Electronic Supplementary Material (ESI) for ChemComm.

Metal-free anomalous [5+1] cycloaddition reactions of donor-acceptor aziridines for the synthesis of *2H*-1,4-Oxazines

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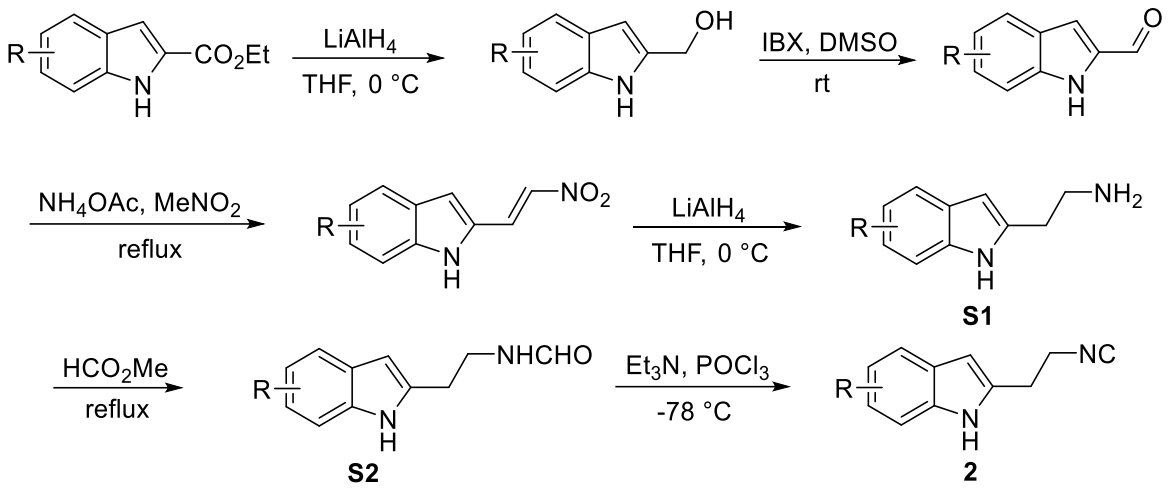
Contents

1. General Information

Reactions were carried out using commercial reagents in over-dried apparatus. $CHCl_3$ was dried over powdered CaH_2 and distilled under nitrogen just before use. ^1H NMR spectra were recorded on commercial instruments (400 MHz and 600 MHz). Chemical shifts are recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26 ppm; DMSO-d_6, δ = 2.50 ppm). Spectra are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), integration and assignment. ^{13}C NMR data were collected on commercial instruments (101 MHz and 151 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ= 77.0; DMSO-d_6, δ = 39.5 ppm). ^{19}F NMR data were collected on commercial instruments (376 MHz) with complete proton decoupling. Melting points (m. p.) were measured on the electrothermal digital melting point apparatus. HRMS was recorded on a commercial apparatus (ESI Source). All 2,2-diester aziridines **1**[1] were prepared according to the literature.

2. Preparing of isocyanides 2.



Isocyanides **2** were prepared according to the literature.[2]

For the synthesis of 2-(1H-indol-2-yl)ethan-1-amine **S1**: Under an inert nitrogen atmosphere, to a solution of $LiAlH_4$ (60 mmol, 3 equiv.) in THF (30 mL, 2 M) was added dropwise the solution of ethyl indole-2-carboxylate (20 mmol, 1 equiv.) in THF over 15 min at 0 °C, and the mixture was stirred at 0 °C for 1 h under nitrogen. Then H_2O was carefully added, the cooling bath was removed, and the mixture was stirred at room temperature for 15 min. Next, a mixture of MeOH and CH_2Cl_2 (1:8) was added, the obtained emulsion was stirred vigorously for 30 min and then extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford the crude alcohol as a slightly yellow oil, which was directly further used without purification.

To the solution of the above alcohol (18 mmol, 1 equiv.) in DMSO (35 mL, 0.5 M) was added IBX (27 mmol, 1.5 equiv.). The reaction mixture was stirred at room temperature for 2 h. Then the reaction mixture was diluted with water and extracted with ethyl acetate. The organic phase was combined, dried with anhydrous Na_2SO_4. The precipitate was filtered out and the mixture was concentrated under reduced pressure. The obtained residue was purification by flash column chromatography by using petroleum ether/ethyl acetate = 4/1 as eluent to afford the desired aldehyde.

The aldehyde (20 mmol, 1 equiv.) and ammonium acetate (4 mmol, 0.2 equiv.) were refluxed in nitromethane (28 mL) for 2 h. The solvent was removed in vacuo and the residue was washed with water, filtered and concentrated in vacuo to furnish the desired nitroolefin. The crude nitroolefin was used directly without further transformation.

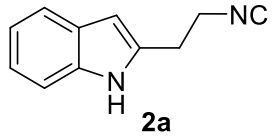
Under an inert nitrogen atmosphere, to a stirred slurry of $LiAlH_4$ (60 mmol, 3.3 equiv.) in THF

(80 mL, 0.75 M) was added a solution of crude nitroolefin (18 mmol, 1 equiv.) in THF at 0 °C. The mixture ware allowed to warm to room temperature and stirred for 3 h. The reaction was quenched by dropwise addition of water until effervescence ceased. The mixture was then diluted with diethyl ether before addition of a saturated aqueous solution of Rochelle's salt and the subsequent biphasic mixture was stirred for 1 h. The layers were extracted with diethyl ether, dried with anhydrous Na_2SO_4, filtered and concentrated in vacuo to furnish the desired 2-(1H-indol-2-yl)ethan-1-amine **S1** which was directly used without that further purification.

For the synthesis of isocyanide **2**: A mixture of crude **S1** in HCO_2Me (6 mL per 10 mol) was refluxed for 4 h. The crude mixture was concentrated in vacuo and purified by flash column chromatography by using petroleum ether/ethyl acetate = 1/2 as eluent to afford formamide **S2**.

Under an inert nitrogen atmosphere, to a solution of formamide **S2** (17.0 mmol, 1equiv.), Et_3N (0.85 mol, 5 equiv.), anhydrous DCM (30 mL, 0.57 M) was added dropwise $POCl_3$ (25 mmol, 1.5 equiv.) at -78 °C over 15 min. After stirring at -78 °C for 3 h, the reaction mixture was poured into ice-cold water carefully and extracted with CH_2Cl_2. The combined organic layer was washed with water and brine, dried over Na_2SO_4, concentrated and purified by column chromatography to give isocyanide **2** as a yellow solid.

2-(2-isocyanoethyl)-1H-indole 2a



2a

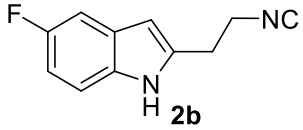
Yellow solid. R_f = 0.4 (PE:EA = 4:1), m.p. 45-47 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.60 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.37 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.17 – 7.13 (m, 1H), 6.39 (dd, *J* = 2.0, 0.8 Hz, 1H), 3.74 – 3.69 (m, 2H), 3.17 – 3.13 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4 (t, *J* = 7.0 Hz), 136.2, 133.9, 128.4, 122.0, 120.3, 120.1, 110.8, 101.2, 41.6 (t, *J* = 7.0 Hz), 28.6.

HRMS (ESI-TOF) calcd for $C_{11}H_{11}N_2^+$ ([M+H$^+$]) = 171.0917, Found 171.0918.

5-fluoro-2-(2-isocyanoethyl)-1H-indole 2b



2b

Yellow liquid. R_f = 0.3 (PE:EA = 4:1).

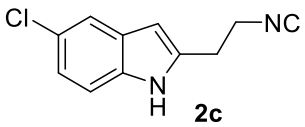
^{1}H (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.28 – 7.21 (m, 2H), 6.94 (td, *J* = 9.2, 2.4 Hz, 1H), 6.35 (d, *J* = 2.4 Hz, 1H), 3.75 – 3.71 (m, 2H), 3.17 – 3.12 (m, 2H).

^{13}C (101 MHz, $CDCl_3$) 158.1 (d, *J* = 231.0 Hz), 157.4 (t, *J* = 6.0 Hz), 132.8, 132.7, 128.7 (d, *J* = 10.0 Hz), 111.3 (d, *J* = 9.0 Hz), 110.2 (d, *J* = 26.0 Hz), 105.1 (d, *J* = 24.0 Hz), 101.4 (d, *J* = 4.0 Hz), 41.5 (t, *J* = 7.0 Hz), 28.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -124.45.

HRMS (ESI-TOF) calcd for $C_{11}H_{10}FN_2^+$ ([M+H$^+$]) = 189.0823, Found 189.0835.

5-chloro-2-(2-isocyanoethyl)-1H-indole 2c



2c

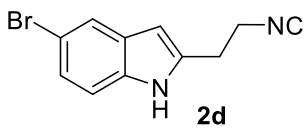
Yellow liquid. R_f = 0.4 (PE:EA = 4:1), m.p. 58-60 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 7.14 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.31 (d, *J* = 2.4 Hz, 1H), 3.72 – 3.68 (m, 2H), 3.13 – 3.09 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3 (t, *J* = 6.0 Hz), 135.5, 134.5, 129.5, 125.6, 122.2, 119.6, 111.8, 100.9, 41.5 (t, *J* = 7.0 Hz), 28.5.

HRMS (ESI-TOF) calcd for $C_{11}H_{10}ClN_2^+$ ([M+H$^+$]) = 205.0527, Found 205.0528.

5-bromo-2-(2-isocyanoethyl)-1H-indole 2d



2d

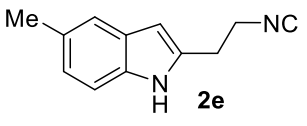
Yellow solid. R_f = 0.4 (PE:EA = 4:1), m.p. 66-68 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.26 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.17 (d, *J* = 8.8 Hz, 1H), 6.28 (d, *J* = 2.0 Hz, 1H), 3.68 – 3.64 (m, 2H), 3.08 – 3.04 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ156.9 (t, *J* = 6.0 Hz), 135.5, 134.8, 130.2, 124.6, 122.7, 113.1, 112.4, 100.7, 41.4 (t, *J* = 7.0 Hz), 28.4.

HRMS (ESI-TOF) calcd for $C_{11}H_{10}BrN_2^+$ ([M+H$^+$]) = 249.0022, Found 249.0020.

2-(2-isocyanoethyl)-5-methyl-1H-indole 2e



2e

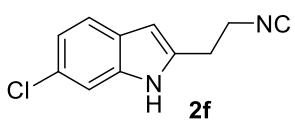
Yellow solid. R_f = 0.4 (PE:EA = 4:1), m.p. 55-57 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.39 (t, *J* = 1.6 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.30 (d, *J* = 2.0 Hz, 1H), 3.72 – 3.67 (m, 2H), 3.14 – 3.09 (m, 2H), 2.48 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 134.5, 133.9, 129.3, 128.7, 123.6, 119.9, 110.4, 100.7, 41.6 (t, *J* = 7.0 Hz), 28.7, 21.5.

HRMS (ESI-TOF) calcd for $C_{12}H_{13}N_2^+$ ([M+H$^+$]) = 185.1073, Found 185.1073.

6-chloro-2-(2-isocyanoethyl)-1H-indole 2f



2f

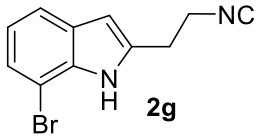
Yellow solid. R_f = 0.4 (PE:EA = 4:1), m.p. 68-70 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.29 – 7.28 (m, 1H), 7.11 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.35 (d, *J* = 2.0 Hz, 1H), 3.70 – 3.65 (m, 2H), 3.09 – 3.05 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8 (t, *J* = 6.0 Hz), 136.5, 134.9, 127.5, 127.0, 121.1, 120.7, 110.8, 101.2, 41.4 (t, *J* = 7.0 Hz), 28.4.

HRMS (ESI-TOF) calcd for $C_{11}H_{10}ClN_2^+$ ([M+H$^+$]) = 205.0527, Found 205.0530.

7-bromo-2-(2-isocyanoethyl)-1H-indole 2g



2g

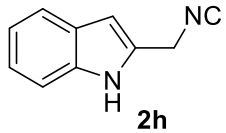
Light yellow solid. R_f = 0.4 (PE:EA = 4:1), m.p. 100-102 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 8.0 Hz, 1H), 6.47 (d, *J* = 2.4 Hz, 1H), 3.74 – 3.69 (m, 2H), 3.17 – 3.13 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4 (t, *J* = 6.0 Hz), 134.9, 134.7, 129.5, 124.3, 121.3, 119.5, 104.2, 102.4, 41.3 (t, *J* = 7.0 Hz), 28.4.

HRMS (ESI-TOF) calcd for $C_{11}H_{10}BrN_2^+$ ([M+H$^+$]) = 249.0022, Found 249.0021.

2-(isocyanomethyl)-1H-indole 2h



2h

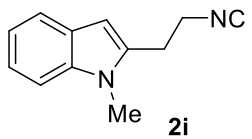
Light yellow solid. R_f = 0.4 (PE:EA = 4:1), m.p. 119-121 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.63 (d, *J* = 6.8 Hz, 1H), 7.40 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.18 (td, *J* = 7.6, 1.2 Hz, 1H), 6.51 (dd, *J* = 2.4, 1.2 Hz, 1H), 4.79 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 136.6, 128.5, 127.8, 123.0, 120.9, 120.5, 111.2, 102.5, 39.7 (t, *J* = 7.0 Hz).

HRMS (ESI-TOF) calcd for $C_{10}H_9N_2^+$ ([M+H$^+$]) = 157.0760, Found 157.0761.

2-(2-isocyanoethyl)-1-methyl-indole 2i



2i

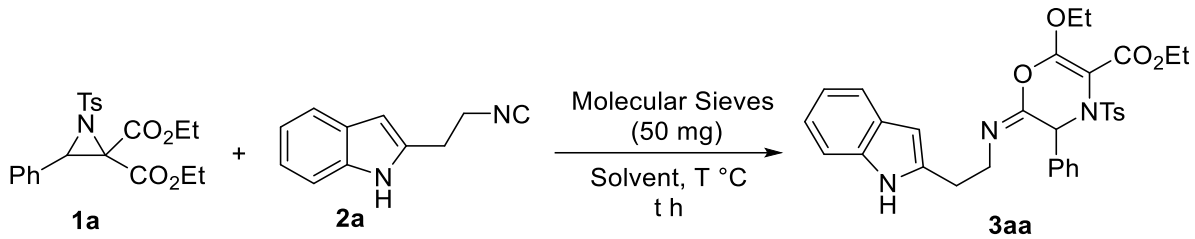
Yellow solid. R_f = 0.4 (PE:EA = 4:1), m.p. 77-79 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.33 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.17 – 7.13 (m, 1H), 6.39 (d, *J* = 1.0 Hz, 1H), 3.84 – 3.62 (m, 5H), 3.21 (t, *J* = 7.3 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.5 (t, *J* = 6.0 Hz), 137.5, 135.1, 127.6, 121.6, 120.3, 119.8, 109.1, 100.1, 40.8 (t, *J* = 7.0 Hz), 29.7, 27.1.

HRMS (ESI-TOF) calcd for $C_{12}H_{13}N_2^+$ ([M+H$^+$]) = 185.1073, Found 185.1072.

3. Optimization of Reaction Conditions



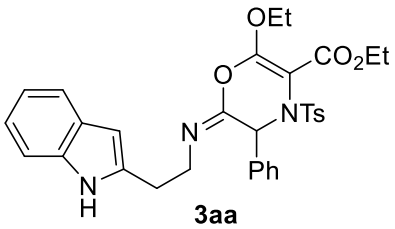
Entry[a]	Molecular Sieves	Solvent	**1a**:**2a**	T (°C)	Yield (%)[b] **3aa**
1	4 Å MS	CH_2Cl_2	1.5:1	35	54
2	4 Å MS	$CHCl_3$	1.5:1	35	68
3	4 Å MS	$ClCH_2CH_2Cl$	1.5:1	35	50
4	4 Å MS	THF	1.5:1	35	N.R.
5	4 Å MS	Toluene	1.5:1	35	30
6	4 Å MS	EtOAc	1.5:1	35	N.R.
7	4 Å MS	Et_2O	1.5:1	35	25
8	4 Å MS	CH_3CN	1.5:1	35	N.R.
9	4 Å MS	DMF	1.5:1	35	N.R.
10	4 Å MS	$CHCl_3$	2:1	35	71
11	4 Å MS	$CHCl_3$	2:1	rt	37
12	4 Å MS	$CHCl_3$	2:1	50	75
13	4 Å MS	$CHCl_3$	2:1	60	55
14		$CHCl_3$	2:1	50	53
15	3 Å MS	$CHCl_3$	2:1	50	79
16	5 Å MS	$CHCl_3$	2:1	50	68
17[c]	3 Å MS	$CHCl_3$	2:1	50	82
18[d]	3 Å MS	$CHCl_3$	2:1	50	64
19[e]	3 Å MS	$CHCl_3$	2:1	50	78

[a]Unless otherwise noted, the reactions were performed with 4 Å MS (50 mg), **1a** (0.15 mmol or 0.2 mmol) and **2a** (0.10 mmol) in indicated solvent (0.5 mL) at indicated temperature for 24 h or 6 h. [b]The yield of isolated product for **3aa**. [c]with 3 Å MS (25 mg). [d]with 3 Å MS (100 mg). [e]With $CHCl_3$ (1.0 mL).

4. General Procedure and Spectral Data of Products 3

A dry reaction tube was charged with aziridines **1** (0.2 mmol, 2 equiv.), isocyanides **2** (0.1 mmol, 1 equiv.) and 3 Å MS (25 mg), $CHCl_3$ (0.5 mL, 0.25 M) was added. The reaction mixture continued stirring at 50 ℃ for 7 h. The residue was directly purified by flash chromatography on silica gel using petroleum ether/ethyl acetate= 2/1 as eluent to afford the desired products **3**.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-phenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3aa



3aa

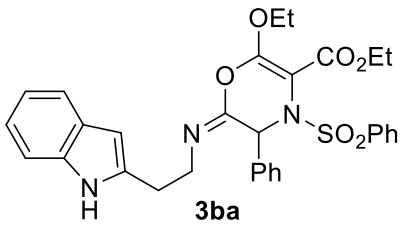
The reaction was run at 50 ℃ for 7 h, affording product **3aa** in 82% yield (48.2 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 111-113 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.58 (dd, *J* = 6.8 Hz, 1H), 7.41 – 7.36 (m, 3H), 7.31 – 7.26 (m, 1H), 7.24 – 7.15 (m, 3H), 7.14 – 7.09 (m, 3H), 6.29 (d, *J* = 1.2 Hz, 1H), 5.70 (s, 1H), 4.33 – 4.22 (m, 2H), 4.05 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.90 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.68 – 3.61 (m, 1H), 3.15 – 2.94 (m, 3H), 2.35 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.10 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 156.6, 146.0, 144.7, 138.1, 136.2, 133.3, 132.8, 129.6, 128.7, 128.7, 128.4, 128.3, 126.3, 121.4, 119.8, 119.7, 110.7, 100.0, 93.0, 67.1, 60.9, 58.0, 46.4, 28.7, 21.5, 14.4, 14.2.

HRMS (ESI-TOF) calcd for $C_{32}H_{34}N_3O_6S^+$ ([M+H$^+$]) = 588.2163, Found 588.2166.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-phenyl-4-(phenylsulfonyl)-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ba



3ba

The reaction was run at 50 ℃ for 7 h, affording product **3ba** in 63% yield (36.1 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 119-121 °C.

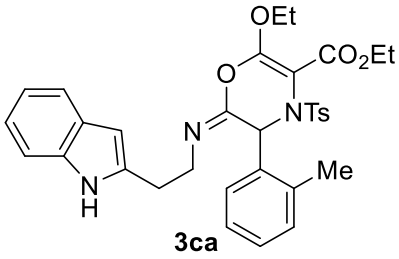
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.95 – 7.93 (m, 2H), 7.59 – 7.55 (m, 2H), 7.39 – 7.35 (m, 5H), 7.30 – 7.25 (m, 1H), 7.22 – 7.09 (m, 4H), 6.28 (d, *J* = 1.2 Hz, 1H), 5.74 (s, 1H), 4.32 – 4.23 (m, 2H), 4.03 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.88 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.66 – 3.59 (m, 1H), 3.17 – 2.99 (m, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 156.7, 145.8, 138.0, 136.1, 136.1, 133.6, 132.8, 129.0, 128.7,

128.7, 128.4, 128.3, 126.2, 121.4, 119.8, 119.7, 110.7, 100.1, 92.8, 67.1, 60.9, 58.2, 46.3, 28.7, 14.4, 14.2.

HRMS (ESI-TOF) calcd for $C_{31}H_{32}N_3O_6S^+$ ([M+H$^+$]) = 574.2006, Found 574.2011.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(o-tolyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ca



3ca

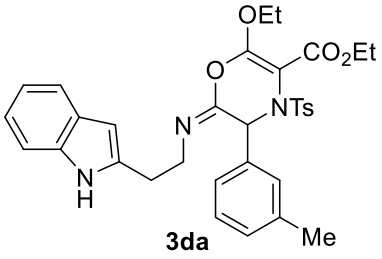
The reaction was run at 50 ℃ for 7 h, affording product **3ca** in 50% yield (29.9 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 123-125 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.69 – 7.67 (m, 2H), 7.58 – 7.55 (m, 1H), 7.31 – 7.28 (m, 1H), 7.26 – 7.19 (m, 2H), 7.17 – 7.09 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.84 (td, *J* = 7.6, 2.0 Hz, 1H), 6.46 (d, *J* = 7.6 Hz, 1H), 6.25 (d, *J* = 0.8 Hz, 1H), 5.93 (s, 1H), 4.16 (dq, *J* = 9.6, 6.8 Hz, 1H), 4.09 – 3.95 (m, 3H), 3.63 – 3.54 (m, 1H), 3.03 – 2.92 (m, 3H), 2.73 (s, 3H), 2.37 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 157.8, 147.0, 144.5, 139.2, 138.0, 136.1, 132.7, 131.7, 131.0, 129.4, 129.1, 128.4, 128.4, 126.0, 125.6, 121.4, 119.8, 119.7, 110.7, 100.0, 92.1, 67.2, 60.5, 57.5, 46.3, 28.6, 21.5, 19.9, 14.9, 13.9.

HRMS (ESI-TOF) calcd for $C_{33}H_{36}N_3O_6S^+$ ([M+H$^+$]) = 602.2319, Found 602.2325.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(m-tolyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3da



3da

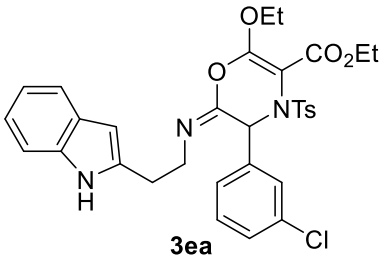
The reaction was run at 50 ℃ for 7 h, affording product **3da** in 68% yield (40.9 mg) as a white solid. R_f = 0.2 (PE:EA = 2:1), m.p. 68-70 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.80 – 7.78 (m, 2H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.36 (m, 2H), 7.19 – 7.07 (m, 7H), 6.28 (d, *J* = 1.2 Hz, 1H), 5.69 (s, 1H), 4.33 – 4.24 (m, 2H), 4.05 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.91 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.65 – 3.59 (m, 1H), 3.11 – 2.96 (m, 3H), 2.34 (s, 3H), 2.28 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 156.5, 146.0, 144.7, 138.6, 138.2, 136.2, 133.3, 132.8, 129.6, 129.5, 128.5, 128.4, 128.3, 127.1, 123.1, 121.4, 119.8, 119.7, 110.7, 99.9, 93.0, 67.1, 60.8, 58.0, 46.31, 28.6, 21.5, 21.4, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{33}H_{36}N_3O_6S^+$ ([M+H$^+$]) = 602.2319, Found 602.2326.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-3-(3-chlorophenyl)-6-ethoxy-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ea



3ea

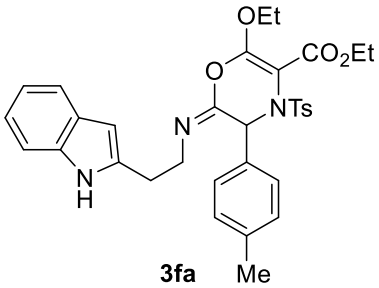
The reaction was run at 50 ℃ for 7 h, affording product **3ea** in 77% yield (47.8 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 56-58 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.78 – 7.76 (m, 2H), 7.65 (q, *J* = 1.6 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.20 – 7.05 (m, 6H), 6.29 (d, *J* = 1.2 Hz, 1H), 5.68 (s, 1H), 4.35 – 4.25 (m, 2H), 4.06 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.92 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.66 – 3.59 (m, 1H), 3.11 – 2.97 (m, 3H), 2.35 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 156.4, 145.4, 144.9, 137.9, 136.2, 135.0, 134.9, 133.0, 130.0, 129.6, 129.0, 128.4, 128.3, 126.8, 124.2, 121.4, 119.9, 119.7, 110.7, 100.1, 92.8, 67.3, 61.1, 57.7, 46.4, 28.7, 21.5, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{32}H_{33}ClN_3O_6S^+$ ([M+H$^+$]) = 622.1773, Found 622.1780.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(p-tolyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3fa



3fa

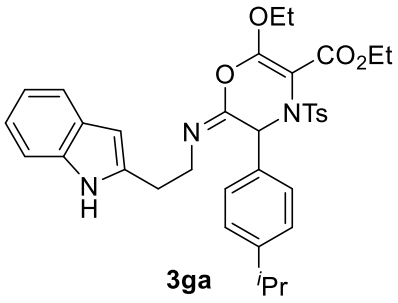
The reaction was run at 50 ℃ for 7 h, affording product **3fa** in 87% yield (52.3 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 140-142 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.81 (dd, *J* = 6.8, 2.0 Hz, 2H), 7.58 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.37 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.26 (dd, *J* = 8.4, 0.8 Hz, 2H), 7.19 – 7.08 (m, 4H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.28 (d, *J* = 1.6 Hz, 1H), 5.66 (s, 1H), 4.32 – 4.24 (m, 2H), 4.05 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.90 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.56 – 3.59 (m, 1H) , 3.16 – 2.94 (m, 3H), 2.35 (s, 3H), 2.31 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 156.6, 146.2, 144.7, 138.5, 138.2, 136.2, 133.4, 129.8, 129.6, 129.4, 128.4, 128.3, 126.2, 121.3, 119.8, 119.7, 110.8, 99.9, 92.8, 67.1, 60.8, 57.9, 46.4, 28.6, 21.5, 21.1, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{33}H_{36}N_3O_6S^+$ ([M+H$^+$]) = 602.2319, Found 602.2320.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(4-isopropylphenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ga



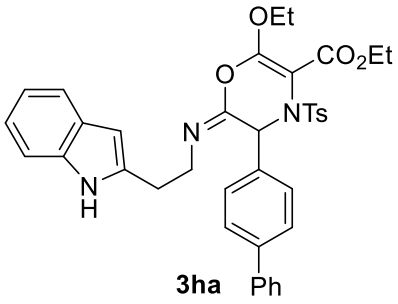
The reaction was run at 50 ℃ for 7 h, affording product **3ga** in 87% yield (54.8 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 127-129 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.83 – 7.81 (m, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.28 – 7.25 (m, 2H), 7.19 – 7.15 (m, 1H), (td, J = 8.0, 7.6, 1.4 Hz, 1H), 7.15 – 7.10 (m, 3H), 7.05 – 7.03 (m, 2H), 6.28 (d, *J* = 2.0 Hz, 1H), 5.65 (s, 1H), 4.33 – 4.24 (m, 2H), 4.05 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.91 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.71 – 3.58 (m, 1H), 3.17 – 3.11 (m, 1H), 3.09 – 2.95 (m, 2H), 2.89 – 2.80 (m, 1H), 2.36 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.22 (d, *J* = 2.4 Hz, 3H), 1.20 (d, *J* = 2.8 Hz, 3H), 1.10 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 156.6, 149.4, 146.2, 144.6, 138.2, 136.2, 133.4, 130.1, 129.6, 128.4, 128.4, 126.8, 126.2, 121.3, 119.8, 119.7, 110.8, 100.0, 93.0, 67.1, 60.8, 57.9, 46.4, 33.7, 28.7, 23.8, 23.8, 21.5, 14.4, 14.2.

HRMS (ESI-TOF) calcd for $C_{35}H_{40}N_3O_6S^+$ ([M+H$^+$]) = 630.2632, Found 630.2638.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-3-([1,1'-biphenyl]-4-yl)-6-ethoxy-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ha



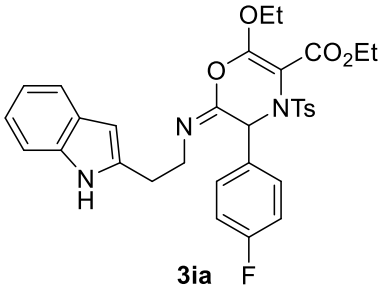
The reaction was run at 50 ℃ for 7 h, affording product **3ha** in 87% yield (57.7 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 123-125°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.85 – 7.82 (m, 2H), 7.59 (d, *J* = 6.4 Hz, 1H), 7.55 – 7.53 (m, 2H), 7.49 – 7.35 (m, 8H), 7.18 (td, *J* = 7.2, 1.2 Hz, 1H), 7.15 – 7.11 (m, 3H), 6.30 (d, *J* = 1.2 Hz, 1H), 5.72 (s, 1H), 4.36 – 4.24 (m, 2H), 4.08 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.93 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.72 – 3.65 (m, 1H), 3.18 – 2.97 (m, 3H), 2.37 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 156.6, 146.0, 144.7, 141.5, 140.2, 138.1, 136.2, 133.3, 131.8, 129.6, 128.8, 128.5, 128.4, 127.6, 127.4, 127.0, 126.7, 121.4, 119.9, 119.7, 110.8, 100.0, 92.9, 67.2, 60.9, 58.0, 46.4, 28.7, 21.6, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{38}H_{38}N_3O_6S^+$ ([M+H$^+$]) = 664.2476, Found 664.2476.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(4-fluorophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ia



3ia

The reaction was run at 50 ℃ for 7 h, affording product **3ia** in 83% yield (50.2 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 124-126 °C.

