Supporting Information

Diastereoselective synthesis of chiral 3-substituted isoindolinones via rhodium(III)-catalyzed oxidative C-H olefination/annulation

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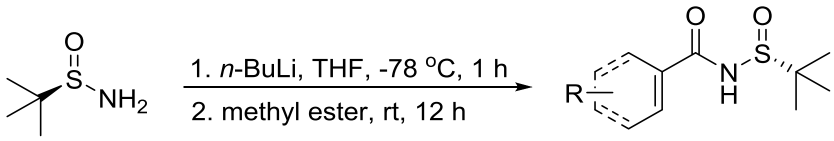
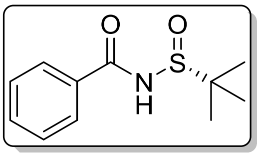
1 General procedure for the preparation of substrates



1

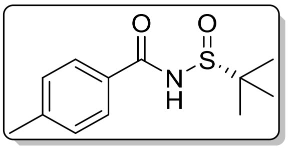
Following the literature reported method,[1] and at a temperature of -78 °C, *n*-BuLi (12.0 mL, 30.0 mmol, 3.0 equiv, 2.5 M in THF) was added dropwise to the solution of *R*-(+)-2-methyl-2-propanesulfinamide (1.21 g, 10.0 mmol) dissolved in dry THF (40.0 mL) under Ar atmosphere. Upon stirring for 1 h, methyl ester (3.0 equiv) was slowly added, followed by stirring for additional 12 h at room temperature. The reaction was then quenched by addition of the saturated NH_4Cl aqueous solution and the organic phase was extracted three times using EtOAc (50 mL). The organic phase was combined, washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography using petroleum ether/EtOAc as the eluent to give substrate **1**.

(*R*)-*N*-(*tert*-butylsulfinyl)benzamide (1a).



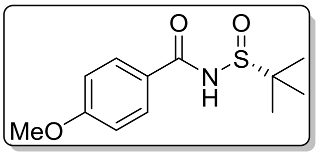
R_f = 0.3 (Petroleum ether/EtOAc =3/2). White solid (1.13 g, 50%), mp. 145-146 °C. $[\alpha]_D^{20}$ = -26.4 (*c* 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 7.4 Hz, 2H), 7.57-7.53 (m, 1H), 7.46-7.43 (m, 2H), 1.33 (s, 9H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ 168.0, 132.9, 132.3, 128.7, 127.9, 57.6, 22.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{11}H_{15}NNaO_2S^+$: 248.0716. Found: 248.0713.

(*R*)-*N*-(*tert*-butylsulfinyl)-4-methylbenzamide (1b).



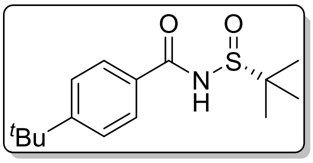
R_f = 0.2 (Petroleum ether/EtOAc =3/2). White solid (1.32 g, 55%), mp. 166-167 °C. $[\alpha]_D^{20}$ = -16.7 (*c* 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 8.2 Hz, 2H), 7.65 (br s, 1H), 7.27 (d, J = 5.8 Hz, 2H), 2.42 (s, 3H), 1.34 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.4, 143.8, 129.5, 129.3, 127.8, 57.5, 22.1, 21.6. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{12}H_{17}NNaO_2S^+$: 262.0872. Found: 262.0870.

(*R*)-*N*-(*tert*-butylsulfinyl)-4-methoxybenzamide (1c).



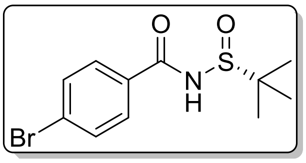
R_f = 0.3 (Petroleum ether/EtOAc =3/2). White solid (1.58 g, 62%), mp. 139-140 ºC. $[\alpha]_D^{20}$ = -13.5 (*c* 0.600, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (br s, 1H), 7.83 (d, J = 8.9 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H), 1.34 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.0, 163.4, 130.0, 124.3, 114.0, 57.5, 55.5, 22.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{12}H_{17}NNaO_3S^+$: 278.0821. Found: 278.0819.

(*R*)-4-(*tert*-butyl)-*N*-(*tert*-butylsulfinyl)benzamide (1d).



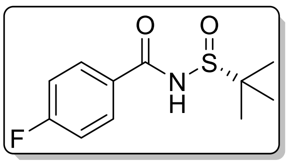
R_f = 0.4 (Petroleum ether/EtOAc =3/2). Yellow solid (1.27 g, 45%), mp. 132-133 ºC. $[\alpha]_D^{20}$ = -12.8 (*c* 0.600, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.78 (d, J = 8.3 Hz, 2H), 7.63 (br s, 1H), 7.49 (d, J = 8.4 Hz, 2H), 1.342 (s, 9H), 1.338 (s, 9H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 167.3, 156.8, 129.3, 127.7, 125.9, 57.5, 35.1, 31.1, 22.1. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{15}H_{23}NNaO_2S^+$: 304.1342. Found: 304.1339.

(*R*)-4-bromo-*N*-(*tert*-butylsulfinyl)benzamide (1e).



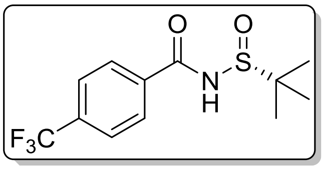
R_f = 0.3 (Petroleum ether/EtOAc =3/2). Yellow solid (2.04 g, 67%), mp. 78-79 ºC. $[\alpha]_D^{20}$ = +20.3 (*c* 0.600, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (br s, 1H), 7.73 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 1.34 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 132.1, 130.9, 129.5, 128.0, 57.9, 22.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{11}H_{14}BrNNaO_2S^+$: 325.9821. Found: 325.9820.

(*R*)-*N*-(*tert*-butylsulfinyl)-4-fluorobenzamide (1f).



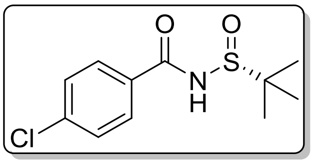
R_f = 0.3 (Petroleum ether/EtOAc =3/2). Pale yellow solid (1.02 g, 42%), mp. 144-145 °C. $[\alpha]_D^{20}$ = -27.9 (*c* 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (br s, 1H), 7.91-7.88 (m, 2H), 7.17-7.12 (m, 2H), 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.6, 165.6 (d, J_{C-F} = 253.1 Hz), 130.5 (d, J_{C-F} = 9.1 Hz), 128.2 (d, J_{C-F} = 2.9 Hz), 116.0 (d, J_{C-F} = 22.0 Hz), 57.8, 22.2. ^{19}F NMR (565 MHz, $CDCl_3$): δ -105.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{11}H_{14}FNNaO_2S^+$: 266.0621. Found: 266.0618.

(*R*)-*N*-(*tert*-butylsulfinyl)-4-(trifluoromethyl)benzamide (1g).



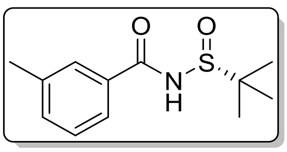
R_f = 0.3 (Petroleum ether/EtOAc =3/2). Pale yellow solid (1.80 g, 61%), mp. 141-142 °C. $[\alpha]_D^{20}$ = -49.8 (*c* 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 9.06 (br s, 1H), 8.00 (d, *J* = 6.0 Hz, 2H), 7.65 (br s, 2H), 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.2, 135.3, 134.1 (q, *J* = 32.8 Hz), 128.7, 125.6, 123.6 (q, J_{C-F} = 270.6 Hz), 58.4, 22.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{12}H_{14}F_3NNaO_2S^+$: 316.0590. Found: 316.0629.

(*R*)-*N*-(*tert*-butylsulfinyl)-4-chlorobenzamide (1h).



R_f = 0.3 (Petroleum ether/EtOAc =3/2). Yellow solid (1.68 g, 65%). mp. 156-157 °C. $[\alpha]_D^{20}$ = +14.2 (*c* 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.62 (br s, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 139.4, 130.3, 129.5, 129.0, 58.0, 22.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{11}H_{14}ClNNaO_2S^+$: 282.0326. Found: 282.0359.

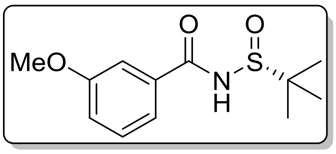
(*R*)-*N*-(*tert*-butylsulfinyl)-3-methylbenzamide (1i).



R_f = 0.3 (Petroleum ether/EtOAc =3/2). White solid (1.13 g, 47%). mp. 171-172 °C. $[\alpha]_D^{20}$ =

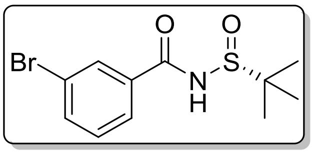
-13.0 (c 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (br s, 1H), 7.66 (br s, 1H), 7.62 (d, J = 7.2 Hz, 1H), 7.39-7.32 (m, 2H), 2.41 (s, 3H), 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.8, 138.8, 133.7, 132.1, 128.7, 128.5, 124.8, 57.7, 22.2, 21.3. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{12}H_{17}NNaO_2S^+$: 262.0872. Found: 262.0870.

(*R*)-*N*-(*tert*-butylsulfinyl)-3-methoxybenzamide (1j).



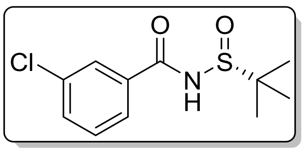
R_f = 0.3 (Petroleum ether/EtOAc =3/2). Brown solid (1.23 g, 48%). mp. 98-99 ºC. $[\alpha]_D^{20}$ = -16.9 (c 0.600, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$): δ 7.83 (br s, 1H), 7.40 (br s, 1H), 7.38-7.35 (m, 2H), 7.12-7.10 (m, 1H), 3.85 (s, 3H), 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 167.4, 160.0, 133.5, 129.8, 119.7, 119.4, 112.8, 57.7, 55.5, 22.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{12}H_{18}NO_3S^+$: 256.1002. Found: 256.1030.

(*R*)-3-bromo-*N*-(*tert*-butylsulfinyl)benzamide (1k).



R_f = 0.3 (Petroleum ether/EtOAc =3/2). Pale yellow solid (1.32 g, 43%). mp. 134-135 ºC. $[\alpha]_D^{20}$ = +12.2 (c 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.74 (br s, 1H), 8.04 (s, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.9 Hz, 1H), 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.5, 135.8, 133.9, 131.3, 130.2, 126.5, 122.9, 58.2, 22.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{11}H_{14}BrNNaO_2S^+$: 325.9821. Found: 325.9864.

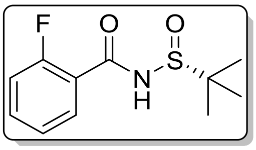
(*R*)-*N*-(*tert*-butylsulfinyl)-3-chlorobenzamide (1l).



R_f = 0.3 (Petroleum ether/EtOAc =3/2). Yellow solid (1.56 g, 60%), mp. 142-143 ºC. $[\alpha]_D^{20}$ = +7.7 (c 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (br s, 1H), 7.86 (t, J = 1.8 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.54 (dd, J = 0.9, 8.0 Hz, 1H), 7.41 (t, J = 7.9 Hz, 1H), 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.5, 135.0, 133.8, 132.9, 130.1, 128.3, 126.0, 58.0, 22.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{11}H_{14}ClNNaO_2S^+$: 282.0326. Found:

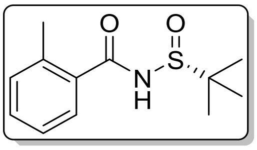
282.0323.

(*R*)-*N*-(*tert*-butylsulfinyl)-2-fluorobenzamide (1m).



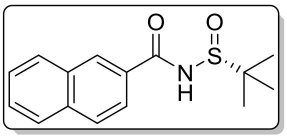
R_f = 0.3 (Petroleum ether/EtOAc =3/2). White solid (0.82 g, 34%), mp. 153-154 °C. $[\alpha]_D^{20}$ = -58.6 (*c* 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.14-8.10 (m, 1H), 7.97 (d, *J* = 14.2 Hz, 1H), 7.60-7.55 (m, 1H), 7.34-7.30 (m, 1H), 7.18 (dd, *J* = 8.3, 12.2 Hz, 1H), 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 162.5 (d, J_{C-F} = 257.1 Hz), 160.0, 135.1 (d, J_{C-F} = 9.4 Hz), 132.5, 125.3 (d, J_{C-F} = 3.0 Hz), 119.3 (d, J_{C-F} = 10.5 Hz), 116.3 (d, J_{C-F} = 24.8 Hz), 57.0, 22.1. ^{19}F NMR (565 MHz, $CDCl_3$): δ -111.9. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{11}H_{14}FNNaO_2S^+$: 266.0621. Found: 266.0619.

(*R*)-*N*-(*tert*-butylsulfinyl)-2-methylbenzamide (1n).



R_f = 0.3 (Petroleum ether/EtOAc =3/2). White solid (1.50 g, 63%), mp. 138-139 °C. $[\alpha]_D^{20}$ = -10.8 (*c* 0.600, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (br s, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.39-7.35 (m, 1H), 7.27-7.22 (m, 2H), 2.45 (s, 3H), 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 167.3, 137.0, 133.5, 131.5, 131.2, 127.1, 125.9, 57.3, 22.2, 20.0. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{12}H_{17}NNaO_2S^+$: 262.0872. Found: 262.0871.

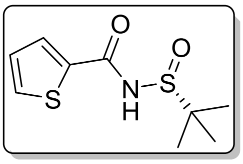
(*R*)-*N*-(*tert*-butylsulfinyl)-2-naphthamide (1o).



R_f = 0.3 (Petroleum ether/EtOAc =3/2). White solid (1.85 g, 67%), mp. 192-193 °C. $[\alpha]_D^{20}$ = +9.6 (*c* 0.600, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$): δ 8.36 (br s, 1H), 7.96-7.92 (m, 2H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.63-7.57 (m, 3H), 1.39 (s, 9H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 167.6, 135.4, 132.4, 129.4, 129.2, 128.93, 128.87, 128.6, 127.9, 127.2, 123.6, 57.6, 22.2. HRMS (positive ESI): $[M+H]^+$ calcd for $C_{15}H_{18}NO_2S^+$: 276.1053.

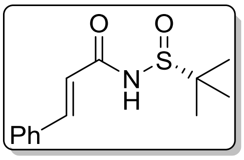
Found: 276.1050.

(*R*)-*N*-(*tert*-butylsulfinyl)thiophene-2-carboxamide (1p).



R_f = 0.3 (Petroleum ether/EtOAc =3/2). White solid (1.50 g, 65%), mp. 178-179 ºC. $[\alpha]_D^{20}$ = -11.3 (*c* 0.600, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (br s, 1H), 7.76 (dd, J = 1.1, 3.8 Hz, 1H), 7.61 (dd, J = 1.0, 5.0 Hz, 1H), 7.13 (dd, J = 3.8, 5.0 Hz, 1H), 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 161.7, 136.5, 132.7, 130.9, 128.1, 57.8, 22.1. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_9H_{13}NNaO_2S_2^+$: 254.0280. Found: 254.0281.

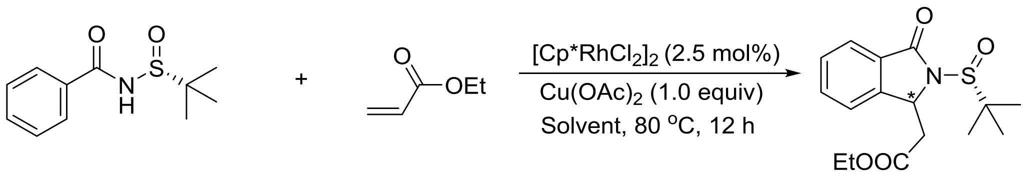
(*R*)-*N*-(*tert*-butylsulfinyl)cinnamamide (1q).



R_f = 0.3 (Petroleum ether/EtOAc =3/2). White solid (1.10 g, 44%), mp. 150-151ºC. $[\alpha]_D^{20}$ = +18.0 (*c* 0.600, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (br s 1H), 7.74 (d, J = 15.6 Hz, 1H), 7.55-7.52 (m, 2H), 7.39-7.37 (m, 3H), 6.70 (d, J = 15.4 Hz, 1H), 1.33 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 145.1, 134.2, 130.6, 128.9, 128.4, 117.9, 57.6, 22.1. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{13}H_{17}NNaO_2S^+$: 274.0872. Found: 274.0871.

2 Optimization of the reaction conditions

Table S1 Screening of the solvent[a]



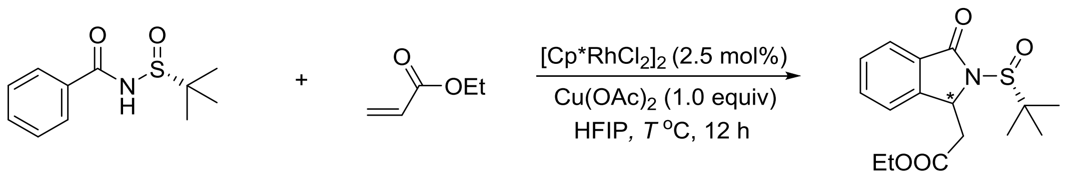
1a **2a** **3aa**

entry	solvent	yield (%)[b]	ratio (*RS*/*RR*)[c]
1	*n*-BuOH	trace	/
2	CF_3CH_2OH	27	2.7:1
3	EtOH	trace	/
4	MeOH	trace	/
5	**HFIP**	**30**	**4.6:1**

6	*t*-AmOH	0	/
7	CH_3CN	0	/
8	dioxane	0	/
9	toluene	0	/

[a]Reaction conditions: **1a** (0.15 mmol), **2a** (0.45 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%), $Cu(OAc)_2$ (1.0 equiv), solvent (1.0 mL), 80 °C, Ar, 12 h. [b]Isolated yield. [c]The *dr* values were determined from ^1H NMR spectra of crude products.

Table S2 Screening of the reaction temperature[a]

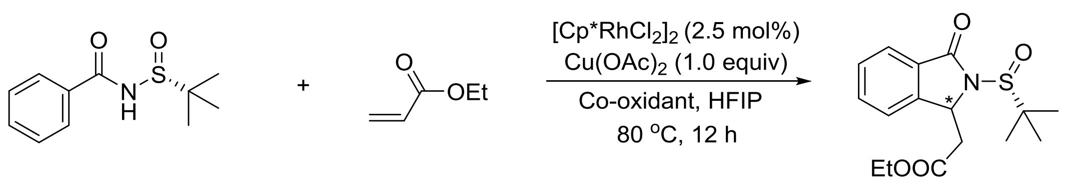


1a 2a 3aa

entry	temp (°C)	yield (%)[b]	ratio (*RS*/*RR*)[c]
1	**80**	**30**	**4.6:1**
2	90	26	3.6:1
3	70	21	4.7:1
4	60	trace	/

[a]Reaction conditions: **1a** (0.15 mmol), **2a** (0.45 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%), $Cu(OAc)_2$ (1.0 equiv), HFIP (1.0 mL), Ar, 12 h. [b]Isolated yield. [c]The *dr* values were determined from ^1H NMR spectra of crude products.

Table S3 Screening of the co-oxidant[a]



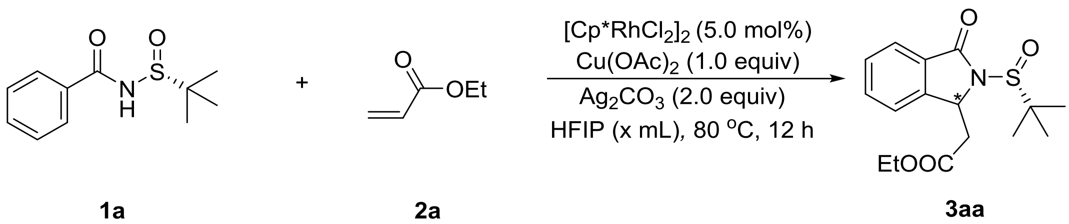
1a 2a 3aa

entry	co-oxidant (equiv)	yield (%)[b]	ratio (*RS*/*RR*)[c]
1[d]	/	28	4.0:1

2[e]	Ag_2CO_3 (2.0)	trace	/
3[f]	$AgSbF_6$ (0.1)	18	4.0:1
4[f]	$AgSbF_6$ (0.2)	13	3.5:1
5	Ag_2CO_3 (1.0)	40	5.3:1
6	Ag_2CO_3 (2.0)	50	4.7:1
7	AgOAc (2.0)	25	2.5:1
8	Ag_2O (2.0)	40	2.2:1
9	AgOTf (2.0)	0	/
10	$AgNO_3$ (2.0)	0	/
11[g]	**Ag_2CO_3 (2.0)**	**57**	**5.0:1**

[a]Reaction conditions: **1a** (0.15 mmol), **2a** (0.45 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%), $Cu(OAc)_2$ (1.0 equiv), co-oxidant, HFIP (1.0 mL), 80 °C, Ar, 12 h. [b]Isolated yield. [c]The *dr* values were determined from ^{1}H NMR spectra of crude products. [d]$Cu(OAc)_2$ (2.0 equiv). [e]Without $Cu(OAc)_2$. [f]$AgSbF_6$ was used as the additive. [g]$[Cp^*RhCl_2]_2$ (5.0 mol%).

Table S4 Screening of solvent volume, reaction time and further screening of oxidant[a]



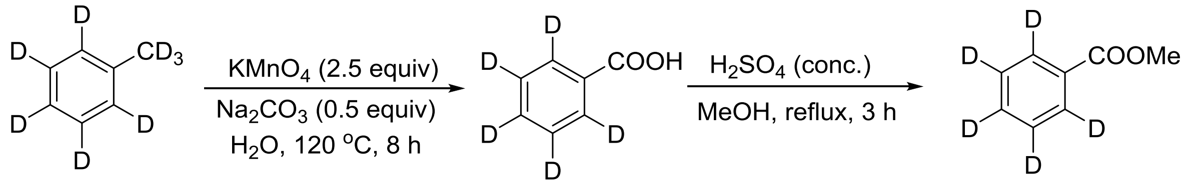
entry	HFIP (mL)	yield (%)[b]	ratio (*RS*/*RR*)[c]
1	1.0	57	5.0:1
2	0.5	63	5.0:1
3	0.25	67	5.0:1
4[d]	**0.25**	**82**	**5.5:1**
5[e]	0.25	80	5.0:1
6[df]	0.25	11	3.1:1
7[dg]	0.25	0	/

8[dh]	0.25	0	/

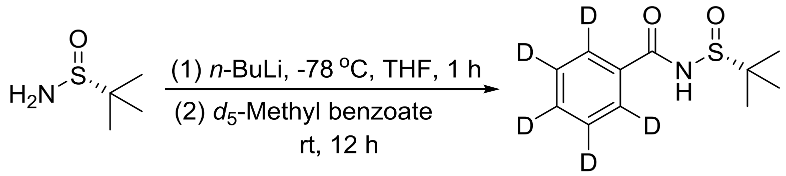
[a]Reaction conditions: **1a** (0.15 mmol), **2a** (0.45 mmol), $[Cp^*RhCl_2]_2$ (5.0 mol%), $Cu(OAc)_2$ (1.0 equiv), Ag_2CO_3 (2.0 equiv), HFIP (x mL), 80 °C, Ar, 12 h. [b]Isolated yield. [c]The *dr* values were determined from ^{1}H NMR spectra of crude products. [d]The reaction time was 16 h. [e]The reaction time is 20 h. [f]Under O_2 atmosphere without Ag_2CO_3. [g]Under air without Ag_2CO_3. [h]TBHP (1.0 equiv) instead of $Cu(OAc)_2$ and Ag_2CO_3 was used as the oxidant.

3 Mechanistic investigations

3.1 Synthesis of [D5]-1a



d_5-Methyl benzoate



[D5]-**1a**

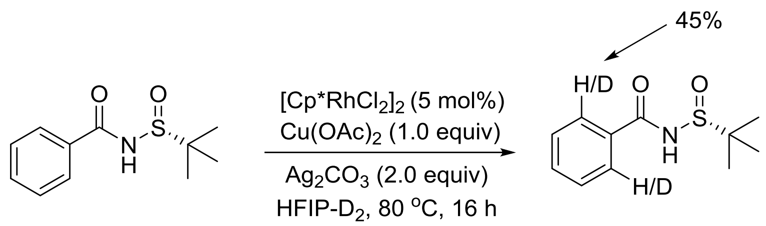
According to the literature report,[2] D_8-toluene (99.9% atom D) (2.5 g, 25.0 mmol), $KMnO_4$ (9.9 g, 62.5 mmol), Na_2CO_3 (1.33 g, 12.5 mmol) and water (75.0 mL) were added to a 250 mL round-bottom flask. The reaction system was refluxed at 120 °C for 8 h and then allowed to cool to room temperature. Next, the mixture was filtered through a pad of celite and the obtained filtrate was subjected to acidification with HCl (12.0 M) and then extracted with EtOAc. The organic layer was washed with water and subsequently concentrated *in vacuo*. The crude product was recrystallized from water to give C_6D_5COOH as white needles (1.78 g, 56%).

H_2SO_4 (conc.) (2.0 mL) was added to the solution of C_6D_5COOH (1.78 g, 14.0 mmol) dissolved in MeOH (30.0 mL) in a round-bottom flask with a magnetic stir bar and a condenser. The reaction mixture was refluxed until the reaction was completed (monitored by TLC) and followed by cooling to room temperature. Then the solvent was removed under reduced pressure. The residue was neutralized with saturated $NaHCO_3$ aqueous solution at 0 °C. Then, the resulted mixture was extracted with EtOAc and the organic layer was combined, dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give d_5-methyl benzoate for the next step without further purification.

At -78 °C, *n*-BuLi (5.6 mL, 14.0 mmol, 3.0 equiv, 2.5 M in THF) was added dropwise to the solution of *R*-(+)-2-methyl-2-propanesulfinamide (557.5 mg, 4.6 mmol, 1.0 equiv) dissolved in dry THF (30.0 mL) under Ar atmosphere. Upon stirring for 1 h, d_5-methyl benzoate (1.98 g, 3.0 equiv) was slowly added and the mixture was stirred for 12 h at room temperature. Then, the reaction was quenched by addition of saturated NH_4Cl aqueous solution at 0 °C and the organic phase was extracted with EtOAc. The organic layer was combined, washed with brine, dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography using petroleum ether/EtOAc as eluent to give [D_5]-**1a** (0.48 g, 45%).

(*R*)-*N*-(*tert*-butylsulfinyl)benzamide-2,3,4,5,6-*d*5 (D5-1a): White solid (0.48 g, 45%). mp. 145-146 °C. $[\alpha]_D^{20}$ = -19.7 (*c* 0.400, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (br s, 1H), 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 167.5, 132.5 (t, J = 24.7 Hz), 132.0, 128.3 (t, J = 24.5 Hz), 127.4, (t, J = 24.5 Hz), 57.6, 22.2. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{11}H_{10}D_5NNaO_2S^+$: 253.1030. Found: 253.1028.

3.2 H/D exchange experiments



1a [Dn]-**1a**

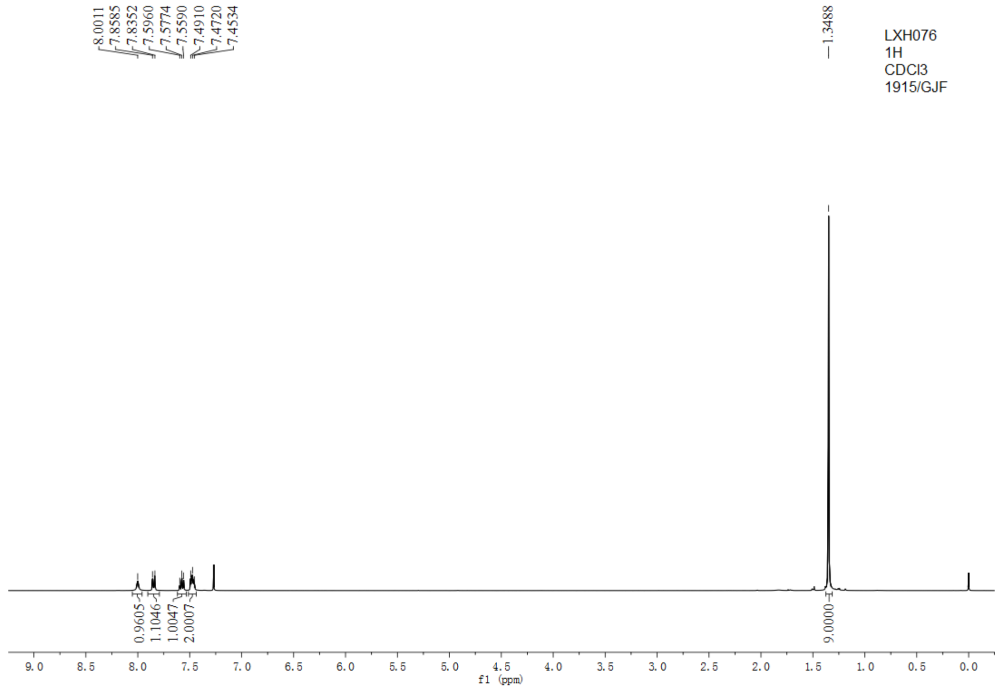
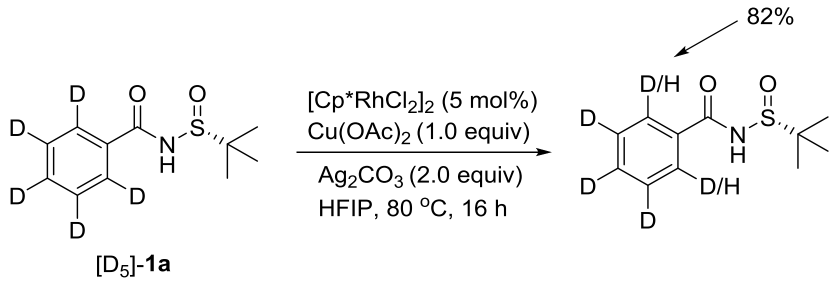


Figure S1 [1]H NMR spectrum of the [Dn]-**1a** from the H/D exchange experiment



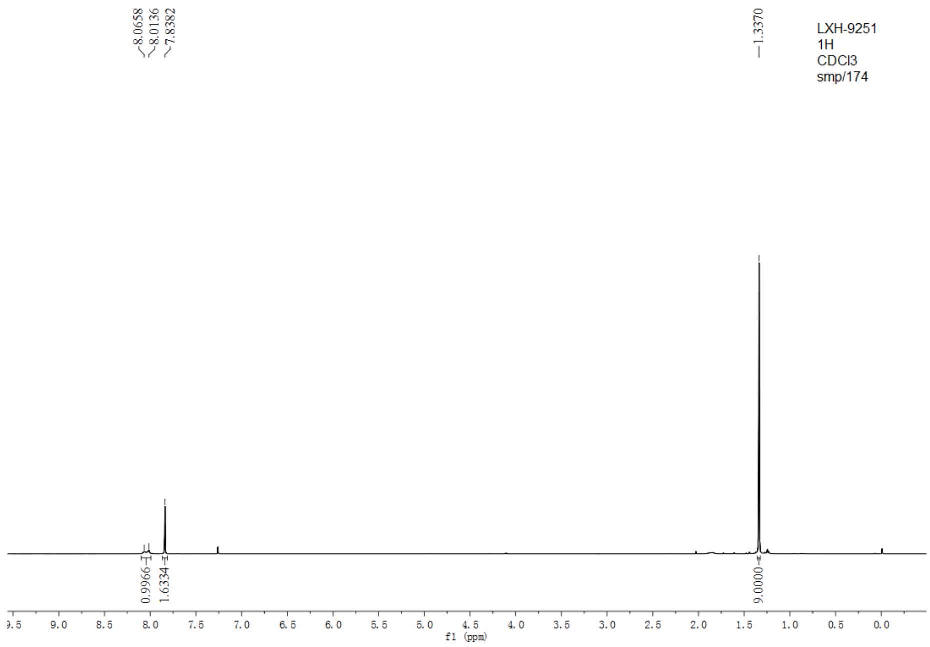
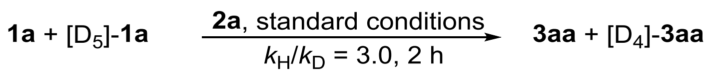


Figure S2 [1]H NMR spectrum of the [Dn]-**1a** from the D/H exchange experiment

3.3 Intermolecular competition KIE.



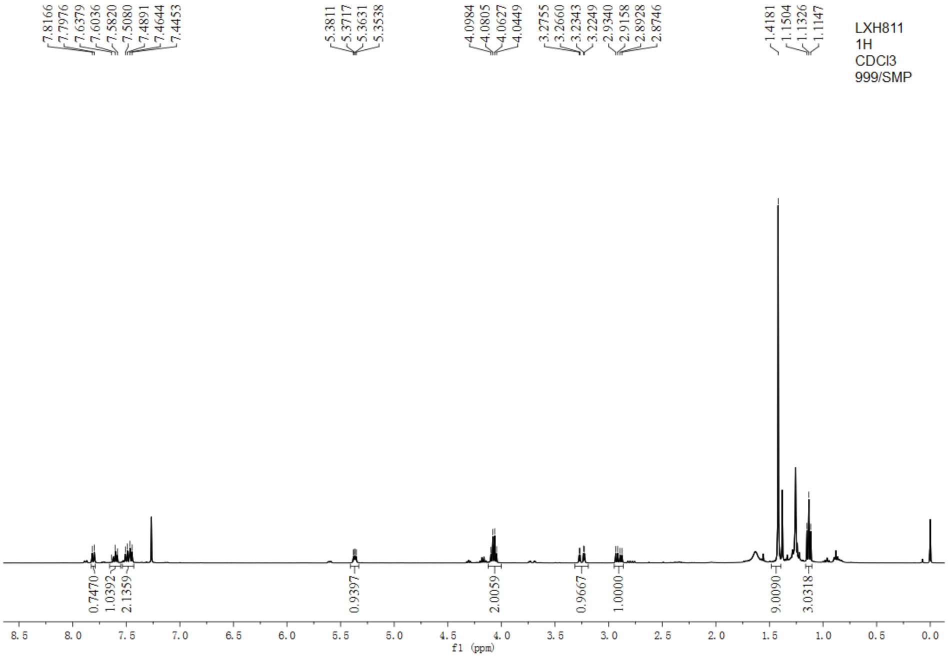
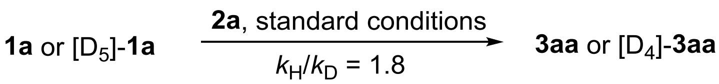


Figure S3 [1]H NMR spectrum of product from intermolecular competition KIE experiment

3.4 Parallel experiments



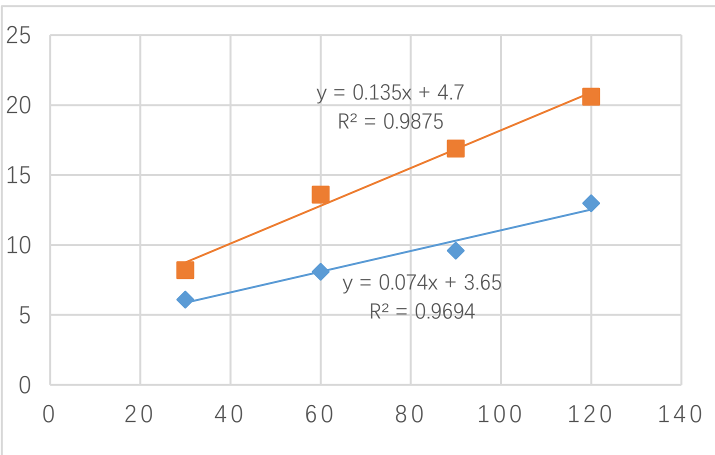
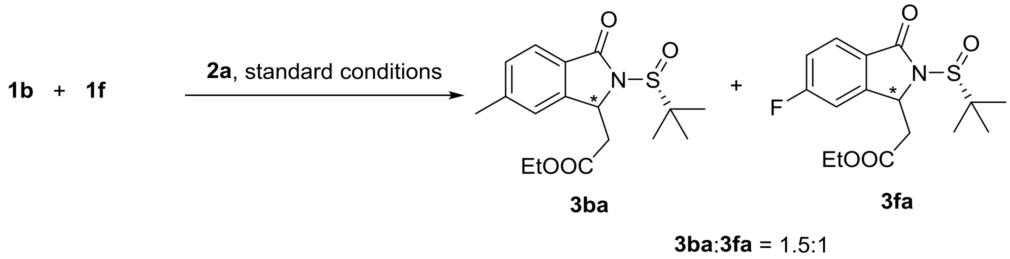


Figure S4 The parallel KIE was calculated as $k_H/k_D = 0.135/0.074 = 1.8$

3.5 Competition experiment



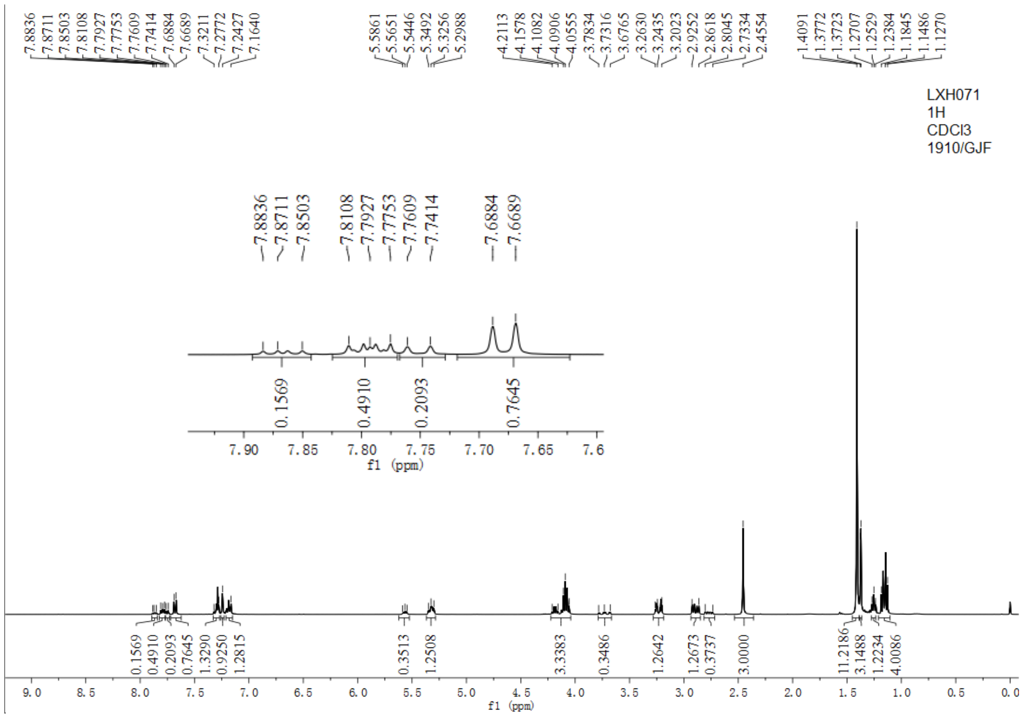
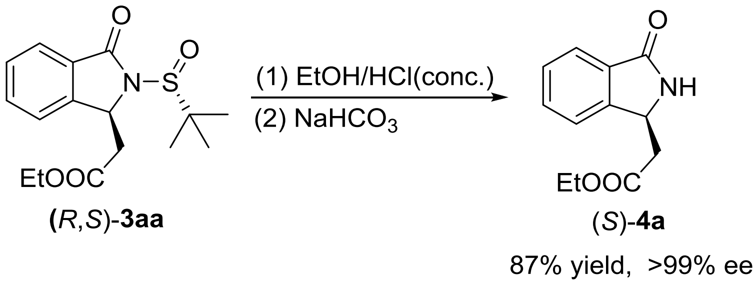


Figure S5 ^{1}H NMR spectrum of products from the competition experiment

4 Removal of *N*-sulfinyl and further transformations

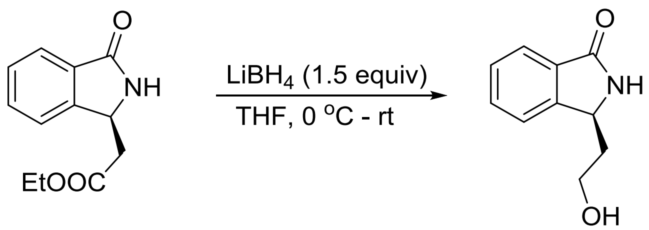
4.1 Removal of *N*-sulfinyl



Following the literature report,[3] 0.6 mL HCl (conc.) dissolved in EtOH (6.0 mL) was added dropwise to the compound (*R*,*S*)-**3aa** (39.0 mg, 0.12 mmol) in a round bottom flask at 0 ºC. The mixture was stirred at room temperature until the reaction was completed (monitored by TLC). Then, the solvent was removed under reduced pressure and the residue was neutralized with saturated $NaHCO_3$ aqueous solution at 0 °C. Next, the mixture was extracted with EtOAc (3×20 mL) and the organic layer was dried with anhydrous Na_2SO_4, filtered and evaporated. The residue was purified by preparative TLC on silica gel plates using petroleum ether/EtOAc (3/2) as the eluent to give (*S*)-**4a** as a white solid (23.0 mg, 87%).

Ethyl (*S*)-2-(3-oxoisoindolin-1-yl)acetate ((*S*)-4a). White solid (23.0 mg, 87%). $[\alpha]_D^{20}$ = -128.8 (*c* 0.24, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.52-7.49 (m, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 7.7 Hz, 1H), 4.87 (dd, *J* = 3.5, 10.3 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.93 (dd, *J* = 3.7, 17.0 Hz, 1H), 2.41 (dd, *J* = 10.3, 17.0 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 171.2, 170.1, 145.9, 132.1, 131.8, 128.7, 124.1, 122.3, 61.3, 52.9, 39.6, 14.2. The enantiomeric excess was determined on a Daicel Chiralpak IB column with *n*-hexane/2-propanol (85/15) and flow rate 0.3 mL/min and detected at a UV wavelength of 254 nm. Retention times: 33.2 min (major), 36.6 min (minor), >99% *ee*. HRMS (positive ESI): $[M+Na]^+$ calcd for $C_{12}H_{13}NNaO_3^+$: 242.0788. Found: 242.0785.

4.2 Synthesis of (*S*)-PD172938

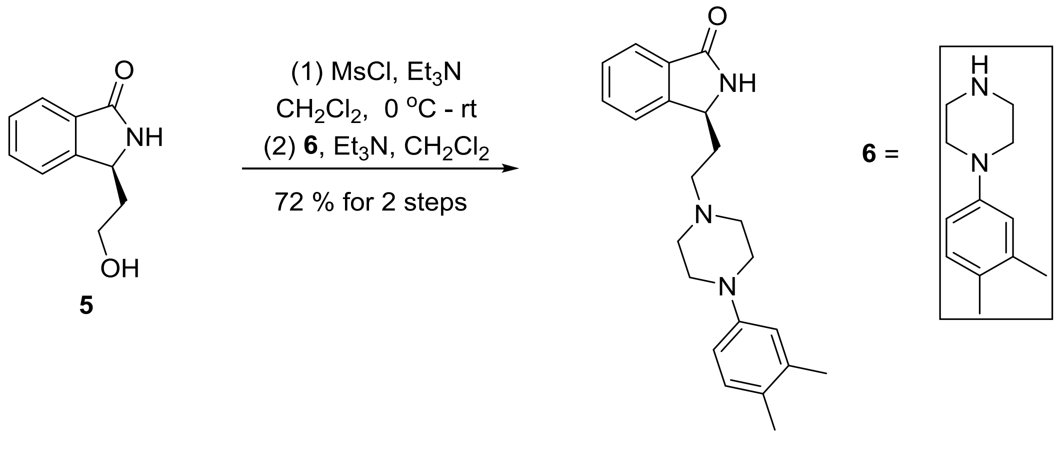


(*S*)-**4a** **5**

According to the literature method,[4] reduction of the ethyl ester (*S*)-**4a** (0.2 mmol, 43.9 mg, 1.0 equiv) by $LiBH_4$ afforded the compound **5**.

(*S*)-3-(2-hydroxyethyl)isoindolin-1-one (5).

White solid (28.4 mg, 80%). $[\alpha]_D^{20}$ = -66.2 (*c* 0.280, CH_2Cl_2). Spectroscopic data are in agreement with those reported in the literature.[4] The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (60/40) and flow rate 0.8 mL/min and detected at a UV wavelength of 254 nm. Retention times: 14.4 min (minor), 18.5 min (major), >99% *ee*.



