

Supporting Information

for

**Aza-Diels–Alder reaction between *N*-aryl-1-oxo-1*H*-isoindolium ions and *tert*-enamides: Steric effects on reaction outcome**

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**Synthetic procedure and characterization data for all compounds and crystallographic data for 1a, 1h, 2b and 3a**

Contents

1. Experimental S2
2. General procedure for the synthesis of *N*-aryl-1*H*-pyrrole-2,5-diones and their spectral data S2
3. General procedure for the synthesis of *N*-aryl-3-hydroxyisoindolinones and their spectral data S5
4. General procedure for the synthesis of 5-(2-oxopyrrolidin-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-ones (**1a–h**), 5-(2-oxoazepan-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-ones (**2a–h**) and (*E*)-2-(2-substitued-phenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-ones (**3a–i**), and their spectral data S10
5. <sup>1</sup>H and <sup>13</sup>C NMR spectra of 5-(2-oxopyrrolidin-1-yl)-6,6a-dihydro-

|                                                                                                                                                              |     |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| isoindolo[2,1- <i>a</i> ]quinolin-11(5 <i>H</i> )-ones ( <b>1a–h</b> )                                                                                       | S23 |
| 6. <sup>1</sup> H and <sup>13</sup> C NMR spectra of 5-(2-oxazepan-1-yl)-6,6a-dihydro-isoindolo[2,1- <i>a</i> ]quinolin-11(5 <i>H</i> )-ones ( <b>2a–h</b> ) | S31 |
| 7. <sup>1</sup> H and <sup>13</sup> C NMR spectra of ( <i>E</i> )-2-(2-substitued-phenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-ones ( <b>3a–i</b> ) | S39 |
| 8. <sup>1</sup> H and <sup>13</sup> C NMR spectra of intermediate <i>N</i> -aryl-1 <i>H</i> -pyrrole-2,5-diones                                              | S48 |
| 9. <sup>1</sup> H and <sup>13</sup> C NMR spectra of intermediate <i>N</i> -aryl-3-hydroxy-isoindolinones                                                    | S65 |
| 10. X-ray crystal structure of compound <b>1b</b>                                                                                                            | S82 |
| 11. X-ray crystal structure of compound <b>1h</b>                                                                                                            | S86 |
| 12. X-ray crystal structure of compound <b>2b</b>                                                                                                            | S90 |
| 13. X-ray crystal structure of compound <b>3a</b>                                                                                                            | S94 |
| 14. References                                                                                                                                               | S98 |

## Experimental

### General information

All reagents were purchased from Aldrich Chemical Co. and were used without purification. Melting points were recorded on a MEL-TEMP II apparatus and are uncorrected. TLCs were performed on pre-coated Merck silica gel 60F<sub>254</sub> plates with the spots detected under UV light. Silica gel (100–200 mesh) was used for column chromatography. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Bruker AC-300 Avance spectrometer at 300 MHz and 75 MHz respectively in CDCl<sub>3</sub>, Acetone-*d*<sub>6</sub>, CD<sub>3</sub>OD or DMSO-*d*<sub>6</sub>. <sup>1</sup>H NMR spectra were reported relative to residual CHCl<sub>3</sub> (δ 7.26), acetone (δ 2.05), methanol (δ 3.31) or DMSO (δ 2.50). <sup>13</sup>C NMR spectra were reported relative to CHCl<sub>3</sub> (δ 77.16), acetone (δ 29.92), methanol (δ 49.15) or DMSO (δ 39.52). IR spectra were recorded on Nicolet Avatar 330FT-IT spectrophotometer. High-Resolution Mass Spectra (HRMS) were recorded in positive ion mode on an Ion Spec Fourier transform mass spectrometer.

### General procedure for the synthesis of *N*-aryl-1*H*-pyrrole-2,5-diones

Phthalic anhydride (10 mmol) was mixed with the corresponding anilines (12 mmol) in

dichloromethane (50 ml) for 30 minutes at room temperature to form the corresponding 2-(arylcarbamoyl)benzoic acid. Vacuum filtration gave excellent yields of the products. The solids were then dried, dissolved in acetic anhydride and were heated at 90 °C for 2–4 hours with freshly fused anhydrous sodium acetate as a catalyst (15 mol %). The solvent was evaporated under low pressure and the crude solids were dissolved in dichloromethane to assist in removal of insoluble sodium acetate by filtration. The organic solvent was evaporated under vacuum and the solid thus obtained was recrystallized from hot methanol to yield pure *N*-aryl-1*H*-pyrrole-2,5-diones.

2-Phenylisoindoline-1,3-dione: Yield: 88%. Mp: 201-203 °C (lit. mp 208-210 °C [1]). Its <sup>1</sup>H and <sup>13</sup>C NMR spectra were found to be identical to the literature report [1].

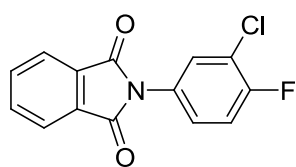
2-*p*-Tolylisoindoline-1,3-dione: Yield: 95%. Mp: 199-201 °C (lit. mp 207-209 °C [1]). Its <sup>1</sup>H and <sup>13</sup>C NMR spectra were found to be identical to the literature report [1].

2-(4-Methoxyphenyl)isoindoline-1,3-dione: Yield: 72%. Mp: 160-162 °C (lit. mp 143-145 °C [1]). Its <sup>1</sup>H and <sup>13</sup>C NMR spectra were found to be identical to the literature report [1].

2-(4-Chlorophenyl)isoindoline-1,3-dione: Yield: 78%. Mp: 194-195 °C (lit. mp 194-196 °C [1]). Its <sup>1</sup>H and <sup>13</sup>C NMR spectra were found to be identical to the literature report [1].

2-(3,5-Dimethylphenyl)isoindoline-1,3-dione: Yield: 96%. Mp: 132-133 °C (lit. mp 133 °C [2]). Its <sup>1</sup>H NMR spectra were found to be identical to the literature report [2].

2-(3-Chloro-4-fluorophenyl)isoindoline-1,3-dione: Yield: 73%. Mp: 185-186°C.  $^1\text{H}$  NMR



( $\text{CDCl}_3$ ):  $\delta$  7.22-7.32 (m, 1H), 7.33-7.40 (m, 1H), 7.56 (dd,  $J$ = 2.4, 6.5Hz, 1H), 7.81 (dd,  $J$ = 3.0, 5.4Hz, 2H), 7.96 (dd,  $J$ = 3.0, 5.4Hz, 2H).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  117.0 (d,  $J$ =22.5 Hz), 121.8 (d,  $J$ =18.7 Hz), 124.1,

126.4 (d,  $J$ =7.5 Hz), 128.65, 129.0, 131.9, 134.8, 157.7 (d,  $J$ =249.0 Hz), 166.9.

2-(Naphthalen-1-yl)isoindoline-1,3-dione: Yield: 77%. Mp: 183-185 °C (lit. mp 159-161 °C [3]).

Its  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were found to be identical to the literature report [3].

2-(Naphthalen-2-yl)isoindoline-1,3-dione: Yield: 75%. Mp: 213-215 °C (lit. mp 214-216 °C [3]).

Its  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were found to be identical to the literature report [3].

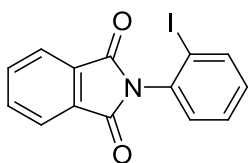
2-(2-Fluorophenyl)isoindoline-1,3-dione: Yield: 74%. Mp: 188-190 °C (lit. mp 194-195 °C [4]).

Its  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were found to be identical to the literature report [4].

2-(2-Chlorophenyl)isoindoline-1,3-dione: Yield: 70%. Mp: 141-142 °C (lit. mp 143-143.6 °C [4]).

Its  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were found to be identical to the literature report [4].

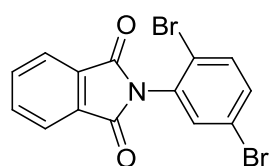
2-(2-Iodophenyl)isoindoline-1,3-dione: Yield: 83%. Mp: 188-190°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  7.20 (t,



$J$ = 7.5Hz, 1H), 7.32 (d,  $J$ = 7.5Hz, 1H), 7.51 (t,  $J$ = 7.5Hz, 1H), 7.79-7.85 (m, 2H), 7.96-8.02 (m, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  99.0, 124.0, 129.4, 130.4,

131.0, 132.2, 134.6, 135.4, 140.0, 166.5.

2-(2,5-Dibromophenyl)isoindoline-1,3-dione: Yield: 69%. Mp: 214-215°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$



7.51 (d,  $J$  = 8.1Hz, 2H), 7.62 (d,  $J$  = 8.4Hz, 1H), 7.85 (dd,  $J$  = 3.0, 5.4Hz, 2H), 8.00 (dd,  $J$  = 3.3, 4.8Hz, 2H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  121.7, 122.6, 124.3, 124.3, 132.2, 133.3, 134.2, 134.9, 134.9, 166.3.

2-(2-Nitrophenyl)isoindoline-1,3-dione: Yield: 81%. Mp: 195-197 °C (lit. mp 198-199 °C [2]). Its

$^1\text{H}$  spectrum was found to be identical to the literature report [2].

2-(2-Ethylphenyl)isoindoline-1,3-dione: Yield: 69%. Mp: 133-134 °C (lit. mp 132-133 °C [2]). Its

$^1\text{H}$  spectrum was found to be identical to the literature report [2].

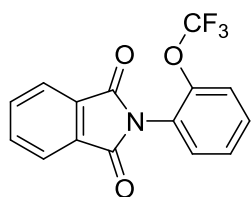
2-(2-*tert*-Butylphenyl)isoindoline-1,3-dione: Yield: 55%. Mp: 119-121 °C (lit. mp 123 °C [2]). Its

$^1\text{H}$  spectrum was found to be identical to the literature report [2].

2-(2-Methoxyphenyl)isoindoline-1,3-dione: Yield: 81%. Mp: 150-151 °C (lit. mp 158 °C [2]). Its

$^1\text{H}$  spectrum was found to be identical to the literature report [2].

2-(2-(Trifluoromethoxy)phenyl)isoindoline-1,3-dione: Yield: 71%. Mp: 90-93°C.  $^1\text{H}$  NMR



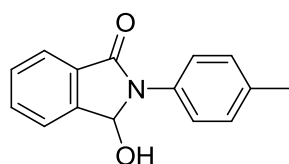
( $\text{CDCl}_3$ ):  $\delta$  7.38-7.58 (m, 4H), 7.79-7.85 (m, 2H), 7.93-8.02 (m, 2H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  119.0, 122.4, 124.2, 124.8, 127.5, 130.7, 130.9, 132.4, 134.7, 146.0, 166.6.

### General procedure for the synthesis of *N*-aryl-3-hydroxyisoindolinones

Appropriate *N*-aryl-1*H*-pyrrole-2,5-diones (700 mg) from the previous step were taken in MeOH (75 ml) and the mixture was stirred in an ice bath for 10 minutes followed by the addition of powdered NaBH<sub>4</sub> (1.0 equiv) in portions over 10 minutes. The reaction progress was monitored by TLC. The reduction reaction took approximately 1 hour to go to completion. Once the TLC showed only one single spot which was more polar than the starting material, the remaining NaBH<sub>4</sub> was quenched by adding diluted HCl solution (0.5 N, 10 ml). The solvent was evaporated under reduced pressure. The residue was extracted with ethyl acetate (100 ml) and water (50 ml × 3). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and vacuum evaporated to dryness, yielding pure reduced products.

3-Hydroxy-2-phenylisoindolin-1-one: Yield: 78%. Mp: 167-168°C (lit. mp 167-168 °C [5]). Its <sup>1</sup>H NMR spectrum was found to be identical to the literature report [5].

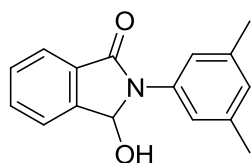
3-Hydroxy-2-*p*-tolylisoindolin-1-one: Yield: 99%. Mp: 166-168°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.35 (s, 3H), 5.70-5.77 (m, 1H), 6.45-6.62 (m, 1H), 7.24 (d, *J*= 7.5Hz, 2H), 7.68-7.76 (m, 5H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 20.3, 82.9, 122.7, 123.2, 123.7, 129.4, 129.9, 132.5, 132.7, 134.4, 136.0, 144.6, 165.9.



3-Hydroxy-2-(4-methoxyphenyl)isoindolin-1-one: Yield: 89%. Mp: 135-137 °C (lit. mp 147-149 °C [5]). Its <sup>1</sup>H NMR spectrum was found to be identical to the literature report [5].

2-(4-Chlorophenyl)-3-hydroxyisoindolin-1-one: Yield: 85%. Mp: 198-200 °C (lit. mp 198-200 °C [6]). Its  $^1\text{H}$  NMR spectrum was found to be identical to the literature report [6].

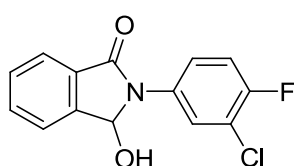
2-(3,5-Dimethylphenyl)-3-hydroxyisoindolin-1-one: Yield: 85%. Mp: 133-135°C.  $^1\text{H}$  NMR



( $\text{CDCl}_3$ ):  $\delta$  2.10 (s, 3H), 2.33 (s, 3H), 3.02 (br s, 1H), 6.34 (m, 1H), 6.88 (s, 1H), 7.30 (s, 2H), 7.50 (t,  $J = 7.2\text{Hz}$ , 1H), 7.57-7.69 (m, 2H), 7.76 (d,  $J = 7.5\text{Hz}$ , 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  21.6, 83.2, 122.2, 123.4, 124.2, 127.8,

130.5, 132.3, 132.9, 137.3, 138.1, 148.2, 166.4.

2-(3-Chloro-4-fluorophenyl)-3-hydroxyisoindolin-1-one: Yield: 87%. Mp: 163-165°C.  $^1\text{H}$  NMR

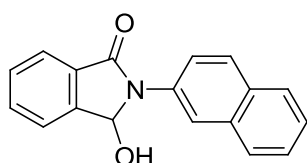


( $\text{DMSO}-d_6$ ):  $\delta$  3.62 (br s, 1H), 6.28 (m, 1H), 7.15 (t,  $J = 8.7\text{Hz}$ , 1H), 7.47 (t,  $J = 7.2\text{Hz}$ , 1H), 7.60-7.70 (m, 3H), 7.89 (d,  $J = 4.5\text{Hz}$ , 1H), 8.09 (s, 1H).  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ ):  $\delta$  83.1, 117.5 (d,  $J = 21.8\text{ Hz}$ ), 120.2 (d,

$J = 18.0\text{ Hz}$ ), 123.4 (d,  $J = 6.5\text{ Hz}$ ), 123.8, 124.4, 124.6, 130.5, 131.7, 133.8, 135.7, 145.1, 155.1 (d,  $J = 243.0\text{ Hz}$ ), 166.4.

3-Hydroxy-2-(naphthalen-1-yl)isoindolin-1-one: Yield: 96%. Mp: 178-180°C (lit. mp 179-181 °C [7]). Its  $^1\text{H}$  NMR spectrum was found to be identical to the literature report [7].

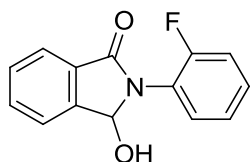
3-Hydroxy-2-(naphthalen-2-yl)isoindolin-1-one: Yield: 90%. Mp: 209-210°C.  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ):



$\delta$  6.61 (s, 1H), 7.45-7.56 (m, 2H), 7.60-7.69 (m, 1H), 7.72-7.78 (m, 2H), 7.86-7.99 (m, 6H), 8.20 (br s, 1H).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$  83.5,

121.5, 122.7, 123.3, 123.6, 125.8, 126.4, 127.6, 127.8, 128.6, 130.0, 131.9, 133.1, 134.2, 134.9, 138.0, 144.2, 167.8.

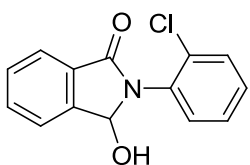
2-(2-Fluorophenyl)-3-hydroxyisoindolin-1-one: Yield: 98%. Mp: 173-175°C.  $^1\text{H}$  NMR



(DMSO- $d_6$ ):  $\delta$  4.71 (br s, 1H), 6.34 (d,  $J$ = 5.7Hz, 1H), 7.20-7.30 (m, 2H), 7.33-7.36 (m, 1H), 7.50-7.68 (m, 4H), 7.90 (d,  $J$ = 6.9Hz, 1H).  $^{13}\text{C}$  NMR

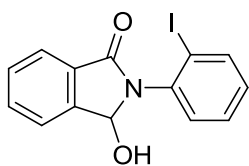
(DMSO- $d_6$ ):  $\delta$  63.3, 115.3 (d,  $J$ =19.2 Hz), 124.3 (d,  $J$ =15.8 Hz), 125.6 (d,  $J$ =7.5 Hz), 127.1, 127.9, 129.1, 130.0, 131.0, 135.7, 136.1, 140.0, 154.8 (d,  $J$ =249.0 Hz), 167.7.

2-(2-Chlorophenyl)-3-hydroxyisoindolin-1-one: Yield: 67%. Mp: 172-173°C.  $^1\text{H}$  NMR



(DMSO- $d_6$ ):  $\delta$  6.17 (d,  $J$ = 8.7Hz, 1H), 6.88 (d,  $J$ = 7.8Hz, 1H), 7.40-7.46 (m, 3H), 7.55-7.75 (m, 5H).  $^{13}\text{C}$  NMR (DMSO- $d_6$ ):  $\delta$  83.7, 123.7, 124.7, 128.6, 130.4, 130.6, 131.7, 132.5, 133.5, 135.0, 137.0, 139.2, 146.0, 166.3.

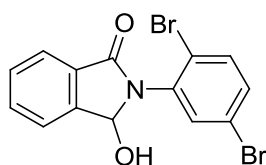
3-Hydroxy-2-(2-iodophenyl)isoindolin-1-one: Yield: 88%. Mp: 176-177°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$



2.96 (br s, 1H), 6.19 (d,  $J$ = 3.9Hz, 1H), 7.15 (t,  $J$ = 7.5Hz, 1H), 7.32 (d,  $J$ = 7.5Hz, 1H), 7.44 (t,  $J$ = 7.5Hz, 1H), 7.54-7.62 (m, 1H), 7.64-7.70 (m, 2H), 7.86 (d,  $J$ = 7.2Hz, 1H), 7.96 (d,  $J$ = 7.8Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  84.1,

99.0, 123.7, 124.5, 129.5, 130.4, 131.3, 131.8, 133.0, 137.2, 139.2, 140.1, 144.0, 166.2.

2-(2,5-Dibromophenyl)-3-hydroxyisoindolin-1-one: Yield: 77%. Mp: 161-163°C.  $^1\text{H}$  NMR

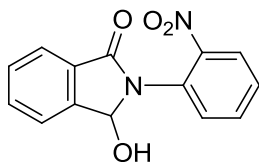


( $\text{CDCl}_3$ ):  $\delta$  6.24 (br s, 1H), 6.96 (d,  $J$ = 9.3Hz, 1H), 7.57-7.85 (m, 5H),



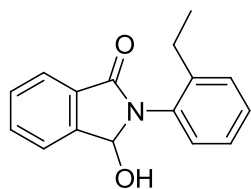
7.94-8.03 (m, 2H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  83.7, 121.4, 123.6, 124.7, 130.5, 131.4, 132.3, 133.5, 135.0, 135.2, 136.0, 138.2, 145.9, 166.7.

3-Hydroxy-2-(2-nitrophenyl)isoindolin-1-one: Yield: 68%. Mp: 177-179°C.  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$



3.32 (m, 1H), 6.32 (m, 1H), 7.60-7.88 (m, 7H), 8.12 (d,  $J$  = 8.1Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$  84.6, 123.5, 123.8, 125.4, 129.0, 130.0, 130.2, 130.8, 131.0, 133.5, 134.0, 145.3, 147.5, 168.1.

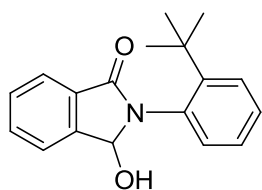
2-(2-Ethylphenyl)-3-hydroxyisoindolin-1-one: Yield: 68%. Mp: 147-148°C.  $^1\text{H}$  NMR



(Acetone- $\text{d}_6$ ):  $\delta$  1.19 (t,  $J$  = 7.2Hz, 3H), 2.63 (q,  $J$  = 7.2Hz, 2H), 5.81 (m, 1H), 6.29 (br s, 1H), 7.19-7.80 (m, 8H).  $^{13}\text{C}$  NMR (Acetone- $\text{d}_6$ ):  $\delta$  14.1, 24.2, 84.6, 123.2, 124.0, 126.4, 126.5, 128.3, 129.0, 129.6, 129.8, 132.4,

135.8, 143.8, 145.6, 166.2.

2-(2-*tert*-Butylphenyl)-3-hydroxyisoindolin-1-one: Yield: 68%. Mp: 126-128°C.  $^1\text{H}$  NMR



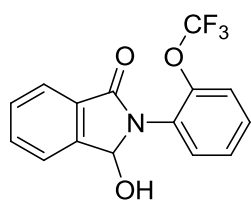
(Acetone- $\text{d}_6$ ):  $\delta$  1.41 (s, 9H), 4.77 (m, 1H), 5.15 (m, 1H), 7.23-7.30 (m, 2H), 7.35-7.39 (m, 1H), 7.41-7.57 (m, 3H), 7.78-7.84 (m, 1H), 9.49 (br s, 1H).  $^{13}\text{C}$  NMR (Acetone- $\text{d}_6$ ):  $\delta$  31.2, 35.1, 63.4, 126.7, 127.0, 127.3, 127.9,

128.4, 130.0, 130.9, 131.4, 136.2, 136.5, 140.8, 146.5, 168.1.

3-Hydroxy-2-(2-methoxyphenyl)isoindolin-1-one: Yield: 89%. Mp: 178-180°C (lit. mp 178-179

°C [5]). Its  $^1\text{H}$  NMR spectrum was found to be identical to the literature report [5].

3-Hydroxy-2-(2-(trifluoromethoxy)phenyl)isoindolin-1-one: Yield: 55%. Semi-solid.  $^1\text{H}$  NMR



( $\text{CDCl}_3$ ):  $\delta$  3.57 (br s, 1H), 6.22 (s, 1H), 7.25-7.55 (m, 5H), 7.60-7.62 (m, 2H), 7.69 (d,  $J$  = 7.2Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  83.8, 120.8 (q,  $J$ =265.5Hz), 121.4, 123.8, 124.3, 127.5, 128.8, 129.4, 130.4, 131.3, 133.1,

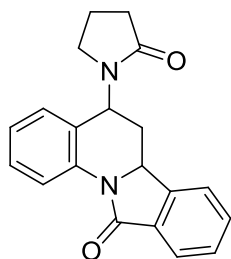
134.2, 144.3, 146.0, 166.8.

**General procedure for the synthesis of 5-(2-oxopyrrolidin-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-ones (1a–h); 5-(2-oxoazepan-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-ones (2a–h) and (*E*)-2-(2-substitued-phenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-ones (3a–i)**

Appropriate *N*-aryl-3-hydroxyisoindolinones (500 mg) from the previous step were dissolved in dichloromethane (10 ml) in a 50 ml round bottom flask which was then sealed with a rubber septum.  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (1.5 equiv) was added to the mixture slowly through the septum by a syringe. This resulted in the formation of a transparent solution. Appropriate *tert*-enamide (1.5 equiv) dissolved in dichloromethane (5 ml) was slowly added to the flask through a syringe over a period of 5 minutes. The reaction was then allowed to stir at room temperature until the precipitates formed. The reaction progress was monitored by TLC. Upon completion of the reaction, the residue was suction filtered and the solid obtained was extracted with ethyl acetate (60 ml) and washed with water (30 ml  $\times$  3). The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated in vacuum to dryness to obtain pure products. In the cases where precipitates did not form, the solvents were evaporated to dryness under reduced pressure. The residue was extracted by ethyl acetate (60 ml) and washed with water (30 ml  $\times$  3). The organic layer was dried over

anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated in vacuum to dryness. The purification of the crude product was achieved by column chromatography (silica gel mesh size 230–240; eluent 50–100% EtOAc/hexane).

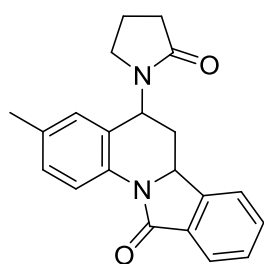
5-(2-Oxopyrrolidin-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-one (**1a**): Yield: 56%.



White solid. Mp: 225-227°C. <sup>1</sup>H NMR (CD<sub>3</sub>OD): δ 1.68-1.84(m, 1H), 1.98-2.14(m, 2H), 2.57-2.65(m, 2H), 2.68-2.78(m, 1H), 3.03-3.18(m, 1H), 3.22-3.32(m, 1H), 5.04(d, *J*= 12.0Hz, 1H), 5.73-5.75(m, 1H), 7.10-7.25(m, 2H), 7.32(d, *J*= 6.6Hz, 1H), 7.50-7.70(m, 3H), 7.83 (d, *J*= 7.2Hz, 1H), 8.45

(d, *J*= 8.1Hz, 1H). <sup>13</sup>C NMR (CD<sub>3</sub>OD): δ 18.9, 32.0, 32.2, 44.3, 50.0, 59.7, 121.5, 123.5, 124.7, 125.2, 125.7, 127.9, 129.3, 130.0, 133.0, 133.8, 137.8, 145.6, 167.8, 178.9. FT-IR *v*<sub>max</sub> (NaCl): 3051, 2953, 2921, 1689, 1490, 1456, 1380, 1282, 1213, 1094, 906, 759, 730 cm<sup>-1</sup>. HRMS (amu): calcd for C<sub>20</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 341.1260; found [M+Na]<sup>+</sup>: 341.1252.

3-Methyl-5-(2-oxopyrrolidin-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-one (**1b**):

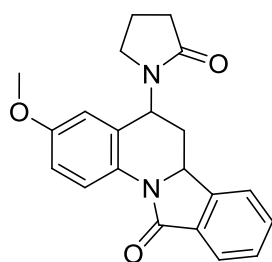


Yield: 62%. White solid. Mp: 202-204°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.68-1.78(m, 1H), 2.01-2.10(m, 2H), 2.35(s, 3H), 2.50-2.61(m, 2H), 2.62-2.71(m, 1H), 3.11(t, *J*= 6.9Hz, 2H), 4.92(d, *J*= 12.0Hz, 1H), 5.80 (dd, *J*= 6.3, 12.0Hz, 1H), 6.90(s, 1H), 7.20(d, *J*= 8.4Hz, 1H), 7.48-7.66(m,

3H), 7.96(d, *J*= 7.5Hz, 1H), 8.45(d, *J*= 8.4Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 18.3, 21.2, 31.4, 31.8, 42.5, 48.2, 58.4, 120.8, 122.0, 123.6, 124.5, 127.2, 129.0, 129.4, 132.3, 132.9, 134.2, 134.6, 143.9, 165.8, 175.9. FT-IR *v*<sub>max</sub> (NaCl): 3047, 2921, 1682, 1499, 1458, 1421, 1383, 1343, 1286, 1213,

1168, 1098, 730  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 355.1422; found  $[\text{M}+\text{Na}]^+$ : 355.1418.

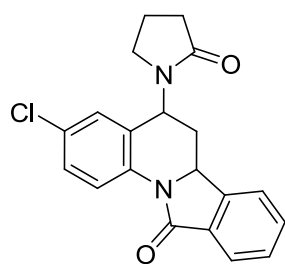
3-Methoxy-5-(2-oxopyrrolidin-1-yl)-6,6a-dihydroisoidolo[2,1-*a*]quinolin-11(5*H*)-one (**1c**):



Yield: 82%. White solid. Mp: 227-230°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.65-1.81(m, 1H), 1.95-2.10(m, 2H), 2.40-2.60(m, 2H), 2.61-2.70(m, 1H), 3.07-3.15(m, 2H), 3.79(s, 3H), 4.88(d,  $J$ = 12.0Hz, 1H), 5.78(dd,  $J$ = 5.7, 11.1Hz, 1H), 6.62(s, 1H), 6.92(d,  $J$ = 7.5Hz, 1H), 7.51(dd,  $J$ = 7.2, 15.3Hz,

2H), 7.60(d,  $J$ = 7.2Hz, 1H), 7.92(d,  $J$ = 6.9Hz, 1H), 8.48(d,  $J$ = 9.0Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  18.3, 31.2, 31.7, 42.5, 48.3, 55.7, 58.3, 112.4, 113.9, 121.9, 122.1, 124.4, 125.4, 129.0, 130.5, 132.2, 132.8, 143.7, 156.6, 165.6, 175.8. FT-IR  $\nu_{\text{max}}$  (NaCl): 3098, 2921, 1682, 1497, 1417, 1384, 1283, 1232, 1098, 1066, 906, 728  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_3$   $[\text{M}+\text{Na}]^+$ : 371.1366; found  $[\text{M}+\text{Na}]^+$ : 371.1361.

3-Chloro-5-(2-oxopyrrolidin-1-yl)-6,6a-dihydroisoidolo[2,1-*a*]quinolin-11(5*H*)-one (**1d**): Yield:

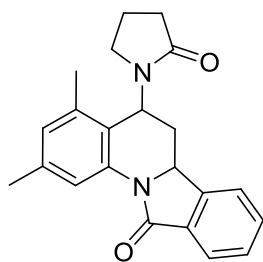


41%. White solid. Mp: 229-230°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.77-1.91(m, 1H), 2.02-2.13(m, 2H), 2.46-2.64(m, 2H), 2.71-2.78(m, 1H), 3.07-3.17(m, 1H), 3.29-3.37(m, 1H), 5.13(d,  $J$ = 12.3Hz, 1H), 5.75(dd,  $J$ = 6.3, 11.8Hz, 1H), 7.12(s, 1H), 7.37(d,  $J$ = 9.0Hz, 1H), 7.56-7.64(m, 1H), 7.70-7.74(m,

2H), 7.89(d,  $J$ = 7.5Hz, 1H), 8.52(d,  $J$ = 8.7Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  18.4, 31.2, 31.4, 42.5, 48.1, 58.3, 122.1, 122.2, 124.7, 125.8, 128.9, 129.2, 130.0, 132.4, 132.7, 135.6, 143.7, 166.0, 176.0. FT-IR  $\nu_{\text{max}}$  (NaCl): 3043, 2953, 2917, 1686, 1593, 1482, 1380, 1343, 1282, 1164, 1094,

1025, 902, 755, 730, 698  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{20}\text{H}_{17}\text{ClN}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 375.0871; found  $[\text{M}+\text{Na}]^+$ : 375.0878.

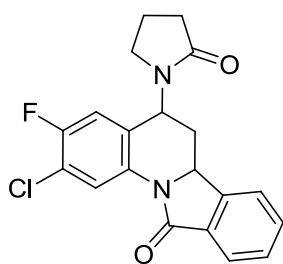
2,4-Dimethyl-5-(2-oxopyrrolidin-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-one (**1e**):



Yield: 59%. White solid. Mp: 232-235°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.55-1.69(m, 1H), 1.88-1.94(m, 2H), 2.14(s, 3H), 2.32-2.50(m, 5H), 2.67-2.77(m, 1H), 2.87-3.03(m, 2H), 4.75(d,  $J$ = 12.6Hz, 1H), 5.73(t,  $J$ = 9.0Hz, 1H), 6.82(s, 1H), 7.44-7.7.64(m, 3H), 7.95(d,  $J$ = 7.5Hz, 1H), 8.19(s,

1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  17.9, 19.5, 21.1, 30.8, 33.0, 42.0, 46.2, 57.8, 119.2, 119.6, 121.9, 124.3, 128.0, 128.7, 132.1, 132.8, 137.7(2C), 138.3, 143.9, 165.2, 174.2. FT-IR  $\nu_{\text{max}}$  (NaCl): 3043, 2953, 2921, 1698, 1605, 1572, 1420, 1379, 1282, 1213, 1090, 1033, 853, 759, 735, 702  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 369.1573; found  $[\text{M}+\text{Na}]^+$ : 369.1563.

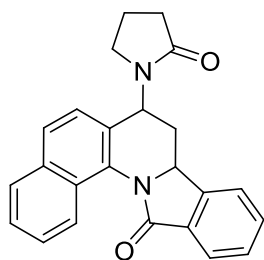
2-Chloro-3-fluoro-5-(2-oxopyrrolidin-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-one (**1f**):



Yield: 33%. White solid. Mp: >260°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.63-1.82(m, 1H), 2.00-2.19(m, 2H), 2.40-2.62(m, 2H), 2.63-2.72(m, 1H), 3.00-3.20(m, 2H), 4.92(d,  $J$ = 12.3Hz, 1H), 5.77(t,  $J$ = 5.4Hz, 1H), 6.87(d,  $J$ = 9.0Hz, 1H), 7.45-7.61(m, 2H), 7.64(d,  $J$ = 7.2Hz, 1H), 7.94(d,  $J$ = 6.9Hz, 1H),

8.79(d,  $J$ = 6.6Hz, 1H).  $^{13}\text{C}$  ( $\text{CDCl}_3$ ) NMR:  $\delta$  18.5, 31.2, 31.4, 42.6, 48.2, 58.4, 114.4, 114.7, 121.2, 121.5, 122.2, 122.9, 124.9, 129.5, 132.3, 132.9, 133.7, 143.7, 166.0, 176.0. FT-IR  $\nu_{\text{max}}$  (NaCl): 3041, 2962, 2892, 1680, 1484, 1409, 1384, 1288, 1215, 1080, 1027, 890, 726, 681  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{20}\text{H}_{16}\text{ClFN}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 393.0777; found  $[\text{M}+\text{Na}]^+$ : 393.0770.

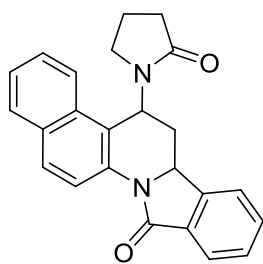
7-(2-Oxopyrrolidin-1-yl)-8,8a-dihydrobenzo[*h*]isoindolo[2,1-*a*]quinolin-13(7*H*)-one (**1g**): Yield:



47%. Pale purple needle-like crystal. Mp: 197-199°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.64-1.79(m, 1H), 1.95-2.10(m, 2H), 2.40-2.65(m, 2H), 2.76-2.87(m, 1H), 3.08-3.17(t, *J*= 6.9Hz, 2H), 5.09(d, *J*= 10.5Hz, 1H), 5.93(dd, *J*= 3.3Hz, 10.6Hz, 1H), 7.13-7.28(m, 2H), 7.42-7.70(m, 5H), 7.75(d, *J*= 8.7Hz, 1H),

7.81-7.86(m, 1H), 8.02(d, *J*= 6.9Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 18.4, 31.4, 35.1, 42.7, 48.6, 59.8, 122.2, 124.0, 124.1, 125.2, 125.8, 126.7, 126.8, 127.3, 127.6, 128.0, 129.1, 132.2, 132.5, 133.5, 134.4, 146.5, 166.0, 176.3. FT-IR *v*<sub>max</sub> (NaCl): 3051, 2925, 1681, 1613, 1470, 1397, 1282, 1209, 1123, 1025, 820, 755, 730cm<sup>-1</sup>. HRMS (amu): calcd for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 391.1417; found [M+Na]<sup>+</sup>: 391.1398.

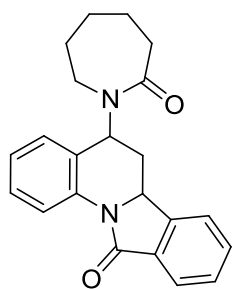
7-(2-Oxopyrrolidin-1-yl)-8,8a-dihydrobenzo[*f*]isoindolo[2,1-*a*]quinolin-13(7*H*)-one (**1h**): Yield:



50%. White solid. Mp: 242-244°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.69-1.83(m, 3H), 2.31-2.45(m, 3H), 2.88-2.98(m, 1H), 3.09-3.19(m, 1H), 4.86(dd, *J*=2.7, 13.0Hz, 1H), 6.25(t, *J*= 9.0Hz, 1H), 7.43-7.60(m, 4H), 7.62-7.69(m, 1H), 7.76(d, *J*= 8.4Hz, 1H), 7.83-7.93(m, 2H), 7.99(d, *J*= 7.5Hz, 1H), 8.72(d,

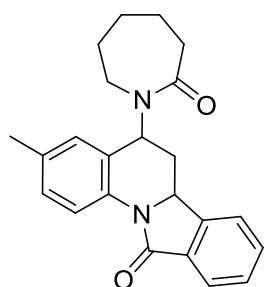
*J*= 9.0Hz, H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 18.2, 31.2, 33.4, 42.3, 46.0, 58.0, 117.6, 120.0, 122.2, 123.2, 124.8, 125.3, 127.5, 129.0, 129.9, 131.1, 131.8, 132.6, 132.9, 136.8, 144.1, 165.8, 174.9. FT-IR *v*<sub>max</sub> (NaCl): 3047, 2974, 2921, 2876, 1677, 1617, 1515, 1470, 1404, 1356, 1298, 1210, 1172, 824, 747, 686 cm<sup>-1</sup>. HRMS (amu): calcd for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 391.1417; found [M+Na]<sup>+</sup>: 391.1409.

5-(2-Oxazepan-1-yl)-6,6a-dihydroisoidolo[2,1-*a*]quinolin-11(5*H*)-one (**2a**): Yield: 47%.



