Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting information for

Copper nitrate-catalyzed oxidative coupling of unactivated C(sp^3)–H bonds of ethers and alkanes with *N*-hydroxyphthalimide: synthesis of *N*-hydroxyimide esters

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1. General information:

All reagents were obtained from commercial suppliers and used without further purification (*Tert*-butyl ethers were synthesized according to *Tetrahedron Lett.*, 2012, **53**, 641). TLC analysis was performed using pre-coated glass plates Silica gel for column chromatography was purchased from Qingdao Haiyang Chemical Co., Ltd. ^{1}H NMR and ^{13}C NMR were recorded with Bruker instrument at 600 and 150 MHz, respectively, and TMS was used as internal standard. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, *J* were reported in Hertz unit (Hz). Mass spectra were measured with Thermo Finnigan LCQ-Advantage. High resolution mass spectral (HRMS) analyze were measured on a Bruker micr OTOF-Q II instrument using ESI or EI techniques. The structures of known compounds were further corroborated by comparing their ^{1}H NMR, ^{13}C NMR and MS data with those of literature.

2. General experimental procedure:

General procedure for the $Cu(NO_3)_2{\cdot}3H_2O$ catalyzed coupling reaction of ethers and alkanes with NHPI.

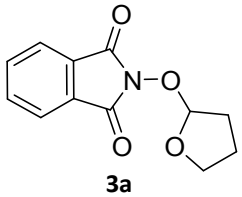
The ethers or alkanes **1** (4.0 mL), NHPI (1.0 mmol) and $Cu(NO_3)_2{\cdot}3H_2O$ (0.05 mmol) were added to CH_3CN (4.0 mL) in a 25 mL flame-dried flask. The solution was stirred for given reaction time as shown in scheme 2 under O_2 (balloon) at 80 ^{o}C. After the reaction, the solvents were removed under reduced pressure and the residue was washed with saturated $NaHCO_3$ and then extracted with EtOAc (2 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc) to afford the corresponding products.

General procedure for synthesis of *N*-hydroxyimide esters from *tert*-butyl ethers.

The *tert*-butyl ethers **4** (2.0 mL), NHPI (1.0 mmol) and $Cu(NO_3)_2{\cdot}3H_2O$ (0.05 mmol) were added to CH_3CN (4.0 mL) in a 25 mL flame-dried flask. The solution was stirred for 10 h under O_2 (balloon) at 80 ^{o}C. After the reaction, the solvents were removed under reduced pressure and the residue was washed with saturated $NaHCO_3$ and then extracted with EtOAc (2 × 20 mL). The combined

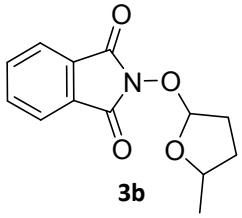
organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc) to afford the corresponding products.

^{1}H and ^{13}C NMR data



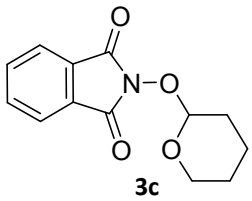
3a

2-(tetrahydrofuran-2-yloxy)isoindoline-1,3-dione (3a):[1] White solid, m.p. 132-133 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.82 (m, 2H), 7.76-7.73 (m, 2H), 5.80 (d, J = 4.8 Hz, 1H), 4.38-4.34 (m, 1H), 4.05-4.01 (m, 1H), 2.34-2.29 (m, 1H), 2.28-2.22 (m, 1H), 2.15-2.10 (m, 1H), 2.00-1.94 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.9, 134.3, 129.1, 123.4, 108.8, 69.2, 30.8, 22.6. IR (KBr): v 3443, 3010, 2999, 2978, 1731, 1380, 1138, 971, 879, 700, 520 cm^{-1}.



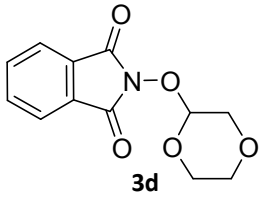
3b

2-(5-methyltetrahydrofuran-2-yloxy)isoindoline-1,3-dione (3b):[1] White solid, m.p. 124-126 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.83 (m, 2H), 7.76-7.74 (m, 2H), 5.81-5.79 (m, 1H), 4.74-4.71 (m, 1H), 2.34-2.31 (m, 1H), 2.28-2.25 (m, 2H), 1.54-1.49 (m, 1H), 1.27 (dd, J = 6.6, 3.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.9, 134.3, 129.1, 123.42, 123.38, 108.9, 30.6, 30.2, 20.5.



3c

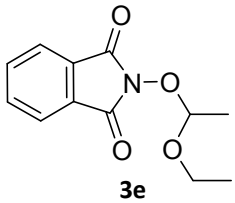
2-(tetrahydro-*2H*-pyran-2-yloxy)isoindoline-1,3-dione (3c):[1] White solid, m.p. 123-124 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84-7.82 (m, 2H), 7.75-7.72 (m, 2H), 5.42 (d, J = 1.8 Hz, 1H), 4.54-4.50 (m, 1H), 3.68-3.65 (m, 1H), 2.13-2.10 (m, 1H), 1.99-1.92 (m, 1H), 1.87-1.81 (m, 1H), 1.74-1.68 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8, 134.3, 129.2, 123.4, 103.1, 62.3, 27.7, 24.8, 17.6.



3d

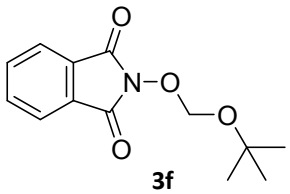
2-(1,4-dioxan-2-yloxy)isoindoline-1,3-dione (3d):[1] White solid, m.p. 185-187 °C. ^{1}H NMR (600

MHz, $CDCl_3$) δ 7.88-7.86 (m, 2H), 7.78-7.77 (m, 2H), 5.27 (d, *J* = 1.8, 1H), 4.90-4.85 (m, 1H), 4.18 (d, *J* = 12.6 Hz, 1H), 3.91 (dd, *J* = 11.4, 2.4 Hz, 1H), 3.85-3,80 (m, 2H), 3.57 (dd, *J* = 11.4, 2.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 134.5, 129.0, 123.6, 99.5, 66.2, 66.0, 60.9.



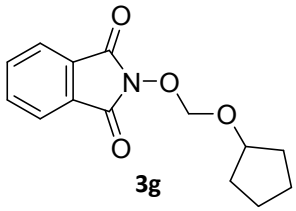
3e

2-(1-ethoxyethoxy)isoindoline-1,3-dione (3e):[1] Oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.83 (m, 2H), 7.77-7.75 (m, 2H), 5.32 (q, *J* = 5.4 Hz, 1H), 4.19-4.15 (m, 1H), 3.85-3.80 (m, 1H), 1.53 (d, *J* = 5.4 Hz, 3H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 134.4, 129.1, 123.4, 106.4, 63.6, 18.9, 15.0. IR (KBr): *v* 3441, 3015, 2990, 2978, 1737, 1710, 1463, 1137, 976, 881, 698, 522 cm^{-1}.



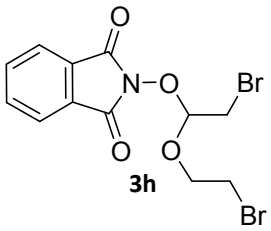
3f

2-(*tert*-butoxymethoxy)isoindoline-1,3-dione (3f):[1] White solid, m.p. 93-95 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.82 (m, 2H), 7.76-7.74 (m, 2H), 5.28 (s, 2H), 1.39 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8, 134.4, 129.1, 123.4, 95.0, 28.3. IR (KBr): *v* 3441, 3015, 2990, 2978, 1737, 1710, 1463, 1137, 976, 881, 698, 522 cm^{-1}.



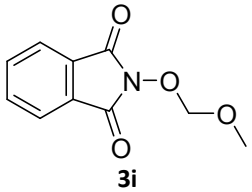
3g

2-(cyclopentyloxymethoxy)isoindoline-1,3-dione (3g):[1] White solid, m.p. 71-73 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.82 (m, 2H), 7.76-7.73 (m, 2H), 5.17 (s, 2H), 4.79-4.76 (m, 1H), 1.86-1.81 (m, 2H), 1.72-1.68 (m, 4H), 1.60-1.57 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.7, 134.4, 129.1, 123.4, 97.8, 80.3, 32.1, 23.4. IR (KBr): *v* 3426, 3013, 2946, 2869, 1727, 1466, 1136, 968, 870, 701, 520 cm^{-1}.



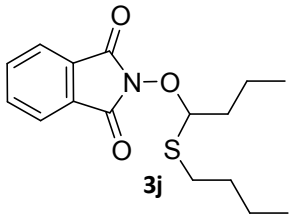
3h

2-(2-bromo-1-(2-bromoethoxy)ethoxy)isoindoline-1,3-dione (3h):[1] White solid, m.p. 112-114 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89-7.88 (m, 2H), 7.82-7.81 (m, 2H), 5.30 (dd, J = 8.4, 3.0 Hz, 1H), 4.58-4.54 (m, 1H), 4.23-4.19 (m, 2H), 3.78 (dd, J = 10.8, 3.0 Hz, 1H), 3.60-3.58 (m, 2H), 3.56-3.52 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.1, 134.9, 128.9, 123.8, 107.9, 69.9, 29.5.



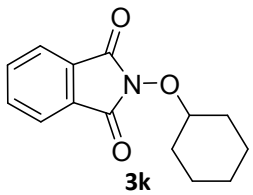
3i

2-(methoxymethoxy)isoindoline-1,3-dione (3i):[2] White solid, m.p. 122-124 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.86 (m, 2H), 7.78-7.77 (m, 2H), 5.14 (s, 2H), 3.74 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 134.5, 129.0, 123.5, 101.3, 57.8. IR (KBr): v 3454, 3027, 2961, 2831, 1718, 1637, 1132, 1098, 967, 878, 701, 519 cm^{-1}.



3j

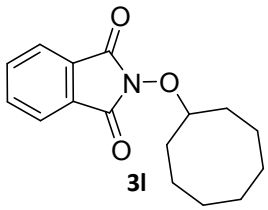
2-(1-(butylthio)butoxy)isoindoline-1,3-dione (3j):[1] Oil. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.90-7.87 (m, 4H), 5.37-5.35 (m, 1H), 2.89-2.85 (m, 1H), 2.75-2.70 (m, 1H), 2.00-1.96 (m, 1H), 1.81-1.76 (m, 1H), 1.52-1.47 (m, 4H), 1.37-1.32 (m, 2H), 0.93 (t, J =7.2 Hz, 3H), 0.87-0.86 (m, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.1, 135.4, 129.0, 123.8, 93.9, 35.7, 31.7, 29.0, 21.9, 19.2, 14.0, 13.9. IR (KBr): v 3456, 3047, 2961, 2866, 1735, 1685, 1136, 1082, 881, 698, 522 cm^{-1}.



3k

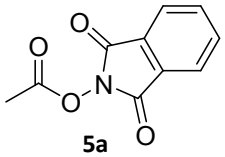
2-(cyclohexyloxy)isoindoline-1,3-dione (3k):[1] White solid, m.p. 116-118 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78-7.75 (m, 2H), 7.69-7.66 (m, 2H), 4.18-4.14 (m, 1H), 1.97-1.95 (m, 2H), 1.79-1.78 (m,

2H), 1.55-1.47 (m, 3H), 1.24-1.18 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 134.4, 129.0, 123.4, 85.7, 30.8, 25.3, 23.7. IR (KBr): *v* 3449, 3027, 2940, 2853, 1731, 1635, 1186, 1038, 978, 878, 698, 519cm^{-1}.



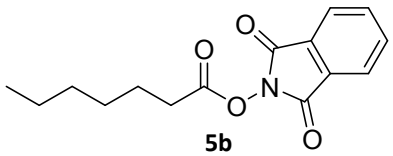
3l

2-(cyclooctyloxy)isoindoline-1,3-dione (3l):[1] White solid, m.p. 107-109 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.82 (m, 2H), 7.76-7.73 (m, 2H), 4.43-4.39 (m, 1H), 2.02-1.98 (m, 2H), 1.95-1.89 (m, 2H), 1.85-1.79 (m, 2H), 1.61-1.47 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 134.4, 129.1, 123.4, 88.8, 30.0, 27.1, 25.3, 22.9. IR (KBr): *v* 3451, 3031, 2967, 2859, 1741, 1637, 1196, 1045, 979, 890, 696, 519 cm^{-1}.



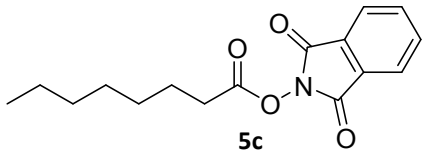
5a

1,3-dioxoisoindolin-2-yl-acetate (5a):[3] White solid, m.p. 188-190 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90-7.88 (m, 2H), 7.80-7.79 (m, 2H), 2.4 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 161.9, 134.8, 128.9, 124.0, 17.6. IR (KBr): *v* 3442, 3037, 2930, 2843, 1787, 1743, 1639, 1141, 1004, 969, 879, 697, 521 cm^{-1}.