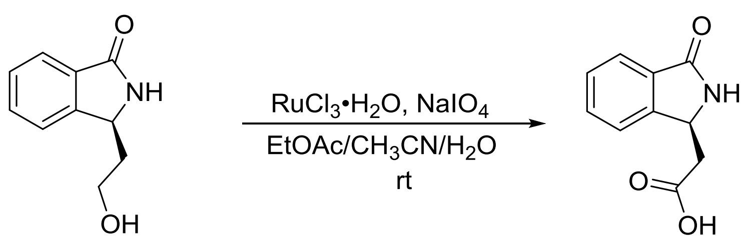
5

7 95% ee
(*S*)-PD172938

The compound **7** was synthesized from **5** (35.4 mg, 0.2 mmol, 1.0 equiv) according to the literature method.[4]

(*S*)-3-(2-(4-(3,4-dimethylphenyl)piperazin-1-yl)ethyl)isoindolin-1-one (7). White solid (50.3 mg, 72%). $[\alpha]_D^{20}$ = -6.0 (*c* 0.20, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 7.5 Hz, 1H), 7.57 (dt, *J* = 1.0, 7.5 Hz, 1H), 7.53 (br s, 1H), 7.49-7.43 (m, 2H), 7.02 (d, *J* = 8.2 Hz, 1H), 6.75 (d, *J* = 2.2 Hz, 1H), 6.69 (dd, *J* = 2.5, 8.2 Hz, 1H), 4.65 (dd, *J* = 2.8, 9.6 Hz, 1H), 3.24-3.15 (m, 4H), 2.75-2.56 (m, 6H), 2.23 (s, 3H), 2.18 (s, 3H), 2.16-2.15 (m, 1H), 1.82-1.73 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.3, 149.5, 147.5, 137.1, 132.0, 131.7, 130.2, 128.3, 128.2, 123.9, 122.3, 118.3, 114.0, 57.1, 56.5, 53.4, 49.9, 31.4, 20.2, 18.8. The enantiomeric excess was determined on a Daicel Chiralpak AD-H column with *n*-hexane/2-propanol (70/30) and flow rate 0.9 mL/min and detected at a UV wavelength of 254 nm. Retention times: 8.0 min (minor), 9.6 min (major), 95% *ee*.

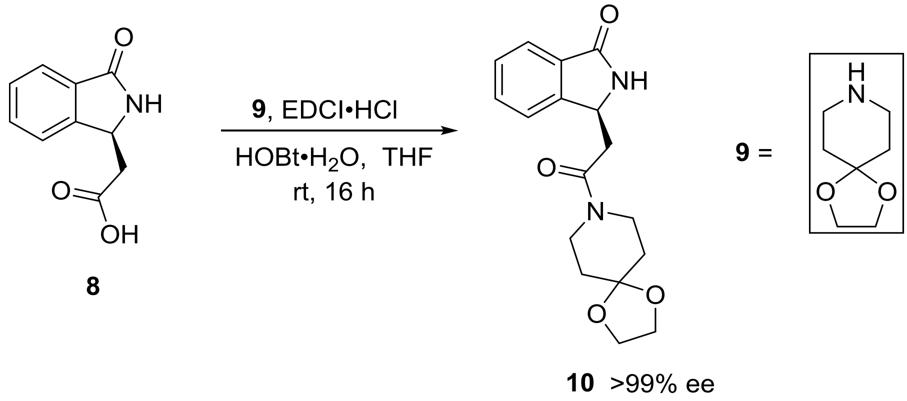
4.3 Synthesis of compound 8



5 8

The compound **8 (**30.6 mg, 80%**)** was synthesized by oxidation of the alcohol **5** (35.4 mg, 0.2 mmol, 1.0 equiv) according to the literature method.[4]

4.4 Synthesis of compound 10



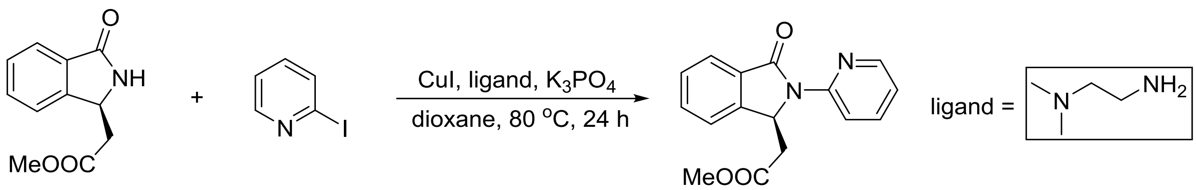
The compound **10** was prepared by the condensation reaction of **8** (38.3 mg, 0.2 mmol, 1.0 equiv) with **9** according to the literature method.[4]

(*S*)-3-(2-oxo-2-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)ethyl)isoindolin-1-one (10).

White solid (47.5 mg, 75% yield). $[\alpha]_D^{20}$ = -242.9 (*c* 0.400, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.5 Hz, 1H), 7.59-7.55 (m, 1H), 7.50-7.44 (m, 2H), 7.12 (br s, 1H), 5.03 (dd, J = 2.7, 10.5 Hz, 1H), 4.00-3.96 (m, 4H), 3.80-3.69 (m, 2H), 3.49-3.46 (m, 2H), 3.06 (dd, J = 3.2, 16.5 Hz, 1H), 2.42 (dd, J = 10.6, 16.5 Hz, 1H), 1.73-1.67 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.8, 168.3, 146.5, 132.2, 131.8, 128.4, 124.1, 122.3, 106.6, 64.5, 53.4, 43.4, 39.9, 38.9, 35.4, 34.7. The enantiomeric excess was determined on a Daicel Chiralpak AD column with *n*-hexane/2-propanol (75/25) and flow rate 0.5 mL/min and detected at a UV wavelength of 254 nm. Retention times: 50.5 min (major), >99% *ee*.

4.5 Synthesis of compound 11 by *N*-arylation of isoindolinone (*S*)-4b

According to the literature reported method [5] and under Ar atmosphere, a 15 mL Schlenk tube was charged with CuI (15.2 mg, 0.05 mmol), K_3PO_4 (78.6 mg, 0.23 mmol), 2-iodopyridine (29.0 µL, 0.17 mmol), *N*,*N*-dimethylethylenediamine (12.5 µL, 0.07 mmol) and (*S*)-**4b** (50.0 mg, 0.15 mmol) dissolved in dioxane (1.6 mL). The reaction mixture was heated at 80 °C for 24 h and then quenched by addition of EtOAc followed by filtration through a celite pad. The solvent was removed under reduced pressure and the residue was purified by preparative TLC on silica gel plates using petroleum ether/EtOAc as the eluent to afford **11**. (Note: (*S*)-**4b** was obtained as described in **4.1**).



Methyl (*S*)-2-(3-oxo-2-(pyridin-2-yl)isoindolin-1-yl)acetate (11).

White solid (38.0 mg, 90%). $[\alpha]_D^{20}$ = +190.5 (*c* 0.400, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.56 (dt, J = 0.8, 8.4 Hz, 1H), 8.43-8.41 (m, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.79-7.75 (m, 1H), 7.64-7.50 (m, 3H), 7.09-7.06 (m, 1H), 6.00 (dd, J = 3.7, 8.2 Hz, 1H), 3.67 (s, 3H), 3.41 (dd, J = 3.7, 16.0 Hz, 1H), 2.73 (dd, J = 8.2, 16.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.1, 167.5, 150.9, 147.7, 145.0, 138.0, 132.9, 131.8, 128.7, 124.3, 122.8, 119.6, 115.7, 56.5, 51.8, 38.1. The enantiomeric excess was determined on a Daicel Chiralpak AD column with *n*-hexane/2-propanol (80/20) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 8.2 min (minor), 9.2 min (major), >99% *ee*.

5 Crystal data of (*R*,*R*)-3aa and (*R*,*S*)-3ab

Crystals of (*R*,*R*)-**3aa** (CCDC 1971954) and (*R*,*S*)-**3ab** (CCDC 2046609) were obtained by recrystallization at ambient temperature from EtOAc/petroleum ether, dichloromethane/ petroleum ether, respectively. The data were collected on an Oxford Diffraction Gemini ES8 diffractometer with graphite-monochromated Cu Kα radiation (λ = 1.54184 Å) for compounds (*R*,*R*)-**3aa** and (*R*,*S*)-**3ab**.

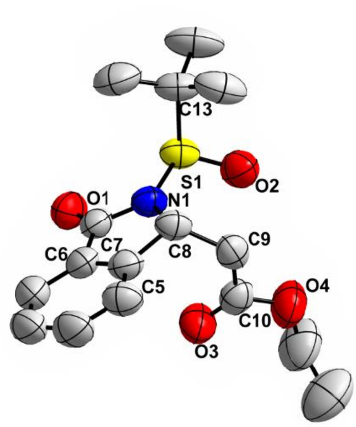


Figure S6 Molecular structure of (*R*,*R*)-**3aa** with thermal ellipsoids drawn at the 50%

probability level (Hydrogen atoms are omitted for clarity; one of the two independent molecules shown).

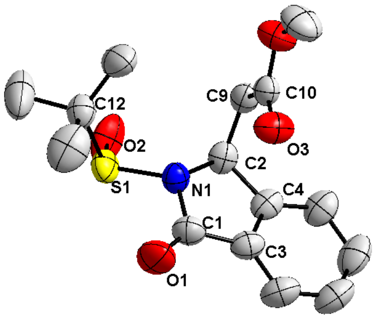


Figure S7 Molecular structure of (*R*,*S*)-**3ab** with thermal ellipsoids drawn at the 50% probability level (Hydrogen atoms are omitted for clarity).

Table S5. Summary of crystal structure determination for (*R*,*R*)-3aa and (*R*,*S*)-3ab

	(*R*,*R*)-3aa	**(*R*,*S*)-3ab**
Empirical formula	$C_{16}H_{21}NO_4S$	$C_{15}H_{19}NO_4S$
Formula weight	323.40	309.37
Temperature/K	293(2)	293(2)
Crystal system	monoclinic	orthorhombic
Space group	$P2_1$	$P2_12_12_1$
a/Å	9.4481(4)	8.6665(5)
b/Å	10.3898(5)	9.0914(5)
c/Å	17.9970(9)	20.0289(10)
α/°	90	90
β/°	96.944(4)	90
γ/°	90	90
Volume/Å^3	1753.69(14)	1578.09(15)
Z	4	4
ρ_{calc}g/cm^3	1.225	1.302
μ/mm^{-1}	1.782	1.957
F(*000*)	688.0	656.0
Crystal size/mm^3	0.19 × 0.16 × 0.14	0.16 × 0.14 × 0.1

Radiation	CuKα (λ = 1.54184)	CuKα (λ = 1.54184)
2Θ range for data collection/ °	9.43 to 134.158	8.83 to 134.094
Index ranges	-11 ≤ h ≤ 10,	-10 ≤ h ≤ 10,
	-11 ≤ k ≤ 12,	-9 ≤ k ≤ 10,
	-20 ≤ 1 ≤ 21	-23 ≤ 1 ≤ 20
Reflections collected	14681	5764
Independent reflections	5731 [R_{int} = 0.0322,	2812 [R_{int}= 0.0316,
	R_{sigma}= 0.0362]	R_{sigma}= 0.0434]
Data/restraints/parameters	5731/3/413	2812/49/207
Goodness-of-fit on F^2	1.071	1.062
Final R indexes [$I>=2\sigma (I)$]	R_1 = 0.0477,	R_1 = 0.0447,
	wR_2 = 0.1380	wR_2 = 0.1087
Final R indexes [all data]	R_1 = 0.0629,	R_1 = 0.0515,
	wR_2 = 0.1557	wR_2 = 0.1158
peak/hole [e $Å^{-3}$]	0.27/-0.23	0.18/-0.24
CCDC number	1971954	2046609

Table S6. Selected bond lengths (Å) and angles (°) for (*R*,*R*)-3aa and (*R*,*S*)-3ab

(*R*,*R*)-3aa		**(*R*,*S*)-3ab**	
C5-C8	1.509 (6)	C1-C3	1.473 (6)
C6-C7	1.476 (7)	C1-O1	1.213 (5)
C7-N1	1.387 (6)	C1-N1	1.406 (5)
C7-O1	1.205 (7)	C2-C4	1.505 (5)
C8-N1	1.487 (6)	C2-C9	1.514 (6)
N1-S1	1.704 (4)	N1-S1	1.720 (3)
C5-C6-C7	109.5 (4)	C1-N1-C2	111.7 (3)
N1-C7-C6	105.5 (4)	S1-N1-C1	116.9 (3)
O1-C7-C6	128.9 (5)	N1-C2-C4	101.9 (3)
O1-C7-N1	125.6 (5)	C2-C9-C10	115.1 (3)

C8-N1-S1	128.0 (3)	C1-C3-C4	109.3 (3)
C7-N1-C8	113.4 (4)	N1-C1-C3	106.2 (3)
N1-S1-C13	102.7 (2)	O2-S1-N1	104.66 (18)
O2-S1-N1	107.5(2)	C3-C4-C2	110.8 (3)

6 References

[1] (a) F. Xue, F. Wang, J. Liu, J. Di, Q. Liao, H. Lu, M. Zhu, L. He, H. He, D. Zhang, H. Song, X.-Y. Liu and Y. Qin, *Angew. Chem. Int. Ed*., 2018, **57**, 6667; (b) Z.-Y. Xu, Y. Luo, D.-W. Zhang, H. Wang, X.-W. Sun and Z.-T. Li, *Green Chem.*, 2020, **22**, 136.

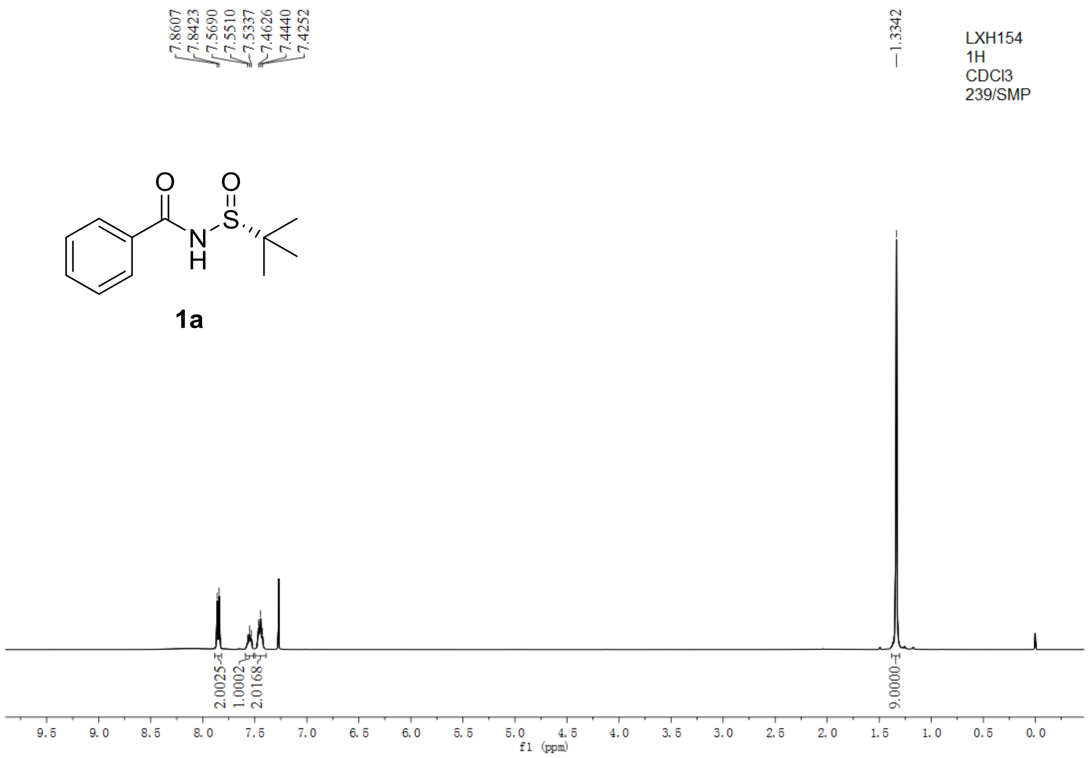
[2] Q.-L. Yang, X.-Y. Wang, T.-L. Wang, X. Yang, D. Liu, X. Tong, X.-Y. Wu and T.-S. Mei, *Org. Lett.*, 2019, **21**, 2645.

[3] M. F. Jacobsen and T. Skrydstrup, *J. Org. Chem.*, 2003, **68**, 7112.

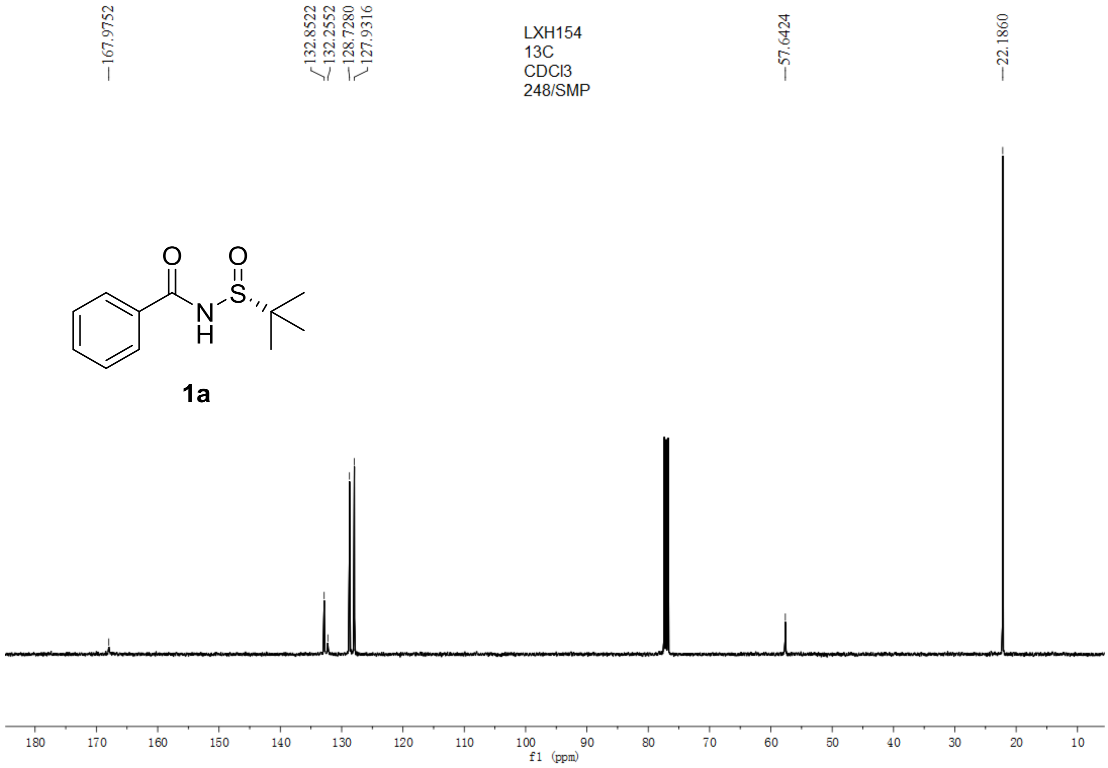
[4] S. K. Ray, M. M. Sadhu, R. G. Biswas, R. A. Unhale and V. K. Singh, *Org. Lett.*, 2019, **21**, 417.

[5] A. Di Mola, M. Tiffner, F. Scorzelli, L. Palombi, R. Filosa, P. De Caprariis, M. Waser and A. Massa, *Beilstein J. Org. Chem.*, 2015, **11**, 2591.

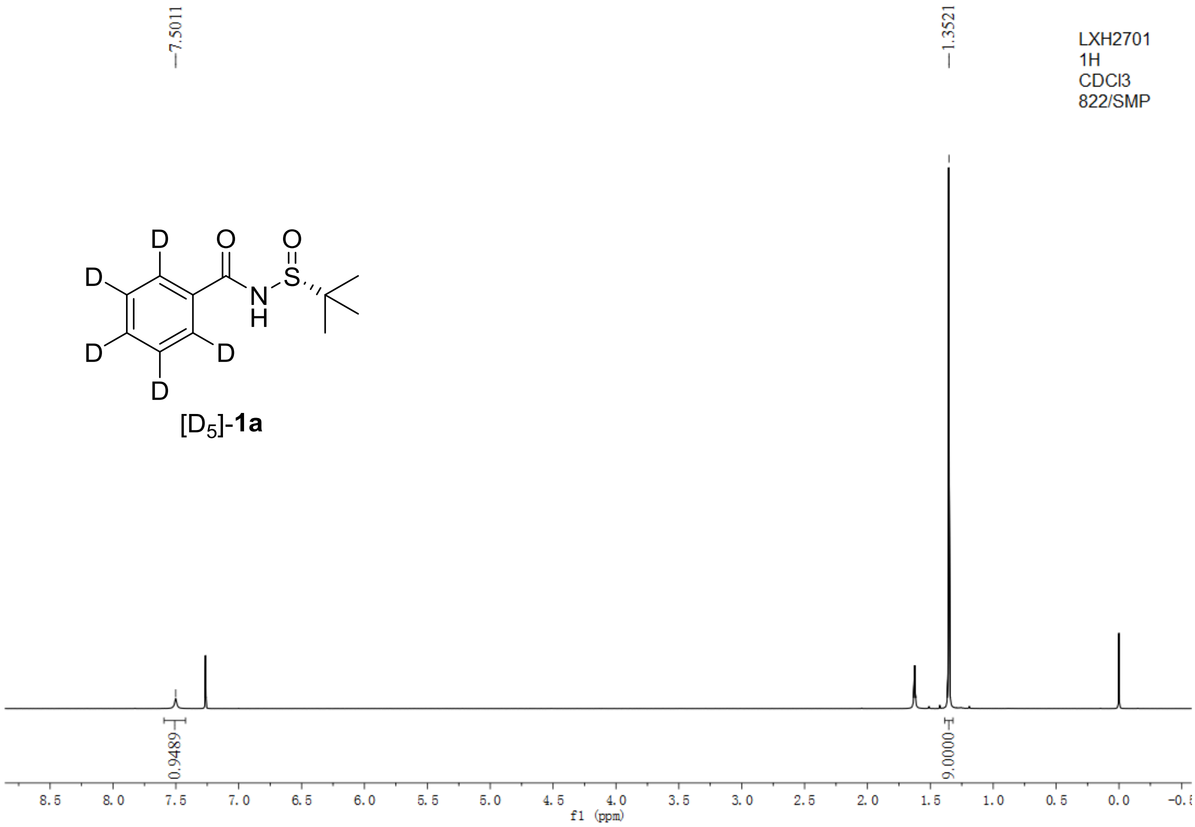
7 NMR and HPLC spectra



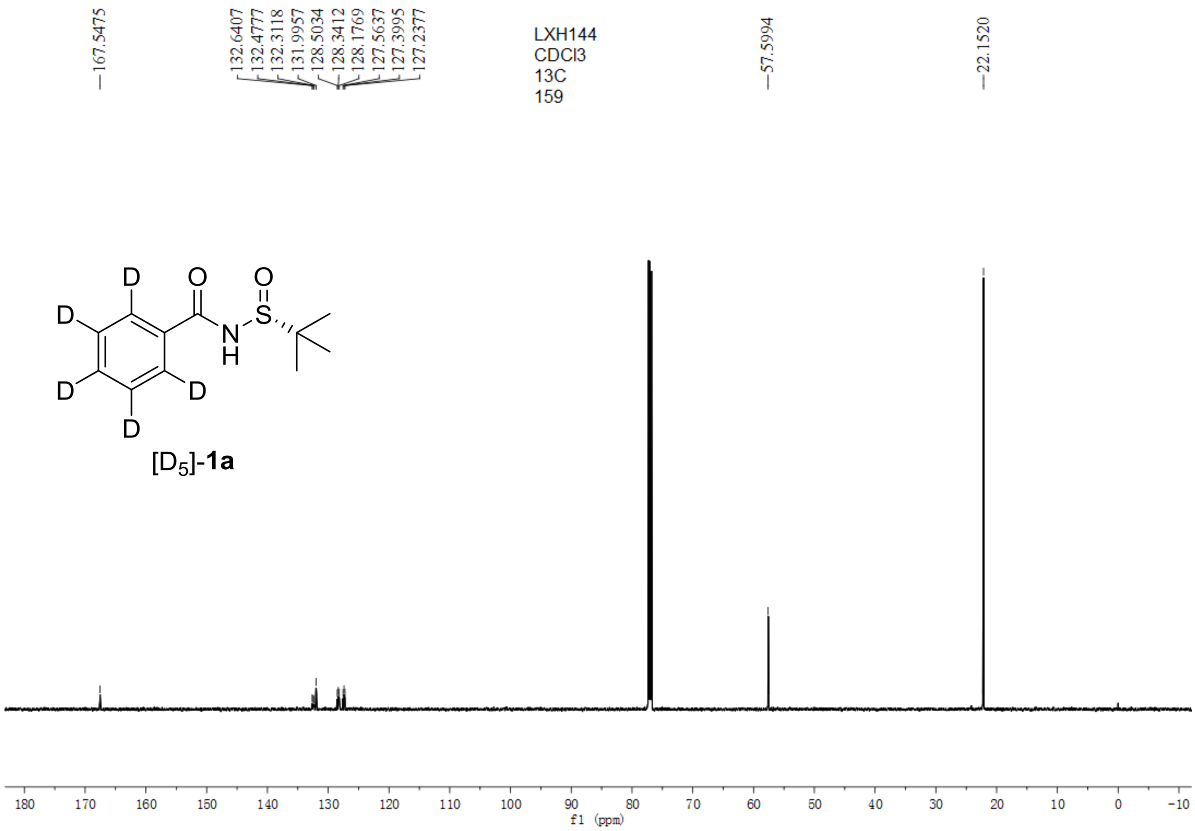
^{1}H NMR (400 MHz, $CDCl_3$) of **1a**



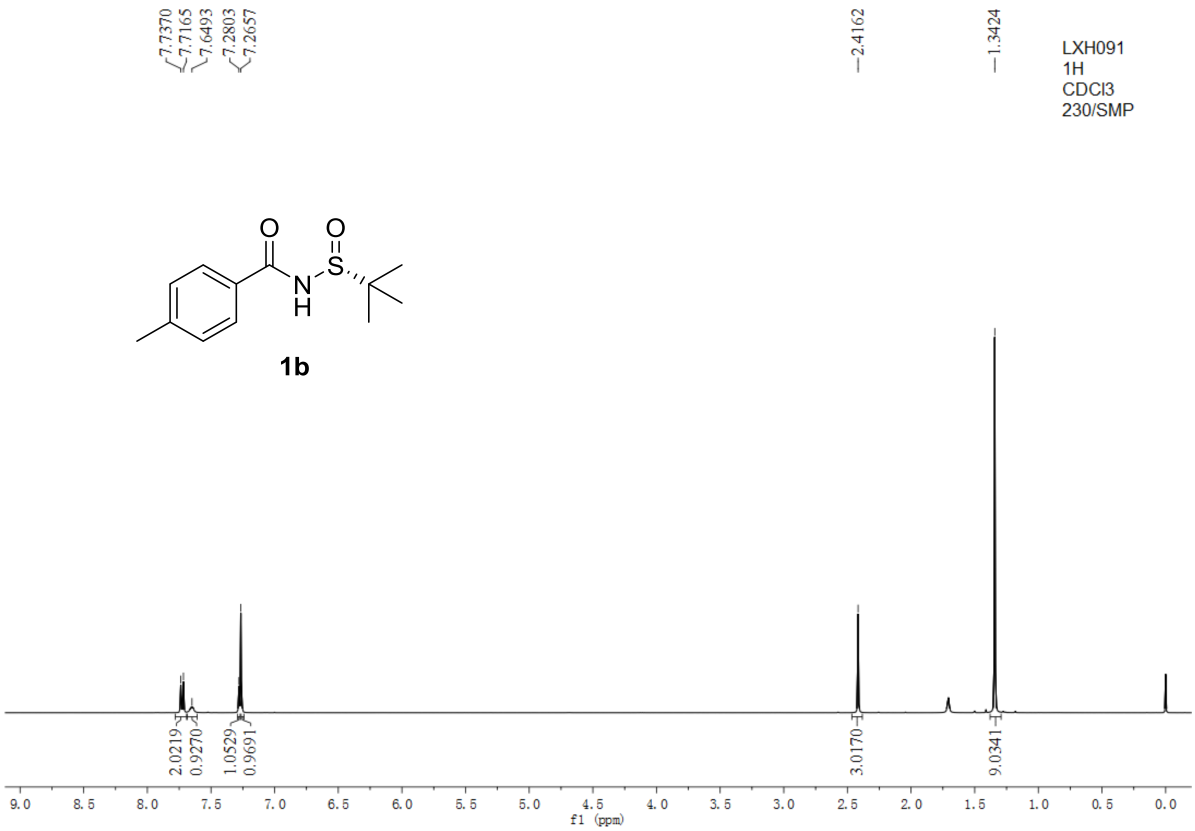
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **1a**



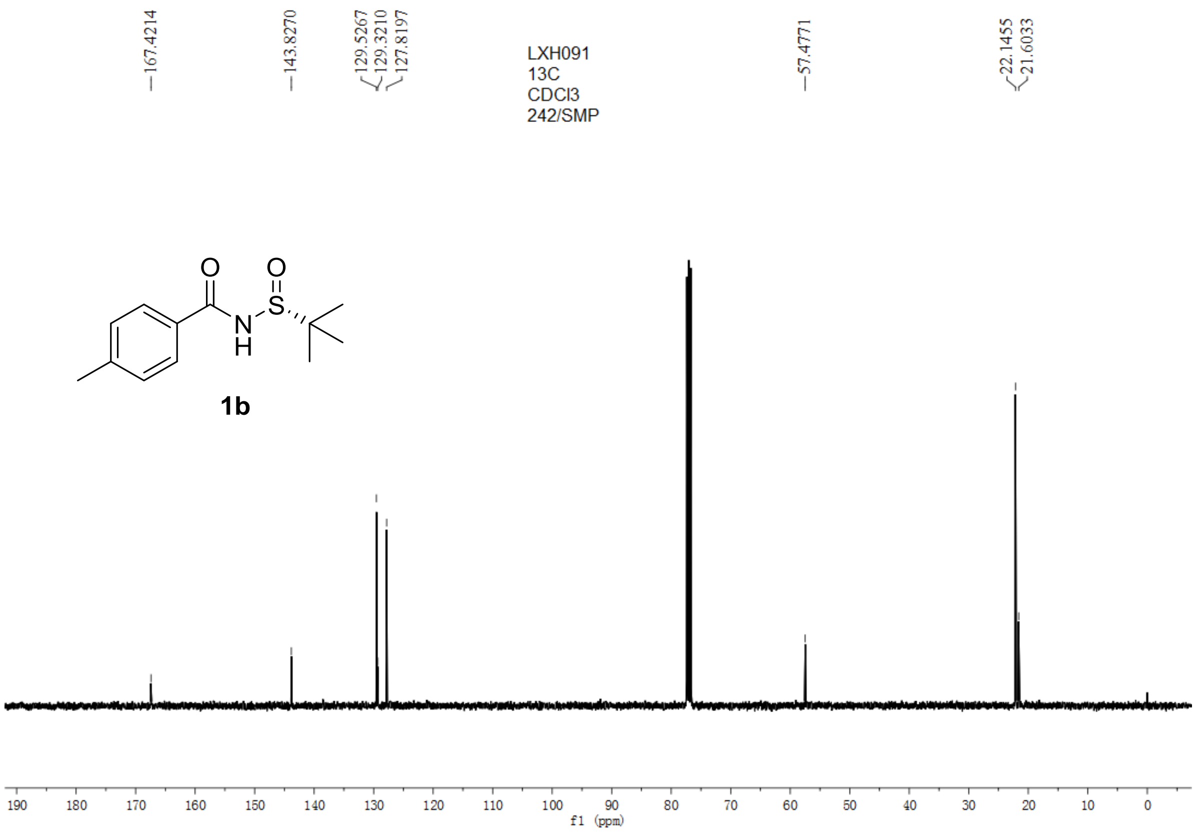
^{1}H NMR (400 MHz, $CDCl_3$) of [D_5]-**1a**



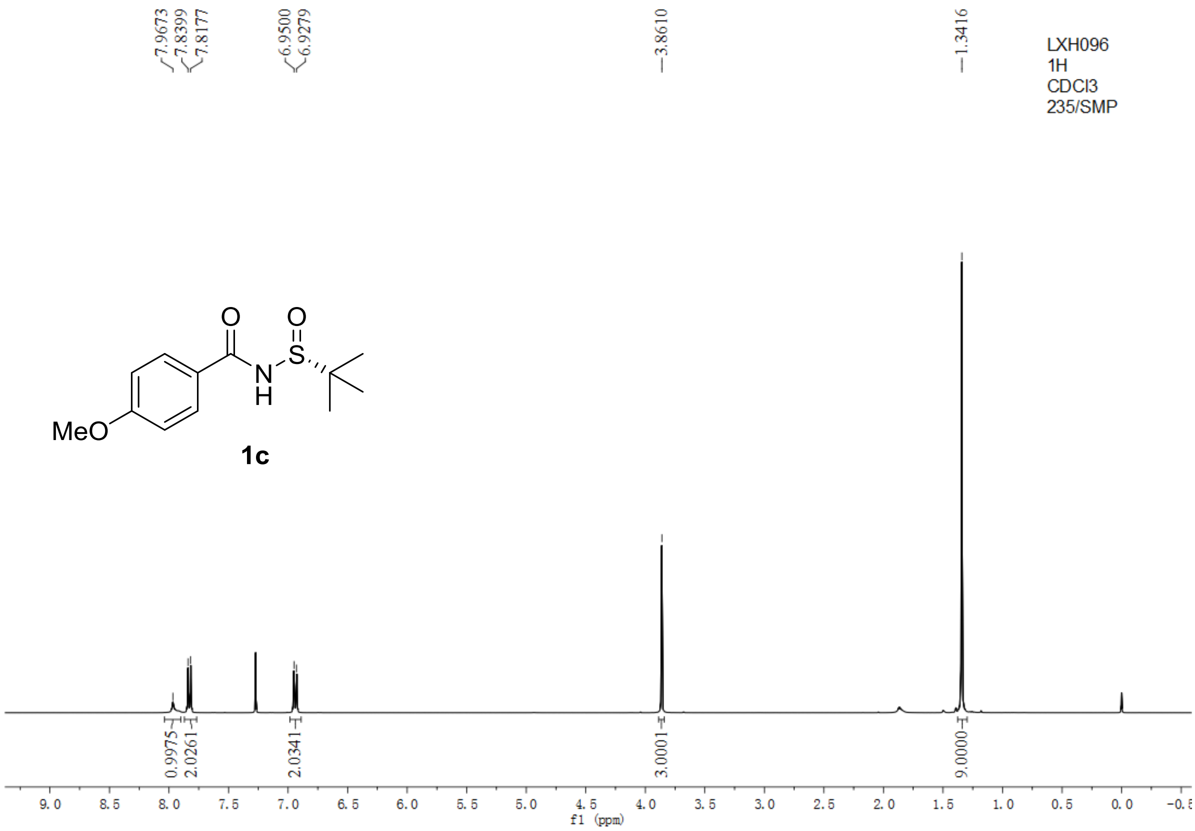
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) of [D_5]-**1a**



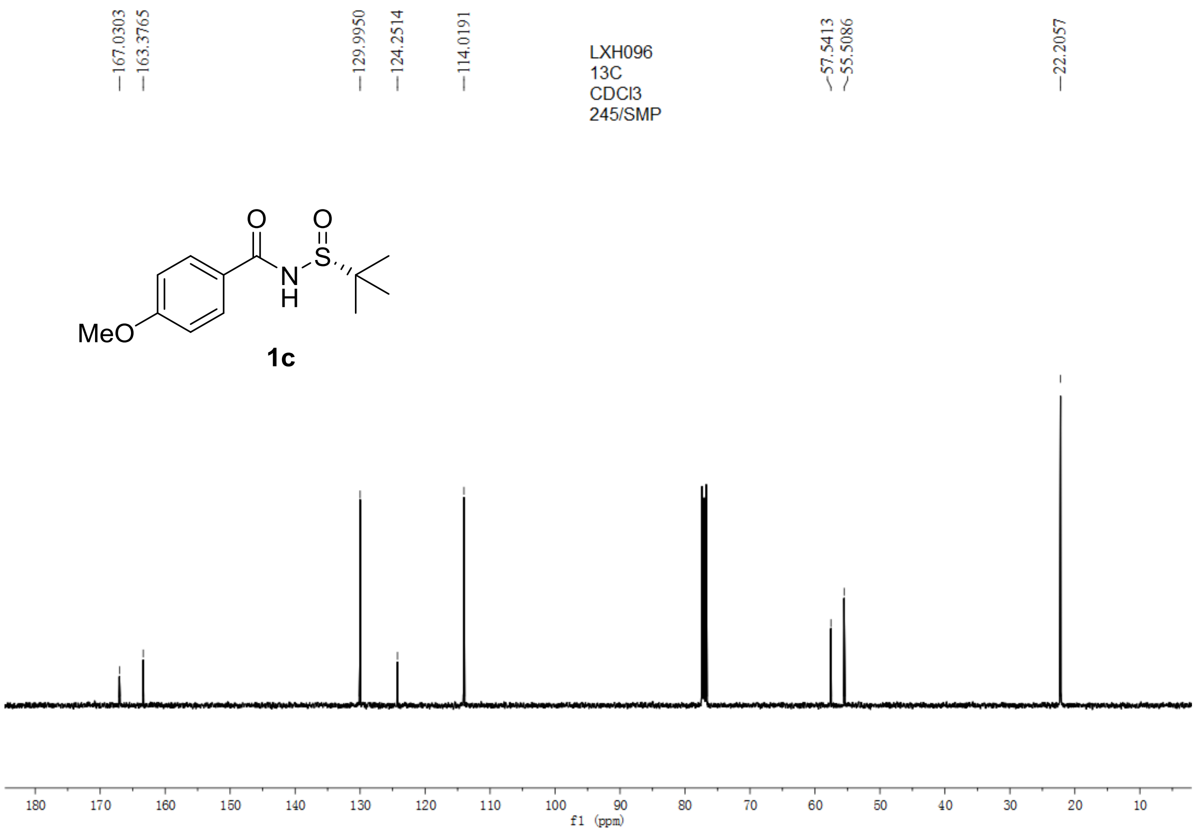
^{1}H NMR (400 MHz, $CDCl_3$) of **1b**



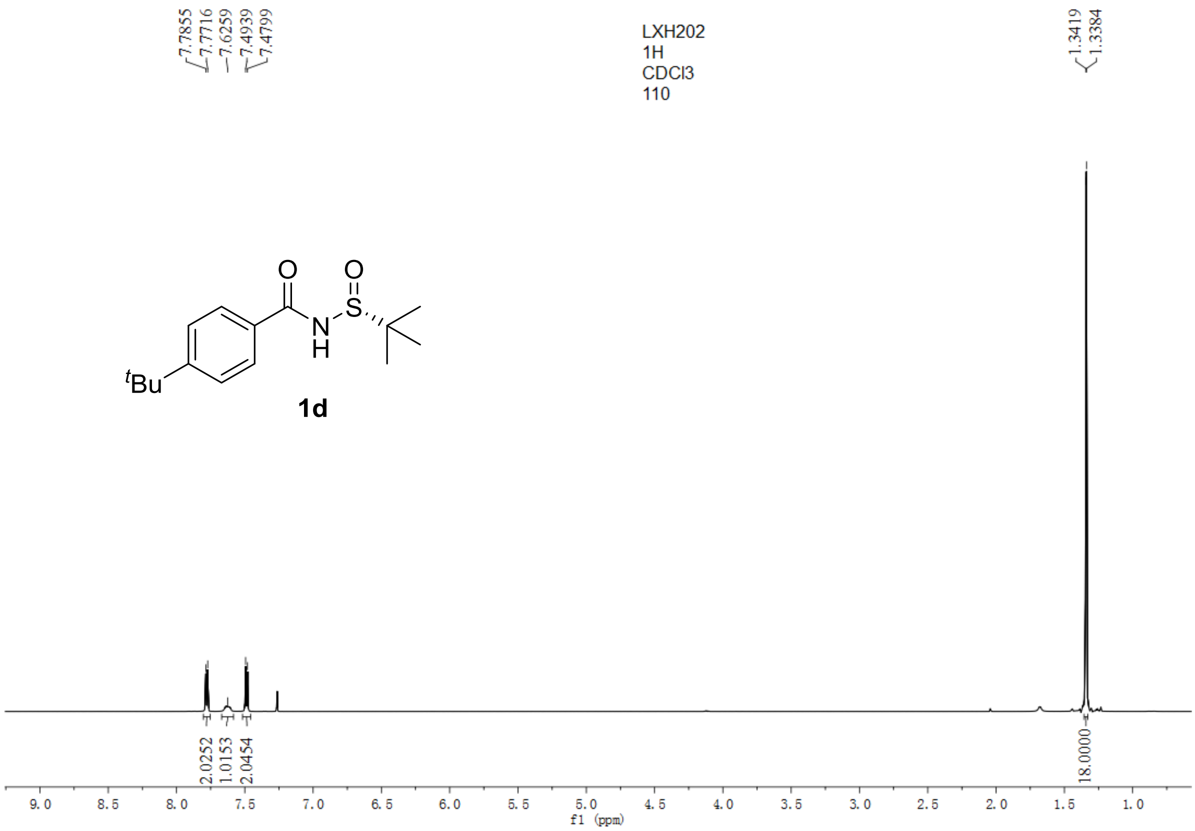
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **1b**



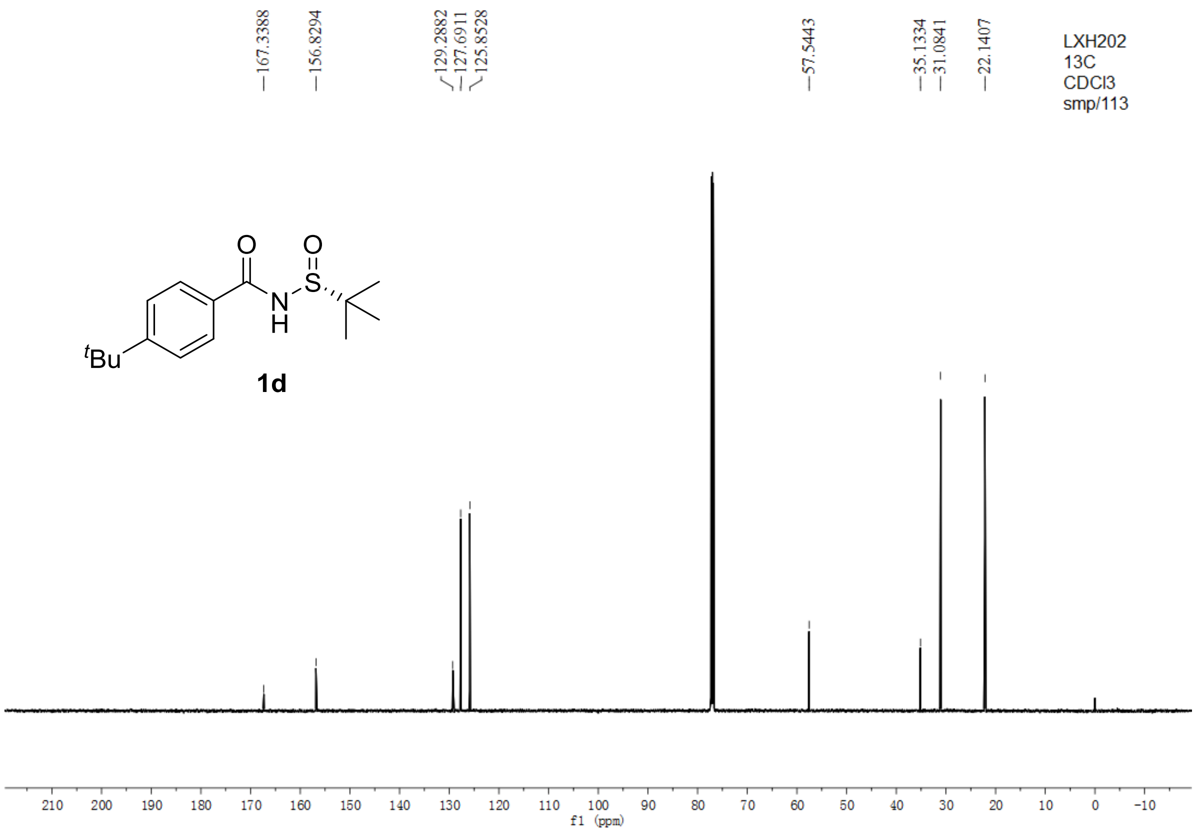
^{1}H NMR (400 MHz, CDCl$_3$) of **1c**



^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) of **1c**



[1]H NMR (600 MHz, $CDCl_3$) of **1d**



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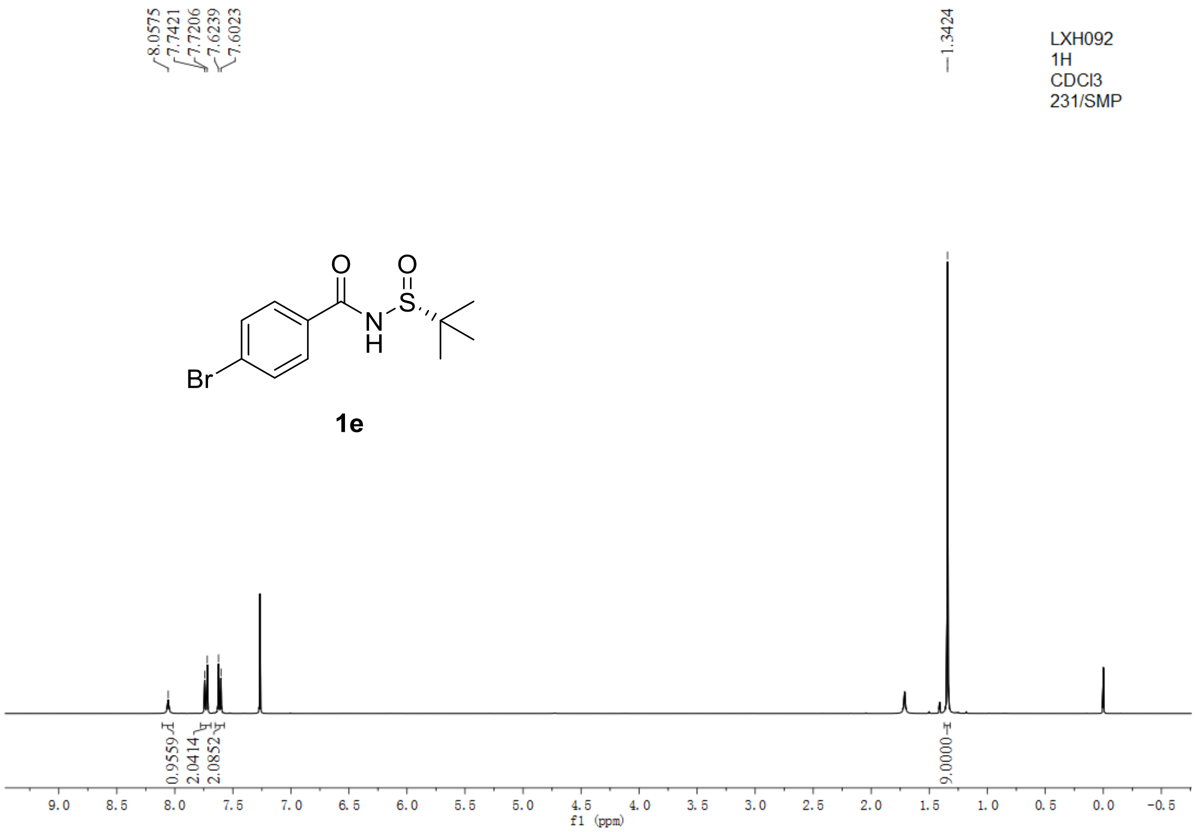
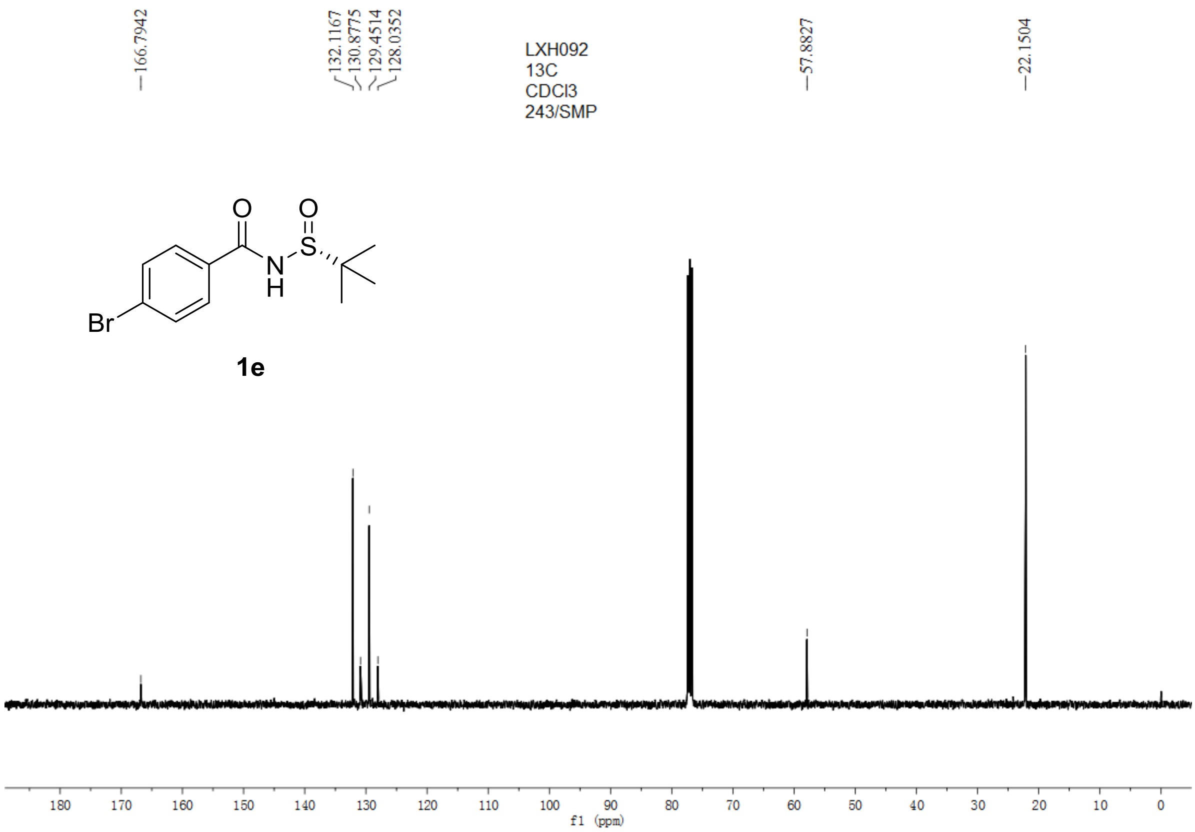


