Supporting Information

Stereodivergent Access to *Cis*- and *Trans*-3,5-Disubstituted-1,4-Thiazane 1-Oxides by Cyclization of Homochiral β-Amino Sulfoxides and Sulfones. The Preparation of Isomeric Ant Venom Alkaloids.

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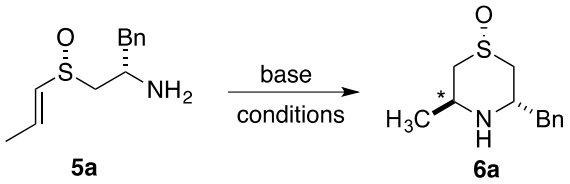
Table 1. Cyclization Optimization of β-Amino Sulfoxide 5a to 6a



5a 6a

entry	base (eq.)	solvent	T	time	yield	*dr*
1	$CsCO_3$(1.0)	DCM	RT	96 h	SM	-
2	$CsCO_3$(1.0)	DCM	reflux	16 h	SM	-
3	NEt_3 (1.0)	DCM	RT	48 h	SM	-
4	NEt_3 (1.0)	DCM	reflux	5 h	SM	-
5	K_2CO_3 (1.0)	DCM	RT	96 h	SM	-
6	K_2CO_3 (1.0)	DCM	reflux	15 h	SM	-
7	K_2CO_3(0.96)	MeOH	reflux	10 h	OMe incorp.	-
8	Triton B (1.0)	MeOH	reflux	2 h	OMe incorp.	-
9	NEt_3 (1.0)	MeOH	reflux	5 h	95	>95:5
10	NEt_3 (0.2)	MeOH	reflux	19.5 h	85	>95:5
11	NEt_3 (1.0)	IPA	reflux	12 h	O*i*Pr incorp.	-

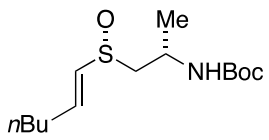
General Experimental

Many general experimental methods have recently been reported.[1] All dry and pure solvents were obtained from a solvent purification system expect for methanol which was distilled over calcium hydride. All chemicals were obtained from commercial sources unless otherwise noted. All air and water sensitive reagents were transferred via oven-dried nitrogen-purged syringes into flame-dried flasks. Homochiral amino iodides and β-amino sulfoxides were prepared as previously described.[1,2] Thiirane S-oxides were prepared and purified as previously described.[3-6]

Synthesis of Boc Protected β-Amino Sulfoxides 4.

The synthesis of the chiral amino iodides, thiirane S-oxides and most of the Boc-protected β-amino sulfoxides including **4a-c, e**, (*R*$_S$, 2*S*)-*N*-Boc-1-phenyl-3-((*E*)-4-phenyl-1-butenylsulfinyl)propan-2-amine, (*R*$_S$, 2*S*)-*N*-Boc-1-(cyclohexenylsulfinyl)-3-phenylpropan-2-amine, (*R*$_S$, 2*S*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfinyl)-3-phenylpropan-2-amine, (*S*$_S$, 1*R*)-*N*-Boc-2-((*E*)-3,3-dimethyl-1-butenylsulfinyl)-1-phenylethanamine and (*S*$_S$, 2*R*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfinyl)butan-2-amine have been previously reported.[1,2,5,7]

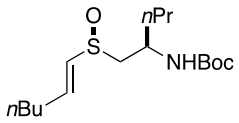
Synthesis of (*S*$_S$, 2*R*)-*N*-Boc-1-((*E*)-1-hexenylsulfinyl)propan-2-amine (4d).



Under anhydrous conditions under an inert N_2(g) atmosphere a solution of LiHMDS (1.0 M in THF, 3.30 mL, 3.30 mmol) in Et_2O (25 mL) at -78 °C was added dropwise a solution of the *n*-butyl thiirane *S*-oxide (0.400 g, 3.03 mmol) in Et_2O/THF (5:2 mL) at -78 °C. The mixture was allowed to

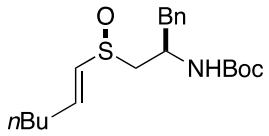
stir for ca. 15 min, at which time a precooled (-78 °C) solution of the (*S*)-2-(*N*)-*t*-butoxylcarbonylamino)-iodopropane (1.14 g, 4.0 mmol) in THF (4 mL) was added dropwise via syringe. After 1 h of stirring at -78 °C the reaction vessel was removed from the cold bath and allowed to warm to rt stirring for ~12 h. Following completion of the reaction, solvent was removed under reduced pressure, and the residue was dissolved in EtOAc. The organic layer was washed with sat'd ammonium chloride solution, water, and brine and then dried over $MgSO_4$. The organic layer was then filtered, and solvent was removed under reduced pressure. The crude reaction mixture was subjected to flash chromatography (40% EtOAc/hexanes), which yielded the β-amino sulfoxide **4d** as a mixture of diastereomers (82%, 0.714 g, *dr* = 89:11 from ^{1}H NMR analysis of reaction mixture). Recrystallization with EtOAc/hexanes provided the pure major diastereomer **4d** as a white solid (58%, 0.509 g). Mp: 120-121 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.50 (dt, *J* = 15.2, 6.8 Hz, 1H), 6.26 (d, *J* = 15.2 Hz, 1H), 5.34 (br m, 1H), 4.14 (br m, 1H), 2.90 (br m, 1H), 2.85-2.82 (m, 2H), 2.25 (m, 2H), 1.42-1.33 (m, 6H), 1.44 (s, 9H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 155.0, 141.8, 132.0, 79.5, 59.8, 43.9, 31.8, 30.2, 28.4, 22.1, 20.4, 13.8; IR (neat) cm^{-1} 3225, 3035, 3001, 2964, 2928, 2875, 2859, 1698, 1546, 1275, 1175, 1077, 1047, 1030, 772; $[\alpha]_D^{25}$ +2.5 (*c* = 0.8, $CHCl_3$); Anal. calcd for $C_{14}H_{27}NO_3S$: C, 58.10; H, 9.40; Found: C, 57.95; H, 9.36. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.32 (d, *J* = 15.1 Hz, 1H); 4.05 (br m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 141.5, 131.7, 79.5, 61.0, 43.3, 31.8, 30.1, 28.4, 22.2, 21.1, 13.8.

Synthesis of (R_S, 2*S*)-*N*-Boc-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (10).



Under anhydrous conditions under an inert N_2(g) atmosphere a solution of LiHMDS (1.0 M in THF, 3.81 mL, 3.81 mmol) in Et_2O (35 mL) at -78 °C was added dropwise a solution of the *n*-butyl thiirane *S*-oxide (0.458 g, 3.47 mmol) in Et_2O/THF (5:2 mL) at -78 °C. The mixture was allowed to stir for ca. 15 min, at which time a precooled (-78 °C) solution of (*R*)-2-(*N*)-*t*-butoxylcarbonylamino)-iodopentane (1.30 g, 4.15 mmol) in THF (4 mL) was added dropwise via syringe. After 1 h of stirring at -78 °C the reaction vessel was removed from the cold bath and allowed to warm to rt stirring for ~8 h. Following completion of the reaction, workup as for **10** provided crude material. The crude reaction mixture was subjected to flash chromatography (40% EtOAc/hexanes), which yielded the β-amino sulfoxide as a mixture of diastereomers **10:4h** (74%, 0.931 g, *dr* = 91:9 from ^{1}H NMR analysis of reaction mixture). Flash chromatography (5% to 40% EtOAc/hexanes) provided the pure major diastereomer **10** as a white solid (65%, 0.827 g). Mp: 73-74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.49 (dt, *J* = 15.2, 6.8 Hz, 1H), 6.25 (d, *J* = 15.2 Hz, 1H), 5.27 (br d, *J* = 7.9 Hz, 1H), 4.01 (sex, *J* = 5.9 Hz, 1H), 2.96-2.82 (m, 2H), 2.24 (m, 2H), 1.78-1.62 (m, 2H), 1.51-1.29 (m, 6H), 1.43 (s, 9H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 141.7, 132.2, 79.4, 58.4, 47.6, 36.4, 31.8, 30.2, 28.4, 22.1, 19.4, 13.8 (CH_3's overlapping); IR (neat) cm^{-1} 3226, 3038, 3003, 2960, 2930, 2873, 1702, 1541, 1454, 1363, 1270, 1253, 1175, 1041, 1025, 971, 742, 704; $[\alpha]_D^{25}$ -29.8 (*c* = 1.3, $CHCl_3$); Anal. calcd for $C_{16}H_{31}NO_3S$: C, 60.53; H, 9.84; Found: C, 60.74; H, 9.90.

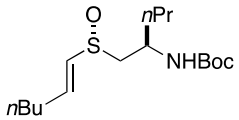
Synthesis of (R_S, 2*S*)-*N*-Boc-1-phenyl-3-((*E*)-1-hexenylsulfinyl)propan-2-amine (4g).



Under anhydrous conditions under an inert N_2(g) atmosphere a solution of LiHMDS (1.0 M in THF, 3.30 mL, 3.30 mmol) in Et_2O (25 mL) at -78 °C was added dropwise a solution of the *n*-butyl thiirane *S*-oxide (0.400 g, 3.03 mmol) in Et_2O/THF (5:2 mL) at -78 °C. The mixture was allowed to stir for ca. 15 min, at which time a precooled (-78 °C) solution of the (*R*)-2-(*N*-*t*-butoxycarbonylamino)-3-phenyl-iodopropane (1.31 g, 3.64 mmol) in THF (4 mL) was added dropwise via syringe. After 1 h of stirring at -78 °C the reaction vessel was removed from the cold bath and allowed to warm to rt stirring for ~12 h. Following completion of the reaction, workup as for **4g** provided crude material. The crude reaction mixture was subjected to flash chromatography (40% EtOAc/hexanes), which yielded the β-amino sulfoxide **4g** as a mixture of diastereomers (77%, 0.850 g, *dr* = 87:13 from ^{1}H NMR analysis of reaction mixture). Flash chromatography with (40% EtOAc/hexanes) provided the pure major diastereomer **4g** as a white solid (68%, 0.751 g). Mp: 101-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.22 (m, 5H), 6.49 (dt, *J* = 15.2, 6.8 Hz, 1H), 6.20 (d, *J* = 15.2 Hz, 1H), 5.51 (br d, *J* = 7.3 Hz, 1H), 4.22 (br m, 1H), 3.20 (dd, *J* = 13.6, 6.6 Hz, 1H), 3.00 (dd, *J* = 13.6, 8.1 Hz, 1H), 2.86 (AB of ABX, J_{AB} = 13.3 Hz, J_{AX} = 7.4 Hz, J_{BX} = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 141.8, 137.5, 131.7, 129.4, 128.7, 126.7, 79.6, 56.5, 49.5, 39.8, 31.8, 30.1, 28.4, 22.2, 13.9; IR (neat) cm^{-1} 3358, 3023, 2958, 2927, 2857, 1691, 1523, 1366, 1267, 1250, 1171, 1048, 1020, 970, 700; $[\alpha]_D^{25}$ -8.3 (*c* = 1.6, $CHCl_3$); Anal. calcd for $C_{20}H_{31}NO_3S$: C, 65.72; H, 8.55; Found: C, 65.81; H, 8.35. Minor

isomer, partial characterization: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.24 (d, *J* = 15.2 Hz, 1H), 5.14 (br d, *J* = 7.8 Hz, 1H), 4.10 (br m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 141.8, 137.0, 131.7, 129.5, 128.9, 126.8, 79.7, 58.4, 48.3, 40.8, 31.7, 30.2, 28.4, 22.1, 13.8.

Synthesis of (*S*$_S$, 2*S*)-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (4h).



A sample of β-amino sulfoxide **10/4h** mixture collected from the mother liquors of several recrystallization attempts (*dr* ~ 70:30 (**10**: **4h**), 0.504 g) was subjected to flash chromatography (10% to 30% EtOAC/hexanes) to give pure major isomer (*R*$_S$, 2*S*)-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (**10**) (326 mg) and pure minor diastereomer (*S*$_S$, 2*S*)-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (**4h**) (111 mg). Minor diastereomer **4h**: Mp 82-83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (dt, *J* = 15.2, 6.8 Hz, 1H), 6.34 (d, *J* = 15.2 Hz, 1H), 4.73 (br d, *J* = 8.0 Hz, 1H), 3.90 (m, 1H), 2.96-2.86 (m, 2H), 2.26 (m, 2H), 1.61-1.57 (m, 2H), 1.48-1.32 (m, 6H), 1.44 (s, 9H), 0.93 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 155.2, 141.5, 132.0, 79.7, 60.5, 47.0, 37.2, 31.8, 30.3, 28.4, 22.2, 19.1, 13.8, 13.7; IR (neat) cm^{-1} 3347, 3025, 2957, 2928, 2872, 1683, 1526, 1463, 1366, 1354, 1170, 1038, 1001, 969, 772; $[\alpha]_D^{25}$ -58.7 (*c* = 0.7, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{16}H_{31}NO_3S$ $[M+H]^+$ 318.2097; found: 318.2104.

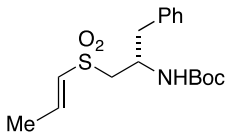
Synthesis of Sulfones 7

General Procedure for the Oxidation of Sulfoxides to Sulfones

β-Amino sulfoxide **4** (1.0 equiv.) was dissolved in DCM (20 mL/mmol) and stirred at

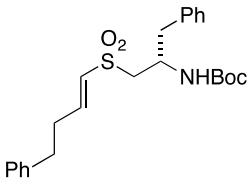
-78 °C. MCPBA (calibrated to 77 or 83%, 1.2–1.5 equiv) was added, and the reaction was slowly warmed to rt stirring for 4-8 h. The crude reaction mixture was washed with saturated $Na_2S_2O_3$ (aq.), $NaHCO_3$ (aq.), H_2O and brine. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed *in vacuo*. The crude sulfone was purified by flash chromatography using EtOAc/hexanes as the eluent.

Synthesis of (2*S*)-*N*-Boc-1-phenyl-3-((*E*)-propenylsulfonyl)propan-2-amine.



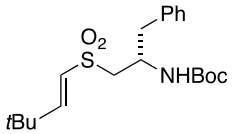
A mixture of diastereomers populated principally by (*R*$_S$, 2*S*)-*N*-Boc-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-amine (**4a**) (0.487 g, 1.51 mmol) in DCM (30 mL) and MCPBA (ca ~77%, 0.507 g, ca ~ 2.26 mmol) in DCM (25 mL) afforded (2*S*)-*N*-Boc-1-phenyl-3-((*E*)-propenylsulfonyl)propan-2-amine (N-Boc protected precursor of β-amino sulfone **7a**) as a white solid (76%, 0.388 g) following flash chromatography (50% EtOAc/hexanes). Mp 190-191 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33-7.30 (m, 2H), 7.26-7.19 (m, 3H), 6.92 (dq, *J* = 14.9, 7.0 Hz, 1H), 6.32 (d, *J* = 14.9 Hz, 1H), 4.92 (br s, 1H), 4.18 (m, 1H), 3.27 (m, 1H), 3.12 (dd, *J* = 14.5, 4.6 Hz, 1H), 3.06 (m, 1H), 3.00 (dd, *J* = 13.6, 7.0 Hz, 1H), 1.96 (dd, *J* = 6.9, 1.1 Hz, 3H), 1.42 (s, 9H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 155.0, 145.3, 136.8, 130.0, 129.5, 128.8, 126.7, 79.9, 56.8, 48.5, 40.0, 28.4, 17.5; IR (neat) cm^{-1} 3358, 3045, 3031, 2979, 2922, 2852, 1689, 1530, 1443, 1277, 1171, 1127, 1117, 1048, 954; $[\alpha]_D^{25}$ +0.2 (*c* = 0.4, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{17}H_{26}NO_4S$ $[M+H]^+$ 340.1577; found: 340.1569.

Synthesis of (2*S*)-*N*-Boc-1-phenyl-3-((*E*)-4-phenyl-1-butenylsulfonyl)propan-2-amine.



A mixture of diastereomers populated principally by (*R*$_S$, 2*S*)-*N*-Boc-1-phenyl-3-((*E*)-4-phenyl-1-butenylsulfinyl)propan-2-amine (1.02 g, 2.46 mmol) in DCM (40 mL) and MCPBA (ca ~77%, 0.720 g, ca ~ 3.22 mmol) in DCM (25 mL) afforded (2*S*)-*N*-Boc-1-phenyl-3-((*E*)-4-phenyl-1-butenylsulfonyl)propan-2-amine (N-Boc protected precursor of β-amino sulfone **7b**) as a white solid (61%, 0.645 g) following flash chromatography (50% EtOAc/hexanes). Mp: 123-124 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33-7.24 (m, 5H), 7.21-7.19 (m, 3H), 7.15 (d, *J* = 7.2 Hz, 2H), 6.93 (dt, *J* = 15.1, 6.8 Hz, 1H), 6.27 (d, *J* = 15.1 Hz, 1H), 4.84 (br s, 1H), 4.14 (m, 1H), 3.21 (m, 1H), 3.07 (dd, *J* = 14.6, 4.7 Hz, 1H), 3.04 (m, 1H), 2.97 (dd, *J* = 13.4, 6.9 Hz, 1H), 2.80 (t, *J* = 7.6 Hz, 2H), 2.59 (m, 2H), 1.42 (s, 9H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 155.0, 148.5, 140.0, 136.8, 129.5, 129.3, 128.7, 128.6, 128.4, 127.0, 126.5, 79.9, 56.9, 48.4, 40.0, 33.8, 33.3, 28.4; IR (neat) cm^{-1} 3086, 3059, 3028, 3010, 2979, 2967, 2928, 2859, 1691, 1527, 1497, 1443, 1367, 1319, 1282, 1250, 1218, 1171, 1126, 1046, 1027 ; $[\alpha]_D^{25}$ -4.8 (*c* = 1.3, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{24}H_{31}NO_4S$ $[M+H]^+$ 430.2047; found: 430.2030.

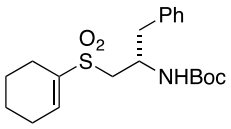
Synthesis of (2*S*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-3-phenylpropan-2-amine.



A mixture of diastereomers populated principally by (*R*$_S$, 2*S*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfinyl)-3-phenylpropan-2-amine (0.740 g, 2.02 mmol) in DCM (30 mL) and MCPBA (ca ~77%, 0.524 g, ca ~

2.34 mmol) in DCM (20 mL) afforded (2*S*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-3-phenylpropan-2-amine (N-Boc protected precursor of **7c**) as a white solid (90%, 0.697 g) following flash chromatography (50% EtOAc/hexanes). Mp: 137-138 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32-7.30 (m, 2H), 7.26-7.24 (m, 1H), 7.21 (d, *J* = 7.2 Hz, 2H), 6.89 (d, *J* = 15.3 Hz, 1H), 6.18 (d, *J* = 15.3 Hz, 1H), 4.94 (br s, 1H), 4.19 (app sex, *J* = 7.2 Hz, 1H), 3.29-3.25 (m, 1H), 3.13 (dd, *J* = 14.4, 4.2 Hz, 1H), 3.08 (m, 1H), 3.00 (dd, *J* = 13.5, 7.2 Hz, IH), 1.42 (s, 9H), 1.11 (s, 9H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 159.0, 154.9, 136.9, 129.4, 128.7, 126.9, 124.8, 79.9, 56.9, 48.7, 40.0, 34.3, 28.4(*t*Bu $\underline{C}H_3$s overlapping); IR (neat) cm^{-1}: 3385, 3057, 3029, 2974, 2933, 2872, 1698, 1514, 1440, 1391, 1365, 1321, 1284, 1250, 1172, 1127, 1026, 873, 825, 774; $[\alpha]_D^{25}$: -4.53 (*c* = 1.7, $CHCl_3$); Anal. calcd for $C_{20}H_{31}NO_4S$: C, 62.96 ; H, 8.19 ; Found: C, 62.77 ; H, 8.02.

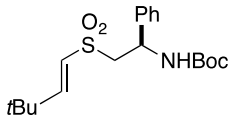
Synthesis of (2*S*)-*N*-Boc-1-(cyclohexenylsulfonyl)-3-phenylpropan-2-amine.



A mixture of diastereomers populated principally by (*R*$_S$, 2*S*)-*N*-Boc-1-(cyclohexenylsulfinyl)-3-phenylpropan-2-amine (0.329 g, 0.906 mmol) in DCM (30 mL) and MCPBA (ca ~83%, 0.207 g, ca ~ 1.00 mmol) in DCM (25 mL) afforded (2*S*)-*N*-Boc-1-(cyclohexenylsulfonyl)-3-phenylpropan-2-amine (N-Boc protected precursor of β-amino sulfone **7d**) as a white solid (70%, 0.240 g) following flash chromatography (30% EtOAc/hexanes). Mp 115-116 °C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.36-7.21 (m, 5H), 6.93 (m, 1H), 4.97 (br s, 1H), 4.10 (m, 1H), 3.19 (dd, *J* = 14.4, 7.2 Hz, 1H), 3.09-3.05 (m, 2H), 2.98 (dd, *J* = 13.6, 7.2 Hz, 1H), 2.30-2.14 (m, 4H), 1.76-1.61 (m, 4H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 140.9, 138.2, 137.0, 129.5, 128.7, 126.9, 79.8, 53.6, 48.7, 40.1, 28.4, 25.6, 23.2,

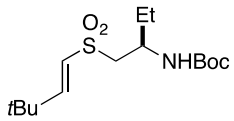
21.8, 20.7; IR (neat) cm^{-1} 3367, 3084, 3061, 3028, 2975, 2934, 2863, 1699, 1646, 1517, 1453, 1306, 1289, 1250, 1167, 1131, 1079, 1047, 1022; $[\alpha]_D^{25}$ -9.8 (*c* = 0.9, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{20}H_{29}NO_4S$ $[M+H]^+$ 380.1890; found: 380.1876.

Synthesis of (1*R*)-*N*-Boc-2-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-1-phenylethanamine.



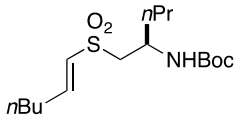
A mixture of diastereomers populated principally by (*S*$_S$, 1*R*)-*N*-Boc-2-((*E*)-3,3-dimethyl-1-butenylsulfinyl)-1-phenylethanamine (0.603 g, 1.72 mmol) in DCM (30 mL) and MCPBA (ca ~77%, 0.503 g, ca ~ 2.92 mmol) in DCM (25 mL) afforded (1*R*)-*N*-Boc-2-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-1-phenylethanamine (N-Boc protected precursor of β-amino sulfone **7e**) as a white solid (77%, 0.485 g) following flash chromatography (50% EtOAc/hexanes). Mp: 83-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 5H), 6.76 (d, *J* = 15.3 Hz, 1H), 5.69 (br s, 1H), 5.66 (d, *J* = 15.3 Hz, 1H), 5.21 (br m, 1H), 3.56 (dd, *J* = 14.2, 6.6 Hz, 1H), 3.44 (dd, *J* = 14.5, 4.0 Hz, 1H), 1.42 (s, 9H), 0.96 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.9, 154.8, 139.6, 129.0, 128.2, 126.4, 124.7, 80.2, 60.5, 50.5, 34.1, 28.3, 28.2; IR (neat) cm^{-1} 3361, 3063, 3031, 2965, 2933, 2907, 2870, 1702, 1626, 1512, 1366, 1293, 1249, 1169, 1121, 1045, 1019, 757, 732, 699; $[\alpha]_D^{25}$ 4.8 (*c* = 1.1, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{19}H_{29}NO_4S$ $[M+H]^+$ 368.1890; found: 368.1880.

Synthesis of (2*R*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)butan-2-amine.



A mixture of diastereomers populated principally by (S_S, 2*R*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfinyl)butan-2-amine (0.460 g, 1.52 mmol) in DCM (25 mL) and MCPBA (ca ~77%, 0.387 g, ca ~ 1.72 mmol) in DCM (20 mL) afforded (2*R*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)butan-2-amine (N-Boc protected precursor of β-amino sulfone **7f**) as a white solid (82%, 0.393 g) following flash chromatography (30% EtOAc/hexanes). Mp: 75-76 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.90 (d, *J* = 15.3 Hz, 1H), 6.25 (d, *J* = 15.3 Hz, 1H), 4.90 (br s, 1H), 3.91 (m, 1H), 3.20 (AB of ABX, J_{AB} = 14.4 Hz, J_{AX} = 6.8 Hz, J_{BX} = 4.8 Hz, 2H), 1.84-1.60 (m, 2H), 1.45 (s, 9H), 1.12 (s, 9H), 0.96 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 155.1, 125.1, 79.5, 58.2, 48.5, 34.1, 28.3 (*t*Bu's overlapping), 27.6, 10.3; IR (neat) cm^{-1} 3361, 3053, 2966, 2934, 2874, 1709, 1518, 1460, 1391, 1365, 1292, 1246, 1171, 1127, 979, 772; $[\alpha]_D^{25}$ + 22.7 (*c* = 0.7, $CHCl_3$); Anal. calcd for $C_{15}H_{29}NO_4S$: C, 56.40; H, 9.15; Found: C, 56.40; H, 8.97.

Synthesis of (2*S*)-*N*-Boc-1-((*E*)-1-hexenylsulfonyl)pentan-2-amine.



A mixture of diastereomers populated principally by (R_S, 2*S*)-*N*-Boc-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (**10**) (1.92 g, 5.26 mmol) in DCM (30 mL) and MCPBA (ca ~83%, 1.92 g, ca ~ 7.86 mmol) in DCM (25 mL) afforded (2*S*)-*N*-Boc-1-((*E*)-1-hexenylsulfonyl)pentan-2-amine (**16**) (N-Boc protected precursor of β-amino sulfone **7g**) as a white solid (95%, 1.90 g) after standard workup procedure. Mp: 82-83 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.93 (dt, *J* = 15.6, 6.6 Hz, 1H), 6.34 (d, *J* = 15.6 Hz, 1H), 4.90 (br d, *J* = 6.6 Hz, 1H), 3.98 (m, 1H), 3.19 (ABX, J_{AB} = 14.4 Hz, J_{AX} = 6.4 Hz, J_{BX} = 3.9 Hz, 2H), 2.28 (m, 2H), 1.72-1.66 (m,

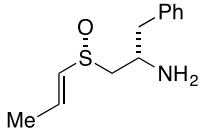
2H), 1.50-1.35 (m, 6H), 1.44 (s, 9H), 0.93 (t, J = 7.3 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 155.2, 149.7, 128.7, 79.7, 58.4, 46.9, 36.5, 31.3, 29.6, 28.3, 22.1, 19.1, 13.7, 13.6; IR (neat) cm^{-1} 3355, 3045, 3010, 2982, 2961, 2934, 2860, 1687, 1526, 1462, 1389, 1364, 1301, 1268, 1251, 1171, 1129, 1092, 1064, 976, 902, 861; $[\alpha]_D^{25}$ +17.5 (c = 0.2, $CHCl_3$); Anal. calcd for $C_{16}H_{31}NO_4S$: C, 57.63; H, 9.37; Found: C, 57.41; H, 9.25.

Deprotection Protocols of β-Amino Sulfones/Sulfoxides

General Deprotection of Boc-Protected β-Amino Sulfones and Sulfoxides to Free Amines.

To a 1:1 solution of TFA:DCM (10 mL/mmol) at 0°C was added a solution of protected β-amino sulfone or sulfoxide in DCM (1.5 mL/mmol). The reaction mixture was stirred for 1 hr at rt to reach completion. Following completion solvent was removed *in vacuo* to give an oily residue. The residue was dissolved in DCM (10 mL/mmol) and washed with a 2 M NaOH solution until a basic pH (pH ~ 8) was achieved. The aqueous layer was extracted with DCM. The organic layers were combined, washed sequentially with water, brine, then dried over MgSO4, filtered and concentrated under reduced pressure to yield the free amine.

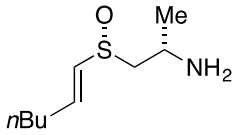
Synthesis of (S_S, 2*R*)-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-amine (5a).



A mixture of a 1:1 solution of TFA:DCM (22 mL) and (S_S, 2*R*)-*N*-Boc-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-amine (**4a**) (0.725 g, 2.24 mmol) in DCM (3 mL) provided (S_S, 2*R*)-1-phenyl-3-((*E*)-

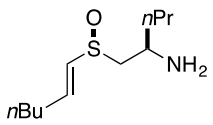
propenylsulfinyl)propan-2-amine (**5a**) as a clear colorless solid (80%, 0.399 g); Mp 41-42 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33-7.31 (m, 2H), 7.26-7.24 (m, 1H), 7.21-7.19 (m, 2H), 6.49 (dq, *J* = 15.0, 6.8 Hz, 1H), 6.19 (dq, *J* = 15.0, 1.5 Hz, 1H), 3.70 (m, 1H), 2.89 (dd, *J* = 13.5, 5.9 Hz, 1H), 2.81-2.76 (m, 2H), 2.67 (dd, *J* = 13.2, 10.0 Hz, 1H), 2.03 (br s, 2H), 1.93 (dd, *J* = 6.8, 1.6 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 137.5, 136.8, 133.2, 129.4, 128.8, 126.9, 60.4, 47.9, 44.0, 17.9; IR (neat) cm^{-1} 3364, 3286, 3038, 3060, 3004, 2914, 2852, 1633, 1601, 1494, 1453, 1440, 1396, 1353, 1091, 1030, 951, 880, 825, 800, 746, 701; $[\alpha]_D^{25}$ +24.0 (*c* = 0.8, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{12}H_{17}NOS$ $[M+H]^+$ 224.1104; found: 224.1109.

Synthesis of (*S*$_S$, 2*R*)-1-((*E*)-1-hexenylsulfinyl)propan-2-amine (5d).



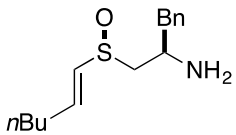
A mixture of a 1:4 solution of TFA:DCM (25 mL) and (*S*$_S$, 2*R*)-*N*-Boc-3-((*E*)-1-hexenylsulfinyl)propan-2-amine (**4d**) (0.487 g, 1.68 mmol) in DCM (3 mL) provided (*S*$_S$, 2*R*)-1-((*E*)-1-hexenylsulfinyl)propan-2-amine (**5d**) as a clear colorless oil (73%, 0.231 g); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.50 (dt, *J* = 15.1, 6.9 Hz, 1H), 6.23 (d, *J* = 15.1 Hz, 1H), 3.57 (br m, 1H), 2.68 (AB of ABX, J_{AB} = 13.0 Hz, J_{AX} = 9.7 Hz, J_{BX} = 3.1 Hz, 2H), 2.26 (m, 2H), 1.85 (br s, 2H), 1.48-1.43 (m, 2H), 1.39-1.32 (m, 2H), 1.24 (d, *J* = 6.5 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 131.9, 63.4, 42.3, 31.8, 30.2, 24.2, 22.1, 13.8; IR (neat) cm^{-1} 3408, 3296, 2958, 2930, 2871, 1677, 1459, 1378, 1201, 1173, 1129, 1018, 772; $[\alpha]_D^{25}$ +3.8 (*c* = 1.2, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_9H_{19}NOS$ $[M+H]^+$ 190.1260; found: 190.1253.

Synthesis of (R_S, 2*S*)-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (5f).



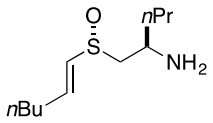
A mixture of a 1:1 solution of TFA:DCM (30 mL) and (R_S, 2*S*)-N-Boc-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (**10**) (1.19 g, 3.27 mmol) in DCM (3 mL) provided (R_S, 2*S*)-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine **5f** as a clear colorless semi-solid (91%, 0.647); ^{1}H NMR (600 MHz, CD_3OD) δ 6.53 (dt, *J* = 15.0, 7.2 Hz, 1H), 6.44 (d, *J* = 15.0 Hz, 1H), 3.35 (br m, 1H), 2.84-2.77 (m, 2H), 2.32 (m, 2H), 1.53-1.37 (m, 8H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150.6 MHz, CD_3OD) δ 143.3, 132.6, 61.4, 47.4, 40.7, 32.8, 31.5, 23.2, 20.0, 14.2, 15.0; IR (neat) cm^{-1} 3288, 2957, 2929, 2871, 1665, 1630, 1464, 1378, 1200, 1127, 1034, 970; $[\alpha]_D^{25}$ -5.0 (*c* = 0.50, $CHCl_3$); Anal. calcd for $C_{11}H_{23}NOS$: C, 60.78; H, 10.66; Found: C, 60.87; H, 10.47.

Synthesis of (R_S, 2*S*)-1-phenyl-3-((*E*)-1-hexenylsulfinyl)propan-2-amine (5g).



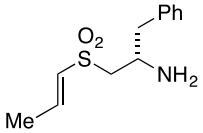
A mixture of a 1:4 solution of TFA:DCM (25 mL) and (R_S, 2*S*)-N-Boc-1-phenyl-3-((*E*)-1-hexenylsulfinyl)propan-2-amine (**4g**) (0.701 g, 1.92 mmol) in DCM (3 mL) provided (R_S, 2*S*)-1-phenyl-3-((*E*)-1-hexenylsulfinyl)propan-2-amine (**5g**) as a clear colorless oil (79%, 0.401 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.19 (m, 5H), 6.49 (dt, *J* = 15.1, 6.8 Hz, 1H), 6.15 (d, *J* = 15.1 Hz, 1H), 3.71 (br m, 1H), 2.92-2.68 (m, 4H), 2.36 (br s, 2H), 2.24 (m, 2H), 1.48-1.30 (m, 4H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 137.4, 131.6, 129.3, 128.7, 126.9, 60.2, 47.8, 43.8, 31.8, 30.2, 22.2, 13.9; IR (neat) cm^{-1} 3307, 3273, 3025, 2955, 2926, 2869, 2857, 1494, 1454, 1029, 968; $[\alpha]_D^{25}$ +7.8 (*c* = 0.8, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{15}H_{23}NOS$ $[M+H]^+$ 266.1573; found: 266.1564.

Synthesis of (S_S, 2*S*)-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (5h).



To a 0°C solution of (S_S, 2*S*)-1-((*E*)-1-hexenylsulfinyl)pentan-2-amine (**4h**) (0.075 g, 0.21 mmol) in DCM (5 mL) was added TFA (4 mL) via syringe. The ice bath was removed and the reaction mixture was stirred for 1 hr at rt. Following completion the reaction mixture was poured into a saturated solution of $NaHCO_3$. The pH was tested to ensure a basic pH (pH ~ 8) was achieved. The aqueous layer was extracted with DCM (3 × 5 mL). Organic layers were combined, washed with brine (1 × 5 mL), then dried over $MgSO_4$, filtered and concentrated under reduced pressure. (S_S, 2*S*)-1-((*E*)-1-Hexenylsulfinyl)pentan-2-amine (**5h**) was obtained as a clear colorless oil (93%, 0.042 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (dt, *J* = 15.2, 6.8 Hz, 1H), 6.29 (d, *J* = 15.2 Hz, 1H), 3.30 (m, 1H), 2.79-2.68 (m, 2H), 2.25 (m, 2H), 1.60 (br s, 2H), 1.57-1.31 (m, 9H), 0.94 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 141.4, 132.5, 61.9, 47.9, 40.2, 31.8, 30.2, 22.1, 18.9, 13.9, 13.8; IR (neat) cm^{-1} 3363, 3280, 2957, 2929, 2872, 1659, 1630, 1464, 1379, 1131, 1028, 970, 772; $[\alpha]_D^{25}$ -4.8 (*c* = 0.5, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{11}H_{23}NOS$ $[M+H]^+$ 218.1573; found: 218.1566.

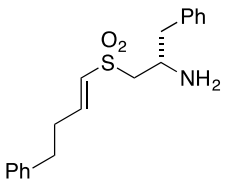
Synthesis of (2*S*)-1-phenyl-3-((*E*)-propenylsulfonyl)propan-2-amine (7a).



A mixture of a 1:1 solution of TFA:DCM (14 mL) and (2*S*)-*N*-Boc-1-phenyl-3-((*E*)-propenylsulfonyl)propan-2-amine (0.333 g, 0.982 mmol) in DCM (3 mL) provided (2*S*)-1-phenyl-3-((*E*)-propenylsulfonyl)propan-2-amine (**7a**) and its corresponding thiazane (**8a**) (~5:1) as a clear colorless oil (77%, 0.181 g); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.24 (m, 3H), 7.19-7.18 (m, 2H), 6.90 (dq,

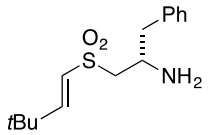
J = 15.0, 6.9 Hz, 1H), 6.32 (dq, *J* = 15.0, 1.4 Hz, 1H), 3.68 (m, 1H), 3.08 (dd, *J* = 14.2, 2.5 Hz, 1H), 2.96 (dd, *J* = 14.2, 9.5 Hz, 1H), 2.76 (m, 2H), 1.95 (dd, *J* = 6.9, 1.7 Hz, 3H), 1.74 (br s, 2H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 144.7, 137.2, 130.24, 129.4, 128.8, 127.0, 60.9, 48.0, 42.1, 16.9. See below for full characterization data of cyclized heterocycle **8a**.

Synthesis of (2*S*)-1-phenyl-3-((*E*)-4-phenyl-1-butenylsulfonyl)propan-2-amine (7b).



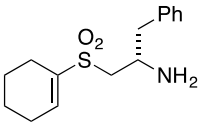
A mixture of a 1:1 solution of TFA:DCM (20 mL) and (2*S*)-*N*-Boc-1-phenyl-3-((*E*)-4-phenyl-1-butenylsulfonyl)propan-2-amine (0.636 g, 2.48 mmol) in DCM (3 mL) provided (2*S*)-1-phenyl-3-((*E*)-4-phenyl-1-butenylsulfonyl)propan-2-amine (**7b**) as a cloudy oil (74%, 0.359 g); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34-7.25 (m, 5H), 7.22-7.19 (m, 1H), 7.17-7.15 (m, 4H), 6.91 (dt, *J* = 15.2, 7.2 Hz, 1H), 6.26 (d, *J* = 15.2 Hz, 1H), 3.59 (m, 1H), 3.01 (dd, *J* = 14.2, 2.5 Hz, 1H), 2.88 (dd, *J* = 14.2, 9.5 Hz, 1H), 2.80 (m, 1H), 2.72 (m, 4H), 2.59 (m, 2H), 1.71 (br s, 2H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 147.9, 139.9, 137.2, 129.6, 129.4, 128.8, 128.7, 128.4, 127.0, 126.5, 61.0, 48.0, 43.9, 33.8, 33.2; IR (neat) cm^{-1} 3308, 3083, 3060, 3026, 3003, 2923, 2854, 1754, 1494, 1453, 1382, 1296, 1129, 1029, 879, 750, 700; $[\alpha]_D^{25}$ +6.7 (*c* = 0.9, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{19}H_{23}NO_2S$ $[M+H]^+$ 330.1522; found: 330.1507.

Synthesis of (2*S*)-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-3-phenylpropan-2-amine (7c).



A mixture of a 1:1 solution of TFA:DCM (25 mL) and (2*S*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-3-phenylpropan-2-amine (0.548 g, 1.44 mmol) in DCM (3 mL) provided (2*S*)-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-3-phenylpropan-2-amine (**7c**) as a cloudy oil (77%, 0.312 g); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.27-7.24 (m, 1H), 7.19-7.17 (m, 2H), 6.88 (d, *J* = 15.6 Hz, 1H), 6.15 (d, *J* = 15.6 Hz, 1H), 3.66 (m, 1H), 3.09 (dd, *J* = 9.0, 2.4 Hz, 1H), 2.95 (dd, *J* = 13.8, 9.0 Hz, 1H), 2.75 (m, 2H), 1.64 (br s, 2H), 1.09 (s, 9H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 158.7, 137.3, 129.3, 128.8, 127.0, 124.9, 61.0, 48.2, 43.9, 34.3, 28.4; IR (neat) cm^{-1} 3377, 3312, 3060, 3027, 2962, 2932, 2869, 1624, 1603, 1495, 1476, 1366, 1293, 1240, 1127, 1030, 877, 830, 764, 702; $[\alpha]_D^{25}$ -1.1 (*c* = 1.1, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{15}H_{23}NO_2S$ $[M+H]^+$ 282.1522; found: 282.1511.

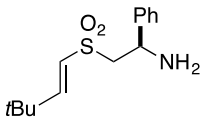
Synthesis of (2*S*)-1-(cyclohexenylsulfonyl)-3-phenylpropan-2-amine (7d).



A mixture of a 1:1 solution of TFA:DCM (15 mL) and (2*S*)-*N*-Boc-1-(cyclohexenylsulfonyl)-3-phenylpropan-2-amine (0.203 g, 0.535 mmol) in DCM (3 mL) provided (2*S*)-1-(cyclohexenylsulfonyl)-3-phenylpropan-2-amine (**7d**) as a clear colorless oil (90%, 0.134 g); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.34-7.18 (m, 5H), 6.91 (m, 1H), 3.57 (m, 1H), 3.05 (dd, *J* = 14.1, 2.2 Hz, 1H), 2.86 (dd, *J* = 14.1, 9.3 Hz, 1H), 2.74 (AB of ABX, J_{AB} = 13.4 Hz, J_{AX} = 7.2 Hz, J_{BX} = 6.9 Hz, 2H), 2.30-2.25 (m, 3H), 1.96-1.89 (m, 1H), 1.75 (br s, 2H), 1.72-1.54 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 138.2, 137.4, 129.3, 128.8, 126.9, 57.5, 48.3, 43.7, 25.5, 23.2, 21.8, 20.8; IR (neat) cm^{-1} 3376, 3310, 3060, 3026, 2933, 2860, 1643, 1495, 1452,

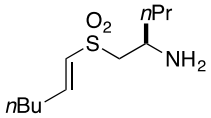
1304, 1289, 1129, 1049, 1026, 941, 856, 749, 702; $[\alpha]_D^{25}$ +7.2 (*c* = 0.8, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{15}H_{21}NO_2S$ $[M+H]^+$ 280.1366; found: 280.1357.

Synthesis of (1*R*)-2-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-1-phenylethanamine (7e).



A mixture of a 1:1 solution of TFA:DCM (15 mL) and (1*R*)-*N*-Boc-2-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-1-phenylethanamine (0.404 g, 1.10 mmol) in DCM (3 mL) provided (1*R*)-2-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-1-phenylethanamine (**7e**) as a white solid (86%, 0.252 g); Mp: 75-76 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39-7.27 (m, 5H), 6.90 (d, *J* = 15.4 Hz, 1H), 6.12 (d, *J* = 15.4 Hz, 1H), 4.64 (dd, *J* = 9.3, 3.2 Hz, 1H), 3.27 (AB of ABX, J_{AB} = 14.1 Hz, J_{AX} = 9.3 Hz, J_{BX} = 3.2 Hz, 2H), 1.92 (br s, 2H), 1.08 (s, 9H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 158.7, 143.1, 130.0, 128.1, 126.4, 125.0, 63.3, 51.2, 34.3, 28.4; IR (neat) cm^{-1} 3361, 3274, 3194, 3045, 3026, 2961, 2933, 2907, 2869, 1475, 1314, 1306, 1270, 1130, 1098, 982, 899, 830; $[\alpha]_D^{25}$ -14.1 (*c* = 1.3, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{14}H_{21}NO_2S$ $[M+H]^+$ 268.1366; found: 268.1360.

Synthesis of (2*R*)-1-((*E*)-1-hexenylsulfonyl)-2-pentanamine (7g).



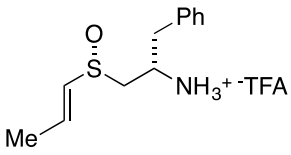
A mixture of a 1:1 solution of TFA:DCM (25 mL) and protected β-amino sulfone **16** (1.89 g, 24.9 mmol) in DCM (3 mL) provided the deprotected β-amino sulfone **7g** as a clear colorless oil (95%, 1.10 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (dt, *J* = 15.1, 6.9 Hz, 1H), 6.34 (dt, *J* = 15.1, 1.6 Hz, 1H), 3.41 (m, 1H), 2.98 (AB of ABX, J_{AB} = 14.0 Hz, J_{AX} = 9.5 Hz, J_{BX} = 2.4 Hz, 2H), 2.30 (m, 2H), 1.64 (br s, 2H), 1.52-1.32 (m, 8H), 0.94 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 149.4, 128.8, 61.9, 46.4, 39.9, 31.3, 29.7, 22.2, 18.9, 13.8, 13.7; IR (neat) cm^{-1} 3382, 3322, 3045, 2958, 2931, 2872, 1634, 1465, 1380, 1306, 1287, 1123, 977, 816; $[\alpha]_D^{25}$ -14.3 (*c* = 0.4, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{11}H_{23}NO_2S$ $[M+H]^+$ 234.1522; found: 234.1532.

General Deprotection of Boc-Protected β-Amino Sulfones and Sulfoxides to Ammonium TFA Salts.

To a 1:1 solution of TFA:DCM (10 mL/mmol) at 0°C was added a solution of protected β-amino sulfone or sulfoxide in DCM (1.5 mL/mmol). The reaction mixture was stirred for 1 hr at rt to reach completion. Solvent was removed under reduced pressure, and then 20 mL of hexanes was added to the residue and removed under reduced pressure. This process was repeated three times in order to ensure removal of trifluoroacetic acid. Excess solvent was removed *in vacuo* to yield the TFA ammonium salt. The product was purified by flash chromatography if necessary.

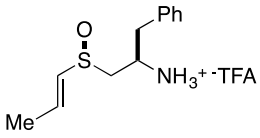
Synthesis of (*R*$_S$, 2*S*)-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-ammonium TFA salt of 5a.



