

**Supporting Information**  
**for Asymmetric Substitution at Tetrasubstituted Chiral Carbon: Catalytic Ring-Opening**  
**Alkylation of Racemic 2,2-Disubstituted Aziridines with 3-Substituted Oxindoles**

Kohsuke Ohmatsu,<sup>†</sup> Yuichiro Ando,<sup>†</sup> and Takashi Ooi<sup>\*,†,‡</sup>

<sup>†</sup>*Institute of Transformative Bio-Molecules (WPI-ITbM), and Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Nagoya, 464-8603, Japan.*

<sup>‡</sup>*CREST, Japan Science and Technology Agency (JST), Nagoya, 464-8603, Japan.*

tooi@apchem.nagoya-u.ac.jp

**General Information:** Infrared spectra were recorded on a Shimadzu IRAffinity-1 spectrometer. <sup>1</sup>H NMR spectra were recorded on a JEOL JNM-ECS400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from the solvent resonance (C<sub>6</sub>D<sub>6</sub>; 7.16 ppm) or the tetramethylsilane (0.0 ppm) resonance as the internal standard [(CD<sub>3</sub>)<sub>2</sub>CO and CDCl<sub>3</sub>]. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, and br = broad) and coupling constants (Hz). <sup>13</sup>C NMR spectra were recorded on a JEOL JNM-ECS400 (101 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the solvent resonance as the internal standard [(CD<sub>3</sub>)<sub>2</sub>CO; 29.84 ppm, CDCl<sub>3</sub>; 77.16 ppm, and C<sub>6</sub>D<sub>6</sub>; 128.06 ppm]. <sup>19</sup>F NMR spectra were recorded on a JEOL JNM-ECS400 (376 MHz) spectrometer. Chemical shifts are reported in ppm from benzotrifluoride (−64.0 ppm) resonance as the external standard. Optical rotations were measured on a HORIBA SEPA-500 polarimeter. The high resolution mass spectra were conducted on Thermo Fisher Scientific Exactive. Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Flash column chromatography was performed on PSQ60AB (spherical, av. 55 μm; Fuji Silysia Chemical Ltd.) and Silica gel 60 (Merck 1.09385.9929, 230-400 mesh). Enantiomeric excesses were determined by HPLC analysis using chiral columns [ϕ 4.6 mm x 250 mm, DAICEL CHIRALCEL OD-3 (OD3), CHIRALCEL OJ-3 (OJ3), CHIRALCEL OZ-3 (OZ3), CHIRALPAK AD-3 (AD3), CHIRALPAK ID-3 (ID3), and CHIRALPAK IE-3 (IE3)] with hexane (Hex), isopropyl alcohol (IPA) and ethanol (EtOH) as eluent.

All air- and moisture-sensitive reactions were performed under an atmosphere of argon (Ar) in dried glassware. Dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>), diethyl ether (Et<sub>2</sub>O), and tetrahydrofuran (THF) were supplied from Kanto Chemical Co., Inc. as “Dehydrated” and further purified by passing through neutral alumina under nitrogen atmosphere. 1,2,3-Triazolium salts **1·X** were synthesized by following the literature methods.<sup>1</sup> Other simple chemicals were purchased and used as such.

---

<sup>1</sup> Ohmatsu, K.; Kiyokawa, M.; Ooi, T. *J. Am. Chem. Soc.* **2011**, *133*, 1307.

## Additional Experimental Data and Discussion:

### (A) Initial Rate Kinetics

#### General Procedure for Kinetic Experiments:

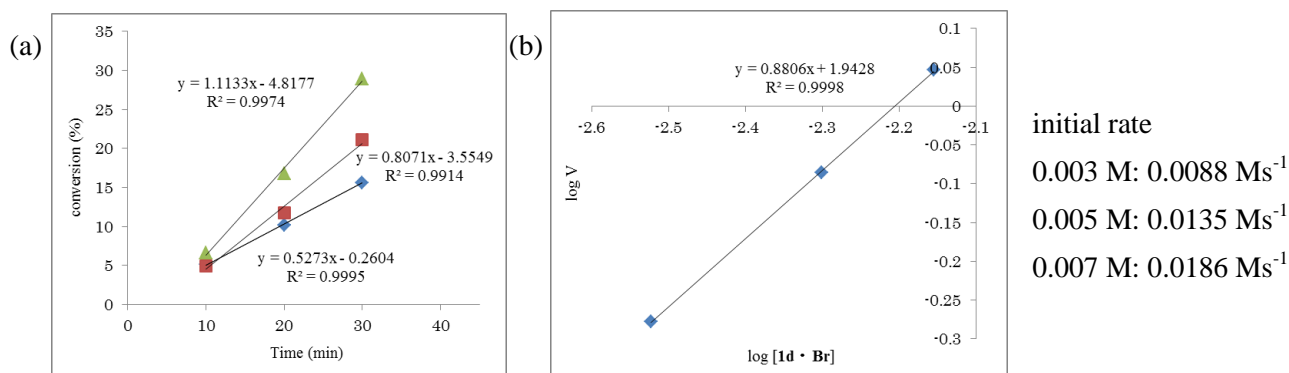
[**2b**] = 0.2 M, [**3a**] = 0.1 M, [**1d·Br**] = 0.005 M, [ $\text{K}_2\text{CO}_3$ ] = 0.1 mmol, [anisole] = 0.25 M.

A solution of **1d·Br** (4.76 mg, 0.005 mmol), aziridine **2b** (63.1 mg, 0.20 mmol), and oxindole **3a** (24.7 mg, 0.10 mmol) in  $\text{Et}_2\text{O}$  (1.0 mL) was degassed by alternating vacuum evacuation/Ar backfill. To this solution was added  $\text{K}_2\text{CO}_3$  (13.8 mg, 0.10 mmol) and the mixture was stirred at room temperature. After stirring for 10, 20, or 30 min, the reaction was quenched by the addition of a saturated aqueous solution of  $\text{NH}_4\text{Cl}$  and the extractive work-up was performed with  $\text{CHCl}_3$ . After evaporation to remove solvent, the residue was dissolved into  $\text{C}_6\text{D}_6$  (1 mL). To this solution was added anisole (27.2  $\mu\text{L}$ , 0.25 mmol) as an internal standard. The sample thus prepared was analyzed by  $^1\text{H}$  NMR at room temperature. The yield of product **4b** was measured by comparison of the integrated area of the methyl protons of anisole.

**Note:** Taking out the aliquots of the reaction mixture from liquid–solid biphasic system to analyze the conversion at the first stage of the reaction (10 min) caused an error of the following reaction rate, probably due to the deviation of the relative amount of  $\text{K}_2\text{CO}_3$  salt. Therefore, we analyzed the conversion at recorded times by quenching each reaction experiments. The reproducibility of data was confirmed by performing all experiments twice.

#### Kinetics on catalyst **1d·Br**:

[**2b**] = 0.2 M, [**3a**] = 0.1 M, [**1d·Br**] = 0.003 ~ 0.007 M, [ $\text{K}_2\text{CO}_3$ ] = 0.1 mmol.

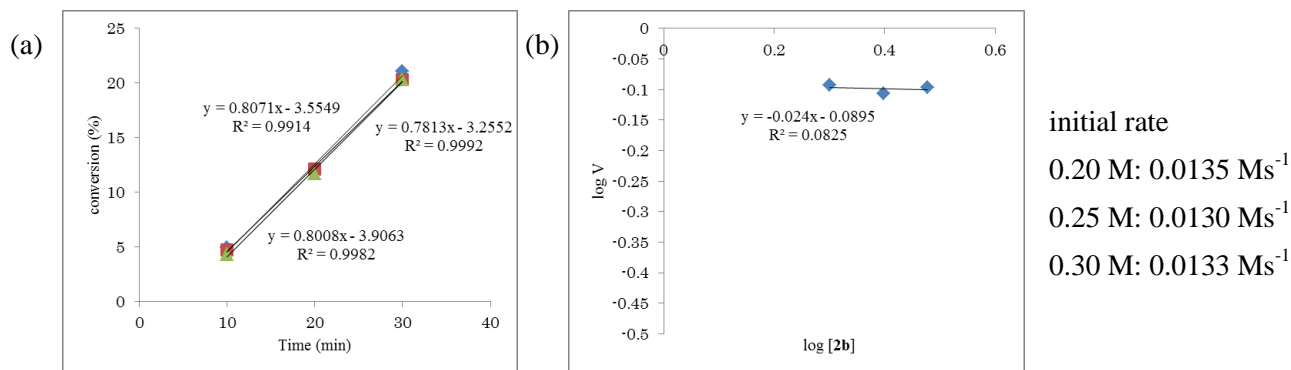


**Figure S1.** (a) Initial rate kinetics (catalyst) (b) Kinetics on catalyst **1d·Br**

*Pseudo-first-order* dependence on the concentration of catalyst **1d·Br**

### Kinetics on aziridine **2b**:

[**2b**] = 0.2 ~ 0.3 M, [**3a**] = 0.1 M, [**1d·Br**] = 0.005 M, [ $\text{K}_2\text{CO}_3$ ] = 0.1 mmol.

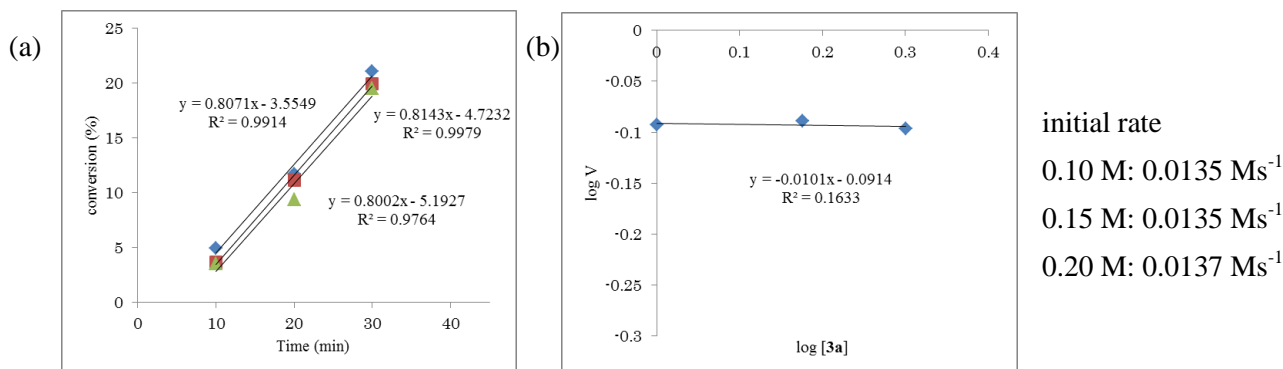


**Figure S2.** (a) Initial rate kinetics (aziridine) (b) Kinetics on aziridine **2b**

Zero-order dependence on the concentration of aziridine **2b**

### Kinetics on oxindole **3a**:

[**2b**] = 0.2 M, [**3a**] = 0.1 ~ 0.2 M, [**1d·Br**] = 0.005 M, [ $\text{K}_2\text{CO}_3$ ] = 0.1 mmol.

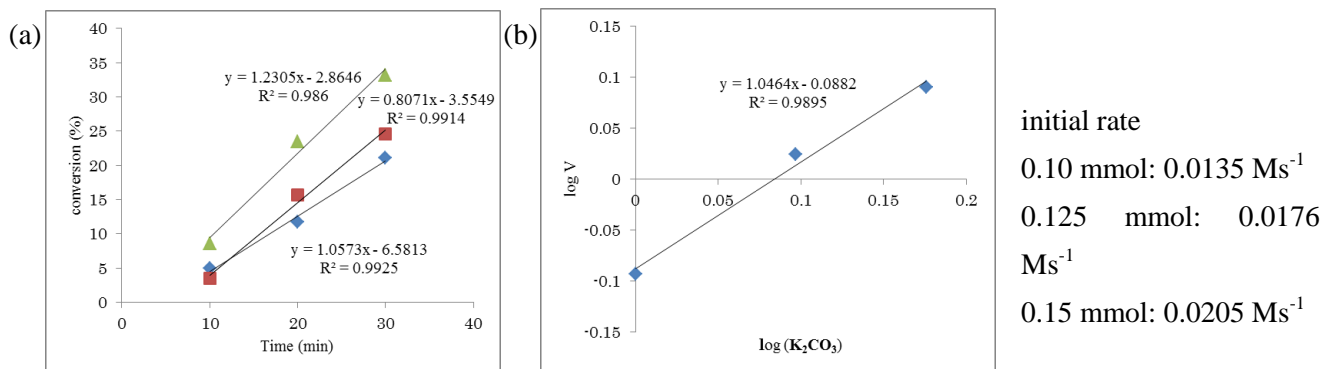


**Figure S3.** (a) Initial rate kinetics (oxindole) (b) Kinetics on oxindole **3a**

Zero-order dependence on the concentration of oxindole **3a**

### Kinetics on $\text{K}_2\text{CO}_3$ :

[**2b**] = 0.2 M, [**3a**] = 0.1M, [**1d·Br**] = 0.005 M, [ $\text{K}_2\text{CO}_3$ ] = 0.1 ~ 0.15 mmol.



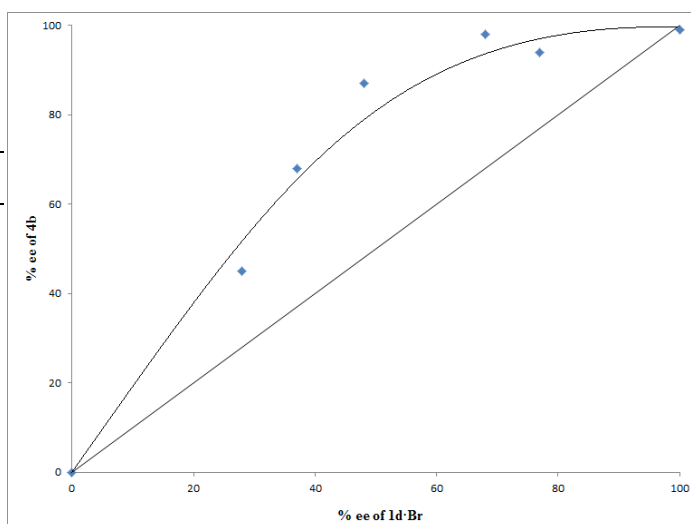
**Figure S4.** (a) Initial rate kinetics (base) (b) Kinetics on  $\text{K}_2\text{CO}_3$

First-order dependence on the amount of  $\text{K}_2\text{CO}_3$

These definitive data clearly indicated that the rate-limiting step is not carbon-carbon bond formation between oxindole-derived chiral triazolium enolate with aziridine but ion-exchange process for the generation of the requisite enolate.

## (B) Nonlinear Effect

$\text{2b} + \text{3a} \xrightarrow[\text{Et}_2\text{O, r.t., 24 h}]{\text{1d}\cdot\text{Br (28-100\% ee, 5 mol\%)}, \text{K}_2\text{CO}_3 (1 \text{ equiv})} \text{4b}$			
entry	ee (%) of <b>1d</b> ·Br	yield (%) of <b>4b</b>	ee (%) of <b>4b</b>
1	28	92	45
2	37	84	68
3	48	92	87
4	68	96	98
5	77	80	94
6	100	97	99



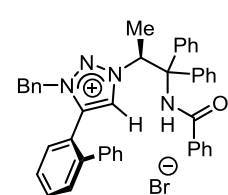
**Table S1.** Asymmetric Amplification

**Figure S5.** Nonlinear effect

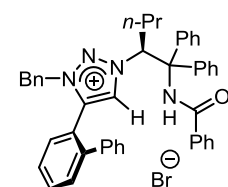
The data of Table S1 and the graph of Figure S5 demonstrated a pronounced positive nonlinear effect, which suggested that more than one catalyst is involved in the stereo-determining step.

## Experimental Section:

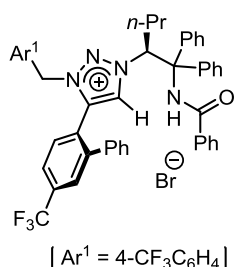
### Characterization of 1,2,3-Triazolium Salt **1**·Br



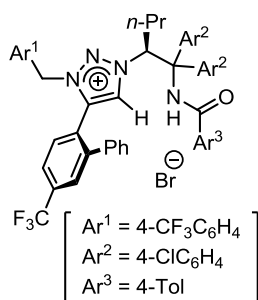
**1a**·Br:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  10.2 (1H, brs), 8.65 (1H, brs), 8.20 (2H, d,  $J = 6.9$  Hz), 7.87-7.82 (3H, m), 7.64 (1H, t,  $J = 7.6$  Hz), 7.45-7.29 (8H, m), 7.27-7.22 (2H, m), 7.20-7.14 (4H, m), 7.03-6.97 (4H, m), 6.91-6.84 (4H, m), 6.55 (2H, d,  $J = 7.8$  Hz), 4.85 (2H, s), 1.63 (3H, d,  $J = 7.3$  Hz);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.4, 142.9, 140.3, 139.9, 138.5, 135.3, 133.7, 132.9, 132.4, 132.0, 131.9, 131.1, 130.2, 129.9, 129.4, 129.2, 129.0, 128.9, 128.8, 128.5, 128.4, 128.3, 128.2, 127.8, 127.6, 127.2, 120.3, 69.4, 65.9, 55.2, 15.8, two peaks for aromatic carbons were not found probably due to overlapping; IR 3221, 2934, 1672, 1520, 1275, 1148, 746, 702  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{43}\text{H}_{37}\text{N}_4\text{O}^+$  ( $[\text{M}]^+$ ) 625.2962. Found 625.2969.;  $[\alpha]_{\text{D}}^{22} = -44.3$  ( $c = 1.0$ , MeOH).



**1b**·Br:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.94 (1H, brs), 8.51 (1H, brs), 8.20 (2H, d,  $J = 6.2$  Hz), 7.79 (2H, brs), 7.66 (2H, td,  $J = 7.7, 1.2$  Hz), 7.51-7.35 (9H, m), 7.30-7.15 (9H, m), 7.07 (2H, t,  $J = 7.6$  Hz), 6.85 (2H, d,  $J = 7.1$  Hz), 6.64 (2H, d,  $J = 7.5$  Hz), 5.07 (2H, brs), 2.13-2.07 (1H, m), 1.90-1.81 (1H, m), 1.33-1.25 (1H, m), 0.84-0.75 (4H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.9, 142.8, 140.6, 138.6, 133.7, 133.1, 132.4, 132.2, 131.9, 130.8, 130.6, 129.8, 129.3, 129.2, 129.0, 128.8, 128.7, 128.6, 128.6, 128.4, 128.3, 128.3, 127.8, 127.7, 127.4, 120.3, 70.4, 69.1, 55.8, 31.9, 19.3, 13.7, three peaks for aromatic carbons were not found probably due to overlapping; IR 3235, 2932, 1674, 1485, 1285, 1146, 748, 704  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{45}\text{H}_{41}\text{N}_4\text{O}^+$  ( $[\text{M}]^+$ ) 653.3275. Found 653.3270.;  $[\alpha]_{\text{D}}^{22} = -27.7$  ( $c = 1.0$ , MeOH).

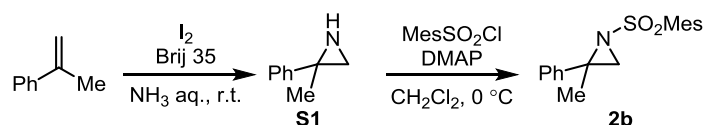


**1c·Br:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.92 (1H, brs), 8.42 (1H, brs), 8.09 (2H, d,  $J$  = 7.3 Hz), 7.80 (1H, d,  $J$  = 8.2 Hz), 7.70 (1H, s), 7.55 (2H, d,  $J$  = 6.8 Hz), 7.48-7.29 (15H, m), 7.17 (2H, t,  $J$  = 7.8 Hz), 7.11 (1H, brs), 6.89 (2H, d,  $J$  = 8.0 Hz), 6.82 (2H, d,  $J$  = 7.6 Hz), 5.69 (1H, brs), 5.37 (1H, d,  $J$  = 15.3 Hz), 2.16-2.10 (1H, m), 1.60-1.57 (1H, m), 1.25-1.19 (1H, m), 0.81-0.73 (4H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.7, [Ar<sup>1</sup> = 4- $\text{CF}_3\text{C}_6\text{H}_4$ ] 143.4, 141.6, 140.0, 137.3, 137.0, 134.5 (q,  $J_{\text{C-F}}$  = 33.9 Hz), 134.0, 133.5, 132.3, 132.0 (q,  $J_{\text{C-F}}$  = 32.9 Hz), 129.7, 129.5, 129.2, 129.1, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.0, 128.0, 127.4 (q,  $J$  = 2.9 Hz), 126.1 (q,  $J_{\text{C-F}}$  = 3.9 Hz), 125.7 (q,  $J_{\text{C-F}}$  = 2.9 Hz), 125.5 (q,  $J_{\text{C-F}}$  = 276 Hz), 123.3 (q,  $J_{\text{C-F}}$  = 277 Hz), 69.7, 68.7, 56.1, 32.7, 19.4, 13.6, three peaks for aromatic carbons were not found probably due to overlapping; IR 3026, 2934, 1674, 1485, 1325, 1130, 752, 706  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{47}\text{H}_{39}\text{N}_4\text{OF}_6^+$  ( $[\text{M}]^+$ ) 789.3023. Found 789.3015.;  $[\alpha]_{\text{D}}^{22} = -25.1$  ( $c$  = 0.4, MeOH).



**1d·Br:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.37 (1H, brs), 8.18 (1H, brs), 8.04 (2H, d,  $J$  = 8.0 Hz), 7.79 (1H, d,  $J$  = 8.0 Hz), 7.73 (1H, s), 7.56 (2H, brs), 7.48 (2H, d,  $J$  = 8.2 Hz), 7.36-7.32 (4H, m), 7.24-7.14 (9H, m), 6.88-6.83 (4H, m), 5.49 (1H, brs), 5.22 (1H, d,  $J$  = 15.3 Hz), 2.34, (3H, s), 2.05-1.96 (1H, m), 1.62 (1H, br), 1.24 (1H, br), 0.82-0.70 (4H, m);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.6, 143.6, 143.1, 140.1, 139.5, 137.2, 134.8, 134.8 (q,  $J_{\text{C-F}}$  = 33.9 Hz), 134.5, 134.1, 133.6, 133.0, 132.3 (q,  $J_{\text{C-F}}$  = 32.9 Hz), 130.9, 130.3, 130.1, 129.6, 129.4, 129.4, 129.3, 128.8, 128.6, 128.3, 128.0, 127.6, 126.2 (q,  $J_{\text{C-F}}$  = 3.9 Hz), 125.6 (q,  $J_{\text{C-F}}$  = 3.9 Hz), 123.5, 123.4 (q,  $J_{\text{C-F}}$  = 278 Hz), 123.2 (q,  $J_{\text{C-F}}$  = 278 Hz), 69.6, 68.2, 55.9, 32.2, 21.6, 19.3, 13.6, one peak for aromatic carbon was not found probably due to overlapping; IR 3026, 2934, 2361, 1674, 1325, 1132, 752  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{48}\text{H}_{39}\text{N}_4\text{OF}_6\text{Cl}_2^+$  ( $[\text{M}]^+$ ) 871.2400. Found 871.2390.;  $[\alpha]_{\text{D}}^{22} = -17.2$  ( $c$  = 1.0, MeOH).

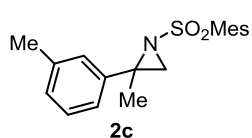
## Preparation and Characterization of 2,2-Disubstituted Aziridines 2:



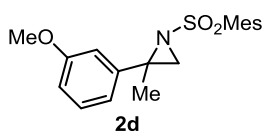
To a solution of  $\text{I}_2$  (5.08 g, 20 mmol) and Brij 35 (0.60 g) in  $\text{NH}_3$  aq. (30 mL) was added  $\alpha$ -methylstyrene (1.30 mL, 10 mmol), and the reaction mixture was stirred for 2 h at room temperature. The resulting solution was diluted with a saturated aqueous solution of  $\text{Na}_2\text{SO}_3$  and EtOAc. The extractive work-up was performed with EtOAc. After drying over  $\text{Na}_2\text{SO}_4$ , filtration, and removal of solvent, the resulting crude residue was purified by column chromatography (Hex/EtOAc = 1:1 as eluent) to afford **S1** (915 mg, 6.9 mmol, 69% yield) as a yellow liquid. **S1:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36 (2H, d,  $J$  = 7.3 Hz), 7.31 (2H, t,  $J$  = 7.3 Hz), 7.22 (1H, t,  $J$  = 7.3 Hz), 1.94 (2H, s), 1.60 (3H, s), 0.63 (1H, br).

To a solution of **S1** (915 mg, 6.9 mmol) in  $\text{CH}_2\text{Cl}_2$  (15 mL) were added 2-mesitylenesulfonyl chloride (1.51 g, 6.9 mmol), and  $N,N$ -dimethyl-4-aminopyridine (0.84 g, 6.9 mmol) at 0  $^\circ\text{C}$ , and the whole reaction mixture was stirred for 3 h at the same temperature. The mixture was then diluted with water and the extractive work-up was conducted with  $\text{CHCl}_3$ . The organic extracts were dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated. Purification of the crude residue by column chromatography on silica gel (Hex/EtOAc = 30:1 as eluent) gave **2b** (631 mg, 2.0 mmol, 29% yield) as a white solid.

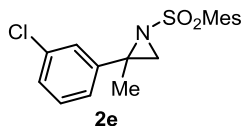
**2b:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 (2H, d,  $J = 7.3$  Hz), 7.33 (2H, t,  $J = 7.3$  Hz), 7.28 (1H, t,  $J = 7.3$  Hz), 6.96 (2H, s), 3.02 (1H, s), 2.71 (6H, s), 2.54 (1H, s), 2.30 (3H, s), 2.06 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.8, 141.3, 139.7, 135.1, 131.9, 128.5, 127.8, 126.6, 51.1, 42.0, 23.3, 21.1, 21.0; IR 3152, 2938, 1314, 1121, 1105, 1024, 862, 800, 775  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{18}\text{H}_{22}\text{NO}_2\text{S}^+$  ( $[\text{M}+\text{H}]^+$ ) 316.1366. Found 316.1366.; HPLC conditions for the recovered aziridine **2b** (Scheme 1), OZ3, H/IPA = 10:1, flow rate = 0.5 mL/min,  $\lambda = 210$  nm, 13.2 min (major), 14.5 min (minor);  $[\alpha]_{\text{D}}^{22} = -22.0$  ( $c = 3.5$ ,  $\text{CHCl}_3$ , 76% ee).



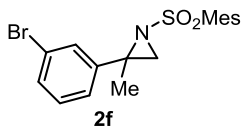
**2c:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21 (1H, td,  $J = 7.1, 1.4$  Hz), 7.18 (1H, s), 7.17 (1H, dd,  $J = 7.1, 1.4$  Hz), 7.08 (1H, d,  $J = 7.1$  Hz), 6.95 (2H, s), 2.99 (1H, s), 2.71 (6H, s), 2.53 (1H, s), 2.33 (3H, s), 2.30 (3H, s), 2.04 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.7, 141.3, 139.8, 138.2, 135.2, 131.9, 128.5, 128.4, 127.4, 123.7, 51.2, 41.9, 23.3, 21.6, 21.1, one peak for methyl carbon was not found probably due to overlapping; IR 2940, 2920, 1601, 1452, 1321, 1038, 905, 719  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{19}\text{H}_{24}\text{NO}_2\text{S}^+$  ( $[\text{M}+\text{H}]^+$ ) 330.1522. Found 330.1522.



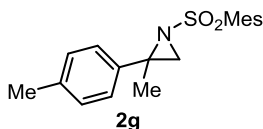
**2d:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.23 (1H, t,  $J = 9.4$  Hz), 6.97 (1H, dd,  $J = 9.4, 0.9$  Hz), 6.96 (2H, s), 6.93 (1H, t,  $J = 0.9$ ), 6.81 (1H, dd,  $J = 9.4, 0.9$  Hz), 3.79 (3H, s), 3.01 (1H, s), 2.72 (6H, s), 2.51 (1H, s), 2.30 (3H, s), 2.05 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  159.7, 143.1, 142.8, 139.8, 135.1, 131.9, 129.6, 118.9, 113.4, 112.3, 55.3, 51.1, 42.0, 23.3, 21.1, 20.9; IR 2967, 2918, 1601, 1315, 1111, 905, 698  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{19}\text{H}_{24}\text{NO}_3\text{S}^+$  ( $[\text{M}+\text{H}]^+$ ) 346.1471. Found 346.1472.



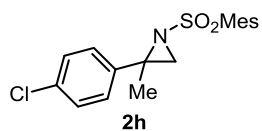
**2e:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 (1H, t,  $J = 1.4$  Hz), 7.30-7.28 (3H, m), 6.97 (2H, s), 3.01 (1H, s), 2.71 (6H, s), 2.50 (1H, s), 2.31 (3H, s), 2.04 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.3, 143.0, 139.8, 134.9, 134.4, 132.0, 129.9, 128.0, 126.9, 124.9, 50.1, 42.0, 23.3, 21.1, 20.6; IR 3472, 3148, 1599, 1314, 1130, 1053, 878  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{SCl}^+$  ( $[\text{M}+\text{H}]^+$ ) 350.0976. Found 350.0977.



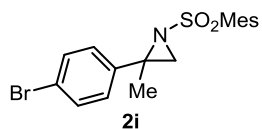
**2f:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 (1H, t,  $J = 1.8$  Hz), 7.40 (1H, dt,  $J = 7.8, 1.8$  Hz), 7.33 (1H, dt,  $J = 7.8, 1.8$  Hz), 7.20 (1H, t,  $J = 7.8$  Hz), 6.97 (2H, s), 3.01 (1H, s), 2.71 (6H, s), 2.50 (1H, s), 2.31 (3H, s), 2.04 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.6, 143.0, 139.8, 134.9, 132.0, 130.9, 130.2, 129.9, 125.4, 122.6, 50.1, 42.0, 23.3, 21.2, 20.6; IR 3144, 2943, 1601, 1315, 1144, 876, 683  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{SBr}^+$  ( $[\text{M}+\text{H}]^+$ ) 394.0471. Found 394.0472.



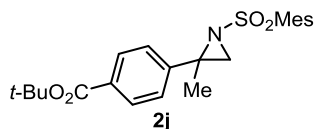
**2g:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27 (2H, d,  $J = 8.2$  Hz), 7.13 (2H, d,  $J = 8.2$  Hz), 6.95 (2H, s), 2.99 (1H, s), 2.70 (6H, s), 2.53 (1H, s), 2.33 (3H, s), 2.30 (3H, s), 2.03 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.7, 140.0, 138.3, 137.5, 135.2, 131.9, 129.2, 126.6, 51.0, 42.1, 23.3, 21.2, 21.1, one peak for methyl carbon was not found probably due to overlapping; IR 3028, 2938, 1603, 1319, 1157, 820, 692  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{19}\text{H}_{24}\text{NO}_2\text{S}^+$  ( $[\text{M}+\text{H}]^+$ ) 330.1522. Found 330.1536.



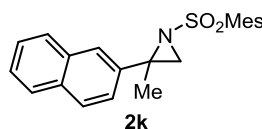
**2h:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 (2H, dd,  $J = 6.1, 2.8$  Hz), 7.29 (2H, dd,  $J = 6.1, 2.8$  Hz), 6.96 (2H, s), 3.00 (1H, s), 2.70 (6H, s), 2.51 (1H, s), 2.30 (3H, s), 2.03 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.9, 139.8, 139.7, 135.0, 133.6, 131.9, 128.7, 128.1, 50.2, 42.0, 23.3, 21.1, 20.8; IR 3159, 2943, 2633, 1317, 1148, 868, 696  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{SCl}^+$  ( $[\text{M}+\text{H}]^+$ ) 350.0976. Found 350.0978.



**2i:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (2H, dd,  $J = 6.7, 1.8$  Hz), 7.26 (2H, dd,  $J = 6.7, 1.8$  Hz), 6.96 (2H, s), 3.00 (1H, s), 2.70 (6H, s), 2.50 (1H, s), 2.31 (3H, s), 2.03 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.9, 140.4, 139.7, 134.9, 131.9, 131.6, 128.4, 121.8, 50.2, 42.0, 23.3, 21.1, 20.7; IR 3275, 2932, 1321, 1161, 1055, 872, 723  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{SBr}^+$  ( $[\text{M}+\text{H}]^+$ ) 394.0471. Found 394.0468.

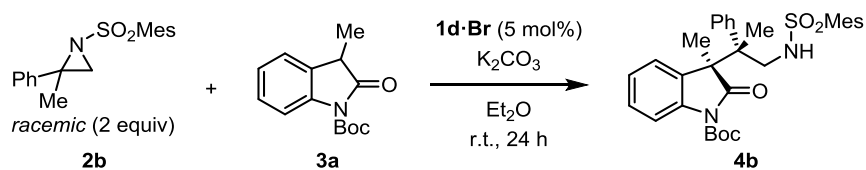


**2j:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (2H, dt,  $J = 8.7, 1.8$  Hz), 7.43 (2H, dt,  $J = 8.7, 1.8$  Hz), 6.96 (2H, s), 3.03 (1H, s), 2.71 (6H, s), 2.52 (1H, s), 2.31 (3H, s), 2.06 (3H, s), 1.59 (9H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.5, 145.7, 143.0, 139.8, 135.0, 132.0, 131.5, 129.7, 126.5, 81.3, 50.5, 42.1, 28.3, 23.3, 21.2, 20.6; IR 2976, 1721, 1452, 1300, 1049, 858, 569  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{23}\text{H}_{29}\text{NO}_4\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 438.1710. Found 438.1710.



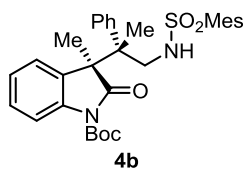
**2k:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.82-7.79 (4H, m), 7.51-7.45 (3H, m), 6.96 (2H, s), 3.09 (1H, s), 2.73 (6H, s), 2.66 (1H, s), 2.30 (3H, s), 2.15 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.8, 139.8, 138.7, 135.2, 133.1, 132.8, 131.9, 128.4, 128.1, 127.8, 126.5, 126.4, 125.6, 124.6, 51.2, 42.1, 23.3, 21.2, 20.9; IR 3472, 2932, 2658, 1314, 1130, 935, 854, 696  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{22}\text{H}_{24}\text{NO}_2\text{S}^+$  ( $[\text{M}+\text{H}]^+$ ) 366.1522. Found 366.1523.; HPLC conditions for the recovered aziridine **2k** (Scheme 1), AD3, Hex/IPA = 10:1, flow rate = 1.0 mL/min,  $\lambda = 210$  nm, 6.9 min (*S*), 8.1 min (*R*);  $[\alpha]_{\text{D}}^{22} = +11.5$  ( $c = 1.5$ ,  $\text{CHCl}_3$ , 76% ee).

### General Procedure for **1d·Br**-Catalyzed Asymmetric Ring-Opening Alkylation of 2,2-Disubstituted Aziridines **2** with Oxindole **3**:

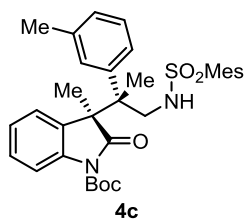


A solution of **1d·Br** (4.76 mg, 0.005 mmol), aziridine **2b** (63.1 mg, 0.20 mmol), and oxindole **3a** (24.7 mg, 0.10 mmol) in  $\text{Et}_2\text{O}$  (1.0 mL) was degassed by alternating vacuum evacuation/Ar backfill. To this solution was added  $\text{K}_2\text{CO}_3$  (13.8 mg, 0.10 mmol) and the mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with a saturated aqueous solution of  $\text{NH}_4\text{Cl}$  and the extractive work-up was performed with  $\text{CHCl}_3$ . After drying over  $\text{Na}_2\text{SO}_4$ , filtration, and removal of solvent, the resulting crude residue was purified by column chromatography (Hex/ $\text{CHCl}_3$ / $\text{EtOAc} = 8:2:1$  as eluent) to afford **4b** (55.7 mg, 0.10 mmol, 99% yield) as a white solid.

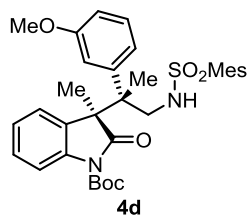
#### Characterization of Alkylation Products 4:



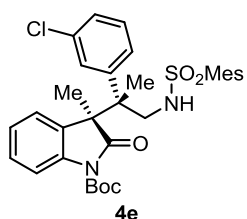
**4b:**  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.97 (1H, d,  $J = 7.8$  Hz), 6.96-6.90 (2H, m), 6.83 (2H, t,  $J = 7.6$  Hz), 6.63 (1H, td,  $J = 7.8, 1.0$  Hz), 6.58 (2H, s), 6.54 (2H, d,  $J = 7.6$  Hz), 6.03 (1H, d,  $J = 7.6$  Hz), 4.26 (1H, dd,  $J = 8.7, 5.5$  Hz), 3.90 (1H, dd,  $J = 12.4, 8.7$  Hz), 3.71 (1H, dd,  $J = 12.4, 5.5$  Hz), 2.59 (6H, s), 1.91 (3H, s), 1.42 (9H, s), 1.24 (3H, s), 1.05 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  177.0, 149.4, 141.8, 140.3, 139.6, 139.4, 134.5, 132.1, 130.7, 128.5, 127.3, 125.1, 123.3, 114.7, 83.3, 54.1, 47.4, 46.8, 28.0, 23.2, 20.7, 18.9, 18.5, two peaks for aromatic carbons were not found probably due to overlapping; IR 2978, 2371, 1732, 1605, 1479, 1348, 1153, 754  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{32}\text{H}_{38}\text{N}_2\text{O}_5\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 585.2394. Found 585.2390.; HPLC ID3, Hex/IPA = 10:1, flow rate = 0.5 mL/min,  $\lambda = 210$  nm, 40.7 min (major isomer of major diastereomer), 63.8 min (minor isomer of major diastereomer), 73.8 min (minor diastereomer), 78.6 min (minor diastereomer).