^{1}H NMR (400 MHz, $CDCl_3$) of **1e**



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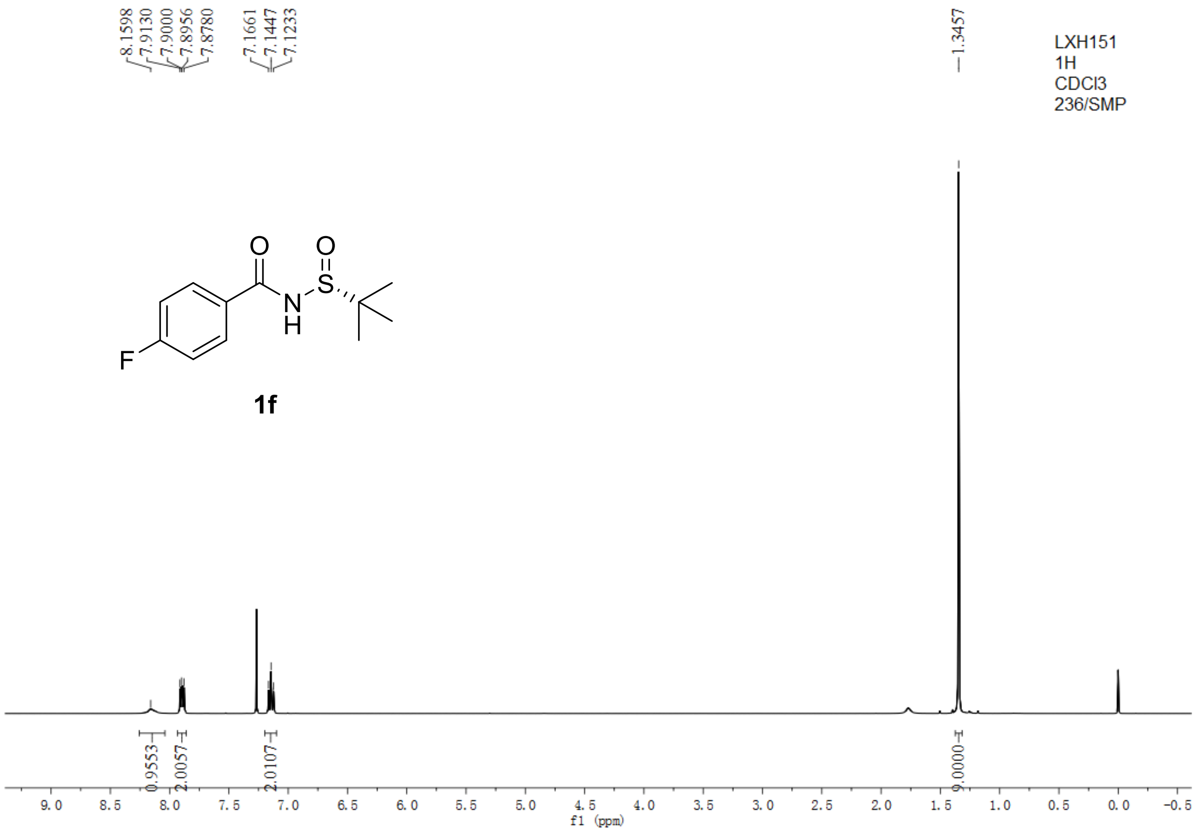
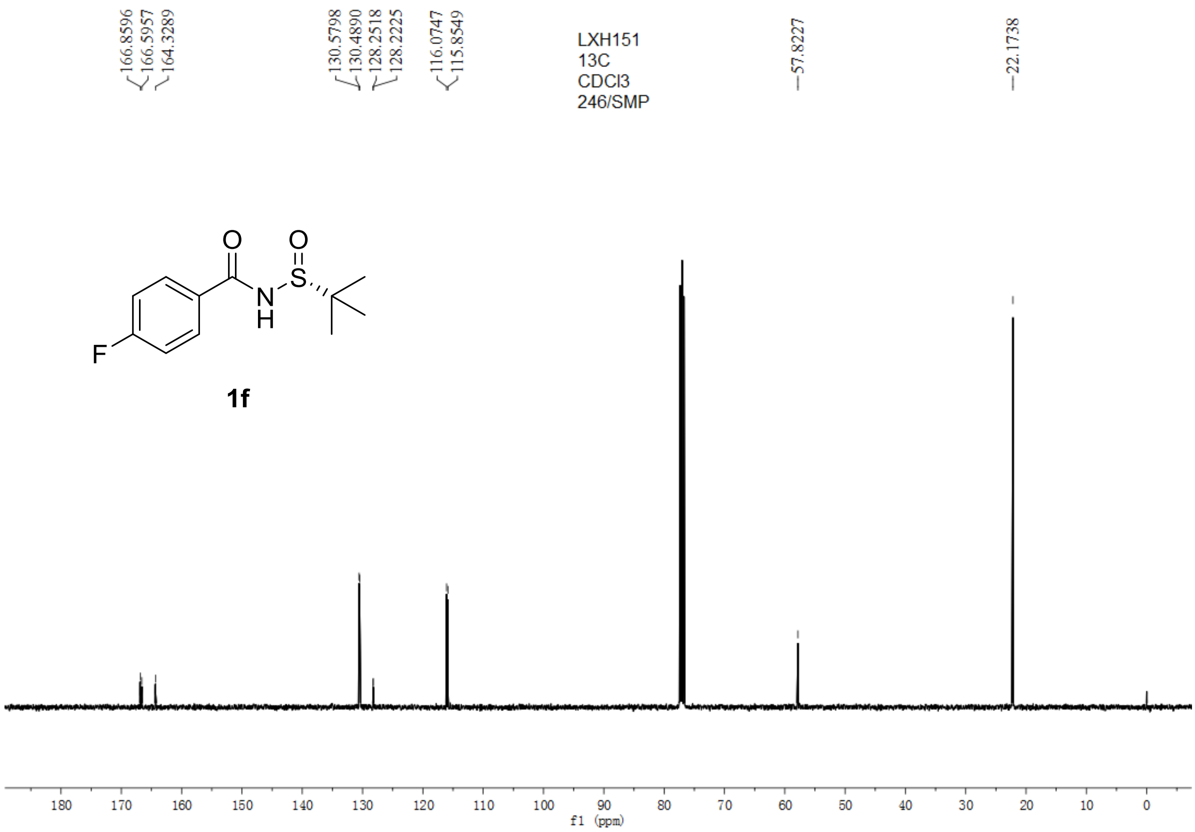
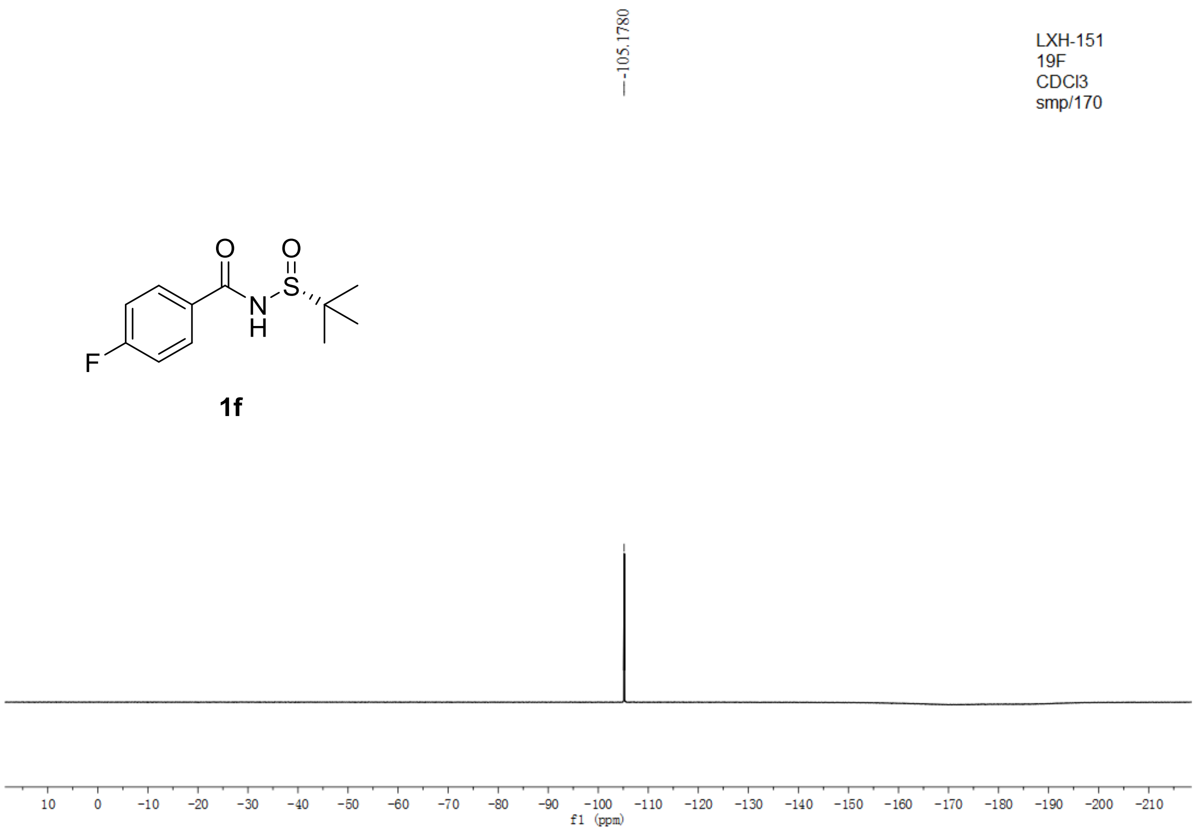


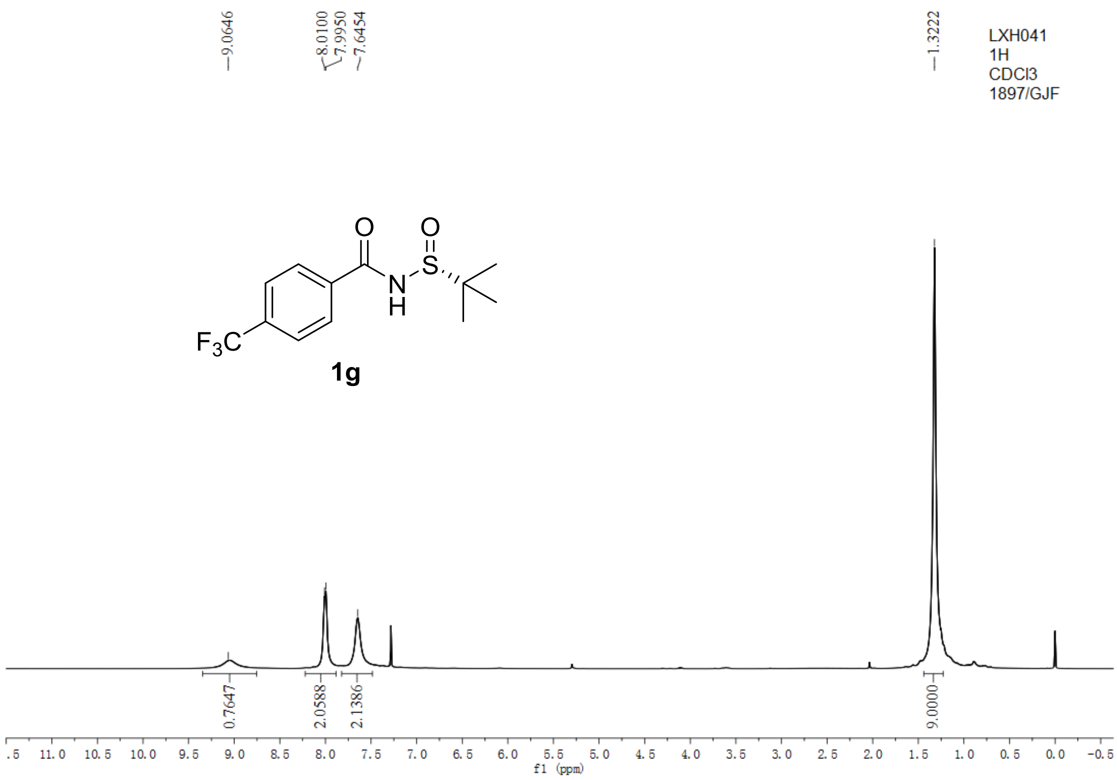
^{1}H NMR (400 MHz, $CDCl_3$) of **1f**



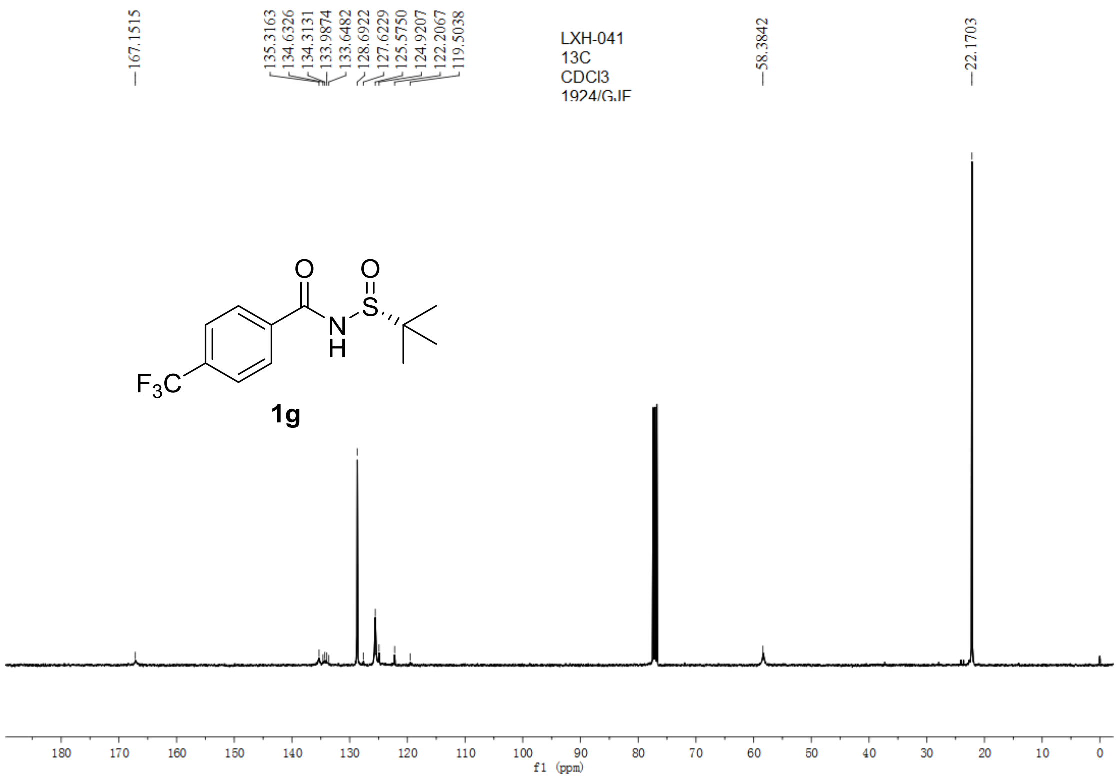
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **1f**



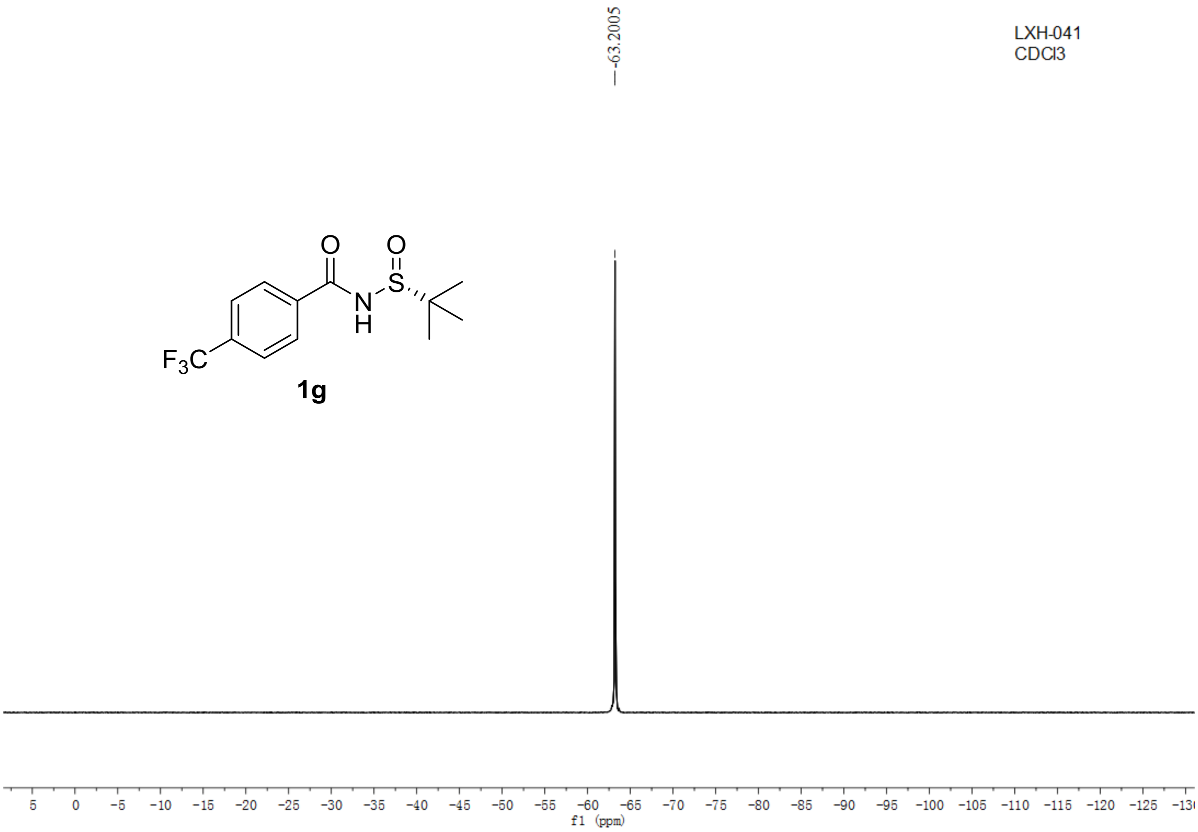
^{19}F NMR (565 MHz, CDCl$_3$) of **1f**



^{1}H NMR (400 MHz, CDCl$_3$) of **1g**



$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) of **1g**



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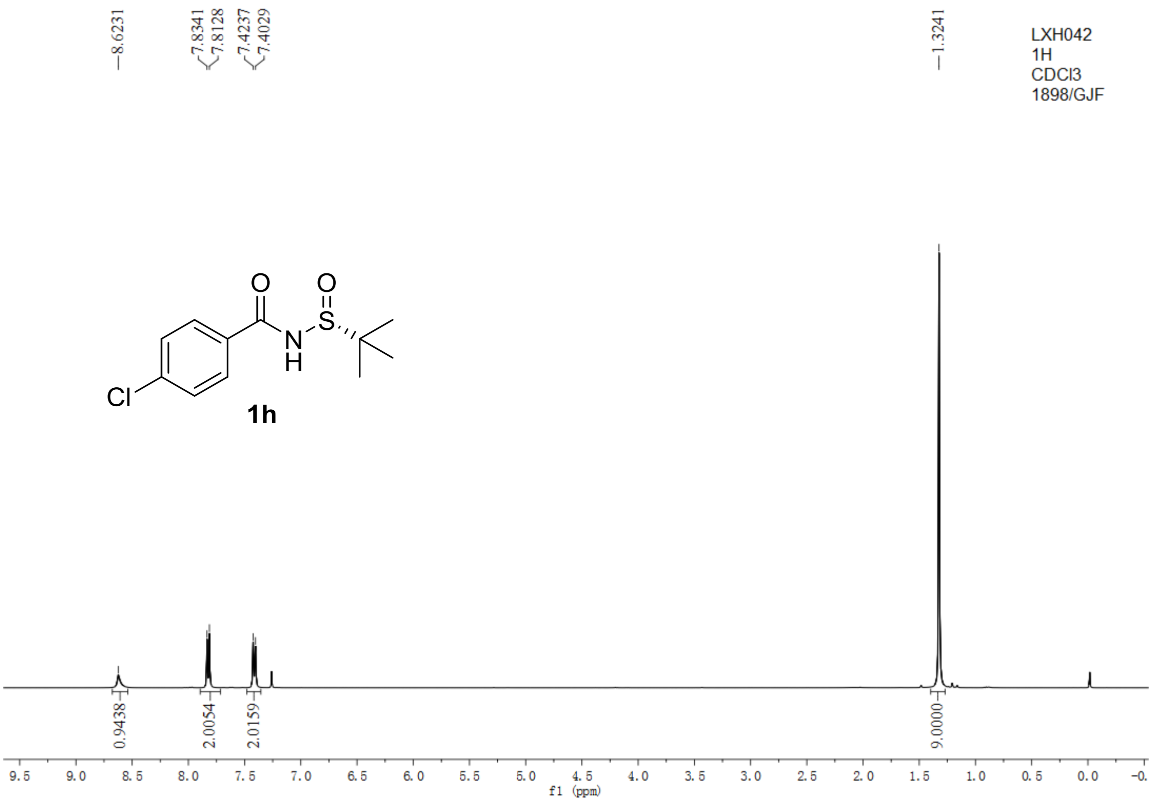
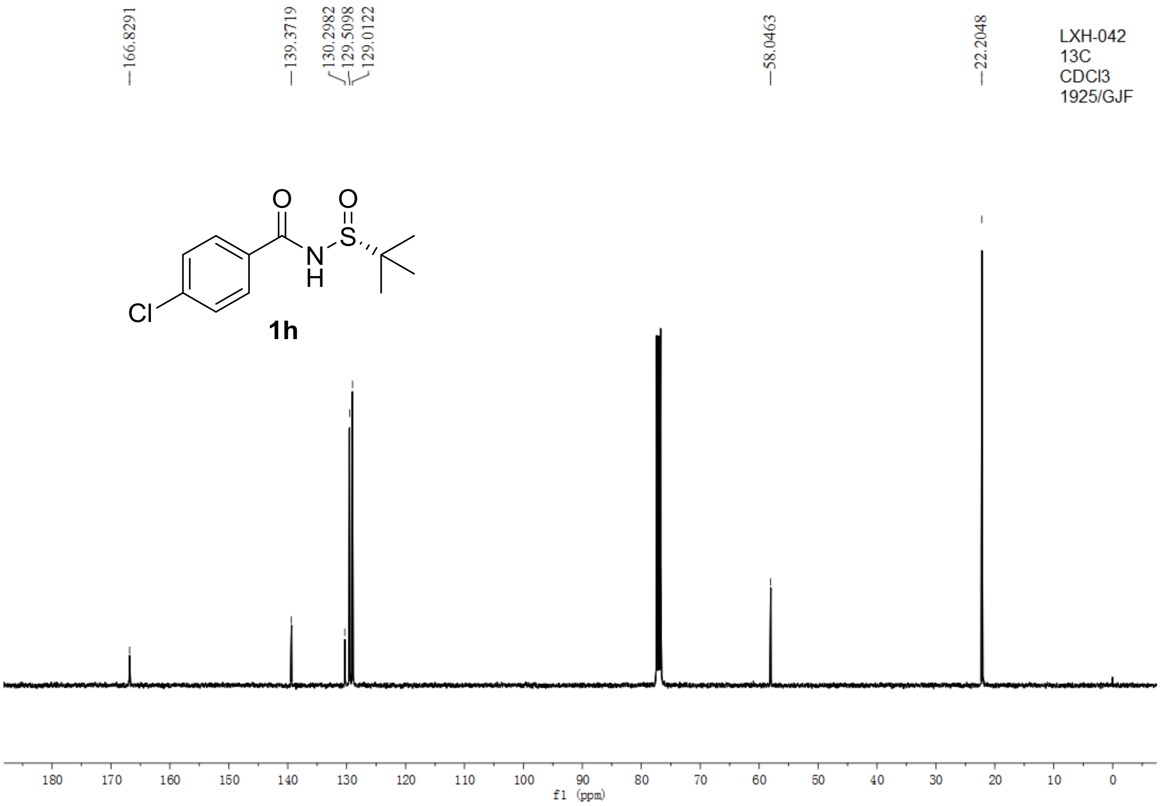
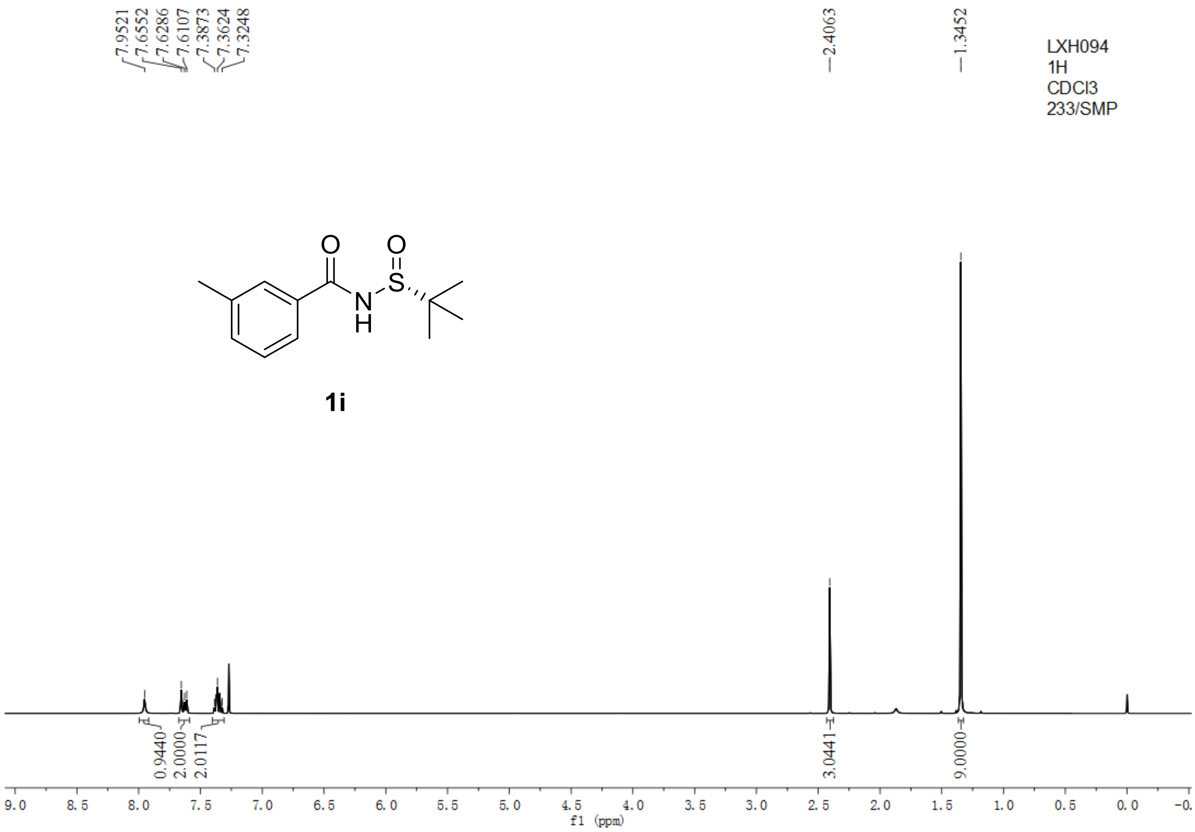


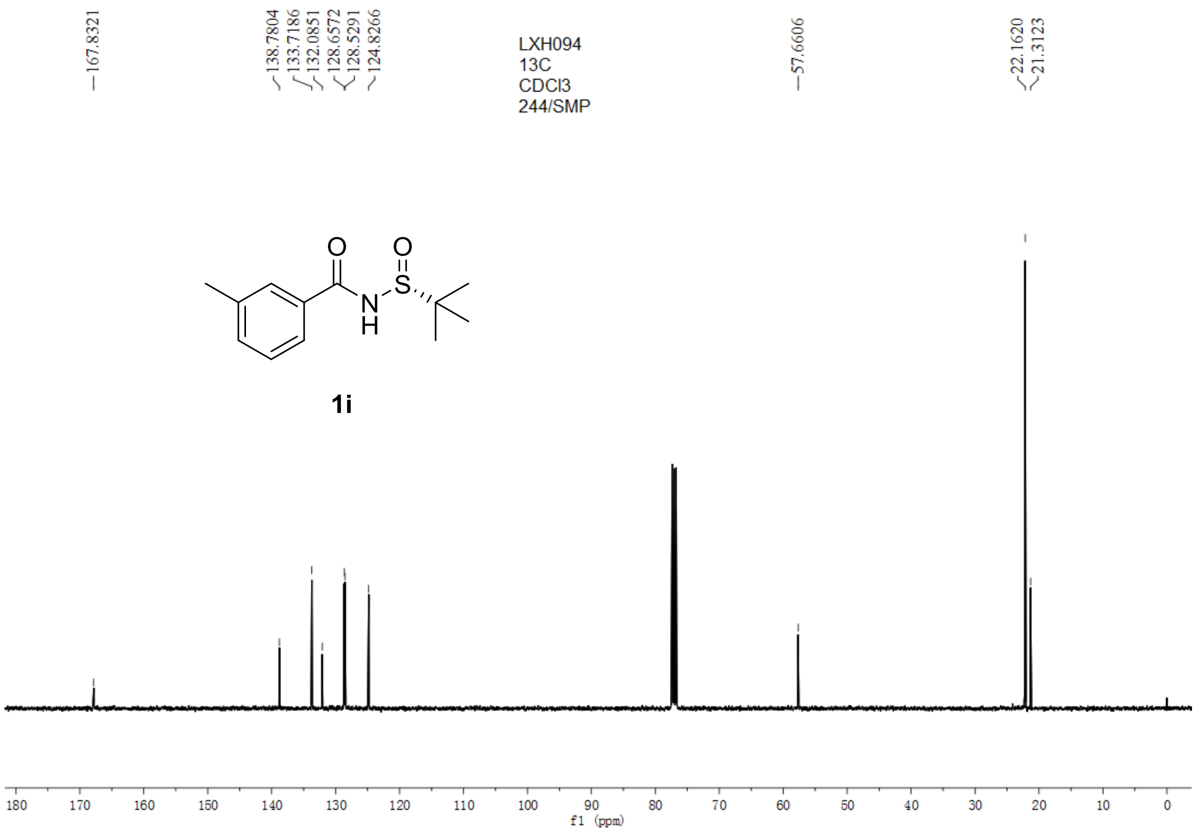
^{1}H NMR (400 MHz, $CDCl_3$) of **1h**



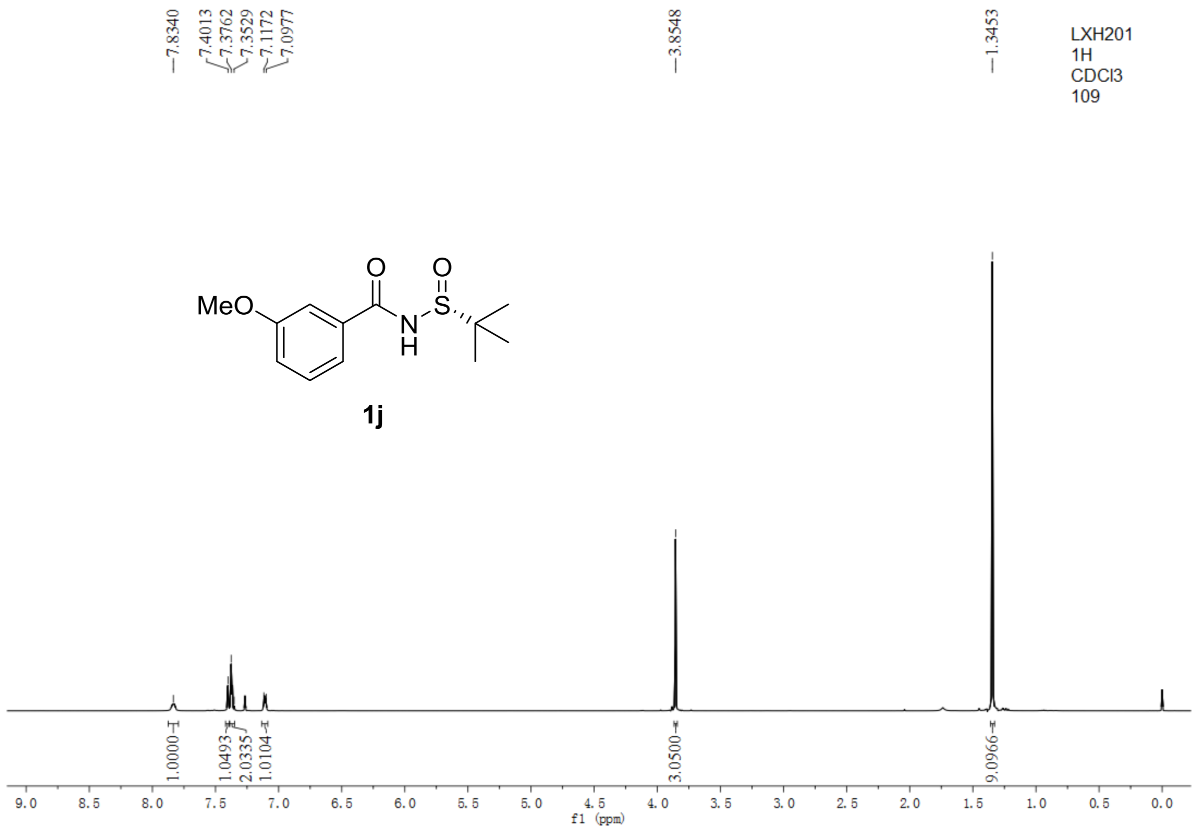
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **1h**



^{1}H NMR (400 MHz, $CDCl_3$) of **1i**

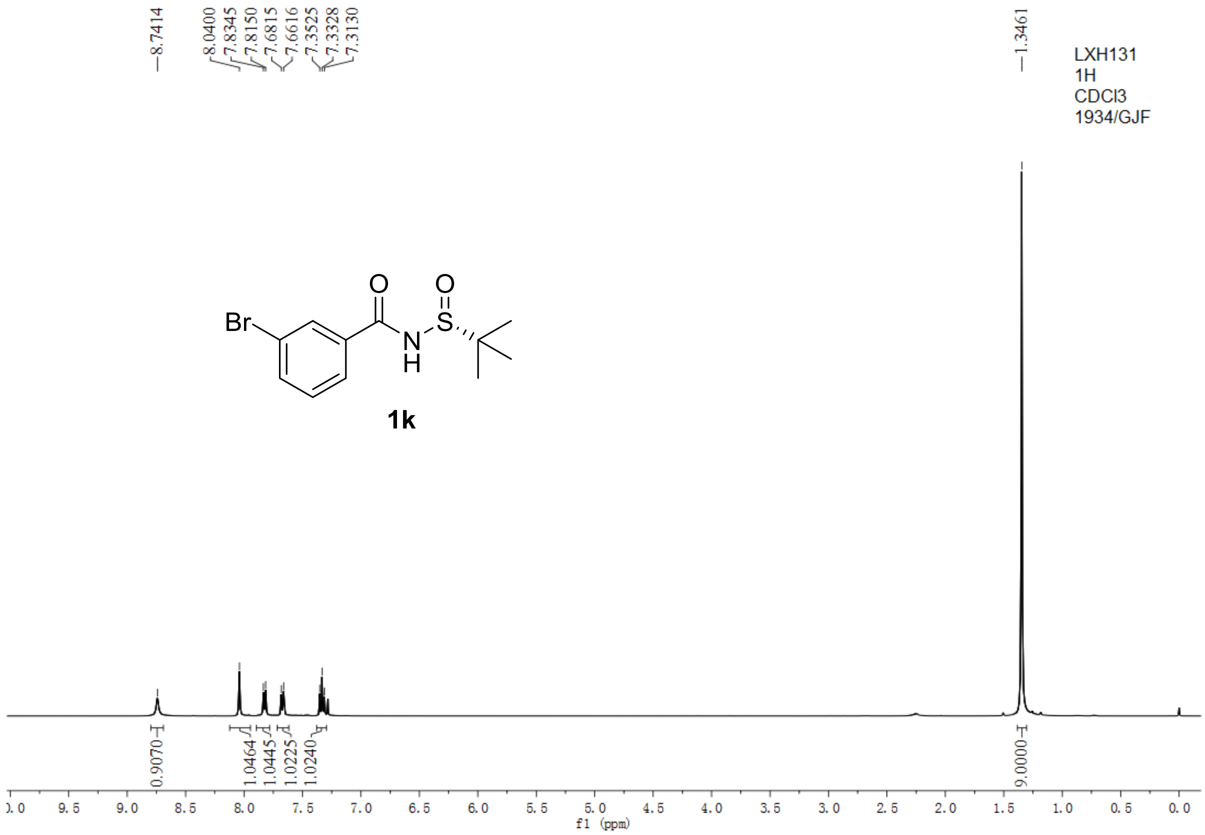


$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **1i**

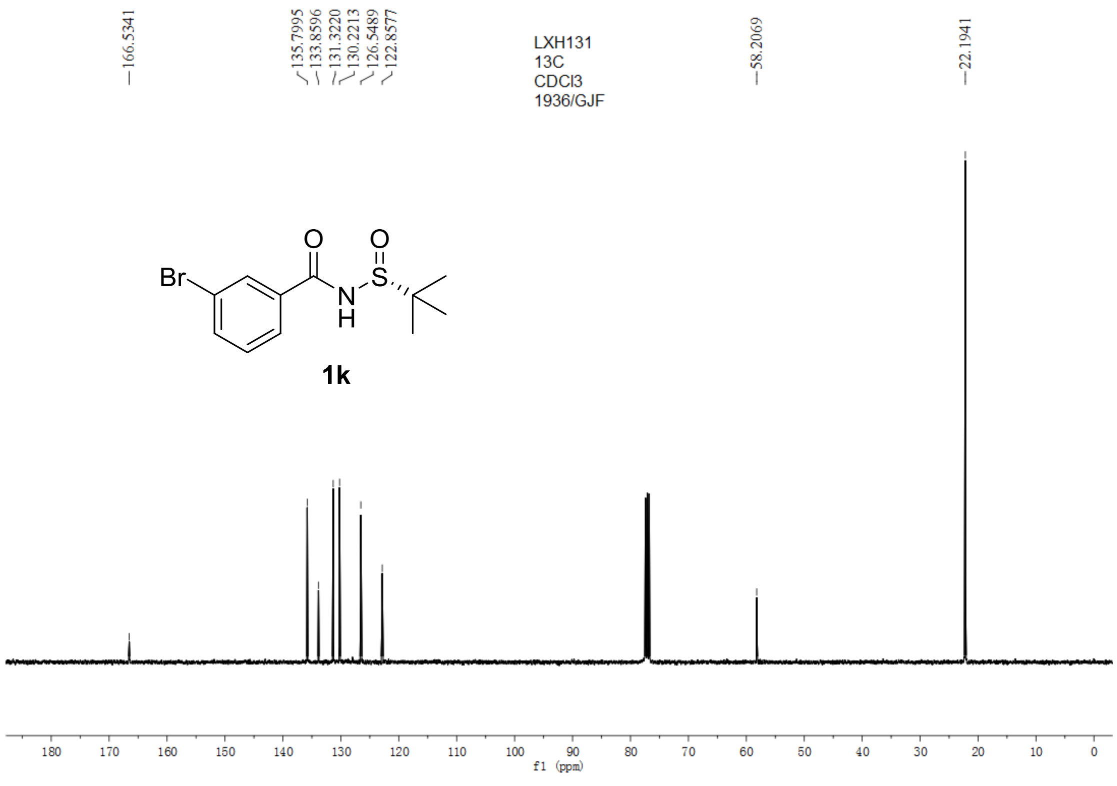


^1H NMR (600 MHz, $CDCl_3$) of **1j**

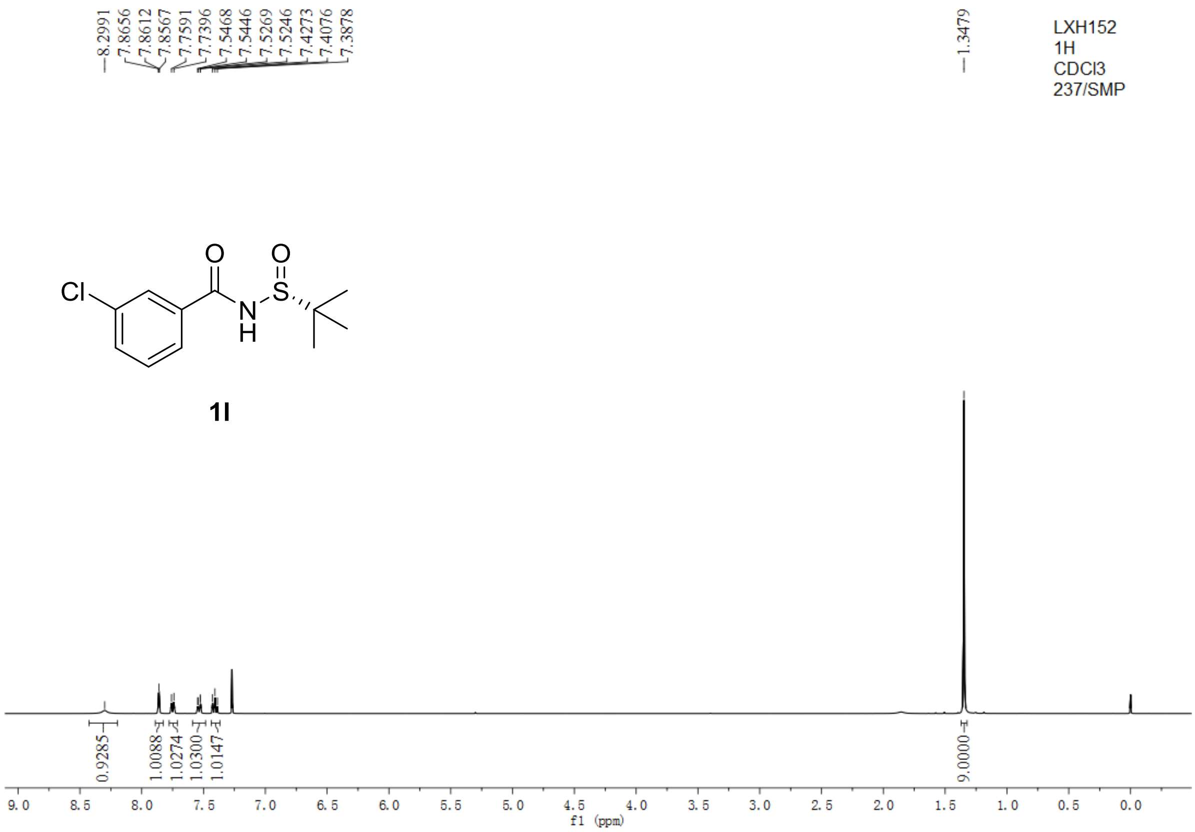
$^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) of **1j**