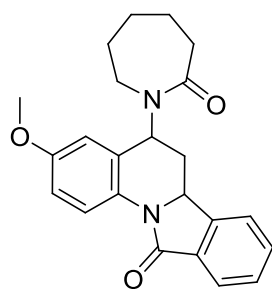
White solid. Mp: 228-230°C.  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$  1.30-1.40(m, 1H), 1.48-1.90(m, 6H), 2.50-2.67(m, 1H), 2.68-2.85(m, 2H), 2.90-3.34(m, 2H), 5.03(d,  $J$ = 12.0Hz, 1H), 6.15-6.23(m, 1H), 7.15(d,  $J$ = 3.9Hz, 2H), 7.28-7.37(m, 1H), 7.52-7.60(m, 1H), 7.68(d,  $J$ = 3.9Hz, 2H), 7.85(d,  $J$ = 7.5Hz, 1H), 8.43(d,  $J$ = 8.7Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$  24.5, 30.3, 30.7, 33.2, 38.1, 46.3, 53.0, 60.0, 121.7, 123.4, 124.8, 125.6, 126.5, 128.5, 129.1, 130.0, 133.2, 133.8, 138.4, 146.0, 167.8, 179.4. FT-IR  $\nu_{\text{max}}$  (NaCl): 3047, 2929, 2851, 1695, 1683, 1597, 1489, 1454, 1380, 1198, 1070, 759  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 369.1573; found  $[\text{M}+\text{Na}]^+$ : 369.1560.

3-Methyl-5-(2-oxazepan-1-yl)-6,6a-dihydroisoidolo[2,1-*a*]quinolin-11(5*H*)-one (**2b**): Yield:



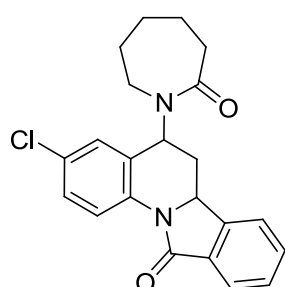
80%. White solid. Mp: 218-221°C.  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$  1.16-1.30(m, 1H), 1.40-1.85(m, 6H), 2.28(s, 3H), 2.45-2.55(m, 2H), 2.61-2.99(m, 3H), 3.08-3.20(m, 1H), 5.13(d,  $J$ = 11.7Hz, 1H), 6.09(s, 1H), 6.92(s, 1H), 7.14(d,  $J$ = 8.1Hz, 1H), 7.57(t,  $J$ = 7.2Hz, 1H), 7.69(t,  $J$ = 7.2Hz, 1H), 7.79(t,  $J$ = 6.6Hz, 2H), 8.33(d,  $J$ = 8.4Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$  21.0, 24.5, 30.3, 30.7, 33.3, 38.1, 46.3, 53.0, 60.0, 121.6, 123.5, 124.8, 126.3, 128.7, 129.8, 130.0, 133.3, 133.7, 135.6, 135.9, 145.9, 167.7, 179.4. FT-IR  $\nu_{\text{max}}$  (NaCl): 3051, 2925, 2855, 1694, 1639, 1499, 1383, 1294, 1192, 1029, 972, 820, 726  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 361.1911; found  $[\text{M}+\text{H}]^+$ : 361.1894.

3-Methoxy-5-(2-oxoazepan-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-one (**2c**): Yield:



48%. White solid. Mp: 216-217°C.  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$  1.25-1.36(m, 1H), 1.56-1.90(m, 6H), 2.60-2.80(m, 3H), 2.90-3.31(m, 1H), 3.10-3.21(m, 1H), 3.82(s, 3H), 4.88(d,  $J$ = 12.0Hz, 1H), 6.29(dd,  $J$ = 6.0, 11.7Hz, 1H), 6.70(s, 1H), 6.94(d,  $J$ = 9.0Hz, 1H), 7.54(dd,  $J$ = 7.5, 14.4Hz, 3H), 7.62(d,  $J$ = 14.4Hz, 1H), 7.96(d,  $J$ = 7.5Hz, 1H), 8.48(d,  $J$ = 9.0Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ):  $\delta$  23.7, 29.7, 30.1, 32.6, 37.7, 45.2, 51.6, 55.7, 58.5, 112.9, 113.8, 122.0, 122.1, 124.4, 126.6, 129.0, 131.0, 132.2, 132.9, 144.0, 156.6, 165.6, 176.9. FT-IR  $\nu_{\text{max}}$  (NaCl): 3047, 2929, 2851, 1692, 1639, 1497, 1384, 1280, 1232, 1188, 1070, 1030, 976, 735  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_3$   $[\text{M}+\text{Na}]^+$ : 399.1679; found  $[\text{M}+\text{Na}]^+$ : 399.1689.

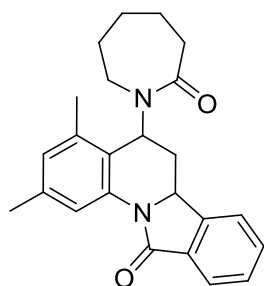
3-Chloro-5-(2-oxoazepan-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-one (**2d**): Yield:



34%. White solid. Mp: 248-250°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.22-1.38(m, 1H), 1.52-1.78(m, 4H), 1.79-1.98(m, 2H), 2.65-2.81(m, 3H), 2.88-3.00(m, 1H), 3.12-3.25(m, 1H), 4.91(d,  $J$ = 12.3Hz, 1H), 6.25-6.36(m, 1H), 7.12(s, 1H), 7.28-7.38(m, 1H), 7.55(dd,  $J$ = 7.2, 13.5Hz, 2H), 7.65(d,  $J$ = 7.2Hz, 1H), 7.96(d,  $J$ = 7.2Hz, 1H), 8.52(d,  $J$ = 8.7Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  23.7, 29.7, 30.0, 32.2, 37.6, 45.2, 51.2, 58.3, 122.1(2C), 124.6, 127.0, 127.2, 128.6, 129.2, 129.8, 132.4, 132.6, 136.0, 143.9, 166.0, 176.9. FT-IR  $\nu_{\text{max}}$  (NaCl): 3047, 2929, 2851, 1692, 1639, 1497, 1384, 1280, 1232, 1190, 1070, 1029, 976, 820, 735  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{22}\text{H}_{21}\text{ClN}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 403.1184; found  $[\text{M}+\text{Na}]^+$ : 403.1182.



2,4-Dimethyl-5-(2-oxoazepan-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-one (2e):



Yield: 33%. White solid. After three chromatographic purification attempts,

the product still contained small amount of an impurity (apparent in its

NMR spectra). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.23-1.98 (m, 7H), 2.20 (s, 3H), 2.28

(s, 3H), 2.33-2.38 (m, 3H), 2.56 (bs, 1H), 2.90-2.97 (m, 1H), 4.71(1H, d,

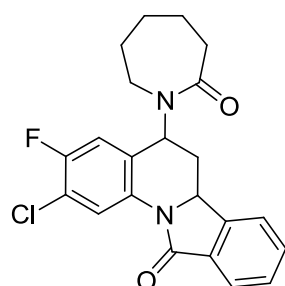
*J*=12.6 Hz), 6.19-6.24 (m, 1H), 7.18-7.28 (m, 2H), 7.47-7.70 (m, 4H), 7.95-7.98 (m, 1H). <sup>13</sup>C

NMR (CDCl<sub>3</sub>): δ 19.5, 21.6, 23.5, 29.2, 30.2, 34.2, 37.7, 44.3, 49.9, 58.6, 119.4, 121.4, 122.2,

124.7, 127.4, 129.0, 130.3, 132.6, 132.9, 138.1, 138.6, 144.4, 165.1, 175.3. HRMS (amu): calcd

for C<sub>24</sub>H<sub>26</sub>N<sub>2</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 397.1892; found [M+Na]<sup>+</sup>: 397.1865.

2-Chloro-3-fluoro-5-(2-oxoazepan-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinolin-11(5*H*)-one (2f):



Yield: 42%. White solid. Mp: >260°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.21-1.34(m,

1H), 1.56-1.75(m, 4H), 1.77-1.95(m, 2H), 2.69(s, 3H), 2.84-2.98(m, 1H),

3.05-3.17(m, 1H), 4.88(d, *J*= 12.3Hz, 1H), 6.22-6.30(m, 1H), 6.91(d, *J*=

9.6Hz, 1H), 7.54(dd, *J*= 7.2, 12.0Hz, 2H), 7.65(t, *J*= 7.5Hz, 1H), 7.93(d,

*J*= 7.2Hz, 1H), 8.65(d, *J*= 6.9Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 23.6, 29.7, 30.0, 32.0, 37.5, 45.2,

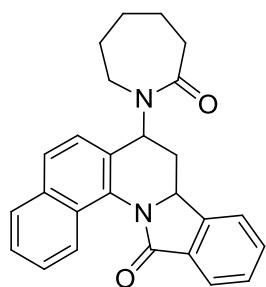
51.1, 58.4, 114.6, 114.9, 120.8, 121.0, 122.1, 122.7, 124.7, 125.8, 129.3, 132.1, 132.8, 133.9,

143.7, 153.3, 156.6, 165.8, 177.0. FT-IR ν<sub>max</sub> (NaCl): 3047, 2929, 2851, 1700, 1639, 1489, 1409,

1380, 1188, 1078, 914, 730 cm<sup>-1</sup>. HRMS (amu): calcd for C<sub>22</sub>H<sub>20</sub>ClFN<sub>2</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 421.1090;

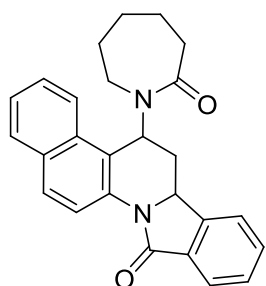
found [M+Na]<sup>+</sup>: 421.1471.

7-(2-Oxoazepan-1-yl)-8,8a-dihydrobenzo[*h*]isoindolo[2,1-*a*]quinolin-13(7*H*)-one (**2g**): Yield:



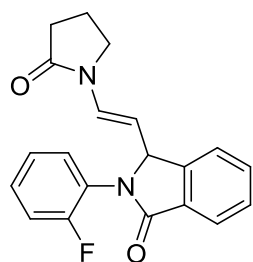
34%. White solid. Mp: 260-262°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.21-1.39(m, 2H), 1.50-1.98(m, 5H), 2.59-2.80(m, 2H), 2.80-3.00(m, 1H), 2.98-3.22(m, 2H), 5.08(d,  $J=11.7\text{Hz}$ , 1H), 6.37-6.52(m, 1H), 7.29(d,  $J=7.8\text{Hz}$ , 2H), 7.50-7.65(m, 3H), 7.65-7.69(m, 1H), 7.75(d,  $J=8.4\text{Hz}$ , 1H), 7.83-7.88(m, 1H), 8.05(d,  $J=6.3\text{Hz}$ , 2H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  14.4, 23.8, 29.8, 30.1, 36.0, 45.2, 52.0, 60.2, 122.1, 124.7, 125.1, 125.2, 125.8, 126.6, 126.7, 127.1, 127.6, 128.0, 129.0, 132.2, 132.4, 133.9, 134.3, 146.6, 165.9, 176.9. FT-IR  $\nu_{\text{max}}$  (NaCl): 3047, 2929, 2851, 1701, 1637, 1470, 1397, 1196, 1127, 1033, 976, 755, 730  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 419.1730; found  $[\text{M}+\text{Na}]^+$ : 419.1725.

7-(2-Oxoazepan-1-yl)-8,8a-dihydrobenzo[*f*]isoindolo[2,1-*a*]quinolin-13(7*H*)-one (**2h**): Yield:



32%. White solid. Mp: 238-240°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  0.60-0.80(m, 1H), 0.93-1.12(m, 1H), 1.44(s, 2H), 1.50-1.76(m, 3H), 2.50-2.78(m, 3H), 2.78-3.91(m, 1H), 3.14(t,  $J=9.3\text{Hz}$ , 1H), 4.79(d,  $J=12.6\text{Hz}$ , 1H), 6.72(t,  $J=9.0\text{Hz}$ , 1H), 7.40-7.59(m, 4H), 7.60-7.65(m, 1H), 7.78-7.85(m, 3H), 7.98(d,  $J=7.2\text{Hz}$ , 1H), 8.68(d,  $J=9.0\text{Hz}$ , 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  24.0, 28.7, 30.6, 34.8, 38.4, 45.4, 49.8, 59.8, 120.7(2C), 123.7, 125.1, 125.3, 126.4, 128.0, 129.8, 130.0, 130.5, 132.7, 133.1, 133.4, 134.0, 138.3, 146.1, 167.7, 178.3. FT-IR  $\nu_{\text{max}}$  (NaCl): 3056, 2925, 2855, 1696, 1631, 1511, 1470, 1403, 1348, 1298, 1263, 1200, 1172, 1029, 816, 751, 726  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 419.1730; found  $[\text{M}+\text{Na}]^+$ : 419.1719.

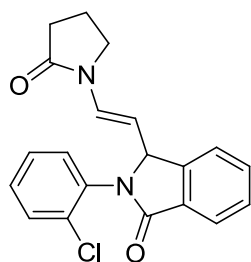
(*E*)-2-(2-Fluorophenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3a**): Yield: 39%.



Colorless solid, mp 260-262°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.98-2.10(m, 2H), 2.41-2.48(m, 2H), 3.24-3.44(m, 2H), 4.62(dd, *J*= 9.6, 14.1Hz, 1H), 5.55(d, *J*= 9.6Hz, 1H), 7.12-7.33(m, 4H), 7.40-7.47(m, 1H), 7.57(dt, *J*= 7.2, 26.4Hz, 2H), 7.94(d, *J*= 7.2Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 17.5, 31.1, 45.2, 64.2,

107.5, 116.6, 116.9, 123.4, 124.4, 124.6, 125.0, 125.2, 128.9 (2C), 129.9, 131.7, 132.4, 145.8, 156.6, 159.9, 167.3, 173.3. FT-IR ν<sub>max</sub> (NaCl): 3068, 2937, 1701, 1655, 1503, 1407, 1375, 1269, 758 cm<sup>-1</sup>. HRMS (amu): calcd for C<sub>20</sub>H<sub>17</sub>FN<sub>2</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 359.1166; found [M+Na]<sup>+</sup>: 359.1149.

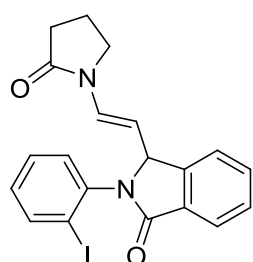
(*E*)-2-(2-Chlorophenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3b**): Yield: 51%.



Colorless solid, mp 97-101°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.04-2.12(m, 2H), 2.42-2.50(m, 2H), 3.36-3.47(m, 2H), 4.61-4.80(m, 1H), 5.50(bs, 1H), 7.17(d, *J*=14.3Hz, 1H), 7.27-7.35(m, 2H), 7.43(d, *J*=7.4Hz, 1H), 7.50-7.60 (m, 2H), 7.63(t, *J*=7.4Hz, 1H), 7.96(d, *J*=7.4Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 20.7,

34.3, 48.4, 67.7, 110.5, 126.6, 127.7, 130.9, 132.0, 132.1, 132.7, 133.9, 134.4, 134.8, 135.6, 137.0, 138.1, 149.0, 170.6, 176.6. FT-IR ν<sub>max</sub> (NaCl): 3068, 2962, 2242, 1704, 1655, 1482, 1407, 1375, 1265, 758 cm<sup>-1</sup>. HRMS (amu): calcd for C<sub>20</sub>H<sub>17</sub>ClN<sub>2</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 375.0876; found [M+Na]<sup>+</sup>: 375.0856.

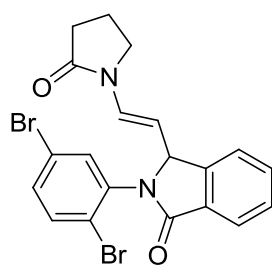
(*E*)-2-(2-Iodophenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3c**). Yield: 57%.



Colorless solid, mp: 118-120°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.72-1.75 (m, 1H), 2.01-2.13 (m, 2H), 2.40-2.51 (m, 2H), 3.34-3.47 (m, 2H), 4.85 (m, 1H), 5.38

(m, 1H), 7.06-7.25 (m, 2H), 7.20 (d,  $J$  = 7.5Hz, 1H), 7.33-7.46 (m, 2H), 7.48-7.58 (m, 1H), 7.62 (t,  $J$  = 7.5Hz, 1H), 7.93 (d,  $J$  = 7.5Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  17.4, 31.1, 45.2, 63.5, 66.6, 99.3, 102.1, 107.3, 123.5, 124.5, 128.4, 129.0, 130.2, 131.8, 132.1, 132.4, 140.1, 145.5, 167.5, 173.5. FT-IR  $\nu_{\text{max}}$  (NaCl): 3047, 2974, 1700, 1655, 1470, 1407, 1372, 1270, 1143, 759, 690  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{20}\text{H}_{17}\text{IN}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 467.0227; found  $[\text{M}+\text{Na}]^+$ : 467.0219.

(*E*)-2-(2,5-Dibromophenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3d**). Yield: 45%.

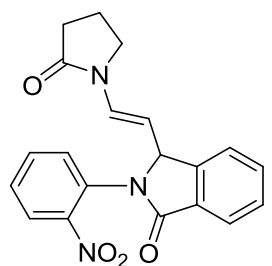


Colorless solid, mp: 248-250°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  2.02-2.18 (m, 3H), 2.49 (t,  $J$  = 8.1Hz, 2H), 4.63-4.85 (m, 1H), 5.35-5.57 (m, 1H), 7.18 (d,  $J$  = 14.1Hz, 1H). 7.33-7.45 (m, 2H), 7.50-7.57 (m, 2H), 7.63 (t,  $J$  = 7.5Hz, 1H), 7.94 (d,  $J$  = 7.5Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  17.5, 31.1, 45.3, 60.5,

106.8, 121.4, 123.5, 124.6, 129.0 (2C), 131.2, 132.7, 133.0, 134.8, 137.8, 145.6, 167.0, 173.6.

FT-IR  $\nu_{\text{max}}$  (NaCl): 3043, 2925, 1702, 1655, 1467, 1404, 1269, 1030, 751, 686  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{20}\text{H}_{16}\text{BrN}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 496.9471; found  $[\text{M}+\text{Na}]^+$ : 496.9452.

(*E*)-2-(2-Nitrophenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3e**): Yield: 66%. Pale

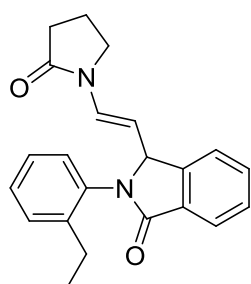


yellow solid, mp: 112-115°C.  $^1\text{H}$  NMR ( $\text{DMSO-d}_6$ ):  $\delta$  1.61 (m, 1H), 2.00-2.13 (m, 2H), 2.47 (t,  $J$  = 9.0 Hz, 2H), 3.30-3.49 (m, 2H), 4.83 (dd,  $J$  = 9.6, 14.2Hz, 1H), 5.55 (d,  $J$  = 9.6Hz, 1H), 7.30-7.37 (m, 1H), 7.41-7.49 (m, 2H), 7.53 (t,  $J$  = 7.5Hz, 1H), 7.60-7.70 (m, 2H), 7.90 (d,  $J$  = 7.5Hz, 1H),

8.10 (dd,  $J$  = 1.2, 8.1Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{DMSO-d}_6$ ):  $\delta$  16.6, 30.3, 44.4, 63.0, 105.8, 123.2, 123.5, 124.9 (2C), 127.4, 128.4, 128.7 (2C), 128.8, 129.8, 133.7, 145.8, 165.9, 172.9. FT-IR

$\nu_{\text{max}}$  (NaCl): 3047, 2921, 1702, 1655, 1601, 1529, 1405, 1373, 1262, 1139, 739  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_4$   $[\text{M}+\text{Na}]^+$ : 386.1106; found  $[\text{M}+\text{Na}]^+$ : 386.1101.

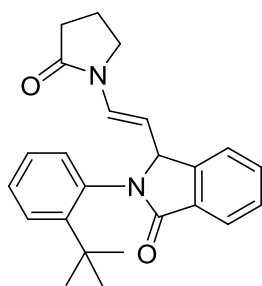
(*E*)-2-(2-Ethylphenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3f**): Yield: 63%. Colourless solid, mp 155-157°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.22(t,  $J=7.6\text{Hz}$ , 3H), 2.05-2.10(m, 2H), 2.43-2.56(m, 4H), 3.28-3.42(m, 2H), 4.63-4.72(m, 1H), 4.67-5.44(AB quartet, 1H), 7.08-7.38(m,



4H), 7.43(d,  $J=7.3\text{Hz}$ , 1H), 7.54(dt,  $J=7.3, 1.2\text{Hz}$ , 1H), 7.60(dt,  $J=7.4, 1.2\text{Hz}$ , 1H), 7.94(d,  $J=7.3\text{Hz}$ , 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  14.2, 17.2, 23.9, 30.8, 44.9, 123.1, 124.0, 126.4, 128.3, 128.6, 128.9, 131.9, 134.9, 142.6, 145.3, 173.2. FT-IR  $\nu_{\text{max}}$  (NaCl): 3053, 2962, 2929, 1689, 1655, 1492, 1413, 1284,

1151, 760  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 369.1579; found  $[\text{M}+\text{Na}]^+$ : 369.1559.

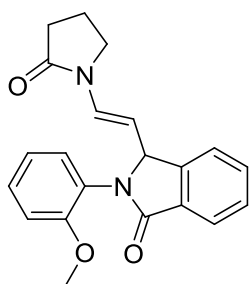
(*E*)-2-(2-*tert*-Butylphenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3g**): Yield: 56%.



Colorless solid, mp: 246-248°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.36(s, 9H), 2.09(t,  $J=7.4\text{ Hz}$ , 2H), 2.47(t,  $J=7.4\text{ Hz}$ , 2H), 3.35-3.49 (m, 2H), 4.69(dd,  $J=14.2, 9.5\text{ Hz}$ , 1H), 5.31 (d,  $J=9.5\text{ Hz}$ , 1H), 6.91 (dd,  $J=7.7, 1.3\text{ Hz}$ , 1H), 7.05 (d,  $J=14.2\text{Hz}$ , 1H), 7.20 (t,  $J=7.7\text{ Hz}$ , 1H), 7.33 (t,  $J=7.7\text{Hz}$ , 1H), 7.43, d,

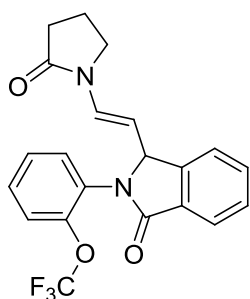
$J=7.4\text{Hz}$ , 1H), 7.53-7.62(m, 3H), 7.94(d,  $J=7.5\text{Hz}$ , 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  17.2, 30.8, 32.0, 32.5, 35.9, 45.0, 66.0, 108.2, 123.2, 124.1, 126.3, 128.1, 128.6, 128.9, 131.9, 133.6, 134.2, 145.4, 149.6, 168.5, 173.1. FT-IR  $\nu_{\text{max}}$  (NaCl): 3054, 2959, 2917, 1688, 1655, 1489, 1437, 1241, 1145, 758  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{24}\text{H}_{26}\text{N}_2\text{O}_2$   $[\text{M}+\text{Na}]^+$ : 397.1892; found  $[\text{M}+\text{Na}]^+$ : 397.1872.

(*E*)-2-(2-Methoxyphenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3h**): Yield: 53%.

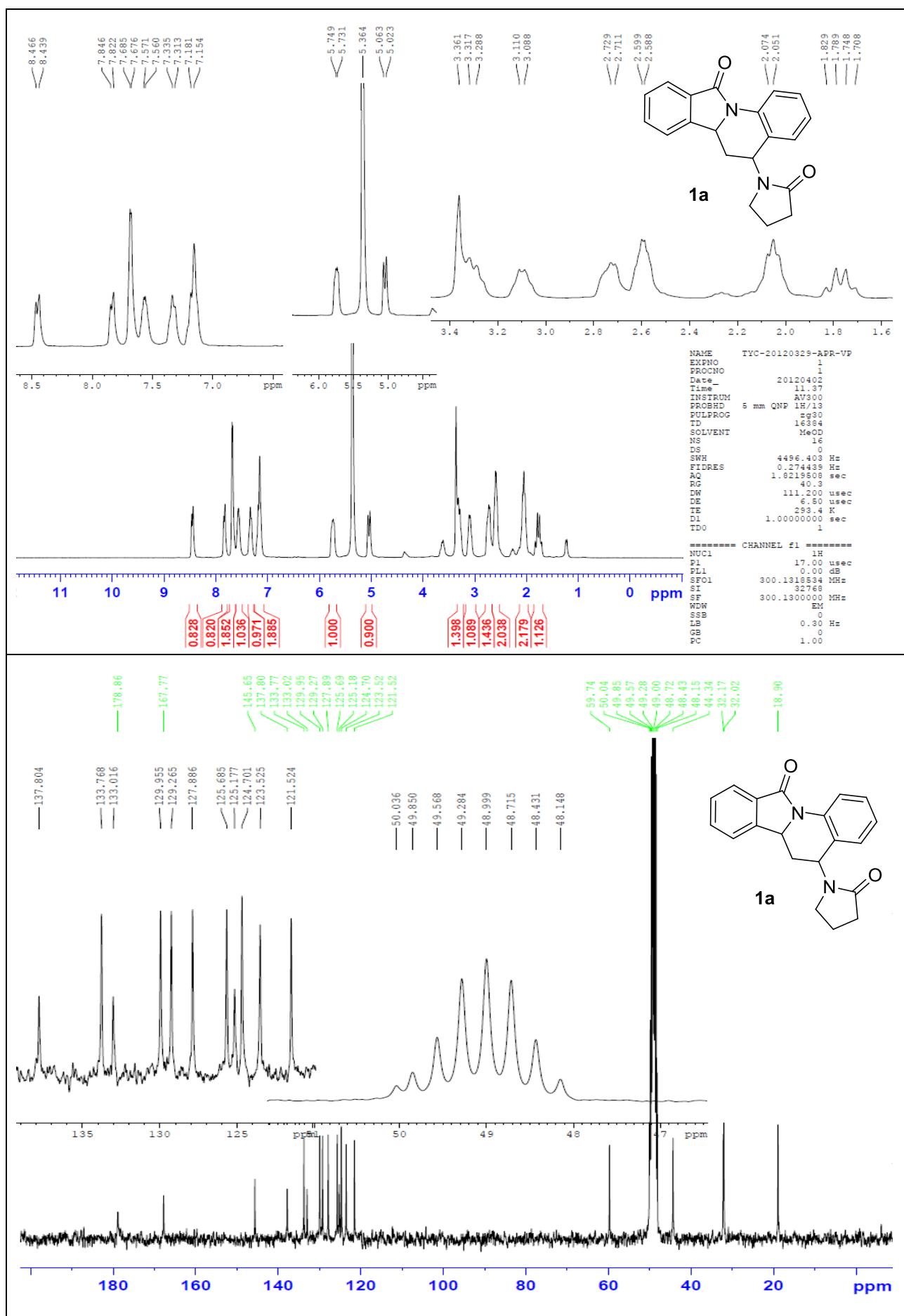


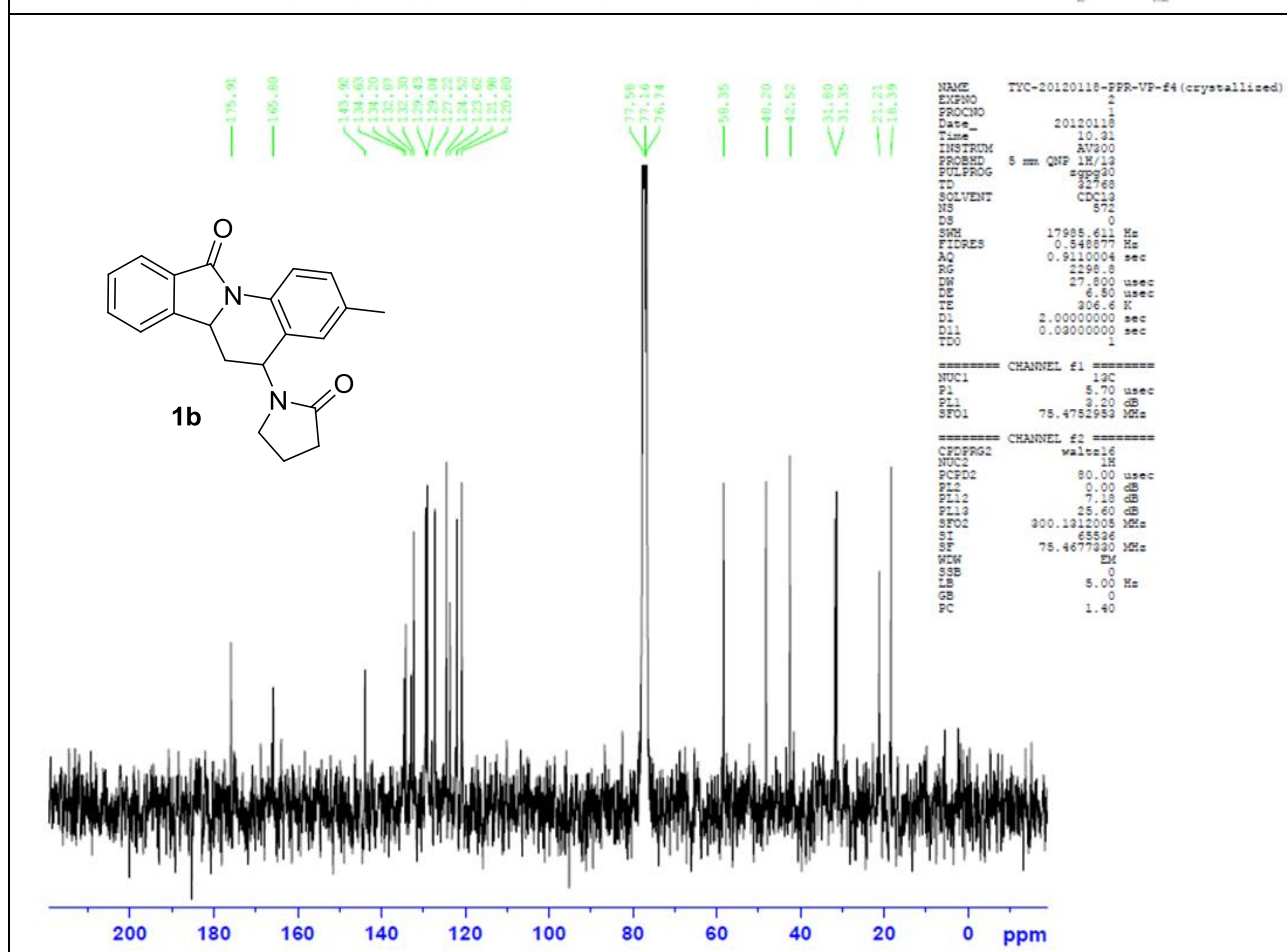
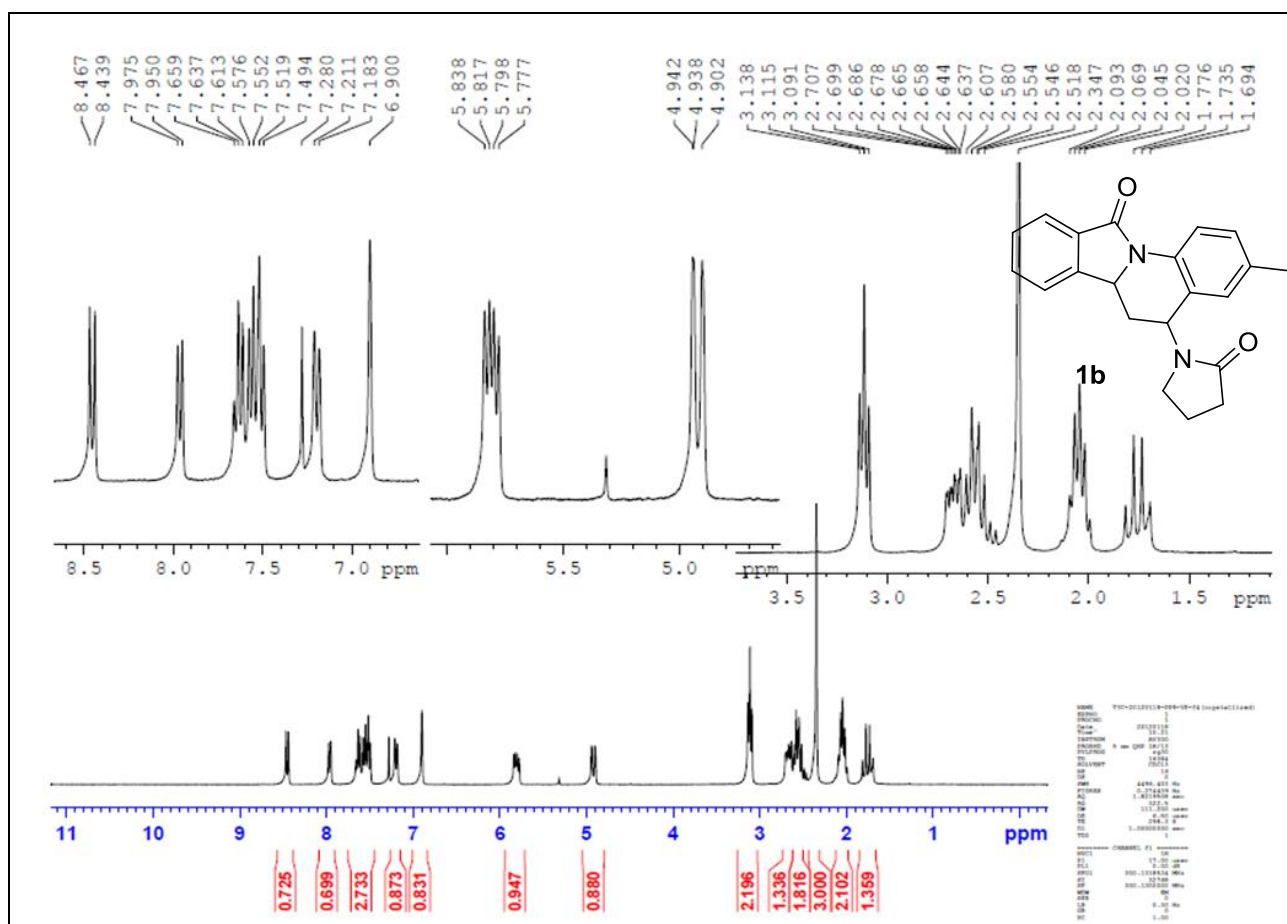
mp: 86-89°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.92-2.02(m, 2H), 2.32-2.40(m, 2H), 3.17-3.38(m, 2H), 3.75(s, 3H), 4.59(dd,  $J$ = 9.6, 14.1Hz, 1H), 5.56(d,  $J$ = 9.6Hz, 1H), 6.89-6.96(m, 2H), 7.12(d,  $J$ = 15.0Hz, 1H), 7.18-7.26(m, 2H), 7.36(d,  $J$ = 7.5Hz), 7.44(t,  $J$ = 7.2Hz, 1H), 7.53(t,  $J$ = 7.2Hz, 1H), 7.85(d,  $J$ = 7.5Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  17.1, 30.8, 44.9, 55.6, 63.4, 107.7, 112.1, 120.6, 123.0, 123.7, 125.4, 128.0, 128.2, 128.7, 130.0, 131.8(2C), 145.7, 155.3, 167.3, 173.1. FT-IR  $\nu_{\text{max}}$  (NaCl): 3051, 2929, 2839, 1697, 1655, 1503, 1407, 1261, 1143, 747  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_3$   $[\text{M}+\text{Na}]^+$ : 371.1366; found  $[\text{M}+\text{Na}]^+$ : 371.1353.