5b

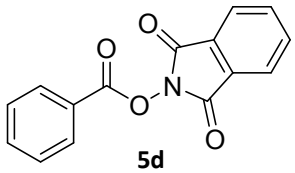
1,3-dioxoisoindolin-2-yl-heptanoate (5b): Yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89-7.87 (m, 2H), 7.80-7.78 (m, 2H), 2.67 (t, *J* =7.2 Hz, 2H), 1.81-1.76 (m, 2H), 1.47-1.43 (m, 2H), 1.35-1.33 (m, 4H), 0.91 (t, *J* =7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 162.0, 134.7, 128.9, 123.9, 31.3, 31.0, 28.5, 24.6, 22.4, 14.0. IR (KBr): *v* 3448, 3037, 2954, 2869, 1788, 1740, 1638, 1139, 1081, 877, 699, 521 cm^{-1}. HRMS (ESI) calcd for $[M+Na]^+$ $C_{15}H_{17}NNaO_4$, m/z 298.1050, found 298.1041.



5c

1,3-dioxoisoindolin-2-yl-octanoate (5c): Yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90-7.86 (m, 2H),

7.80-7.77 (m, 2H), 2.67-2.65 m, 2H), 1.801-1.76 (m, 2H), 1.43 (s, 2H), 1.33-1.30 (m, 6H), 0.90 (t, *J* =3.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 169.7, 162.0, 134.7, 129.0, 123.9, 31.6, 31.0, 28.8, 24.7, 22.6, 14.1. IR (KBr): *v* 3448, 3035, 3026, 2964, 2879, 1789, 1743, 1642, 1149, 1077, 879, 698, 520 cm^{-1}. HRMS (ESI) calcd for $[M+Na]^+$ $C_{16}H_{19}NNaO_4$, m/z 312.1206, found 312.1202.



5d

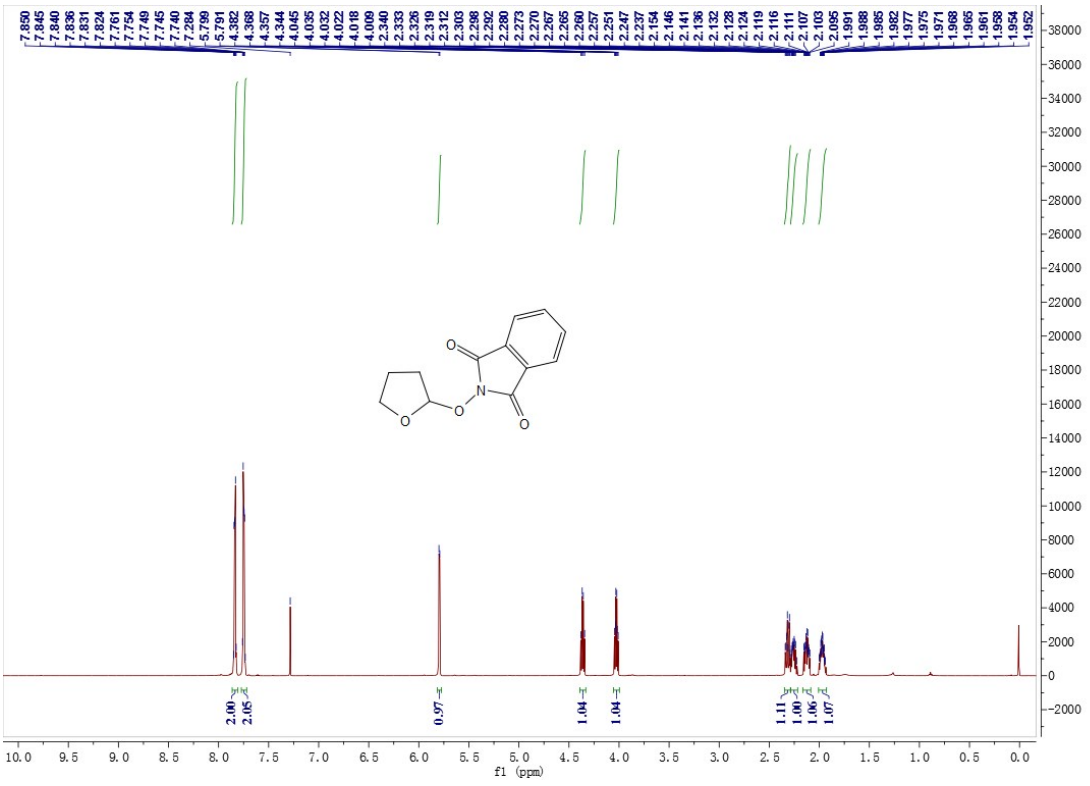
1,3-dioxoisoindolin-2-yl-benzoate (5d) :[4] White solid, m.p. 168-170 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ* 8.22 (d, *J* = 7.8 Hz, 2H), 7.96-7.93 (m, 2H), 7.85-7.83 (m, 2H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 162.8, 162.1, 134.9, 134.8, 130.7, 129.0, 128.9, 125.3, 124.0. IR (KBr): *v* 3438, 3043, 3024, 2984, 2879, 1772, 1734, 1643, 1140, 1037,1022, 1008, 875, 697, 520 cm^{-1}.

References

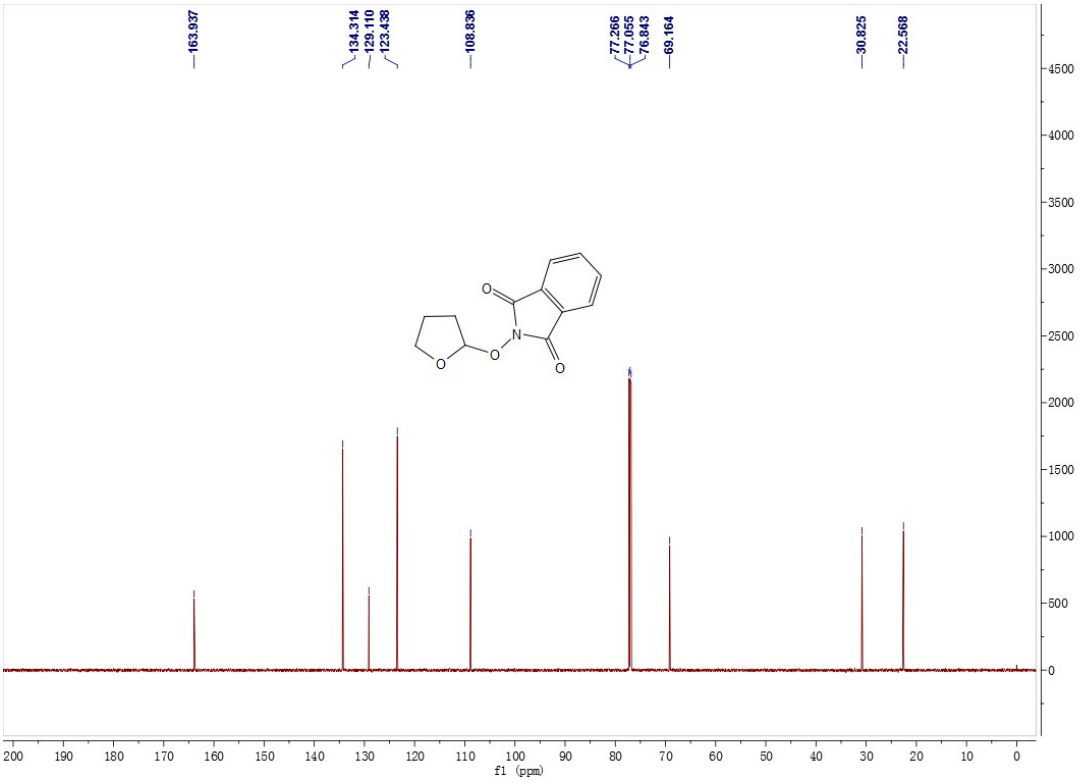
1. Zh. Ch. Guo, C. Jin, J. D. Zhou and W. K. Su, *RSC Adv.*, 2016, **6**, 79016.
2. S. M. Canham, D. J. France and L. E. Overman, *J. Am. Chem. Soc.*, 2010, **132**, 7876.
3. D. E. Ames and T. F. Grey, *J. Org. Chem.*, 1955, 3518.
4. X. H. Xu, P. P. Li, Y. Y. Huang, Ch. Tong, Y. Y. Yan and Y. Y. Xie, T*etrahedron Lett*., 2017, **58***,* 1742.

Copies of ^{1}H and ^{13}C spectrum

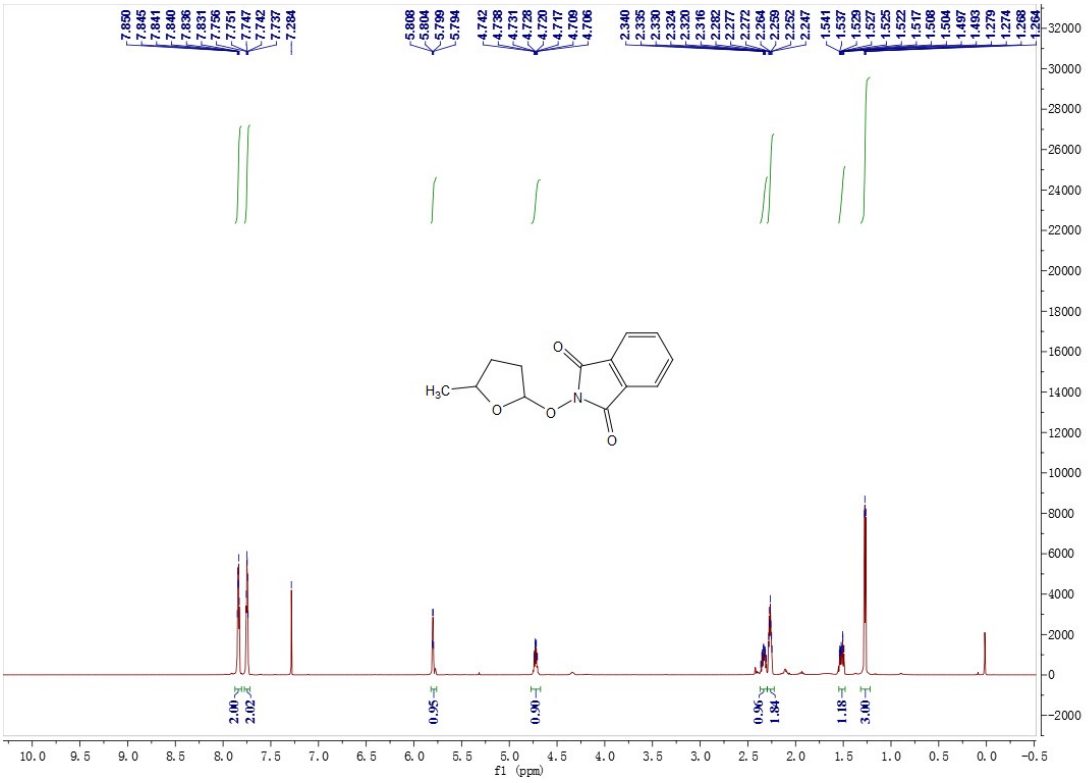
3a (^{1}H, $CDCl_3$)



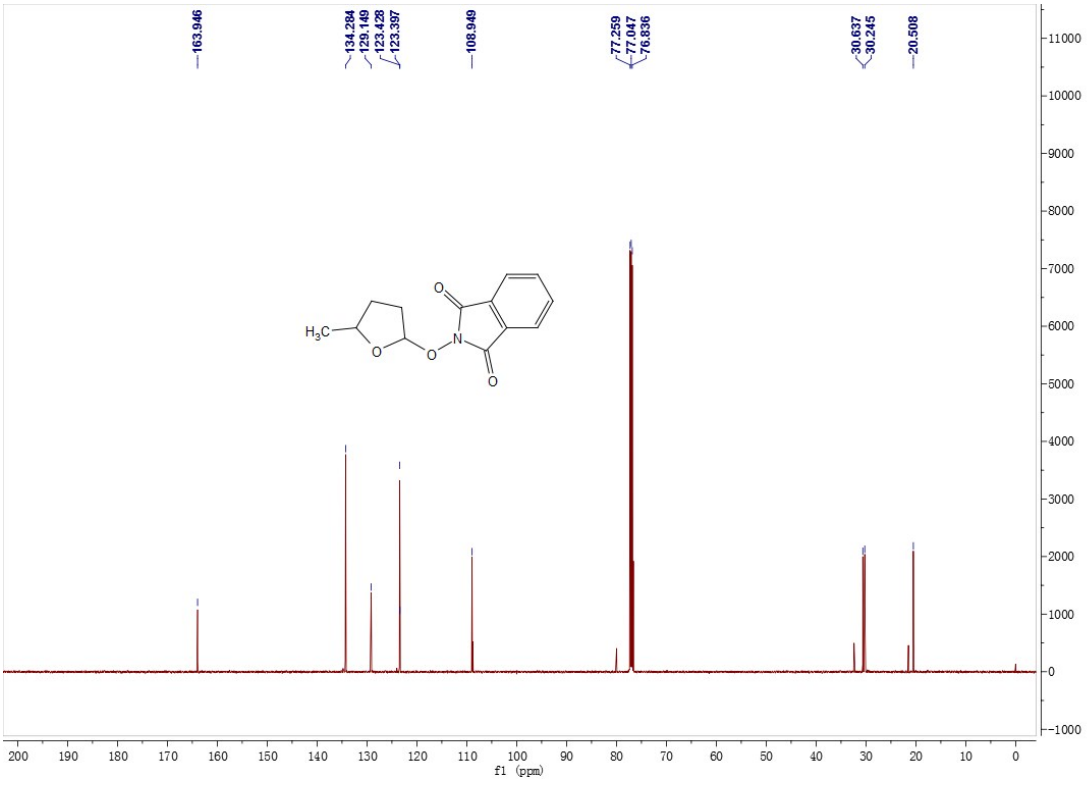
3a (^{13}C, $CDCl_3$)



