Supporting Information

Eco-friendly metal-/catalyst-free one-pot three-component thioamination of 1,4-naphthoquinone in green solvent

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1. General information

Solvents, naphthoquinones, thiophenols, and amines were purchased from commercial suppliers and used without further purification. Silica gel was purchased from Qing Dao Hai Yang Chemical Industry. The ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and ^{19}F NMR (376 MHz) NMR spectra data were recorded on Bruker Avance 400 MHz spectrometer using $CDCl_3$ as solvent at room temperature (20 ± 2 °C). To display multiplicities and signal forms correctly the following abbreviations were used: s = singlet, d = doublet, t = triplet, m = multiplet.^{1}H NMR and ^{13}C NMR spectra were recorded with tetramethylsilane (δ = 0.00 ppm) as an internal reference. High-resolution mass spectra (HRMS) were obtained with a Waters Micromass Q-Tof Micro instrument using the ESI technique.

2. Experimental operation process

2.1 Preparation of deep eutectic solvents

Choline chloride (ChCl) : Urea: ChCl (0.03 mol, 4.1887 g) and urea (0.06 mol, 3.6033 g) were mixed in a small flask at a ratio of 1 : 2, then the two solids were slowly heated to 80 °C, stirred for 30 minutes and cooled to room temperature. Then the deep eutectic solvent with 100% atomic economy was obtained.

ChCl : p-toluenesulfonic acid (p-TsOH) : ChCl (0.02 mol, 2.7925 g) and *p*-TsOH (0.02 mol, 3.4440 g) were mixed in a small flask at a ratio of 1 : 1, then the two solids were slowly heated to 100 °C under N_2 atmosphere, stirred for 40 minutes and cooled to room temperature. Then the colorless deep eutectic solvent was obtained.

ChCl:Glycerol : ChCl (0.015 mol, 2.0944 g) and glycerol (0.03 mol, 2.7627 g) were mixed in a small flask at a ratio of 1 : 2, then the two compounds were slowly heated to 80 °C, stirred for 30 minutes and cooled to room temperature. Then the colourless homogenous deep eutectic solvent was obtained.

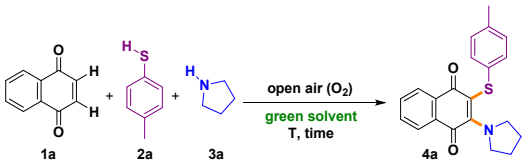
2.2 Experimental procedure for the synthesis of 4a-4o

In a 25 mL reaction tube, 1,4-naphthoquinone **1a** (0.2 mmol), thiophenols **2** (0.3 mmol) and pyrrolidine **3a** (0.3 mmol) were dissolved in CPME (1.5 mL), and then the reaction tube was stirred in air at 70 °C for 6 h. After the reaction, the mixture was collected, and the residue was purified by silica gel column chromatography to obtain the desired products **4**.

2.3 Experimental procedure for the synthesis of 5a-5f

In a 25 mL reaction tube, 1,4-naphthoquinone **1a** (0.2 mmol), *p*-methylthiophenol **2a** (0.3 mmol), and aliphatic amines **3** (0.3 mmol) were dissolved in CPME (1.5 mL), and then the reaction tube was stirred in air at 70 °C for 6 h. After the reaction, the mixture was collected, and the residue was purified by silica gel column chromatography to obtain the desired products **5**.

2.4 Condition optimization

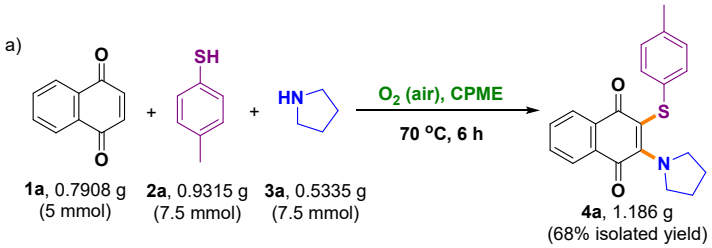


Entry	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	H_2O	35	12	10
2	CH_3CH_2OH	35	12	26
3	PEG-200	35	12	28
4	2-MeTHF	35	12	49
5	MBTE	35	12	42
6	CPME	35	12	55
7	DMC	35	12	50
8	EC	35	12	Trace
9	PC	35	12	Trace
10	$BMIMBF_4$	35	12	Trace
11	ChCl:Urea (1:2)	35	12	20
12	ChCl:*p*-TsOH (1:1)	35	12	Trace
13	ChCl:Glycerol (1:2)	35	12	17
14	CPME	35	9	55
15	CPME	35	6	56
16	CPME	35	3	51
17	CPME	0	6	37
18	CPME	60	6	75
19	**CPME**	**70**	**6**	**78**
20	CPME	80	6	65
21	CPME	90	6	64

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), **3a** (0.3 mmol), solvent (1.5 mL), open air. PEG-200 = polyethylene glycol (molecular weight = 200), MBTE = methyl *tert*-butyl ether, DMC = dimethyl carbonate, EC = ethylene carbonate, PC = propylene carbonate, $BMIMBF_4$ = 1-butyl-3-methylimidazolium tetrafluoroborate, ChCl = choline chloride, *p*-TsOH = *p*-toluenesulfonic acid. [b]Yield was determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as the internal standard.

2.5 Application of this one-pot thioamination in green solvent

To a 250 mL flask, 1,4-naphthoquinone **1a** (5 mmol), *p*-methylthiophenol **2a** (7.5 mmol) and pyrrolidine **3a** (7.5 mmol) were dissolved in CPME (75 mL), and then the reaction flask was stirred in air at 70 °C for 6 h. After the reaction, the mixture was collected, and the residue was purified by column chromatography on silica gel to afford the desired products **4a** (Scheme S1a).



Scheme S1. Application of this one-pot thioamination in green solvent

2.6 Experimental procedure for control experiments

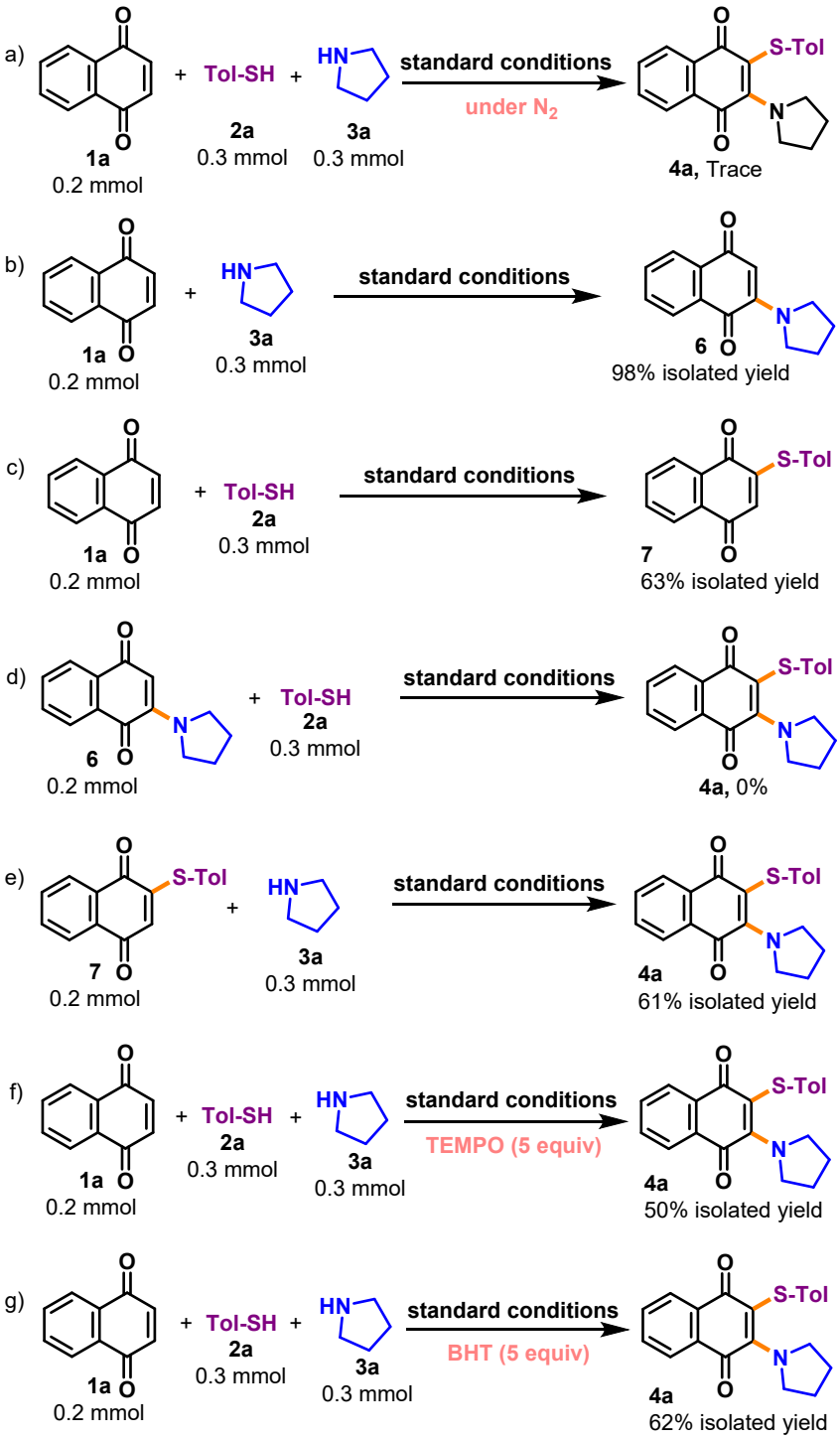
Experimental procedure for **Scheme S2(a)**: The 25 mL reaction tube containing the solution of 1,4-naphthoquinone **1a** (0.2 mmol), *p*-methylthiophenol **2a** (0.3 mmol) and pyrrolidine **3a** (0.3 mmol) in CPME (1.5 mL) was filled with nitrogen three times, and then the reaction tube was stirred in air at 70 °C for 6 h. After the reaction, product **4a** was detected by TLC.

Experimental procedure for **Scheme S2(c)**: In a 25 mL reaction tube, 1,4-naphthoquinone **1a** (0.2 mmol) and *p*-methylthiophenol **2a** (0.3 mmol) were dissolved in CPME (1.5 mL), and then the reaction tube was stirred in air at 70 °C for 6 h. After the reaction, the mixture was collected, and the residue was purified by silica gel column chromatography to obtain the desired product **7** in 63% yield.

Experimental procedure for **Scheme S2(d)**: In a 25 mL reaction tube, compound **6** (0.2 mmol) and *p*-methylthiophenol **2a** (0.3 mmol) were dissolved in CPME (1.5 mL), and then the reaction tube was stirred in air at 70 °C for 6 h. After the reaction, no product **4a** was detected by TLC.

Experimental procedure for **Scheme S2(e)**: In a 25 mL reaction tube, compound **7** (0.2 mmol) and pyrrolidine **3a** (0.3 mmol) were dissolved in CPME (1.5 mL), and then the reaction tube was stirred in air at 70 °C for 6 h. After the reaction, the mixture was collected, and the residue was purified by silica gel column chromatography to obtain the desired product **4a** in 61% yield.

Experimental procedure for **Scheme S2(f** and **g)**: In a 25 mL reaction tube, 1,4-naphthoquinone **1a** (0.2 mmol), *p*-methylthiophenol **2a** (0.3 mmol) and pyrrolidine **3a** (0.3 mmol) were dissolved in CPME (1.5 mL), in addition, a corresponding amount of additive (TEMPO or BQ) was added to the reaction system, and then the reaction tube was stirred in air at 70 °C for 6 h. After the reaction, the yield was determined by ^{1}H NMR (1,1,2,2-tetrachloroethane as the internal standard).

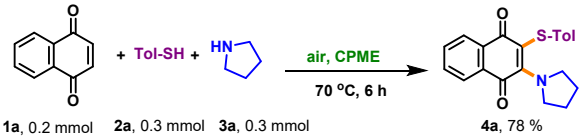


Scheme S2. Control Experiments

2.7 The calculation of green chemistry metrics

Entry	This work	Previous work (Ref 13)
AU (Atom Utilization)	0.63	0.63
E-factor	1.53	1.86
RME (Reaction Mass Efficiency)	0.39	0.35
MI (Mass Intensity)	38.53	88.29

Table S1 Green metrics of this work



1a, 0.2 mmol **2a**, 0.3 mmol **3a**, 0.3 mmol **4a**, 78 %

Item	Reactant 1	Reactant 2	Reactant 3	Product
	1a	**2a**	**3a**	**4a**
Mmol	0.2 mmol	0.3 mmol	0.3 mmol	0.156 mmol
MW	158.04	124.03	71.07	226.09
Mass	31.61 mg	37.21 mg	21.32 mg	35.27 mg

$$AU(atom\ utilization) = \frac{MW\ of\ desired\ products}{MW\ Reactant\ 1 + Reactant\ 2 + Reactant\ 3}$$

$$= \frac{226.09}{158.01 + 124.07 + 71.07}$$

$$= 0.63$$

$$E\text{-}factor = \frac{\Sigma MW\ of\ stoichiometric\ reactants - \Sigma MW\ of\ desired\ products}{\Sigma MW\ of\ desired\ products}$$

$$= \frac{31.6 + 37.2 + 21.3 - 35.27}{35.27}$$

$$= 1.54$$

$$RME(Reaction\ mass\ efficiency) = \frac{\Sigma MW\ of\ desired\ products}{\Sigma MW\ of\ stoichiometric\ reacta}$$

$$= \frac{35.27}{31.6 + 37.2 + 21.32}$$

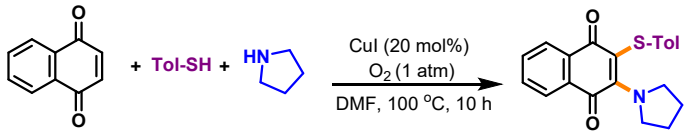
$$= 0.39$$

$$MI(mass\ intensity) = \frac{\Sigma MW\ of\ all\ substances\ (excluding}{\Sigma MW\ of\ desired\ products}$$

$$= \frac{31.6 + 37.2 + 21.3 + 21.5 \times 0.8 \times 1000}{35.27}$$

$$= 38.53$$

Table S2 Green metrics of the previous work



1a, 0.2 mmol **2a**, 0.2 mmol **3a**, 0.7 mmol **4a**, 82 %

Item	**Reactant 1**	**Reactant 1**	**Reactant 1**	**Product**
	1a	**2a**	**3a**	**4a**
Mmol	0.2 mmol	0.2 mmol	0.7 mmol	0.164 mmol
MW	158.04	124.03	71.07	226.09
Mass	31.61 mg	24.81 mg	49.75 mg	37.08 mg

$$AU(atom\ utilization) = \frac{MW\ of\ desired\ products}{MW\ Reactant\ 1 + MW\ Reactant\ 2 + MW\ Reactant\ 3}$$

$$= \frac{226.09}{158.01 + 124.07 + 31.07}$$

$$= 0.63$$

$$E\text{-}factor = \frac{\Sigma MW\ of\ stoichiometric\ reactants - \Sigma MW\ of\ desired\ products}{\Sigma MW\ of\ desired\ products}$$

$$= \frac{31.6 + 124.8 + 149.7 - 37.08}{37.08}$$

$$= 1.86$$

$$RME\ (reaction\ mass\ efficiency) = \frac{\Sigma MW\ of\ desired\ products}{\Sigma MW\ of\ stoichiometric\ reactants}$$

$$= \frac{37.08}{31.6 + 124.8 + 149.7}$$

$$= 0.35$$

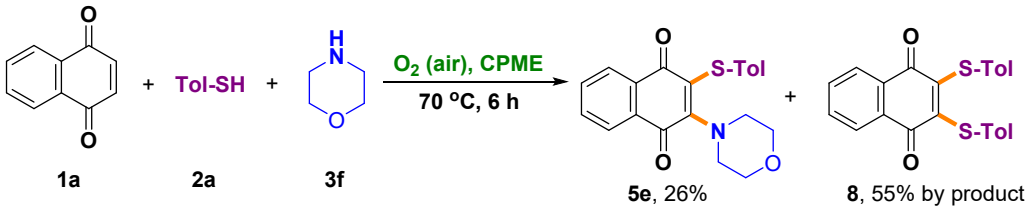
$$MI\ (mass\ intensity) = \frac{\Sigma MW\ of\ all\ substances\ (excluding\ O_2) + MW\ of\ O_2 \times 2.5}{\Sigma MW\ of\ desired\ products}$$

$$= \frac{31.6 + 124.8 + 149.7 + 190.4 \times 5.2 + 32.0 \times 2.0 + 32.0 \times 0.9 + 100 + 101.2}{37.08}$$

$$= 88.29$$

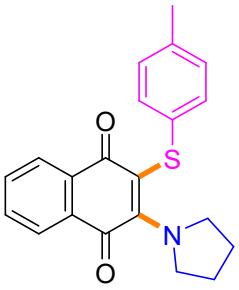
(The weight of O_2 balloon is approximately 1.28 g)

2.8 Byproduct analysis



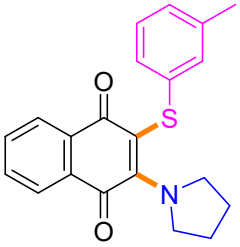
Experimental procedure: To 25 mL reaction tube, 1,4-naphthoquinone **1a** (0.2 mmol), *p*-methylthiophenol **2a** (0.3 mmol) and morpholine **3f** (0.3 mmol), CPME (1.5 mL) were added, and then the reaction tube was stirred in air at 70 °C for 6 h. After the reaction, the mixture was collected, and the residue was purified by silica gel column chromatography to obtain the desired product **5e** and byproduct **8** with yields of 26% and 55%, respectively.