A mixture of a 1:1 solution of TFA:DCM (15 mL) and (*R*$_S$, 2*S*)-*N*-Boc-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-amine (**4a**) (0.673 g, 2.08 mmol) in DCM (3 mL) provided the (*R*$_S$, 2*S*)-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-ammonium trifluoroacetate (**5a.TFA**) as a clear colorless oil (95%, 0.668 g) following flash chromatography (10

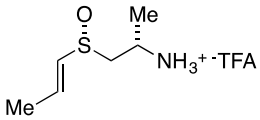
% MeOH/DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (br s, 3H), 7.34-7.16 (m, 5H), 6.51 (dq, *J* = 14.8, 6.8 Hz, 1H), 5.87 (dd, *J* = 14.8, 1.6 Hz, 1H), 4.06 (m, 1H), 3.41 (dd, *J* = 14.8, 9.6 Hz, 1H), 3.34 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.98 (dd, *J* = 13.6, 10.8 Hz, 1H), 2.53 (dd, *J* = 14.8, 1.6 Hz, 1H), 1.94 (dd, *J* = 6.8, 1.6 Hz, 3H); 13C NMR (100.6 MHz, $CDCl_3$) δ 140.5, 134.2, 129.2, 129.1, 128.6, 127.9, 49.4, 48.3, 38.6, 17.8; IR (neat) cm^{-1} 3420, 3032, 2977, 2923, 1680, 1497, 1436, 1203, 1135, 1009, 952, 837, 801, 747; $[\alpha]_D^{25}$ -56.8 (c = 2.0, $CHCl_3$). Anal. calcd for $C_{14}H_{18}F_3NO_3S$: C, 49.84; H, 5.38. Found: C, 49.83; H, 5.31.

Synthesis of (*S*$_S$, 2*R*)-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-ammonium TFA salt of 5e.



A mixture of a 1:1 solution of TFA:DCM (15 mL) and (*S*$_S$, 2*R*)-*N*-Boc-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-amine (**4e**) (0.502 g, 1.55 mmol) in DCM (3 mL) provided (*S*$_S$, 2*R*)-1-phenyl-3-((*E*)-propenylsulfinyl)propan-2-ammonium trifluoroacetate (**5e.TFA**) as a clear colorless oil (94%, 0.493 g) following flash chromatography (10 % MeOH/DCM); Spectral data identical as above for TFA salt of **5a**; $[\alpha]_D^{25}$ +55.8 (*c* = 2.0, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{12}H_{17}NOS$ $[M+H]^+$ 224.1109; found: 224.1104.

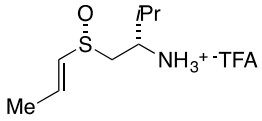
Synthesis of (*R*$_S$, 2*S*)-((*E*)-1-propenylsulfinyl)propan-2-ammonium TFA salt of 5b.



A mixture of a 1:1 solution of TFA:DCM (15 mL) and (*R*$_S$, 2*S*)-*N*-Boc-((*E*)-1-propenylsulfinyl)propan-2-amine (**4b**) (0.237 g, 0.959 mmol) in DCM (3 mL) provided (*R*$_S$, 2*S*)-((*E*)-1-propenylsulfinyl)propan-2-

ammonium trifluoroacetate (**5b.TFA**) as a clear colorless oil (52%, 0.137 g) following flash chromatography (10% MeOH/DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (br s, 3H), 6.58 (dq, *J* = 15.0, 6.8 Hz, 1H), 6.24 (app dd, *J* = 15.0, 1.6 Hz, 1H), 3.95 (m, 1H), 3.43 (dd, *J* = 14.6, 9.2 Hz, 1H), 2.69 (dd, *J* = 14.6, 2.5 Hz, 1H), 1.99 (dd, *J* = 6.8, 1.5 Hz, 3H), 1.48 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 130.0, 51.6, 44.3, 18.9, 17.9; IR (neat) cm^{-1} 3428, 2980, 2923, 2853, 2739, 1677, 1429, 1202, 1132, 1026, 1016, 955; $[\alpha]_D^{25}$ +3.3 (*c* = 0.3, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_6H_{13}NOS$ $[M+H]^+$ 148.0791; found: 148.0797.

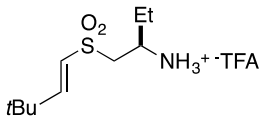
Synthesis of (*R*$_S$, 2*S*)-3-methyl-1-((*E*)-1-propenylsulfinyl)butan-2-ammmonium TFA salt of 5c.



A mixture of a 1:1 solution of TFA:DCM (15 mL) and (*R*$_S$, 2*S*)-*N*-Boc-3-methyl-1-((*E*)-1-propenylsulfinyl)butan-2-amine (**4c**) (0.431 g, 1.33 mmol) in DCM (3 mL) provided (*R*$_S$, 2*S*)-3-methyl-1-((*E*)-1-propenylsulfinyl)butan-2-ammmonium trifluoroacetate (**5c.TFA**) as a clear colorless oil (98%, 0.337 g) following flash chromatography (10% MeOH/DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (br s, 3H), 6.57 (dq, *J* =14.9, 6.6 Hz, 1H), 6.23 (d, *J* = 14.9 Hz, 1H), 3.60-3.59 (m, 1H), 3.46 (m, 1H), 2.67 (m, 1H), 2.15 (m, 1H), 1.98 (d, *J* = 6.0 Hz, 3H), 1.01 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 129.7, 52.6, 48.3, 30.9, 18.4, 17.8, 17.4; IR (neat) cm^{-1} 3436, 2973, 1677, 1634, 1524, 1428, 1400, 1202, 1180, 1026, 956; $[\alpha]_D^{25}$ +2.8 (*c* = 0.3, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_8H_{17}NOS$ $[M+H]^+$ 176.1104; found: 176.1110.

Synthesis of (2*R*)-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)butan-2-ammonium

TFA Salt of 7f



A mixture of a 1:1 solution of TFA:DCM (15 mL) and (2*R*)-*N*-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)butan-2-amine (0.220 g, 0.689 mmol) in DCM (3 mL) provided (2*R*)-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)butan-2-ammonium trifluoroacetate (**7f.TFA**) as a white solid (98%, 0.224 g) following flash chromatography (10 % MeOH/DCM); Mp: 100-101 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (br s, 3H), 7.04 (d, *J* = 15.0 Hz, 1H), 6.31 (d, *J* = 15.0 Hz, 1H), 3.80 (m, 1H), 3.58 (m, 1H), 3.35 (m, 1H), 1.94 (m, 1H), 1.83 (m, 1H), 1.13 (s, 9H), 1.05 (t, *J* = 5.9 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 162.4, 123.2, 54.3, 49.1, 34.7, 28.0, 25.9, 9.3; IR (neat) cm^{-1}: 3188, 3052, 2968, 2910, 2874, 1674, 1622, 1530, 1464, 1295, 1202, 1181, 1133, 836, 799, 772, 721; $[\alpha]_D^{25}$ -7.5 (*c* = 0.9, $CHCl_3$); Anal. calcd for $C_{12}H_{22}F_3NO_4S$: C, 43.24; H, 6.65; Found: C, 43.34; H, 6.55.

Cyclization Reaction Experiments

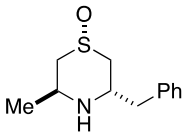
General Procedure for Cyclizations of TFA Salts (Cyclization Method A)

The TFA salt (1.0 equiv.) was dissolved in MeOH (30 mL/mmol) and stirred at rt. Triethylamine (2.0-2.5 equiv.) was added to the reaction mixture via syringe which was stirred at the indicated temperature until completion (monitored by TLC). The solvent was removed *in vacuo* to give a crude residue, which was dissolved into DCM (30 mL/mmol) and transferred to a separatory funnel. The organic layer was successively with 1 M aqueous NaOH, H_2O, and brine then dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the cyclized product.

General Procedure for Cyclizations of Free Amines (Cyclization Method B)

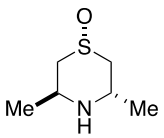
The free amine (1.0 equiv.) was dissolved in MeOH (30 mL/mmol) and stirred at rt. Triethylamine (1.0-10.0 equiv.) was added to the reaction mixture via syringe which was stirred at the indicated temperature until completion (monitored by TLC). The solvent and excess triethylamine was removed *in vacuo* to give the cyclized product.

Synthesis of (1*S*, 3*S*, 5*S*)-5-methyl-3-phenylmethylthiomorpholine-1-oxide (6a).



Using *Cyclization Method A*, a mixture of the TFA salt **5a** (0.333 g, 0.99 mmol) and triethylamine (0.34 mL, 2.5 mmol) in methanol (15 mL) refluxed for 8 h provided (1*S*, 3*S*, 5*S*)-5-methyl-3-phenylmethylthiomorpholine-1-oxide (**6a**) as a single diastereomer (93%, 0.124 g). Greyish solid. Mp: 59-60 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.32 (m, 2H), 7.27-7.25 (m, 1H), 7.21 (d, *J* = 7.2 Hz, 2H), 3.87 (m, 1H), 3.45 (m, 1H), 3.21 (dd, *J* = 13.2, 8.4 Hz, 1H), 3.06 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.98 (dd, *J* = 13.2, 2.4 Hz, 1H), 2.89-2.85 (m, 1H), 2.82 (dd, *J* = 12.8 Hz, 2.6 Hz, 1H), 2.72 (dd, *J* = 13.2, 6.6 Hz, 1H), 1.78 (br s, 1H), 1.20 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 129.2, 128.8, 126.7, 54.4, 51.6, 51.0, 41.3, 41.2, 21.0; IR (neat) cm^{-1} 3447, 3284, 3060, 3025, 2965, 2915, 1601, 1494, 1453, 1376, 1249, 1200, 1050, 1028, 913, 743, 701; $[\alpha]_D^{25}$ -18.7 (*c* = 0.95, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{12}H_{17}NOS$ $[M+H]^+$ 224.1104; found: 224.1099.

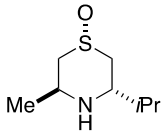
Synthesis of (1*S*, 3*S*, 5*S*)-3,5-dimethylthiomorpholine-1-oxide (6b).



Using *Cyclization Method A*, a mixture of the TFA salt **5b** (0.103 g, 0.394 mmol) and triethylamine (0.110 mL, 0.788 mmol) in methanol

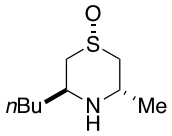
(15 mL) refluxed for 8 h provided (1*S*, 3*S*, 5*S*)-3,5-dimethylthiomorpholine-1-oxide (**6b**) as a single diastereomer (91%, 0.053 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (m, 1H), 3.35 (m, 1H), 3.17 (dt, *J* = 12.3, 2.4 Hz, 1H), 3.07 (dq, *J* = 12.3, 2.1 Hz, 1H), 2.69 (dd, *J* = 12.3, 3.6 Hz, 1H), 2.46 (dd, *J* = 12.3, 9.1 Hz, 1H), 1.65 (br s, 1H), 1.34 (d, *J* = 6.6 Hz, 3H), 1.28 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.3, 55.2, 44.6, 43.9, 22.3, 20.6; IR (neat) cm^{-1} 3398, 3279, 2972, 1650, 1134, 1005, 772; $[\alpha]_D^{25}$ +0.3 (*c* = 0.6, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_6H_{13}NOS$ $[M+H]^+$ 148.0791; found: 148.0797.

Synthesis of (1*S*, 3*S*, 5*S*)-5-methyl-3-(1-methylethyl)thiomorpholine-1-oxide (6c).



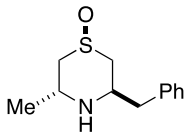
Using *Cyclization Method A*, a mixture of the TFA salt **5c** (0.095 g, 0.33 mmol) and triethylamine (0.092 mL, 0.66 mmol) in methanol (15 mL) refluxed for 7 h provided (1*S*, 3*S*, 5*S*)-5-methyl-3-(1-methylethyl)thiomorpholine-1-oxide (**6c**) as a single diastereomer (97%, 0.056 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.76 (m, 1H), 3.20-3.06 (m, 2H), 2.88-2.82 (m, 1H), 2.68 (dd, *J* = 12.3, 3.6 Hz, 1H), 2.55 (dd, *J* = 12.3, 9.6 Hz, 1H), 2.04 (app sex, *J* = 6.8 Hz, 1H), 1.54 (br s, 1H), 1.25 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.7, 53.6, 52.5, 44.8, 31.8, 20.5, 18.9, 18.8; IR (neat) cm^{-1} 3445, 3293, 2962, 2930, 2872, 1465, 1375, 1025, 772; $[\alpha]_D^{25}$ -8.3 (*c* = 4.1, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_8H_{17}NOS$ $[M+H]^+$ 176.1104; found: 176.1107.

Synthesis of (1*R*, 3*S*, 5*S*)-3-butyl-5-methylthiomorpholine-1-oxide (6d).



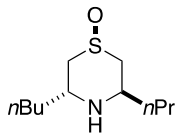
Using *Cyclization Method B*, a mixture of the amine **5d** (0.107 g, 0.57 mmol) and triethylamine (0.079 mL, 0.57 mmol) in methanol (10 mL) refluxed for 8 h provided (1*R*, 3*S*, 5*S*)-3-butyl-5-methylthiomorpholine-1-oxide (**6d**) as a single diastereomer (93%, 0.100 g). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.50 (m, 1H), 3.26 (m, 1H), 3.19-3.16 (m, 2H), 2.70 (dd, *J* = 12.2, 3.6 Hz, 1H), 2.44 (dd, *J* = 11.8, 9.7 Hz, 1H), 1.83 (br s, 1H), 1.62-1.52 (m, 2H), 1.37-1.27 (m, 7H), 0.92 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 56.8, 54.1, 50.0, 43.7, 33.0, 28.6, 22.4, 22.3, 14.0; IR (neat) cm^{-1} 3291, 2957, 2929, 2860, 1650, 1459, 1338, 1032, 1011, 772; $[\alpha]_D^{25}$ -4.7 (*c* = 0.9, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_9H_{19}NOS$ $[M+H]^+$ 190.1260; found: 190.1264.

Synthesis of (1*R*, 3*R*, 5*R*)-5-methyl-3-phenylmethylthiomorpholine-1-oxide (6e)



Using *Cyclization Method A*, a mixture of the TFA salt **5e** (0.201 g, 0.596 mmol) and triethylamine (0.17 mL, 1.2 mmol) in methanol (15 mL) refluxed for 8 h provided (1*R*, 3*R*, 5*R*)-5-methyl-3-phenylmethylthiomorpholine-1-oxide (**6e**) as a single diastereomer (93%, 0.124 g). Greyish solid. Mp 59-60 °C; Spectral data as above for **6a**; $[\alpha]_D^{25}$ +18.3 (*c* = 0.2, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{12}H_{17}NOS$ $[M+H]^+$ 224.1104; found: 224.1107.

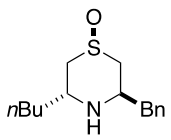
Synthesis of (1*S*, 3*R*, 5*R*)-3-butyl-5-propylthiomorpholine-1-oxide (6f).



Using *Cyclization Method B*, a mixture of the amine **5f** (0.304 g, 1.4 mmol) and triethylamine (0.975 mL, 7.0 mmol) in methanol (20 mL)

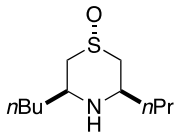
was refluxed for 8 h affording (1*S*, 3*R*, 5*R*)-3-butyl-5-propylthiomorpholine-1-oxide (**6f**) as single diastereomer (96%, 292 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.47 (m, 1H), 3.21-3.10 (m, 2H), 3.05 (m, 1H), 2.71 (dd, *J* = 12.0, 3.2 Hz, 1H), 2.46 (dd, *J* = 12.0, 9.2 Hz, 1H), 1.74-1.26 (m, 11H), 0.96-0.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 54.5, 49.4, 47.9, 37.9, 33.1, 28.5, 22.4, 19.3, 14.0, 13.9; IR (neat) cm^{-1} 3442, 3287, 2956, 2929, 2871, 1465, 1378, 1203, 1168, 1035, 771; $[\alpha]_D^{25}$ +21.0 (*c* = 0.5, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{11}H_{23}NOS$ $[M+H]^+$ 218.1573; found: 218.1568.

Synthesis of (1*R*, 3*R*, 5*R*)-5-butyl-3-phenylmethylthiomorpholine-1-oxide (6g).



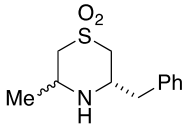
Using *Cyclization Method B*, a mixture of the amine **5g** (0.214 g, 0.81 mmol) and triethylamine (0.11 mL, 0.81 mmol) in methanol (20 mL) refluxed for 8 h provided (1*R*, 3*R*, 5*R*)-5-butyl-3-phenylmethylthiomorpholine-1-oxide (**6g**) and unreacted starting material **5g** in a 92:8 molar ratio (^{1}H NMR of crude reaction mixture). Flash chromatography with MeOH/DCM (5:95) as the eluent provided **6g** as a single diastereomer (84%, 0.180 g). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34-7.30 (m, 2H), 7.26-7.25 (m, 1H), 7.24-7.20 (m, 2H), 3.52 (m, 1H), 3.32 (m, 1H), 3.10-3.04 (m, 2H), 2.97 (app dd, *J* = 13.3, 5.7 Hz, 2H), 2.80 (dd, *J* = 12.5, 3.2 Hz, 1H), 2.66 (dd, *J* = 12.5, 8.0 Hz, 1H), 1.50 (br s, 1H), 1.49-1.41 (m, 2H), 1.26 (m, 2H), 1.10 (m, 2H), 0.84 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 129.2, 128.7, 126.8, 53.8, 53.2, 50.2, 47.3, 41.6, 33.4, 28.0, 22.3, 13.9; IR (neat) cm^{-1} 3273, 3061, 3025, 2954, 2858, 1602, 1453, 1038, 915, 770; $[\alpha]_D^{25}$ +96.2 (*c* = 0.4, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{15}H_{23}NOS$ $[M+H]^+$ 266.1573; found: 266.1586.

Synthesis of (1*R*, 3*S*, 5*R*)-3-butyl-5-propylthiomorpholine-1-oxide (6h).



Using *Cyclization Method B*, a mixture of the amine **5h** (0.040 g, 0.184 mmol) and triethylamine (0.256 mL, 1.84 mmol) in methanol (8 mL) refluxed for 42 h. ^{1}H NMR analysis of the crude reaction mixture revealed a single diastereomer of cyclized product and 20% unreacted starting material. Flash chromatography (5% MeOH/DCM) afforded (1*R*, 3*S*, 5*R*)-3-butyl-5-propylthiomorpholine-1-oxide (**6h**) as a clear colorless oil (75%; 94% based on consumed starting material, 30 mg). ^{1}H NMR (400 MHz, C_6D_6) δ 3.61-3.53 (m, 2H), 2.41 (m, 2H), 1.54 (dd, *J* = 13.2, 11.2 Hz, 2H, overlapping axial methylene ring protons), 1.18-0.98 (m, 11H), 0.82 (t, *J* = 7.2 Hz, 3H), 0.77 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 50.4, 46.0, 45.8, 38.6, 36.2, 27.4, 22.7, 18.4, 13.9, 13.8; IR (neat) cm^{-1} 3438, 3267, 2957, 2929, 2871, 1678, 1465, 1380, 1328, 1153, 1139, 1068, 1026; $[\alpha]_D^{25}$ -3.6 (*c* = 1.4, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{11}H_{23}NOS$ $[M+H]^+$ 218.1573; found: 218.1566.

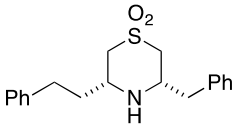
Synthesis of Thiazane 8a.



Using *Cyclization Method B*, a ~ 5:1 (uncyclized/cyclized) mixture of amine (**7a/8a**) (0.175 g, 0.73 mmol) and triethylamine (0.102 mL, 0.73 mmol) in methanol (15 mL) at 0 °C slow warming to rt over 1 h gave the cyclized product **8a** as a yellow solid (97%, 90 mg, *dr* = 91:9 by ^{1}H NMR analysis of the crude reaction mixture). Major isomer ((3*S*, 5*R*)-5-methyl-3-phenylmethylthiomorpholine-1,1-dioxide): ^{1}H NMR (600MHz, $CDCl_3$) δ 7.28-7.26 (m, 2H), 7.22-7.19 (m, 1H), 7.15-7.10 (m, 2H), 3.36 (m, 1H), 3.18 (m, 1H), 2.91-2.84

(m, 2H), 2.72-2.66 (m, 2H), 2.63 (dd, *J* = 13.4, 11.6 Hz, 1H), 2.60 (dd, *J* = 13.1, 11.4 Hz, 1H); 1.74 (br s, 1H), 1.08 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2, 129.2, 129.0, 127.3, 58.3, 56.4, 55.4, 49.9, 42.1, 21.6; IR (neat) cm^{-1} 3320, 3083, 3061, 3027, 2971, 2925, 2852, 1495, 1455, 1298, 1257, 1124, 755, 701; $[\alpha]_D^{25}$ -2.9 (*c* = 2.3, $CHCl_3$, for 91:9 mixture); HRMS (TOF, ESI) calcd for $C_{12}H_{17}NO_2S$ $[M+H]^+$ 240.1053; found: 240.1044. Minor isomer, partial characterization: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.68-3.60 (m, 2H), 3.03-2.98 (m, 4H), 1.18 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 137.0, 129.3, 128.9, 126.9, 57.8, 54.2, 52.8, 45.6, 38.6, 20.4.

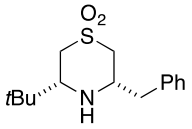
Synthesis of Thiazane 8b.



Using *Cyclization Method B*, a mixture of the amine **7b** (0.096 g, 0.29 mmol) and triethylamine (0.04 mL, 0.29 mmol) in methanol (15 mL) refluxed for ~7 h to give the cyclized product **8b** as a pale pink solid (94%, 90 mg, *dr* = 91:9 by ^{1}H NMR analysis of the crude reaction mixture. Recrystallization from EtOAc/hexanes gave the major *cis*-isomer as a white solid. Major isomer ((3*S*, 5*R*)-5-(2-phenylethyl)-3-phenylmethylthiomorpholine-1,1-dioxide): Mp 104-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.17 (m, 8H), 6.93-6.90 (m, 2H), 3.33 (m, 1H), 3.06-2.92 (m, 3H), 2.80 (dd, *J* = 13.4, 5.2 Hz, 1H), 2.72 (app t, *J* = 15.7 Hz, 1H), 2.70 (app t, *J* = 11.5 Hz, 2H), 2.54 (m, 2H), 1.74 (q, *J* = 6.8 Hz, 2H), 1.61 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 136.4, 129.3, 129.0, 128.7, 128.2, 127.4, 126.4, 57.2, 57.0, 55.3, 53.3, 42.0, 37.0, 31.6; IR (neat) cm^{-1} 3542, 3306, 3061, 3026, 2922, 2853, 1602, 1494, 1454, 1297, 1129, 1071; $[\alpha]_D^{25}$ +12.7 (*c* = 2.8, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{19}H_{23}NO_2S$ $[M+H]^+$ 330.1522; found: 330.1534. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03-7.02 (m, 2H), 1.26 (br s, 1H); ^{13}C

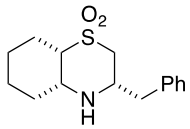
NMR (100 MHz, $CDCl_3$) δ 140.5, 137.3, 129.2, 128.9, 128.5, 128.3, 127.1, 126.2, 56.1, 55.9, 55.2, 53.2, 42.5, 39.7, 32.1.

Synthesis of Thiazane 8c.



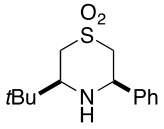
Using *Cyclization Method B*, a mixture of the amine **7c** (0.246 g, 0.878 mmol) and triethylamine (0.488 mL, 3.50 mmol) in methanol (15 mL) refluxed for 8 h to give the cyclized product **8c** as a pale pink solid (99%, 0.244 g, *dr* = 92:8 by ^{1}H NMR analysis of the crude reaction mixture). Recrystallization from EtOAc/hexanes provided the major cis diastereomer (76%, 0.187 g). Major *cis*-isomer ((3*R*, 5*S*)-3-(2,2-dimethylethyl)-5-phenylmethylthiomorpholine-1,1-dioxide): Mp 133-134 °C; ^{1}H NMR (600 MHz, C_6D_6) δ 7.07-7.05 (m, 2H), 7.02-7.00 (m, 1H), 6.84 (d, *J* = 7.2 Hz, 2H), 3.19 (m, 1H), 2.72 (m, 1H), 2.64-2.60 (m, 2H), 2.32 (dd, *J* = 13.2, 12.0 Hz, 1H), 2.24 (dd, *J* = 13.2, 11.4 Hz, 1H), 2.17 (AB of ABX, J_{AB} = 13.8 Hz, J_{AX} = 9.1 Hz, J_{BX} = 4.8 Hz, 2H), 1.11 (br s, 1H), 0.45 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.4, 129.3, 129.0, 127.2, 63.0, 57.3, 55.1, 53.7, 41.9, 33.4, 25.8; IR (neat) cm^{-1} 3355, 3312, 3084, 3062, 3025, 2961, 2904, 2868, 2842, 1493, 1477, 1454, 1291, 1263, 1125, 893, 775, 747, 701; $[\alpha]_D^{25}$ -13.6 (*c* = 1.2, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{15}H_{23}NO_2S$ $[M+H]^+$ 282.1522; found: 282.1530. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (m, 1H), 3.22-3.17 (m, 3H), 3.01-3.05 (m, 2H), 0.87 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 138.6, 129.5, 128.7, 126.7, 56.9, 54.1, 54.0, 52.6, 36.7, 33.7, 26.3.

Synthesis of Thiazane 8d.



Using *Cyclization Method B*, a mixture of the amine **7d** (0.119 g, 0.43 mmol) and triethylamine (0.06 mL, 0.43 mmol) in methanol (15 mL) refluxed for 7 h. ^{1}H NMR analysis of the crude reaction mixture revealed a single diastereomer of cyclized product (2*S*, 3*R*, 5*S*)-2,3-tetramethylene-5-phenylmethylthiomorpholine-1,1-dioxide (**8d**) and 5% unreacted starting material. Flash chromatography (50% EtOAc/hexanes) afforded heterocycle as a white solid (79%, 94 mg). Mp 149-150 °C; ^{1}H NMR (600 MHz, C_6D_6) δ 7.13-7.10 (m, 2H), 7.07-7.05 (m, 1H), 6.93 (d, *J* = 7.2 Hz, 2H), 3.30 (m, 1H), 3.28 (m, 1H), 2.54 (m, 1H), 2.48 (dd, *J* = 13.8, 11.4 Hz, 1H), 2.40 (ddd, *J* = 13.2, 3.6, 2.4 Hz, 1H), 2.27 (AB of ABX, J_{AB} = 13.8 Hz, J_{AX} = 7.8 Hz, J_{BX} = 6.0 Hz, 2H), 1.94 (m, 1H), 1.71 (m, 1H), 1.48 (m, 1H), 1.32 (m, 1H), 1.05 (m, 1H), 0.95 (m, 1H), 0.89 (m, 1H), 0.82-0.74 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.4, 129.5, 129.0, 127.1, 61.6, 55.6, 52.7, 52.2, 42.1, 32.2, 25.4, 22.1, 19.4; IR (neat) cm^{-1} 3330, 3082, 3063, 3029, 2987, 2969, 2936, 2892, 2854, 1446, 1290, 1255, 1221, 1114, 1104, 1067,1011, 766, 748; $[\alpha]_D^{25}$ -38.4 (*c* = 1.0, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{15}H_{21}NO_2S$ $[M+H]^+$ 280.1366; found: 280.1360.

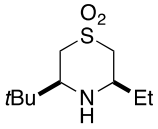
Synthesis of Thiazane 8e.



Using *Cyclization Method B*, a mixture of the amine **7e** (0.095 g, 0.36 mmol) and triethylamine (0.05 mL, 0.36 mmol) in methanol (15 mL) refluxed for 10 h. ^{1}H NMR analysis of the crude reaction mixture revealed a single diastereomer of cyclized product (3*R*, 5*S*)-5-(2,2-dimethylethyl)-3-phenylthiomorpholine-1,1-dioxide (**8e**) and 5% unreacted starting material. Flash chromatography with EtOAc/hexanes/TEA (30:65:5) afforded **8e** as a white solid (79%, 75 mg). Mp 125-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.33 (m, 5H), 4.24

(dd, *J* = 11.2, 1.6 Hz, 1H), 3.09 (app br d, *J* = 12.8 Hz, 2H), 3.03-2.95 (m, 2H), 2.83 (app t, *J* = 12.0 Hz, 1H), 1.85 (br s, 1H), 0.99 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 129.1, 128.6, 126.7, 63.3, 58.8, 58.4, 53.1, 33.8, 26.3; IR (neat) cm^{-1} 3316, 3062, 3031, 2959, 2903, 2871, 2838, 1704, 1494, 1299, 1130, 878, 769, 751, 699; $[\alpha]_D^{25}$ -51.0 (*c* = 4.1, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{14}H_{21}NO_2S$ $[M+H]^+$ 268.1366; found: 268.1360.

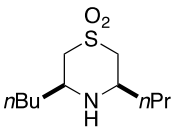
Synthesis of Thiazane 8f.



Using *Cyclization Method A*, a mixture of the TFA salt **7f** (0.164 g, 0.49 mmol) and triethylamine (0.14 mL, 0.98 mmol) in methanol (15 mL) refluxed for 8 h provided **8f** as a pale yellow solid (70%, 75 mg, *dr* = 91:9 by ^{1}H NMR analysis). Diastereomers were separated by flash chromatography (50% EtOAc/hexanes) as the eluent (68 mg of *cis*-isomer; 7 mg of *trans*-isomer). *cis*-Isomer [(3*S*, 5*R*)-5-ethyl-3-(2,2-dimethylethyl)thiomorpholine-1,1-dioxide]: Mp: 76-77 °C; ^{1}H NMR (400 MHz, C_6D_6), δ: 2.84-2.77 (m, 2H), 2.73 (dd, *J* = 11.6, 1.6 Hz, 1H), 2.61 (dt, *J* = 13.2, 2.4 Hz, 1H), 2.30 (dd, *J* = 12.9, 11.9 Hz, 1H), 2.07 (dd, *J* = 12.8, 11.6 Hz, 1H), 0.97 (m, 2H), 0.59-0.53 (m, 4H), 0.58 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6), δ: 62.8, 56.6, 55.5, 53.4, 33.2, 28.6, 25.7, 9.7; IR (neat) cm^{-1} 3313, 2961, 2875, 1465, 1368, 1294, 1242, 1151, 1130, 874, 772; $[\alpha]_D^{25}$ +7.64 (*c* = 1.4, $CHCl_3$); Anal. calcd for $C_{10}H_{21}NO_2S$: C, 54.76; H, 9.65; Found: C, 55.12; H, 9.57. Minor isomer, partial characterization: Mp 84-85 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.39 (br m, 1), 3.12 (m, 1H), 3.02 (m, 3H), 2.73 (m, 1H), 2.04 (m, 1H), 1.71 (m, 1H), 1.49 (br s, 1H), 0.97 (s,

9H), 0.94 (t, *J* = 7.8 Hz, 3H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 56.6, 54.2, 53.9, 33.8, 29.7, 26.2, 23.3, 11.4; IR (neat) cm^{-1} 3399, 2964, 2938, 2869, 1295, 1219, 1130, 798.

Synthesis of Thiazane 8g.

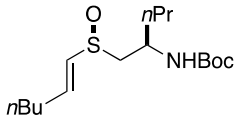


Using *Cyclization Method B*, a mixture of the amine **7g** (0.854 g, 3.7 mmol) and triethylamine (0.51 mL, 3.7 mmol) in methanol (15 mL) was stirred for 1 h at 40 °C to give the cyclized product **8g** as a white (99%, 852 mg, *dr* = 92:8 by ^{1}H NMR analysis of the mixture). Flash chromatography (30% EtOAc/hexanes) on 1.16 g of the diastereomeric mixture (*dr* = 92:8) from multiple combined different reactions provided the pure major diastereomer (82%, 0.966 g) ((3*S*, 5*R*)-3-butyl-5-propylthiomorpholine-1,1-dioxide). Mp: 34-35 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.19-3.12 (m, 2H), 2.97 (app d, *J* = 13.4 Hz, 2H), 2.63 (app t, *J* = 12.3 Hz, 2H), 1.53-1.34 (m, 11H), 0.97-0.91 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 57.1 (overlapping SO_2-$\underline{CH_2}$'s), 54.4, 54.1, 37.9, 35.5, 27.6, 22.4, 18.7, 13.9 (overlapping terminal $\underline{CH_3}$'s); IR (neat) cm^{-1} 3305, 2958, 2931, 2872, 1466, 1380, 1300, 1236, 1128, 1082, 992, 957, 904, 870, 770; $[\alpha]_D^{25}$ + 1.33 (*c* = 0.75, $CHCl_3$); Anal. calcd for $C_{11}H_{23}NO_2S$: C, 56.61; H, 9.93; Found: C, 56.38; H, 9.87. Minor isomer, partial characterization: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.42 (m, 1H), 3.07 (m, 1H), 2.86-2.82 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 56.3, 56.2, 50.5, 50.2, 35.2, 32.8, 28.4, 22.4, 19.4, 14.0, 13.8.

Synthesis of Venom Alkaloids 15 & 20

The syntheses of butyl thiirane *S*-oxide[7] and chiral iodide **9**[8] have been reported previously. Spectral data for these compounds was in good agreement with literature reports.

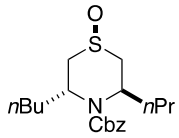
Synthesis of Boc-Protected Sulfoxide 10



Under anhydrous conditions under an inert N_2(g) atmosphere a solution of LiHMDS (1.0 M in THF, 3.81 mL, 3.81 mmol) in Et_2O (35 mL) at -78 °C was added dropwise a solution of the *n*-butyl thiirane *S*-oxide **8** (0.458 g, 3.47 mmol) in Et_2O/THF (5:2 mL) at -78 °C. The mixture was allowed to stir for ca. 15 min, at which time a precooled (-78 °C) solution of the amino iodide **9** (1.30 g, 4.15 mmol) in THF (4 mL) was added dropwise via syringe. After 1 h of stirring at -78 °C the reaction vessel was removed from the cold bath and allowed to warm to rt stirring for ~8 h. Following completion the solvent was removed under reduced pressure, and the residue was dissolved in EtOAc. The organic layer was washed with sat'd ammonium chloride solution, water, and brine and then dried over $MgSO_4$. The organic layer was then filtered, and solvent was removed under reduced pressure. The crude reaction mixture was subjected to flash chromatography (40% EtOAc/hexanes), which yielded the β-amino sulfoxide as a mixture of diastereomers (74%, 0.931 g, *dr* = 91:9 from ^{1}H NMR analysis of reaction mixture). Flash chromatography (5% to 40% EtOAc/hexanes) provided the pure major diastereomer **10** as a white solid (65%, 0.827 g). Mp: 73-74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.49 (dt, *J* = 15.2, 6.8 Hz, 1H), 6.25 (d, *J* = 15.2 Hz, 1H), 5.27 (br d, *J* =

7.9 Hz, 1H), 4.01 (sex, *J* = 5.9 Hz, 1H), 2.96-2.82 (m, 2H), 2.24 (m, 2H), 1.78-1.62 (m, 2H), 1.51-1.29 (m, 6H), 1.43 (s, 9H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 141.7, 132.2, 79.4, 58.4, 47.6, 36.4, 31.8, 30.2, 28.4, 22.1, 19.4, 13.8 (CH_3's overlapping); IR (neat) cm^{-1} 3226, 3038, 3003, 2960, 2930, 2873, 1702, 1541, 1454, 1363, 1270, 1253, 1175, 1041, 1025, 971, 742, 704; $[\alpha]_D^{25}$ -29.8 (*c* = 1.3, $CHCl_3$); Anal. calcd for $C_{16}H_{31}NO_3S$: C, 60.53; H, 9.84; Found: C, 60.74; H, 9.90.

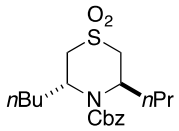
Synthesis of Cbz-Protected Heterocycle 11



Compound **5f** was prepared from **10** as on page S15 above and from it, thiazine **6f** was prepared as per Table 1**.** To a solution of Na_2CO_3 (4.00 g, 37.8 mmol) in H_2O/DCM (12 mL: 15 mL) at rt was added a solution of unprotected amine **6f** (0.547 g, 2.52 mmol, prepared from **5f**, as per Table 1) in DCM (3 mL). Next, the reaction mixture was cooled to 0 °C and benzyl chloroformate (1.21 mL, 12.6 mmol) was added via syringe. Reaction completion was reached after 2 h of stirring at rt. The reaction mixture was extracted with DCM (3 × 10 mL) then the organic layers were combined and washed sequentially with a saturated solution of NH_4Cl, H_2O, and brine. The organic phase was dried over $MgSO_4$, filtered and solvent was removed *in vacuo* to give the crude sulfoxide. The sulfoxide was purified via column chromatography eluting first with EtOAc/hexanes (50%), followed by elution with EtOAc/MeOH (50%) to give the pure Cbz-protected sulfoxide **11** as a white solid (0.638 g, 72%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.14 (m, 2H), 4.43 (m, 1H), 4.10 (m, 1H), 3.12 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.85-2.76 (m, 3H), 2.28 (m, 1H), 1.97 (m, 1H), 1.82 (m, 1H), 1.55-1.48 (m, 1H), 1.37-1.31

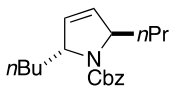
(m, 6H), 0.93-0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$), mixture of rotamers δ 156.1, 136.2, 128.6, 128.3, 128.2, 67.5, 52.1, 51.8, 50.6, 50.5, 49.1, 49.0, 47.6, 47.4, 35.5, 35.3, 33.1, 33.0, 29.0, 28.6, 22.3, 22.2, 20.1, 19.7, 14.0, 13.9, 13.7, 13.6; IR (neat) cm^{-1} 3063, 3032, 2957, 2930, 2871, 1700, 1455, 1406, 1316, 1285, 1233, 1218, 1087, 1039, 770; $[\alpha]_D^{25}$ +13.4 (*c* = 0.8, $CHCl_3$); Anal. calcd for $C_{19}H_{29}NO_3S$: C, 64.92; H, 8.32; Found: C, 64.64; H, 8.22.

Synthesis of Heterocyclic Sulfone 12



Using the general method for oxidizing β-amino sulfoxides to β-amino sulfones. A mixture of sulfoxide **11** (0.547 g, 1.55 mmol) in DCM (30 mL) and MCPBA (ca ~83%, 0.612 g, ca ~ 2.95 mmol) in DCM (25 mL) afforded (3*R*, 5*R*)-3-butyl-5-propylthiomorpholine-1,1-dioxide (**12**) as a clear colorless oil (90%, 0.511 g) after standard workup procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39-7.33 (m, 5H), 5.14 (m, 2H), 4.22 (br m, 2H), 3.12-3.03 (m, 4H), 2.15-2.09 (m, 2H), 1.72-1.64 (m, 2H), 1.39-1.24 (m, 6H), 0.93-0.88 (m, 6H); ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 155.8, 135.8, 128.7, 128.5, 128.3, 67.9, 55.1, 52.0, 51.8, 33.8, 31.5, 29.7, 28.6, 22.2, 19.7, 13.9, 13.6; IR (neat) cm^{-1} 3065, 3023, 2958, 2932, 2872, 1703, 1456, 1430, 1379, 1237, 1129, 1088, 998, 770, 752, 698; $[\alpha]_D^{25}$ +13.1 (*c* = 0.6, $CHCl_3$); Anal. calcd for $C_{19}H_{29}NO_4S$: C, 62.10; H, 7.95; Found: C, 62.30; H, 7.86.

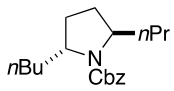
Synthesis of Pyrroline 13



Sulfone **12** (472 mg, 1.29 mmol) was dissolved in THF:*t*BuOH (5 mL/15 mL) and stirred at rt. KOH-Al_2O_3 (24.5 mmol, 3.09 g) was added to the reaction mixture followed by a solution of 1,2-

dibromotetrachloroethane (0.755 g, 2.32 mmol) in THF (2 mL) was added slowly via syringe. The reaction mixture was stirred for 45 min at 70 °C to reach completion. The reaction mixture was flushed through a silica plug with EtOAc to remove inorganic components. Fractions were combined and concentrated. Purification by flash chromatography (5% EtOAc/hexanes) gave the pure (2*R*, 5*R*)-N-Cbz-2-butyl-5-propyl-3-pyrroline (**13**) as a clear colorless oil (50%, 0.195). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 5.67 (m, 2H), 5.23 (dd, *J* = 12.3, 2.4 Hz, 1H), 5.07 (dd, *J* = 12.4, 6.7 Hz, 1H), 4.55 (m, 2H), 1.95-1.60 (m, 4H), 1.32-1.03 (m, 6H), 0.92-0.85 (m, 3H), 0.81-0.77 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$), mixture of rotamers δ 154.1, 137.0, 136.9, 129.2, 129.1, 128.4, 128.1, 128.0, 127.9, 66.5, 66.4, 64.6, 35.7, 34.1, 33.1, 31.5, 26.3, 25.8, 22.8, 22.7, 17.5, 17.0, 14.2, 14.1, 14.0; IR (neat) cm^{-1} 3089, 3065, 3033, 2958, 2932, 2872, 1717, 1525, 1498, 1455, 1393, 1351, 1304, 1239, 1103, 1054, 1028, 984, 773; $[\alpha]_D^{25}$ -25.7 (*c* = 0.9, $CHCl_3$); Anal. calcd for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03; Found: C, 75.88; H, 8.79.

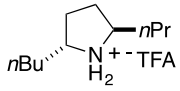
Synthesis of Pyrrolidine 14



To a suspension of Pt/C (10% by wt., 15 mg) in MeOH (10 mL) under H_2 (g)(1 atm) a solution of pyrroline **13** (0.111 g, 0.368 mmol) in MeOH (1 mL) was added. Reaction completion was reached after stirring for 15 min at rt. The reaction mixture was filtered through Celite® column, which was washed with EtOAc. The solvent was removed *in vacuo* to yield a diastereomeric mixture of pyrrolidine **14** [96%, 0.107 g, *dr* = 93:7 by ^{1}H NMR integration; major isomer: (2*R*, 5*R*)-N-Cbz-2-butyl-5-propylpyrrolidine]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31-7.19 (m,

5H), 5.14-4.97 (m, 2H), 3.72-3.67 (m, 2H), 1.88-1.77 (m, 3H), 1.62-1.51 (m, 3H), 1.28-1.12 (m, 8H), 0.87-0.74 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$)(mixture of rotamers) δ 154.3, 137.2, 128.4, 127.9, 127.8, 127.7, 66.4, 66.3, 58.2, 58.0, 57.7, 57.5, 36.2, 34.9, 33.7, 32.3, 28.9, 28.8, 27.6, 26.7, 22.7, 22.6, 19.9, 19.8, 14.2, 14.1, 14.0, 13.9; IR (neat) cm^{-1} 3023, 2957, 2931, 2872, 2862, 1695, 1405, 1206, 1135, 790; $[\alpha]_D^{25}$ -14.8 (*c* = 0.3, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{19}H_{29}NO_2$ $[M+H]^+$ 304.2271; found: 304.2264.

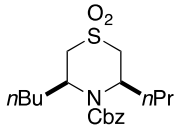
Synthesis of TFA Salt 15



To a suspension of Pd/C (10% by wt., 20 mg) in MeOH (10 mL) under H_2 (g) (1 atm) a solution of pyrrolidine **14** (0.094 g, 0.31 mmol) in MeOH (1 mL) was added. Reaction completion was reached after stirring for 15 min at rt. The reaction mixture was filtered through Celite® column, which was washed with EtOAc. The solvent was removed *in vacuo* to give crude pyrrolidine as a clear oily residue. The residue was immediately dissolved in DCM (10 mL) and chilled to 0 °C. Trifluoroacetic acid (5 mL) was added via syringe and the mixture was stirred for 1 h at rt. Solvent was removed *in vacuo* and then 20 mL of hexanes was added and evaporated three times to ensure removal of excess TFA which provided TFA salt **15** as a diastereomeric mixture (84%, 0.074 g, *dr* = 93:7). Major trans diastereomer ((2*R*, 5*R*)-2-butyl-5-propylpyrrolidine): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (br s, 2H), 3.54 (m, 2H), 2.18 (m, 2H), 1.81-1.55 (m, 6H), 1.43-1.30 (m, 6H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 59.6, 59.4, 34.6, 32.2, 30.8 (CH_2's overlapping), 28.5, 22.3, 19.9, 13.7, 13.6. NMR spectra are in good agreement with literature values.[9] $[\alpha]_D^{25}$ -2.7 (*c* = 0.5, $CHCl_3$,

for 93:7 diastereomeric mixture). To get a comparative optical rotation the TFA salt was converted to the free amine. TFA salt **15** (0.074 g, 0.261 mmol) was dissolved in 5 mL DCM and washed with an aqueous solution of 2M NaOH (4 mL). The organic layer was washed with brine (1 mL) dried over $MgSO_4$, filtered, and then concentrated by blowing N_2(g) over the solution to give the corresponding free amine of **15** in an improved diastereomeric ratio (70%, 31 mg, *dr* = 95:5 (trans/cis) by ^{1}H NMR analysis. Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.51 (m, 2H), 2.14-2.11 (m, 2H), 1.87-1.82 (m, 2H), 1.63-1.50 (m, 4H), 1.48-1.25 (m, 7H), 0.96-0.84 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.5, 58.4, 37.6, 35.2, 31.7 ($\underline{C}H_2$'s overlapping), 29.2, 22.7, 20.3, 14.1, 14.0; GC–MS: m/z 170 $[M+H]^+$ (100), 168 (8), 126 (9), 111 (10); $[\alpha]_D^{25}$ -2.0 (*c* = 1.6, $CHCl_3$); lit. value for 94% ee of enantiomer $[\alpha]_D^{25}$ + 2.0 (*c* = 0.5, $CHCl_3$).[9] (See page S43 for ^{13}C NMR comparison to literature data)

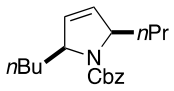
Synthesis of Cbz-protected Heterocycle 17



Sulfone **16** was prepared from **10** as describe on page S12 above. Sulfone **16** is deprotected to the free amine **7g** as described on p S19 above. To a solution of Na_2CO_3 (2.13 g, 20.1 mmol) in H_2O/DCM (12 mL: 15 mL) at rt was added a solution of unprotected amine **8g** (0.312 g, 1.34 mmol, obtained by cyclization of **7g** as per Table 2) in DCM (3 mL). Next, the reaction mixture was cooled to 0 °C and benzyl chloroformate (0.941 mL, 6.69 mmol) was added via syringe. Reaction completion was reached after 48 h of stirring at rt. The reaction mixture was extracted with DCM (3 × 10 mL) then the organic layers were combined and washed sequentially with a saturated solution of NH_4Cl, H_2O, and brine. The organic phase was dried over $MgSO_4$, filtered and solvent was removed *in*

vacuo to give the crude sulfone. The sulfone was purified via column chromatography eluting first with EtOAc/Hexanes (50%), followed by elution with EtOAc/MeOH (50%) to give the pure Cbz-protected sulfone **17** as a white solid (53%, 0.262 g); Mp: 85-86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 5H), 5.15 (s, 2H), 4.85 (br m, 2H), 3.21-3.05 (m, 4H), 2.03-1.84 (m, 4H), 1.39-1.25 (m, 6H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 6.8 Hz, 3H) ^{13}C NMR (150.6 MHz, $CDCl_3$) δ 155.6, 135.8, 128.6, 128.4, 128.2, 68.3, 53.1, 52.9, 51.6 (overlapping $\underline{CH_2}$'s), 35.4, 33.0, 29.2, 22.3, 20.3, 13.9, 13.6; IR (neat) cm^{-1} 3065, 3033, 2958, 2932, 2871, 1693, 1456, 1413, 1386, 1319, 1218, 1114, 1088, 1002, 771; $[\alpha]_D^{25}$ +2.67 (*c* = 0.5, $CHCl_3$); Anal. calcd for $C_{19}H_{29}NO_4S$: C, 62.10; H, 7.95; Found: C, 62.14; H, 8.17.