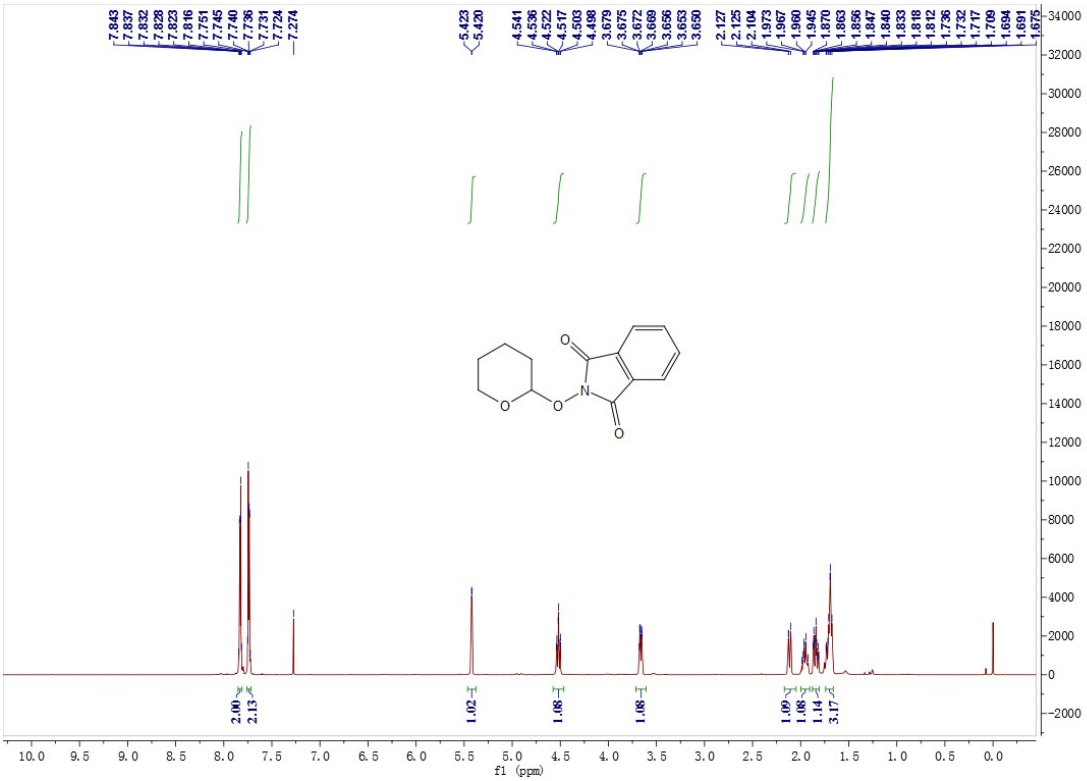
3b (^{1}H, $CDCl_3$)



3b (^{13}C, $CDCl_3$)



3c (^{1}H, $CDCl_3$)



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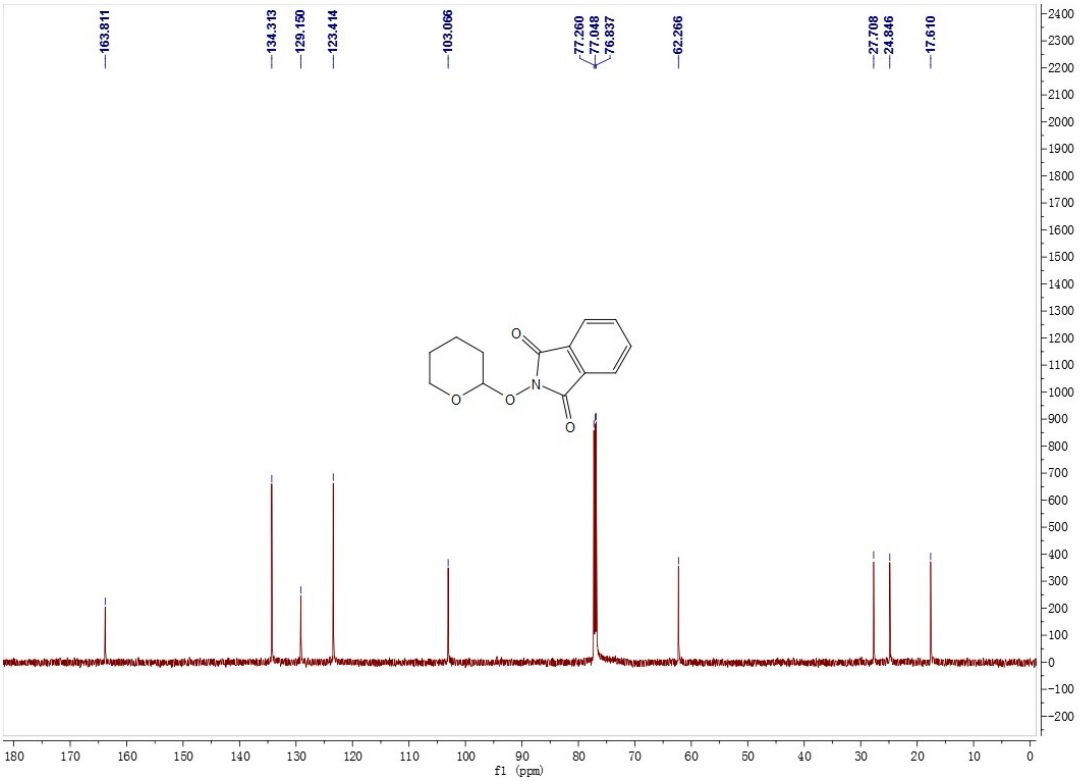

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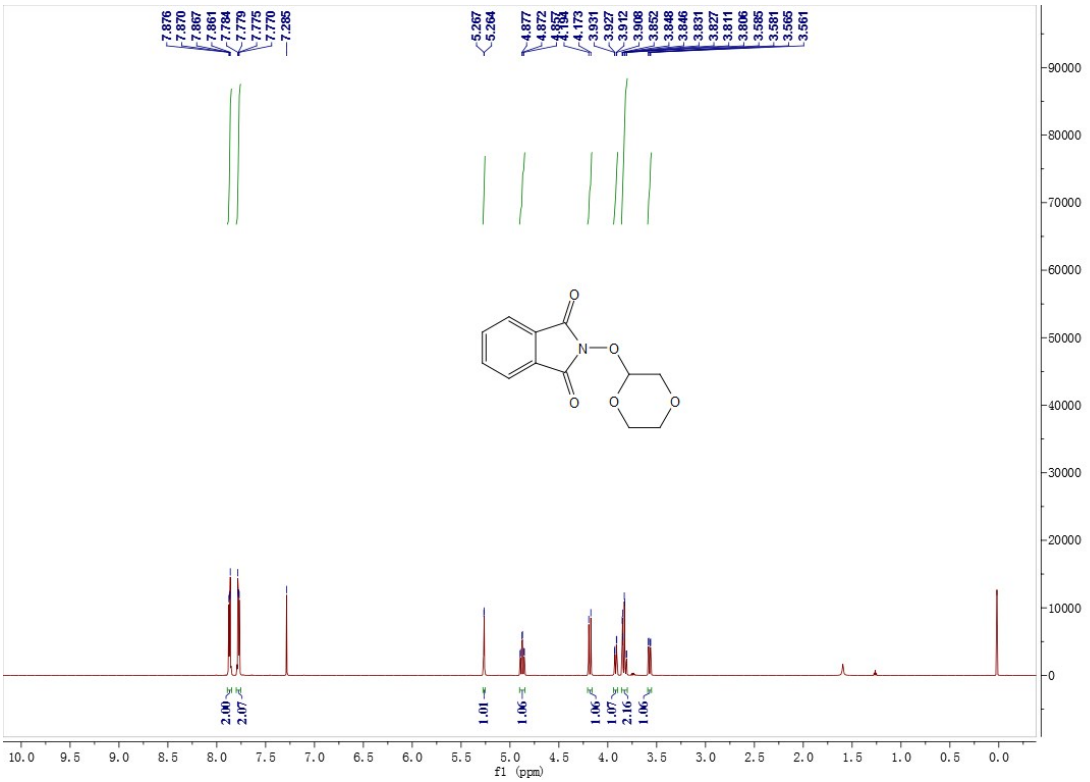
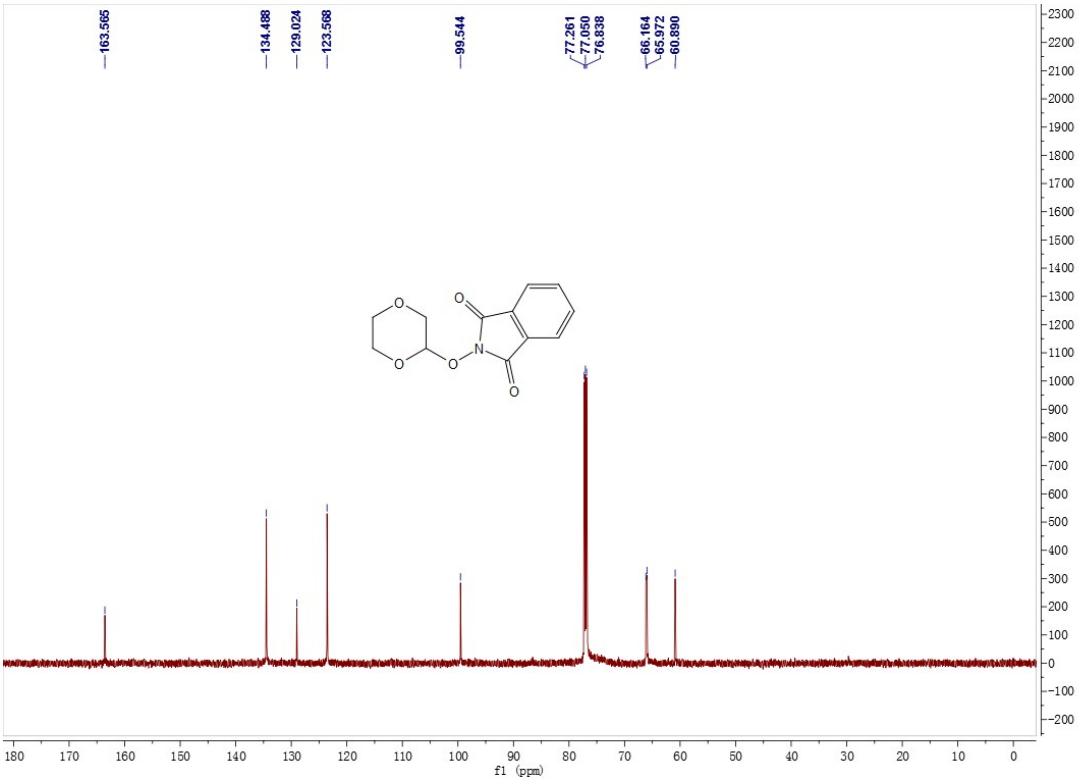
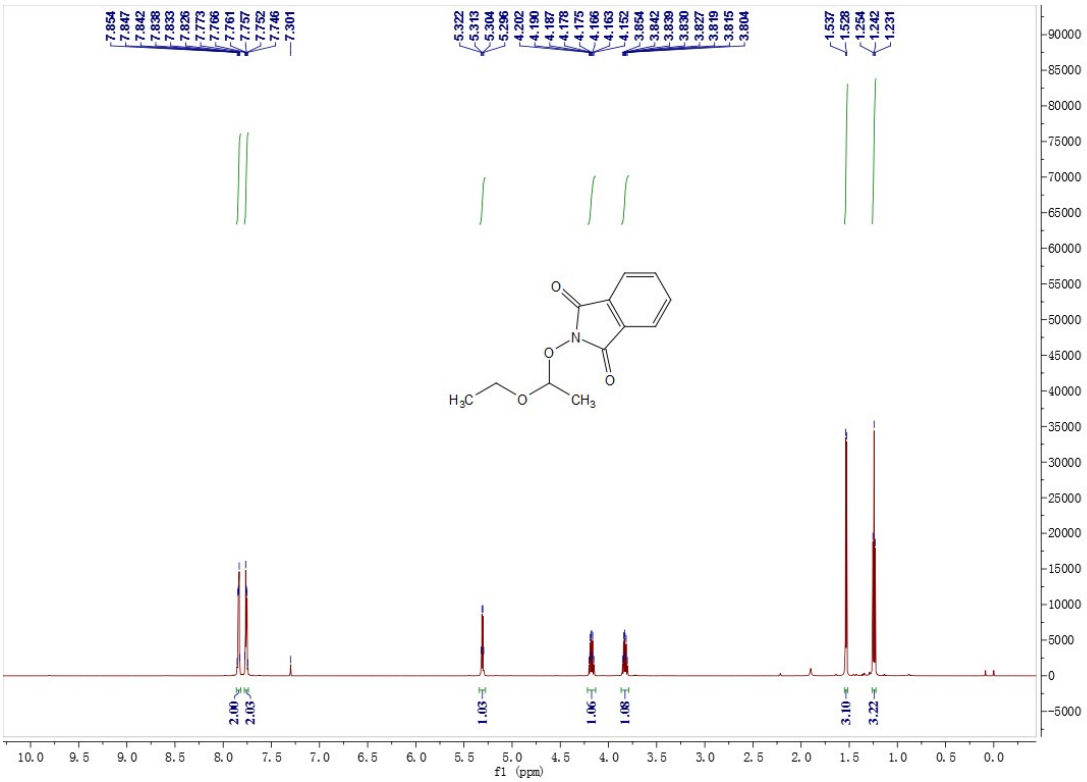


