Supplementary Information

Visible Light-Induced Aerobic Dioxygenation of α,β-unsaturated amides/Alkenes toward Selective Synthesis of β-Oxy Alcohols Using Rose Bengal as a Photosensitizer

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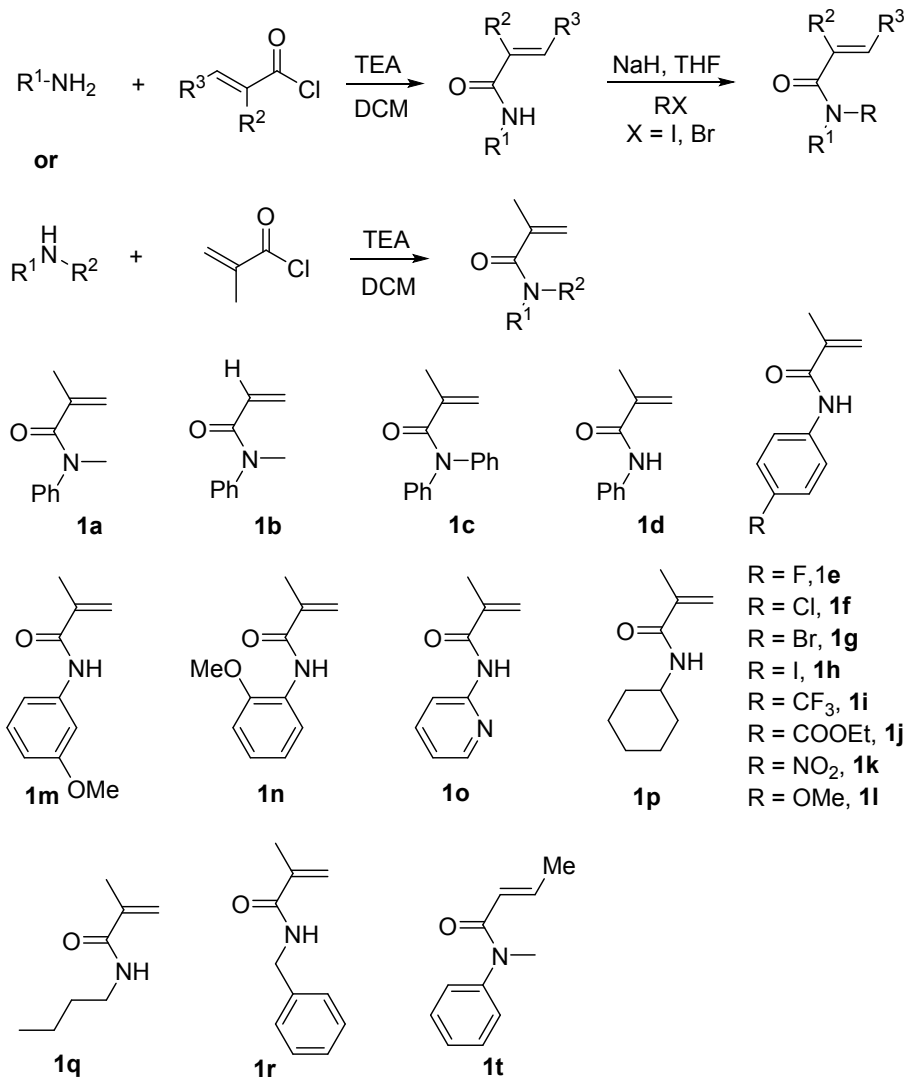
1. General information

All reagents were used in analytical grades and were obtained from common commercial sources. Rose bengal catalyst was purchased from Adamas (high purity) and $^{18}O_2$ was purchased from Wuhan Isotope Technology Co., Ltd. (^{18}O atom ≥ 97%). Solvents were purified by standard methods. Products were purified by flash chromatography on silica gel (300-400 mesh, *Qingdao Haiyang Chemical Co. Ltd. Gel*). ^1H and ^{13}C NMR spectra were recorded on 400 MHz and 500 MHz spectrometer (Bruker ADVANCE III). Chemical shifts are reported relative to the residual solvent peak ($CHCl_3$). High-resolution mass spectra (HRMS) were obtained by the ESI model from an ab sciex 500R QTOF or micrOTOF-Q II instrument.

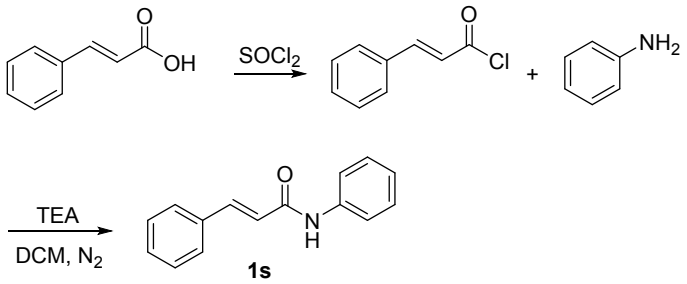
2. General procedures for the synthesis of substrates

The *α,β*-unsaturated amides **1a-1r** and **1t**[1,2] were synthesized according to previously described methods.



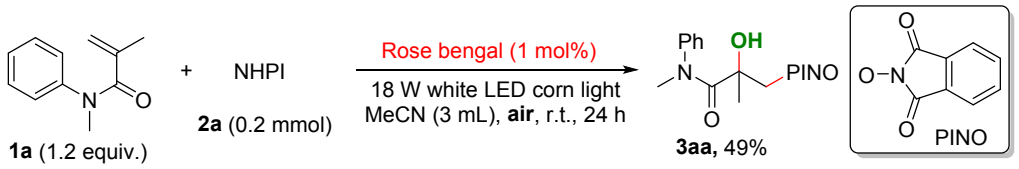
Scheme S1. Synthesis of *α,β*-unsaturated amides **1a-1r** and **1t**

According to the literature,[3] substrate **1s** was prepared easily as described below:



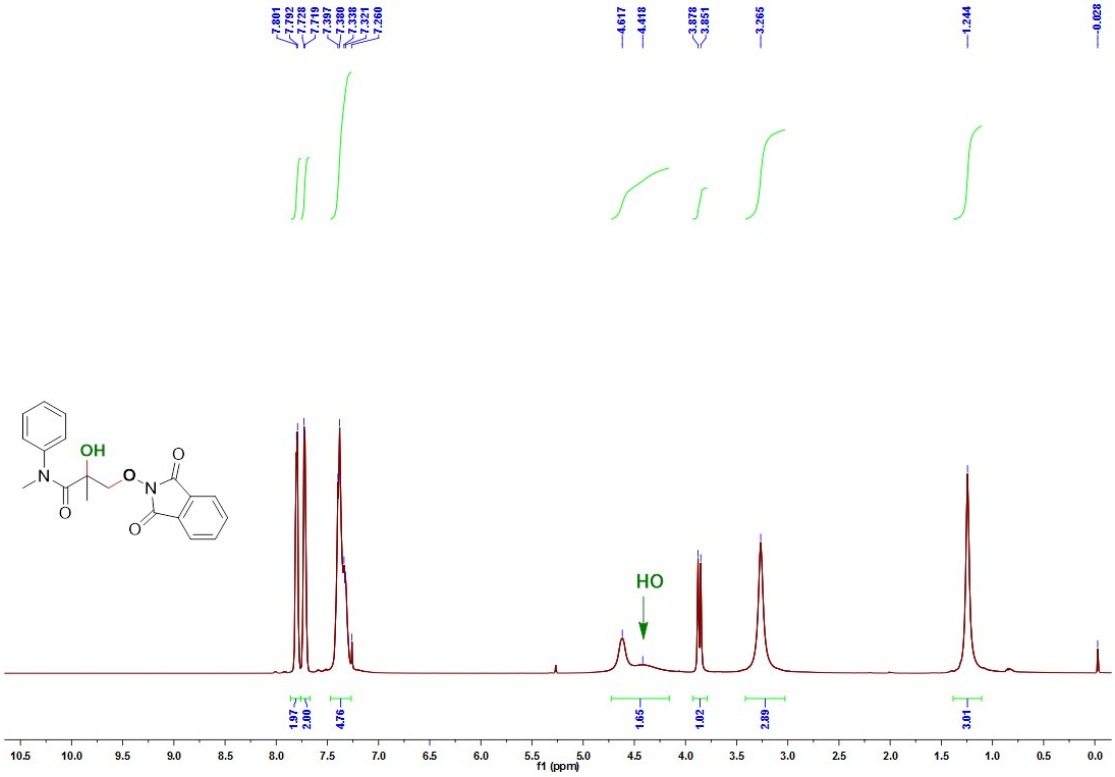
Scheme S2. Synthesis of substrate **1s**

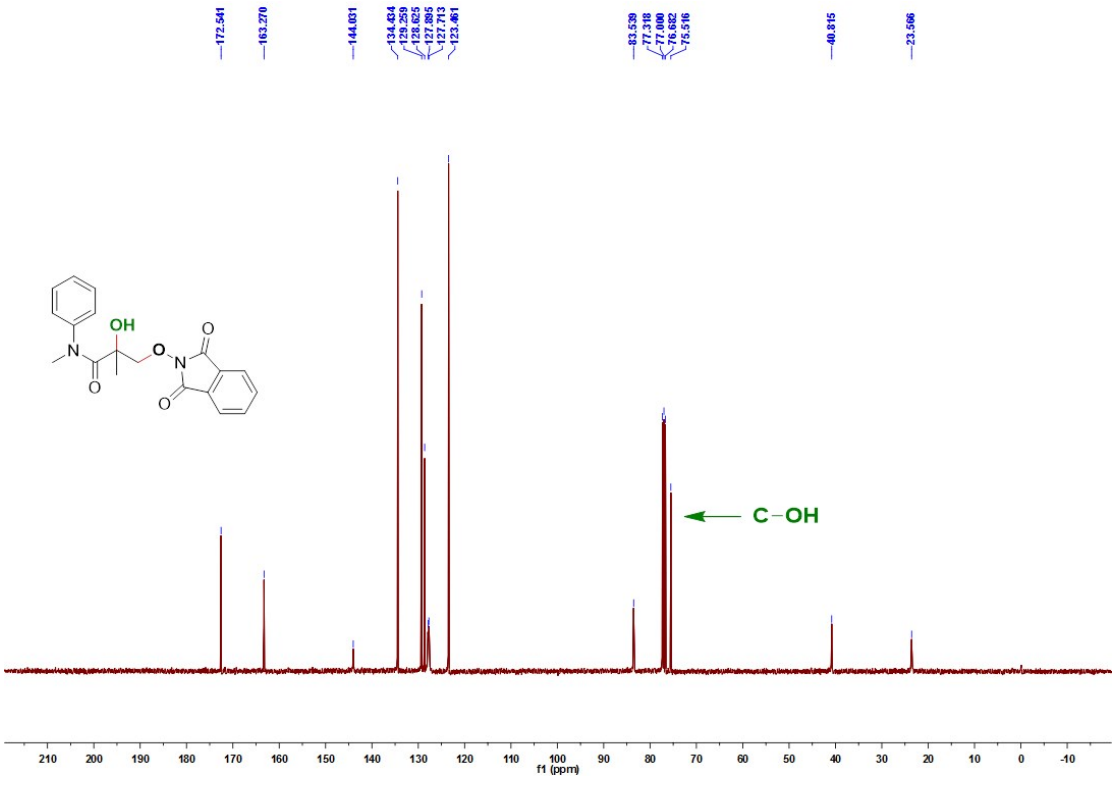
3. Determine the structure of *β*-oxy alcohol 3aa



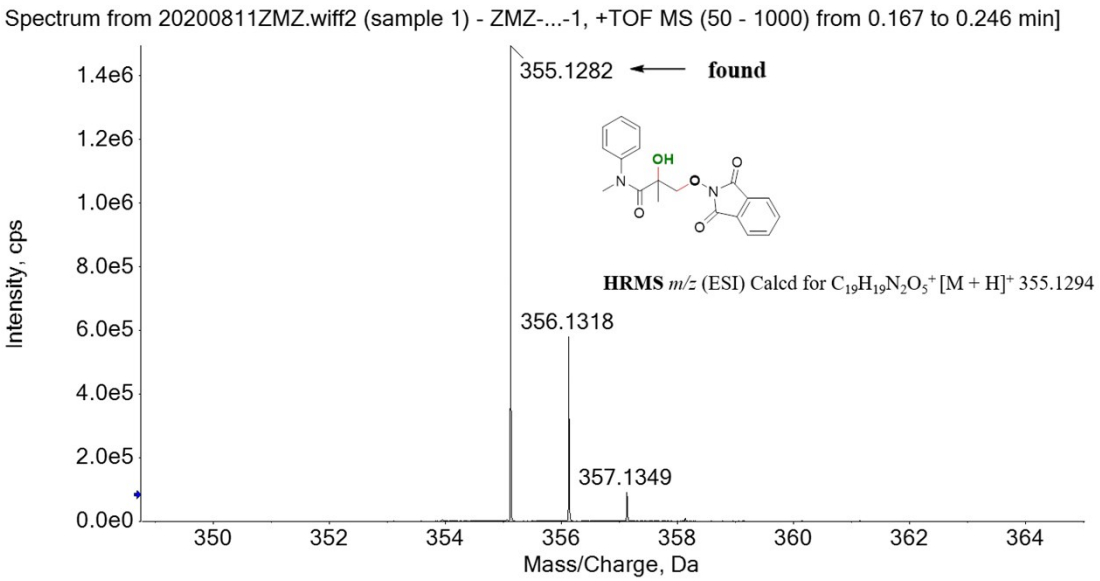
After careful analysis by NMR, HRMS and references,[4] the new product was confirmed as a *β*-oxy alcohol **3aa** (see below).

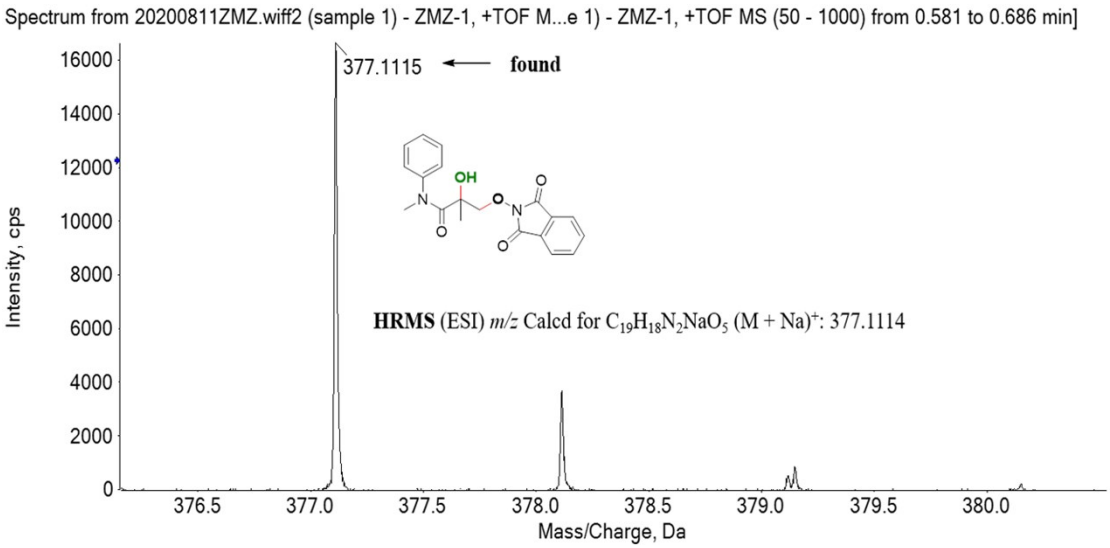
NMR analysis of *β*-oxy alcohol (**3aa**)[4]



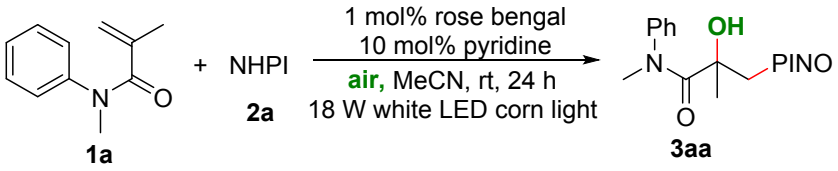


HRMS analysis of β-oxy alcohol (**3aa**)





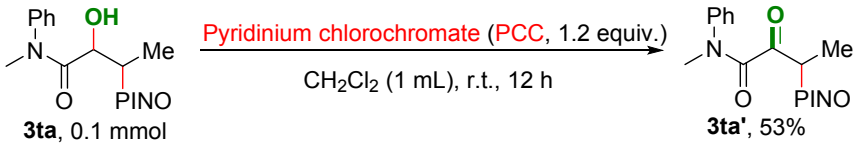
4. Table S1. Screening of the solvents



Entry	Solvent	Yield of **3aa** (%)[b]
1	MeCN	92
2	PhCN	88
3	THF	Trace
4	Benzene	38
5	DCE	15
6	DMSO	Trace
7	DMF	Trace

[a]Reaction conditions: **1a** (0.24 mmol), **2a** (0.2 mmol), rose bengal (1 mol%), pyridine (10 mol%), solvent (3 mL), open to air, irradiation under a 18 W white LED corn light at room temperature for 24 h. [b]Isolated yields based on NHPI, and the excess **1a** was recovered.

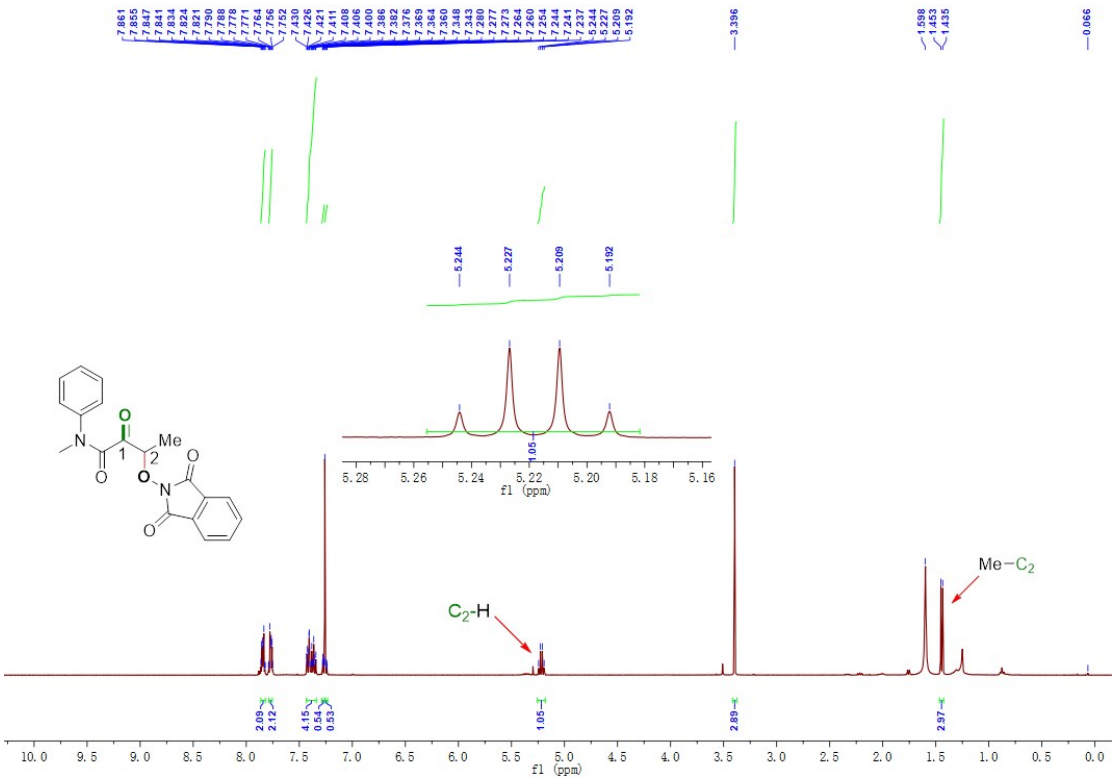
5. Conversion from product 3ta to *α*-oxygenated ketones 3ta'

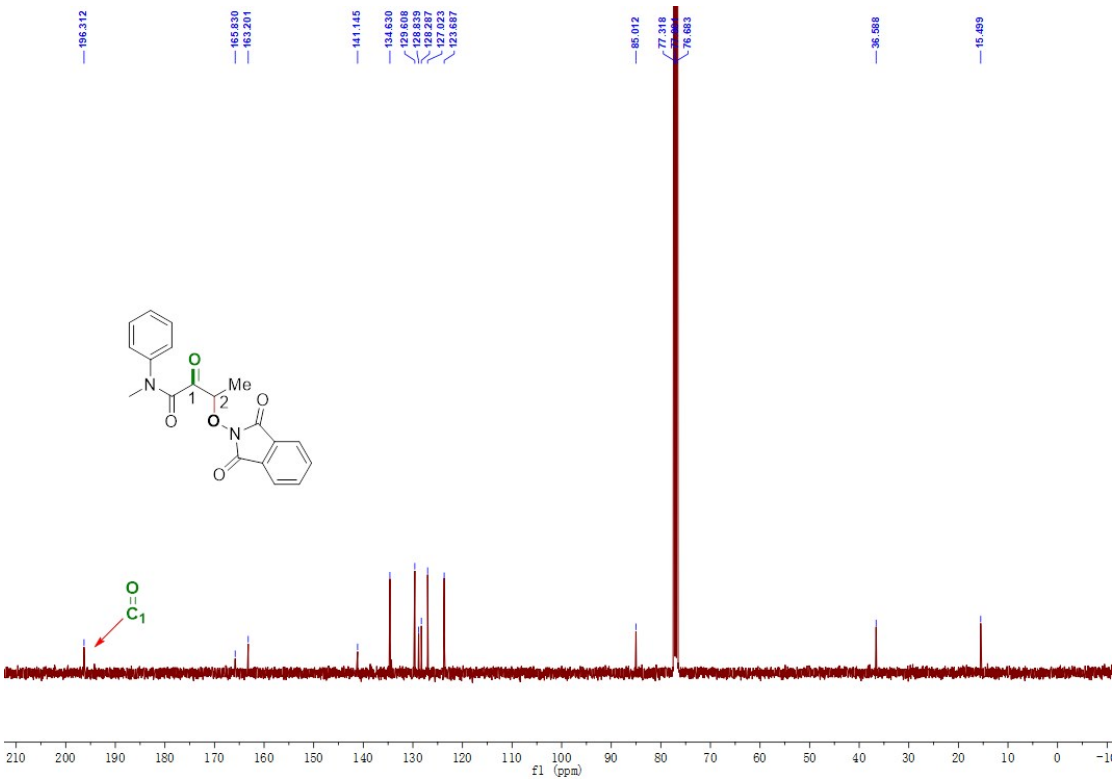


3ta, 0.1 mmol

3ta', 53%

NMR analysis of *α*-oxygenated ketones (**3ta'**)



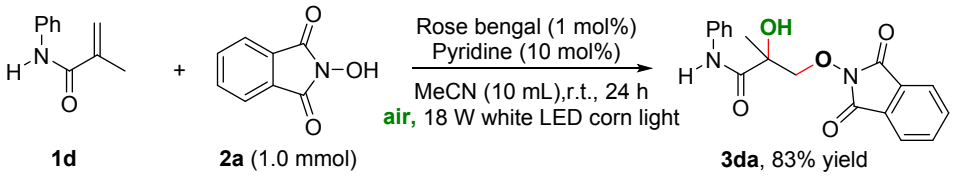


6. General procedures for the selective dioxygenation reaction

A mixture of alkenes **1** or **4** (1.2 euqiv.), *N*-hydroxy compound **2** (0.2 or 0.3 mmol), rose bengal (1 mol%), and pyridine (10 mol%) was stirred in anhydrous MeCN (3.0 mL) at room temperature under air with 18 W white LED corn light irradiation for 24 h. When the reaction was completed (monitored by TLC), water (6 mL) was added to the reaction mixture, and the resulting mixture was extracted with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and then concentrated in a vacuum. The residue was purified by flash chromatography on silica gel to afford the corresponding product **3** or **5** (using the mixture of petroleum ether and acetone as eluents).

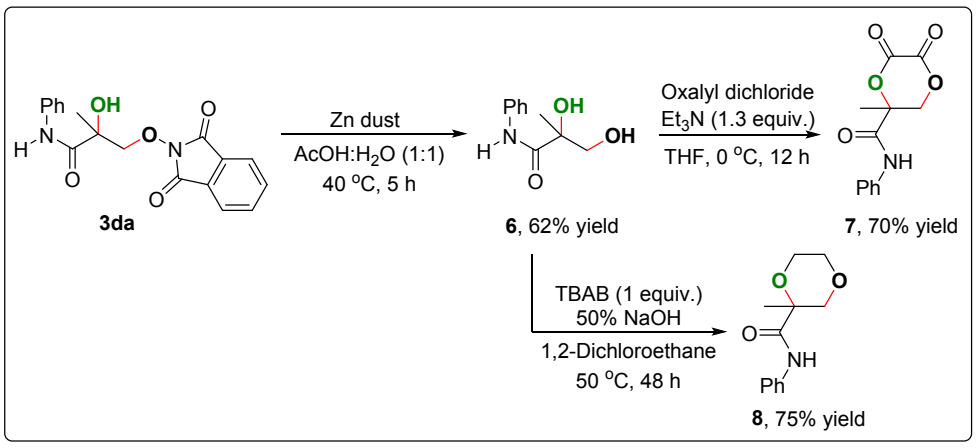
7. Synthesis applications

7.1 1.0 mmol-scale dioxygenation reaction



To an oven-dried 50 mL Schlenk tube were added *N*-phenylmethacrylamide **1d** (0.193 g, 1.2 mmol), NHPI **2a** (0.163 g, 1 mmol), Rose bengal (0.013 g, 1 mol%), pyridine (0.008 g, 10 mol%), and anhydrous MeCN (10 mL). Then the tube was stirred at room temperature under open air with 18 W white LED corn light irradiation for 24 h. Upon completion, the solvent was evaporated under vacuum. Then, the residue was diluted by dichloromethane and washed with H_2O. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and the solvent was then removed under vacuum. The resulting residue was purified by silica gel column chromatography (petroleum ether/acetone, 10:1 to 6:1) to afford the desired product **3da** in 83% yield (0.282 g).

7.2 Synthetic transformations



Preparation of 2,3-dihydroxy-2-methyl-*N*-phenylpropanamide (6):

To a 100 mL Schlenk tube were added **3da** (0.282 g, 0.83 mmol), AcOH (4 mL), Zn powder (0.54 g 8.3 mmol), and H_2O (4 mL). Then the tube was stirred at 40 °C for

5 h. Upon completion, the reaction mixture was filtered through Celite and was further extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuum. The resulting residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate; 4:1 to 2:1) to afford the desired product **6** in 62% yield (0.1 g).

Preparation of 2-methyl-5,6-dioxo-*N*-phenyl-1,4-dioxane-2-carboxamide (7):[5]

The mixture of **6** (0.05 g, 0.256 mmol) and Et_3N (0.037 g, 0.33 mmol) were placed in a 25 mL Schlenk tube with 5 mL of anhydrous THF and put into an ice bath, oxalyl dichloride (0.03 mL, 0.33 mmol) was added dropwise, the resulting mixture was allowed to warm to room temperature and stirred overnight. Upon completion, the solvent was evaporated under vacuum. Then, the residue was diluted by dichloromethane and washed with brine. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and the solvent was then removed under vacuum. The resulting residue was purified by silica gel column chromatography (petroleum ether/acetone, 6:1) to afford the desired product **7** in 70% yield (0.0447 g).

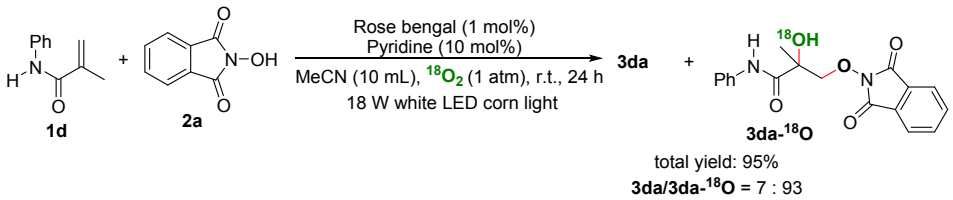
Preparation of 2-methyl-*N*-phenyl-1,4-dioxane-2-carboxamide (8):[6]

To a 25 mL Schlenk tube were added **6** (0.05 g, 0.256 mmol), tetrabutylammonium bromide (TBAB: 0.09 g, 0.256 mmol), 50% NaOH aqueous solution (1.6 mL), and 1,2-dichloroethane (DCE, 3.0 mL). Then the reaction mixture was stirred at 50 °C for 48 h, cooled to rt, and diluted with H_2O and dichloromethane. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 30 mL).

The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and the solvent was then removed under vacuum. The resulting residue was purified by silica gel column chromatography (petroleum ether/acetone, 5:1) to afford the desired product **8** in 75% yield (0.0425 g).

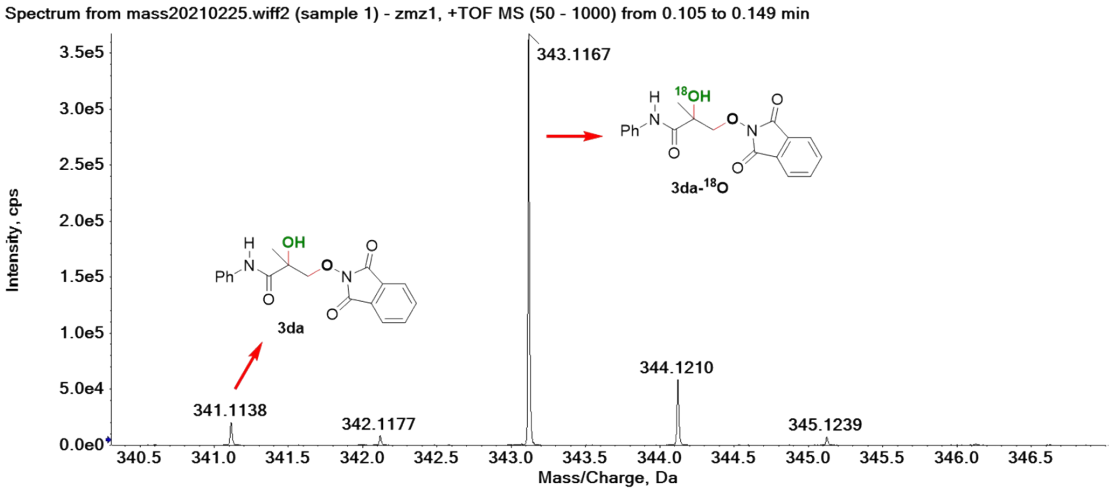
8. Preliminary mechanistic studies

8.1 $^{18}O_2$-labeling experiment



HRMS with $^{18}O_2$ labeling

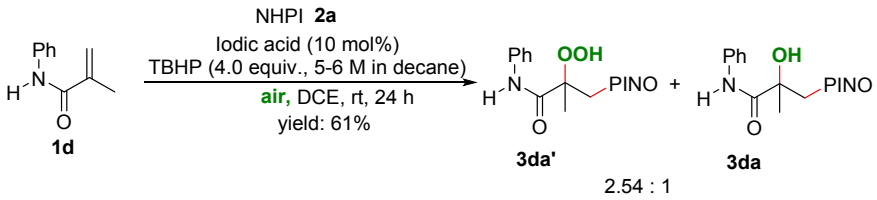
^{16}O-labeled product 3da: HRMS m/z (ESI) **Calcd for** $C_{18}H_{17}N_2O_5^+$ $(M + H)^+$ 341.1137, **found** 341.1138; **^{18}O-labeled product 3da-^{18}O:** HRMS m/z (ESI) **Calcd for** $C_{18}H_{17}N_2O_4{}^{18}O^+$ $(M + H)^+$ 343.1180, **found** 343.1167.



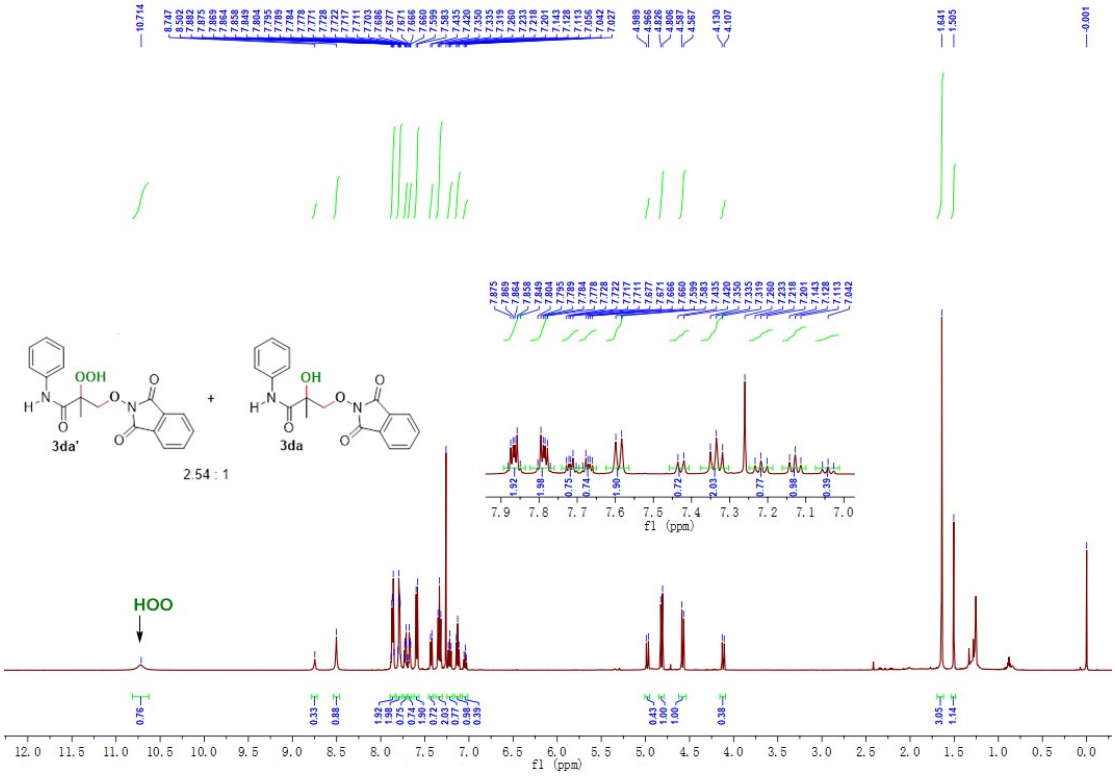
Mass/Char	Area	Height	Width	Width at 50%	Resolution
148.0396	60.69912	8405.833	0.034752	0.006573758	22519.78
163.039	572.6187	72429.5	0.069033	0.006643882	24539.72
164.0427	60.18452	7225.333	0.037889	0.007170586	22877.17
191.0354	47.81233	5369.167	0.052166	0.007257169	26323.69
222.065	128.0859	12400.67	0.076006	0.008660822	25640.18
279.094	177.4818	13613.83	0.069871	0.010701906	26078.9
282.0866	105.0961	8417.333	0.056539	0.010458204	26972.76
341.1138	326.8022	20361	0.090434	0.013384953	25484.87
342.1177	134.7412	8548	0.073586	0.013225777	25867.49
343.1167	4391.068	367437.7	0.105817	0.009981826	34374.14
344.121	889.4607	58827.83	0.130568	0.012735023	27021.62
345.1239	120.5829	7578.5	0.085278	0.013279291	25989.63

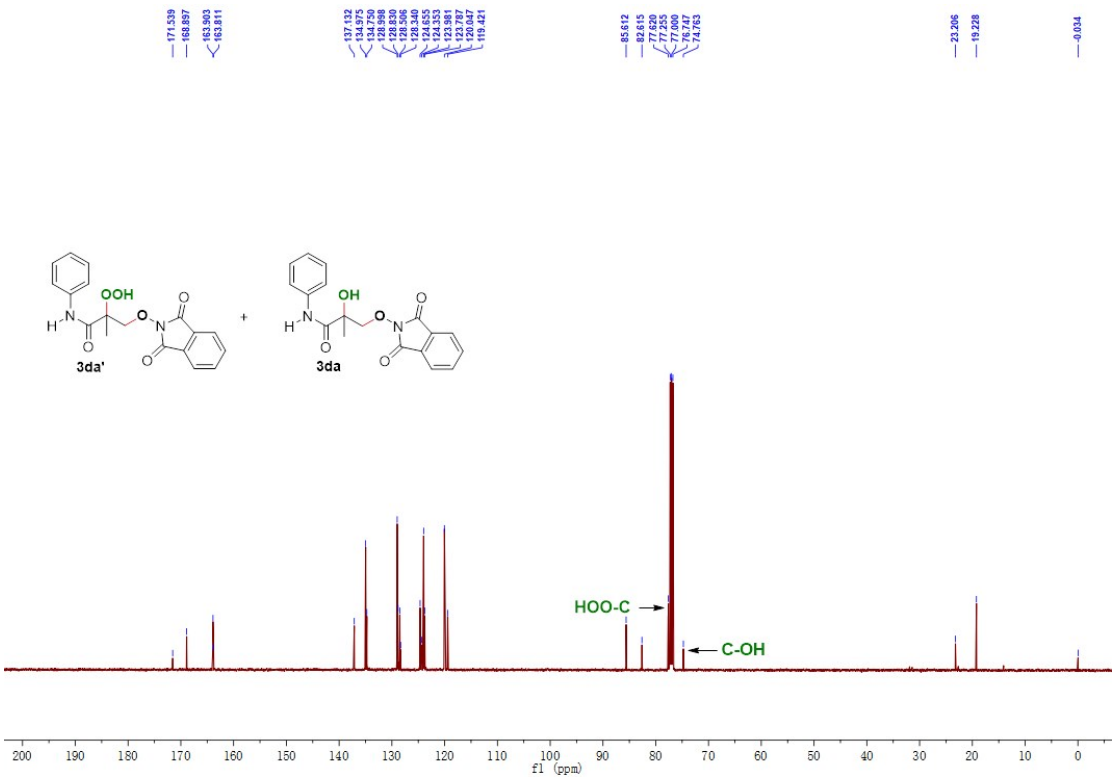
8.2 Intermediate verification experiments

When the reaction was performed under the reaction conditions similar to a TBHP/acid-mediated dioxygenation, a mixture of hydroperoxide (**3da'**) and alcohol (**3da**) was given (the ratio of **3da'**/**3da** was ca. 2.54:1).