3. Characterization data



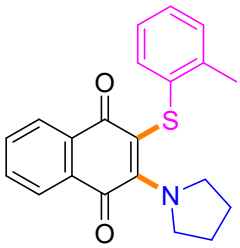
2-(pyrrolidin-1-yl)-3-(p-tolylthio)naphthalene-1,4-dione ***(4a)***[1]

Reddish brown solid, 75% yield (52 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.93 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.69 (td, *J* = 7.6, 1.5 Hz, 1H), 7.60 (td, *J* = 7.5, 1.3 Hz, 1H), 7.07 (d, *J* = 8.3 Hz, 2H), 7.03 (d, *J* = 8.3 Hz, 2H), 3.95 – 3.84 (m, 4H), 2.28 (s, 3H), 1.87 – 1.75 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.39, 180.29, 155.61, 135.06, 134.78, 134.09, 133.48, 131.96, 131.90, 129.59, 126.40, 126.25, 125.90, 105.66, 53.82, 25.50, 20.93.



2-(pyrrolidin-1-yl)-3-(m-tolylthio)naphthalene-1,4-dione ***(4b)***

Reddish brown solid, 58% yield (41 mg), mp 50.8 – 51.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 – 8.04 (m, 1H), 7.92 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.67 (td, *J* = 7.5, 1.4 Hz, 1H), 7.59 (td, *J* = 7.5, 1.4 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 1.7 Hz, 1H), 6.95 – 6.90 (m, 1H), 6.87 (d, *J* = 7.5 Hz, 1H), 3.96 – 3.82 (m, 4H), 2.26 (s, 3H), 1.87 – 1.71 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.44, 180.23, 155.89, 138.51, 134.12, 133.48, 131.98, 131.91, 128.68, 126.48, 126.42, 125.92, 125.88, 122.98, 104.85, 53.87, 25.50, 21.47. HRMS Calcd for $C_{27}H_{20}NO_2S$ [M + H]$^{+}$: m/z 350.1209, found: 350.1213.



2-(pyrrolidin-1-yl)-3-(o-tolylthio)naphthalene-1,4-dione ***(4c)***

Reddish brown solid, 56% yield (39 mg), mp 80.8 – 81.0 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.93 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.68 (td, *J* = 7.6, 1.4 Hz, 1H), 7.60 (td, *J* = 7.5, 1.3 Hz, 1H), 7.11 (dd, *J* = 7.1, 1.7 Hz, 1H), 7.06 – 6.94 (m, 2H), 6.87 (dd, *J* = 7.6, 1.6 Hz, 1H), 3.95 – 3.82 (m, 4H), 2.45 (s, 3H), 1.85 – 1.75 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.44, 180.18, 156.55, 137.67, 134.43, 134.15, 133.52, 132.02, 131.91, 130.07, 126.44, 126.34, 125.94, 125.20, 124.52, 103.82, 53.78, 25.49, 20.02. HRMS Calcd for $C_{27}H_{20}NO_2S$ [M + H]$^{+}$: m/z 350.1209, found: 350.1208.

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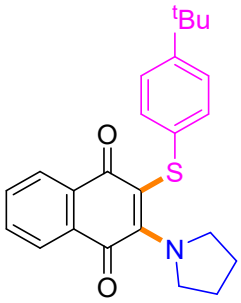
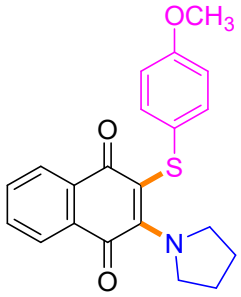
[1] F.L. Zeng, X. Chen, S.Q. He, *et al*., *Org. Chem. Front. 6* (**2019**) *1476–1480.*



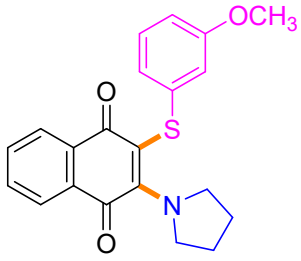
*2-((4-(tert-butyl)phenyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4d**)*[1]

Reddish brown solid, 71% yield (56 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 7.7 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 3.89 – 3.86 (m, 4H), 1.85 – 1.68 (m, 4H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.40, 180.29, 155.69, 148.03, 135.03, 134.07, 133.46, 131.95, 131.90, 126.36, 125.91, 125.89, 125.84, 105.52, 53.85, 34.33, 31.33, 25.48.



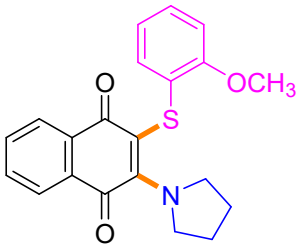
*2-((4-methoxyphenyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4e**)*[1]

Reddish brown solid, 65% yield (47 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.90 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.66 (td, *J* = 7.5, 1.4 Hz, 1H), 7.58 (td, *J* = 7.5, 1.3 Hz, 1H), 7.16 – 7.08 (m, 2H), 6.81 – 6.72 (m, 2H), 3.91 – 3.82 (m, 4H), 3.74 (s, 3H), 1.85 – 1.74 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.35, 180.43, 157.80, 155.15, 134.05, 133.43, 131.90, 129.11, 128.42, 126.34, 125.88, 114.58, 107.21, 55.35, 53.83, 25.52.



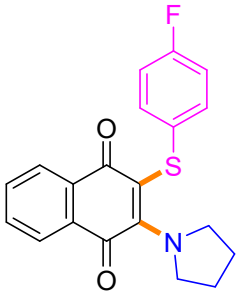
*2-((3-methoxyphenyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4f**)*

Reddish brown solid, 54% yield (39 mg), mp 38.8 – 39.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.89 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.66 (td, *J* = 7.4, 1.4 Hz, 1H), 7.57 (td, *J* = 7.6, 1.4 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.78 – 6.67 (m, 2H), 6.61 (dd, *J* = 8.1, 2.4 Hz, 1H), 3.97 – 3.82 (m, 4H), 3.71 (s, 3H), 1.90 – 1.71 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.39, 180.10, 159.88, 156.11, 140.32, 134.12, 133.43, 131.96, 131.92, 129.65, 126.36, 125.91, 118.18, 111.41, 110.57, 104.16, 55.20, 53.88, 25.47. HRMS Calcd for $C_{21}H_{20}NO_3S$ $[M + H]^+$: m/z 366.1158, found: 366.1160.



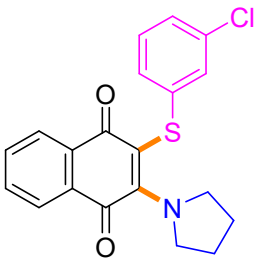
*2-((2-methoxyphenyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4g**)*[1]

Reddish brown solid, 76% yield (55 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.92 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.67 (td, *J* = 7.6, 1.4 Hz, 1H), 7.59 (td, *J* = 7.5, 1.3 Hz, 1H), 7.08 – 7.03 (m, 1H), 6.90 – 6.78 (m, 3H), 3.92 – 3.89 (m, 7H), 1.85 – 1.74 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.50, 180.09, 156.73, 155.51, 134.11, 133.59, 132.03, 131.85, 127.10, 126.42, 126.37, 125.90, 125.61, 121.16, 110.36, 103.00, 55.87, 53.80, 25.50.



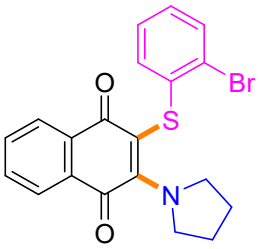
*2-((4-fluorophenyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4h**)*[1]

Reddish brown solid, 60% yield (42 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.91 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.68 (td, *J* = 7.5, 1.4 Hz, 1H), 7.59 (td, *J* = 7.5, 1.3 Hz, 1H), 7.18 – 7.08 (m, 2H), 6.97 – 6.87 (m, 2H), 3.95 – 3.83 (m, 4H), 1.88 – 1.77 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.33, 180.21, 162.03, 159.60, 156.04, 134.20, 133.88, 133.84, 133.35, 132.01, 131.89, 127.92, 127.85, 126.38, 125.97, 116.02, 115.80, 105.03, 54.03, 25.50. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -117.70.



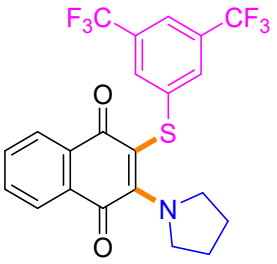
*2-((3-chlorophenyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4i**)*[1]

Reddish brown solid, 55% yield (41 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (t, *J* = 8.6 Hz, 1H), 7.92 (t, *J* = 8.7 Hz, 1H), 7.72 – 7.66 (m, 1H), 7.61 (t, *J* = 8.6 Hz, 1H), 7.19 – 6.89 (m, 4H), 4.00 – 3.68 (m, 4H), 1.94 – 1.55 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.25, 179.98, 156.49, 141.32, 134.69, 134.25, 133.33, 132.05, 131.95, 129.85, 126.43, 126.05, 125.41, 124.98, 123.84, 103.00, 54.09, 25.47.



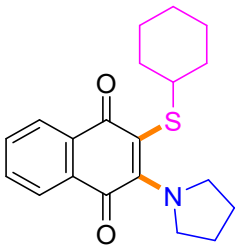
*2-((2-bromophenyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4j**)*[1]

Reddish brown solid, 63% yield (52 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.95 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.71 (td, *J* = 7.6, 1.4 Hz, 1H), 7.63 (td, *J* = 7.5, 1.3 Hz, 1H), 7.49 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.14 (td, *J* = 7.6, 1.4 Hz, 1H), 6.97 – 6.91 (m, 2H), 3.94 – 3.90 (m, 4H), 1.91 – 1.77 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.41, 179.90, 157.05, 139.95, 134.31, 133.43, 132.72, 132.03, 132.00, 127.67, 126.92, 126.49, 126.05, 125.82, 120.24, 102.74, 54.06, 25.49.



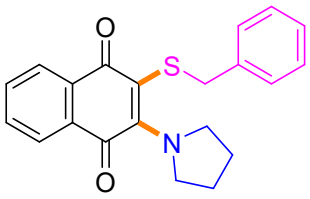
*2-((3,5-bis(trifluoromethyl)phenyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4k**)*

Reddish brown solid, 49% yield (46 mg), mp 169.1 – 169.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 7.6 Hz, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 6.7 Hz, 3H), 3.94 – 3.91 (m, 4H), 1.96 – 1.78 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 183.92, 179.62, 156.93, 142.98, 134.44, 133.15, 132.39, 132.25, 132.06, 131.88, 131.73, 131.40, 126.40, 126.23, 125.18, 124.49, 121.78, 100.58, 54.27, 25.39. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.02. HRMS Calcd for $C_{22}H_{16}F_6NO_2S$ $[M + H]^+$: m/z 472.0800, found: 472.0803.



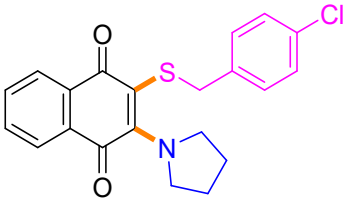
*2-(cyclohexylthio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4l**)*[1]

Purple solid, 22% yield (15 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.87 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.66 (td, *J* = 7.6, 1.4 Hz, 1H), 7.57 (td, *J* = 7.5, 1.3 Hz, 1H), 3.96 – 3.85 (m, 4H), 2.90 – 2.83 (m, 1H), 1.98 – 1.90 (m, 4H), 1.90 – 1.82 (m, 2H), 1.73 – 1.68 (m, 2H), 1.61 – 1.52 (m, 1H), 1.31 – 1.15 (m, 5H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.58, 181.00, 156.28, 133.85, 133.56, 131.90, 131.69, 126.14, 125.60, 108.36, 54.37, 46.05, 32.85, 26.10, 25.90, 25.65.



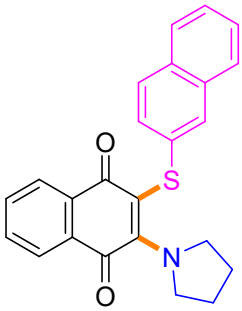
*2-(benzylthio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4m**)*[1]

Purple solid, 62% yield (43 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.82 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.66 (td, *J* = 7.6, 1.3 Hz, 1H), 7.55 (td, *J* = 7.6, 1.3 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.14 (td, *J* = 6.3, 5.9, 1.6 Hz, 3H), 3.82 (s, 2H), 3.72 – 3.58 (m, 4H), 1.85 – 1.70 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.19, 180.65, 156.55, 138.24, 133.91, 133.70, 131.76, 131.65, 128.96, 128.17, 126.90, 126.04, 125.69, 106.61, 54.32, 40.13, 25.45.



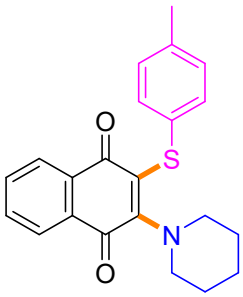
*2-((4-chlorobenzyl)thio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4n**)*[1]

Purple solid, 64% yield (49 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.95 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.75 – 7.61 (m, 2H), 7.21 – 7.14 (m, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 4.09 (s, 2H), 3.59 – 3.44 (m, 4H), 2.78 – 2.60 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 181.96, 181.64, 156.45, 136.57, 133.83, 133.06, 132.93, 132.74, 131.94, 130.26, 128.50, 126.70, 126.34, 125.31, 55.05, 38.27, 28.04.



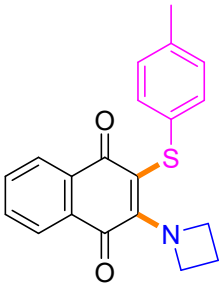
*2-(naphthalen-2-ylthio)-3-(pyrrolidin-1-yl)naphthalene-1,4-dione (**4o**)*

Reddish brown solid, 55% yield (42 mg), mp 49.6 – 50.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.97 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.75 – 7.68 (m, 3H), 7.67 – 7.59 (m, 2H), 7.48 (d, *J* = 1.8 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.31 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.02 – 3.82 (m, 4H), 1.88 – 1.66 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.38, 180.27, 155.99, 136.40, 134.20, 133.85, 133.48, 132.02, 131.37, 128.42, 127.72, 126.93, 126.46, 126.03, 125.18, 124.64, 123.64, 104.40, 53.91, 25.45. HRMS Calcd for $C_{24}H_{20}NO_2S$ $[M + H]^+$: m/z 386.1209, found: 386.1210.



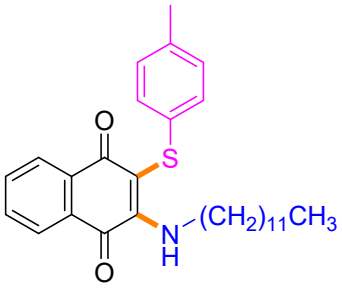
*2-(piperidin-1-yl)-3-(p-tolylthio)naphthalene-1,4-dione (**5a**)*[1]

Reddish brown solid, 81% yield (59 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 – 7.98 (m, 2H), 7.68 – 7.61 (m, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 3.38 – 3.41 (m, 4H), 2.29 (s, 3H), 1.73 – 1.67 (m, 4H), 1.63 – 1.57 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 182.39, 181.71, 155.02, 135.94, 133.79, 133.20, 132.81, 132.66, 132.26, 129.64, 127.95, 126.65, 126.45, 120.01, 53.39, 26.87, 24.10, 21.06.



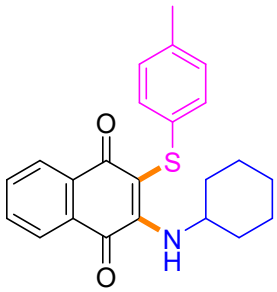
*2-(azetidin-1-yl)-3-(p-tolylthio)naphthalene-1,4-dione (**5b**)*

Reddish brown solid, 60% yield (40 mg), mp 68.5 – 69.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.98 – 7.88 (m, 1H), 7.66 (td, *J* = 7.6, 1.5 Hz, 1H), 7.55 (td, *J* = 7.6, 1.4 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 4.79 (t, *J* = 8.0 Hz, 4H), 2.34 – 2.26 (m, 2H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 182.70, 179.51, 151.22, 136.39, 134.59, 134.51, 133.58, 131.77, 131.30, 129.77, 126.59, 126.05, 125.92, 102.58, 58.77, 20.92, 18.31. HRMS Calcd for $C_{20}H_{18}NO_2S$ [M + H]$^{+}$: m/z 336.1053, found: 336.1053.



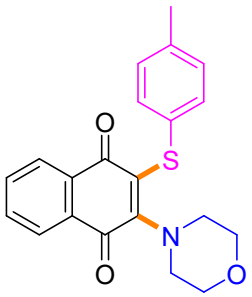
*2-(dodecylamino)-3-(p-tolylthio)naphthalene-1,4-dione (**5c**)*[1]

Reddish brown solid, 37% yield (34 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 7.6 Hz, 1H), 8.05 (d, *J* = 7.5 Hz, 1H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 3.89 – 3.83 (m, 2H), 2.26 (s, 3H), 1.59 (t, *J* = 7.2 Hz, 2H), 1.31 – 1.17 (m, 18H), 0.88 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 181.59, 135.25, 134.97, 133.85, 132.13, 129.82, 127.15, 126.81, 126.60, 45.65, 31.93, 30.49, 29.65, 29.57, 29.49, 29.36, 29.20, 26.64, 22.71, 20.94, 14.15.



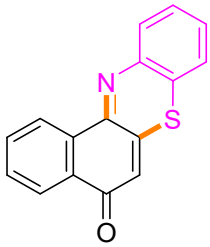
*2-(cyclohexylamino)-3-(p-tolylthio)naphthalene-1,4-dione (**5d**)*[1]

Reddish brown solid, 40% yield (30 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 7.1 Hz, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.69 (td, *J* = 7.5, 1.3 Hz, 1H), 7.59 (td, *J* = 7.5, 1.2 Hz, 1H), 7.14 (s, 2H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.54 (d, *J* = 9.1 Hz, 1H), 4.60 (d, *J* = 10.8 Hz, 1H), 2.25 (s, 3H), 2.01 – 1.85 (m, 2H), 1.69 (dt, *J* = 13.0, 3.9 Hz, 2H), 1.62 – 1.57 (m, 1H), 1.40 – 1.15 (m, 5H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 181.60, 179.88, 135.33, 134.91, 133.81, 132.13, 130.47, 129.80, 127.06, 126.61, 52.91, 34.17, 25.33, 24.53, 20.98.



