Supporting Information

A Solvent-specific DAST-mediated intramolecular Friedel-Crafts reaction: access to dibenzoxepine-fused spirooxindoles

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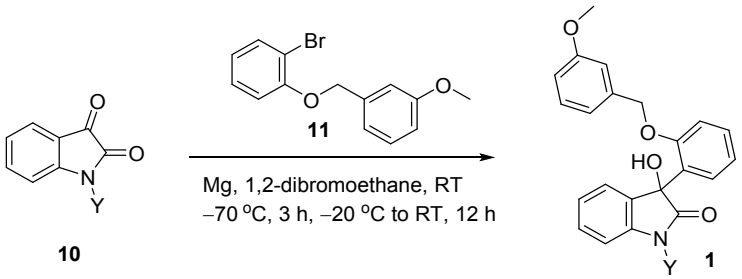
1. General

All reactions were performed under a nitrogen atmosphere unless otherwise specified. Reactions were monitored by thin-layer chromatography (TLC) using Merck silica gel 60 F_{254} pre-coated plates and visualized by a UV lamp for reaction monitoring. ^{1}H NMR (400 MHz) and ^{19}F NMR spectra were measured, and chemical shifts were reported in ppm using TMS or the residual solvent peak as a reference. LC-MS analyses conducted using the Agilent 6140 quadrupole LCMS instrument using C18 columns.

2. Procedure and data for the starting materials (1a – 1aa)

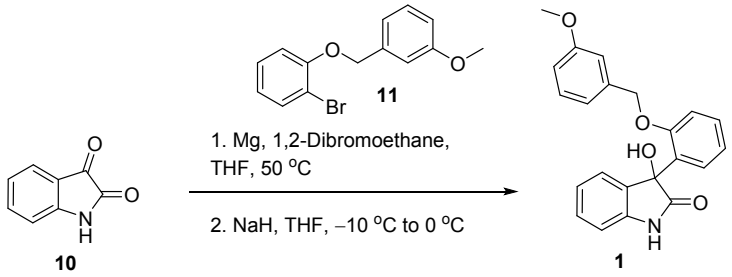
a. General Method – A.[1]



To a stirred suspension of magnesium turnings (2.5 eq.), in dry THF, was added 1,2-dibromoethane (0.1 eq.) under nitrogen and allowed to stir for 15 minutes. After 15 minutes, a solution of 1-bromo-2-((3-methoxybenzyl)oxy)benzene (**11**) (1.5 eq.) in dry THF was added dropwise and the reaction suspension was occasionally heated with a hot gun (50 °C) for initiation. After 30 minutes, the reaction suspension was refluxed for 1 h under nitrogen and then cooled to ambient temperature. To a separate flask, was added isatin, **10** (1 eq.) in dry THF and the solution was cooled to –20 °C under nitrogen. After 10 minutes, the above prepared Grignard reagent was added dropwise over 5 minutes. The reaction mixture was slowly warmed to ambient temperature and stirred for 12 h. After cooling to 0 °C, a saturated NH_4Cl solution (20 mL) was added slowly at 0 °C, followed by the addition of ethyl acetate (3 x 50 mL). The organic layer was separated, washed with water (3 x 50 mL) and brine (40 mL), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was purified by flash chromatography using a mixture of petroleum ether and EtOAc as eluent to afford pure compound **1**.

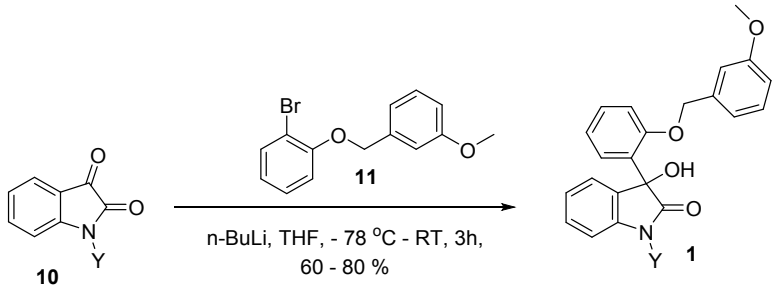
b. General Method – B. [2]

A Schlenk round bottom flask was charged with magnesium (0.062 g, 2.56 mmol), dry THF (5 mL) and 1,2-dibromoethane (0.1 eq.) under a nitrogen atmosphere and stirred until an exothermic reaction occurred (~10 minutes). 2-Bromo-4-chloro-1-((3-methoxybenzyl)oxy)benzene (**11**, 0.571 g, 1.743 mmol) in dry THF (3 mL) was added slowly over 10 minutes. Once the exothermic reaction had subsided, the reaction mixture was heated at reflux for 1 h and then allowed to cool to room temperature.



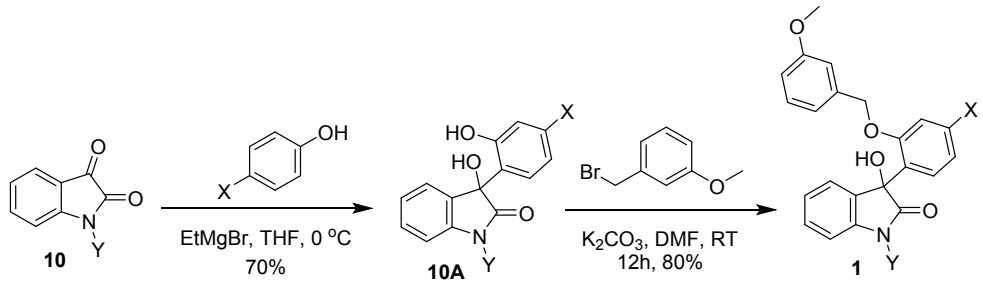
A separate round bottom flask was charged with 6-(trifluoromethyl)indoline-2,3-dione (**10**) (1.162 mmol) and dry THF (5 mL) under nitrogen. The solution was cooled to 0 °C, NaH (0.056 g, 1.394 mmol) added portion-wise and the mixture stirred until gas evolution ceased. The resulting suspension of the sodium salt of 6-(trifluoromethyl)indoline-2,3-dione (**10**) (1.162 mmol) was cooled to −30 °C, and the above Grignard reagent added *via* a syringe. The reaction mixture was allowed to warm to room temperature and stirred for 30 minutes. The progress of the reaction was monitored by TLC or LCMS. Upon completion of the reaction, the mixture was quenched with a saturated solution of NH_4Cl (20 mL) and extracted with ethyl acetate (3 x 50 mL). The organic extract was washed with brine (40 mL), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to give the crude product which was purified by flash column chromatography using a mixture of petroleum ether and EtOAc as eluent to furnish the compound **1.**

c. General Method – C. [3]



A solution of 1-bromo-2-((3-methoxybenzyl)oxy)benzene (**11**) (2.5 eq.) in anhydrous THF (10 vol.) was cooled to –78 °C under argon. After 15 minutes, a solution of *n*-BuLi (1.6 M in hexane, 2.5 eq.) was added dropwise over 15 minutes. The resulting pale yellow solution was stirred for 30 minutes before being added via cannula to cooled solution of isatin (**10**) (1 eq.) in anhydrous THF maintained at –78 °C. The reaction mixture was slowly warmed to ambient temperature. The reaction progress was monitored by TLC for the consumption of isatin starting material. Upon completion, the reaction mixture was cooled to 0 °C and quenched with a saturated solution of NH_4Cl (20 mL), followed by extraction with ethyl acetate (3 x 50 mL). The combined organic layers were washed with water (3 x 50 mL) and brine (40 mL), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography using a mixture of petroleum ether and EtOAc as eluent to afford pure **1**.

d. <u>General Method – D.</u> [4]

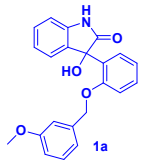


<u>Step 1.</u> <u>Addition of magnesium phenolates to isatins.</u> A solution of EtMgBr (1.1 eq., 1 M in THF) was added dropwise to a solution of phenol (1.2 eq., both unsubstituted and substituted analogues) in anhydrous THF (10 vol) maintained at 0 °C. The white suspension was stirred for 15 mins and the reaction mixture concentrated to dryness. The white bromo magnesium phenolate residue obtained was dissolved in DCM (10 vol), and the isatin (**10**,1 eq.) was added. The reaction mixture was stirred at room temperature and the progress monitored by TLC (if there was no any reaction at RT, the reaction mixture was heated at reflux until the isatin was consumed). The reaction mixture was quenched by the addition of 1N HCl (20 mL), the organic layer was separated and washed with water (2 x 30 mL), brine (30 mL) and dried over sodium sulfate. The crude product was purified either by flash chromatography using a mixture of petroleum ether and EtOAc as eluent or by recrystallization to afford the intermediate **10A**.

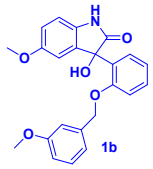
<u>Step-2.</u> <u>Benzylation of phenolic OH</u>. To a solution of the intermediate **10A** in anhydrous DMF at 25 °C was added anhydrous K_2CO_3 (2 eq.) and 1-(bromomethyl)-3-methoxybenzene (1.2 eq). The reaction mixture was stirred at ambient temperature for

12 h, before quenching with ice-cold water (15 mL), followed by extraction with ethyl acetate (3 x 30 mL). The combined organic layers were washed with water (2 x 20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue obtained was purified either by flash chromatography using a mixture of petroleum ether and EtOAc as eluent or by recrystallization to afford pure **1**.

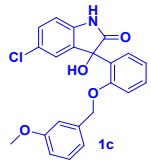
2.e. Spectral data of the synthesized starting materials 1a – 1aa.



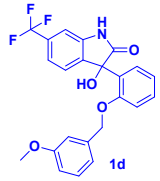
Compound 1a. 3-hydroxy-3-(2-((3-methoxybenzyl)oxy)- phenyl)indolin-2-one was prepared according to the Method B. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.17 (s, 1H), 7.88 (dd, J = 7.8, 1.7 Hz, 1H), 7.07–7.26 (m, 4H), 6.92–7.07 (m, 1H), 6.71–6.89 (m, 6H), 6.62 (s, 1H), 6.42–6.47 (m, 2H), 4.72–4.86 (m, 2H), 3.70 (s, 3H); LCMS (ESI) calcd for $(M–H)^+$ $C_{22}H_{19}NO_4$ 360.40; found 360.12.



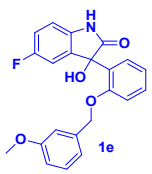
Compound 1b. 3-hydroxy-5-methoxy-3-(2-((3-methoxy-benzyl)oxy) phenyl)indolin-2-one was prepared according to the Method B. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.02 (s, 1H), 7.86 (dd, J = 7.8, 1.7 Hz, 1H), 7.08-7.26 (m, 2H), 7.02 (td, J = 7.6, 1.0 Hz, 1H), 6.59–6.88 (m, 6H), 6.50 (d, J = 8.0 Hz, 1H), 6.45 (s, 1H), 6.37 (d, J = 2.7 Hz, 1H), 4.77–4.87 (m, 2H), 3.68–3.79 (m, 3H), 3.62 (s, 3H); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.08–7.28 (m, 2H), 6.66–6.89 (m, 5H), 4.77–4.87 (m, 2H), 3.65–3.75 (m, 3H), 3.60–3.73 (m, 3H); LCMS (ESI) calcd for $(M–H)^+$ $C_{23}H_{21}NO_5$ 390.42; found 390.12.



Compound 1c. 5-chloro-3-hydroxy-3-(2-((3-methoxybenzyl)oxy)phenyl) indolin-2-one was prepared according to the Method B. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.35 (s, 1H), 7.84 (d, J = 7.6 Hz, 1H), 6.99–7.29 (m, 4H), 6.64–6.89 (m, 5H), 6.59 (s, 1H), 6.44 (d, J = 7.3 Hz, 1H), 4.75–4.90 (m, 2H), 3.70 (s, 3H); LCMS (ESI) calcd for $(M–H)^+$ $C_{22}H_{18}ClNO_4$ 394.84, found 394.05.

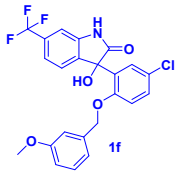


Compound 1d. 3-hydroxy-3-(2-((3-methoxybenzyl)oxy)phenyl)-6-(trifluoro methyl)indolin-2-one was prepared according to the Method B. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.47 (s, 1H), 7.87 (d, J = 7.3 Hz, 1H), 7.17–7.29 (m, 2H), 6.78–7.12 (m, 6H), 6.73 (s, 1H), 6.55 (s, 1H), 6.35 (d, J = 7.3 Hz, 1H), 4.69–4.88 (m, 2H), 3.68 (s, 3H); ^{19}F NMR ($CDCl_3$, 377 MHz) δ -61.73 (s, 3F); LCMS (ESI) calcd for $(M–H)^+$ $C_{23}H_{18}F_3NO_4$ 428.40, found 428.11.

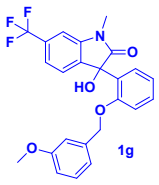


Compound 1e. 5-fluoro-3-hydroxy-3-(2-((3-methoxybenzyl)oxy)phenyl) indolin-2-one was prepared according to the Method B. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.23 (s, 1H), 7.86 (dd, J = 7.8, 1.8 Hz, 1H), 7.24 (td, J = 7.8, 1.5 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H), 6.95–7.07 (m, 2H), 6.87 (d, J = 8.1 Hz, 1H),

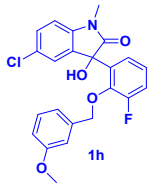
6.80 (d, J = 8.4 Hz, 1H), 6.58–6.69 (m, 4H), 6.49 (d, J = 7.5 Hz, 1H), 4.76–4.88 (m, 2H), 3.70 (s, 3H); ^{19}F NMR (DMSO-d_6, 377 MHz) δ 120.8 (s, 1F); LCMS (ESI) calcd for $(M + NH_4)^+$, $C_{22}H_{18}F_3NO_4$ 397.39; found 397.20.



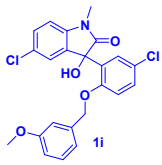
Compound 1f. 3-(5-chloro-2-((3-methoxybenzyl)oxy)phenyl)-3-hydroxy-6-(trifluoromethyl)indolin-2-one was prepared according to the Method B. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.94 (d, J = 2.5 Hz, 1H), 7.52 (br s, 1H), 7.30–7.37 (m, 1H), 7.15–7.27 (m, 3H), 6.90 (dd, J = 8.0, 2.0 Hz, 1H), 6.80 (d, J = 9.0 Hz, 1H), 6.77 (s, 1H), 6.57–6.65 (m, 2H), 4.80 (d, J = 10.5 Hz, 1H), 4.71 (d, J = 10.5 Hz, 1H), 3.77 (s, 3H), 3.40 (br s, 1H); ^{19}F NMR ($CDCl_3$, 377 MHz) δ -62.73 (s, 3F); HRMS m/z (ESI): calcd. for $C_{23}H_{17}ClF_3NO_4$ $[M+H]^+$ 464.84; found 464.80.



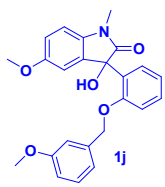
Compound 1g. 3-hydroxy-3-(2-((3-methoxybenzyl)oxy) phenyl)-1-methyl-6-(trifluoromethyl)indolin-2-one was prepared according to the Method C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90 (dd, J = 7.5, 1.5 Hz, 1H), 7.18–7.34 (m, 4H), 6.95–7.15 (m, 2H), 6.82-6.90 (m, 2H), 6.69–6.79 (m, 1H), 6.49–6.63 (m, 2H), 4.61–4.74 (m, 2H), 3.68-3.83 (m, 3H), 3.36 (s, 1H), 2.62 (s, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ -62.55 (s, 3F); LCMS (ESI) calcd for $(M+H)^+$ $C_{24}H_{20}F_3NO_4$ 444.42; found 444.20.



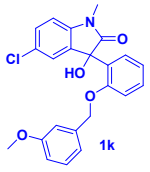
Compound 1h. 5-chloro-3-(3-fluoro-2-((3-methoxybenzyl) oxy)phenyl)-3-hydroxy-1-methylindolin-2-one was prepared according to the Method D. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59–7.68 (m, 1H), 7.08–7.28 (m, 5H), 7.02 (d, J = 2.0 Hz, 1H), 6.84 (dd, J = 8.3, 2.3 Hz, 1H), 6.63–6.72 (m, 2H), 6.46 (d, J = 8.0 Hz, 1H), 4.92 (d, J = 10.5 Hz, 1H), 4.60 (d, J = 10.5 Hz, 1H), 3.79 (s, 3H), 3.56 (br s, 1H), 2.61 (s, 3H); ^{19}F NMR (DMSO-d_6, 377 MHz): δ -129.95 (s, 1F); LCMS (ESI) calcd for $(M+H)^+$ $C_{23}H_{19}ClFNO_4$ 428.86; found 428.20



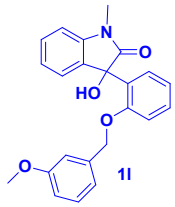
Compound 1i. 5-chloro-3-(5-chloro-2-((3-methoxybenzyl)oxy) phenyl)-3-hydroxy-1-methylindolin-2-one was prepared according to the Method D. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.83 (d, J = 3.0 Hz, 1H), 7.30–7.38 (m, 2H), 7.22 (t, J = 7.8 Hz, 1H), 6.97 (d, J = 8.5 Hz, 1H), 6.85–6.93 (m, 3H), 6.73 (d, J = 8.0 Hz, 1H), 6.52 (s, 1H), 6.46 (d, J=7.5 Hz, 1H), 4.74 (s, 2H), 3.74 (s, 3H), 2.66 (s, 3H); LCMS (ESI) calcd for $(M+2H)^+$ $C_{23}H_{19}Cl_2NO_4$ 446.31; found 446.20.



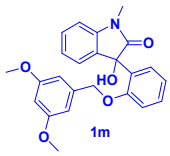
Compound 1j. 3-hydroxy-5-methoxy-3-(2-((3-methoxybenzyl)oxy)phenyl) -1-methylindolin-2-one was prepared according to the Method C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.87 (d, J = 7.5 Hz, 1H), 7.17–7.33 (m, 3H), 7.07 (t, J = 7.5 Hz, 1H), 6.76–6.90 (m, 3H), 6.58–6.71 (m, 3H), 6.48 (d, J = 8.5 Hz, 1H), 4.66–4.80 (m, 2H), 3.78 (s, 3H), 3.71 (s, 3H), 3.24 (s, 1H), 2.64 (s, 3H); LCMS (ESI) calcd for $(M + H)^+$ $C_{24}H_{23}NO_5$ 406.45; found 406.25.



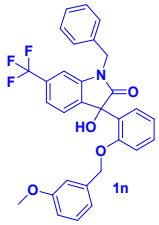
Compound 1k. 5-chloro-3-hydroxy-3-(2-((3-methoxybenzyl) oxy)phenyl)-1-methylindolin-2-one was prepared according to the Method C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (dd, J = 7.5, 1.5 Hz, 1H), 7.18–7.34 (m, 3H), 7.09 (t, J = 7.5 Hz, 1H), 7.02 (d, J = 2.0 Hz, 1H), 6.79–6.93 (m, 2H), 6.63 (d, J = 7.0 Hz, 1H), 6.56 (s, 1H), 6.45 (d, J = 8.5 Hz, 1H), 4.66–4.77 (m, 2H), 3.72–3.84 (m, 3H), 3.22 (s, 1H), 2.61 (s, 3H); LCMS (ESI) calcd for (M + H)$^+$ $C_{23}H_{20}ClNO_4$ 410.87; found 410.20.



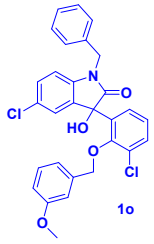
Compound 1l. 3-hydroxy-3-(2-((3-methoxybenzyl)oxy)phenyl)-1-methyl indolin-2-one was prepared according to the Method A. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.89 (dd, J = 7.5, 1.5 Hz, 1H), 7.81–7.97 (m, 1H), 7.14–7.29 (m, 2H), 7.13–7.30 (m, 1H), 7.00–7.09 (m, 1H), 7.05 (t, J = 7.5 Hz, 1H), 6.80–6.93 (m, 3H), 6.78–6.93 (m, 1H), 6.66–6.72 (m, 1H), 6.70 (d, J = 7.5 Hz, 1H), 6.50–6.55 (m, 1H), 6.53 (s, 1H), 6.48 (s, 1H), 6.45 (d, J = 7.6 Hz, 1H), 6.42–6.49 (m, 1H), 4.61–4.74 (m, 2H), 3.72 (s, 3H), 2.64 (s, 3H); LCMS (ESI) calcd for (M + H)$^+$ $C_{23}H_{21}NO_4$ 376.15;found 376.20.



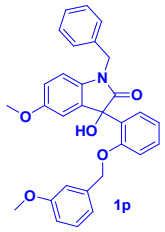
Compound 1m. 3-(2-((3,5-dimethoxybenzyl)oxy)phenyl)-3-hydroxy-1-methylindolin-2-one was prepared according to the Method C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.89 (d, J = 7.7 Hz, 1H), 7.27–7.21 (m, 2H), 7.05 (dt, J = 1.0, 7.5 Hz, 1H), 6.92–6.82 (m, 3H), 6.71 (d, J = 7.5 Hz, 1H), 6.50 (s, 1H), 6.42 (t, J = 2.3 Hz, 1H), 6.16 (d, J = 2.0 Hz, 2H), 4.70–4.60 (m, 2H), 3.71 (s, 6H), 2.73 (s, 3H); LCMS (ESI) calcd for (M + H)$^+$ $C_{24}H_{23}NO_5$ 406.45; found 406.45.



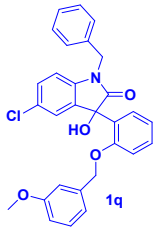
Compound 1n .1-benzyl-3-hydroxy-3-(2-((3-methoxybenzyl) oxy)phenyl)-6-(trifluoromethyl)indolin-2-one was prepared according to the Method C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (dd, J = 7.8, 1.3 Hz, 1H), 7.06–7.32 (m, 9H), 6.91 (dd, J = 8.3, 2.3 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 6.61 (d, J = 13.6 Hz, 2H), 6.52 (d, J = 7.5 Hz, 1H), 4.85 (d, J = 15.6 Hz, 1H), 4.63–4.71 (m, 2H), 3.77 (s, 3H), 3.61 (d, J = 16.1 Hz, 1H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ -62.6 (s, 3F); LCMS (ESI) calcd for (M + H)$^+$ $C_{30}H_{24}F_3NO_4$ 520.52; found 520.20.



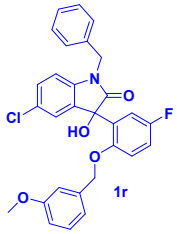
Compound 1o. 1-benzyl-5-chloro-3-(3-chloro-2-((3-methoxy benzyl)oxy) phenyl)-3-hydroxyindolin-2-one was prepared according to the Method D. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (br d, J = 8.0 Hz, 1H), 7.40 (dd, J = 8.0, 1.5 Hz, 1H), 7.06–7.30 (m, 8H), 6.90 (dd, J = 8.3, 2.3 Hz, 1H), 6.75–6.85 (m, 2H), 6.36 (d, J = 8.5 Hz, 1H), 5.05 (d, J = 11.5 Hz, 1H), 4.94 (d, J = 16.1 Hz, 1H), 4.26 (br d, J = 11.0 Hz, 1H), 3.82 (s, 3H), 3.55 (br d, J = 16.1 Hz, 1H); LCMS (ESI) calcd for (M +H)$^+$ $C_{29}H_{23}Cl_2NO_4$ 521.41; found 521.2.



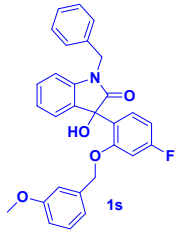
Compound 1p. 1-benzyl-3-hydroxy-5-methoxy-3-(2-((3-methoxybenzyl) oxy)phenyl)indolin-2-one was prepared according to the Method C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (br d, J = 7.5 Hz, 1H), 7.14–7.30 (m, 7H), 7.06 (t, J = 7.5 Hz, 1H), 6.80–6.92 (m, 2H), 6.58–6.71 (m, 4H), 6.39 (d, J = 8.5 Hz, 1H), 4.70–4.85 (m, 3H), 3.74–3.85 (m, 4H), 3.59–3.74 (m, 3H); LCMS (ESI) calcd for $(M + H)^+$ $C_{30}H_{27}NO_5$ 482.55; found 482.20.



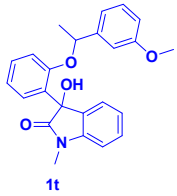
Compound 1q. 1-benzyl-5-chloro-3-hydroxy-3-(2-((3-methoxybenzyl) oxy) phenyl)indolin-2-one was prepared according to the Method C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90–7.95 (m, 1H), 7.12–7.37 (m, 11H), 7.07 (d, J = 2.0 Hz, 1H), 6.87–6.98 (m, 2H), 6.63–6.71 (m, 2H), 6.40 (d, J = 8.5 Hz, 1H), 4.88 (d, J = 16.1 Hz, 1H), 4.76 (s, 2H), 3.82 (s, 3H), 3.70 (d, J = 15.6 Hz, 1H), 3.32 (br s, 1H); LCMS (ESI) calcd for $(M + H)^+$ $C_{29}H_{24}ClNO_4$ 486.96; found 486.20.



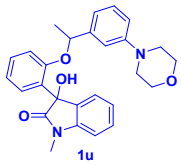
Compound 1r. 1-benzyl-5-chloro-3-(5-fluoro-2-((3-methoxybenzyl)oxy) phenyl)-3-hydroxyindolin-2-one was prepared according to the Method D. ^{1}H NMR (DMSO-d_6, 400 MHz) δ.66 (dd, J = 9.8, 3.3 Hz, 1H), 7.20–7.33 (m, 7H), 7.12 (td, J = 8.5, 3.0 Hz, 1H), 7.04 (s, 1H), 6.87–6.95 (m, 3H), 6.64 (d, J = 8.0 Hz, 1H), 6.54 (s, 1H), 6.43 (d, J = 7.5 Hz, 1H), 4.68–4.84 (m, 2H), 4.58–4.66 (m, 1H), 3.97 (d, J = 16.1 Hz, 1H), 3.69-3.77 (m, 3H); ^{19}F NMR (DMSO-d_6, 377 MHz) δ –123.3 (s, 1F); LCMS (ESI) calcd for $(M+H)^+$ $C_{29}H_{23}ClFNO_4$ 504.95; found 504.20.



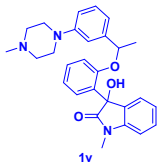
Compound 1s. 1-benzyl-3-(4-fluoro-2-((3-methoxybenzyl) oxy)phenyl)-3-hydroxyindolin-2-one was prepared according to the Method A. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.66 (dd, J = 9.8, 3.3 Hz, 1H), 7.20–7.33 (m, 7H), 7.12 (td, J = 8.5, 3.0 Hz, 1H), 7.04 (s, 1H), 6.87–6.95 (m, 3H), 6.64 (d, J = 8.0 Hz, 1H), 6.54 (s, 1H), 6.43 (d, J = 7.5 Hz, 1H), 4.68–4.84 (m, 2H), 4.58–4.66 (m, 1H), 3.97 (d, J = 16.1 Hz, 1H), 3.69-3.77 (m, 3H); ^{19}F NMR (DMSO-d_6, 376 MHz) δ 123.5 (s, 1F); LCMS (ESI) calcd for $(M + H)^+$ $C_{29}H_{24}FNO_4$ 470.51; found 470.20.



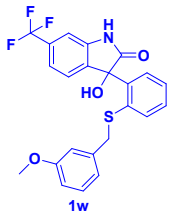
Compound 1t. Diastereomeric mixture (50 :50). 3-hydroxy-3-(2-(1-(3-methoxy phenyl)ethoxy)phenyl)-1-methylindolin-2-one was prepared according to the Method C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.87 (dd, J = 7.5, 1.5 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 6.90–7.10 (m, 5H), 6.75–6.87 (m, 4H), 6.54 (s, 1H), 6.48 (d, J = 8.0 Hz, 1H), 5.06 (q, J=6.0 Hz, 1H), 3.74 (s, 3H), 3.19 (s, 3H), 0.89 (d, J = 6.5 Hz, 3H); LCMS (ESI) calcd for $(M + H)^+$ $C_{23}H_{21}NO_4$ 390.45; found 390.20.



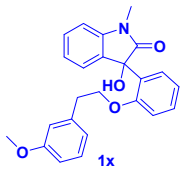
Compound 1u. 3-hydroxy-1-methyl-3-(2-(1-(3-morpholinophenyl)ethoxy) phenyl)indolin-2-one was prepared according to the Method C as a diastereomeric mixture in a ratio of 50:50. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.86 (ddd, J = 1.5, 4.3, 7.8 Hz, 1H), 7.37–7.22 (m, 1H), 7.16–7.03 (m, 2H), 7.00–6.83 (m, 4H), 6.81–6.74 (m, 1H), 6.72–6.60 (m, 1H), 6.54 (d, J = 8.2 Hz, 1H), 6.52–6.46 (m, 1H), 6.25 (s, 1H), 5.90 (d, J = 7.5 Hz, 1H), 5.13 (q, J = 6.0 Hz, 1H), 3.70 (td, J = 4.8, 16.1 Hz, 4H), 3.38–3.24 (m, 1H), 3.18 (d, J = 2.5 Hz, 3H), 3.15–3.07 (m, 2H), 2.93–2.77 (m, 2H), 1.18 (d, J = 6.5 Hz, 2H), 0.89 (d, J = 6.5 Hz, 1H); HRMS m/z (ESI) calcd. for $C_{27}H_{28}N_2O_4$ $[M+H]^+$ 445.2127; found 445.2109.



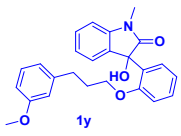
Compound 1v. 3-hydroxy-1-methyl-3-(2-(1-(3-(4-methylpiperazin-1-yl) phenyl)ethoxy)phenyl)indolin-2-one was prepared according to the Method C as a diastereomeric mixture in a ratio of 60:40. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88–7.82 (m, 1H), 7.61–7.41 (m, 1H), 7.38–7.26 (m, 1H), 7.11–7.02 (m, 2H), 7.00–6.73 (m, 4H), 6.67–6.57 (m, 1H), 6.56–6.45 (m, 1H), 6.24 (s, 1H), 5.86 (d, J = 7.5 Hz, 1H), 5.12 (q, J = 6.0 Hz, 1H), 3.22–3.07 (m, 4H), 2.95–2.77 (m, 3H), 2.73–2.52 (m, 1H), 2.46–2.26 (m, 4H), 2.20 (s, 3H), 1.90 (s, 1H), 1.61–1.37 (m, 1H), 1.34–1.07 (m, 3H), 0.93–0.83 (m, 1H), 0.83–0.66 (m, 1H); HRMS m/z (ESI) calcd. for $C_{28}H_{31}N_3O_3$ $[M+H]^+$ 458.2444; found 458.2435.



Compound 1w. 3-hydroxy-3-(2-((3-methoxybenzyl)thio) phenyl)-6-(trifluoromethyl)indolin-2-one was prepared according to the Method B. ^{1}H NMR (DMSO-d_6, 400MHz) δ (7.62 (d, J = 8.0 Hz, 1H), 7.54 (s, 2H), 7.13–7.32 (m, 3H), 6.99–7.09 (m, 2H), 6.70–6.98 (m, 6H), 6.55 (d, J = 7.5 Hz, 1H), 6.46-6.52 (m, 1H), 6.34–6.44 (m, 1H), 6.21 (s, 1H), 6.14 (d, J = 7.5 Hz, 1H), 4.07 (s, 1H), 3.27–3.35 (s, 3H); ^{19}F NMR (DMSO-d_6, 376MHz) δ -61.08 (s, 3F); LCMS (ESI) calcd for $(M-1)^+$ $C_{23}H_{18}F_3NO_3S$ 444.46; found 444.42.

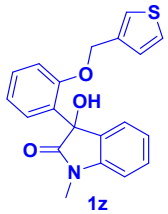


Compound 1x. 3-hydroxy-3-(2-(3-methoxyphenethoxy) phenyl)-1-methy lindolin-2-one was prepared according to the Method C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (dd, J = 8.0, 1.5 Hz, 1H), 7.21–7.39 (m, 4H), 7.03–7.17 (m, 3H), 6.78–6.88 (m, 3H), 6.65–6.77 (m, 2H), 4.11 (td, J = 9.0, 6.5 Hz, 1H), 3.88–3.99 (m, 1H), 3.81 (s, 3H), 3.38–3.52 (m, 1H), 3.25 (s, 3H), 2.79–2.89 (m, 1H), 2.71 (ddd, J = 14.0, 8.5, 6.0 Hz, 1H); LCMS (ESI) calcd for $(M-18)^+$ $C_{23}H_{21}NO_4$ 372.45; found 372.20.

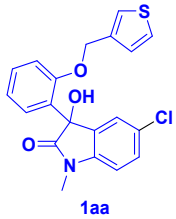


Compound 1y. 3-hydroxy-3-(2-(3-(3-methoxyphenyl)propoxy) phenyl)-1-methylindolin-2-one was prepared according to the Method C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.91 (dd, J = 1.8, 7.8 Hz, 1H), 7.26 (td, J = 7.7, 11.7 Hz, 1H), 7.26 (td, J = 7.9, 11.3 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.05 (t, J = 7.3 Hz, 1H), 7.00 (d, J = 7.5 Hz, 1H), 6.95–6.90 (m, 1H), 6.88–6.85 (m, 1H),

6.78–6.71 (m, 2H), 6.58–6.52 (m, 3H), 3.67–3.63 (m, 1H), 3.68 (s, 4H), 3.47 (td, J = 6.5, 9.2 Hz, 1H), 3.35 (s, 1H), 3.17 (s, 3H), 2.35–2.30 (m, 1H), 2.25–2.19 (m, 1H), 1.63–1.55 (m, 2H); HRMS m/z (ESI) calcd. for $C_{25}H_{25}NO_4$ $[M+H]^+$ 404.1862; found 404.1837.



Compound 1z. 3-hydroxy-1-methyl-3-(2-(thiophen-3-ylmethoxy)phenyl) indolin-2-one was prepared according to the Method D. ^{1}H NMR (CD_3OD, 400 MHz) δ 7.97–8.02 (m, 2H), 7.28–7.38 (m, 5H), 6.88–7.16 (m, 10H), 6.76 (d, J = 8.0 Hz, 2H), 6.61–6.71 (m, 2H), 4.75–4.85 (m, 1H), 4.58–4.73 (m, 1H), 2.67–2.74 (m, 3H); LCMS (ESI) calcd for $(M + H)^+$ $C_{23}H_{21}NO_4$ 352.42; found 352.40.