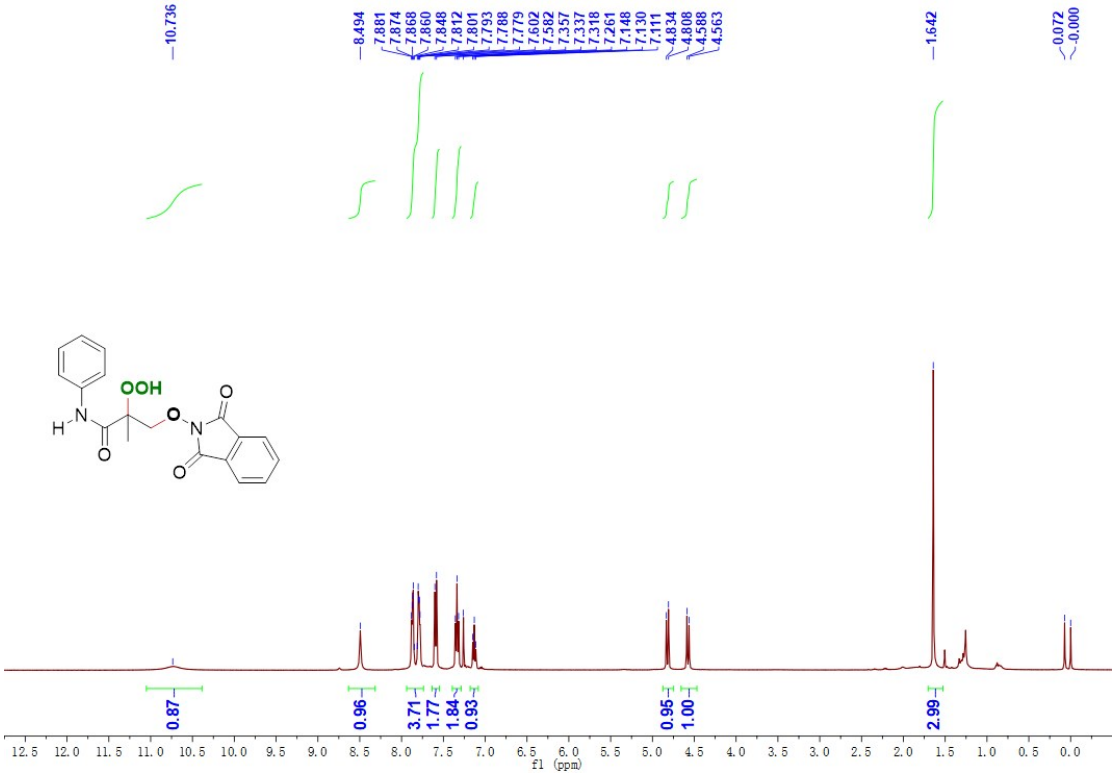
NMR analysis of hydroperoxide (**3da'**)[4a,7] and alcohol (**3da**)[4]

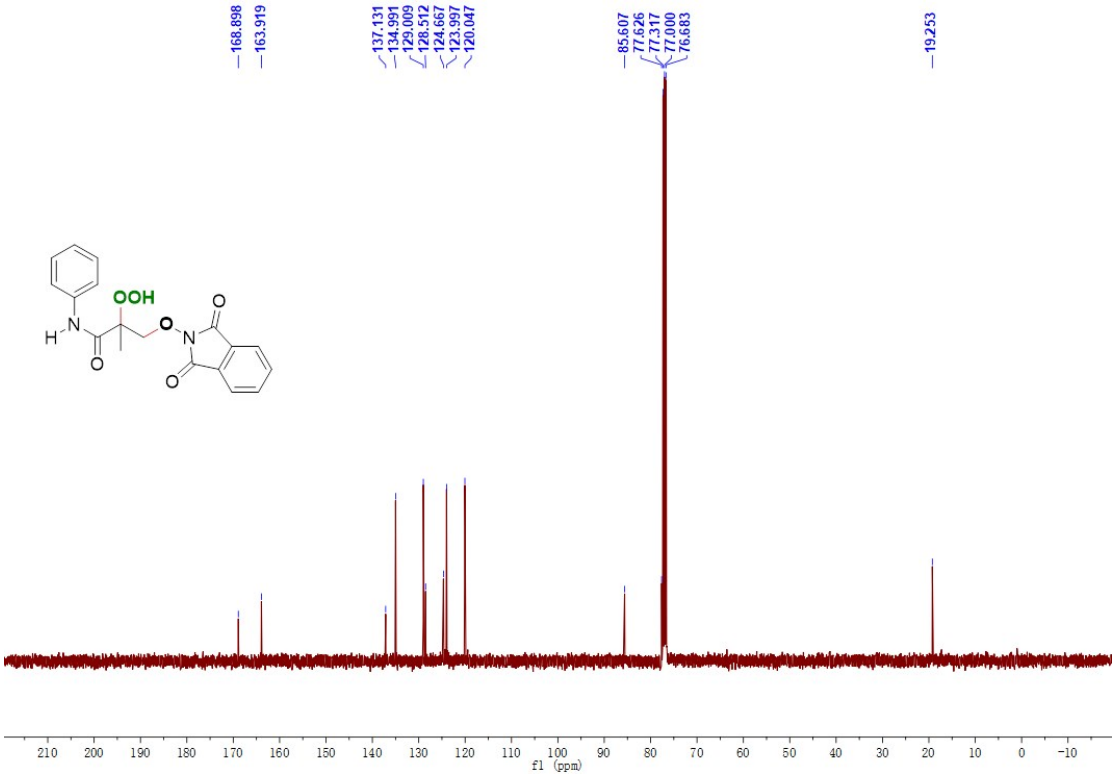




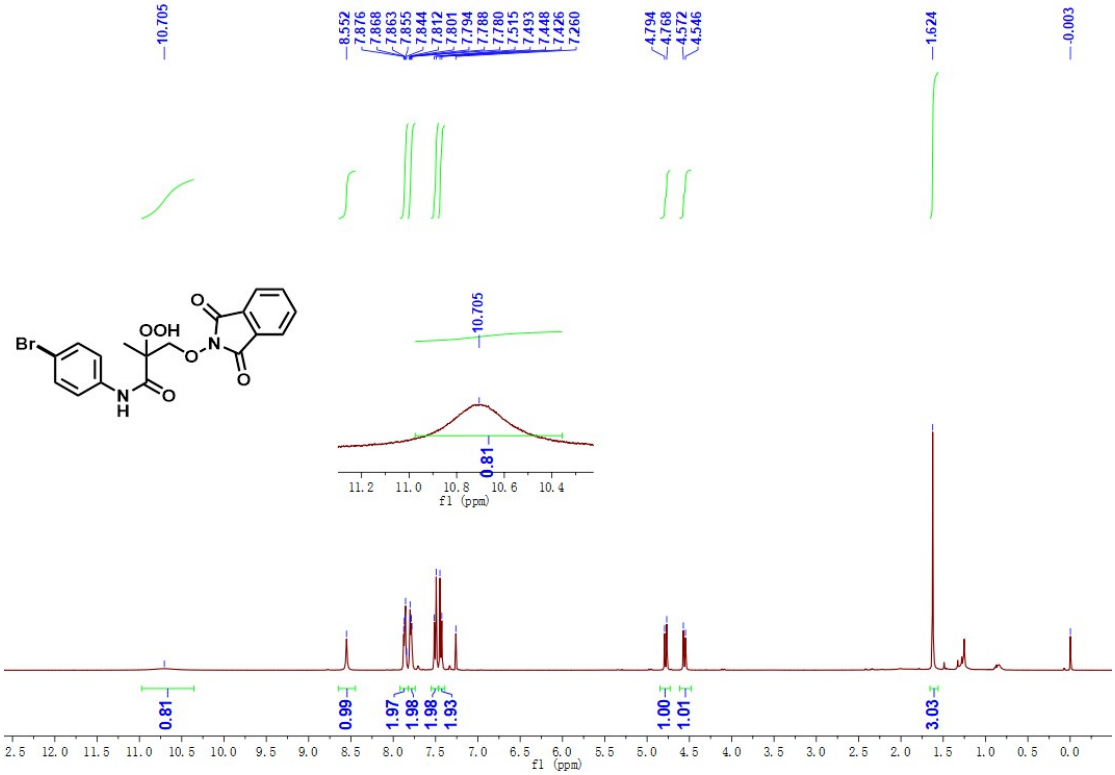
We synthesized hydroperoxides[4a] **3da'**, **3ga'**, **3pa'** and **5i'** and found that these compounds could be converted into the corresponding alcohols **3da**, **3ga**, **3pa** and **5i** in excellent yields under our standard reaction conditions in the presence of 1.0 equiv. of NHPI and 10 mol% of pyridine.

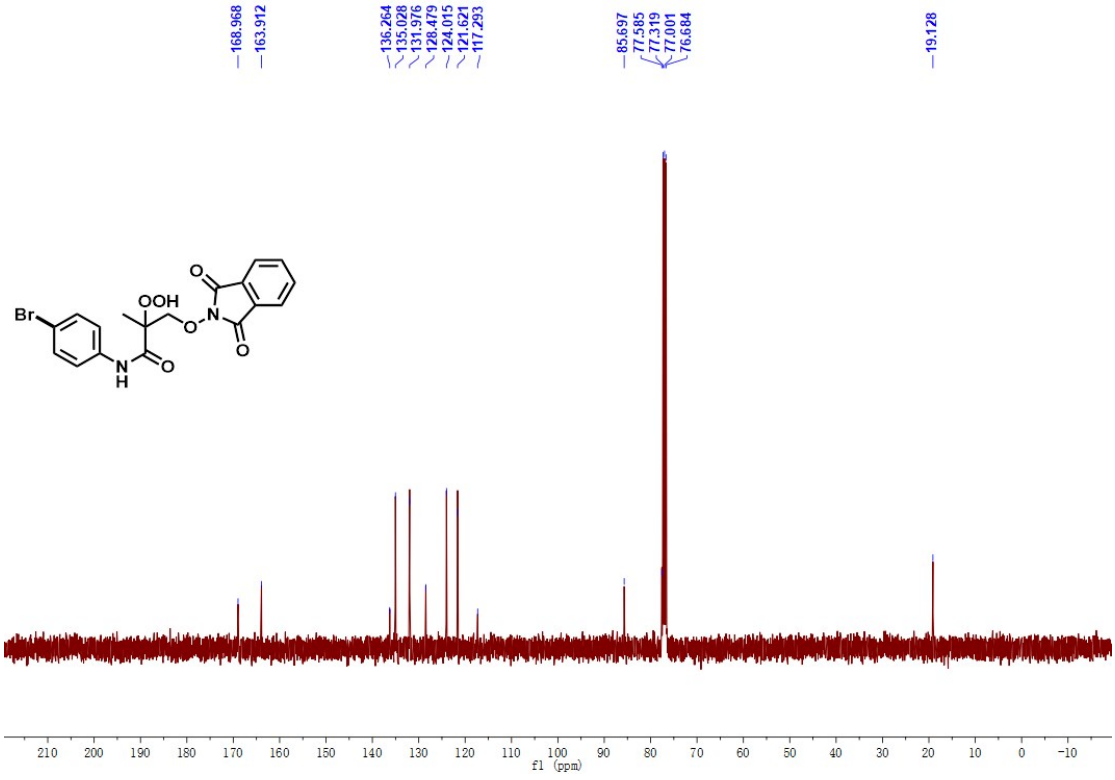
NMR Spectra of hydroperoxide **3da'**[4a,7]



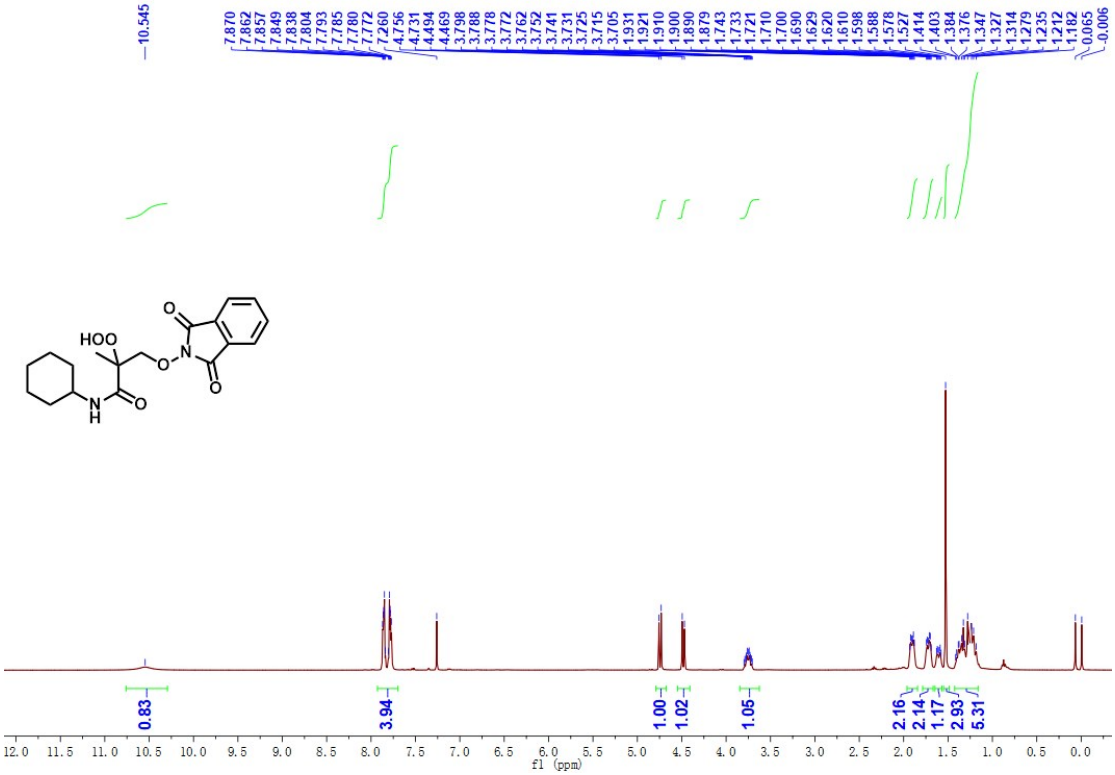


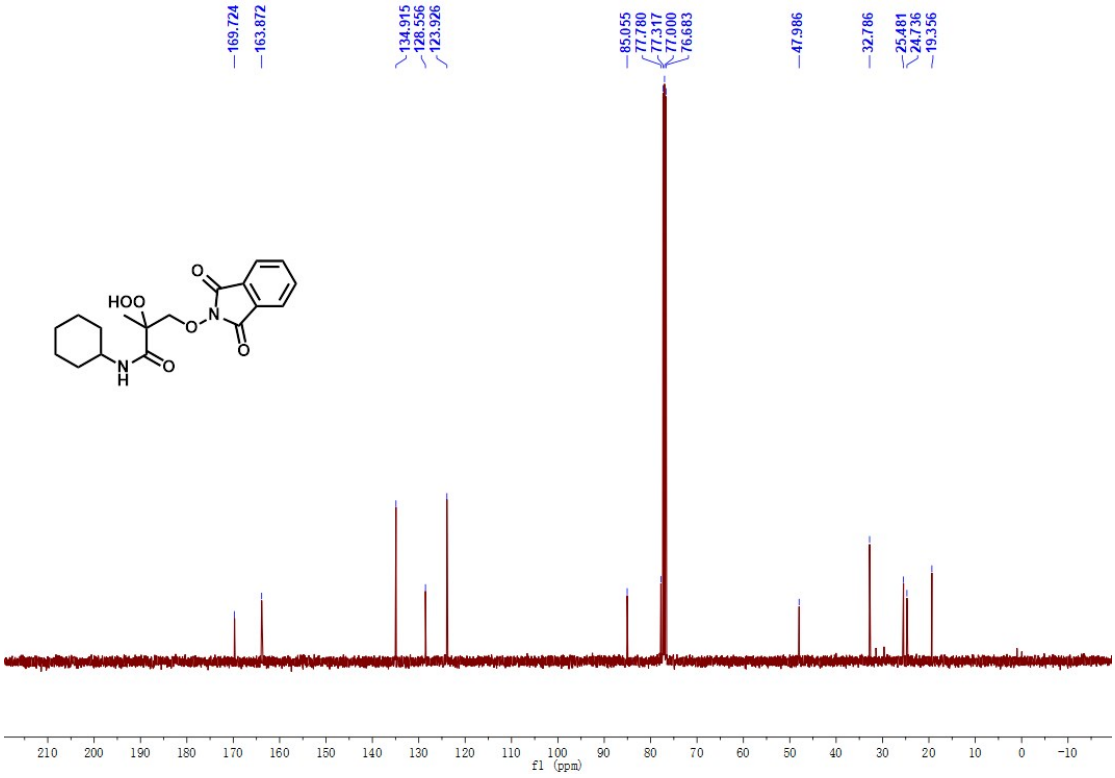
NMR Spectra of hydroperoxide **3ga'**[4a,7]



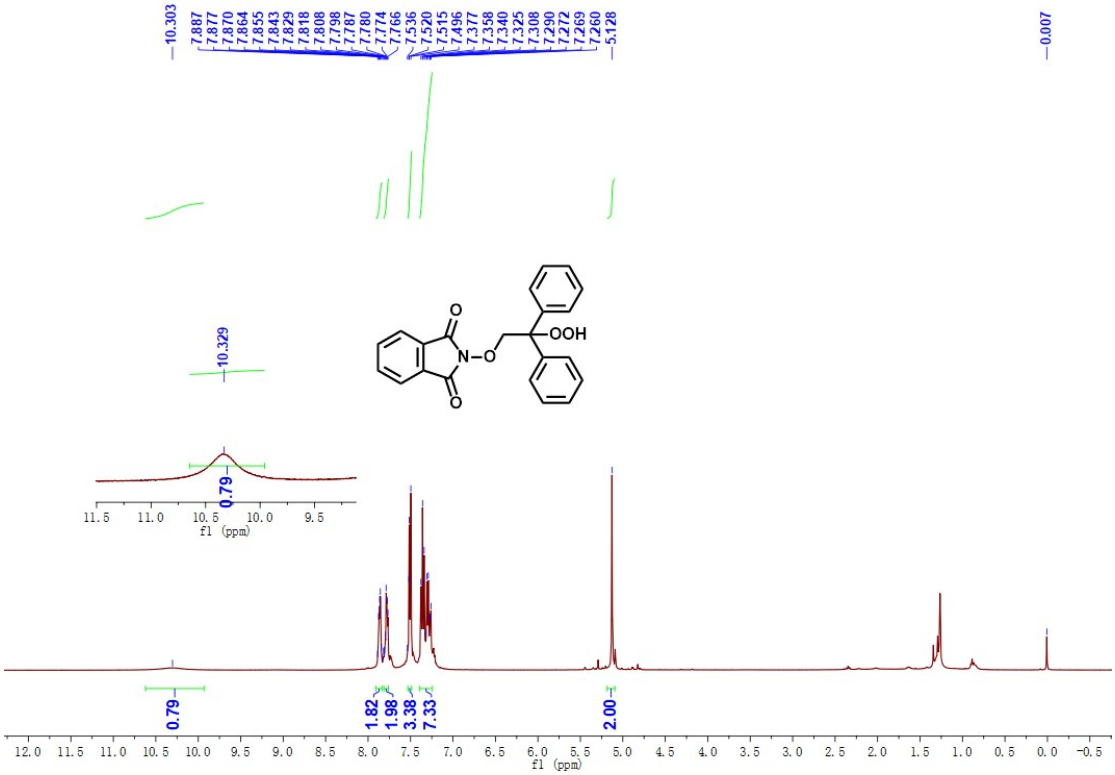


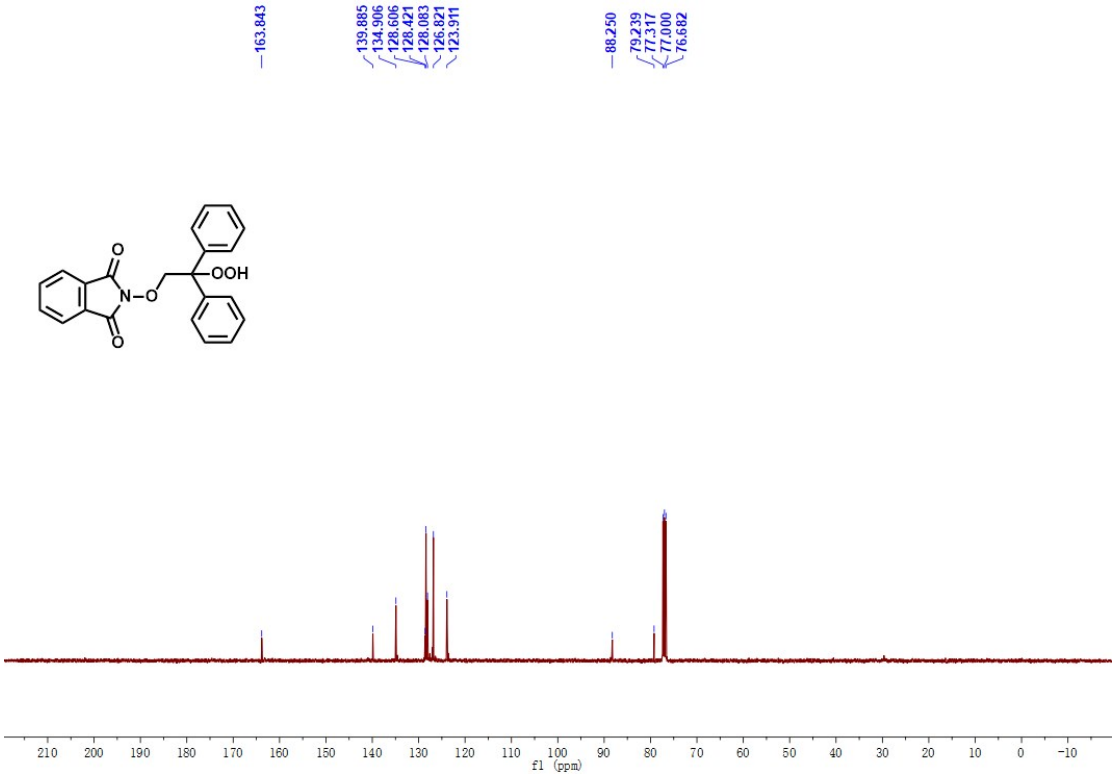
NMR Spectra of hydroperoxide **3pa'**[4a,7]



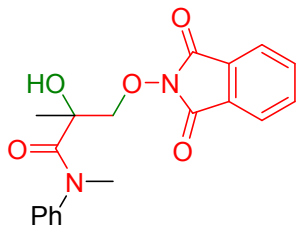


NMR Spectra of hydroperoxide **5i'**[4a,7]

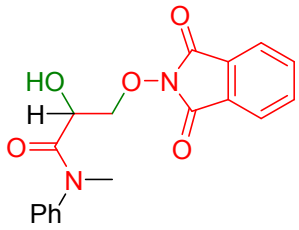




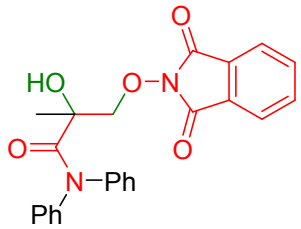
9. Characterization data of products



3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-*N*,2-dimethyl-*N*-phenylpropanamide (3aa): By following the typical procedure, the product was obtained as a white solid (65.2 mg, 92% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.80 (d, J = 3.8 Hz, 2H), 7.72 (d, J = 3.8 Hz, 2H), 7.40-7.32 (m, 5H), 4.52 (d, J = 79.6 Hz, CH-H + O-H), 3.86 (d, J = 10.8 Hz, 1H), 3.27 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 172.5, 163.3, 144.0, 134.4, 129.3, 128.6, 127.9, 127.7, 123.5, 83.5, 75.5, 40.8, 23.6; HRMS *m/z* (ESI) Calcd for $C_{19}H_{19}N_2O_5^+$ $(M + H)^+$ 355.1294, found 355.1282.

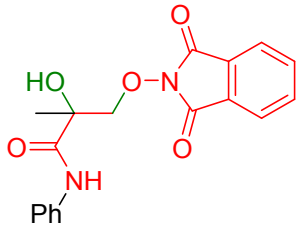


3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-*N*-methyl-*N*-phenylpropanamide (3ba): By following the typical procedure, the product was obtained as a white solid (59.2 mg, 87% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.81-7.75 (m, 4H), 7.34-7.28 (m, 4H), 7.12 (t, J = 7.3 Hz, 1H), 4.53 (d, J = 6.4 Hz, 1H), 4.15 (d, J = 10.8 Hz, 1H), 4.03 (dd, J = 11.2, 6.3 Hz, 1H), 3.98 (s, 1H), 3.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 170.0, 163.1, 141.8, 134.5, 129.9, 128.7, 128.3, 127.3, 123.5, 79.6, 67.5, 38.2; HRMS *m/z* (ESI) Calcd for $C_{18}H_{17}N_2O_5^+$ $(M + H)^+$ 341.1137, found 341.1132.



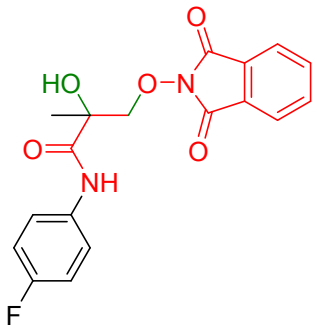
3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methyl-*N*,*N*-diphenylpropanamid

(3ca): By following the typical procedure, the product was obtained as a white solid (77.5 mg, 93% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.88-7.83 (m, 2H), 7.78-7.73 (m, 2H), 7.45-7.35 (m, 8H), 7.28-7.25 (m, 2H), 4.66 (d, J = 10.8 Hz, 1H), 4.45 (s, 1H), 3.98 (d, J = 10.8 Hz, 1H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 173.6, 163.5, 143.4, 134.6, 129.3, 128.8, 128.1, 127.5, 123.7, 83.9, 76.3, 24.2; HRMS *m/z* (ESI) Calcd for $C_{24}H_{21}N_2O_5^+$ $(M + H)^+$ 417.1450, found 417.1448.

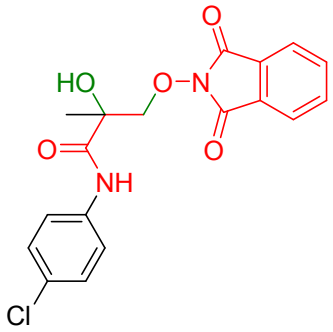


3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methyl-*N*-phenylpropanamide

(3da): By following the typical procedure, the product was obtained as a white solid (65.3 mg, 96% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.75 (s, 1H), 7.73-7.66 (m, 4H), 7.43 (d, J = 8.0 Hz, 2H), 7.22 (t, J = 7.6 Hz, 2H), 7.04 (t, J = 7.4 Hz, 1H), 4.97 (d, J = 11.6 Hz, 1H), 4.94 (s, 1H), 4.12 (d, J = 11.6 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 171.5, 163.8, 137.1, 134.7, 128.8, 128.3, 124.3, 123.8, 119.4, 82.6, 74.8, 23.2; HRMS *m/z* (ESI) Calcd for $C_{18}H_{17}N_2O_5^+$ $(M + H)^+$ 341.1137, found 341.1138.

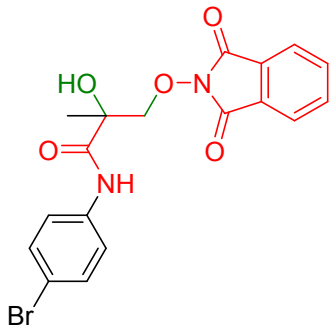


3-((1,3-dioxoisoindolin-2-yl)oxy)-*N*-(4-fluorophenyl)-2-hydroxy-2-methylpropanamide (3ea): By following the typical procedure, the product was obtained as a white solid (63.1 mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.75 (s, 1H), 7.74-7.68 (m, 4H), 7.40 (dd, J = 8.1, 5.0 Hz, 2H), 6.91 (t, J = 8.4 Hz, 2H), 4.97 (d, J = 11.6 Hz, 1H), 4.11 (d, J = 11.6 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 171.5, 163.8, 159.3 (d, J = 242.2 Hz), 134.8, 133.2 (d, J = 2.8 Hz), 128.3, 123. 8, 121.1 (d, J = 7.8 Hz), 115.4 (d, J = 22.3 Hz), 82.6, 74.7, 23.2; HRMS *m/z* (ESI) Calcd for $C_{18}H_{16}FN_2O_5^+$ $(M + H)^+$ 359.1043, found 359.1047.

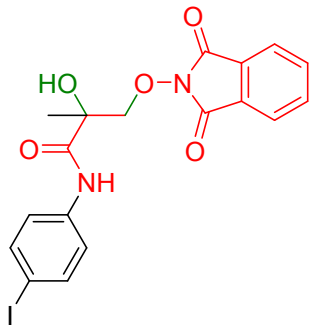


***N*-(4-chlorophenyl)-3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methylpropanamide (3fa):** By following the typical procedure, the product was obtained as a white solid (68.2 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.79 (s, 1H), 7.69 (t, J = 5.8 Hz, 4H), 7.39 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 4.96 (d, J = 11.5 Hz, 1H), 4.10 (d, J = 11.5 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 171.6, 163.8, 135.7, 134.8, 129.3, 128.8, 128.3, 123.8, 120.6,

82.5, 74.8, 23.1; HRMS *m/z* (ESI) Calcd for $C_{18}H_{16}ClN_2O_5^+$ $(M + H)^+$ 375.0747, found 375.0741.

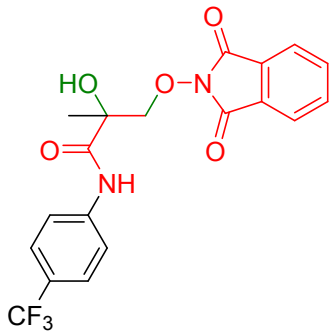


***N*-(4-bromophenyl)-3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methylpropanamide (3ga):** By following the typical procedure, the product was obtained as a white solid (80.5 mg, 96% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.76 (s, 1H), 7.74-7.69 (m, 4H), 7.36-7.31 (m, 4H), 4.98 (d, J = 11.6 Hz, 1H), 4.93 (s, 1H), 4.11 (d, J = 11.6 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 171.7, 163.8, 136.3, 134.9, 131.8, 128.3, 123.8, 120.9, 117.0, 82.5, 74.8, 23.2; HRMS *m/z* (ESI) Calcd for $C_{18}H_{16}BrN_2O_5^+$ $(M + H)^+$ 419.0242, found 419.0237.

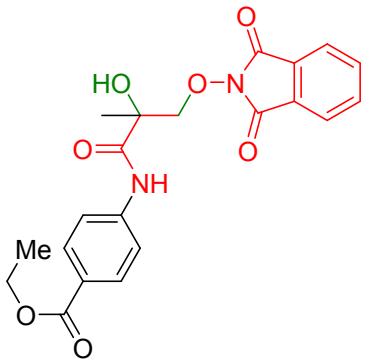


3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-*N*-(4-iodophenyl)-2-methylpropanamide (3ha): By following the typical procedure, the product was obtained as a white solid (86.7 mg, 93% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.77 (s, 1H), 7.72-7.68 (m, 4H), 7.50 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.2 Hz, 2H), 4.95 (d, J = 11.2 Hz, 2H), 4.10 (d, J = 11.6 Hz, 1H), 1.48 (s, 3H); ^{13}C NMR (100

MHz, $CDCl_3$, ppm) δ: 171.7, 163.7, 137.7, 136.9, 134.8, 128.3, 123.8, 121.2, 87.6, 82.5, 74.8, 23.1; HRMS *m/z* (ESI) Calcd for $C_{18}H_{16}IN_2O_5^+$ $(M + H)^+$ 467.0104, found 467.0108.

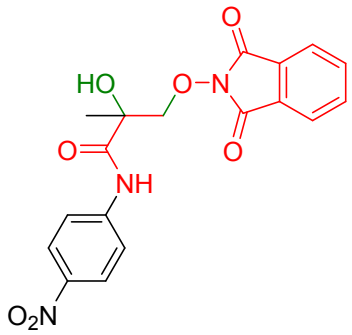


3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methyl-*N*-(4-(trifluoromethyl)phenyl)propenamide (3ia): By following the typical procedure, the product was obtained as a white solid (62.9 mg, 77% yield); ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.95 (s, 1H), 7.71-7.65 (m, 4H), 7.57 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 5.01 (d, J = 11.6 Hz, 1H), 4.99 (s, 1H), 4.11 (d, J = 11.6 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 172.1, 163.8, 140.1, 134.9, 128.2, 126.1 (q, J = 32.5 Hz), 126.1 (q, J = 3.8 Hz), 124.0 (q, J = 270.0 Hz), 123.8, 119.0, 82.4, 74.9, 23.1; HRMS *m/z* (ESI) Calcd for $C_{19}H_{16}F_3N_2O_5^+$ $(M + H)^+$ 409.1011, found 409.1015.

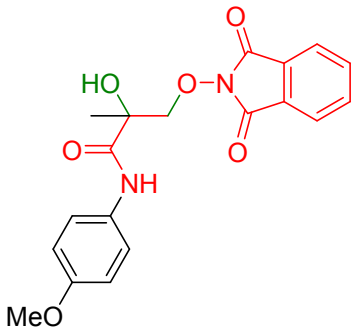


Ethyl-4-(3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methylpropanamido)benzoate (3ja): By following the typical procedure, the

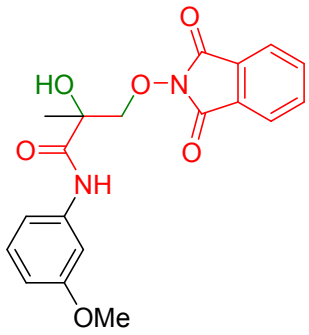
product was obtained as a white solid (61 mg, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.92 (s, 1H), 7.92 (d, J = 8.4 Hz, 2H), 7.74-7.67 (m, 4H), 7.52 (d, J = 8.4 Hz, 2H), 4.99 (d, J = 11.6 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 4.12 (d, J = 11.6 Hz, 1H), 1.51 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 171.9, 164.2, 163.8, 141.1, 134.9, 130.6, 128.3, 126.1, 123.8, 118.6, 82.6, 74.9, 60.9, 23.2, 14.3; HRMS *m/z* (ESI) Calcd for $C_{21}H_{21}N_2O_7^+$ $(M + H)^+$ 413.1349, found 413.1346.



3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methyl-*N*-(4-nitrophenyl)propanamide (3ka): By following the typical procedure, the product was obtained as a yellow solid (53.2 mg, 69% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 9.15 (s, 1H), 8.15-8.12 (m, 2H), 7.76-7.65 (m, 6H), 5.04 (s, 1H), 4.98 (d, J = 11.6 Hz, 1H), 4.12 (d, J = 11.6 Hz, 1H), 1.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 172.3, 163.8, 143.6, 142.9, 135.0, 128.2, 124.9, 123.9, 119.0, 82.7, 75.0, 23.1; HRMS *m/z* (ESI) Calcd for $C_{18}H_{16}N_3O_7^+$ $(M + H)^+$ 386.0988, found 386.0991.

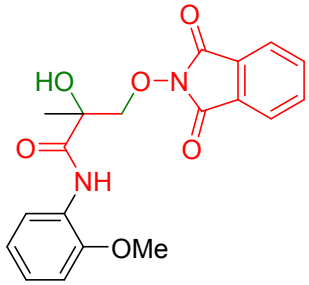


3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-*N*-(4-methoxyphenyl)-2-methylpropanamide (3la): By following the typical procedure, the product was obtained as a white solid (59.3 mg, 80% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.68 (s, 1H), 7.74-7.67 (m, 4H), 7.30 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 4.97 (d, J = 11.6 Hz, 1H), 4.12 (d, J = 11.6 Hz, 1H), 2.27 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 171.3, 163.8, 134.7, 134.6, 133.9, 129.3, 128.4, 123.8, 119.4, 82.7, 74.7, 23.2, 20.8; HRMS *m/z* (ESI) Calcd for $C_{19}H_{19}N_2O_6^+$ $(M + H)^+$ 371.1243, found 371.1239.

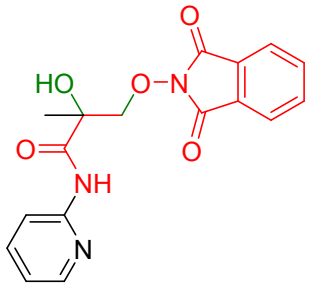


3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-*N*-(3-methoxyphenyl)-2-methylpropanamide (3ma)： By following the typical procedure, the product was obtained as a colorless oil (49.6 mg, 67% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.73 (s, 1H), 7.74-7.67 (m, 4H), 7.20 (t, J = 2.2 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 6.90 (ddd, J = 8.0, 2.0, 0.9 Hz, 1H), 6.60 (ddd, J = 8.3, 2.6, 1.0 Hz, 1H), 5.00 (d, J = 11.2

Hz, 1H), 4.11 (d, J = 11.6 Hz, 1H), 3.72 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 171.6, 163.8, 160.0, 138.3, 134.8, 129.5, 128.3, 123.8, 111.5, 110.6, 104.5, 82.6, 74.8, 55.2, 23.2; HRMS *m/z* (ESI) Calcd for $C_{19}H_{19}N_2O_6^+$ $(M + H)^+$ 371.1243, found 371.1237.

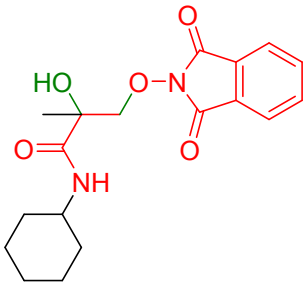


3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-*N*-(2-methoxyphenyl)-2-methylpropanamide (3na): By following the typical procedure, the product was obtained as a colorless oil (43 mg, 58% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 9.33 (s, 1H), 8.07 (dd, J = 8.1, 1.6 Hz, 1H), 7.74-7.67 (m, 4H), 6.98 (td, J = 7.9, 1.6 Hz, 1H), 6.85 (dd, J = 8.2, 1.2 Hz, 1H), 6.77 (td, J = 7.8, 1.2 Hz, 1H), 5.01 (d, J = 11.2 Hz, 1H), 4.93 (s, 1H), 4.13 (d, J = 11.6 Hz, 1H), 3.92 (s, 3H), 1.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 171.3, 163.8, 148.3, 134.7, 128.3, 126.9, 123.9, 123.7, 120.7, 119.0, 109.9, 83.0, 75.1, 55.8, 23.2; HRMS *m/z* (ESI) Calcd for $C_{19}H_{19}N_2O_6^+$ $(M + H)^+$ 371.1243, found 371.1240.

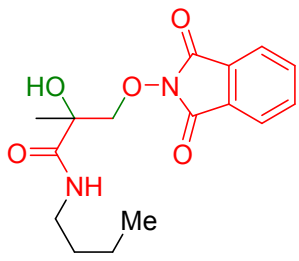


3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methyl-*N*-(pyridin-2-yl)propanamide (3oa): By following the typical procedure, the product was obtained

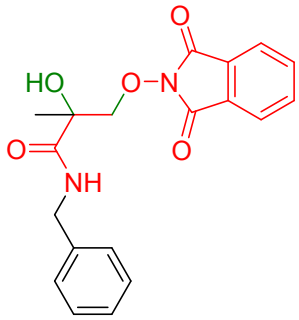
as a white solid (49.8 mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 9.35 (s, 1H), 8.30 (ddd, J = 4.9, 2.0, 0.9 Hz, 1H), 7.99 (dt, J = 8.4, 1.0 Hz, 1H), 7.79-7.68 (m, 4H), 7.57 (ddd, J = 8.3, 7.3, 1.9 Hz, 1H), 7.01 (ddd, J = 7.4, 4.9, 1.0 Hz, 1H), 4.99 (d, J = 11.4 Hz, 1H), 4.13 (d, J = 11.4 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 172.3, 163.7, 150.6, 147.9, 138.1, 134.8, 128.4, 123.8, 120.0, 113.5, 83.1, 74.9, 23.0; HRMS *m/z* (ESI) Calcd for $C_{17}H_{16}N_3O_5^+$(M + H)$^+$ 342.1090, found 342.1088.



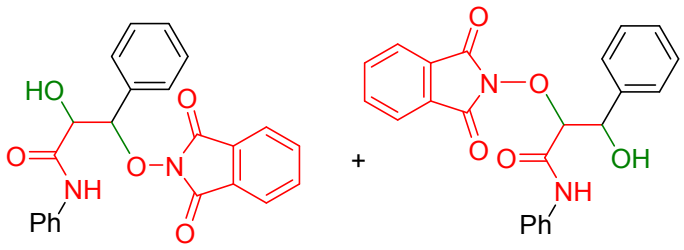
***N*-Cyclohexyl-3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methylpropanamide(3pa):** By following the typical procedure, the product was obtained as a colorless oil (45.7 mg, 66% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.84-7.80 (m, 2H), 7.78-7.73 (m, 2H), 6.81 (d, J = 8.4 Hz, 1H), 4.84 (d, J = 11.6 Hz, 1H), 4.66 (s, 1H), 4.05 (d, J = 11.2 Hz, 1H), 3.57-3.47 (m, 1H), 1.70-1.54 (m, 4H), 1.39 (s, 3H), 1.34-1.04 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 172.4, 163.8, 134.8, 128.6, 123.8, 82.6, 74.0, 48.1, 32.9, 25.4, 24.7, 23.5; HRMS *m/z* (ESI) Calcd for $C_{18}H_{23}N_2O_5^+$ (M + H)$^+$ 347.1607, found 347.1603.



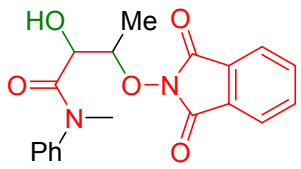
***N*-Butyl-3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methylpropanamide (3qa):** By following the typical procedure, the product was obtained as a colorless oil (54.5 mg, 85% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.85-7.80 (m, 2H), 7.78-7.74 (m, 2H), 6.96 (s, 1H), 4.83 (d, J = 11.2 Hz, 1H), 4.05 (d, J = 11.6 Hz, 1H), 3.18-3.04 (m, 2H), 2.13 (s, 1H), 1.45-1.37 (m, 2H), 1.41 (s, 3H), 1.34-1.24 (m, 3H), 0.87 (t, J = 7.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 173.3, 163.8, 134.8, 128.5, 123.8, 82.9, 74.3, 39.0, 31.5, 23.3, 19.9, 13.7; HRMS *m/z* (ESI) Calcd for $C_{16}H_{21}N_2O_5^+$(M + H)$^+$ 321.1450, found 321.1448.