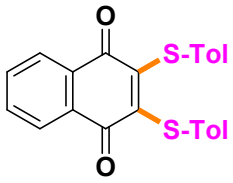
*2-morpholino-3-(p-tolylthio)naphthalene-1,4-dione (**5e**)*[1]

Reddish brown solid, 26% yield (19 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 – 8.07 (m, 1H), 8.07 – 8.02 (m, 1H), 7.75 – 7.64 (m, 2H), 7.22 – 7.15 (m, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 3.83 – 3.72 (m, 4H), 3.52 – 3.42 (m, 4H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 182.07, 181.90, 153.09, 136.48, 133.96, 132.97, 132.57, 132.19, 132.05, 129.79, 128.18, 126.74, 126.55, 122.13, 67.45, 51.81, 21.06.



*5H-benzo[a]phenothiazin-5-one (**5f**)*[1]

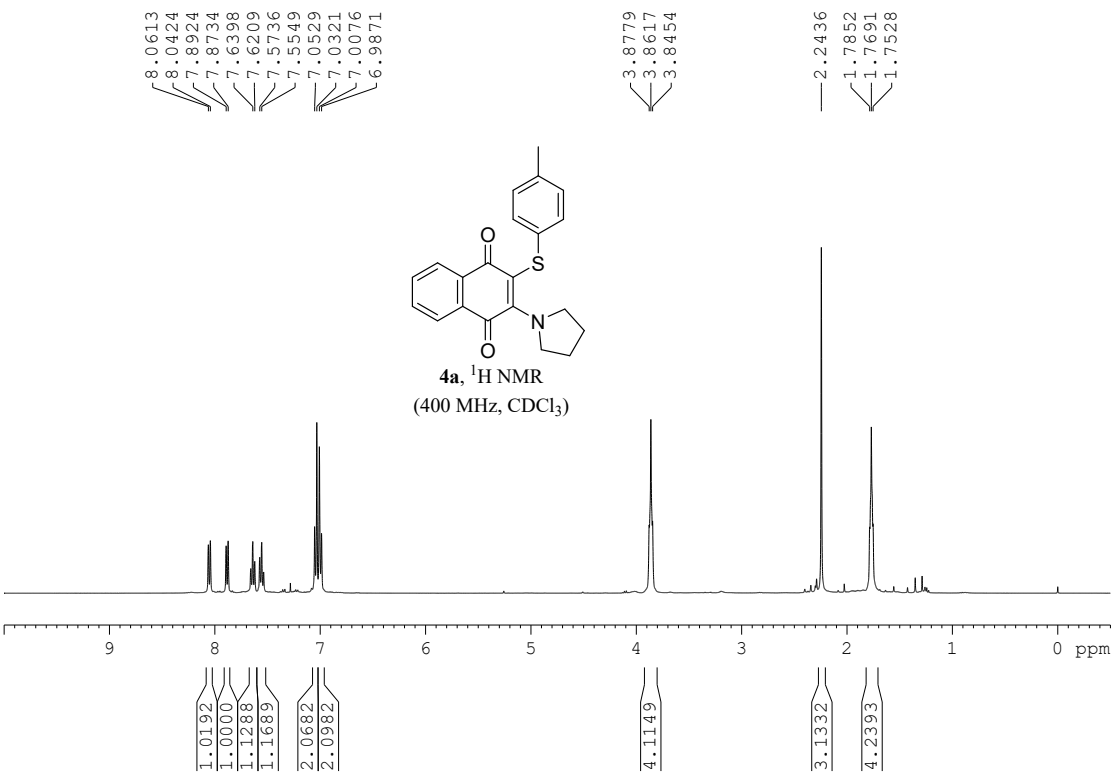
Yellow solid, 92% yield (48 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.79 – 8.63 (m, 1H), 8.30 – 8.08 (m, 1H), 7.85 – 7.74 (m, 1H), 7.67 (td, *J* = 8.0, 7.1, 4.2 Hz, 2H), 7.40 – 7.26 (m, 3H), 6.71 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 180.16, 144.65, 138.53, 137.75, 134.16, 133.34, 132.56, 131.59, 131.27, 129.93, 127.71, 125.73, 125.57, 124.63, 122.88, 120.20.



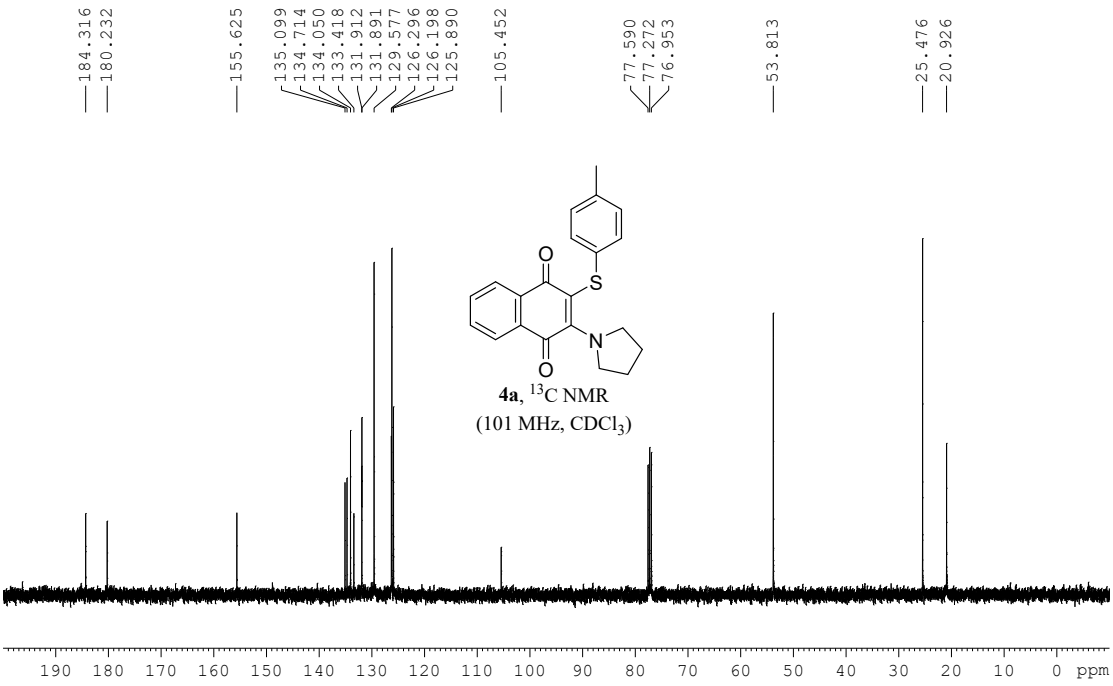
*2,3-bis(p-tolylthio)naphthalene-1,4-dione (**8**)*[1]

Reddish brown solid, 55% yield (44 mg). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 5.7, 3.3 Hz, 2H), 7.68 (dd, *J* = 5.8, 3.3 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 4H), 7.17 – 7.11 (m, 4H), 2.36 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.78, 148.32, 137.98, 133.68, 132.86, 131.43, 130.21, 129.95, 127.13, 21.27.

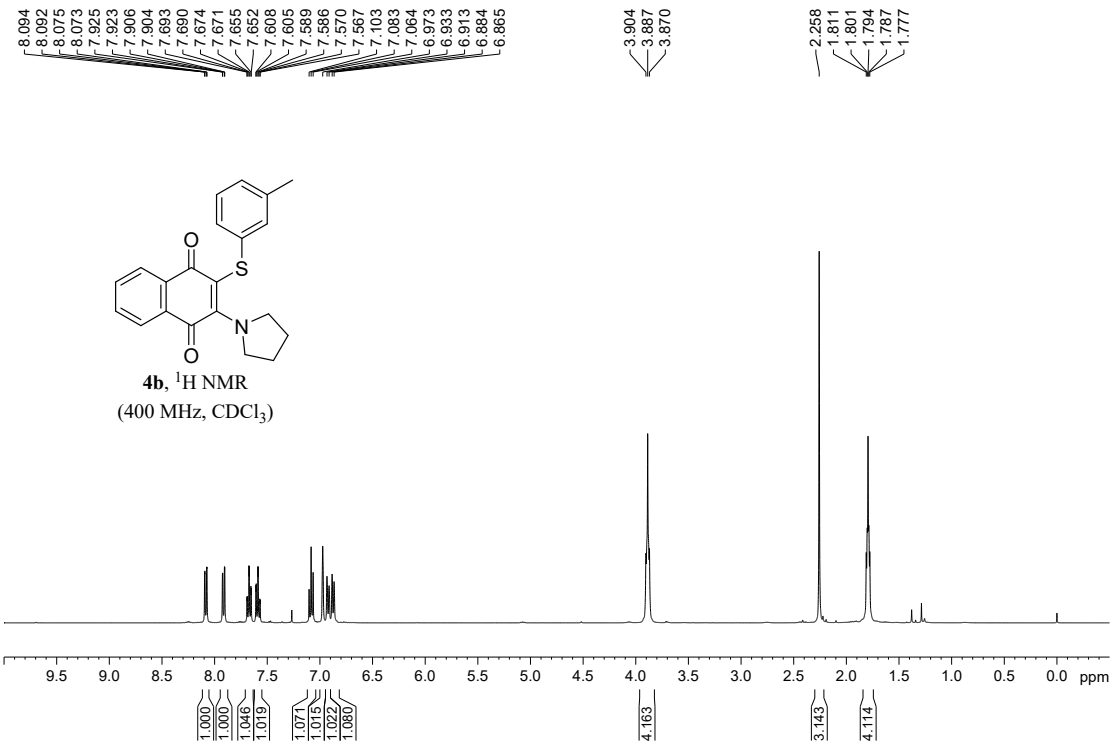
4. ^{1}H, ^{13}C, and ^{19}F NMR spectra



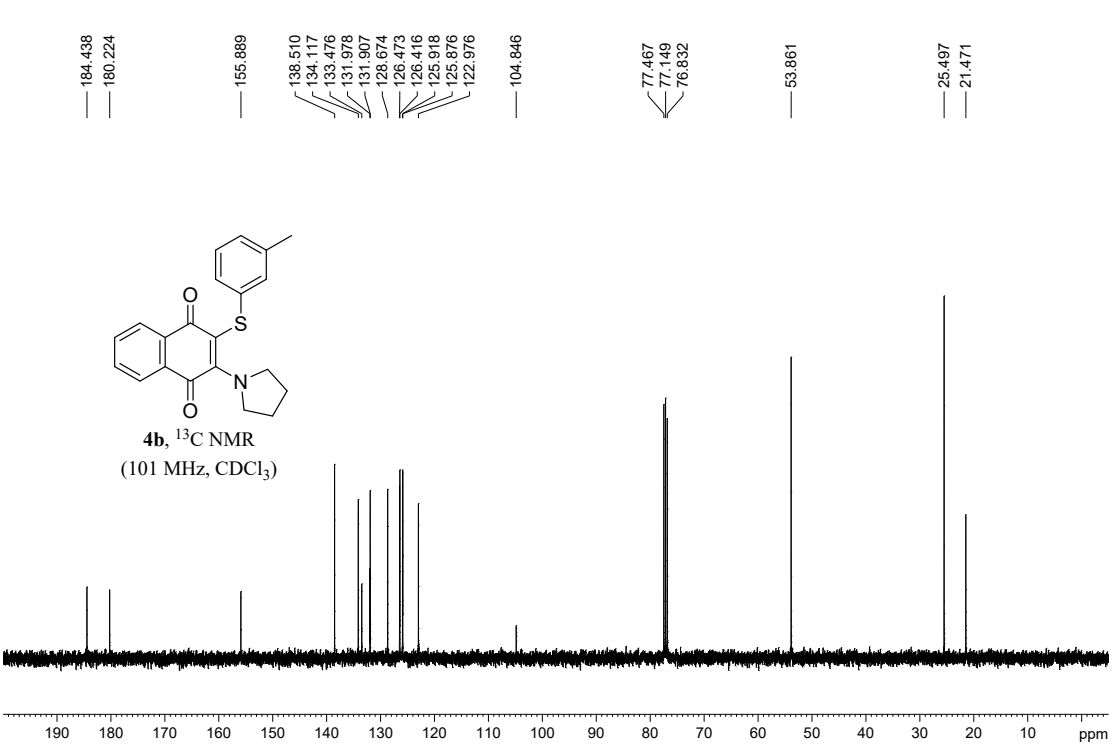
4a, ^{1}H NMR
(400 MHz, $CDCl_3$)



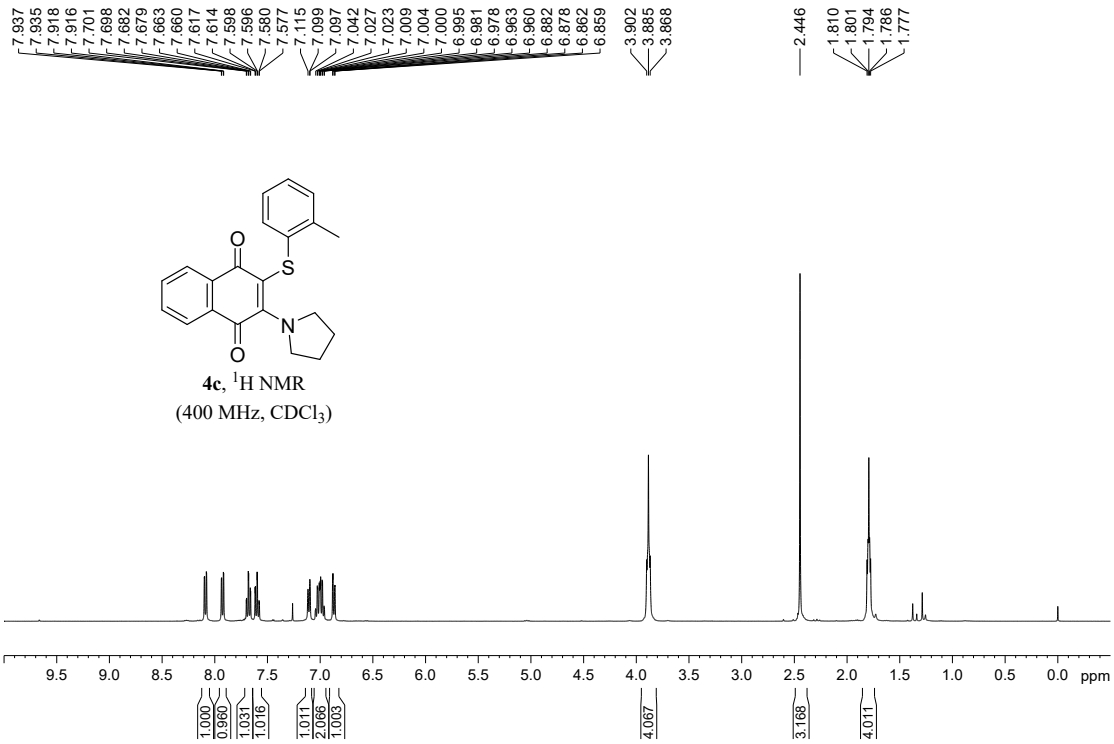
4a, ^{13}C NMR
(101 MHz, $CDCl_3$)



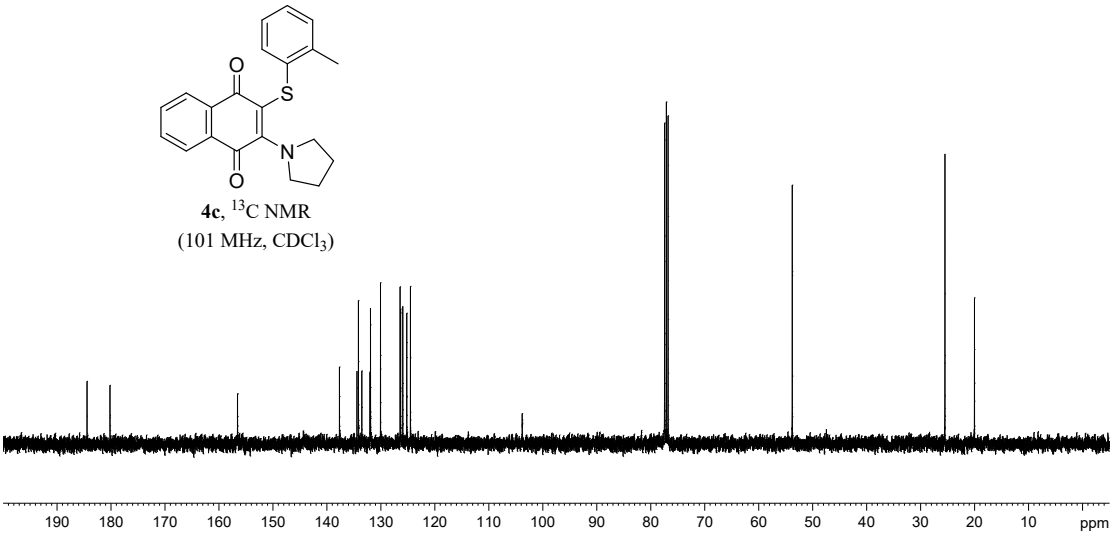
4b, ^{1}H NMR
(400 MHz, $CDCl_3$)