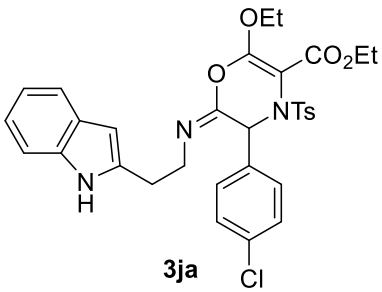
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.80 – 7.78 (m, 2H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.20 – 7.10 (m, 4H), 6.86 – 6.82 (m, 2H), 6.28 (d, *J* = 1.2 Hz, 1H), 5.64 (s, 1H), 4.32 – 4.24 (m, 2H), 4.05 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.90 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.68 – 3.60 (m, 1H), 3.13 – 2.97 (m, 3H), 2.36 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 162.8 (d, *J* = 246.0 Hz), 156.4, 145.7, 144.8, 137.9, 136.1, 133.2, 129.6, 128.5 (d, *J* = 4.0 Hz), 128.5, 128.3, 128.2, 128.1, 121.5, 119.8, 119.8, 115.7 (d, *J* = 22.0 Hz), 110.7, 100.0, 92.9, 67.2, 61.0, 57.5, 46.4, 29.7, 28.7, 21.5, 14.5, 14.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.09.

HRMS (ESI-TOF) calcd for $C_{32}H_{33}FN_3O_6S^+$ ([M+H$^+$]) = 606.2069, Found 606.2078.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(4-chlorophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ja



3ja

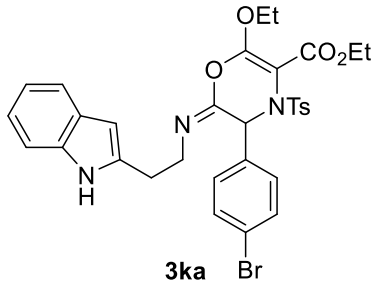
The reaction was run at 50 ℃ for 7 h, affording product **3ja** in 86% yield (53.4 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 141-143 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.80 – 7.77 (m, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.21 – 7.10 (m, 6H), 6.28 (d, *J* = 1.2 Hz, 1H), 5.63 (s, 1H), 4.32 – 4.24 (m, 2H), 4.05 (dq, *J* = 10.0, 7.0 Hz, 1H), 3.90 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.67 – 3.55 (m, 1H), 3.14 – 2.94 (m, 3H), 2.36 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 156.4, 145.6, 144.8, 137.9, 136.1, 134.7, 133.1, 131.4, 129.6, 128.9, 128.4, 128.3, 127.7, 121.5, 119.9, 119.8, 110.7, 100.0, 92.8, 67.2, 61.0, 57.6, 46.4, 28.7, 21.6, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{32}H_{33}ClN_3O_6S^+$ ([M+H$^+$]) = 622.1773, Found 622.1773.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(4-bromophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ka



3ka

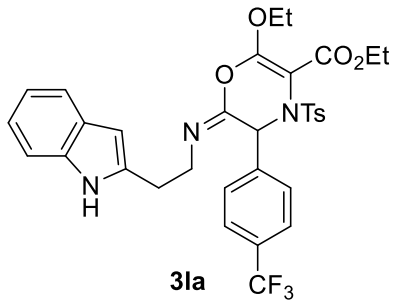
The reaction was run at 50 ℃ for 7 h, affording product **3ka** in 81% yield (53.9 mg) as a white solid. R_f = 0.2 (PE:EA = 2:1), m.p. 142-144 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.80 – 7.78 (m, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.28 – 7.07 (m, 9H), 6.27 (d, *J* = 0.8 Hz, 1H), 5.60 (s, 1H), 4.32 – 4.24 (m, 2H), 4.05 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.90 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.67 – 3.61 (m, 1H), 3.14 – 2.94 (m, 3H), 2.36 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 156.5, 145.5, 144.8, 137.9, 136.1, 133.1, 132.0, 131.9, 129.6, 128.5, 128.3, 128.0, 122.9, 121.5, 119.9, 119.8, 110.7, 100.0, 92.8, 67.2, 61.0, 57.7, 46.4, 28.7, 21.6, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{32}H_{33}BrN_3O_6S^+$ ([M+H$^+$]) = 666.1268, Found 666.1267.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(4-(trifluoromethyl)phenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3la



3la

The reaction was run at 50 ℃ for 7 h, affording product **3la** in 72% yield (47.2 mg) as a yellow solid. R_f = 0.3 (PE:EA = 2:1), m.p. 134-136 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 3H), 7.20 – 7.11 (m, 4H), 6.28 (d, *J* = 0.8 Hz, 1H), 5.69 (s, 1H), 4.35 – 4.23 (m, 2H), 4.06 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.91 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.71 – 3.64 (m, 1H), 3.18 – 2.96 (m, 3H), 2.37 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H).

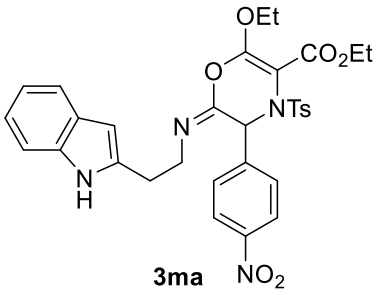
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.1, 156.4, 145.4, 144.9, 137.8, 136.9, 136.1, 133.0, 130.9 (q, *J* = 31.5 Hz), 129.7, 128.5, 128.4, 126.7, 125.7 (q, *J* = 3.0 Hz), 123.8 (q, *J* = 271.5 Hz), 121.5, 119.9, 119.9, 110.7, 100.1, 92.8, 67.3, 61.1, 57.8, 46.4, 28.7, 21.6, 14.4, 14.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.80.

HRMS (ESI-TOF) calcd for $C_{33}H_{33}F_3N_3O_6S^+$ ([M+H$^+$]) = 656.2037, Found 656.2041.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(4-nitrophenyl)-4-tosyl-3,4-dihydro-

2H-1,4-oxazine-5-carboxylate 3ma



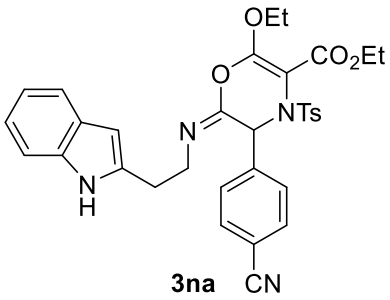
The reaction was run at 50 ℃ for 7 h, affording product **3ma** in 36% yield (22.7 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 143-145 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.93 – 7.89 (m, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.50 – 7.48 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.23 – 7.13 (m, 4H), 6.29 (d, *J* = 1.6 Hz, 1H), 5.70 (s, 1H), 4.33 – 4.25 (m, 2H), 4.06 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.91 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.73 – 3.66 (m, 1H), 3.18 – 3.01 (m, 3H), 2.39 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 156.4, 148.2, 145.1, 145.0, 140.0, 137.6, 136.0, 132.9, 129.7, 128.5, 128.4, 127.4, 123.9, 121.7, 120.0, 119.9, 110.7, 100.2, 92.8, 67.4, 61.2, 57.8, 46.5, 28.7, 21.6, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{32}H_{33}N_4O_8S^+$ ([M+H$^+$]) = 633.2014, Found 633.1984.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(4-cyanophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3na



The reaction was run at 50 ℃ for 7 h, affording product **3na** in 35% yield (21.4 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 150-152 °C.

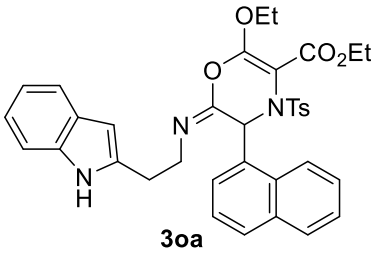
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.79 – 7.77 (m, 2H), 7.57 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.38 – 7.33 (m, 3H), 7.22 – 7.18 (m, 1H), 7.16 – 7.11 (m, 3H), 6.28 (d, *J* = 2.4 Hz, 1H), 5.67 (s, 1H), 4.28 (qt, *J* = 7.2, 3.6 Hz, 2H), 4.06 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.90 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.71 – 3.60 (m, 1H), 3.15 – 2.96 (m, 3H), 2.38 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 156.4, 145.0, 145.0, 138.2, 137.6, 136.1, 132.9, 132.5, 129.7, 128.5, 128.3, 127.1, 121.6, 120.0, 119.9, 118.2, 112.7, 110.7, 100.1, 92.8, 67.3, 61.1, 57.9, 46.4, 28.7, 21.6, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{33}H_{33}N_4O_6S^+$ ([M+H$^+$]) = 613.2115, Found 613.2118.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(naphthalen-1-yl)-4-tosyl-3,4-dihydro-

2H-1,4-oxazine-5-carboxylate 3oa



3oa

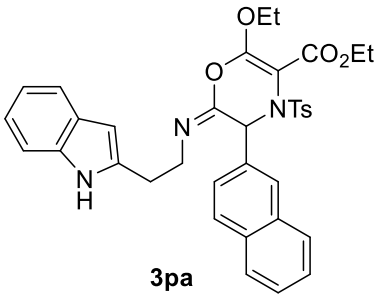
The reaction was run at 50 ℃ for 7 h, affording product **3oa** in 40% yield (25.5 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 113-115 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 9.2 Hz, 1H), 8.46 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.76 – 7.74 (m, 2H), 7.71 – 7.67 (m, 1H), 7.60 – 7.54 (m, 2H), 7.26 – 7.24 (m, 1H), 7.18 – 7.09 (m, 2H), 7.07 – 7.00 (m, 3H), 6.67 (d, *J* = 7.2 Hz, 1H), 6.49 (s, 1H), 6.26 (d, *J* = 0.8 Hz, 1H), 4.19 (dq, *J* = 10.0, 7.2 Hz, 1H), 4.02 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.80 – 3.71 (m, 2H), 3.70 – 3.60 (m, 1H), 3.04 – 2.94 (m, 3H), 2.39 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 0.69 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 157.8, 146.9, 144.6, 138.1, 136.1, 134.1, 132.7, 131.3, 130.3, 129.5, 128.7, 128.5, 128.4, 128.4, 128.2, 126.8, 126.3, 125.1, 124.4, 124.3, 121.4, 119.8, 119.7, 110.8, 100.0, 92.1, 67.3, 60.1, 57.2, 46.4, 28.6, 21.6, 14.9, 13.4.

HRMS (ESI-TOF) calcd for $C_{36}H_{36}N_3O_6S^+$ ([M+H$^+$]) = 638.2319, Found 638.2325.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-(naphthalen-2-yl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3pa



3pa

The reaction was run at 50 ℃ for 7 h, affording product **3pa** in 47% yield (29.9 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 115-117 °C.

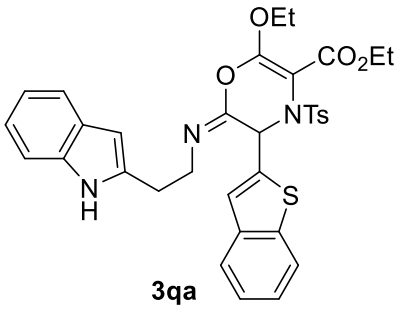
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.85 – 7.78 (m, 4H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.61 – 7.56 (m, 3H), 7.52 – 7.44 (m, 2H), 7.38 – 7.35 (m, 1H), 7.21 – 7.08 (m, 4H), 6.32 (d, *J* = 1.2 Hz, 1H), 5.88 (s, 1H), 4.28 (qt, *J* = 6.8, 3.6 Hz, 2H), 4.05 (dq, *J* = 10.0, 7.0 Hz, 1H), 3.89 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.74 – 3.67 (m, 1H), 3.18 – 2.97 (m, 3H), 2.36 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 156.6, 146.0, 144.8, 138.2, 136.2, 133.3, 133.2, 133.0, 130.3, 129.6, 128.7, 128.5, 128.4, 128.2, 127.6, 126.6, 126.4, 125.5, 123.9, 121.4, 119.9, 119.7, 110.8, 100.0, 92.9, 67.1, 60.9, 58.2, 46.4, 28.7, 21.6, 14.5, 14.3.

HRMS (ESI-TOF) calcd for $C_{36}H_{36}N_3O_6S^+$ ([M+H$^+$]) = 638.2319, Found 638.2322.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-3-(benzo[b]thiophen-2-yl)-6-ethoxy-4-tosyl-3,4-

dihydro-2H-1,4-oxazine-5-carboxylate 3qa



3qa

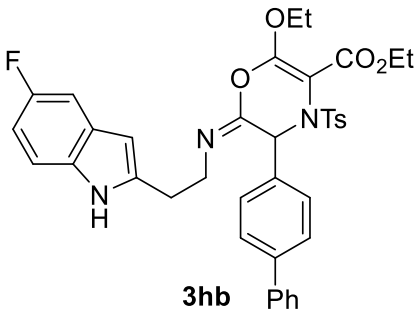
The reaction was run at 50 ℃ for 7 h, affording product **3qa** in 73% yield (47.1 mg) as a white solid. R_f = 0.2 (PE:EA = 2:1), m.p. 81-83 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.90 – 7.88 (m, 2H), 7.75 – 7.70 (m, 1H), 7.59 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.38 – 7.36 (m, 1H), 7.35 – 7.30 (m, 2H), 7.27 (d, *J* = 1.6 Hz, 1H), 7.21 – 7.11 (m, 4H), 6.31 (d, *J* = 1.2 Hz, 1H), 5.92 (d, *J* = 1.6 Hz, 1H), 4.42 – 4.28 (m, 2H), 4.10 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.95 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.71 – 3.64 (m, 1H), 3.30 – 3.23 (m, 1H), 3.13 – 3.01 (m, 2H), 2.39 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 156.8, 146.0, 145.0, 139.9, 139.2, 138.1, 137.4, 136.3, 133.0, 129.7, 128.5, 128.5, 124.8, 124.5, 123.9, 123.1, 122.3, 121.4, 119.8, 119.7, 110.8, 100.0, 92.4, 67.2, 61.0, 55.9, 46.6, 28.7, 21.6, 14.6, 14.3.

HRMS (ESI-TOF) calcd for $C_{34}H_{34}N_3O_6S_2^+$ ([M+H$^+$]) = 644.1884, Found 644.1885.

Ethyl (Z)-3-([1,1'-biphenyl]-4-yl)-6-ethoxy-2-((2-(5-fluoro-1H-indol-2-yl)ethyl)imino)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3hb



3hb

The reaction was run at 50 ℃ for 7 h, affording product **3hb** in 87% yield (59.2 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 141-143 °C.

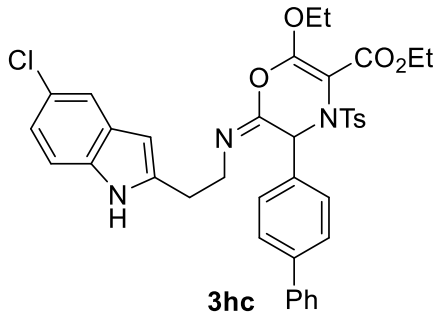
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.07 (d, *J* = 2.0 Hz, 1H), 7.70 – 7.62 (m, 2H), 7.59 – 7.53 (m, 2H), 7.47 – 7.34 (m, 5H), 7.32 – 7.22 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.88 (td, *J* = 9.2, 2.4 Hz, 1H), 6.22 (d, *J* = 2.0 Hz, 1H), 5.54 (s, 1H), 4.16 – 4.07 (m, 3H), 3.96 (dq, *J* = 10.4, 6.8 Hz, 1H), 3.78 – 3.69 (m, 1H), 3.00 – 2.93 (m, 3H), 2.40 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H), 0.96 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.9, 157.5 (d, *J* = 229.0 Hz), 156.7, 145.4, 144.1, 140.7, 140.6, 139.5, 133.2, 132.8, 132.3, 130.3, 129.6, 129.4, 129.4, 129.2, 129.1, 128.3, 128.2, 127.1, 127.0, 112.0 (d, *J* = 10.0 Hz), 108.6 (d, *J* = 26.0 Hz), 104.4 (d, *J* = 23.0 Hz), 100.1 (d, *J* = 5.0 Hz), 92.2, 67.3, 60.6, 57.7, 45.7, 28.9, 21.6, 14.6, 14.5.

^{19}F NMR (376 MHz, DMSO-d_6) δ -125.70.

HRMS (ESI-TOF) calcd for $C_{38}H_{37}FN_3O_6S^+$ ([M+H$^+$]) = 682.2382, Found 682.2382.

Ethyl (Z)-3-([1,1'-biphenyl]-4-yl)-6-ethoxy-2-((2-(5-chloro-1H-indol-2-yl)ethyl)imino)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3hc



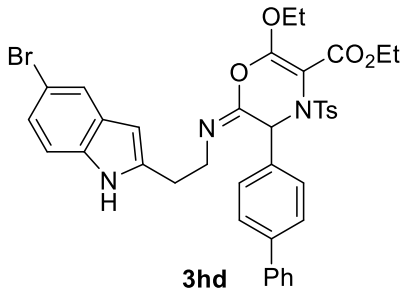
The reaction was run at 50 ℃ for 7 h, affording product **3hc** in 73% yield (50.9 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 131-133 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.19 (d, *J* = 2.0 Hz, 1H), 7.68 – 7.63 (m, 2H), 7.56 – 7.53 (m, 3H), 7.49 – 7.42 (m, 4H), 7.39 – 7.31 (m, 2H), 7.23 – 7.18 (m, 2H), 7.05 (dd, *J* = 8.4, 2.0 Hz, 3H), 6.23 (d, *J* = 2.0 Hz, 1H), 5.52 (s, 1H), 4.17 – 4.06 (m, 3H), 3.96 (dq, *J* = 10.4, 6.8 Hz, 1H), 3.82 – 3.72 (m, 1H), 2.99 – 2.93 (m, 3H), 2.41 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.9, 156.7, 145.4, 144.1, 140.5, 140.5, 139.4, 135.1, 132.8, 132.2, 130.3, 130.1, 129.4, 128.3, 128.2, 127.4, 127.2, 127.2, 127.0, 127.0, 123.9, 120.7, 119.0, 112.7, 99.8, 92.2, 67.3, 60.6, 57.7, 45.6, 28.8, 21.6, 21.2, 14.5.

HRMS (ESI-TOF) calcd for $C_{38}H_{37}ClN_3O_6S^+$ ([M+H$^+$]) = 698.2086, Found 698.2081.

Ethyl (Z)-3-([1,1'-biphenyl]-4-yl)-6-ethoxy-2-((2-(5-bromo-1H-indol-2-yl)ethyl)imino)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3hd



The reaction was run at 50 ℃ for 7 h, affording product **3hd** in 73% yield (54.2 mg) as a white solid. R_f = 0.2 (PE:EA = 2:1), m.p. 160-162 °C.

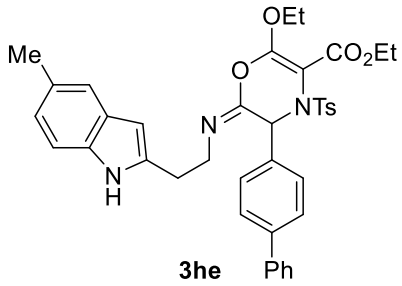
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.21 (d, *J* = 2.4 Hz, 1H), 7.70 – 7.66 (m, 3H), 7.57 – 7.54 (m, 2H), 7.50 – 7.42 (m, 4H), 7.39 – 7.33 (m, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.18 – 7.15 (m, 3H), 7.04 – 7.01 (m, 2H), 6.23 (d, *J* = 2.0 Hz, 1H), 5.51 (s, 1H), 4.18 – 4.06 (m, 3H), 3.96 (dq, *J* = 10.4, 6.8 Hz, 1H), 3.84 – 3.73 (m, 1H), 2.99 – 2.94 (m, 3H), 2.41 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.9, 156.7, 145.4, 144.1, 140.4, 140.4, 139.3, 135.3, 132.8, 132.2, 130.8, 130.3, 129.5, 128.3, 128.2, 127.0, 127.0, 126.9, 123.2, 122.0, 113.2, 111.9, 99.7, 92.2, 67.3, 60.6, 57.7, 45.6, 28.8, 21.6, 21.2, 14.5.

HRMS (ESI-TOF) calcd for $C_{38}H_{37}BrN_3O_6S^+$ ([M+H$^+$]) = 742.1581, Found 742.1574.

Ethyl (Z)-3-([1,1'-biphenyl]-4-yl)-6-ethoxy-2-((2-(5-methyl-1H-indol-2-yl)ethyl)imino)-4-tosyl-

3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3he



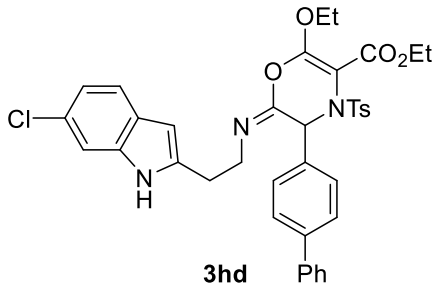
The reaction was run at 50 ℃ for 7 h, affording product **3he** in 90% yield (61.0 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 130-132 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.82 (d, *J* = 2.1 Hz, 1H), 7.70 – 7.66 (m, 2H), 7.54 – 7.48 (m, 2H), 7.49 – 7.43 (m, 4H), 7.28 – 7.34 (m, 1H), 7.26 (s, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.12 – 7.09 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.88 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.12 (d, *J* = 2.0 Hz, 1H), 5.50 (s, 1H), 4.18 – 4.03 (m, 3H), 3.96 (dq, *J* = 10.4, 6.8 Hz, 1H), 3.83 – 3.74 (m, 1H), 2.99 – 2.93 (m, 3H), 2.42 (s, 3H), 2.37 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.9, 156.8, 145.4, 143.9, 140.4, 139.5, 138.4, 135.0, 132.8, 132.2, 130.3, 129.4, 129.2, 128.3, 128.2, 127.5, 127.4, 127.2, 127.1, 127.0, 126.9, 122.3, 119.5, 111.0, 99.5, 92.2, 67.3, 60.5, 57.8, 45.8, 28.9, 21.7, 21.6, 14.6, 14.5.

HRMS (ESI-TOF) calcd for $C_{39}H_{40}N_3O_6S^+$ ([M+H$^+$]) = 678.2632, Found 678.2633.

Ethyl (Z)-3-([1,1'-biphenyl]-4-yl)-6-ethoxy-2-((2-(6-chloro-1H-indol-2-yl)ethyl)imino)-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3hf



The reaction was run at 50 ℃ for 7 h, affording product **3hf** in 92% yield (64.2 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 142-144 °C.

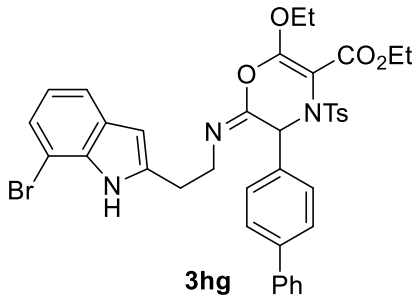
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.87 – 7.80 (m, 2H), 7.56 – 7.53 (m, 2H), 7.48 – 7.43 (m, 3H), 7.41 – 7.32 (m, 6H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.09 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.27 (d, *J* = 1.2 Hz, 1H), 5.70 (s, 1H), 4.37 – 4.25 (m, 2H), 4.07 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.93 (dq, *J* = 10.0, 7.2 Hz, 1H), 3.73 – 3.65 (m, 1H), 3.24 – 3.18 (m, 1H), 3.10 – 2.97 (m, 2H), 2.38 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 156.6, 146.2, 144.8, 141.5, 140.1, 139.0, 136.5, 133.3, 131.7, 129.6, 128.9, 128.4, 127.6, 127.4, 127.1, 127.1, 127.0, 126.6, 120.6, 120.4, 110.8, 100.0, 92.9, 67.2, 60.9, 57.9, 46.3, 28.6, 21.6, 14.5, 14.2.

HRMS (ESI-TOF) calcd for $C_{38}H_{37}ClN_3O_6S^+$ ([M+H$^+$]) = 698.2086, Found 698.2083.

Ethyl (Z)-3-([1,1'-biphenyl]-4-yl)-6-ethoxy-2-((2-(7-bromo-1H-indol-2-yl)ethyl)imino)-4-tosyl-

3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3hg



3hg

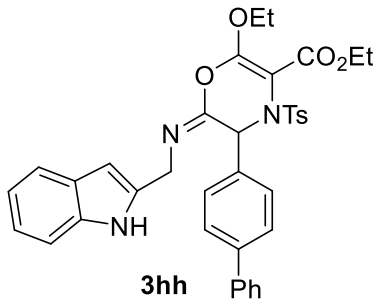
The reaction was run at 50 ℃ for 7 h, affording product **3hg** in 86% yield (63.7 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 158-160 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.15 (d, *J* = 2.0 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.55 – 7.51 (m, 2H), 7.50 – 7.42 (m, 5H), 7.40 – 7.36 (m, 1H), 7.27 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.24 – 7.20 (m, 2H), 7.10 – 7.07 (m, 2H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.37 (d, *J* = 2.0 Hz, 1H), 5.50 (s, 1H), 4.16 – 4.05 (m, 3H), 3.93 (dq, *J* = 10.4, 6.8 Hz, 1H), 3.89 – 3.80 (m, 1H), 3.10 – 2.96 (m, 3H), 2.43 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.9, 156.8, 145.4, 144.0, 140.6, 140.1, 139.5, 134.9, 132.8, 132.2, 130.6, 130.4, 129.4, 128.3, 128.2, 127.0, 127.0, 123.3, 120.7, 119.3, 104.1, 101.4, 92.1, 67.3, 60.5, 57.8, 45.8, 28.6, 21.6, 14.6, 14.5.

HRMS (ESI-TOF) calcd for $C_{38}H_{37}BrN_3O_6S^+$ ([M+H$^+$]) = 742.1581, Found 742.1571.

Ethyl (Z)-2-(((1H-indol-2-yl)methyl)imino)-3-([1,1'-biphenyl]-4-yl)-6-ethoxy-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3hh



3hh

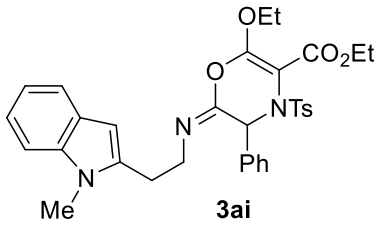
The reaction was run at 50 ℃ for 7 h, affording product **3hh** in 85% yield (55.2 mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p. 93-95°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.89 – 7.81 (m, 2H), 7.68 – 7.53 (m, 7H), 7.52 – 7.42 (m, 3H), 7.42 – 7.35 (m, 1H), 7.26 – 7.20 (m, 1H), 7.17 (t, *J* = 7.7 Hz, 3H), 6.34 (s, 1H), 5.85 (s, 1H), 4.65 (d, *J* = 17.2 Hz, 1H), 4.40 – 4.28 (m, 3H), 4.25 – 4.16 (m, 1H), 4.06 (dq, *J* = 10.1, 7.0 Hz, 1H), 2.31 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 156.6, 146.0, 144.7, 138.1, 136.2, 133.3, 132.8, 129.6, 128.7, 128.7, 128.4, 128.3, 126.3, 121.4, 119.8, 119.7, 110.7, 100.0, 93.0, 67.1, 60.9, 58.1, 46.4, 28.7, 21.5, 14.4, 14.2.

HRMS (ESI-TOF) calcd for $C_{37}H_{36}N_3O_6S^+$ ([M+H$^+$]) = 650.2319, Found 650.2325.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-6-ethoxy-3-phenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 3ai



3ai

The reaction was run at 50 ℃ for 7 h, affording product **3ai** in 15% yield (12.6mg) as a white solid. R_f = 0.3 (PE:EA = 2:1), m.p.129-130 °C.

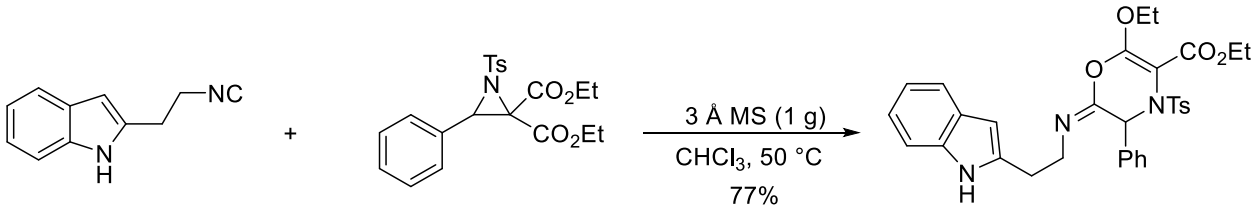
^{1}H NMR (600 MHz, DMSO-d_6) δ 7.70 – 7.65 (m, 2H), 7.46 (dd, J = 7.9, 2.9 Hz, 3H), 7.40 (d, J = 8.3 Hz, 1H), 7.28 – 7.23 (m, 3H), 7.15 (t, J = 7.5 Hz, 2H), 7.10 (t, J = 7.7 Hz, 1H), 7.00 (t, J = 7.4 Hz, 1H), 6.23 (s, 1H), 5.51 (s, 1H), 4.15 – 4.03 (m, 3H), 3.96 – 3.88 (m, 1H), 3.69 (s, 3H), 3.64 – 3.60 (m, 3H), 3.03 – 2.90 (m, 3H), 2.39 (s, 3H), 1.22 – 1.18 (m, 3H), 0.98 – 0.92 (m, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 162.9, 156.7, 145.4, 144.2, 139.4, 137.5, 133.3, 132.9, 130.4, 129.1, 129.1, 128.3, 127.8, 126.5, 120.8, 119.8, 119.4, 109.9, 99.6, 92.3, 67.3, 60.6, 57.9, 45.6, 30.0, 27.2, 21.6, 14.6, 14.5.

HRMS (ESI-TOF) calcd for $C_{33}H_{36}N_3O_6S^+$ ([M+H$^+$]) = 602.2319, Found 602.2316.

5. Experimental procedure for the scale-up reaction and transformations of the product

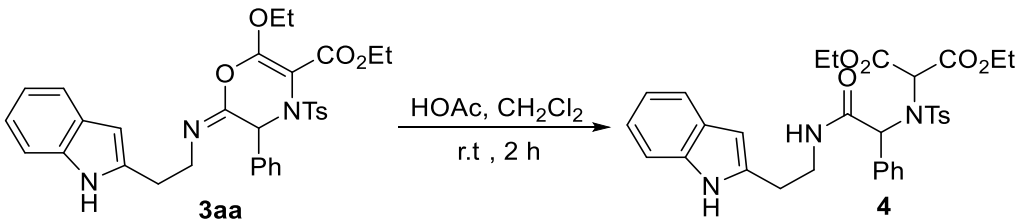
a) Scale-up version of the reaction



1a (4 mmol) **2a** (8 mmol) **3aa**

Procedure: A dry reaction tube was charged with **1a** (4 mmol, 0.68 g, 1 equiv.), **2a** (8 mmol, 3.33 g, 2 equiv.) and 3 Å MS (1.00 g). $CHCl_3$ (20 mL, 0.25 M) was added. The reaction mixture was stirred at 50 ℃ for 7 h. The residue was directly purified by flash chromatography on silica gel using petroleum ether/ethyl acetate= 2/1 as eluent to afford the desired product **3aa** in 77% yield (1.82 g).

