The *N,S*-Bidentate Ligand Assisted Pd-Catalyzed C(sp^2)-H Carbonylation using Langlois Reagent as CO Source

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Supporting Information

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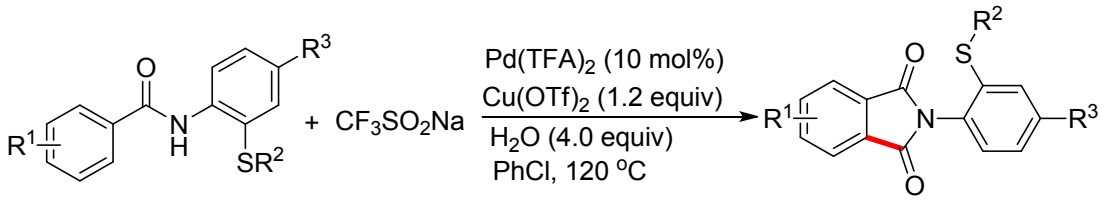
1. General Information.

Chemicals were either purchased or purified by standard techniques. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz spectrometer (^{1}H: 500 MHz, ^{13}C: 125 MHz), using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as an internal standard at 120 ^{o}C temperature. Chemical shifts are given in δ relative to TMS, the coupling constants J are given in Hz. High resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometry. All reactions under air atmosphere were conducted using standard Schlenk techniques. Melting points were measured on X4 melting point apparatus and uncorrected. Column chromatography was performed using EM Silica gel 60 (300-400 mesh).

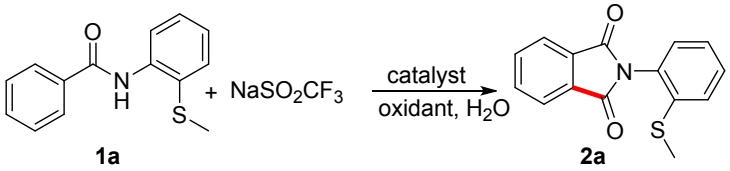
2. General Procedure for the Synthesis of isoindoline-1,3-diones 2a-2u, 4a-4h



2a - 2u, 4a-4h

To a flame-dried Schlenk tube with a magnetic stirring bar was charged with **1** (0.2 mmol), CF_3SO_2Na (0.54 mmol), $Pd(TFA)_2$ (13.3 mg, 0.4 mmol), H_2O (4.0 equiv) in dry PhCl (2 mL) under air atmosphere. The reaction mixture was stirred at 120 ^{o}C until complete consumption of starting material as detected by TLC or GC−MS analysis. After the reaction was finished, the mixture was poured into ethyl acetate and evaporated under vacuum. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired products **2a-2u, 4a-4h.**

3. S-Table 1. Optimization of the Reaction Conditions [a,b]

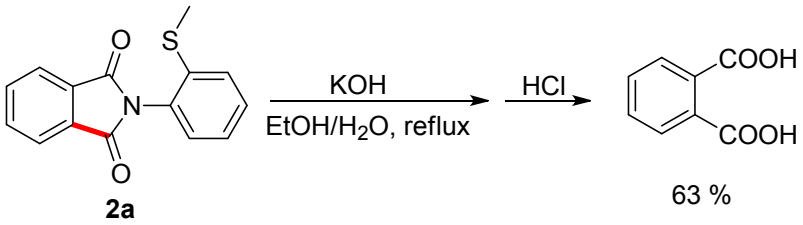


1a **2a**

Entry	**CF_3SO_2Na** (equiv)	**Catalyst**	**Oxidant** (equiv)	**Solvent**	**Yield (%)**
1	2.0	$Pd(OAc)_2$	$Cu(OTf)_2$ (1.0)	Dioxane	5
2	2.0	$Pd(OAc)_2$	$Cu(OTf)_2$(1.0)	DMSO	0
3	2.0	$Pd(OAc)_2$	$Cu(OTf)_2$(1.0)	DCE	18
4	2.0	$Pd(OAc)_2$	$Cu(OTf)_2$ (1.0)	DMF	NR
5	2.0	$Pd(OAc)_2$	$Cu(OTf)_2$(1.0)	AcOH	6%
6	2.0	$Pd(OAc)_2$	$Cu(OTf)_2$(1.0)	THF	NR
7	2.0	$Pd(OAc)_2$	$Cu(OTf)_2$(1.0)	PhCl	21
8	2.0	$PdCl_2$	$Cu(OTf)_2$(1.0)	PhCl	8
9	2.0	$Pd(MeCN)_2Cl_2$	$Cu(OTf)_2$(1.0)	PhCl	32
10	2.0	$Pd(TFA)_2$	$Cu(OTf)_2$(1.0)	PhCl	50
11	2.0	$PdBr_2$	$Cu(OTf)_2$(1.0)	PhCl	20
12	2.0	$Ni(dppp)_2Cl_2$	$Cu(OTf)_2$(1.0)	PhCl	NR
13	2.0	$Co(acac)_2$	$Cu(OTf)_2$(1.0)	PhCl	NR
14	2.0	$Pd(TFA)_2$	$CuCl_2$(1.0)	PhCl	12
15	2.0	$Pd(TFA)_2$	$Cu(BF_4)_2$(1.0)	PhCl	33
16	2.0	$Pd(TFA)_2$	$Cu(NO_3)_2$(1.0)	PhCl	6
17	2.7	$Pd(TFA)_2$	AgOAc (1.2)	PhCl	NR
18	2.7	$Pd(TFA)_2$	Ag_2CO_3 (1.2)	PhCl	NR
19	2.0	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	55
20	2.5	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	66
21	2.7	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	77
22	3.0	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	75
23 [c]	2.7	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	72
24 [d]	2.7	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	56

25 [e]	2.7	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	71
26 [f]	2.7	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	60
27 [g]	2.7	$Pd(TFA)_2$	$Cu(OTf)_2$(1.2)	PhCl	54
[a] Reaction conditions: **1a** (0.2 mmol), CF_3SO_2Na (2.0-3.0 equiv), Pd catalyst (10 mol %), oxidant (1.0 equiv), H_2O (4.0 equiv) in solvent (2 mL) at 120°C under air atmosphere for 24 h; [b] Isolated yield; [c] 130 °C; [d] for 18h; [e] N_2 atmosphere; [f] H_2O (6.0 equiv); [g] H_2O (2.0 equiv).					

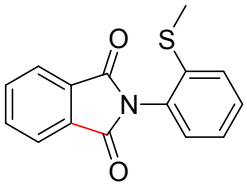
4. The hydrolysis of compound 2a



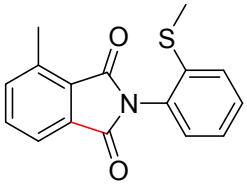
2a 63 %

2a (26.9 mg, 0.1 mmol) was refluxed with KOH (33.6 mg, 0.6 mmol) in 2 mL EtOH/H_2O (1:3) for 6 h. After the reaction was finished, dilute hydrochloric acid (1.2 N) was added in ice-bath and precipitated white solid was isolated by filtration, washed with water and dried. The phthalic acid was obtained. Yield (10.5 mg, 63 % yield.

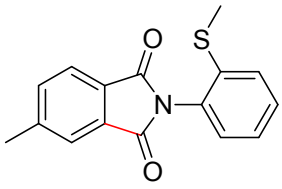
5. Data for All Compounds.



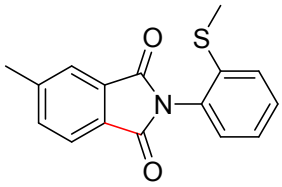
2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2a**): White solid (41.4 mg, 77% yield). m.p. 158-160 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97-7.96 (m, 2H), 7.81-7.79 (m, 2H), 7.48-7.42 (m, 2H), 7.33-7.30 (m, 1H), 7.26-7.24 (m, 1H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 138.6, 134.5, 132.1, 130.28, 130.25, 129.7, 128.1, 126.3, 124.0, 16.4. HRMS (ESI) Calcd for $C_{15}H_{11}NO_2SNa^+$ ([M + Na]$^+$) 292.0403, Found: 292.0413.



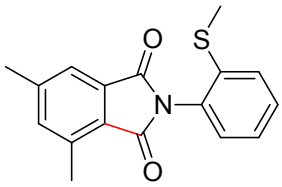
4-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2b**): Yellow solid (31.1 mg, 55% yield). m.p. 129-131 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.0 Hz, 1H), 7.65-7.62 (m, 1H), 7.53 (d, J = 7.5 Hz, 1H), 7.47-7.41 (m, 2H), 7.31-7.28 (m, 1H), 7.24 (d, J = 7.5 Hz, 1H), 2.74 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 167.2, 138.7, 138.6, 136.8, 133.9, 132.5, 130.3, 130.1, 129.7, 128.8, 127.8, 126.2, 121.6, 17.8, 16.2. HRMS (ESI) Calcd for $C_{16}H_{13}NO_2SNa^+$ ([M + Na]$^+$) 306.0559, Found: 306.0561.



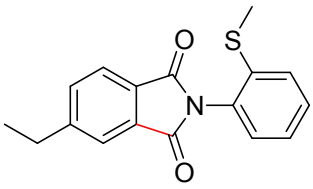
5-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2c**): Yellow solid (40.8 mg, 72% yield). m.p. 146-148 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 7.5 Hz, 1H), 7.77 (s, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.47-7.41 (m, 2H), 7.32-7.29 (m, 1H), 7.24 (d, J = 8.0 Hz, 1H), 2.55 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 167.3, 145.8, 138.7, 135.0, 132.5, 130.4, 130.2, 129.8, 129.6, 128.0, 126.3, 124.5, 123.9, 22.2, 16.4. HRMS (ESI) Calcd for $C_{16}H_{13}NO_2SNa^+$ ([M + Na]$^+$) 306.0559, Found: 306.0562.



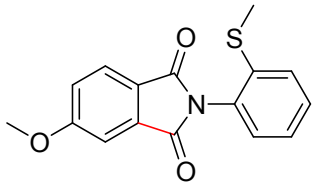
5-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2d**): Yellow solid (36.3 mg, 64% yield). m.p. 146-148 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.76 (s, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.46-7.41 (m, 2H), 7.32 - 7.29 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 2.54 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 167.3, 145.8, 138.6, 135.0, 132.5, 130.4, 130.1, 129.7, 129.5, 128.0, 126.3, 124.5, 123.9, 22.2, 16.3. HRMS (ESI) Calcd for $C_{16}H_{13}NO_2SNa^+$ ([M + Na]$^+$) 306.0559, Found: 306.0557.



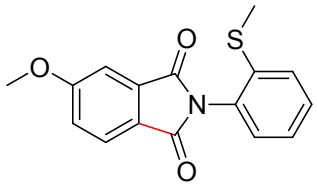
4,6-dimethyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2e**): Yellow solid (33.3 mg, 56% yield). m.p. 141-143 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.46-7.43 (m, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.33 (s, 1H), 7.31-7.28 (m, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 2.69 (s, 3H), 2.48 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 167.5, 145.2, 138.7, 138.5, 137.3, 132.9, 130.4, 130.0, 129.8, 127.7, 126.3, 126.1, 122.3, 21.9, 17.8, 16.2. HRMS (ESI) Calcd for $C_{17}H_{15}NO_2SNa^+$ ([M + Na]$^+$) 320.0716, Found: 320.0711.



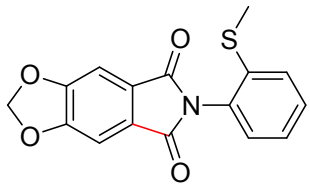
5-ethyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2f**): Yellow solid (35.5 mg, 61% yield). m.p. 141-143 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.5 Hz, 1H), 7.80 (s, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.47-7.41 (m, 2H), 7.32-7.29 (m, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 2.84 (q, *J* = 7.5 Hz, 2H), 2.42 (s, 3H), 1.32 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 167.3, 152.0, 138.6, 134.0, 132.6, 130.4, 130.1, 129.8, 129.7, 128.0, 126.3, 124.0, 123.3, 29.4, 16.4, 15.3. HRMS (ESI) Calcd for $C_{17}H_{15}NO_2SNa^+$ ([M + Na]$^+$) 320.0716, Found: 320.0729.



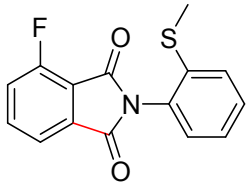
5-methoxy-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2g**): Yellow solid (31.1 mg, 52% yield). m.p. 164-166 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.5 Hz, 1H), 7.46-7.41 (m, 3H), 7.31-7.28 (m, 1H), 7.25-7.22 (m, 2H), 3.94 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 167.0, 165.1, 138.7, 134.7, 130.5, 130.1, 129.8, 128.0, 126.3, 125.7, 124.0, 120.5, 108.4, 56.2, 16.3. HRMS (ESI) Calcd for $C_{16}H_{13}NO_3SNa^+$ ([M + Na]$^+$) 322.0508, Found: 322.0520.



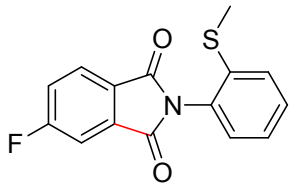
5-methoxy-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2h**): Yellow solid (28.7 mg, 48% yield). m.p. 164-166 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.5 Hz, 1H), 7.46-7.40 (m, 3H), 7.31 - 7.28 (m, 1H), 7.24 - 7.22 (m, 2H), 3.93 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 166.9, 165.0, 138.6, 134.6, 130.3, 130.1, 129.7, 127.8, 126.2, 125.6, 123.9, 120.5, 108.4, 56.2, 16.2. HRMS (ESI) Calcd for $C_{16}H_{13}NO_3SNa^+$ ([M + Na]$^+$) 322.0508, Found: 322.0513.



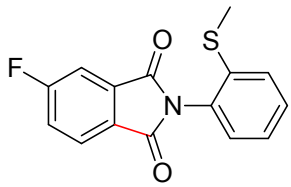
6-(2-(methylthio)phenyl)-5H-[1,3]dioxolo[4,5-f]isoindole-5,7(6H)-dione (**2i**): Yellow solid (21.9 mg, 35% yield). m.p. 225-227 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46-7.43 (m, 1H), 7.41 - 7.40 (m, 1H), 7.32 - 7.31 (m, 2H), 7.29 - 7.25 (m, 1H), 7.23 - 7.22 (m, 1H), 6.19 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 153.1, 138.7, 130.4, 130.2, 129.8, 127.9, 127.7, 126.3, 104.3, 103.2, 16.3. HRMS (ESI) Calcd for $C_{16}H_{12}NO_4S^+$ ([M + H]$^+$) 314.0482, Found: 314.0499.



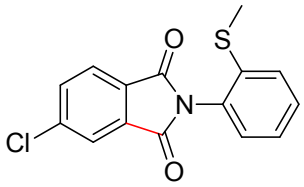
4-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2j**): Yellow solid (11.5 mg, 20% yield). m.p. 136-138 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81-7.78 (m, 2H), 7.48-7.43 (m, 3H), 7.33-7.30 (m, 1H), 7.24 (d, J = 8.0 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 163.8, 158.0 (d, $J_{C\text{-}F}$ = 265 Hz), 138.6, 137.0, 134.3, 130.4, 130.0, 129.7, 128.4, 126.5, 122.8 (d, $J_{C\text{-}F}$ = 20.0 Hz), 120.2, 118.0 (d, $J_{C\text{-}F}$ = 12.5 Hz), 16.5. HRMS (ESI) Calcd for $C_{15}H_{10}NFO_2SNa^+$ ([M +Na]$^+$) 310.0308, Found: 310.0309.



5-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2k**): Yellow solid (28.1 mg, 49% yield). m.p. 161-163 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97-7.95 (m, 1H), 7.63 (d, J = 7.0 Hz, 1H), 7.48-7.42 (m, 3H), 7.32-7.29 (m, 1H), 7.24 (d, J = 7.5 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7 (d, $J_{C\text{-}F}$ = 256.3 Hz), 166.1, 165.8, 138.5, 134.9, 130.4, 130.0, 129.6, 128.1, 127.8, 126.4 (d, $J_{C\text{-}F}$ = 10 Hz), 126.3, 121.5 (d, $J_{C\text{-}F}$ = 23.8 Hz), 111.7 (d, $J_{C\text{-}F}$ = 25 Hz), 16.3. HRMS (ESI) Calcd for $C_{15}H_{11}NFO_2S^+$ ([M +H]$^+$) 288.0489, Found: 288.0499.

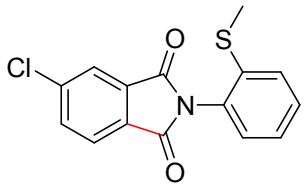


5-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2l**): Yellow solid (24 mg, 42% yield). m.p. 161-163 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 - 7.95 (m, 1H), 7.63 (d, J = 6.5 Hz, 1H), 7.47-7.42 (m, 3H), 7.32 - 7.29 (m, 1H), 7.24 (d, J = 8.0 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7 (d, $J_{C\text{-}F}$ = 255 Hz), 166.1, 165.8, 138.5, 134.9, 130.4, 130.1, 129.6, 128.1, 127.9, 126.4, (d, $J_{C\text{-}F}$ = 10 Hz), 126.3, 121.5 (d, J = 23.8 Hz), 111.7 (d, J = 25 Hz), 16.4. HRMS (ESI) Calcd for $C_{15}H_{11}NFO_2S^+$ ([M +H]$^+$) 288.0489, Found: 288.0495.

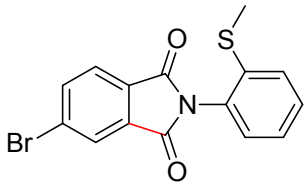


5-chloro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2m**): Yellow solid (35.3 mg, 60% yield). m.p. 157-159 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.89 (d, J =

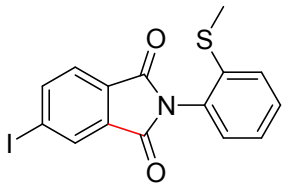
8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.48-7.41 (m, 2H), 7.32 - 7.29 (m, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 165.8, 141.1, 138.5, 134.5, 133.7, 130.4, 130.1, 129.9, 129.6, 128.1, 126.3, 125.2, 124.3, 16.3. HRMS (ESI) Calcd for $C_{15}H_{11}NClO_2S^+$ ([M +H]$^+$) 304.0194, Found: 304.0199.



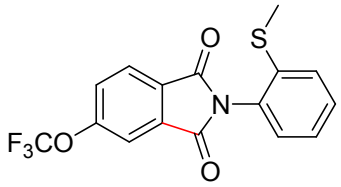
5-chloro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2n**): Yellow solid (34.1 mg, 58% yield). m.p. 157-159 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.47-7.41 (m, 2H), 7.32-7.29 (m, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 165.9, 141.1, 138.5, 134.5, 133.7, 130.3, 130.1, 130.0, 129.6, 128.1, 126.3, 125.2, 124.3, 16.4. HRMS (ESI) Calcd for $C_{15}H_{11}NClO_2S^+$ ([M +H]$^+$) 304.0194, Found: 304.0205.



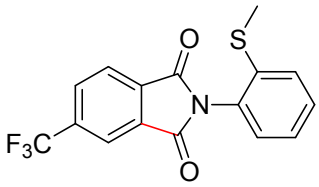
5-bromo-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2o**): Yellow solid (36.0 mg, 52% yield). m.p. 156-158 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.48-7.45 (m, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.33-7.30 (m, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 165.9, 138.5, 137.5, 133.7, 130.6, 130.4, 130.0, 129.6, 129.4, 128.2, 127.3, 126.4, 125.4, 16.4. HRMS (ESI) Calcd for $C_{15}H_{11}NBrO_2S^+$ ([M +H]$^+$) 347.9688, Found: 347.9703.



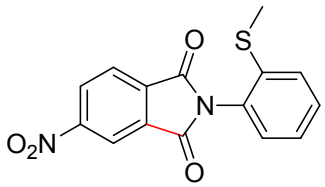
5-iodo-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (**2p**): White solid (18.1 mg, 23% yield). m.p. 98-100 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.48-7.45 (m, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.33-7.30 (m, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 165.8, 143.5, 138.6, 133.4, 133.1, 131.2, 130.4, 130.0, 129.7, 128.3, 126.4, 125.3, 101.4, 16.5. HRMS (ESI) Calcd for $C_{15}H_{11}NIO_2S^+$ ([M +H]$^+$) 395.9550, Found: 395.9564.



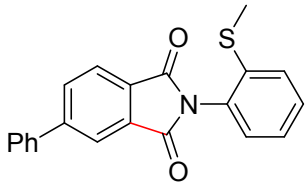
2-(2-(methylthio)phenyl)-5-(trifluoromethoxy)isoindoline-1,3-dione (**2q**): Yellow solid(37.4 mg, 53% yield). m.p. 86-88 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.80 (s, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.50-7.47 (m, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.34-7.31 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 165.7, 153.9, 138.5, 134.4, 130.5, 130.0, 129.9, 129.6, 128.3, 126.47, 126.45, 126.0, 120.4 (q, *J* = 258.8 Hz), 116.1, 16.4. HRMS (ESI) Calcd for $C_{16}H_{10}NF_3O_3SNa^+$ ([M +Na]$^+$) 376.0226, Found: 376.0241.



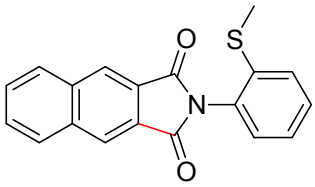
2-(2-(methylthio)phenyl)-5-(trifluoromethyl)isoindoline-1,3-dione (**2r**): Yellow solid (30.3 mg, 45% yield). m.p. 147-149 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.12-8.08 (m, 2H), 7.51-7.48 (m, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.35-7.32 (m, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 165.8, 138.5, 136.6 (q, *J* = 34.0 Hz), 134.9, 132.8, 131.6, 130.6, 129.8, 129.6, 128.3, 126.5, 124.6, 123.2 (q, *J* = 272.5 Hz), 121.3, 16.4. HRMS (ESI) Calcd for $C_{16}H_{11}NF_3OS^+$ ([M +H]$^+$) 338.0457, Found: 376.0480.



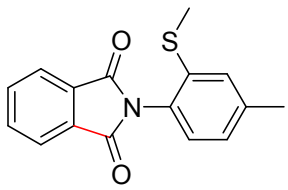
2-(2-(methylthio)phenyl)-5-nitroisoindoline-1,3-dione (**2s**): Yellow solid (11.3 mg, 18% yield). m.p. 162-164 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.67 (d, *J* = 8.0 Hz, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.52-7.49 (m, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.35-7.32 (m, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 164.9, 152.2, 138.4, 136.4, 133.5, 130.7, 129.7, 129.5, 128.5, 128.4, 126.6, 125.3, 119.4, 16.5. HRMS (ESI) Calcd for $C_{15}H_{11}N_2O_4S^+$ ([M +H]$^+$) 315.0434, Found: 315.0438.



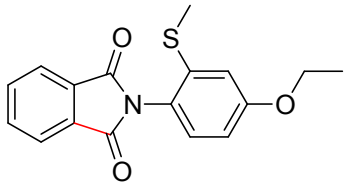
2-(2-(methylthio)phenyl)-5-phenylisoindoline-1,3-dione (**2t**): Yellow solid (38.6 mg, 56% yield). m.p. 204-206 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.00-7.96 (m, 2H), 7.65 (d, *J* = 7.5 Hz, 2H), 7.51-7.48 (m, 2H), 7.45-7.43 (m, 3H), 7.31-7.28 (m, 1H), 7.24 (d, *J* = 6.0 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 167.1, 147.9, 139.1, 138.6, 133.0, 132.9, 130.5, 130.3, 130.2, 129.7, 129.3, 129.0, 128.1, 127.5, 126.3, 124.4, 122.5, 16.4. HRMS (ESI) Calcd for $C_{21}H_{16}NO_2S^+$ ([M +H]$^+$) 346.0896, Found: 346.0895.



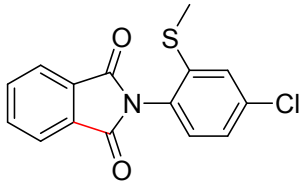
2-(2-(methylthio)phenyl)-1H-benzo[f]isoindole-1,3(2H)-dione (**2u**): Yellow solid (35.1 mg, 55% yield). m.p. 196-198 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (s, 2H), 8.10 - 8.08 (m, 2H), 7.73 -7.71 (m, 2H), 7.49-7.45 (m, 2H), 7.35-7.30 (m, 2H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 138.5, 135.8, 130.6, 130.5, 130.2, 129.6, 129.4, 128.2, 127.8, 126.4, 125.5, 16.4. HRMS (ESI) Calcd for $C_{19}H_{14}NO_2S^+$ ([M +H]$^+$) 320.0740, Found: 320.0734.



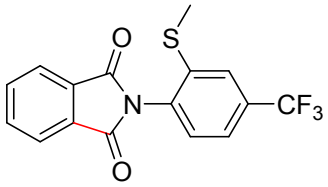
2-(4-methyl-2-(methylthio)phenyl)isoindoline-1,3-dione (**4a**): White solid (35.1mg, 62% yield), m.p. 168-170°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 - 7.94 (m, 2H), 7.79 - 7.77 (m, 2H), 7.22 (s, 1H), 7.14 - 7.10 (m, 2H), 2.41 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 140.4, 138.0, 134.4, 132.1, 129.4, 128.7, 127.6, 127.2, 123.9, 21.5, 16.4. HRMS (ESI) Calcd for $C_{16}H_{13}NNaO_2S^+$ ([M + Na]$^+$) 306.0559, Found: 306.0554.



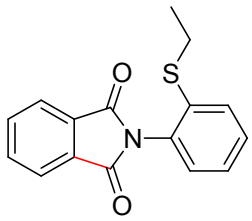
2-(4-ethoxy-2-(methylthio)phenyl)isoindoline-1,3-dione (**4b**): White solid (40.7mg, 65% yield), m.p. 138-140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 -7.93 (m, 2H), 7.79 - 7.77 (m, 2H), 7.14 (d, *J* = 8.8 Hz, 1H), 6.90 (s, 1H), 6.79 (d, *J* = 8.8 Hz, 1H), 4.07 (q, *J* = 6.8 Hz, 2H), 2.40 (s, 3H), 1.44 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.6, 160.2, 139.8, 134.4, 132.1, 130.5, 123.9, 122.4, 114.3, 111.5, 64.0, 16.1, 14.9. HRMS (ESI) Calcd for $C_{17}H_{16}NO_3S^+$ ($[M + H]^+$) 314.0845, Found: 314.0842.