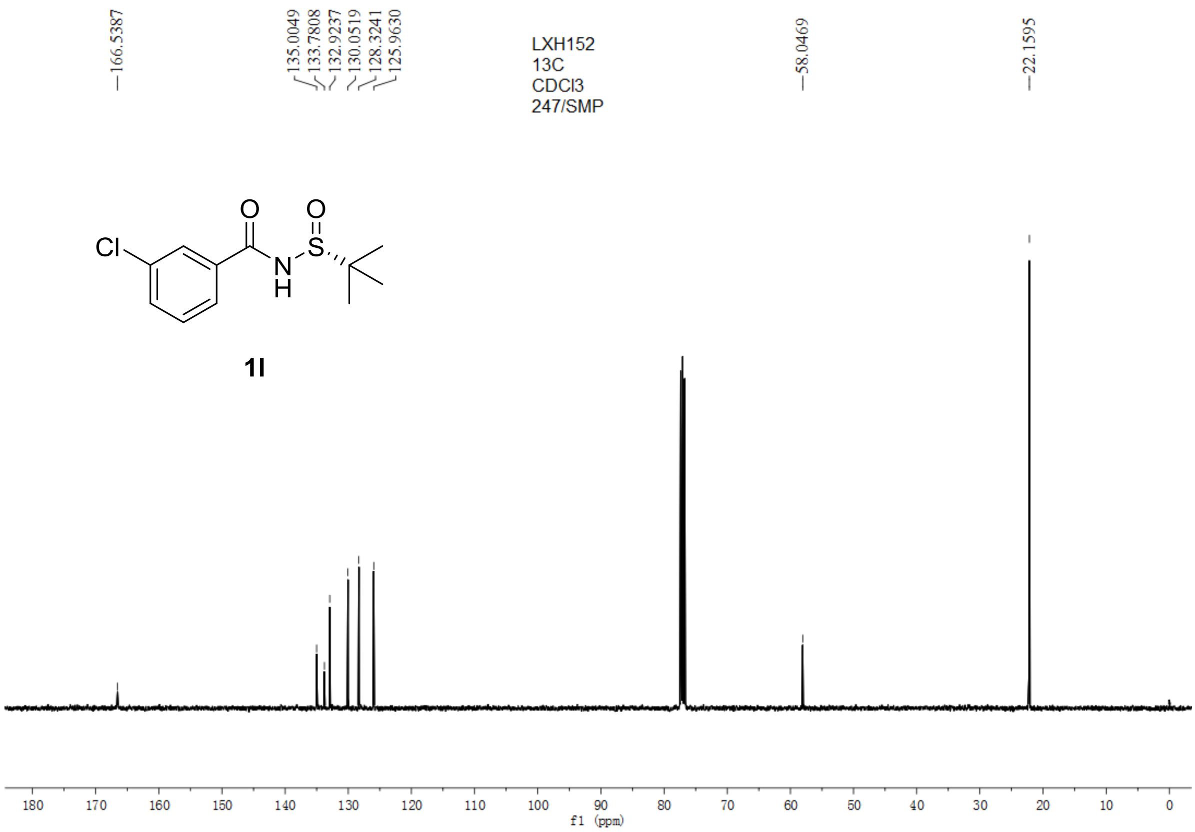
^{1}H NMR (400 MHz, CDCl$_3$) of **1k**



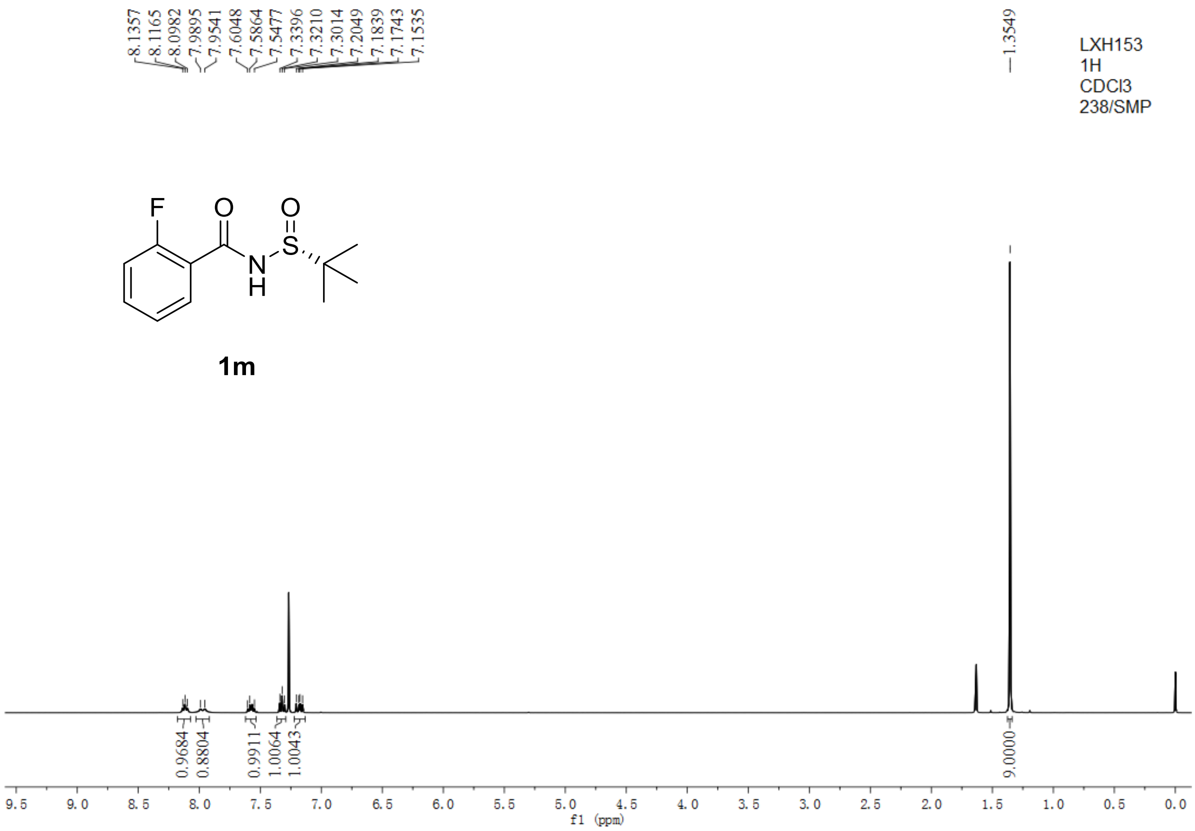
^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) of **1k**



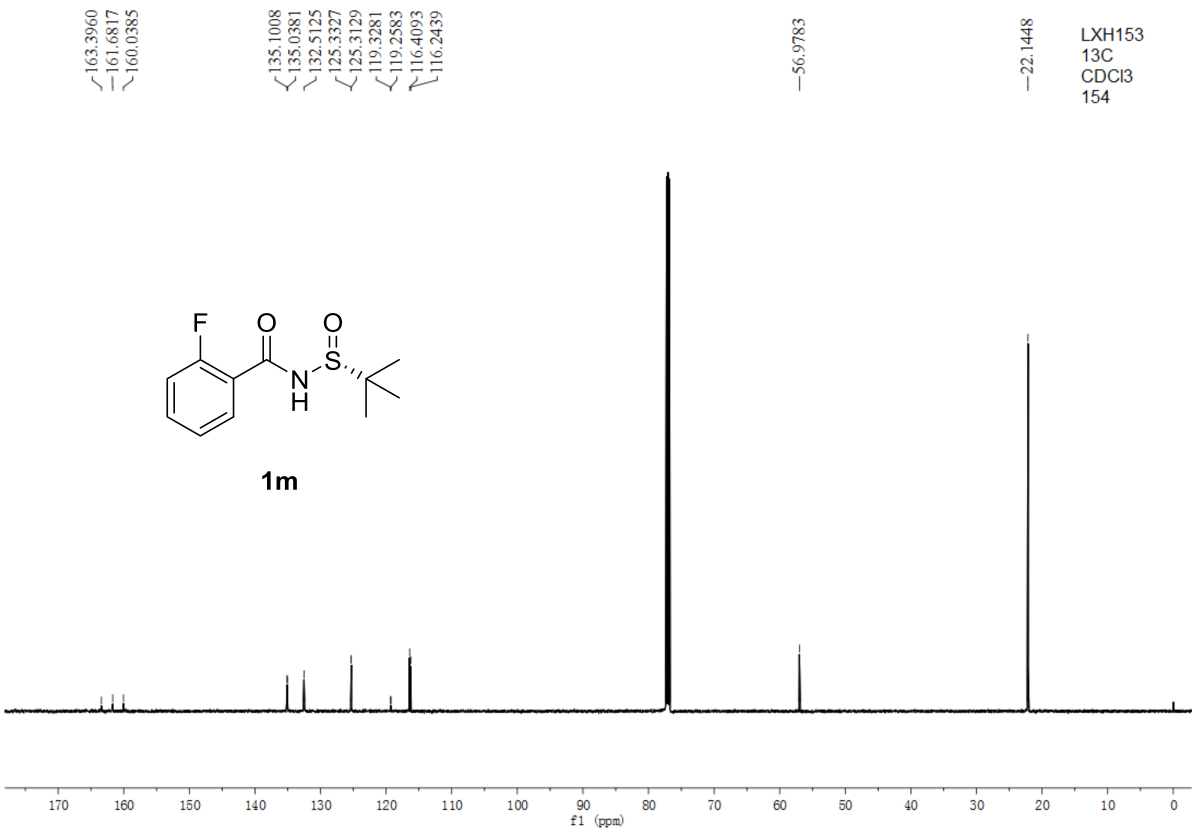
^{1}H NMR (400 MHz, $CDCl_3$) of **1l**



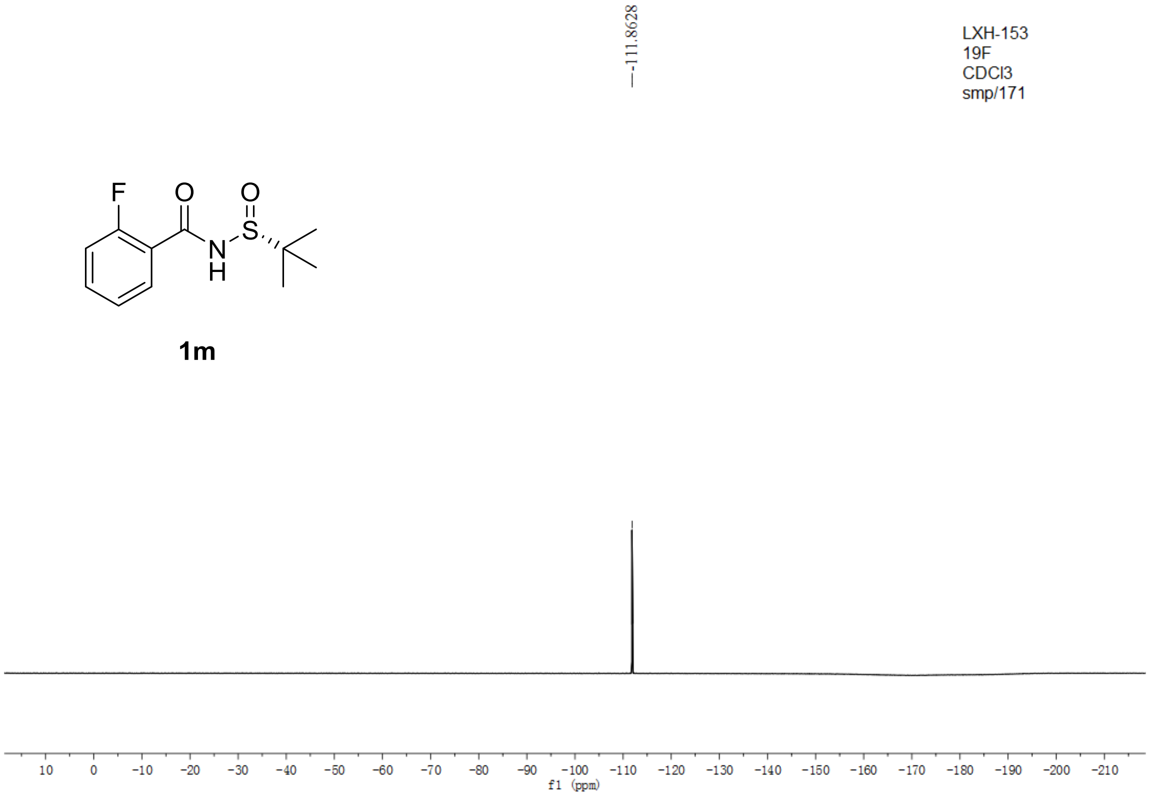
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **1l**



^{1}H NMR (400 MHz, CDCl$_3$) of **1m**

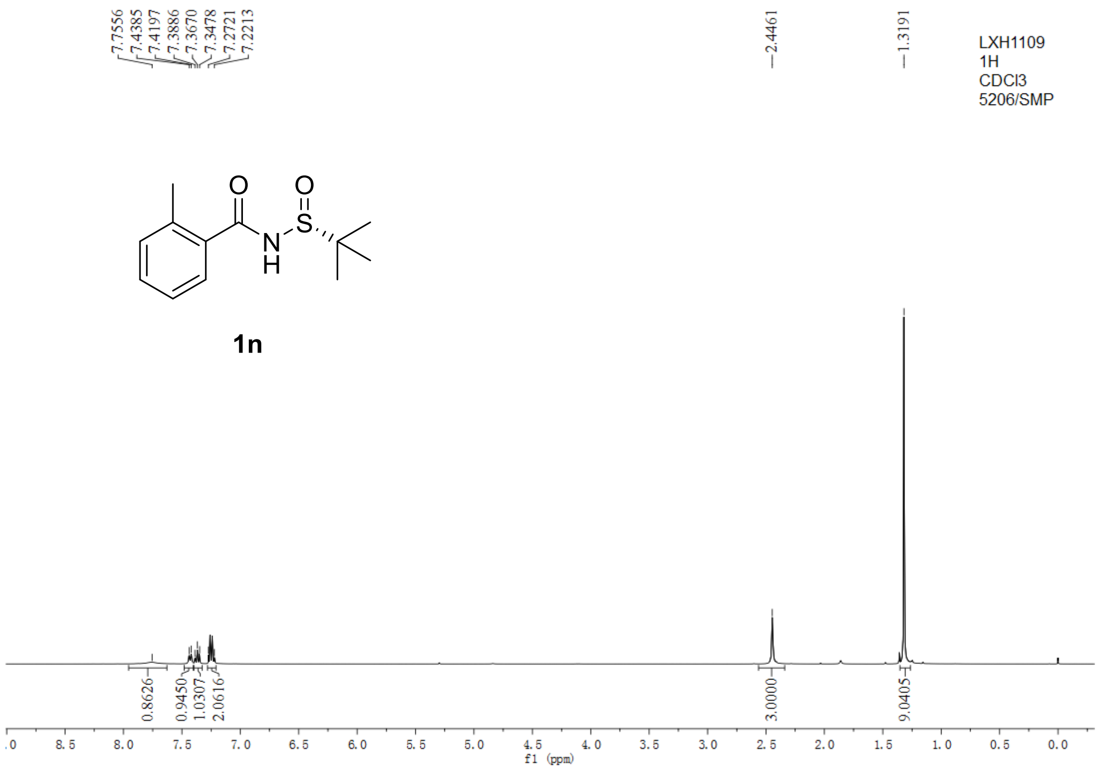


^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) of **1m**



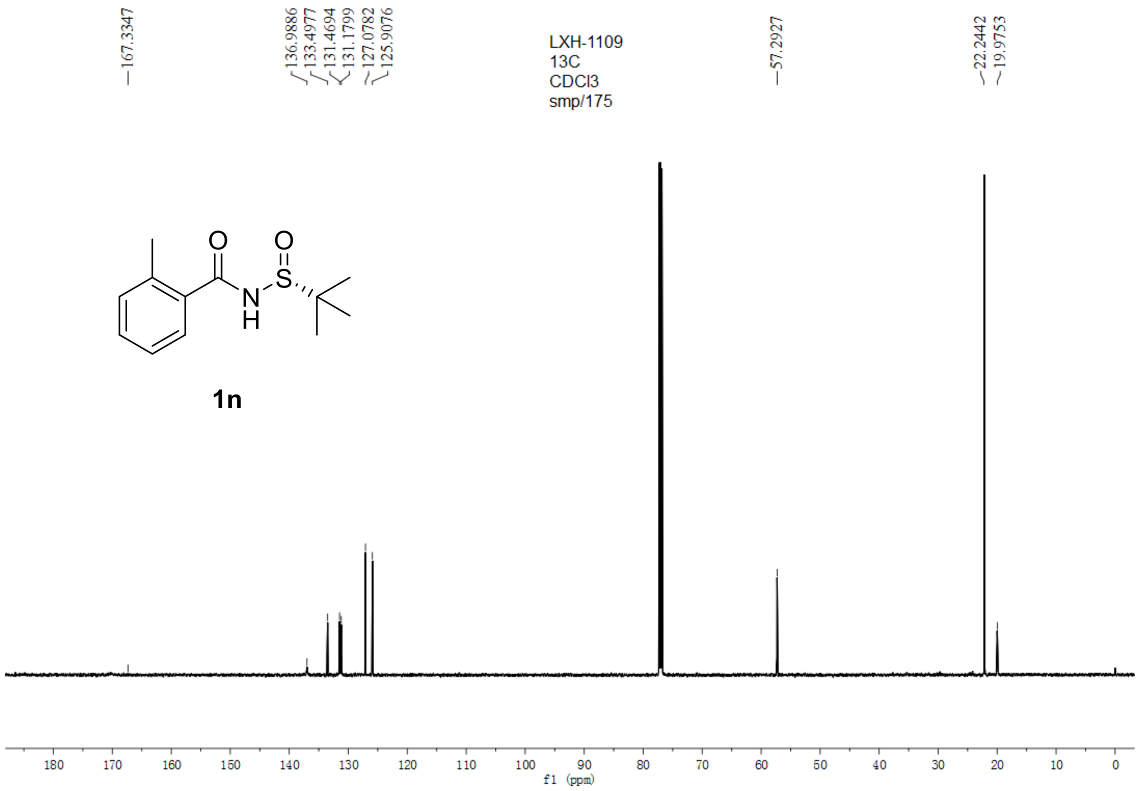
1m

^{19}F NMR (565 MHz, $CDCl_3$) of **1m**

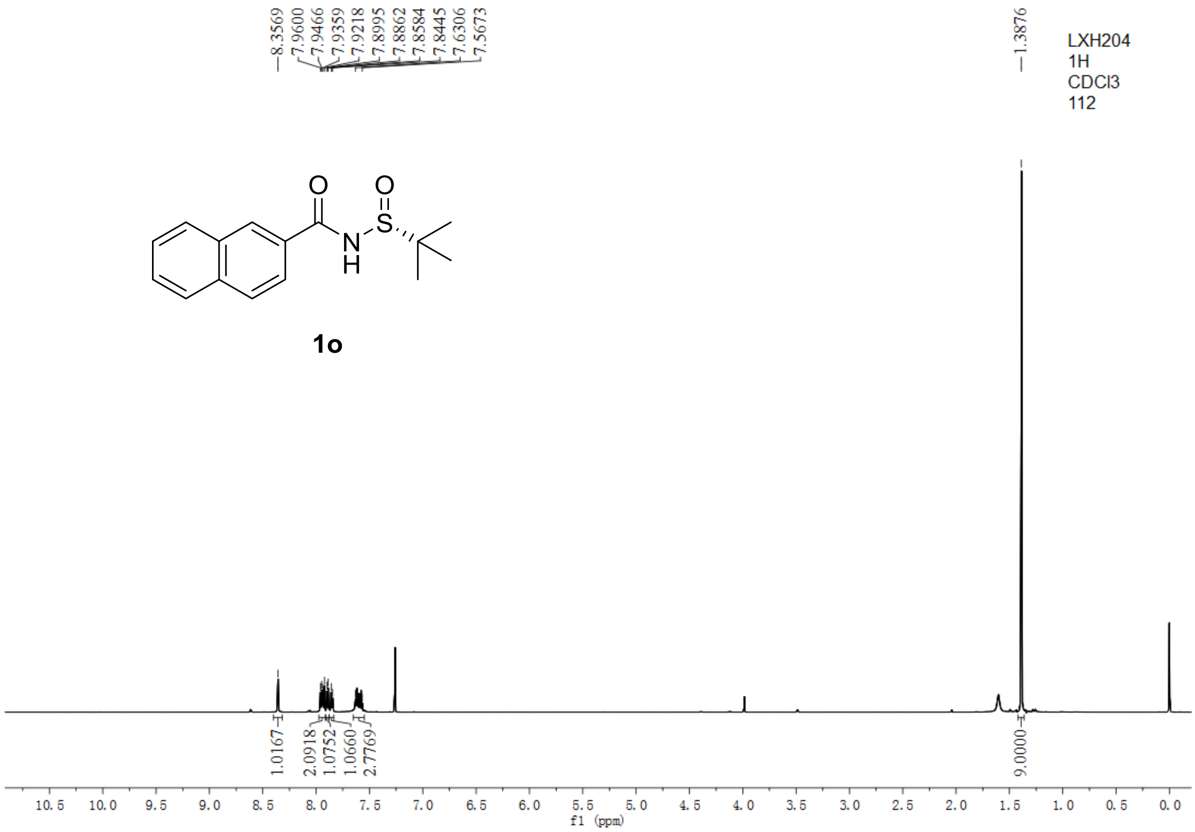


1n

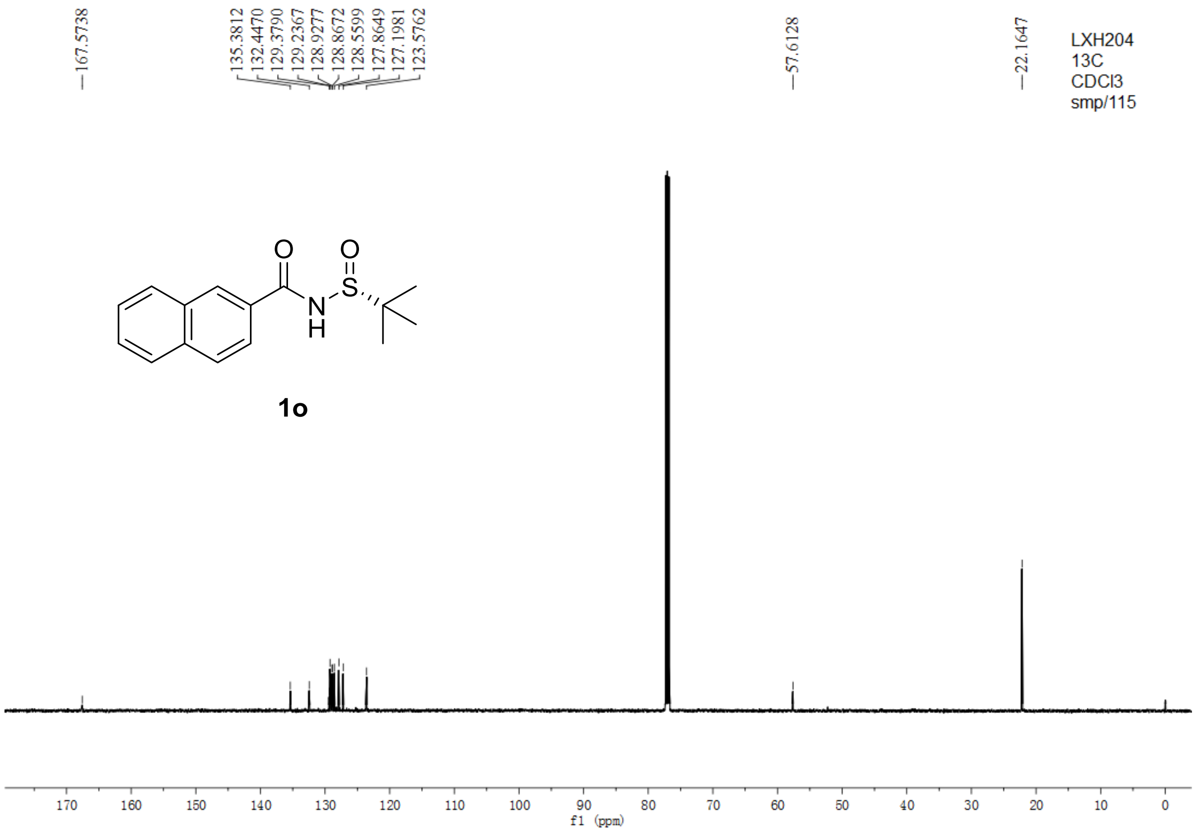
^{1}H NMR (400 MHz, $CDCl_3$) of **1n**



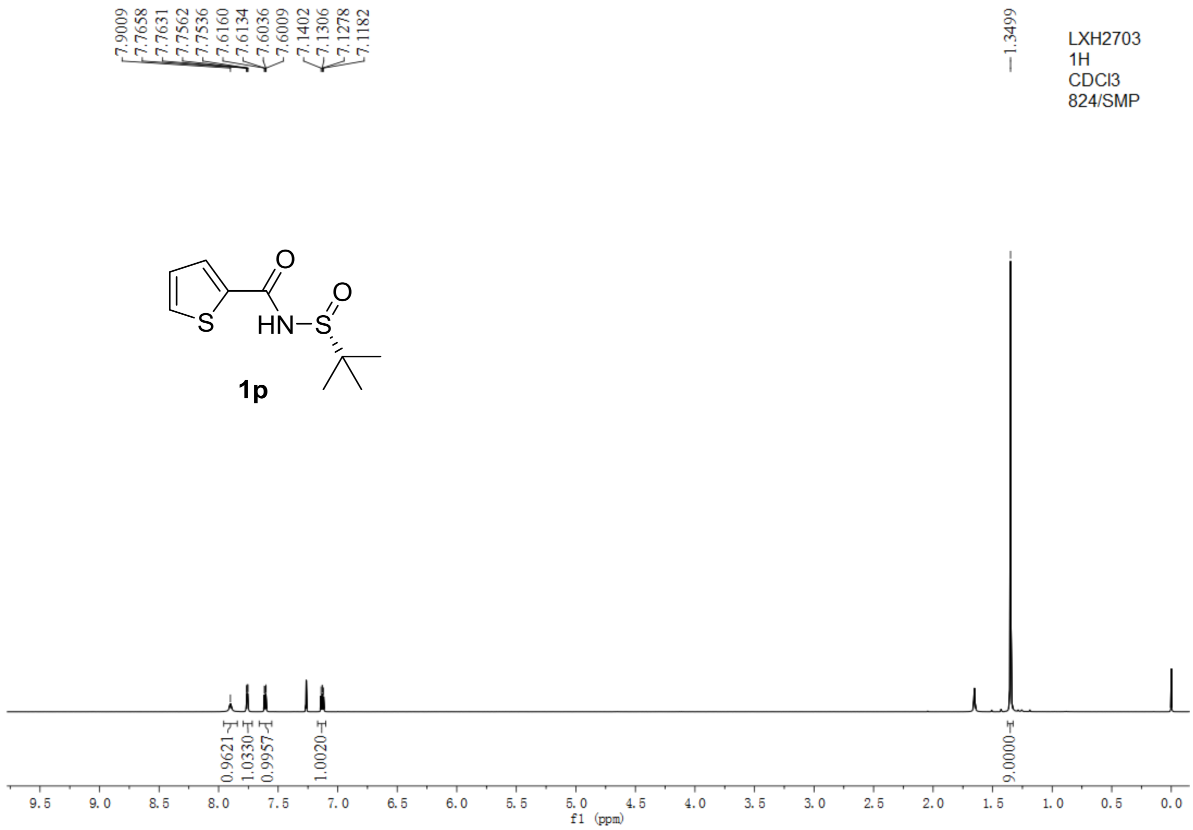
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **1n**



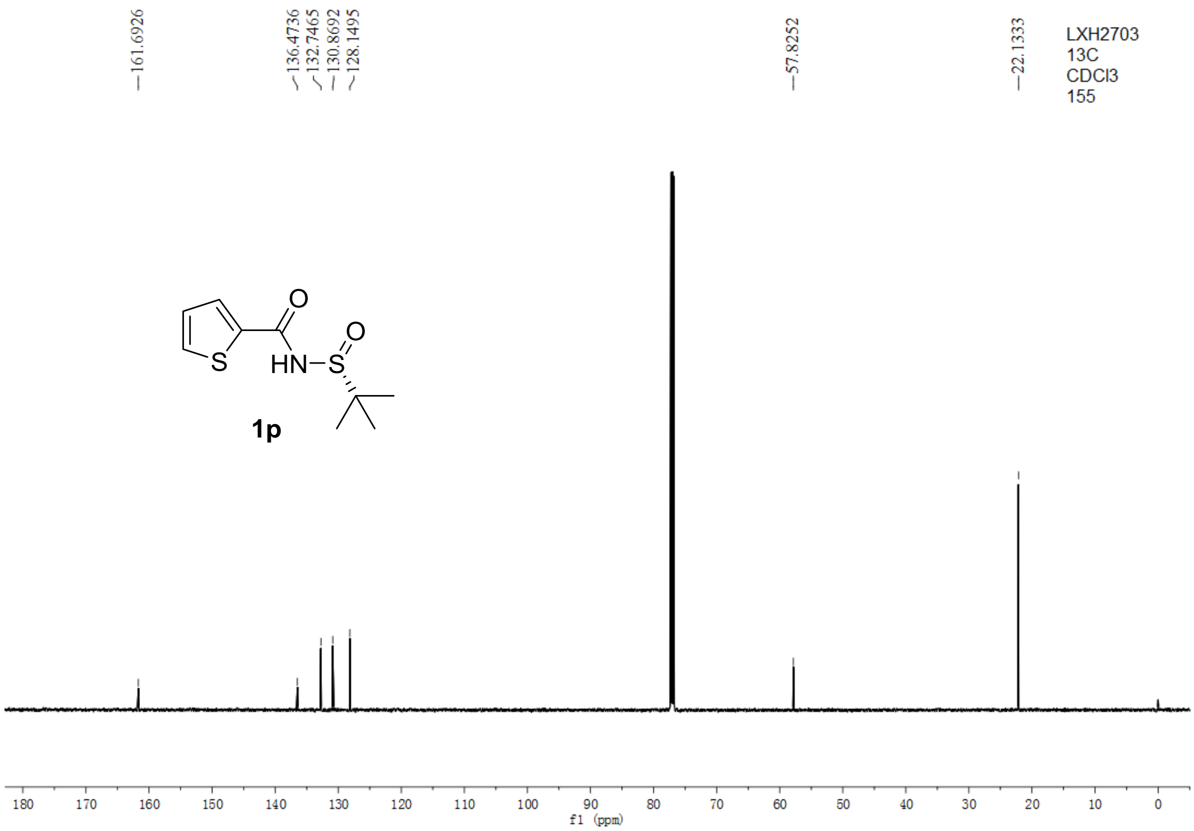
^{1}H NMR (600 MHz, $CDCl_3$) of **1o**



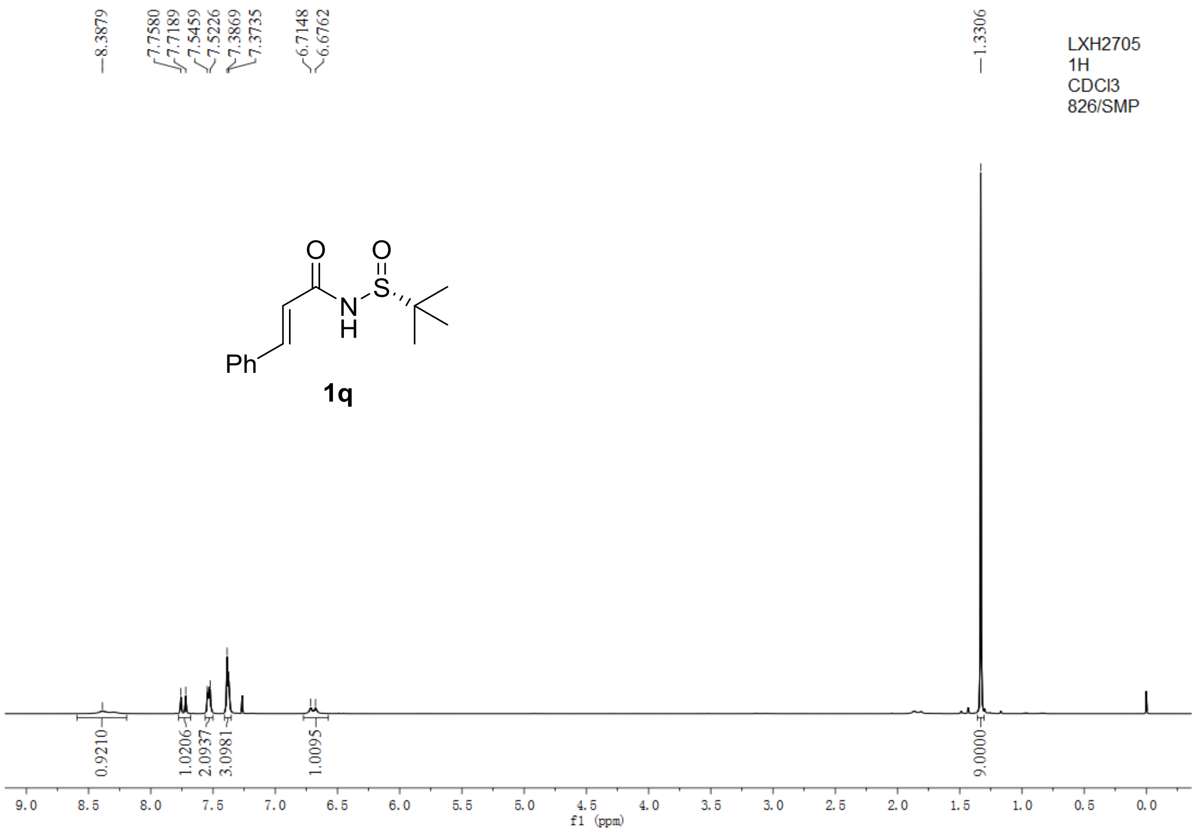
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **1o**



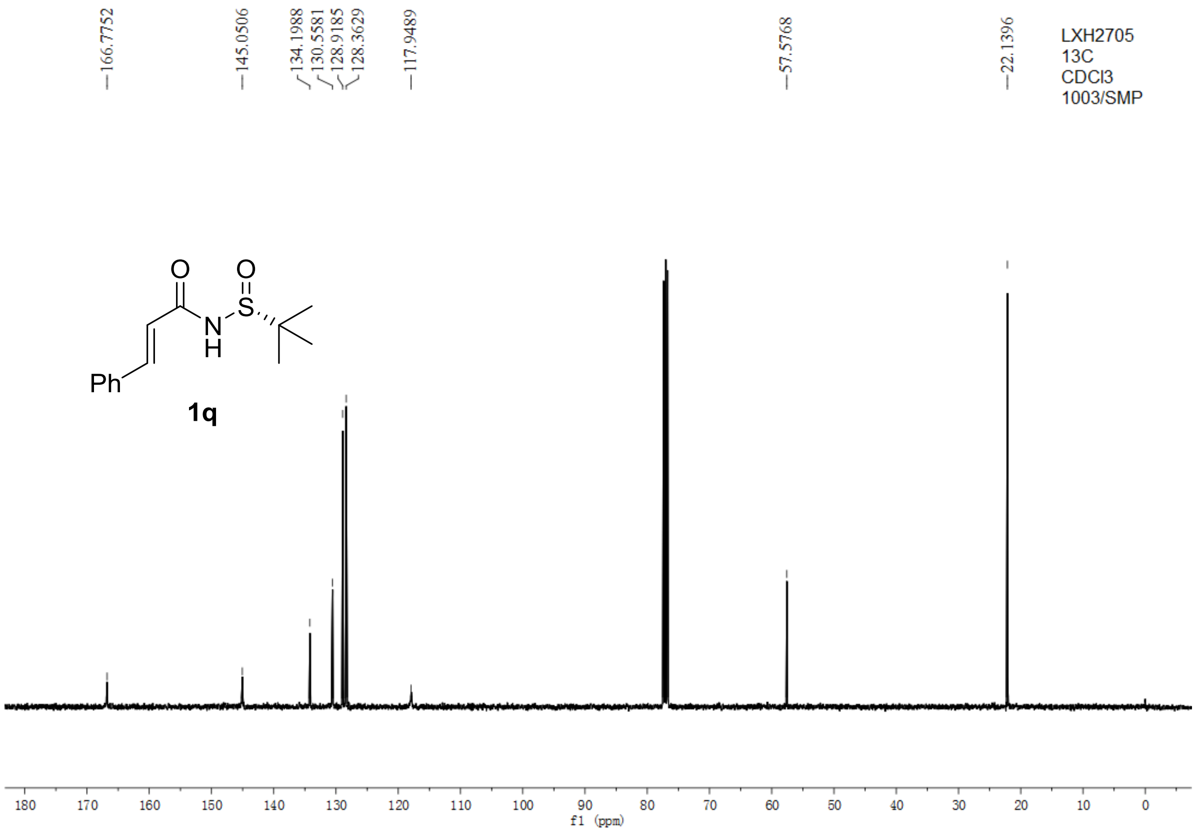
^{1}H NMR (400 MHz, $CDCl_3$) of **1p**



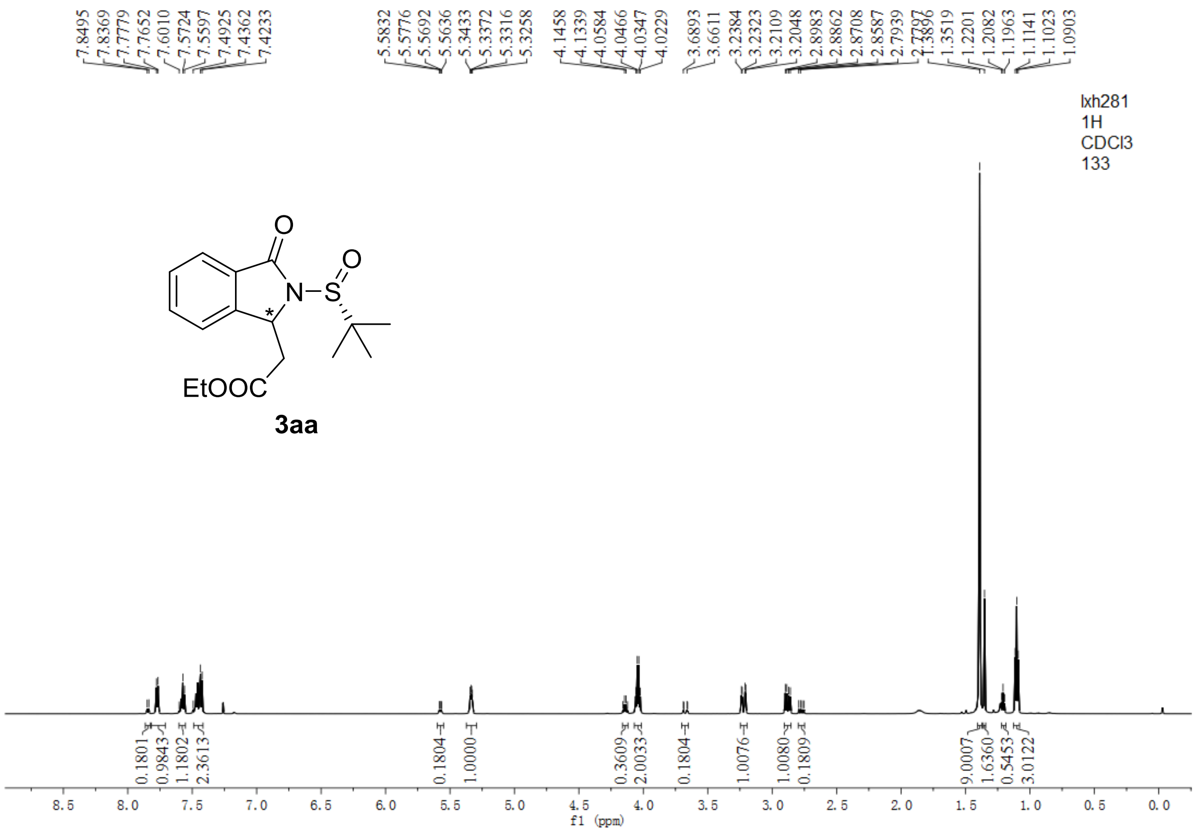
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **1p**