(*E*)-2-(2-(Trifluoromethoxy)phenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3i**): Yield:

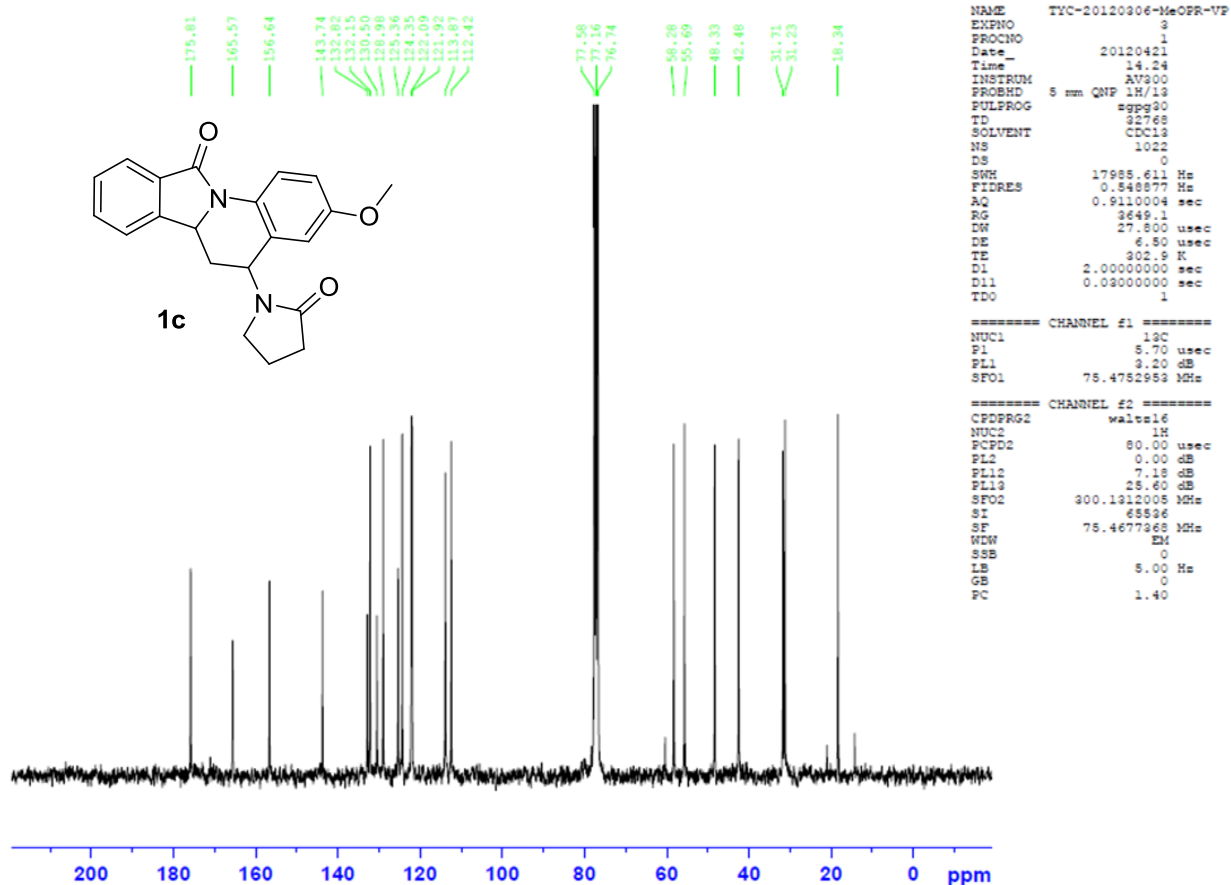
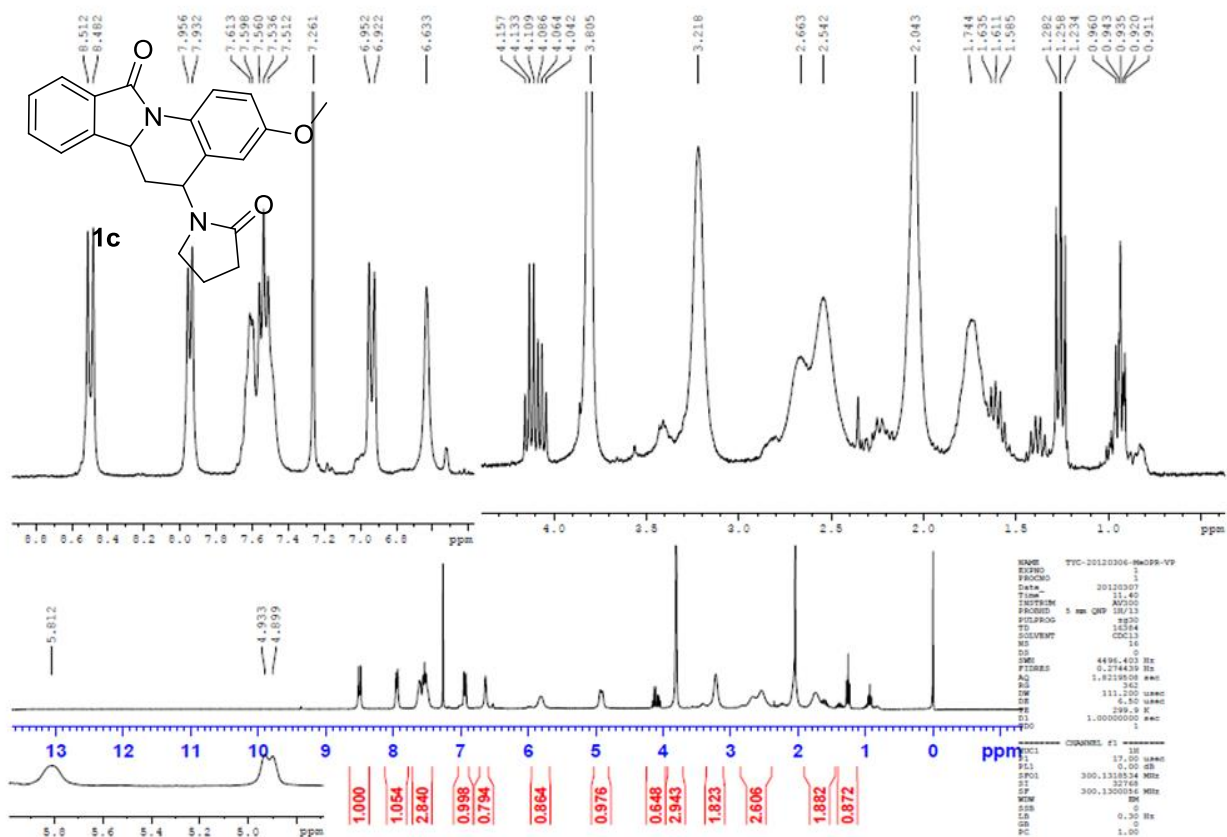


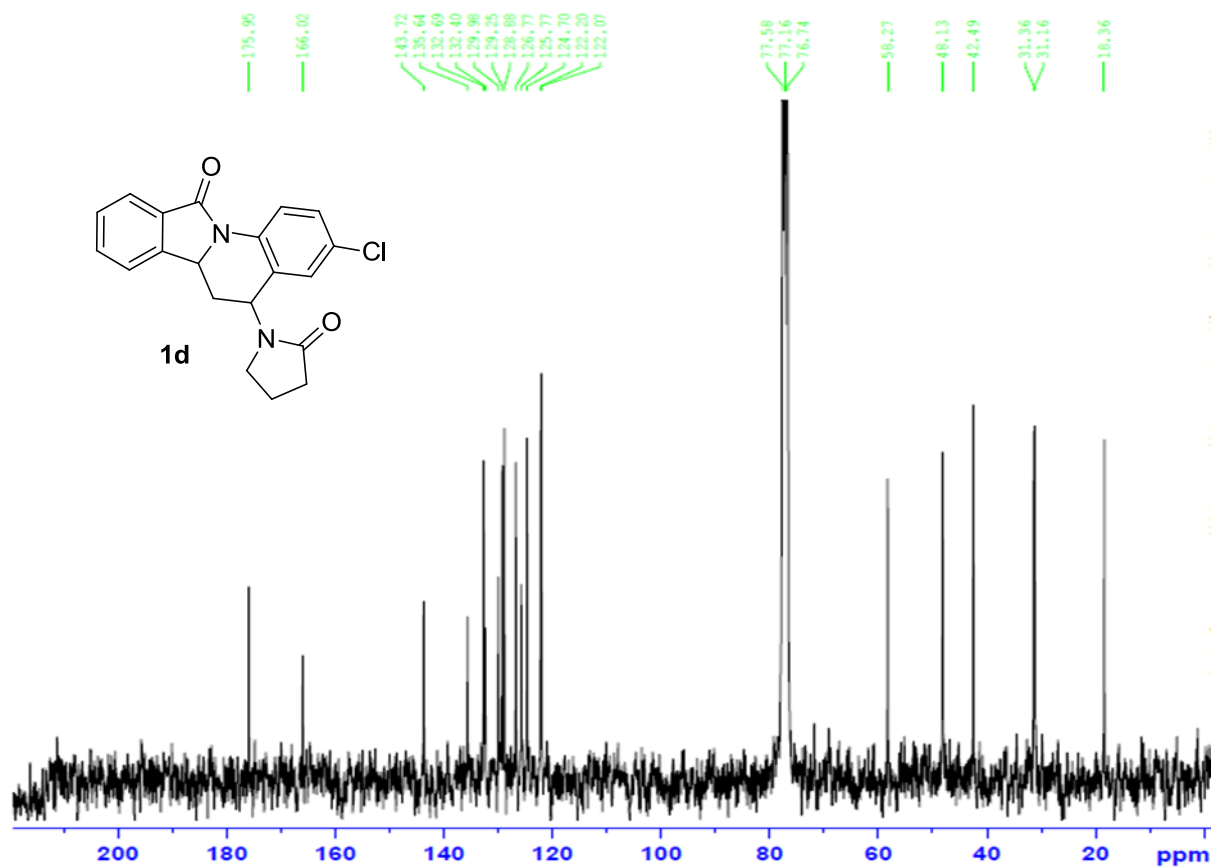
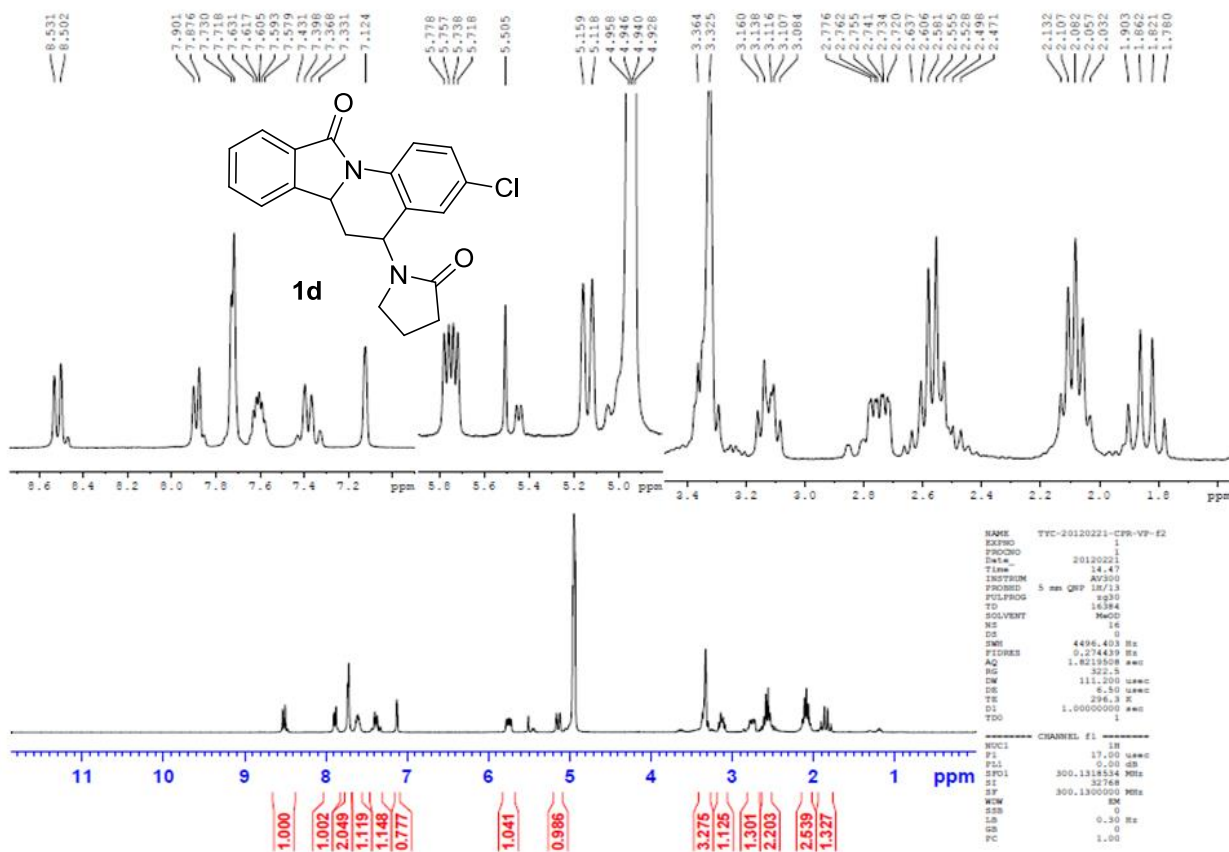
58%. Colorless solid, mp: >260°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.20-1.40 (m, 1H), 2.00-2.13 (m, 2H), 2.47 (t,  $J$ = 8.4Hz, 2H), 3.23-3.47 (m, 2H), 4.62 (dd,  $J$ = 9.6, 14.3Hz, 1H), 5.30 (d,  $J$ = 9.6Hz, 1H), 7.30 (d,  $J$ =14.4Hz, 1H), 7.30-7.43 (m, 3H), 7.48 (d,  $J$ = 7.8Hz, 1H), 7.55 (t,  $J$ = 7.5Hz, 1H), 7.64 (t,  $J$ = 7.5Hz, 1H), 7.96 (d,  $J$ = 7.5Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  17.4, 18.1, 31.0, 45.0, 64.2, 107.2, 121.3, 123.4, 124.4, 127.3, 128.7, 128.9(2C), 129.5, 130.5, 131.2, 132.5, 145.6, 167.3, 173.4. FT-IR  $\nu_{\text{max}}$  (NaCl): 2917, 1705, 1655, 1503, 1405, 1366, 1249, 1169, 759  $\text{cm}^{-1}$ . HRMS (amu): calcd for  $\text{C}_{21}\text{H}_{17}\text{F}_3\text{N}_2\text{O}_3$   $[\text{M}+\text{Na}]^+$ : 425.1083; found  $[\text{M}+\text{Na}]^+$ : 425.1100.

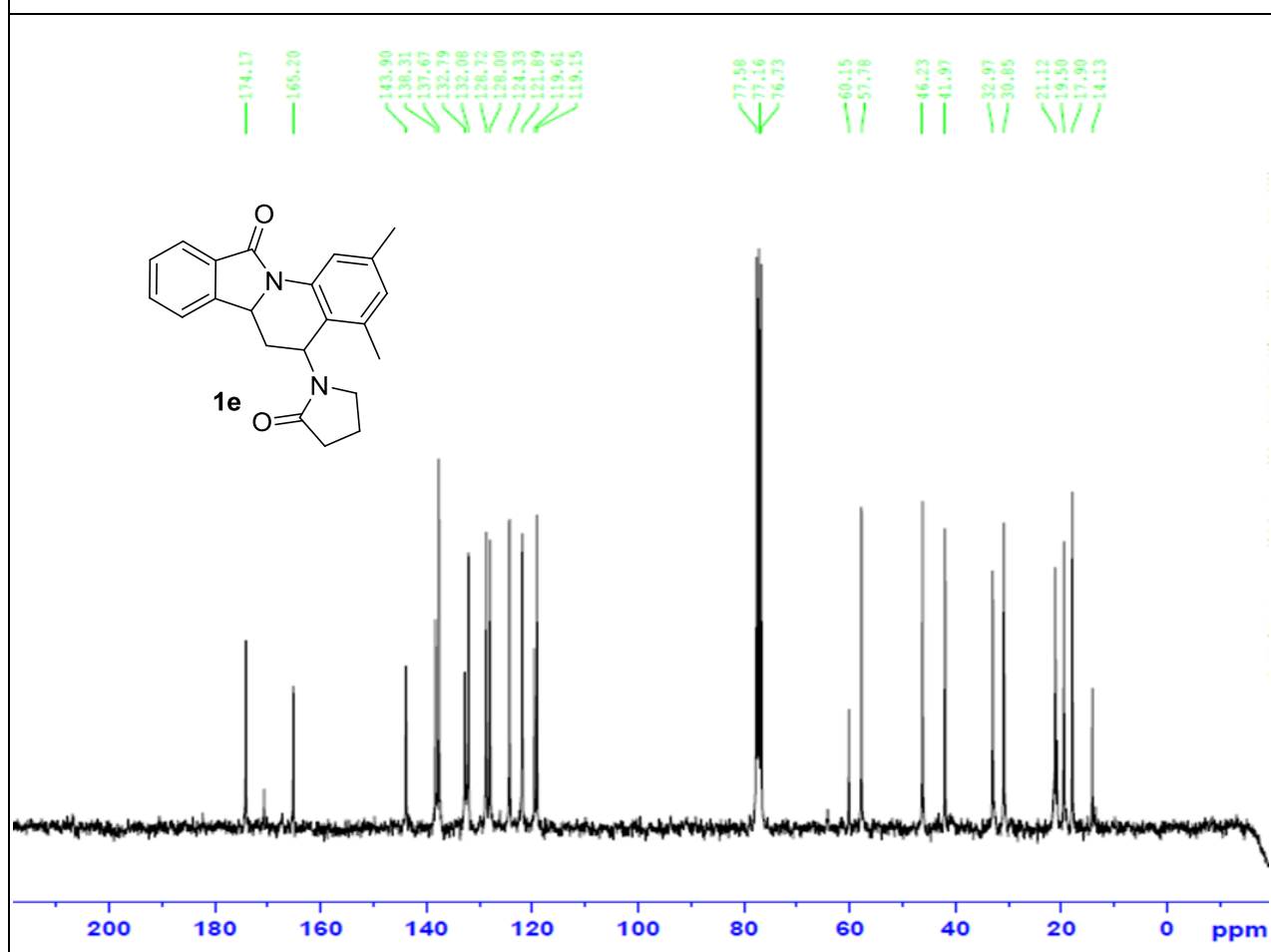
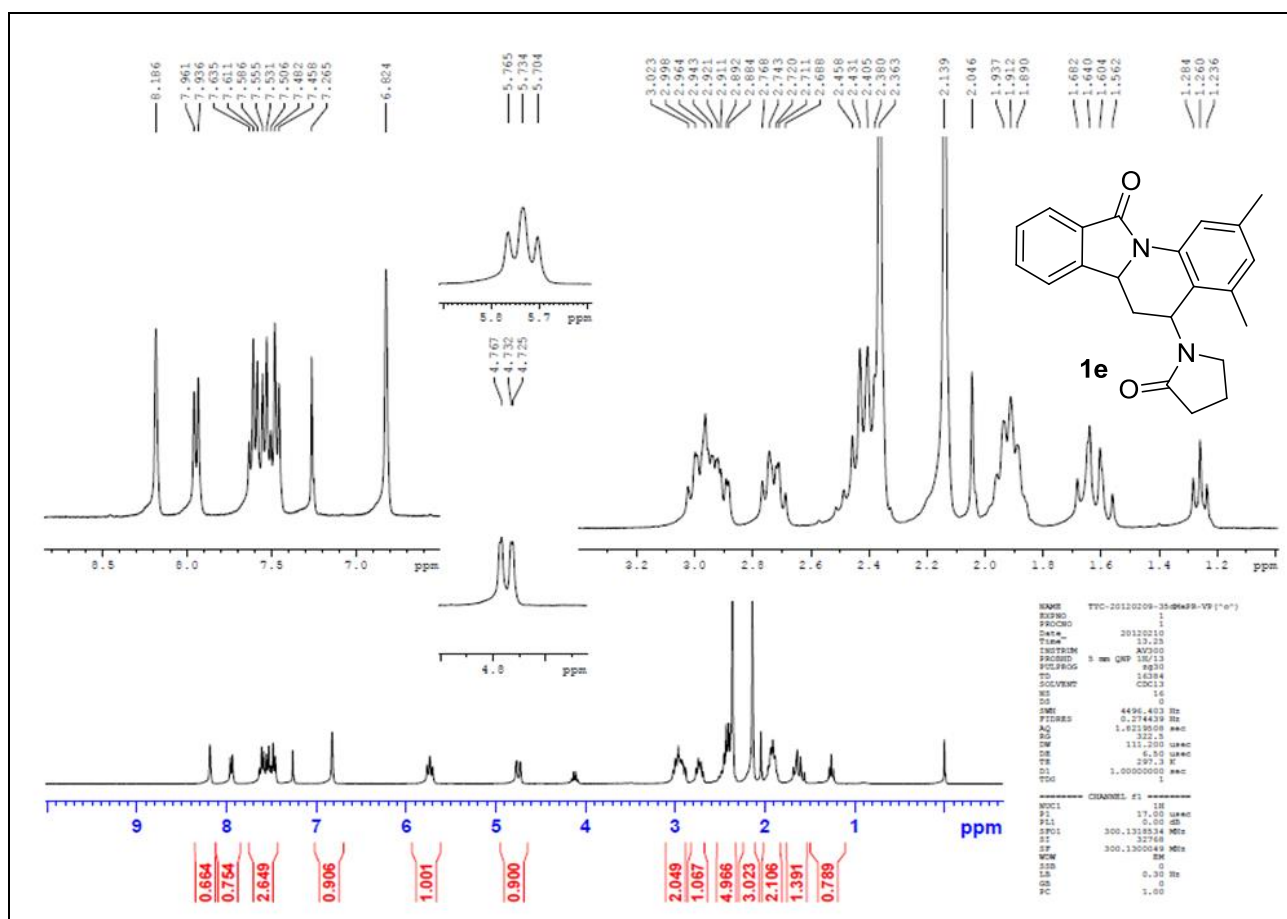


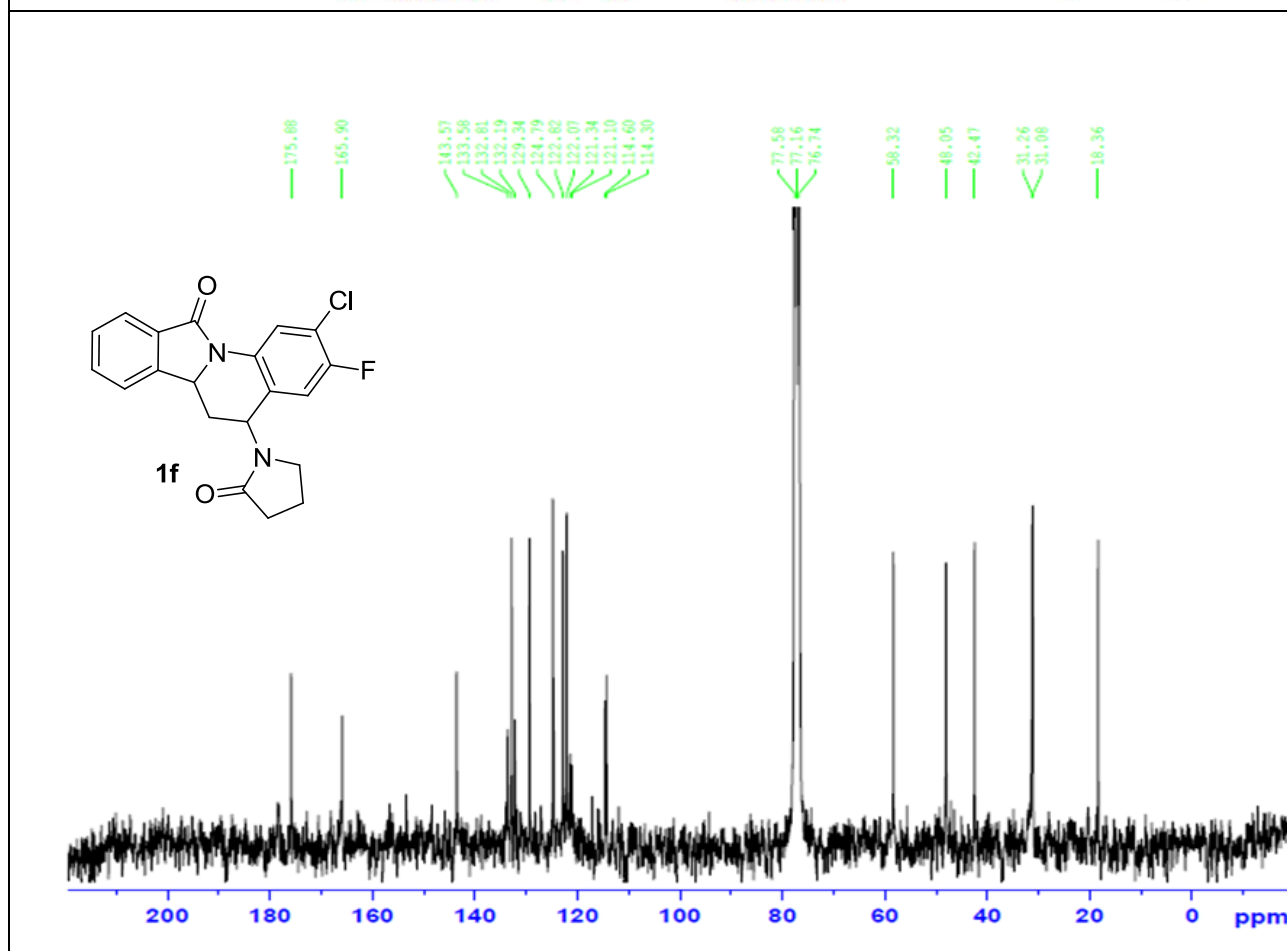
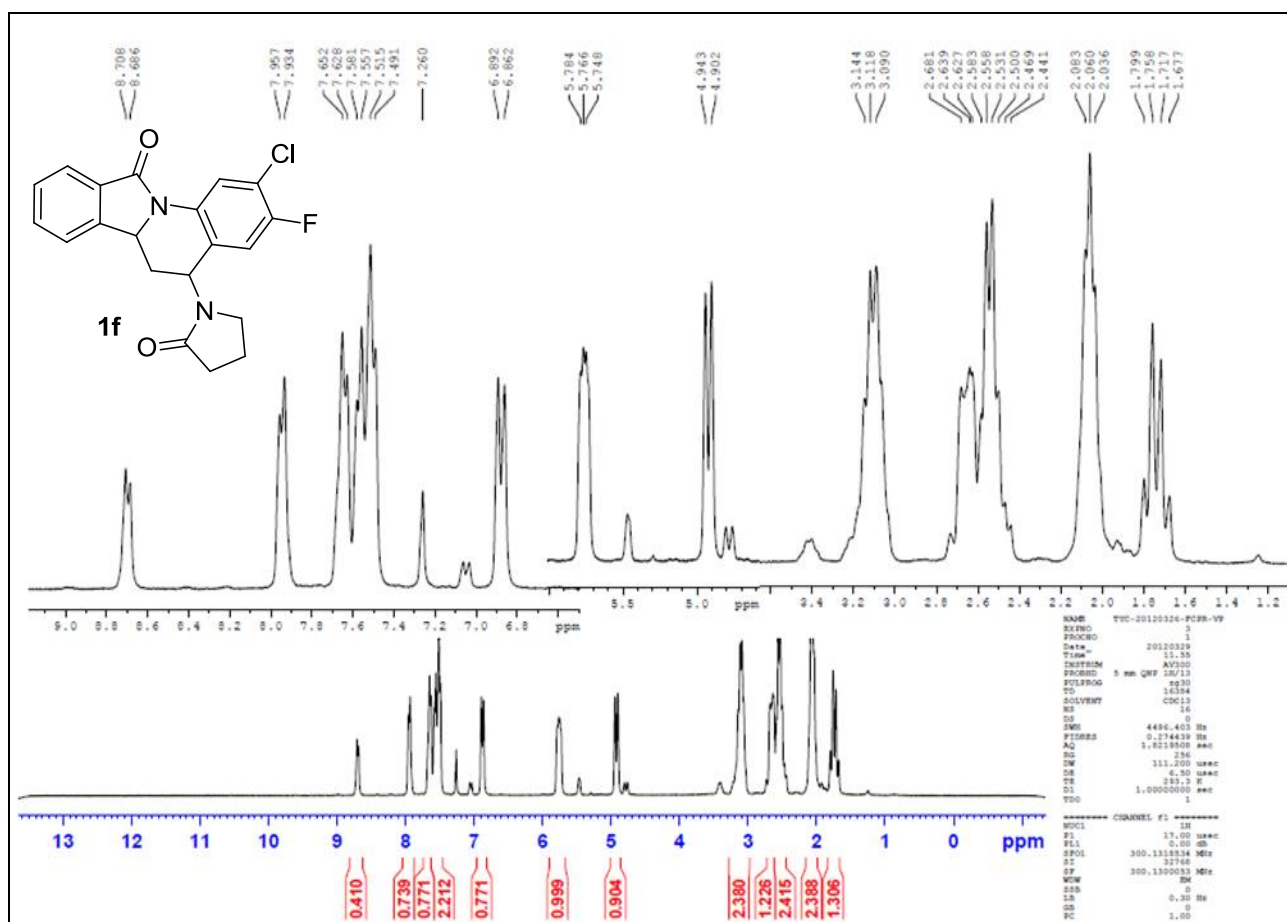


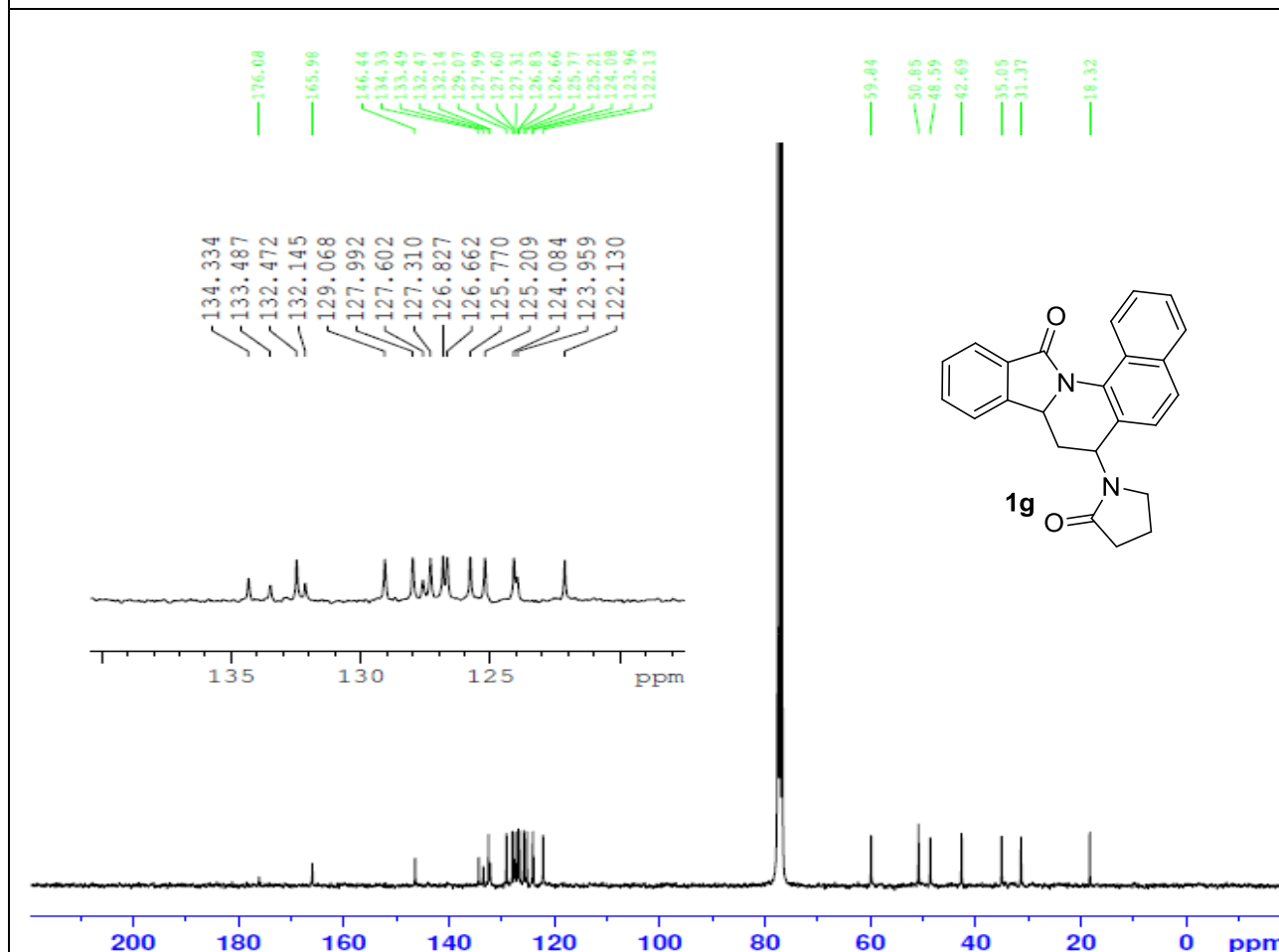
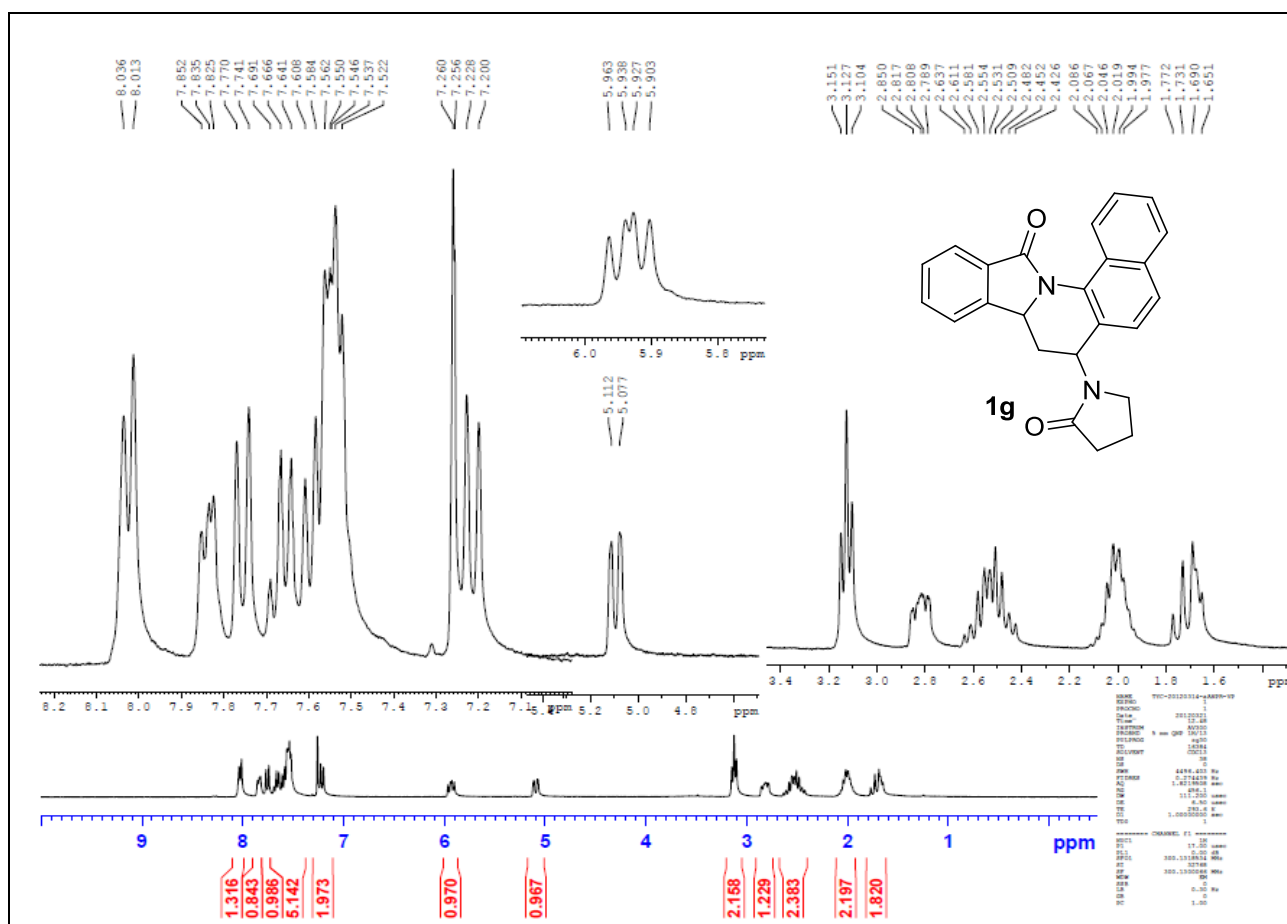


