

Supporting Information

Metal-free C(sp³)-H functionalization: Oxidative carbo-oxygenation of α -diazo carbonyls *via* radical dediazotization

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Context

General Information.....	S2
X-Ray Structure of 4a	S2
Control Experiments.....	S2
Competing Kinetic Isotope Effect (KIE) Experiment.....	S3
General Procedure for the Synthesis of Product 4a	S4
Characterization Data of Compounds 4a-4x	S4-S14
General Procedure for the Synthesis of Product 5	S14
Copies of ¹ H and ¹³ C NMR Spectra for Compounds 4a-4x	S15-S37
Copies of ¹ H NMR Spectra for Compounds 5	S38

Experimental

General Information

^1H NMR (^{13}C NMR) spectra were measured on a Bruker DPX 400 MHz spectrometer in CDCl_3 ($\text{DMSO-}d_6$) with chemical shift (δ) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (ESI) was determined by using microTOF-QII HRMS/MS instrument (BRUKER). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

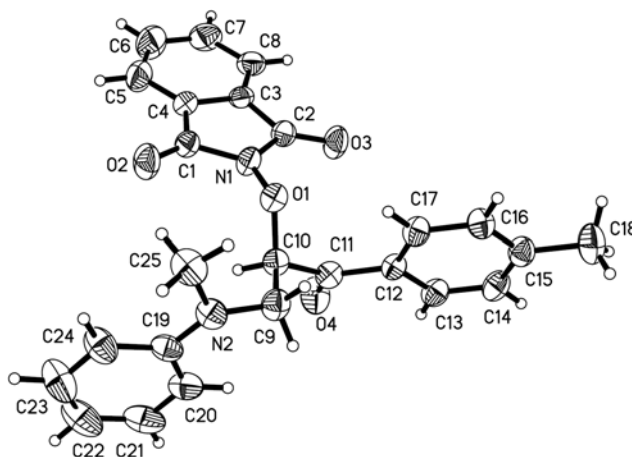
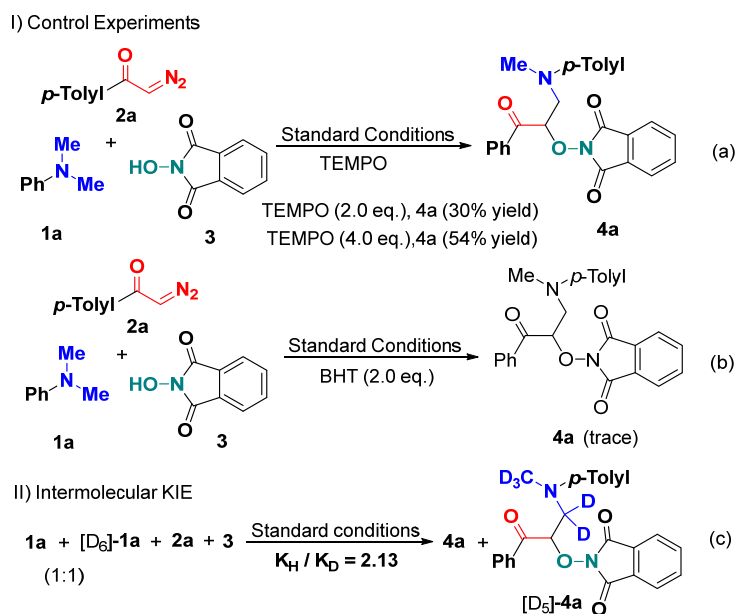


Figure 1 The ORTEP Drawing of **4a** (Thermal ellipsoids are set at 30% probability level)

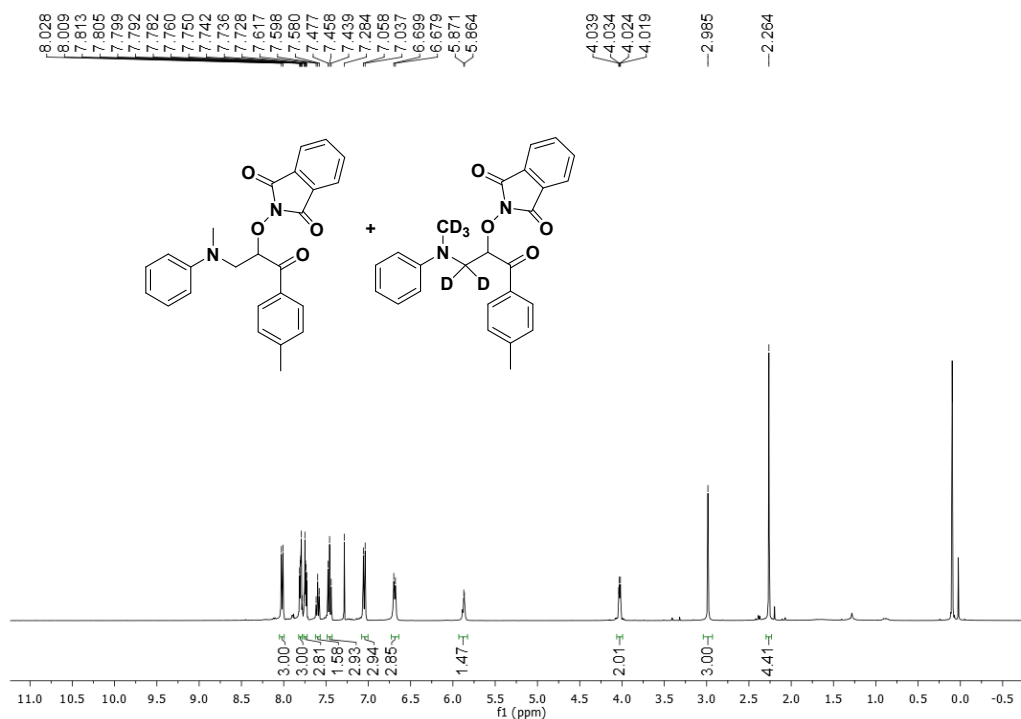
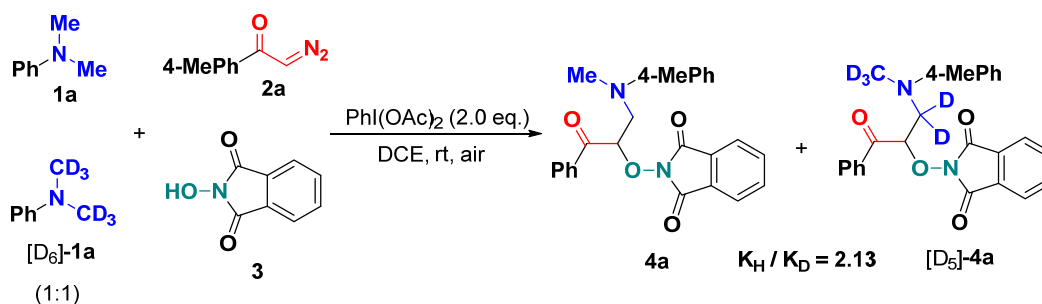


Scheme 1. Control experiments

Competing Kinetic Isotope Effect (KIE) Experiment:

KIE experimental procedure:

A mixture of *N,N*-dimethyl aniline (**1a**, 0.5 mmol, 1.0 equiv.), [D_6]-*N,N*-dimethyl aniline ([D_6]-**1a**, 0.5 mmol, 1.0 equiv.), *N*-hydroxyphthalimide (**3**, 0.50 mmol, 1.0 equiv.), 2-diazo-1-(*p*-tolyl)ethan-1-one (**2a**, 1.0 mmol, 2.0 equiv.), and phenyliodine diacetate (PIDA, 1.0 mmol, 2.0 equiv.) in dry 1,2-dichloroethane (DCE, 2.0 mL) was stirred at room temperature for about 12 hour. After the reaction finished, the mixture was evaporated under vacuum and purified by column chromatography to afford a mixture of products **4a** and [D_5]-**4a**. The KIE value was determined by 1H NMR spectra of the mixture of **4a** and [D_5]-**4a**, which has been described in details as follows.



1H NMR spectra of products **4a** and [D_5]-**4a**

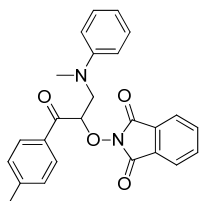
Note: The value of k_H/k_D was calculated from the 1H NMR spectra above. $K_H/K_D = 2.13$

$K_H/K_D = 1/(1.47-1) = 2.13$

General procedure for the synthesis of 4

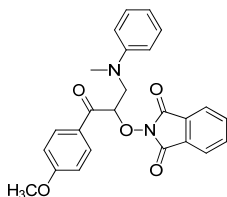
Example for the synthesis of **4a**

N,N-Dimethyl aniline (**1a**, 1.0 mmol, 2.0 equiv.), *N*-hydroxyphthalimide (**3**, 0.50 mmol, 1.0 equiv.) and 2-diazo-1-(*p*-tolyl)ethan-1-one (**2a**, 1.0 mmol, 2.0 equiv.) were introduced in a 10-mL Schlenk tube, dry 1,2-dichloroethane (DCE, 2.0 mL) and phenyliodine diacetate (PIDA, 1.0 mmol, 2.0 equiv.) were then successively added and the mixture stirred at room temperature for about 12 hours (monitored by TLC). After the reaction finished, the mixture was evaporated under vacuum and purified by column chromatography (petroleum ether/ethyl acetate) to afford the desired product **4a**.
2-(1-(Methyl(phenyl)amino)-3-oxo-3-(p-tolyl)propoxy)isoindoline-1,3-dione (4a)



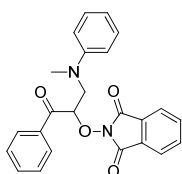
Yellow solid, mp 129-130 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.07–7.62 (m, 6H), 7.29–7.12 (m, 4H), 6.77 (d, *J* = 8.4 Hz, 3H), 5.84 (s, 1H), 4.06-4.02 (m, 2H), 3.01 (s, 3H), 2.40 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 195.0, 163.2, 148.2, 145.1, 134.6, 132.9, 129.5, 129.3, 129.1, 128.7, 123.7, 117.3, 112.7, 84.9, 53.9, 39.7, 21.8; IR (KBr, ν, cm⁻¹) 3067, 2910, 1791, 1739, 1660, 1505, 1376, 1182, 1082, 973, 836, 699; HRMS (APCI) *m/z* Calcd. For C₂₅H₂₂N₂O₄Na, 437.1477 [M+Na]⁺, found 437.1488.

2-((1-(4-Methoxyphenyl)-3-(methyl(phenyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4b)



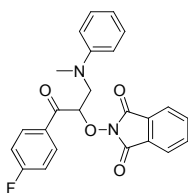
Yellow solid, mp 119-120 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.07-7.99 (m, 2H), 7.83-7.71 (m, 4H), 7.28-7.24 (m, 2H), 6.95-6.90 (m, 2H), 6.94-6.90 (m, 2H), 5.85 (s, 1H), 4.08-4.04 (m, 2H), 3.88 (s, 3H), 3.02 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 193.7, 164.2, 163.2, 146.3, 134.6, 131.4, 129.8, 128.8, 128.4, 126.5, 123.7, 113.9, 113.1, 84.8, 55.5, 54.2, 39.8, 20.3; IR (KBr, ν, cm⁻¹) 3054, 2931, 1792, 1732, 1677, 1597, 1348, 1254, 1171, 973, 873, 700; HRMS (APCI) *m/z* Calcd. For C₂₅H₂₂N₂O₅Na, 453.1426 [M+Na], found 453.1428.

2-((3-(Methyl(phenyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (4c)



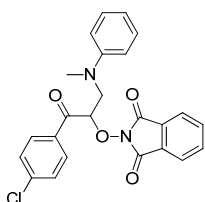
Yellow solid, mp 113-114 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.06-7.98 (m, 2H), 7.77-7.75 (m, 4H), 7.60-7.59 (m, 1H), 7.46 (m, 2H), 7.31-7.20 (m, 2H), 6.83-6.72 (m, 3H), 5.87-5.85 (m, 1H), 4.08-4.04 (m, 2H), 3.02 (s, 3H), 3.02 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 195.6, 163.2, 148.2, 135.3, 134.9, 134.7, 134.0, 129.4, 129.3, 129.0, 128.9, 128.8, 128.7, 128.7, 123.9, 123.7, 117.4, 112.7, 85.0, 53.9, 39.7; IR (KBr, ν, cm⁻¹) 3065, 2911, 1785, 1727, 1690, 1597, 1507, 1375, 1185, 977, 880, 750, 690; HRMS (APCI) m/z Calcd. For C₂₄H₂₀N₂O₄Na, 423.1321 [M+Na]⁺, found 423.1302.

2-((1-(4-Fluorophenyl)-3-(methyl(phenyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4d)



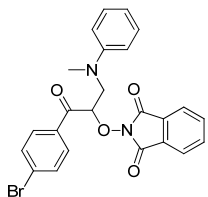
Yellow solid, mp 113-114 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.02-7.93 (m, 2H), 7.72-7.63 (m, 4H), 7.15-6.99 (m, 4H), 6.68-6.66 (m, 3H), 5.66 (t, *J* = 6.0 Hz 1H), 3.99-3.95 (m, 2H), 2.90 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 194.0, 166.2 (*J* = 255.2 Hz), 163.2, 148.1, 134.7, 134.3, 131.9 (*J* = 9.5 Hz), 131.7 (*J* = 3.0 Hz), 129.4, 128.7, 123.8, 123.6, 117.6, 115.9 (*J* = 21.8), 112.8, 85.2, 53.9, 39.8; IR (KBr, ν, cm⁻¹) 3055, 2924, 1774, 1687, 1596, 1508, 1352, 1230, 1081, 975, 701; HRMS (APCI) m/z Calcd. For C₂₄H₁₉FN₂O₄Na, 441.1227 [M+Na]⁺, found 441.1206.

2-((1-(4-Chlorophenyl)-3-(methyl(phenyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4e)



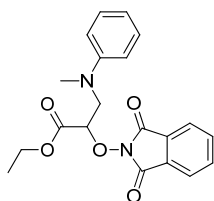
Yellow solid, mp 112-113 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.03-7.95 (m, 2H), 7.90-7.89 (m, 1H), 7.83-7.74 (m, 5H), 7.44-7.42 (m, 1H), 7.26-7.23 (m, 2H), 6.76 (d, *J* = 8.0 Hz, 2H), 5.76-5.72 (m, 1H), 4.09-4.05 (m, 2H), 3.01 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 194.4, 167.8, 163.2, 140.6, 134.8, 134.4, 133.6, 132.6, 130.5, 129.4, 129.1, 128.7, 123.8, 123.6, 117.7, 112.9, 85.3, 53.9, 39.9; IR (KBr, ν, cm⁻¹) 3199, 2920, 1737, 1604, 1500, 1373, 1185, 969, 875, 700; HRMS (APCI) m/z Calcd. For C₂₄H₁₉ClN₂O₄Na, 457.0931 [M+Na]⁺, found 457.0924.

2-((1-(4-Bromophenyl)-3-(methyl(phenyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4f**)



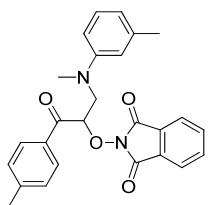
Yellow solid, mp 152-153 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 7.94-7.88 (m, 2H), 7.83-7.73 (m, 4H), 7.63-7.54 (m, 2H), 7.28-7.22 (m, 2H), 6.79-6.75 (m, 3H), 5.72 (d, $J = 6.0$ Hz, 1H), 4.09-4.05 (m, 2H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 194.7, 163.2, 148.1, 134.8, 134.3, 134.0, 132.0, 130.5, 129.4, 128.6, 123.8, 123.6, 117.5, 112.7, 85.4, 53.8, 39.8; IR (KBr, ν , cm^{-1}) 3054, 1793, 1774, 1686, 1507, 1350, 1257, 1061, 972, 873, 700; HRMS (APCI) m/z Calcd. For $\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_4\text{BrNa}$, 501.0426 $[\text{M}+\text{Na}]^+$, found 501.0420.

Ethyl 2-((1,3-dioxoisoindolin-2-yl)oxy)-3-(methyl(phenyl)amino)propanoate (**4g**)



Yellow solid, mp 99-100 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 7.82-7.72 (m, 4H), 7.29-7.25 (m, 2H), 6.84-6.67 (m, 3H), 4.98-4.95 (m, 1H), 4.22 (q, $J = 7.2$ Hz, 2H), 3.99-3.95 (m, 2H), 3.12 (s, 3H), 1.27 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 168.6, 162.9, 148.4, 134.7, 129.3, 128.8, 123.7, 117.2, 112.6, 84.0, 62.0, 53.2, 39.4, 14.0; IR (KBr, ν , cm^{-1}) 2996, 1792, 1730, 1599, 1508, 1374, 1264, 1121, 1025, 971, 878, 701; HRMS (APCI) m/z Calcd. For $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_5\text{Na}$, 391.1270 $[\text{M}+\text{Na}]^+$, found 391.1274.

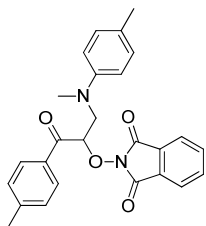
2-((3-(Methyl(m-tolyl)amino)-1-oxo-1-(p-tolyl)propan-2-yl)oxy)isoindoline-1,3-dione (**4h**)



Yellow solid; mp 99-100 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 7.94 (d, $J = 8.4$ Hz, 2H), 7.83-7.72 (m, 4H), 7.26 (d, $J = 8.0$ Hz, 2H), 7.14 (m, 1H), 6.60 (d, $J = 7.6$ Hz, 3H), 5.87 (t, $J = 5.6$ Hz, 1H), 4.05-4.03 (m, 2H), 3.01 (s, 3H), 2.42 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 194.9, 167.9, 163.2, 148.3, 145.1, 139.0, 134.6, 134.3, 132.8, 132.6, 129.5, 129.2, 129.1, 128.7, 123.7, 123.6, 118.2, 113.5, 110.0, 85.0, 53.9, 39.7, 29.7, 21.9, 21.8; IR (KBr, ν , cm^{-1}) 3199,

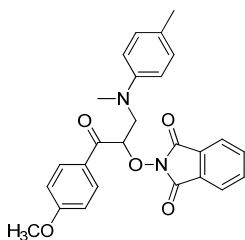
1791, 1737, 1655, 1604, 1500, 1185, 1053, 969, 875, 700; HRMS (APCI) m/z Calcd. For $C_{26}H_{24}N_2O_4Na$, 451.1634 $[M+Na]^+$, found 451.1633.

2-((3-(Methyl(p-tolyl)amino)-1-oxo-1-(p-tolyl)propan-2-yl)oxy)isoindoline-1,3-dione (4i)



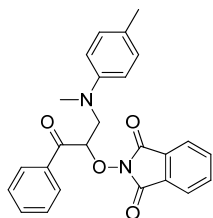
Yellow solid; mp 138-139 °C; 1H NMR (400 MHz, $CDCl_3$; δ , ppm) 7.93 (d, J = 8.0 Hz, 2H), 7.80-7.78 (m, 4H), 7.26 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.4 Hz, 2H), 5.85 (t, J = 6.0 Hz, 1H), 4.03-4.01 (m, 2H), 2.99 (s, 3H), 2.42 (s, 3H), 2.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; δ , ppm) 195.0, 163.2, 146.3, 145.0, 134.6, 132.9, 129.8, 129.5, 129.1, 128.7, 126.6, 123.7, 113.1, 85.0, 54.2, 39.8, 21.8, 20.3; IR (KBr, ν , cm^{-1}) 2910, 1736, 1664, 1522, 1372, 1261, 1187, 1121, 970, 810, 702; HRMS (APCI) m/z Calcd. For $C_{26}H_{24}N_2O_4Na$, 451.1634 $[M+Na]^+$, found 451.1631.

2-((1-(4-Methoxyphenyl)-3-(methyl(p-tolyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (4j)



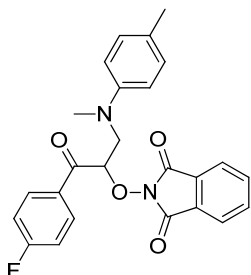
Yellow solid, mp 126-127 °C; 1H NMR (400 MHz, $CDCl_3$; δ , ppm) 8.02 (d, J = 8.8 Hz, 2H), 7.83-7.70 (m, 4H), 7.05 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 6.70 (d, J = 7.2 Hz, 2H), 5.83 (s, 1H), 4.03-4.01 (m, 2H), 3.88 (s, 3H), 2.98 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ , ppm) 193.7, 164.2, 163.2, 148.3, 134.6, 131.4, 129.3, 128.7, 128.4, 123.7, 117.2, 114.0, 112.6, 84.7, 55.5, 53.7, 39.6; IR (KBr, ν , cm^{-1}) 2912, 1735, 1600, 1522, 1256, 1174, 970, 842, 702 ; HRMS (APCI) m/z Calcd. For $C_{26}H_{24}N_2O_5Na$, 467.1583 $[M+Na]^+$, found 467.1555.

2-((3-(Methyl(p-tolyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (4k)



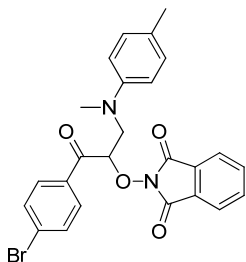
Yellow solid; mp 138-139 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.06-7.99 (m, 2H), 7.81-7.72 (m, 4H), 7.60 (s, 1H), 7.48-7.44 (m, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.69 (d, *J* = 8.4 Hz, 2H), 5.87 (t, *J* = 6.0 Hz, 1H), 4.04-4.02 (m, 2H), 2.98 (s, 3H), 2.26 (s, 3H); ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 195.6, 167.9, 163.2, 146.2, 135.3, 134.6, 134.3, 133.9, 132.6, 129.8, 129.0, 128.7, 126.7, 123.7, 123.6, 113.2, 85.1, 54.2, 39.8, 20.3; IR (KBr, ν, cm⁻¹) 2911, 1774, 1736, 1667, 1523, 1377, 1257, 1156, 970, 877, 701, 634; HRMS (APCI) *m/z* Calcd. for C₂₅H₂₂N₂O₄Na, 437.1477 [M+Na]⁺, found 437.1476.

2-((1-(4-Fluorophenyl)-3-(methyl(*p*-tolyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4l**)



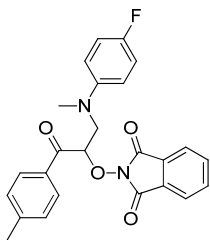
Yellow solid; mp 141-142 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 8.10-8.07 (m, 2H), 7.85-7.69 (m, 4H), 7.19-6.98 (m, 4H), 6.68 (d, *J* = 7.9 Hz, 2H), 5.77 (t, *J* = 6.0 Hz, 1H), 4.05-4.02 (s, 2H), 2.97 (s, 3H), 2.26 (s, 3H); ¹³CNMR (100 MHz, CDCl₃; δ, ppm) 194.0, 166.2 (*J*_{CF} = 255.0 Hz), 163.2, 146.1, 134.7, 134.3, 131.9 (*J*_{CF} = 9.5 Hz), 131.7 (*J*_{CF} = 2.9 Hz), 129.9, 128.7, 123.7, 123.6, 115.9 (*J*_{CF} = 21.8), 113.2, 85.3, 54.2, 39.9, 20.3; IR (KBr, ν, cm⁻¹) 3199, 2909, 1774, 1736, 1666, 1596, 1522, 1307, 1186, 1053, 971, 804, 714; HRMS (APCI): *m/z* Calcd. for C₂₅H₂₁FN₂O₄Na, 455.1383 [M+Na]⁺, found 455.1377.

2-((1-(4-Bromophenyl)-3-(methyl(*p*-tolyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4m**)



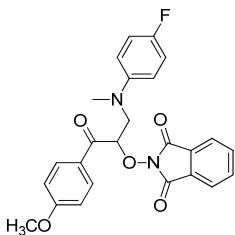
Yellow solid; mp 160-161 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 7.92-7.89 (m, 2H), 7.82-7.74 (m, 4H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 7.6 Hz, 2H), 5.73 (t, *J* = 6.0 Hz, 1H), 4.04-4.02 (m, 2H), 2.97 (s, 3H), 2.26 (s, 3H); ¹³CNMR (100 MHz, CDCl₃; δ, ppm) 194.7, 167.9, 163.2, 134.7, 134.3, 134.0, 132.6, 132.0, 130.5, 129.9, 129.3, 128.7, 123.8, 123.6, 113.2, 85.4, 54.2, 40.0, 20.3; IR (KBr, ν, cm⁻¹) 3067, 2911, 1791, 1735, 1660, 1596, 1520, 1375, 1186, 1053, 971, 714; HRMS (APCI): *m/z* Calcd. for: C₂₅H₂₁BrN₂O₄, 515.0582 [M+Na]⁺, found 515.0580.

