

Neat synthesis of isothiazole compounds, studies on their synthetic applications and photophysical properties

Anirban Bera,^{ac} Prasanta Patra,^b Abulkalam Azad,^a Sk Asraf Ali,^a Susanta Kumar Manna,^a Amit Saha,^{*c} Shubhankar Samanta^{*a}

^aDepartment of Chemistry, Bidhannagar College, Kolkata 700064, India

^bJhargram Raj College, Jhargram, West Bengal 721507, India

^cDepartment of Chemistry, Jadavpur University, Kolkata 700032, India

Email: chemshubha@gmail.com; Fax : (9133) 2337 4782 Mobile: 919775550193

Contents:

1. General information :	2 - 3
2. Characterization of data:	4 - 14
3. ¹H and ¹³C Spectra:	15–44
4. HRMS spectra:	45 - 57

General information:

^1H NMR spectra of all the synthesized compounds were recorded on a 400 MHz and 500 MHz spectrometers in CDCl_3 solvent using TMS as the internal standard. ^{13}C NMR was recorded in the same MHz instruments. 60-120 or 100-200 mesh silica gels (SRL) were used for column chromatographic purification. Progress of the reaction was monitored by using precoated silica gel 60 F254 TLC sheets (Merck). Petroleum ether (boiling range 60-80 °C) or n-hexane and ethyl acetate (b.p. 77.1 °C) were used as the eluent for column chromatographic separation. Solvents were distilled, dried and stored over molecular sieves (4 Å). The UV-Vis absorption spectra were recorded on UV-Vis spectrophotometer (Labtronics Model LT-291) and the fluorescence emission spectra were recorded on PerkinElmer Fluorescence Spectrometer (Model LS 45).

General Procedure for the preparation of 1a – 1o:

At first distilled chloroform (2 mL), DMF (3 mmol) were taken in a dry in a two-neck round-bottom flask and this round-bottom flask was placed in an ice-bath. Then PBr_3 (2.7 mmol) was added dropwise into the round-bottom flask and the resulting mixture was allowed to stir until a white complex formed. After that substrate was dissolved in distilled chloroform and slowly added to the resulting reaction. Finally, the reaction mixture was allowed for stirring 8 h at room temperature. The crude residue was purified by silica-gel (60-120 mesh) in column chromatography using petroleum ether and ethyl acetate (30:1) as an eluent to get the desired product **1**.

General Procedure for the preparation of 2a – 2o:

β -Bromovinyl aldehyde **1** (1mmol) and NH_4SCN (10 mmol) were taken in a one-neck round-bottom flask and it was placed in a heating oil bath. The reaction was heated for 10 minutes at 130 °C under neat conditions. The progress of the reaction was monitored by TLC. The crude residue was purified by silica-gel (100-200 mesh) in column chromatography using petroleum ether and ethyl acetate (20:1) as an eluent to get the desired product **2**.

General Procedure for the preparation of 3a – 3e:

β -Bromovinyl aldehyde **1** (1mmol), NH_4SCN (1 mmol) and *p*-toluidine (1 mmol) were taken in a one-neck round-bottom flask. A instantaneous change will occur by the change of colour within

2-3 minutes at room temperature under the neat condition. The crude residue was purified by silica-gel (100-200 mesh) in column chromatography using petroleum ether and ethyl acetate (30:1) as an eluent to get the desired product **3**.

General Procedure for the preparation of *N*-*p*-tolylformamide **3da:**

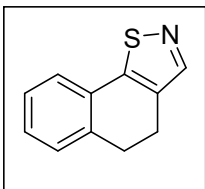
Substrate **3da** (1mmol) was taken in a one-neck round-bottom flask and dissolved in DMSO (3 mL). Then K₂CO₃ (1 mmol) was added to this reaction mixture and allowed for stirring 3h at 120 °C. The progress of the reaction was monitored by TLC. The crude residue was purified by silica-gel (100-200 mesh) in column chromatography using petroleum ether and ethyl acetate (5:1) as an eluent to get the desired product.

General Procedure for the preparation of **4a – 4g:**

Substrate **1** or **2** (1 mmol) was taken in a two-neck round-bottom flask. Then NBS (1 mmol) was dissolved in CH₂Cl₂ (3 mL) and added into this reaction mixture. After that AcOH (1 drop) was dissolved in CH₂Cl₂ and added to it. Finally, the reaction mixture was allowed for stirring under inert conditions at room temperature. The progress of the reaction was monitored by TLC. The crude residue was purified by silica-gel (100-200 mesh) in column chromatography using petroleum ether and ethyl acetate (50:1) as an eluent to get the desired product **4**.

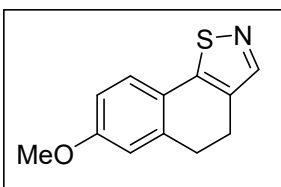
Characterization of data:

4,5-Dihydronaphtho[2,1-d]isothiazole: (2a)



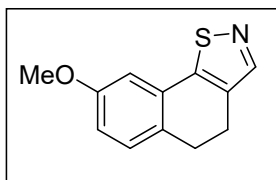
Brown liquid (50.0 mg, 72%). ^1H NMR (500 MHz, CDCl_3) δ 8.31 (s, 1H), 7.42 – 7.41 (m, 1H), 7.29 – 7.23 (m, 3H), 2.99 – 2.96 (m, 2H), 2.92 – 2.89 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 158.4, 156.8, 135.4, 134.0, 129.2, 128.6, 128.5, 127.3, 125.2, 29.0, 21.3. HRMS calcd. for $\text{C}_{11}\text{H}_{10}\text{NS}$: (M+H) $^+$ 188.0536, found : 188.0534.

7-Methoxy-4,5-dihydronaphtho[2,1-d]isothiazole: (2b)



Brown solid (48.0 mg, 90%), mp. 59 °C. ^1H NMR (500 MHz, CDCl_3) δ 8.20 (s, 1H), 7.28 (d, J = 8.5 Hz, 1H), 6.76 (d, J = 2.5 Hz, 1H), 6.70 (dd, J = 8.5, 2.5 Hz, 1H), 3.77 (s, 3H), 2.90 – 2.87 (m, 2H), 2.82 – 2.80 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 160.3, 158.4, 156.6, 137.4, 132.6, 126.5, 121.8, 114.2, 112.3, 55.4, 29.5, 21.3. HRMS calcd. for $\text{C}_{12}\text{H}_{12}\text{NOS}$: (M+H) $^+$ 218.0641, found : 218.0644.

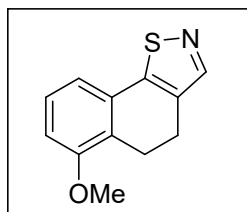
8-Methoxy-4,5-dihydronaphtho[2,1-d]isothiazole:(2c)



Brown solid (44.0 mg, 88%), mp. 64 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.31 (s, 1H), 7.19 (d, J = 8.4 Hz, 1H), 6.95 (d, J = 2.6 Hz, 1H), 6.82 (dd, J = 8.3, 2.6 Hz, 1H), 3.82 (s, 3H), 2.89 – 2.88 (m,

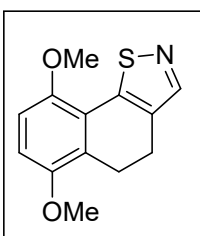
4H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.8, 158.5, 157.0, 134.5, 131.0, 129.4, 127.7, 114.8, 110.5, 55.6, 28.3, 21.8. HRMS calcd. for $\text{C}_{12}\text{H}_{12}\text{NOS}$: $(\text{M}+\text{H})^+$ 218.0641, found : 218.0638.

6-Methoxy-4,5-dihydronaphtho[2,1-d]isothiazole: (2d)



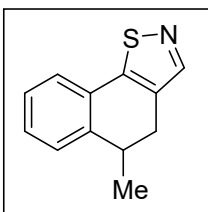
Yellow solid (24 mg, 83%), mp. 82 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.35 (s, 1H), 8.17 – 8.07 (m, 1H), 7.49 (d, J = 8.8 Hz, 1H), 6.76 (d, J = 8.8 Hz, 1H), 3.86 (s, 3H), 3.01 (t, J = 7.6 Hz, 2H), 2.89 – 2.85 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 156.1, 154.9, 153.9, 134.9, 131.9, 127.2, 122.9, 121.2, 112.4, 56.1, 22.4, 21.0. HRMS calcd. for $\text{C}_{12}\text{H}_{12}\text{NOS}$: $(\text{M}+\text{H})^+$ 218.0641, found : 218.0643.

6,9-Dimethoxy-4,5-dihydronaphtho[2,1-d]isothiazole: (2e)



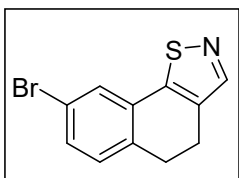
Yellow solid (32.0 mg, 76%), mp. 101 °C. ^1H NMR (500 MHz, CDCl_3) δ 8.28 (s, 1H), 6.84 (d, J = 9.0 Hz, 1H), 6.79 (d, J = 9.0 Hz, 1H), 3.95 (s, 3H), 3.83 (s, 3H), 3.00 (d, J = 8.0 Hz, 2H), 2.92 (d, J = 8.0 Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 154.5, 153.0, 151.0, 149.4, 132.7, 124.9, 119.8, 111.7, 108.8, 56.2, 56.0, 21.6, 20.8. HRMS calcd. for $\text{C}_{13}\text{H}_{14}\text{NO}_2\text{S}$: $(\text{M}+\text{H})^+$ 248.0747, found : 248.0744.

5-Methyl-4,5-dihydronaphtho[2,1-d]isothiazole: (2f)



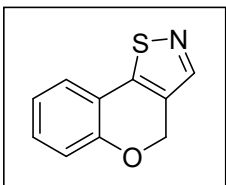
Brown liquid (45.0 mg, 68%). ^1H NMR (500 MHz, CDCl_3) δ 8.31 (s, 1H), 7.43 (d, $J = 7.5$ Hz, 1H), 7.32 – 7.28 (m, 2H), 7.26 – 7.23 (m, 1H), 3.14 (q, $J = 6.8$ Hz, 1H), 3.02 (dd, $J = 15.5$, 6.5 Hz, 1H), 2.73 (dd, $J = 15.5$, 6.0 Hz, 1H), 1.23 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 157.7, 157.3, 140.4, 132.7, 129.5, 127.7, 127.3, 127.1, 125.4, 33.5, 29.0, 20.5. HRMS calcd. for $\text{C}_{12}\text{H}_{12}\text{NS}$: $(\text{M}+\text{H})^+$ 202.0692, found : 202.0690.

8-Bromo-4,5-dihydronaphtho[2,1-d]isothiazole: (2g)



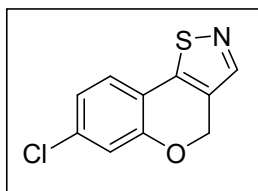
White solid (38.0 mg, 90%), mp. 70 °C. ^1H NMR (500 MHz, CDCl_3) δ 8.34 (s, 1H), 7.57 (d, $J = 1.7$ Hz, 1H), 7.40 (dd, $J = 8.1$, 1.7 Hz, 1H), 7.18 (d, $J = 8.1$ Hz, 1H), 2.96 – 2.94 (m, 4H). ^{13}C NMR (126 MHz, CDCl_3) δ 156.9, 156.8, 134.5, 134.2, 131.8, 130.4, 130.0, 127.8, 120.6, 28.6, 21.2. HRMS calcd. for $\text{C}_{11}\text{H}_9\text{BrNS}$: $(\text{M}+\text{H})^+$ 265.9641, found : 265.9642.

4H-chromeno[3,4-d]isothiazole: (2h)



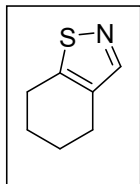
Red liquid (70.0 mg, 67%). ^1H NMR (500 MHz, CDCl_3) δ 8.23 (s, 1H), 7.35 (dd, $J = 7.7$, 1.2 Hz, 1H), 7.25 – 7.23 (m, 1H), 6.99 – 6.96 (m, 2H), 5.34 (s, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 154.8, 153.3, 152.2, 131.4, 128.5, 125.3, 122.3, 117.5, 117.2, 64.7. HRMS calcd. for $\text{C}_{10}\text{H}_8\text{NOS}$: $(\text{M}+\text{H})^+$ 190.0328, found : 190.0327.

7-Chloro-4H-chromeno[3,4-d]isothiazole: (2i)



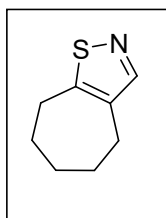
Yellow solid (22.0 mg, 65%), mp. 105 °C. ^1H NMR (500 MHz, CDCl_3) δ 8.29 (s, 1H), 7.38 (s, 1H), 7.24 – 7.21 (m, 1H), 6.96 (dd, J = 8.7, 1.2 Hz, 1H), 5.41 (s, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 153.6, 153.1, 150.6, 136.5, 130.9, 127.2, 124.8, 118.7, 118.6, 64.8. HRMS calcd. for $\text{C}_{10}\text{H}_7\text{ClNOS}$: $(\text{M}+\text{H})^+$ 223.9939, found : 223.9936.

4,5,6,7-Tetrahydrobenzo[d]isothiazole: (2j)



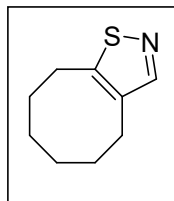
Yellow oil (39.0 mg, 62%). ^1H NMR (400 MHz, CDCl_3) δ 8.19 (s, 1H), 2.86 (t, J = 6.1 Hz, 2H), 2.68 (t, J = 6.1 Hz, 2H), 1.88 – 1.76 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 157.6, 131.0, 128.9, 23.4, 23.1, 22.9, 22.4. HRMS calcd. for $\text{C}_7\text{H}_{10}\text{NS}$: $(\text{M}+\text{H})^+$ 140.0536, found : 140.0533.

5,6,7,8-Tetrahydro-4H-cyclohepta[d]isothiazole: (2k)



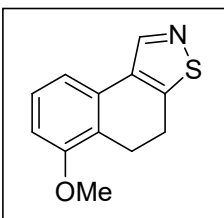
Yellow oil (72.0 mg, 70%). ^1H NMR (400 MHz, CDCl_3) δ 8.10 (s, 1H), 2.92 – 2.88 (m, 2H), 2.77 – 2.73 (m, 2H), 1.89 – 1.85 (m, 2H), 1.72 – 1.67 (m, 2H), 1.64 – 1.60 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.4, 138.8, 131.7, 32.2 (2C), 27.8, 27.8, 27.7. HRMS calcd. for $\text{C}_8\text{H}_{12}\text{NS}$: $(\text{M}+\text{H})^+$ 154.0692, found : 154.0688.

4,5,6,7,8,9-Hexahydrocycloocta[d]isothiazole: (2l)



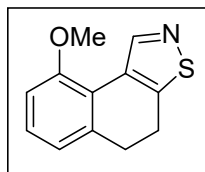
Yellow oil (62.0 mg, 86%). ^1H NMR (400 MHz, CDCl_3) δ 8.17 (s, 1H), 2.97 – 2.94 (m, 2H), 2.74 – 2.71 (m, 2H), 1.65 – 1.64 (m, 4H), 1.41 – 1.40 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.7, 145.6, 131.5, 31.4, 30.8, 25.6, 25.3, 24.7, 24.4. HRMS calcd. for $\text{C}_9\text{H}_{14}\text{NS}$: $(\text{M}+\text{H})^+$ 168.0849, found : 168.0848.

6-Methoxy-4,5-dihydronaphtho[1,2-d]isothiazole: (2m)



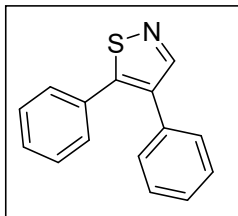
Yellow solid (36.0 mg, 66%), mp. 86 °C. ^1H NMR (500 MHz, CDCl_3) δ 10.21 (s, 1H), 7.31 – 7.28 (m, 1H), 7.20 (t, J = 7.5 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 3.91 (s, 3H), 3.07 – 2.98 (m, 4H). ^{13}C NMR (126 MHz, CDCl_3) δ 189.1, 156.3, 144.4, 132.1, 130.0, 127.8, 122.6, 114.4, 110.8, 55.5, 31.7, 20.4. HRMS calcd. for $\text{C}_{12}\text{H}_{12}\text{NOS}$: $(\text{M}+\text{H})^+$ 218.0641, found : 218.0638.

9-Methoxy-4,5-dihydronaphtho[1,2-d]isothiazole: (2n)



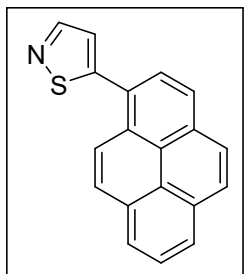
Yellow solid (35.0 mg, 71%), mp. 97 °C. ^1H NMR (400 MHz, CDCl_3) δ 10.04 (s, 1H), 7.28 (t, J = 7.9 Hz, 1H), 6.91 – 6.87 (m, 2H), 3.86 (s, 3H), 3.00 – 2.88 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.2, 168.1, 136.9, 131.7, 128.4, 126.9, 124.1, 115.0, 111.6, 61.6, 31.1, 21.1. HRMS calcd. for $\text{C}_{12}\text{H}_{12}\text{NOS}$: $(\text{M}+\text{H})^+$ 218.0641, found : 218.0644.

4,5-Diphenylisothiazole: (2o)



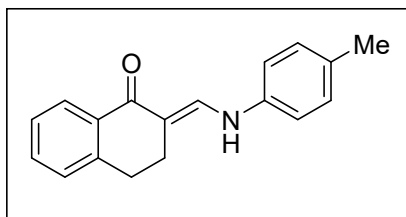
Yellow solid (23.0 mg, 80%), mp. 86 °C. ^1H NMR (300 MHz, CDCl_3) δ 8.52 (s, 1H), 7.34 - 7.32 (m, 10H). ^{13}C NMR (76 MHz, CDCl_3) δ 161.7, 159.3, 135.7, 133.0, 130.6, 129.2, 129.1 (2C), 129.0 (2C), 128.9 (2C), 128.8 (2C), 127.8. HRMS calcd. for $\text{C}_{15}\text{H}_{12}\text{NS}$: $(\text{M}+\text{H})^+$ 238.0692, found : 238.0690.

5-(Pyren-1-yl)isothiazole: (2p)



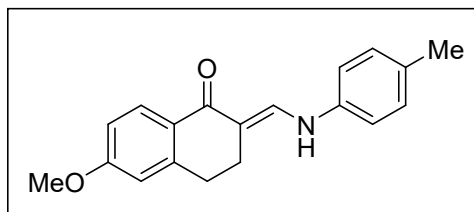
Brown solid (35.0 mg, 78%), mp. 108 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.66 (s, 1H), 8.30 (d, J = 9.2 Hz, 1H), 8.22 – 8.15 (m, 3H), 8.12 – 8.01 (m, 5H), 7.53 (s, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.1, 157.7, 132.0, 131.4, 130.8, 128.8, 128.6, 128.5, 127.8, 127.3, 126.5, 126.0, 125.6, 125.5, 125.0, 124.7, 124.6, 124.5, 124.1. HRMS calcd. for $\text{C}_{19}\text{H}_{12}\text{NS}$: $(\text{M}+\text{H})^+$ 286.0692, found : 286.0688.

(E)-2-((p-tolylamino)methylene)-3,4-dihydronaphthalen-1(2H)-one: (3a)



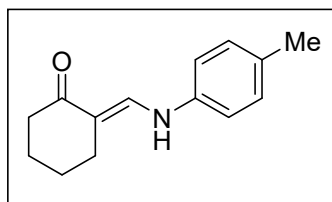
Brown solid (65.0 mg, 66%), mp. 116 °C. ^1H NMR (300 MHz, CDCl_3) δ 11.89 (d, J = 12.0 Hz, 1H), 7.95 (dd, J = 7.5, 1.5 Hz, 1H), 7.35 – 7.23 (m, 3H), 7.19 – 7.12 (m, 1H), 7.04 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 2.88 - 2.81 (m, 2H), 2.61 – 2.57 (m, 2H), 2.23 (s, 3H). ^{13}C NMR (76 MHz, CDCl_3) δ 187.5, 142.3, 142.1, 138.3, 135.3, 132.7, 131.9, 130.3(2C), 128.0, 126.9, 126.6, 116.1 (2C), 104.8, 29.9, 27.8, 20.8. HRMS calcd. for $\text{C}_{18}\text{H}_{18}\text{NO}$: $(\text{M}+\text{H})^+$ 264.1390, found : 264.1386.

(E)-6-methoxy-2-((p-tolylamino)methylene)-3,4-dihydronaphthalen-1(2H)-one: (3b)



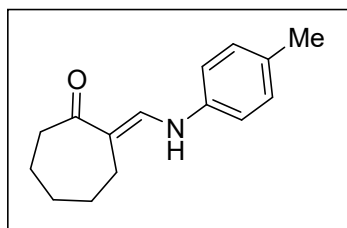
Brown solid (34.0 mg, 69%), mp. 122 °C. ¹H NMR (300 MHz, CDCl₃) δ 11.87 (d, *J* = 11.8 Hz, 1H), 8.02 (d, *J* = 8.6 Hz, 1H), 7.35-7.31 (m, 1H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.99 (d, *J* = 8.5 Hz, 2H), 6.89 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.73 (d, *J* = 2.4 Hz, 1H), 3.88 (s, 3H), 2.93 – 2.89 (m, 2H), 2.71 – 2.66 (m, 2H), 2.33 (s, 3H). ¹³C NMR (76 MHz, CDCl₃) δ 187.1, 162.6, 144.4, 141.5, 138.5, 132.4, 130.3 (2C), 128.9, 128.7, 121.4, 115.9 (2C), 112.7, 104.6, 55.5, 30.4, 28.1, 20.8. HRMS calcd. for C₁₉H₂₀NO₂: (M+H)⁺ 294.1496, found : 294.1494.

(E)-2-((p-tolylamino)methylene)cyclohexan-1-one: (3c)



Yellow solid (34.0 mg, 62%), mp. 85 °C. ¹H NMR (300 MHz, CDCl₃) δ 11.87 (d, *J* = 12.1 Hz, 1H), 7.14 – 7.08 (m, 3H), 6.92 (d, *J* = 8.4 Hz, 2H), 2.46 – 2.35 (m, 4H), 2.29 (s, 3H), 1.82 – 1.70 (m, 4H). ¹³C NMR (76 MHz, CDCl₃) δ 204.5, 142.2, 138.5, 132.2, 130.1 (2C), 115.8 (2C), 109.9, 44.7, 32.9, 31.8, 31.1, 25.2. HRMS calcd. for C₁₄H₁₈NO: (M+H)⁺ 216.1390, found : 216.1393.

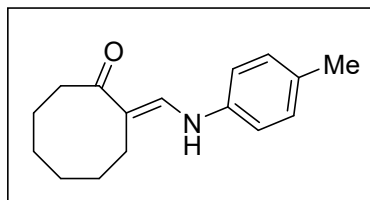
(E)-2-((p-tolylamino)methylene)cycloheptan-1-one: (3d)



Yellow solid (56.0 mg, 73%), mp. 91 °C. ¹H NMR (400 MHz, CDCl₃) δ 11.49 (d, *J* = 11.0 Hz, 1H), 7.15 (d, *J* = 12.0 Hz, 1H), 7.08 (d, *J* = 8.2 Hz, 2H), 6.89 (d, *J* = 8.3 Hz, 2H), 2.57 – 2.54 (m,

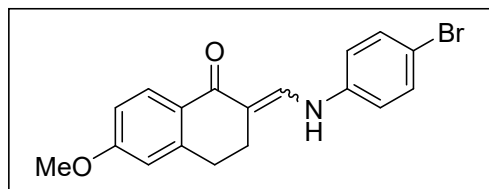
2H), 2.38 – 2.35 (m, 2H), 2.28 (s, 3H), 1.74 – 1.64 (m, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 204.5, 142.2, 138.6, 132.2, 130.2 (2C), 115.8 (2C), 110.0, 44.8, 38.2, 33.0, 32.0, 29.8, 22.8. HRMS calcd. for $\text{C}_{15}\text{H}_{20}\text{NO}$: $(\text{M}+\text{H})^+$ 230.1547, found : 230.1545.

(E)-2-((p-tolylamino)methylene)cyclooctan-1-one: (3e)



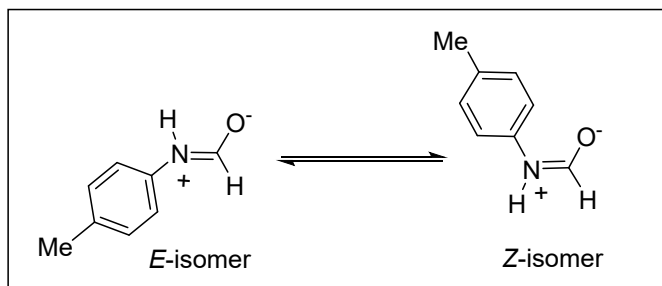
Yellow solid (90.0 mg, 76%), mp. 75 °C. ^1H NMR (400 MHz, CDCl_3) δ 11.87 (d, J = 11.7 Hz, 1H), 7.13 – 7.06 (m, 3H), 6.90 (d, J = 8.5 Hz, 2H), 2.57 – 2.53 (m, 2H), 2.44 – 2.40 (m, 2H), 2.27 (s, 3H), 1.77 – 1.71 (m, 2H), 1.59 – 1.50 (m, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 204.2, 142.7, 138.4, 132.4, 130.2(2C), 116.0(2C), 108.8, 39.7, 33.7, 30.5, 29.0, 26.3, 26.0, 20.8. HRMS calcd. for $\text{C}_{16}\text{H}_{22}\text{NO}$: $(\text{M}+\text{H})^+$ 244.1703, found : 244.1701.

2-(((4-bromophenyl)amino)methylene)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one: (3f)



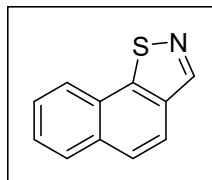
Brown solid (55 mg, 65%, Diastereomeric mixture). mp. 92-94 °C. ^1H NMR (300 MHz, CDCl_3) Z (major) δ 11.73 (d, J = 11.7 Hz, 1H), 7.90 (d, J = 8.6 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.17 – 7.16 (m, 2H), 6.84 – 6.80 (m, 2H), 6.79 – 6.75 (m, 1H), 3.76 (s, 3H), 2.81 – 2.77 (m, 2H), 2.59 – 2.54 (m, 2H); ^1H NMR (300 MHz, CDCl_3) E (minor) δ 7.21 – 7.18 (m, 2H), 7.03 – 6.97 (m, 1H), 6.89 – 6.86 (m, 1H), 6.69 – 6.62 (m, 2H), 6.47 – 6.45 (m, 2H), 3.71 (s, 3H), 2.74 – 2.69 (m, 2H), 2.48 – 2.39 (m, 2H). ^{13}C NMR (76 MHz, CDCl_3) δ 189.9, 187.6, 162.8, 144.6, 144.2, 143.0, 140.1, 140.0, 132.6, 132.3, 132.1, 132.0, 131.9, 130.6, 129.7, 129.1, 128.4, 124.3, 122.2, 121.4, 117.2, 116.8, 116.6, 115.5, 114.9, 113.6, 112.8, 112.7, 111.4, 111.2, 110.7, 109.9, 105.8, 55.5, 55.4, 30.4, 30.2, 28.1, 26.9, 23.5. HRMS calcd. for $\text{C}_{18}\text{H}_{17}\text{BrNO}_2$: $(\text{M}+\text{H})^+$ 358.0444, found : 358.0448.