**4c:**  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.95 (1H, brd,  $J = 6.0$  Hz), 6.94 (1H, t,  $J = 8.0$  Hz), 6.83-6.77 (2H, m), 6.65 (1H, t,  $J = 7.6$  Hz), 6.58 (2H, s), 6.44 (1H, brd,  $J = 7.4$  Hz), 6.35 (1H, s), 6.12 (1H, brd,  $J = 6.9$  Hz), 4.35-4.19 (1H, m), 3.88 (1H, dd,  $J = 12.4, 8.7$  Hz), 3.70 (1H, dd,  $J = 12.4, 4.6$  Hz), 2.58 (6H, s), 1.92 (3H, s), 1.91 (3H, s), 1.41 (9H, s), 1.30 (3H, s), 1.07 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  176.9, 149.4, 141.7, 140.4, 139.5, 139.2, 137.2, 134.5, 134.4, 132.1, 130.8, 128.9, 128.5, 125.3, 125.1, 123.2, 114.6, 83.2, 54.1, 47.5, 46.8, 27.9, 23.1, 21.5, 20.7, 18.8, 18.5, one peak for aromatic carbon was not found probably due to overlapping; IR 3319, 2978, 1730, 1605, 1479, 1290, 847, 652  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{33}\text{H}_{40}\text{N}_2\text{O}_5\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 599.2550. Found 599.2549.; HPLC ID3, Hex/IPA = 19:1, flow rate = 0.5 mL/min,  $\lambda = 210$  nm, 70.5 min (major isomer of major diastereomer), 106 min (minor isomer of major diastereomer), 124 min (minor diastereomer), 132 min (minor diastereomer).



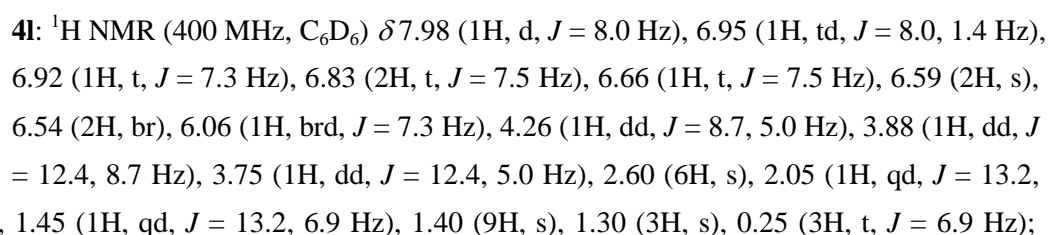
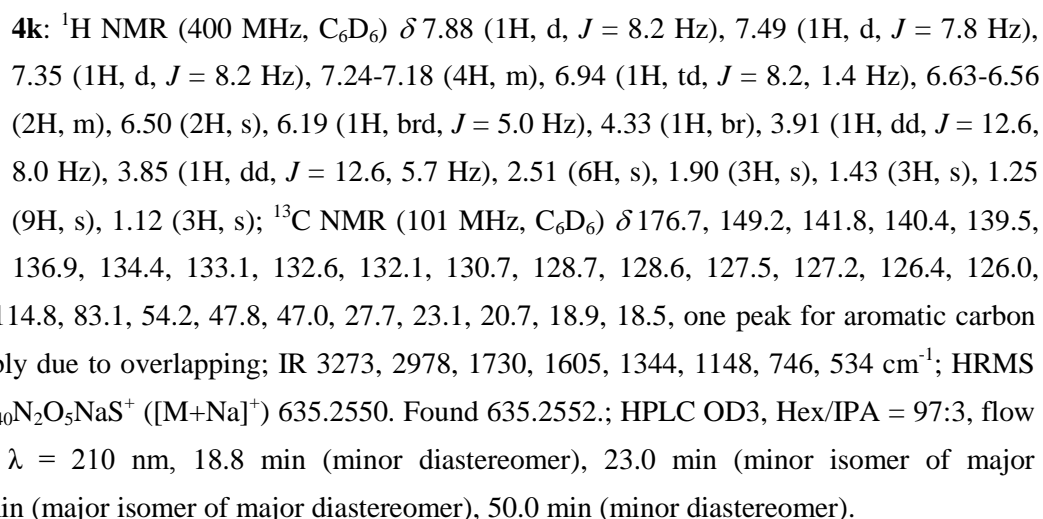
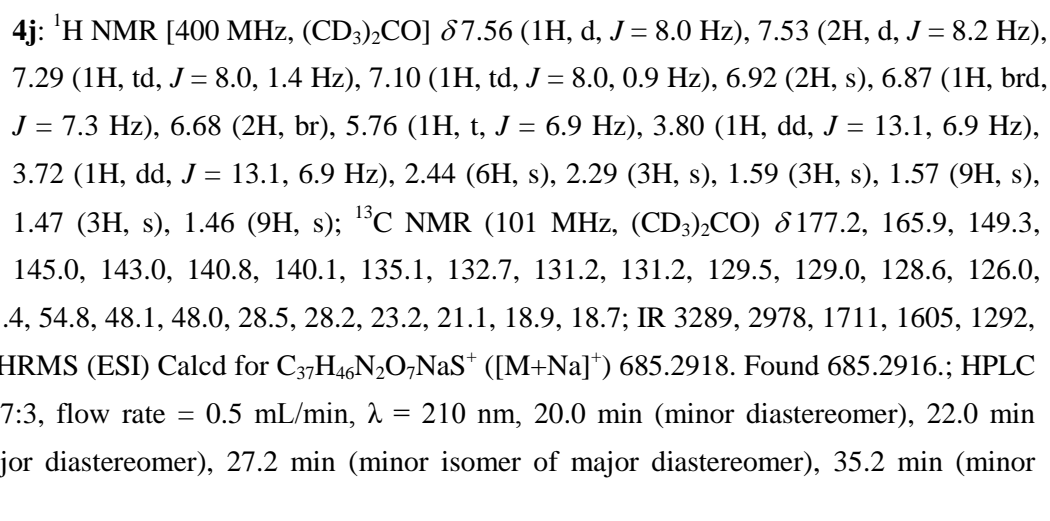
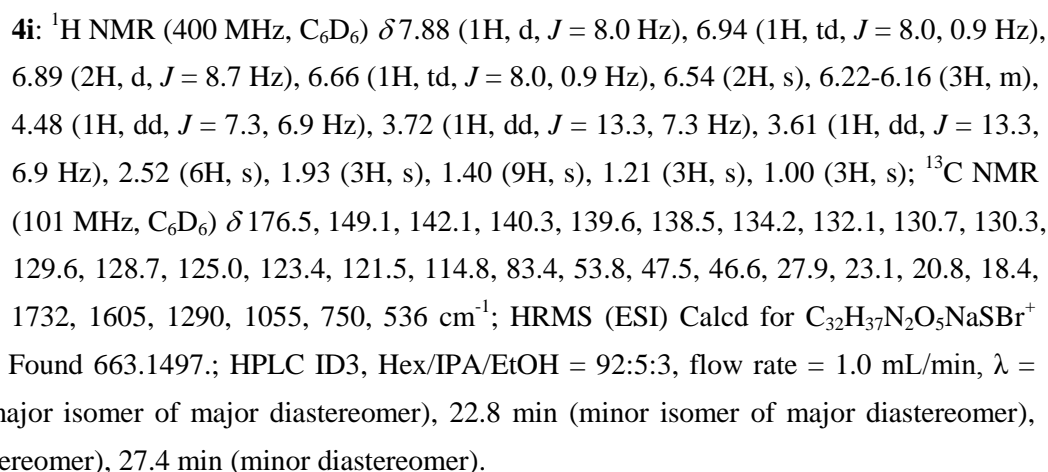
**4d:**  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.93 (1H, d,  $J = 8.2$  Hz), 6.93 (1H, td,  $J = 7.8, 1.4$  Hz), 6.78 (1H, t,  $J = 7.8$  Hz), 6.66 (1H, t,  $J = 7.3$  Hz), 6.59-6.56 (3H, m), 6.28 (1H, brs), 6.25 (1H, d,  $J = 7.3$  Hz), 6.19 (1H, d,  $J = 7.8$  Hz), 4.42 (1H, dd,  $J = 8.7, 4.8$  Hz), 3.85 (1H, dd,  $J = 12.5, 8.7$  Hz), 3.70 (1H, dd,  $J = 12.5, 4.8$  Hz), 3.19 (3H, s), 2.58 (6H, s), 1.92 (3H, s), 1.41 (9H, s), 1.33 (3H, s), 1.08 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  176.8, 159.5, 149.4, 141.8, 140.9, 140.4, 139.5, 134.4, 132.1, 130.8, 128.9, 128.5, 125.1, 123.3, 120.3, 114.7, 114.1, 113.3, 83.2, 54.5, 54.0, 47.7, 46.9, 27.9, 23.1, 20.7, 18.8, 18.5; IR 3315, 2978, 1730, 1602, 1290, 1147, 750  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{33}\text{H}_{40}\text{N}_2\text{O}_6\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 615.2499. Found 615.2495.; HPLC ID3, Hex/EtOH = 10:1, flow rate = 1.0 mL/min,  $\lambda = 210$  nm, 16.1 min (major isomer of major diastereomer), 18.5 min (minor isomer of major diastereomer), 21.5 min (minor diastereomer), 23.8 min (minor diastereomer).



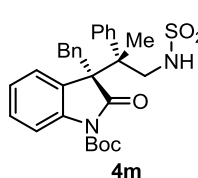
**4e:**  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.92 (1H, d,  $J = 8.2$  Hz), 6.93 (1H, td,  $J = 8.2, 1.4$  Hz), 6.89 (1H, dd,  $J = 7.8, 1.4$  Hz), 6.70-6.66 (2H, m), 6.57 (2H, s), 6.48 (1H, t,  $J = 7.8$  Hz), 6.24 (1H, brd,  $J = 7.3$  Hz), 6.18 (1H, brd,  $J = 6.9$  Hz), 4.32 (1H, dd,  $J = 7.8, 6.2$  Hz), 3.71 (1H, dd,  $J = 12.7, 7.8$  Hz), 3.58 (1H, dd,  $J = 12.7, 6.2$  Hz), 2.54 (6H, s), 1.91 (3H, s), 1.42 (9H, s), 1.19 (3H, s), 0.99 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  176.4, 149.3,





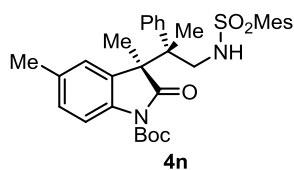


$^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  176.4, 149.3, 141.8, 141.5, 139.6, 139.5, 134.5, 132.1, 128.6, 127.2, 125.3, 123.3, 114.7, 83.3, 60.2, 47.5, 47.3, 27.9, 24.4, 23.2, 20.7, 19.1, 9.5, three peaks for aromatic carbons were not found probably due to overlapping; IR 3283, 2978, 1730, 1605, 1296, 1152, 754, 660  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{33}\text{H}_{40}\text{N}_2\text{O}_5\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 599.2550. Found 599.2550.; HPLC ID3, Hex/EtOH = 97:3, flow rate = 1.0 mL/min,  $\lambda$  = 210 nm, 23.8 min (major isomer of major diastereomer), 31.9 min (minor isomer of major diastereomer), 34.2 min (minor diastereomer), 41.9 min (minor diastereomer).



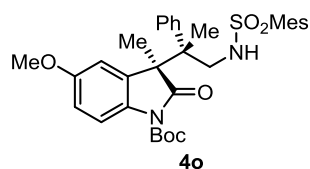
**4m:**  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.69 (1H, d,  $J$  = 8.0 Hz), 6.97 (1H, t,  $J$  = 7.3 Hz), 6.89 (2H, t,  $J$  = 7.8 Hz), 6.81 (1H, td,  $J$  = 8.0, 1.4 Hz), 6.77-6.63 (8H, m), 6.60 (2H, s), 6.20 (1H, brd,  $J$  = 7.3 Hz), 4.43 (1H, dd,  $J$  = 8.7, 5.0 Hz), 4.23 (1H, dd,  $J$  = 12.5, 8.7 Hz), 3.92 (1H, dd,  $J$  = 12.5, 5.0 Hz), 3.45 (1H, d,  $J$  = 12.8 Hz), 2.83 (1H, d,  $J$  = 12.8

Hz), 2.64 (6H, s), 1.91 (3H, s), 1.34 (9H, s), 1.31 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  176.1, 149.0, 141.8, 141.2, 139.8, 139.6, 135.7, 134.7, 132.2, 130.7, 128.6, 127.4, 126.7, 126.3, 122.7, 114.6, 83.2, 61.0, 47.6, 38.2, 27.9, 23.2, 20.7, 19.5, four peaks for aromatic carbons and one peak for aliphatic carbon were not found probably due to overlapping; IR 3292, 2980, 1730, 1605, 1252, 1032, 748, 654  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{38}\text{H}_{42}\text{N}_2\text{O}_5\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 661.2707. Found 661.2702.; HPLC ID3, Hex/EtOH = 10:1, flow rate = 1.0 mL/min,  $\lambda$  = 210 nm, 15.5 min (major isomer of major diastereomer), 21.1 min (minor diastereomer), 28.9 min (minor isomer of major diastereomer), 53.1 min (minor diastereomer).



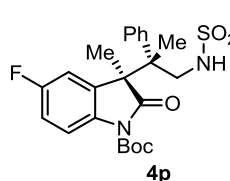
**4n:**  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.90 (1H, d,  $J$  = 8.2 Hz), 6.93 (1H, t,  $J$  = 7.4 Hz), 6.83 (2H, t,  $J$  = 7.4 Hz), 6.77 (1H, dd,  $J$  = 8.2, 1.4 Hz), 6.59 (2H, s), 6.54 (2H, d,  $J$  = 7.4 Hz), 5.89 (1H, brs), 4.39-4.31 (1H, m), 3.92 (1H, dd,  $J$  = 12.6, 8.5 Hz), 3.70 (1H, dd,  $J$  = 12.6, 5.0 Hz), 2.59 (6H, s), 1.93 (3H, s), 1.91 (3H, s), 1.42 (9H, s),

1.27 (3H, s), 1.09 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  177.1, 149.5, 141.8, 139.6, 139.5, 138.0, 134.4, 132.6, 132.1, 130.7, 129.0, 127.3, 125.9, 114.5, 83.1, 54.1, 47.4, 46.8, 28.0, 23.2, 20.9, 20.7, 18.9, 18.6, two peaks for aromatic carbons were not found probably due to overlapping; IR 3291, 2978, 1728, 1605, 1304, 1055, 750, 656  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{33}\text{H}_{40}\text{N}_2\text{O}_5\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 599.2550. Found 599.2544.; HPLC AD3, Hex/IPA = 97:3, flow rate = 1.0 mL/min,  $\lambda$  = 210 nm, 22.6 min (minor diastereomer), 28.8 min (minor isomer of major diastereomer), 36.4 min (major isomer of major diastereomer), 44.2 min (minor diastereomer).



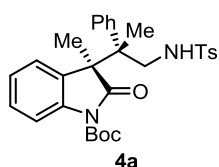
**4o:**  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.96 (1H, d,  $J$  = 8.7 Hz), 6.92 (1H, t,  $J$  = 7.3 Hz), 6.85 (2H, t,  $J$  = 7.3 Hz), 6.61-6.58 (5H, m), 5.62 (1H, brs), 4.40 (1H, dd,  $J$  = 8.7, 5.0 Hz), 4.00 (1H, dd,  $J$  = 12.8, 8.7 Hz), 3.73 (1H, dd,  $J$  = 12.8, 5.0 Hz), 3.15 (3H, s), 2.61 (6H, s), 1.92 (3H, s), 1.45 (9H, s), 1.22 (3H, s), 1.06 (3H, s);

$^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  177.2, 156.2, 149.6, 141.8, 139.5, 139.5, 134.5, 133.5, 132.1, 132.0, 127.3, 115.6, 113.7, 111.5, 83.2, 54.9, 54.4, 47.2, 46.8, 28.0, 23.2, 20.7, 19.0, 18.9, two peaks for aromatic carbons were not found probably due to overlapping; IR 3283, 2978, 1726, 1605, 1277, 1150, 748, 656  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{33}\text{H}_{40}\text{N}_2\text{O}_6\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 615.2499. Found 615.2497.; HPLC ID3, Hex/EtOH = 19:1, flow rate = 1.0 mL/min,  $\lambda$  = 210 nm, 35.1 min (major isomer of major diastereomer), 43.5 min (minor diastereomer), 48.3 min (minor diastereomer), 51.3 min (minor isomer of major diastereomer).



**4p:**  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.82 (1H, dd,  $J = 9.1$ ,  $J_{\text{F-H}} = 4.6$  Hz), 6.91 (1H, t,  $J = 7.4$  Hz), 6.82 (2H, t,  $J = 7.4$  Hz), 6.63-6.58 (3H, m), 6.48 (2H, d,  $J = 7.4$  Hz), 5.70 (1H, brd,  $J = 6.4$  Hz), 4.26 (1H, dd,  $J = 8.7$ , 5.0 Hz), 3.89 (1H, dd,  $J = 12.6$ , 8.7 Hz), 3.62 (1H, dd,  $J = 12.6$ , 5.0 Hz), 2.59 (6H, s), 1.92 (3H, s), 1.42 (9H, s), 1.16 (3H, s),

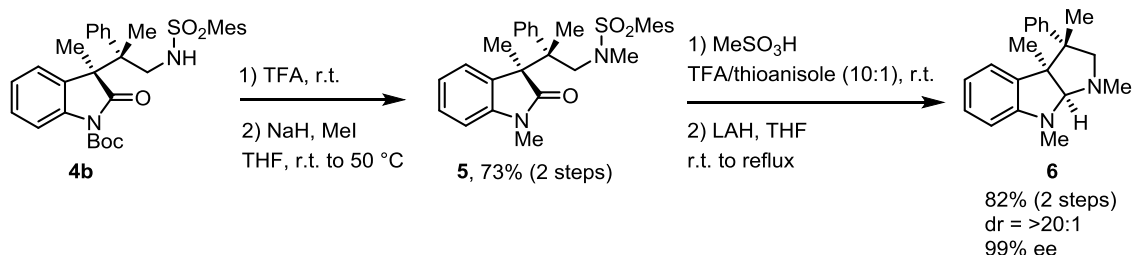
0.93 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  176.6, 159.3 (d,  $J_{\text{F-C}} = 247.7$  Hz), 149.4, 141.9, 139.6, 139.0, 136.1, 134.5, 132.6 (d,  $J_{\text{F-C}} = 7.7$  Hz), 132.1, 127.6, 115.9 (d,  $J_{\text{F-C}} = 6.8$  Hz), 114.9 (d,  $J_{\text{F-C}} = 23.2$  Hz), 112.8 (d,  $J_{\text{F-C}} = 25.2$  Hz), 83.6, 54.3, 47.1, 46.7, 27.9, 23.2, 20.7, 18.9, 18.4, two peaks for aromatic carbons were not found probably due to overlapping;  $^{19}\text{F}$  NMR (376 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  -118.4; IR 3286, 2980, 1732, 1605, 1477, 1152, 754, 658  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{32}\text{H}_{37}\text{N}_2\text{O}_5\text{FNaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 603.2299. Found 603.2296.; HPLC IE3, H/EtOH = 19:1, flow rate = 1.0 mL/min,  $\lambda = 220$  nm, 38.7 (major isomer of major diastereomer), 42.1 min (minor isomer of major diastereomer), 48.1 (minor diastereomer), 50.4 min (minor diastereomer).



**4a:**  $^1\text{H}$  NMR (400 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  7.74 (2H, d,  $J = 8.2$  Hz), 7.60 (1H, d,  $J = 8.0$  Hz), 7.41 (2H, d,  $J = 8.2$  Hz), 7.25 (1H, td,  $J = 8.0$ , 1.4 Hz), 7.17 (1H, t,  $J = 7.3$  Hz), 7.09 (2H, t,  $J = 7.5$  Hz), 7.01 (1H, td,  $J = 7.7$ , 0.9 Hz), 6.82 (2H, d,  $J = 7.3$  Hz), 6.63 (1H, d,  $J = 7.3$  Hz), 5.78 (1H, brt,  $J = 6.6$  Hz), 3.85 (1H, dd,  $J = 12.8$ , 5.6 Hz), 3.74 (1H, dd,  $J = 12.8$ ,

7.8 Hz), 2.44 (3H, s), 1.53 (3H, s), 1.52 (9H, s), 1.45 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  177.5, 149.4, 143.7, 140.6, 140.0, 139.0, 131.4, 130.4, 129.0, 128.9, 128.2, 127.9, 127.7, 126.0, 124.0, 114.8, 83.8, 54.8, 48.2, 47.6, 28.1, 21.4, 19.0, 18.7; IR 3300, 2978, 1734, 1477, 1290, 1060, 754  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{30}\text{H}_{34}\text{N}_2\text{O}_5\text{NaS}^+$  ( $[\text{M}+\text{Na}]^+$ ) 557.2081. Found 557.2080.; HPLC OZ3, H/IPA/EtOH = 92:5:3, flow rate = 0.5 mL/min,  $\lambda = 210$  nm, 48.8 (minor diastereomer), 59.1 min (minor diastereomer), 65.5 min (major isomer of major diastereomer), 89.0 min (minor isomer of major diastereomer).

## Derivatization of 4b to Pyrrolidinoindoline 6



The alkylated product **4b** (169 mg, 0.30 mmol, dr = >20:1.0, 99% ee) was placed in a test tube and dissolved into trifluoroacetic acid (TFA) (0.3 mL). The resulting solution was stirred for 2.5 h at room temperature. After cooling to 0  $^{\circ}\text{C}$ , the reaction mixture was poured onto ice and the aqueous solution thus obtained was neutralized by NaOH. The aqueous phase was extracted with EtOAc and the organic phase was dried over  $\text{Na}_2\text{SO}_4$ . Filtration and concentration of the organic phase gave crude material. This crude material was dissolved into THF (3.0 mL), and NaH (36 mg, 0.9 mmol) was carefully introduced into the solution under Ar at 0  $^{\circ}\text{C}$ . After stirring for 30 min at room temperature, methyl iodide (0.050 mL, 0.9 mmol) was added to the solution and whole reaction mixture was stirred for 12 h at 50  $^{\circ}\text{C}$ . The mixture was then diluted with water and the extractive workup was performed with EtOAc. After drying over  $\text{Na}_2\text{SO}_4$ ,

filtration, and removal of solvent, the resulting crude residue was purified by column chromatography (Hex/EtOAc = 3:1 as eluent) to afford **5** (108 mg, 0.22 mmol, 73% yield for 2 steps) as a white solid.

**5**:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 (1H, t,  $J$  = 7.8 Hz), 7.16-7.11 (4H, m), 6.99-6.96 (3H, m), 6.90 (2H, t,  $J$  = 7.8 Hz), 6.58 (1H, d,  $J$  = 7.8 Hz), 4.41 (1H, d,  $J$  = 14.1 Hz), 3.68 (1H, d,  $J$  = 14.1 Hz), 2.71 (3H, s), 2.65 (6H, s), 2.32 (3H, s), 2.11 (3H, s), 1.33 (6H, s).

To a solution of **5** (108 mg, 0.22 mmol) in TFA (0.2 mL) and thioanisole (0.02 mL) was added  $\text{MeSO}_3\text{H}$  (0.02 mL, 0.33 mmol) and the resulting solution was stirred for 6 h at room temperature. After cooling to 0 °C, the reaction mixture was poured onto ice and the aqueous solution thus obtained was neutralized by NaOH. The aqueous phase was extracted with EtOAc and the organic phase was dried over  $\text{Na}_2\text{SO}_4$ . Filtration and concentration of the organic phase gave crude material. To a solution of this crude material in THF (4.4 mL) was carefully added  $\text{LiAlH}_4$  (83 mg, 2.2 mmol) and the mixture was refluxed for 2 h. After cooling to 0 °C, the reaction was quenched by the addition of  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$  (3.2 g 10 mmol), and the resulting suspension was vigorously stirred overnight at room temperature. The mixture was filtered with the aid of EtOAc and the filtrates were concentrated. Purification of the crude residue by column chromatography (Hex/EtOAc = 1:1 as eluent) furnished **6** (52.6 mg, 0.18 mmol, 82% yield for 2 steps, dr = >20:1.0, 99% ee) as a white solid. **6**:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (2H, dd,  $J$  = 8.0, 1.4 Hz), 7.35 (2H, t,  $J$  = 8.0 Hz), 7.24 (1H, td,  $J$  = 8.0, 1.4 Hz), 7.13 (1H, td,  $J$  = 7.6, 1.4 Hz), 7.11 (1H, dd,  $J$  = 7.6, 1.1 Hz), 6.71 (1H, td,  $J$  = 7.8, 1.1 Hz), 6.43 (1H, d,  $J$  = 8.0 Hz), 4.02 (1H, s), 3.50 (1H, d,  $J$  = 8.9 Hz), 3.08 (1H, d,  $J$  = 8.9 Hz), 2.92 (3H, s), 2.73 (3H, s), 1.32 (3H, s), 0.95 (3H, s);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.7, 145.6, 133.4, 128.3, 128.2, 127.1, 126.3, 123.7, 117.0, 106.5, 102.4, 66.4, 58.3, 51.3, 43.0, 35.2, 26.4, 26.0; IR 2926, 1605, 1491, 1240, 1022, 908, 700  $\text{cm}^{-1}$ ; HRMS (ESI) Calcd for  $\text{C}_{20}\text{H}_{25}\text{N}_2^+$  ( $[\text{M}+\text{H}]^+$ ) 293.2012. Found 293.2007.; HPLC OJ3, H/IPA = 97:3, flow rate = 0.5 mL/min,  $\lambda$  = 210 nm, 10.6 min (major), 14.0 min (minor).

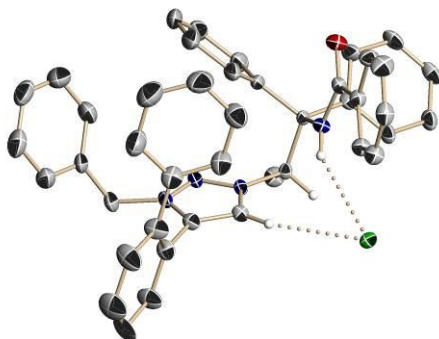
### Crystallographic Structure Determination:

**Recrystallization of 1a·Cl, 4b, 4k, 2k, and 6:** A single crystal of **1a·Cl** was obtained from toluene at room temperature. Single crystals of **4b** and **4k** were obtained from  $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$  solvent system at room temperature. A single crystal of **2k** was obtained from  $\text{Et}_2\text{O}/\text{Hex}$  solvent system at room temperature. A single crystal of **6** was obtained from Hex at room temperature. The single crystals thus obtained were mounted on CryoLoop. Data of X-ray diffraction were collected at 133 K on a Bruker SMART APEX CCD diffractometer with graphite-monochromated Mo  $\text{K}\alpha$  radiation ( $\lambda$  = 0.71073 Å). An absorption correction was made using SADABS. The structure was solved by direct methods and Fourier syntheses, and refined by full-matrix least squares on  $F^2$  by using SHELXTL.<sup>2</sup> All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms bonded to oxygen atoms were located from a difference synthesis and their coordinates and isotropic thermal parameters refined. The other hydrogen atoms were placed in calculated positions. The crystallographic data were summarized in **Tables S2, S3, S4, S5, and S6**.

<sup>2</sup> Sheldrick, G. M. SHELXTL 5.1, Bruker AXS Inc., Madison, Wisconsin, 1997.

**Table S2.** Crystal data, structure refinement for **1a-Cl**.

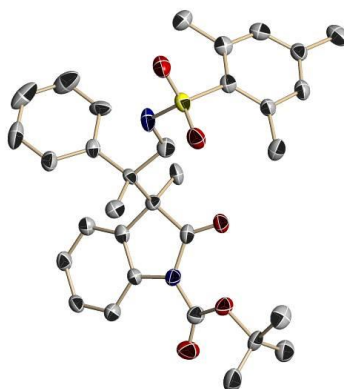
Empirical formula	C <sub>43</sub> H <sub>37</sub> Cl N <sub>4</sub> O	
Formula weight	661.22	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 11.727(3) Å	α = 81.252(4)°.
	b = 11.746(3) Å	β = 72.971(4)°.
	c = 15.471(4) Å	γ = 60.415(4)°.
Volume	1772.0(7) Å <sup>3</sup>	
Z	2	
Density (calculated)	1.239 Mg/m <sup>3</sup>	
Absorption coefficient	0.147 mm <sup>-1</sup>	
F(000)	696	
Crystal size	0.50 x 0.40 x 0.20 mm <sup>3</sup>	
Theta range for data collection	1.99 to 28.42°.	
Index ranges	-13 ≤ h ≤ 15, -13 ≤ k ≤ 15, -20 ≤ l ≤ 18	
Reflections collected	12521	
Independent reflections	10248 [R(int) = 0.0285]	
Completeness to theta = 28.42°	96.1 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	10248 / 3 / 885	
Goodness-of-fit on F <sup>2</sup>	1.062	
Final R indices [I > 2σ(I)]	R1 = 0.0801, wR2 = 0.2197	
R indices (all data)	R1 = 0.0831, wR2 = 0.2225	
Absolute structure parameter	0.14(8)	
Largest diff. peak and hole	1.860 and -0.398 e.Å <sup>-3</sup>	

**Figure S6.** Molecular structure of ion-paired ligand **1a-Cl**. Calculated hydrogen atoms are omitted for clarity.

Blue = nitrogen, red = oxygen, green = chlorine, black = carbon.

**Table S3.** Crystal data and structure refinement for **4b**.

Empirical formula	C <sub>32</sub> H <sub>38</sub> N <sub>2</sub> O <sub>5</sub> S	
Formula weight	562.70	
Temperature	103(2) K	
Wavelength	0.71075 Å	
Crystal system	Orthorhombic	
Space group	P <sub>2</sub> <sub>1</sub> <sub>2</sub> <sub>1</sub> <sub>2</sub> <sub>1</sub>	
Unit cell dimensions	a = 6.4319(16) Å	α = 90°.
	b = 16.382(4) Å	β = 90°.
	c = 27.793(7) Å	γ = 90°.
Volume	2928.4(13) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.276 Mg/m <sup>3</sup>	
Absorption coefficient	0.154 mm <sup>-1</sup>	
F(000)	1200	
Crystal size	0.30 x 0.02 x 0.02 mm <sup>3</sup>	
Theta range for data collection	3.18 to 27.48°.	
Index ranges	-8 ≤ h ≤ 8, -21 ≤ k ≤ 21, -36 ≤ l ≤ 31	
Reflections collected	23968	
Independent reflections	6696 [R(int) = 0.1223]	
Completeness to theta = 27.48°	99.8 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9969 and 0.9553	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	6696 / 0 / 369	
Goodness-of-fit on F <sup>2</sup>	1.035	
Final R indices [I > 2σ(I)]	R1 = 0.0933, wR2 = 0.2105	
R indices (all data)	R1 = 0.1421, wR2 = 0.2481	
Absolute structure parameter	-0.29(16)	
Largest diff. peak and hole	0.721 and -0.402 e.Å <sup>-3</sup>	

**Figure S7.** Molecular structure of ion-paired ligand **4b**. All calculated hydrogen atoms are omitted for clarity. Blue = nitrogen, red = oxygen, yellow = sulfur, black = carbon.

**Table S4.** Crystal data and structure refinement for **4k**.

Empirical formula	C <sub>36</sub> H <sub>41</sub> N <sub>2</sub> O <sub>5</sub> S	
Formula weight	613.77	
Temperature	293(2) K	
Wavelength	0.71075 Å	
Crystal system	Orthorhombic	
Space group	P <sub>21</sub> <sub>21</sub> <sub>21</sub>	
Unit cell dimensions	a = 6.493(2) Å	α = 90°.
	b = 16.778(6) Å	β = 90°.
	c = 30.179(11) Å	γ = 90°.
Volume	3288(2) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.240 Mg/m <sup>3</sup>	
Absorption coefficient	0.143 mm <sup>-1</sup>	
F(000)	1308	
Crystal size	0.30 x 0.05 x 0.05 mm <sup>3</sup>	
Theta range for data collection	3.16 to 27.37°.	
Index ranges	-8 ≤ h ≤ 8, -19 ≤ k ≤ 21, -38 ≤ l ≤ 38	
Reflections collected	26453	
Independent reflections	7433 [R(int) = 0.0952]	
Completeness to theta = 27.37°	99.6 %	
Max. and min. transmission	0.9929 and 0.9584	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	7433 / 0 / 405	
Goodness-of-fit on F <sup>2</sup>	1.016	
Final R indices [I > 2σ(I)]	R1 = 0.0784, wR2 = 0.1907	
R indices (all data)	R1 = 0.1011, wR2 = 0.2145	
Absolute structure parameter	0.06(13)	
Largest diff. peak and hole	0.726 and -0.540 e.Å <sup>-3</sup>	

**Table S5.** Crystal data and structure refinement for **2k**.

Empirical formula	C <sub>32</sub> H <sub>38</sub> N <sub>2</sub> O <sub>5</sub> S	
Formula weight	562.70	
Temperature	103(2) K	
Wavelength	0.71075 Å	
Crystal system	Orthorhombic	
Space group	P <sub>21</sub> <sub>21</sub> <sub>21</sub>	
Unit cell dimensions	a = 6.4319(16) Å	α = 90°.
	b = 16.382(4) Å	β = 90°.
	c = 27.793(7) Å	γ = 90°.