2-(((3-((4-Fluorophenyl)(methyl)amino)-1-oxo-1-(*p*-tolyl)propan-2-yl)oxy)isoindoline-1,3-dione (**4n**)



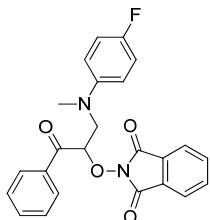
Yellow solid; mp 146-147 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 7.91 (d, $J = 8.4$ Hz, 2H), 7.85-7.65 (m, 4H), 7.28 (d, $J = 6.8$ Hz, 2H), 6.99-6.87 (m, 2H), 6.77-6.66 (m, 2H), 5.83 (t, $J = 6.0$ Hz, 1H), 4.02-4.00 (m, 2H), 2.99 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 194.8, 163.2, 156.0 ($J_{\text{CF}} = 236.4$ Hz), 145.2, 144.9 ($J_{\text{CF}} = 1.0$ Hz), 134.6, 132.8, 129.5, 129.0, 128.7, 123.7, 115.7 ($J_{\text{CF}} = 21.9$ Hz), 114.3 ($J_{\text{CF}} = 6.3$ Hz), 84.9, 54.7, 40.1, 21.8; IR (KBr, ν , cm^{-1}) 2913, 1791, 1738, 1663, 1510, 1226, 1124, 971, 817, 689; HRMS (APCI) m/z Calcd. For $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_4$ Na, 455.1383 $[\text{M}+\text{Na}]^+$, found 455.1382.

2-((3-((4-Fluorophenyl)(methyl)amino)-1-(4-methoxyphenyl)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4o**)



Yellow solid, mp 135-136 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 8.05-7.92 (m, 2H), 7.781-7.73 (m, 4H), 7.10-6.80 (m, 4H), 6.78-6.63 (m, 2H), 5.80 (t, $J = 6.0$ Hz, 1H), 4.02-4.00 (m, 2H), 3.88 (s, 3H), 2.98 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 193.5, 164.3, 163.2, 156.0 ($J_{\text{CF}} = 235.0$ Hz), 145.0 ($J_{\text{CF}} = 5.9$ Hz), 134.7, 131.4, 128.7, 128.3, 123.7, 115.7 ($J_{\text{CF}} = 22.0$ Hz), 114.2 ($J_{\text{CF}} = 5.6$ Hz), 114.0, 84.7, 55.6, 54.7, 40.1; IR (KBr, ν , cm^{-1}) 2912, 1790, 1738, 1599, 1511, 1255, 1023, 971, 816, 701; HRMS (APCI) m/z Calcd. For $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_5\text{FNa}$, 471.1332 $[\text{M}+\text{Na}]^+$, found 471.1335.

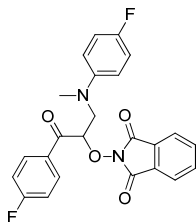
2-((3-((4-Fluorophenyl)(methyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (**4p**)



Yellow solid, mp 114-115 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 8.02-8.00 (m, 2H), 7.86-7.71 (m, 4H), 7.65-7.56 (m, 1H), 7.49-7.48 (m, 2H), 6.96-6.92 (m, 2H), 6.75-6.71 (m, 2H), 5.86 (t, $J = 6.0$ Hz, 1H), 4.04-4.01 (m, 2H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 195.4, 163.2, 156.0 ($J_{\text{CF}} = 235.6$ Hz), 144.9 ($J_{\text{CF}} = 0.9$ Hz), 135.3, 134.7, 134.0, 128.9, 128.8, 128.7, 123.7, 115.9 ($J_{\text{CF}} =$

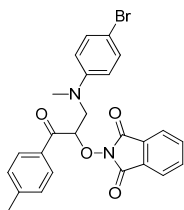
21.8 Hz), 114.4 ($J_{CF} = 7.2$ Hz), 85.0, 54.6, 40.1; IR (KBr, ν , cm^{-1}) 3067, 2912, 1791, 1738, 1599, 1511, 1255, 1228, 1173, 971, 816, 701; HRMS (APCI) m/z Calcd. For $\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_4\text{FNa}$, 441.1227 $[\text{M}+\text{Na}]^+$, found 441.1219.

2-((1-(4-Fluorophenyl)-3-((4-fluorophenyl)(methyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4q**)



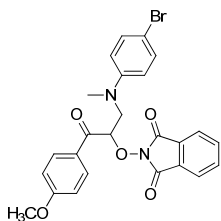
Yellow solid, mp 123-124 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 8.10-8.06 (m, 2H), 7.87-7.72 (m, 4H), 7.14 (m, 2H), 6.96-6.91 (m, 2H), 6.76-6.63 (m, 2H), 5.72 (t, $J = 6.0$ Hz, 1H), 4.03-4.01 (m, 2H), 2.97 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 193.9, 166.2 ($J_{CF} = 255.3$ Hz), 163.2, 156.0 ($J_{CF} = 235.2$ Hz), 145.0 ($J_{CF} = 1.6$ Hz), 134.8, 131.8 ($J_{CF} = 9.5$ Hz), 131.7 ($J_{CF} = 3.0$ Hz), 128.6, 123.8, 115.9 ($J_{CF} = 22.3$ Hz), 115.7 ($J_{CF} = 22.5$ Hz), 114.3 ($J_{CF} = 7.4$ Hz), 85.4, 54.6, 40.2; IR (KBr, ν , cm^{-1}) 2911, 1790, 1737, 1664, 1595, 1512, 1230, 969, 817, 700; HRMS (APCI) m/z Calcd. For $\text{C}_{24}\text{H}_{18}\text{N}_2\text{O}_4\text{F}_2\text{Na}$, 459.1132 $[\text{M}+\text{Na}]^+$, found 459.1146.

2-((3-((4-Bromophenyl)(methyl)amino)-1-oxo-1-(p-tolyl)propan-2-yl)oxy)isoindoline-1,3-dione (**4r**)



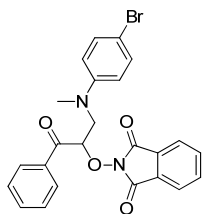
Yellow solid, mp 159-160 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 7.96-7.71 (m, 6H), 7.35-7.29 (m, 2H), 7.27 (d, $J = 8.0$ Hz, 2H), 6.73-6.56 (m, 2H), 5.81-5.78 (m, 1H), 4.04-4.00 (m, 2H), 3.00 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 194.8, 163.2, 147.2, 145.3, 134.7, 132.7, 132.0, 129.5, 129.0, 128.7, 123.7, 114.3, 109.4, 84.8, 53.8, 39.8, 21.8; IR (KBr, ν , cm^{-1}) 2912, 1735, 1659, 1591, 1498, 1257, 1121, 970, 810, 701; HRMS (APCI) m/z Calcd. For $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_4\text{BrNa}$, 515.0582 $[\text{M}+\text{Na}]^+$, found 515.0585.

2-((3-((4-Bromophenyl)(methyl)amino)-1-(4-methoxyphenyl)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4s**)



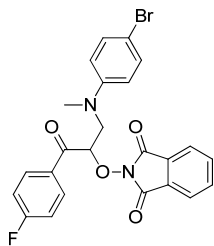
Yellow solid; mp 146-147 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 8.04-7.99 (m, 2H), 7.83-7.72 (m, 4H), 7.36-7.30 (m, 2H), 6.97-6.91 (m, 2H), 6.71 (d, $J = 8.8$ Hz, 2H), 5.83 (t, $J = 6.0$ Hz, 1H), 4.05-4.01 (m, 2H), 3.88 (s, 3H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 193.5, 164.3, 163.2, 147.2, 134.7, 132.0, 131.4, 128.7, 123.7, 114.2, 114.0, 100.0, 84.6, 55.6, 53.8, 39.7; IR (KBr, ν , cm^{-1}) 2932, 1735, 1598, 1499, 1373, 1255, 1174, 1027, 968, 810, 701; HRMS (APCI) m/z Calcd. For $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_5\text{BrNa}$, 508.0634 $[\text{M}+\text{Na}]^+$, found 503.0635.

2-((3-((4-bromophenyl)(methyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (**4t**)



Yellow solid, mp 147-148 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 8.10-7.97 (m, 2H), 7.94-7.68 (m, 4H), 7.66-7.51 (m, 1H), 7.51-7.40 (m, 2H), 7.33-7.29 (m, 2H), 6.76-6.50 (m, 2H), 5.82 (t, $J = 6.0$ Hz, 1H), 4.06-4.02 (m, 2H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 195.3, 163.2, 147.2, 135.2, 134.7, 134.1, 132.0, 128.9, 128.8, 128.7, 123.8, 114.4, 109.5, 84.9, 53.8, 39.7; IR (KBr, ν , cm^{-1}) 3068, 2914, 1789, 1735, 1666, 1499, 1256, 1016, 968, 812, 700; HRMS (APCI) m/z Calcd. For $\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_4\text{BrNa}$, 501.0426 $[\text{M}+\text{Na}]^+$, found 501.0401.

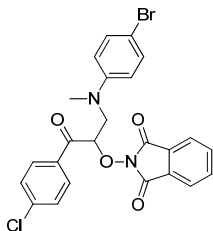
2-((3-((4-bromophenyl)(methyl)amino)-1-(4-fluorophenyl)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4u**)



Yellow solid; mp 166-167 °C; ^1H NMR (400 MHz, CDCl_3 ; δ , ppm) 8.13-7.99 (m, 2H), 7.93-7.69 (m, 4H), 7.42-7.30 (m, 2H), 7.17-7.13 (m, 2H), 6.68 (d, $J = 9.2$ Hz, 2H), 5.74 (t, $J = 6.0$ Hz, 1H), 4.18-3.88 (m, 2H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 ; δ , ppm) 193.8, 166.3 ($J_{\text{CF}} = 255.8$ Hz), 163.2, 147.2, 135.0, 134.8, 134.2, 131.6 ($J_{\text{CF}} = 3.1$ Hz), 132.0, 130.1 ($J_{\text{CF}} = 8.9$ Hz), 128.6, 123.8, 116.0 ($J_{\text{CF}} = 21.8$ Hz), 114.3, 85.3, 53.7, 39.8; IR (KBr, ν , cm^{-1}) 2913, 1788, 1735, 1664,

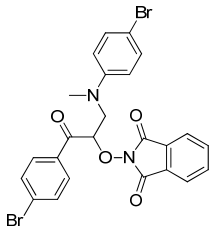
1592, 1498, 969, 810, 709; HRMS (APCI) m/z Calcd. For $C_{24}H_{18}N_2O_4BrFNa$, 519.0332 $[M+Na]^+$, found 519.0340.

2-((3-((4-Bromophenyl)(methyl)amino)-1-(4-chlorophenyl)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4v**)



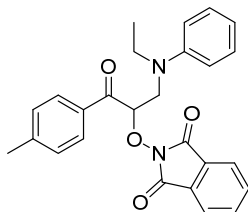
Yellow solid, mp 164-165 °C; 1H NMR (400 MHz, $CDCl_3$; δ , ppm) 8.06-7.96 (m, 2H), 7.91-7.66 (m, 4H), 7.53-7.40 (m, 2H), 7.38-7.29 (m, 2H), 6.66 (d, $J = 9.2$ Hz, 2H), 5.69 (t, $J = 6.0$ Hz, 1H), 4.06-4.03 (m, 2H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ , ppm) 194.2, 163.2, 147.0, 140.7, 134.8, 133.5, 132.1, 130.5, 129.1, 128.6, 123.8, 114.5, 85.4, 53.8, 39.9; IR (KBr, ν , cm^{-1}) 2911, 1735, 1666, 1587, 1497, 1258, 969, 875, 700; HRMS (APCI) m/z Calcd. For $C_{24}H_{18}N_2O_4BrClNa$, 535.0036 $[M+Na]^+$, found 535.0040.

2-((1-(4-Bromophenyl)-3-((4-bromophenyl)(methyl)amino)-1-oxopropan-2-yl)oxy)isoindoline-1,3-dione (**4w**)

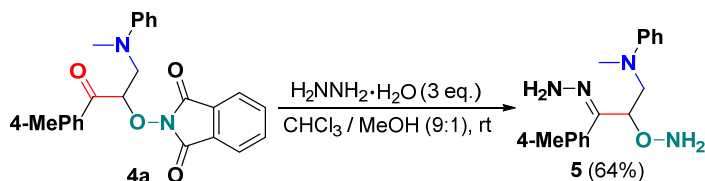


Yellow solid; mp 147-148 °C; 1H NMR (400 MHz, $CDCl_3$; δ , ppm) 7.95-7.88 (m, 2H), 7.85-7.73 (m, 4H), 7.66-7.59 (m, 2H), 7.35-7.26 (m, 3H), 6.66 (d, $J = 9.0$ Hz, 2H), 5.68 (t, $J = 6.0$ Hz, 1H), 4.06-4.02 (s, 2H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ , ppm) 194.5, 163.2, 147.0, 134.8, 133.9, 132.1, 132.1, 130.5, 129.6, 128.6, 123.8, 114.4, 109.7, 85.4, 53.8, 39.9; IR (KBr, ν , cm^{-1}) 2911, 1735, 1666, 1587, 1497, 1258, 969, 875, 700; HRMS (APCI) m/z Calcd. For $C_{24}H_{18}N_2O_4Br_2Na$, 578.9531 $[M+Na]^+$, found 578.9533.

2-((3-(Ethyl(phenyl)amino)-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (**4x**) (major)



Yellow solid; mp 99-100 °C; ¹H NMR (400 MHz, CDCl₃; δ, ppm) 7.94–7.71 (m, 7H), 7.27-7.22 (m, 3H), 6.79-6.73 (m, 3H), 5.88-5.85 (m, 1H), 4.09-3.94 (m, 2H), 3.46-3.33 (m, 2H), 2.41 (s, 3H), 1.10 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃; δ, ppm) 195.1, 163.2, 147.0, 145.1, 134.6, 133.0, 129.4, 129.1, 128.7, 123.7, 123.6, 117.1, 113.0, 84.1, 51.6, 46.0, 21.8, 11.7. IR (KBr, ν, cm⁻¹): 3060, 2965, 1791, 1736, 1661, 1604, 1506, 1353, 1187, 1080, 971, 876, 702; HRMS (APCI): *m/z* Calcd. For: C₂₆H₂₄N₂O₄, 451.1634 [M+Na], found: 451.1635.



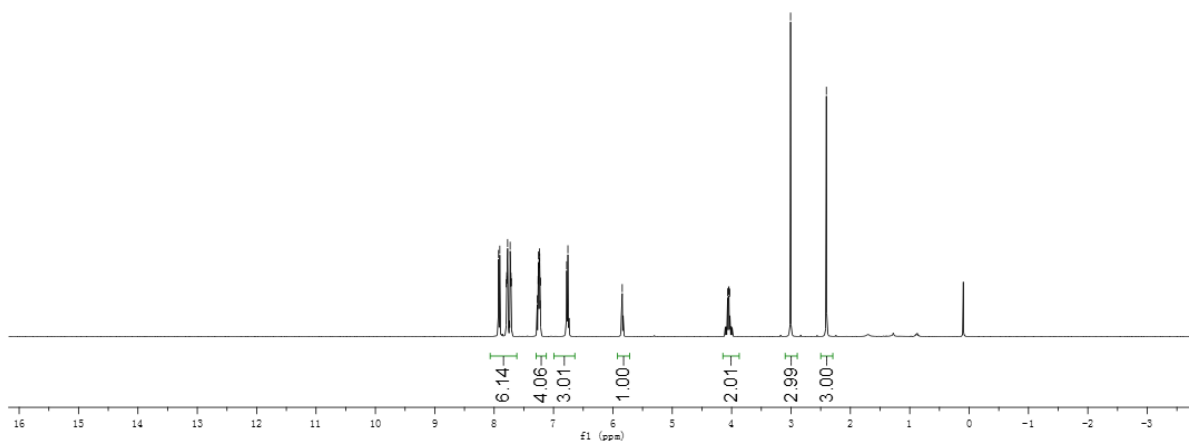
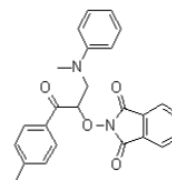
Scheme 2. Further synthetic transformations

To a solution of **4a** (53 mg, 0.2 mmol) in a mixed solvent of MeOH and CHCl₃ (2.0 mL V/V = 9:1), hydrazine monohydrate (80% in water, 0.03 mL, 0.6 mmol) was added. The reaction mixture was stirred at room temperature for about 16 hours. After the reaction finished, the mixture was evaporated under vacuum and purified by column chromatography to afford a product **5** as a colorless oil (64%).

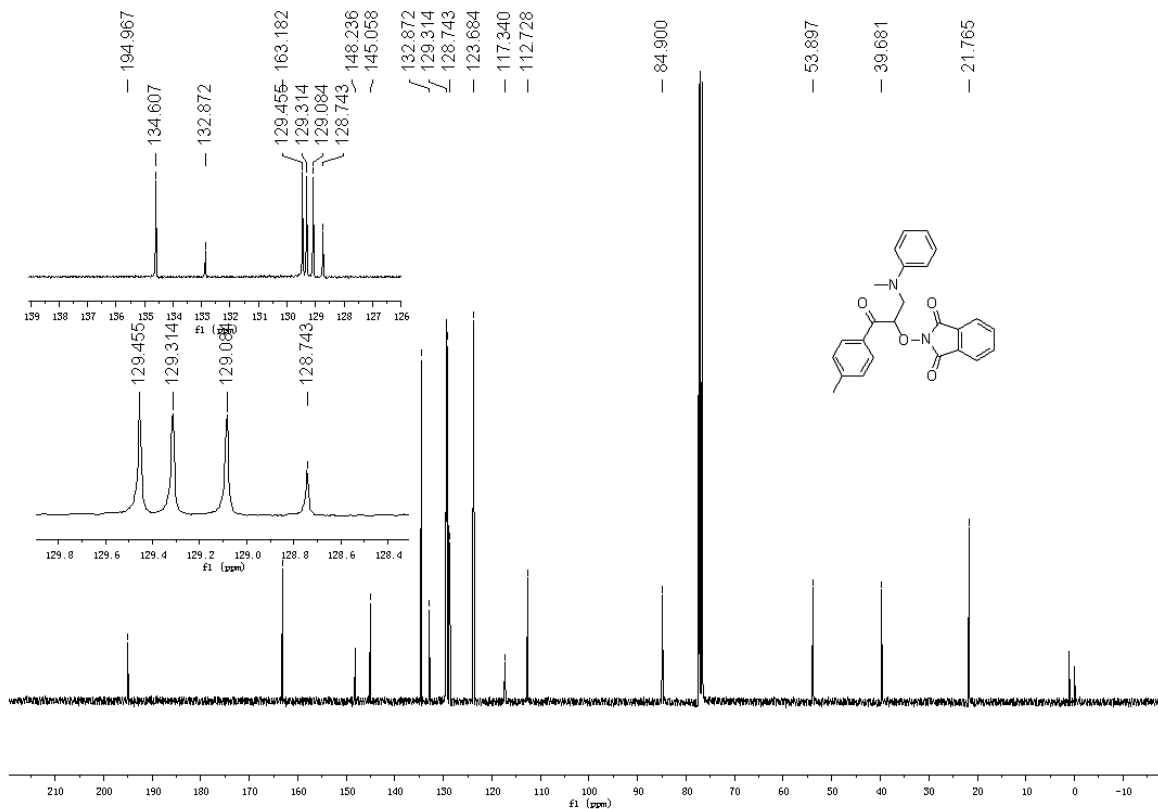
¹H NMR (400 MHz, CDCl₃; δ, ppm) 7.93 (d, *J* = 8.0 Hz, 2H), 7.42-7.18 (m, 5H), 6.82 (s, 2H), 5.65 (s, 1H), 4.06– 3.73 (m, 2H), 3.00 (s, 3H), 2.43 (s, 3H), 1.84 (s, 2H), 1.80 (s, 2H). IR (KBr, ν, cm⁻¹) 3350, 3320, 3257, 3107, 1601, 1523, 1432, 1080, 965, 821; HRMS (APCI) *m/z* Calcd. for C₁₇H₂₁N₄O, 297.1715 [M-H]⁻, found 297.1721.

