Electronic Supplementary Material (ESI) for ChemComm.
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Palladium-catalyzed Interannular C-H Amination of Biaryl Amines

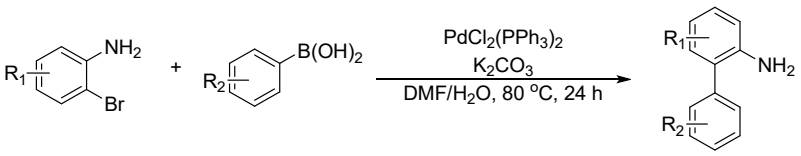
Supporting Information

General Information and Procedure

1. General Information

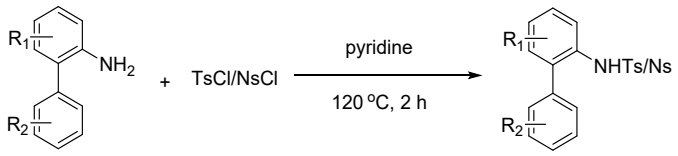
$Pd(OAc)_2$ (Energy Chemical) were purchased from above mentioned company and used without additional purification. Other chemical reagents were commercially available and directly used without any further purification.^{1}H NMR spectra were recorded at 400 MHz and 500 MHz NMR spectrometers using TMS as an internal standard, ^{13}C NMR spectra were recorded at 100 MHz and 125 MHz NMR spectrometers using TMS as an internal standard, and were fully decoupled by broad band proton decoupling. ^{19}F NMR spectra were recorded at a 376 MHz NMR spectrometer using TMS as an internal standard and were fully decoupled by broad band proton decoupling. Data for ^{1}H NMR are reported as follows: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and integration. Mass spectra were obtained on a Bruker Apex IV RTMS.

2. General Procedure for the Preparation of Amine Substrates



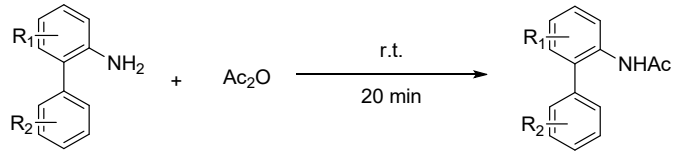
A

Aryl boronic acids (1.2-1.5 equiv.), K_2CO_3 (2.0-4.0 equiv.), and $PdCl_2(PPh_3)_2$ (5%-10% mol%) were added to DMF/H_2O (v/v 13:3) in a flame-dried round bottom flask containing 2-bromoanilines. The resulting mixture was stirred at 80 °C for 24 h under a nitrogen atmosphere. After completion of the reaction, the reaction mixture was allowed to cool down to room temperature and was extracted several times with CH_2Cl_2. The combined organic layer was washed twice with sat. NaCl and dried over anhydrous Na_2SO_4. The organic layer was then concentrated under vacuum, and the crude residue was purified using flash silica gel column chromatography (hexanes/EtOAc) to produce the coupling product 2-aminobiaryls **A**.[1]



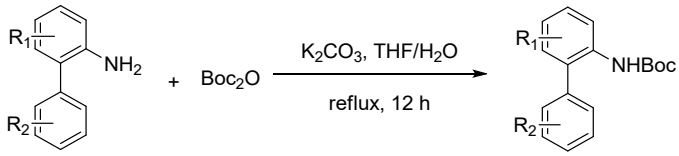
A **1** (Ts)/**C**(Ns)

To a flame-dried round-bottom flask containing the solution of **A** in pyridine was added 4-methylbenzenesulfonyl chloride or 4-nitrobenzenesulfonyl chloride (1.5 equiv.) and the resulting mixtures were refluxed at 120 °C for 2 h. After the completion of the reaction, the reaction mixture was allowed to cool to room temperature and extracted with CH_2Cl_2 for several times. The combined organic layer was washed with saturated NaCl for two times and dried over anhydrous Na_2SO_4. The organic layer was then concentrated under vacuum, and the crude residue was purified by silica gel column chromatography (hexanes/EtOAc) to afford **1**/**C**.[2]



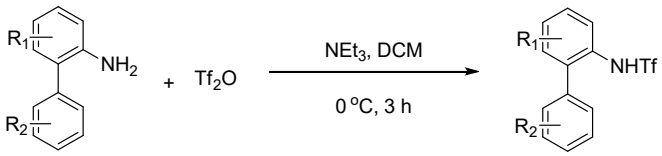
A **D**

A was dissolved in Ac_2O and was stirred at room temperature for 20 min. The reaction mixture was added dropwise to an aqueous 4 M K_2CO_3-solution and the formed precipitate was filtered and washed with H_2O until the filtrate became pH neutral. Drying in vacuo gave **D** as an off-white solid.[3]



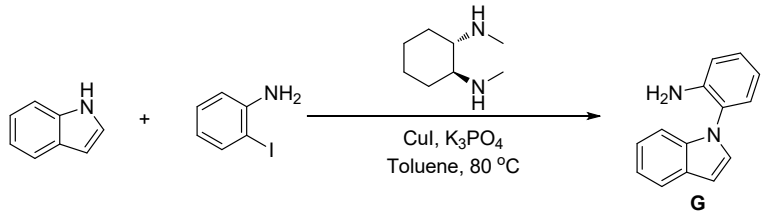
A **E**

To a mixture of **A** and K_2CO_3 (2.0 equiv.) in THF/H_2O (v/v 1:1) was added Boc_2O (2.0 equiv.) at room temperature. The reaction mixture was then refluxed for 12 h. The mixture was cooled to room temperature and quenched by saturated aqueous NH_4Cl. After evaporation of THF, the resulting solution was extracted with ethyl acetate for three times. The organic extracts were washed with brine and dried over Na_2SO_4. After evaporation of solvents, the residue was purified by flash column chromatography on silica gel (hexane/ethyl acetate as eluent) to afford **E**.[4]



A **F**

To a solution of **A** in dichloromethane under Ar atmosphere was added triethylamine (1.2 equiv.) at 0 °C. Then trifluoromethanesulfonic anhydride (1.2 equiv.) was added dropwise. The reaction was stirred at 0 °C for 3 hours and quenched with saturated NH_4Cl aqueous solution. The resulting mixture was extracted with dichloromethane and dried over anhydrous sodium sulfate. Evaporation of the solvent followed by purification column flash chromatography on silica gel affording **F**.[5]

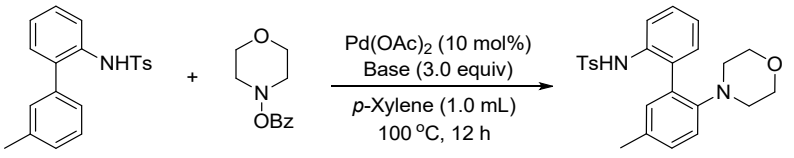


G

Following the general procedure, indole was coupled with 2-iodoaniline (1.20 equiv.) using K_3PO_4 (2.1 equiv.), CuI (0.5 equiv.), Dimethylcyclohexanediamine (20 mol%), and toluene at 80 °C. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 5:1) to provide (90% yield) of the desired product **G** as a light yellow oil[6].

3. Optimization of Reaction Conditions

Screening of Bases



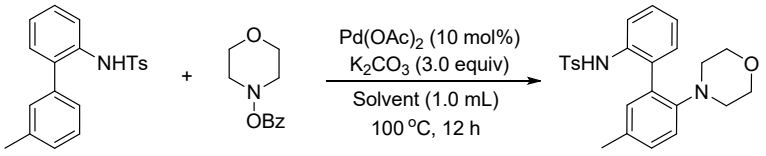
1aa **2a** **3aa**

Entry[a]	Base	Yield(%)[b]
1	K_3PO_4	61
2	K_2HPO_4	44
3	KH_2PO_4	<3
4	K_2CO_3	62
5	$KHCO_3$	33
6	KOH	6
7	*t*-BuOK	n.d.
8	KOAc	26
9	Cs_2CO_3	23

10	CsF	61
11	NaOAc	20
12	Na_2HPO_4	11
13	Na_2CO_3	14
14	$NaHCO_3$	16
15	NaTFA	trace
16	LiOAc	12
17	LiTFA	trace

[a] Reactions conditons: **1aa** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (0.02 mmol), Base (0.6 mmol), *p*-Xylene (1.0 mL), 100 °C, 12 h. [b]Isolated yield by flash column chromatography.

Screening of Solvents

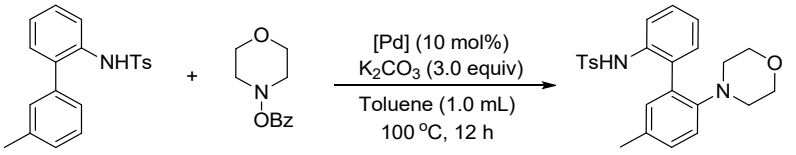


1aa **2a** **3aa**

Entry[a]	Solvent	Yield(%)[b]
1	DME	35
2	*o*-Xylene	67
3	*m*-Xylene	44
4	Mesitylene	65
5	Toluene	83(12 [c])
6	Ph-Cl	59
7	Ph-Br	60
8	Ph-CF_3	71
9	DCM	61
10	DCE	68
11	$CHCl_3$	72
12	DMF	<3
13	DMSO	trace
14	Dioxane	37
15	NMP	<3
16	THF	30
17	MeCN	19
18	TBME	27
19	*t*-Amyl-OH	45

[a]Reactions conditons: **1aa** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (0.02 mmol), K_2CO_3 (0.6 mmol), Solvent (1.0 mL), 100 °C, 12 h. [b]Isolated yield by flash column chromatography. [c]**1aa** recovery.

Screening of [Pd]

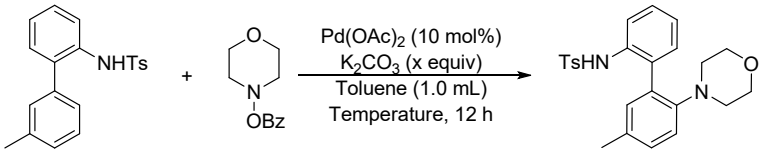


1aa **2a** **3aa**

Entry[a]	[Pd]	Yield(%)[b]
1	$PdCl_2$	39
2	$PdCl_2(MeCN)_2$	73
3	$Pd_2(dba)_3$	66
4	$Pd(TFA)_2$	57
5	$Pd(acac)_2$	63
6	$Pd(OAc)_2$	83
7[c]	$Pd(OAc)_2$	59
8[d]	$Pd(OAc)_2$	36
9[e]	$Pd(OAc)_2$	21

[a]Reactions conditons: **1aa** (0.2 mmol), **2a** (0.4 mmol), [Pd] (0.02 mmol), K_2CO_3 (0.6 mmol), Toluene (1.0 mL), 100 °C, 12 h. [b]Isolated yield by flash column chromatography. [c]0.016 mmol $Pd(OAc)_2$ was used. [d]0.01 mmol $Pd(OAc)_2$ was used. [e]0.004 mmol $Pd(OAc)_2$ was used.

Others

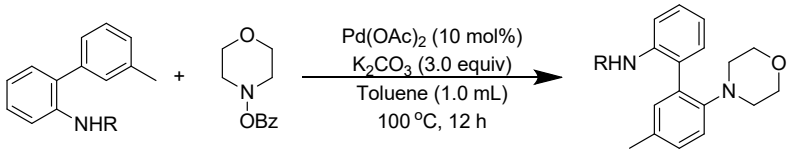


1aa **2a** **3aa**

Entry[a]	Addition	x (equiv)	Temperature(°C)	Yield(%)[b]
1	-	2.0	100	53
2	-	2.5	100	80
3	-	3.5	100	78
4	-	4.0	100	80
5	KOAc (1.0 equiv.)	3.0	100	81
6	NaOAc (1.0 equiv.)	3.0	100	84
7	-	3.0	80	61
8	-	3.0	90	74
9	-	3.0	110	77
10	-	3.0	120	62
11[c]	-	3.0	100	77

[a]Reactions conditons: **1aa** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (0.02 mmol), K_2CO_3 (x equiv.), Toluene (1.0 mL), Temperature, 12 h. [b]Isolated yield by flash column chromatography. [c]24 h.

Protecting Groups



1aR **2a** **3aR**

Entry[a]	R	Yield (%)[b]
1	H	0
2	Ac	0
3	Boc	0

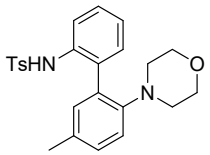
4	Ns	57
5	Tf	22

[a]Reaction conditions: **1aR** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (10 mmol %), K_2CO_3 (0.6 mmol), Toluene (1.0 mL), 100 °C, 12 h. [b]Isolated yields by flash column chromatography.

4. General Procedure for Palladium-catalyzed Interannular C-H Amination of Biaryl Amines

To an oven-dried 25 mL Schlenk tube was added substrate **1** (0.2 mmol), **2** (0.4 mmol), $Pd(OAc)_2$ (0.01 mmol), K_2CO_3 (0.6 mmol), toluene (1.0 mL). The mixture was stirred for 12 h at 100 °C followed by cooling. The resulting mixture was quenched by filtered through a celite pad and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to afford the product **3**.

5. Analytic Data of Products



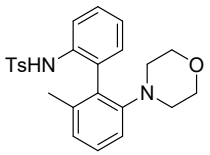
4-methyl-*N*-(5'-methyl-2'-morpholino-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3aa)

White solid. 83% yield; mp: 129-131 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.73-7.71 (m, 1H), 7.42-7.37 (m, 1H), 7.29-7.25 (m, 1H), 7.17-7.11 (m, 2H), 6.97-6.94 (m, 3H), 6.85-6.83 (m, 2H), 6.27 (s, 1H), 3.78-3.76 (m, 4H), 2.92-2.83 (m, 4H), 2.30 (s, 3H), 2.18 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 145.5, 142.1, 136.5, 136.3, 134.3, 133.6, 133.4, 132.8, 130.8, 129.2, 128.8, 128.6, 127.4, 127.1, 126.5, 117.7, 66.7, 52.3, 21.5, 20.6.

HRMS (ESI) Calcd for $C_{24}H_{27}N_2O_3S$ $(M+H)^+$: 423.1737, Found: 423.1742.



4-methyl-*N*-(2'-methyl-6'-morpholino-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3ba)

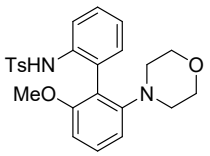
White solid. 92% yield; mp: 167-168 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.80-7.78 (m, 1H), 7.38-7.34 (m, 1H),

7.29-7.25 (m, 1H), 7.22-7.16 (m, 3H), 7.07-7.05 (m, 1H), 6.98-6.95 (m, 3H), 6.83 (d, *J* = 7.6 Hz, 1H), 3.67-3.54 (m, 4H), 2.93-2.76 (m, 4H), 2.35 (s, 3H), 1.41 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 149.3, 142.8, 139.0, 136.8, 133.2, 132.8, 132.1, 131.8, 129.3, 128.9, 128.5, 126.7, 126.2, 126.0, 125.7, 116.0, 66.9, 52.4, 21.4, 21.1.

HRMS (ESI) Calcd for $C_{24}H_{27}N_2O_3S$ $(M+H)^+$: 423.1737, Found: 423.1730.



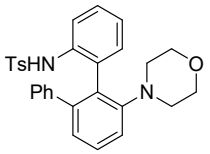
***N*-(2'-methoxy-6'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3ca)**

White solid. 55% yield; mp: 170-171 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.74-7.72 (m, 1H), 7.36-7.28 (m, 2H), 7.22-7.18 (m, 4H), 6.97-6.95 (m, 2H), 6.73-6.71 (m, 1H), 6.52-6.50 (m, 1H), 3.66-3.55 (m, 4H), 3.42 (s, 3H), 2.87-2.74 (m, 4H), 2.34 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.5, 150.1, 142.1, 136.9, 133.5, 133.2, 129.8, 129.7, 129.1, 128.3, 126.6, 125.9, 125.4, 120.3, 110.8, 106.5, 66.8, 55.2, 52.1, 21.5.

HRMS (ESI) Calcd for $C_{24}H_{27}N_2O_4S$ $(M+H)^+$: 439.1686, Found: 439.1680.



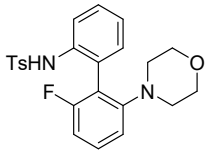
4-methyl-*N*-(6'-morpholino-[1,1':2',1''-terphenyl]-2-yl)benzenesulfonamide (3da)

White solid. 73% yield; mp: 209-210 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.46-7.44 (m, 2H), 7.24-7.21 (m, 1H), 7.16-7.12 (m, 2H), 7.06-7.01 (m, 3H), 6.93-6.89 (m, 2H), 6.73-6.69 (m, 1H), 6.58-6.56 (m, 1H), 6.23-6.21 (m, 2H), 3.76-3.65 (m, 4H), 3.01-2.88 (m, 4H), 2.20 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 149.5, 144.8, 143.5, 141.1, 137.9, 134.3, 133.7, 131.4, 131.1, 129.5, 129.4, 129.2, 128.2, 127.3, 127.2, 126.9, 126.1, 124.7, 123.2, 117.8, 66.8, 52.4, 21.4.

HRMS (ESI) Calcd for $C_{29}H_{29}N_2O_3S$ $(M+H)^+$: 485.1893, Found: 485.1889.



***N*-(2'-fluoro-6'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide**

(3ea)

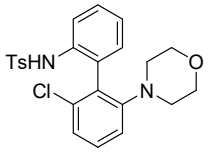
White solid. 55% yield; mp: 168-170 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.79-7.77 (m, 1H), 7.45-7.41 (m, 1H), 7.29-7.24 (m, 2H), 7.21-7.18 (m, 1H), 7.08-7.06 (m, 2H), 6.92-6.90 (m, 2H), 6.85-6.82 (m, 1H), 6.60-6.56 (m, 1H), 3.74-3.65 (m, 4H), 2.92-2.80 (m, 4H), 2.33 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.2 (d, J = 246.1 Hz), 149.9 (d, J = 4.0 Hz), 142.6, 136.0, 133.6, 132.3 (d, J = 3.7 Hz), 129.9 (d, J = 10.4 Hz), 129.3, 129.3, 128.1, 127.8, 126.4, 126.0, 120.2 (d, J = 14.9 Hz), 113.6 (d, J = 3.1 Hz), 111.2 (d, J = 24.2 Hz), 66.6, 52.1, 21.4.

^{19}F NMR (376 MHz, $CDCl_3$, 300 K) δ -114.54.

HRMS (ESI) Calcd for $C_{23}H_{24}FN_2O_3S$ $(M+H)^+$: 427.1486, Found: 427.1491.



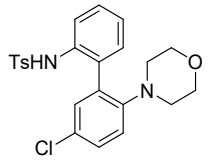
***N*-(2'-chloro-6'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3fa)**

White solid. 42% yield; mp: 159-160 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.78-7.75 (m, 1H), 7.42-7.38 (m, 1H), 7.30-7.25 (m, 2H), 7.24-7.20 (m, 4H), 7.04-6.99 (m, 4H), 3.67-3.54 (m, 4H), 2.92-2.77 (m, 4H), 2.35 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 150.8, 143.1, 136.5, 135.9, 133.2, 132.9, 130.8, 130.7, 129.8, 129.5, 129.2, 126.4, 126.0, 125.6, 125.3, 117.0, 66.7, 52.1, 21.5.

HRMS (ESI) Calcd for $C_{23}H_{24}ClN_2O_3S$ $(M+H)^+$: 443.1191, Found: 443.1184.



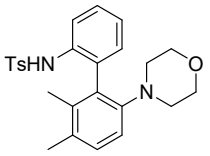
***N*-(5'-chloro-2'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3ga)**

White solid. 41% yield; mp: 188-190 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1H), 7.76-7.74 (m, 1H), 7.47-7.43 (m, 1H), 7.33-7.25 (m, 2H), 6.98-6.89 (m, 5H), 6.35 (d, J = 2.48 Hz, 1H), 3.77-3.74 (m, 4H), 2.91-2.81 (m, 4H), 2.38 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 146.5, 143.2, 135.6, 135.3, 134.5, 133.5, 133.0, 130.6, 129.3, 129.2, 129.1, 128.4, 128.1, 127.6, 126.2, 119.1, 66.6, 52.1, 21.6.

HRMS (ESI) Calcd for $C_{23}H_{24}ClN_2O_3S$ $(M+H)^+$: 443.1191, Found: 443.1193.



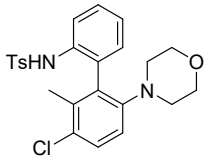
***N*-(2',3'-dimethyl-6'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3ha)**

White solid. 85% yield; mp: 128-130 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.79-7.77 (m, 1H), 7.39-7.34 (m, 1H), 7.22-7.16 (m, 4H), 7.03-7.01 (m, 1H), 6.96-6.95 (m, 2H), 6.90-6.88 (m, 1H), 3.65-3.52 (m, 4H), 2.89-2.72 (m, 4H), 2.36 (s, 3H), 2.15 (s, 3H), 1.27 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.3, 142.6, 137.5, 137.1, 133.6, 133.3, 132.8, 132.5, 132.0, 130.3, 129.1, 128.4, 126.9, 126.3, 125.7, 115.6, 66.9, 52.5, 21.4, 20.3, 17.3.

HRMS (ESI) Calcd for $C_{25}H_{29}N_2O_3S$ $(M+H)^+$: 437.1893, Found: 437.1899.



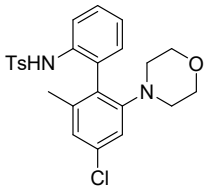
***N*-(3'-chloro-2'-methyl-6'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3ia)**

White solid. 85% yield; mp: 175-176 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.81-7.79 (m, 1H), 7.43-7.36 (m, 2H), 7.26-7.22 (m, 1H), 7.16-7.12 (m, 2H), 7.02-6.98 (m, 3H), 6.92 (d, J = 8.7 Hz, 1H), 3.67-3.56 (m, 4H), 2.90-2.73 (m, 4H), 2.38 (s, 3H), 1.37 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.9, 143.2, 137.1, 136.7, 133.7, 133.0, 132.2, 130.6, 129.5, 129.3, 129.0, 127.4, 126.6, 126.2, 116.2, 66.8, 52.3, 21.5, 18.3.

HRMS (ESI) Calcd for $C_{24}H_{26}ClN_2O_3S$ $(M+H)^+$: 457.1347, Found: 457.1354.



***N*-(4'-chloro-2'-methyl-6'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3ja)**

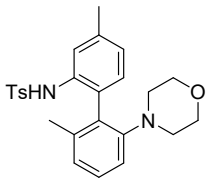
White solid. 37% yield; mp: 164-166 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.78-7.76 (m, 1H), 7.40-7.36 (m, 1H),

7.24-7.19 (m, 3H), 7.04-7.01 (m, 3H), 6.92 (d, J = 2.1 Hz, 1H), 6.79-6.77 (m, 1H), 3.66-3.53 (m, 4H), 2.90-2.74 (m, 4H), 2.38 (s, 3H), 1.42 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 150.4, 143.1, 140.5, 136.8, 134.3, 133.2, 132.0, 131.9, 130.1, 129.3, 128.8, 126.5, 126.0, 125.8, 116.5, 66.7, 52.2, 21.5, 21.1.

HRMS (ESI) Calcd for $C_{24}H_{26}ClN_2O_3S$ $(M+H)^+$: 457.1347, Found: 457.1344.



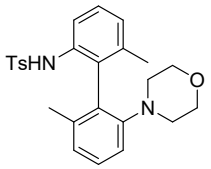
***N*-(2',4-dimethyl-6'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3ka)**

White solid. 95% yield; mp: 177-178 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.61-7.60 (m, 1H), 7.25 (t, J = 7.8 Hz, 1H), 7.15-7.13 (m, 2H), 7.02-6.99 (m, 1H), 6.95-6.91 (m, 4H), 6.80 (d, J = 7.5 Hz, 1H), 3.69-3.57 (m, 4H), 2.94-2.75 (m, 4H), 2.42 (s, 3H), 2.34 (s, 3H), 1.40 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 149.2, 142.6, 139.1, 138.5, 136.8, 132.9, 132.0, 131.9, 130.0, 129.3, 128.6, 126.9, 126.8, 126.6, 126.2, 115.9, 66.9, 52.3, 21.4, 21.3, 21.2.

HRMS (ESI) Calcd for $C_{25}H_{29}N_2O_3S$ $(M+H)^+$: 437.1893, Found: 437.1887.



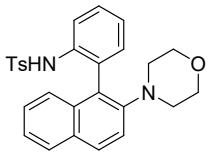
***N*-(2',6-dimethyl-6'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3la)**

White solid. 57% yield; mp: 138-139 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.62-7.60 (m, 1H), 7.42-7.39 (m, 2H), 7.30 (t, J = 7.8 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 7.14-7.10 (m, 3H), 7.04 (d, J = 7.4 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.87 (d, J = 7.6 Hz, 1H), 3.55-3.41 (m, 4H), 2.82-2.73 (m, 4H), 2.38 (s, 3H), 1.94 (s, 3H), 1.38 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 150.1, 143.3, 138.9, 137.6, 137.2, 136.6, 130.8, 130.2, 129.4, 129.2, 128.0, 127.0, 126.9, 125.7, 119.5, 116.6, 67.0, 51.9, 21.5, 20.0, 19.2.

HRMS (ESI) Calcd for $C_{25}H_{29}N_2O_3S$ $(M+H)^+$: 437.1893, Found: 437.1894.



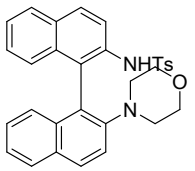
4-methyl-*N*-(2-(2-morpholinonaphthalen-1-yl)phenyl)benzenesulfonamide (3ma)

White solid. 64% yield; mp: 180-182 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.91-7.88 (m, 2H), 7.77-7.74 (m, 1H), 7.49-7.45 (m, 1H), 7.40-7.37 (m, 1H), 7.35-7.29 (m, 2H), 7.21-7.18 (m, 1H), 7.08-7.04 (m, 1H), 6.91-6.87 (m, 3H), 6.44-6.42 (m, 2H), 3.75-3.63 (m, 4H), 3.06-2.90 (m, 4H), 2.00 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 146.0, 142.4, 135.9, 133.9, 133.3, 132.2, 131.9, 130.7, 130.1, 128.8, 128.7, 127.6, 127.2, 127.0, 126.2, 126.1, 125.9, 125.4, 124.3, 117.8, 67.0, 52.2, 21.3.

HRMS (ESI) Calcd for $C_{27}H_{27}N_2O_3S$ $(M+H)^+$: 459.1737, Found: 459.1730.



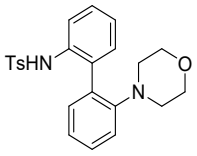
4-methyl-*N*-(2'-morpholino-[1,1'-binaphthalen]-2-yl)benzenesulfonamide(3na)

White solid. 51% yield; mp: 189-190 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.11 (m, 1H), 8.00-7.96 (m, 2H), 7.91-7.88 (m, 2H), 7.79-7.77 (m, 1H), 7.48 (d, J = 8.8 Hz, 1H), 7.42-7.38 (m, 1H), 7.30-7.26 (m, 1H), 7.20-7.16 (m, 1H), 6.99-6.92 (m, 3H), 6.83-6.79 (m, 1H), 6.53-6.50 (m, 2H), 6.22-6.21 (m, 1H), 3.58-3.47 (m, 4H), 2.91 (t, J = 4.6 Hz, 4H), 2.08 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.7, 142.7, 136.1, 133.6, 133.4, 131.8, 131.6, 130.6, 130.2, 129.3, 128.9, 128.9, 127.7, 126.8, 126.6, 126.3, 126.2, 125.8, 125.4, 124.1, 124.1, 123.5, 118.3, 67.0, 51.9, 21.4.

HRMS (ESI) Calcd for $C_{31}H_{29}N_2O_3S$ $(M+H)^+$: 509.1893, Found: 509.1899.



4-methyl-*N*-(2'-morpholino-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3qa)

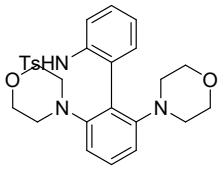
White solid. 44% yield; mp: 203-204 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 7.74-7.72 (m, 1H), 7.42-7.38 (m, 1H), 7.34-7.26 (m, 2H), 7.18-7.16 (m, 1H), 7.06-7.04 (m, 1H), 6.97-6.95 (m, 2H), 6.89-

6.81 (m, 3H), 6.48-6.46 (m, 1H), 3.79-3.77 (m, 4H), 2.96-2.86 (m, 4H), 2.31(s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.8, 142.4, 136.3, 136.0, 133.6, 133.6, 133.0, 130.9, 129.1, 128.8, 128.7, 127.3, 127.1, 126.1, 123.6, 117.8, 66.7, 52.1, 21.4.

HRMS (ESI) Calcd for $C_{23}H_{25}N_2O_3S$ $(M+H)^+$: 409.1580, Found: 409.1587.



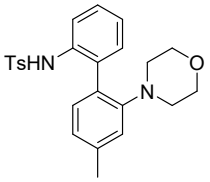
***N*-(2',6'-dimorpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3qa')**

White solid. 15% yield; mp: 226-228 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.74-7.72 (m, 1H), 7.45-7.38 (m, 4H), 7.31-7.27 (m, 1H), 7.17-7.13 (m, 1H), 7.08-7.06 (m, 2H), 6.88-6.86 (m, 2H), 3.52-3.41 (m, 8H), 2.58-2.47 (m, 8H), 2.35 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 151.4, 143.2, 138.4, 133.9, 133.4, 129.9, 129.8, 129.4, 128.5, 127.0, 126.6, 124.66, 123.2, 114.7, 66.7, 51.9, 21.4.

HRMS (ESI) Calcd for $C_{27}H_{32}N_3O_4S$ $(M+H)^+$: 494.2108, Found: 494.2103.



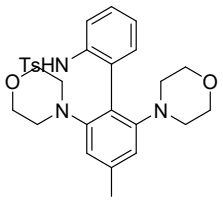
4-methyl-*N*-(4'-methyl-2'-morpholino-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3ra)

White solid. 42% yield; mp: 217-218 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.71-7.69 (m, 1H), 7.40-7.36 (m, 1H), 7.28-7.24 (m, 1H), 7.17-7.15 (m, 1H), 7.00-6.96 (m, 2H), 6.84-6.81 (m, 3H), 6.69-6.67 (m, 1H), 6.37 (d, J = 7.7 Hz, 1H), 3.79-3.76 (m, 4H), 2.95-2.85 (m, 4H), 2.41 (s, 3H), 2.31 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.6, 142.4, 138.8, 136.2, 136.2, 133.6, 133.6, 130.8, 130.1, 128.9, 128.4, 127.2, 127.0, 126.2, 124.4, 118.5, 66.7, 52.1, 21.5, 21.3.

HRMS (ESI) Calcd for $C_{24}H_{27}N_2O_3S$ $(M+H)^+$: 423.1737, Found: 423.1738.



4-methyl-*N*-(4'-methyl-2',6'-dimorpholino-[1,1'-biphenyl]-2-

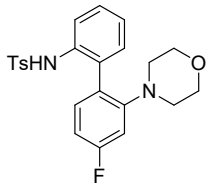
yl)benzenesulfonamide (3ra')

White solid. 13% yield; mp: 227-228 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.71-7.69 (m, 1H), 7.49-7.47 (m, 2H), 7.43-7.40 (m, 1H), 7.29-7.25 (m, 1H), 7.15-7.11 (m, 1H), 7.08 (s, 1H), 7.06 (s, 1H), 6.67 (s, 2H), 3.51-3.40 (m, 8H), 2.58-2.47 (m, 8H), 2.43 (s, 3H), 2.35 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 151.2, 143.2, 139.8, 138.4, 134.0, 133.5, 129.9, 129.3, 128.3, 127.0, 124.6, 123.5, 122.9, 115.5, 66.8, 51.9, 21.8, 21.4.

HRMS (ESI) Calcd for $C_{28}H_{34}N_3O_4S$ $(M+H)^+$: 508.2265, Found: 508.2256.



***N*-(4'-fluoro-2'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3sa)**

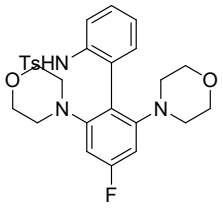
White solid. 50% yield; mp: 175-176 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 7.73-7.71 (m, 1H), 7.43-7.39 (m, 1H), 7.30-7.26 (m, 1H), 7.14-7.12 (m, 1H), 7.02-7.00 (m, 2H), 6.90-6.88 (m, 2H), 6.77-6.73 (m, 1H), 6.55-6.51 (m, 1H), 6.43-6.39 (m, 1H), 3.77-3.75 (m, 4H), 2.92-2.81 (m, 4H), 2.33 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 163.0 (d, J = 246.7 Hz), 149.4 (d, J = 8.1 Hz), 142.7, 136.1, 135.4, 134.7 (d, J = 9.2 Hz), 133.4, 130.7, 129.1, 128.8, 128.7 (d, J = 3.3 Hz), 127.5, 127.3, 126.1, 110.1 (d, J = 21.0 Hz), 105.5 (d, J = 24.0 Hz), 66.5, 51.9, 21.4.

^{19}F NMR (376 MHz, $CDCl_3$, 300 K) δ -112.20.

HRMS (ESI) Calcd for $C_{23}H_{24}FN_2O_3S$ $(M+H)^+$: 427.1486, Found: 427.1491.



***N*-(4'-fluoro-2',6'-dimorpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3sa')**

White solid. 8% yield; mp: 190-192 °C;

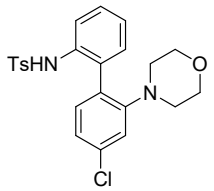
^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 7.73-7.71 (m, 1H), 7.51-7.48 (m, 2H), 7.40-7.38 (m, 1H), 7.32-7.28 (m, 1H), 7.17-7.10 (m, 3H), 6.58 (s, 1H), 6.56 (s, 1H), 3.51-3.40 (m, 8H), 2.55-2.45 (m, 8H), 2.36 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 163.7 (d, J = 246.2 Hz), 152.9 (d, J = 9.8 Hz), 143.4,

138.3, 133.9, 133.3, 129.4, 129.2, 128.6, 127.0, 124.9, 123.2, 122.0 (d, J = 3.7 Hz), 102.0 (d, J = 23.1 Hz), 66.6, 51.7, 21.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -110.10.

HRMS (ESI) Calcd for $C_{27}H_{31}FN_3O_4S$ $(M+H)^+$: 512.2014, Found: 512.2020.



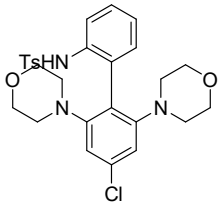
***N*-(4'-chloro-2'-morpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3ta)**

White solid. 21% yield; mp: 153-154 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 7.73-7.71 (m, 1H), 7.45-7.41 (m, 1H), 7.32-7.28 (m, 1H), 7.14-7.12 (m, 1H), 7.01-6.99 (m, 3H), 6.91-6.88 (m, 2H), 6.81-6.78 (m, 1H), 6.37 (d, J = 8.3 Hz, 1H), 3.78-3.75 (m, 4H), 2.93-2.84 (m, 4H), 2.35 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.8, 142.8, 136.1, 135.3, 134.6, 134.5, 133.5, 131.3, 130.5, 129.1, 129.1, 127.8, 127.4, 126.1, 123.5, 118.3, 66.5, 51.9, 21.5.

HRMS (ESI) Calcd for $C_{23}H_{24}ClN_2O_3S$ $(M+H)^+$: 443.1191, Found: 443.1186.



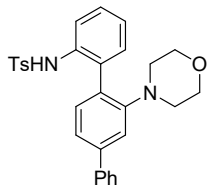
***N*-(4'-chloro-2',6'-dimorpholino-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3ta')**

White solid. 19% yield; mp: 241-243 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.73-7.71 (m, 1H), 7.52-7.49 (m, 2H), 7.40-7.37 (m, 1H), 7.33-7.29 (m, 1H), 7.18-7.11 (m, 3H), 6.82 (s, 2H), 3.51-3.40 (m, 8H), 2.57-2.47 (m, 8H), 2.37 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 152.3, 143.4, 138.2, 135.4, 133.9, 133.0, 129.5, 129.0, 128.8, 127.0, 124.9, 124.7, 123.2, 115.2, 66.6, 51.7, 21.5.

HRMS (ESI) Calcd for $C_{27}H_{31}ClN_3O_4S$ $(M+H)^+$: 528.1718, Found: 528.1715.



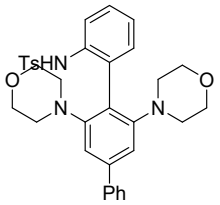
4-methyl-*N*-(2'-morpholino-[1,1':4',1''-terphenyl]-2-yl)benzenesulfonamide (3ua)

White solid. 41% yield; mp: 176-177 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.76-7.74 (m, 1H), 7.64-7.61 (m, 2H), 7.57-7.53 (m, 2H), 7.48-7.41 (m, 2H), 7.34-7.30 (m, 1H), 7.24-7.22 (m, 2H), 7.08-7.06 (m, 1H), 7.01-6.98 (m, 2H), 6.82-6.80 (m, 2H), 6.54 (d, J = 8.0 Hz, 1H), 3.83-3.81 (m, 4H), 3.02-2.97 (m, 4H), 2.28 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.1, 142.5, 141.8, 140.4, 136.1, 136.0, 134.1, 133.6, 131.9, 130.8, 129.1, 129.0, 128.8, 127.9, 127.7, 127.3, 127.0, 126.1, 122.2, 116.6, 66.7, 52.2, 21.5.

HRMS (ESI) Calcd for $C_{29}H_{29}N_2O_3S$ $(M+H)^+$: 485.1893, Found: 485.1891.



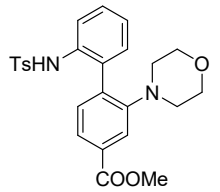
***N*-(2',6'-dimorpholino-[1,1':4',1''-terphenyl]-2-yl)-4-methylbenzenesulfonamide (3ua')**

White solid. 19% yield; mp: 238-240 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.75-7.73 (m, 1H), 7.67-7.64 (m, 2H), 7.56-7.43 (m, 6H), 7.33-7.29 (m, 1H), 7.19-7.15 (m, 1H), 7.08 (s, 1H), 7.05 (s, 3H), 3.55-3.44 (m, 8H), 2.66-2.56 (m, 8H), 2.34 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 151.7, 143.2, 143.0, 140.8, 138.3, 134.0, 133.4, 129.7, 129.4, 129.0, 128.6, 127.9, 127.1, 127.0, 125.3, 124.7, 123.2, 113.6, 66.8, 52.0, 21.4.

HRMS (ESI) Calcd for $C_{33}H_{36}N_3O_4S$ $(M+H)^+$: 570.2421, Found: 570.2427.



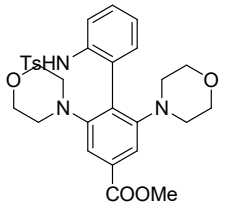
methyl 2'-(4-methylphenylsulfonamido)-2-morpholino-[1,1'-biphenyl]-4-carboxylate (3va)

White solid. 33% yield; mp: 161-162 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.75-7.73 (m, 1H), 7.69 (d, J = 1.5 Hz, 1H), 7.50-7.48 (m, 1H), 7.47-7.43 (m, 1H), 7.34-7.30 (m, 1H), 7.19-7.16 (m, 1H), 6.97-6.94 (m, 2H), 6.82-6.79 (m, 2H), 6.53 (d, J = 8.0 Hz, 1H), 4.01 (s, 3H), 3.80-3.77 (m, 4H), 2.98-2.87 (m, 4H), 2.32 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.5, 147.9, 142.8, 137.6, 135.9, 135.5, 133.7, 133.5, 130.6, 130.4, 129.4, 129.1, 127.9, 127.4, 126.1, 124.6, 118.9, 66.6, 52.4, 52.0, 21.4.

HRMS (ESI) Calcd for $C_{25}H_{27}N_2O_5S$ $(M+H)^+$: 467.1635, Found: 467.1634.



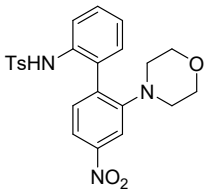
methyl 2'-(4-methylphenylsulfonamido)-2,6-dimorpholino-[1,1'-biphenyl]-4-carboxylate (3va')

White solid. 17% yield; mp: 225-227 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.76-7.73 (m, 1H), 7.52 (s, 2H), 7.47-7.45 (m, 2H), 7.43-7.41 (m, 1H), 7.35-7.30 (m, 1H), 7.19-7.15 (m, 1H), 7.08-7.06 (m, 2H), 4.00 (s, 3H), 3.53-3.42 (m, 8H), 2.62-2.51 (m, 8H), 2.35 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.6, 151.5, 143.4, 138.2, 133.9, 132.9, 131.4, 131.1, 129.4, 129.3, 129.1, 127.0, 124.9, 123.4, 115.8, 66.6, 52.4, 51.8, 21.4.

