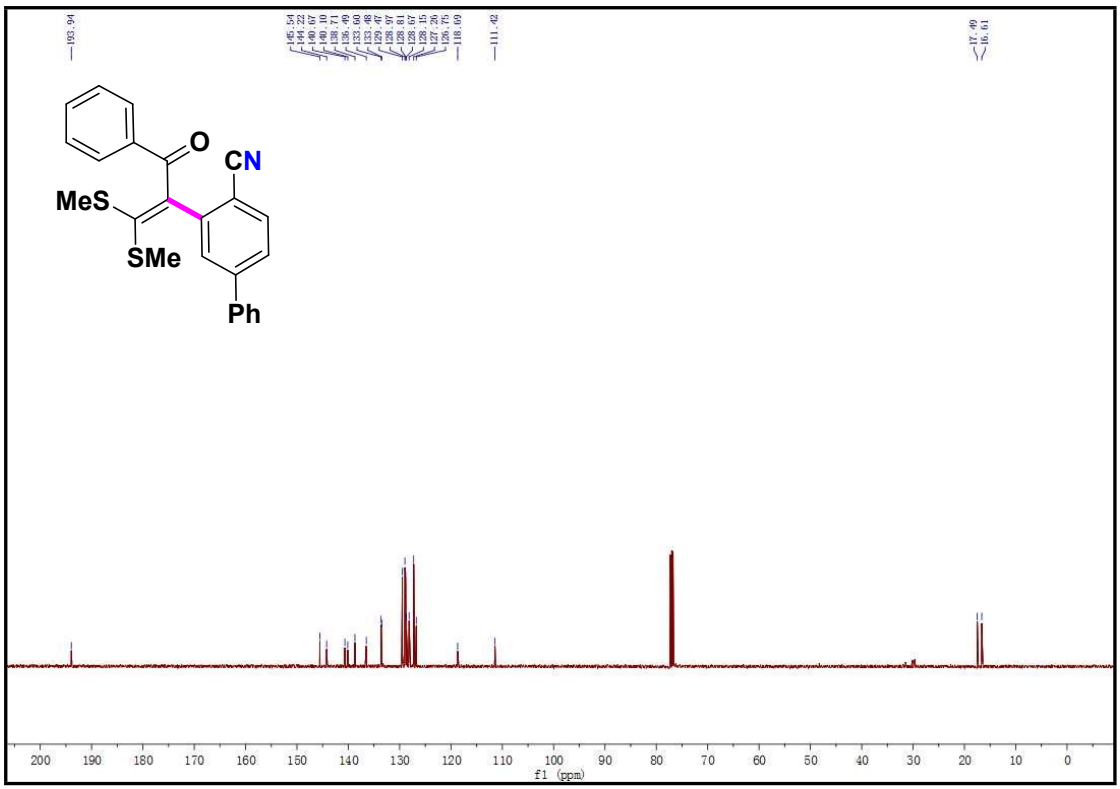
2-(1,1-bis(methylthio)-3-oxo-3-phenylprop-1-en-2-yl)-4-methylbenzonitrile (4m)