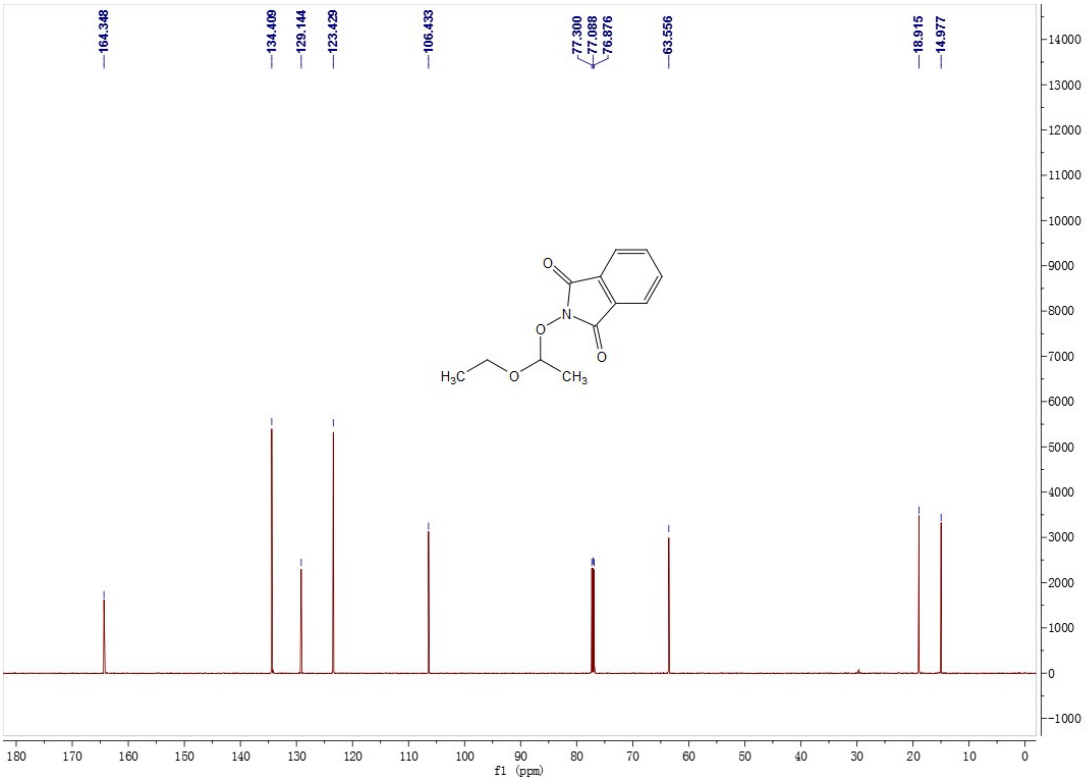
3d (^{13}C, $CDCl_3$)



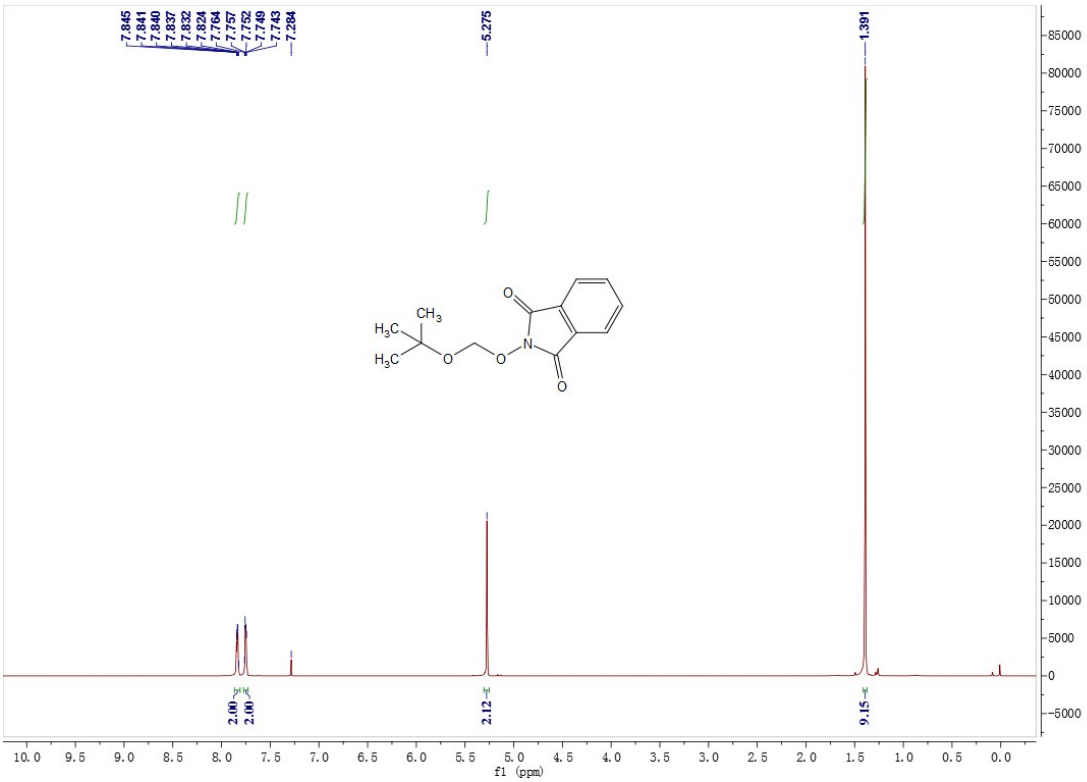
3e (^{1}H, $CDCl_3$)



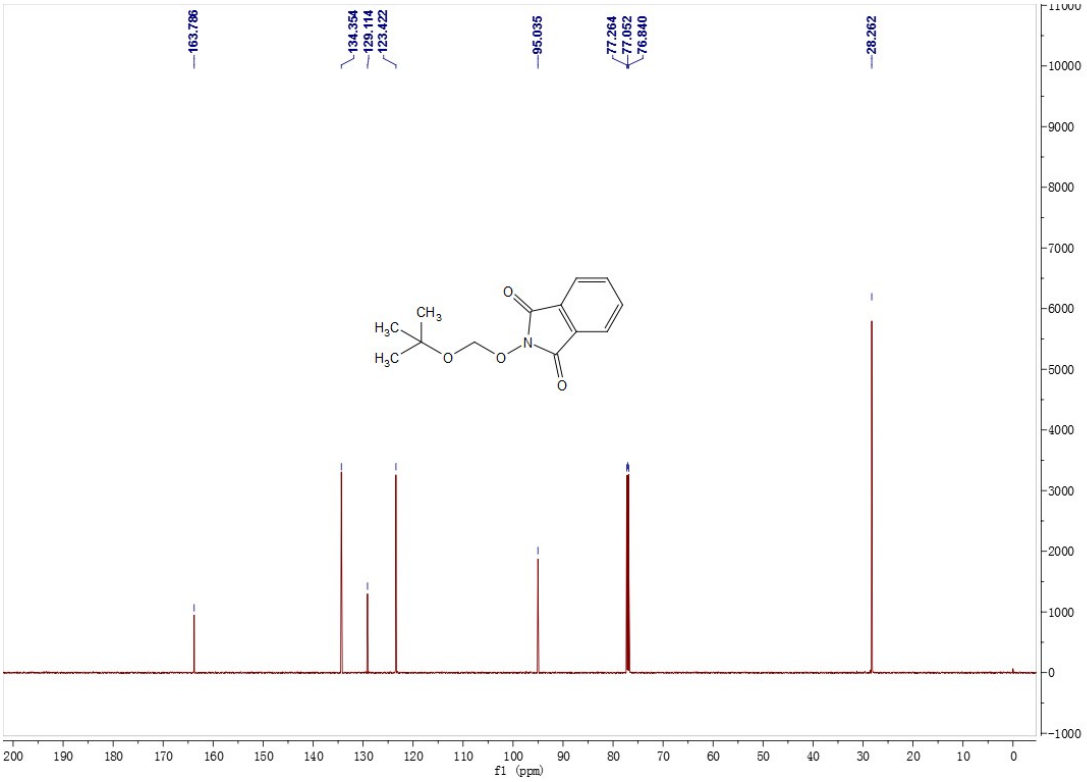
3e (^{13}C, $CDCl_3$)



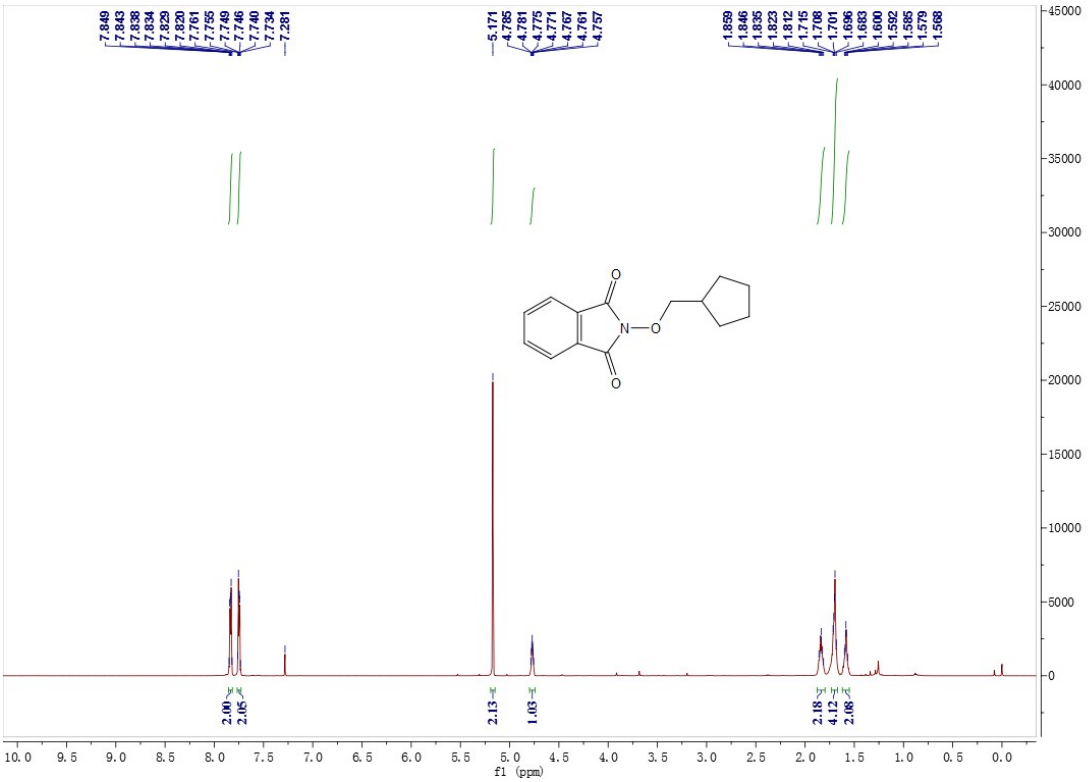
3f (^{1}H, $CDCl_3$)



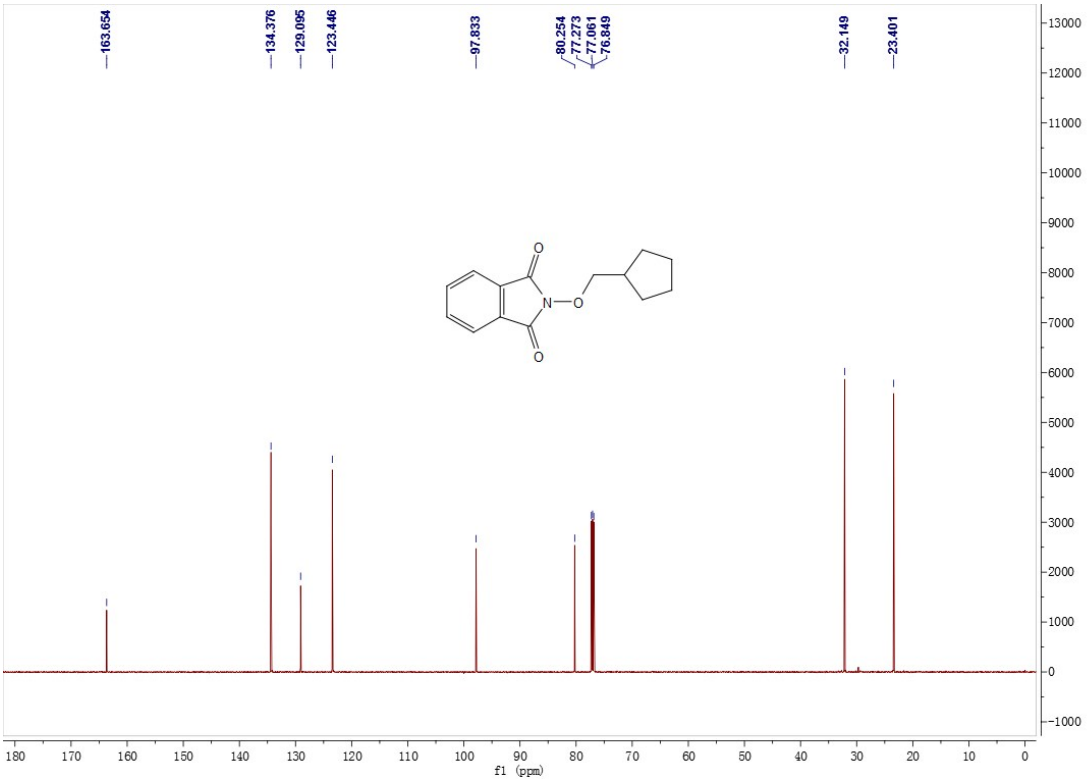
3f (^{13}C, $CDCl_3$)