HRMS (ESI) Calcd for $C_{29}H_{34}N_3O_6S$ $(M+H)^+$: 552.2163, Found: 522.2167.



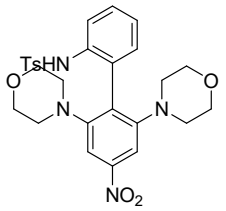
4-methyl-*N*-(2'-morpholino-4'-nitro-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3wa)

Yellow solid. 17% yield; mp: 74-77 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 7.87 (d, J = 2.3 Hz, 1H), 7.77-7.75 (m, 1H), 7.66-7.63 (m, 1H), 7.53-7.49 (m, 1H), 7.39-7.35 (m, 1H), 7.20-7.17 (m, 1H), 7.02-6.98 (m, 2H), 6.87-6.85 (m, 2H), 6.62 (d, J = 8.4 Hz, 1H), 3.80-3.78 (m, 4H), 3.00-2.89 (m, 4H), 2.35 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.8, 147.9, 143.2, 139.4, 136.0, 134.6, 134.2, 133.4, 130.4, 130.1, 129.2, 128.3, 127.7, 126.1, 117.9, 112.9, 66.4, 51.8, 21.4.

HRMS (ESI) Calcd for $C_{23}H_{24}N_3O_5S$ $(M+H)^+$: 454.1431, Found: 454.1436.



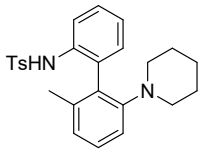
***N*-(2',6'-dimorpholino-4'-nitro-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3wa')**

Yellow solid. 5% yield; mp: 212-213 °C;

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.72-7.70 (m, 1H), 7.66 (s, 2H), 7.52-7.50 (m,2H), 7.39-7.33 (m, 2H), 7.21-7.18 (m, 1H), 7.12-7.10 (m, 2H), 3.51-3.42 (m, 8H), 2.62-2.54 (m, 8H), 2.35 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 152.4, 148.9, 143.8, 138.0, 133.9, 132.5, 132.4, 129.7, 129.6, 128.5, 127.0, 125.3, 123.4, 109.6, 66.5, 51.6, 21.5.

HRMS (ESI) Calcd for $C_{27}H_{31}N_4O_6S$ $(M+H)^+$: 539.1959, Found: 539.1953.



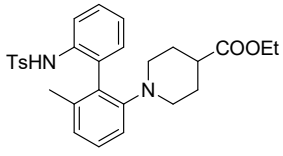
4-methyl-*N*-(2'-methyl-6'-(piperidin-1-yl)-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3bb)

White solid. 38% yield; mp: 179-181 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.79-7.77 (m, 1H), 7.37-7.35 (m, 1H), 7.25-7.18 (m, 2H), 7.11-7.09 (m, 2H), 7.07-7.04 (m, 1H), 6.96 (d, J = 8.1 Hz, 1H), 6.91-6.89 (m, 2H), 6.75 (d, J = 7.5 Hz, 1H), 2.89-2.79 (m, 4H), 2.33 (s, 3H), 1.57-1.48 (m, 6H), 1.39 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 150.5, 142.3, 138.7, 137.0, 133.9, 133.3, 132.5, 132.5, 129.2, 128.5, 127.3, 126.4, 125.8, 125.7, 116.3, 53.7, 26.1, 24.0, 21.4.

HRMS (ESI) Calcd for $C_{25}H_{29}N_2O_2S$ $(M+H)^+$: 421.1944, Found: 421.1952.



ethyl 1-(6-methyl-2'-(4-methylphenylsulfonamido)-[1,1'-biphenyl]-2-yl)piperidine-4-carboxylate (3bc)

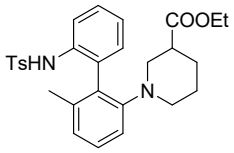
White solid. 50% yield; mp: 124-125 °C;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.78-7.76 (m, 1H), 7.37-7.33 (m, 1H),

7.25-7.18 (m, 2H), 7.15-7.12 (m, 2H), 7.06-7.04 (m, 1H), 6.97-6.92 (m, 3H), 6.78 (d, *J* = 7.4 Hz, 1H), 4.18-4.10 (m, 2H), 3.23 (d, *J* = 11.3 Hz, 1H), 2.98-2.86 (m, 2H), 2.43-2.37 (m, 1H), 2.33 (s, 3H), 2.32-2.28 (m, 1H), 2.06-2.00 (m, 1H), 1.94-1.83 (m, 1H), 1.71-1.65 (m, 1H), 1.39 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.4, 150.0, 142.5, 138.8, 136.9, 133.3, 133.2, 132.3, 132.2, 129.2, 128.6, 128.3, 126.7, 126.6, 126.2, 126.0, 125.8, 116.3, 60.5, 53.3, 50.7, 40.5, 28.5, 28.2, 21.4, 21.2, 14.2.

HRMS (ESI) Calcd for $C_{28}H_{33}N_2O_4S$ $(M+H)^+$: 493.2156, Found: 493.2160.



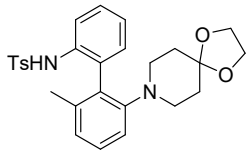
ethyl 1-(6-methyl-2'-(4-methylphenylsulfonamido)-[1,1'-biphenyl]-2-yl)piperidine-3-carboxylate (3bd)

White solid. 23% yield; mp: 121-124 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.78-7.76 (m, 1H), 7.38-7.33 (m, 1H), 7.26-7.15 (m, 4H), 7.08-7.06 (m, 1H), 6.97-6.95 (m, 3H), 6.79 (d, *J* = 7.6 Hz, 1H), 4.03-3.91 (m, 2H), 3.26 (d, *J* = 11.3 Hz, 1H), 3.11-3.06 (m, 1H), 2.89-2.83 (m, 1H), 2.36-2.33 (m, 4H), 2.11-2.04 (m, 1H), 2.01-1.97 (m, 1H), 1.90-1.74 (m, 2H), 1.46-1.39 (m, 4H), 1.13 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.2, 150.0, 142.6, 138.8, 136.9, 133.2, 133.0, 132.3, 132.1, 129.3, 128.6, 128.3, 126.3, 125.9, 125.8, 116.4, 60.2, 56.3, 51.0, 41.8, 26.6, 25.2, 21.4, 21.1, 14.1.

HRMS (ESI) Calcd for $C_{28}H_{33}N_2O_4S$ $(M+H)^+$: 493.2156, Found: 493.2150.



4-methyl-*N*-(2'-methyl-6'-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3be)

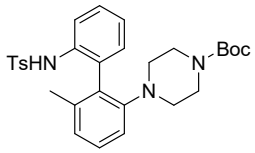
White solid. 41% yield; mp: 180-182 ℃;

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.74-7.72 (m, 1H), 7.33-7.30 (m, 1H), 7.22-7.15 (m, 2H), 7.14-7.11 (m, 2H), 7.04-7.02 (m, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.93-6.91 (m, 2H), 6.77-6.75 (m, 1H), 3.91 (s, 4H), 2.97-2.88 (m, 4H), 2.31 (s, 3H), 1.67-1.58 (m, 4H), 1.37 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ 150.1, 142.9, 139.2, 137.3, 133.7, 133.6, 132.6,

132.6, 129.6, 129.0, 128.6, 127.0, 126.8, 126.3, 126.1, 116.9, 106.9, 64.6, 50.8, 35.5, 21.8, 21.5.

HRMS (ESI) Calcd for $C_{27}H_{31}N_2O_4S$ $(M+H)^+$: 479.1999, Found: 479.2001.



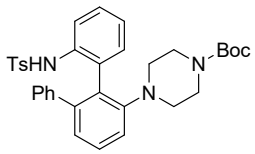
tert-butyl 4-(6-methyl-2'-(4-methylphenylsulfonamido)-[1,1'-biphenyl]-2-yl)piperazine-1-carboxylate (3bf)

White solid. 63% yield; mp: 149-151 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.78-7.75 (m, 1H), 7.38-7.34 (m, 1H), 7.26-7.17 (m, 4H), 7.07-7.05 (m, 1H), 6.99-6.93 (m, 3H), 6.84 (d, J = 7.5 Hz, 1H), 3.40-3.27 (m, 4H), 2.88-2.72 (m, 4H), 2.35 (s, 3H), 1.45 (s, 9H), 1.42 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.6, 149.4, 142.8, 139.0, 136.8, 133.1, 132.6, 132.1, 132.0, 129.3, 128.9, 128.5, 126.7, 126.3, 125.8, 125.7, 116.3, 79.9, 51.9, 28.4, 21.1, 21.0.

HRMS (ESI) Calcd for $C_{29}H_{36}N_3O_4S$ $(M+H)^+$: 522.2421, Found: 522.2426.



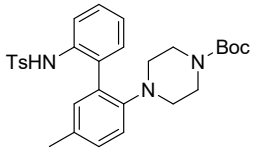
tert-butyl 4-(2''-(4-methylphenylsulfonamido)-[1,1':2',1''-terphenyl]-3'-yl)piperazine-1-carboxylate (3df)

White solid. 31% yield; mp: 212-213 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 7.68-7.66 (m, 1H), 7.52-7.44 (m, 3H), 7.21-7.12 (m, 3H), 7.06-7.01 (m, 3H), 6.92-6.88 (m, 2H), 6.74-6.70 (m, 1H), 6.59-6.56 (m, 1H), 6.25-6.22 (m, 2H), 3.49-3.38 (m, 4H), 2.96-2.83 (m, 4H), 2.20 (s, 3H), 1.47 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.7, 149.6, 144.7, 143.6, 141.1, 137.8, 134.2, 133.6, 131.3, 131.2, 129.5, 129.4, 129.2, 128.2, 127.3, 127.2, 126.9, 126.1, 124.7, 123.1, 118.1, 79.9, 52.0, 28.4, 21.4.

HRMS (ESI) Calcd for $C_{34}H_{38}N_3O_4S$ $(M+H)^+$: 584.2578, Found: 587.2575.



tert-butyl 4-(5-methyl-2'-(4-methylphenylsulfonamido)-[1,1'-biphenyl]-2-

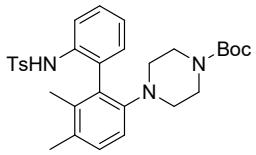
yl)piperazine-1-carboxylate (3af)

White solid. 24% yield; mp: 110-111 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.72-7.70 (m, 1H), 7.42-7.38 (m, 1H), 7.30-7.26 (m, 1H), 7.17-7.15 (m, 1H), 7.13-7.10 (m, 1H), 6.98-6.91 (m, 3H), 6.85-6.83 (m, 2H), 6.28 (d, J = 2.1 Hz, 1H), 3.55-3.45 (m, 4H), 2.87-2.81 (m, 4H), 2.31 (s, 3H), 2.18 (s, 3H), 1.46 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.6, 145.6, 142.1, 136.3, 136.3, 134.2, 133.5, 133.4, 133.0, 130.9, 129.2, 128.8, 128.6, 127.4, 127.1, 126.5, 118.1, 80.0, 51.8, 28.4, 21.5, 20.6.

HRMS (ESI) Calcd for $C_{29}H_{36}N_3O_4S$ $(M+H)^+$: 522.2421, Found: 522.2424.



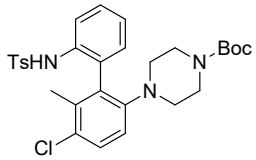
tert-butyl 4-(5,6-dimethyl-2'-(4-methylphenylsulfonamido)-[1,1'-biphenyl]-2-yl)piperazine-1-carboxylate (3hf)

White solid. 15% yield; mp: 96-98 ℃;

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.74-7.72 (m, 1H), 7.36-7.32 (m, 1H), 7.20-7.13 (m, 4H), 7.00-6.98 (m, 1H), 6.95-6.93 (m, 2H), 6.84 (d, J = 8.2 Hz, 1H), 3.35-3.22 (m, 4H), 2.82-2.66 (m, 4H), 2.33 (s, 3H), 2.13 (s, 3H), 1.42 (s, 9H), 1.25 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.7, 147.4, 142.6, 137.5, 137.1, 133.4, 133.2, 132.9, 132.5, 132.2, 130.2, 129.1, 128.4, 126.9, 126.1, 125.7, 115.9, 79.8, 52.0, 28.4, 21.5, 17.3.

HRMS (ESI) Calcd for $C_{30}H_{38}N_3O_4S$ $(M+H)^+$: 536.2578, Found: 536.2577.



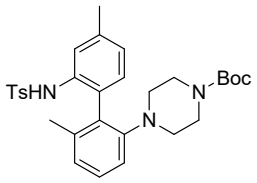
tert-butyl 4-(5-chloro-6-methyl-2'-(4-methylphenylsulfonamido)-[1,1'-biphenyl]-2-yl)piperazine-1-carboxylate (3if)

White solid. 27% yield; mp: 106-108 ℃;

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.76-7.74 (m, 1H), 7.39-7.38 (m, 1H), 7.34 (d, J = 8.7 Hz, 1H), 7.24-7.20 (m, 1H), 7.13-7.11 (m, 2H), 6.99-6.96 (m, 3H), 6.87 (d, J = 8.6 Hz, 1H), 3.36-3.23 (m, 4H), 2.81-2.68 (m, 4H), 2.35 (s, 3H), 1.42 (s, 9H), 1.34 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.7, 147.4, 142.6, 137.5, 137.2, 133.4, 133.3, 132.9, 132.4, 132.2, 130.2, 139.1, 128.4, 126.9, 126.0, 125.7, 116.0, 79.8, 52.0, 28.4, 21.4, 20.3, 17.2.

HRMS (ESI) Calcd for $C_{29}H_{35}ClN_3O_4S$ $(M+H)^+$: 556.2031, Found: 556.2036.



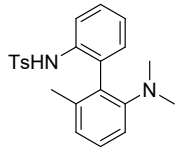
tert-butyl 4-(4',6-dimethyl-2'-(4-methylphenylsulfonamido)-[1,1'-biphenyl]-2-yl)piperazine-1-carboxylate (3kf)

White solid. 17% yield; mp: 190-191 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.58 (s, 1H), 7.23 (t, J = 7.8 Hz, 1H), 7.16-7.13 (m, 2H), 7.03-7.00 (m, 1H), 6.96-6.90 (m, 4H), 6.80 (d, J = 7.4 Hz, 1H), 3.42-3.30 (m, 4H), 2.89-2.72 (m, 4H), 2.41 (s, 3H), 2.34 (s, 3H), 1.45 (s, 9H), 1.40 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.7, 149.3, 142.6, 139.1, 138.5, 136.8, 132.8, 132.1, 131.9, 129.8, 129.3, 128.6, 126.8, 126.8, 126.6, 126.3, 116.2, 79.9, 51.9, 28.4, 21.4, 21.3, 21.3.

HRMS (ESI) Calcd for $C_{30}H_{38}N_3O_4S$ $(M+H)^+$: 536.2578, Found: 536.2572.



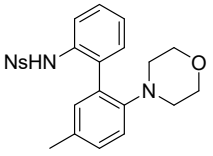
***N*-(2'-(dimethylamino)-6'-methyl-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3bg)**

White solid. 21% yield; mp: 135-137 ℃;

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.74-7.72 (m, 1H), 7.35-7.31 (m, 1H), 7.22-7.16 (m, 2H), 7.14-7.12 (m, 1H), 7.07-7.06 (m, 1H), 6.96 (d, J = 8.1 Hz, 1H), 6.92-6.91 (m, 2H), 6.72 (d, J = 7.5 Hz, 1H), 2.54 (s, 6H), 2.32 (s, 3H), 1.40 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 150.3, 142.5, 138.8, 136.9, 133.6, 132.3, 131.5, 129.2, 128.5, 128.2, 126.5, 126.4, 125.6, 125.4, 115.6, 43.8, 31.0, 21.4, 21.4.

HRMS (ESI) Calcd for $C_{22}H_{25}N_2O_2S$ $(M+H)^+$: 381.1631, Found: 381.1627.



***N*-(5'-methyl-2'-morpholino-[1,1'-biphenyl]-2-yl)-4-nitrobenzenesulfonamide**

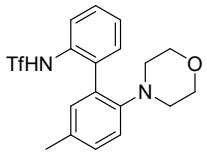
(3aNHNs)

Yellow solid. 57% yield; mp: 188-189 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.50 (s,1H), 7.74-7.71 (m, 1H), 7.56-7.52 (m, 1H), 7.48-7.42 (m, 4H), 7.38-7.34 (m, 1H), 7.14-7.12 (m, 1H), 6.97-6.94 (m, 1H), 6.85-6.83 (m, 1H), 6.14-6.13 (m, 1H), 3.73 (s, 4H), 2.98-2.78 (m, 4H), 2.02 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 146.6, 146.5, 137.4, 13.3, 132.8, 132.4, 132.3, 132.1, 131.9, 131.6, 130.7, 130.6, 130.0, 129.3, 128.6, 128.3, 125.0, 117.9, 67.0, 52.3, 20.4.

HRMS (ESI) Calcd for $C_{23}H_{24}N_3O_5S$ $(M+H)^+$: 454.1431, Found: 454.1428.



1,1,1-trifluoro-*N*-(5'-methyl-2'-morpholino-[1,1'-biphenyl]-2-yl)methanesulfonamide (3aNHTf)

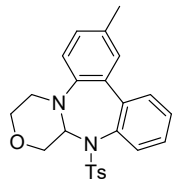
White solid. 22% yield; mp: 139-141 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.43 (s, 1H), 7.62-7.60 (m, 1H), 7.48-7.37 (m, 3H), 7.30-7.28 (m, 1H), 7.19 (d, J = 2.1 Hz, 1H), 7.10 (d, J = 8.2 Hz, 1H), 3.80-3.78 (m, 4H), 2.98-2.90 (m, 4H), 2.40 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 145.0, 135.9, 134.9, 134.8, 132.9, 132.5, 131.3, 130.1, 129.0, 127.7, 125.8, 121.3, 118.4, 118.1, 66.5, 52.5, 20.7.

HRMS (ESI) Calcd for $C_{18}H_{20}F_3N_2O_3S$ $(M+H)^+$: 401.1141, Found: 401.1135.

6. Derivatization of Products



2-methyl-10-tosyl-7,9,9a,10-tetrahydro-6*H*-dibenzo[d,f][1,4]oxazino[4,3-*a*][1,3]diazepine (4)

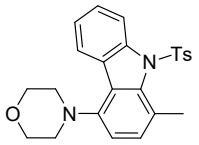
White solid. 39% yield; mp: 174-176 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59-7.57 (m, 1H), 7.50-7.43 (m, 2H), 7.27-7.25 (m, 1H), 7.01-6.98 (m, 1H), 6.96-6.93 (m, 2H), 6.87-6.84 (m, 3H), 6.47 (d, J = 2.2 Hz, 1H), 5.25-5.21 (m, 1H), 4.16-4.12 (m, 1H), 3.86-3.82 (m, 1H), 3.65-3.60 (m, 1H), 3.46 (td, J = 11.2 Hz, 2.1 Hz, 1H), 3.35 (td, J = 11.2 Hz, 2.8 Hz, 1H), 2.88-2.85 (m, 1H), 2.34 (s, 3H), 2.21 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 144.5, 142.2, 140.2, 136.4, 134.5, 133.6, 133.6,

132.5, 129.3, 129.2, 129.1, 128.8, 128.6, 128.1, 126.9, 118.3, 82.1, 70.2, 66.2, 50.0, 21.5, 20.8.

HRMS (ESI) Calcd for $C_{24}H_{25}N_2O_3S$ $(M+H)^+$: 421.1580, Found: 421.1572.



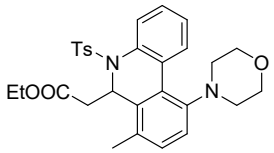
4-(1-methyl-9-tosyl-9*H*-carbazol-4-yl)morpholine (5)

White solid. 47% yield; mp: 188-189 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.32-8.31 (m, 1H), 8.00 (s, 1H), 7.82-7.80 (m, 1H), 7.70-7.66 (m, 3H), 7.46-7.42 (m, 1H), 7.36-7.32 (m, 1H), 7.12-7.10 (m, 2H), 3.96-3.94 (m, 4H), 3.07-3.05 (m, 4H), 2.45 (s, 3H), 2.28 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 151.4, 144.8, 138.6, 137.7, 135.0, 129.6, 129.1, 126.5, 126.5, 126.4, 123.9, 121.9, 121.9, 119.4, 115.2, 106.0, 67.4, 52.7, 21.5, 18.2.

HRMS (ESI) Calcd for $C_{24}H_{25}N_2O_3S$ $(M+H)^+$: 421.1580, Found: 421.1587.



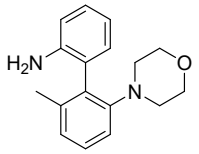
ethyl 2-(7-methyl-10-morpholino-5-tosyl-5,6-dihydrophenanthridin-6-yl)acetate (6)

White solid. 61% yield; mp: 210-212 ℃;

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.88-8.87 (m, 1H), 7.73-7.71 (m, 1H), 7.34-7.30 (m, 1H), 7.26-7.22 (m, 1H), 7.05-7.03 (m, 2H), 7.00 (d, J = 8.2 Hz, 1H), 6.76-6.72 (m, 3H), 6.03-6.00 (m, 1H), 4.30-4.21 (m, 2H), 3.93 (d, J = 11.4 Hz, 1H), 3.76-3.71 (m, 1H), 3.47 (s, 2H), 2.96-2.88 (m, 2H), 2.43 (s, 3H), 2.36-2.32 (m, 1H), 2.23-2.17 (m, 4H), 1.82 (d, J = 12.4 Hz, 1H), 1.67-1.60 (m, 2H), 1.36 (t, J = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.7, 148.0, 142.9, 137.0, 135.5, 132.6, 130.5, 130.0, 129.6, 128.8, 128.4, 127.9, 127.1, 127.1, 126.5, 122.4, 117.9, 66.8, 61.0, 53.7, 53.5, 49.8, 37.4, 21.4, 18.4, 14.4.

HRMS (ESI) Calcd for $C_{29}H_{33}N_2O_5S$ $(M+H)^+$: 521.2105, Found: 521.2104.



2'-methyl-6'-morpholino-[1,1'-biphenyl]-2-amine (7)

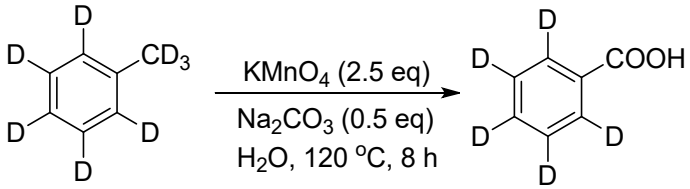
White solid. 67% yield; mp: 104-105 ℃;

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 1H), 7.19-7.15 (m, 1H), 7.06-7.03 (m, 2H), 6.96-6.94 (m, 1H), 6.86-6.79 (m, 2H), 3.50 (t, J = 4.6 Hz, 4H), 2.93-2.78 (m, 4H), 2.12 (s, 3H).

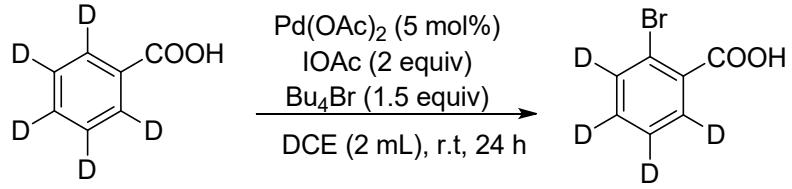
^{13}C-NMR (125 MHz, $CDCl_3$) δ 115.6, 144.0, 139.0, 133.5, 131.7, 128.7, 128.5, 125.7, 125.6, 118.9, 116.8, 116.1, 67.7, 52.5, 20.8.

HRMS (ESI) Calcd for $C_{17}H_{22}N_2OS$ $(M+H)^+$: 269.1648, Found: 269.1654.

7. Deuteration Experiments

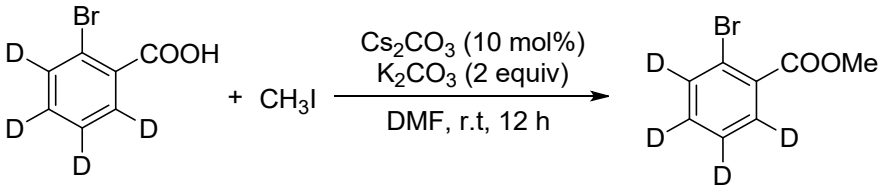


A round-bottom flask equipped with a stir bar and a condenser was charged with d_8-tolune (99.9 atom % D) (1 g, 10 mmol), $KMnO_4$ (4 g, 25 mmol), Na_2CO_3 (0.52 g, 5 mmol), and H_2O (30 mL). The reaction mixture was refluxed for 8 h and then cooled to room temperature. The mixture was filtered through a pad of celite, and the filtrate was acidified with 12 M HCl and extracted with DCM (3 × 30 mL). The organic layer was washed with water and concentrated in vacuo. The crude product was recrystallized from water to give $C_6D_5CO_2H$ as white needle solid (0.64 g, 50% yield). Synthesis of $C_6D_5CO_2H$ was prepared using a similar procedure.

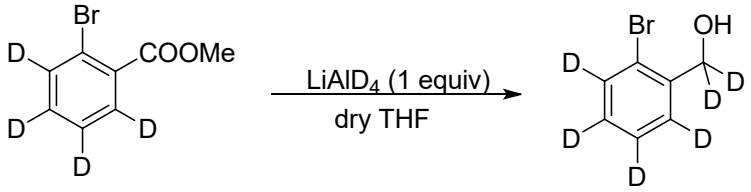


In a 20 mL glass tube, iodobenzene diacetate (128.8 mg, 0.4 mmol) and I_2 (101.6 mg, 0.4 mmol) were dissolved in dichloroethane (2 mL) under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at room temperature for 1 hour to generate iodoacetate in-situ. Substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), and tetrabutylammonium bromide (99.6 mg, 0.3 mmol) were added under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 100 °C for 24 hours. The reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was added. The organic layer was separated and the

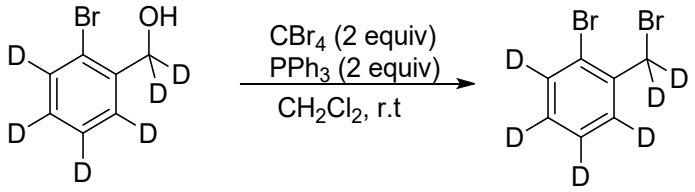
aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (hexane: ether/8:1) to give the [$^2H_4$]-2-bromobenzoic acid (16.3 mg, 40% yield).



[$^2H_4$]-2-bromobenzoic acid (2.04 g, 10 mmol) was dissolved in DMF. Two equivalents (2.76 g, 20 mmol) of K_2CO_3 and 2.82 g (20 mmol, 2.0 equiv) of methyl iodide were added to the solution, as well as a catalytic amount of Cs_2CO_3. The reaction mixture was stirred overnight at room temperature and quenched with acidic water until all the base dissolved. The aqueous solution was extracted with ether. Afterward the organic layer was washed with water, dried over $MgSO_4$, and concentrated to a colourless oil.[7]

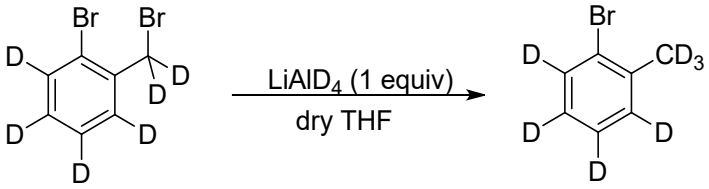


In a flame-dried round-bottom flask immersed in an ice bath, 0.336 g (8 mmol, 2.0 equiv) of lithium aluminum deuteride was suspended in 10 mL of dry THF. [$^2H_4$]-methyl 2-bromobenzoate (1.74 g, 8 mmol) diluted in 5 mL of dry THF was added dropwise at 0 °C. After the addition was complete, the slurry was stirred for 20 min. The reaction mixture was quenched and worked up following the standard procedure,[7] to yield 1.3 g (85%) of a colourless oil.

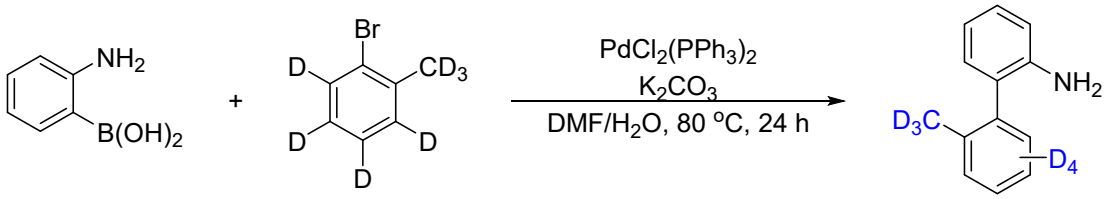


[$^2H_6$]-2-bromobenzyl alcohol (1.15 mg, 6 mmol) was suspended in a solution of CBr_4 (0.664 g, 12 mmol, 2 equiv) in dichloromethane. Triphenylphosphine (3.15 g, 12

mmol, 2 equiv) was added portionwise at room temperature to avoid overheating. After the addition was complete, the clear solution was precipitated in ether and filtered. As the solvent was evaporated, any remaining triphenylphosphine was further filtered. The crude product was purified via column chromatography using 5:1 hexanes- ethyl acetate to yield 1.14 g (75%) of a colourless oil.

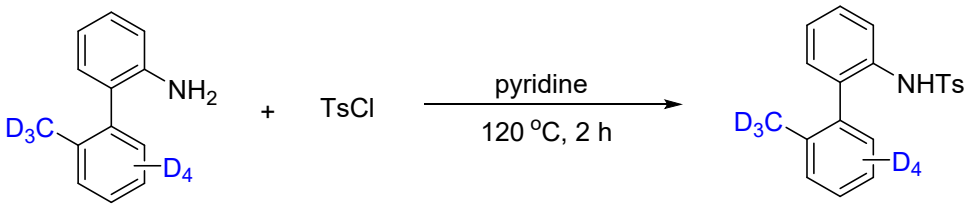


In a flame-dried flask, [$^2H_6$]-2-bromo-benzyl bromide (1.14 g, 4.5 mmol) in THF was added dropwise to a slurry of lithium aluminum deuteride (0.189 g, 4.5 mmol) in dry THF at room temperature. Then, the reaction mixture was quenched and worked up following the standard procedure.[7]



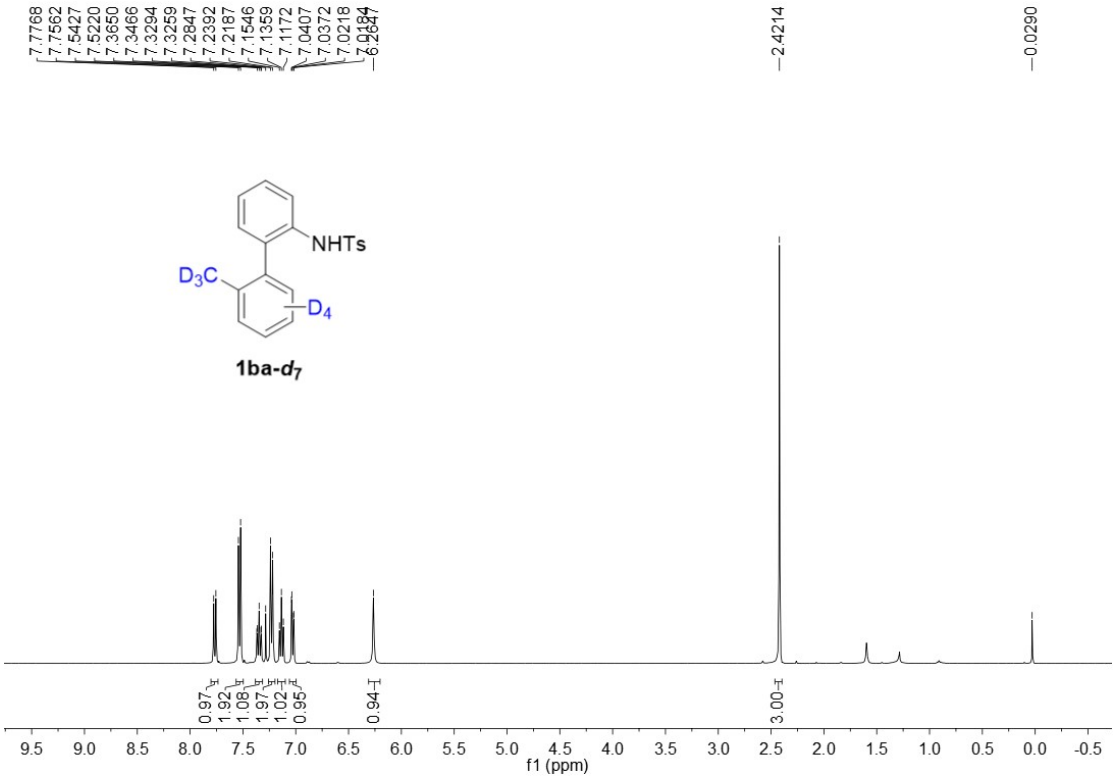
1baNH$_2$-*d*$_7$

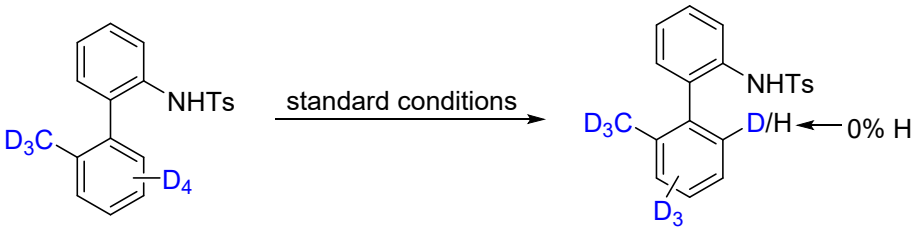
(2-aminophenyl)boronic acid (1.5 equiv.), K_2CO_3 (4.0 equiv.), and $PdCl_2(PPh_3)_2$ (5% mol%) were added to DMF/H_2O (v/v 13:3) in a flame-dried round bottom flask containing 1-bromo-2-(methyl-d_3)benzene-3,4,5,6-d_4. The resulting mixture was stirred at 80 °C for 24 h under a nitrogen atmosphere. After completion of the reaction, the reaction mixture was allowed to cool down to room temperature and was extracted several times with CH_2Cl_2. The combined organic layer was washed twice with sat. NaCl and dried over anhydrous Na_2SO_4. The organic layer was then concentrated under vacuum, and the crude residue was purified using flash silica gel column chromatography (hexane/EtOAc) to produce the coupling product **1baNH$_2$-*d*$_7$**.



1baNH$_2$-*d*$_7$ **1ba-*d*$_7$**

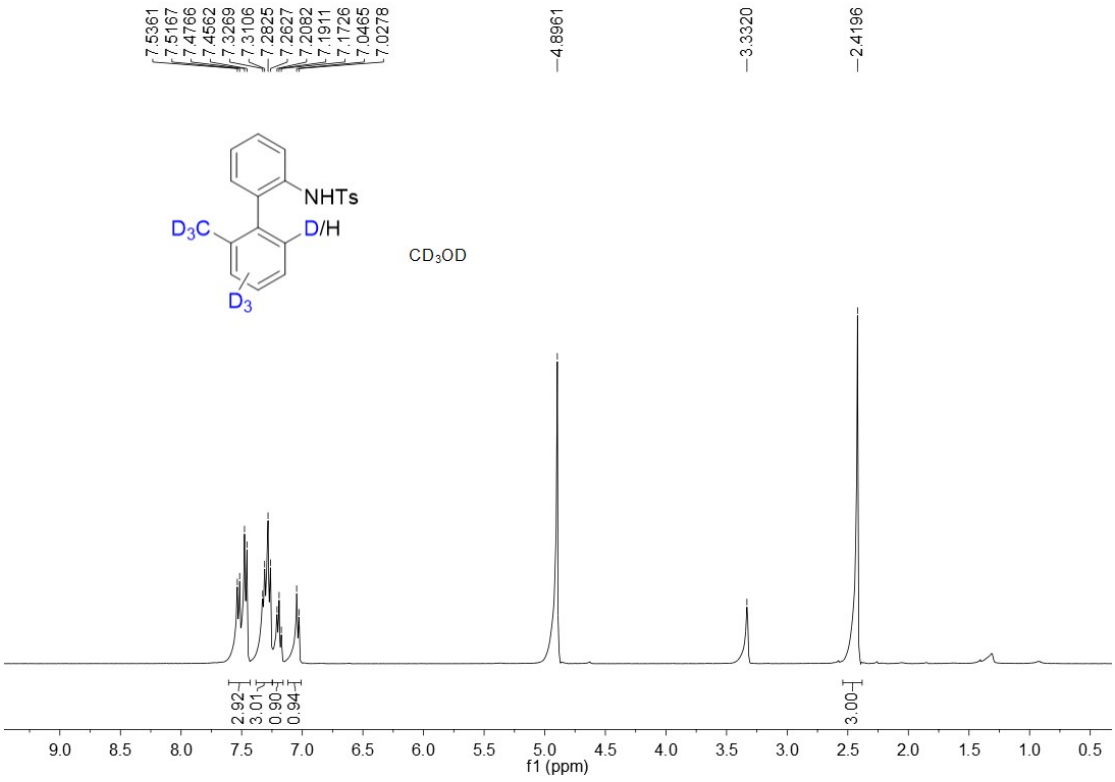
To a flame-dried round-bottom flask containing the solution of **1baNH$_2$-*d*$_7$** in pyridine was added 4-methylbenzenesulfonyl chloride (1.5 equiv.) and the resulting mixtures were refluxed at 120 °C for 2 h. After the completion of the reaction, the reaction mixture was allowed to cool to room temperature and extracted with CH_2Cl_2 for several times. The combined organic layer was washed with saturated NaCl for two times and dried over anhydrous Na_2SO_4. The organic layer was then concentrated under vacuum, and the crude residue was purified by silica gel column chromatography (hexane/EtOAc) to afford **1ba-*d*$_7$**.

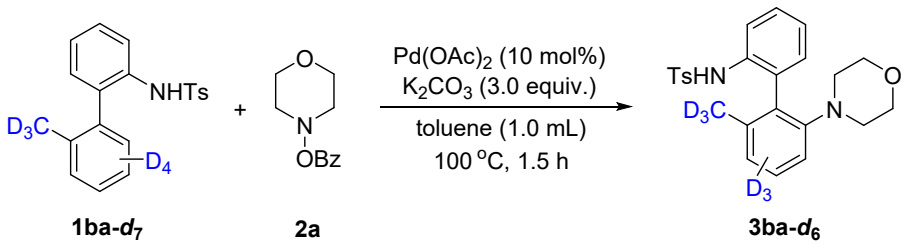




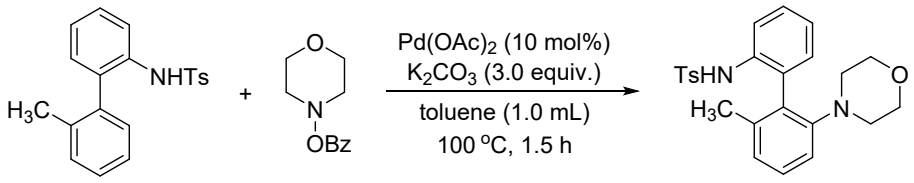
1ba-d_7 **1ba-d_7**, 0% H

To an oven-dried 25 mL Schlenk tube was added substrate **1ba-d_7** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), K_2CO_3 (0.6 mmol), toluene (1.0 mL). The mixture was stirred for 12 h at 100 °C followed by cooling. The resulting mixture was quenched by filtered through a celite pad and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to afford the starting material **1ba-d_7**.