N-p-tolylformamide: (3da)



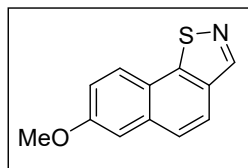
Brown liquid (20 mg, 65%, Diastereomeric mixture). ^1H NMR (500 MHz, CDCl_3) (*E*-isomer) δ 8.64 (d, J = 11.5 Hz, 1H), 7.44 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.3 Hz, 2H), 2.36 (s, 3H). (*Z*-isomer) 8.37 (m, 1H), 7.15 (d, 2H, J = 8.5 Hz), 7.01 (d, J = 8.3 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) (*E*-isomer) δ 162.5, 135.1, 134.4, 130.2 (2C), 129.8, 129.5 (2C), 20.8. (*Z*-isomer) 158.8, 134.2, 133.9, 121.1, 119.9 (2C), 119.2 (2C), 20.7 HRMS calcd. for $\text{C}_8\text{H}_{10}\text{NO}$: ($\text{M}+\text{H}$) $^+$ 136.0764, found : 136.0761.

Naphtho[2,1-d]isothiazole: (4a)



Yellow solid (45 mg, 88%), mp. 126 $^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 8.97 (s, 1H), 8.12 – 8.10 (m, 1H), 7.98 – 7.96 (m, 1H), 7.92 (d, J = 8.7 Hz, 1H), 7.74 (d, J = 8.6 Hz, 1H), 7.64 – 7.62 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.6, 154.6, 153.2, 132.1, 129.0, 128.1, 127.4, 126.7, 126.3, 125.4, 120.6. HRMS calcd. for $\text{C}_{11}\text{H}_8\text{NS}$: ($\text{M}+\text{H}$) $^+$ 186.0379, found : 186.0377.

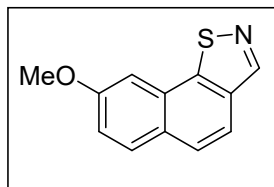
7-Methoxynaphtho[2,1-d]isothiazole:(4b)



Off white solid (20 mg, 67%), mp. 142 $^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 8.93 (s, 1H), 8.18 (d, J = 9.1 Hz, 1H), 8.06 (d, J = 8.9 Hz, 1H), 7.97 (d, J = 9.1 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 7.28 (m, 1H), 4.06 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 157.5, 155.5, 153.4, 132.4, 131.0, 128.9,

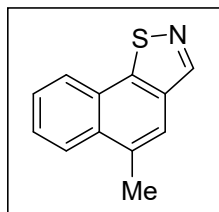
126.1, 125.3, 122.3, 121.9, 113.6, 57.1. HRMS calcd. for $C_{12}H_{10}NOS$: $(M+H)^+$ 216.0485, found : 216.0484.

8-Methoxynaphtho[2,1-d]isothiazole: (4c)



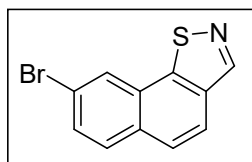
Off white solid (27 mg, 58%), mp. 155 °C. 1H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.16 (s, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.58 (d, J = 8.6 Hz, 1H), 7.46 (s, 1H), 7.30 (s, 1H), 4.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 155.8, 154.7, 133.3, 127.4, 126.3, 125.3, 119.3, 114.7, 108.4, 104.8, 56.6. HRMS calcd. for $C_{12}H_{10}NOS$: $(M+H)^+$ 216.0485, found : 216.0488.

5-Methylnaphtho[2,1-d]isothiazole: (4d)



Yellow liquid (32 mg, 52%). 1H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.06 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 7.7 Hz, 1H), 7.76 – 7.58 (m, 3H), 2.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7, 155.3, 152.4, 134.2, 131.8, 128.7, 127.2, 125.8, 125.7, 120.4, 116.3, 18.6. HRMS calcd. for $C_{12}H_{10}NS$: $(M+H)^+$ 200.0536, found : 200.0539.

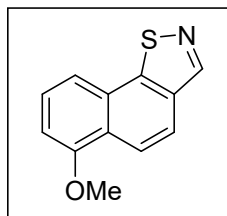
8-Bromonaphtho[2,1-d]isothiazole: (4e)



White solid (48 mg, 72%), mp. 122 °C. 1H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.27 (s, 1H), 7.97 (d, J = 8.7 Hz, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.73 (d, J = 8.6 Hz, 2H). ^{13}C NMR (126 MHz,

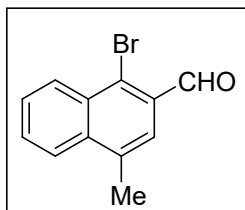
CDCl_3) δ 155.5 (2C), 151.8, 134.4, 131.2, 130.4, 127.6, 127.3, 126.2, 121.2, 121.0. HRMS calcd. for $\text{C}_{11}\text{H}_7\text{BrNS}$: $(\text{M}+\text{H})^+$ 263.9484, found : 263.9481.

6-Methoxynaphtho[2,1-d]isothiazole: (4f)



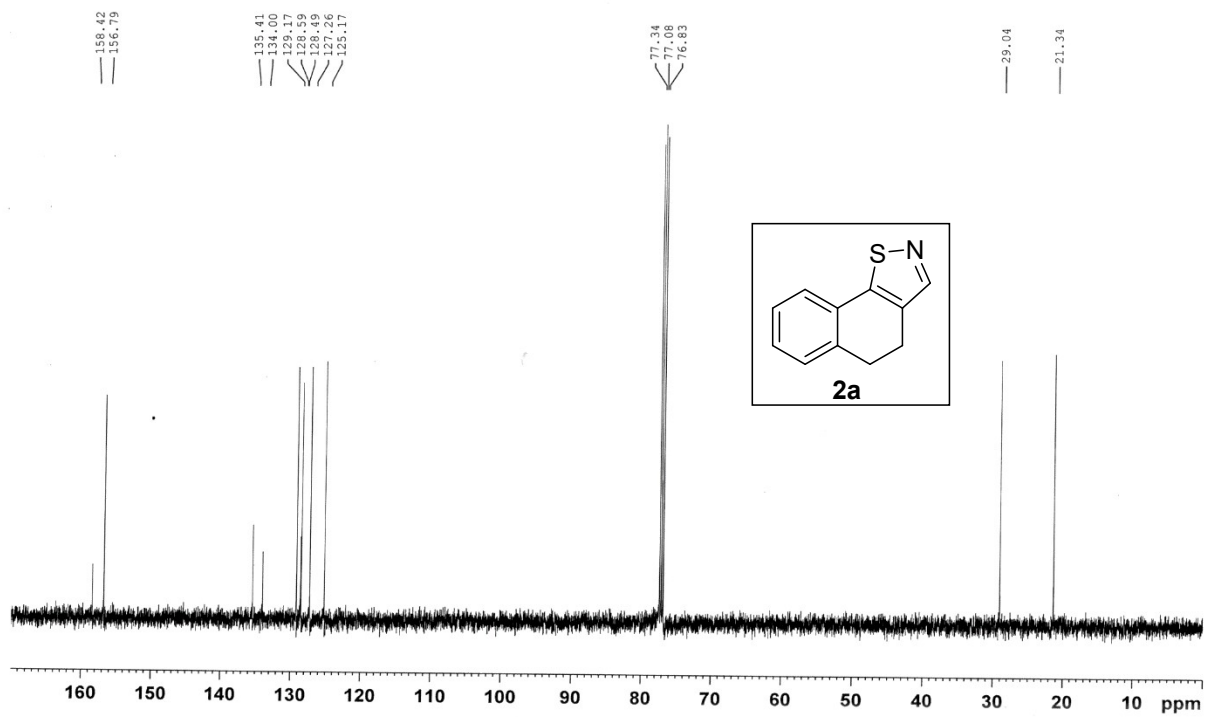
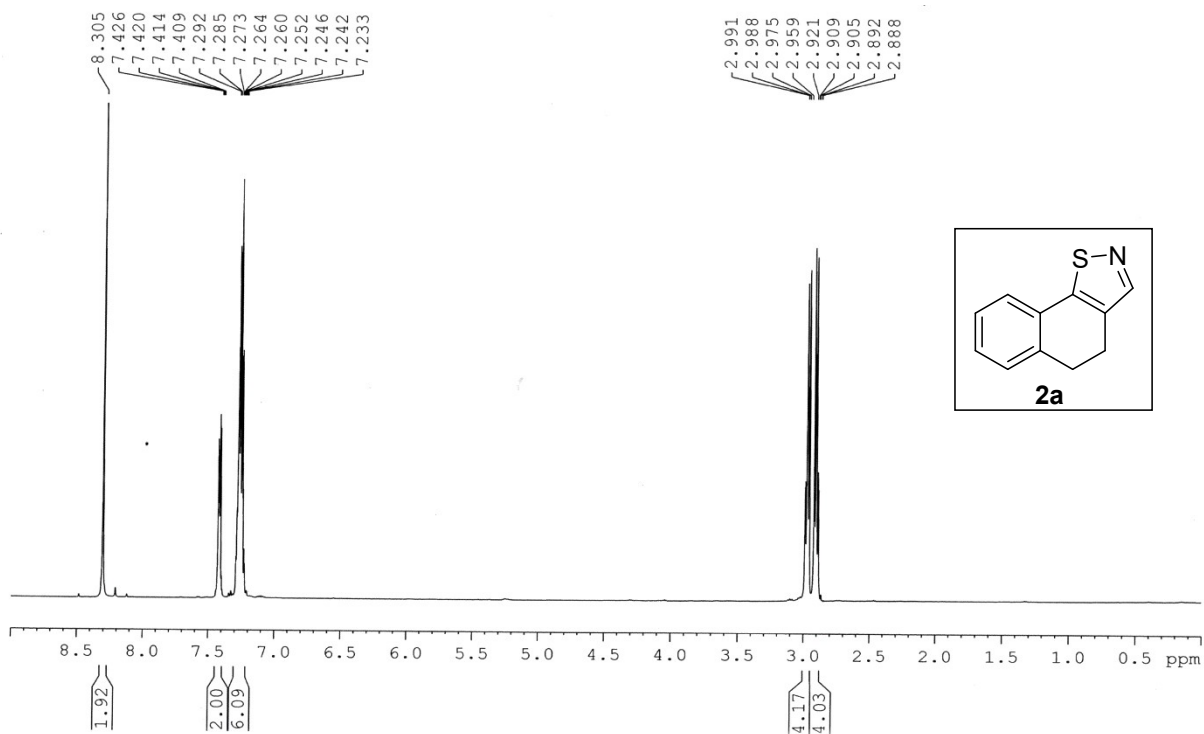
Off white solid (25 mg, 76%), mp. 91 °C. ^1H NMR (300 MHz, CDCl_3) δ 9.05 (s, 1H), 8.37 – 8.31 (m, 2H), 8.02 (d, J = 8.9 Hz, 1H), 7.88 (d, J = 8.5 Hz, 1H), 6.93 (d, J = 8.5 Hz, 1H), 4.06 (s, 3H). ^{13}C NMR (76 MHz, CDCl_3) δ 155.6, 153.9, 152.0, 135.8, 131.5, 128.3, 127.2, 125.8, 121.1, 112.3, 107.3, 56.2. HRMS calcd. for $\text{C}_{12}\text{H}_{10}\text{NOS}$: $(\text{M}+\text{H})^+$ 216.0485, found : 216.0480.

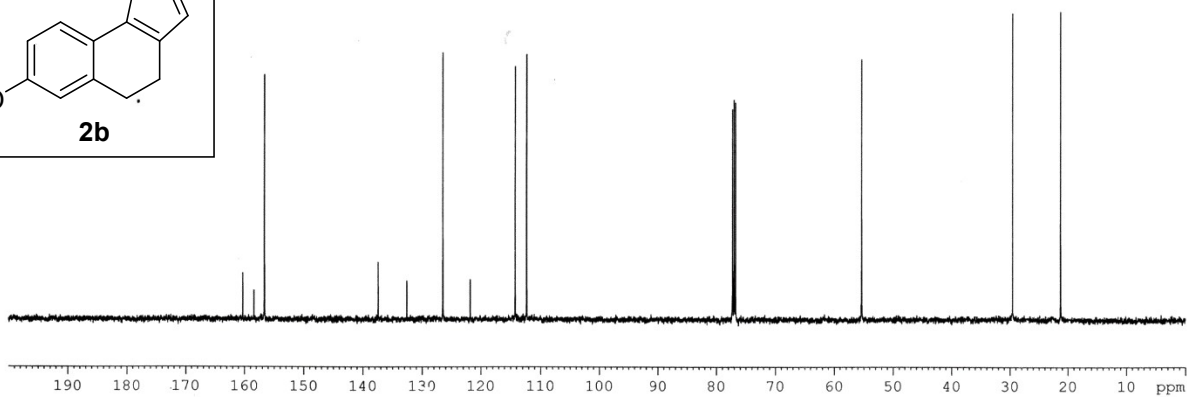
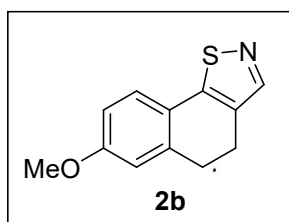
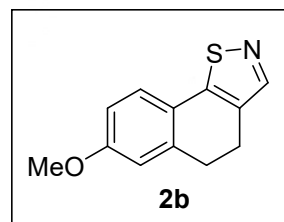
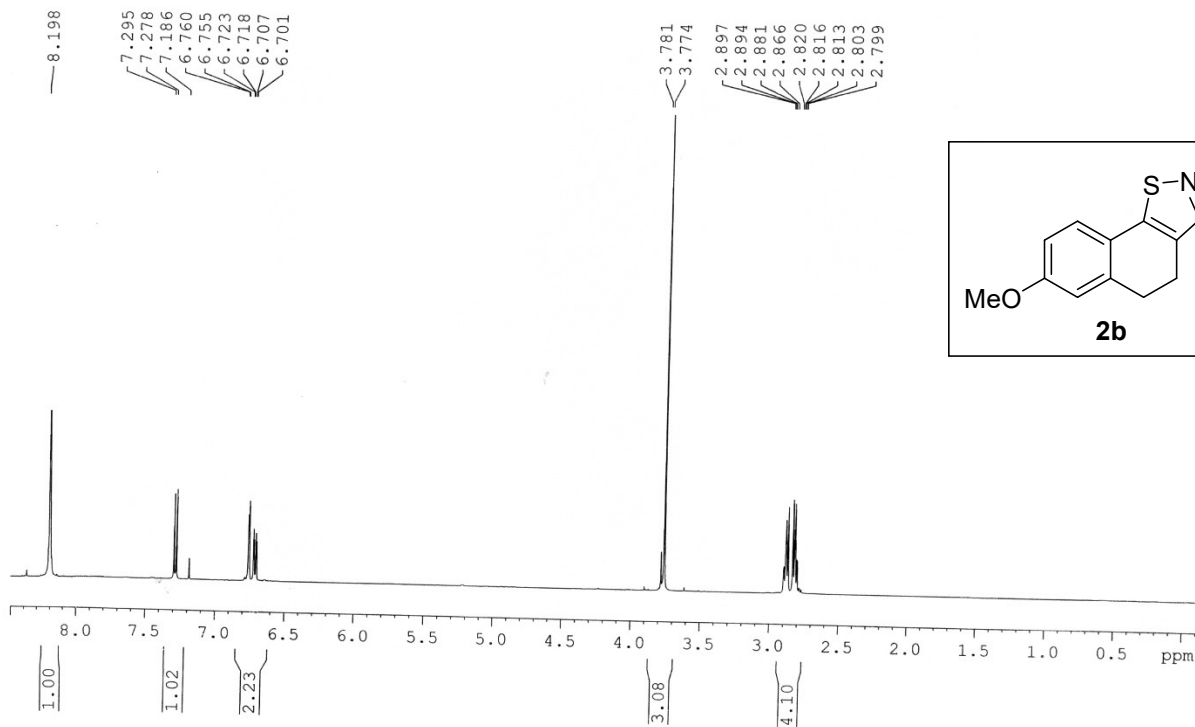
1-Bromo-4-methyl-2-naphthaldehyde: (4g)

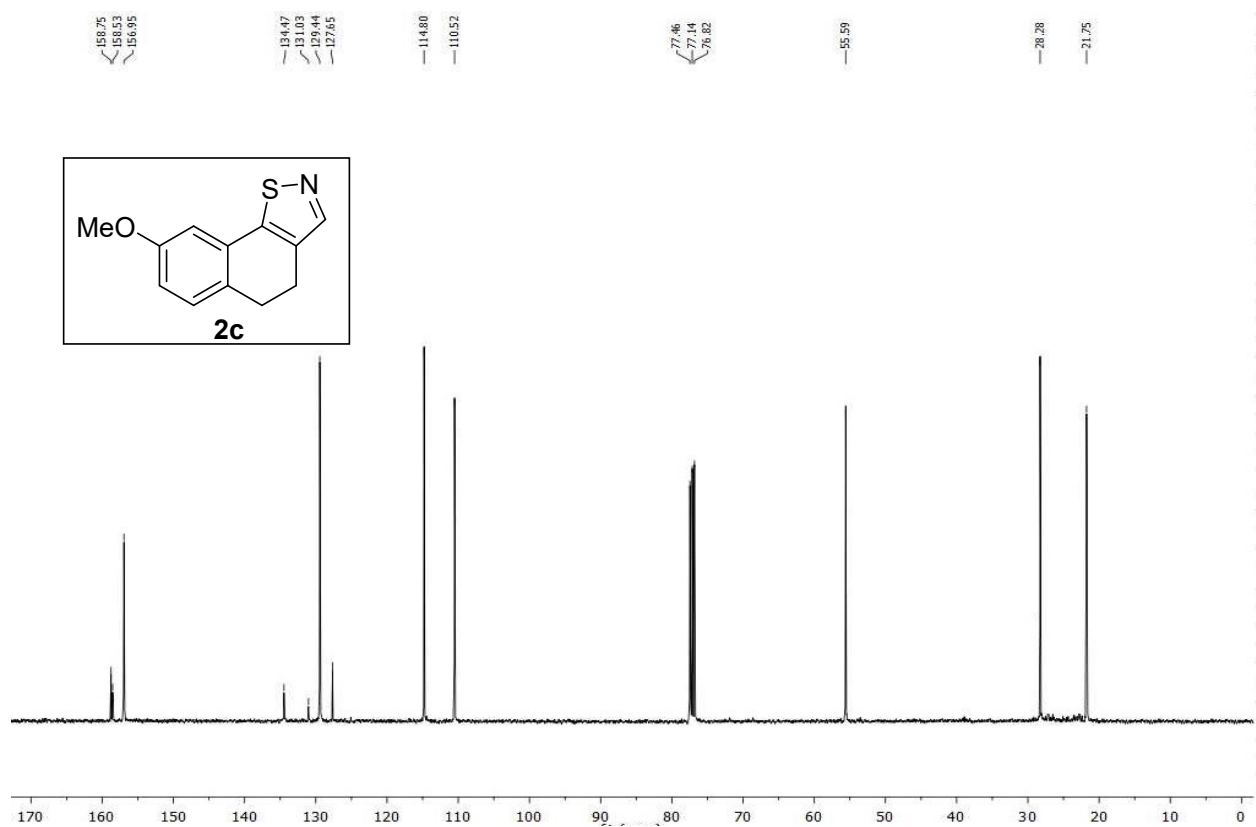
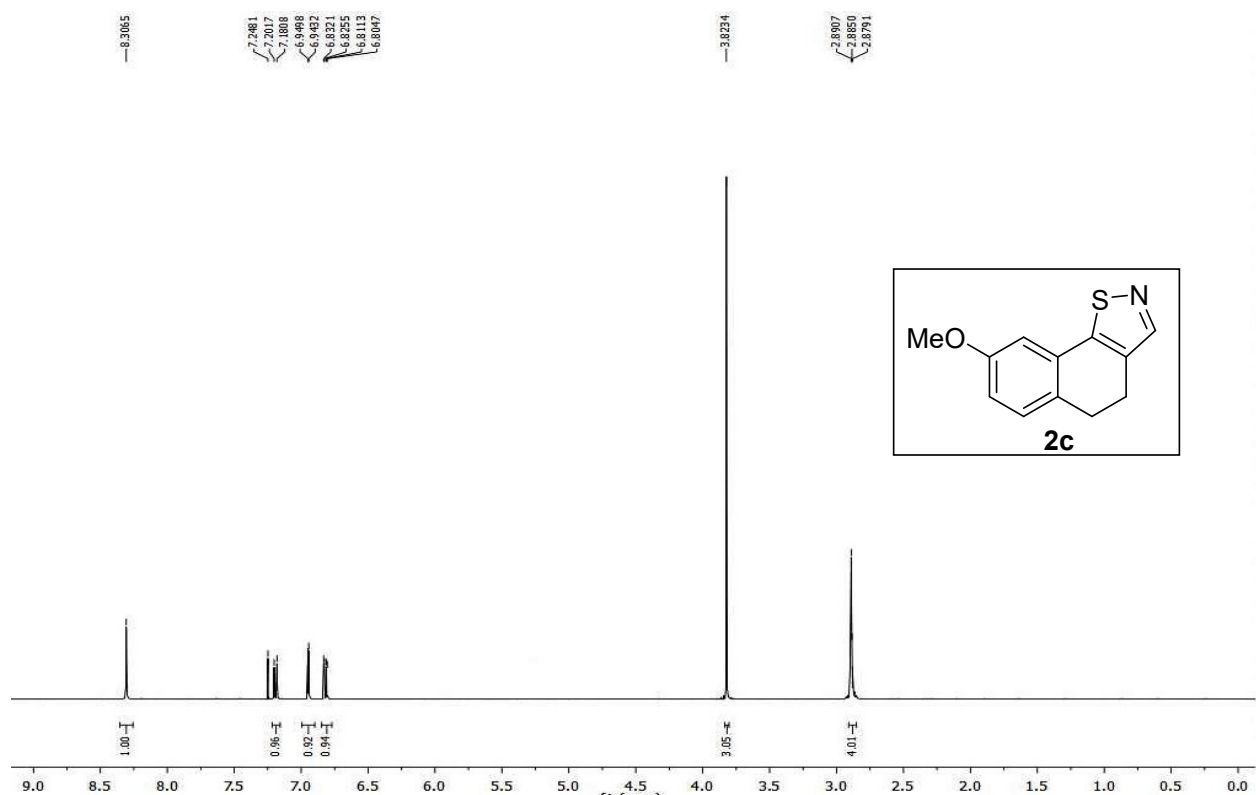


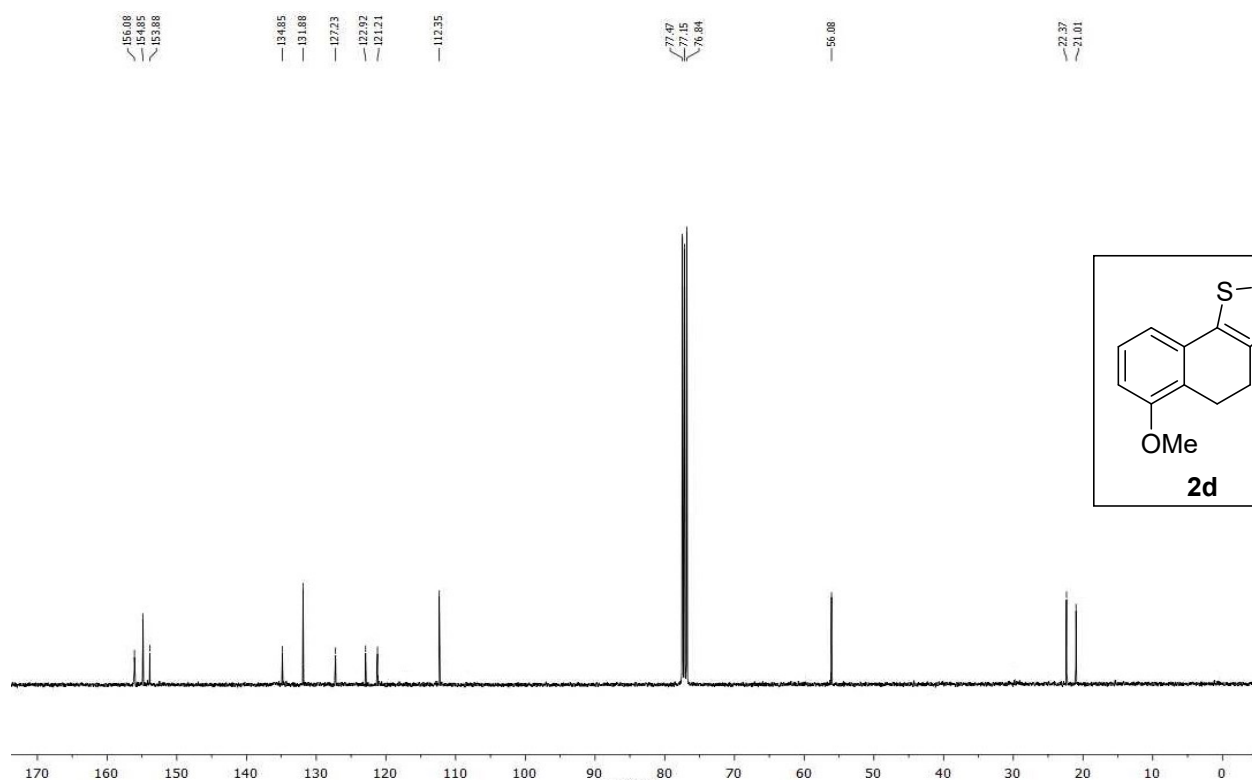
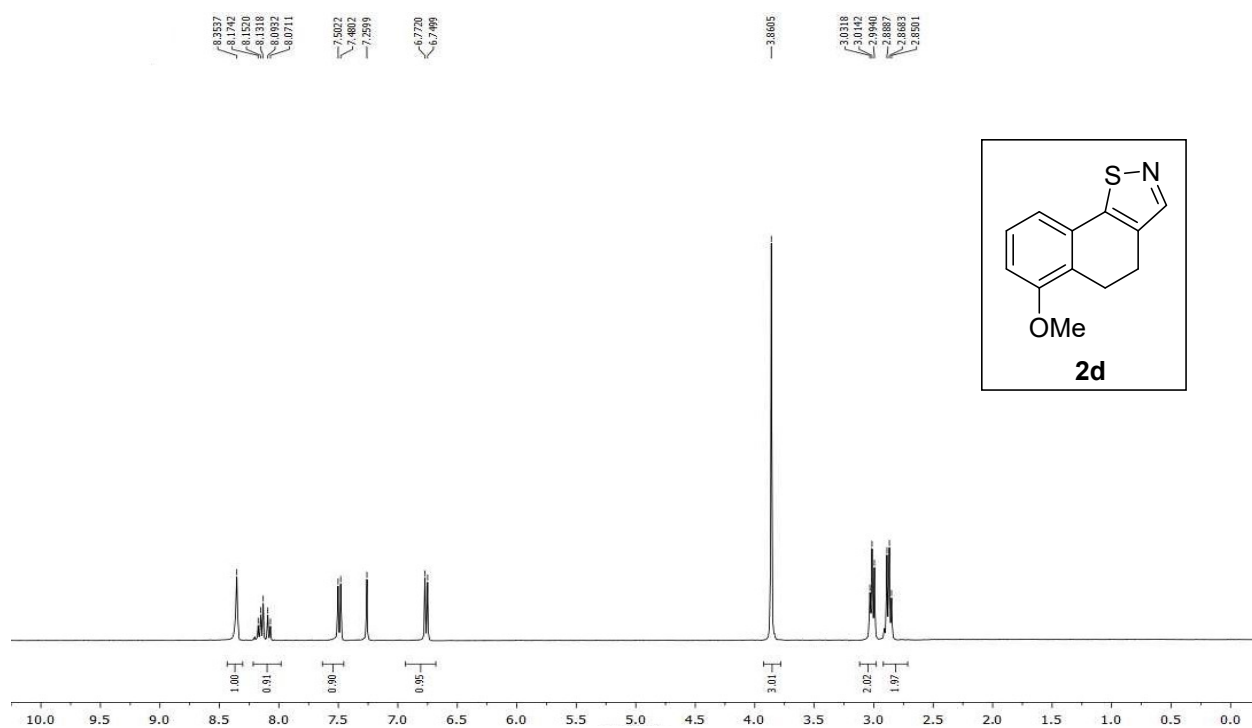
Off white solid (45 mg, 61 %), mp. 86 °C. ^1H NMR (300 MHz, CDCl_3) δ 10.51 (s, 1H), 8.42 – 8.39 (m, 1H), 7.89 – 7.87 (m, 1H), 7.64 – 7.54 (m, 3H), 2.56 (s, 3H). ^{13}C NMR (76 MHz, CDCl_3) δ 193.0, 136.7, 135.0, 132.0, 130.8, 129.7, 129.4, 128.7, 127.7, 124.9, 124.4, 19.3. HRMS calcd. for $\text{C}_{12}\text{H}_{10}\text{BrO}$: $(\text{M}+\text{H})^+$ 248.9917, found : 248.9915.