Copies of ^1H NMR and ^{13}C NMR of compounds

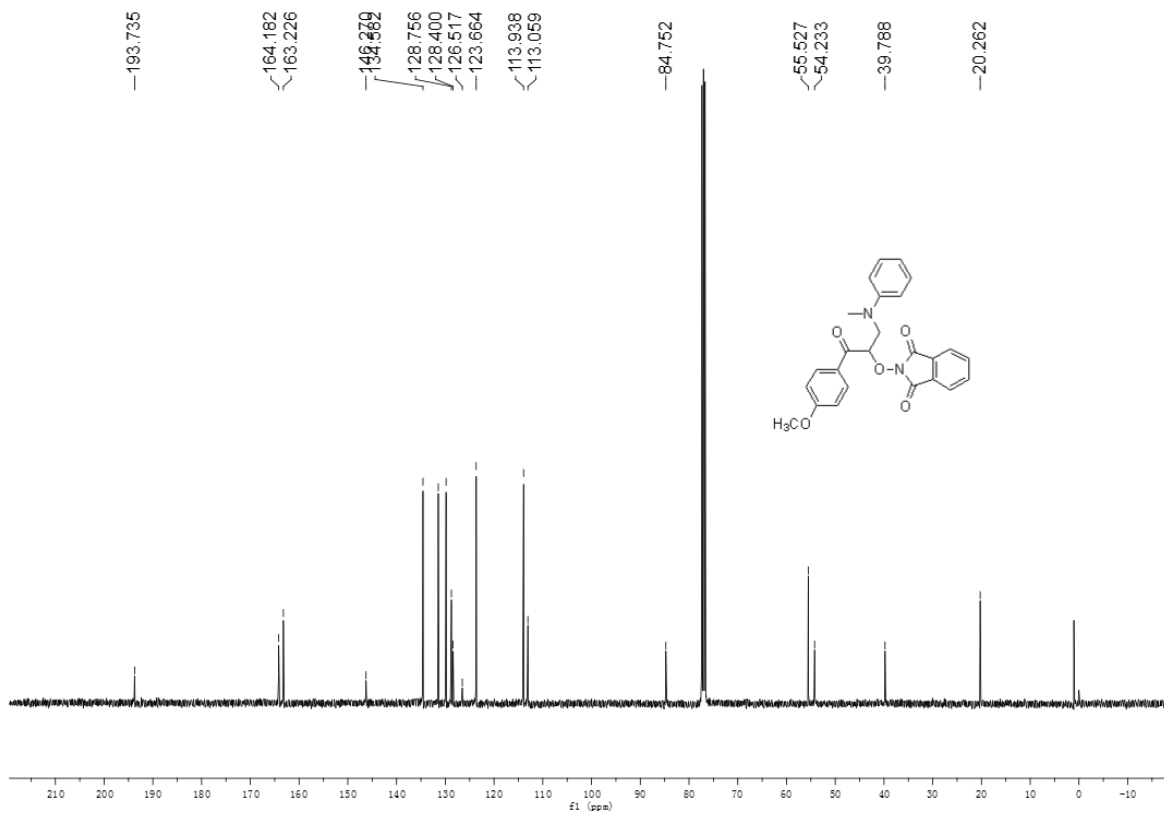
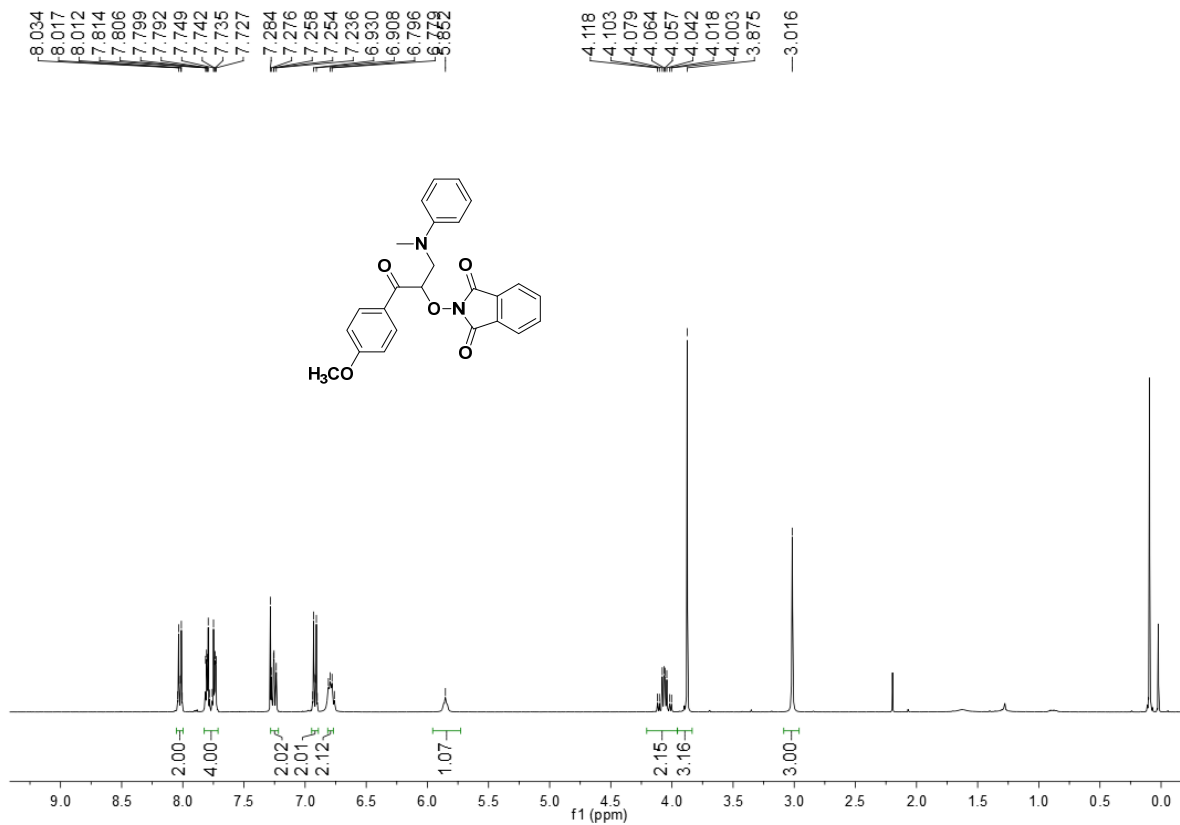
7.926
7.905
7.795
7.787
7.780
7.773
7.731
7.723
7.717
7.709
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6.758
5.842
4.068
4.052
4.045
4.030
3.007
2.405



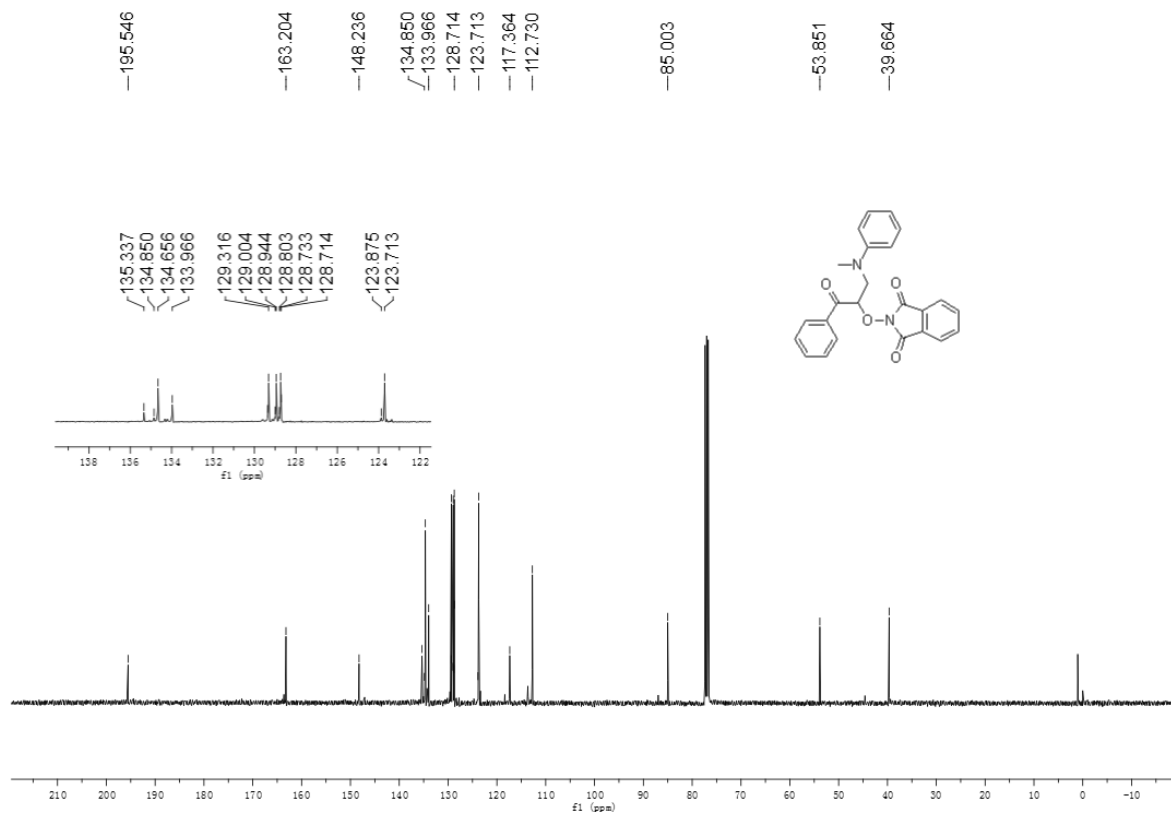
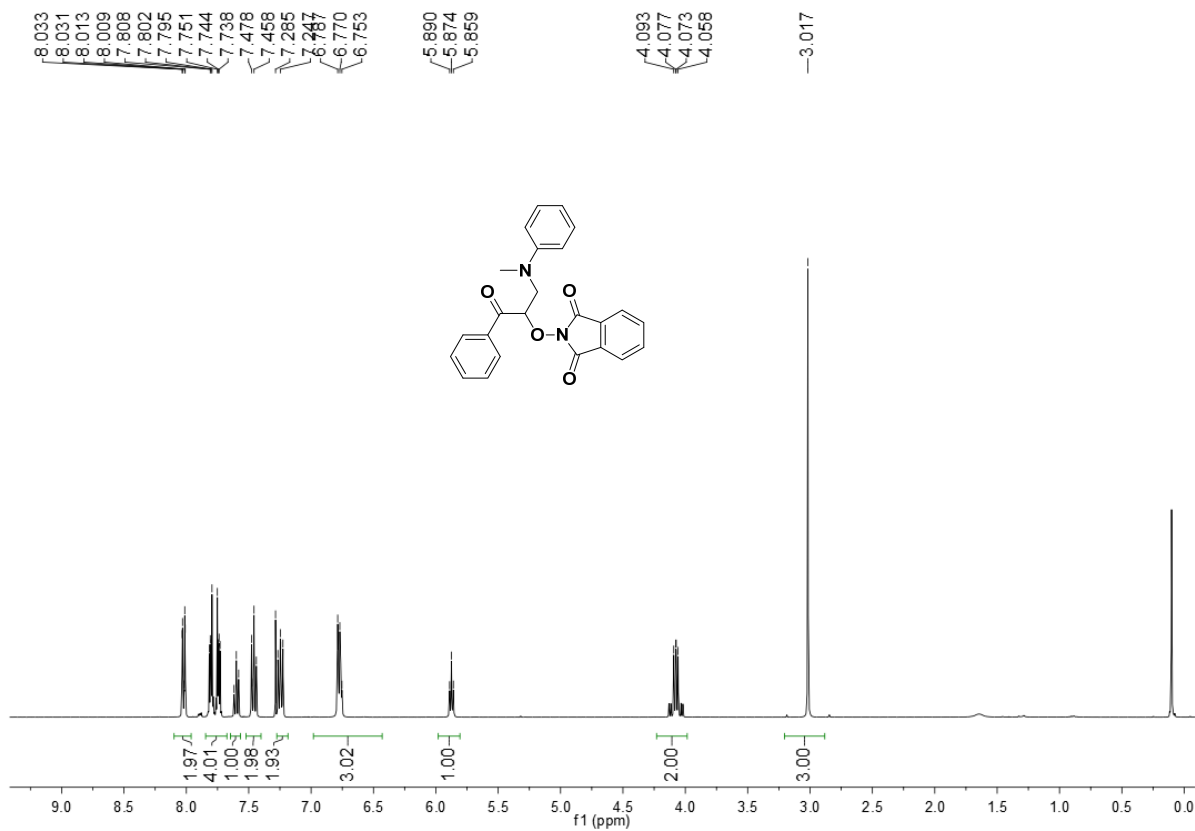
^1H NMR Spectrum of Compound 4a