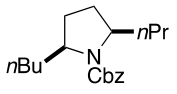
Synthesis of Pyrroline 18



Sulfone **17** (461 mg, 1.26 mmol) was dissolved in THF:*t*BuOH (5 mL/15 mL) and stirred at rt. KOH-Al_2O_3 (23.8 mmol, 3.01 g) was added to the reaction mixture followed by a solution of 1,2-dibromotetrachloroethane (0.766 g, 2.35 mmol) in THF (2 mL) was added slowly via syringe. The reaction mixture was stirred for 3.5 h at rt. The reaction mixture was flushed through a silica plug with EtOAc to remove inorganic components. Fractions were combined and concentrated. Purification by flash chromatography (5% EtOAc/hexanes) gave the pure (2*S*, 5*R*)-N-Cbz-2-butyl-5-propyl-3-pyrroline (**18**) as a clear colorless oil (65%, 0.246 g). ^{1}H NMR (600 MHz, $CDCl_3$), mixture of rotamers δ 7.37-7.29 (m, 5H), 5.76 (m, 2H), 5.19-5.14 (m, 2H), 4.53-4.48 (m, 2H), 1.95-1.75 (m, 2H), 1.44-1.29 (m, 8H), 0.95-0.85 (m, 6H); ^{13}C NMR (150.6 MHz, $CDCl_3$), mixture of rotamers δ 155.1, 137.1, 129.4, 129.3, 129.2, 129.1, 128.4, 127.8, 127.7, 66.5, 65.7,

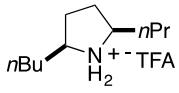
64.9, 64.7, 38.1, 37.6, 35.6, 35.1, 27.8, 27.7, 22.8, 22.7, 19.0, 18.8, 14.2, 14.1, 14.0; IR (neat) cm^{-1} 3067, 3033, 2957, 2931, 2871, 1703, 1455, 1406, 1357, 1312, 1212, 1184, 1094, 1029, 990, 793, 732, 697; $[\alpha]_D^{25}$ 5.3 (*c* = 0.6, $CHCl_3$); Anal. calcd for $C_{19}H_{27}NO_2$: C, 75.71 ; H, 9.03; Found: C, 75.56; H, 8.97.

Synthesis of Pyrrolidine 19



To a suspension of Pt/C (10% by wt., 25 mg) in MeOH (10 mL) under H_2 (g) (1 atm) a solution of pyrroline **18** (0.130 g, 0.431 mmol) in MeOH (1 mL) was added. Reaction completion was reached after stirring for 15 min at rt. The reaction mixture was filtered through Celite® column, which was washed with EtOAc. The solvent was removed *in vacuo* to yield a diastereomerically pure (2*S*, 5*R*)-N-Cbz-2-butyl-5-propylpyrrolidine (**19**) (94%, 0.122 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H), 5.12 (m, 2H), 3.88 (m, 2H), 1.90-1.61 (m, 6H), 1.28-126 (m, 8H), 0.88 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$), mixture of rotamers δ 155.4, 137.2, 128.4, 127.7 (overlapping C-H carbons), 66.4, 59.0, 58.9, 58.3, 58.2, 38.2, 37.9, 35.7, 35.3, 29.7, 29.3, 28.6, 22.7, 19.6, 14.2, 14.1; IR (neat) cm^{-1} 3065, 3033, 2957, 2931, 2872, 1698, 1464, 1456, 1405, 1354, 1317, 1251, 1207, 1131, 1099, 770, 732, 696; $[\alpha]_D^{25}$ +8.3 (*c* = 0.4, $CHCl_3$); HRMS (TOF, ESI) calcd for $C_{19}H_{29}NO_2$ $[M+H]^+$ 304.2271; found: 304.2261.

Synthesis of TFA Salt 20



To a suspension of Pd/C (10% by wt., 15 mg) in MeOH (10 mL) under H_2 (g)(1 atm) a solution of pyrrolidine **19** (0.093 g, 0.31 mmol) in MeOH (1 mL) was added. Reaction completion was reached after stirring for 15 min

at rt. The reaction mixture was filtered through Celite® column, which was washed with EtOAc. The solvent was removed *in vacuo* to give crude pyrrolidine as a clear oily residue. The residue was immediately dissolved in DCM (10 mL) and chilled to 0 °C. Trifluoroacetic acid (5 mL) was added via syringe and the mixture was stirred for 1 h at rt. Solvent was removed *in vacuo* and then 20 mL of hexanes was added and evaporated three times to ensure removal of excess TFA which provided TFA salt **20** as a the pure cis diastereomer [(2*S*, 5*R*)-2-butyl-5-propylpyrrolidine] (95%, 0.083 g). Mp 33-34 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.13 (br s, 1H), 8.62 (br s 1H), 3.46 (m, 2H), 2.20-2.11 (m, 2H), 1.87-1.74 (m, 4H), 1.69-1.58 (m, 2H), 1.44-1.30 (m, 6H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 60.3, 60.0, 34.3, 31.8, 28.8, 28.7, 28.6, 22.2, 21.9, 13.7, 13.6; The ^{1}H NMR and ^{13}C NMR spectra were in good agreement with literature data.[9] $[\alpha]_D^{25}$ 0.0 (*c* = 1.6, $CHCl_3$). To get a comparative optical rotation the TFA salt was converted to the free amine. TFA salt **20** (0.074 g, 0.261 mmol) was dissolved in 5 mL DCM and washed with an aqueous solution of 2M NaOH (4 mL). The organic layer was washed with brine (1 mL) dried over $MgSO_4$, filtered, and then concentrated by blowing N_2(g) over the solution to give the corresponding free amine of **20** (79%, 15 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.95 (m, 2H), 1.87-1.78 (m, 2H), 1.55-1.22 (m, 14H), 0.93-0.85 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 59.4, 59.1, 39.0, 36.5, 31.3 ($\underline{C}H_2$'s overlapping), 29.7, 22.9, 20.7, 14.3, 14.1; The NMR spectra are in good agreement with literature data (See page S43).[9]; GC–MS: m/z 170 [M+H] (50), 126 (81), 112 (100), 95 (12), 67 (19), 56 (17); $[\alpha]_D^{25}$ 0.0 (*c* = 0.75, $CHCl_3$) lit. value: $[\alpha]_D^{25}$ 0.0 (*c* = 0.6, $CHCl_3$).[9]

Comparison of ^{13}C chemical shits of venom alkaloids with published data

The following tables are presented for corroboration of the assigned stereochemistries of compounds **15** and **20** to literature data. [9]

It is well recognized that over time and with exposure to light $CDCl_3$ can decompose to make acidic by-products such as HCl. This is known to have an effect on NMR chemical shifts values for nitrogen containing compounds dissolved in $CDCl_3$ as noted in the literature[10] and by Prof. Coldham for the compounds subjected to this comparison.[9, 11] The phenomenon was also observed in the current work wherein some acquired NMR spectra of the ant venom alkaloids gave variable chemical shifts from sample to sample. Trans compound **15** demonstrated particular variability and the table below shows the data from two different acquisitions using different $CDCl_3$. One set of data matches the literature reasonably well. Spectra for compounds **15** and **20** are shown in the latter part of this Supporting Information

Comparison of ^{13}C NMR data of (2*S*, 5*R*)-2-butyl-5-propylpyrrolidine (**20**, free amine) with that from Coldham and Leonori).[9,11]

Literature data[a]	**20** in current paper
59.4	59.4
59.2	59.1
38.7	39.0
36.2	36.5
31.2 (2 peaks)[b]	31.3 (2 peaks)
29.7	29.7
22.9	22.9
20.6	20.7
14.2	14.3
14.0	14.1

a Data for the (2*R*, 5*S*)-2-butyl-5-propylpyrrolidine enantiomer. The ^{13}C NMR numerical listings of the two venom alkaloid isomers are reversed in the experimental section of Reference 9. The spectra shown in the Supporting Information of that paper are correct. See refs. 9 and 11.

b The two peaks are NOT noted in the literature, but the high intensity of the resonance is recognizable through our inspection of the Supporting Information of ref. 9.

Comparison of ^{13}C NMR data of (2*R*, 5*R*)-2-butyl-5-propylpyrrolidine (**15**, free amine) with that from Coldham and Leonori).[9,11]

Literature data[a]	**15** in current paper (spectrum 1)	**15** in current paper (spectrum 2)
59.6	59.4	58.5
59.3	59.2	58.4
34.6	35.1	37.6
32.2	32.7	35.2
30.8 (2 peaks)[b]	30.6 (2 peaks)	31.7 (2 peaks)
28.5	28.9	29.2
22.3	22.4	22.7
19.8	20.1	20.3
13.7	14.0	14.1
13.6	13.8	14.0

a Data for the (2*S*, 5*S*)-2-butyl-5-propylpyrrolidine enantiomer. The ^{13}C NMR numerical listings of the two venom alkaloid isomers are reversed in the experimental section of Reference 9. The Spectra shown in the Supporting Information of that paper are correct. See refs. 9 and 11.

b The two peaks are NOT noted in the literature, but the high intensity of the resonance is recognizable through our inspection of the Supporting Information of ref. 9.

References for Supporting Information.

(1) Soderman, S. C.; Schwan, A. L. *J. Org. Chem.* **2013**, *78*, 1638.

(2) Soderman, S. C.; Schwan, A. L. *Org. Lett.* **2011**, *13*, 4192.

(3) Schwan, A. L.; Roche, M. R.; Gallagher, J. F.; Ferguson, G. *Can. J. Chem.* **1994**, *72*, 312.

(4) Schwan, A. L.; Strickler, R. R.; Lear, Y.; Kalin, M. L.; Rietveld, T. E.; Xiang, T.-J.; Brillon, D. *J. Org. Chem.* **1998**, *63*, 7825.

(5) Kondo, K.; Negishi, A. *Tetrahedron* **1971**, *27*, 4821.

(6) Kondo, K.; Negishi, A.; Fukuyama, M. *Tetrahedron Lett.* **1969**, 2461.

(7) Refvik, M. D.; Froese, R. D. J.; Goddard, J. D.; Pham, H. H.; Pippert, M. F.; Schwan, A. L. *J. Am. Chem. Soc.* **1995**, *117*, 184.

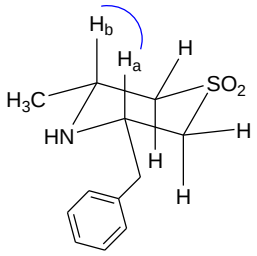
(8) Jo, E.; Na, Y.; Chang, S. *Tetrahedron Lett.* **1999**, *40*, 5581.

(9) Coldham, I.; Leonori, D. *J. Org. Chem.* **2010**, *75*, 4069.

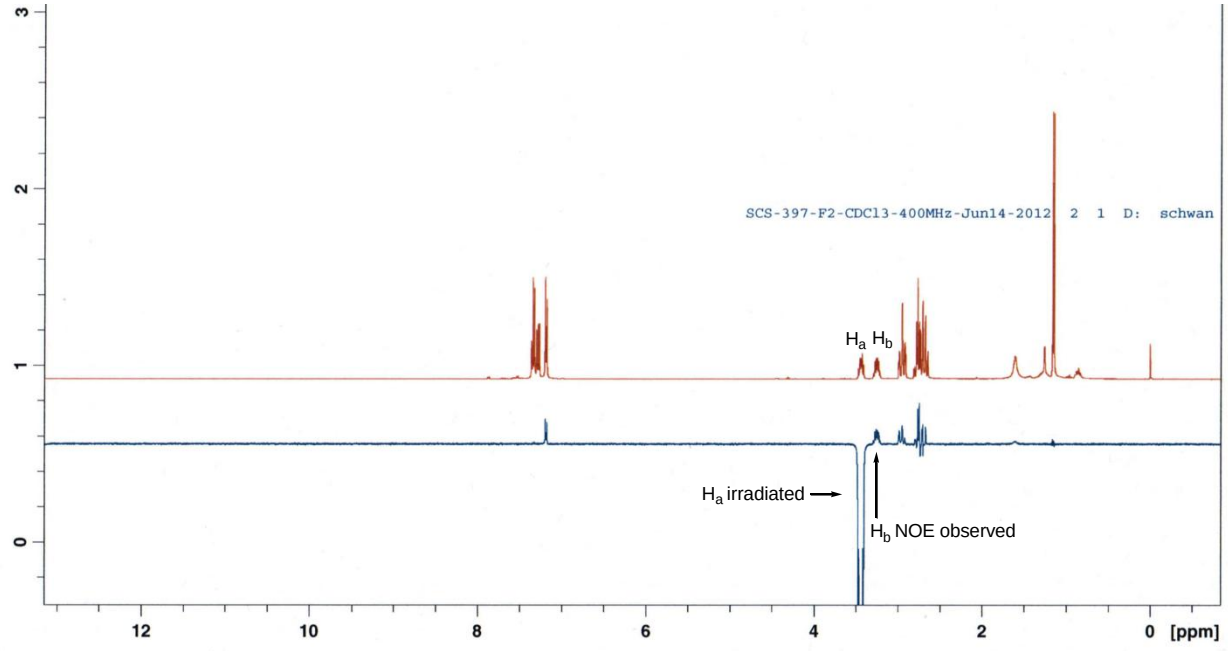
(10) Magolan, J.; Carson, C.A.; Kerr, M.A. *Org. Lett.* **2008**, *10*, 1437.

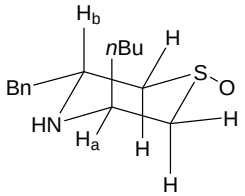
(11) Coldham, I. University of Sheffield, Sheffield, U.K. Personal Communication, 2013.

^{1}H NMR NOESY data



8a, $CDCl_3$; single gradient NOE-400 MHz
H_a irradiated





6g, $CDCl_3$; single gradient NOE-600 MHz
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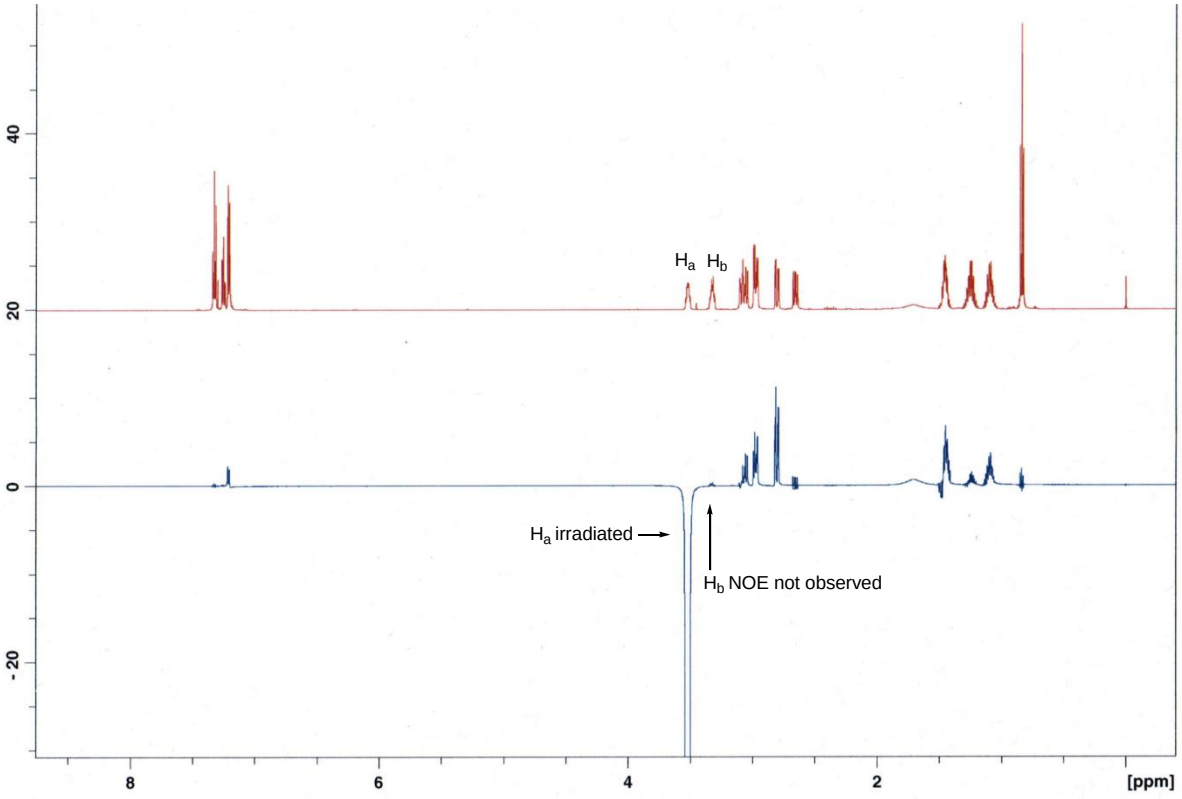
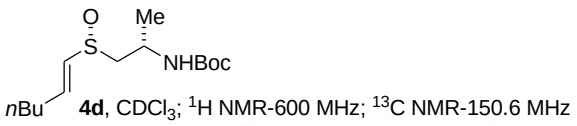
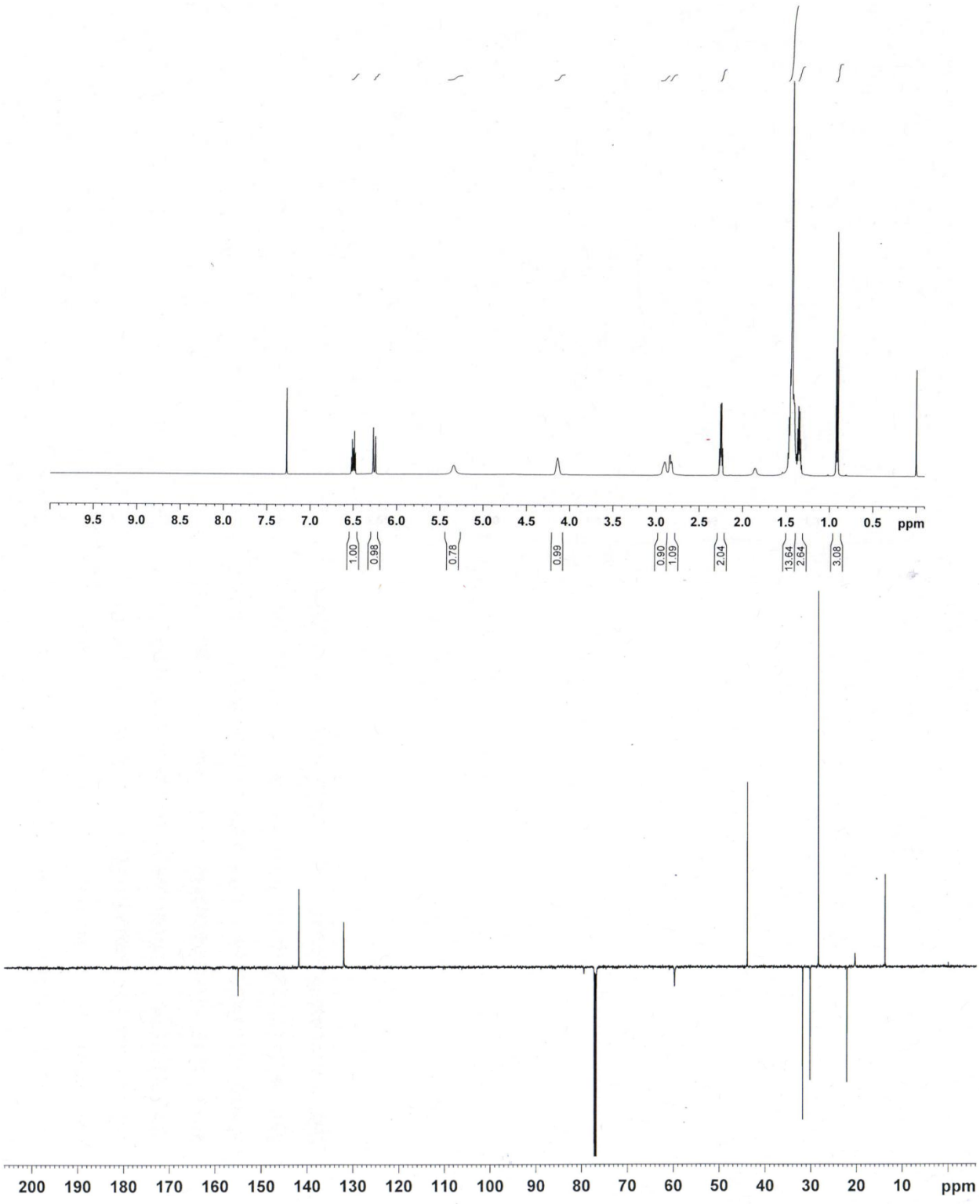
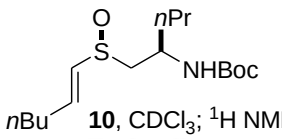




4d, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz





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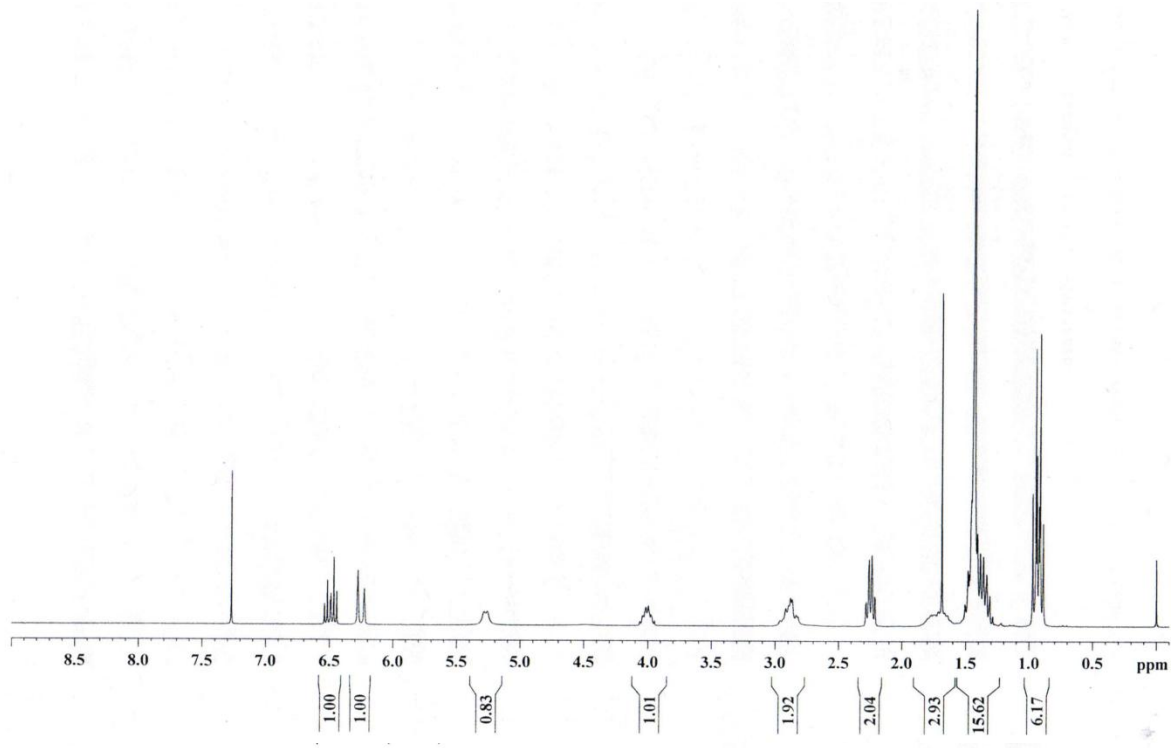
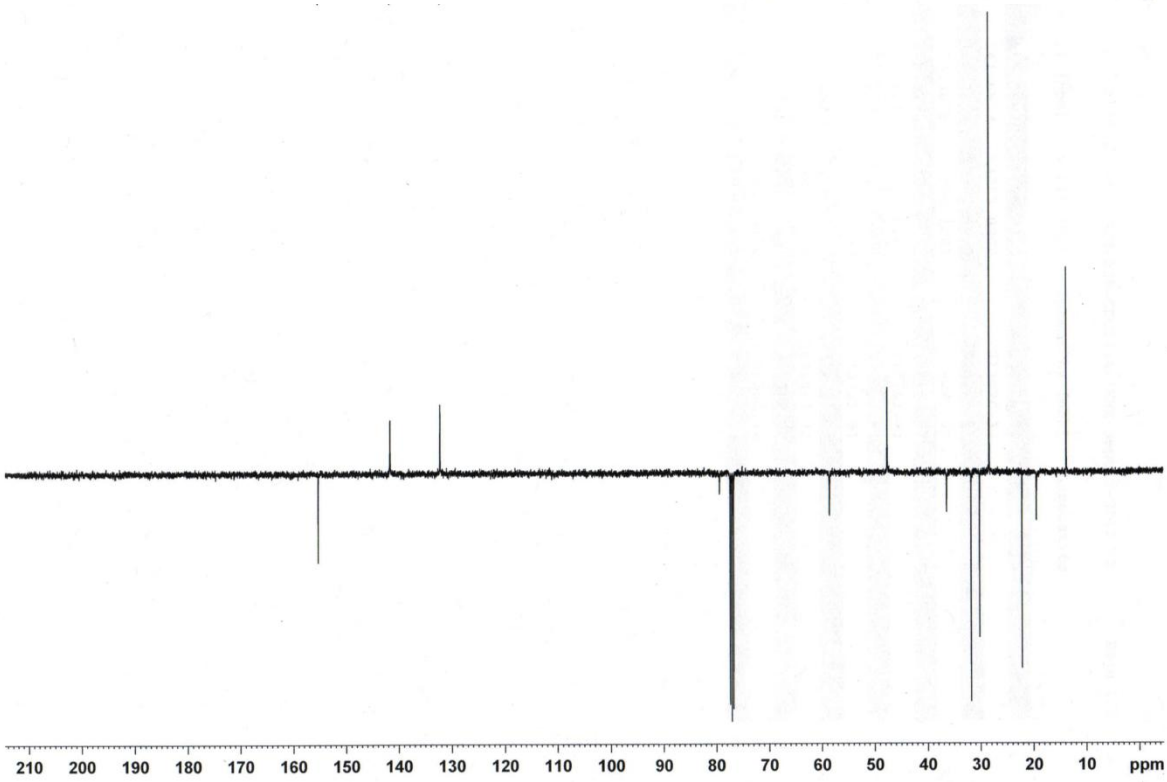
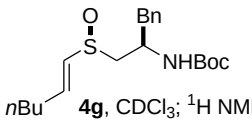
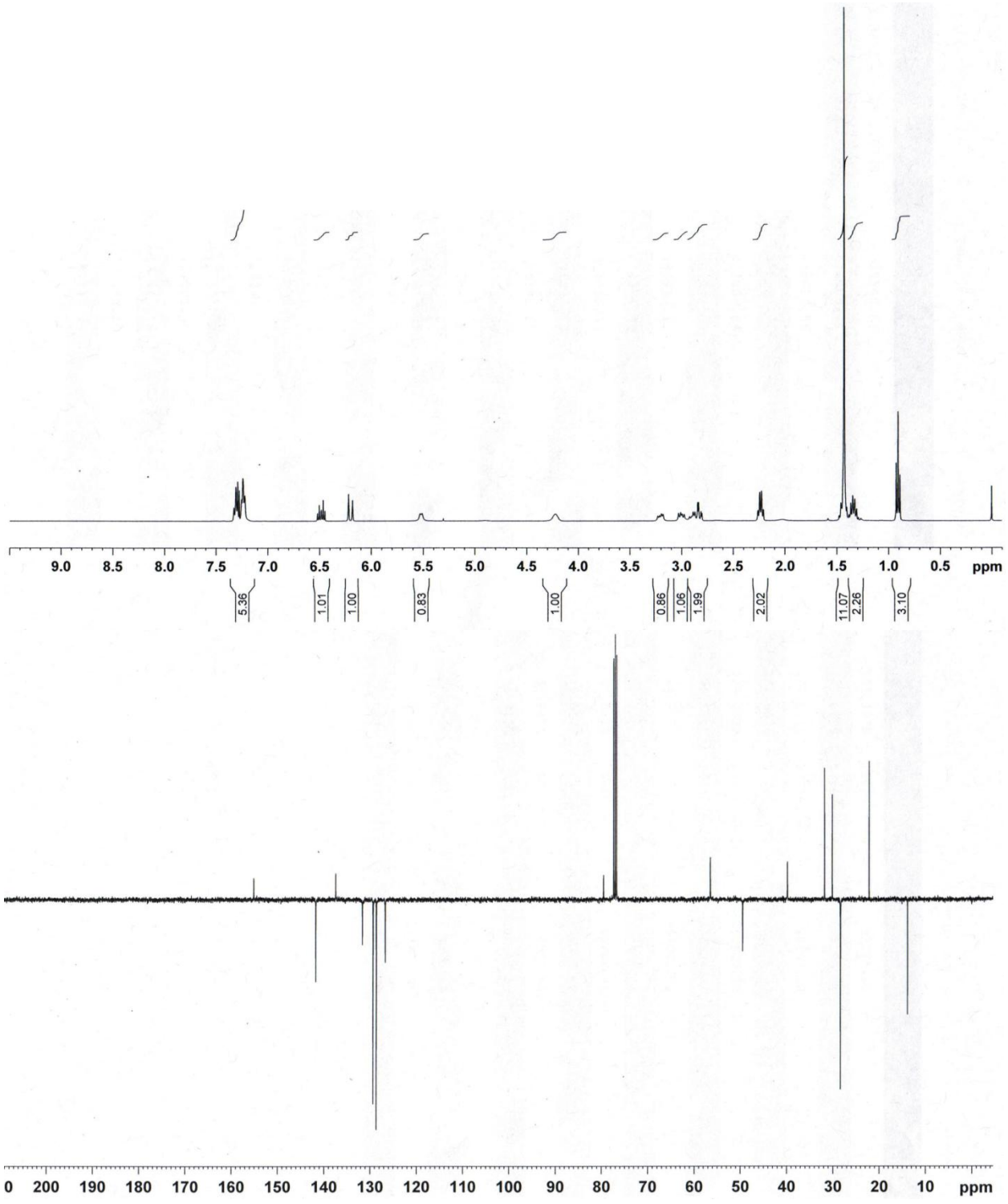
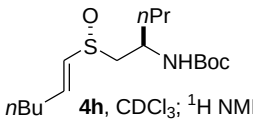




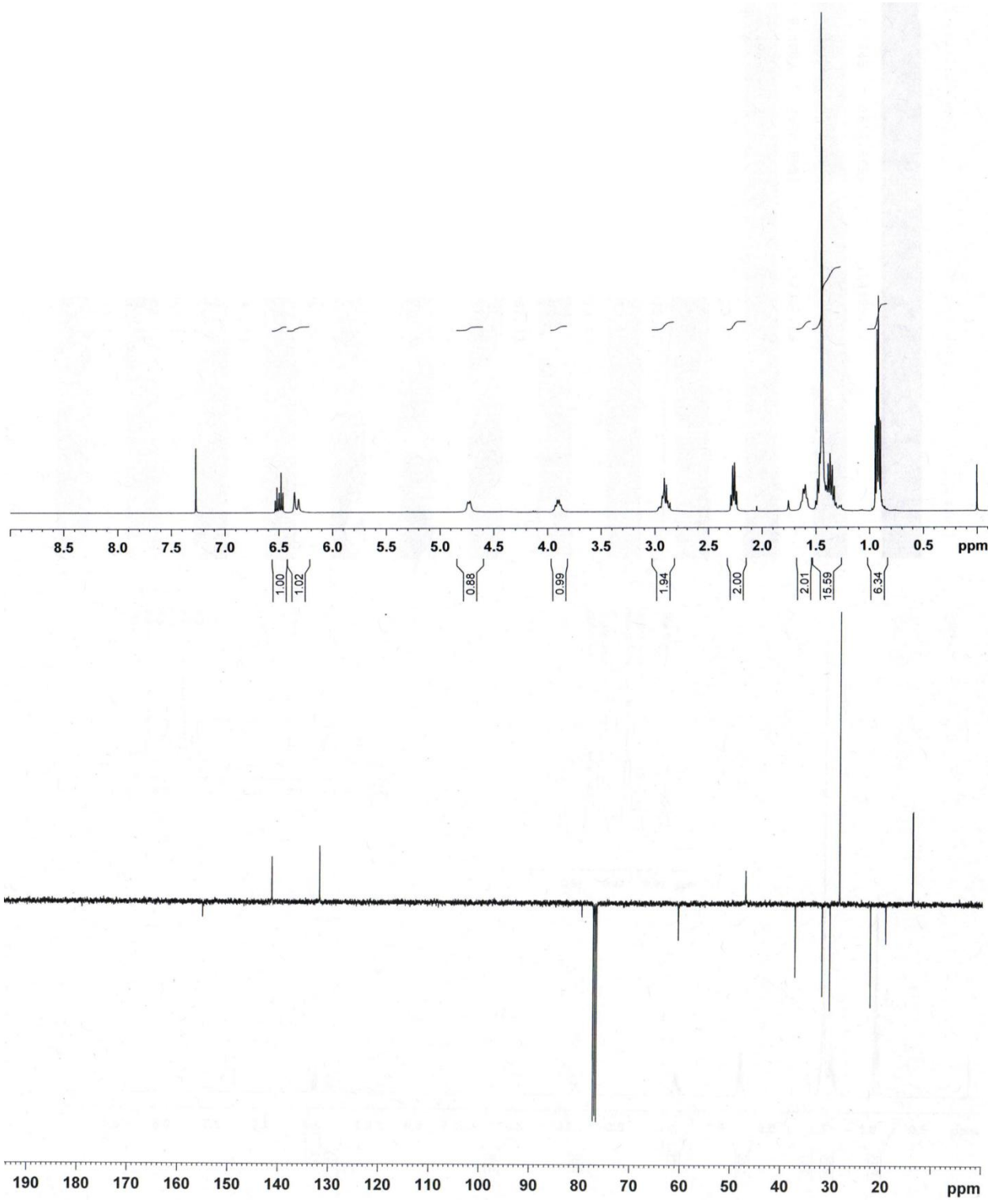


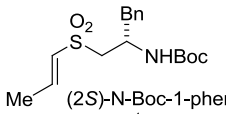
4g, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz



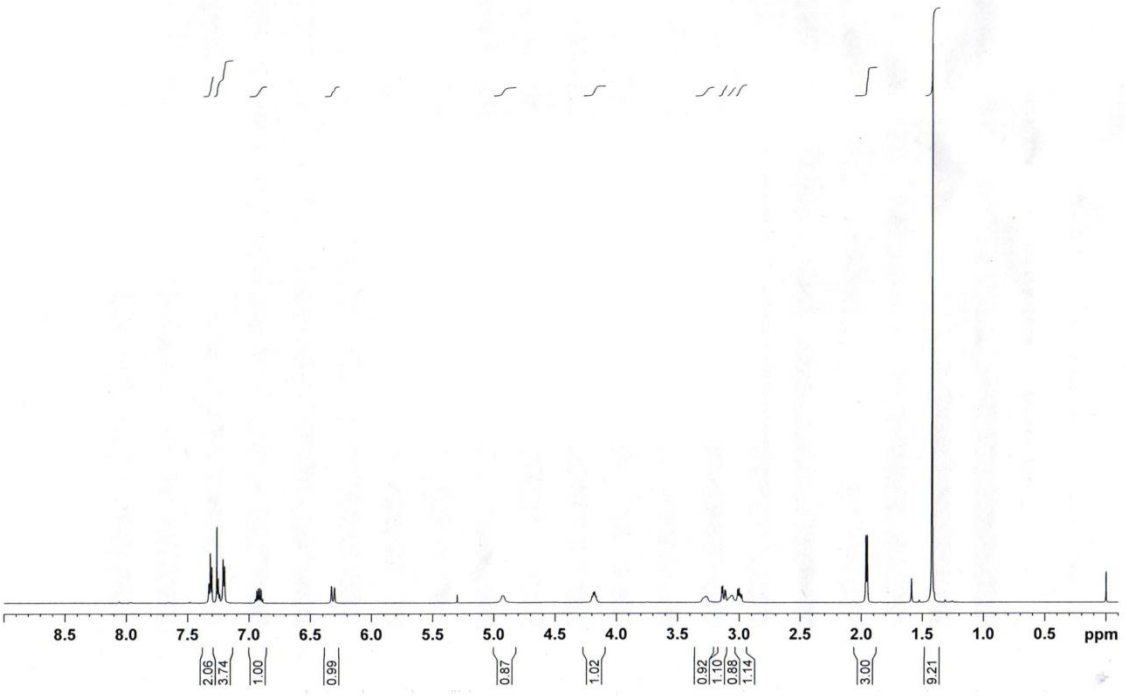


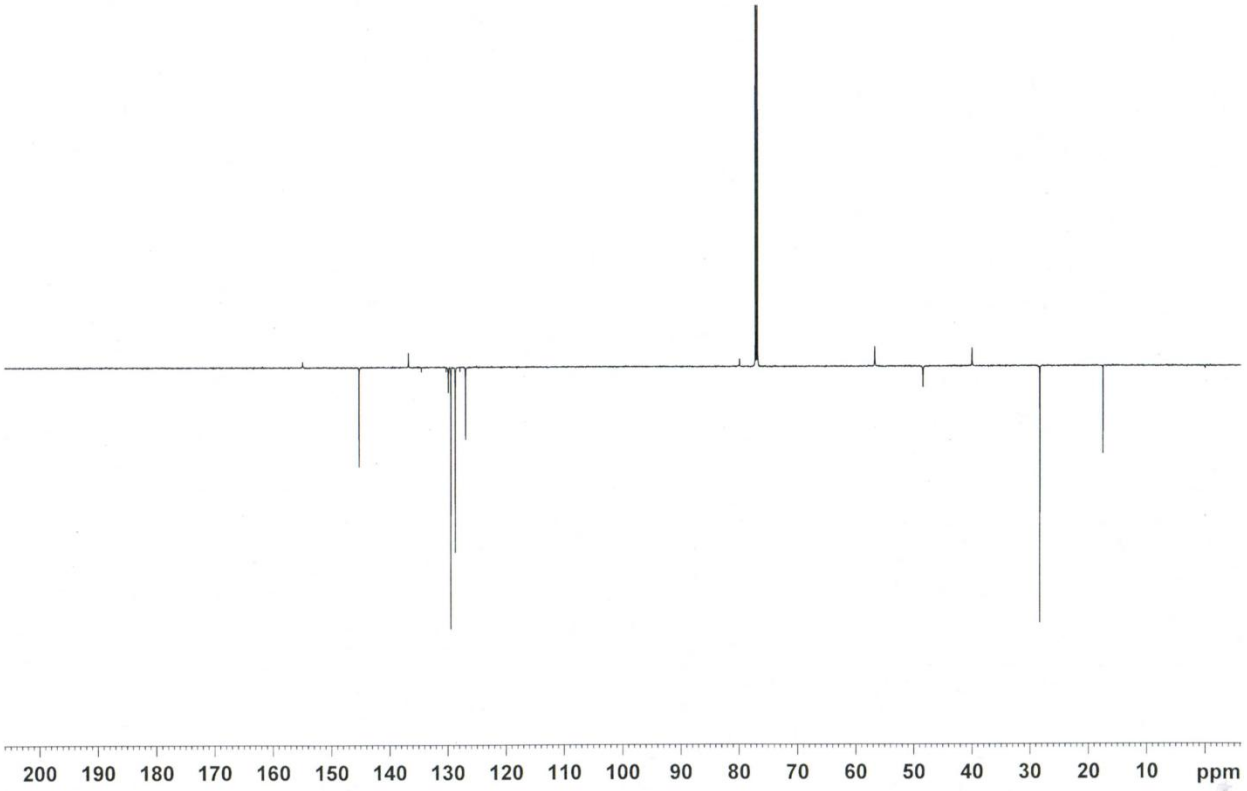
4h, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

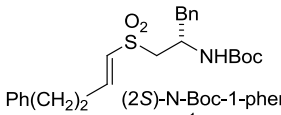




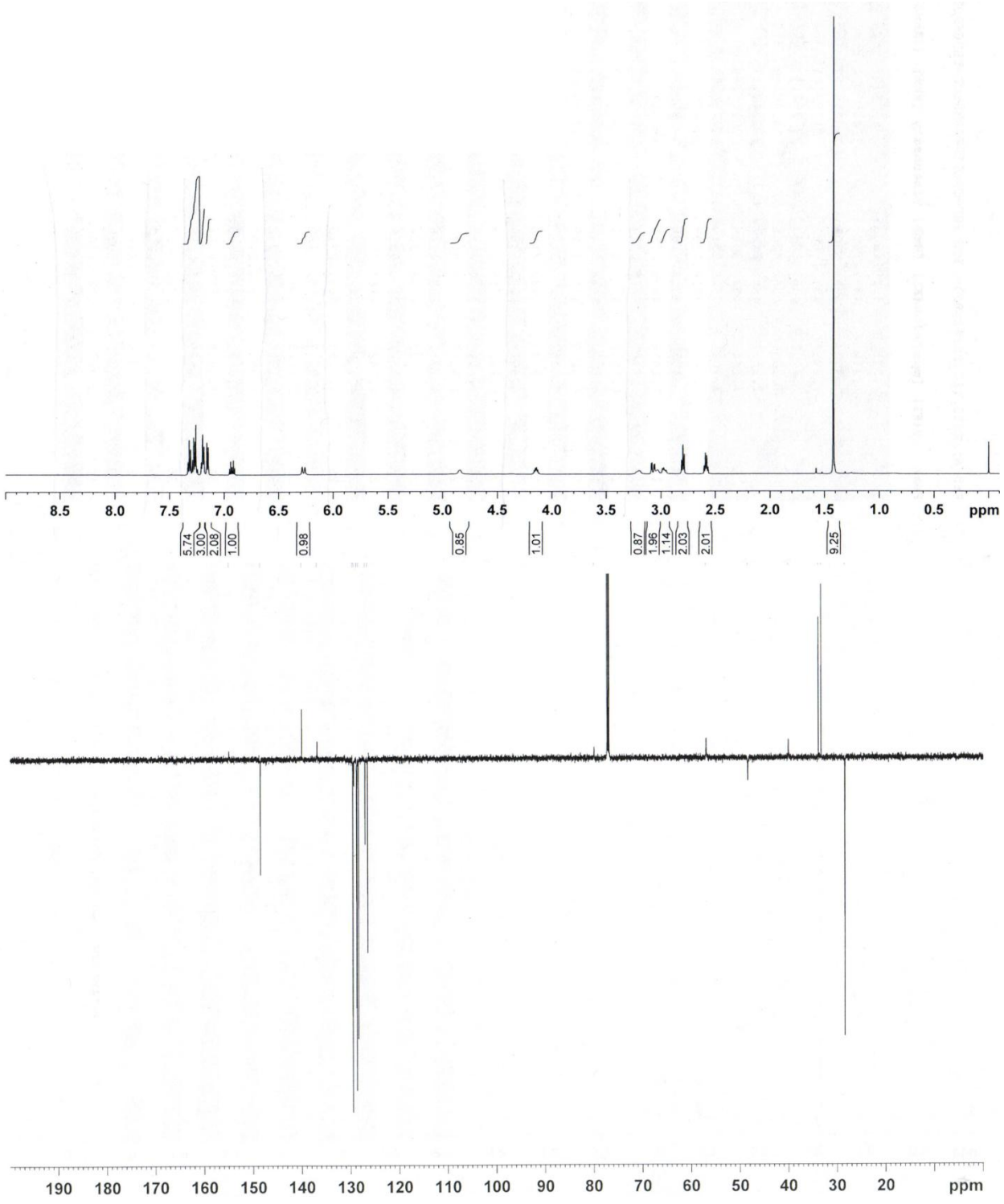
(2*S*)-N-Boc-1-phenyl-3-((*E*)-propenylsulfonyl)propan-2-amine
$CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