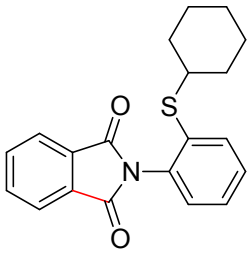
2-(4-chloro-2-(methylthio)phenyl)isoindoline-1,3-dione (**4c**): White solid (36.4mg, 60% yield), m.p. 118-120 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 - 7.98 (m, 2H), 7.85 - 7.83 (m, 2H), 7.37 (s, 1H), 7.30 (d, *J* = 9.6 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 140.9, 136.2, 134.6, 131.9, 130.7, 128.3, 127.0, 126.1, 124.0, 15.9. HRMS (ESI) Calcd for $C_{15}H_{10}ClNNaO_2S^+$ ($[M + Na]^+$) 326.0013, Found: 326.0034.



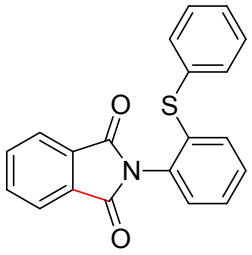
2-(2-(methylthio)-4-(trifluoromethyl)phenyl)isoindoline-1,3-dione **(4d):** White solid (34.3mg, 51% yield). m.p. 87-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 - 7.97 (m, 2H), 7.84 - 7.82 (m, 2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.50 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (125 MHz, CD_3Cl) δ 166.68, 144.33, 134.72, 131.85, 129.72, 128.0 (q, *J* = 33.8 Hz), 126.8, 126.59, 124.11, 123.7 (q, *J* = 271.3 Hz), 113.7, 15.34. HRMS (ESI) Calcd for $C_{16}H_{10}F_3NO_2S^+$ ($[M +H]^+$) 338.0457, Found: 338.0465.



2-(2-(ethylthio)phenyl)isoindoline-1,3-dione (**4e**): White solid (29.4 mg, 52% yield), m.p. 127-129°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 - 7.99 (m, 2H), 7.86 - 7.83 (m, 2H), 7.57 (d, J = 8.0 Hz, 1H), 7.50-7.47 (m, 1H), 7.40-7.37 (m, 1H), 7.31 (d, J = 6.8 Hz, 1H), 2.93 (q, J = 7.6 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 137.0, 134.4, 132.1, 131.6, 130.4, 130.0, 129.8, 127.0, 123.9, 28.2, 14.3. HRMS (ESI) Calcd for $C_{16}H_{14}NO_2S^+$ ([M + H]$^+$), 284.0740, Found: 284.0739.

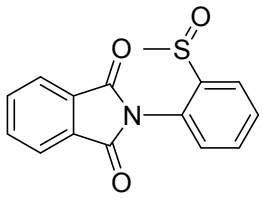


2-(2-(cyclohexylthio)phenyl)isoindoline-1,3-dione (**4f**): White solid (41.1mg, 61% yield), m.p. 108-110°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 - 7.96 (m, 2H), 7.81 - 7.78 (m, 2H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.45-7.41 (m, 1H), 7.39-7.35 (m, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 3.10 - 3.03 (m, 1H), 1.89 - 1.85 (m, 2H), 1.67 - 1.66 (m, 2H), 1.56 - 1.53 (m, 1H), 1.29 - 1.19 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 135.9, 134.4, 133.2, 133.1, 132.2, 129.9, 129.8, 127.8, 124.0, 47.5, 33.5, 26.1, 25.8. HRMS (ESI) Calcd for $C_{20}H_{19}NNaO_2S^+$([M + Na]$^+$) 360.1029, Found: 360.1027.

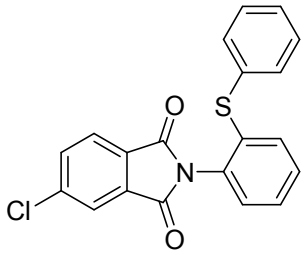


2-(2-(phenylthio)phenyl)isoindoline-1,3-dione (**4g**): Yellow solid (35.1 mg, 53% yield). m.p. 105-107°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 - 7.91 (m, 2H), 7.79 - 7.76 (m, 2H), 7.41 - 7.35 (m, 3H), 7.34 - 7.29 (m , 3H), 7.24 - 7.18 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 136.6, 134.5, 134.3, 133.0, 132.0, 131.9, 131.8, 130.1,

129.9, 129.3, 128.2, 127.6, 123.9. HRMS (ESI) Calcd for $C_{20}H_{13}NO_2SNa^+$ ([M +Na]$^+$) 354.0559, Found: 354.0559.

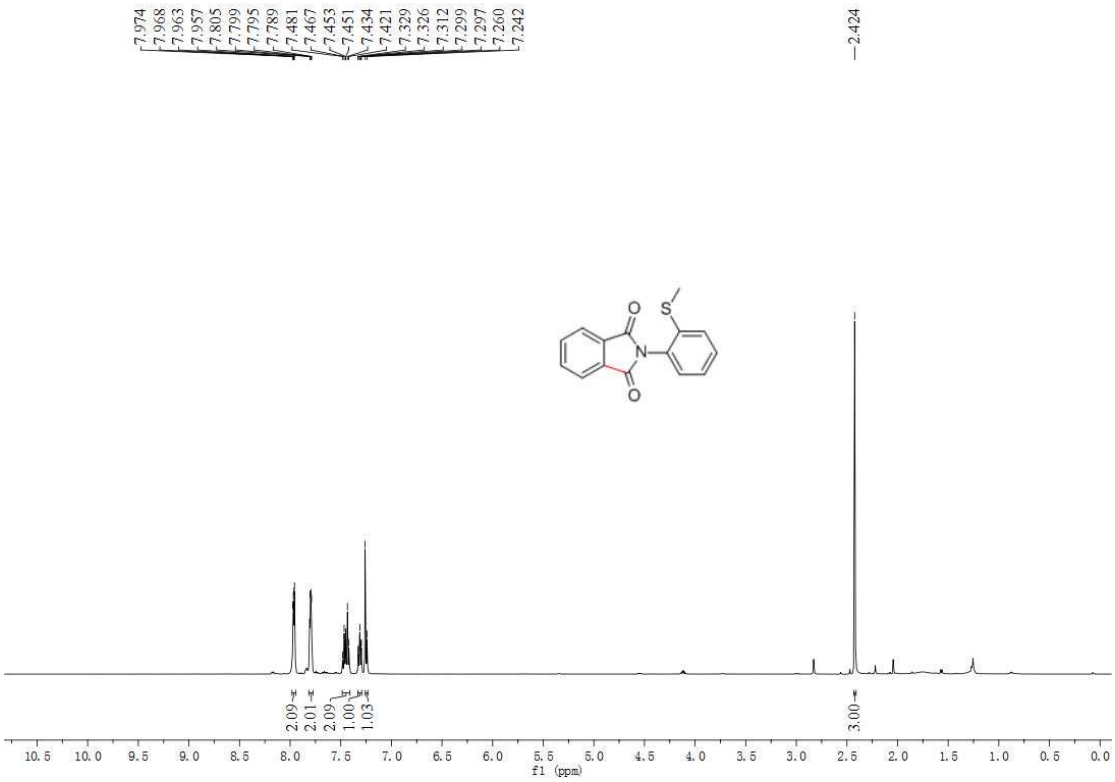


2-(2-(methylsulfinyl)phenyl)isoindoline-1,3-dione (**11**): Yellow solid (24.3 mg, 85% yield). m.p. 161-163 ^{o}C. ^{1}H NMR (500 MHz, DMSO) δ 8.17 (d, *J* = 7.5 Hz, 1H), 8.02 - 8.01 (m, 2H), 7.95 – 7.93 (m, 3H), 7.87 – 7.84 (m, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 3.19 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ 167.5, 138.5, 135.3, 135.2, 132.8, 132.1, 131.2, 131.1, 130.3, 124.0, 44.0. HRMS (ESI) Calcd for $C_{15}H_{12}NO_3S^+$ ([M +H]$^+$) 286.0532, Found: 286.0539.

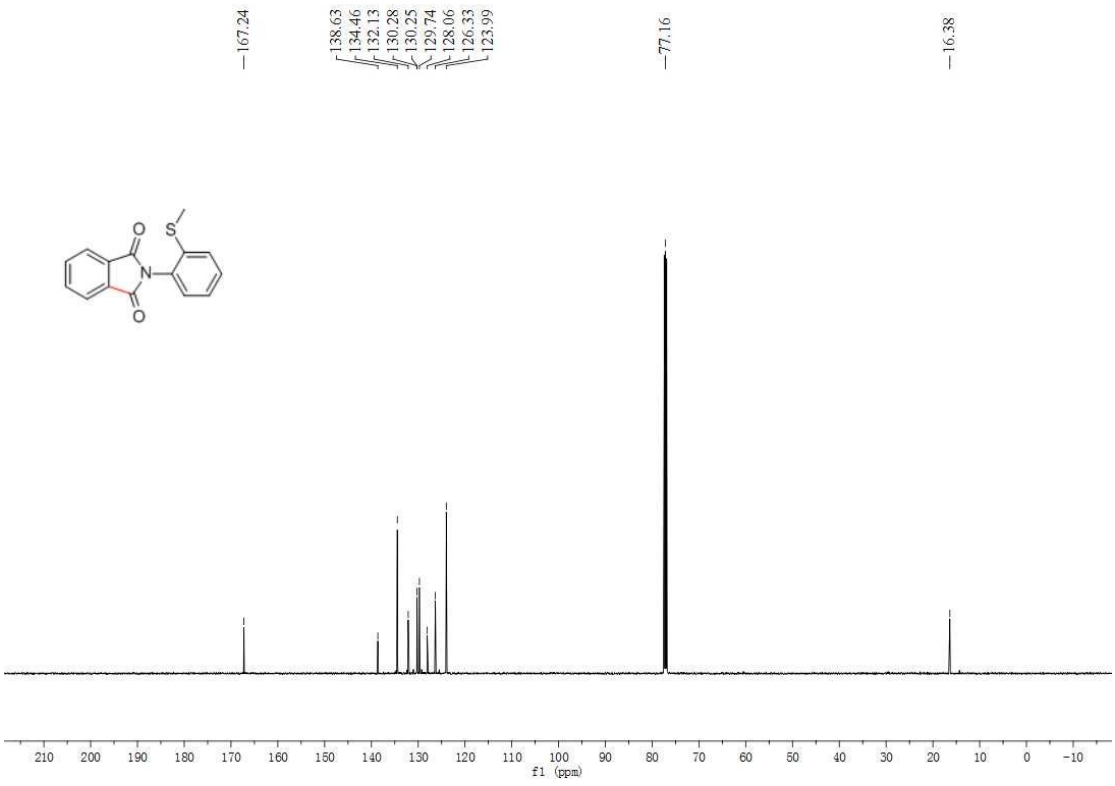


5-chloro-2-(2-(phenylthio)phenyl)isoindoline-1,3-dione (**12**): White solid (27.4 mg, 75% yield), m.p. 112-114^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.39 (s, 3H), 7.32-7.27 (m, 3H), 7.22 (d, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.04, 165.72, 141.04, 136.49, 134.37, 133.57, 133.14, 131.91, 131.56, 130.27, 129.97, 129.82, 129.63, 129.26, 128.23, 127.65, 125.09, 124.26. HRMS (ESI) Calcd for $C_{20}H_{13}ClNO_2S^+$ ([M + H]$^+$) 366.0350, Found: 366.0362.

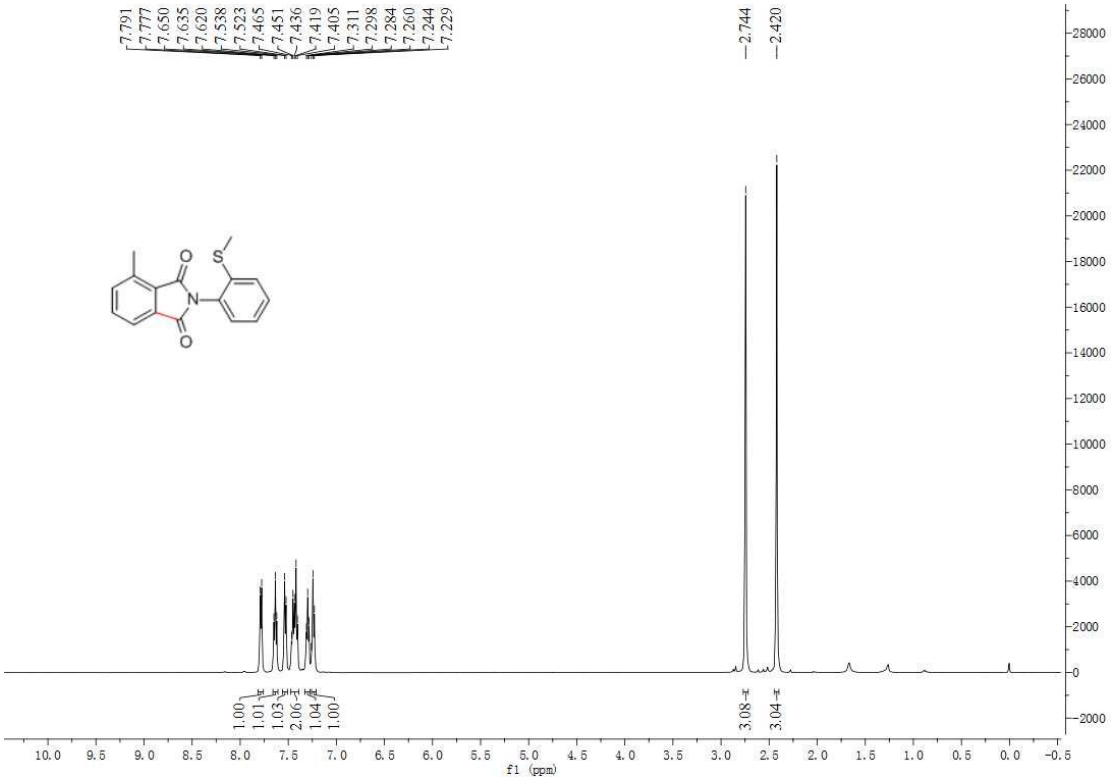
6. NMR Spectra for All Compounds.



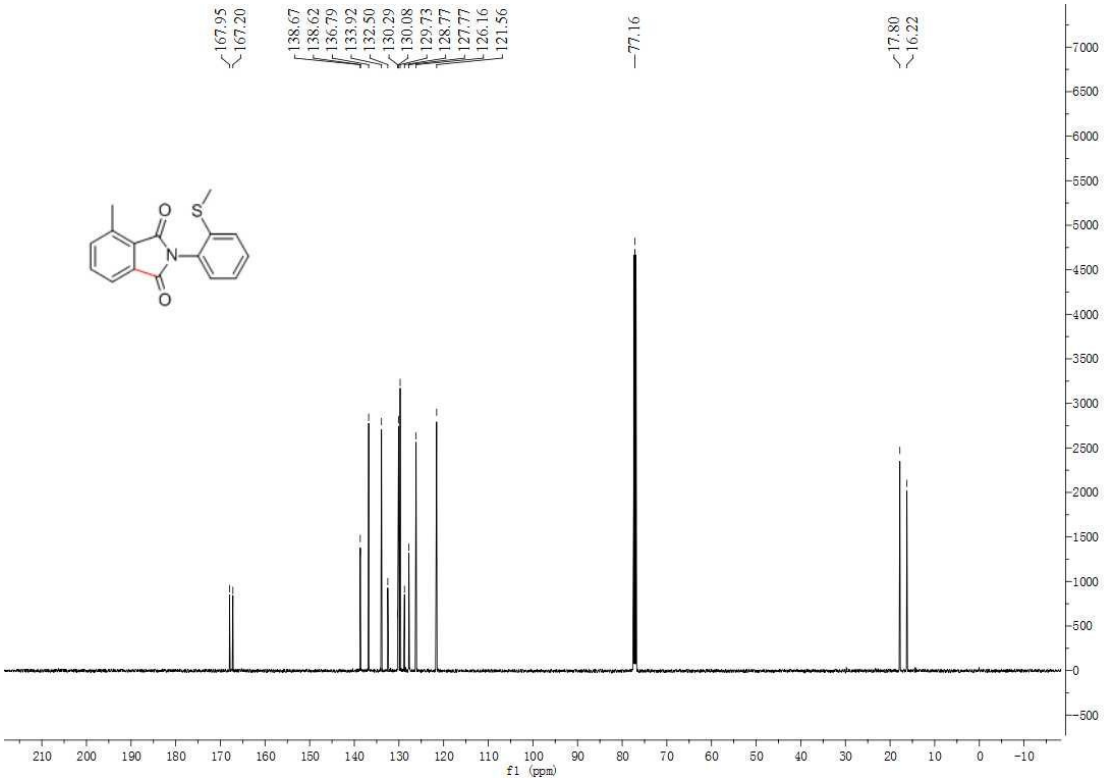
^{1}H NMR:2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2a)



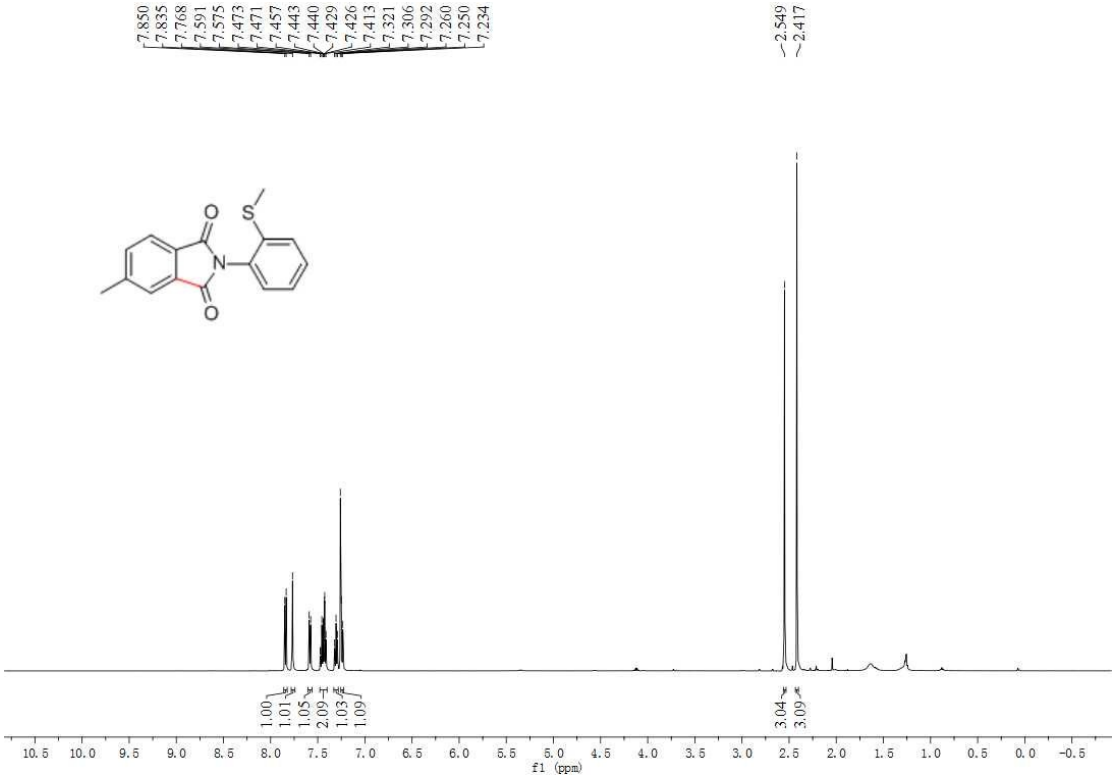
^{13}C NMR:2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2a)



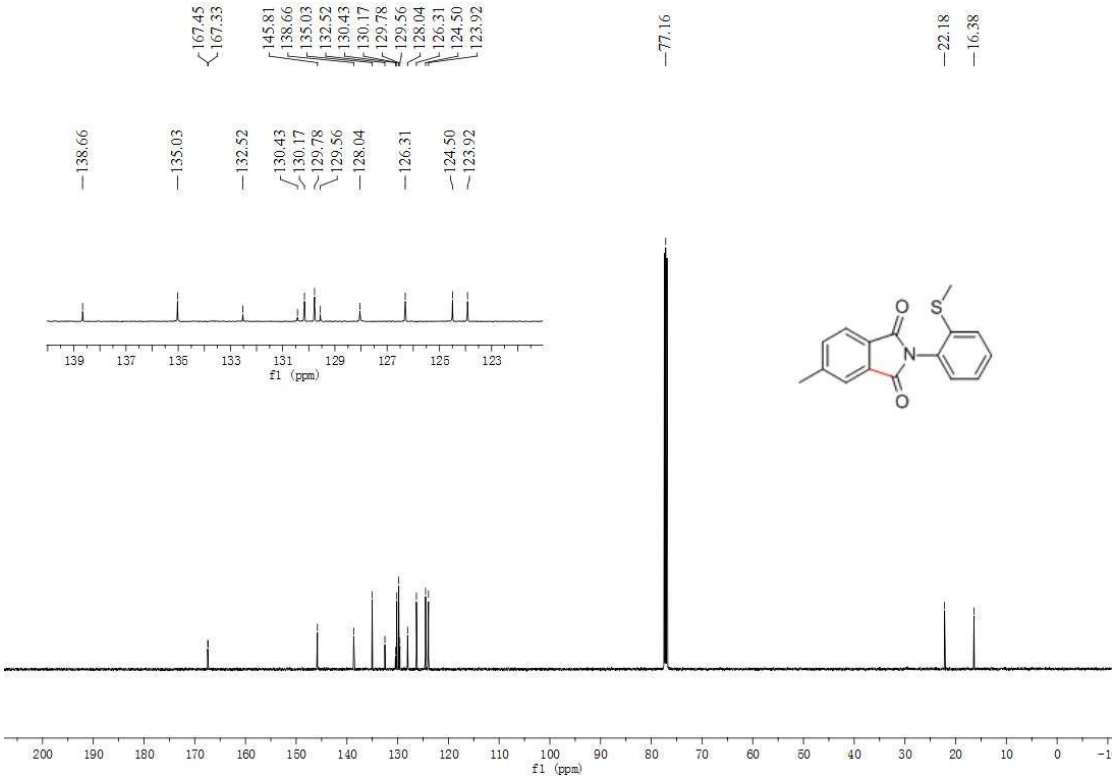
^{1}H NMR:4-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2b)



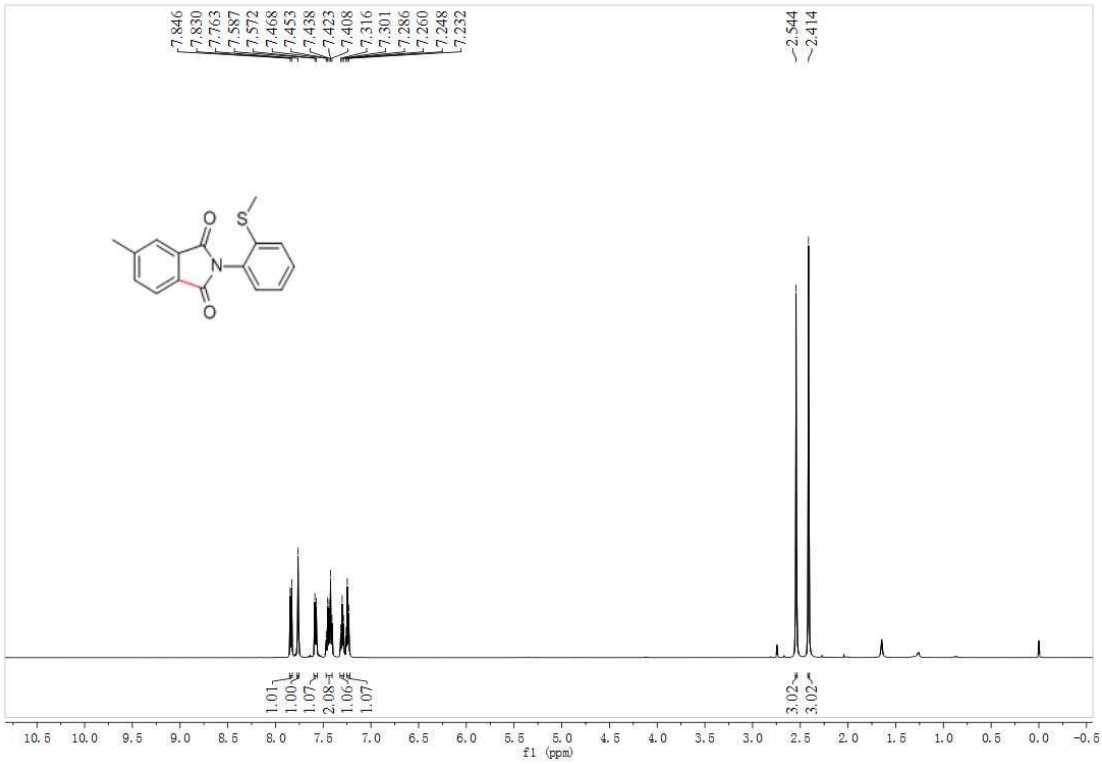
^{13}C NMR:4-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2b)