Compound 1aa. 5-chloro-3-hydroxy-1-methyl-3-(2-(thiophen-3-yl methoxy)phenyl)indolin-2-one was prepared according to the Method D. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (d, J = 7.9 Hz, 1H), 7.21–7.36 (m, 4H), 6.99–7.14 (m, 3H), 6.88 (dd, J = 8.0, 1.0 Hz, 1H), 6.75 (dd, J = 5.0, 1.5 Hz, 1H), 6.53 (d, J = 8.0 Hz, 1H), 4.78–4.86 (m, 1H), 4.70–4.76 (m, 1H), 3.15 (s, 1H), 2.62–2.70 (m, 3H); LCMS (ESI) calcd for $(M +2H)^+$ $C_{23}H_{21}NO_4$ 391.45, found 391.20.

Compound 5. 3-hydroxy-1-methyl-3-(2-((3-methylbenzyl) oxy)phenyl) indolin-2-one was prepared according to the Method C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.89 (dd, J = 1.7, 7.8 Hz, 1H), 7.31–7.23 (m, 2H), 7.20–6.97 (m, 4H), 6.95–6.88 (m, 2H), 6.83 (dd, J = 1.3, 7.2 Hz, 1H), 6.74–6.67 (m, 2H), 6.60 (s, 1H), 6.48 (s, 1H), 5.88 (s, 1H), 5.76 (s, 1H), 4.71–4.60 (m, 2H), 3.31–3.14 (m, 2H), 3.10 (s, 1H), 2.68 (s, 1H), 2.59 (s, 3H), 2.56–2.52 (m, 1H), 2.45–2.31 (m, 1H), 2.27 (s, 3H); LCMS (ESI) calcd for $(M + H)^+$ $C_{23}H_{21}NO_3$ 360.43; found 360.50.

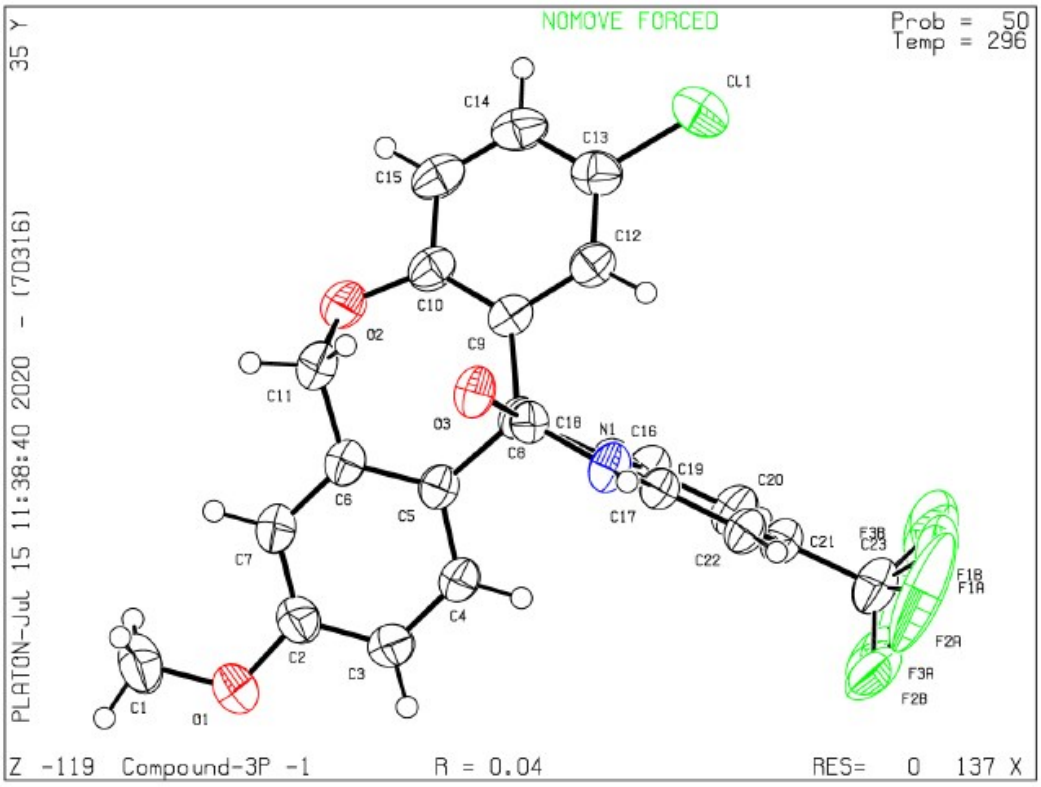
3. Crystal structure data and refinement details for compound-3f

CCDC deposition number	CCDC-2016549
Empirical formula	$C_{23}H_{15}ClF_3NO_3$
Formula weight	445.81
Temperature/K	296.15
Crystal system	triclinic

Space group	P-1
a/Å	7.8400(4)
b/Å	11.8374(6)
c/Å	11.9176(6)
α/°	111.955(2)
β/°	97.653(2)
γ/°	98.734(2)
Volume/Å^3	991.91(9)
Z	2
ρ_{calc}g/cm^3	1.493
μ/mm^{-1}	2.197
F(000)	456.0
Crystal size/mm^3	0.25 × 0.15 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.18 to 130.38
Index ranges	-9 ≤ h ≤ 9, -13 ≤ k ≤ 13, -14 ≤ l ≤ 14
Reflections collected	28674
Independent reflections	3296 [R_{int} = 0.0485, R_{sigma} = 0.0239]
Data/restraints/parameters	3296/0/308
Goodness-of-fit on F^2	1.096
Final R indexes [I>=2σ (I)]	R_1 = 0.0437, wR_2 = 0.1213
Final R indexes [all data]	R_1 = 0.0452, wR_2 = 0.1233
Largest diff. peak/hole / e Å^{-3}	0.30/-0.27

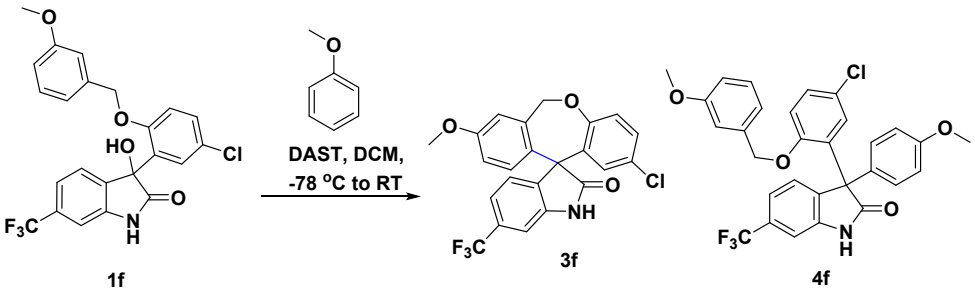
Experimental

Single crystals of Compound-3f {2-Chloro-8-methoxy-6'-(trifluoromethyl)-6H-spiro[dibenzo-[b,e]oxepine-11,3'-indolin]-2'-one} were obtained from methanol solution by solvent evaporation at room temperature. A suitable block shaped crystal was mounted on a nylon cryoloop using paratone oil. Data were collected on a Bruker SMART APEX-II diffractometer, equipped with Apex II area detector, at room temperature (~296 K). Initial structure solution was achieved with 'Intrinsic Phasing' method in Bruker APEX2 software suite. Using Olex2 [5], further structure refinements were performed with the ShelXL [6, 7] refinement package using Least Squares minimization.



ORTEP diagram of compound-3f with 50% probability ellipsoids (notice orientational disorder of the trifluoro methyl group; figure taken from checkCIF/PLATON report).

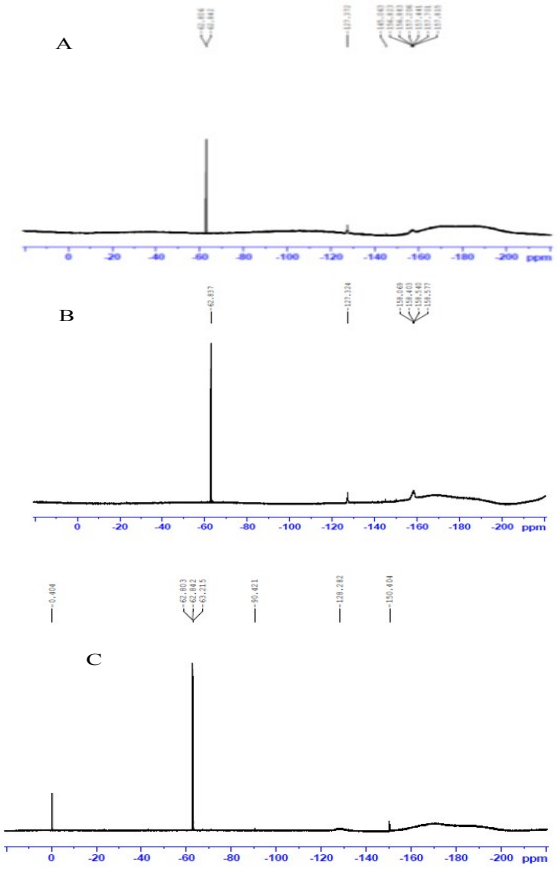
4. Cross over and control experiments



To support the derived mechanism, we have studied a cross over experiment by adding an equivalent of anisole to **1f** to see if the product **4f** is forming by intermolecular nucleophilic substitution. Interestingly, under the given reaction conditions, only the formation of **3f** was observed exclusively and not the product **4f**. This study clearly indicates that the intramolecular FC-Cyclization is preferred under this condition over intermolecular nucleophilic substitution, which supports our proposed plausible mechanism. In non-competitive environment, the nucleophilic substitution is also possible as explained in the potential application of the main manuscript.

In addition, we have performed the control experiment for the conversion **1f** to **3f** under standard reaction conditions by monitoring the reaction every 10 mins interval using ^{1}H-NMR, ^{19}F-NMR and LCMS studies. Since the reaction temperature was −78 °C, we were not able to see the mass for the

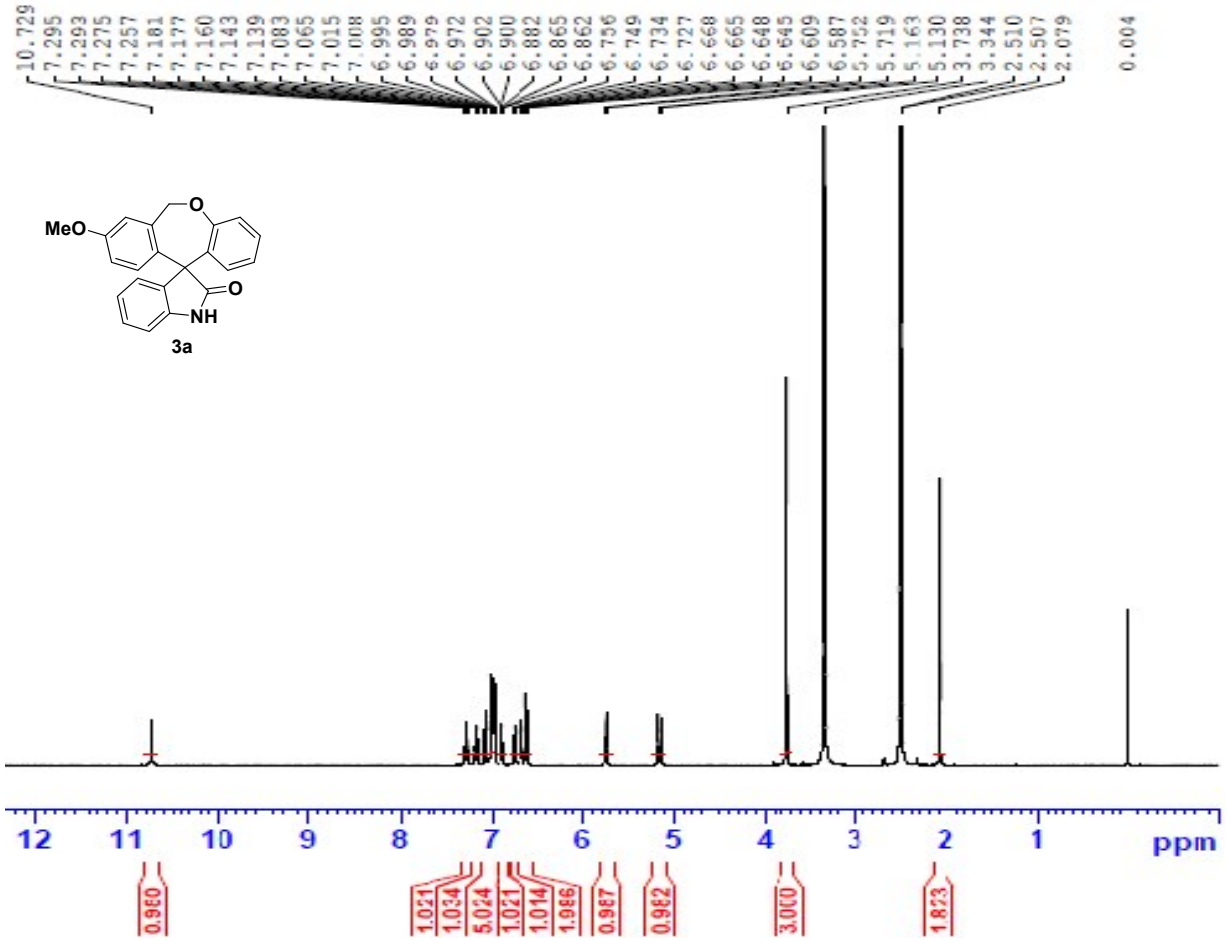
possible intermediates/additives by LCMS/^{1}H-NMR, which normally operates at higher temperature. However, ^{19}F-NMR studies in DCM show some interesting observations, which supports our plausible mechanism. The Signal at –127 ppm could be attributed to F^- from HF, liberated from DAST on interaction with free hydroxyl in the substrate. It clearly indicates the generation of HF during the course of the reaction and since DCM is a non-coordinating solvent, the HF forms strong hydrogen-bond with the carbonyl oxygen of the intermediate C, which in turn makes the adjacent carbon center highly electrophilic in nature. So, before the fluoride ion could attack this position the intramolecular Friedel Craft reaction precedes to form compound **3f**. After completion of the reaction (30 minutes), the signal at –127 ppm disappeared and a new peak appeared at –0.4 ppm [9] due to the formation of $CFCl_3$, from the interaction of F^- with the traces of CD_2Cl_2 in the NMR solvent, which is reported in the literature [10].

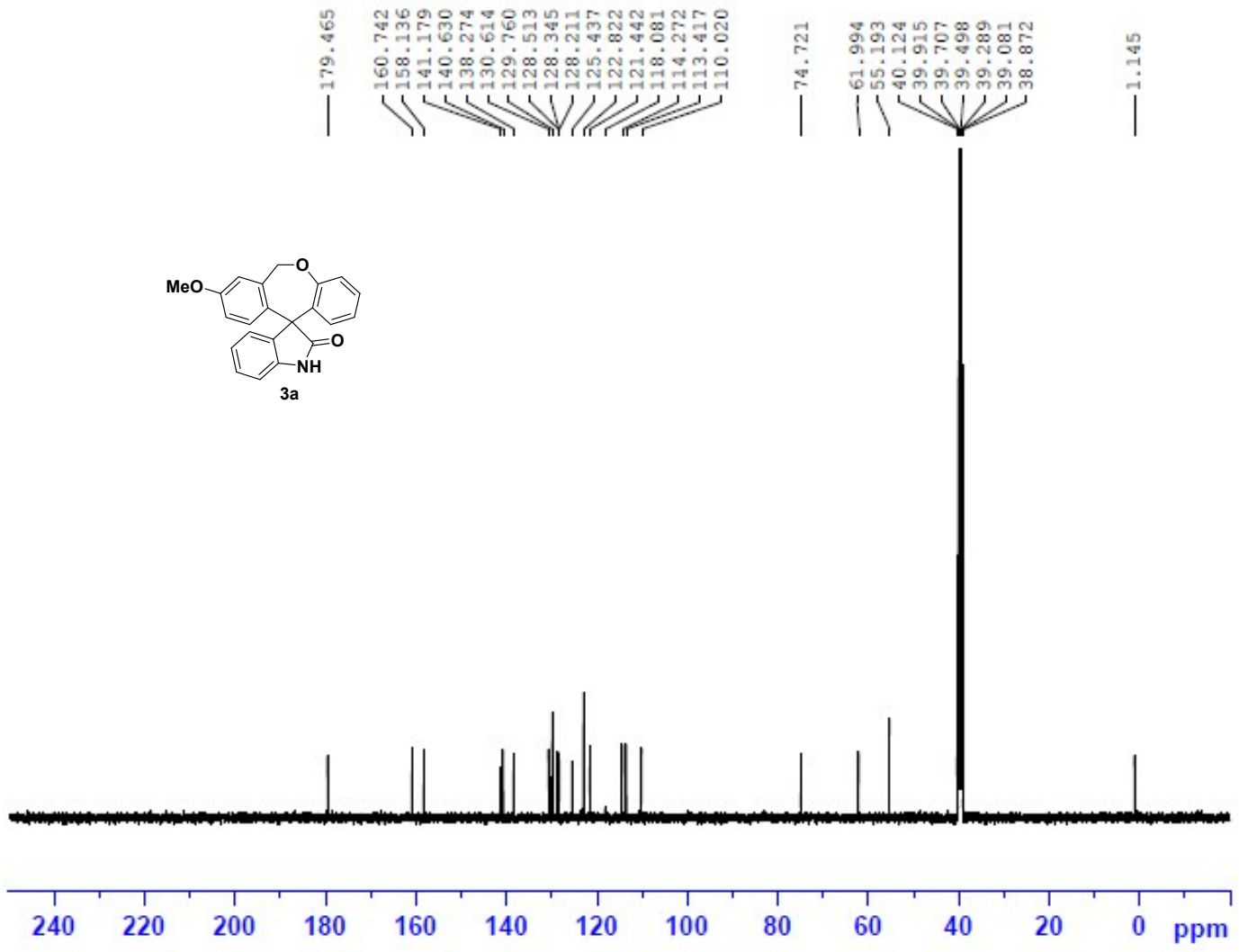


^{19}F-NMR monitoring of the reaction (A) 10 mins (B) in 20 mins (C) in 30 mins

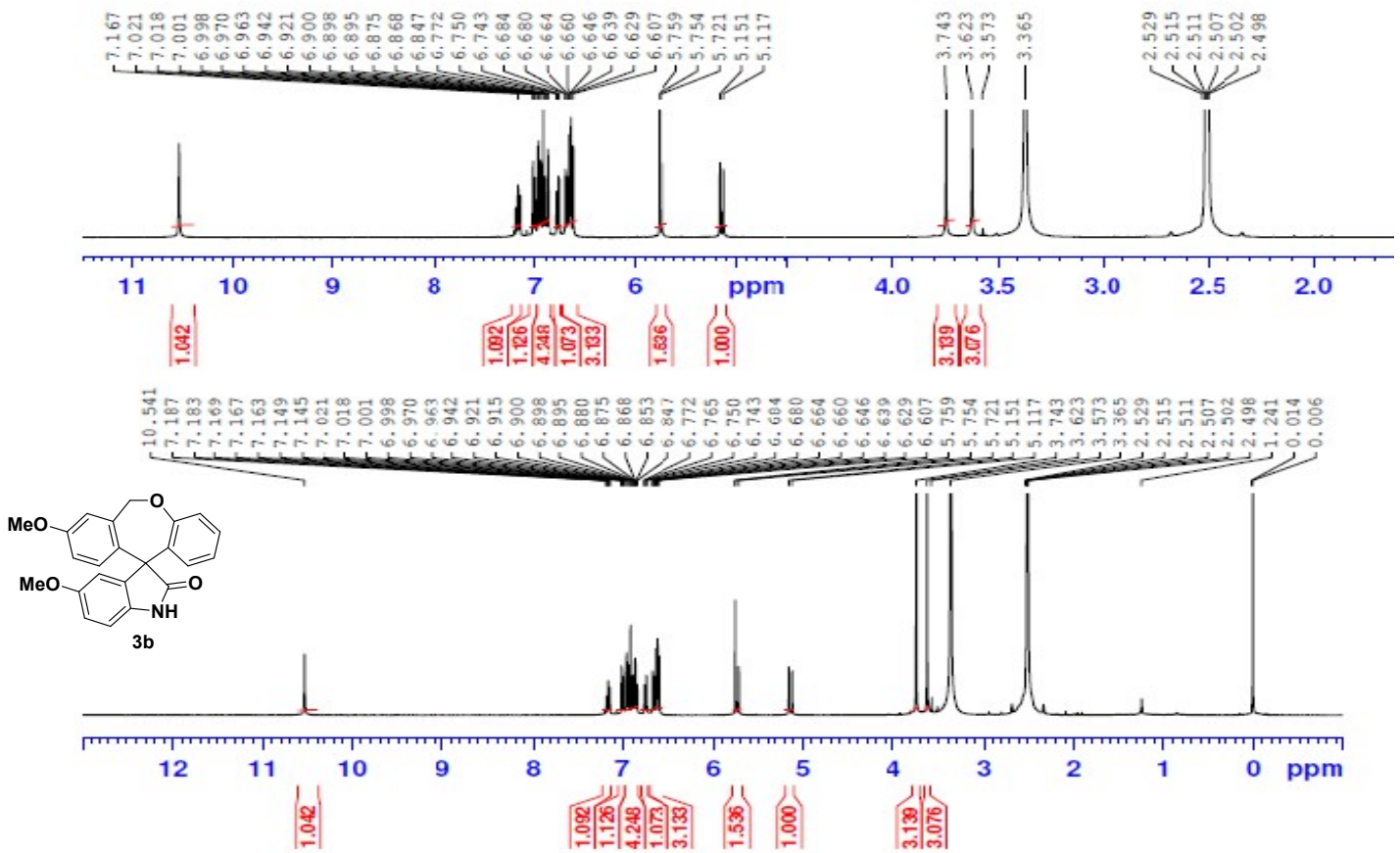
5. **Spectral data for the final compounds (3a to 3aa).**

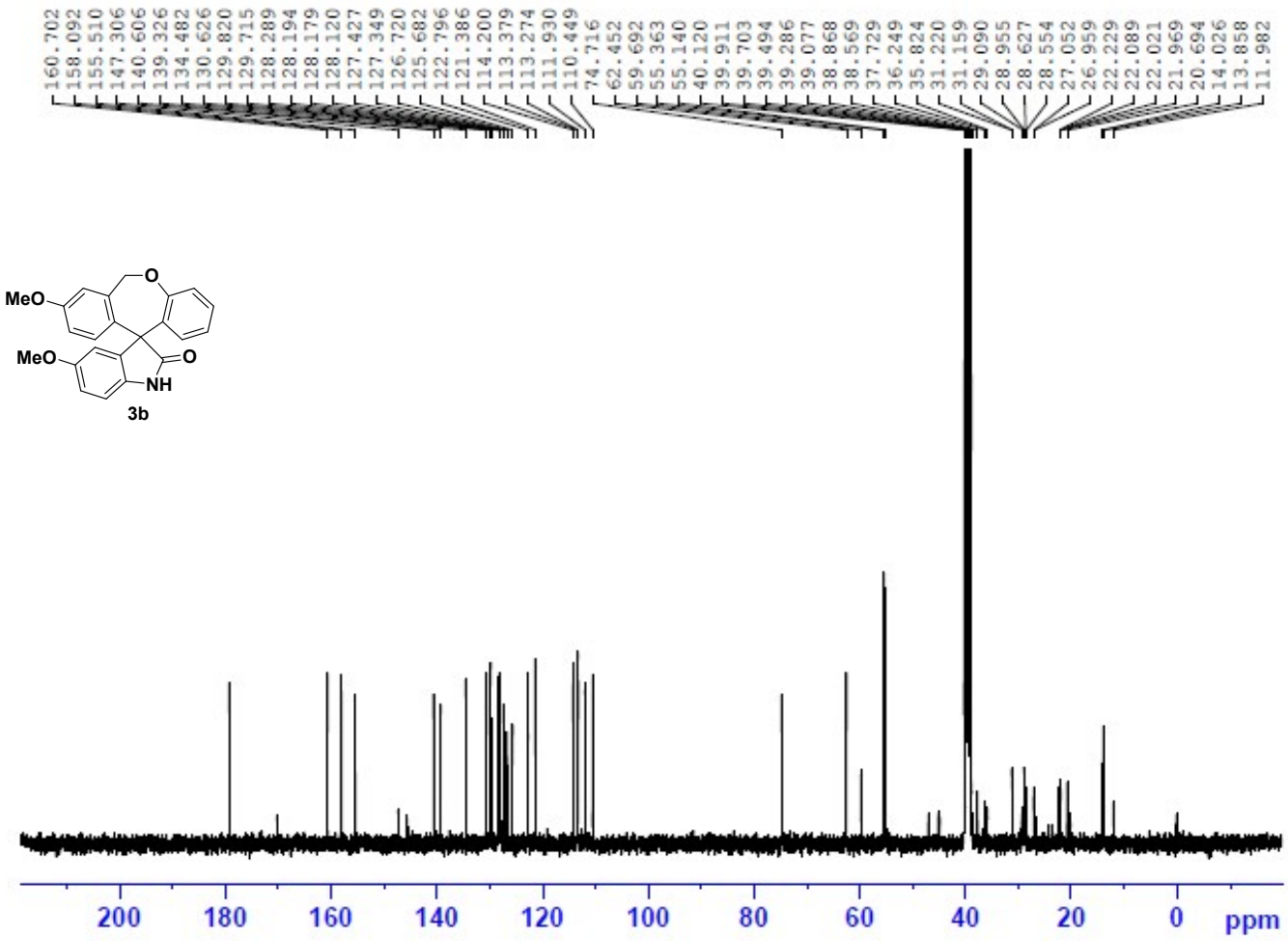
^{1}H and ^{13}C – NMR Data for 3a



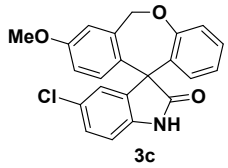

179.465
160.742
158.136
141.179
140.630
138.274
130.614
129.760
128.513
128.345
128.211
125.437
122.822
121.442
118.081
114.272
113.417
110.020
74.721
61.994
55.193
40.124
39.915
39.707
39.498
39.289
39.081
38.872
1.145
MeO
O
O
NH
3a
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

^{1}H and ^{13}C – NMR Data for 3b

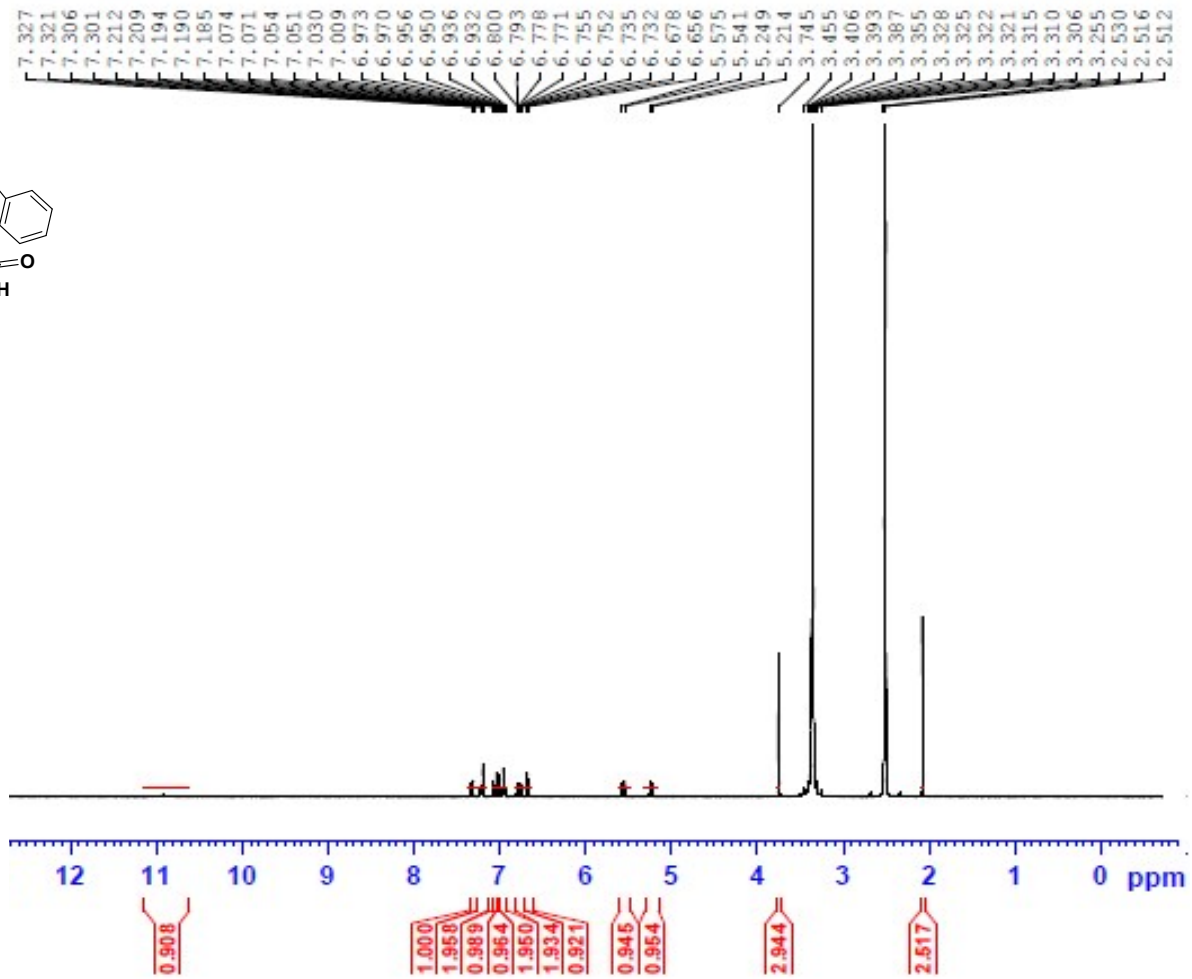


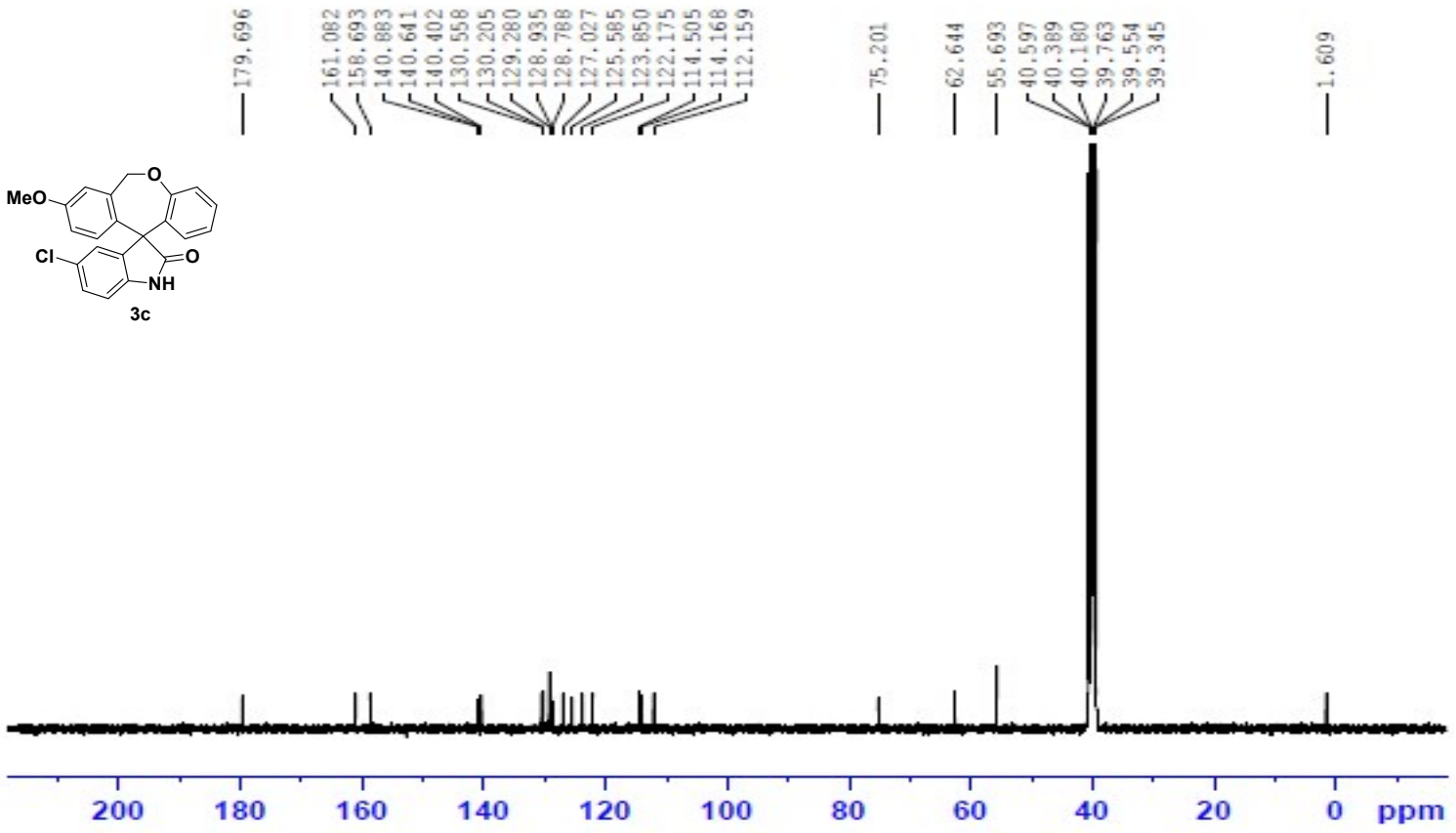

160.702
158.092
155.510
147.306
140.606
139.326
134.482
130.626
129.820
129.715
128.289
128.194
128.179
128.120
127.427
127.349
126.720
125.682
122.796
121.386
114.200
113.379
113.274
111.930
110.449
74.716
62.452
59.692
55.363
55.140
40.120
39.911
39.703
39.494
39.286
39.077
38.868
38.569
37.729
36.249
35.824
31.220
31.159
29.090
28.955
28.627
28.554
27.052
26.959
22.229
22.089
22.021
21.969
20.694
14.026
13.858
11.982
MeO
MeO
O
O
NH
3b
200
180
160
140
120
100
80
60
40
20
0
ppm