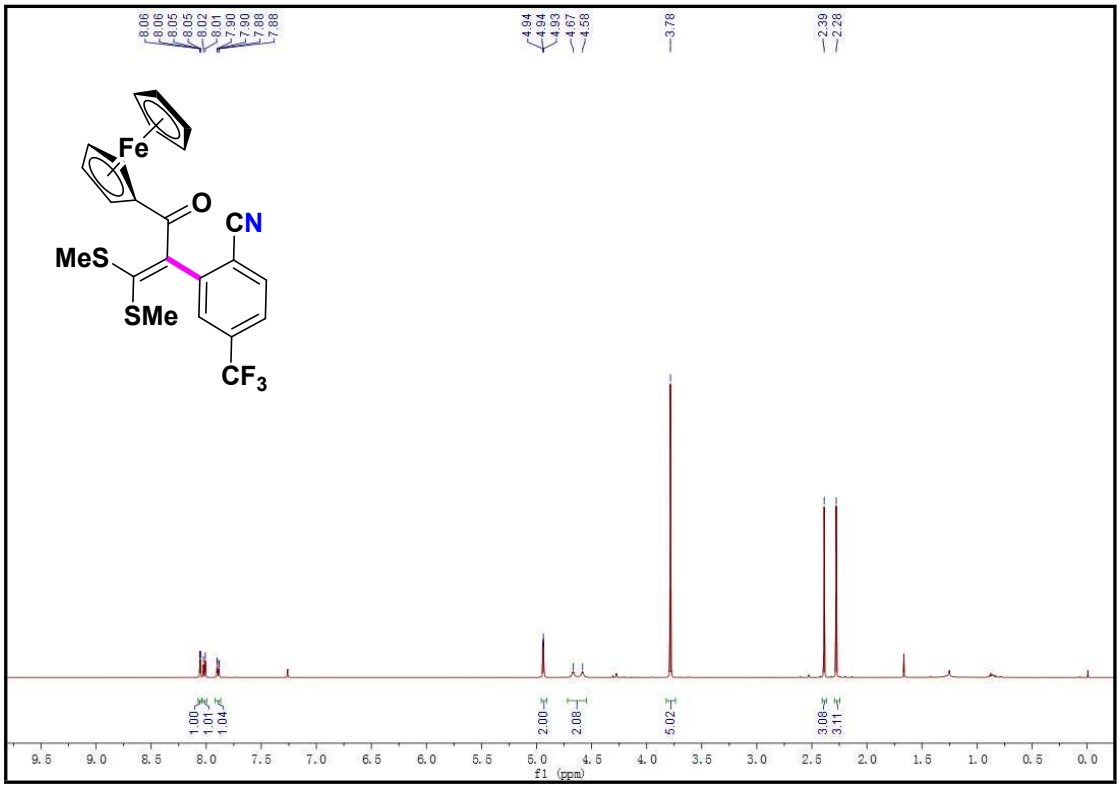


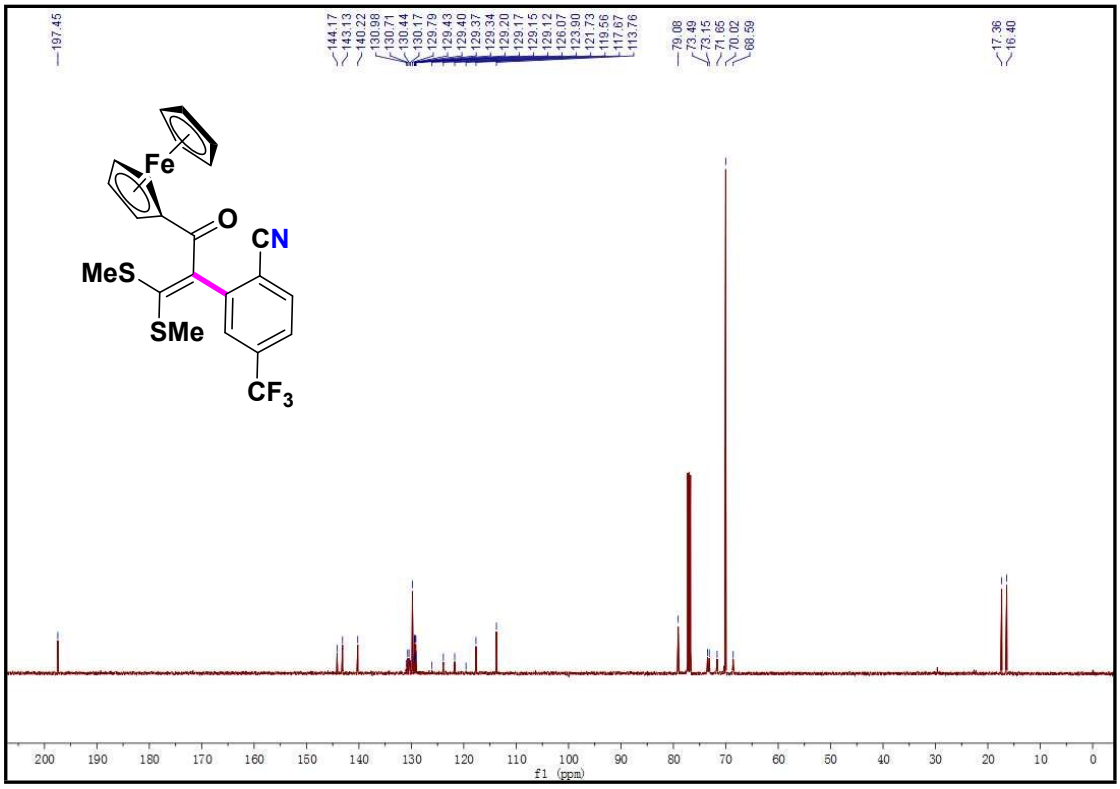
2-(1,1-bis(methylthio)-3-oxo-3-phenylprop-1-en-2-yl)-[1,1'-biphenyl]-4-carbonitrile (4n)