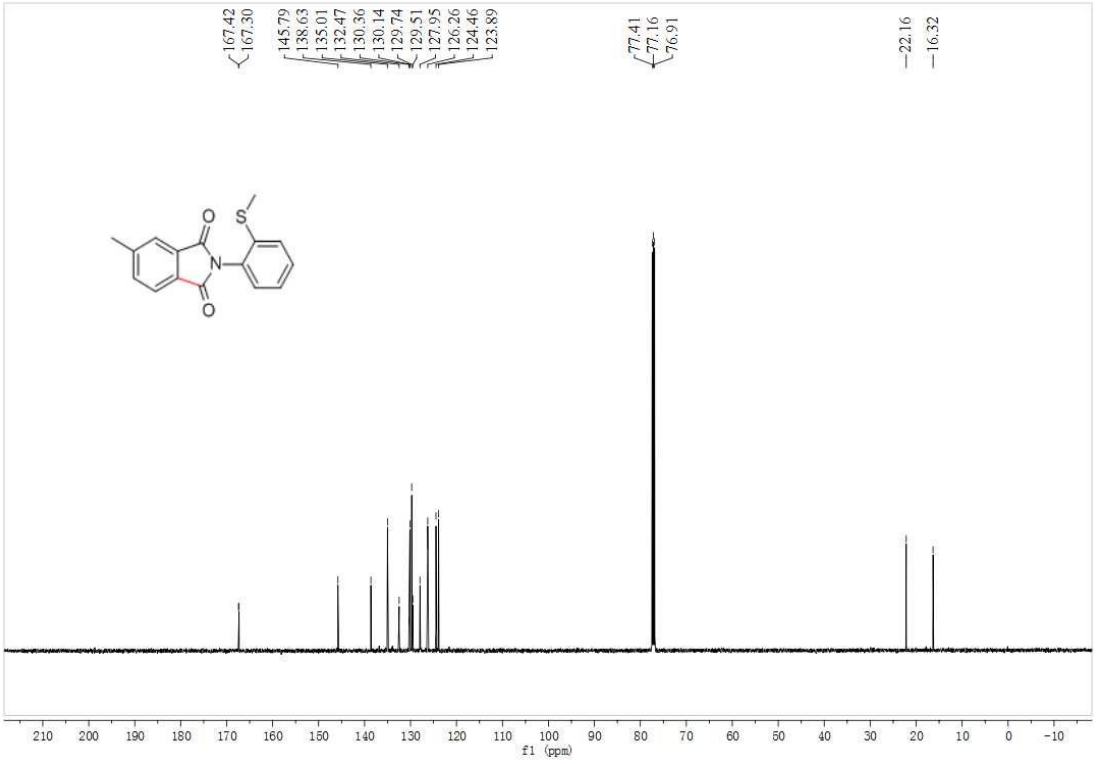
^{1}H NMR:5-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2c)



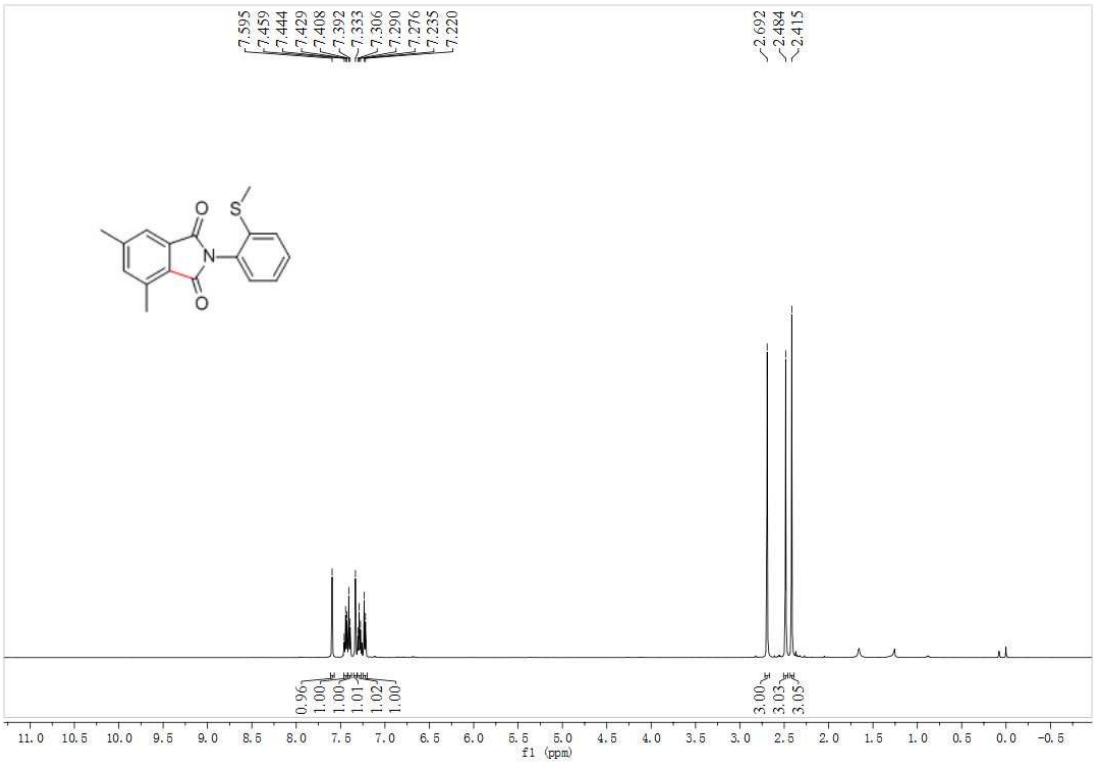
^{13}C NMR:5-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2c)



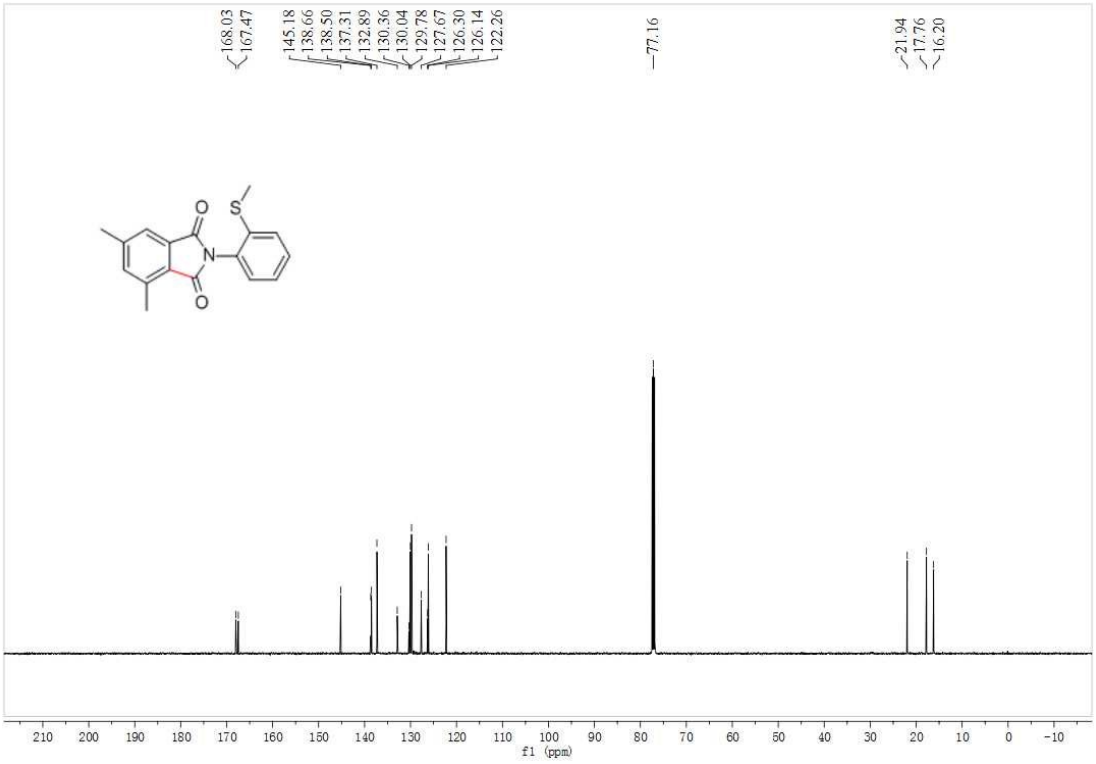
^{1}H NMR:5-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2d)



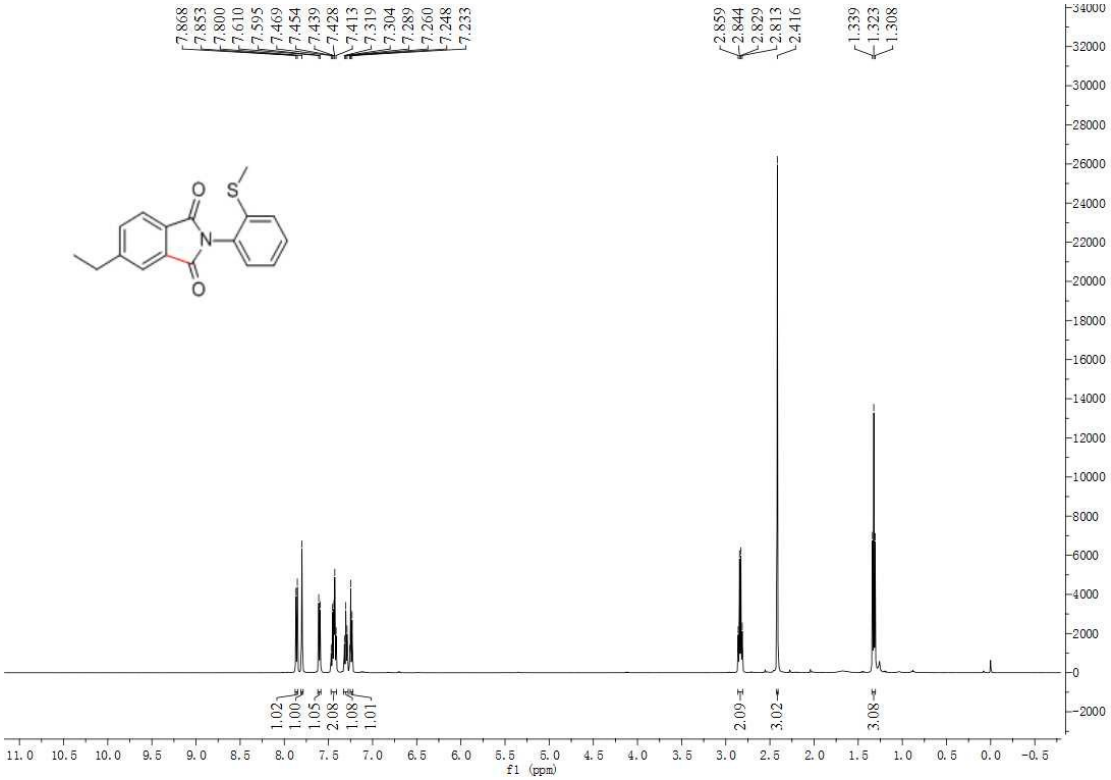
^{13}C NMR:5-methyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2d)



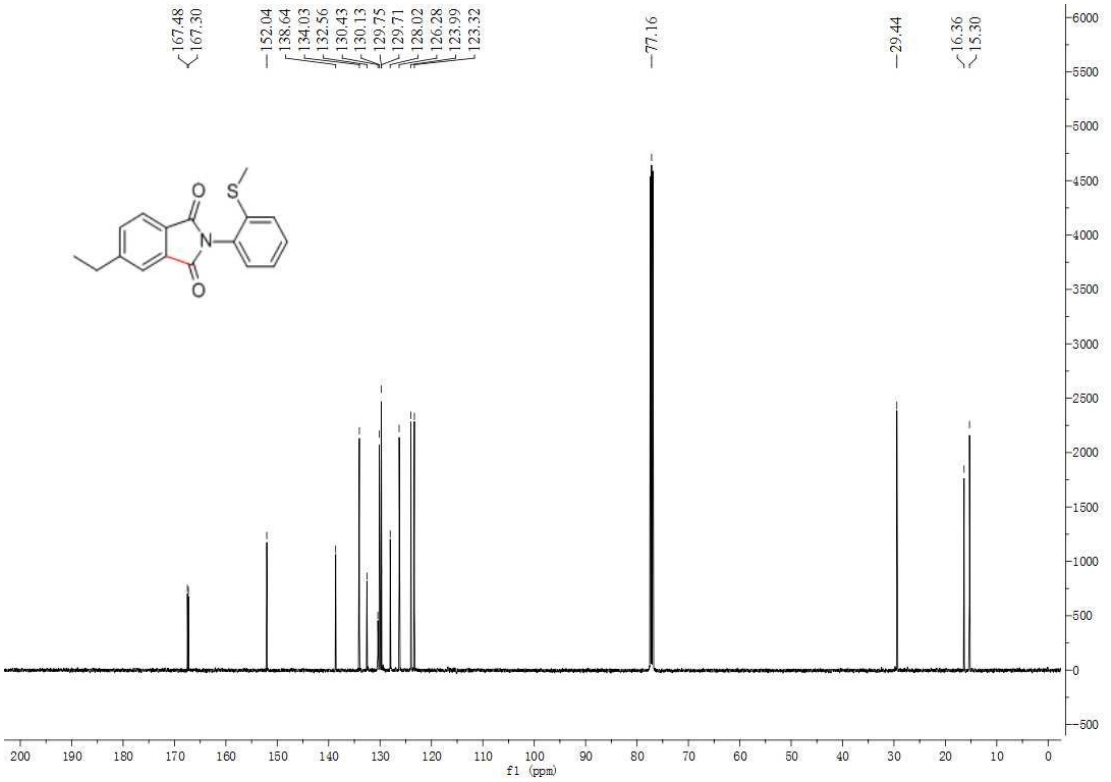
^{1}H NMR:4,6-dimethyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2e)



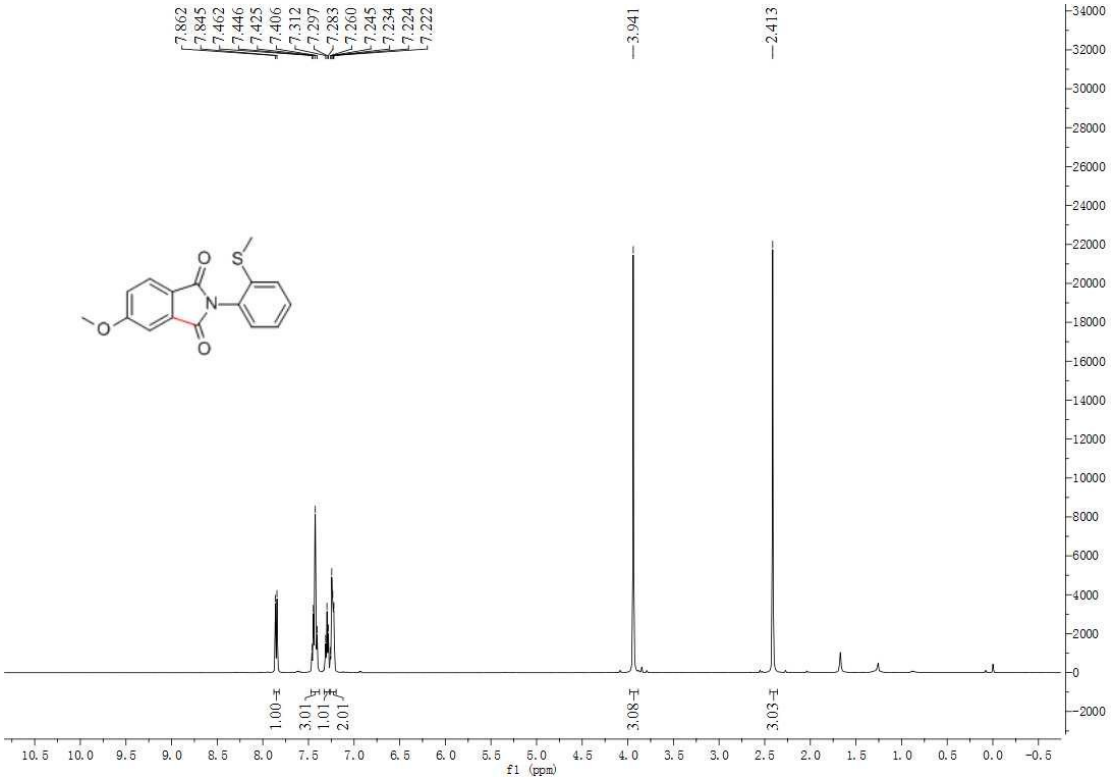
^{13}C NMR:4,6-dimethyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2e)



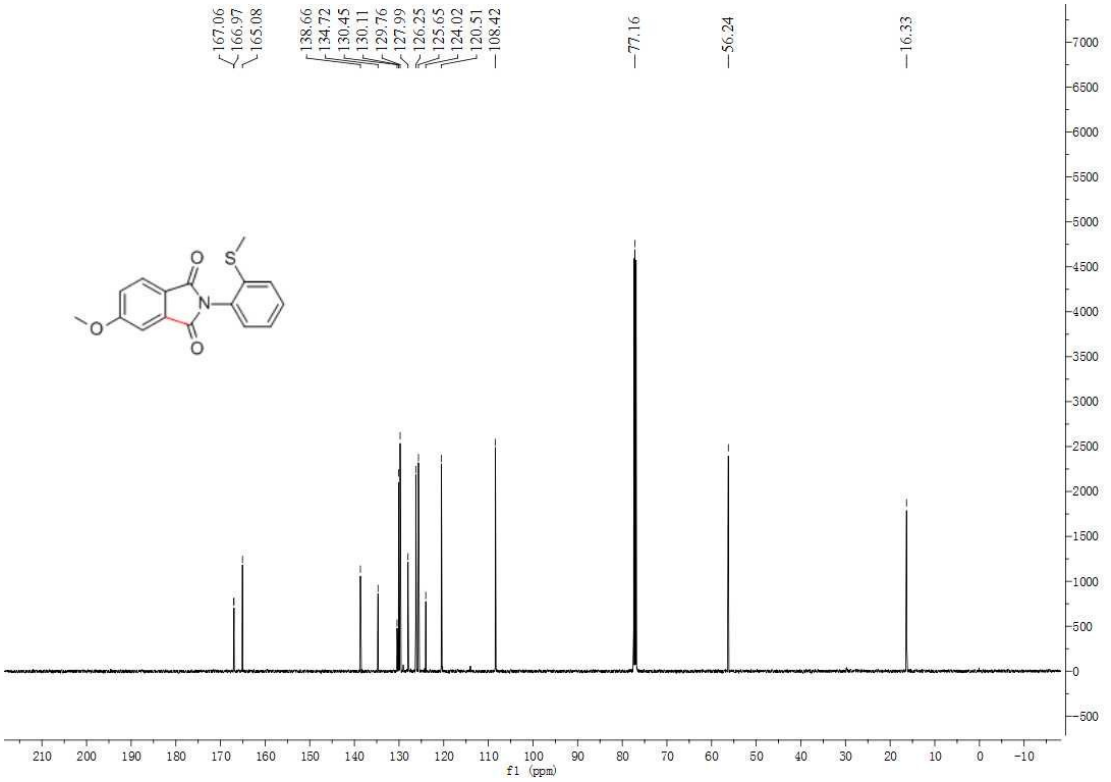
^{1}H NMR:5-ethyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2f)



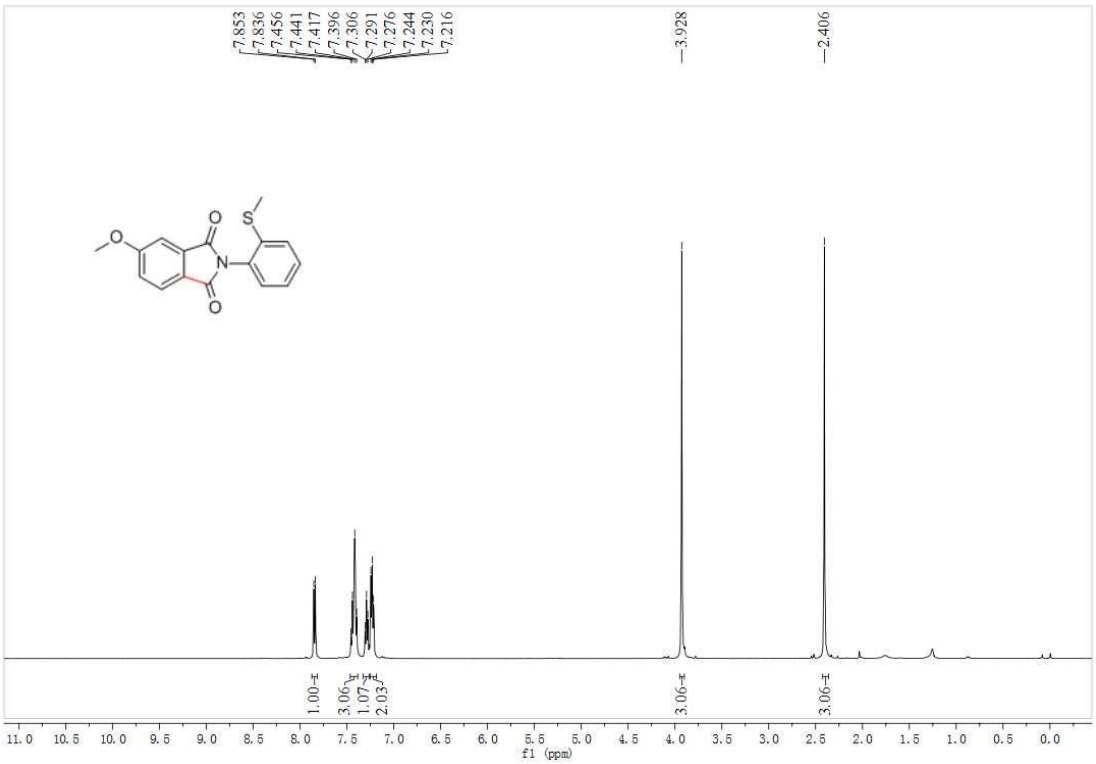
^{13}C NMR:5-ethyl-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2f)



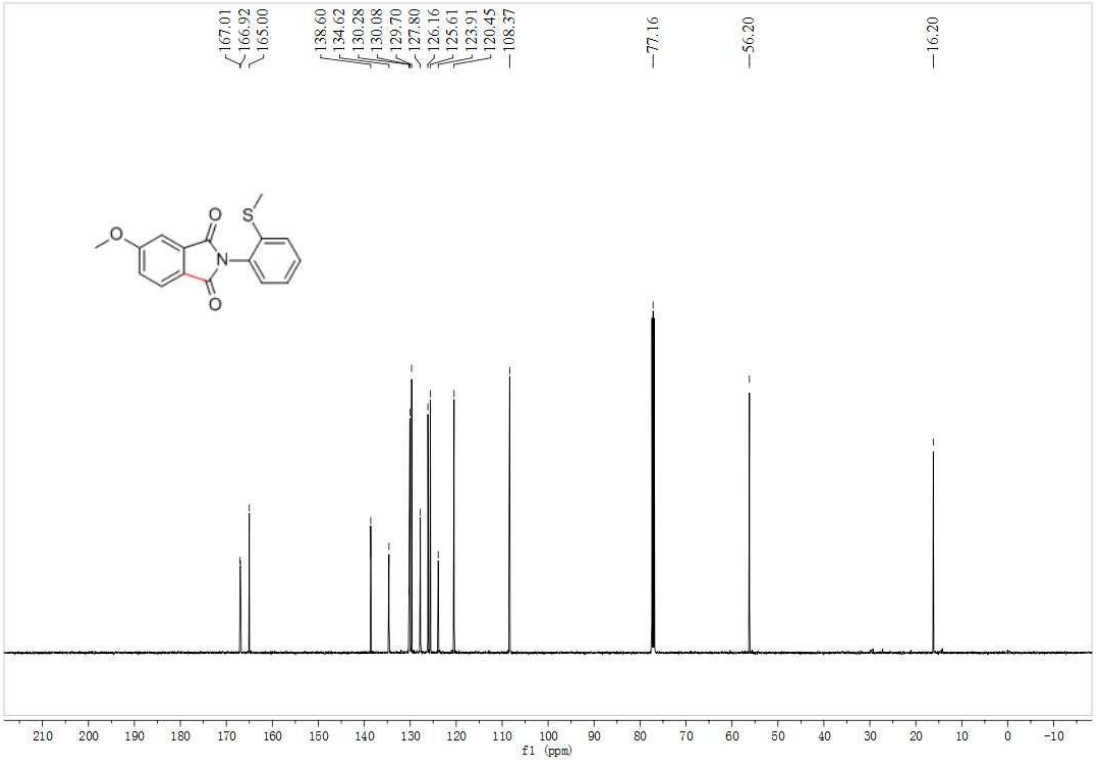
^{1}H NMR:5-methoxy-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2g)



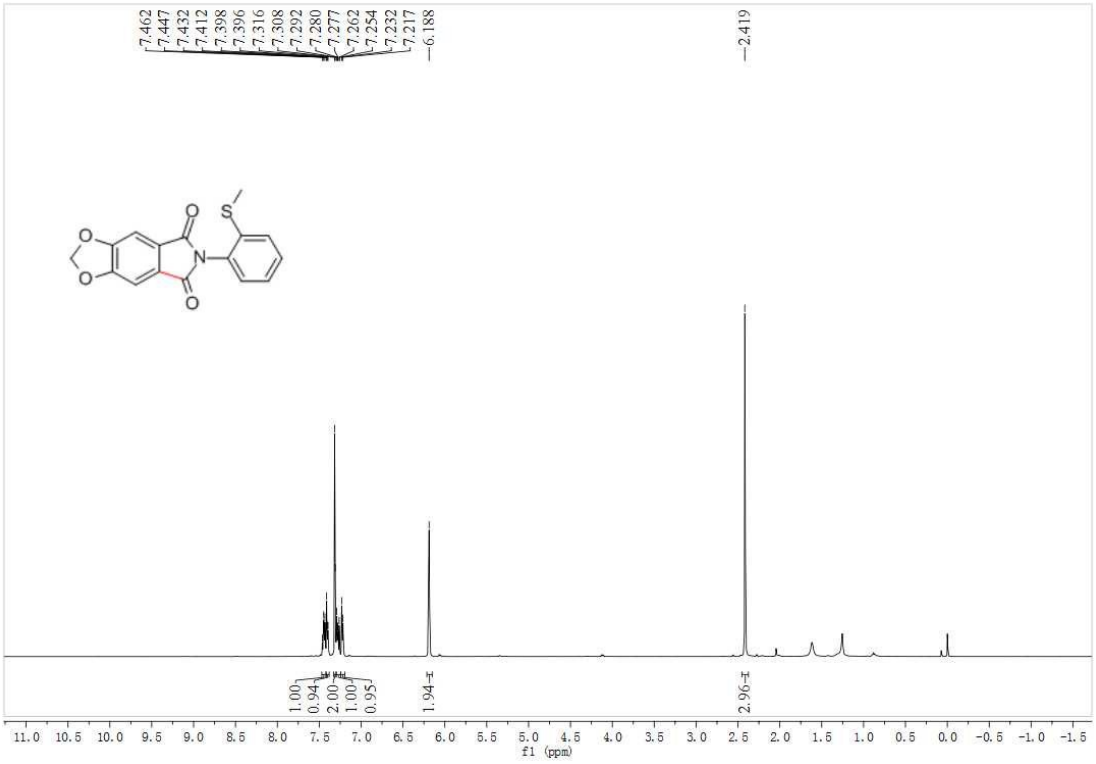
^{13}C NMR:5-methoxy-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2g)