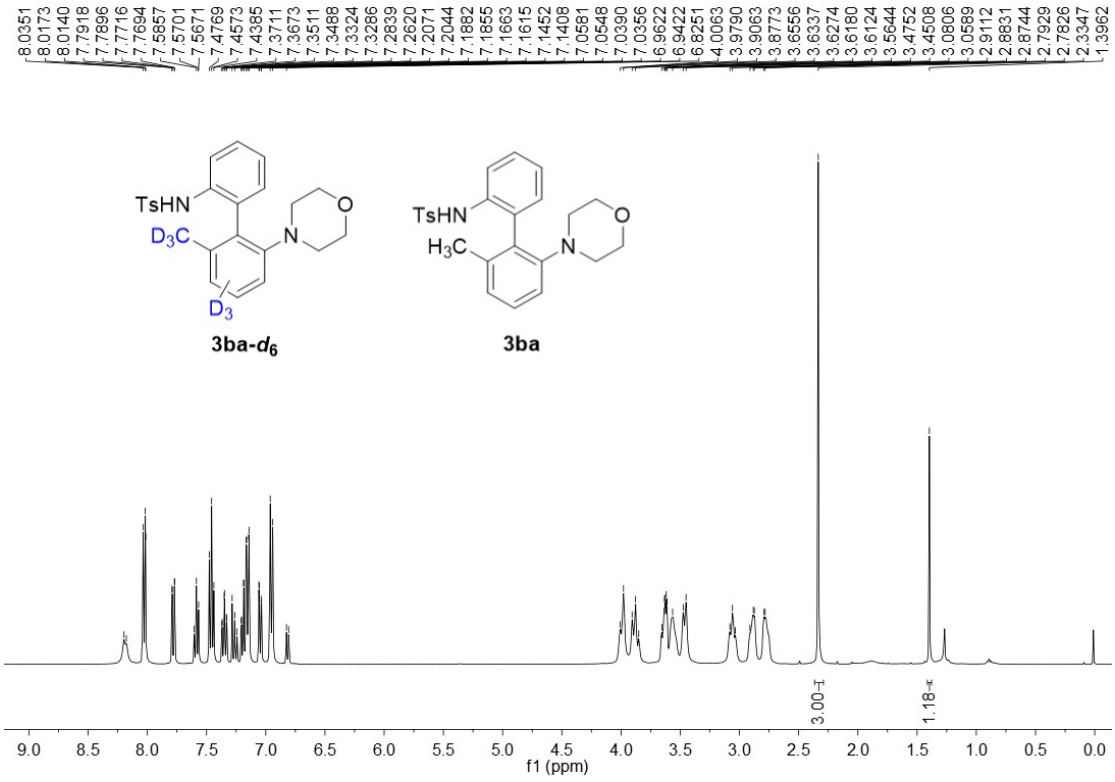


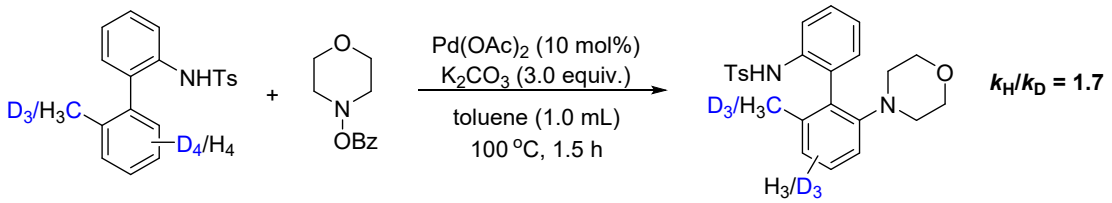


k_H/k_D = 0.7



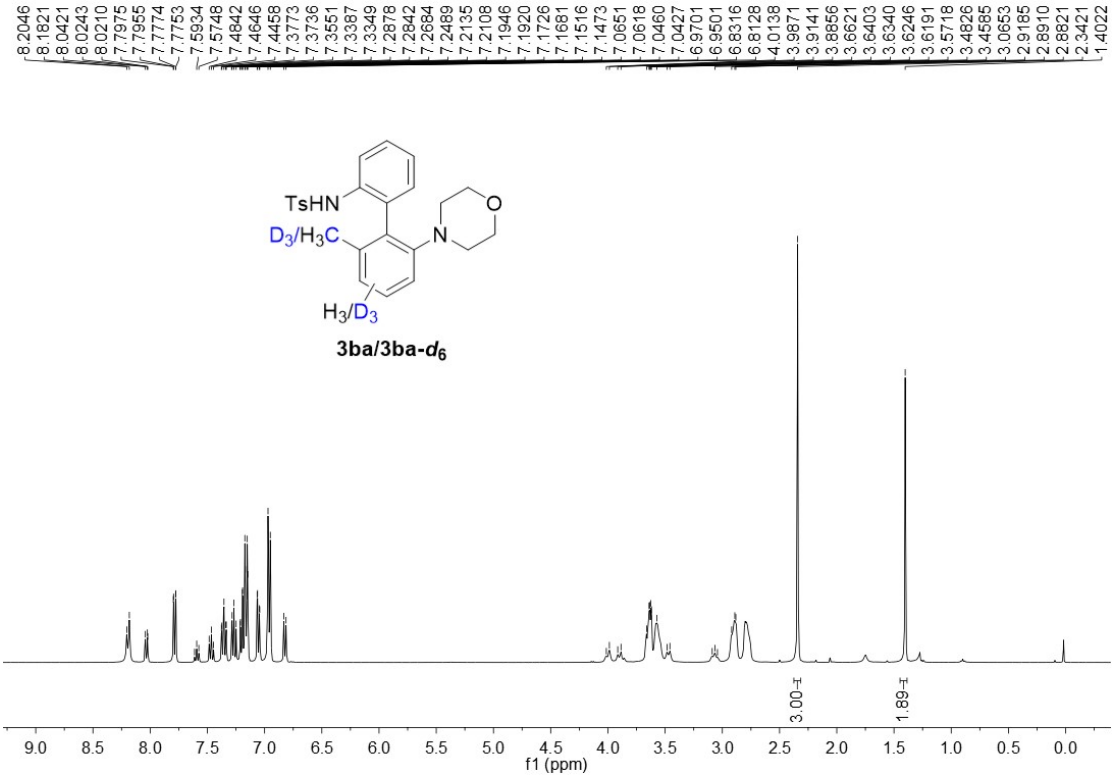
To an oven-dried 25 mL Schlenk tube was added substrate **1ba** or **1ba-d$_7$** (0.2 mmol), **2** (0.4 mmol), $Pd(OAc)_2$ (0.01 mmol), K_2CO_3 (0.6 mmol), toluene (1.0 mL). The mixture was stirred for 12 h at 100 °C followed by cooling. The resulting mixture was quenched by filtered through a celite pad and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to afford a mixture of **3ba** and **3ba-*d*$_6$**.



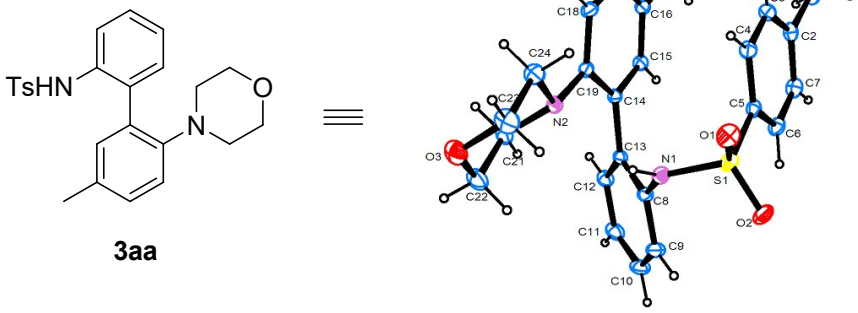


1ba/1ba-d_7 **2a** **3ba/3ba-d_6**

To an oven-dried 25 mL Schlenk tube was added substrate **1ba** (0.1 mmol), **1ba-d_7** (0.1 mmol), **2** (0.4 mmol), $Pd(OAc)_2$ (0.01 mmol), K_2CO_3 (0.6 mmol), toluene (1.0 mL). The mixture was stirred for 12 h at 100 °C followed by cooling. The resulting mixture was quenched by filtered through a celite pad and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to afford a mixture of **3ba** and **3ba-d_6**.



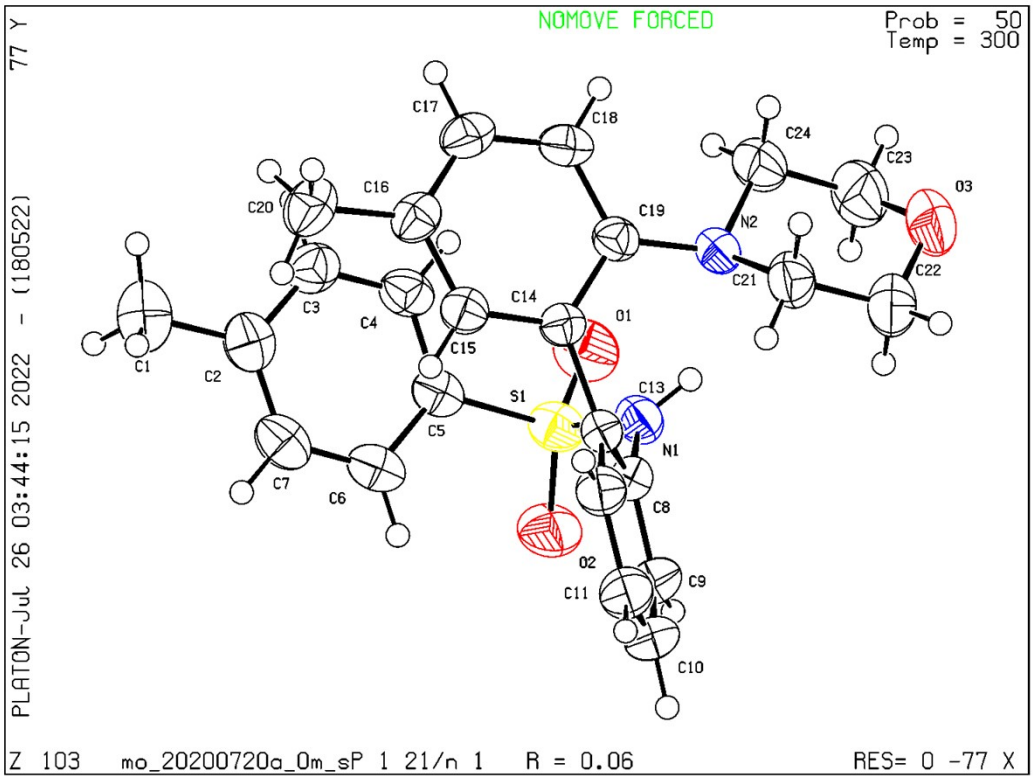
8. X-ray Crystallographic Data

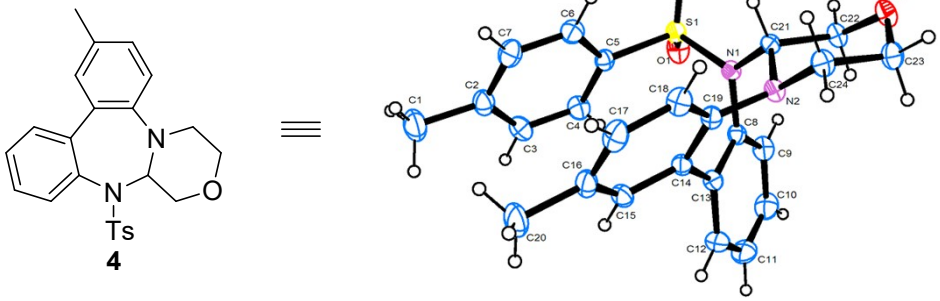


(CCDC 2060398; Displacement ellipsoids are drawn at the 50% probability level)

Identification code	mo_20200720a_0m_sq	
Empirical formula	C_{24} H_{26} N_2 O_3 S	
Formula weight	422.53	
Temperature	300.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 9.5460(6) Å	α= 90°.
	b = 9.1361(5) Å	β= 93.827(2)°.
	c = 29.2032(17) Å	γ = 90°.
Volume	2541.2(3) $Å^3$	
Z	4	
Density (calculated)	1.104 Mg/m^3	
Absorption coefficient	0.151 mm^{-1}	
F(000)	896	
Crystal size	0.24 x 0.23 x 0.21 mm^3	
Theta range for data collection	3.061 to 27.639°.	
Index ranges	-12<=h<=12, -11<=k<=11, -38<=l<=38	
Reflections collected	54642	
Independent reflections	5899 [R(int) = 0.0614]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	None	
Max. and min. transmission	0.7456 and 0.6872	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5899 / 0 / 273	
Goodness-of-fit on F^2	1.017	

Final R indices [I>2sigma(I)]	R1 = 0.0572, wR2 = 0.1512
R indices (all data)	R1 = 0.0948, wR2 = 0.1766
Extinction coefficient	n/a
Largest diff. peak and hole	0.414 and -0.416 e.Å^{-3}

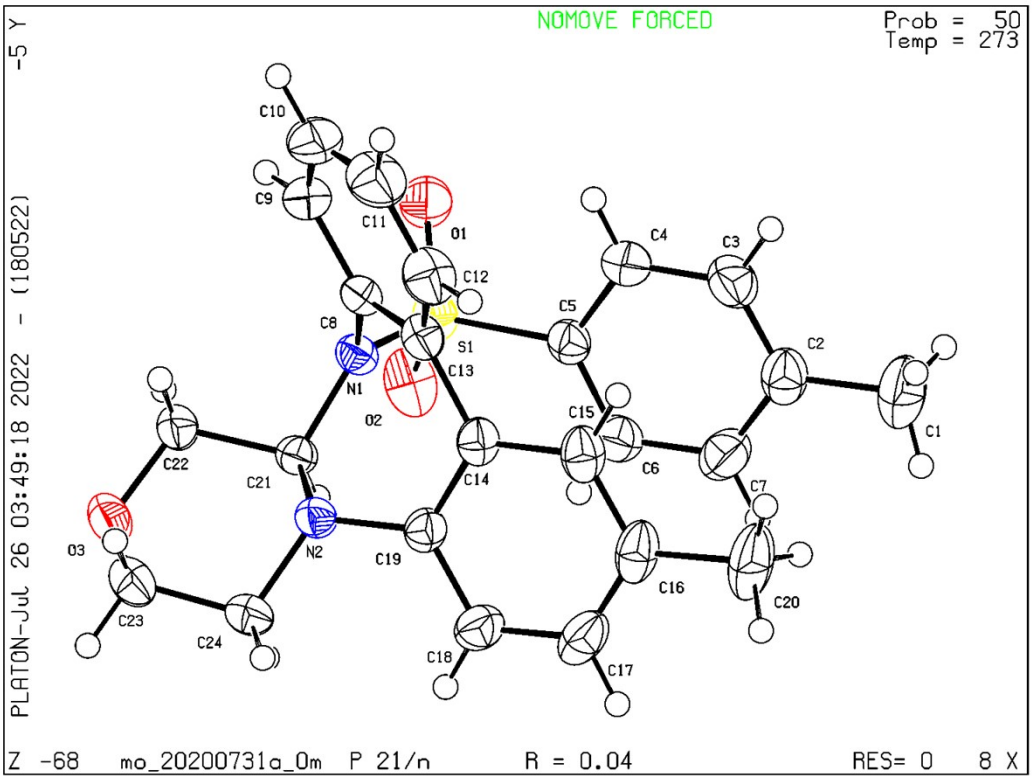




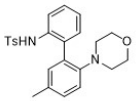
(CCDC 2060400; Displacement ellipsoids are drawn at the 50% probability level)

Identification code	mo_20200731a_0m
Empirical formula	C24 H24 N2 O3 S
Formula weight	420.51
Temperature	273(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic

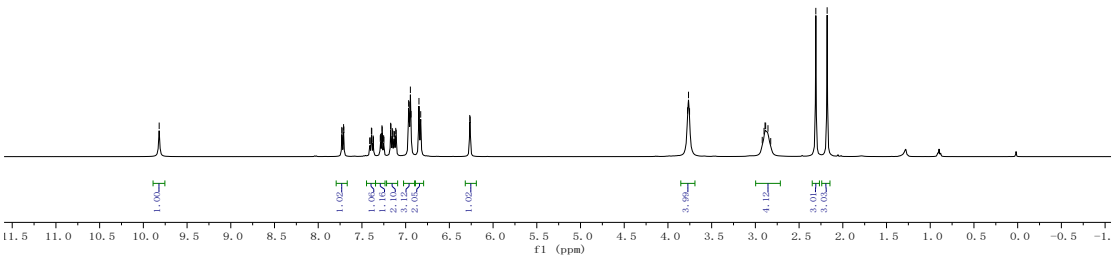
Space group	$P2_1/n$	
Unit cell dimensions	a = 8.8985(3) Å	α= 90°.
	b = 22.3112(9) Å	β= 101.4750(10)°.
	c = 10.5503(5) Å	γ = 90°.
Volume	2052.75(15) $Å^3$	
Z	4	
Density (calculated)	1.361 Mg/m^3	
Absorption coefficient	0.187 mm^{-1}	
F(000)	888	
Crystal size	0.230 x 0.210 x 0.200 mm^3	
Theta range for data collection	2.888 to 27.507°.	
Index ranges	-10<=h<=11, -28<=k<=28, -13<=l<=13	
Reflections collected	50315	
Independent reflections	4707 [R(int) = 0.0412]	
Completeness to theta = 25.242°	99.9 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4707 / 0 / 274	
Goodness-of-fit on F^2	1.026	
Final R indices [I>2sigma(I)]	R1 = 0.0402, wR2 = 0.1041	
R indices (all data)	R1 = 0.0553, wR2 = 0.1155	
Extinction coefficient	0.0083(11)	
Largest diff. peak and hole	0.256 and -0.348 $e.Å^{-3}$	

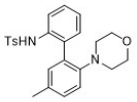

NOMOVE FORCED
Prob = 50
Temp = 273
-5 Y
PLATON-Jul 26 03:49:18 2022 - (180522)
C10
C9
C11
O1
C12
C8
S1
C13
N1
O2
C4
C3
C5
C2
C1
C15
C6
C7
C22
C21
C14
O3
N2
C19
C16
C20
C23
C24
C18
C17
Z -68 mo_20200731a_0m P 21/n R = 0.04 RES= 0 8 X

9. Copies of ^{1}H, ^{13}C and ^{19}F NMR Spectra

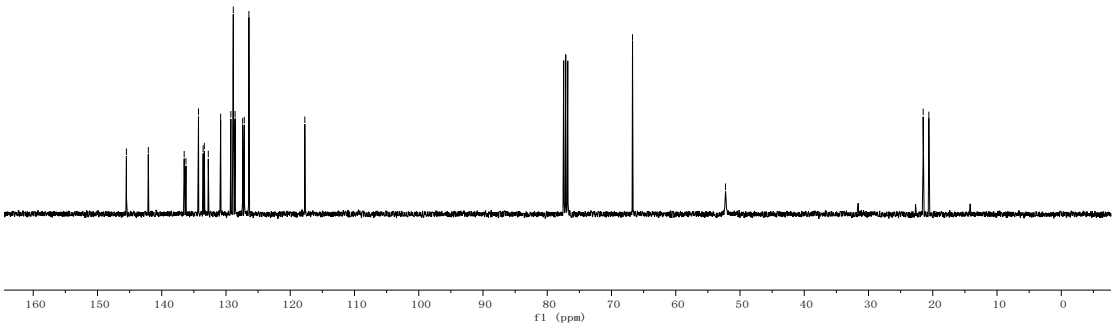


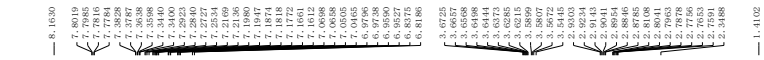
3aa

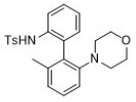




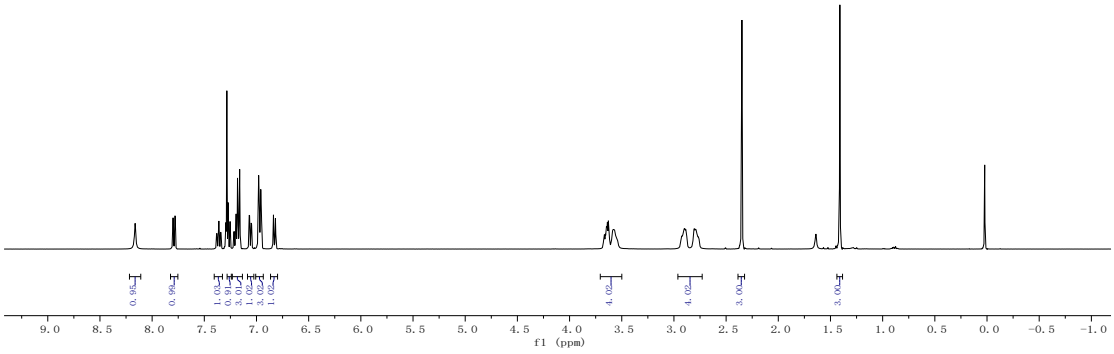
3aa

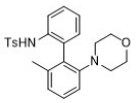




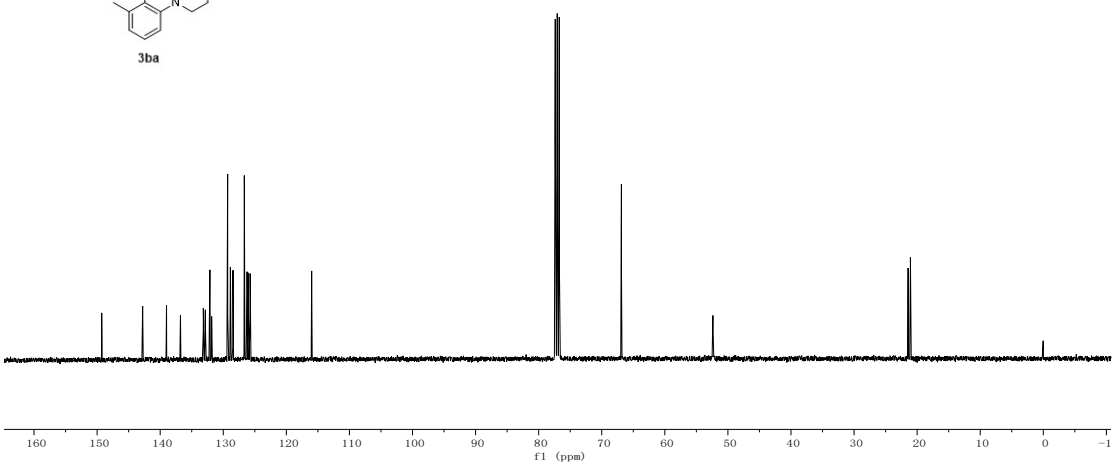

TsHN
N
O

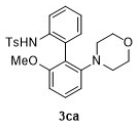
3ba


0.94
0.99
1.03
0.91
0.97
1.02
3.02
1.02
4.02
4.02
3.00
3.00
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 −0.5 −1.0
f1 (ppm)

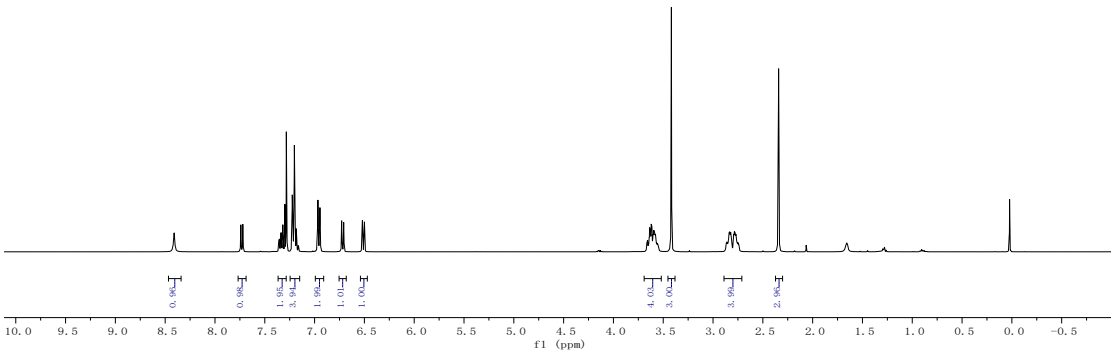

TsHN
N
O

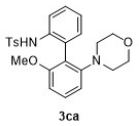
3ba


160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −1
f1 (ppm)

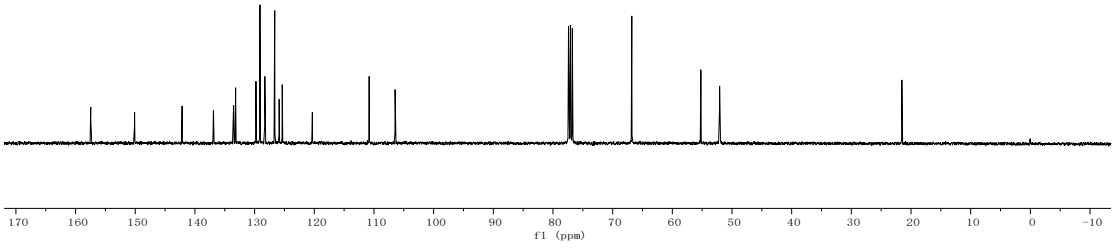

TsHN
MeO
O
N

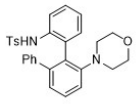
3ca


0.98
0.98
1.95
3.94
1.99
1.01
1.00
4.03
3.00
3.99
2.98
f1 (ppm)

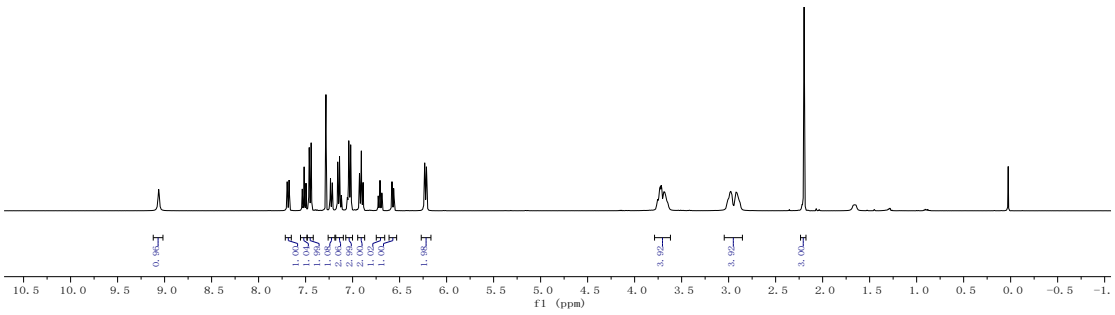

TsHN
MeO
O
N

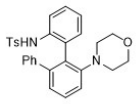
3ca


f1 (ppm)

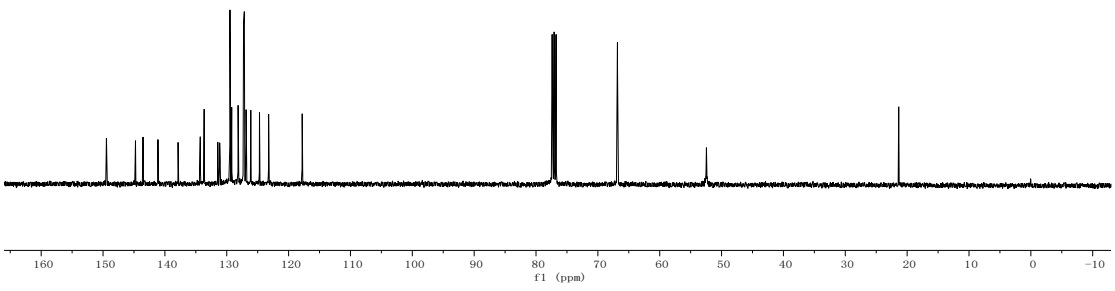


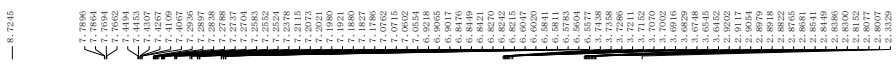
3da

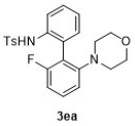




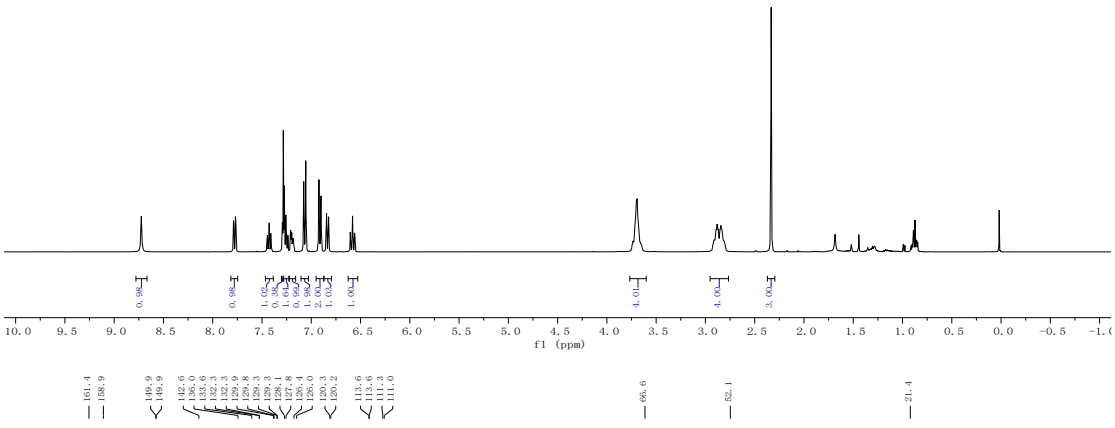
3da

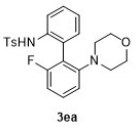




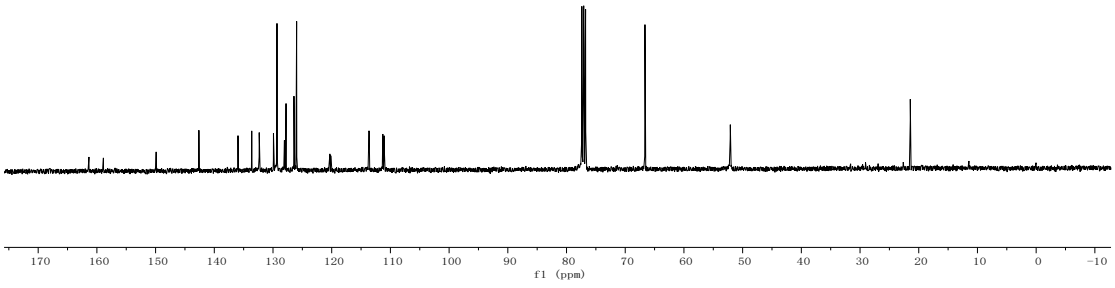


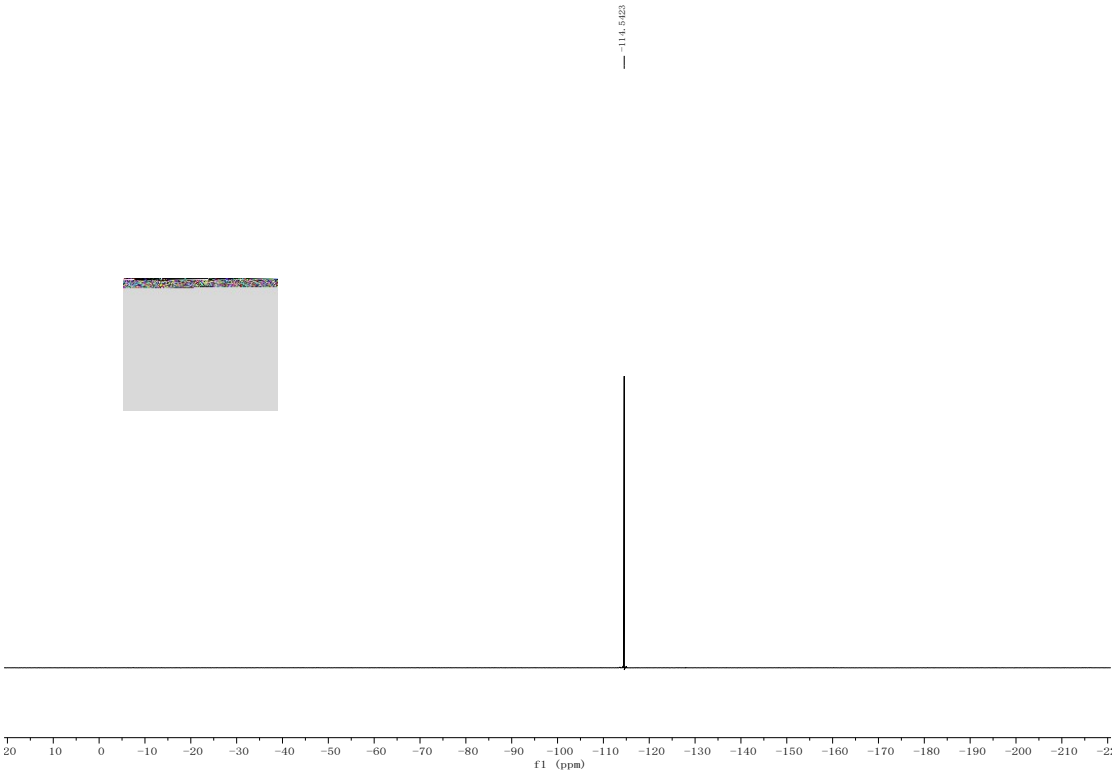
3ea

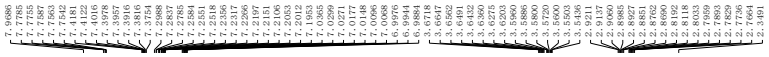


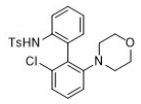


3ea

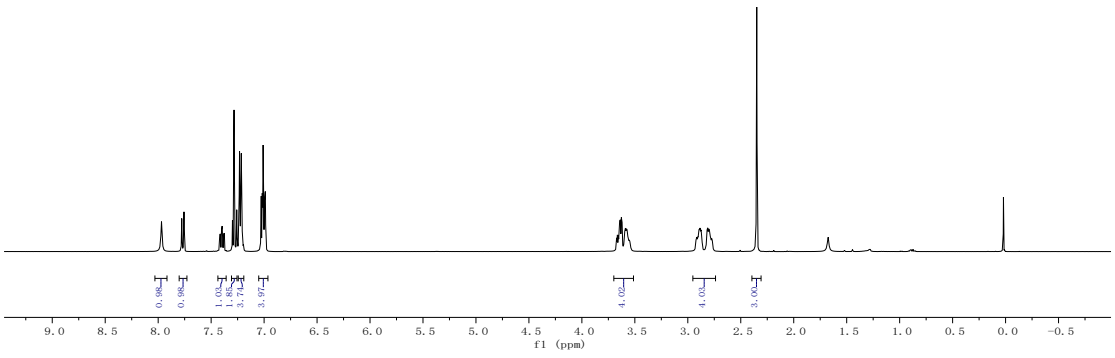



-114.5423
f1 (ppm)




TsHN
Cl
N
O

3fa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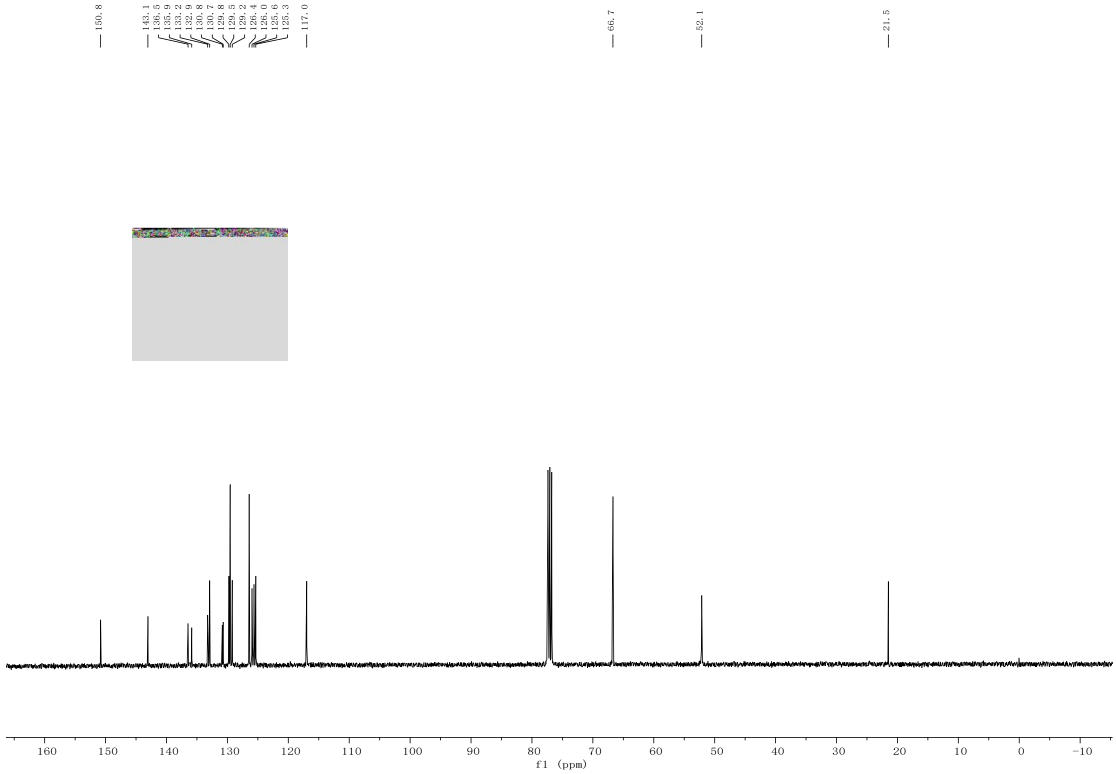
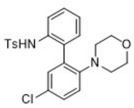
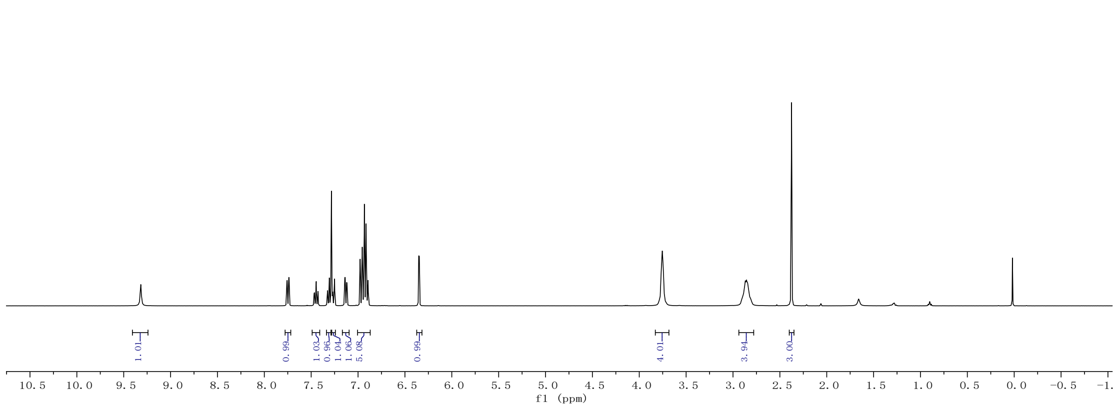
0.98
1.03
1.85
3.71
3.97
4.02
4.03
3.00
f1 (ppm)


150.8
143.1
136.5
135.9
133.2
132.9
130.8
130.7
129.8
129.5
129.2
126.4
126.0
125.6
125.3
117.0
66.7
52.1
21.5
f1 (ppm)