***N*-Benzyl-3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methylpropanamide (3ra):** By following the typical procedure, the product was obtained as a white solid (25.5 mg, 36% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.78-7.74 (m, 2H), 7.72-7.68 (m, 2H), 7.27-7.17 (m, 5H), 4.80 (d, J = 11.2 Hz, 1H), 4.64 (s, 1H), 4.33 (dd, J = 14.8, 6.0 Hz, 1H), 4.21 (dd, J = 14.8, 5.6 Hz, 1H), 4.05 (d, J = 11.2 Hz, 1H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 173.3, 163.8, 137.8, 134.9, 128.7, 128.5, 127.6, 127.5, 123.9, 83.3, 74.5, 43.3, 23.3; HRMS *m/z* (ESI) Calcd for $C_{19}H_{19}N_2O_5^+$ (M + H)$^+$ 355.1294, found 355.1296.

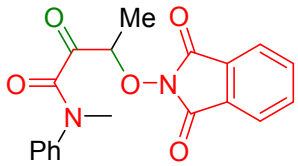


3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-*N*,3-diphenylpropanamide and 2-((1,3-Dioxoisoindolin-2-yl)oxy)-3-hydroxy-*N*,3-diphenylpropanamide (3sa + 3sa'): By following the typical procedure, the product was obtained as a white solid (65.2 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 9.49 (s, 1.34H), 7.91 (td, J = 5.2, 4.7, 1.9 Hz, 1.92H), 7.87-7.77 (m, 3.71H), 7.67-7.61 (m, 2.81H), 7.52 (dd, J = 15.5, 7.3 Hz, 2.89H), 7.38-7.30 (m, 5.85H), 7.30-7.26 (m, 1.1H), 7.18-7.12 (m, 1.43H), 5.62 (dd, J = 9.3, 2.8 Hz, 1H), 5.55 (dd, J = 7.6, 4.6 Hz, 0.48H), 5.30 (s, 0.89H), 5.00-4.98 (m, 1.89H), 4.95 (s, 0.45), 4.27 (d, J = 8.0 Hz, 0.47H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 166.4, 164.7, 164.7, 163.8, 138.7, 137.7, 137.0, 136.8, 135.6, 135.2, 129.0, 129.0, 128.4, 128.3, 128.2, 128.1, 126.9, 126.8, 125.0, 124.9, 124.5, 124.2, 120.3, 120.2, 93.8, 89.1, 73.6, 73.6; HRMS *m/z* (ESI) Calcd for $C_{23}H_{19}N_2O_5^+$ $(M + H)^+$ 403.1294, found 403.1291.

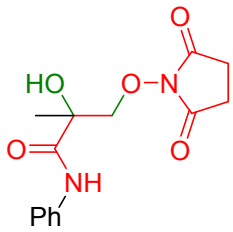


3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroxy-*N*-methyl-*N*-phenylbutanamide (3ta): By following the typical procedure, the product was obtained as a white solid (42.5 mg, 60% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.78-7.72 (m, 4H), 7.11-7.09 (m, 2H), 7.05-7.01 (m, 2H), 6.61 (tt, J = 7.4, 1.3 Hz, 1H), 4.61 (dd, J = 7.5, 1.8 Hz,

1H), 4.11 (qd, J = 6.5, 1.7 Hz, 1H), 3.54 (d, J = 7.6 Hz, 1H), 3.26 (s, 3H), 1.33 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 170.6, 163.3, 141.5, 134.4, 129.7, 128.8, 127.9, 127.3, 123.4, 84.0, 68.7, 38.1, 11.6; HRMS *m/z* (ESI) Calcd for $C_{19}H_{19}N_2O_5^+$(M + H)$^+$ 355.1294, found 355.1292.

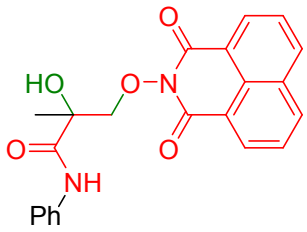


3-((1,3-dioxoisoindolin-2-yl)oxy)-*N*-methyl-2-oxo-*N*-phenylbutanamide (3ta'): The product was obtained as a white solid (18.7 mg, 53% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.86-7.82 (m, 2H), 7.79-7.75 (m, 2H), 7.43-7.34 (m, 4H), 7.28-7.24 (m, 1H), 5.22 (q, J = 6.8 Hz, 1H), 3.40 (s, 3H), 1.44 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 196.3, 165.8, 163.2, 141.1, 134.6, 129.6, 128.8, 128.3, 127.0, 123.7, 85.0, 36.6, 15.5; HRMS *m/z* (ESI) Calcd for $C_{19}H_{17}N_2O_5^+$ (M + H)$^+$ 353.1137, found 353.1133.

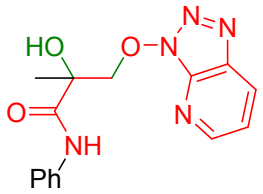


3-((2,5-Dioxopyrrolidin-1-yl)oxy)-2-hydroxy-2-methyl-*N*-phenylpropanamide (3db): By following the typical procedure, the product was obtained as a white solid (53.2 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.69 (s, 1H), 7.57 (d, J = 8.0 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.13 (t, J = 7.4 Hz, 1H), 4.98 (d, J = 12.0 Hz, 1H), 3.93 (d, J = 12.0 Hz, 1H), 2.64-2.56 (m, 2H), 2.52-2.43 (m, 2H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 172.0, 171.6, 137.2, 129.1, 124.7, 119.4, 80.6,

74.5, 25.1, 23.3; HRMS *m/z* (ESI) Calcd for $C_{14}H_{17}N_2O_5^+$ $(M + H)^+$ 293.1137, found 293.1131.

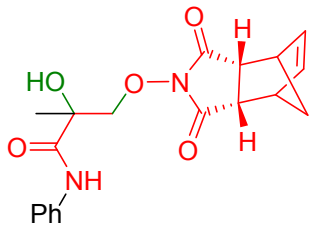


3-((1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)oxy)-2-hydroxy-2-methyl-*N*-phenylpropanamide (3dc): By following the typical procedure, the product was obtained as a white solid (70.3 mg, 90% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.94 (s, 1H), 8.55 (d, J = 7.6 Hz, 2H), 8.21 (d, J = 8.0 Hz, 2H), 7.71 (t, J = 7.7 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.17 (t, J = 7.6 Hz, 2H), 7.00 (t, J = 7.4 Hz, 1H), 6.04 (s, 1H), 5.12 (d, J = 11.2 Hz, 1H), 4.15 (d, J = 11.2 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 172.0, 161.6, 137.4, 135.1, 132.2, 131.6, 128.7, 127.2, 127.1, 124.1, 121.9, 119.3, 82.7, 75.0, 23.2; HRMS *m/z* (ESI) Calcd for $C_{22}H_{19}N_2O_5^+$ $(M + H)^+$ 391.1294, found 391.1290.

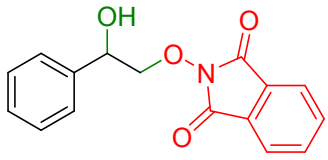


3-((3H-[1,2,3]triazolo[4,5-b]pyridin-3-yl)oxy)-2-hydroxy-2-methyl-*N*-phenylpropanamide (3dd): By following the typical procedure, the product was obtained as a white solid (25 mg, 40% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.88 (s, 1H), 8.68 (d, J = 4.0 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.40 (m, 1H), 7.29 (m, 2H), 7.10 (t, J = 8.0 Hz, 1H), 5.21 (d, J = 12.0 Hz, 1H), 4.64 (d, J = 8.0 Hz, 1H), 1.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 170.7,

150.7, 139.4, 137.1, 135.2, 130.1, 128.9, 124.6, 120.9, 119.6, 86.0, 75.4, 23.3; HRMS *m/z* (ESI) Calcd for $C_{15}H_{16}N_5O_3^+$ $(M + H)^+$ 314.1253, found 314.1251.

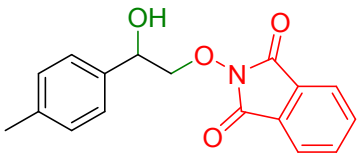


3-(((3a*R*,7a*S*)-1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2*H*-4,7-methanoisoindol-2-yl)oxy)-2-hydroxy-2-methyl-*N*-phenylpropanamide (3de): By following the typical procedure, the product was obtained as a white solid (59.2 mg, 83% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.77 (s, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.12 (t, J = 7.4 Hz, 1H), 6.13 (t, J = 6.8 Hz, 2H), 5.07 (s, 1H), 4.71 (d, J = 11.2 Hz, 1H), 3.87 (d, J = 11.2 Hz, 1H), 3.38 (d, J = 13.6 Hz, 2H), 3.17 (dd, J = 7.0, 4.6 Hz, 1H), 3.01 (dd, J = 7.0, 4.6 Hz, 1H), 1.73 (d, J = 8.8 Hz, 1H), 1.44 (d, J = 6.3 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 173.0, 172.1, 171.5, 137.3, 134.7, 134.4, 129.0, 124.5, 119.4, 82.5, 74.5, 51.4, 44.6, 44.6, 42.5, 42.3, 23.1; HRMS *m/z* (ESI) Calcd for $C_{19}H_{21}N_2O_5^+$ $(M + H)^+$ 357.1450, found 357.1445.

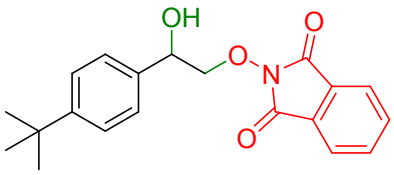


2-(2-Hydroxy-2-phenylethoxy)isoindoline-1,3-dione (5a): By following the typical procedure, the product was obtained as a white solid (60.3 mg, 71% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.84 – 7.79 (m, 2H), 7.75 – 7.70 (m, 2H), 7.33 – 7.19 (m, 5H), 4.94 (dd, J = 9.9, 2.5 Hz, 1H), 4.31 (dd, J = 11.7, 2.5 Hz, 1H), 4.17 (s, 1H), 4.05 (dd, J = 11.7, 9.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.3, 138.1, 134.9,

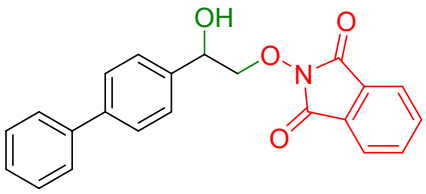
128.7, 128.5, 128.1, 126.2, 123.9, 83.7, 70.8; HRMS *m/z* (ESI) Calcd for $C_{16}H_{14}NO_4^+$ $(M + H)^+$ 284.0923, found 284.0925.



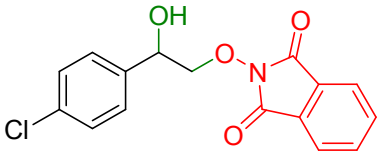
2-(2-Hydroxy-2-(p-tolyl)ethoxy)isoindoline-1,3-dione (5b): By following the typical procedure, the product was obtained as a white solid (67.8 mg, 76% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.90 – 7.86 (m, 2H), 7.81 – 7.77 (m, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 4.97 (dd, J = 9.9, 2.5 Hz, 1H), 4.35 (dd, J = 11.7, 2.5 Hz, 1H), 4.11 (dd, J = 11.7, 9.9 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.3, 137.8, 135.0, 134.8, 129.2, 128.7, 126.1, 123.9, 83.6, 70.6, 21.1; HRMS *m/z* (ESI) Calcd for $C_{17}H_{16}NO_4^+$ $(M + H)^+$ 298.1079, found 298.1083.



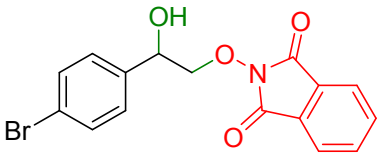
2-(2-(4-(*Tert*-butyl)phenyl)-2-hydroxyethoxy)isoindoline-1,3-dione (5c): By following the typical procedure, the product was obtained as a white solid (84.5 mg, 83% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.90 – 7.86 (m, 2H), 7.82 – 7.77 (m, 2H), 7.38 – 7.35 (m, 2H), 7.31 – 7.29 (m, 2H), 4.98 (dd, J = 9.8, 2.5 Hz, 1H), 4.37 (dd, J = 11.7, 2.5 Hz, 1H), 4.15 (dd, J = 11.7, 9.8 Hz, 2H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.3, 151.1, 135.0, 134.8, 128.8, 125.9, 125.5, 123.9, 83.6, 70.5, 34.5, 31.3; HRMS *m/z* (ESI) Calcd for $C_{20}H_{22}NO_4^+$ $(M + H)^+$ 340.1549, found 340.1551.



2-(2-([1,1'-Biphenyl]-4-yl)-2-hydroxyethoxy)isoindoline-1,3-dione (5d): By following the typical procedure, the product was obtained as a white solid (86.3 mg, 80% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.92 – 7.87 (m, 2H), 7.83 – 7.78 (m, 2H), 7.59 – 7.55 (m, 4H), 7.47 – 7.41 (m, 4H), 7.36 – 7.32 (m, 1H), 5.06 (d, J = 9.7 Hz, 1H), 4.43 (dd, J = 11.7, 2.5 Hz, 1H), 4.28 (s, 1H), 4.17 (dd, J = 11.7, 9.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.4, 141.1, 140.6, 137.0, 134.9, 128.7, 127.4, 127.3, 127.1, 126.6, 123.9, 83.6, 70.5; HRMS *m/z* (ESI) Calcd for $C_{22}H_{18}NO_4^+$ $(M + H)^+$ 360.1236, found 360.1239.

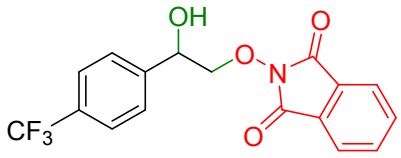


2-(2-(4-Chlorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione (5e): By following the typical procedure, the product was obtained as a white solid (65.8 mg, 69% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.90 – 7.86 (m, 2H), 7.82 – 7.77 (m, 2H), 7.34 – 7.29 (m, 4H), 4.98 (dd, J = 9.8, 2.5 Hz, 1H), 4.34 (dd, J = 11.7, 2.5 Hz, 2H), 4.06 (dd, J = 11.7, 9.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.3, 136.6, 134.9, 133.9, 128.7, 128.7, 127.5, 124.0, 83.4, 70.1; HRMS *m/z* (ESI) Calcd for $C_{16}H_{13}ClNO_4^+$ $(M + H)^+$ 318.0533, found 318.0537.

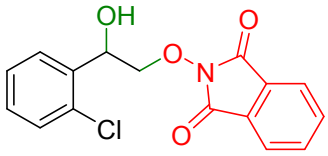


2-(2-(4-Bromophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione (5f): By following

the typical procedure, the product was obtained as a white solid (79.3 mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.90 – 7.85 (m, 2H), 7.81 – 7.77 (m, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 4.97 (dd, J = 9.9, 2.5 Hz, 1H), 4.35 (dd, J = 11.6, 2.5 Hz, 1H), 4.18 (s, 1H), 4.11 (dd, J = 11.7, 9.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.3, 137.8, 135.0, 134.8, 129.2, 128.7, 126.1, 123.9, 83.6, 70.5; HRMS *m/z* (ESI) Calcd for $C_{16}H_{13}BrNO_4^+$ $(M + H)^+$ 362.0028, found 362.0031.

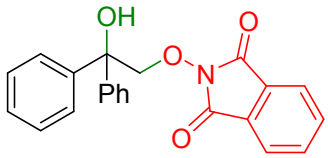


2-(2-Hydroxy-2-(4-(trifluoromethyl)phenyl)ethoxy)isoindoline-1,3-dione (5g): By following the typical procedure, the product was obtained as a white solid (58 mg, 55% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.91 – 7.87 (m, 2H), 7.83 – 7.78 (m, 2H), 7.61 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 5.06 (dd, J = 9.7, 2.5 Hz, 1H), 4.40 (dd, J = 11.7, 2.6 Hz, 2H), 4.10 (dd, J = 11.7, 9.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.3, 142.1, 135.0, 130.3 (q, J = 32.4 Hz), 128.7, 126.5, 125.5 (q, J = 3.7 Hz), 124.0 (q, J = 270.4 Hz), 124.0, 83.3, 70.2; HRMS *m/z* (ESI) Calcd for $C_{17}H_{13}F_3NO_4^+$ $(M + H)^+$ 352.0796, found 352.0799.

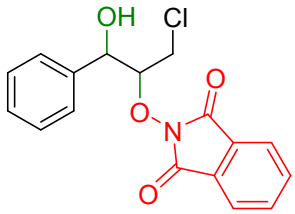


2-(2-(2-Chlorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione (5h): By following the typical procedure, the product was obtained as a white solid (60.1 mg, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.92 – 7.87 (m, 2H), 7.82 – 7.78 (m, 2H), 7.70 (dd, J = 7.7, 1.6 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.25 – 7.21 (m, 1H), 5.37 (dd, J = 9.7,

2.2 Hz, 1H), 4.51 (dd, J = 11.8, 2.2 Hz, 1H), 4.41 (s, 1H), 3.96 (dd, J = 11.8, 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.4, 135.6, 134.9, 131.6, 129.2, 129.1, 128.7, 127.8, 127.3, 124.0, 81. 9, 67.7; HRMS *m/z* (ESI) Calcd for $C_{16}H_{13}ClNO_4^+$ $(M + H)^+$ 318.0533, found 318.0535.

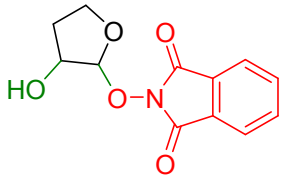


2-(2-Hydroxy-2,2-diphenylethoxy)isoindoline-1,3-dione (5i): By following the typical procedure, the product was obtained as a white solid (69 mg, 64% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.80 – 7.76 (m, 2H), 7.74 – 7.69 (m, 2H), 7.54 – 7.51 (m, 4H), 7.32 – 7.28 (m, 4H), 7.22 – 7.18 (m, 2H), 4.83 (s, 2H), 4.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 163.6, 142.9, 134.6, 128.4, 128.2, 127.4, 126.4, 123.6, 84.4, 77.3; HRMS *m/z* (ESI) Calcd for $C_{22}H_{18}NO_4^+$ $(M + H)^+$ 360.1236, found 360.1238.

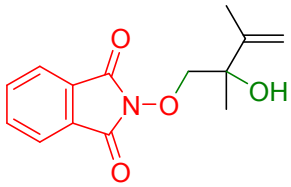


2-((3-Chloro-1-hydroxy-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (5j): By following the typical procedure, the product was obtained as a white solid (52.7 mg, 53% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.89 – 7.84 (m, 2H), 7.81 – 7.77 (m, 2H), 7.49 – 7.46 (m, 2H), 7.36 – 7.27 (m, 3H), 5.20 (dd, J = 7.8, 2.9 Hz, 1H), 4.42 – 4.37 (m, 2H), 4.13 (dd, J = 12.4, 3.6 Hz, 1H), 3.41 (dd, J = 12.4, 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 164.2, 138.2, 135.0, 128.7, 128.6, 128.5, 126.9,

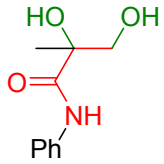
124.0, 92.5, 72.7, 43.3; HRMS *m/z* (ESI) Calcd for $C_{17}H_{15}ClNO_4^+$ $(M + H)^+$ 332.0689, found 332.0693.



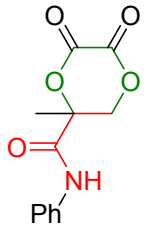
2-((3-Hydroxytetrahydrofuran-2-yl)oxy)isoindoline-1,3-dione (5k): By following the typical procedure, the product was obtained as a white solid (50 mg, 67% yield); ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 7.81 – 7.78 (m, 2H), 7.73 – 7.69 (m, 2H), 5.76 (d, J = 4.8 Hz, 1H), 4.35 – 4.30 (m, 1H), 4.01 – 3.97 (m, 1H), 2.30 – 2.18 (m, 2H), 2.12 – 2.05 (m, 1H), 1.97 – 1.89 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 163.8, 134.2, 129.0, 123.3, 108.7, 69.0, 30.7, 22.5; HRMS *m/z* (ESI) Calcd for $C_{12}H_{12}NO_5^+$ $(M + H)^+$ 250.0715, found 250.0719.



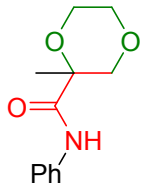
2-((2-Hydroxy-2,3-dimethylbut-3-en-1-yl)oxy)isoindoline-1,3-dione (5l): By following the typical procedure, the product was obtained as a white solid (47.8 mg, 61% yield); ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 7.85 – 7.82 (m, 2H), 7.78 – 7.74 (m, 2H), 5.20 (d, J = 1.0 Hz, 1H), 4.93 (t, J = 1.5 Hz, 1H), 4.49 (d, J = 10.5 Hz, 1H), 4.04 (d, J = 10.5 Hz, 1H), 3.75 (s, 1H), 1.84 (d, J = 0.7 Hz, 3H), 1.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 163.8, 147.1, 134.7, 128.6, 123.7, 111.6, 84.9, 74.2, 23.7, 19.4; HRMS *m/z* (ESI) Calcd for $C_{14}H_{16}NO_4^+$ $(M + H)^+$ 262.1079, found 262.1083.



2,3-Dihydroxy-2-methyl-*N*-phenylpropanamide (6): The product was obtained as a white solid (100 mg, 62% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.71 (s, 1H), 7.57 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 8.0 Hz, 2H), 7.13 (t, J = 7.4 Hz, 1H), 4.15 (d, J = 11.0 Hz, 1H), 3.54 (d, J = 11.0 Hz, 1H), 3.37 (s, 1H), 2.04 (s, 1H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 173.1, 137.2, 129.1, 124.6, 119.6, 76.4, 67.7, 22.6; HRMS *m/z* (ESI) Calcd for $C_{10}H_{14}NO_3^+$ $(M + H)^+$ 196.0973, found 196.0969.

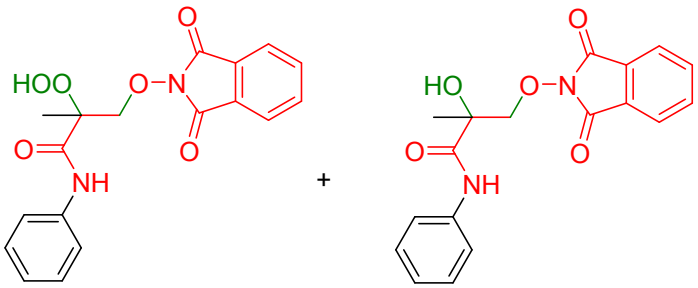


2-Methyl-5,6-dioxo-*N*-phenyl-1,4-dioxane-2-carboxamide (7): The product was obtained as a white solid (44.7 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.24 (s, 1H), 7.56 (dt, J = 8.8, 1.7 Hz, 2H), 7.38-7.33 (m, 2H), 7.21-7.16 (m, 1H), 4.82 (d, J = 9.2 Hz, 1H), 4.34 (d, J = 9.2 Hz, 1H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 167.9, 153.0, 136.1, 129.1, 125.5, 120.3, 82.1, 73.3, 23.7; HRMS *m/z* (ESI) Calcd for $C_{12}H_{12}NO_5^+$ $(M + H)^+$ 250.0715, found 250.0713.

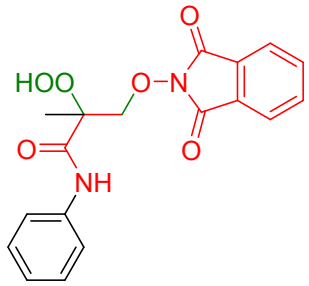


2-Methyl-*N*-phenyl-1,4-dioxane-2-carboxamide (8): The product was obtained as a white solid (42.5 mg, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.40 (s, 1H), 7.61-7.58 (m, 2H), 7.37-7.32 (m, 2H), 7.15-7.11 (m, 1H), 4.05 (d, J = 11.6 Hz, 1H),

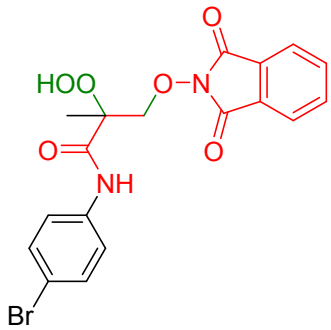
3.94 (ddd, J = 11.9, 6.7, 3.1 Hz, 1H), 3.83 (ddd, J = 11.8, 5.4, 3.3 Hz, 1H), 3.76-3.67 (m, 2H), 3.63 (d, J = 11.6 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 170.9, 137.4, 129.0, 124.4, 119.5, 75.8, 71.1, 66.2, 62.4, 20.4; HRMS *m/z* (ESI) Calcd for $C_{12}H_{16}NO_3^+$ $(M + H)^+$ 222.1130, found 222.1127.



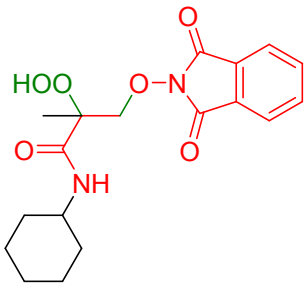
3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroperoxy-2-methyl-*N*-phenylpropanamide (3da') and 3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroxy-2-methyl-*N*- phenylpropanamide (3da): The product was obtained as a white solid (43.7 mg, 61% yield); ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 10.71 (s, 1H), 8.75 (s, 0.33H), 8.50 (s, 1H), 7.87 (dd, J = 5.4, 3.1 Hz, 2H), 7.79 (dd, J = 5.5, 3.1 Hz, 2H), 7.72 (dd, J = 5.4, 3.1 Hz, 0.75H), 7.67 (dd, J = 5.5, 3.1 Hz, 0.74H), 7.59 (d, J = 7.7 Hz, 2H), 7.43 (d, J = 7.7 Hz, 0.72H), 7.33 (t, J = 7.9 Hz, 2H), 7.22 (t, J = 7.9 Hz, 0.77H), 7.13 (t, J = 7.4 Hz, 1H), 7.04 (t, J = 7.0 Hz, 0.39H), 4.98 (d, J = 11.5 Hz, 0.43H), 4.82 (d, J = 10.2 Hz, 1H), 4.58 (d, J = 10.2 Hz, 1H), 4.12 (d, J = 11.5 Hz, 0.38H), 1.64 (s, 3H), 1.51 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ: 171.5, 168.9, 163.9, 163.8, 137.1, 135.0, 134.8, 129.00, 128.8, 128.5, 128.3, 124.7, 124.4, 124.0, 123.8, 120.0, 119.4, 85.6, 82.6, 77.6, 74.8, 23.2, 19.2. HRMS *m/z* (ESI) Calcd for $C_{18}H_{16}N_2NaO_6^+$ $(M + Na)^+$ 379.0906, found 379.0904; HRMS *m/z* (ESI) Calcd for $C_{18}H_{17}N_2O_5^+$ $(M + H)^+$ 341.1137, found 341.1133.



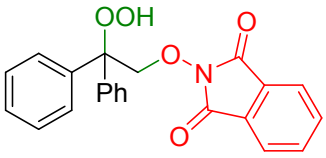
3-((1,3-Dioxoisoindolin-2-yl)oxy)-2-hydroperoxy-2-methyl-*N*-phenylpropanamide (3da'): ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.74 (s, 1H), 8.49 (s, 1H), 7.88-7.78 (m, 4H), 7.59 (d, J = 8.0 Hz, 2H), 7.34 (t, J = 7.7 Hz, 2H), 7.13 (t, J = 7.4 Hz, 1H), 4.82 (d, J = 10.2 Hz, 1H), 4.58 (d, J = 10.2 Hz, 1H), 1.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 168.9, 163.9, 137.1, 135.0, 129.0, 128.5, 124.7, 124.0, 120.0, 85.6, 77.6, 19.3; HRMS *m/z* (ESI) Calcd for $C_{18}H_{16}N_2NaO_6^+$ $(M + Na)^+$ 379.0906, found 379.0904.



***N*-(4-Bromophenyl)-3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroperoxy-2-methylpropanamide (3ga'):** ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.71 (s, 1H), 8.55 (s, 1H), 7.86 (dt, J = 7.5, 3.7 Hz, 2H), 7.79 (dd, J = 5.5, 3.1 Hz, 2H), 7.50 (d, J = 8.9 Hz, 2H), 7.44 (d, J = 8.9 Hz, 2H), 4.78 (d, J = 10.3 Hz, 1H), 4.56 (d, J = 10.3 Hz, 1H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 169.0, 163.9, 136.3, 135.0, 132.0, 128.5, 124.0, 121.6, 117.3, 85.7, 77.6, 19.1; HRMS *m/z* (ESI) Calcd for $C_{18}H_{15}BrN_2NaO_6^+$ $(M + Na)^+$ 457.0011, found 457.0009.



***N*-Cyclohexyl-3-((1,3-dioxoisoindolin-2-yl)oxy)-2-hydroperoxy-2-methylpropanamide (3pa')**: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.55 (s, 1H), 7.87-7.77 (m, 4H), 4.74 (d, J = 10.0 Hz, 1H), 4.48 (d, J = 10.0 Hz, 1H), 3.75 (tdd, J = 10.4, 7.3, 4.0 Hz, 1H), 1.91 (dt, J = 12.4, 4.1 Hz, 2H), 1.72 (dt, J = 12.6, 4.1 Hz, 2H), 1.60 (dt, J = 12.6, 3.8 Hz, 1H), 1.53 (s, 3H), 1.41-1.18 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 169.7, 163.9, 134.9, 128.6, 123.9, 85.1, 77.8, 48.0, 32.8, 25.5, 24.7, 19.4; HRMS *m/z* (ESI) Calcd for $C_{18}H_{22}N_2NaO_6^+$ $(M + Na)^+$ 385.1376, found 385.1373.



2-(2-Hydroperoxy-2,2-diphenylethoxy)isoindoline-1,3-dione (5i'): ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.30 (s, 1H), 7.89-7.84 (m, 2H), 7.83-7.77 (m, 2H), 7.51 (d, J = 7.7 Hz, 3H), 7.38-7.27 (m, 7H), 5.13 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 163.8, 139.9, 134.9, 128.6, 128.4, 128.18, 126.8, 123.9, 88.3, 79.2; HRMS *m/z* (ESI) Calcd for $C_{22}H_{17}NNaO_5^+$ $(M + Na)^+$ 398.1005, found 398.1002.

10. Reference

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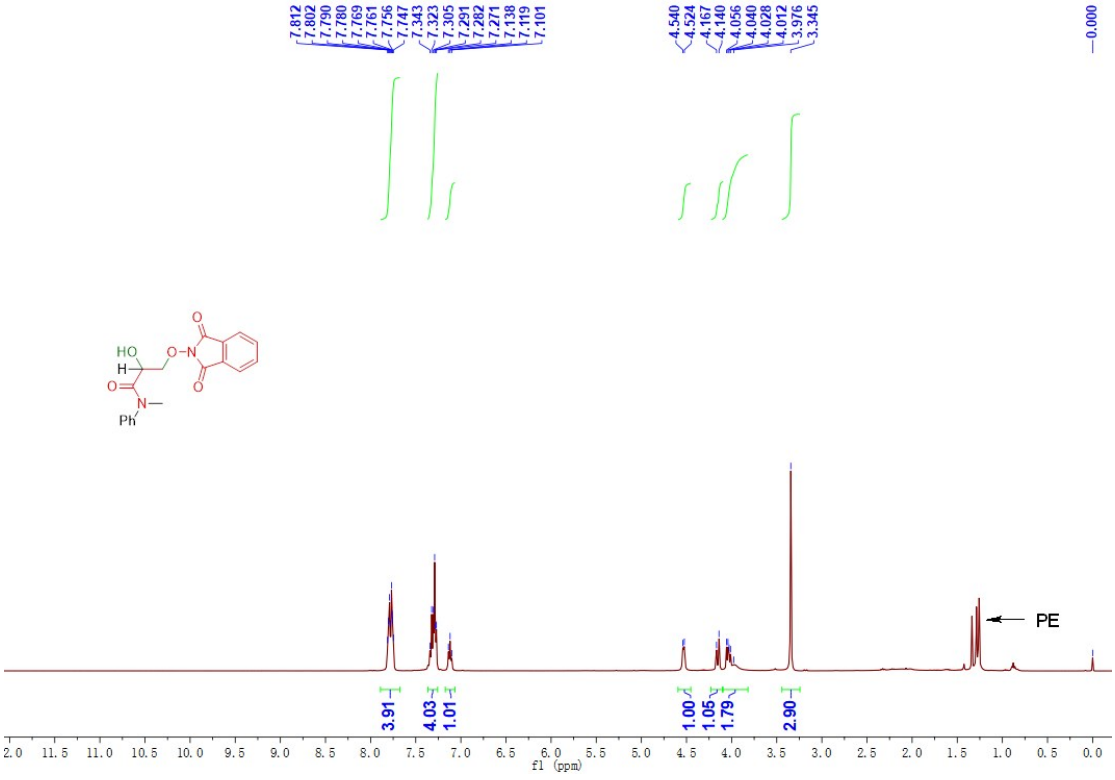
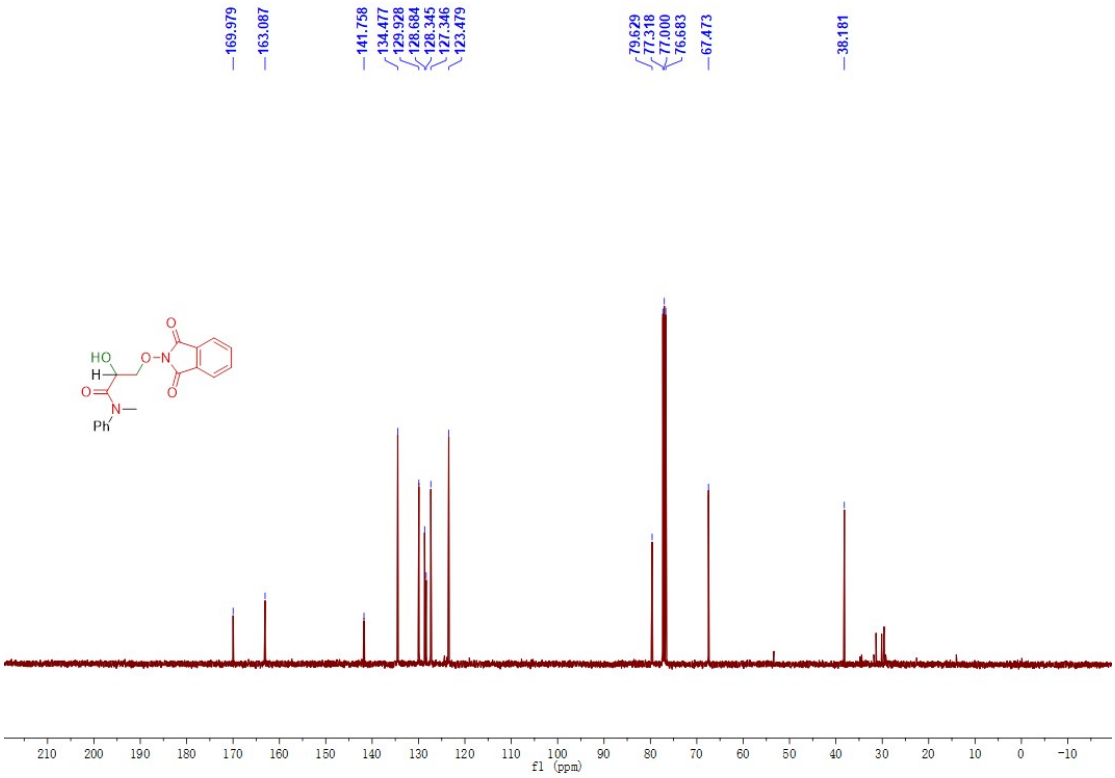
11. ^{1}H and ^{13}C NMR Spectra

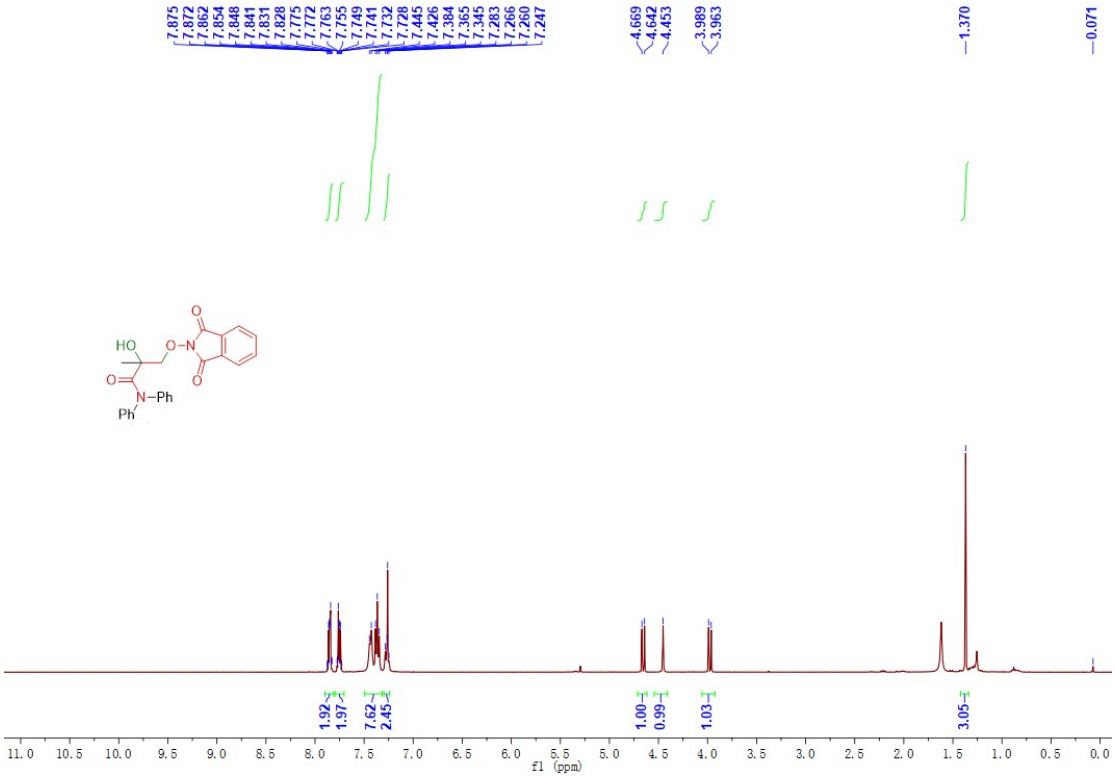
400 MHz ^{1}H NMR of **3ba** in $CDCl_3$



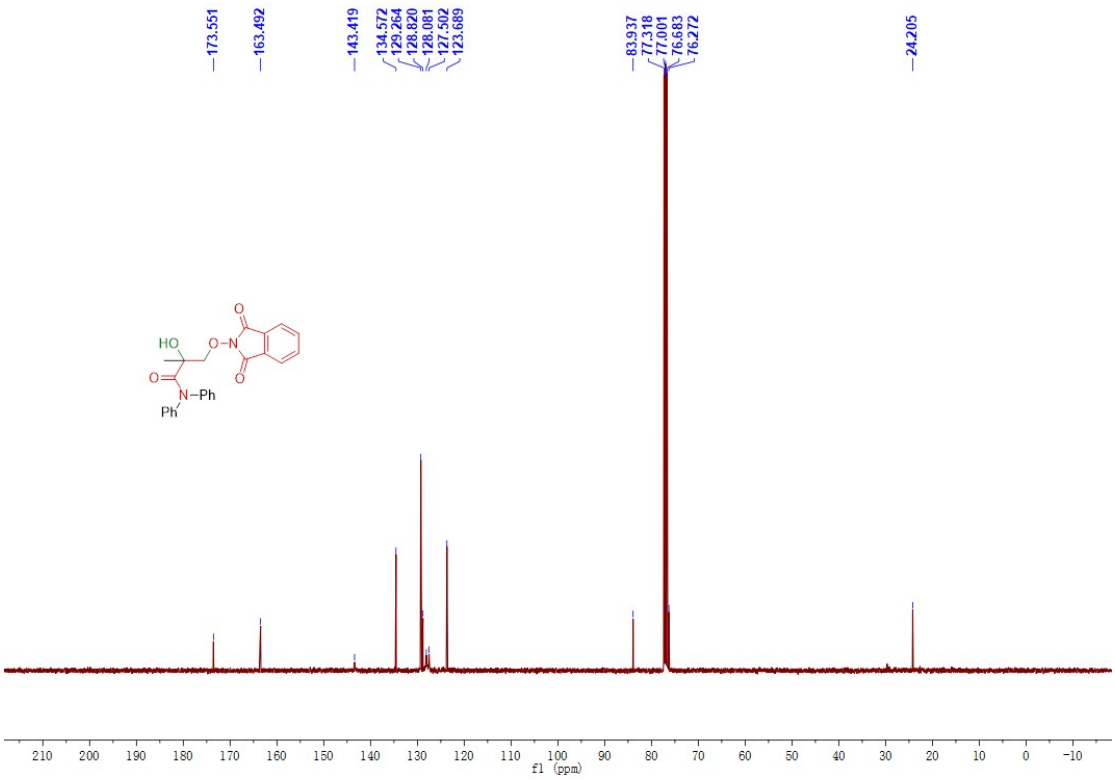
100 MHz ^{13}C NMR of **3ba** in $CDCl_3$