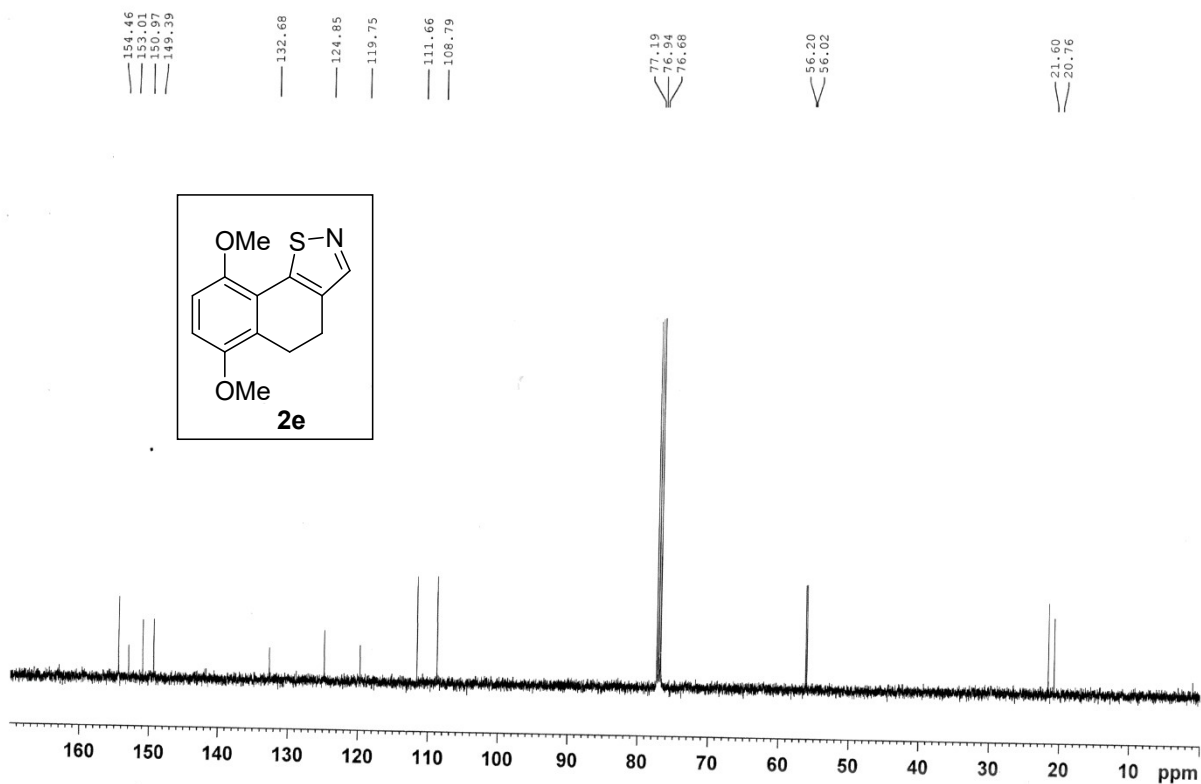
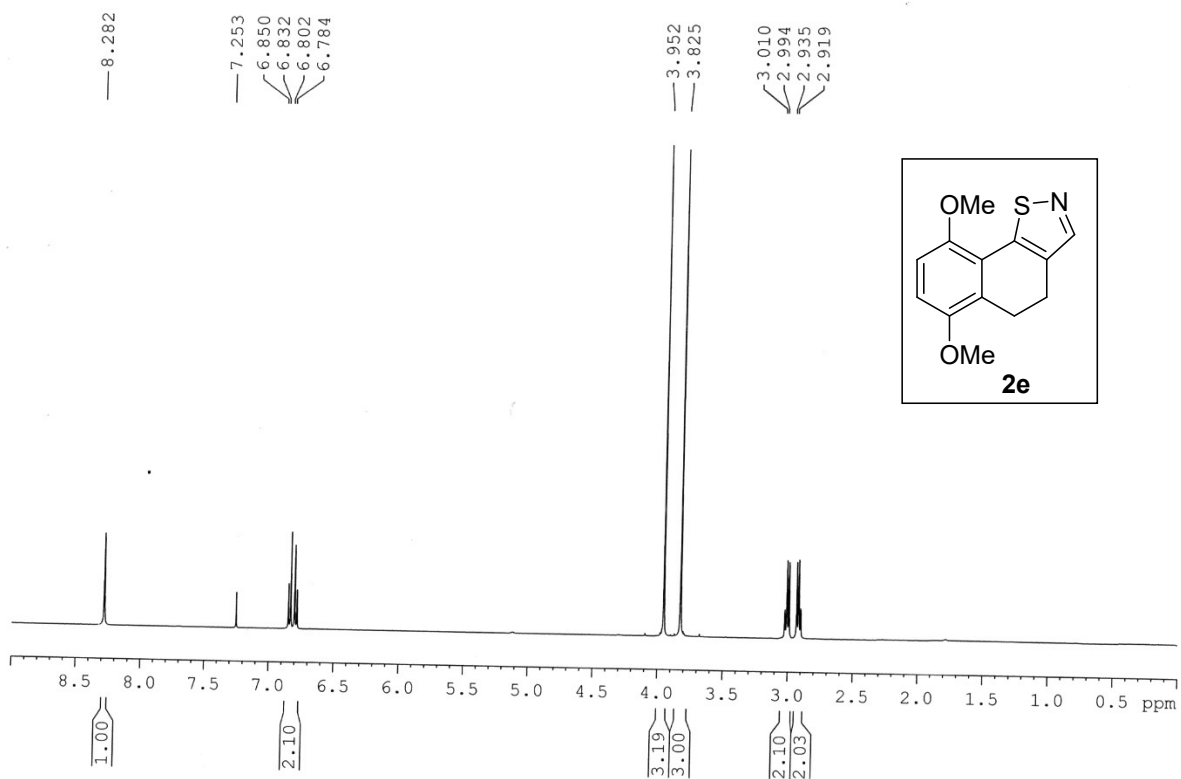
^1H and ^{13}C spectra:

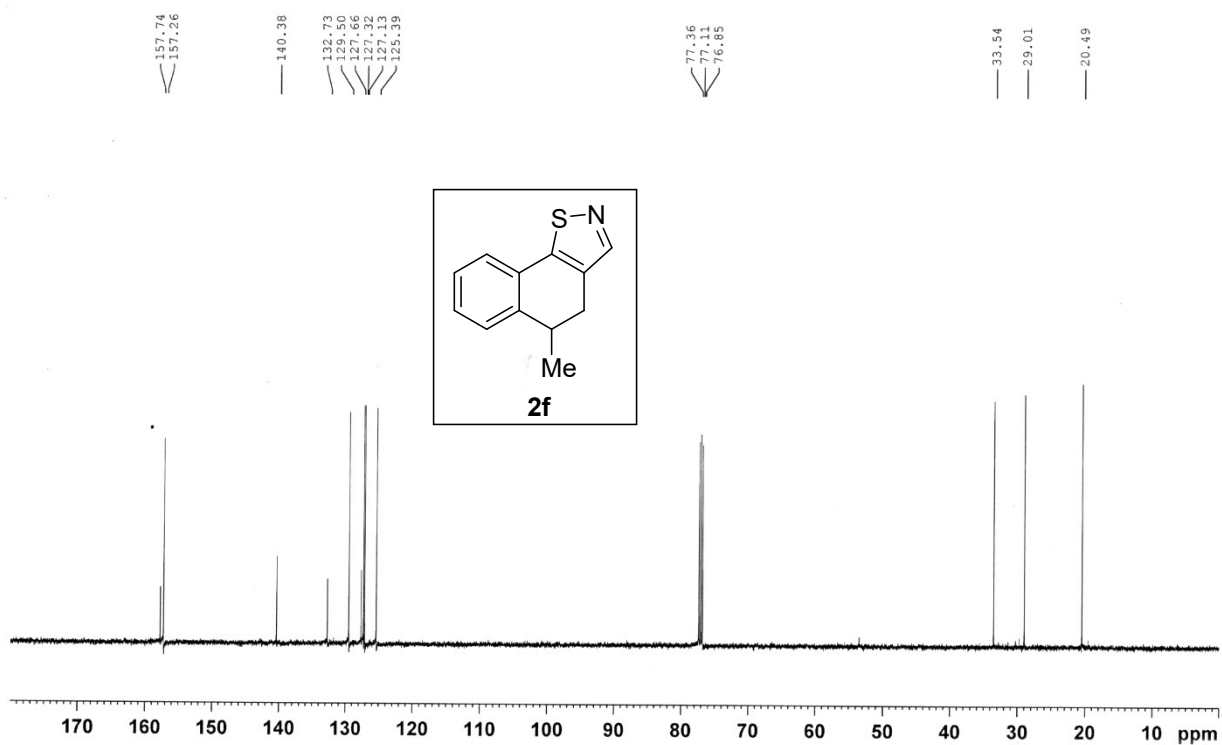
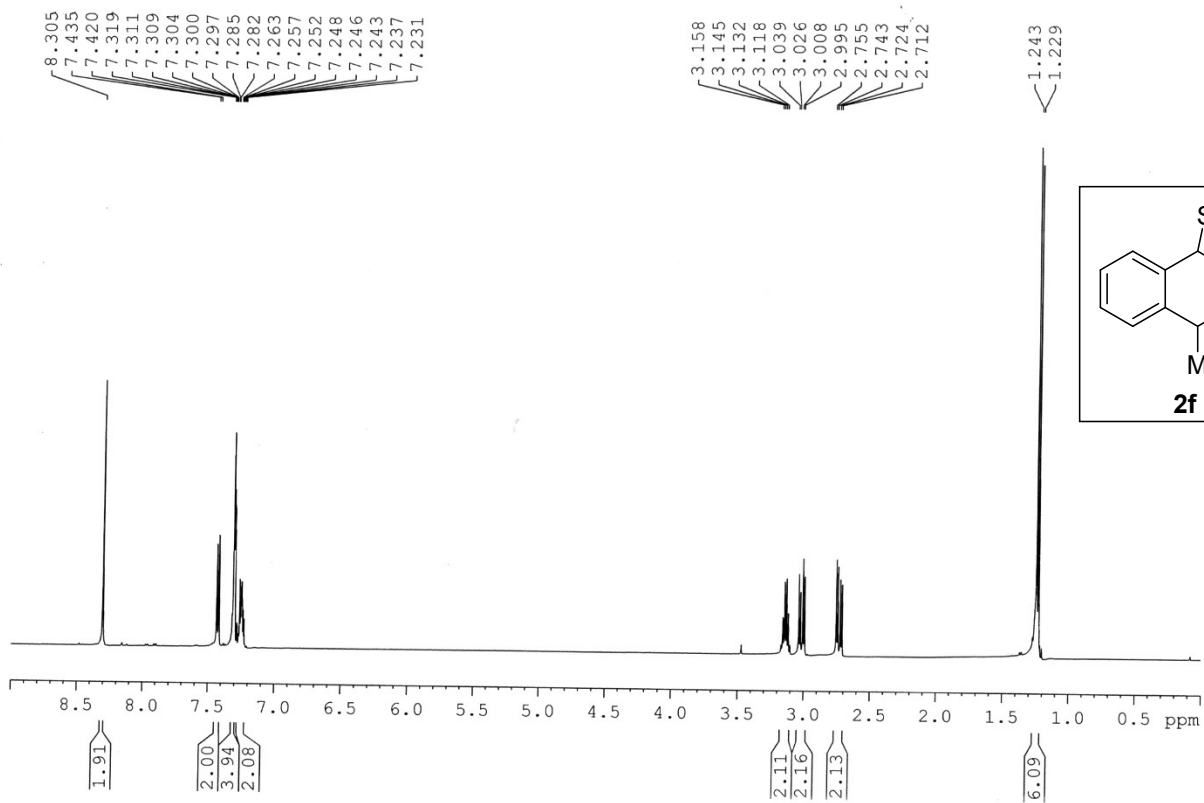


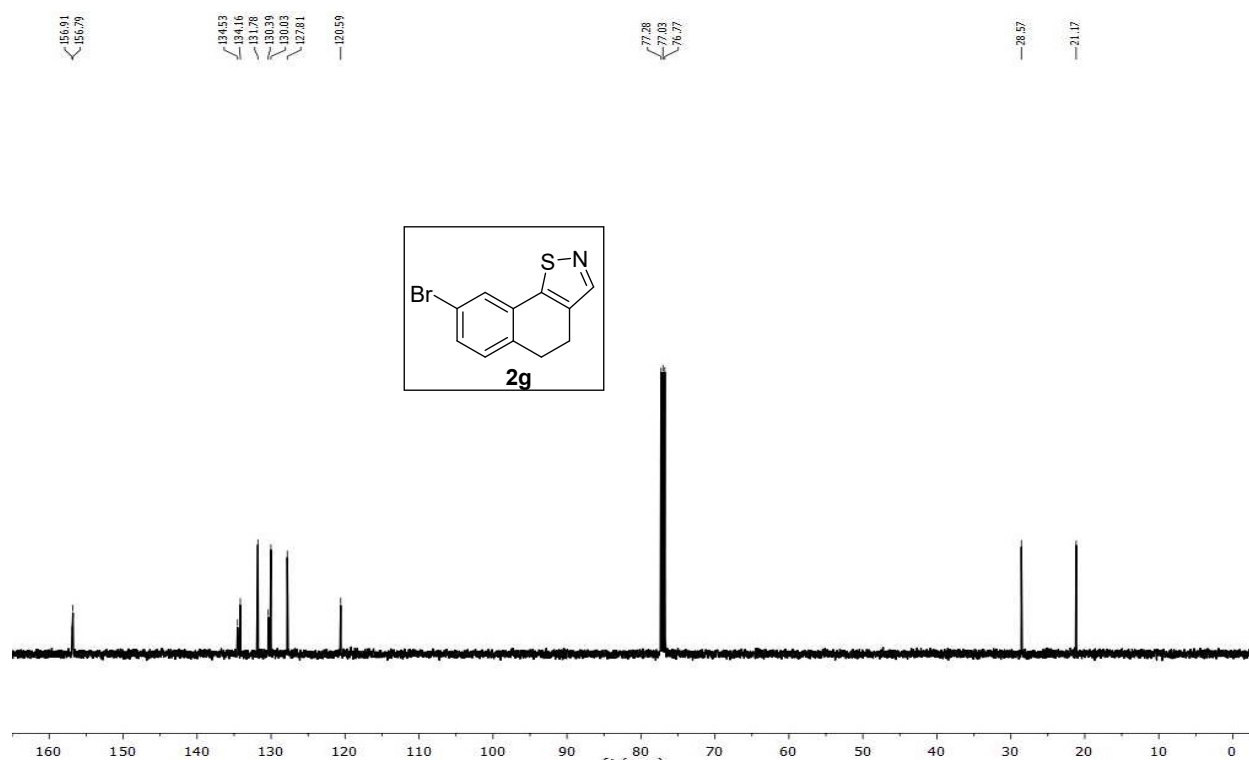
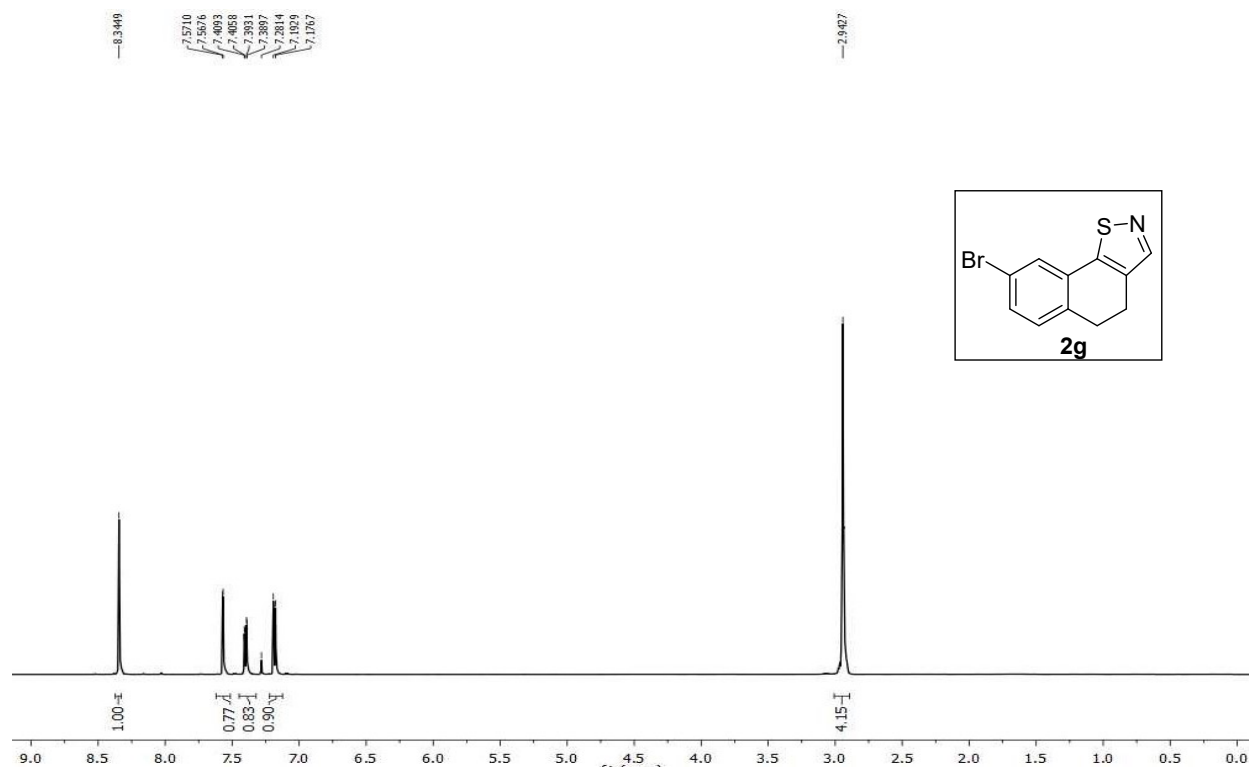


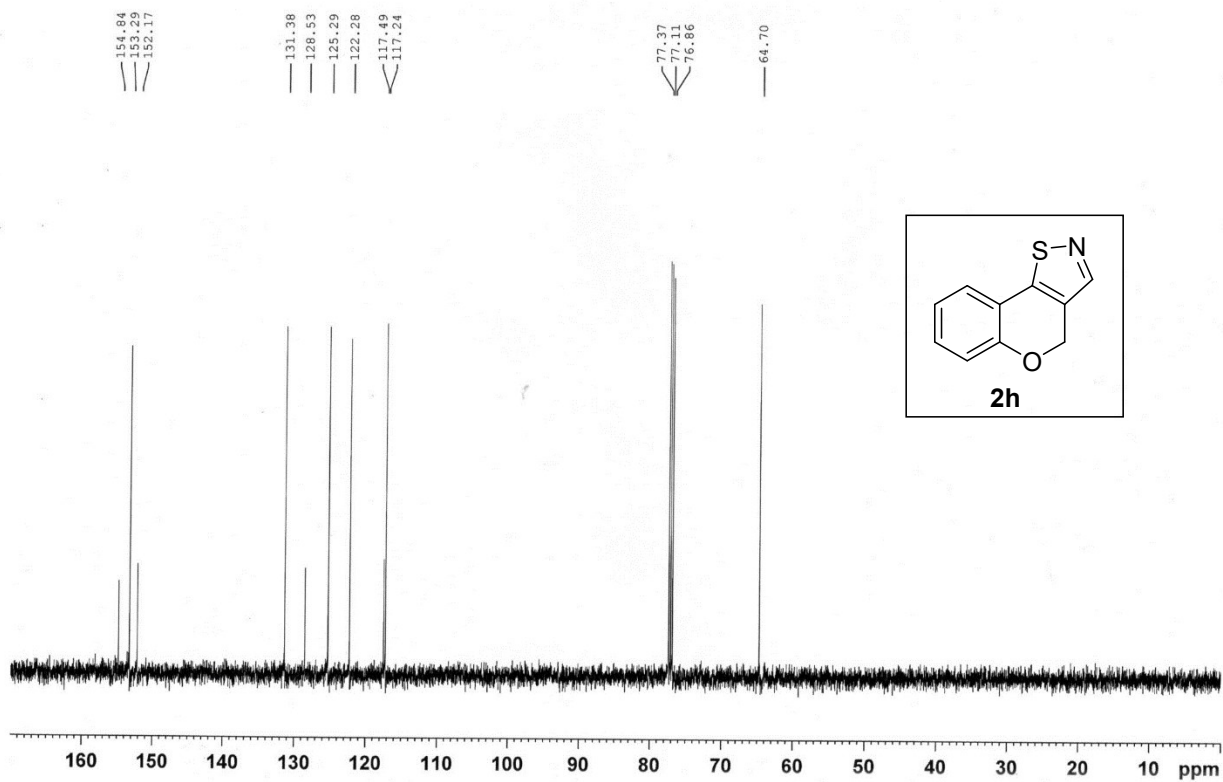
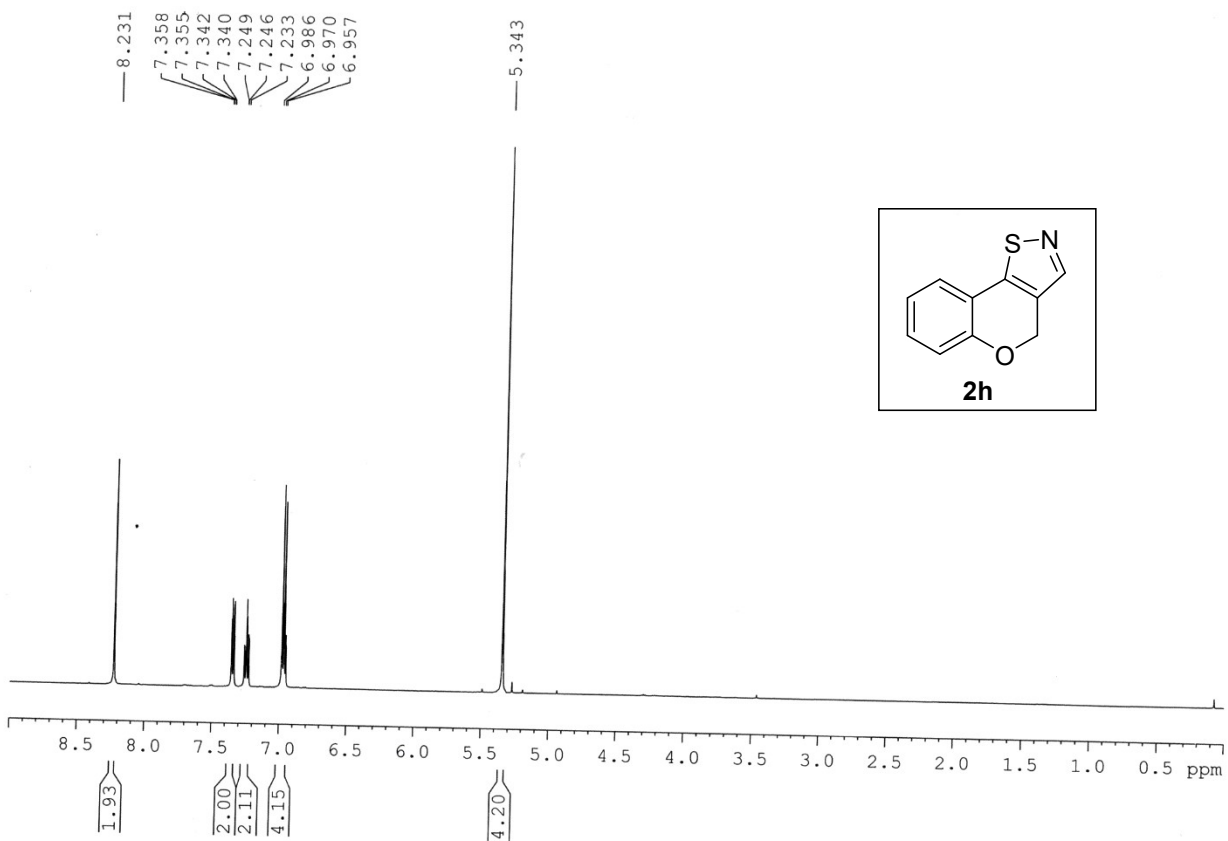