^{1}H and ^{13}C – NMR Data for 3c

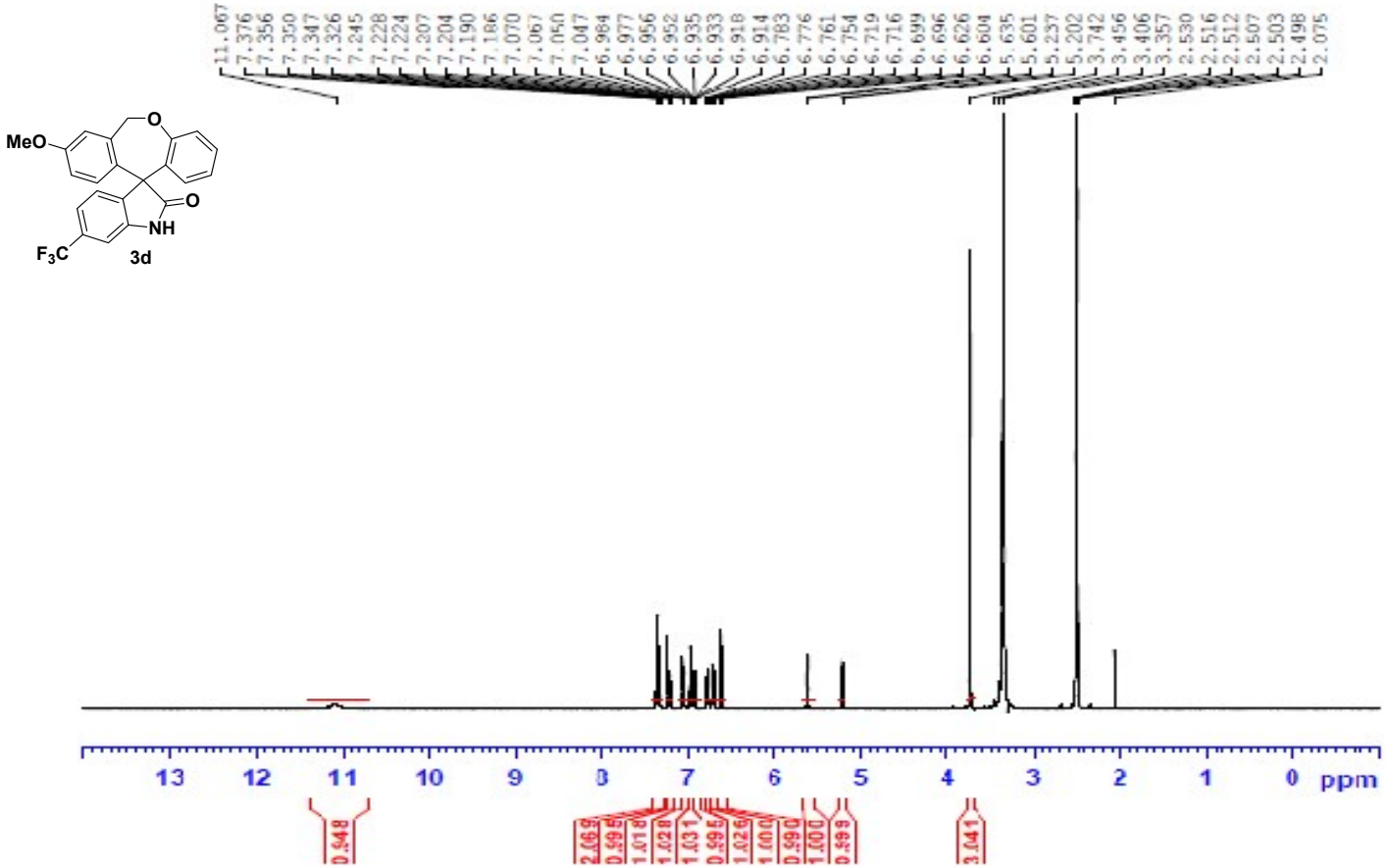


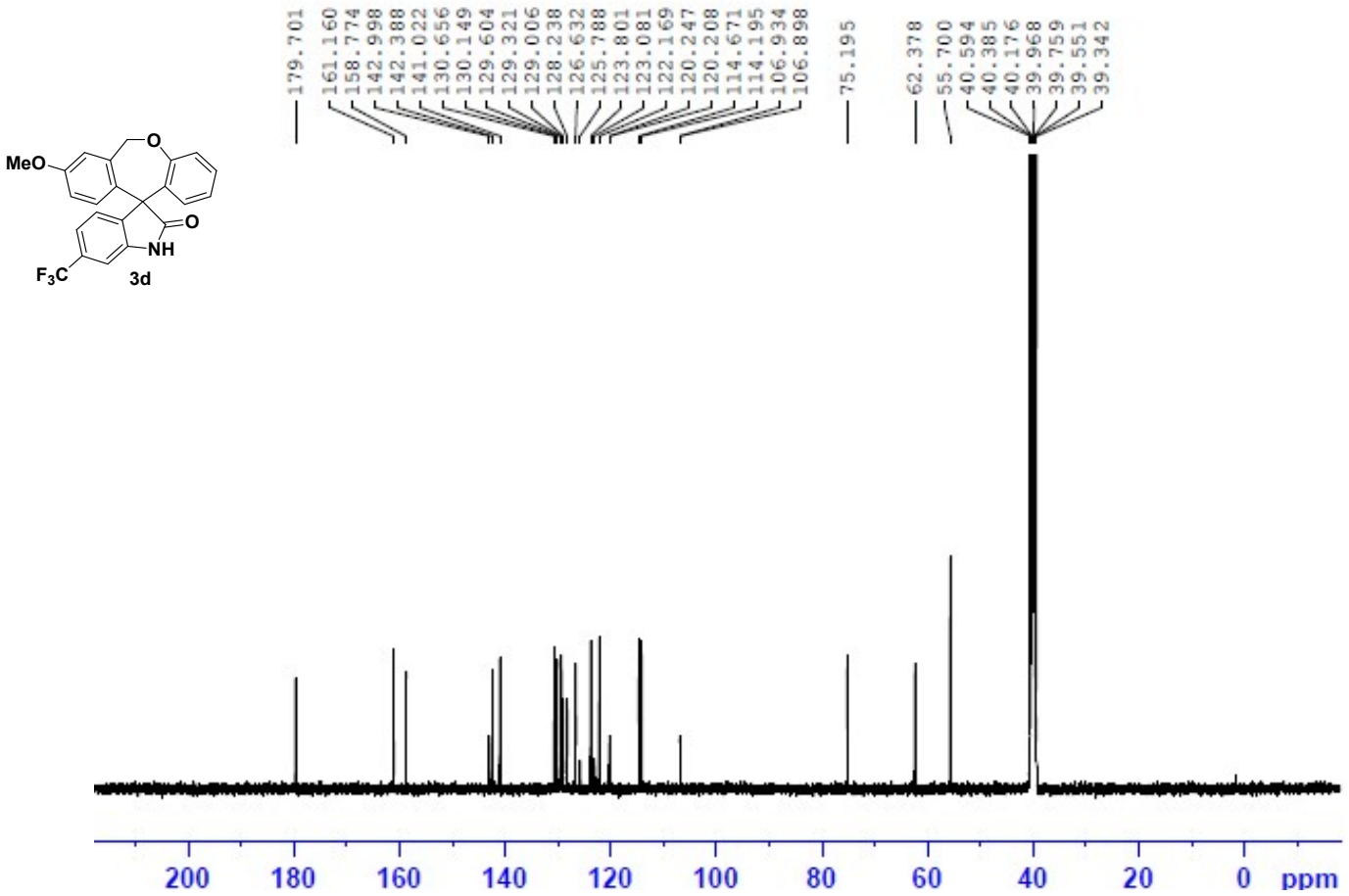
3c

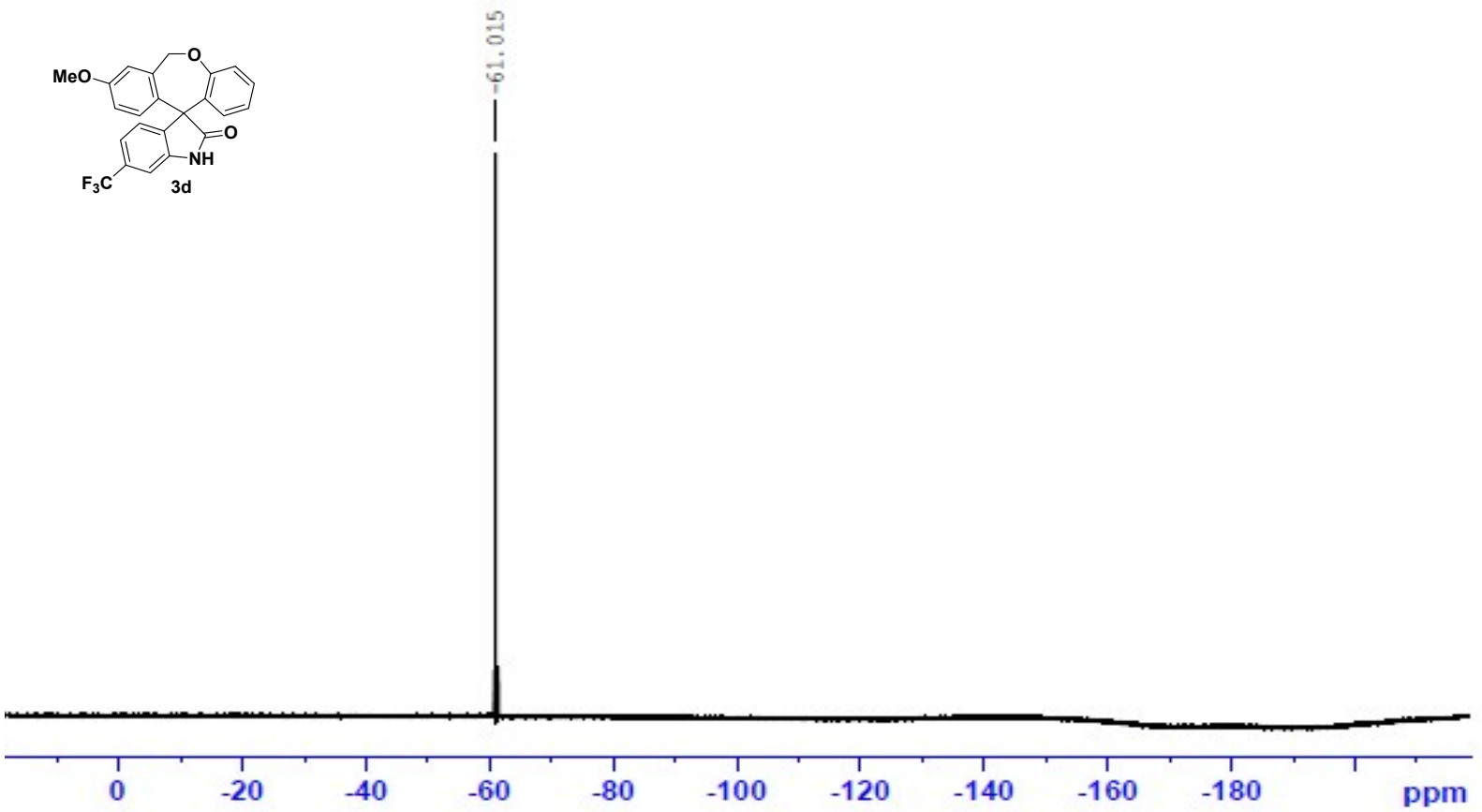



179.696
161.082
158.693
140.883
140.641
140.402
130.558
130.205
129.280
128.935
128.788
127.027
125.585
123.850
122.175
114.505
114.168
112.159
75.201
62.644
55.693
40.597
40.389
40.180
39.763
39.554
39.345
1.609
MeO
O
Cl
O
NH
3c
200
180
160
140
120
100
80
60
40
20
0
ppm

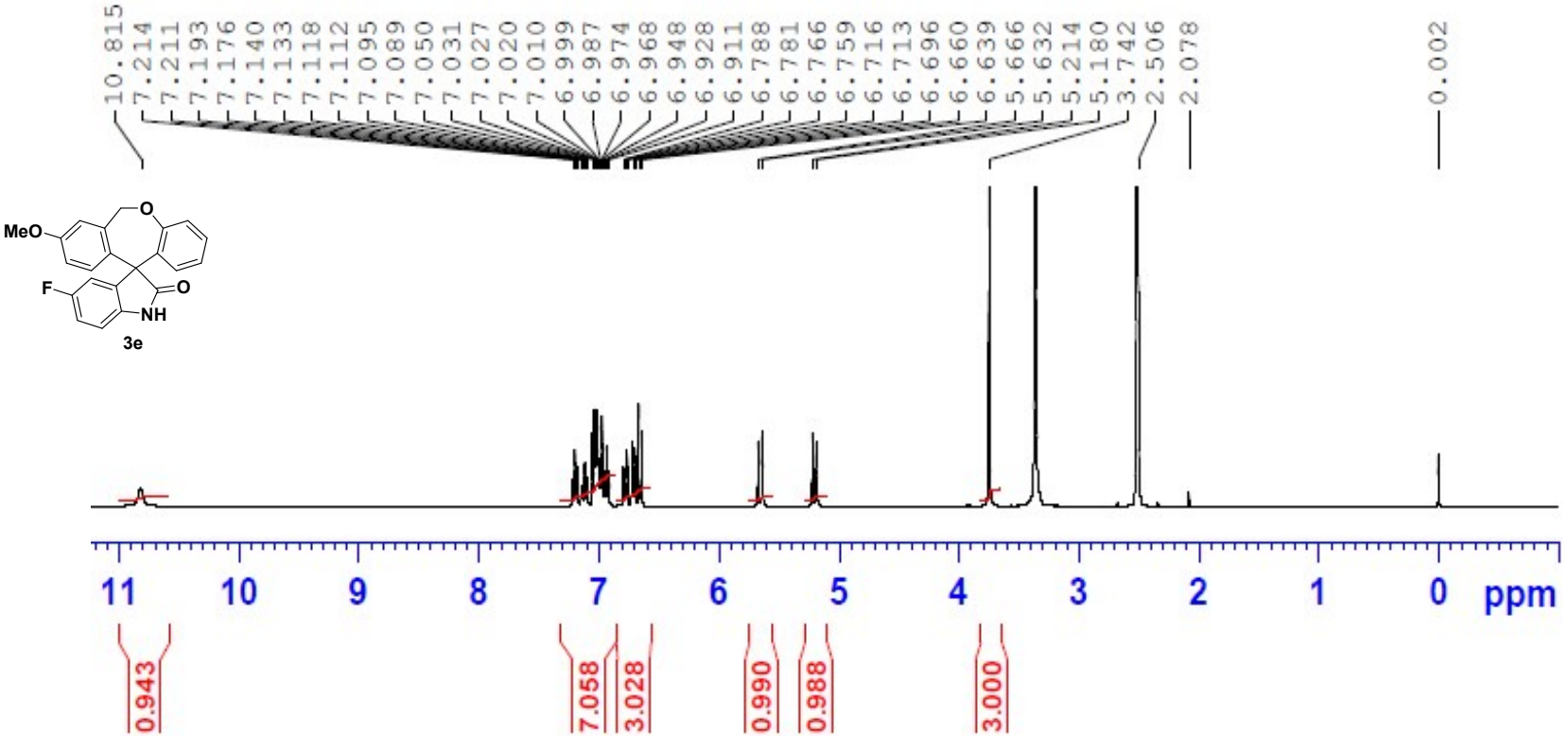
^{1}H ,^{13}C & ^{19}F– NMR Data for 3d

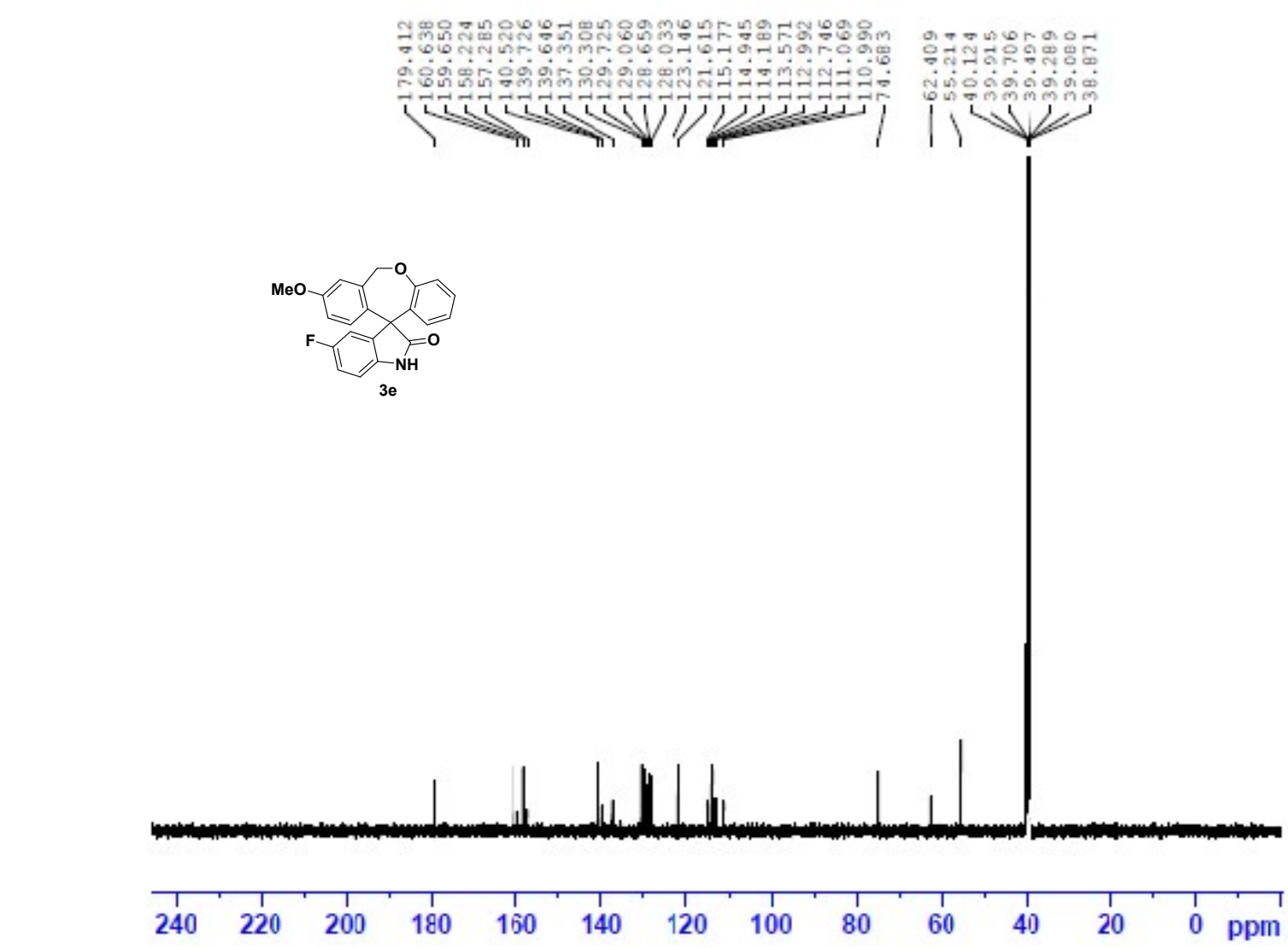


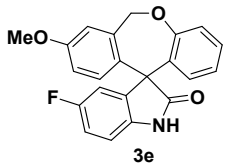

179.701
161.160
158.774
142.998
142.388
141.022
130.656
130.149
129.604
129.321
129.006
128.238
126.632
125.788
123.801
123.081
122.169
120.247
120.208
114.671
114.195
106.934
106.898
75.195
62.378
55.700
40.594
40.385
40.176
39.968
39.759
39.551
39.342
MeO
O
O
NH
F3C
3d
200
180
160
140
120
100
80
60
40
20
0
ppm


MeO
O
O
NH
F3C
3d
-61.015
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

H ,^{13}C & ^{19}F– NMR Data for 3e.

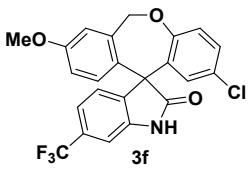


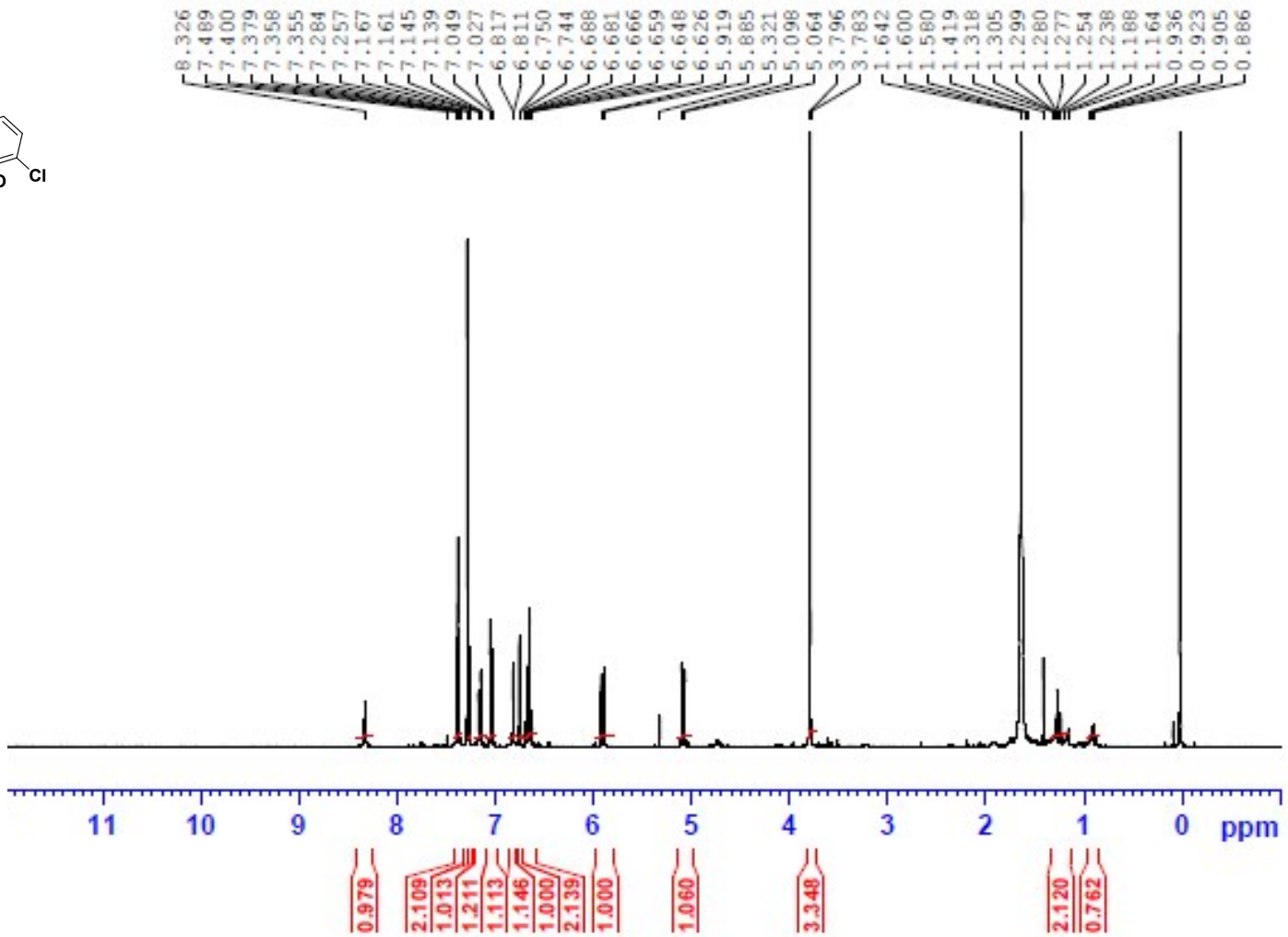

179.412
160.638
159.650
158.224
157.285
140.520
139.726
139.646
137.351
130.308
129.725
129.060
128.659
128.033
123.146
121.615
115.177
114.945
114.189
113.571
112.992
112.746
111.069
110.990
74.683
62.409
55.214
40.124
39.915
39.706
39.497
39.289
39.080
38.871
MeO
O
F
O
NH
3e
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

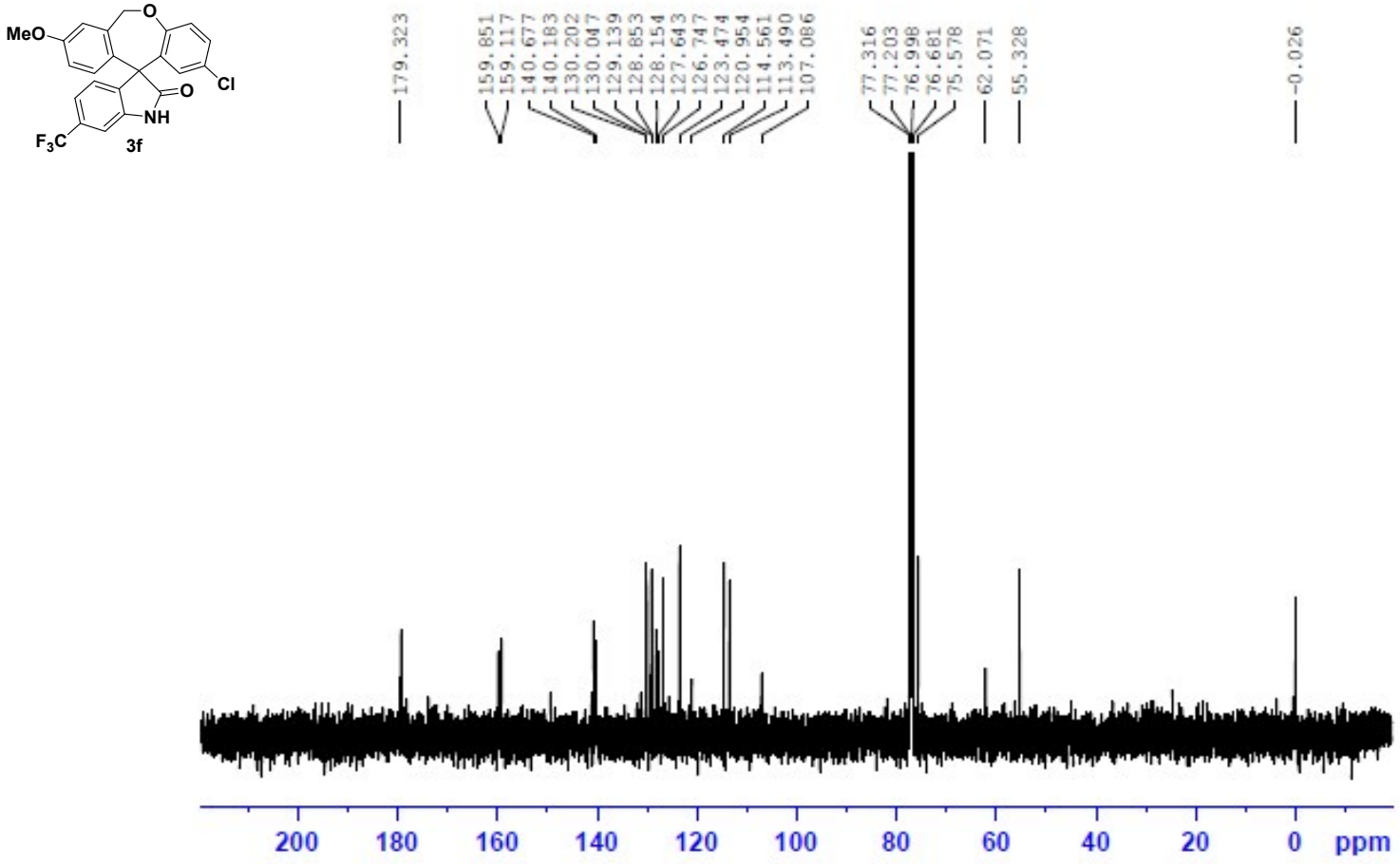


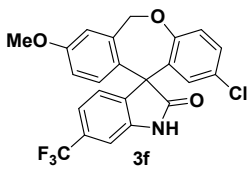
3e

^{1}H ,^{13}C & ^{19}F– NMR Data for 3f



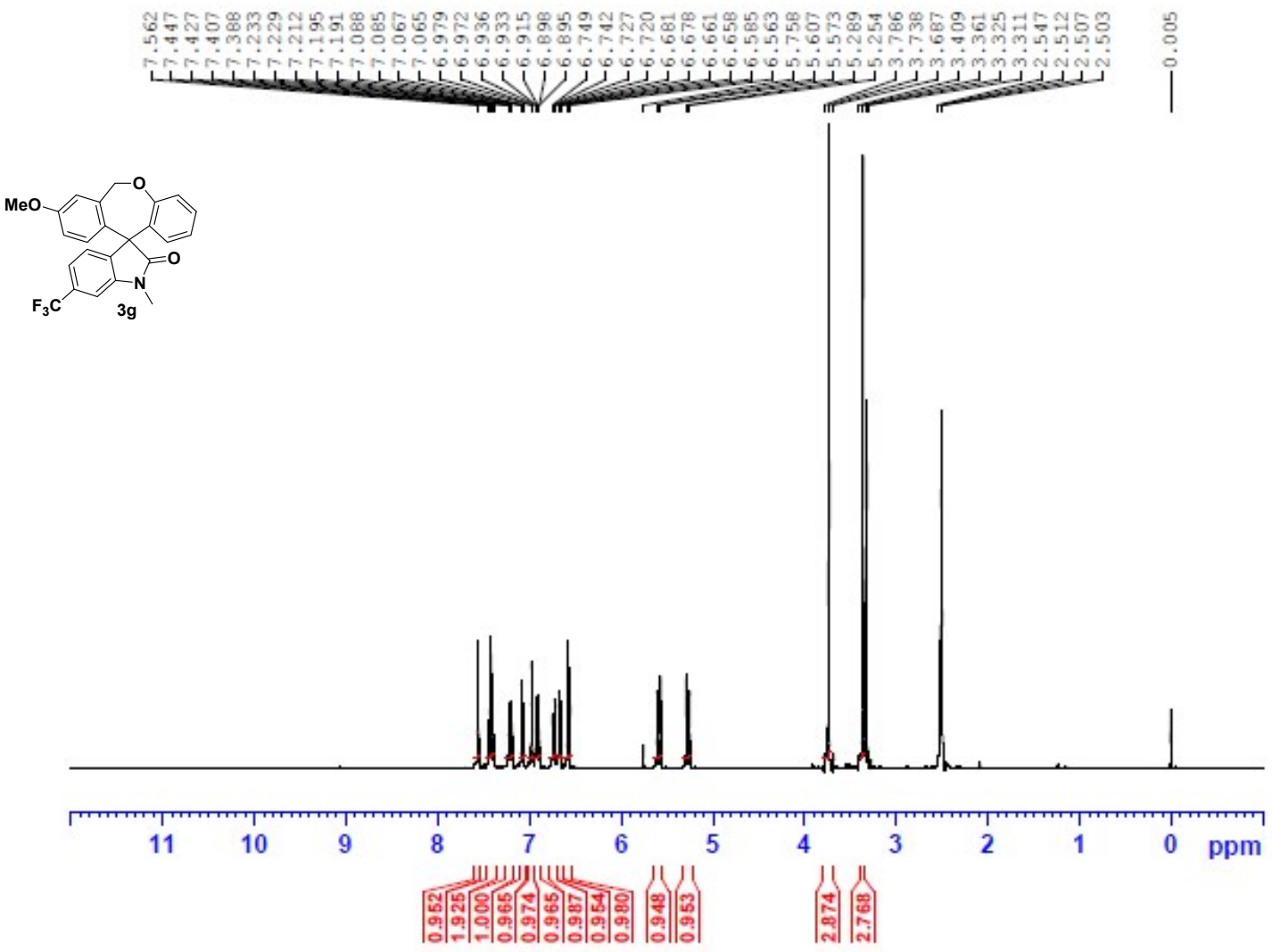


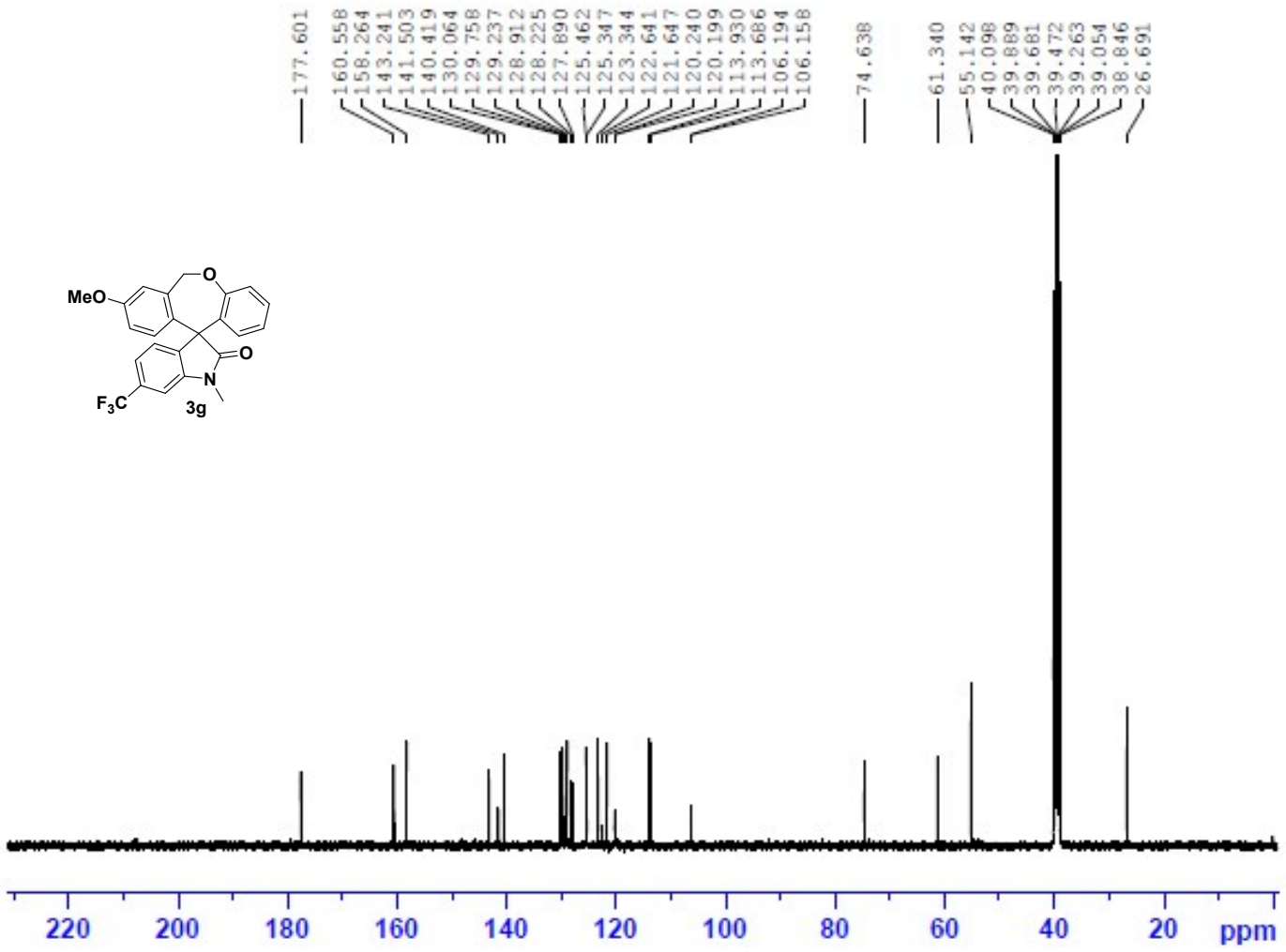

MeO
O
Cl
O
NH
F3C
3f
179.323
159.851
159.117
140.677
140.183
130.202
130.047
129.139
128.853
128.154
127.643
126.747
123.474
120.954
114.561
113.490
107.086
77.316
77.203
76.998
76.681
75.578
62.071
55.328
-0.026
200
180
160
140
120
100
80
60
40
20
0
ppm