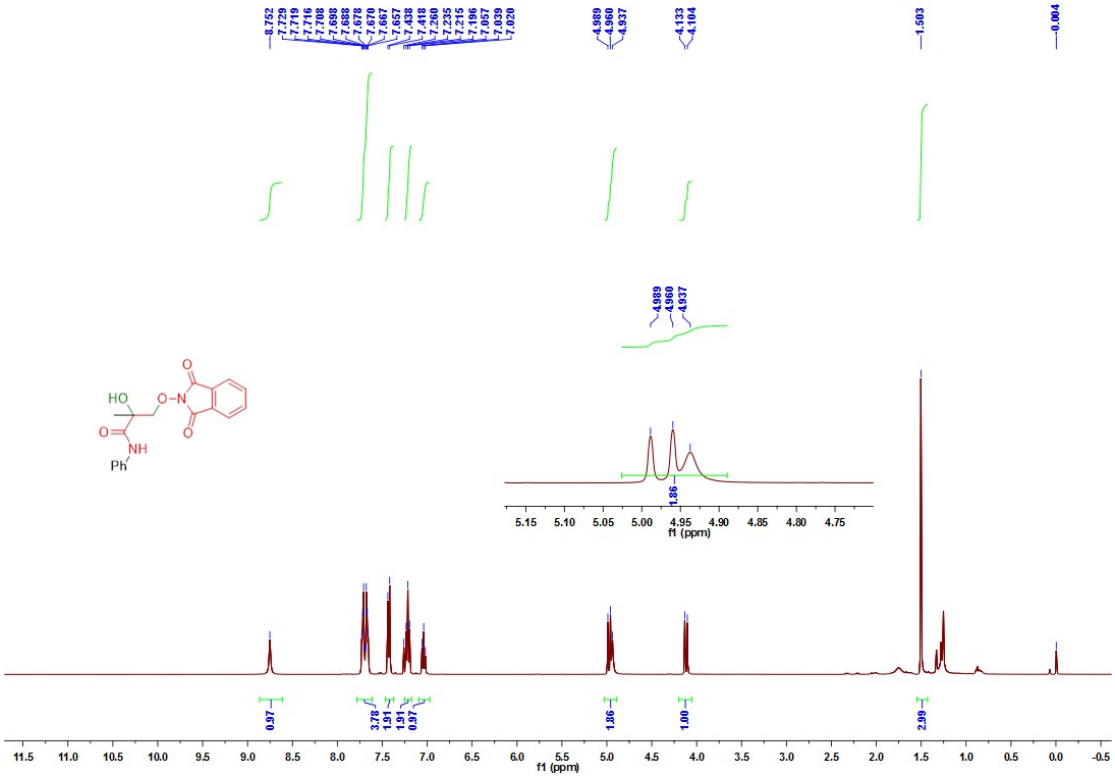
400 MHz ^{1}H NMR of **3ca** in $CDCl_3$



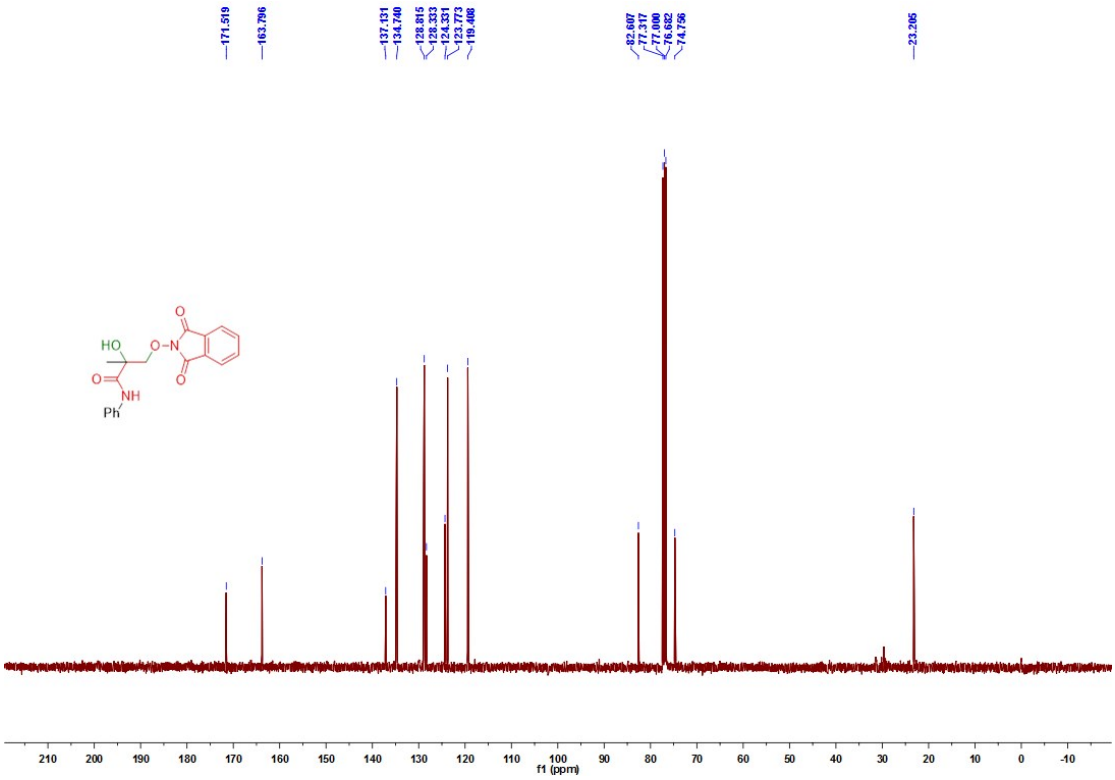
100 MHz ^{13}C NMR of **3ca** in $CDCl_3$



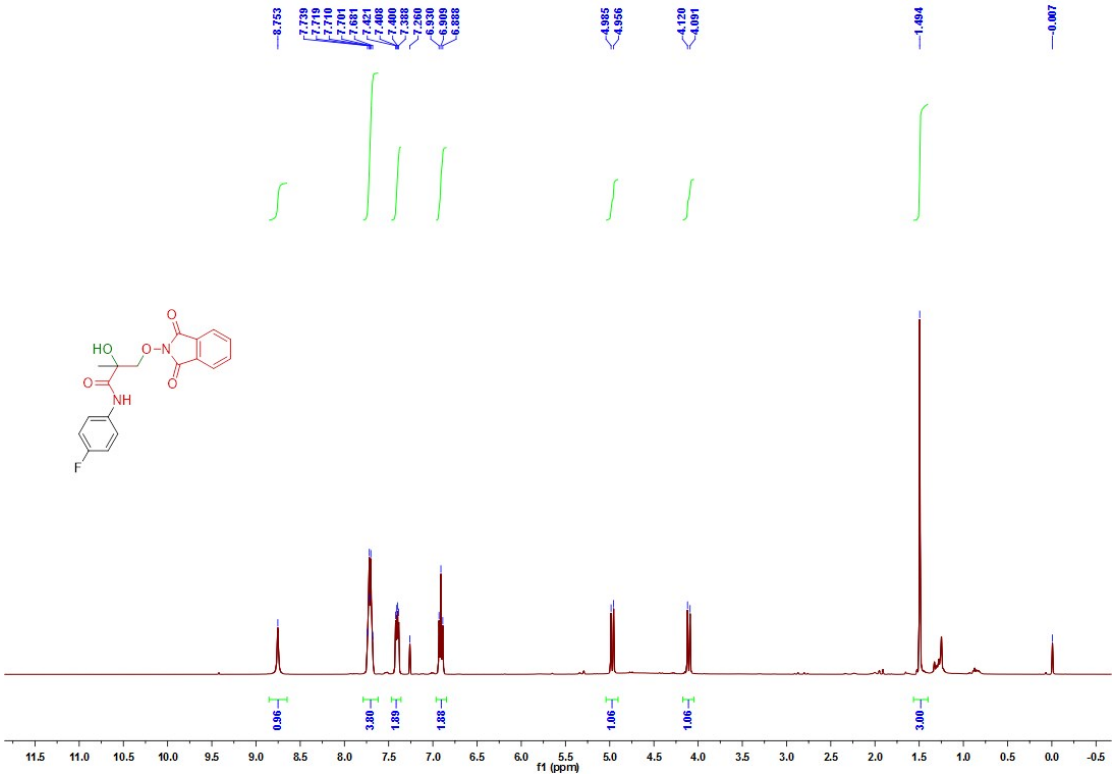
400 MHz ^{1}H NMR of **3da** in $CDCl_3$



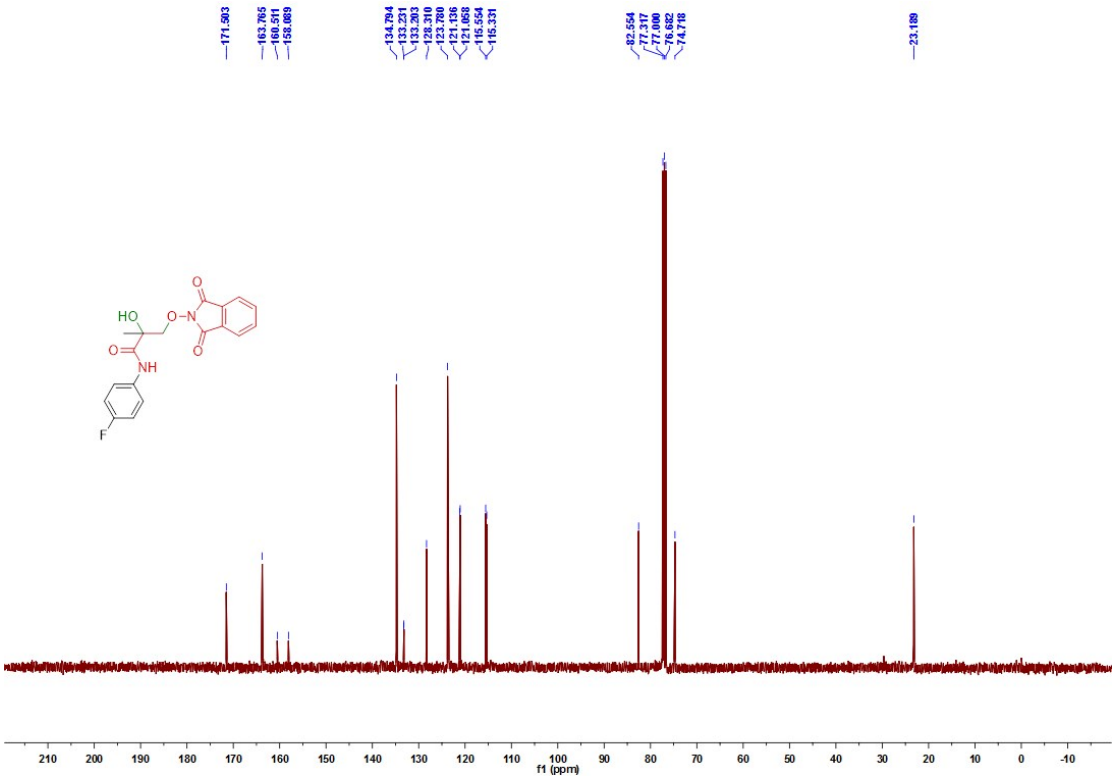
100 MHz ^{13}C NMR of **3da** in $CDCl_3$



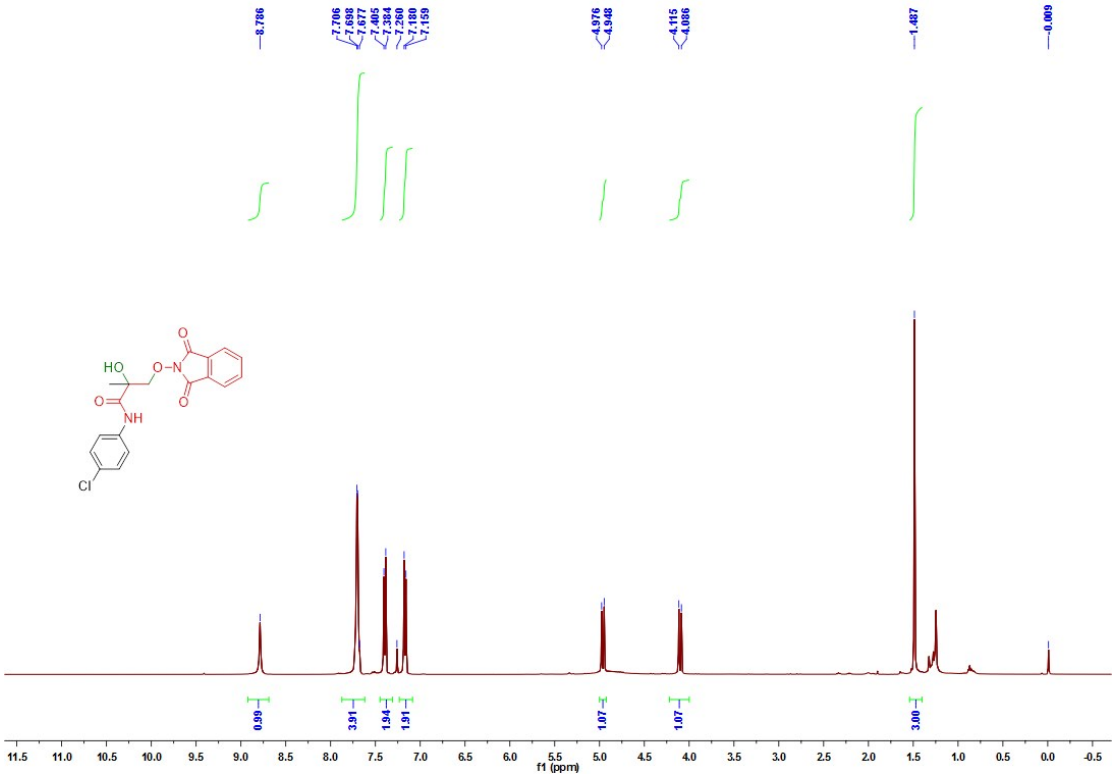
400 MHz ^{1}H NMR of **3ea** in $CDCl_3$



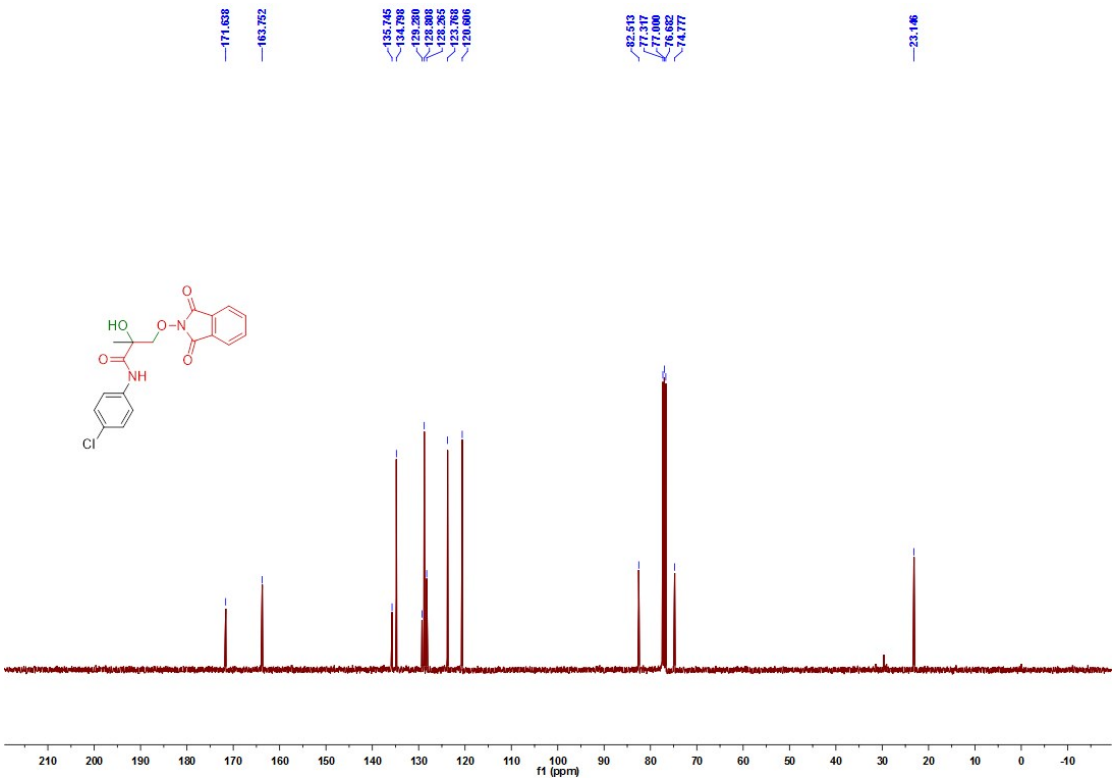
100 MHz ^{13}C NMR of **3ea** in $CDCl_3$



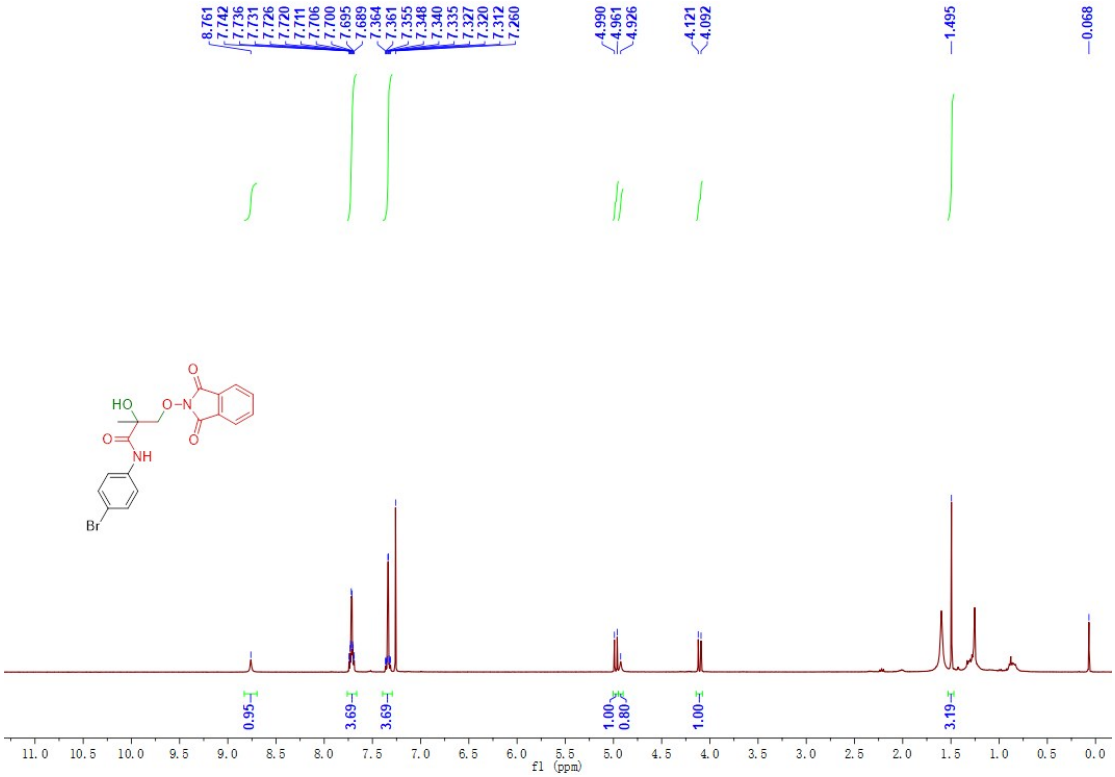
400 MHz ^{1}H NMR of **3fa** in $CDCl_3$



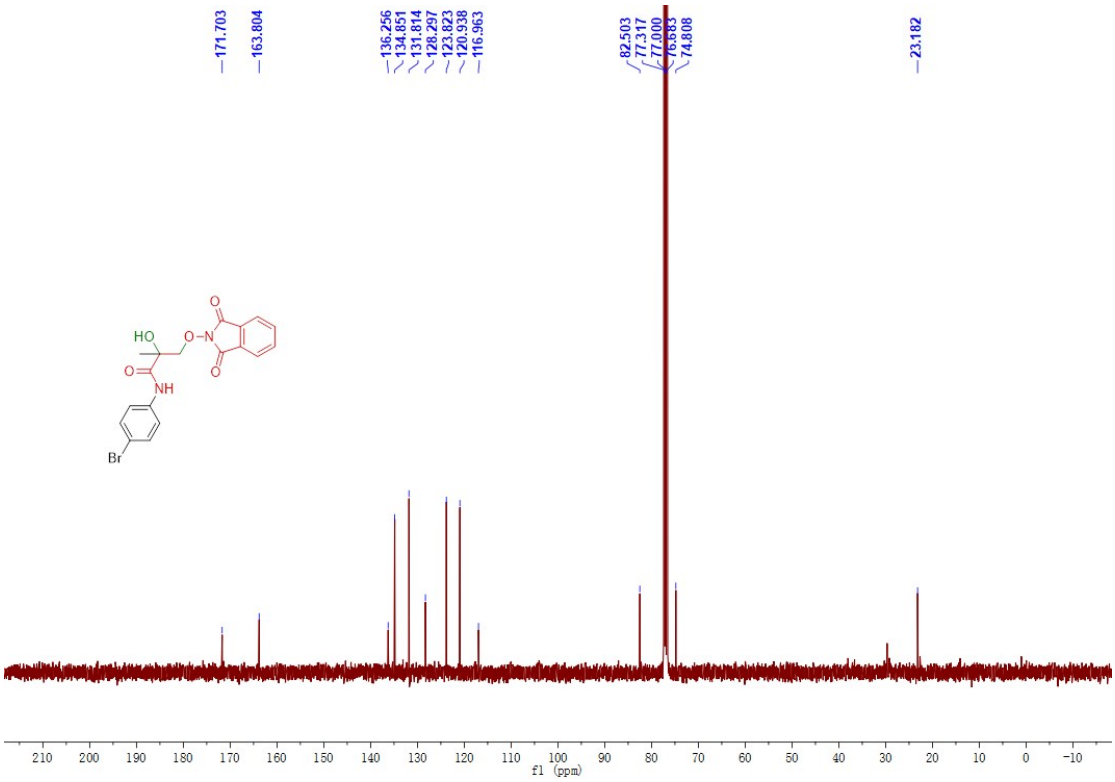
100 MHz ^{13}C NMR of **3fa** in $CDCl_3$



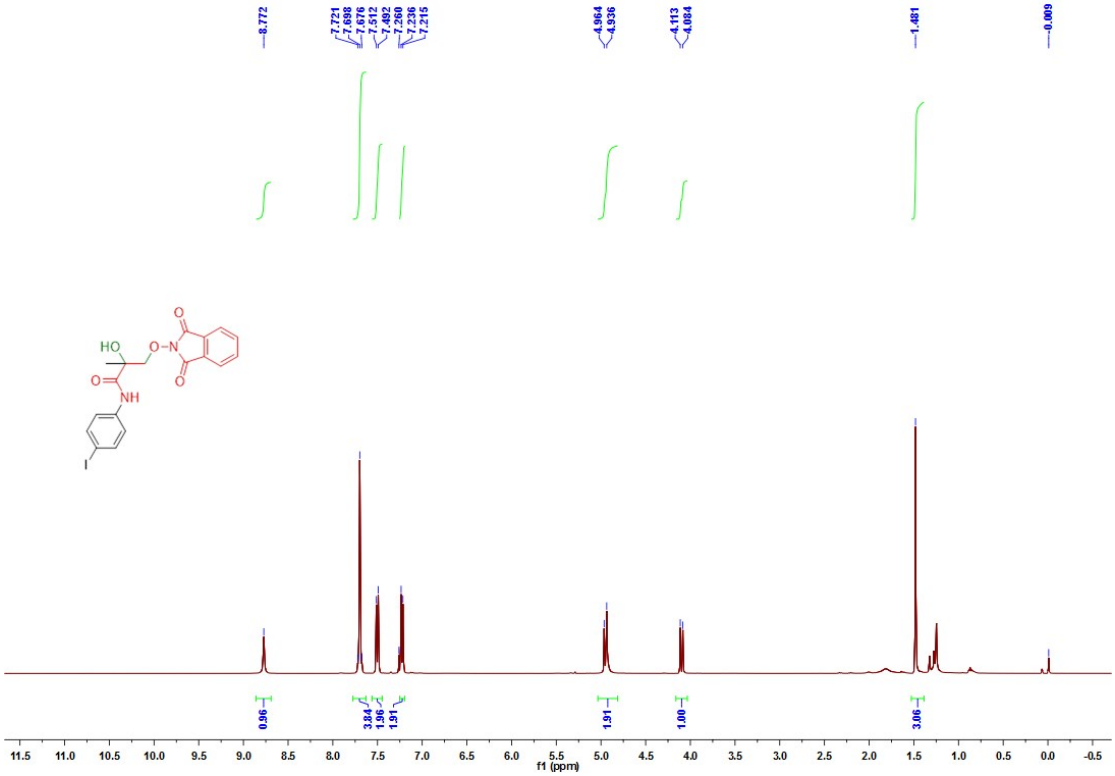
400 MHz ^{1}H NMR of **3ga** in $CDCl_3$



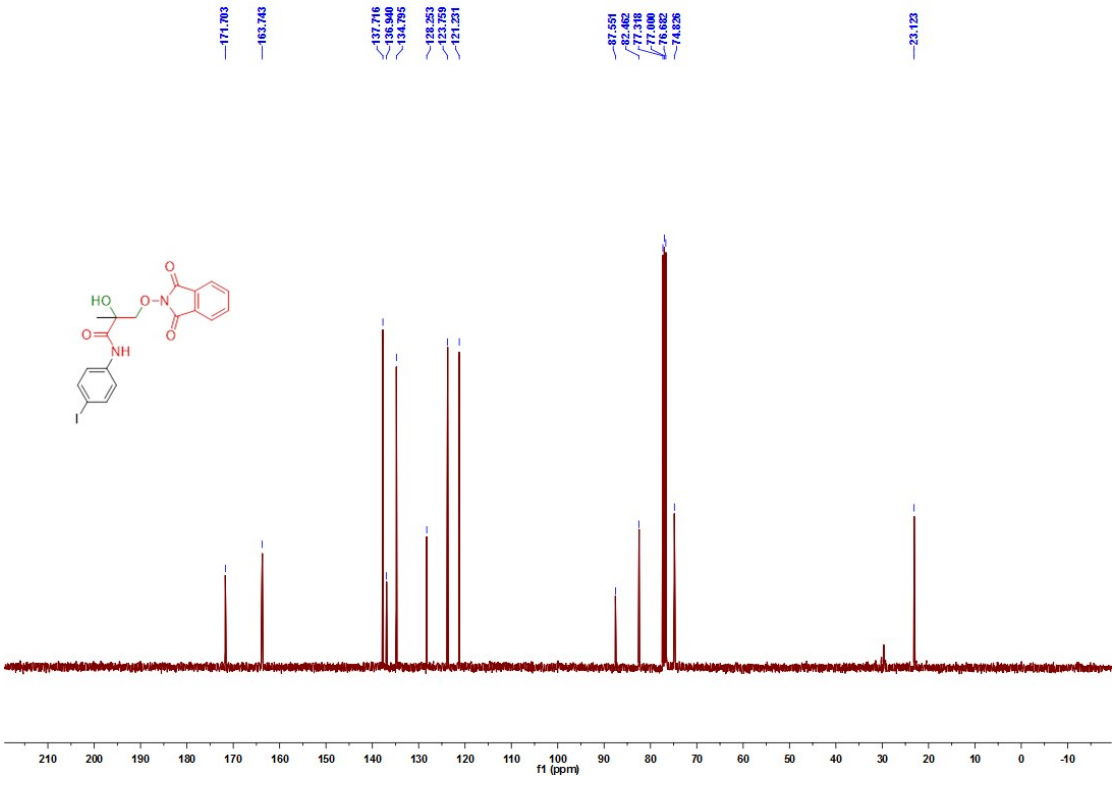
100 MHz ^{13}C NMR of **3ga** in $CDCl_3$



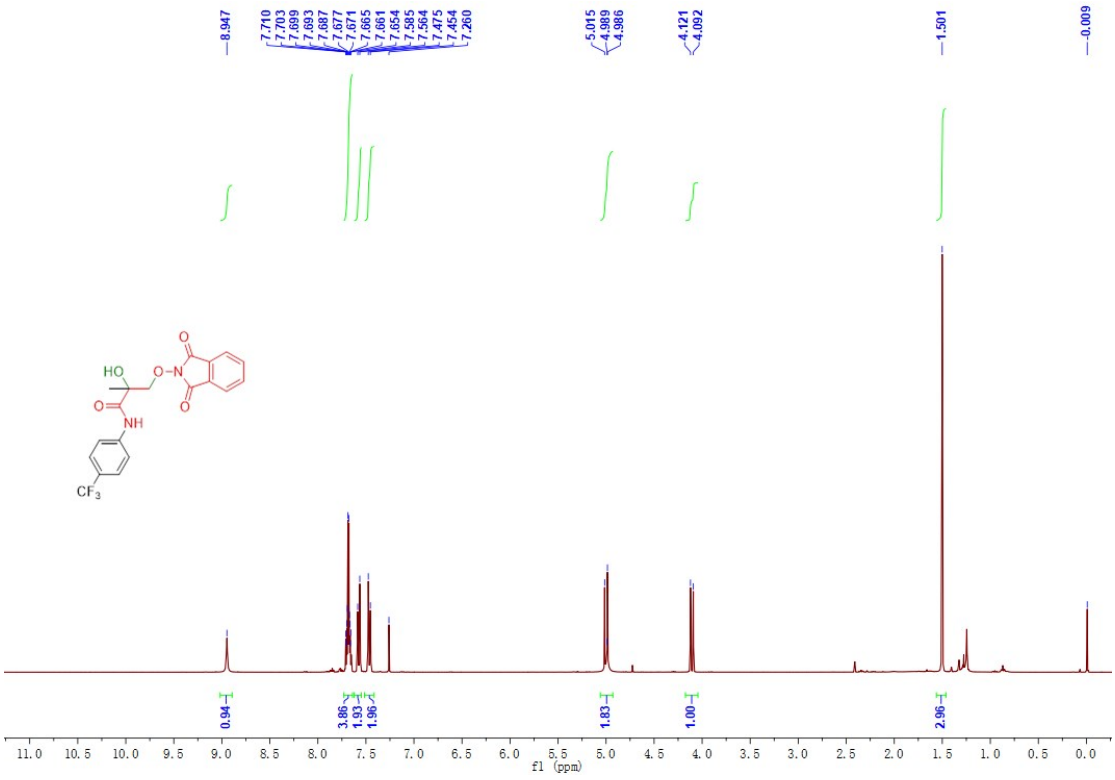
400 MHz ^{1}H NMR of **3ha** in $CDCl_3$



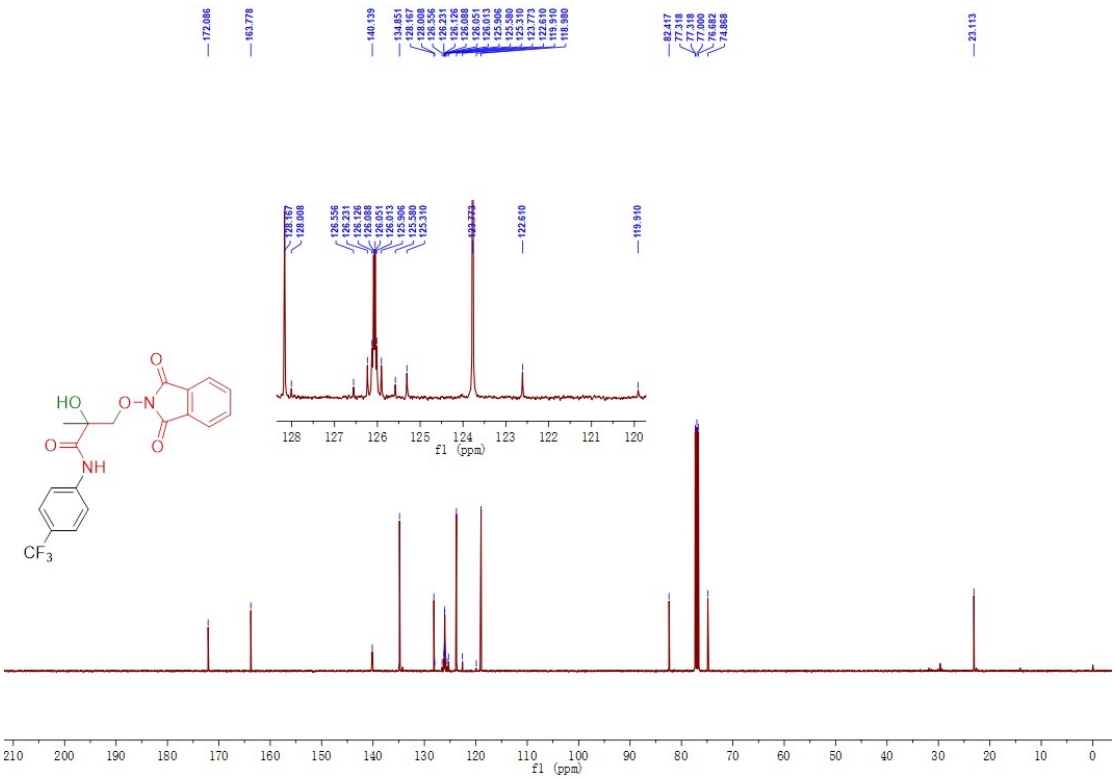
100 MHz ^{13}C NMR of **3ha** in $CDCl_3$



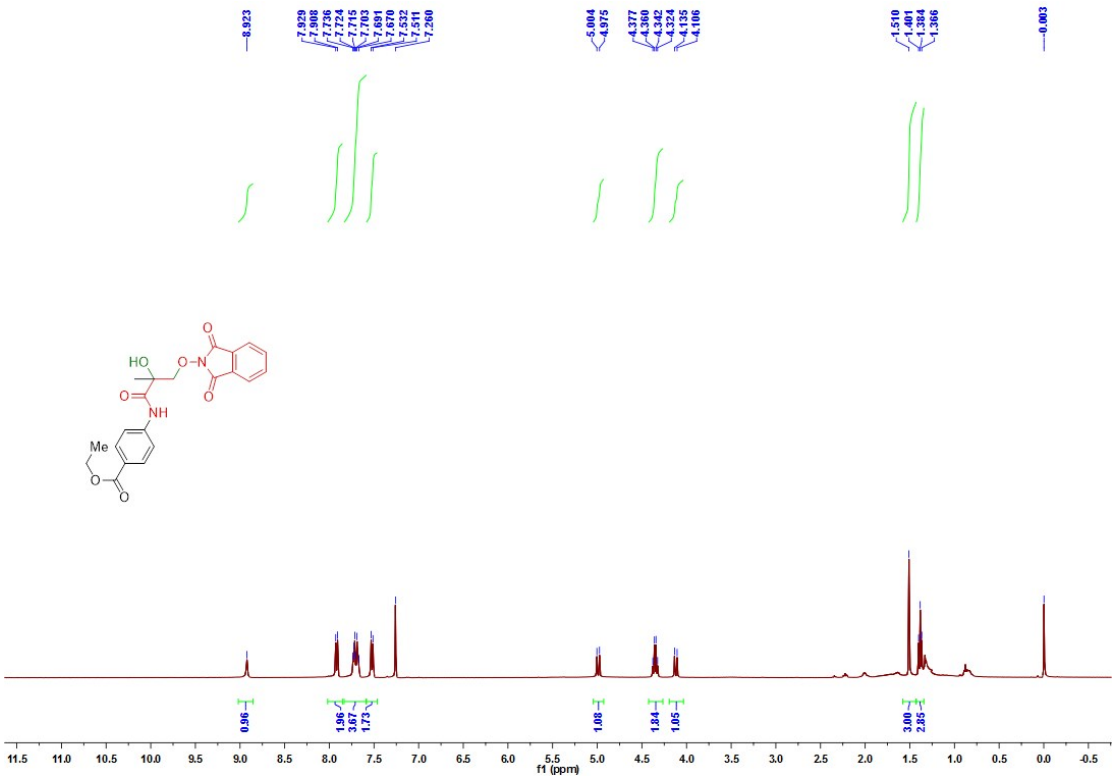
400 MHz ^{1}H NMR of **3ia** in $CDCl_3$



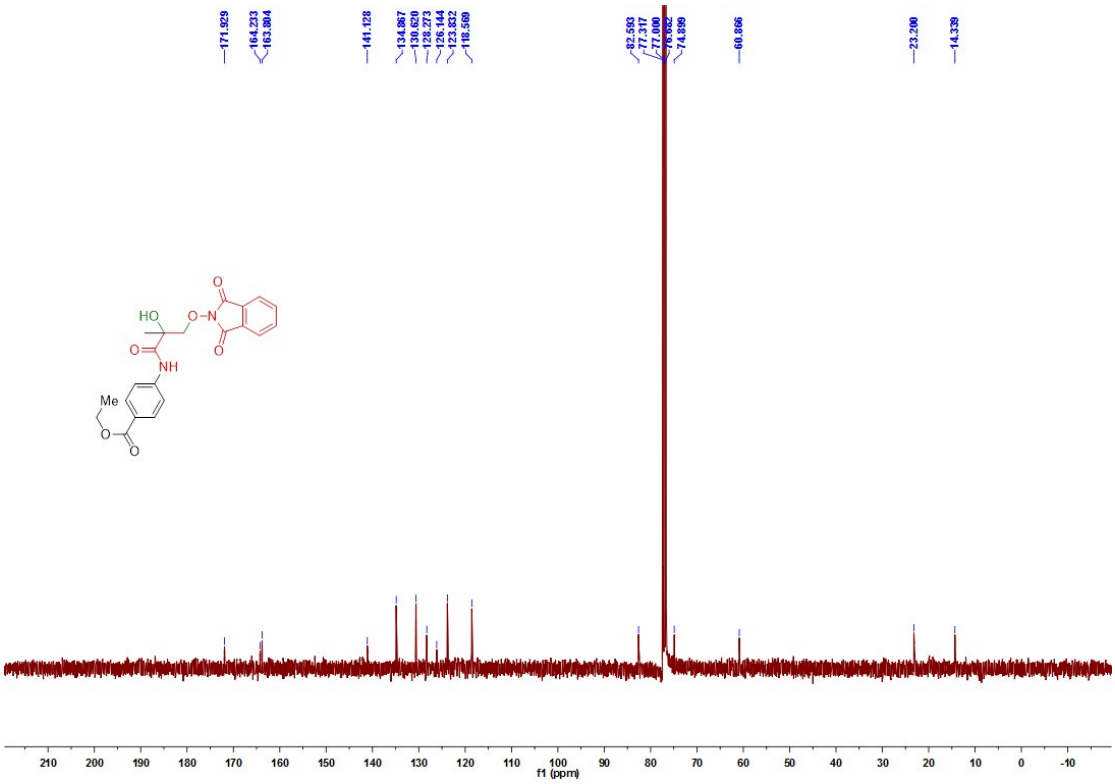
100 MHz ^{13}C NMR of **3ia** in $CDCl_3$