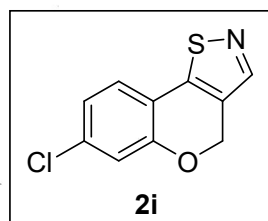
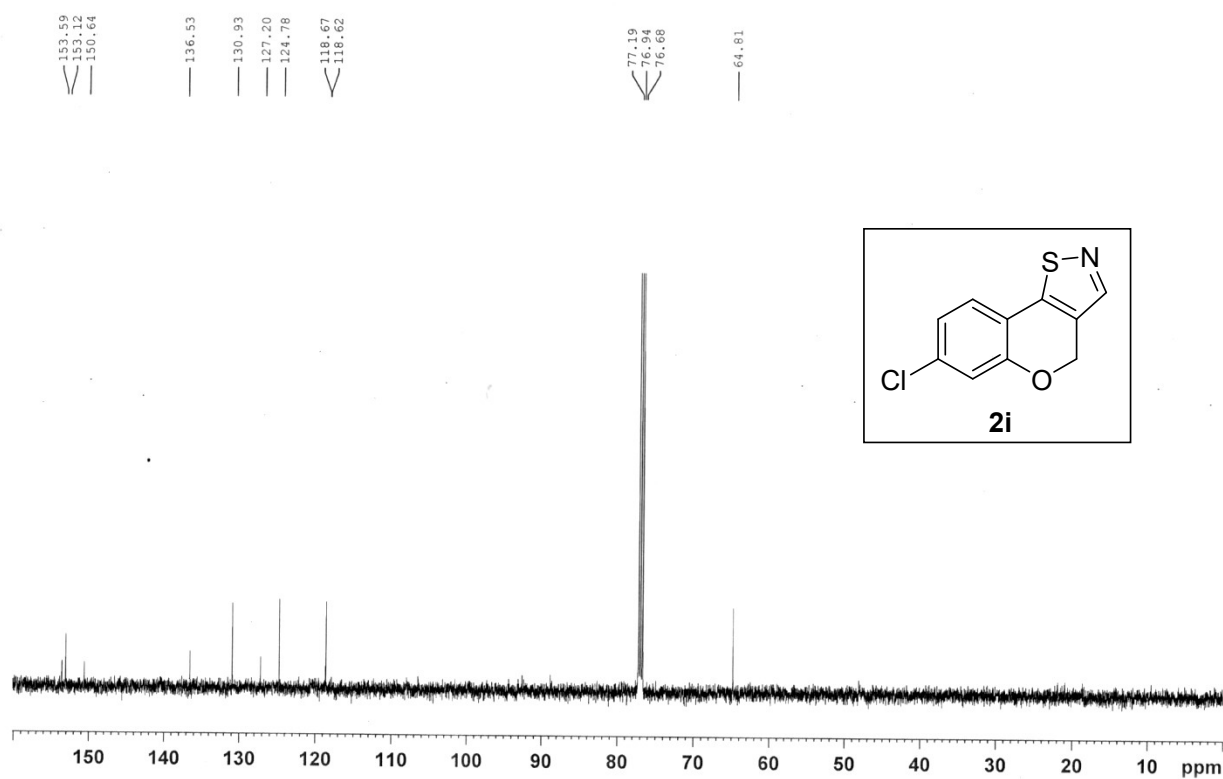
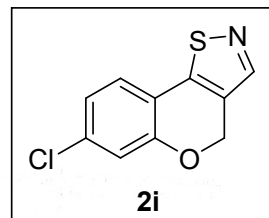
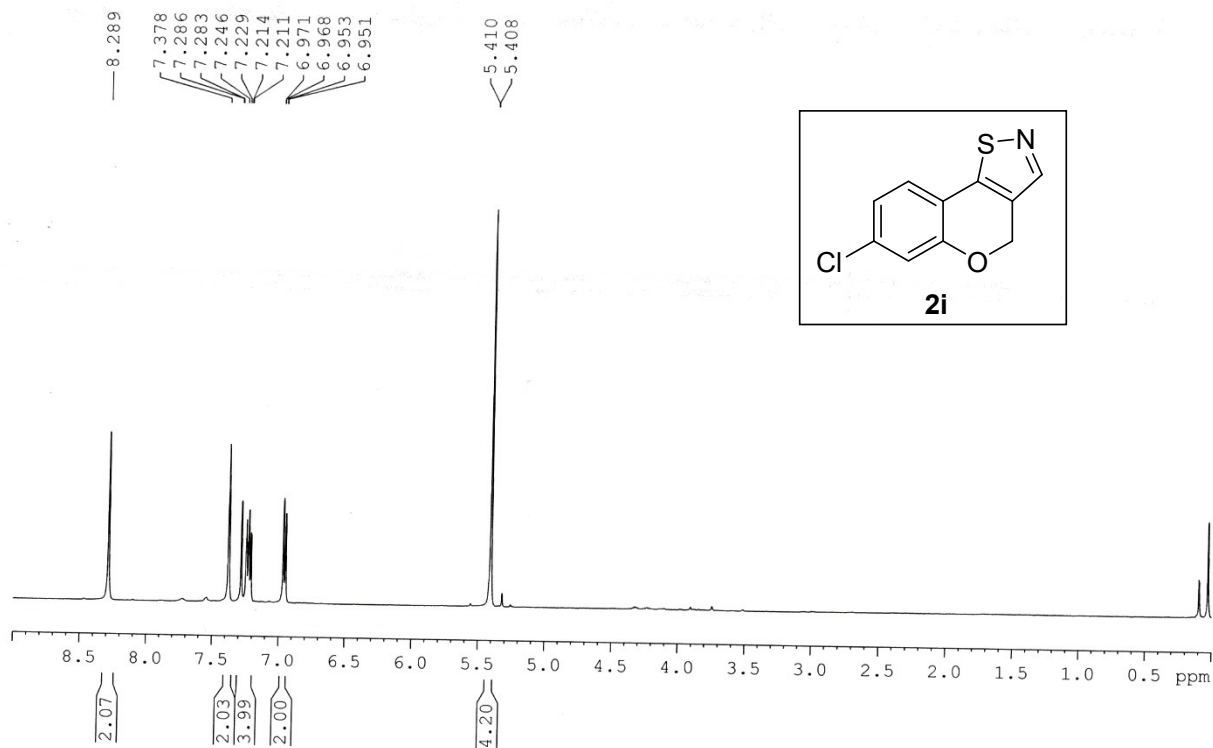


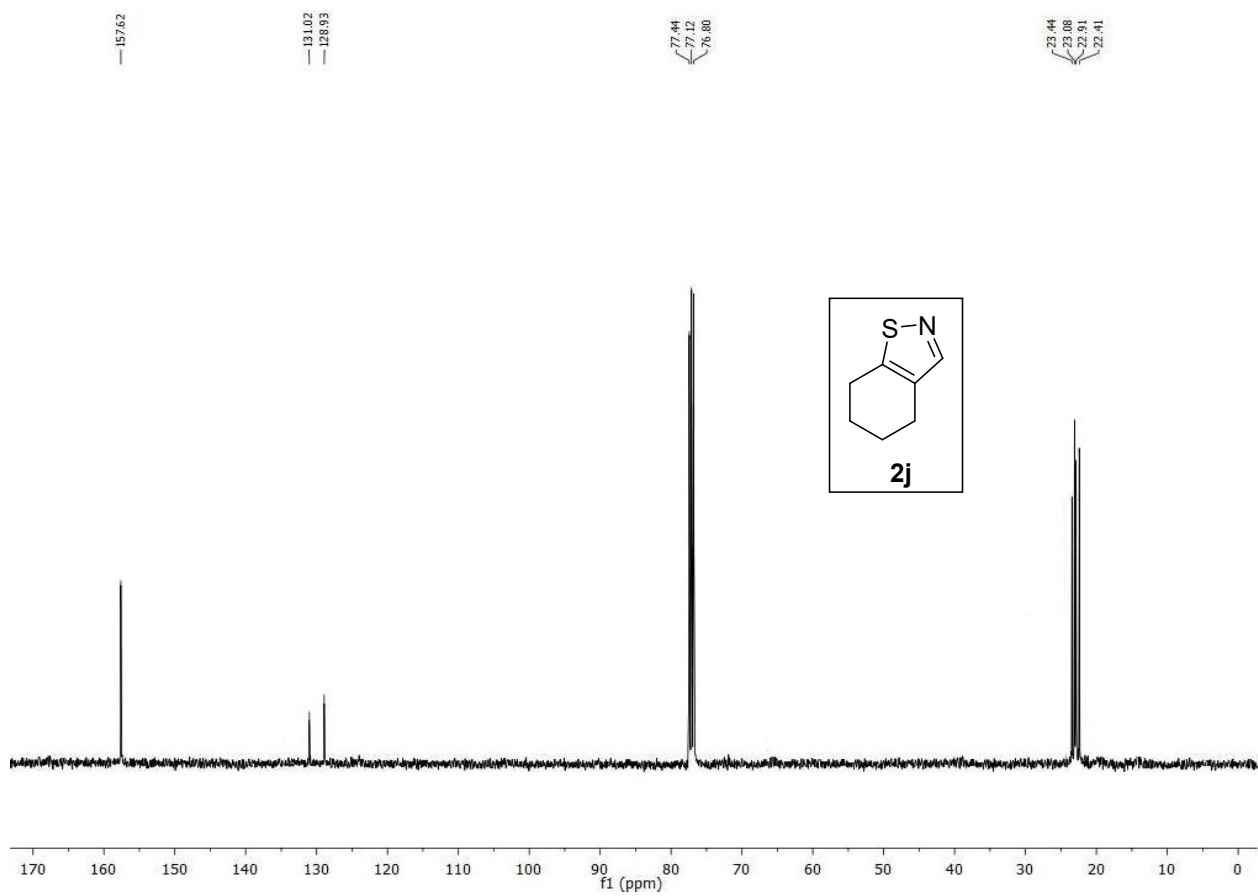
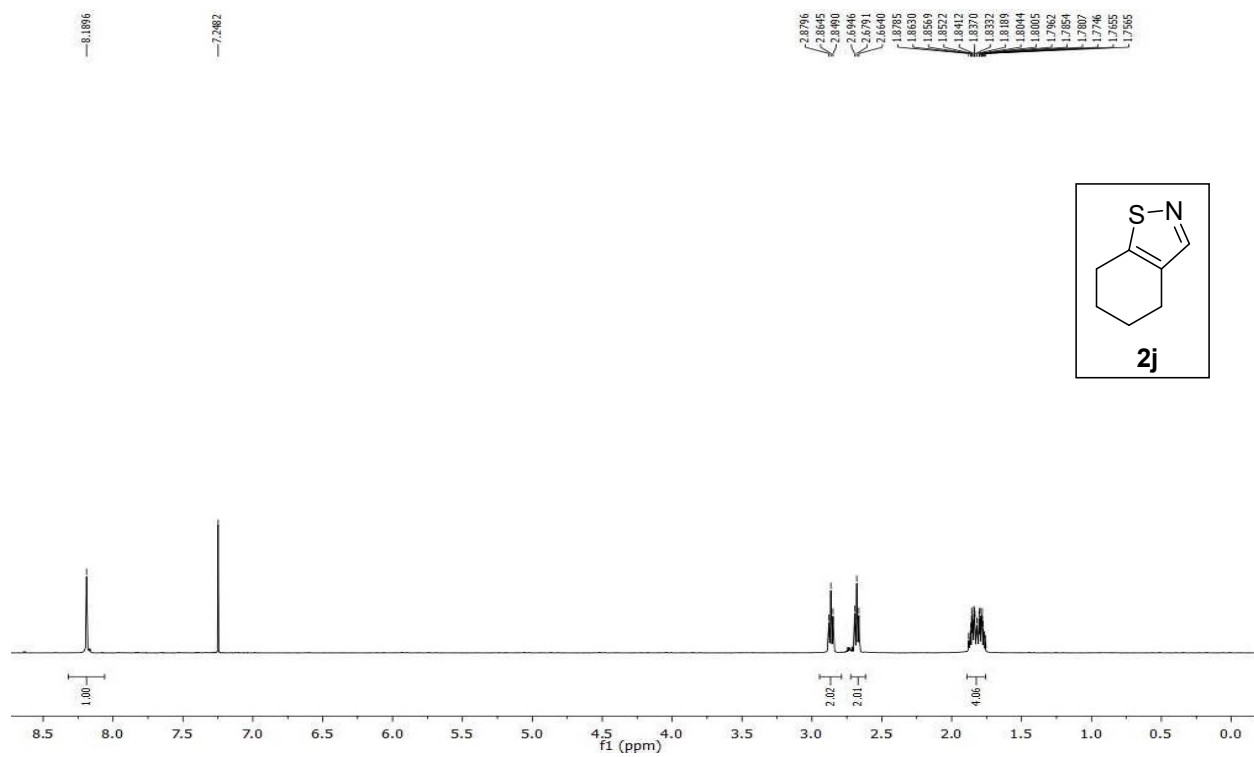


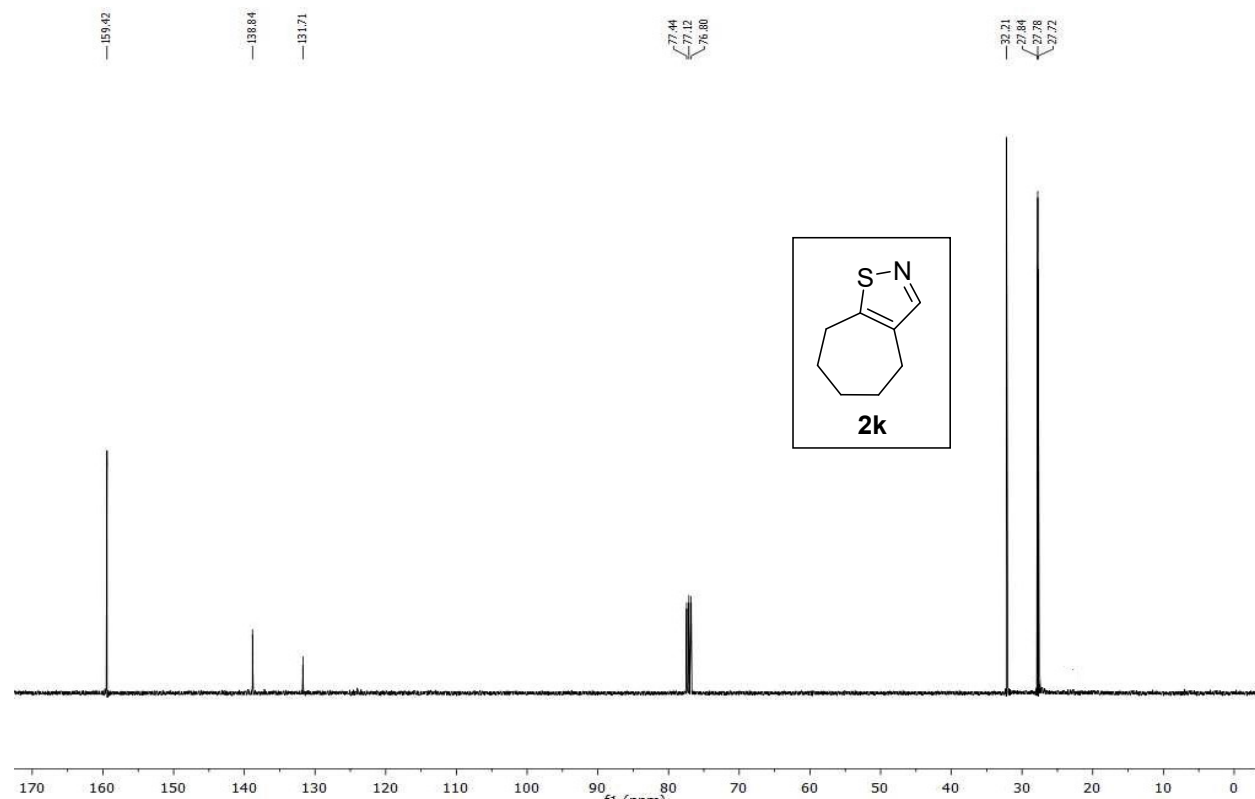
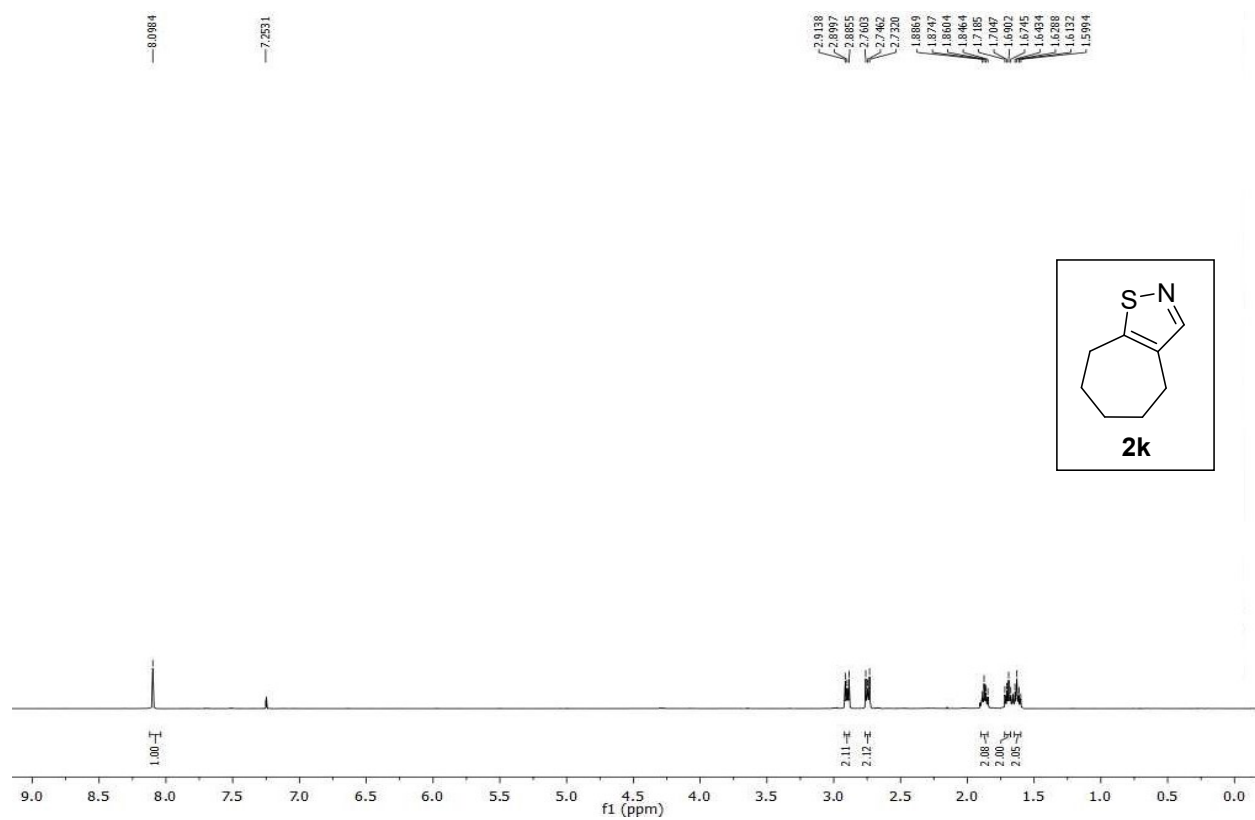


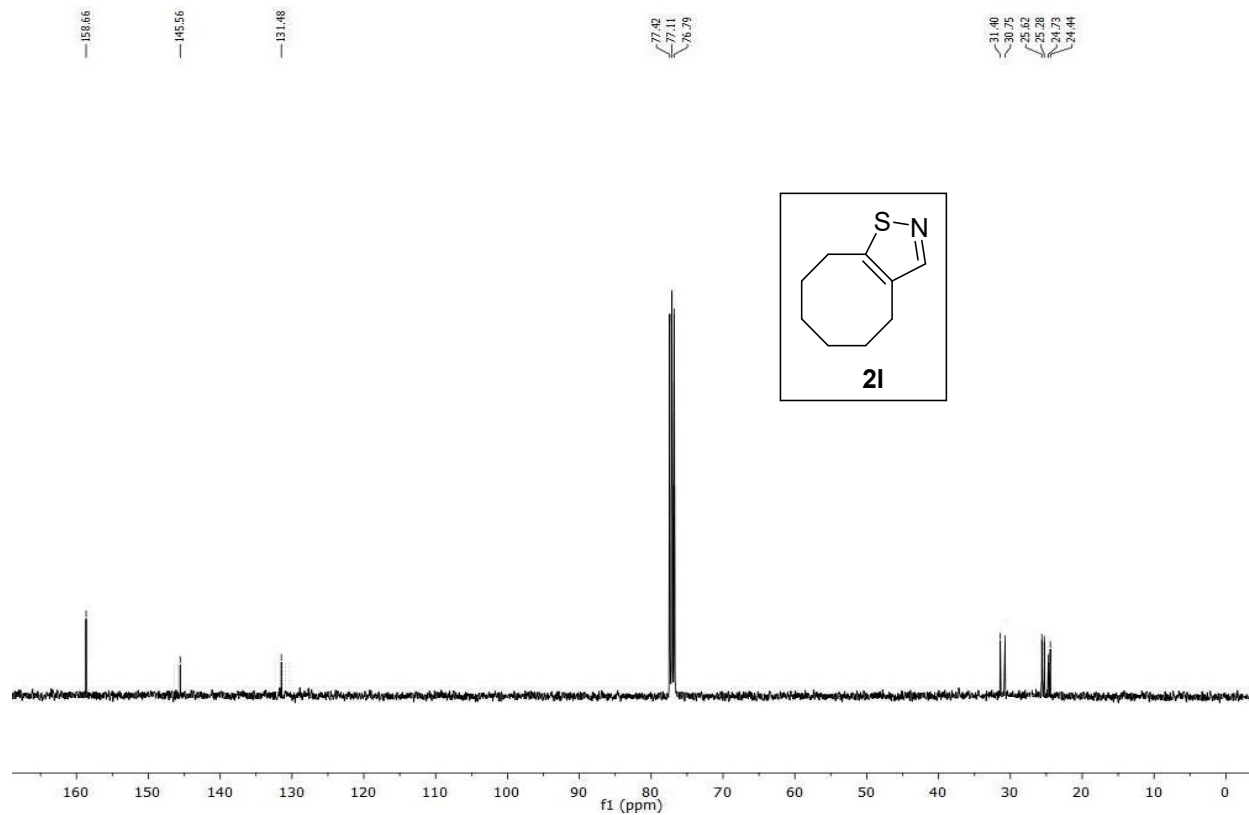
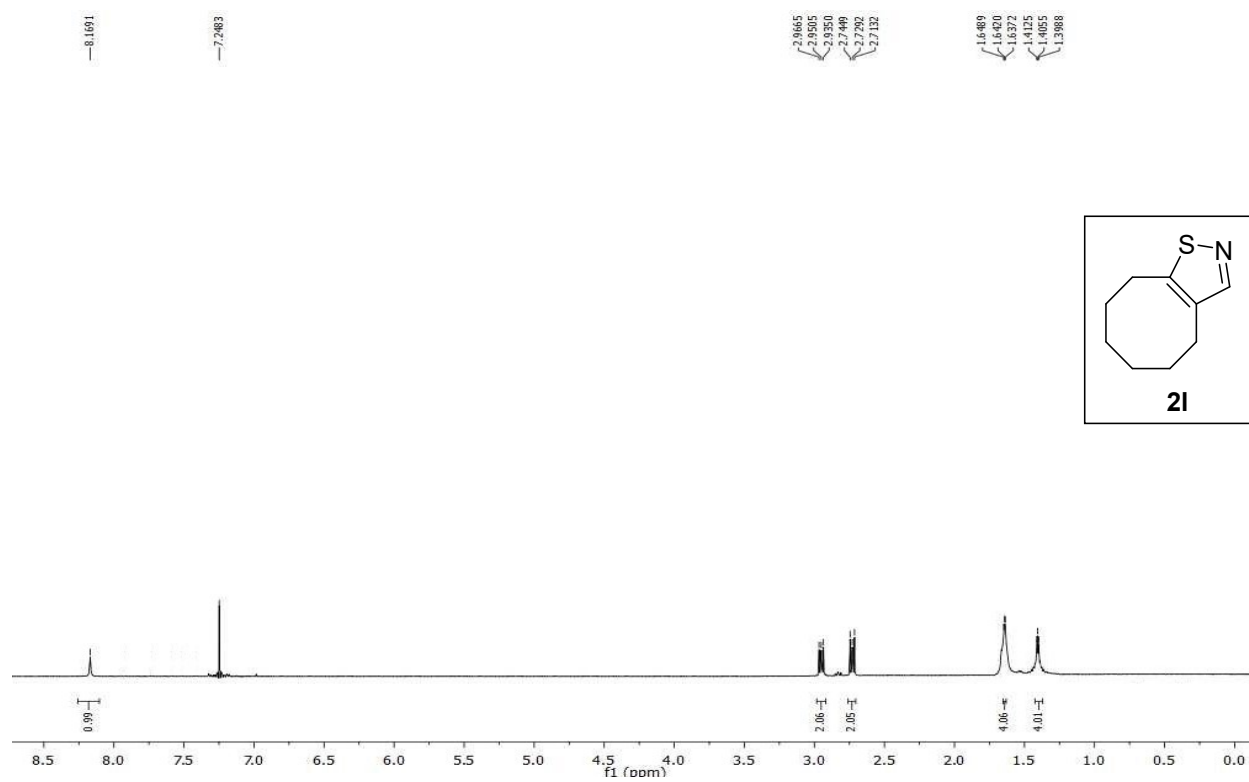