TsHN
N
O
Cl

3ga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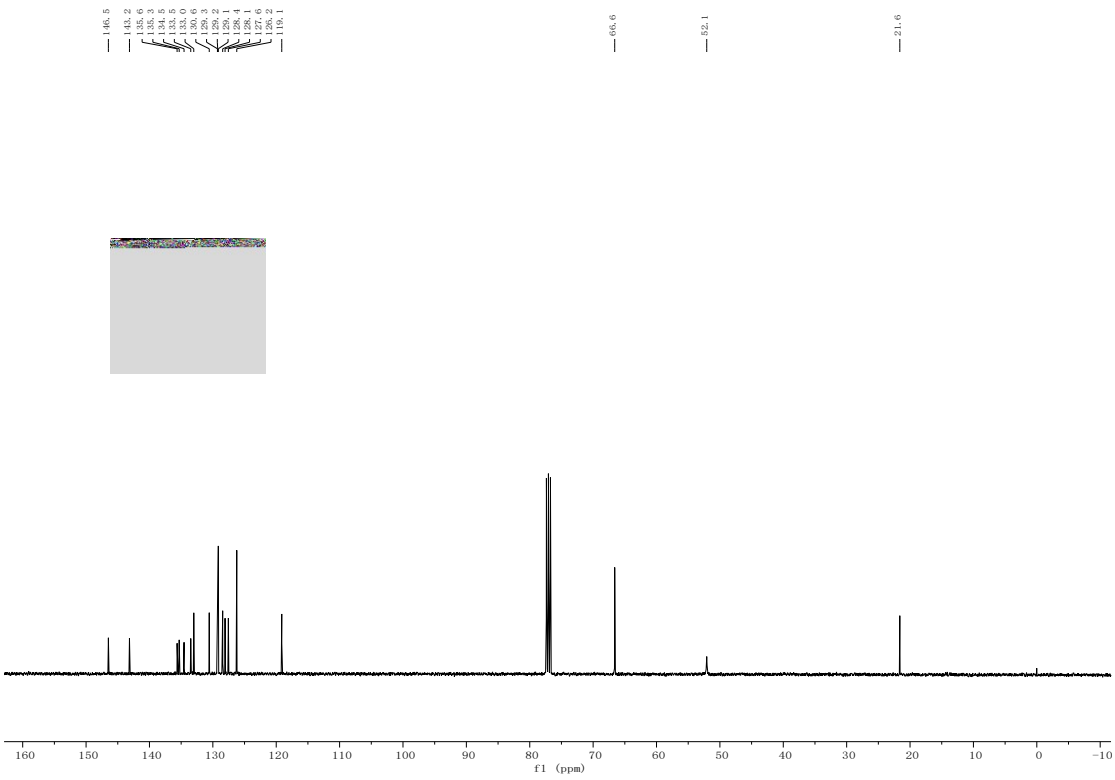
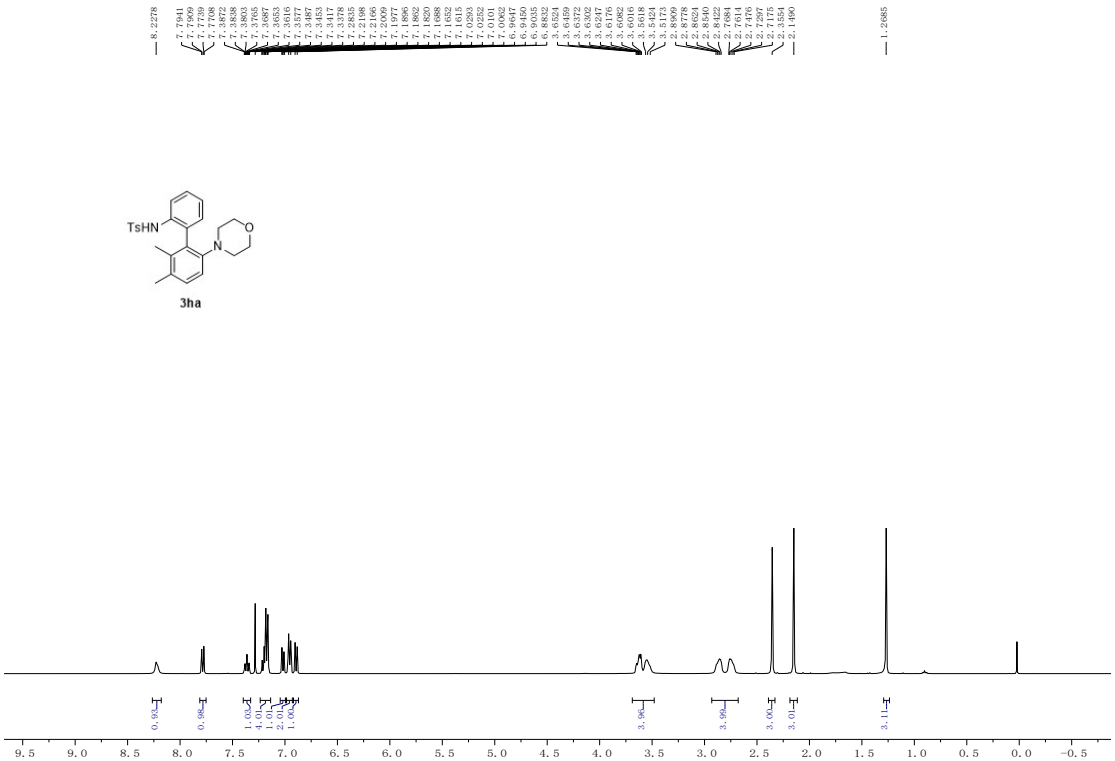
3.7660
3.7544
3.7427
2.9094
2.8992
2.8797
2.8691
2.8482
2.8137
2.3756
f1 (ppm)


146.5
143.2
135.6
135.3
134.5
133.5
133.0
130.6
129.3
129.2
128.1
128.4
128.1
127.6
126.2
110.1
66.6
52.1
21.6
f1 (ppm)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7.7941
7.7909
7.7739
7.7708
7.3872
7.3838
7.3803
7.3756
7.3687
7.3653
7.3616
7.3577
7.3495
7.3453
7.3417
7.3378
7.2955
7.2198
7.2166
7.2009
7.1977
7.1895
7.1882
7.1820
7.1688
7.1652
7.1615
7.0293
7.0252
7.0101
7.0082
6.9647
6.9450
6.9405
6.8832
3.6524
3.6459
3.6372
3.6292
3.6247
3.6176
3.6082
3.6016
3.5618
3.5424
3.5173
3.5096
2.8778
2.8624
2.8540
2.8492
2.8464
2.7614
2.7476
2.7397
2.7175
2.3554
2.1490
1.2685
TsHN
N
O
3ha
0.83
0.98
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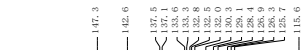
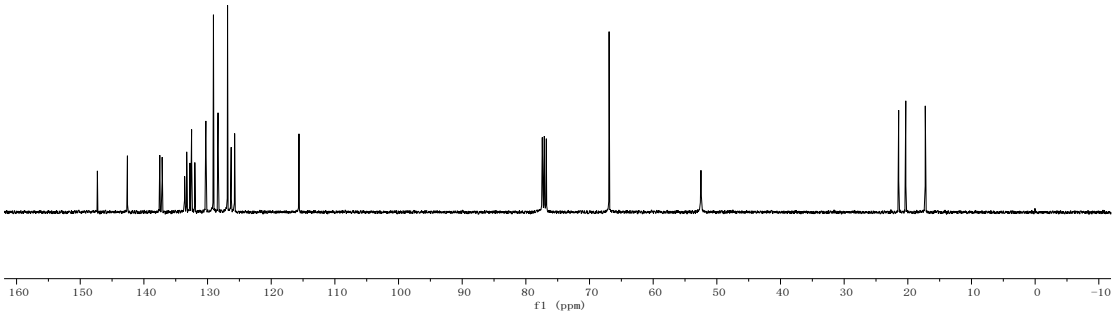
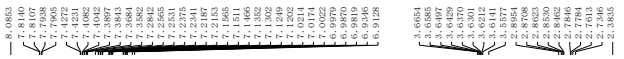
1.01
2.01
1.00
3.96
3.99
3.00
3.01
3.11
f1 (ppm)


147.3
142.6
137.5
137.1
133.6
133.3
132.8
132.5
132.0
130.3
129.1
128.4
126.9
126.3
125.7
115.6
66.9
52.5
21.4
20.3
17.3


160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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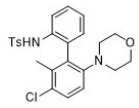
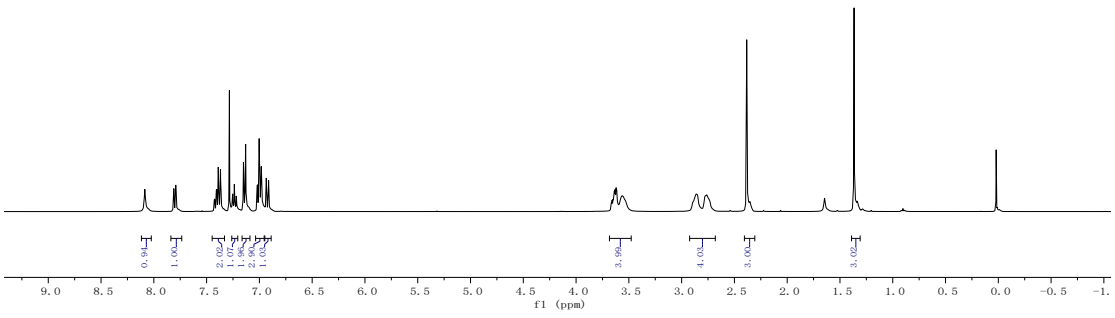
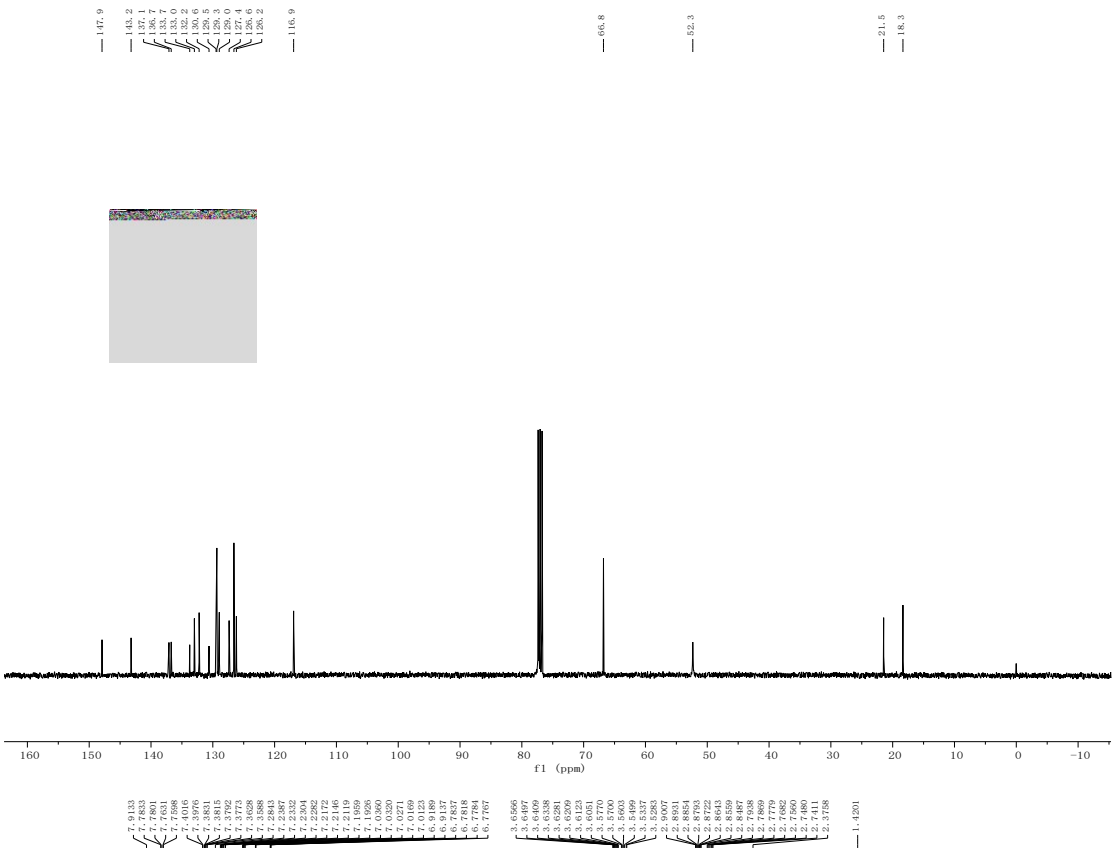
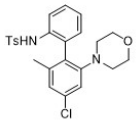
7.8140
7.8107
7.7938
7.7905
7.4472
7.4231
7.4082
7.4042
7.3897
7.3864
7.3684
7.3382
7.2842
7.2695
7.2531
7.2375
7.2341
7.2187
7.2153
7.1565
7.1511
7.1466
7.1352
7.1302
7.1249
7.1202
7.0744
7.0174
7.0022
6.9979
6.9870
6.9819
6.9346
6.9128
3.6654
3.6585
3.6497
3.6370
3.6291
3.6212
3.6141
3.5577
2.8954
2.8896
2.8823
2.8530
2.8462
2.7846
2.7784
2.7613
2.7346
2.3833
1.3665


TsHN
N
O
Cl

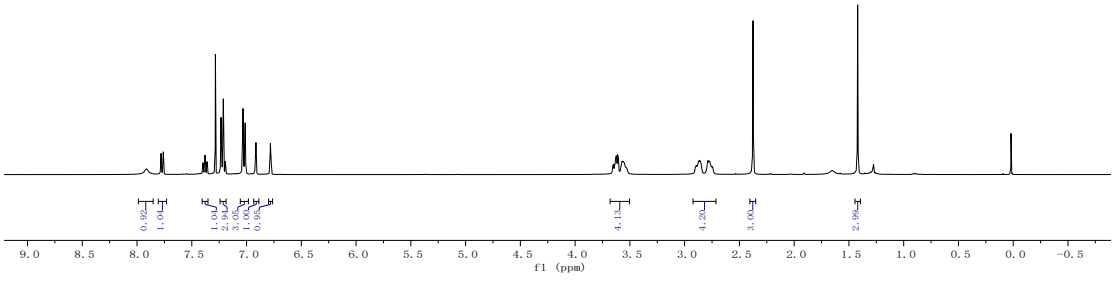
3ia

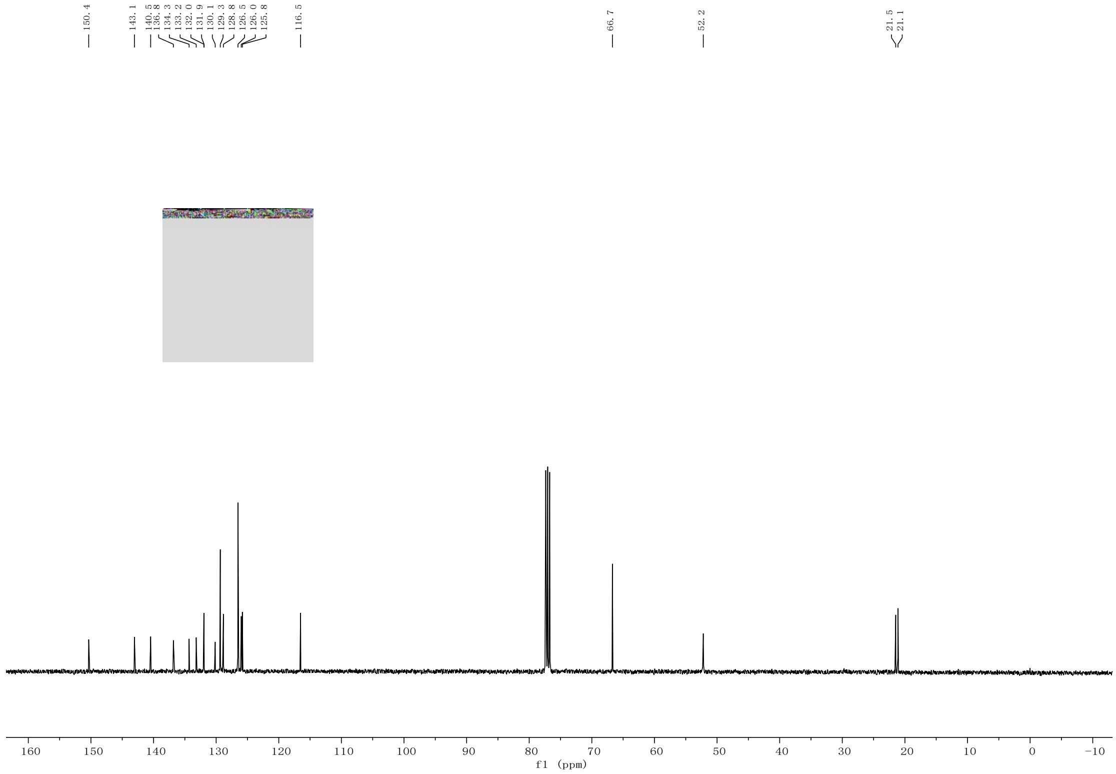

0.94
1.00
2.02
1.07
1.96
2.04
1.03
3.90
4.03
3.00
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)





3ja

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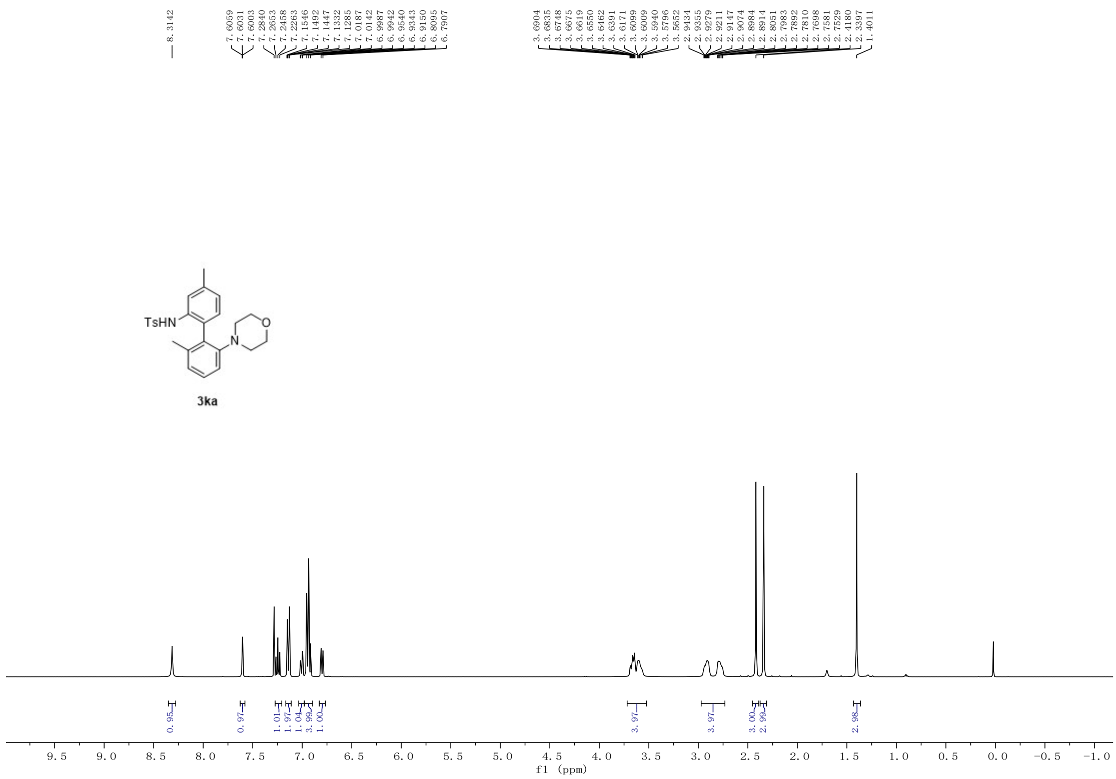
140.5
136.8
134.3
133.2
132.0
131.9
130.1
129.3
128.8
126.5
126.0
125.8
116.5
66.7
52.2
21.5
21.1
f1 (ppm)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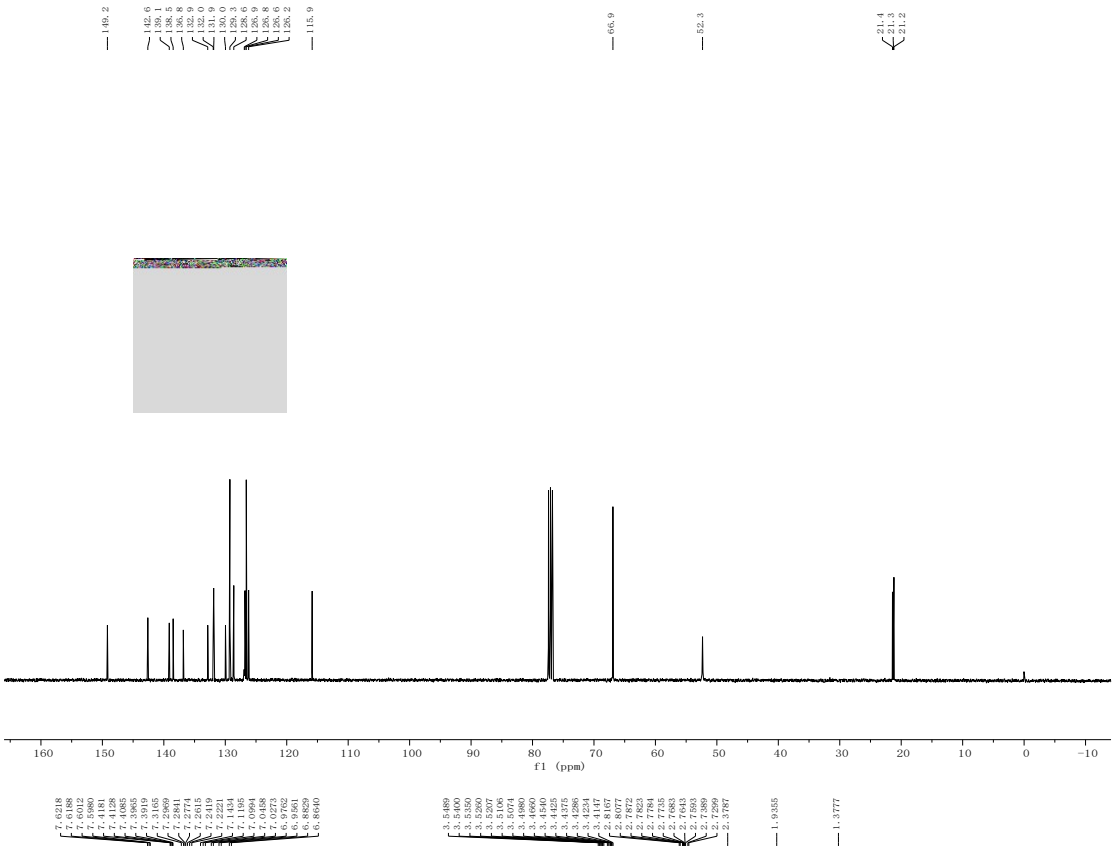
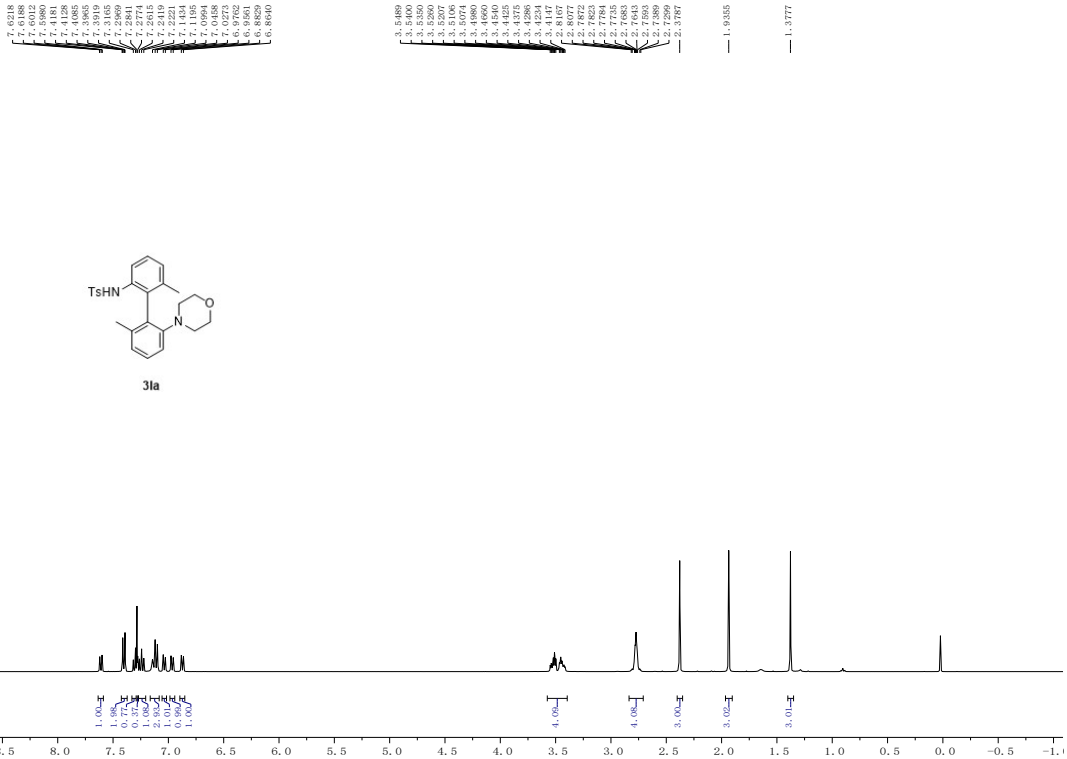
7.6059
7.6031
7.6003
7.2840
7.2653
7.2458
7.2263
7.1546
7.1492
7.1447
7.1332
7.1285
7.0187
7.0142
6.9987
6.9942
6.9540
6.9343
6.9150
6.8095
6.7907
3.6904
3.6835
3.6748
3.6675
3.6619
3.6550
3.6462
3.6391
3.6171
3.6099
3.6009
3.5940
3.5796
3.5652
2.9434
2.9355
2.9279
2.9211
2.9147
2.9074
2.8984
2.8914
2.8051
2.7983
2.7892
2.7810
2.7698
2.7581
2.7529
2.4180
2.3397
1.4011
TsHN
N
O
3ka
0.95
0.97
1.01
1.97
1.04
3.99
1.00
3.97
3.97
3.00
2.99
2.98
f1 (ppm)


149.2
142.6
139.1
138.5
136.8
132.9
132.0
131.9
130.0
129.3
128.6
126.8
126.6
126.2
115.9
66.9
52.3
21.4
21.3
21.2
f1 (ppm)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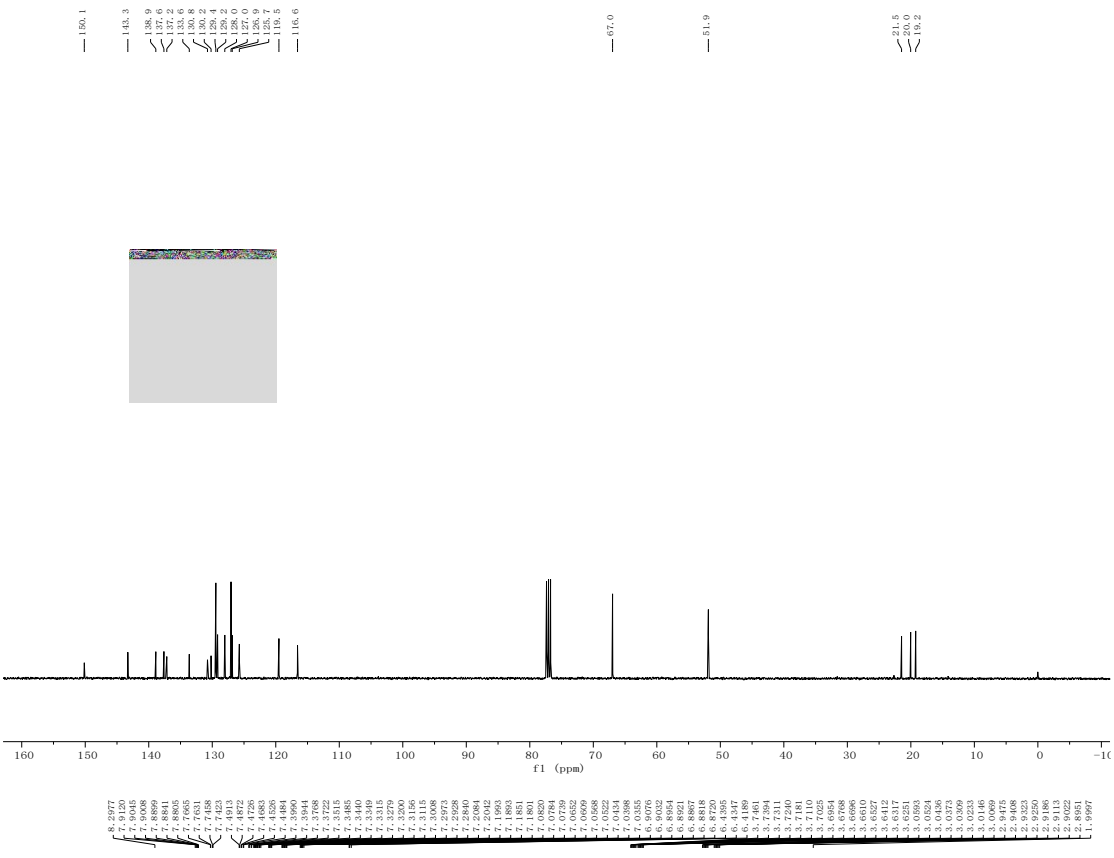
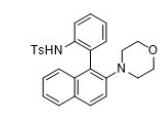
7.6188
7.6012
7.5980
7.4181
7.4128
7.4085
7.3965
7.3919
7.3165
7.2969
7.2841
7.2774
7.2645
7.2419
7.2221
7.1434
7.1195
7.1044
7.0458
7.0273
6.9762
6.9561
6.8829
6.8640
3.5489
3.5400
3.5350
3.5299
3.5207
3.5106
3.5074
3.4980
3.4866
3.4540
3.4425
3.4375
3.4298
3.4234
3.4147
2.8167
2.8077
2.7872
2.7823
2.7784
2.7735
2.7685
2.7643
2.7593
2.7389
2.7299
2.3787
1.9355
1.3777
TsHN
N
O
3la
1.00
1.98
0.77
0.72
1.08
2.92
1.01
0.96
1.00
4.09
4.08
3.00
3.02
3.01
f1 (ppm)





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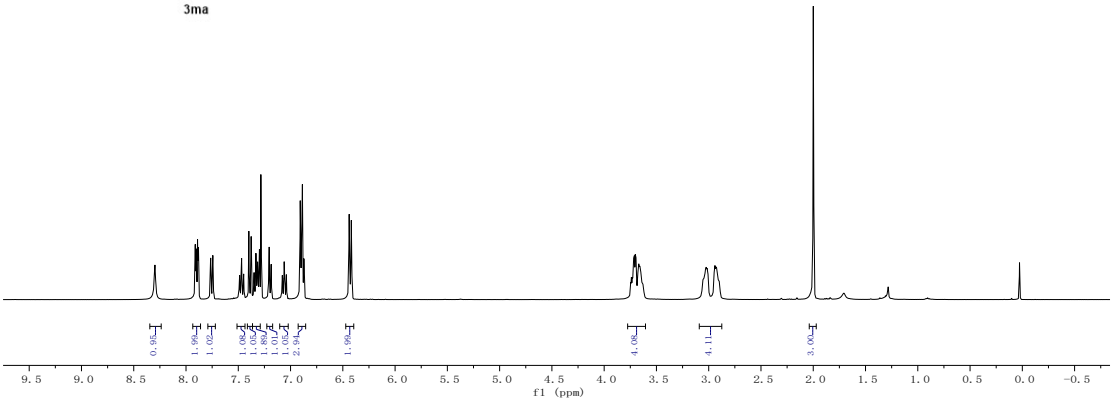

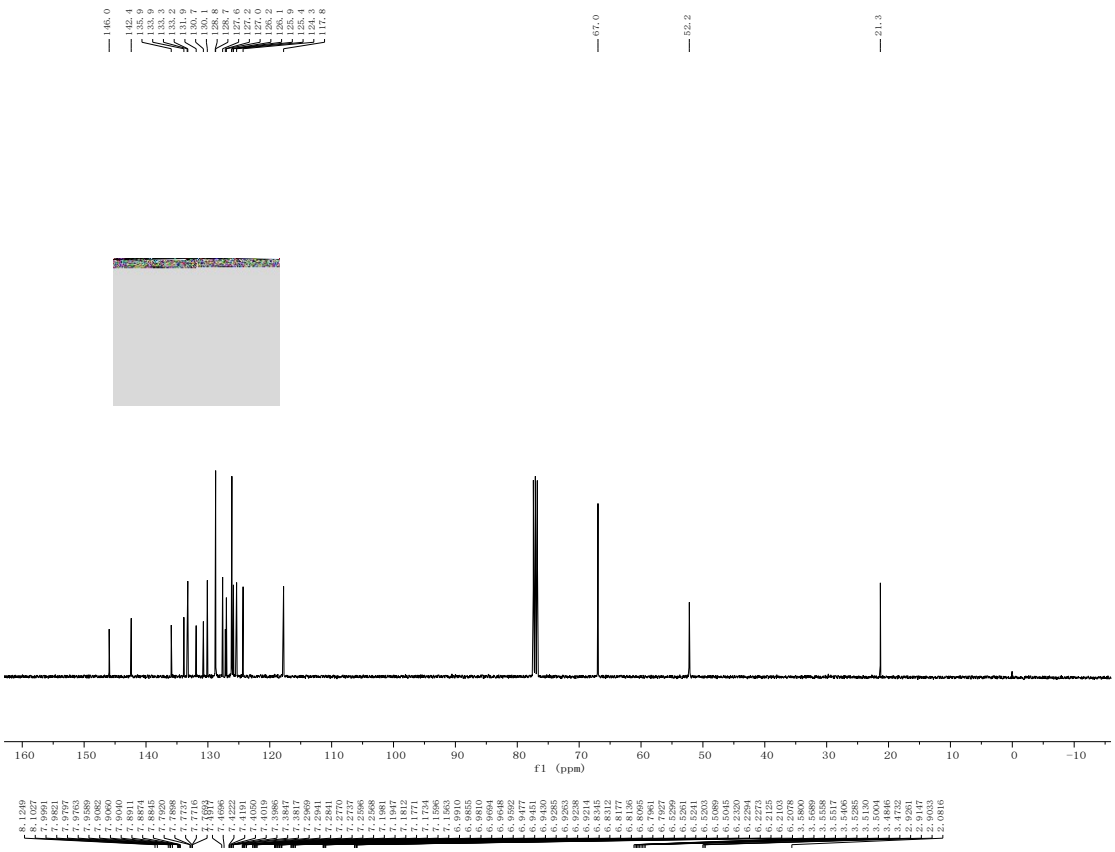

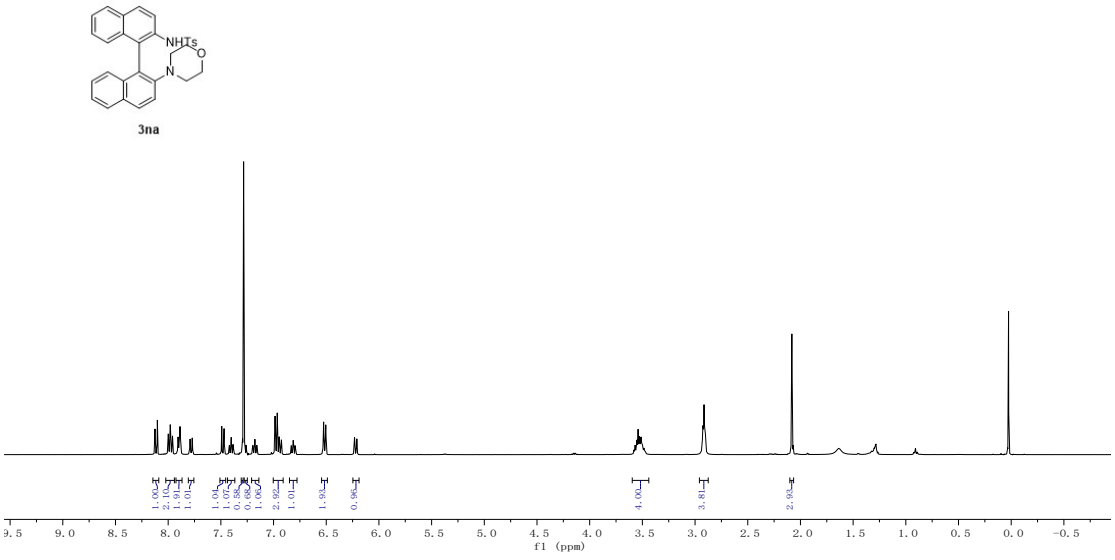

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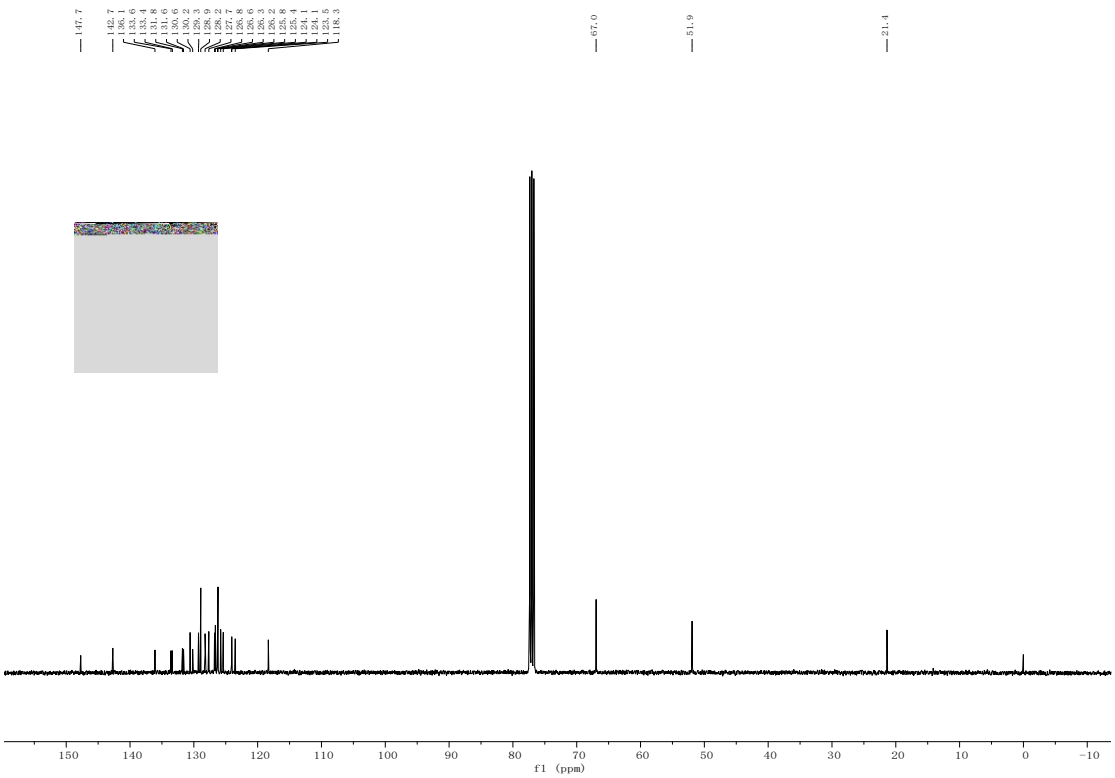
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142.7
136.1
133.6
133.4
131.8
131.6
130.6
130.2
128.3
128.9
128.2
127.7
126.8
126.6
126.3
125.8
125.4
124.1
124.1
123.5
118.3
67.0
51.9
21.4
f1 (ppm)