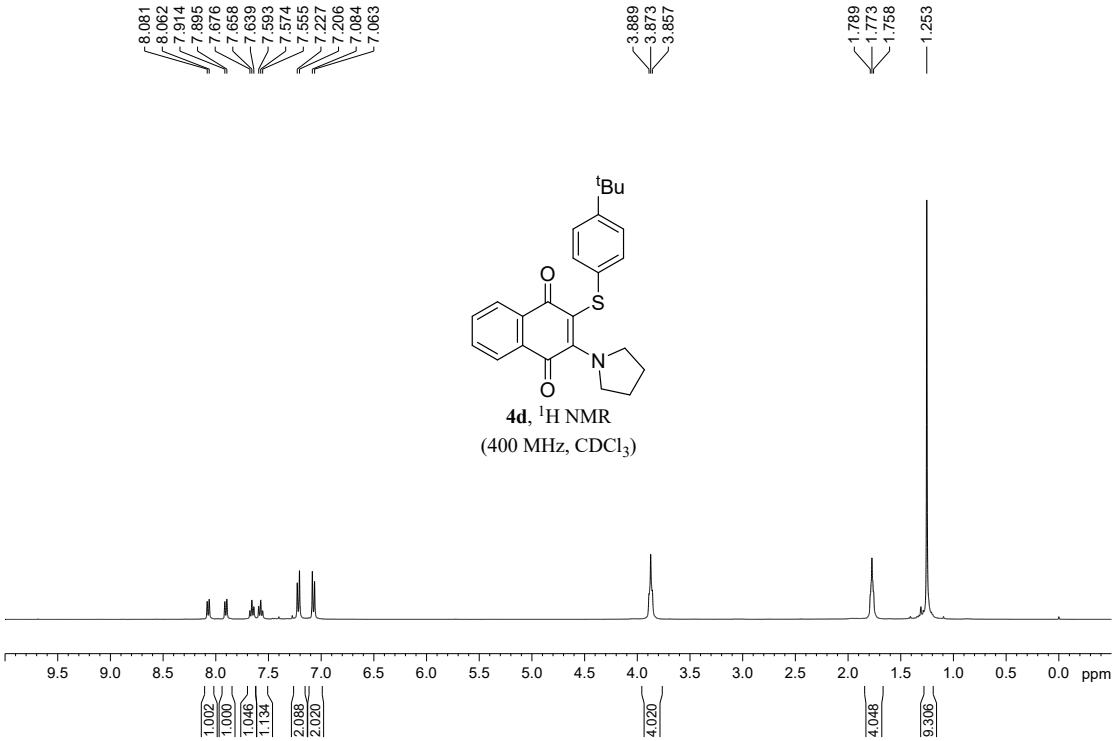
4b, ^{13}C NMR
(101 MHz, $CDCl_3$)



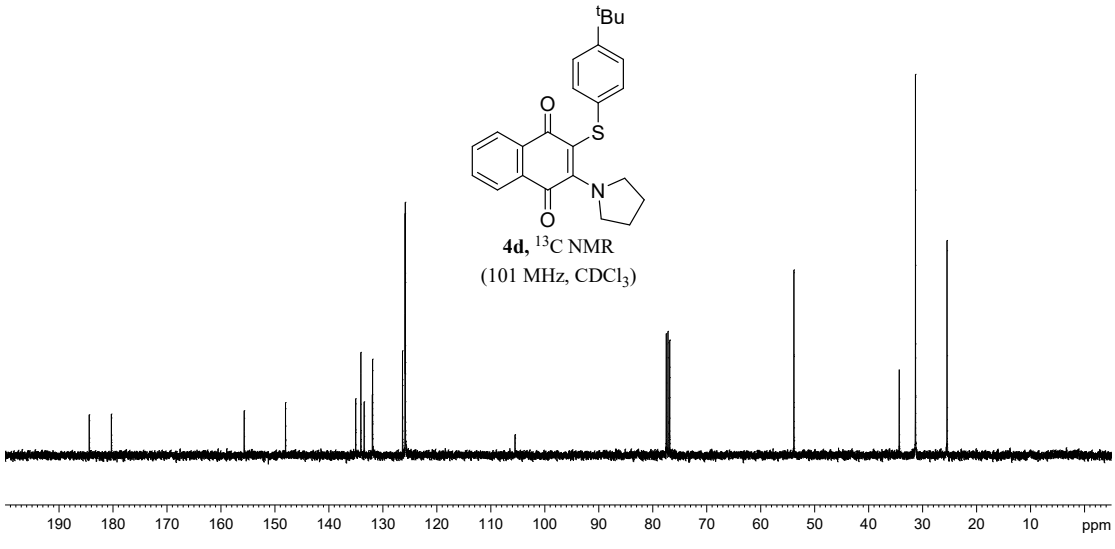
4c, ^{1}H NMR
(400 MHz, $CDCl_3$)



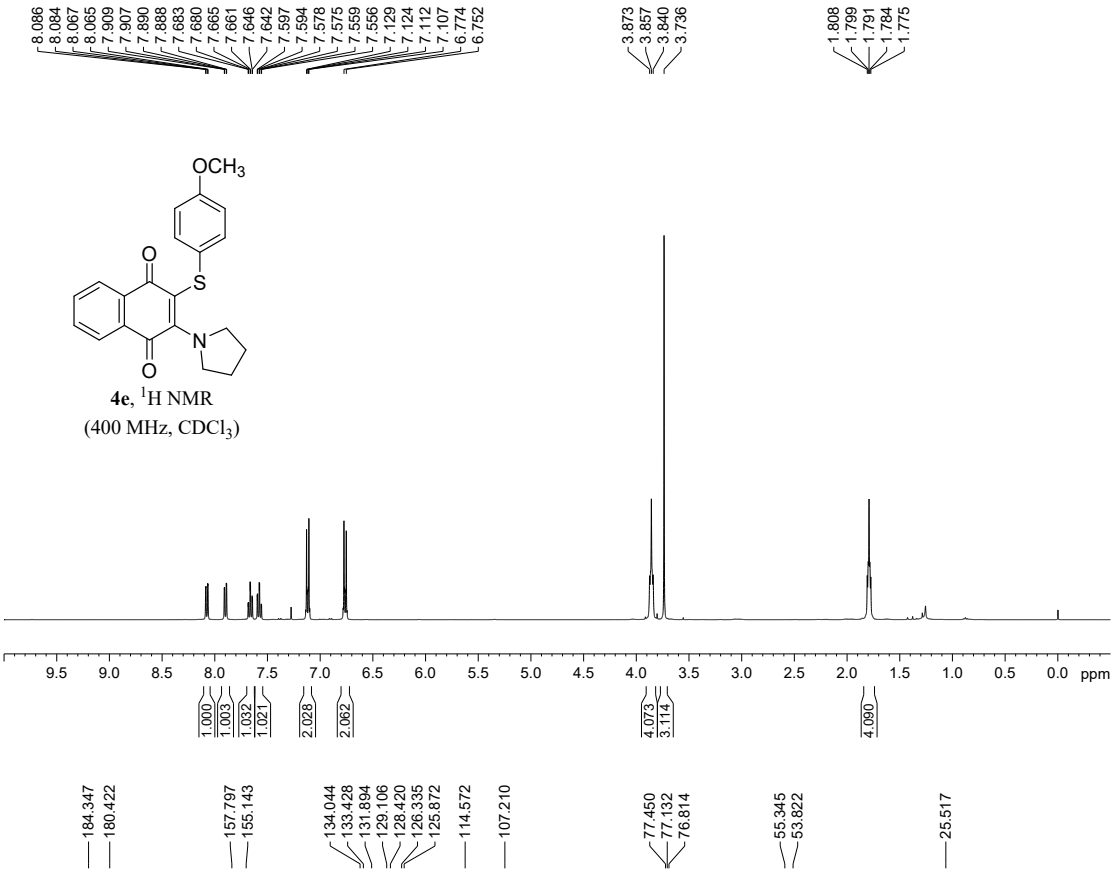
4c, ^{13}C NMR
(101 MHz, $CDCl_3$)



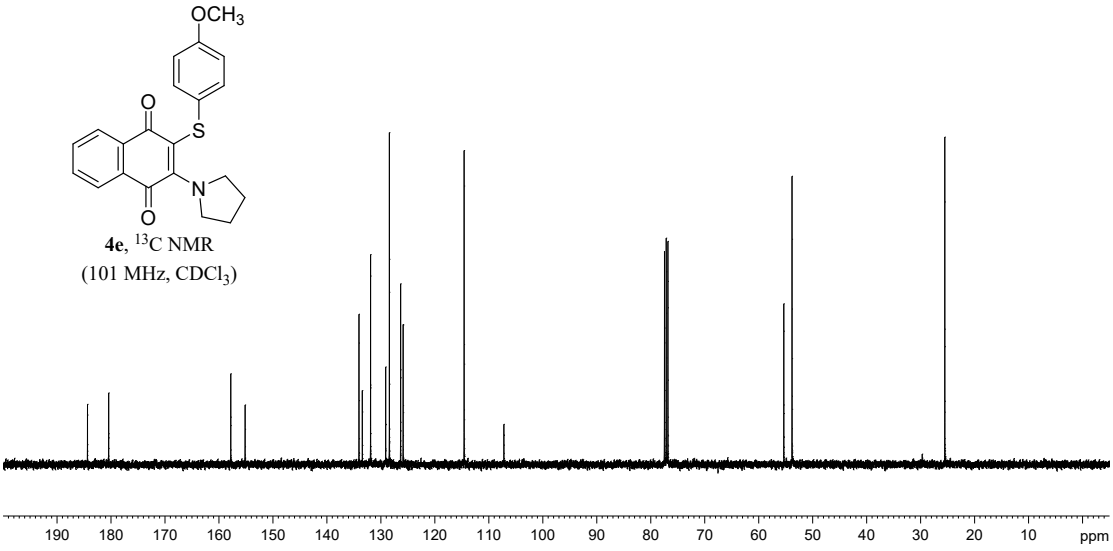
4d, ^{1}H NMR
(400 MHz, $CDCl_3$)



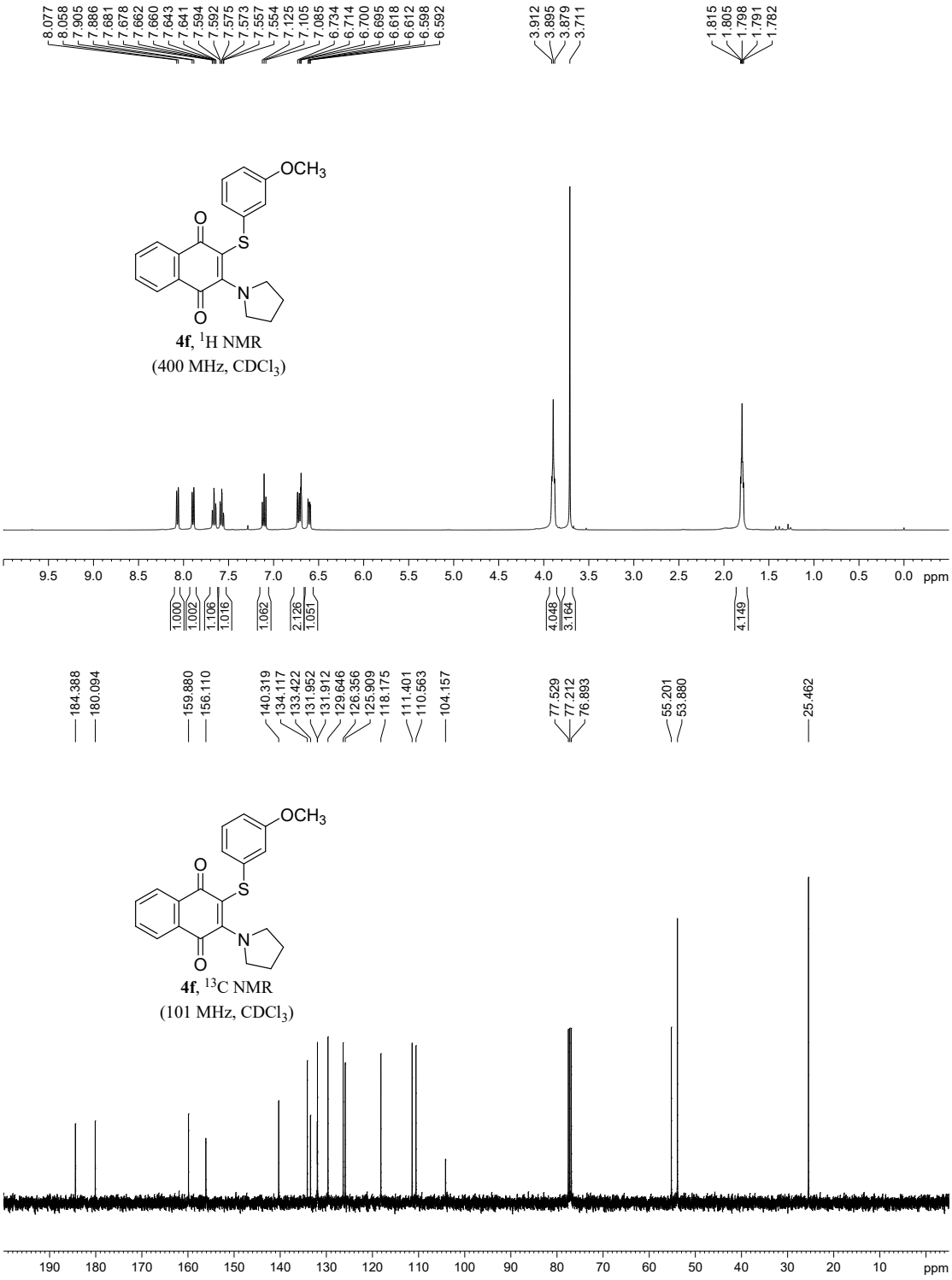
4d, ^{13}C NMR
(101 MHz, $CDCl_3$)



4e, ^{1}H NMR
(400 MHz, $CDCl_3$)



4e, ^{13}C NMR
(101 MHz, $CDCl_3$)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7.886
7.681
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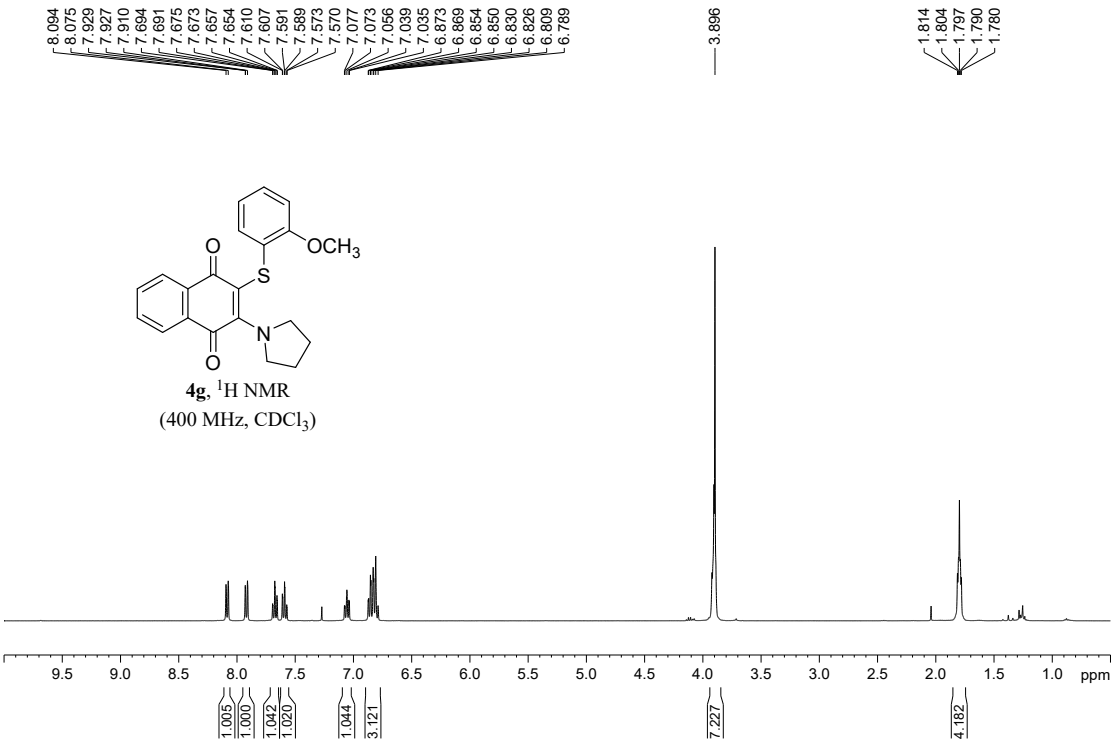
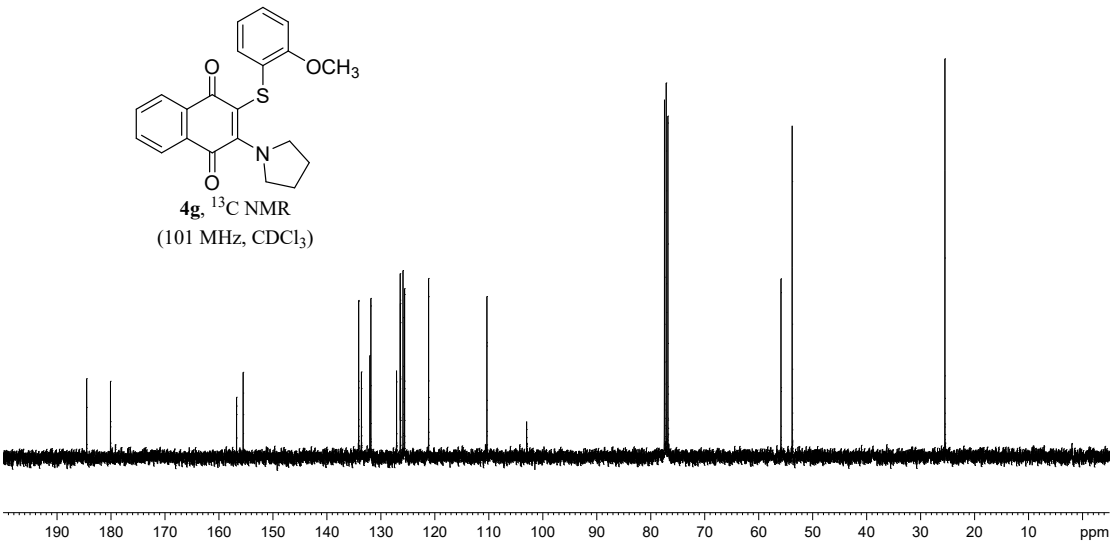
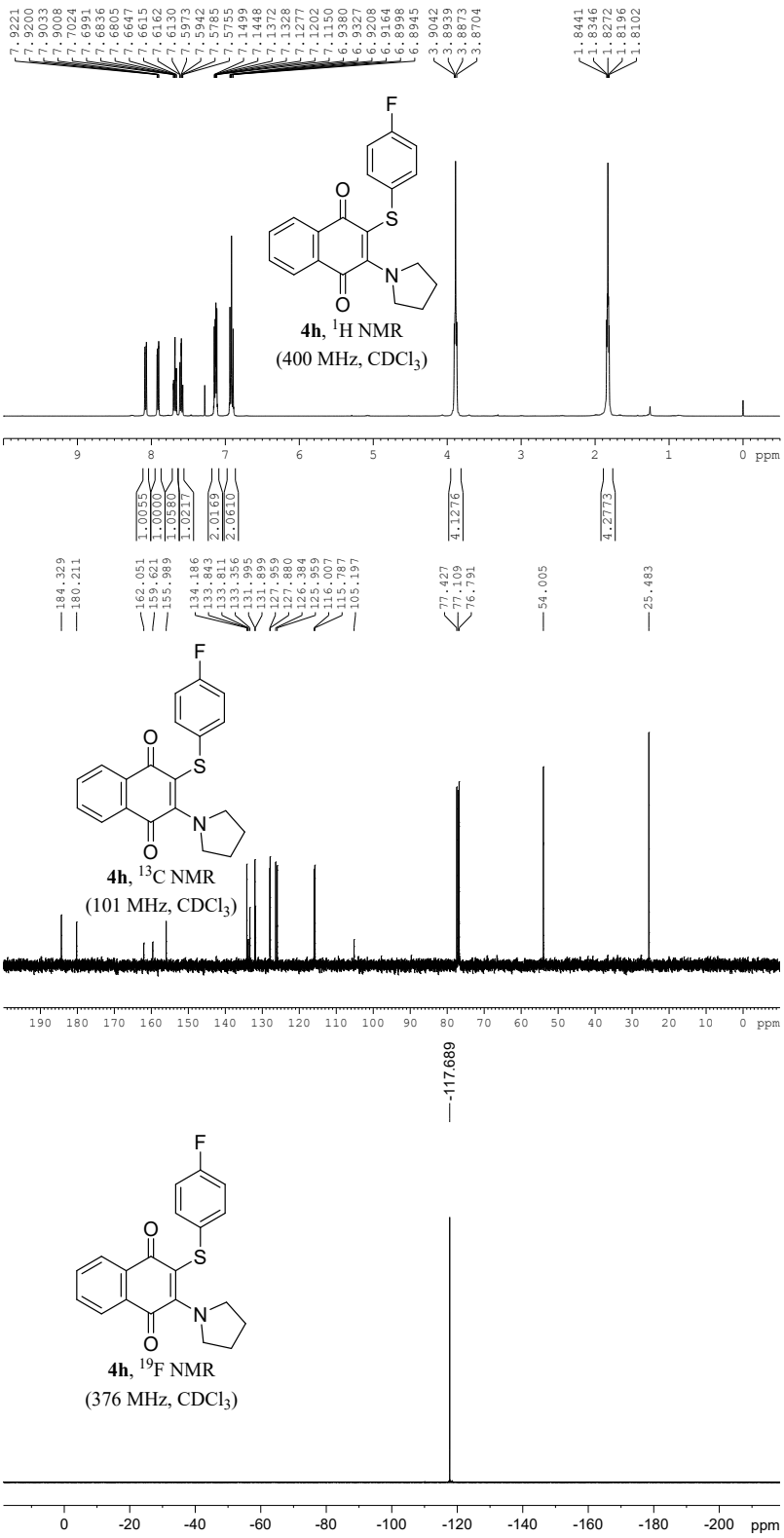
7.643
7.641
7.594
7.592
7.575
7.573
7.557
7.554
7.125
7.105
7.085
6.734
6.714
6.700
6.695
6.618
6.612
6.598
6.592
3.912
3.895
3.879
3.711
1.815
1.805
1.798
1.791
1.782
OCH3
O
S
N
O
4f, 1H NMR
(400 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.000
1.002
1.106
1.016
1.062
2.126
1.051
4.048
3.164
4.149
184.388
180.094
159.880
156.110
140.319
134.117
133.422
131.952
131.912
129.646
126.356
125.909
118.175
111.401
110.563
104.157
77.529
77.212
76.893
55.201
53.880
25.462
OCH3
O
S
N
O
4f, 13C NMR
(101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