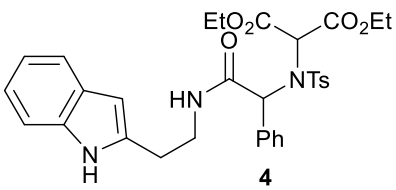
b) Transformation of the product **3aa**



3aa **4**

Procedure： A dry round-bottom flask was charged with **3aa** (0.1 mmol, 58.7 mg), AcOH (1 mL) and CH_2Cl_2 (1 mL). The reaction mixture was stirred at room temperature for 2 h. The precipitate was filtered out and the solvent was removed under reduced pressure. Saturated aqueous Na_2CO_3 was added to the mixture to adjust the pH of solution to 8.0-9.0. Then the solution was diluted with ethyl acetate, washed with water, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was directly purified by flash chromatography on silica gel using petroleum ether/ethyl acetate = 2/1 as eluent to afford the desired product **4** in 58% yield.

Diethyl 2-((N-(2-((2-(1H-indol-2-yl)ethyl)amino)-2-oxo-1-phenylethyl)-4-methylphenyl) sulfonamido)malonate 4



4

The reaction was run at room temperature for 2 h, affording product **4** in 58% yield (34.1 mg) as a white solid. R_f = 0.1 (PE:EA = 2:1), m.p. 62-64 °C.

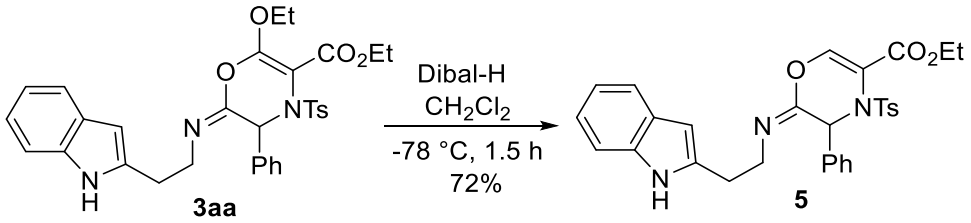
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.28 – 8.25 (m, 1H), 8.05 – 8.02 (m, 2H), 7.54 (d, *J* = 6.8 Hz, 1H), 7.33 (dd, *J* = 8.0, 3.6 Hz, 3H), 7.20 – 7.05 (m, 3H),

7.00 (t, *J* = 8.0 Hz, 2H), 6.71 (d, *J* = 7.2 Hz, 2H), 6.24 (d, *J* = 2.0 Hz, 1H), 5.37 (s, 1H), 4.50 (s, 1H), 4.33 (dq, *J* = 10.8, 7.2 Hz, 1H), 4.22 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.95 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.86 – 3.74 (m, 2H), 3.39 (dt, *J* = 13.6, 5.6 Hz, 1H), 3.04 – 2.96 (m, 2H), 2.45 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.07 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 168.1, 165.4, 144.7, 136.7, 136.6, 135.8, 133.5, 129.7, 129.4, 129.2, 128.6, 128.6, 128.5, 121.2, 119.7, 119.5, 111.1, 100.5, 64.2, 63.5, 62.5, 61.8, 39.4, 28.4, 21.6, 13.8, 13.8.

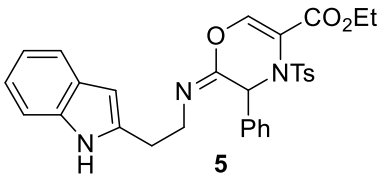
HRMS (ESI-TOF) calcd for $C_{32}H_{36}N_3O_7S^+$ ([M+H$^+$]) = 606.2268, Found 606.2282.

b) Transformation of the product **3aa**



Procedure：Under an inert nitrogen atmosphere, to a solution of **3aa** (58.7 mg, 0.1 mmol) in anhydrous DCM (0.5 mL) was added dropwise Dibal-H (1M in hexane, 0.4 mL, 4 eq.) at over 2 min at -78 ºC. After 1.5 h, the reaction mixture was quenched with methanol. NaOH (aq.) was added to dilute the reaction mixture. The resulting slurry allowed to warm to room temperature and continued to stir for 30 minutes. The layers were separated and the aqueous layer with washed with DCM. The combined organic phase was dried over $MgSO_4$. The residue was directly purified by flash chromatography on silica gel using petroleum ether/ethyl acetate = 3/1 as eluent to afford the desired product **5** in 72% yield.

Ethyl (Z)-2-((2-(1H-indol-2-yl)ethyl)imino)-3-phenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine-5-carboxylate 5

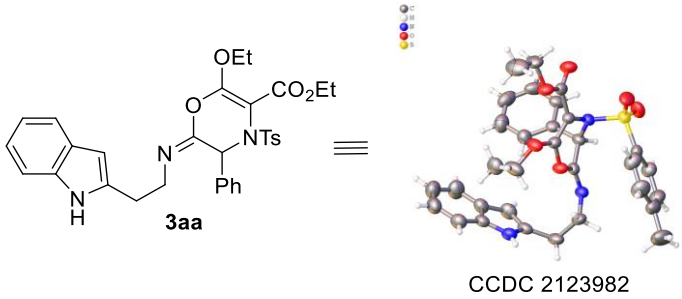


The reaction was run at -78 ℃ for 1.5 h, affording product **5** in 72% yield (39.3 mg) as a white solid. R_f = 0.4 (PE:EA = 3:1), m.p. 68-70 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.91 – 7.81 (m, 2H), 7.58 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.44 – 7.36 (m, 1H), 7.31 (dt, *J* = 8.5, 1.2 Hz, 2H), 7.28 – 7.25 (m, 1H), 7.24 – 7.19 (m, 3H), 7.19 – 7.13 (m, 3H), 7.13 – 7.09 (m, 1H), 6.29 (dd, *J* = 2.1, 0.9 Hz, 1H), 5.67 (d, *J* =

1.0 Hz, 1H), 4.36 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.30 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.72 – 3.68 (m, 1H), 3.25 – 3.21 (m, 1H), 3.06 – 3.00 (m, 1H), 2.98 – 2.94 (m, 1H), 2.34 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.0, 146.0, 145.0, 143.5, 138.3, 136.2, 133.7, 132.7, 130.0, 128.8, 128.7, 128.4, 128.3, 126.0, 121.2, 119.8, 119.6, 113.7, 110.8, 100.0, 61.7, 58.1, 46.4, 28.7, 21.5, 14.1. HRMS (ESI-TOF) calcd for $C_{30}H_{30}N_3O_6S^+$ ([M+H^+]) = 544.1901, Found:544.1899

6. X-ray crystallographic data of 3aa and 3aa'.



The single crystal for compound **3aa** was obtained by vaporization of a mixture solvent of cyclohexane and methanol (v/v = 1:3). The data were collected on a Xcalibur Eos diffractometer equipped with MoKα X-ray sources (λ = 0.71073 Å).

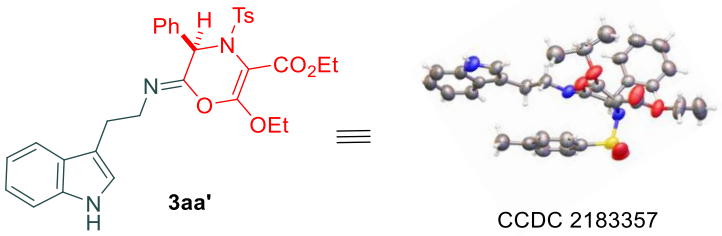
X-ray derived ORTEP of **3aa** with thermal ellipsoids shown at the 30% probability level.

Structure deposited at the Cambridge Crystallographic Data Centre. CCDC 2123982 contains the supplementary crystallographic data which can be obtained free of charge from the Cambridge Crystallographic Data Center via https://www.ccdc.cam.ac.uk/structures/.

Crystal data and structure refinement for CCDC 2123982

Empirical formula	$C_{32}H_{33}N_3O_6S$
Formula weight	587.67
Temperature/K	293.15
Crystal system	triclinic
Space group	P-1
a/Å	9.8721(6)
b/Å	10.9778(7)
c/Å	15.0003(10)
α/°	111.083(6)
β/°	96.959(5)
γ/°	94.009(5)
Volume/Å^3	1494.30(18)
Z	2
ρcalcg/cm^3	1.306
μ/mm^{-1}	0.157
F(000)	620.0
Crystal size/mm^3	0.35 × 0.3 × 0.25
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.894 to 52.744
Index ranges	-12 ≤ h ≤ 12, -10 ≤ k ≤ 13, -18 ≤ l ≤ 13
Reflections collected	12221

Independent reflections	6101 [Rint = 0.0197, Rsigma = 0.0388]
Data/restraints/parameters	6101/0/382
Goodness-of-fit on F2	1.034
Final R indexes [I>=2σ (I)]	R^1 = 0.0462, wR^2 = 0.1049
Final R indexes [all data]	R^1 = 0.0697, wR^2 = 0.1177
Largest diff. peak/hole / e Å^{-3}	0.26/-0.30



The single crystal for compound **3aa'** was obtained by vaporization of a mixture solvent of cyclohexane and methanol (v/v = 1:3). The data were collected on a Xcalibur Eos diffractometer equipped with MoKα X-ray sources (λ = 0.71073 Å).

X-ray derived ORTEP of **3aa** with thermal ellipsoids shown at the 30% probability level.

Structure deposited at the Cambridge Crystallographic Data Centre. CCDC 2123982 contains the supplementary crystallographic data which can be obtained free of charge from the Cambridge Crystallographic Data Center via https://www.ccdc.cam.ac.uk/structures/.

Crystal data and structure refinement for CCDC 2183357

Empirical formula	$C_{32}H_{33}N_3O_6S$
Formula weight	587.67
Temperature/K	293.15
Crystal system	monoclinic
Space group	P21/n
a/Å	8.2530(7)
b/Å	28.894(2)
c/Å	13.2728(14)
α/°	90
β/°	107.124(9)
γ/°	90
Volume/Å3	3024.7(5)
Z	4
ρcalcg/cm3	1.290
μ/mm-1	0.155
F(000)	1240.0

Crystal size/mm3	0.35 × 0.3 × 0.25
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.932 to 52.744
Index ranges	-10 ≤ h ≤ 10, -36 ≤ k ≤ 34, -16 ≤ l ≤ 15
Reflections collected	15399
Independent reflections	6177 [Rint = 0.0637, Rsigma = 0.0815]
Data/restraints/parameters	6177/0/387
Goodness-of-fit on F2	1.061
Final R indexes [I>=2σ (I)]	R_1 = 0.0789, wR_2 = 0.1816
Final R indexes [all data]	R_1 = 0.1383, wR_2 = 0.2242
Largest diff. peak/hole/e Å^{-3}	0.31/-0.39

7. Quantum chemical calculations

The electron correlation effects are considered by employing density functional theory (DFT)[3] at the M06-2X-D3 level[4], which include the London-dispersion correction[5]. The ultrafine grid (99,590), having 99 radial shells and 590 angular points per shell, is used to evaluate the numerical integration accuracy. Geometry optimizations are performed with the double-zeta basis set 6-31G(d,p) in chloroform medium (298.15 K) while using SMD solvation model[6]. Based on the optimized structures, the electronic energy ($E_{electron}$) and solvation free energy (ΔG_{solv}) are calculated at the same theoretical level. The harmonic vibrational frequencies are analyzed after the geometry optimizations to characterize the nature of the stationary point as a minimum with all positive frequencies or as a transition state with only one imaginary frequency, and to provide the zero-point energy (E_{ZPE}), total entropy (S_{tot}) and thermal correction to enthalpy (H_{corr}) at the same theoretical level. Then, the intrinsic reaction coordinate (IRC)[5] calculations are carried out to verify the transition state (TS) associated with the correct reactant complexes (RC), intermediate (IM) and product complexes (PC) at the same level of theory. The Gibbs free energy of free substrates (G_i) are defined as reference-point. All calculations were carried out with Gaussian 16 program.[7]

$$G = E_{electron} + \Delta G_{solv} + E_{ZPE} + H_{corr} - TS_{tot} \quad (1)$$

$$\Delta G = G - \sum_i G_i \quad (2)$$

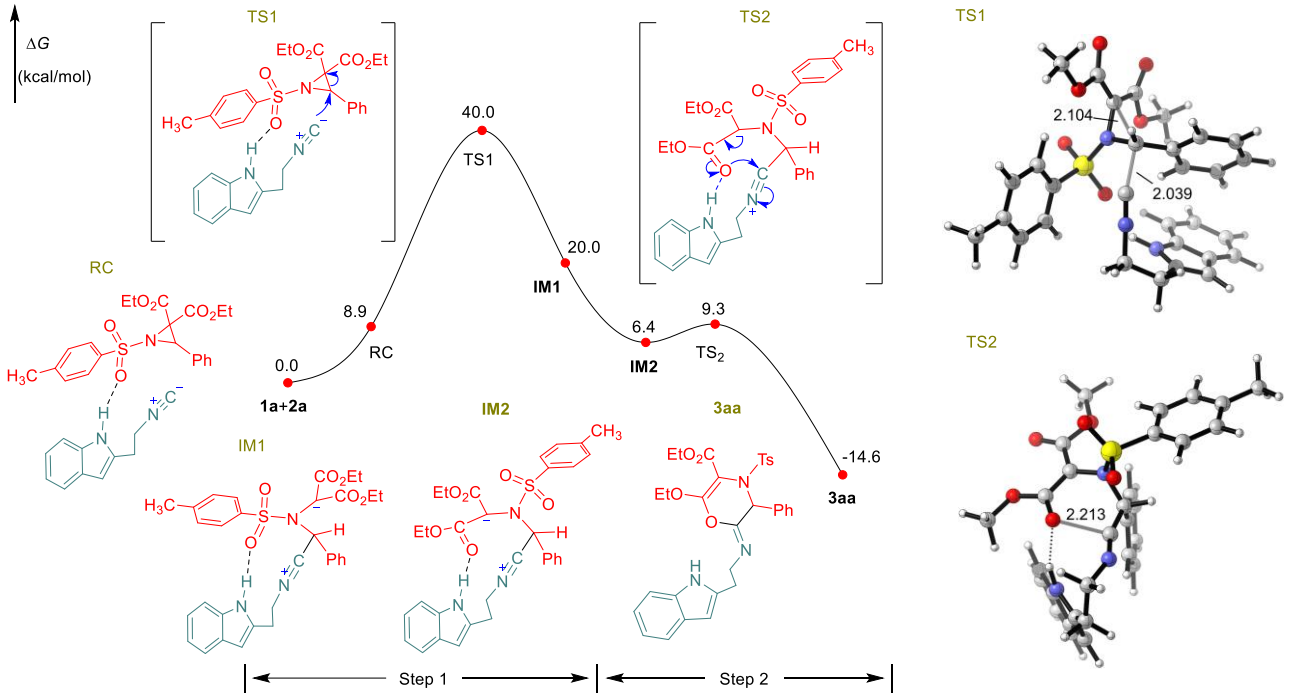


Figure 1. Relative energy profiles (in kcal/mol) of reaction pathway and optimized structures of important transition state (bond lengths, Å) at the M06-2X-D3/6-31G(d,p)/SMD($CHCl_3$) level.

Cartesian coordinate for theoretical calculation

1a

C	-1.33826900	0.69051000	0.00010500
C	-1.51048000	-0.71603400	0.00004600
C	-2.77371600	-1.31601500	-0.00016700
C	-3.87668900	-0.47739200	-0.00031400
C	-3.73039000	0.92425900	-0.00025400
C	-2.47695200	1.51310100	-0.00005000
C	0.07761700	0.93484900	0.00033900
H	-2.88323300	-2.39602000	-0.00021300
H	-4.87292500	-0.90844600	-0.00047700
H	-4.61793200	1.54919100	-0.00036700
H	-2.37254400	2.59422100	0.00000100
N	-0.25669900	-1.27990900	0.00021700
C	0.69876000	-0.28707800	0.00035300
H	0.56559800	1.89942400	0.00043400
C	2.15094900	-0.64657800	0.00056900
H	2.38917900	-1.25192800	0.88258100
H	2.38908200	-1.25326200	-0.88055200
H	-0.05908200	-2.27035400	0.00017000
C	3.02892500	0.60233100	-0.00041800
H	2.83600000	1.21267300	0.88582100
H	2.83585100	1.21137300	-0.88751800
C	5.53611600	-0.07484700	-0.00014200
N	4.41024100	0.24140900	-0.00025700

2a

C	1.30682000	0.05012900	-0.94100500
C	1.52409900	-0.72080200	0.34640100
H	1.44399300	-0.55183500	-1.83772100
C	2.10410800	0.01231800	1.53412100
O	3.29428600	0.09575600	1.70429700
O	1.17848900	0.55819800	2.31355500
C	1.93891300	-2.17570600	0.29355900
O	2.38294600	-2.76564400	1.24453600
O	1.72289200	-2.70087700	-0.90712500
C	1.69406800	1.34353700	3.39755000
H	2.29518900	2.16802000	3.00779800
H	0.82227500	1.72190700	3.92778400
H	2.30522900	0.72361100	4.05593200
C	1.82659600	-4.12902600	-0.98181100
H	1.13784700	-4.58351000	-0.26698900
H	1.54787600	-4.38925900	-2.00095700
H	2.84936700	-4.44400100	-0.76800300
C	1.65671100	1.49660800	-1.04329600
C	1.01670900	2.45814300	-0.25766500
C	2.66895300	1.88058300	-1.92487900
C	1.39704200	3.79417600	-0.35161700
H	0.22043200	2.15334600	0.41480700
C	3.04598300	3.21698100	-2.01507800
H	3.16060000	1.13019200	-2.53795500
C	2.41185700	4.17544100	-1.22707000
H	0.89463400	4.53994500	0.25640500
H	3.83356200	3.50969900	-2.70195700
H	2.70501500	5.21805300	-1.29869200
N	0.20058700	-0.31692200	-0.08408700
S	-0.97506000	-1.45636800	-0.56101300
O	-0.88371200	-1.70844200	-1.99228800
O	-0.87713900	-2.55498800	0.39399800
C	-2.44334200	-0.52495000	-0.24067900
C	-3.31602300	-0.25703000	-1.28601600
C	-2.70077000	-0.10459400	1.06481600
C	-4.48263800	0.45381500	-1.01213600

H	-3.08439400	-0.59574500	-2.29003700
C	-3.86537800	0.60373100	1.31343700
H	-1.99566500	-0.32130800	1.86197600
C	-4.77204300	0.89053500	0.28133900
H	-5.17623900	0.67244700	-1.81843800
H	-4.08149900	0.94313000	2.32254400
C	-6.03472400	1.65157600	0.58061900
H	-6.68620700	1.07079900	1.24129900
H	-5.81010200	2.59310800	1.09033500
H	-6.58880100	1.87692300	-0.33265800

RC

C	1.28277700	-1.22663200	1.29110400
C	1.61465800	-2.23922500	0.17249400
H	2.08329700	-1.06828900	2.01184800
C	0.46206600	-3.09618400	-0.30817100
O	0.14757800	-4.12302100	0.23483000
O	-0.14599800	-2.56653500	-1.36482700
C	2.94456100	-2.95970800	0.18666300
O	3.08398200	-4.11862800	-0.11184100
O	3.93088500	-2.15189000	0.57409400
C	-1.31839700	-3.26370100	-1.81102900
H	-2.10211200	-3.19629800	-1.05169900
H	-1.62864200	-2.76370600	-2.72597500
H	-1.08021500	-4.31076200	-2.00462500
C	5.22909600	-2.76052100	0.62101500
H	5.51492600	-3.11186600	-0.37212000
H	5.90730900	-1.98015800	0.96083700
H	5.22772200	-3.59941600	1.31947200
C	-0.08499800	-1.16042900	1.88732800
C	-1.26304500	-1.07906800	1.14094100
C	-0.15943200	-1.19895100	3.28296900
C	-2.49686800	-1.05703000	1.78615500
H	-1.22569000	-1.00316100	0.05884100
C	-1.39303700	-1.17371600	3.92509100
H	0.75608300	-1.24426900	3.86636600
C	-2.56693700	-1.10733700	3.17665600
H	-3.40461900	-0.98238500	1.19306100
H	-1.43625100	-1.20371100	5.00916400
H	-3.53177000	-1.08614200	3.67364200
N	1.65893600	-0.83330900	-0.03090600
S	1.26922400	0.16165300	-1.29383900
O	1.72333100	-0.55008700	-2.47857300
O	-0.11108500	0.64398100	-1.25393600
C	2.32447600	1.54514400	-0.96625800
C	1.83211600	2.82402800	-1.19593900
C	3.63703500	1.32512700	-0.55380900
C	2.68053000	3.90981100	-1.00199500
H	0.80111800	2.96499600	-1.50349000
C	4.46464800	2.42230300	-0.36309800
H	3.98663200	0.31396100	-0.36493900
C	4.00072500	3.72617300	-0.58407100
H	2.30852100	4.91583100	-1.17178000
H	5.48793100	2.27022400	-0.03105800
C	4.91811800	4.89898700	-0.36740300
H	5.78239000	4.84261000	-1.03643800
H	4.40464300	5.84484400	-0.55129000
H	5.30007900	4.90847400	0.65791800
C	-4.78302000	0.82122600	-0.61869300
C	-3.43471000	0.70047000	-1.04403800
C	-3.06755700	-0.04855600	-2.16956200
C	-4.08322400	-0.67676500	-2.87278400
C	-5.43124000	-0.56253300	-2.47527200
C	-5.78881900	0.17822700	-1.36167900

C	-4.76685500	1.62712800	0.56814000
H	-2.02698300	-0.12718600	-2.46779300
H	-3.83633900	-1.26590800	-3.75098000
H	-6.19877900	-1.06731700	-3.05373400
H	-6.82942000	0.25802000	-1.06050800
N	-2.65763500	1.41277300	-0.16086900
C	-3.45769500	1.94990100	0.82200100
H	-5.61567700	1.93064400	1.16507400
C	-2.89462000	2.70049600	1.99045600
H	-3.65308000	3.40227700	2.34666200
H	-2.68205300	2.00782300	2.81414300
H	-1.64402500	1.40211000	-0.17371500
C	-1.61740700	3.49080600	1.69419300
H	-1.42951300	4.21253900	2.49200200
H	-1.69419300	4.03370200	0.74800700
C	0.45754900	1.92161900	1.62782900
N	-0.47578400	2.62896000	1.62479700

TS1

C	0.74700800	-0.99003000	1.17118000
C	1.53134600	-2.41125100	-0.16697600
H	1.47803500	-1.14850000	1.96197300
C	0.53628800	-3.27354900	-0.78975100
O	0.50868700	-4.48779900	-0.77516900
O	-0.41093000	-2.53953300	-1.42440000
C	2.79347300	-2.94862600	0.30898400
O	3.14869300	-4.10917000	0.29411700
O	3.58153800	-1.97272700	0.85351300
C	-1.52329300	-3.27776400	-1.91736800
H	-1.96952000	-3.88339100	-1.12445700
H	-2.24082900	-2.53663300	-2.27192000
H	-1.21962200	-3.93117500	-2.73896500
C	4.83132200	-2.43412900	1.36032700
H	5.42428200	-2.89748700	0.56861300
H	5.34241700	-1.55092500	1.74473900
H	4.68163800	-3.16086100	2.16232100
C	-0.65157000	-1.35127700	1.49587800
C	-1.71601100	-1.10371300	0.62277400
C	-0.89273400	-1.90938600	2.75629100
C	-3.01033800	-1.44296900	1.00090500
H	-1.52142500	-0.65823300	-0.34507500
C	-2.18842200	-2.24605700	3.12986400
H	-0.06093500	-2.08996600	3.43176700
C	-3.24639800	-2.01524600	2.25103900
H	-3.83347000	-1.25186400	0.31755200
H	-2.37255100	-2.69109400	4.10212100
H	-4.25842200	-2.27855700	2.54234700
N	1.31525000	-1.01618100	-0.10623200
S	1.26387600	0.04678600	-1.39090400
O	1.79924500	-0.70288800	-2.51322200
O	-0.06266300	0.66665500	-1.49502200
C	2.37631300	1.35691800	-0.93883400
C	2.03442500	2.66409500	-1.27254000
C	3.57728400	1.05453600	-0.30160100
C	2.91606900	3.69031100	-0.94685000
H	1.09552600	2.87274800	-1.77587900
C	4.44211200	2.09442300	0.01434700
H	3.80796900	0.02584100	-0.03939100
C	4.12708100	3.42203900	-0.30173400
H	2.66100300	4.71538700	-1.20022400
H	5.37862800	1.87494700	0.51990400
C	5.08807500	4.52972900	0.03417000
H	5.95843400	4.49429700	-0.62923200
H	4.62000000	5.50995200	-0.07709800

H	5.45585800	4.43355800	1.05942300
C	-4.46687600	1.56927300	0.00599300
C	-3.32172000	1.37921600	-0.80552800
C	-3.33787400	0.59159300	-1.96248800
C	-4.54052500	-0.00610400	-2.30444700
C	-5.69877200	0.17724900	-1.51904900
C	-5.67405600	0.95643400	-0.37449800
C	-4.05184300	2.37418000	1.11790300
H	-2.43715200	0.45042900	-2.55249900
H	-4.59327500	-0.62520900	-3.19470600
H	-6.62351300	-0.30491600	-1.82048500
H	-6.56941600	1.08562600	0.22669500
N	-2.27740500	2.04983300	-0.21429200
C	-2.71656200	2.63789500	0.95331700
H	-4.66306900	2.71931900	1.94015300
C	-1.82095100	3.46139700	1.83576600
H	-2.11990900	4.51389500	1.79057700
H	-1.94064000	3.14069200	2.87443700
H	-1.32022400	1.96432700	-0.53696200
C	-0.34173000	3.42385900	1.46610300
H	0.24324500	4.04589600	2.14565900
H	-0.17041500	3.77428800	0.44320800
C	0.60892600	1.01341500	1.52688700
N	0.18622400	2.09262900	1.53637700

IM1

C	0.58275000	0.66267100	-1.15290400
C	1.42899900	2.42000400	0.32654200
H	1.29317300	0.96866100	-1.93528100
C	0.44902800	3.19949000	1.03244200
O	0.42805700	4.40756900	1.20551600
O	-0.54222800	2.40296900	1.54625400
C	2.54290600	3.02142500	-0.33257500
O	2.90612200	4.18585700	-0.32075800
O	3.23431400	2.09640400	-1.10821600
C	-1.62746100	3.10007700	2.13269600
H	-2.08729300	3.78828800	1.41704700
H	-2.35021400	2.33796900	2.43010200
H	-1.30499900	3.66990700	3.00866000
C	4.36728100	2.62712600	-1.78193600
H	5.08376200	3.05270700	-1.07487800
H	4.82235200	1.78944300	-2.31365200
H	4.07628200	3.40523200	-2.49258900
C	-0.79000000	1.26146000	-1.43559900
C	-1.86308000	0.96904600	-0.59315300
C	-0.95896100	2.09378300	-2.53846700
C	-3.11600600	1.50551300	-0.86422200
H	-1.70249100	0.35000900	0.28327700
C	-2.21469300	2.63841000	-2.80144400
H	-0.11197500	2.32459200	-3.17853200
C	-3.29088400	2.34014200	-1.96934900
H	-3.95043400	1.27210500	-0.20827200
H	-2.34828800	3.29813400	-3.65240200
H	-4.26841100	2.76360200	-2.17781100
N	1.18922400	1.03255500	0.13262200
S	1.25538600	-0.05313500	1.39214200
O	1.67261600	0.66494100	2.57989900
O	0.00217300	-0.82827200	1.40945400
C	2.51067300	-1.22951400	0.92178900
C	2.37094300	-2.55253200	1.34202300
C	3.61680000	-0.81281500	0.18797400
C	3.35922300	-3.47044200	1.00805800
H	1.50524900	-2.85255100	1.92453400
C	4.59386800	-1.74979500	-0.13715100

H	3.69774500	0.22262400	-0.13370300
C	4.48060200	-3.08454000	0.26262200
H	3.26508700	-4.50204600	1.33608900
H	5.46194800	-1.43669000	-0.71045600
C	5.52793400	-4.09591700	-0.11718900
H	6.48491300	-3.61375900	-0.32808700
H	5.67541100	-4.82808700	0.68057500
H	5.22589300	-4.64468200	-1.01592000
C	-4.34162500	-1.79351900	-0.28049100
C	-3.35140900	-1.67915100	0.72487000
C	-3.55803700	-0.96323900	1.90953600
C	-4.80177700	-0.37935200	2.08696900
C	-5.81493000	-0.50210000	1.11168600
C	-5.59676900	-1.19683500	-0.06575200
C	-3.74556600	-2.52584100	-1.36063200
H	-2.76873400	-0.86549800	2.64885400
H	-5.00138000	0.18265500	2.99394800
H	-6.77860100	-0.03514000	1.28937800
H	-6.37797300	-1.27506200	-0.81619500
N	-2.22714100	-2.33493600	0.28050100
C	-2.46357900	-2.83150600	-0.98600400
H	-4.20737900	-2.79996600	-2.29886700
C	-1.44895700	-3.62833100	-1.75251100
H	-1.57488900	-4.70040900	-1.56387900
H	-1.61242900	-3.46775200	-2.82047900
H	-1.33518500	-2.28429400	0.75902100
C	0.01059700	-3.33065300	-1.40778000
H	0.69441700	-3.81894300	-2.10335000
H	0.26710500	-3.63494500	-0.38783100
C	0.44391900	-0.79480700	-1.31441300
N	0.28391900	-1.92065200	-1.45092000

IM2

C	0.65176300	-0.37931500	-1.15950300
C	0.19211200	-0.20019700	1.31543000
H	1.52504100	-0.54524400	-1.80437700
C	-0.72636500	-1.17912300	1.77040400
O	-0.96419700	-2.25220200	1.17912100
O	-1.37246300	-0.88746500	2.92112300
C	0.38598400	1.08565300	1.93718400
O	-0.33970000	1.64007600	2.74698600
O	1.52844100	1.69551200	1.49541900
C	-2.31743300	-1.85428900	3.36626700
H	-1.85704500	-2.83933400	3.46627100
H	-2.66343800	-1.49929100	4.33686700
H	-3.17071400	-1.92504700	2.68288500
C	1.69177500	3.03812900	1.92574000
H	1.79180500	3.09592100	3.01289300
H	2.60573300	3.39683600	1.44821000
H	0.84200500	3.65444900	1.61856200
C	0.09057700	1.00385200	-1.42402400
C	-1.26296400	1.23724800	-1.64161100
C	0.99352300	2.06854600	-1.38688400
C	-1.72275700	2.54303500	-1.80877100
H	-1.97076400	0.41388200	-1.68580000
C	0.53274400	3.36772800	-1.55903100
H	2.04538000	1.87258900	-1.19633400
C	-0.82772600	3.60615500	-1.76407000
H	-2.78375600	2.71827400	-1.95581500
H	1.23328900	4.19623000	-1.52641700
H	-1.18684800	4.62299600	-1.88665900
N	1.03191600	-0.57202900	0.23549000
S	2.23842900	-1.73314200	0.44373400
O	2.29759100	-2.04965500	1.85916300