9.6281
7.7400
7.7366
7.7200
7.7166
7.4597
7.4207
7.4061
7.4021
7.3885
7.3823
7.3393
7.3351
7.3191
7.3109
7.3002
7.2964
7.2841
7.2805
7.2772
7.2619
7.2385
7.1996
7.1765
7.1614
7.1573
7.0931
7.0892
7.0416
7.0387
6.9695
6.9659
6.9537
6.9488
6.8855
6.8655
6.8666
6.8637
6.8479
6.8439
6.8333
6.8133
6.4816
6.4776
6.4735
6.4484
3.7927
3.7811
3.7684
2.9589
2.9502
2.9343
2.9214
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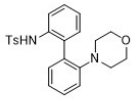
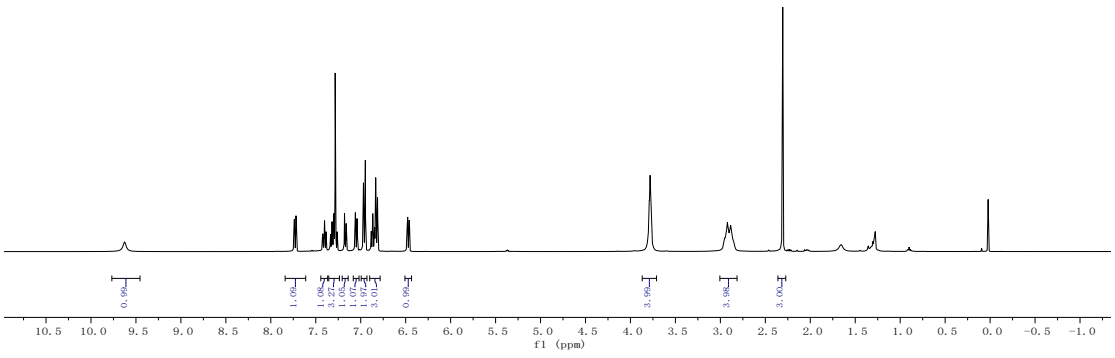
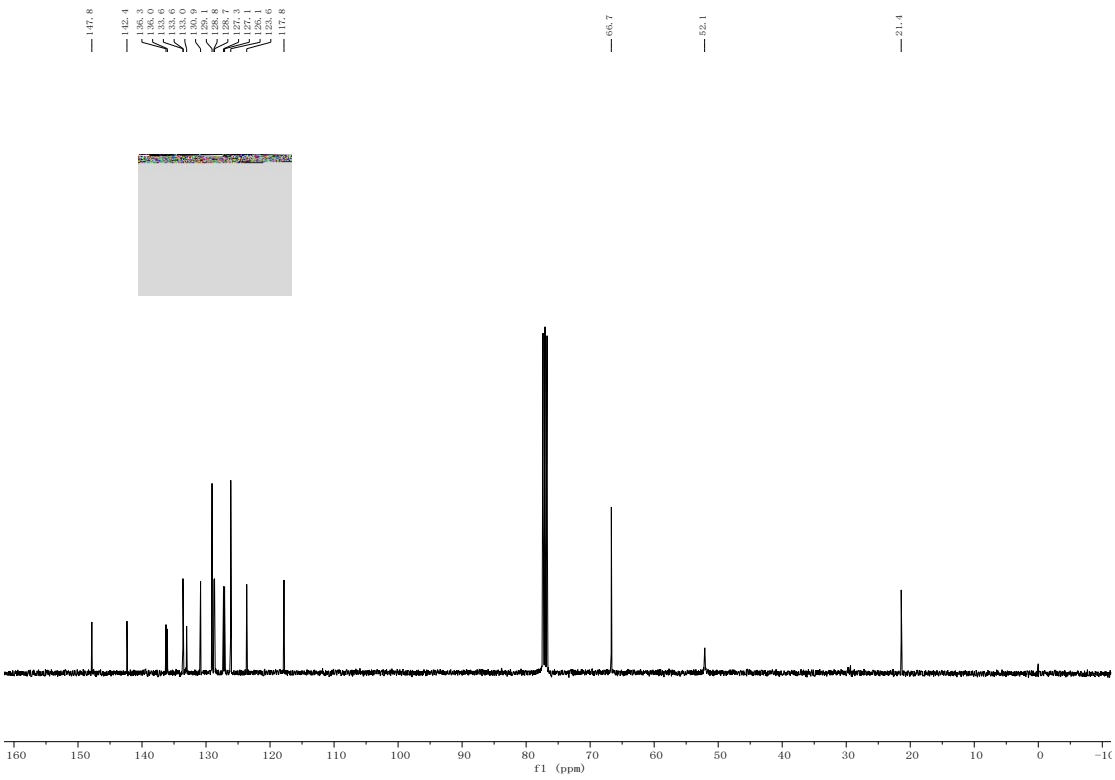
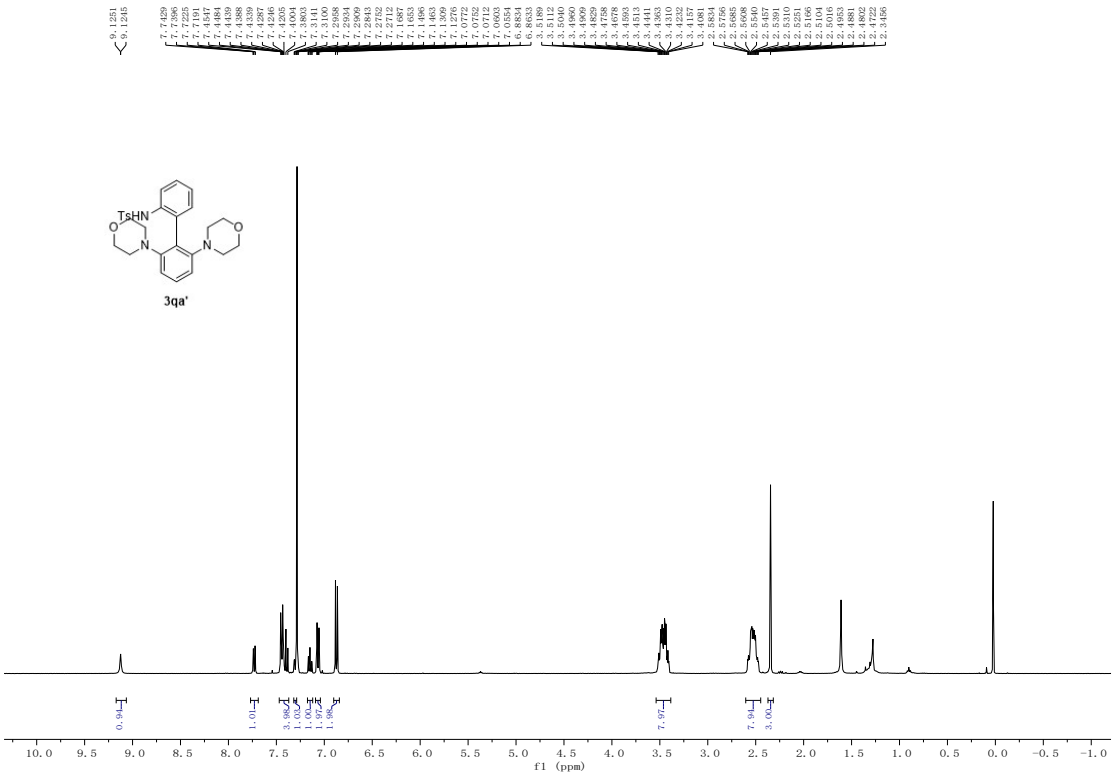
2.8724
2.8584
2.3063

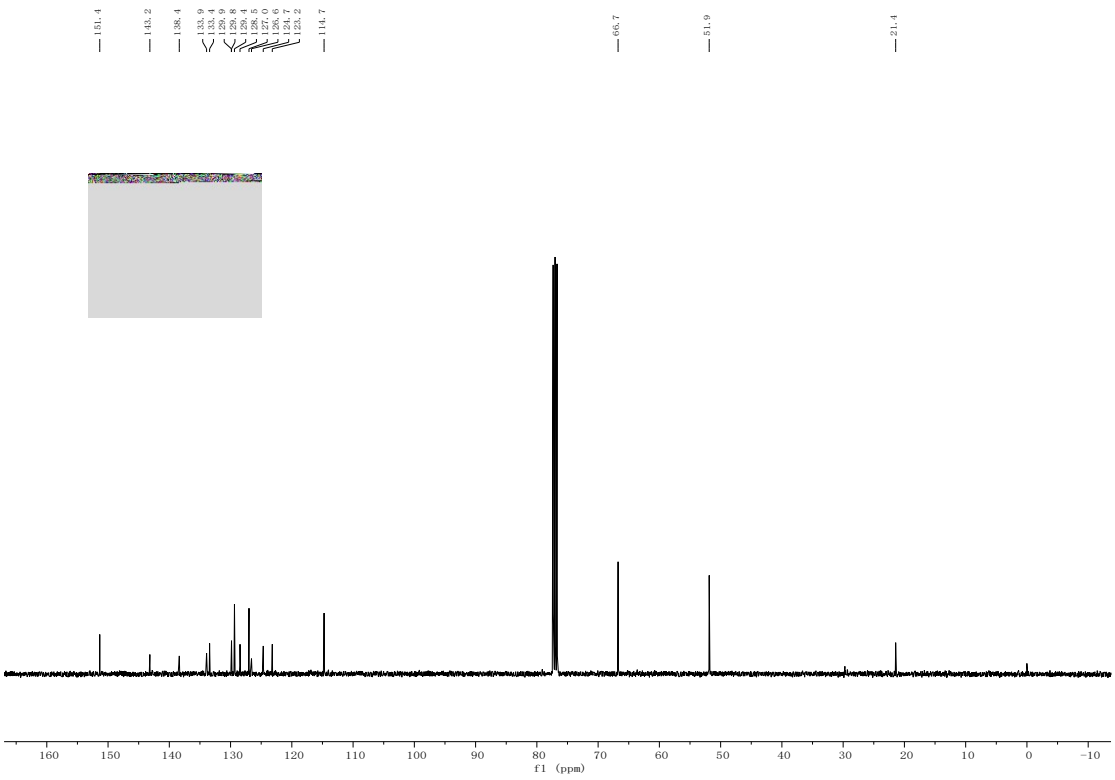

TsHN
N
O

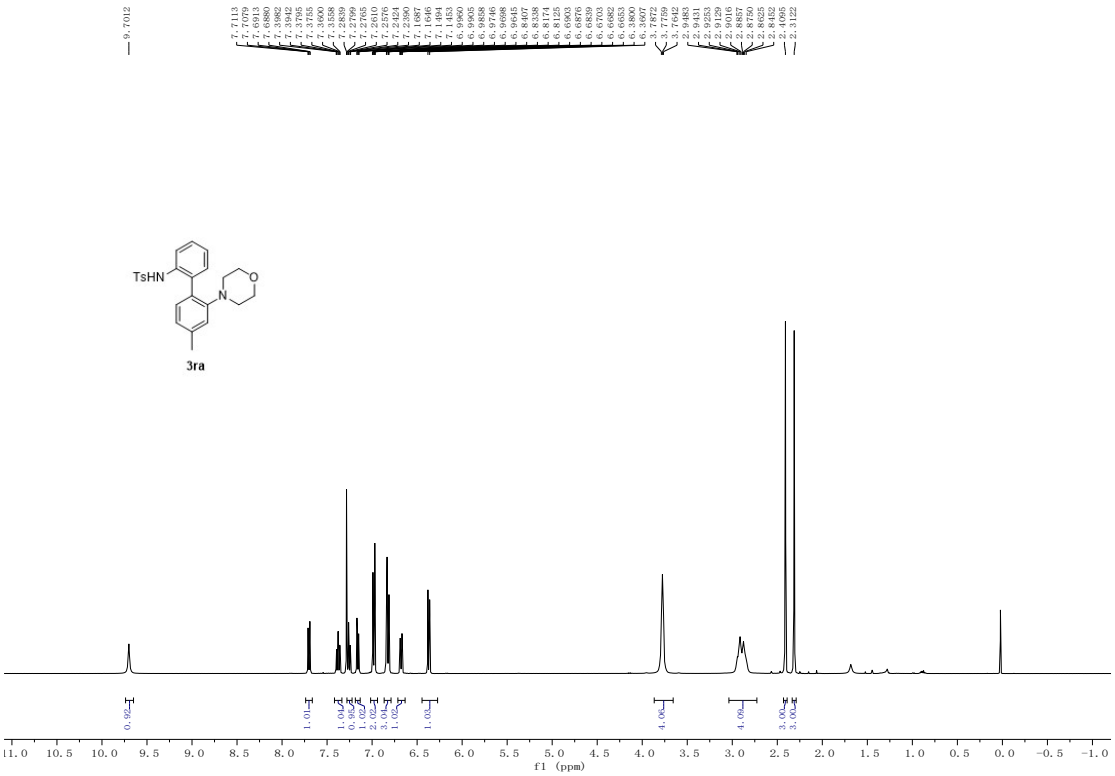
3qa


0.99
1.09
1.08
3.37
1.05
1.07
1.07
3.01
0.99
3.99
3.98
3.00
f1 (ppm)


147.8
142.4
136.3
136.0
133.6
133.6
131.0
130.9
129.1
128.8
128.7
127.3
127.1
125.1
123.6
117.8
66.7
52.1
21.4
f1 (ppm)


TsHN
O
N
N
O
3qa'
0.94
1.01
3.98
1.02
1.04
1.97
1.98
7.97
7.94
3.00
f1 (ppm)


151.4
143.2
138.4
133.9
133.4
129.8
129.4
128.5
127.0
126.6
124.7
123.2
114.7
66.7
51.9
21.4
f1 (ppm)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7.6913
7.6888
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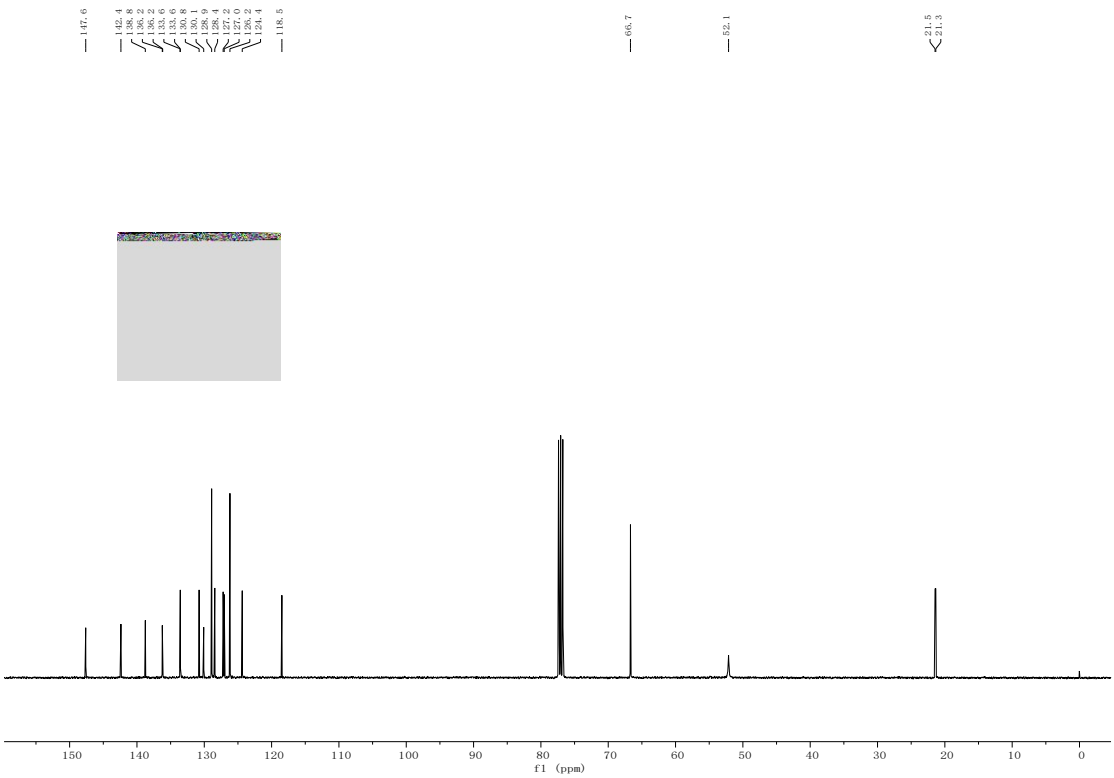
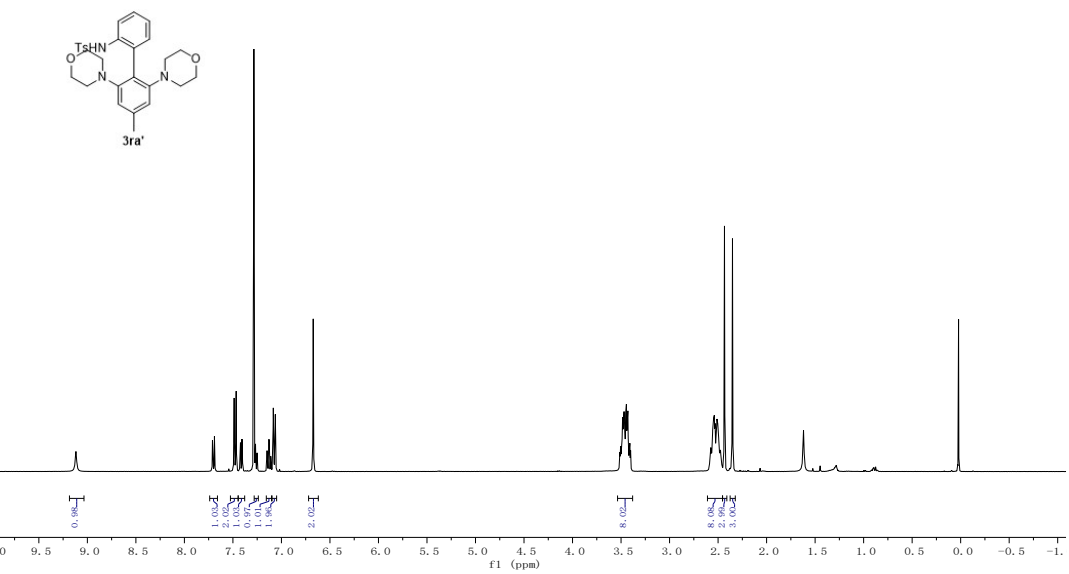
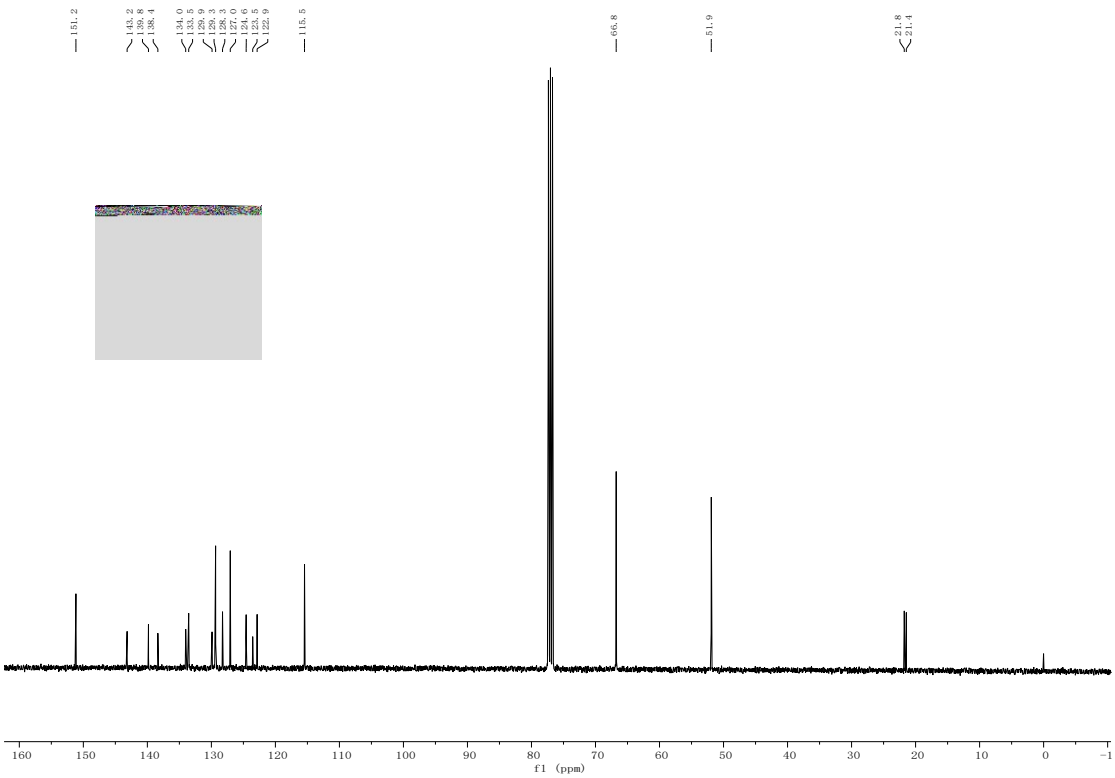
7.3942
7.3795
7.3755
7.3600
7.3558
7.2839
7.2799
7.2705
7.2610
7.2576
7.2424
7.2384
7.1887
7.1646
7.1494
7.1453
6.9960
6.9905
6.9858
6.9706
6.9698
6.9645
6.8407
6.8338
6.8171
6.8125
6.6903
6.6876
6.6698
6.6703
6.6682
6.6653
6.3990
6.3907
3.7872
3.7759
3.7642
3.7525
2.9431
2.9253
2.9129
2.9004
2.8857
2.8750
2.8625
2.8502
2.4095
2.3122
TsHN
3ra
0.92
1.01
1.04
0.94
1.02
2.02
3.04
1.02
1.03
4.06
4.09
3.00
3.00
f1 (ppm)


147.6
142.4
138.8
136.2
136.2
133.6
133.6
130.8
130.1
128.9
128.4
127.2
127.0
126.2
124.4
118.5
66.7
52.1
21.5
21.3
f1 (ppm)


TsHN
3ra'
f1 (ppm)


151.2
143.2
138.8
138.4
134.0
133.5
129.9
128.3
127.0
124.6
123.5
122.9
115.5
66.8
51.9
21.8
21.4
f1 (ppm)


9.2214
7.7903
7.7299
7.7103
7.7069
7.4410
7.4270
7.4120
7.4080
7.3925
7.3584
7.3039
7.3003
7.2839
7.2761
7.2682
7.2628
7.1412
7.1272
7.1225
7.1180
7.0167
7.0122
7.0059
6.9959
6.9911
6.8859
6.8810
6.7635
6.7592
6.7389
6.7346
6.5567
6.5504
6.5378
6.5334
6.5290
6.5163
6.5101
6.4972
6.4058
6.3895
3.7703
3.7638
3.7620
3.7501
3.7376
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2.8831
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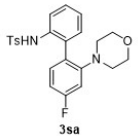
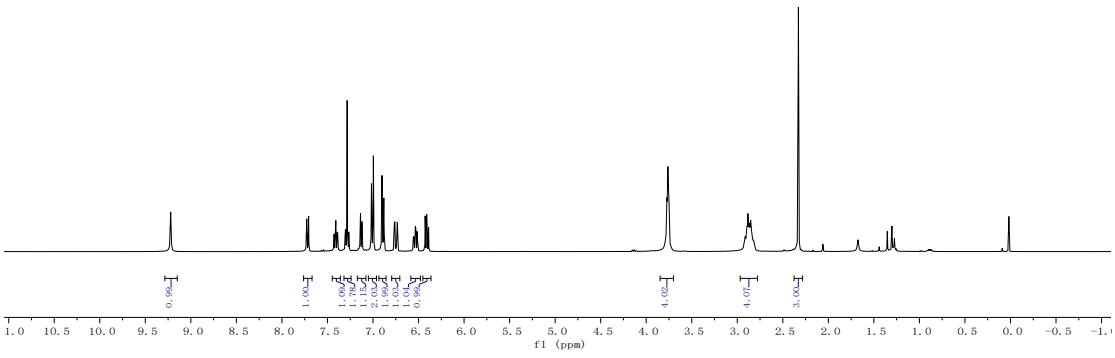
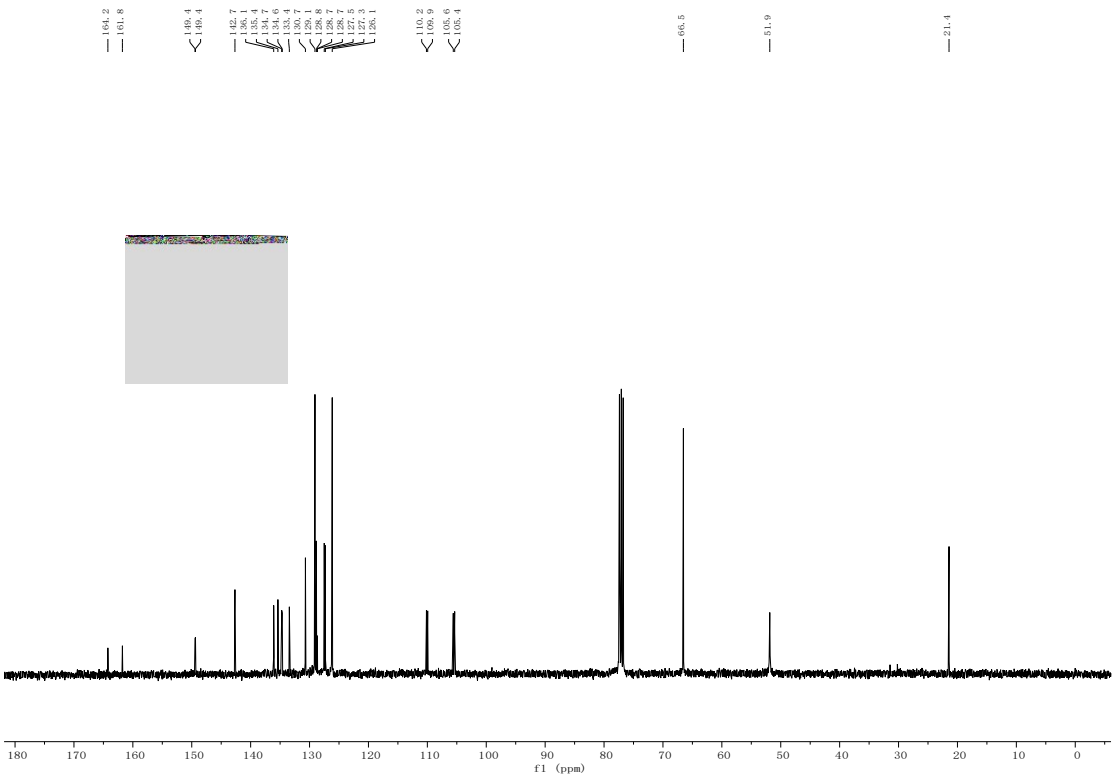
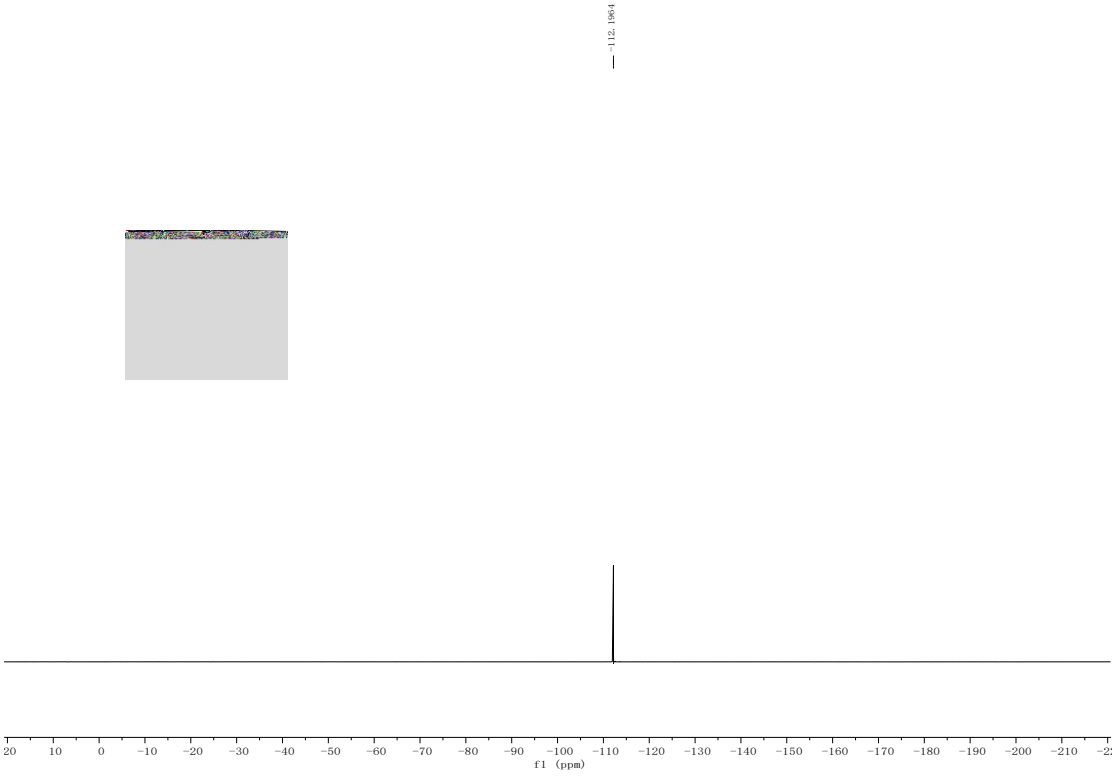
2.8588
2.8525
2.8404
2.8239
2.8198
2.3289

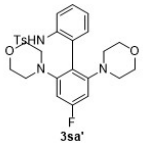

TsHN
N
O
F

3sa

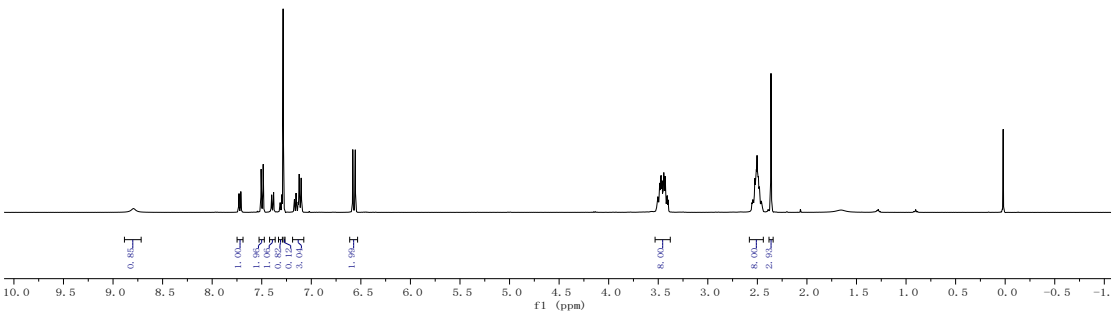

0.89
1.00
1.09
1.79
1.14
2.02
1.99
1.03
1.04
0.98
4.02
4.07
3.00
f1 (ppm)


164.2
161.8
149.4
149.4
142.7
136.1
135.4
134.7
134.6
133.4
130.7
129.1
128.8
128.7
128.7
127.5
127.3
126.1
110.2
109.9
105.6
105.4
66.5
51.9
21.4
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-112.1964
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

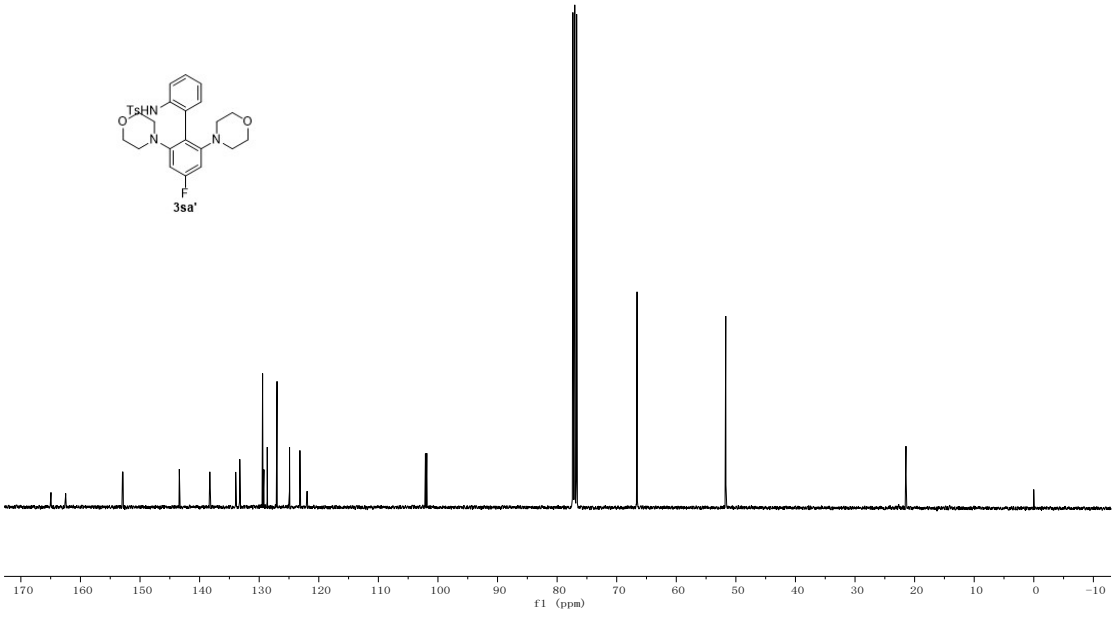

TsHN
O
N
N
O
F

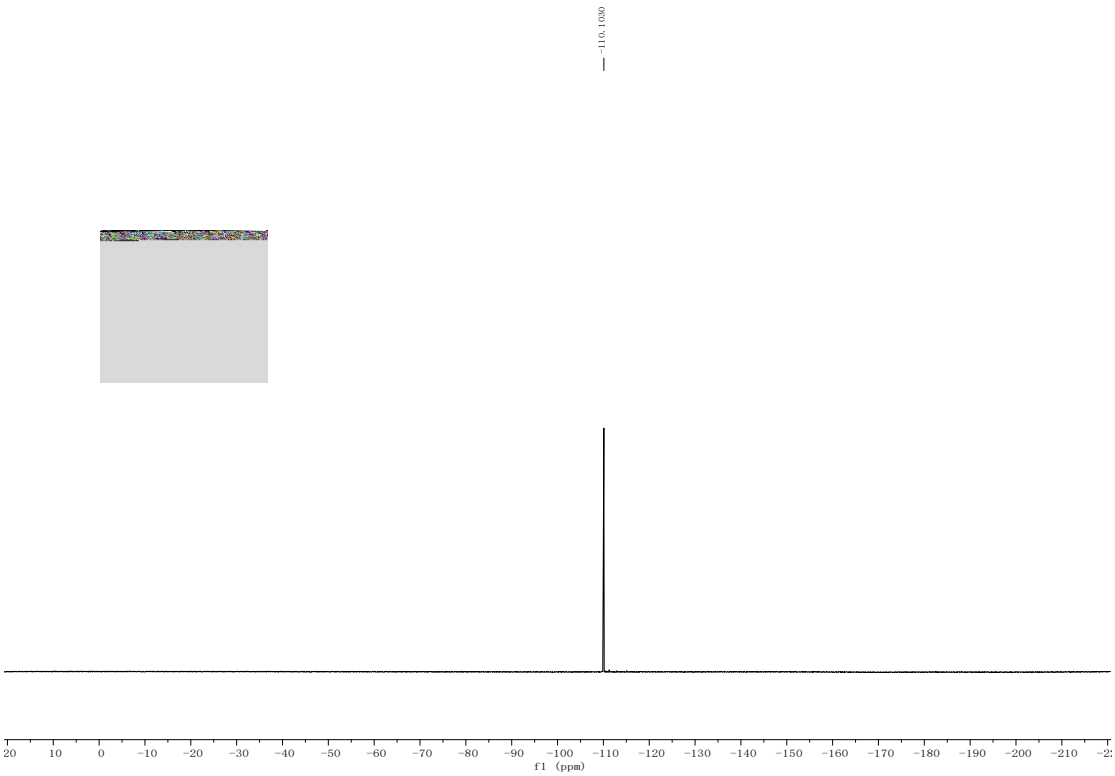
3sa'

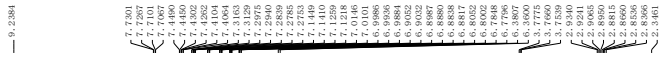

0.84
1.00
1.98
1.06
0.82
0.12
3.00
1.99
8.00
8.00
2.93
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
f1 (ppm)

TsHN
O
N
N
O
F

3sa'


170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


-110.1030
f1 (ppm)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7.7267
7.7101
7.7067
7.4490
7.4450
7.4302
7.4282
7.4104
7.4064
7.3163
7.3129
7.2975
7.2940
7.2839
7.2785
7.2733
7.1449
7.1410
7.1259
7.1218
7.0146
7.0101
6.9986
6.9936
6.9884
6.9032
6.8887
6.8838
6.8817
6.8032
6.7972
6.7848
6.7796
3.8907
3.8769
3.7775
3.7660
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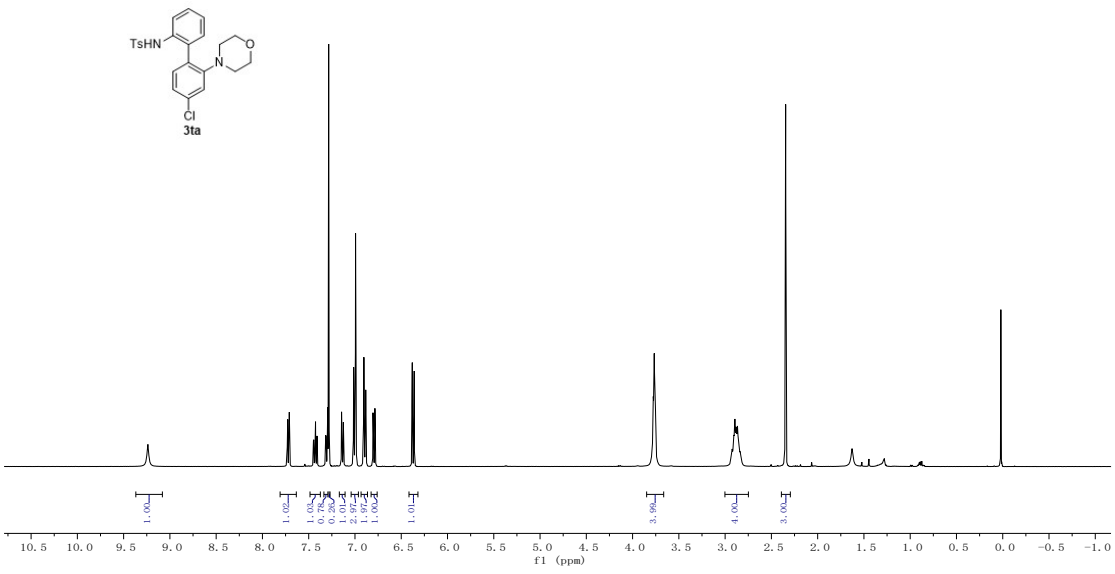
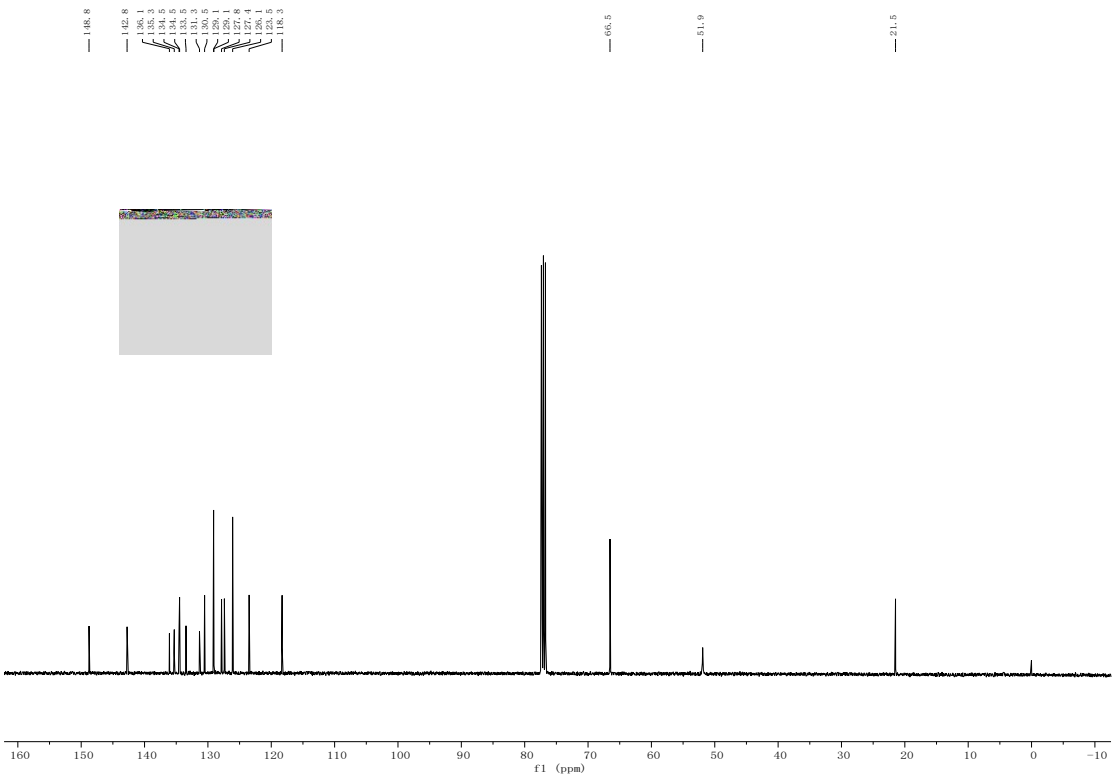
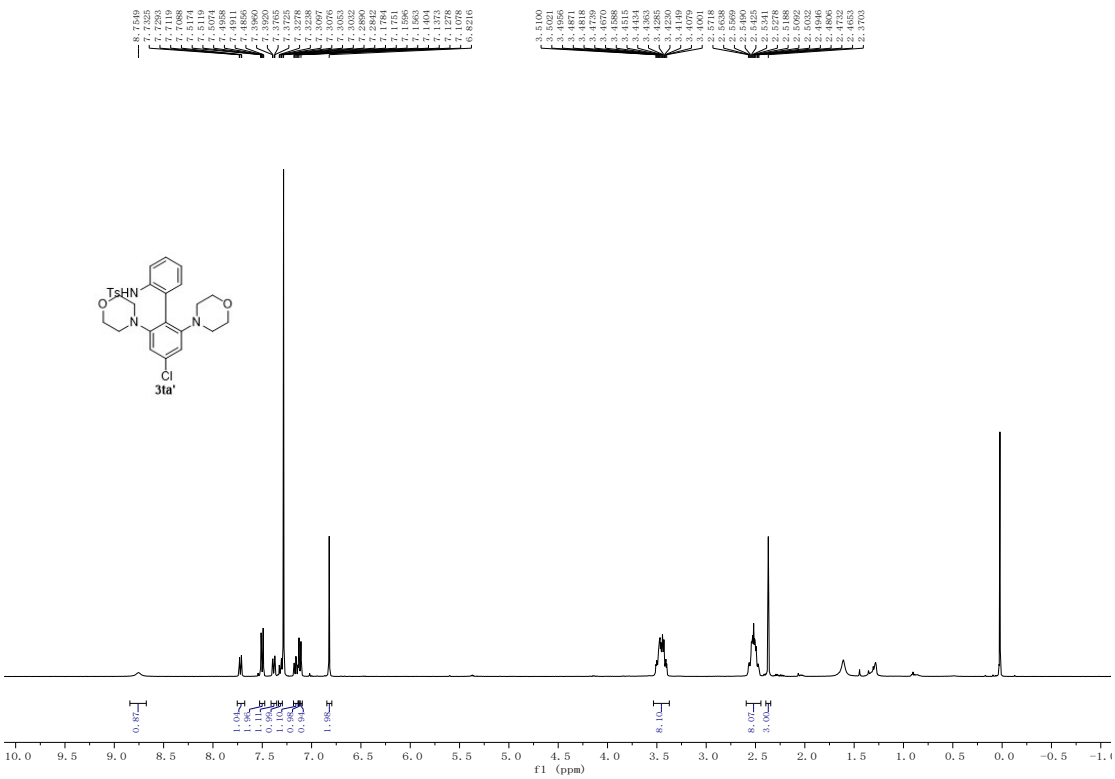
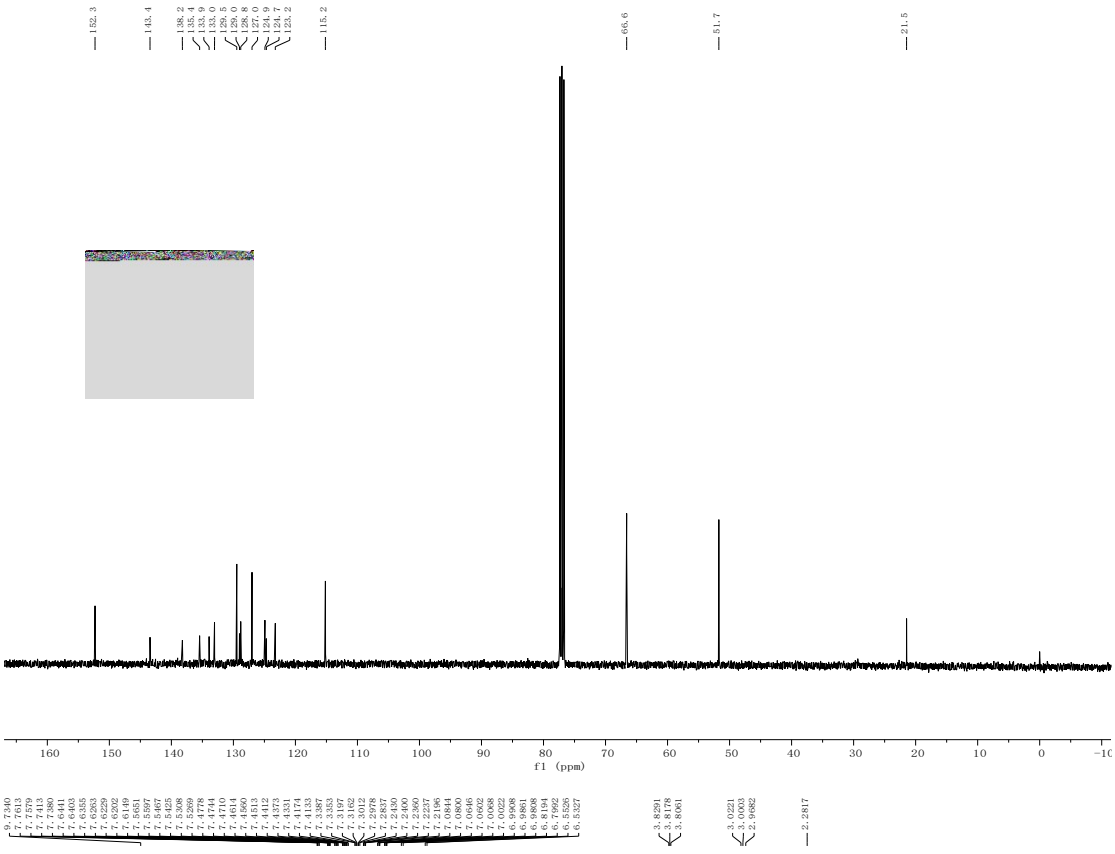
2.8366
2.3461