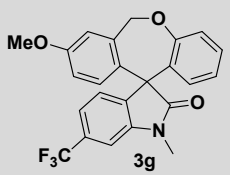


3f

^{1}H ,^{13}C & ^{19}F– NMR Data for 3g

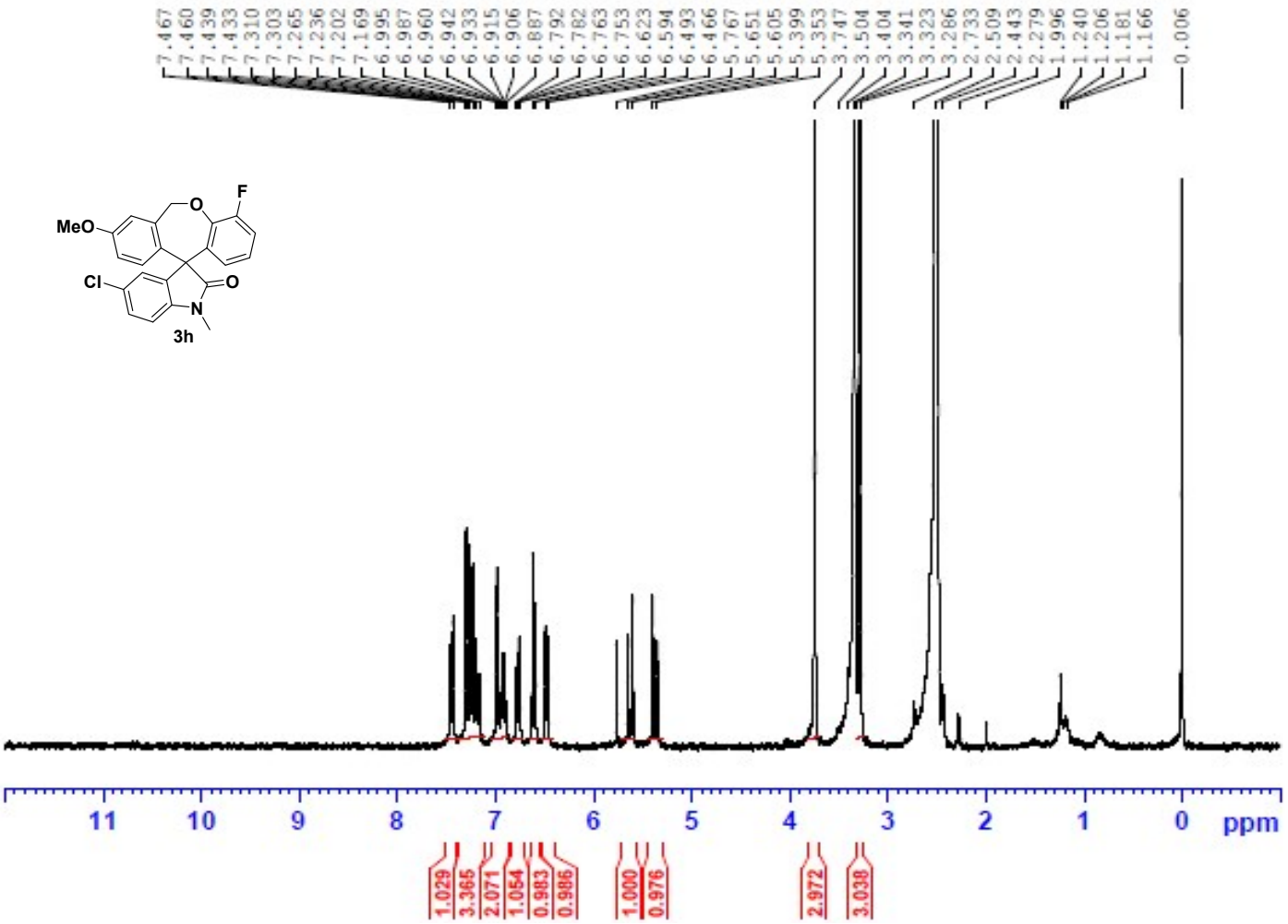


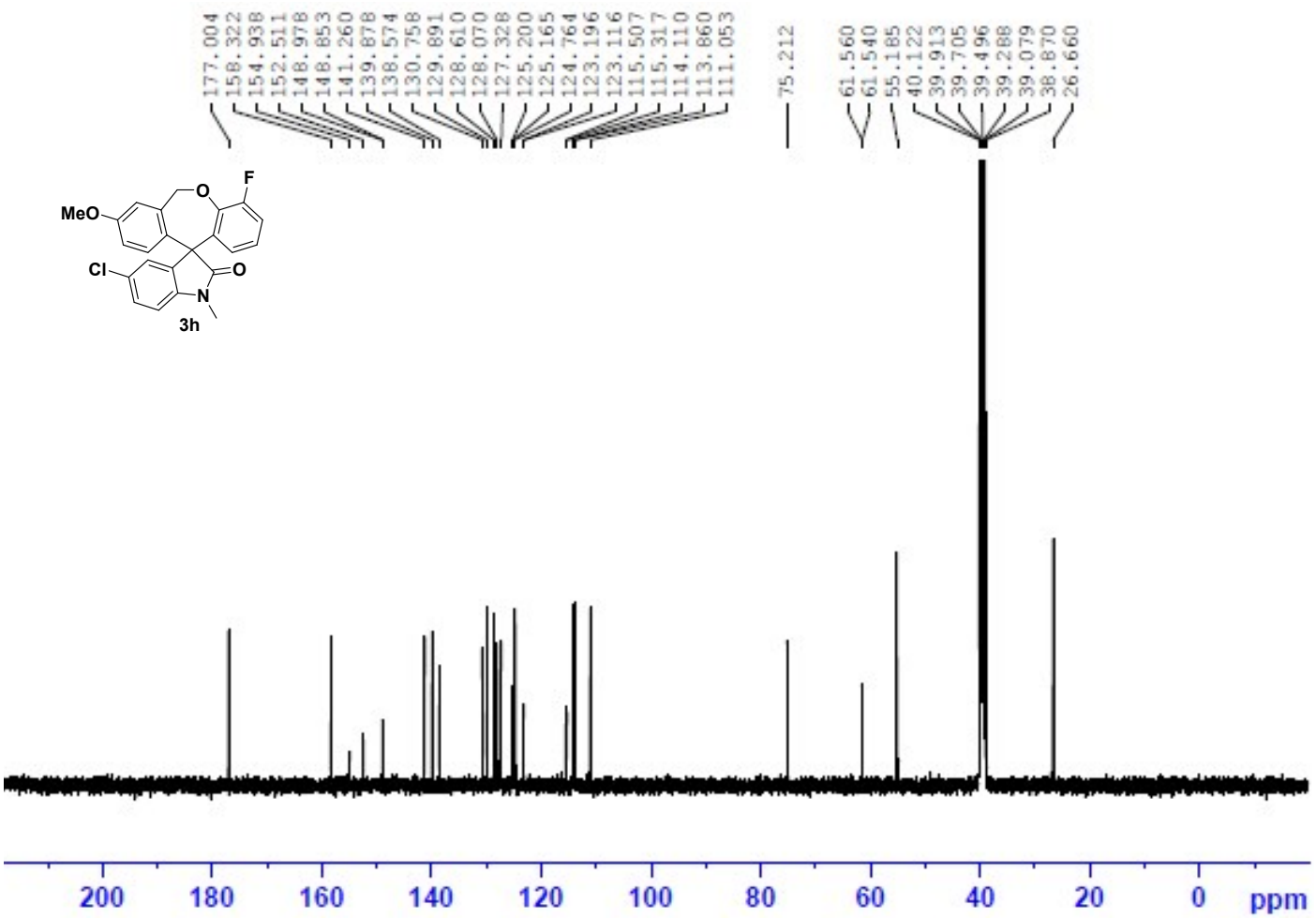

177.601
160.558
158.264
143.241
141.503
140.419
130.064
129.758
129.237
128.912
128.225
127.890
125.462
125.347
123.344
122.641
121.647
120.240
120.199
113.930
113.686
106.194
106.158
74.638
61.340
55.142
40.098
39.889
39.681
39.472
39.263
39.054
38.846
26.691
MeO
O
O
N
F3C
3g
220
200
180
160
140
120
100
80
60
40
20
ppm

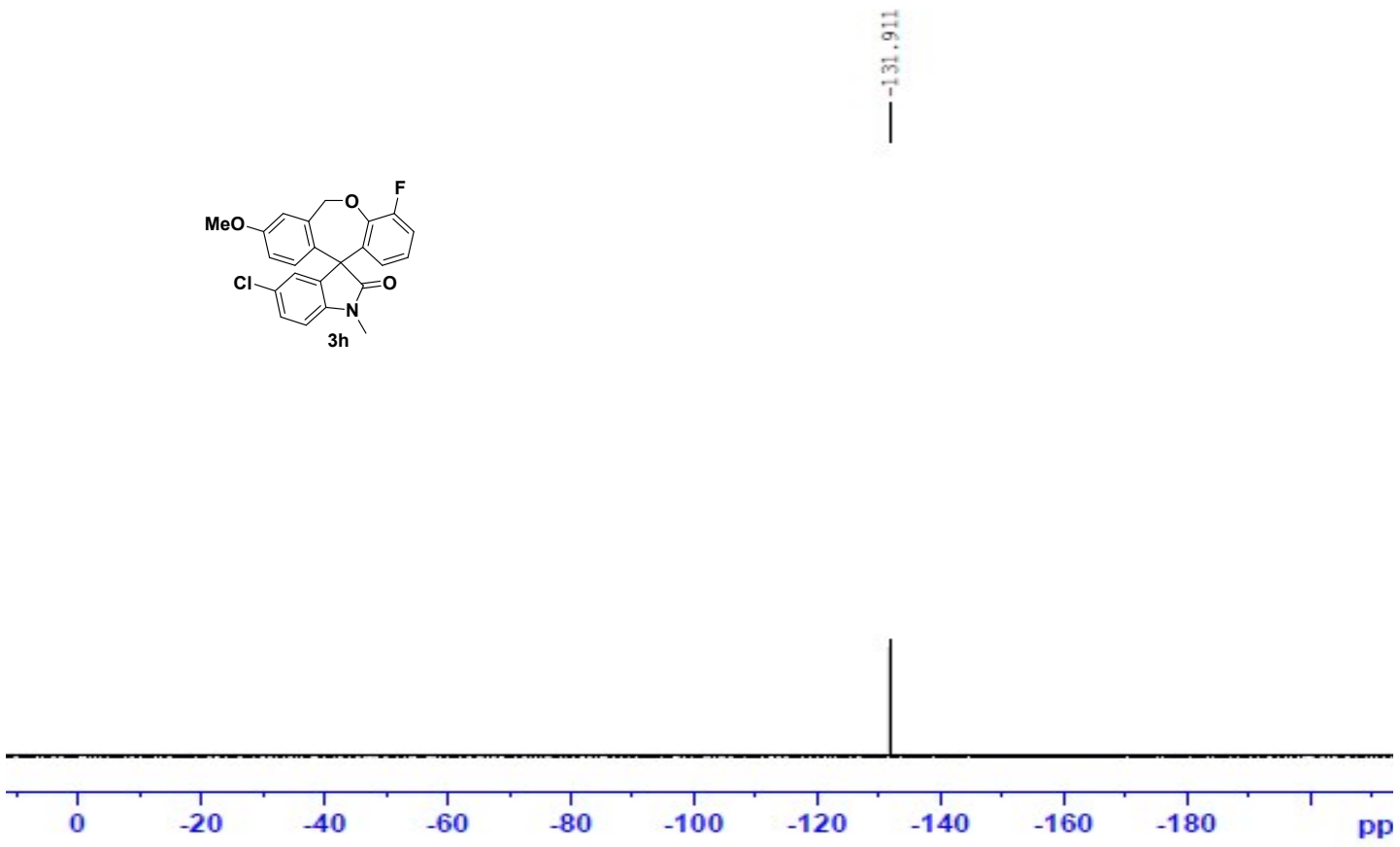


3g

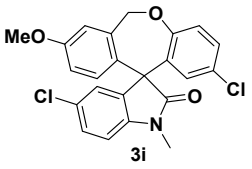
^{1}H ,^{13}C & ^{19}F– NMR Data for 3h

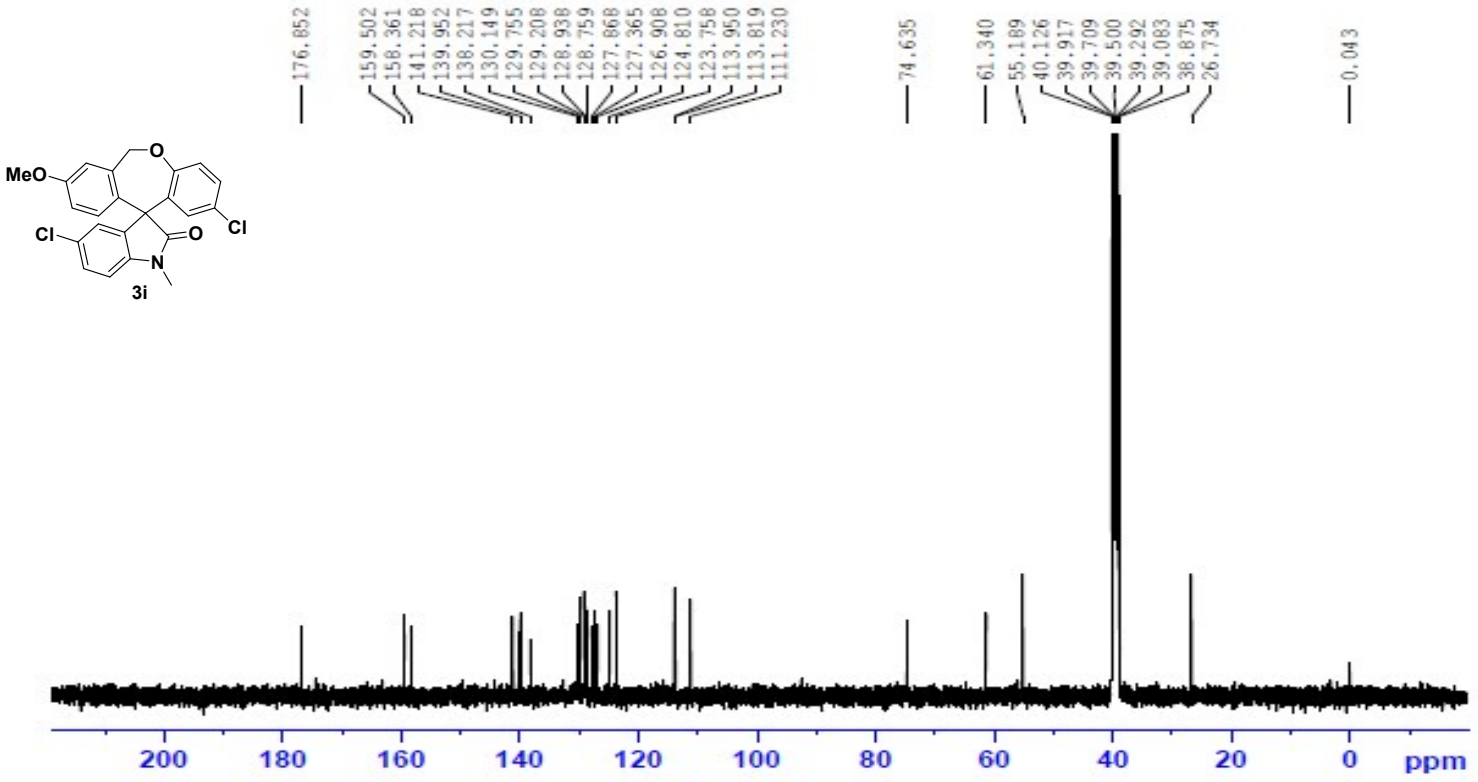



177.004
158.322
154.938
152.511
148.978
148.853
141.260
139.878
138.574
130.758
129.891
128.610
128.070
127.328
125.200
125.165
124.764
123.196
123.116
115.507
115.317
114.110
113.860
111.053
75.212
61.560
61.540
55.185
40.122
39.913
39.705
39.496
39.288
39.079
38.870
26.660
MeO
F
Cl
O
O
N
3h
200
180
160
140
120
100
80
60
40
20
0
ppm

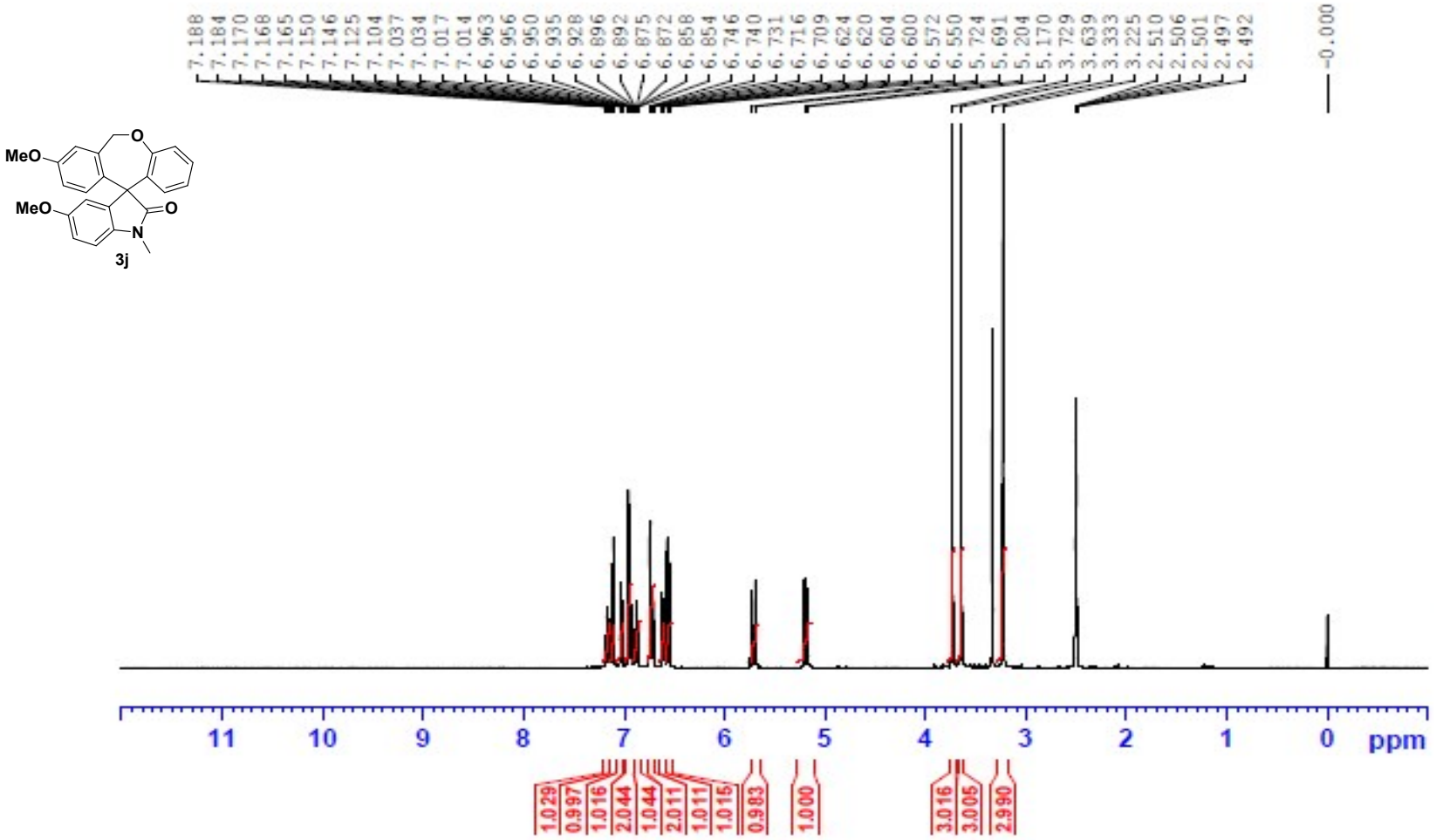

-131.911
F
O
MeO
Cl
O
N
3h
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
pp

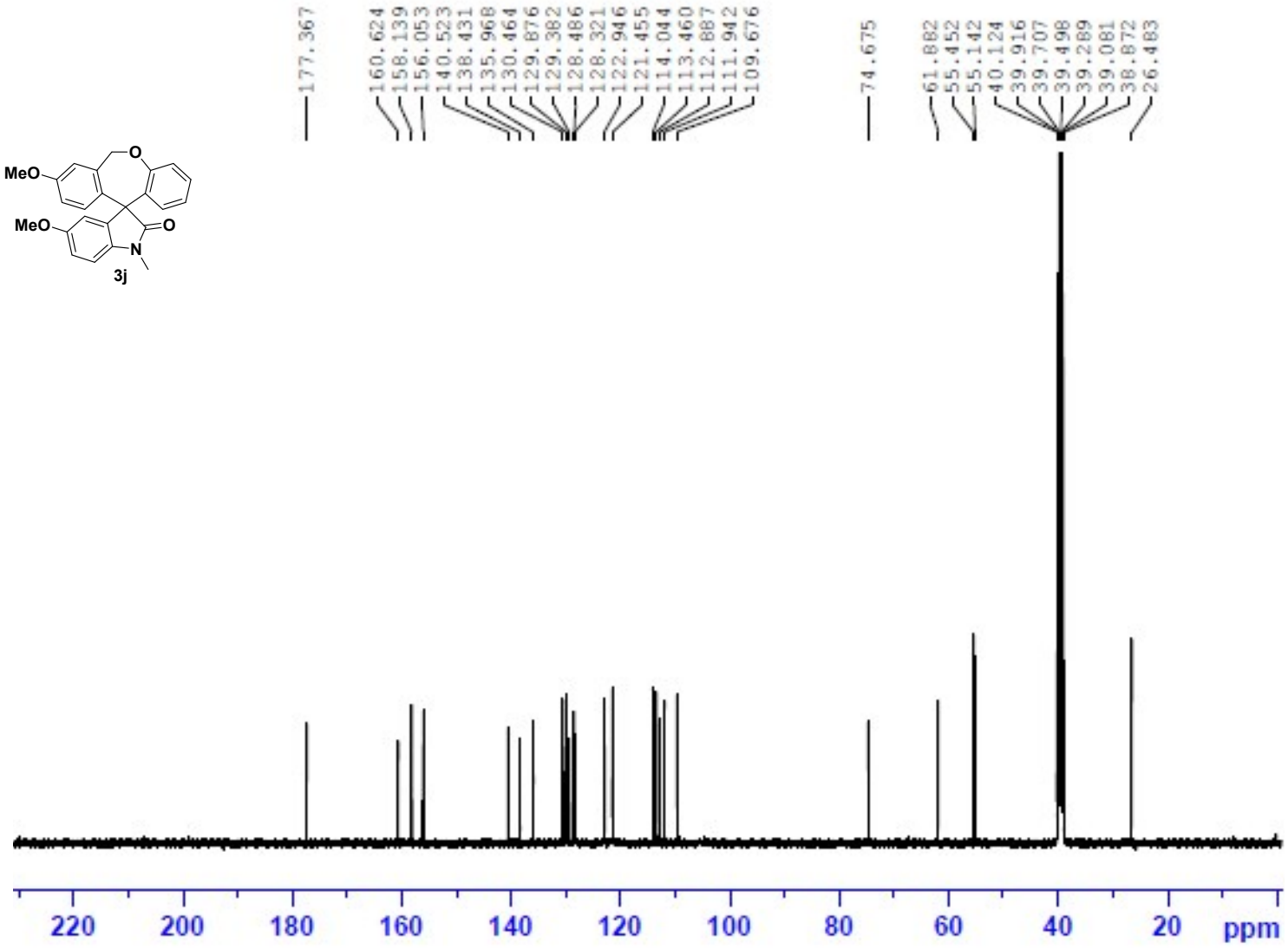
^{1}H ,^{13}C – NMR Data for 3i



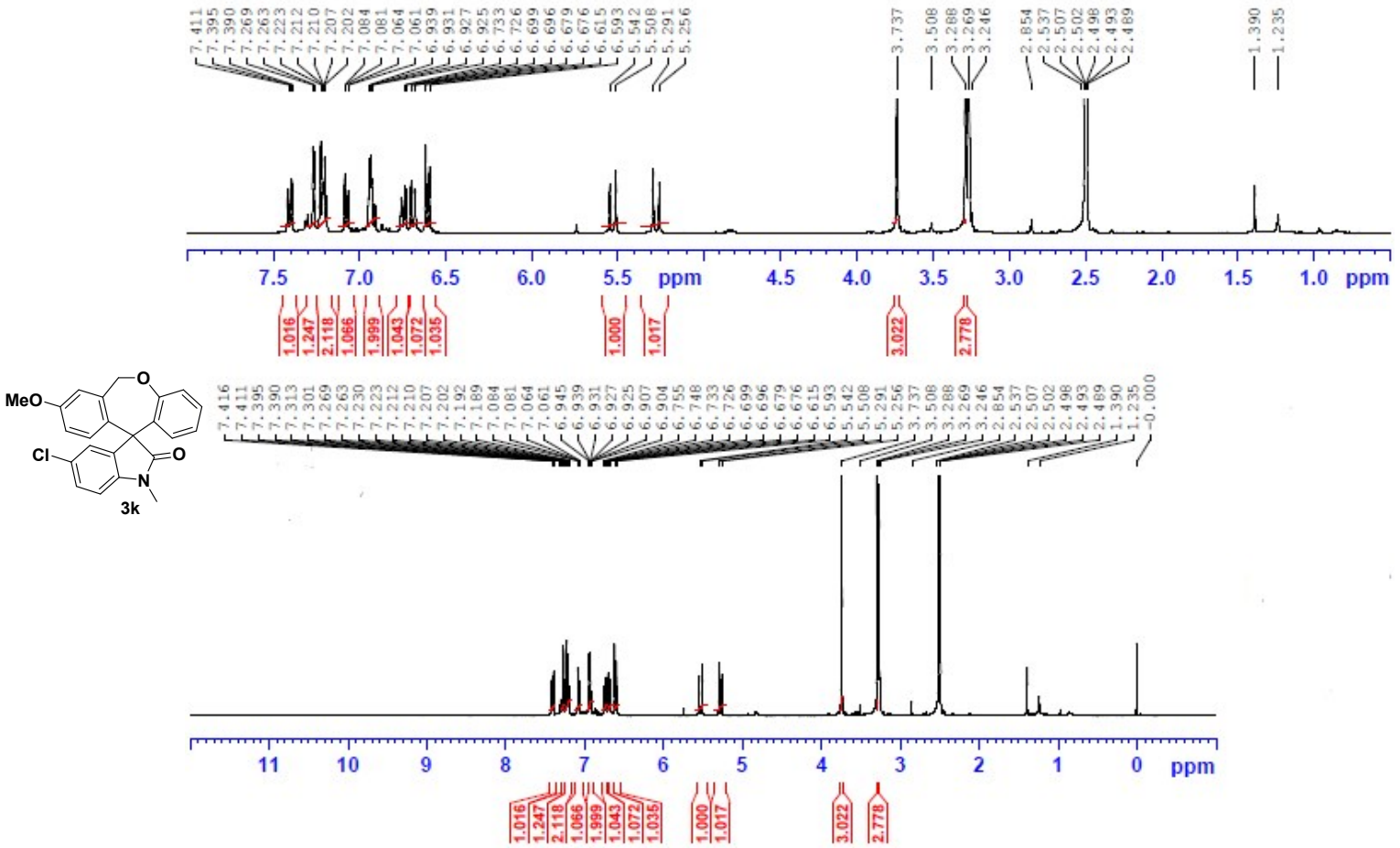

176.852
159.502
158.361
141.218
139.952
138.217
130.149
129.755
129.208
128.938
128.759
127.868
127.365
126.908
124.810
123.758
113.950
113.819
111.230
74.635
61.340
55.189
40.126
39.917
39.709
39.500
39.292
39.083
38.875
26.734
0.043
MeO
Cl
Cl
O
O
N
3i
200
180
160
140
120
100
80
60
40
20
0
ppm

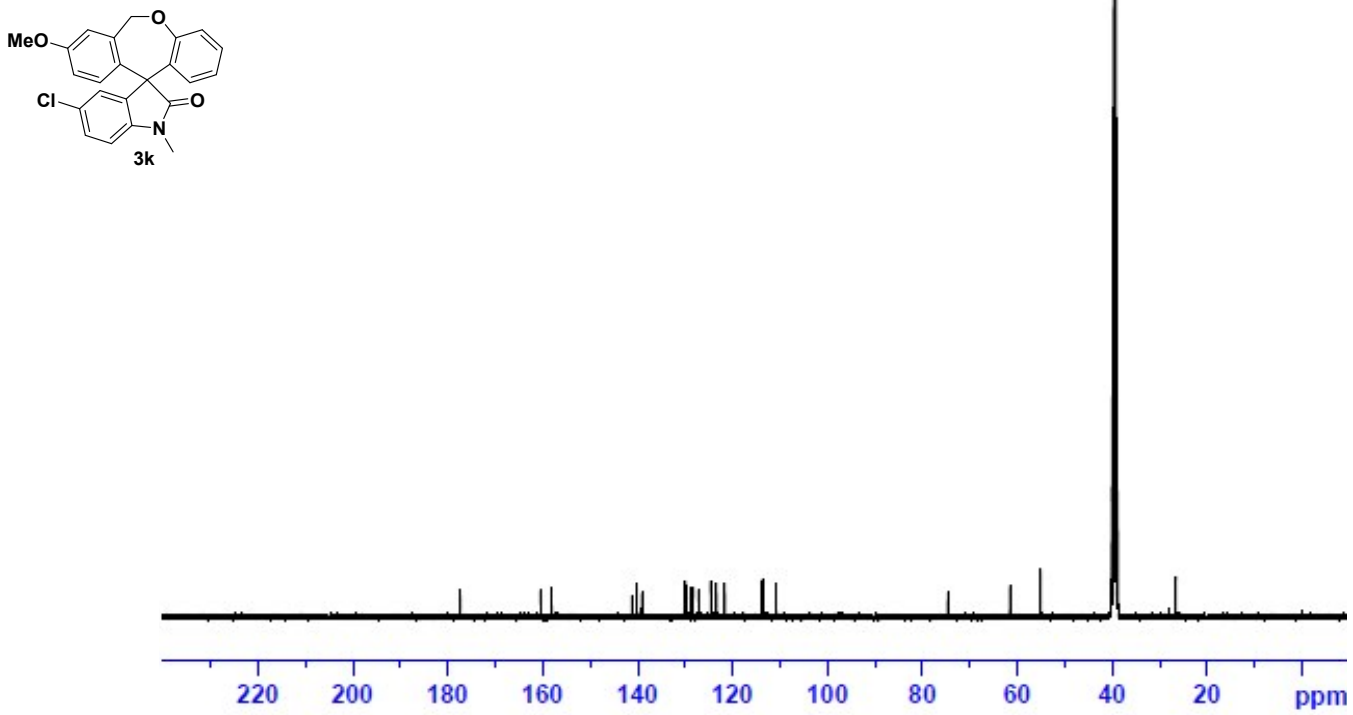
^{1}H ,^{13}C – NMR Data for 3j



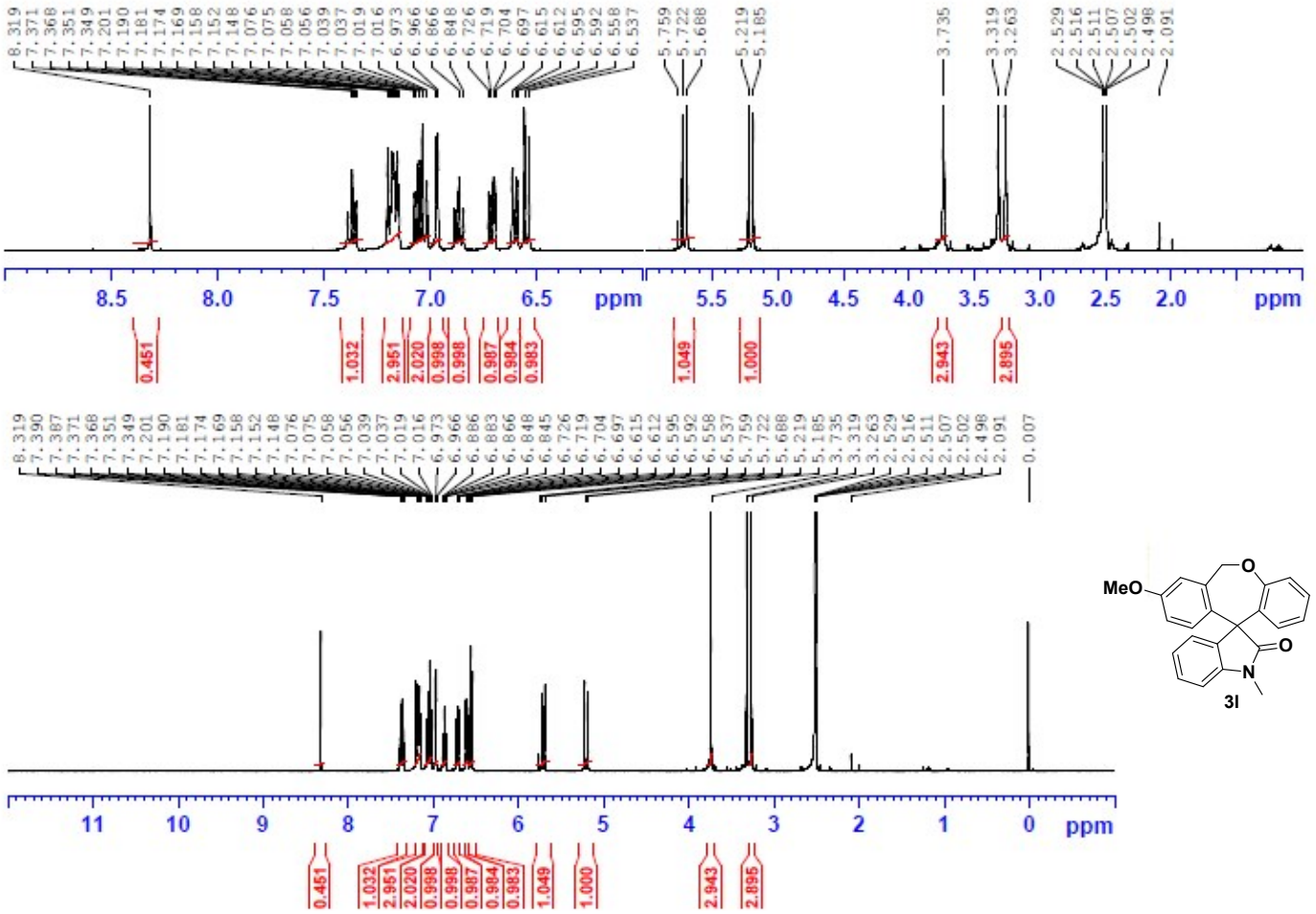

MeO
MeO
O
O
N
3j
177.367
160.624
158.139
156.053
140.523
138.431
135.968
130.464
129.876
129.382
128.486
128.321
122.946
121.455
114.044
113.460
112.887
111.942
109.676
74.675
61.882
55.452
55.142
40.124
39.916
39.707
39.498
39.289
39.081
38.872
26.483
220
200
180
160
140
120
100
80
60
40
20
ppm