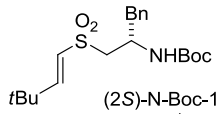




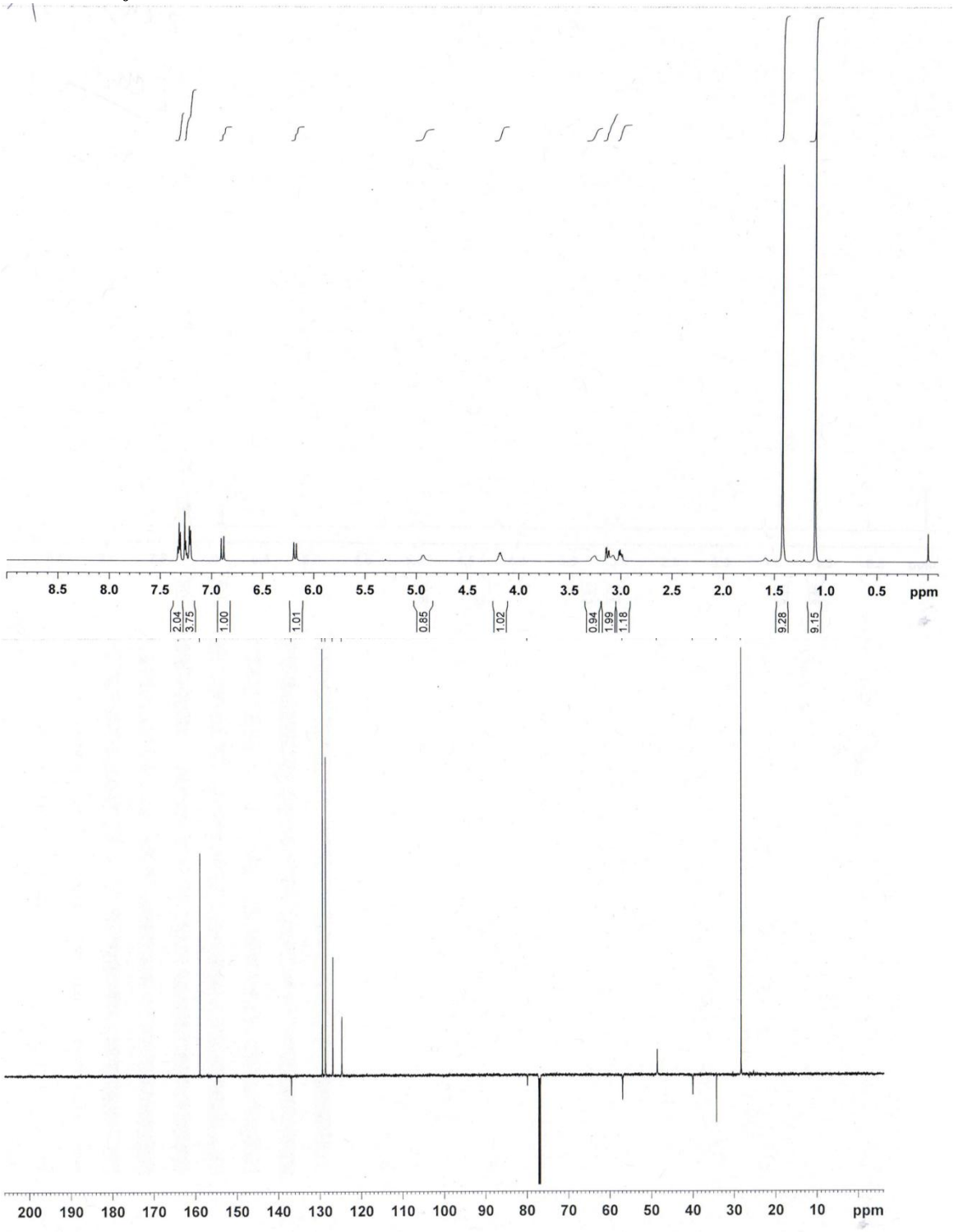


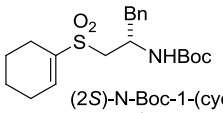
(2*S*)-N-Boc-1-phenyl-3-((*E*)-4-phenyl-1-butenylsulfonyl)propan-2-amine
$CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz



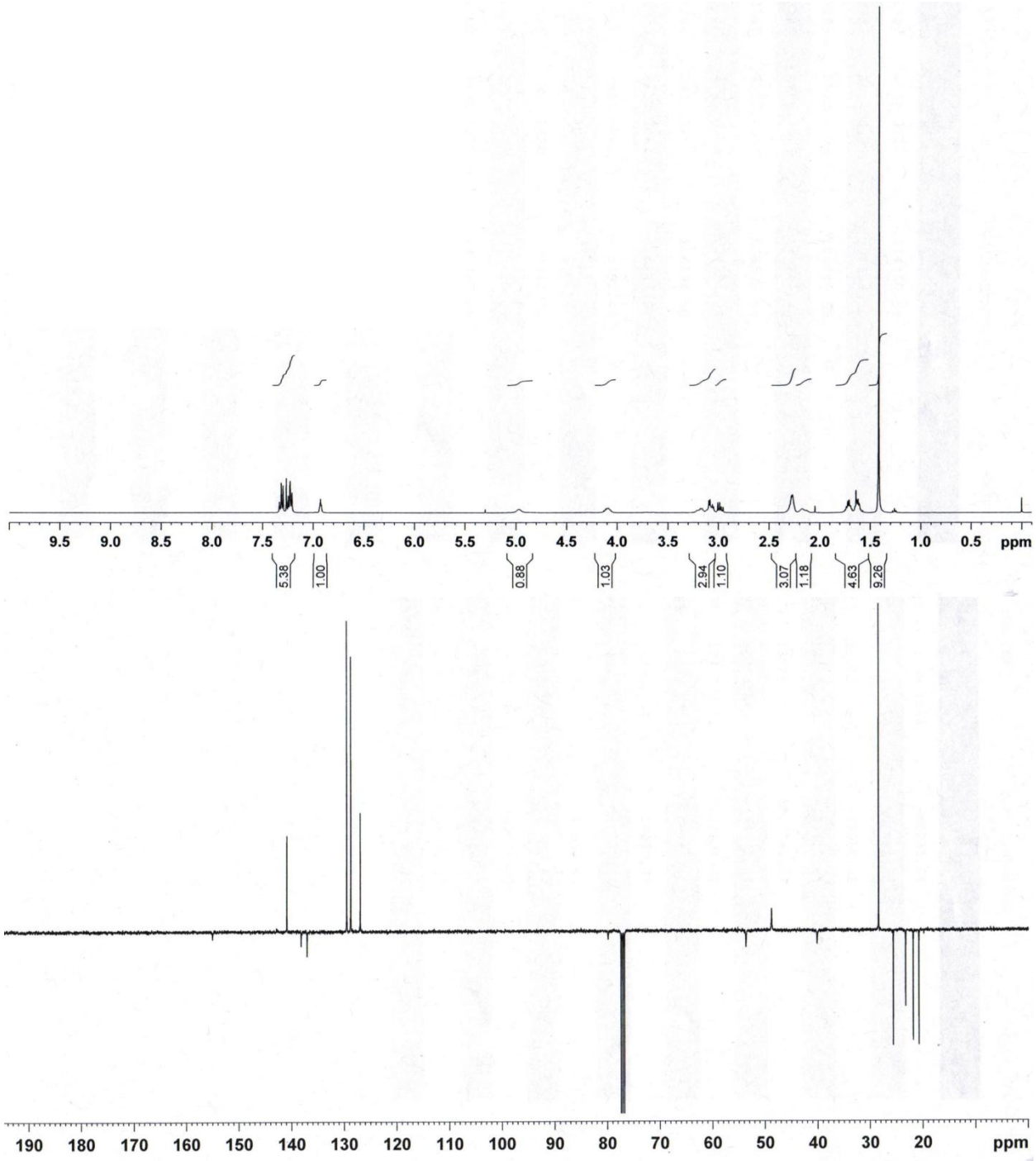


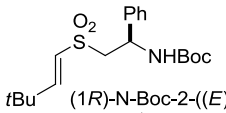
(2*S*)-N-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-3-phenylpropan-2-amine,
$CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz



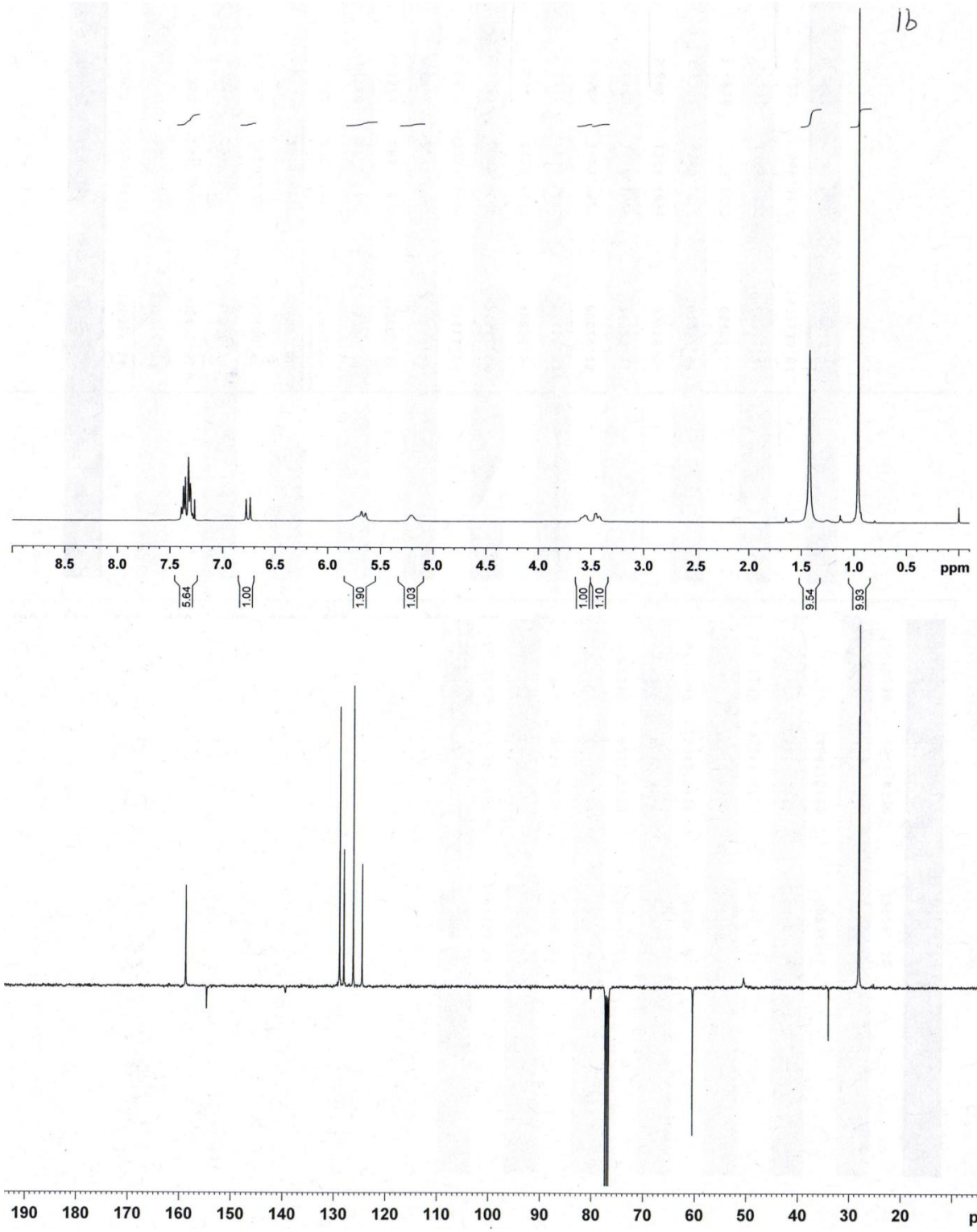


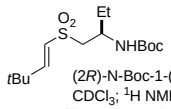
(2*S*)-N-Boc-1-(cyclohexenylsulfonyl)-3-phenylpropan-2-amine,
$CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz



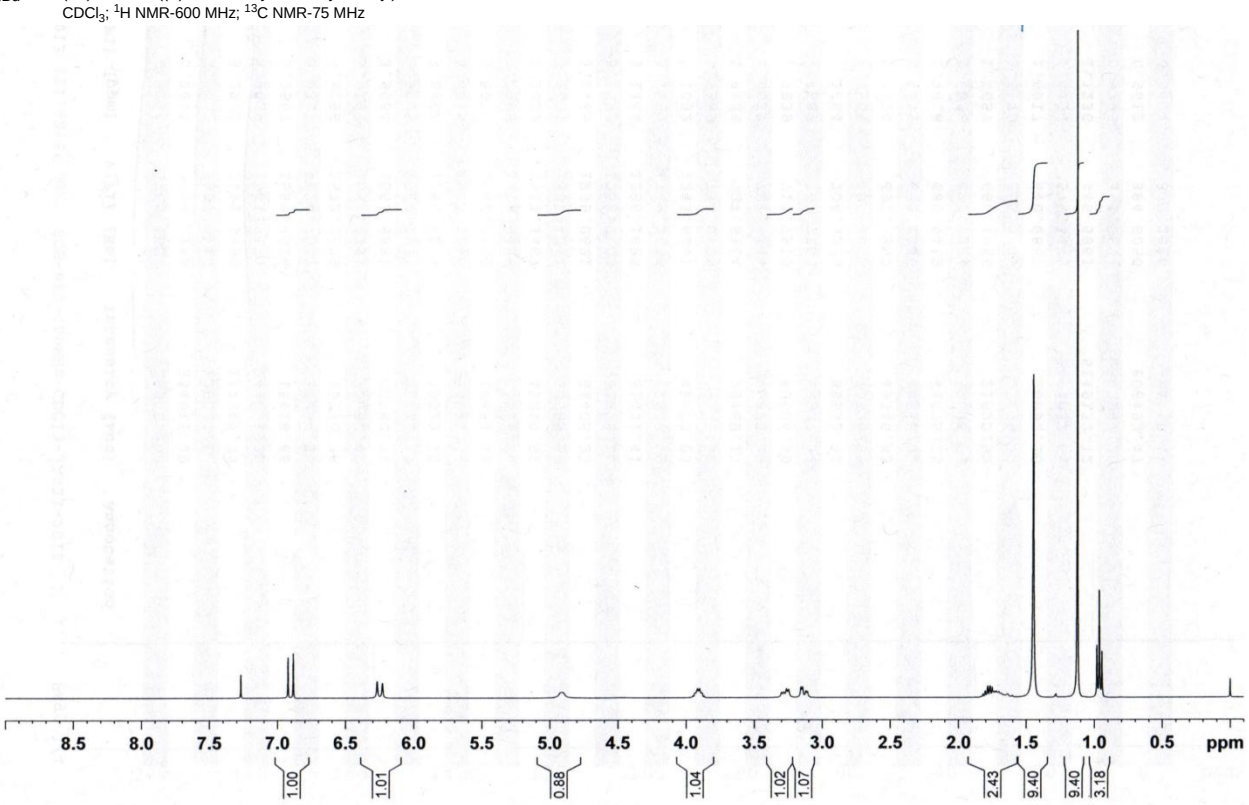


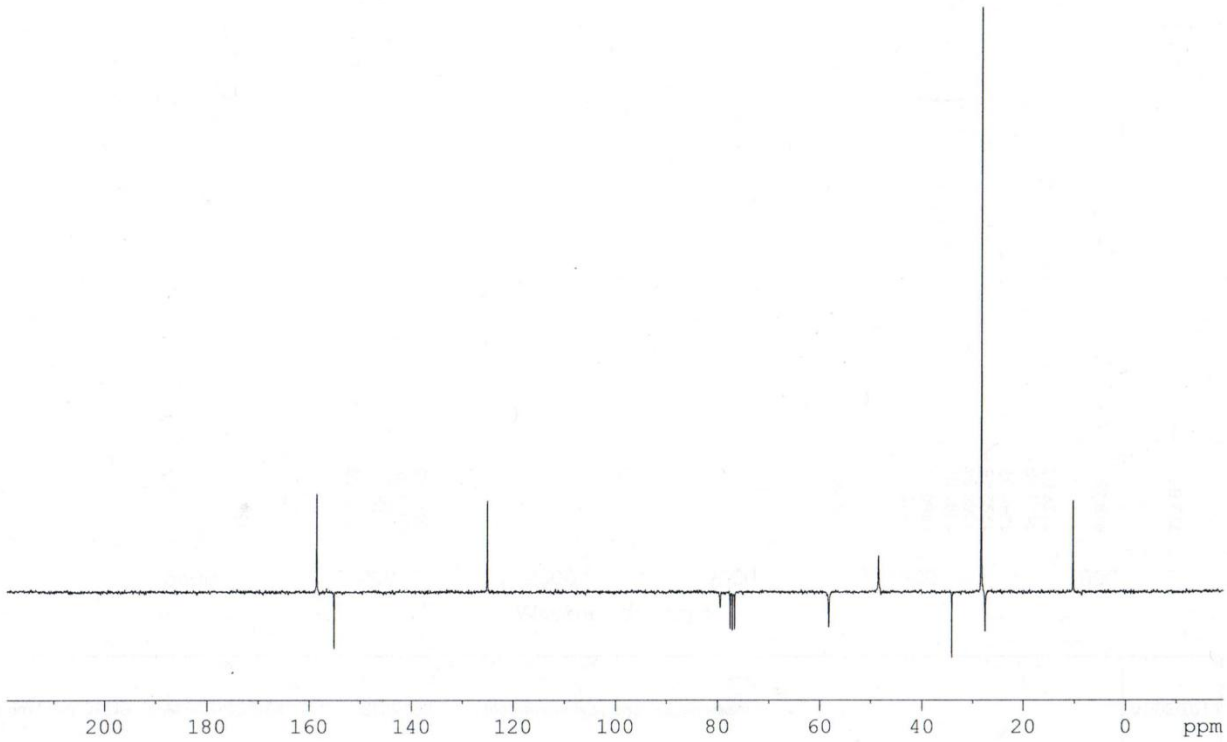
(1*R*)-N-Boc-2-((*E*)-3,3-dimethyl-1-butenylsulfonyl)-1-phenylethanamine,
$CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

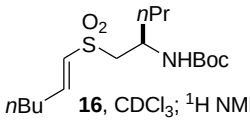




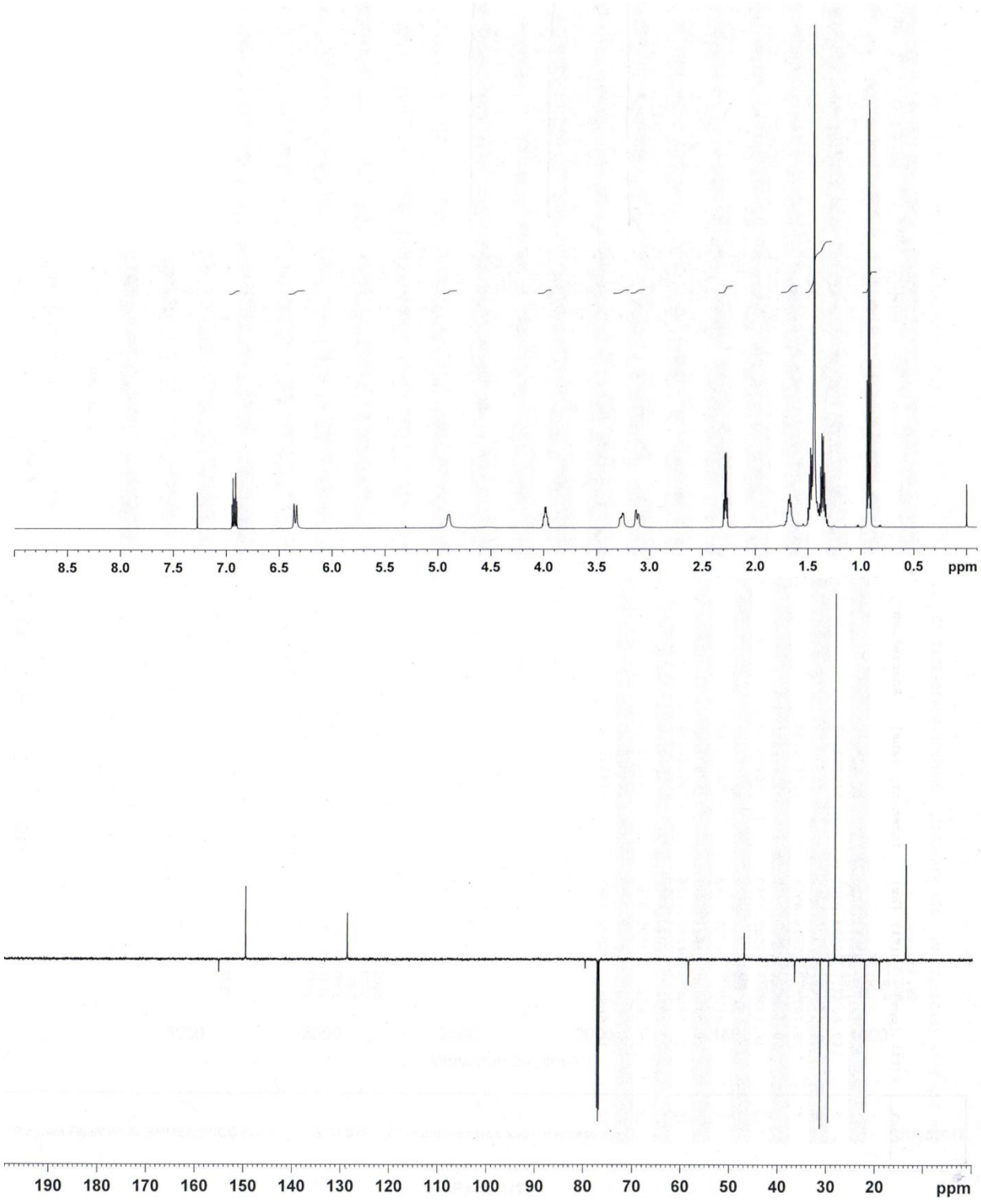
(2*R*)-N-Boc-1-((*E*)-3,3-dimethyl-1-butenylsulfonyl)butan-2-amine,
$CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-75 MHz

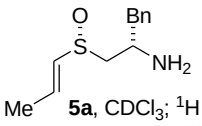




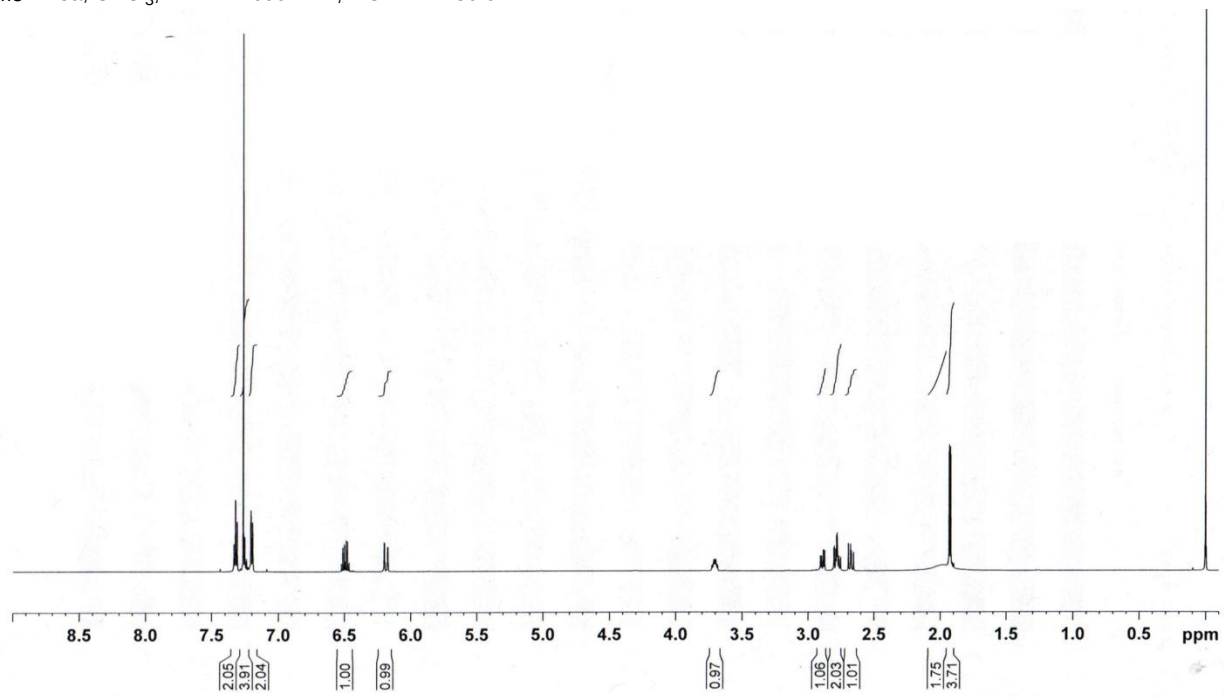


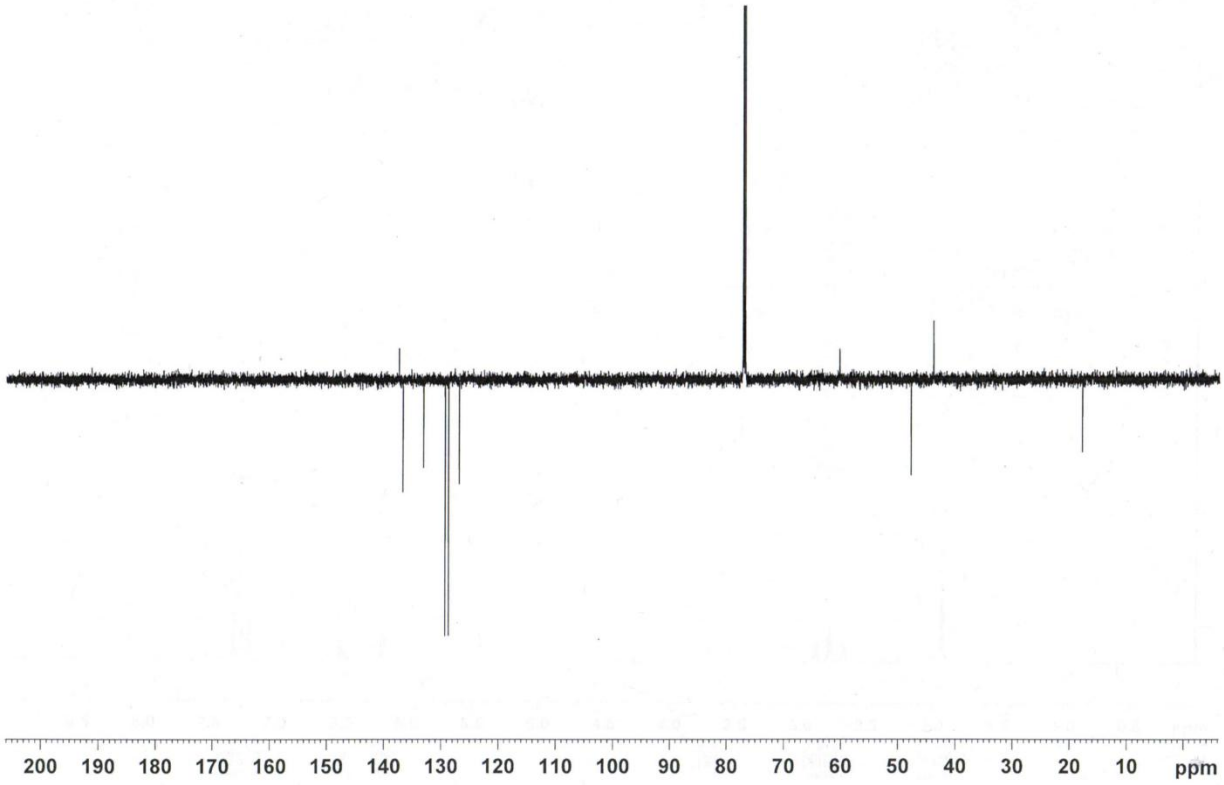
16, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

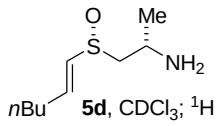




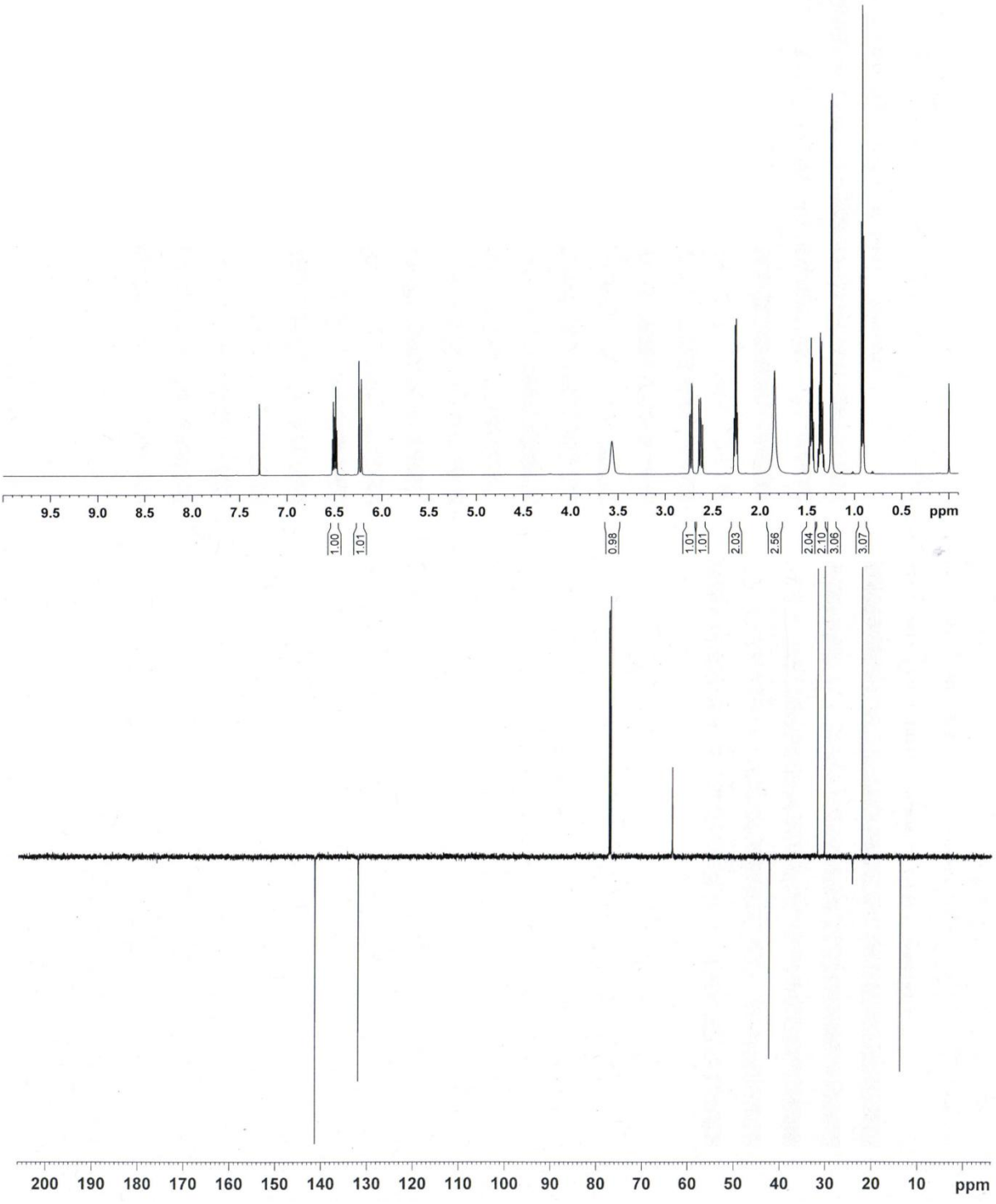
5a, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

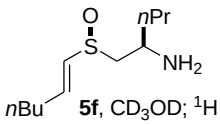




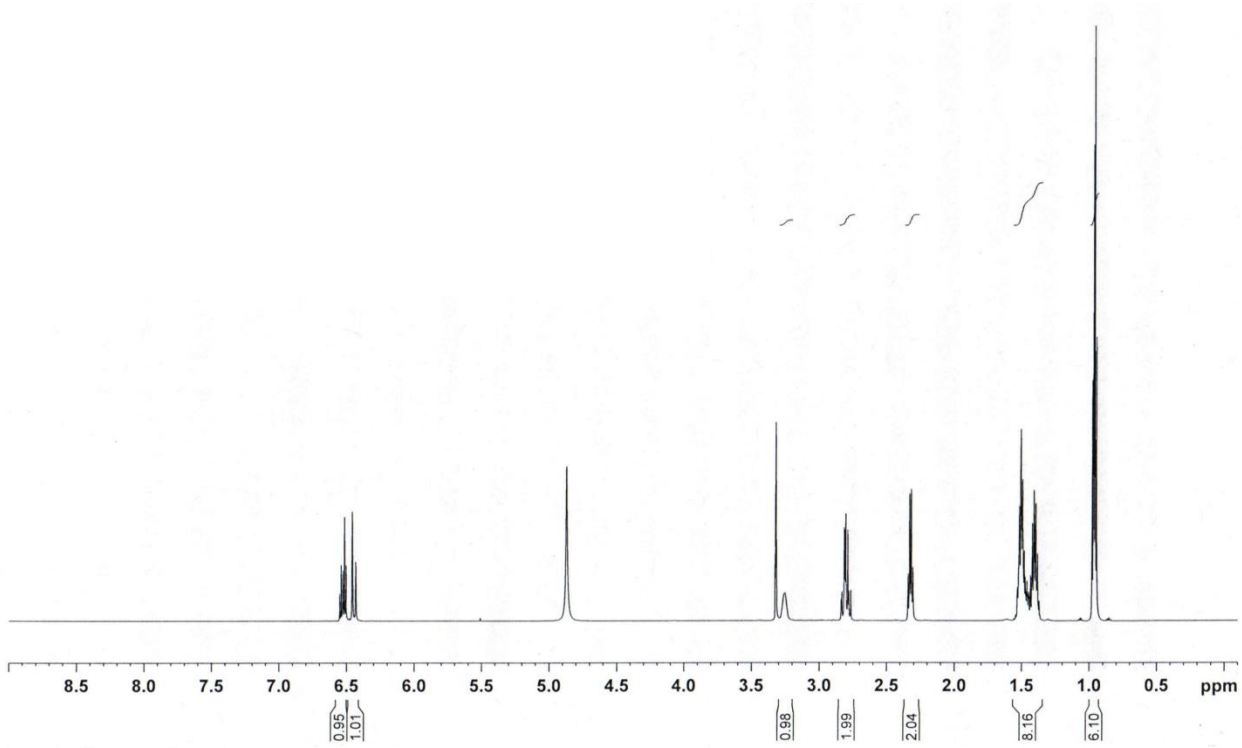


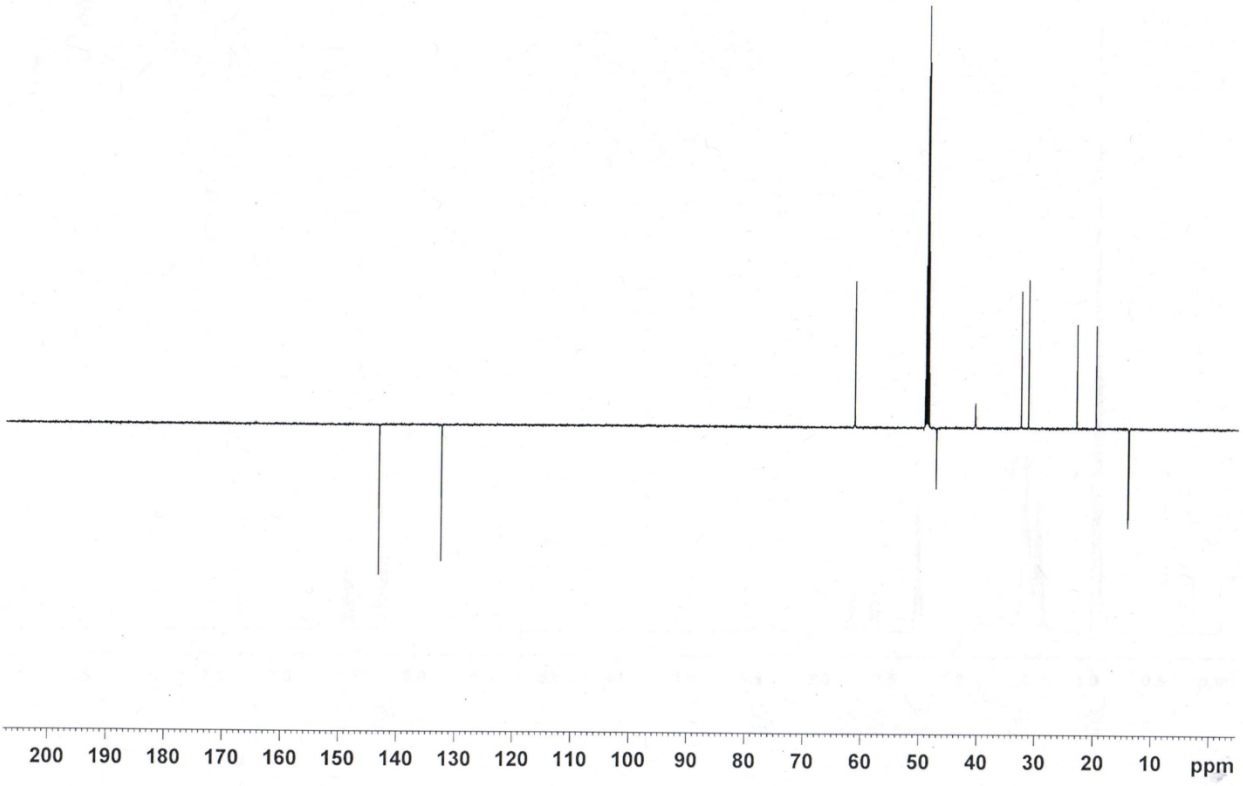
5d, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-100 MHz

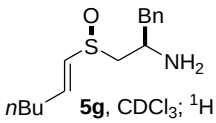




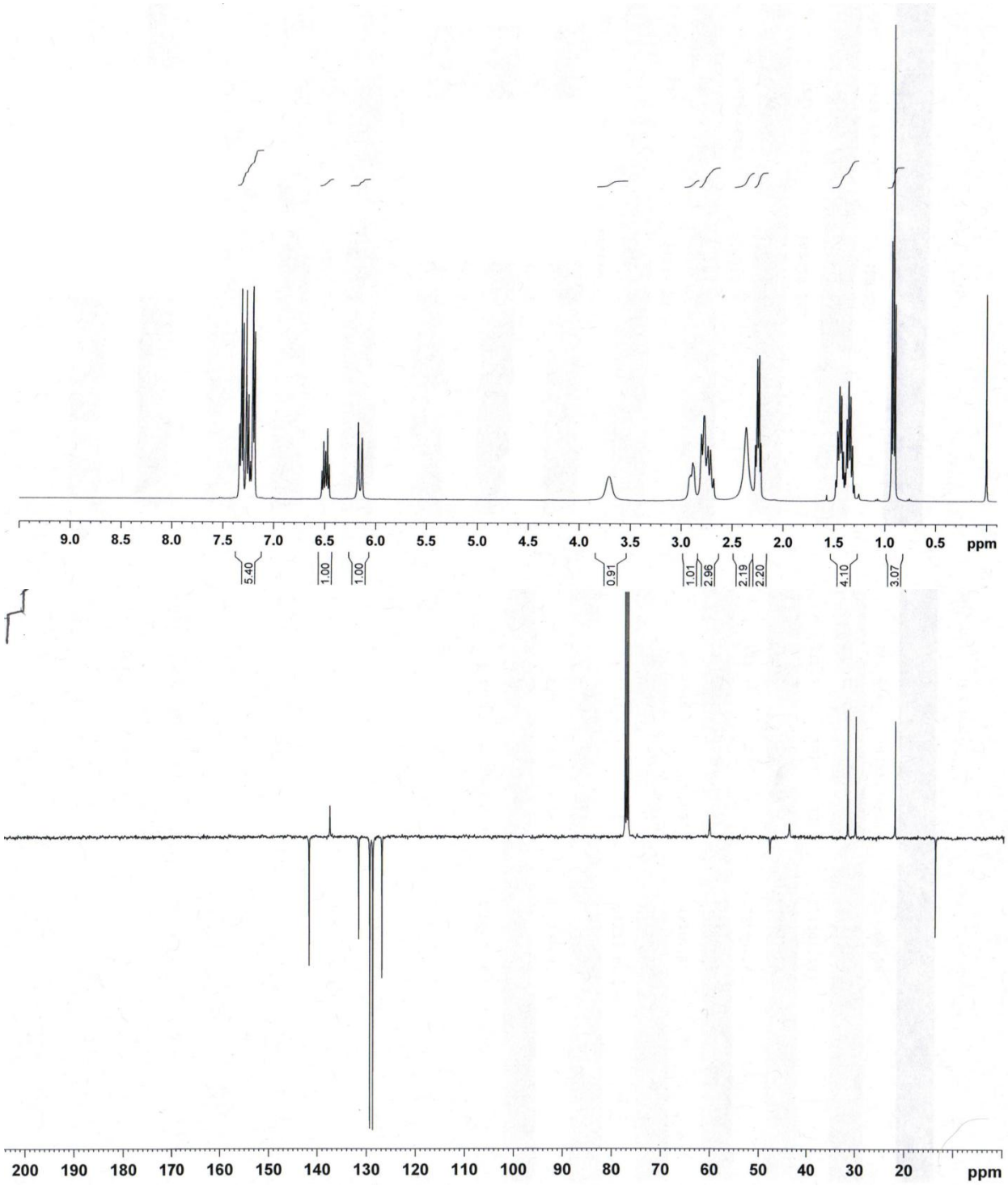
5f, CD_3OD; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

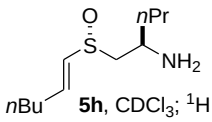




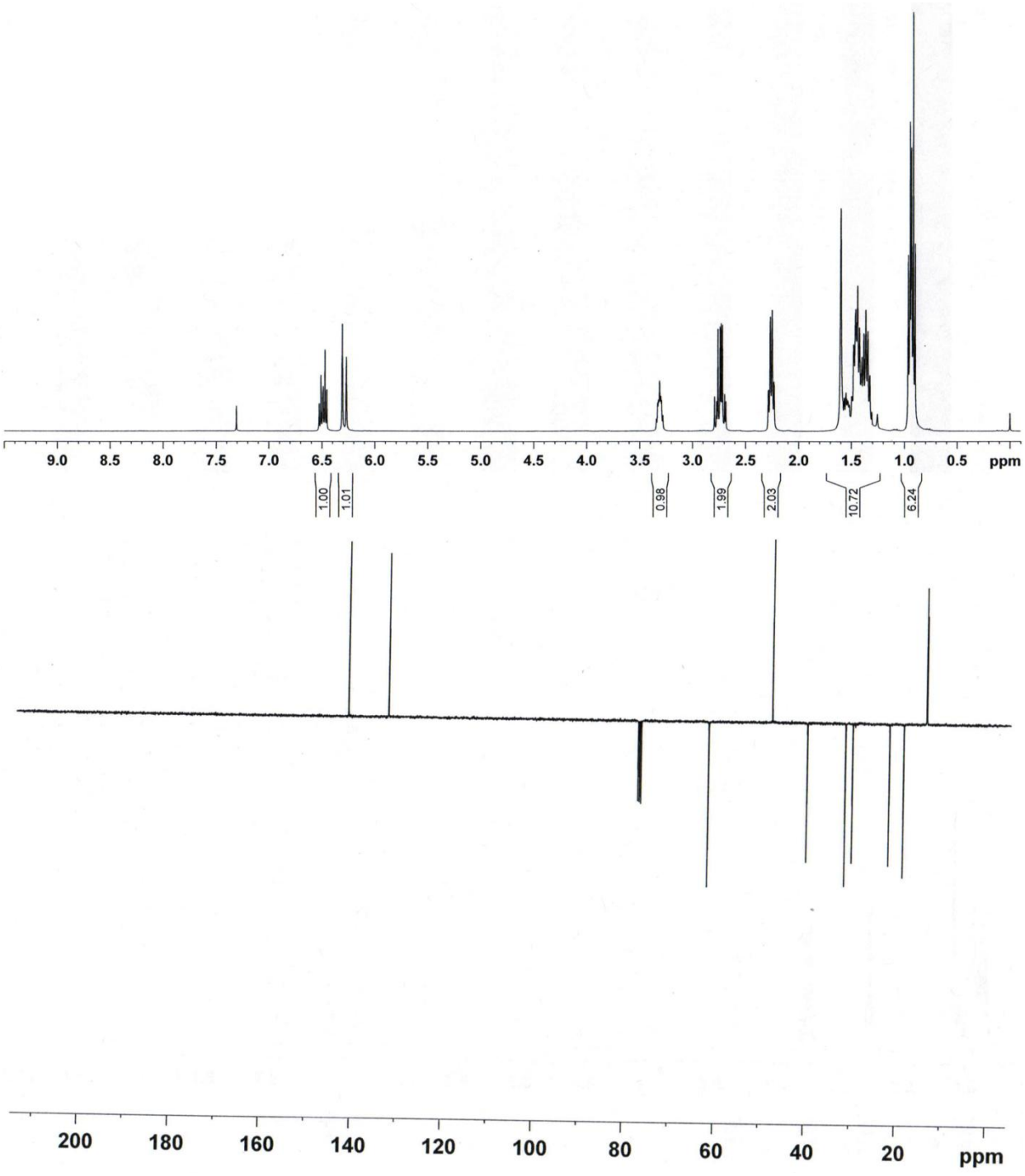


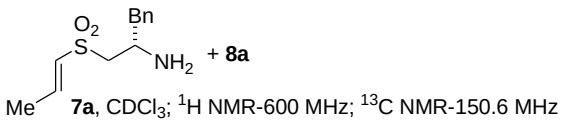
5g, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz