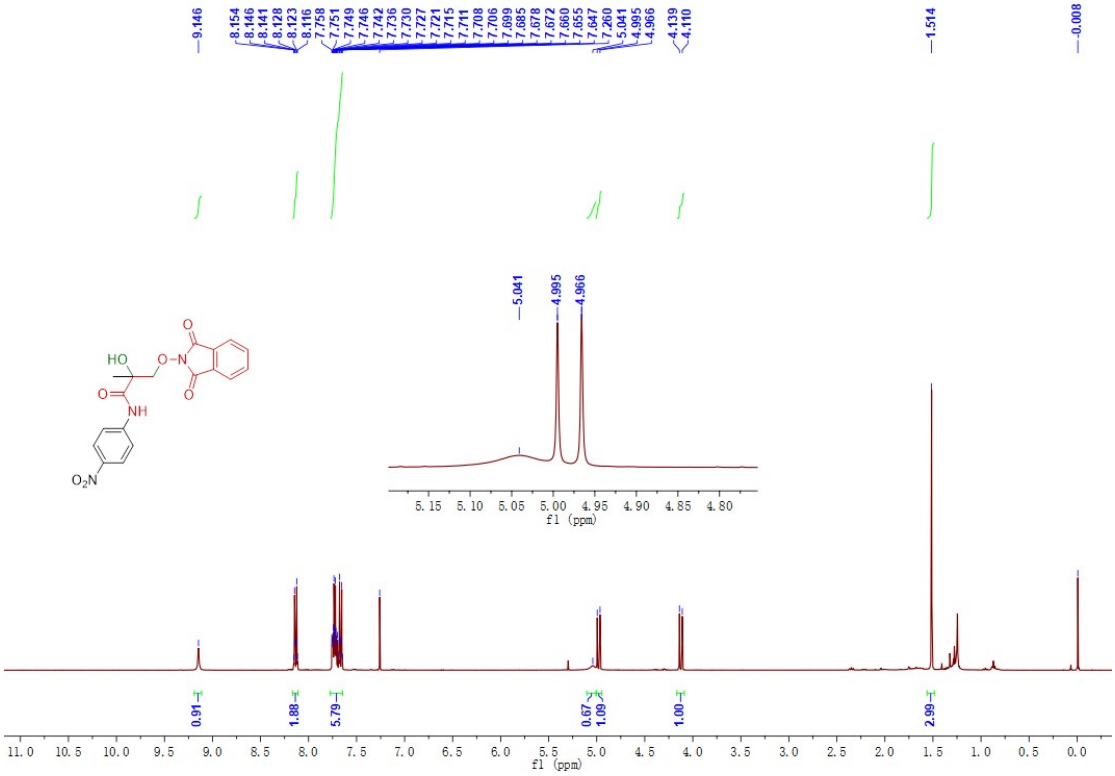
400 MHz ^{1}H NMR of **3ja** in $CDCl_3$



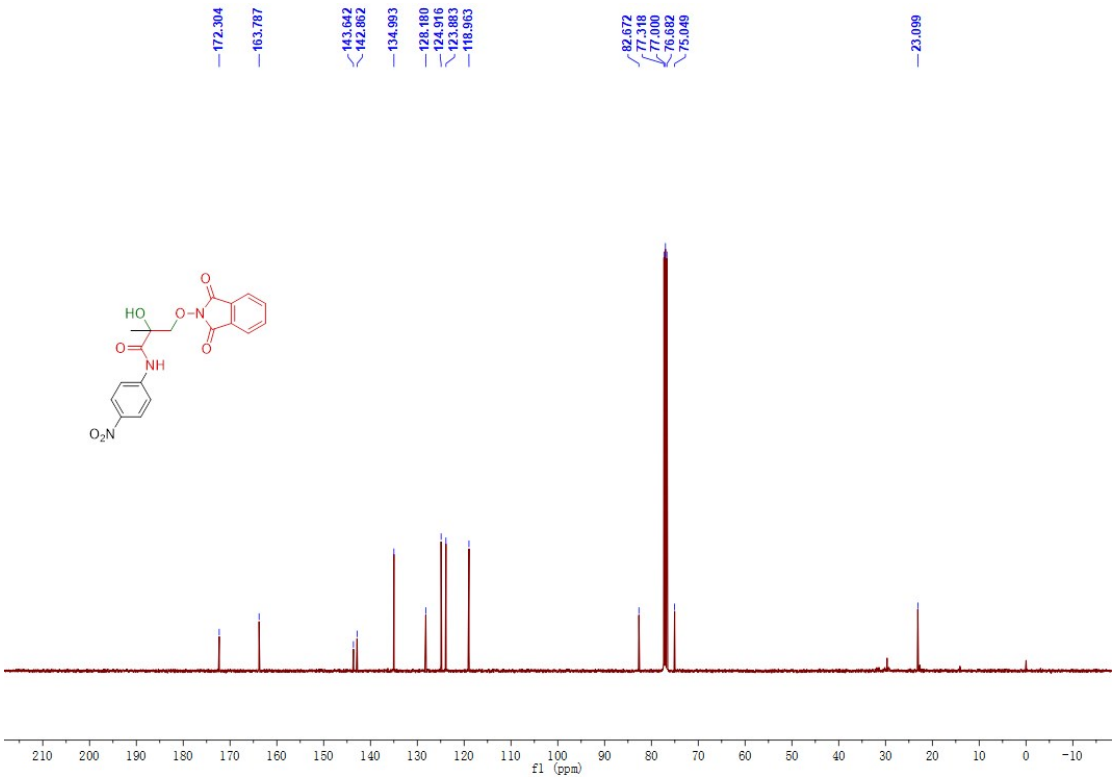
100 MHz ^{13}C NMR **3ja** in $CDCl_3$



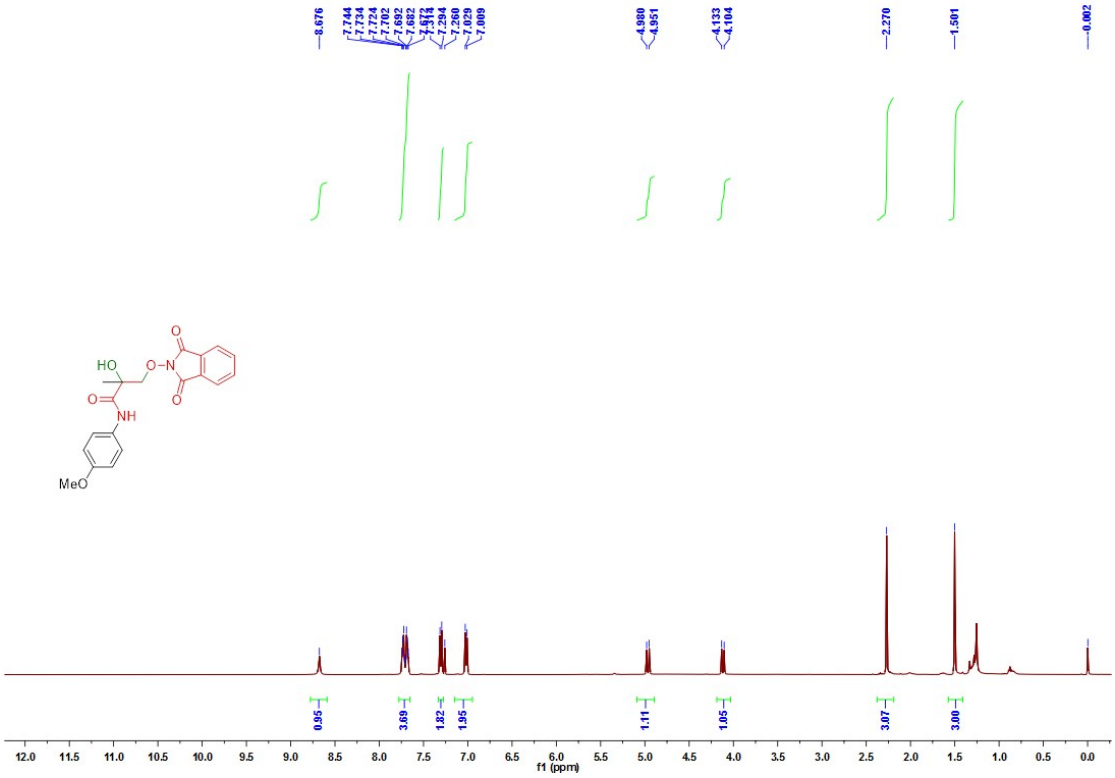
400 MHz ^{1}H NMR of **3ka** in $CDCl_3$



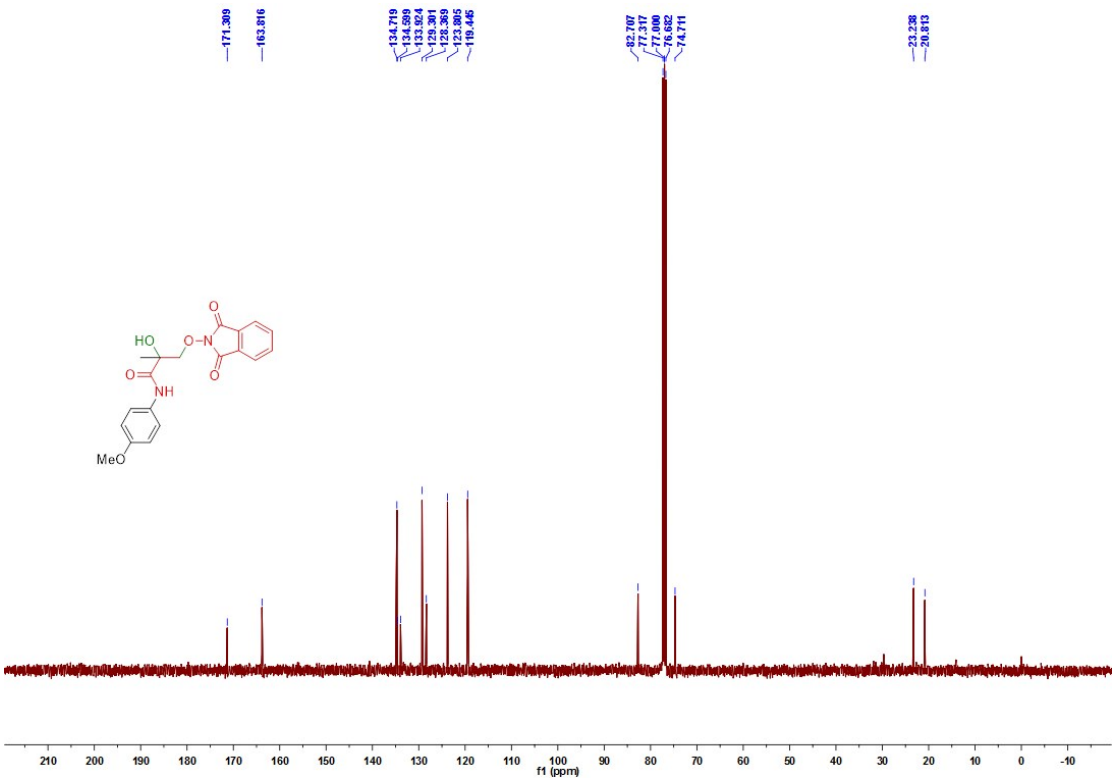
100 MHz ^{13}C NMR of **3ka** in $CDCl_3$



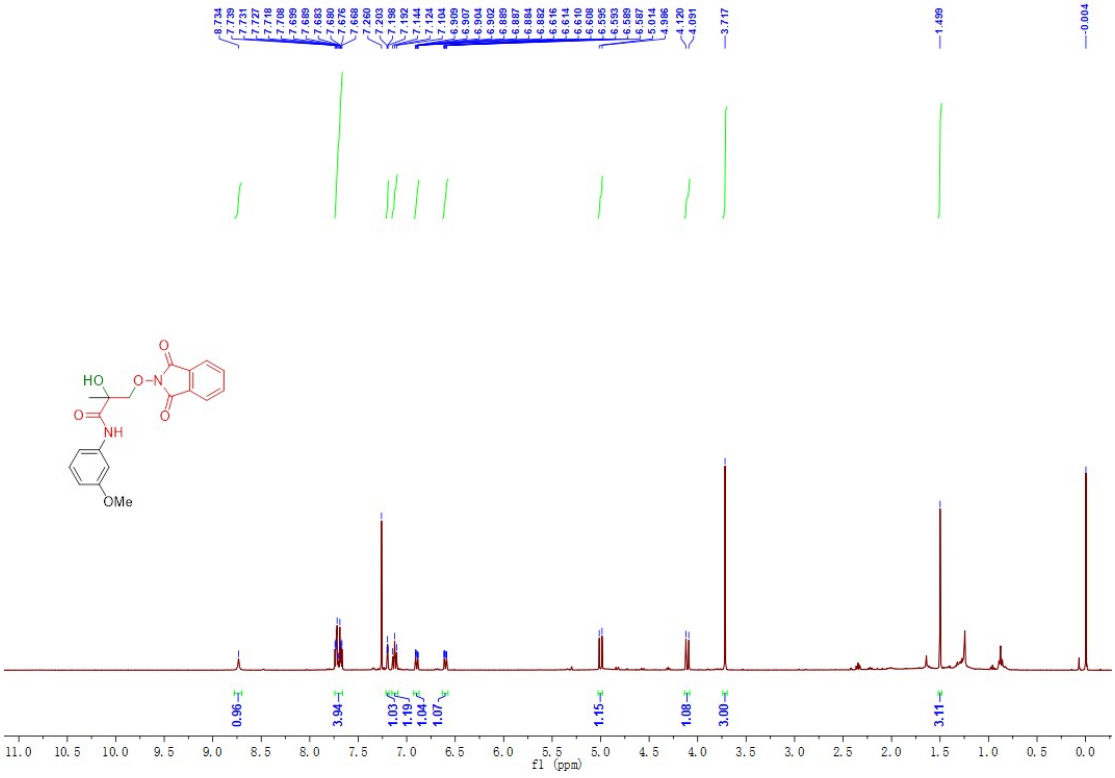
400 MHz ^{1}H NMR of **3la** in $CDCl_3$



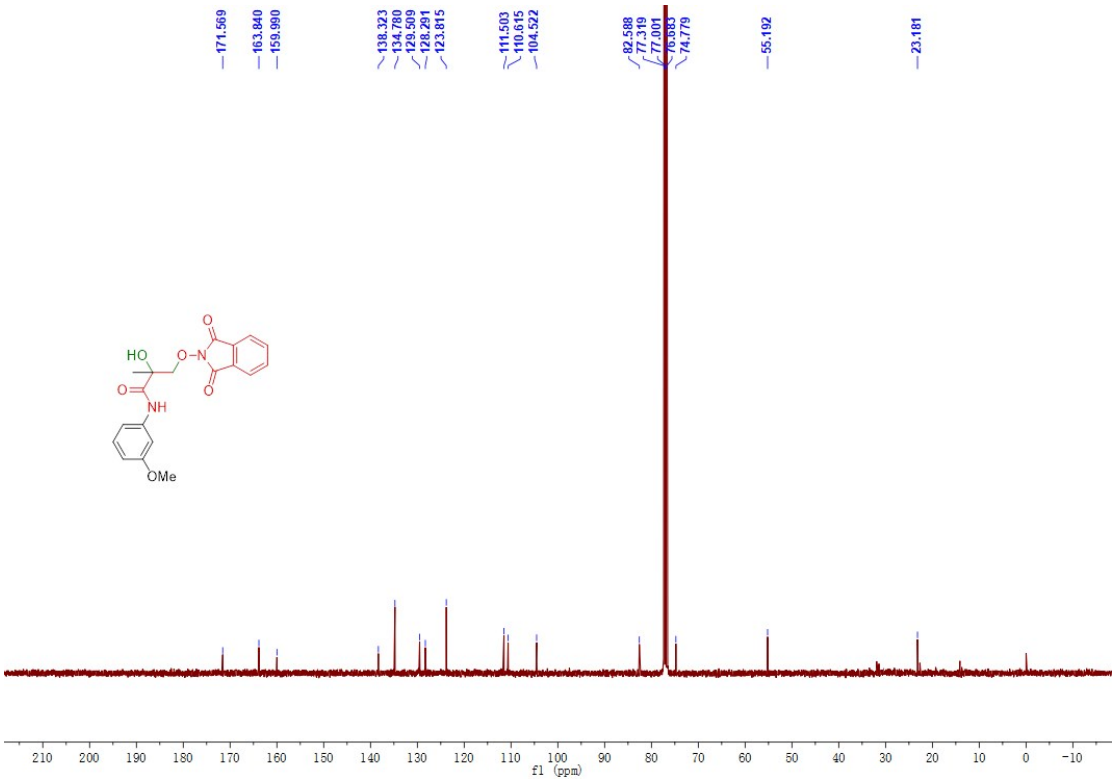
100 MHz ^{13}C NMR of **3la** in $CDCl_3$



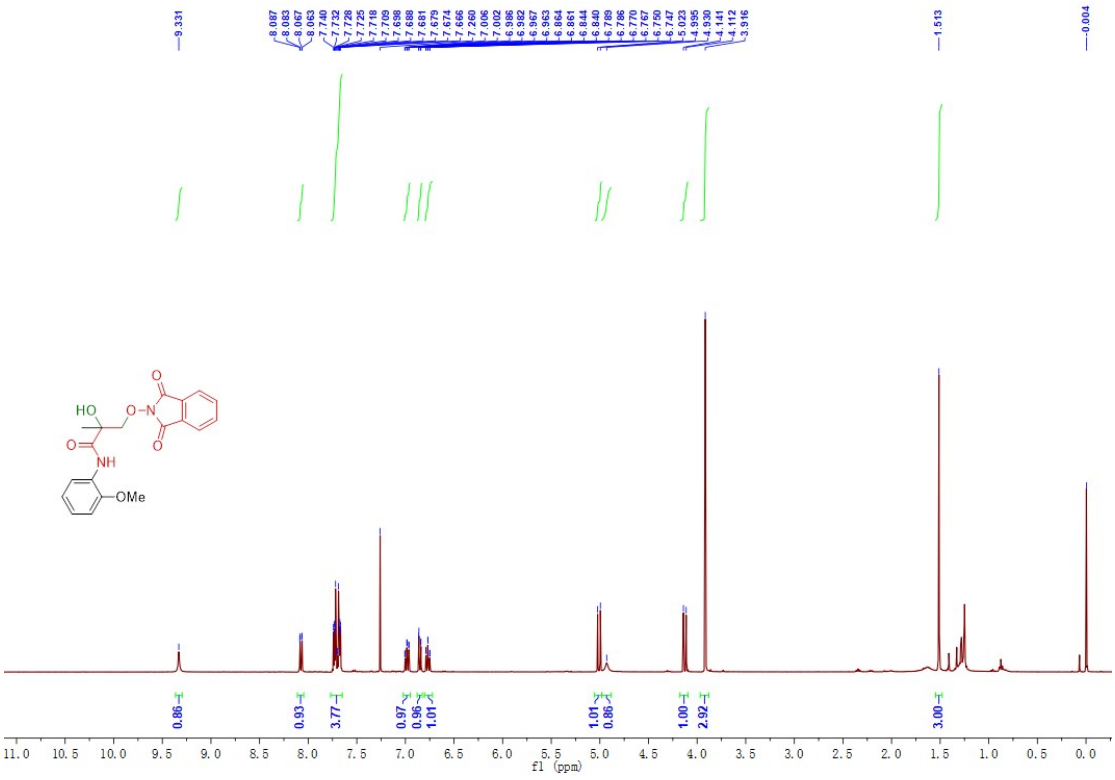
400 MHz ^{1}H NMR of **3ma** in $CDCl_3$



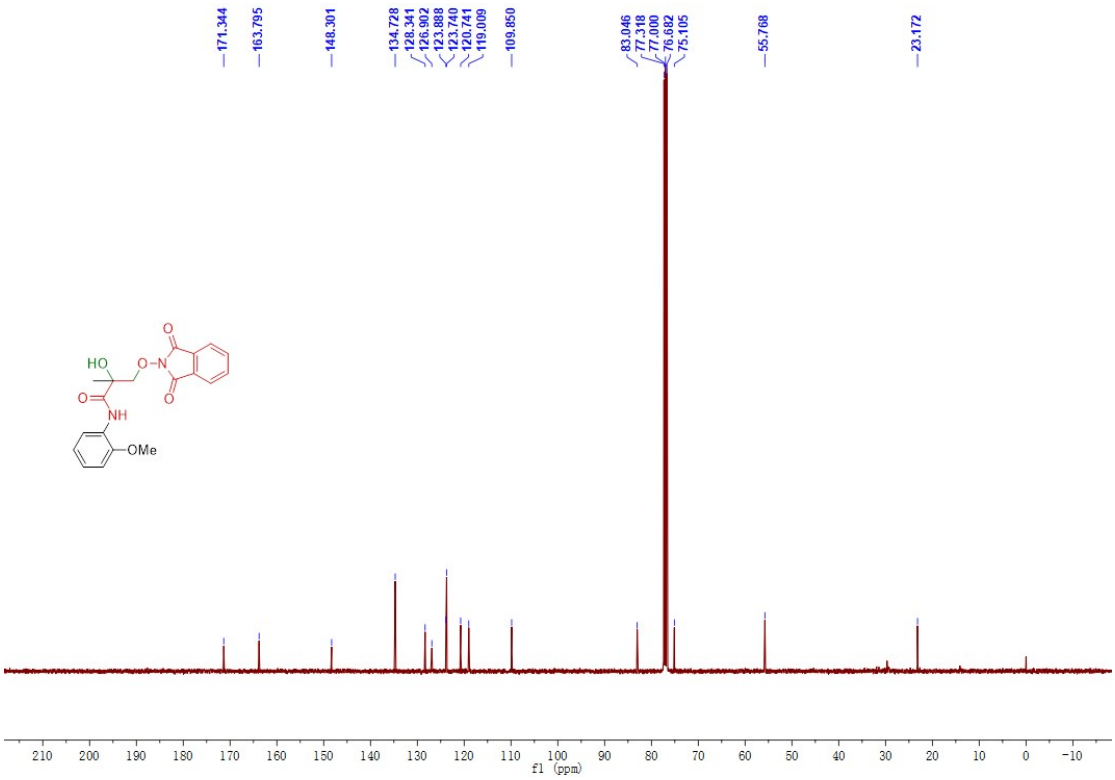
100 MHz ^{13}C NMR of **3ma** in $CDCl_3$



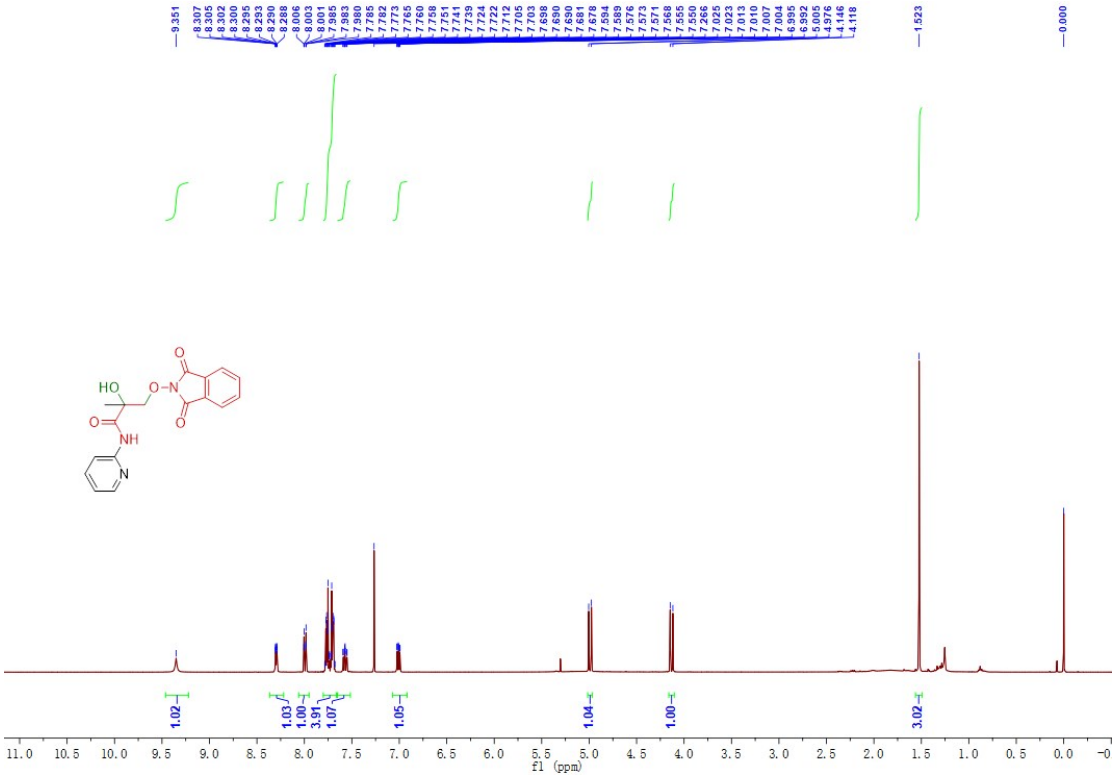
400 MHz ^{1}H NMR of **3na** in $CDCl_3$



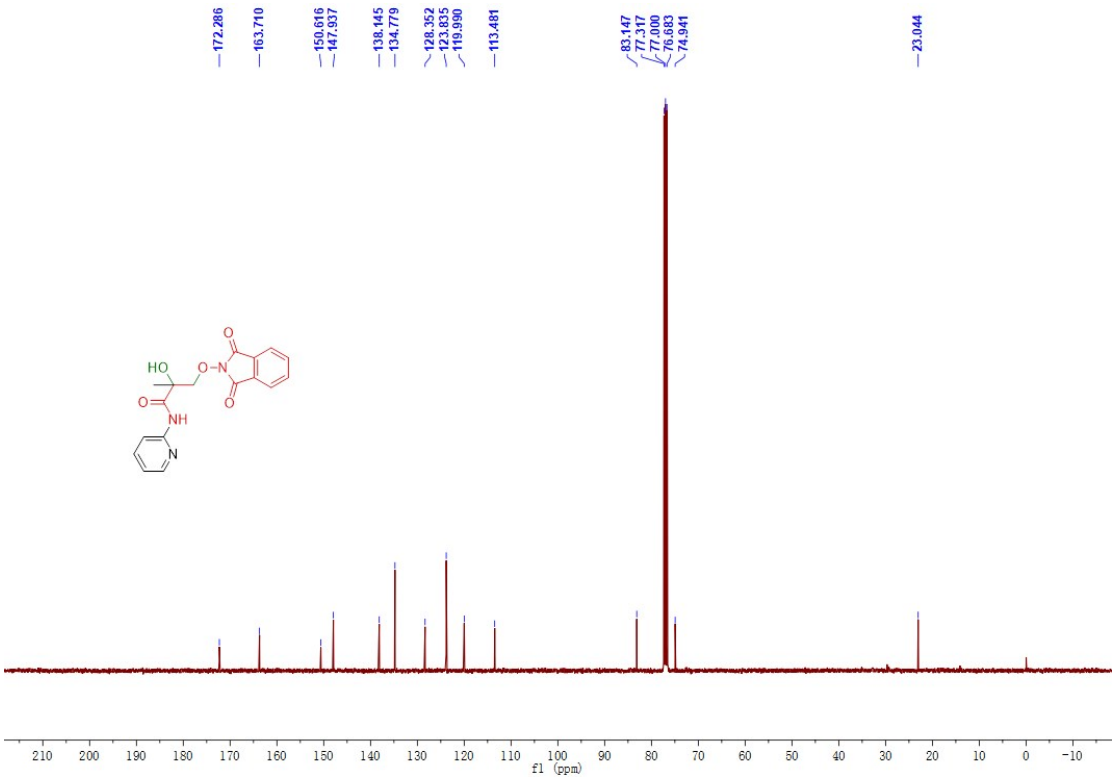
100 MHz ^{13}C NMR of **3na** in $CDCl_3$



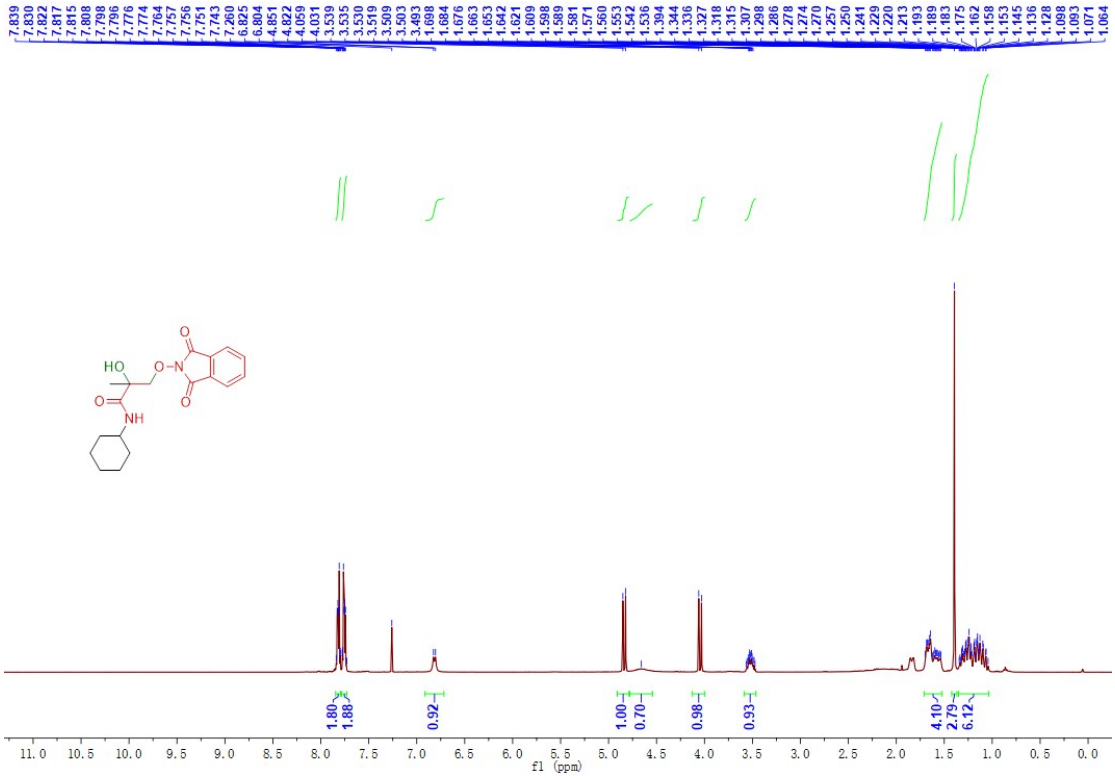
400 MHz ^{1}H NMR of **3oa** in $CDCl_3$



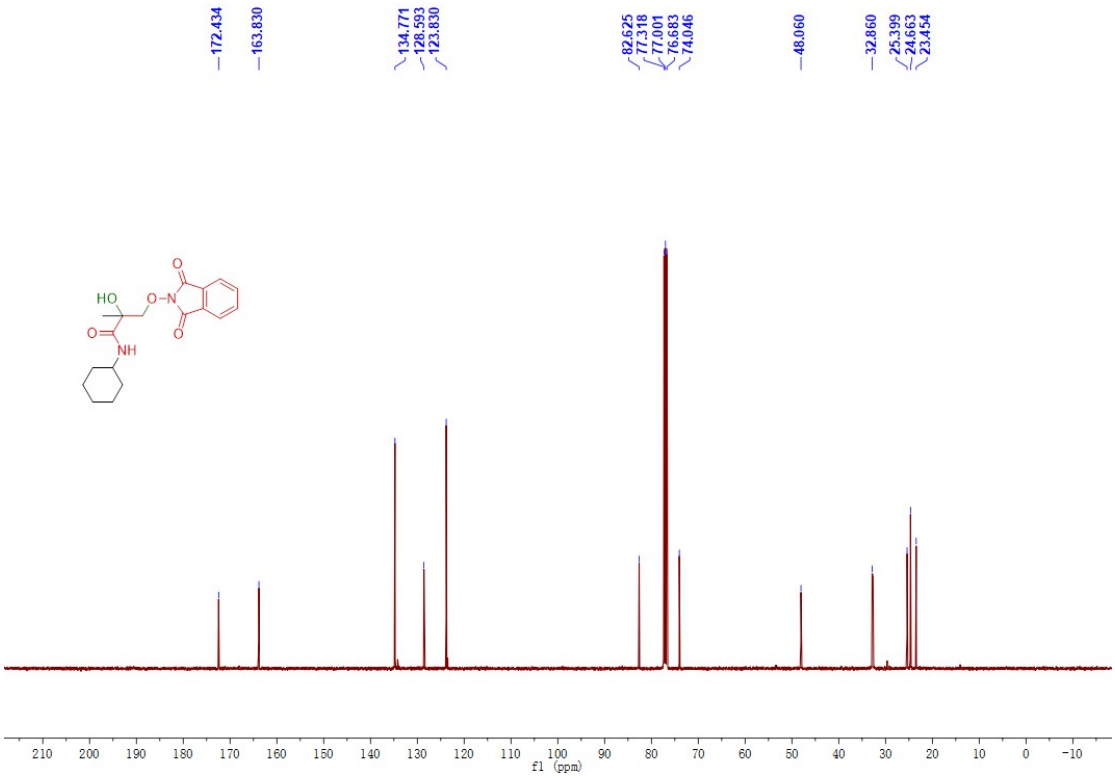
100 MHz ^{13}C NMR of **3oa** in $CDCl_3$



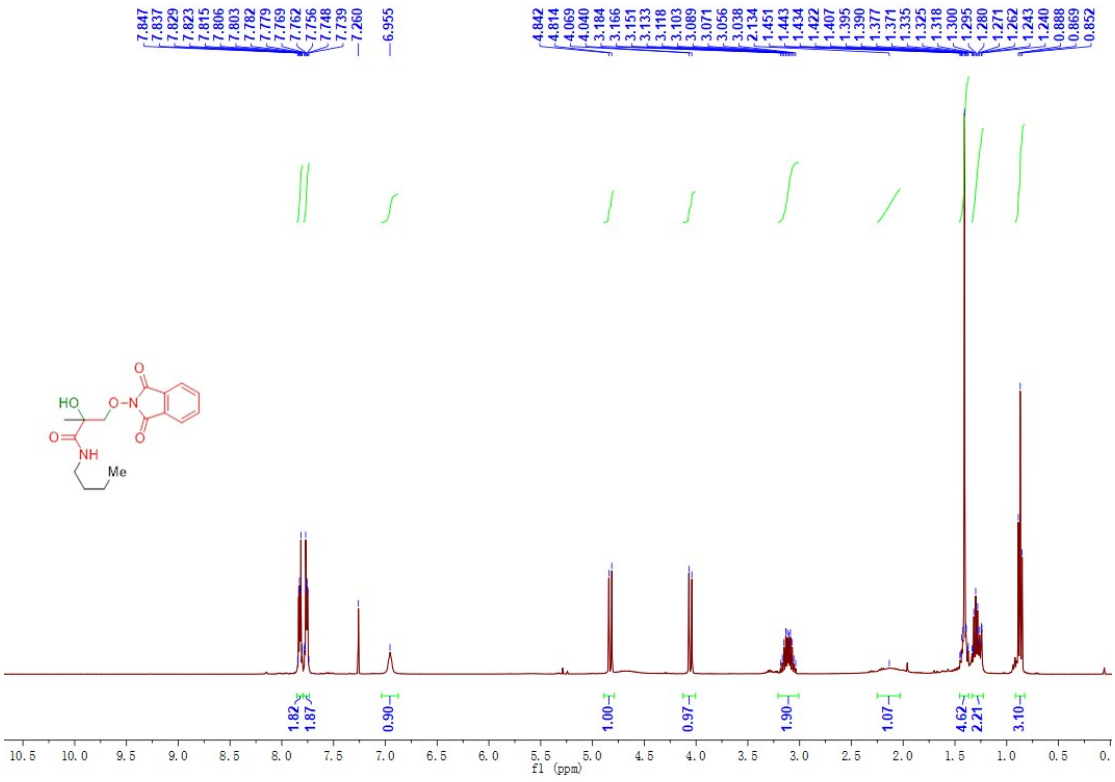
400 MHz ^{1}H NMR of **3pa** in $CDCl_3$



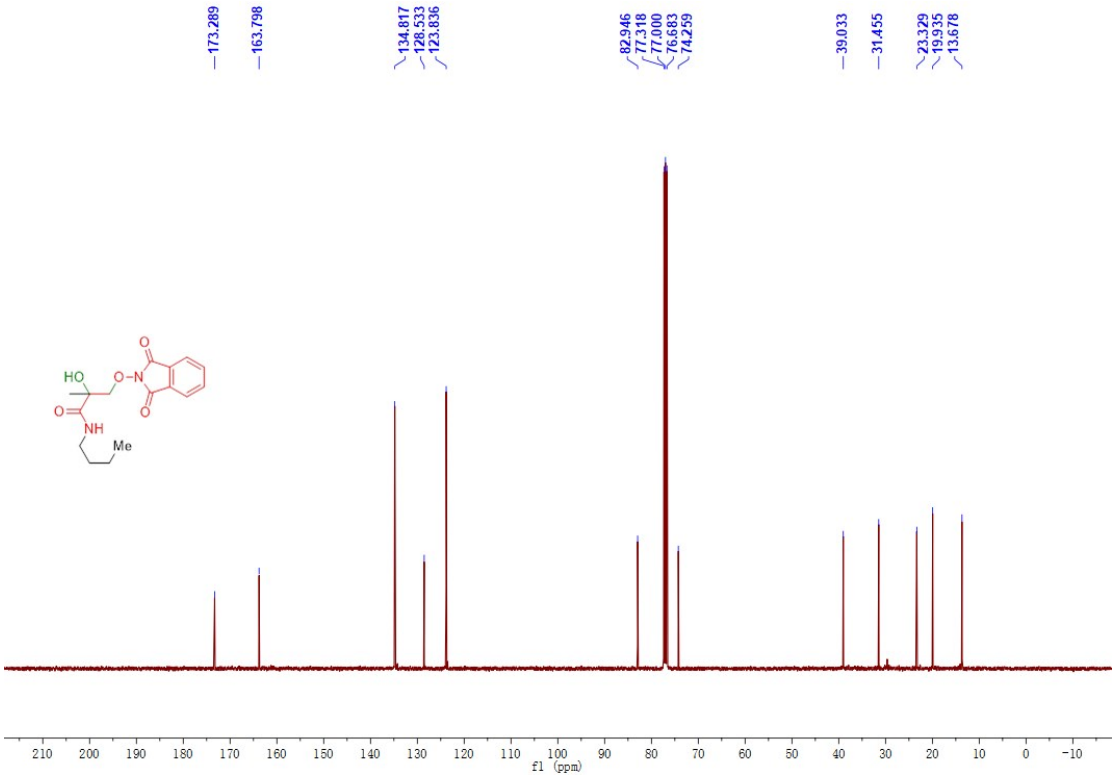
100 MHz ^{13}C NMR of **3pa** in $CDCl_3$



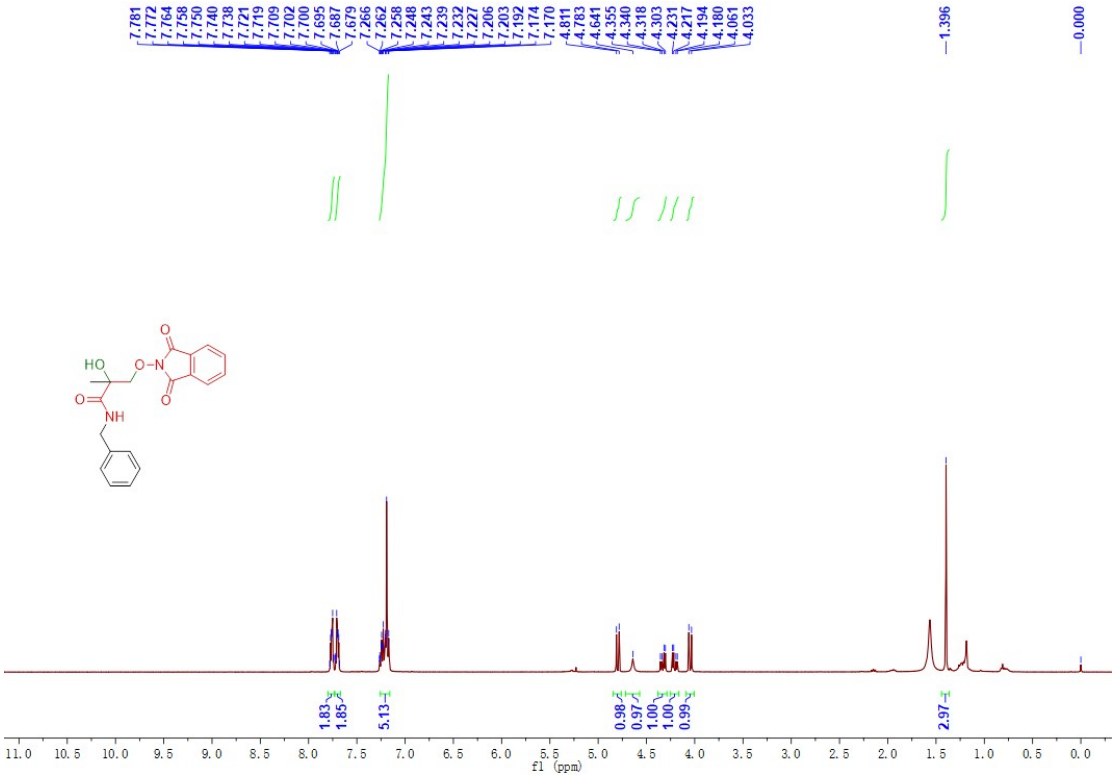
400 MHz ^{1}H NMR of **3qa** in $CDCl_3$