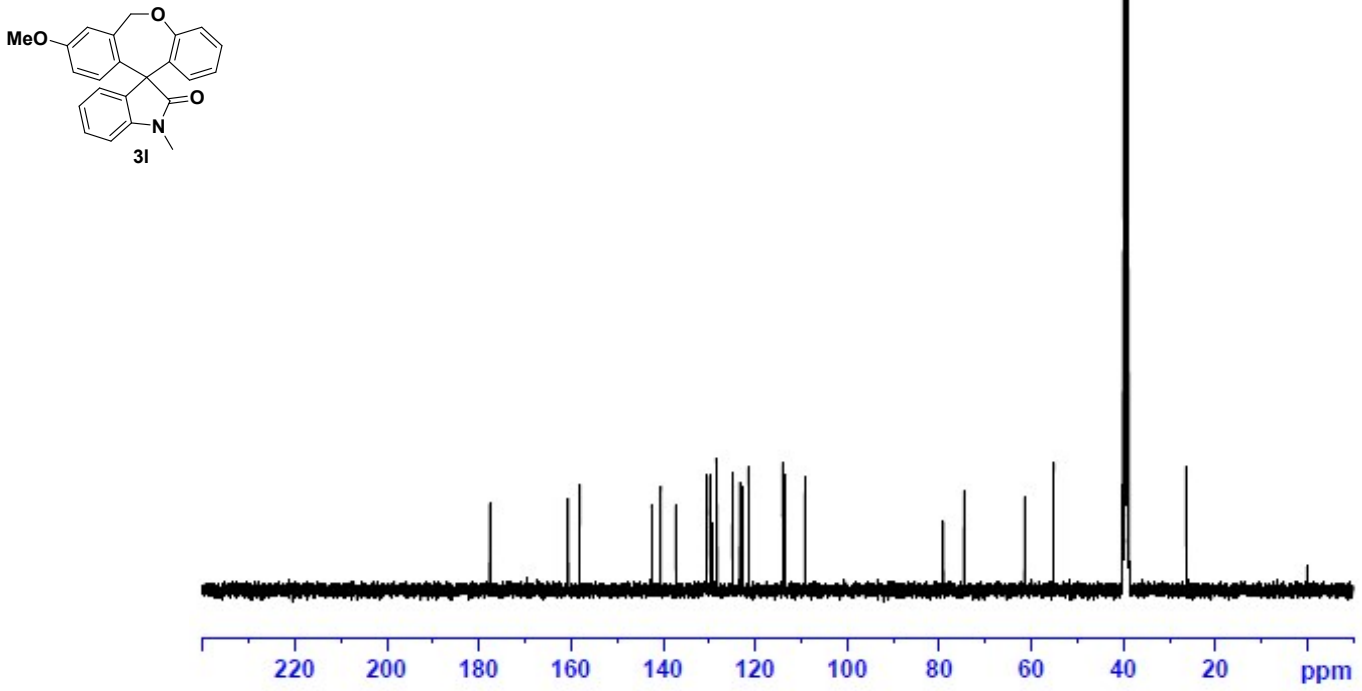
^{1}H ,^{13}C – NMR Data for 3k



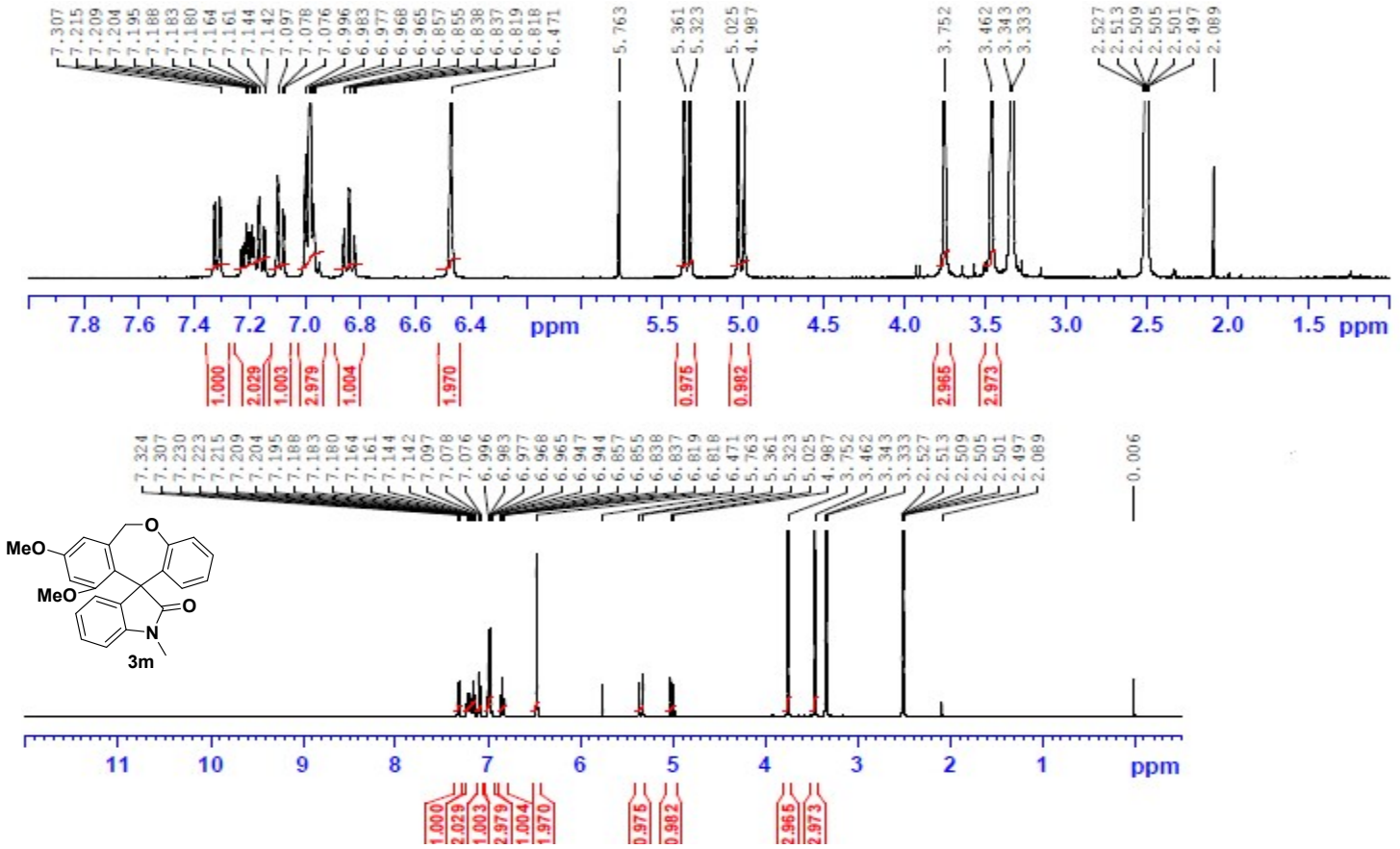

MeO
O
Cl
O
N
3k
177.431
160.493
158.213
141.212
140.303
139.140
129.943
129.807
128.916
128.458
128.410
128.356
127.171
124.659
123.439
121.698
113.795
113.698
110.926
74.651
61.575
55.163
40.122
39.913
39.704
39.496
39.287
39.078
38.870
26.607
220
200
180
160
140
120
100
80
60
40
20
ppm

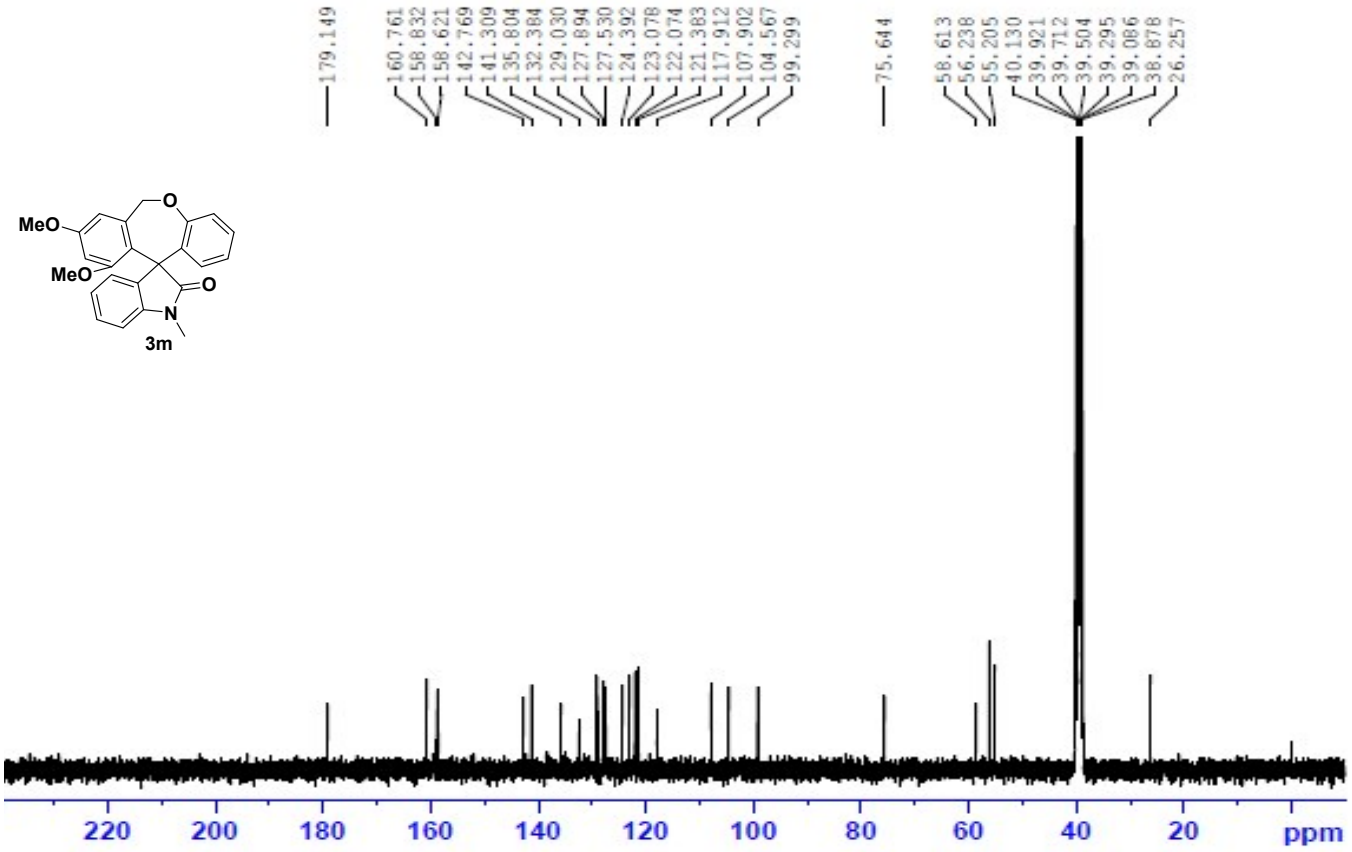
^{1}H ,^{13}C – NMR Data for 3l



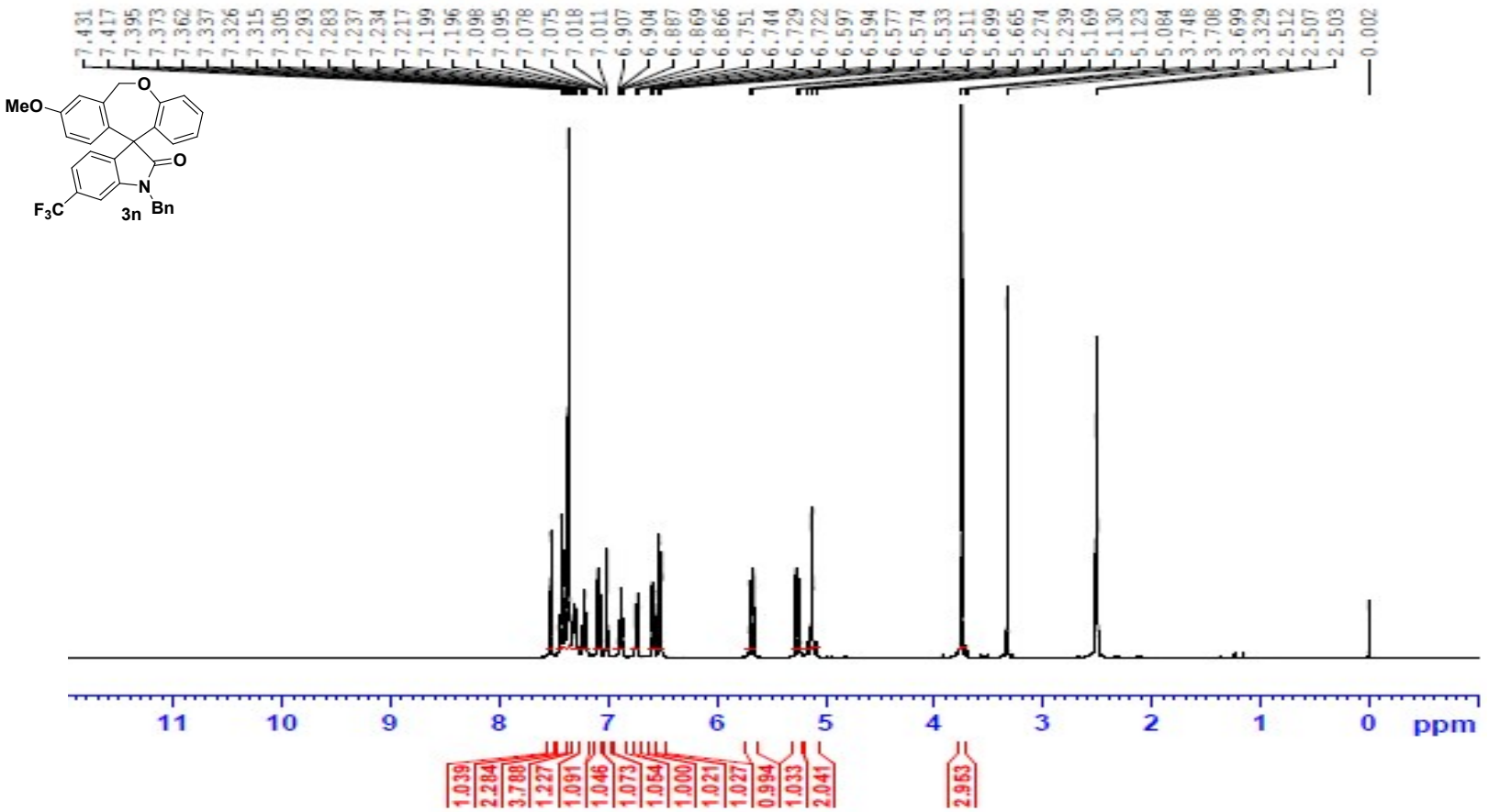

MeO
O
O
N
3l
177.704
160.634
158.145
142.470
140.509
137.343
130.435
129.786
129.408
128.499
128.467
128.286
124.947
123.375
122.900
121.444
114.068
113.450
109.197
79.123
74.646
61.468
55.152
40.124
39.916
39.708
39.499
39.290
39.082
38.873
26.412
0.050
220
200
180
160
140
120
100
80
60
40
20
ppm

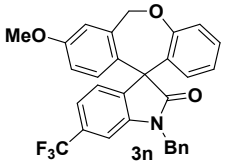
^{1}H ,^{13}C – NMR Data for 3m

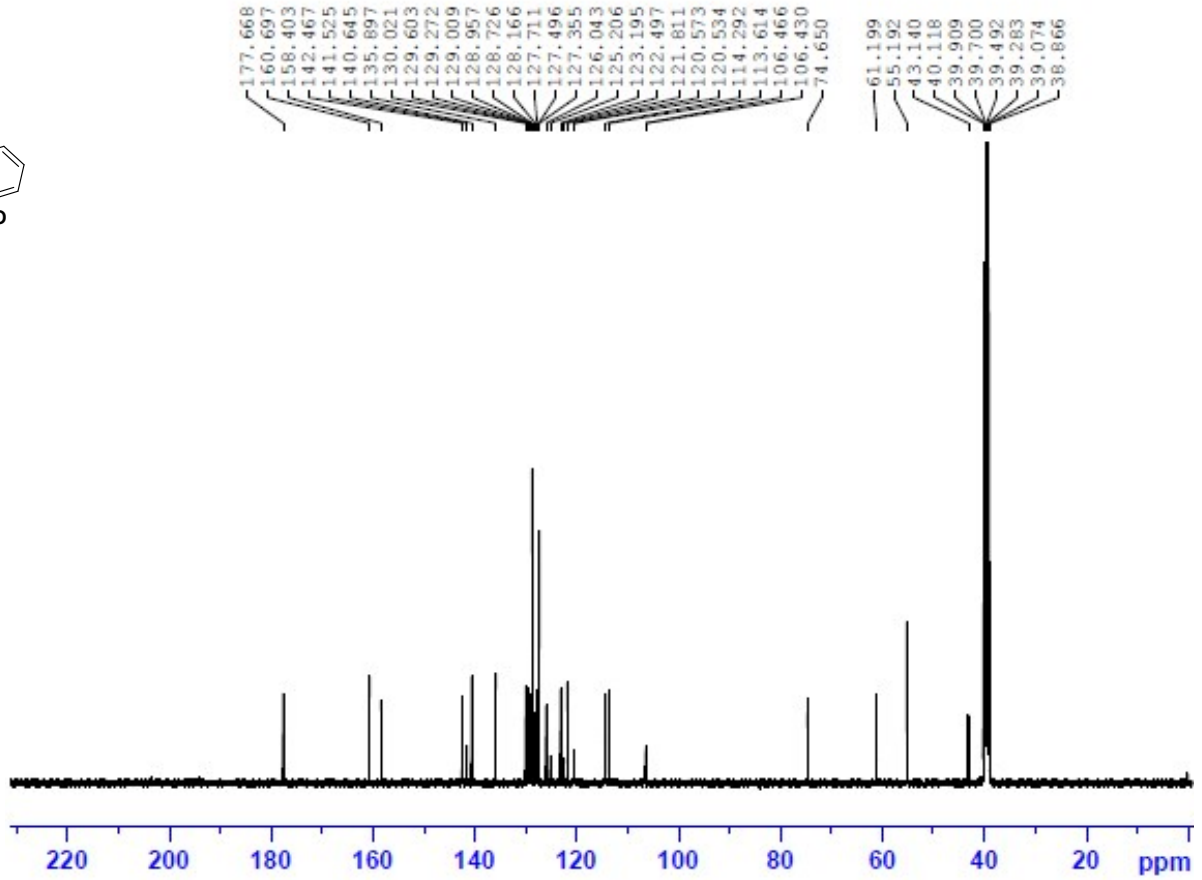


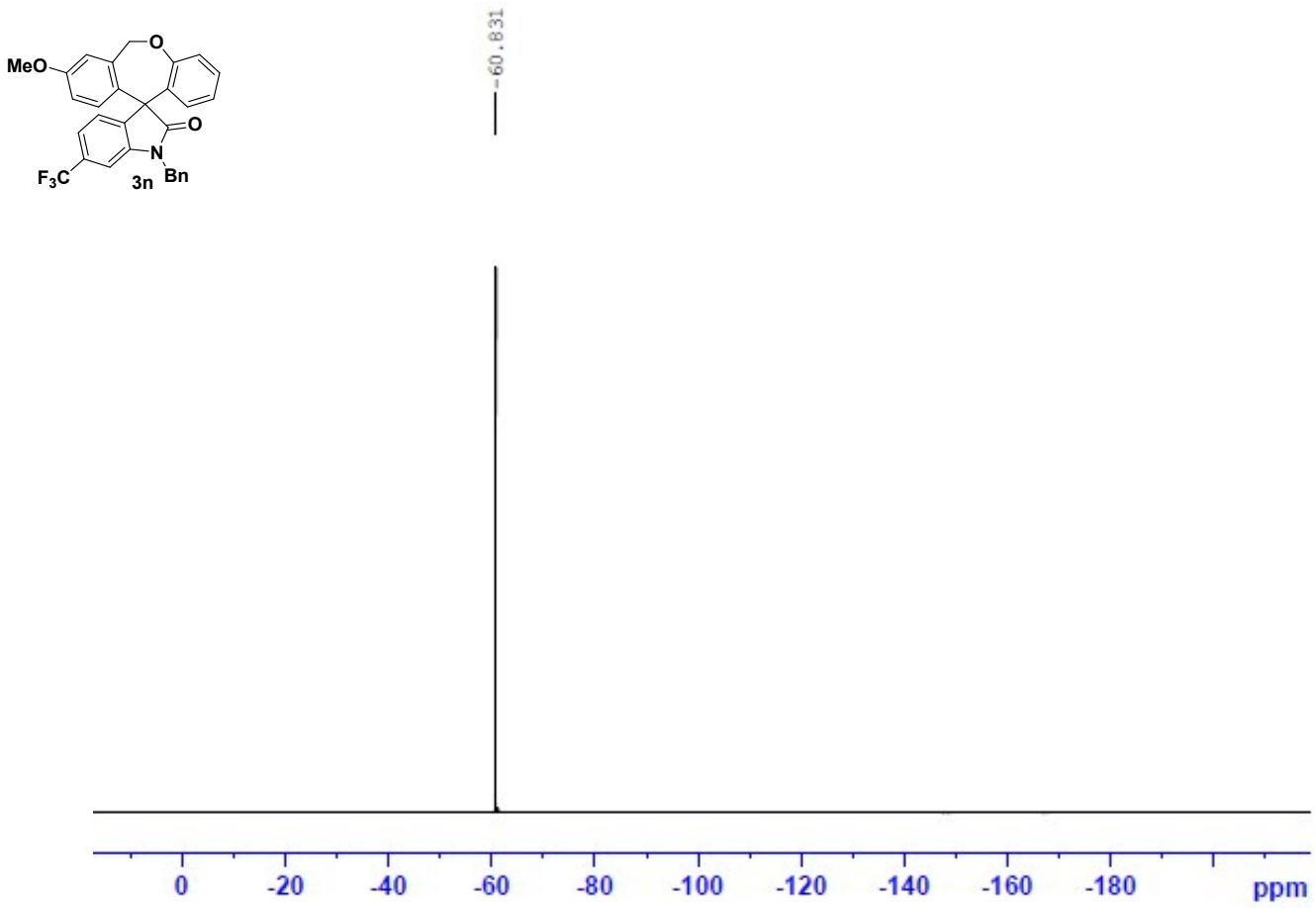

179.149
160.761
158.832
158.621
142.769
141.309
135.804
132.384
129.030
127.894
127.530
124.392
123.078
122.074
121.383
117.912
107.902
104.567
99.299
75.644
58.613
56.238
55.205
40.130
39.921
39.712
39.504
39.295
39.086
38.878
26.257
MeO
MeO
O
O
N
3m
220
200
180
160
140
120
100
80
60
40
20
ppm

^{1}H ,^{13}C & ^{19}F– NMR Data for 3n

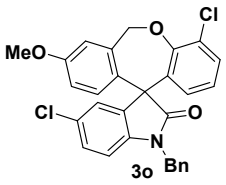


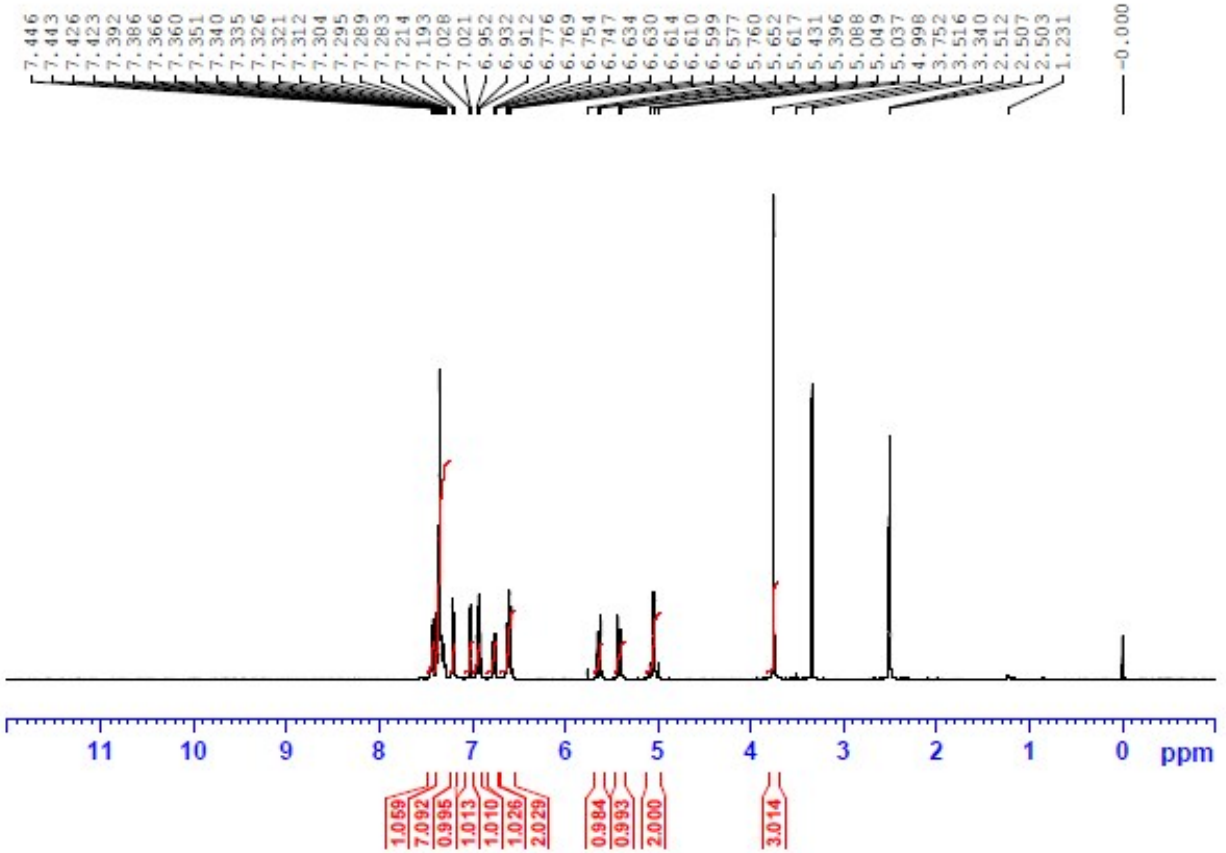

MeO
O
O
N
Bn
F3C
3n

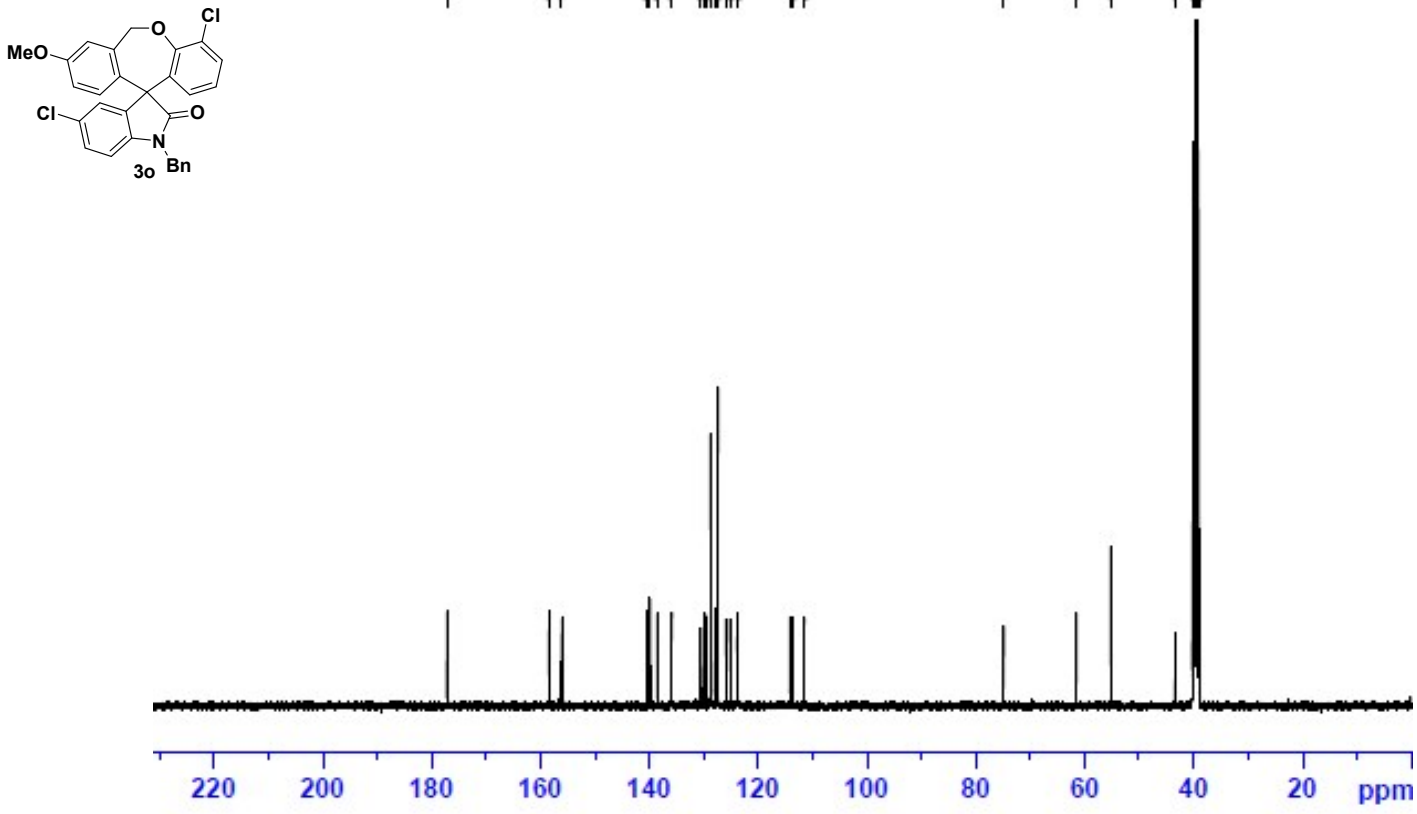

177.668
160.697
158.403
142.467
141.525
140.645
135.897
130.021
129.603
129.272
129.009
128.957
128.726
128.166
127.711
127.496
127.355
126.043
125.206
123.195
122.497
121.811
120.573
120.534
114.292
113.614
106.466
106.430
74.650
61.199
55.192
43.140
40.118
39.909
39.700
39.492
39.283
39.074
38.866
220
200
180
160
140
120
100
80
60
40
20
ppm


MeO
O
O
N
Bn
F_3C
3n
-60.831
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