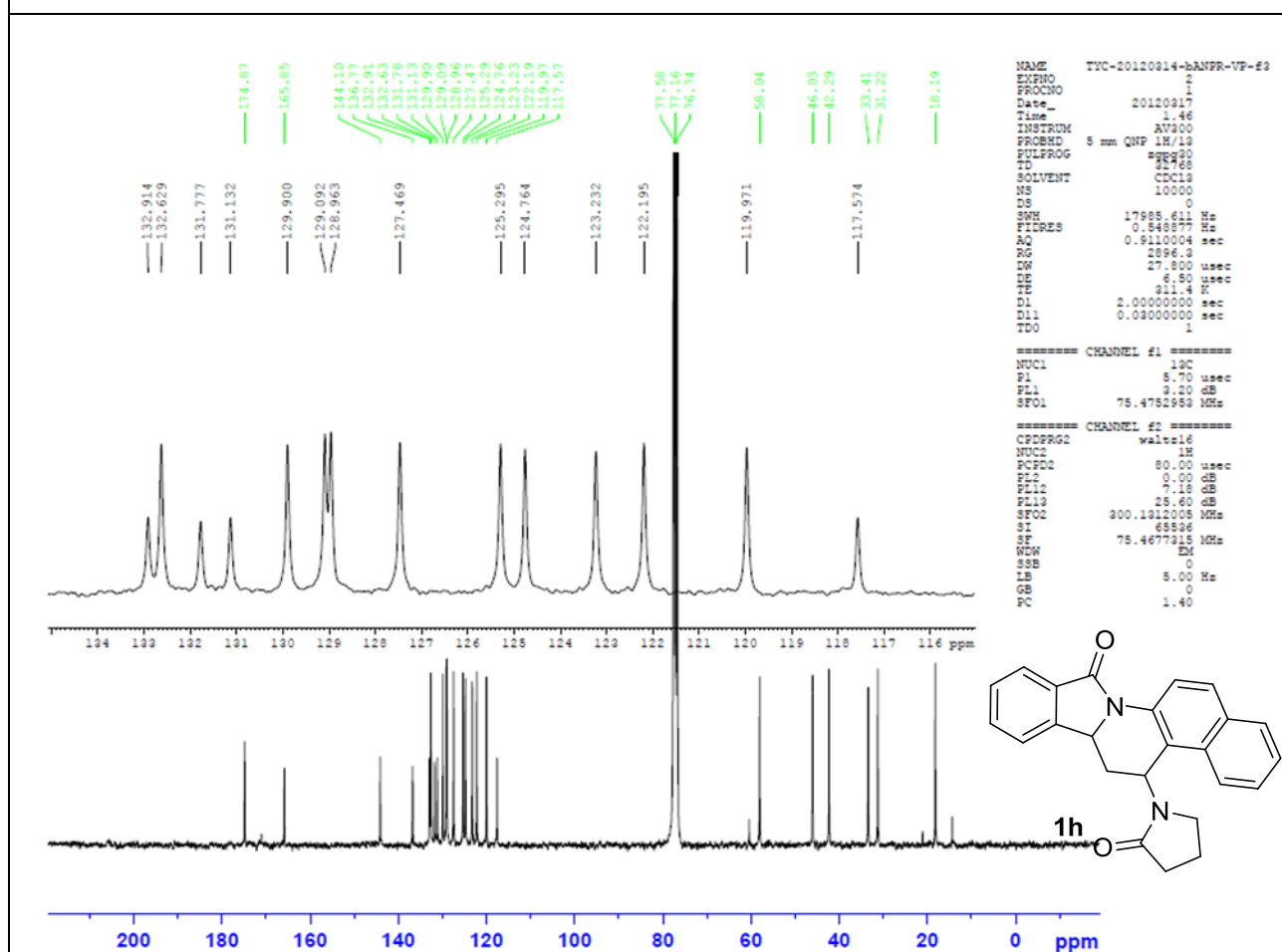
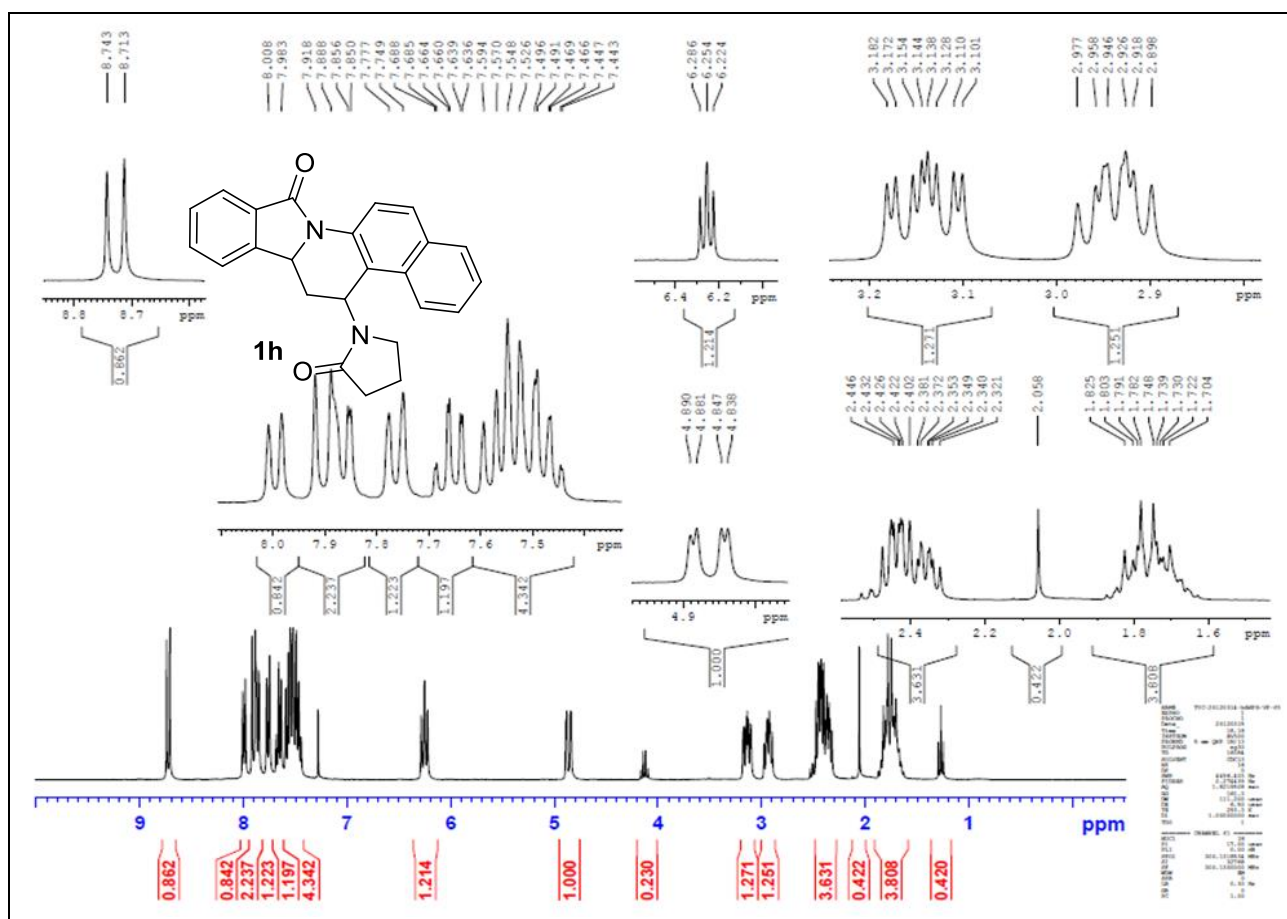




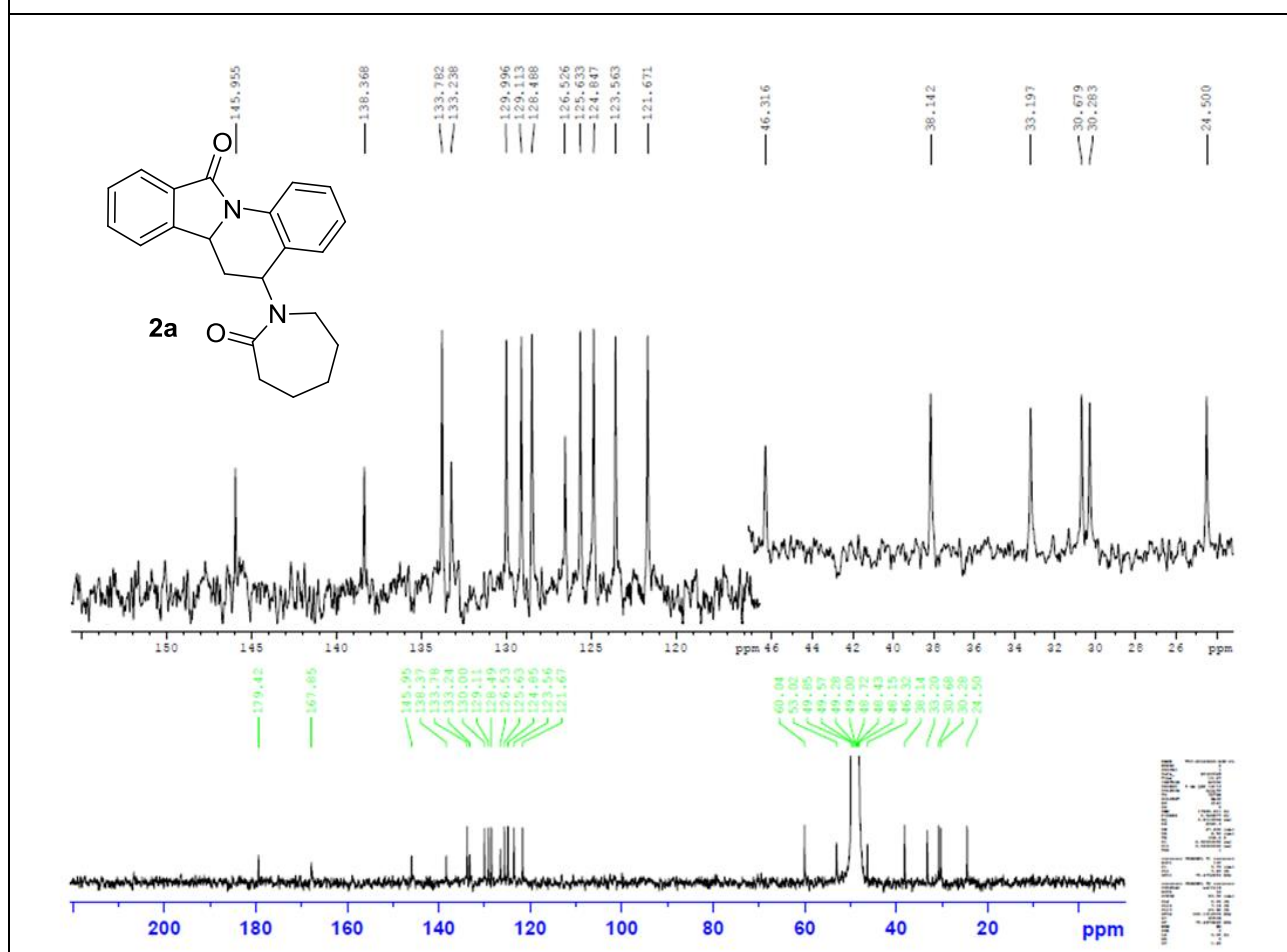
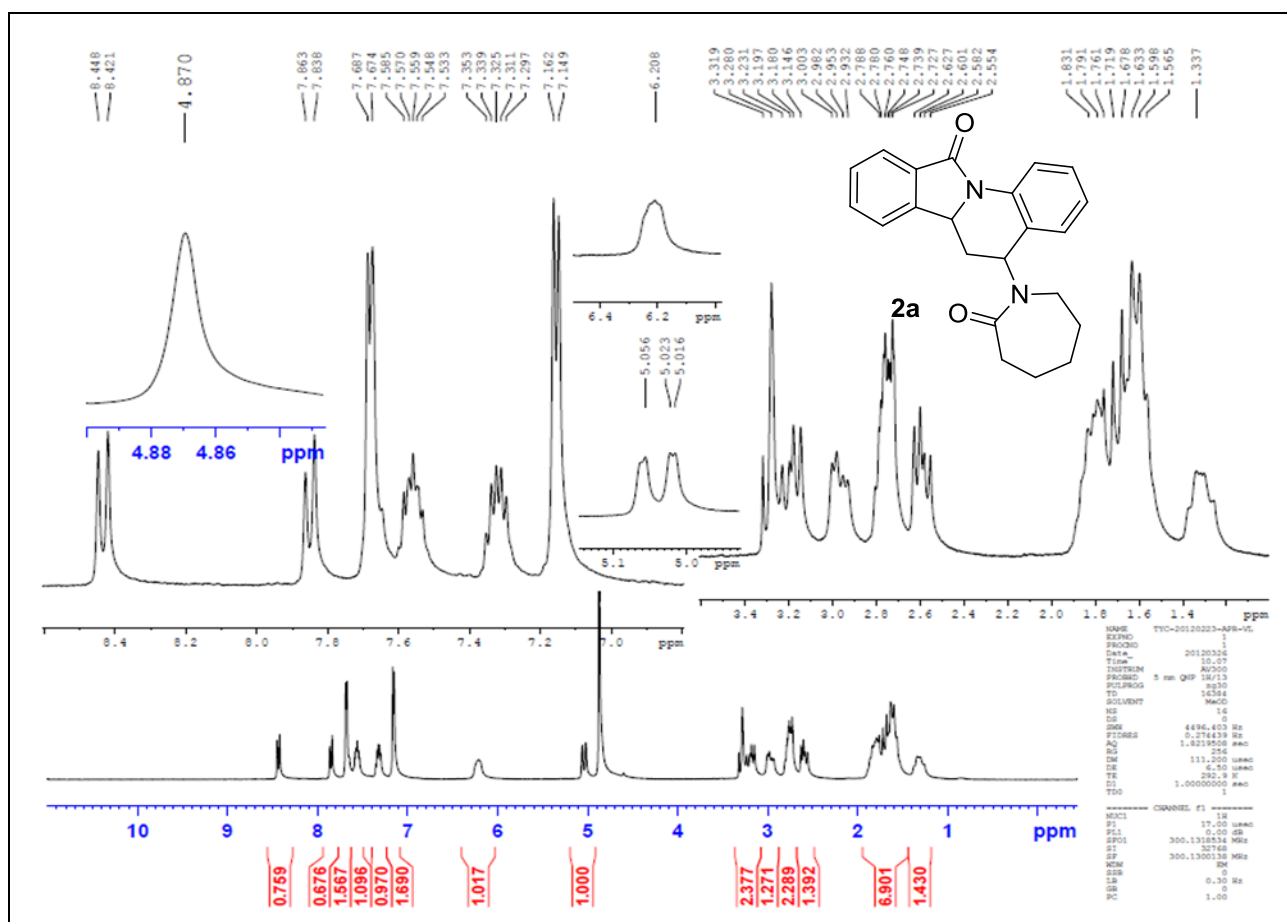


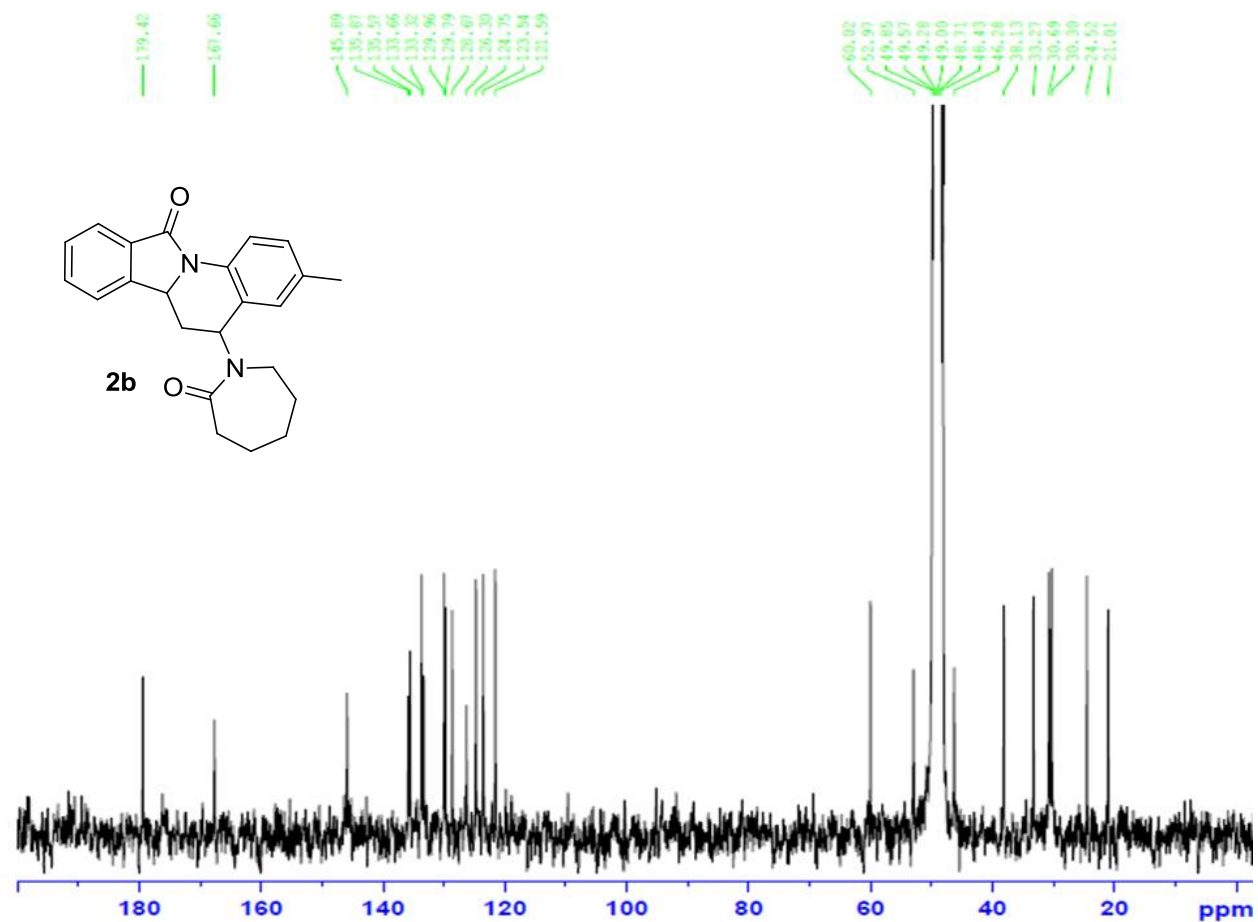
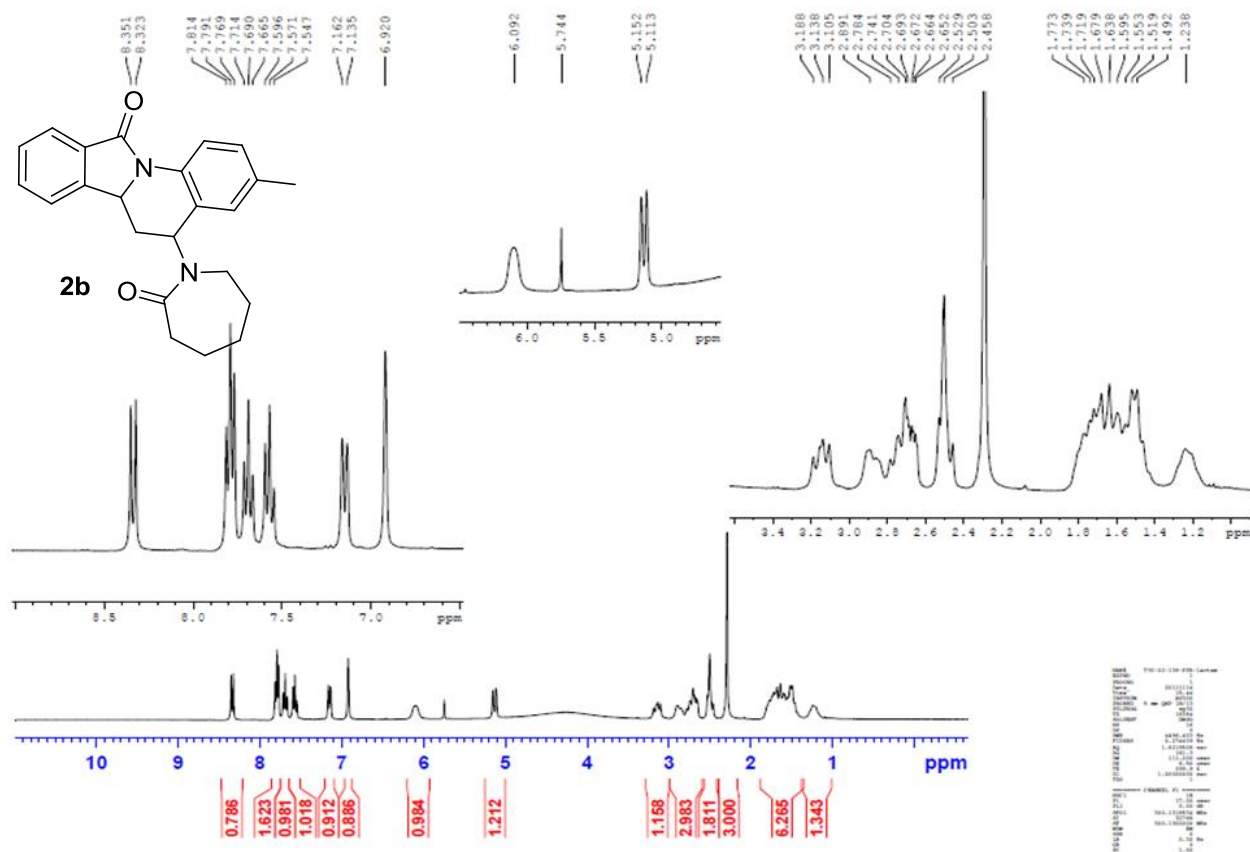




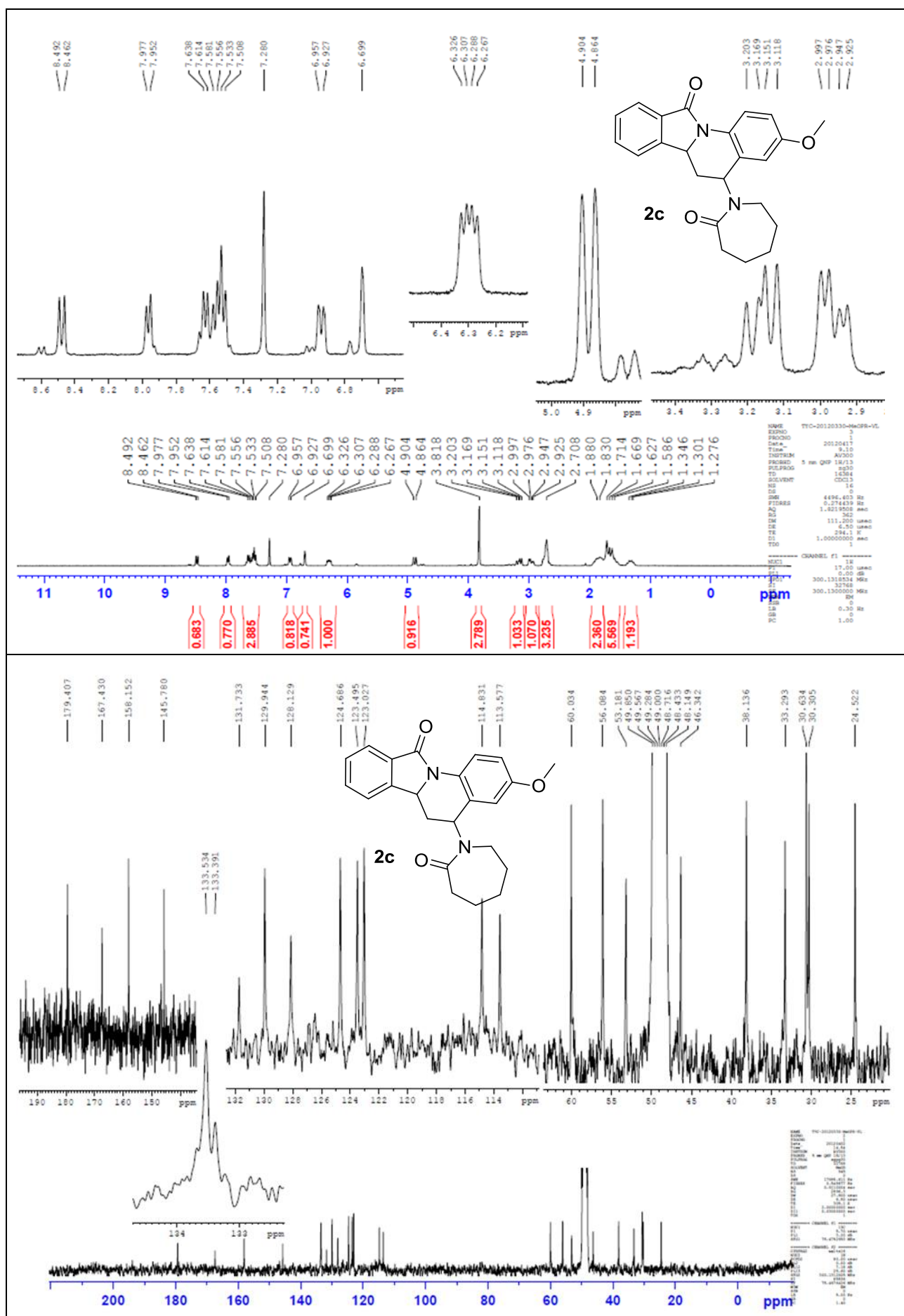


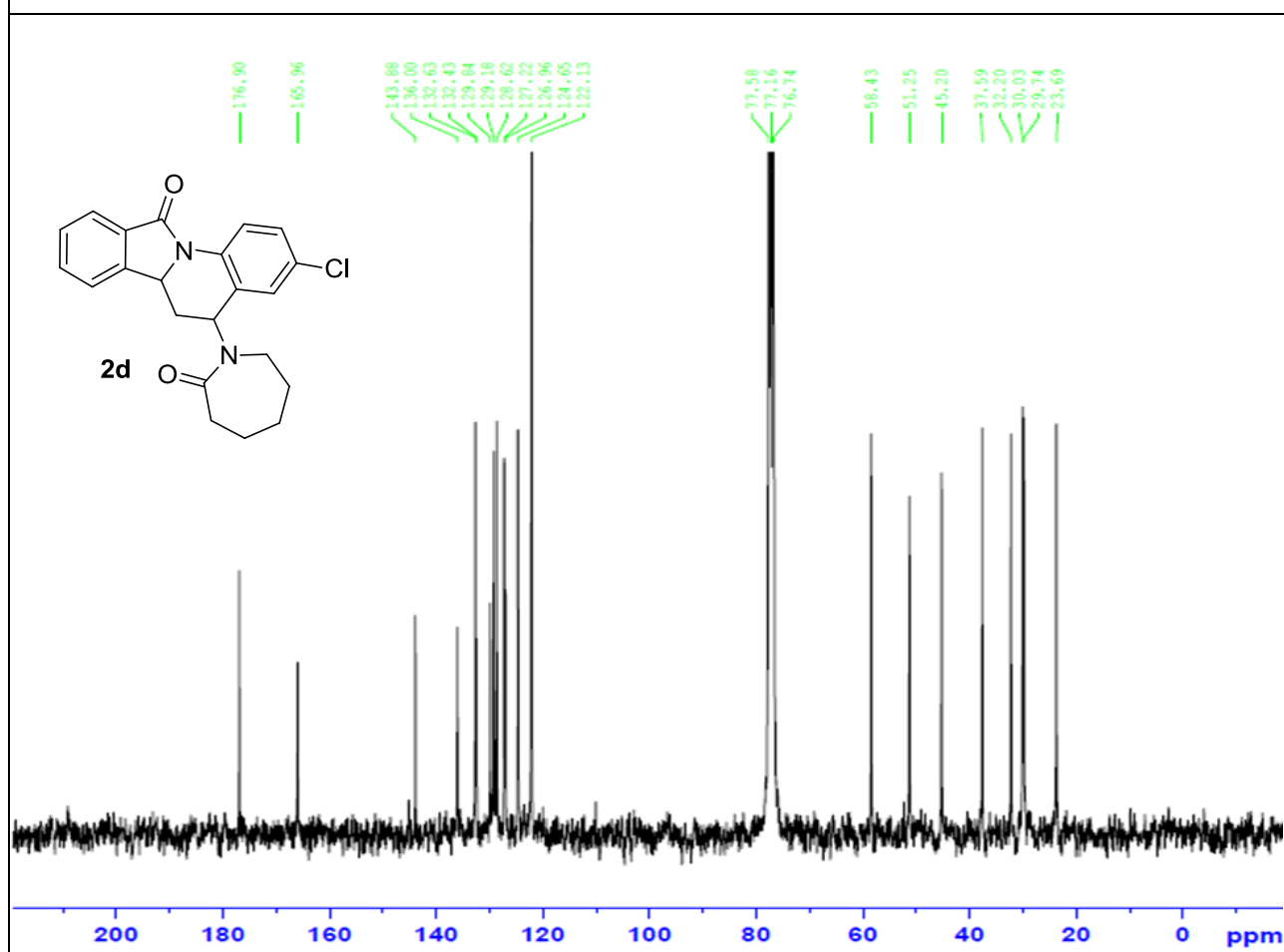
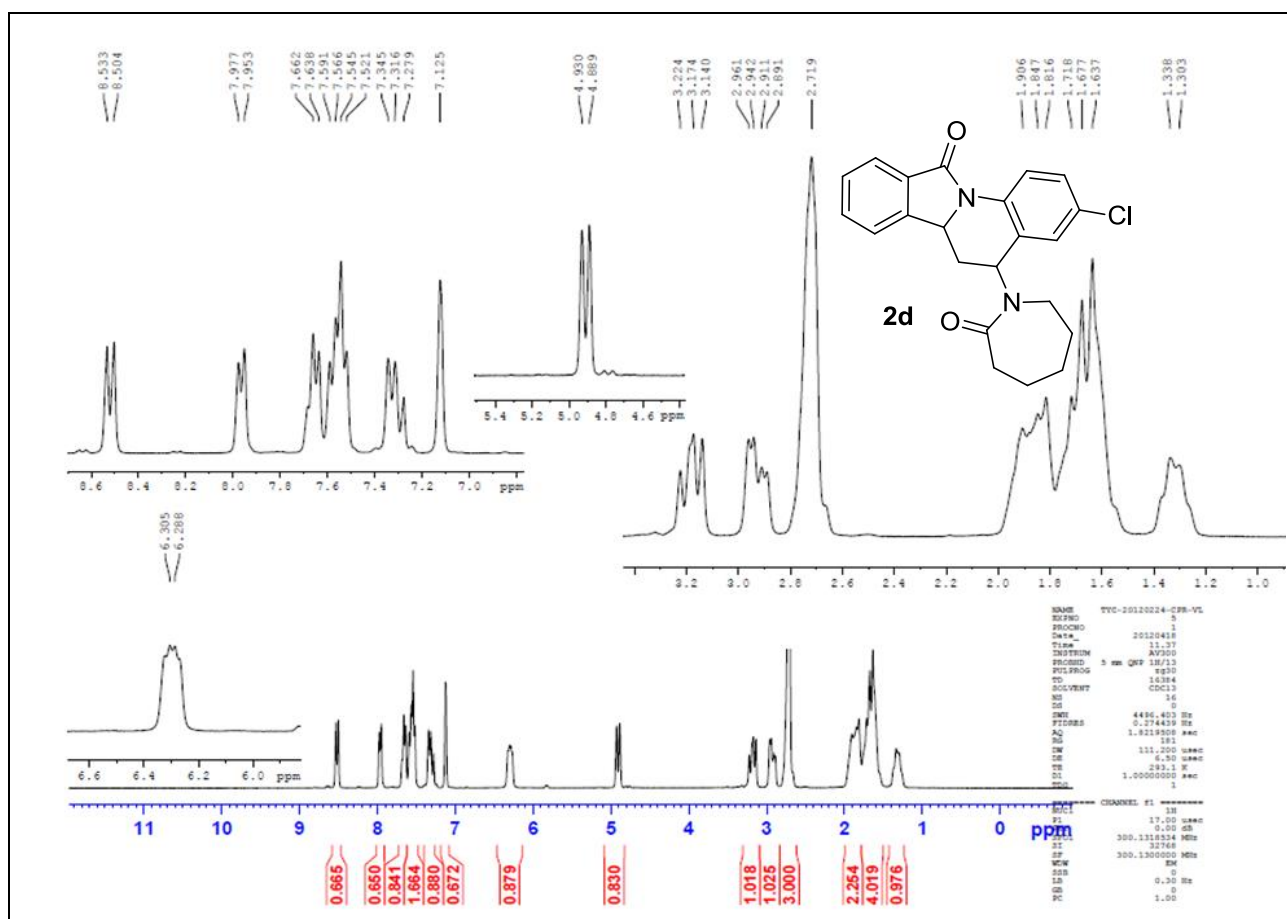


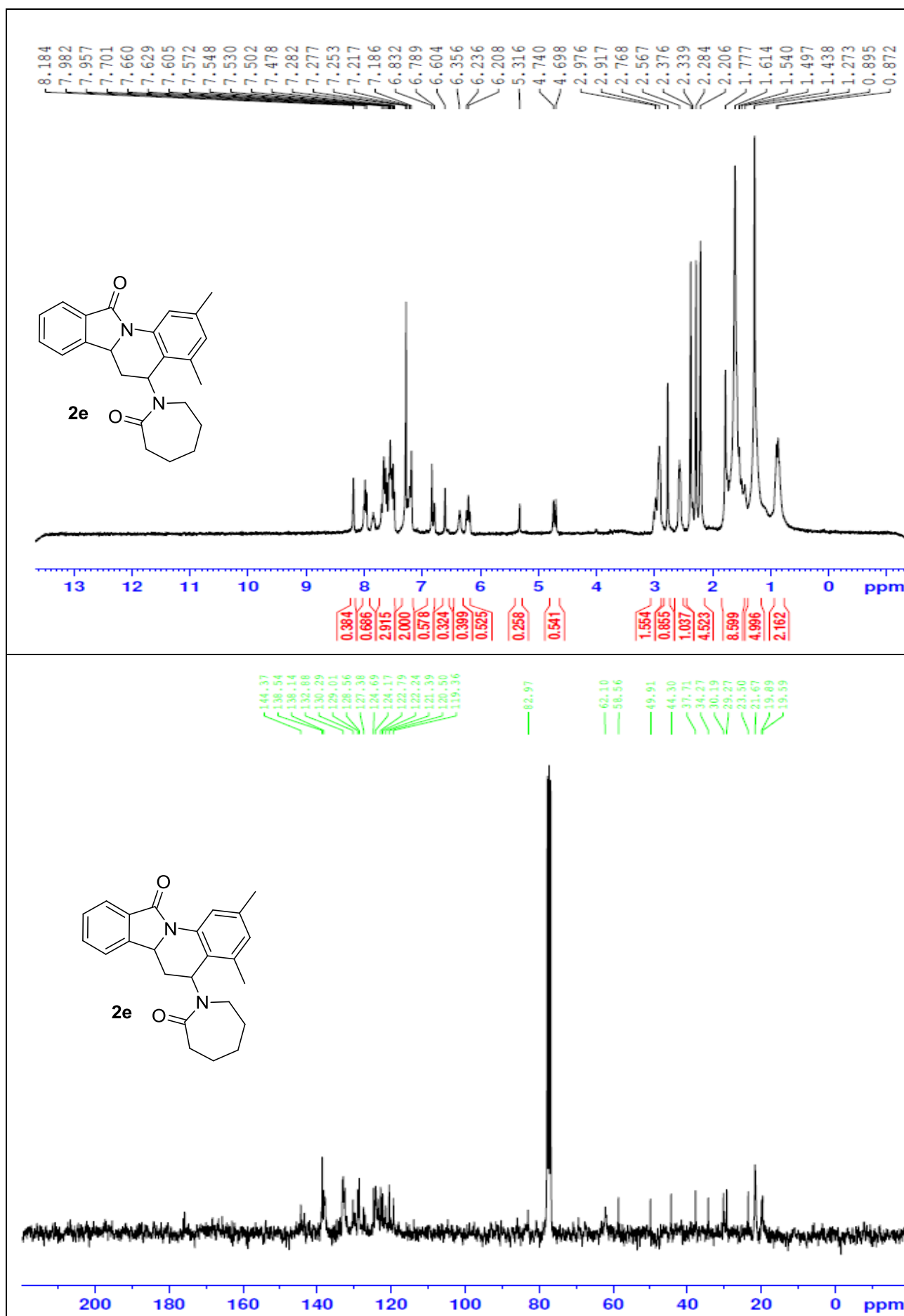


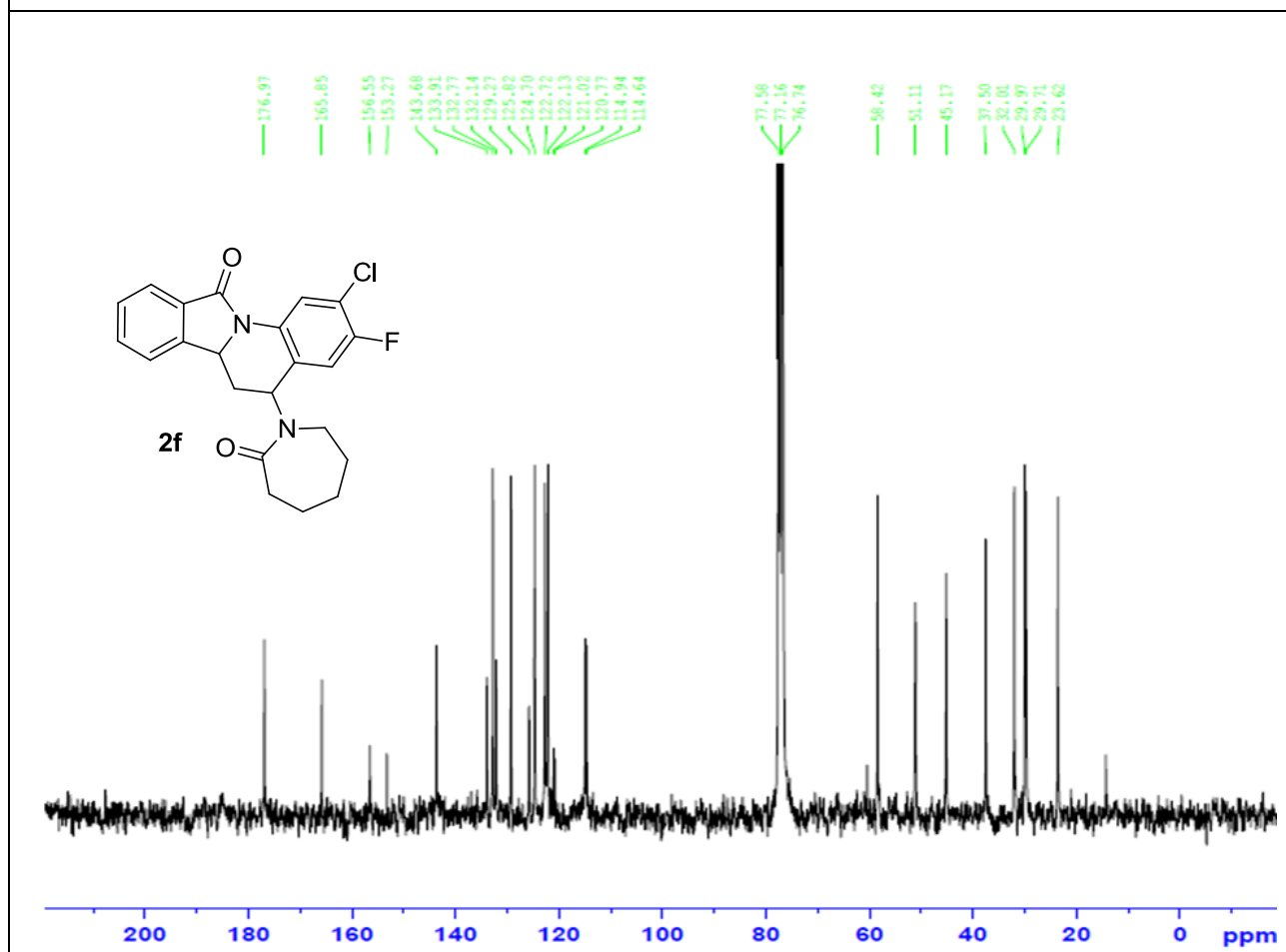
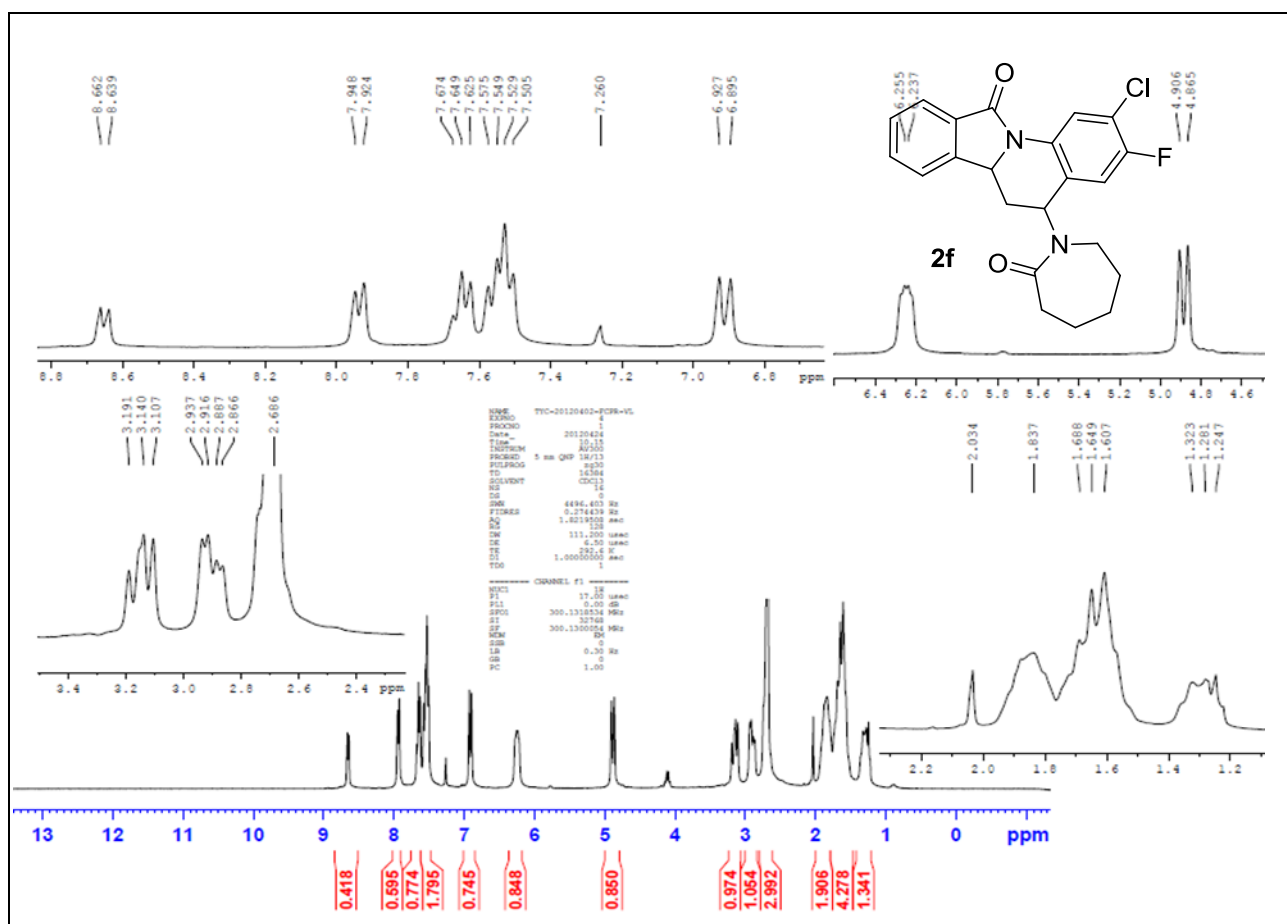