4g, ^{1}H NMR
(400 MHz, $CDCl_3$)



4g, ^{13}C NMR
(101 MHz, $CDCl_3$)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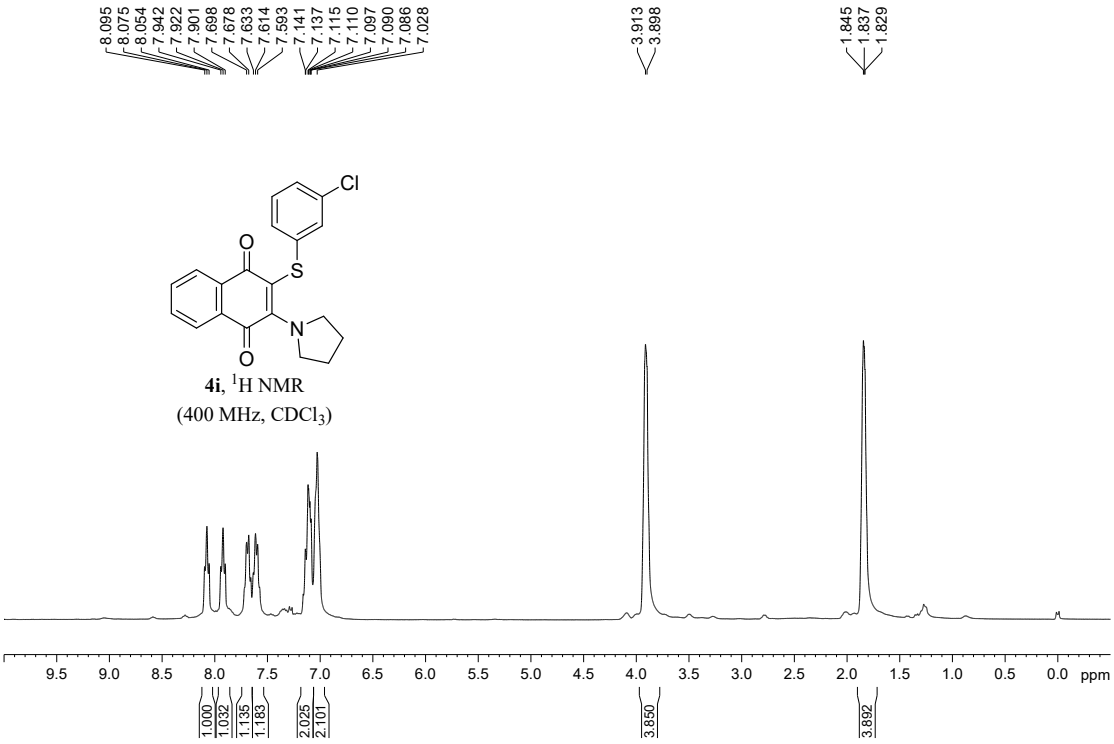
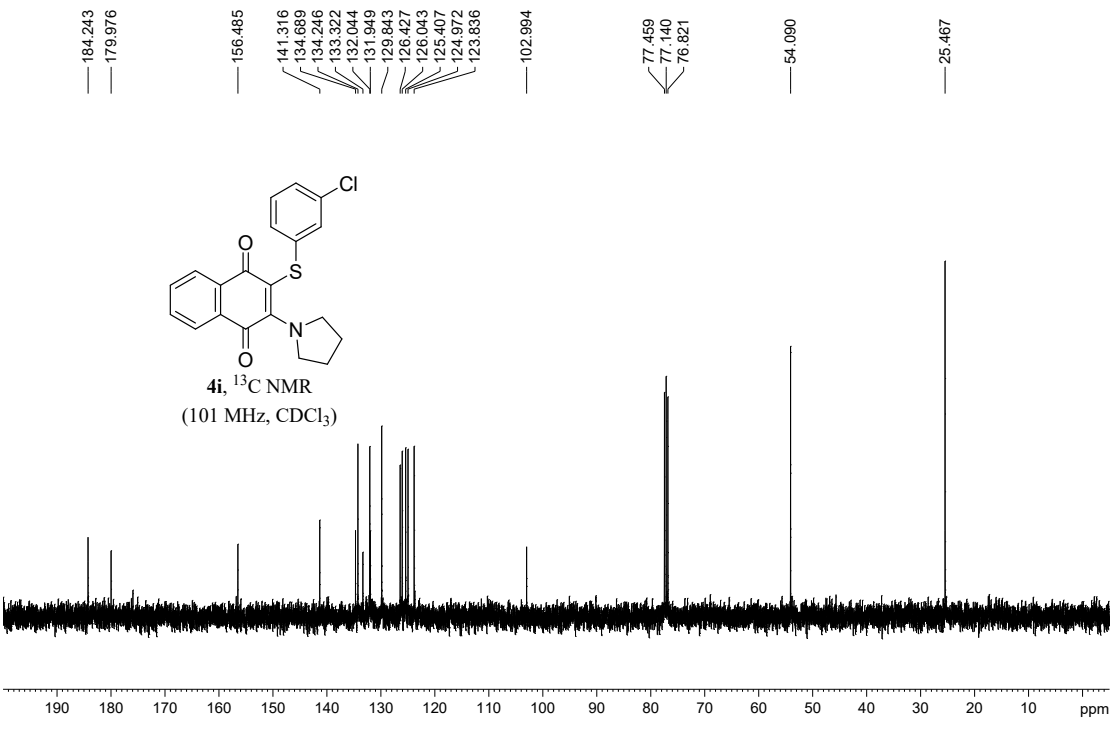
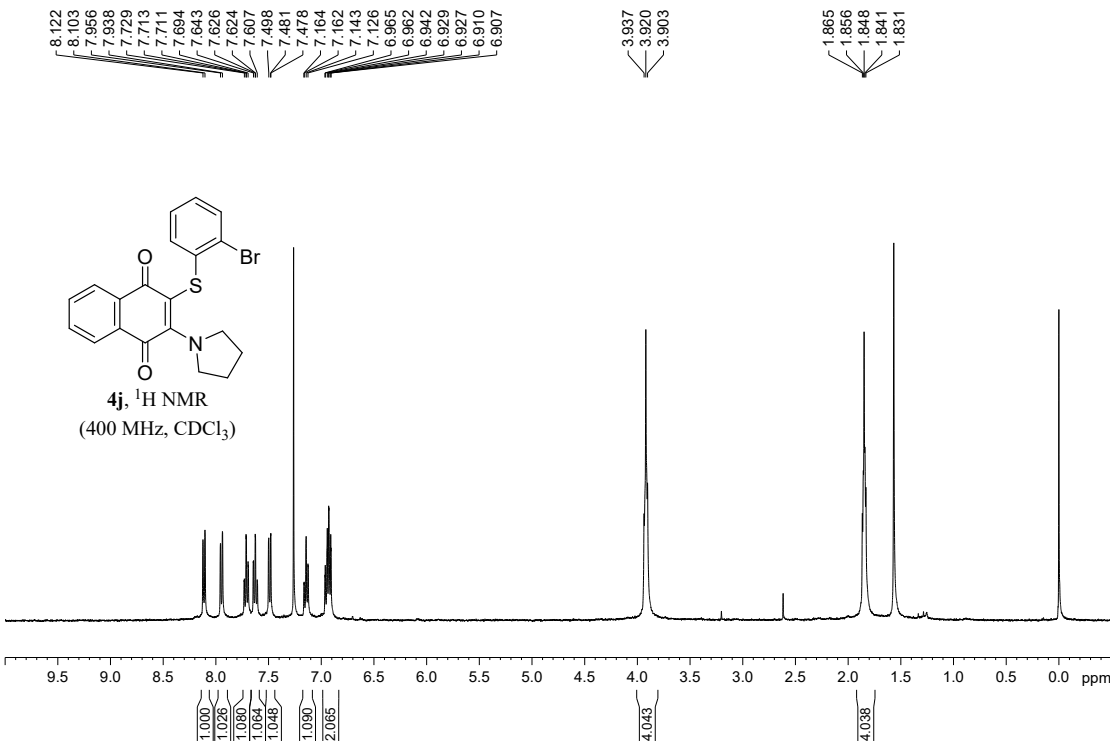
7.9200
7.9033
7.9008
7.7024
7.6991
7.6836
7.6805
7.6647
7.6615
7.6162
7.6130
7.5973
7.5942
7.5785
7.5755
7.1499
7.1448
7.1372
7.1328
7.1277
7.1202
7.1150
6.9380
6.9327
6.9208
6.9164
6.8998
6.8945
3.9042
3.8939
3.8873
3.8704
1.8441
1.8346
1.8272
1.8196
1.8102
F
O
S
N
O
4h, 1H NMR
(400 MHz, CDCl3)
9
8
7
6
5
4
3
2
1
0 ppm
1.0055
1.0000
1.0580
1.0247
2.0169
2.0610
4.1276
4.2773
184.329
180.211
162.051
159.621
155.989
134.186
133.843
133.811
133.356
131.995
131.899
127.959
127.880
126.384
125.959
116.007
115.787
105.197
77.427
77.109
76.791
54.005
25.483
4h, 13C NMR
(101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm
-117.689
4h, 19F NMR
(376 MHz, CDCl3)
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm



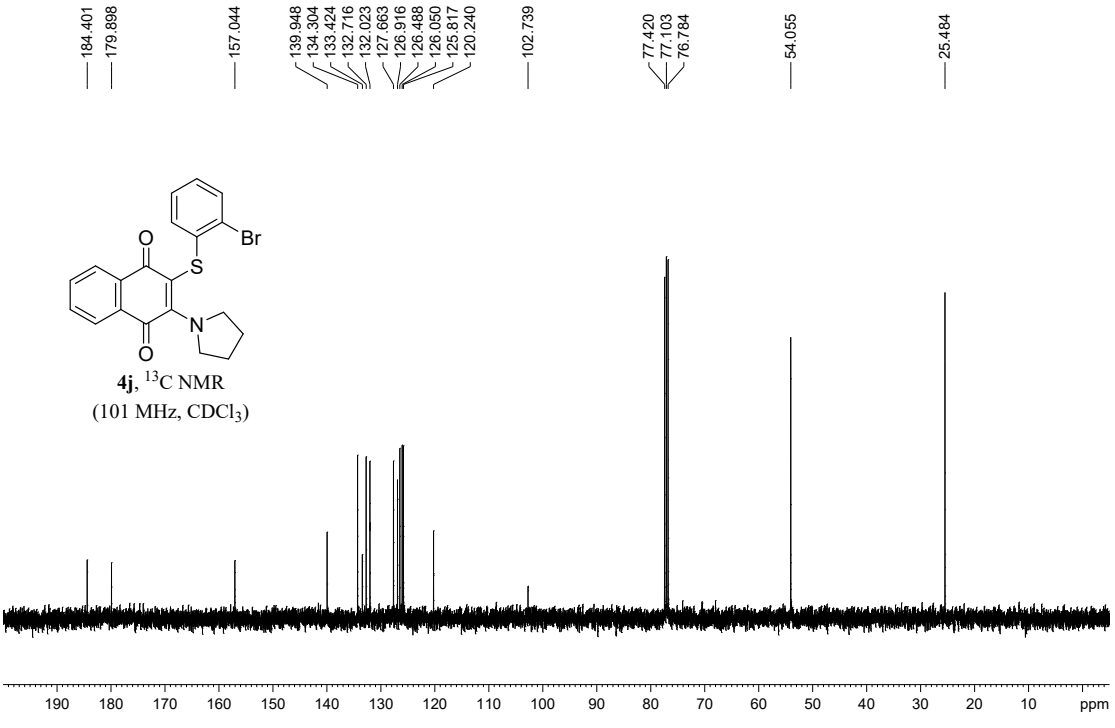
4i, ^{1}H NMR
(400 MHz, $CDCl_3$)



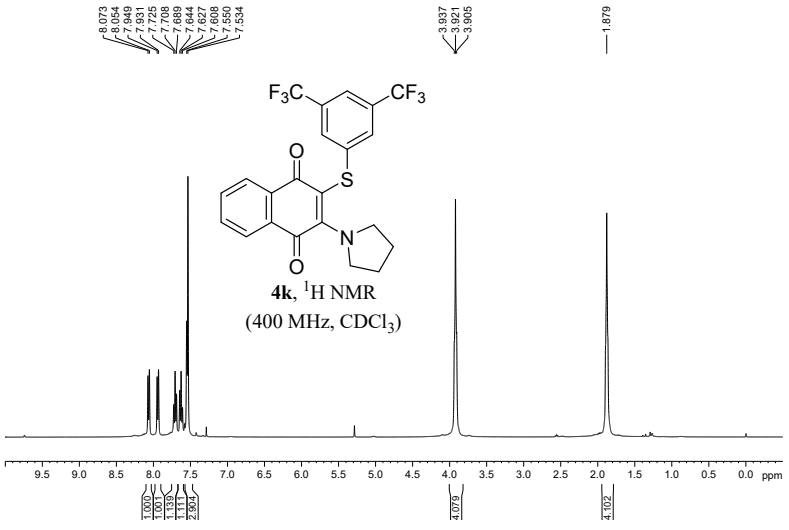
4i, ^{13}C NMR
(101 MHz, $CDCl_3$)



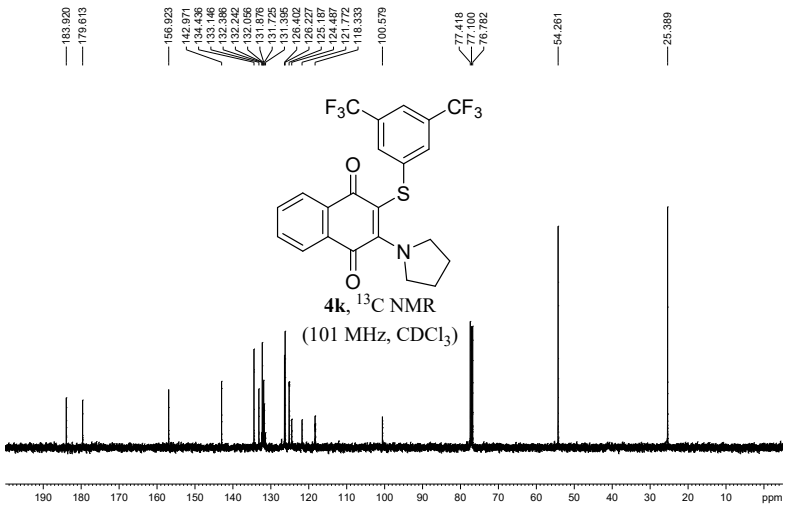
4j, ^{1}H NMR
(400 MHz, $CDCl_3$)