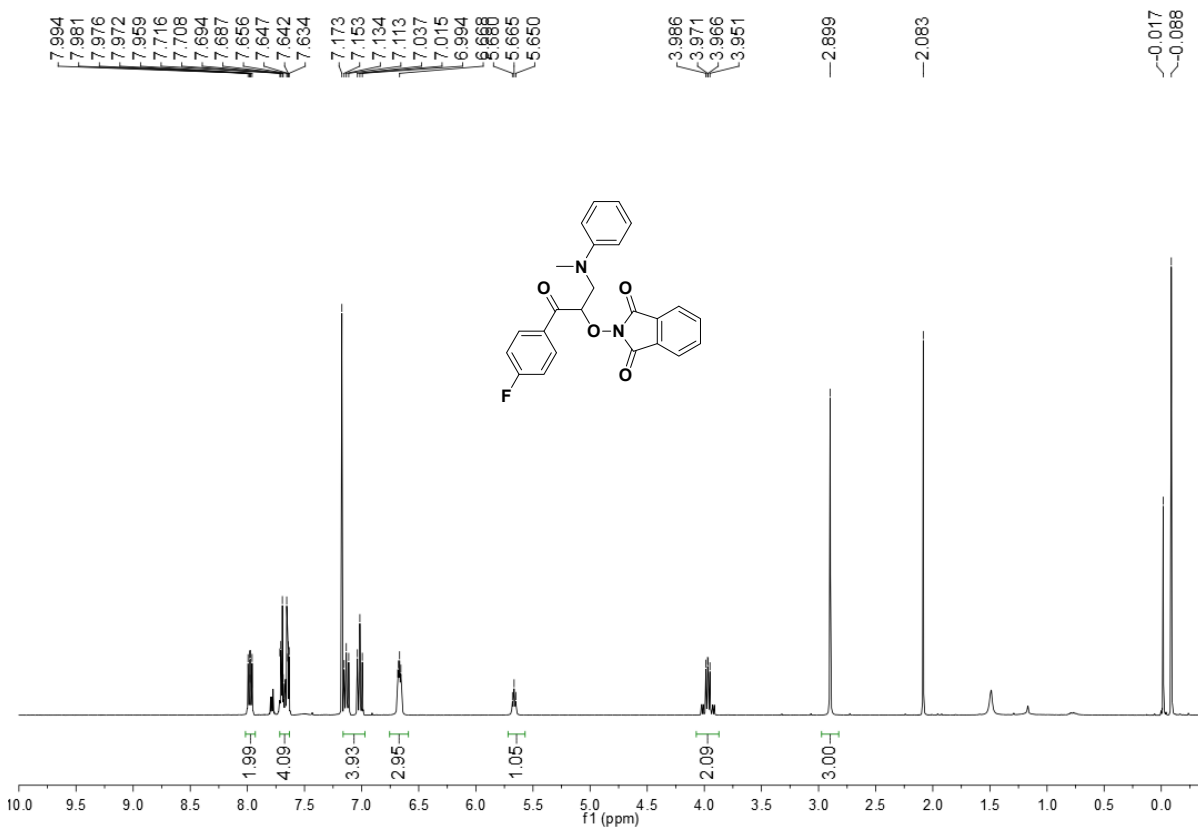
^{13}C NMR Spectrum of Compound 4a



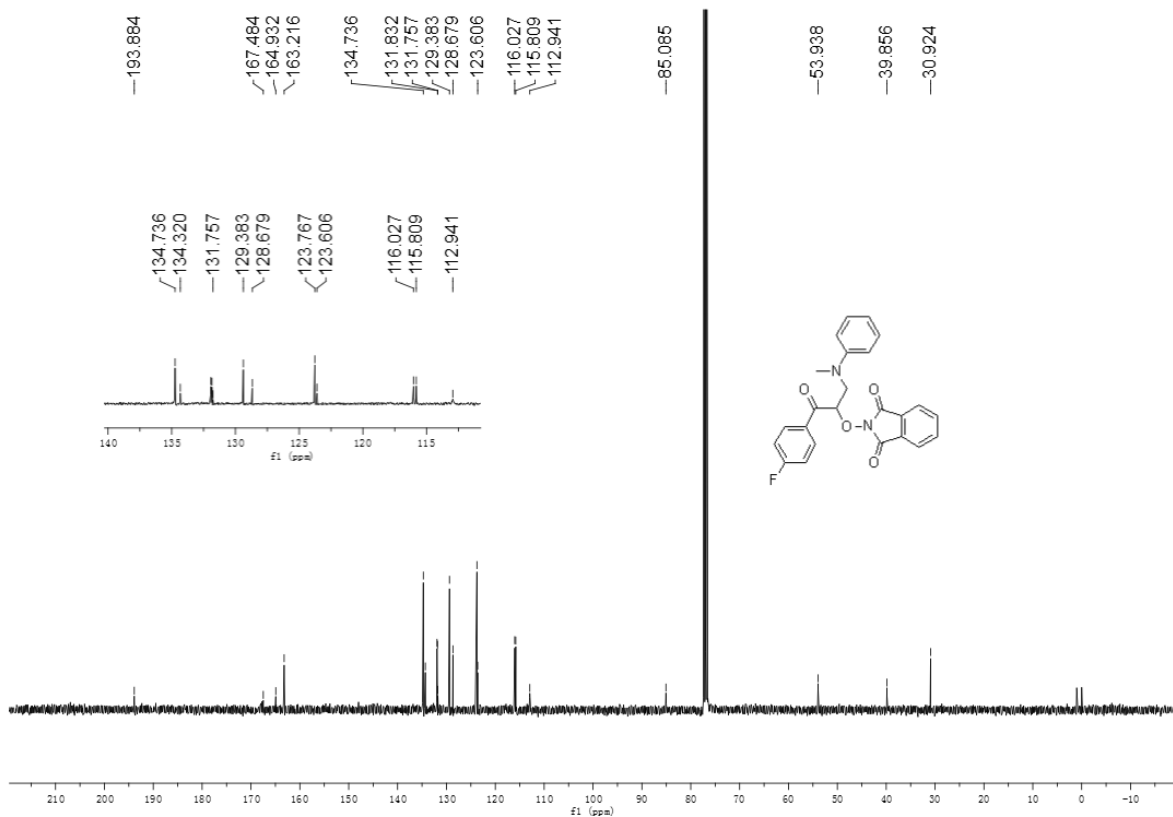
¹³C NMR Spectrum of Compound 4b



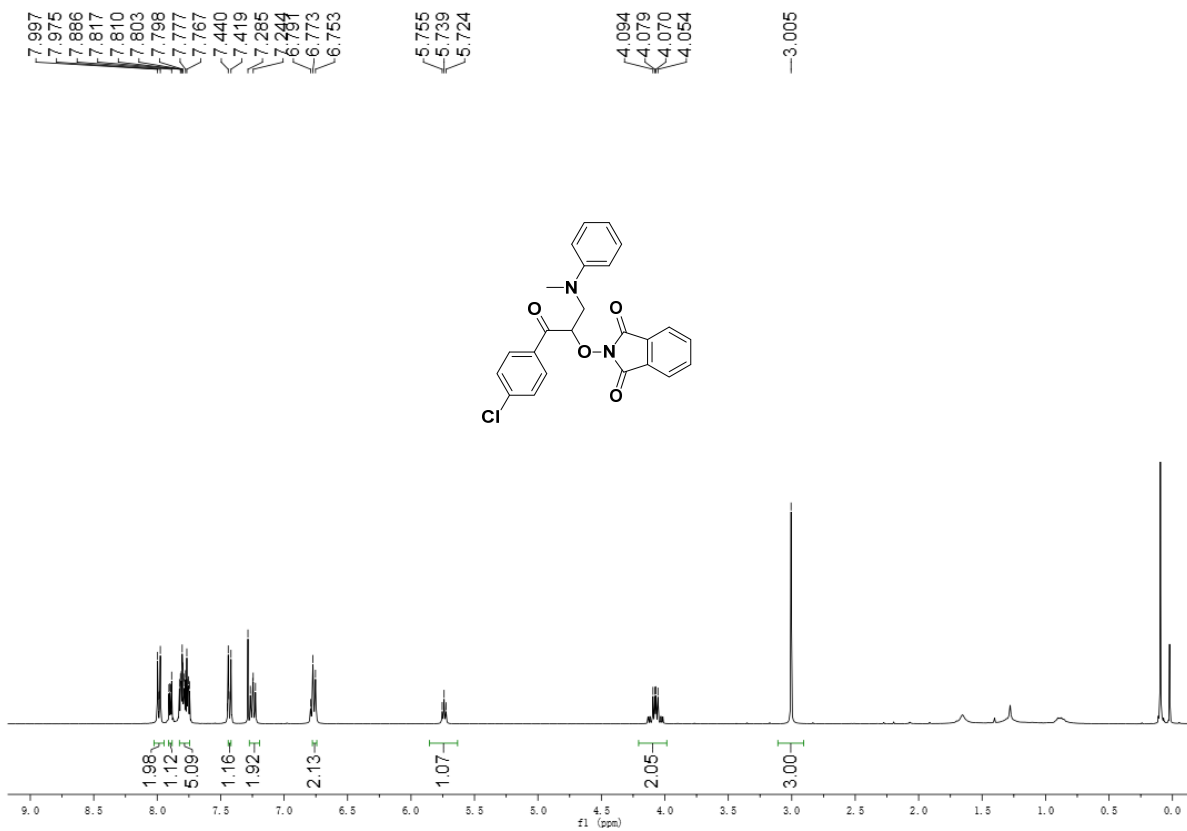
¹³C NMR Spectrum of Compound 4c



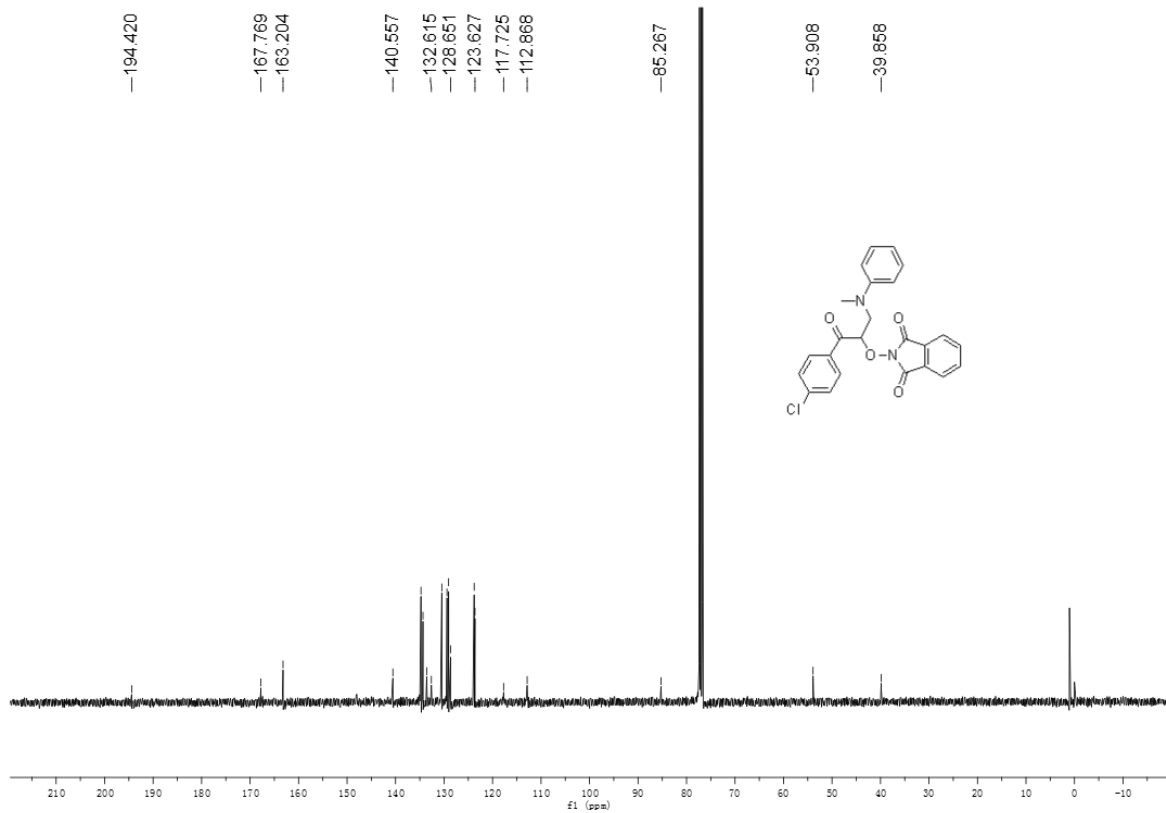
¹H NMR Spectrum of Compound 4d



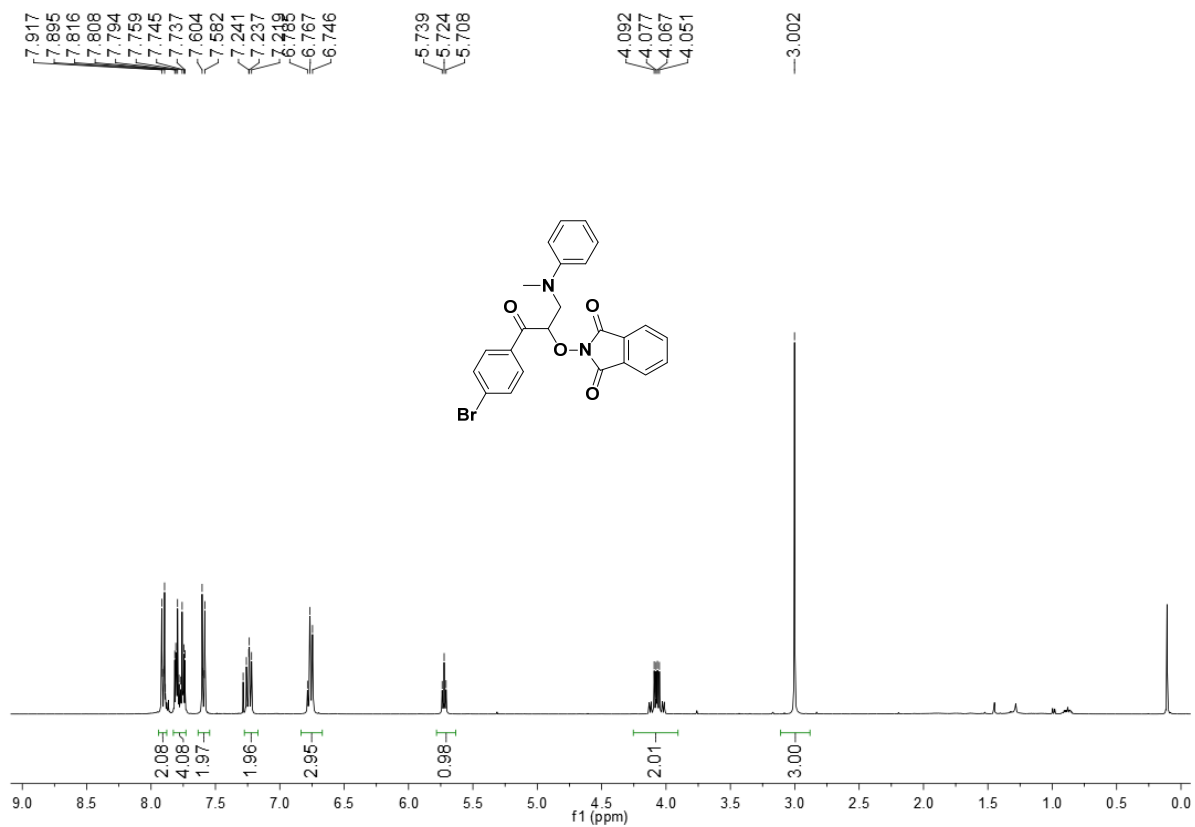
¹³C NMR Spectrum of Compound 4d



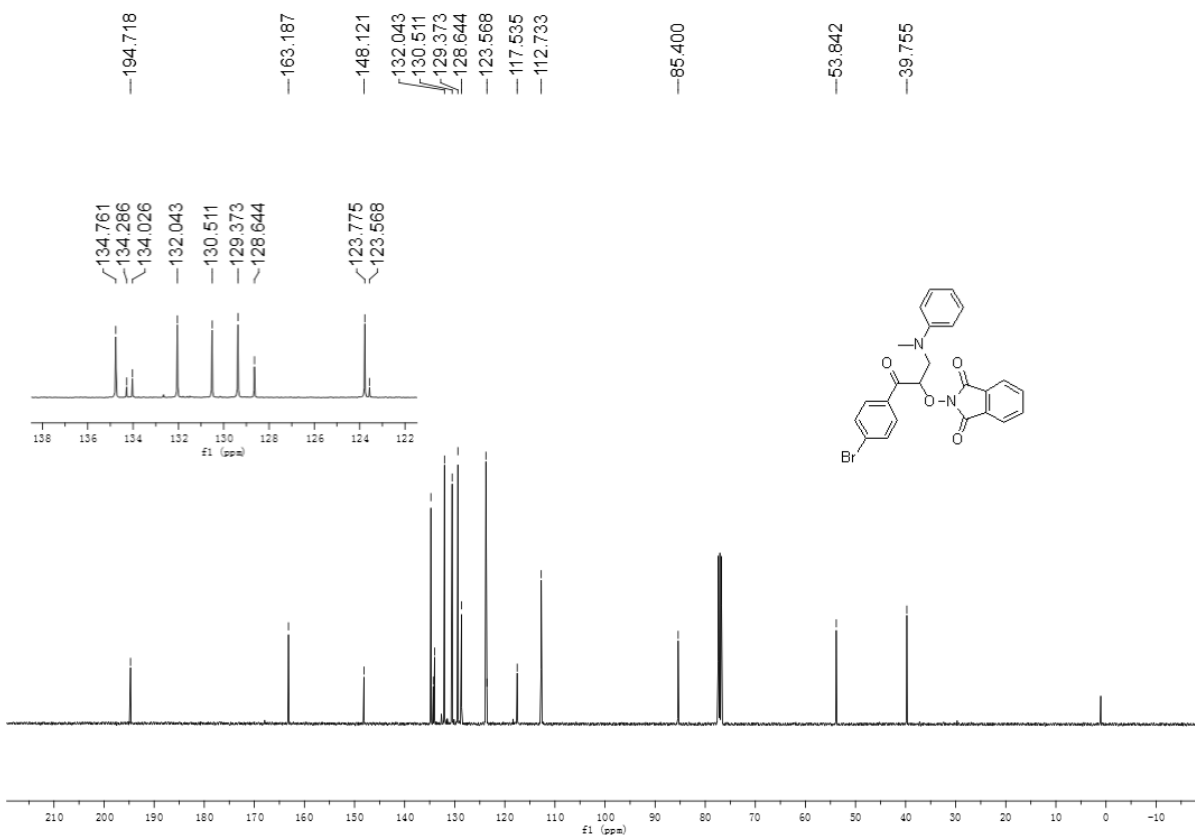
¹H NMR Spectrum of Compound 4e



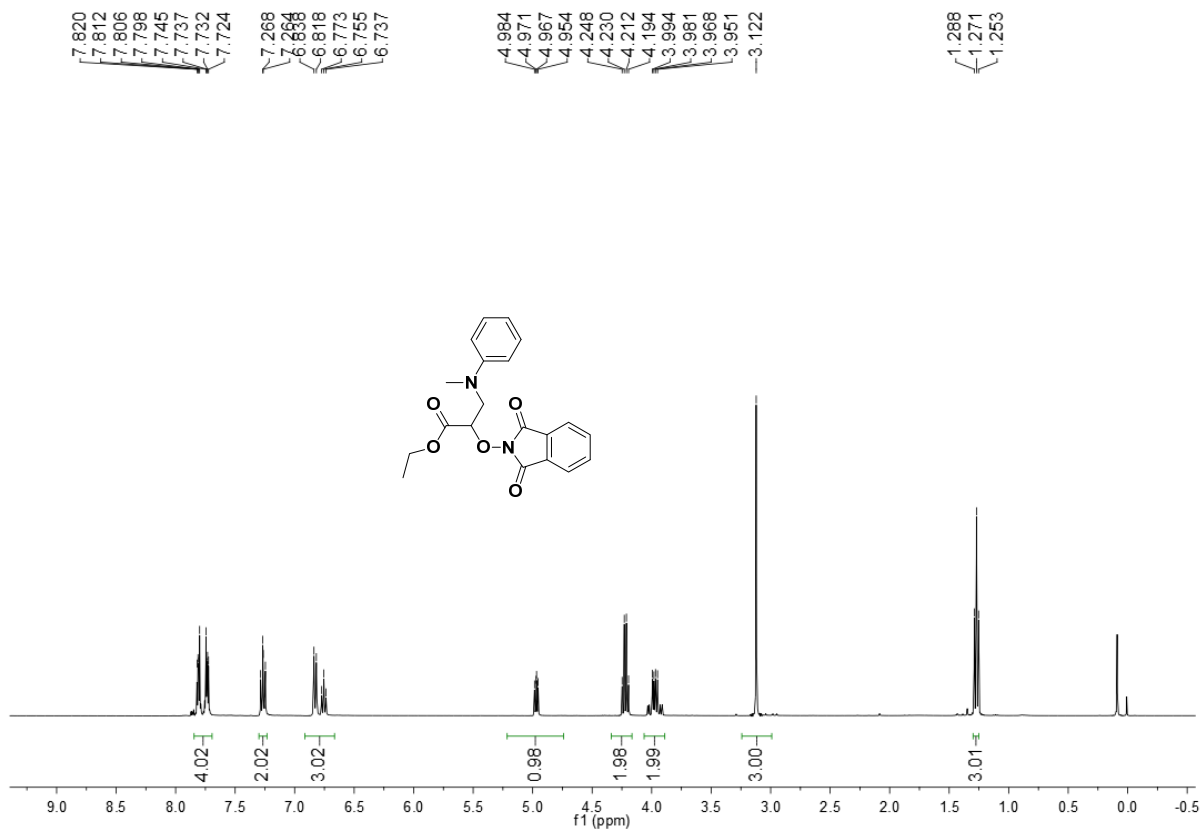
¹³C NMR Spectrum of Compound 4e



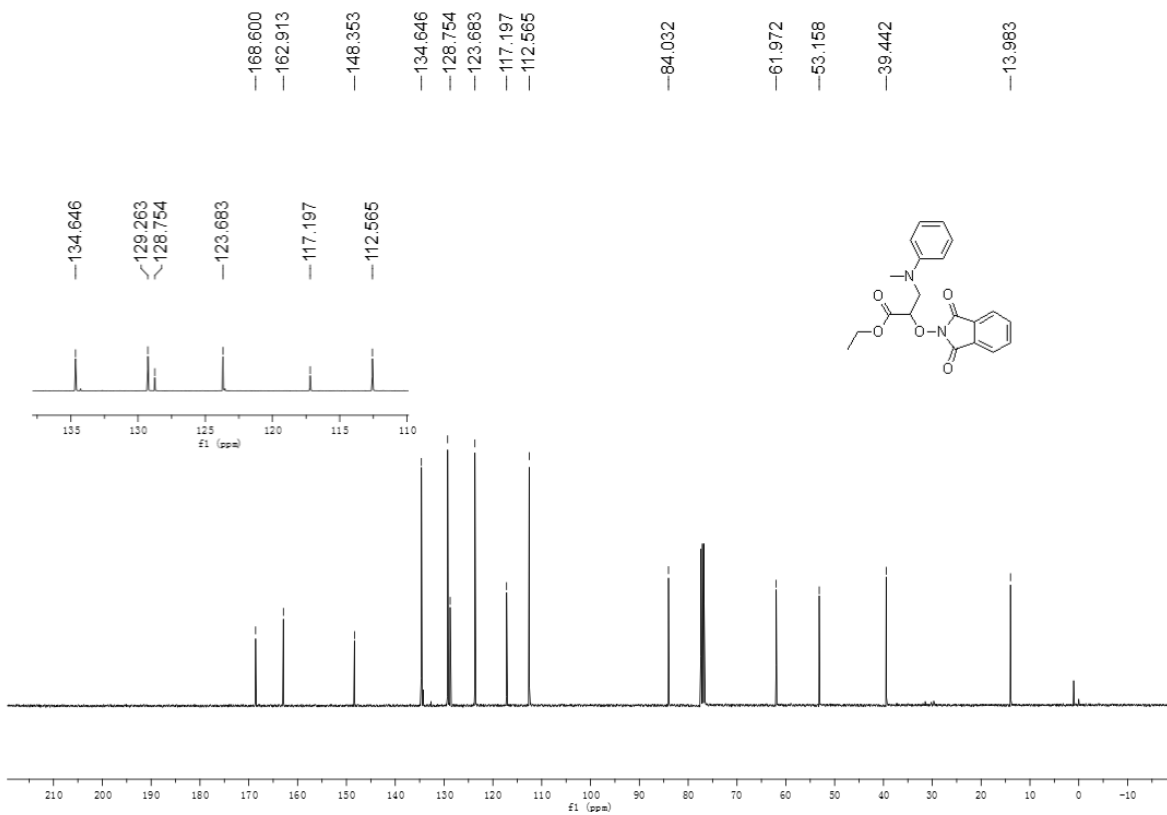
¹H NMR Spectrum of Compound 4f



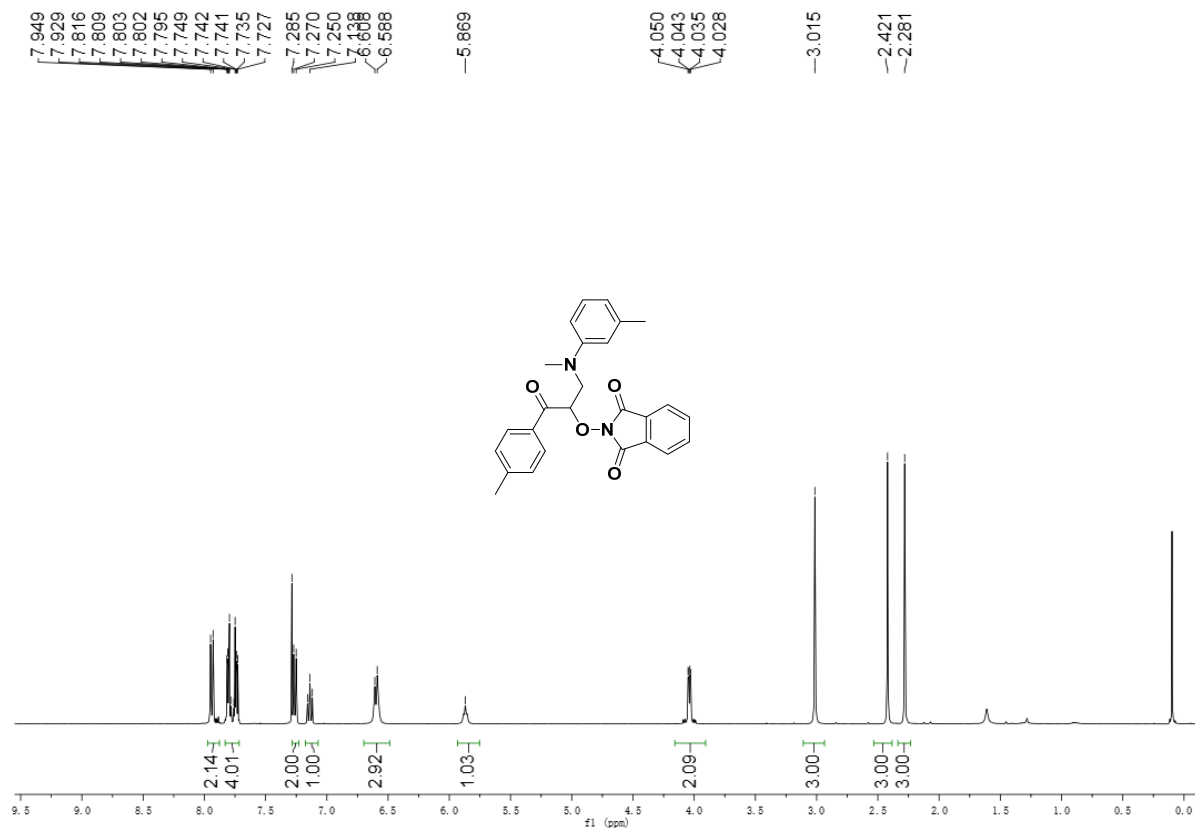
¹³C NMR Spectrum of Compound 4f



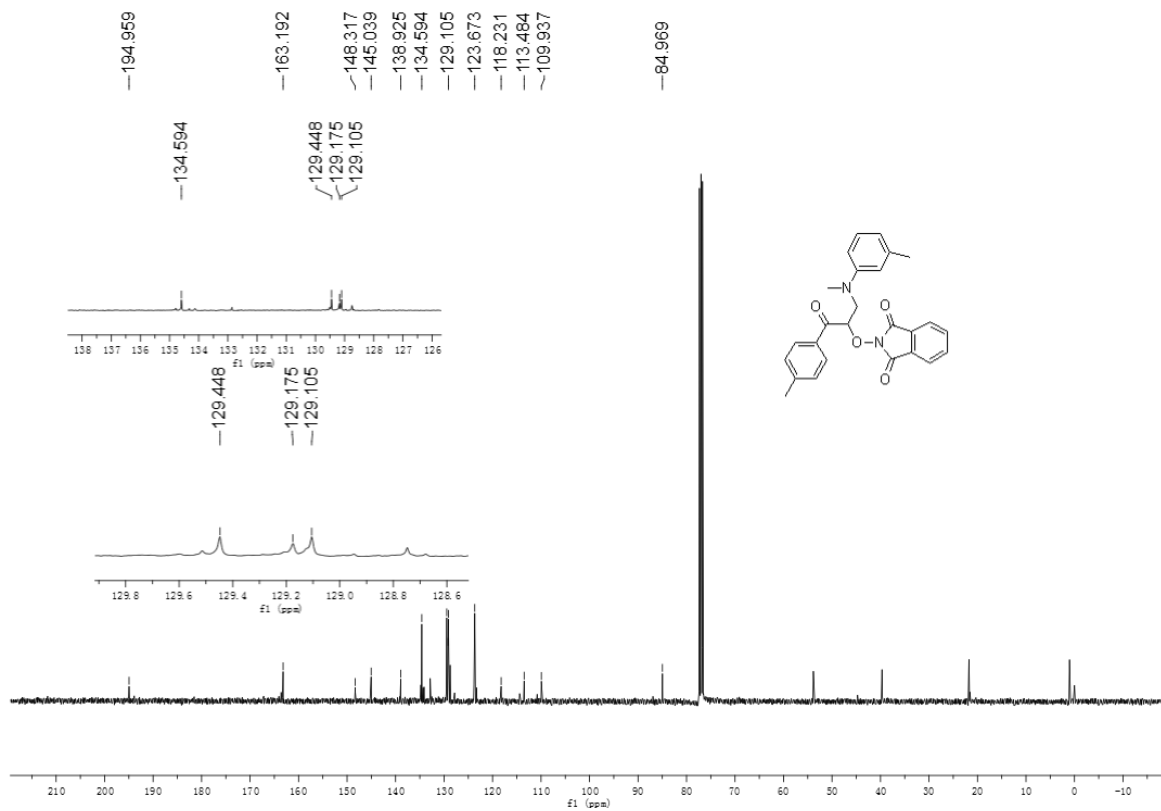
¹H NMR Spectrum of Compound 4g



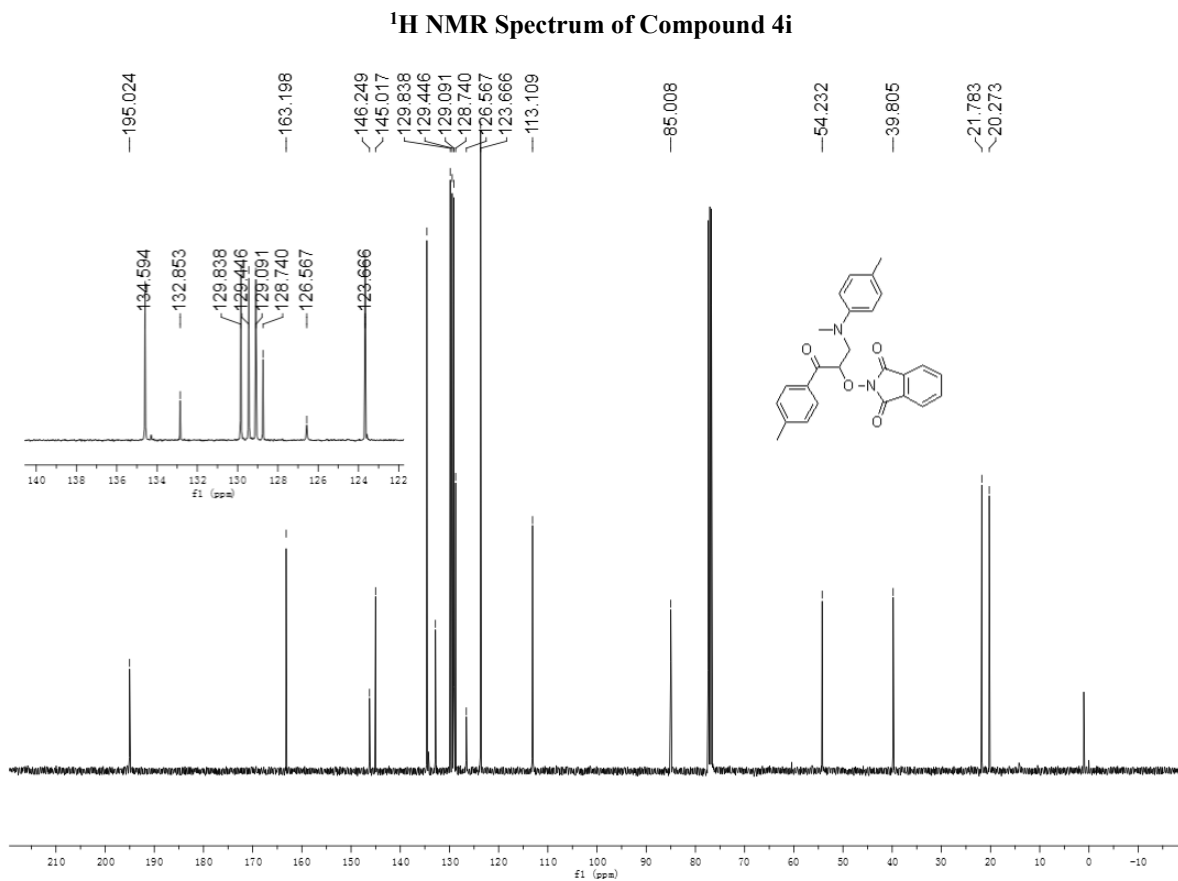
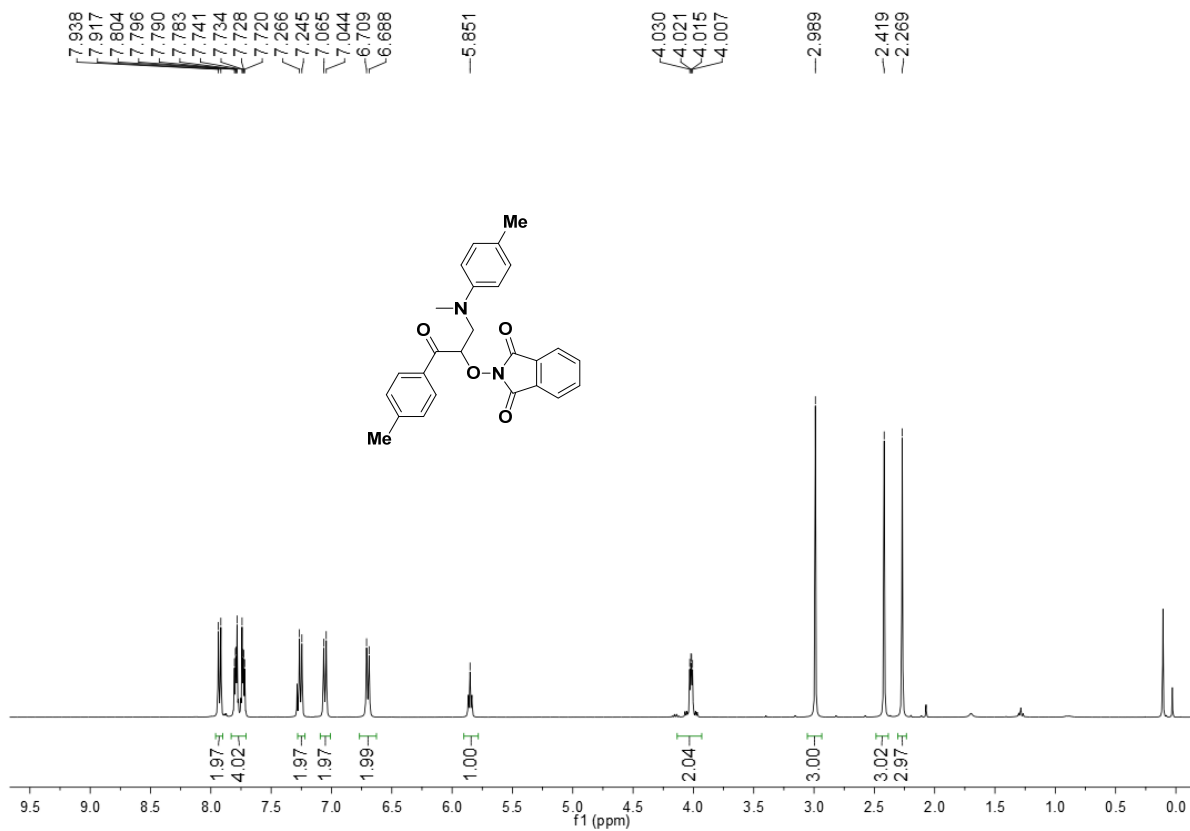
¹³C NMR Spectrum of Compound 4g