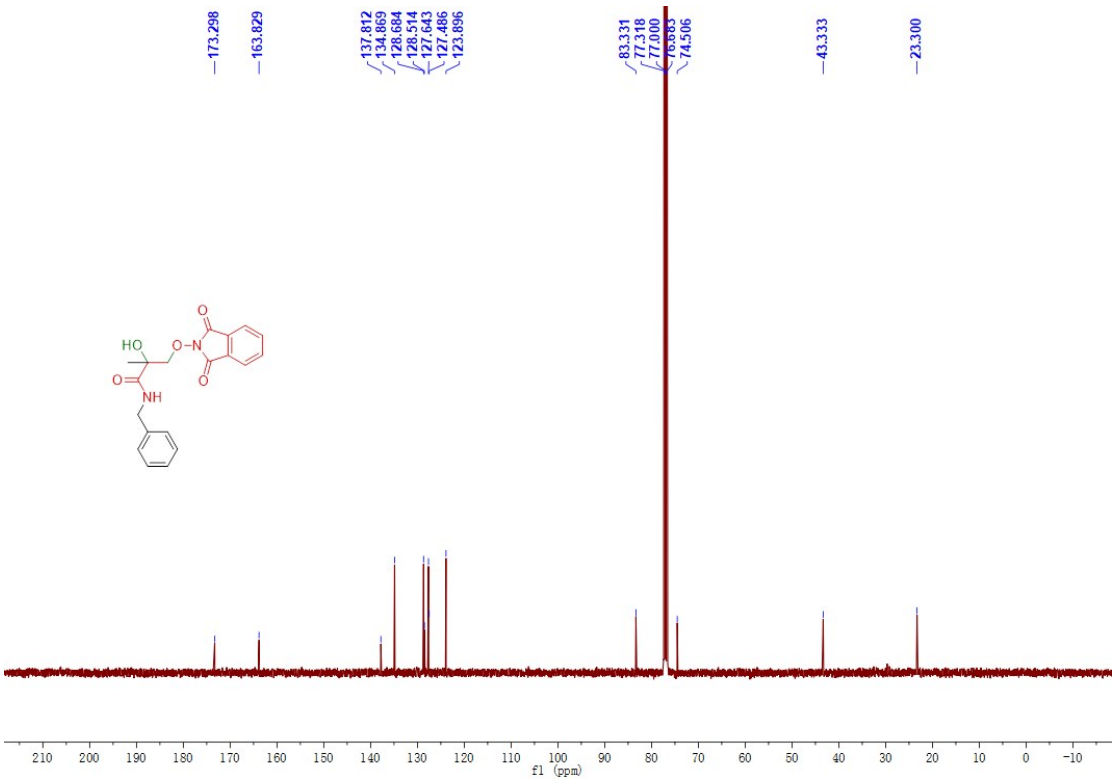
100 MHz ^{13}C NMR of **3qa** in $CDCl_3$



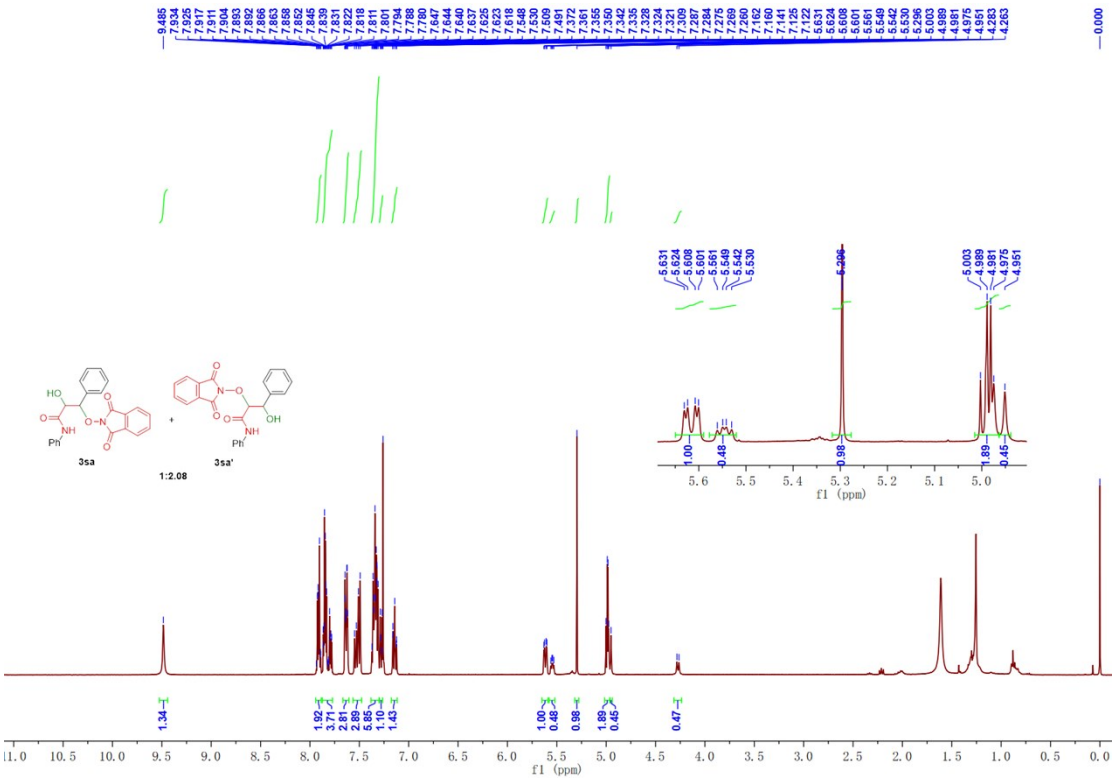
400 MHz ^{1}H NMR of **3ra** in $CDCl_3$



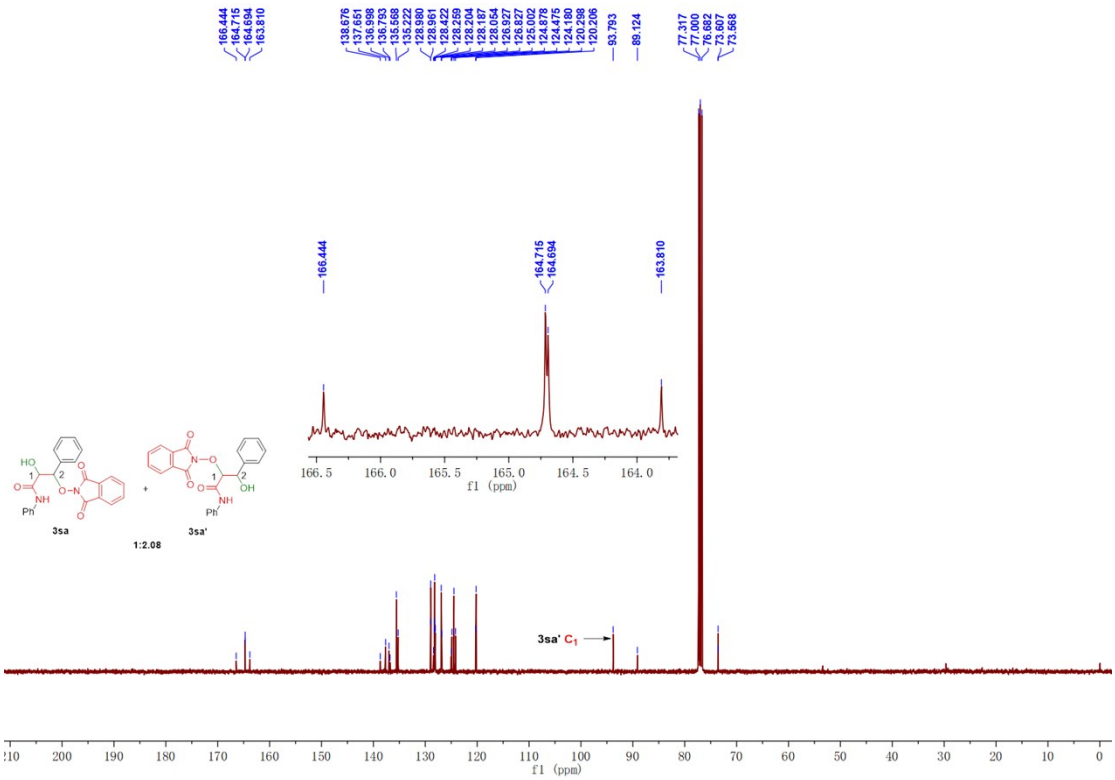
100 MHz ^{13}C NMR of **3ra** in $CDCl_3$



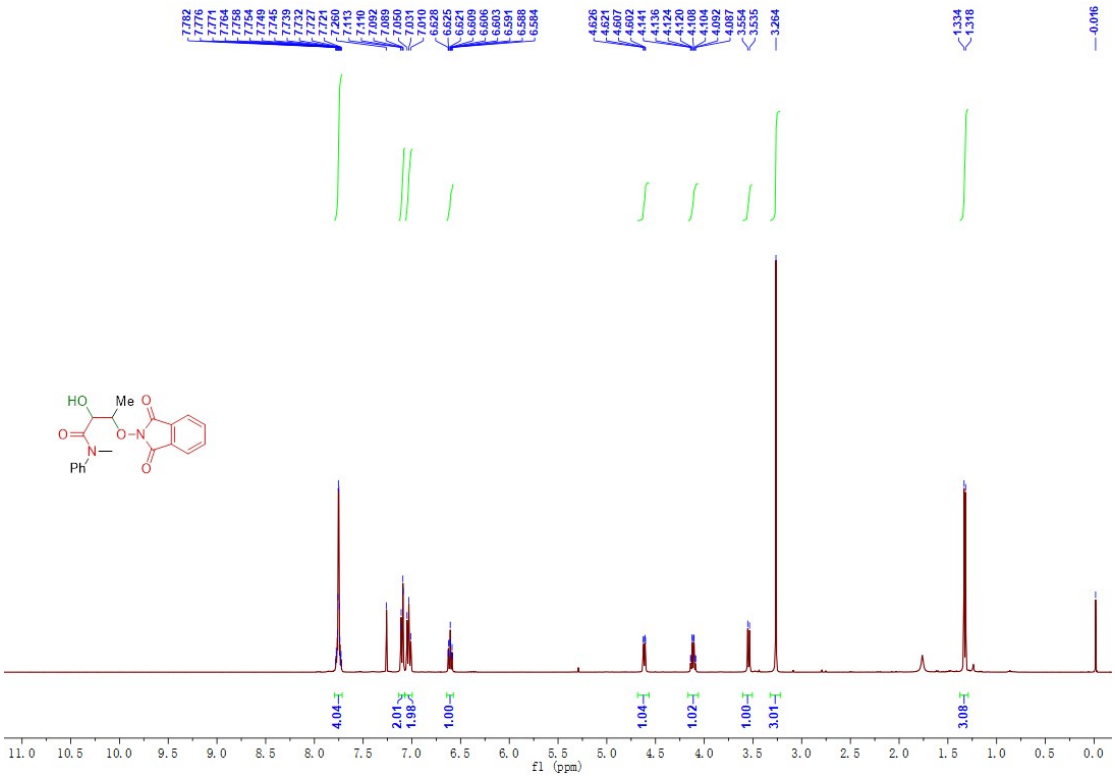
400 MHz ^{1}H NMR of **3sa** and **3sa'** in $CDCl_3$



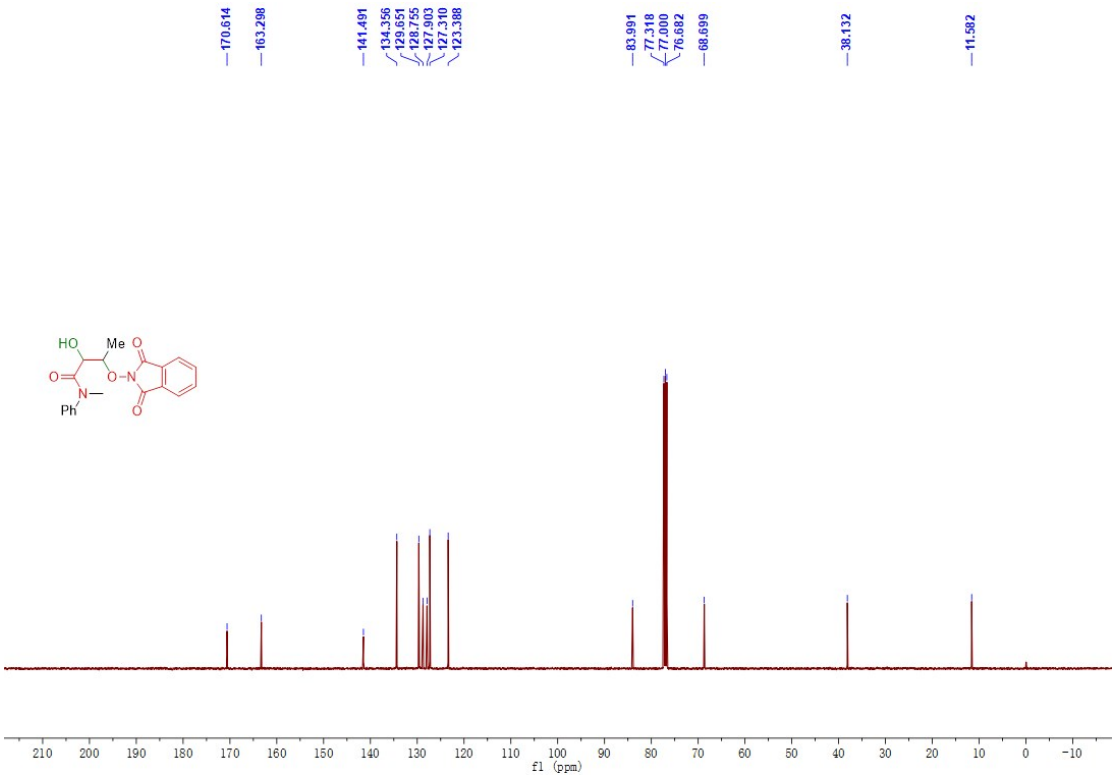
100 MHz ^{13}C NMR of **3sa** and **3sa'** in $CDCl_3$



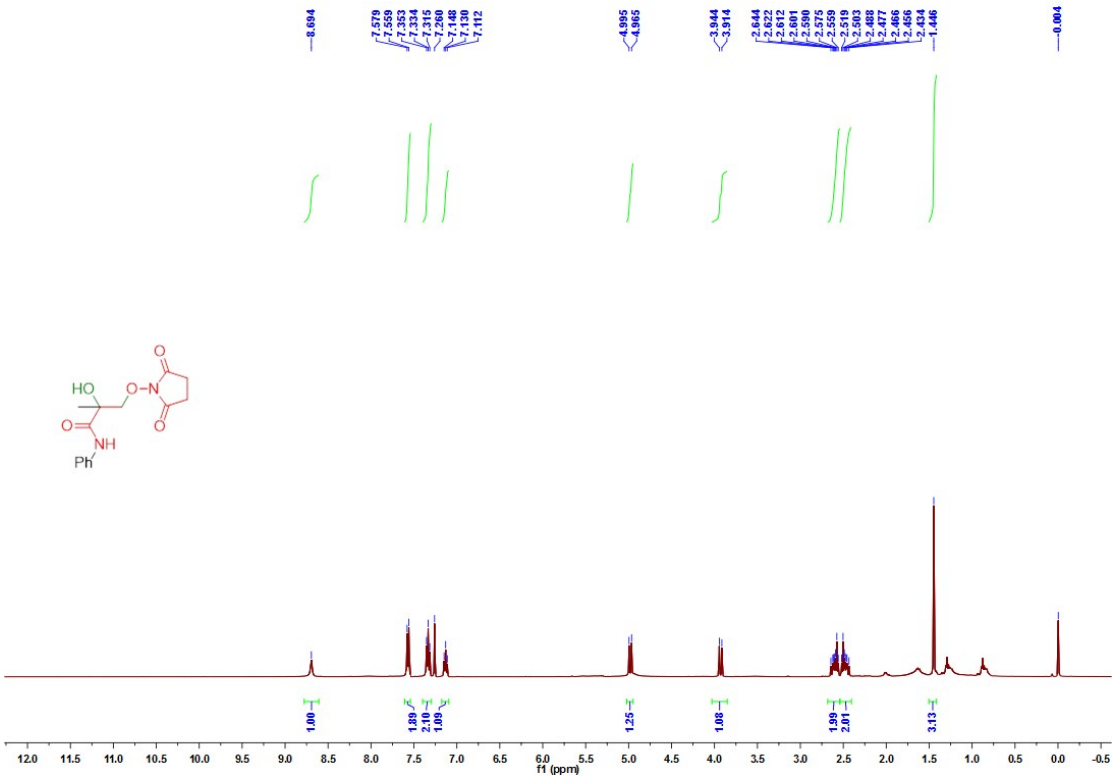
400 MHz ^{1}H NMR of **3ta** in $CDCl_3$



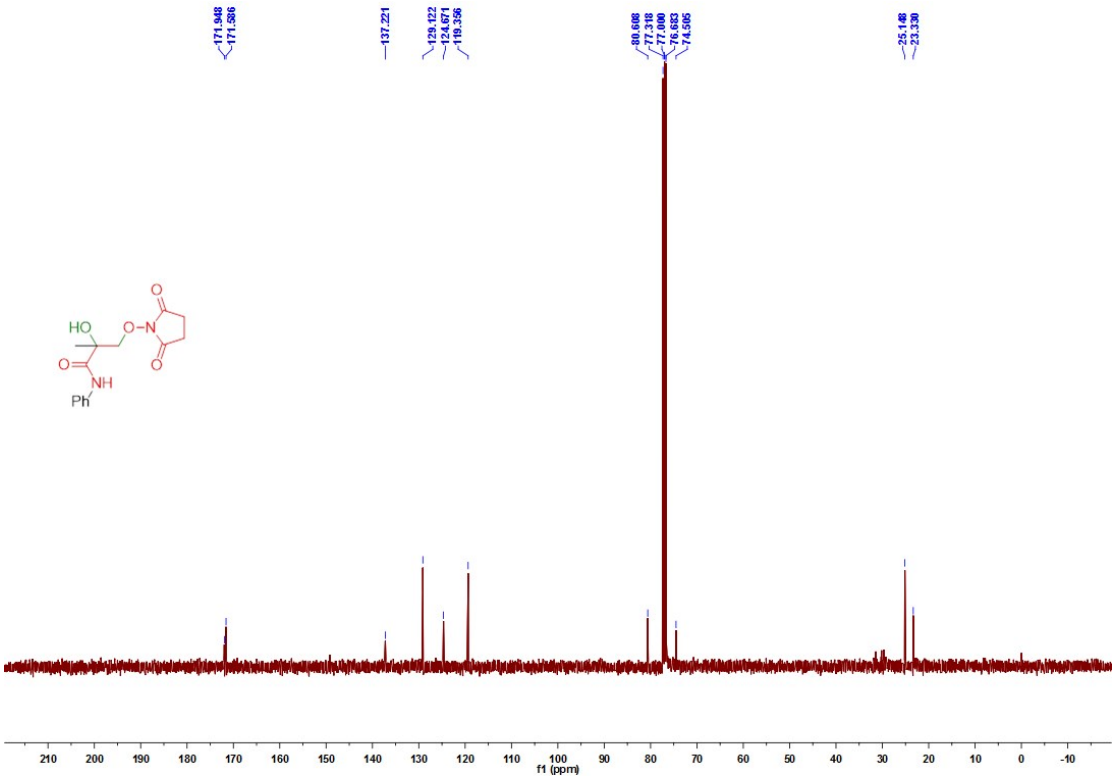
100 MHz ^{13}C NMR of **3ta** in $CDCl_3$



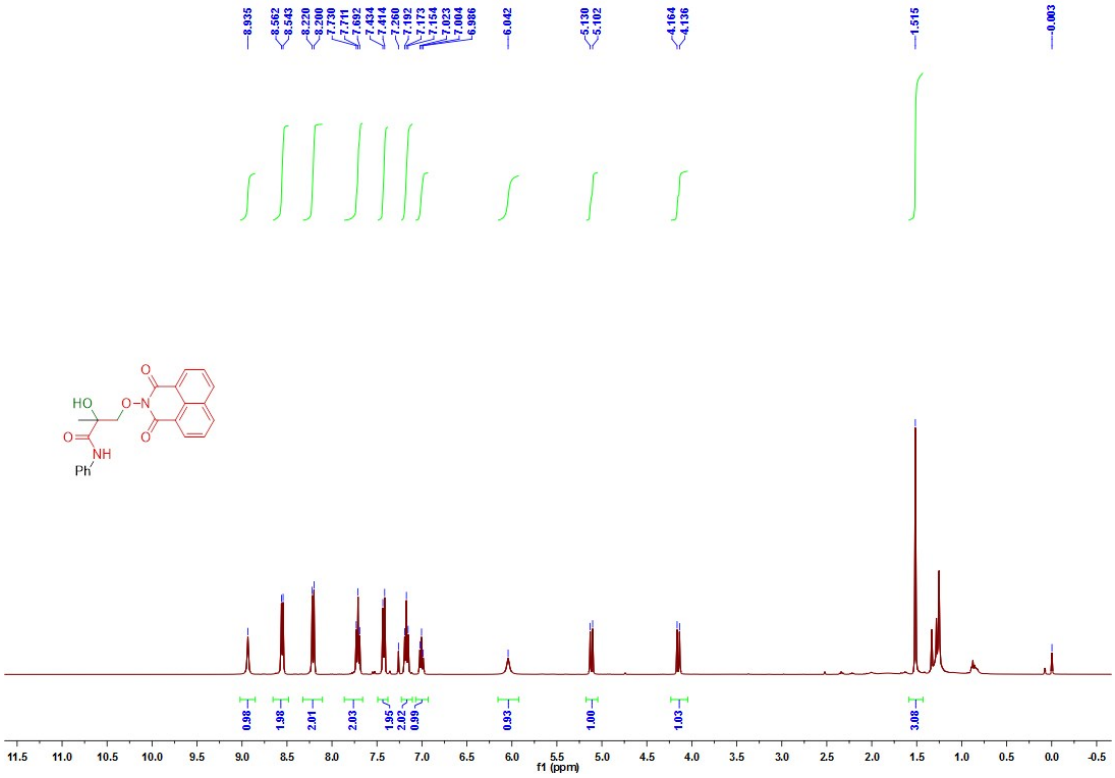
400 MHz ^{1}H NMR of **3db** in $CDCl_3$



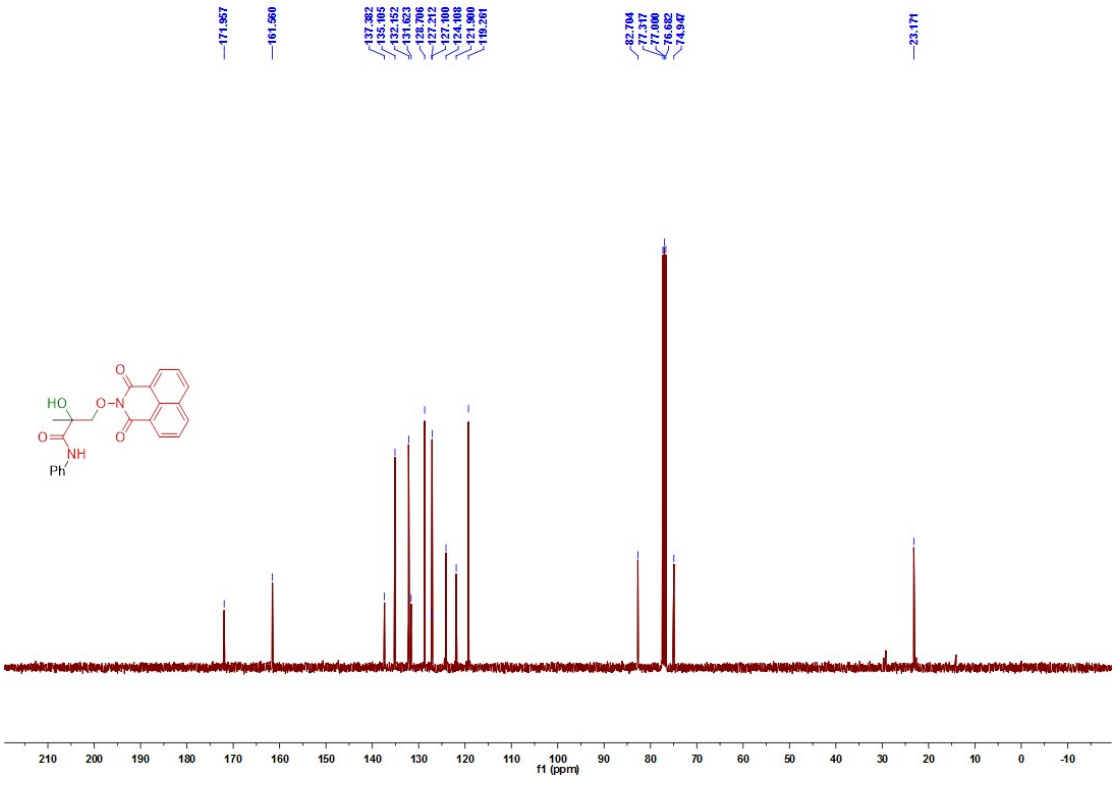
100 MHz ^{13}C NMR of **3db** in $CDCl_3$



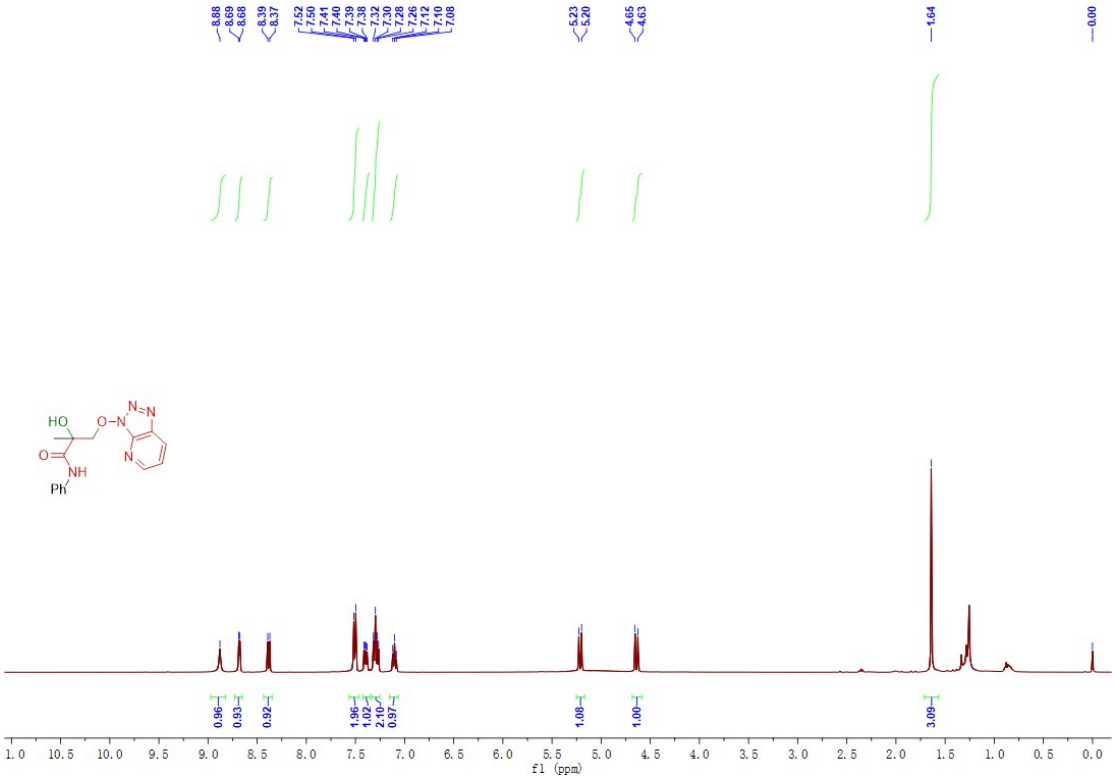
400 MHz ^{1}H NMR of **3dc** in $CDCl_3$



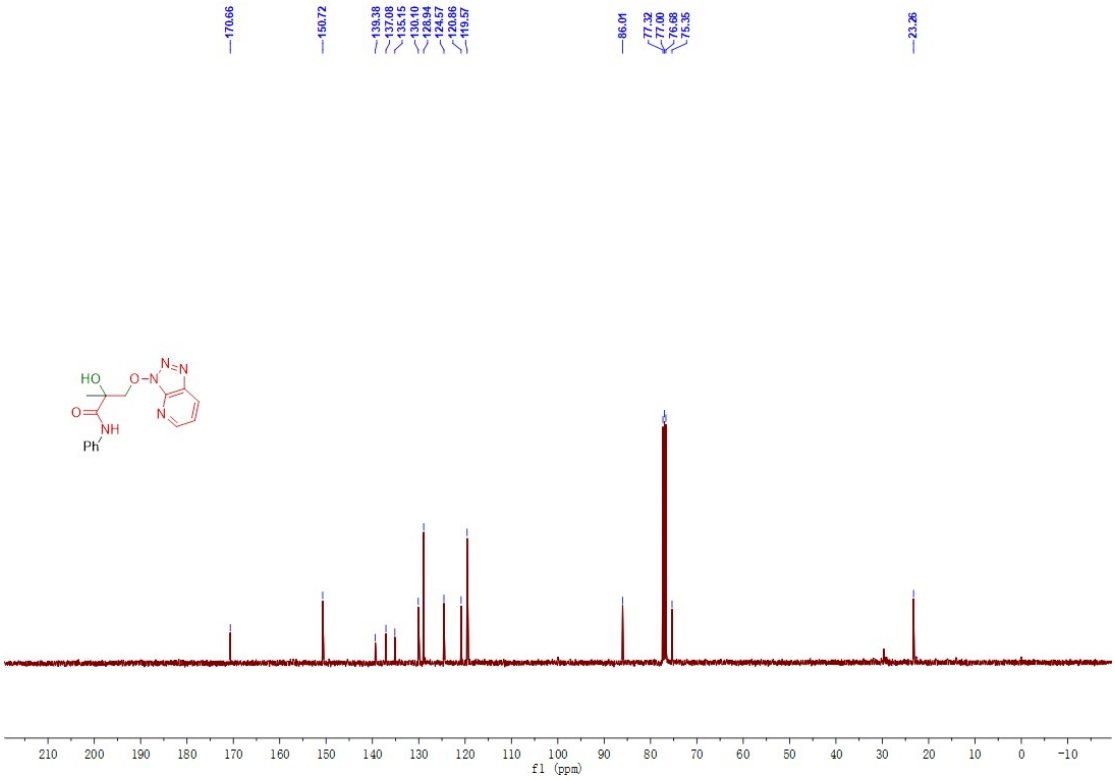
100 MHz ^{13}C NMR of **3dc** in $CDCl_3$



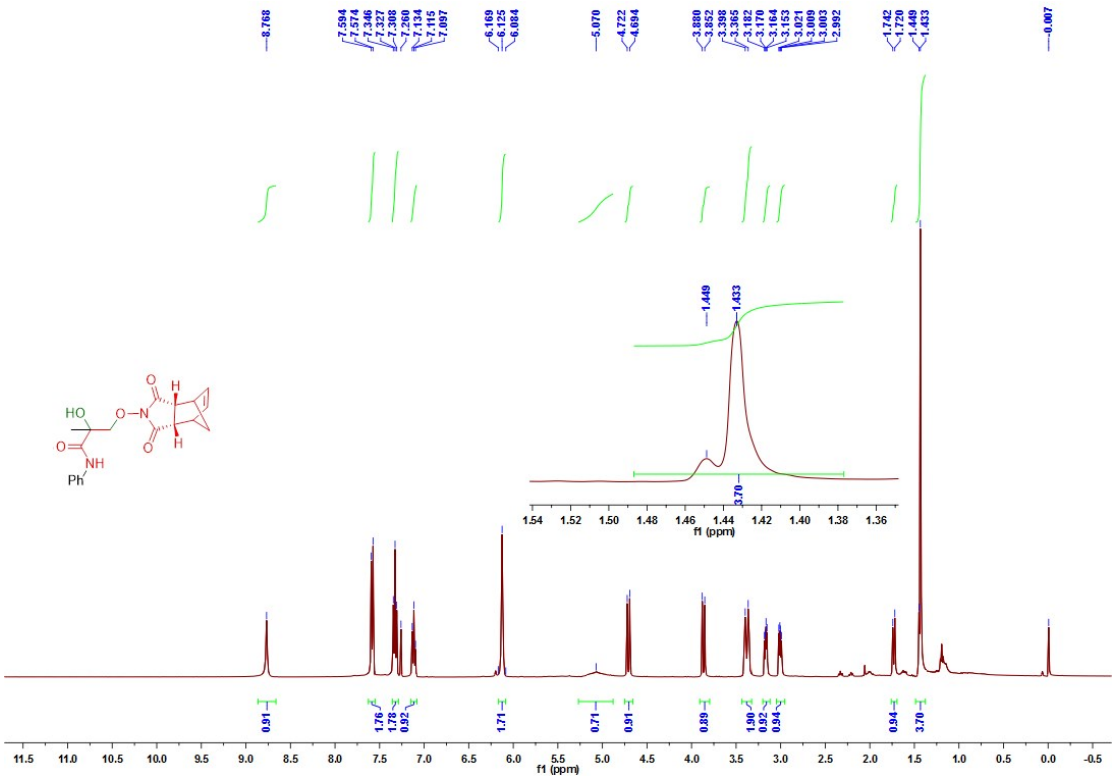
400 MHz ^{1}H NMR of **3dd** in $CDCl_3$



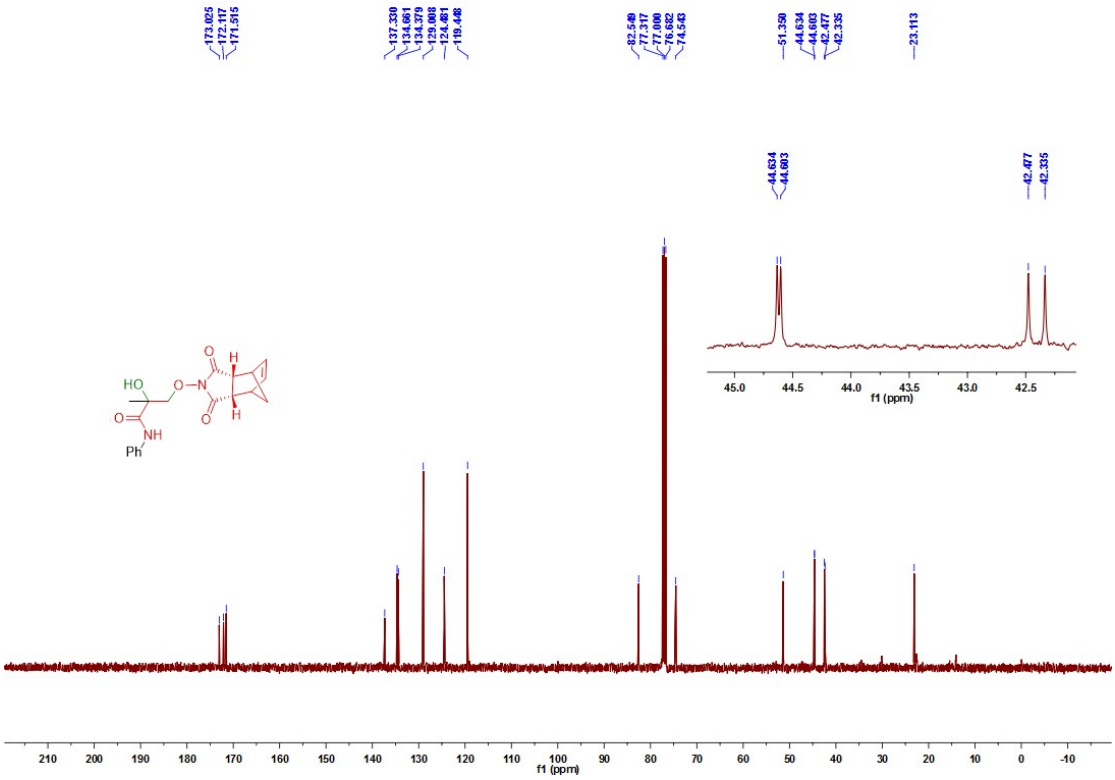
100 MHz ^{13}C NMR of **3dd** in $CDCl_3$



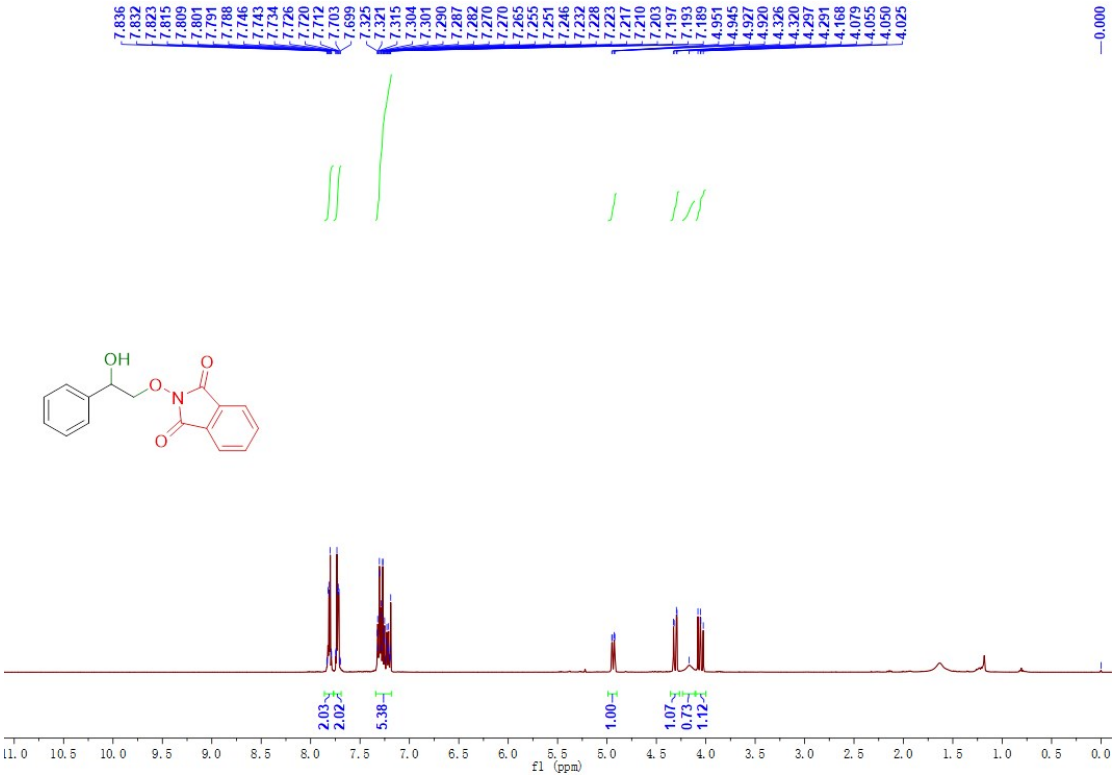
400 MHz ^{1}H NMR of **3de** in $CDCl_3$