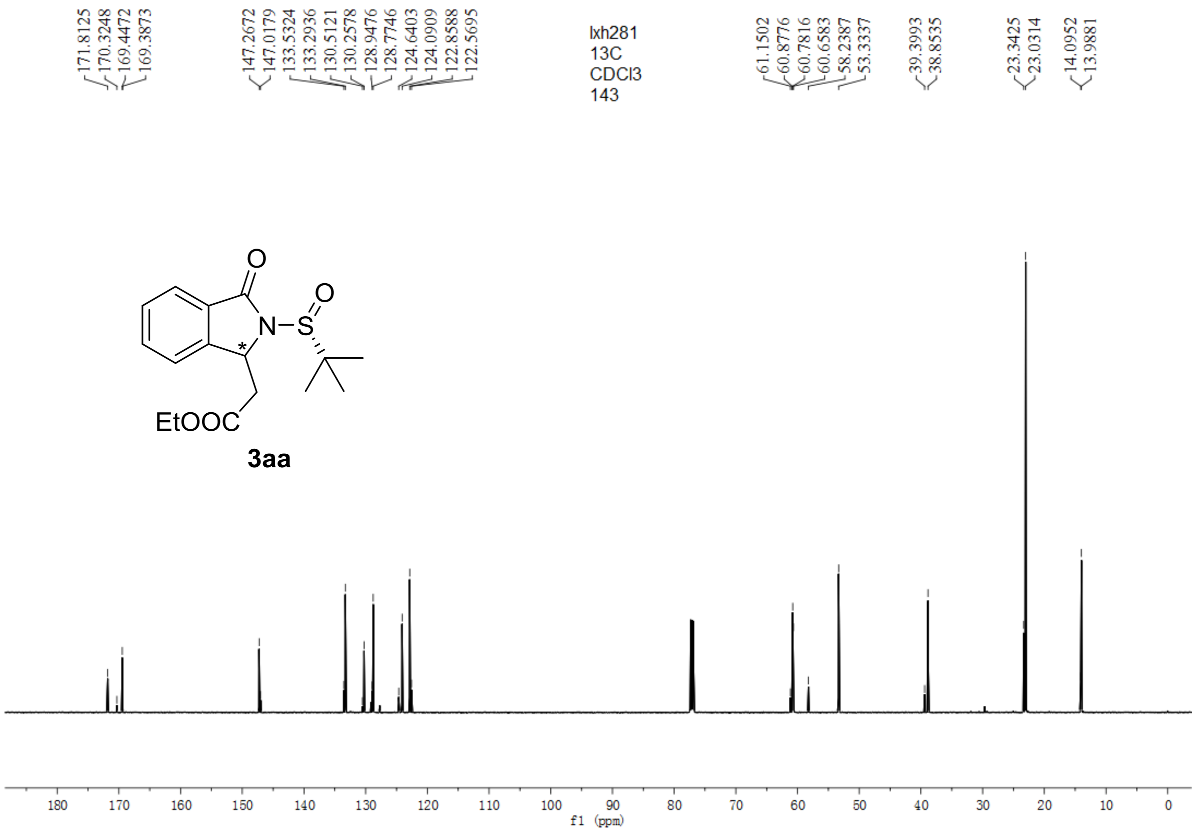
^{1}H NMR (400 MHz, $CDCl_3$) of **1q**



$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **1q**



^{1}H NMR (600 MHz, $CDCl_3$) of **3aa**



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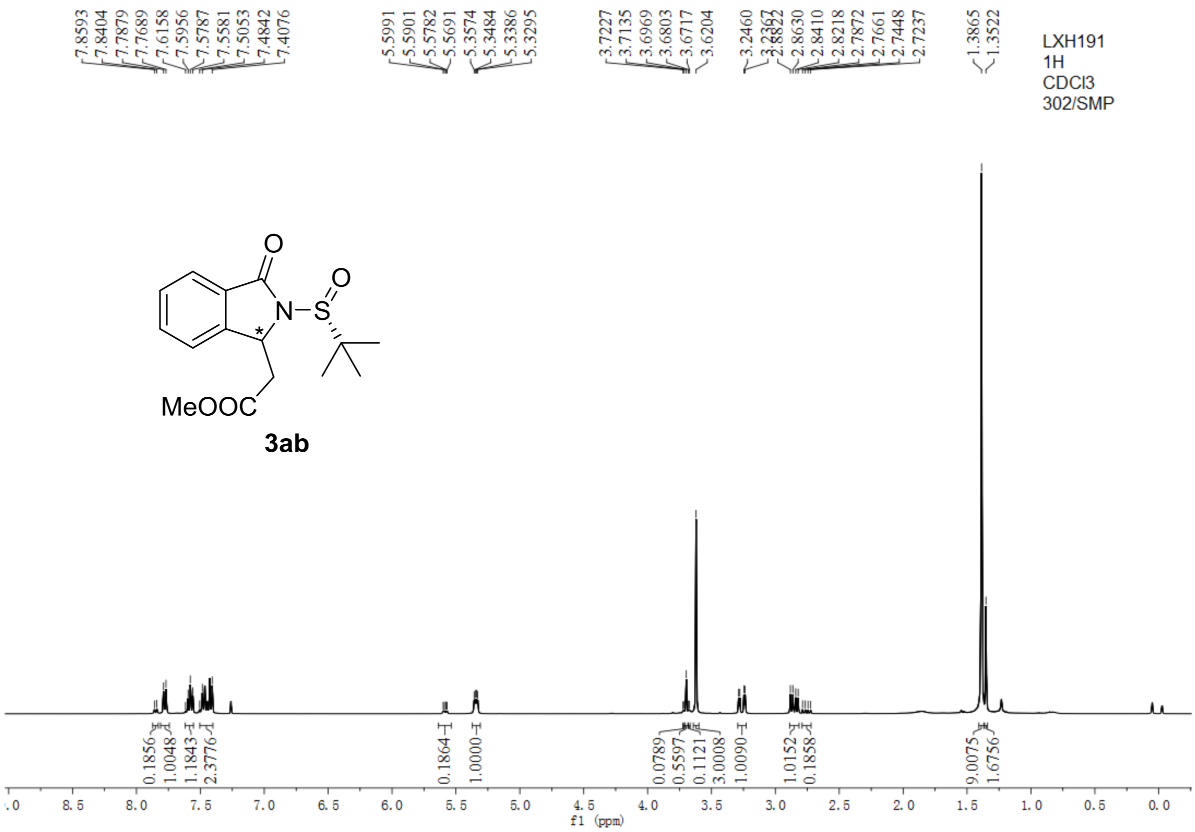

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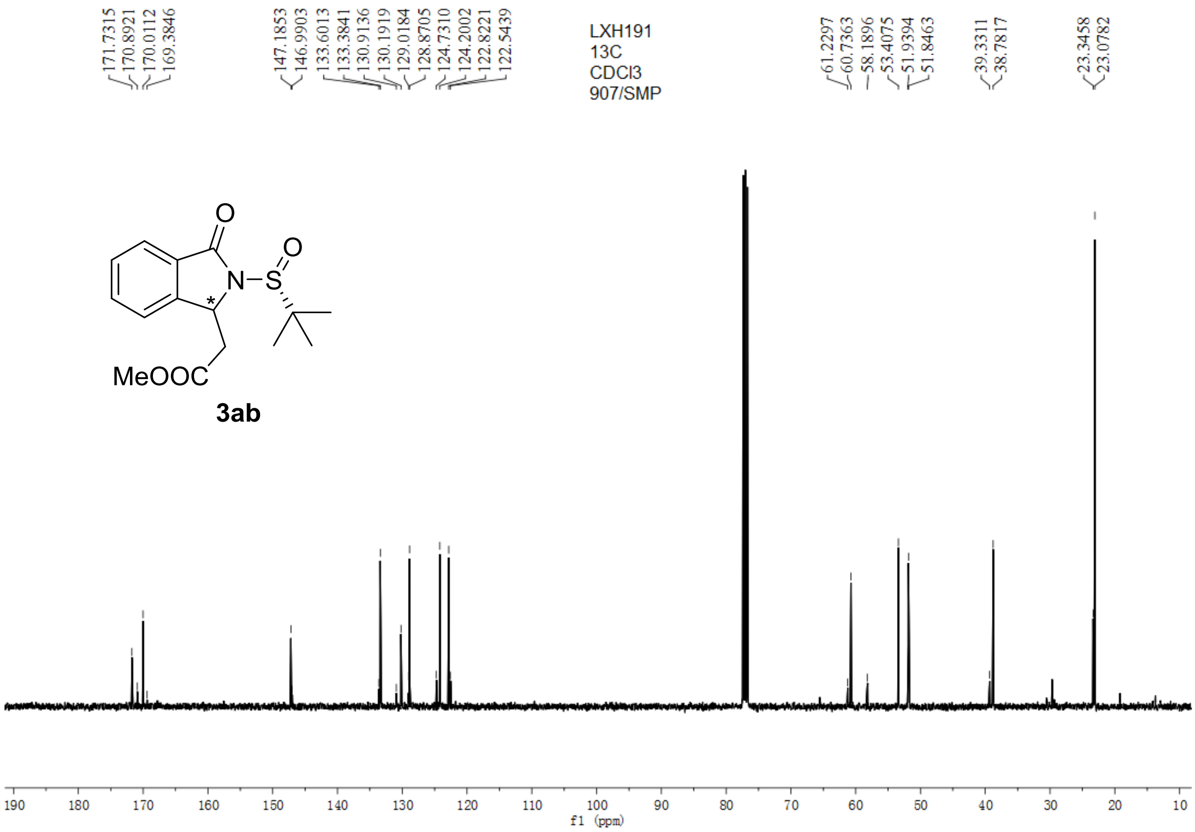

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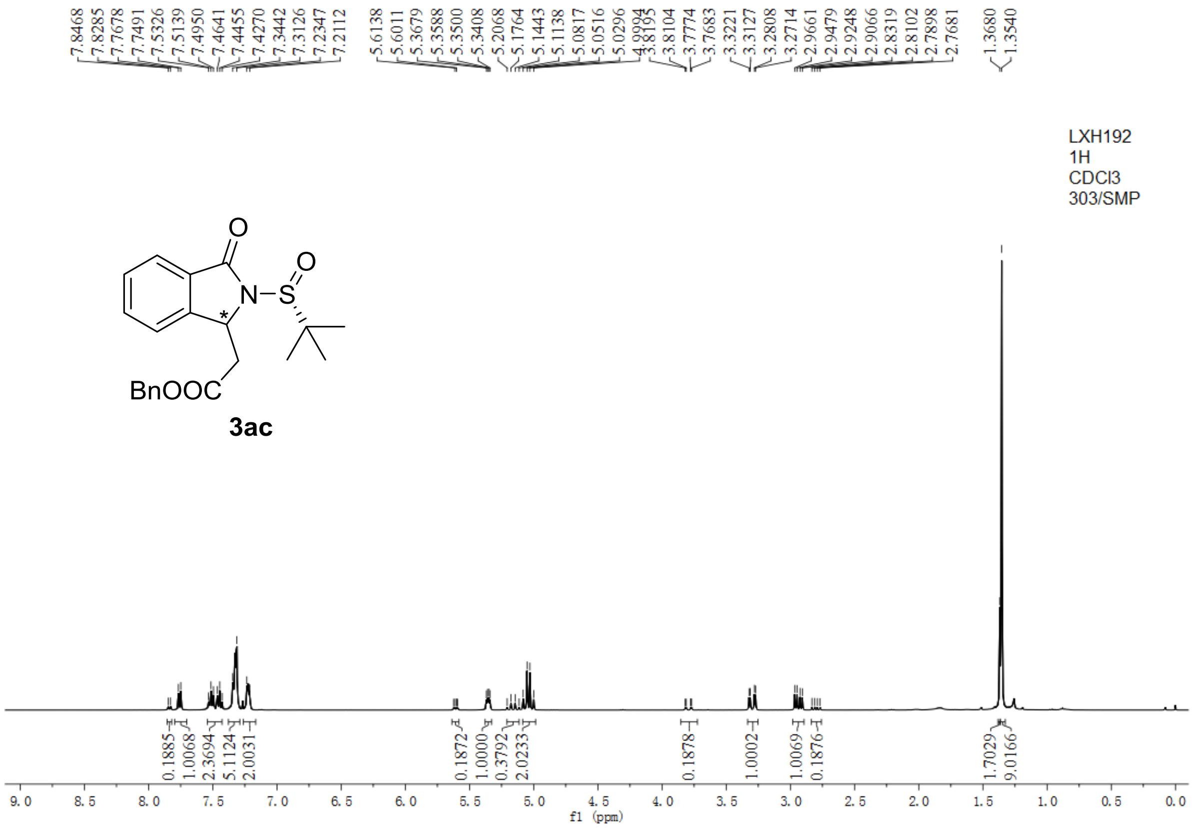

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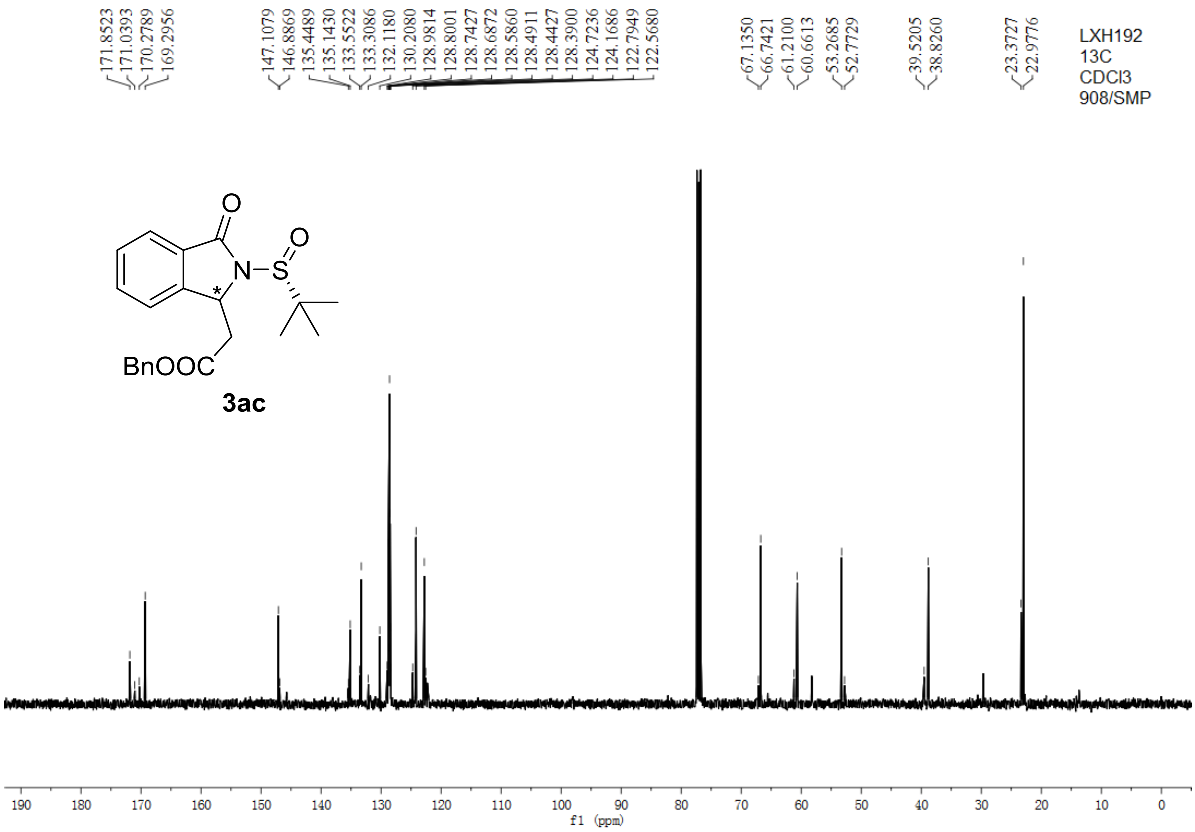

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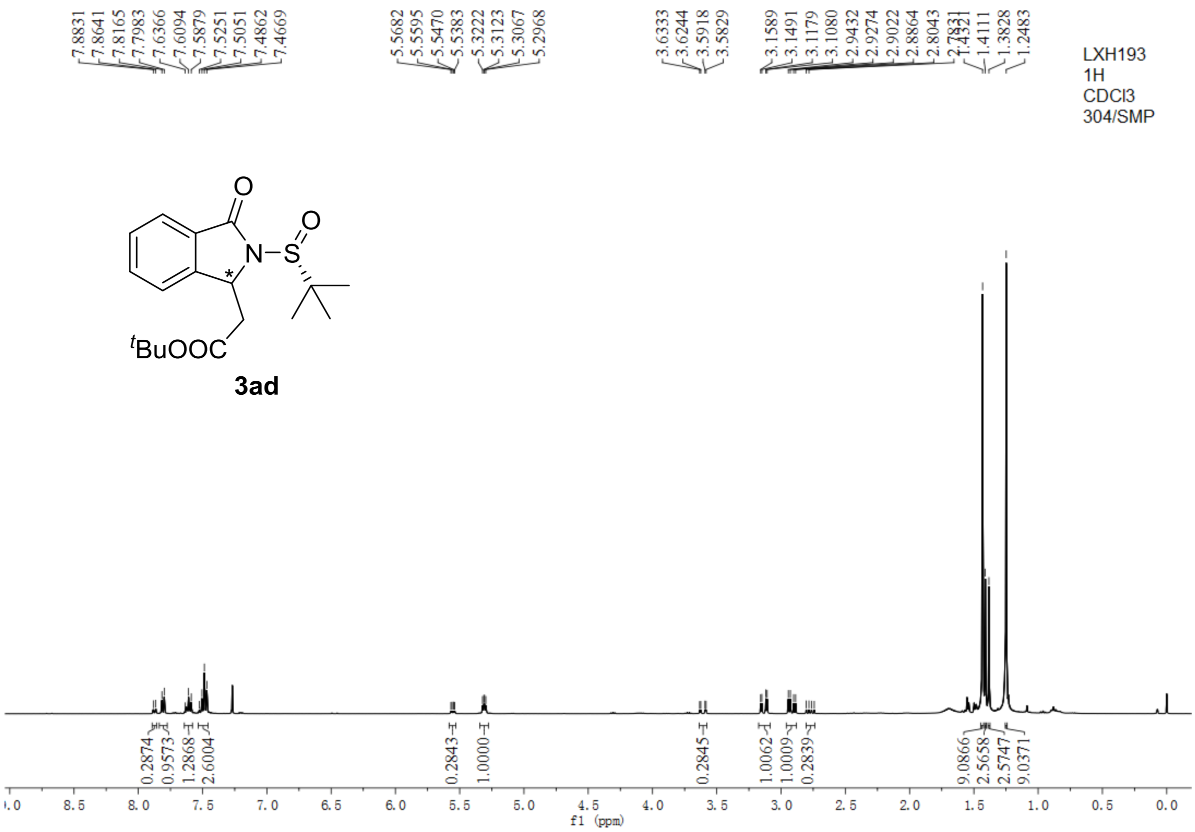

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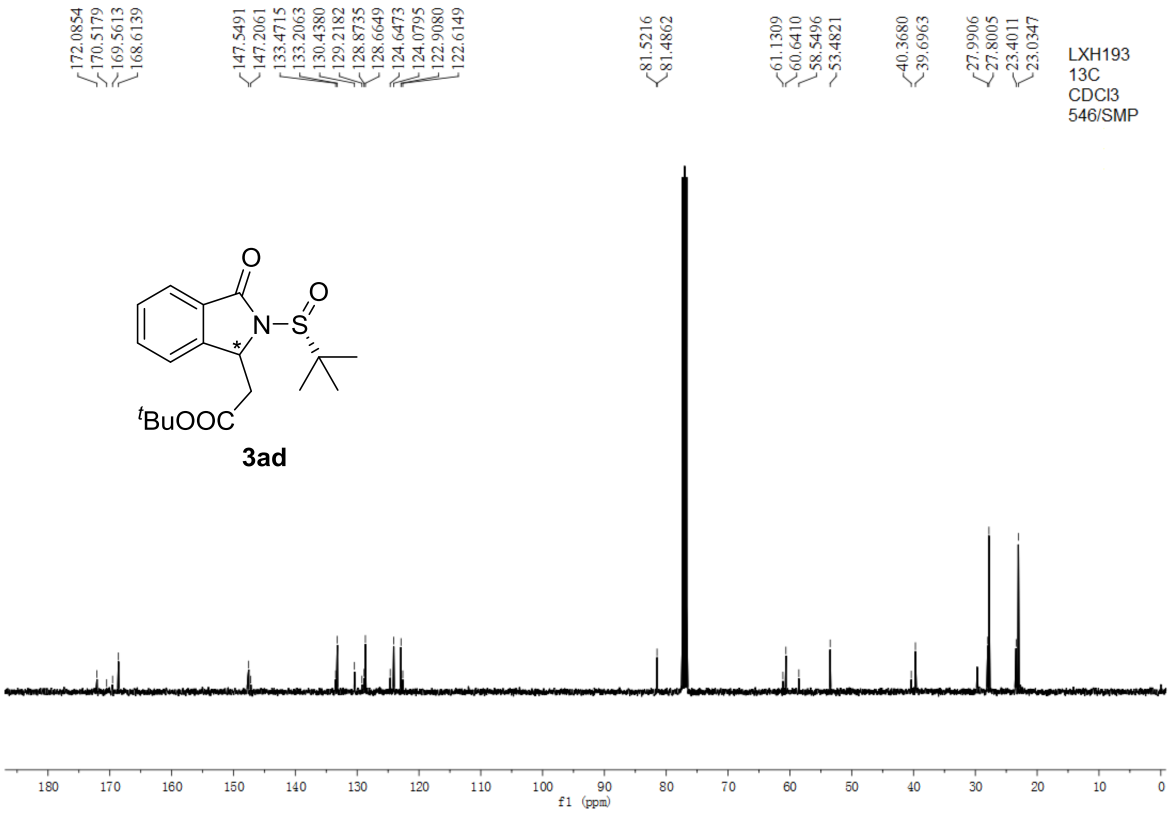

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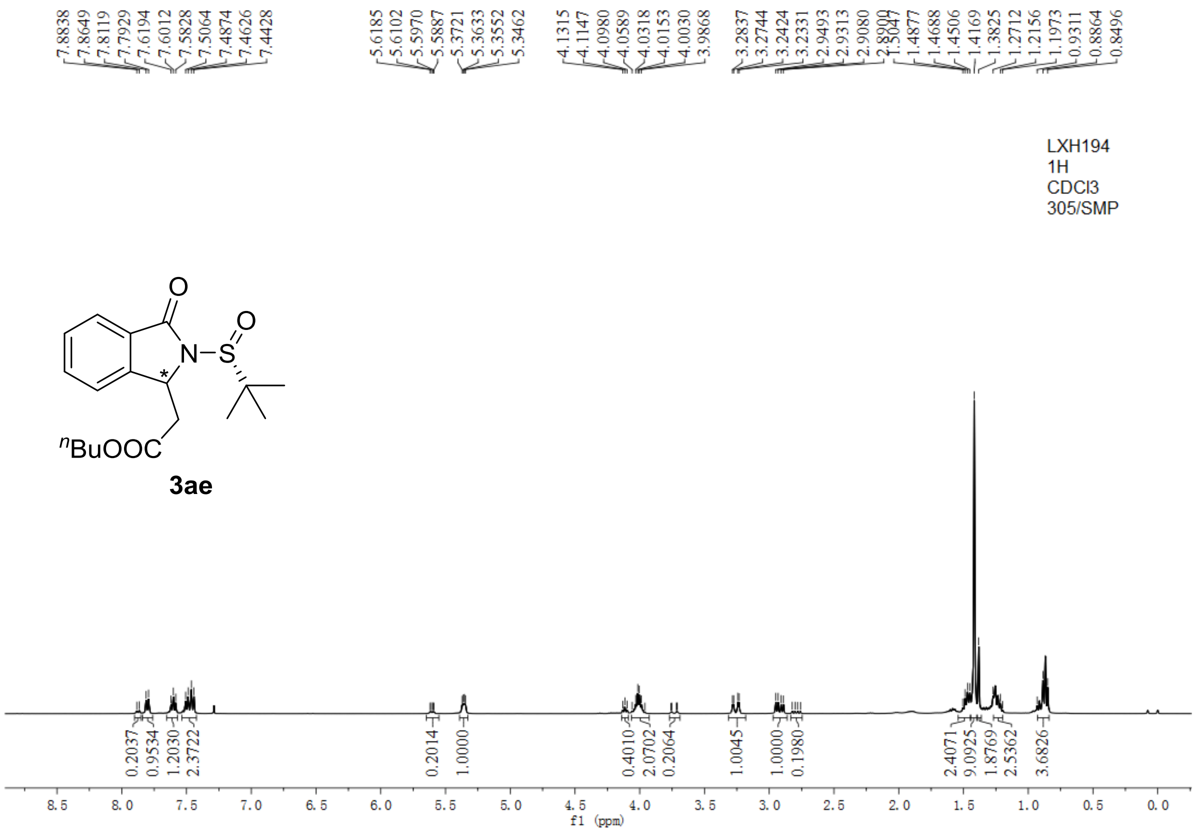

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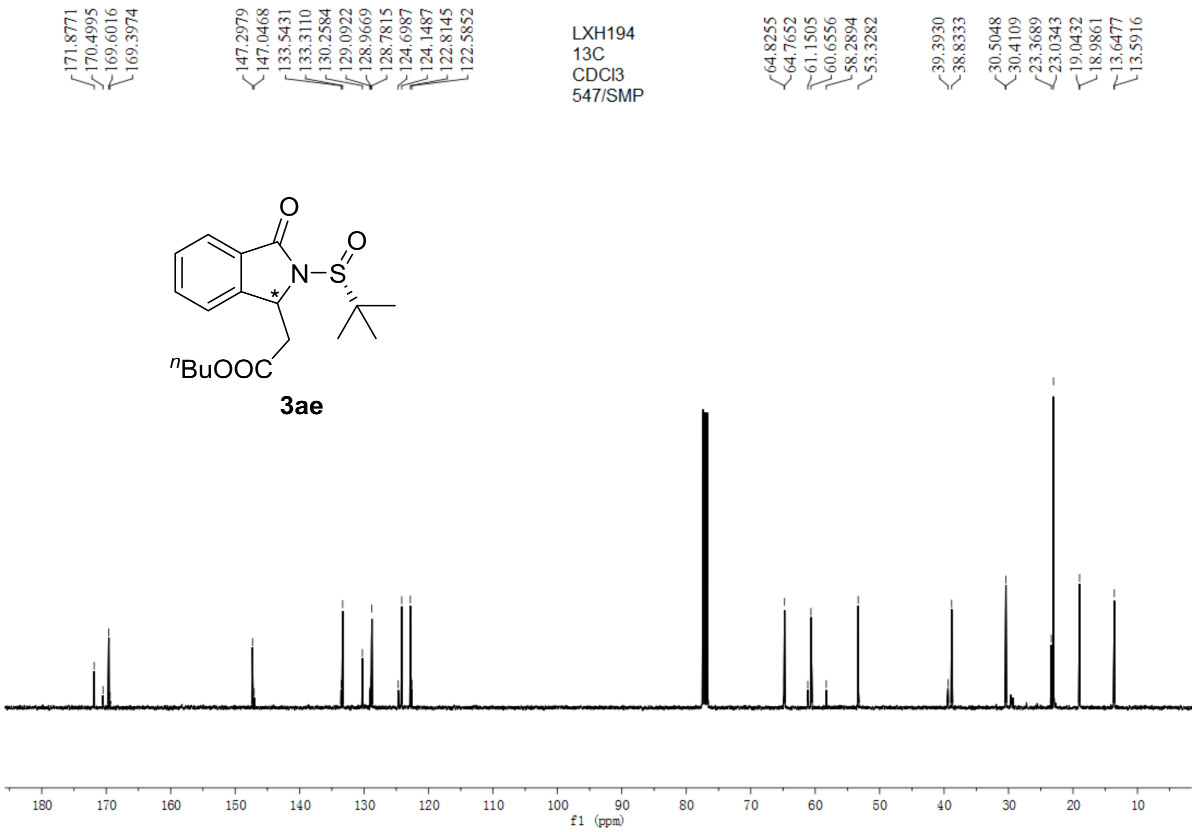

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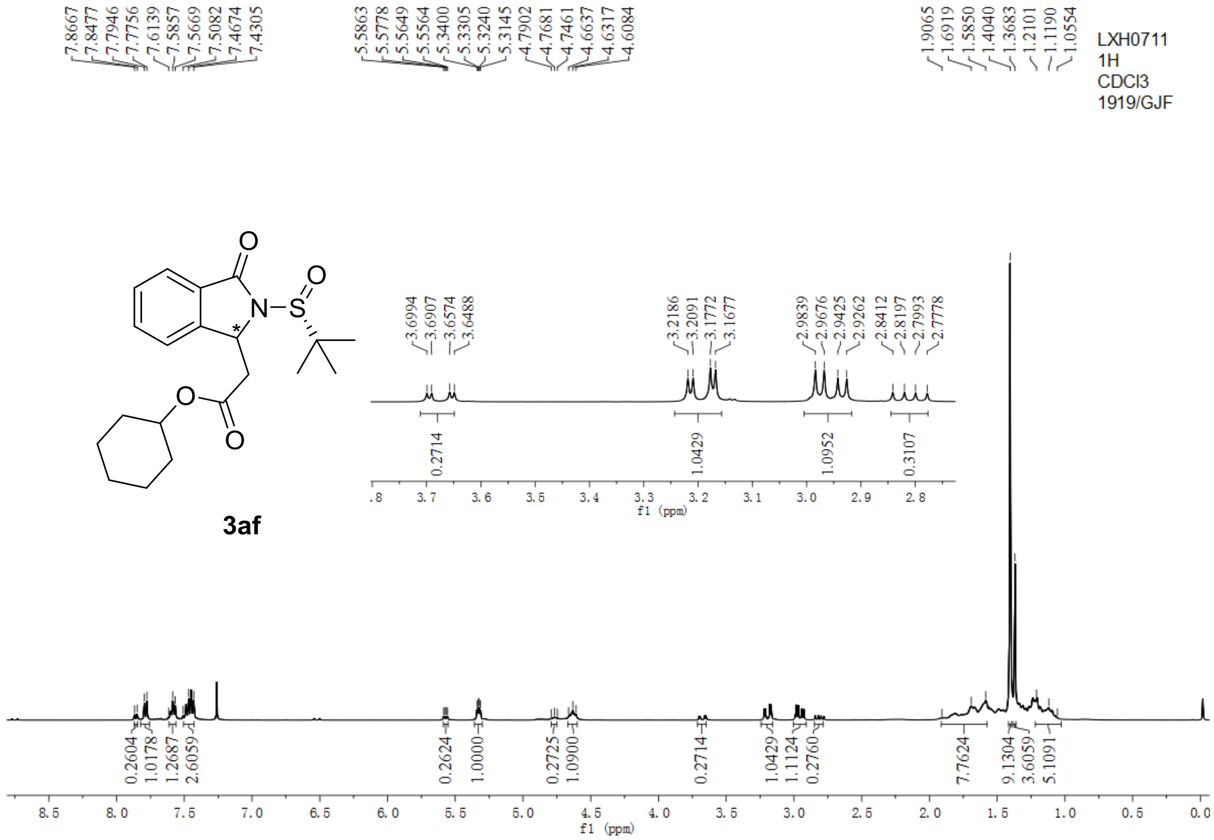

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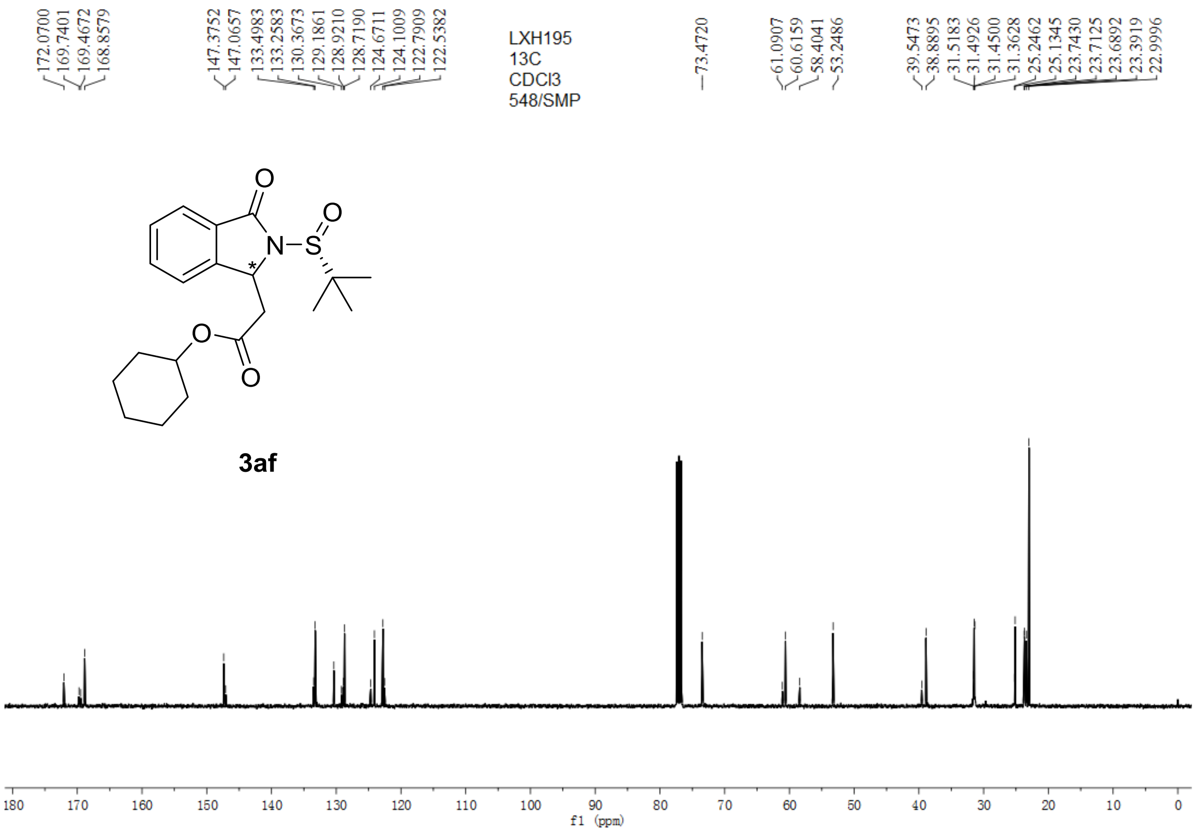

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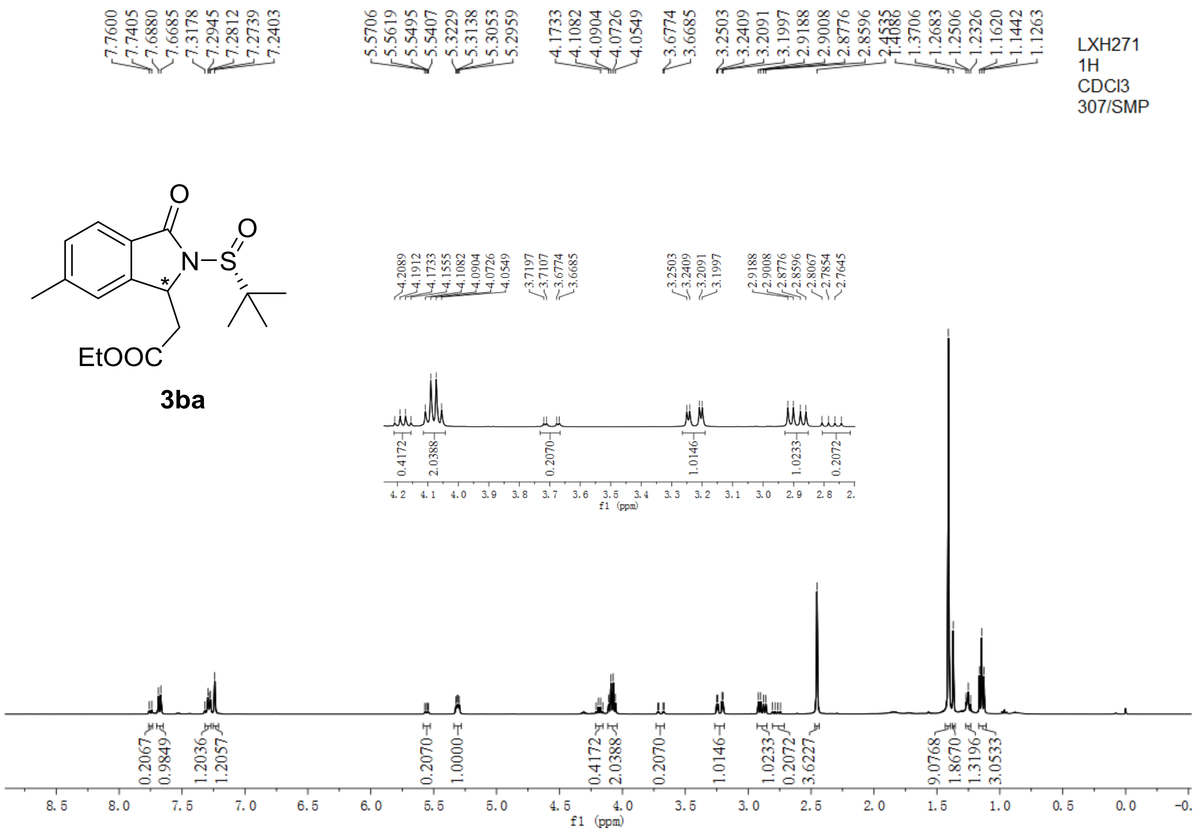

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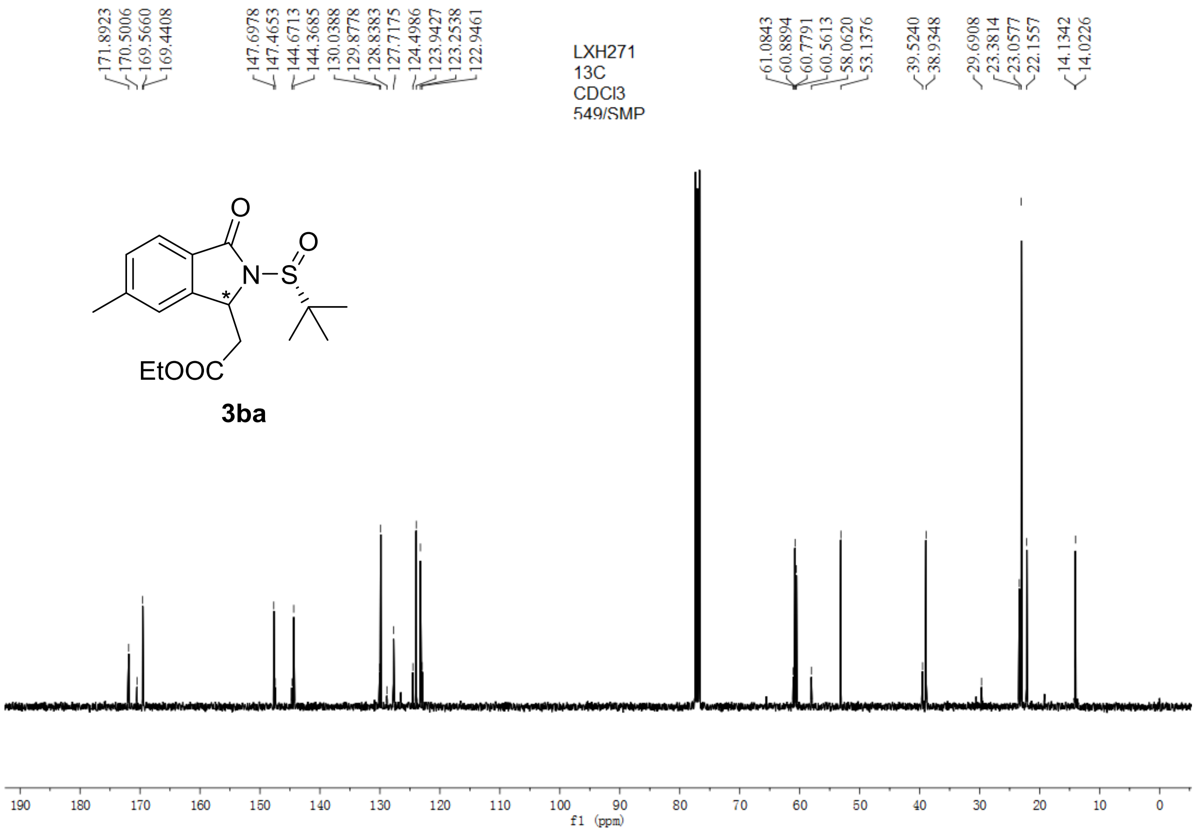

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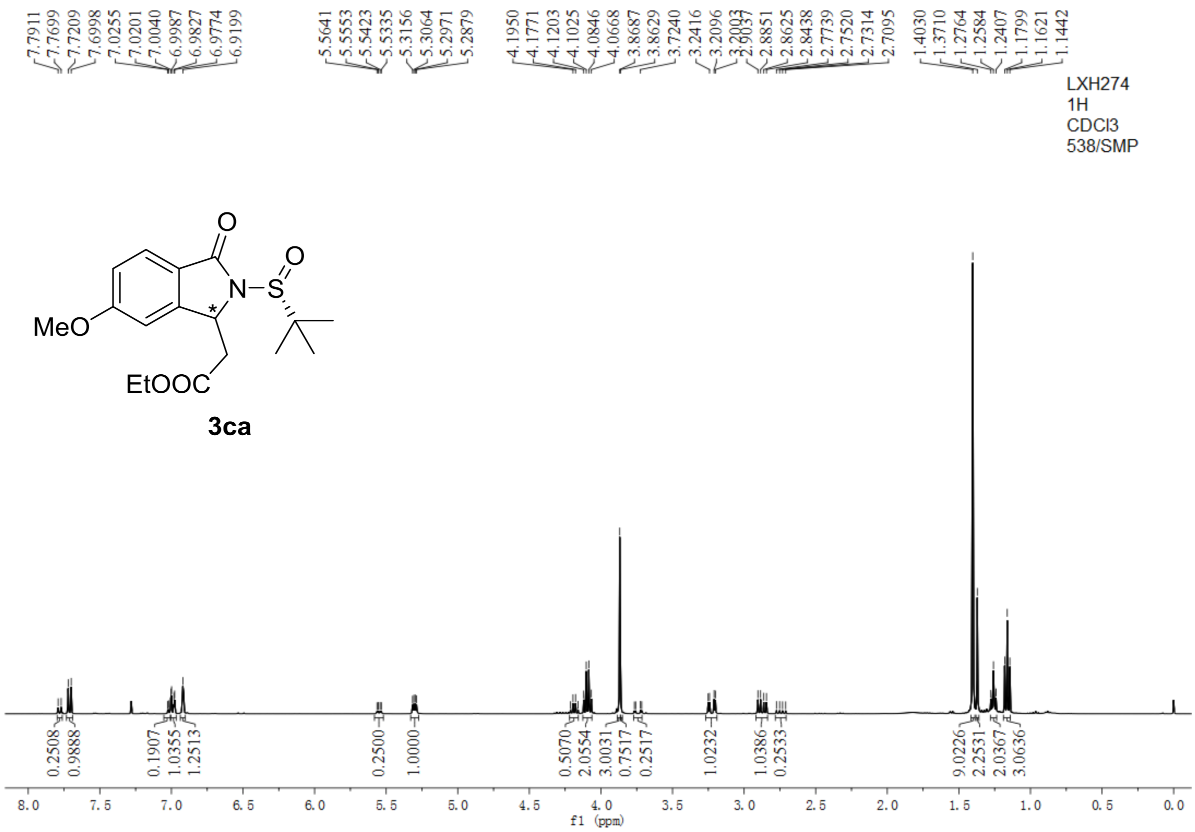

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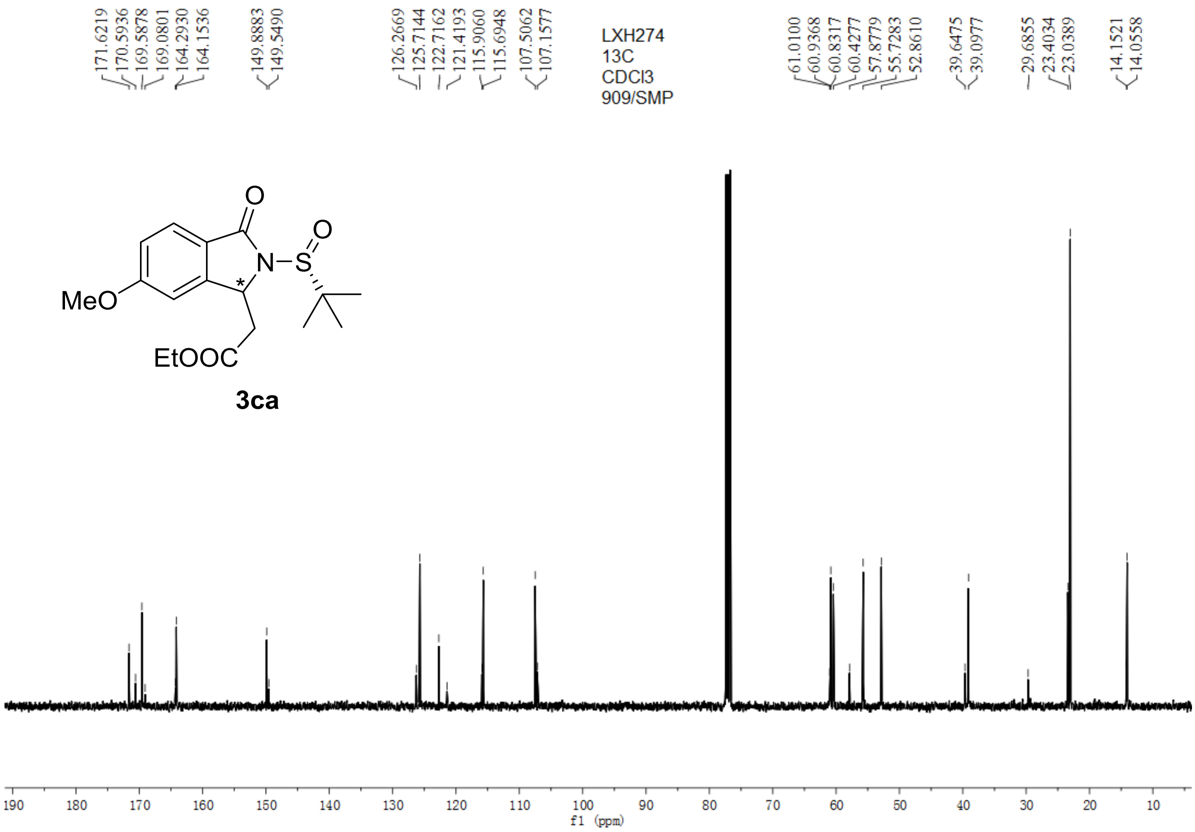