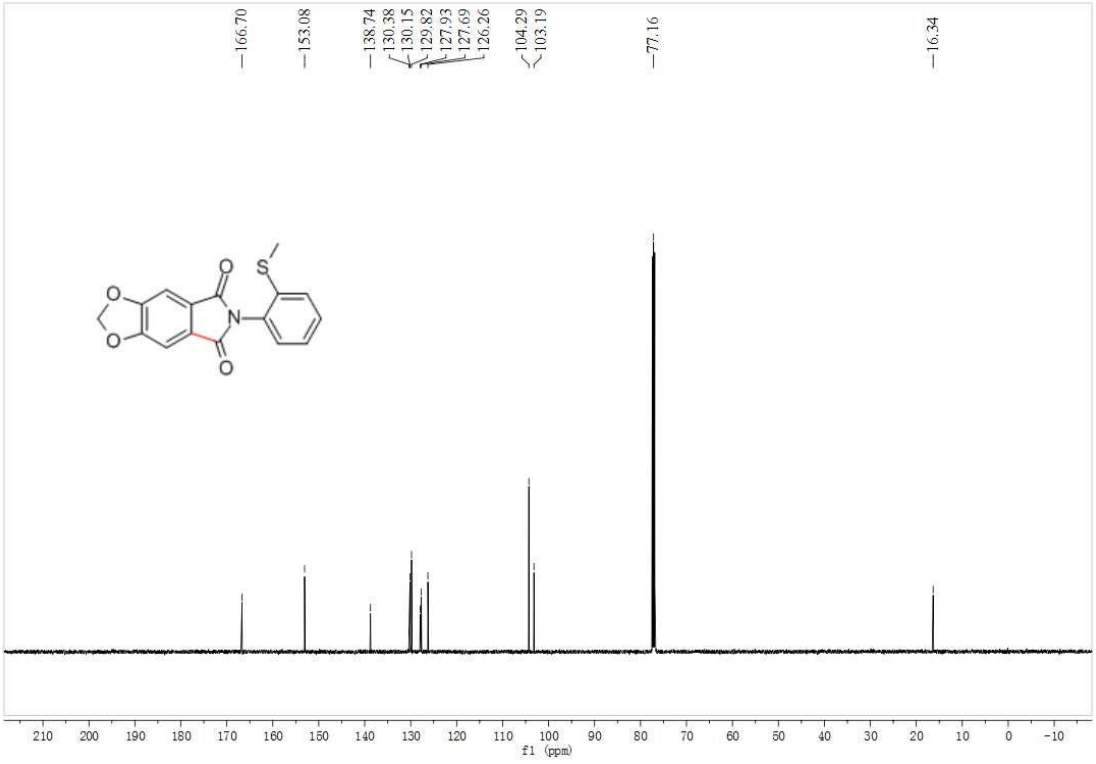
^{1}H NMR:5-methoxy-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2h)



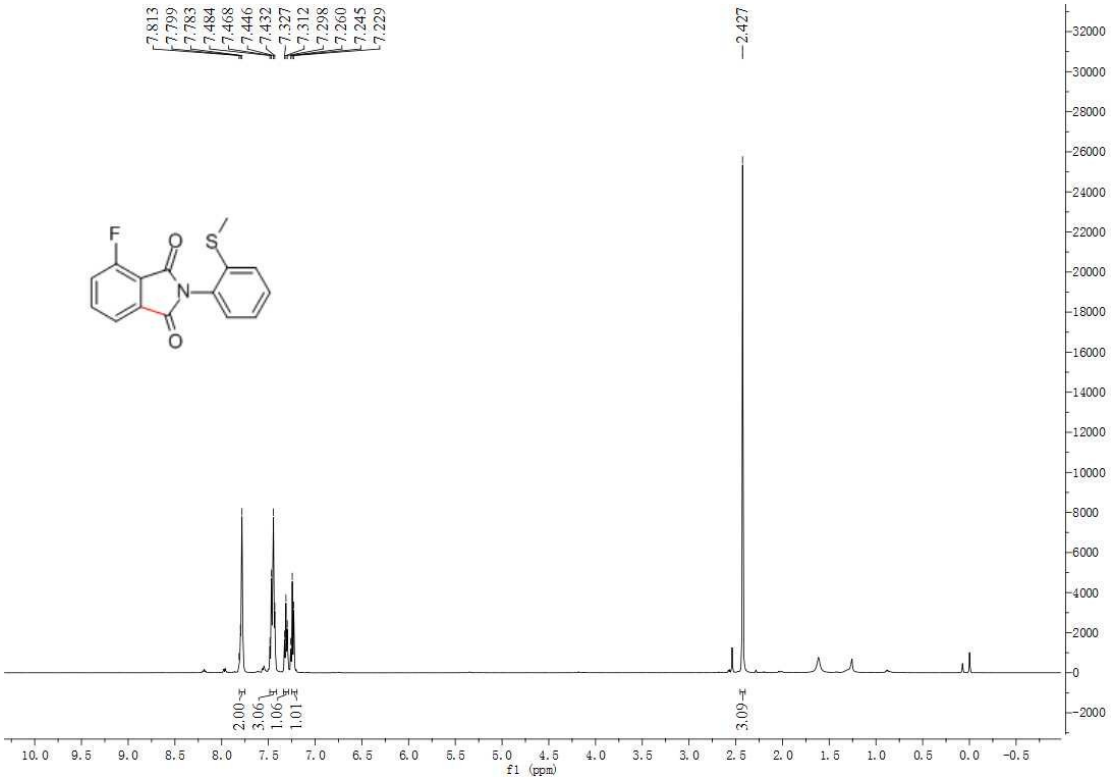
^{13}C NMR:5-methoxy-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2h)



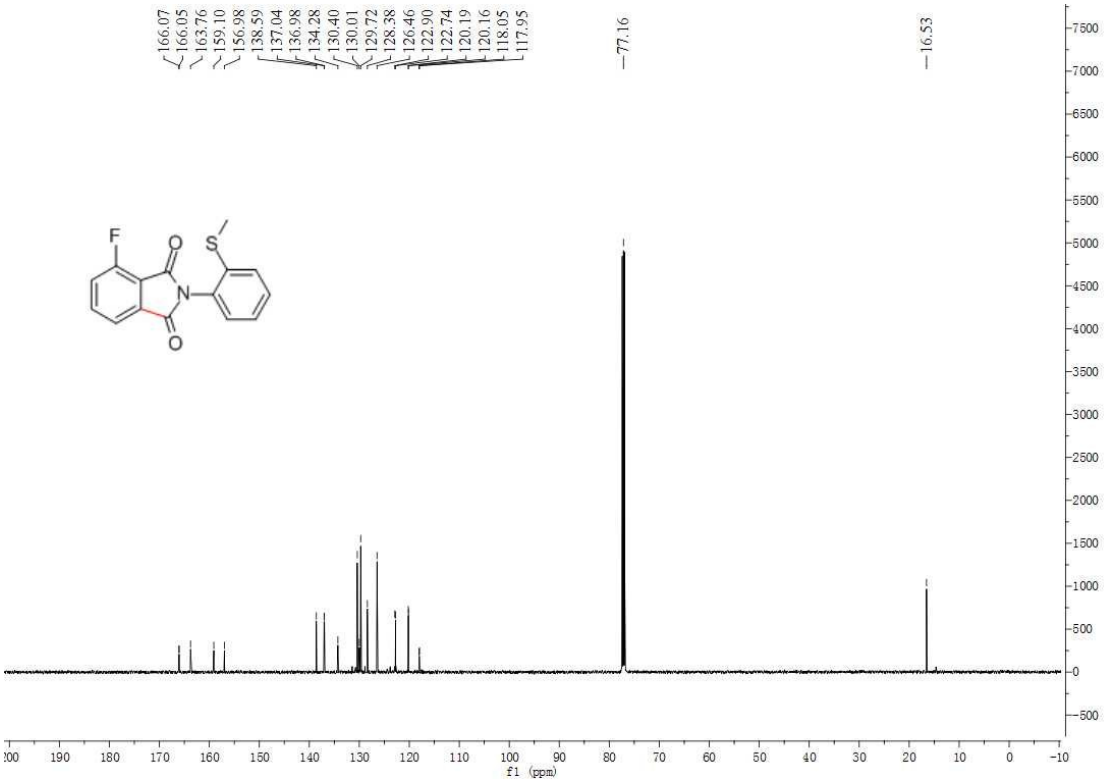
[1]H NMR:6-(2-(methylthio)phenyl)-5H-[1,3]dioxolo[4,5-f]isoindole-5,7(6H)-dione (2i)



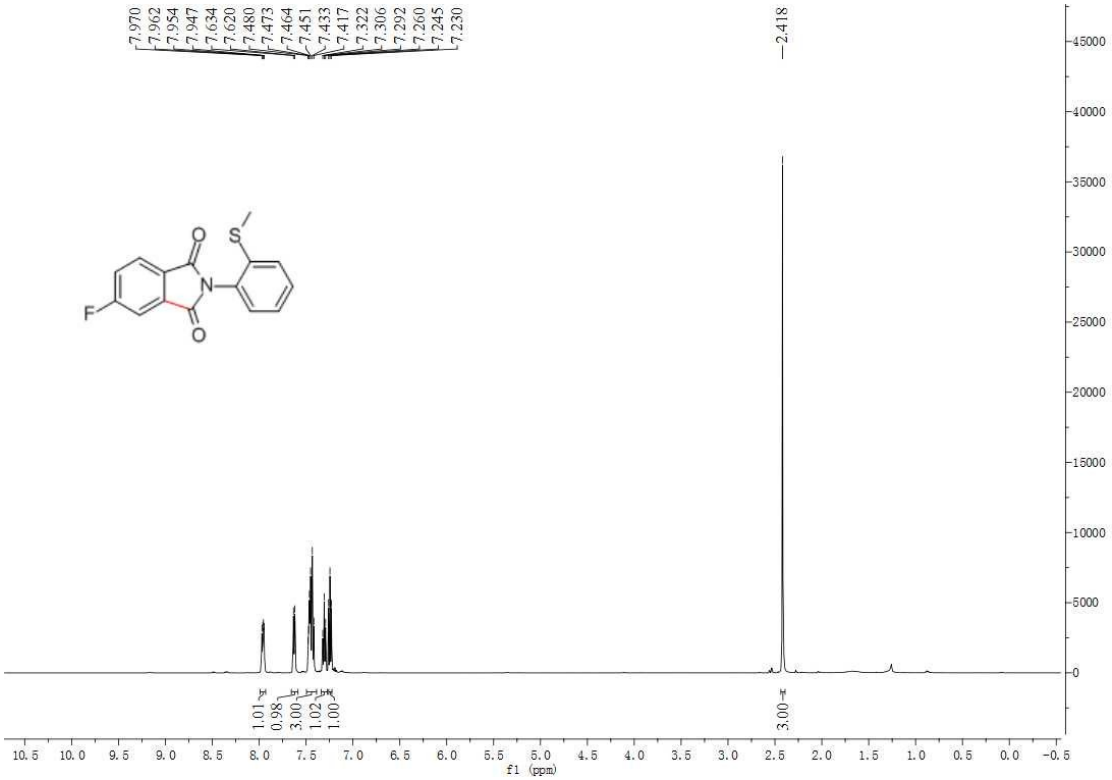
[13]C NMR: 6-(2-(methylthio)phenyl)-5H-[1,3]dioxolo[4,5-f]isoindole-5,7(6H)-dione (2i)



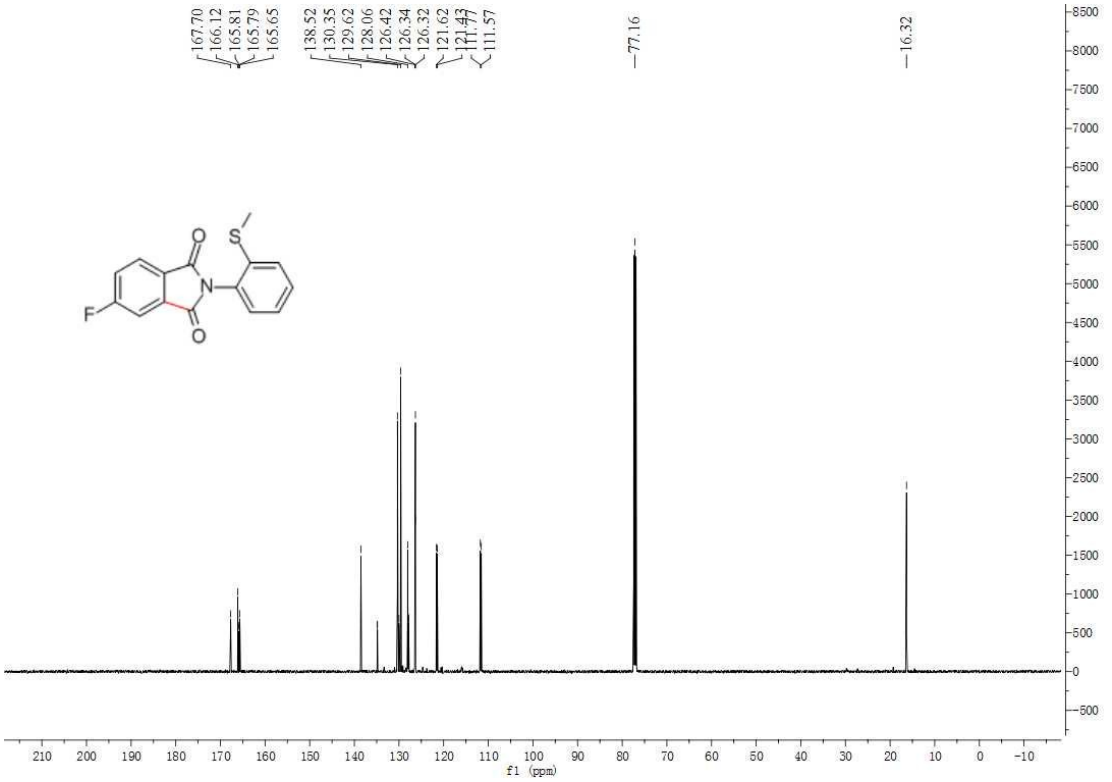
^{1}H NMR:4-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2j)



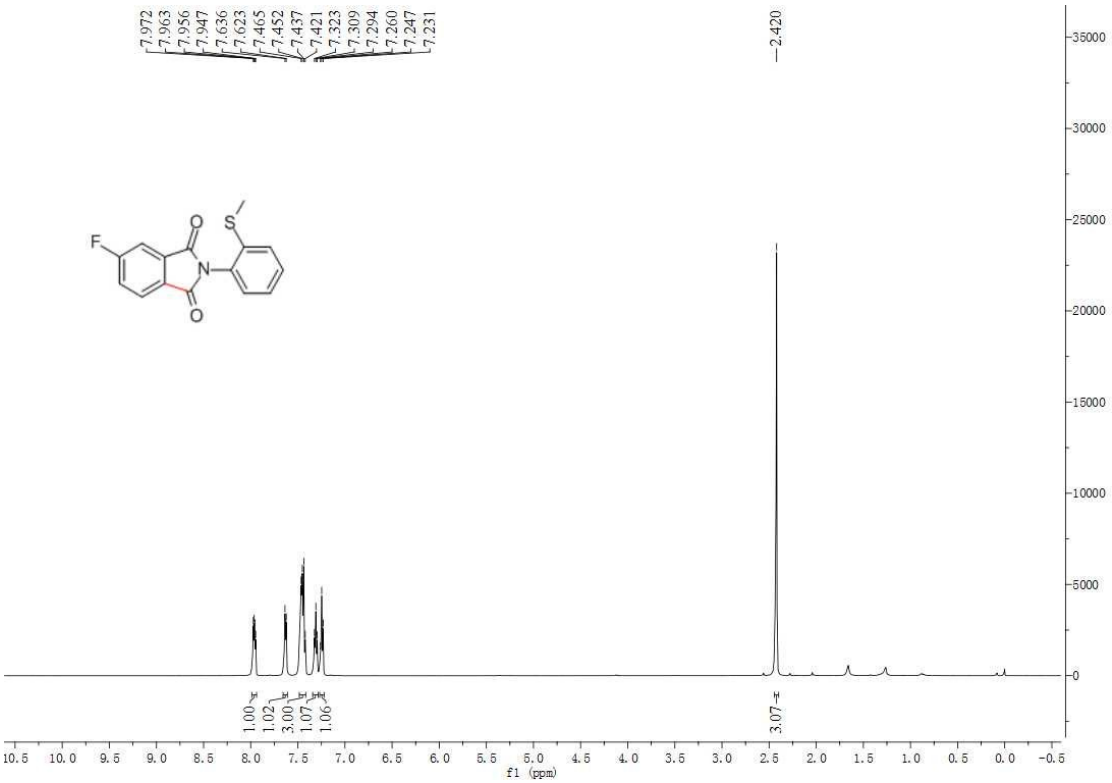
^{13}C NMR:4-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2j)



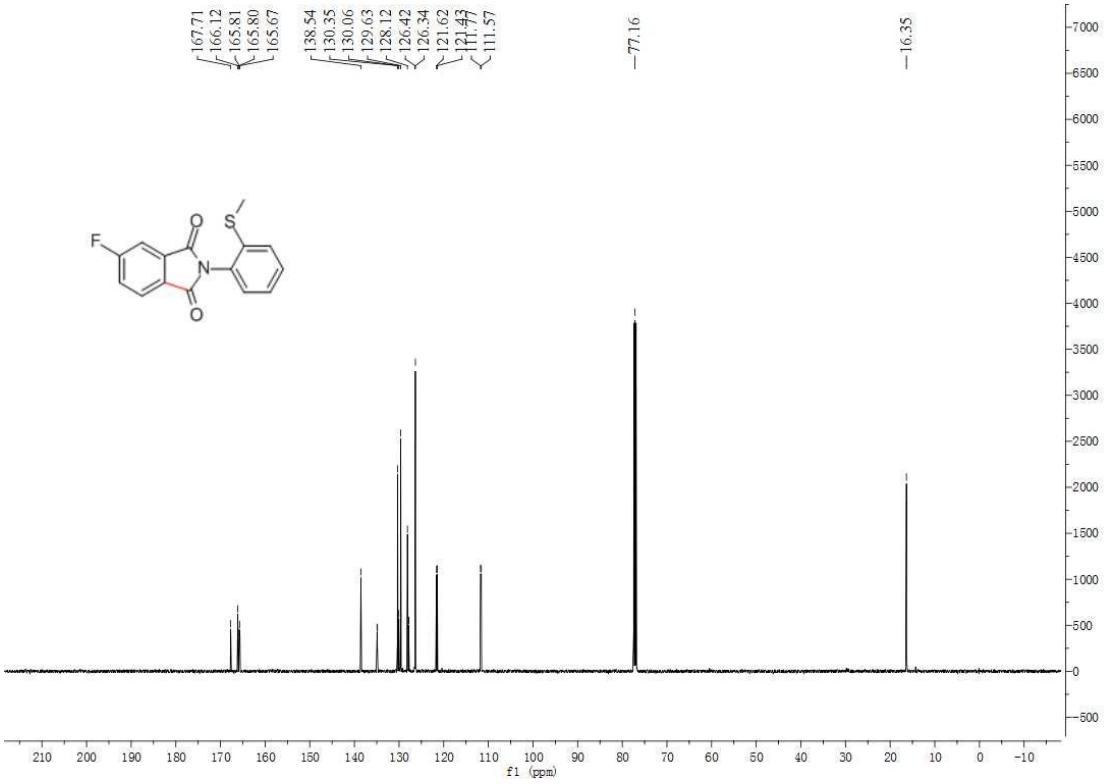
^{1}H NMR:5-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2k)



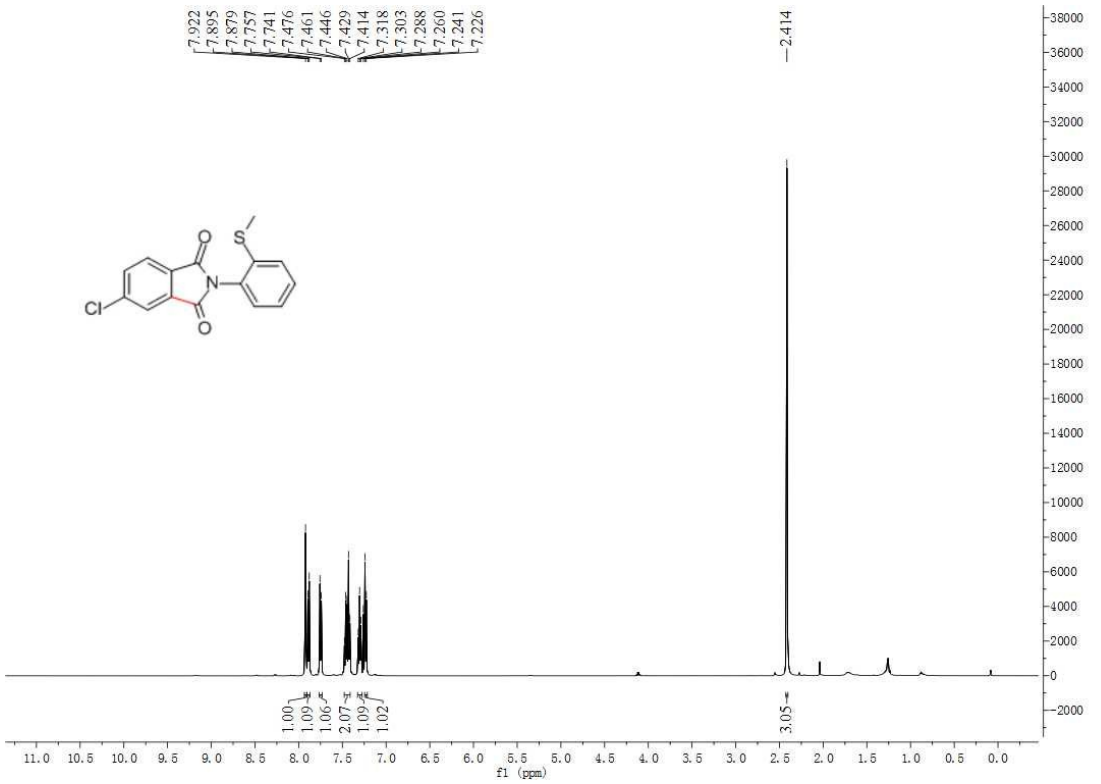
^{13}C NMR: 5-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2k)



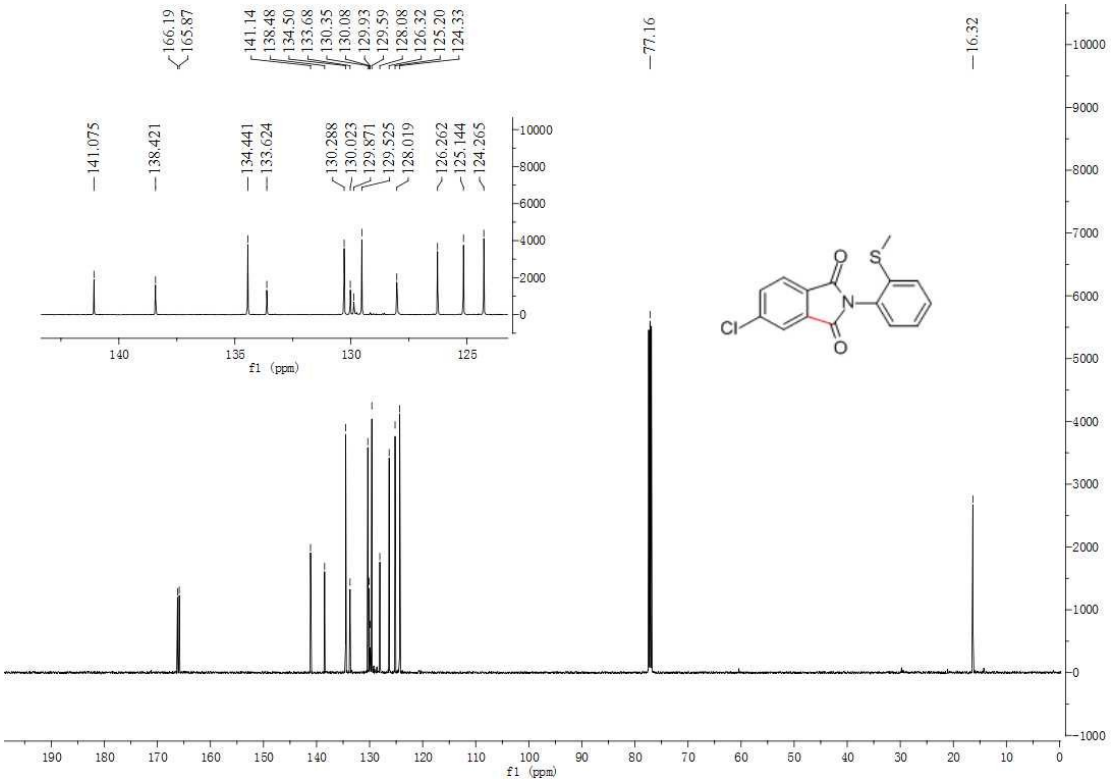
^{1}H NMR:5-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2l)