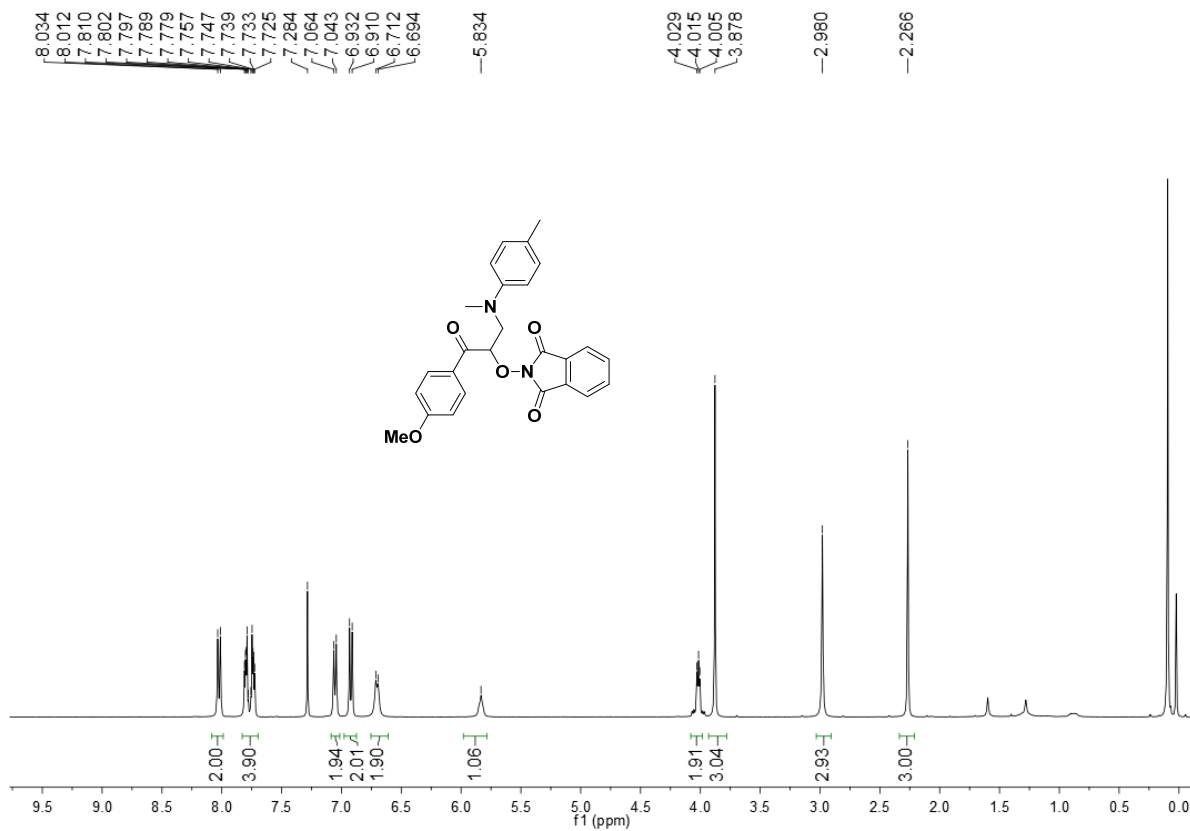
¹H NMR Spectrum of Compound 4h



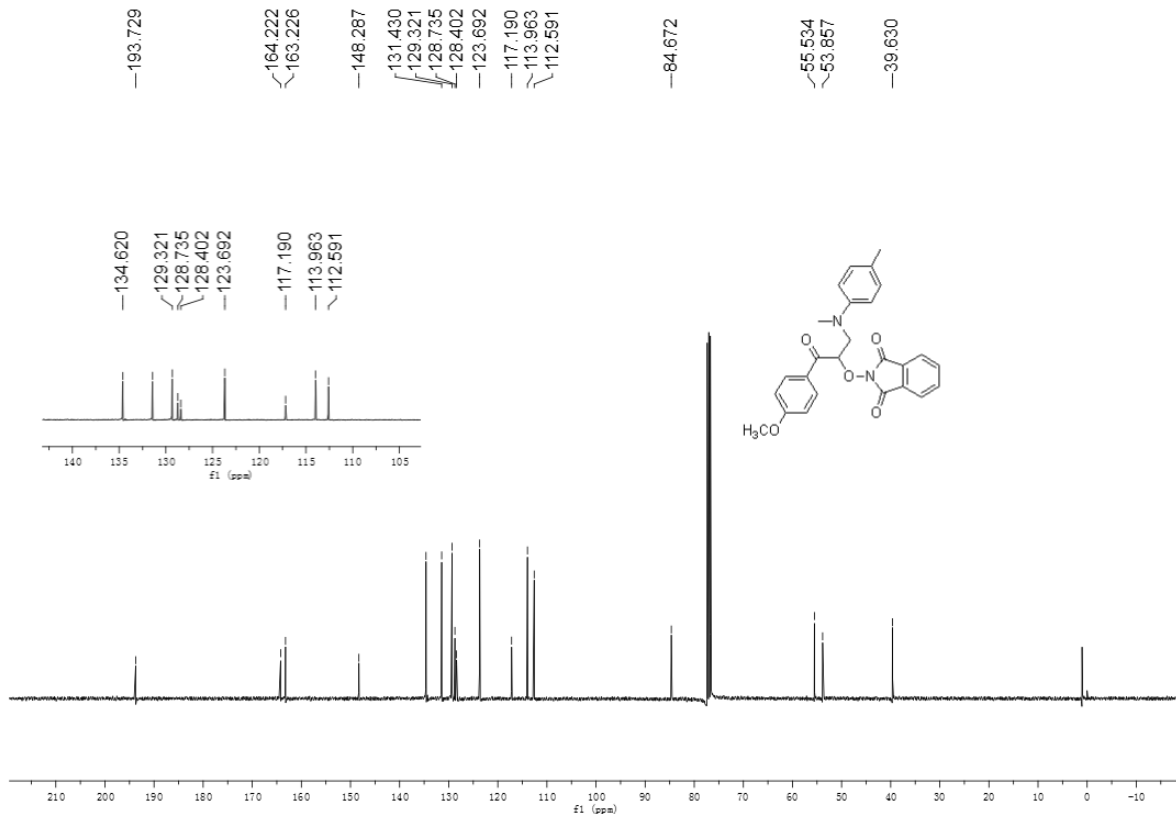
¹³C NMR Spectrum of Compound 4h



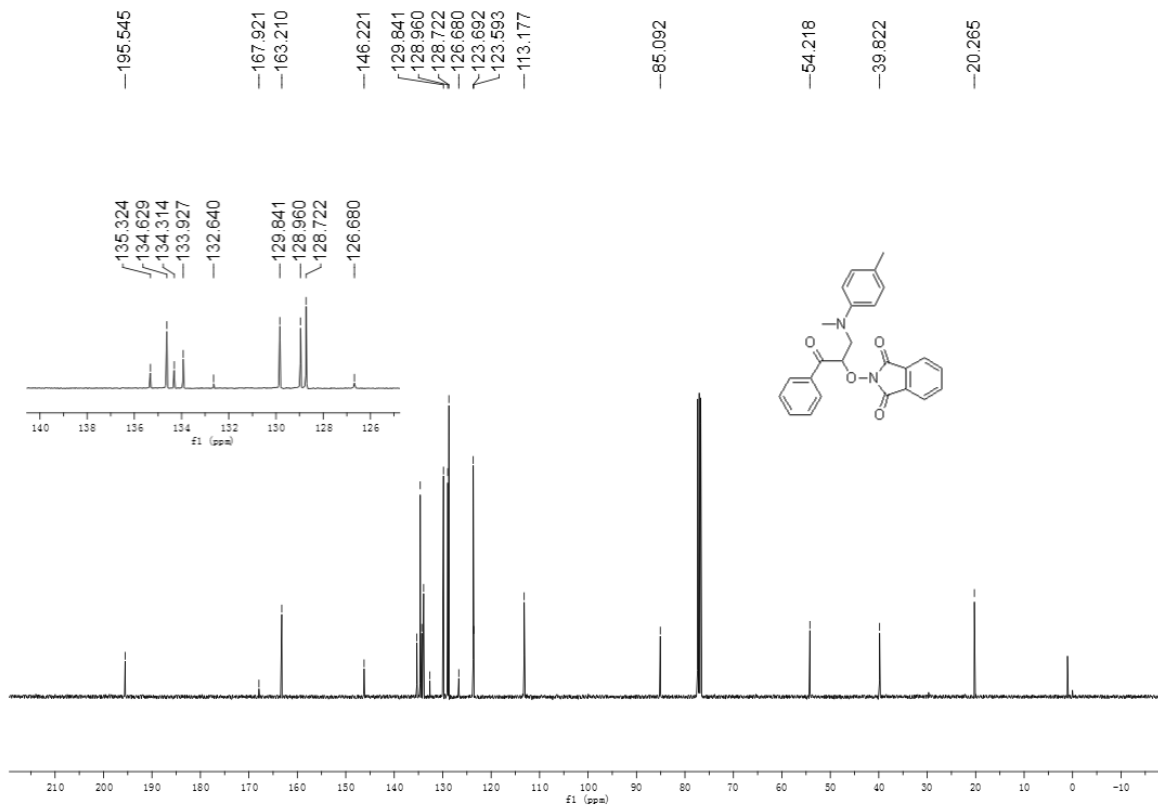
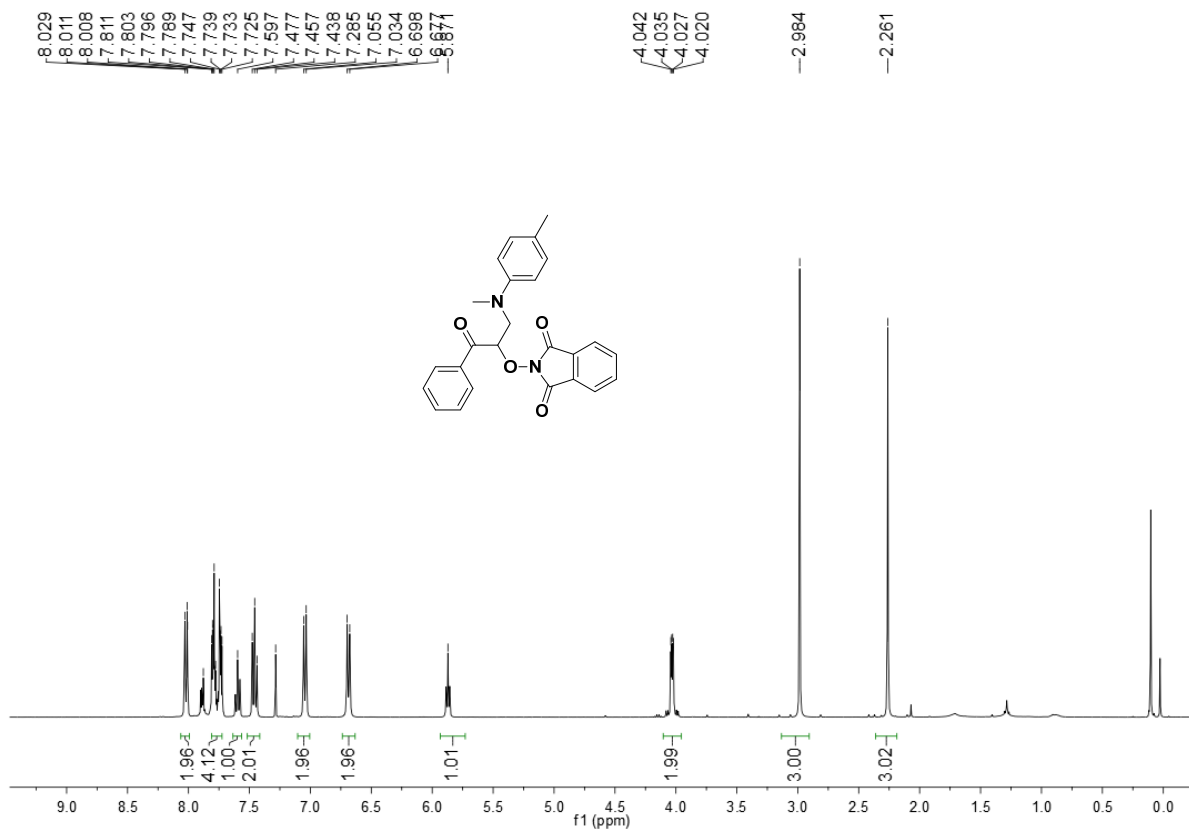
¹³C NMR Spectrum of Compound 4i



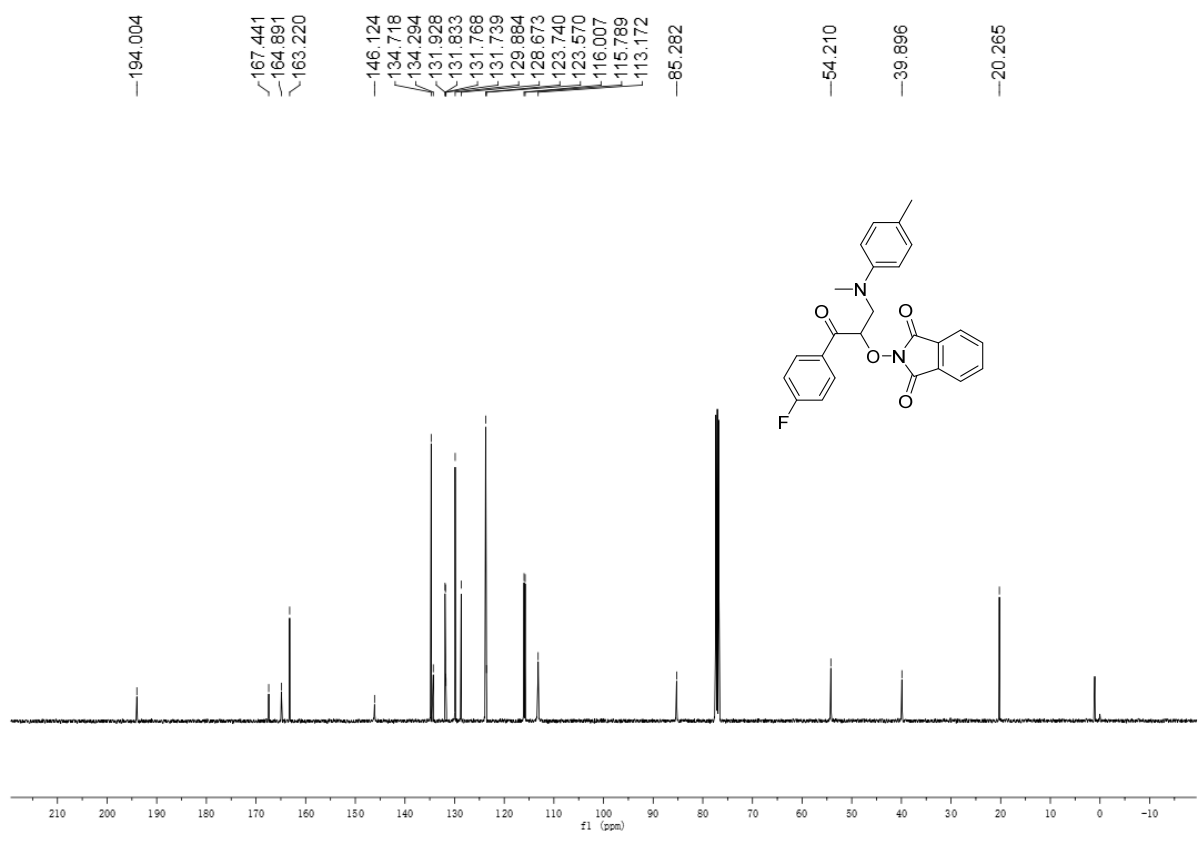
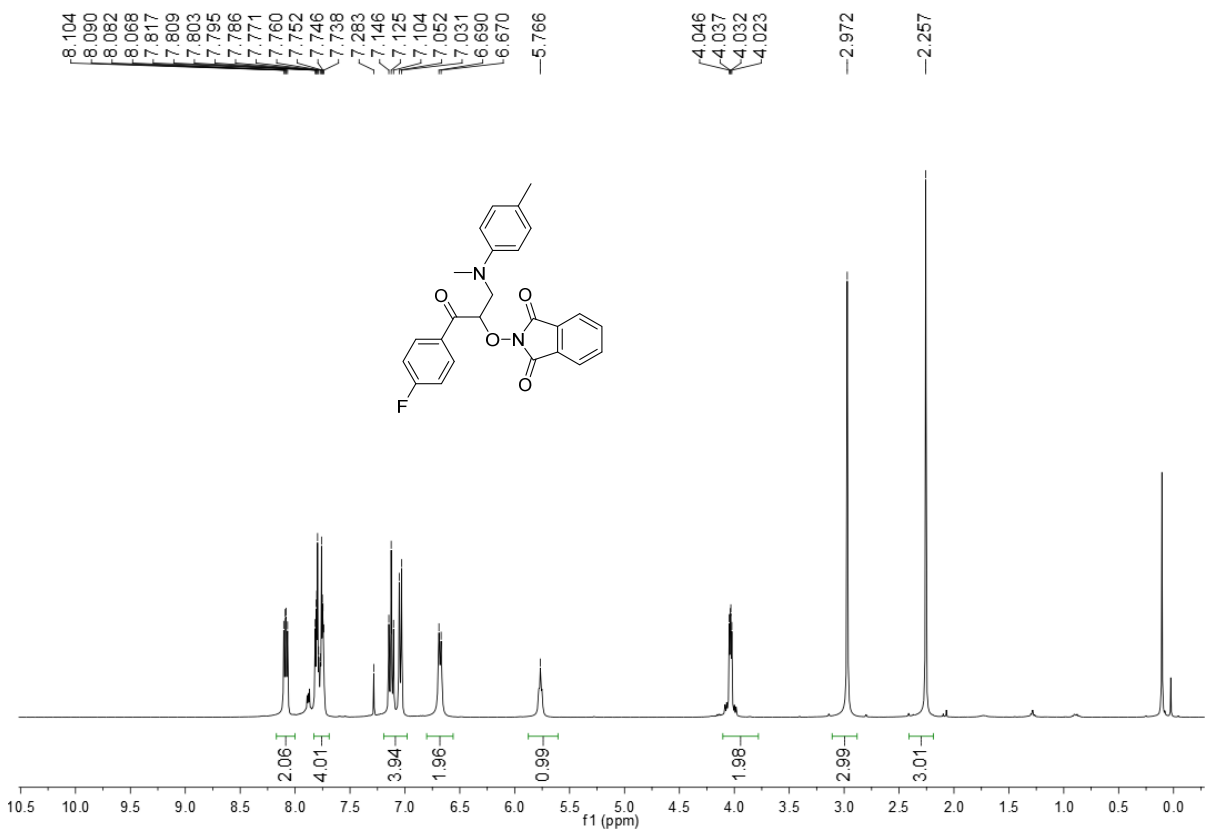
¹H NMR Spectrum of Compound 4j

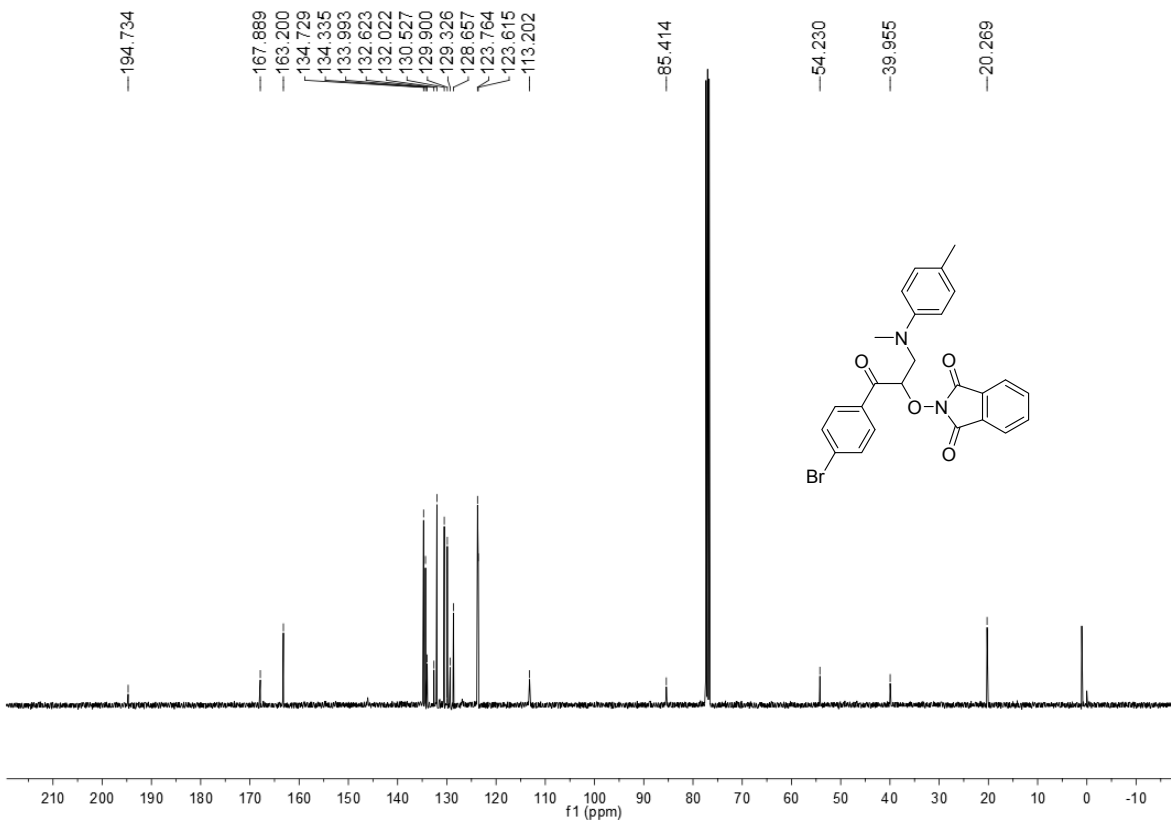
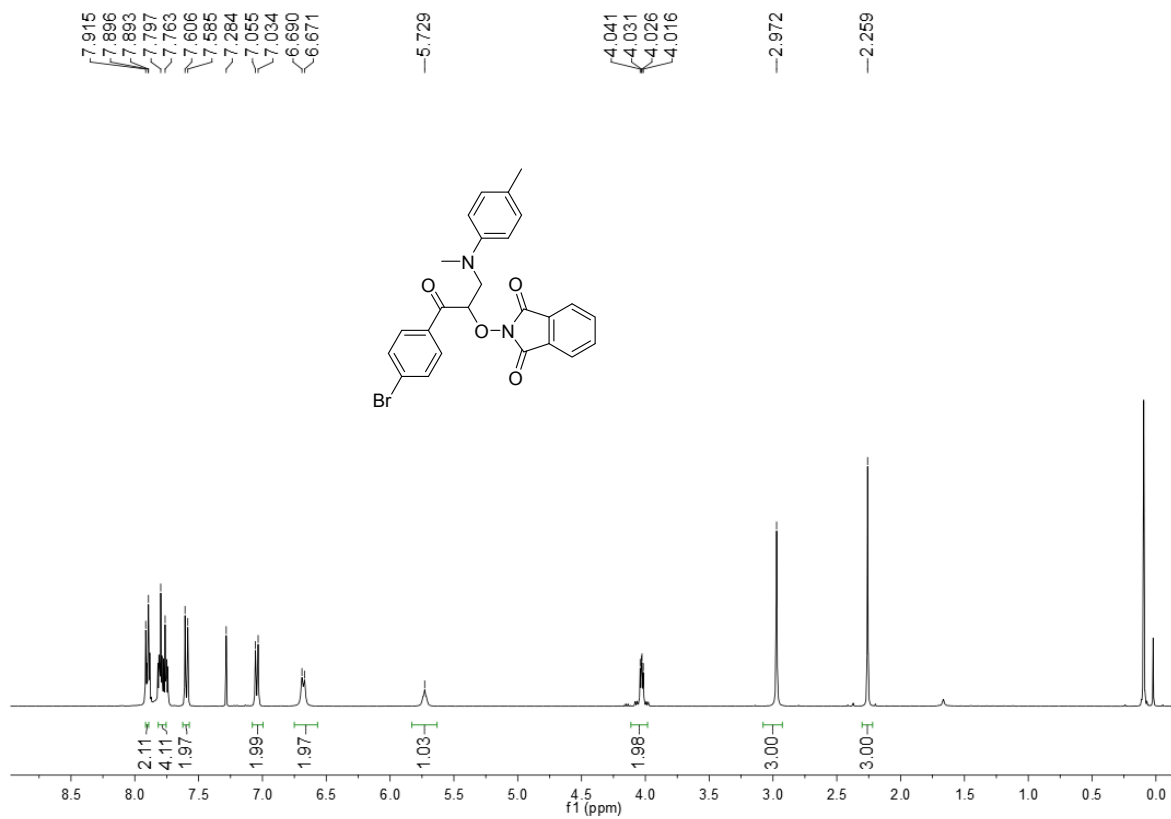