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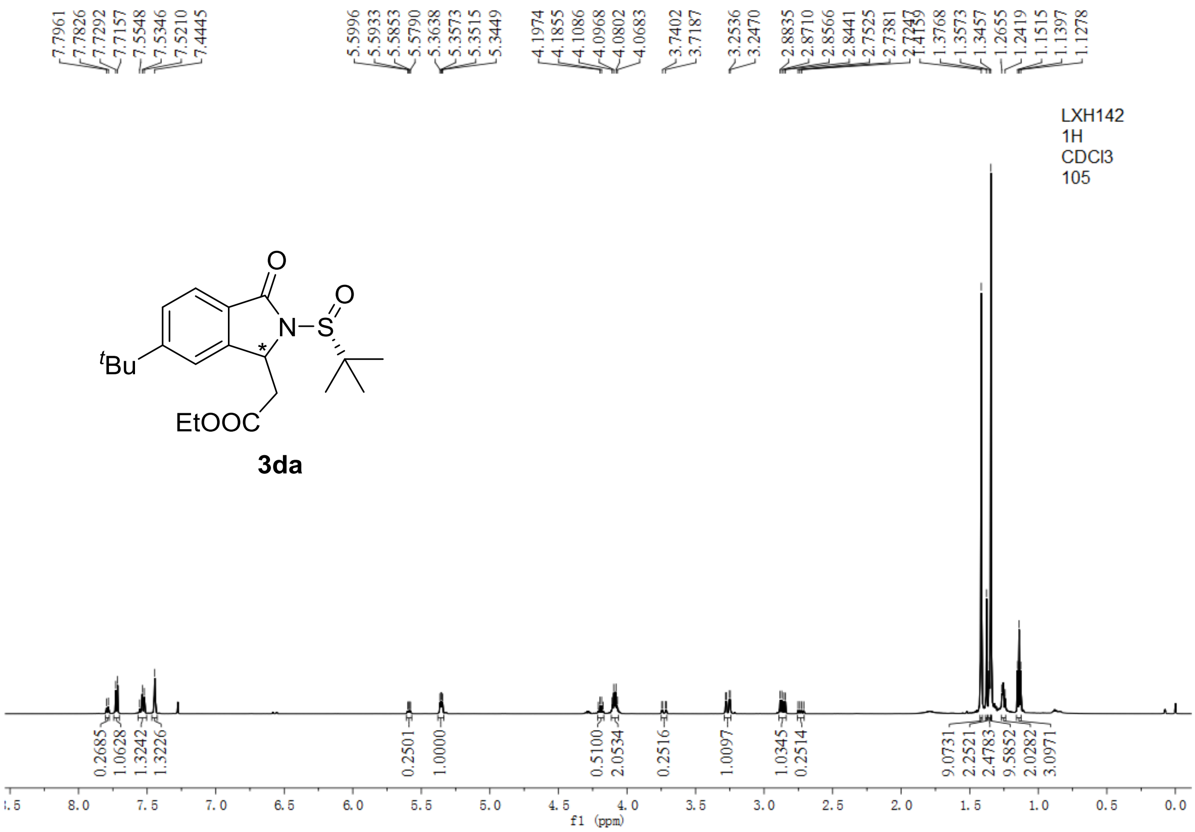

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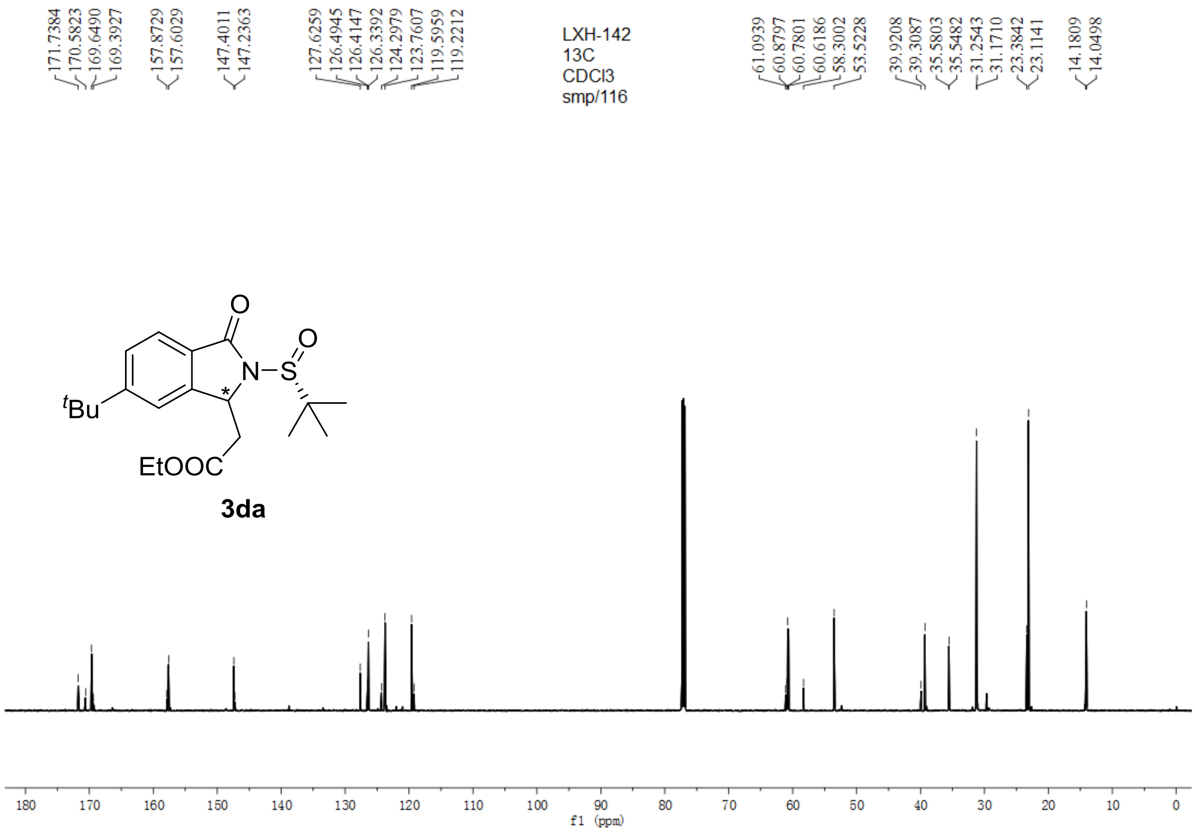

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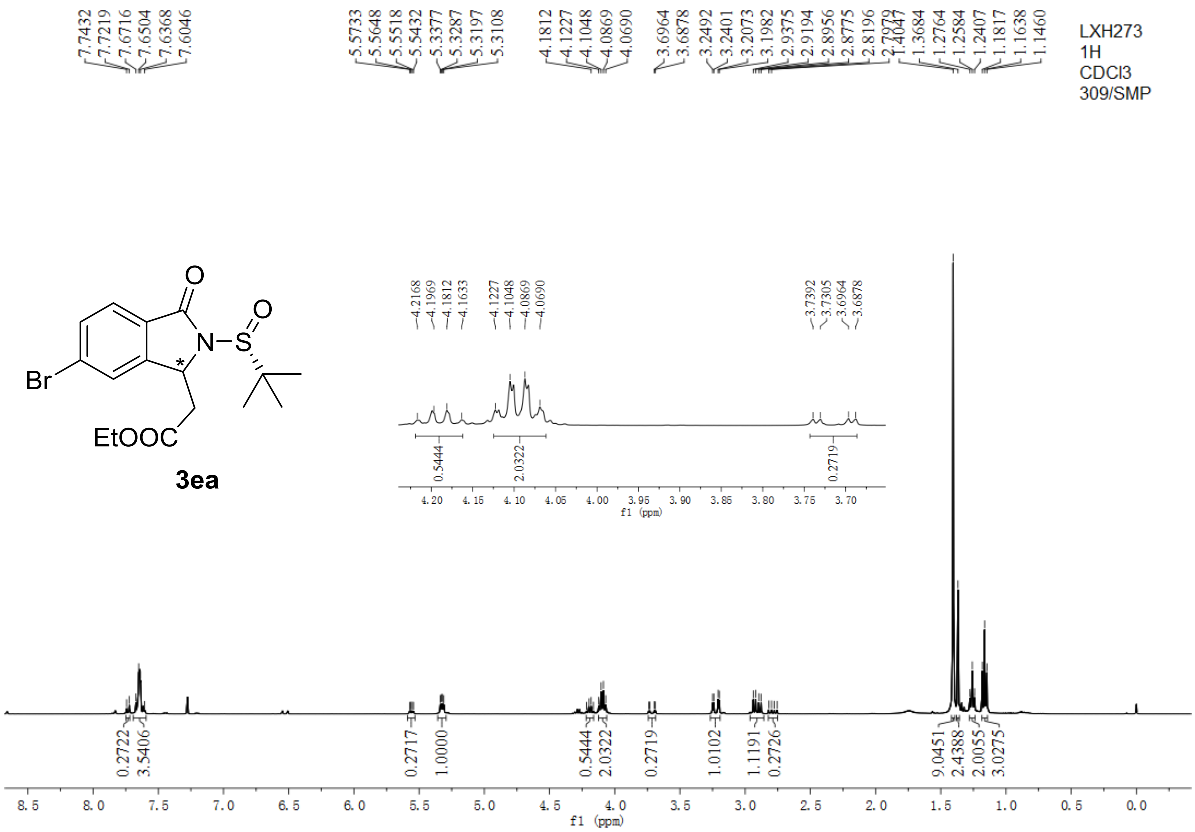

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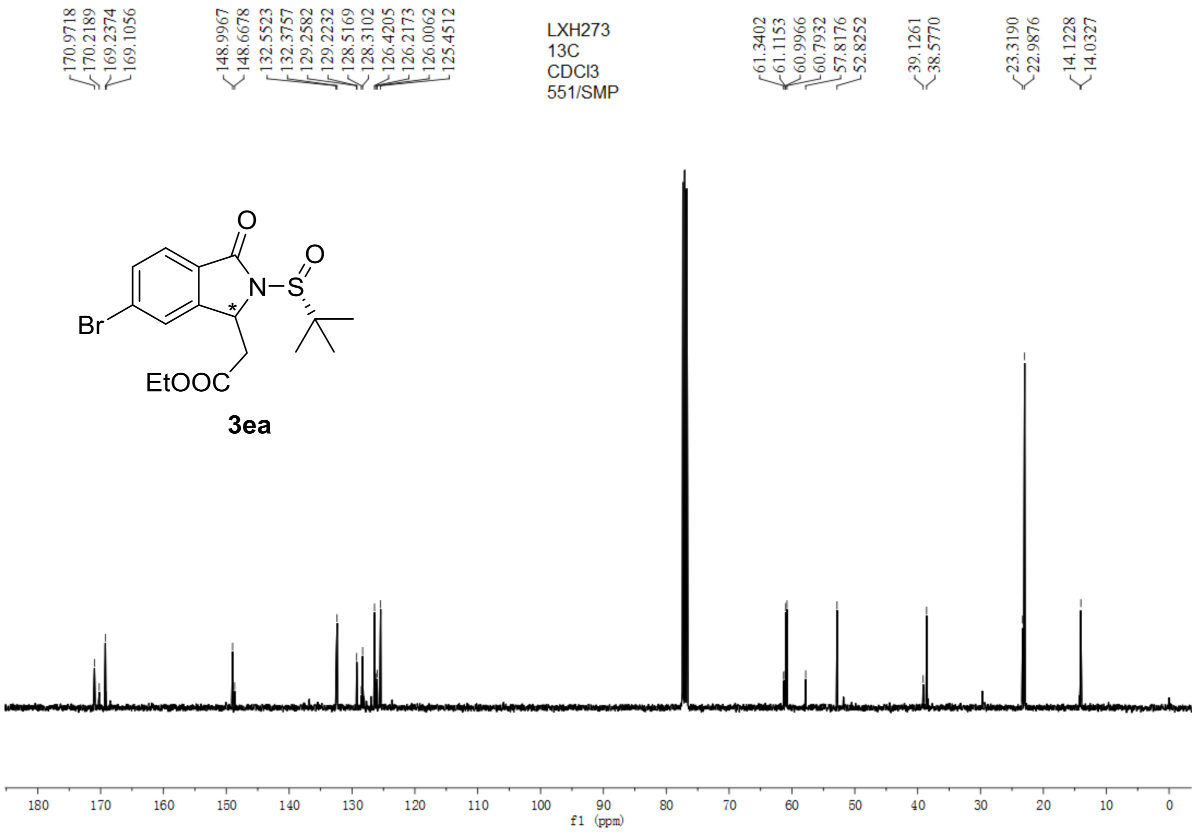
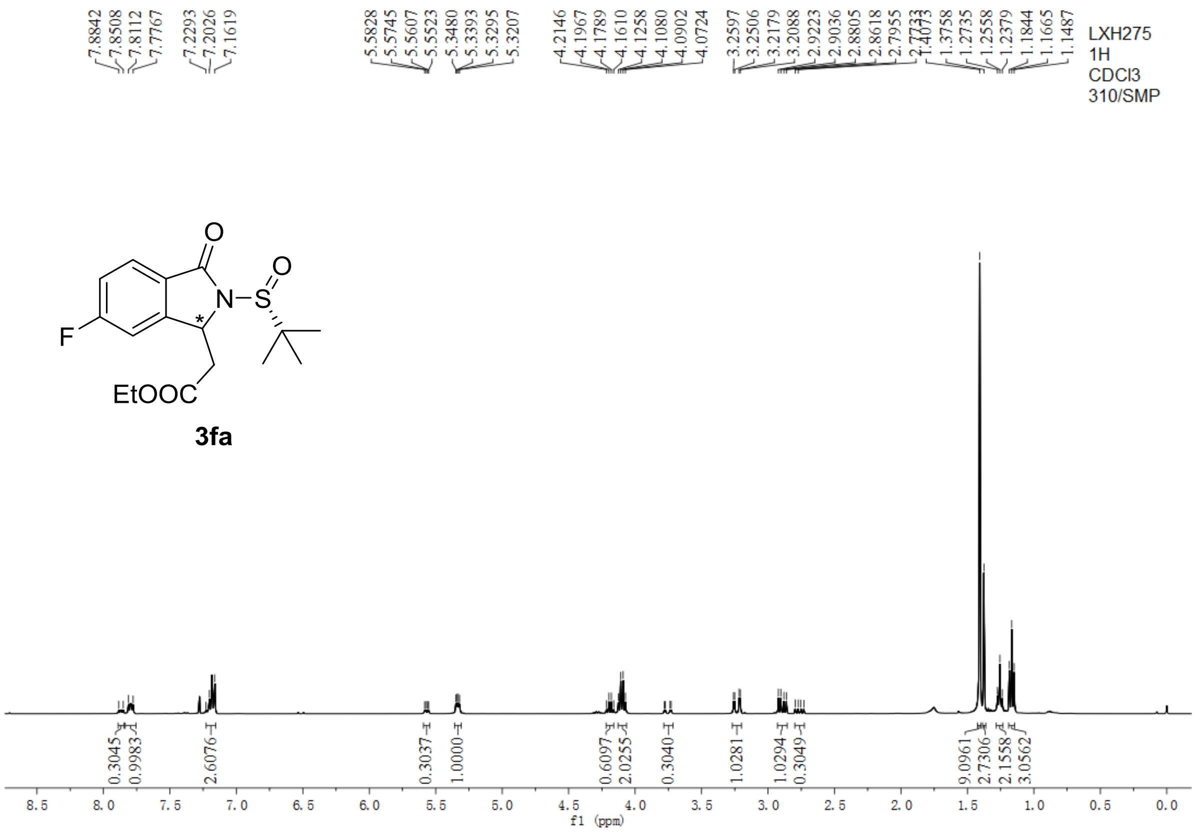
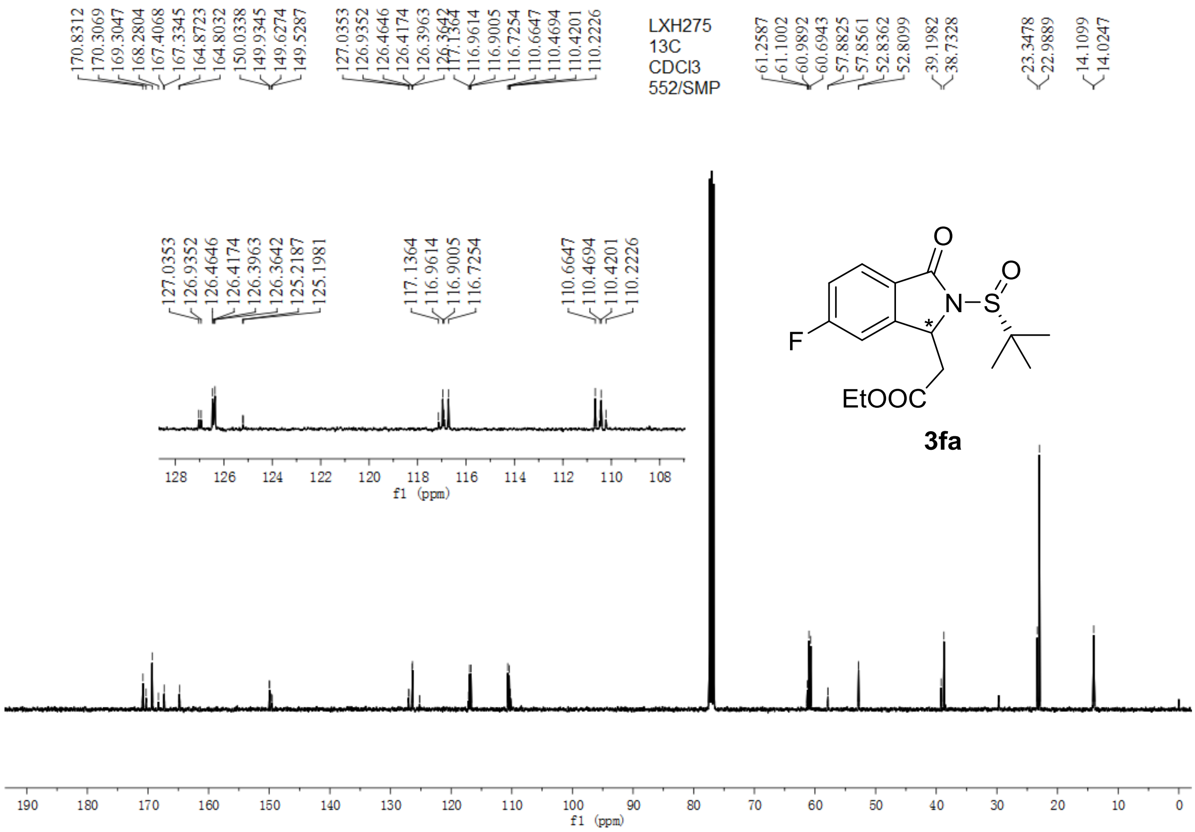


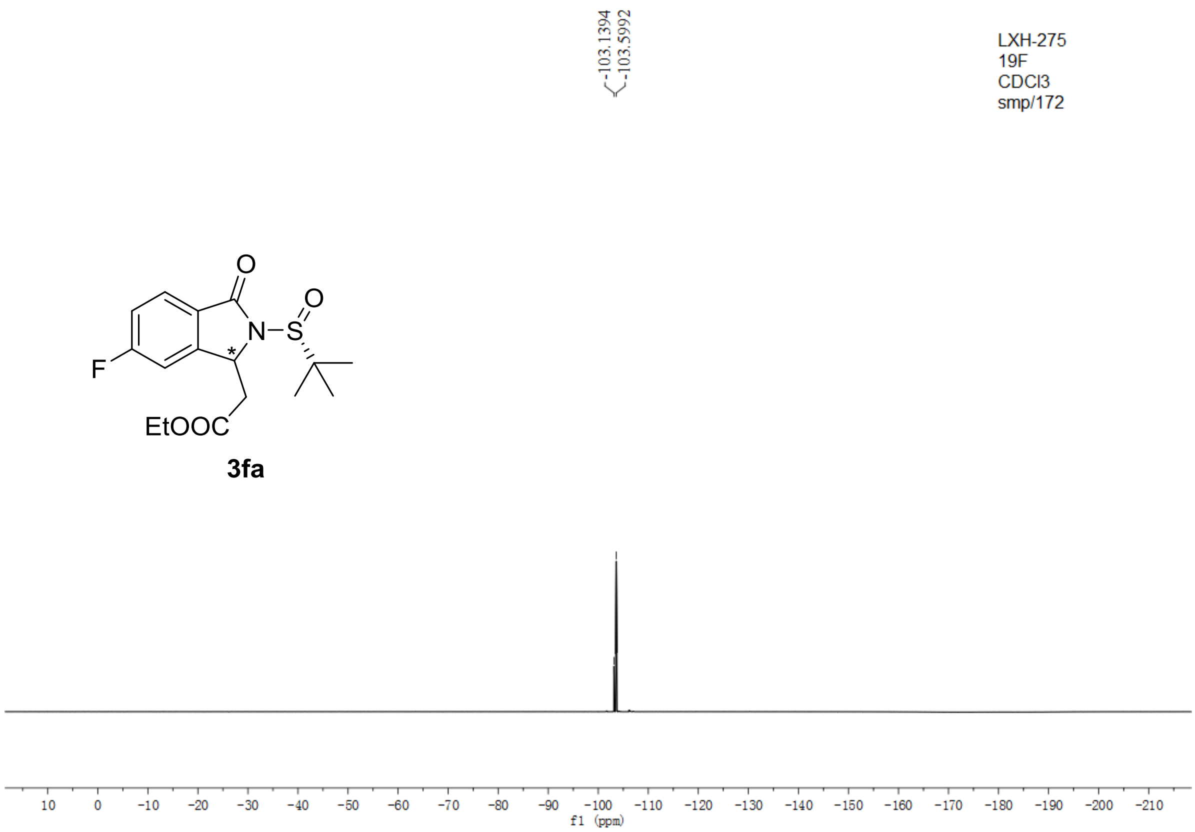
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3ea**



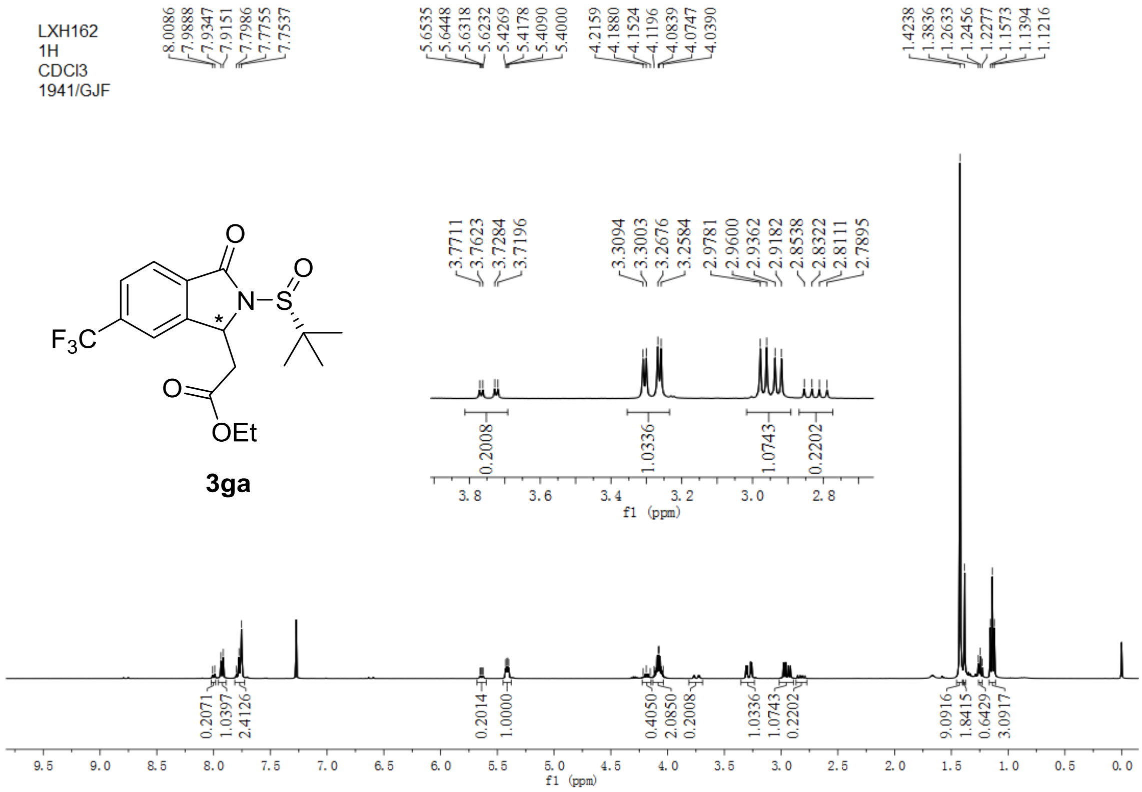
^{1}H NMR (400 MHz, $CDCl_3$) of **3fa**



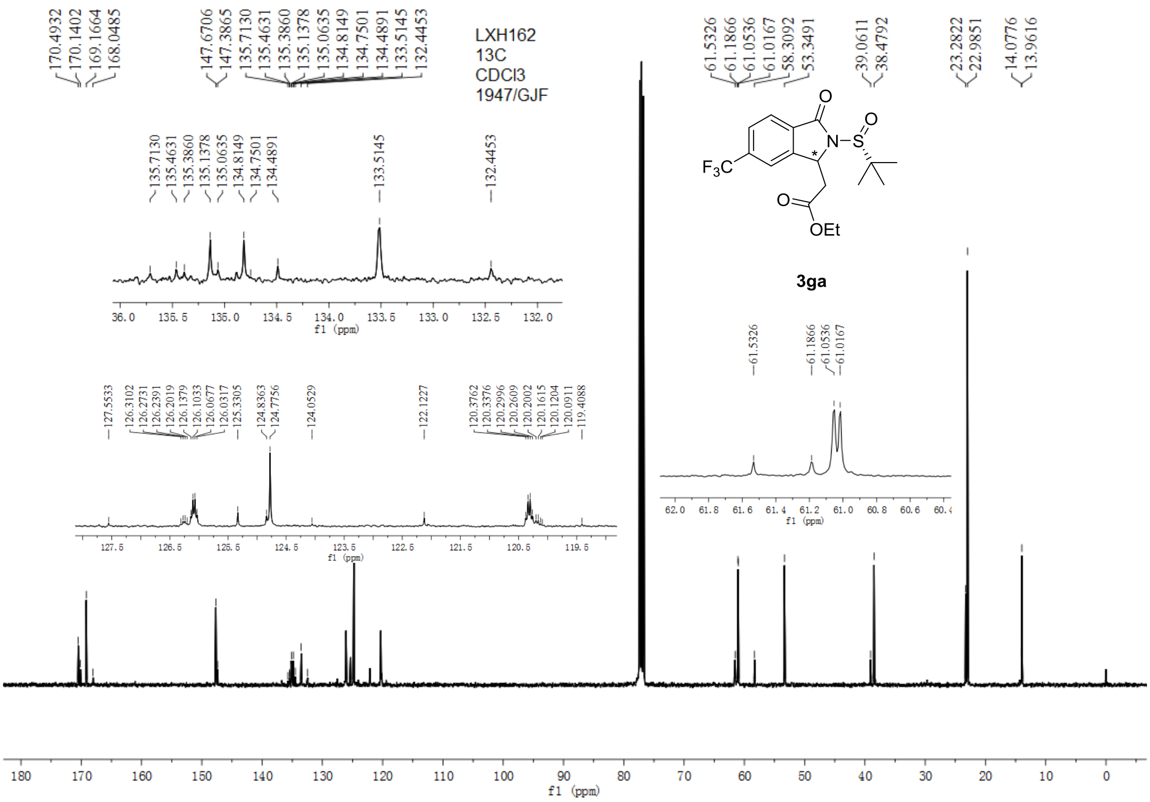
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) of **3fa**



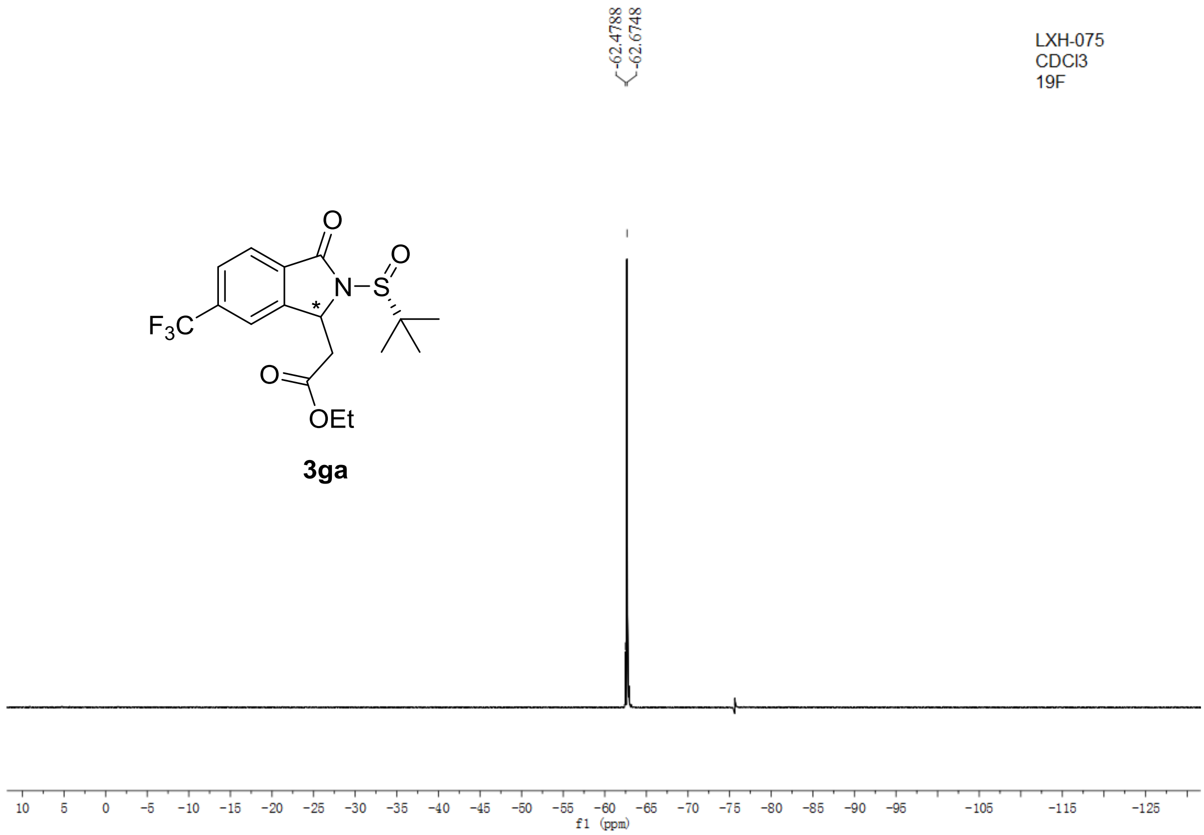
^{19}F NMR (565 MHz, $CDCl_3$) of **3fa**



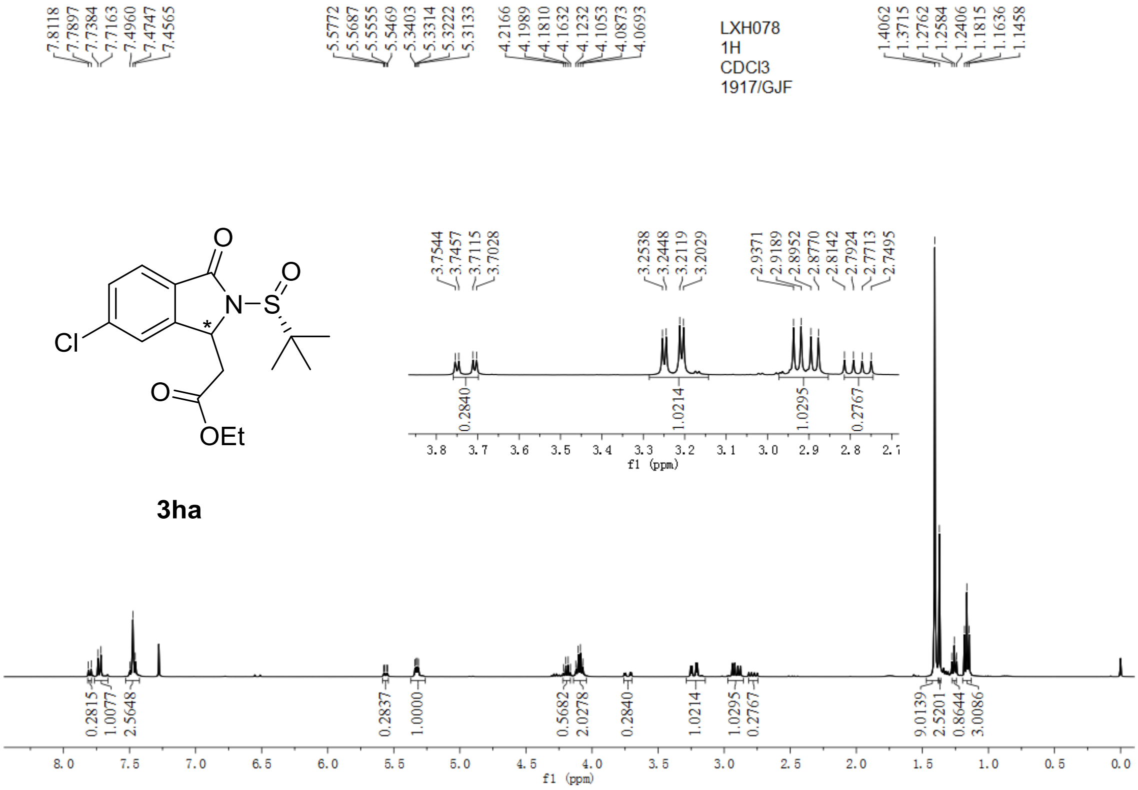
^{1}H NMR (400 MHz, $CDCl_3$) of **3ga**



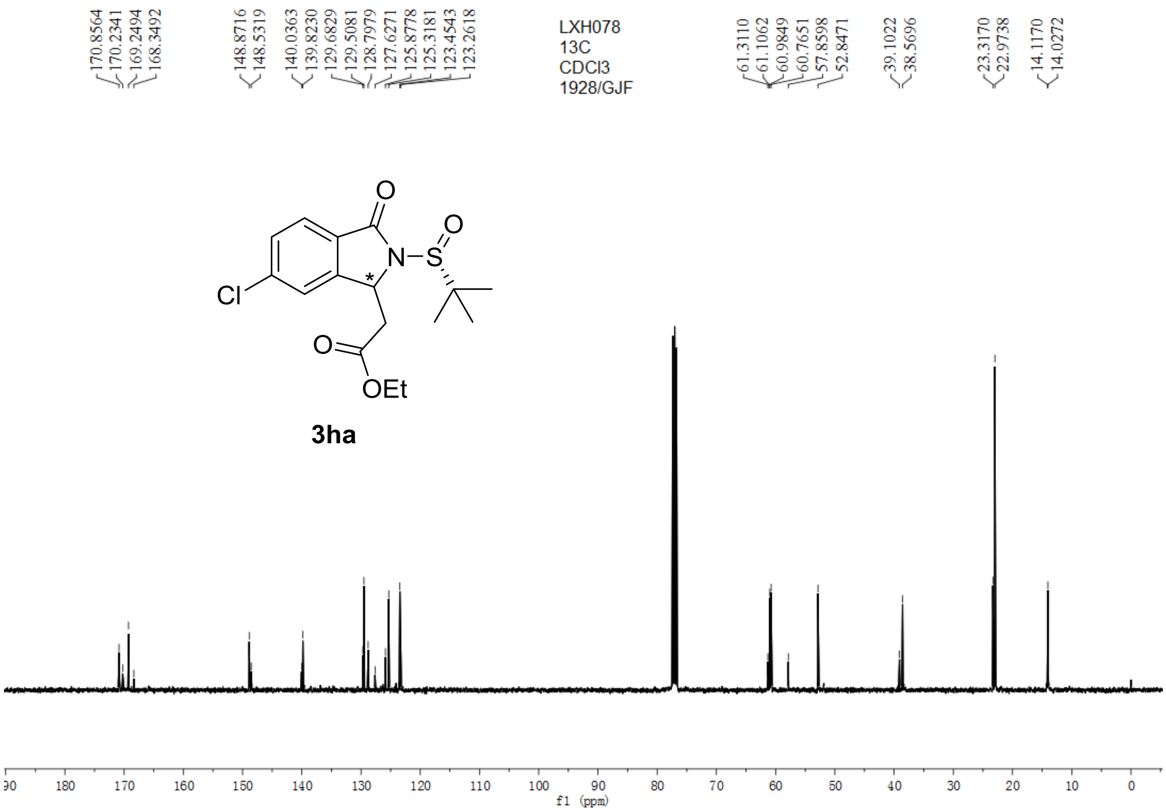
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3ga**



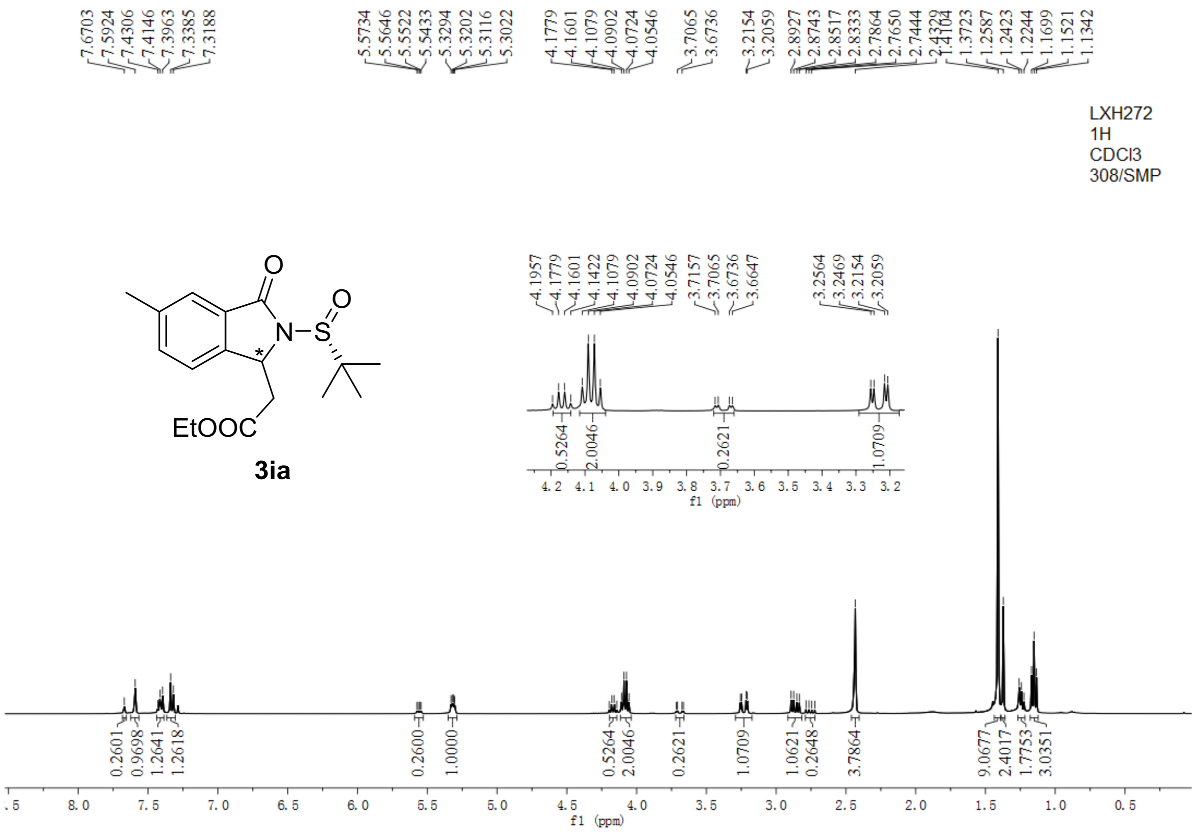
^{19}F NMR (376 MHz, $CDCl_3$) of **3ga**



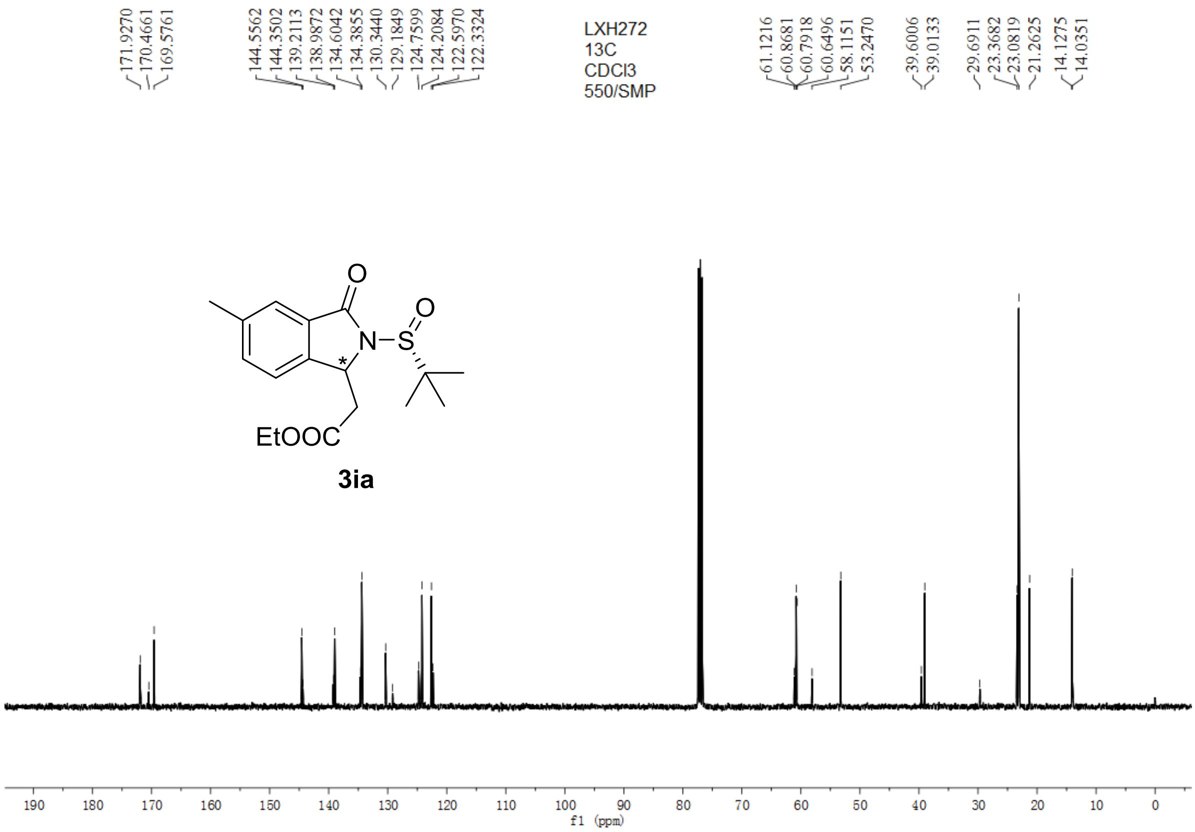
^{1}H NMR (400 MHz, $CDCl_3$) of **3ha**



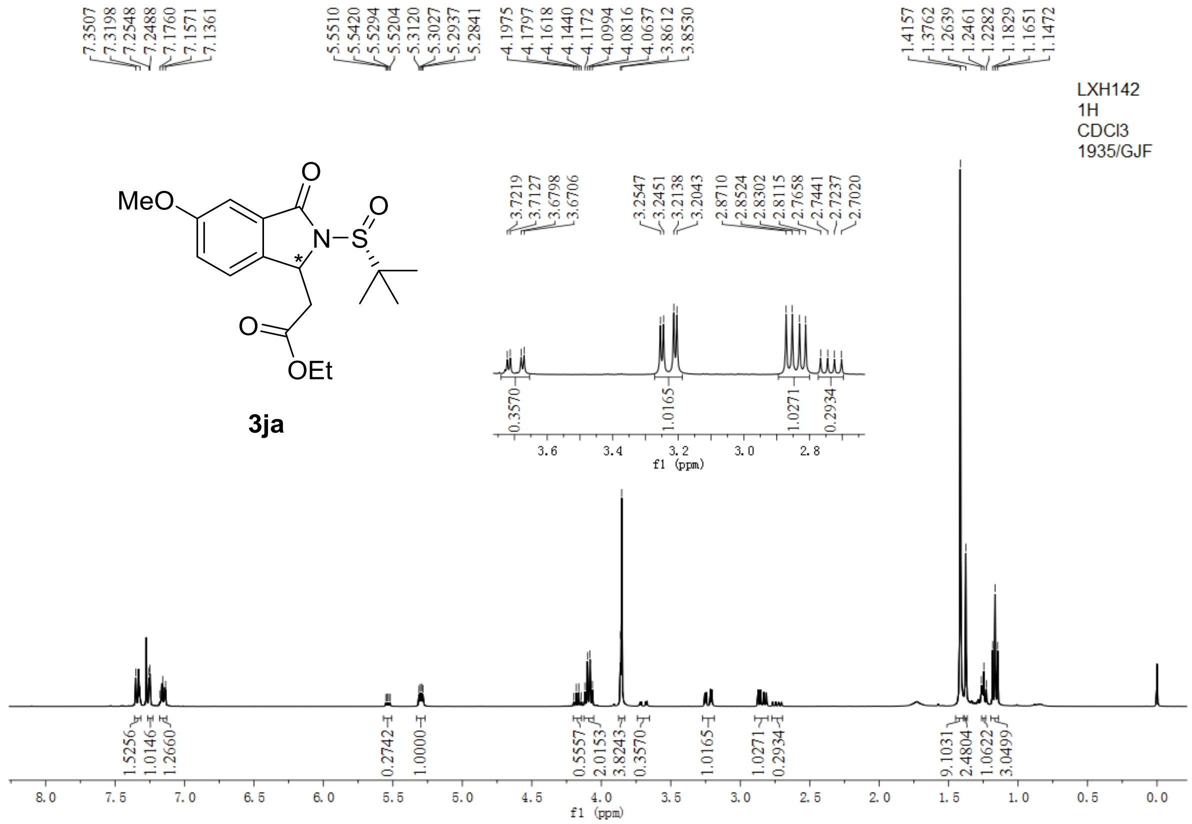
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3ha**