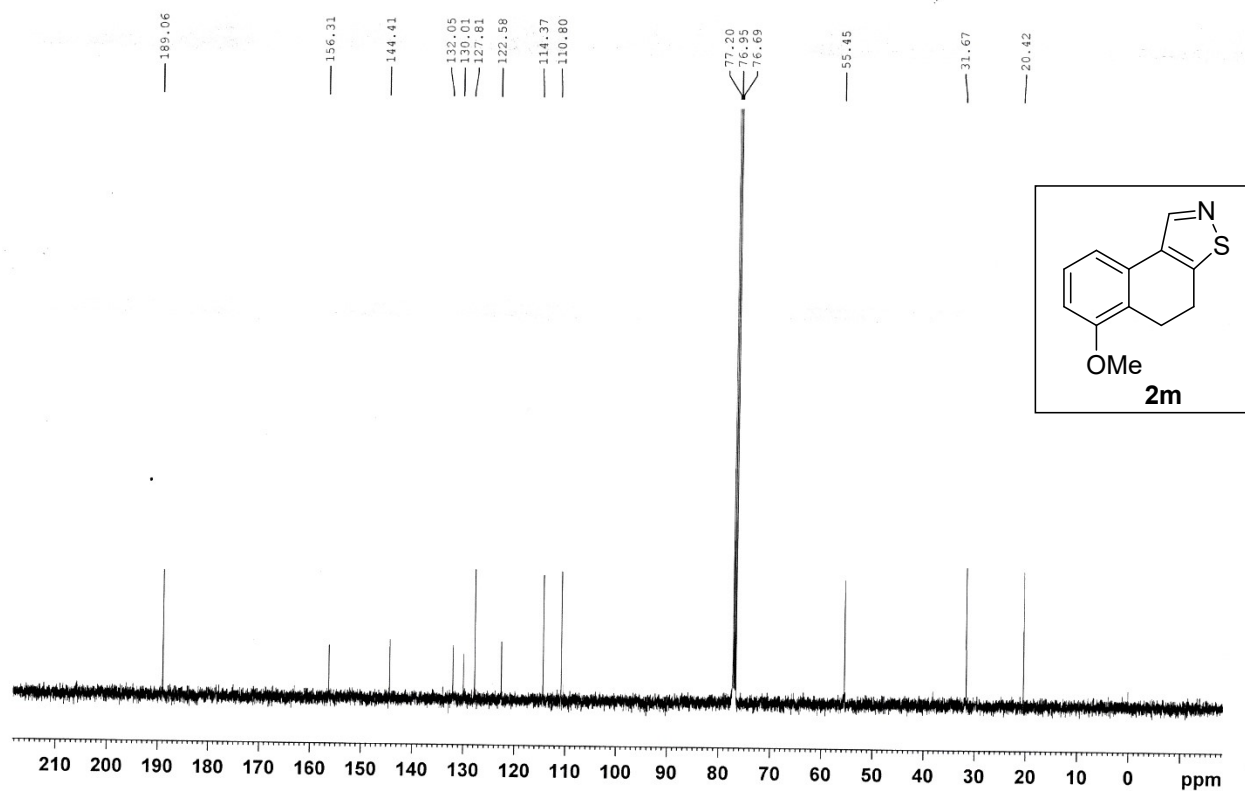
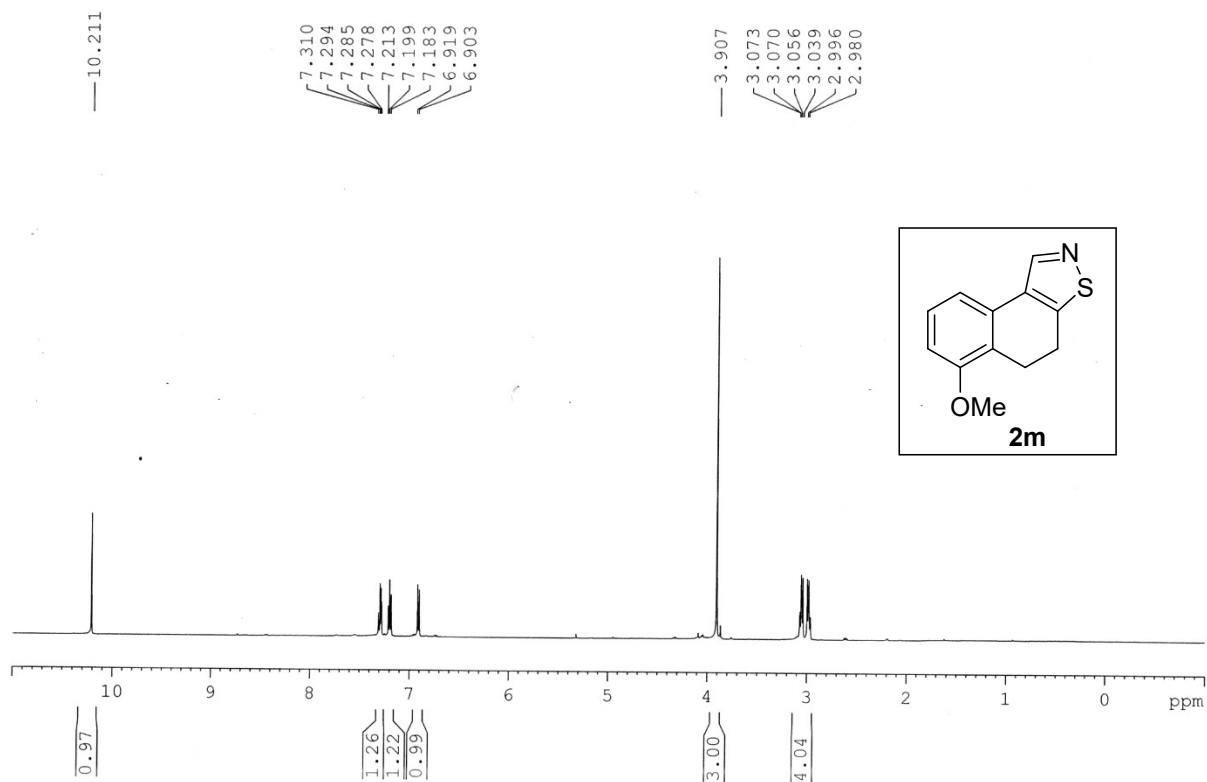


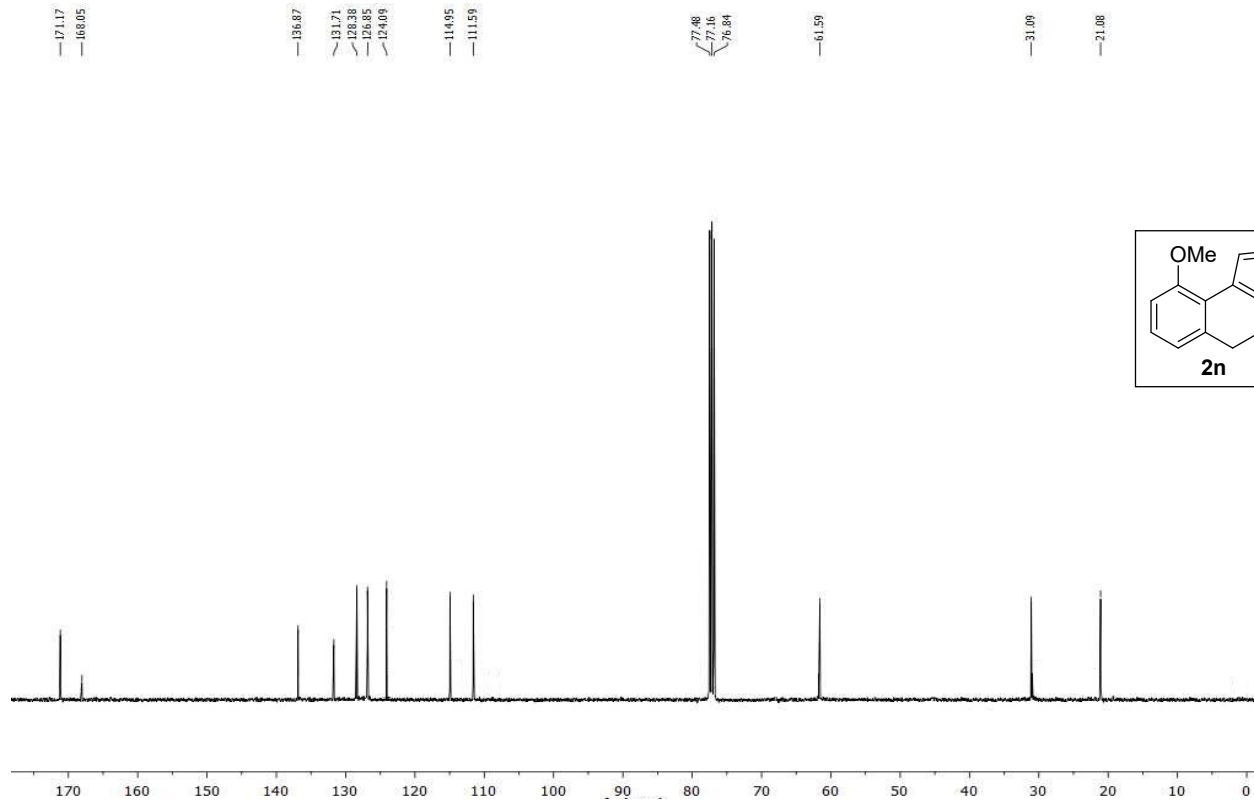
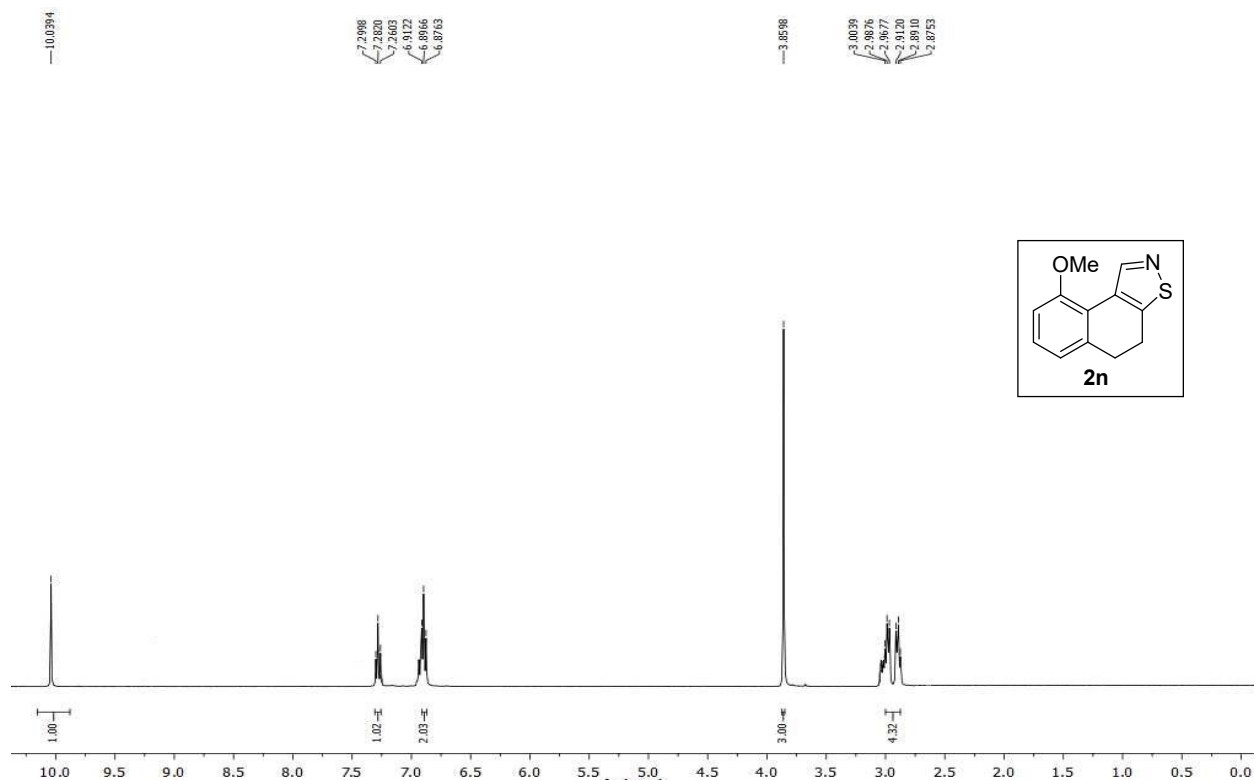


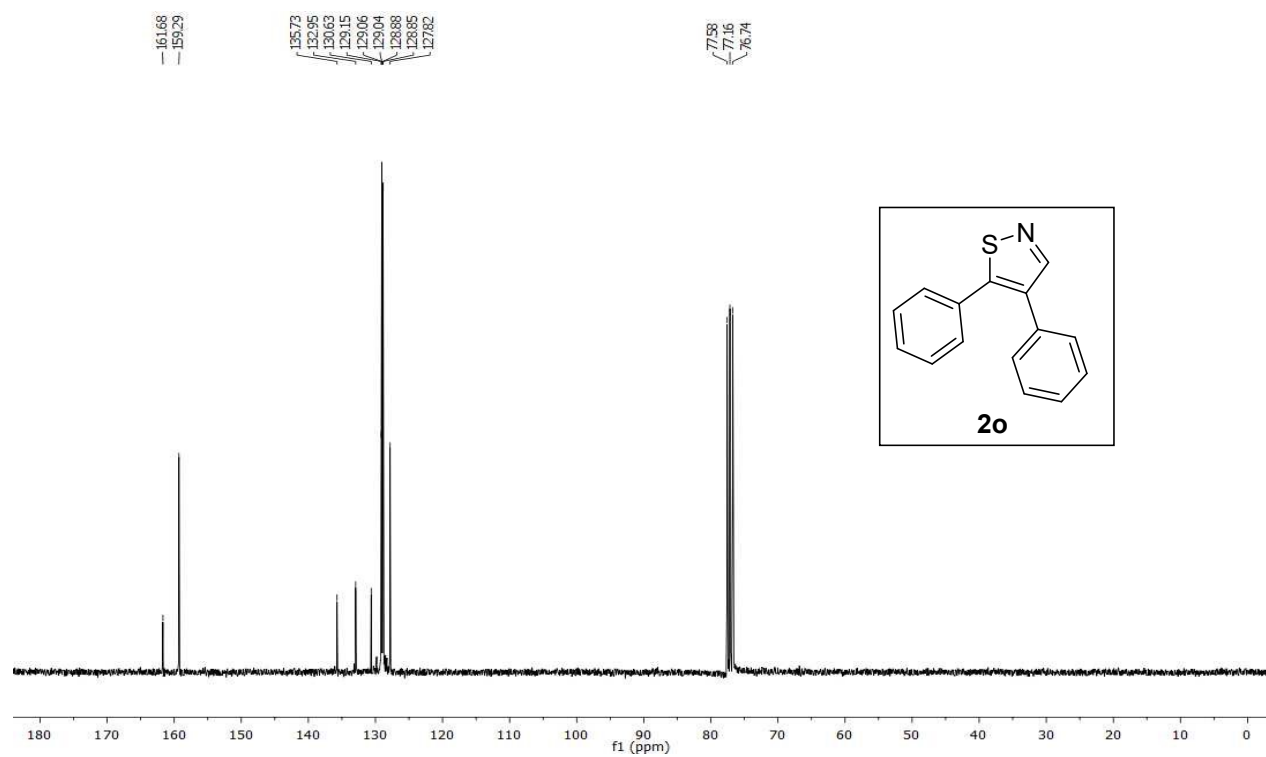
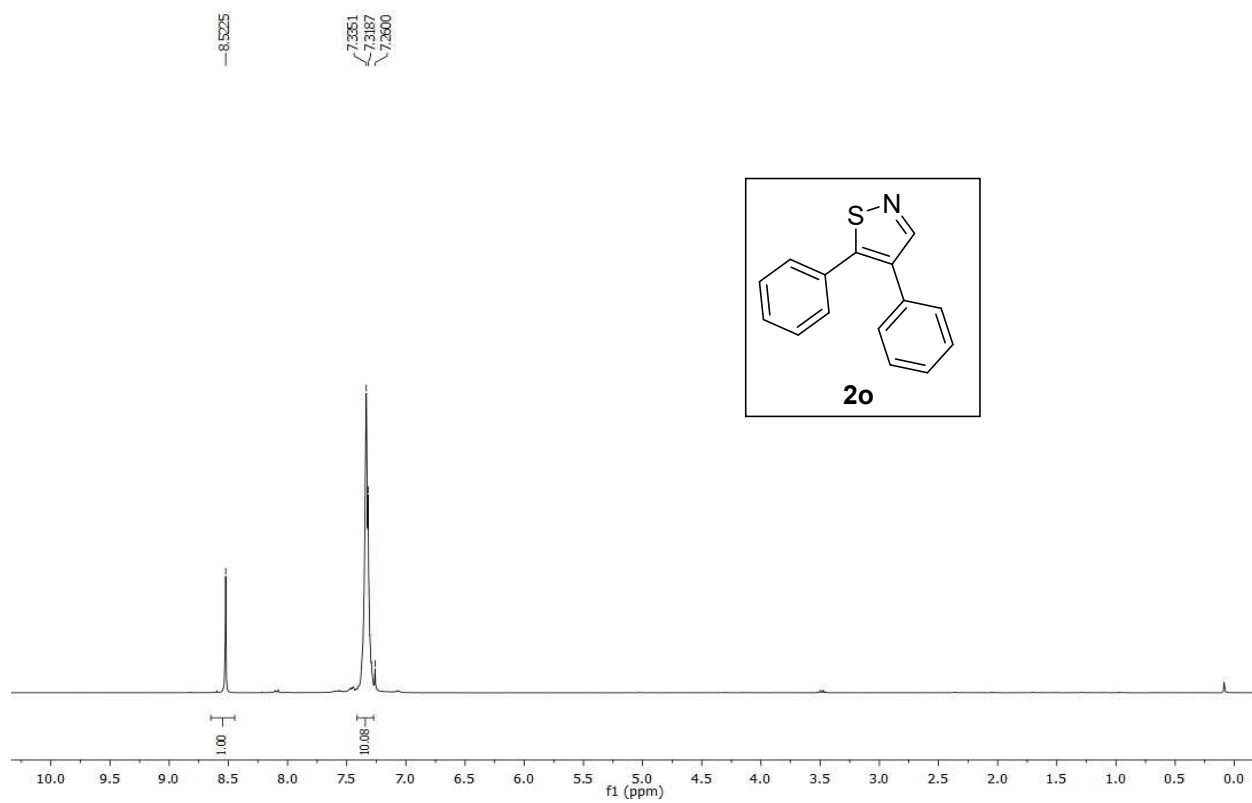




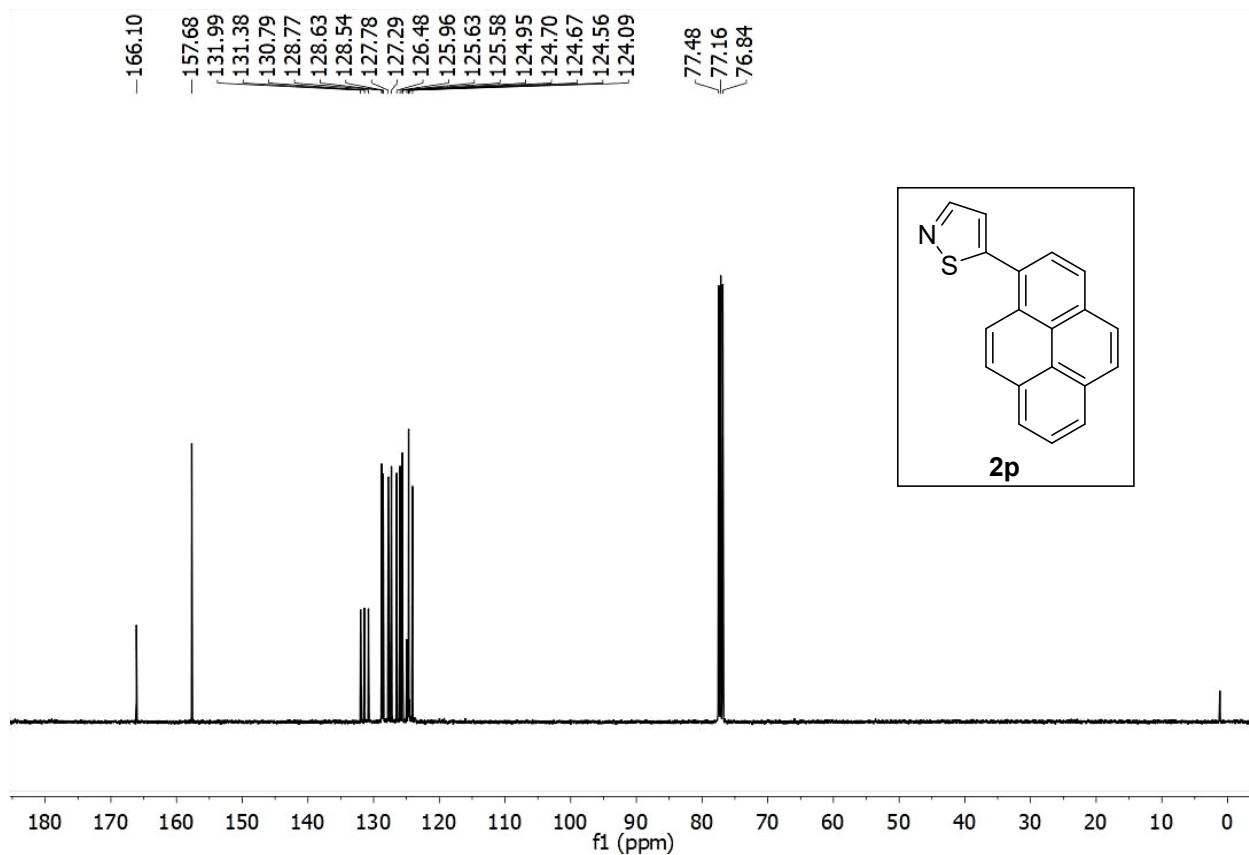
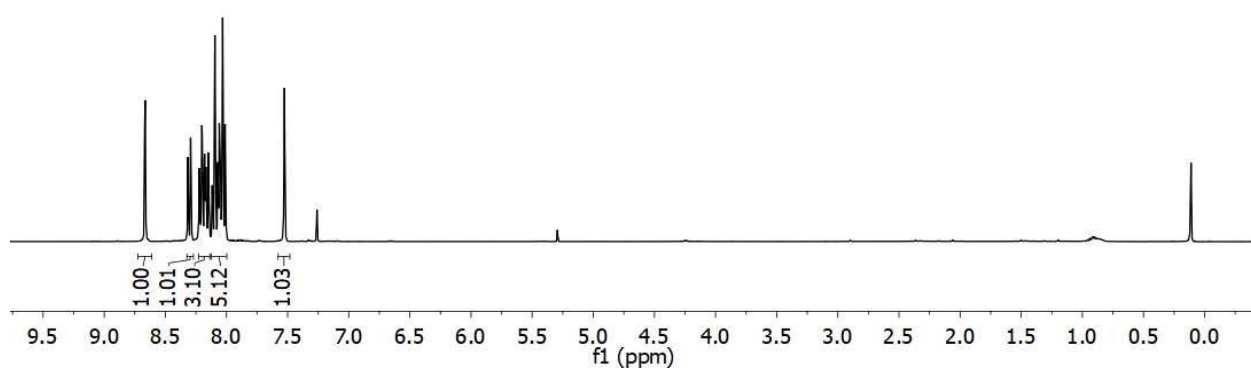
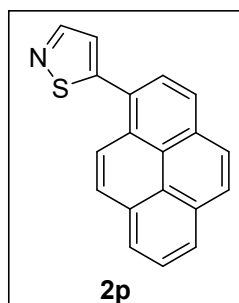


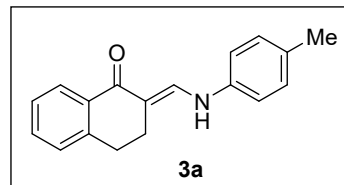
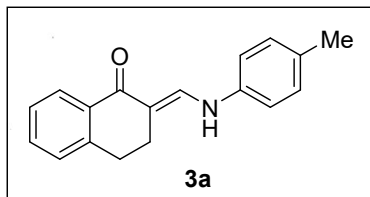