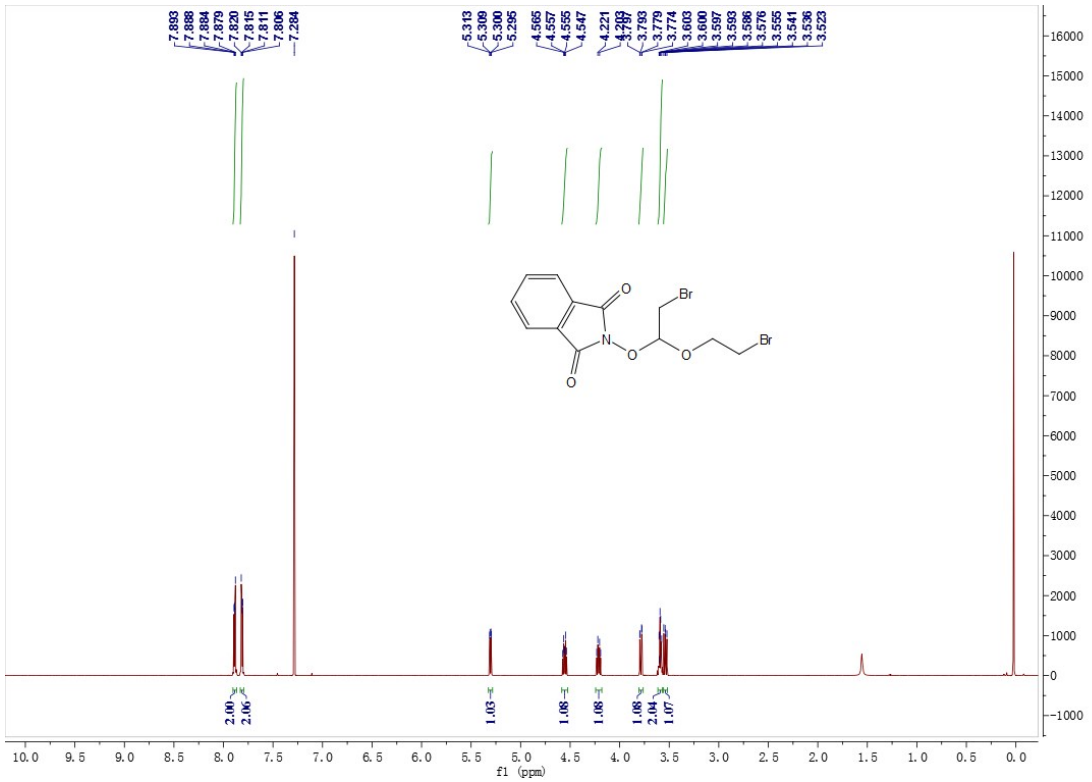
3g (^{1}H, $CDCl_3$)



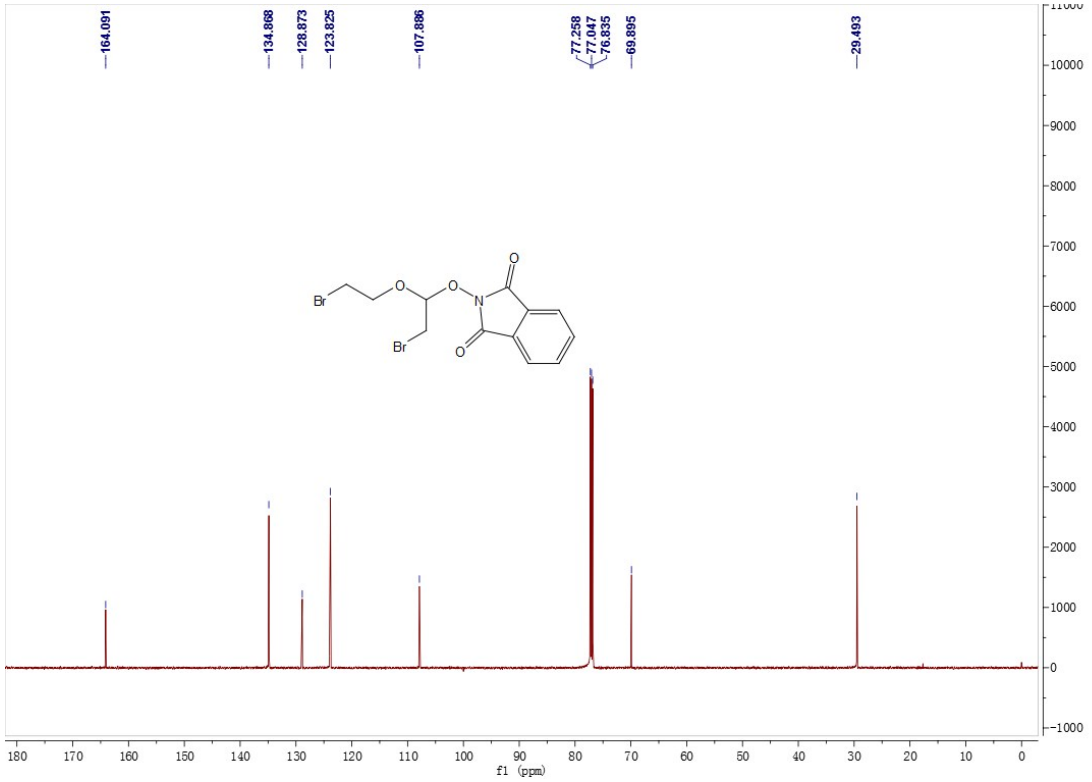
3g (^{13}C, $CDCl_3$)



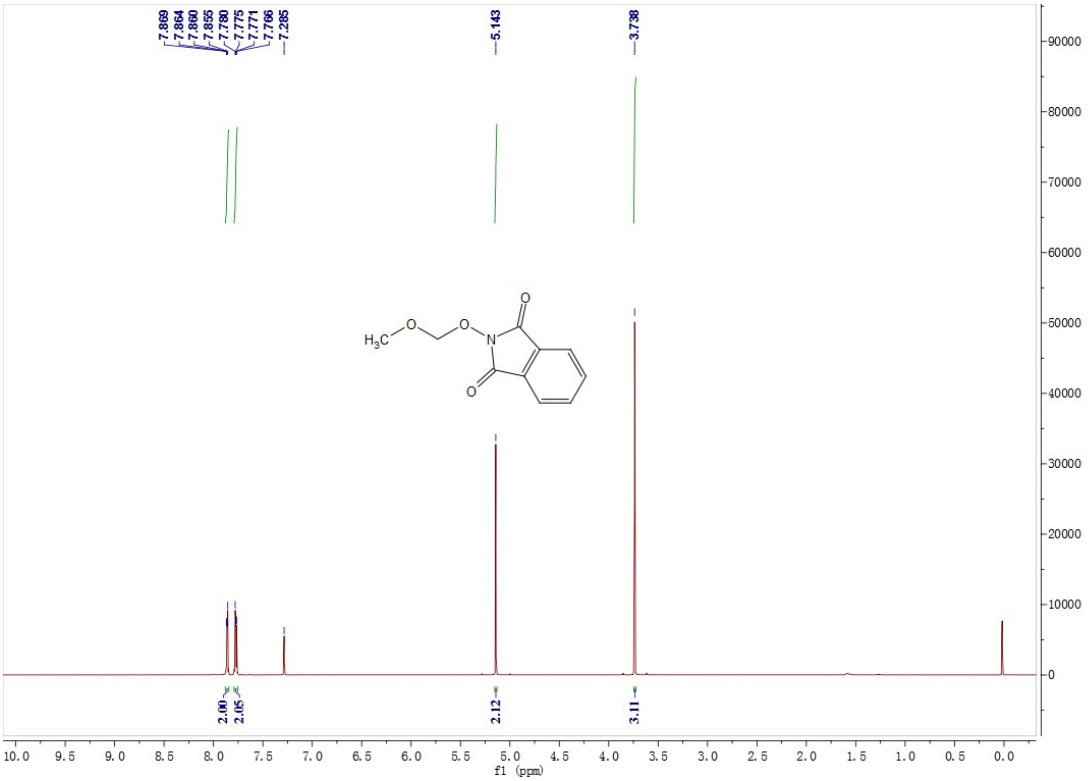
3h (^{1}H, $CDCl_3$)



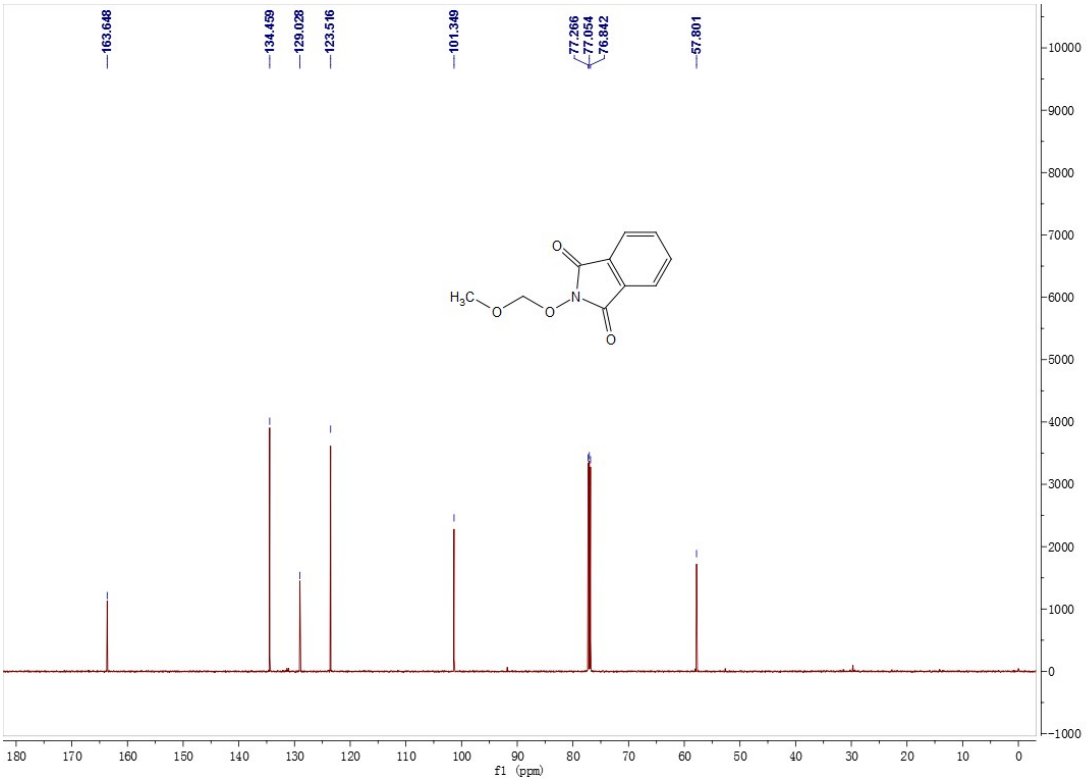
3h (^{13}C, $CDCl_3$)