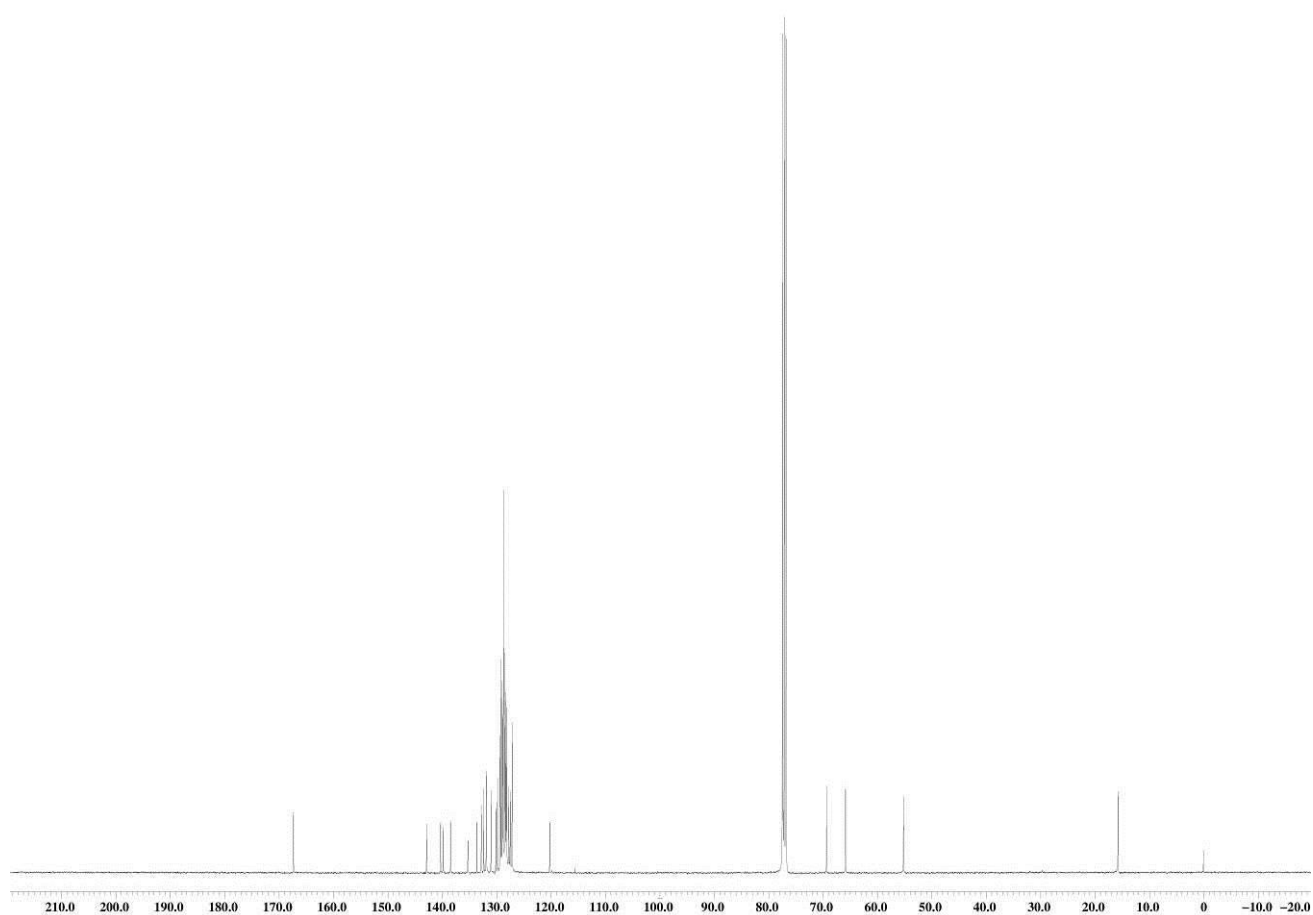
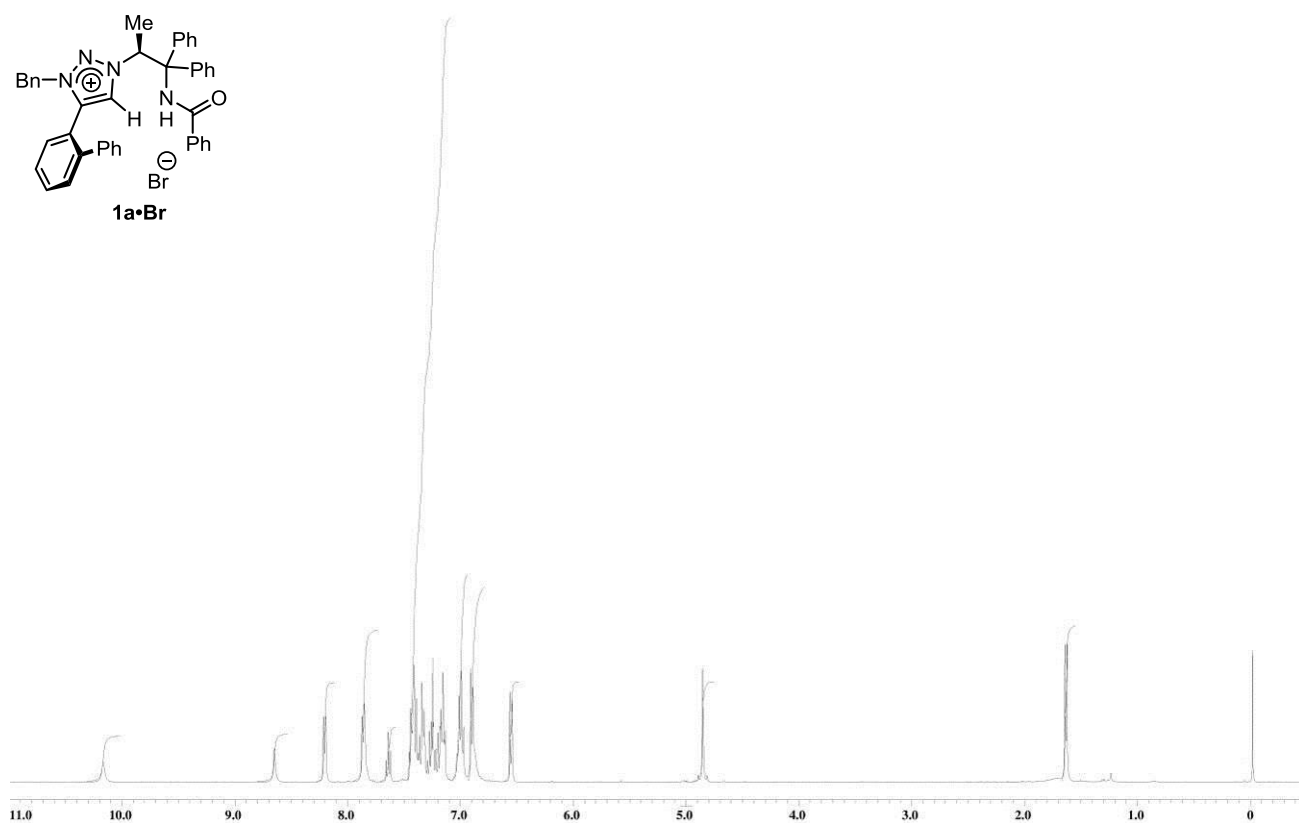
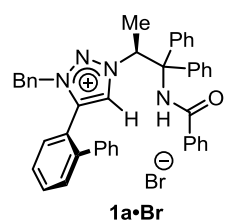
Volume	2928.4(13) Å <sup>3</sup>
Z	4
Density (calculated)	1.276 Mg/m <sup>3</sup>
Absorption coefficient	0.154 mm <sup>-1</sup>
F(000)	1200
Crystal size	0.30 x 0.02 x 0.02 mm <sup>3</sup>
Theta range for data collection	3.18 to 27.48°.
Index ranges	-8<=h<=8, -21<=k<=21, -36<=l<=31
Reflections collected	23968
Independent reflections	6696 [R(int) = 0.1223]
Completeness to theta = 27.48°	99.8 %
Absorption correction	Empirical
Max. and min. transmission	0.9969 and 0.9553
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	6696 / 0 / 369
Goodness-of-fit on F <sup>2</sup>	1.035
Final R indices [I>2sigma(I)]	R1 = 0.0933, wR2 = 0.2105
R indices (all data)	R1 = 0.1421, wR2 = 0.2481
Absolute structure parameter	-0.29(16)
Largest diff. peak and hole	0.721 and -0.402 e.Å <sup>-3</sup>

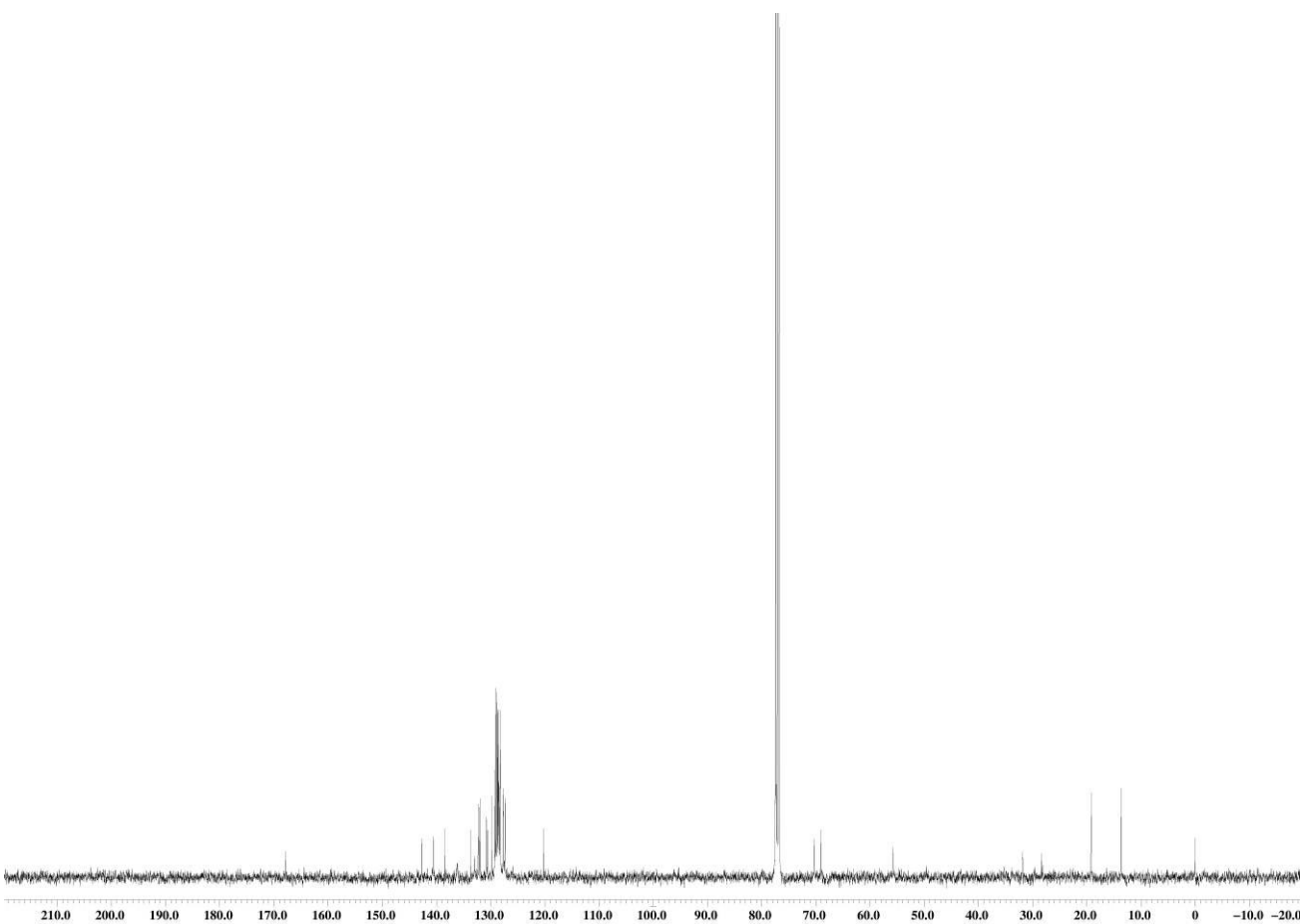
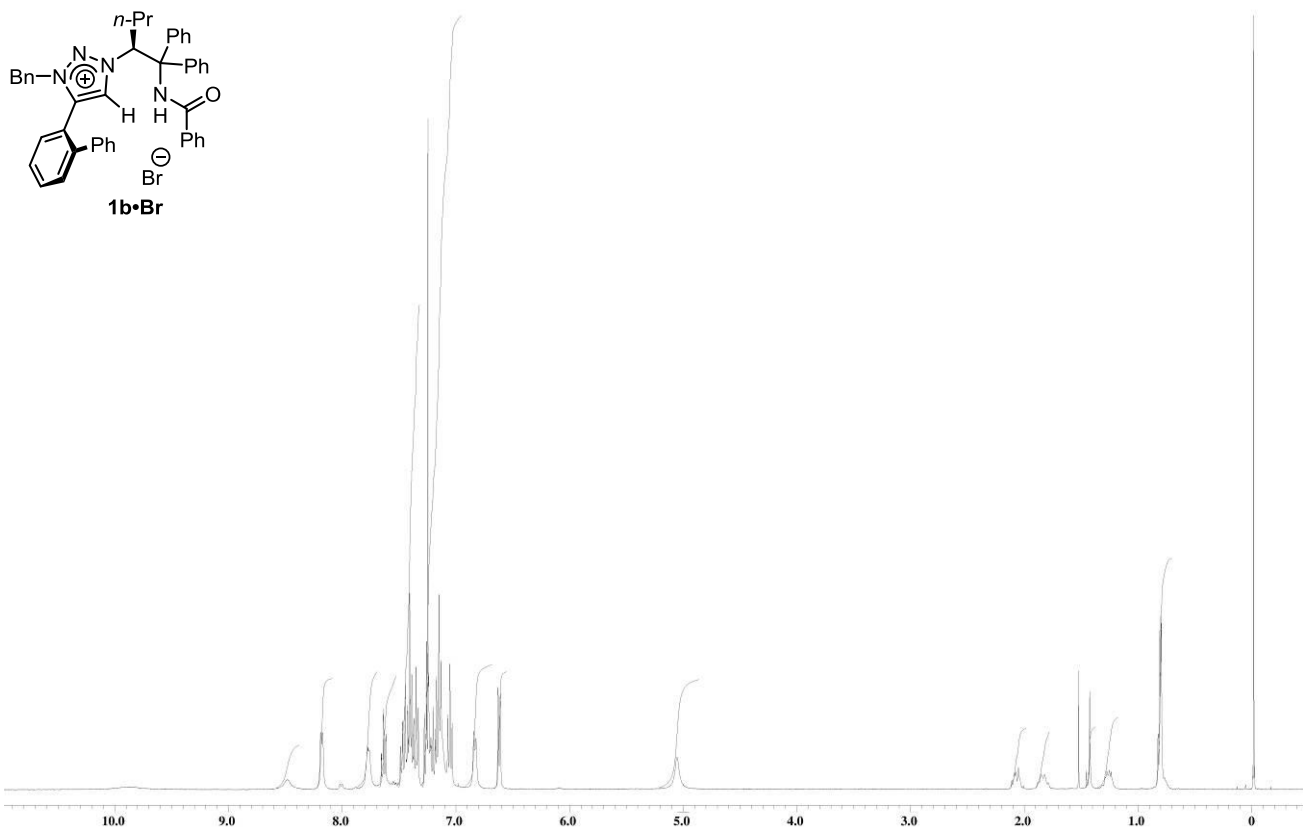
**Table S6.** Crystal data and structure refinement for **6**.

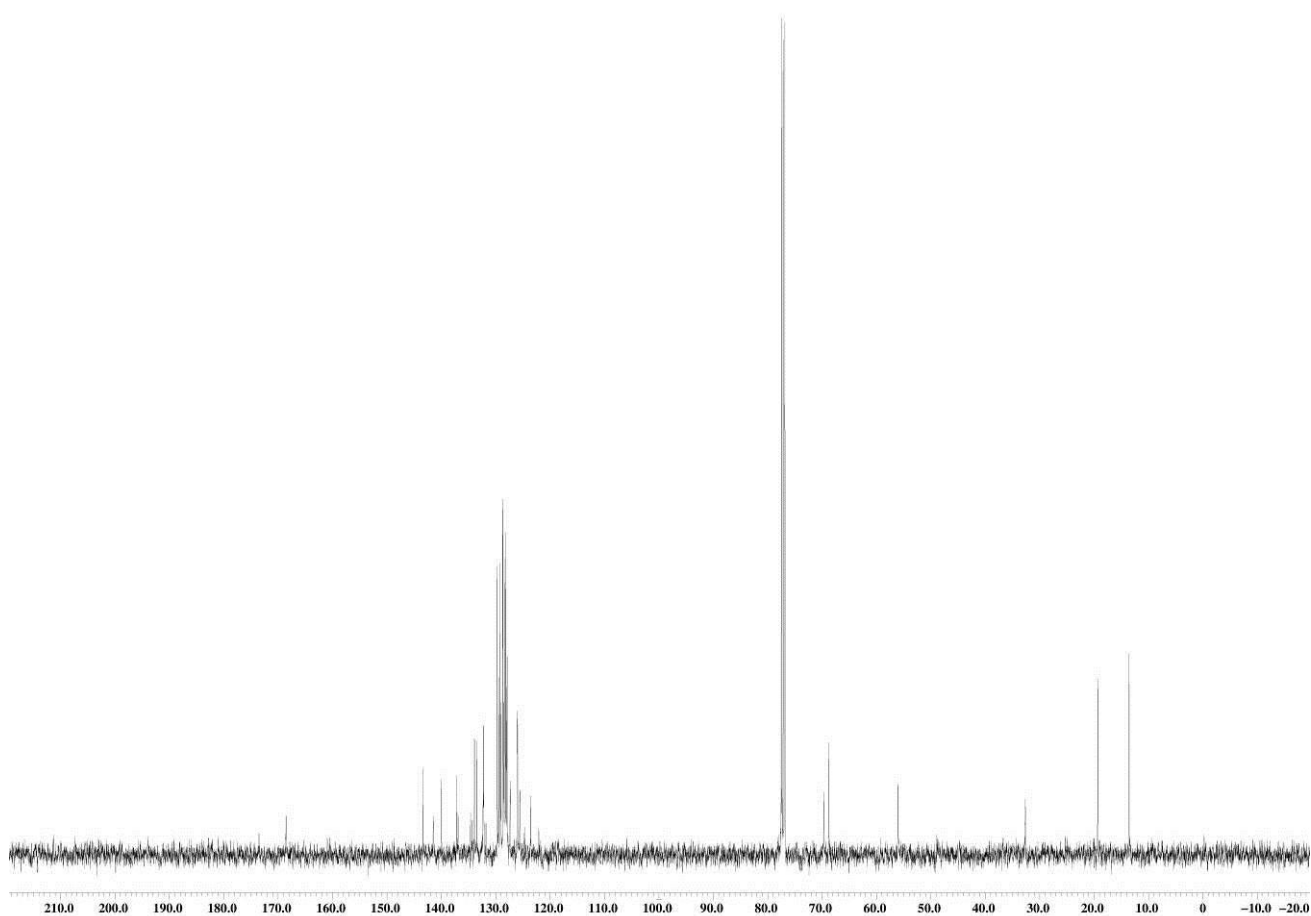
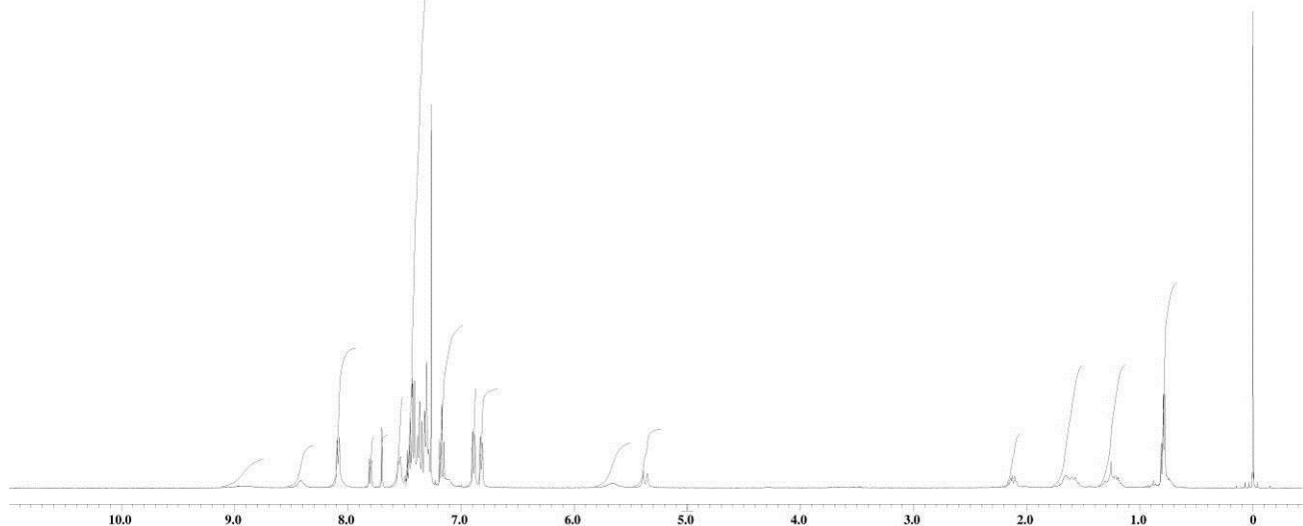
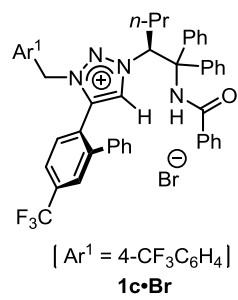
Empirical formula	C20 H24 N2
Formula weight	292.41
Temperature	123(2) K
Wavelength	0.71073 Å
Crystal system	Rhombohedral
Space group	R3
Unit cell dimensions	a = 21.290(6) Å      α = 90°. b = 21.290(6) Å      β = 90°. c = 9.790(4) Å      γ = 120°.
Volume	3843(2) Å <sup>3</sup>
Z	9
Density (calculated)	1.137 Mg/m <sup>3</sup>
Absorption coefficient	0.067 mm <sup>-1</sup>
F(000)	1422
Crystal size	0.30 x 0.20 x 0.10 mm <sup>3</sup>
Theta range for data collection	1.91 to 28.34°.
Index ranges	-28<=h<=24, -27<=k<=28, -13<=l<=12
Reflections collected	7069
Independent reflections	3315 [R(int) = 0.0528]

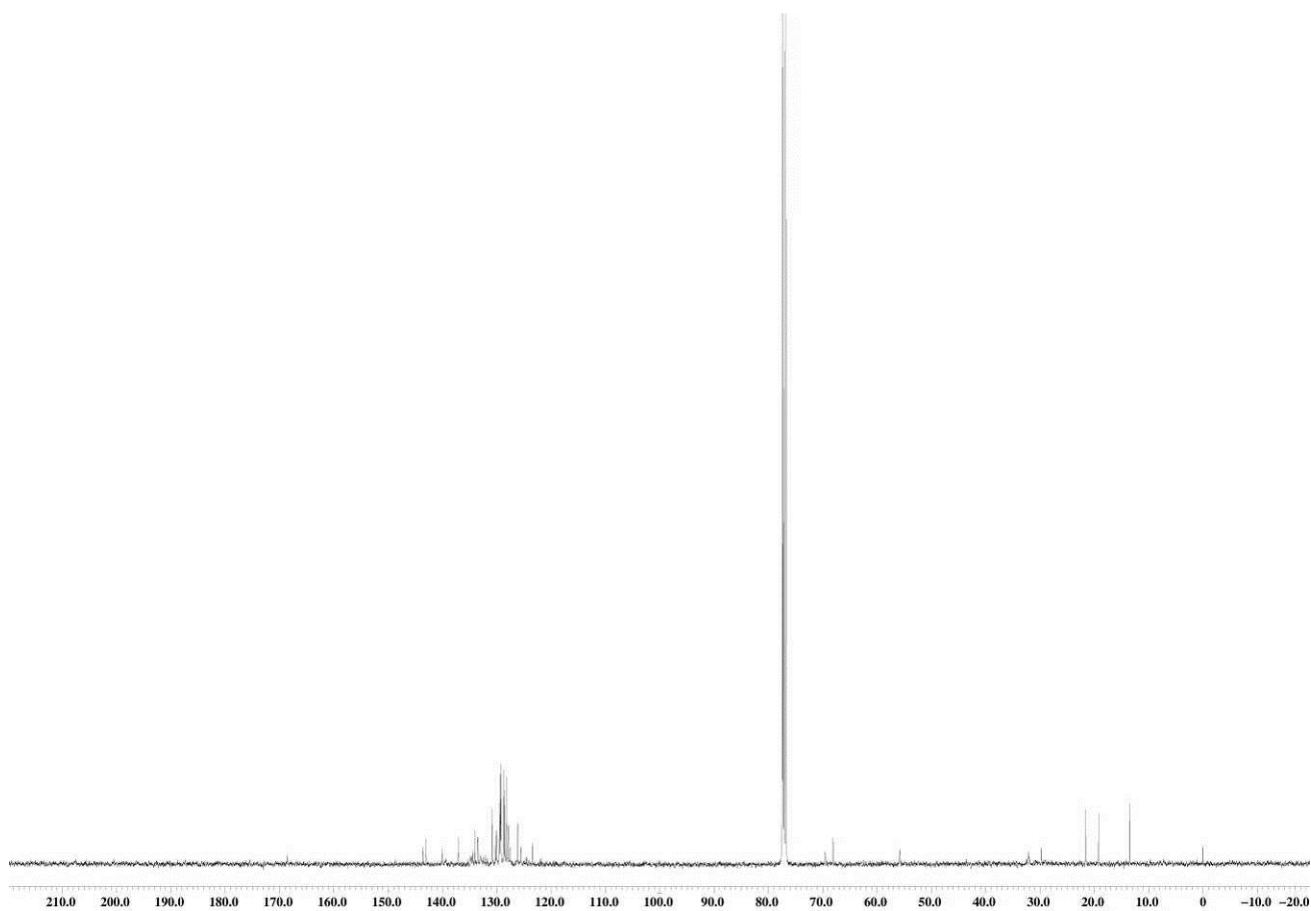
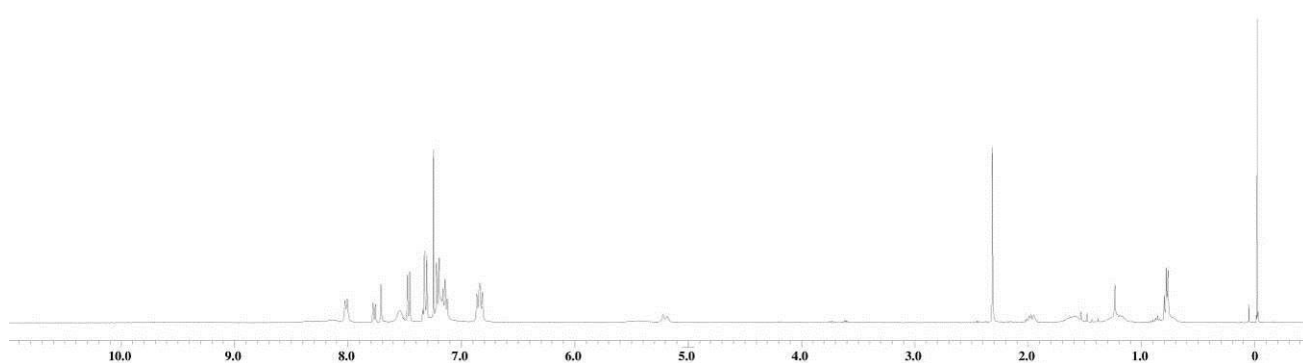
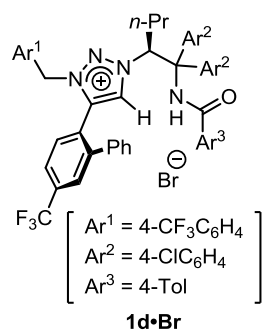
Completeness to $\theta = 28.34^\circ$	87.6 %
Absorption correction	Empirical
Max. and min. transmission	0.9934 and 0.9803
Refinement method	Full-matrix least-squares on $F^2$
Data / restraints / parameters	3315 / 1 / 203
Goodness-of-fit on $F^2$	1.169
Final R indices [ $I > 2\sigma(I)$ ]	$R_1 = 0.0748$ , $wR_2 = 0.1857$
R indices (all data)	$R_1 = 0.0973$ , $wR_2 = 0.1931$
Largest diff. peak and hole	0.235 and -0.220 e. $\text{\AA}^{-3}$

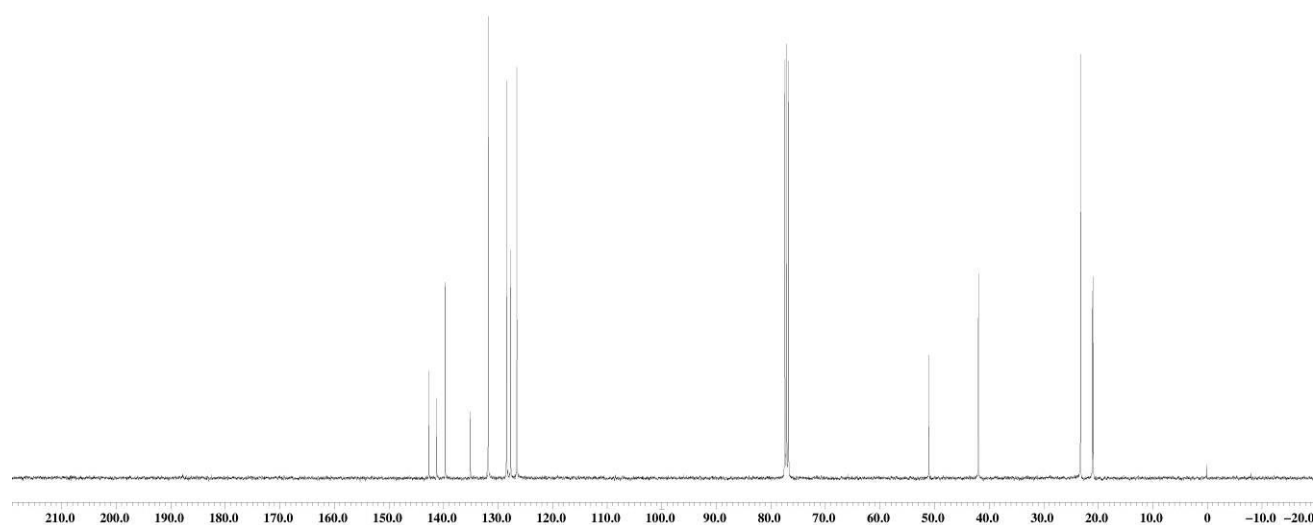
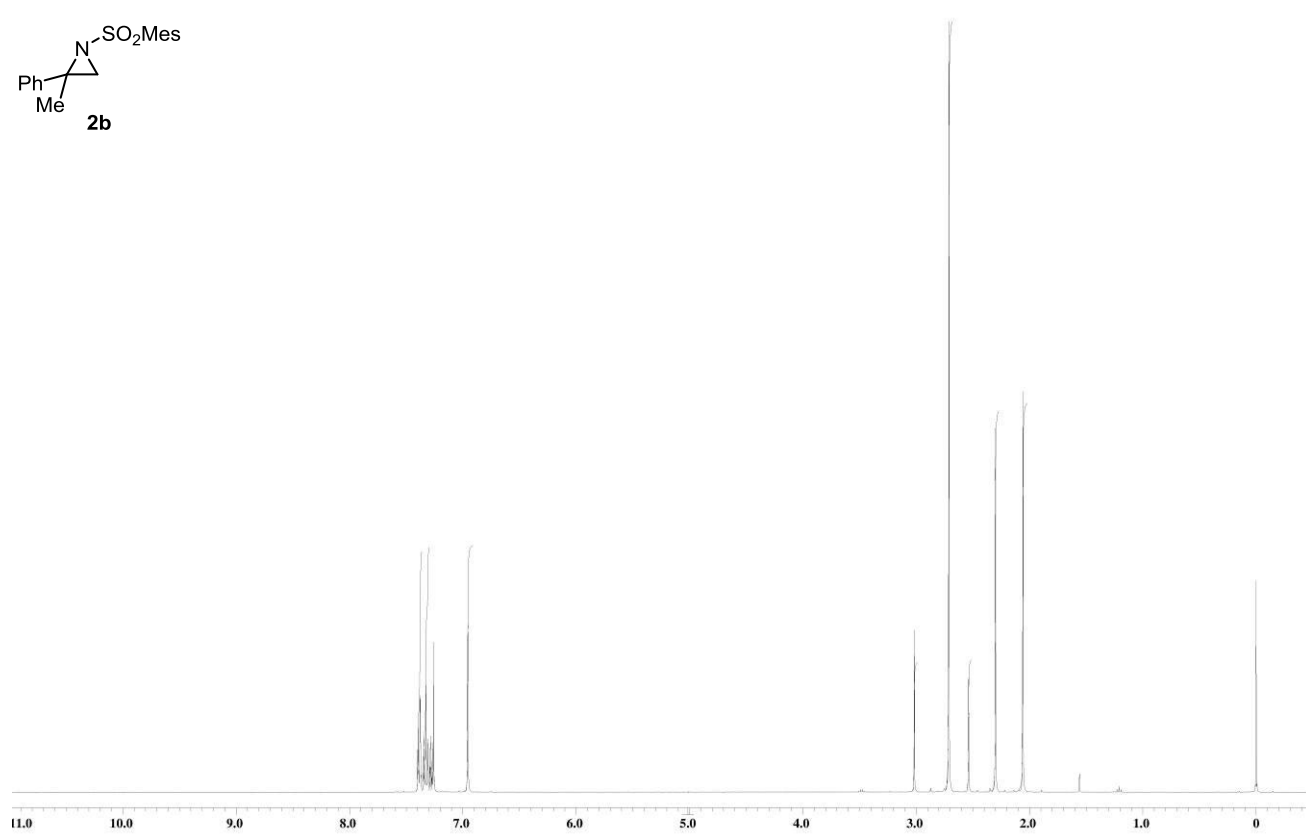
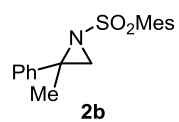
Copies of  $^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra:

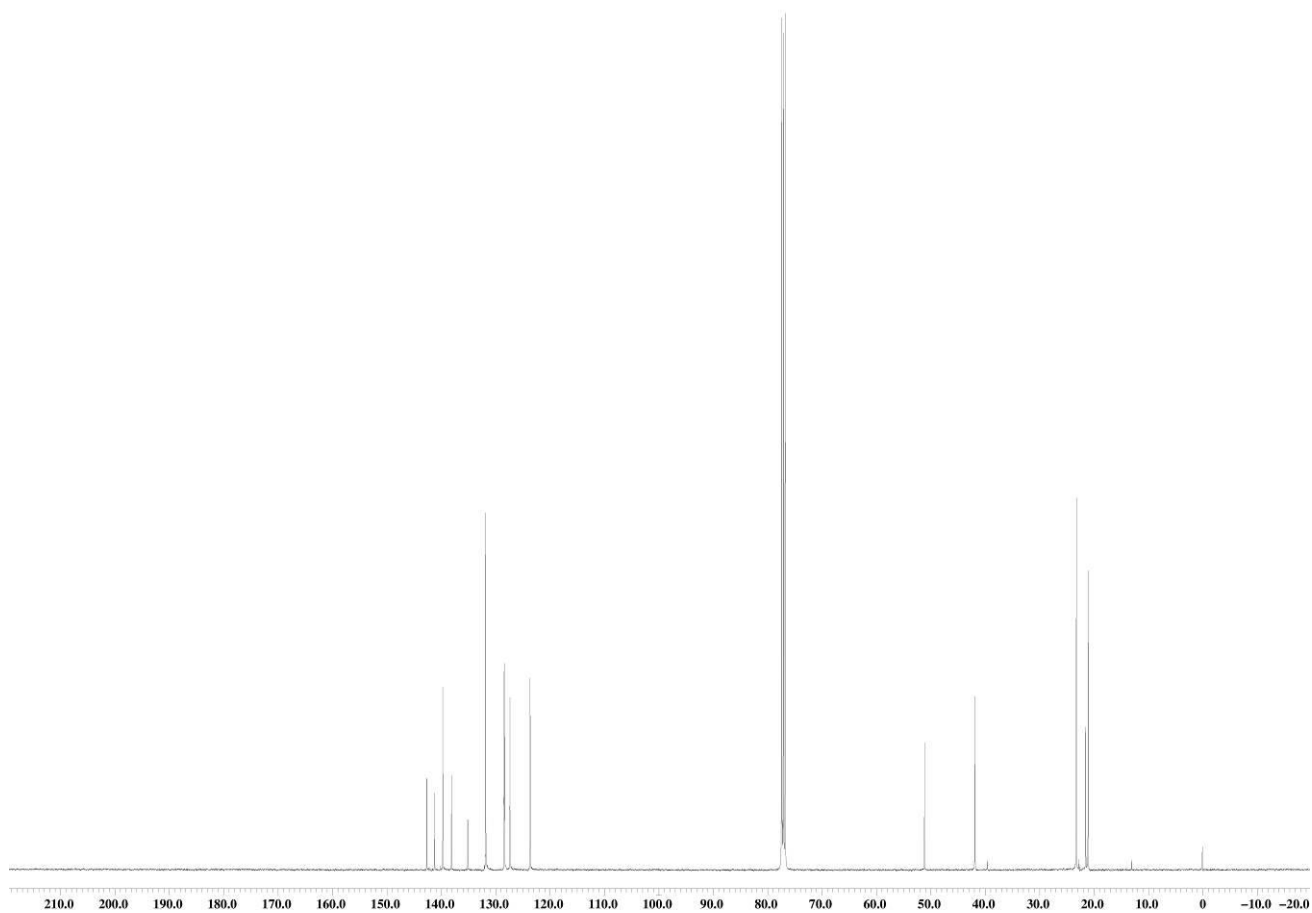
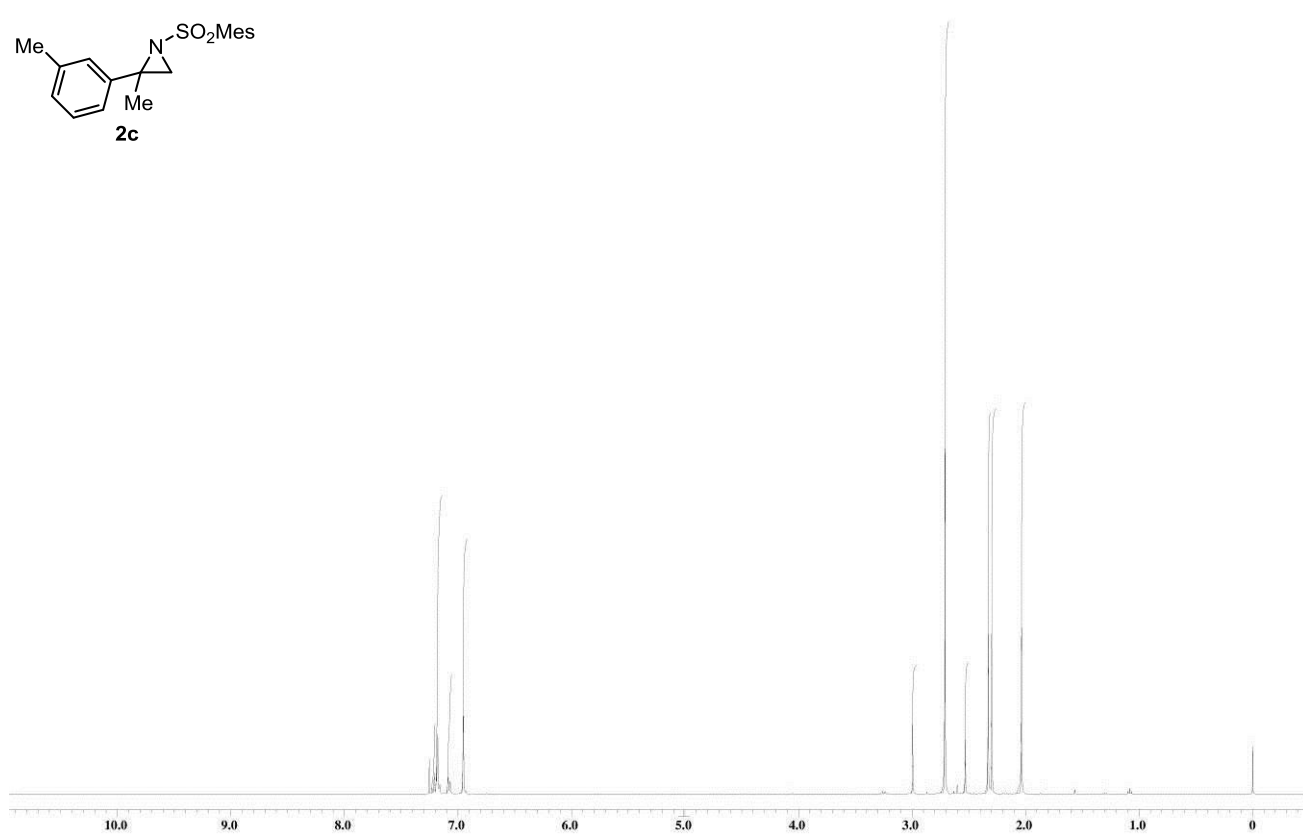
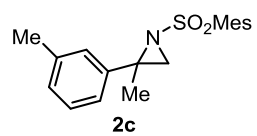