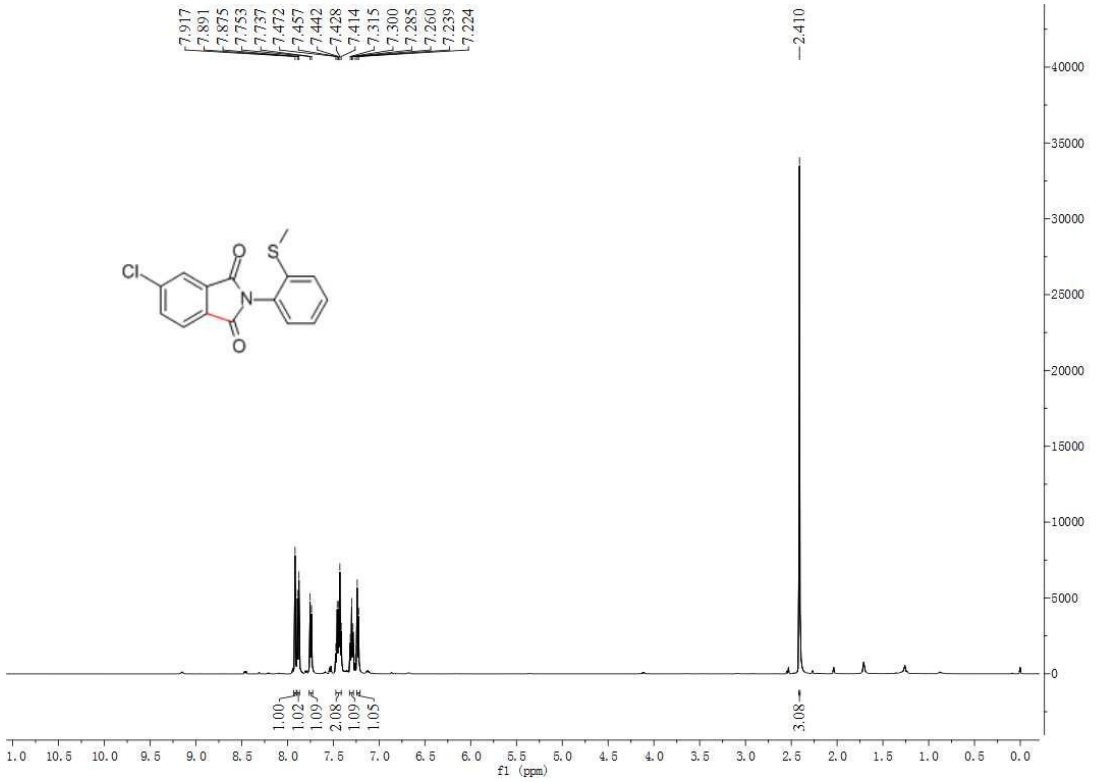
^{13}C NMR: 5-fluoro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2l)



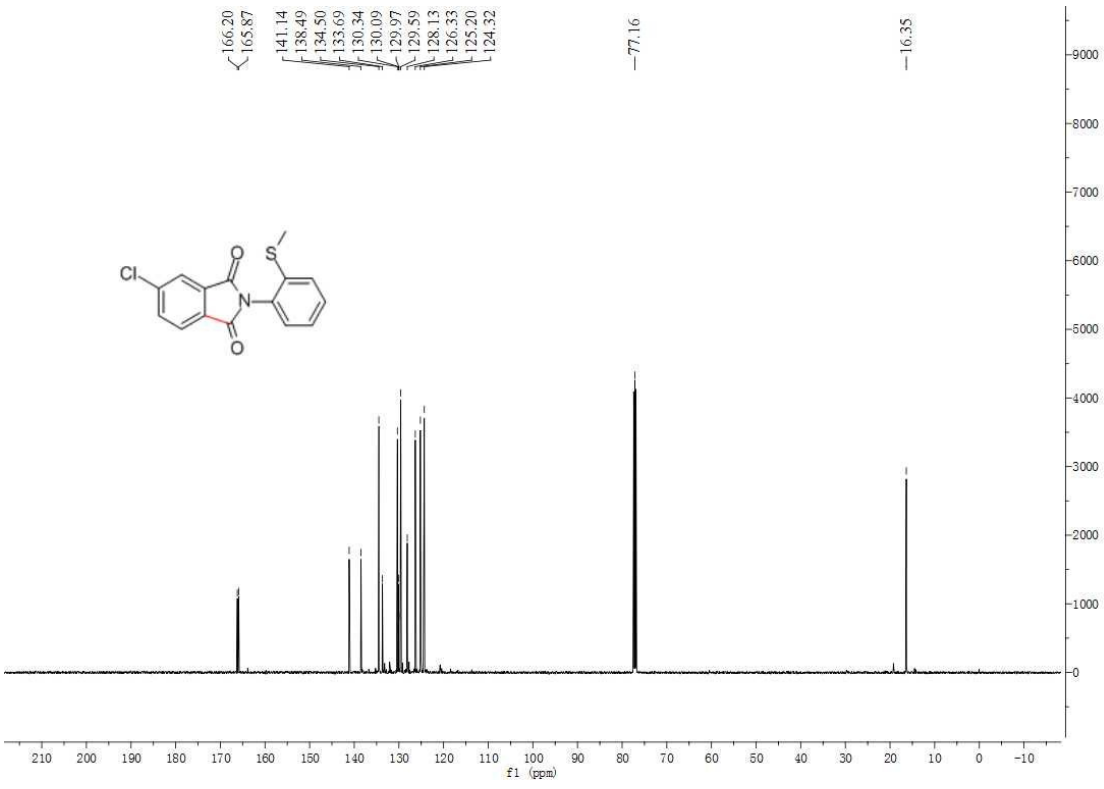
^{1}H NMR:5-chloro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2m)



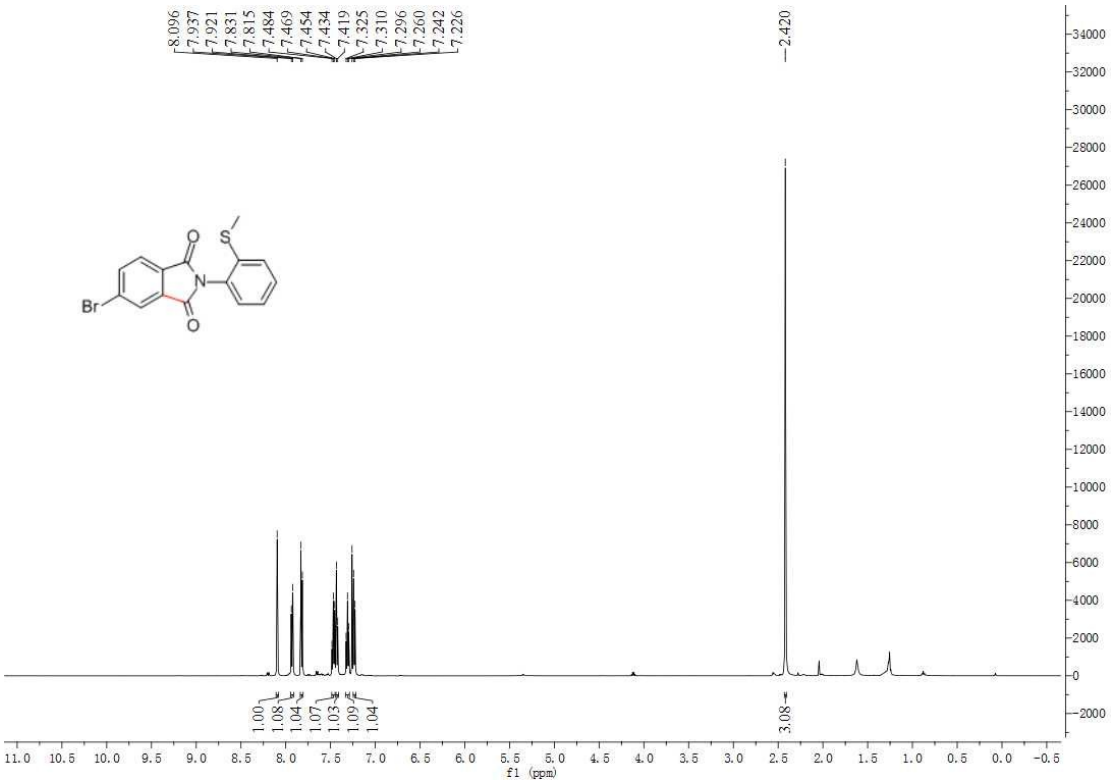
^{13}C NMR:5-chloro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2m)



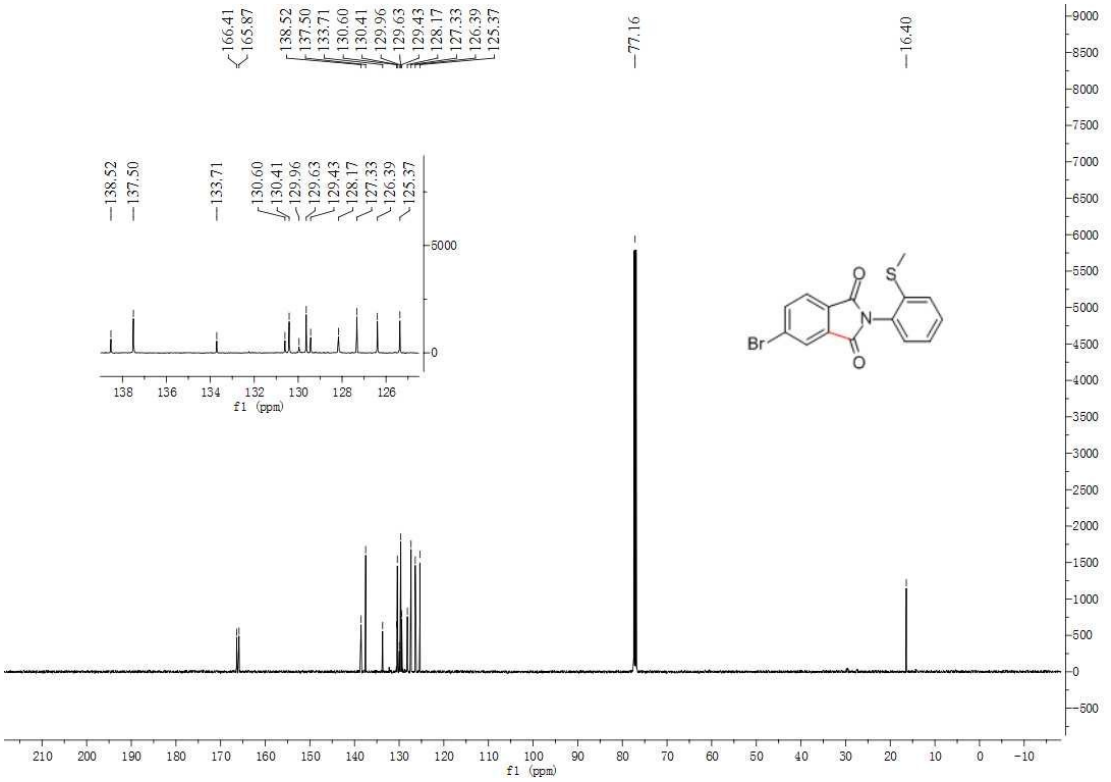
^{1}H NMR:5-chloro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2n)



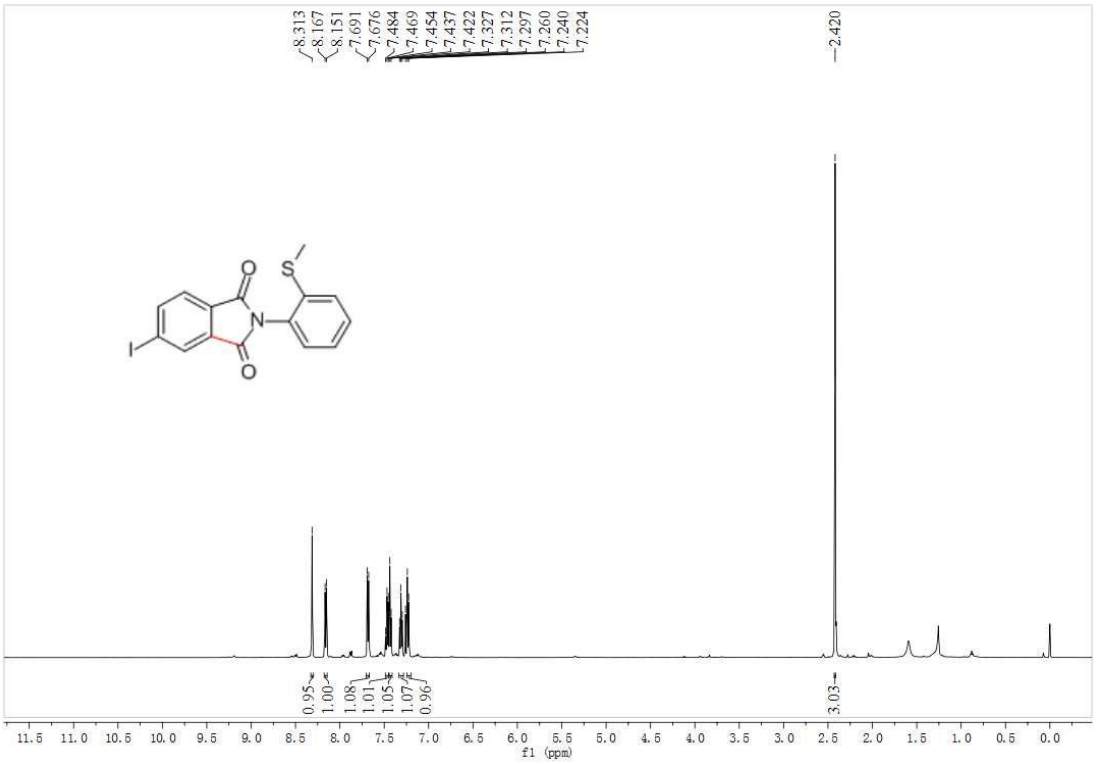
^{13}C NMR:5-chloro-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2n)



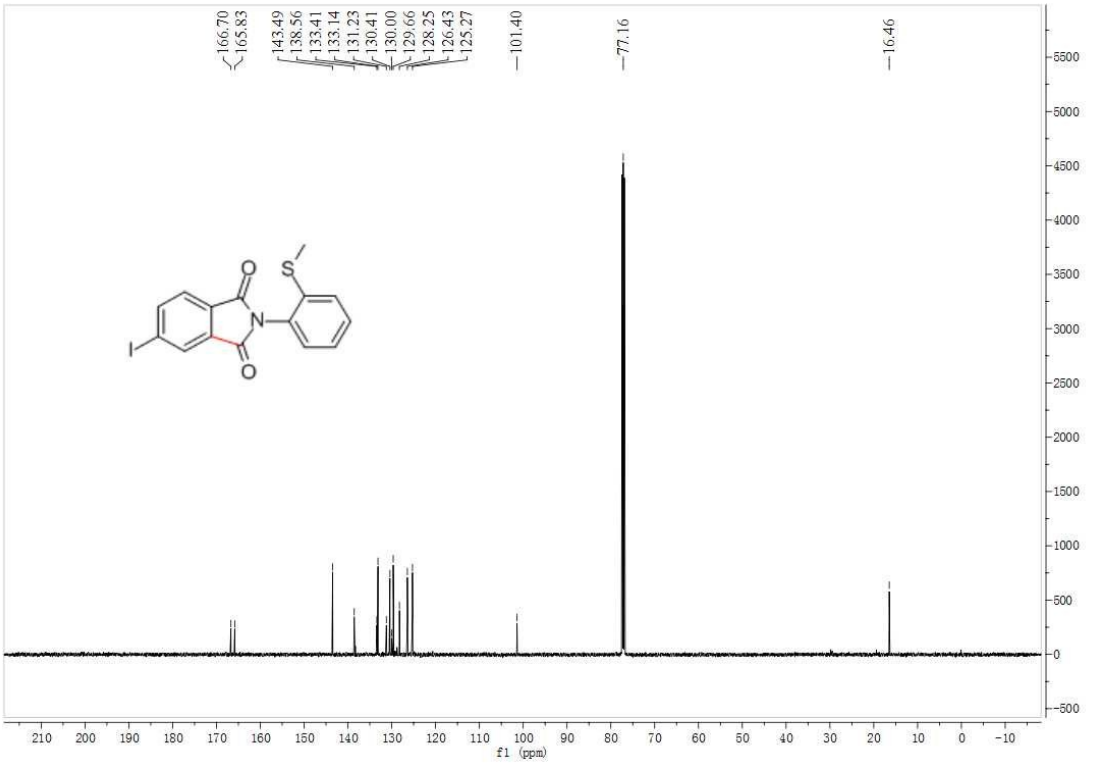
^{1}H NMR:5-bromo-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2o)



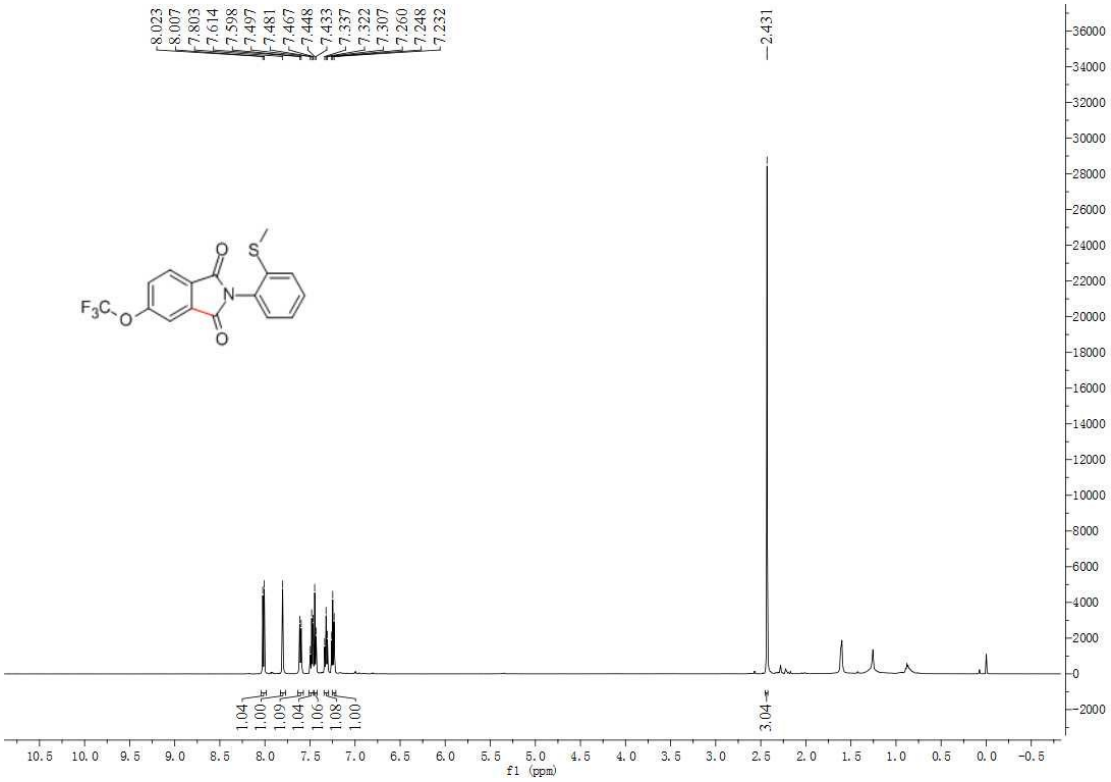
^{13}C NMR: 5-bromo-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2o)



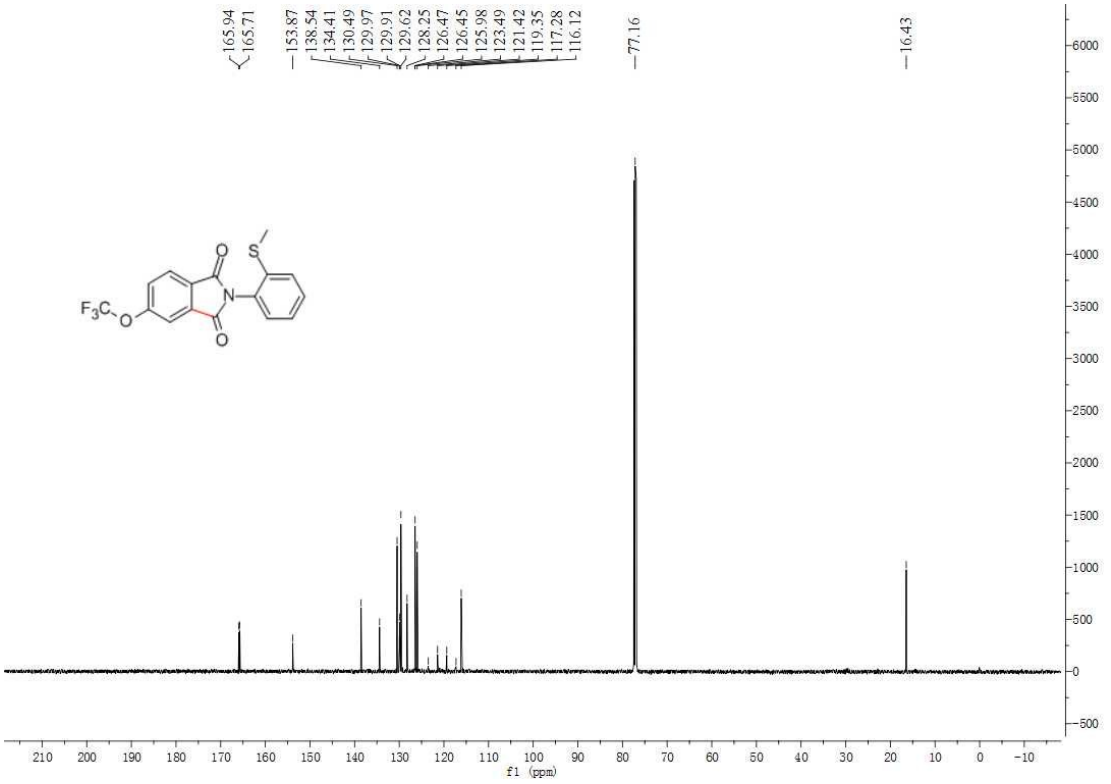
^{1}H NMR: 5-iodo-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2p)



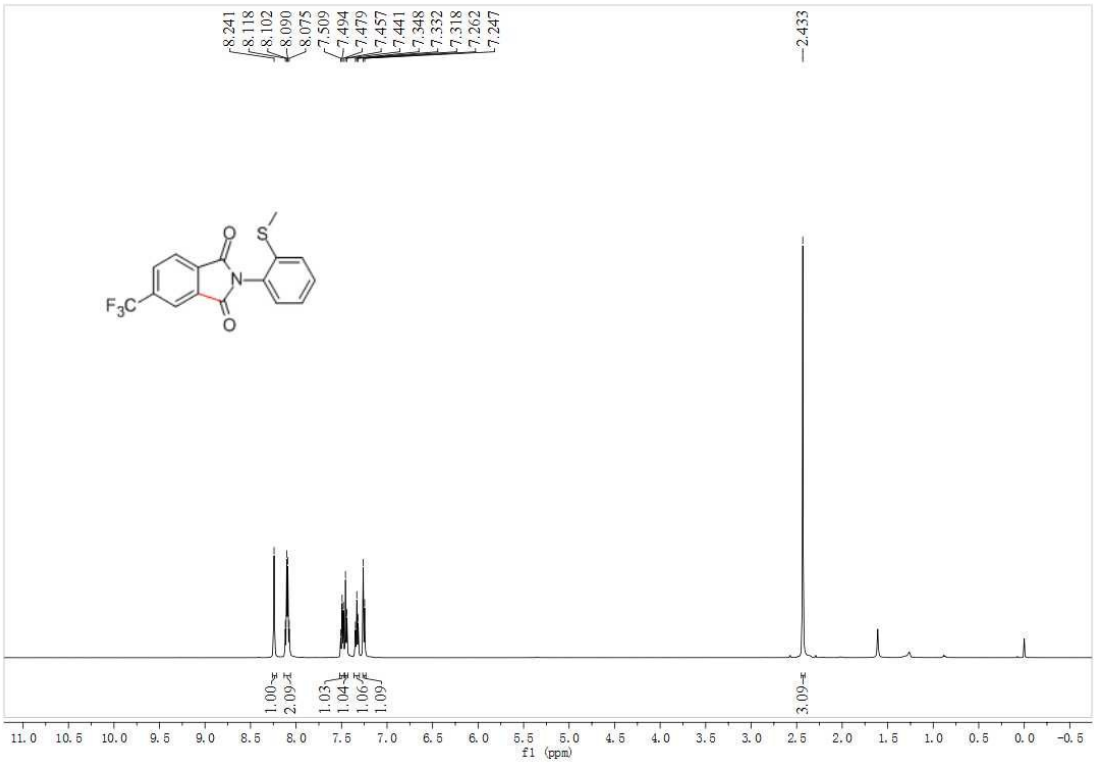
^{13}C NMR: 5-iodo-2-(2-(methylthio)phenyl)isoindoline-1,3-dione (2p)