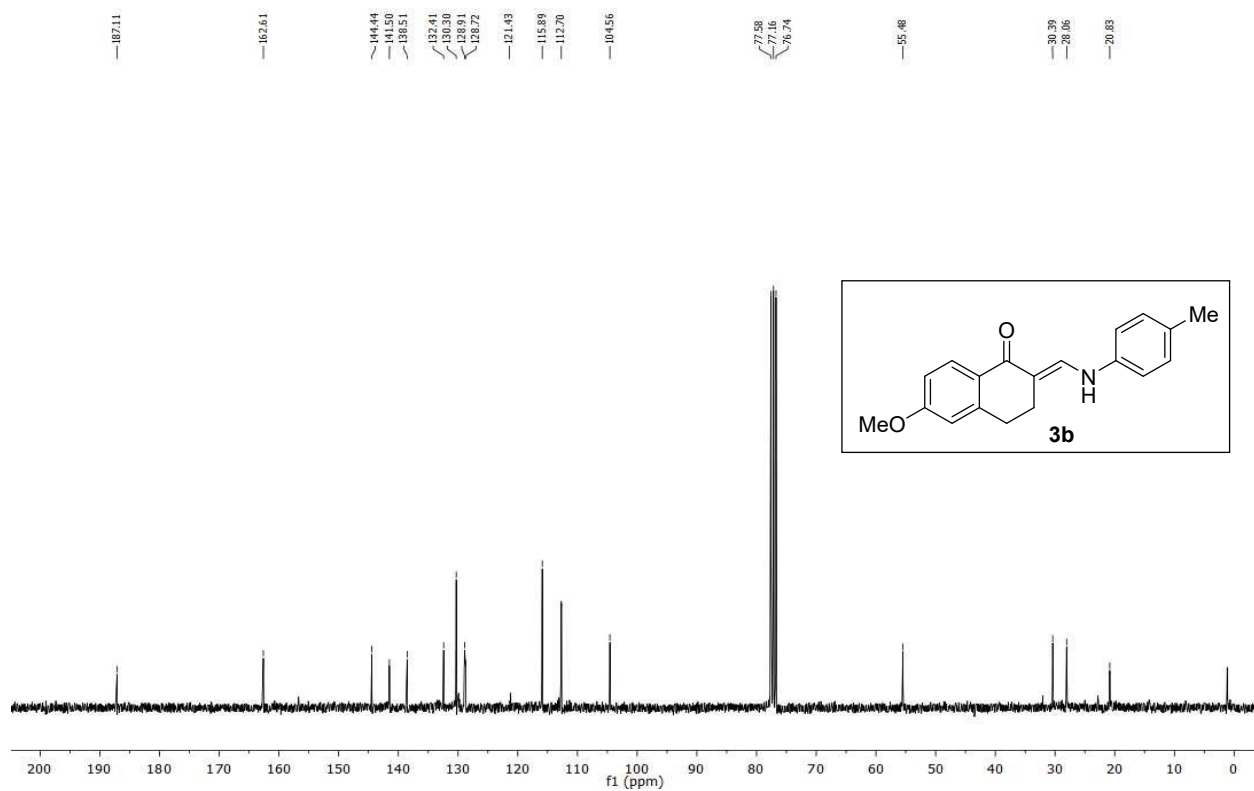
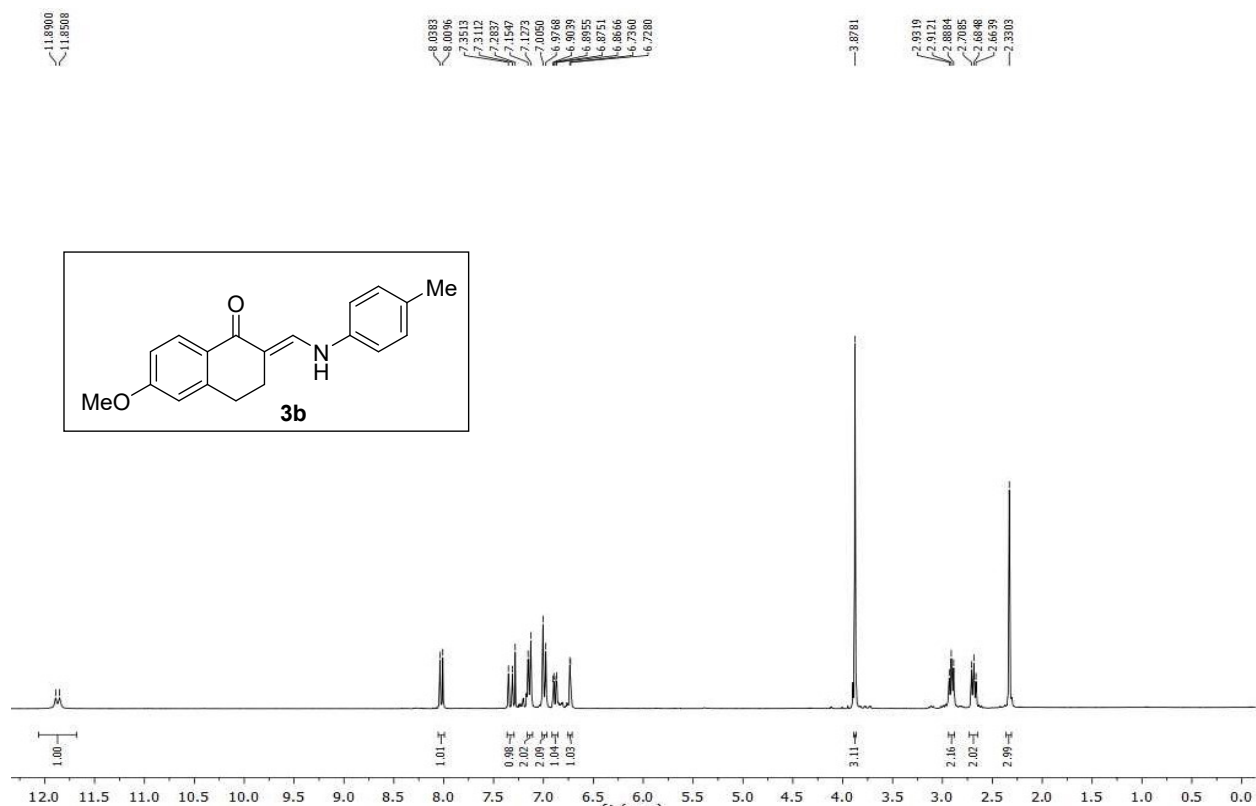


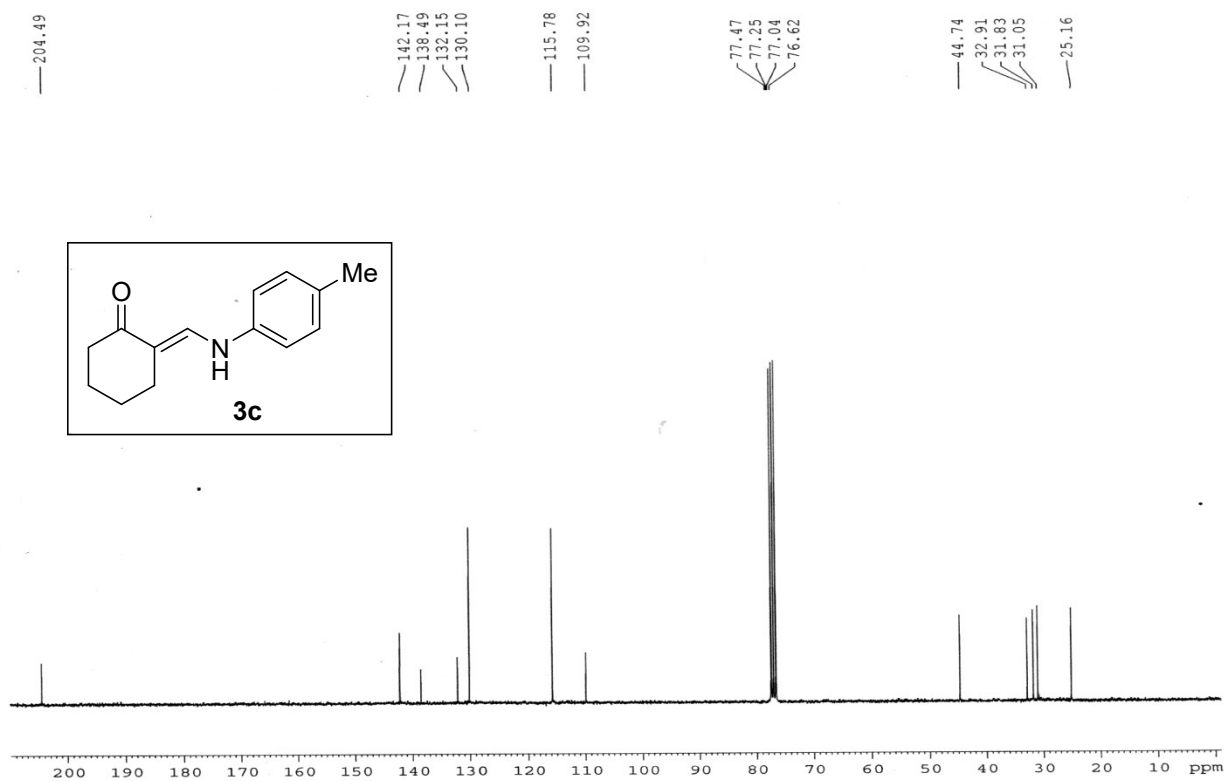
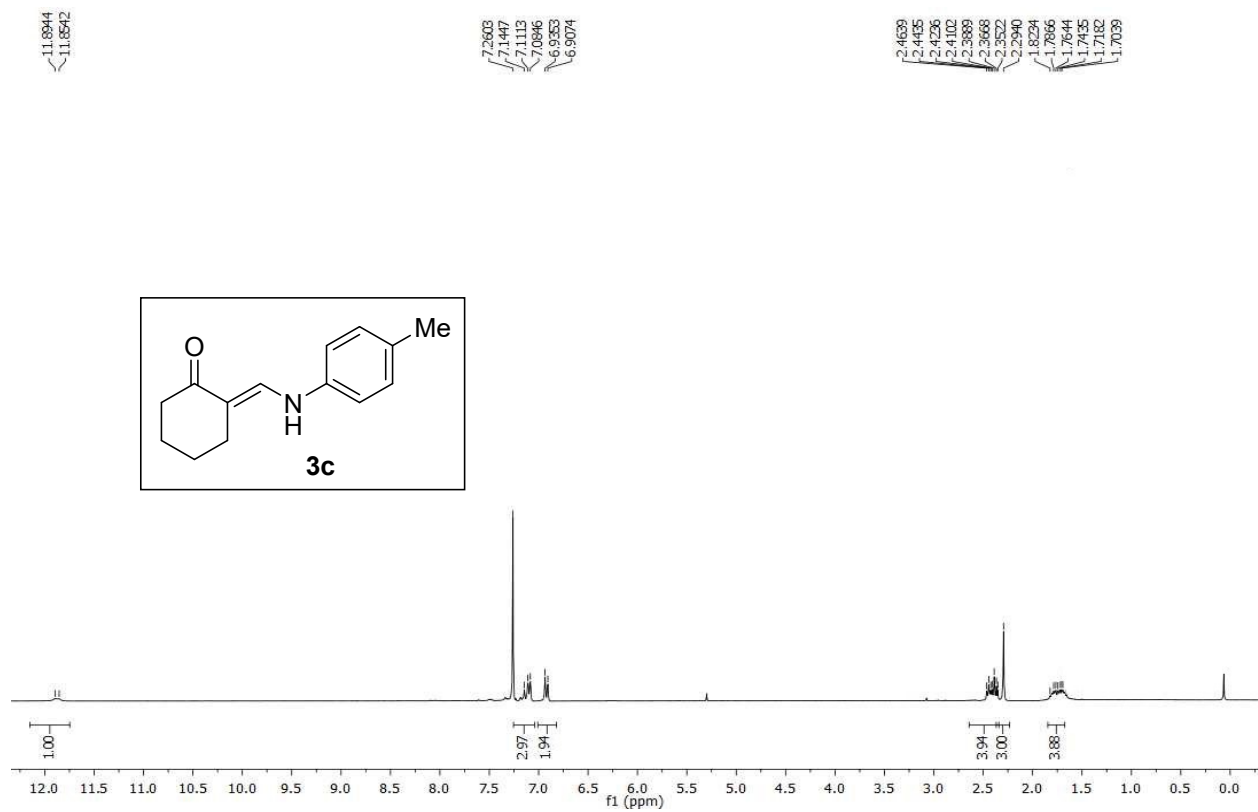


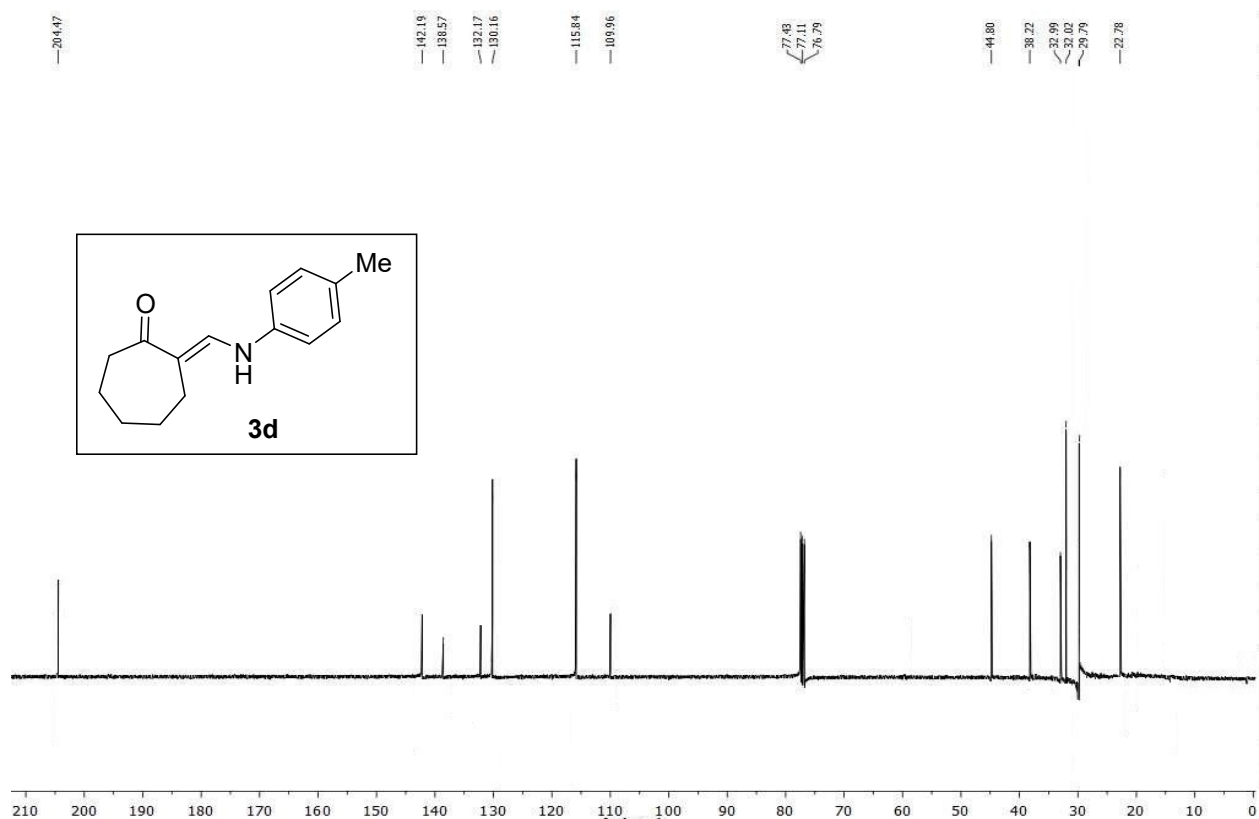
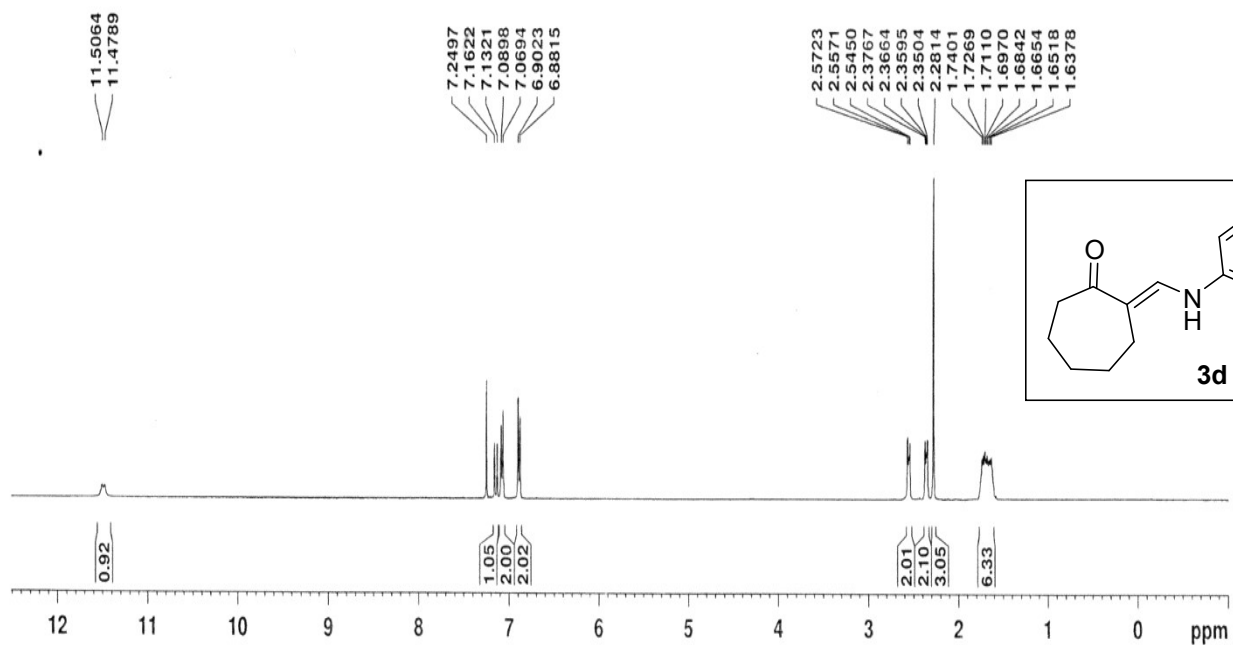
8.6646
8.3157
8.2926
8.2217
8.2011
8.1788
8.1685
8.1485
8.1167
8.0947
8.0719
8.0586
8.0511
8.0312
8.0113
7.5259
7.2599

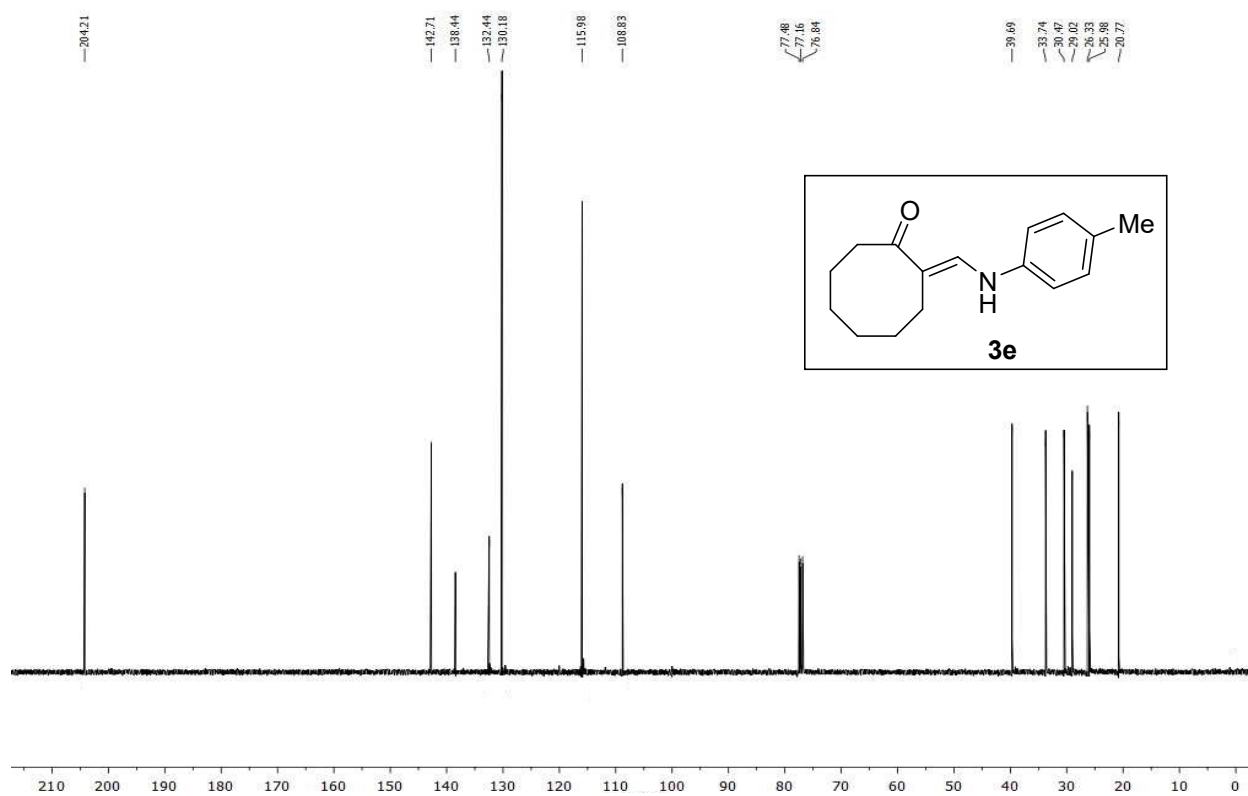
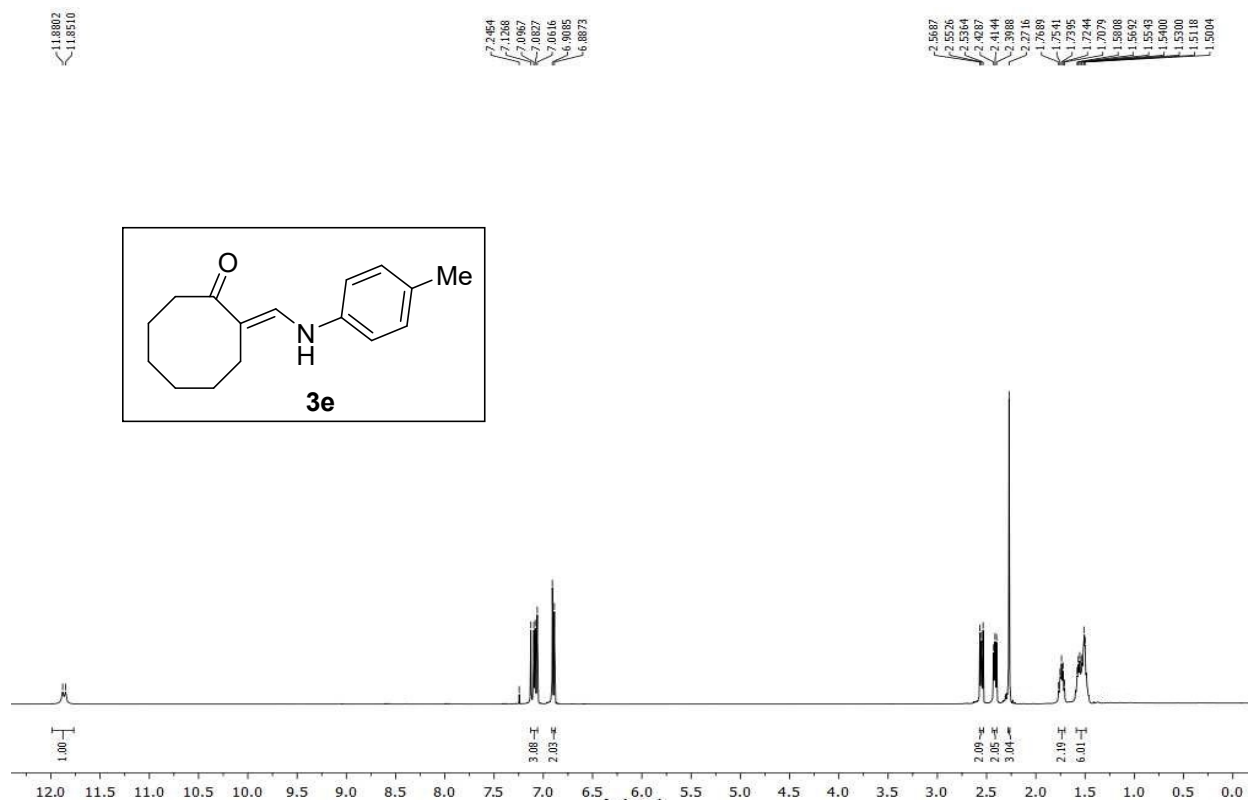


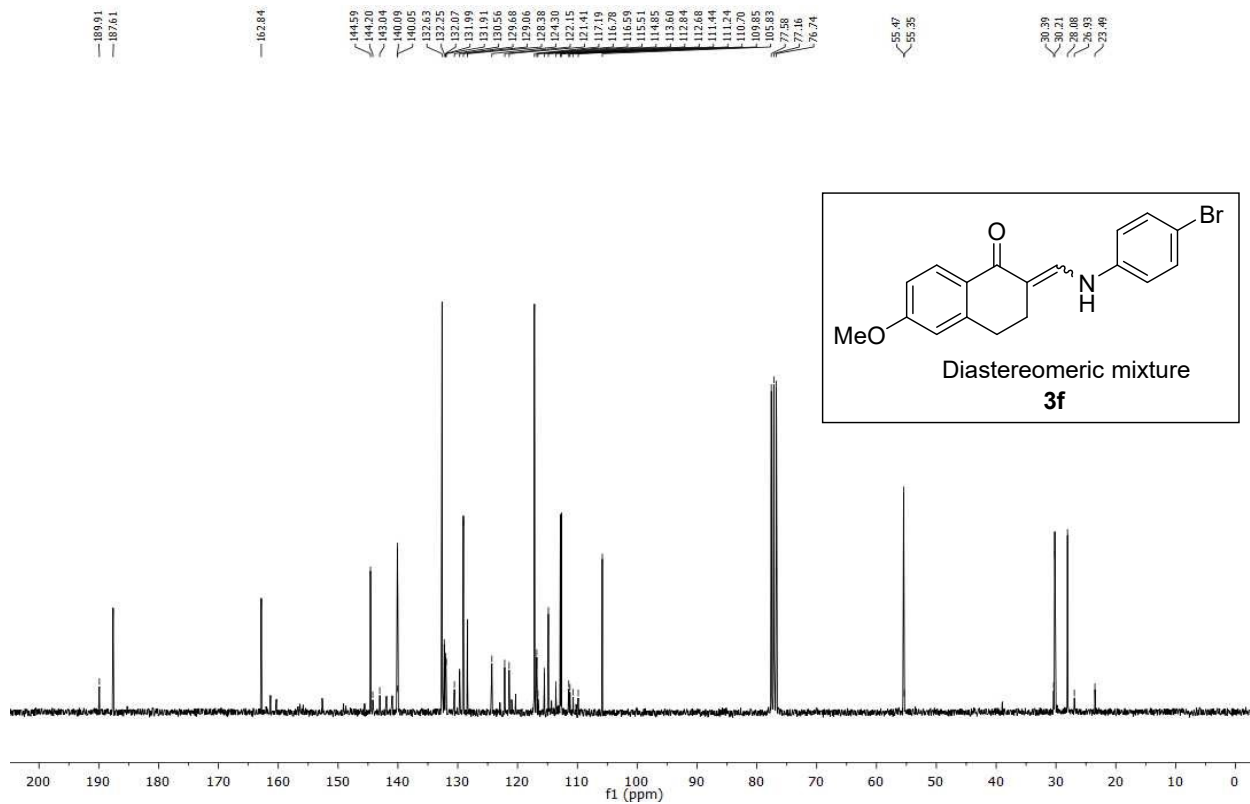
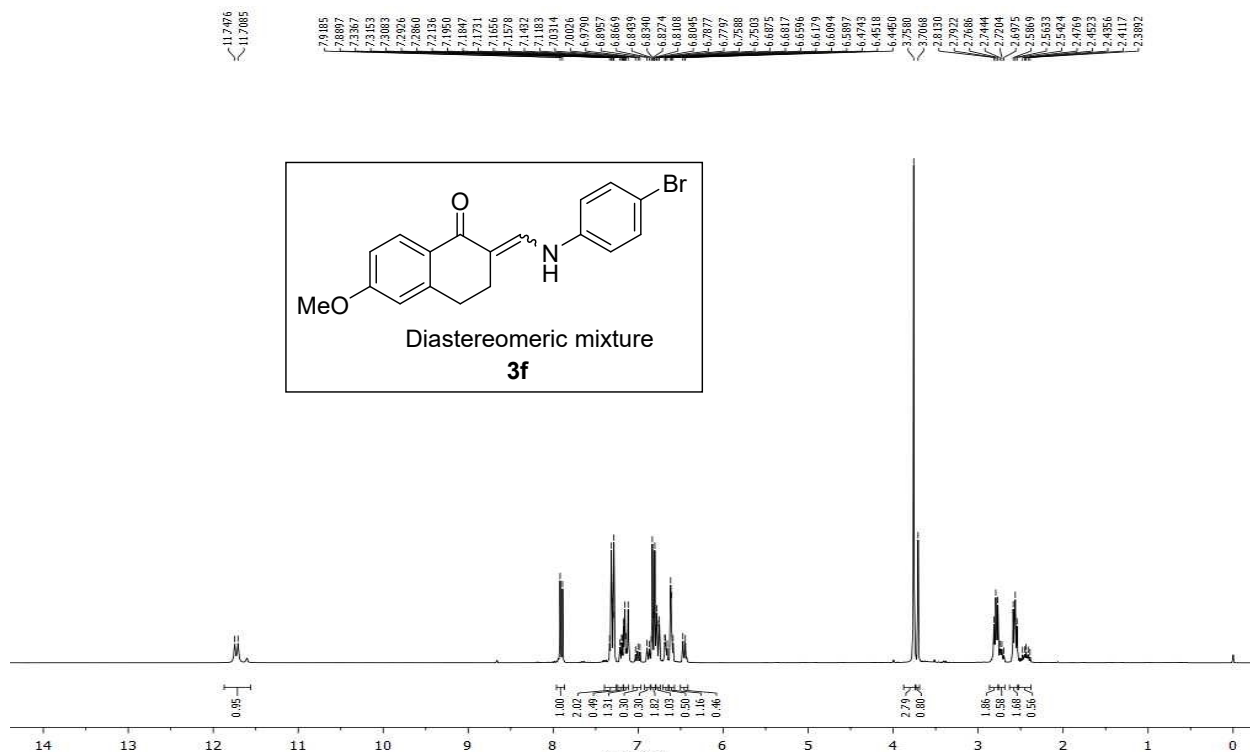