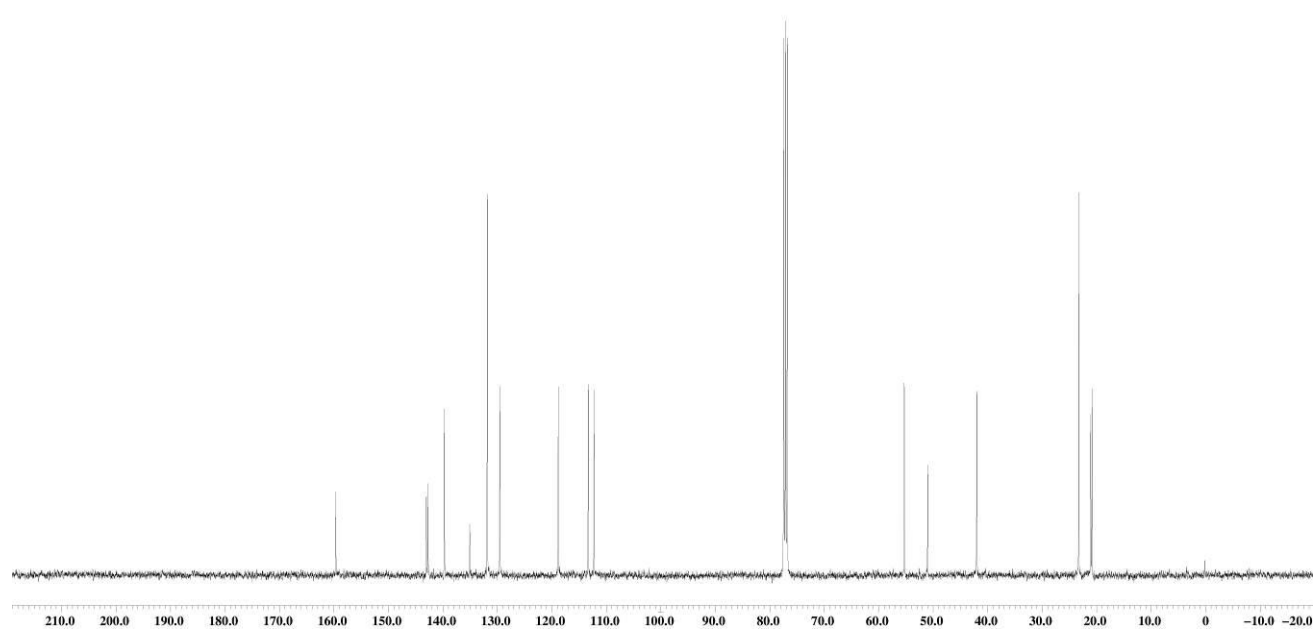
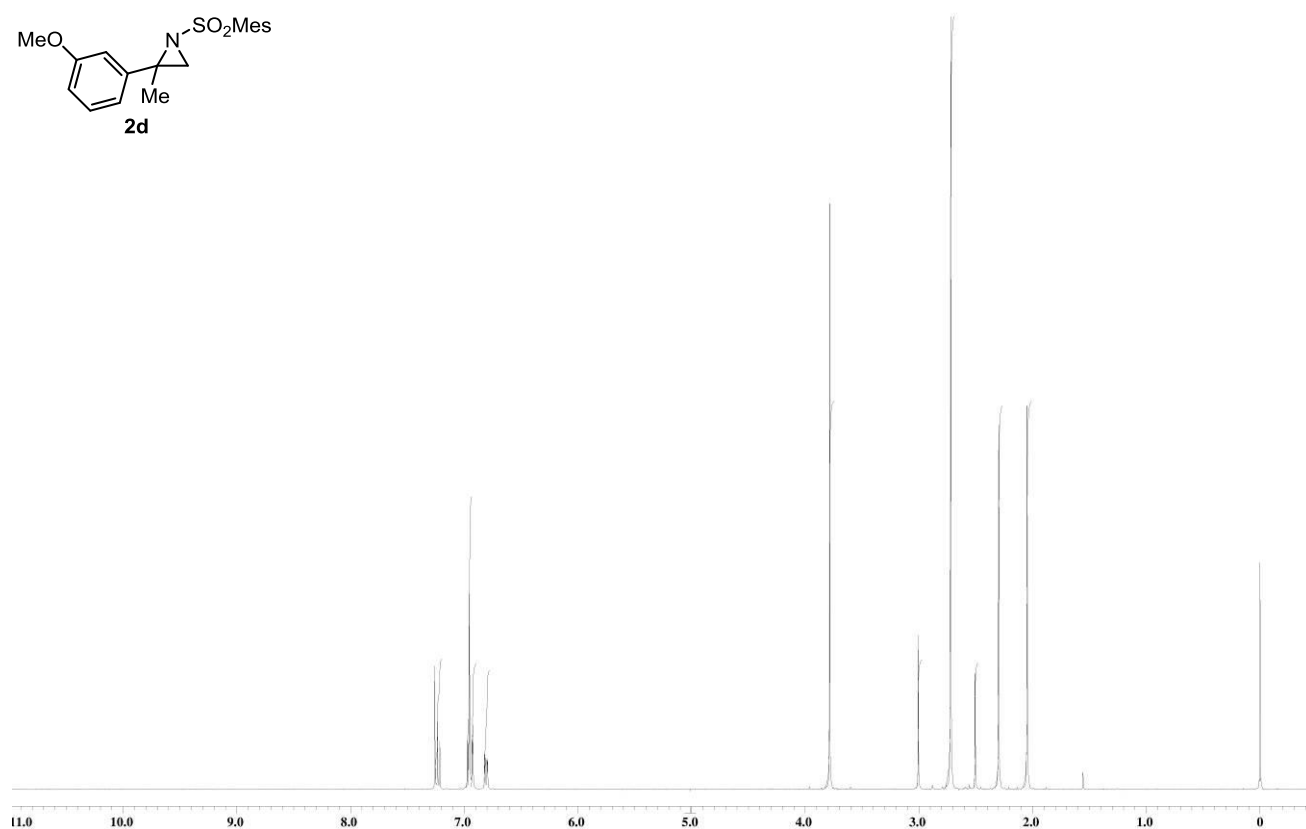
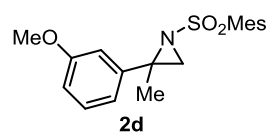


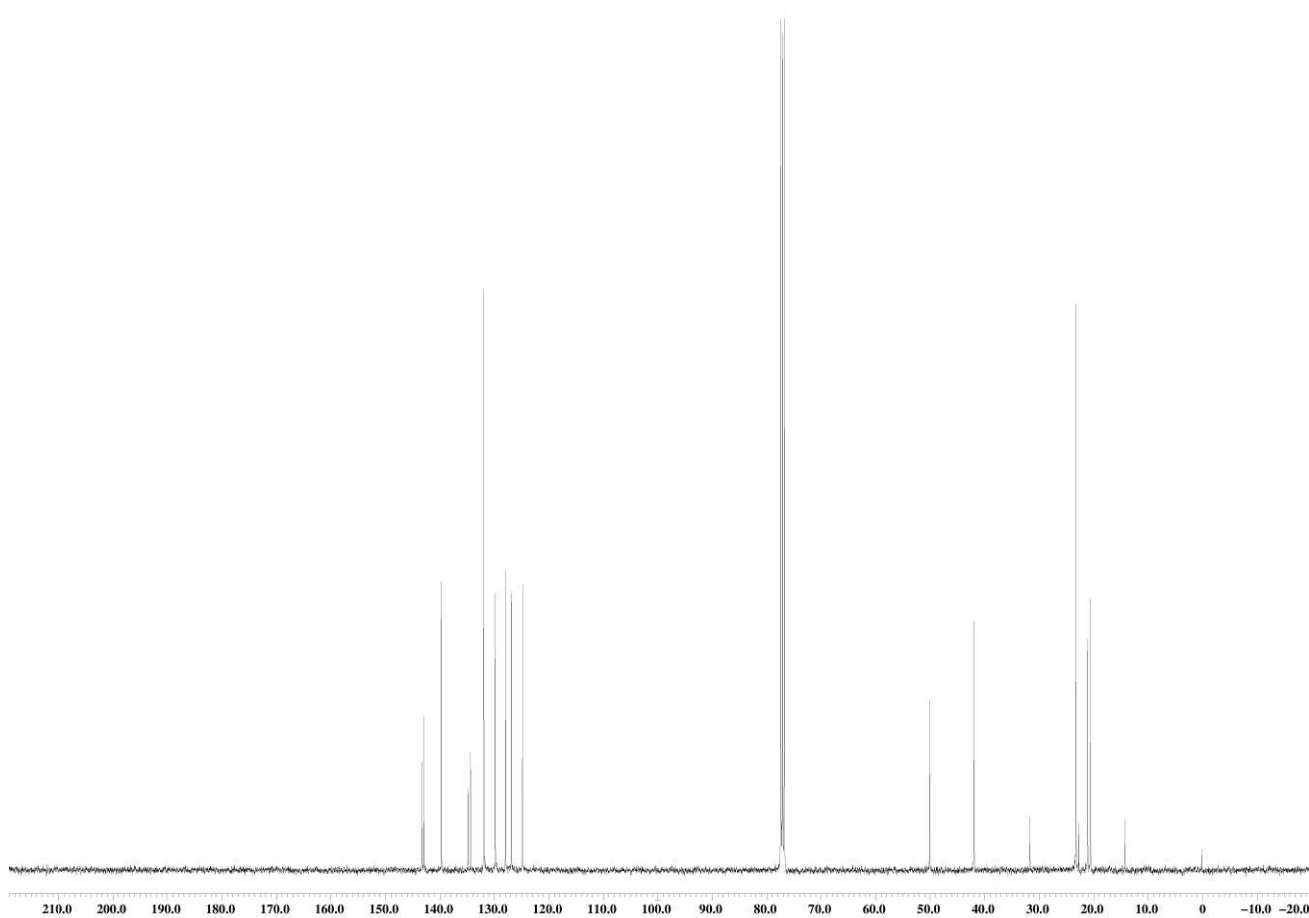
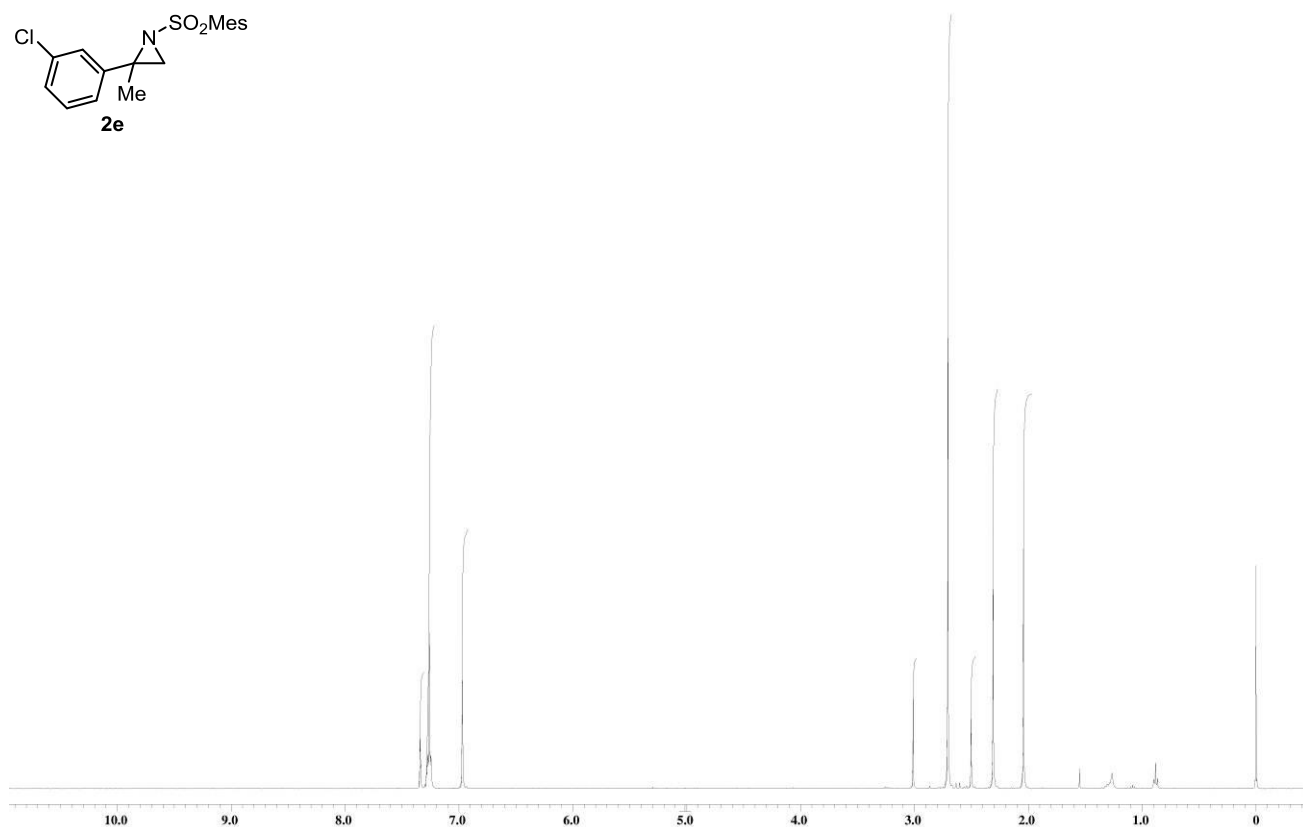
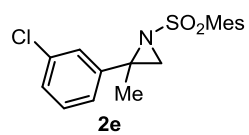


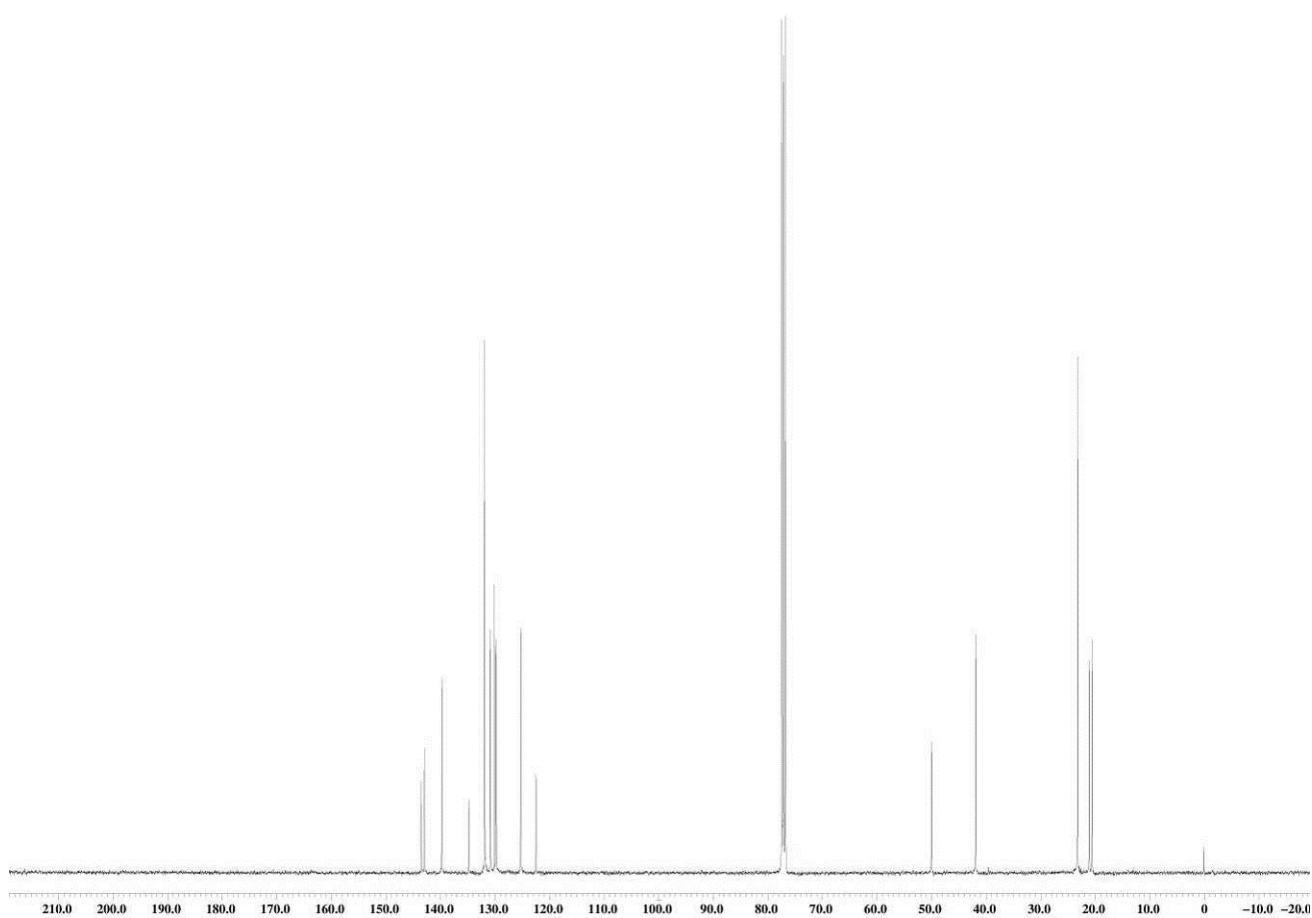
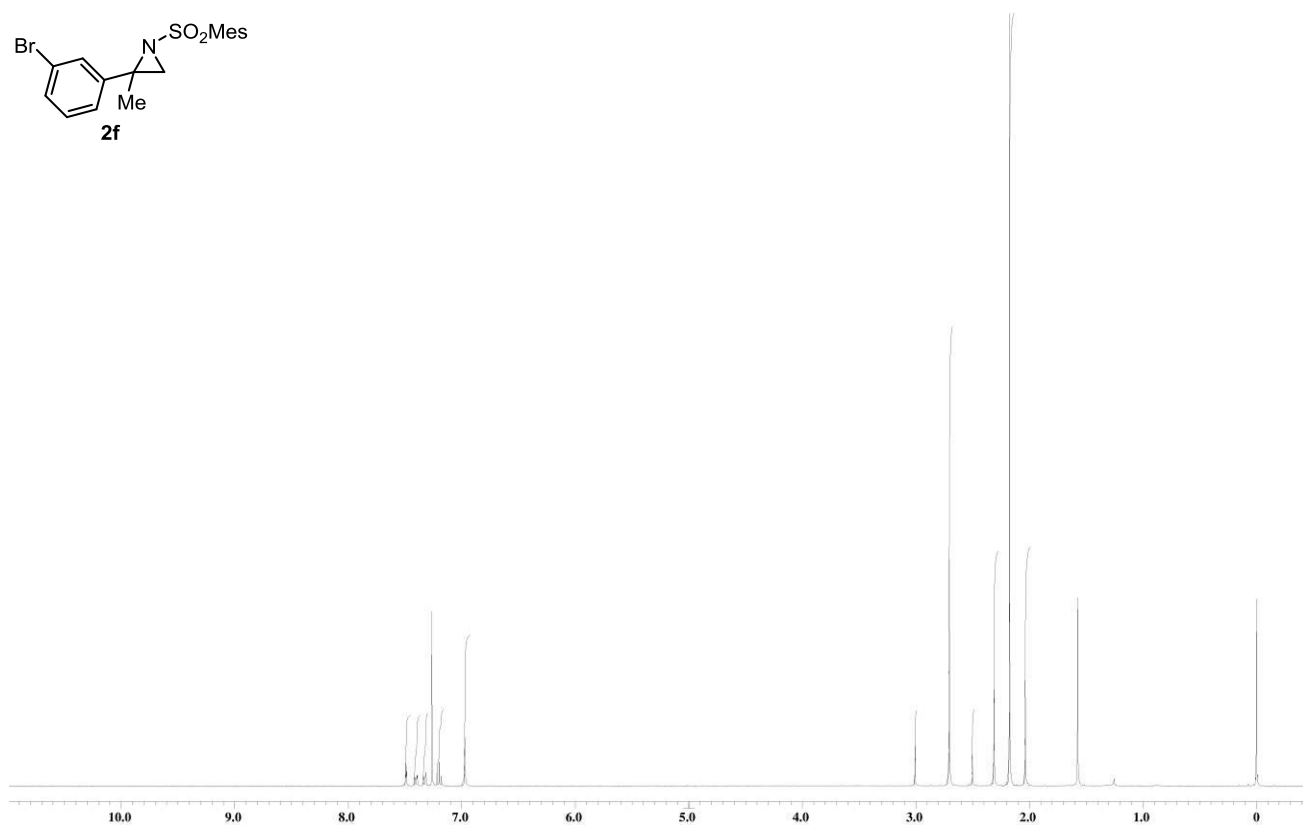
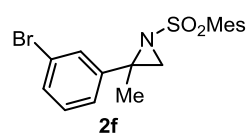


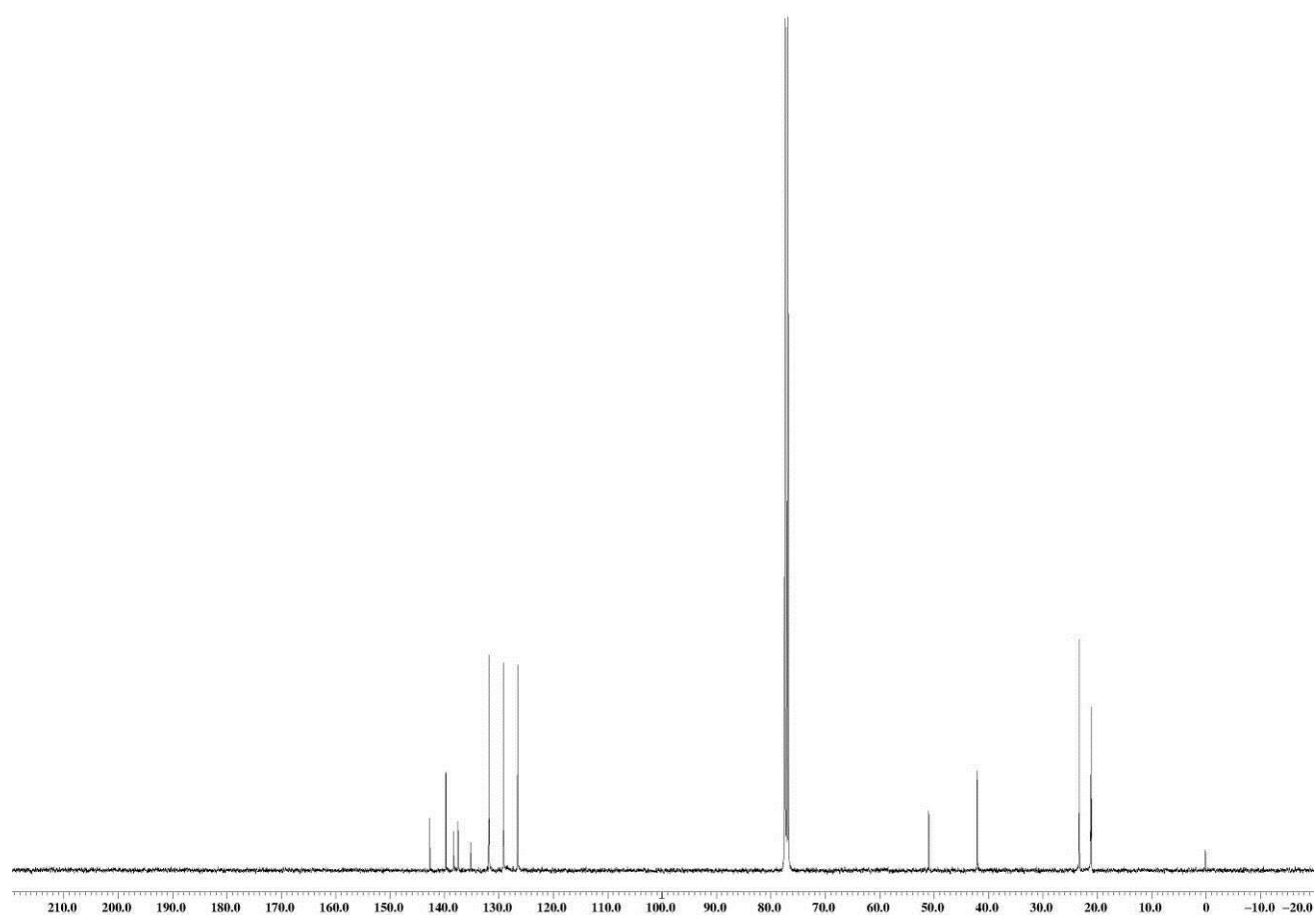
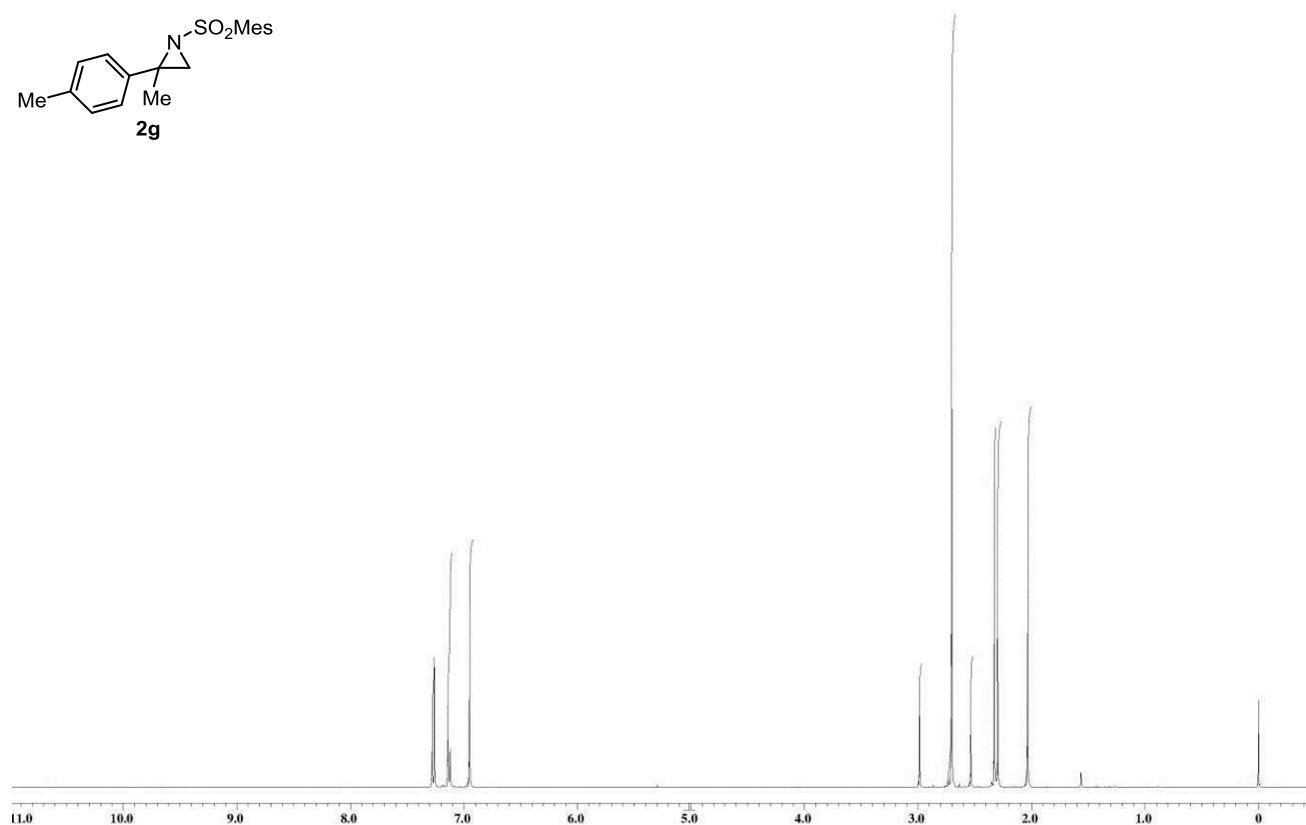
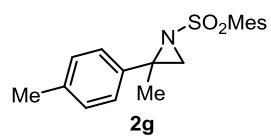


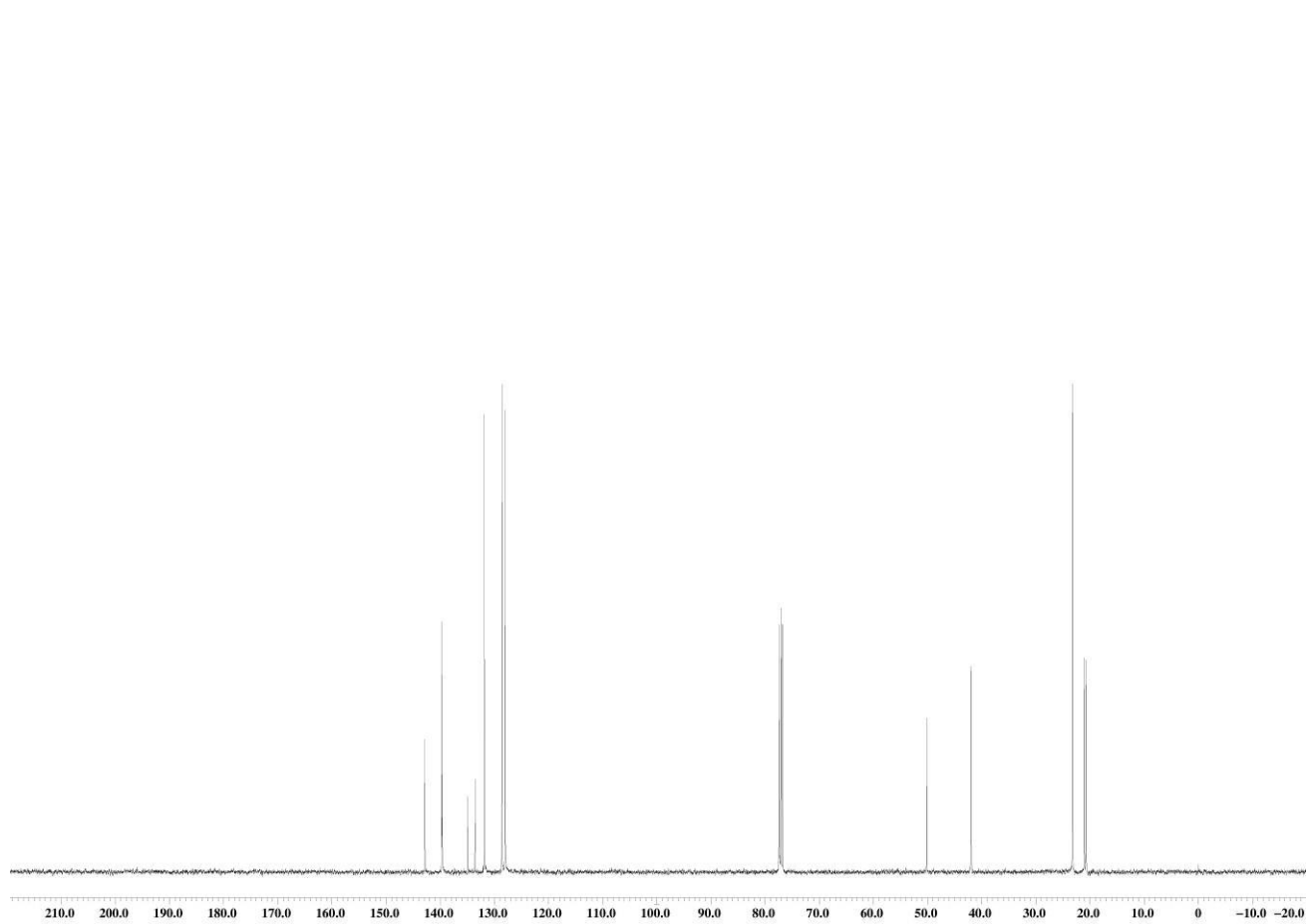
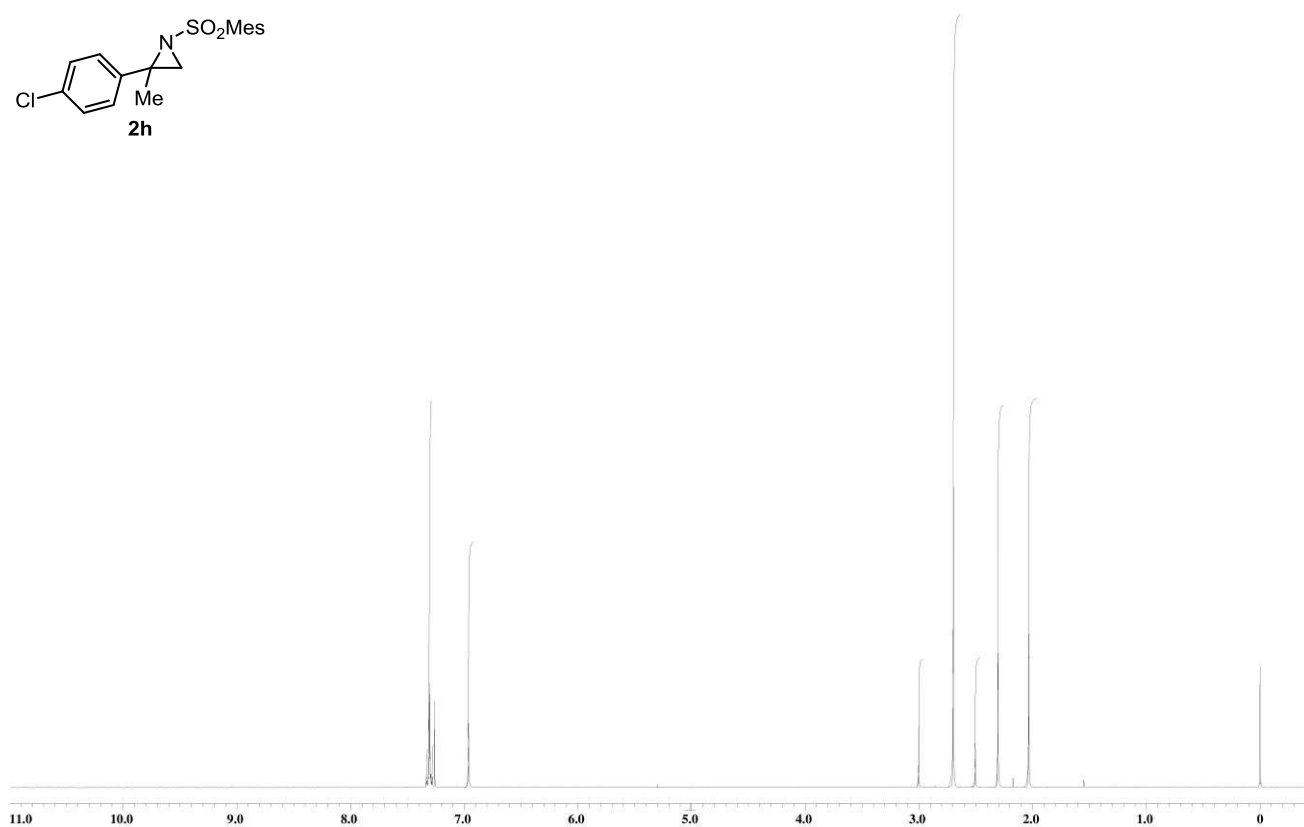
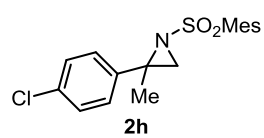


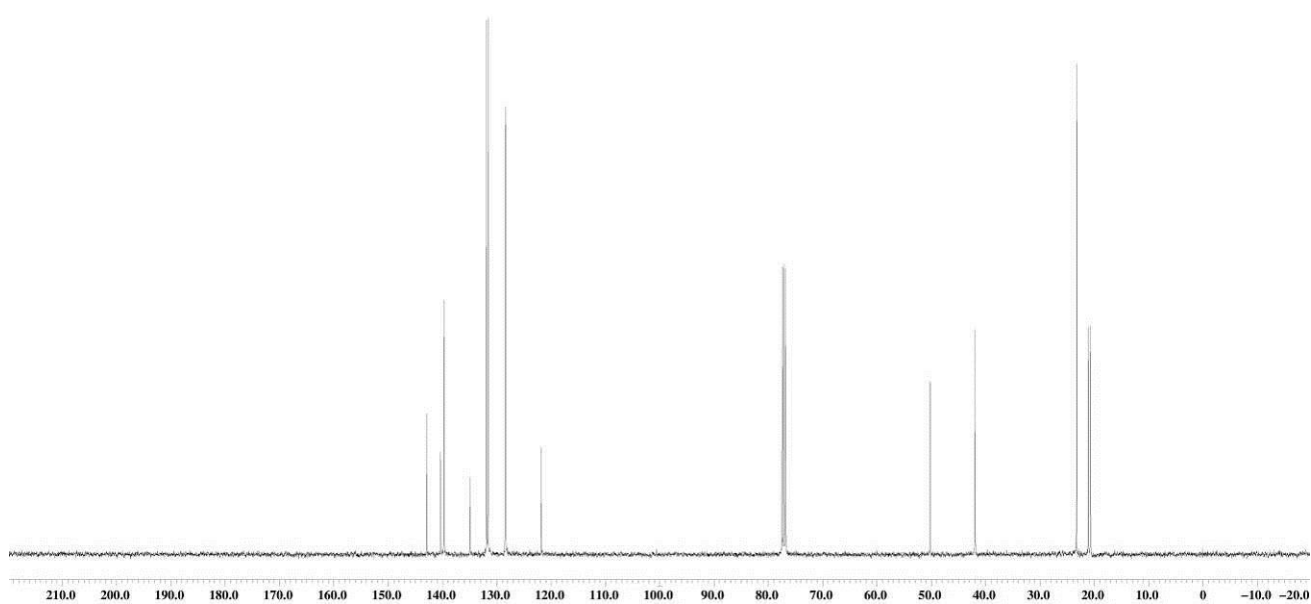
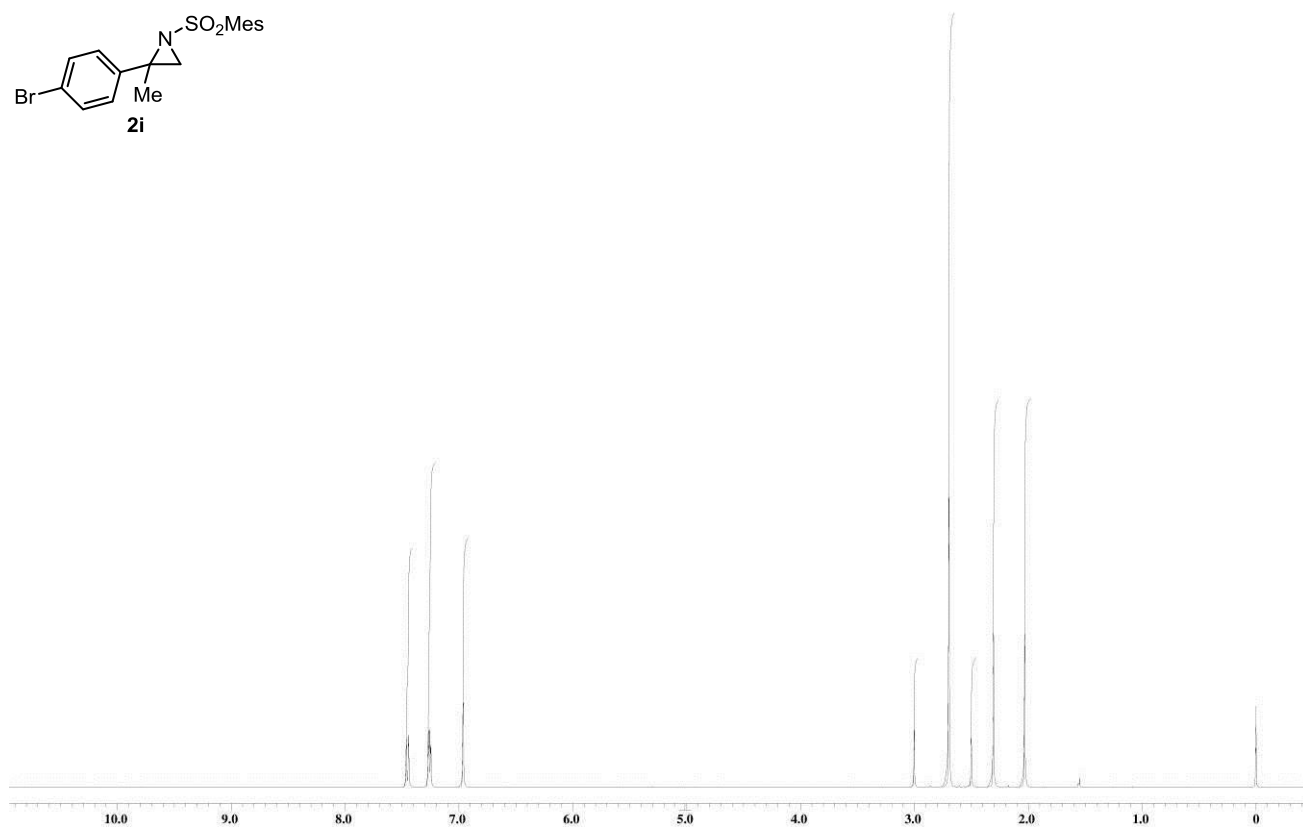
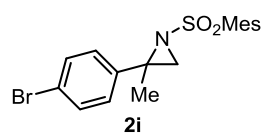