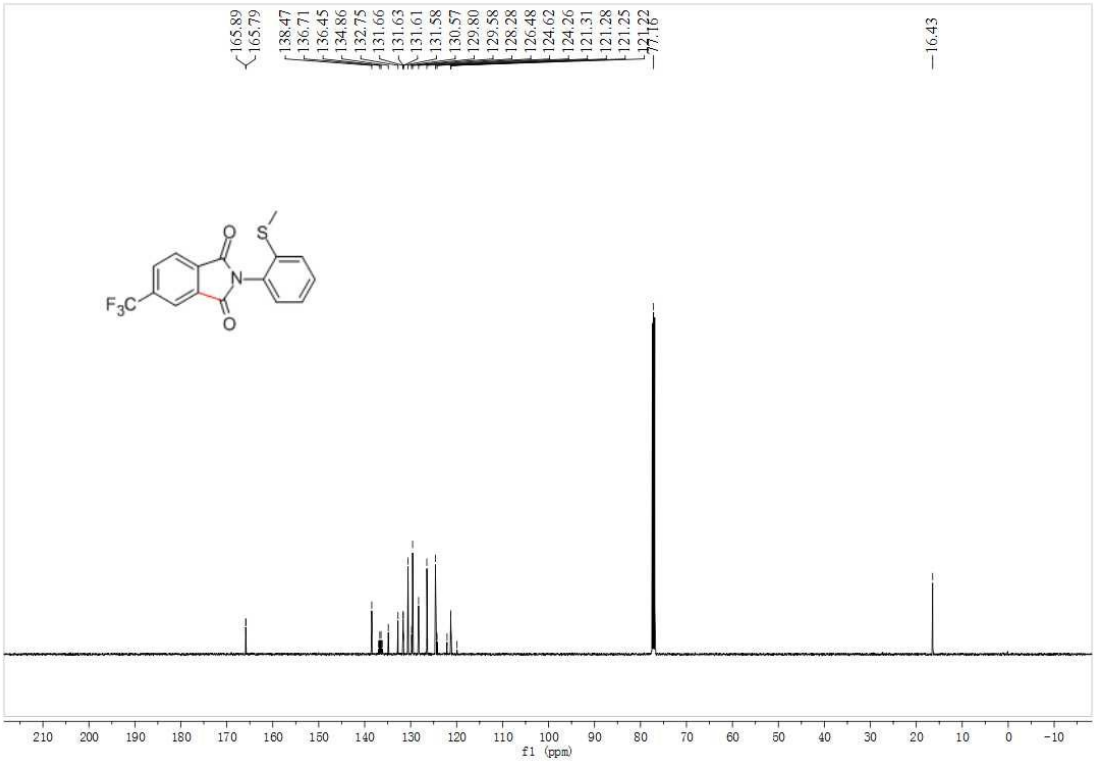
[1]H NMR:2-(2-(methylthio)phenyl)-5-(trifluoromethoxy)isoindoline-1,3-dione (2q)



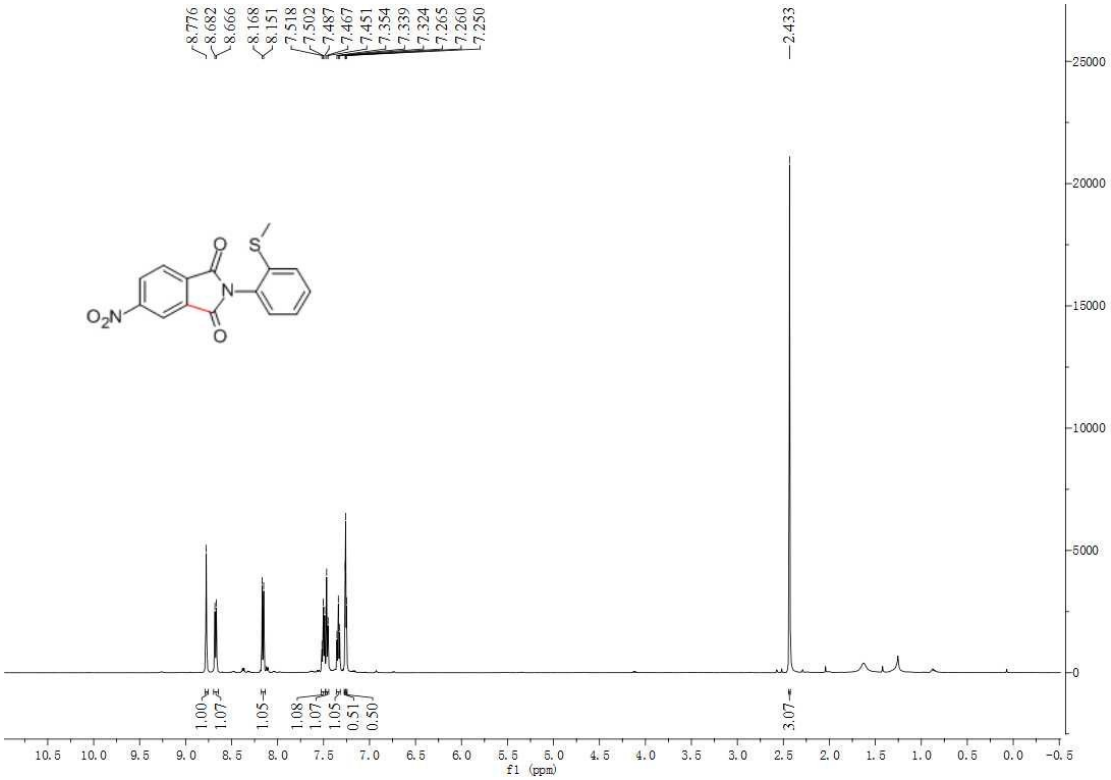
[13]C NMR: 2-(2-(methylthio)phenyl)-5-(trifluoromethoxy)isoindoline-1,3-dione (2q)



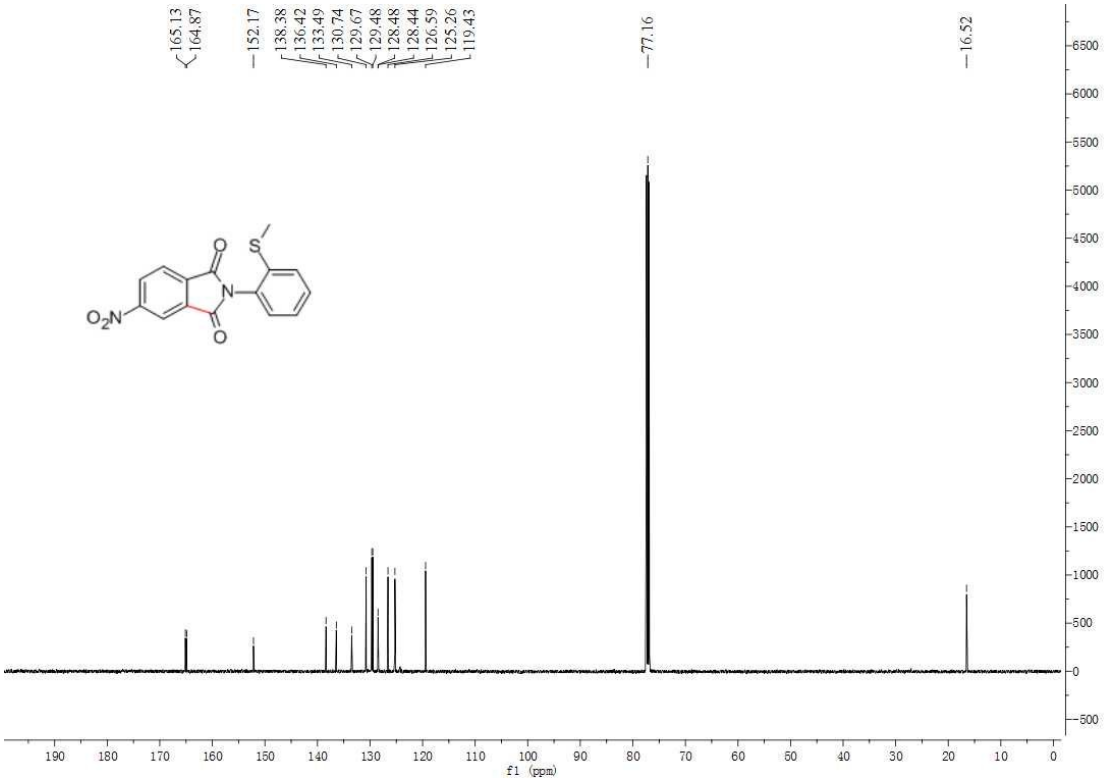
^{1}H NMR:2-(2-(methylthio)phenyl)-5-(trifluoromethyl)isoindoline-1,3-dione(2r)



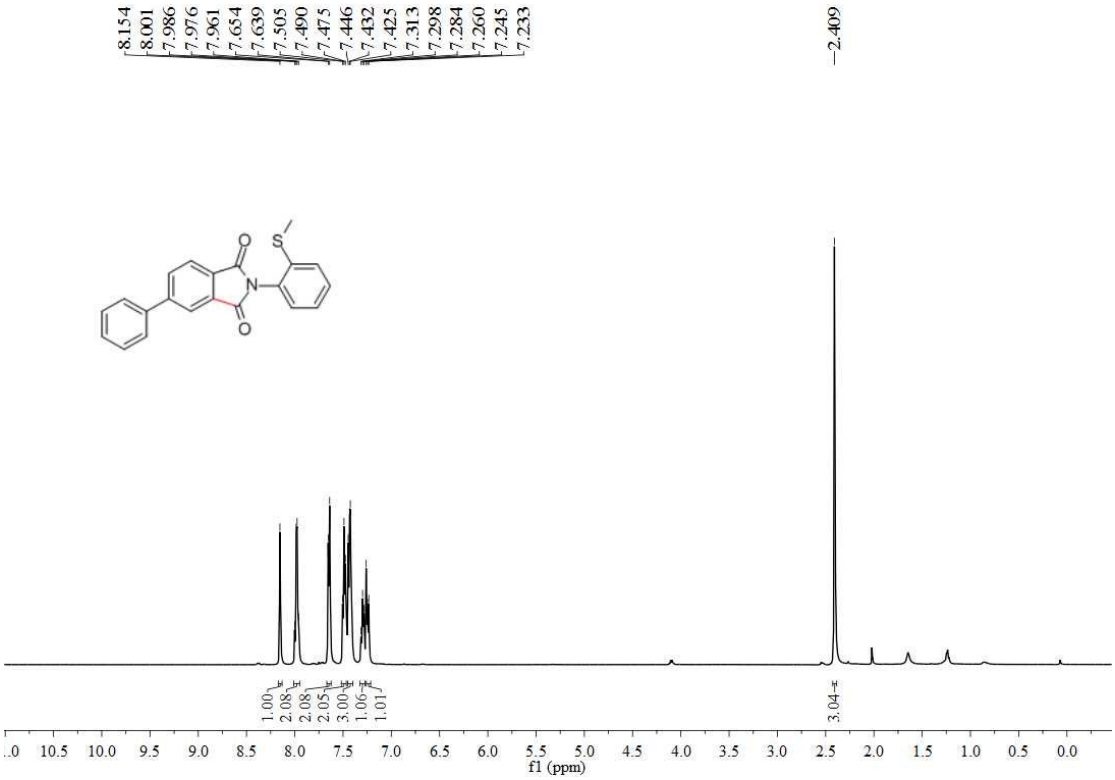
^{13}C NMR:2-(2-(methylthio)phenyl)-5-(trifluoromethyl)isoindoline-1,3-dione(2r)



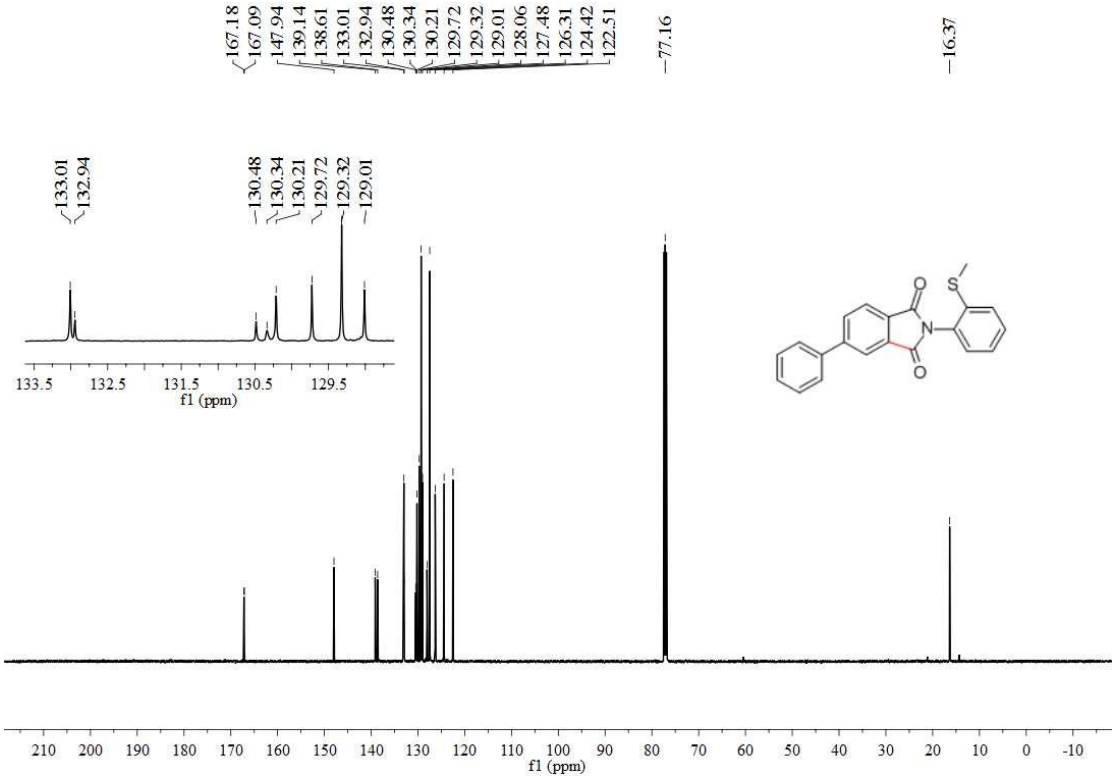
^{1}H NMR:2-(2-(methylthio)phenyl)-5-nitroisoindoline-1,3-dione (2s)



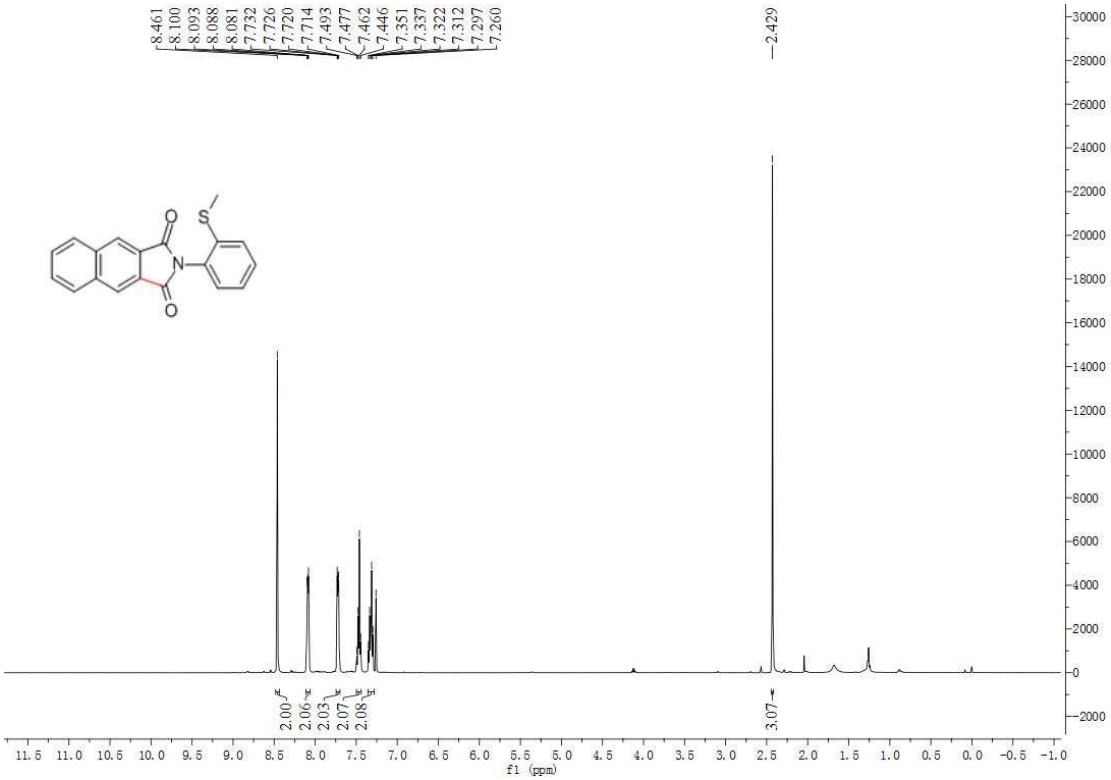
^{13}C NMR: 2-(2-(methylthio)phenyl)-5-nitroisoindoline-1,3-dione (2s)



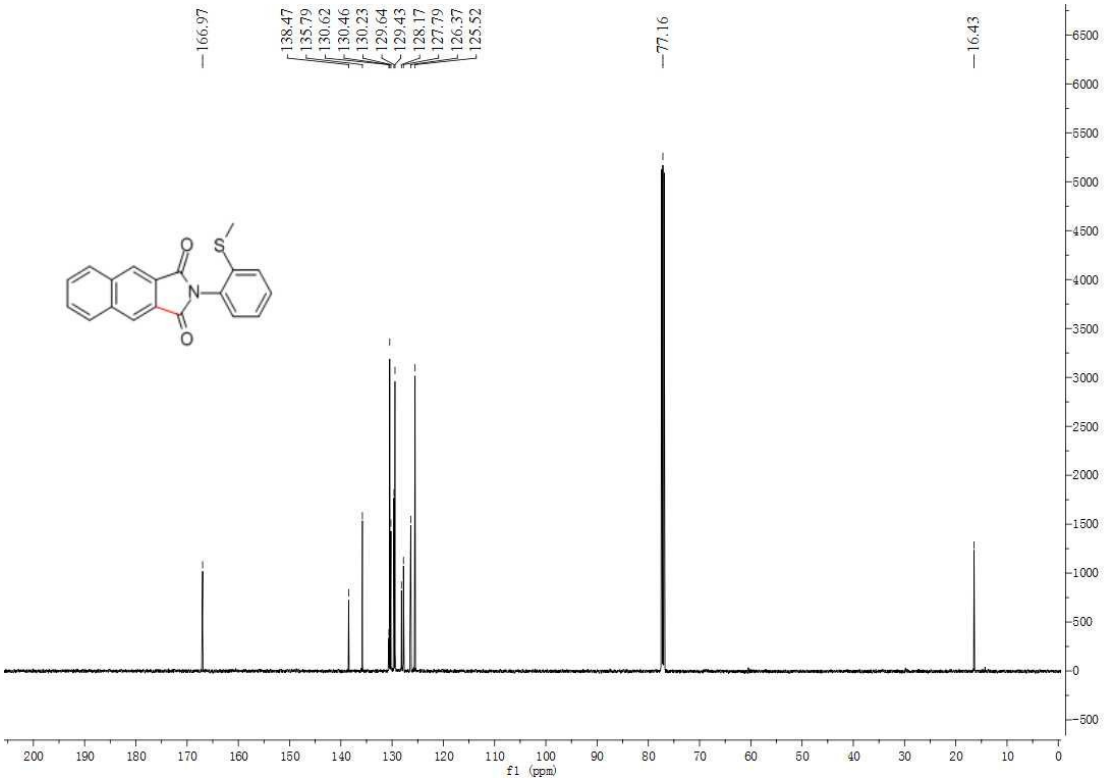
^{1}H NMR:2-(2-(methylthio)phenyl)-5-phenylisoindoline-1,3-dione (2t)



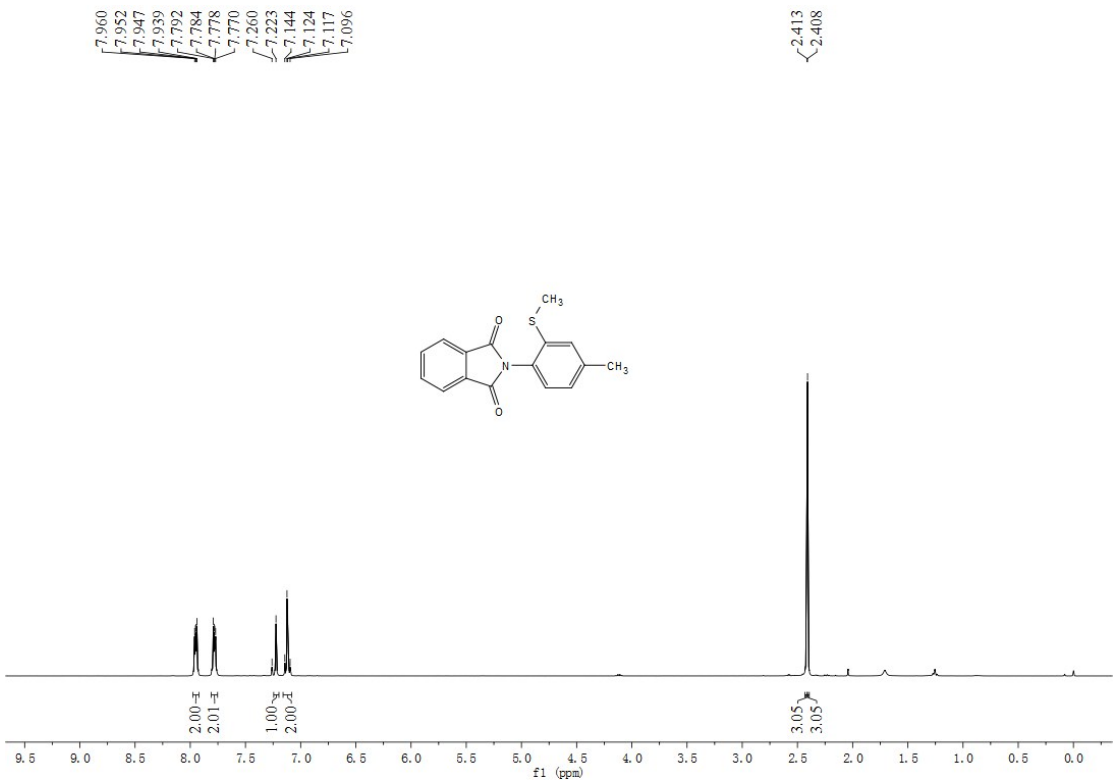
^{13}C NMR:2-(2-(methylthio)phenyl)-5-phenylisoindoline-1,3-dione (2t)



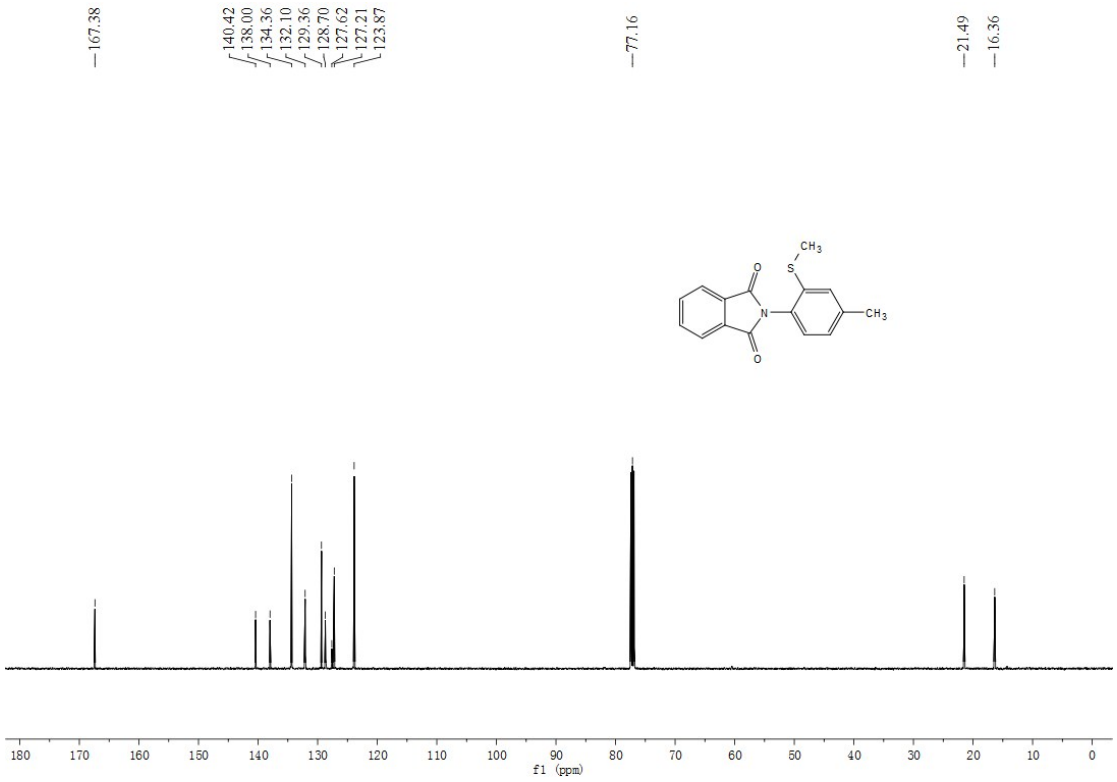
^{1}H NMR: 2-(2-(methylthio)phenyl)-1H-benzo[f]isoindole-1,3(2H)-dione (2u)