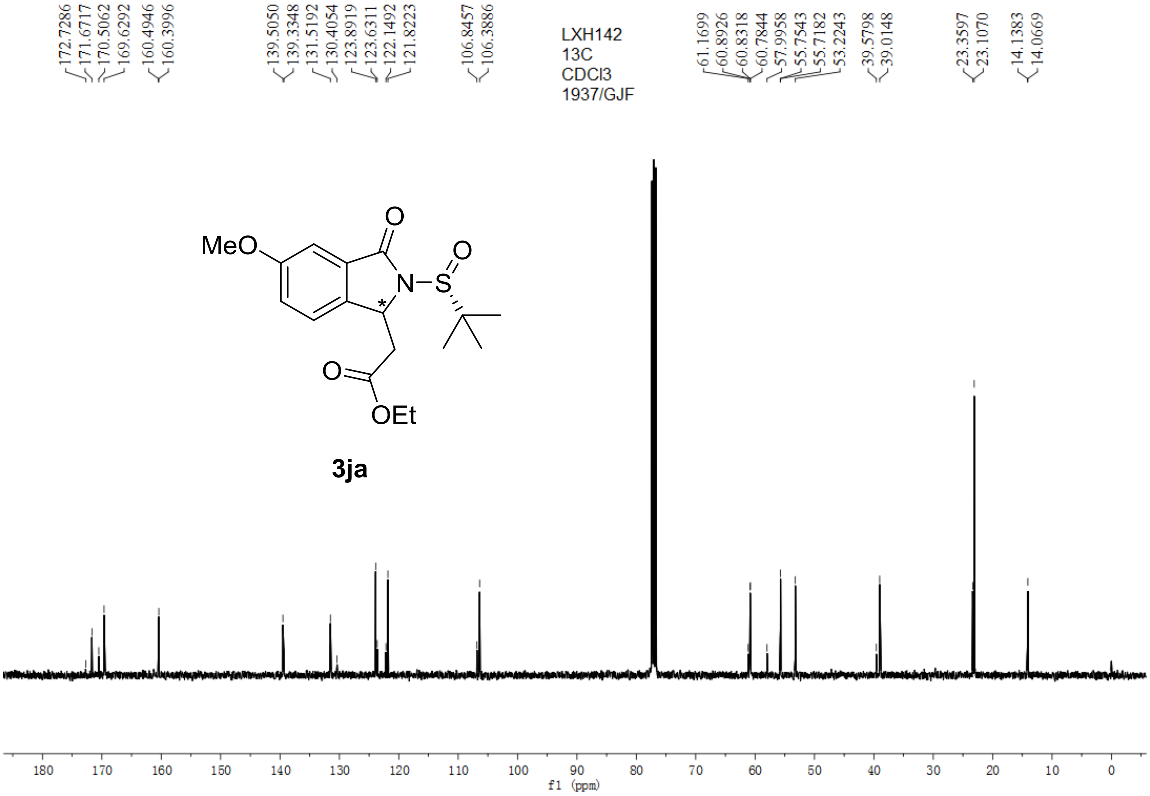
^{1}H NMR (400 MHz, $CDCl_3$) of **3ia**



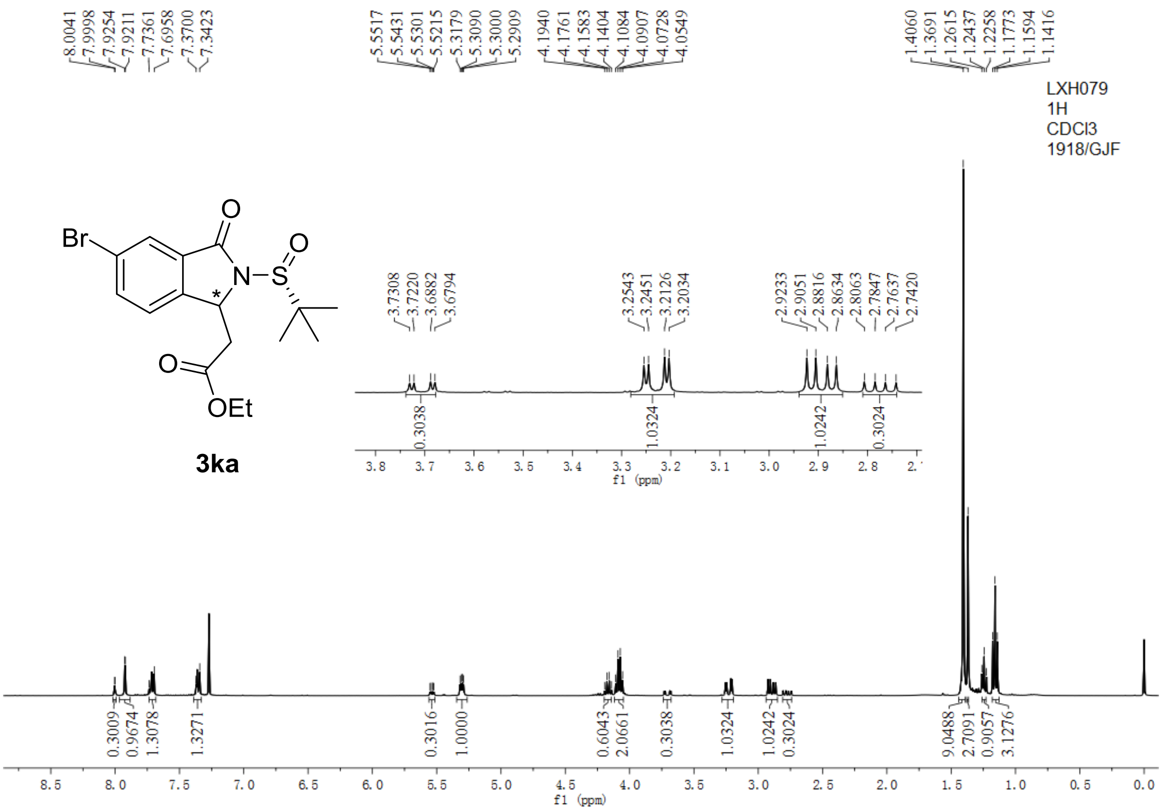
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3ia**



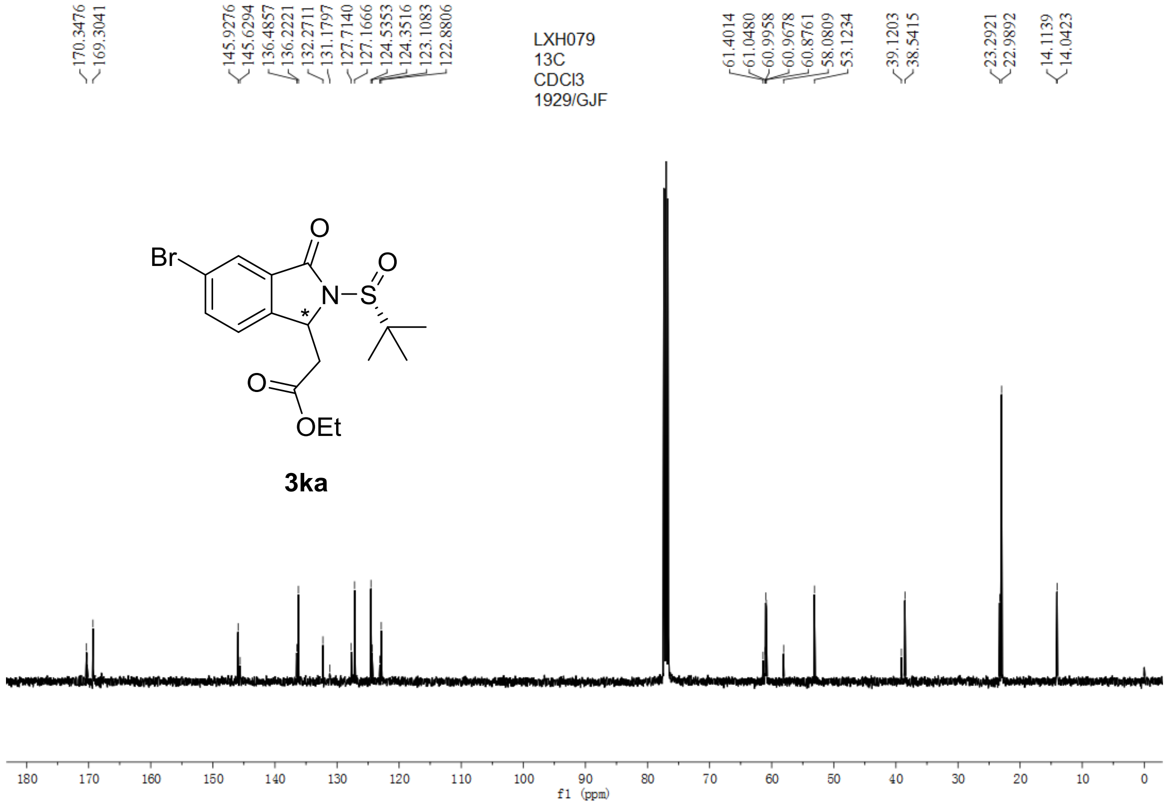
^{1}H NMR (400 MHz, $CDCl_3$) of **3ja**



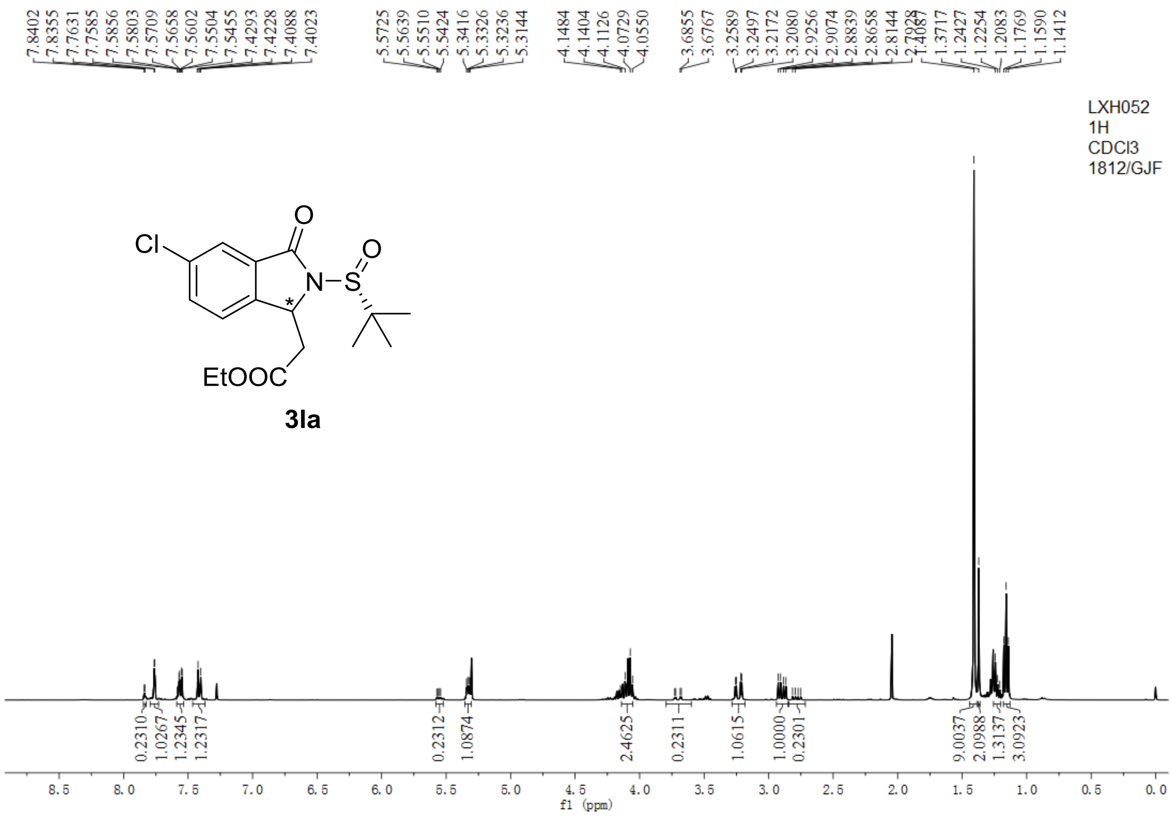
^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) of **3ja**



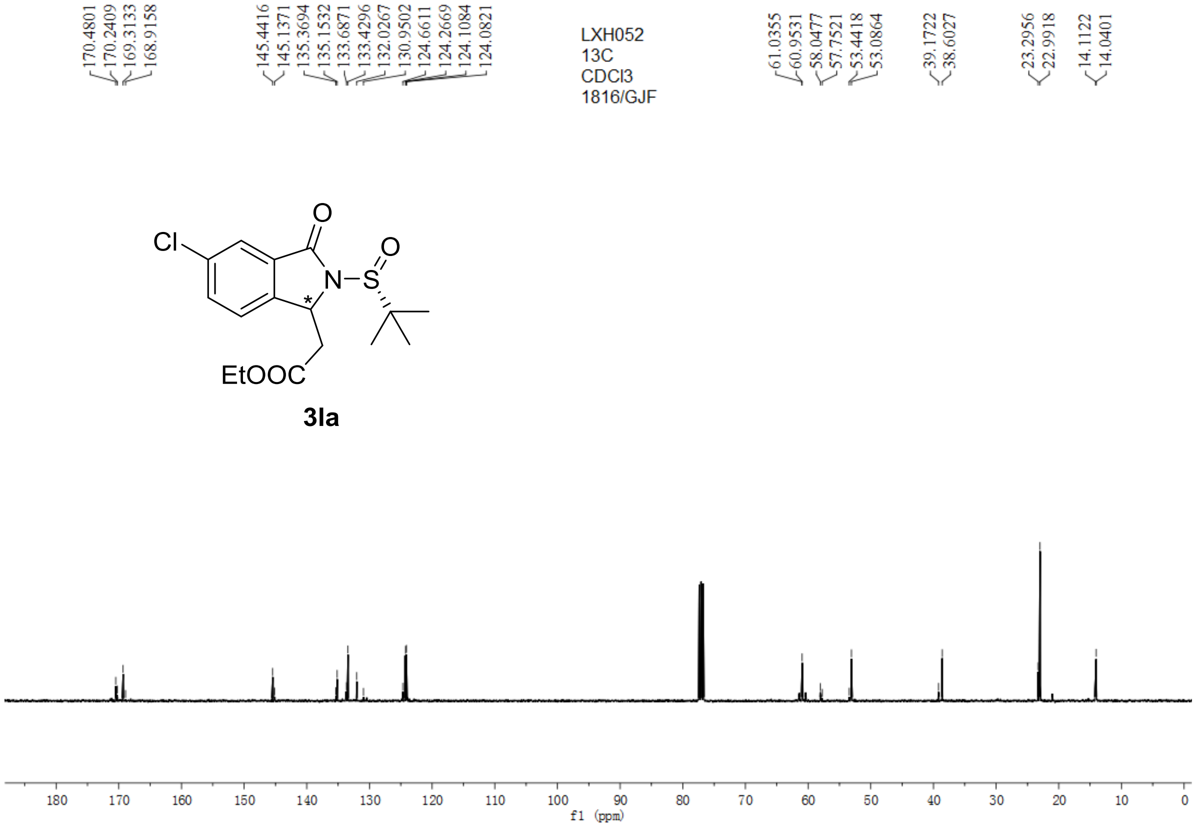
^{1}H NMR (400 MHz, CDCl$_3$) of **3ka**



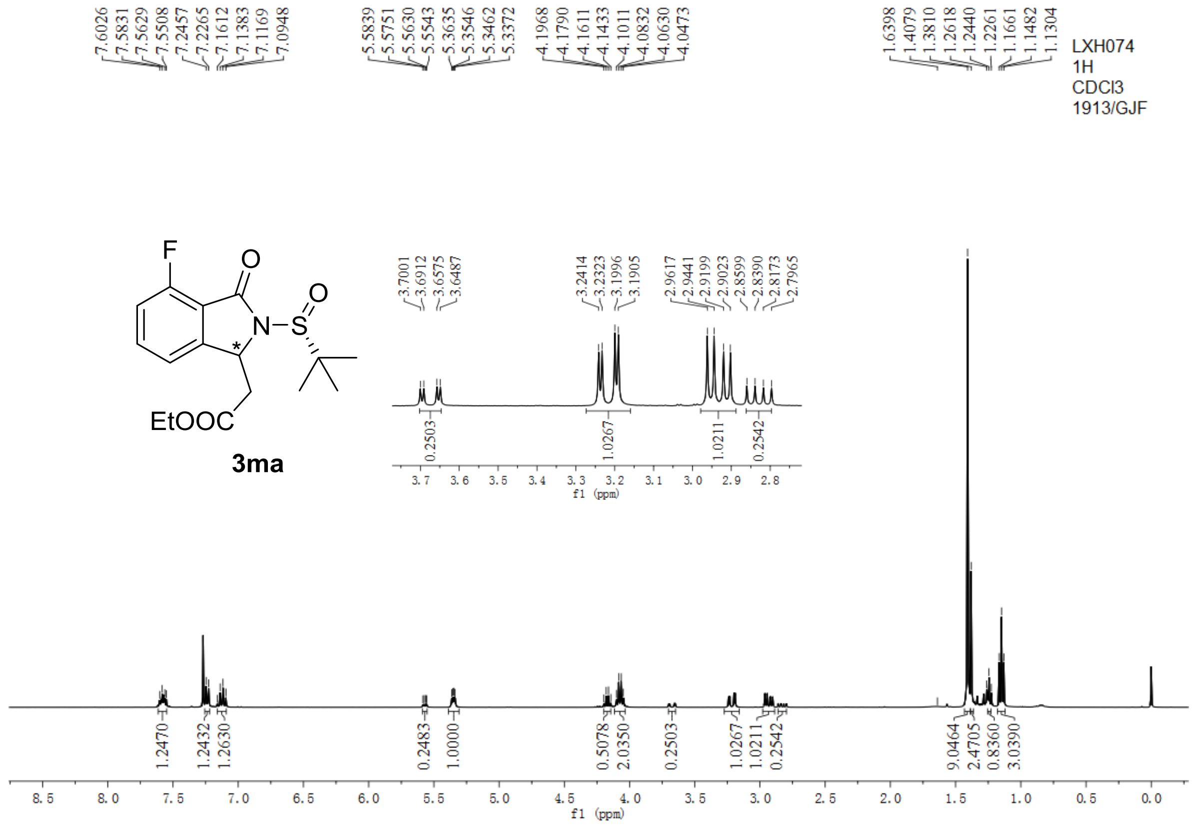
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) of **3ka**



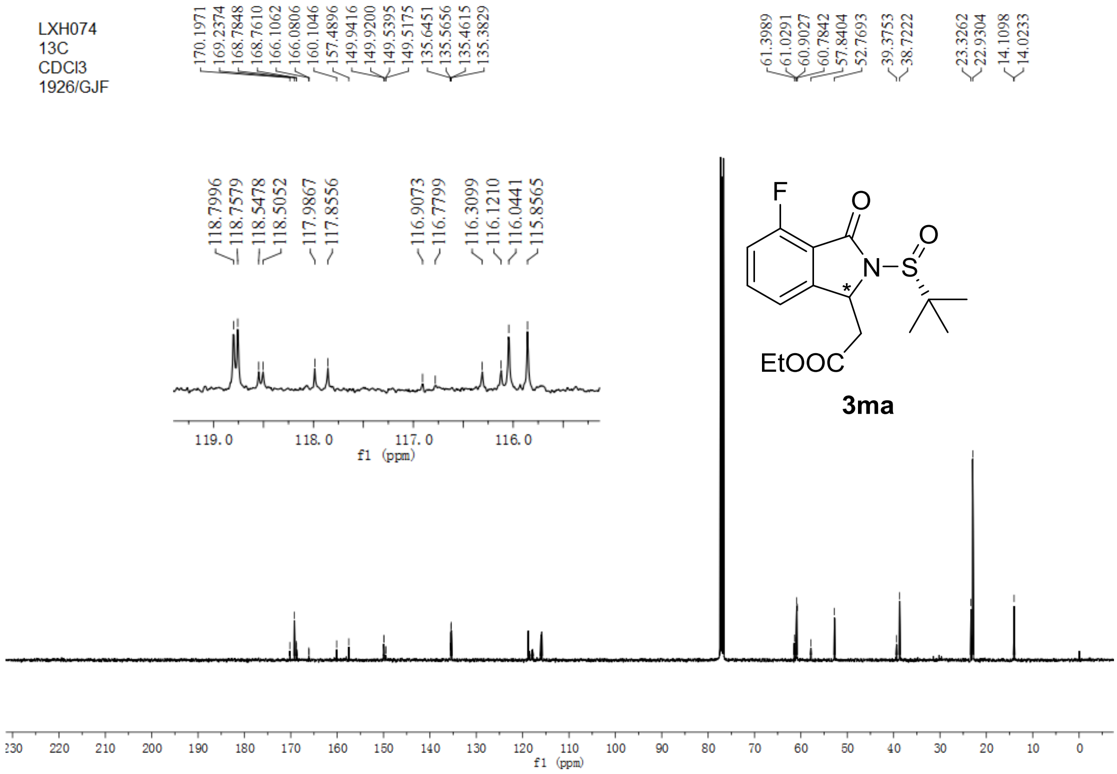
^1H NMR (400 MHz, $CDCl_3$) of **3la**



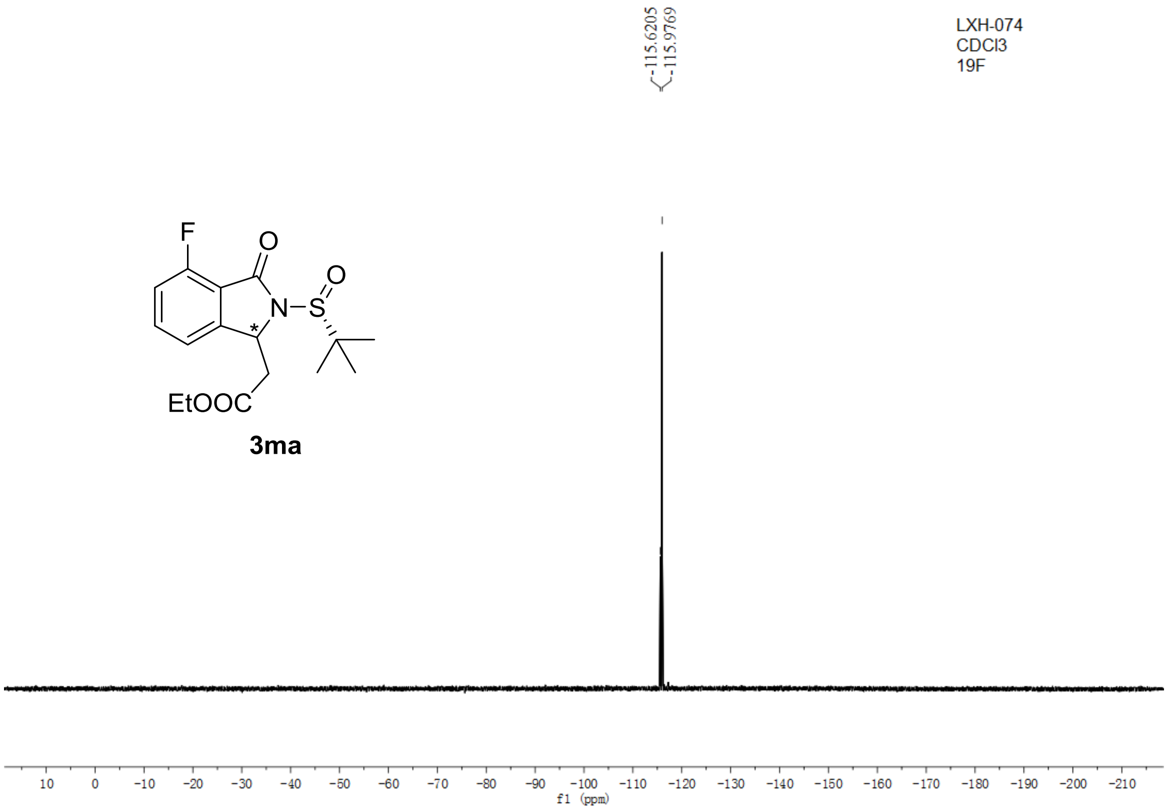
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) of **3la**



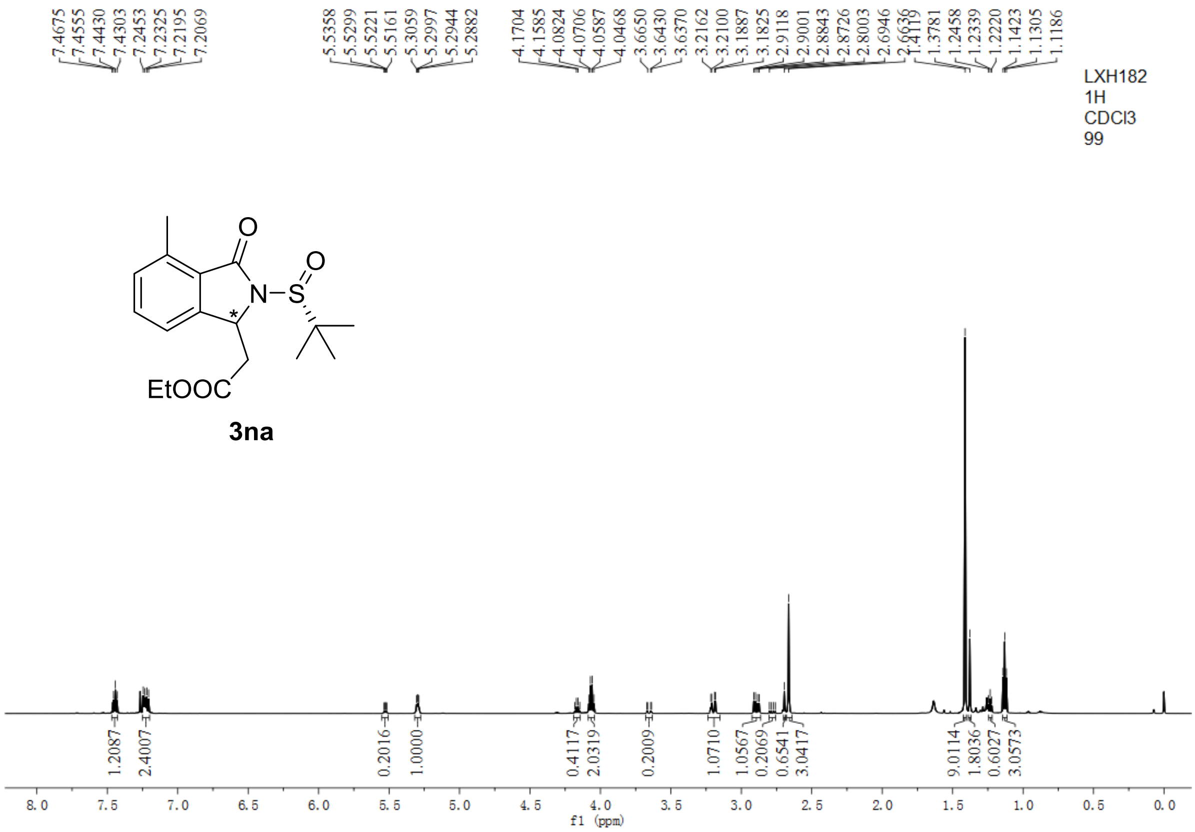
^1H NMR (400 MHz, $CDCl_3$) of **3ma**



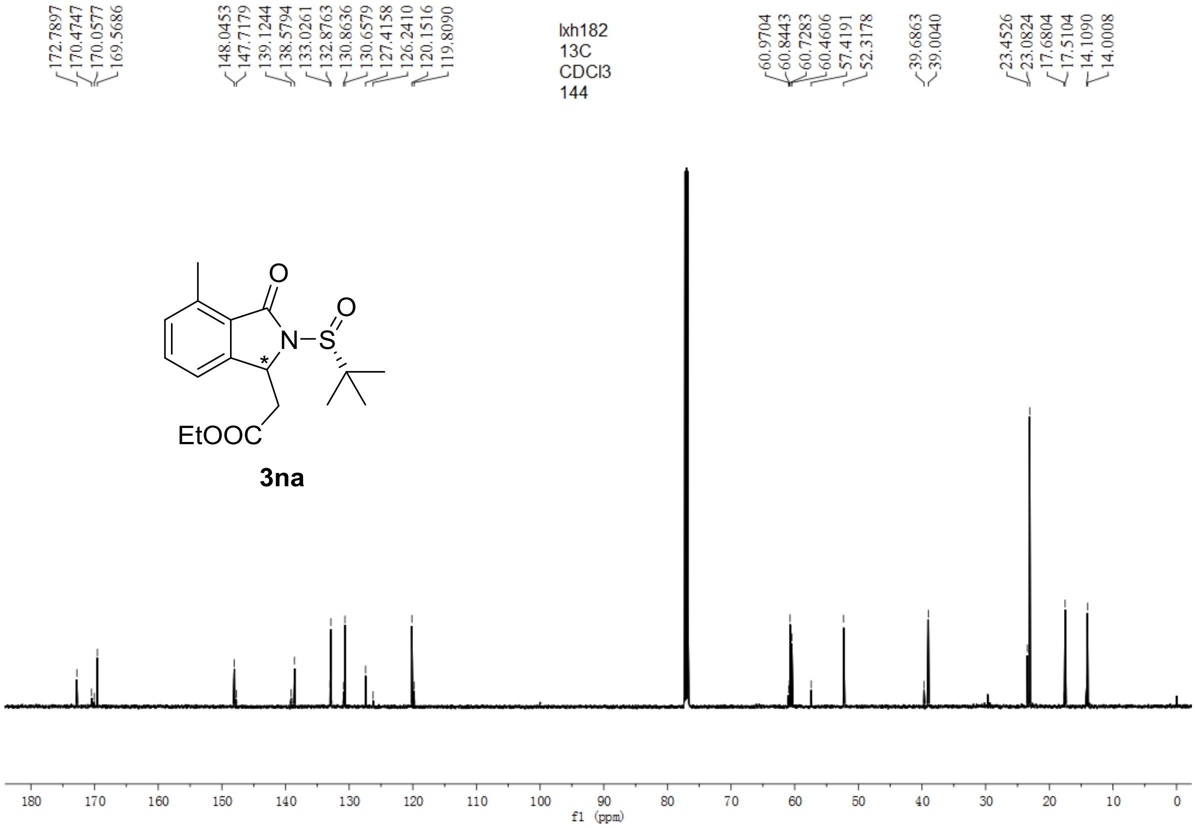
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) of **3ma**



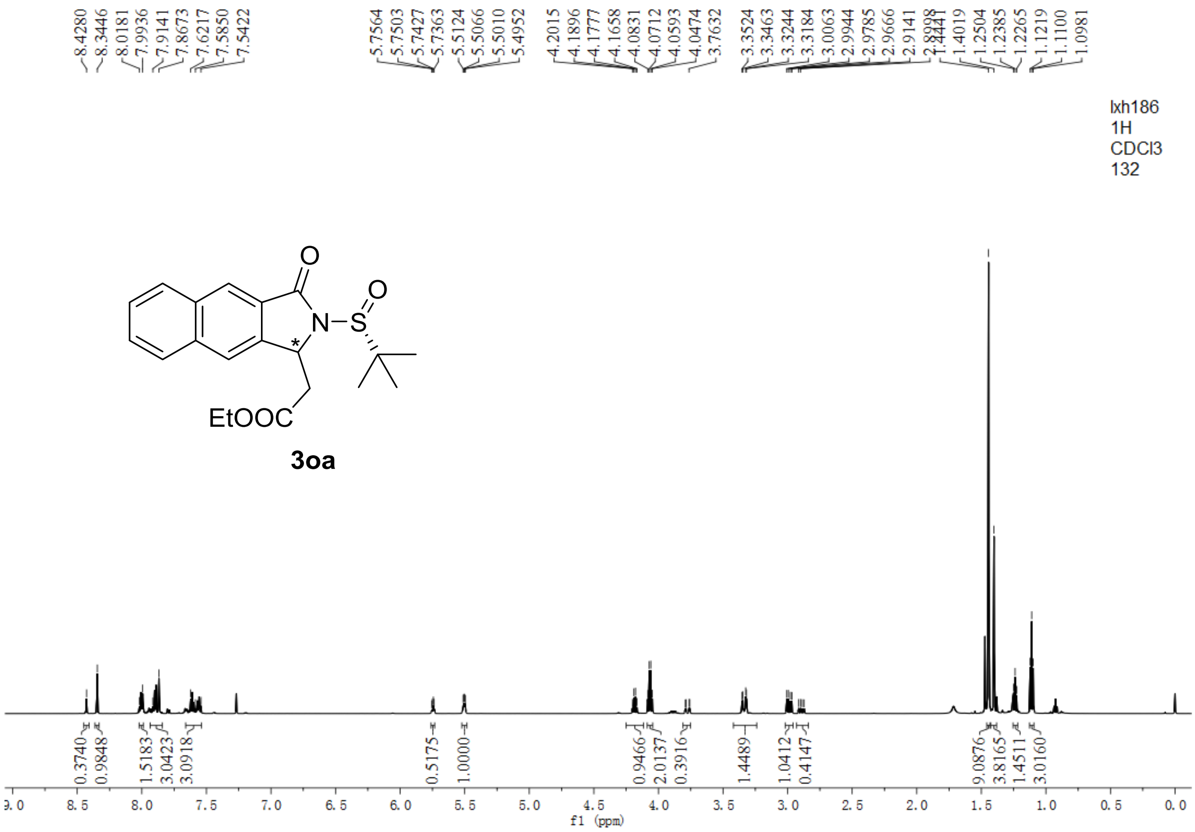
^{19}F NMR (376 MHz, $CDCl_3$) of **3ma**



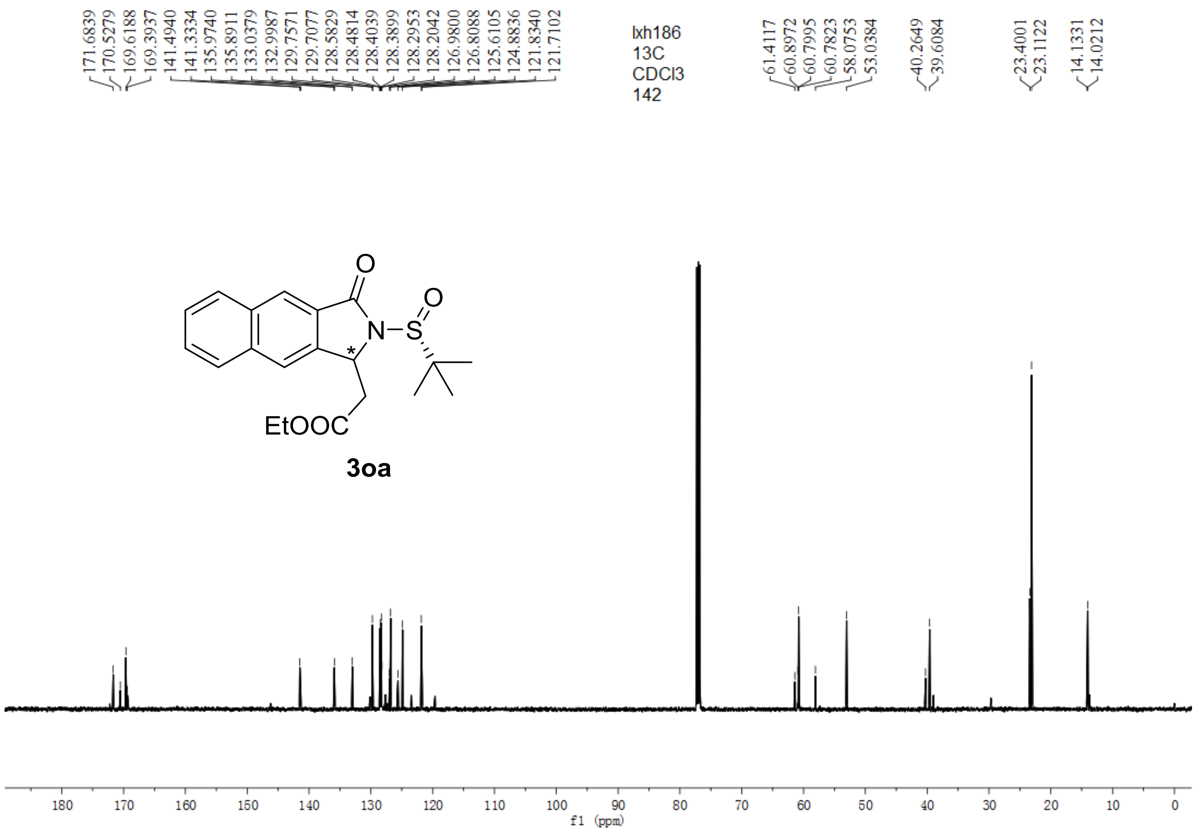
^{1}H NMR (600 MHz, CDCl$_3$) of **3na**



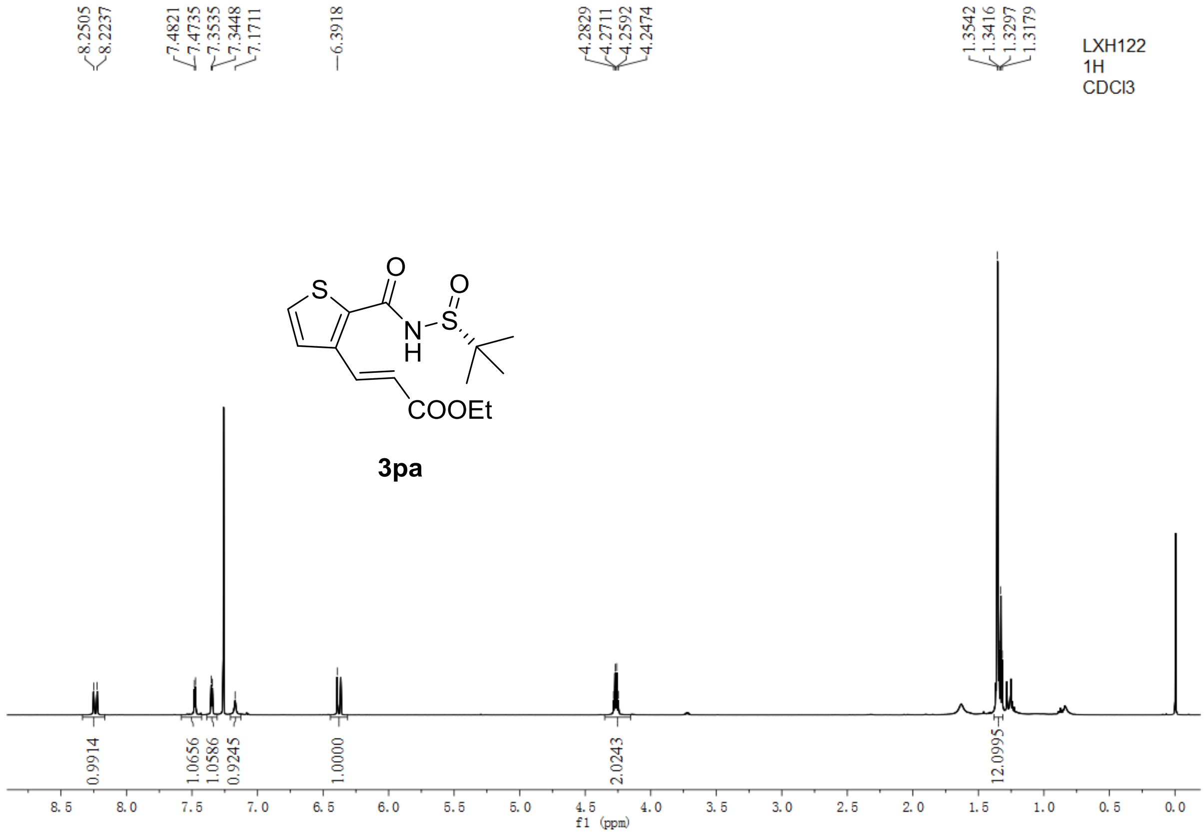
^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) of **3na**



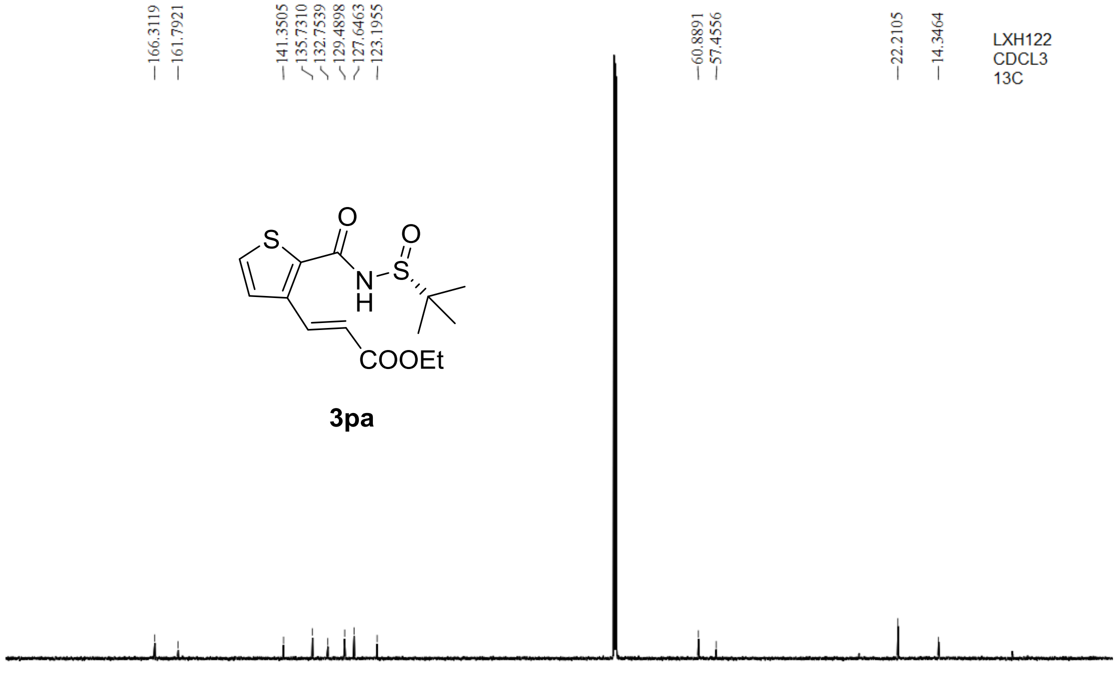
^{1}H NMR (600 MHz, $CDCl_3$) of **3oa**



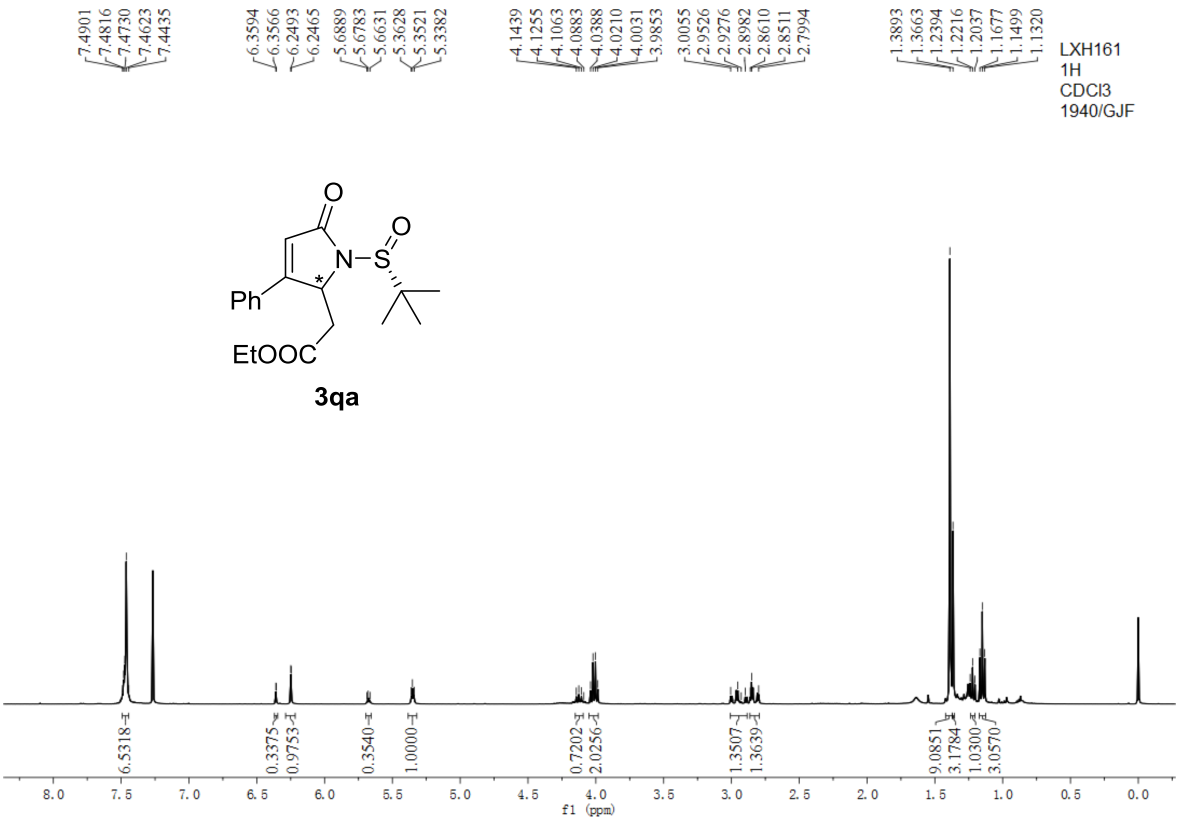
$^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) of **3oa**