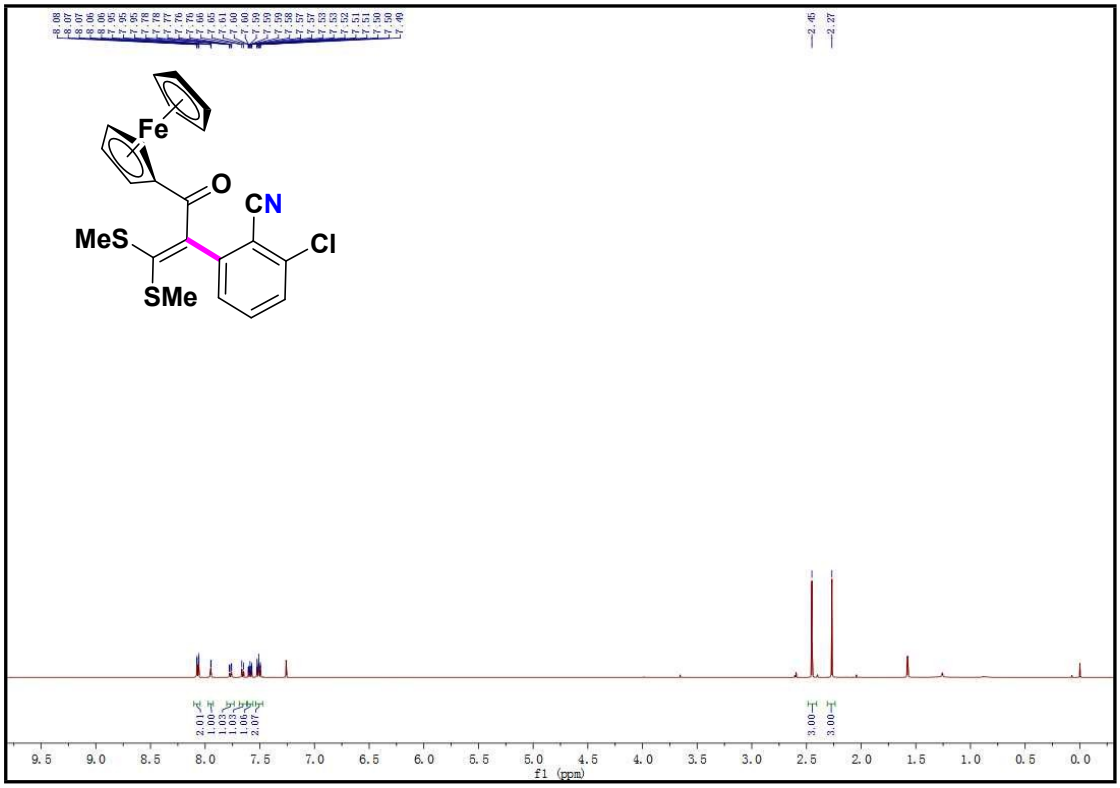


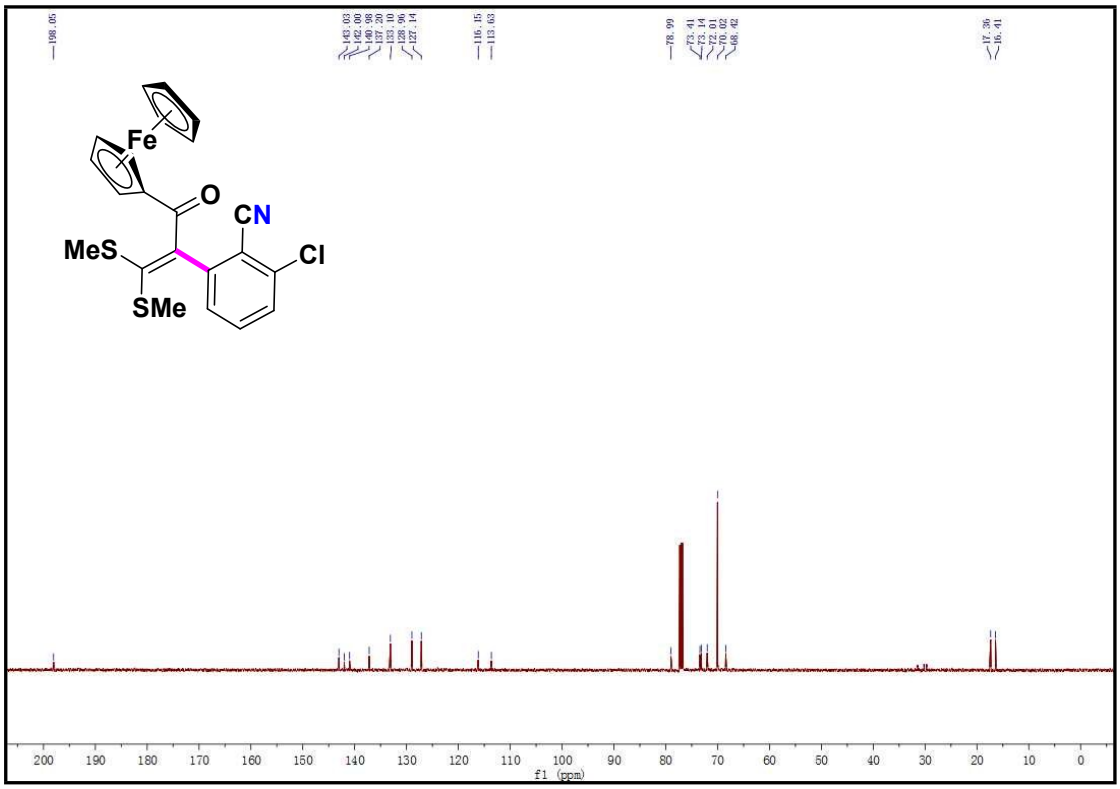
2-(1,1-bis(methylthio)-3-oxoferrocen-1-en-2-yl)-4-(trifluoromethyl)benzonitrile (4o)





2-(1,1-bis(methylthio)-3-oxoferrocen-1-en-2-yl)-6-chlorobenzonitrile (4p)





2-(5-(ethylthio)-3-(thiophen-2-yl)-1H-pyrazol-4-yl)benzonitrile (5)