TsHN
N
O
Cl
3ta
1.00
1.02
1.03
0.78
0.26
1.01
2.97
1.04
1.00
1.01
3.99
4.00
3.00
f1 (ppm)


148.8
142.8
136.1
135.3
134.5
134.5
133.5
131.3
130.5
129.1
128.1
127.8
127.4
126.1
123.5
118.3
66.5
51.9
21.5
f1 (ppm)


TsHN
O
N
N
O
Cl
3ta'
f1 (ppm)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143.4
138.2
135.4
133.9
131.0
129.5
129.0
128.8
127.0
124.9
124.7
123.2
115.2
66.6
51.7
21.5
f1 (ppm)

9.7340
7.7613
7.7579
7.7413
7.7380
7.6441
7.6405
7.6355
7.6263
7.6229
7.6192
7.6149
7.5651
7.5497
7.5467
7.5435
7.5308
7.5269
7.4778
7.4744
7.4710
7.4614
7.4560
7.4513
7.4412
7.4373
7.4331
7.4174
7.4132
7.3387
7.3353
7.3197
7.3162
7.3012
7.2978
7.2857
7.2710
7.2400
7.2360
7.2237
7.2196
7.0844
7.0800
7.0646
7.0602
7.0098
7.0022
6.9908
6.9861
6.9698
6.8194
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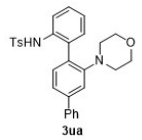
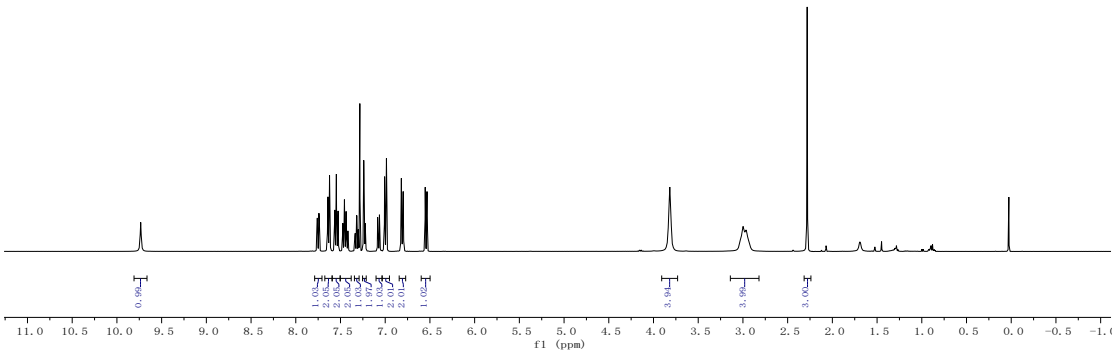
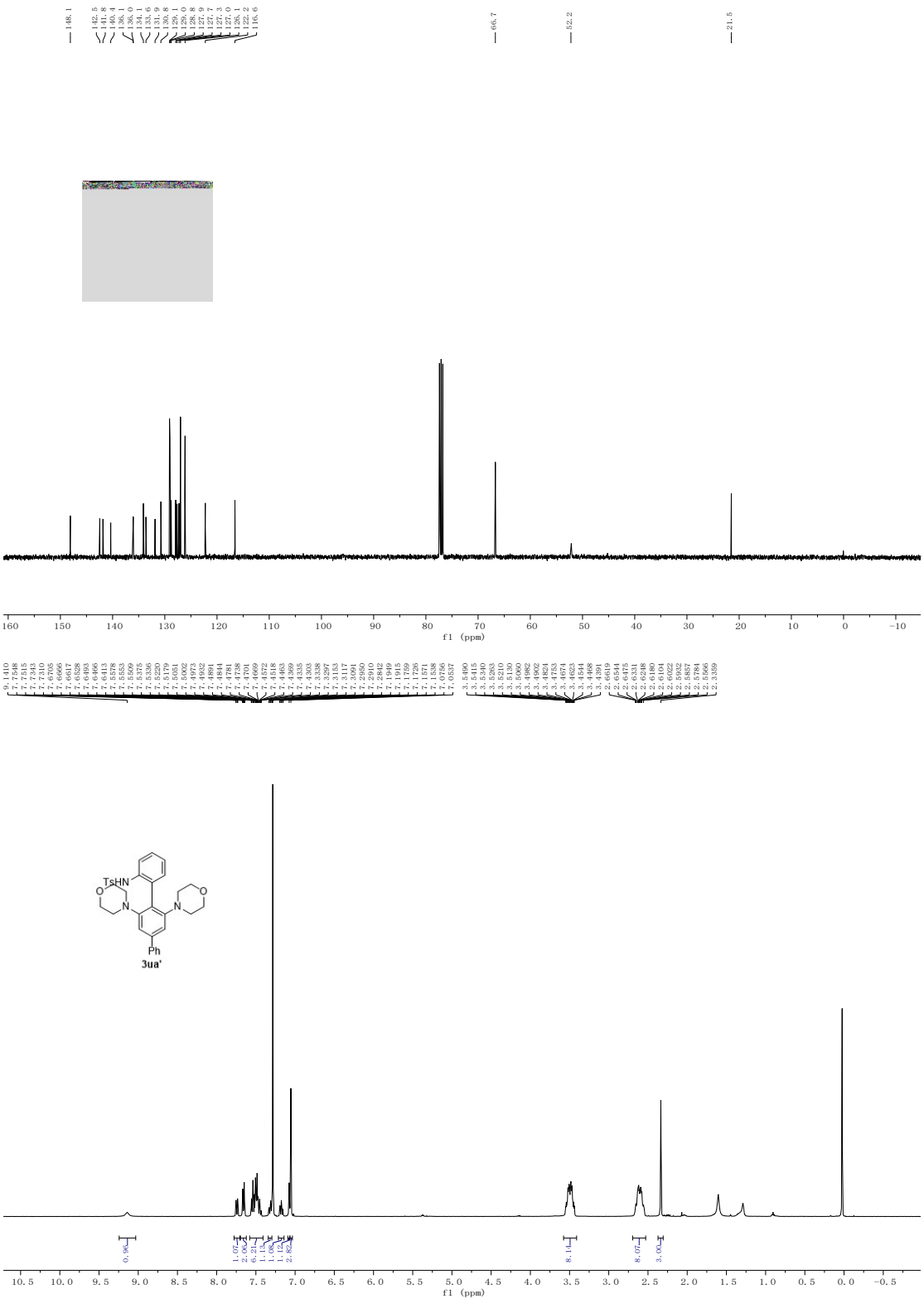
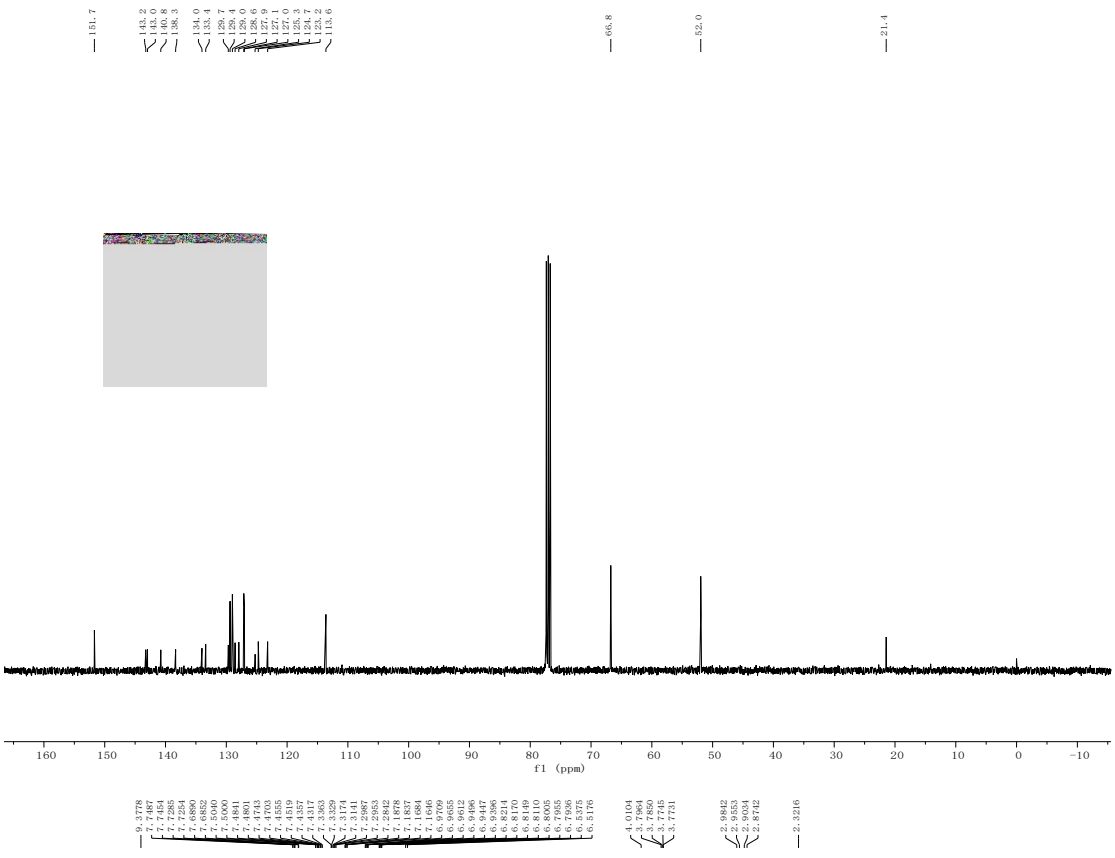
6.5526
6.5327
3.8291
3.8178
3.8061
3.0221
3.0503
2.9682
2.2817


TsHN
N
O
Ph

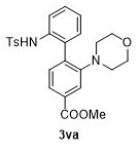
3ua


0.99
1.03
2.02
2.05
1.02
1.97
1.04
2.01
2.01
1.02
3.94
3.99
3.00
f1 (ppm)

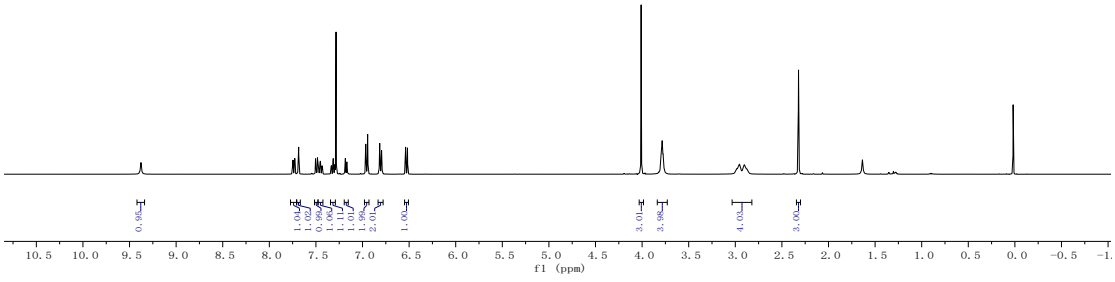

148.1
142.5
141.8
140.4
136.1
136.0
134.1
133.6
131.9
130.8
130.1
129.0
128.8
127.9
127.7
127.3
127.0
126.1
122.2
116.6
66.7
52.2
21.5
f1 (ppm)
TsHN
Ph
3ua'
0.96
1.07
2.04
6.21
1.13
1.08
1.12
2.82
8.14
8.07
3.00
f1 (ppm)

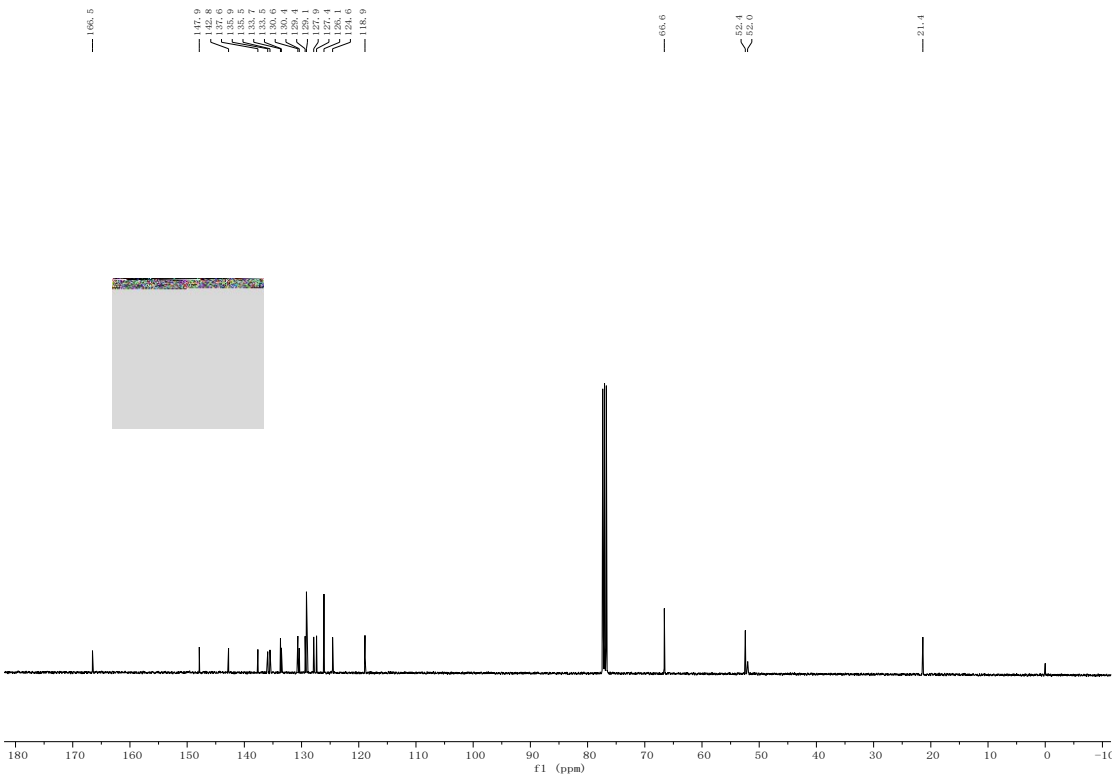

151.7
148.2
145.0
140.8
138.3
134.0
133.4
129.7
129.4
128.0
127.6
127.9
127.1
127.0
125.3
124.7
123.2
113.6
66.8
52.0
21.4
f1 (ppm)

9.3778
7.7487
7.7454
7.7295
7.7285
7.7254
7.6882
7.5000
7.4960
7.4841
7.4801
7.4743
7.4703
7.4555
7.4519
7.4357
7.4317
7.3503
7.3329
7.3174
7.3141
7.2966
7.2953
7.2842
7.1878
7.1837
7.1684
7.1646
6.9709
6.9695
6.9612
6.9496
6.9447
6.9396
6.8214
6.8170
6.8149
6.8110
6.8095
6.7935
6.7936
6.5375
6.5176
4.0104
3.7964
3.7850
3.7745
3.7731
2.9842
2.9553
2.9034
2.8742
2.3216

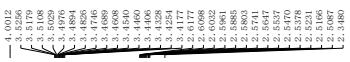

TsHN
N
O
COOMe

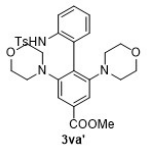
3va


0.95
1.04
1.07
0.99
1.06
1.11
1.04
1.99
2.01
1.00
3.01
3.98
4.03
3.00
f1 (ppm)

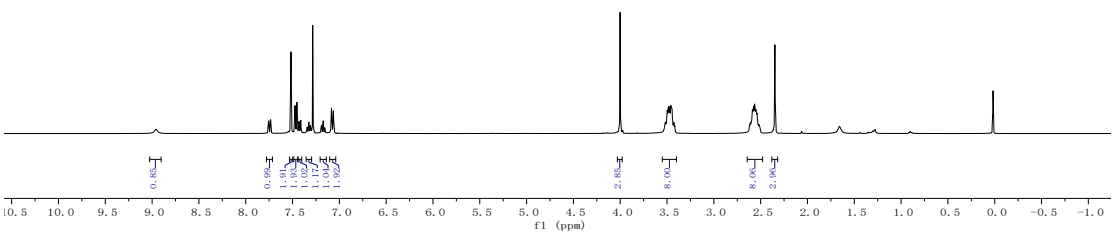

166.5
147.9
142.8
137.6
135.9
135.5
134.7
133.5
130.6
130.4
128.4
128.1
127.9
127.4
126.1
124.6
118.9
66.6
52.4
52.0
21.4
f1 (ppm)

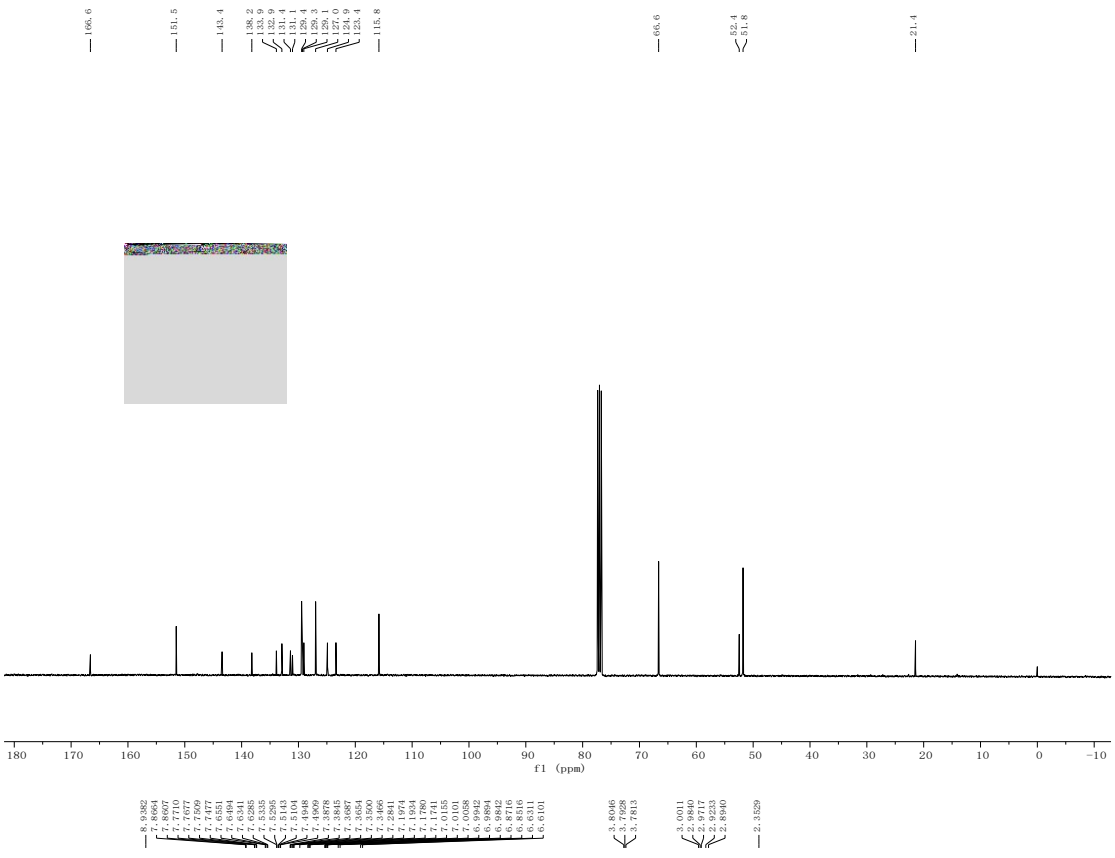

8.9579
7.7669
7.7537
7.7363
7.7232
7.5169
7.4738
7.4694
7.4571
7.4530
7.4476
7.4349
7.4309
7.4155
7.4114
7.3475
7.3434
7.3291
7.3257
7.3230
7.3088
7.3046
7.2843
7.1940
7.1907
7.1732
7.1719
7.1561
7.1529
7.0839
7.0659

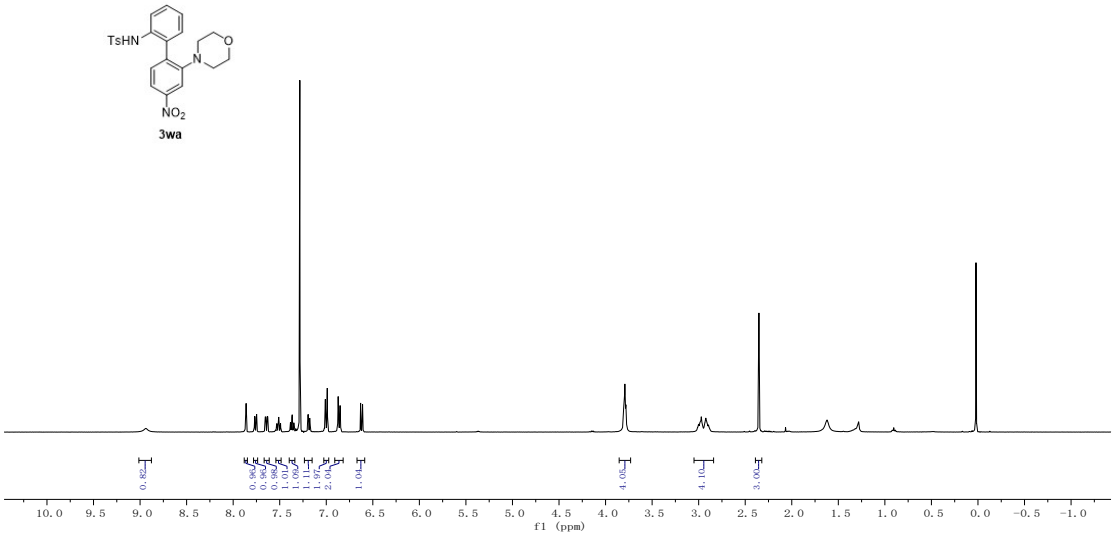

4.0012
3.5295
3.5179
3.5108
3.5029
3.4894
3.4826
3.4706
3.4608
3.4540
3.4460
3.4406
3.4328
3.4254
3.4177
3.4077
2.6098
2.6032
2.5961
2.5885
2.5805
2.5741
2.5647
2.5537
2.5370
2.5378
2.5231
2.5166
2.5087
2.3480

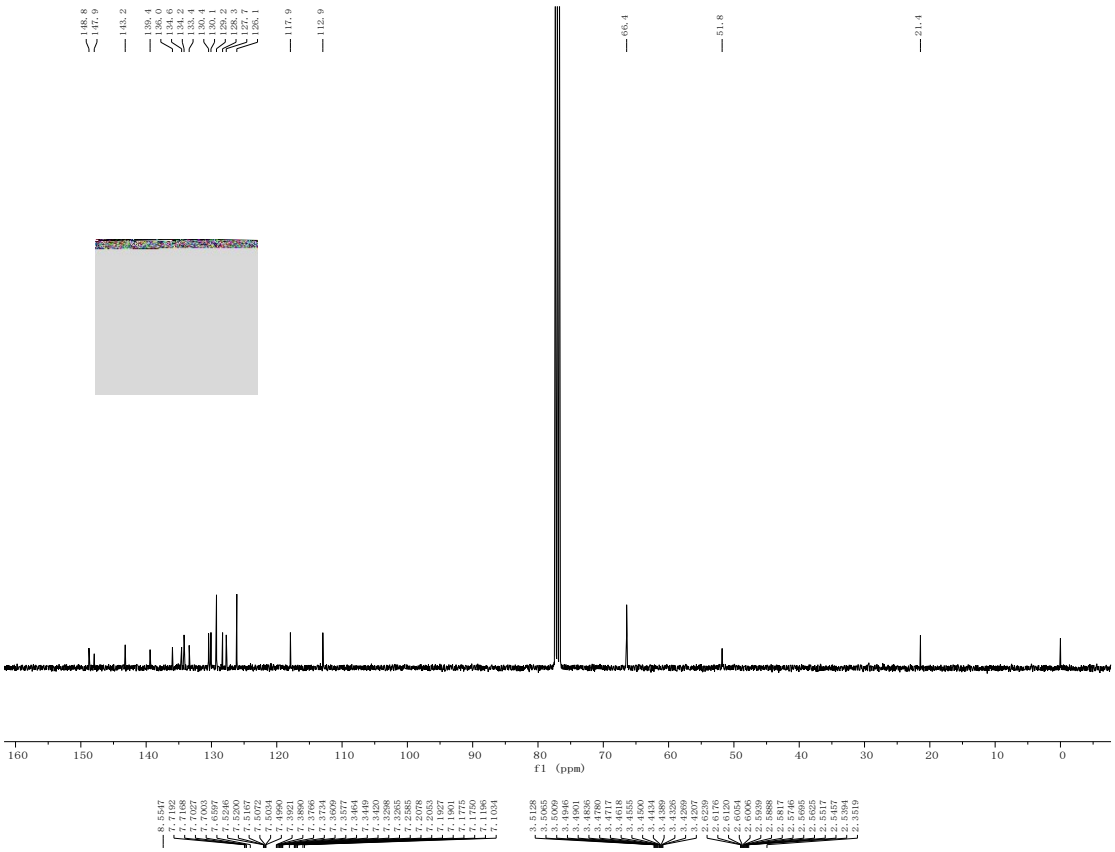

TsHN
O
N
N
O
COOMe

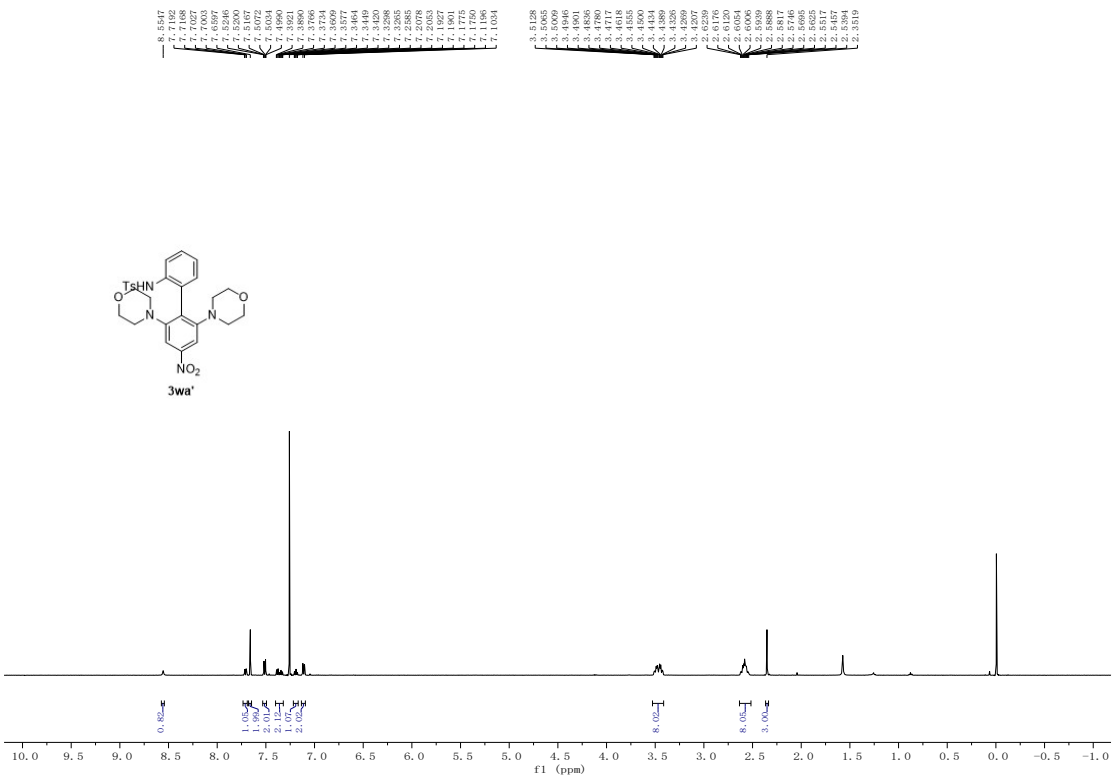
3va'

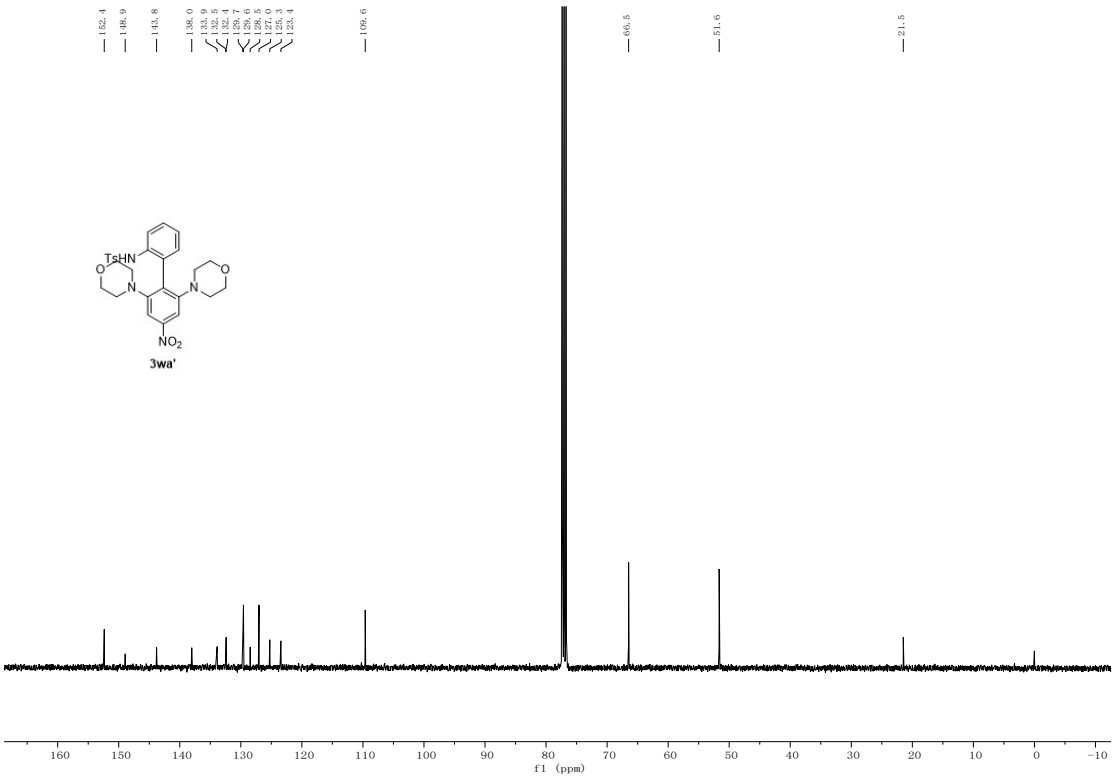

0.85
0.89
1.91
1.84
1.02
1.17
1.04
1.02
2.85
8.00
8.04
2.96
f1 (ppm)

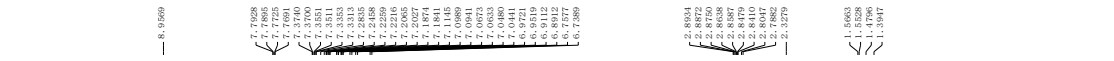

166.6
151.5
143.4
138.2
133.9
132.9
131.4
131.1
129.4
129.3
128.1
125.0
124.9
123.4
115.8
65.6
52.4
51.8
21.4
f1 (ppm)
8.9382
7.8664
7.8607
7.7710
7.7677
7.7599
7.7477
7.6551
7.6494
7.6441
7.6285
7.5295
7.5143
7.5104
7.4948
7.4909
7.3878
7.3845
7.3687
7.3654
7.3500
7.3466
7.2841
7.1974
7.1934
7.1780
7.1741
7.1111
7.0155
7.0101
7.0058
6.9962
6.9894
6.9842
6.8716
6.8676
6.8516
6.6311
6.6101
3.8046
3.7928
3.7813
3.0011
2.9940
2.9777
2.9233
2.8940
2.3529


TsHN
N
O
NO2
3wa
0.82
0.98
0.98
1.01
1.04
1.11
1.97
2.04
1.04
4.05
4.10
3.00
f1 (ppm)


148.8
147.9
143.2
139.4
136.0
134.6
134.2
133.4
130.4
130.1
128.2
128.3
127.7
126.1
117.9
112.9
66.4
51.8
21.4
f1 (ppm)


TsHN
O
N
N
O
NO2
3wa'
0.82
1.05
1.89
2.04
2.12
1.07
2.02
8.02
8.05
3.00
f1 (ppm)