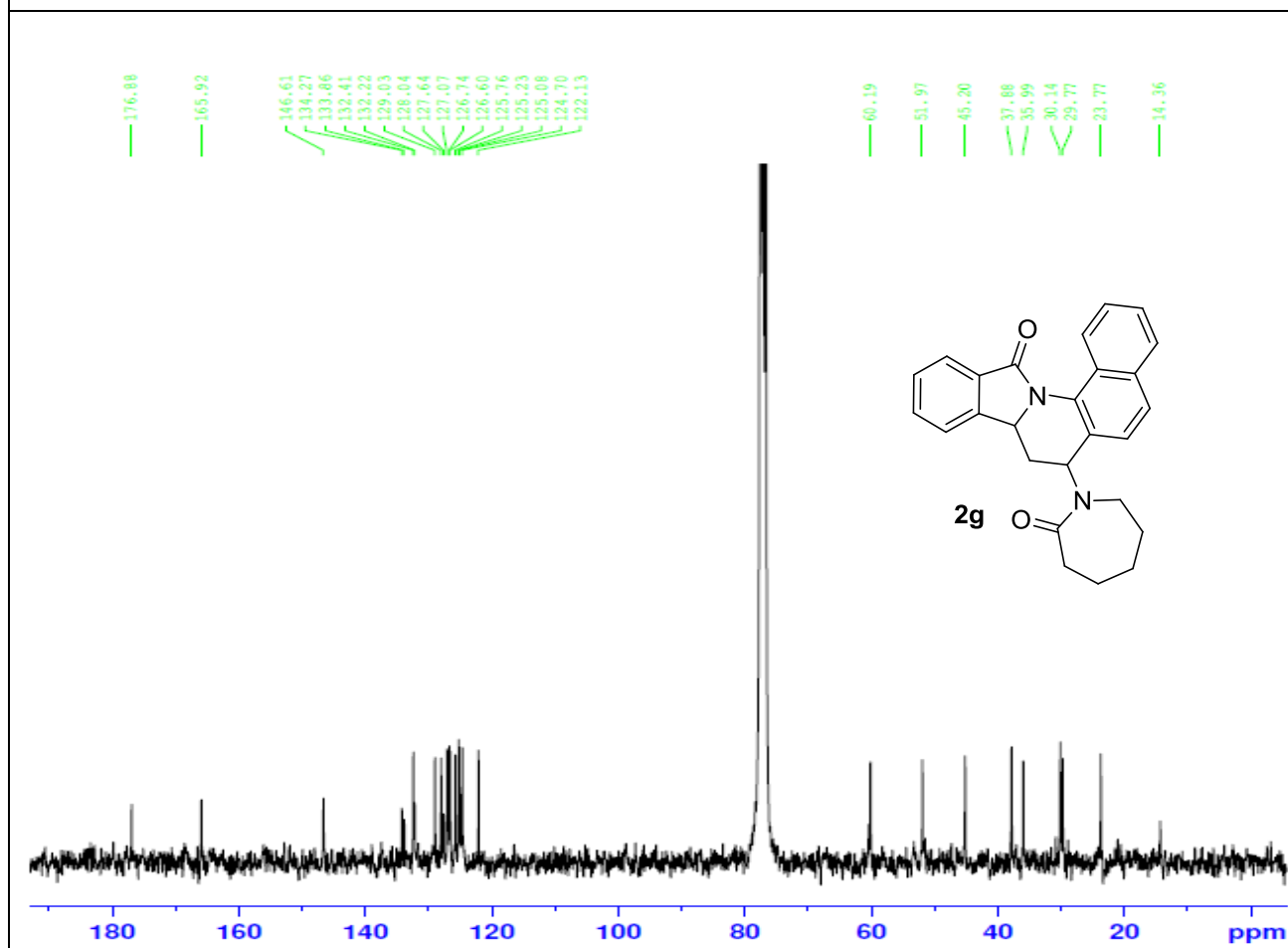
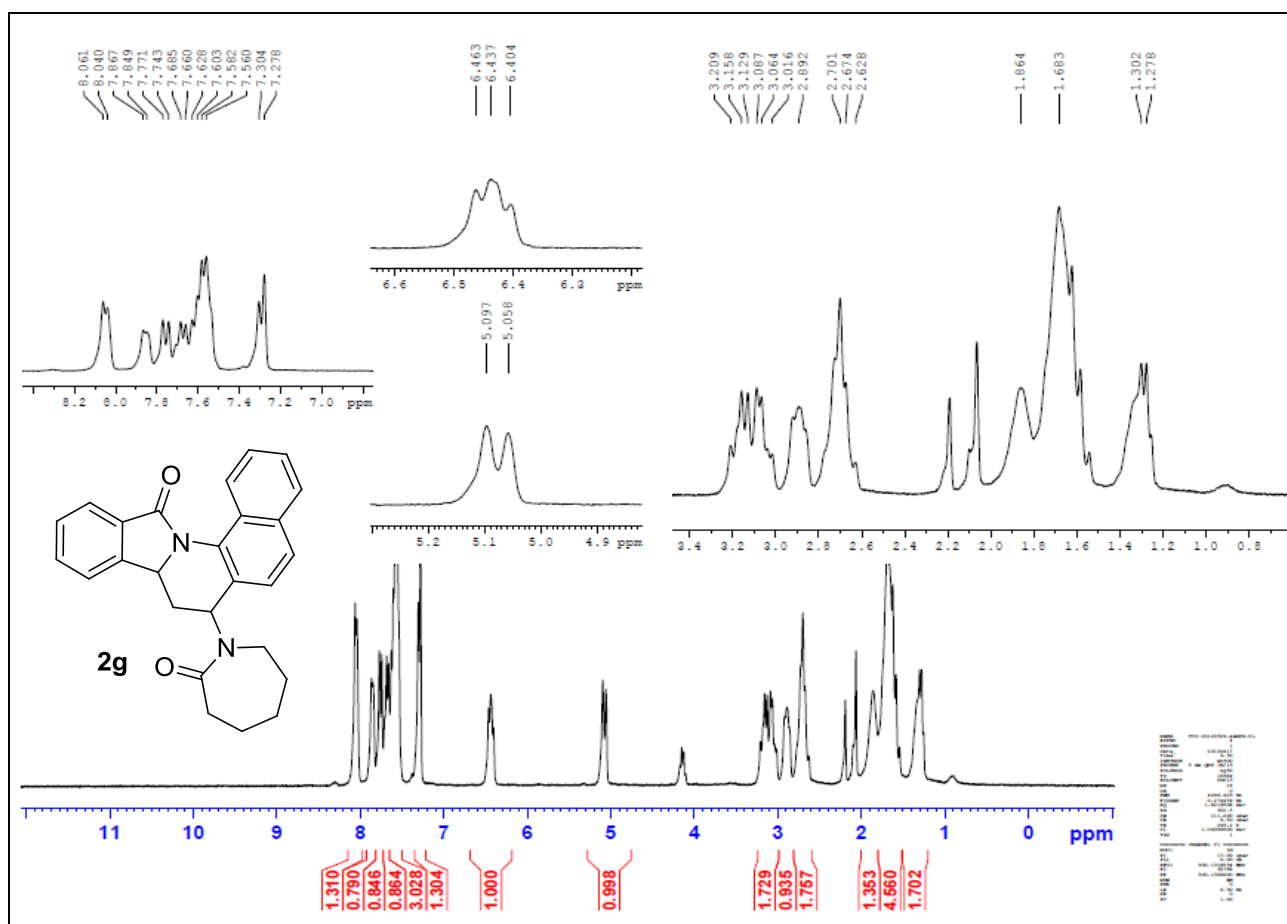


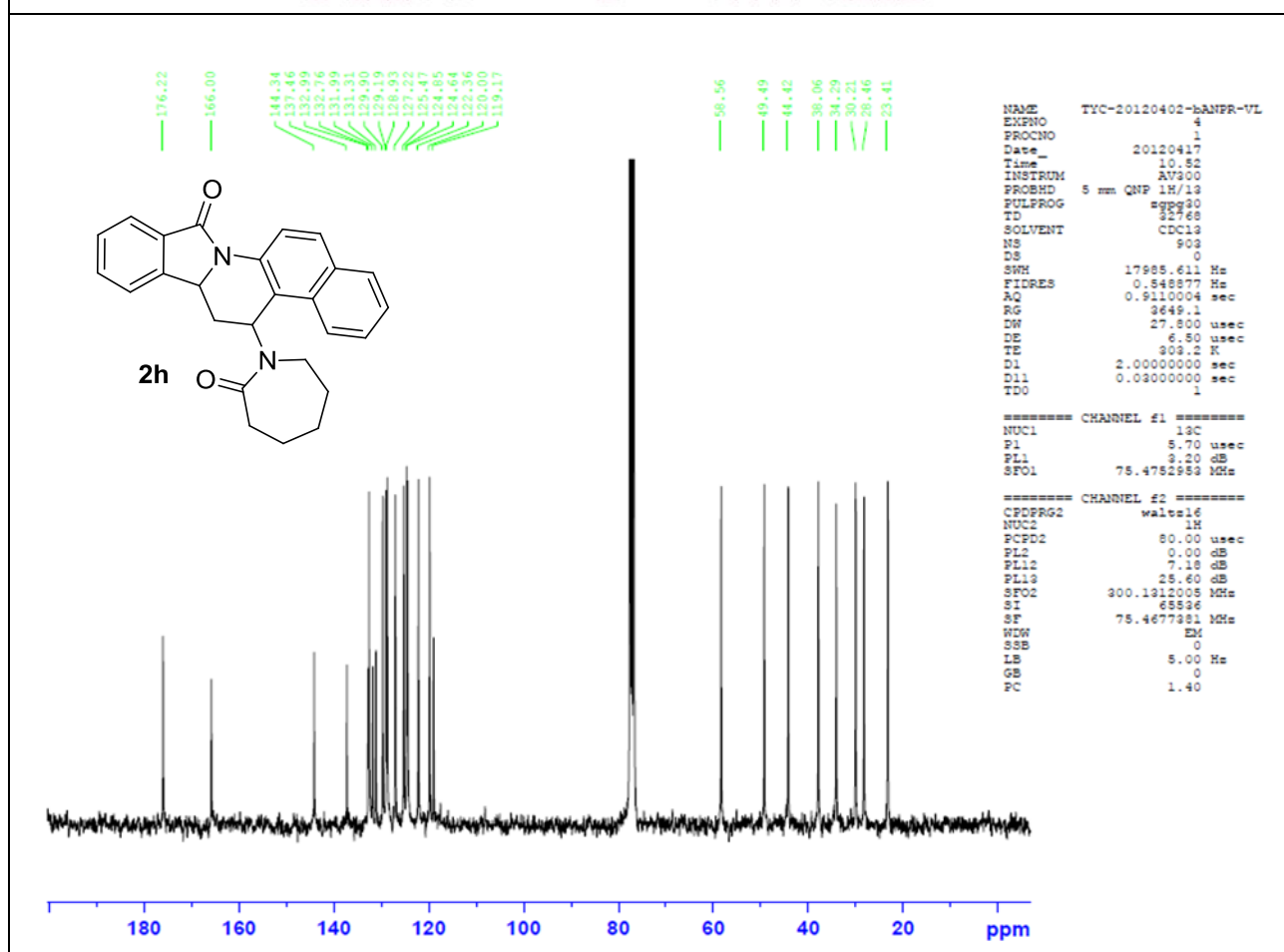
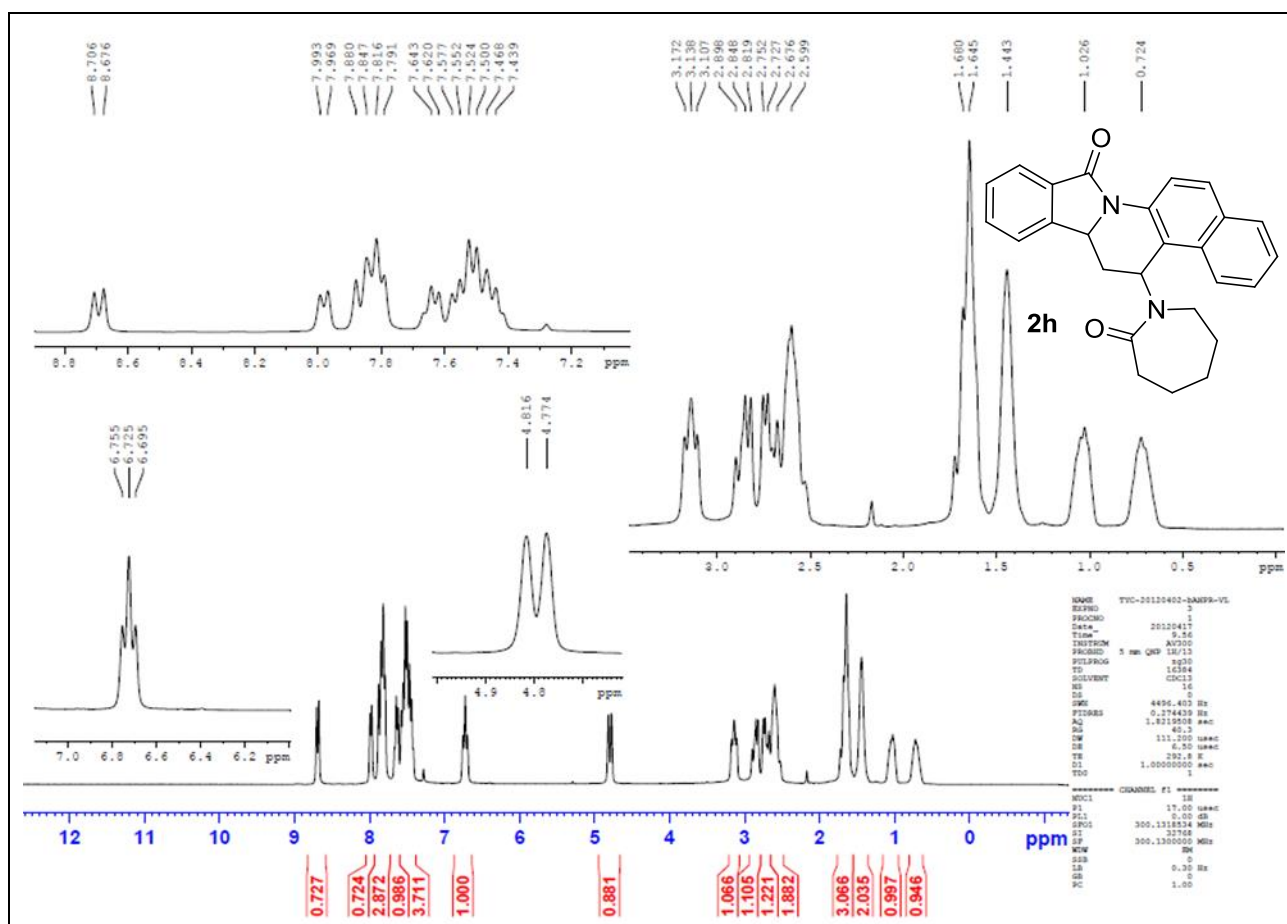






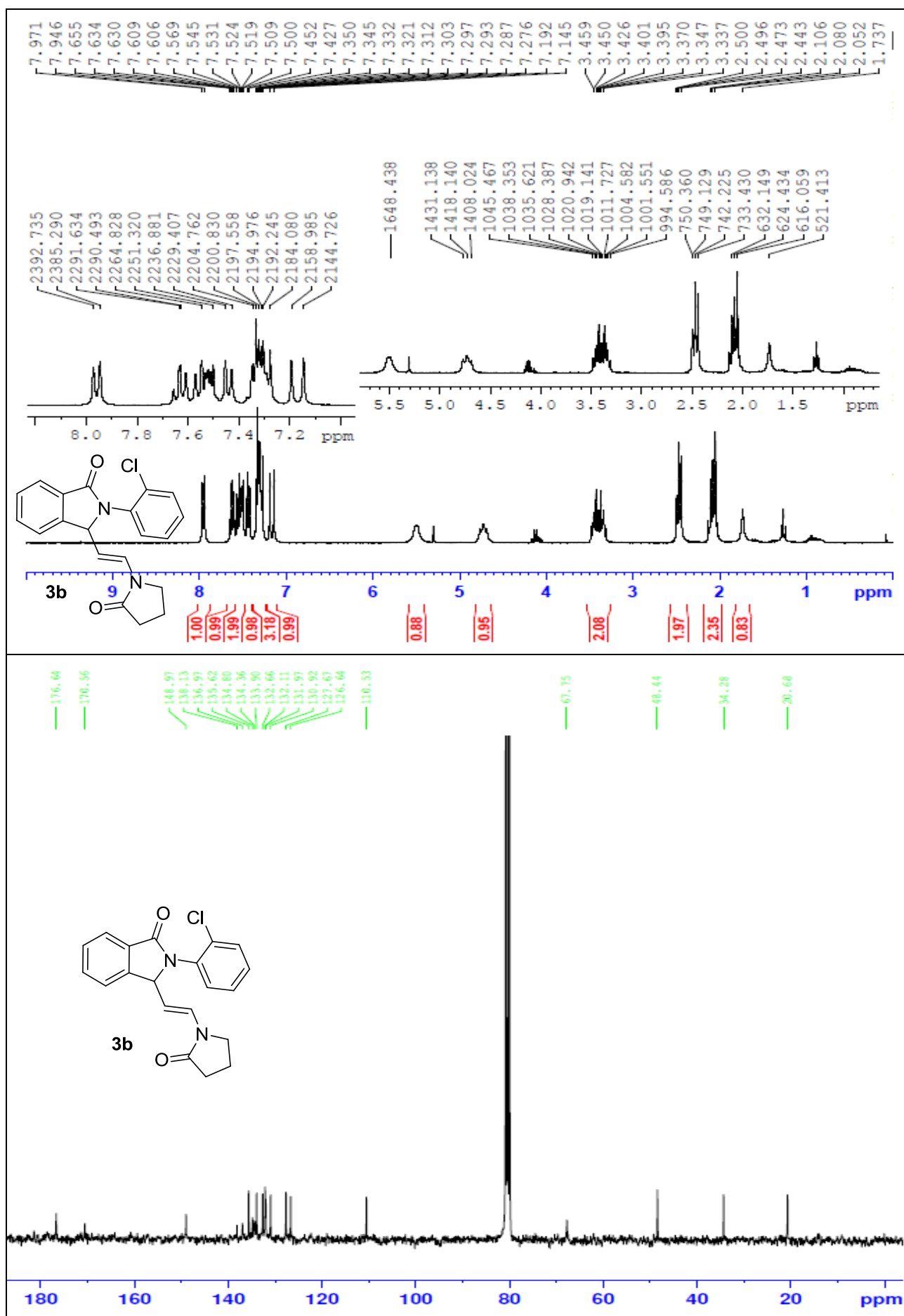




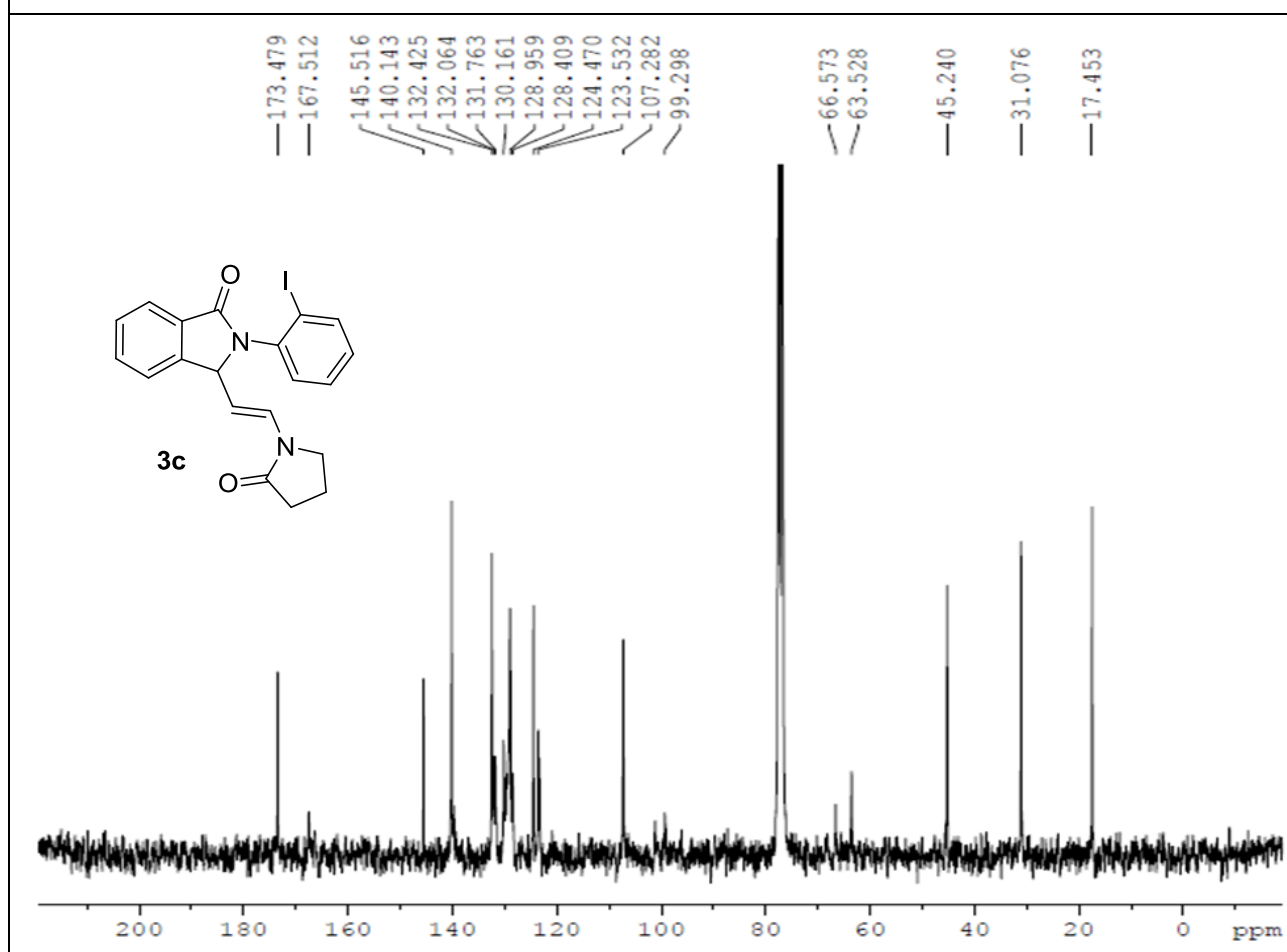
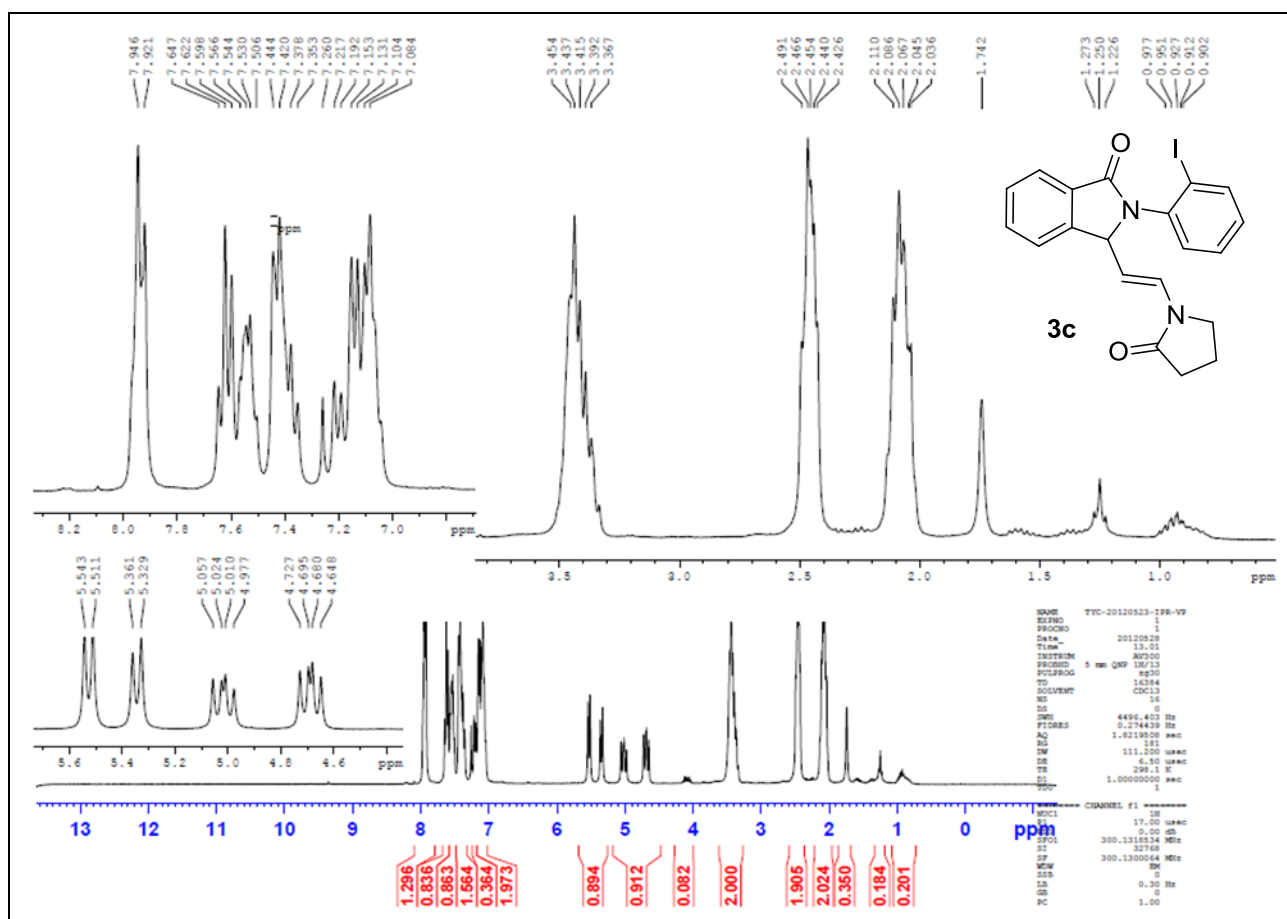