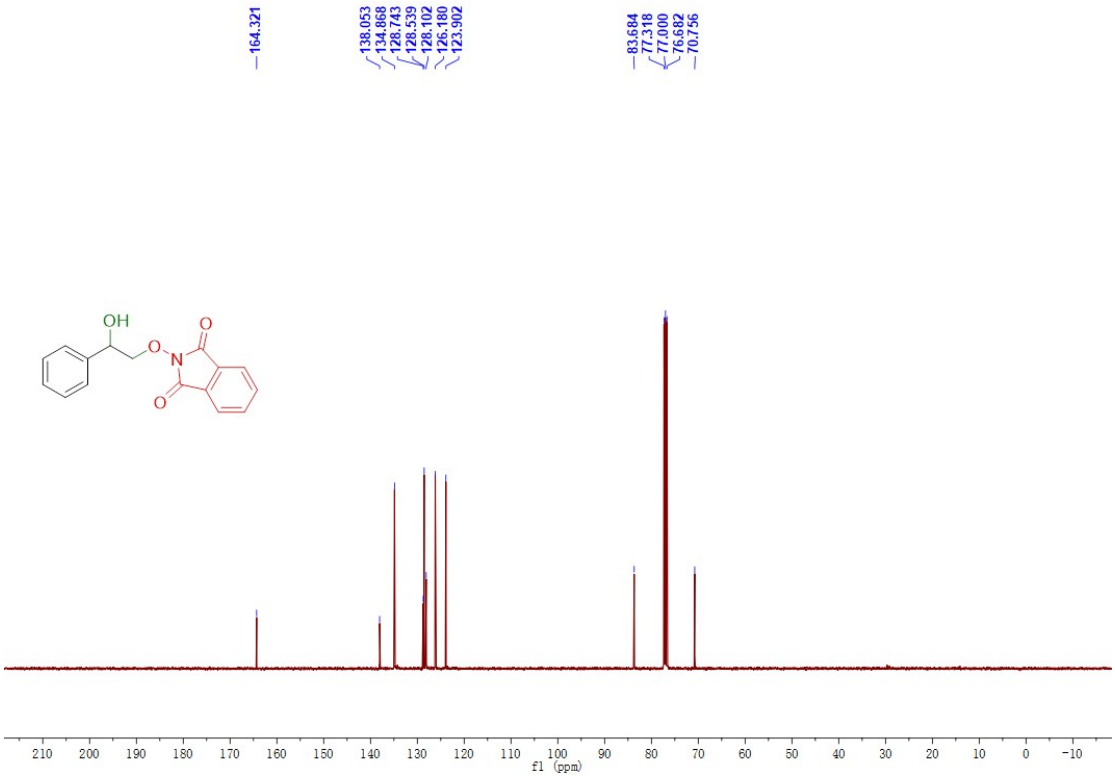
100 MHz ^{13}C NMR of **3de** in $CDCl_3$



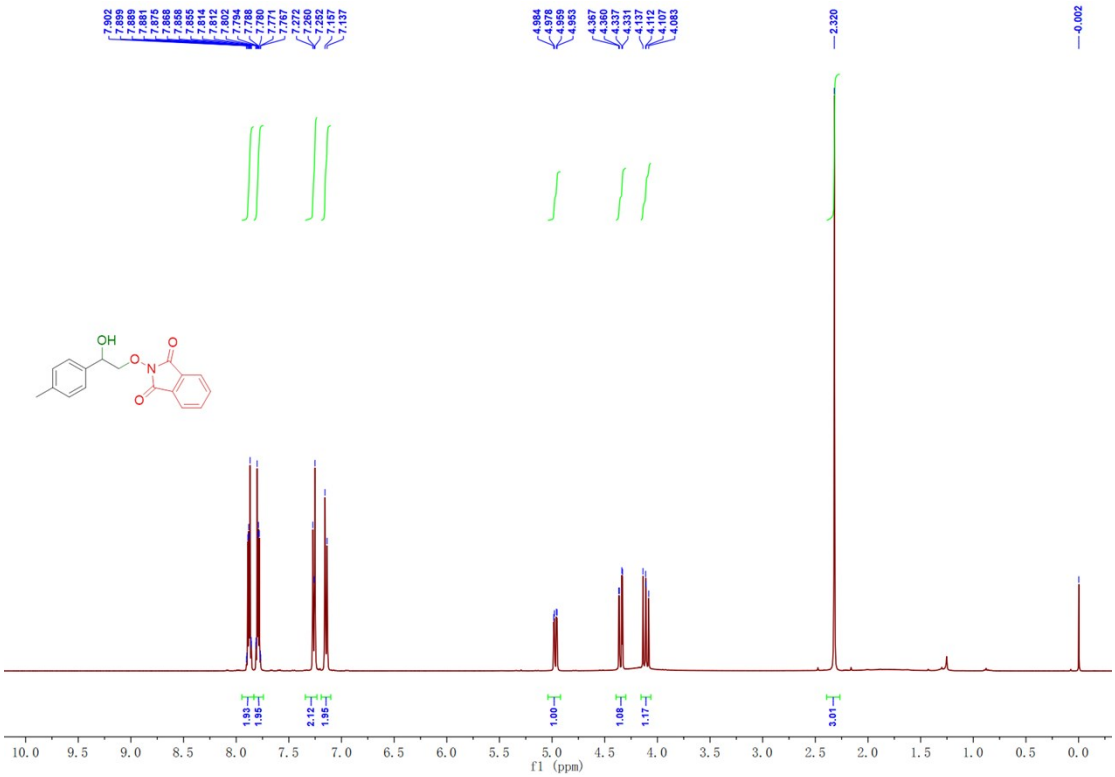
400 MHz ^{1}H NMR of **5a** in $CDCl_3$



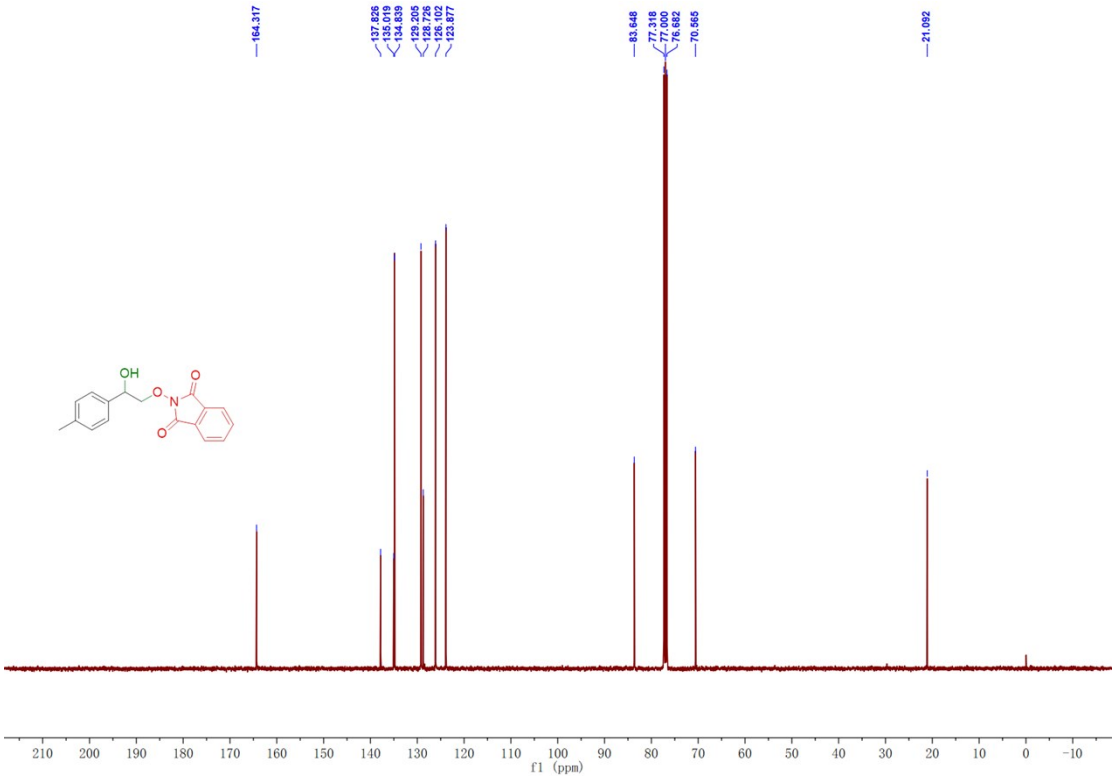
100 MHz ^{13}C NMR of **5a** in $CDCl_3$



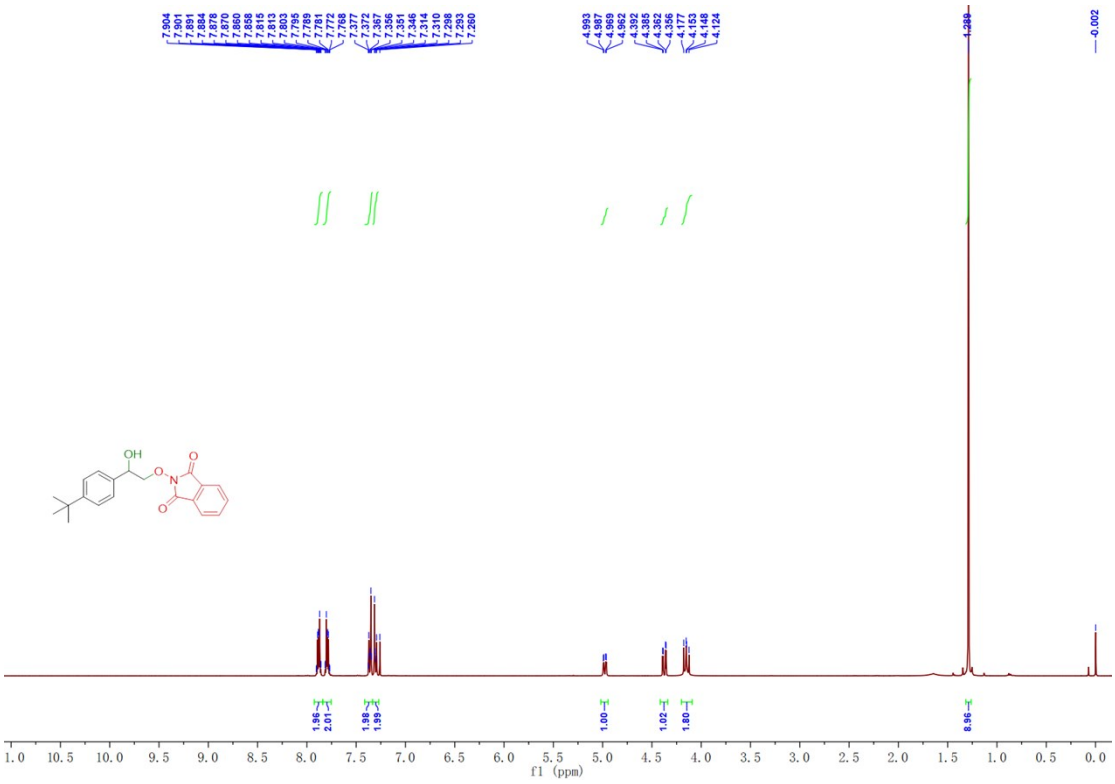
400 MHz ^{1}H NMR of **5b** in $CDCl_3$



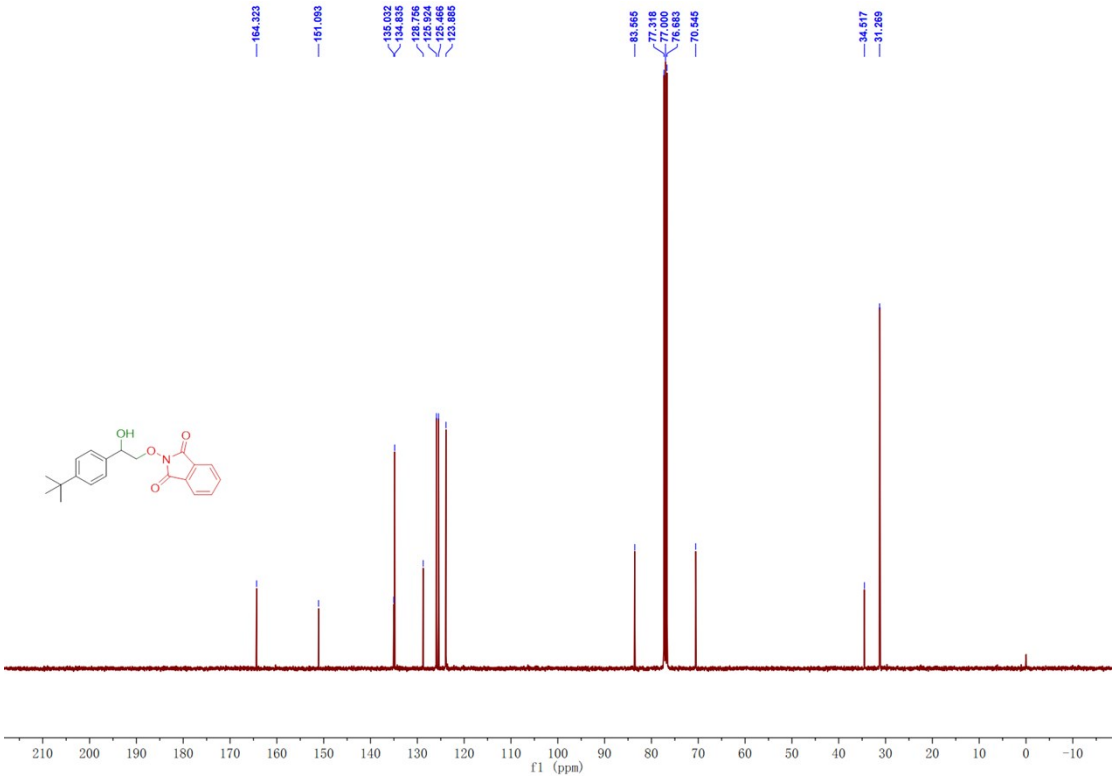
100 MHz ^{13}C NMR of **5b** in $CDCl_3$



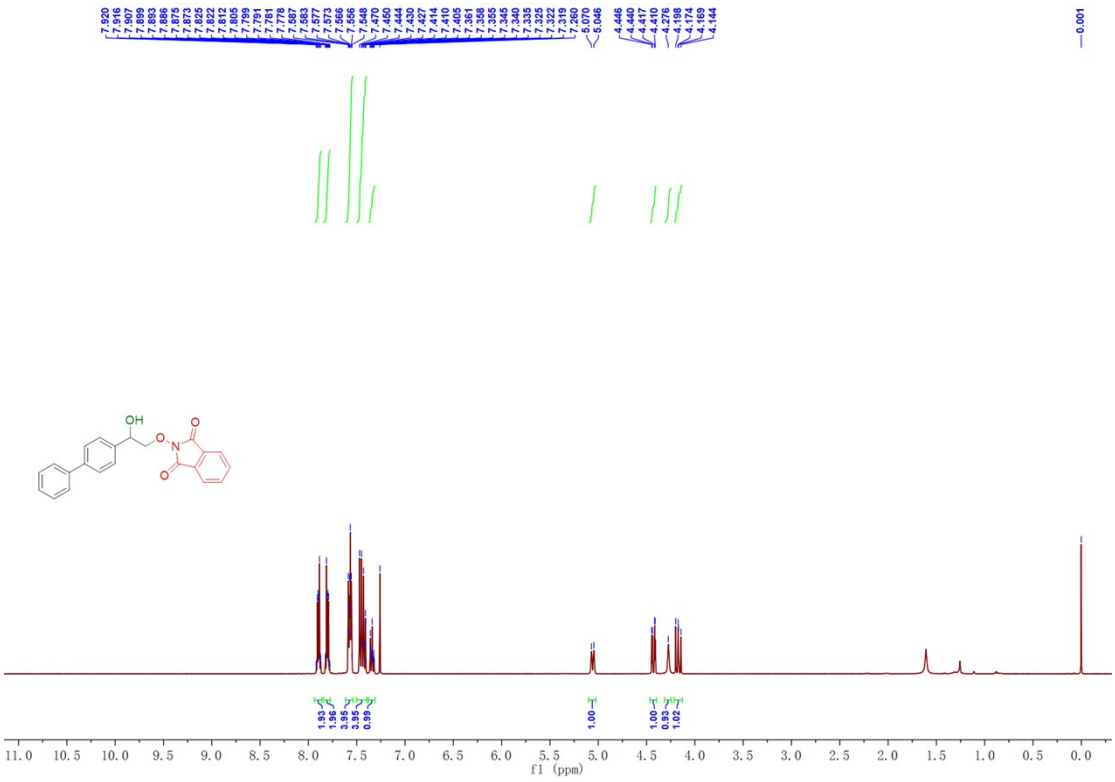
400 MHz ^{1}H NMR of **5c** in $CDCl_3$



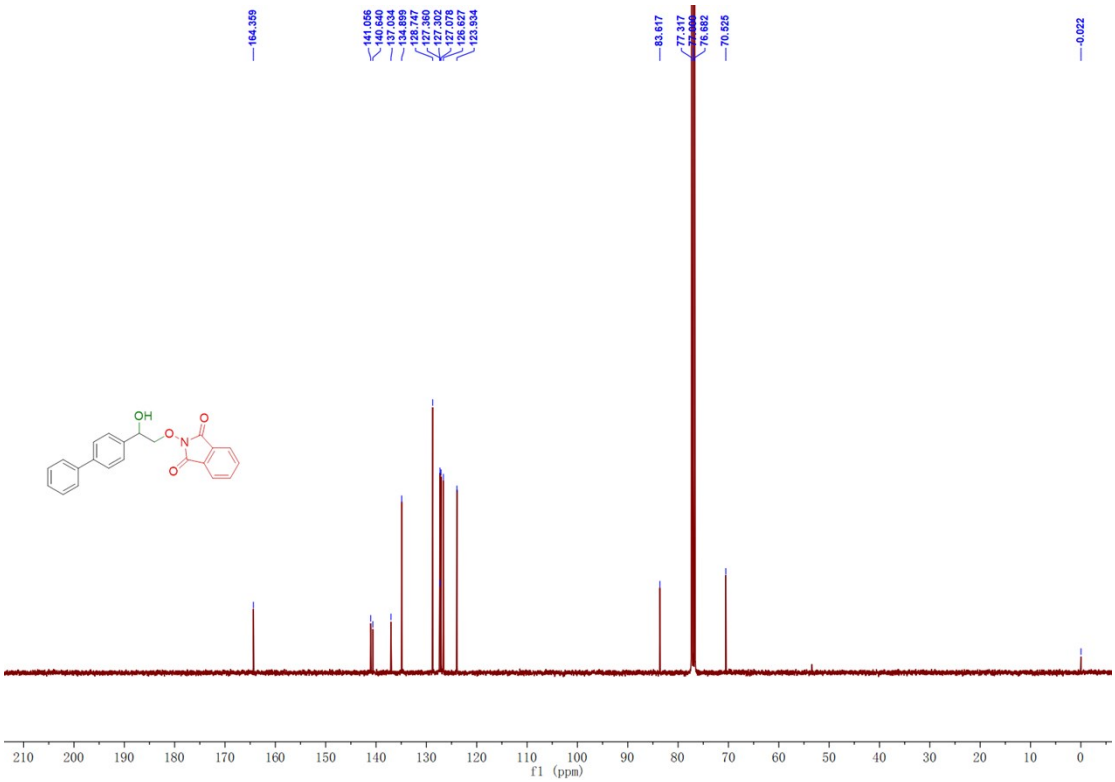
100 MHz ^{13}C NMR of **5c** in $CDCl_3$



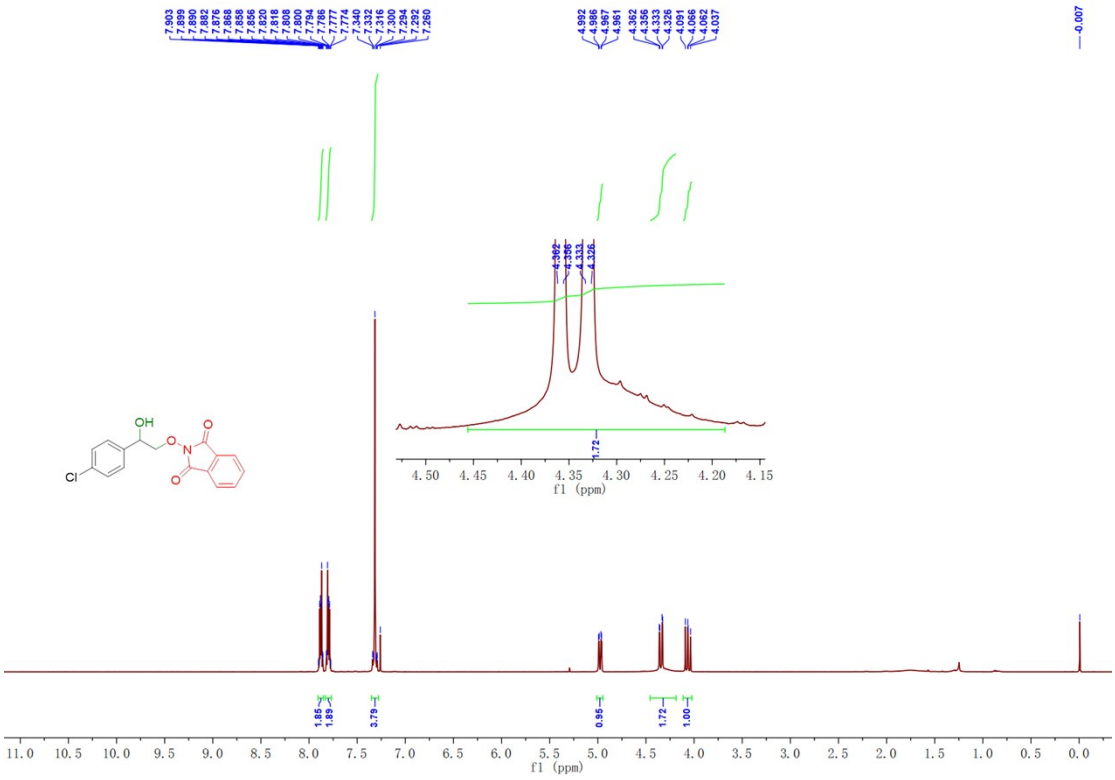
400 MHz ^{1}H NMR of **5d** in $CDCl_3$



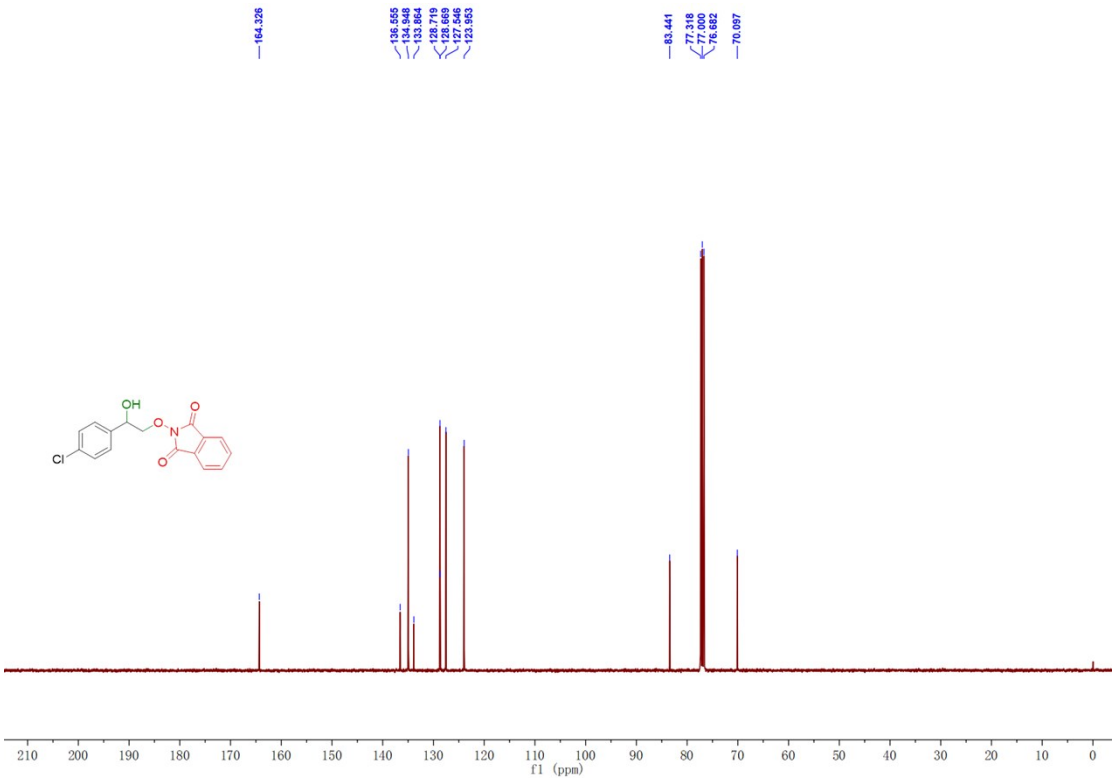
100 MHz ^{13}C NMR of **5d** in $CDCl_3$



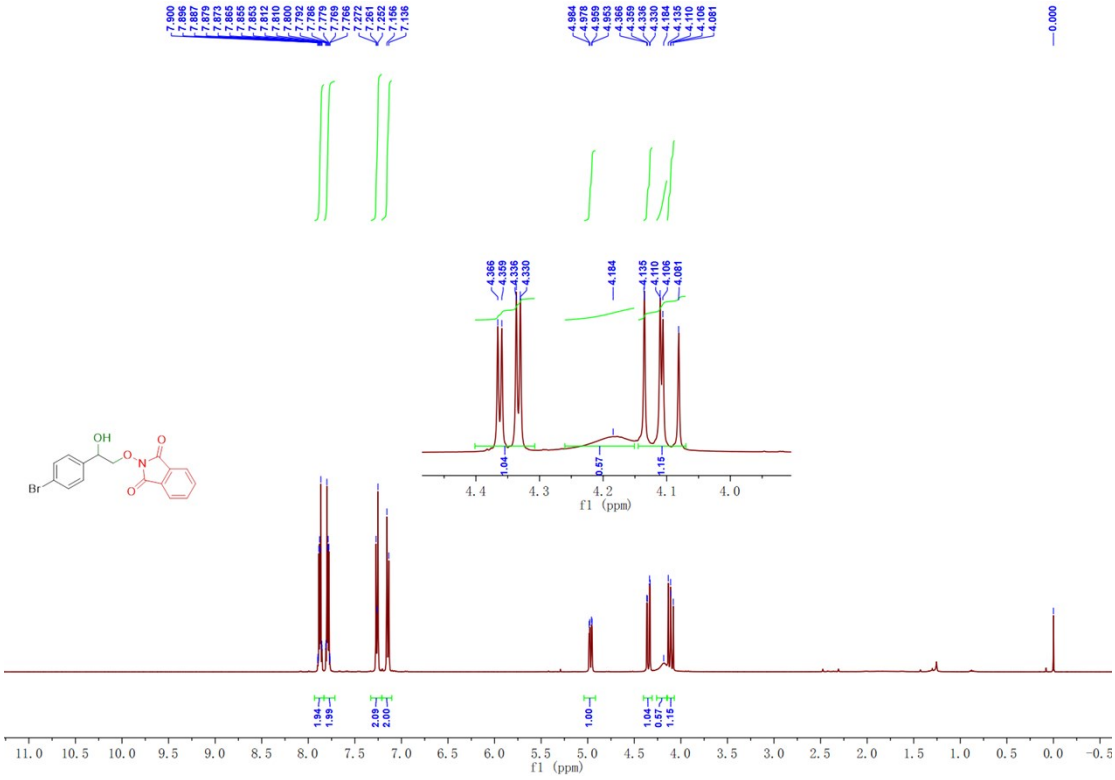
400 MHz ^{1}H NMR of **5e** in $CDCl_3$



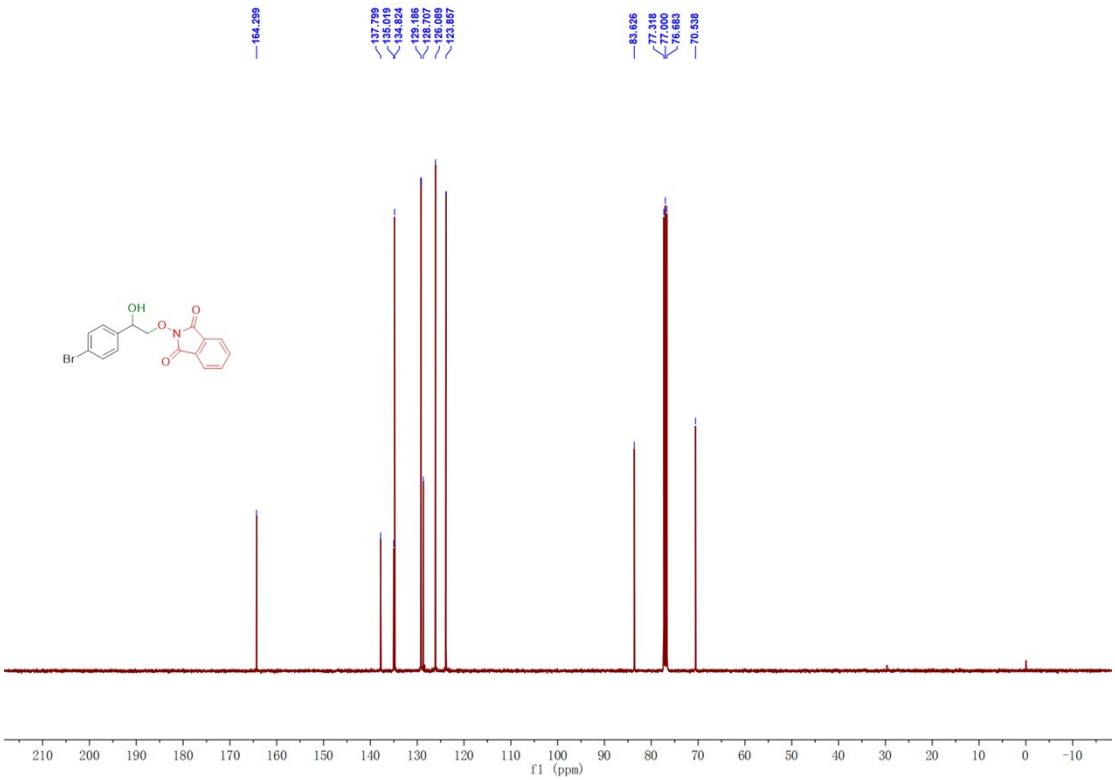
100 MHz ^{13}C NMR of **5e** in $CDCl_3$



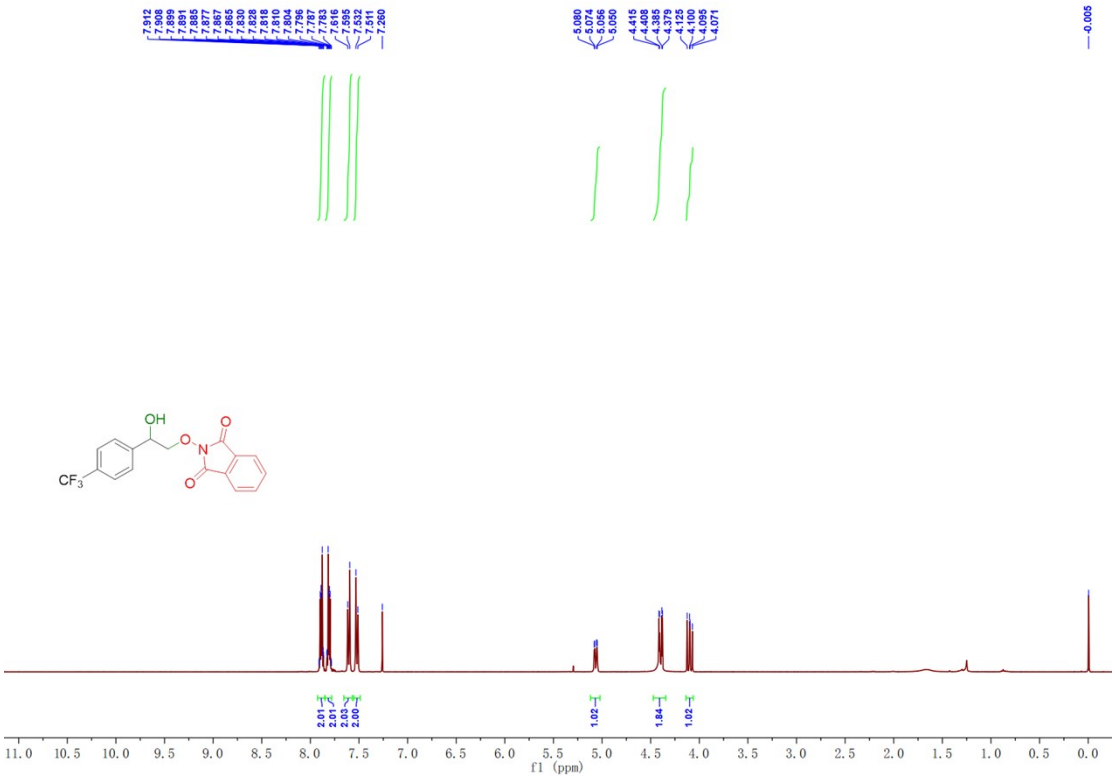
400 MHz ^{1}H NMR of **5f** in $CDCl_3$



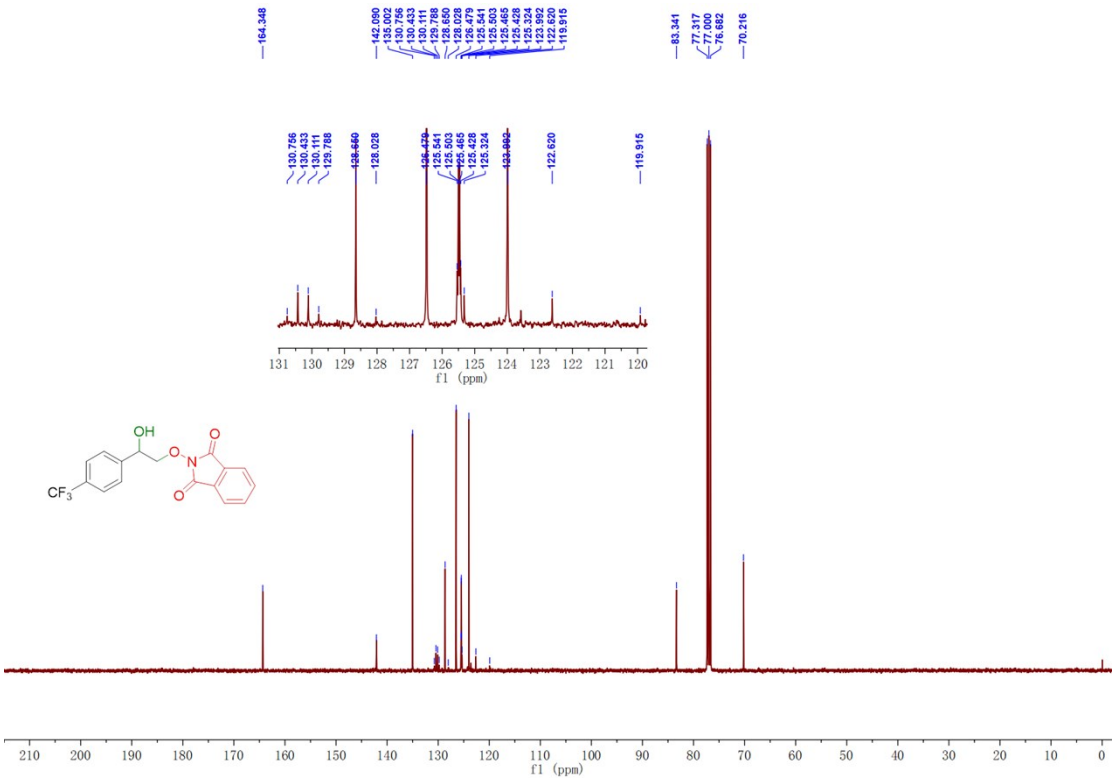
100 MHz ^{13}C NMR of **5f** in $CDCl_3$



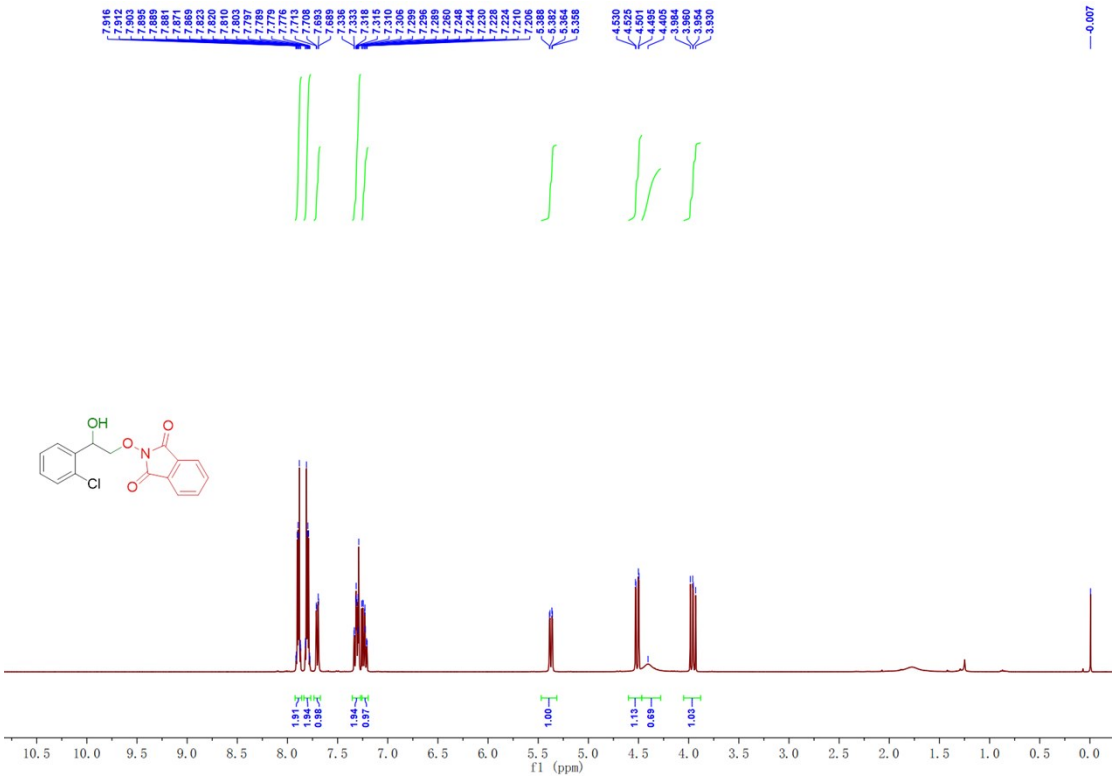
400 MHz ^{1}H NMR of **5g** in $CDCl_3$



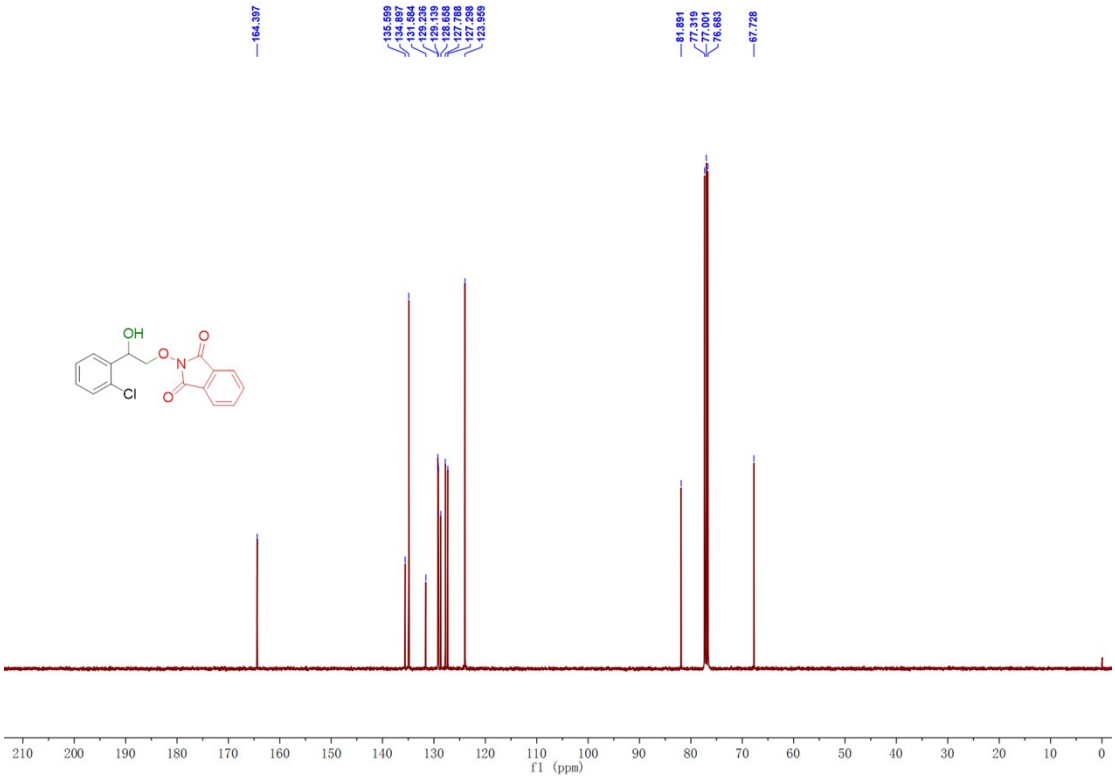
100 MHz ^{13}C NMR of **5g** in $CDCl_3$