O	2.01433200	-2.78159300	-0.55510500
C	3.71584000	-0.86789600	-0.02973100
C	4.37074600	-1.21516600	-1.20485700
C	4.17063300	0.17274000	0.78290100
C	5.50775200	-0.49941400	-1.57640500
H	3.99931500	-2.03531400	-1.81036700
C	5.30239800	0.87274000	0.39358400
H	3.63151200	0.43470400	1.68743300
C	5.98542300	0.54900300	-0.78885600
H	6.03086500	-0.76269400	-2.49099300
H	5.66927500	1.68548600	1.01476800
C	7.21318600	1.32383600	-1.18419700
H	8.00292300	1.20366200	-0.43600400
H	7.60218500	0.98903200	-2.14795100
H	6.99238200	2.39325300	-1.25408900
C	-4.64773700	0.50838800	-0.90125000
C	-3.78419200	0.13369300	0.15904300
C	-3.46571500	1.00130500	1.21280400
C	-4.07437700	2.24470400	1.20840100
C	-4.97278900	2.62474600	0.18894600
C	-5.26011900	1.77491500	-0.86498400
C	-4.63899500	-0.57427800	-1.84359100
H	-2.74636300	0.72984900	1.98125300
H	-3.84397900	2.94584700	2.00431800
H	-5.43360900	3.60703100	0.22813800
H	-5.93706100	2.08067500	-1.65774200
N	-3.31182100	-1.12968400	-0.12086500
C	-3.81542400	-1.54574800	-1.33443400
H	-5.17056500	-0.62907500	-2.78357300
C	-3.43910000	-2.86817100	-1.93424100
H	-4.12042200	-3.66118600	-1.60655900
H	-3.52496600	-2.79580000	-3.02063400
H	-2.62692800	-1.64135200	0.43669100
C	-2.03668500	-3.35249200	-1.55272900
H	-1.71627000	-4.18602600	-2.17860800
H	-1.96476500	-3.63990000	-0.49863200
C	-0.31205100	-1.45611100	-1.51365200
N	-1.06027700	-2.30584100	-1.68297600

TS2

C	-0.56069800	-0.66871800	0.42625300
C	-0.51342700	1.10464300	-1.32323700
H	-1.31756400	-1.24926600	0.97744600
C	0.59328100	0.61295900	-2.02800700
O	0.91765300	-0.60845500	-1.99877900
O	1.33995200	1.48102100	-2.72823400
C	-0.95417800	2.47727600	-1.34276600
O	-0.42762600	3.41237200	-1.91788500
O	-2.09970100	2.66295100	-0.61455000
C	2.37364900	0.91653000	-3.53300400
H	1.97416400	0.15086900	-4.20183900
H	2.77559700	1.74749400	-4.11187700
H	3.17143200	0.48354800	-2.92184100
C	-2.57896900	4.00308600	-0.60100900
H	-2.81444000	4.34384100	-1.61189800
H	-3.48291900	3.99288400	0.00942900
H	-1.84010900	4.67895300	-0.16300500
C	0.23791900	0.16292500	1.42637300
C	1.41155700	-0.30833200	2.00986500
C	-0.28040100	1.40393300	1.80534700
C	2.07436900	0.46673700	2.96109400
H	1.83567500	-1.27002300	1.73121500
C	0.38746600	2.17191700	2.75195600
H	-1.19348400	1.76616900	1.34353100

C	1.56900300	1.70801200	3.32914500
H	2.99822300	0.09877100	3.39482100
H	-0.01367300	3.14056800	3.03272600
H	2.09521700	2.31474500	4.05921900
N	-1.24594800	0.14323800	-0.56536800
S	-2.47082000	-0.72185800	-1.36808200
O	-2.89208000	0.09834100	-2.49015500
O	-2.02166100	-2.09882900	-1.59553500
C	-3.74759400	-0.78308900	-0.13766800
C	-4.23089300	-2.01523100	0.28516000
C	-4.25877100	0.41744000	0.35755700
C	-5.25515500	-2.04277800	1.22923000
H	-3.81238900	-2.93050000	-0.11999900
C	-5.27679400	0.36642800	1.29741100
H	-3.84683800	1.36088900	0.01087500
C	-5.78947000	-0.86049200	1.74478200
H	-5.64355600	-2.99828700	1.56904200
H	-5.68552900	1.29081900	1.69625600
C	-6.89779600	-0.88599300	2.76192900
H	-7.79191100	-0.39111500	2.37025000
H	-7.16482100	-1.90891200	3.03440200
H	-6.60309100	-0.35280900	3.67088600
C	4.77963200	-0.65078300	1.08376300
C	3.97847600	-0.08724900	0.06010200
C	3.84433000	1.29536600	-0.11737600
C	4.56119700	2.11427500	0.73784800
C	5.39493200	1.57687100	1.74173800
C	5.51088300	0.20949900	1.92273100
C	4.57659500	-2.07040800	1.02692300
H	3.18175100	1.70622200	-0.87479900
H	4.47576900	3.19154900	0.63721800
H	5.94704400	2.25276500	2.38748400
H	6.14238700	-0.19428300	2.70913300
N	3.36134300	-1.12130400	-0.60325400
C	3.70315600	-2.31402000	-0.00356300
H	5.01767700	-2.82146000	1.66773400
C	3.14415000	-3.62926000	-0.46178700
H	3.80118300	-4.09829600	-1.20298300
H	3.09685400	-4.30280400	0.39712300
H	2.63546600	-0.98649900	-1.30805900
C	1.76998900	-3.54035800	-1.12915500
H	1.33096700	-4.53156000	-1.24229000
H	1.81914200	-3.05395600	-2.10796100
C	0.28848100	-1.73253400	-0.19900500
N	0.85361400	-2.73217800	-0.35675000

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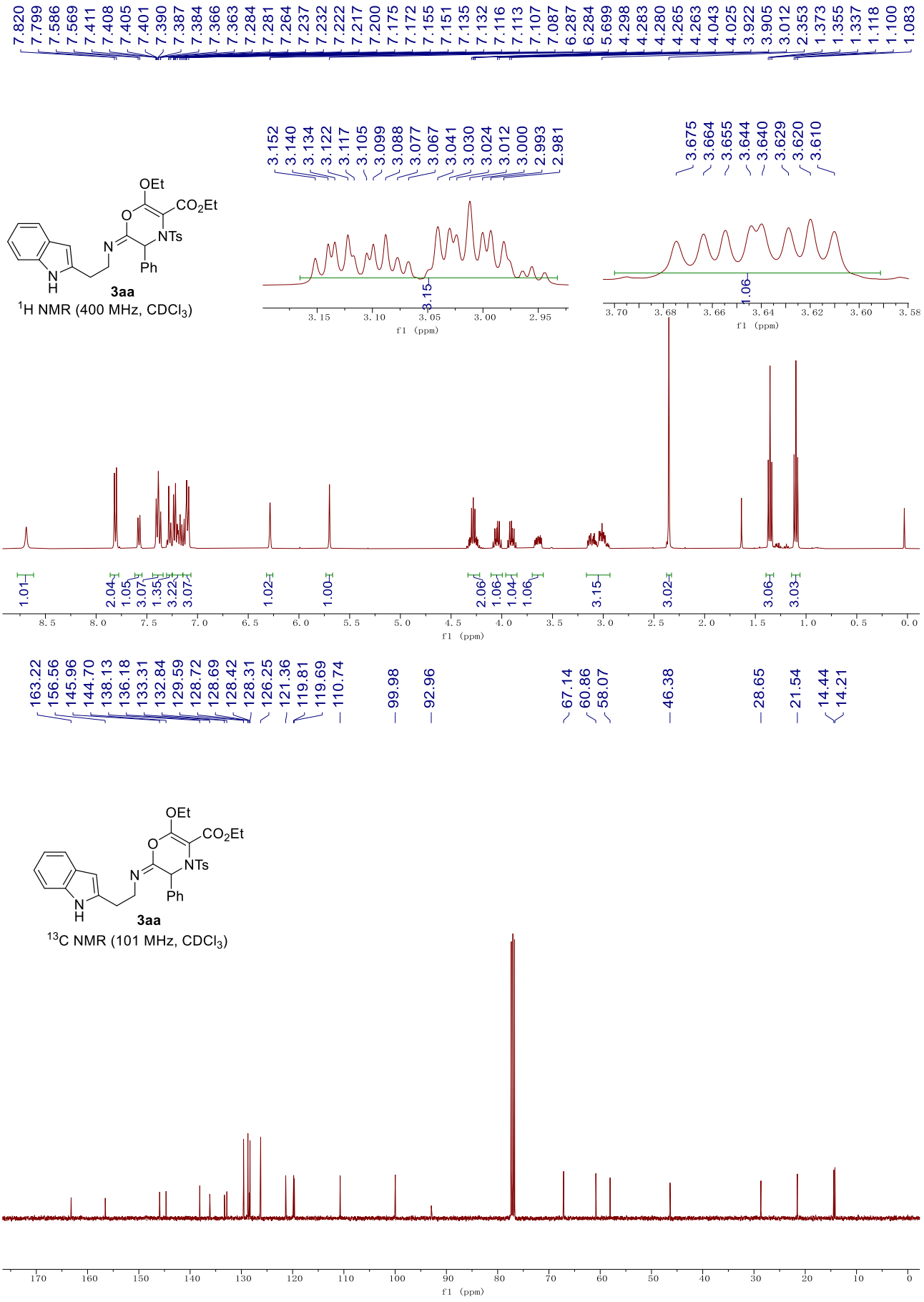
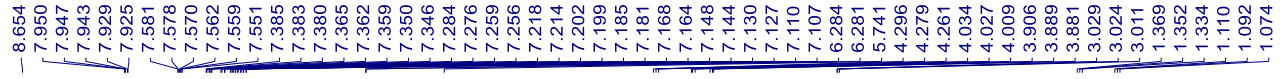
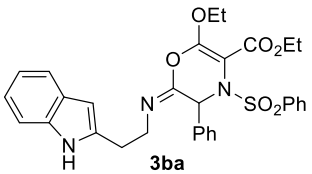
C	-0.43578200	-0.49892800	-0.44823300
C	-0.81072900	1.83156900	0.09636200
H	-0.96139700	-1.36151100	-0.86926900
C	0.41358300	2.09340600	-0.40282000
O	1.03145600	1.25460000	-1.27739500
O	1.19553100	3.11530000	-0.07206500
C	-1.47192100	2.74177100	1.05642000
O	-1.20192900	3.91349400	1.19441800
O	-2.40999400	2.10949900	1.77394300
C	1.04119300	4.28000500	-0.90921700
H	0.02022600	4.65554900	-0.82637400
H	1.74686900	5.01511100	-0.52565500
H	1.28500600	4.03185100	-1.94584000
C	-3.14741300	2.94718200	2.66964000
H	-3.65939100	3.73488800	2.11311300
H	-3.87030700	2.29519100	3.15766300
H	-2.48070900	3.39630800	3.40835500

C	0.25429600	-0.89060700	0.85617800
C	1.49192000	-1.53518900	0.82364400
C	-0.35964100	-0.63554900	2.08450700
C	2.11357300	-1.91354800	2.01189600
H	1.97892800	-1.74319900	-0.12654800
C	0.26396900	-1.01914200	3.26838100
H	-1.31685600	-0.12391100	2.10972200
C	1.50295600	-1.65535200	3.23581100
H	3.08590300	-2.39515600	1.97426600
H	-0.21758200	-0.81085100	4.21883200
H	1.99444000	-1.94260000	4.16010900
N	-1.40514600	0.57680300	-0.21022300
S	-2.71645400	0.63757500	-1.28669500
O	-3.35630900	1.92006000	-1.02860900
O	-2.27859100	0.31144400	-2.64006600
C	-3.70794800	-0.69263200	-0.67710000
C	-4.01666400	-1.75685100	-1.51380400
C	-4.17365400	-0.62287700	0.63679900
C	-4.81695600	-2.78252100	-1.01492900
H	-3.63554000	-1.78006700	-2.52935500
C	-4.96731700	-1.65464500	1.11176700
H	-3.90396200	0.22371400	1.26256400
C	-5.29934900	-2.74632300	0.29456100
H	-5.06699000	-3.62372900	-1.65430600
H	-5.33762700	-1.62161300	2.13255200
C	-6.15791400	-3.85561200	0.83796600
H	-7.11823300	-3.46562500	1.18855900
H	-6.35182000	-4.61670800	0.07986400
H	-5.67099100	-4.33733900	1.69153400
C	4.95927500	-1.46793400	-0.05691500
C	4.43103600	-0.15611000	0.04095200
C	4.56376600	0.62467600	1.19340300
C	5.26148500	0.07495700	2.25614300
C	5.81947800	-1.21787300	2.17492600
C	5.67571500	-1.99083100	1.03428700
C	4.57001300	-1.97143200	-1.34370400
H	4.12293600	1.61539000	1.25117700
H	5.38148600	0.64983000	3.16899500
H	6.36690700	-1.61211500	3.02551800
H	6.10093600	-2.98923000	0.98431000
N	3.78255800	0.11466800	-1.14004100
C	3.85591100	-0.98299600	-1.97256400
H	4.78820100	-2.94564100	-1.75861900
C	3.22674500	-0.98632700	-3.33294600
H	3.91431800	-0.55508100	-4.07040700
H	3.05240400	-2.02633800	-3.62144000
H	3.25956900	0.95970200	-1.32584600
C	1.91159200	-0.20385500	-3.41046400
H	1.48875600	-0.34127200	-4.40942100
H	2.09680800	0.86831100	-3.27942300
C	0.55254300	-0.03192200	-1.49382100
N	0.94646000	-0.73394400	-2.45574700

8. Copy of ^{1}H NMR and ^{13}C NMR Spectra

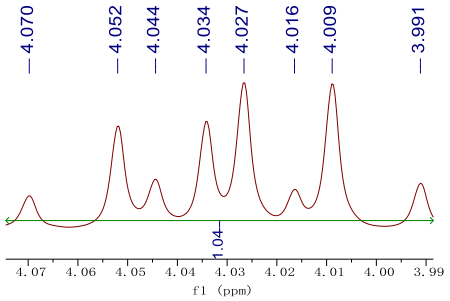


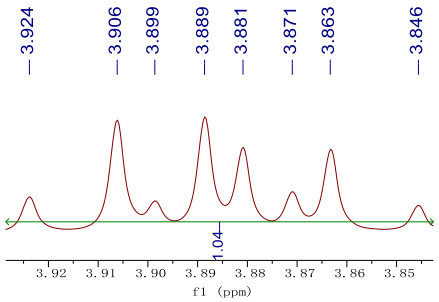


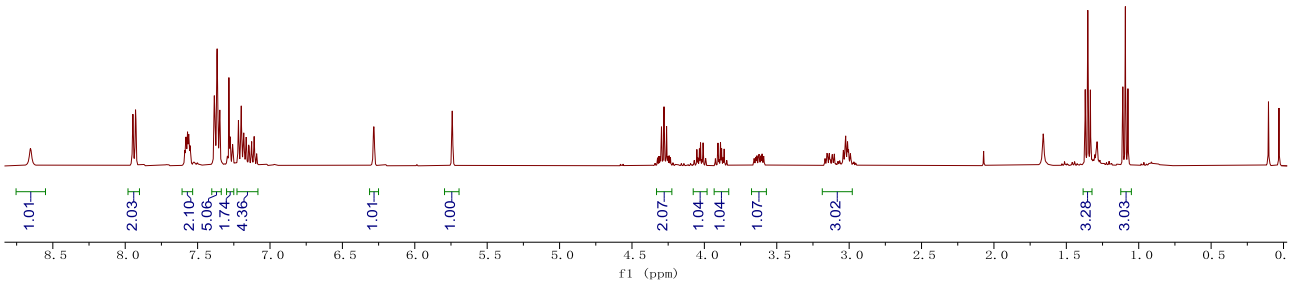


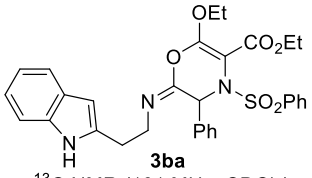
3ba

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



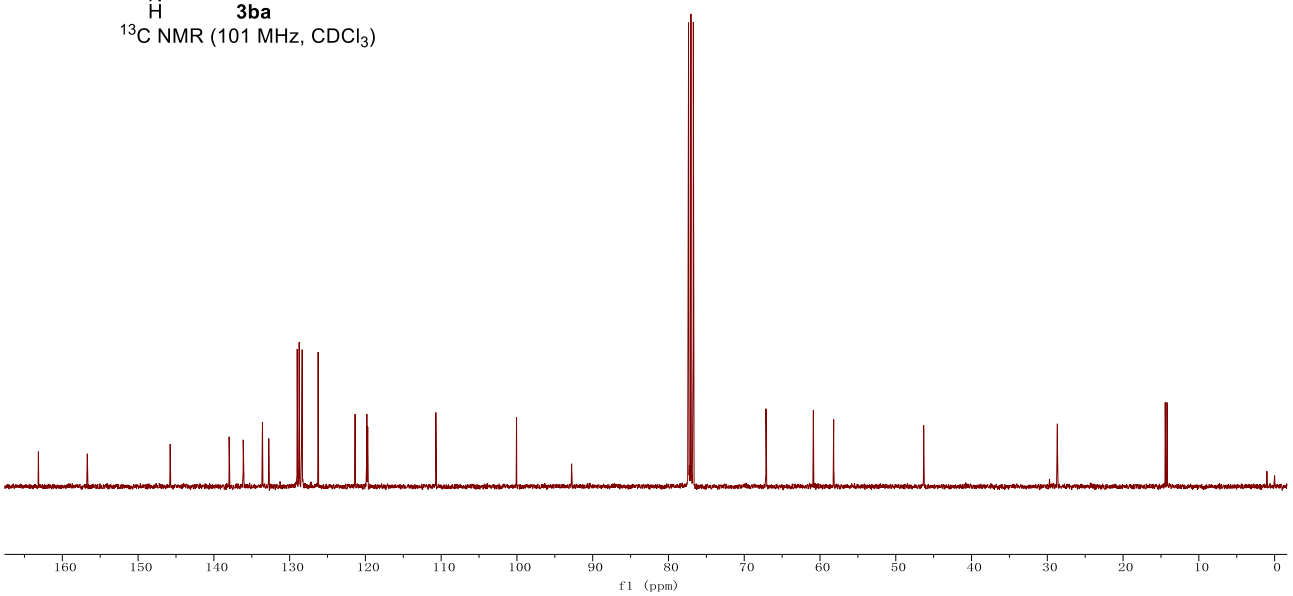


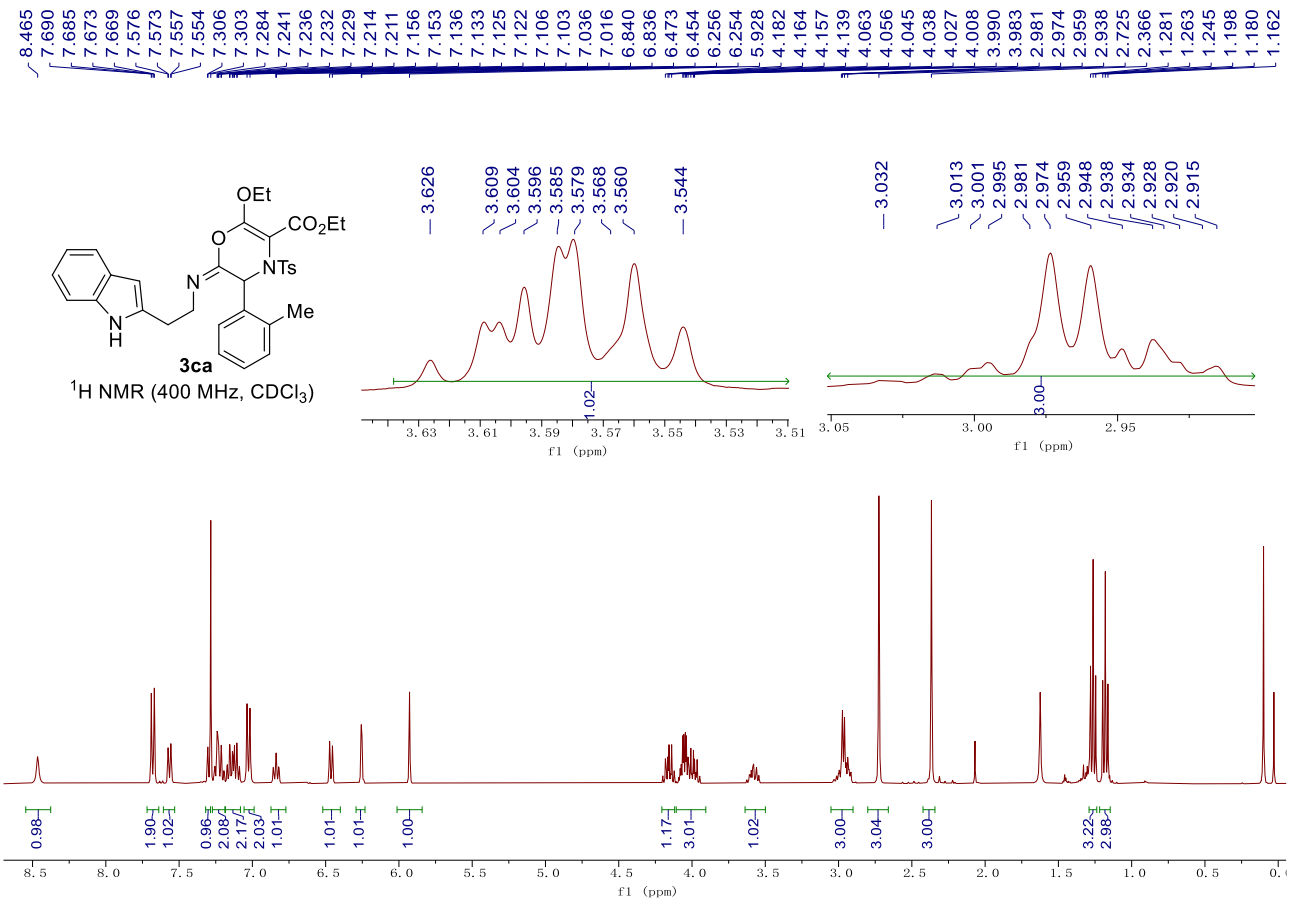


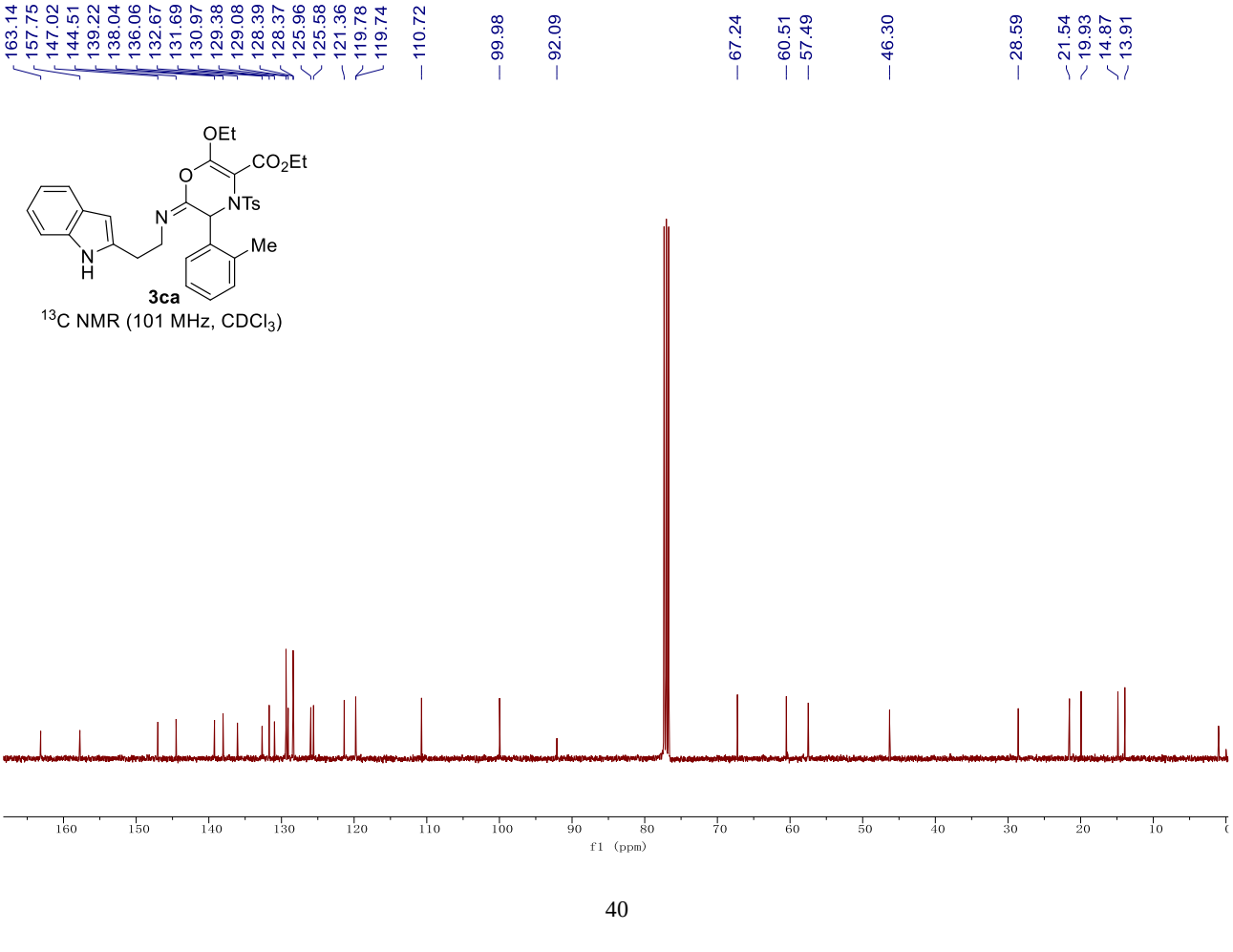


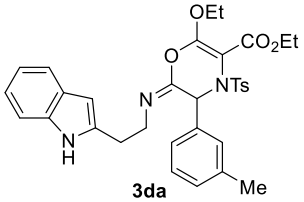
3ba

^{13}C NMR (101 MHz, $CDCl_3$)



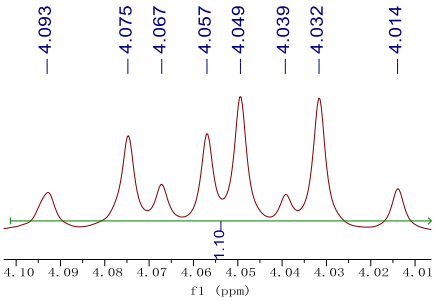

3ca
1H NMR (400 MHz, CDCl3)
f1 (ppm)

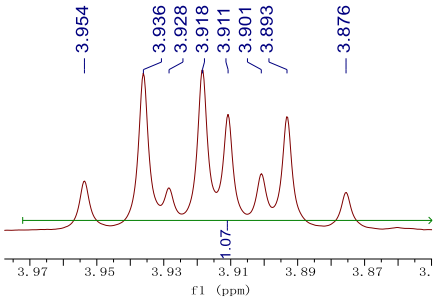

3ca
13C NMR (101 MHz, CDCl3)
f1 (ppm)

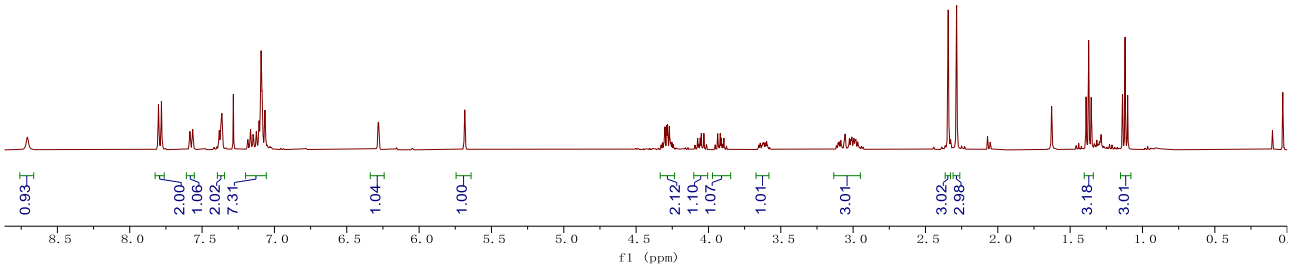


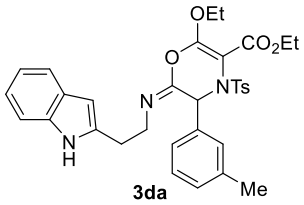
3da

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



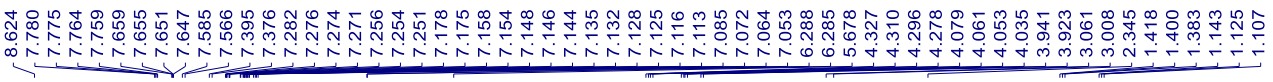


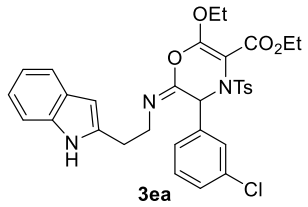




3da

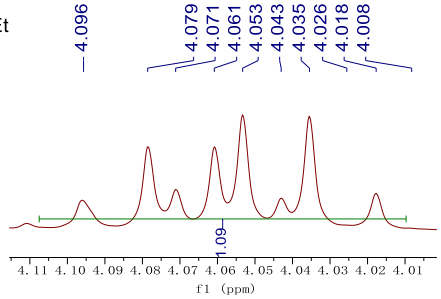
^{13}C NMR (101 MHz, $CDCl_3$)