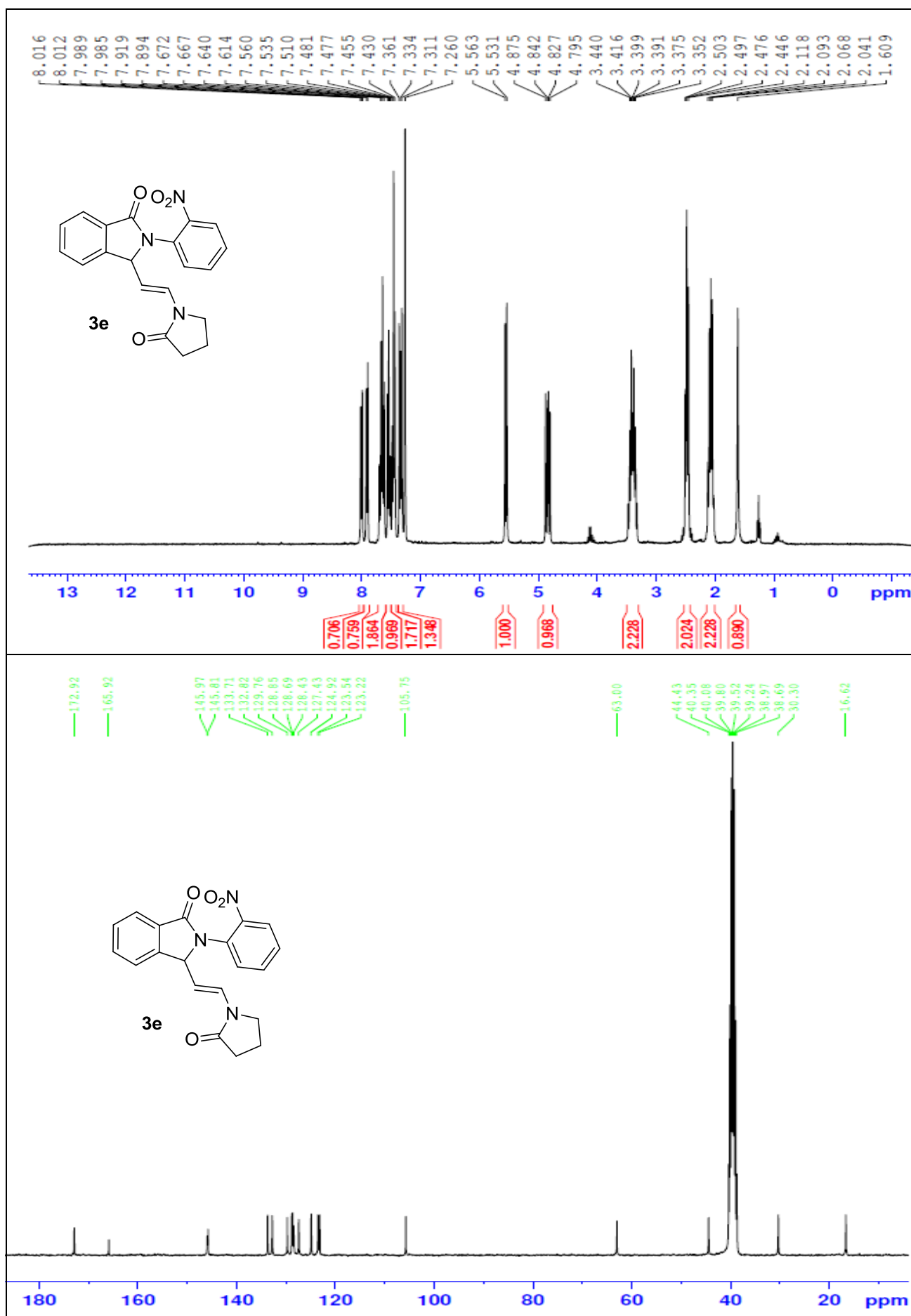


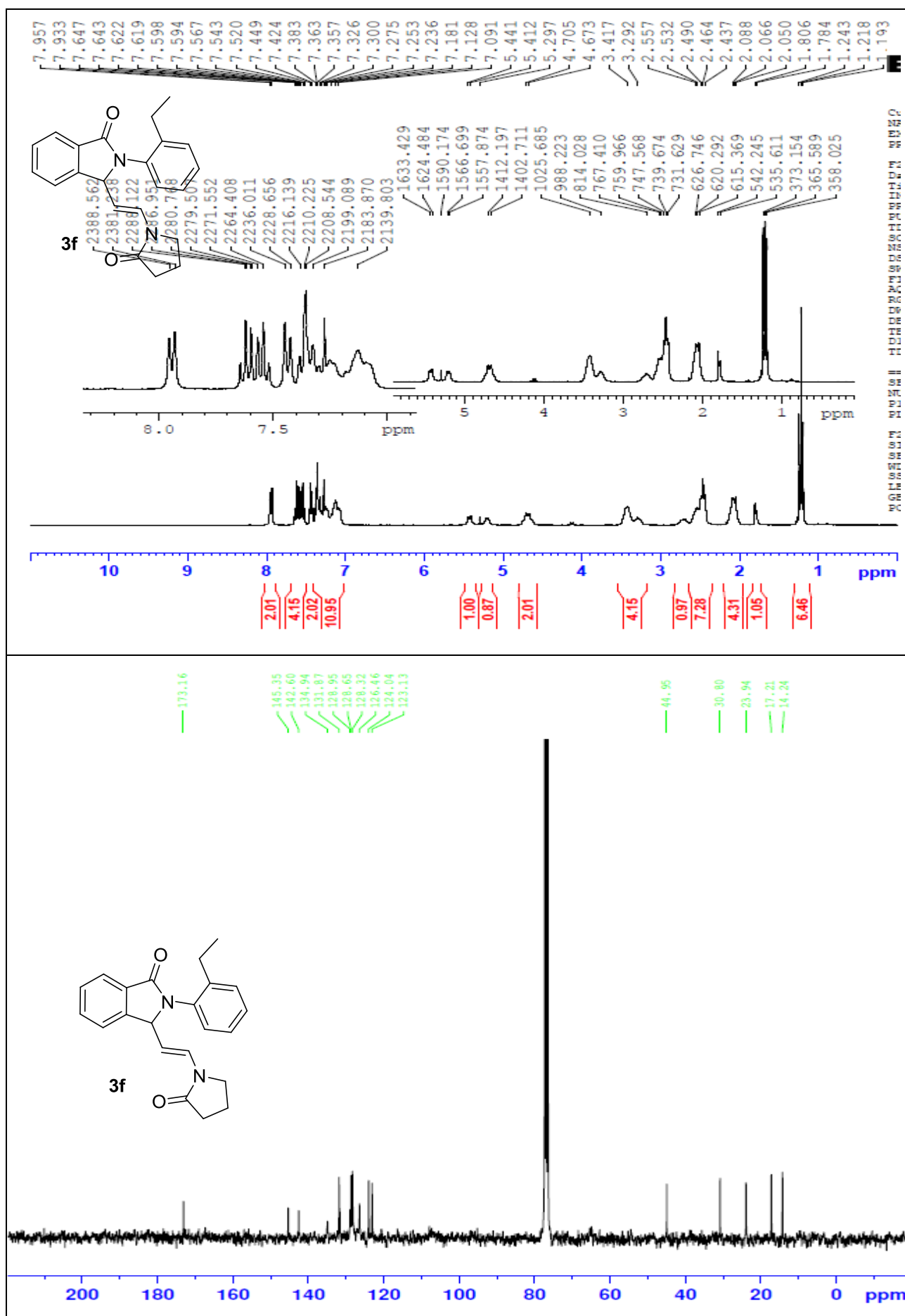


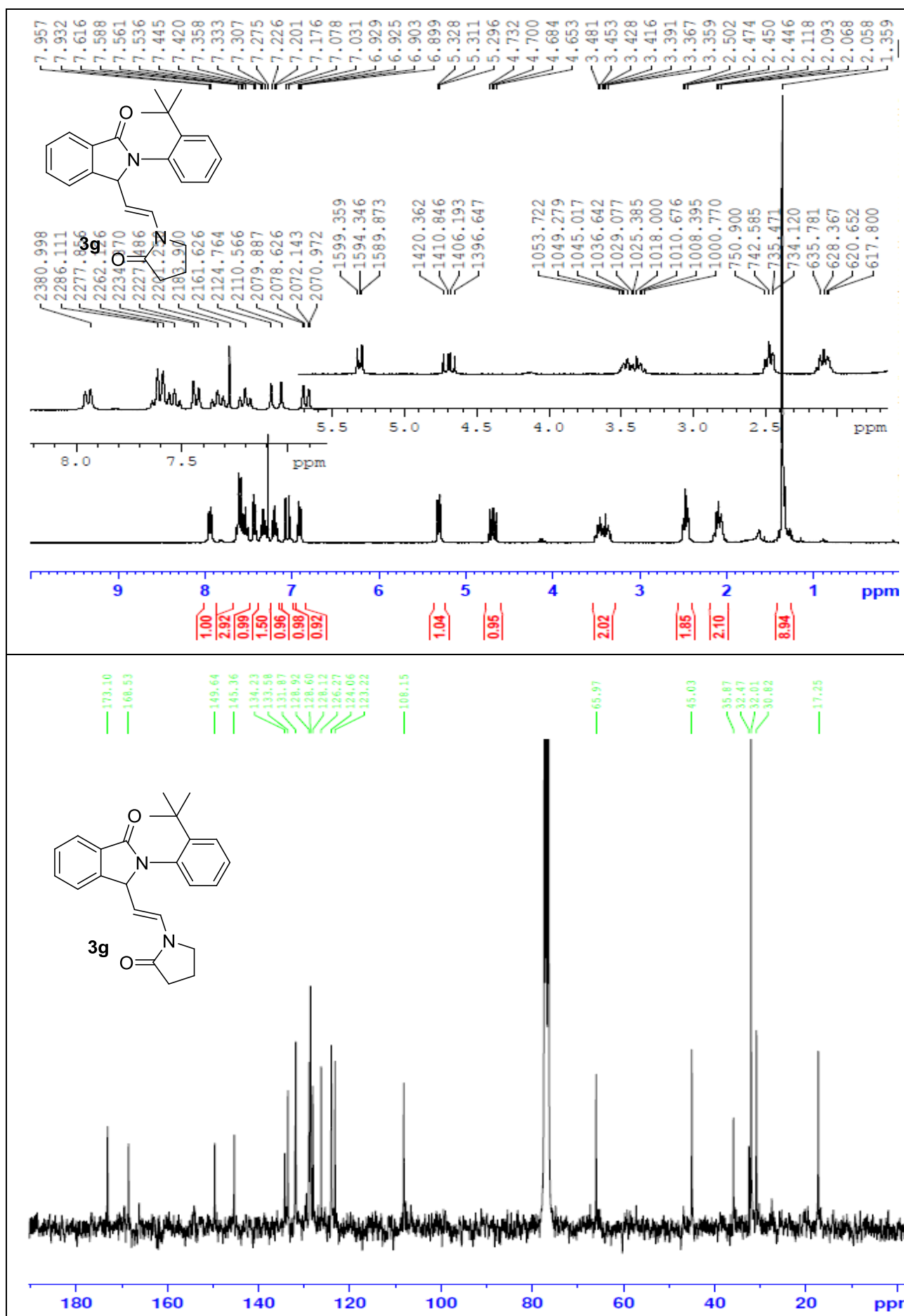


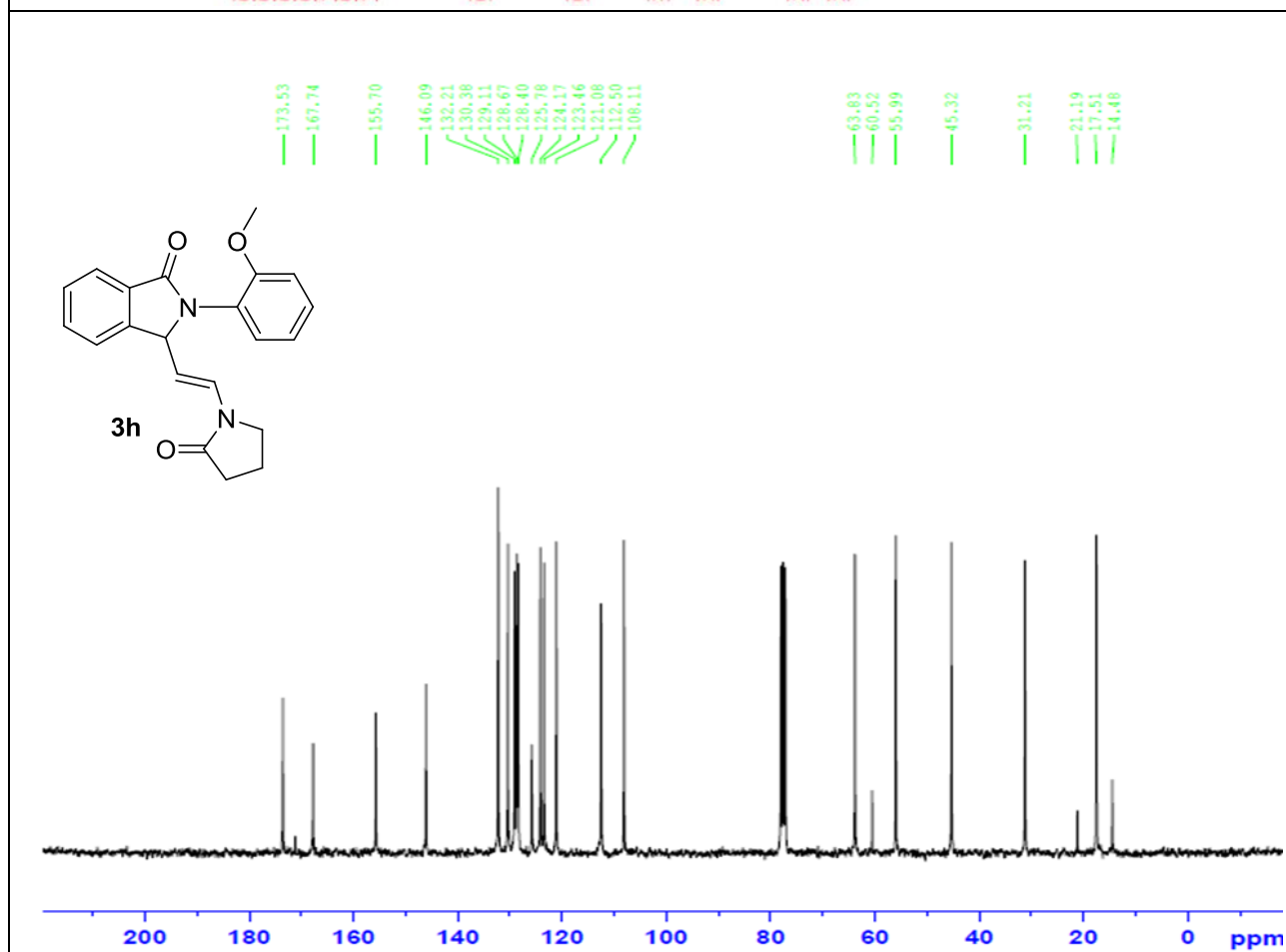
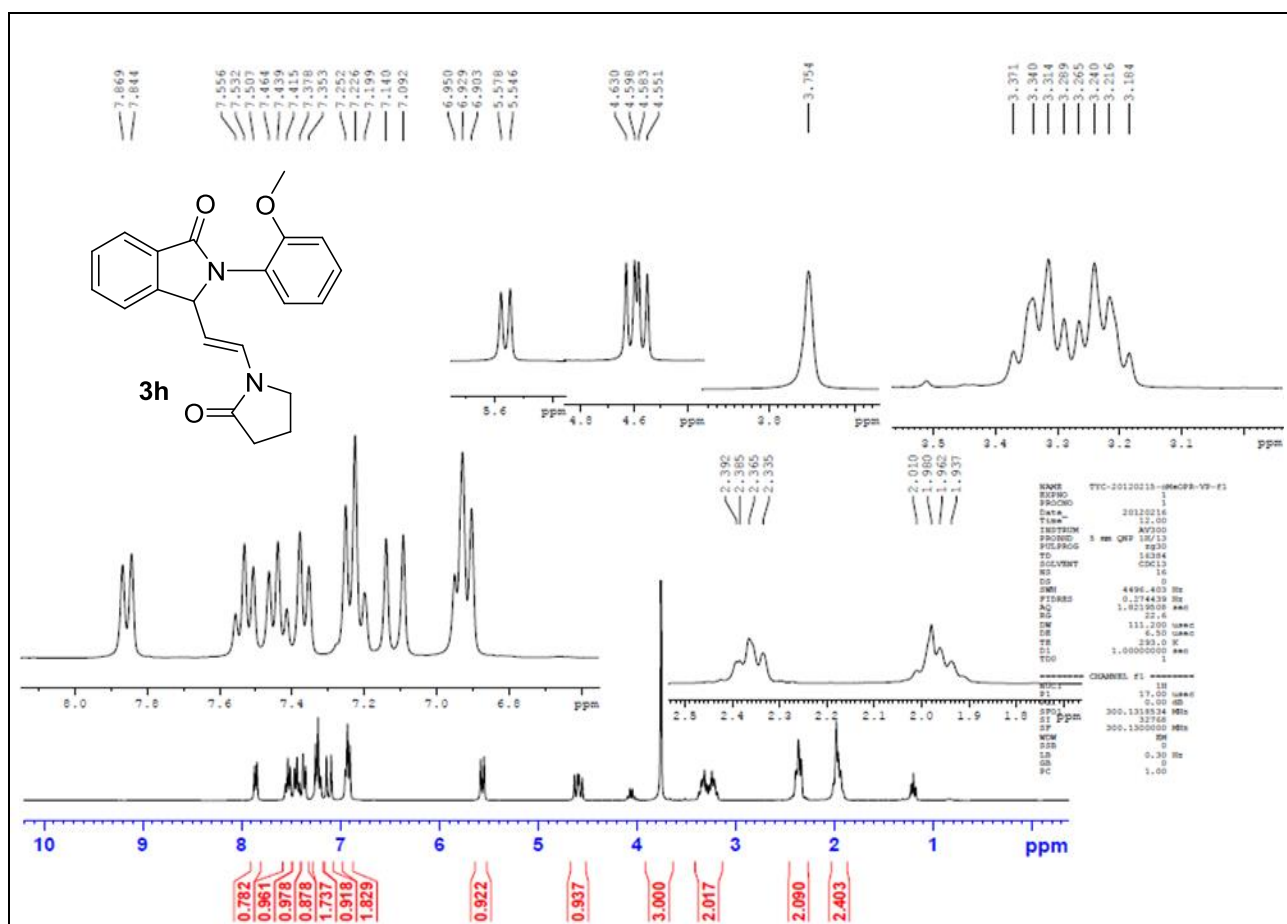


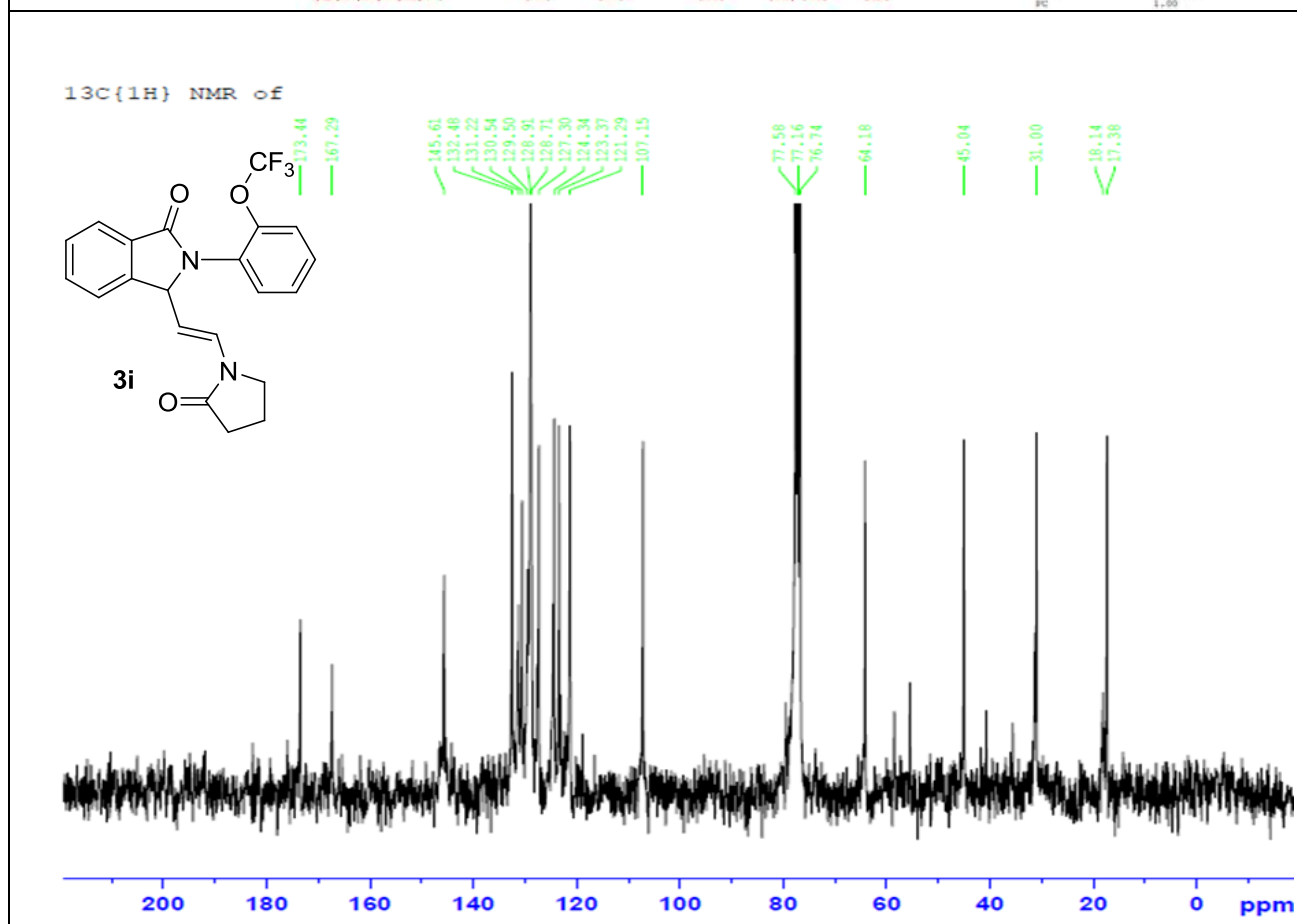
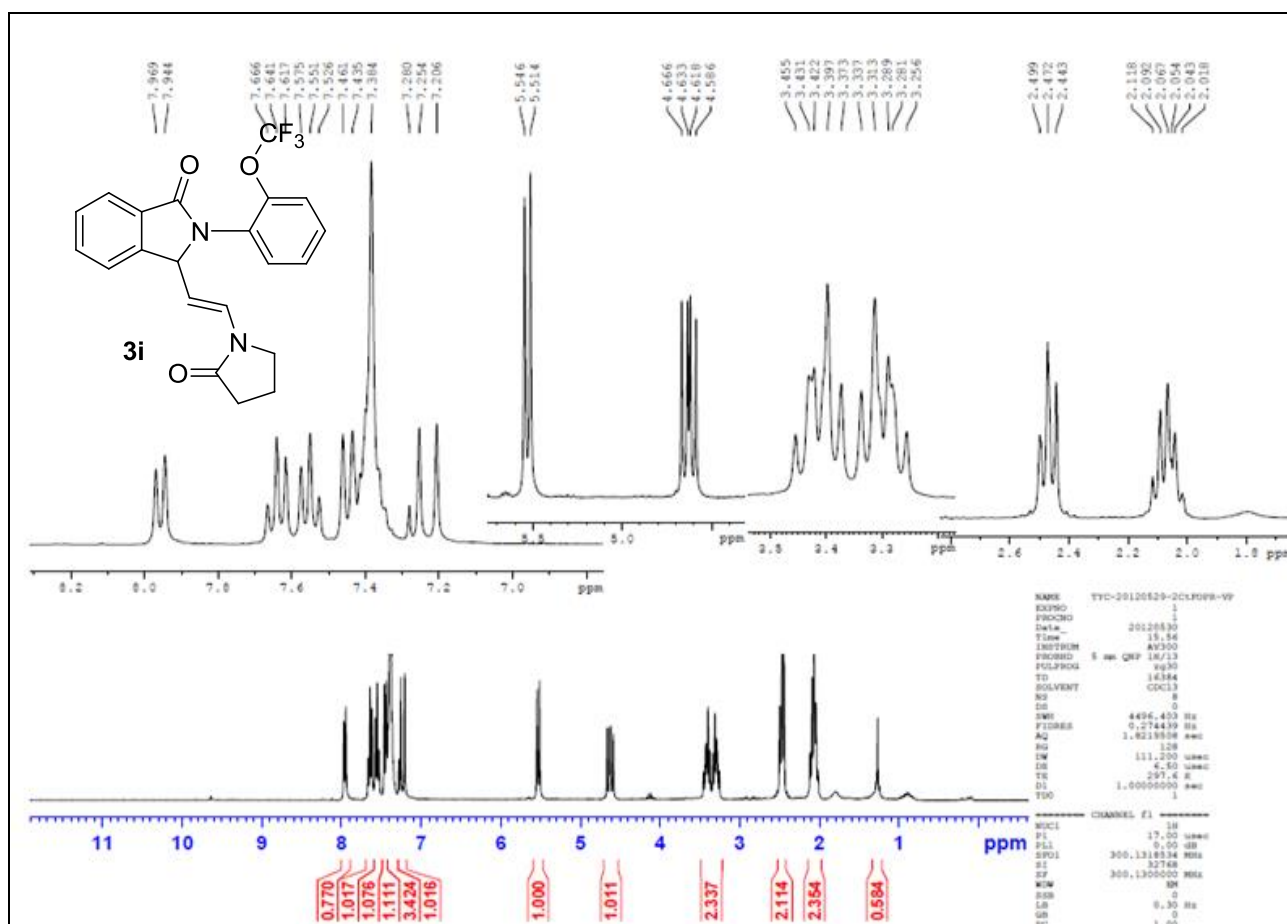


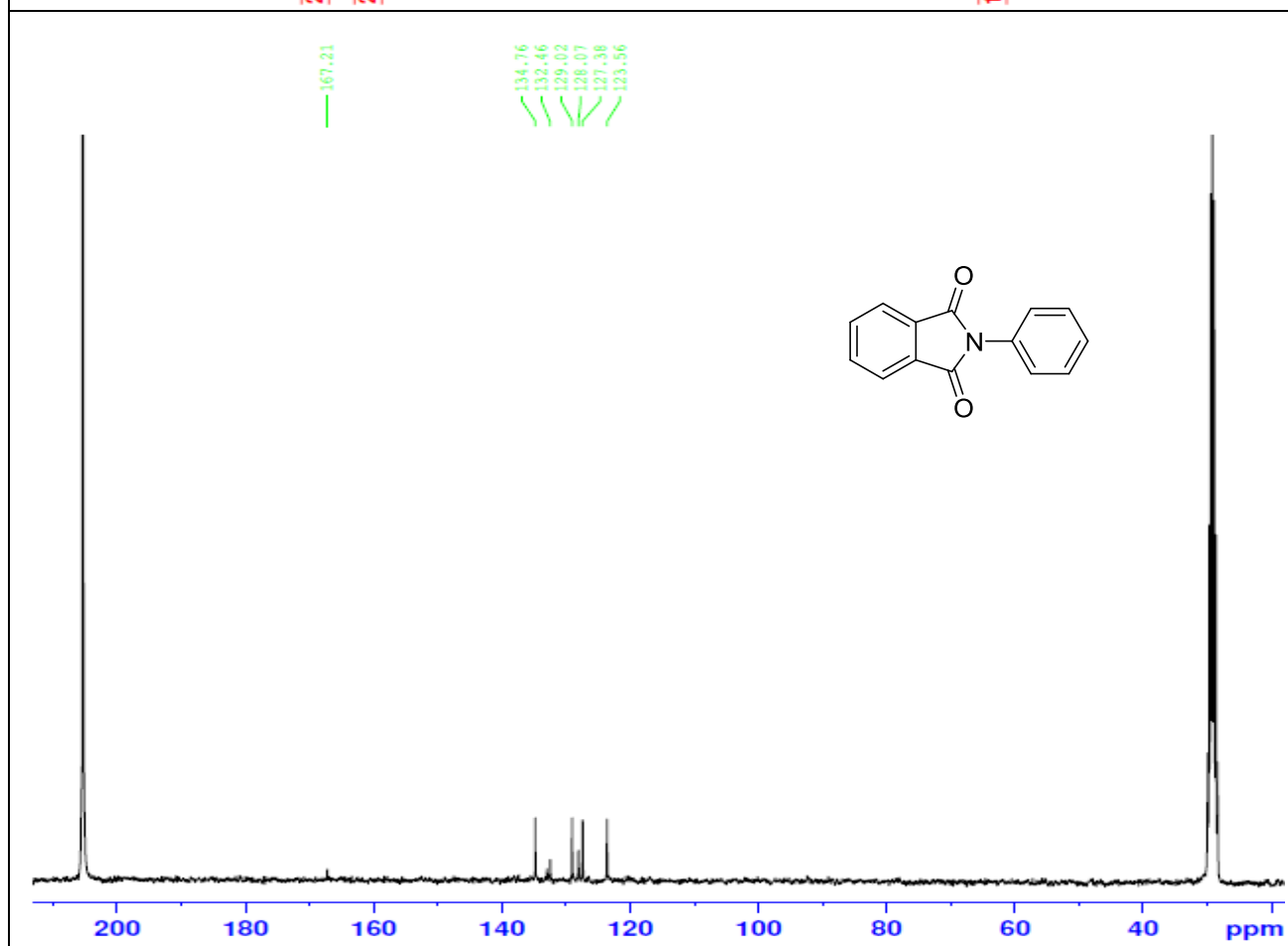
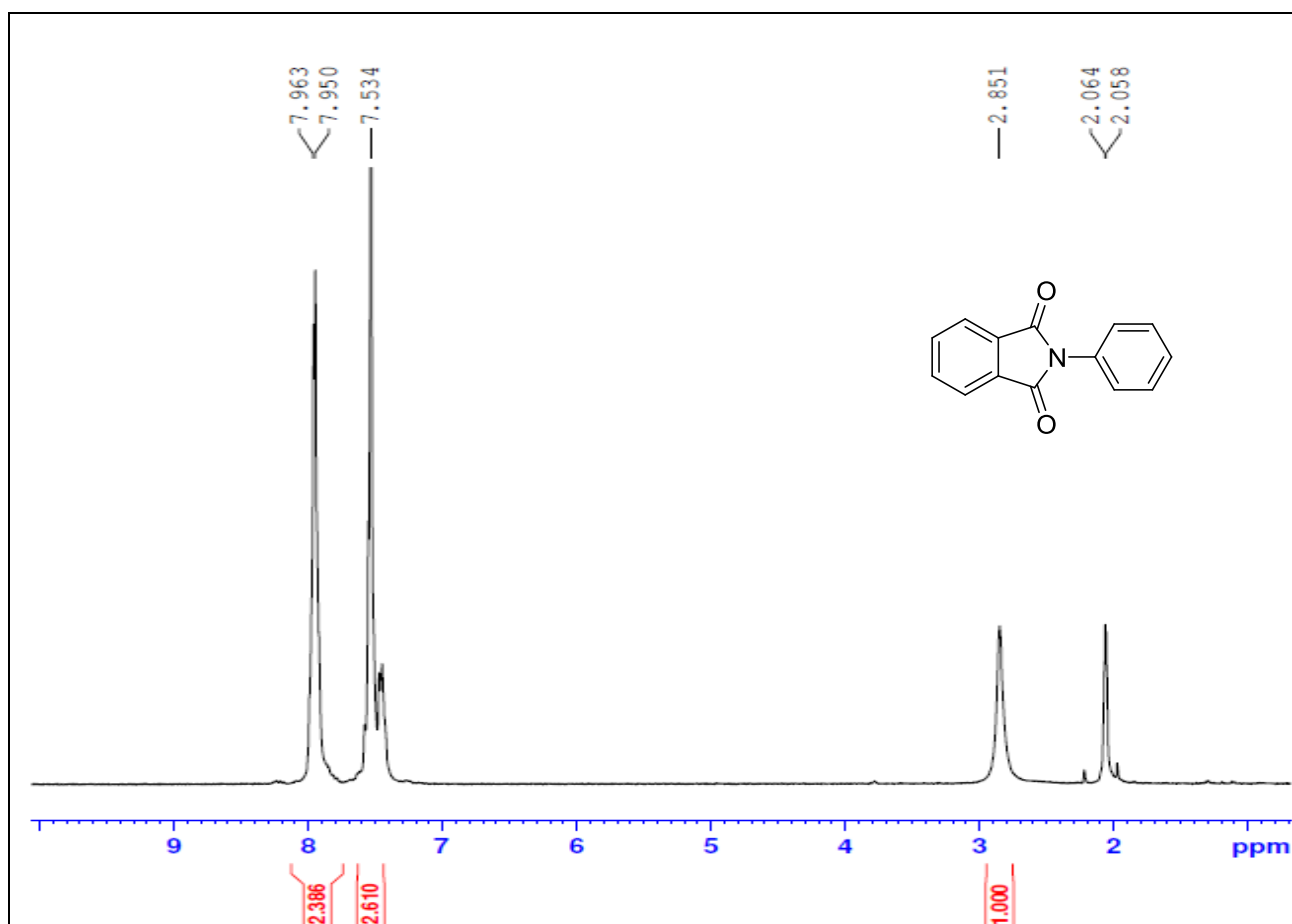




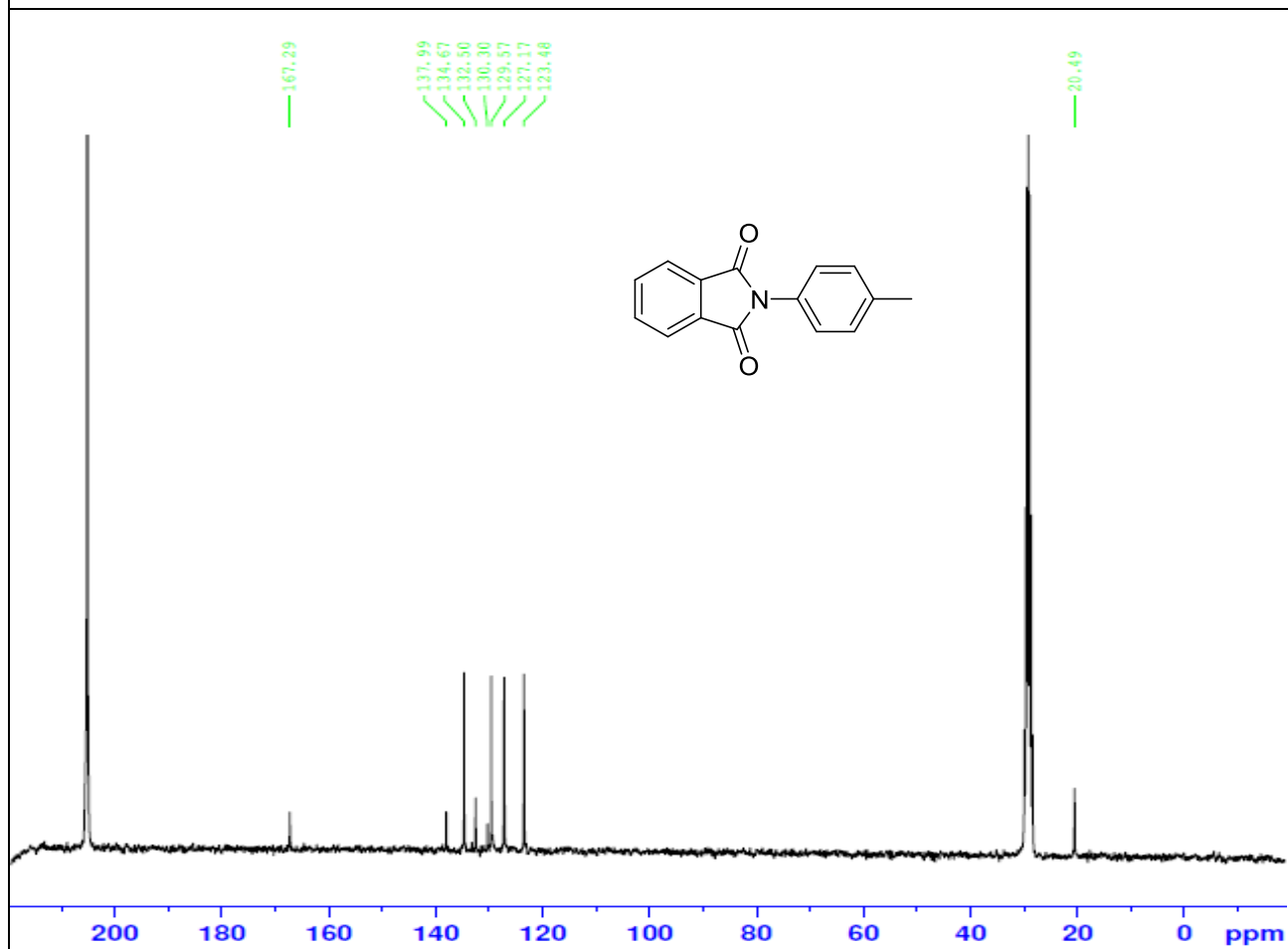
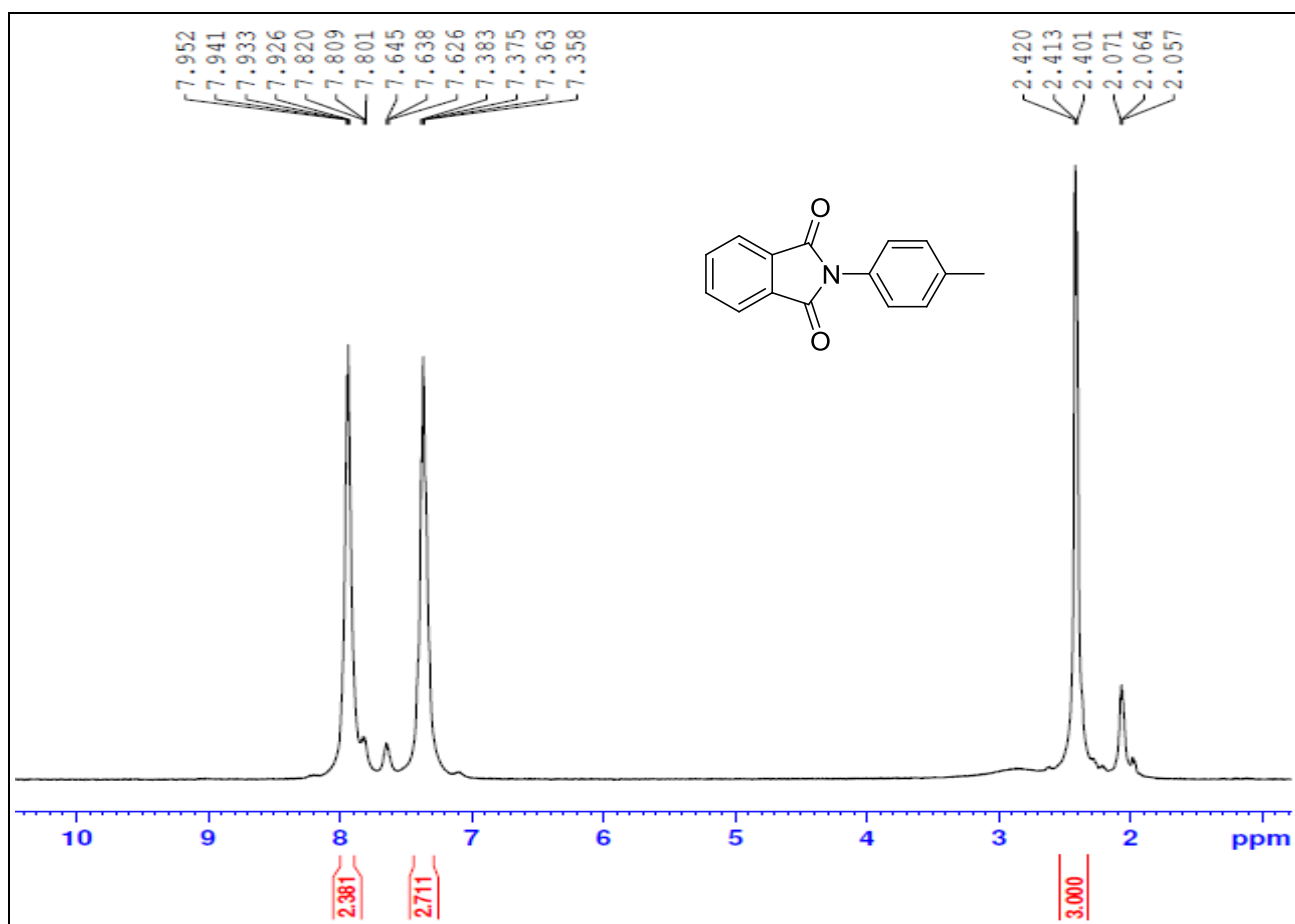


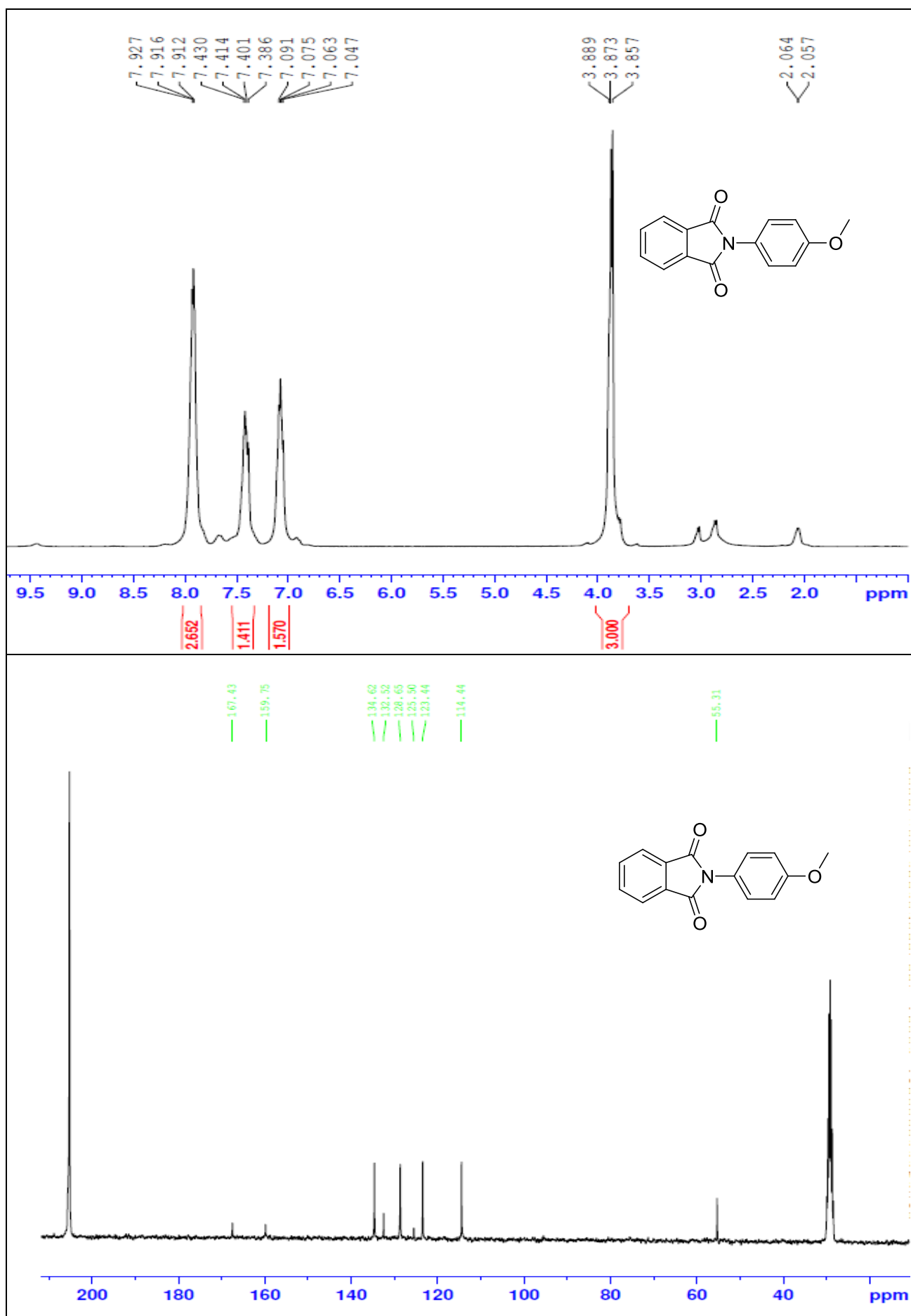


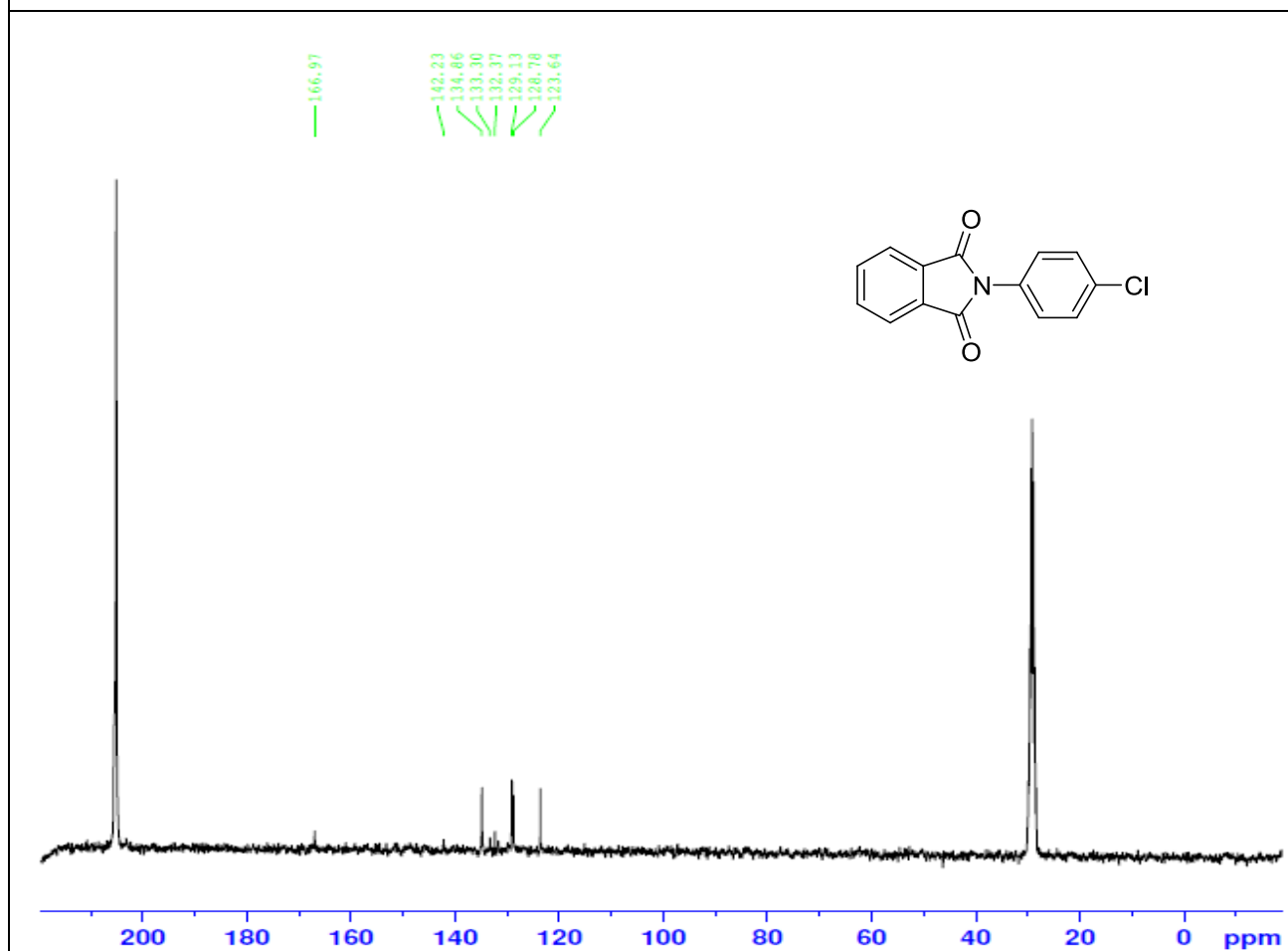
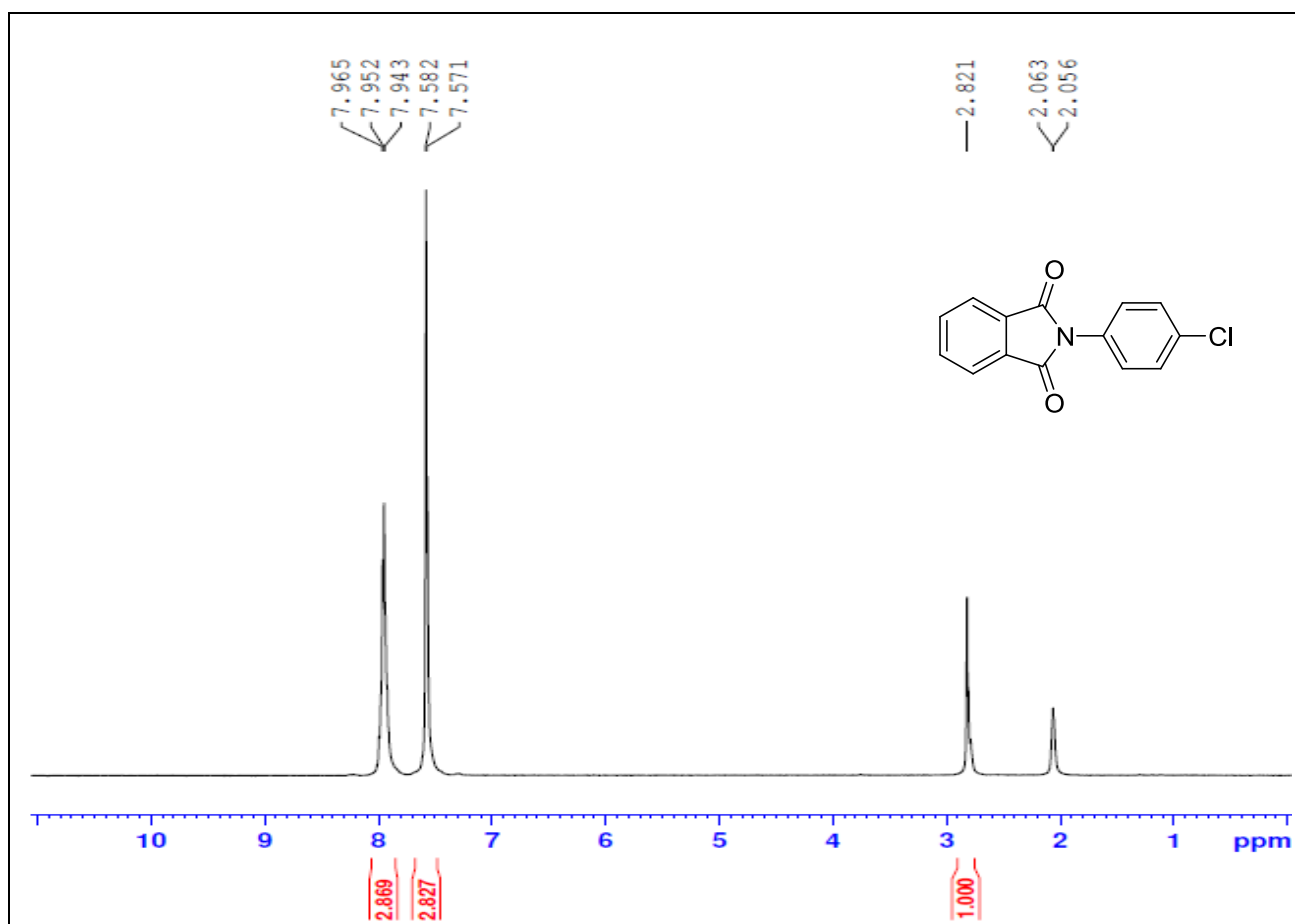


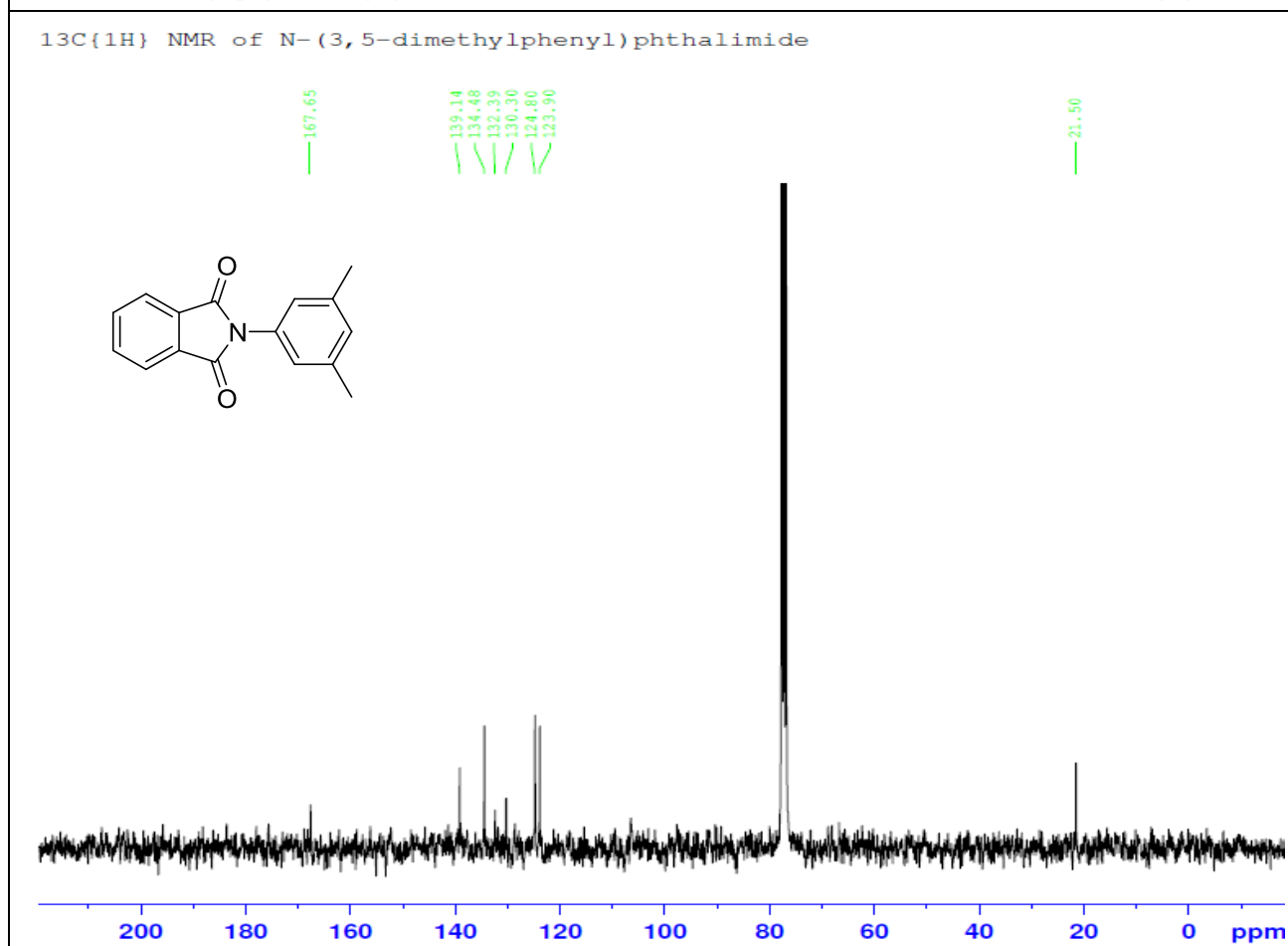
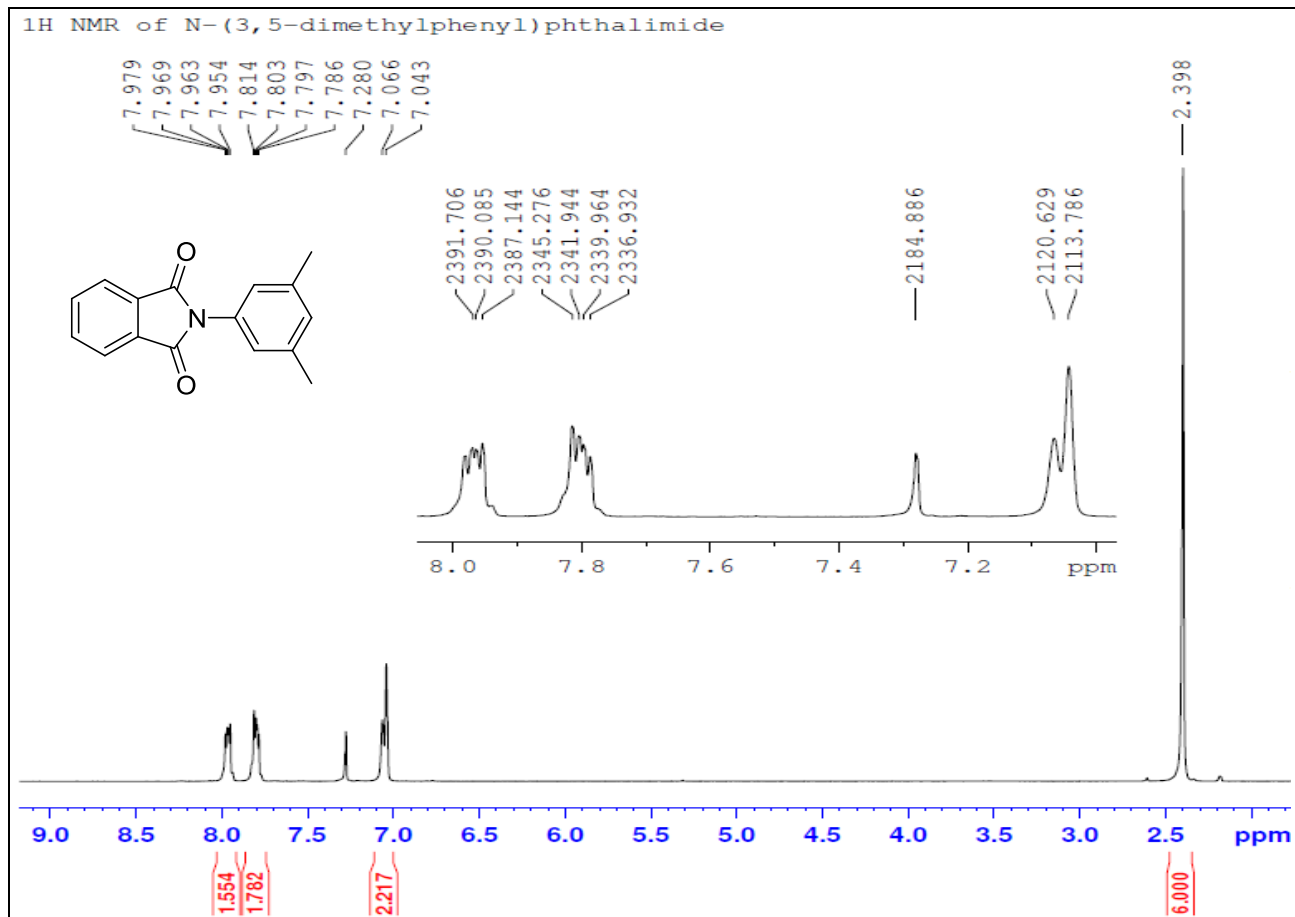




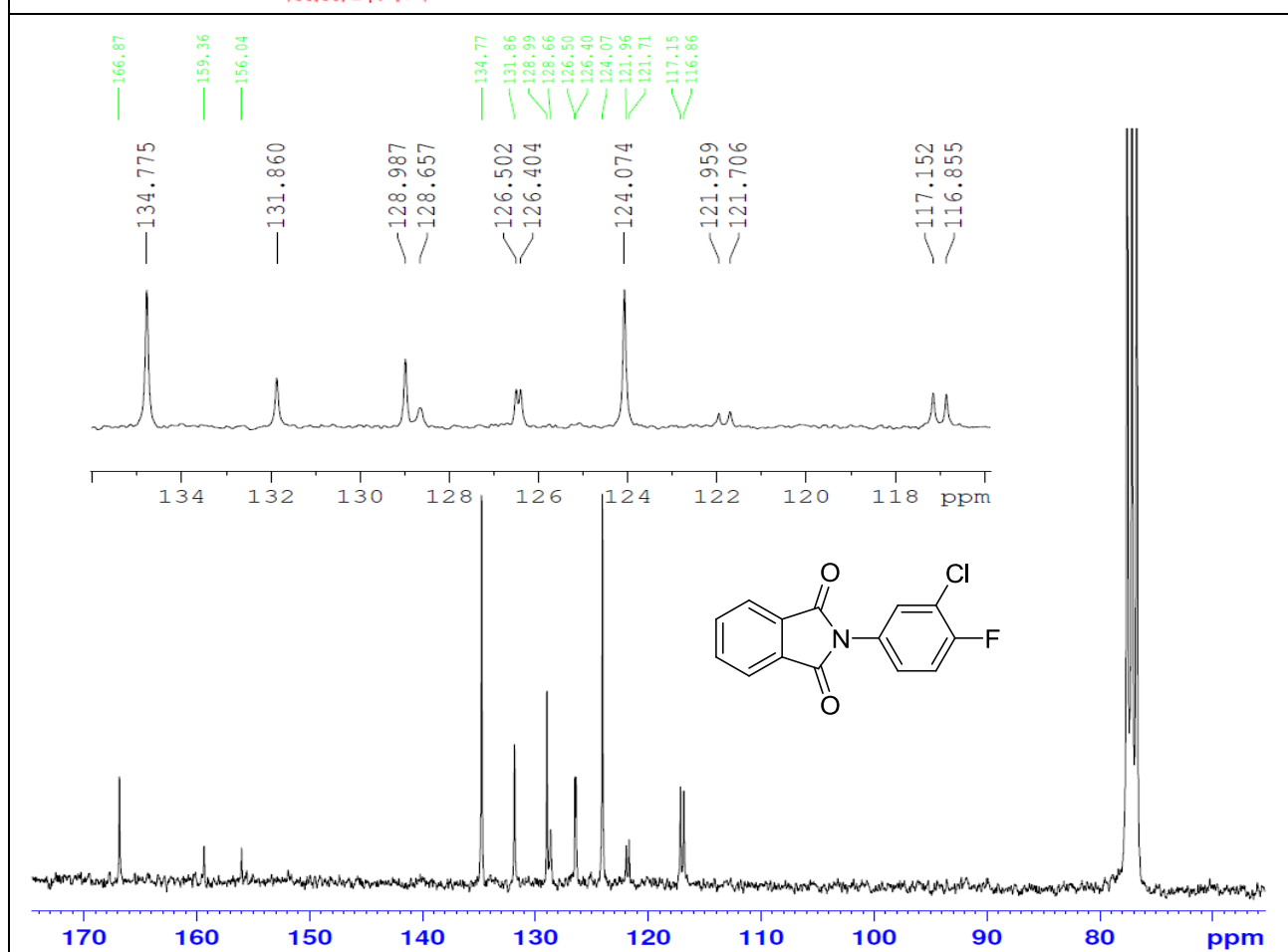
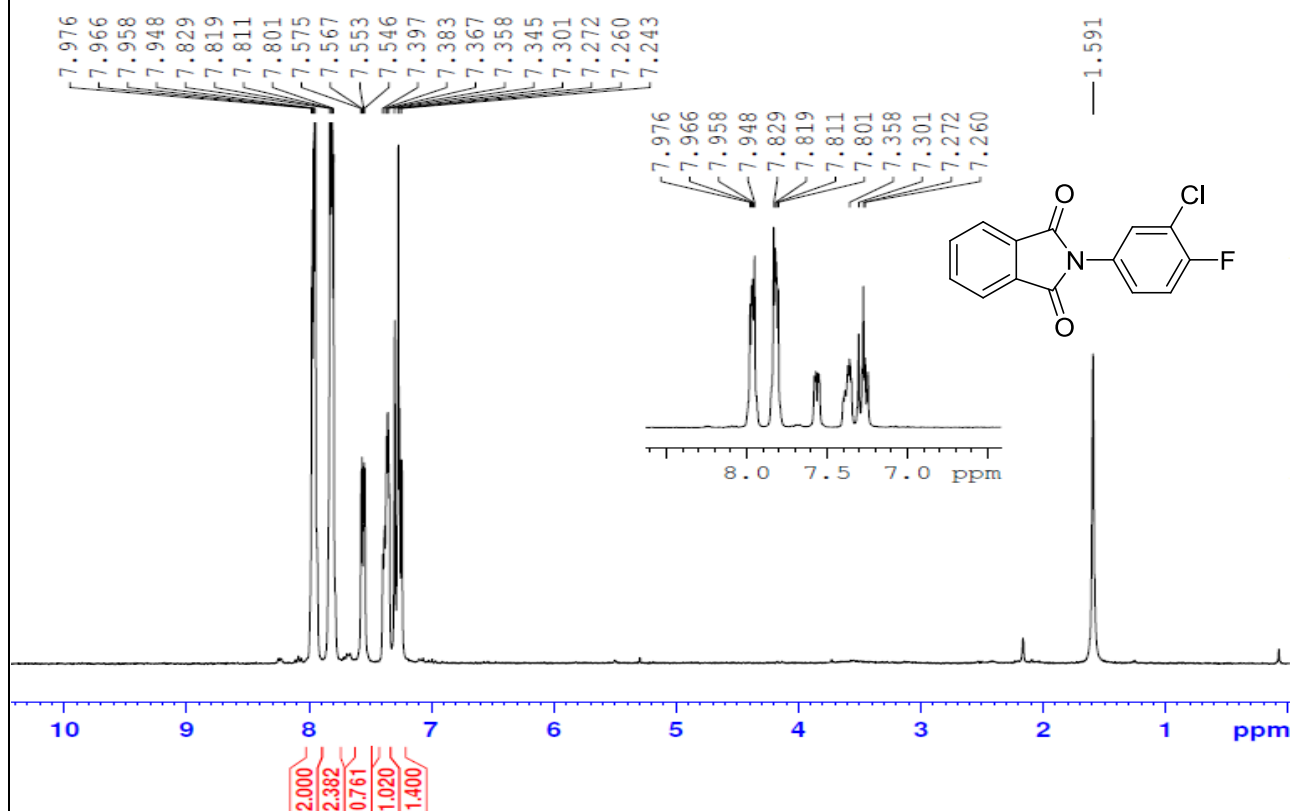


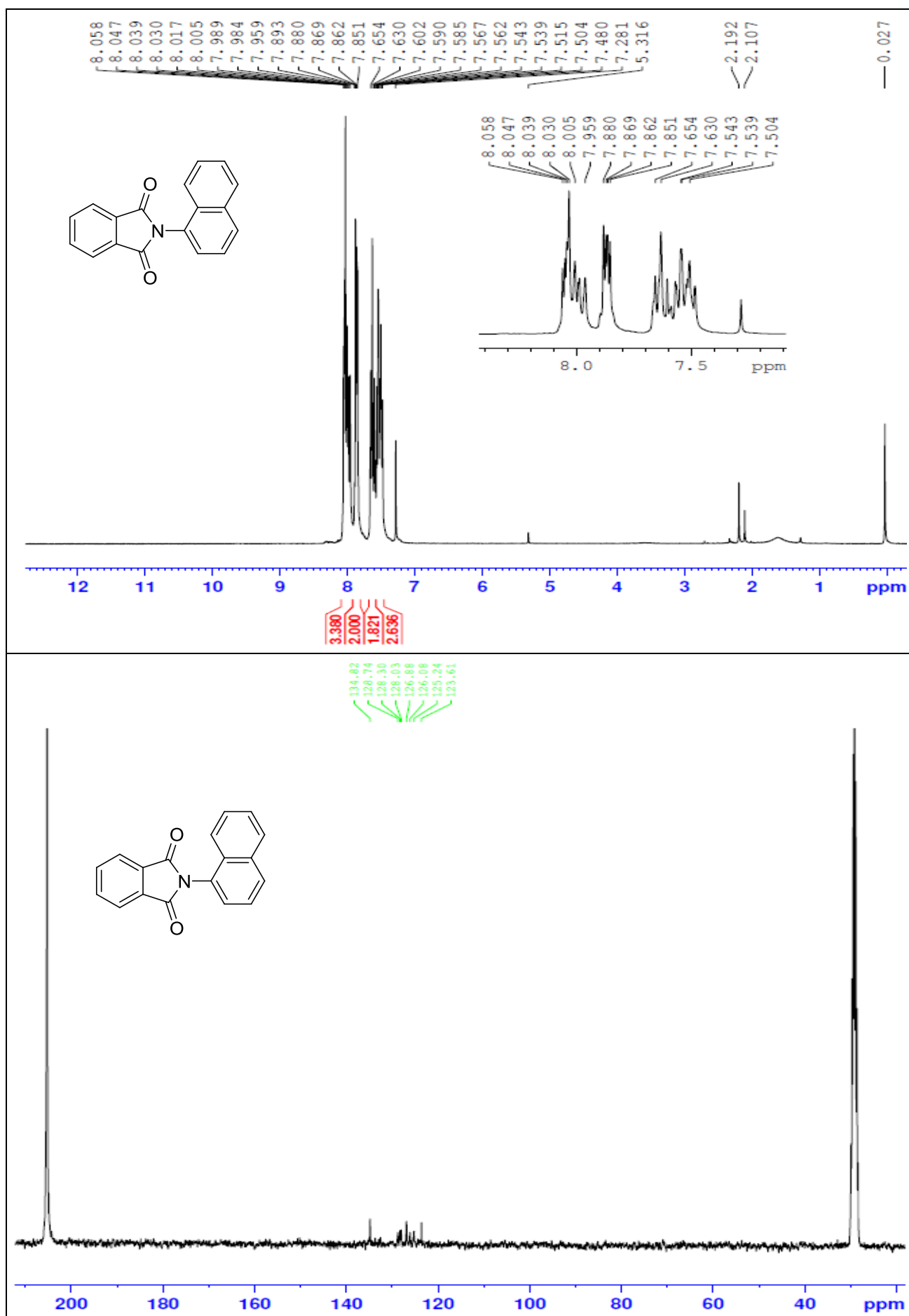


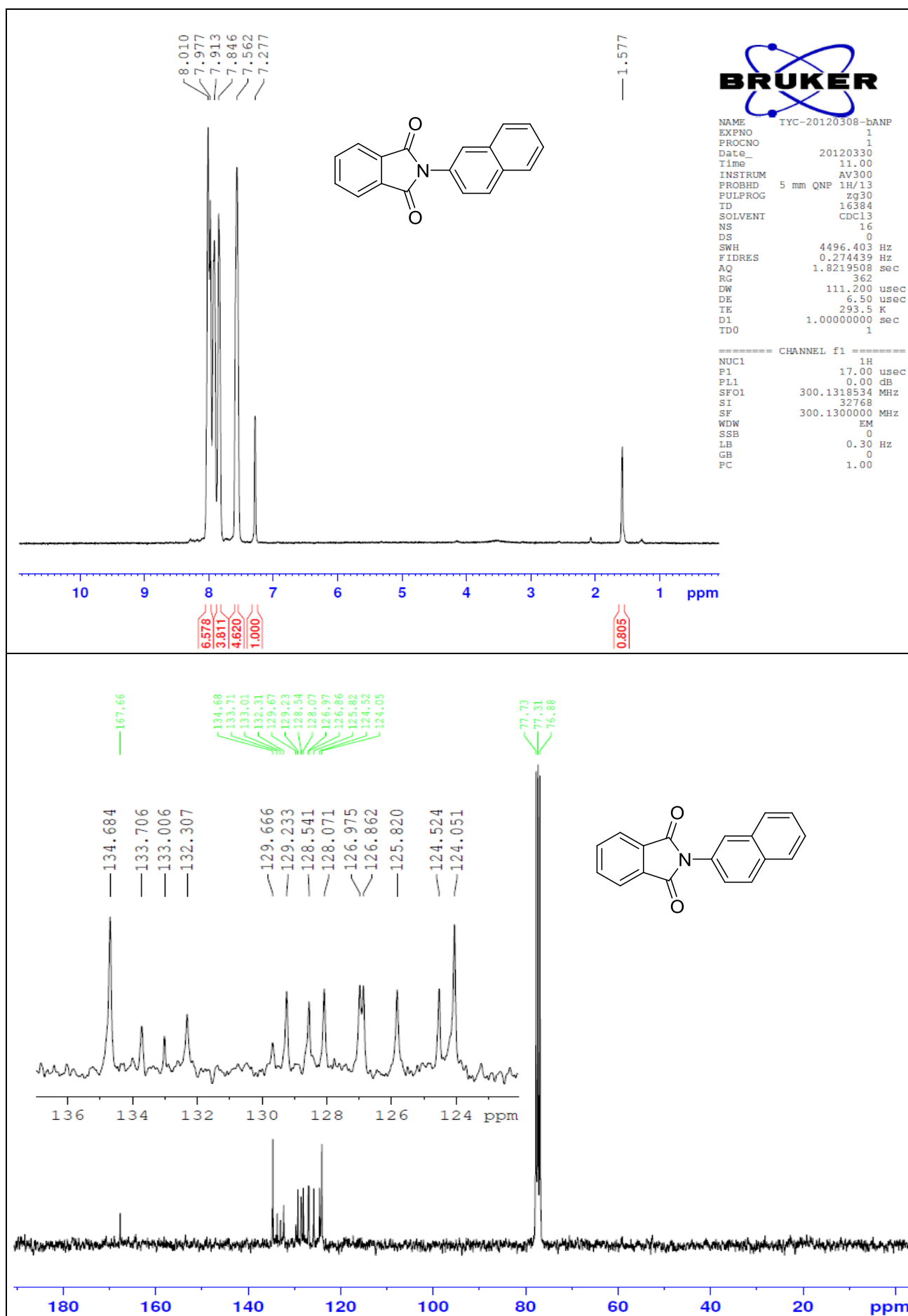


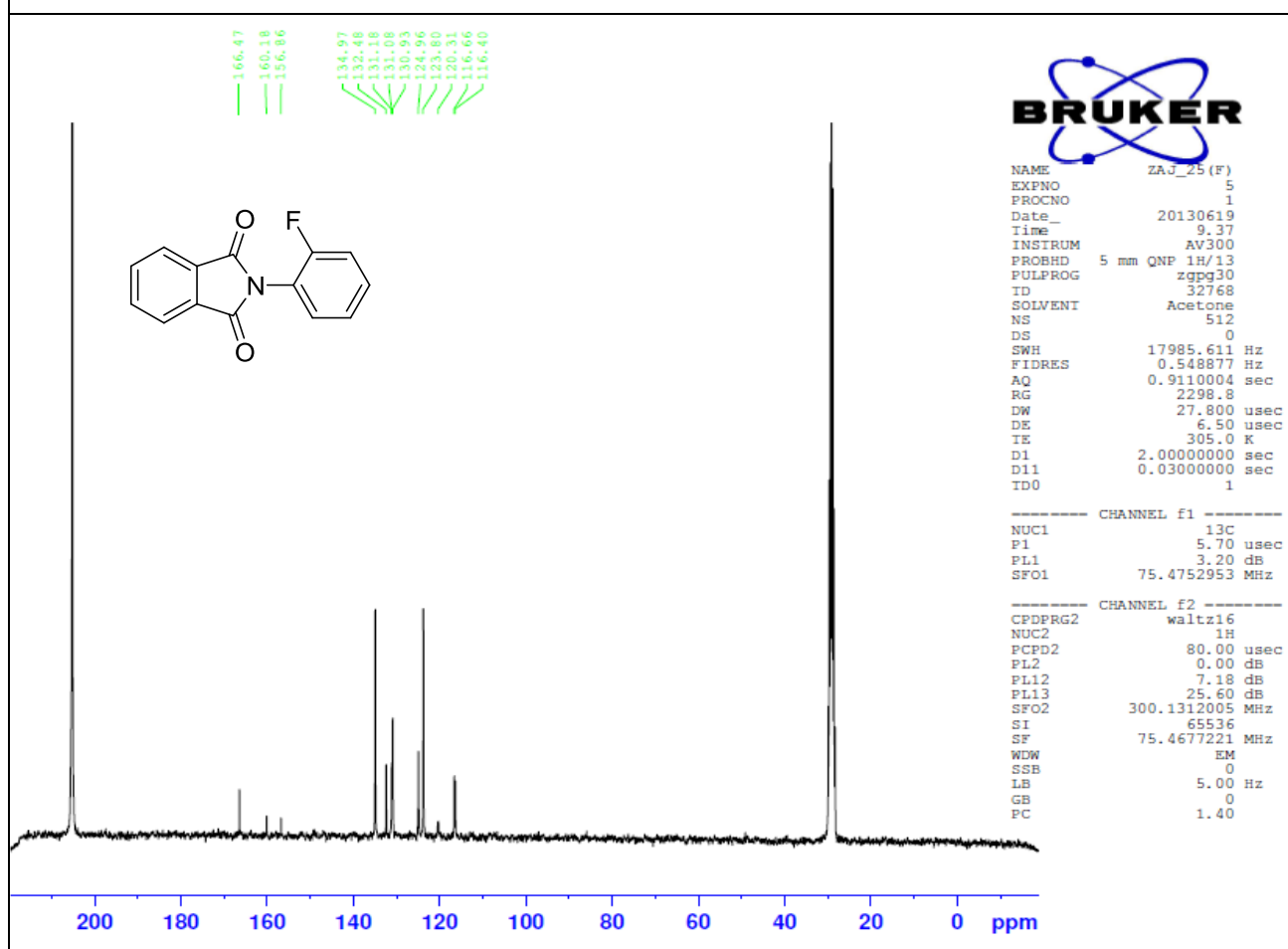
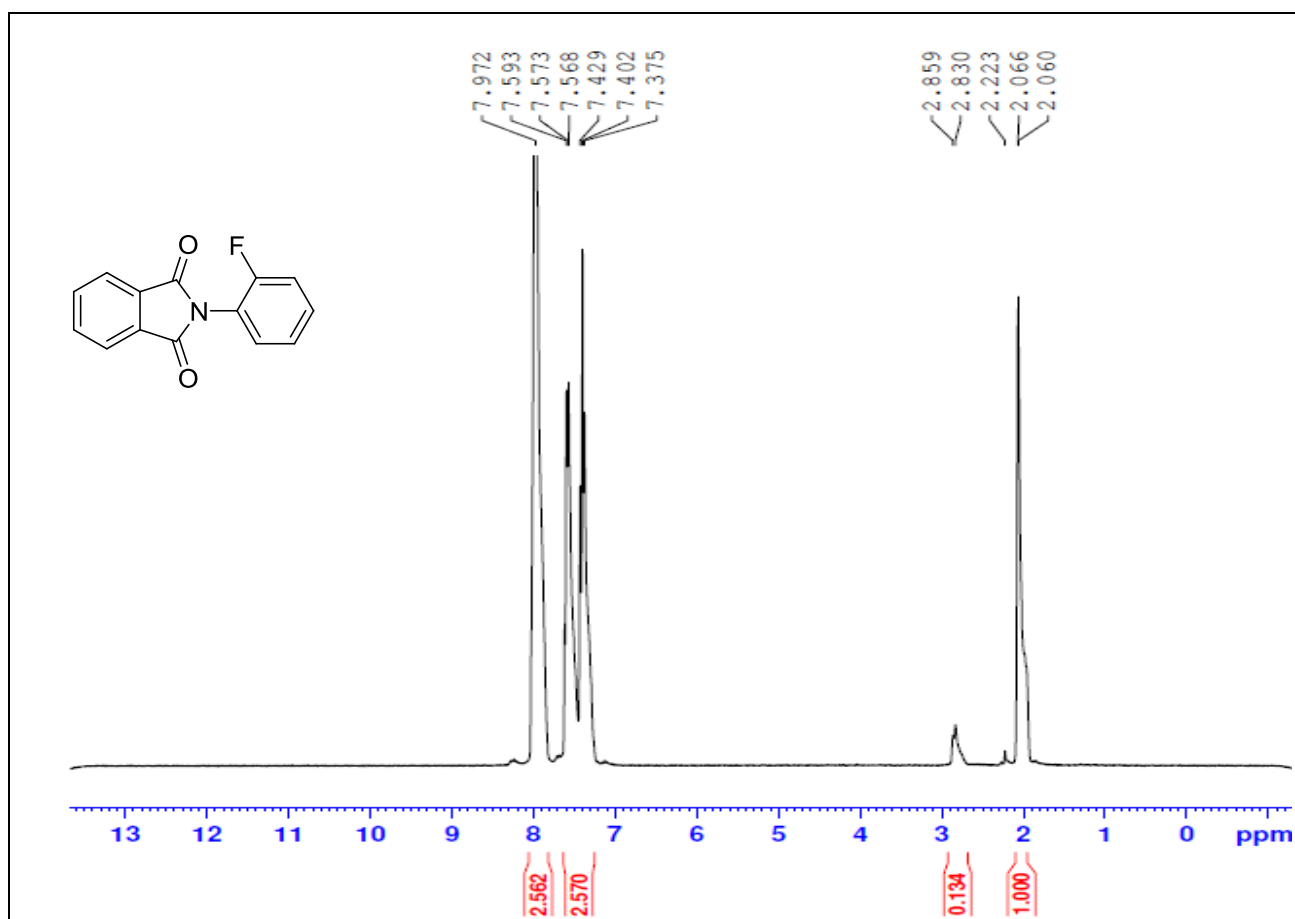