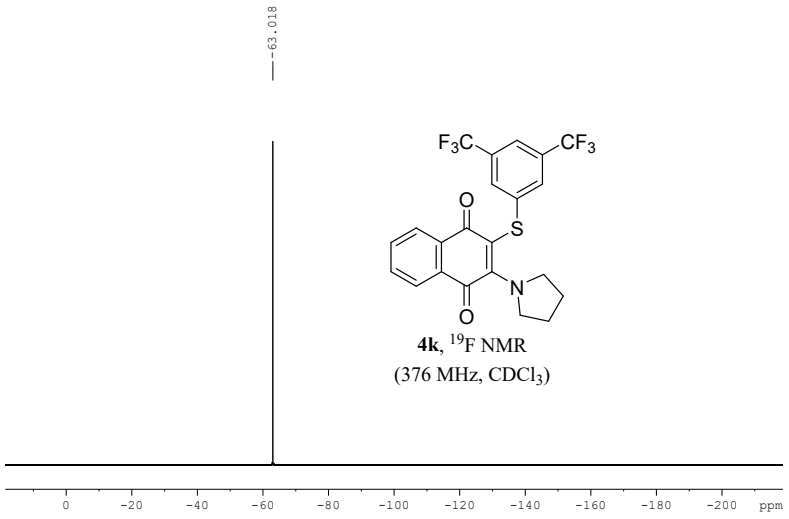
4j, ^{13}C NMR
(101 MHz, $CDCl_3$)



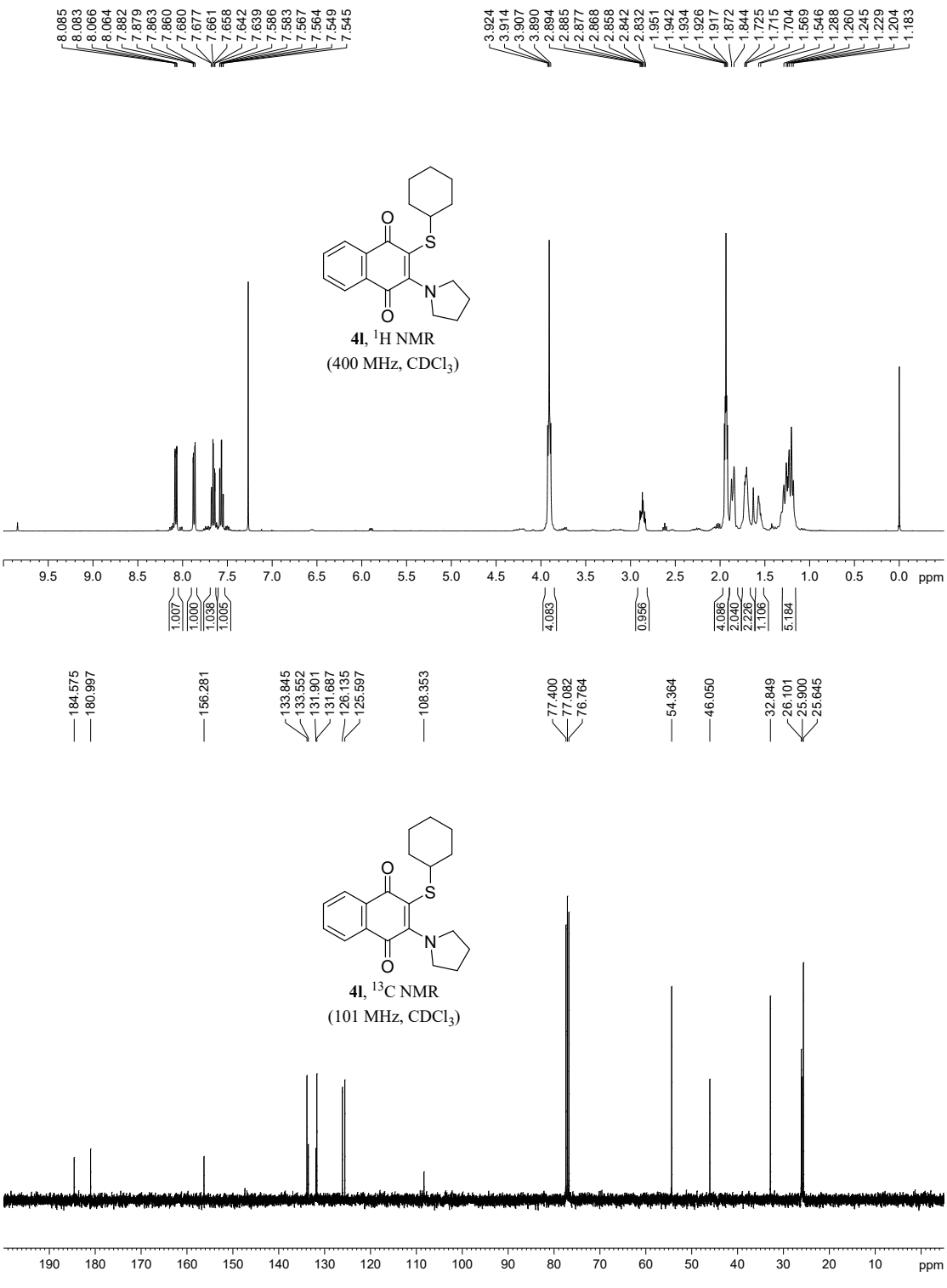
4k, ^{1}H NMR
(400 MHz, $CDCl_3$)

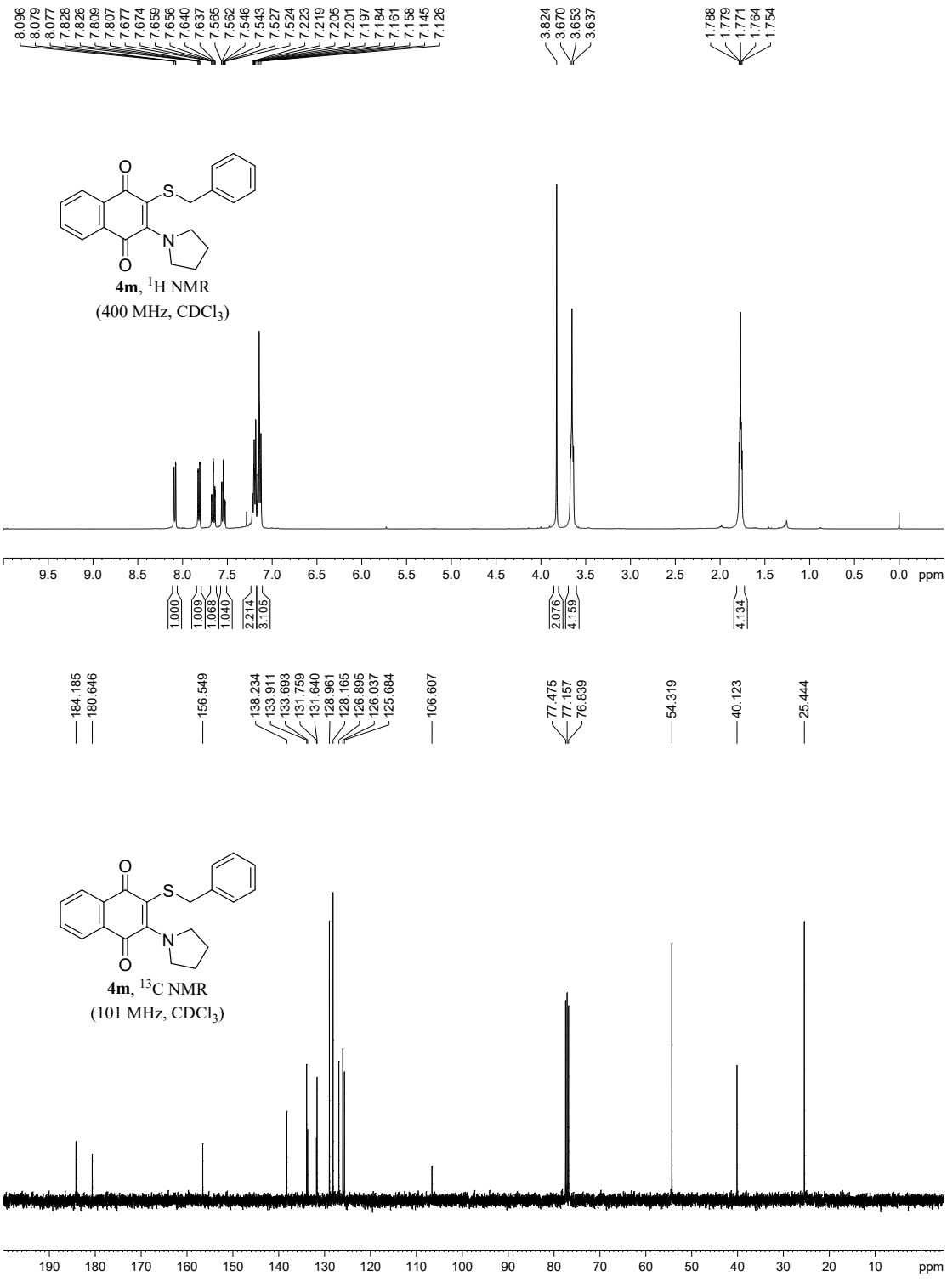


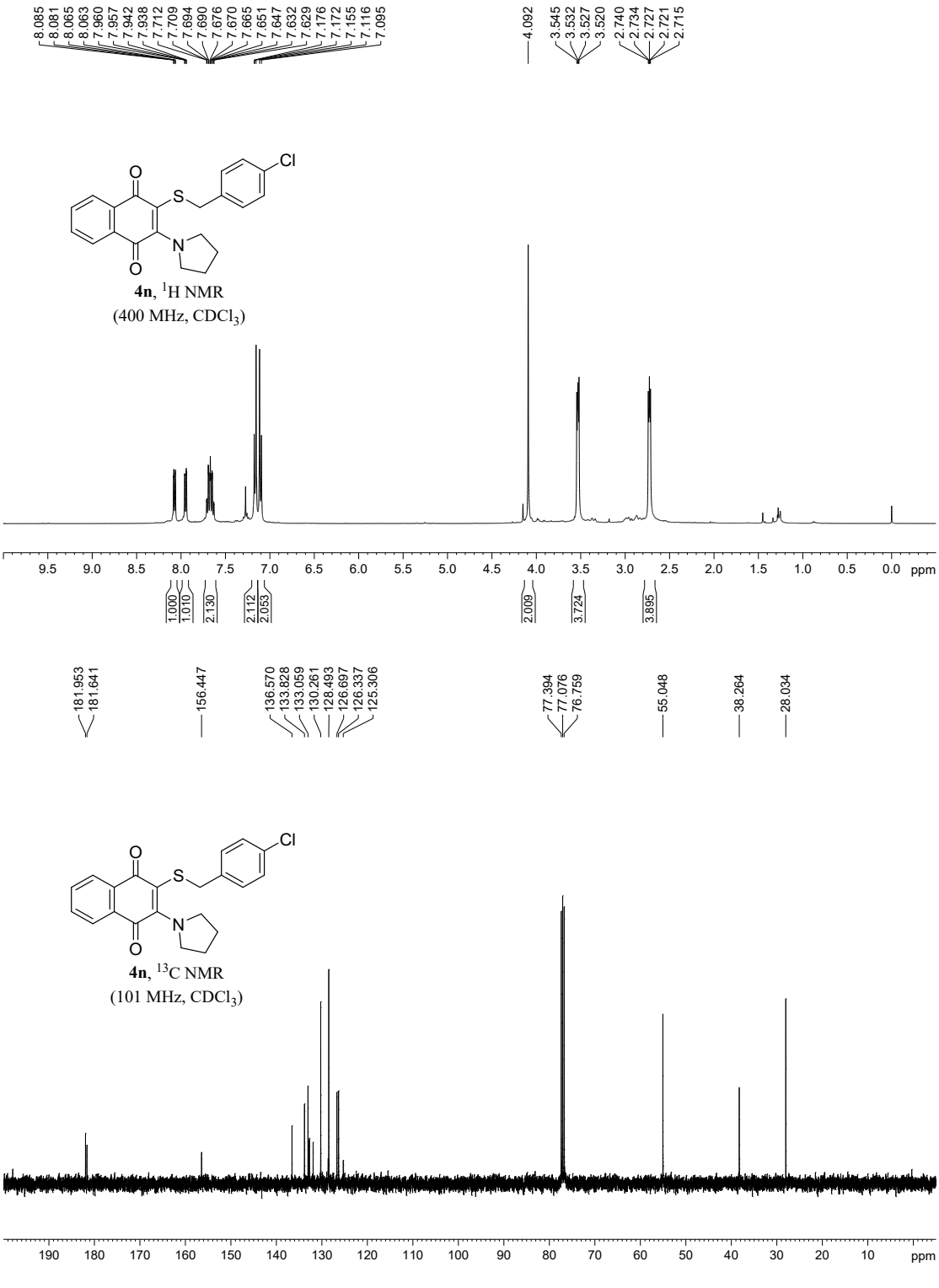
4k, ^{13}C NMR
(101 MHz, $CDCl_3$)

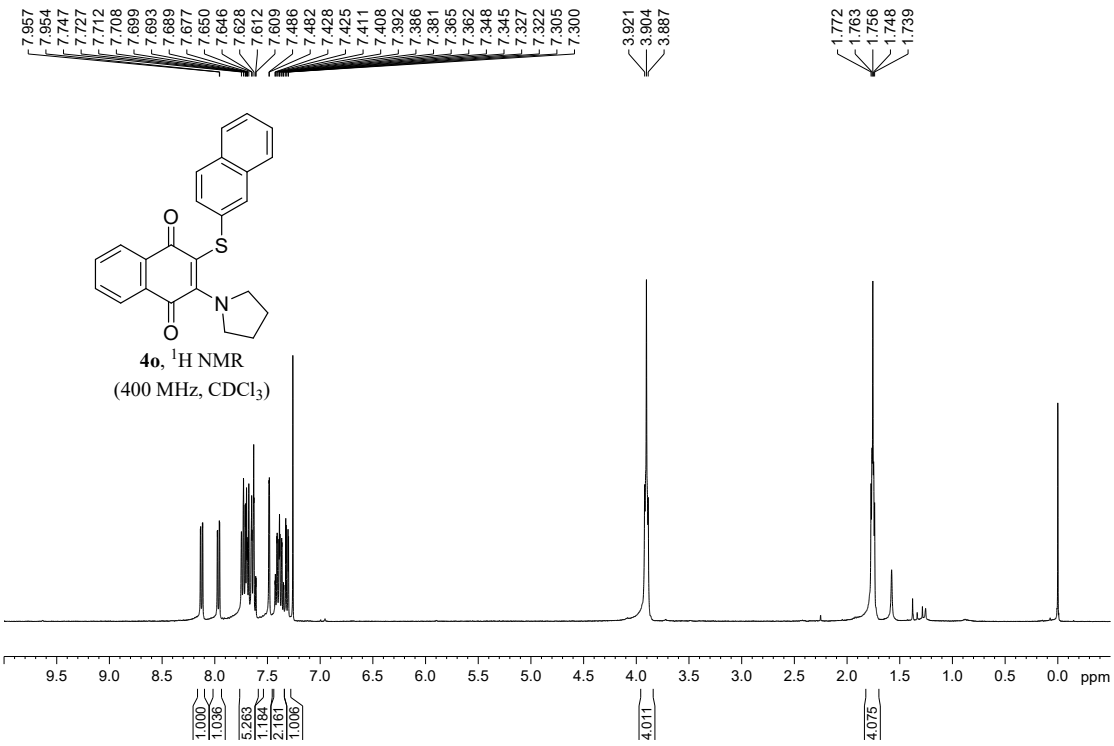


4k, ^{19}F NMR
(376 MHz, $CDCl_3$)

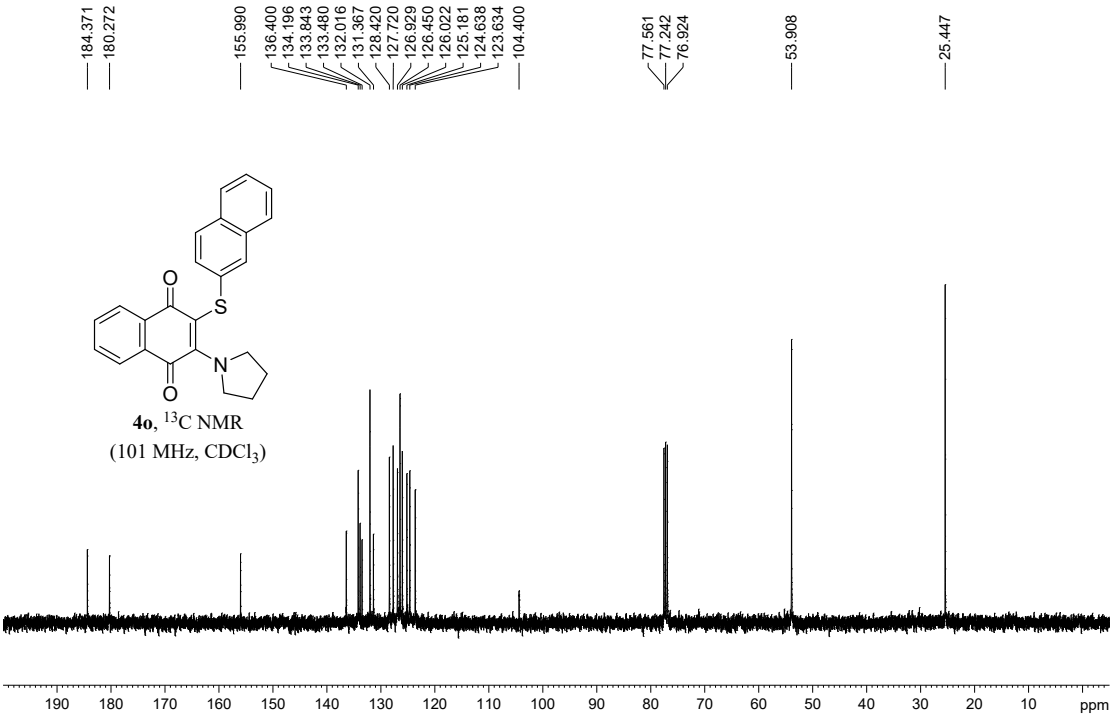

8.085
8.083
8.066
8.064
7.882
7.879
7.863
7.860
7.680
7.677
7.661
7.658
7.642
7.639
7.586
7.583
7.567
7.564
7.549
7.545
3.924
3.914
3.907
3.890
2.894
2.885
2.877
2.868
2.858
2.842
2.832
1.951
1.942
1.934
1.926
1.917
1.872
1.844
1.725
1.715
1.704
1.569
1.546
1.288
1.260
1.245
1.229
1.204
1.183
O
S
N
O
4l, 1H NMR
(400 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.007
1.000
1.038
1.005
4.083
0.956
4.086
2.040
2.226
1.106
5.184
184.575
180.997
156.281
133.845
133.552
131.901
131.687
126.135
125.597
108.353
77.400
77.082
76.764
54.364
46.050
32.849
26.101
25.900
25.645
O
S
N
O
4l, 13C NMR
(101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.096
8.079
8.077
7.828
7.826
7.809
7.807
7.677
7.674
7.659
7.656
7.640
7.637
7.565
7.562
7.546
7.543
7.527
7.524
7.223
7.219
7.205
7.201
7.197
7.184
7.161
7.158
7.145
7.126
3.824
3.670
3.653
3.637
1.788
1.779
1.771
1.764
1.754
O
S
N
O
4m, 1H NMR
(400 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.000
1.009
1.068
1.040
2.214
3.105
2.076
4.159
4.134
184.185
180.646
156.549
138.234
133.911
133.693
131.759
131.640
128.961
128.165
126.895
126.037
125.684
106.607
77.475
77.157
76.839
54.319
40.123
25.444
O
S
N
O
4m, 13C NMR
(101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