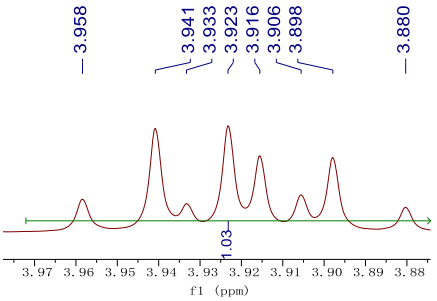


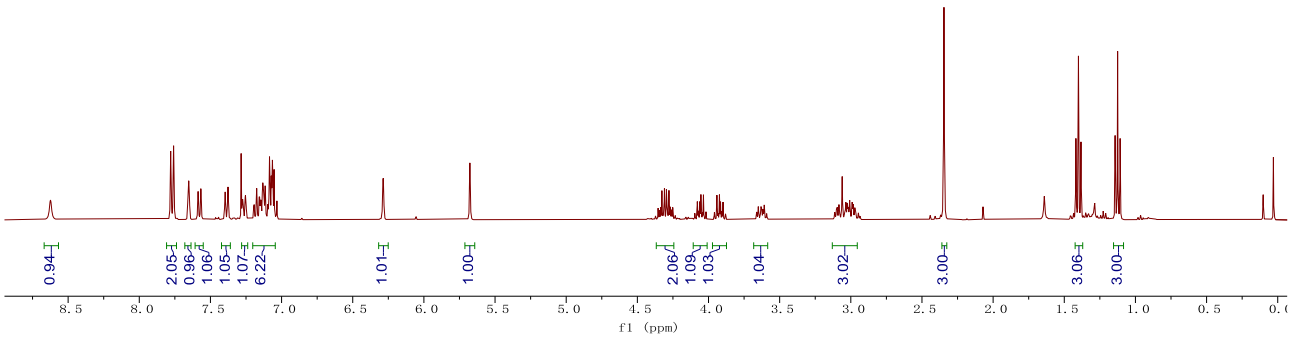


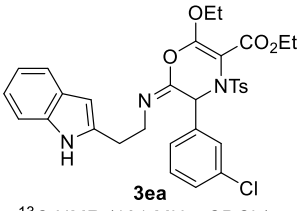
3ea

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



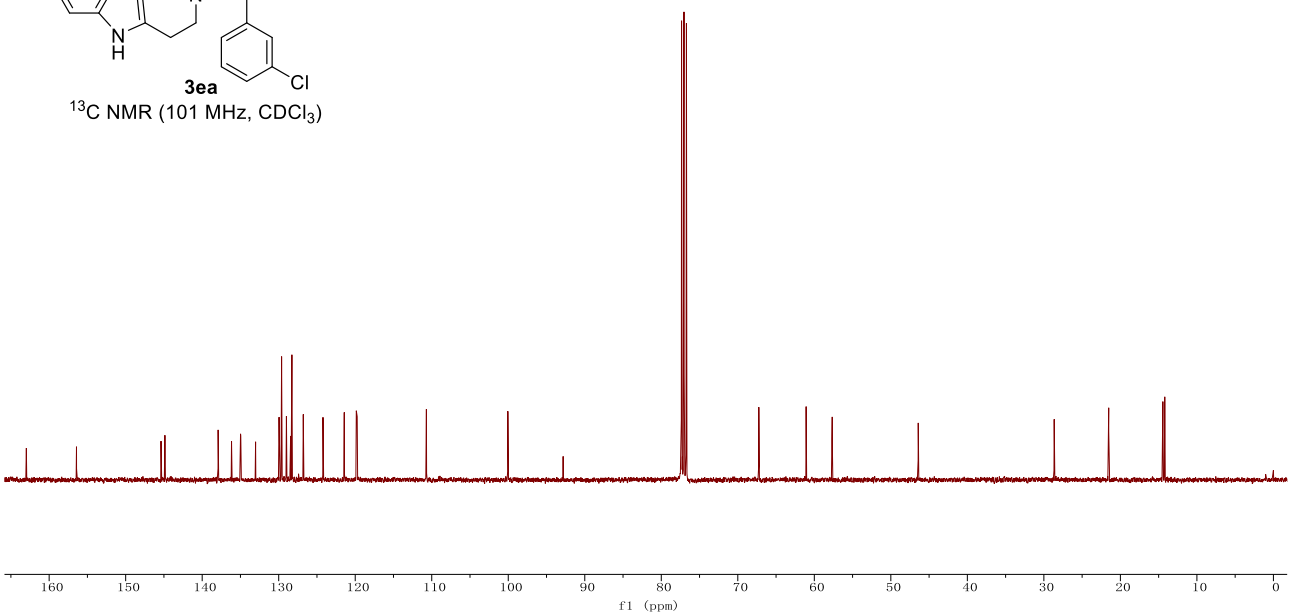


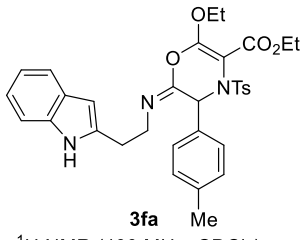




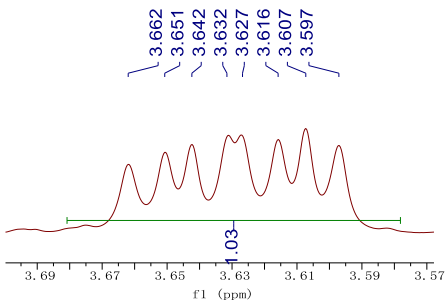
3ea

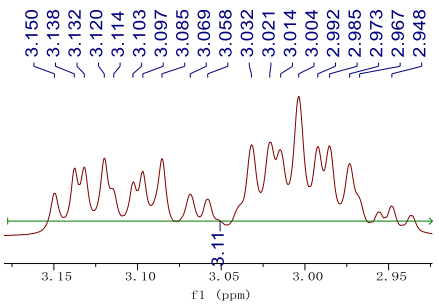
^{13}C NMR (101 MHz, $CDCl_3$)

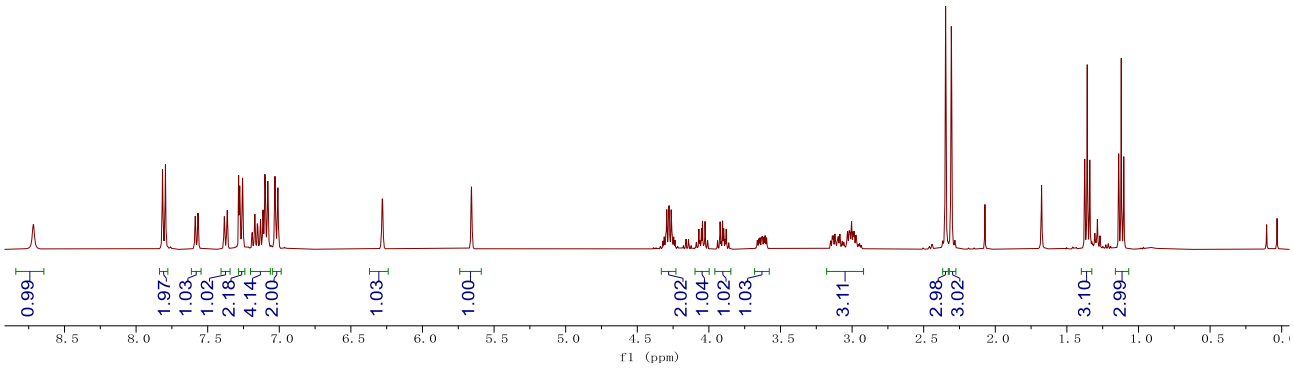


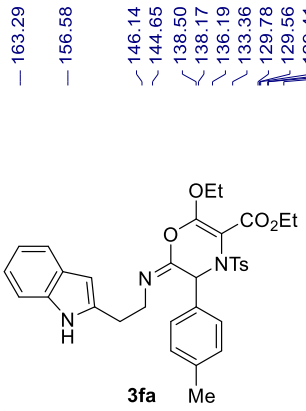


^{1}H NMR (400 MHz, $CDCl_3$)

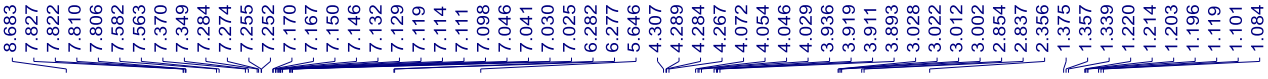


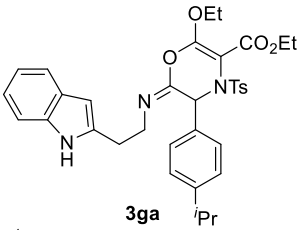




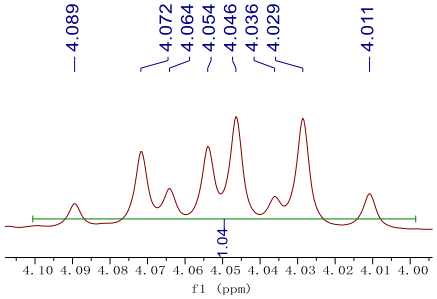


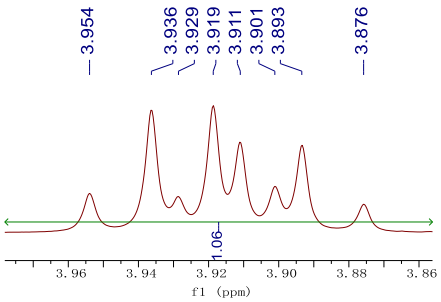
^{13}C NMR (101 MHz, $CDCl_3$)

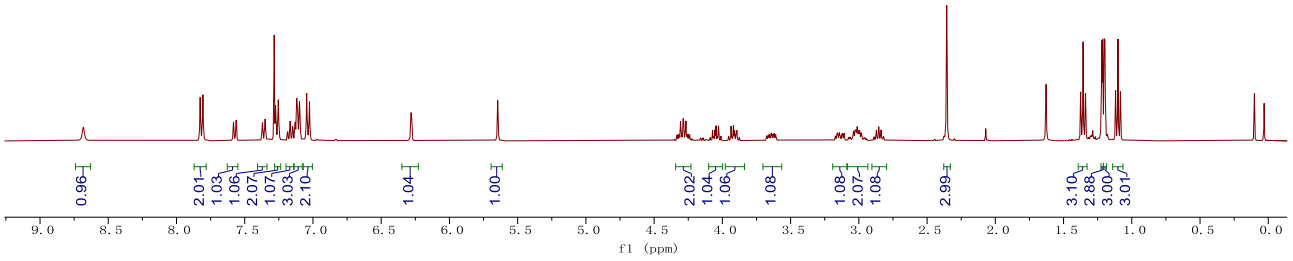


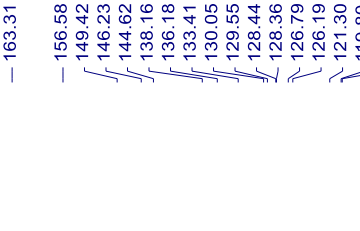


^{1}H NMR (400 MHz, $CDCl_3$)

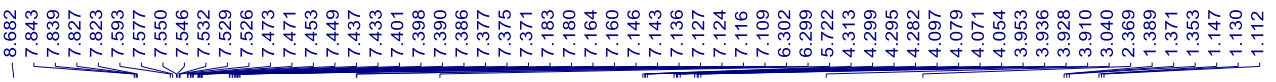


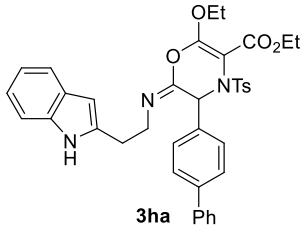






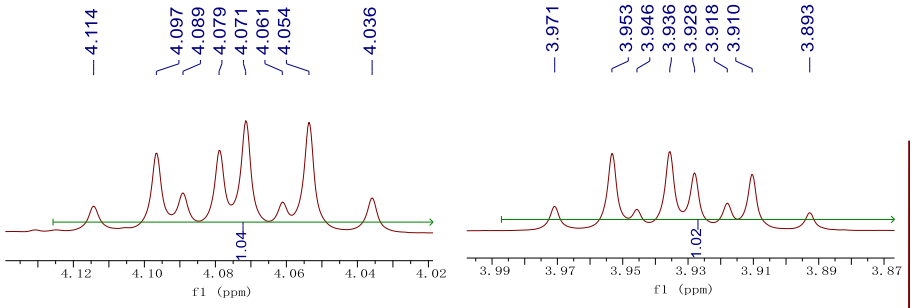
^{13}C NMR (101 MHz, $CDCl_3$)

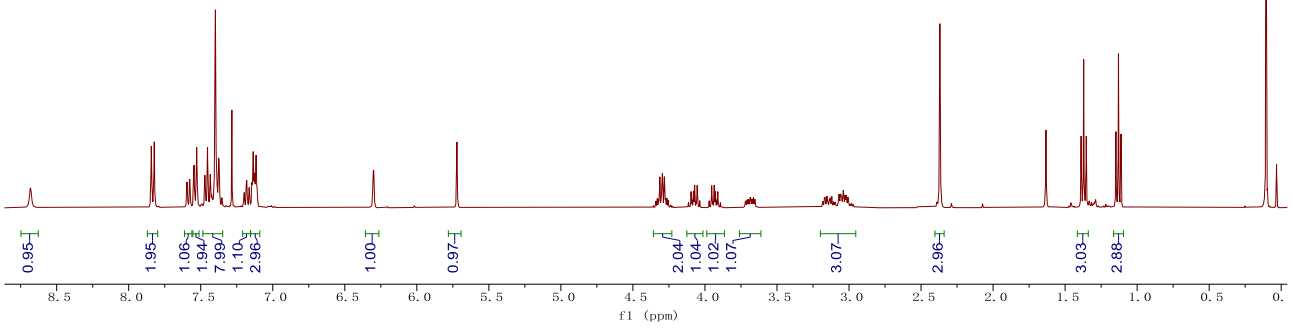


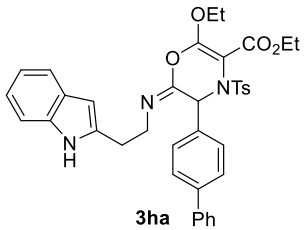


3ha Ph

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

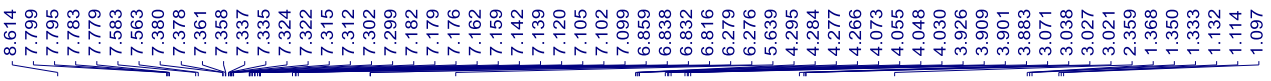


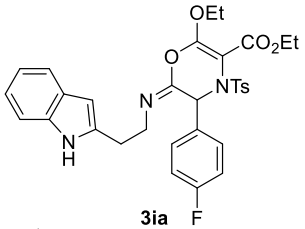




3ha Ph

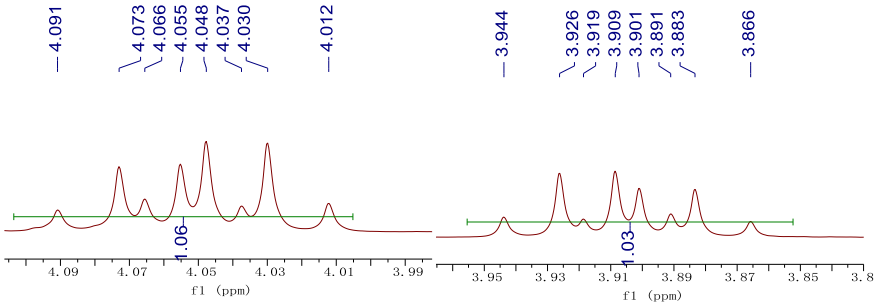
^{13}C NMR (101 MHz, $CDCl_3$)

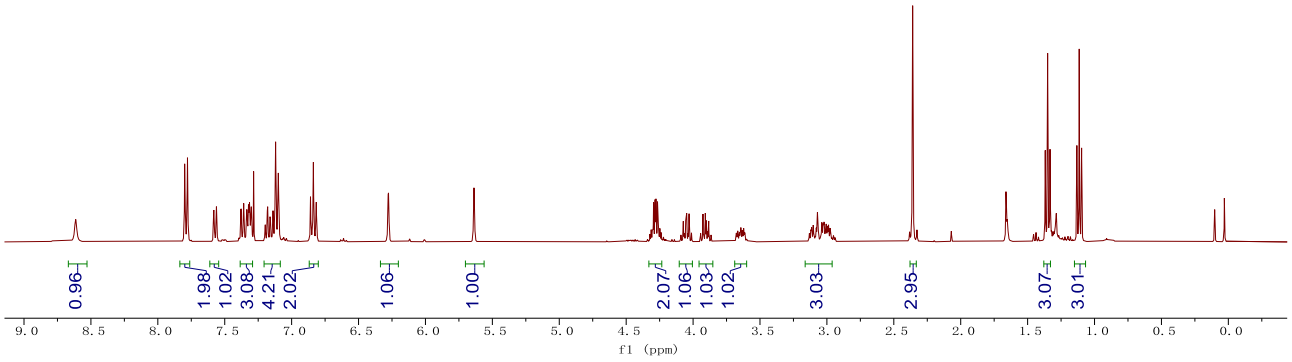


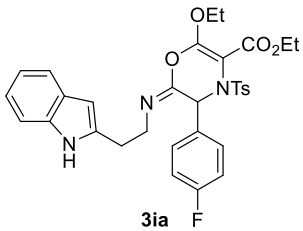


3ia

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

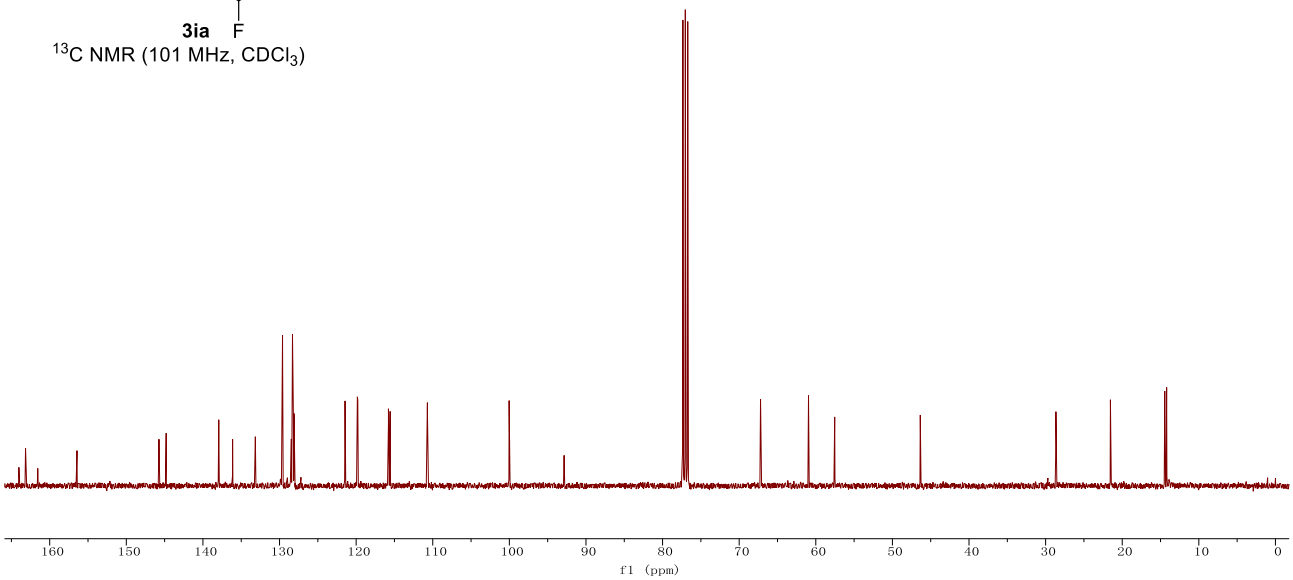


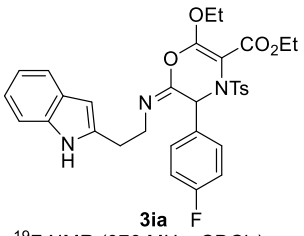




3ia

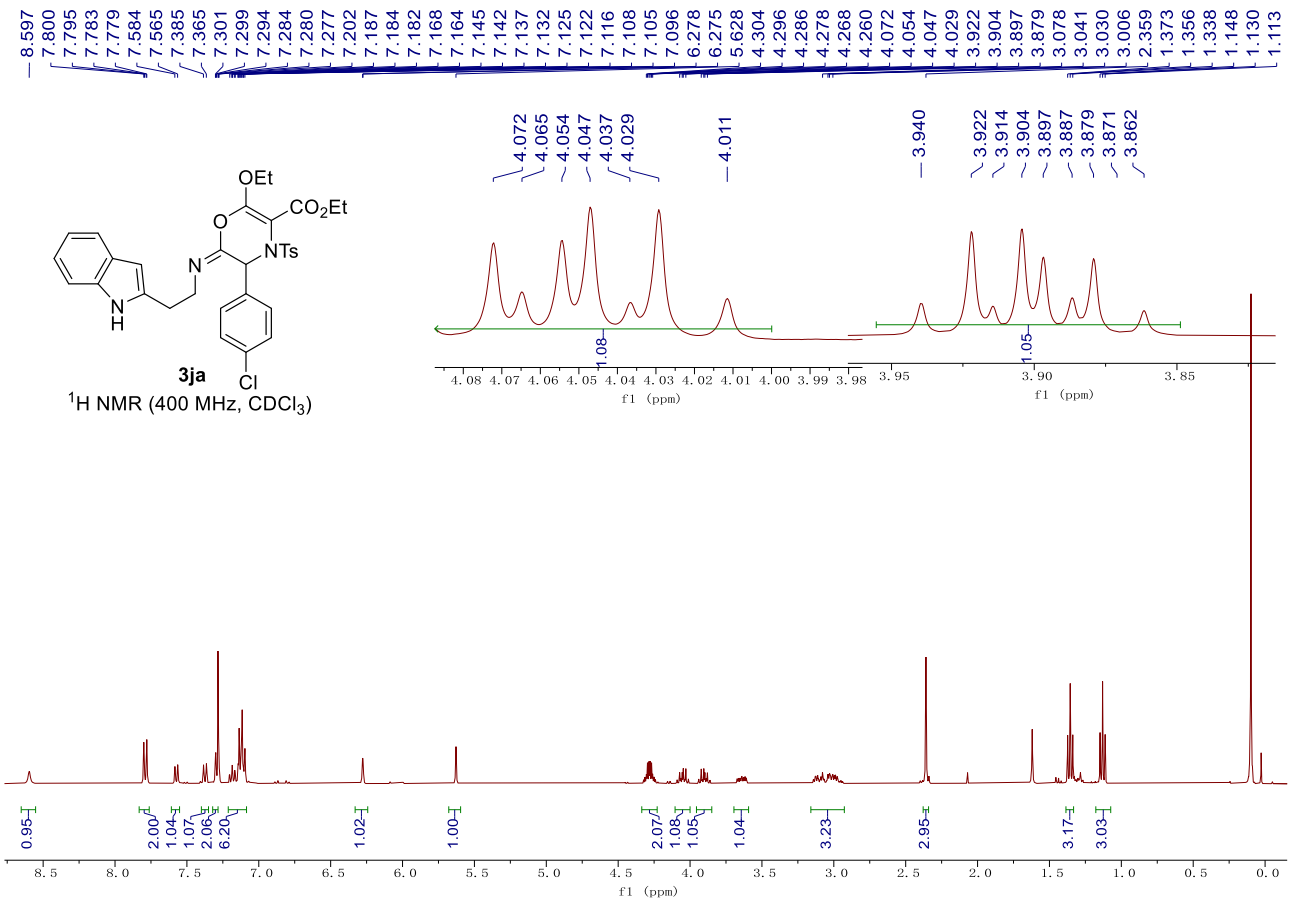
^{13}C NMR (101 MHz, $CDCl_3$)





3ia

^{19}F NMR (376 MHz, $CDCl_3$)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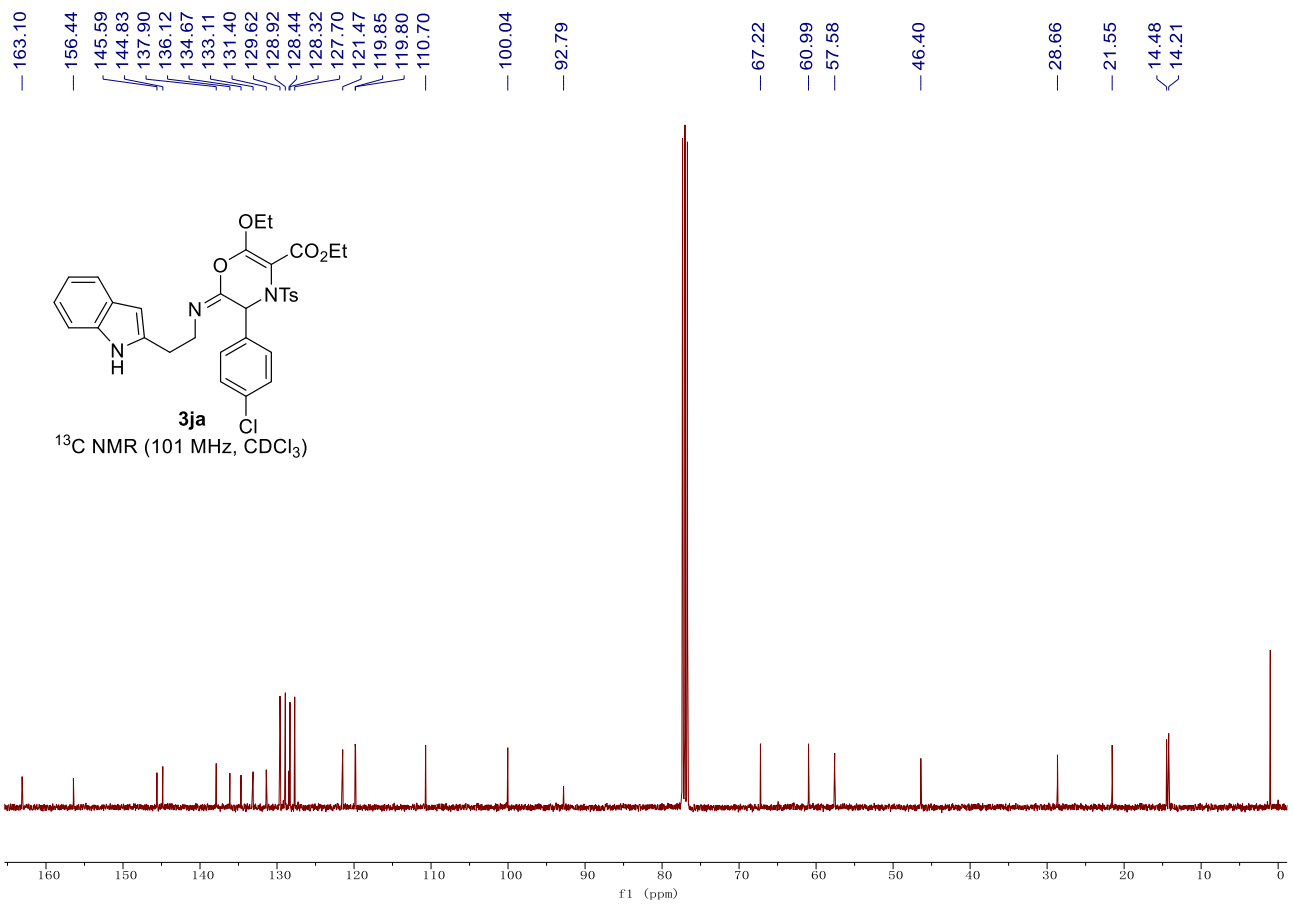
7.795
7.783
7.779
7.584
7.565
7.385
7.365
7.301
7.299
7.294
7.284
7.280
7.277
7.202
7.187
7.184
7.182
7.168
7.164
7.145
7.142
7.137
7.132
7.125
7.122
7.116
7.108
7.105
7.096
6.278
6.275
5.628
4.304
4.296
4.286
4.278
4.268
4.260
4.072
4.054
4.047
4.029
3.922
3.904
3.897
3.879
3.078
3.041
3.030
3.006
2.359
1.373
1.356
1.338
1.148
1.130
1.113
OEt
CO2Et
O
NTs
N
N
H
Cl
3ja
1H NMR (400 MHz, CDCl3)
4.072
4.065
4.054
4.047
4.037
4.029
4.011
3.940
3.922
3.914
3.904
3.897
3.887
3.879
3.871
3.862
1.08
1.05
f1 (ppm)
0.95
2.00
1.04
1.07
2.06
6.20
1.02
1.00
2.07
1.08
1.05
1.04
3.23
2.95
3.17
3.03
f1 (ppm)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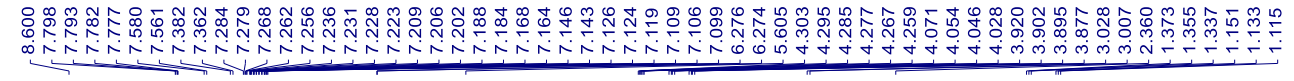
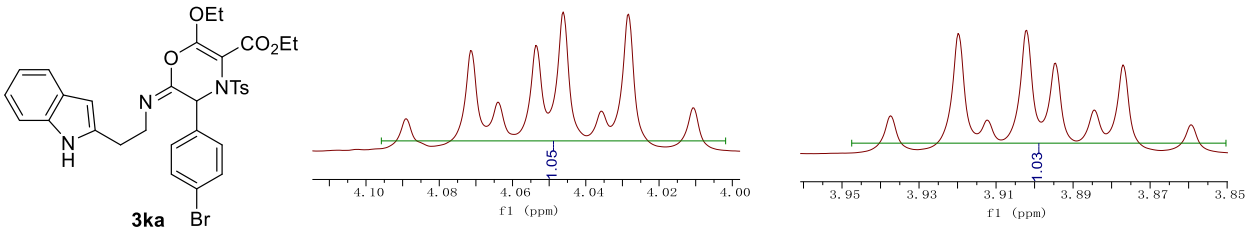
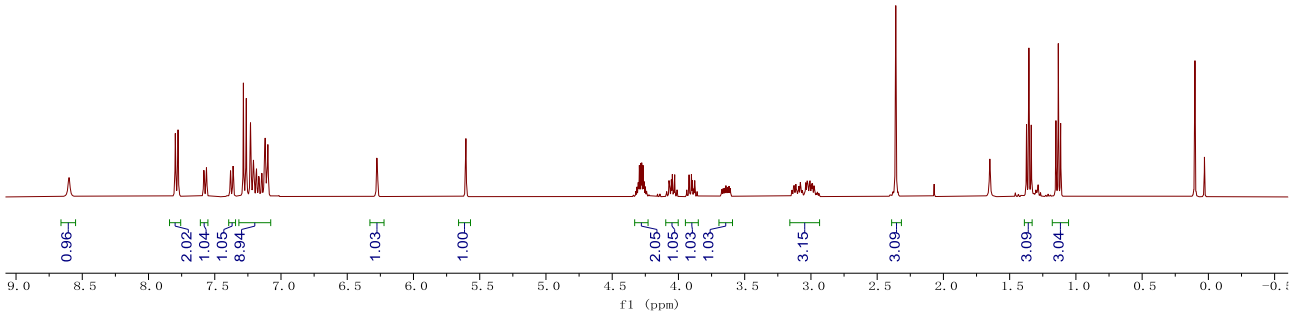
145.59
144.83
137.90
136.12
134.67
133.11
131.40
129.62
128.92
128.44
128.32
127.70
121.47
119.85
119.80
110.70
100.04
92.79
67.22
60.99
57.58
46.40
28.66
21.55
14.48
14.21
OEt
CO2Et
O
NTs
N
N
H
Cl
3ja
13C NMR (101 MHz, CDCl3)
f1 (ppm)