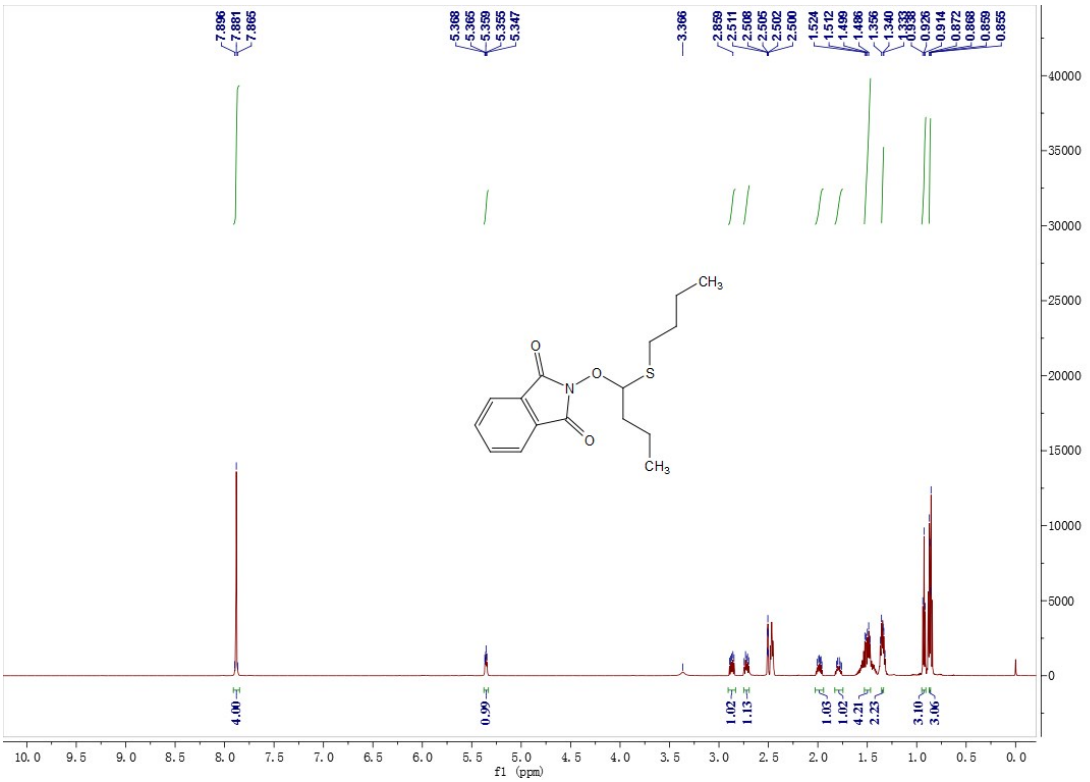
3i (^{1}H, $CDCl_3$)



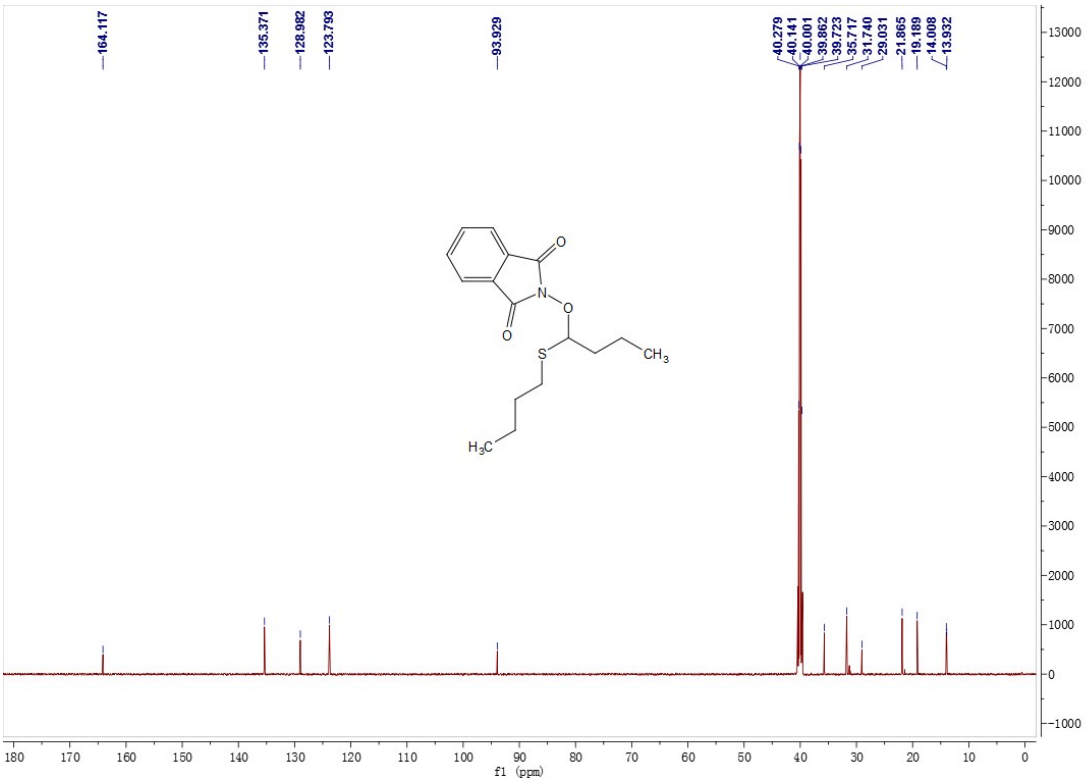
3i (^{13}C, $CDCl_3$)



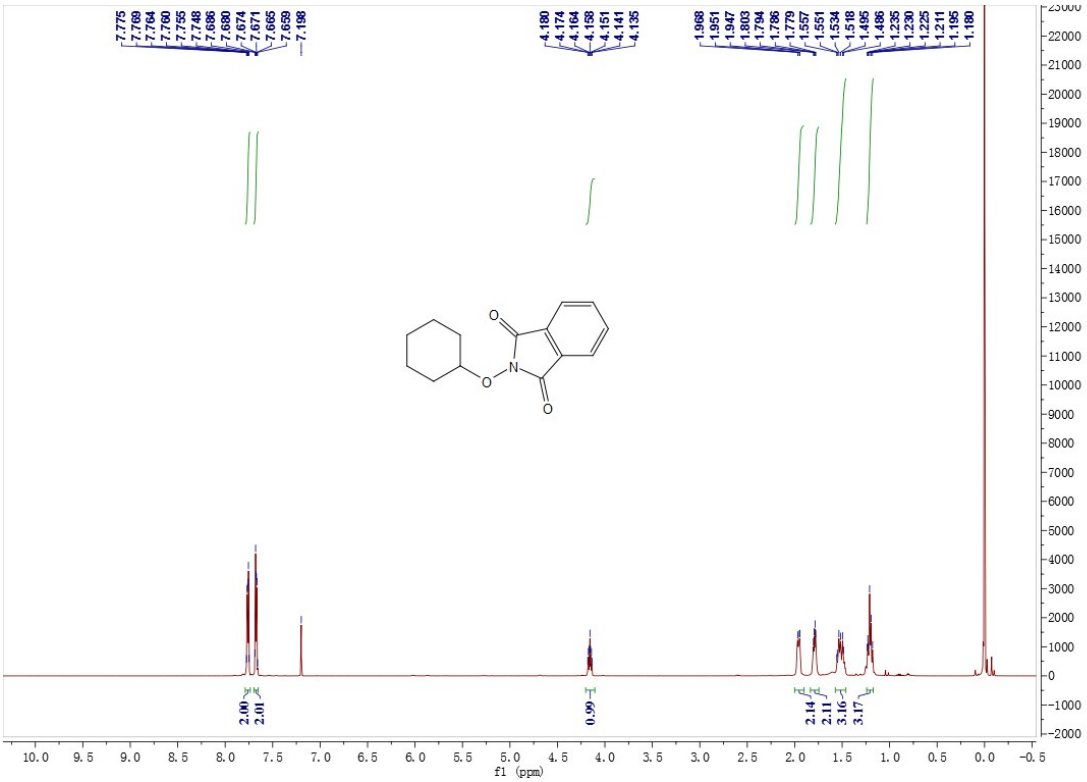
3j (^{1}H, DMSO-d_6)



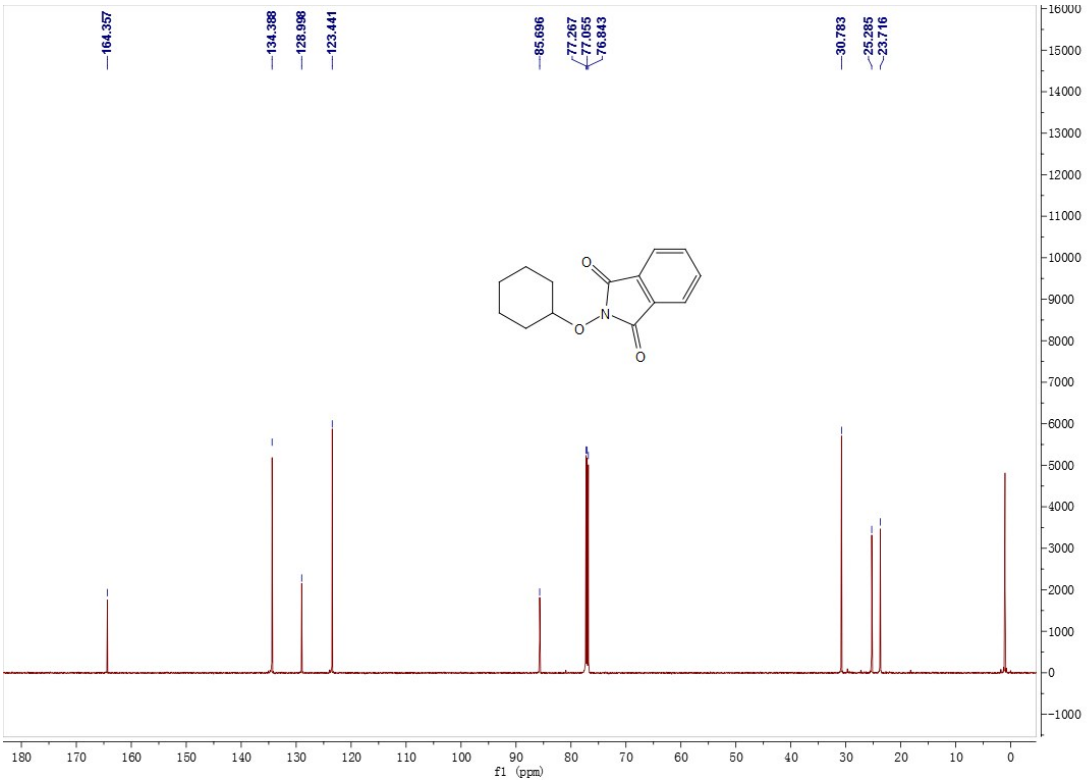
3j (^{13}C, DMSO-d_6)



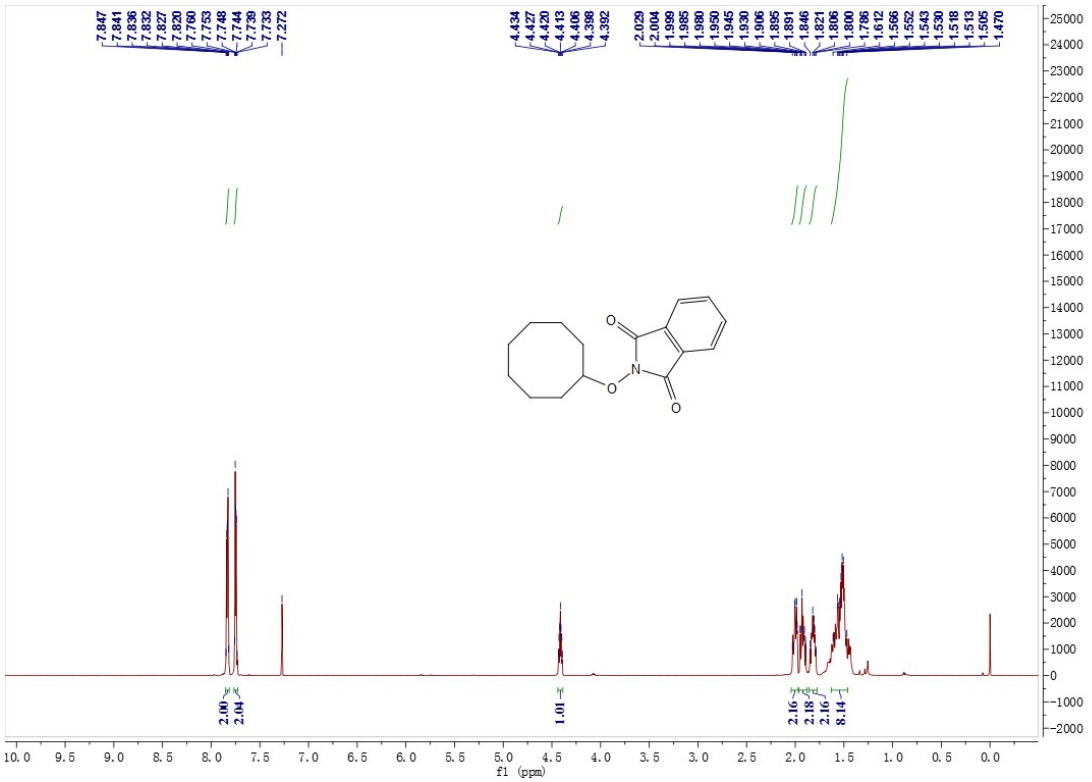
3k (^{1}H, $CDCl_3$)