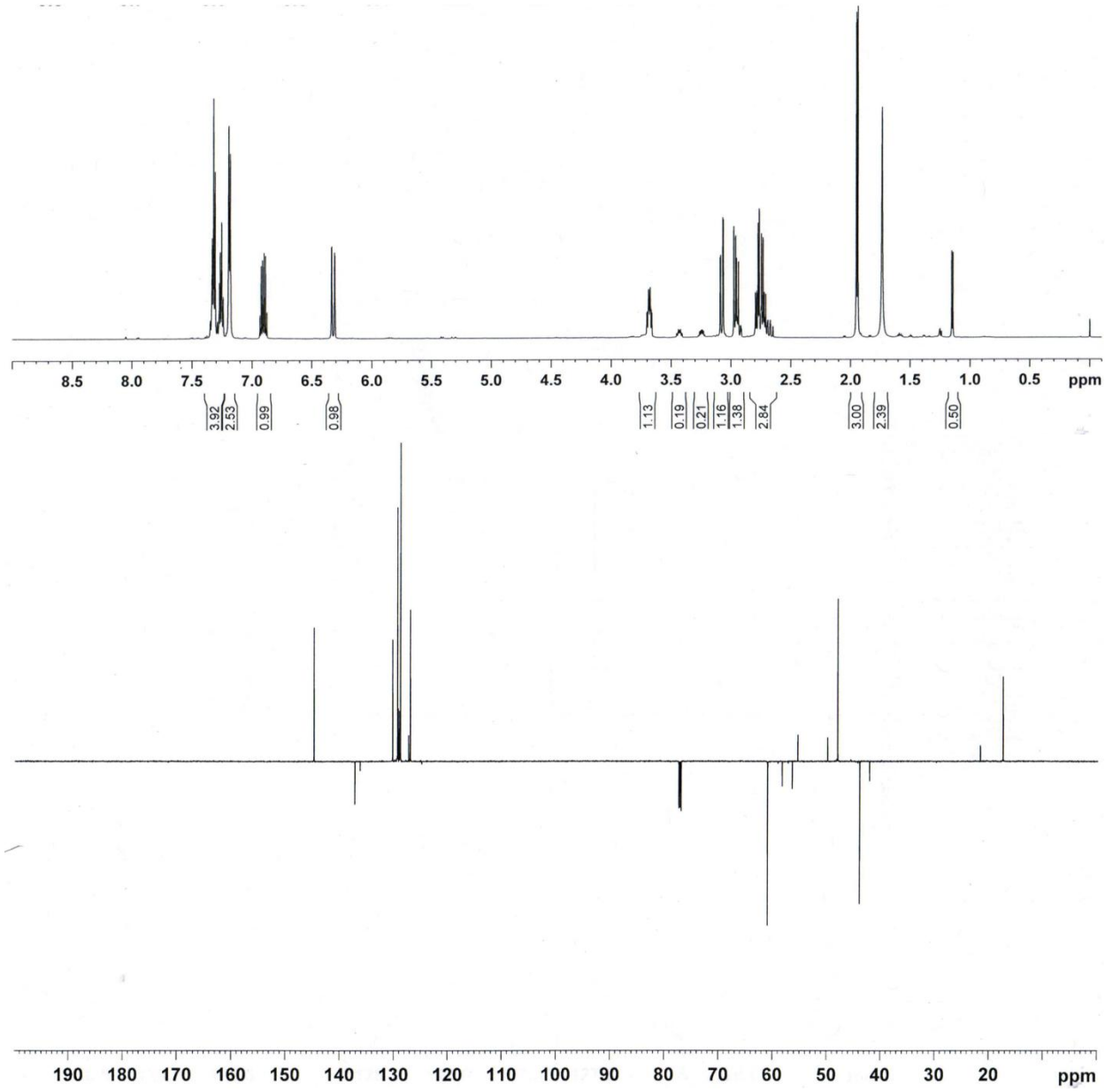


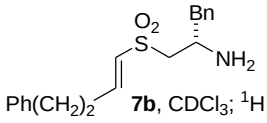
5h, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-150.6 MHz



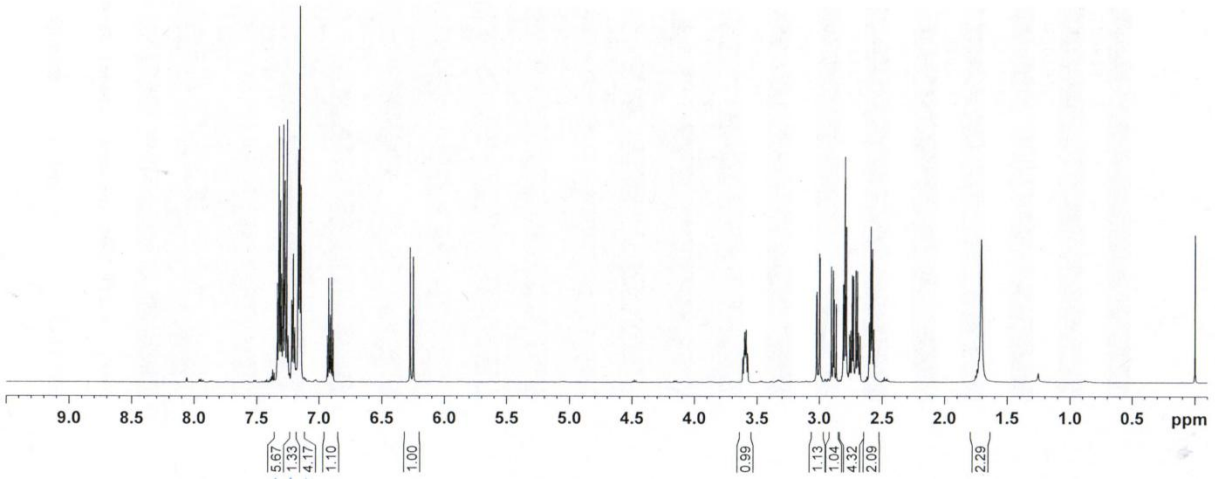


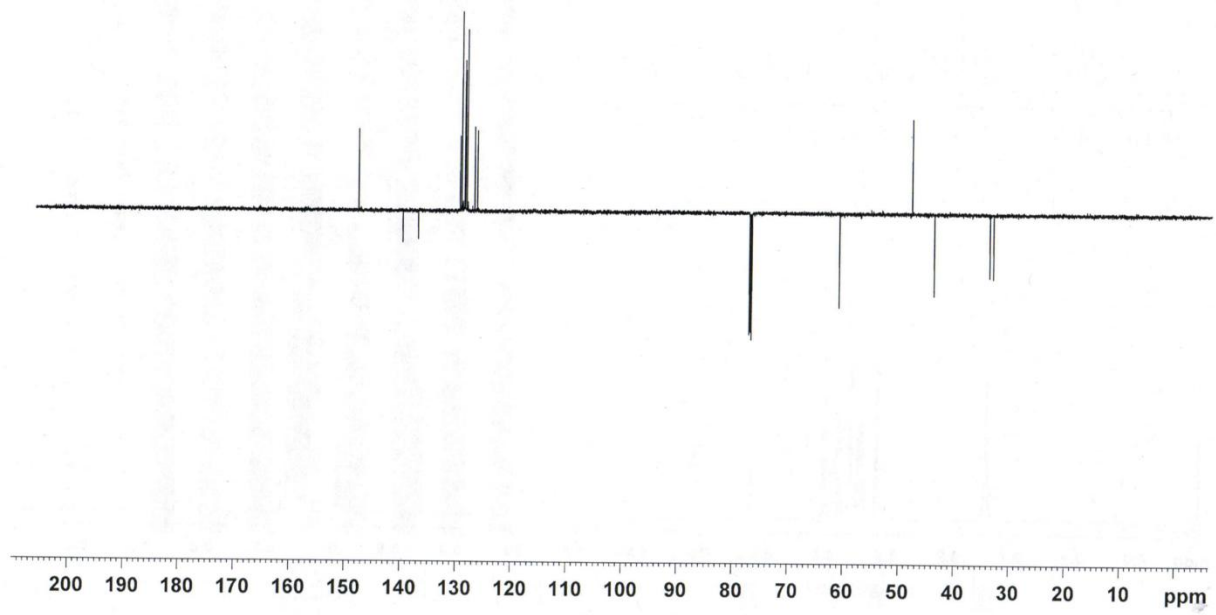
7a, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

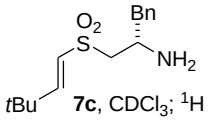




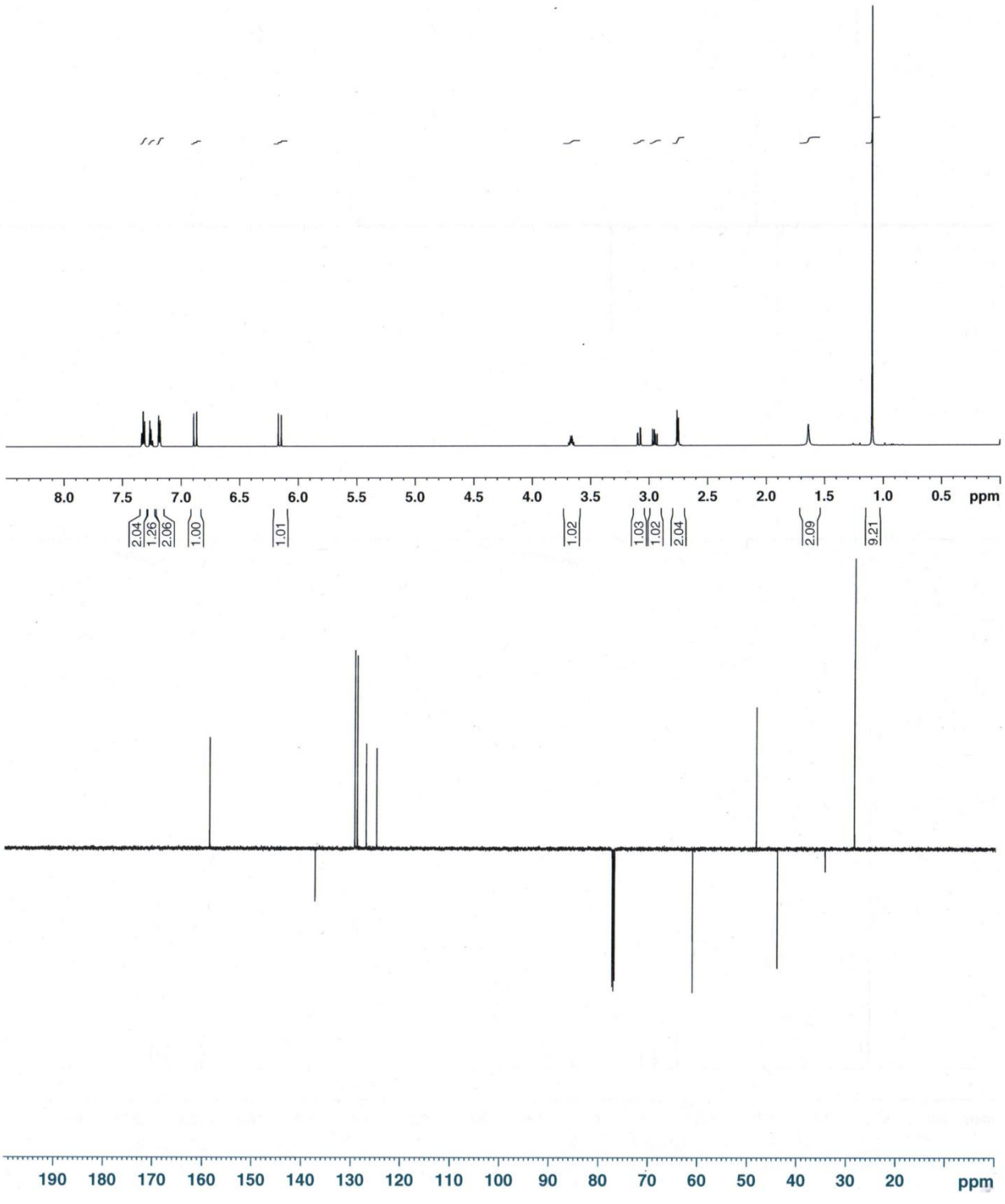
7b, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

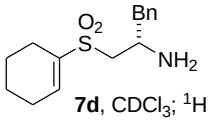




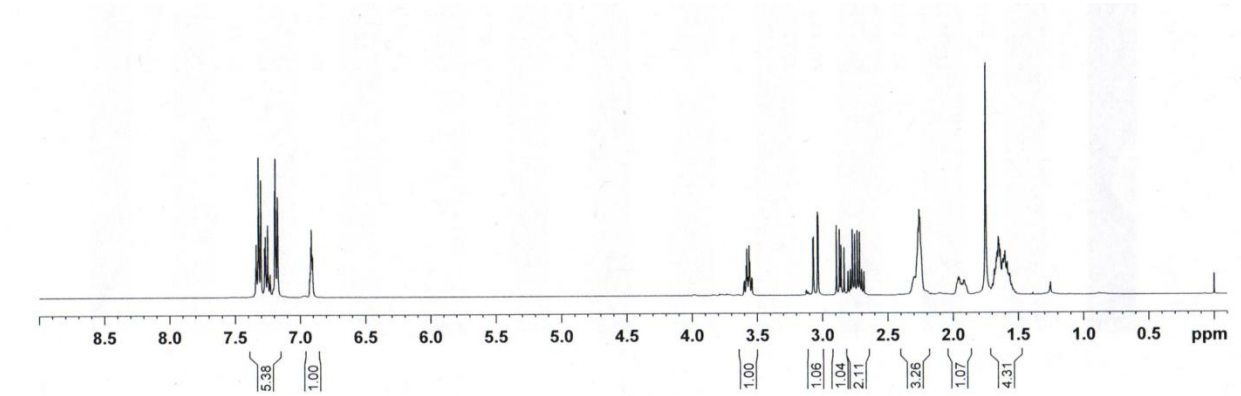


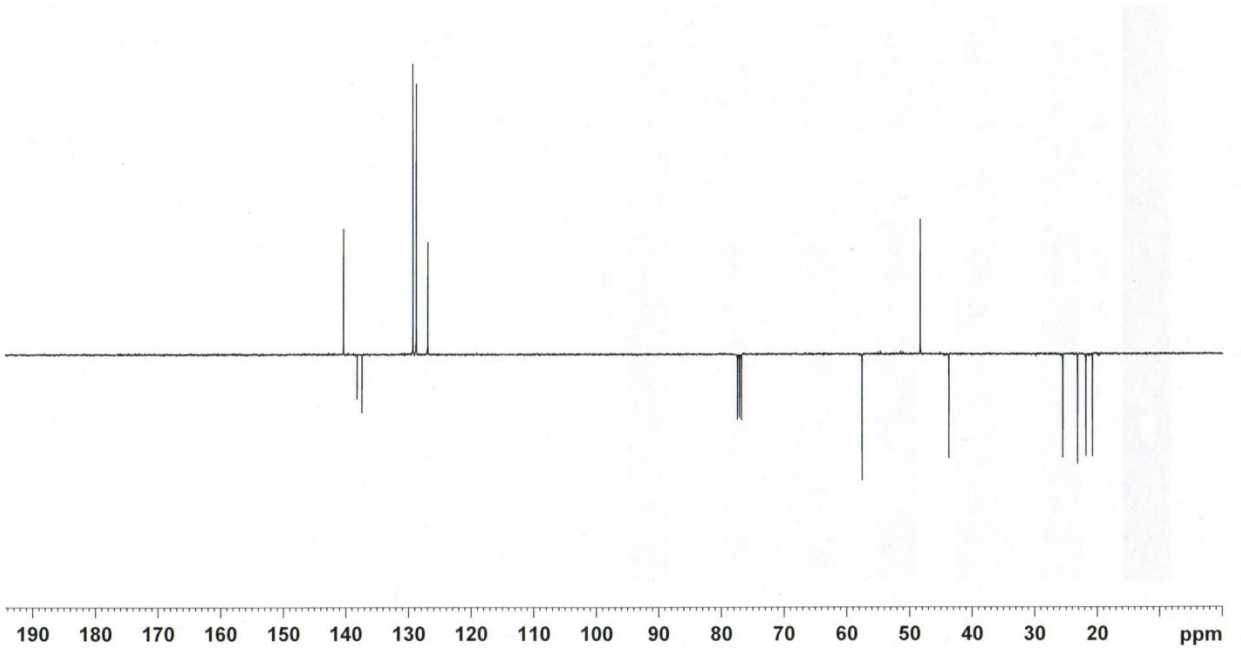
7c, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

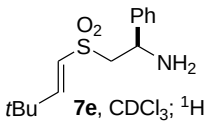




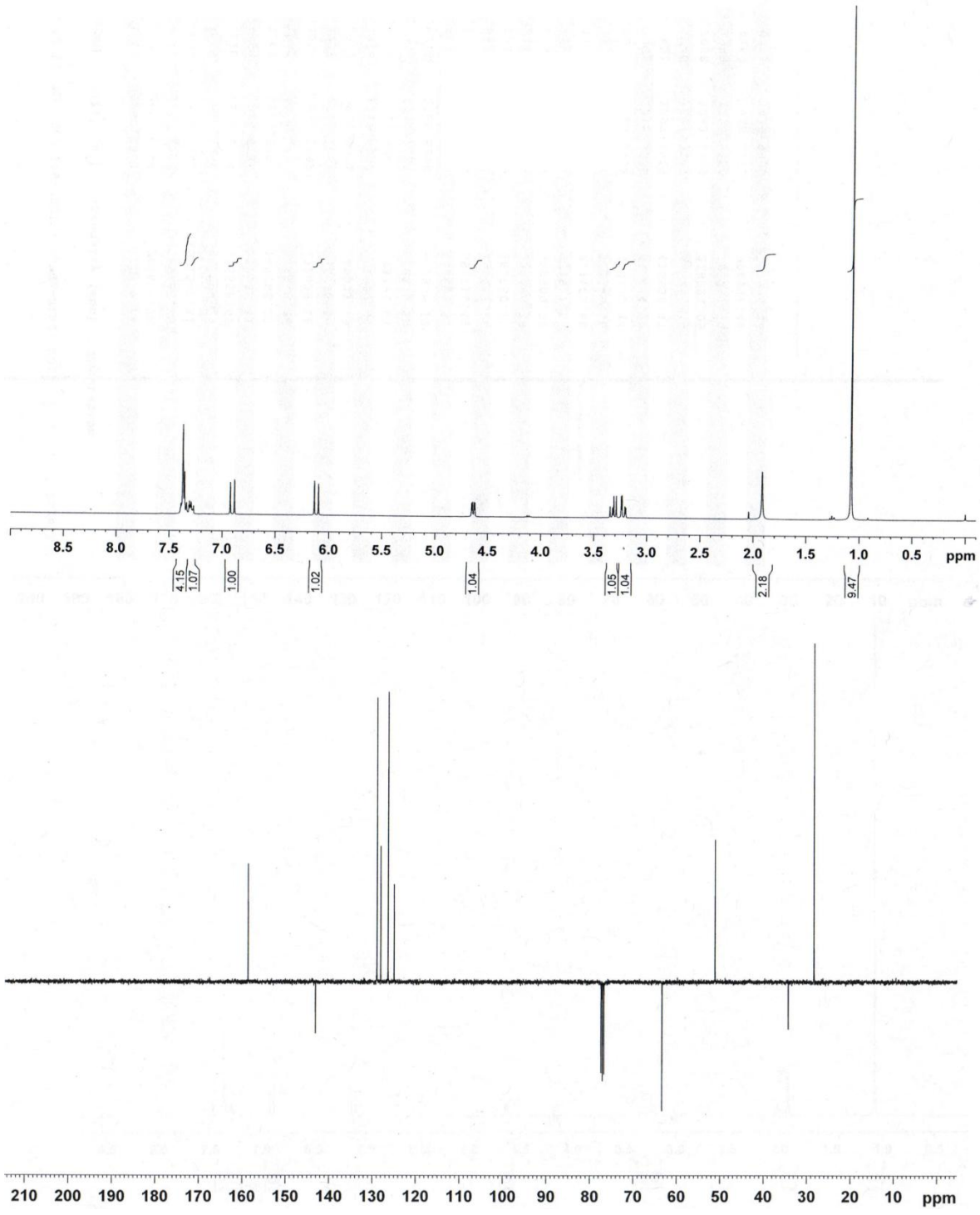
7d, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

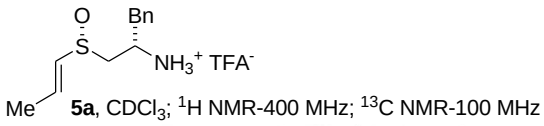




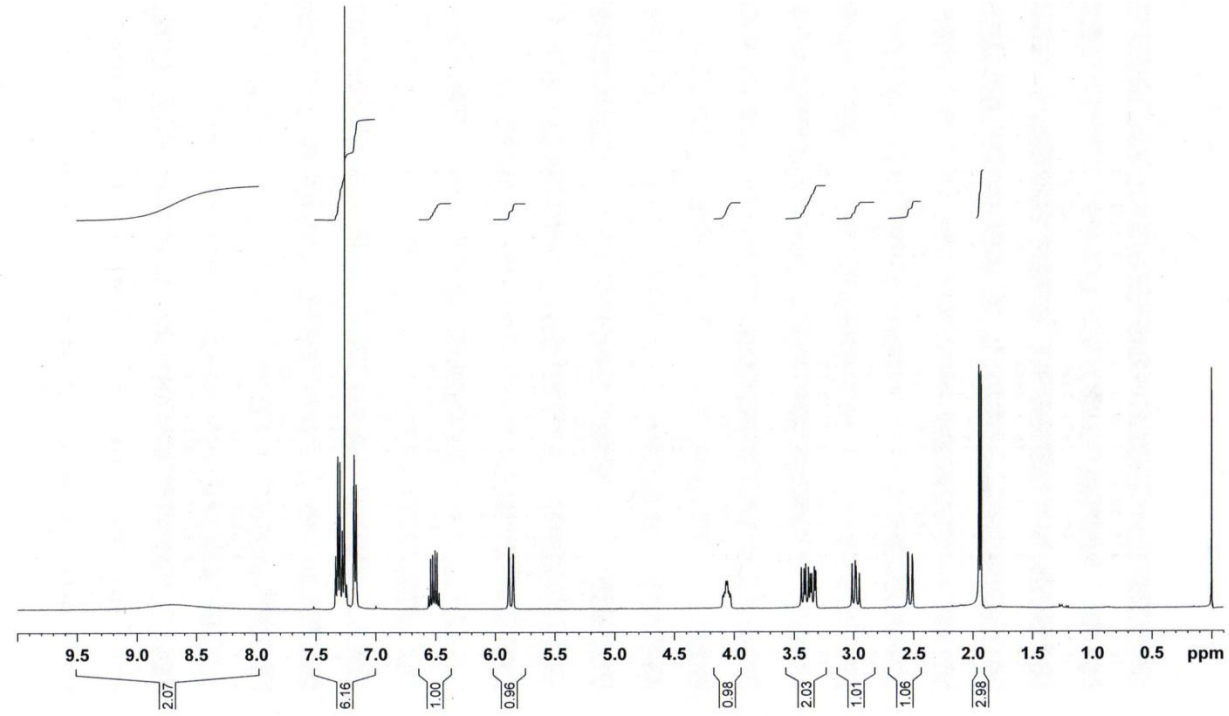


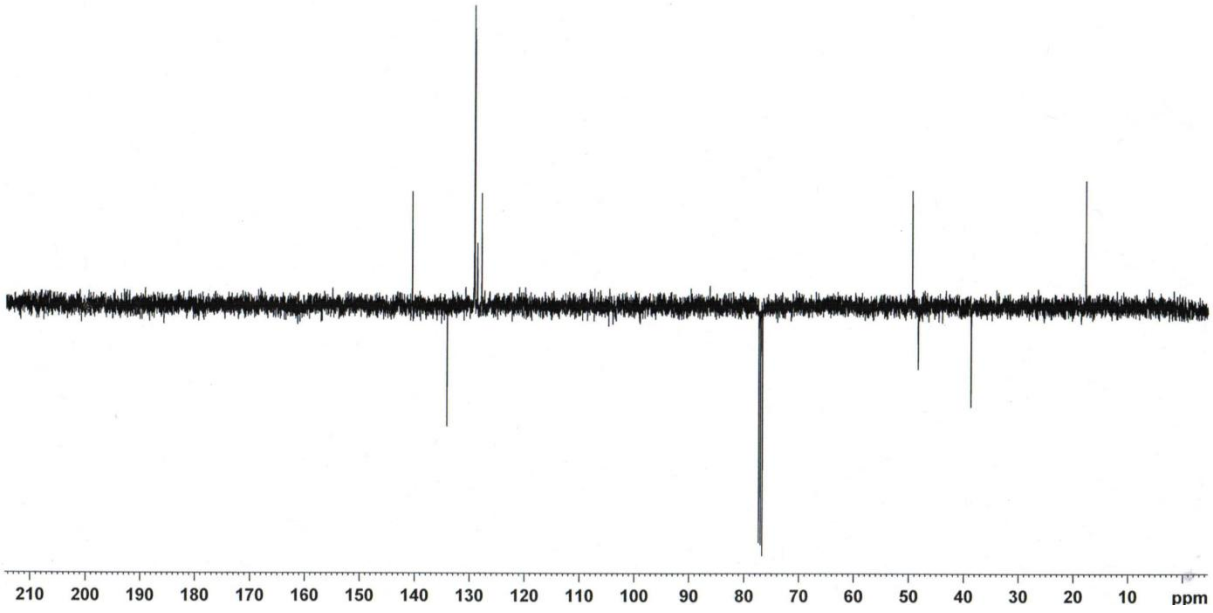
7e, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

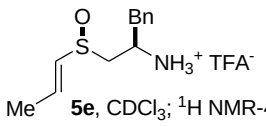




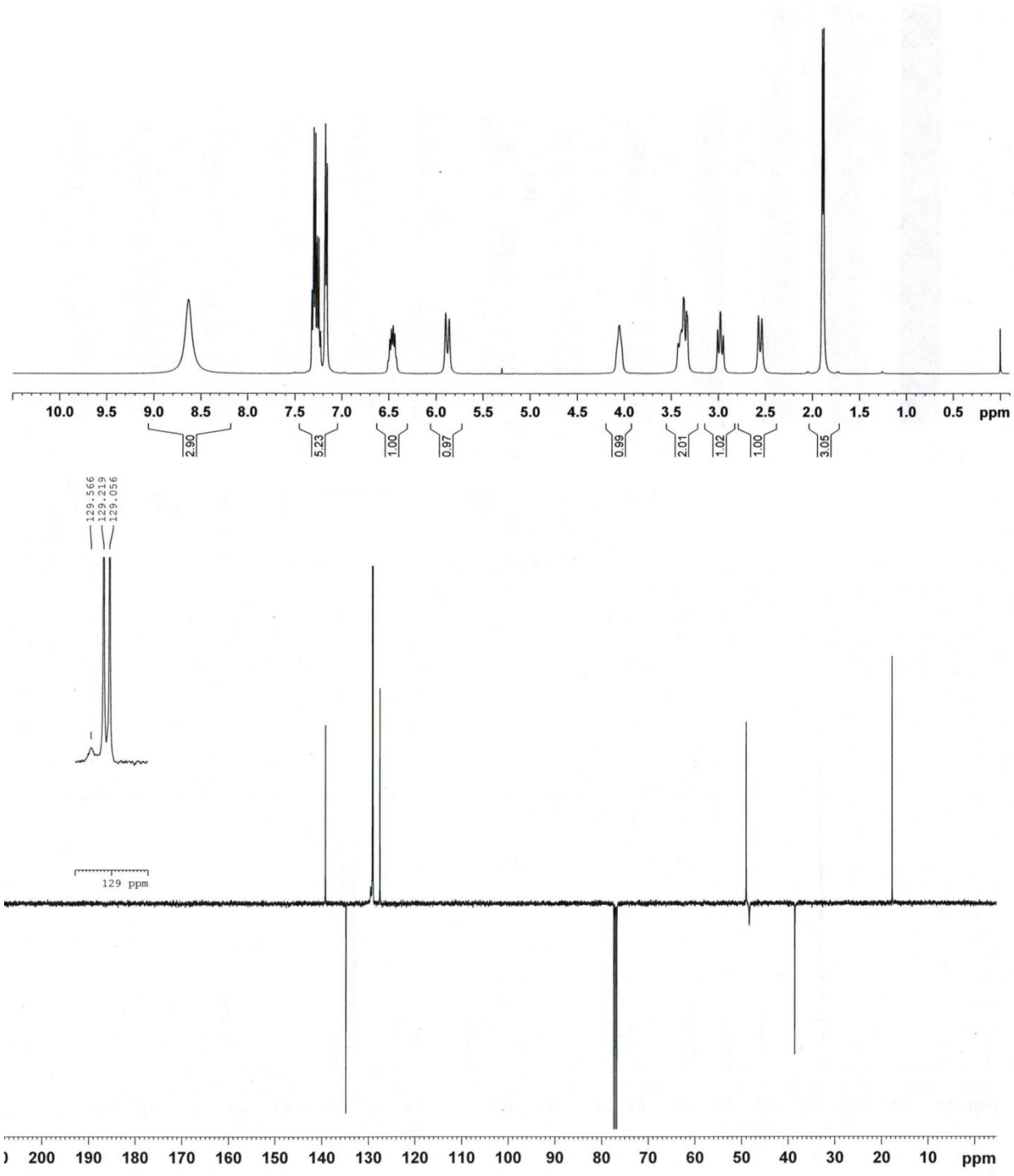
5a, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz



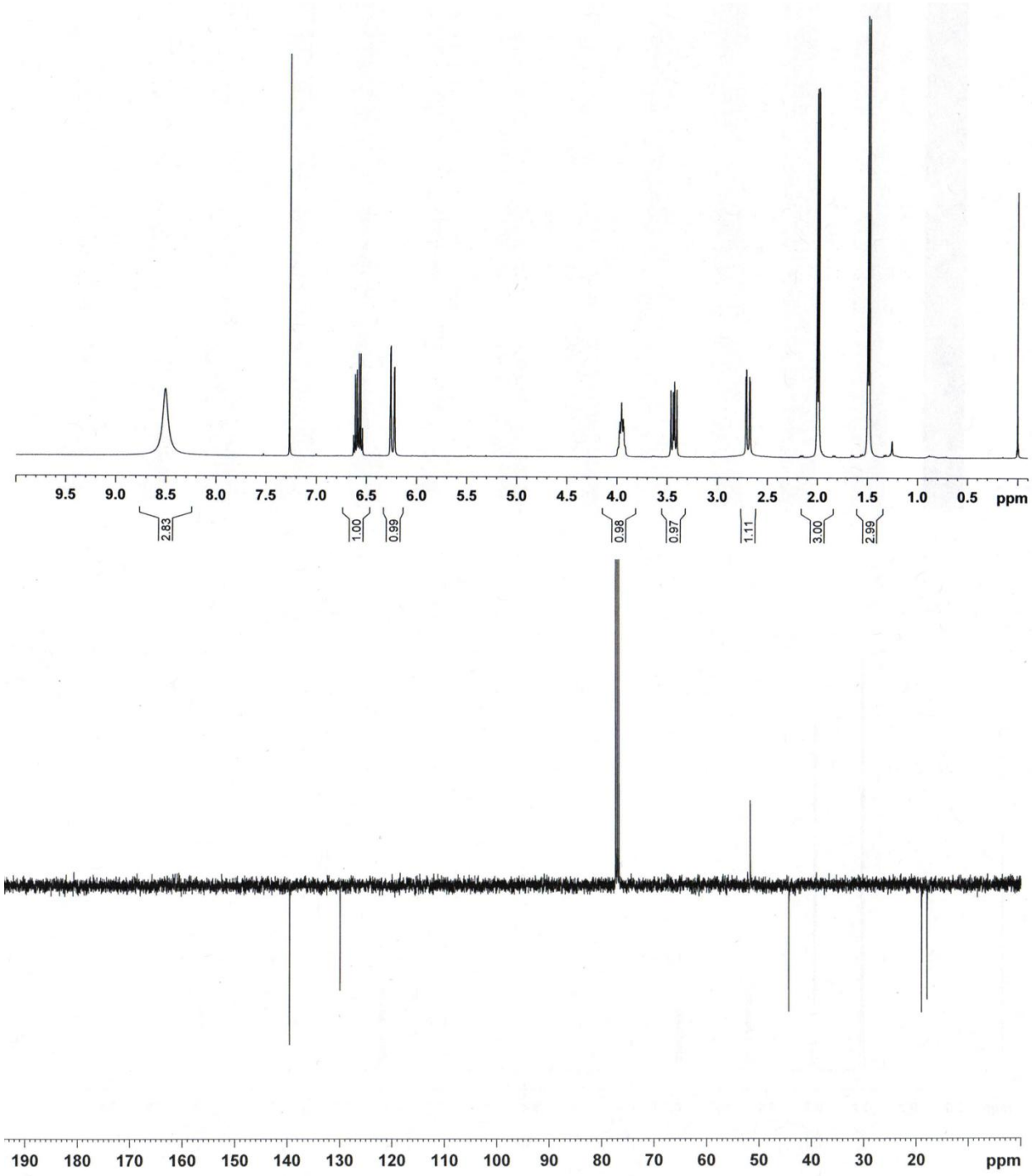


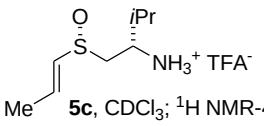


5e, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

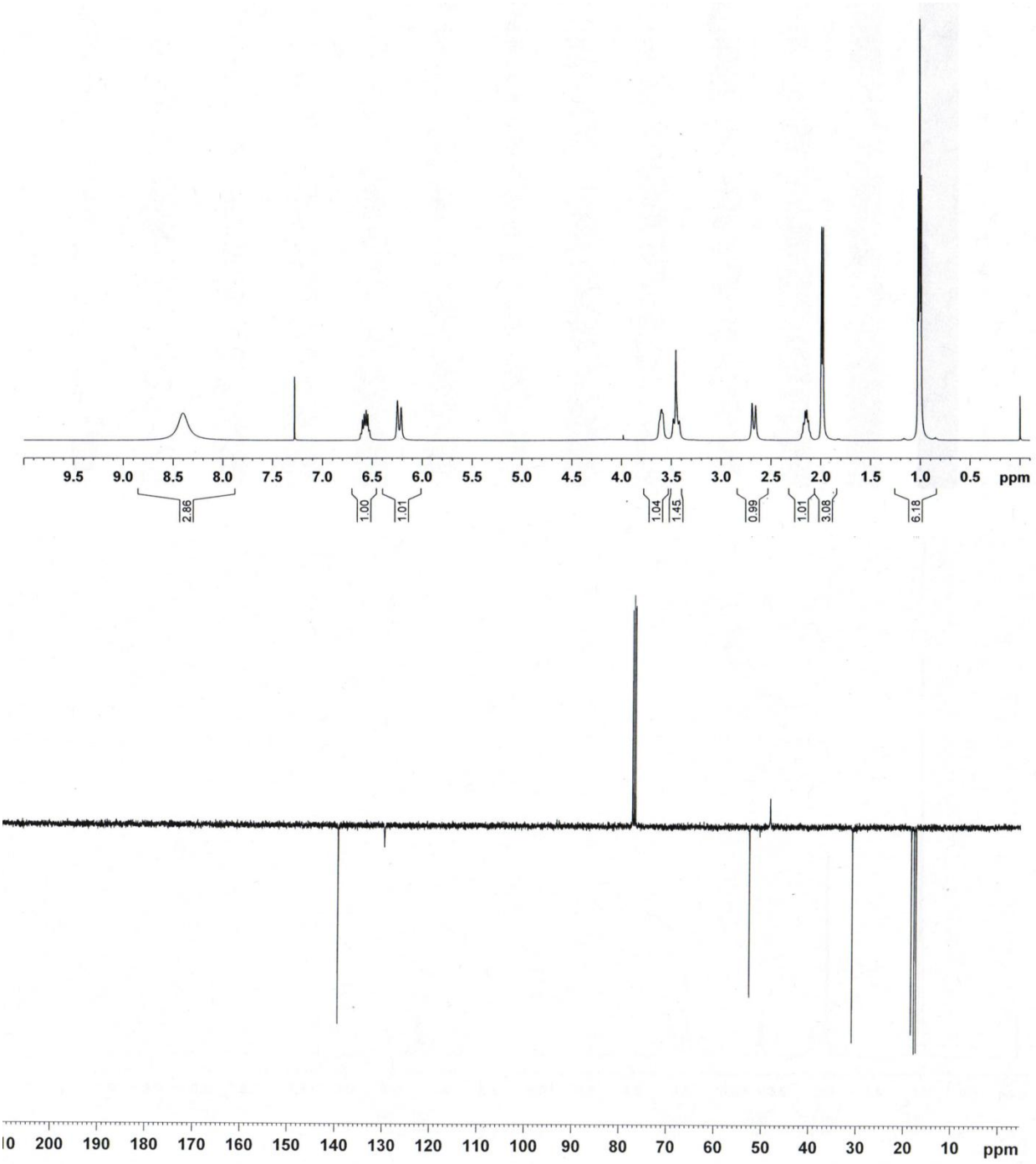


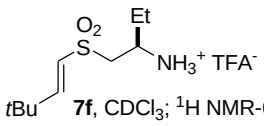
5b, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz



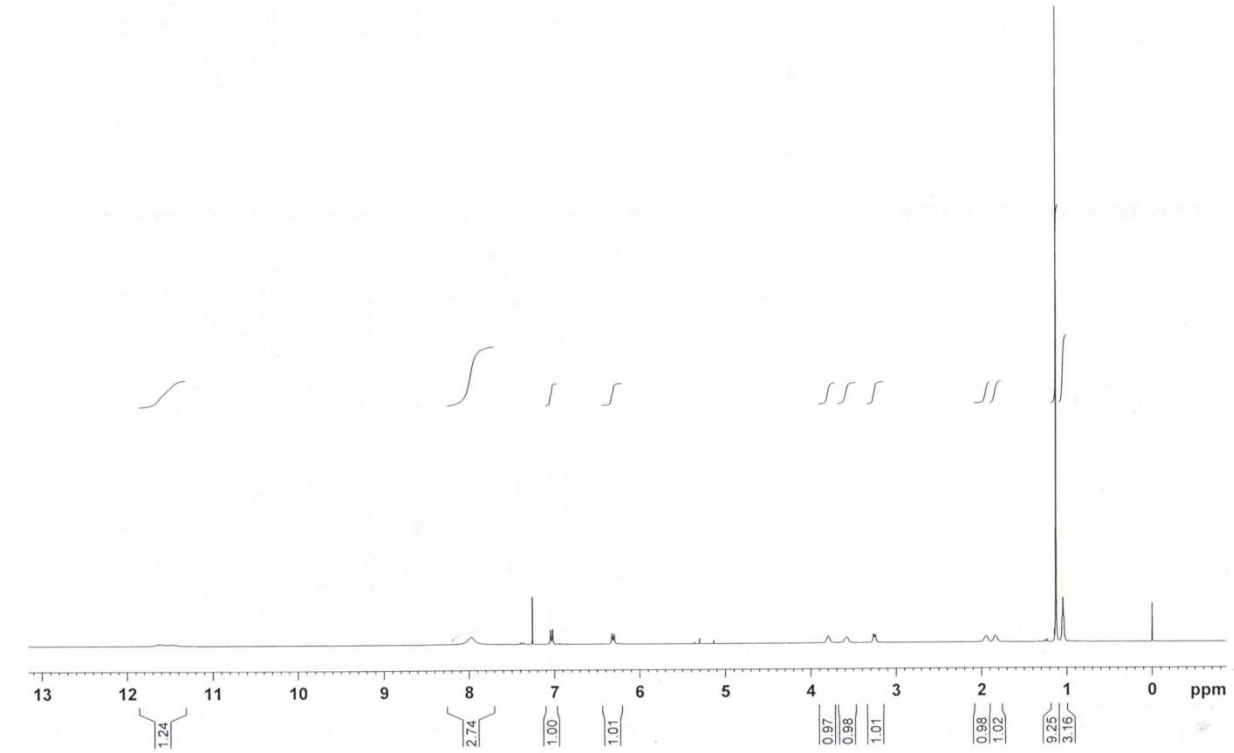


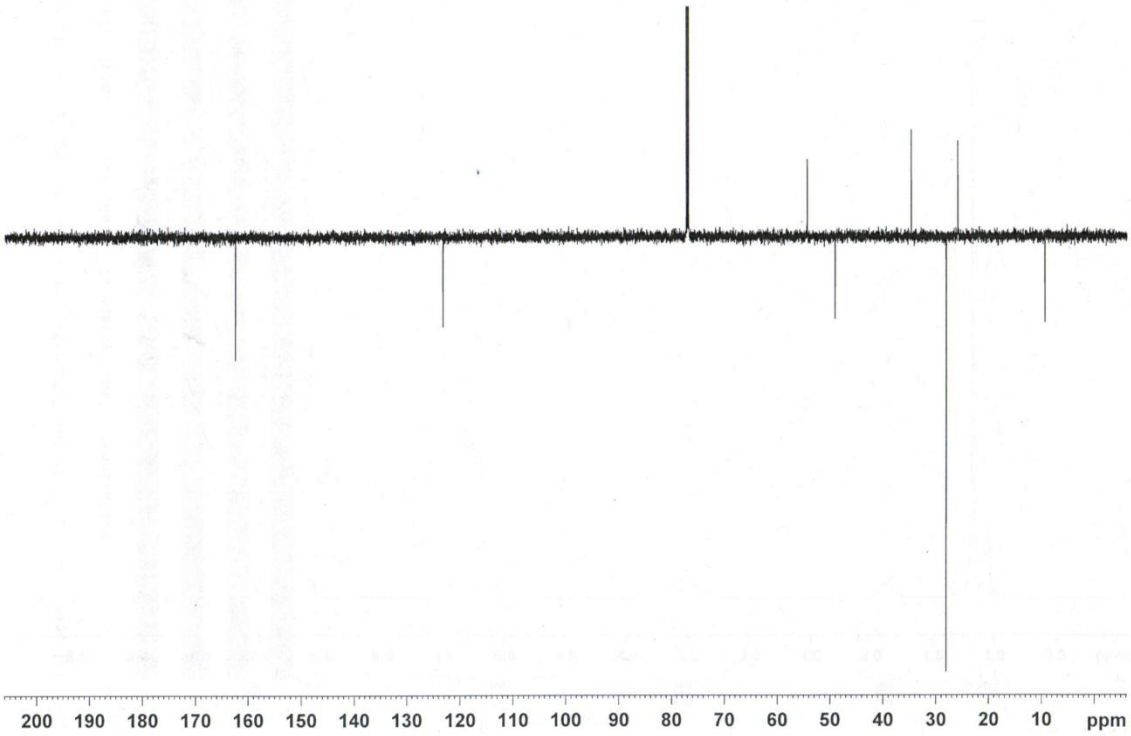
5c, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

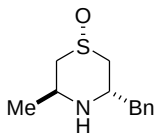




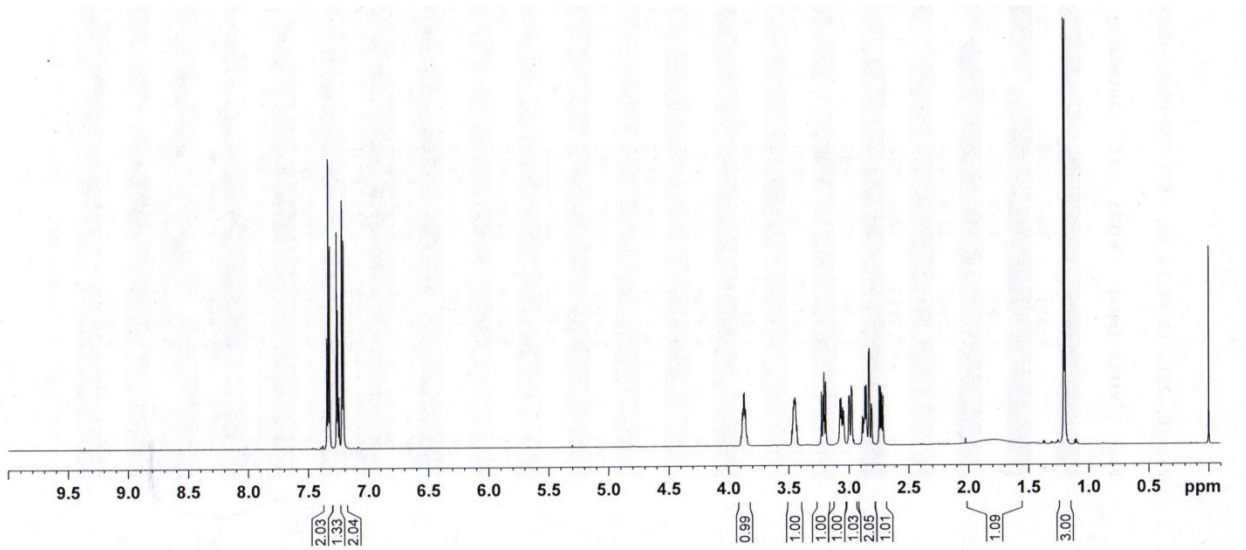
7f, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