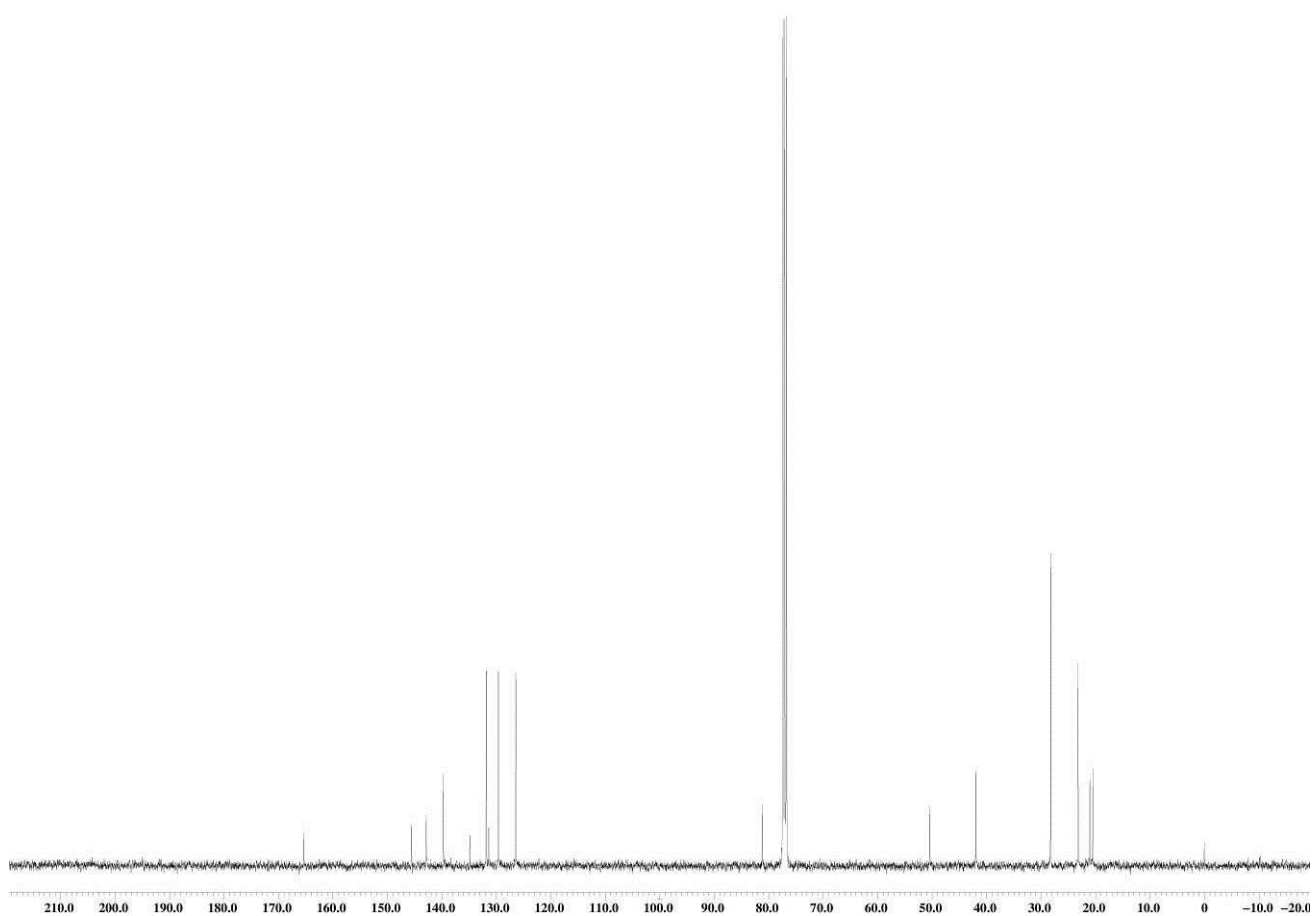
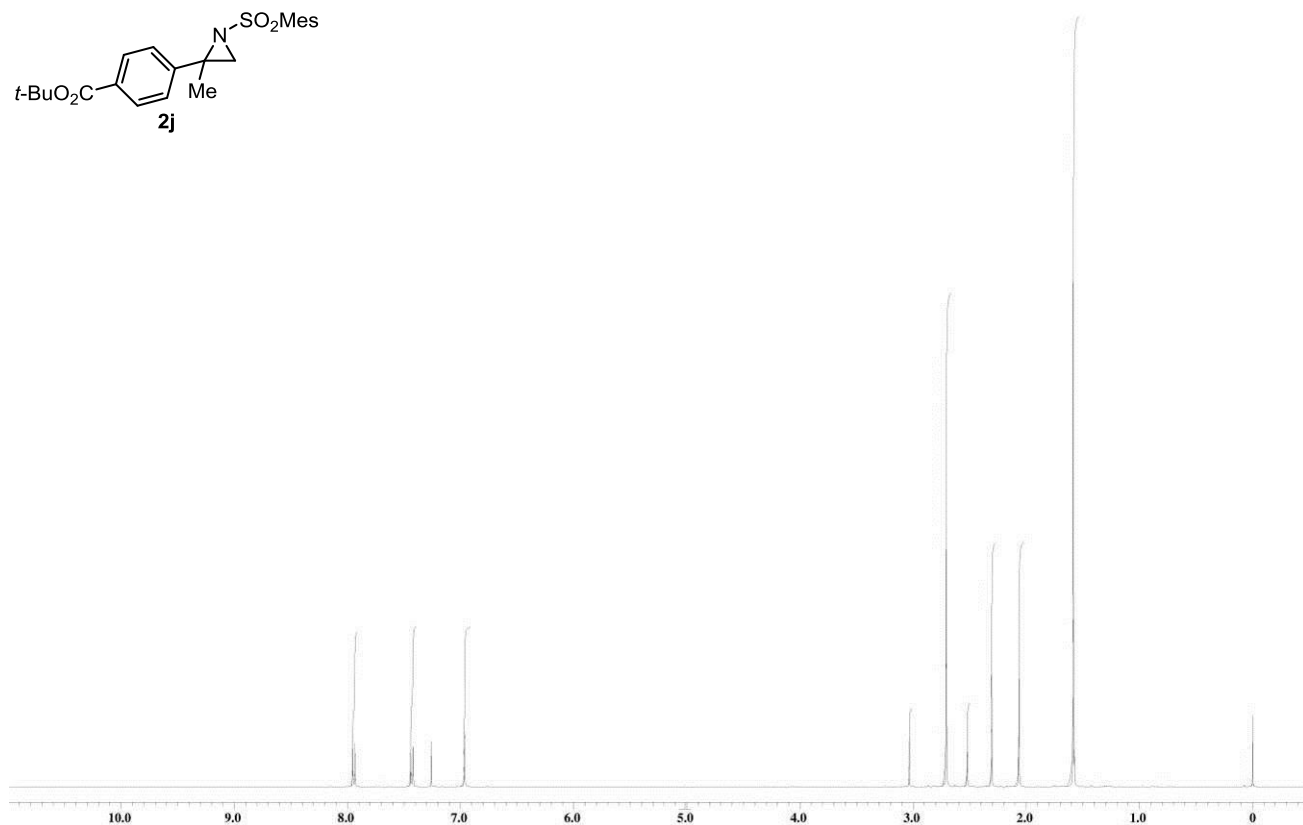
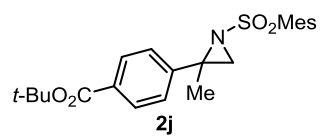


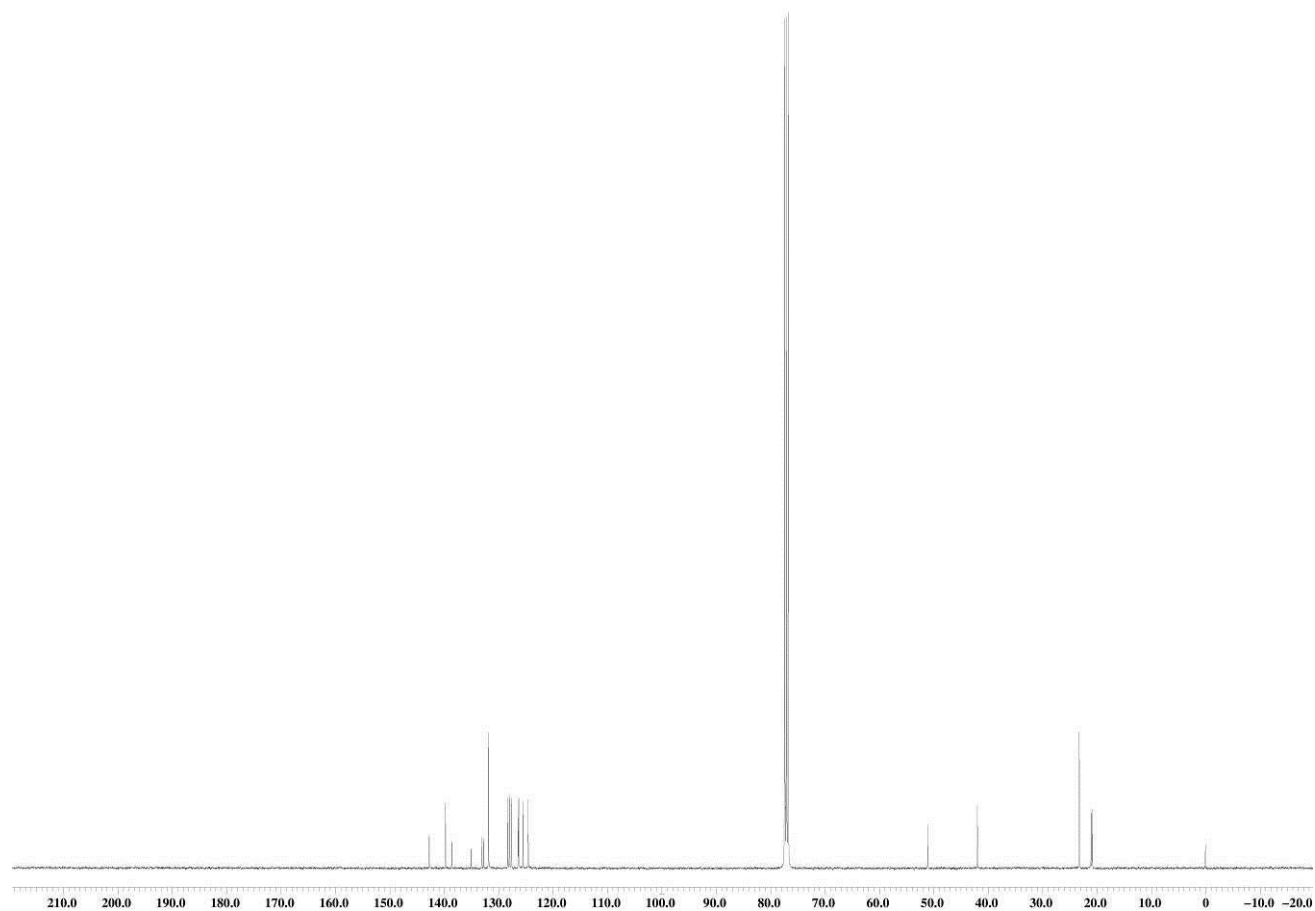
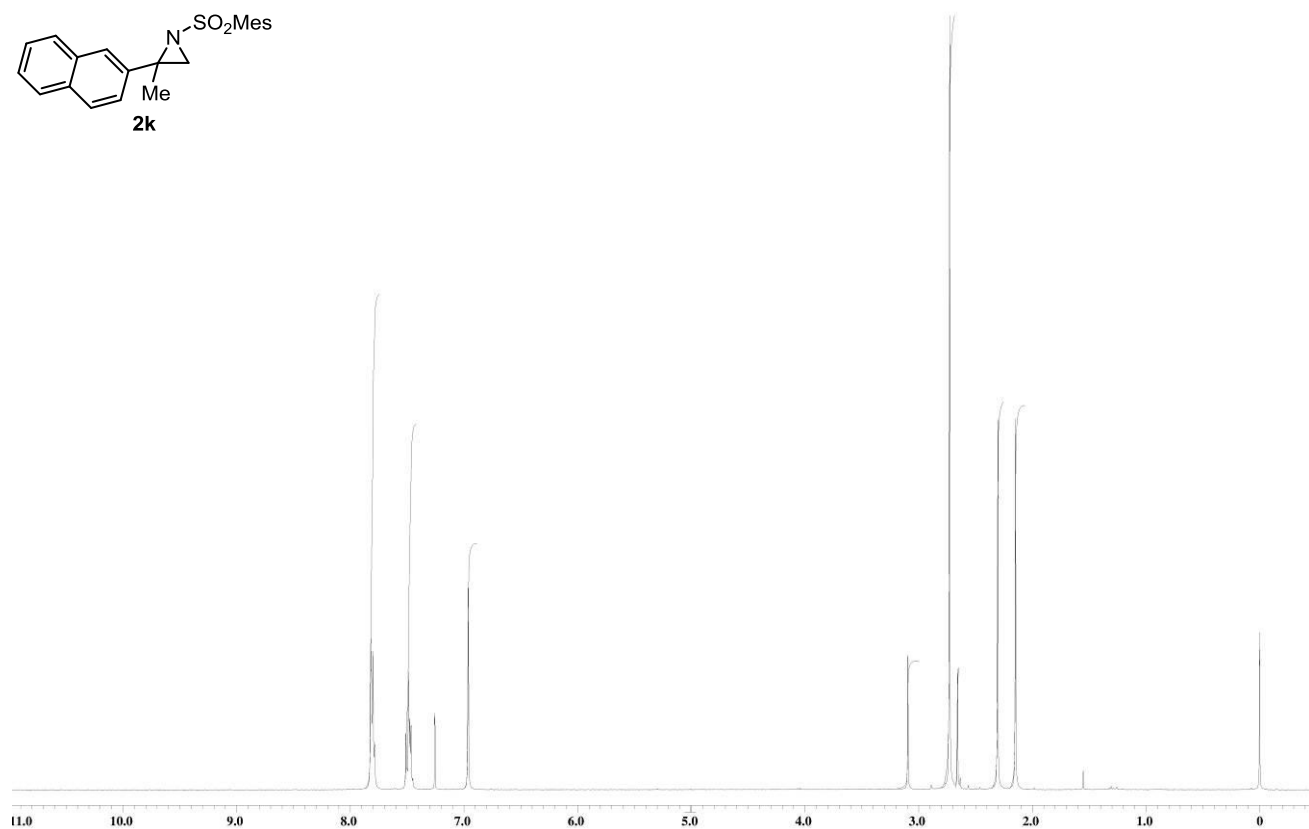
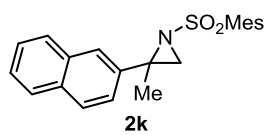




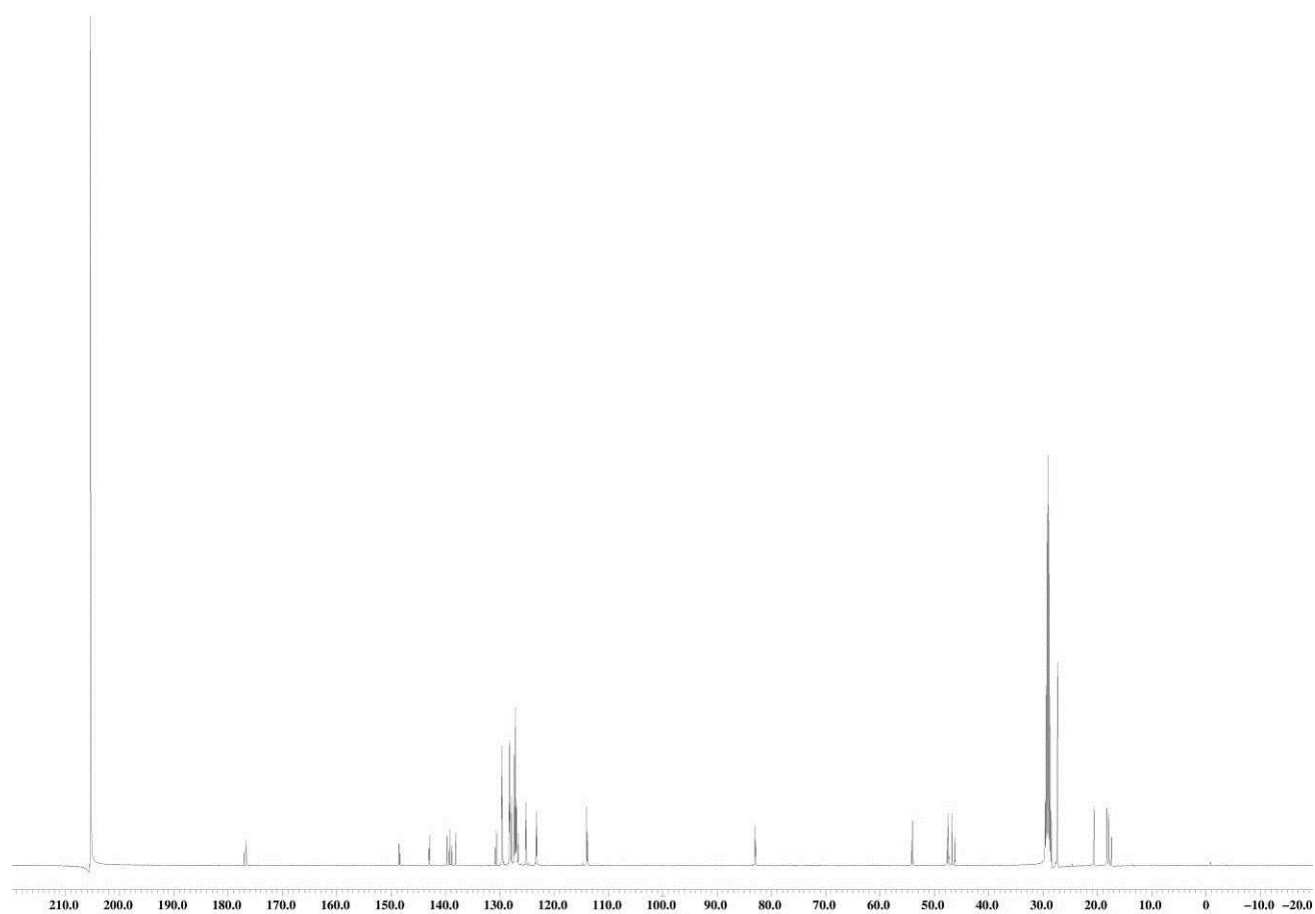
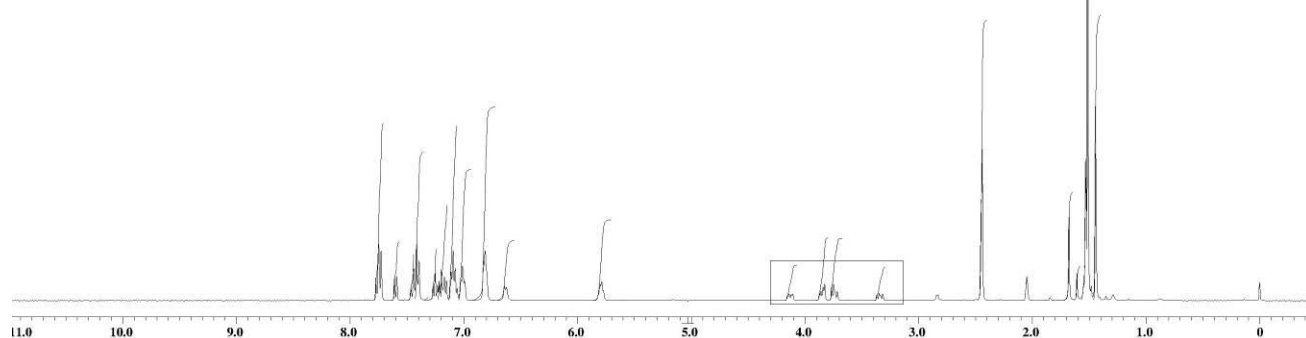
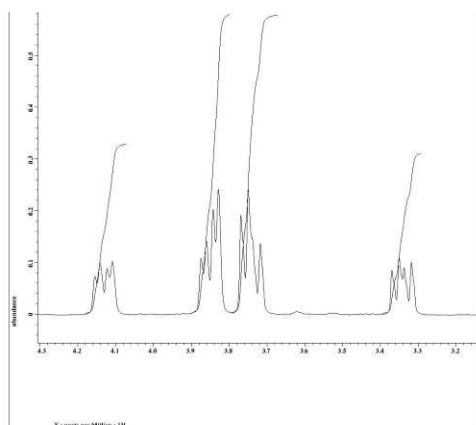
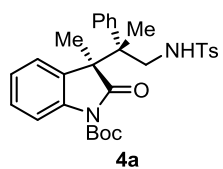


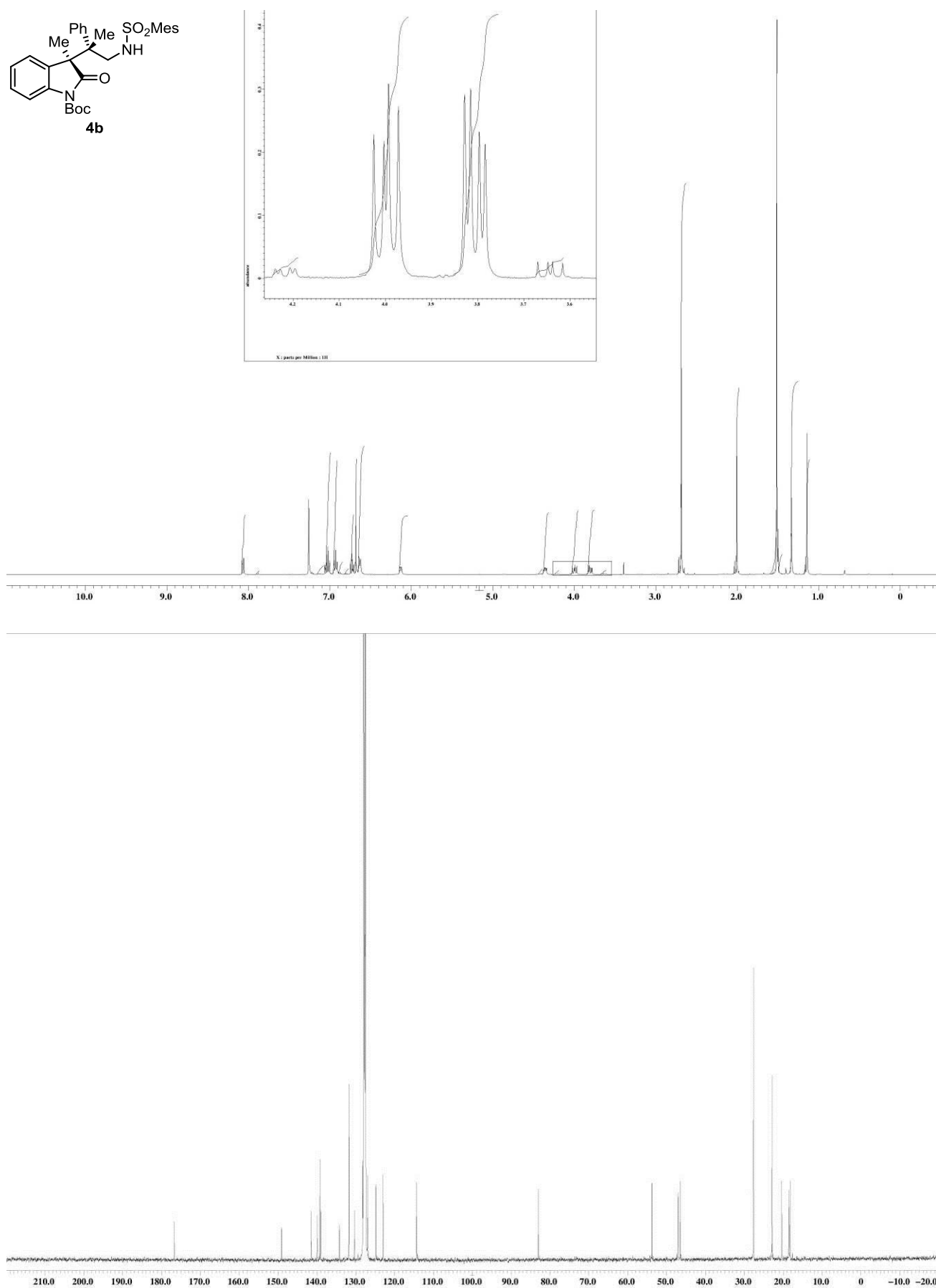
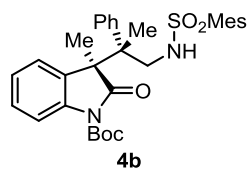


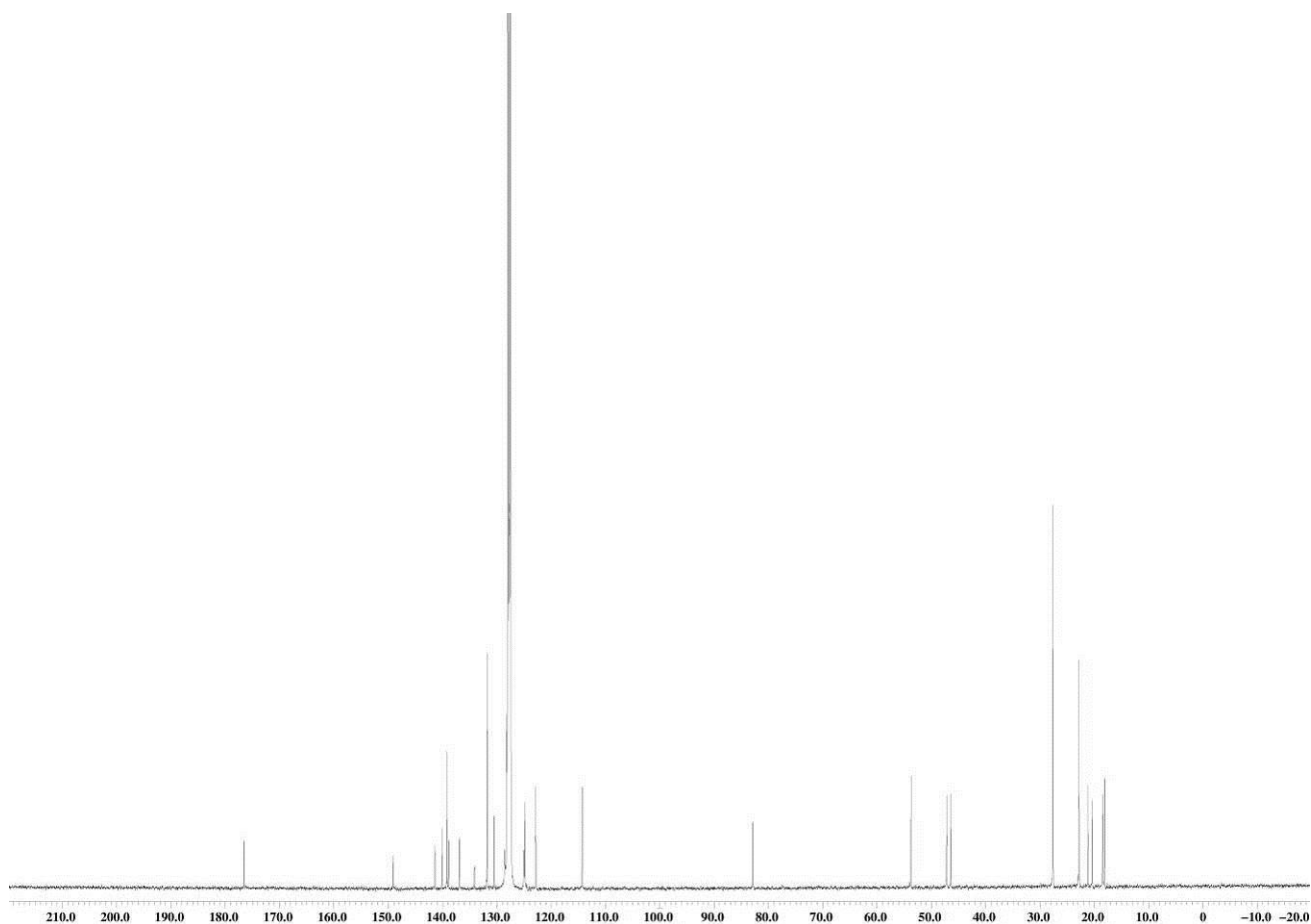
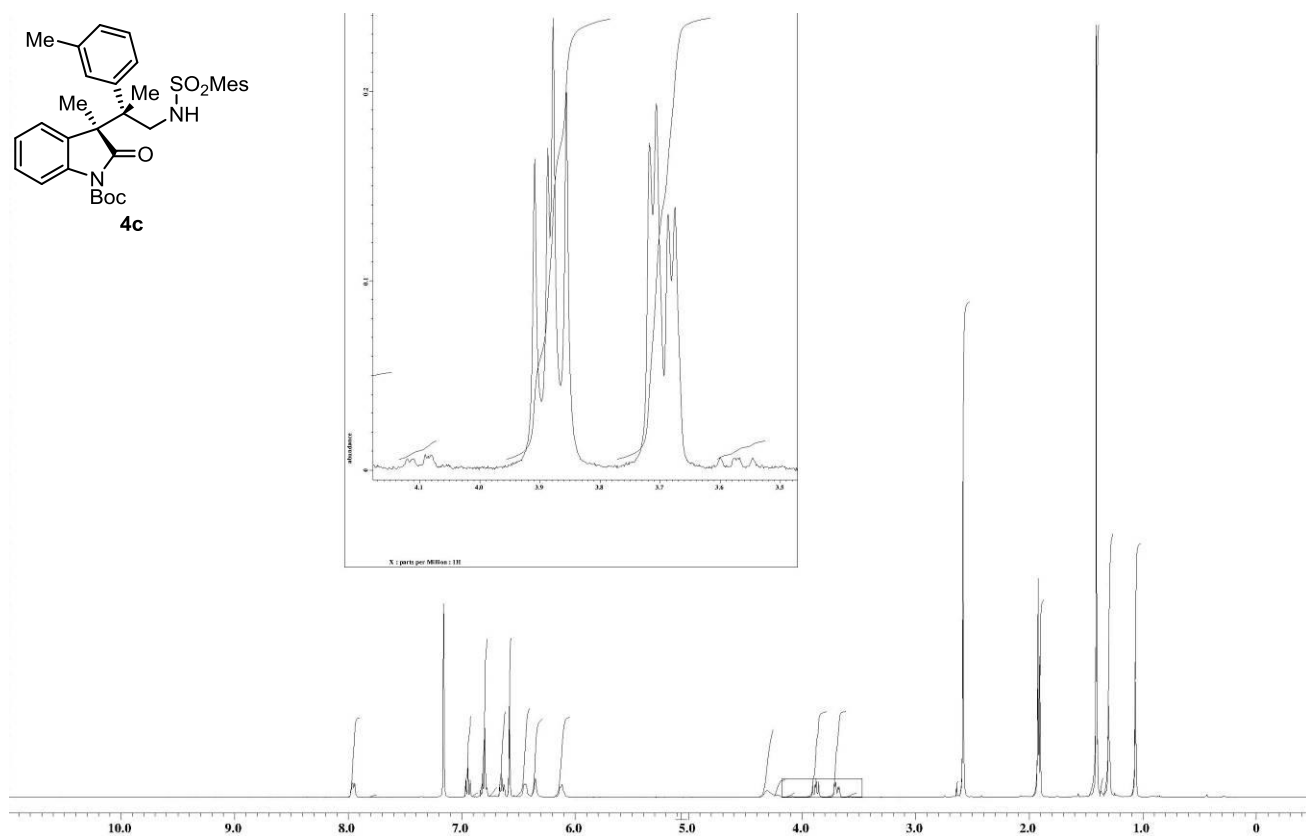
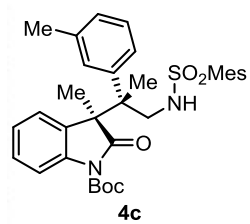


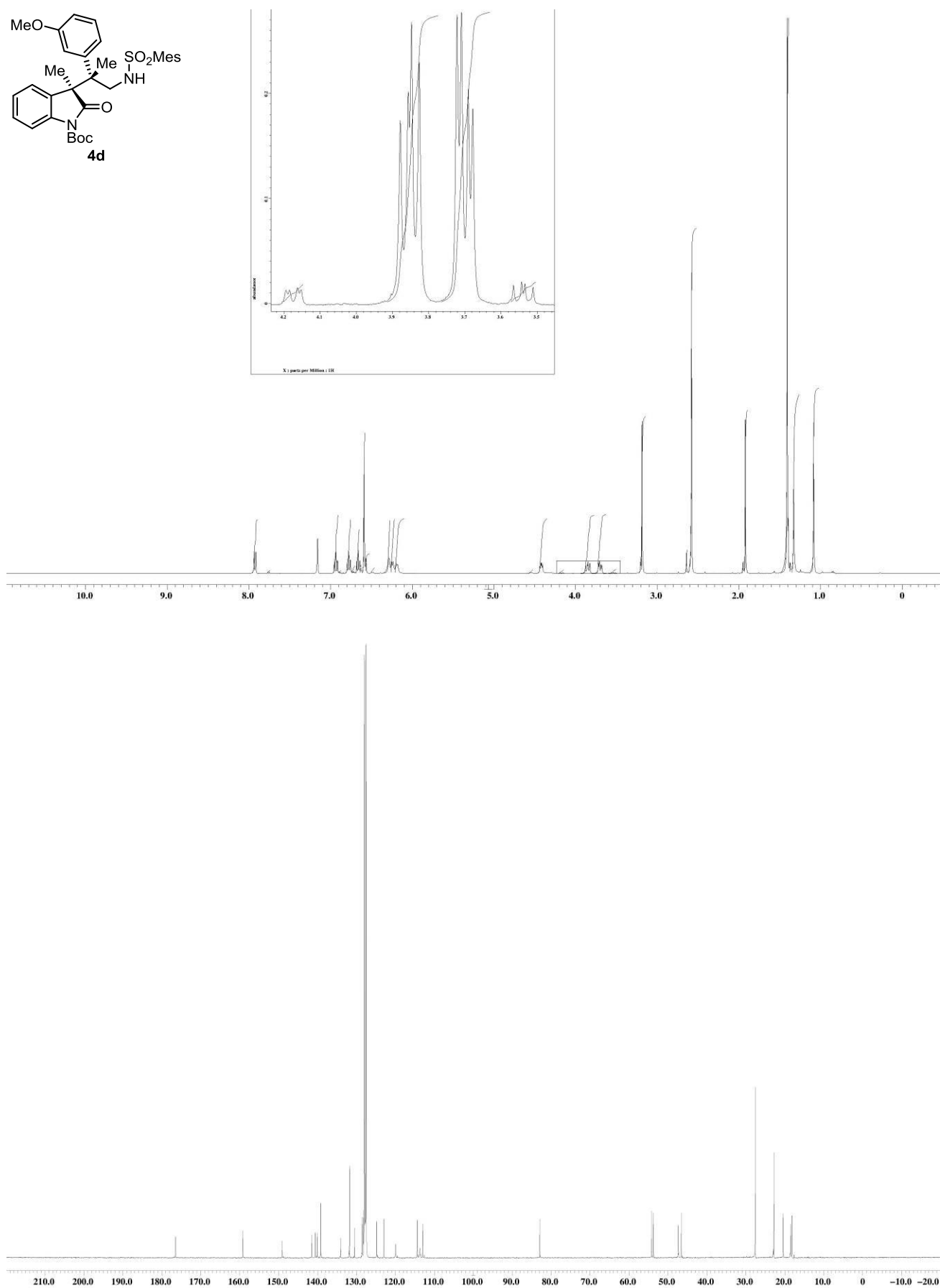
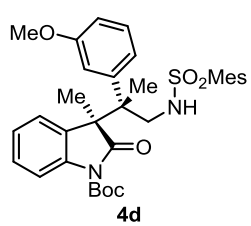