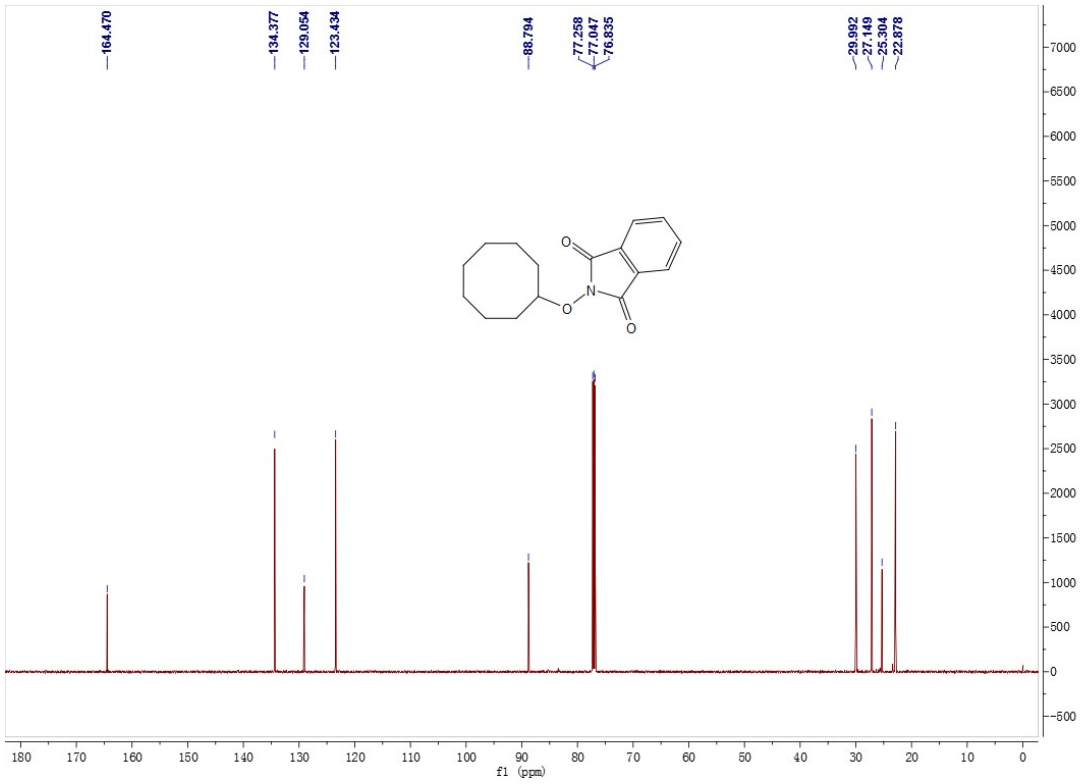
3k (^{13}C, $CDCl_3$)



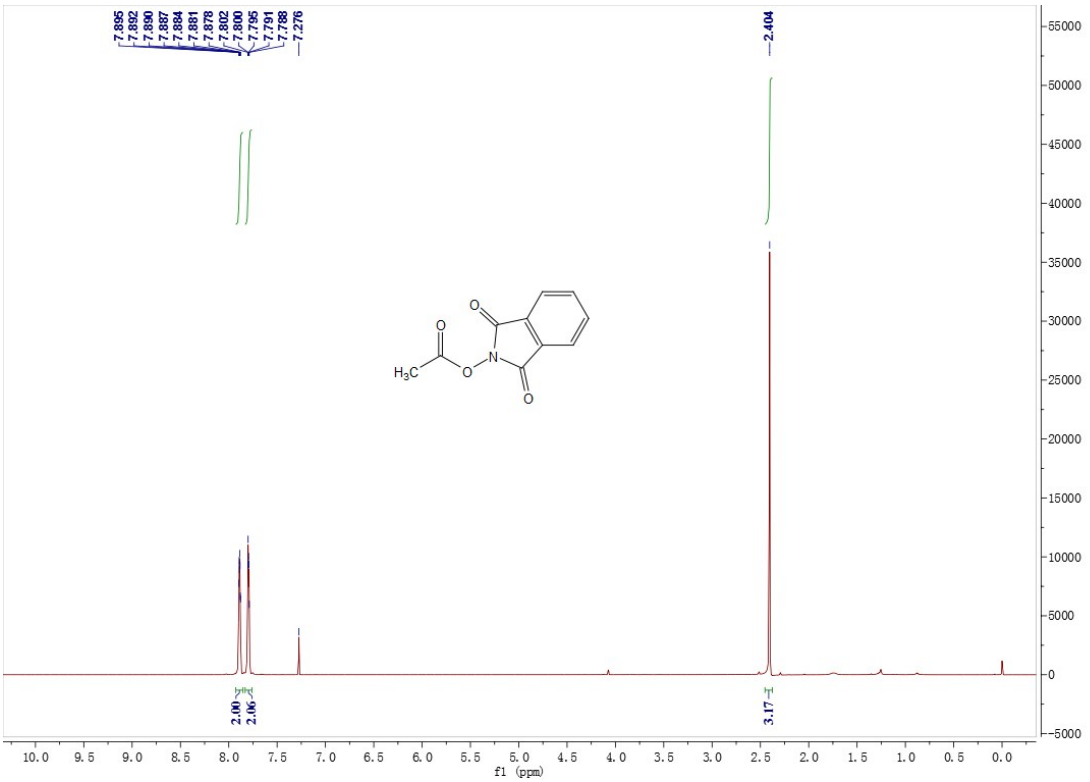
3l (^{1}H, $CDCl_3$)



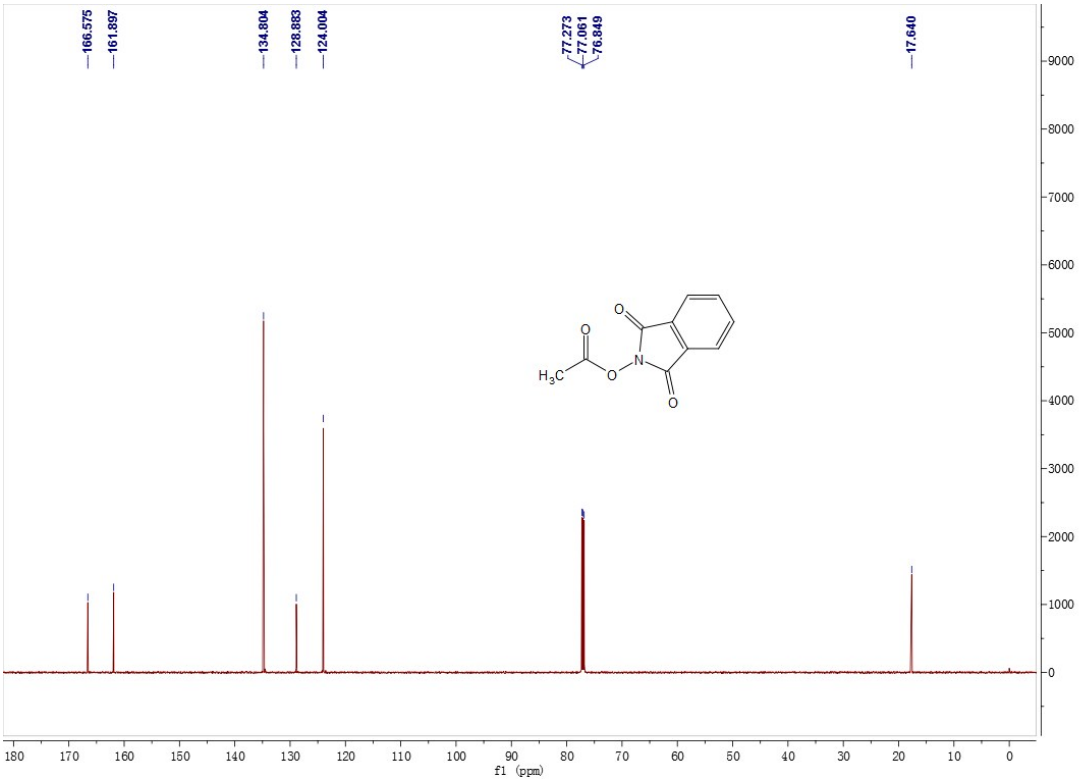
3l (^{13}C, $CDCl_3$)



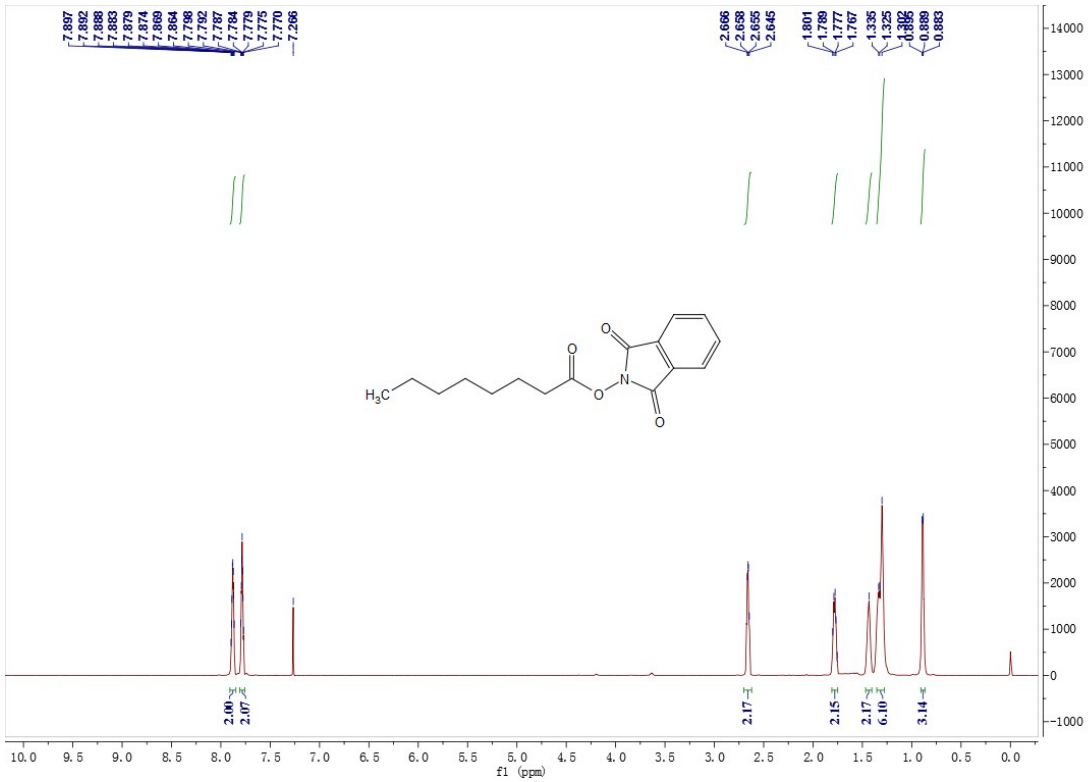
5a (^{1}H, $CDCl_3$)



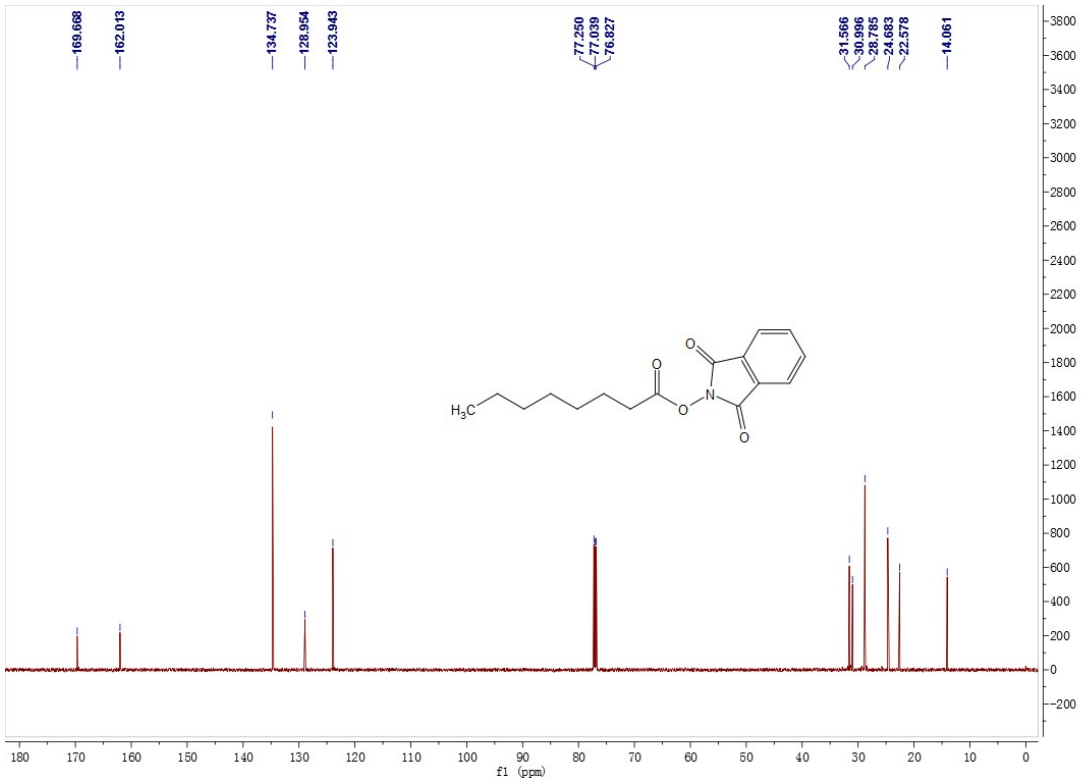
5a (^{13}C, $CDCl_3$)