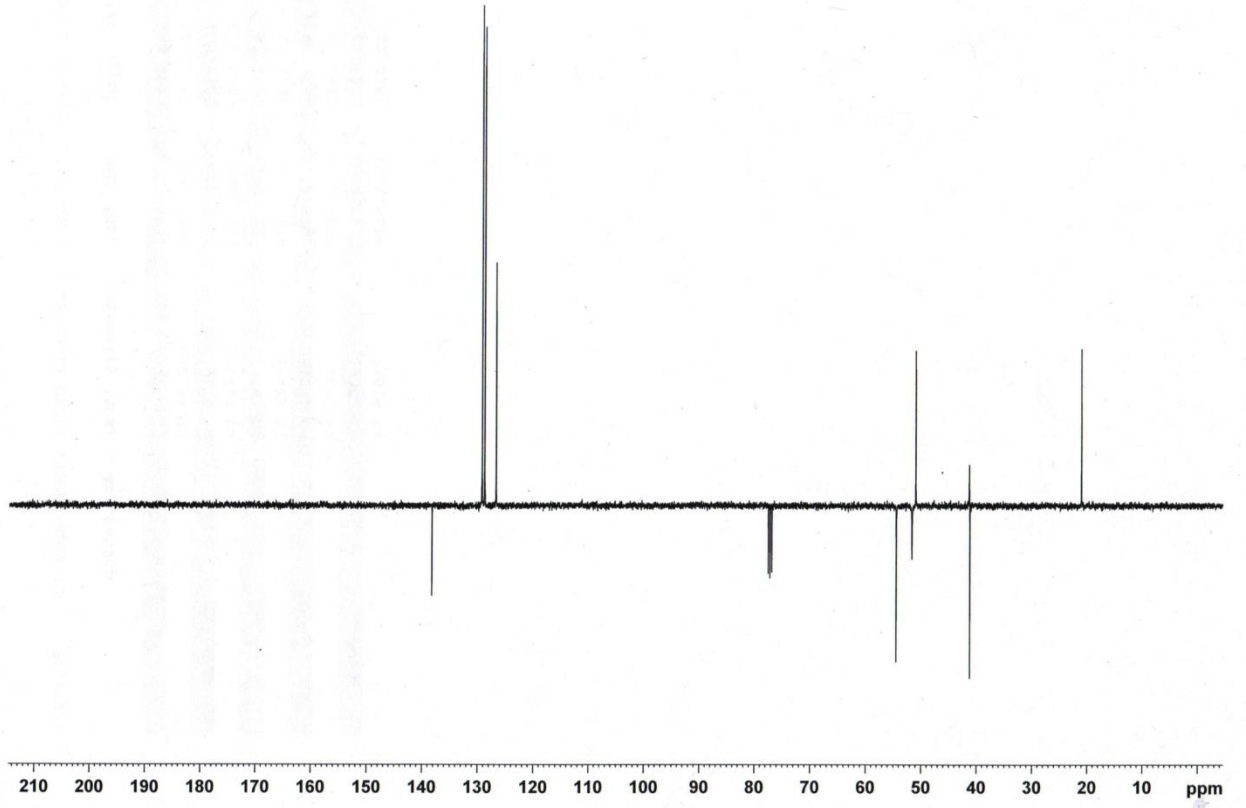


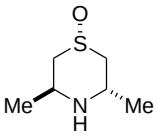




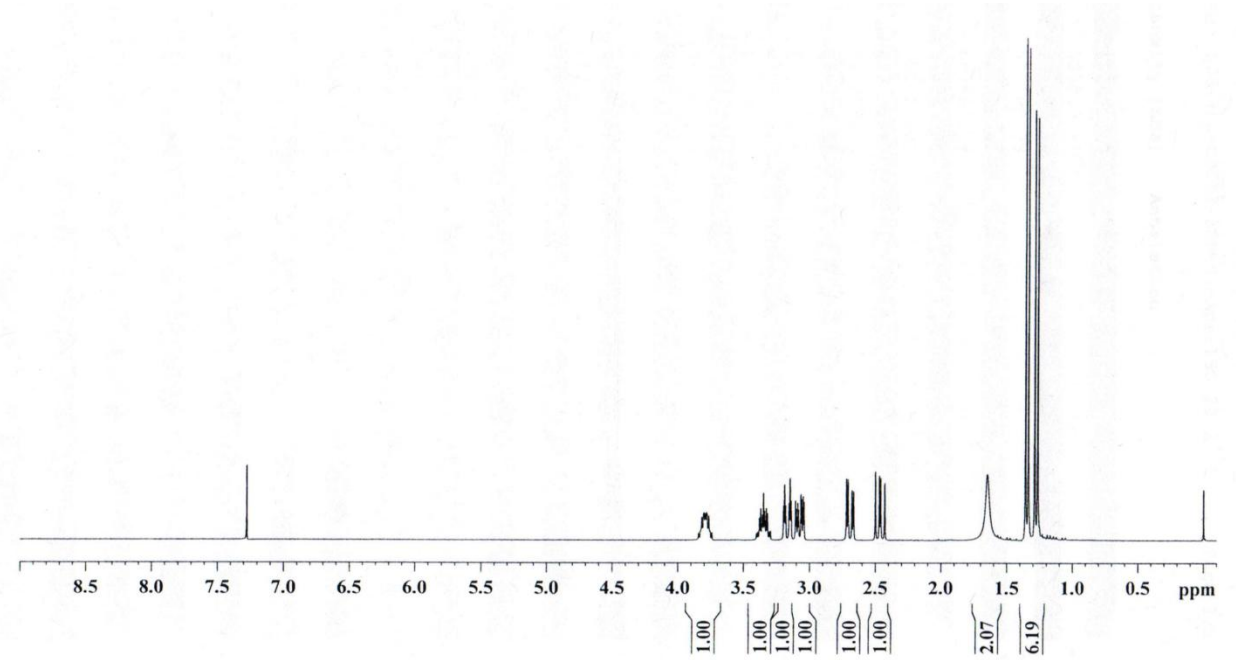
6a, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-100 MHz

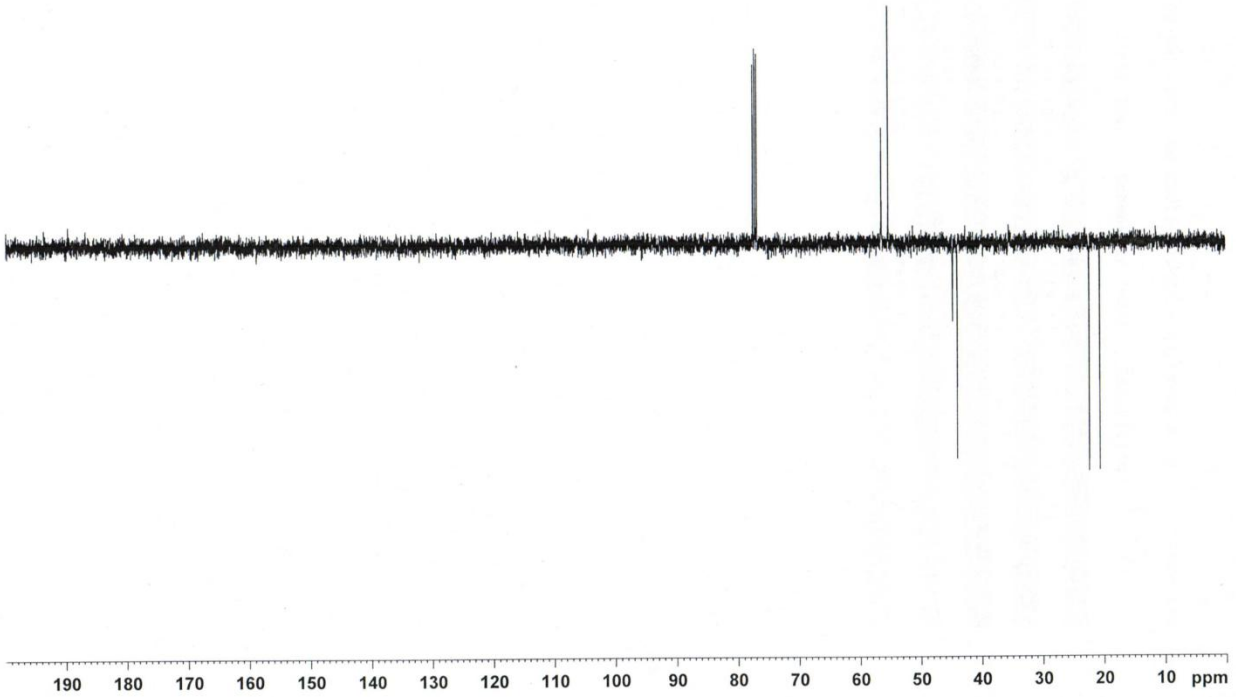


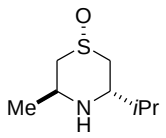




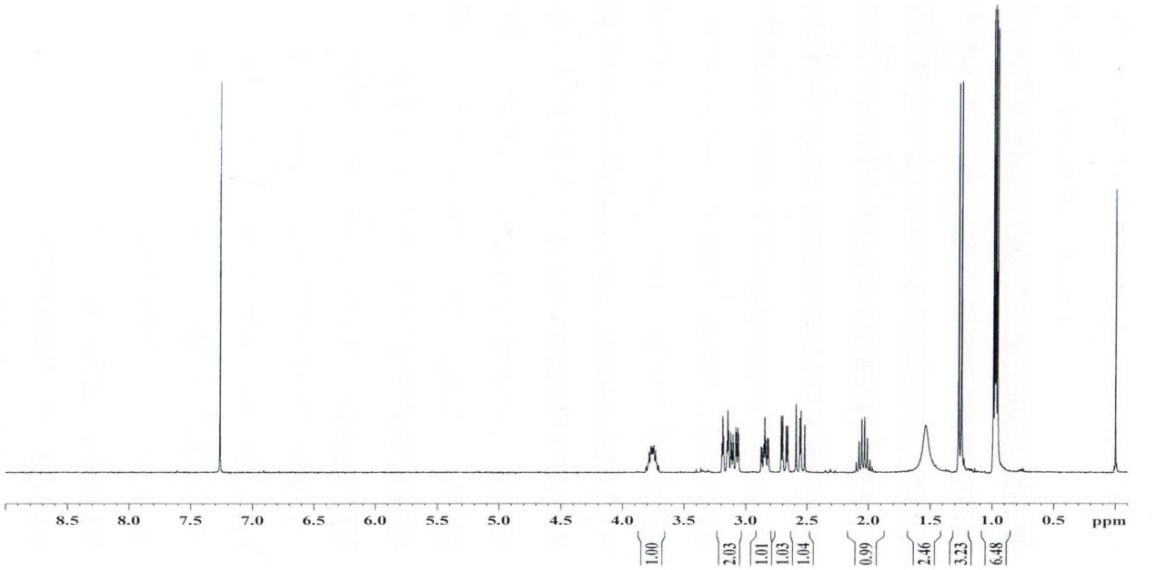
6b, $CDCl_3$; ^1H NMR-300 MHz; ^{13}C NMR-75 MHz

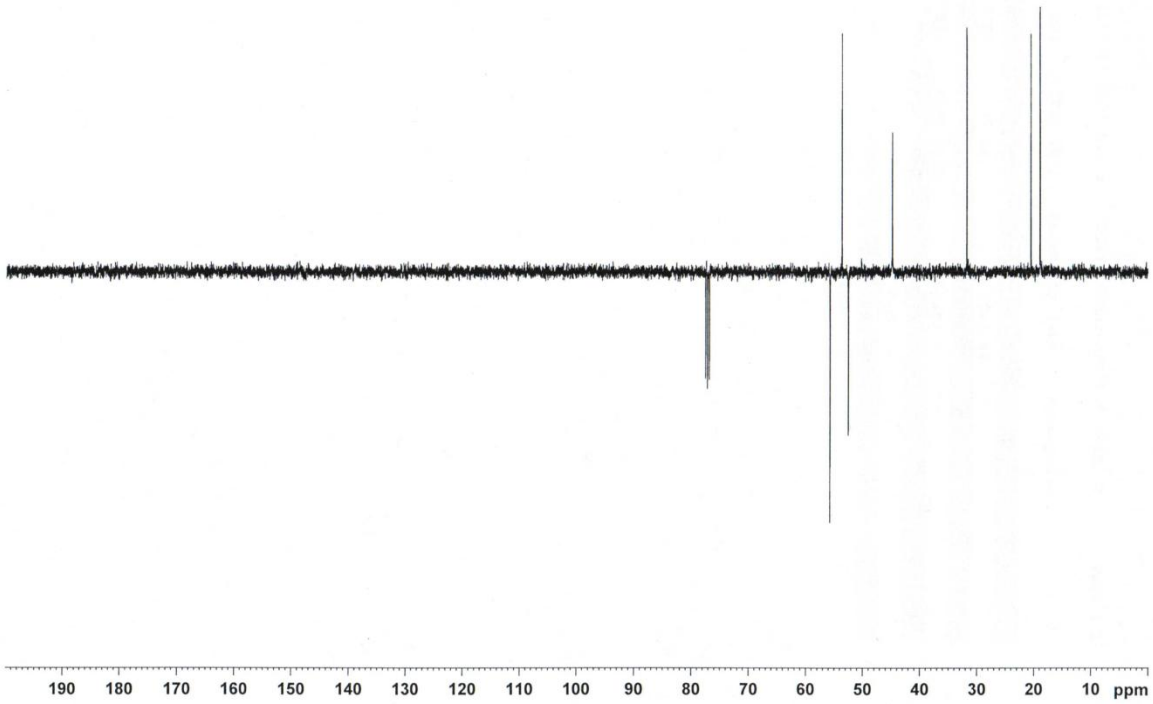


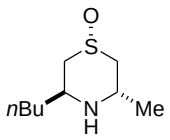




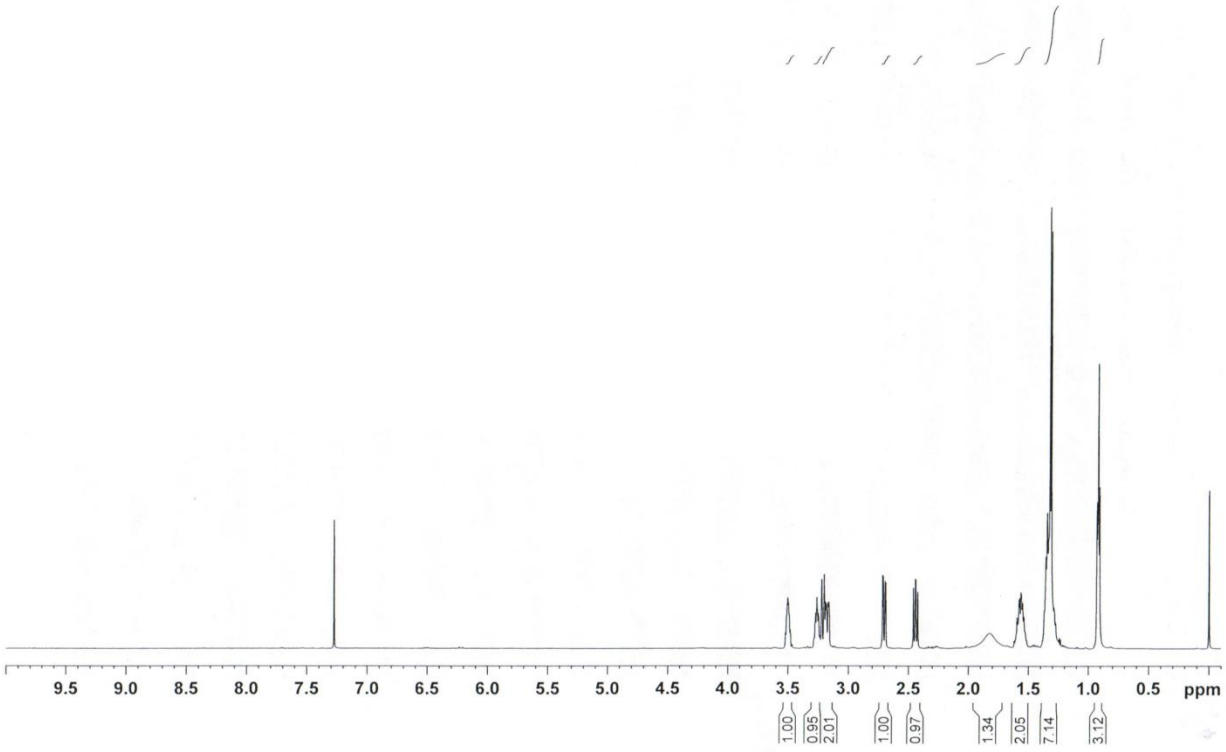
6c, $CDCl_3$; ^1H NMR-300 MHz; ^{13}C NMR-75 MHz

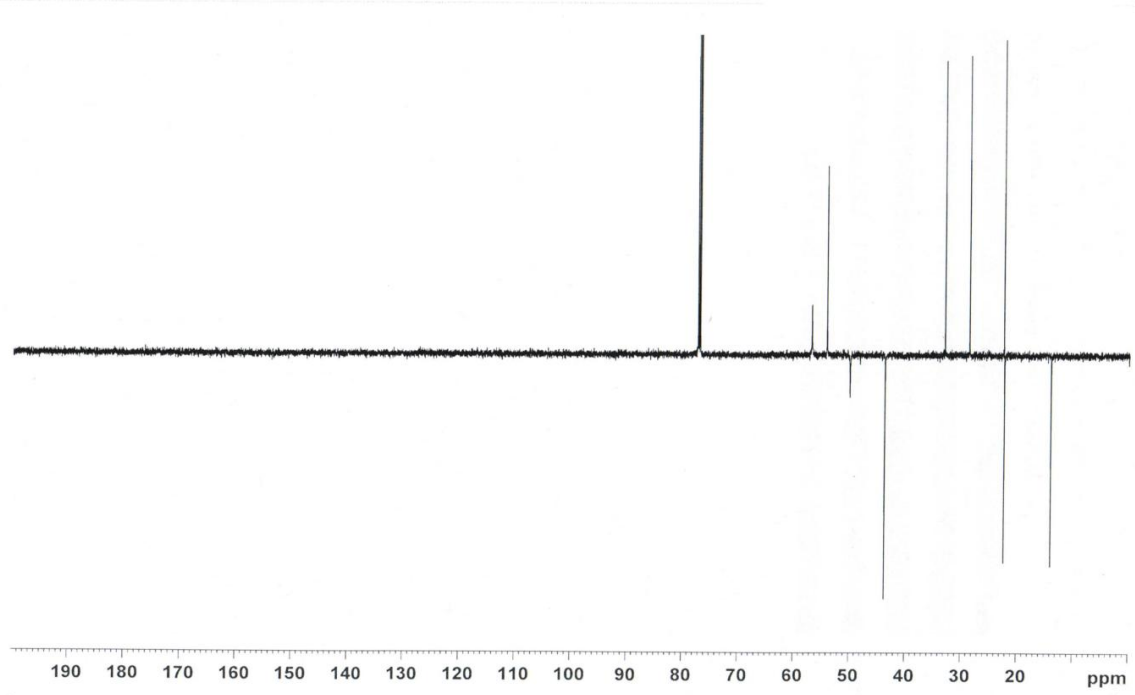


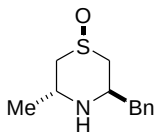




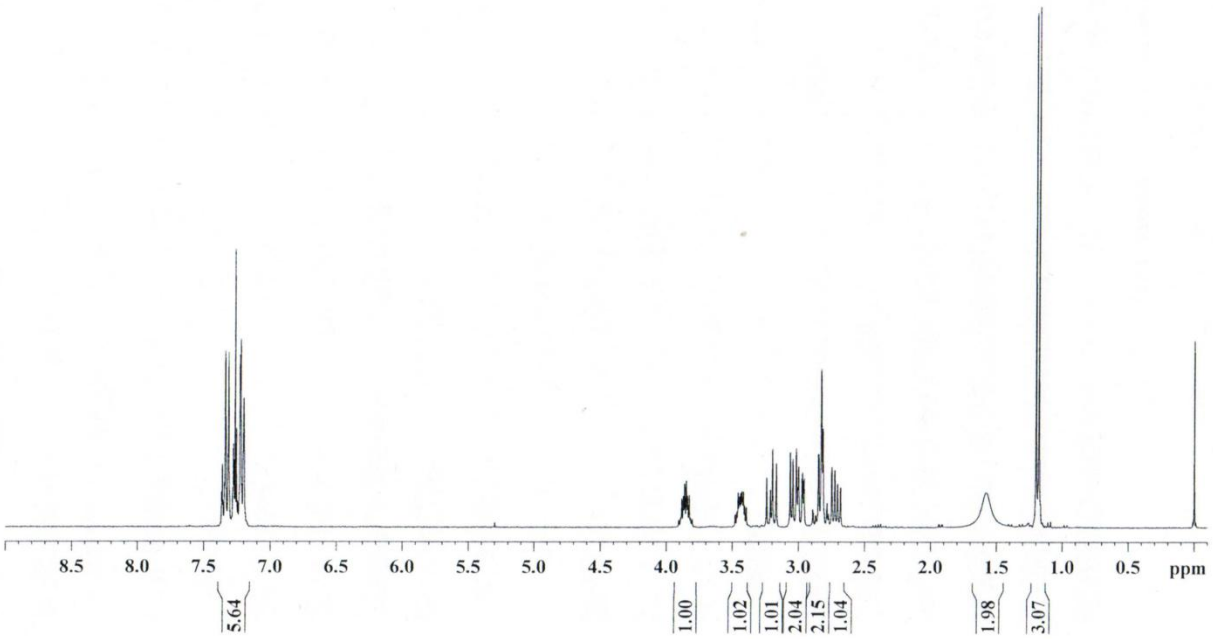
6d, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

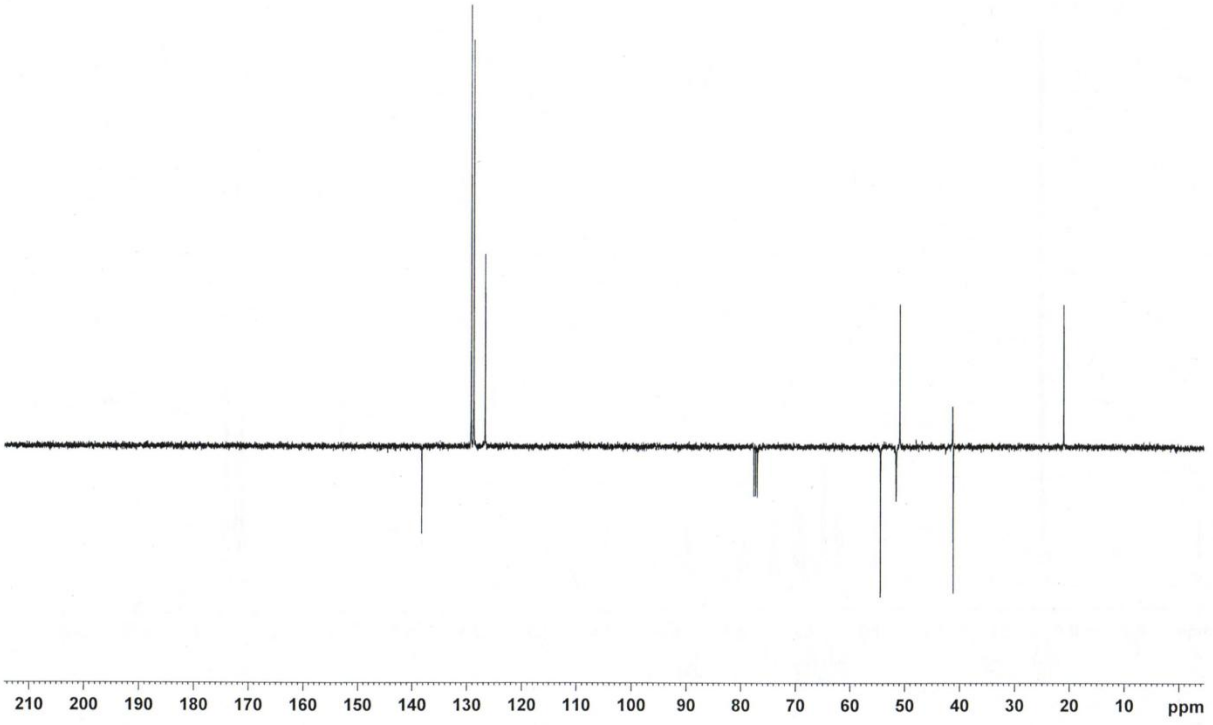


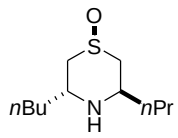




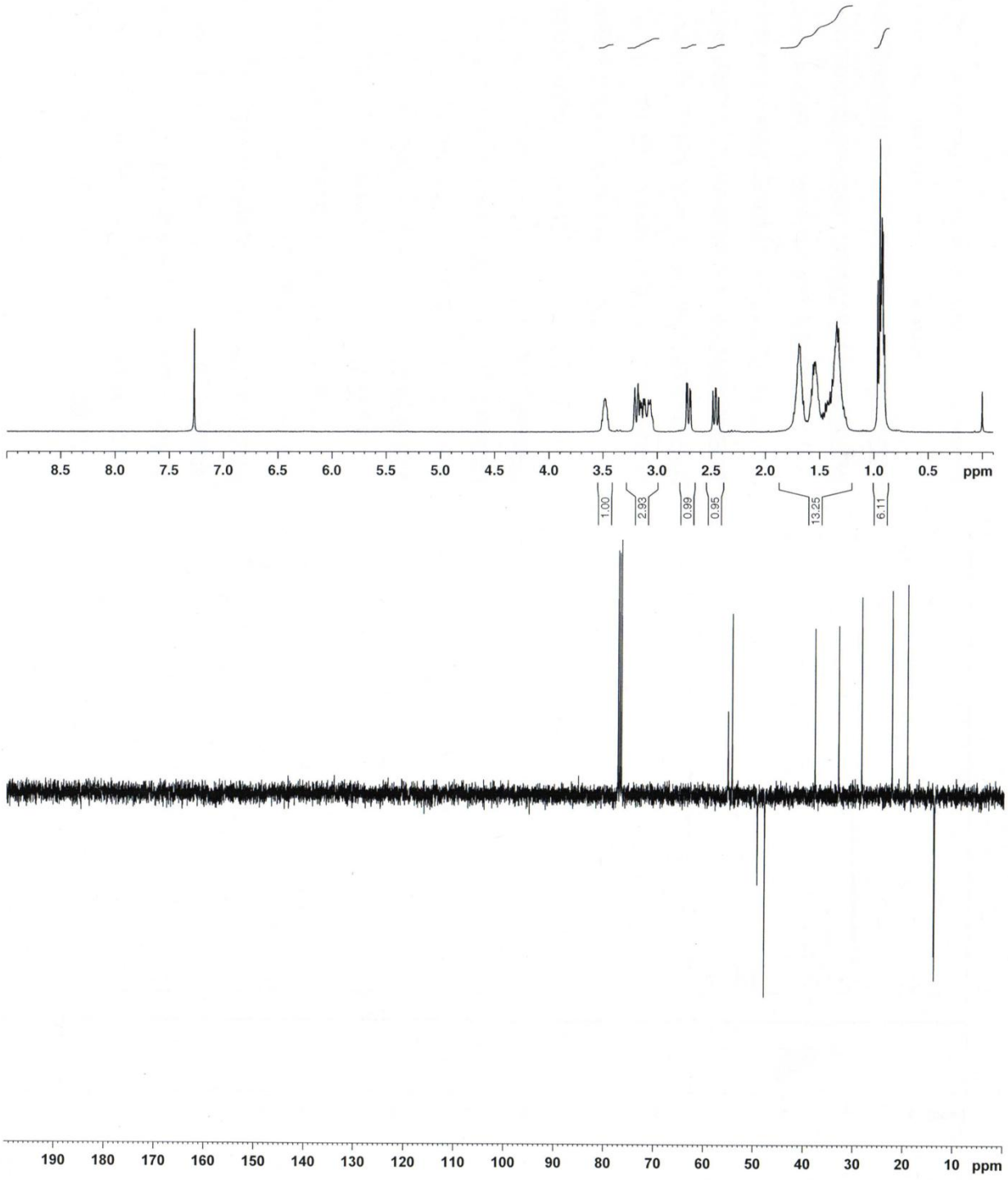
6e, $CDCl_3$; ^1H NMR-300 MHz; ^{13}C NMR-100 MHz

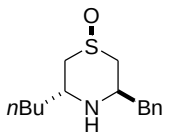




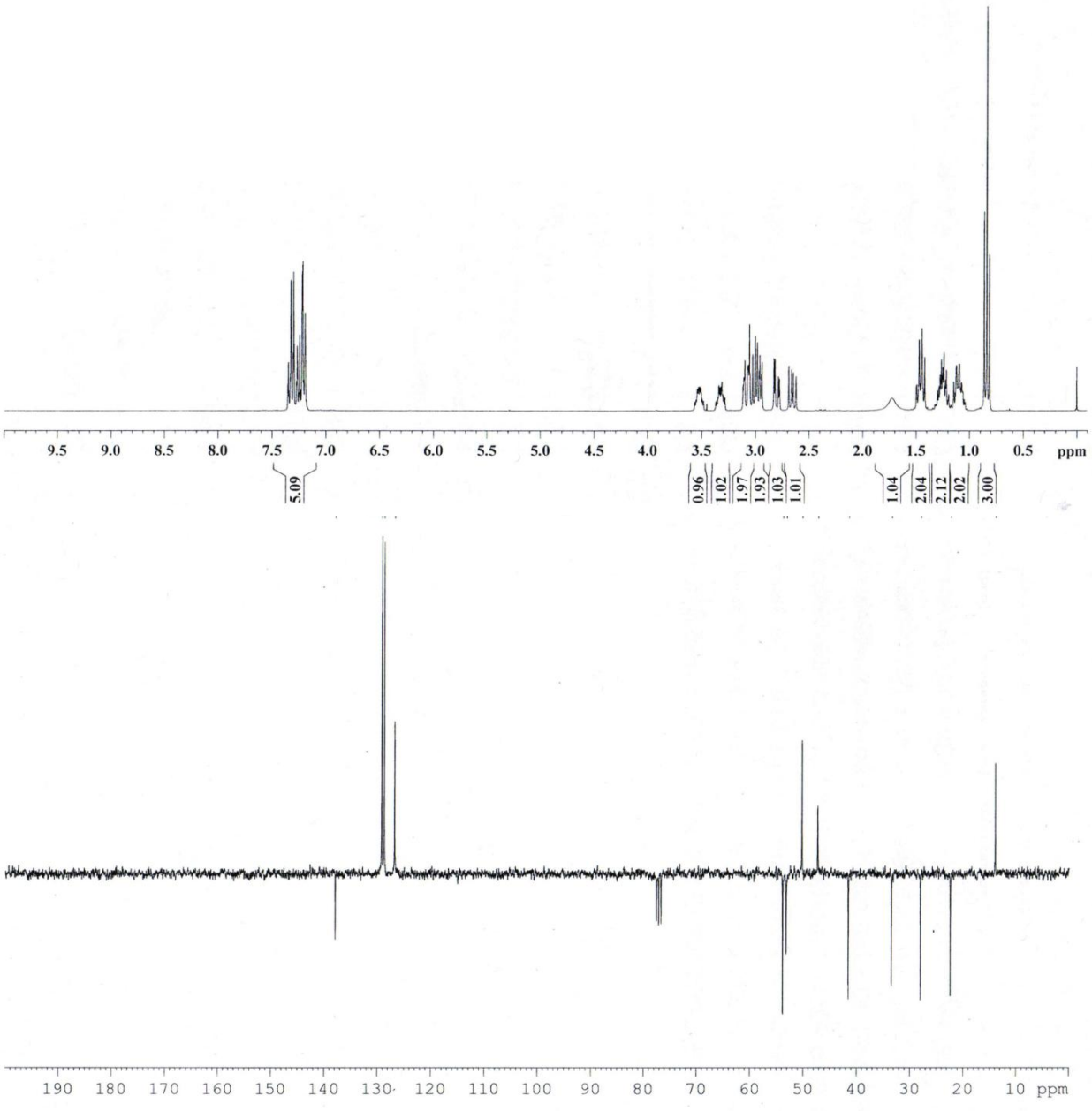


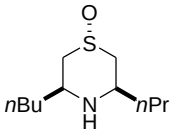
6f, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz



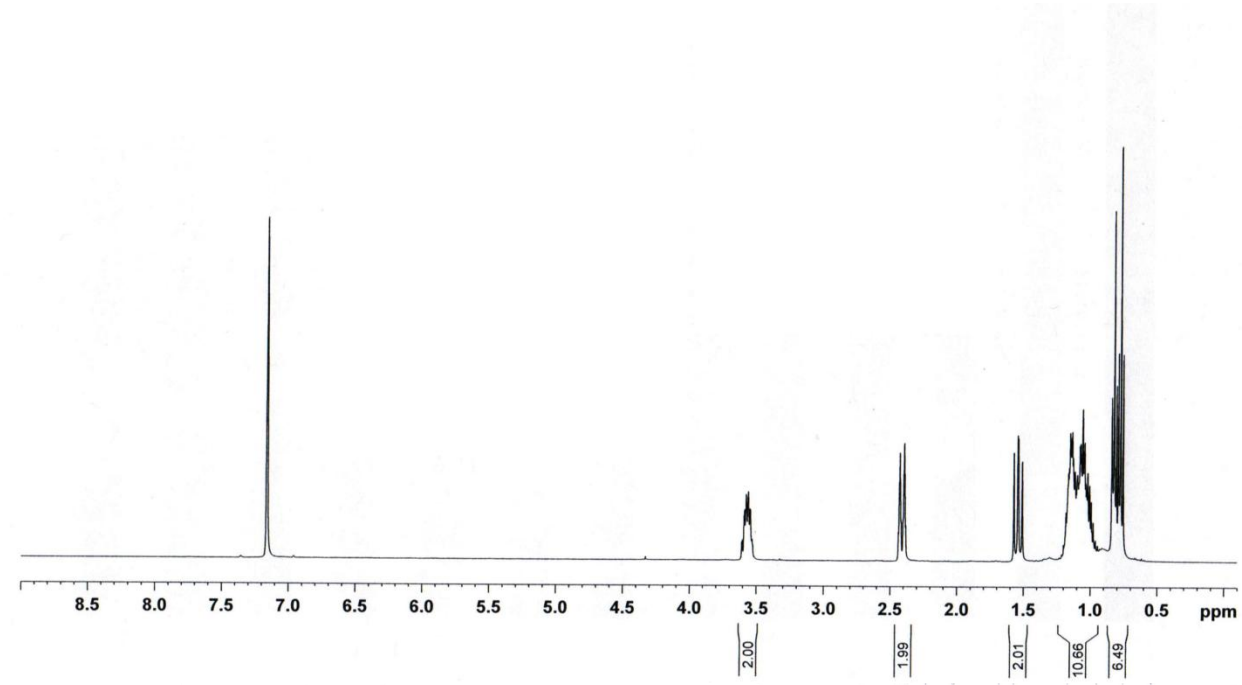


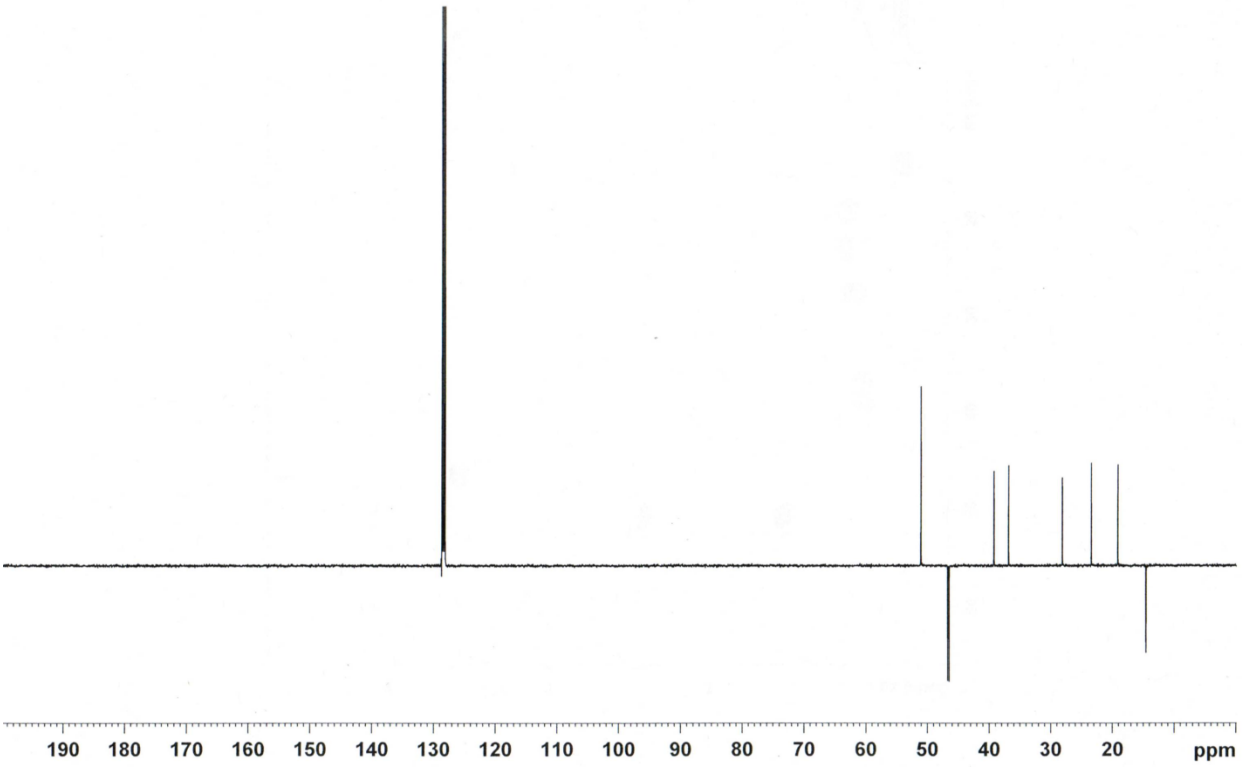
6g, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-75 MHz

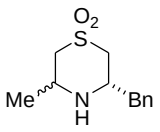




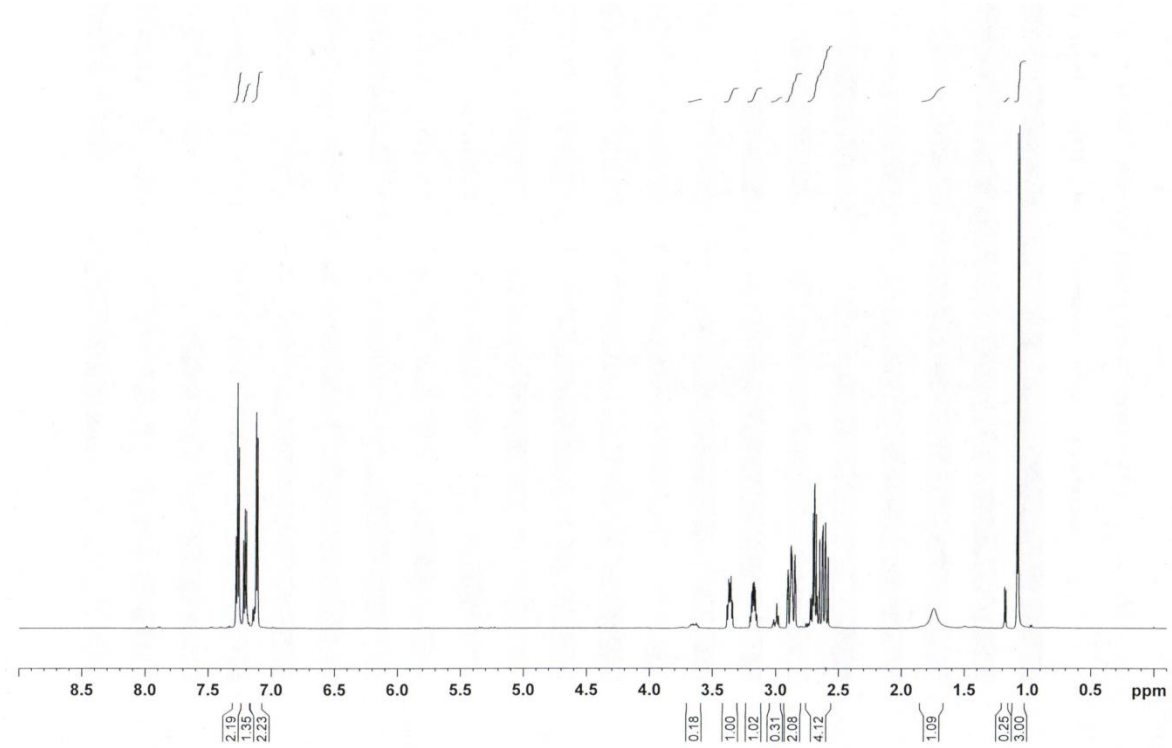
6h, C_6D_6; ^1H NMR-400 MHz; ^{13}C NMR-150.6 MHz

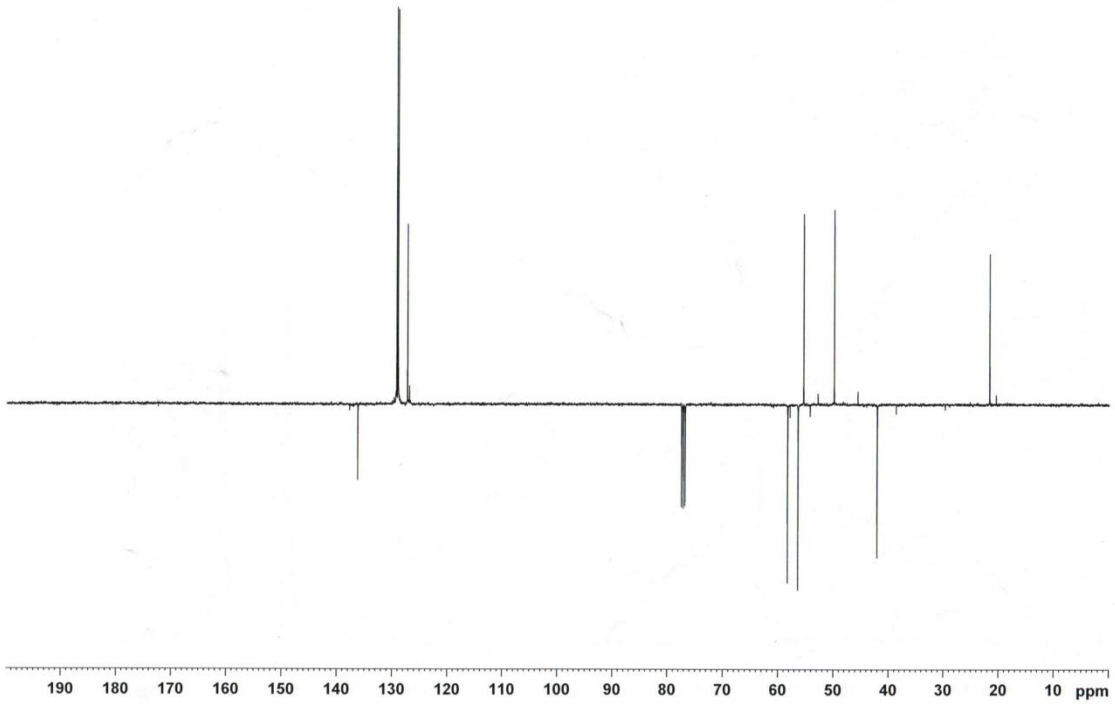


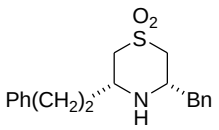




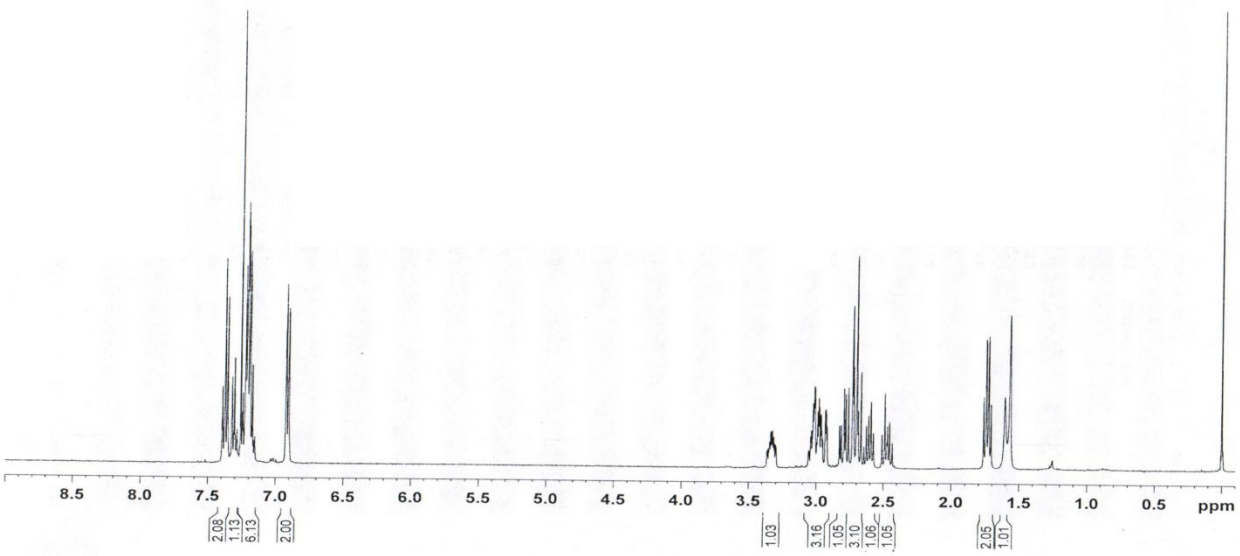
8a, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-100 MHz