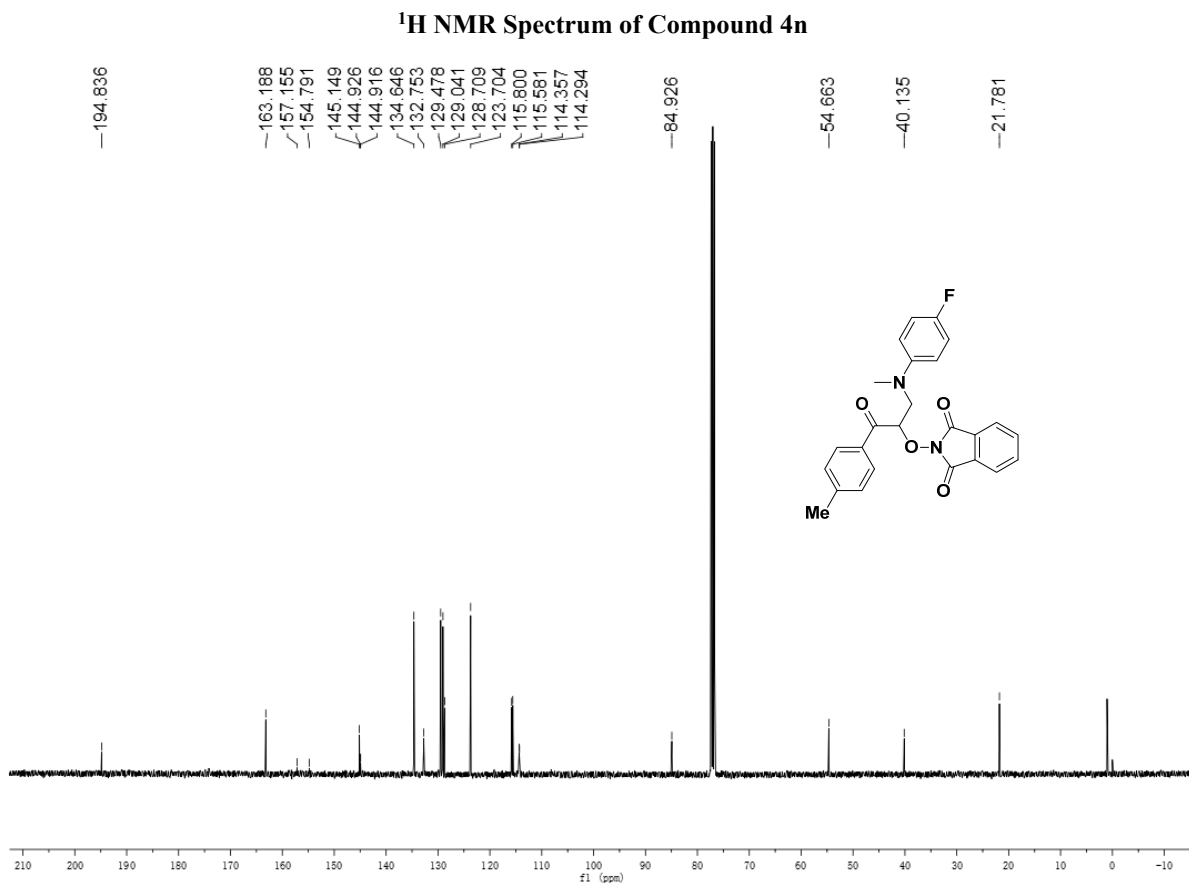
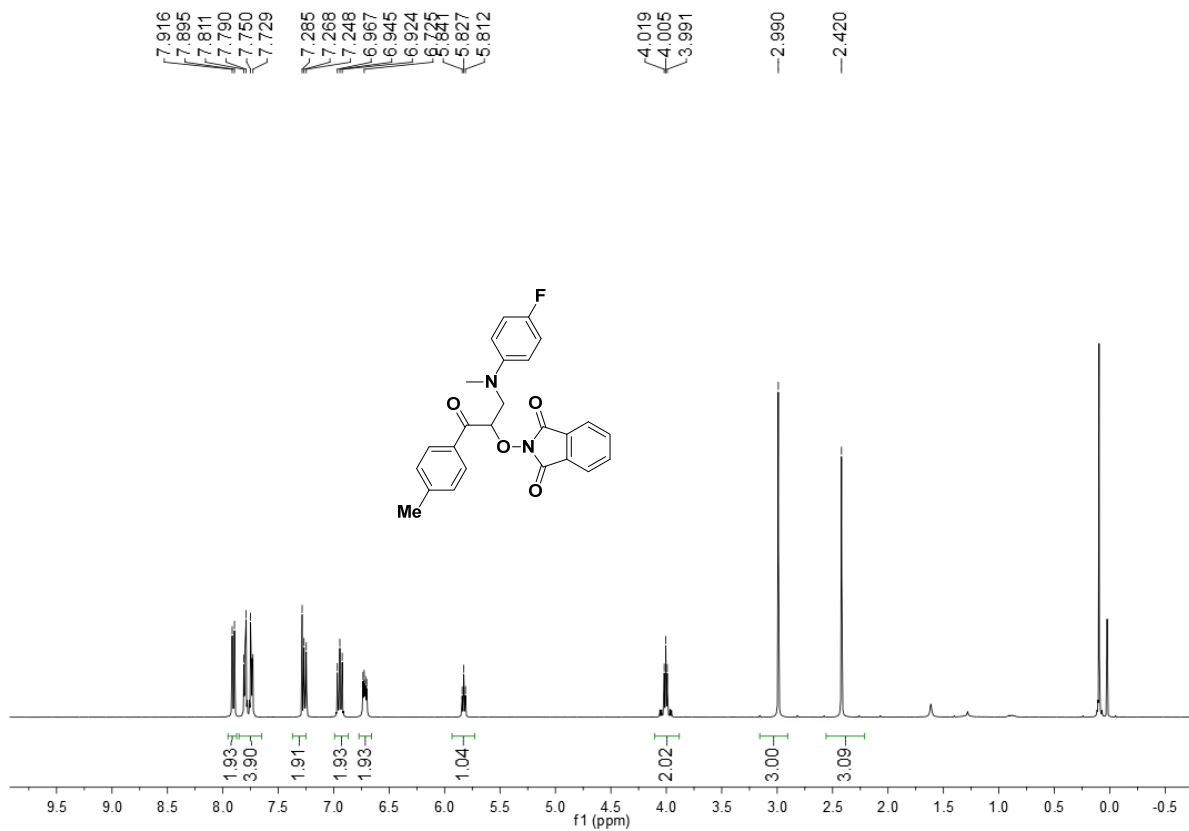
¹³C NMR Spectrum of Compound 4j

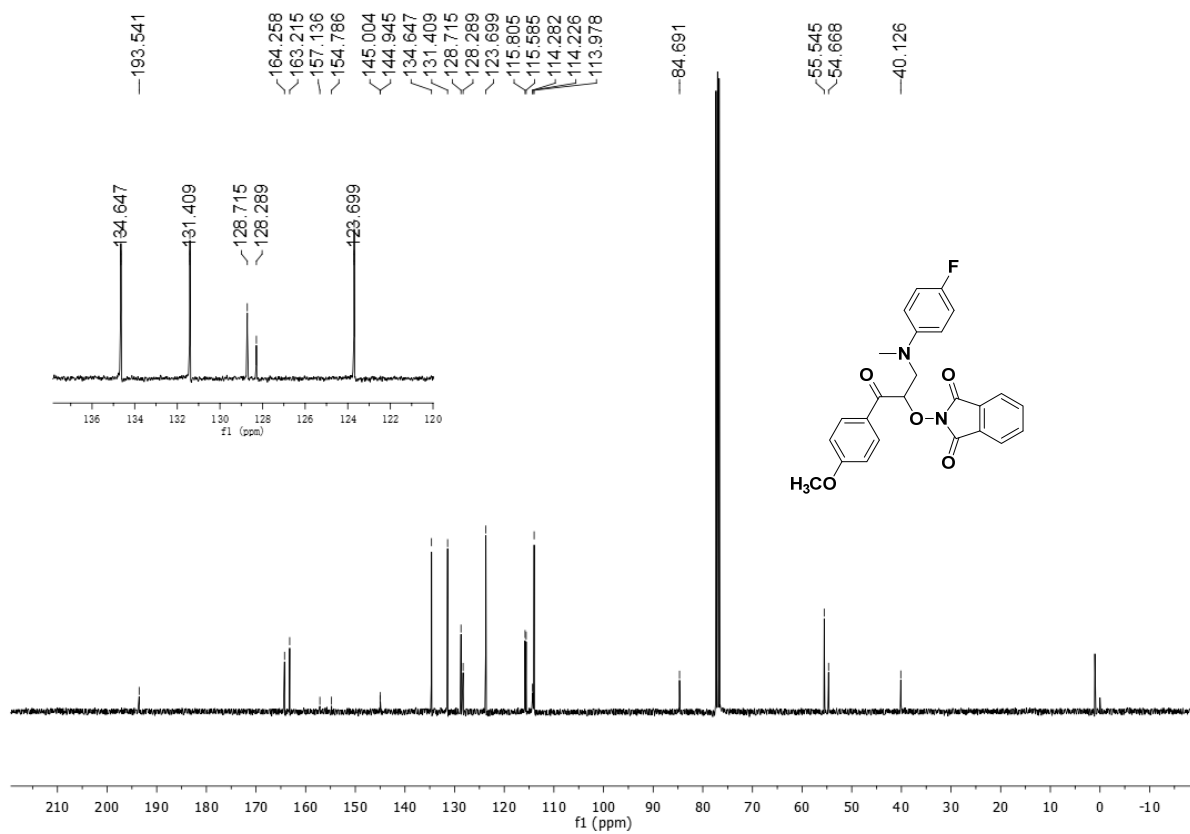
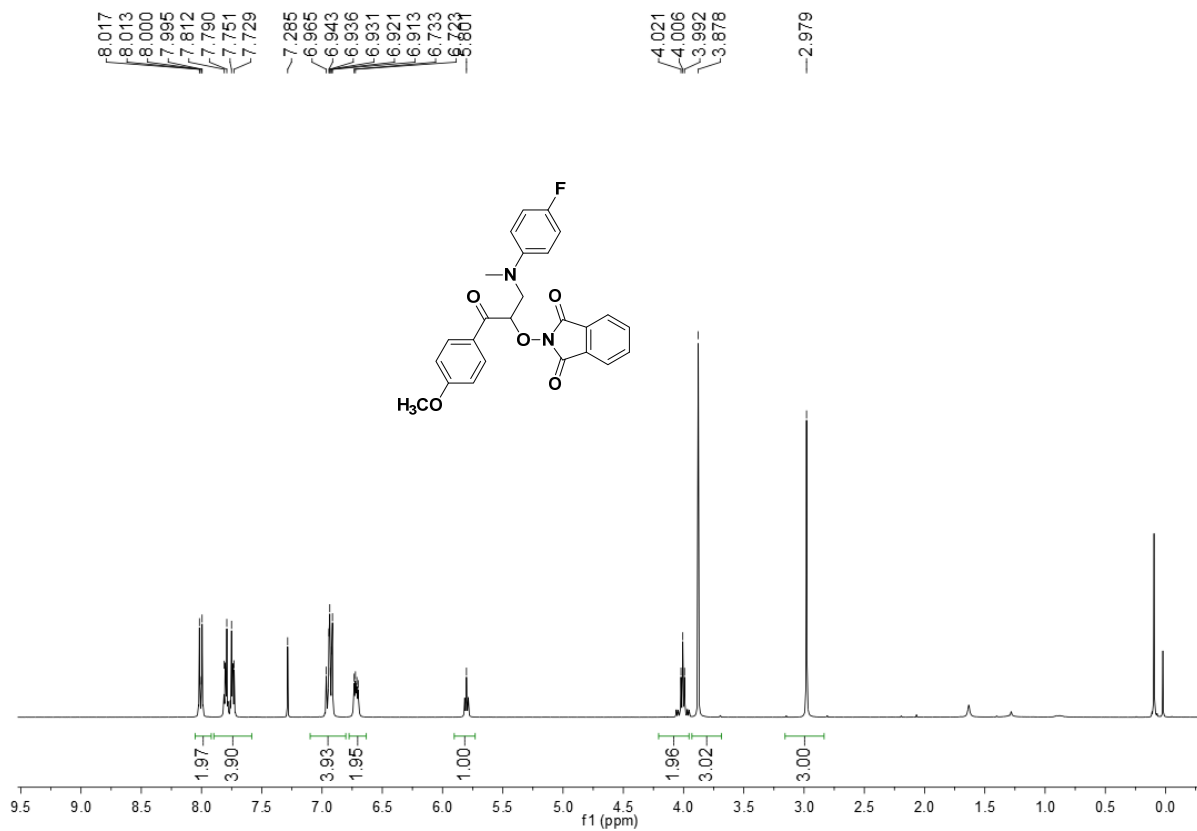


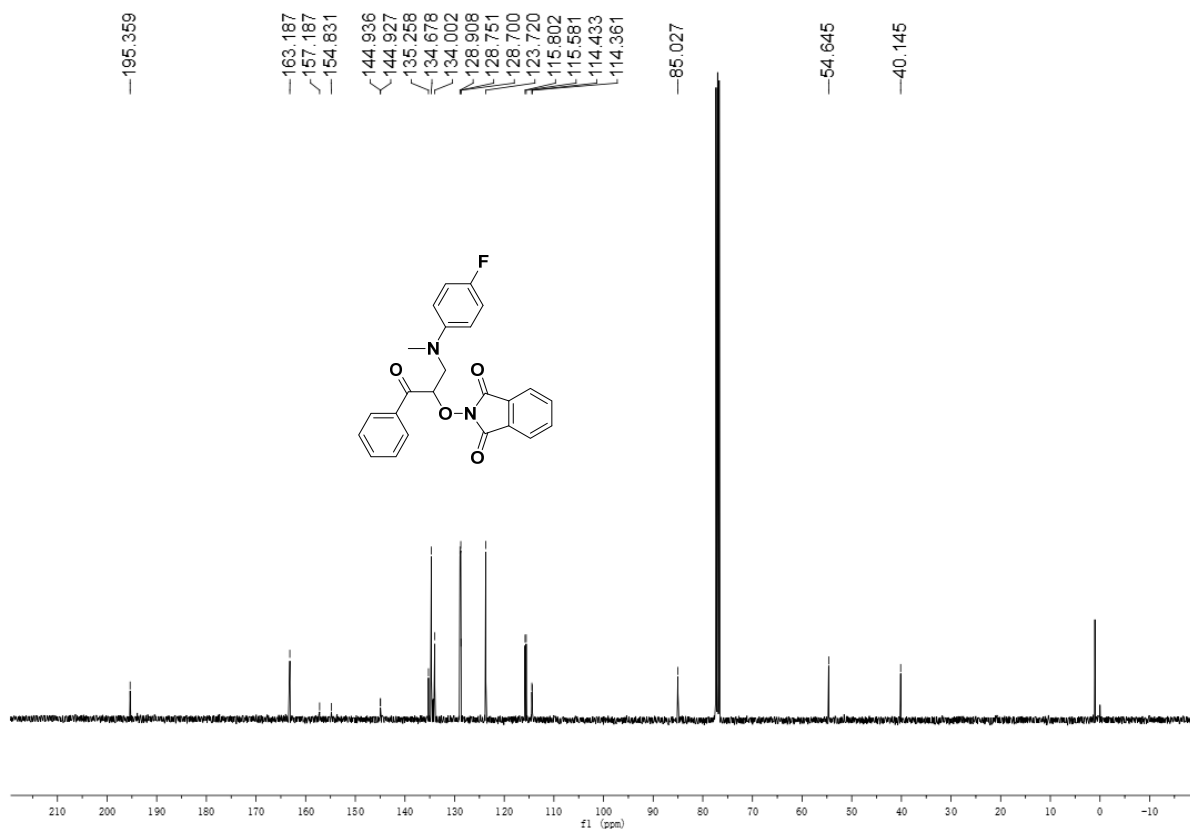
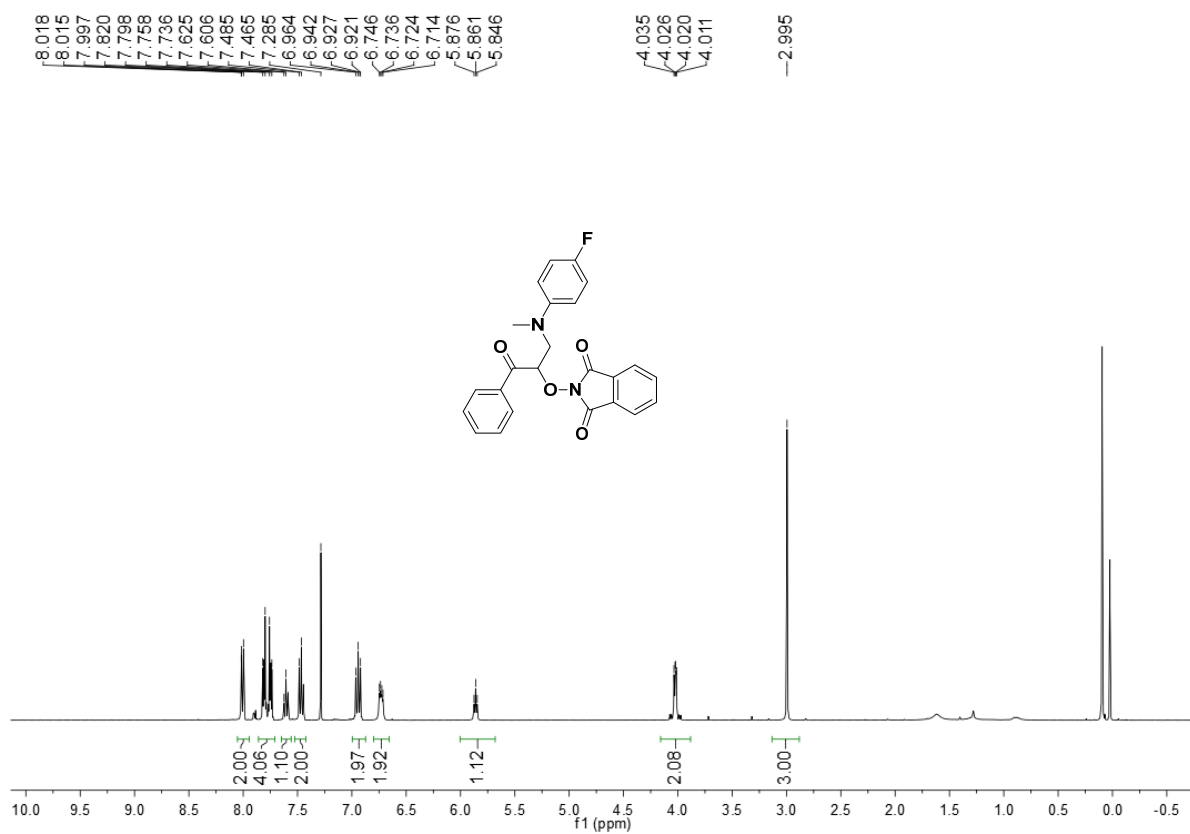
¹³C NMR Spectrum of Compound 4k

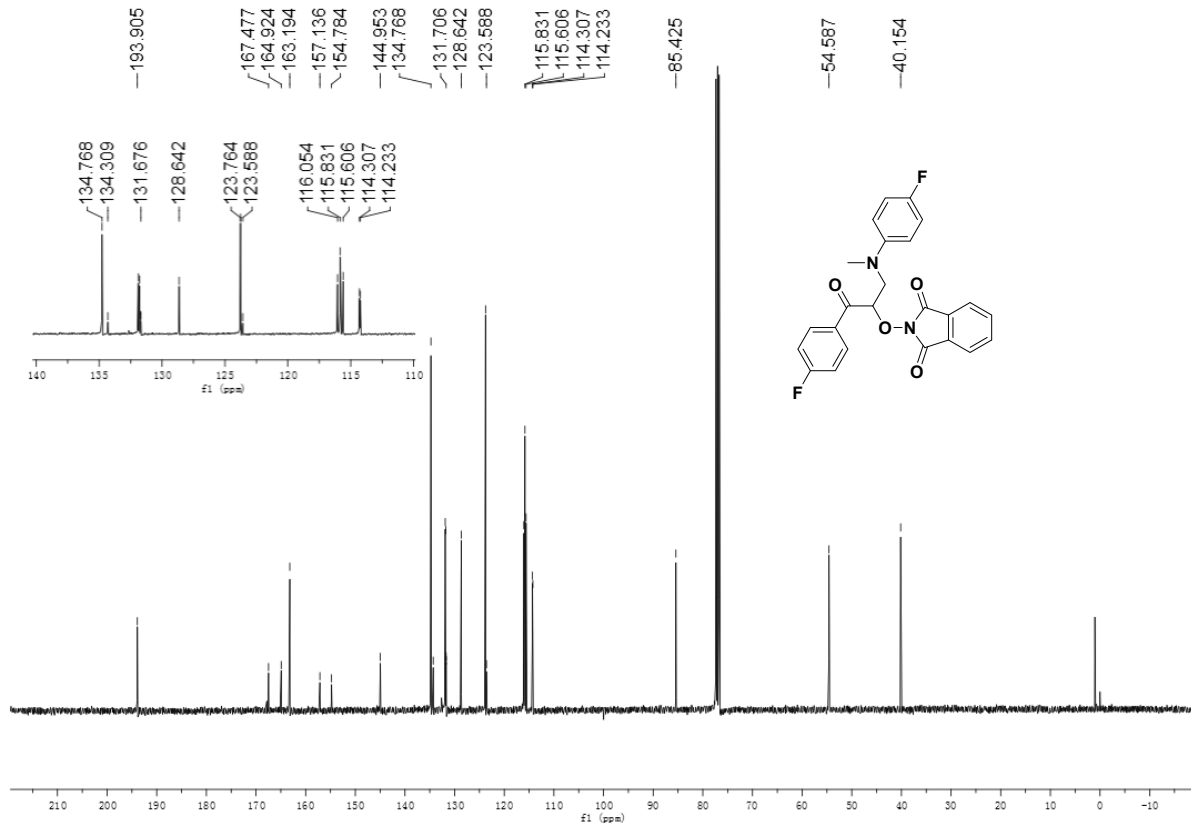
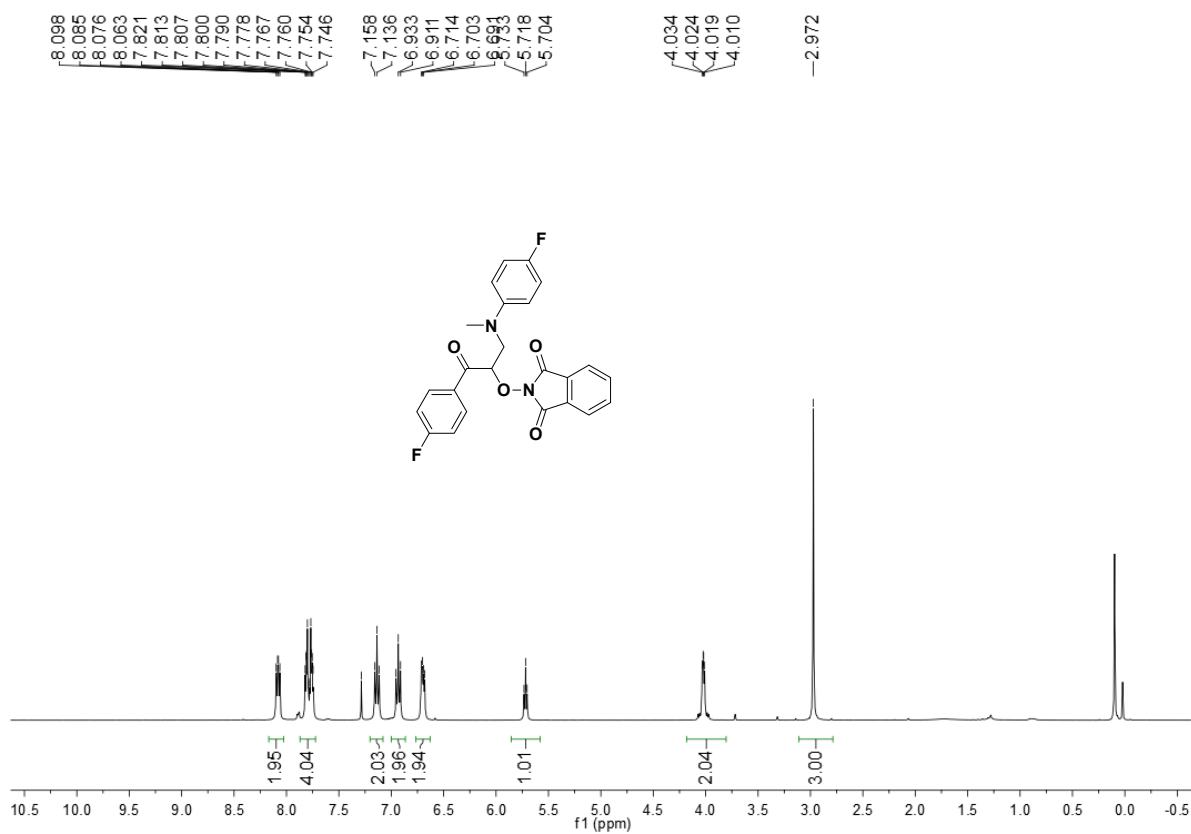