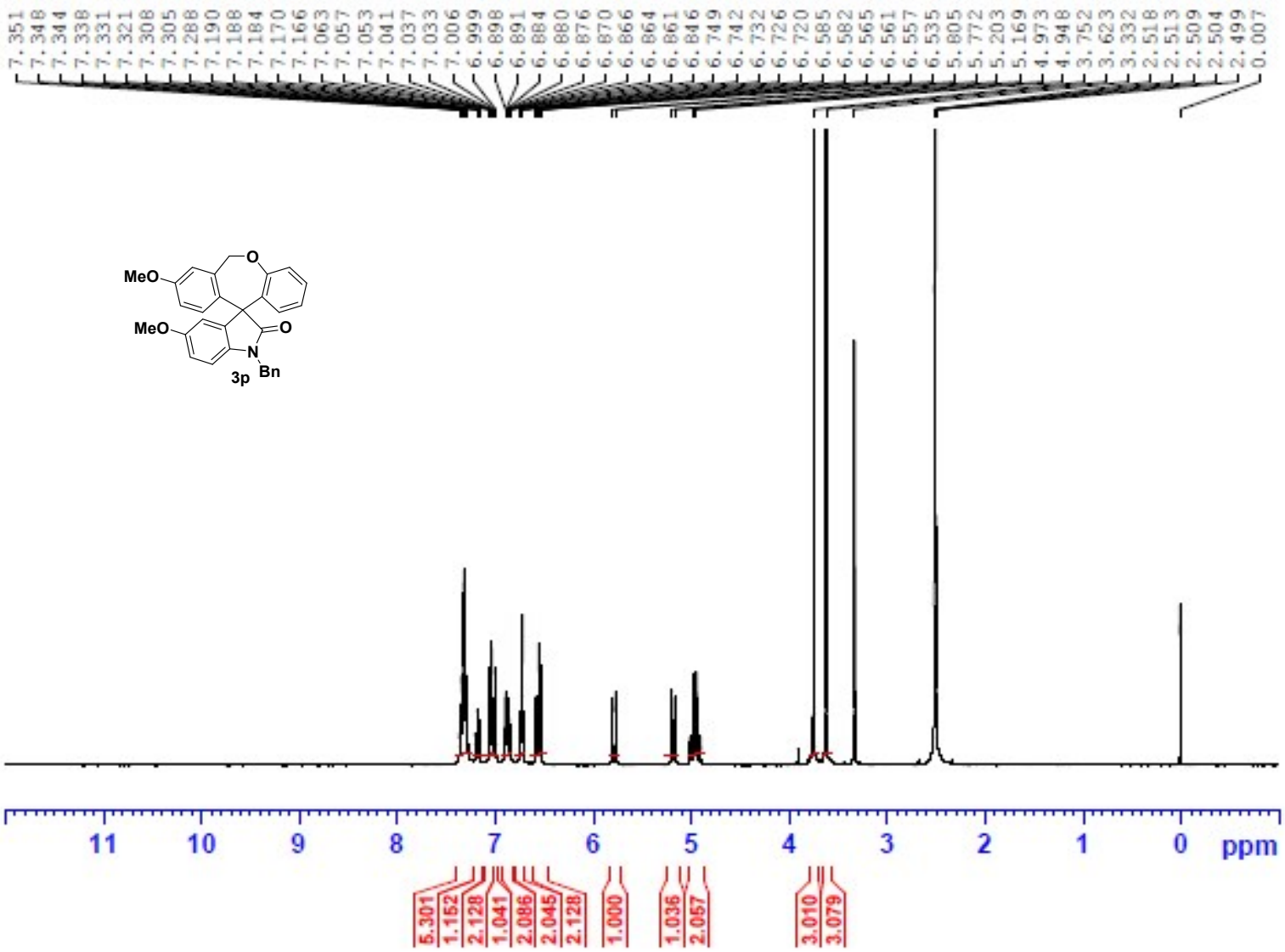
^{1}H ,^{13}C – NMR Data for 3o

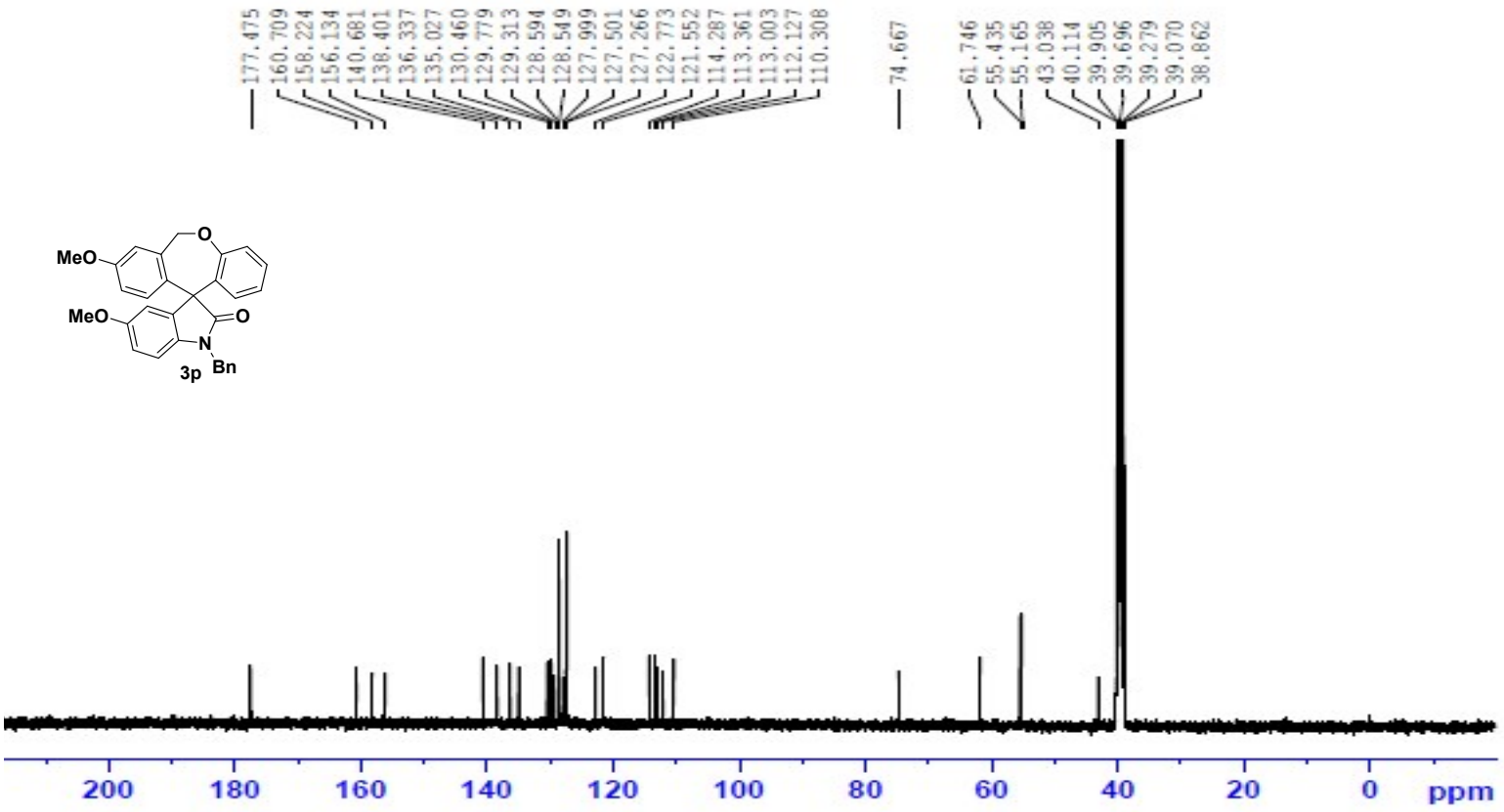




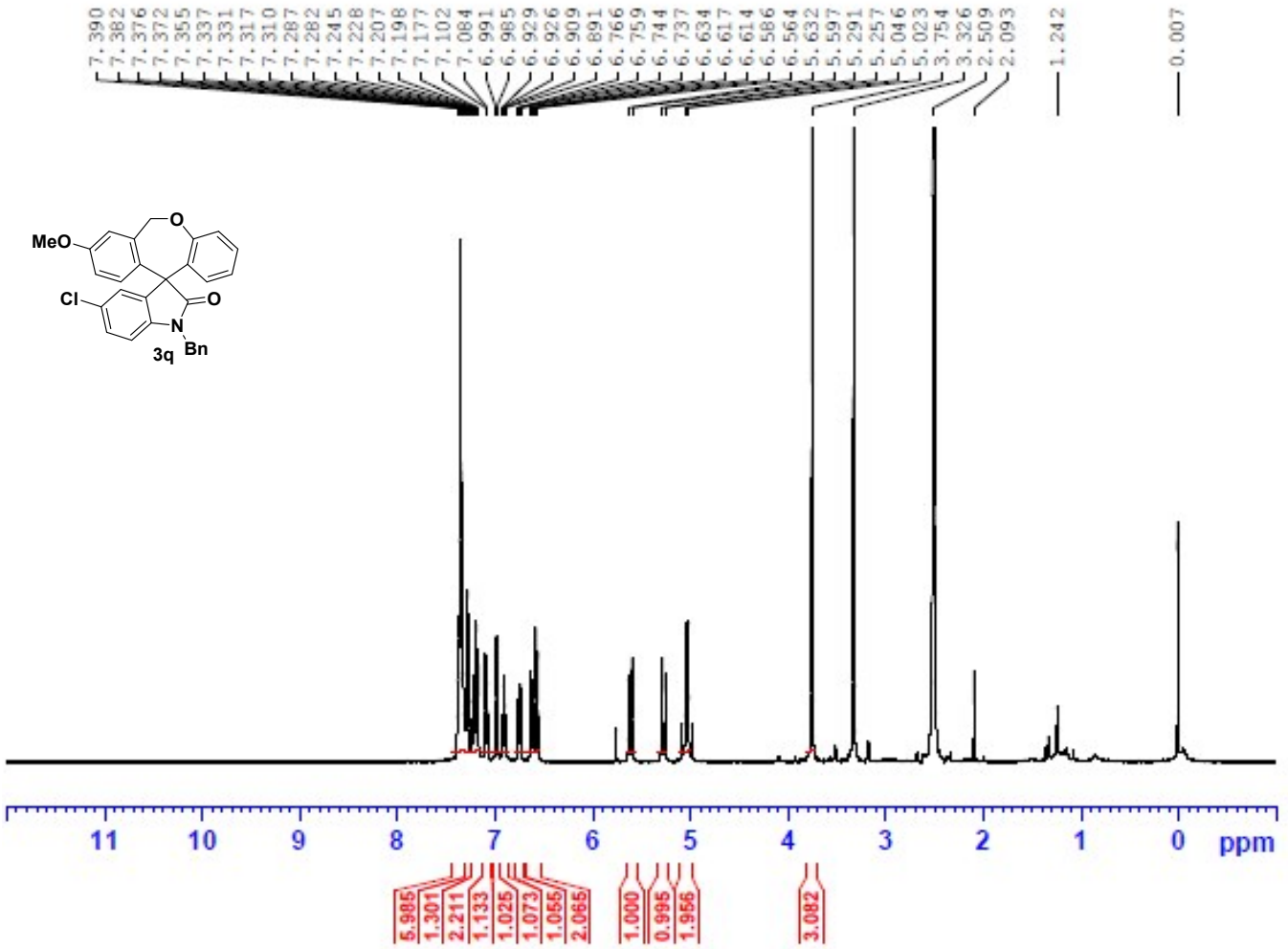

MeO
Cl
O
Cl
O
N
Bn
3o
177.156
158.404
156.057
140.306
139.845
138.559
135.865
130.472
129.738
129.517
128.761
128.730
128.658
127.888
127.708
127.638
127.392
125.898
125.166
123.820
114.109
113.738
111.550
74.839
61.511
55.216
43.291
40.122
39.913
39.705
39.496
39.287
39.079
38.870
220
200
180
160
140
120
100
80
60
40
20
ppm

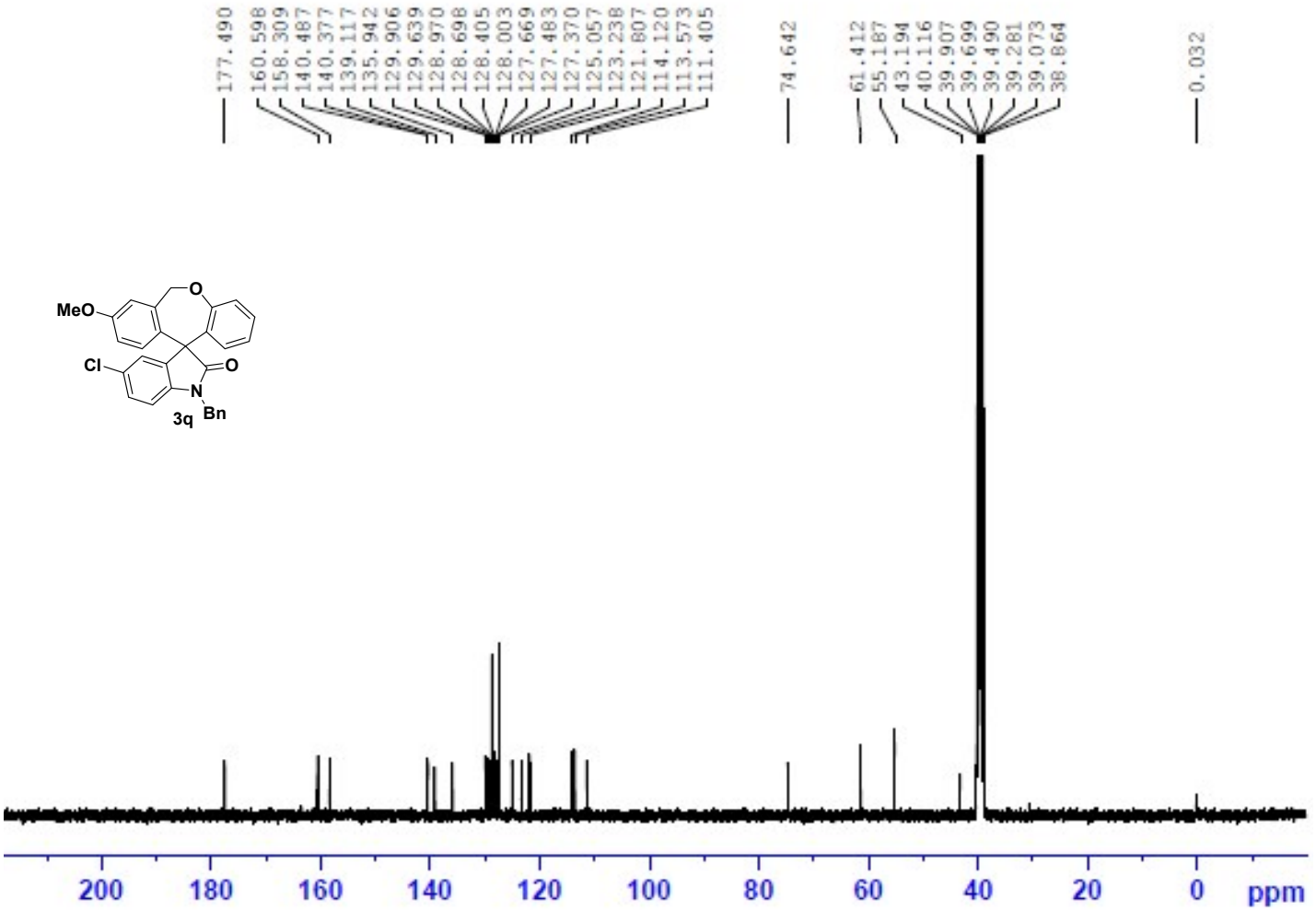
^{1}H ,^{13}C – NMR Data for 3p



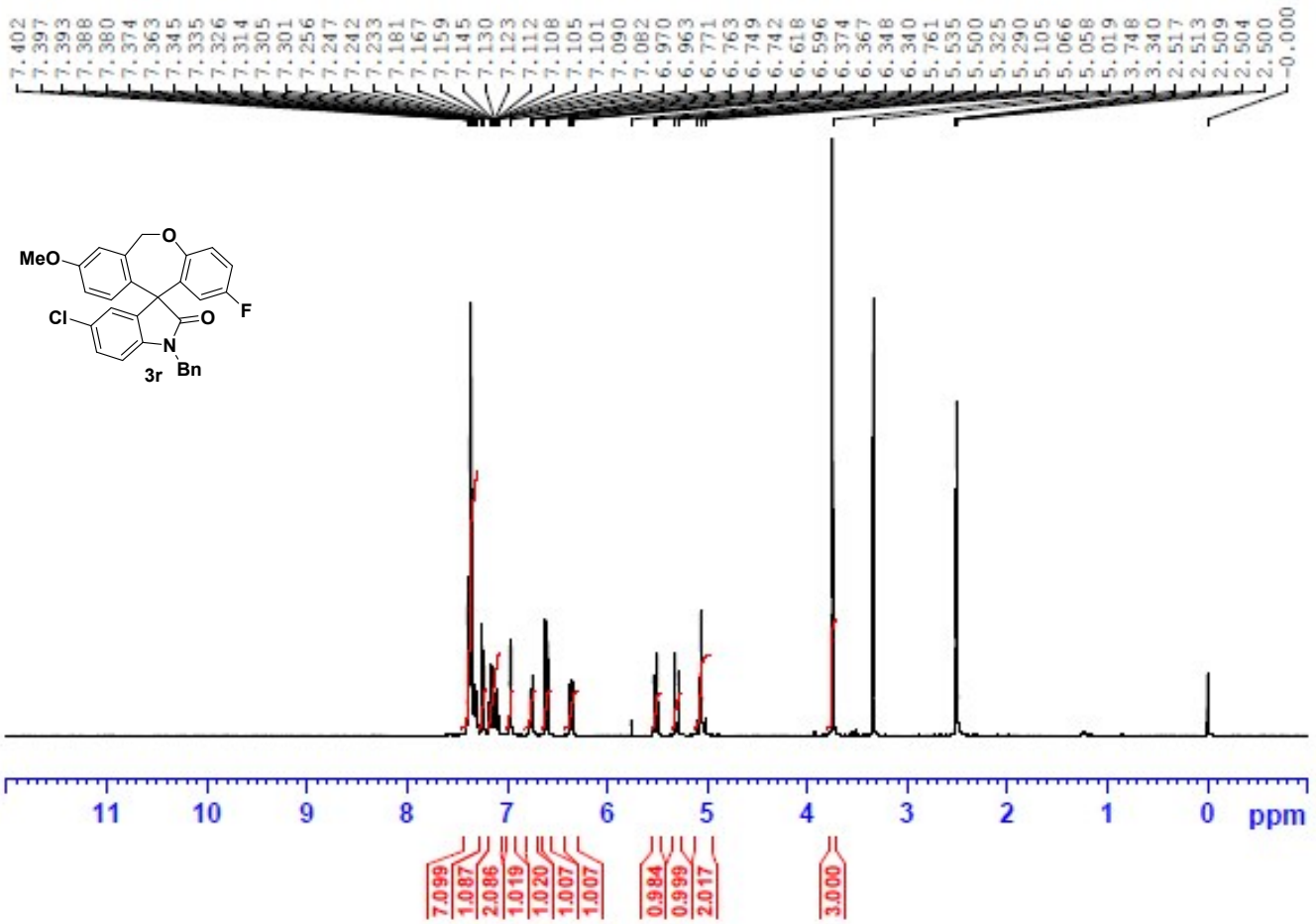

177.475
160.709
158.224
156.134
140.681
138.401
136.337
135.027
130.460
129.779
129.313
128.594
128.549
127.999
127.501
127.266
122.773
121.552
114.287
113.361
113.003
112.127
110.308
74.667
61.746
55.435
55.165
43.038
40.114
39.905
39.696
39.279
39.070
38.862
MeO
MeO
O
O
N
Bn
3p
200
180
160
140
120
100
80
60
40
20
0
ppm

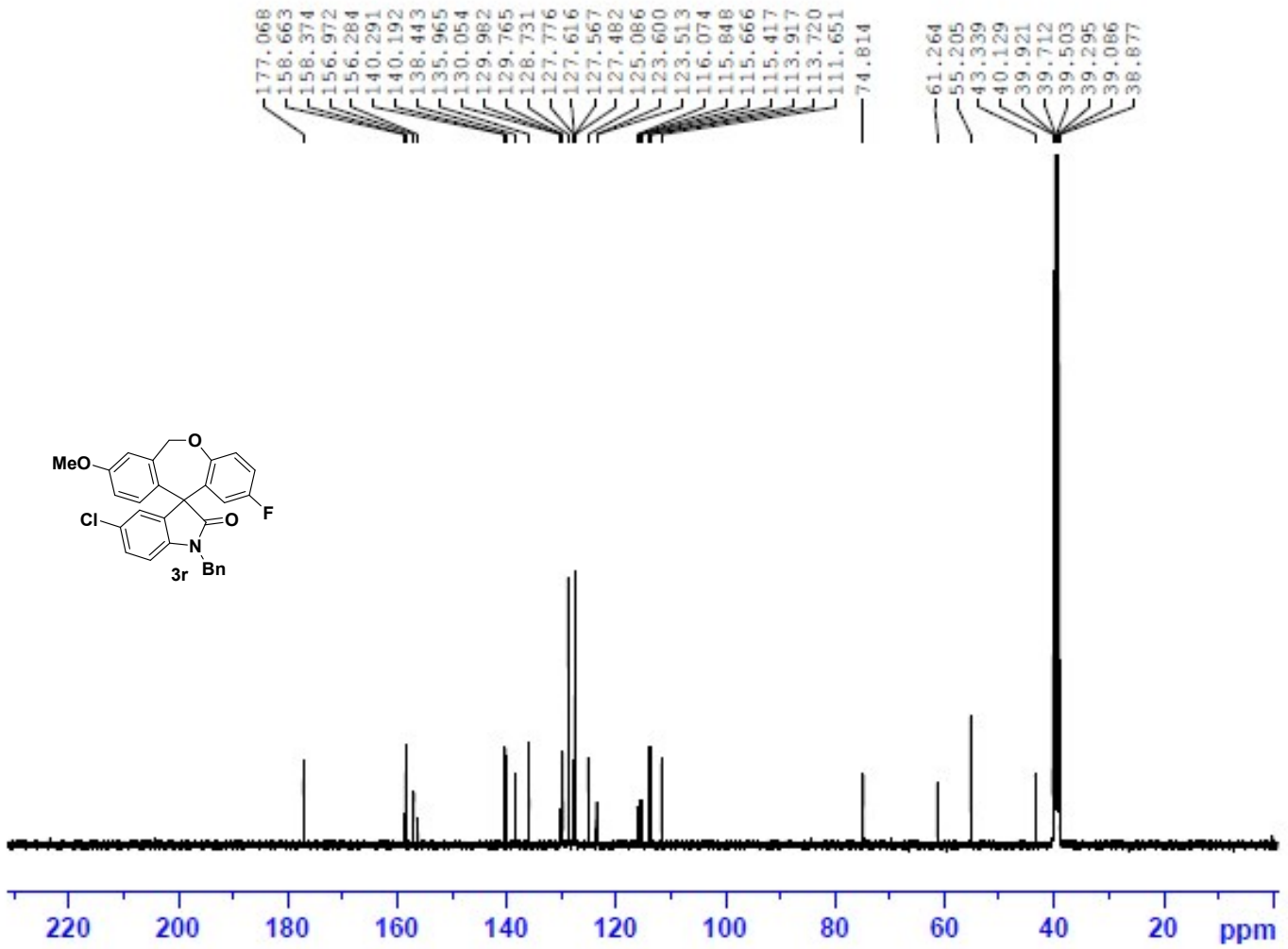
^{1}H ,^{13}C – NMR Data for 3q

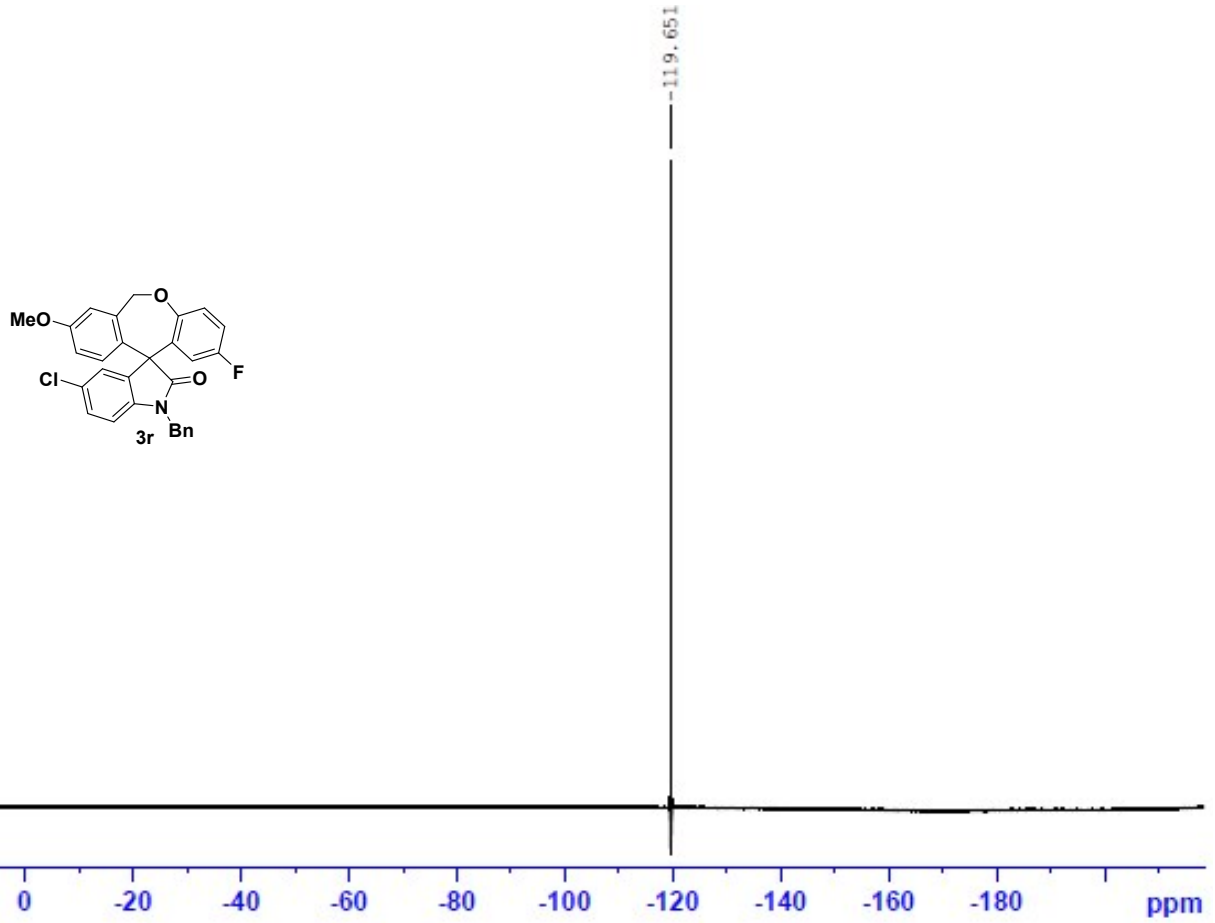



177.490
160.598
158.309
140.487
140.377
139.117
135.942
129.906
129.639
128.970
128.698
128.405
128.003
127.669
127.483
127.370
125.057
123.238
121.807
114.120
113.573
111.405
74.642
61.412
55.187
43.194
40.116
39.907
39.699
39.490
39.281
39.073
38.864
0.032
MeO
Cl
O
O
N
Bn
3q
200
180
160
140
120
100
80
60
40
20
0
ppm

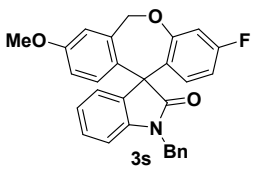
^{1}H ,^{13}C & ^{19}F– NMR Data for 3r

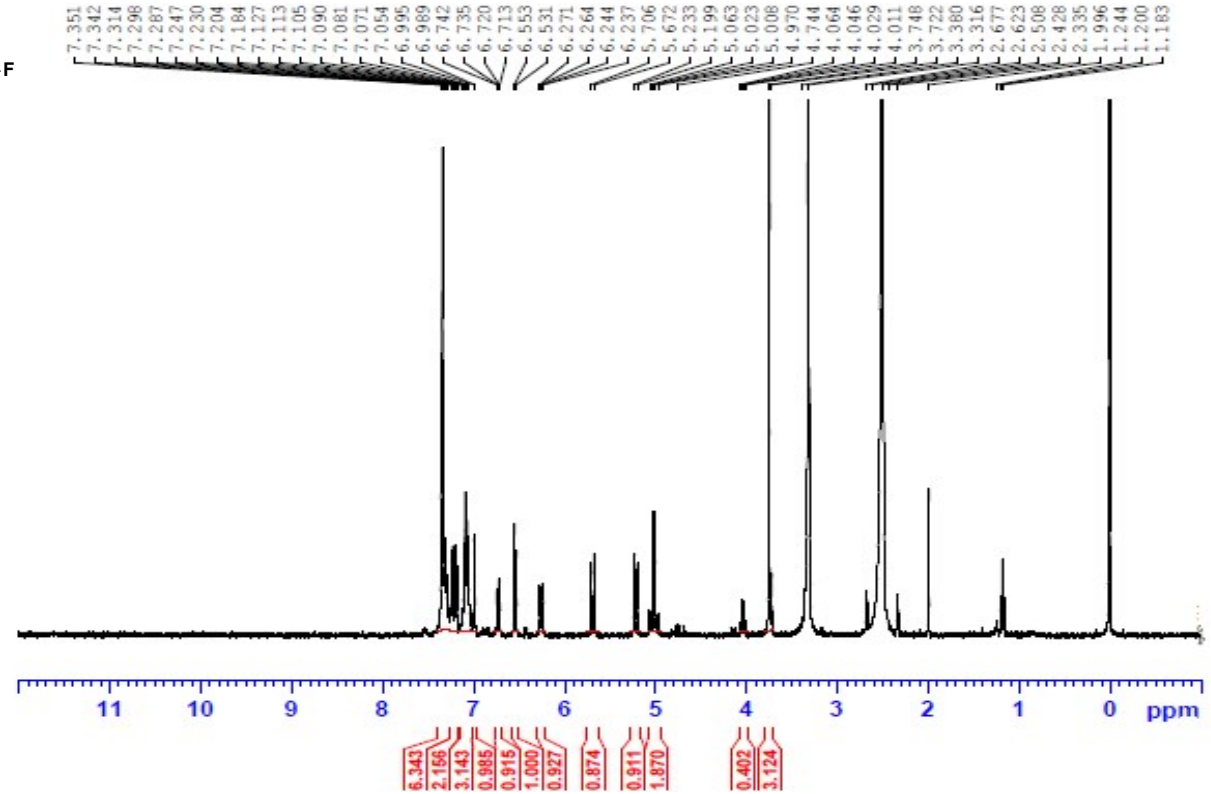


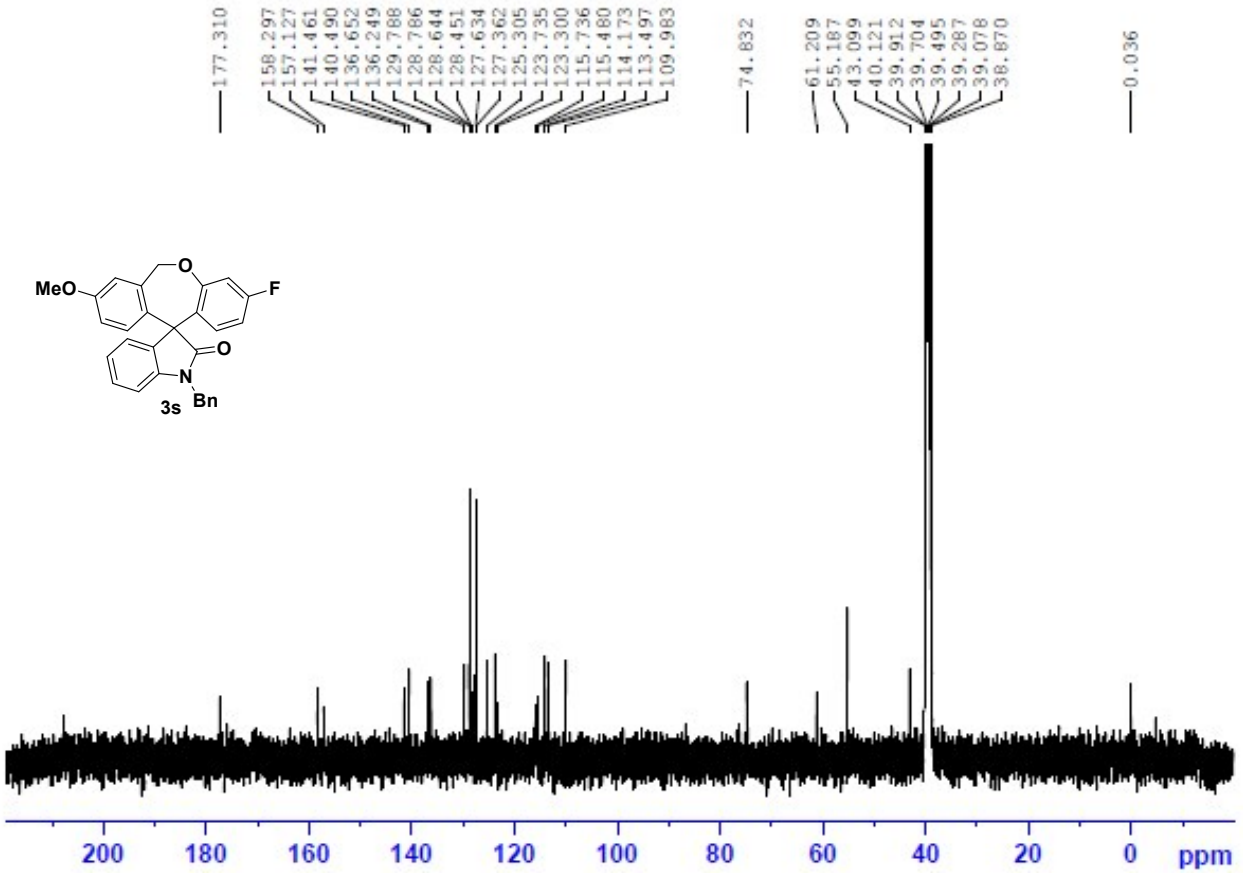

177.068
158.663
158.374
156.972
156.284
140.291
140.192
138.443
135.965
130.054
129.982
129.765
128.731
127.776
127.616
127.567
127.482
125.086
123.600
123.513
116.074
115.848
115.666
115.417
113.917
113.720
111.651
74.814
61.264
55.205
43.339
40.129
39.921
39.712
39.503
39.295
39.086
38.877
MeO
O
F
Cl
O
N
Bn
3r
220
200
180
160
140
120
100
80
60
40
20
ppm

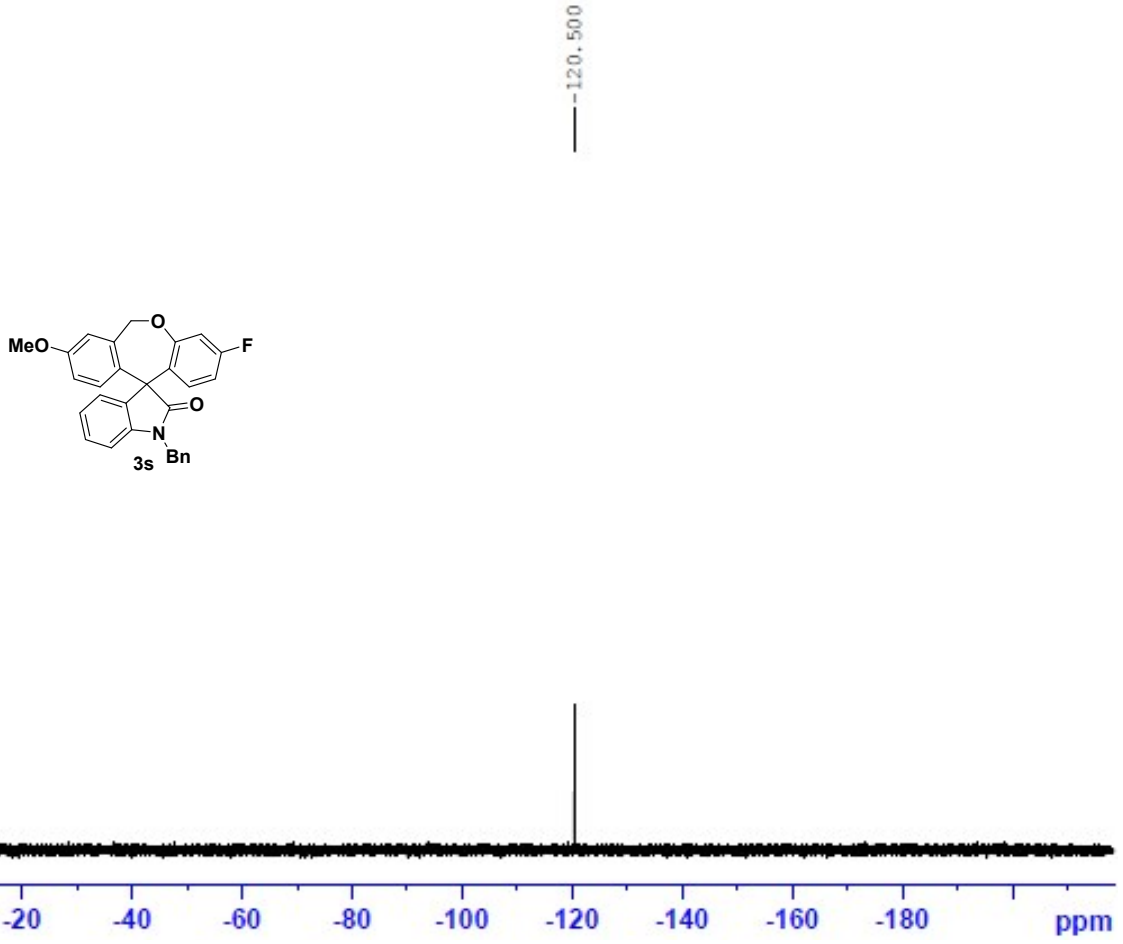

-119.651
MeO
O
F
Cl
O
N
Bn
3r
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

^{1}H ,^{13}C & ^{19}F– NMR Data for 3s

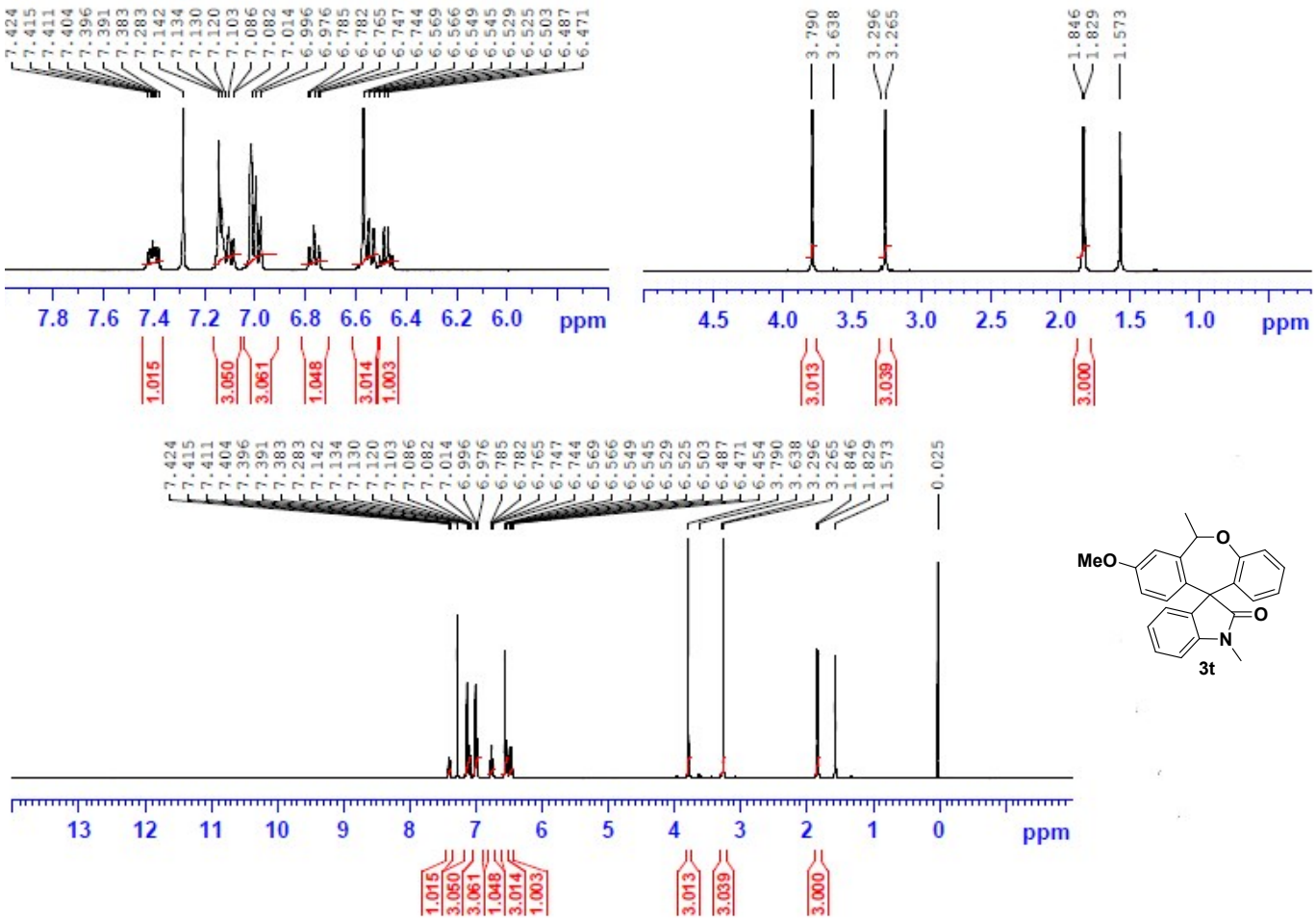


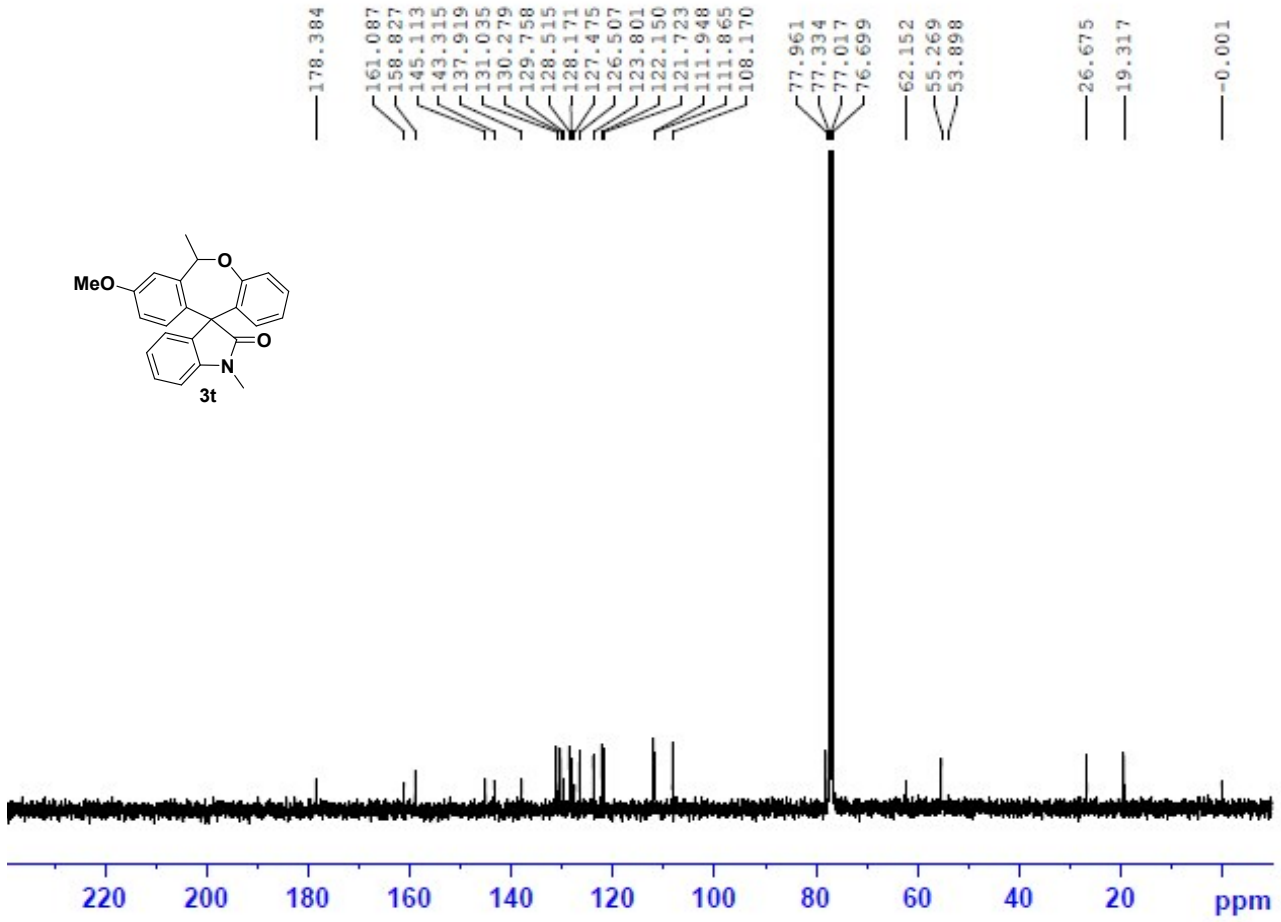



177.310
158.297
157.127
141.461
140.490
136.652
136.249
129.788
128.786
128.644
128.451
127.634
127.362
125.305
123.735
123.300
115.736
115.480
114.173
113.497
109.983
74.832
61.209
55.187
43.099
40.121
39.912
39.704
39.495
39.287
39.078
38.870
0.036
MeO
F
O
O
N
Bn
3s
200
180
160
140
120
100
80
60
40
20
0
ppm

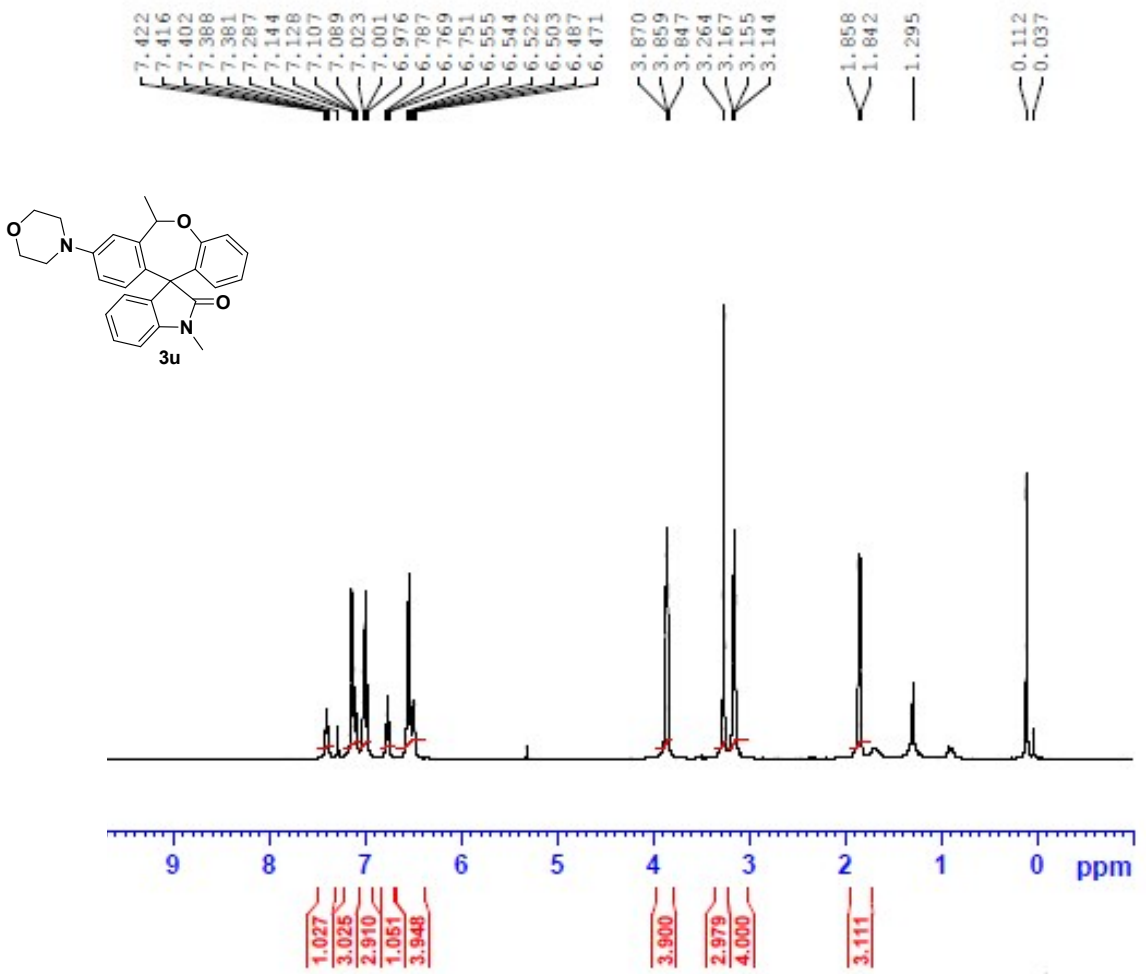

-120.500
MeO
O
F
O
N
Bn
3s
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

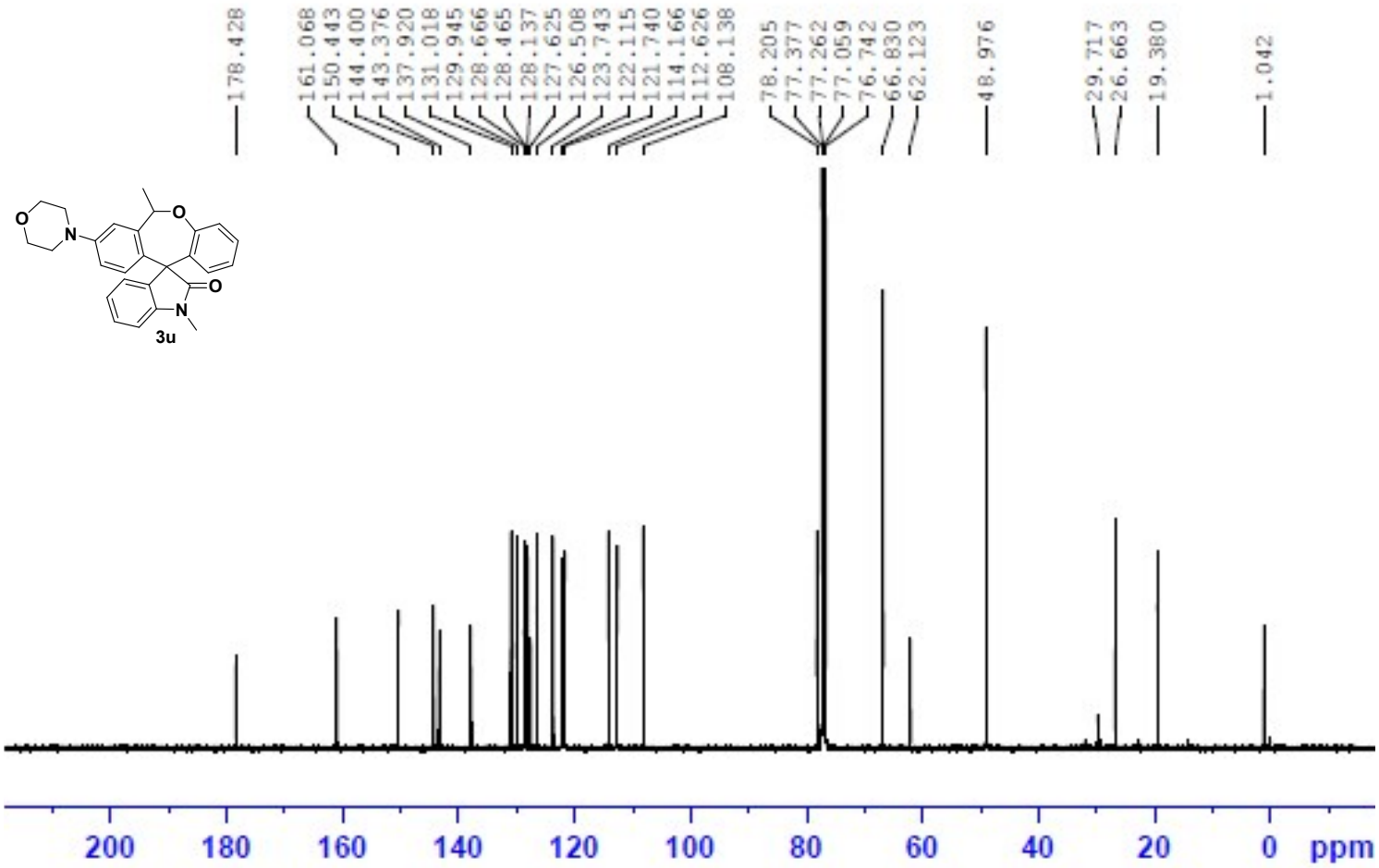
^{1}H ,^{13}C – NMR Data for 3t



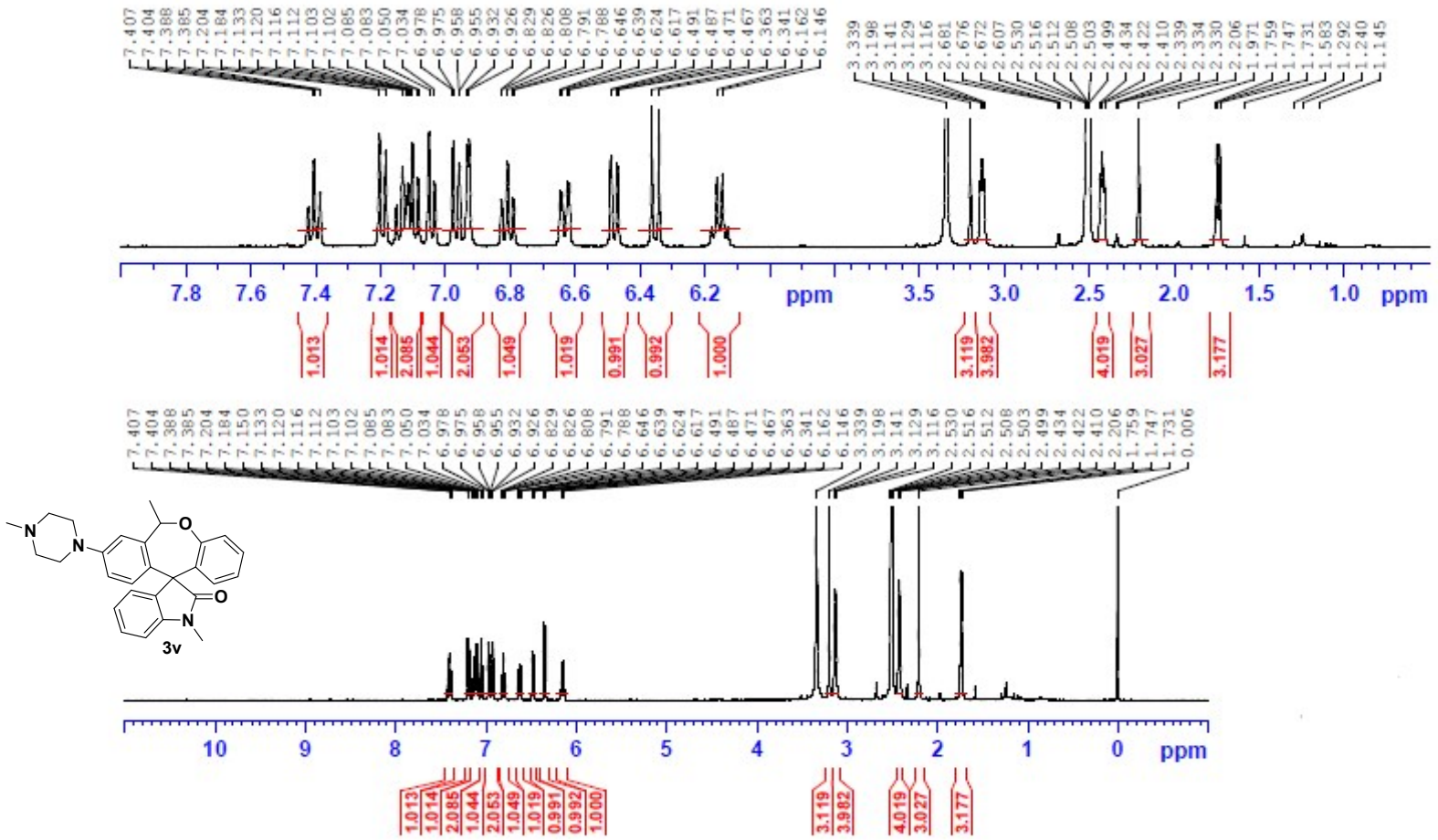

178.384
161.087
158.827
145.113
143.315
137.919
131.035
130.279
129.758
128.515
128.171
127.475
126.507
123.801
122.150
121.723
111.948
111.865
108.170
77.961
77.334
77.017
76.699
62.152
55.269
53.898
26.675
19.317
-0.001
MeO
O
O
N
3t
220
200
180
160
140
120
100
80
60
40
20
ppm

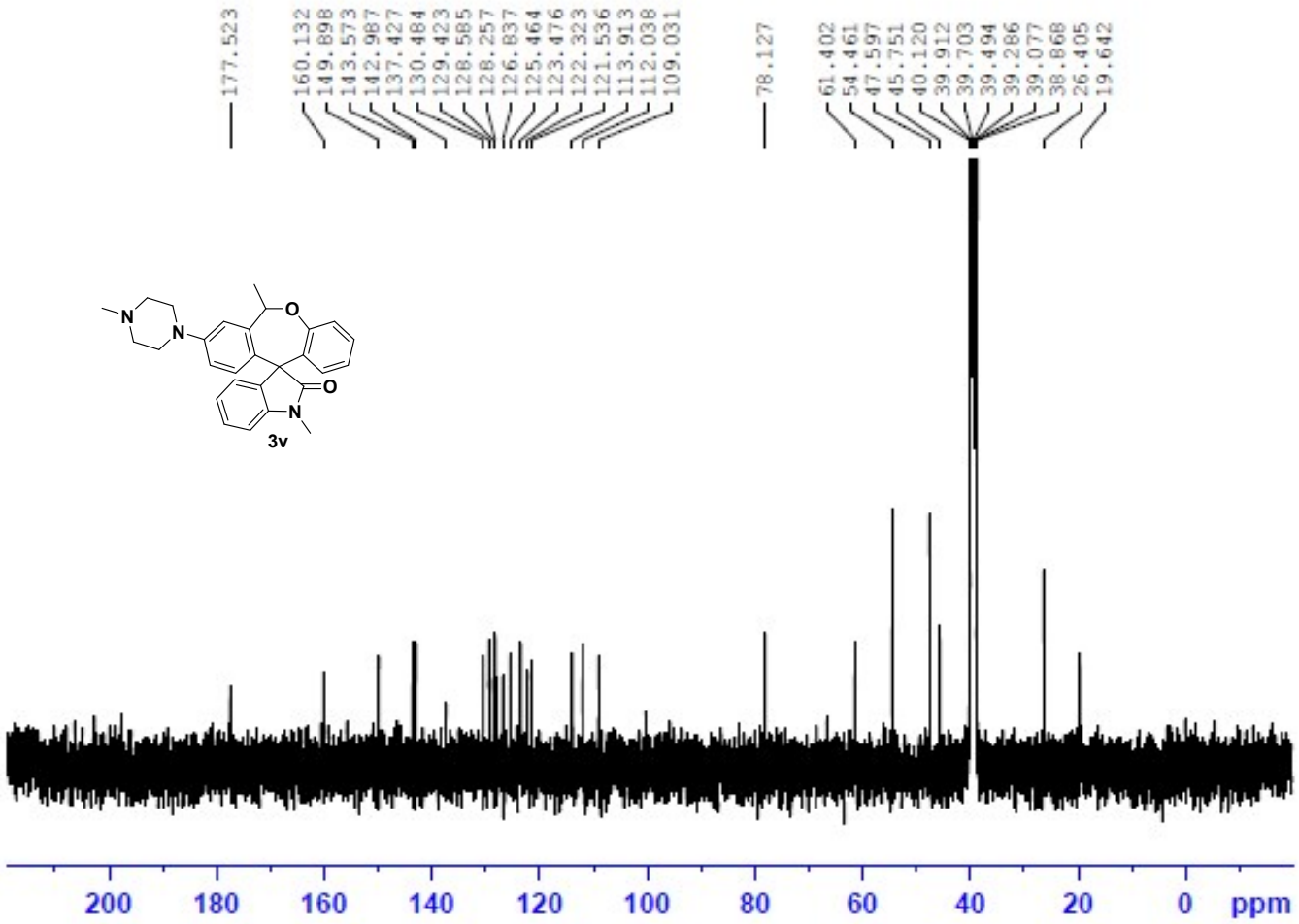
^{1}H ,^{13}C – NMR Data for 3u



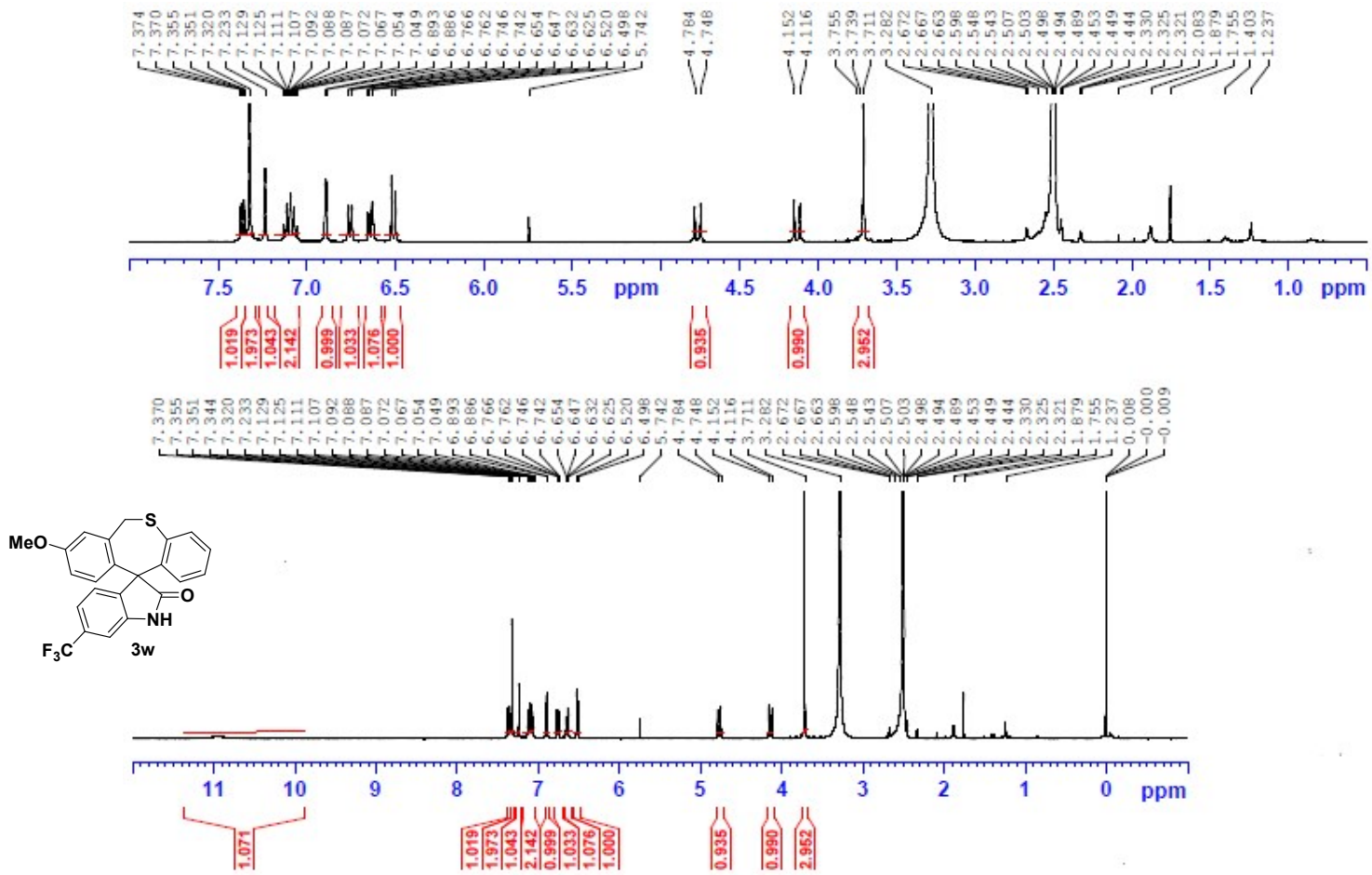

178.428
161.068
150.443
144.400
143.376
137.920
131.018
129.945
128.666
128.465
128.137
127.625
126.508
123.743
122.115
121.740
114.166
112.626
108.138
78.205
77.377
77.262
77.059
76.742
66.830
62.123
48.976
29.717
26.663
19.380
1.042
O
N
O
O
N
3u
200
180
160
140
120
100
80
60
40
20
0
ppm

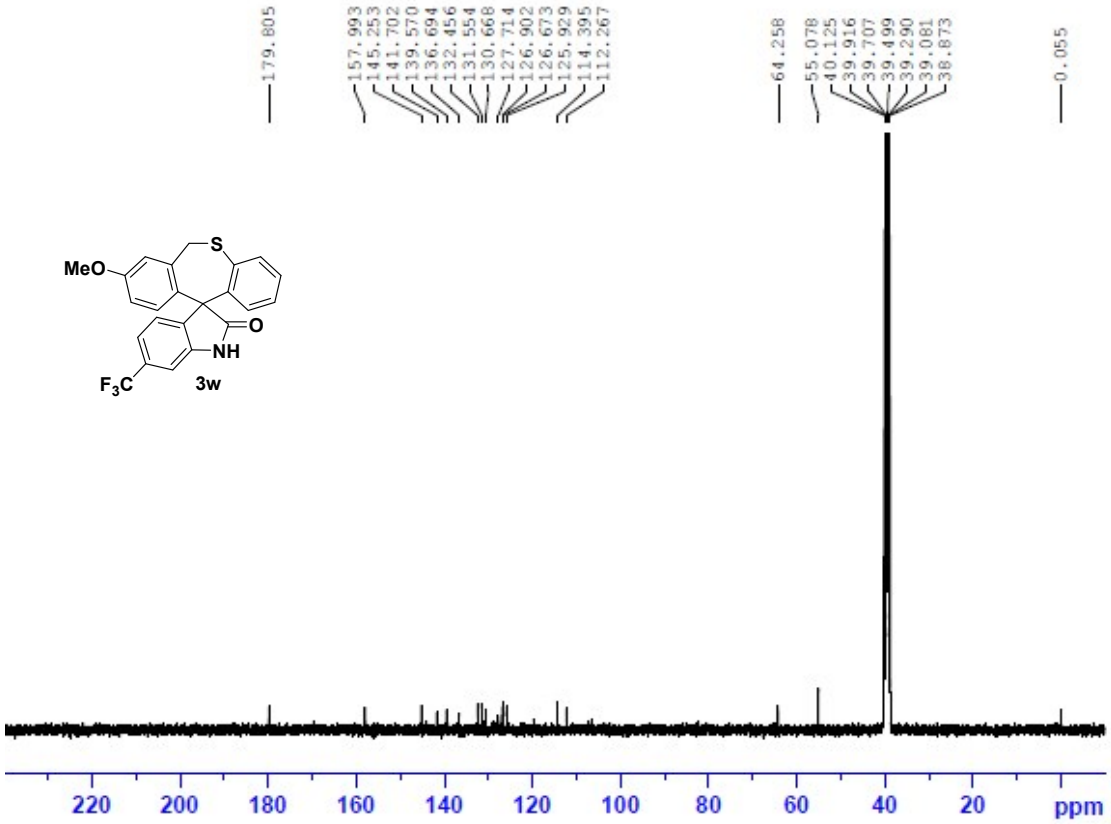
^{1}H ,^{13}C – NMR Data for 3v

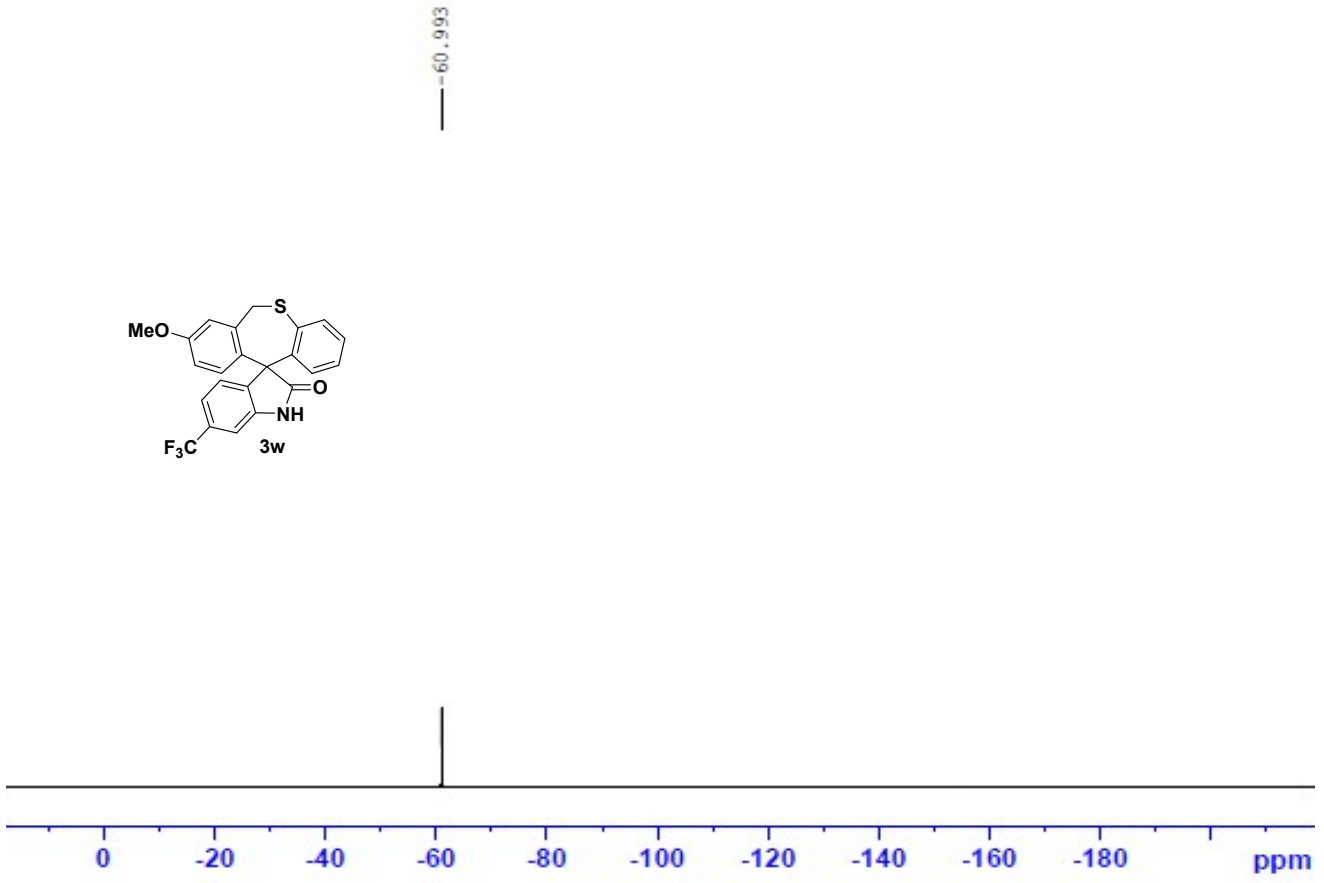



177.523
160.132
149.898
143.573
142.987
137.427
130.484
129.423
128.585
128.257
126.837
125.464
123.476
122.323
121.536
113.913
112.038
109.031
78.127
61.402
54.461
47.597
45.751
40.120
39.912
39.703
39.494
39.286
39.077
38.868
26.405
19.642
3v
200
180
160
140
120
100
80
60
40
20
0
ppm