152.4
148.9
143.8
138.0
133.9
132.5
132.4
129.7
129.6
128.5
127.0
125.3
123.4
109.6
66.5
51.6
21.5
TsHN
O
N
O
N
NO2
3wa'
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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7.7865
7.7725
7.7691
7.3700
7.3700
7.3551
7.3511
7.3333
7.3313
7.2835
7.2458
7.2239
7.2216
7.2065
7.2027
7.1874
7.1444
7.1145
7.0989
7.0941
7.0873
7.0693
7.0480
7.0441
6.9721
6.9519
6.9112
6.8912
6.7577
6.7389
2.8934
2.8872
2.8750
2.8638
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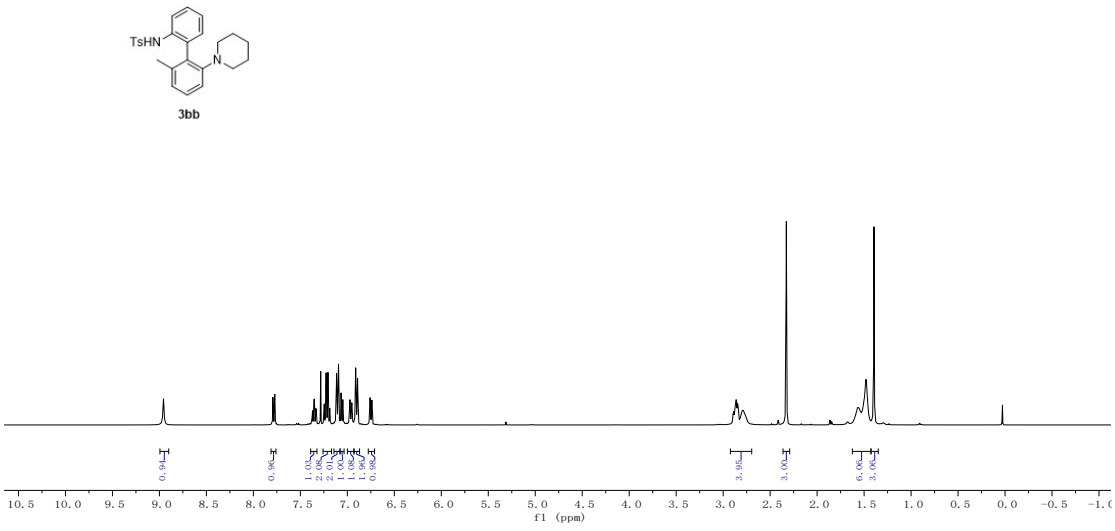
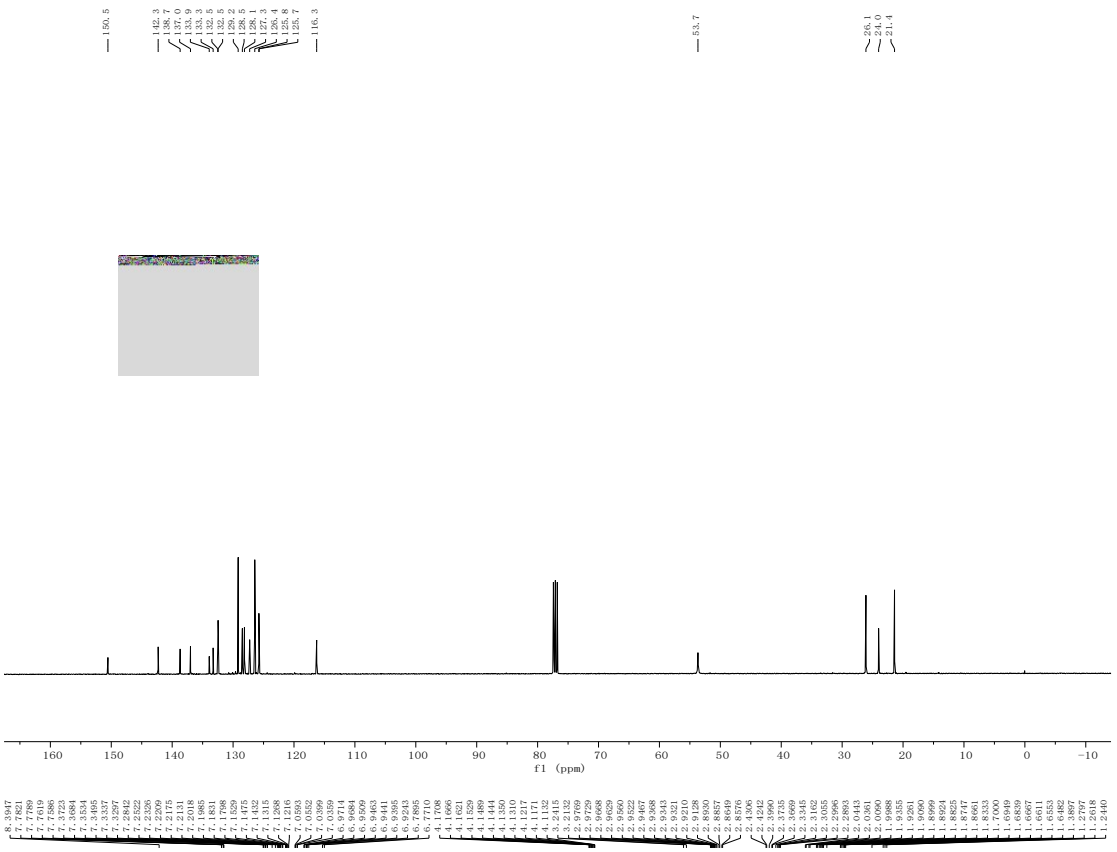
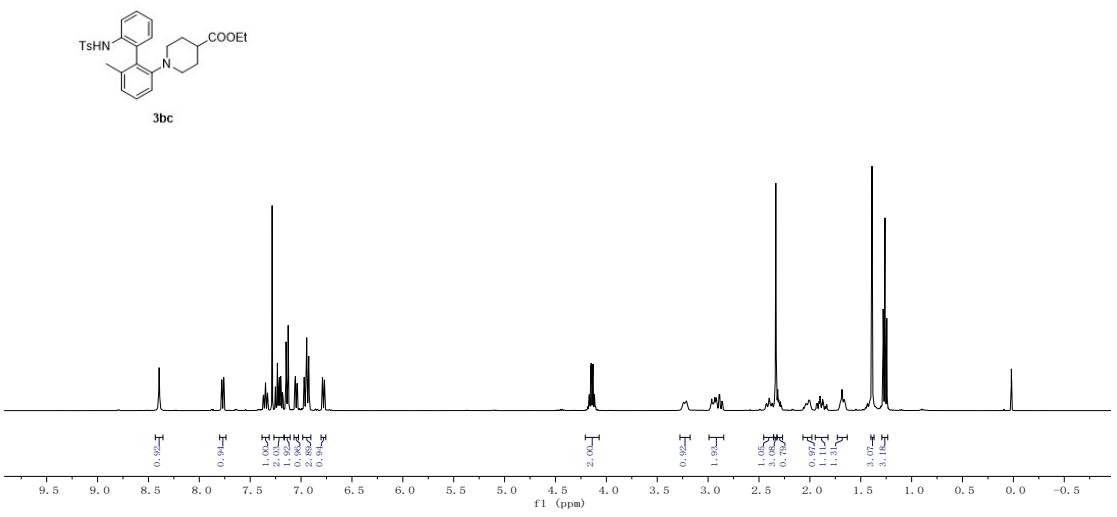
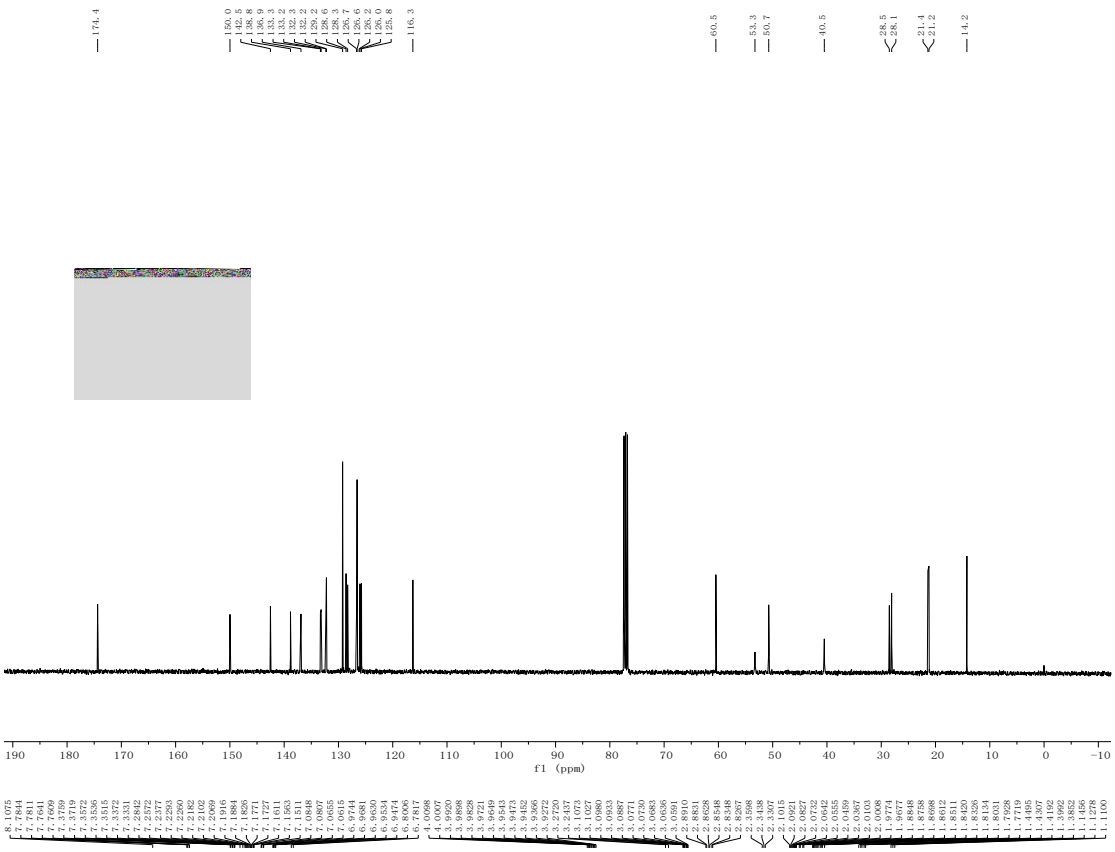
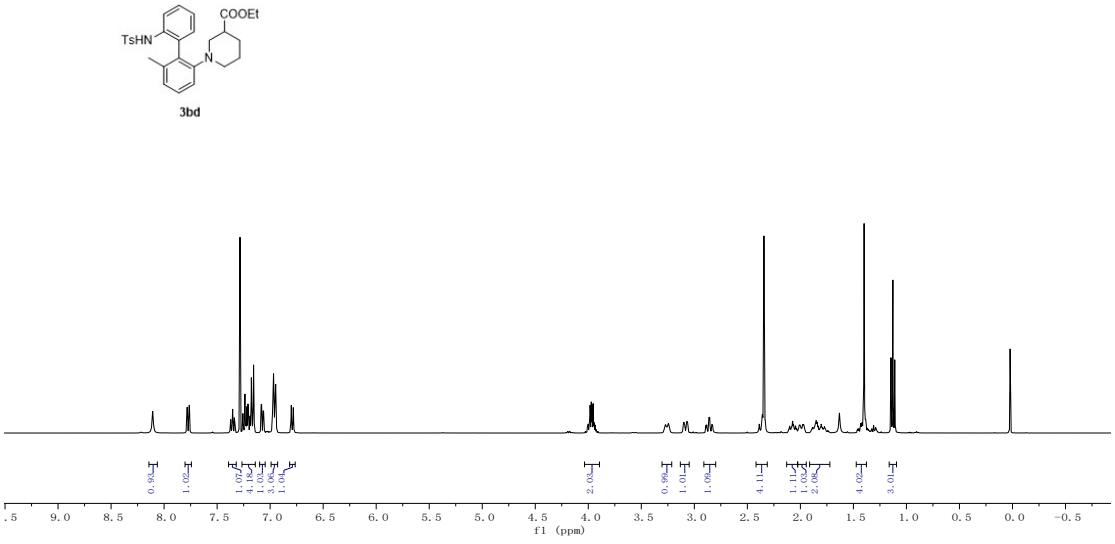
2.8479
2.8410
2.8047
2.7882
2.3570
1.5663
1.5528
1.4096
1.3947

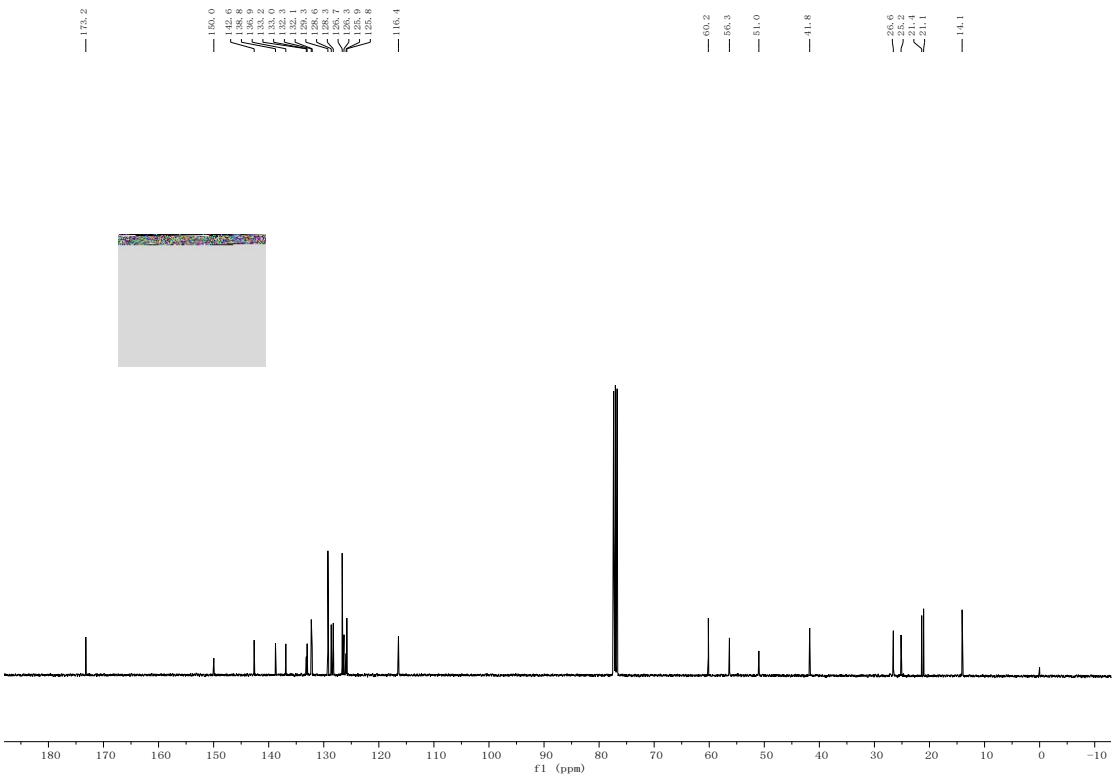

TsHN
N
3bb
0.94
0.96
1.03
2.08
2.01
1.00
1.96
0.98
3.95
3.00
6.00
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

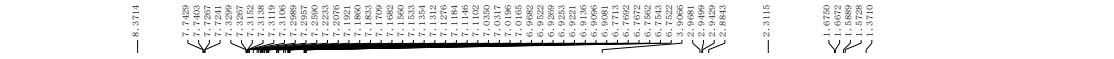

150.5
142.3
138.7
137.0
133.9
133.3
132.5
132.5
129.2
128.5
128.1
127.3
126.4
125.8
125.7
116.3
53.7
26.1
24.0
21.4
f1 (ppm)

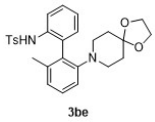

TsHN
COOEt
N
3bc
f1 (ppm)



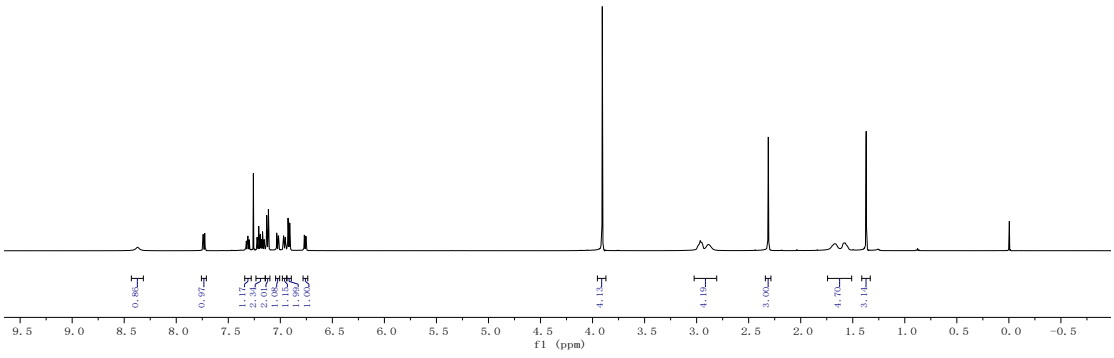

COOEt
TsHN
N
3bd

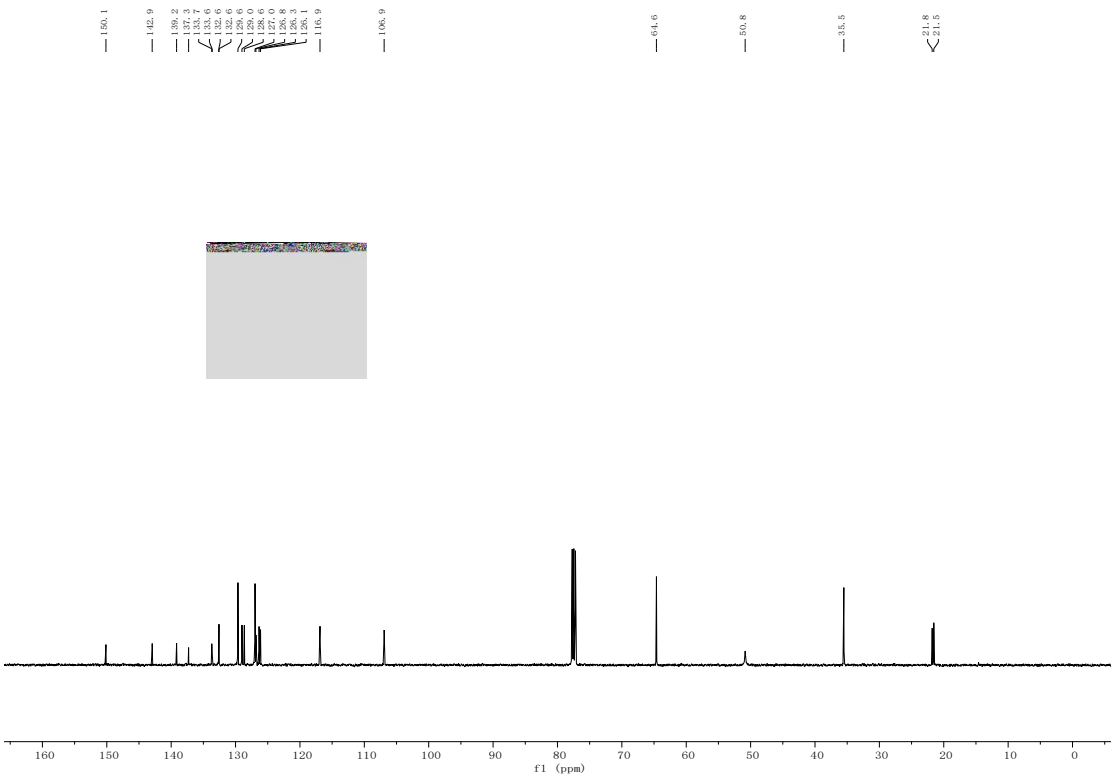


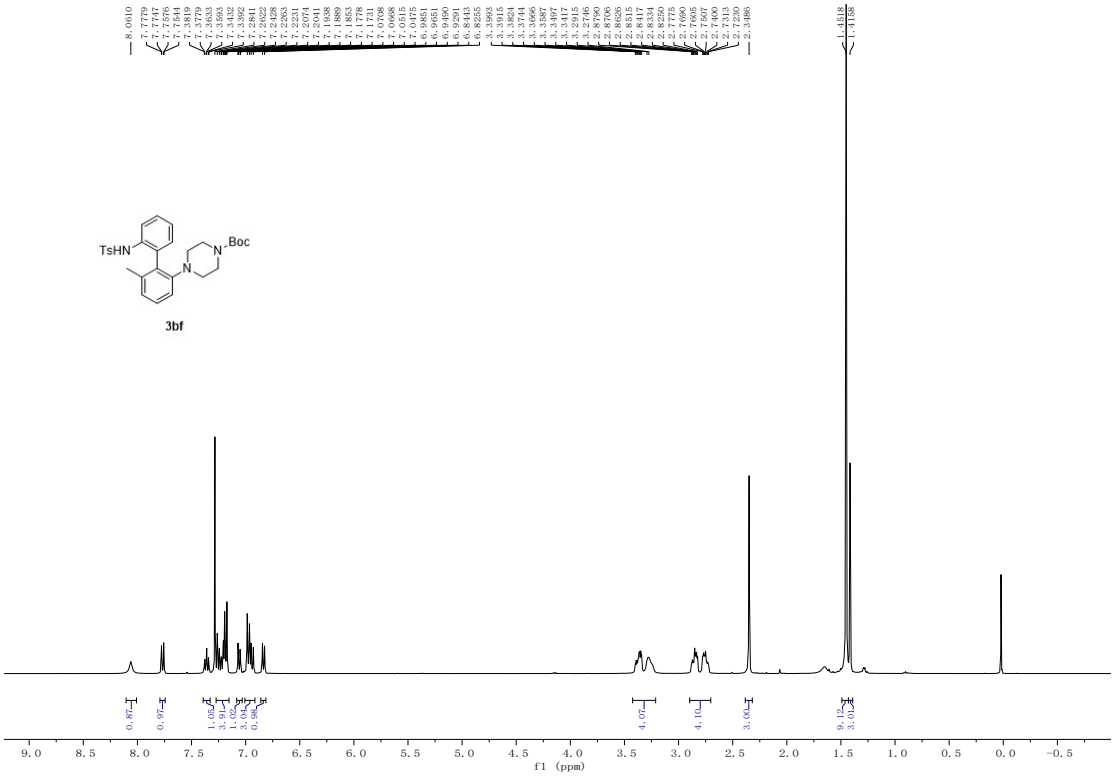




3be




150.1
142.9
139.2
137.3
134.7
133.6
132.6
129.6
129.0
128.6
127.0
126.8
126.5
126.1
116.9
106.9
64.6
50.8
35.5
21.8
21.5
f1 (ppm)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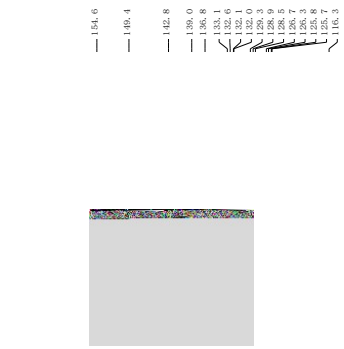
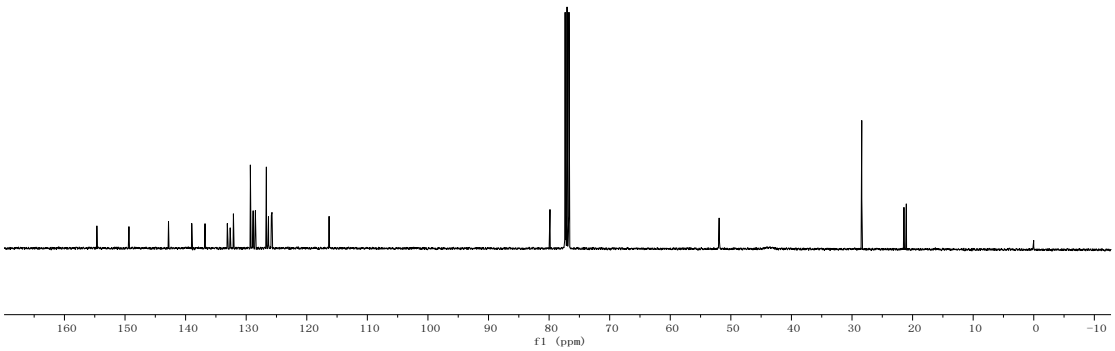
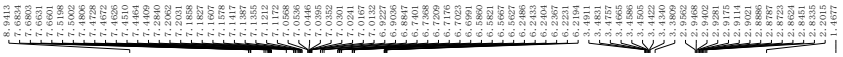
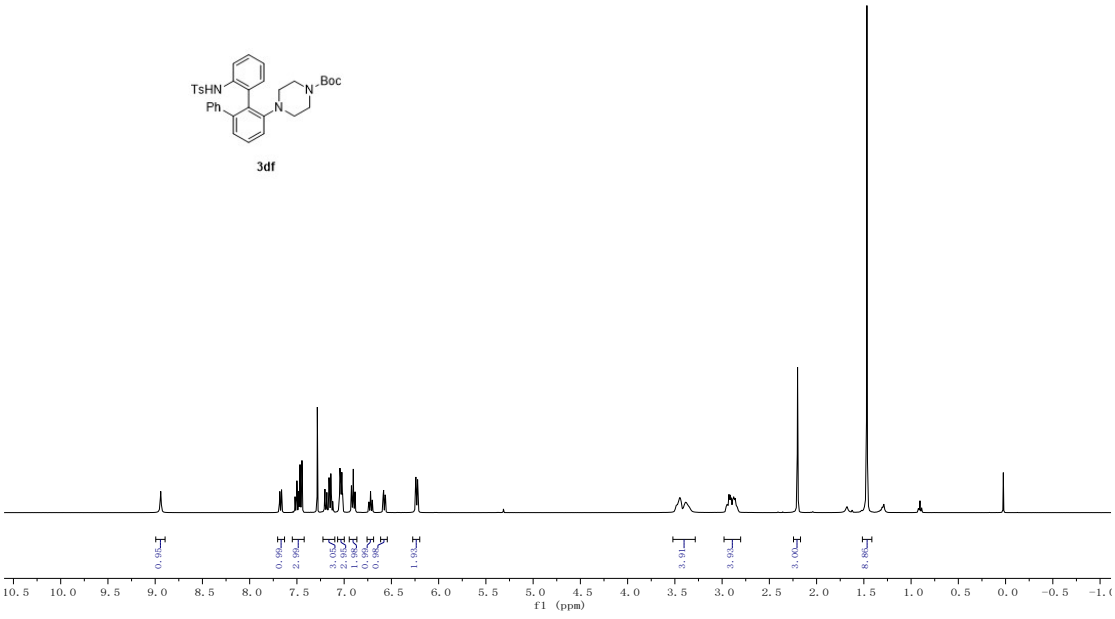
7.7747
7.7576
7.7544
7.3819
7.3779
7.3533
7.3493
7.3432
7.3392
7.2941
7.2622
7.2428
7.2283
7.2271
7.2074
7.2041
7.1938
7.1898
7.1883
7.1778
7.1731
7.1098
7.1068
7.0515
7.0475
6.9851
6.9491
6.9290
6.8443
6.8435
3.3993
3.3915
3.3824
3.3744
3.3666
3.3587
3.3497
3.3417
3.2916
3.2746
2.8790
2.8706
2.8595
2.8515
2.8417
2.8334
2.8259
2.7775
2.7690
2.7605
2.7507
2.7440
2.7313
2.7230
2.3486
1.4518
1.4138
TsHN
N
N
Boc
3bf
0.87
0.97
1.05
3.91
1.02
3.04
0.98
4.07
4.10
3.00
9.12
3.01
f1 (ppm)

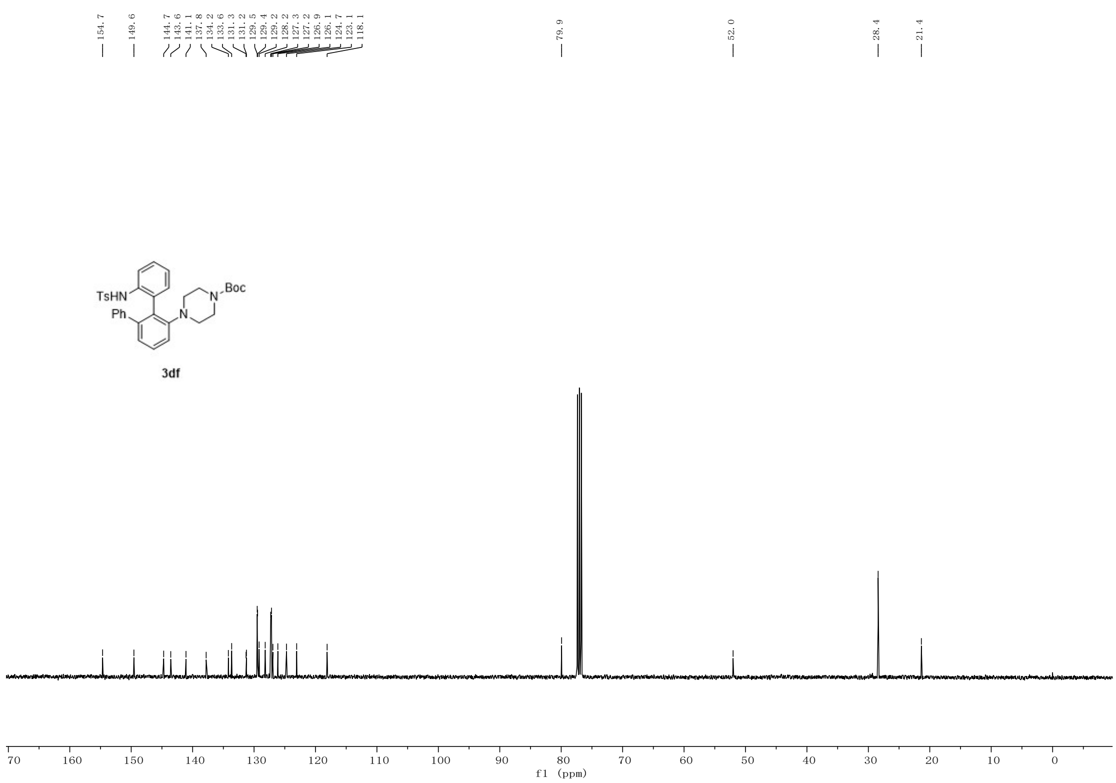






3df

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133.6
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131.2
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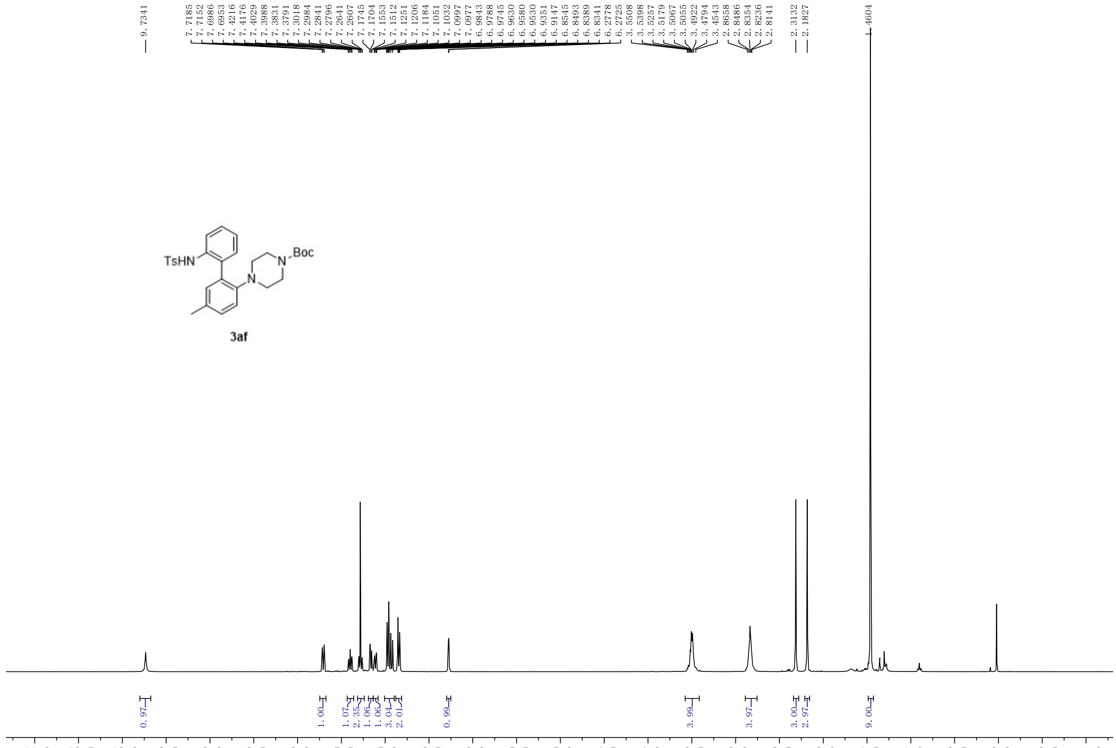
129.4
129.2
128.2
127.3
127.2
126.9
126.1
124.7
123.1
118.1
79.9
52.0
28.4
21.4
TsHN
Ph
N
Boc
3df
f1 (ppm)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7.3831
7.3791
7.3018
7.2984
7.2841
7.2796
7.2641
7.2607
7.1745
7.1704
7.1553
7.1512
7.1251
7.1206
7.1184
7.1051
7.1032
7.0997
7.0977
6.9843
6.9788
6.9745
6.9630
6.9580
6.9530
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6.9147
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6.8389
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6.2725
3.5508
3.5398
3.5257
3.5179
3.5067
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3.4794
3.4543
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2.8486
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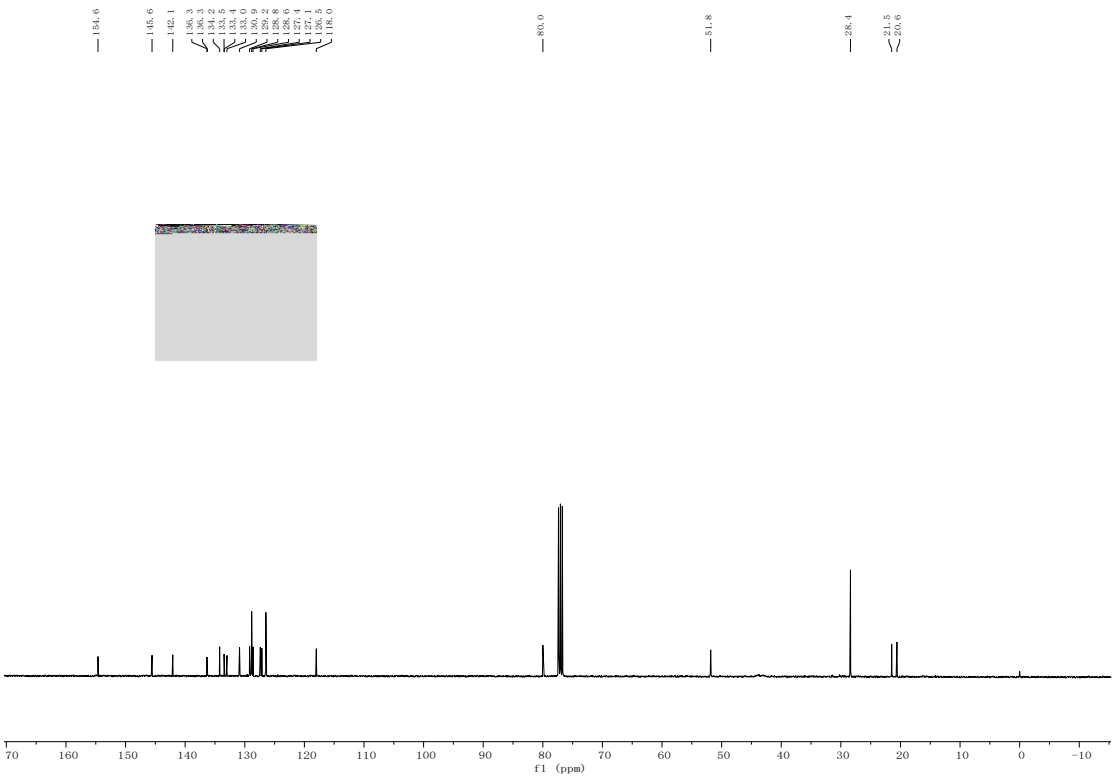
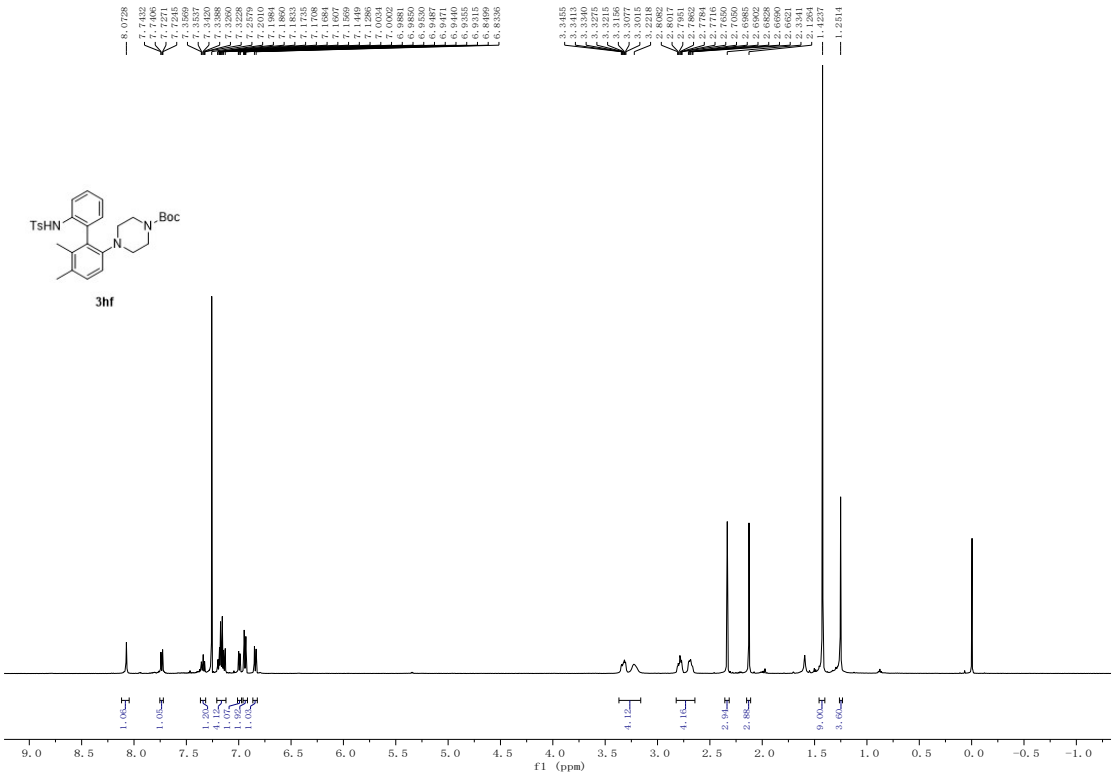
TsHN
N
Boc
3af
f1 (ppm)

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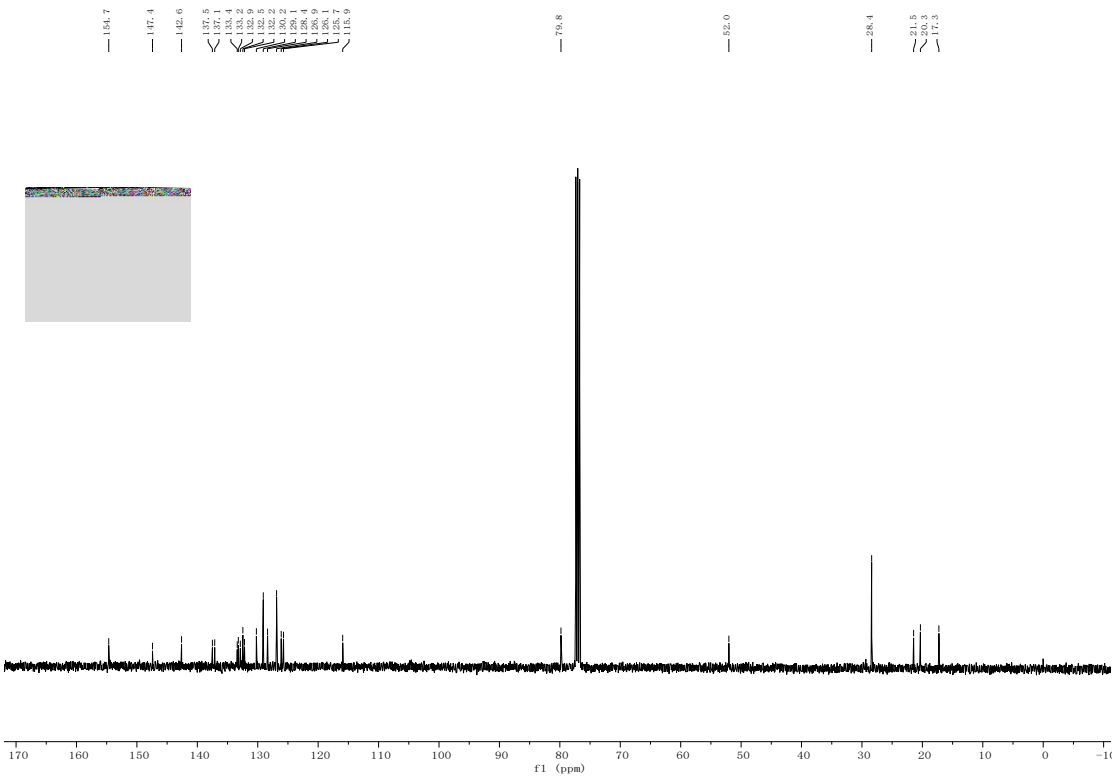
N
N
Boc
3hf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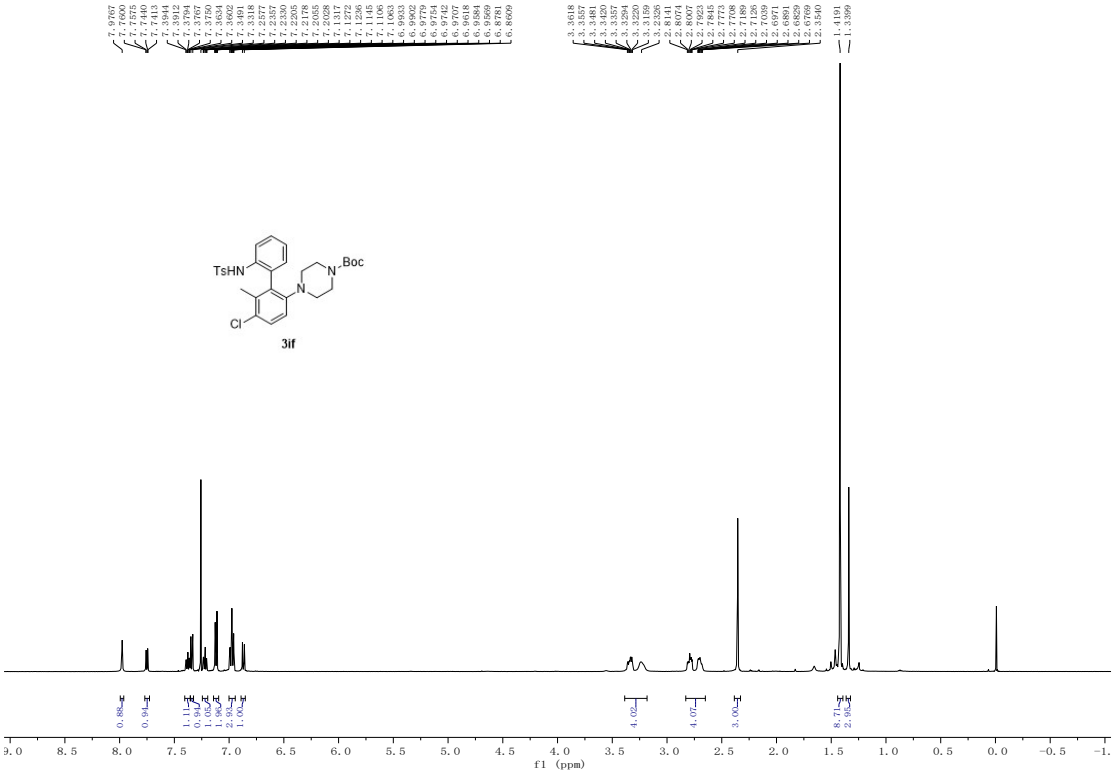
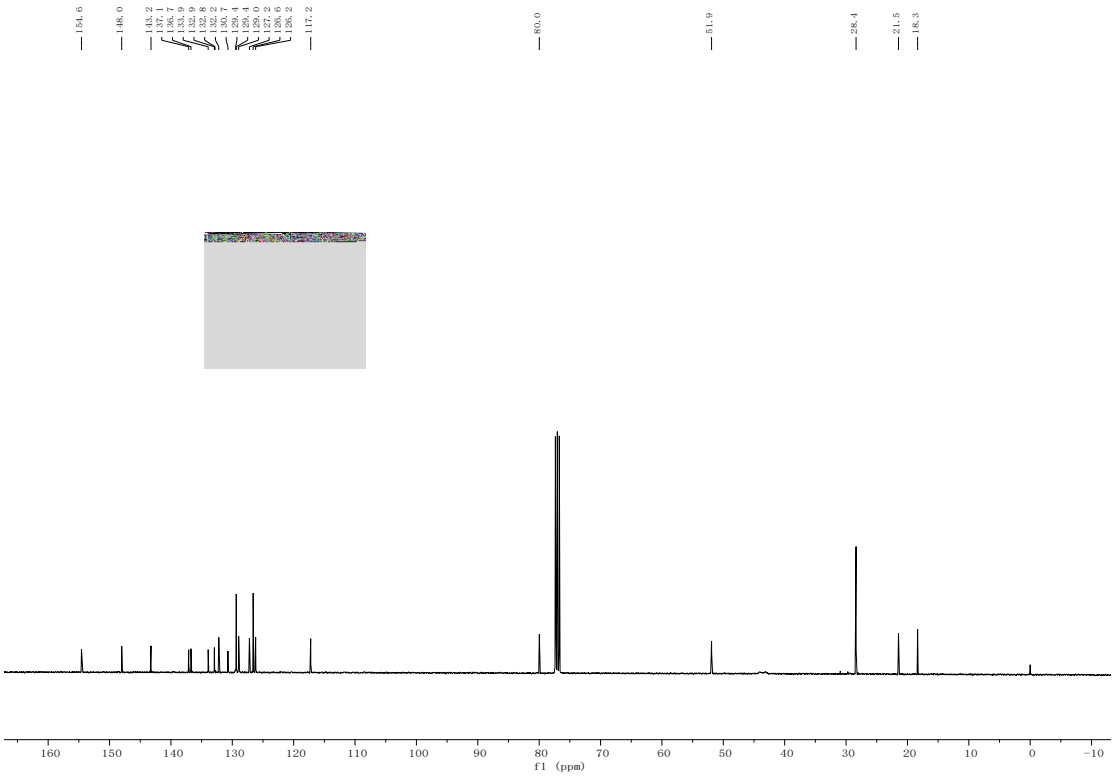
132.9
132.5
132.2
130.2
130.1
128.4
126.9
126.1
125.7
115.9
79.8
52.0
28.4
21.5
20.3
17.3
f1 (ppm)