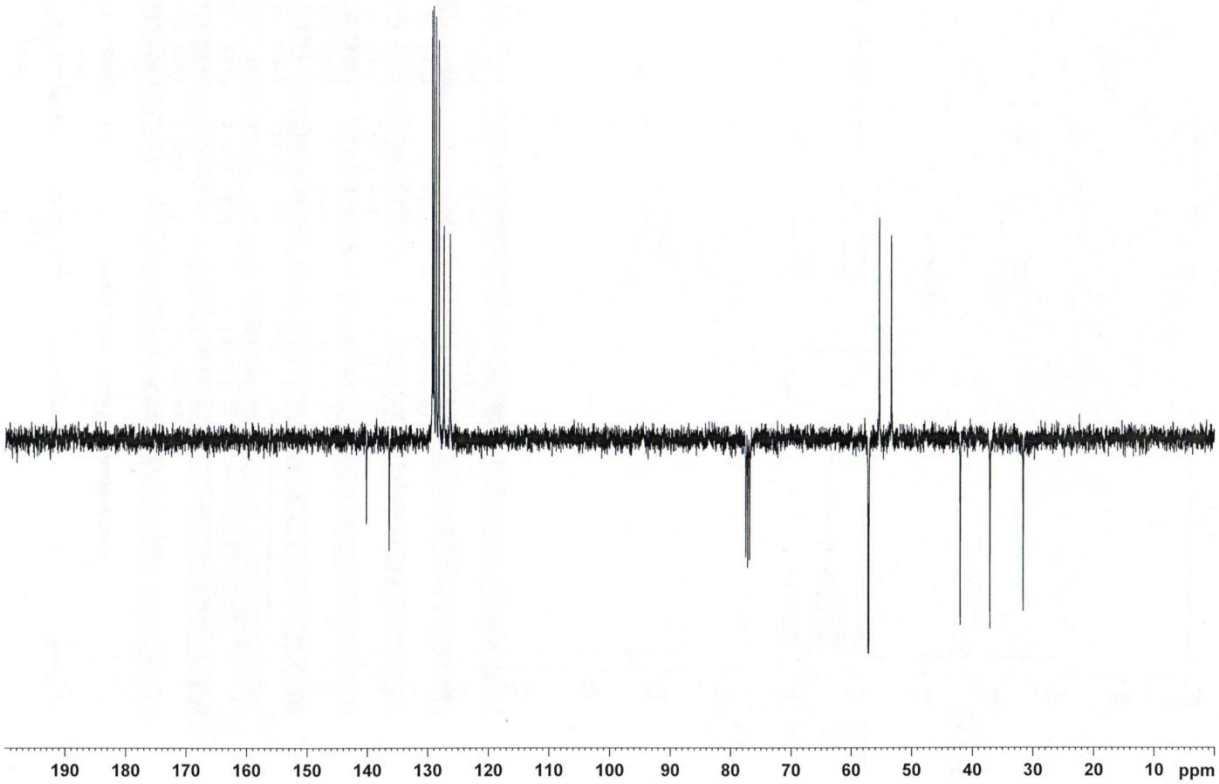


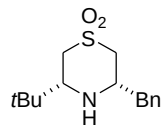




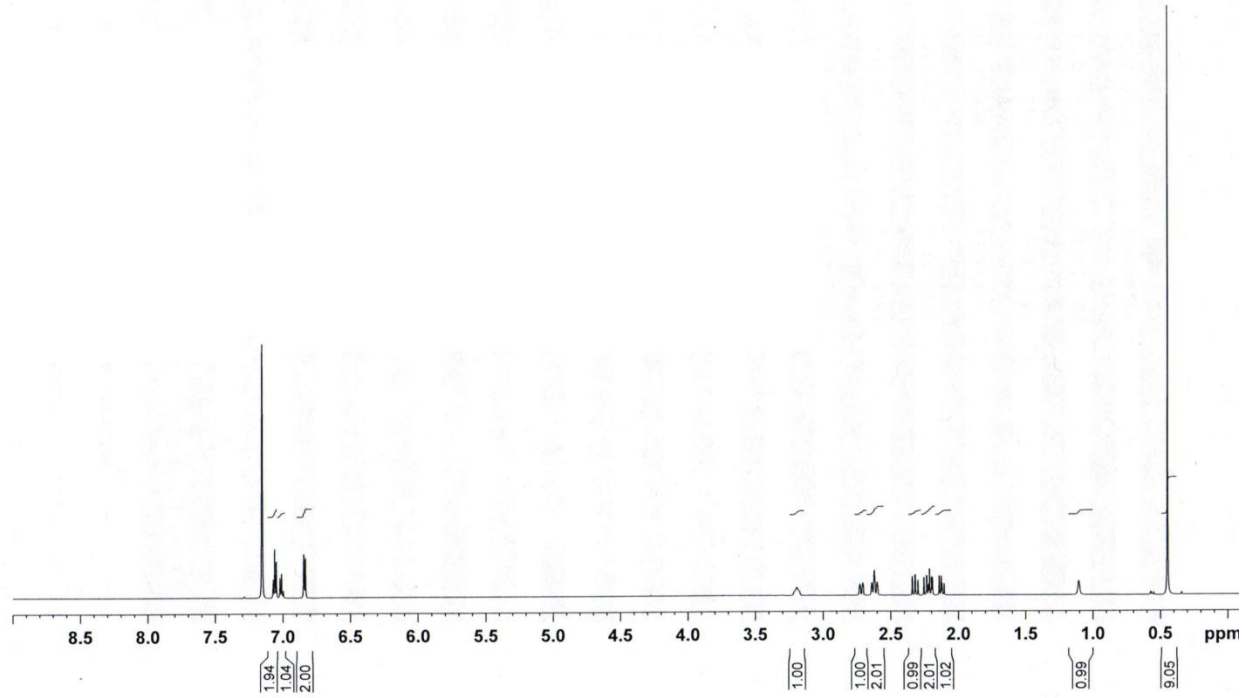
8b, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

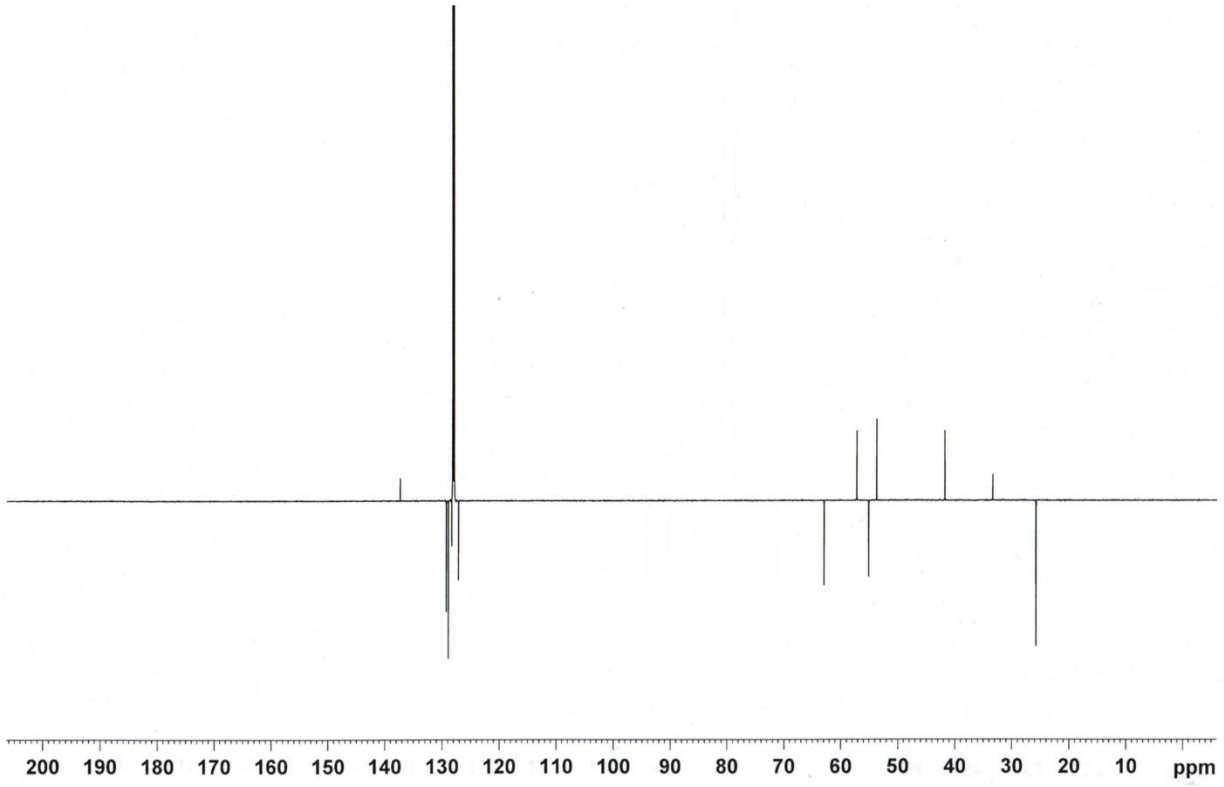


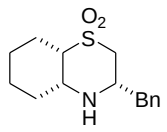




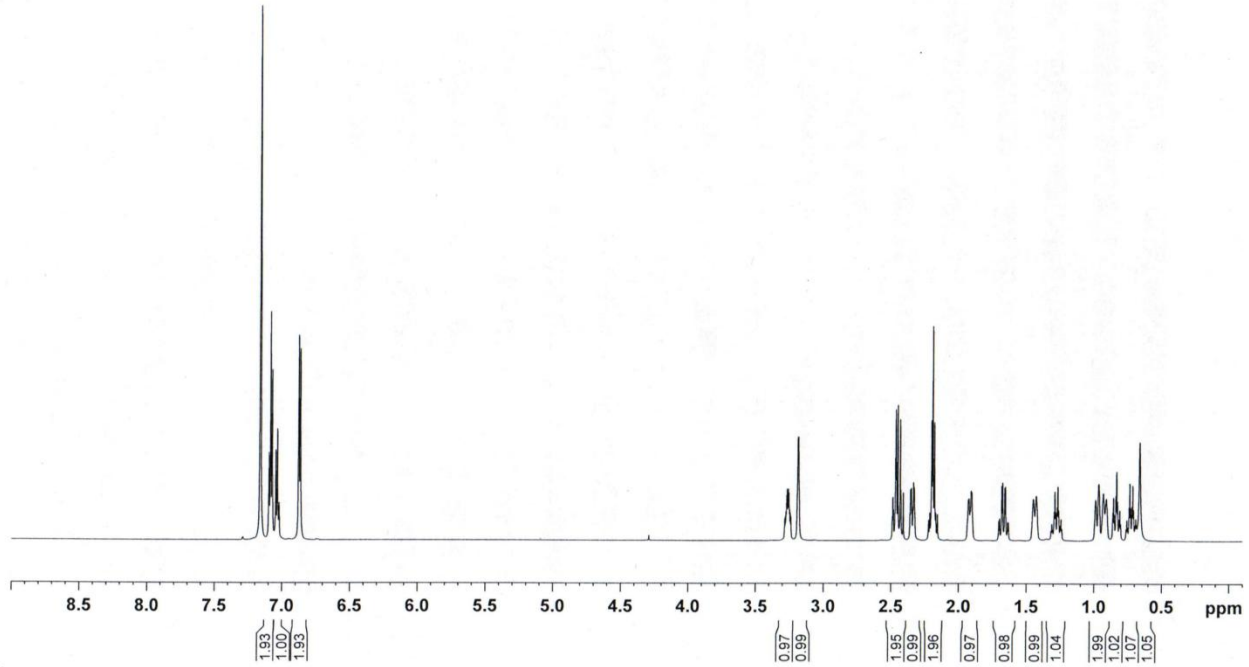
8c, C_6D_6; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

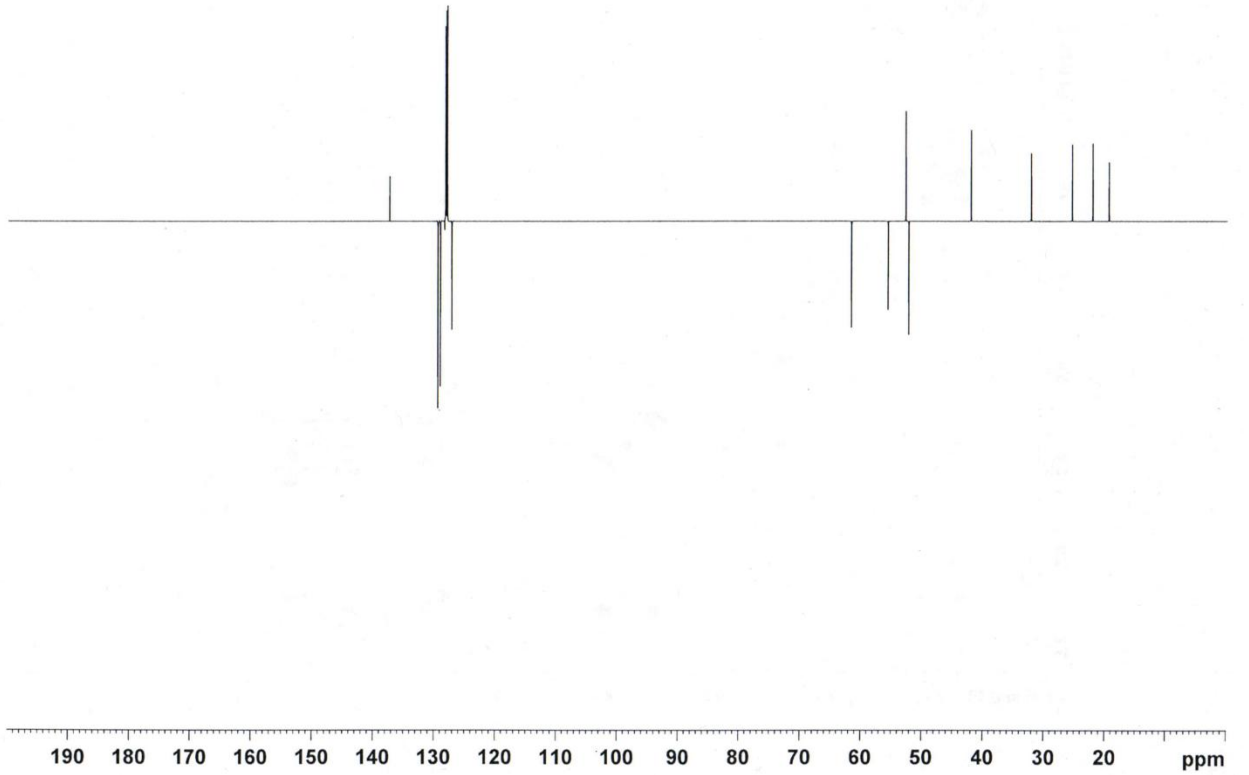


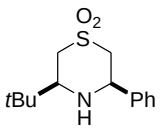




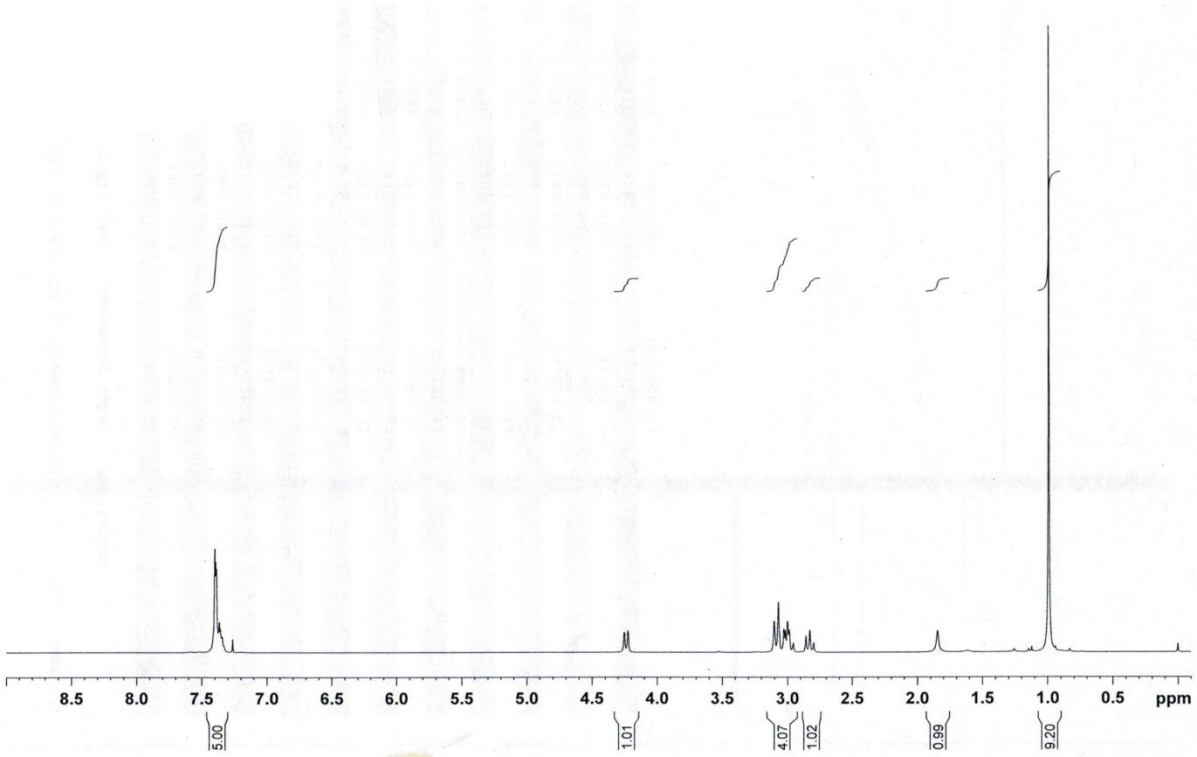
8d, C_6D_6; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

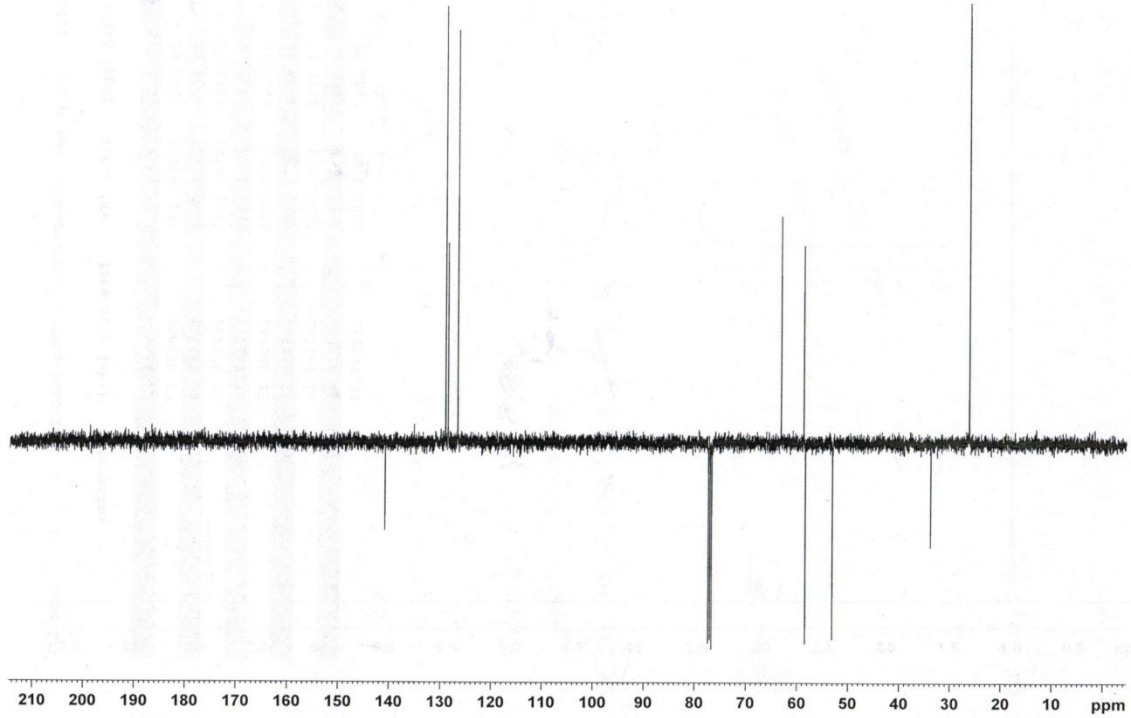


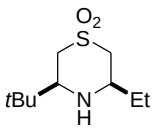




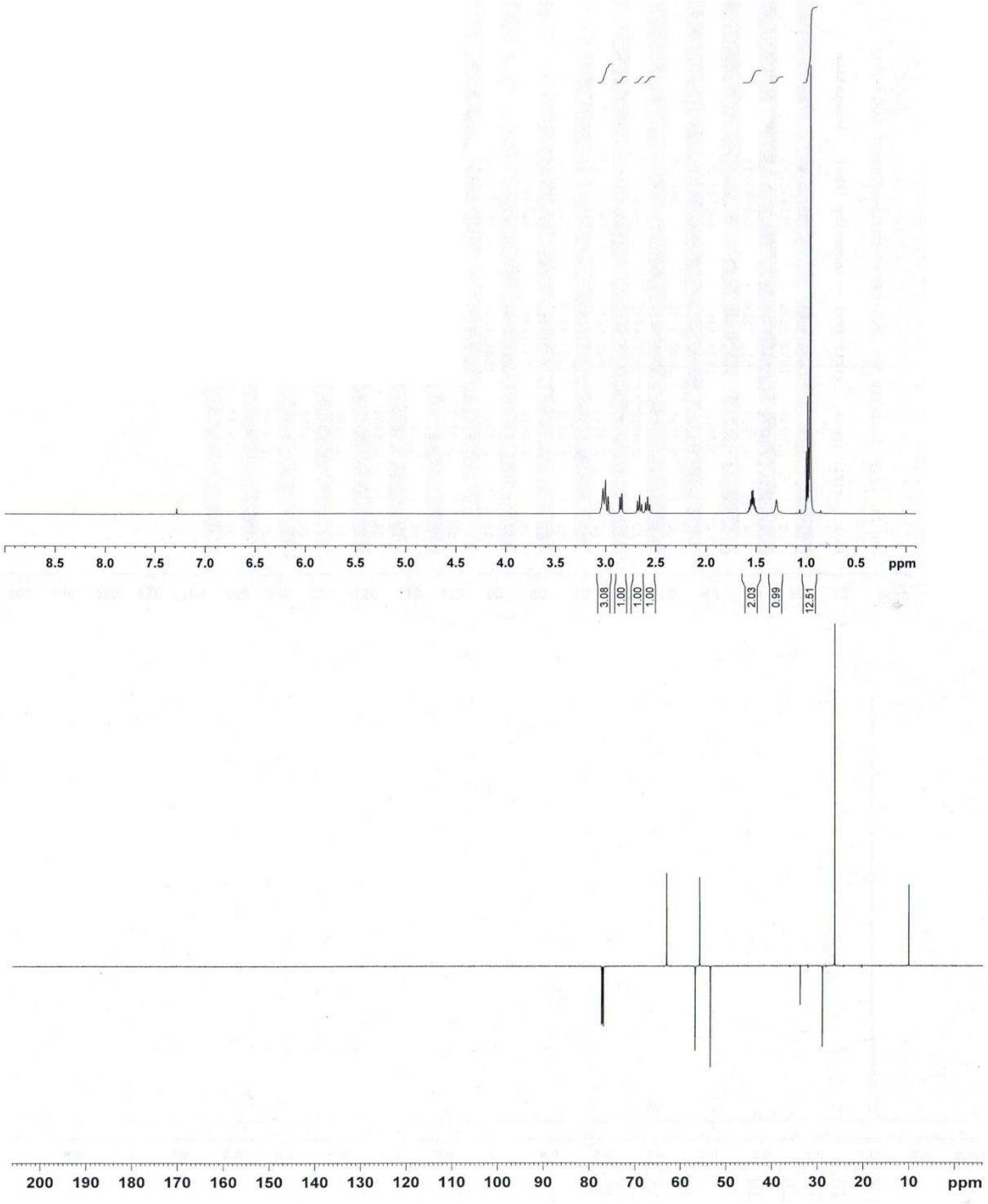
8e, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

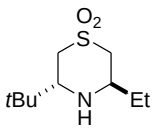




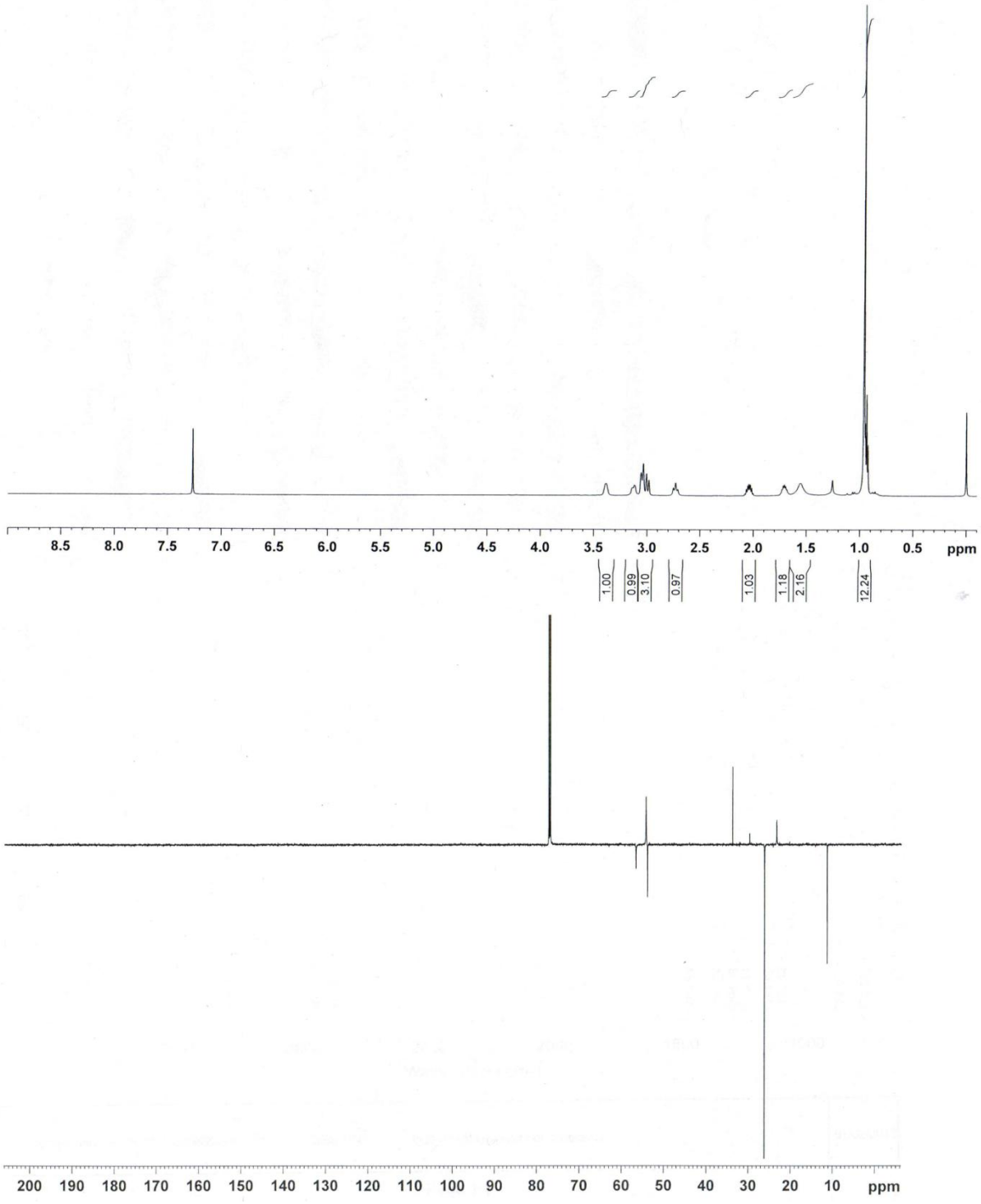


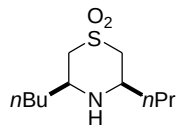
8f, C_6D_6; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz



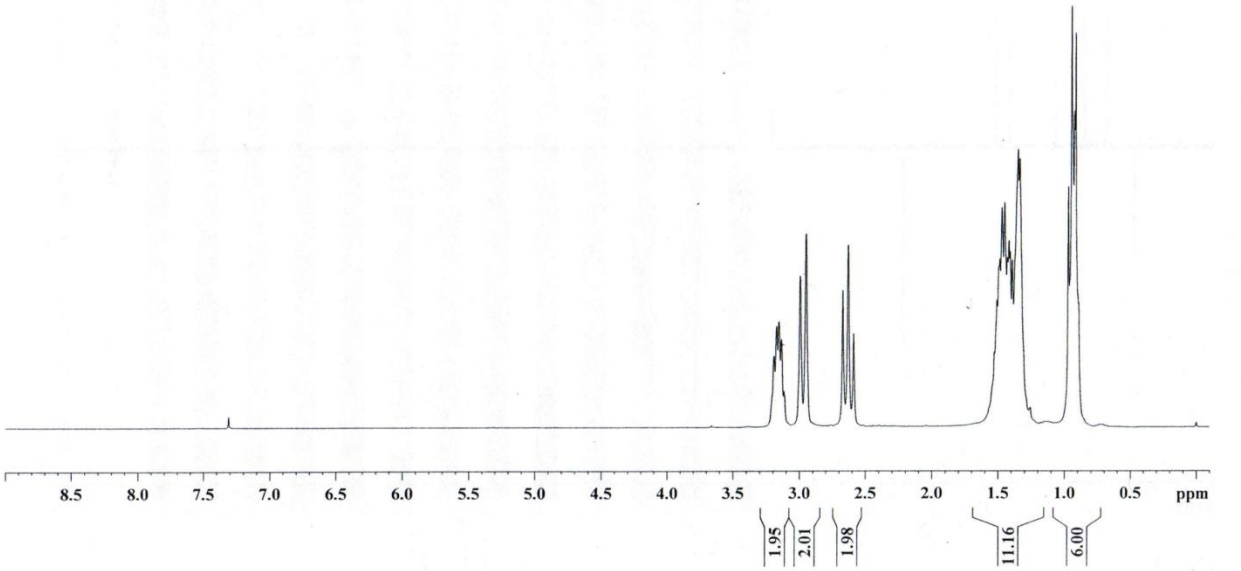


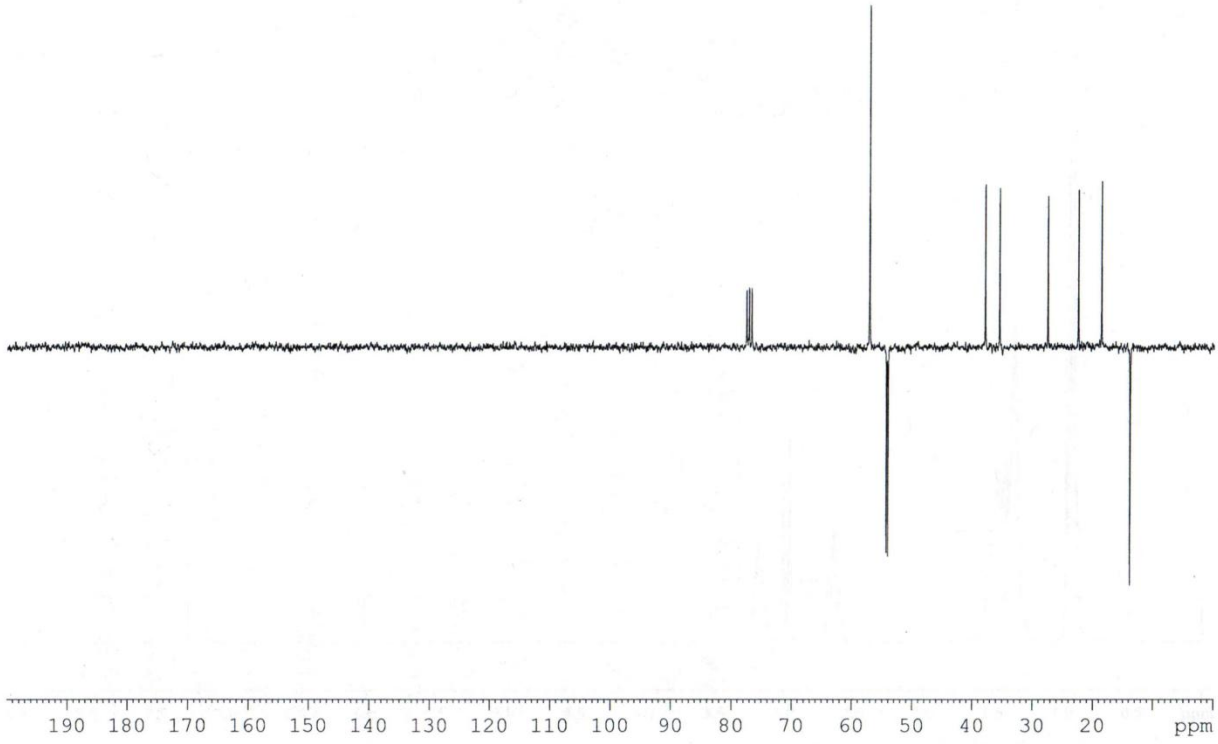
8f, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

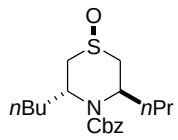




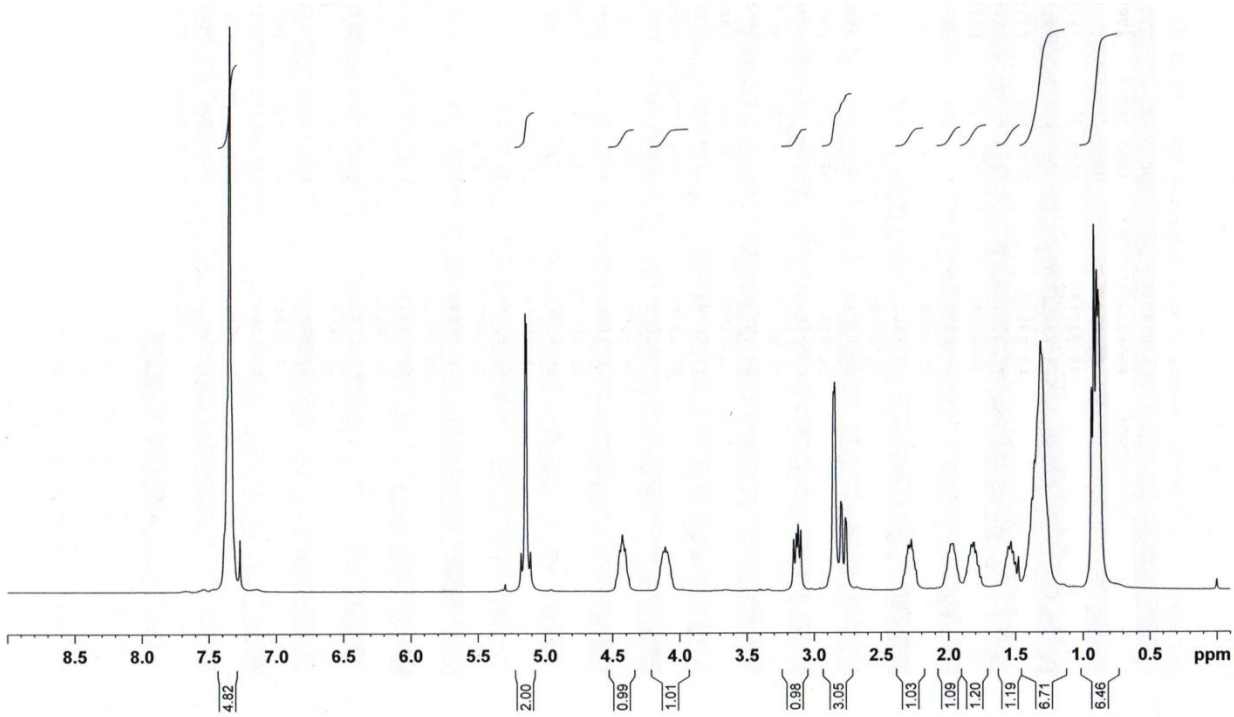
8g, $CDCl_3$; ^1H NMR-300 MHz; ^{13}C NMR-75 MHz

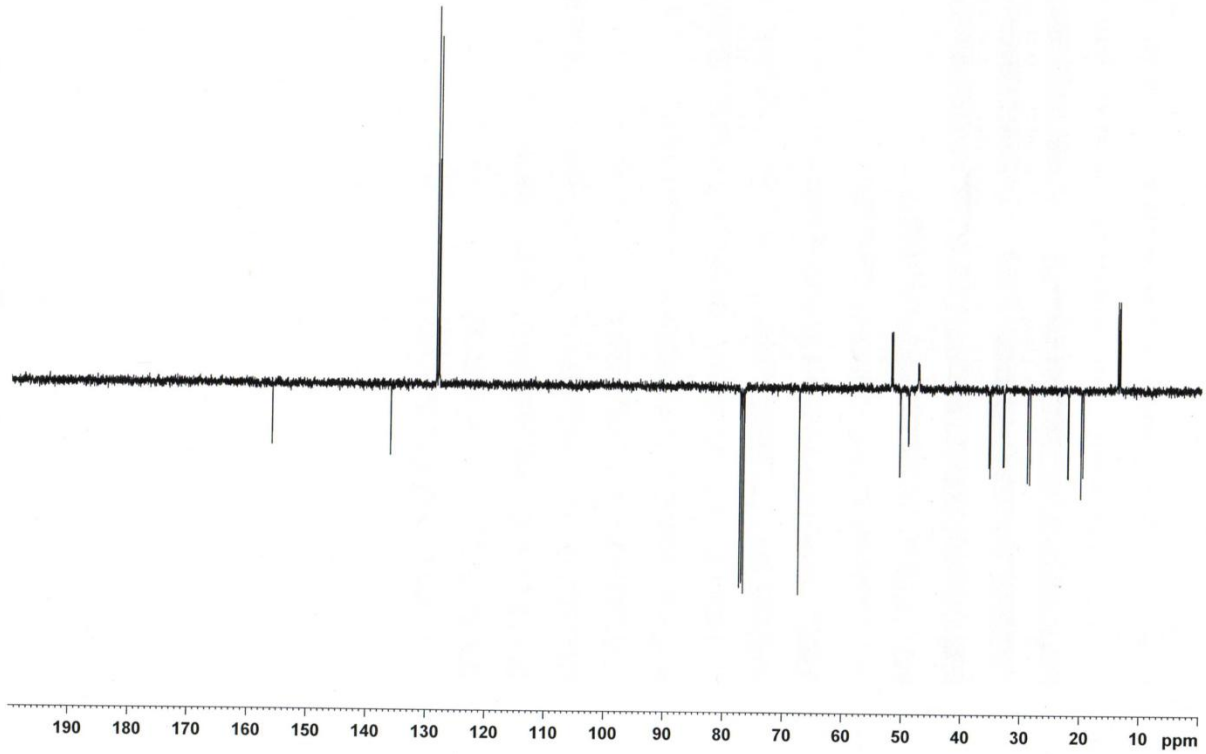


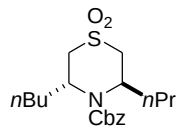




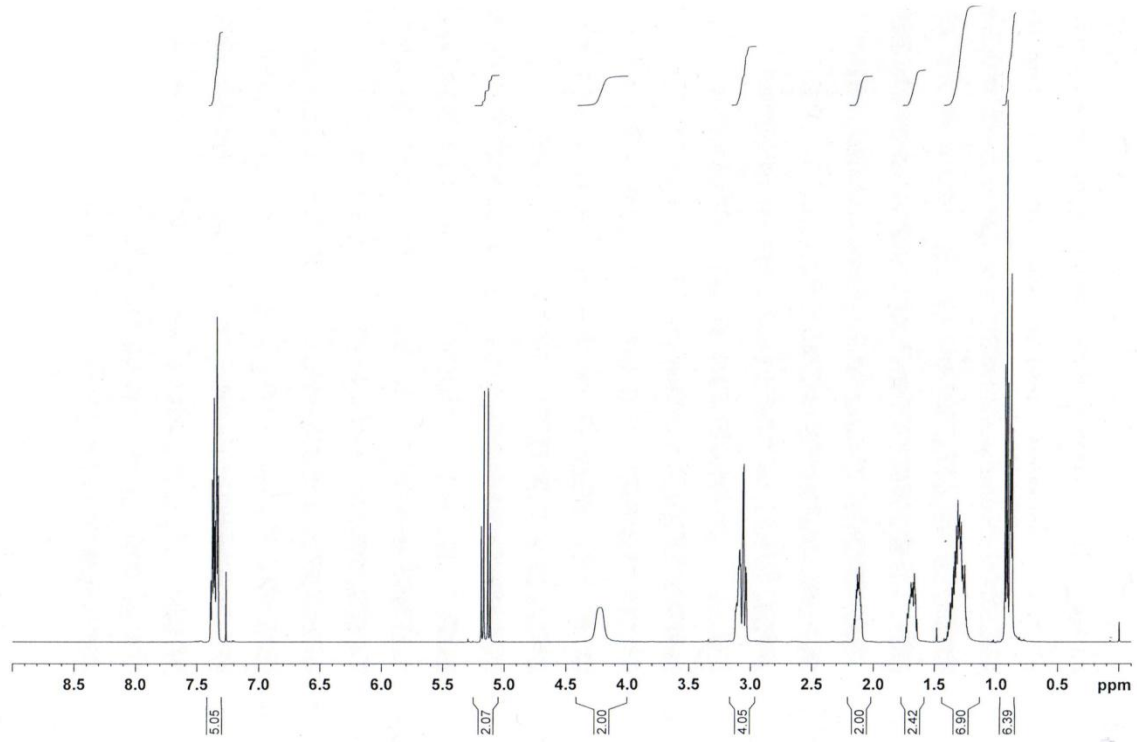
11, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

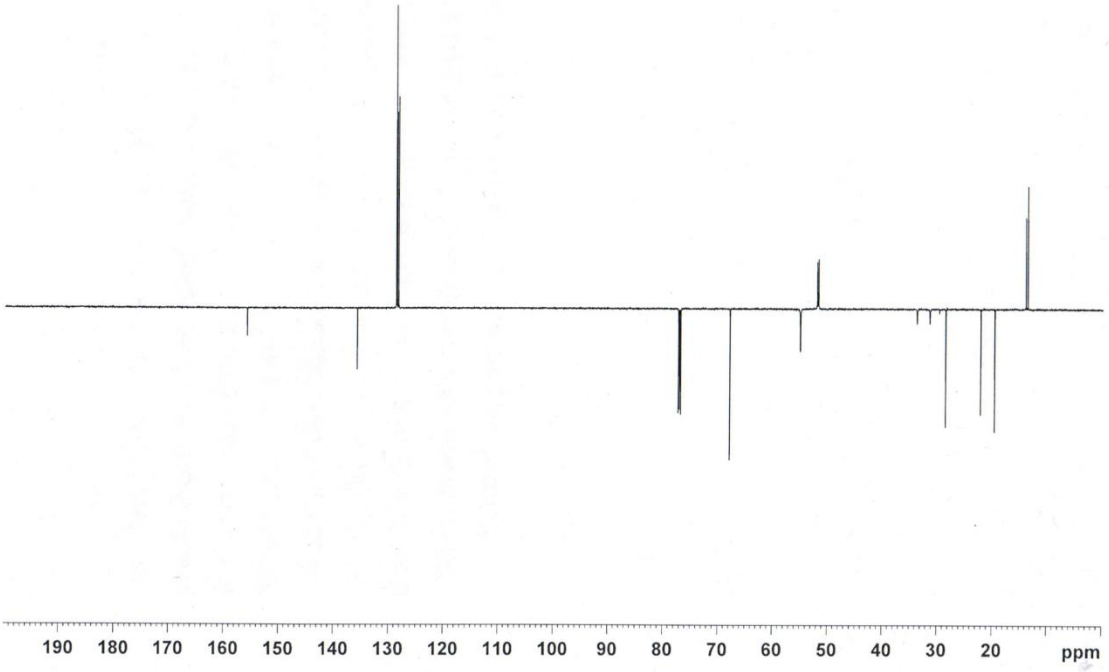


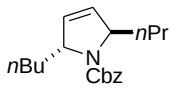




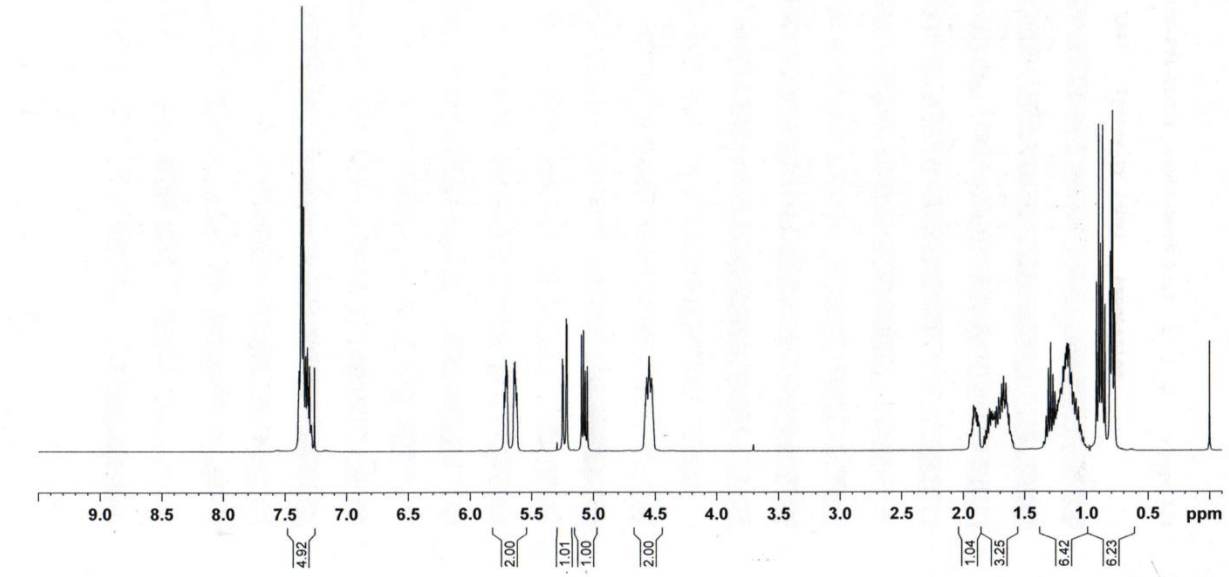
12, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