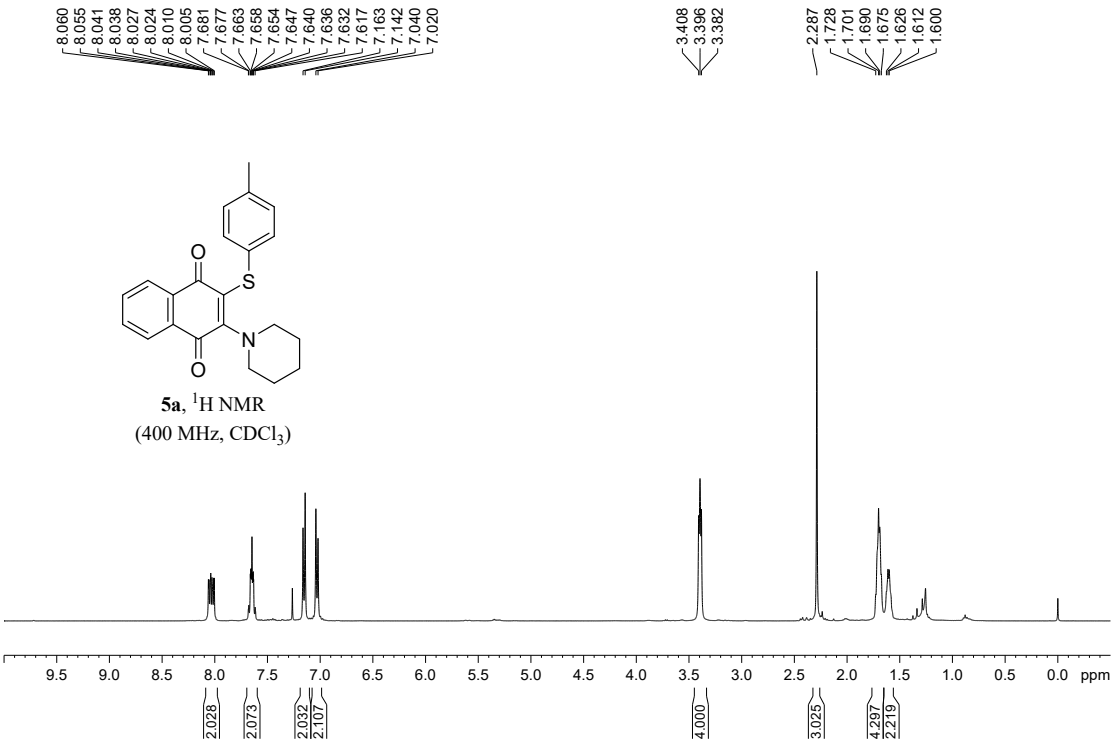

8.085
8.081
8.065
8.063
7.960
7.957
7.942
7.938
7.712
7.709
7.694
7.690
7.676
7.670
7.665
7.651
7.647
7.632
7.629
7.176
7.172
7.155
7.116
7.095
4.092
3.545
3.532
3.527
3.520
2.740
2.734
2.727
2.721
2.715
Cl
O
S
N
O
4n, 1H NMR
(400 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.000
1.010
2.130
2.112
2.053
2.009
3.724
3.895
181.953
181.641
156.447
136.570
133.828
133.059
130.261
128.493
126.697
126.337
125.306
77.394
77.076
76.759
55.048
38.264
28.034
Cl
O
S
N
O
4n, 13C NMR
(101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



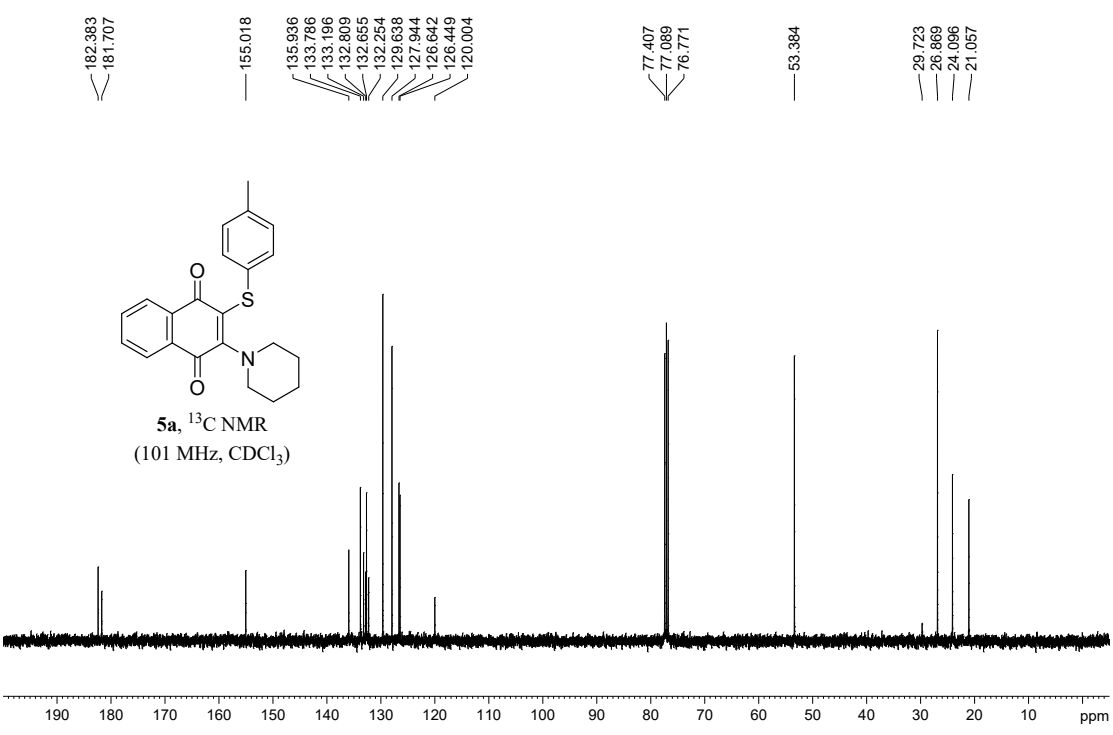
4o, ^{1}H NMR
(400 MHz, $CDCl_3$)



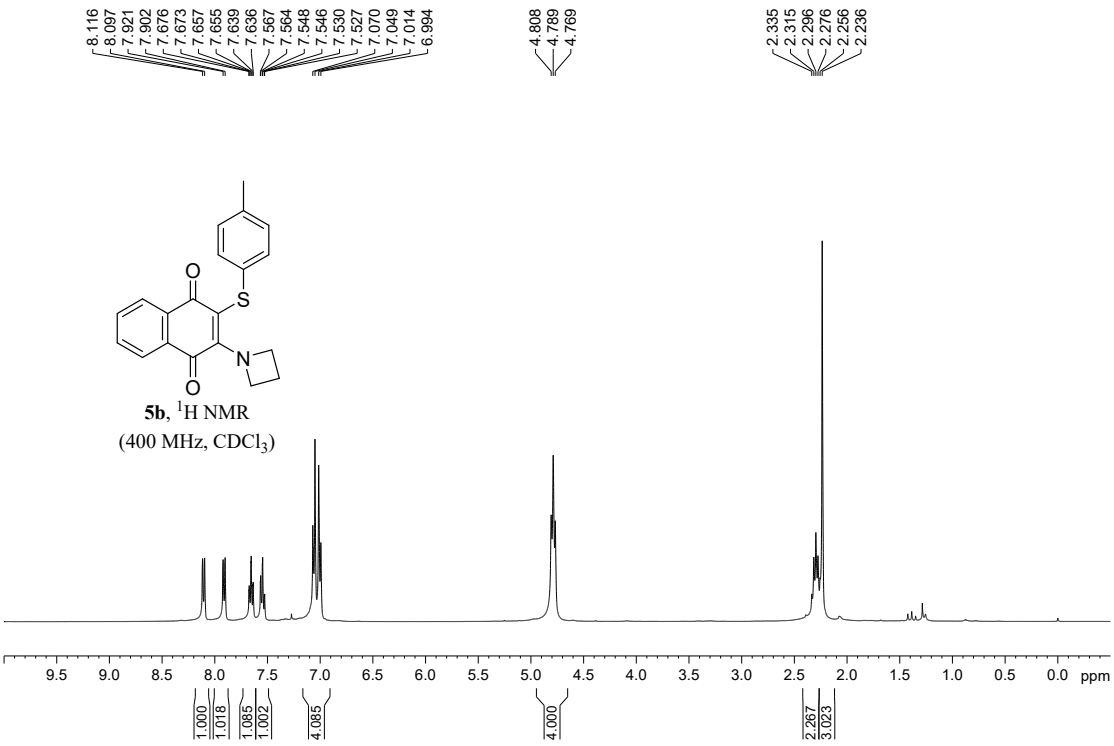
4o, ^{13}C NMR
(101 MHz, $CDCl_3$)



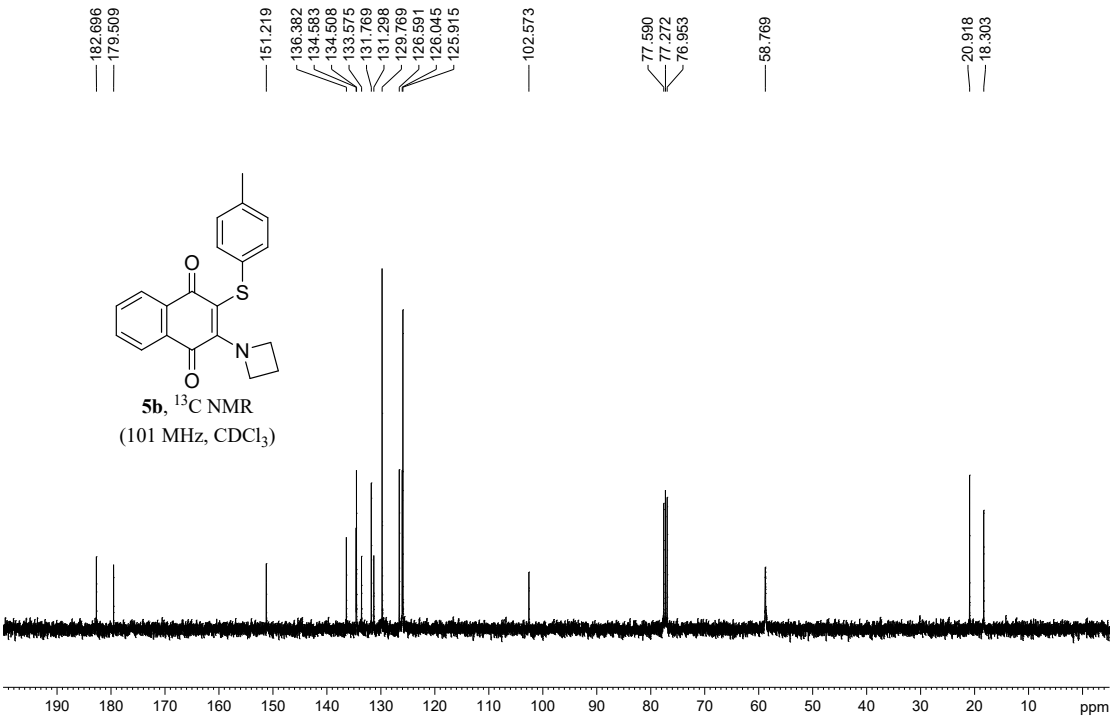
5a, ^{1}H NMR
(400 MHz, $CDCl_3$)



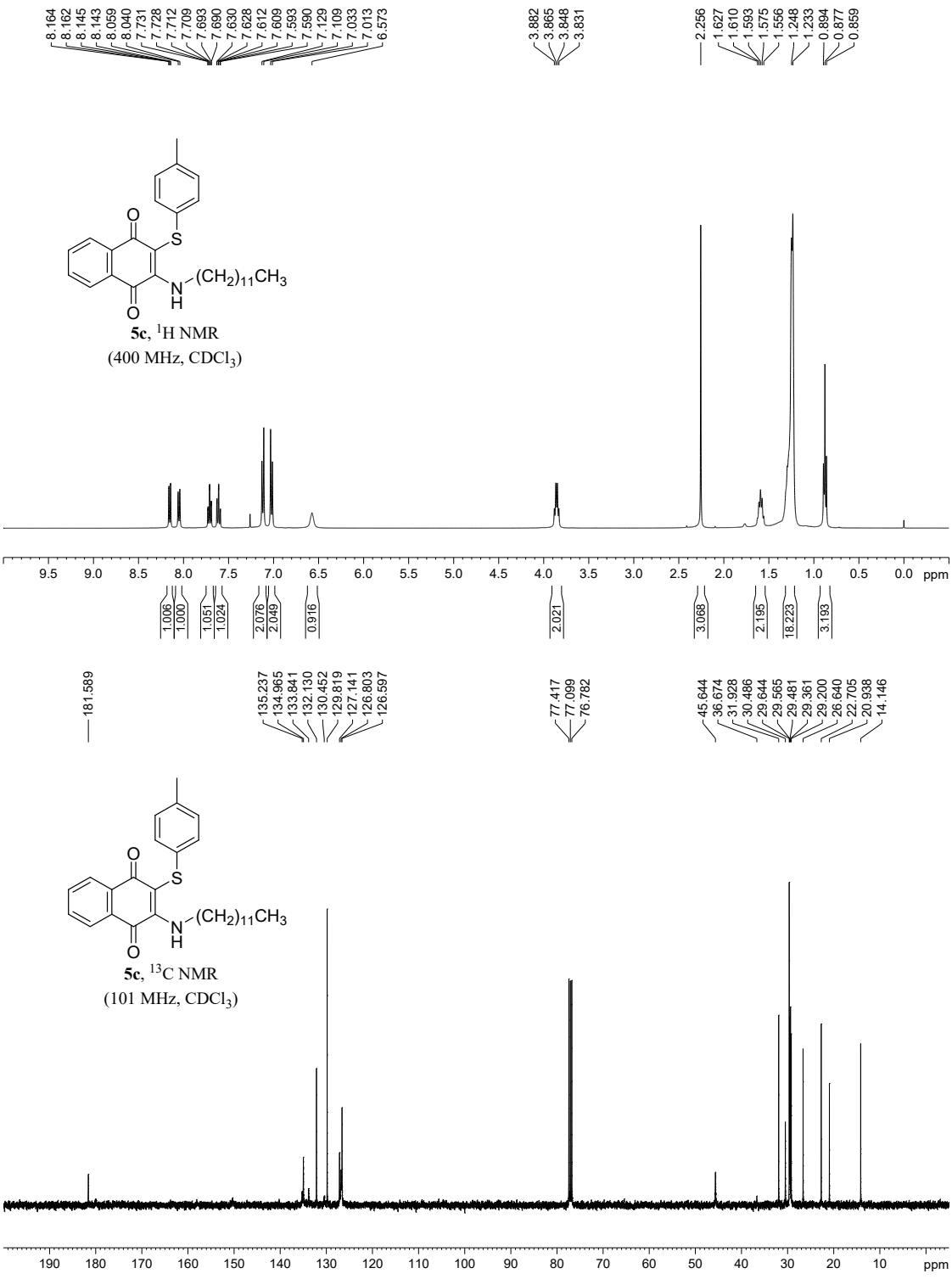
5a, ^{13}C NMR
(101 MHz, $CDCl_3$)