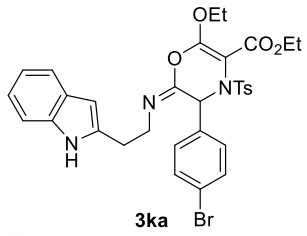




3ka

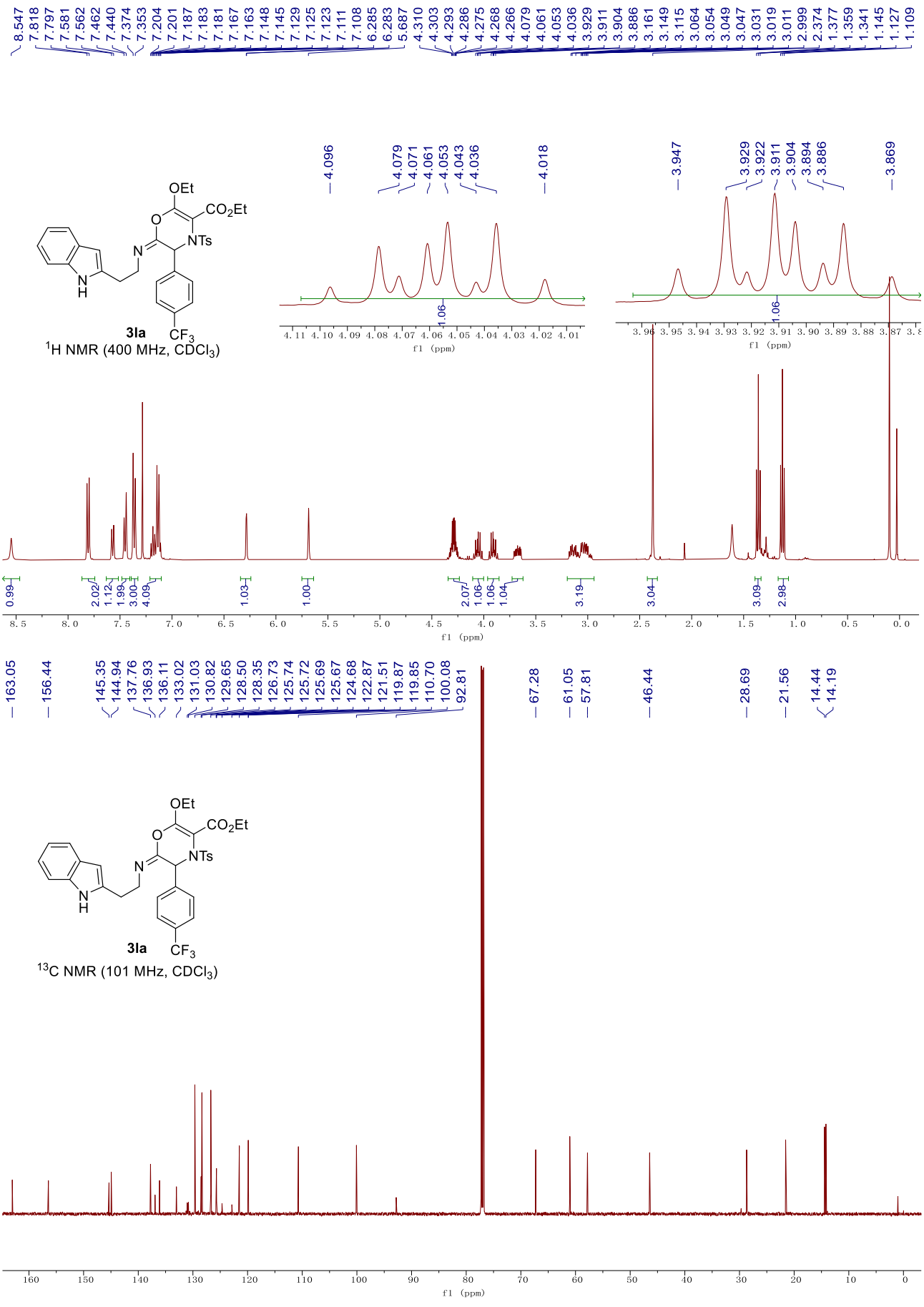
^{1}H NMR (400 MHz, $CDCl_3$)

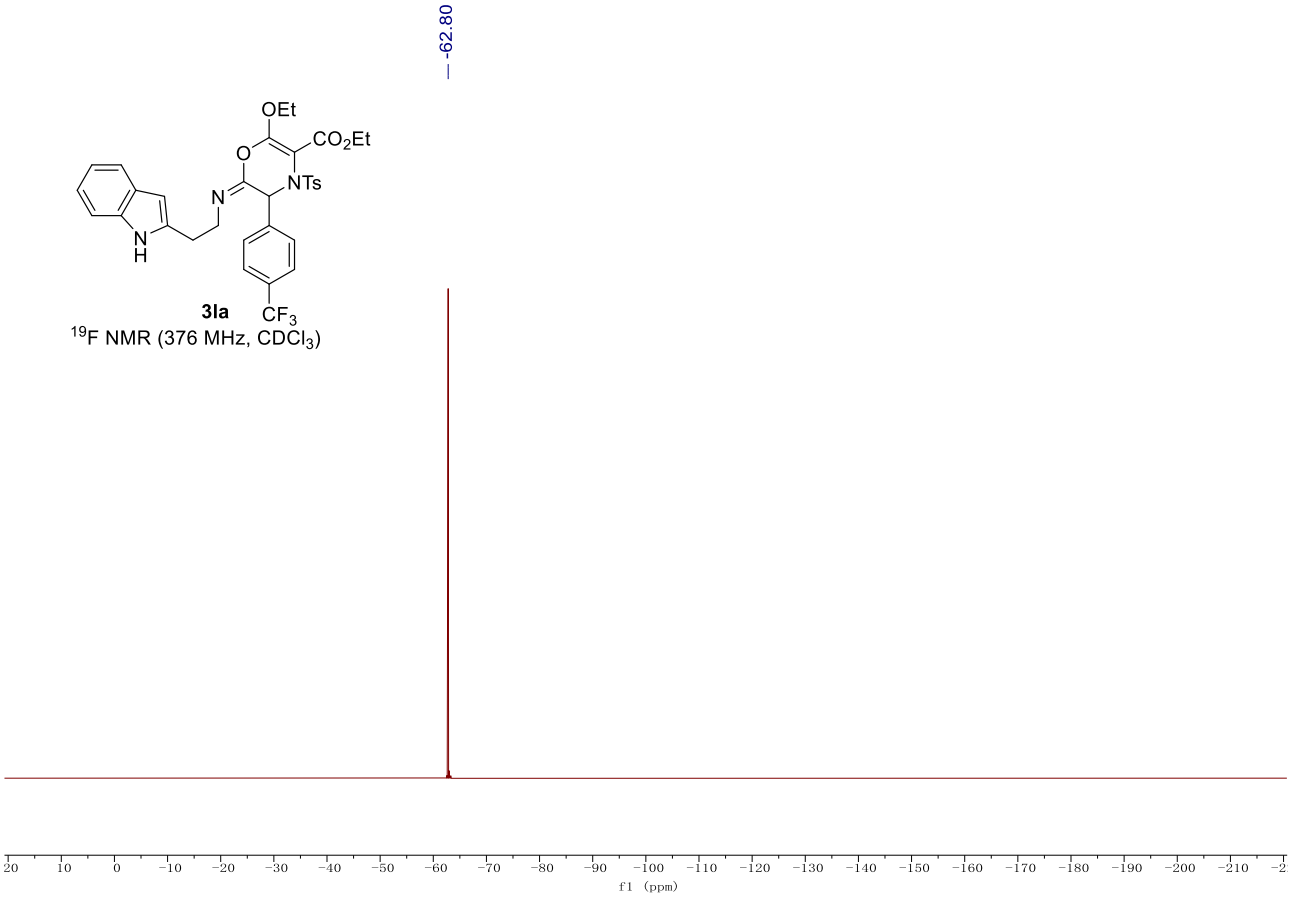




3ka

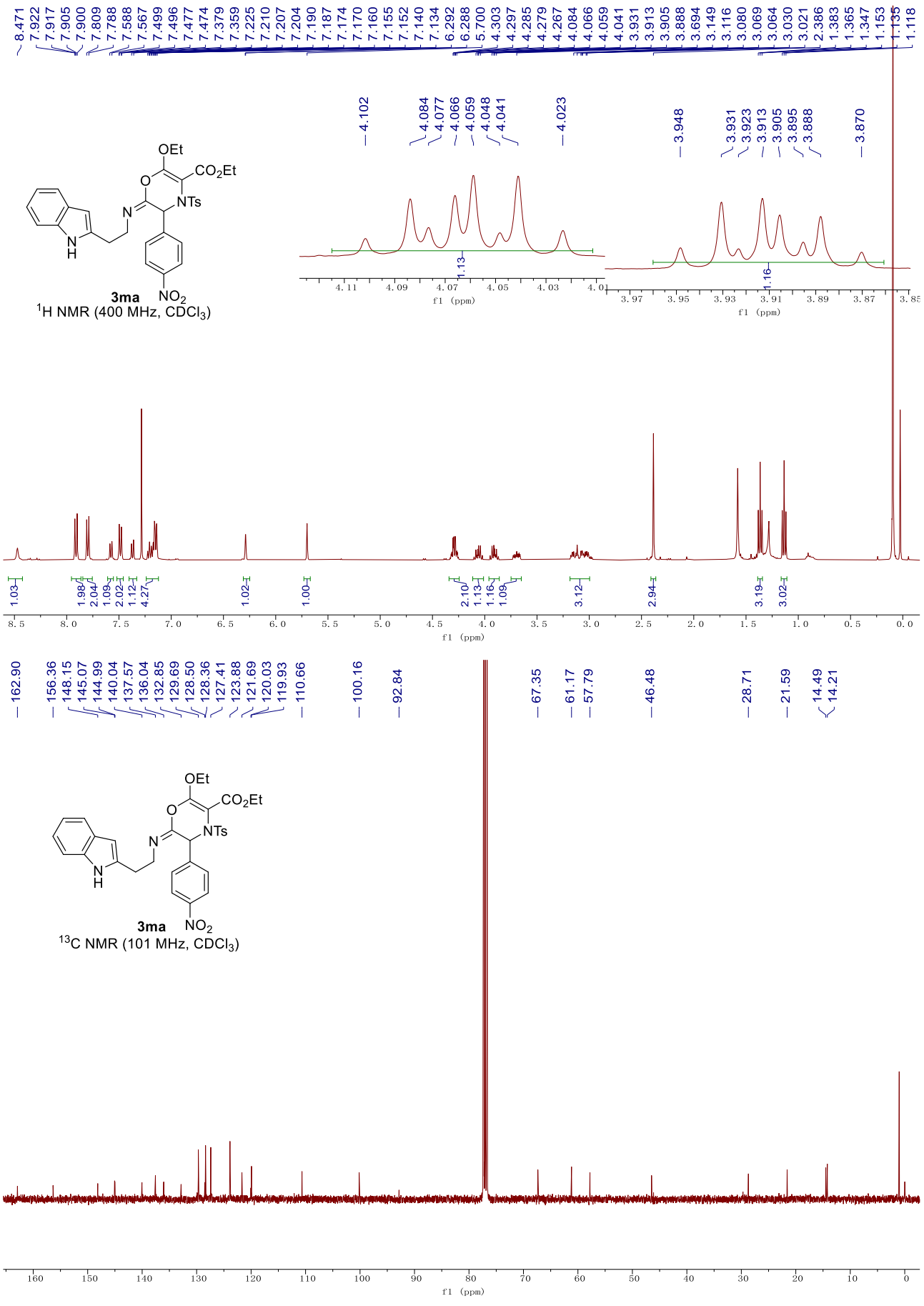
^{13}C NMR (101 MHz, $CDCl_3$)

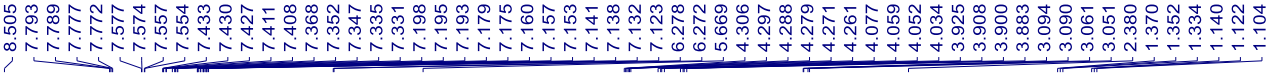

8.547 7.818 7.797 7.581 7.562 7.462 7.440 7.374 7.353 7.204 7.201 7.187 7.183 7.181 7.167 7.163 7.148 7.145 7.129 7.125 7.123 7.111 7.108 6.285 6.283 5.687 4.310 4.303 4.293 4.286 4.275 4.268 4.266 4.079 4.061 4.053 4.036 3.929 3.911 3.904 3.886 3.161 3.149 3.115 3.064 3.054 3.049 3.047 3.031 3.019 3.011 2.999 2.374 1.377 1.359 1.341 1.145 1.127 1.109
OEt
CO2Et
O
NTs
N
N
H
CF3
3la
1H NMR (400 MHz, CDCl3)
4.096 4.079 4.071 4.061 4.053 4.043 4.036 4.018
3.947 3.929 3.922 3.911 3.904 3.894 3.886 3.869
1.06
1.06
f1 (ppm)
0.99 2.02 1.12 1.99 3.00 4.09 1.03 1.00 2.07 1.06 1.04 3.19 3.04 3.09 2.98
f1 (ppm)
163.05 156.44 145.35 144.94 137.76 136.93 136.11 133.02 131.03 130.82 129.65 128.50 128.35 126.73 125.74 125.72 125.69 125.67 124.68 122.87 121.51 119.87 119.85 110.70 100.08 92.81 67.28 61.05 57.81 46.44 28.69 21.56 14.44 14.19
OEt
CO2Et
O
NTs
N
N
H
CF3
3la
13C NMR (101 MHz, CDCl3)
f1 (ppm)

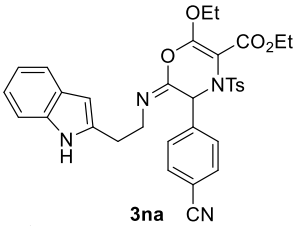


3la

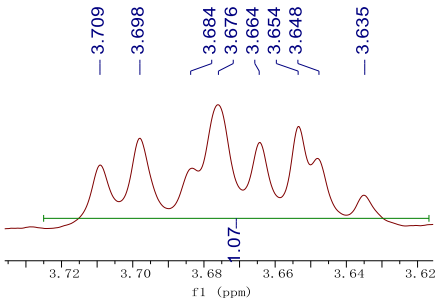
^{19}F NMR (376 MHz, $CDCl_3$)

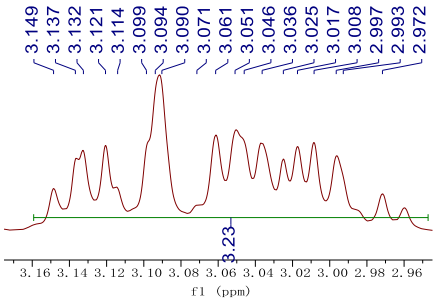

OEt
CO2Et
O
NTs
N
N
H
NO2
3ma
1H NMR (400 MHz, CDCl3)
f1 (ppm)
13C NMR (101 MHz, CDCl3)

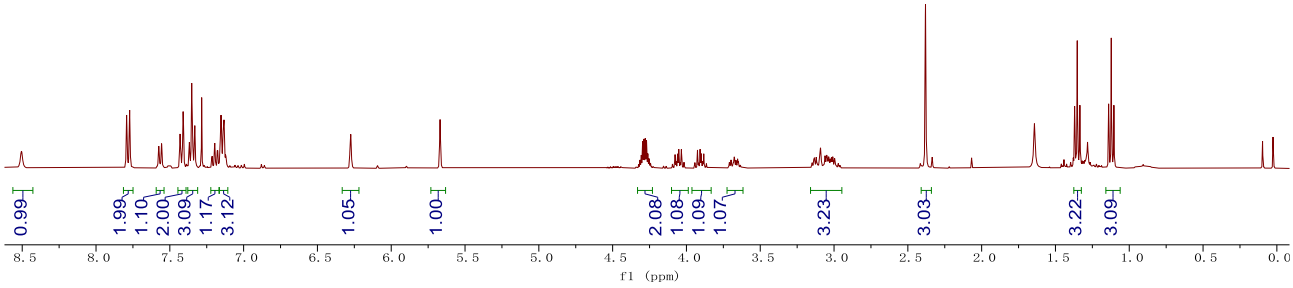


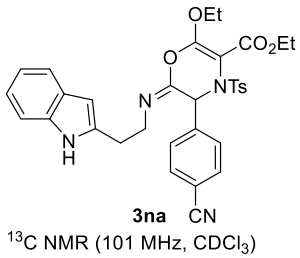


^{1}H NMR (400 MHz, $CDCl_3$)

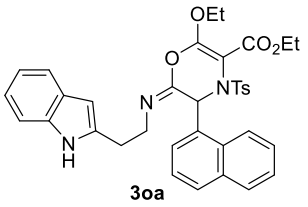






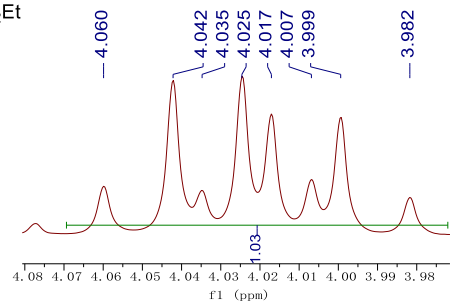


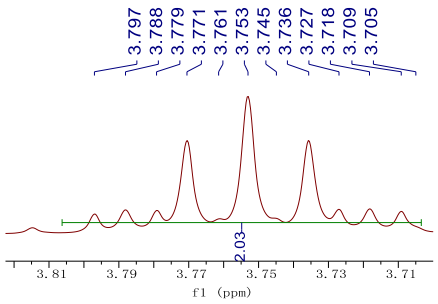
^{13}C NMR (101 MHz, $CDCl_3$)

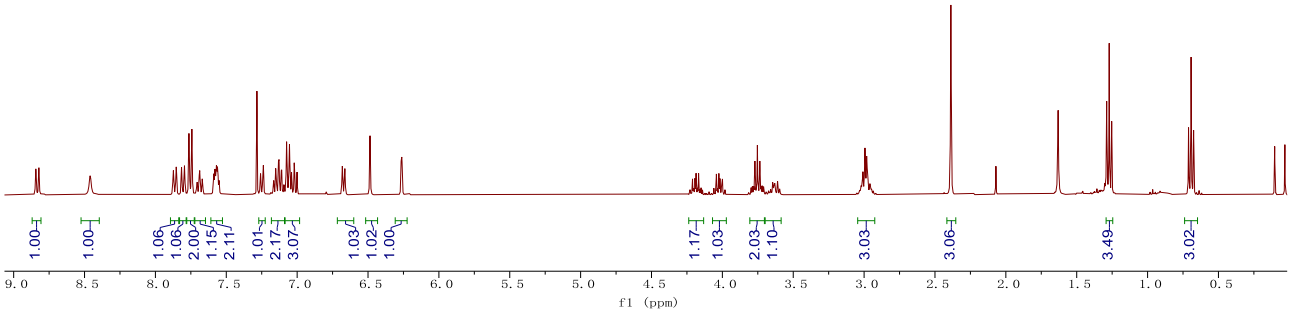


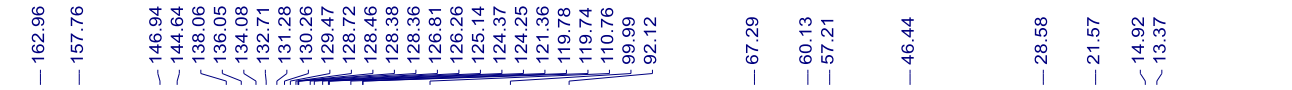
3oa

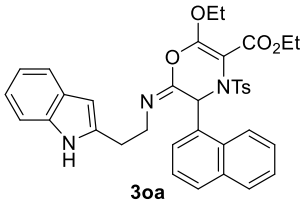
^{1}H NMR (400 MHz, $CDCl_3$)





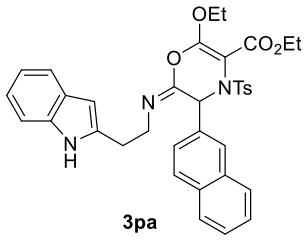






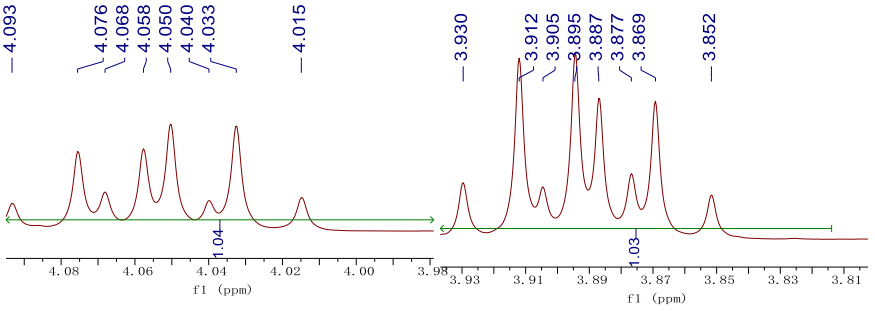
3oa

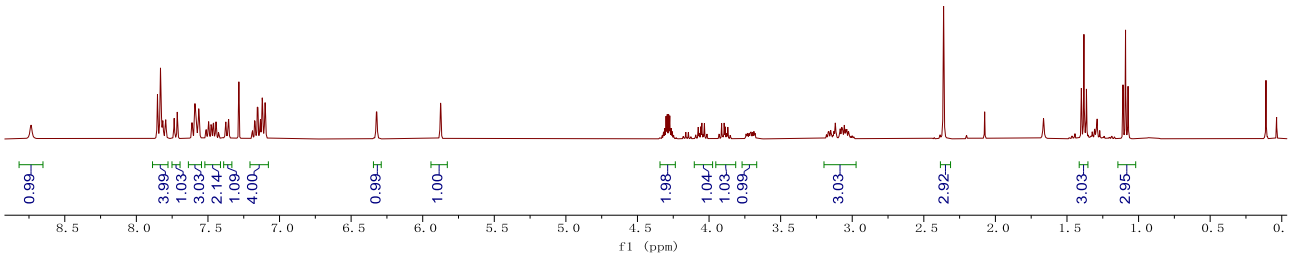
^{13}C NMR (101 MHz, $CDCl_3$)

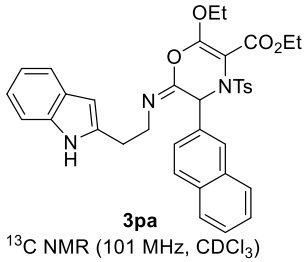


3pa

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

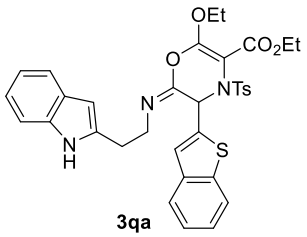






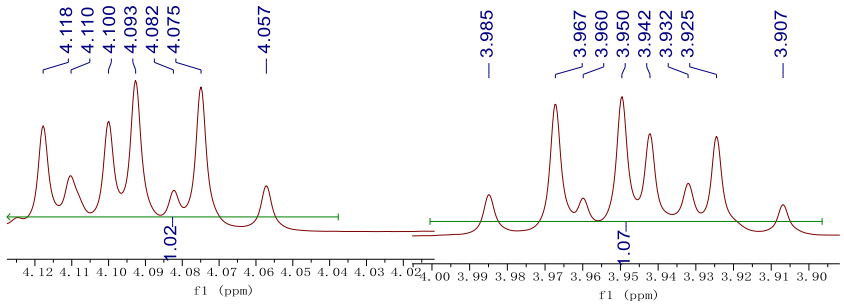
3pa

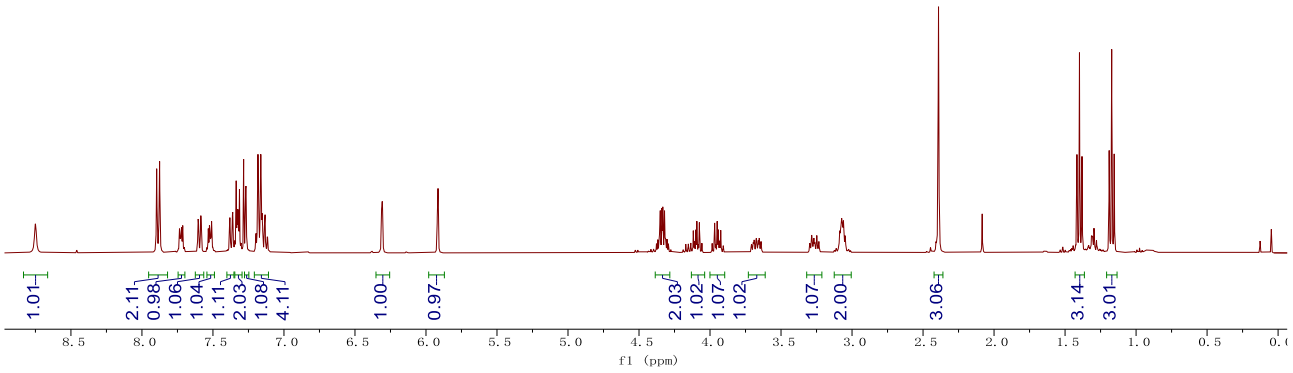
^{13}C NMR (101 MHz, $CDCl_3$)

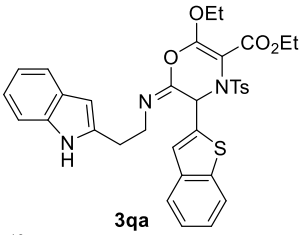


3qa

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

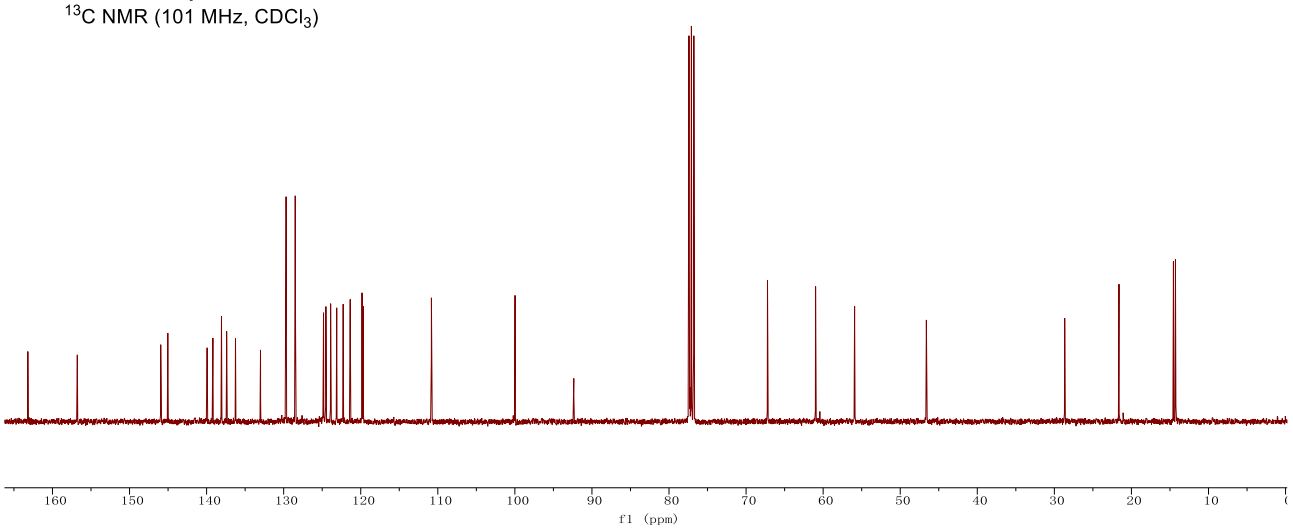


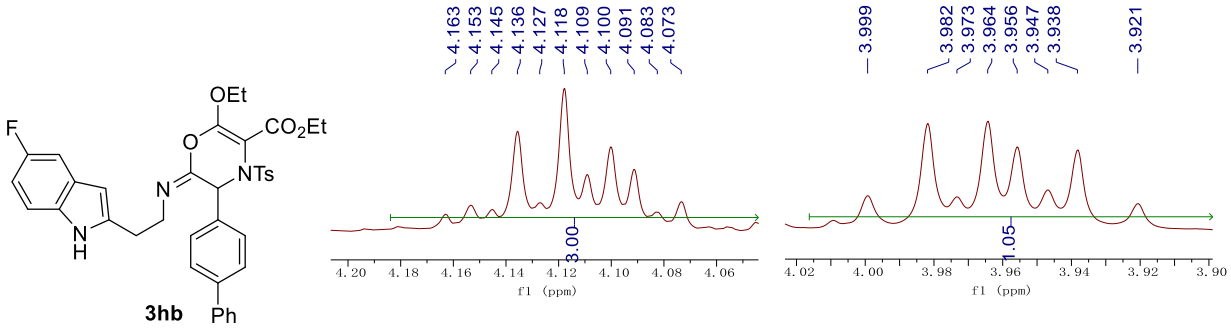




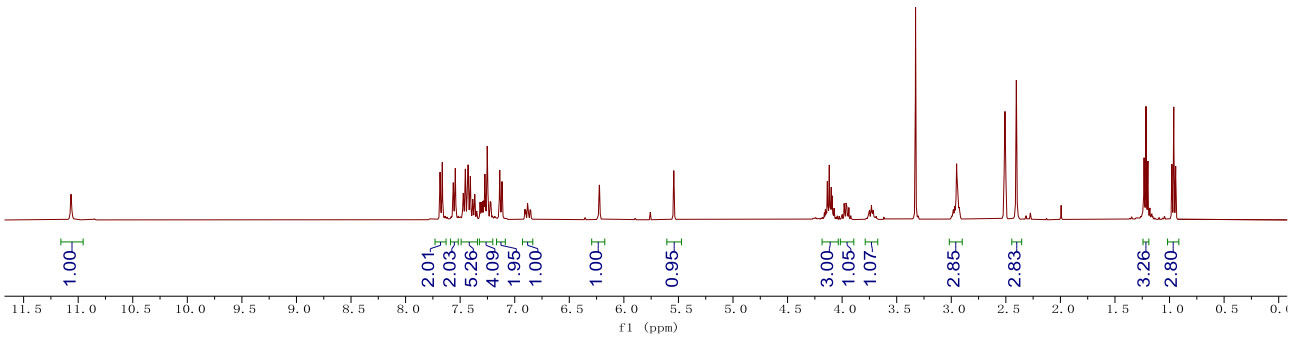
3qa

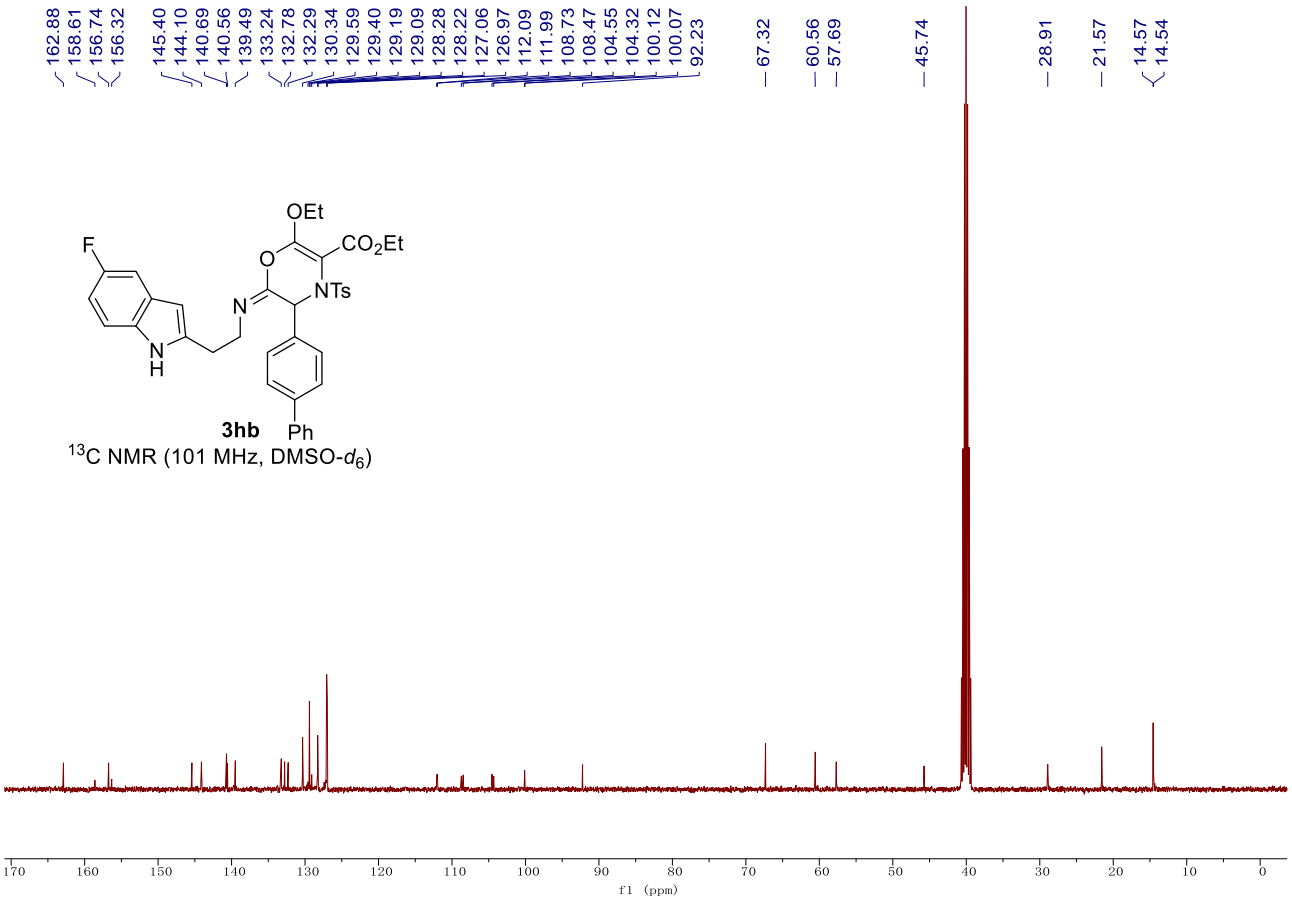
^{13}C NMR (101 MHz, $CDCl_3$)