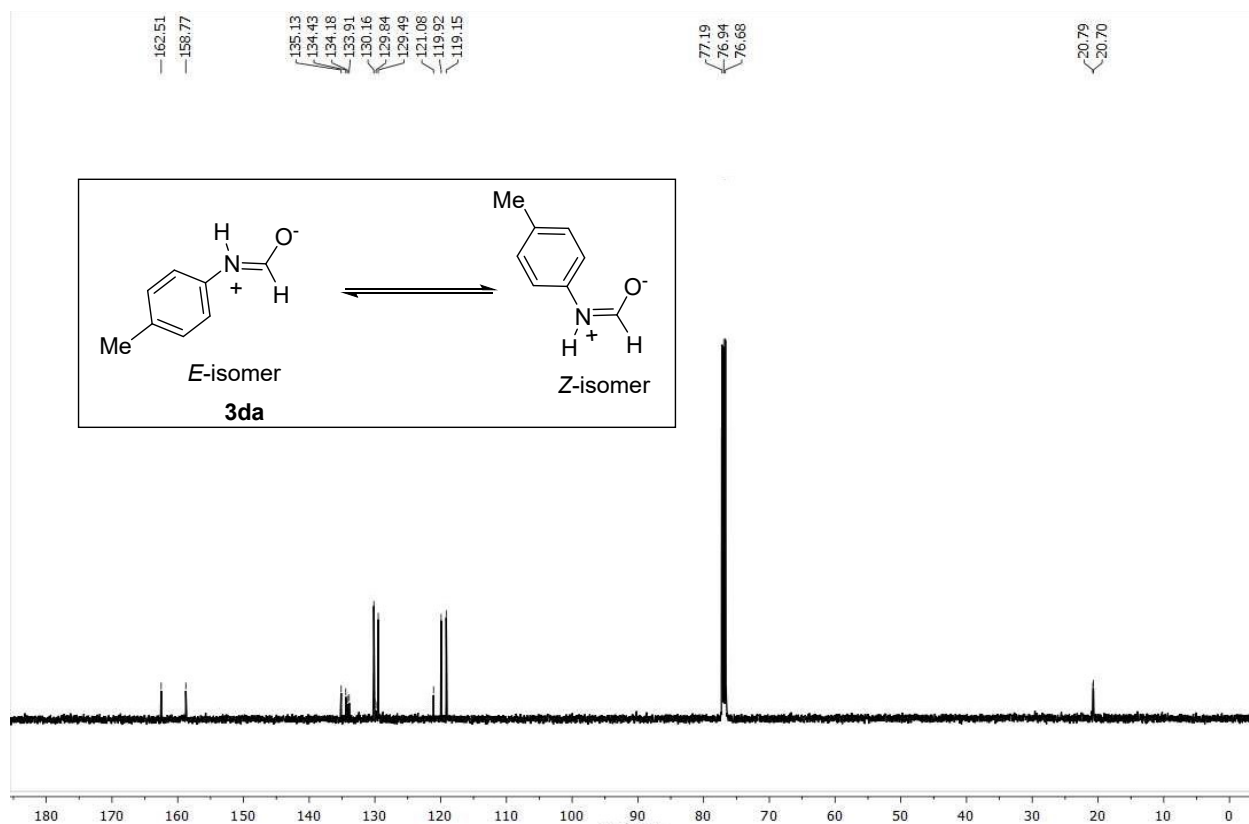
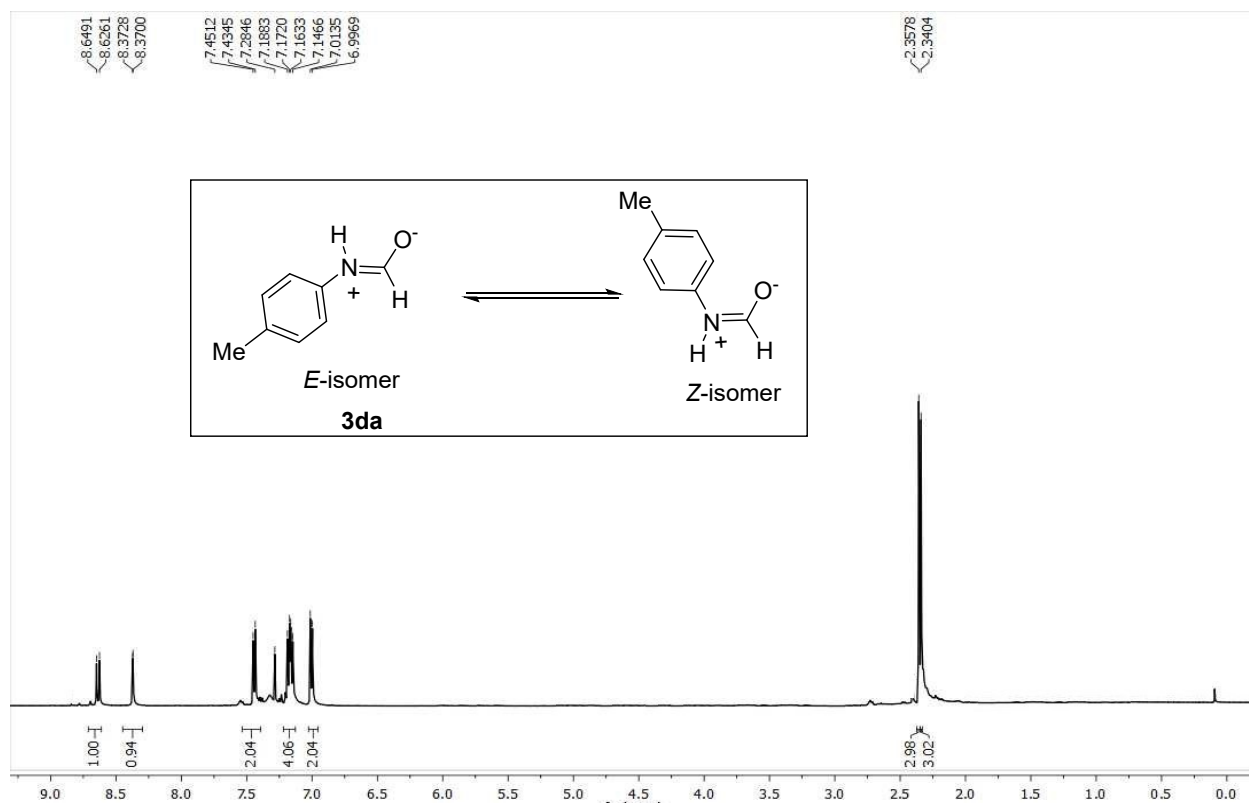


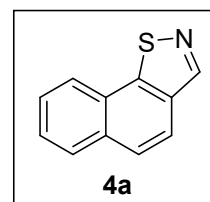
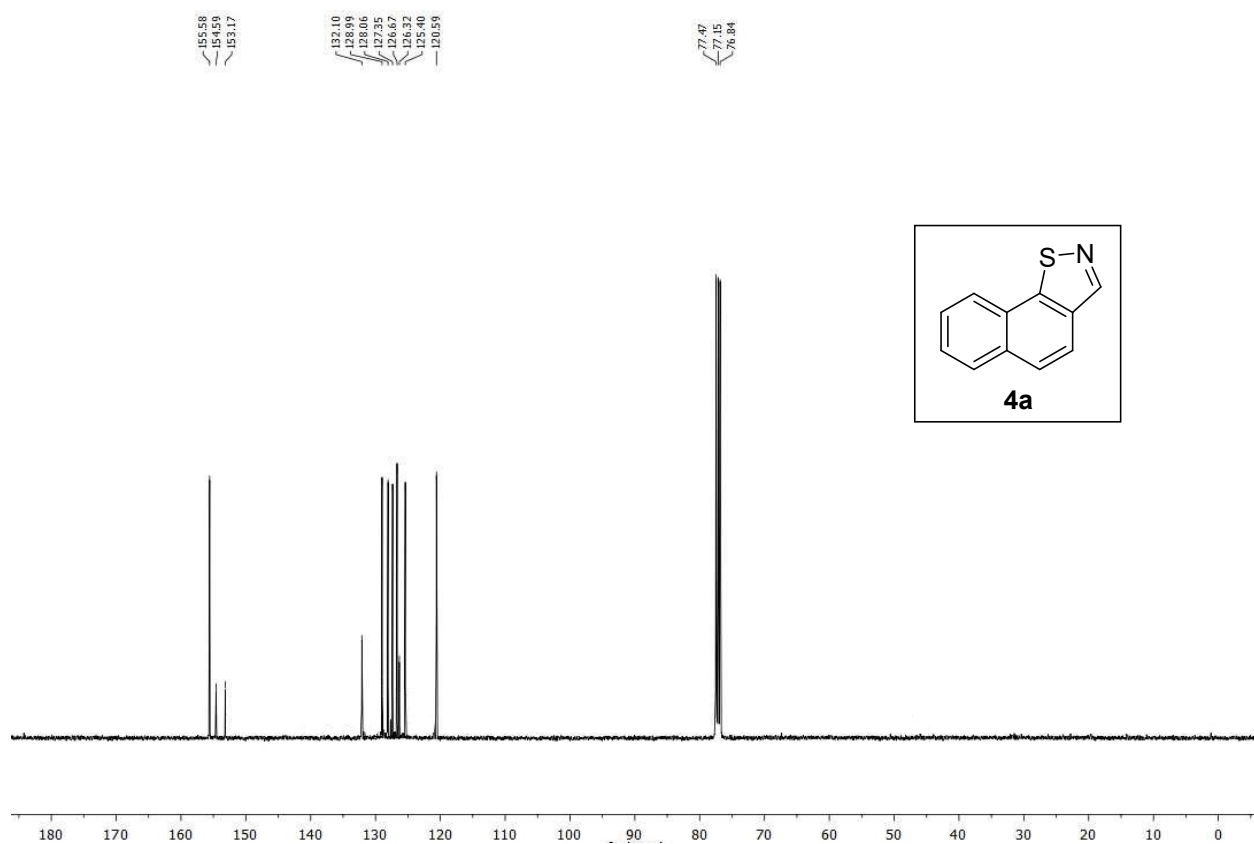
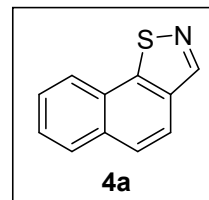
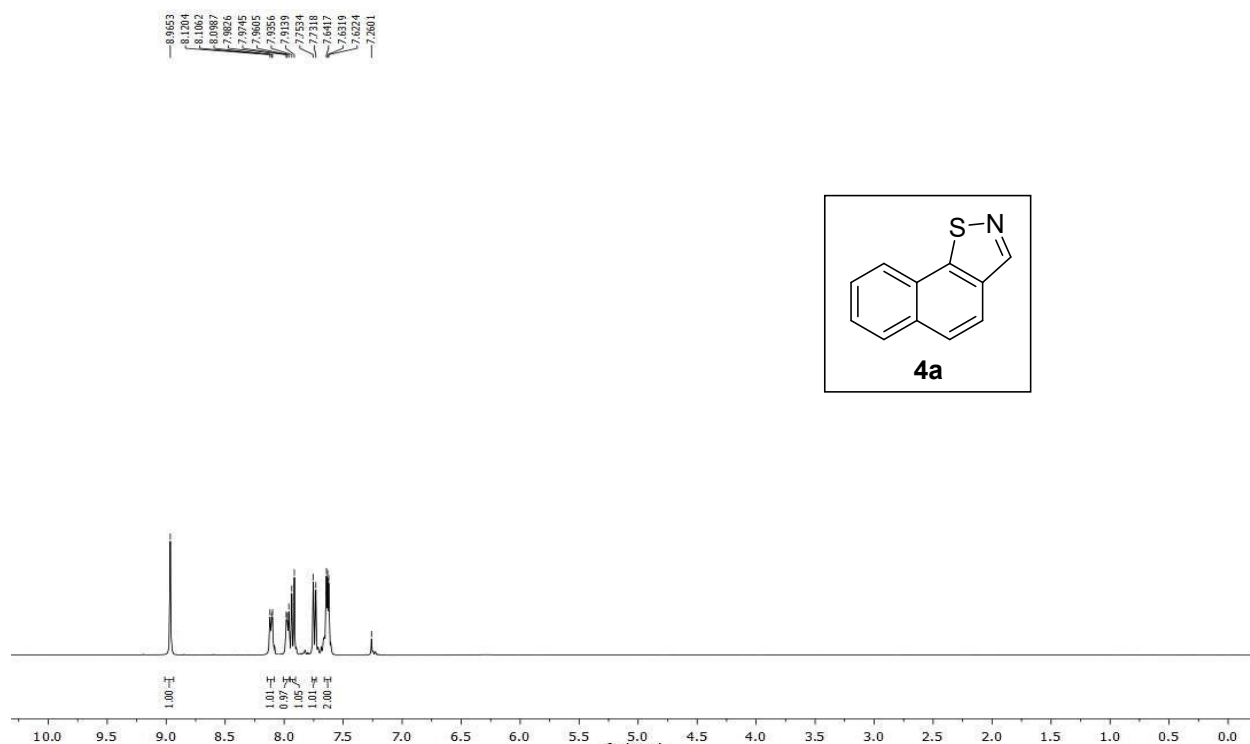


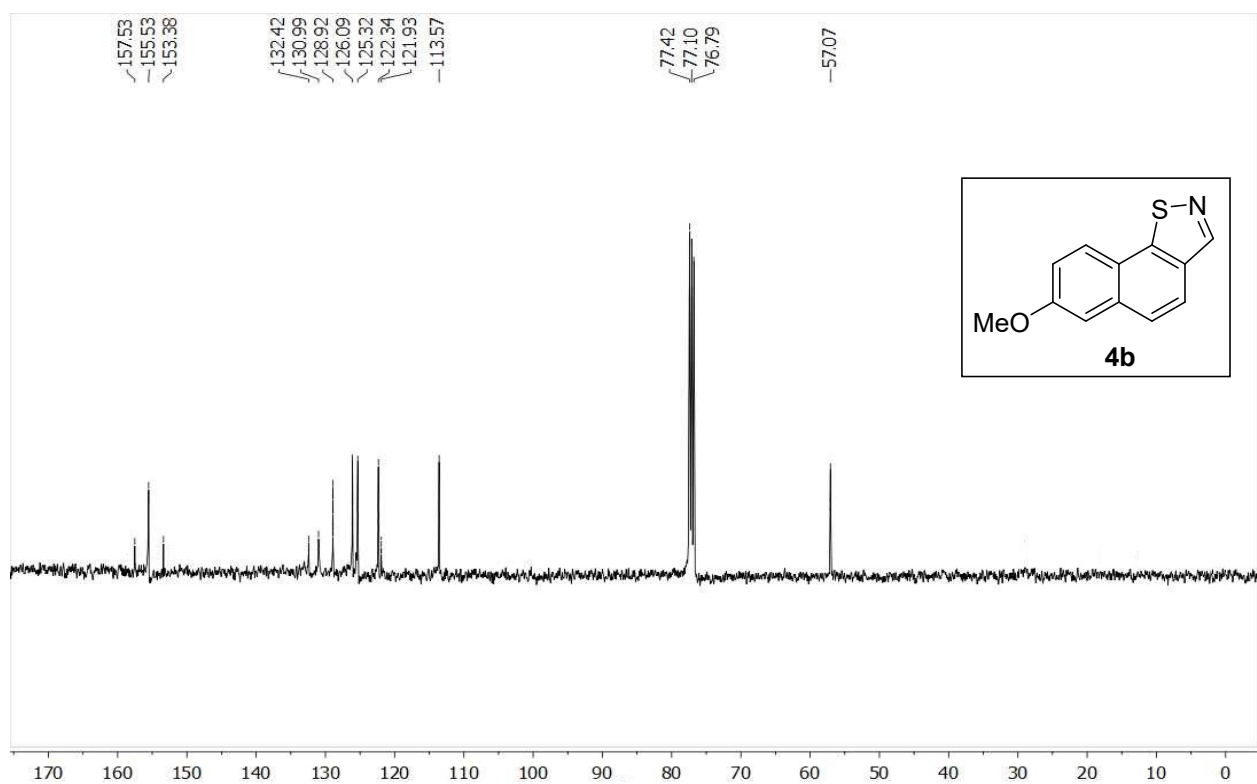
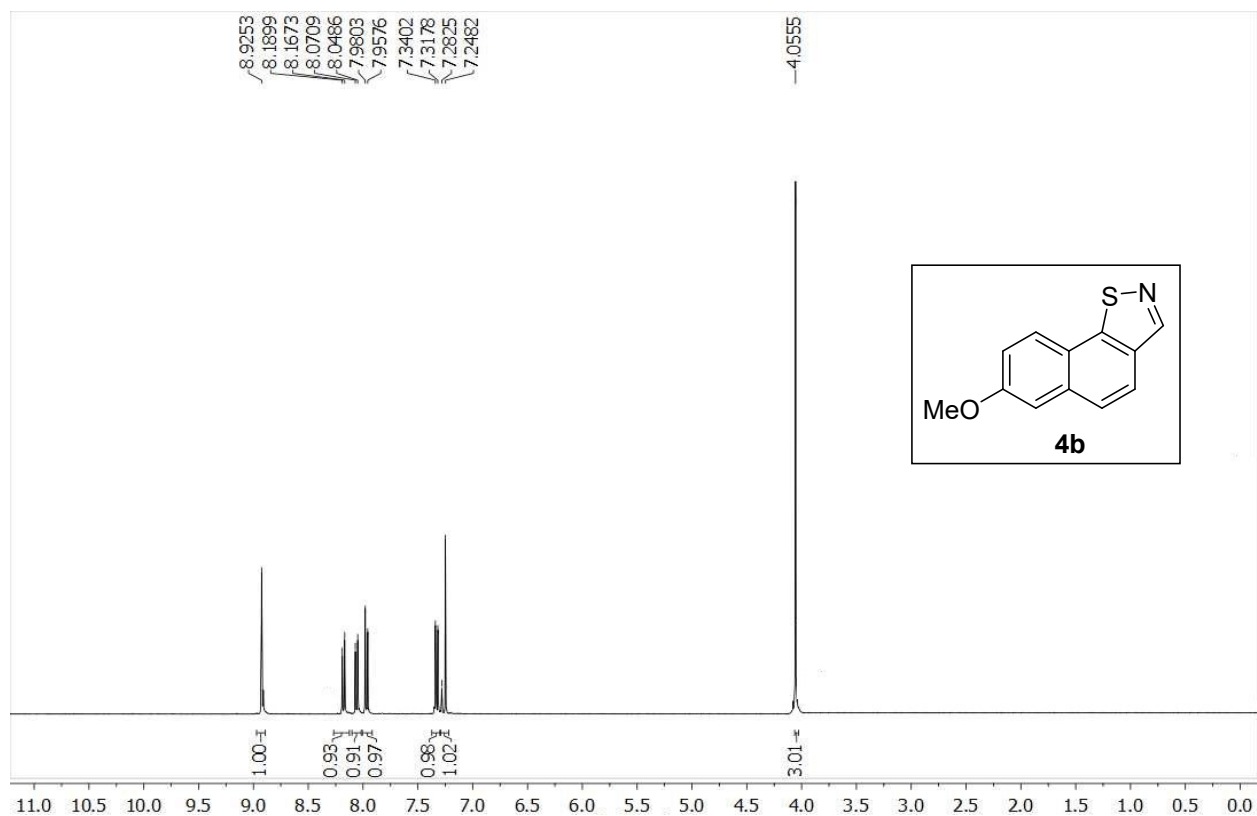


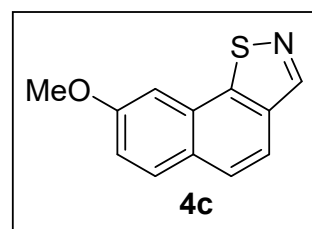
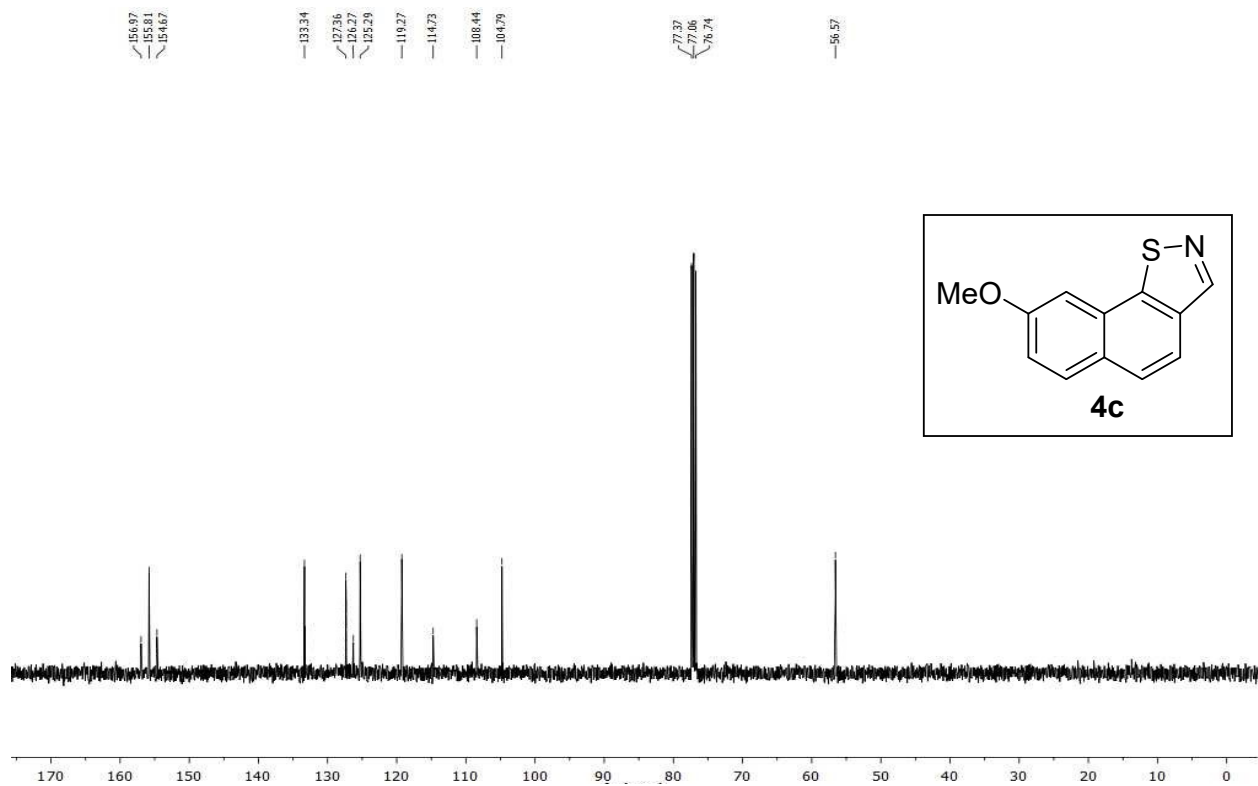
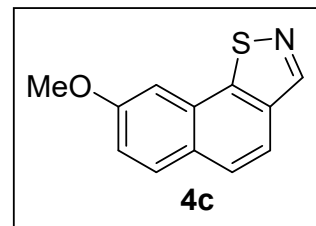
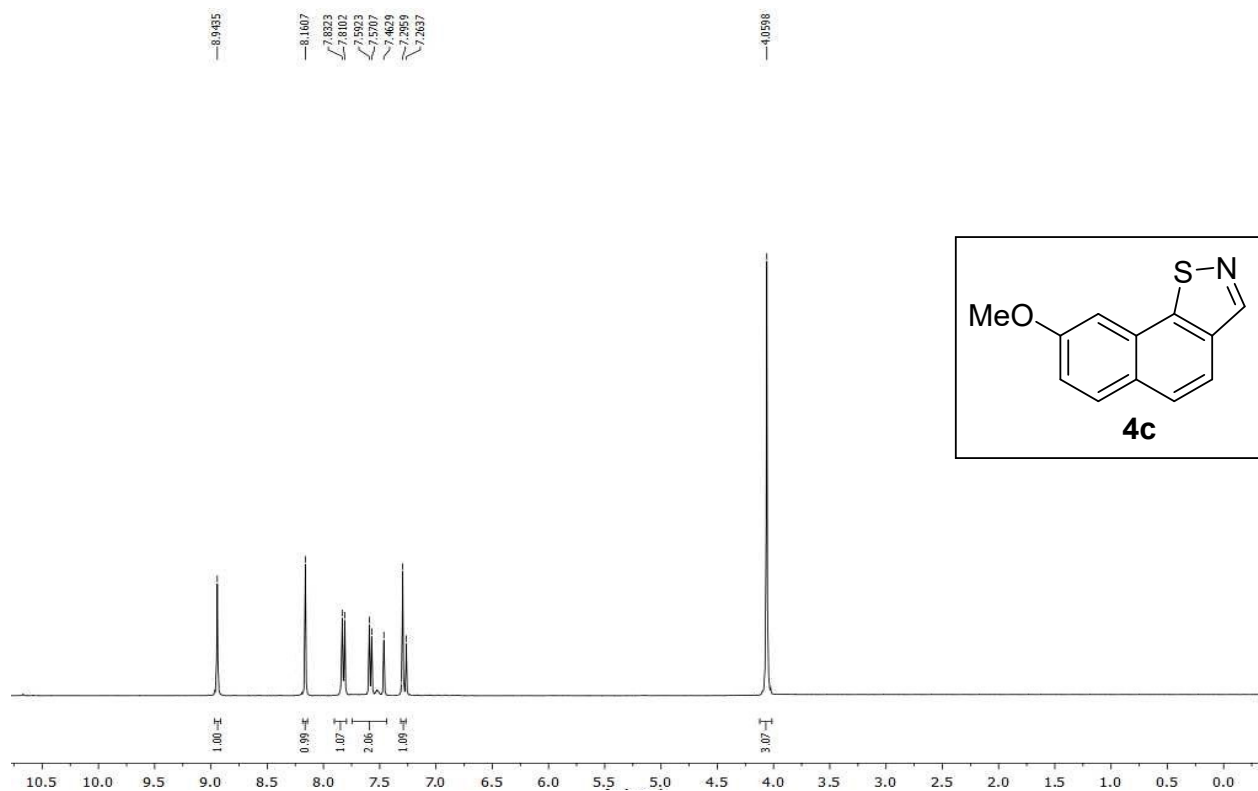