TsHN
Boc
Cl
3if
f1 (ppm)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132.9
132.8
132.2
130.7
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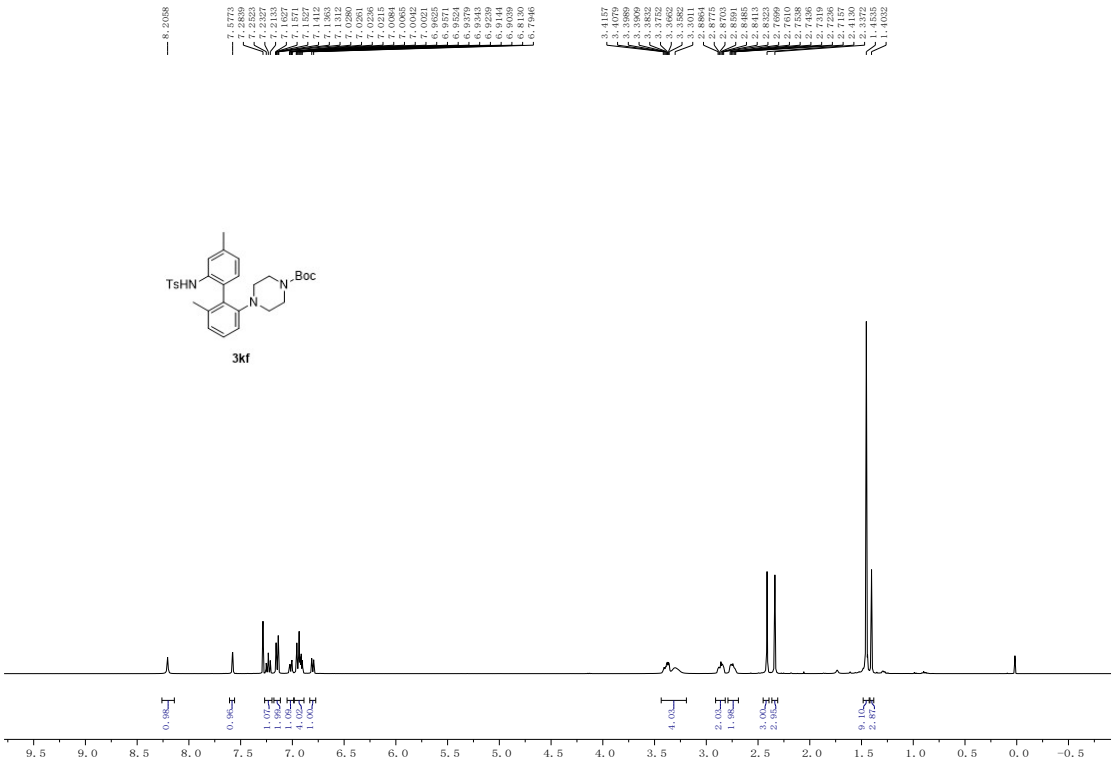
127.2
126.6
126.2
117.2
80.0
51.9
28.4
21.5
18.3
f1 (ppm)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7.1412
7.1363
7.1212
7.0280
7.0261
7.0236
7.0215
7.0084
7.0065
7.0042
7.0021
6.9965
6.9571
6.9524
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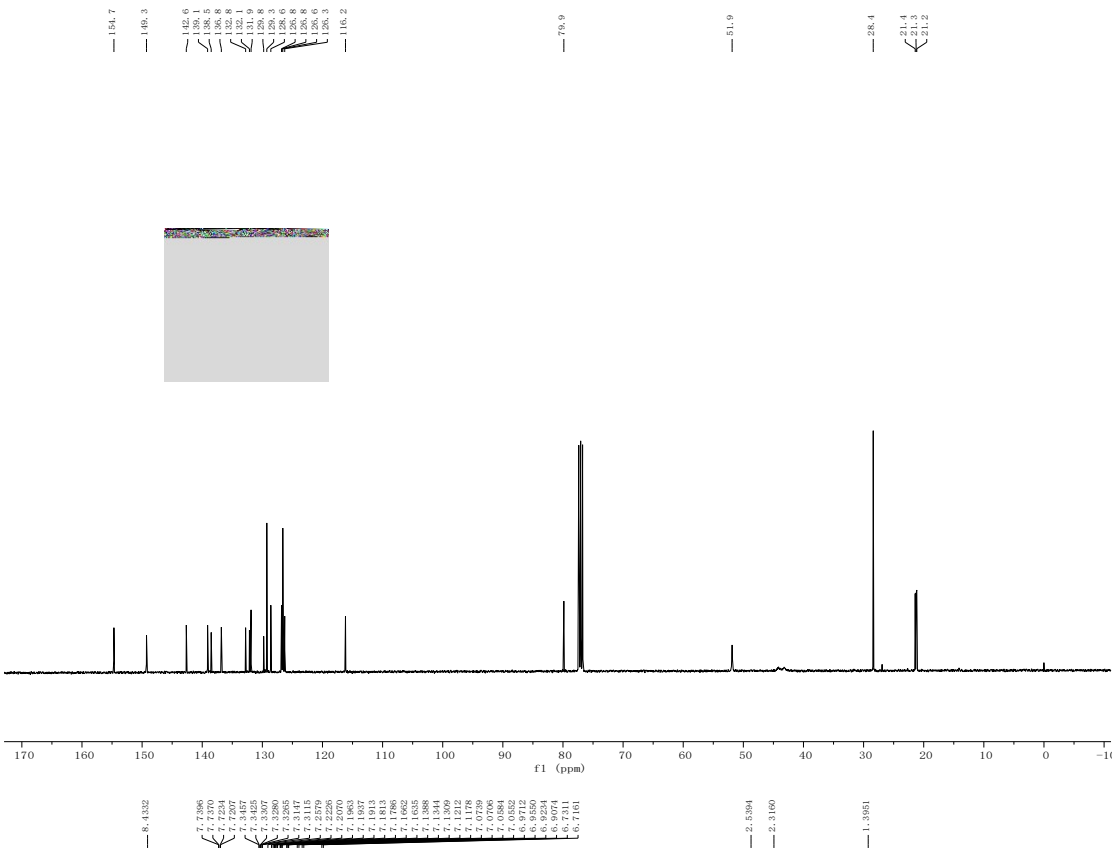
6.9239
6.9144
6.9039
6.8930
6.7946
3.4157
3.4079
3.3989
3.3909
3.3832
3.3752
3.3682
3.3582
3.3011
2.9084
2.8775
2.8703
2.8591
2.8445
2.8413
2.8323
2.7699
2.7610
2.7458
2.7436
2.7319
2.7236
2.7157
2.4130
2.3372
1.4535
1.4032
f1 (ppm)

TsHN
N
N
Boc
3kf
0.98
0.96
1.07
1.99
1.09
4.02
1.00
4.03
2.02
1.98
3.00
2.95
9.10
2.87
f1 (ppm)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142.6
138.1
138.5
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132.8
132.1
131.9
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129.3
128.6
128.5
126.8
126.6
126.3
116.2
78.9
51.9
28.4
21.4
21.3
21.2
f1 (ppm)

8.4332
7.7986
7.7970
7.7234
7.7207
7.3457
7.3435
7.3307
7.3280
7.3265
7.3147
7.3115
7.2579
7.2226
7.2070
7.1962
7.1837
7.1813
7.1788
7.1682
7.1635
7.1388
7.1344
7.1309
7.1212
7.1178
7.0739
7.0708
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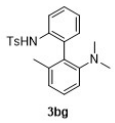
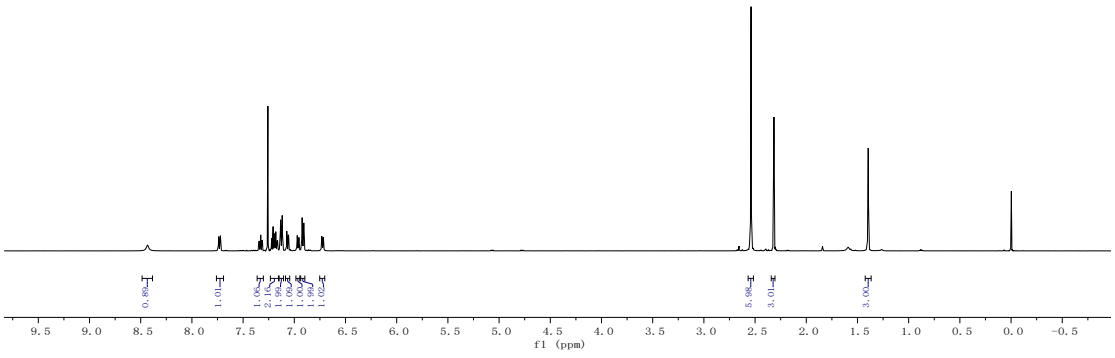
2.3160
1.3951


TsHN
N

3bg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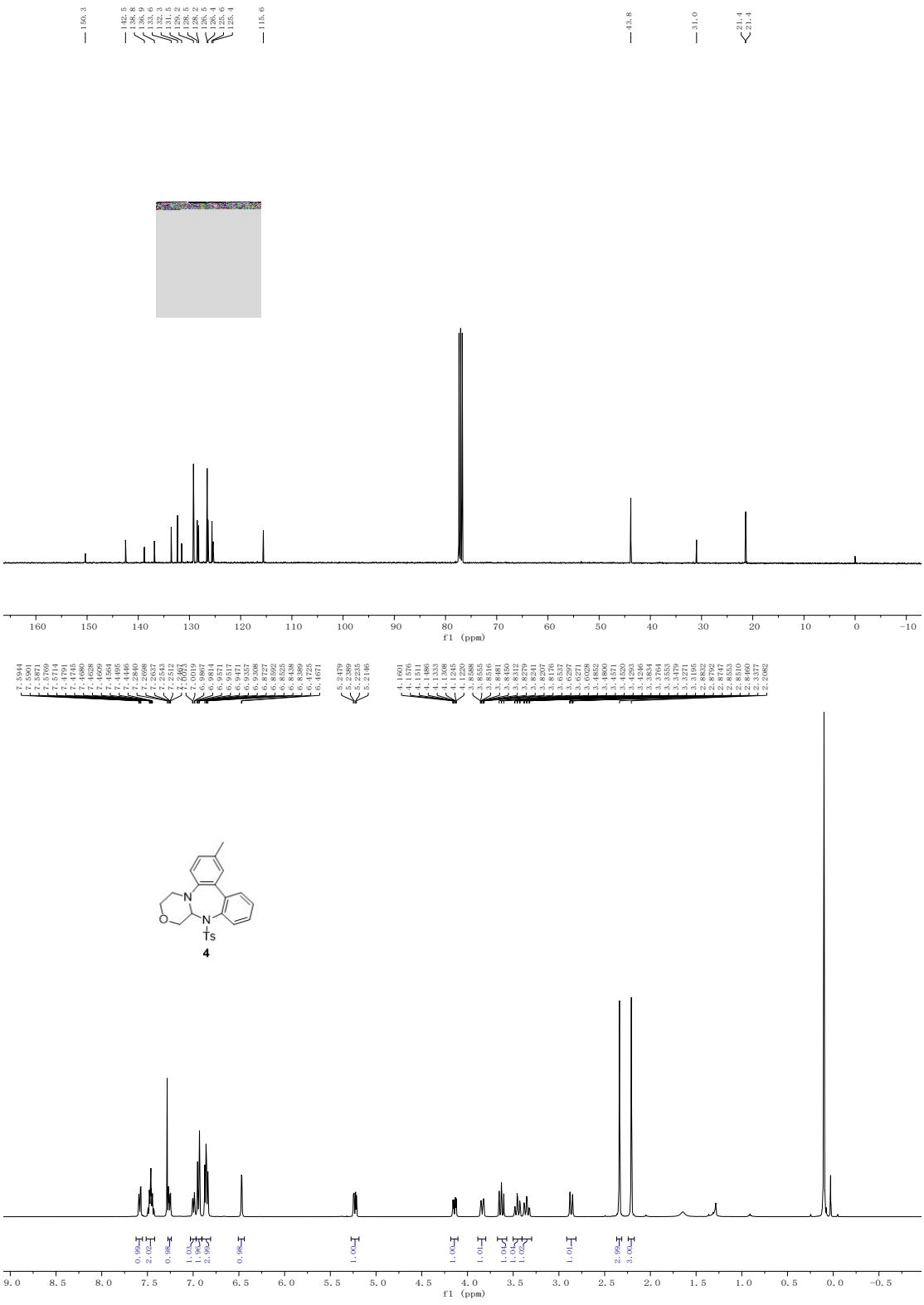
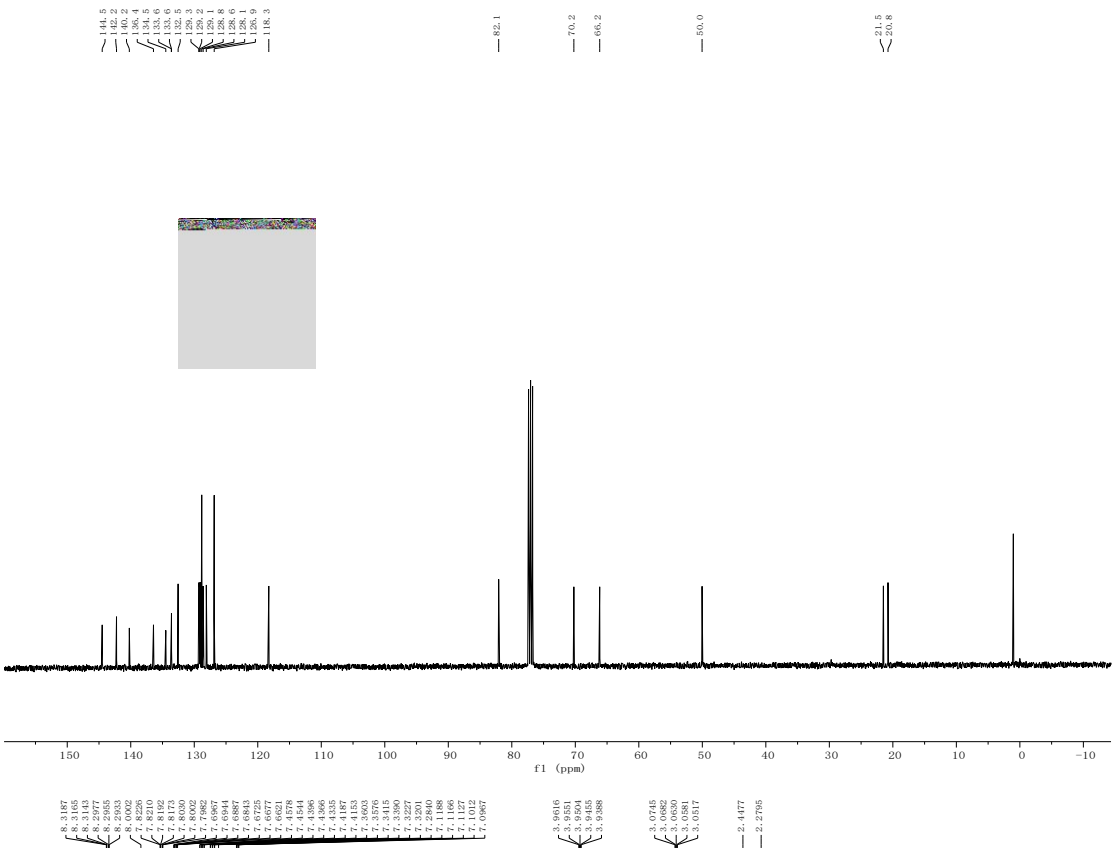
1.05
2.16
1.98
1.09
1.00
1.09
1.02
5.98
3.01
3.00
f1 (ppm)


150.3
142.5
138.8
138.0
135.6
132.3
131.5
129.2
128.5
128.2
126.5
126.4
125.6
125.4
115.6
43.8
31.0
21.4
21.4
f1 (ppm)
Ts
4
f1 (ppm)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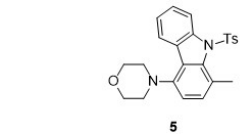
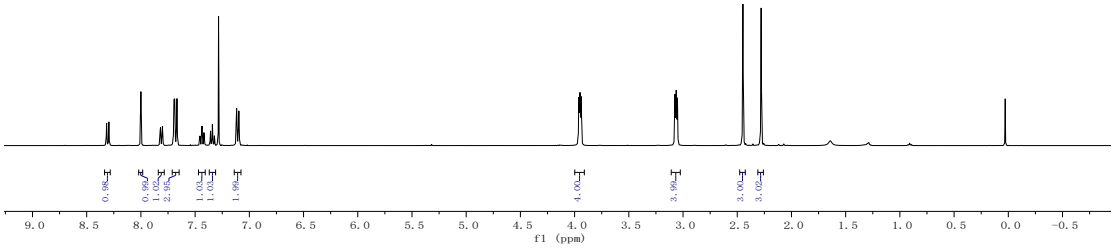
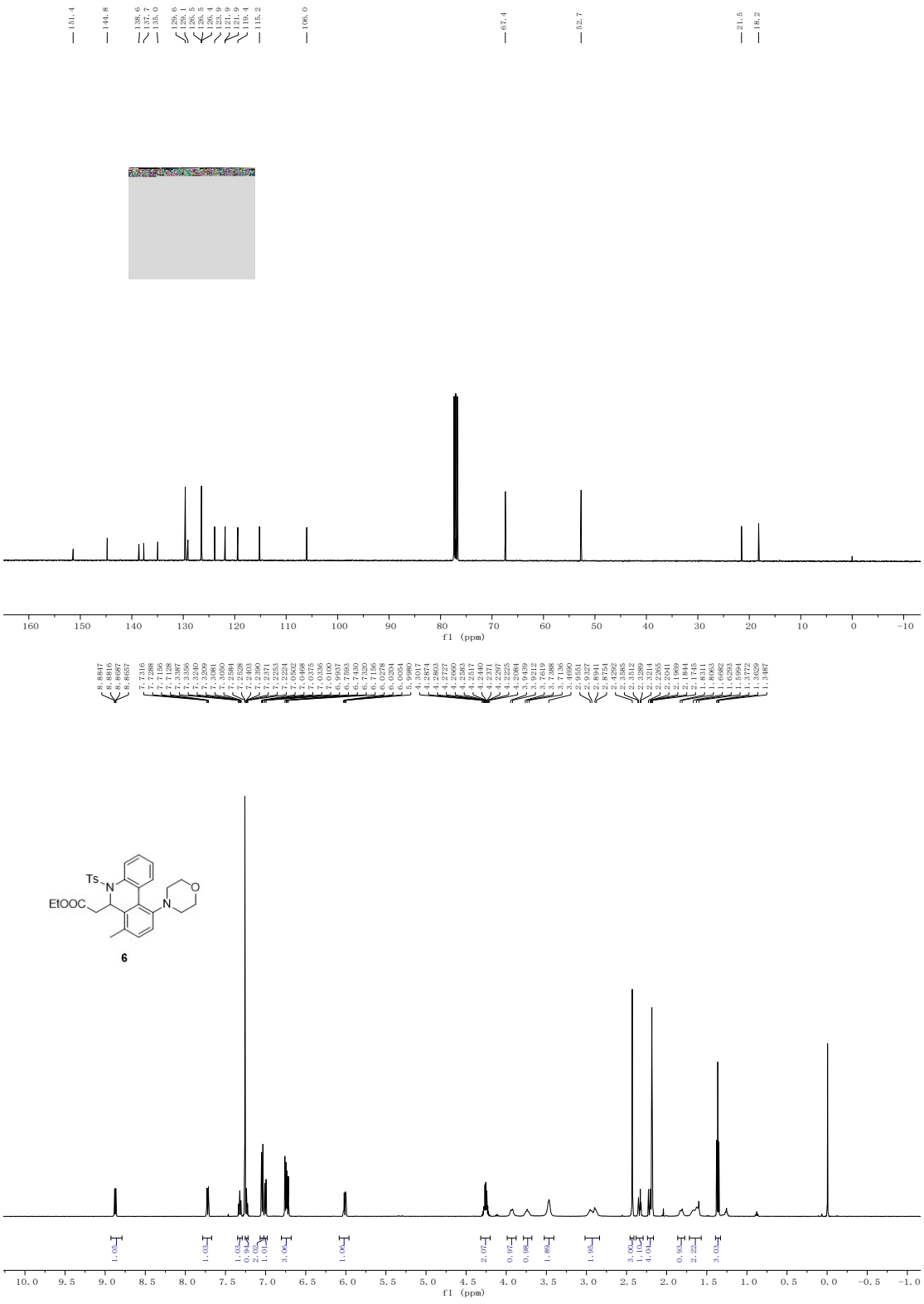
142.2
140.2
136.4
134.5
133.6
133.5
132.5
129.3
129.2
129.1
128.8
128.6
128.1
126.9
118.3
82.1
70.2
66.2
50.0
21.5
20.8
f1 (ppm)


N
Ts
O
N

5


0.98
0.99
1.05
2.95
1.02
1.02
1.99
4.00
3.89
3.00
3.02
f1 (ppm)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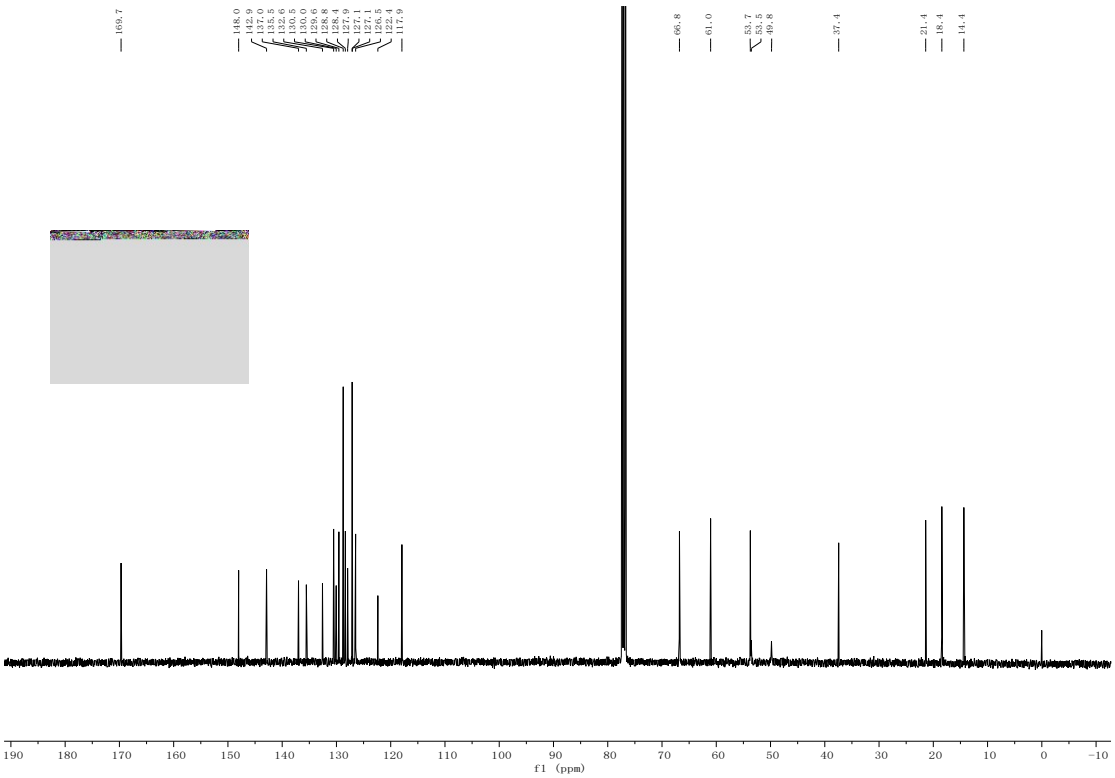
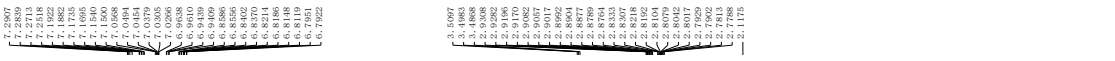
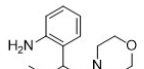
144.8
138.6
137.7
135.0
129.6
129.1
126.5
126.4
123.9
121.9
121.9
119.4
115.2
106.0
67.4
52.7
21.5
18.2
f1 (ppm)
Ts
N
EtOOC
O
6







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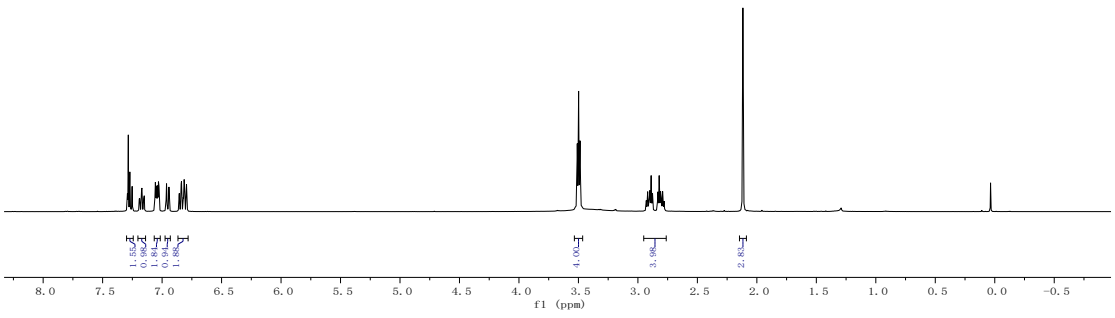
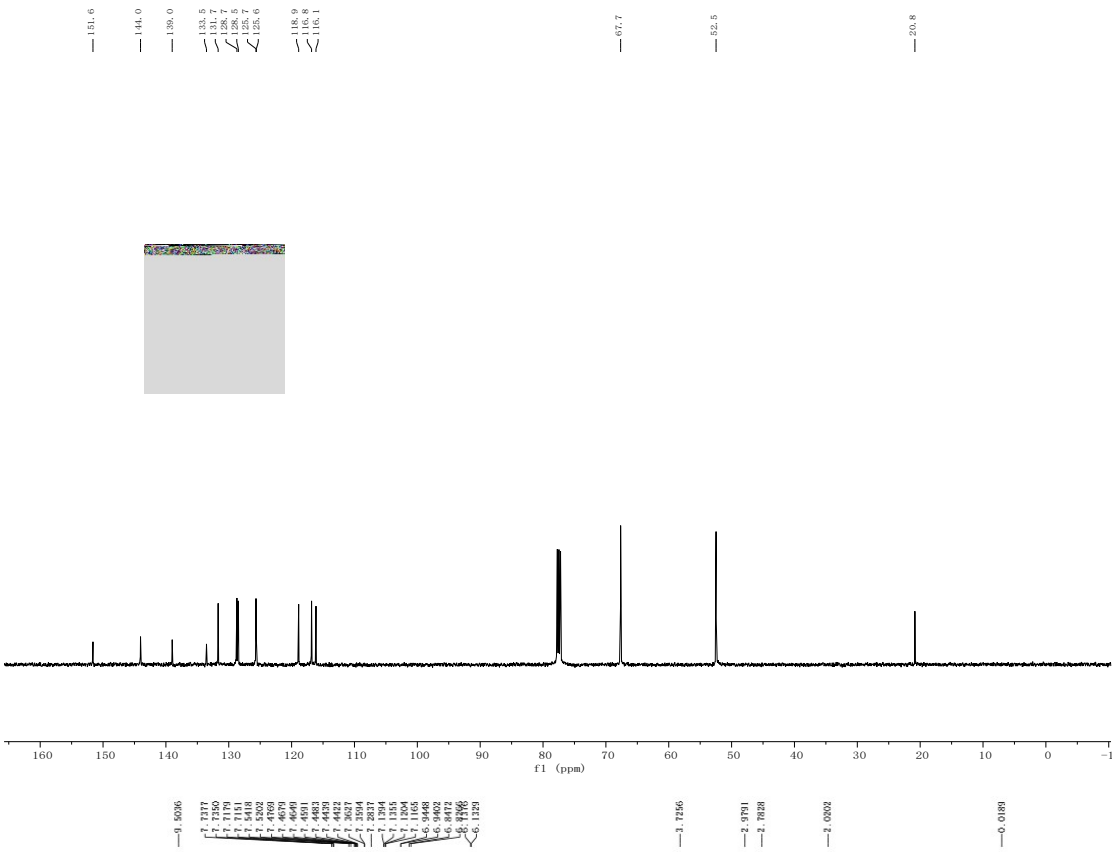
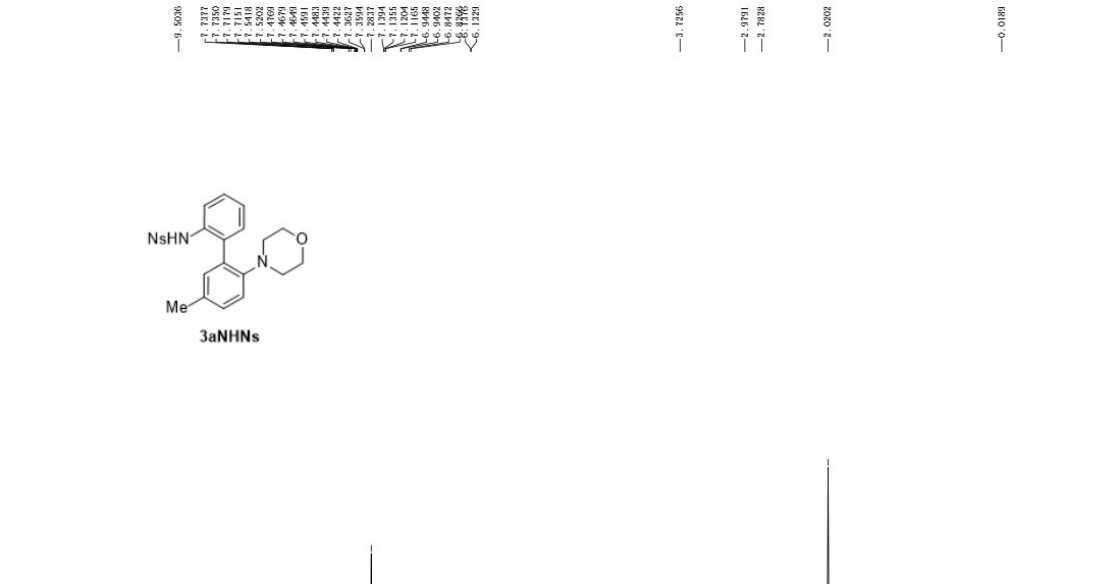
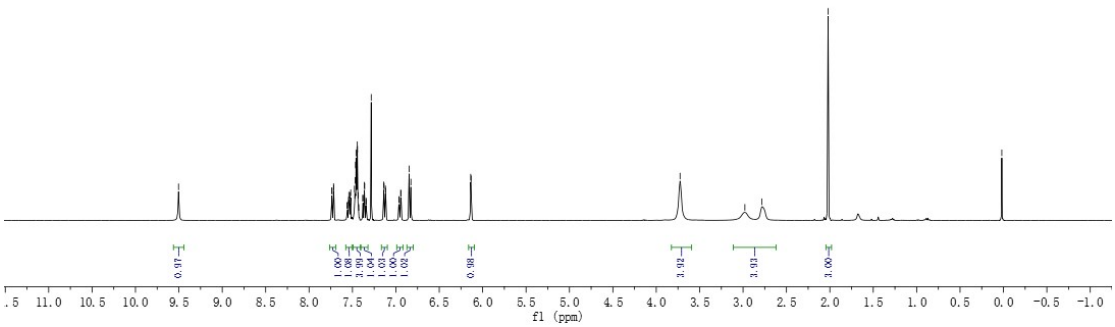
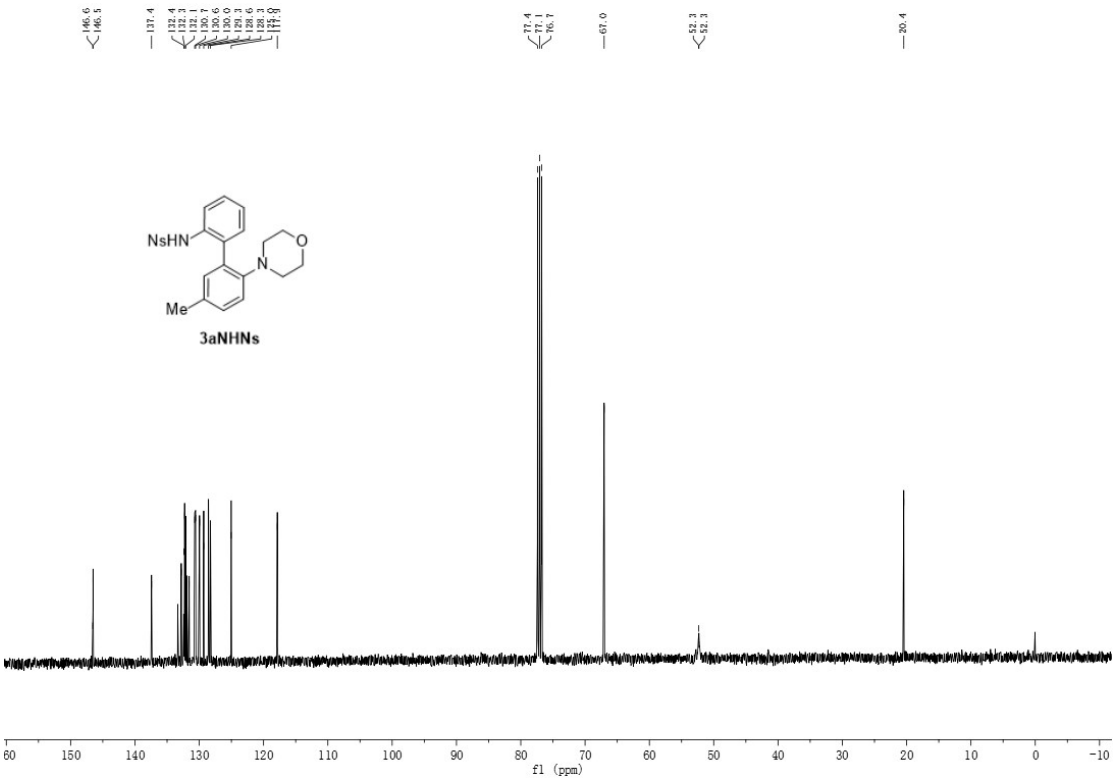


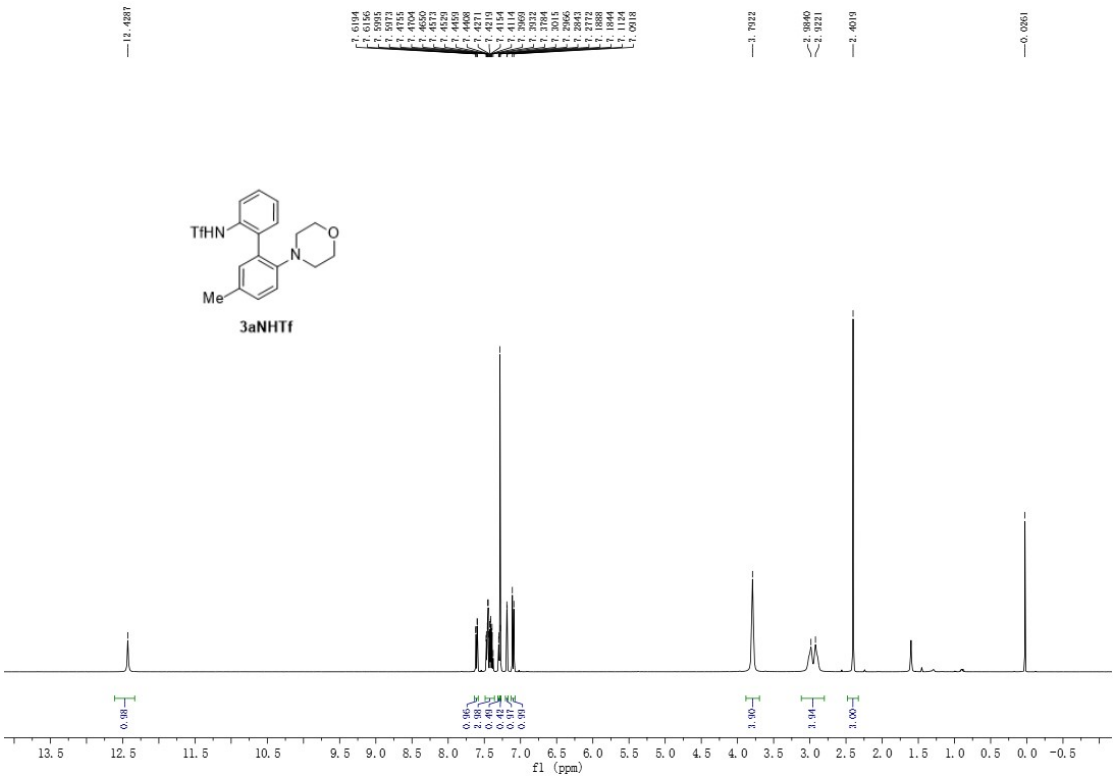


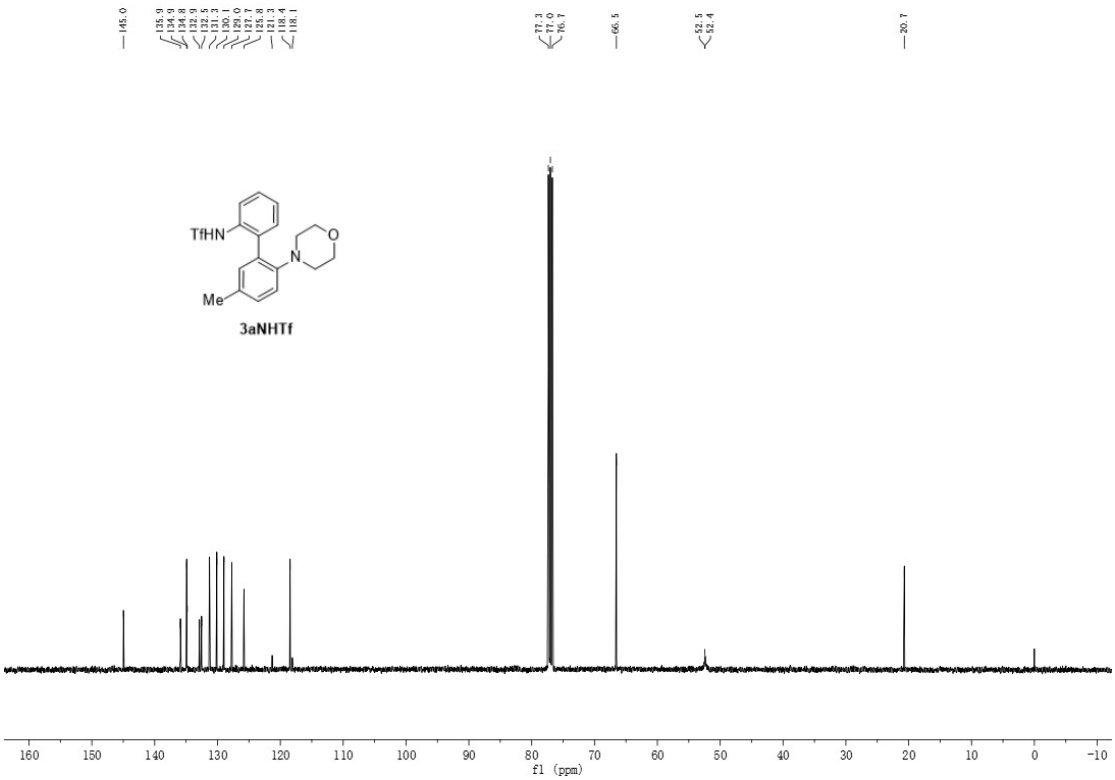


3aNHNs




NsHN
N
O
Me
3aNHNs
f1 (ppm)


TfHN
N
O
Me
3aNHTf
f1 (ppm)



10. References

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