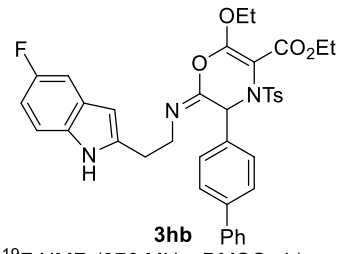


^{1}H NMR (400 MHz, DMSO-d_6)



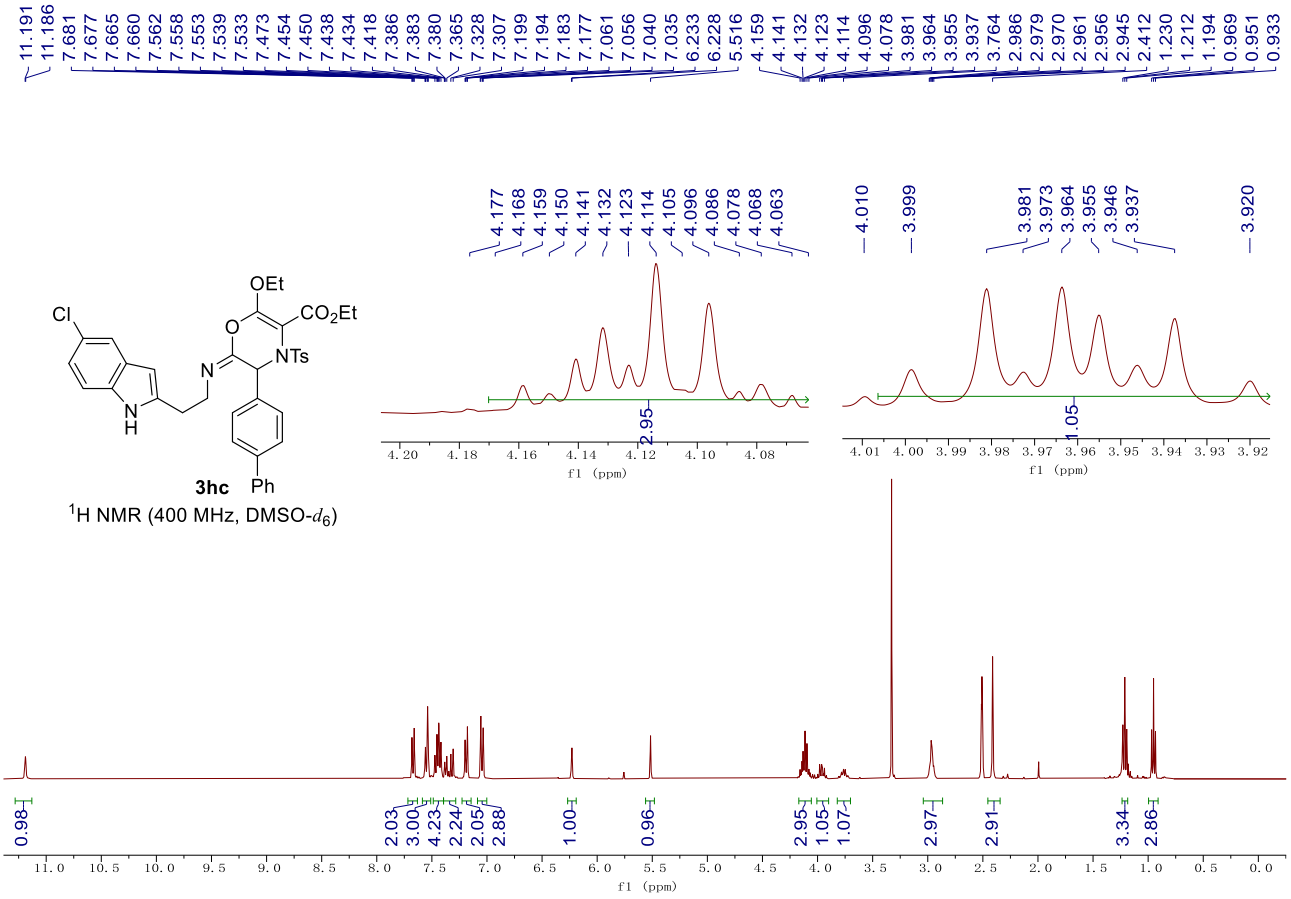


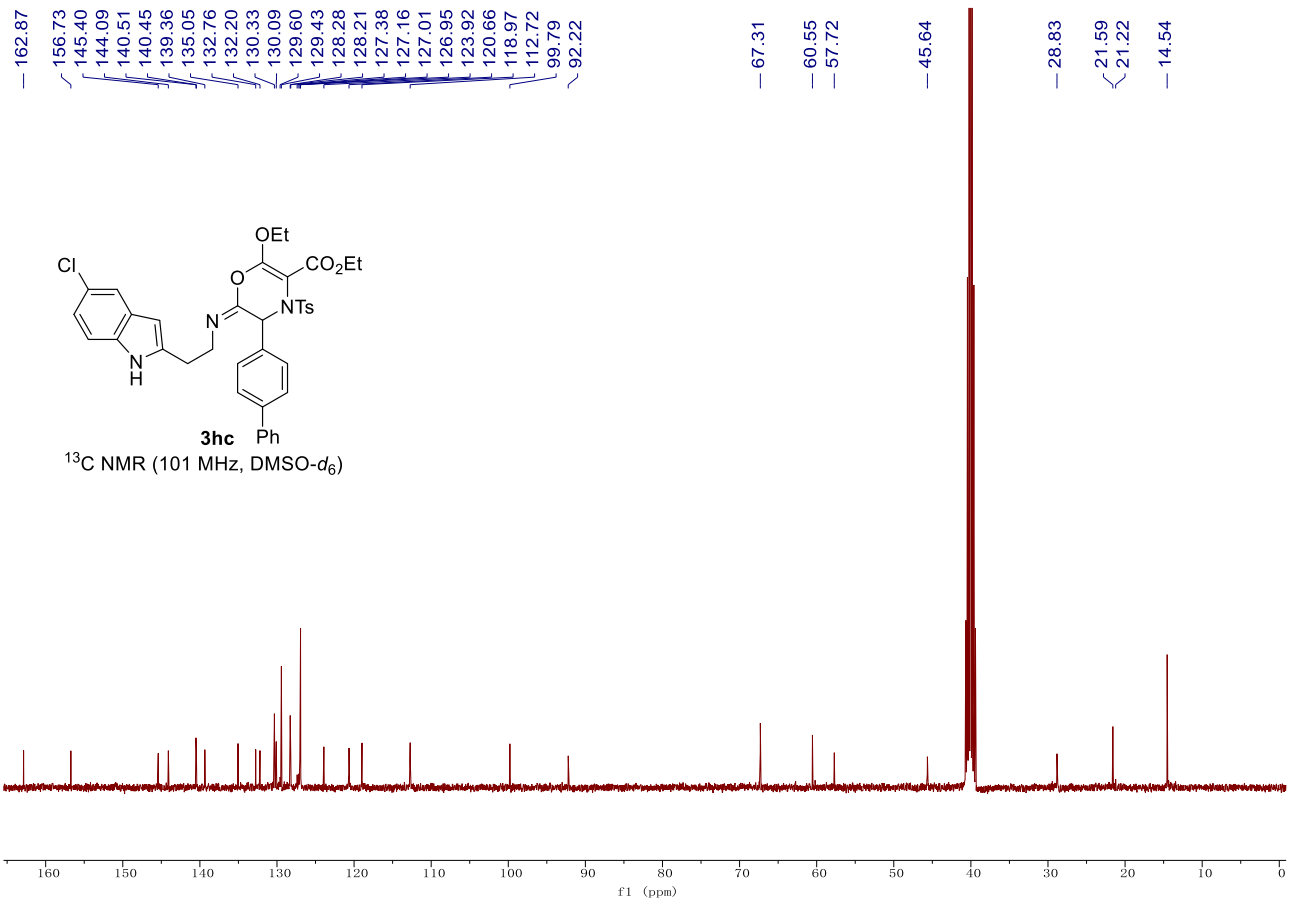
^{13}C NMR (101 MHz, DMSO-d_6)

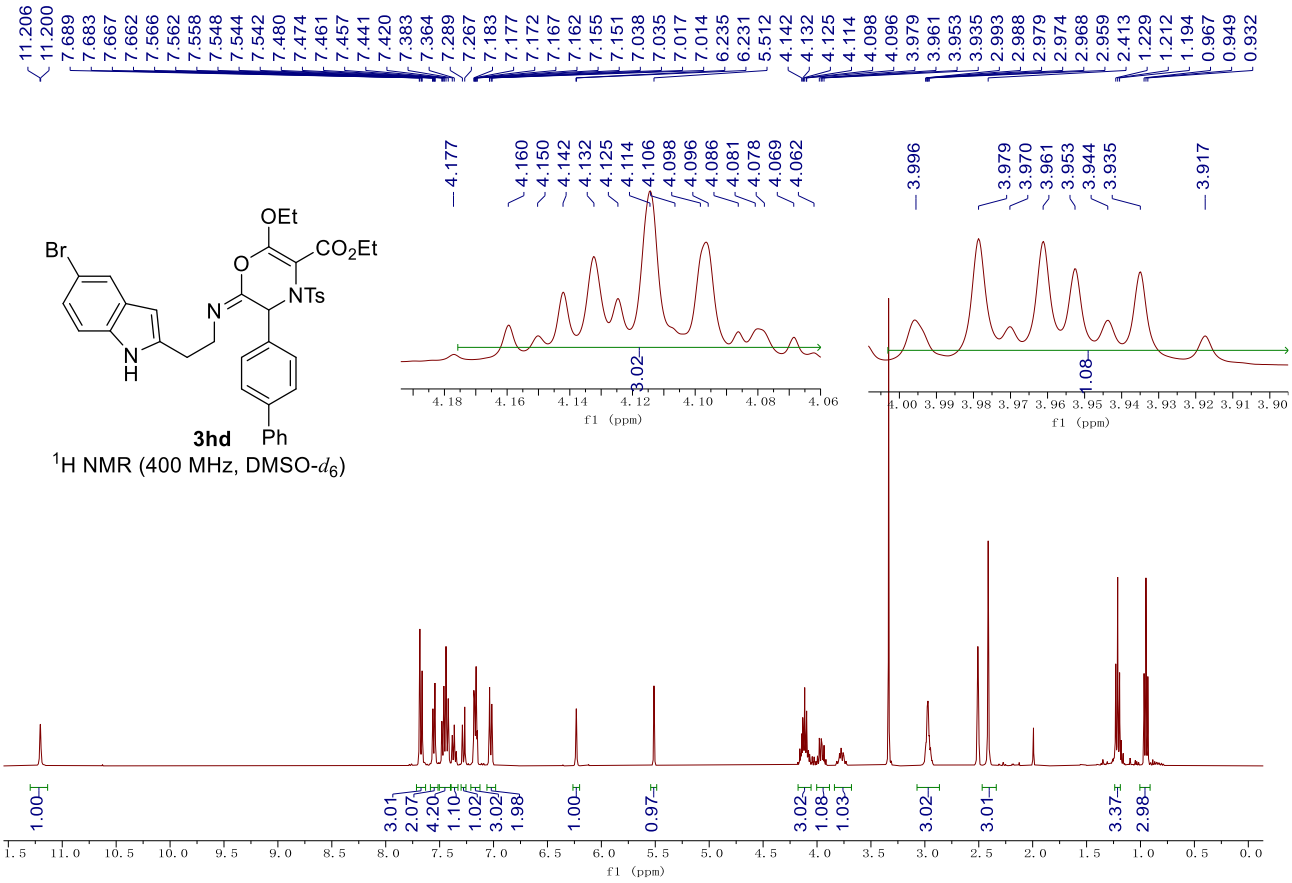


3hb

^{19}F NMR (376 MHz, DMSO-d_6)

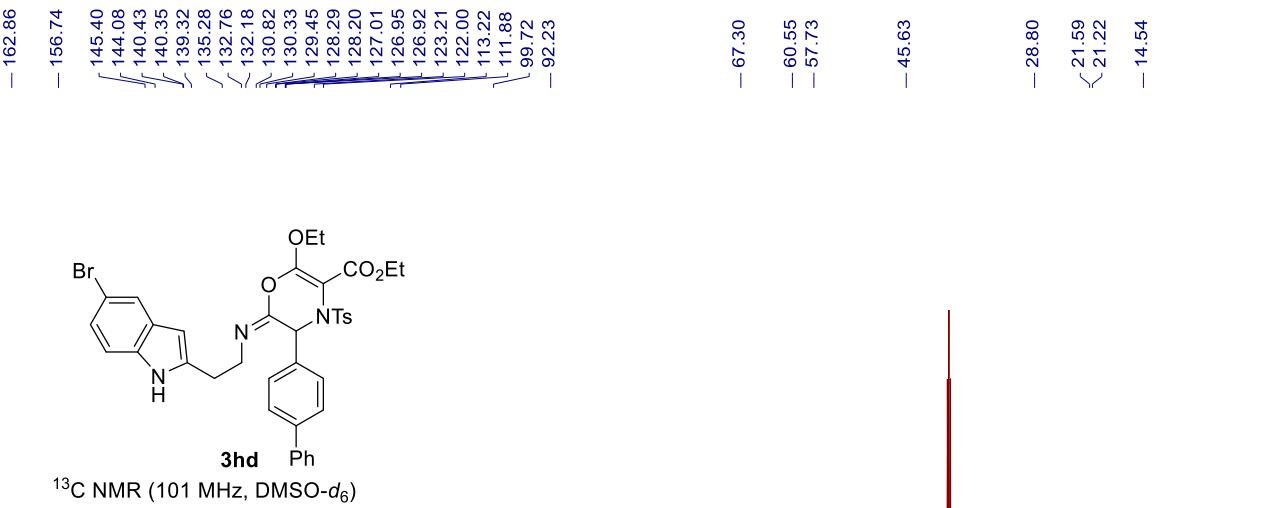

11.191
11.186
7.681
7.677
7.665
7.660
7.562
7.558
7.553
7.539
7.533
7.473
7.454
7.450
7.438
7.434
7.418
7.386
7.383
7.380
7.365
7.328
7.307
7.199
7.194
7.183
7.177
7.061
7.056
7.040
7.035
6.233
6.228
5.516
4.159
4.141
4.132
4.123
4.114
4.096
4.078
3.981
3.964
3.955
3.937
3.764
2.986
2.979
2.970
2.961
2.956
2.945
2.412
1.230
1.212
1.194
0.969
0.951
0.933
4.177
4.168
4.159
4.150
4.141
4.132
4.123
4.114
4.105
4.096
4.086
4.078
4.068
4.063
4.010
3.999
3.981
3.973
3.964
3.955
3.946
3.937
3.920
2.95
1.05
f1 (ppm)
OEt
CO2Et
Cl
O
N
NTs
N
H
Ph
3hc
1H NMR (400 MHz, DMSO-d6)
0.98
2.03
3.00
4.23
2.24
2.05
2.88
1.00
0.96
2.95
1.05
1.07
2.97
2.91
3.34
2.86
f1 (ppm)


162.87
156.73
145.40
144.09
140.51
140.45
139.36
135.05
132.76
132.20
130.33
130.09
129.60
129.43
128.28
128.21
127.38
127.16
127.01
126.95
123.92
120.66
118.97
112.72
99.79
92.22
67.31
60.55
57.72
45.64
28.83
21.59
21.22
14.54
OEt
CO2Et
Cl
O
N
NTs
N
H
Ph
3hc
13C NMR (101 MHz, DMSO-d6)
f1 (ppm)



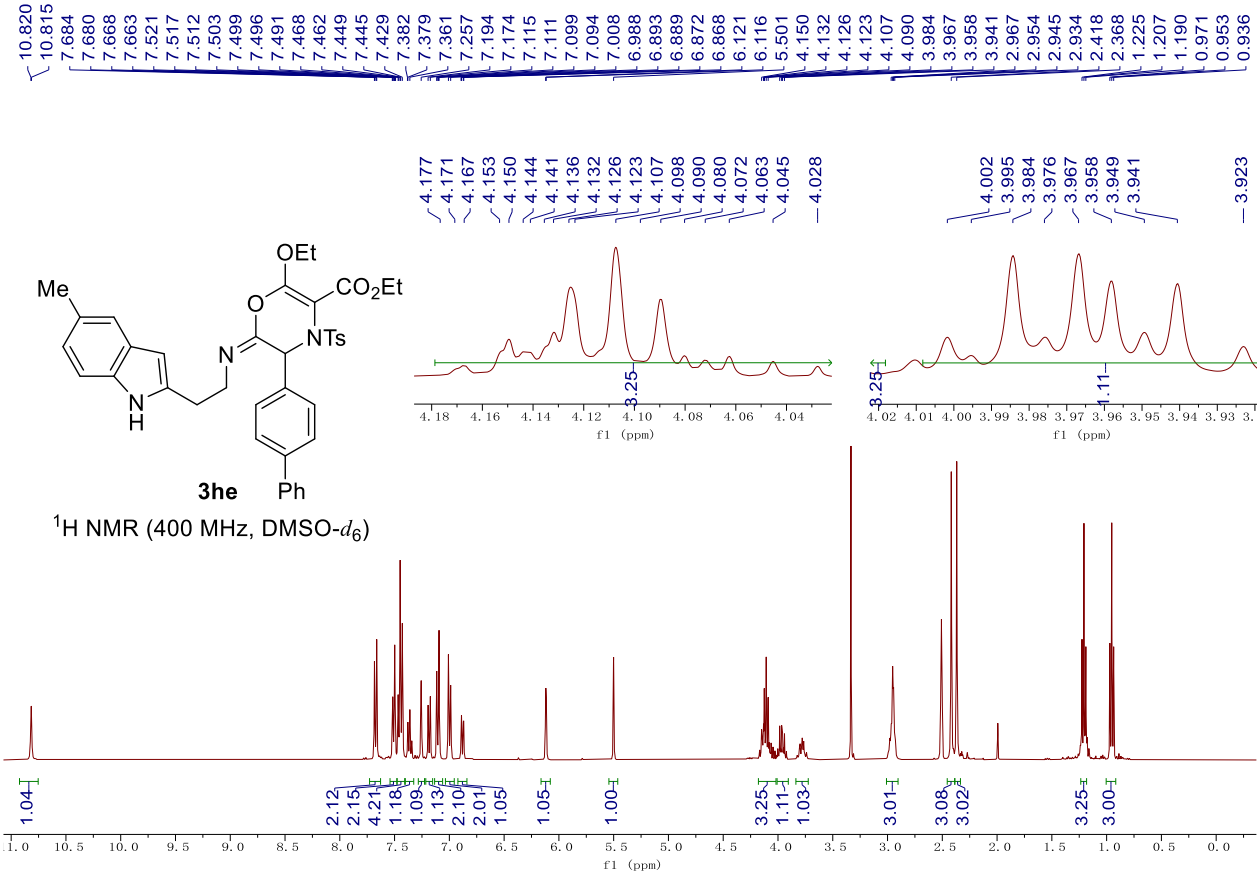
3hd

^{1}H NMR (400 MHz, DMSO-d_6)



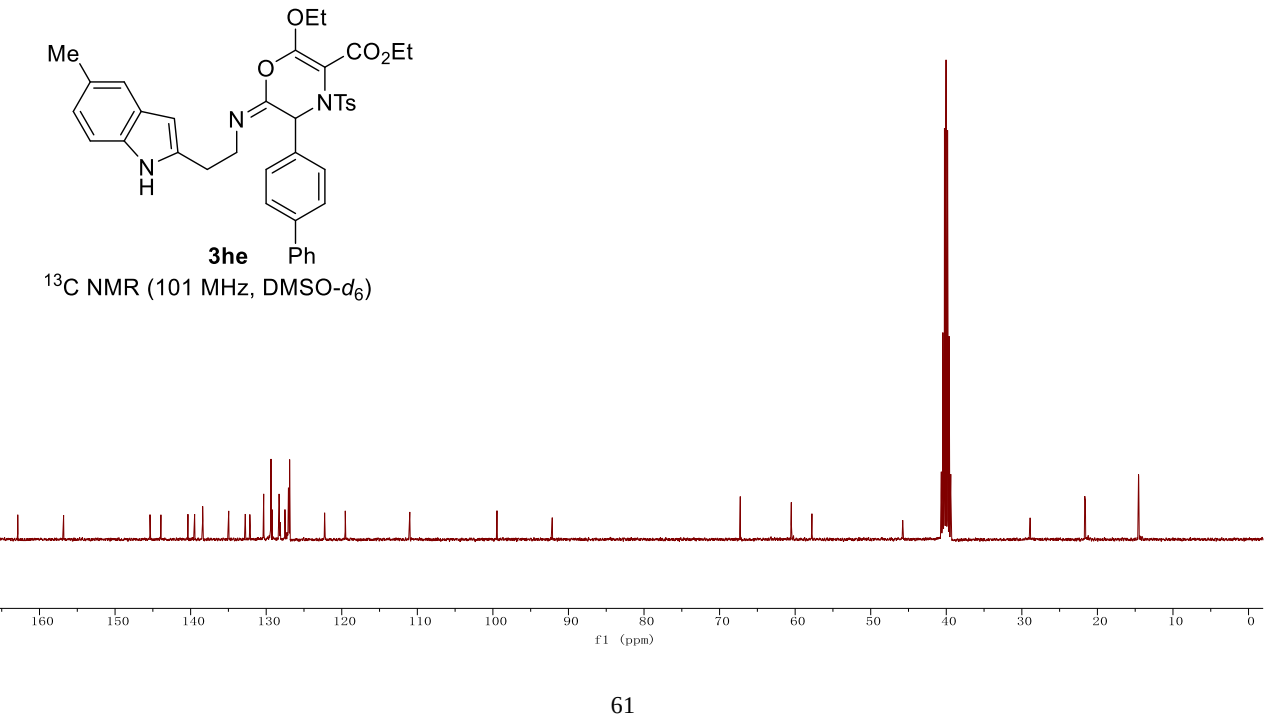
3hd

^{13}C NMR (101 MHz, DMSO-d_6)



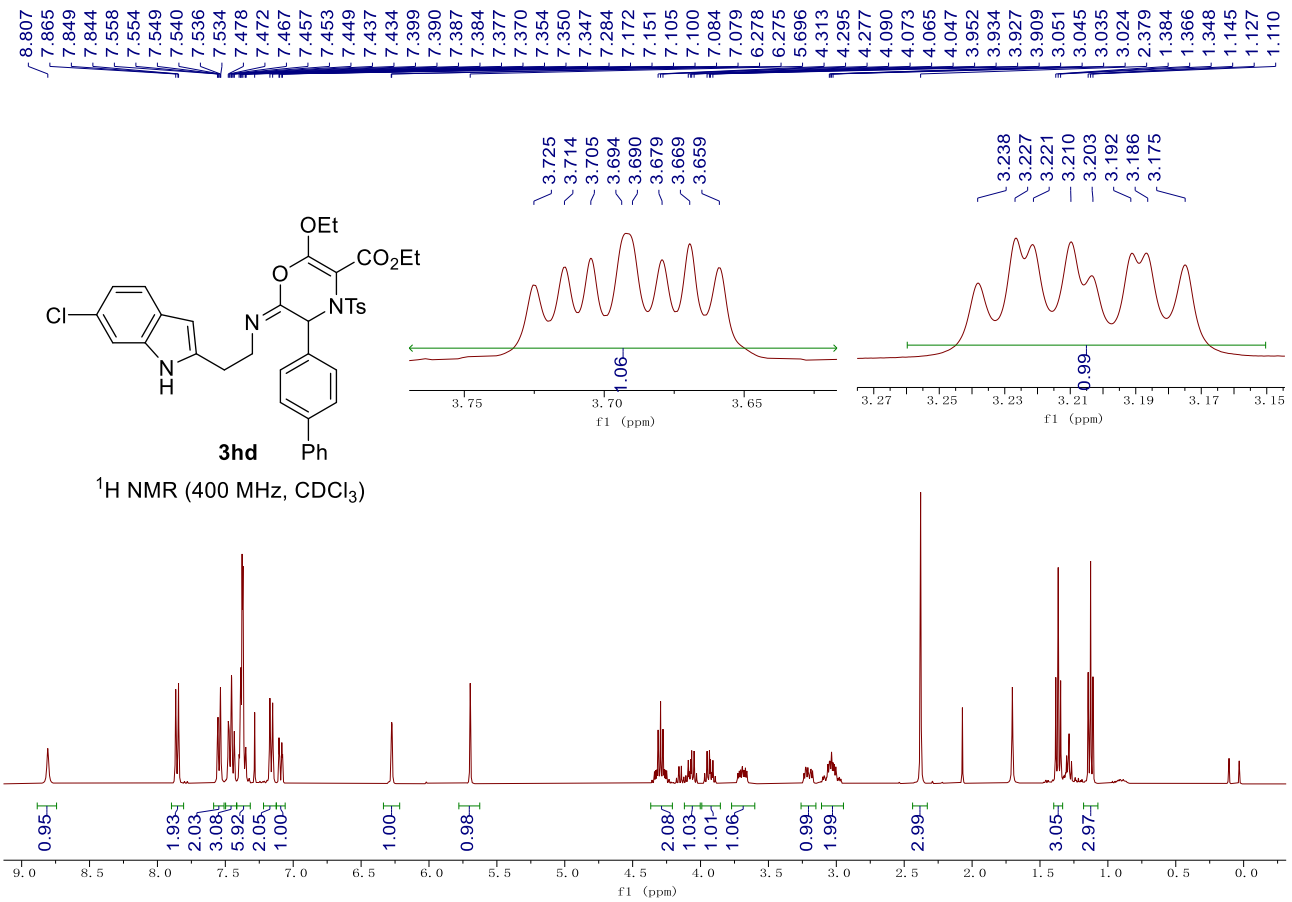
3he Ph

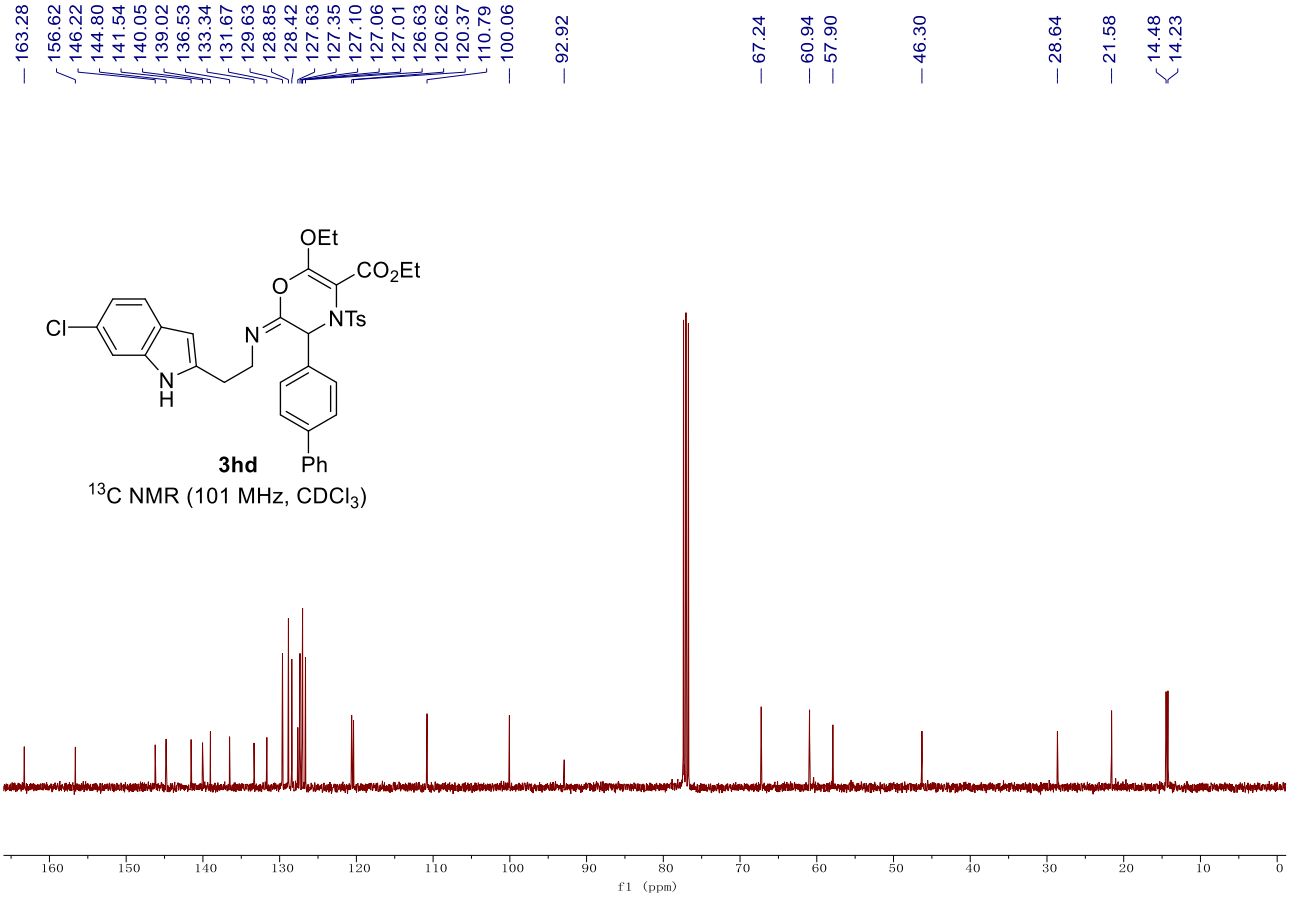
^{1}H NMR (400 MHz, DMSO-d_6)