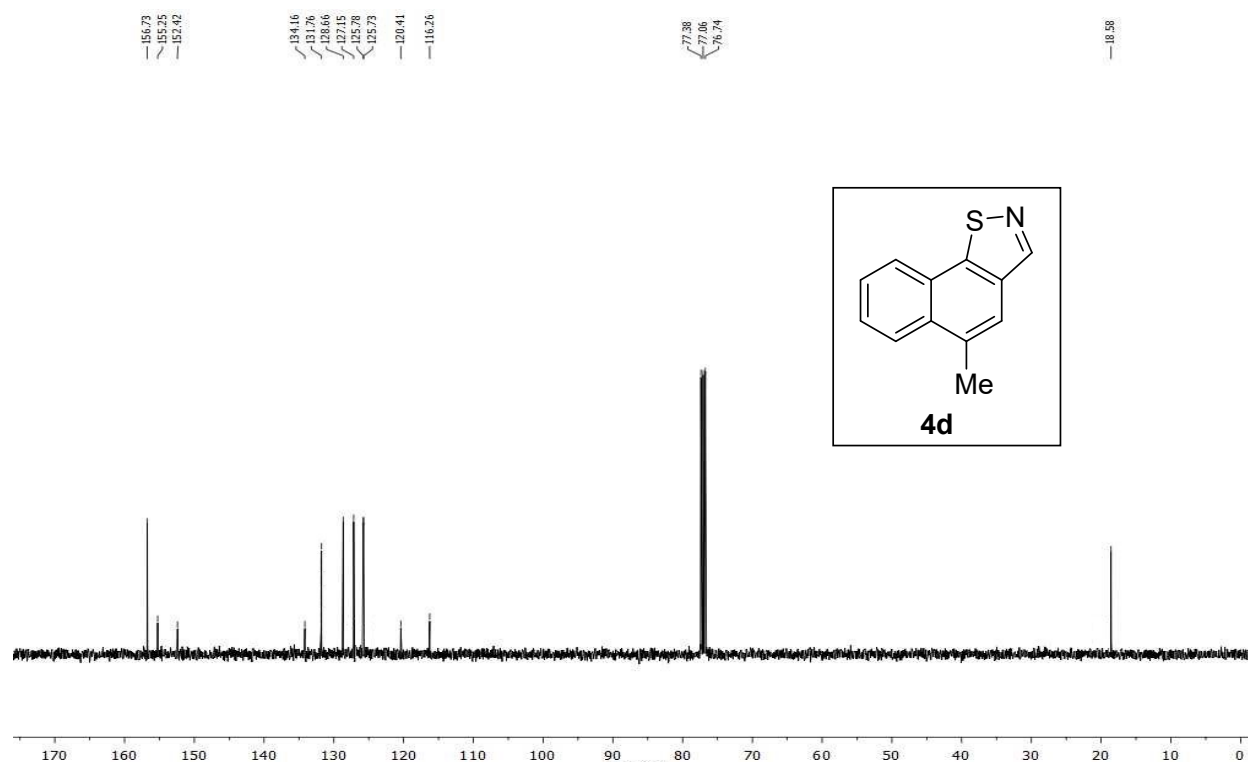
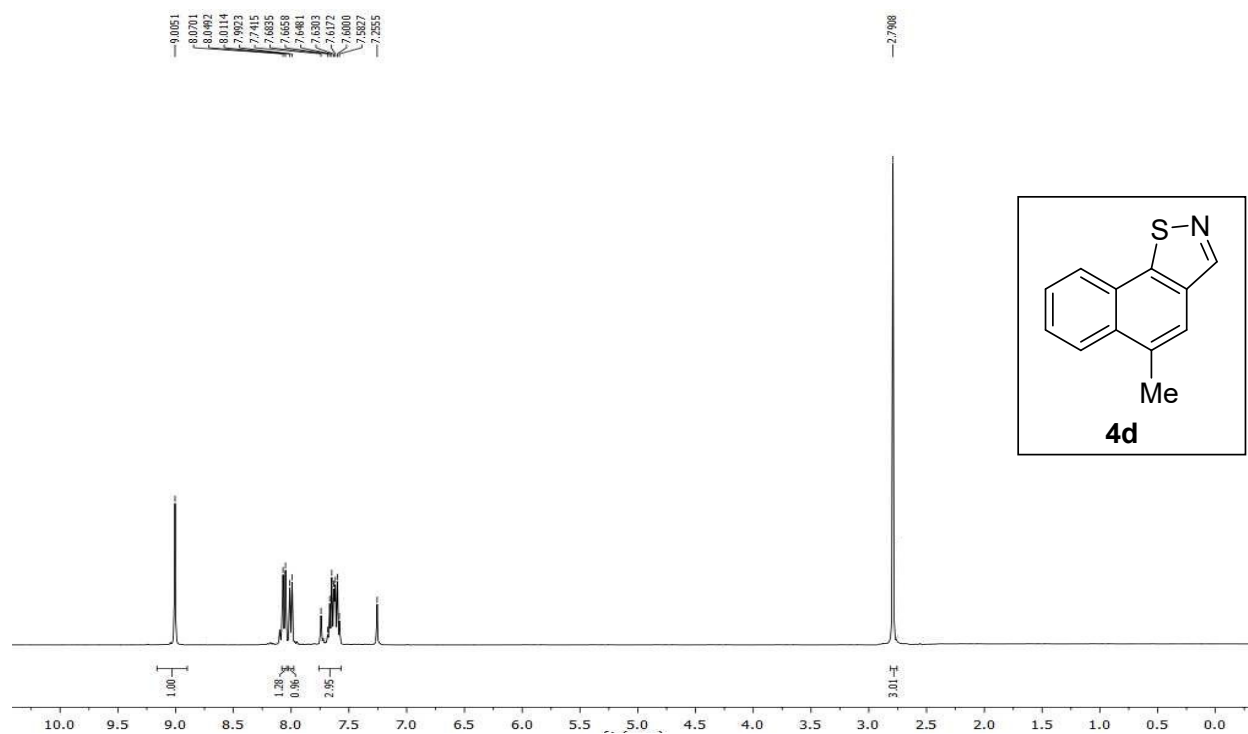


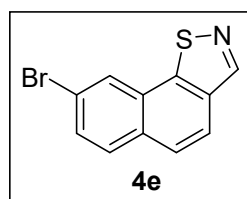
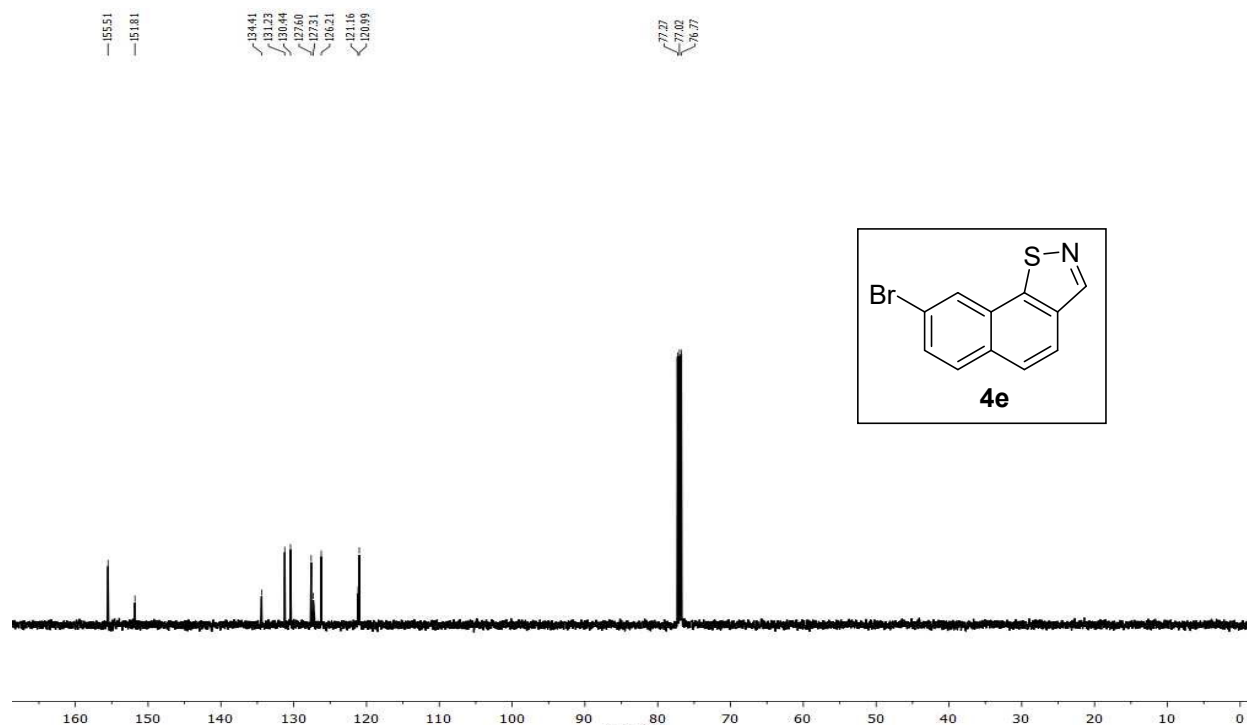
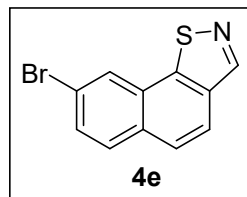
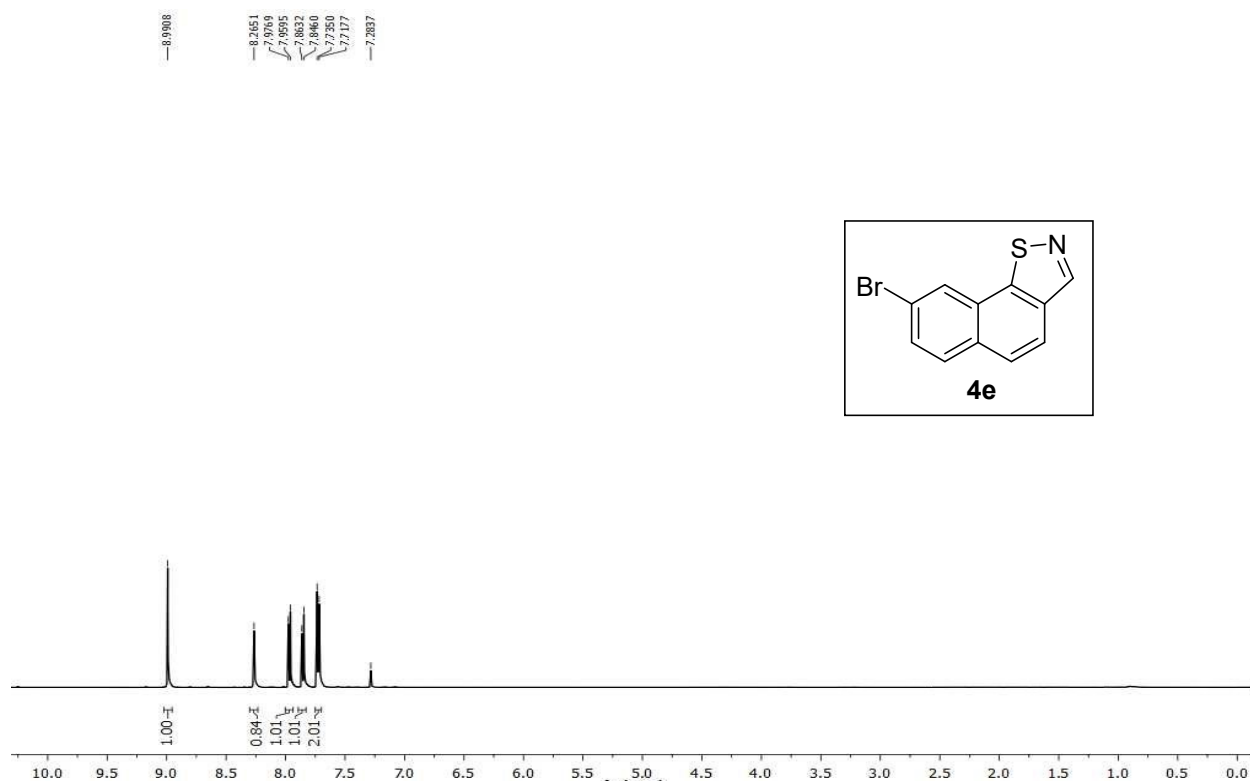


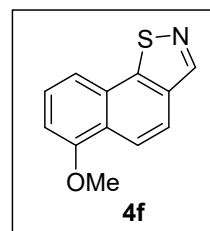
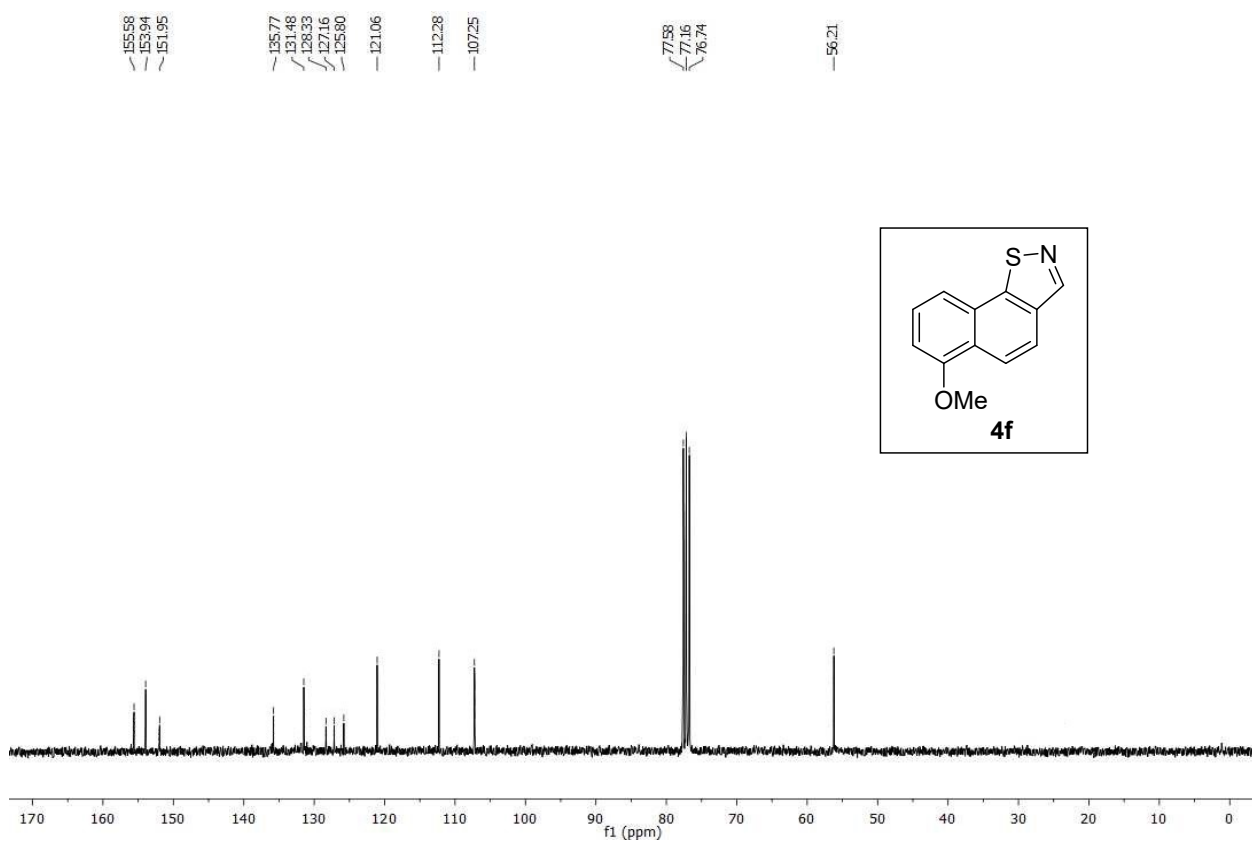
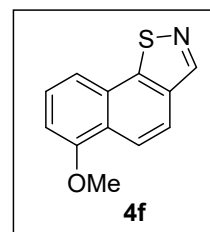
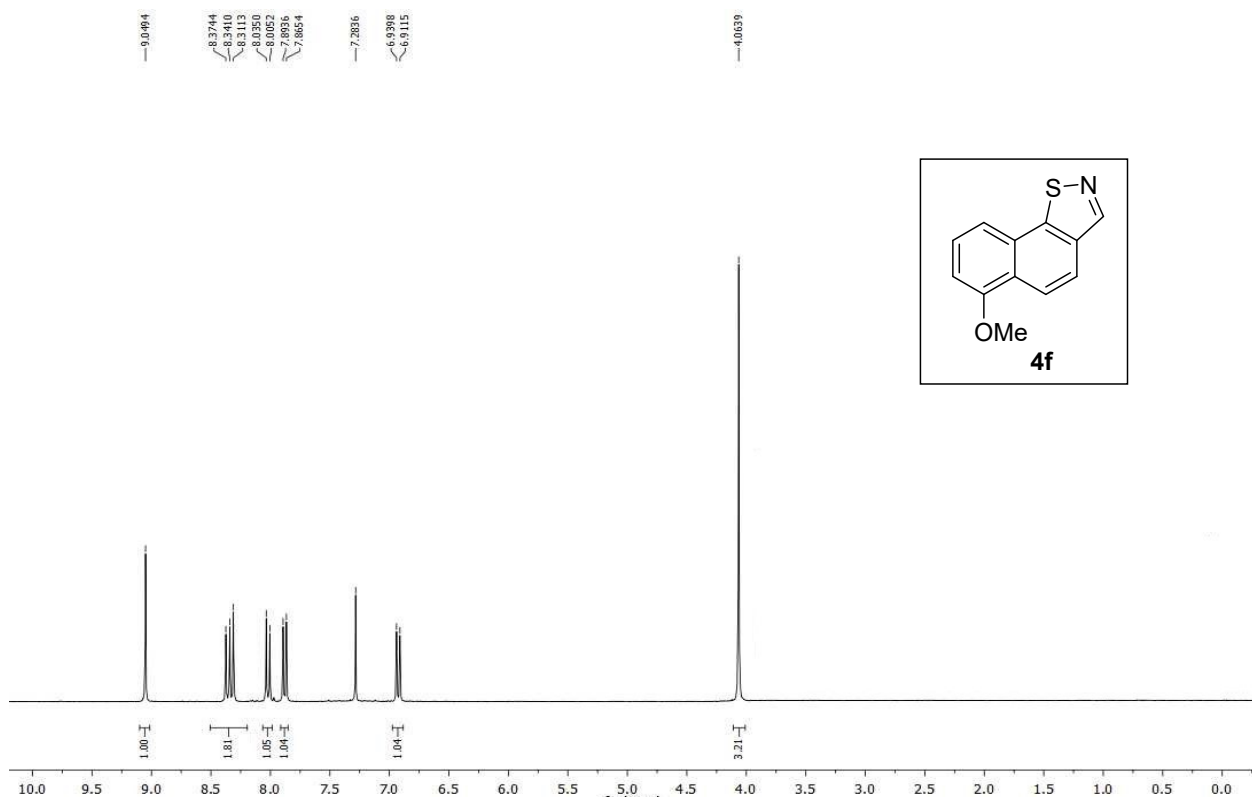


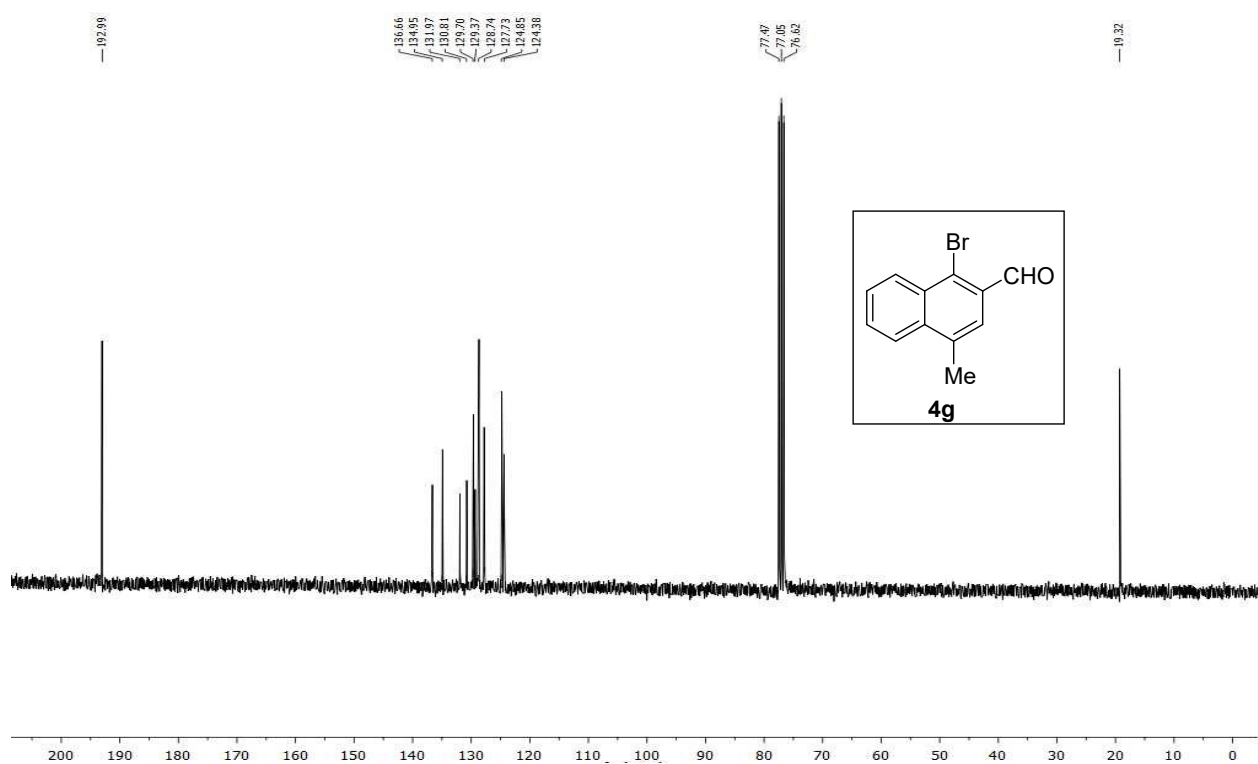
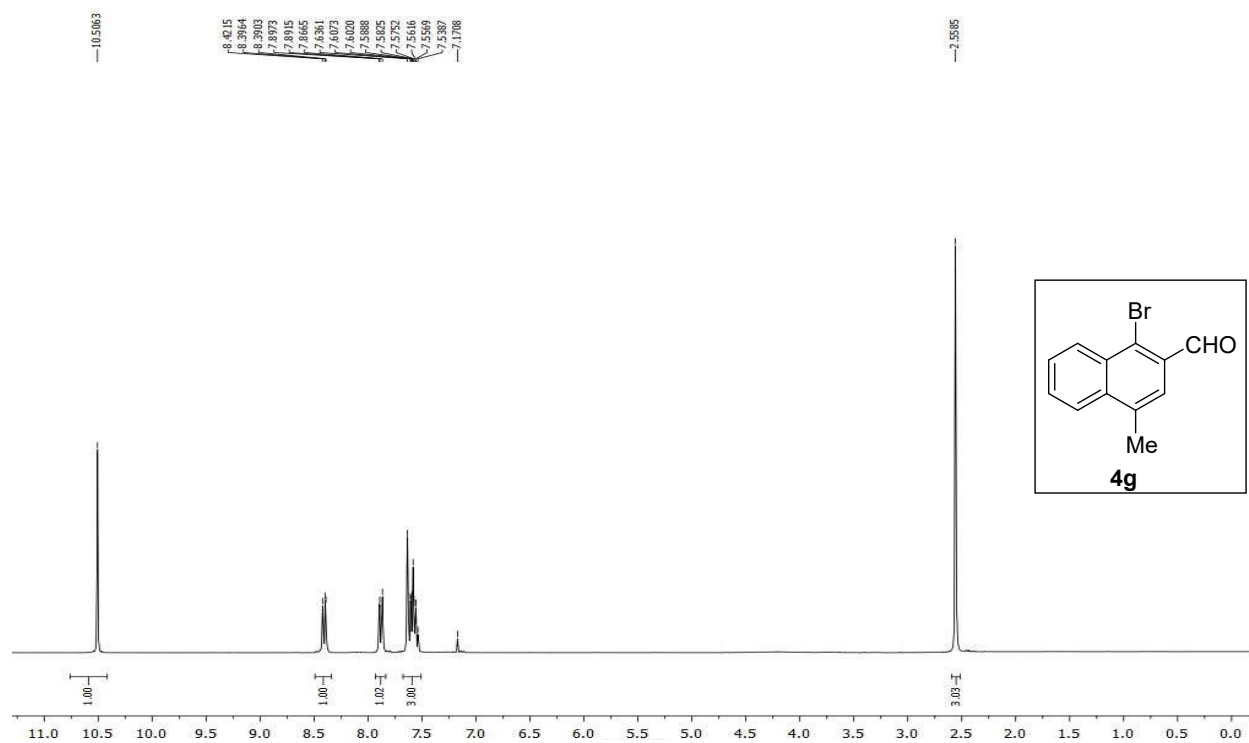












HRMS Spectra:

