

# Transition-metal free thiocyanooxygenation of functionalized alkenes: facile routes to SCN-containing dihydrofurans and lactones

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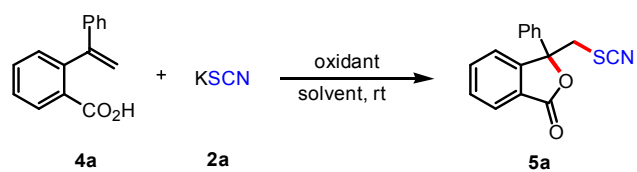
## General Information

All reactions were carried out under an atmosphere of nitrogen with the strict exclusion of air. Column chromatography was carried out on silica gel.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker Advance III-400 in solvents as indicated. Chemical shift are reported in ppm from TMS with the solvent resonance as internal standard ( $\text{CDCl}_3$ :  $^1\text{H}$ -NMR:  $\delta = 7.26$ ;  $^{13}\text{C}$ -NMR:  $\delta = 77.0$ ). IR spectra were recorded on a Bruker Tensor 27 spectrometer and only major peaks are reported in  $\text{cm}^{-1}$ . HRMS were obtained on a Q-TOF micro spectrometer.

## Starting Materials

All of olefinic dicarbonyl compounds **1** were synthesized according to the literature.<sup>1</sup> 2-vinyl benzoic acids **4** were prepared by the direct Wittig olefination of the corresponding acids according to the reported procedure.<sup>2</sup> Benzyl alcohol **6** was prepared by the direct reduction of the corresponding acids according to the reported procedure.<sup>3</sup> All the NMR spectroscopy were in full accordance with the data in the literatures.

## Optimization of the reaction conditions of **4a** and **2a**<sup>a</sup>

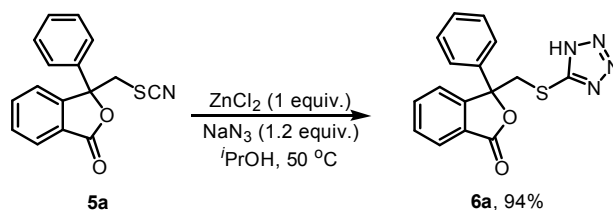


Entry	Oxidant (equiv.)	Solvent	Yield <sup>b</sup> (%)
1	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	HOAc	98%
2	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	CH <sub>3</sub> CN	44%
6	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	DCE	88%
7	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	EtOAc	n.r
3	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	DMF	n.r
8	Na <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	HOAc	97%
9	(NH <sub>4</sub> ) <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	HOAc	89%
10	Oxone (1.5)	HOAc	90%
11	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	HOAc	80% <sup>c</sup>
12	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.5)	HOAc	80% <sup>d</sup>
16	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (1.2)	HOAc	91%
17	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> (2.0)	HOAc	80%

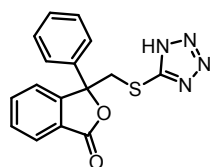
<sup>a</sup> Reaction conditions: **4a** (0.2 mmol, 1 equiv.), **2a** (0.4 mmol, 2 equiv.), solvent (2 mL), oxidant (1.5 equiv.), room temperature, 24 h, under N<sub>2</sub>. <sup>b</sup> Yield of isolated product. <sup>c</sup> NaSCN (0.4 mmol, 2 equiv.) was used. <sup>d</sup> NH<sub>4</sub>SCN (0.4 mmol, 2 equiv.) was used.

## Derivatization of products **5a**

### 1. [3+2] Cycloaddition of product **5a**.<sup>4a</sup>

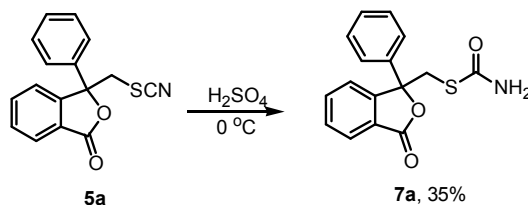


A 10 mL oven-dried Schlenk-tube was charged with ZnCl<sub>2</sub> (0.2 mmol, 1.0 equiv.) and NaN<sub>3</sub> (0.24 mmol, 1.2 equiv.). A solution of **5a** (0.2 mmol, 1.0 equiv.) in *i*PrOH (1 mL) was then injected into the tube by syringe. The resulting mixture was heated to 50 °C and stirred vigorously for 1.5 h. Upon completion of the reaction, the mixture was diluted with EtOAc. The solvent was then removed under vacuo. After the usual workup, the desired thiotetrazole **6a** was isolated in 94% (60.9 mg) yield.

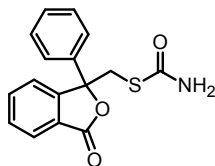


**6a**: White solid; R<sub>f</sub> 0.1 (EtOAc); <sup>1</sup>H NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ = 7.83 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.64-7.52 (m, 4H), 7.42-7.32 (m, 3H), 4.37 (d, *J* = 13.6 Hz, 1H), 4.25 (d, *J* = 14.0 Hz, 1H), 3.41 (s, 1H); <sup>13</sup>C NMR (100 MHz, (CD<sub>3</sub>)<sub>2</sub>SO): δ = 168.9, 156.7, 150.5, 139.3, 134.6, 129.9, 128.9, 128.6, 125.0, 123.3, 88.2, 41.3; IR (KBr): ν<sub>max</sub> 1766 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>16</sub>H<sub>12</sub>KN<sub>4</sub>O<sub>2</sub>S [M+K]<sup>+</sup> 363.0313, found 363.0313.

### 2. Acid hydrolysis of product **5a**.<sup>4b</sup>

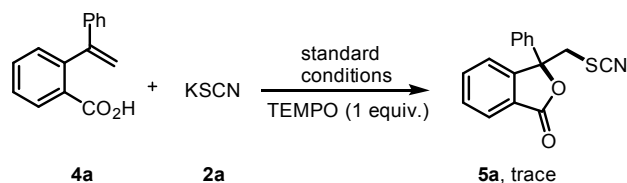


**5a** (0.2 mmol, 1.0 equiv.) was added slowly to a solution of 95% sulfuric acid (0.5 mL) and the mixture was stirred at 0 °C for 15h. Upon completion of the reaction, the mixture was diluted with EtOAc. The solvent was then removed under vacuo. After the usual workup, the product **7a** was isolated in 35% (20.9 mg) yield.

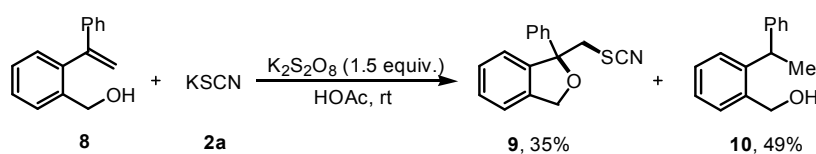


**7a:** Yellow Liquid;  $R_f$  0.5 (EtOAc/petroleum ether = 1:2);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.86 (d,  $J$  = 7.6 Hz, 1H), 7.67-7.50 (m, 5H), 7.40-7.31 (m, 3H), 5.36 (s, 2H), 4.08 (d,  $J$  = 14.4 Hz, 1H), 3.90 (d,  $J$  = 14.4 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 169.5, 167.1, 150.3, 139.0, 134.1, 129.5, 128.8, 128.7, 126.3, 125.4, 125.1, 123.1, 88.8, 39.4; IR (KBr):  $\nu_{\text{max}}$  1766  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{13}\text{NNaO}_3\text{S}$   $[\text{M}+\text{Na}]^+$  322.0508, found 322.0504.

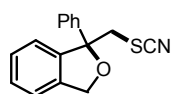
## Investigation of the Reaction Mechanism



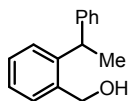
When 1.0 equiv of TEMPO was added to the reaction of **4a** with **2a** under the standard conditions, only trace amount of desired product **5a** was detected. The result indicates that the radical intermediate probably be involved in the catalytic cycle of the reaction.



A 10 mL oven-dried Schlenk-tube was charged with 2-vinyl benzyl alcohol **8** (0.2 mmol, 1 equiv.), KSCN (0.4 mmol, 2 equiv.) and  $\text{K}_2\text{S}_2\text{O}_8$  (0.3 mmol, 1.5 equiv.). The tube was evacuated and backfilled with nitrogen (three times). 2 mL of HOAc was injected by syringe. The tube was then sealed and the mixture was stirred for 24 h at room temperature. Upon completion of the reaction, the reaction was quenched by the slow addition of a saturated solution of  $\text{Na}_2\text{CO}_3$ . After the usual workup, the cyclized product **9** was isolated in 35% (18.7 mg) yield along with the protonated product **10** in 49% (20.8 mg) yield. The result indicates that a carbocation intermediate is probably involved in this transformation.



**1-Phenyl-1-thiocyanatomethyl-1,3-dihydroisobenzofuran (9):** Yellow liquid;  $R_f$  0.4 (EtOAc/petroleum ether = 1:10);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.53 (dd,  $J$  = 8.8, 1.6 Hz, 2H), 7.41-7.35 (m, 5H), 7.32-7.27 (m, 2H), 5.31 (d,  $J$  = 12.4 Hz, 1H), 5.21 (d,  $J$  = 12.4 Hz, 1H), 3.85 (d,  $J$  = 13.2 Hz, 1H), 3.73 (d,  $J$  = 13.6 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 141.9, 140.4, 139.5, 128.9, 128.8, 128.2, 128.0, 125.0, 122.1, 121.5, 112.9, 89.9, 72.8, 45.6; IR (KBr):  $\nu_{\text{max}}$  2153, 1262, 1020  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{13}\text{NNaOS}$   $[\text{M}+\text{Na}]^+$  290.0610, found 290.0606.



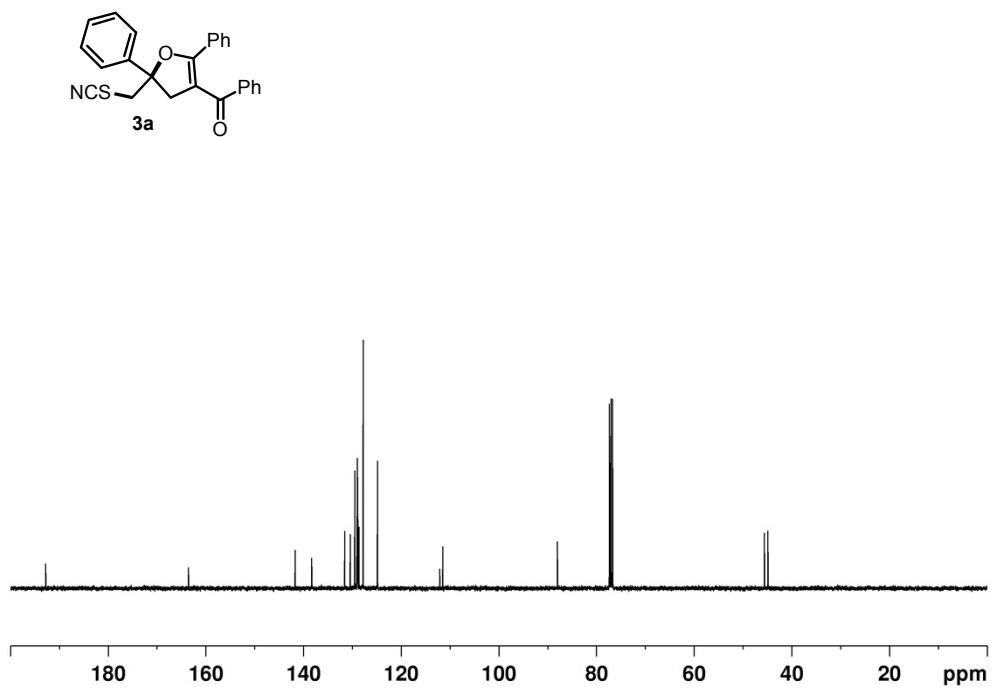
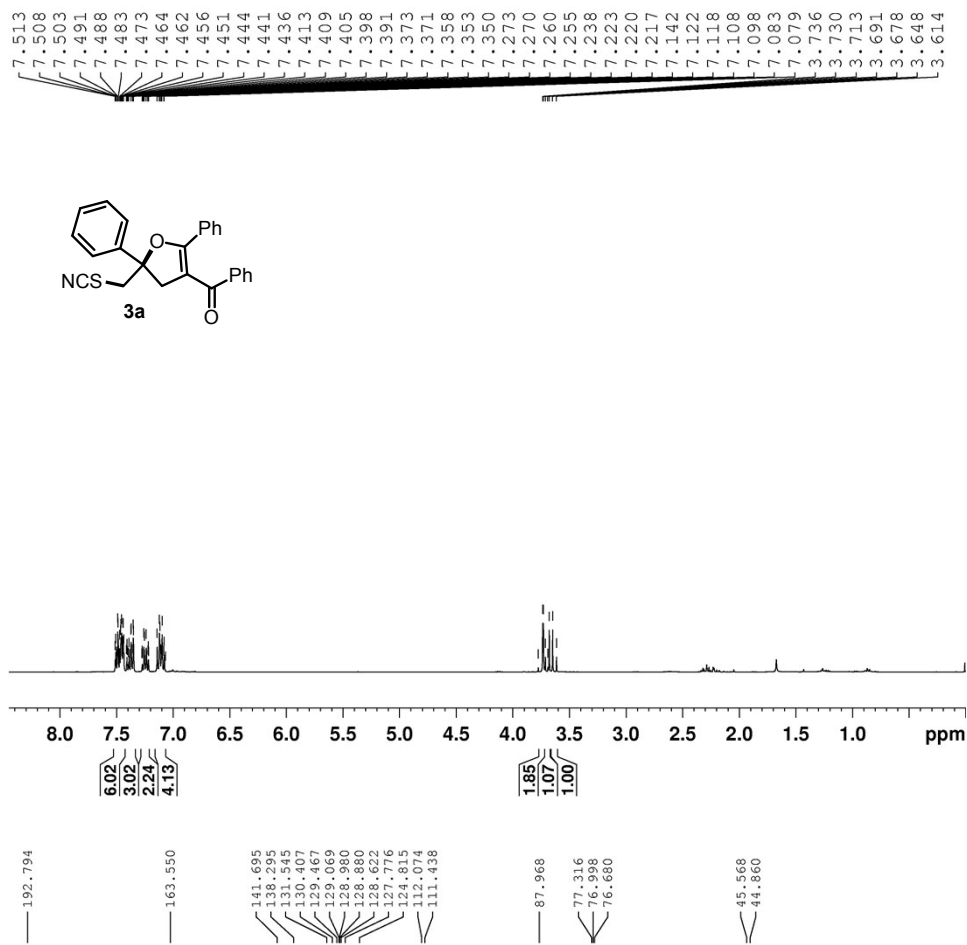
**[2-(1-Phenylethyl)phenyl]methanol (10)<sup>2</sup>:** Yellow liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.39-7.23 (m, 6H), 7.19-7.15 (m, 3H), 4.70 (d,  $J$  = 12.8 Hz, 1H), 4.62 (d,  $J$  = 12.8 Hz, 1H), 4.50 (q,  $J$  = 7.2 Hz, 1H), 1.64 (d,  $J$  = 7.2 Hz, 3H), 1.50 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 146.3, 143.8, 138.2, 128.6, 128.5, 128.1, 127.5, 127.3, 126.5, 126.1, 63.2, 40.0, 22.4.

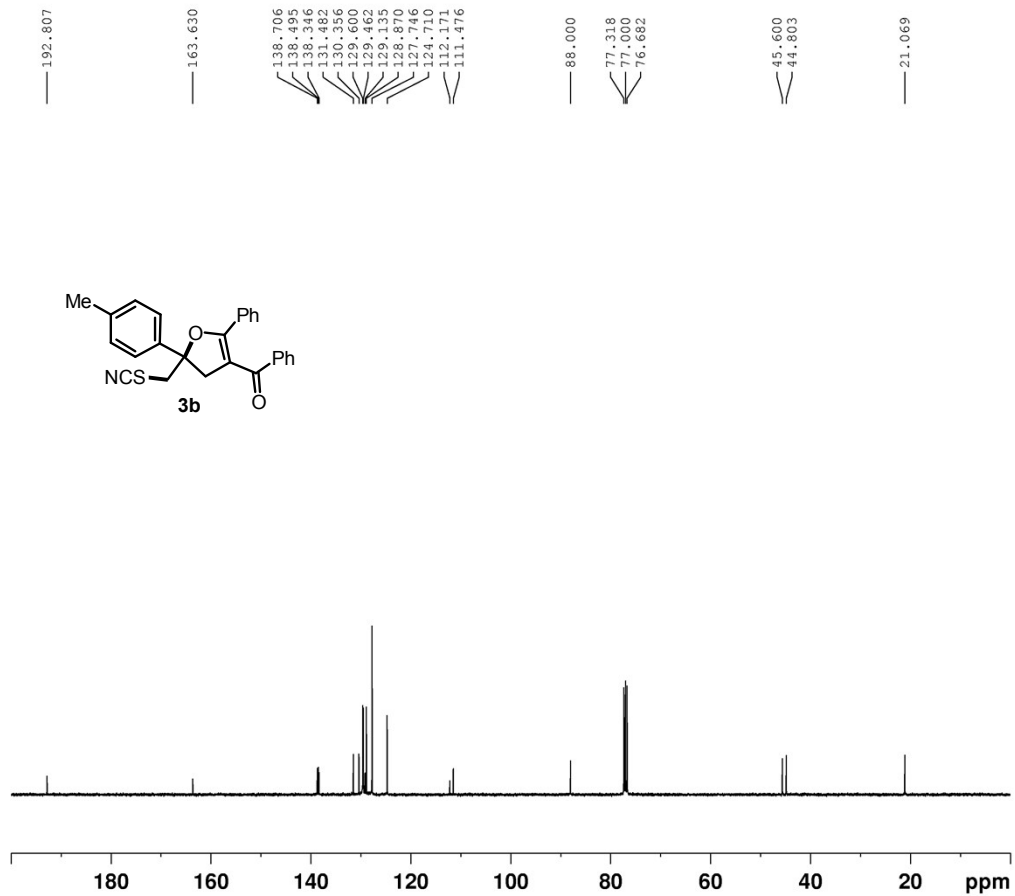
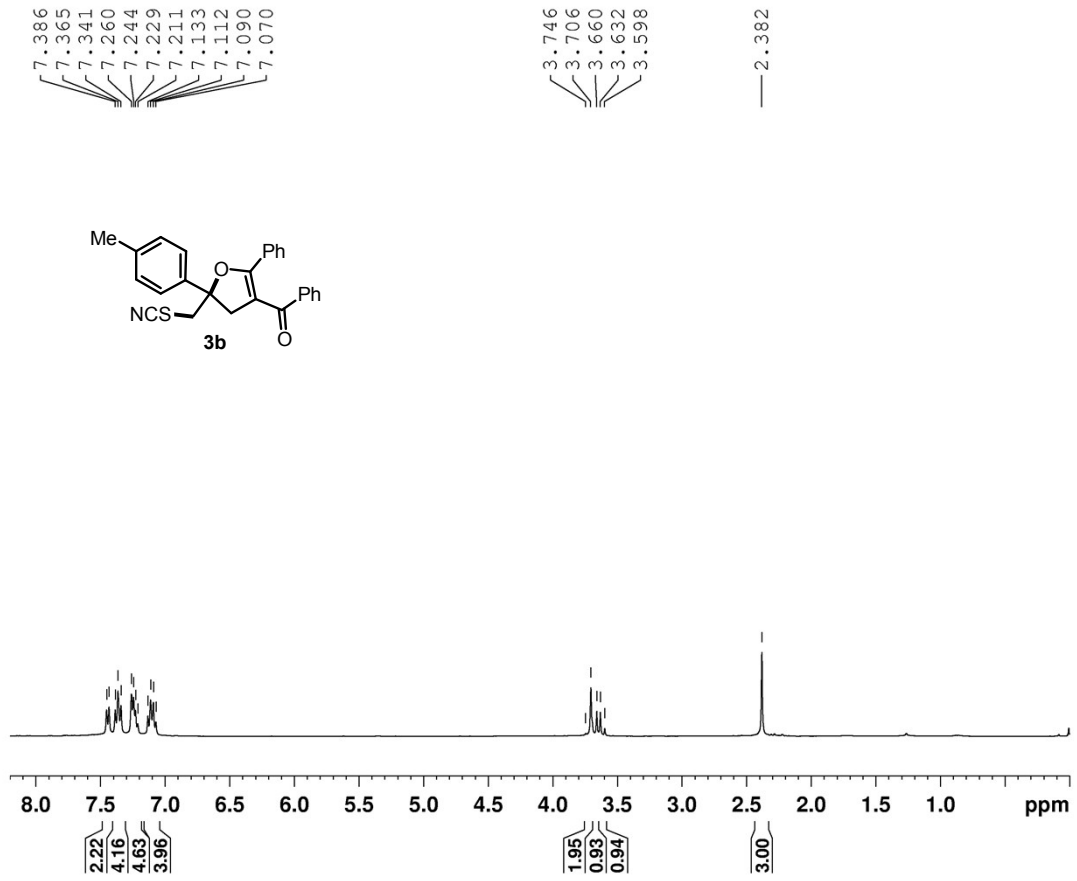
## References

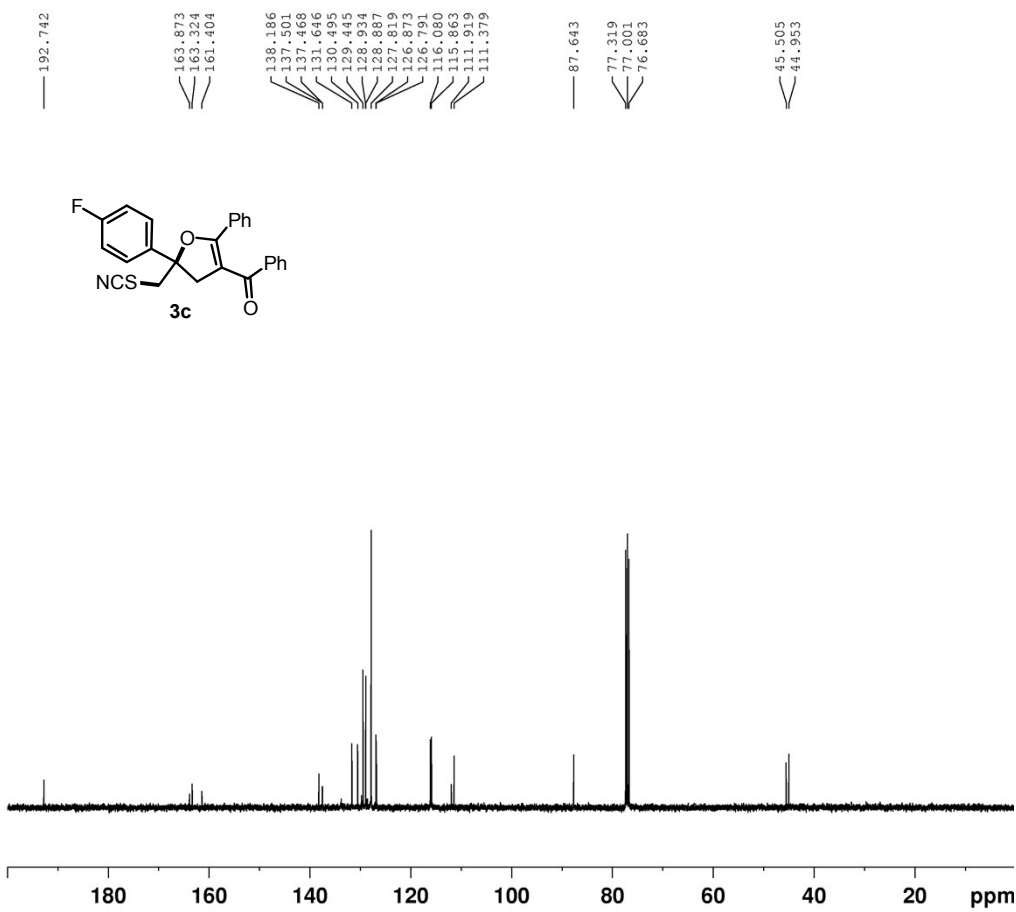
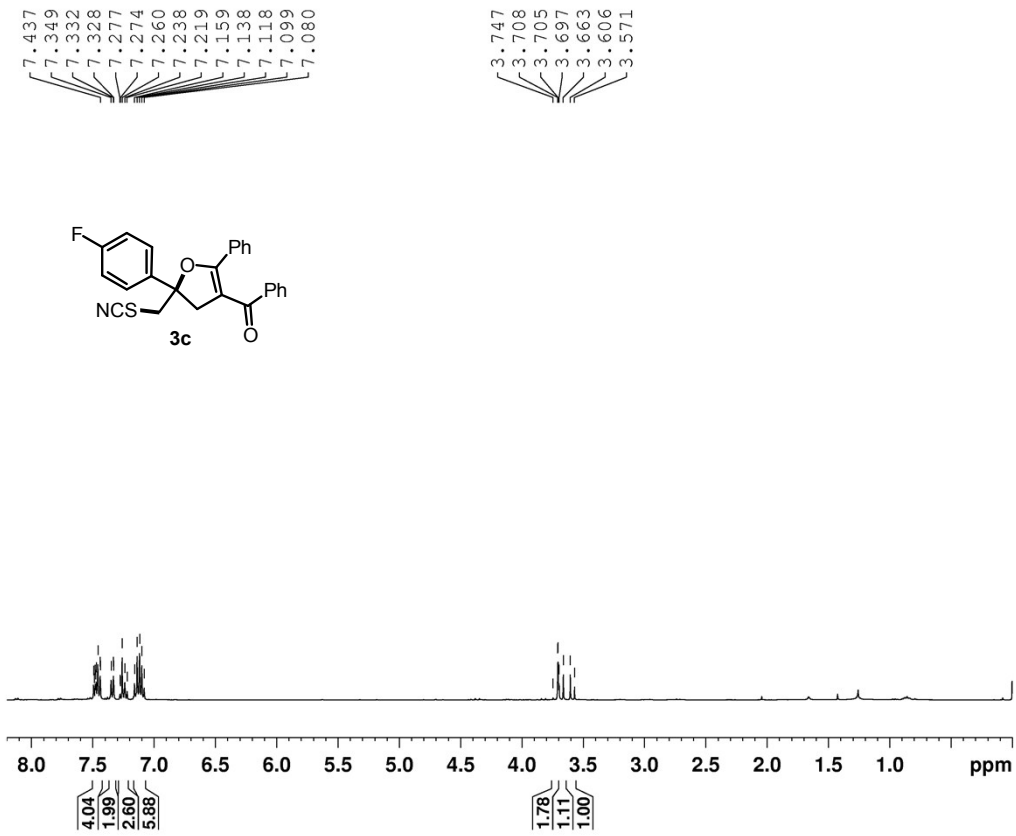
- 1 Y. Zhao, X. Jiang and Y.-Y. Yeung, *Angew. Chem., Int. Ed.*, 2013, **52**, 8597.
- 2 S. Song, S.-F. Zhu, Y.-B. Yu and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2013, **52**, 1556.
- 3 R. M. Trend, Y. K. Ramtohul and B. M. Stoltz, *J. Am. Chem. Soc.*, 2005, **127**, 17778.
- 4 (a) S. Vorona, T. Artamonova, Y. Zevatskii and L. Myznikov, *Synthesis*, 2014, **46**, 781; (b) R. Riemschneider, F. Wojahn and G. Orlick, *J. Am. Chem. Soc.*, 1951, **73**, 5905.



# <sup>1</sup>H NMR and <sup>13</sup>C NMR Spectra of Products 3

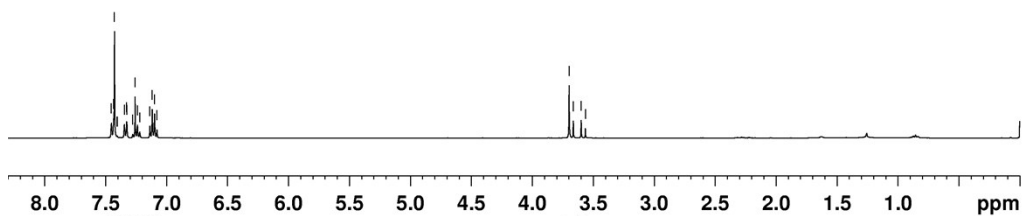
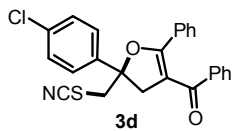






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7.119  
7.100  
7.081

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4.00

2.94  
1.00

192.700

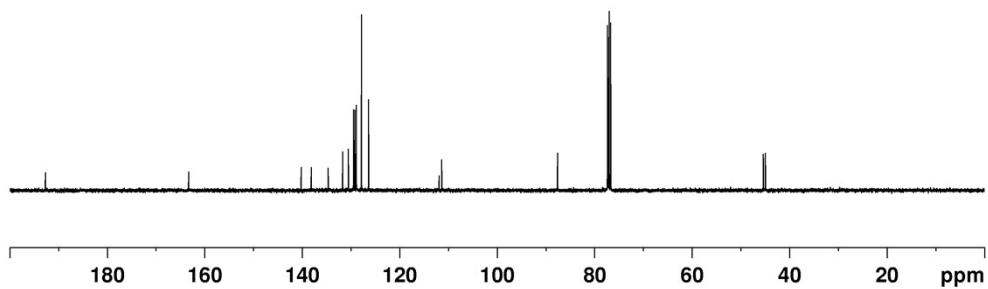
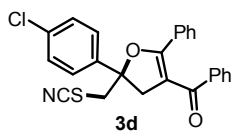
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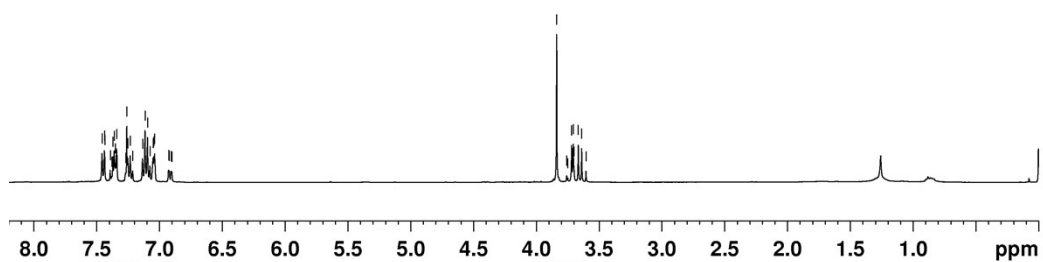
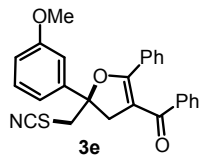
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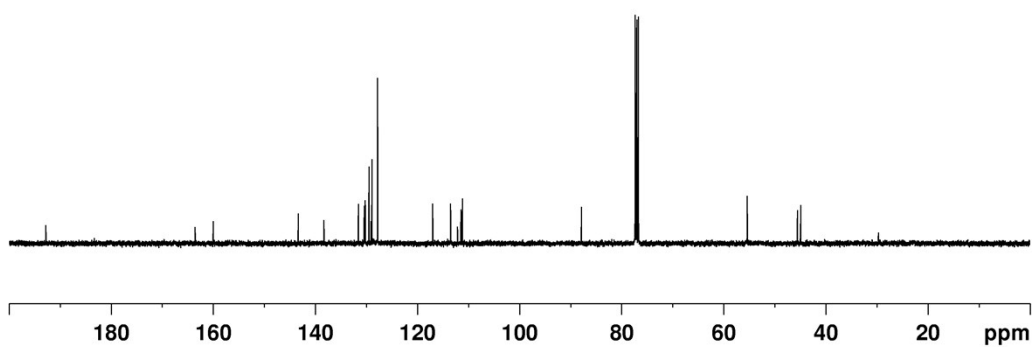
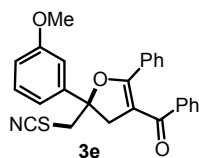
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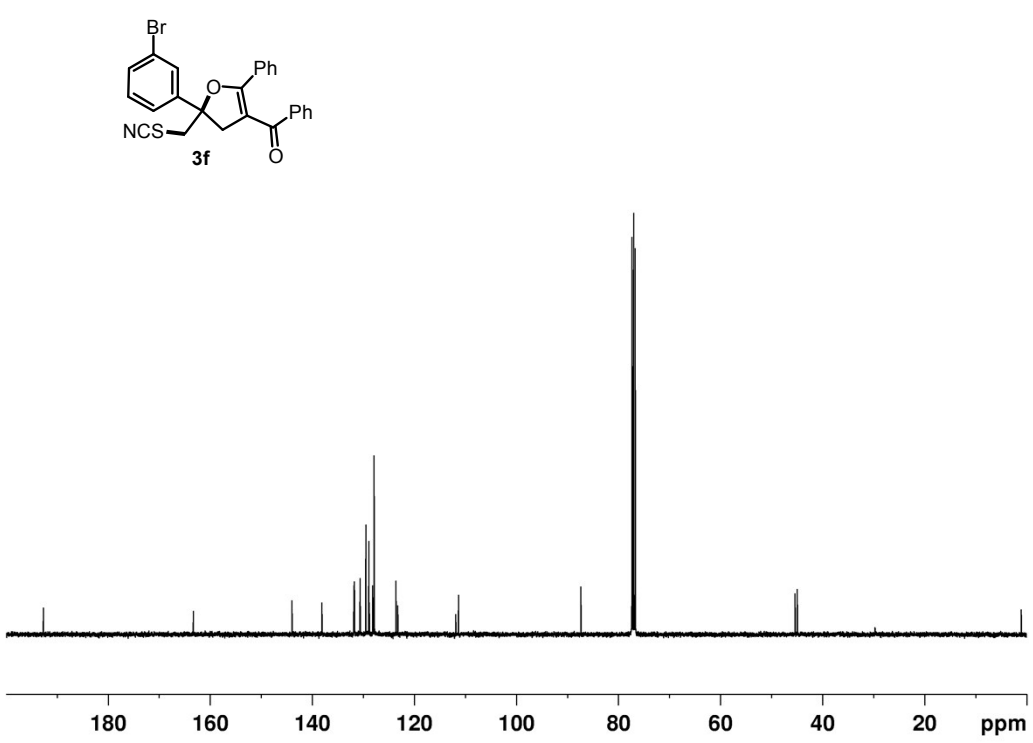
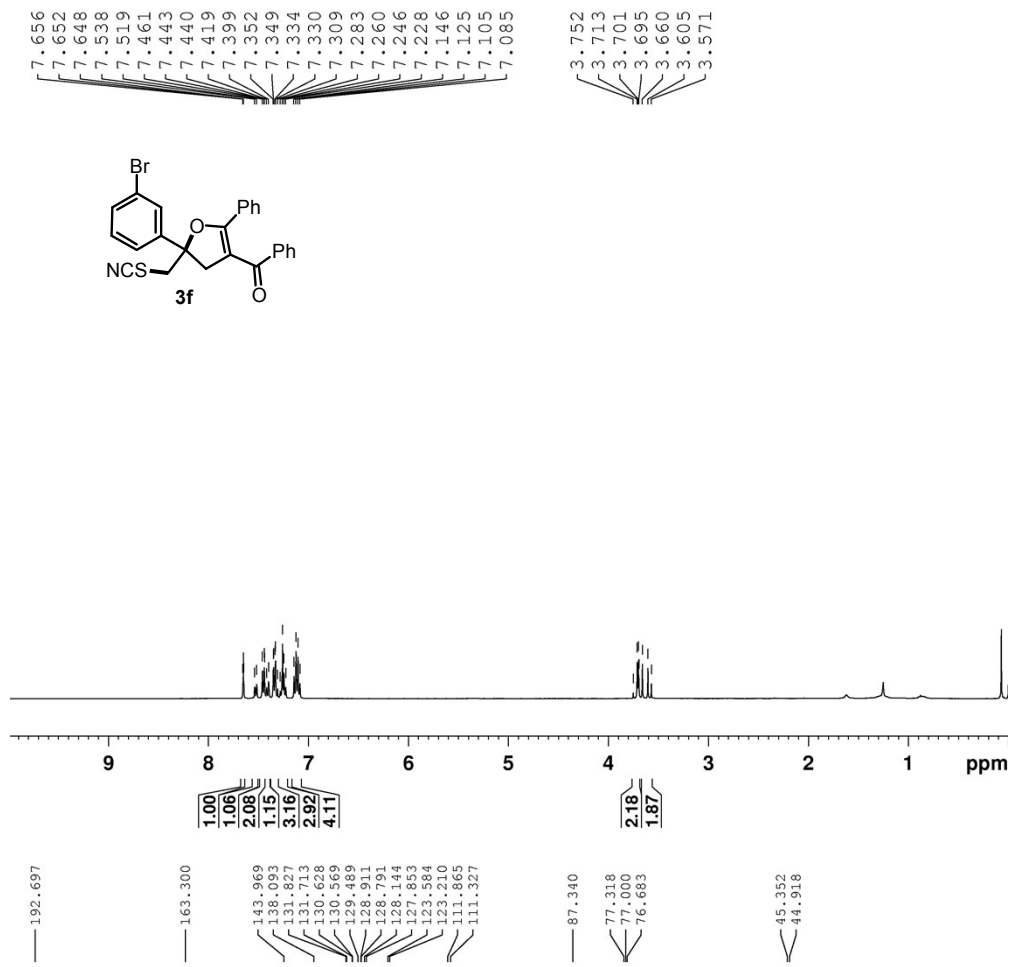
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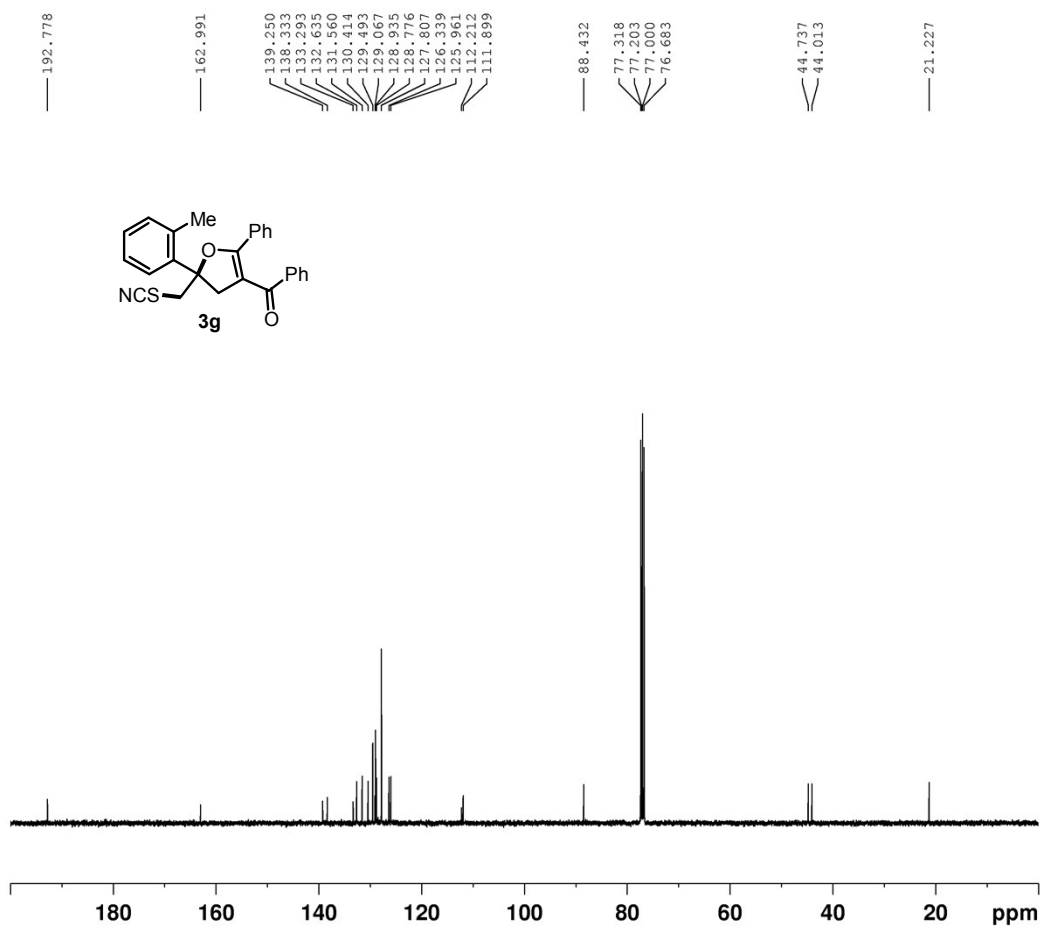
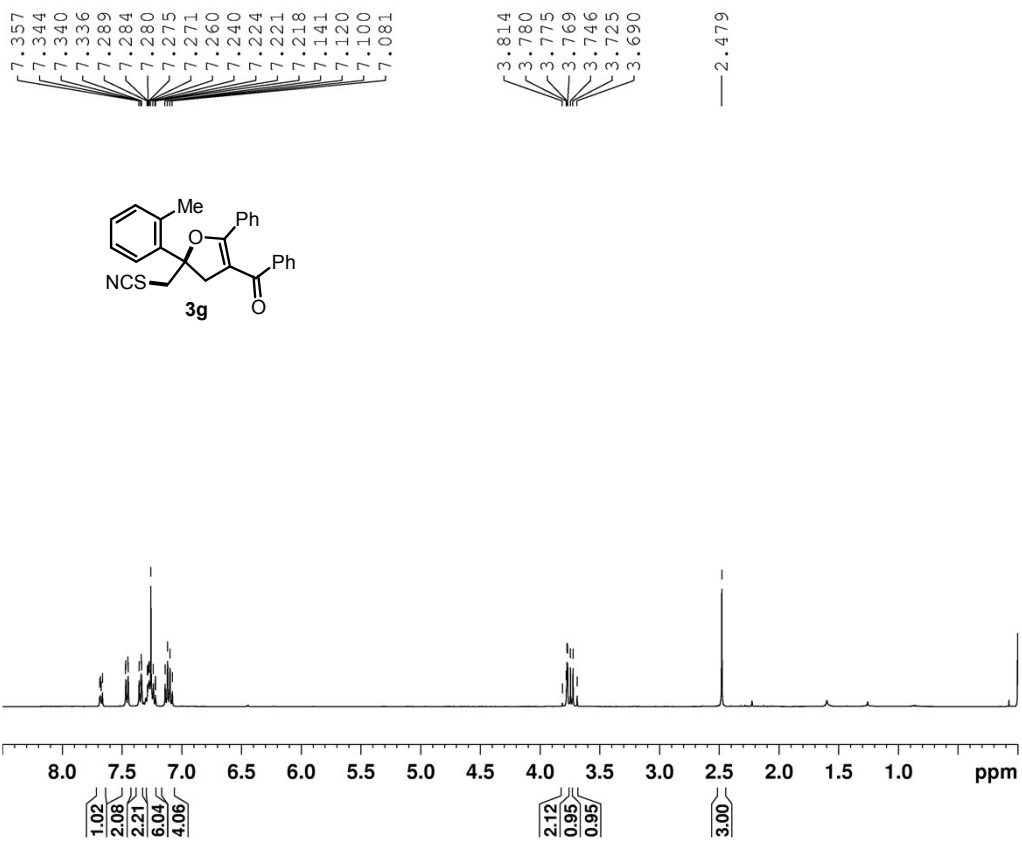
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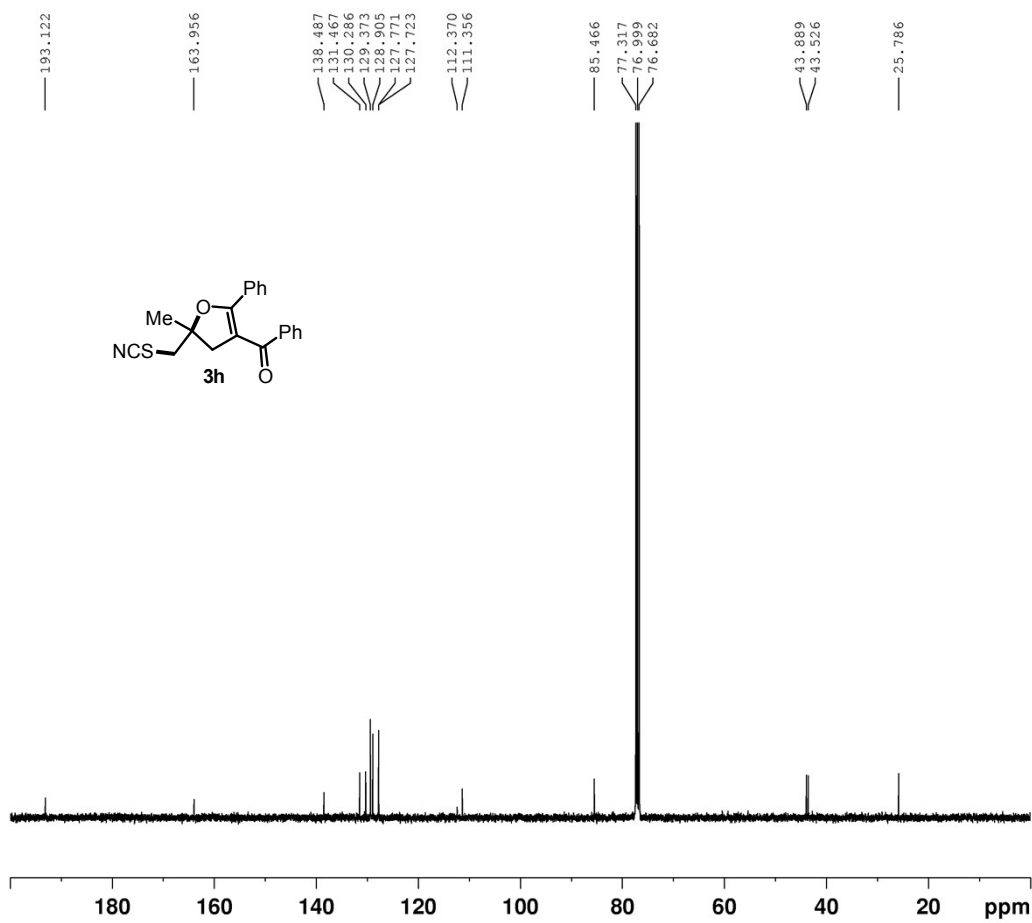
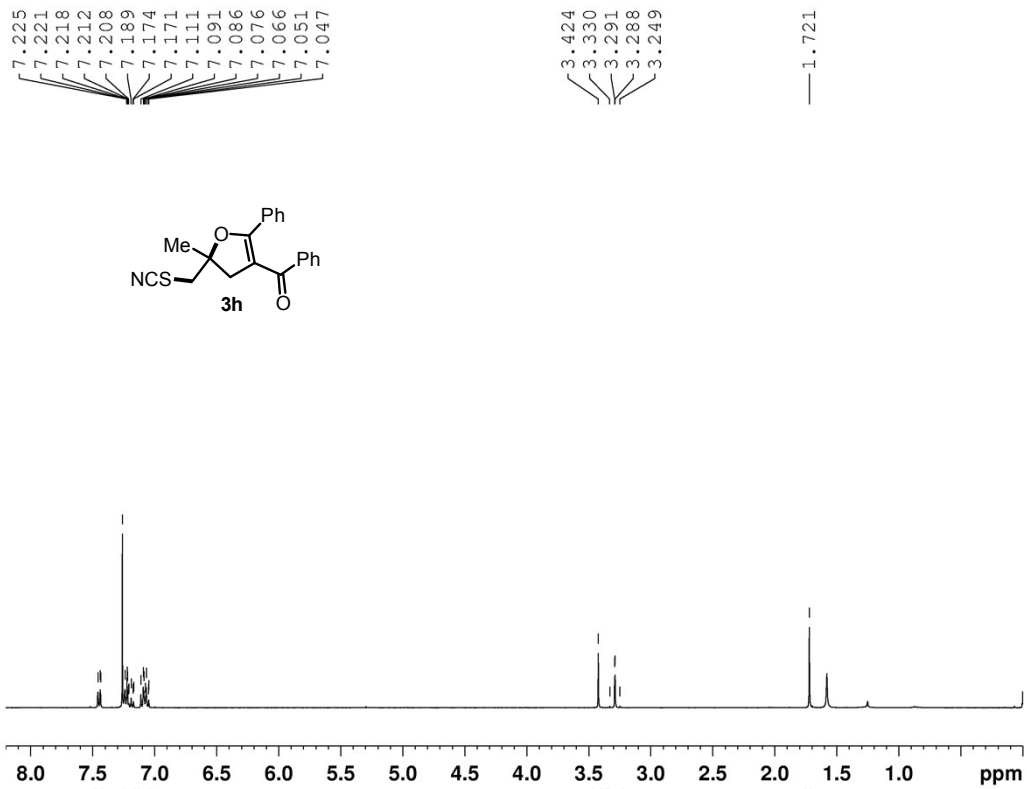
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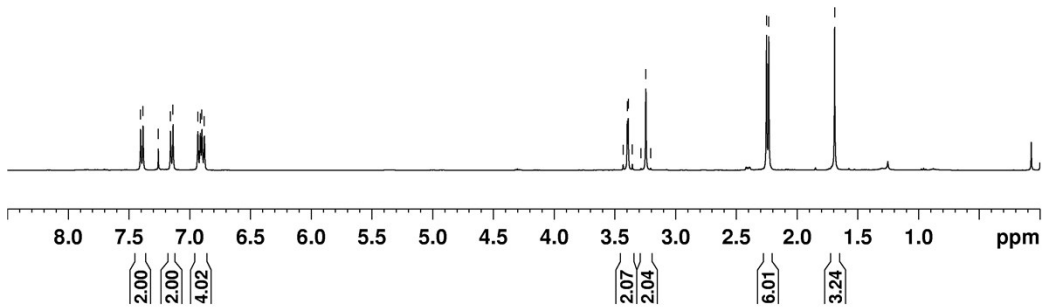
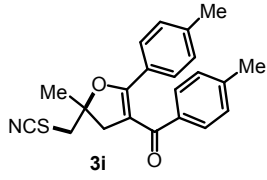


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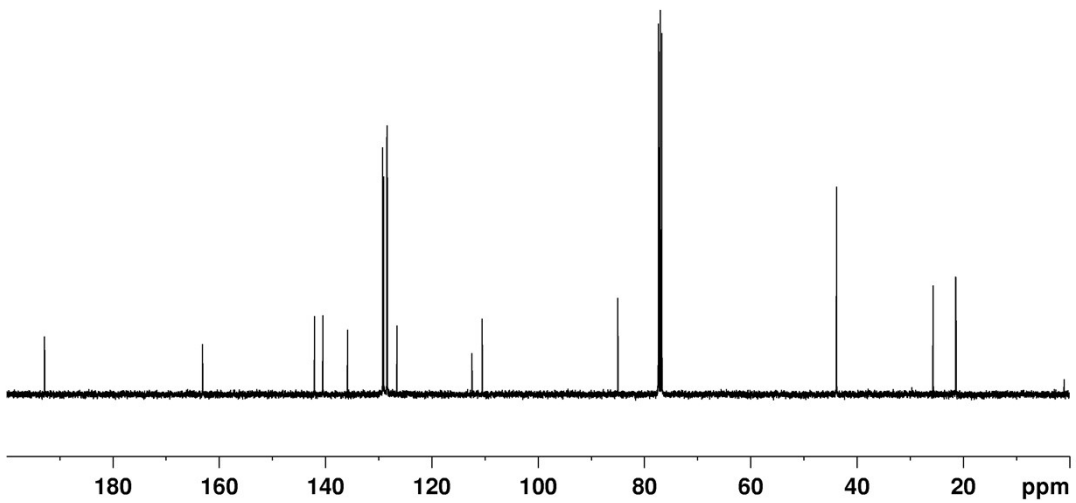
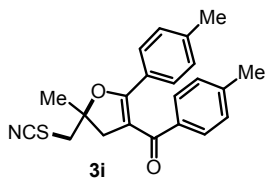
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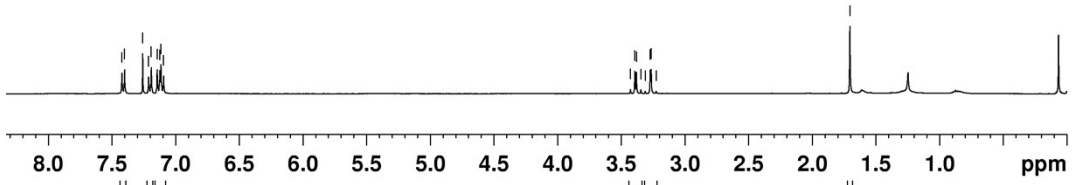
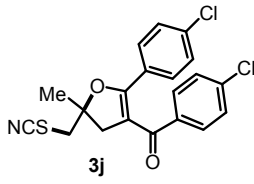
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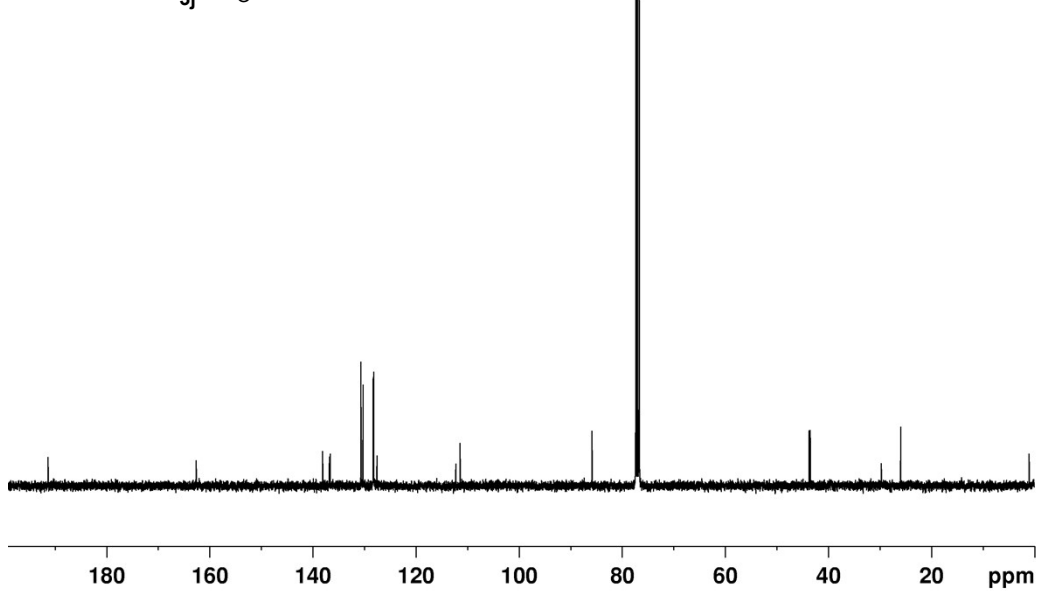
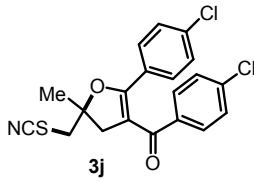
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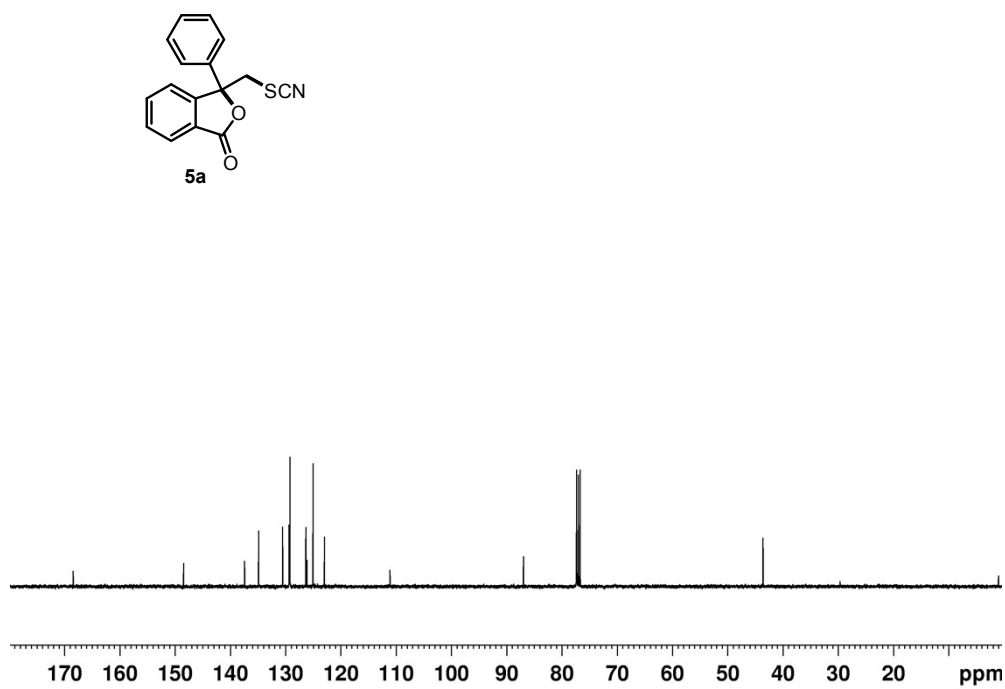
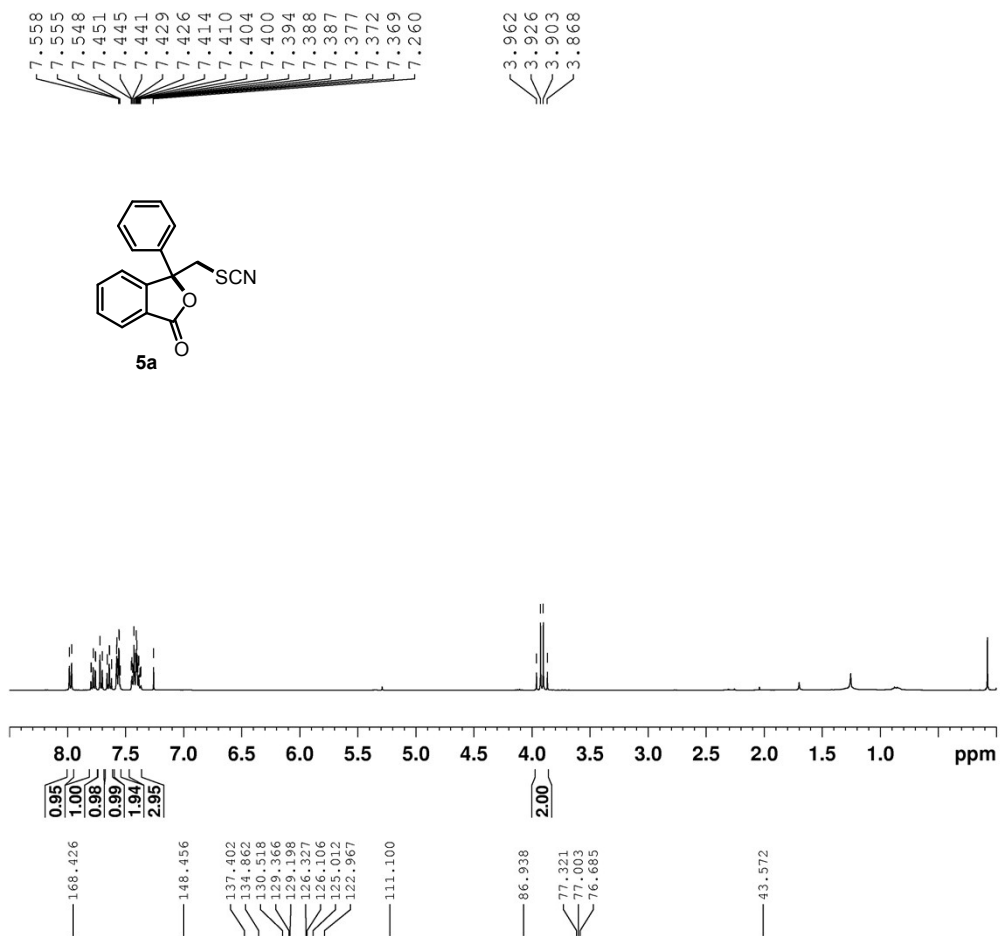
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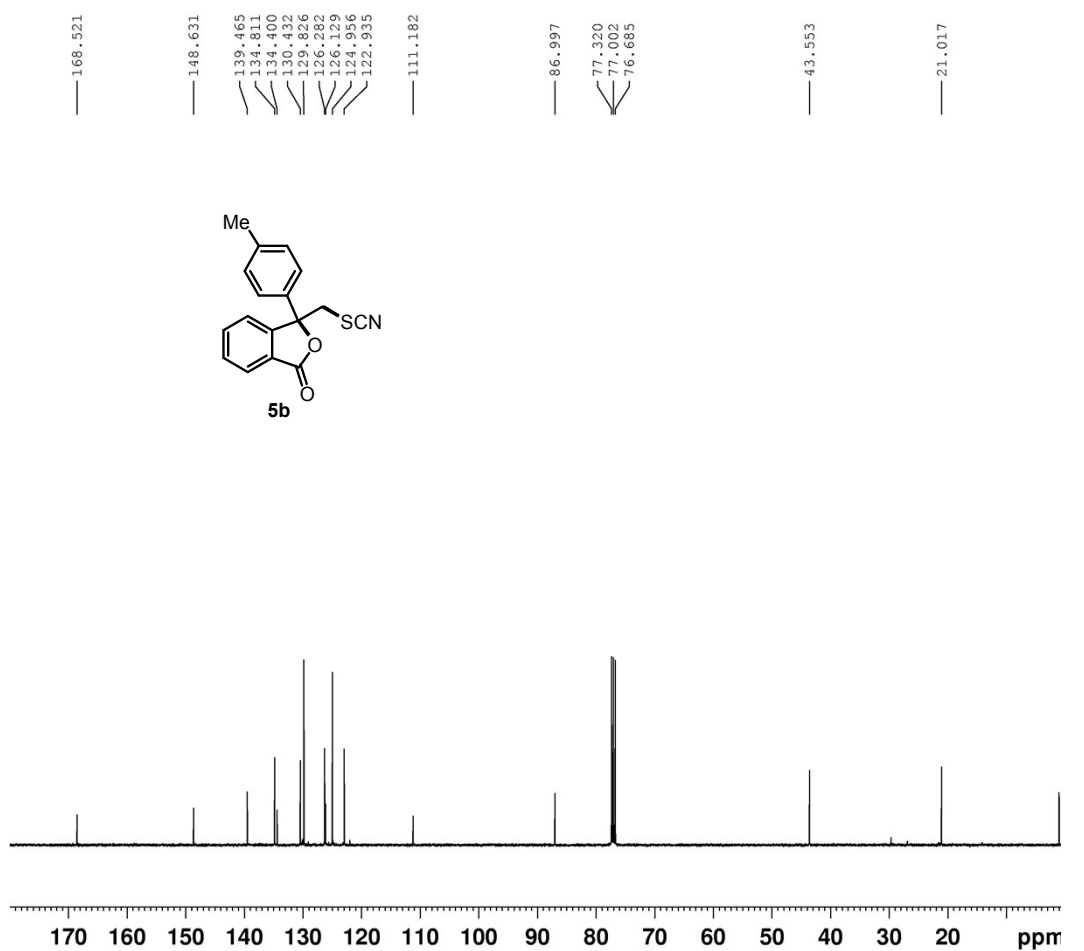
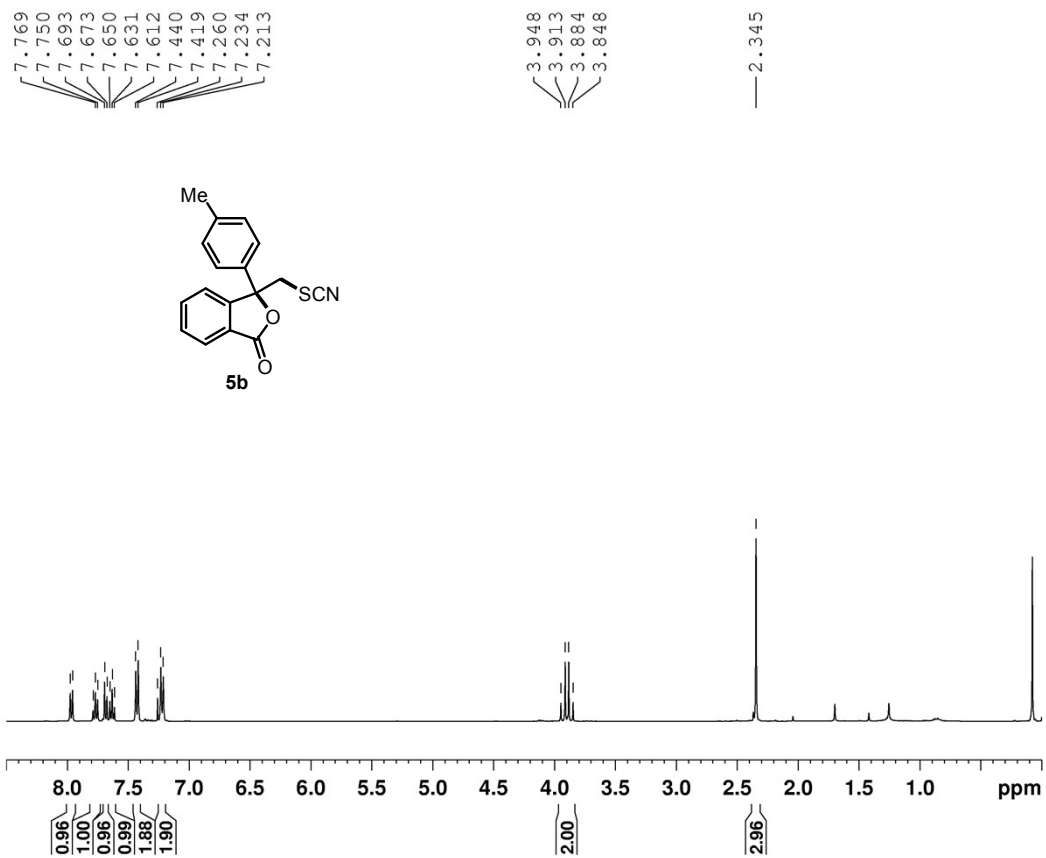
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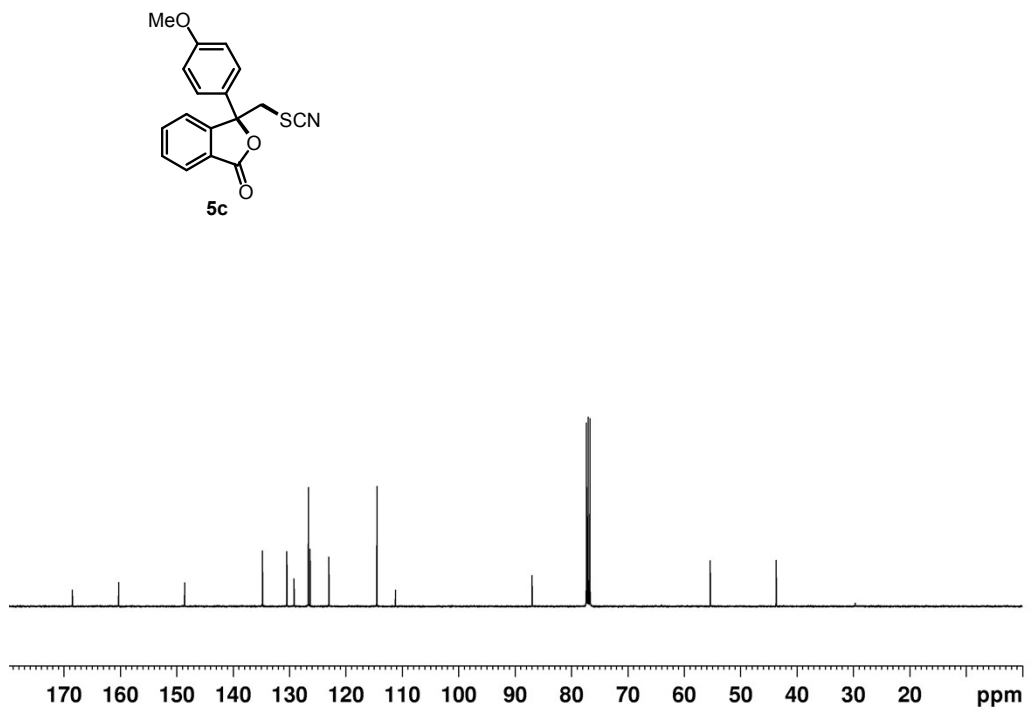
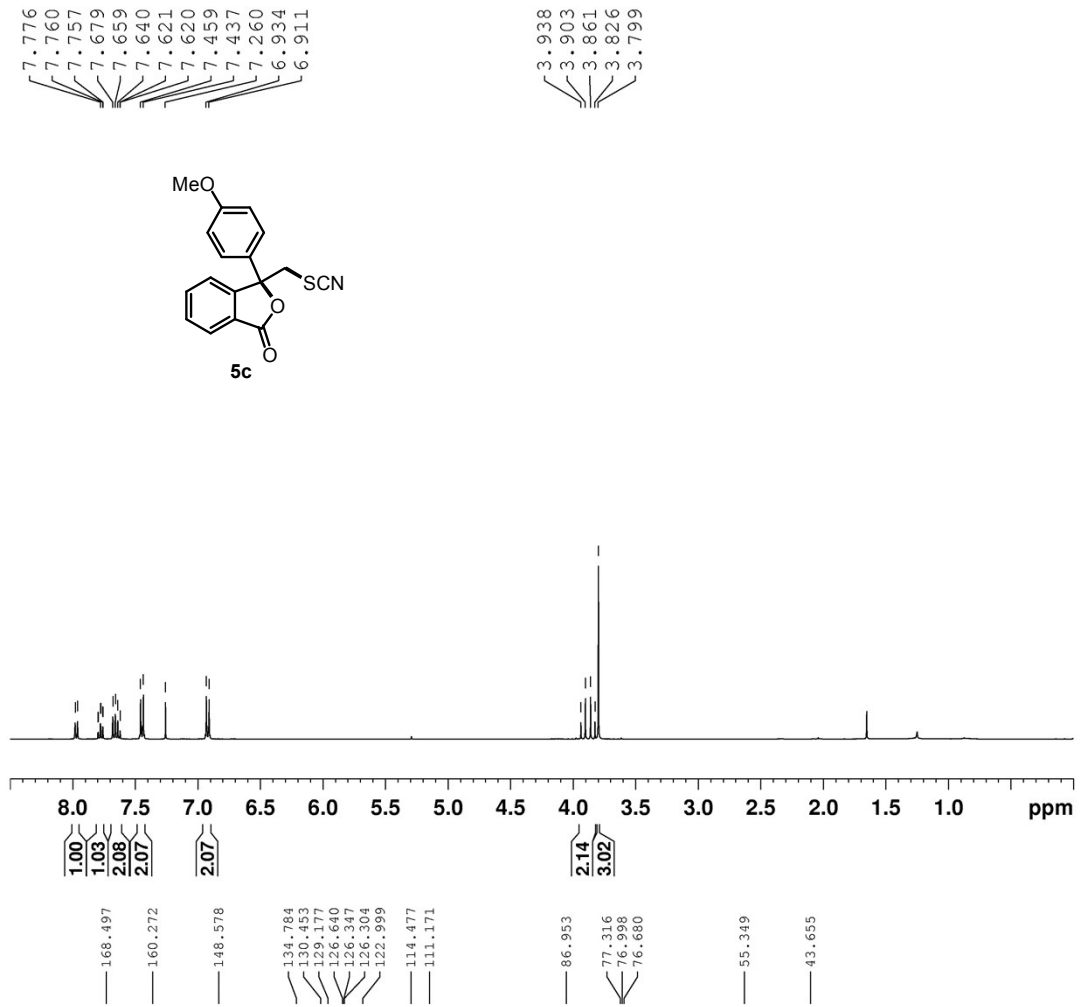
25.917

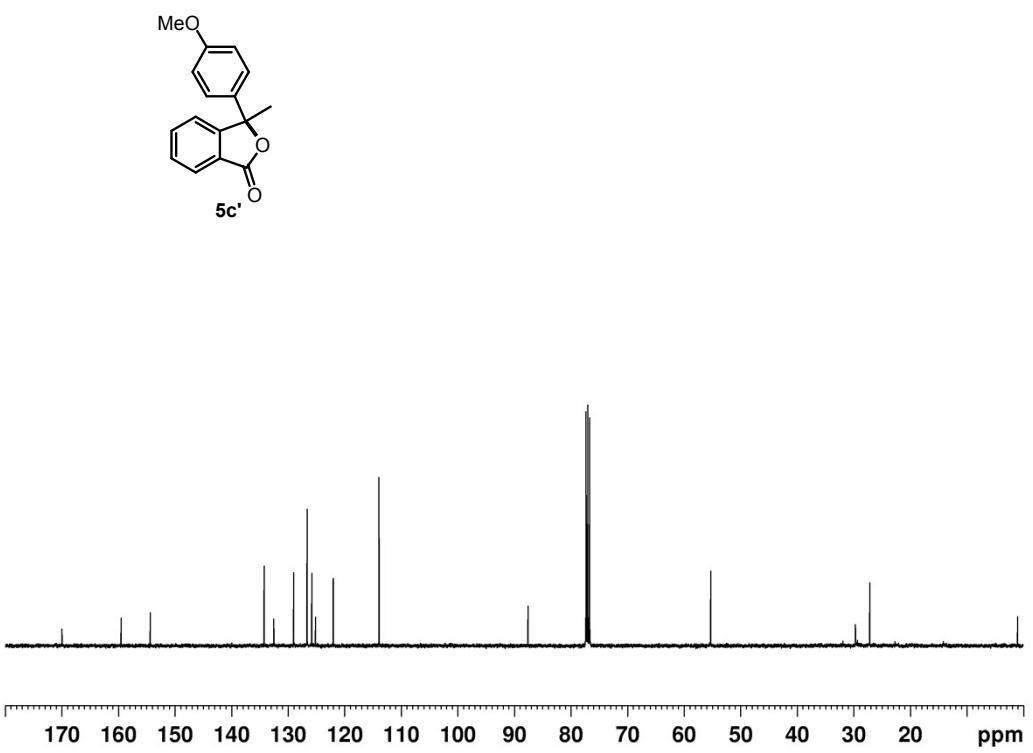
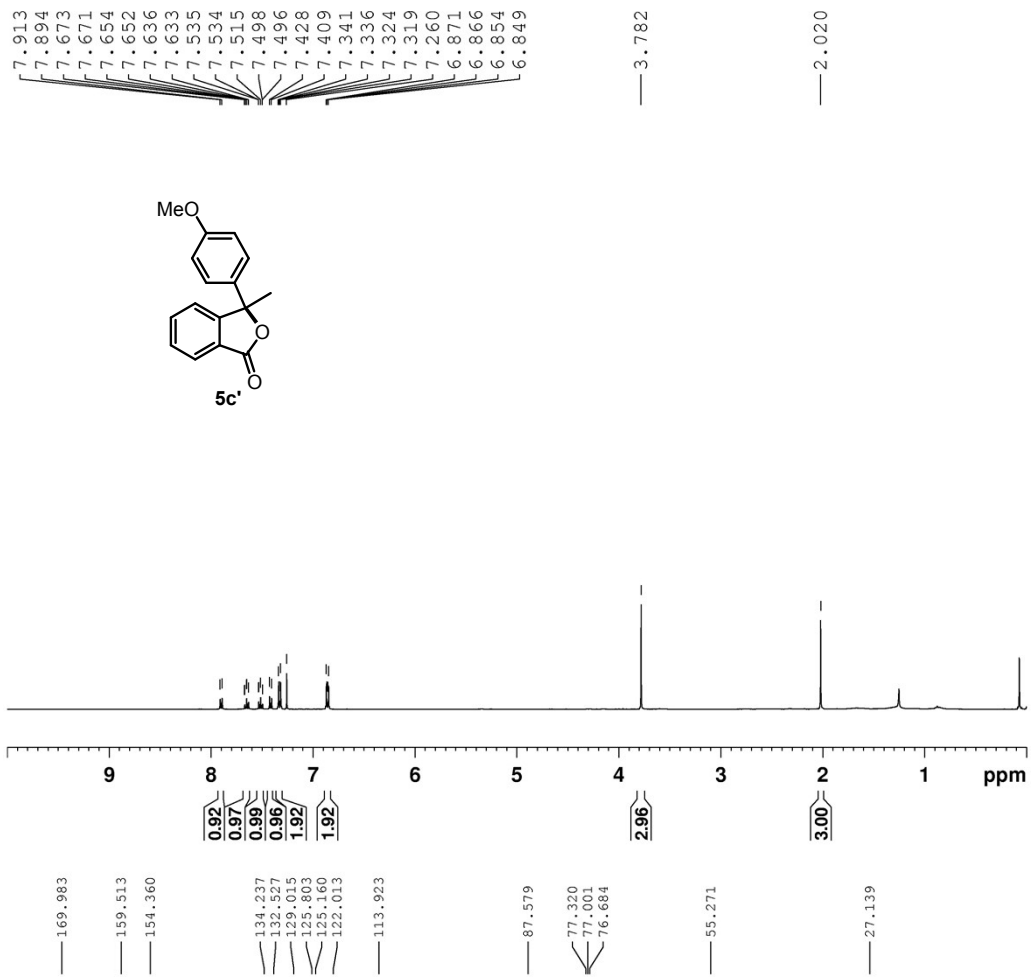


# <sup>1</sup>H NMR and <sup>13</sup>C NMR Spectra of Products 5



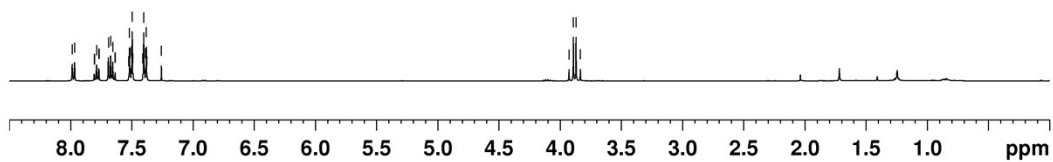
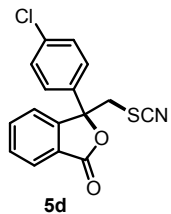






7.655  
7.637  
7.635  
7.527  
7.520  
7.515  
7.504  
7.498  
7.492  
7.410  
7.404  
7.399  
7.387  
7.382  
7.376  
7.260

3.928  
3.893  
3.871  
3.835



0.96  
0.99  
1.98  
1.97  
1.95

1.00  
1.01

168.157

148.075

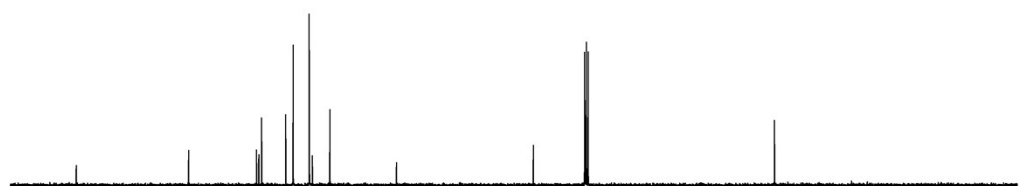
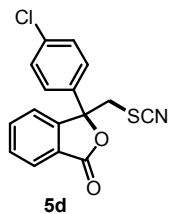
135.943  
135.329  
133.721  
129.390  
126.537  
126.478  
125.973  
122.825

110.941

86.484

77.318  
77.000  
76.682

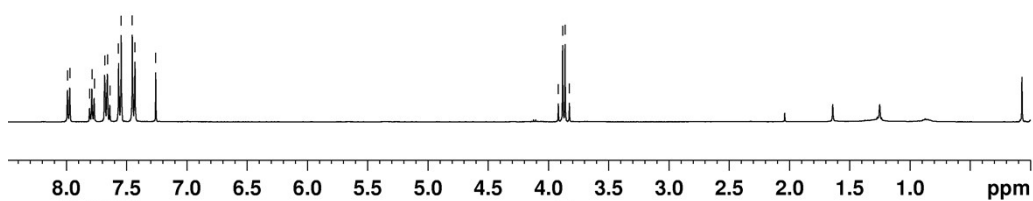
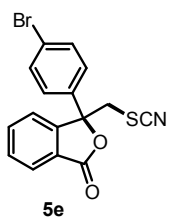
43.394



170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

7.787  
7.768  
7.682  
7.659  
7.639  
7.568  
7.547  
7.454  
7.433  
7.260

3.918  
3.883  
3.863  
3.827



0.95  
0.99  
1.97  
1.92  
1.97

2.00

168.103

148.025

136.530

135.037

132.393

130.754

126.784

126.525

126.012

123.750

122.810

110.903

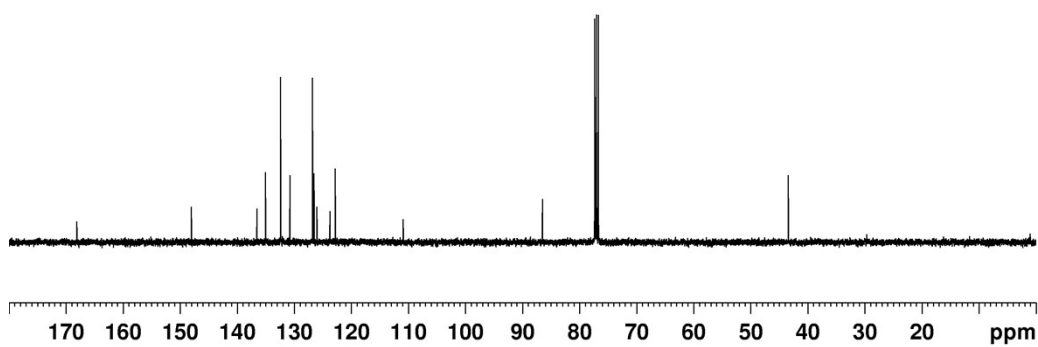
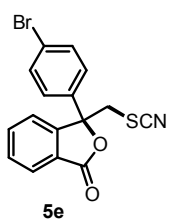
86.486

77.315

76.398

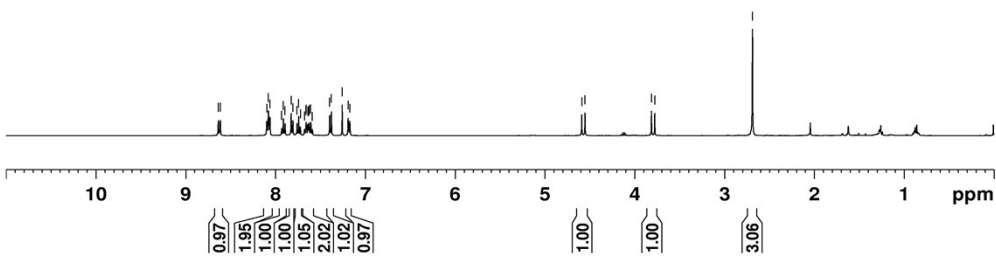
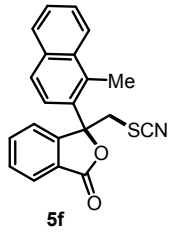
76.680

43.386

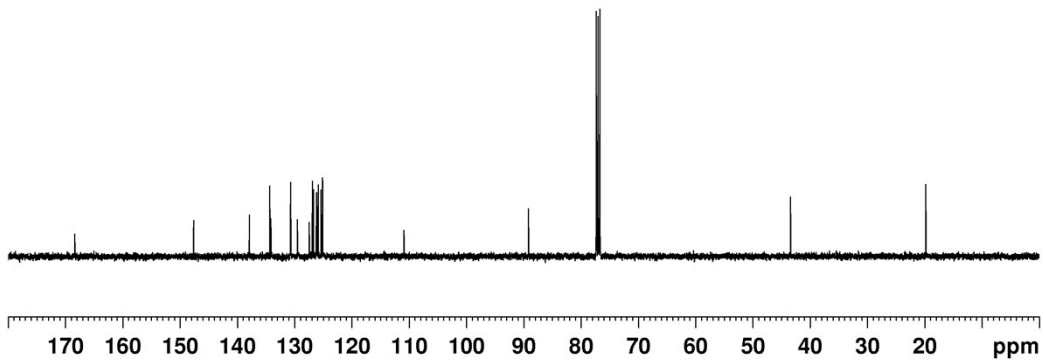
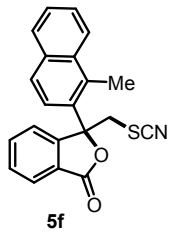


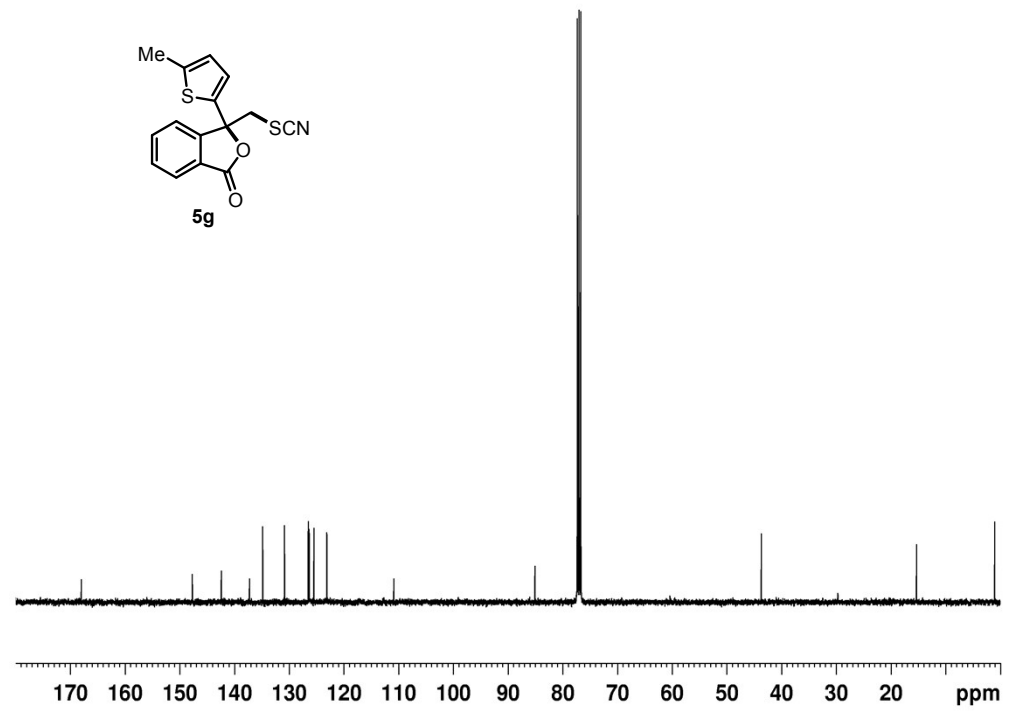
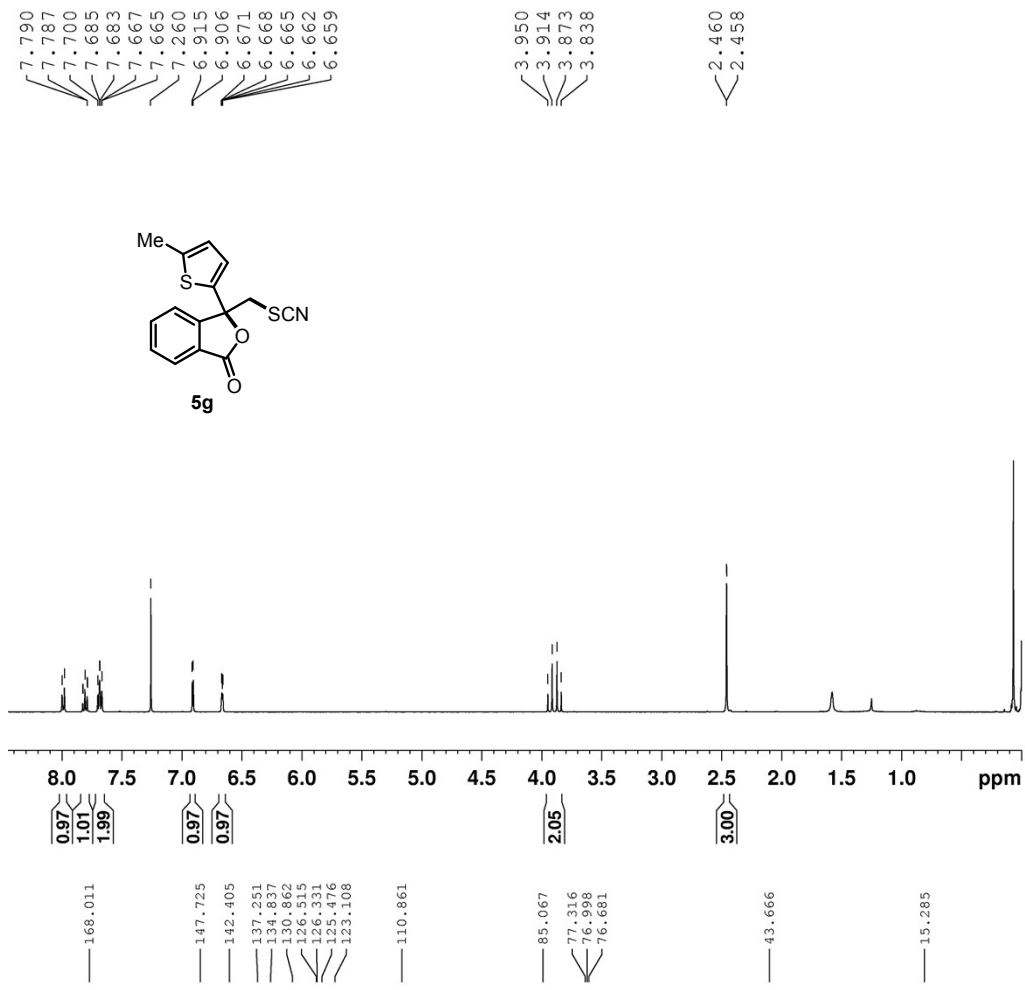


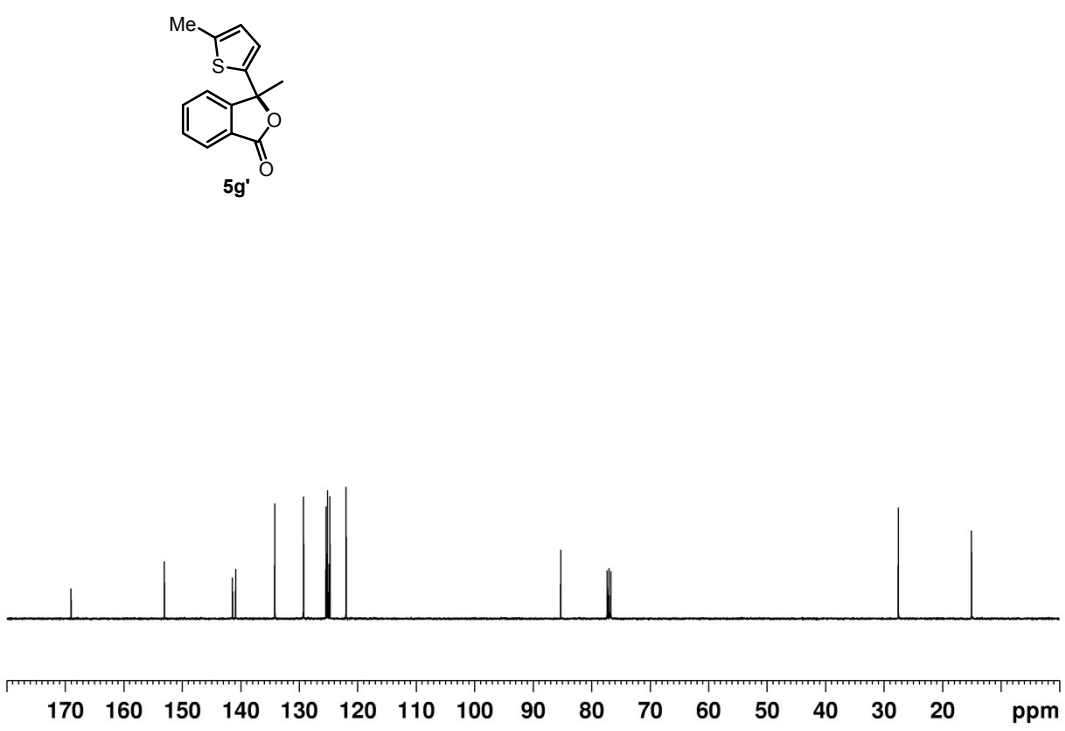
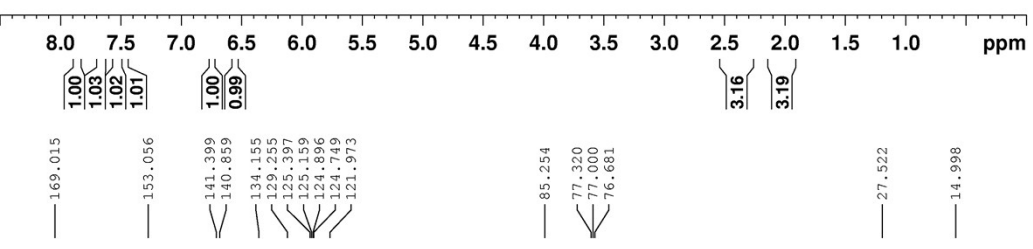
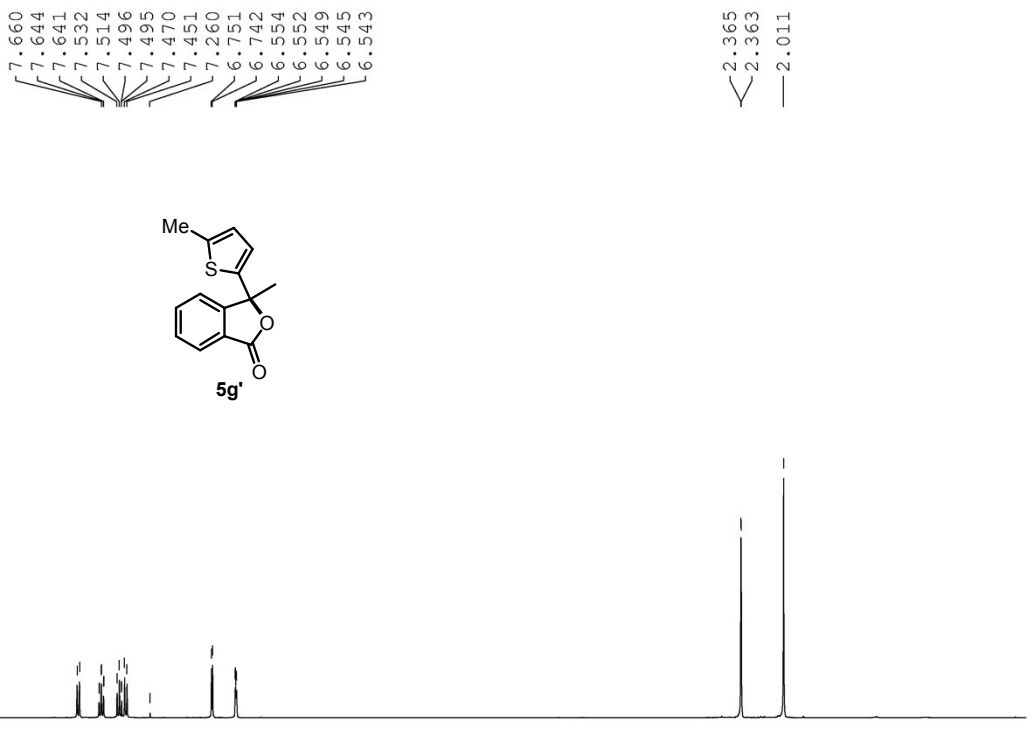
8.638  
8.617  
8.099  
8.081  
8.065  
7.933  
7.915  
7.896  
7.828  
7.809  
7.762  
7.743  
7.724  
7.678  
7.663  
7.660  
7.643  
7.639  
7.630  
7.627  
7.610  
7.592  
7.399  
7.380  
7.260  
7.193  
7.174  
4.591  
4.555  
3.815  
3.779  
— 2.690

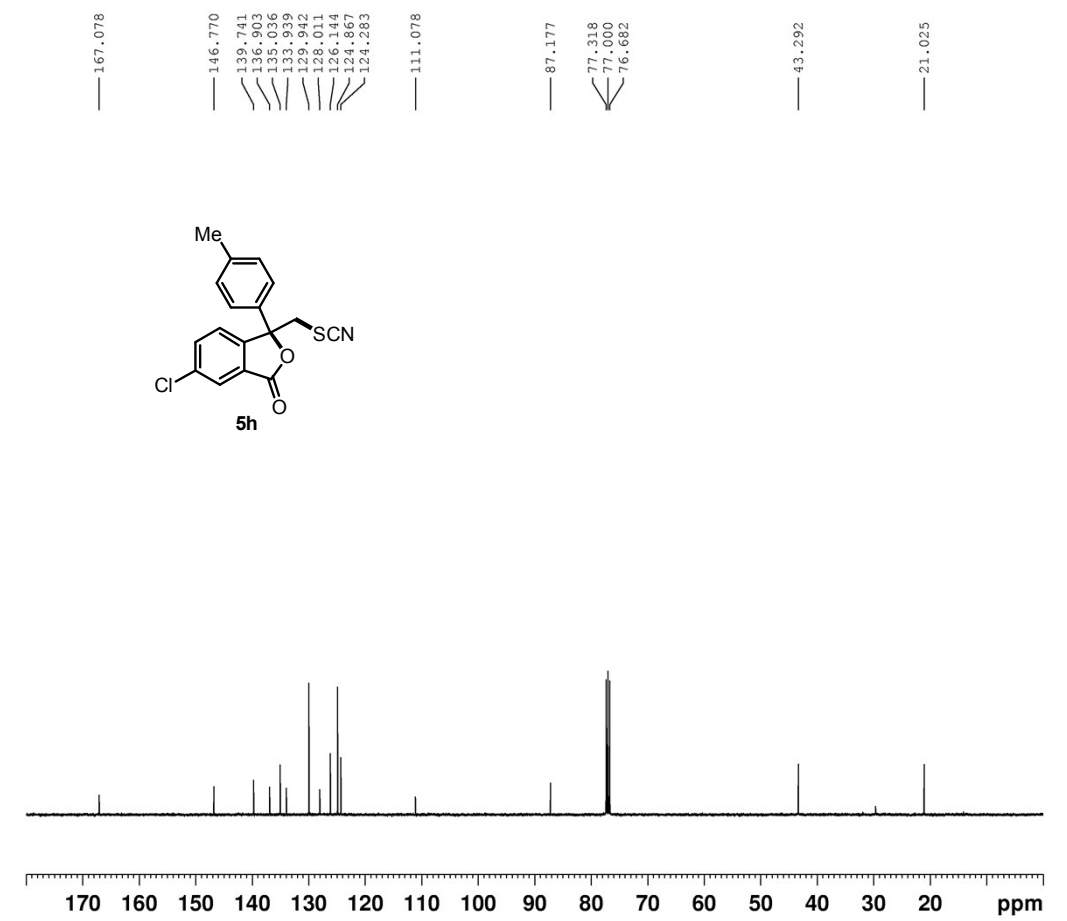
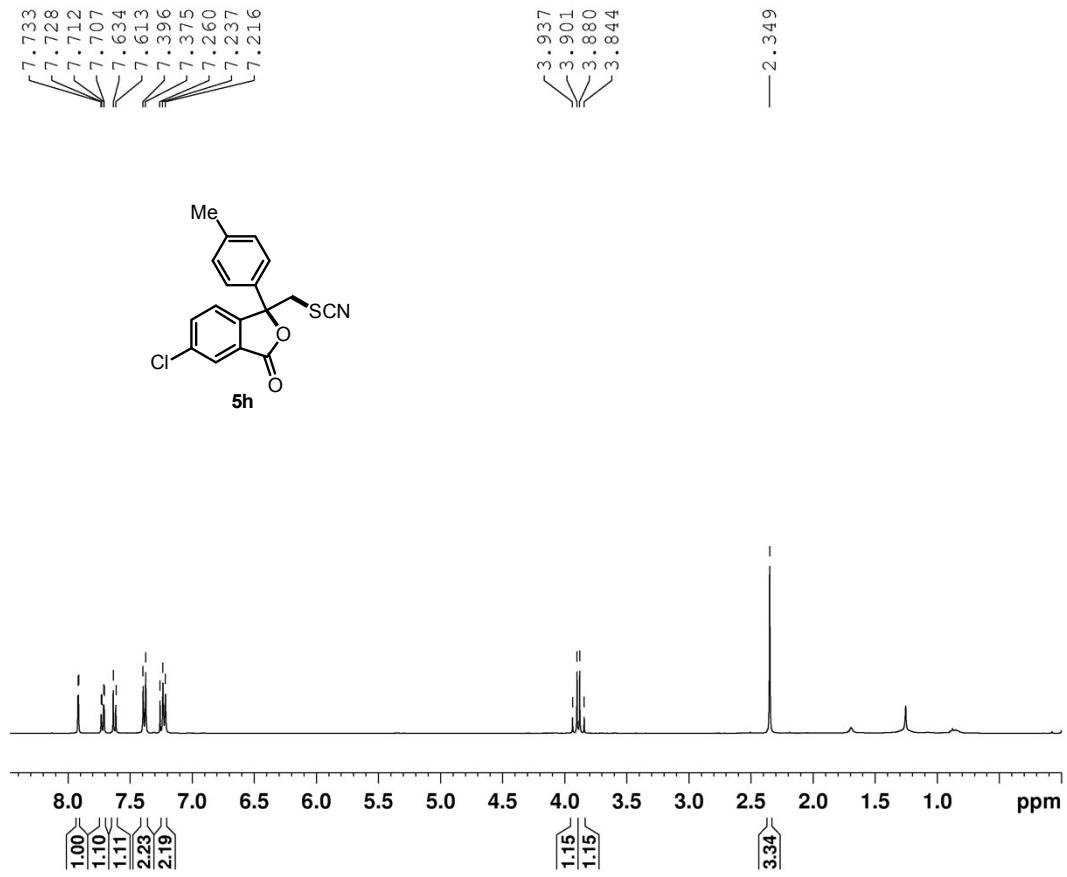


168.374  
147.624  
137.876  
134.319  
134.120  
130.700  
129.633  
129.441  
127.441  
126.896  
126.715  
126.175  
126.089  
125.873  
125.389  
125.122  
125.077  
110.883  
89.163  
77.315  
76.997  
76.679  
43.381  
19.778





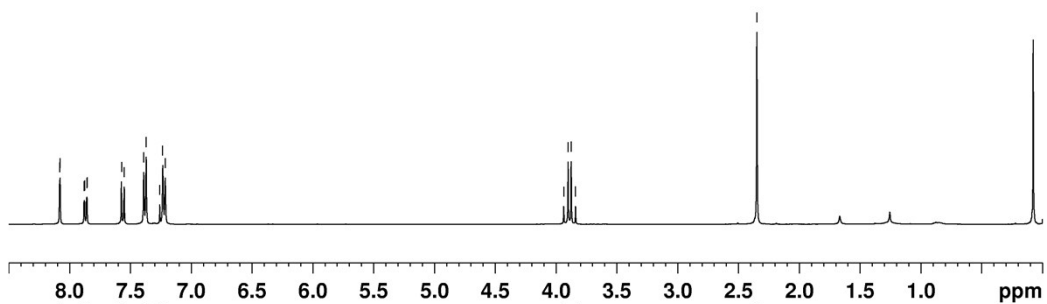
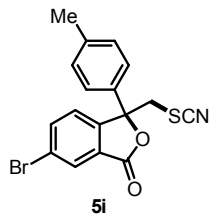




7.880  
7.877  
7.860  
7.856  
7.573  
7.553  
7.393  
7.372  
7.260  
7.236  
7.215

3.938  
3.902  
3.876  
3.841

— 2.349



1.00  
1.07  
1.10  
2.18  
2.16

2.31

3.25

— 166.931

— 147.296

— 139.745

— 137.810

— 133.877

— 129.943

— 129.214

— 128.208

— 124.861

— 124.498

— 111.069

— 87.230

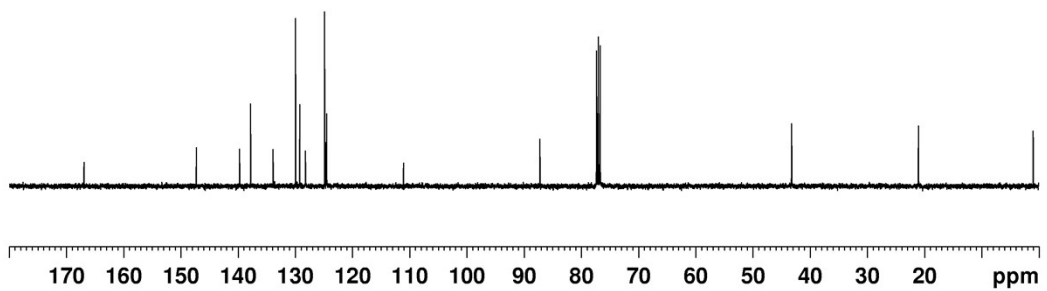
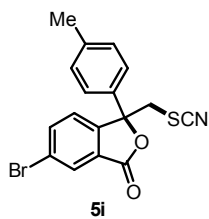
— 77.317

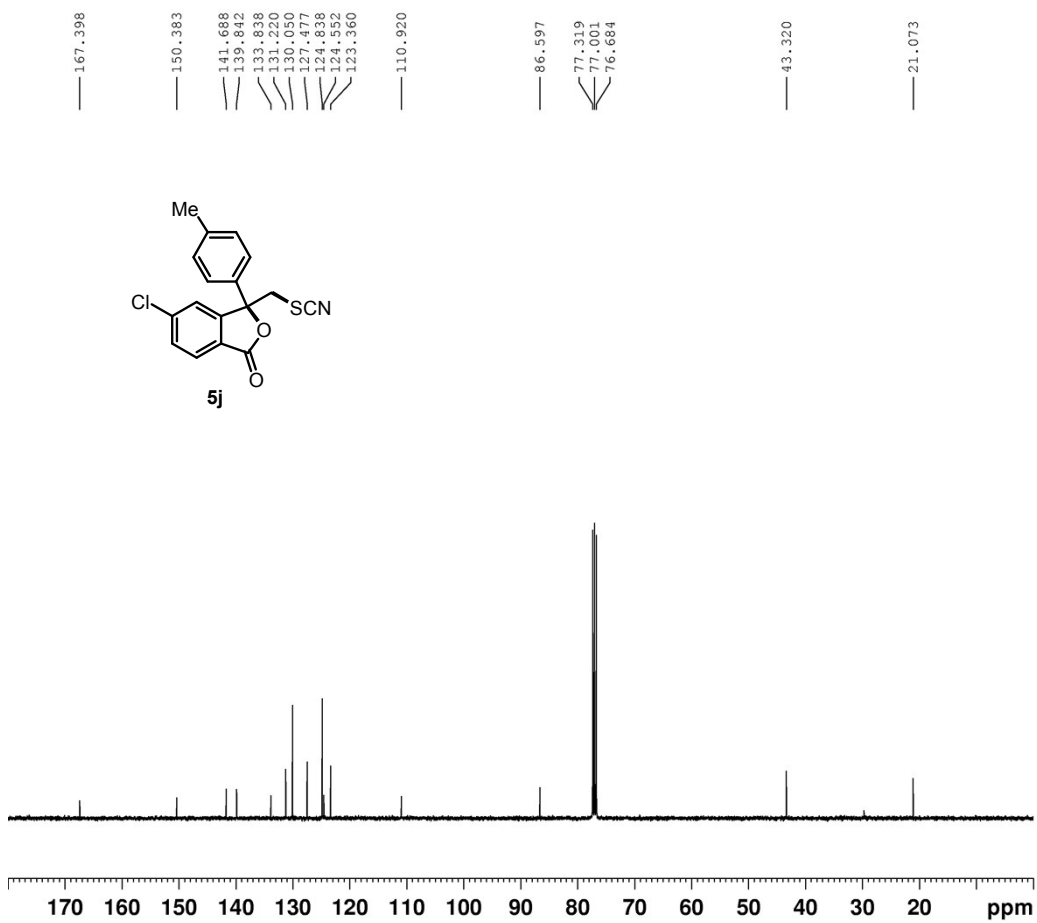
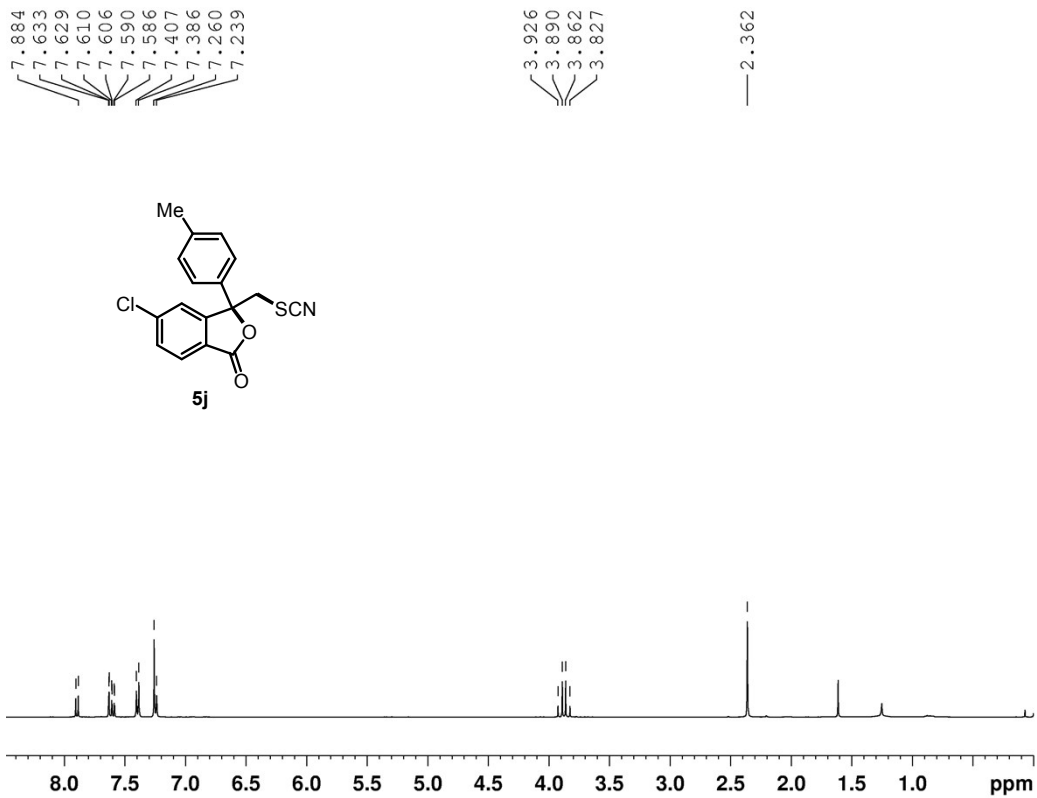
— 76.999

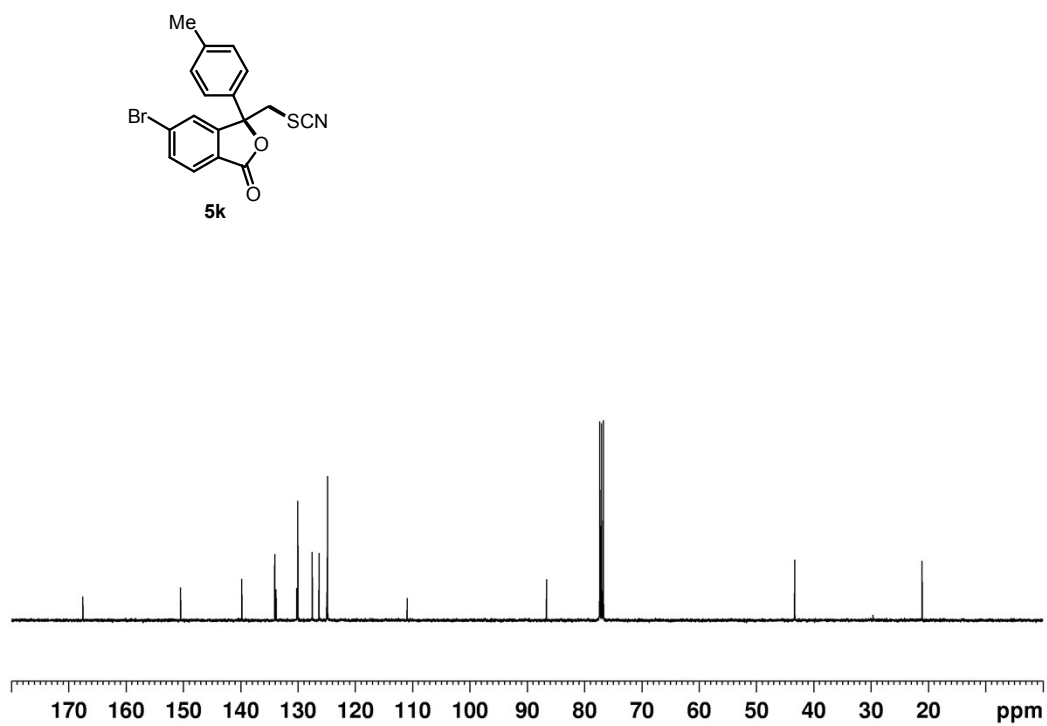
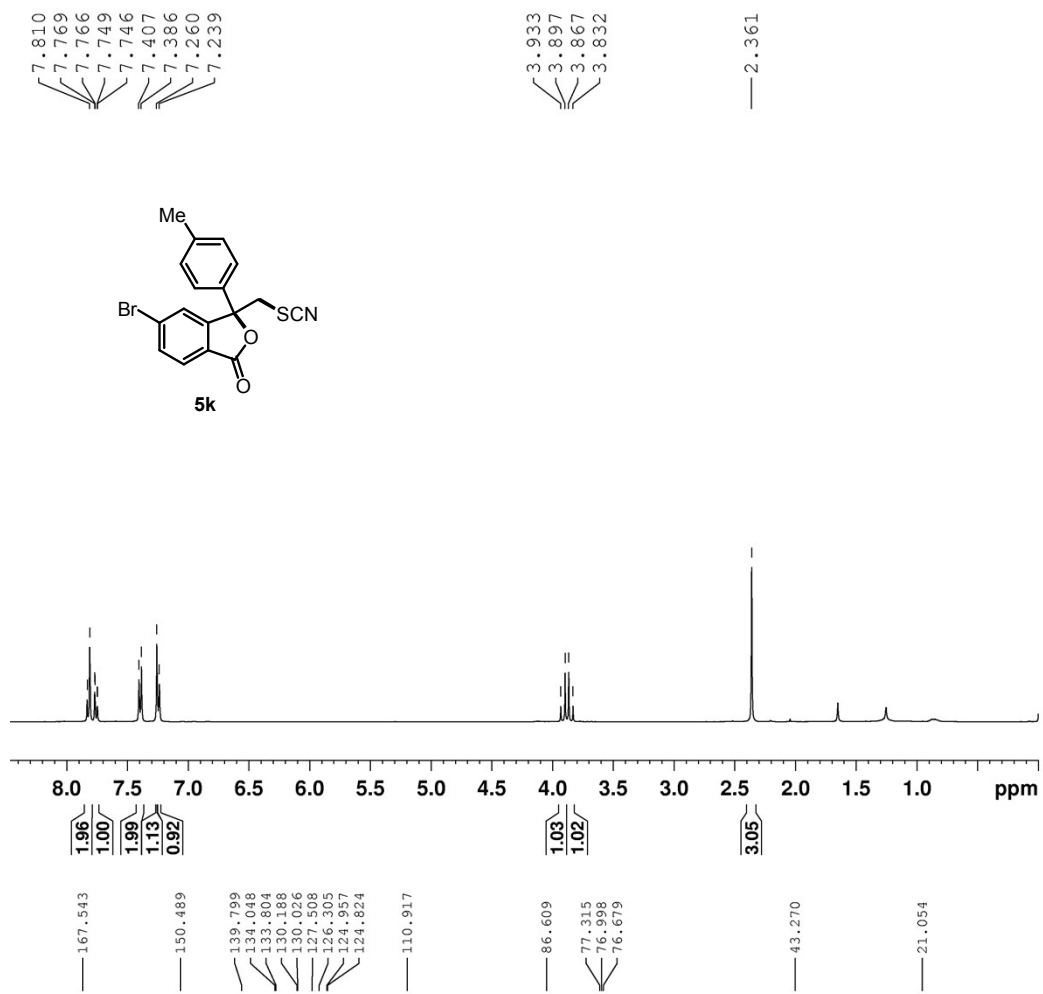
— 76.682

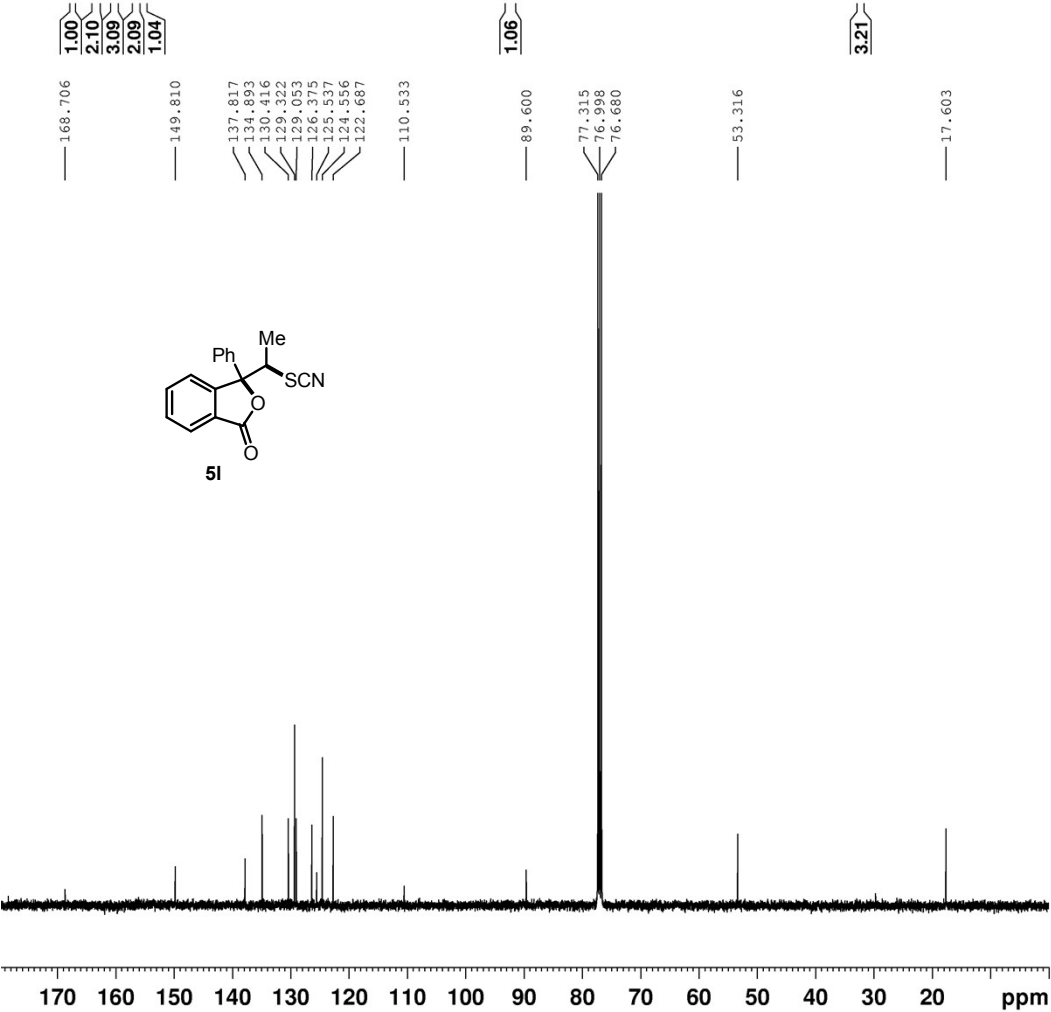
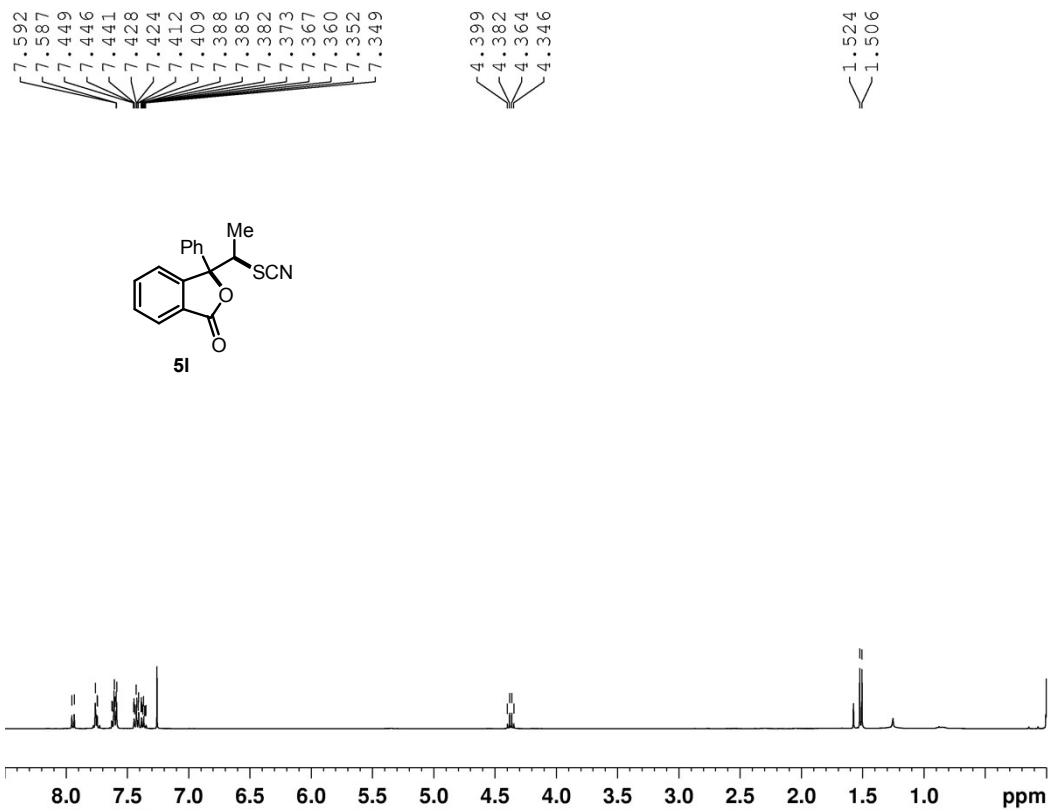
— 43.209

— 21.028

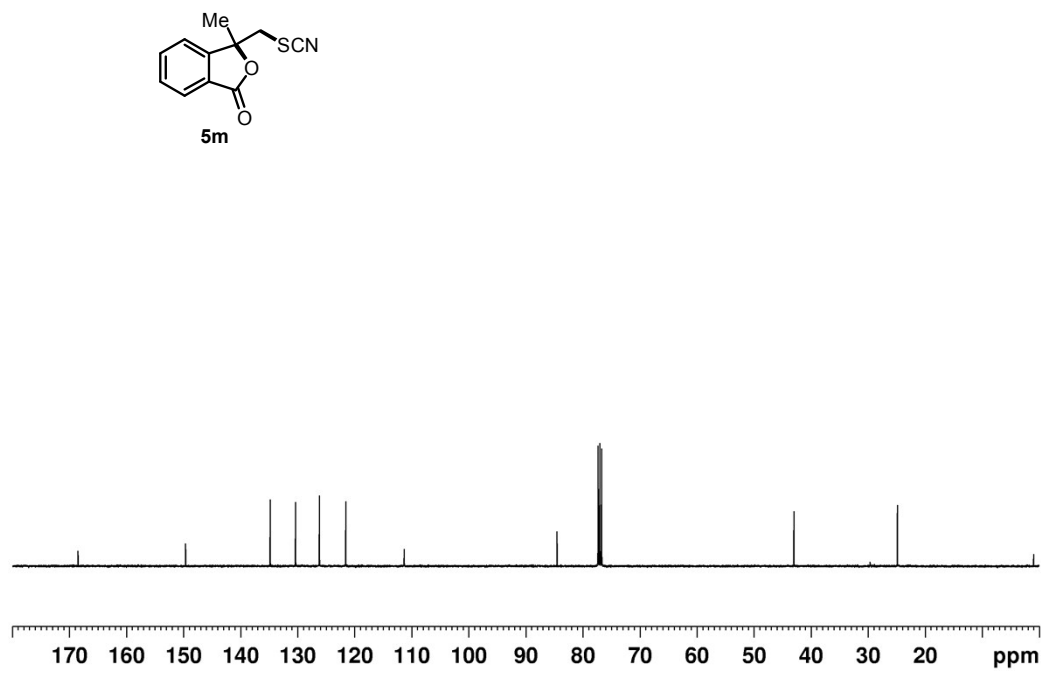
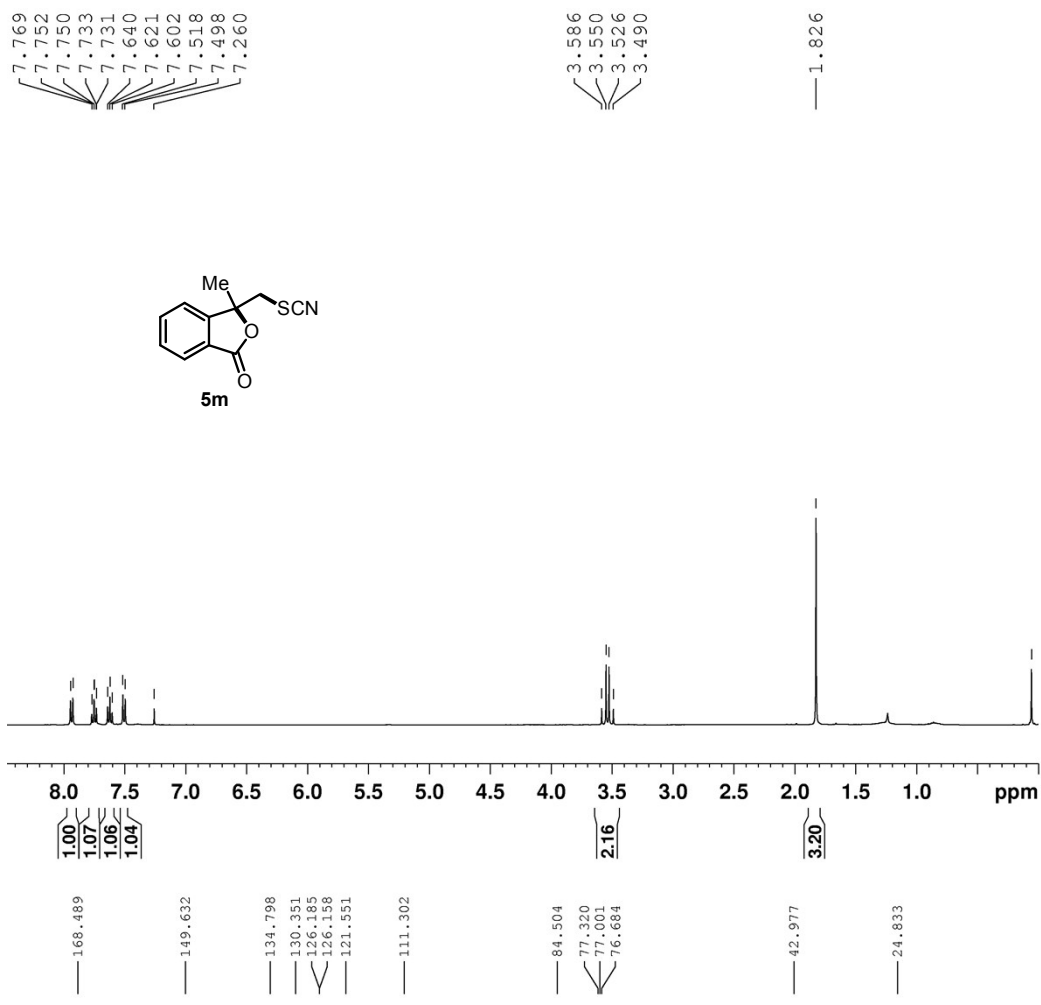




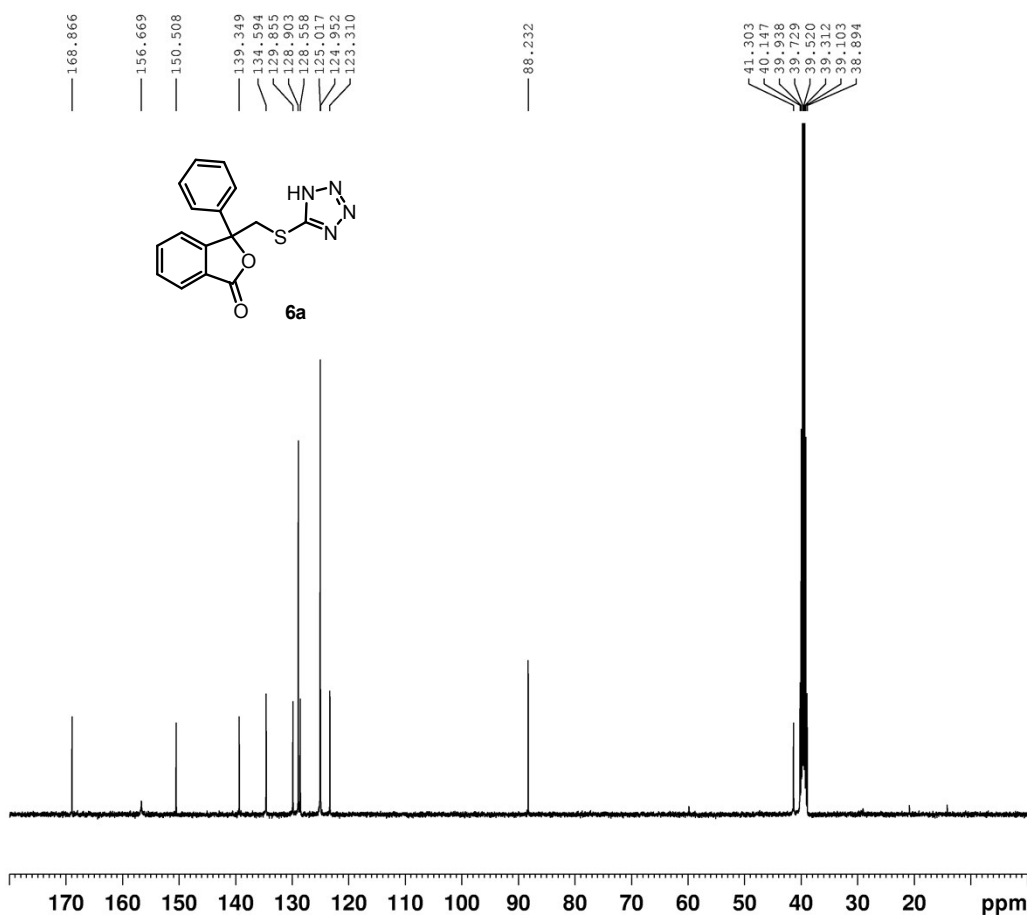
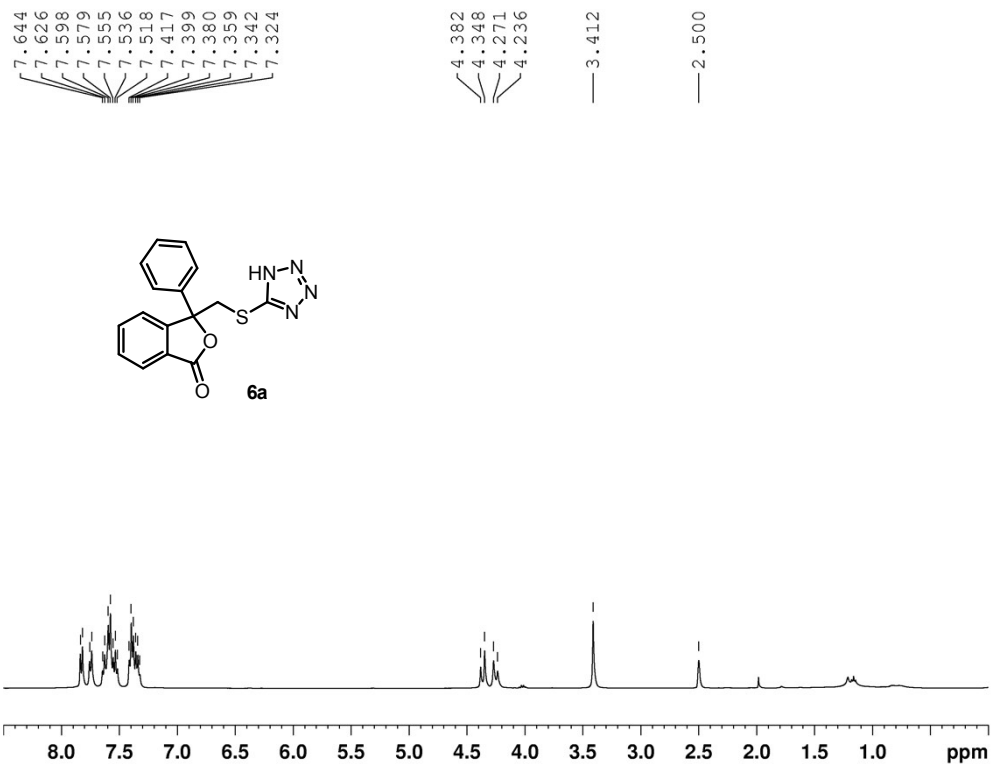






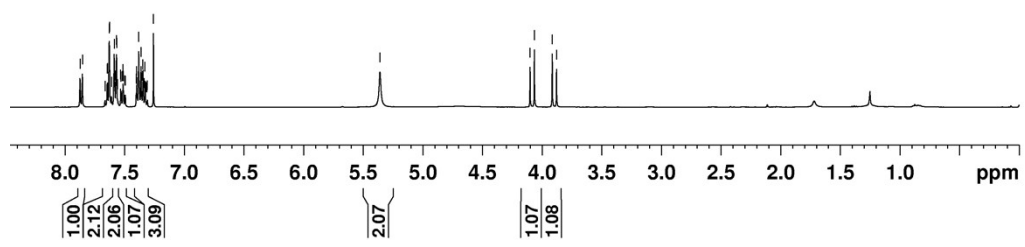
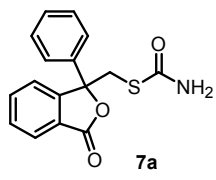


# <sup>1</sup>H NMR and <sup>13</sup>C NMR Spectra of Products 6a, 7a, 9 and 10



7.519  
7.516  
7.512  
7.500  
7.496  
7.404  
7.400  
7.396  
7.383  
7.364  
7.351  
7.348  
7.344  
7.336  
7.330  
7.322  
7.315  
7.312  
7.260  
5.361

4.102  
4.066  
3.916  
3.880



169.543  
167.068  
150.265  
139.042  
134.083  
129.548  
128.839  
128.695  
126.340  
125.421  
125.123  
123.147

88.768  
77.320  
77.003  
76.685

39.398