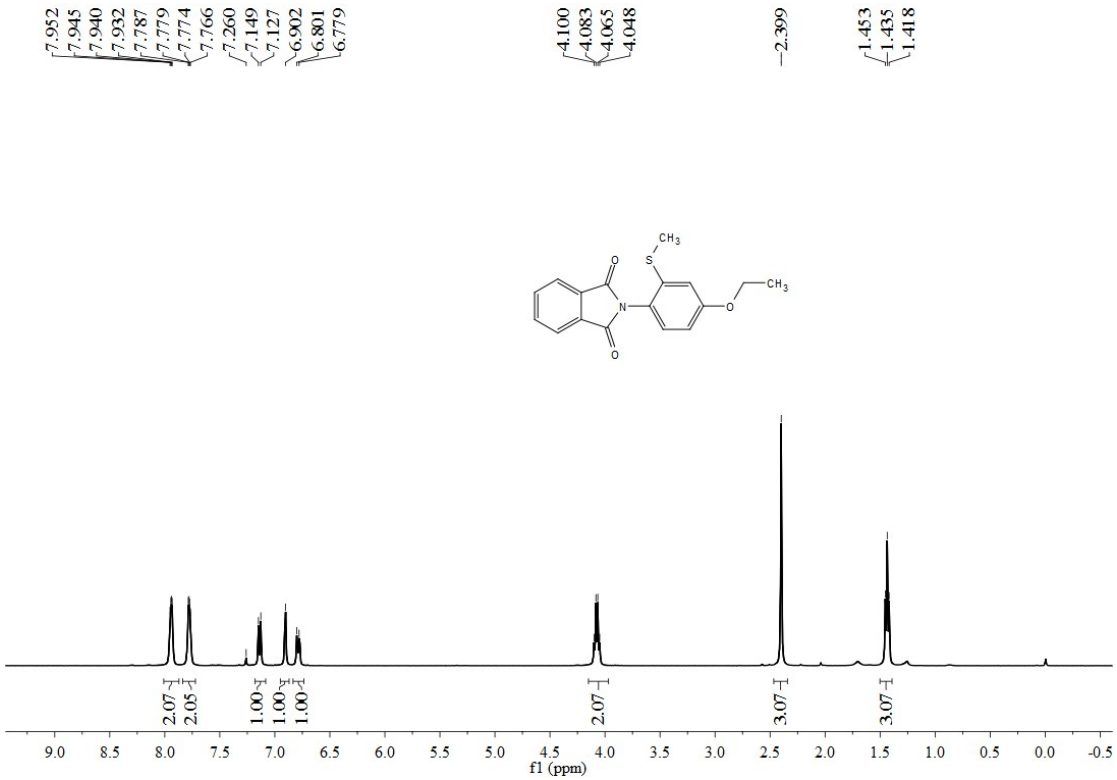
^{13}C NMR: 2-(2-(methylthio)phenyl)-1H-benzo[f]isoindole-1,3(2H)-dione (2u)



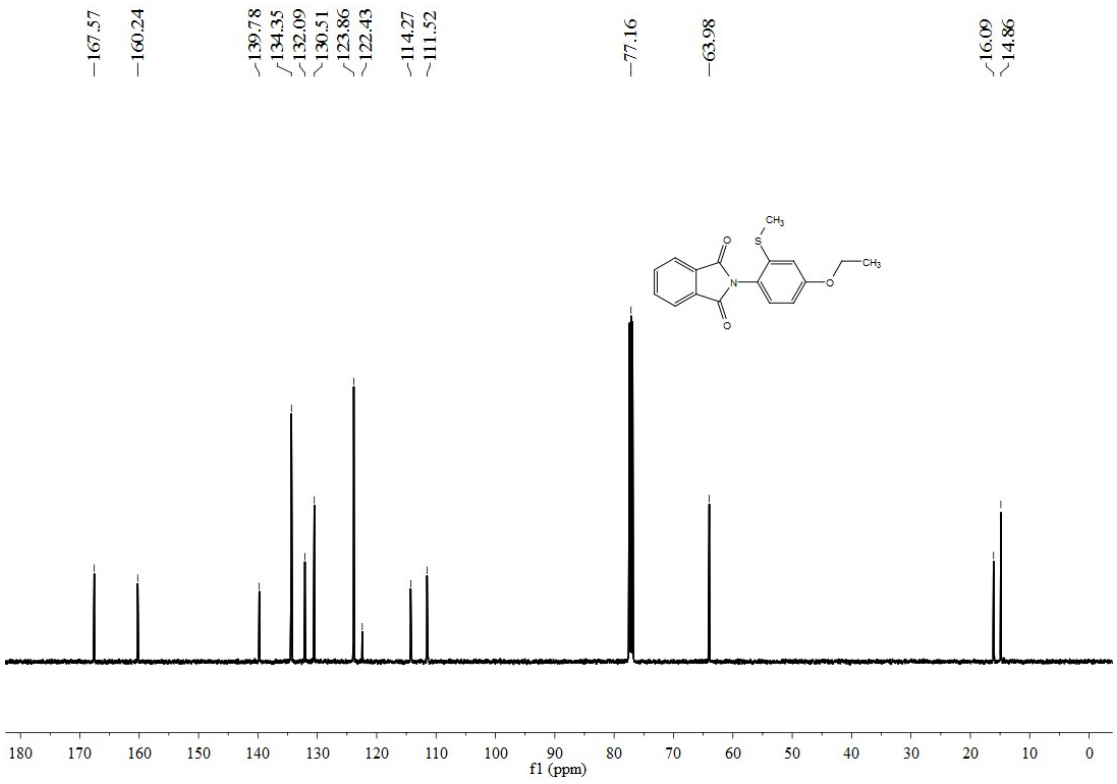
^{1}H NMR: 2-(4-methyl-2-(methylthio)phenyl)isoindoline-1,3-dione (4a)



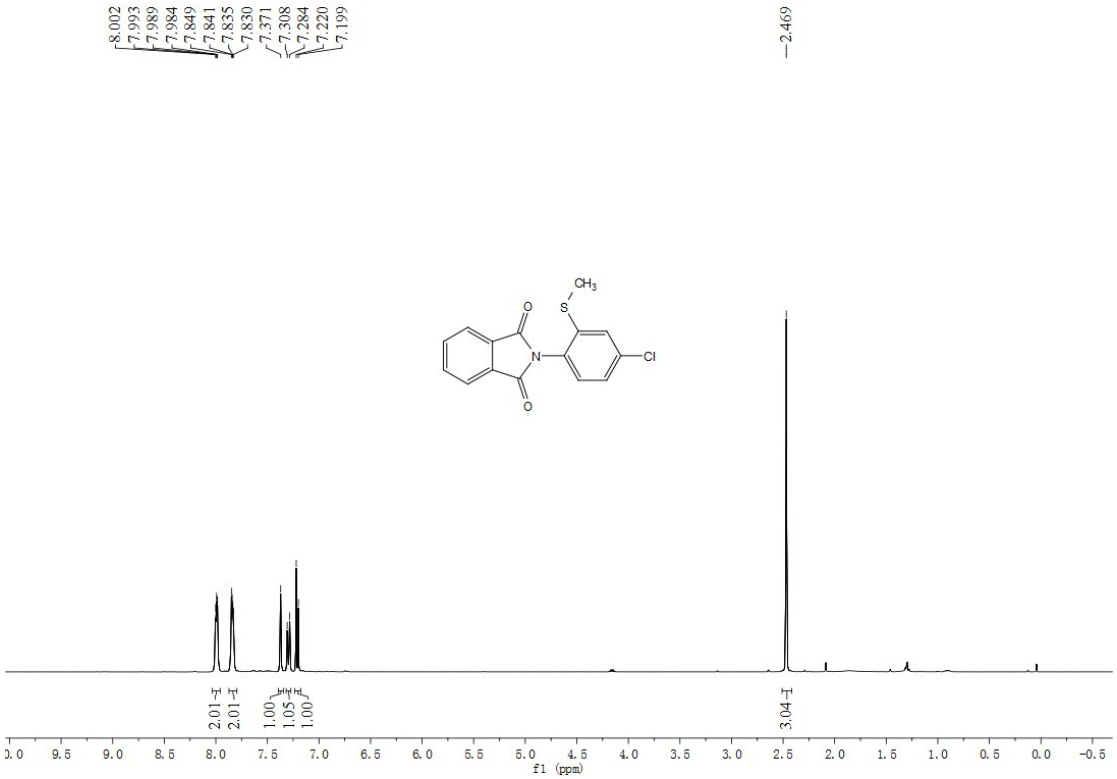
^{13}C NMR: 2-(4-methyl-2-(methylthio)phenyl)isoindoline-1,3-dione (4a)



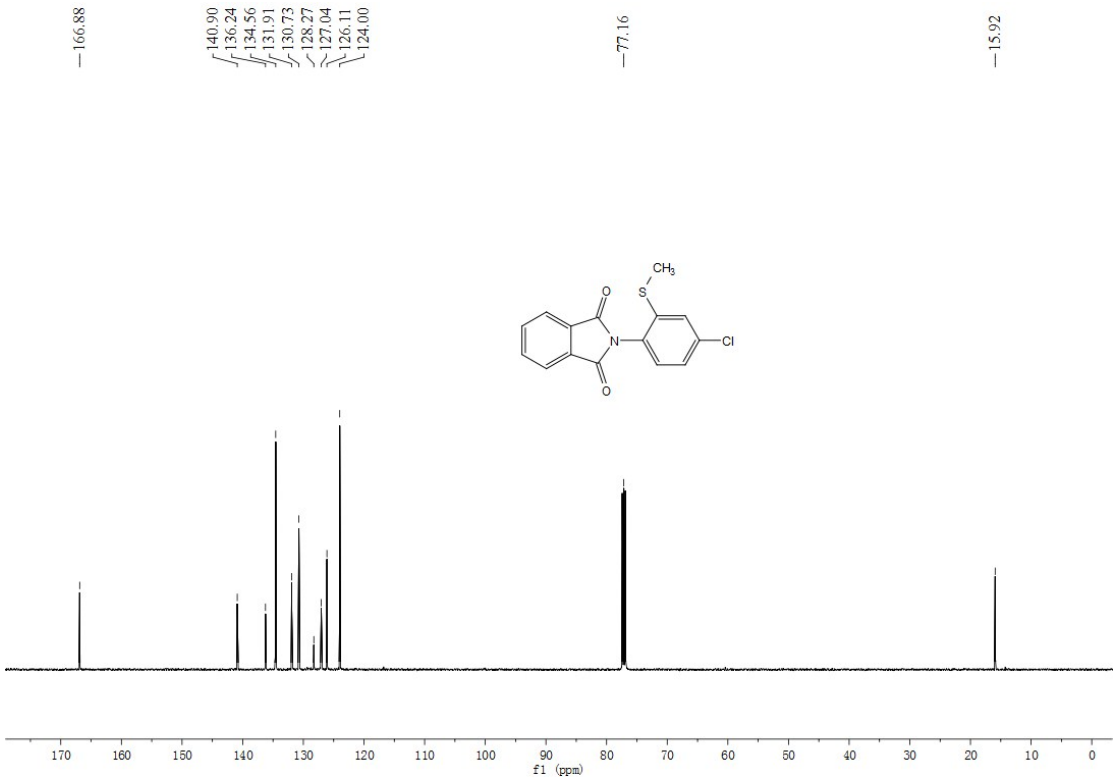
^{1}H NMR: 2-(4-ethoxy-2-(methylthio)phenyl)isoindoline-1,3-dione (4b)



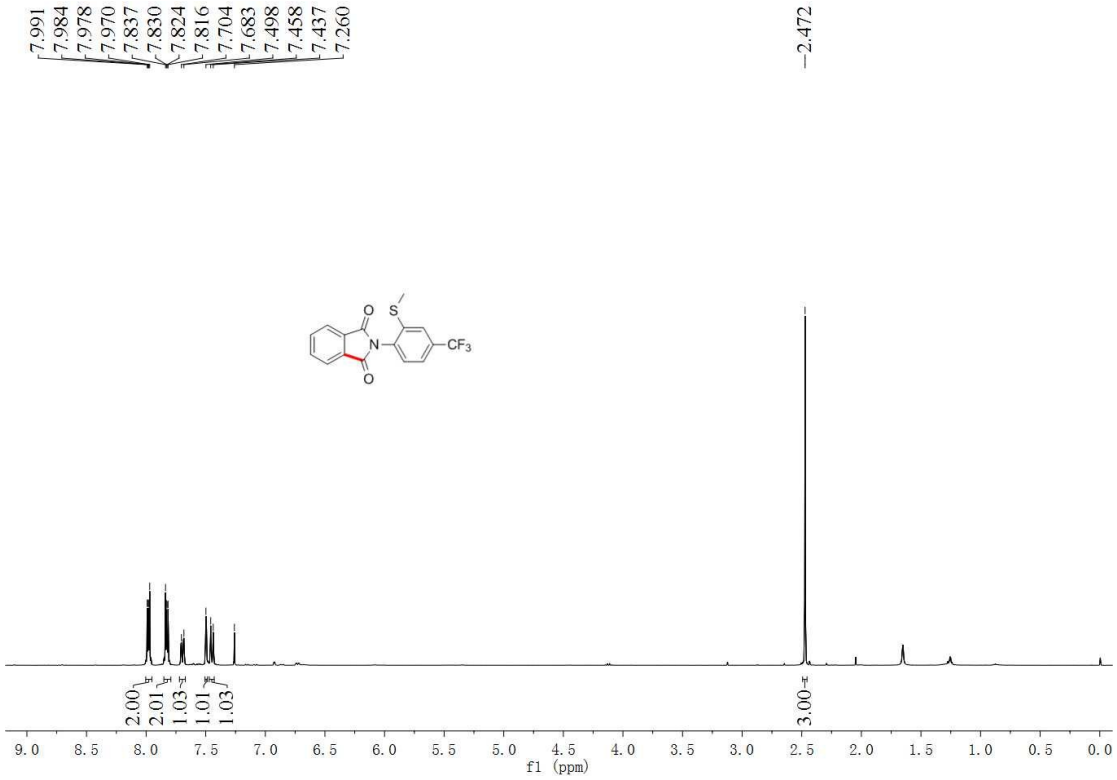
^{13}C NMR: 2-(4-ethoxy-2-(methylthio)phenyl)isoindoline-1,3-dione (4b)



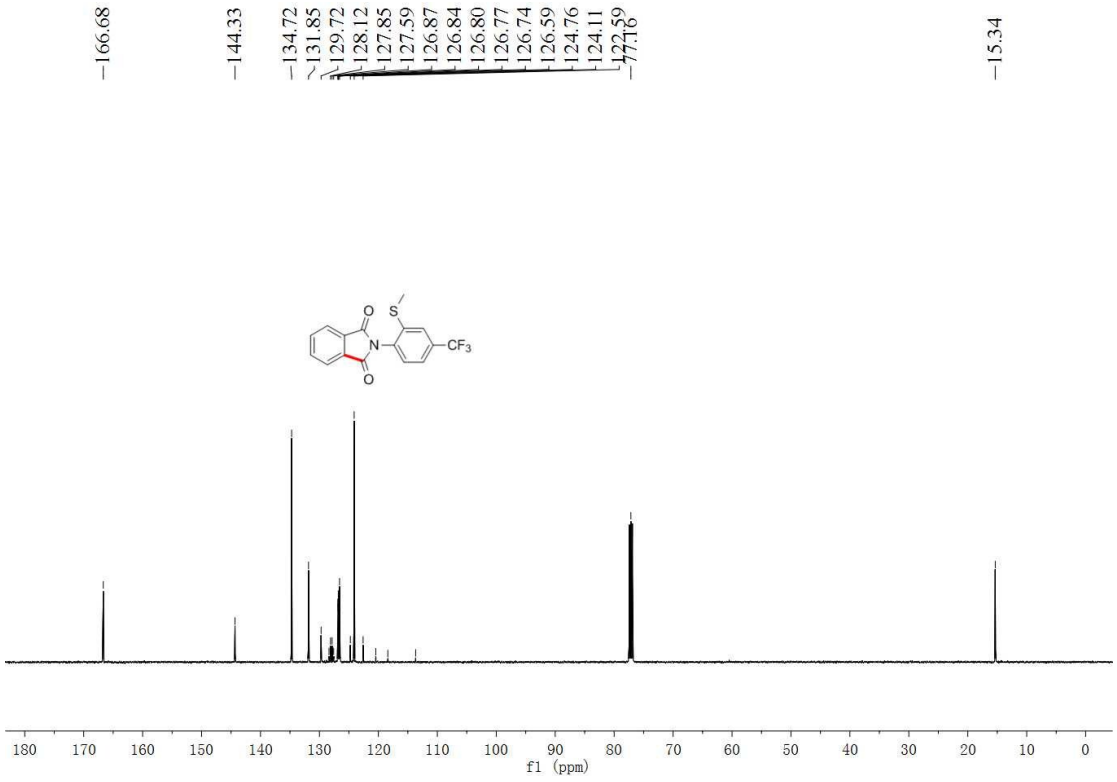
[1]H NMR: 2-(4-chloro-2-(methylthio)phenyl)isoindoline-1,3-dione (4c)



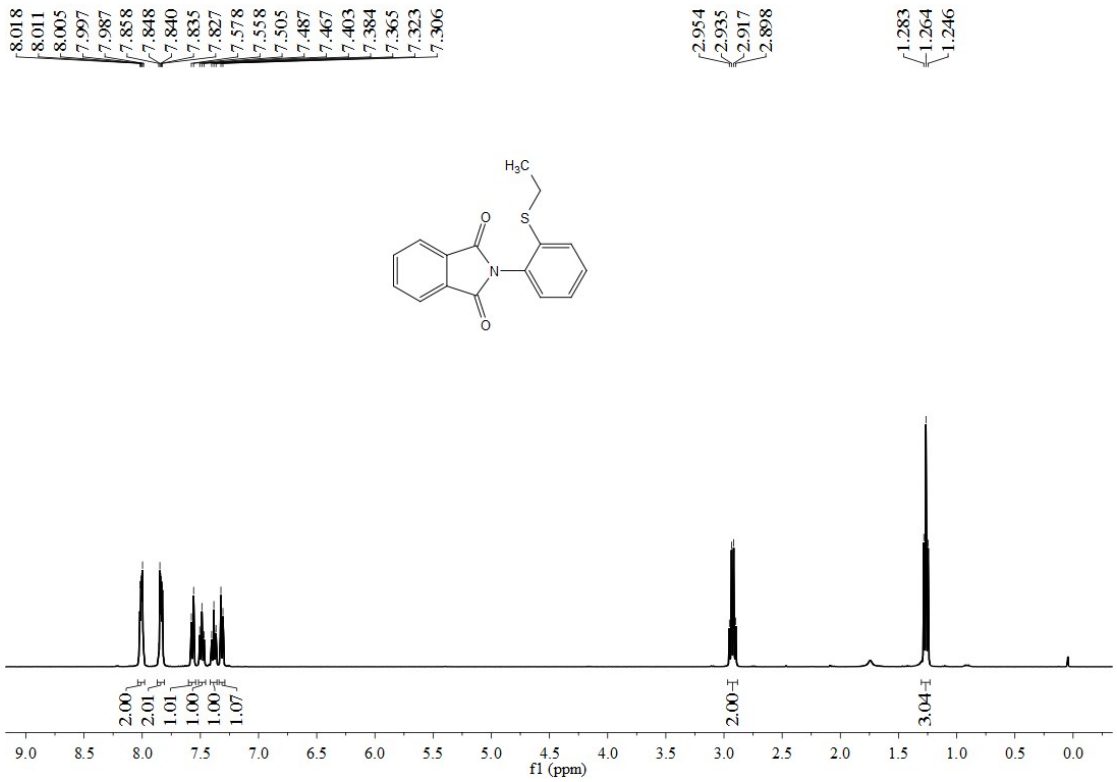
[13]C NMR: 2-(4-chloro-2-(methylthio)phenyl)isoindoline-1,3-dione (4c)



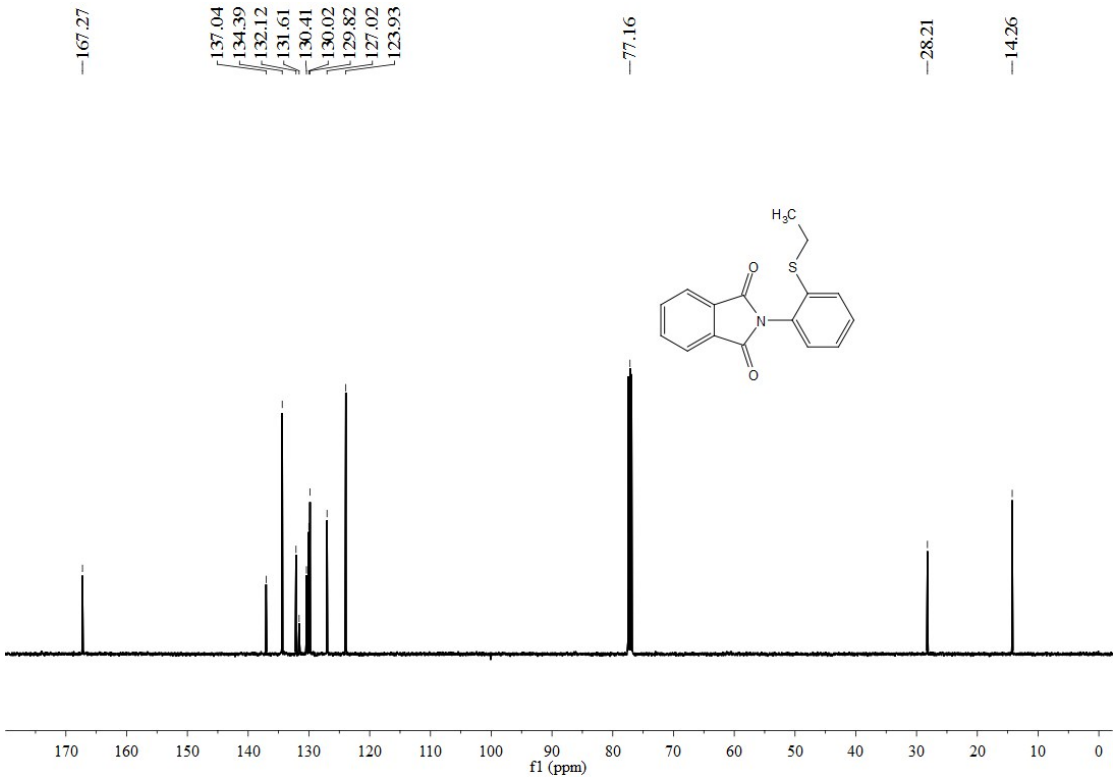
^{1}H NMR: 2-(2-(methylthio)-4-(trifluoromethyl)phenyl)isoindoline-1,3-dione (4d)



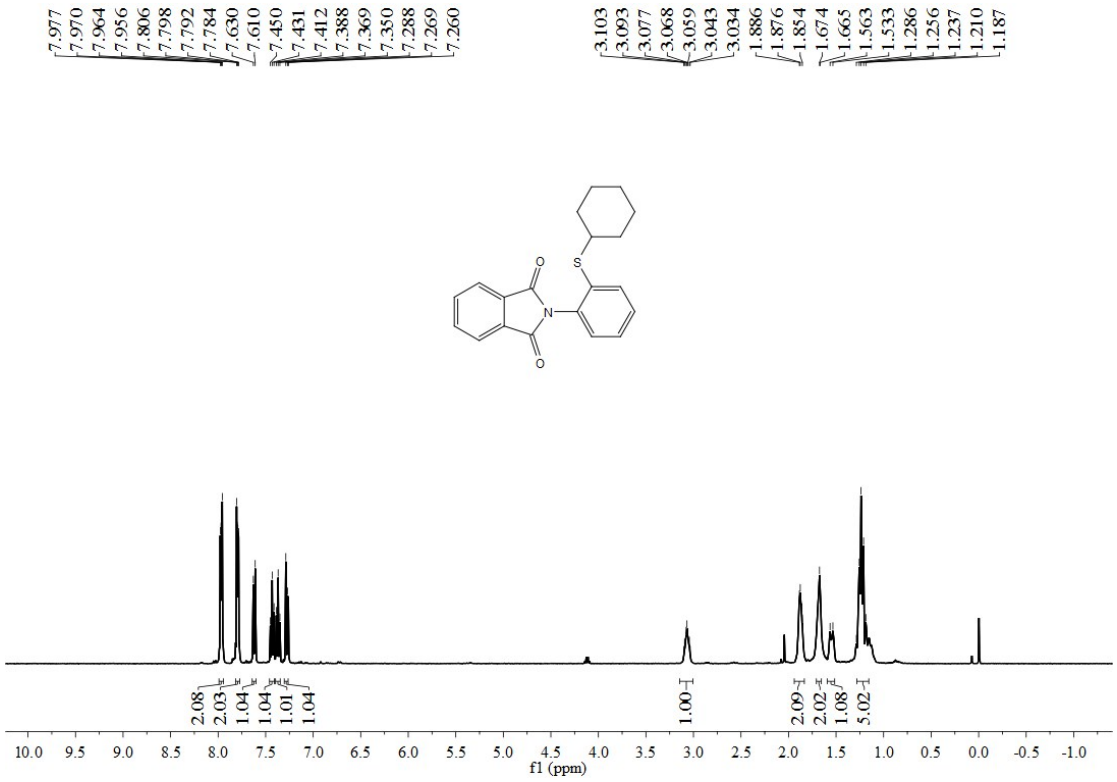
^{13}C NMR: 2-(2-(methylthio)-4-(trifluoromethyl)phenyl)isoindoline-1,3-dione (4d)



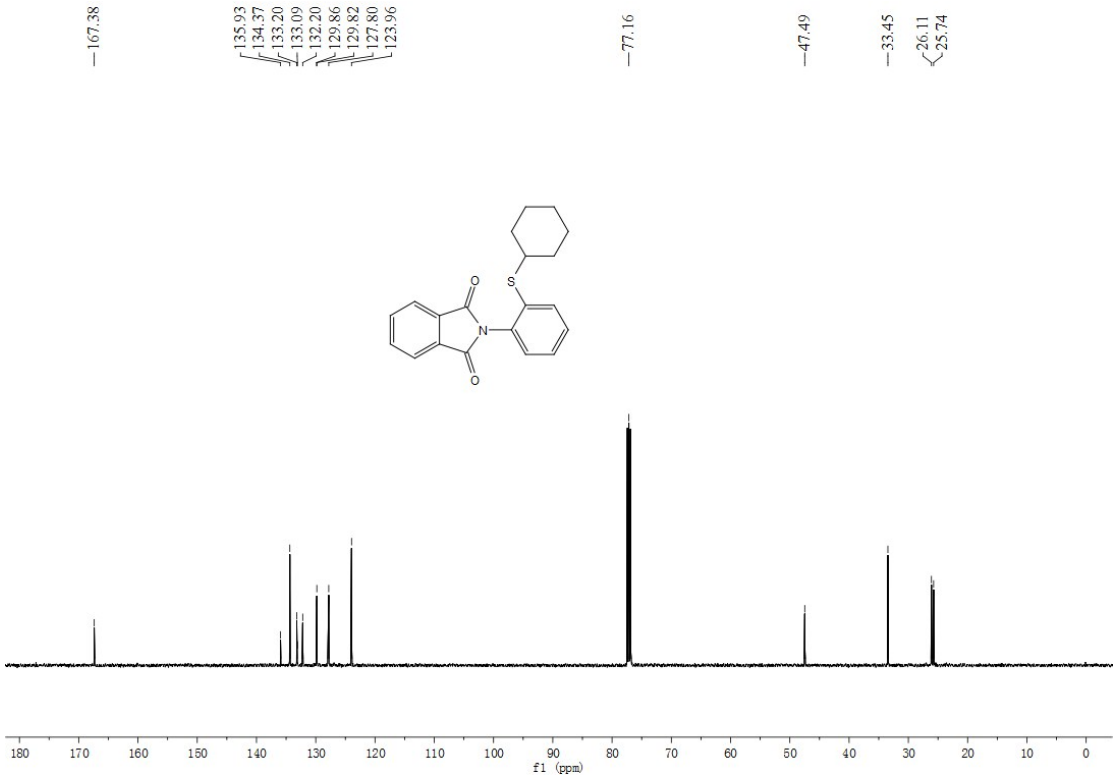
^{1}H NMR: 2-(2-(ethylthio)phenyl)isoindoline-1,3-dione (4e)