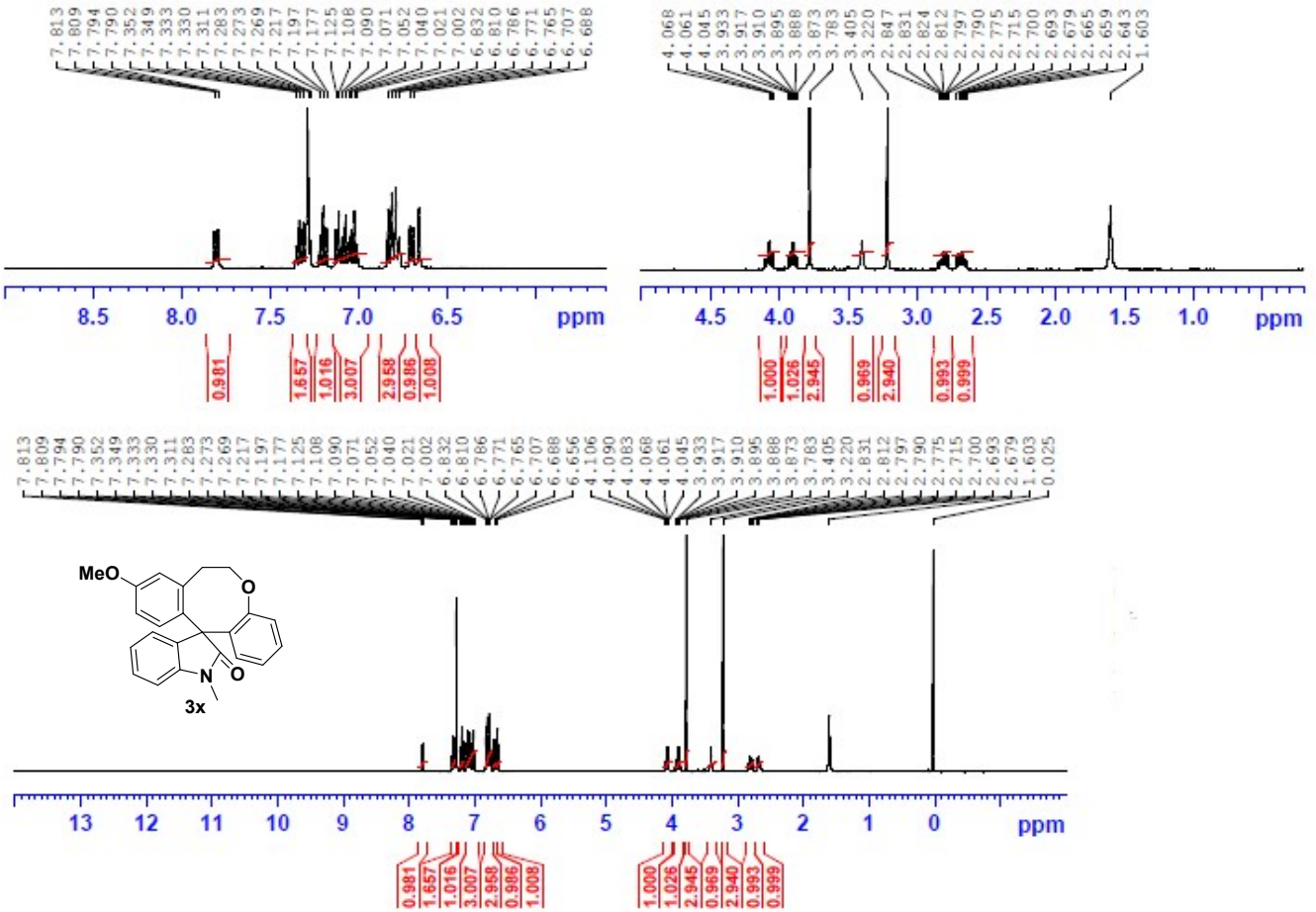
^{1}H ,^{13}C, ^{19}F – NMR Data for 3w

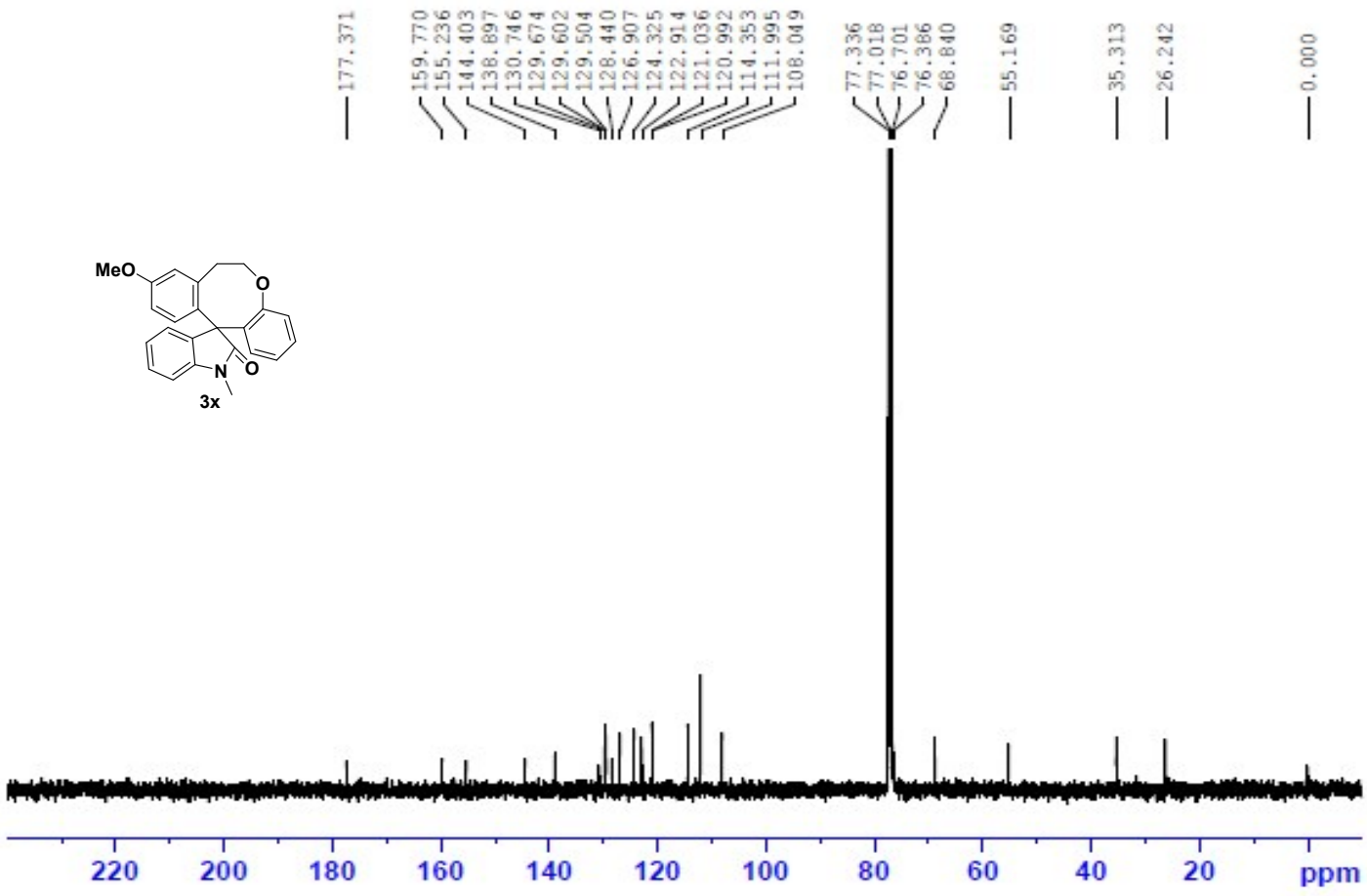



179.805
157.993
145.253
141.702
139.570
136.694
132.456
131.554
130.668
127.714
126.902
126.673
125.929
114.395
112.267
64.258
55.078
40.125
39.916
39.707
39.499
39.290
39.081
38.873
0.055
MeO
S
O
NH
F3C
3w
220
200
180
160
140
120
100
80
60
40
20
ppm

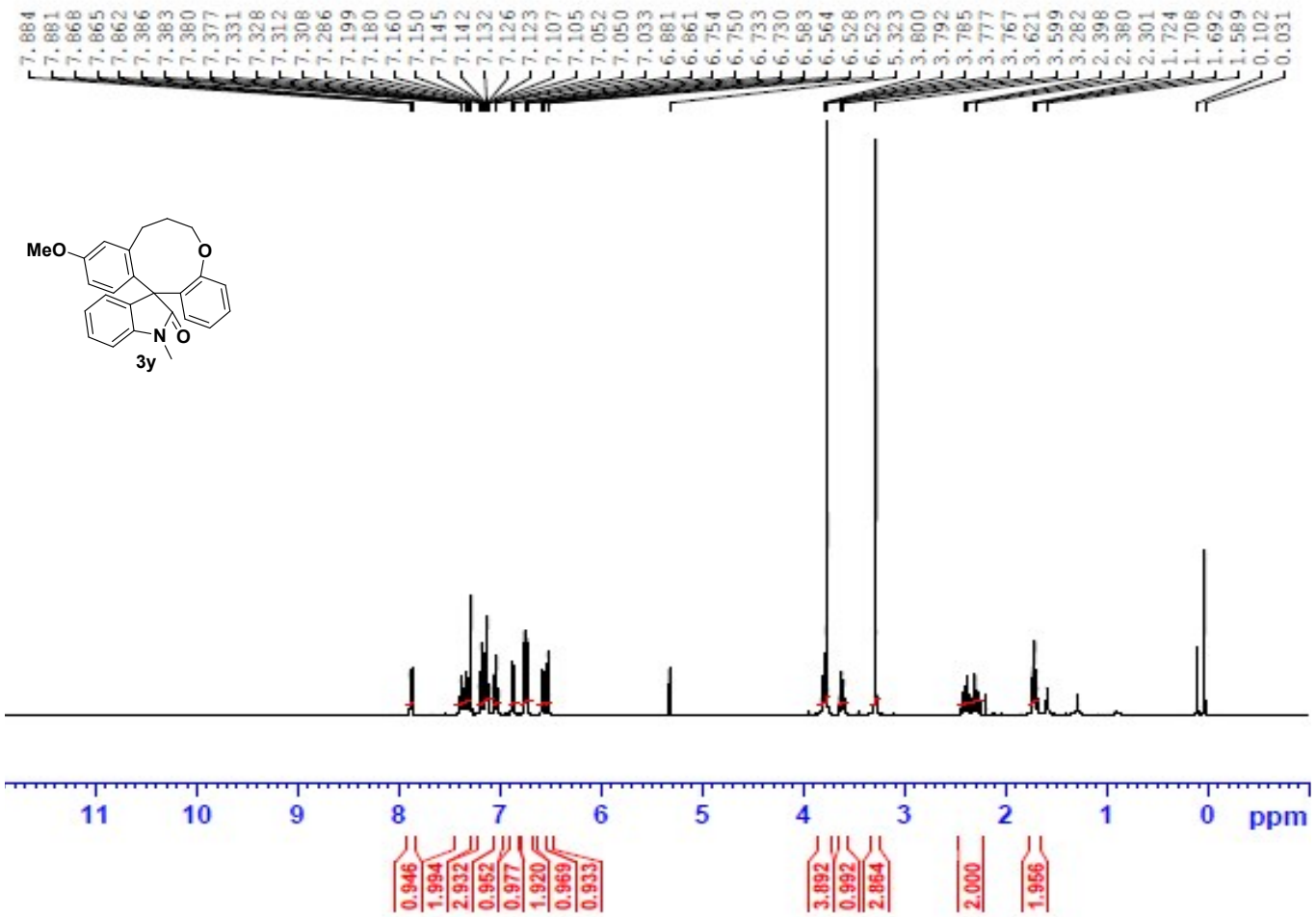

-60.993
MeO
S
O
NH
F3C
3w
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

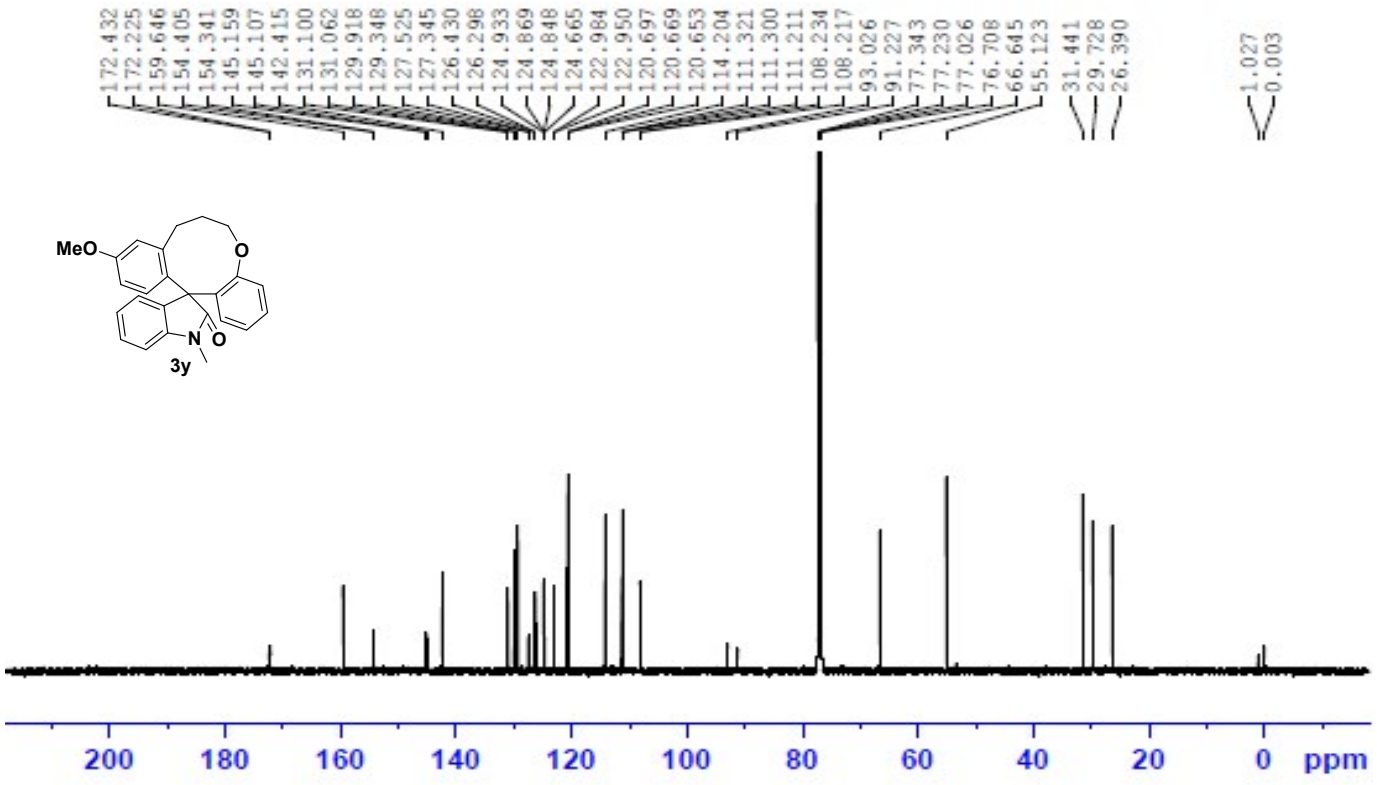
^{1}H ,^{13}C – NMR Data for 3x



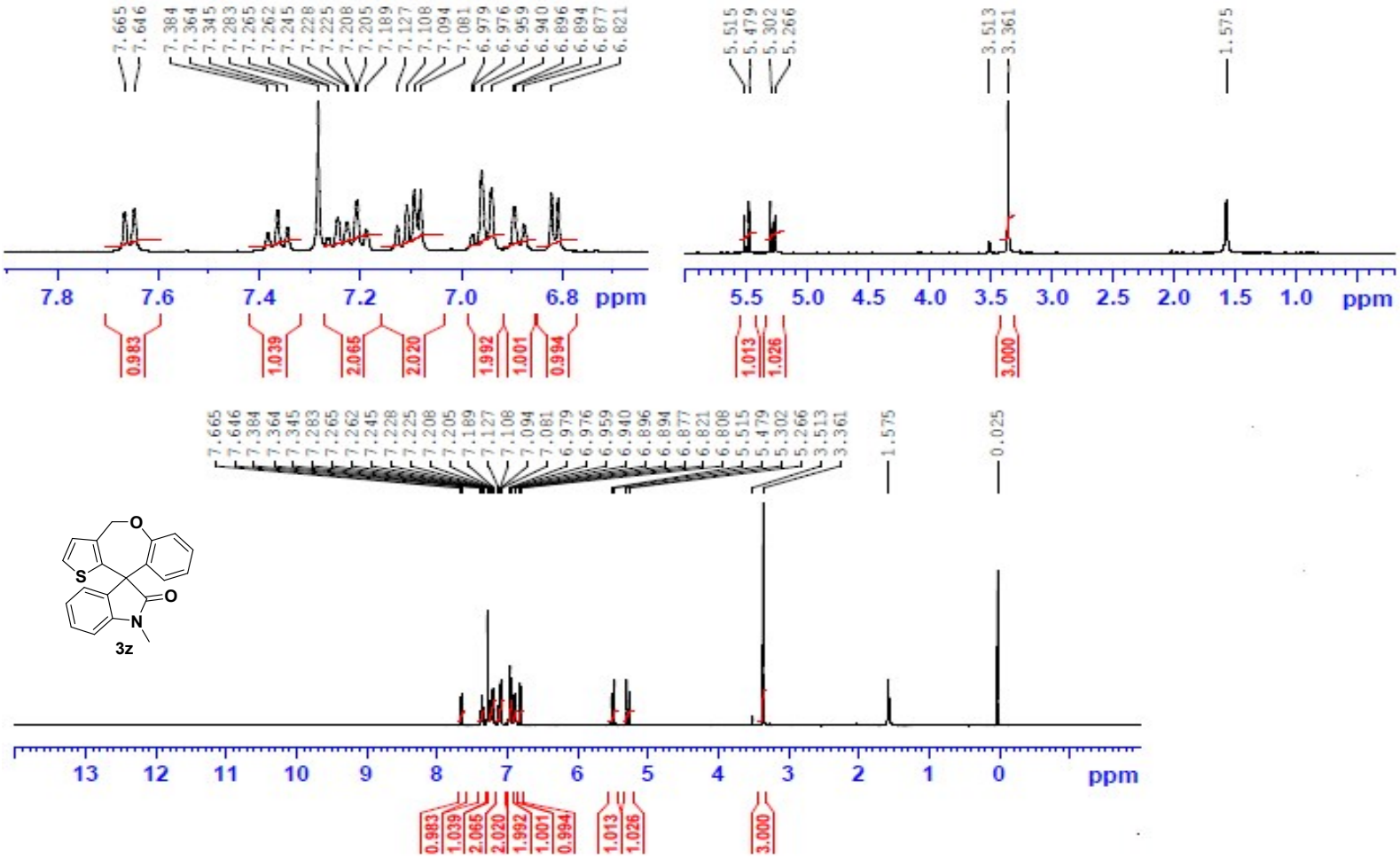

177.371
159.770
155.236
144.403
138.897
130.746
129.674
129.602
129.504
128.440
126.907
124.325
122.914
121.036
120.992
114.353
111.995
108.049
77.336
77.018
76.701
76.386
68.840
55.169
35.313
26.242
0.000
MeO
O
N
O
3x
220
200
180
160
140
120
100
80
60
40
20
ppm

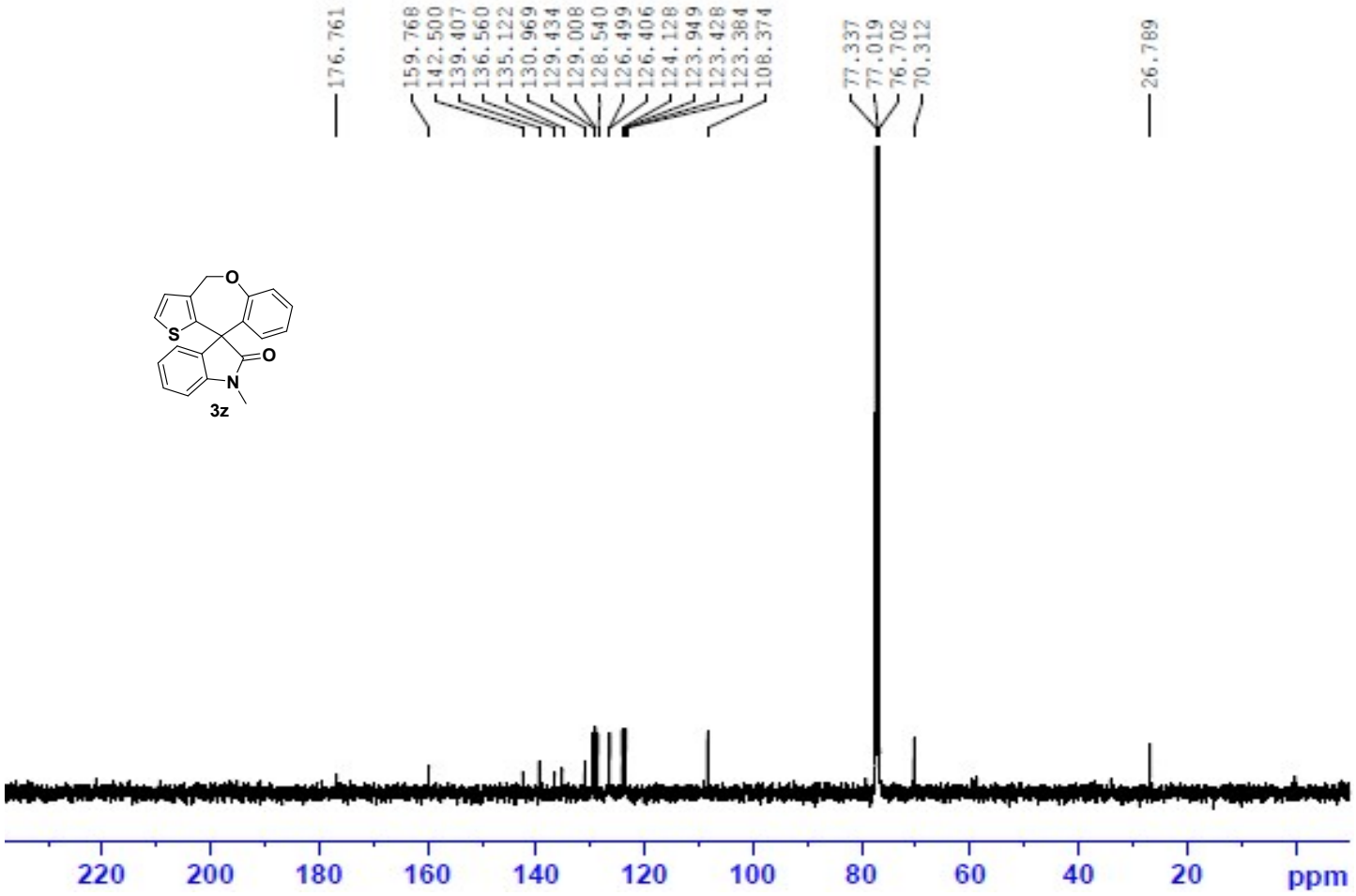
^{1}H ,^{13}C – NMR Data for 3y



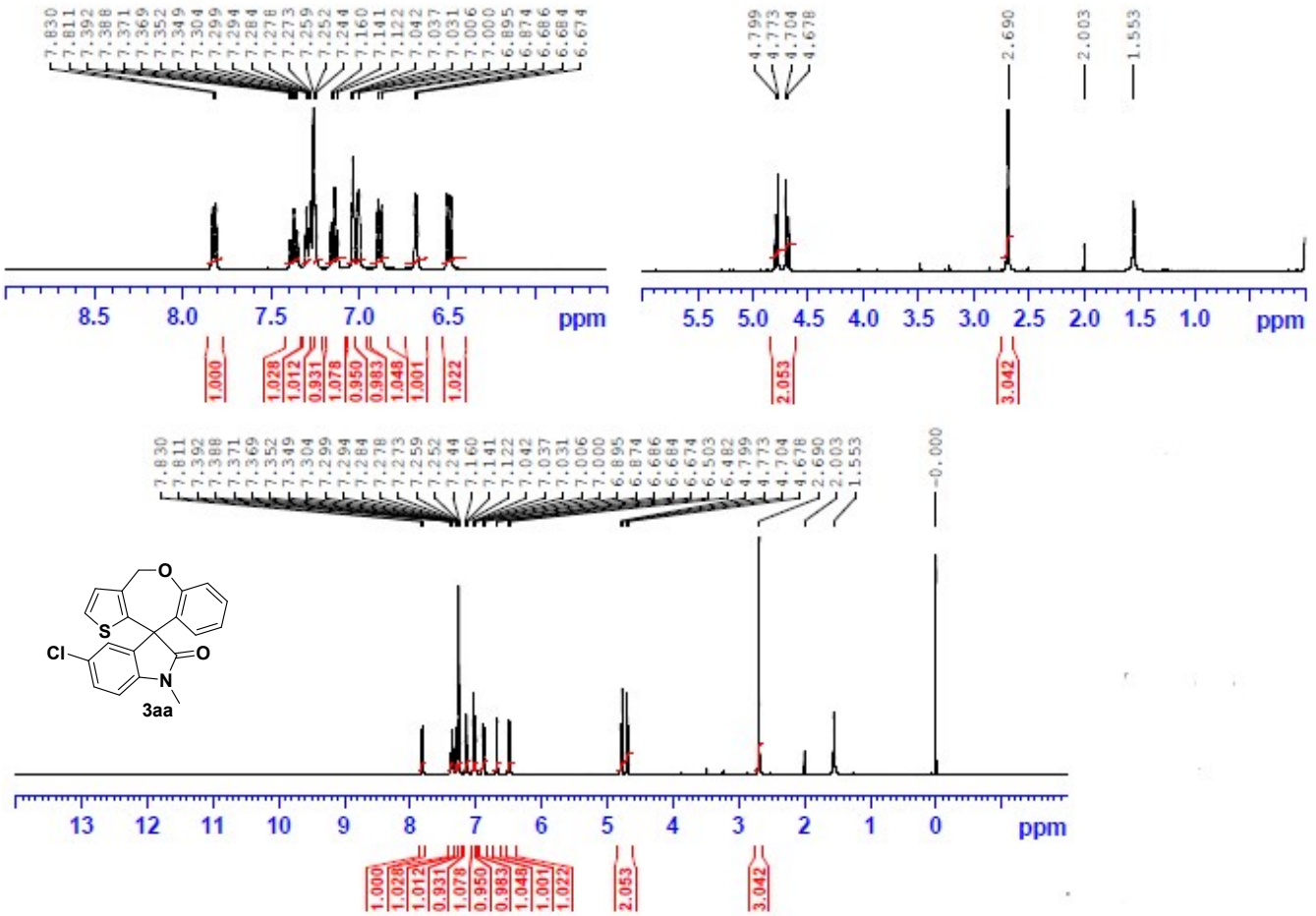

172.432
172.225
159.646
154.405
154.341
145.159
145.107
142.415
131.100
131.062
129.918
129.348
127.525
127.345
126.430
126.298
124.933
124.869
124.848
124.665
122.984
122.950
120.697
120.669
120.653
114.204
111.321
111.300
111.211
108.234
108.217
93.026
91.227
77.343
77.230
77.026
76.708
66.645
55.123
31.441
29.728
26.390
1.027
0.003
MeO
O
N
O
3y
200
180
160
140
120
100
80
60
40
20
0
ppm

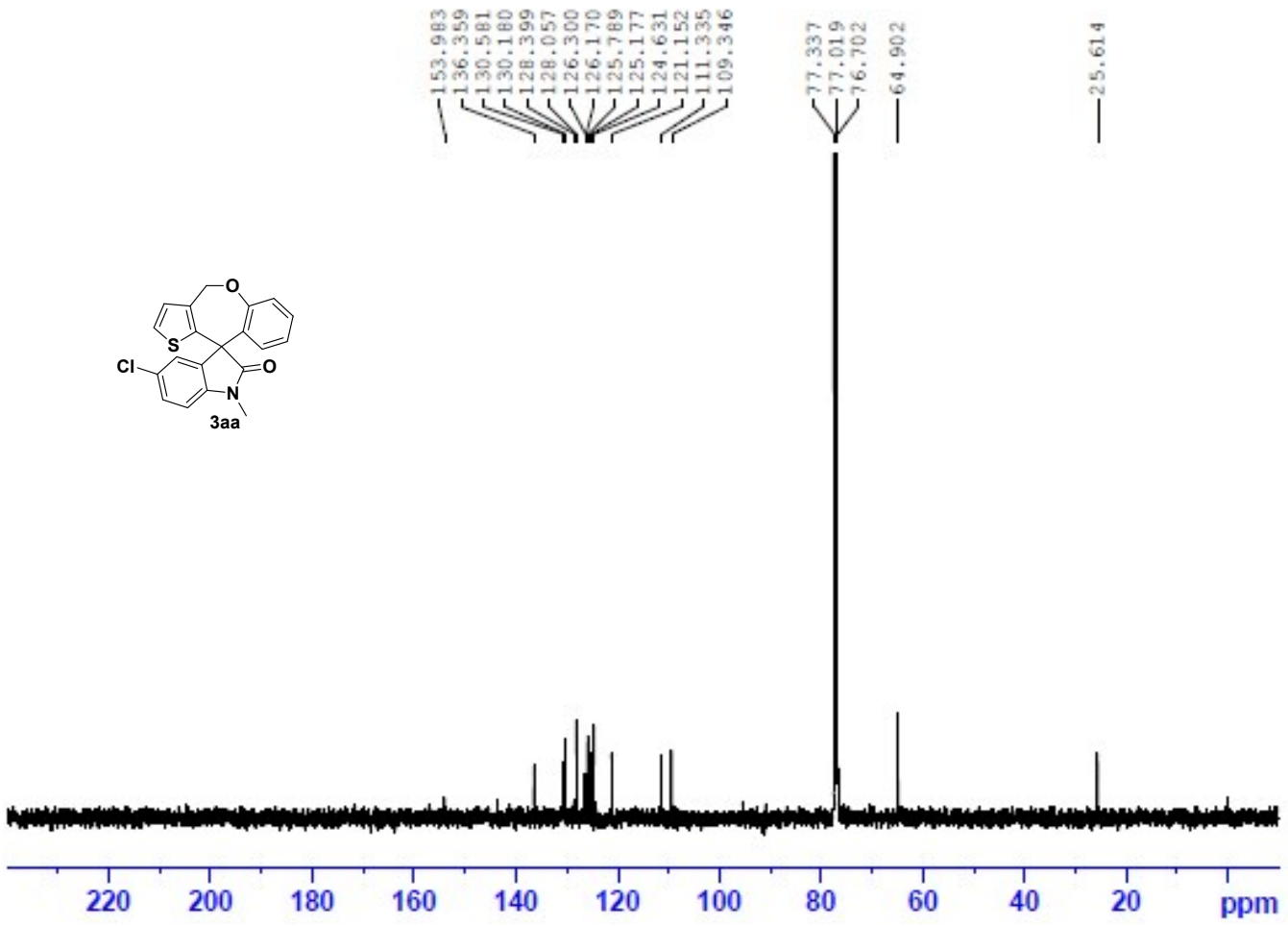
^{1}H ,^{13}C – NMR Data for 3z




176.761
159.768
142.500
139.407
136.560
135.122
130.969
129.434
129.008
128.540
126.499
126.406
124.128
123.949
123.428
123.384
108.374
77.337
77.019
76.702
70.312
26.789
O
S
O
N
3z
220
200
180
160
140
120
100
80
60
40
20
ppm

^{1}H ,^{13}C – NMR Data for 3aa




153.983
136.359
130.581
130.180
128.399
128.057
126.300
126.170
125.789
125.177
124.631
121.152
111.335
109.346
77.337
77.019
76.702
64.902
25.614
O
S
Cl
O
N
3aa
220
200
180
160
140
120
100
80
60
40
20
ppm

6. References

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