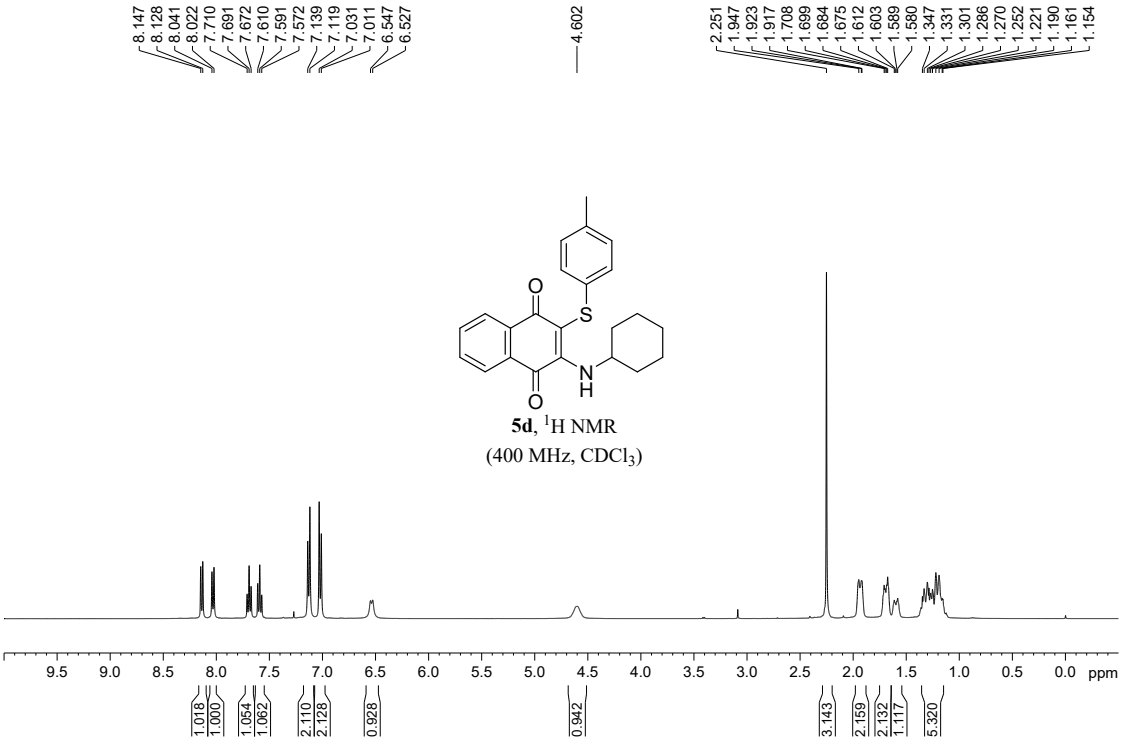


5b, ^{1}H NMR
(400 MHz, $CDCl_3$)

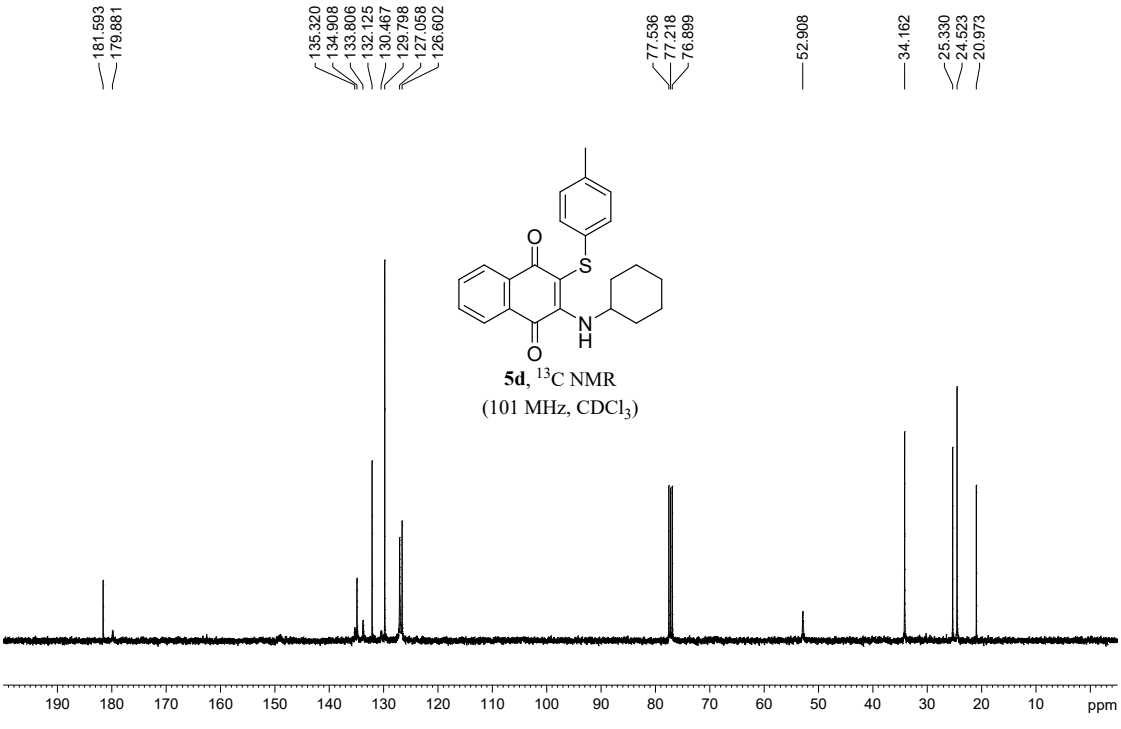


5b, ^{13}C NMR
(101 MHz, $CDCl_3$)

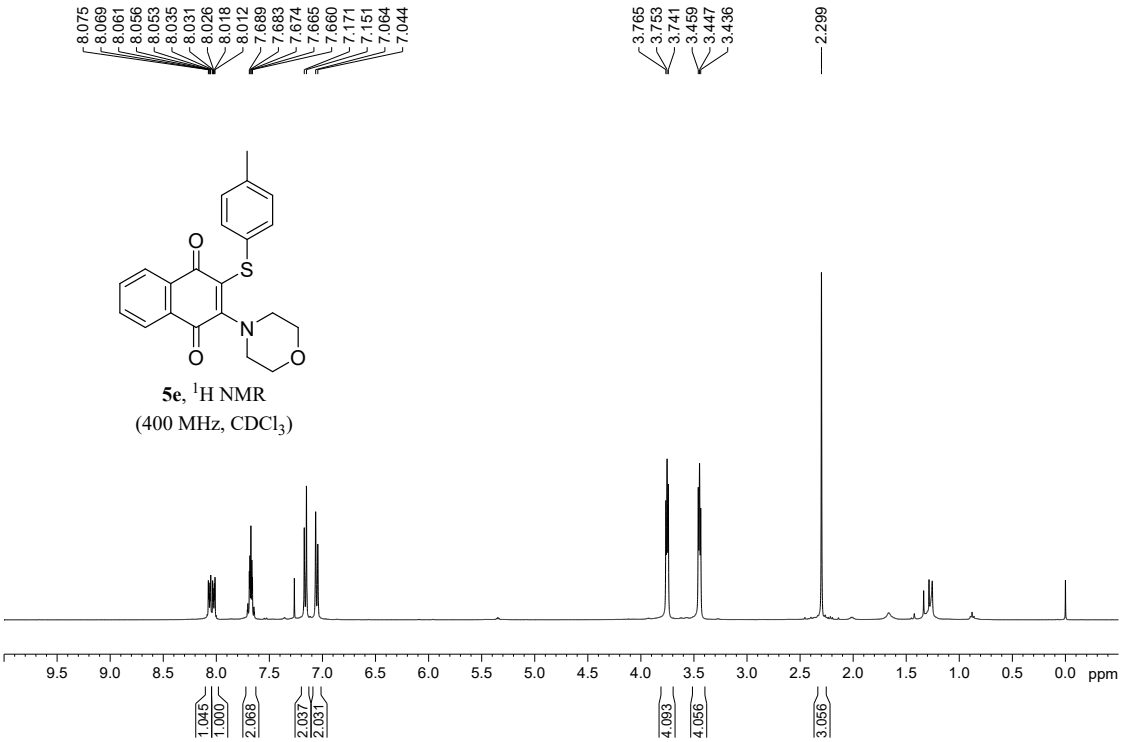

8.164
8.162
8.145
8.143
8.059
8.040
7.731
7.728
7.712
7.709
7.693
7.690
7.630
7.628
7.612
7.609
7.593
7.590
7.129
7.109
7.033
7.013
6.573
3.882
3.865
3.848
3.831
2.256
1.627
1.610
1.593
1.575
1.556
1.248
1.233
0.894
0.877
0.859
O
S
N
H
(CH2)11CH3
O
5c, 1H NMR
(400 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.006
1.000
1.051
1.024
2.076
2.049
0.916
2.021
3.068
2.195
18.223
3.193
181.589
135.237
134.965
133.841
132.130
130.452
129.819
127.141
126.803
126.597
77.417
77.099
76.782
45.644
36.674
31.928
30.486
29.644
29.565
29.481
29.361
29.200
26.640
22.705
20.938
14.146
O
S
N
H
(CH2)11CH3
O
5c, 13C NMR
(101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



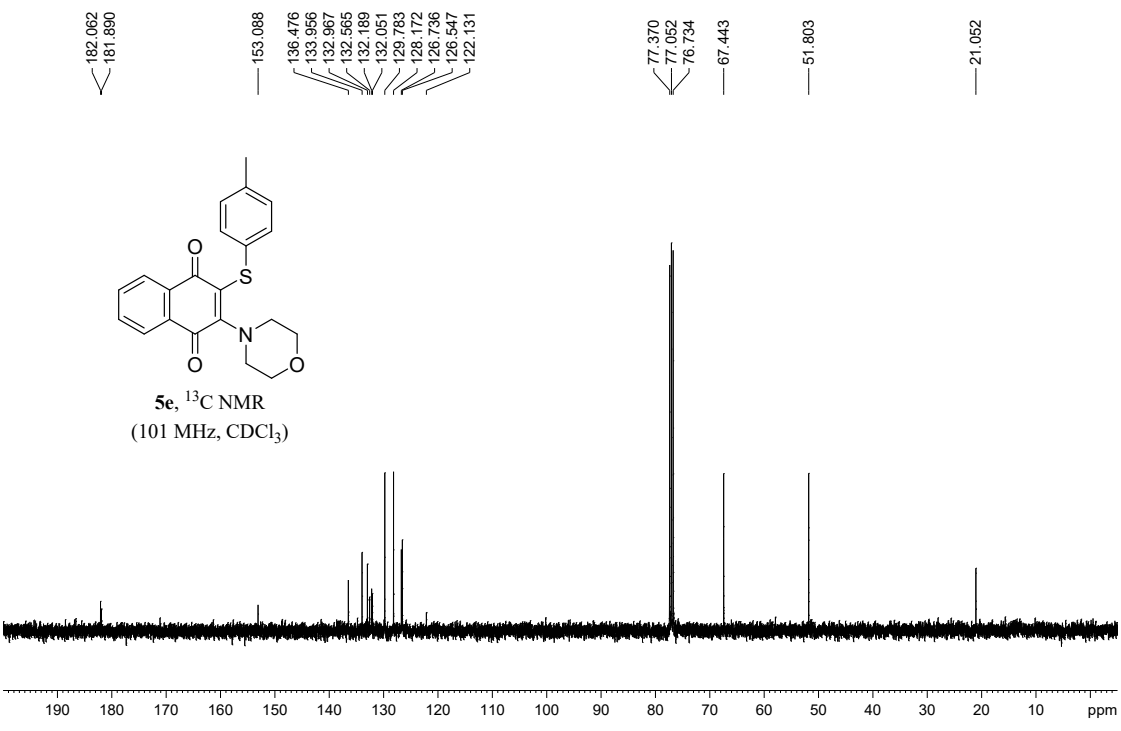
5d, ^{1}H NMR
(400 MHz, $CDCl_3$)



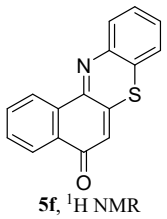
5d, ^{13}C NMR
(101 MHz, $CDCl_3$)



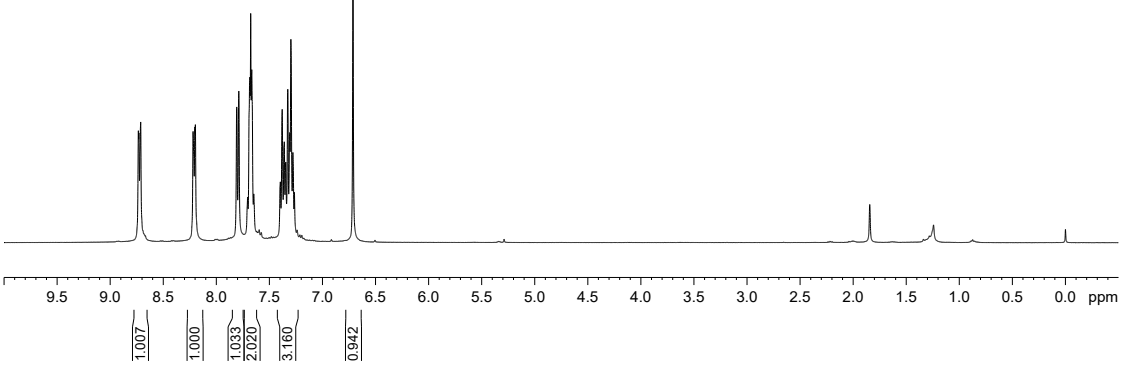
5e, ^{1}H NMR
(400 MHz, $CDCl_3$)

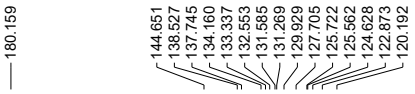


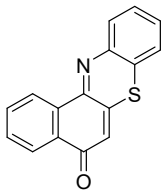
5e, ^{13}C NMR
(101 MHz, $CDCl_3$)



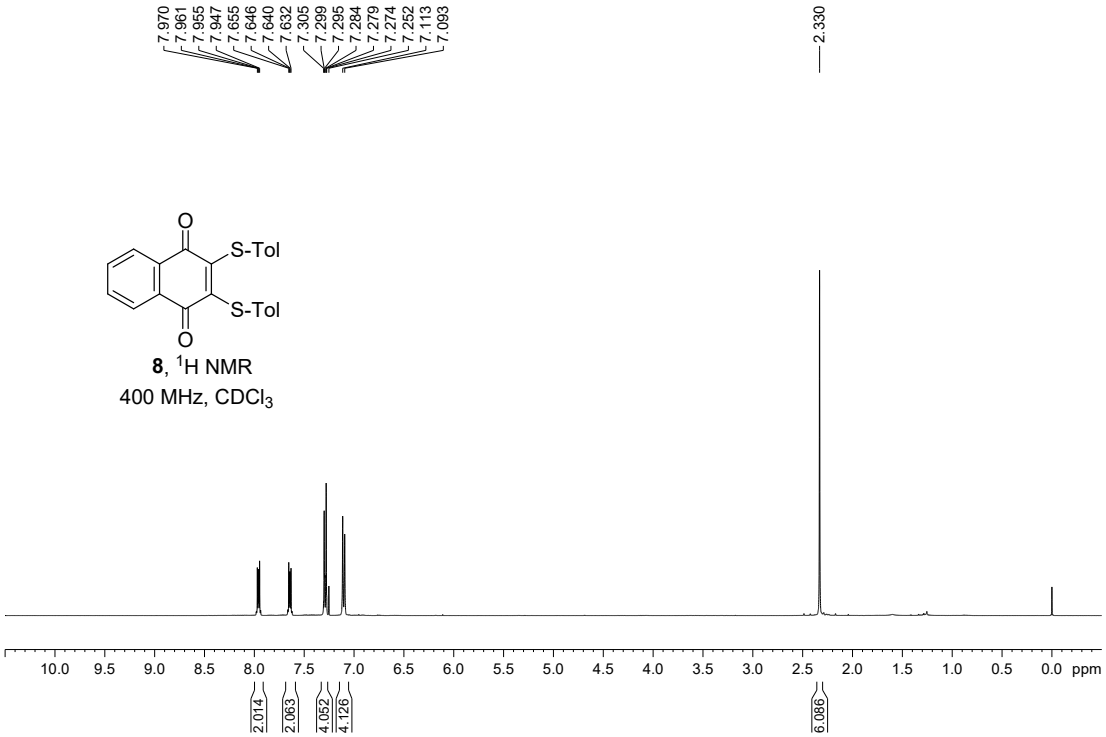
5f, ^{1}H NMR
(400 MHz, $CDCl_3$)



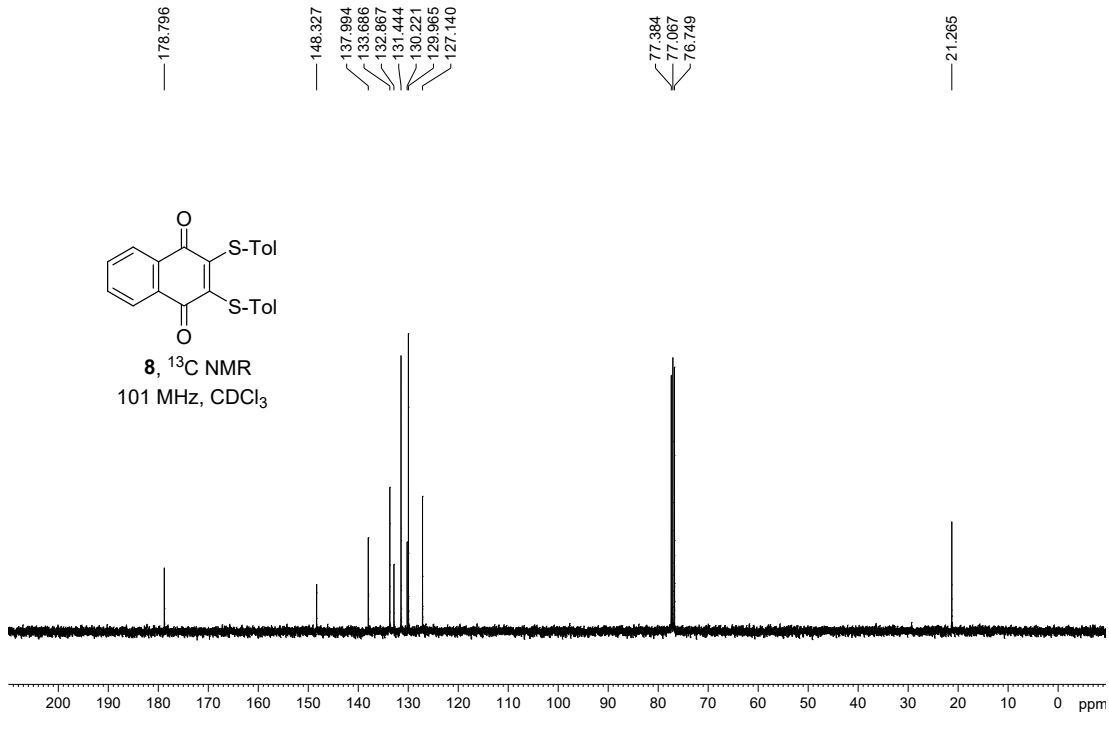




5f, ^{13}C NMR
(101 MHz, $CDCl_3$)



8, ^{1}H NMR
400 MHz, $CDCl_3$



8, ^{13}C NMR
101 MHz, $CDCl_3$