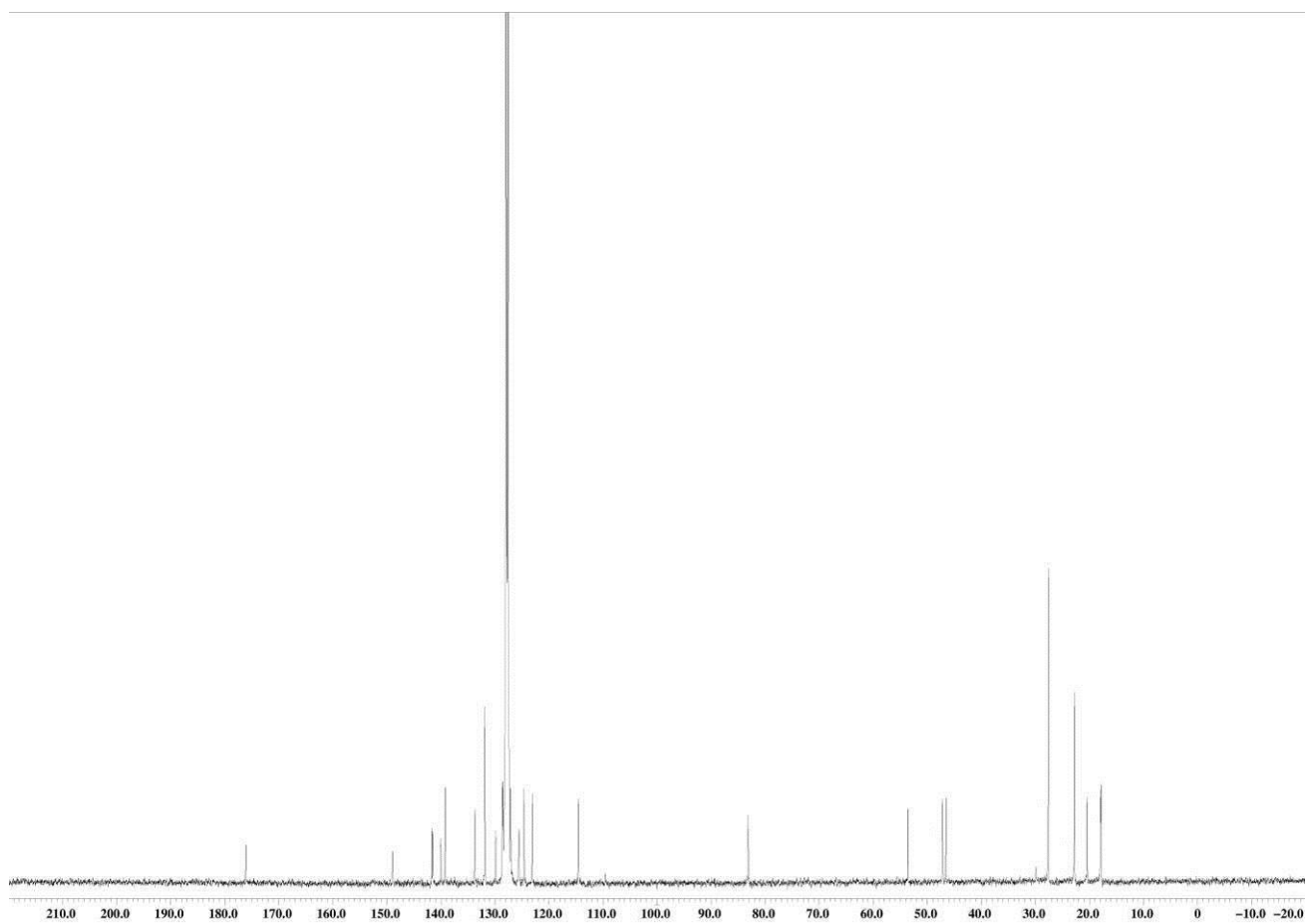
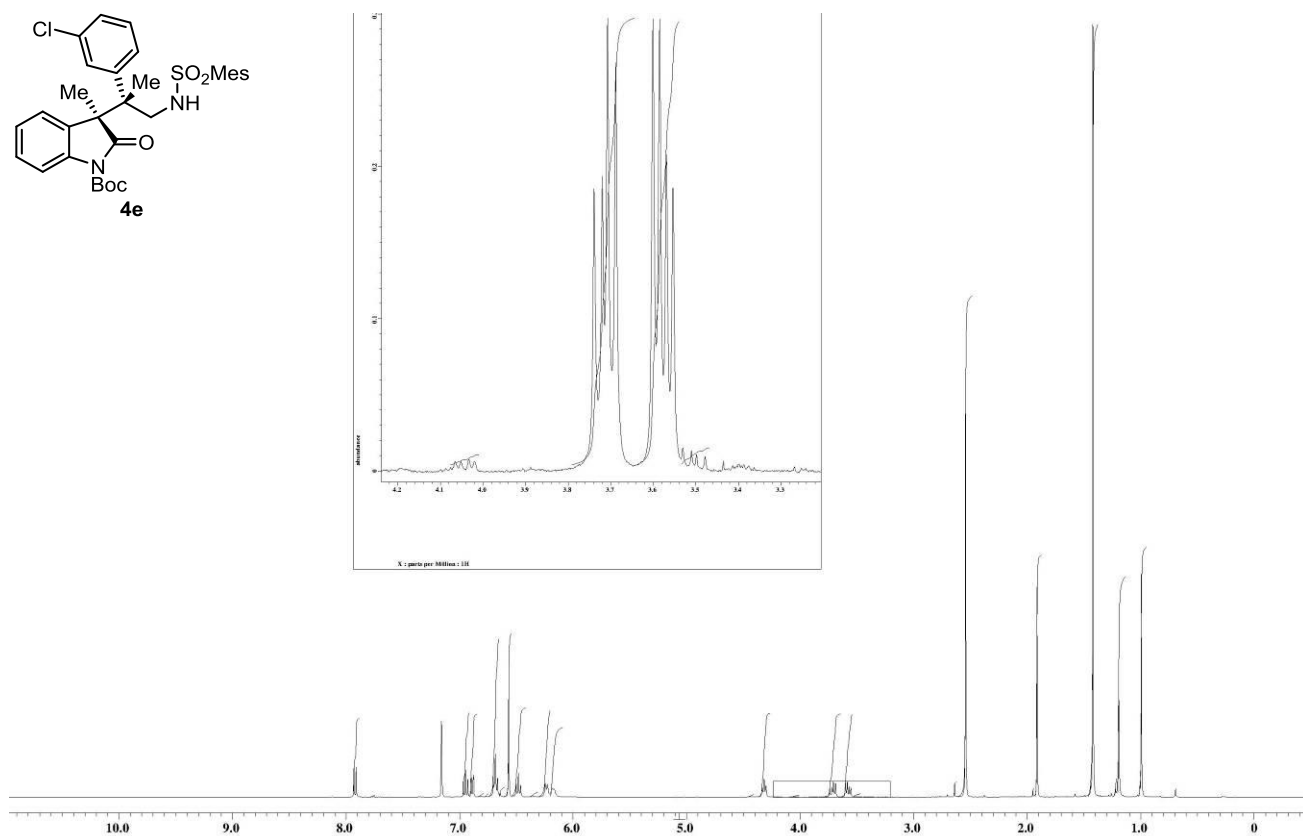
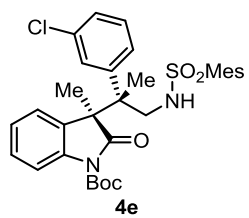


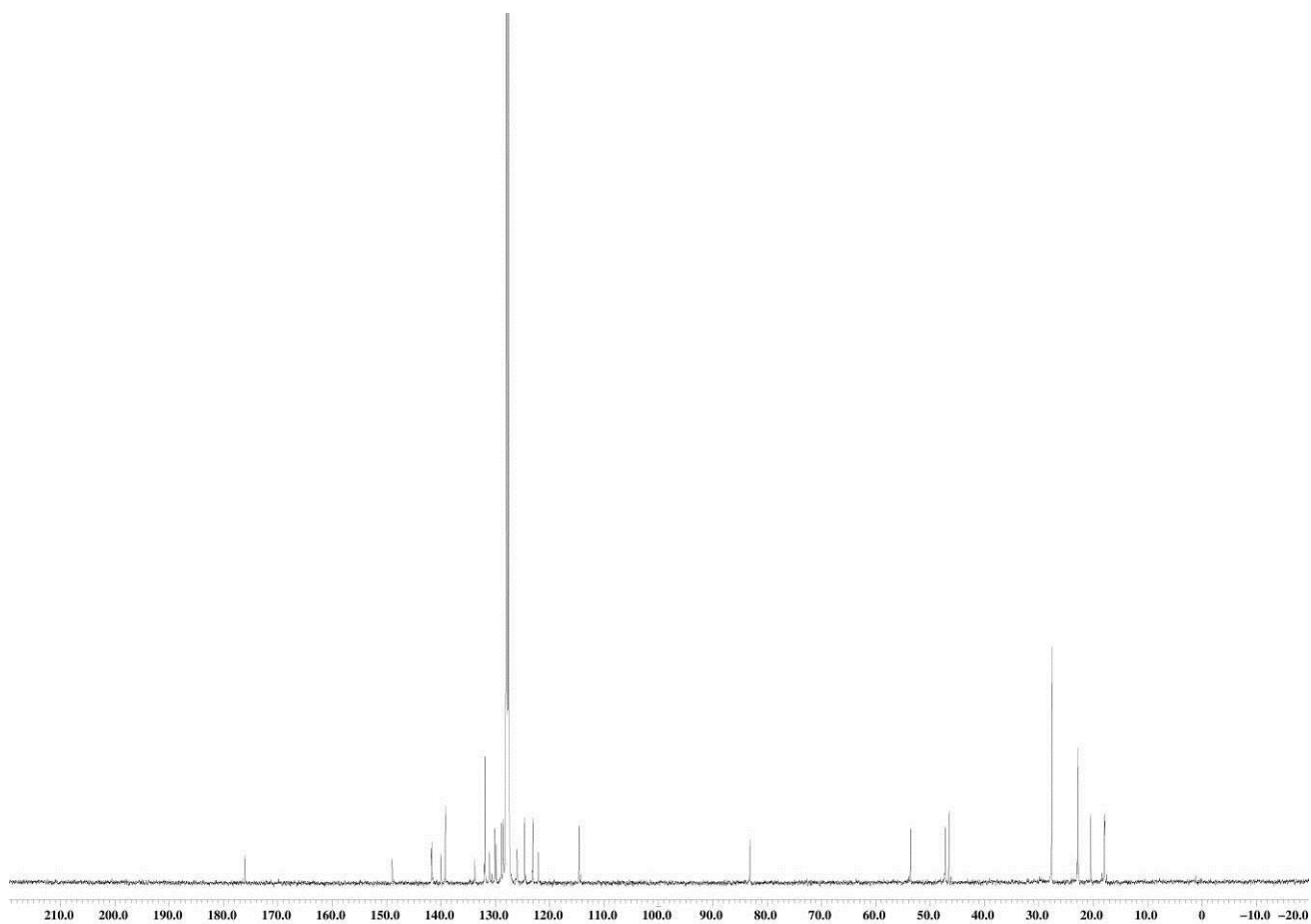
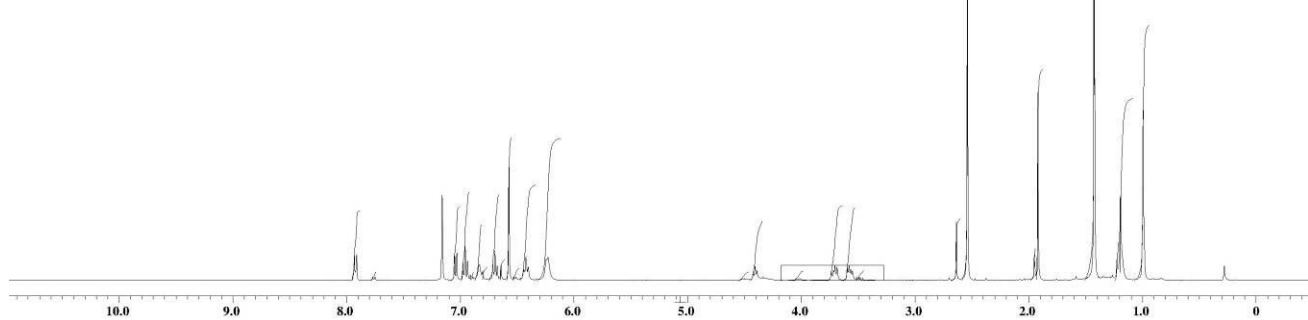
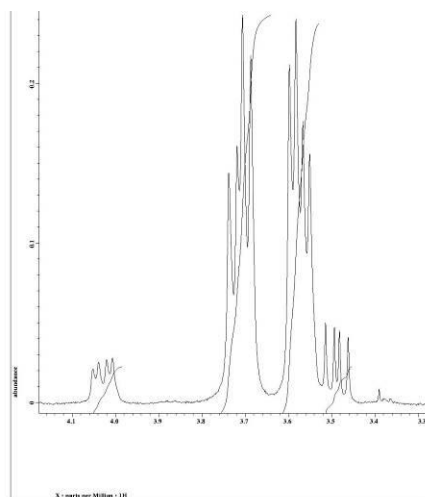


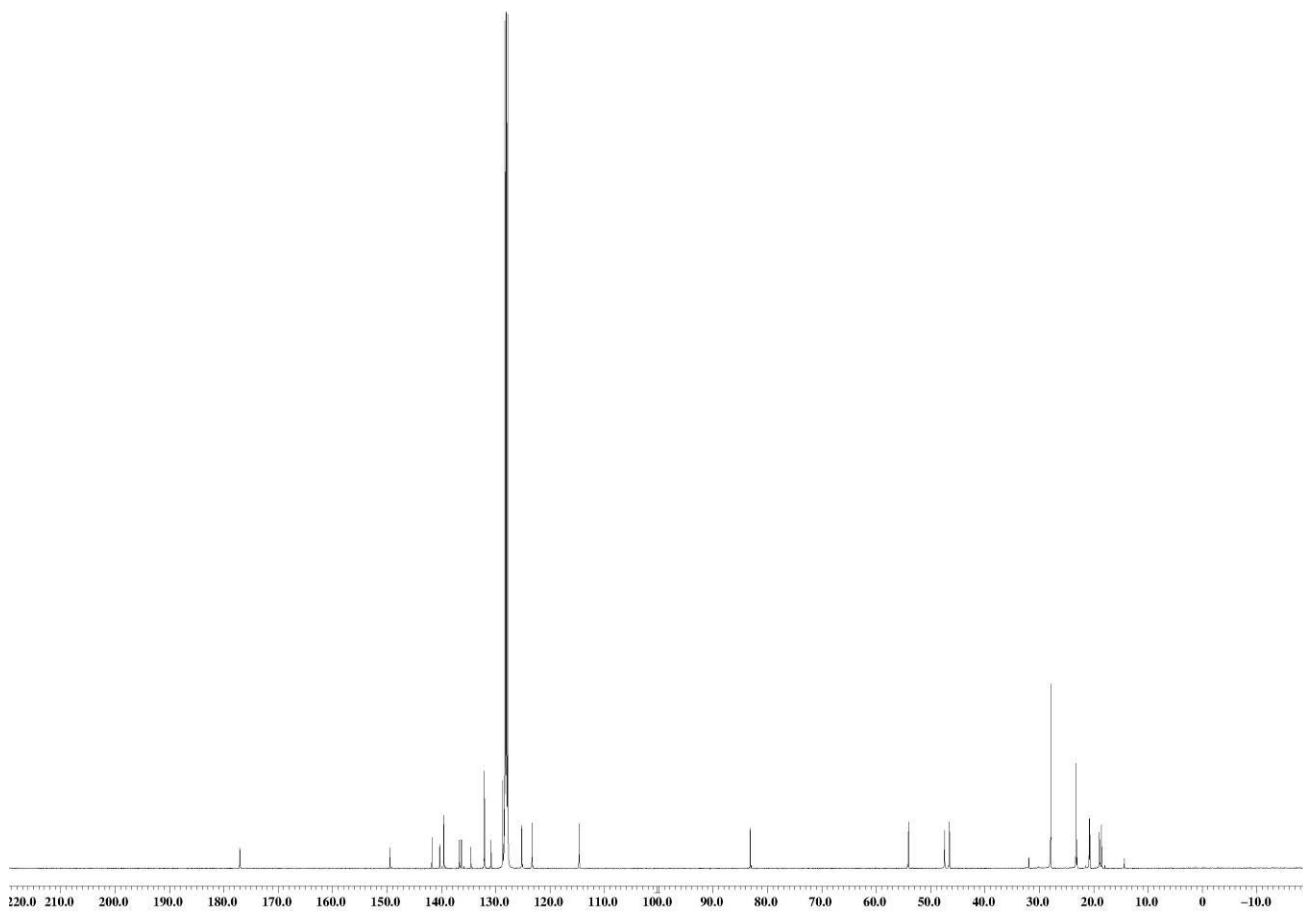
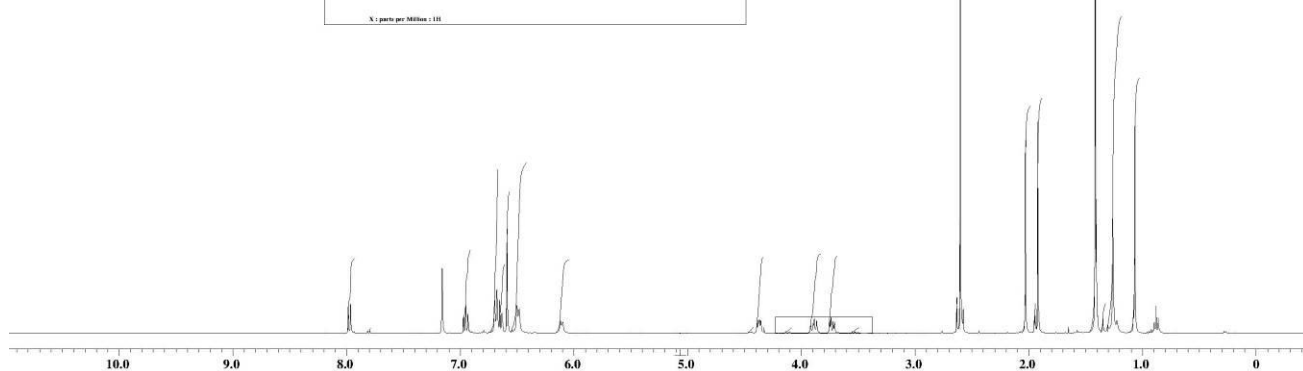
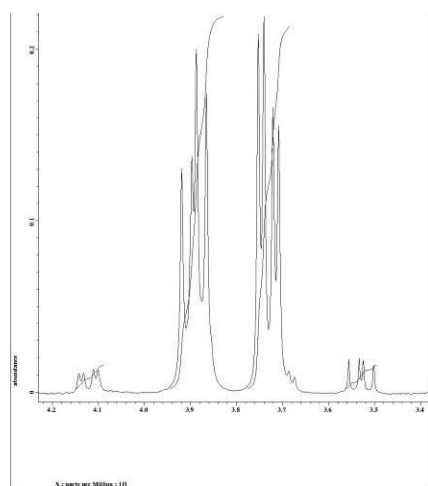
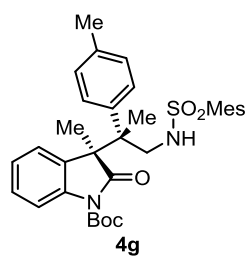


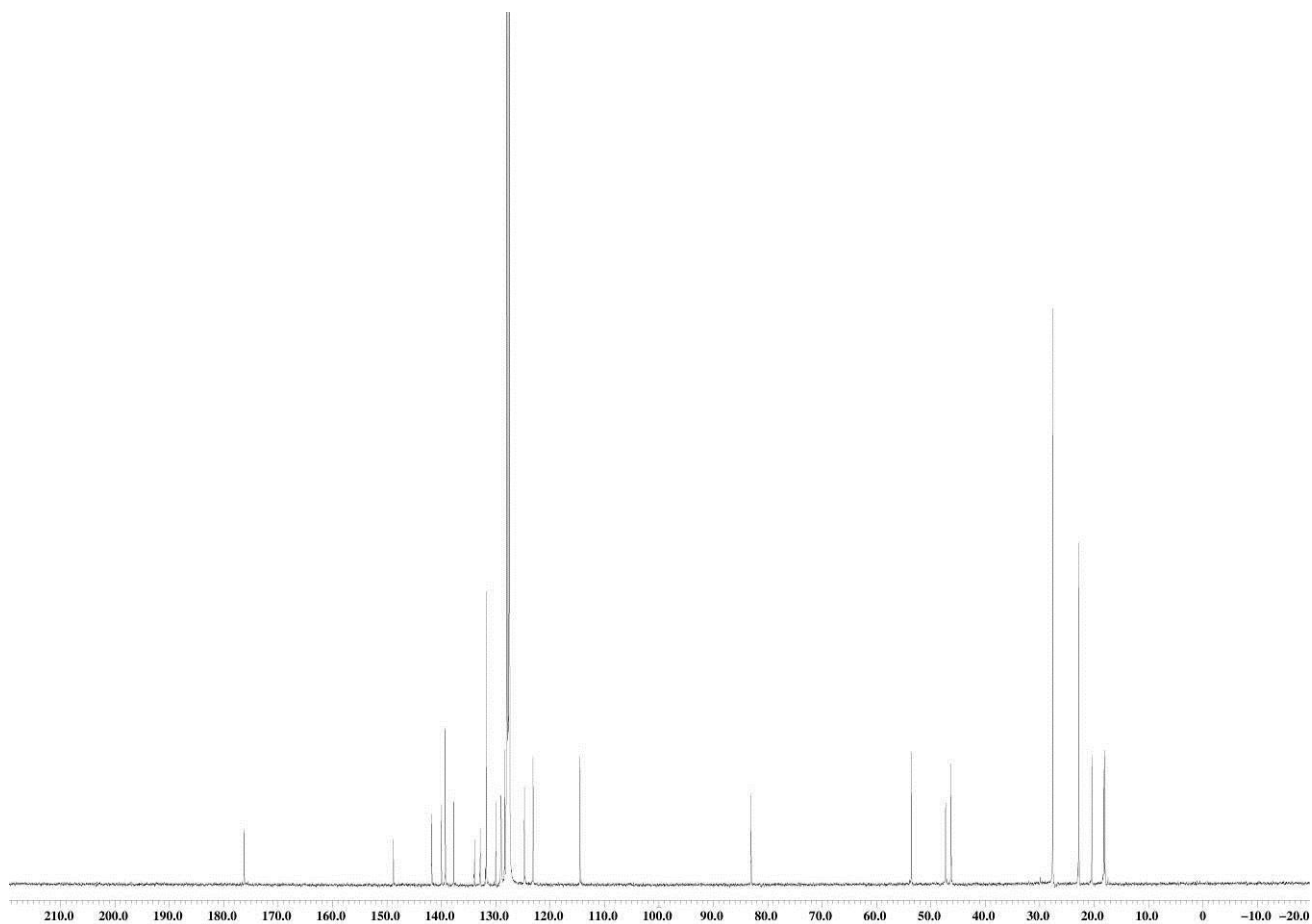
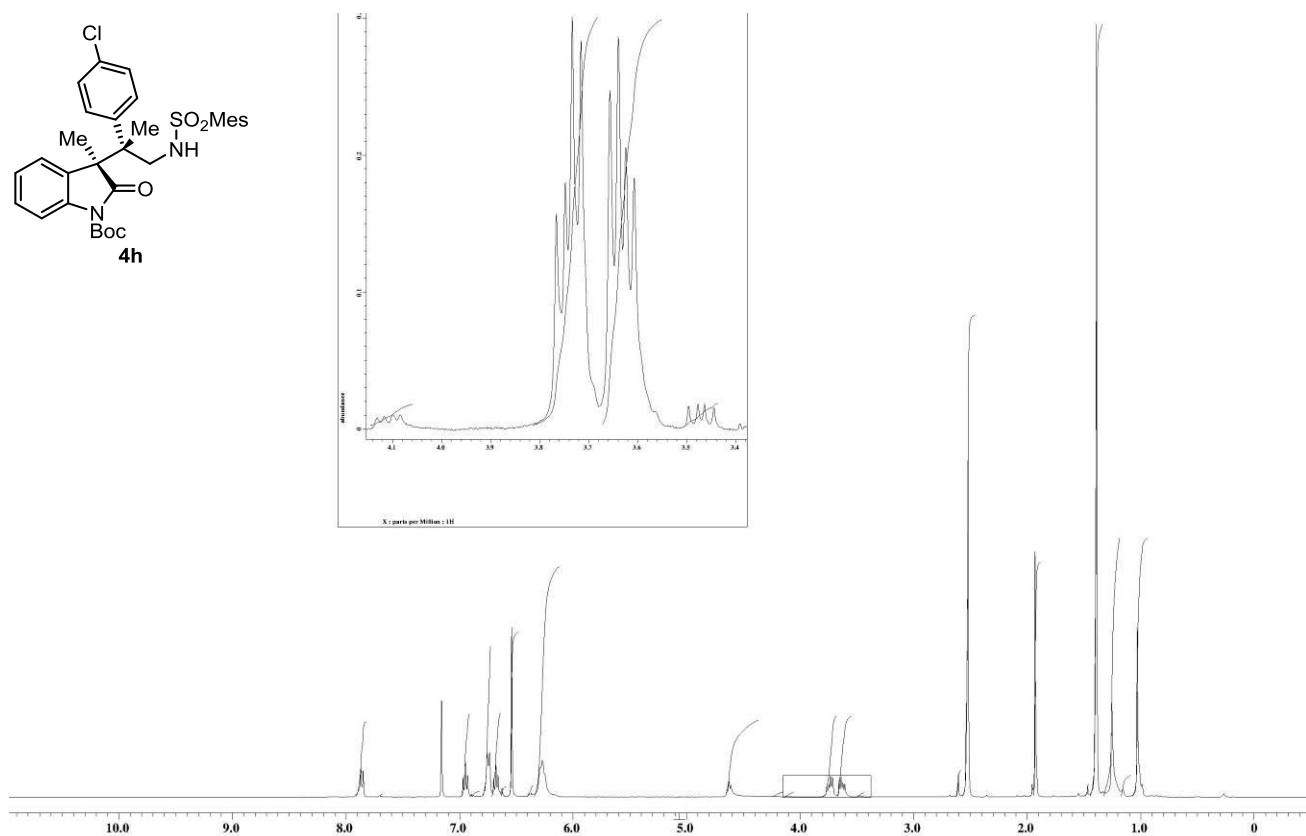
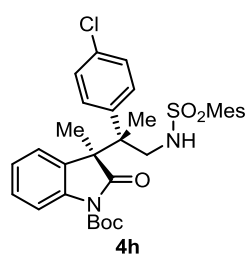




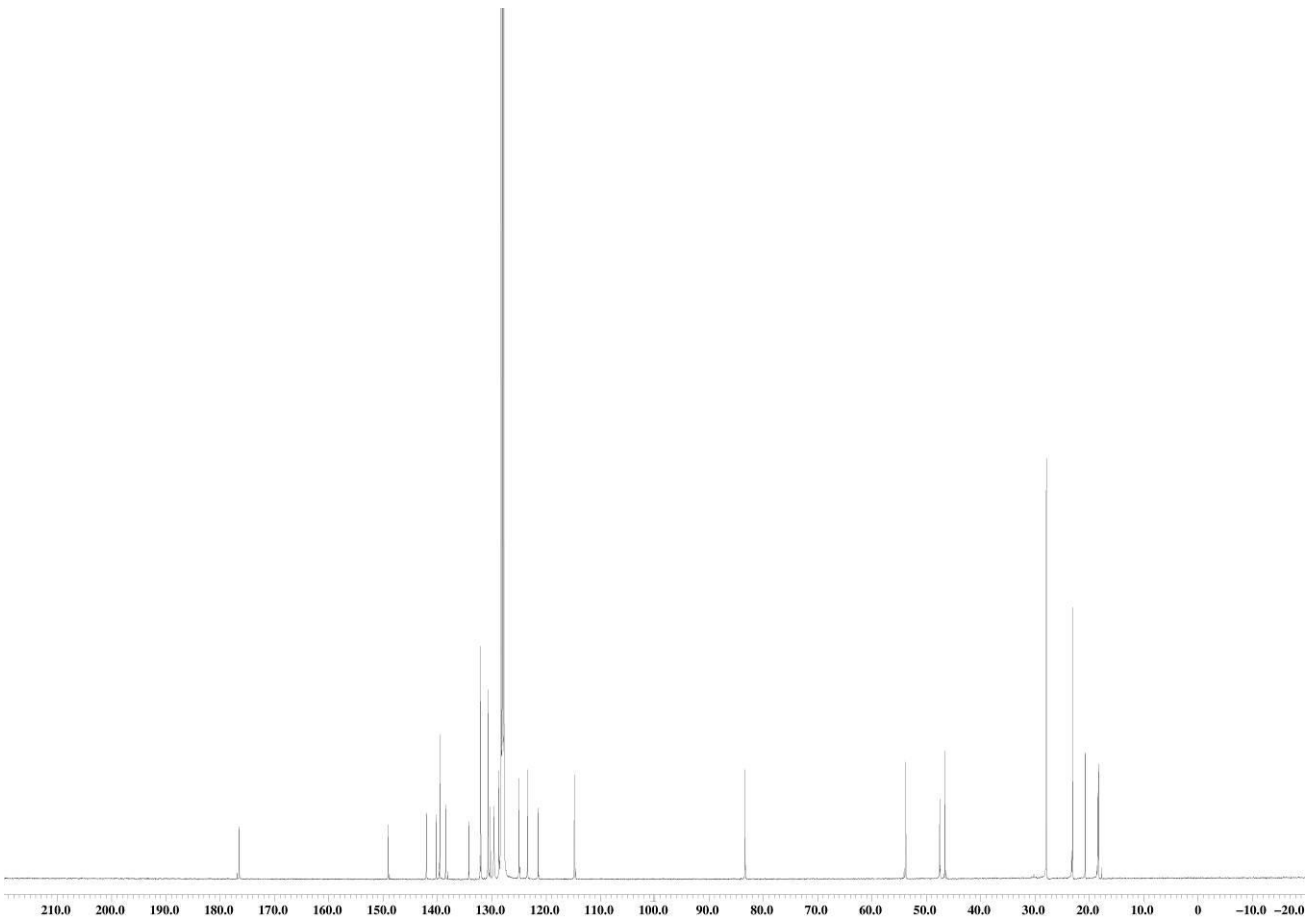
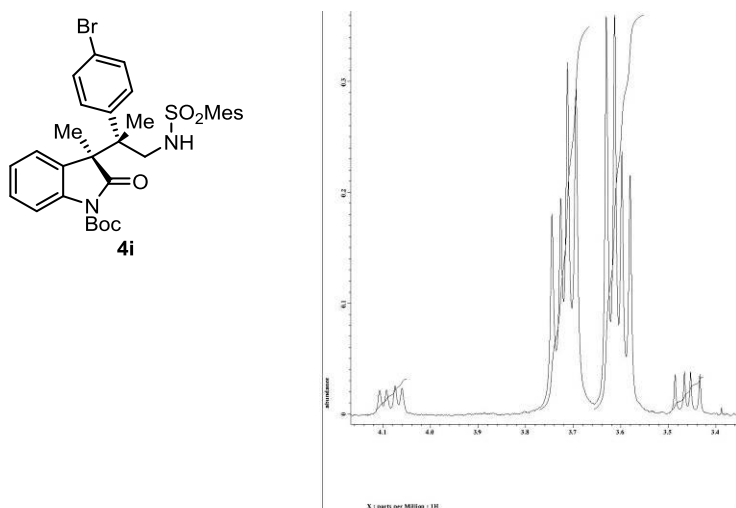


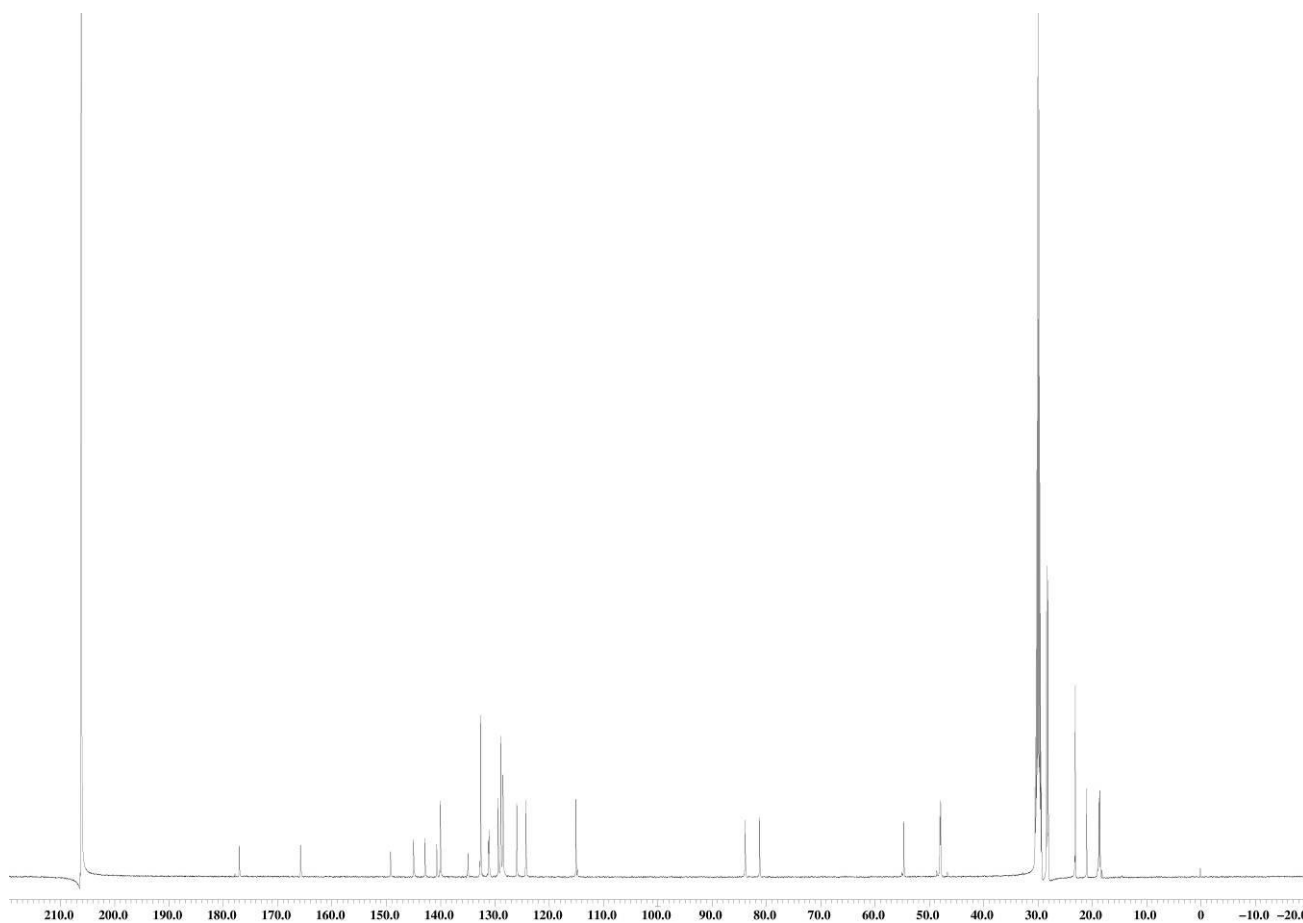
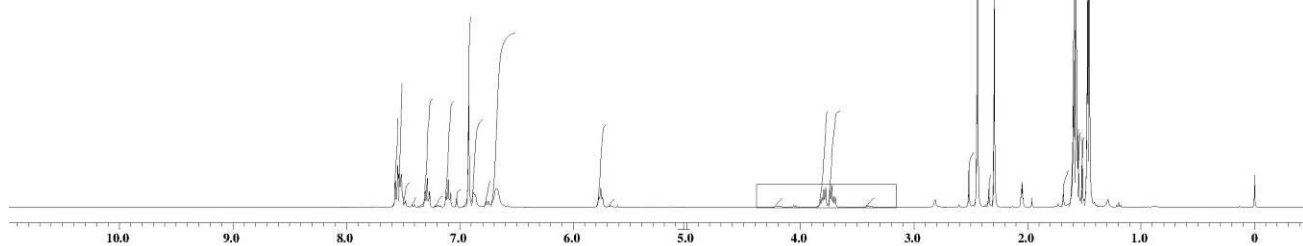
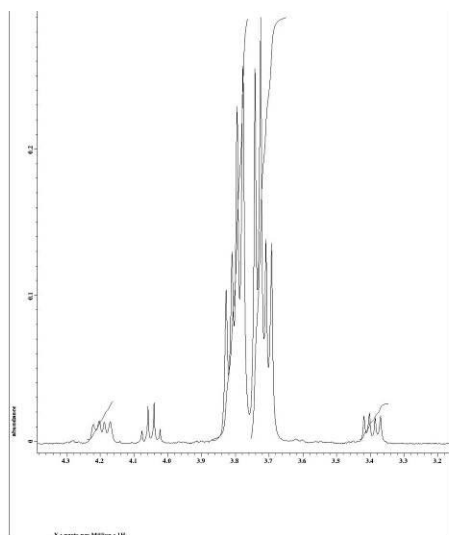
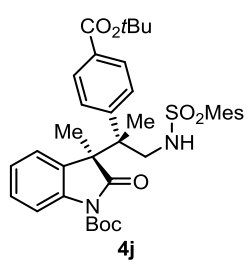