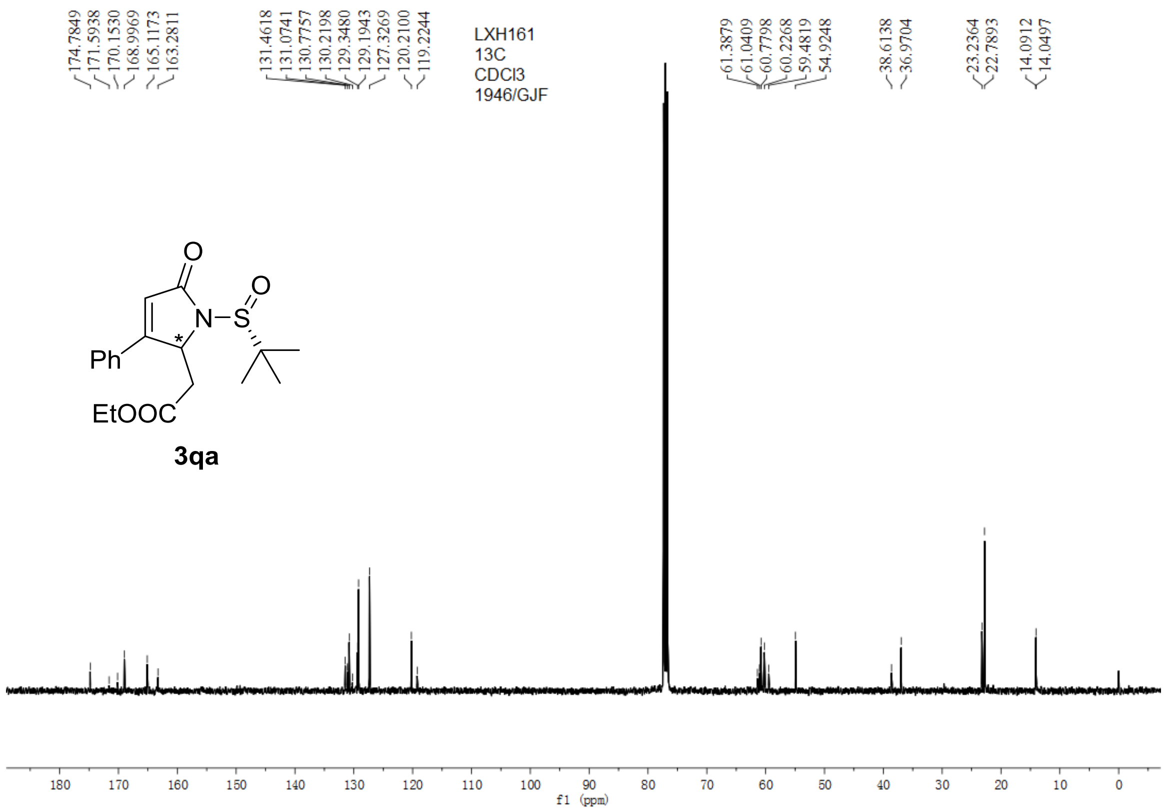
^{1}H NMR (600 MHz, $CDCl_3$) of **3pa**



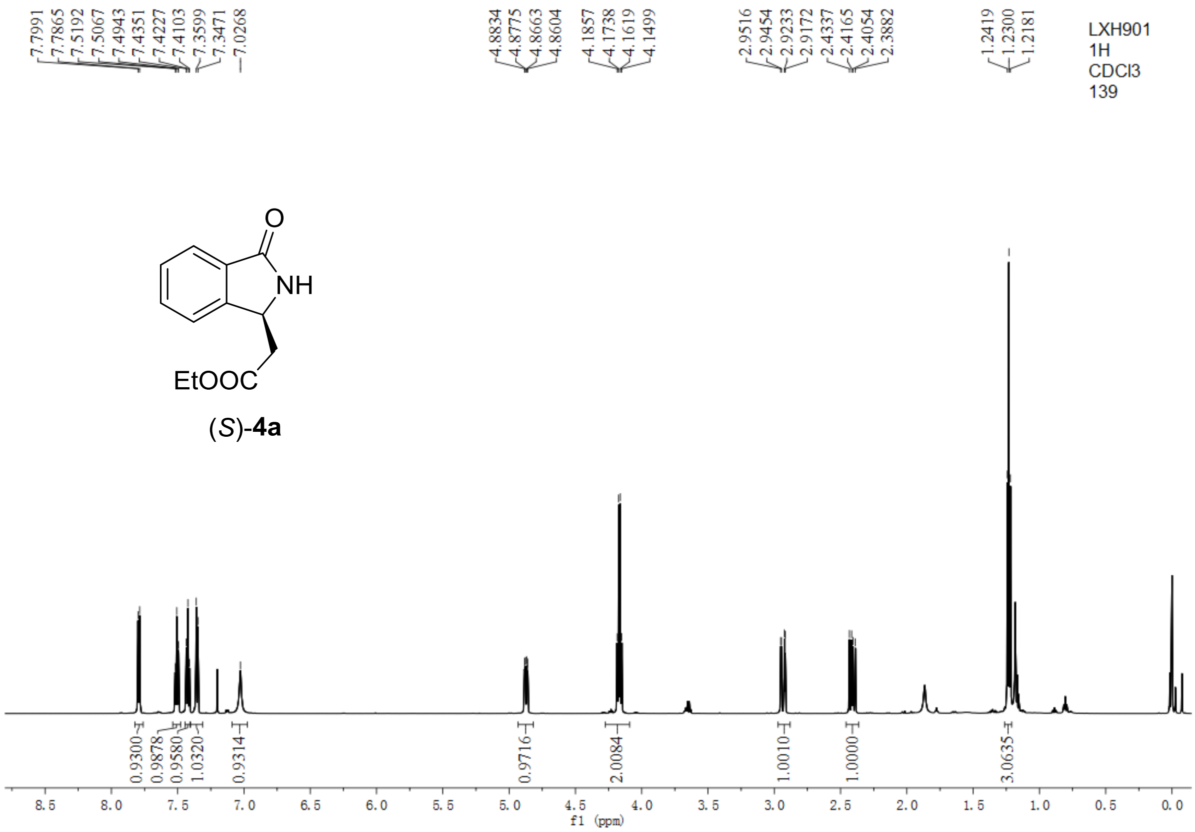
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) of **3pa**



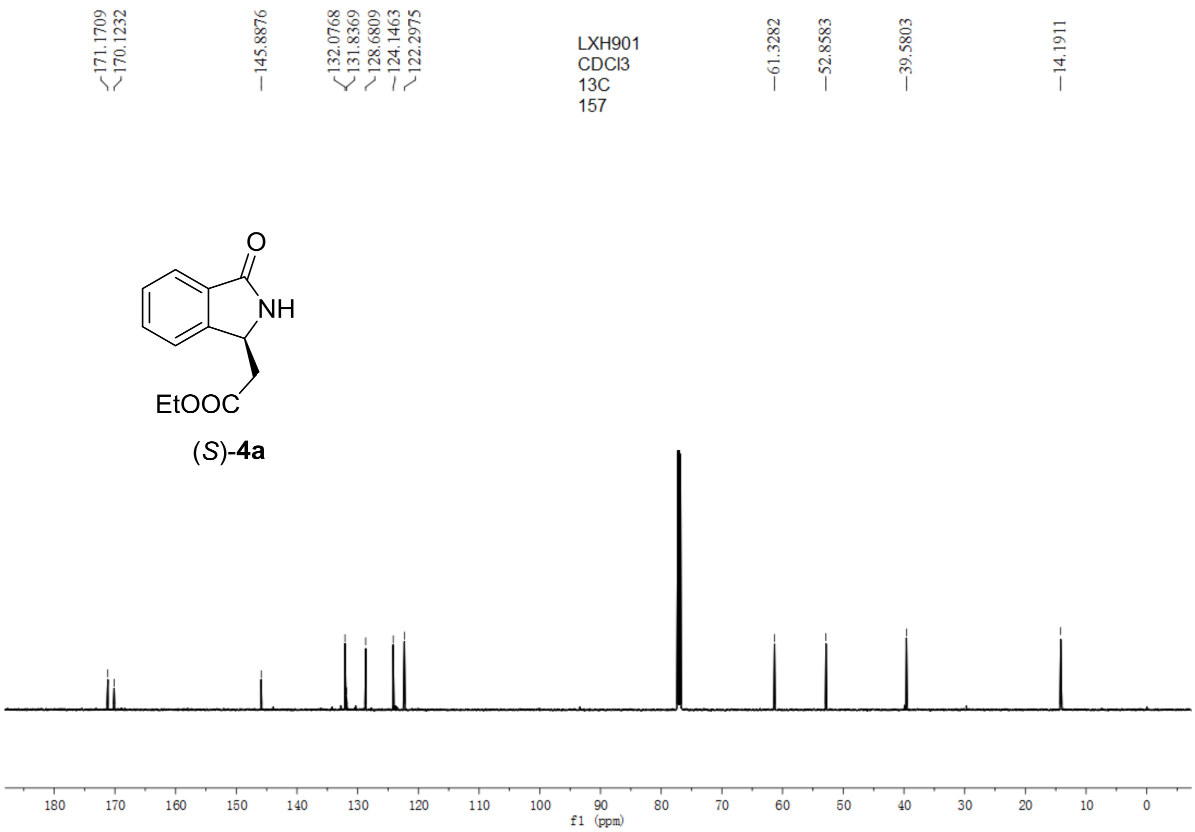
^{1}H NMR (400 MHz, $CDCl_3$) of **3qa**



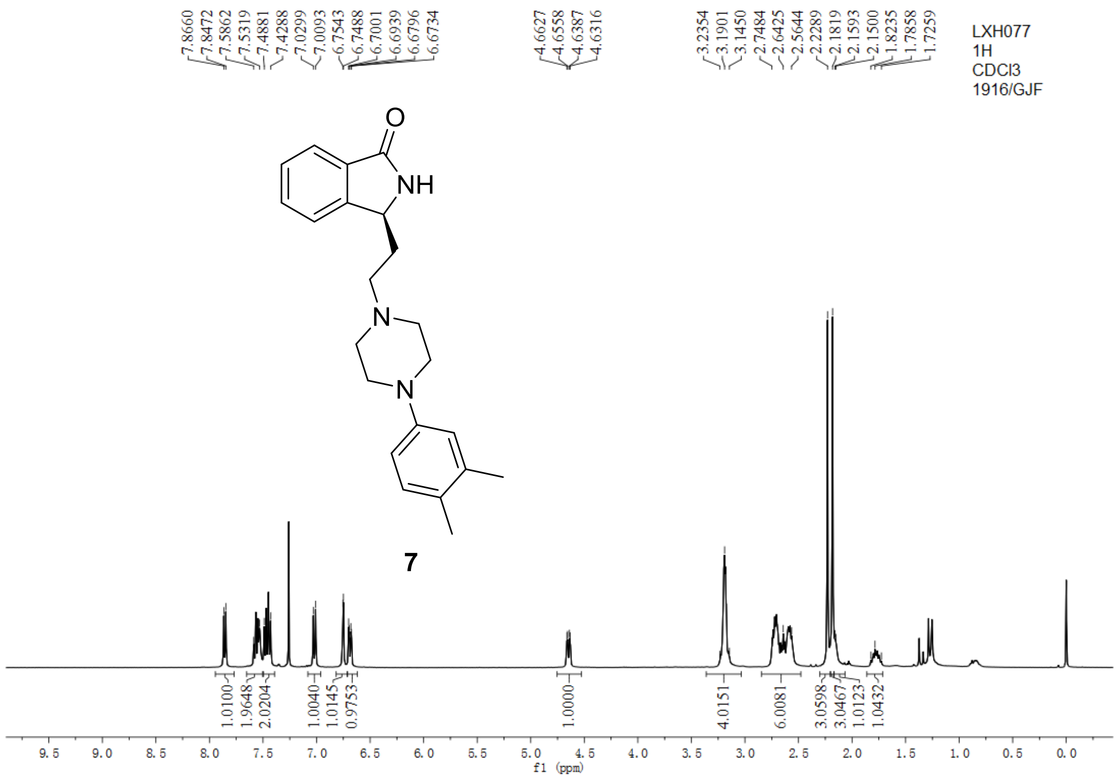
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3qa**



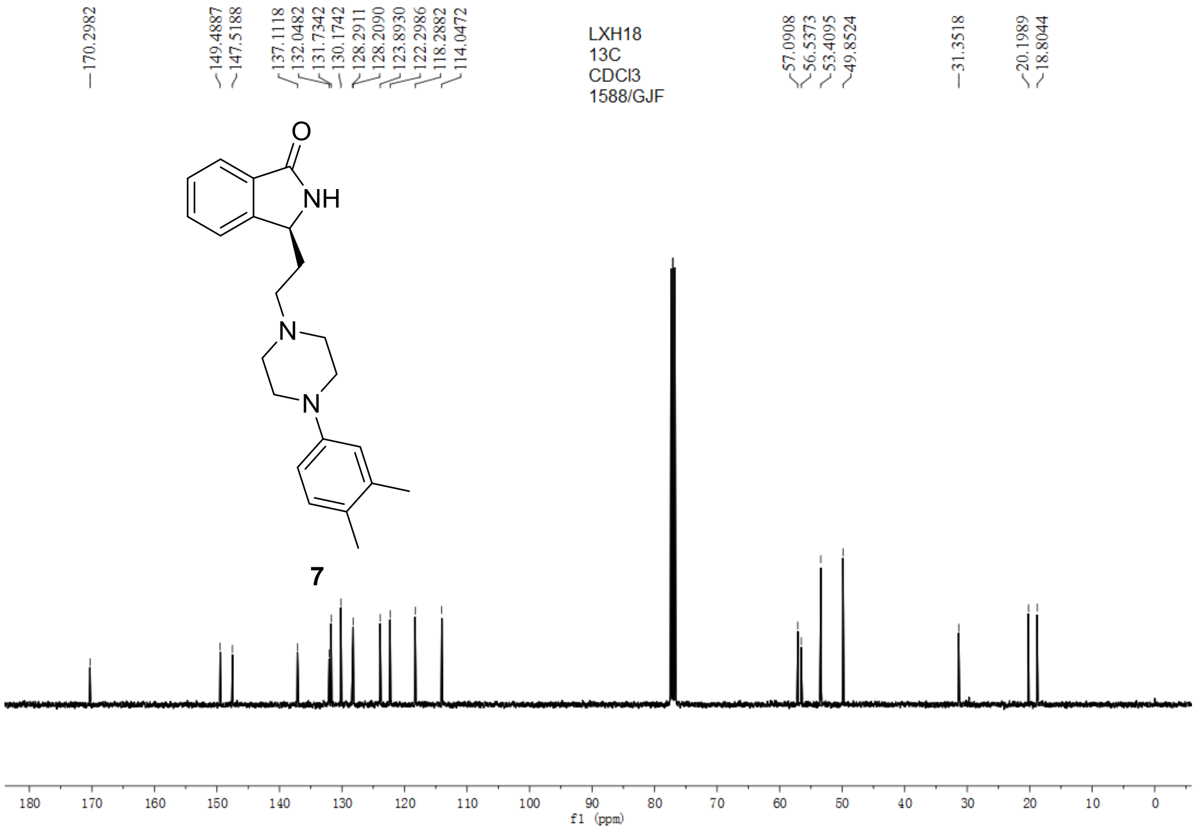
^{1}H NMR (600 MHz, CDCl$_3$) of (*S*)-**4a**



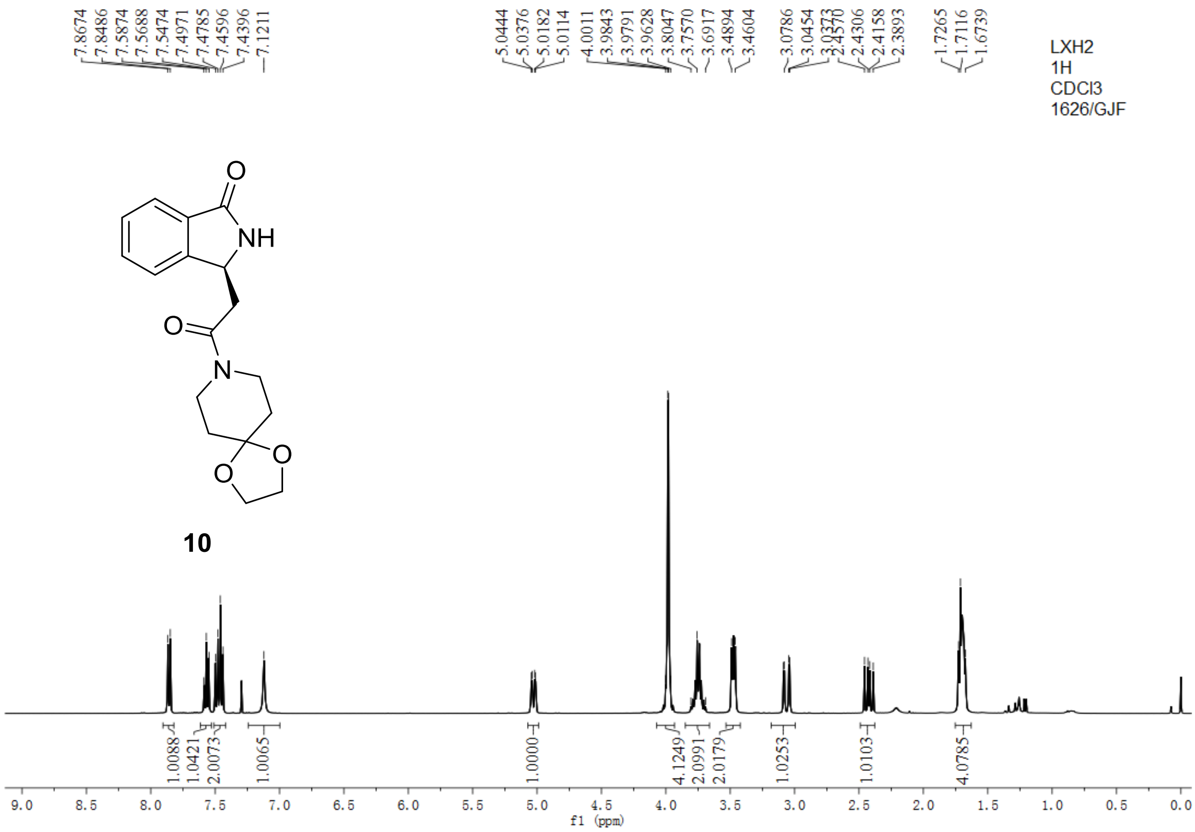
^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) of (*S*)-**4a**



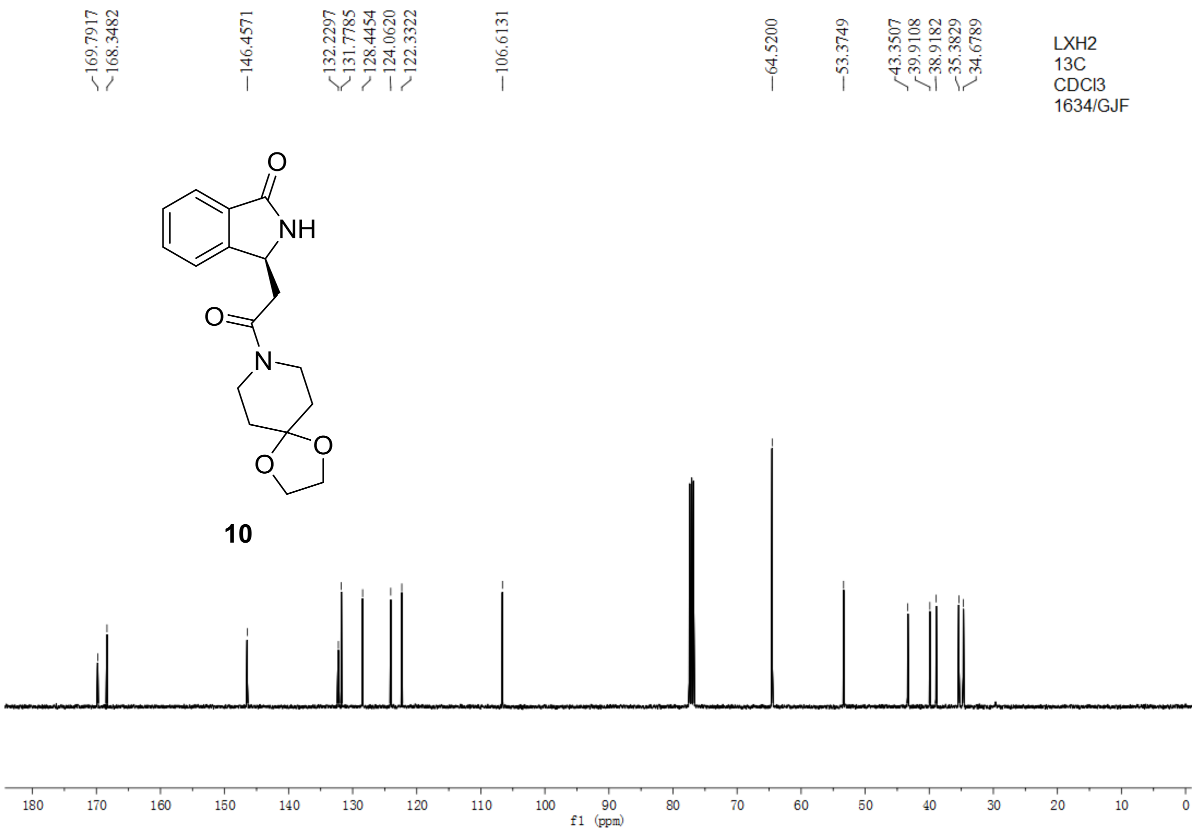
^{1}H NMR (400 MHz, $CDCl_3$) of **7**



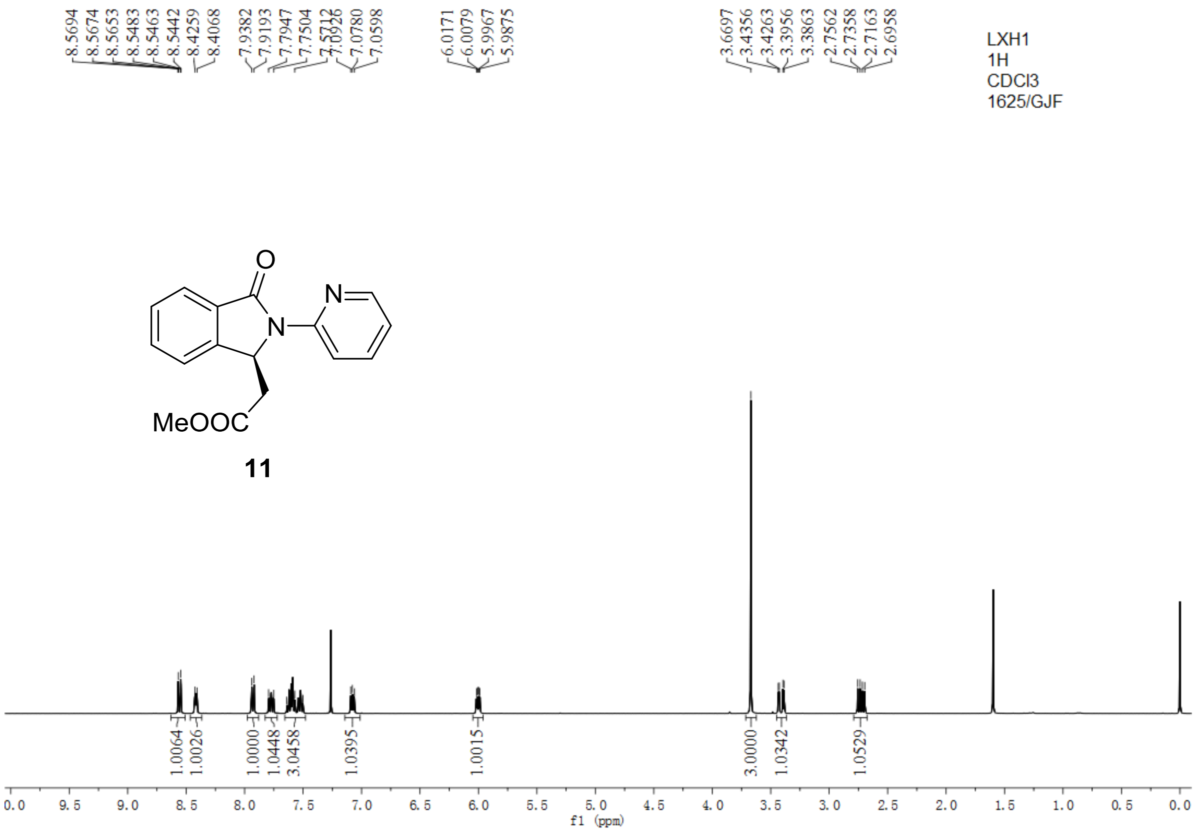
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **7**



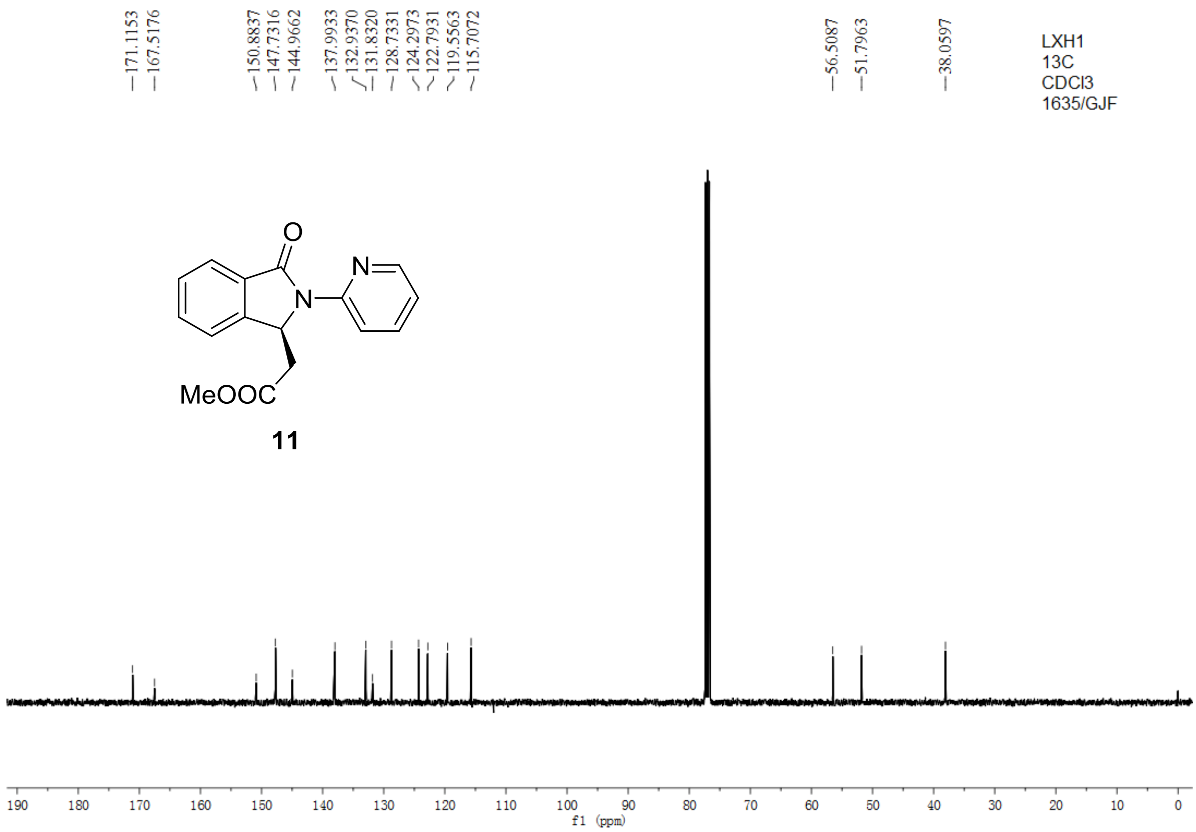
^{1}H NMR (400 MHz, $CDCl_3$) of **10**



$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **10**

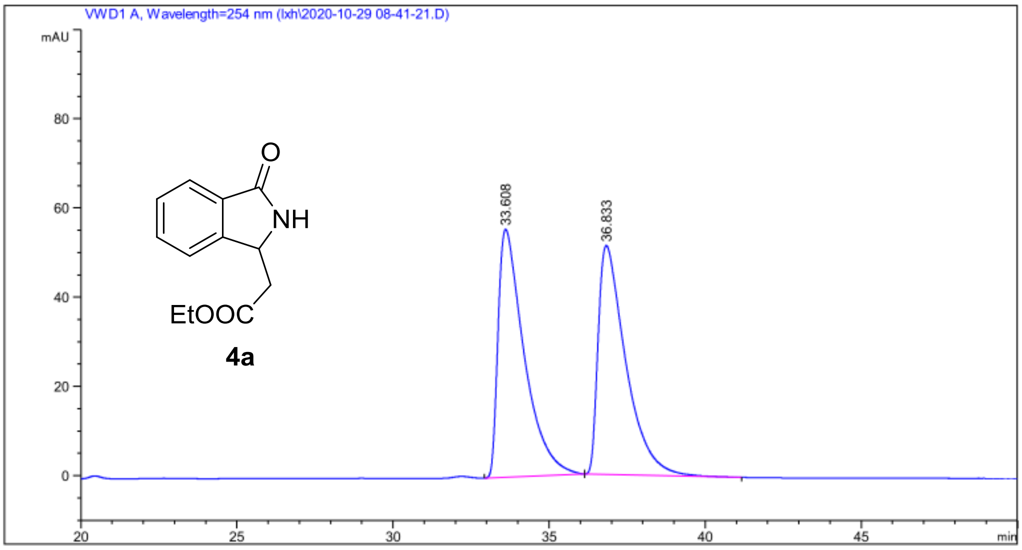


^1H NMR (400 MHz, $CDCl_3$) of **11**



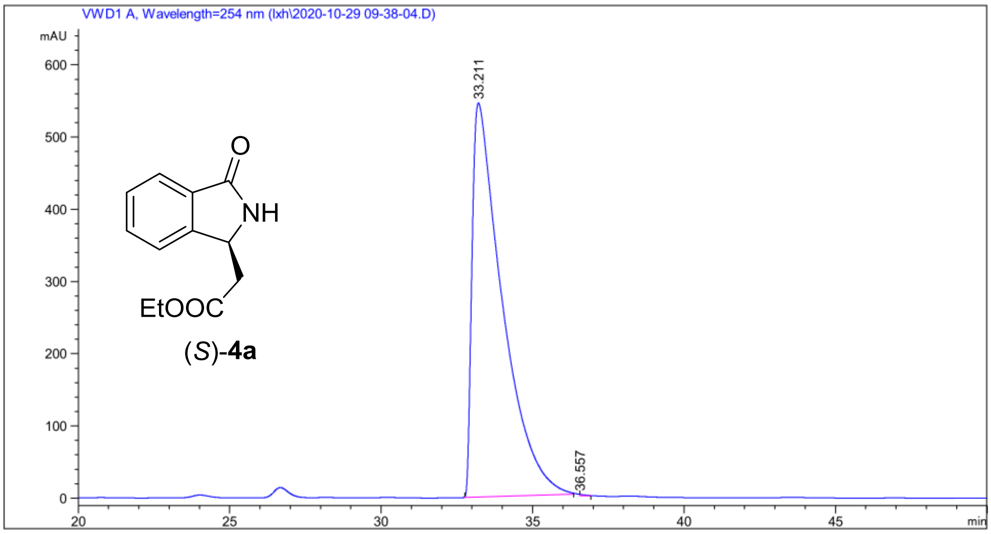
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) of **11**

HPLC Spectra.



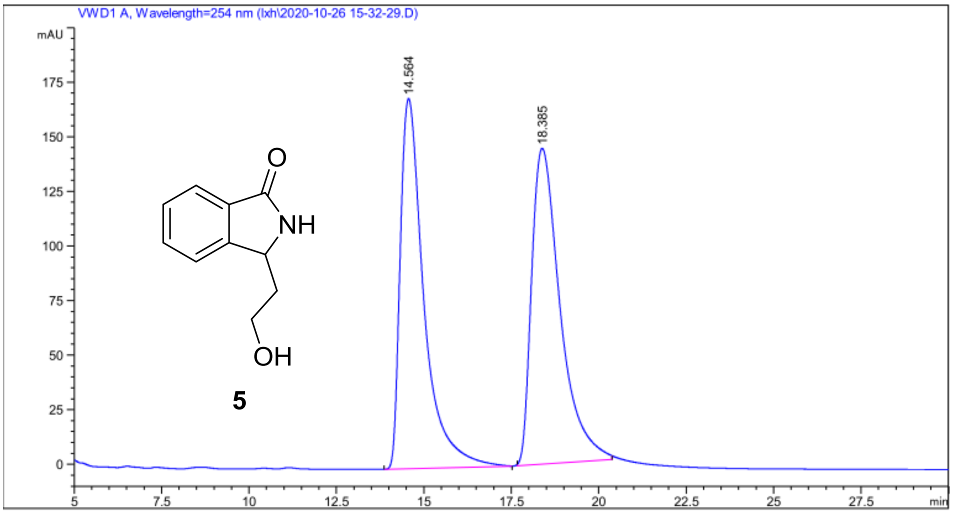
PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	33.608	55.60484	3224.21680	50.4983
2	36.833	51.36386	3160.58936	49.5017

Chiral HPLC chromatogram for racemic 4a



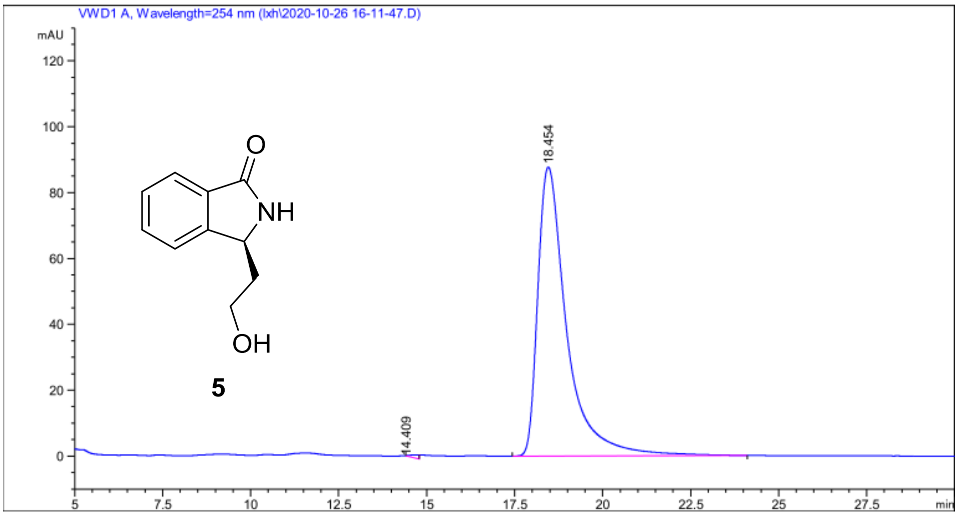
PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	33.211	545.38116	3.76698e4	99.9560
2	36.557	1.73080	16.57049	0.0440

Chiral HPLC chromatogram for enantioenriched (*S*)-4a



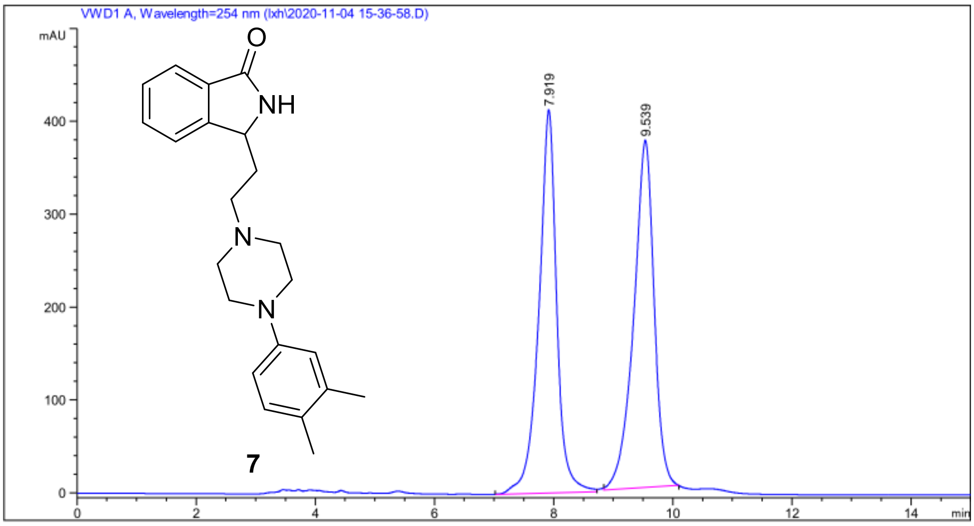
PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	14.564	169.56108	7965.42432	49.2525
2	18.385	144.59998	8207.21387	50.7475

Chiral HPLC chromatogram for racemic 5



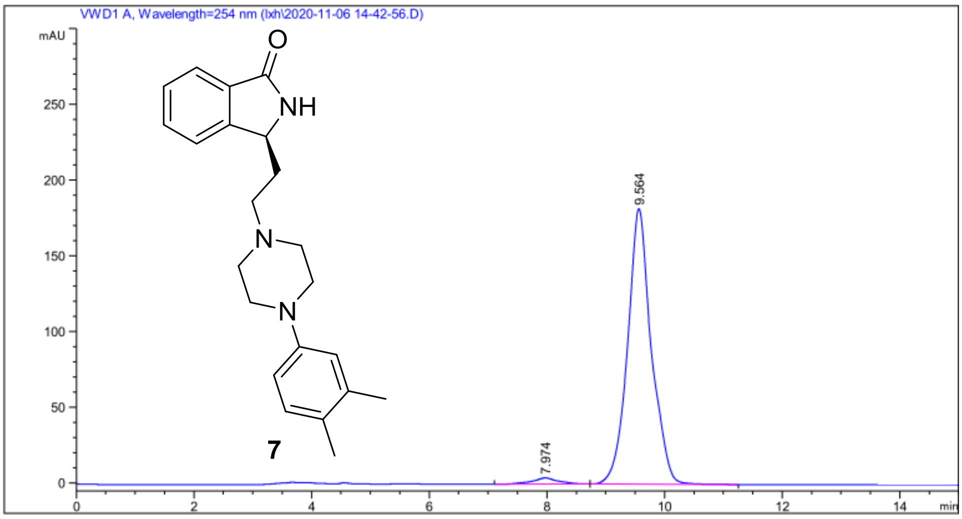
PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	14.409	3.64892e-2	15.71862	0.3121
2	18.454	87.75197	5020.24023	99.6879

Chiral HPLC chromatogram for enantioenriched 5



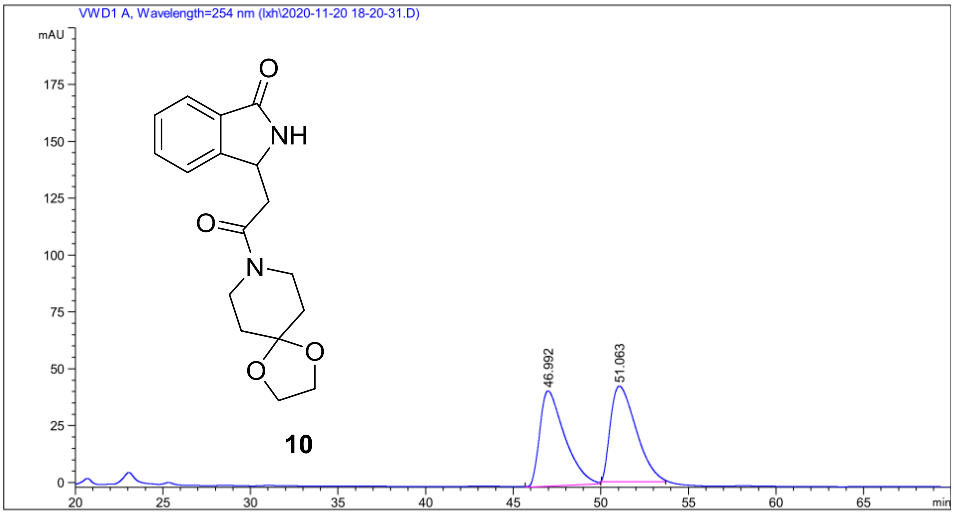
PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	7.919	412.30762	8576.43945	49.1058
2	9.539	373.75912	8888.79102	50.8942

Chiral HPLC chromatogram for racemic 7



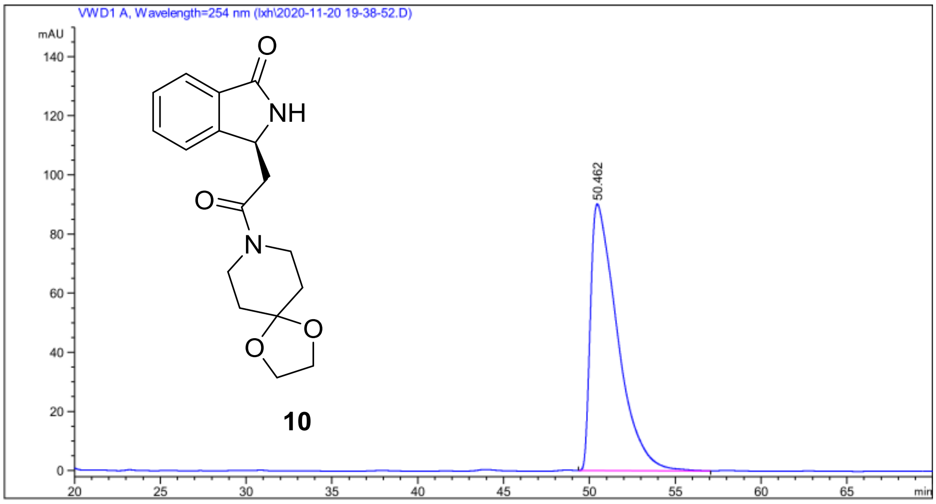
PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	7.974	4.10645	128.32562	2.4610
2	9.564	181.66975	5086.11035	97.5390

Chiral HPLC chromatogram for enantioenriched 7



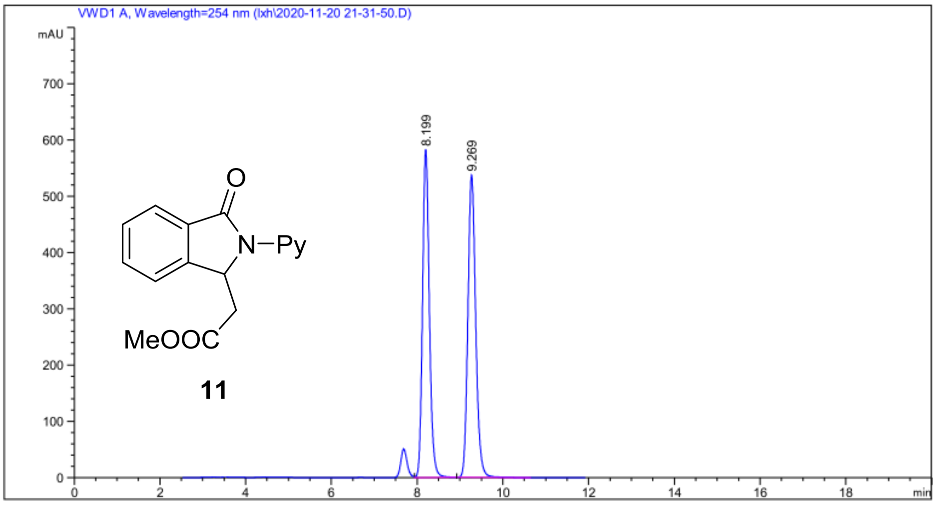
PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	46.992	41.98966	4167.18164	49.1988
2	51.063	42.11304	4302.90430	50.8012

Chiral HPLC chromatogram for racemic 10



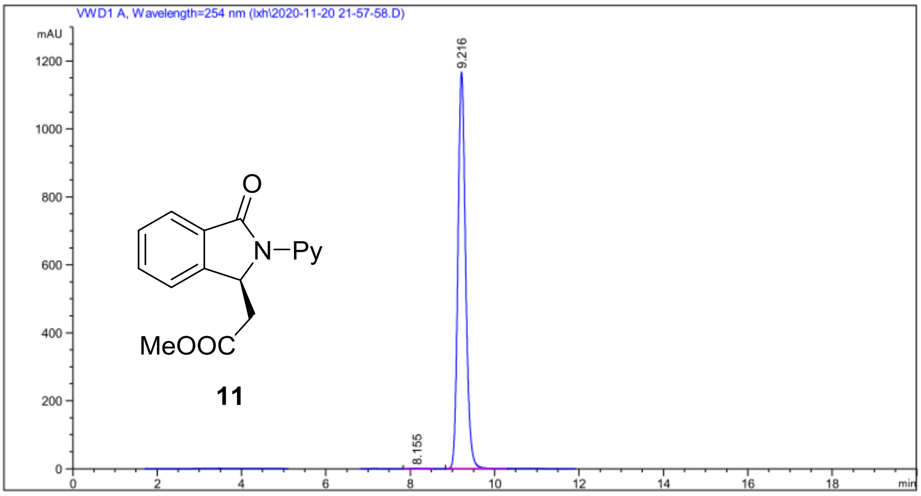
PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	50.462	90.15623	9818.70215	100

Chiral HPLC chromatogram for enantioenriched 10



PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	8.199	582.74756	6411.64014	48.5559
2	9.269	537.28802	6793.02295	51.4441

Chiral HPLC chromatogram for racemic 11



PeakNO.	Ret.Time	PeakHeight	PeakArea	Area%
1	8.155	1.86769	21.23161	0.1432
2	9.216	1167.37207	1.48092e4	99.8568

Chiral HPLC chromatogram for enantioenriched 11