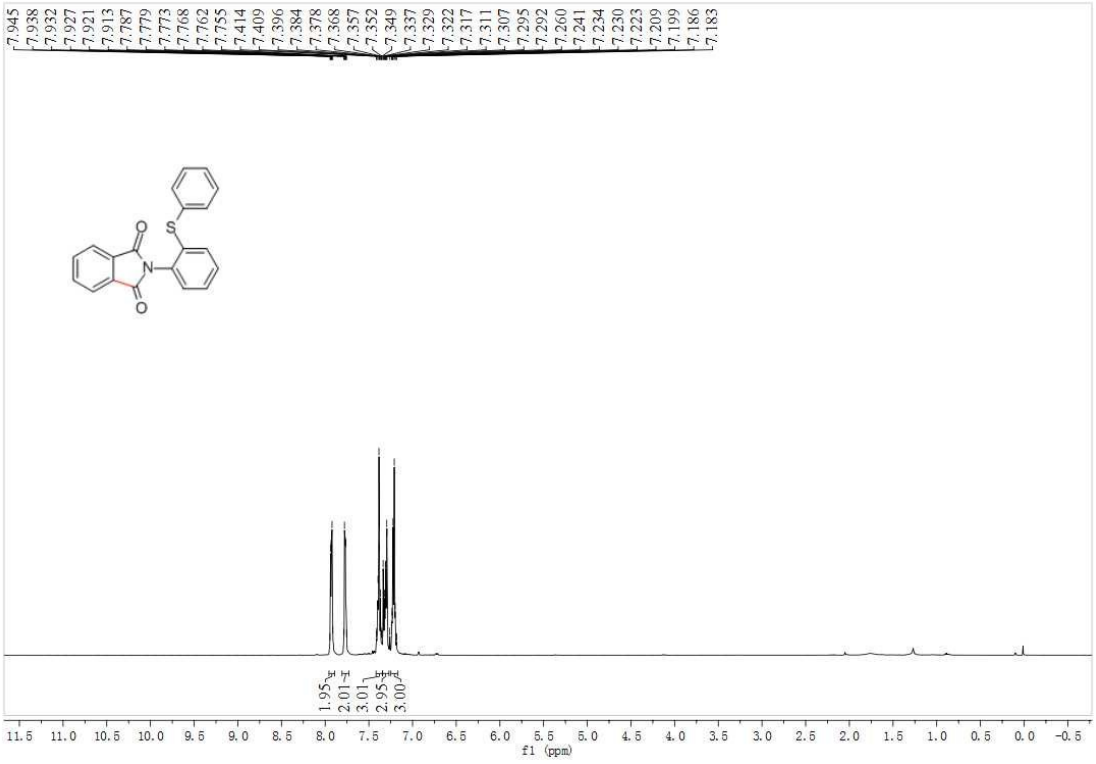
^{13}C NMR: 2-(2-(ethylthio)phenyl)isoindoline-1,3-dione (4e)



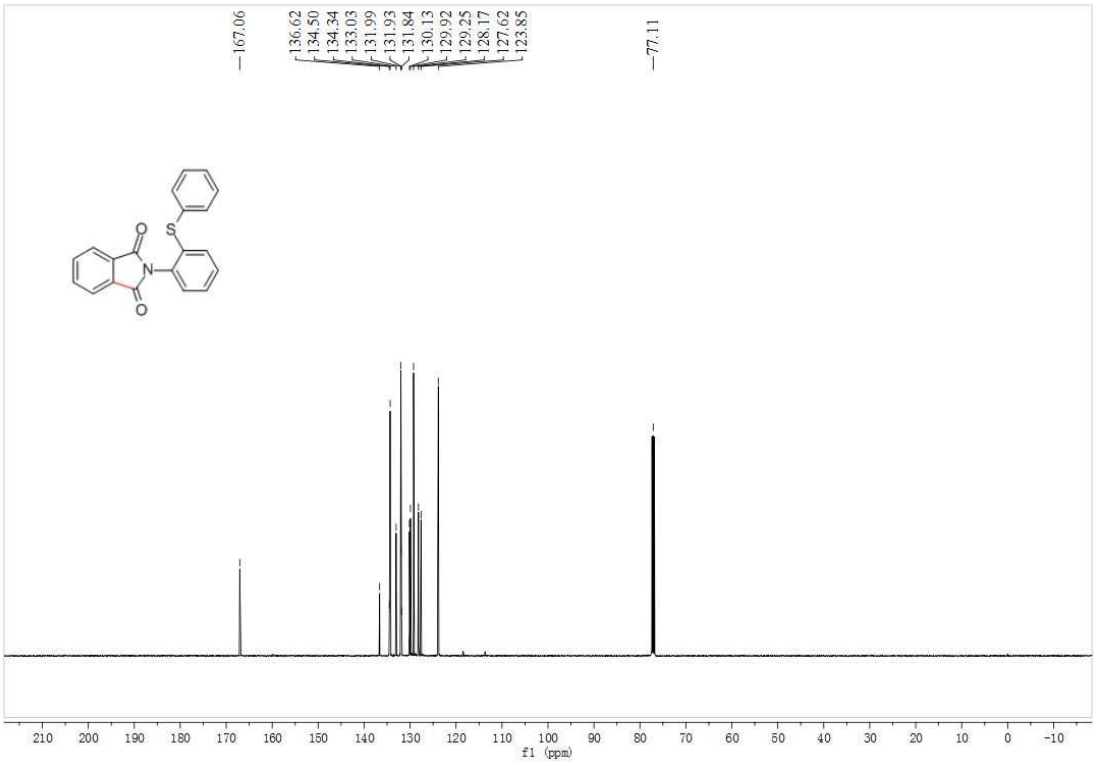
^{1}H NMR: 2-(2-(cyclohexylthio)phenyl)isoindoline-1,3-dione (4f)



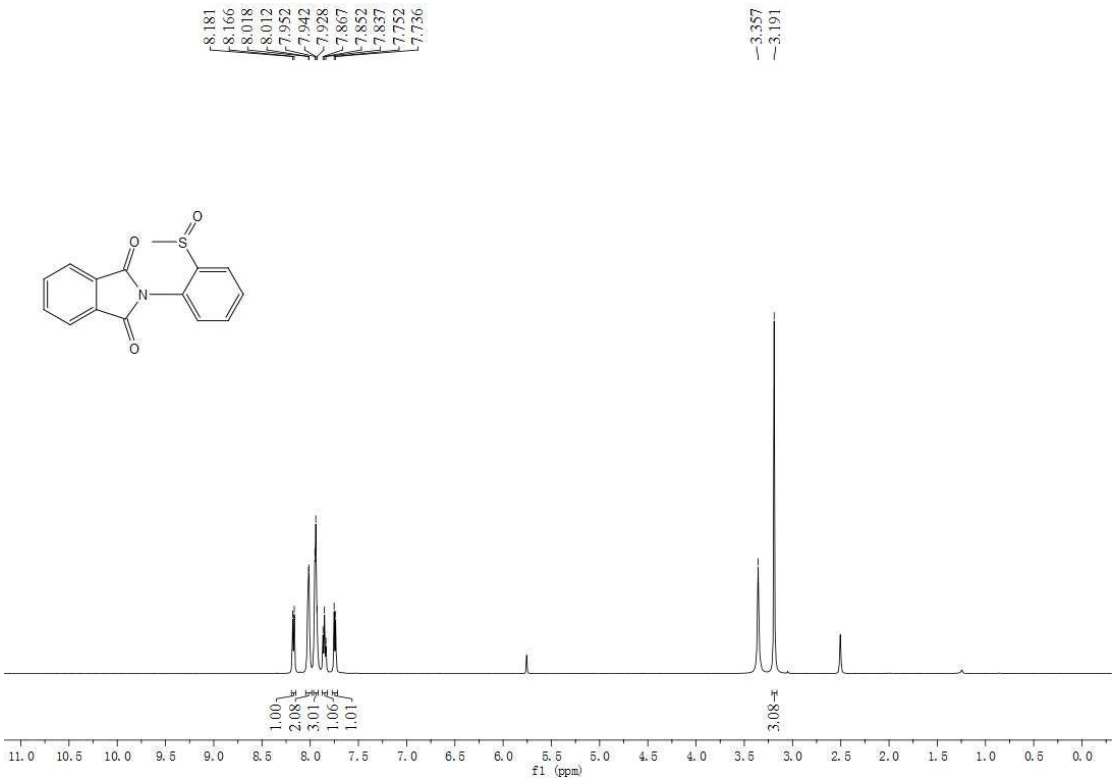
^{13}C NMR: 2-(2-(cyclohexylthio)phenyl)isoindoline-1,3-dione (4f)



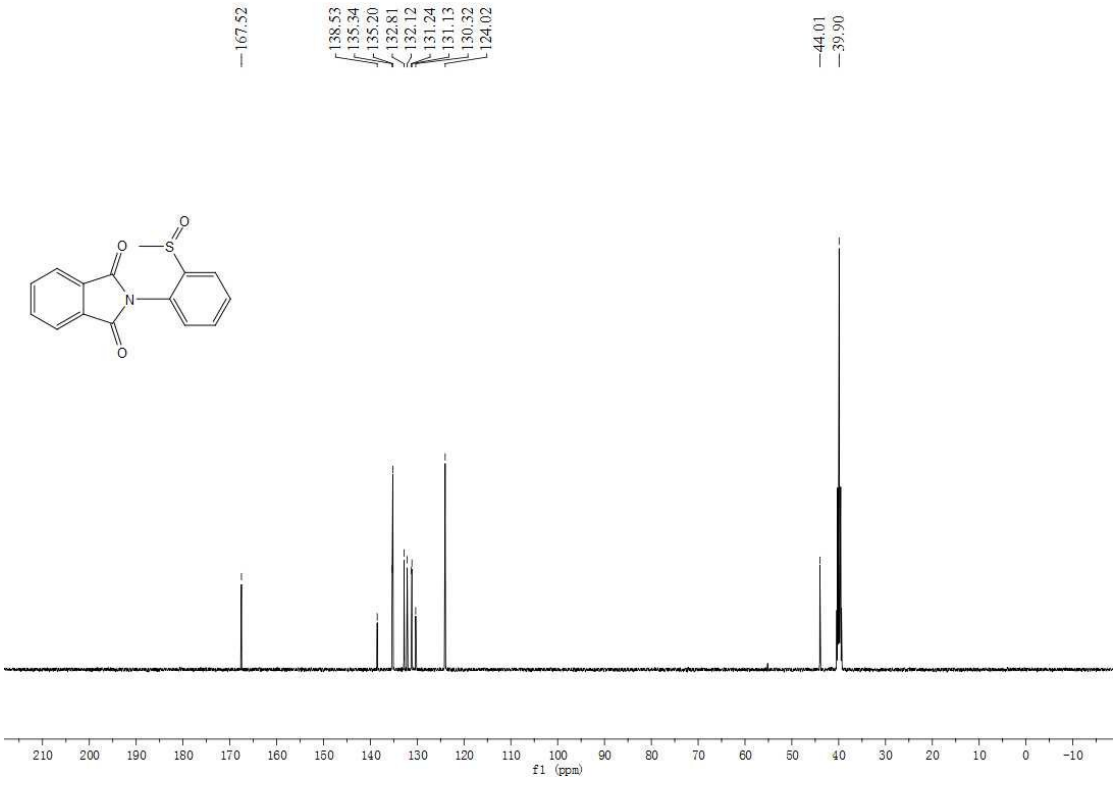
^{1}H NMR:2-(2-(phenylthio)phenyl)isoindoline-1,3-dione(4g)



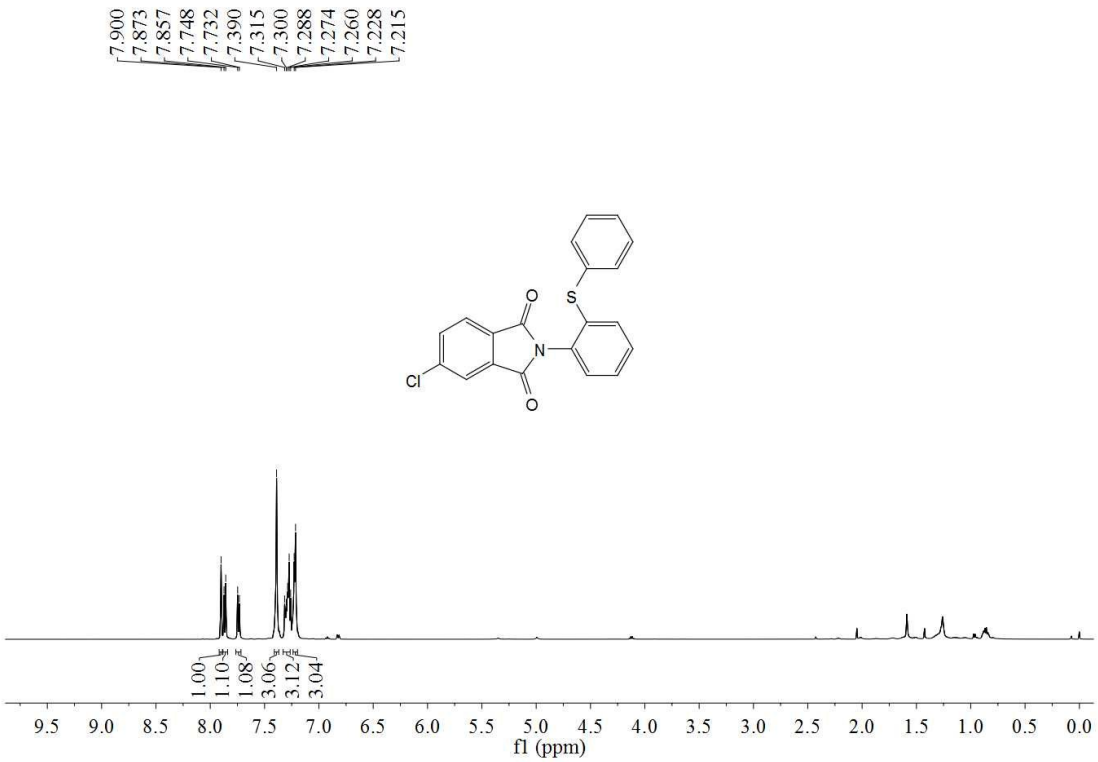
^{13}C NMR:2-(2-(phenylthio)phenyl)isoindoline-1,3-dione(4g)



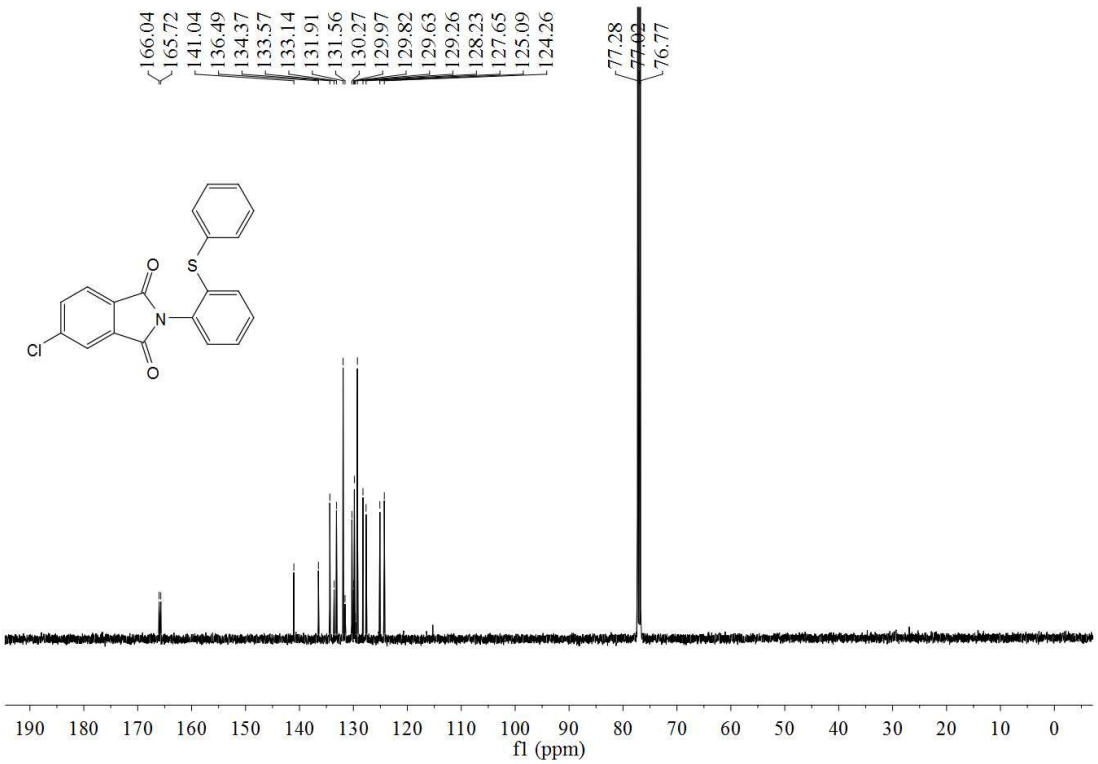
^{1}H NMR:2-(2-(methylsulfinyl)phenyl)isoindoline-1,3-dione (11)



^{13}C NMR:2-(2-(methylsulfinyl)phenyl)isoindoline-1,3-dione (11)



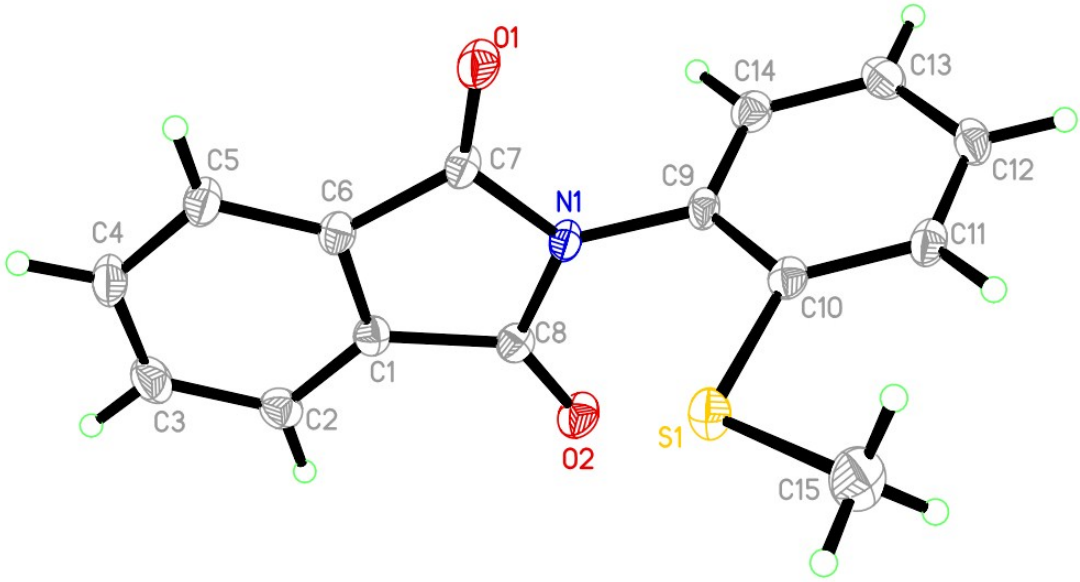
^{1}H NMR: 5-chloro-2-(2-(phenylthio)phenyl)isoindoline-1,3-dione (12)



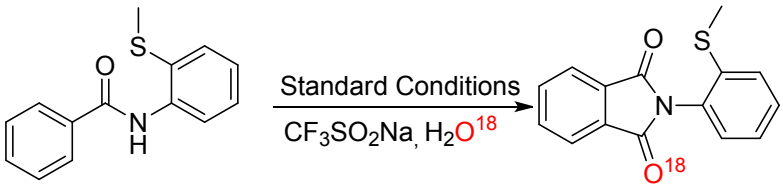
^{13}C NMR: 5-chloro-2-(2-(phenylthio)phenyl)isoindoline-1,3-dione (12)

7. X-ray crystal structure of compound 2a

Supplementary crystallographic data was deposited at the Cambridge Crystallographic Data Centre (CCDC) under the numbers CCDC-1821829 (**2a**) and can be obtained free of charge from via www.ccdc.cam.ac.uk/data_request.cif.



8. Data for Control Experiments

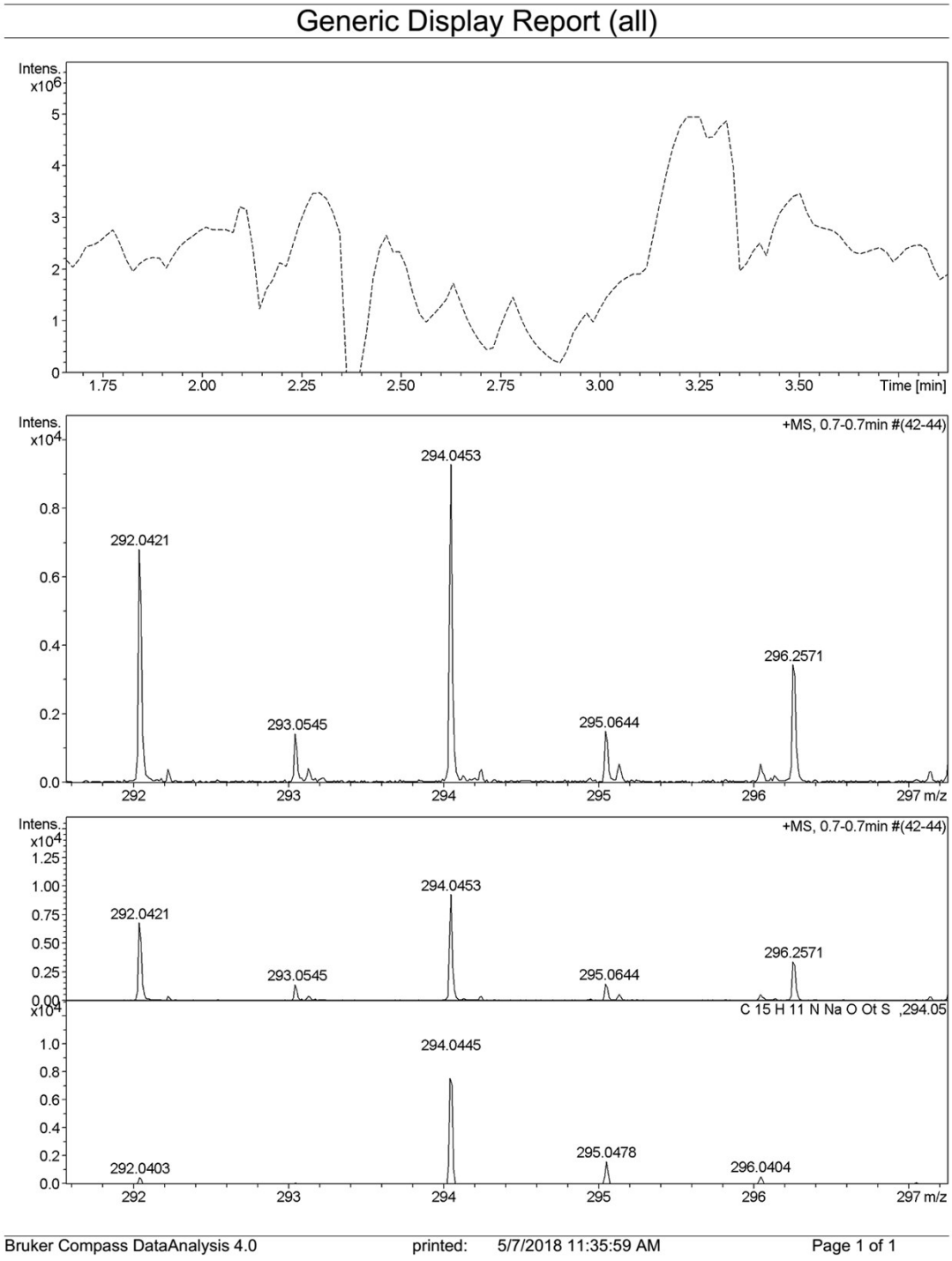


72% ^{18}O:^{16}O = 4 : 3

To a flame-dried Schlenk tube with a magnetic stirring bar was charged with **1a** (0.2 mmol), CF_3SO_2Na (0.54 mmol), $Pd(CF_3CO_2)_2$ (13.3 mg, 0.4 mmol), H_2O^{18} (4.0 equiv, 16 mg, 0.8 mmol) in dry PhCl (2 mL) under air atmosphere. The reaction mixture was stirred at 120 °C until complete consumption of starting material as detected by TLC or GC−MS analysis. After the reaction was finished, the mixture was poured into ethyl acetate and evaporated under vacuum. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired products ^{18}O-**2a**.

O^{18}-2a HRMS (ESI):

Calcd for $C_{15}H_{11}NOO^{18}S\ Na^+$ ([M + Na]$^+$) 294.0445, Found: 294.0453.



O^{18}-**2a** GC analysis