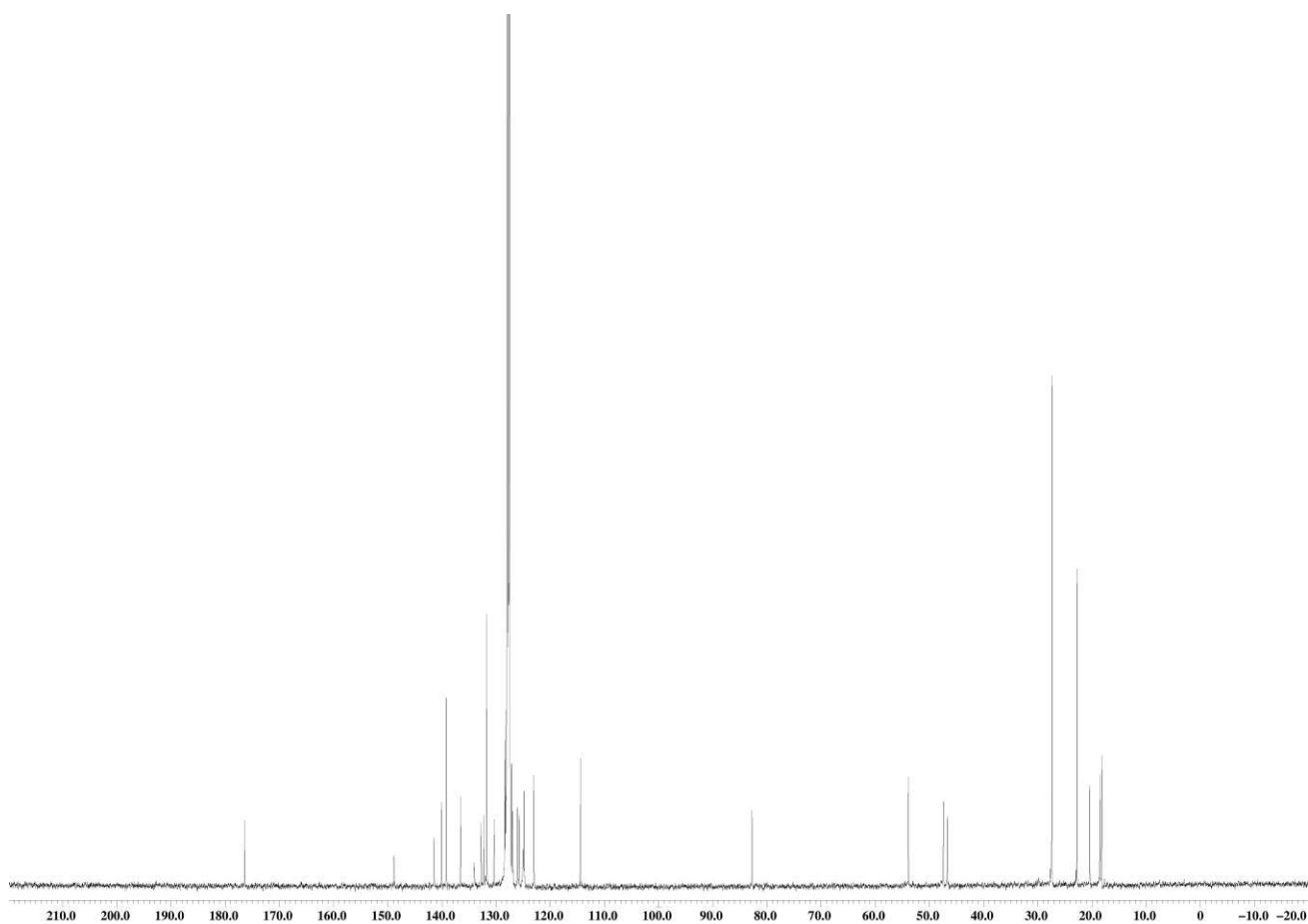
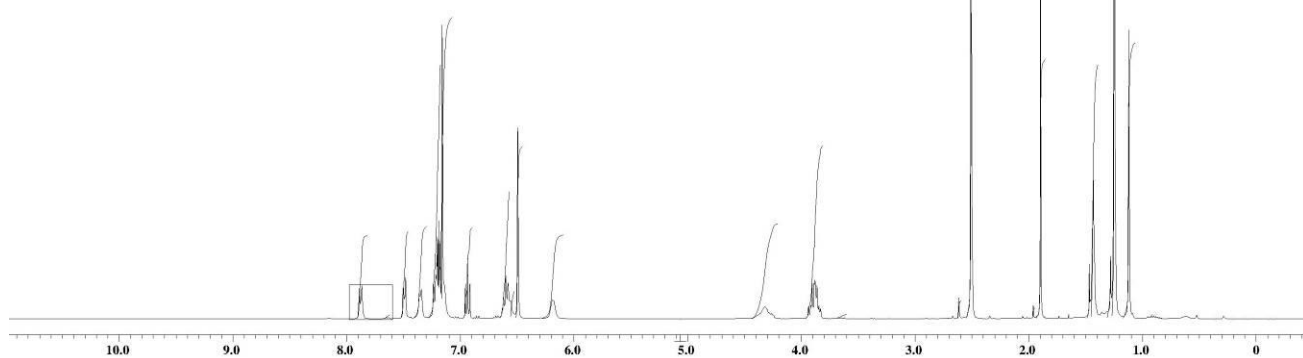
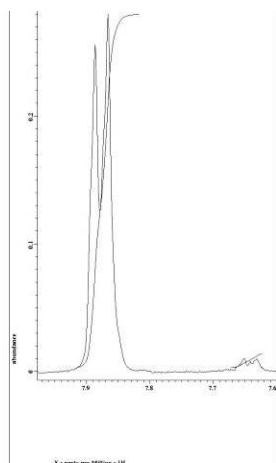


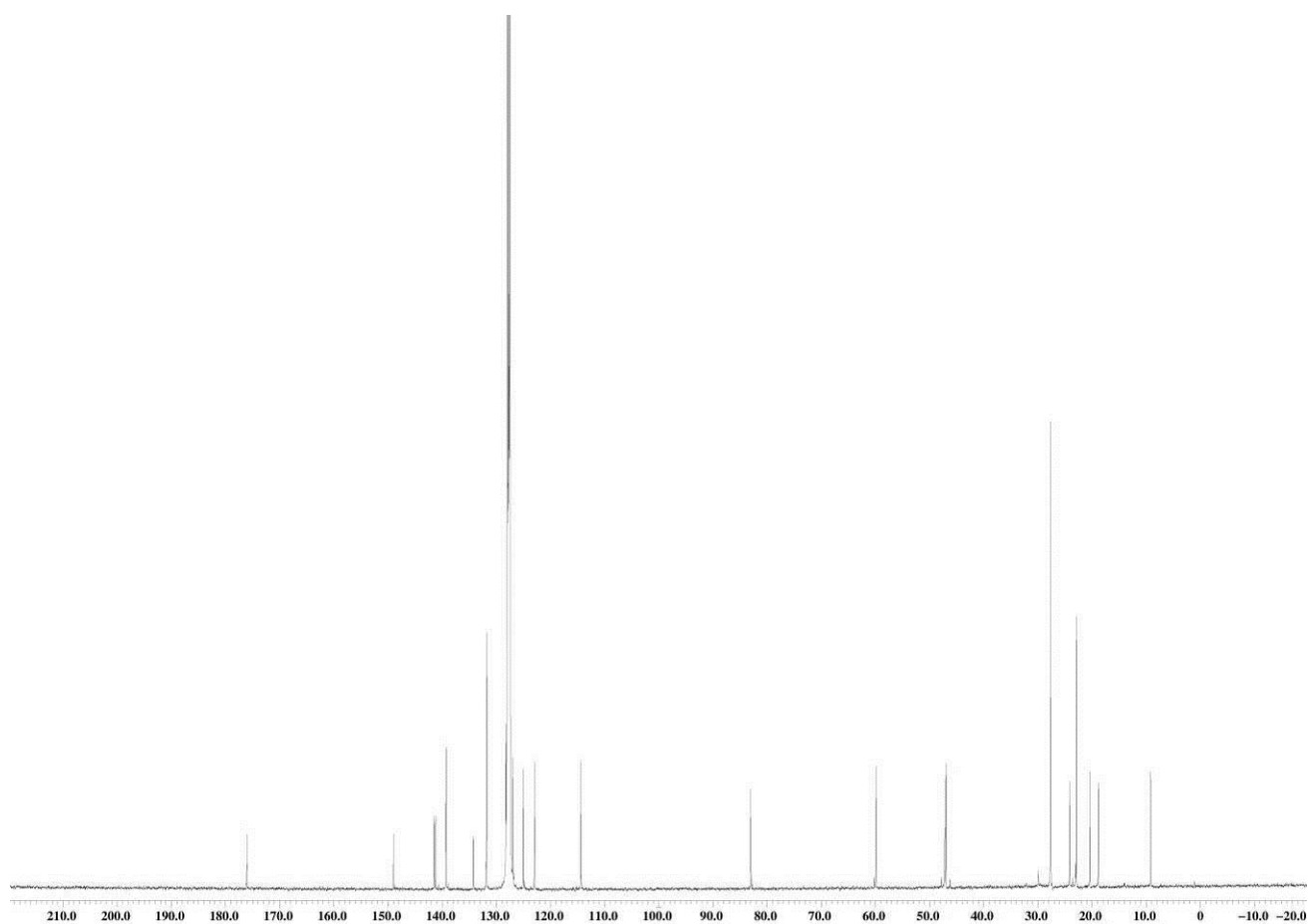
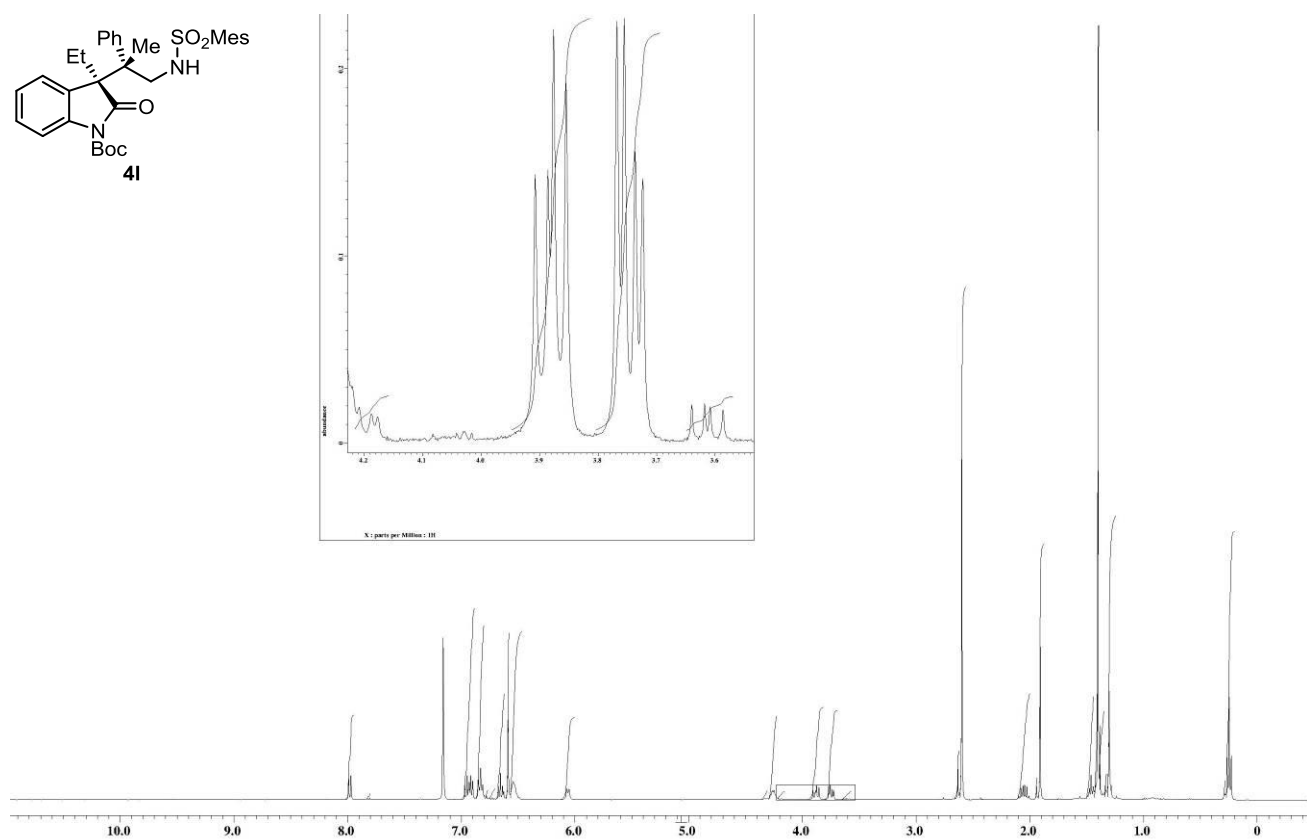
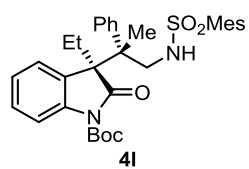


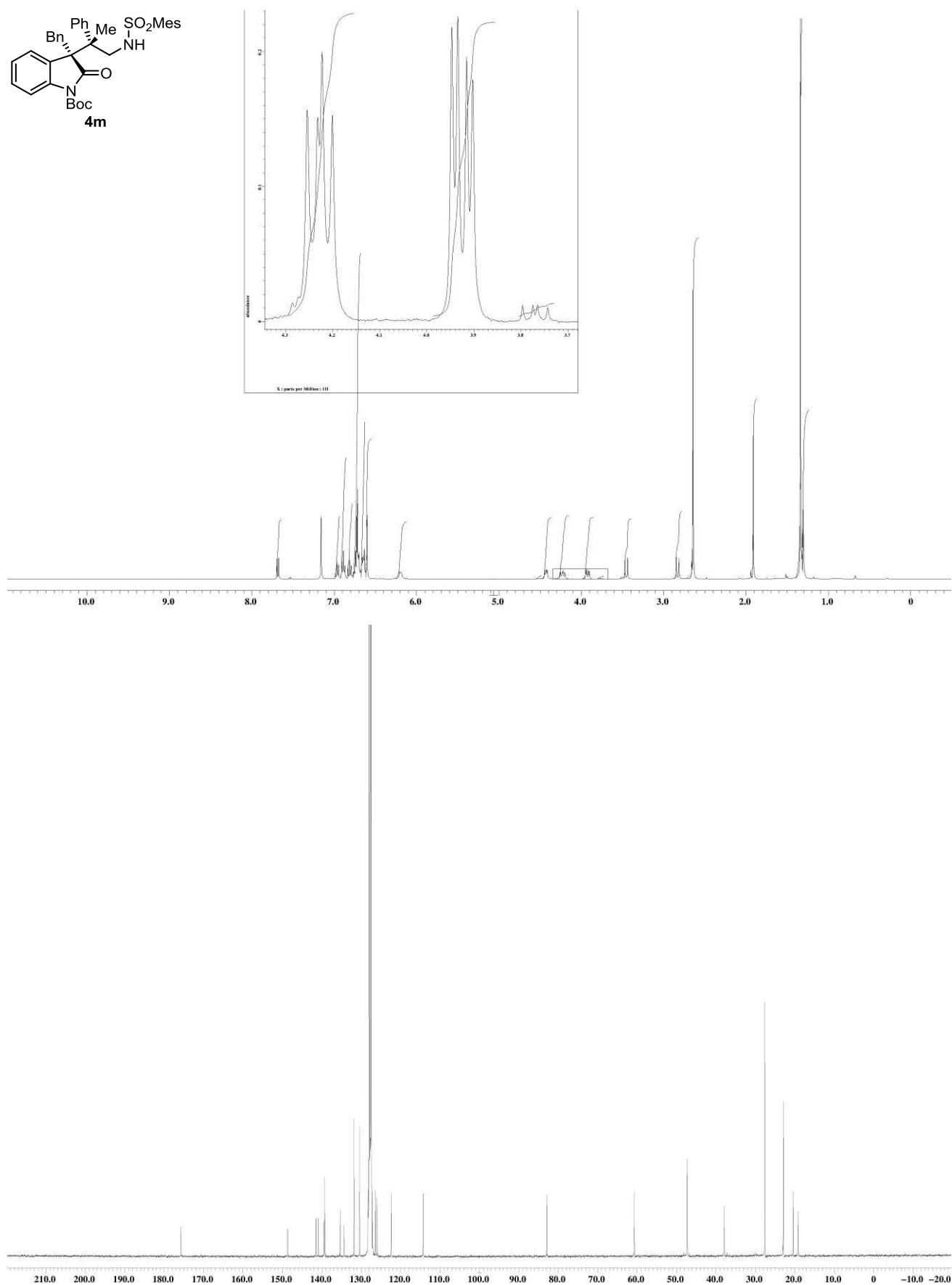
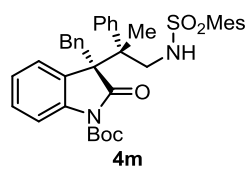


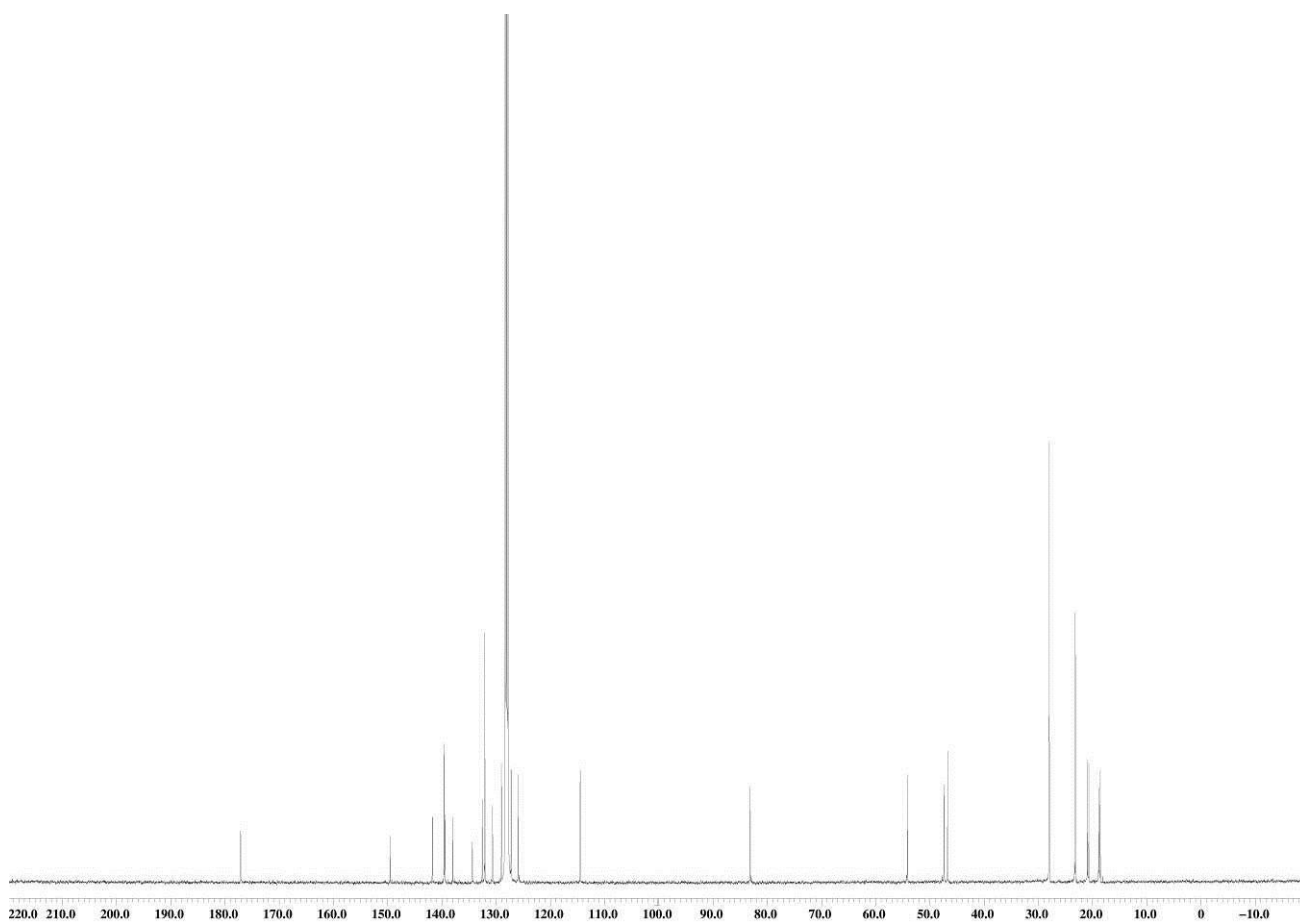
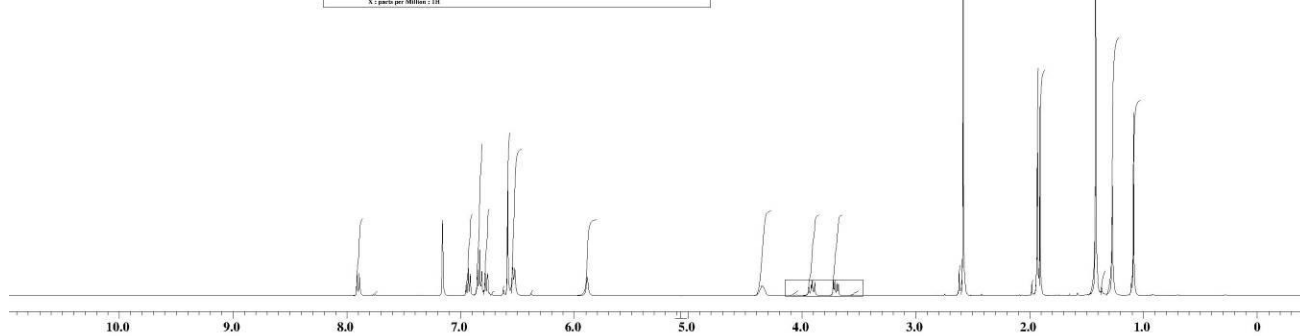
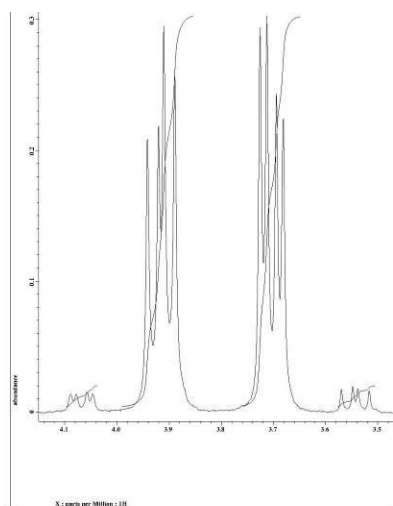
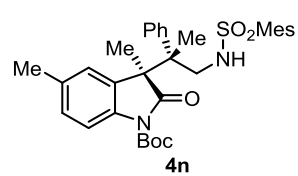


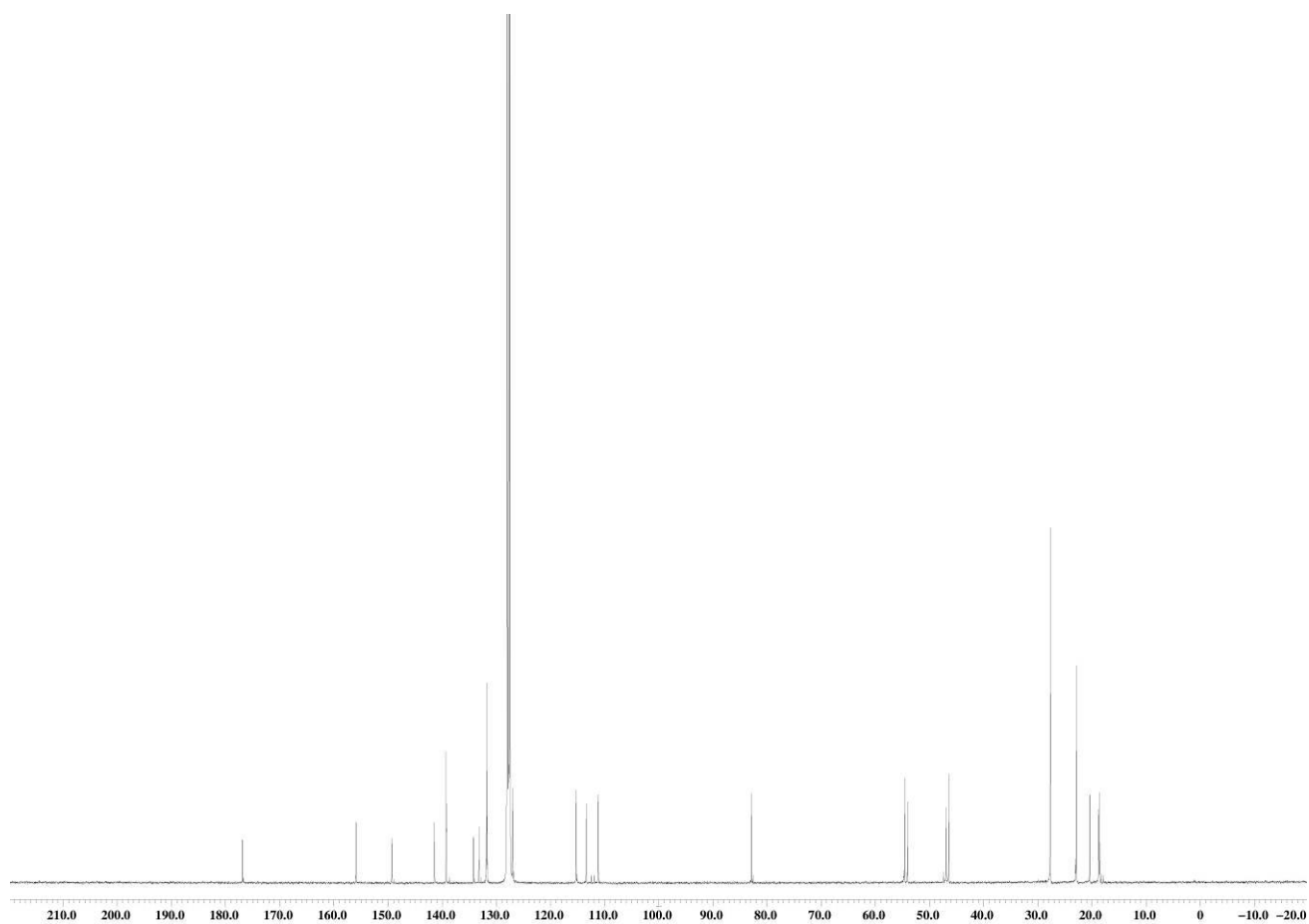
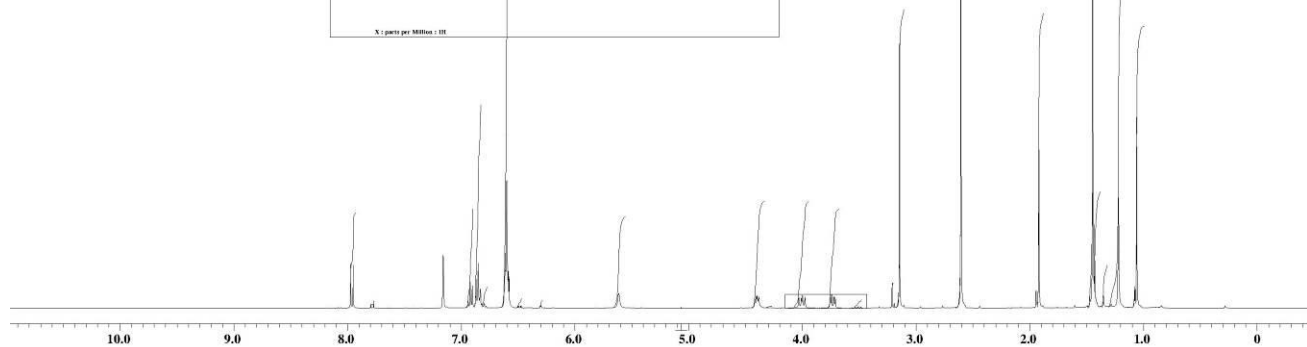
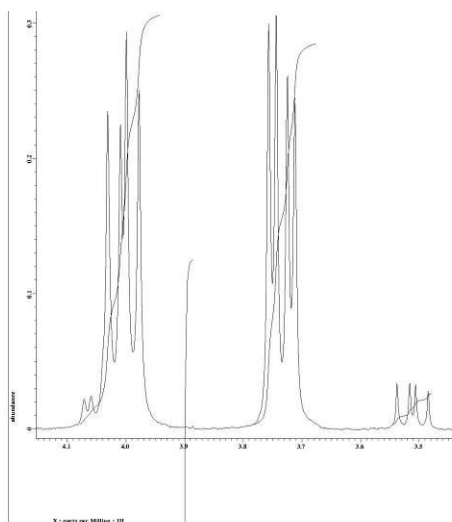


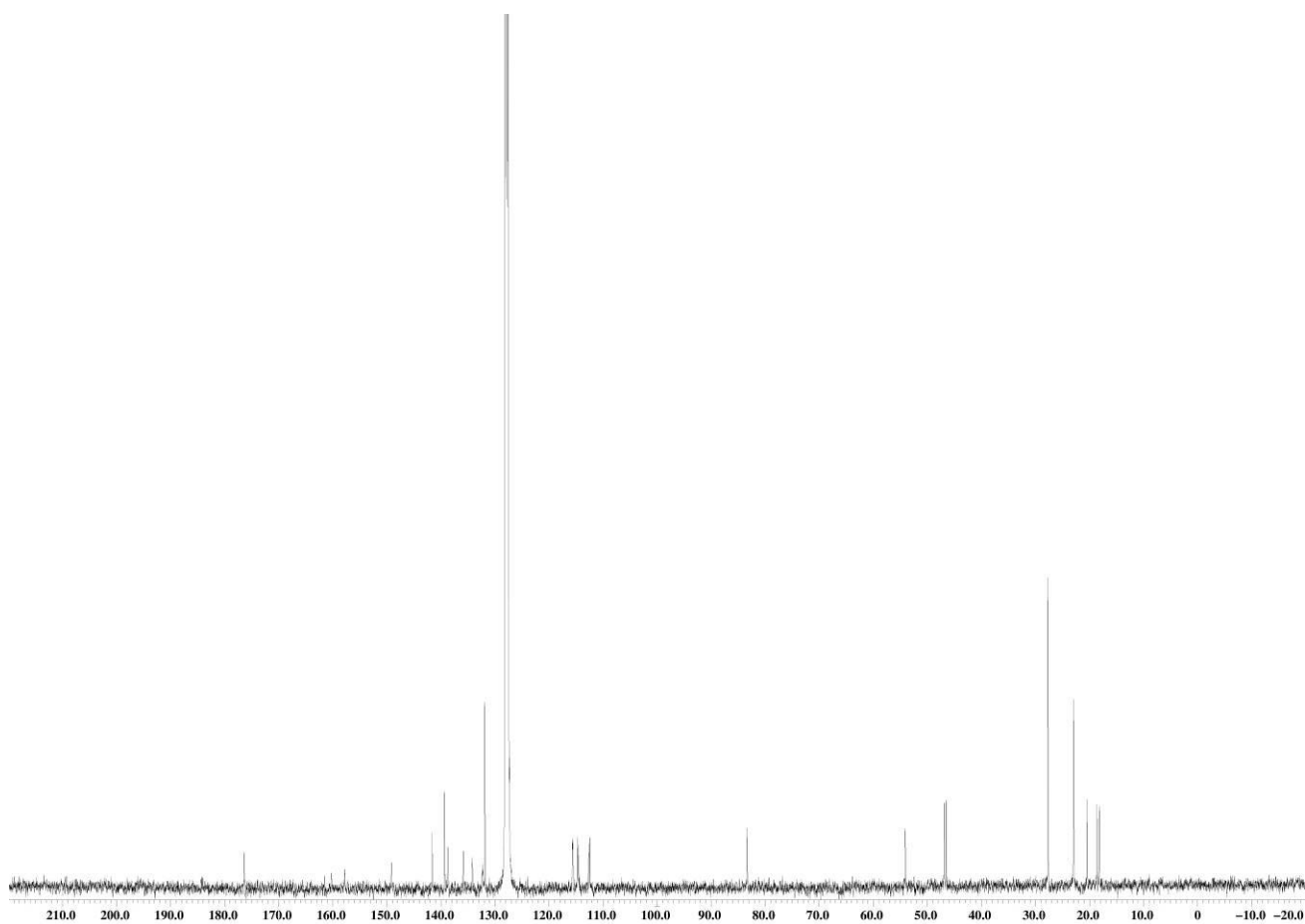
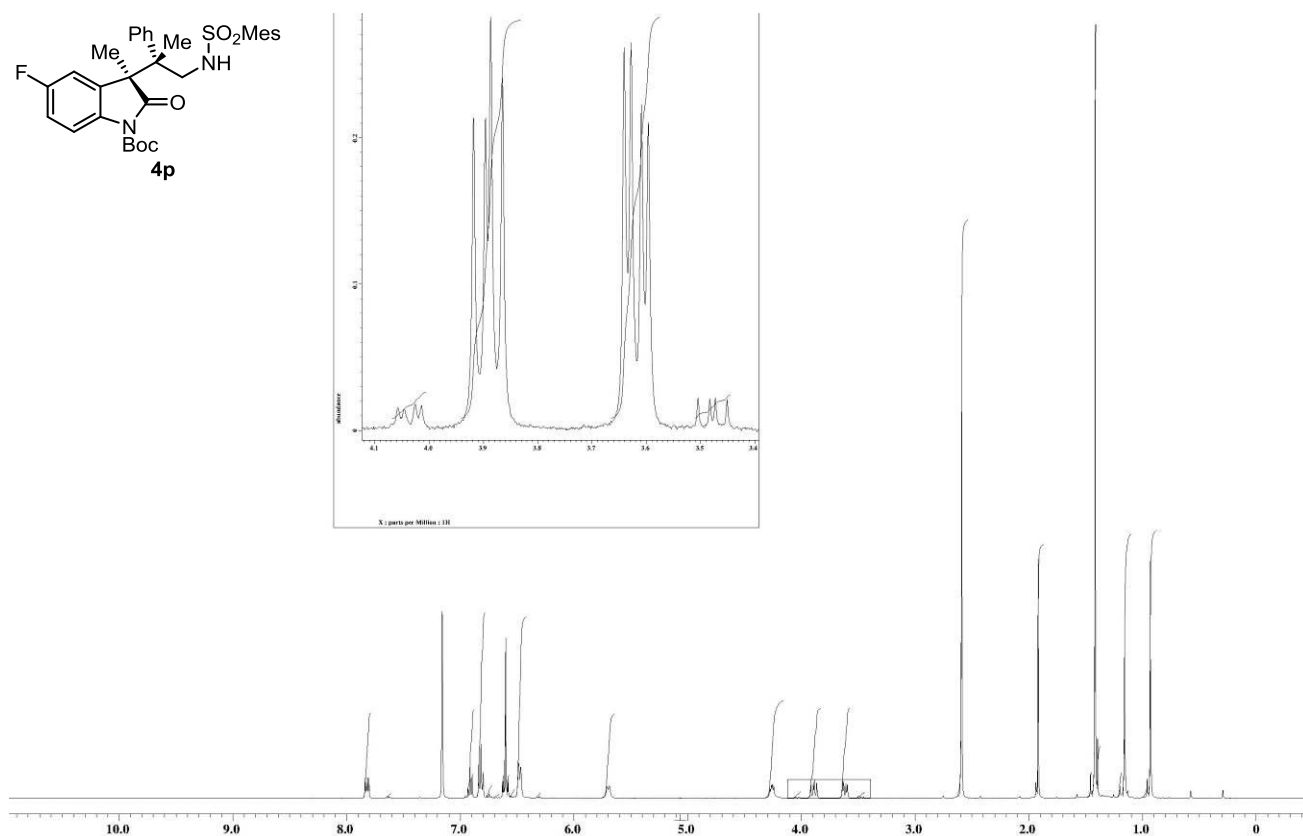
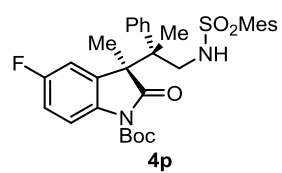