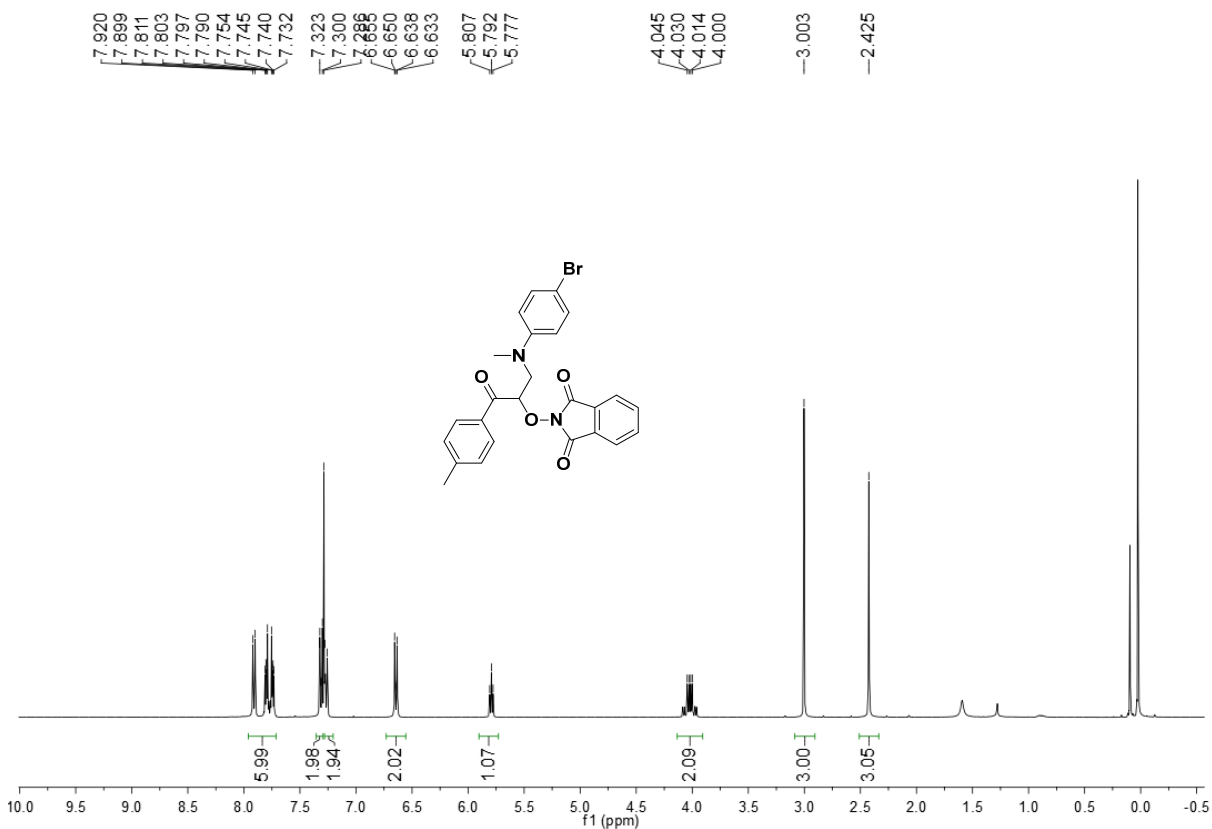




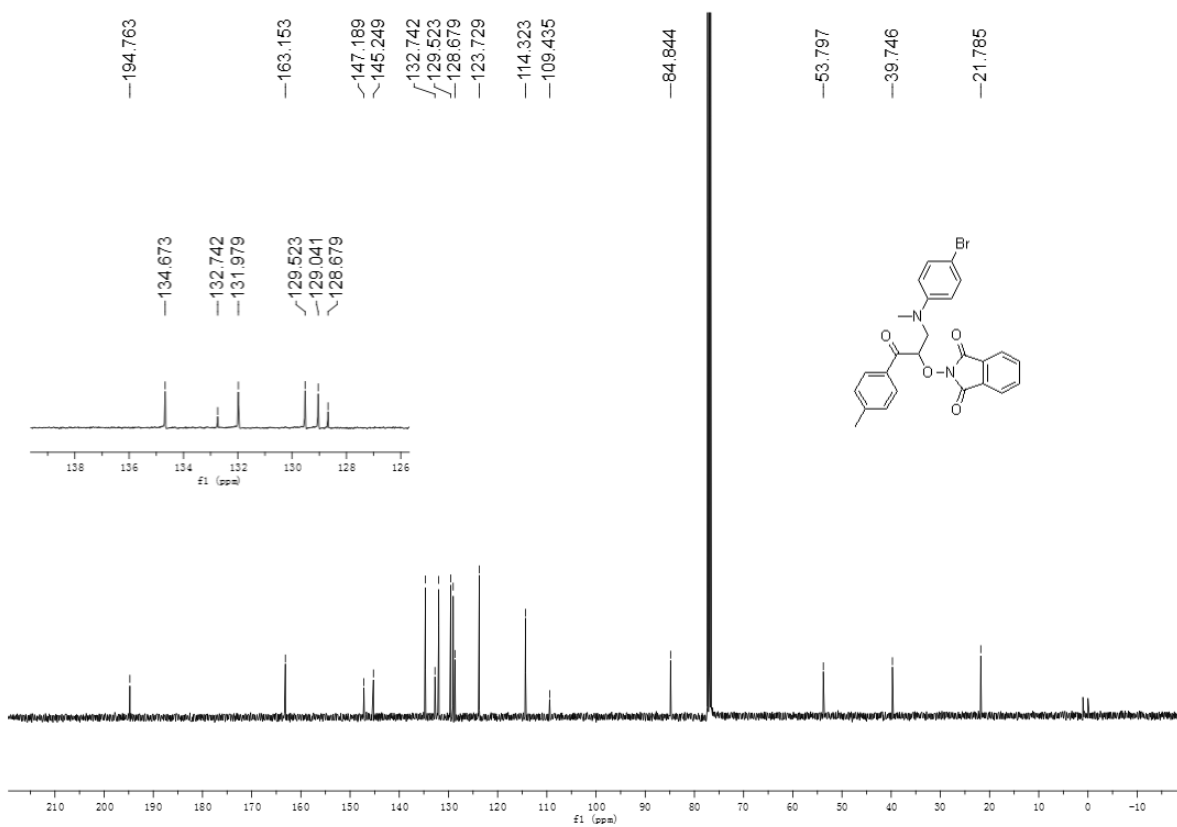




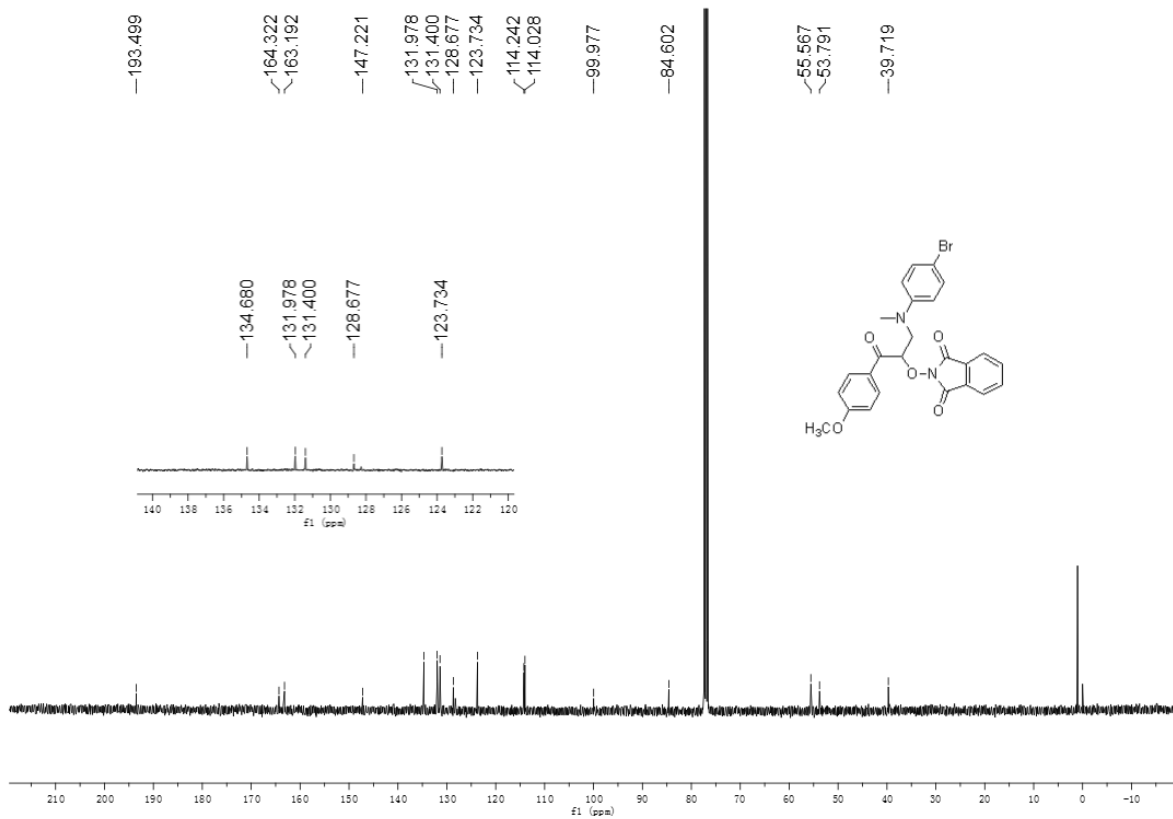
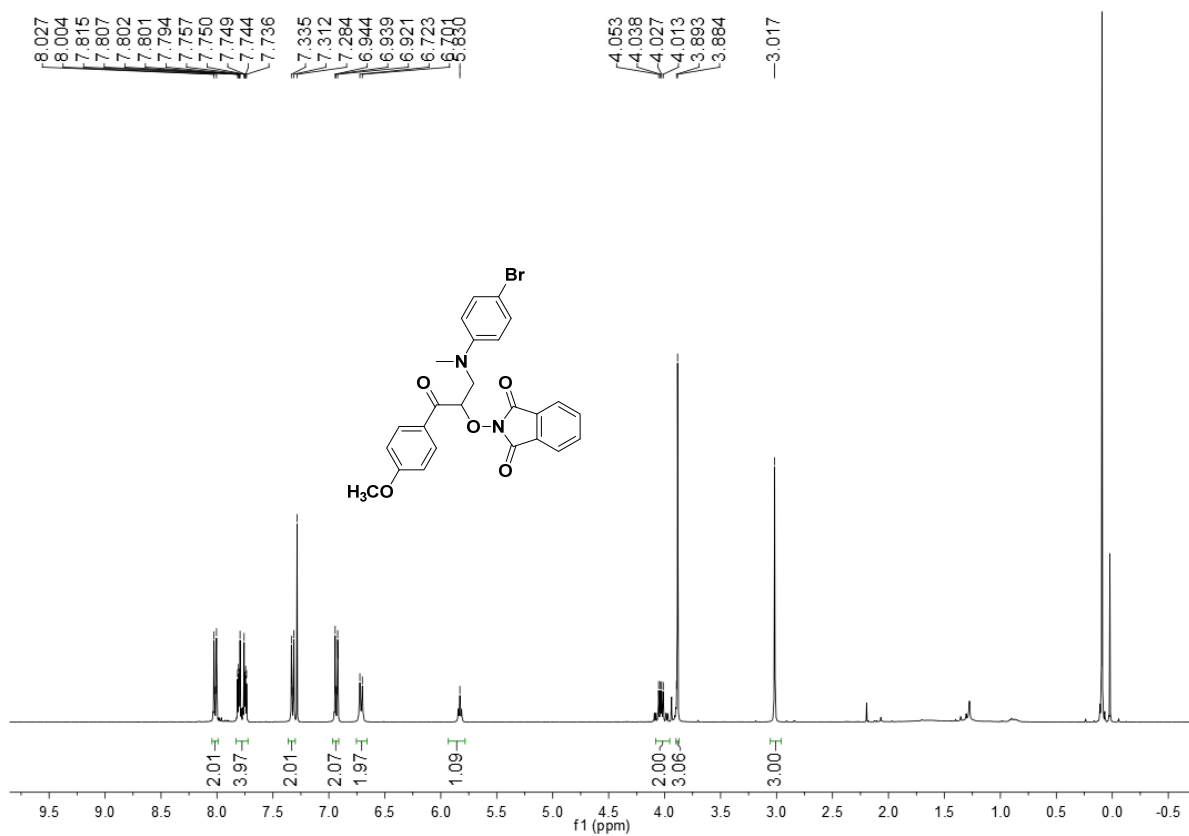
¹³C NMR Spectrum of Compound 4q



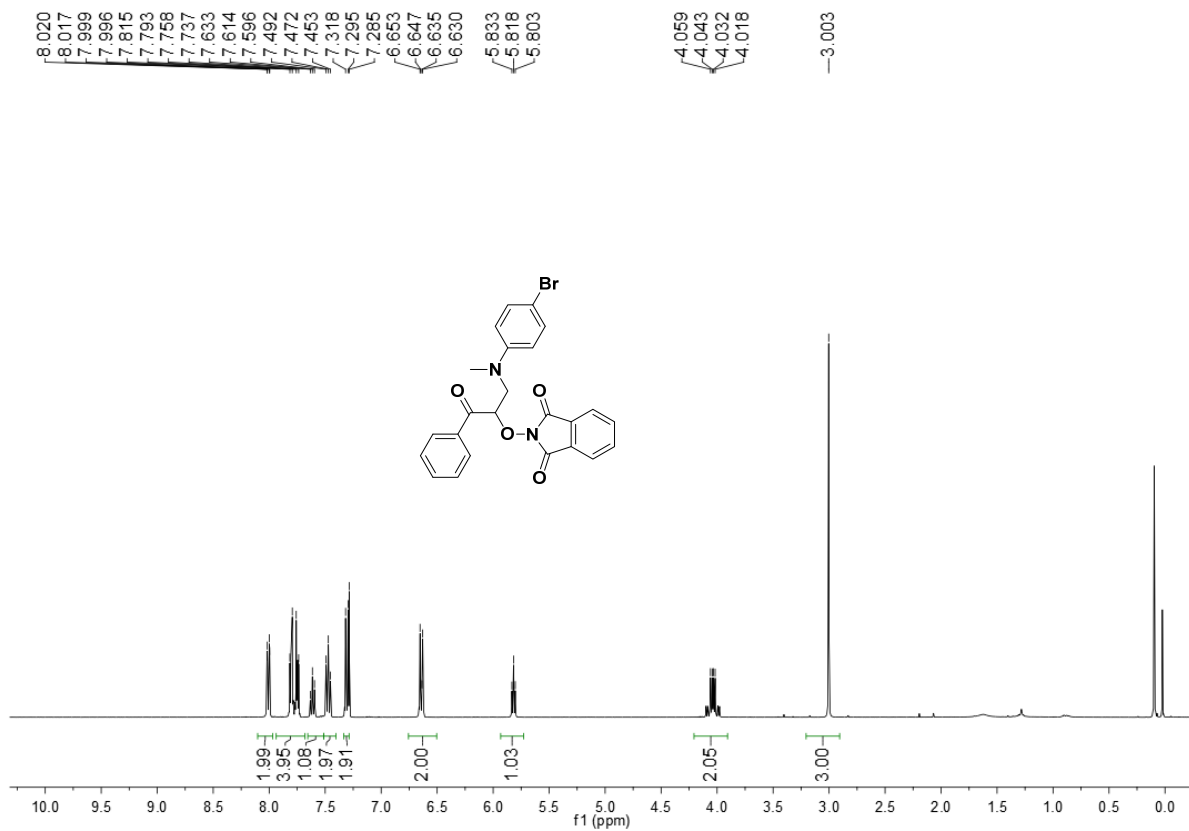
¹H NMR Spectrum of Compound 4r



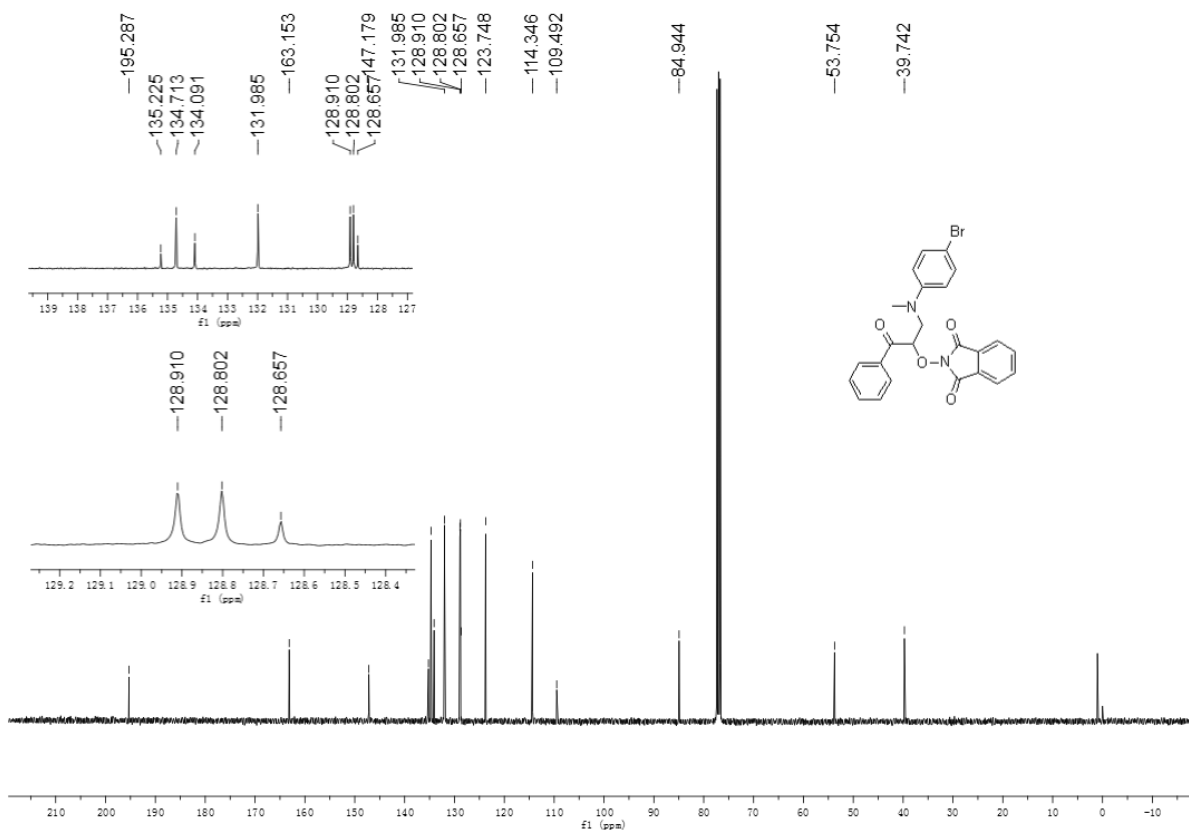
¹³C NMR Spectrum of Compound 4r



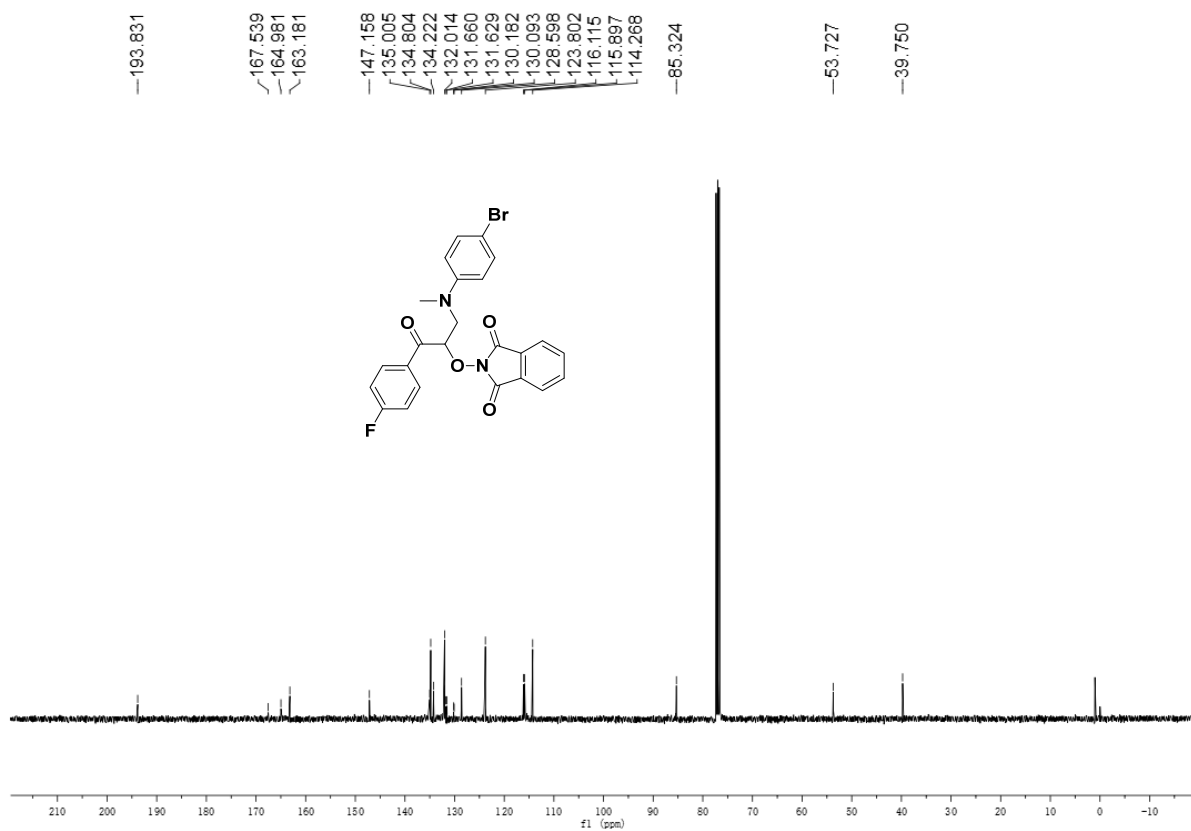
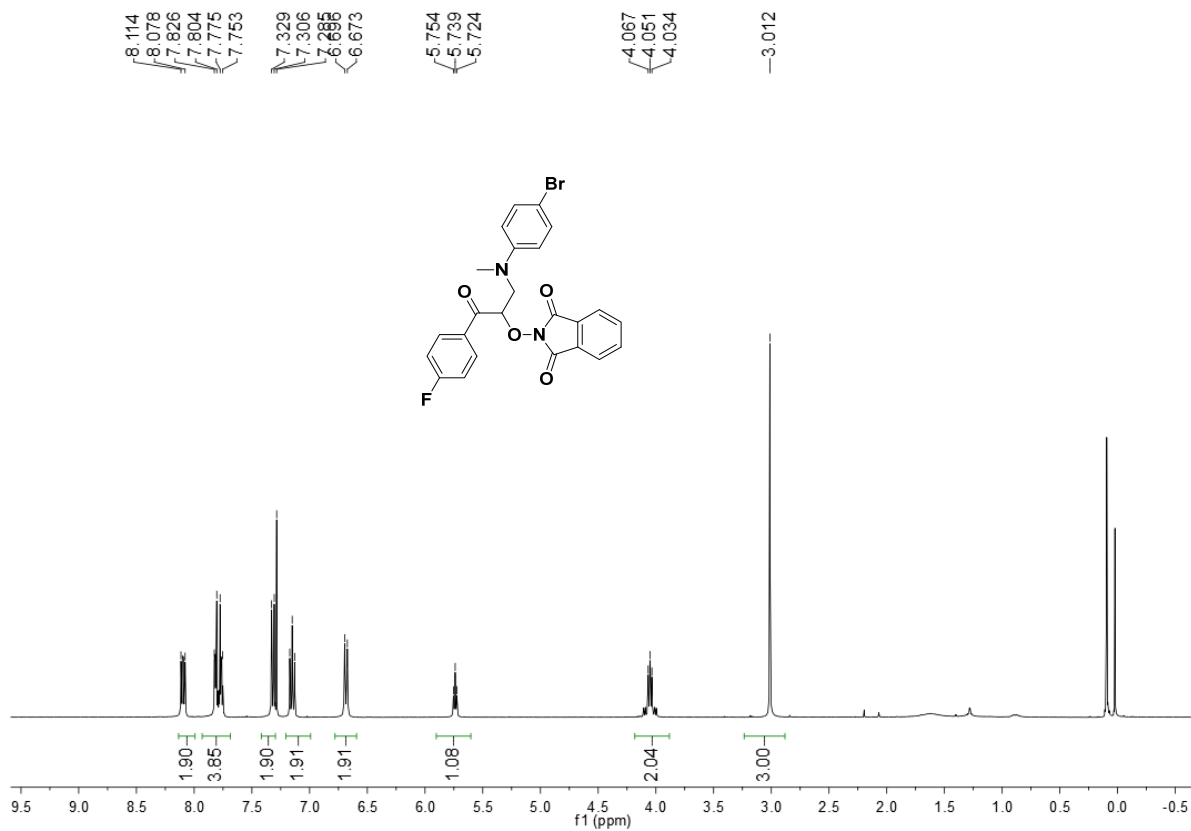
¹³C NMR Spectrum of Compound 4s