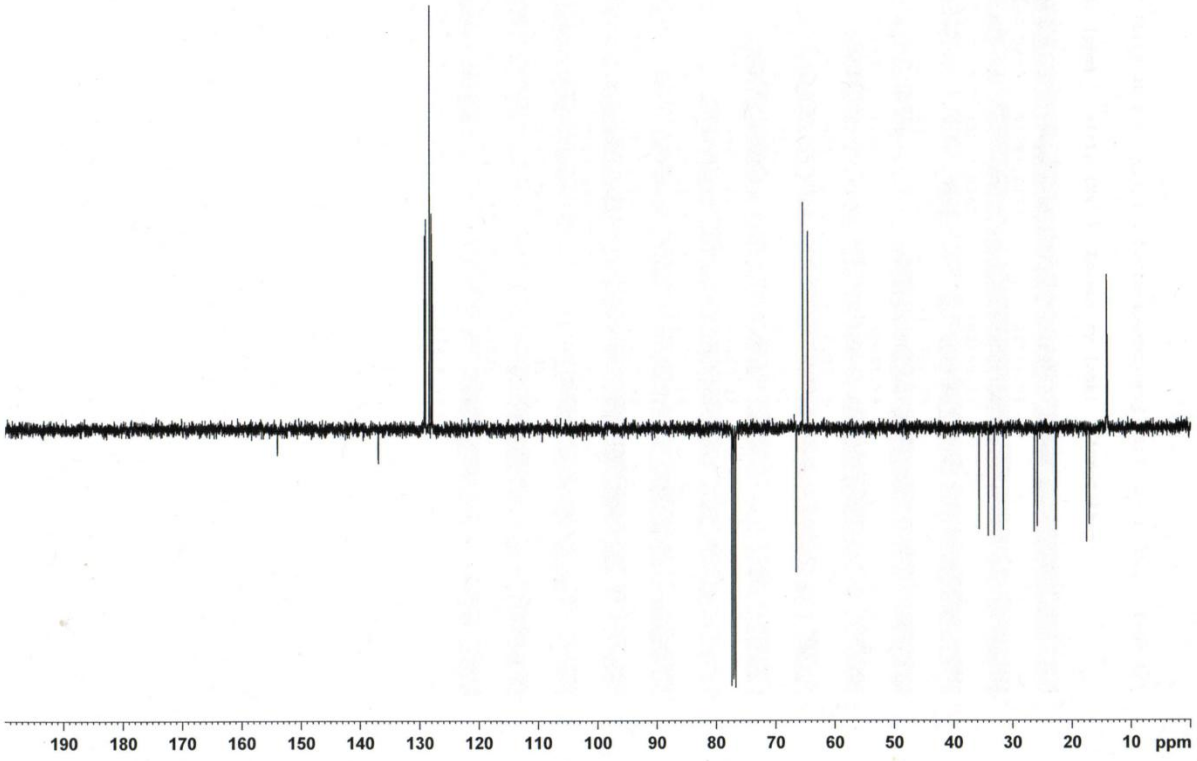


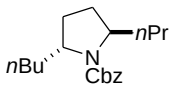




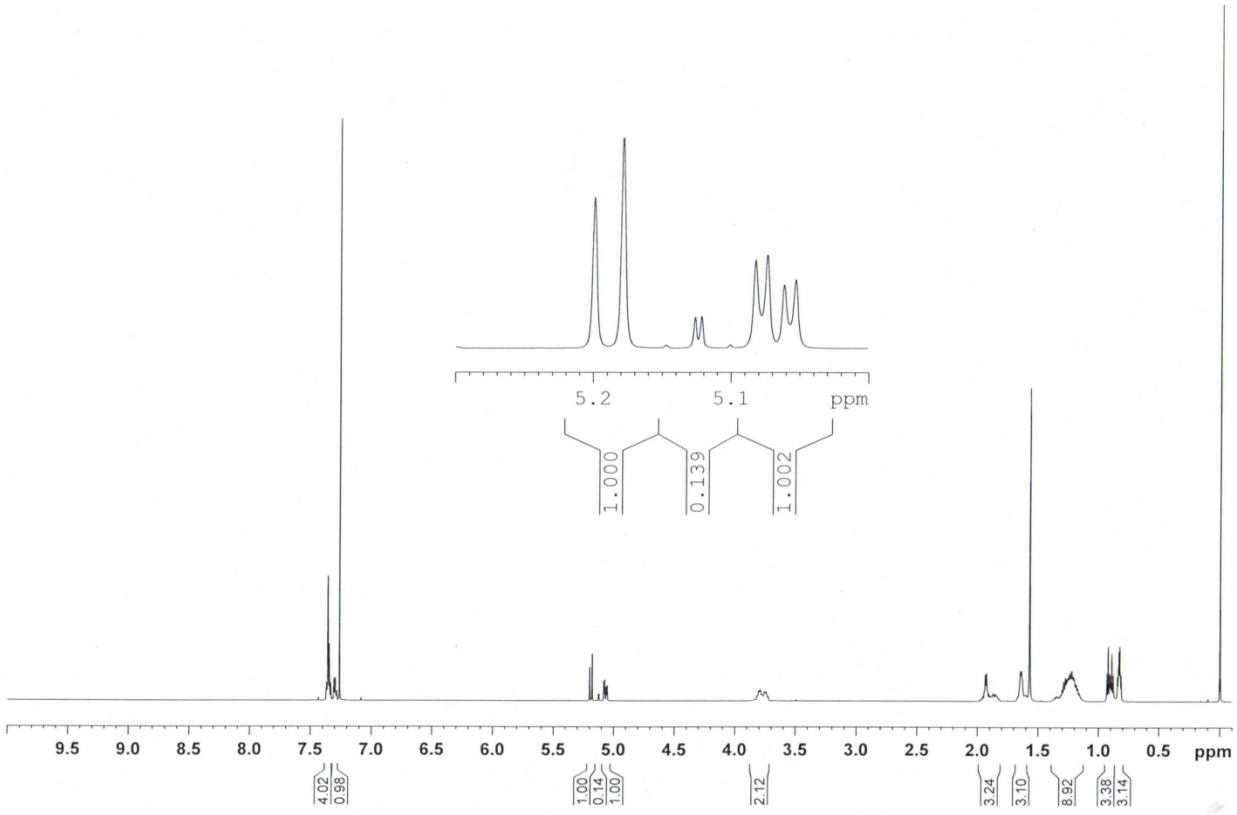
13, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

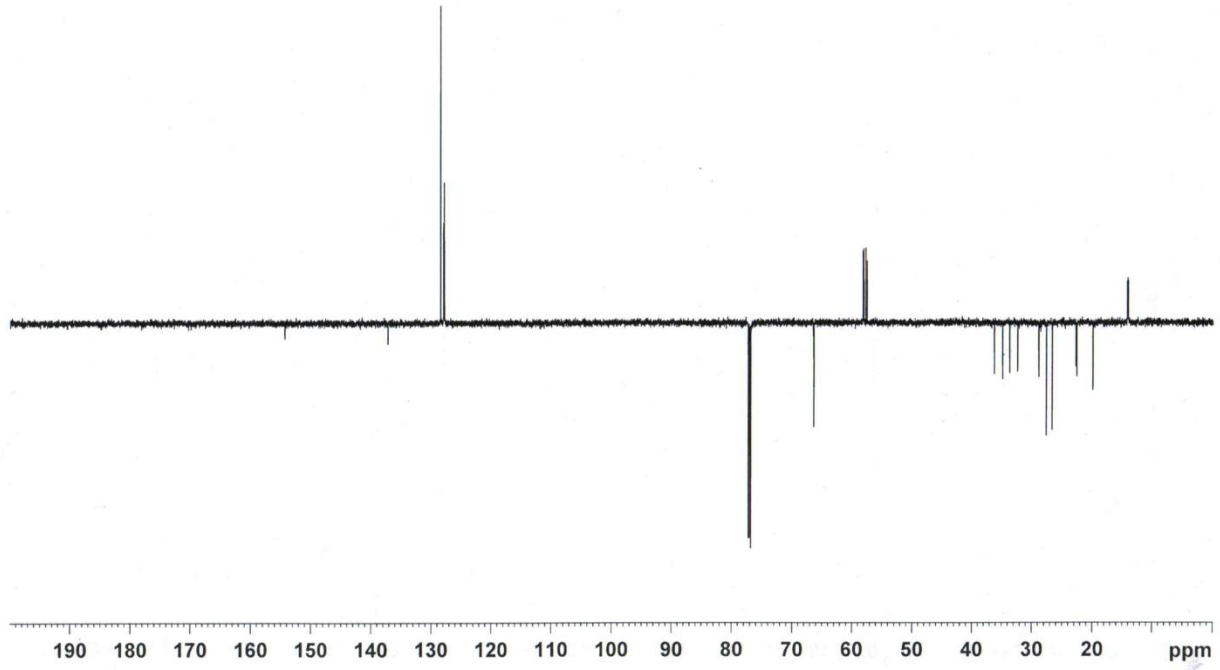


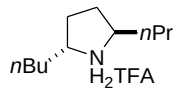




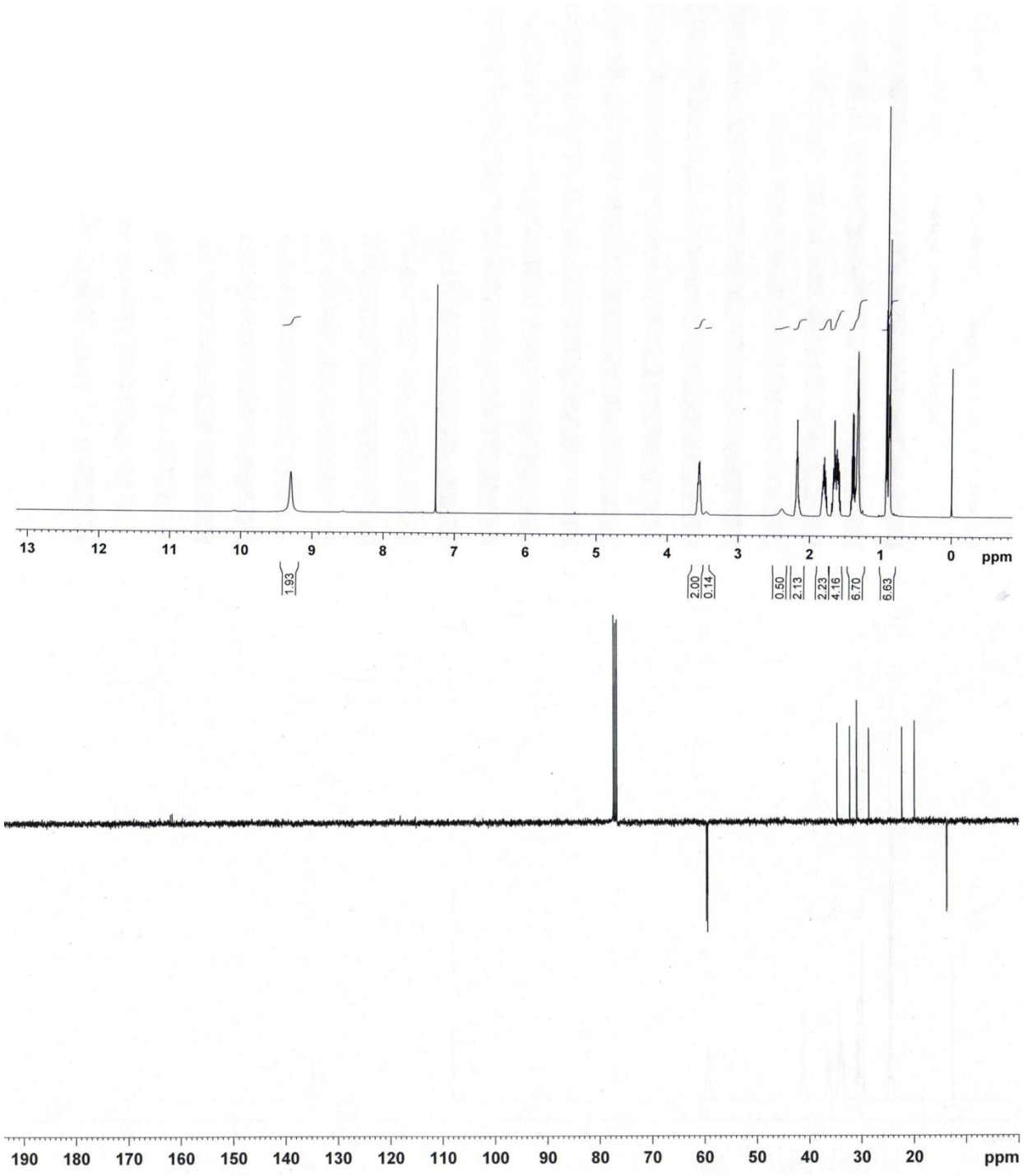
14 dr = 93:7, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz

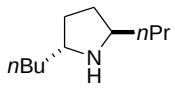




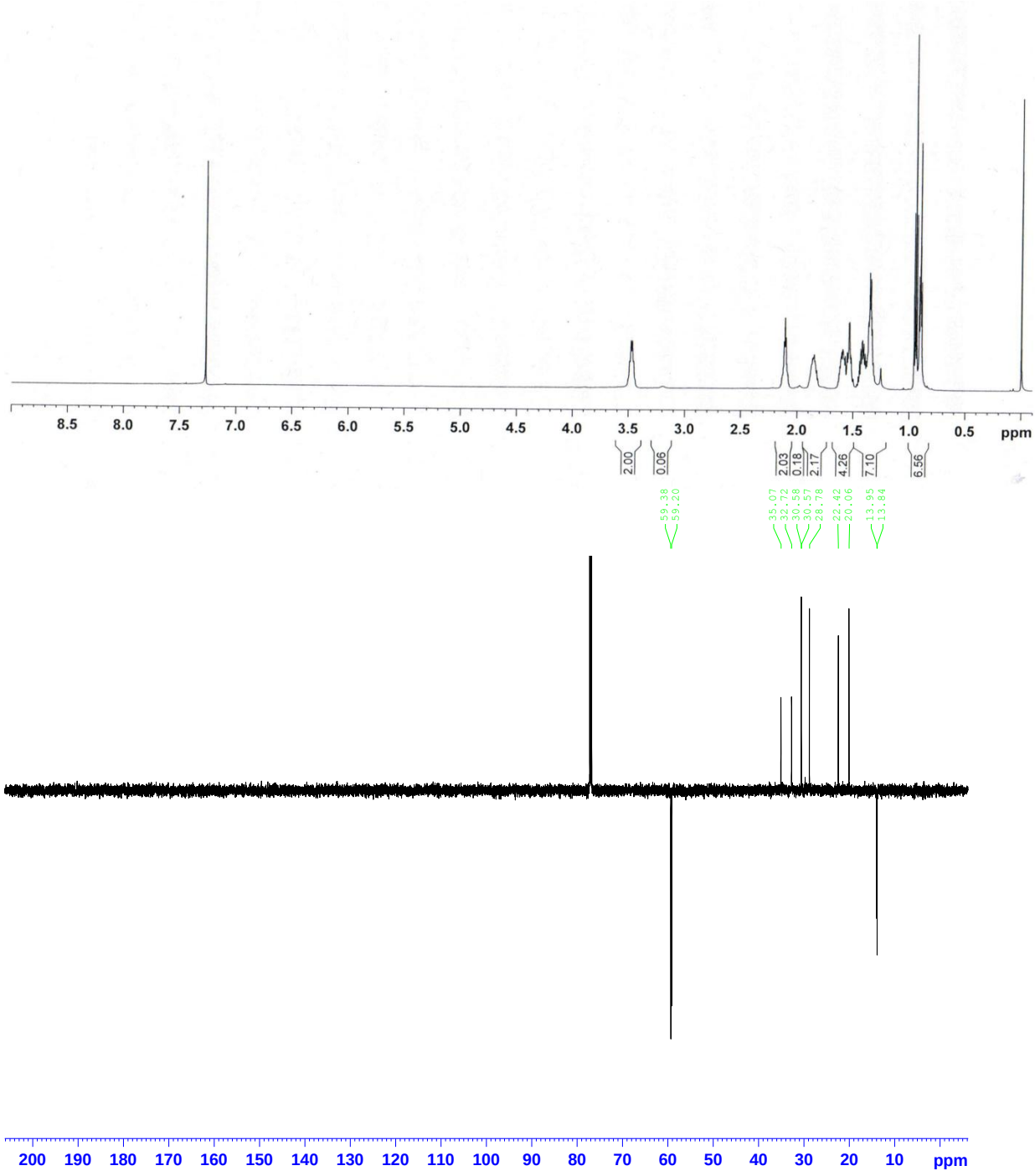


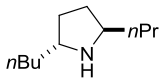
15 (TFA salt), dr = 93:7, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-100 MHz



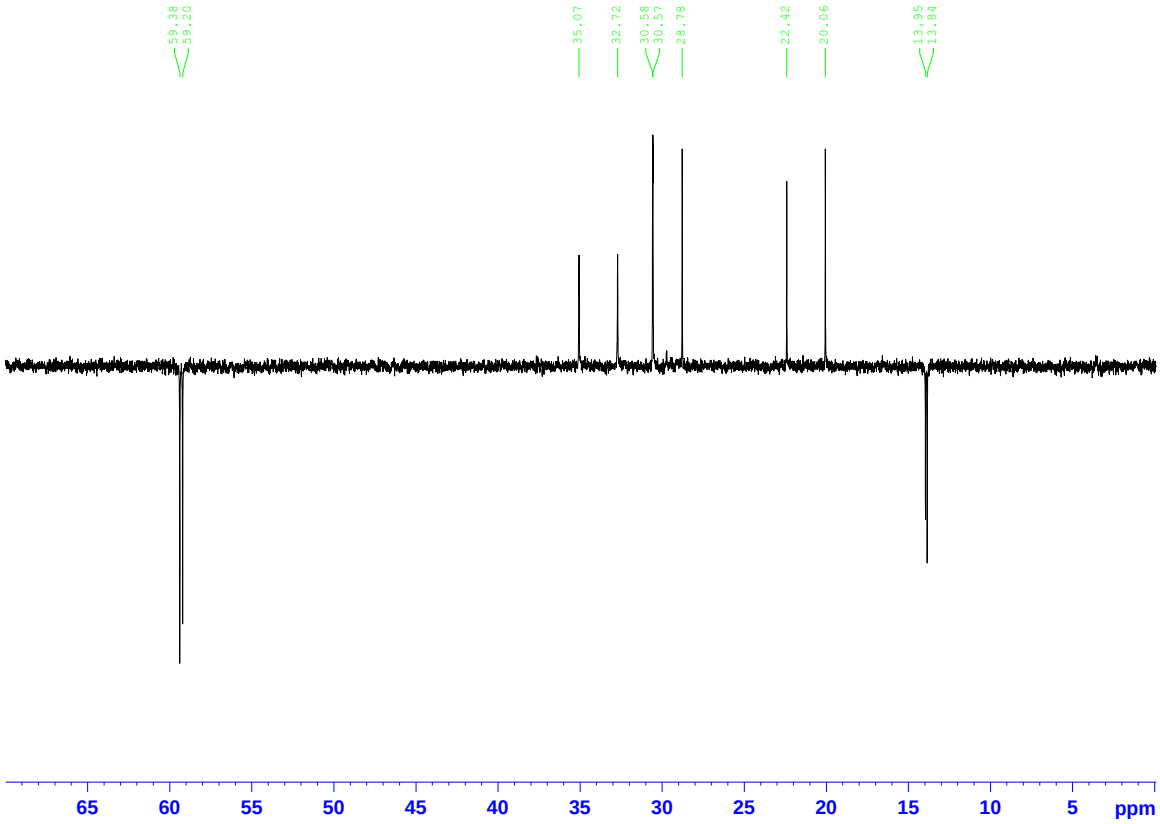


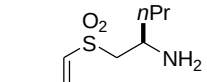
15 (free amine), dr = 95:5, $CDCl_3$; ^{1}H NMR-400 MHz; ^{13}C NMR-100 MHz



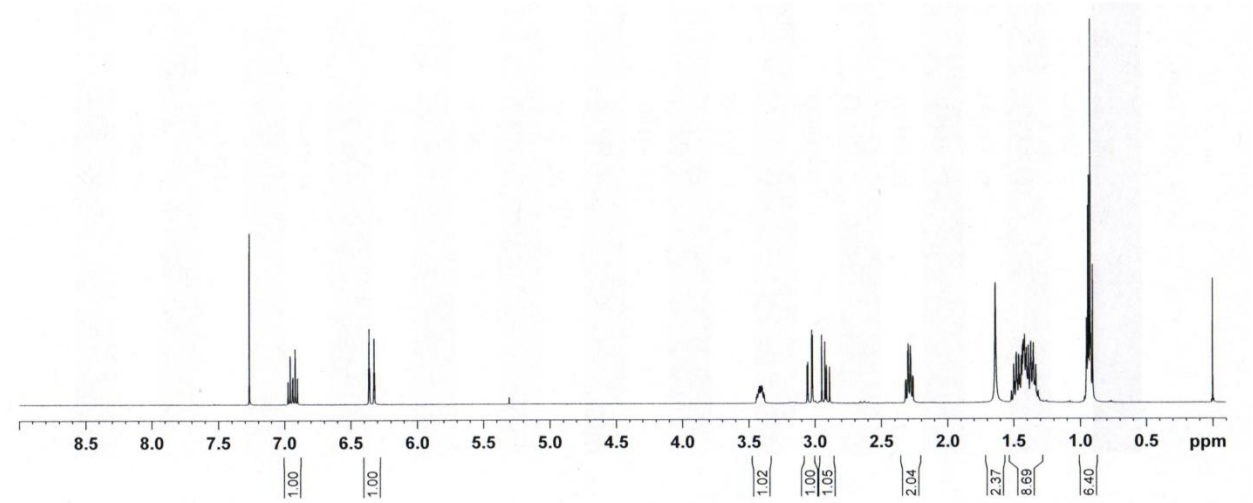


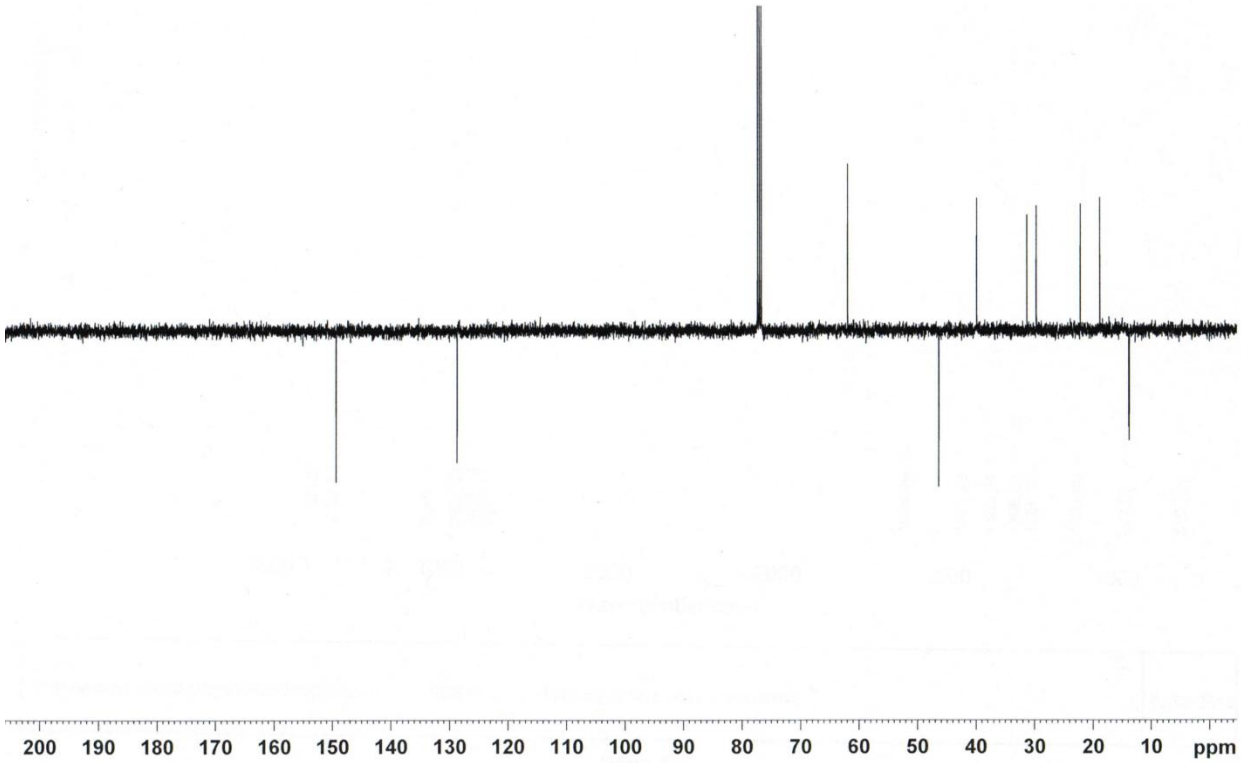
15 (free amine), dr = 95:5, $CDCl_3$;expansion of ^{13}C NMR-100 MHz

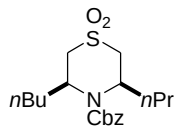




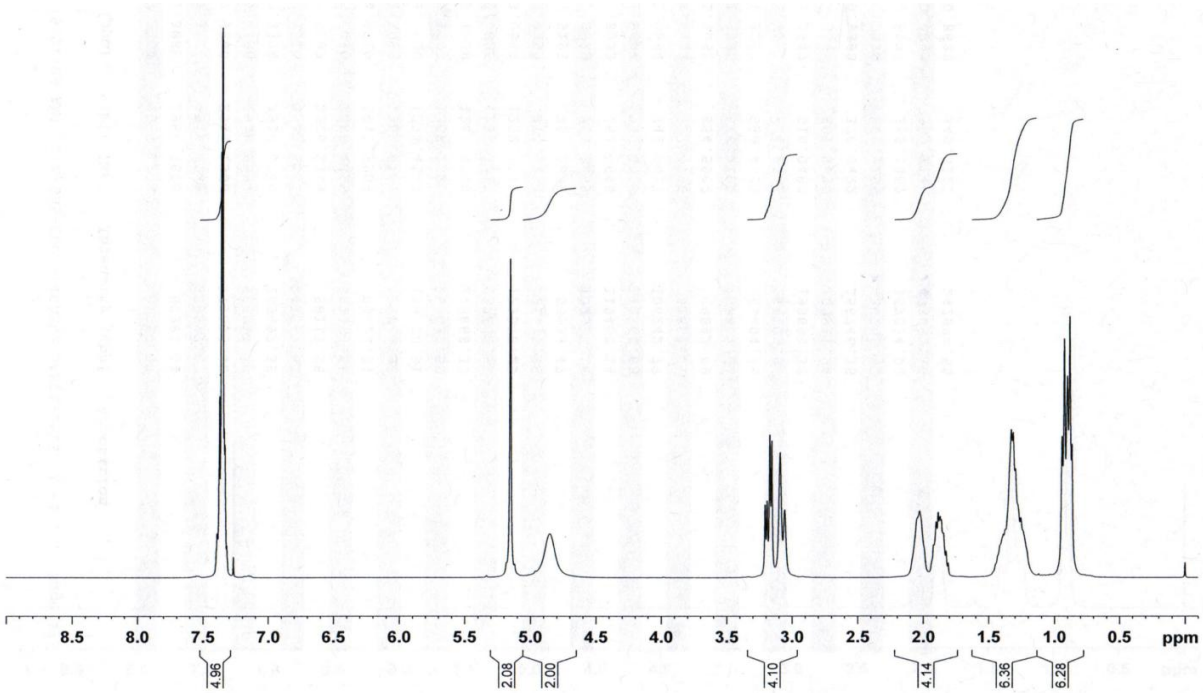
7g, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz

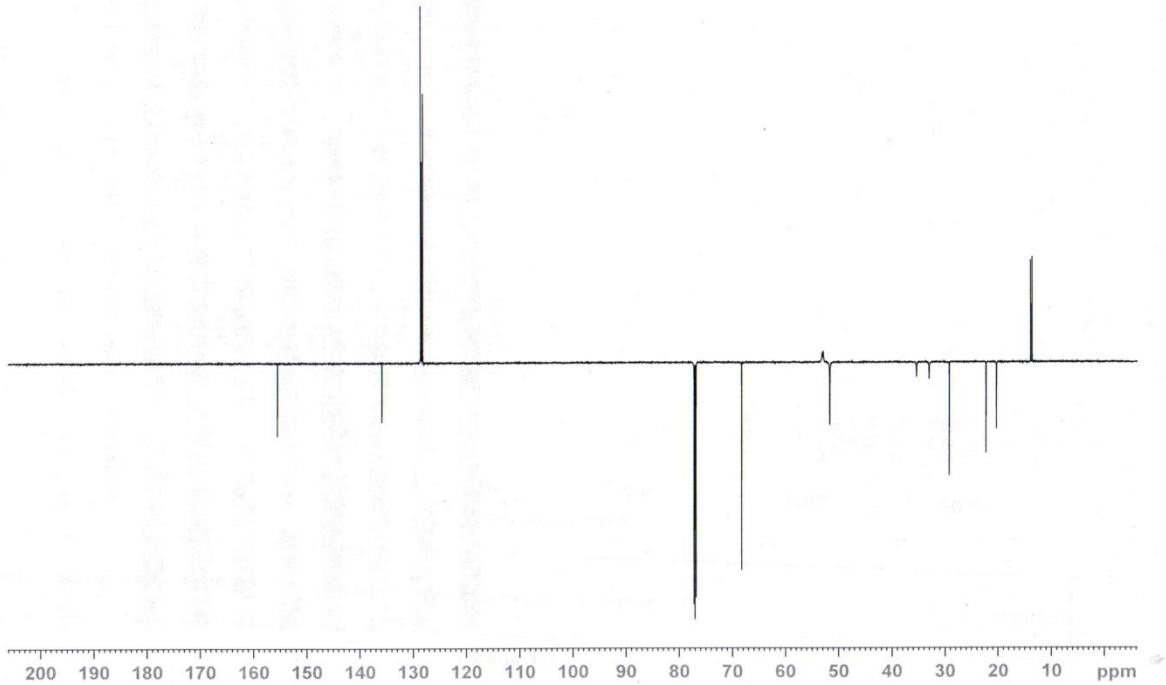


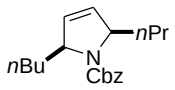




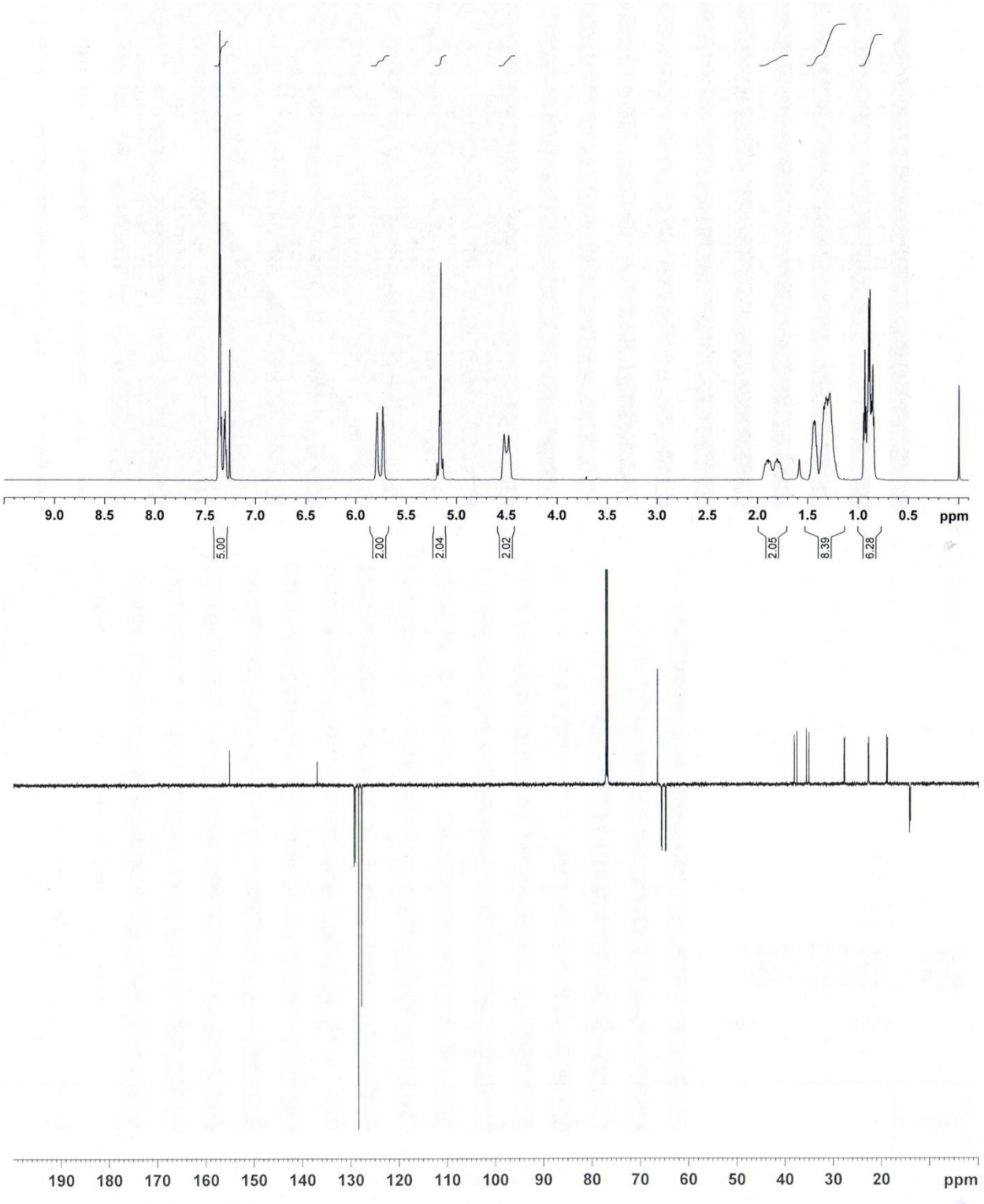
17, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-150.6 MHz

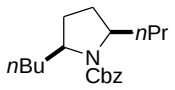




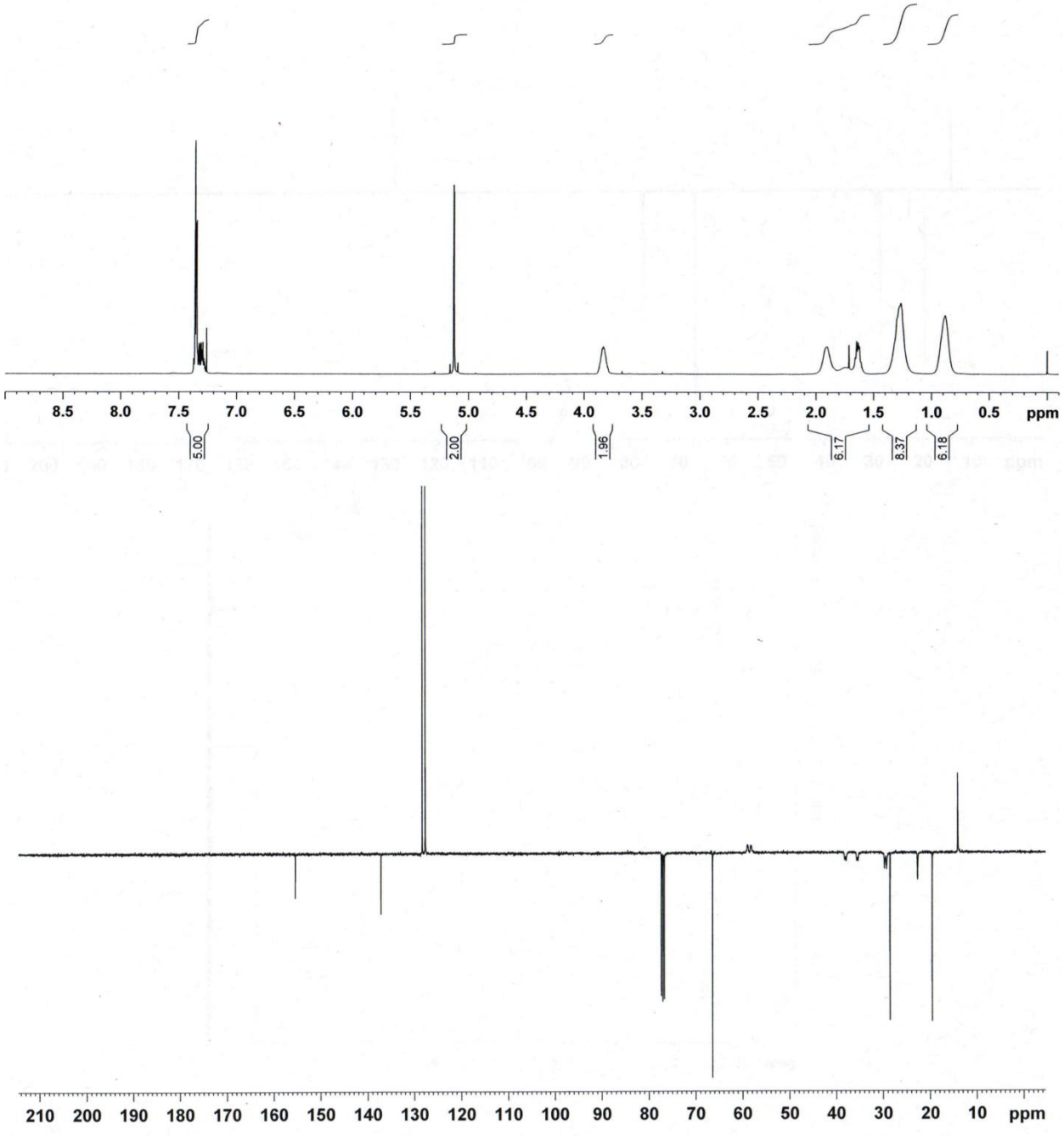


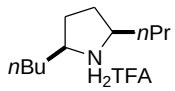
18, $CDCl_3$; ^1H NMR-600 MHz; ^{13}C NMR-150.6 MHz



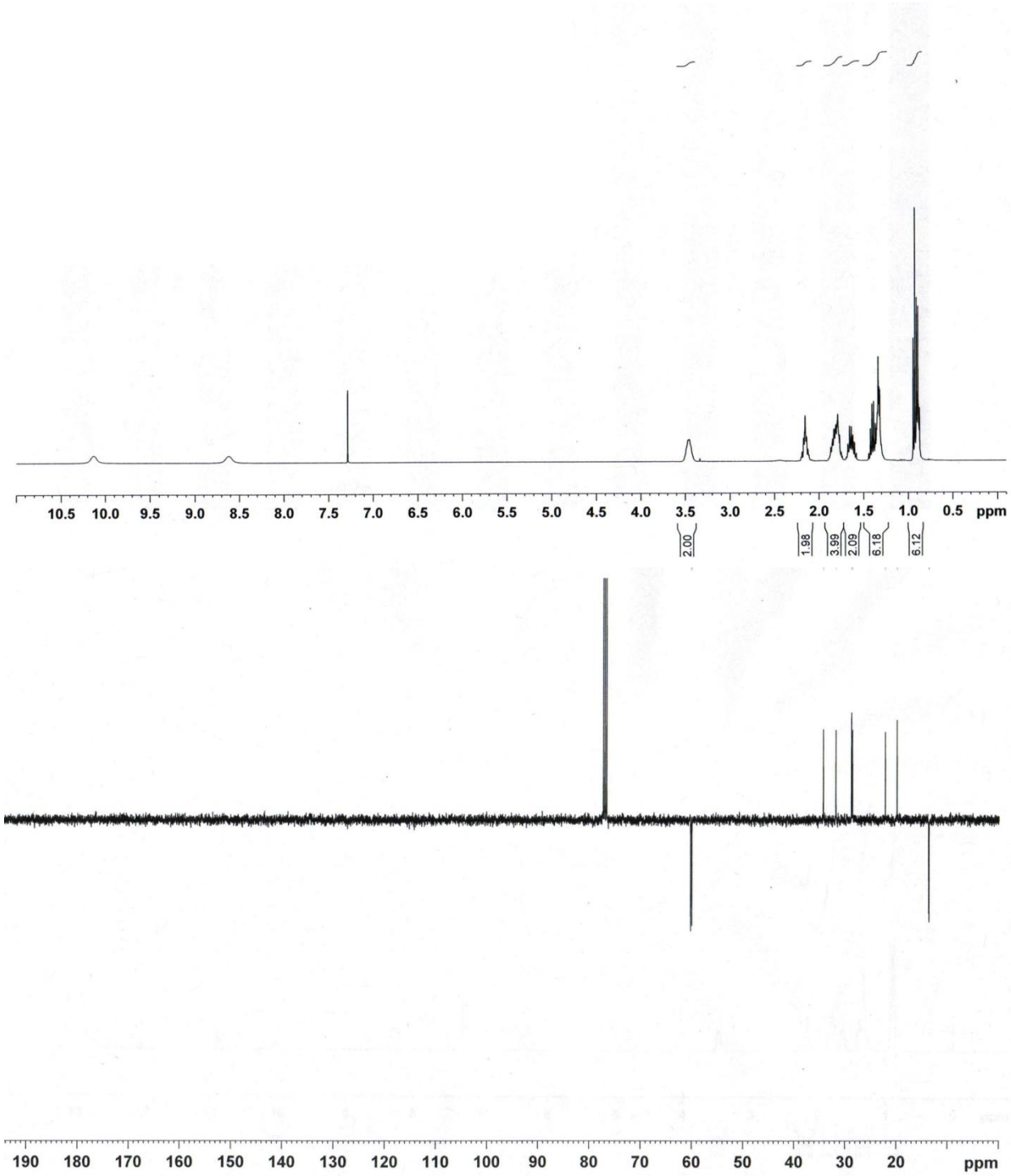


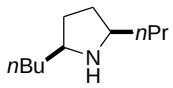
19, $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz



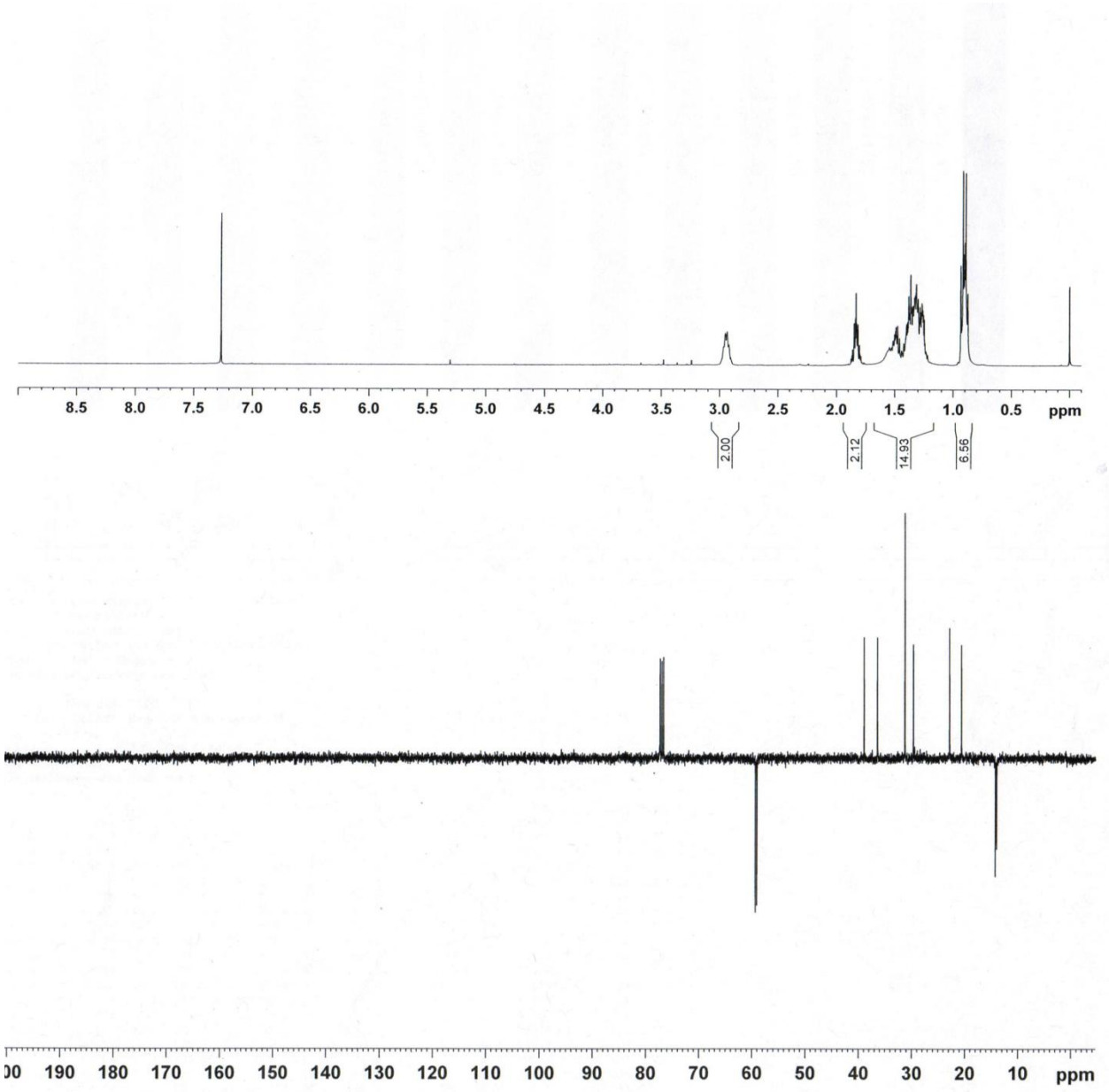


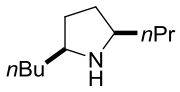
20 (TFA salt), $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz





20 (free amine), $CDCl_3$; ^1H NMR-400 MHz; ^{13}C NMR-100 MHz





20 (free amine), $CDCl_3$; expansion of ^{13}C NMR-100 MHz