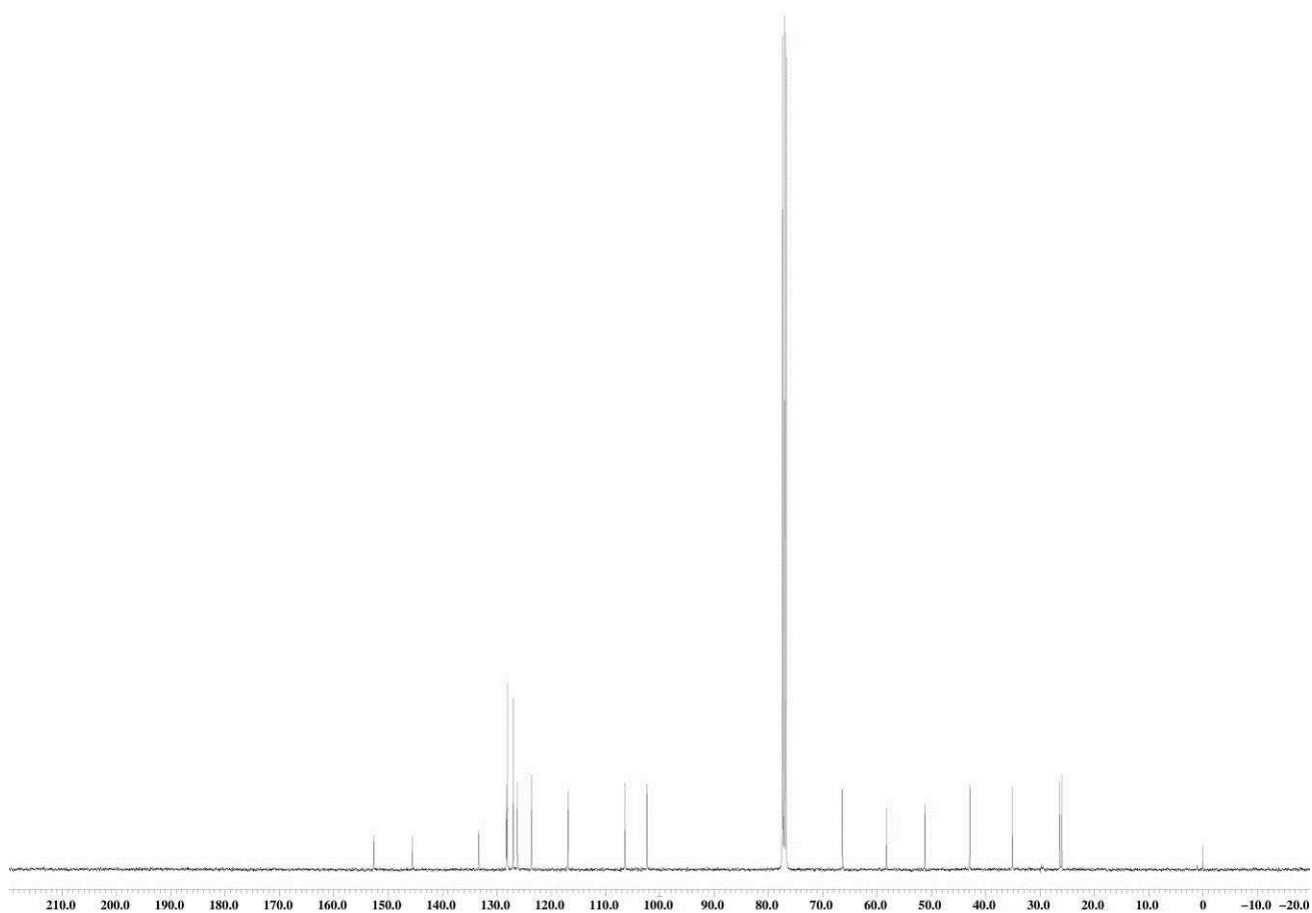
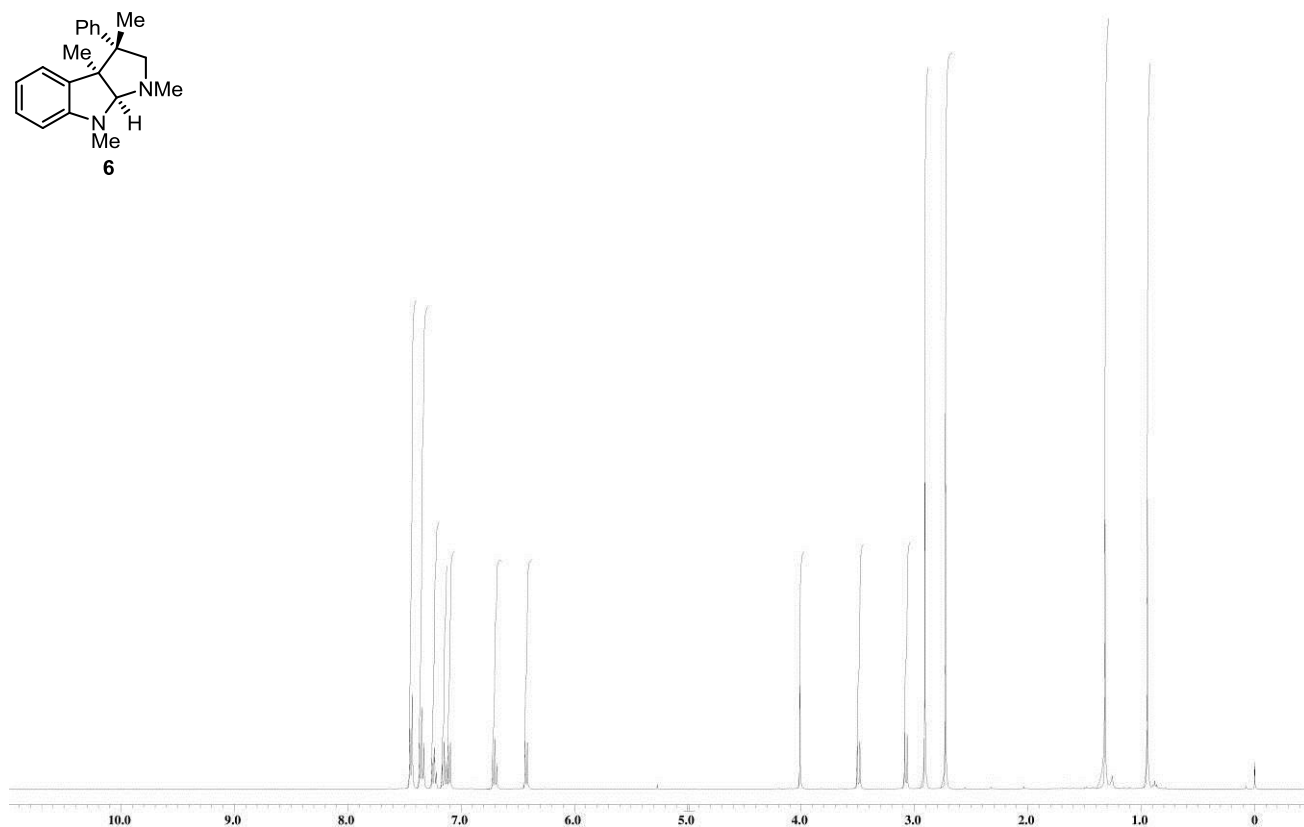
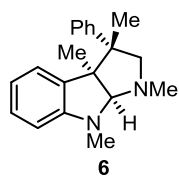






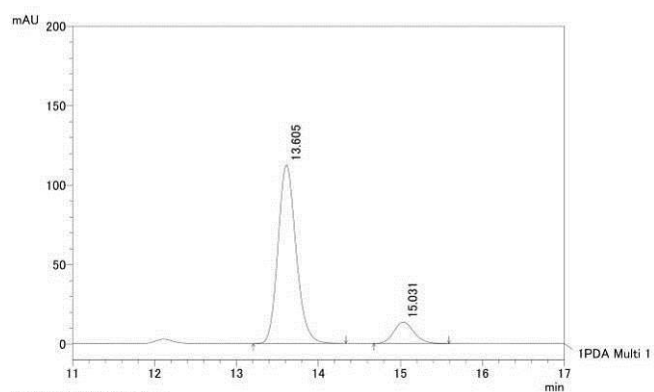
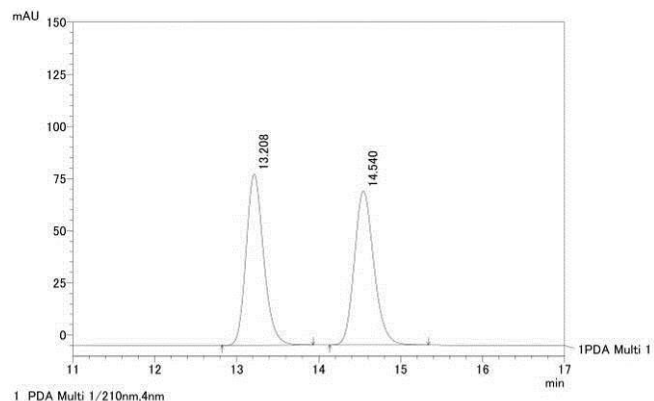






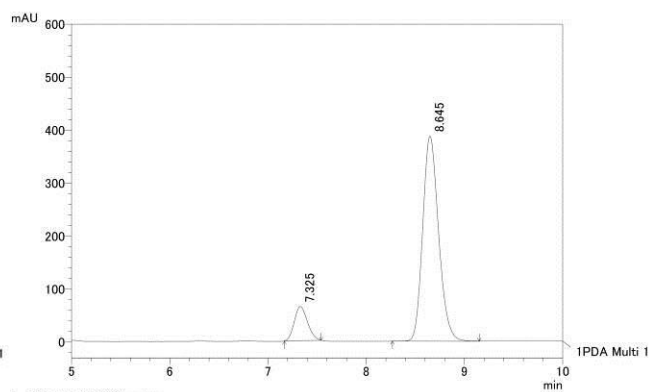
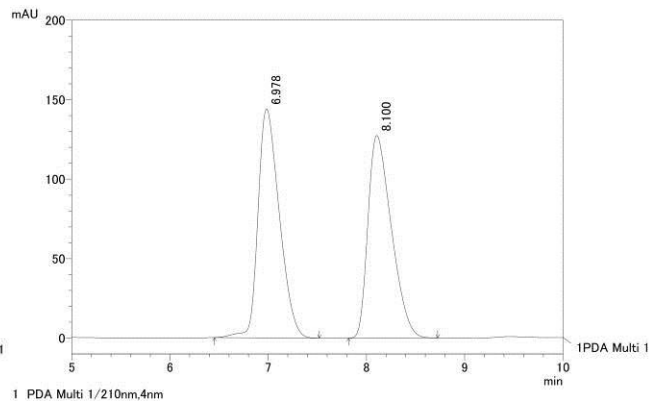
## HPLC Chromatograms:

2b



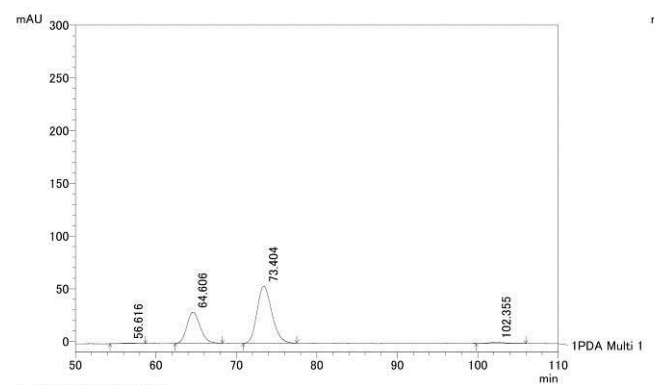
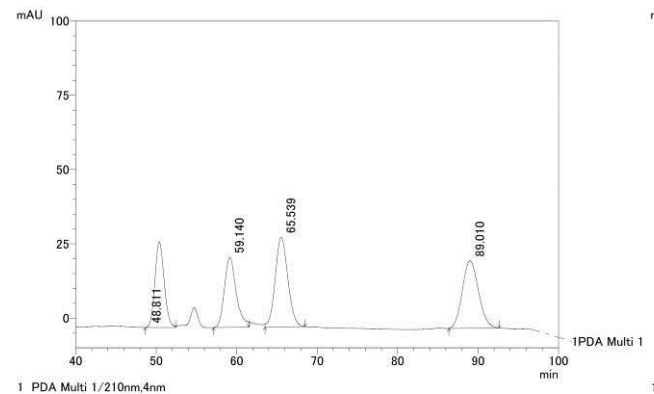
ピーク#	保持時間	面積%
1	13.605	88.181
2	15.031	11.819
合計		100.000

2k



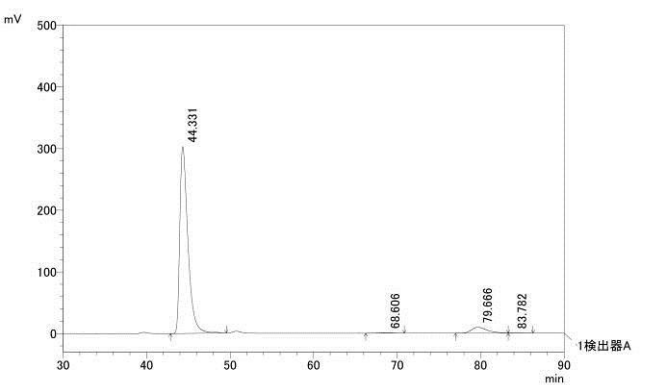
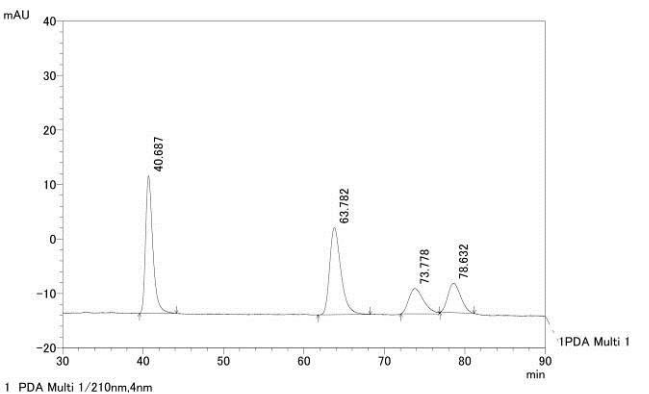
ピーク#	保持時間	面積%
1	7.325	12.122
2	8.645	87.878
合計		100.000

4a



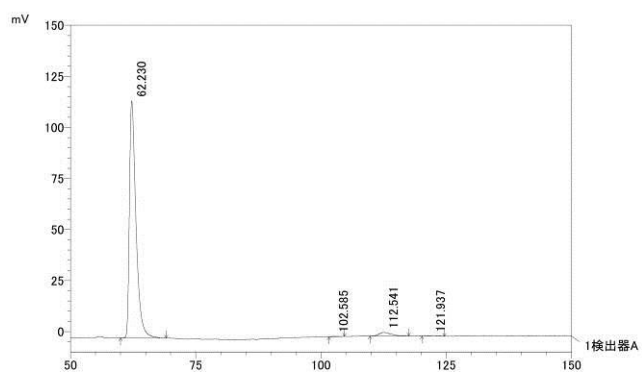
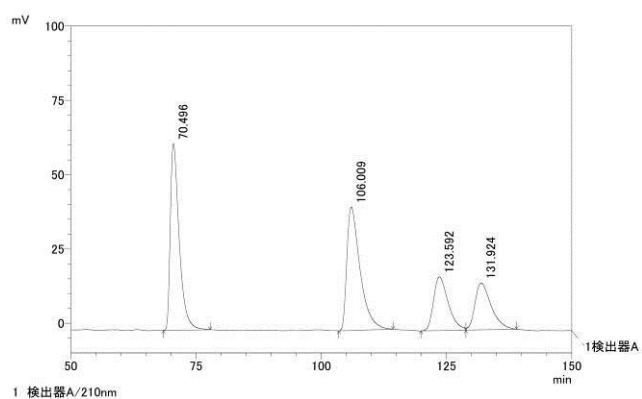
ピーク#	保持時間	面積%
1	56.616	0.485
2	64.606	32.057
3	73.404	66.026
4	102.355	1.431
合計		100.000

4b



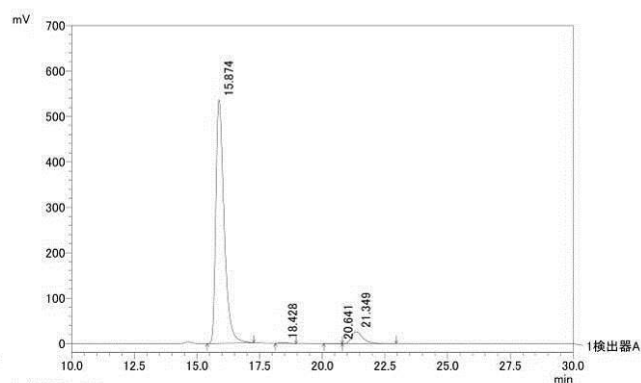
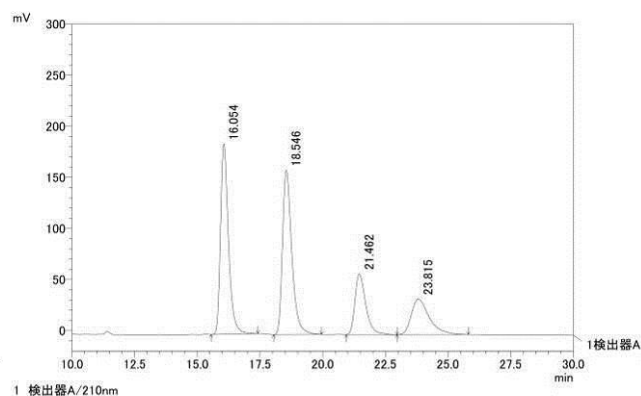
ピーク#	保持時間	面積%
1	44.331	93.593
2	68.606	0.452
3	79.666	5.768
4	83.782	0.187
合計		100.000

4c



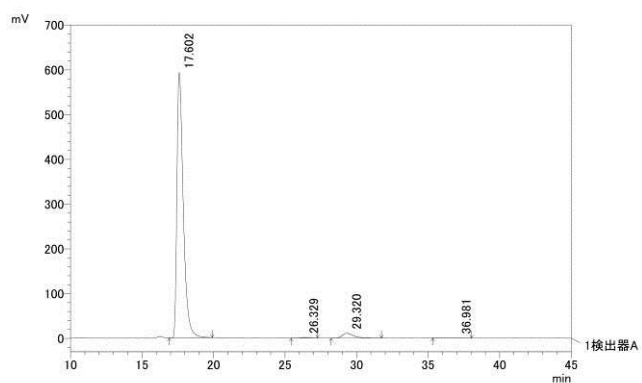
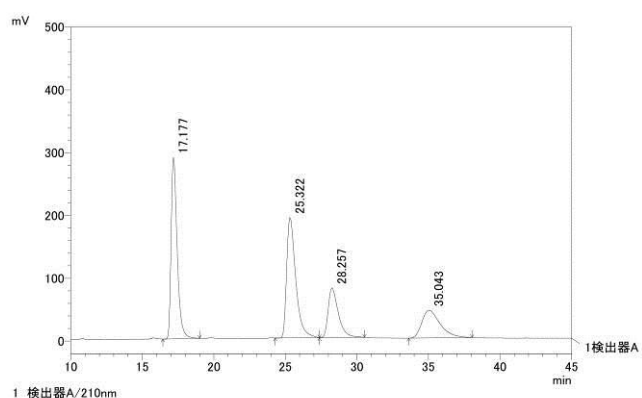
ピーク#	保持時間	面積%
1	62.230	96.890
2	102.585	0.168
3	112.541	2.707
4	121.937	0.234
合計		100.000

4d



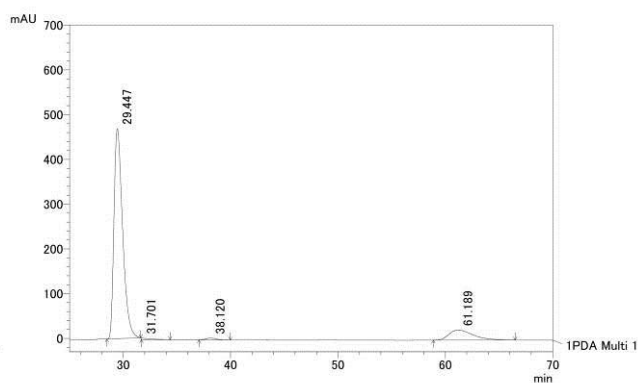
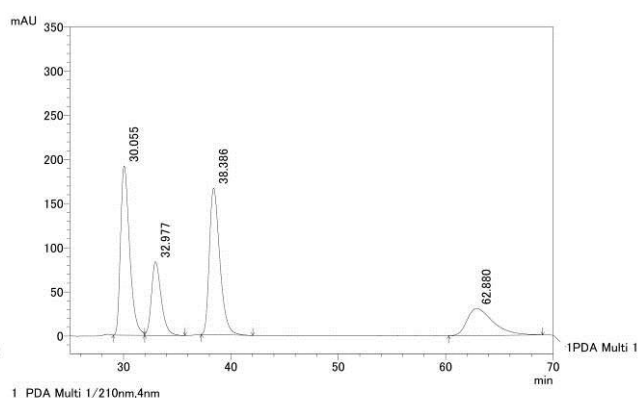
ピーク#	保持時間	面積%
1	15.874	93.609
2	18.428	0.322
3	20.641	0.012
4	21.349	6.058
合計		100.000

4e



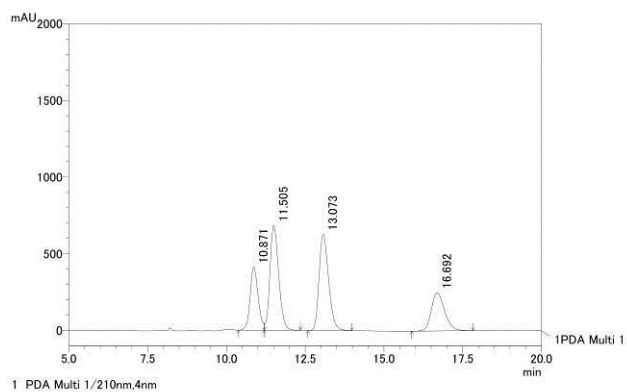
ピーク#	保持時間	面積%
1	17.602	96.534
2	26.329	0.278
3	29.320	3.060
4	36.981	0.129
合計		100.000

4f

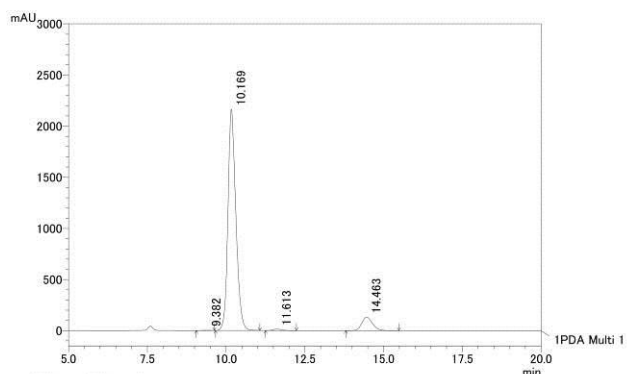
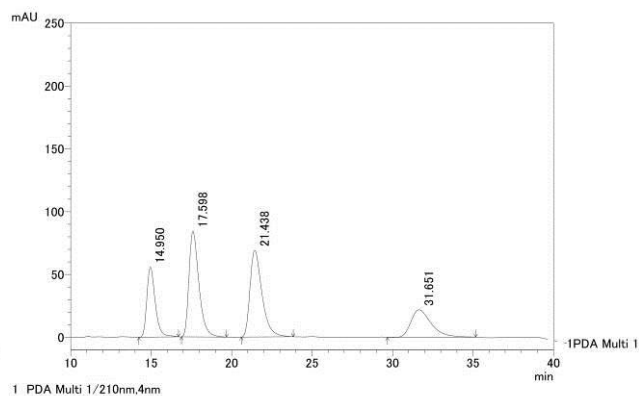


ピーク#	保持時間	面積%
1	29.447	86.836
2	31.701	0.662
3	38.120	0.880
4	61.189	11.622
合計		100.000

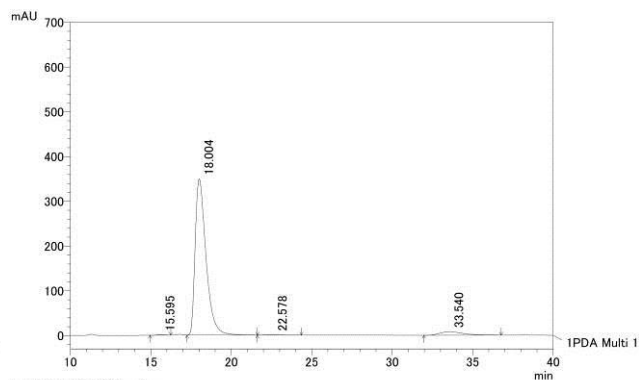
4g



4h

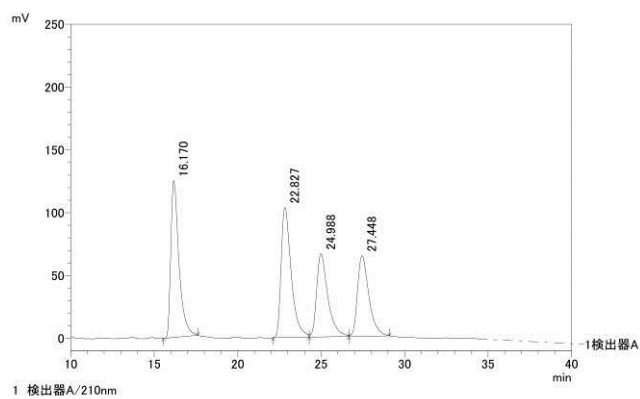


ピーク#	保持時間	面積%
1	9.382	0.103
2	10.169	91.677
3	11.613	0.627
4	14.463	7.593
合計		100.000

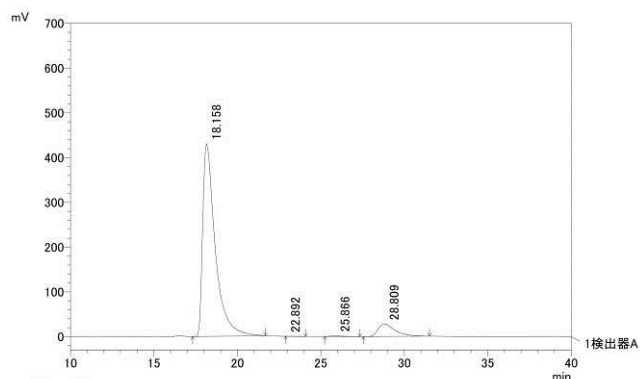
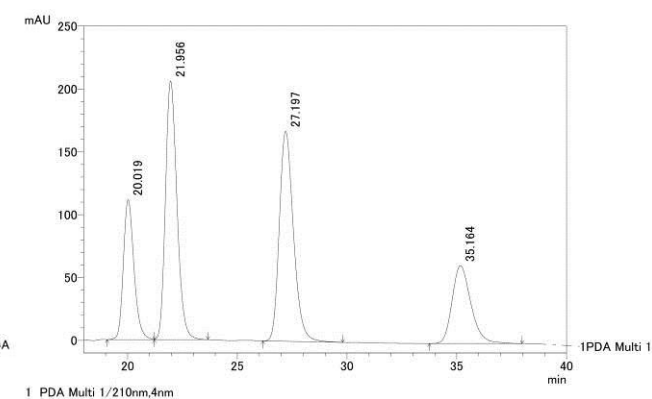


ピーク#	保持時間	面積%
1	15.595	0.206
2	18.004	94.986
3	22.578	0.252
4	33.540	4.557
合計		100.000

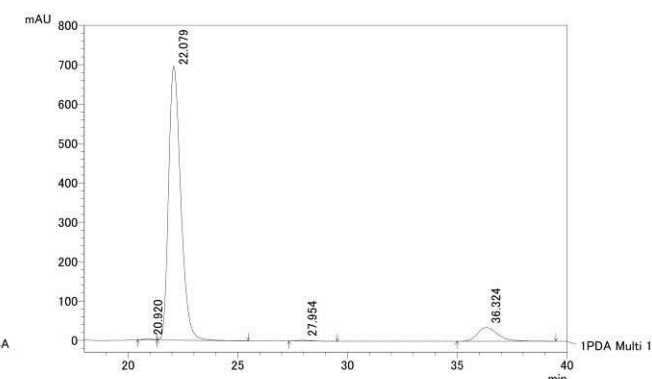
4i



4j

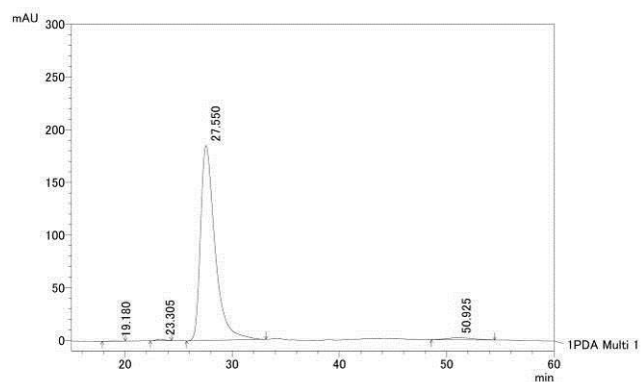
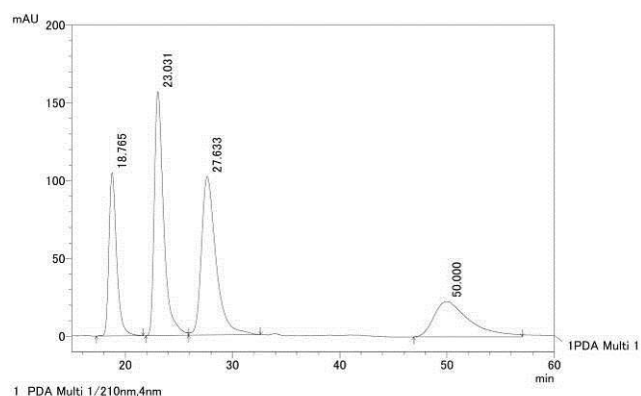


ピーク#	保持時間	面積%
1	18.158	91.544
2	22.892	0.005
3	25.866	0.354
4	28.809	8.097
合計		100.000



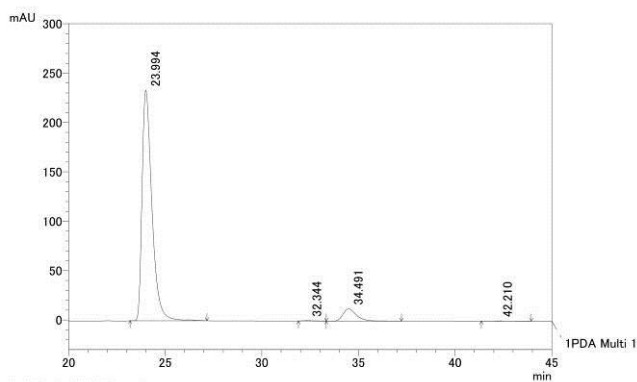
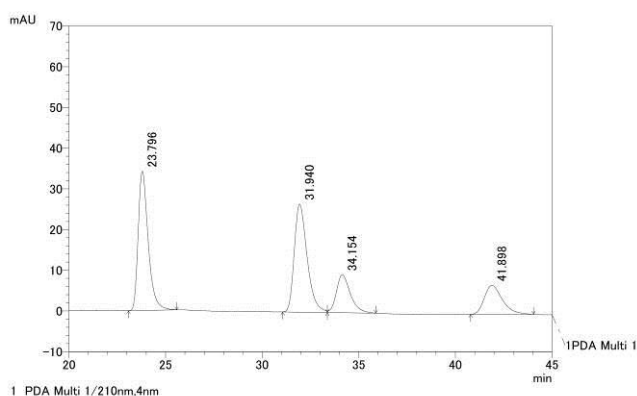
ピーク#	保持時間	面積%
1	20.920	0.202
2	22.079	91.656
3	27.954	0.289
4	36.324	7.853
合計		100.000

4k



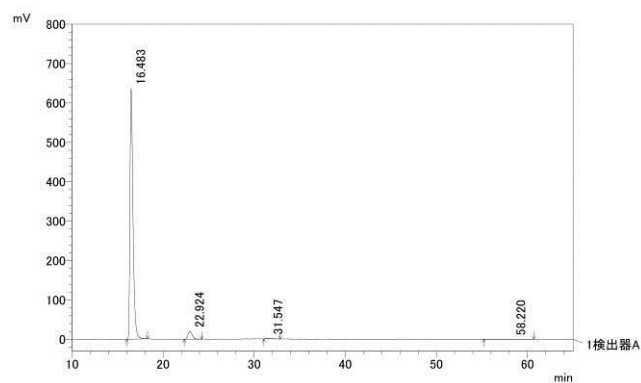
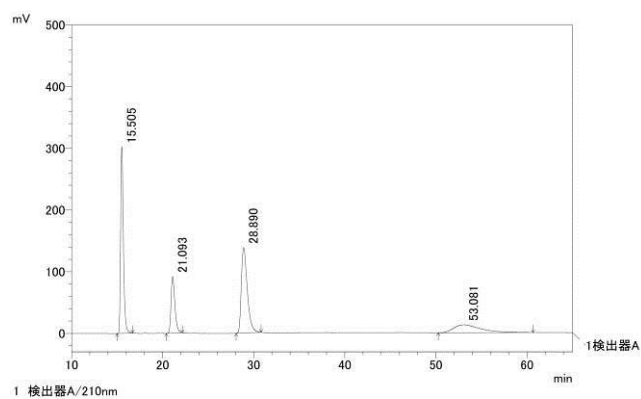
ピーク#	保持時間	面積%
1	19.180	0.097
2	23.305	0.415
3	27.550	97.601
4	50.925	1.887
合計		100.000

4l



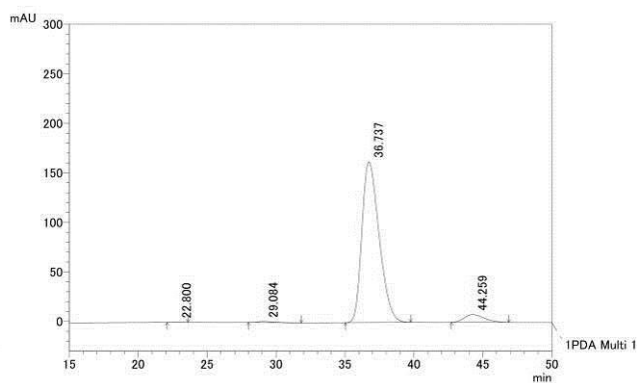
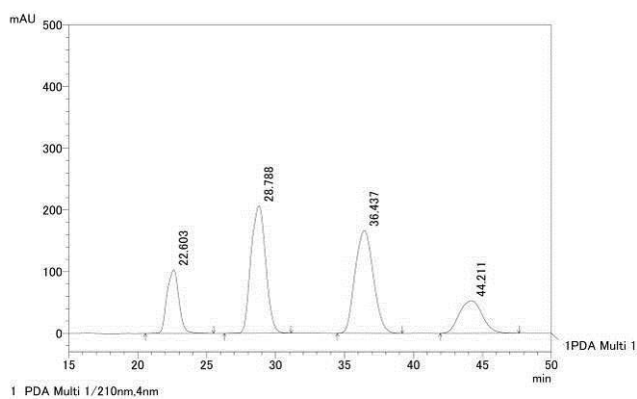
ピーク#	保持時間	面積%
1	23.994	93.006
2	32.344	0.183
3	34.491	6.671
4	42.210	0.140
合計		100.000

4m



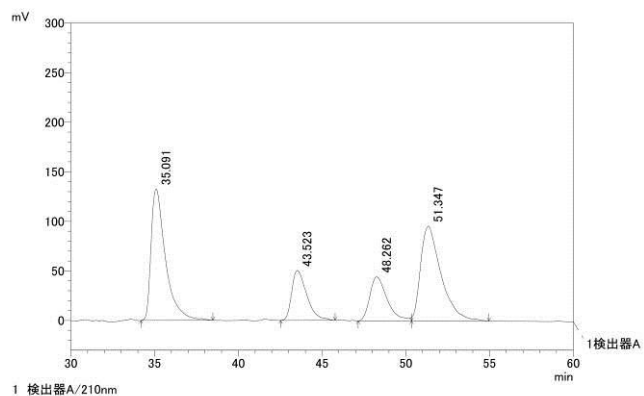
ピーク#	保持時間	面積%
1	16.483	95.535
2	22.924	4.185
3	31.547	0.253
4	58.220	0.027
合計		100.000

4n

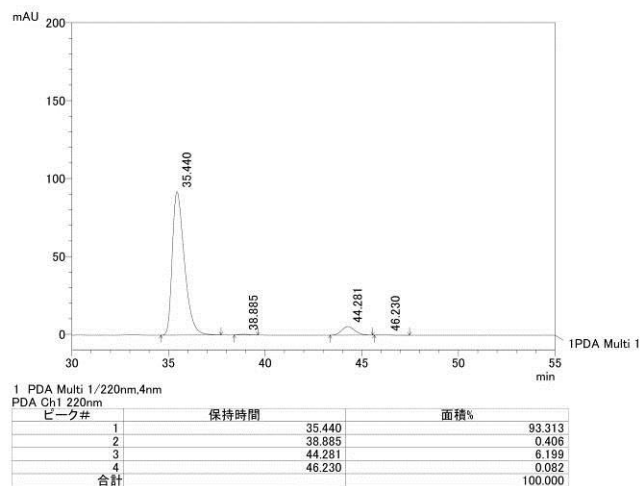
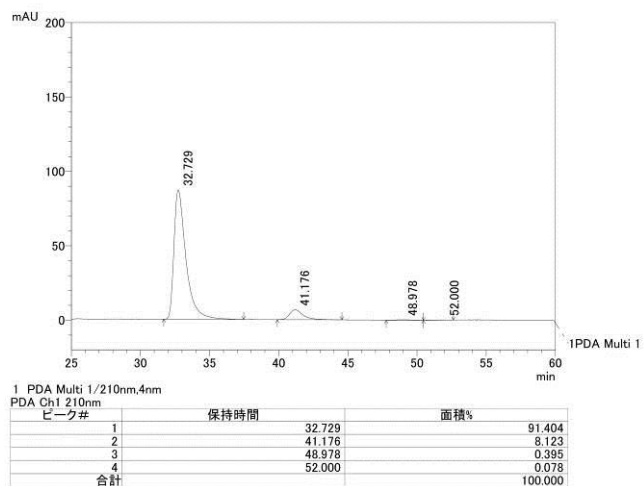
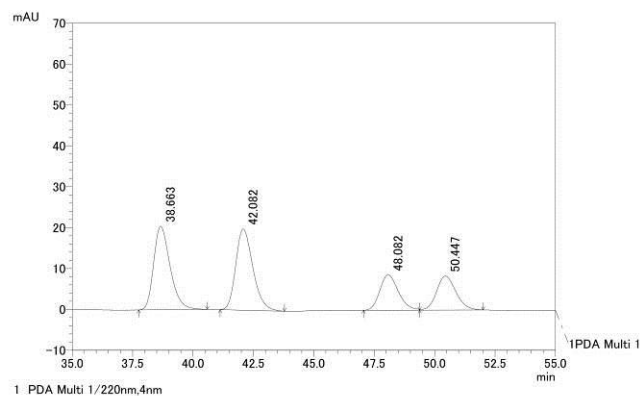


ピーク#	保持時間	面積%
1	22.800	0.042
2	29.084	0.538
3	36.737	94.190
4	44.259	5.230
合計		100.000

4o



4p



6