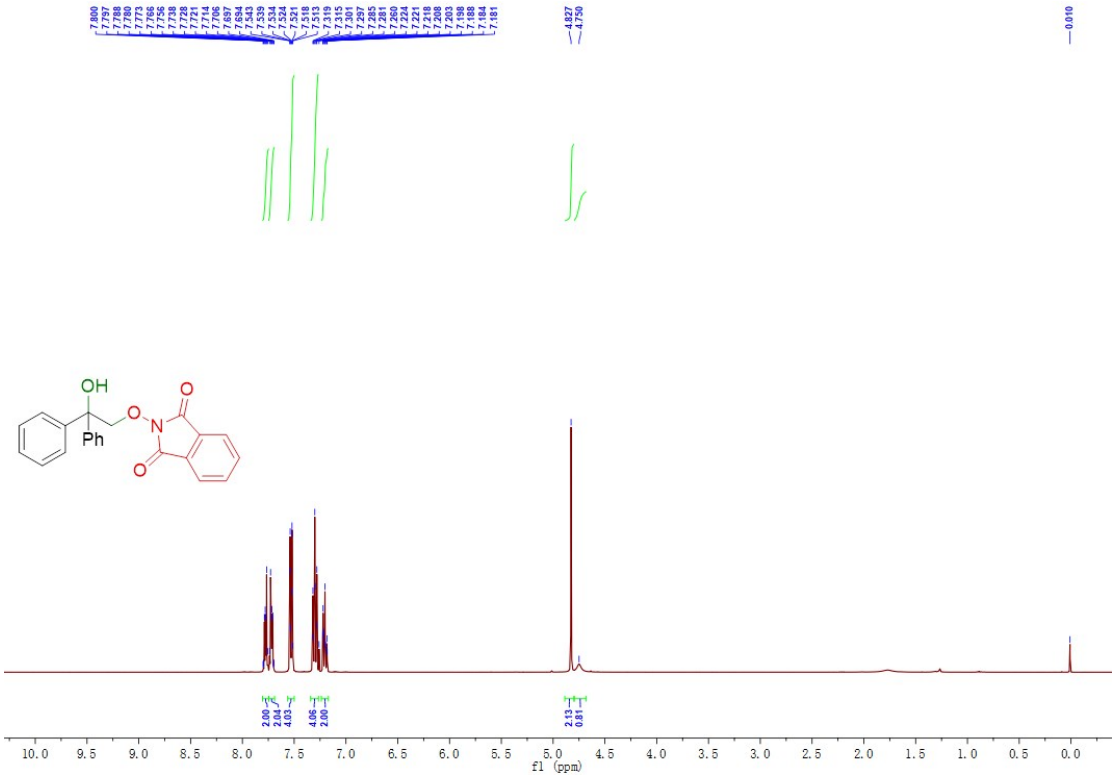
400 MHz ^{1}H NMR of **5h** in $CDCl_3$



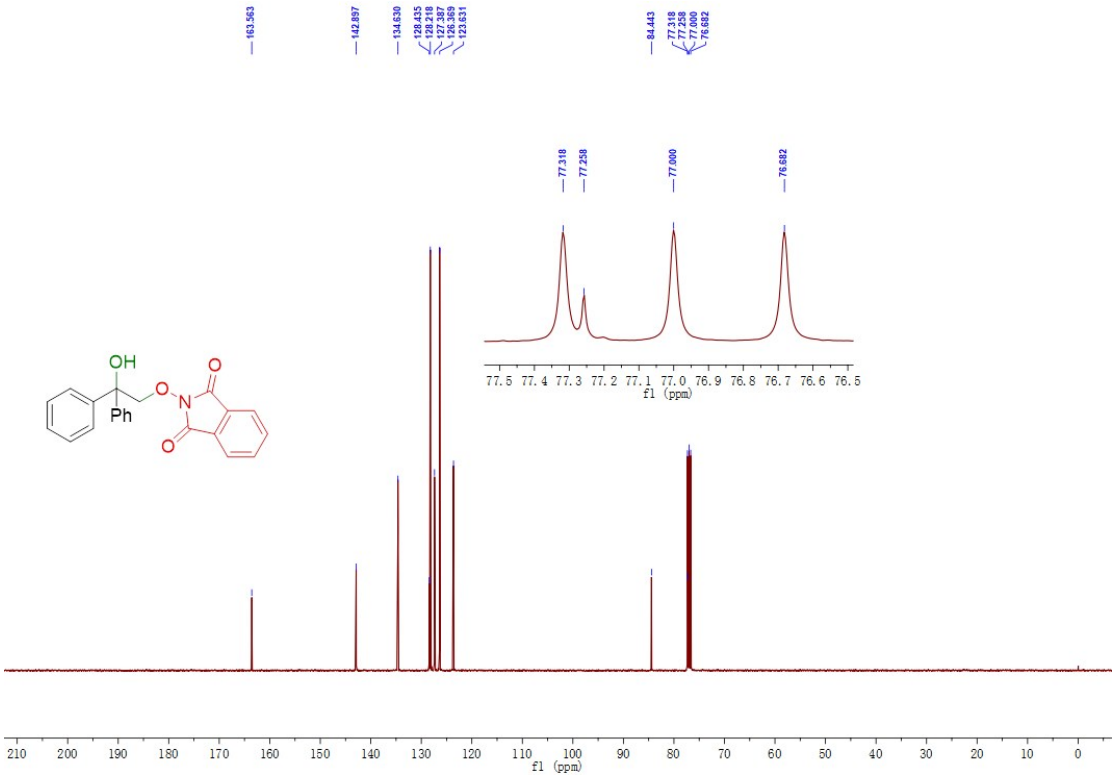
100 MHz ^{13}C NMR of **5h** in $CDCl_3$



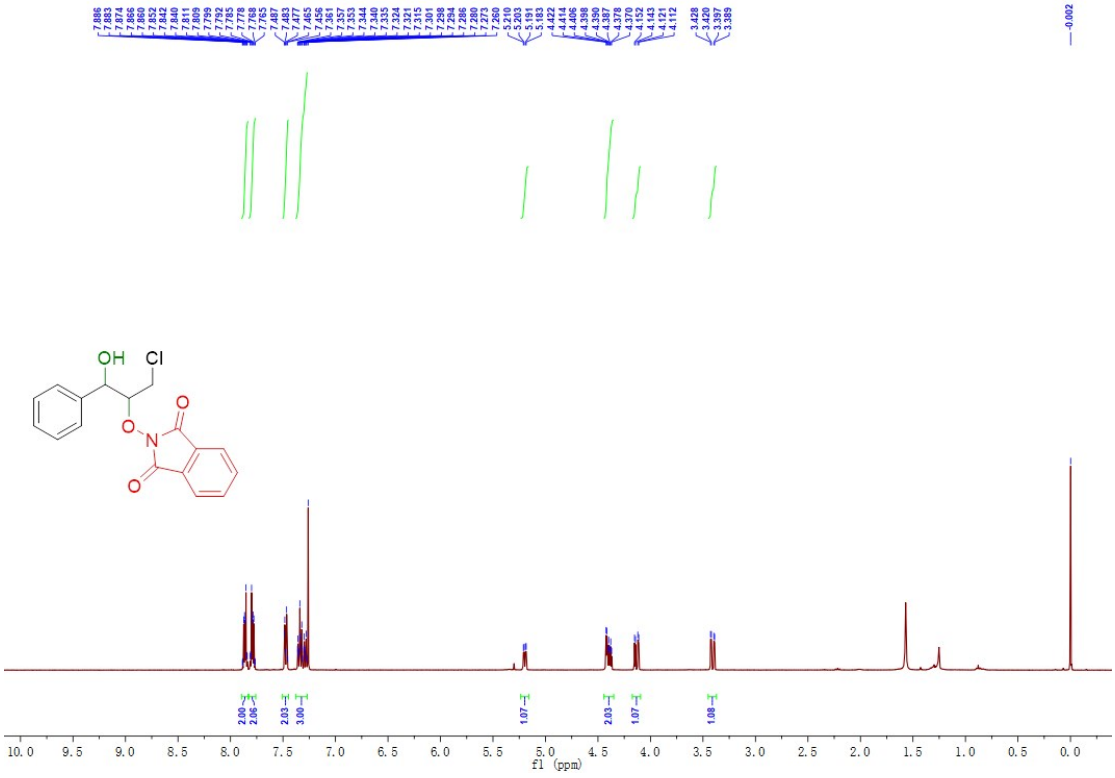
400 MHz ^{1}H NMR of **5i** in $CDCl_3$



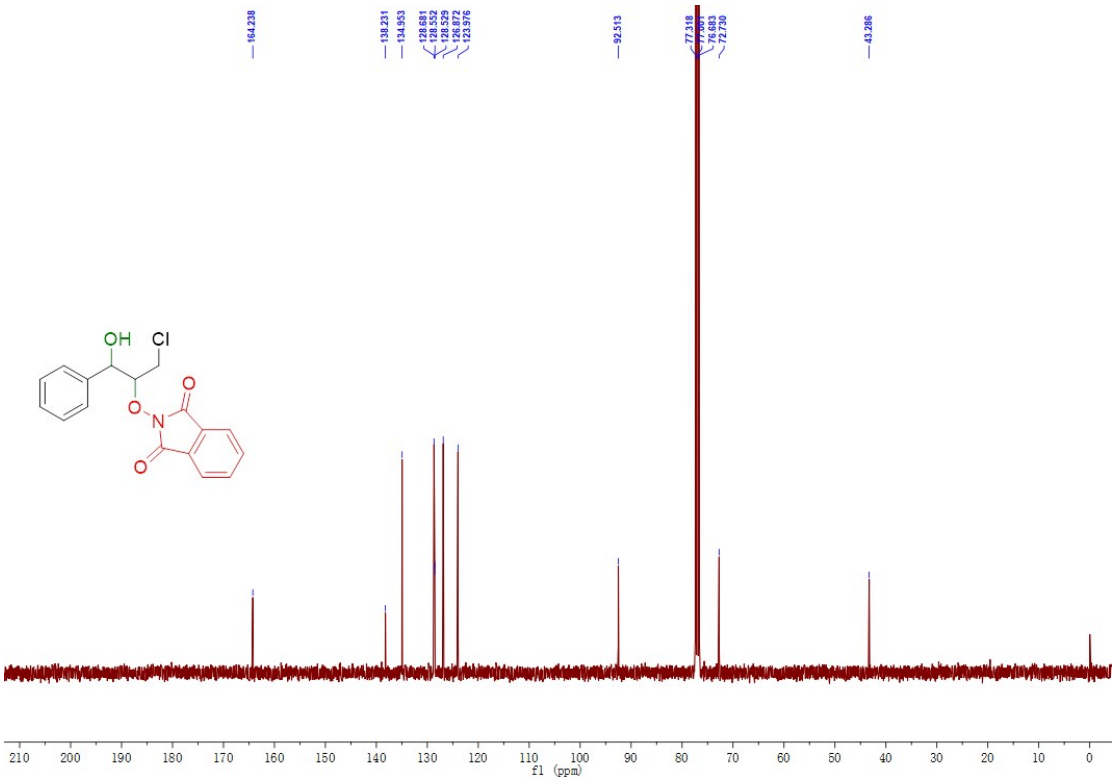
100 MHz ^{13}C NMR of **5i** in $CDCl_3$



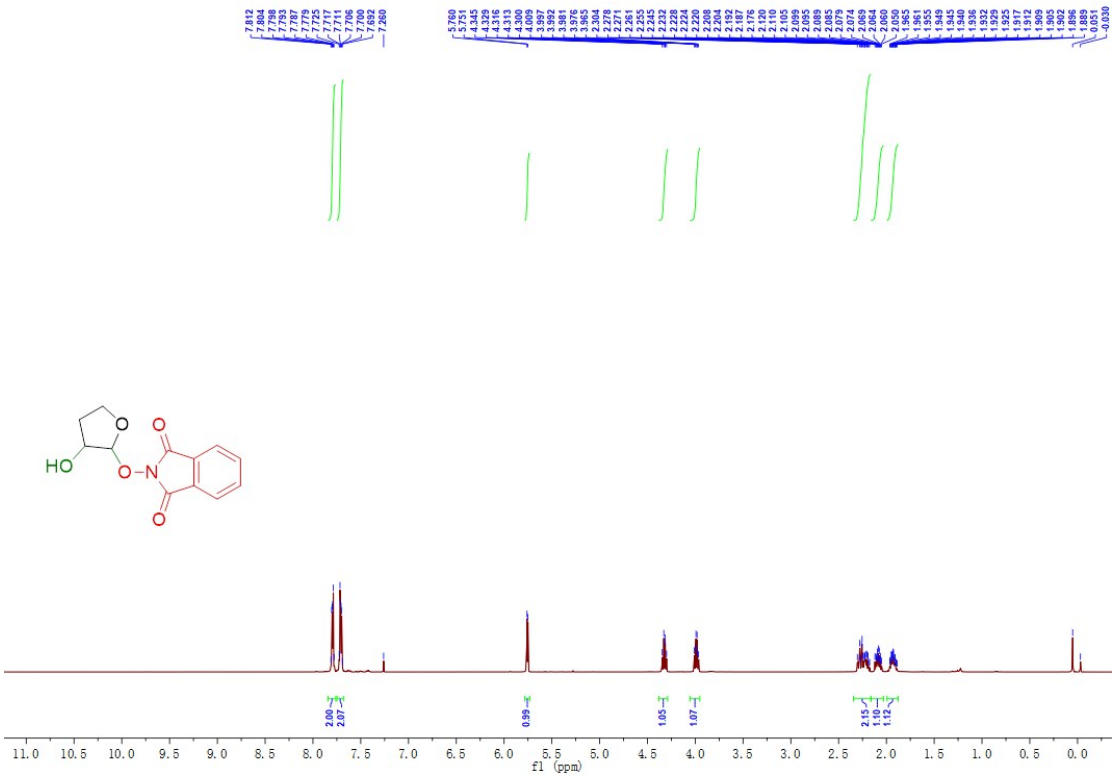
400 MHz ^{1}H NMR of **5j** in $CDCl_3$



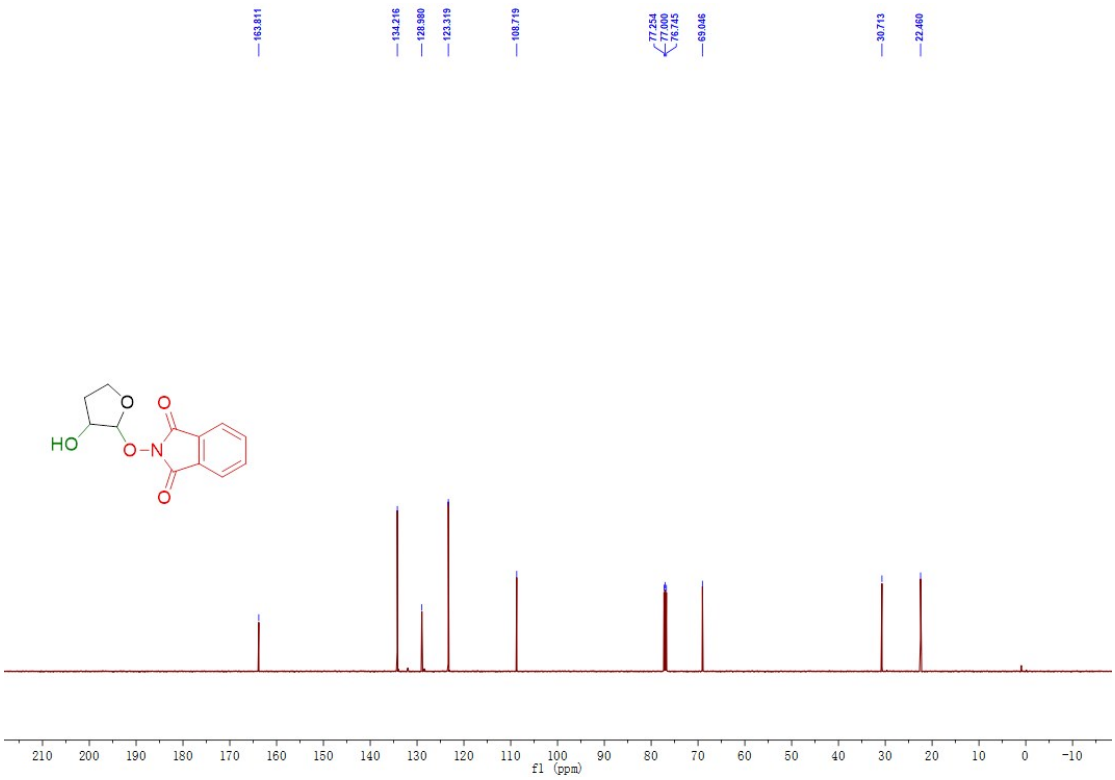
100 MHz ^{13}C NMR of **5j** in $CDCl_3$



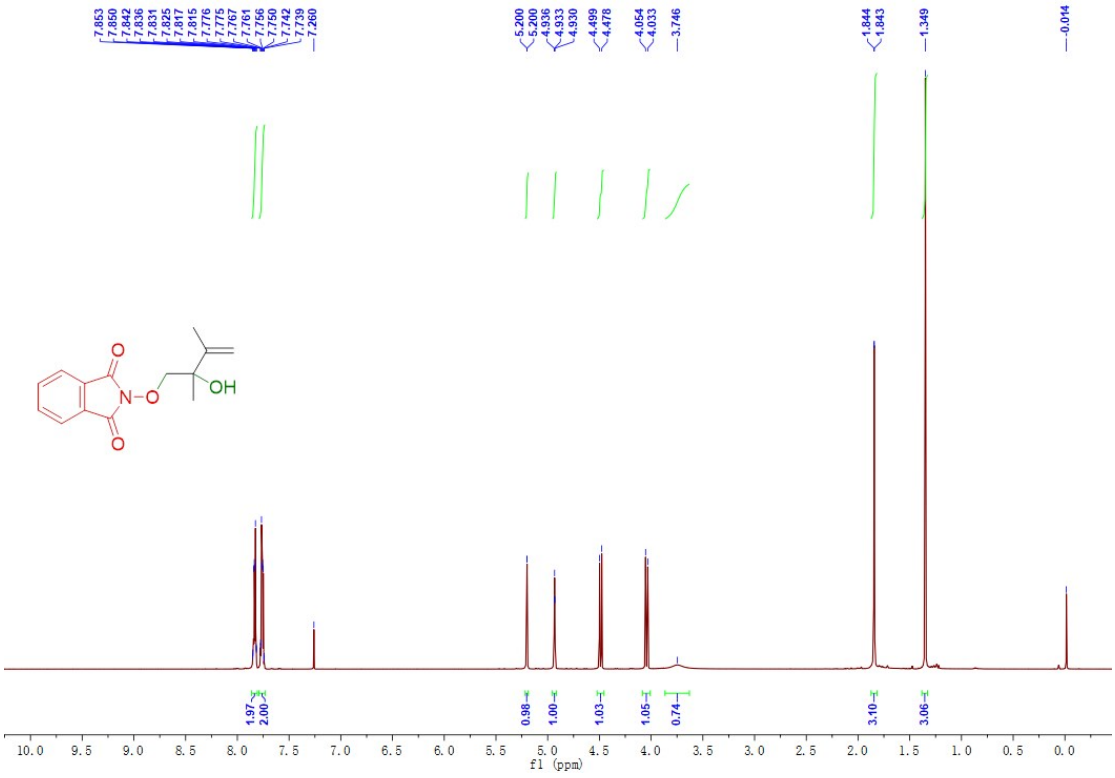
500 MHz ^{1}H NMR of **5k** in $CDCl_3$



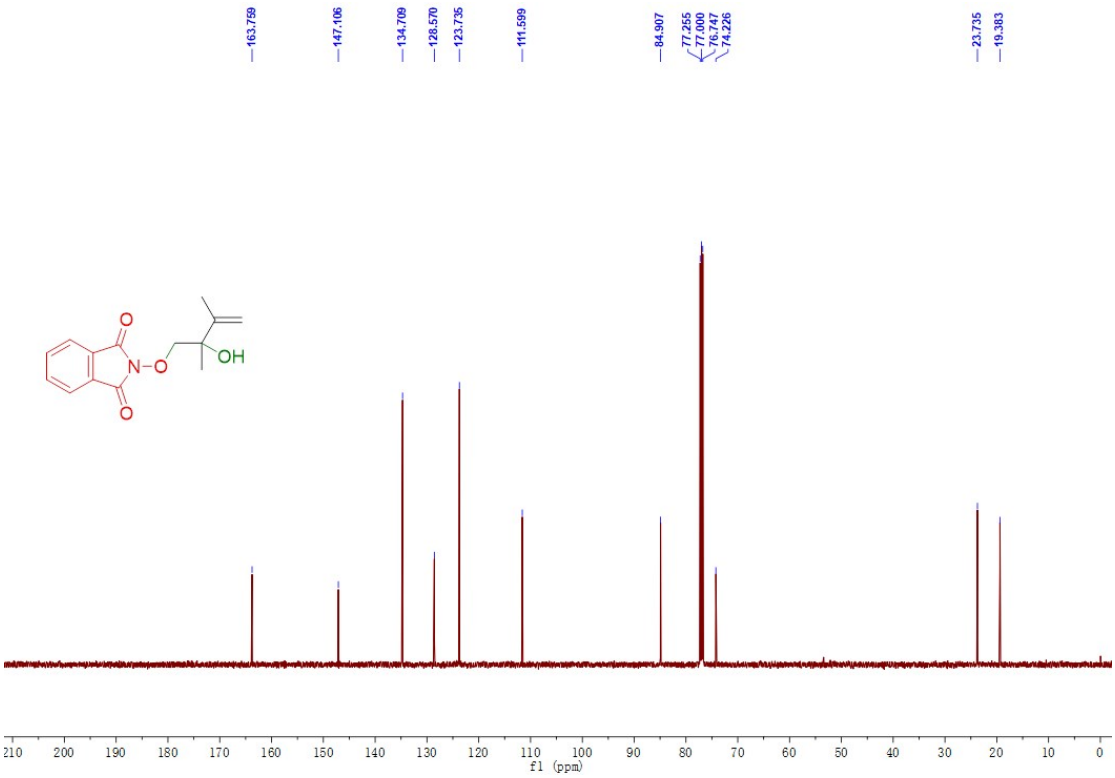
125 MHz ^{13}C NMR of **5k** in $CDCl_3$



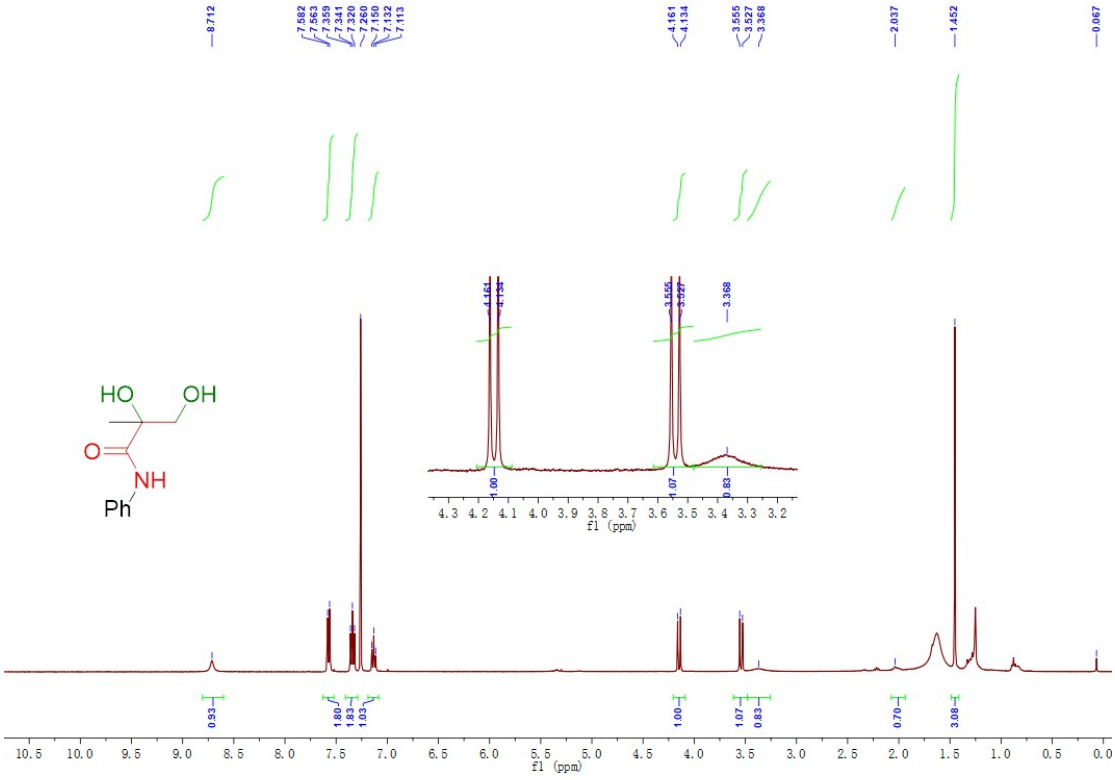
500 MHz ^{1}H NMR of **5l** in $CDCl_3$



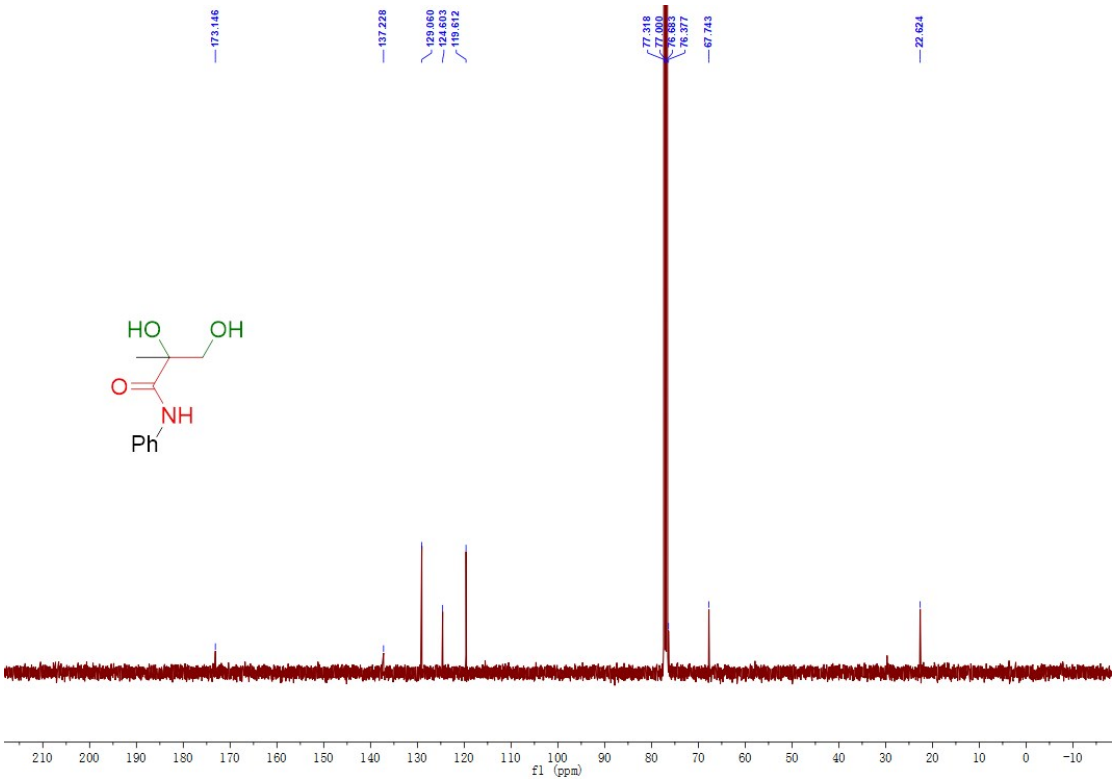
125 MHz ^{13}C NMR of **5l** in $CDCl_3$



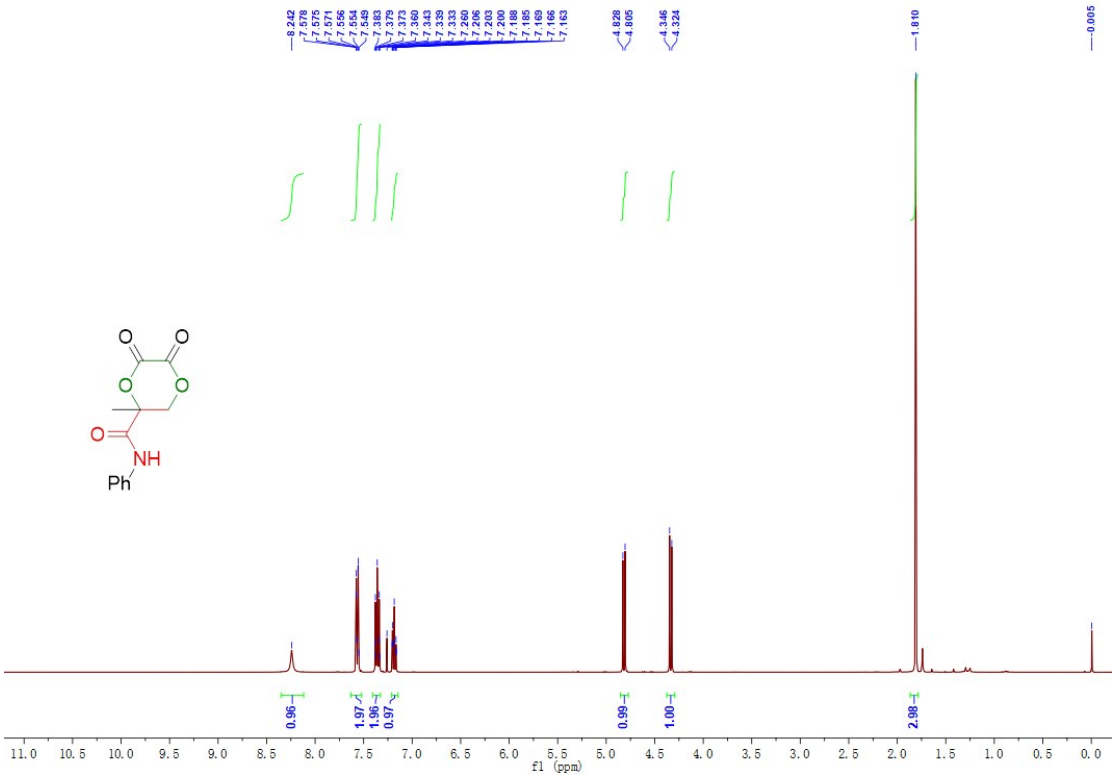
400 MHz ^{1}H NMR of **6** in $CDCl_3$



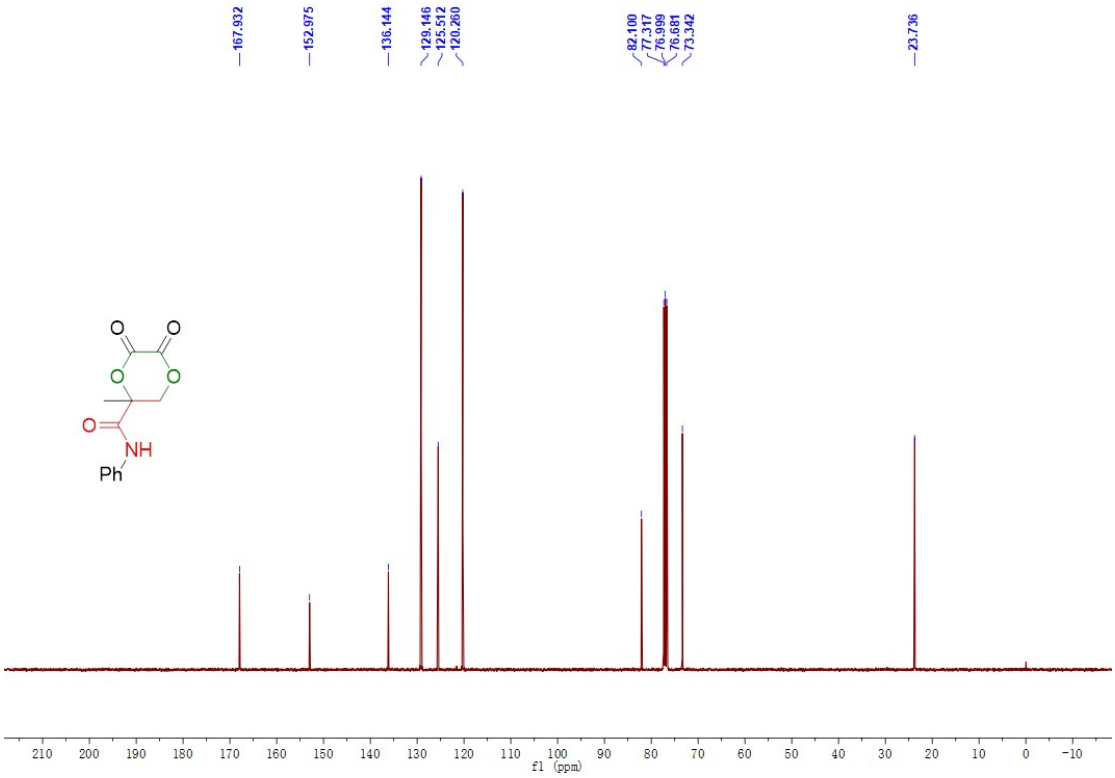
100 MHz ^{13}C NMR of **6** in $CDCl_3$



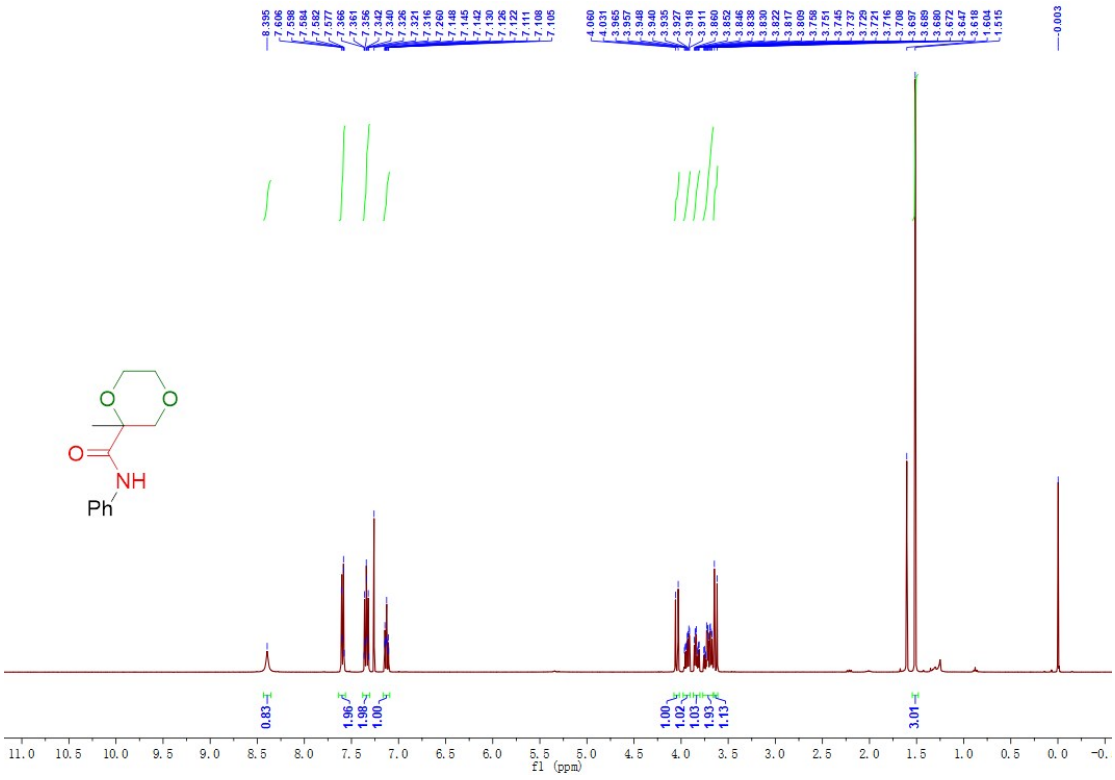
400 MHz ^{1}H NMR of **7** in $CDCl_3$



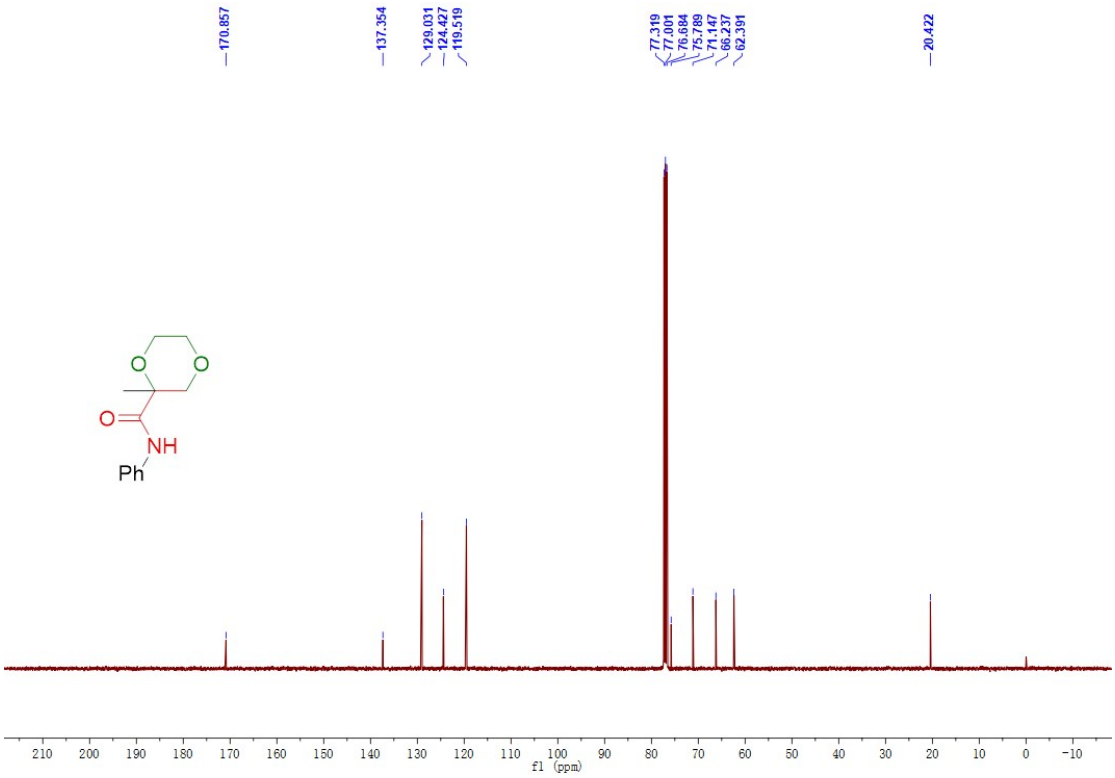
100 MHz ^{13}C NMR of **7** in $CDCl_3$



400 MHz ^{1}H NMR of **8** in $CDCl_3$



100 MHz ^{13}C NMR of **8** in $CDCl_3$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O
O
O
NH
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)