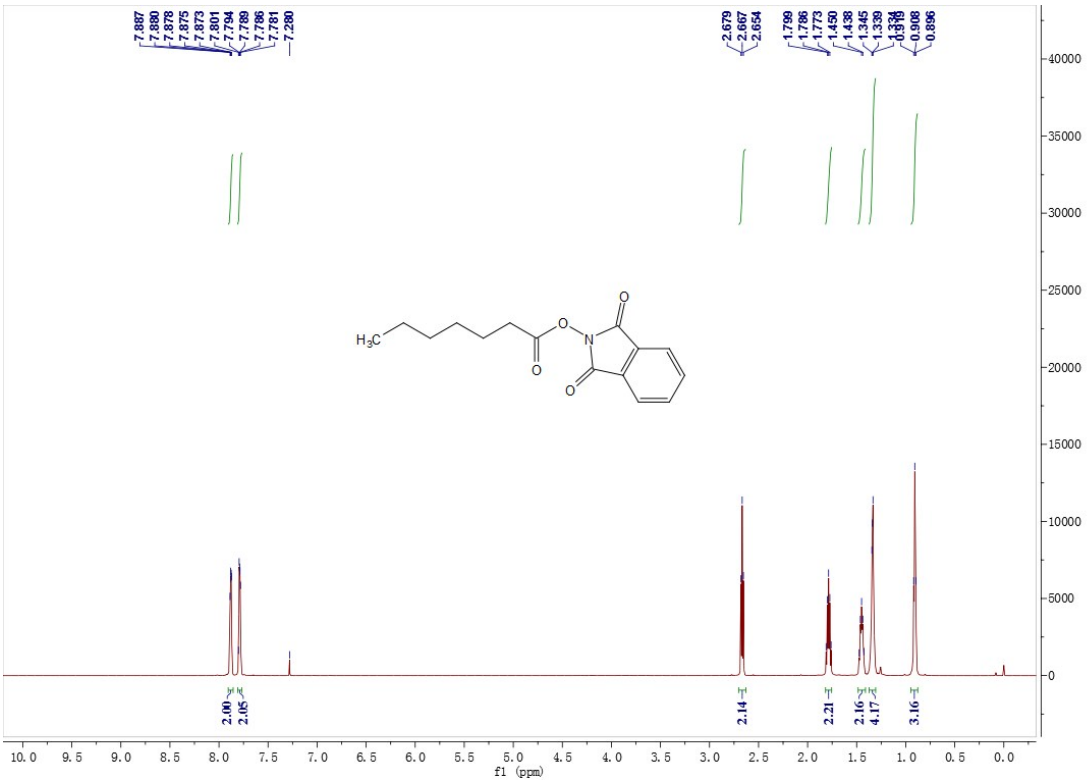
5b (^{1}H, $CDCl_3$)



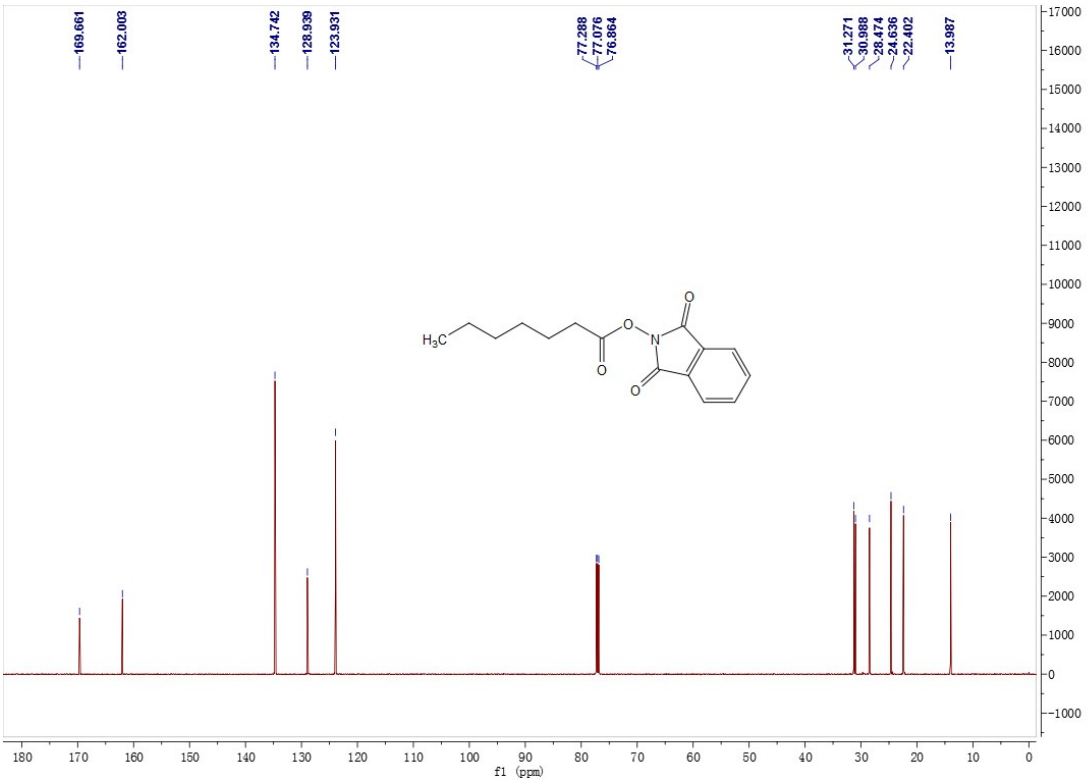
5b (^{13}C, $CDCl_3$)



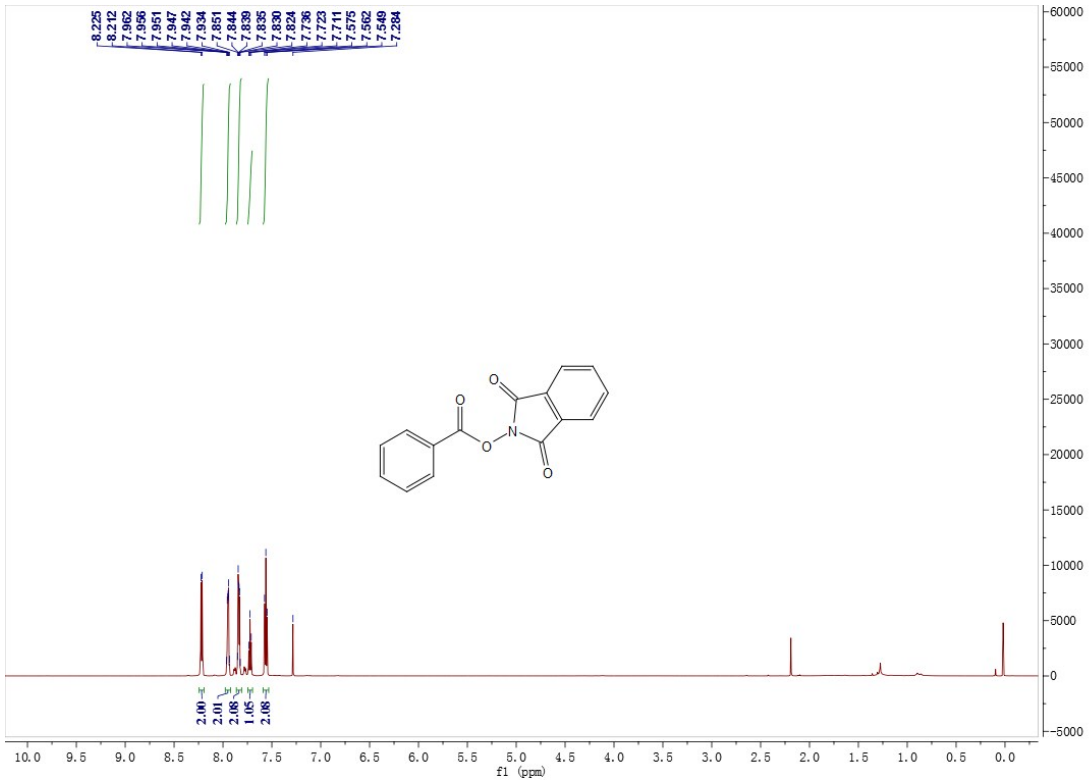
5c (^{1}H, $CDCl_3$)



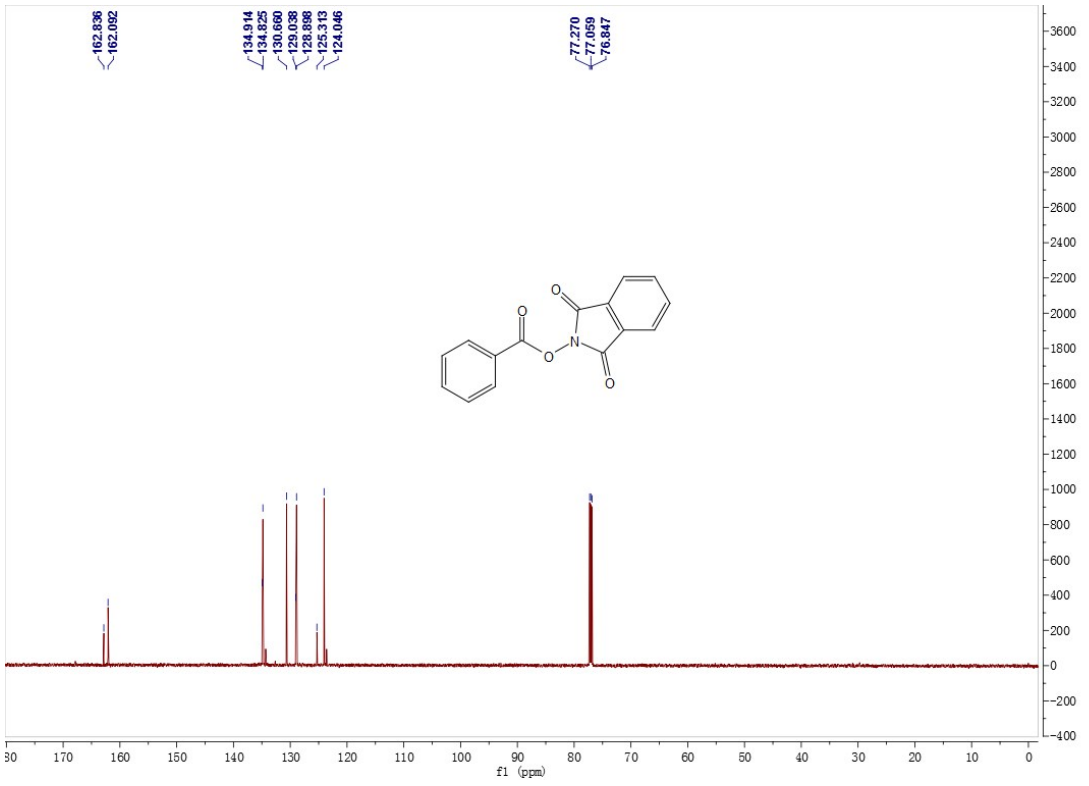
5c (^{13}C, $CDCl_3$)



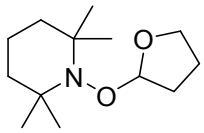
5d (^{1}H, $CDCl_3$)



5d (^{13}C, $CDCl_3$)



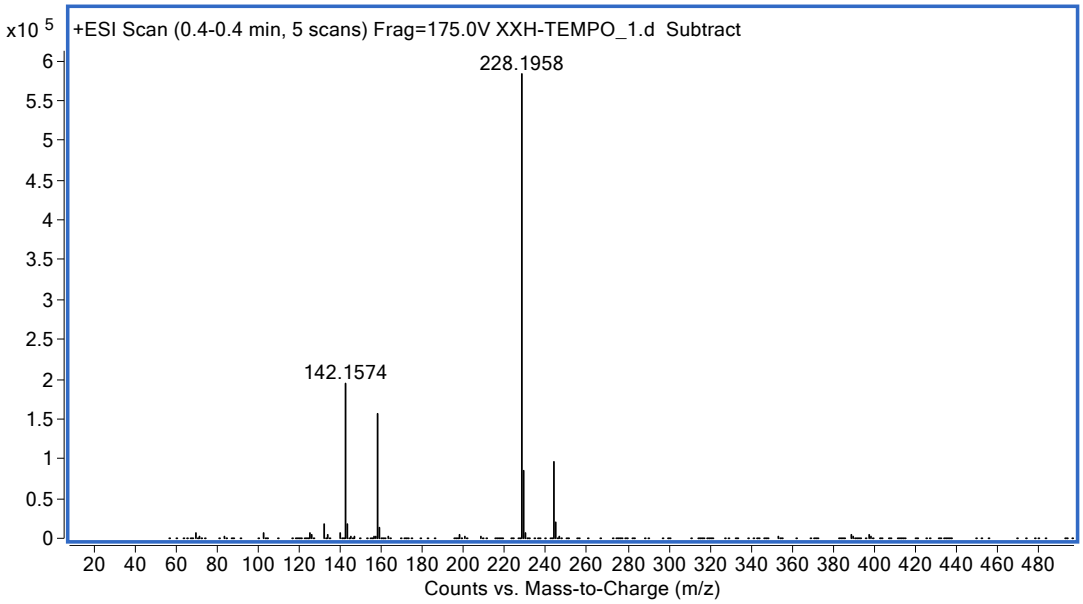
HRMS (ESI) spectra of 2,2,6,6-tetramethyl-1-(tetrahydrofuran-2-yloxy)piperidine (6)



2,2,6,6-tetramethyl-1-(tetrahydrofuran-2-yloxy)piperidine

Chemical Formula: $C_{13}H_{25}NO_2$

Exact Mass: 227.1885



Formula (M)	Ion Formula	m/z	Calc m/z	Diff (ppm)
C13 H25 N O2	C13 H26 N O2	228.1958	228.1958	0.02