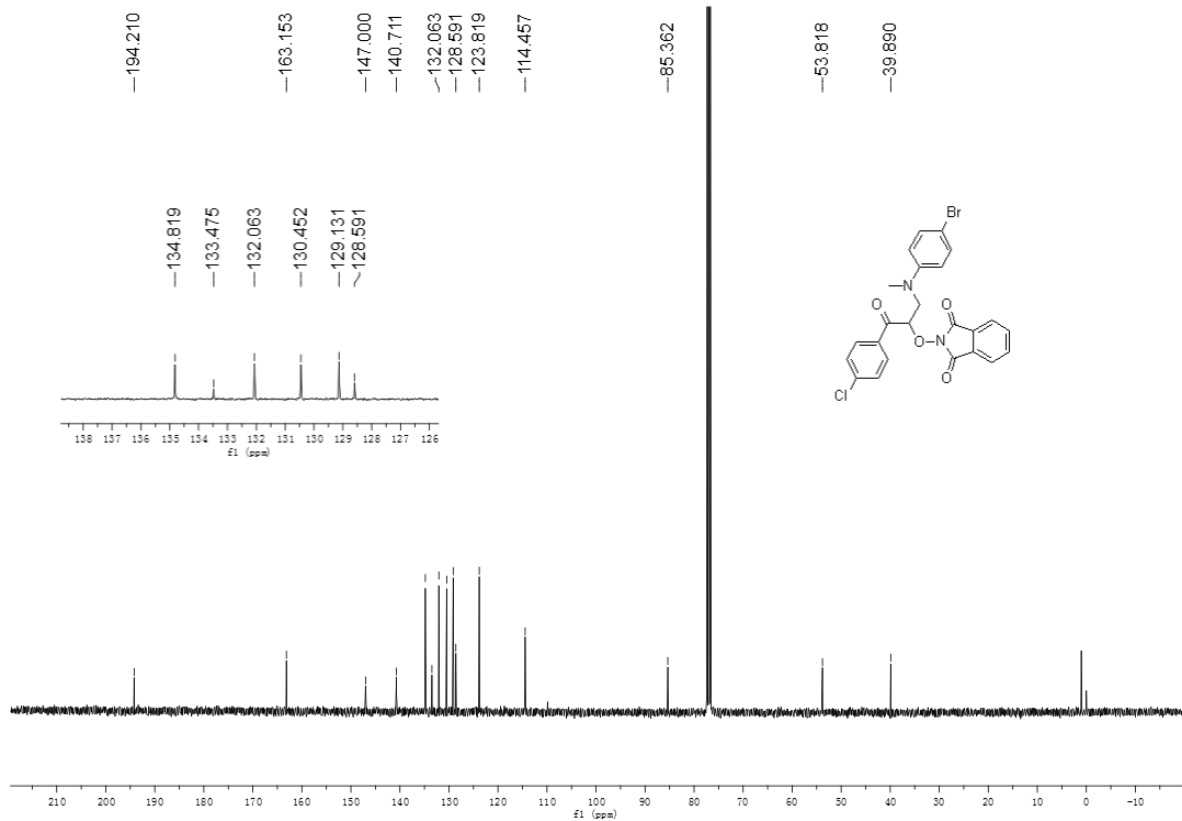
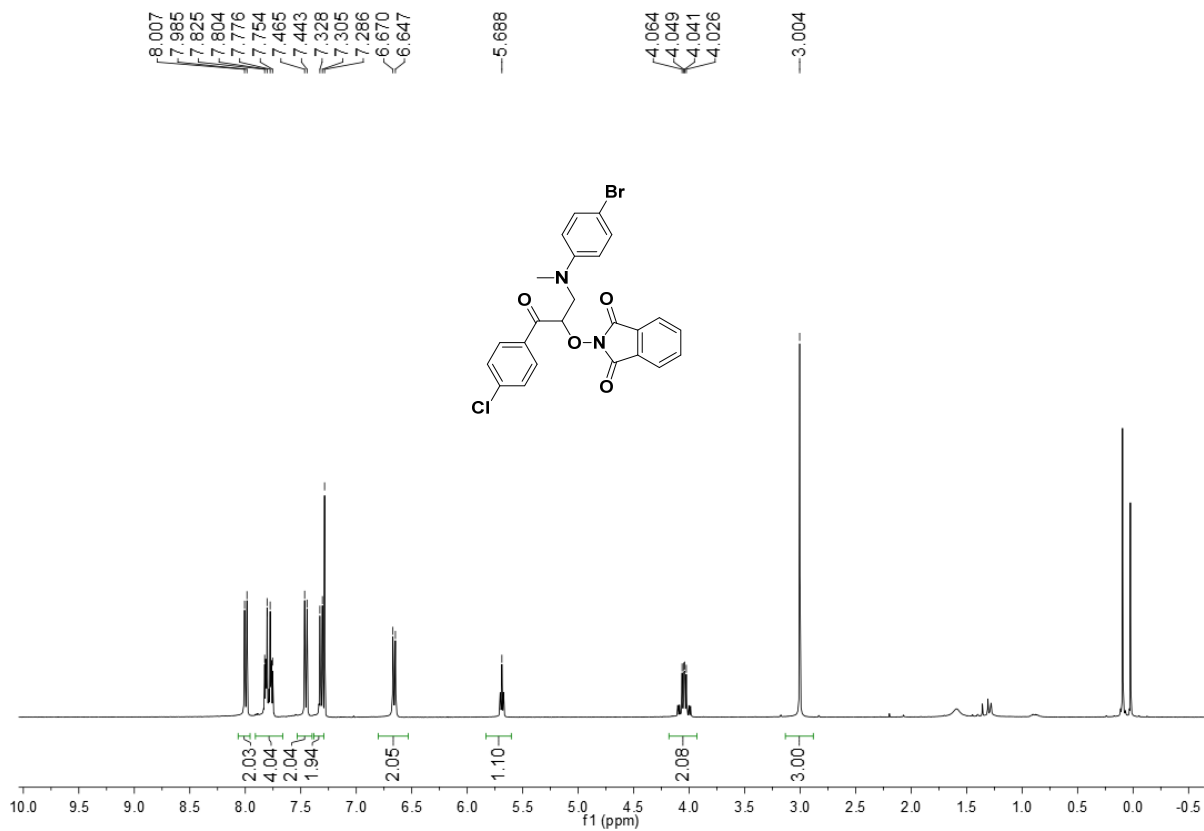


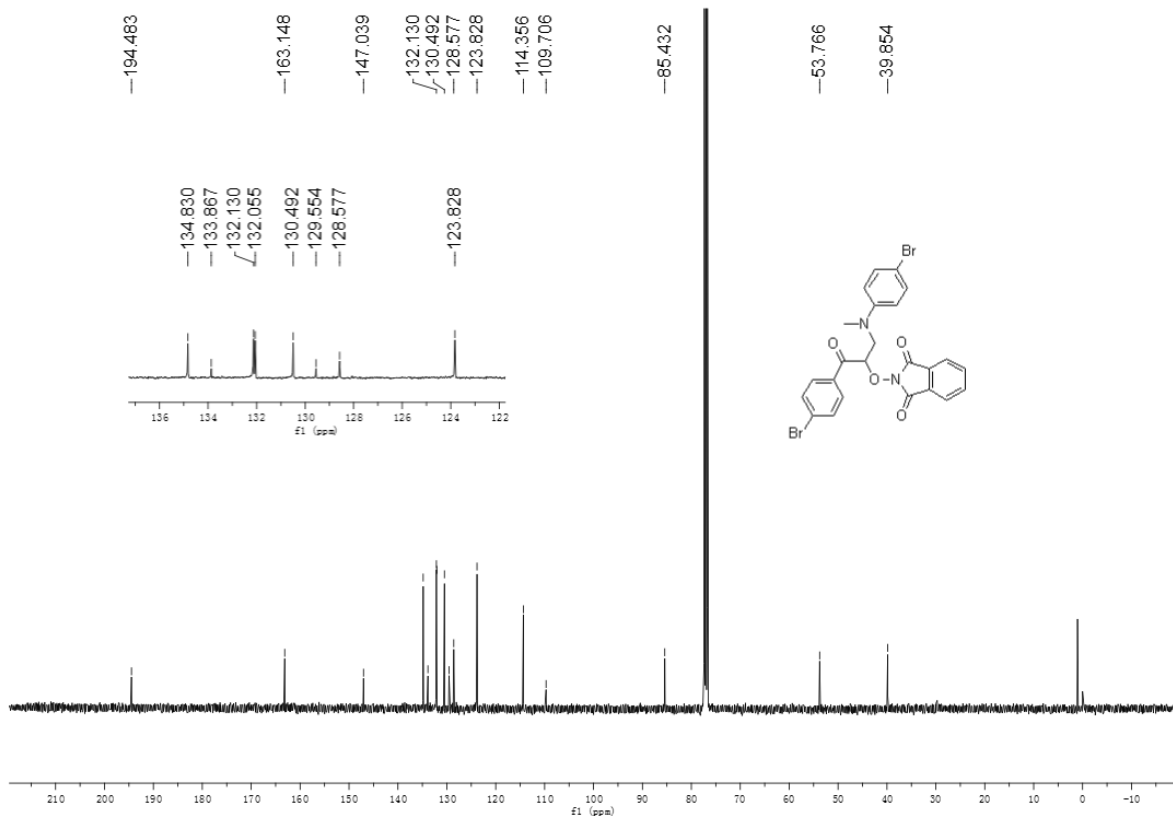
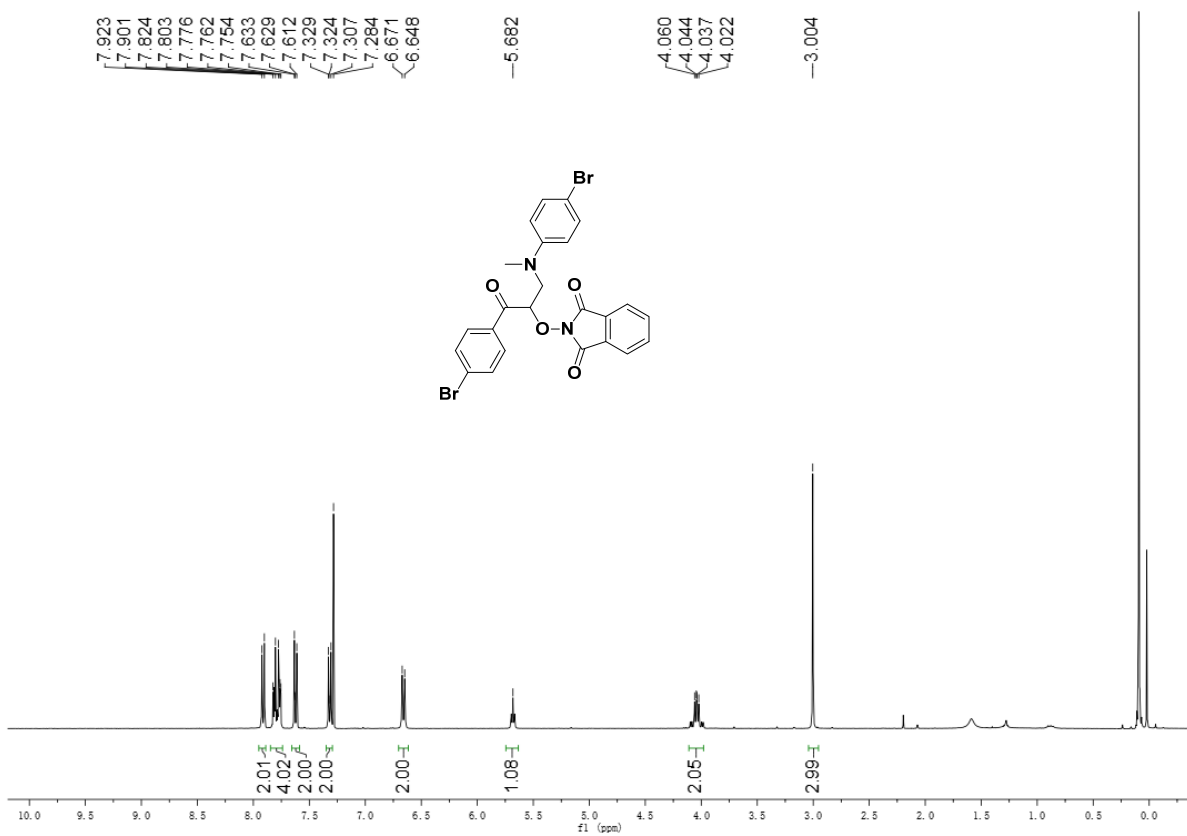
¹H NMR Spectrum of Compound 4t



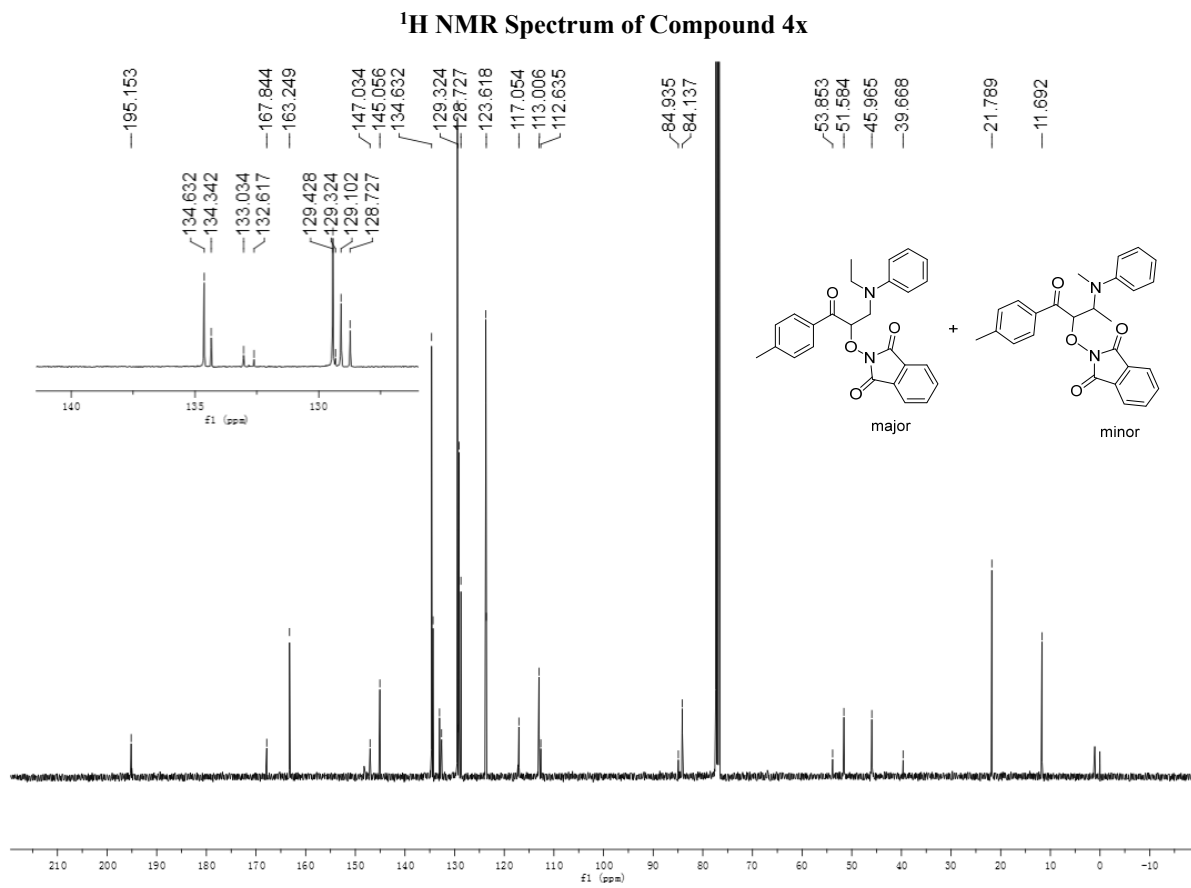
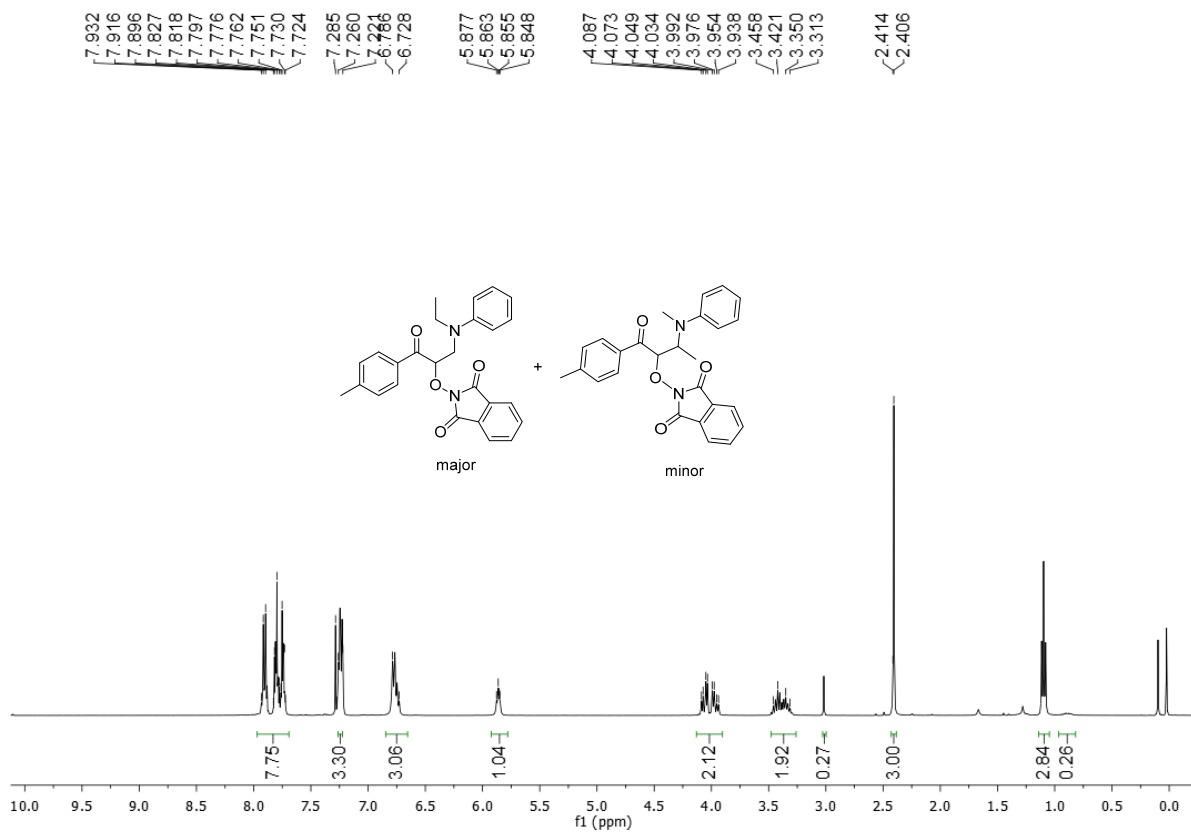
¹³C NMR Spectrum of Compound 4t

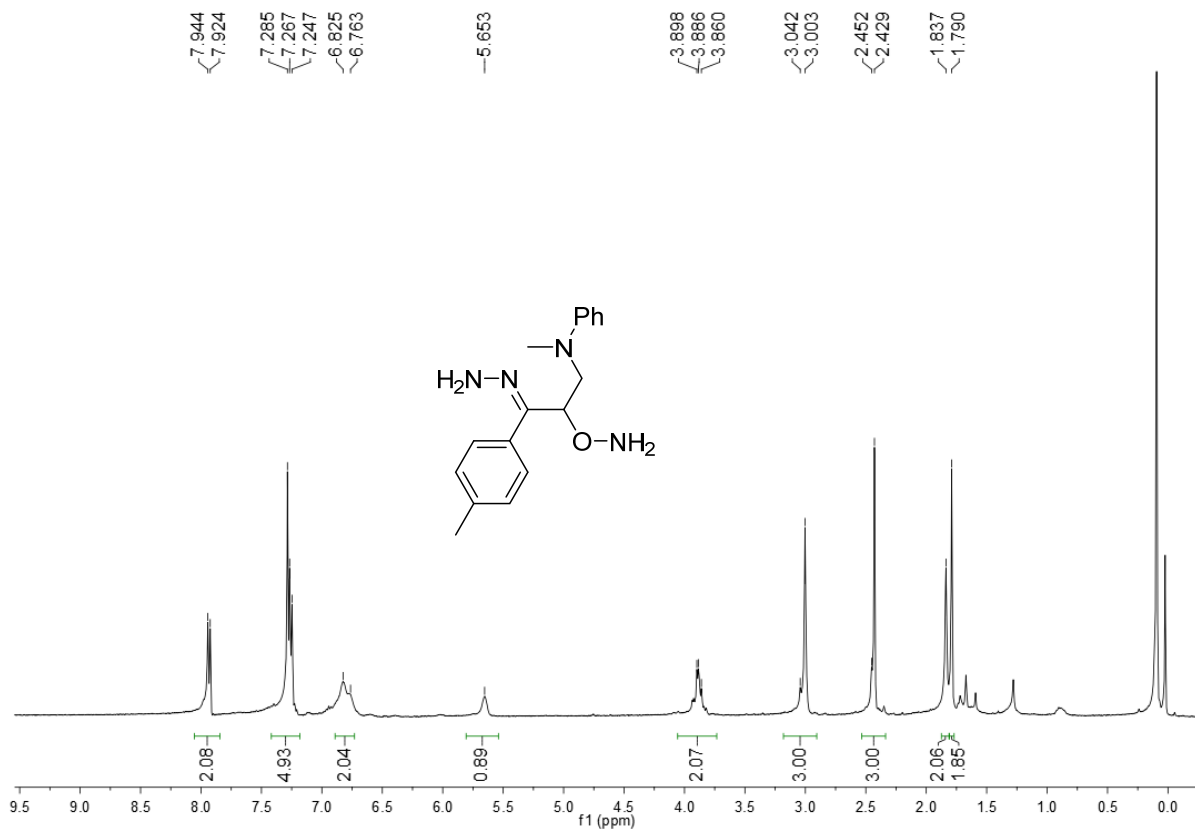






¹³C NMR Spectrum of Compound 4w





¹H NMR Spectrum of Compound 5