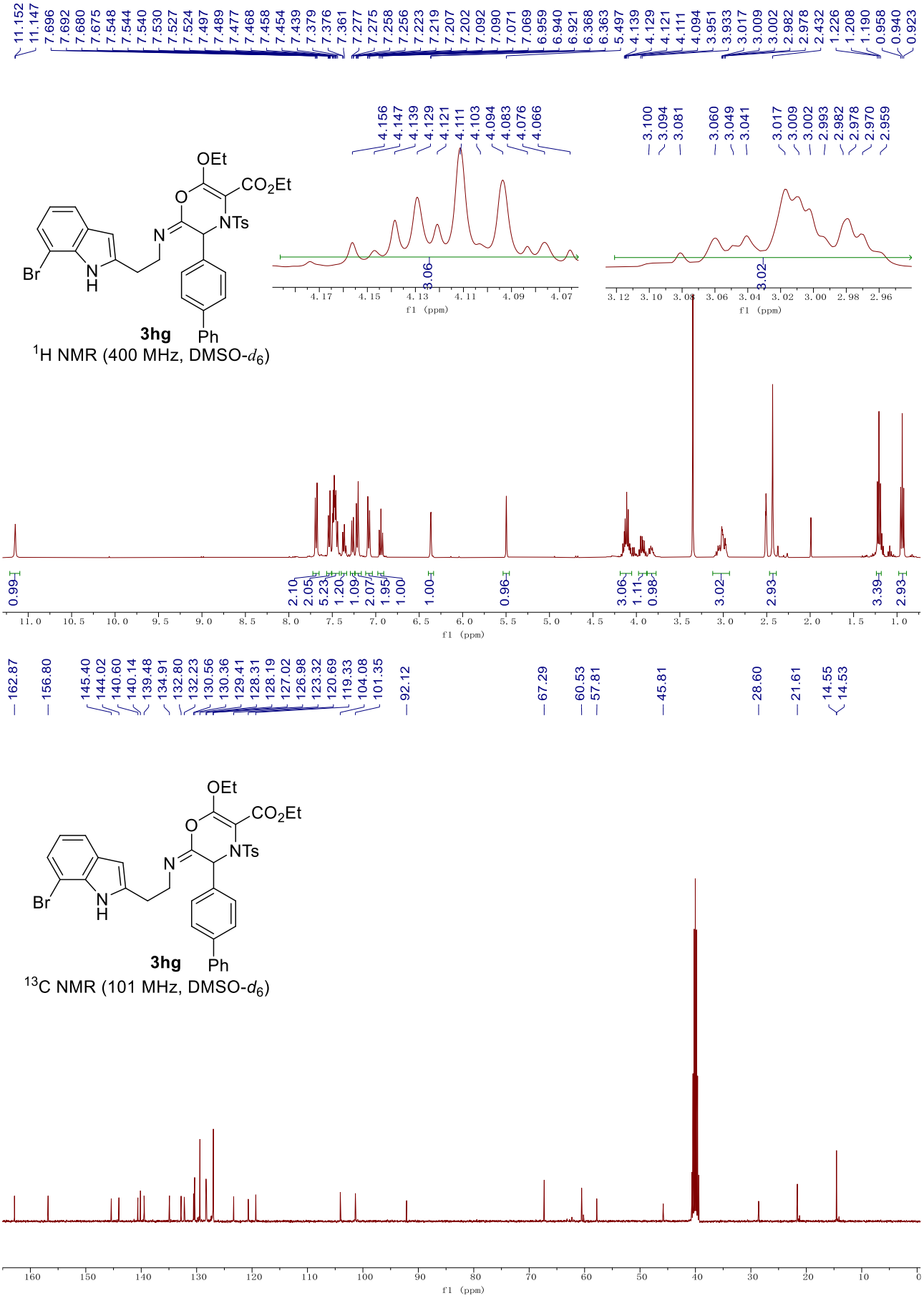


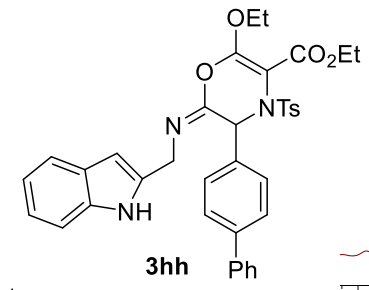
3he Ph

^{13}C NMR (101 MHz, DMSO-d_6)


8.807 7.865 7.849 7.844 7.558 7.554 7.549 7.540 7.536 7.534 7.478 7.472 7.467 7.457 7.453 7.449 7.437 7.434 7.399 7.390 7.387 7.384 7.377 7.370 7.354 7.350 7.347 7.284 7.172 7.151 7.105 7.100 7.084 7.079 6.278 6.275 5.696 4.313 4.295 4.277 4.090 4.073 4.065 4.047 3.952 3.934 3.927 3.909 3.051 3.045 3.035 3.024 2.379 1.384 1.366 1.348 1.145 1.127 1.110
3.725 3.714 3.705 3.694 3.690 3.679 3.669 3.659
3.238 3.227 3.221 3.210 3.203 3.192 3.186 3.175
OEt
CO2Et
O
NTs
N
Cl
N
H
Ph
3hd
1.06
0.99
3.75 3.70 3.65
3.27 3.25 3.23 3.21 3.19 3.17 3.15
f1 (ppm)
1H NMR (400 MHz, CDCl3)
0.95 1.93 2.03 3.08 5.92 2.05 1.00 1.00 0.98 2.08 1.03 1.01 1.06 0.99 1.99 2.99 3.05 2.97
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

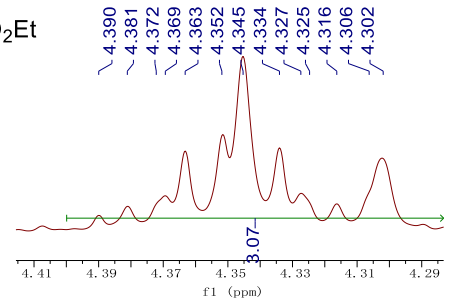

163.28 156.62 146.22 144.80 141.54 140.05 139.02 136.53 133.34 131.67 129.63 128.85 128.42 127.63 127.35 127.10 127.06 127.01 126.63 120.62 120.37 110.79 100.06 92.92 67.24 60.94 57.90 46.30 28.64 21.58 14.48 14.23
OEt
CO2Et
O
NTs
N
Cl
N
H
Ph
3hd
13C NMR (101 MHz, CDCl3)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

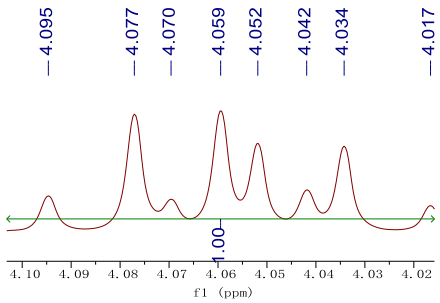

11.152
11.147
7.696
7.692
7.680
7.675
7.548
7.544
7.540
7.530
7.527
7.524
7.497
7.489
7.477
7.468
7.458
7.454
7.439
7.379
7.376
7.361
7.277
7.275
7.258
7.256
7.223
7.219
7.207
7.202
7.092
7.090
7.071
7.069
6.959
6.940
6.921
6.368
6.363
5.497
4.139
4.129
4.121
4.111
4.094
3.951
3.933
3.017
3.009
3.002
2.982
2.978
2.432
1.226
1.208
1.190
0.958
0.940
0.923
OEt
CO2Et
O
NTs
N
Br
N
H
Ph
3hg
1H NMR (400 MHz, DMSO-d6)
4.156
4.147
4.139
4.129
4.121
4.111
4.103
4.094
4.083
4.076
4.066
3.06
f1 (ppm)
3.100
3.094
3.081
3.060
3.049
3.041
3.017
3.009
3.002
2.993
2.982
2.978
2.970
2.959
3.02
f1 (ppm)
0.99
2.10
2.05
5.23
1.20
1.09
2.07
1.95
1.00
1.00
0.96
3.06
1.11
0.98
3.02
2.93
3.39
2.93
f1 (ppm)
162.87
156.80
145.40
144.02
140.60
140.14
139.48
134.91
132.80
132.23
130.56
130.36
129.41
128.31
128.19
127.02
126.98
123.32
120.69
119.33
104.08
101.35
92.12
67.29
60.53
57.81
45.81
28.60
21.61
14.55
14.53
OEt
CO2Et
O
NTs
N
Br
N
H
Ph
3hg
13C NMR (101 MHz, DMSO-d6)
f1 (ppm)

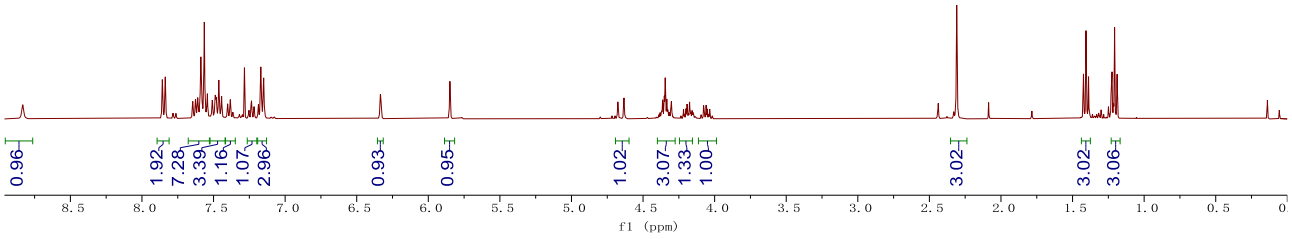


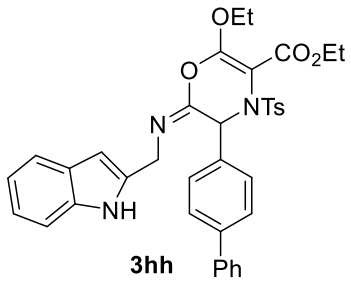
3hh

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



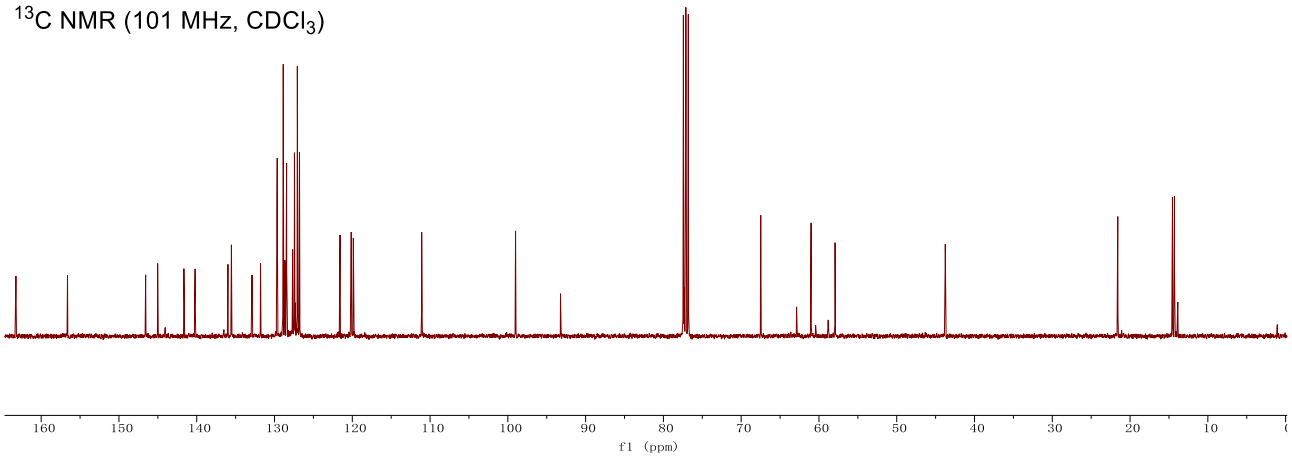


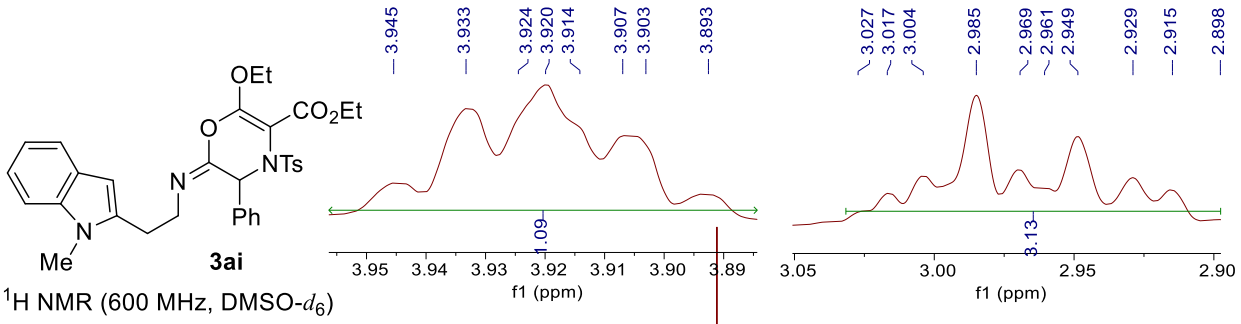




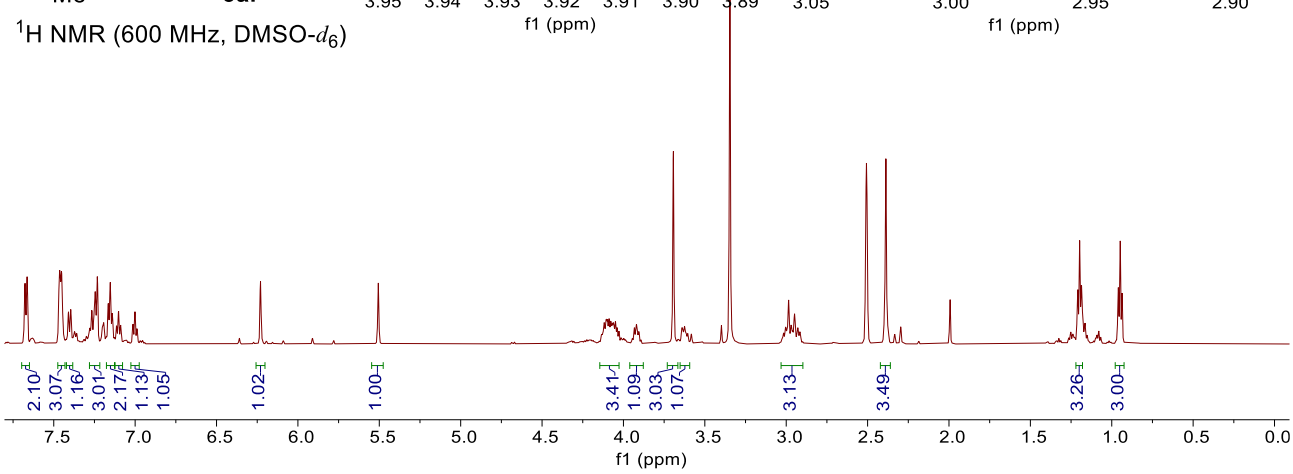
3hh

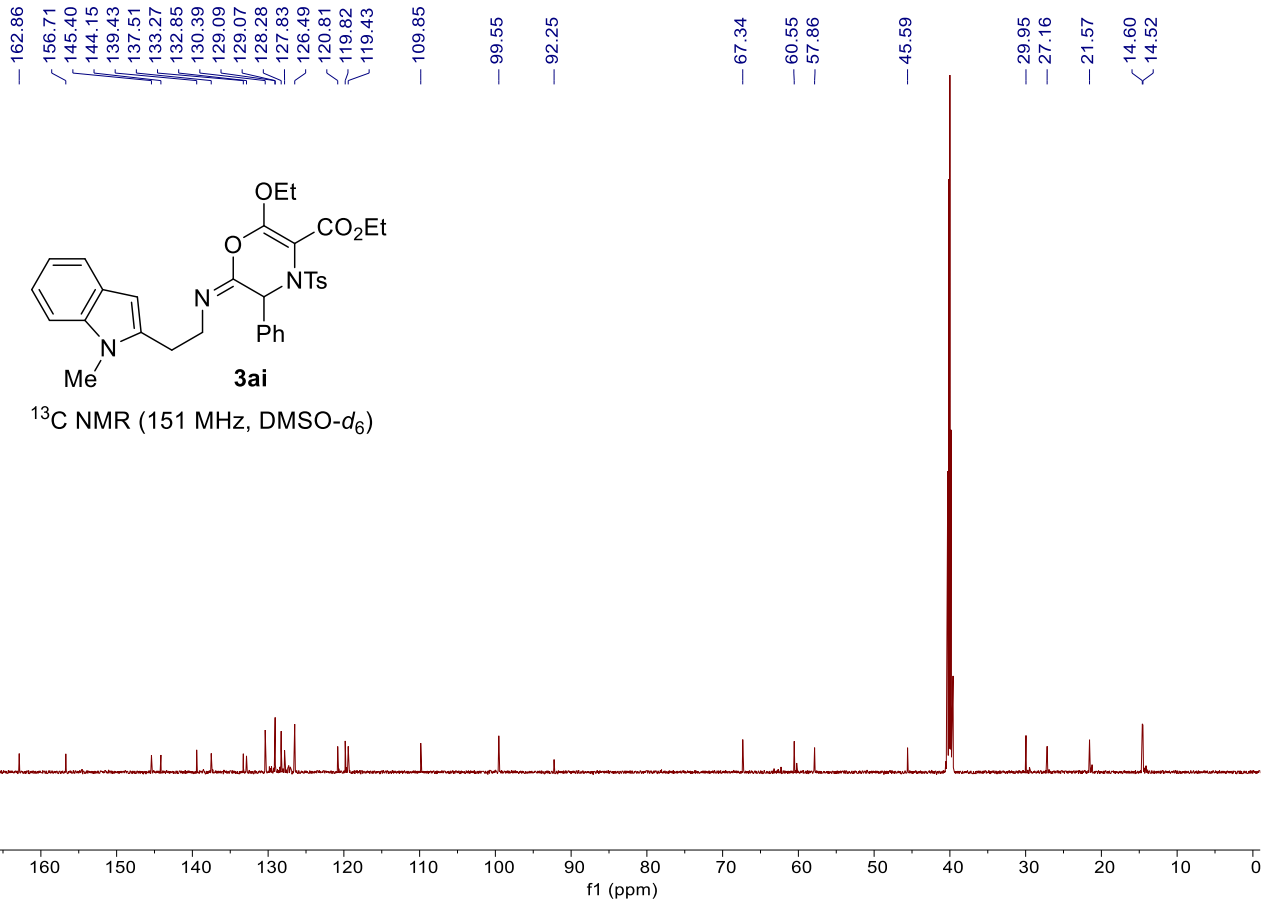
^{13}C NMR (101 MHz, $CDCl_3$)



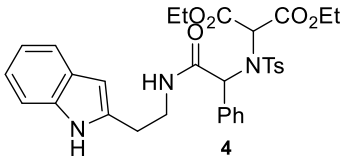


^{1}H NMR (600 MHz, DMSO-d_6)



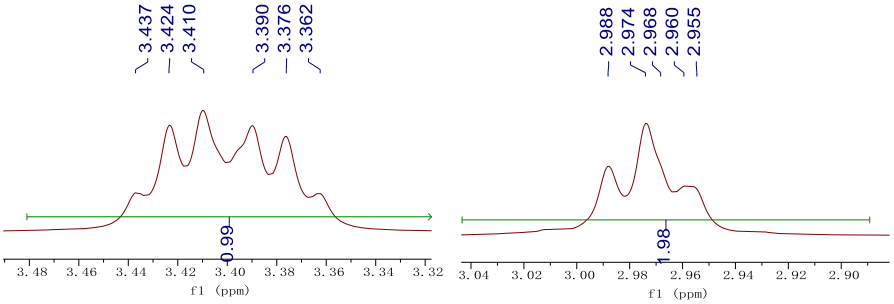


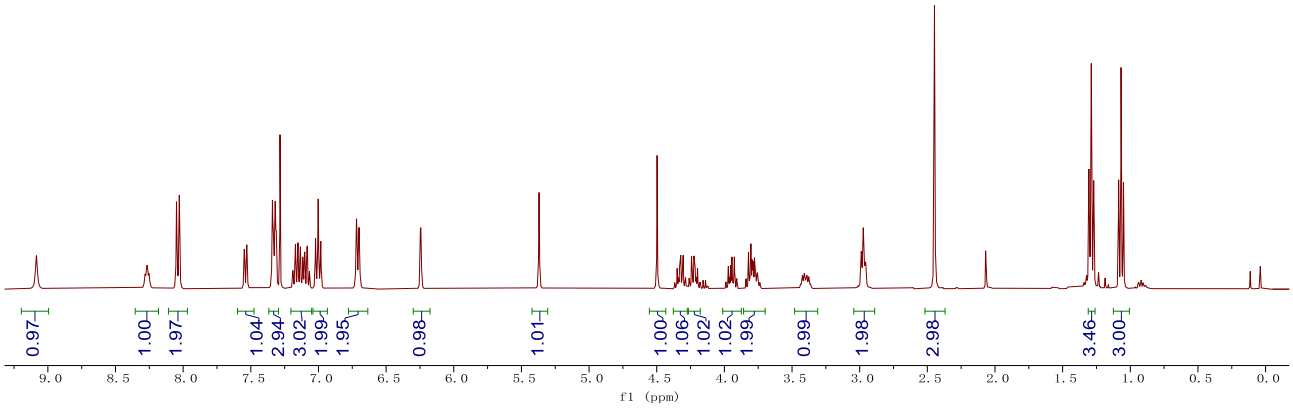
^{13}C NMR (151 MHz, DMSO-d_6)

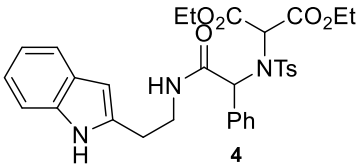


4

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

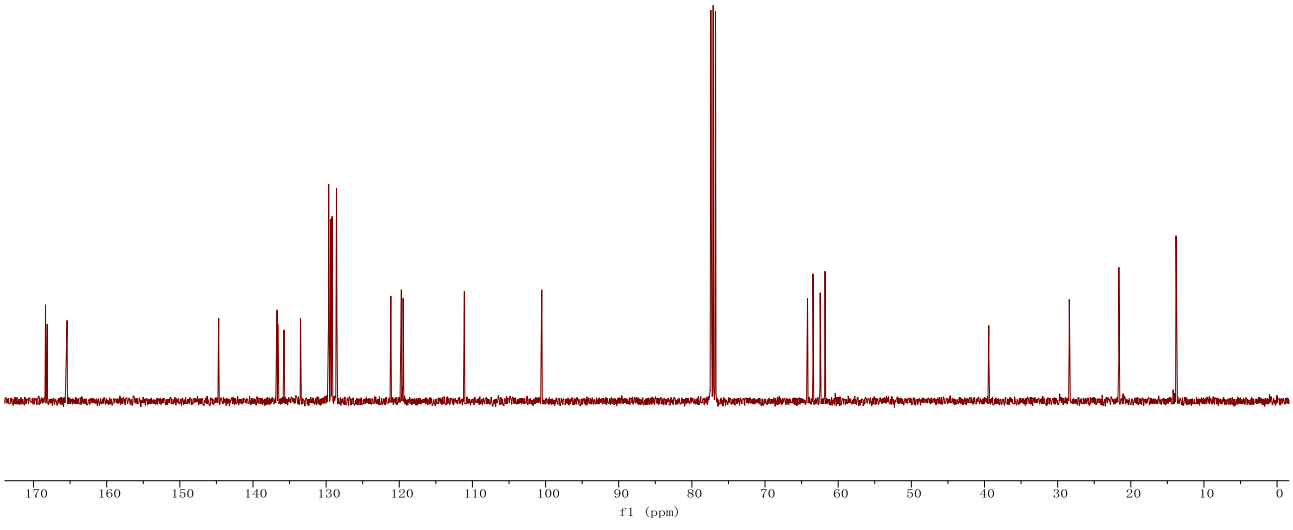


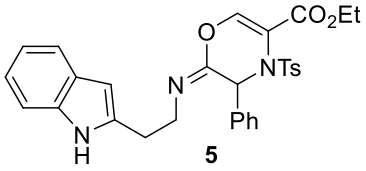




4

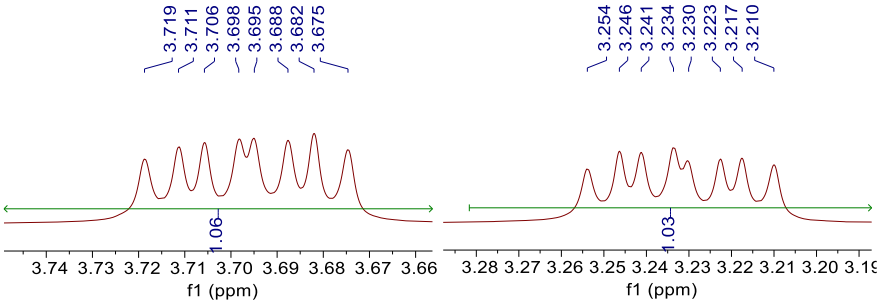
^{13}C NMR (101 MHz, $CDCl_3$)

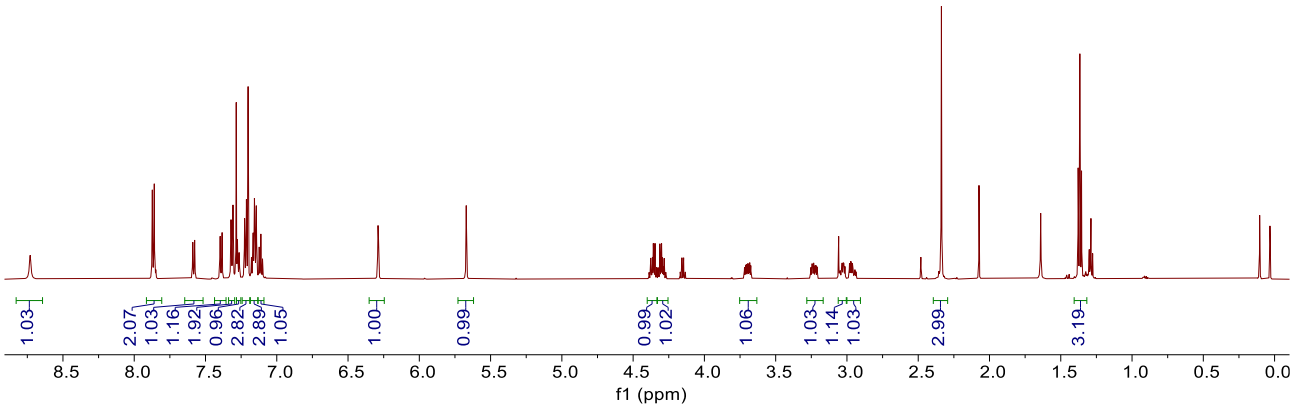


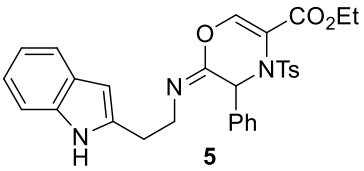


5

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







5

^{13}C NMR (151 MHz, $CDCl_3$)

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