<sup>1</sup>H NMR of N-(3-chloro-4-fluorophenyl)phthalimide



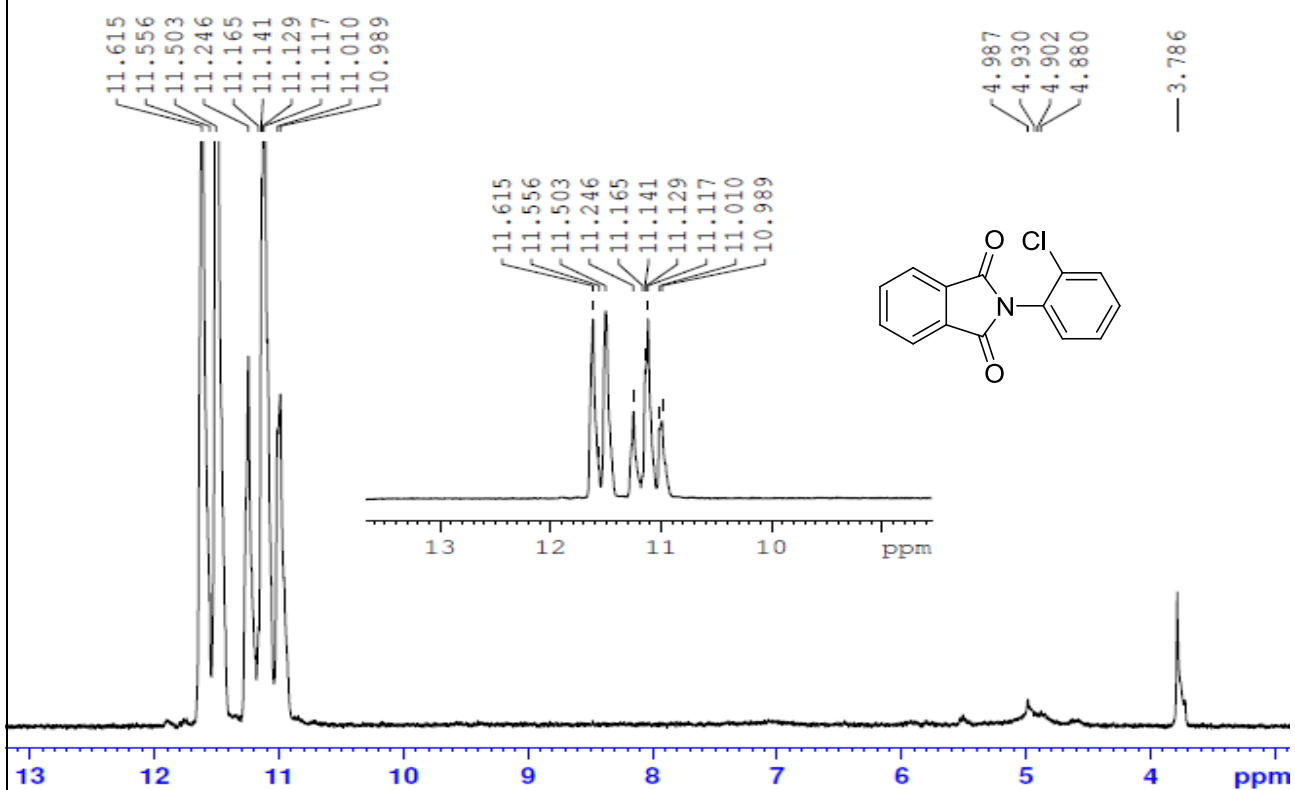




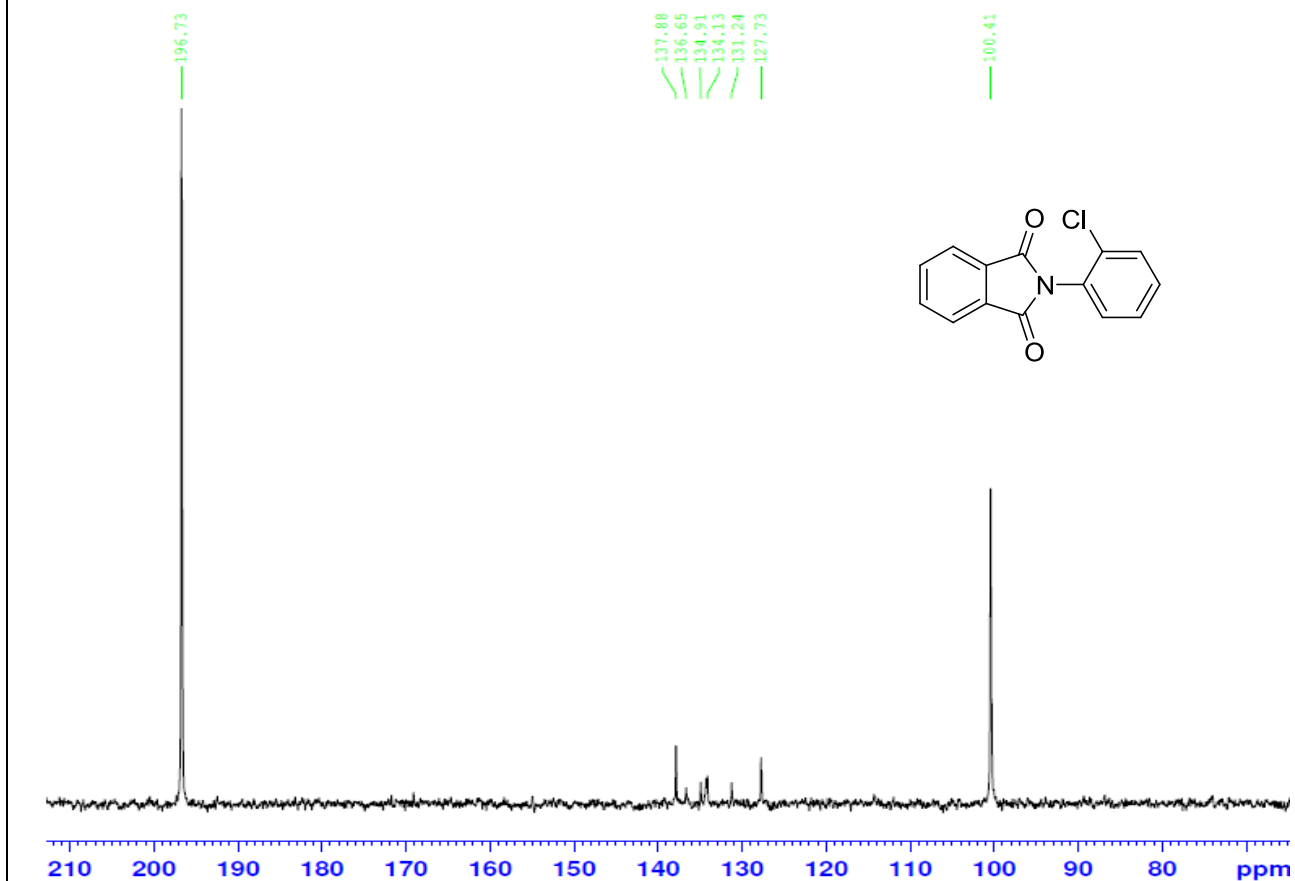


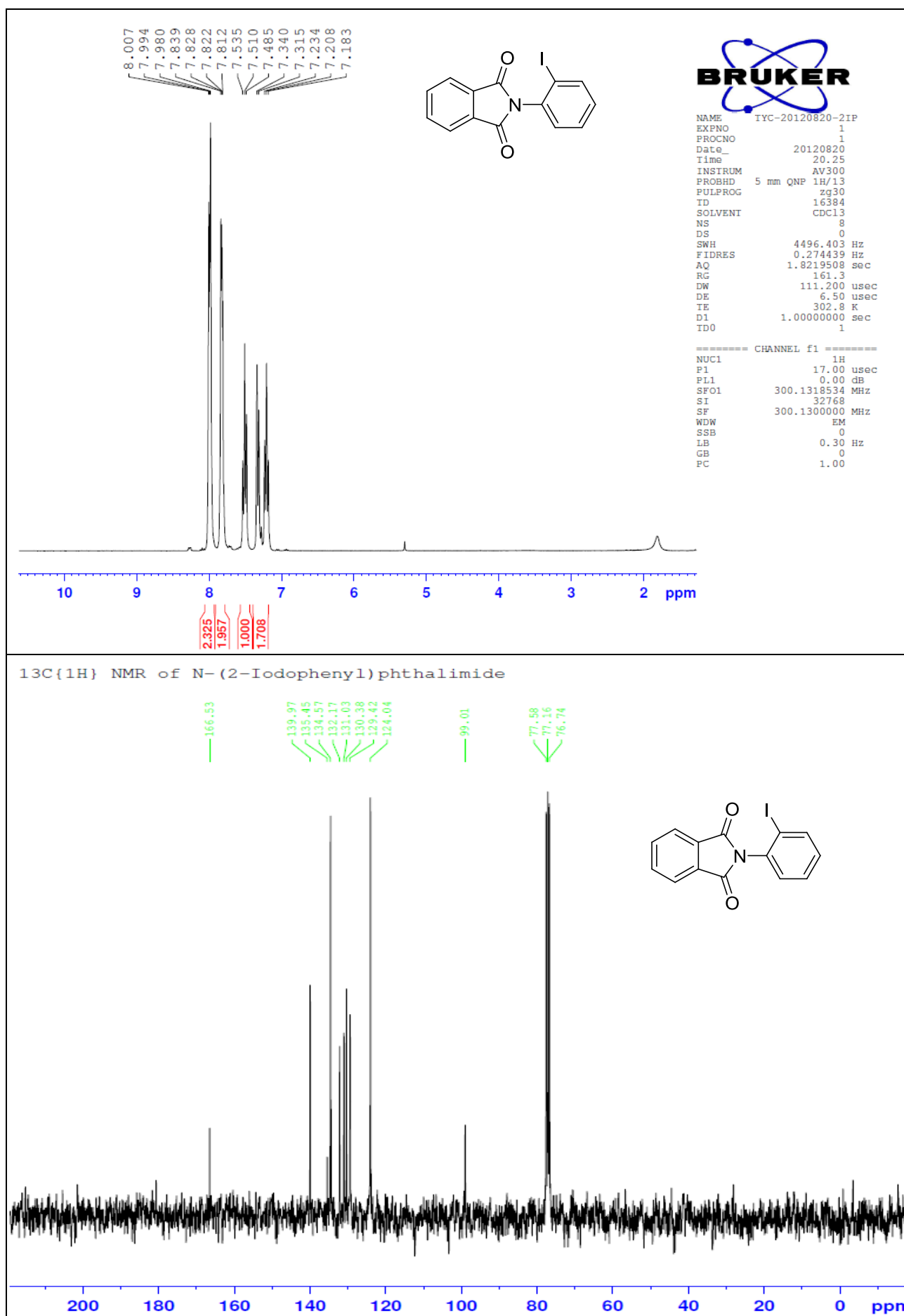


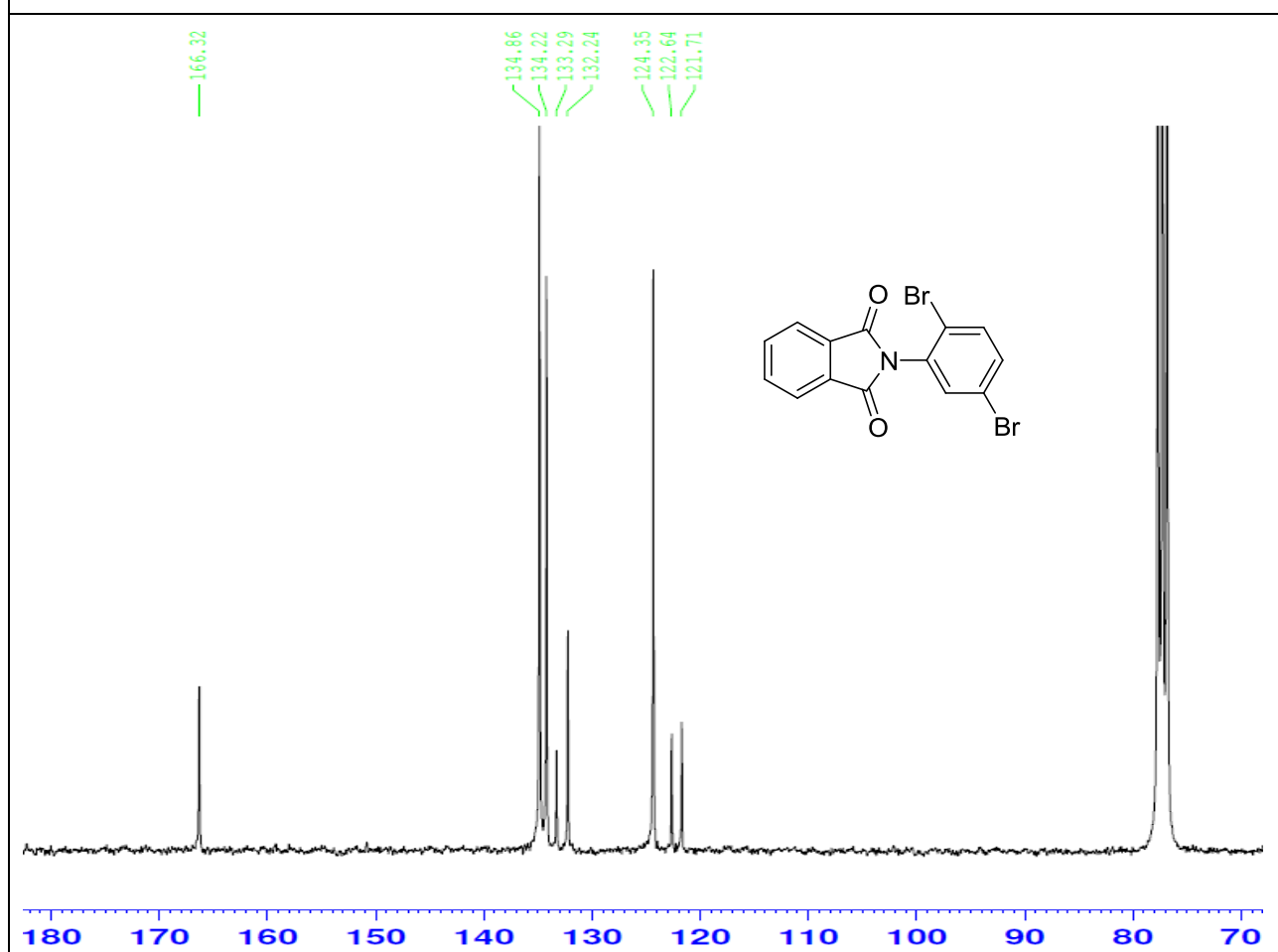
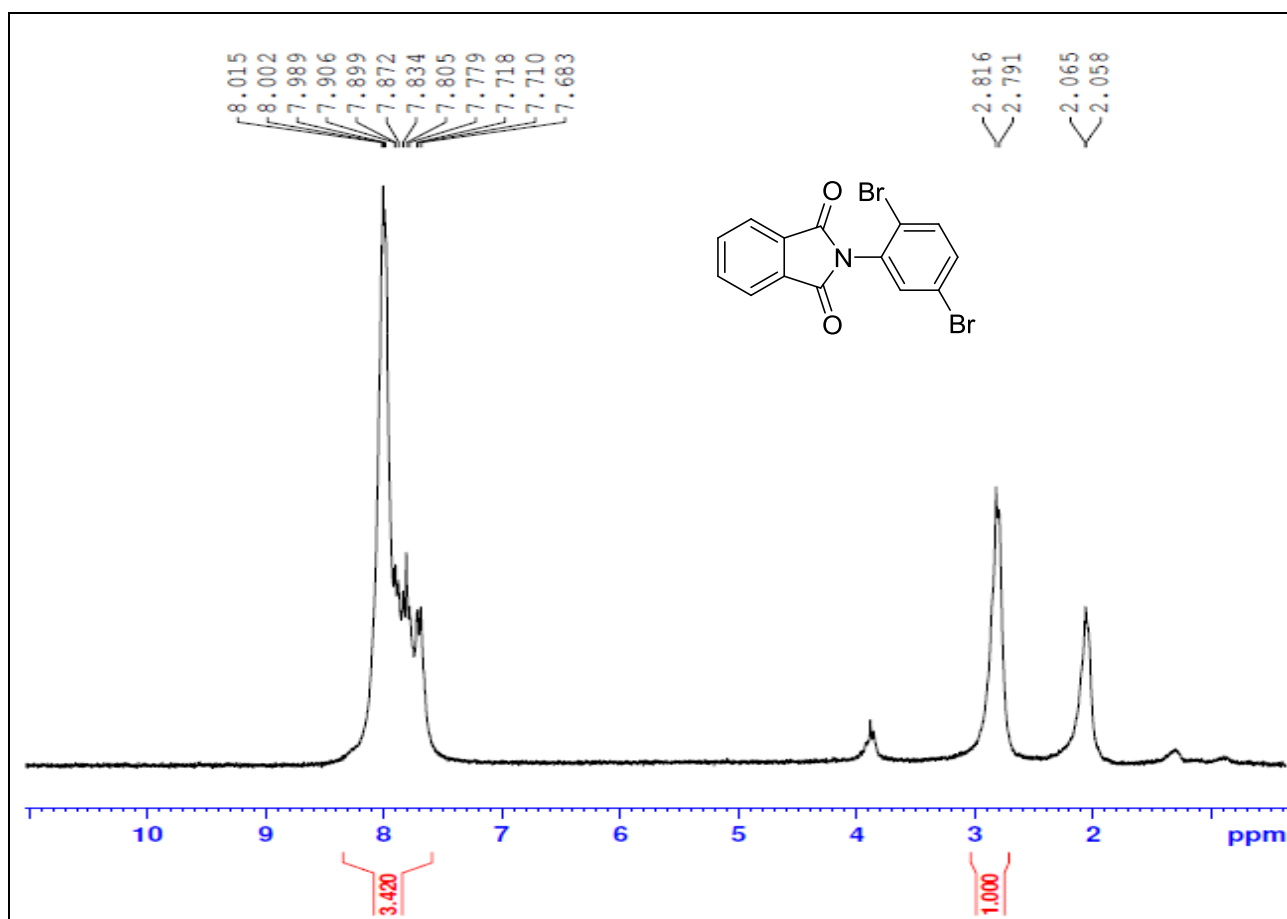
<sup>1</sup>H NMR of 2CP

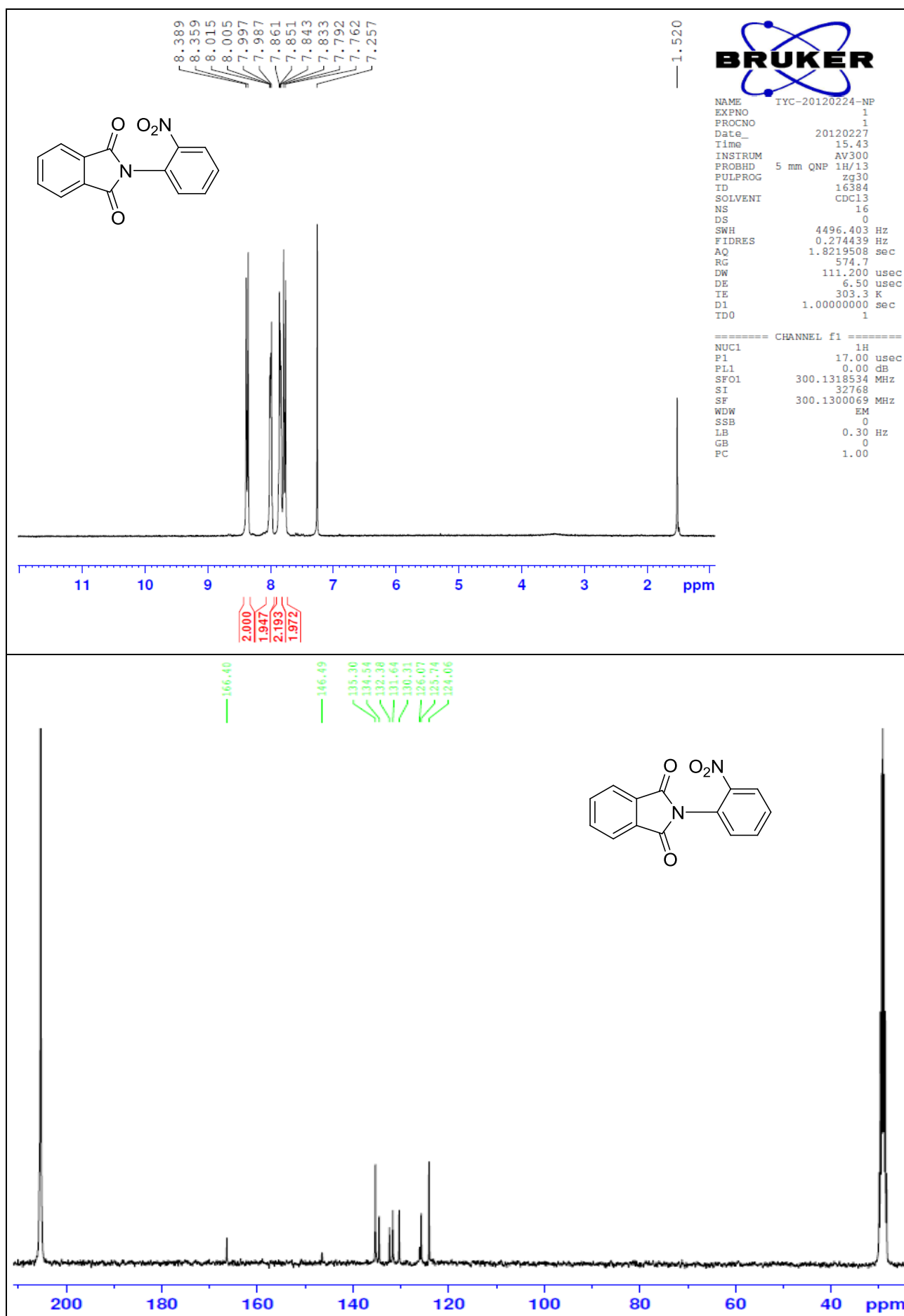


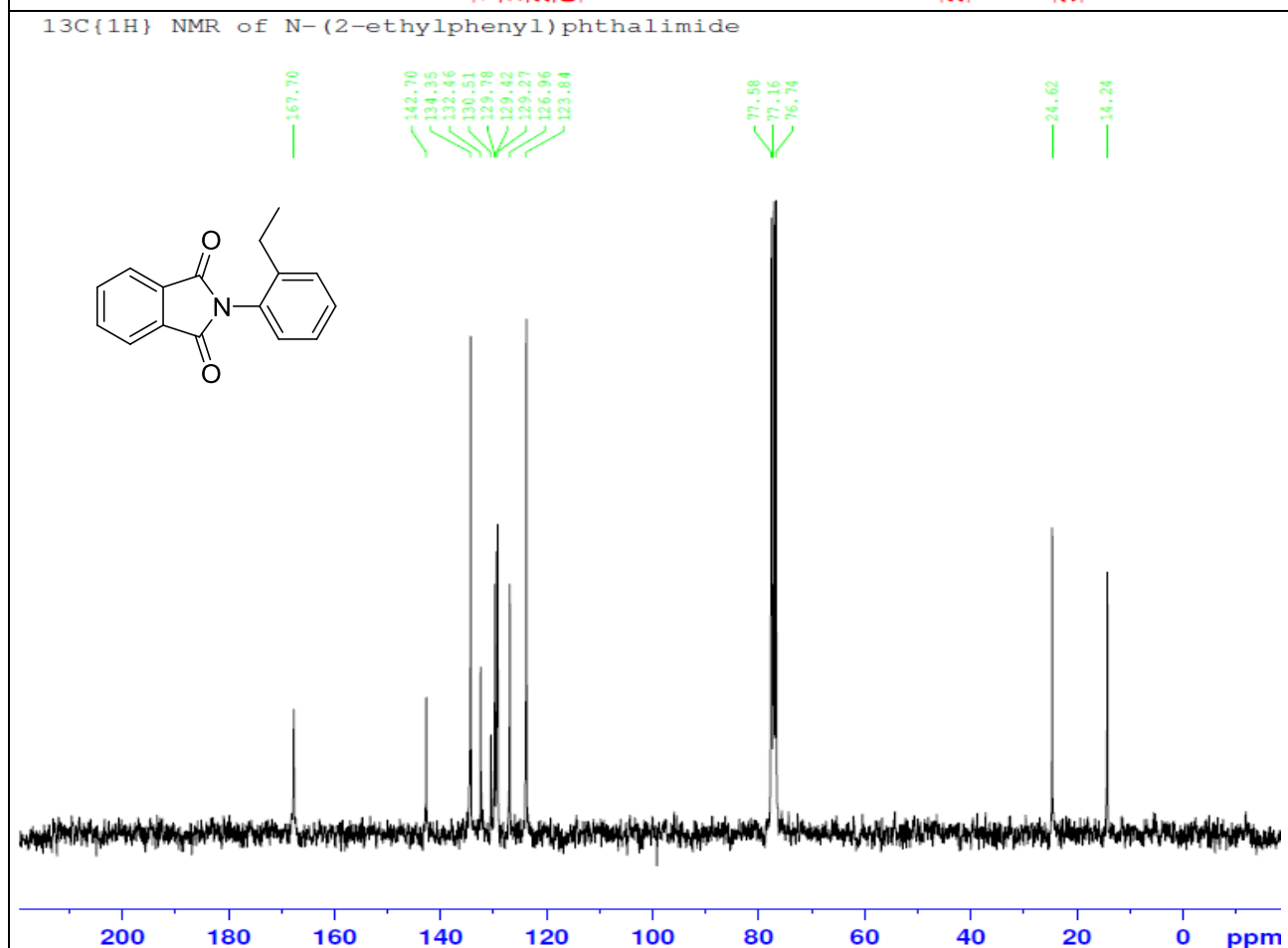
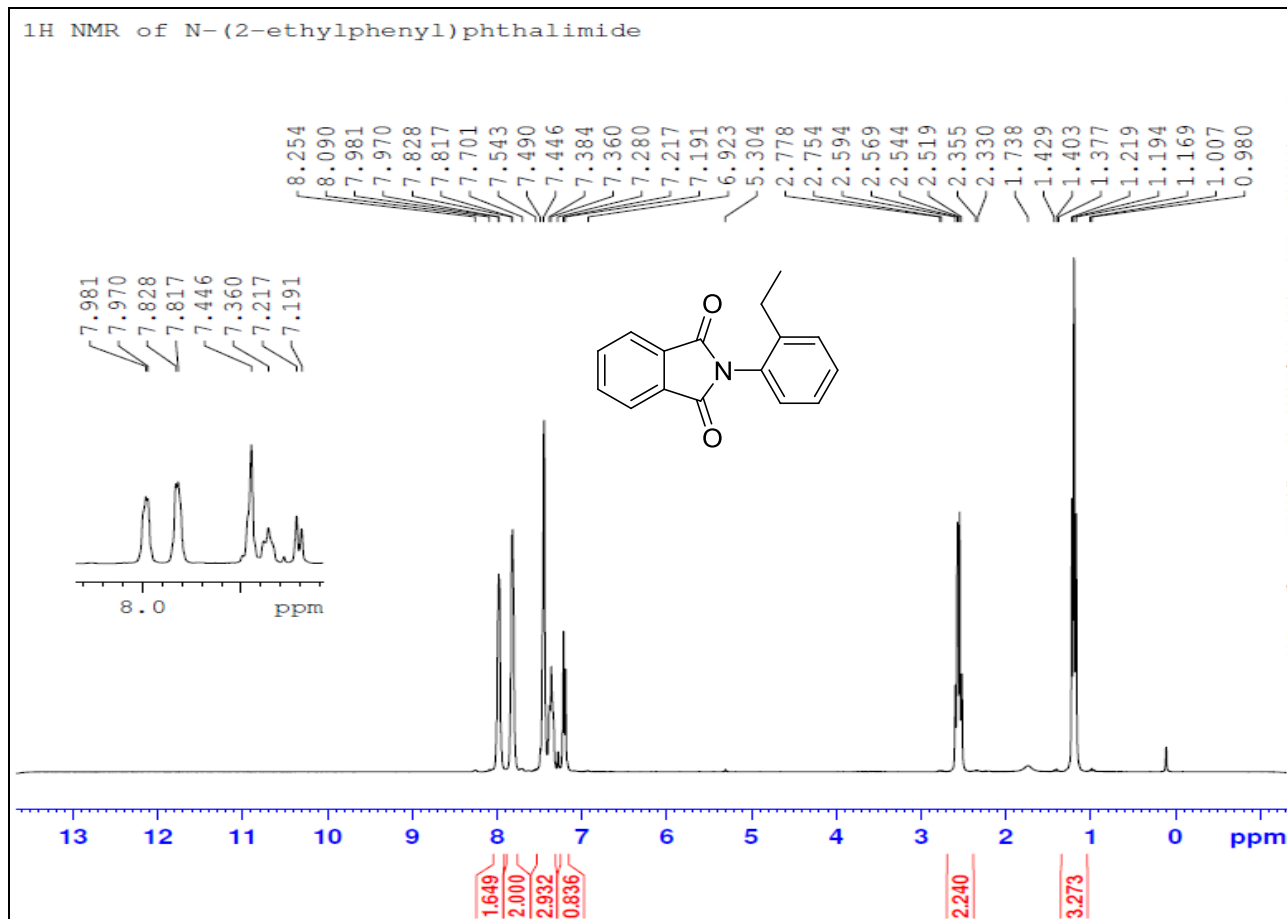
<sup>13</sup>C{<sup>1</sup>H} NMR of 2CP

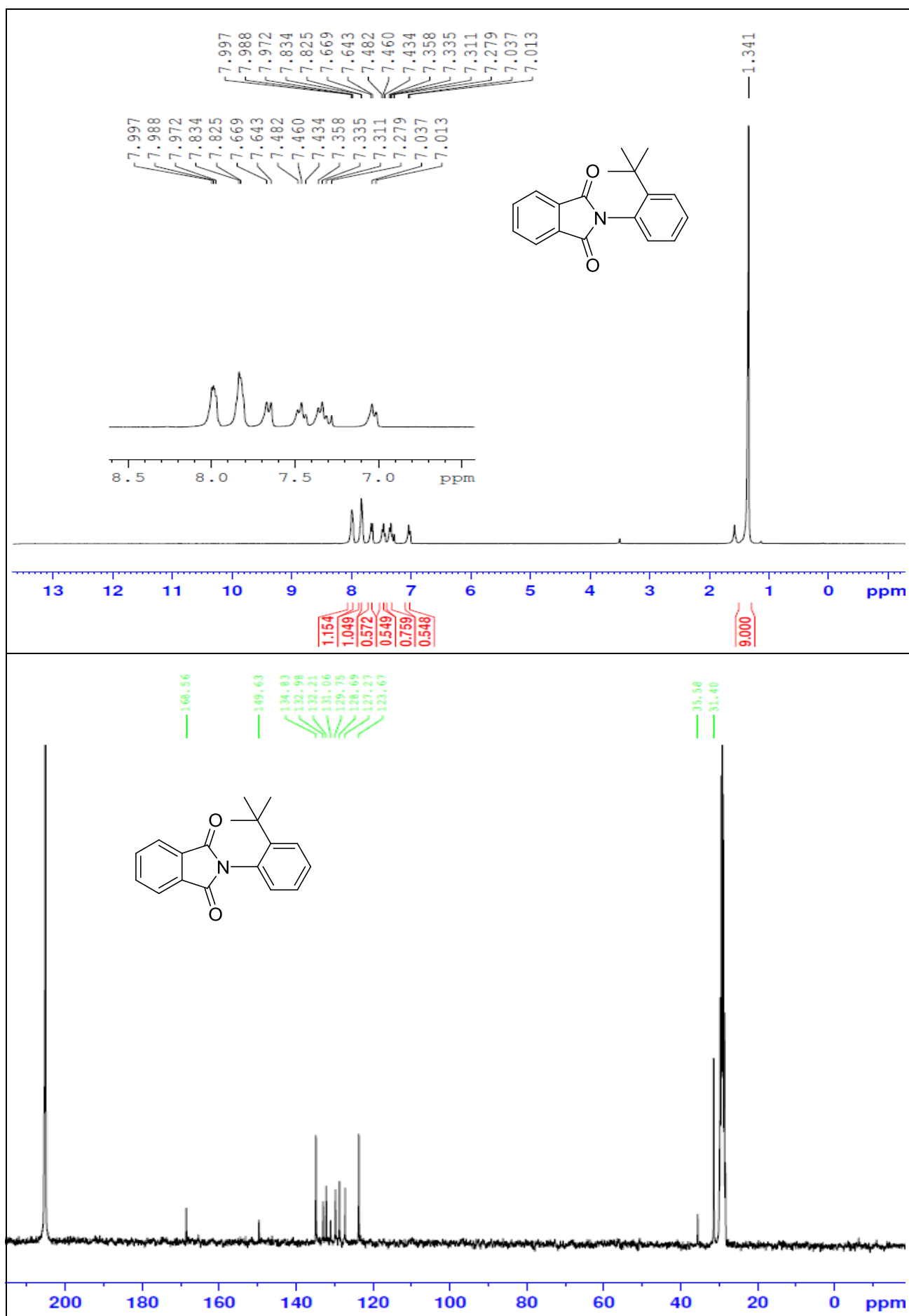


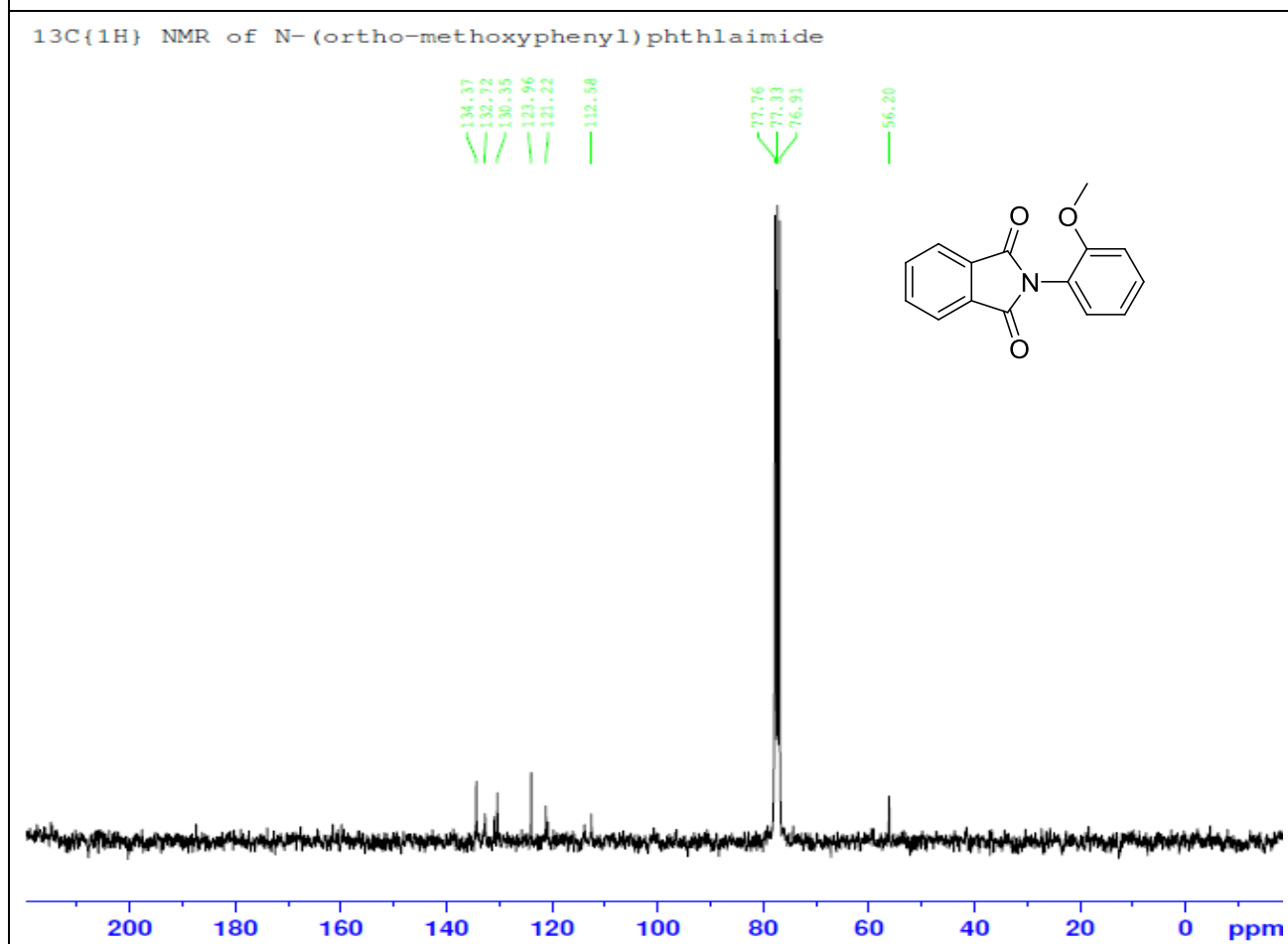
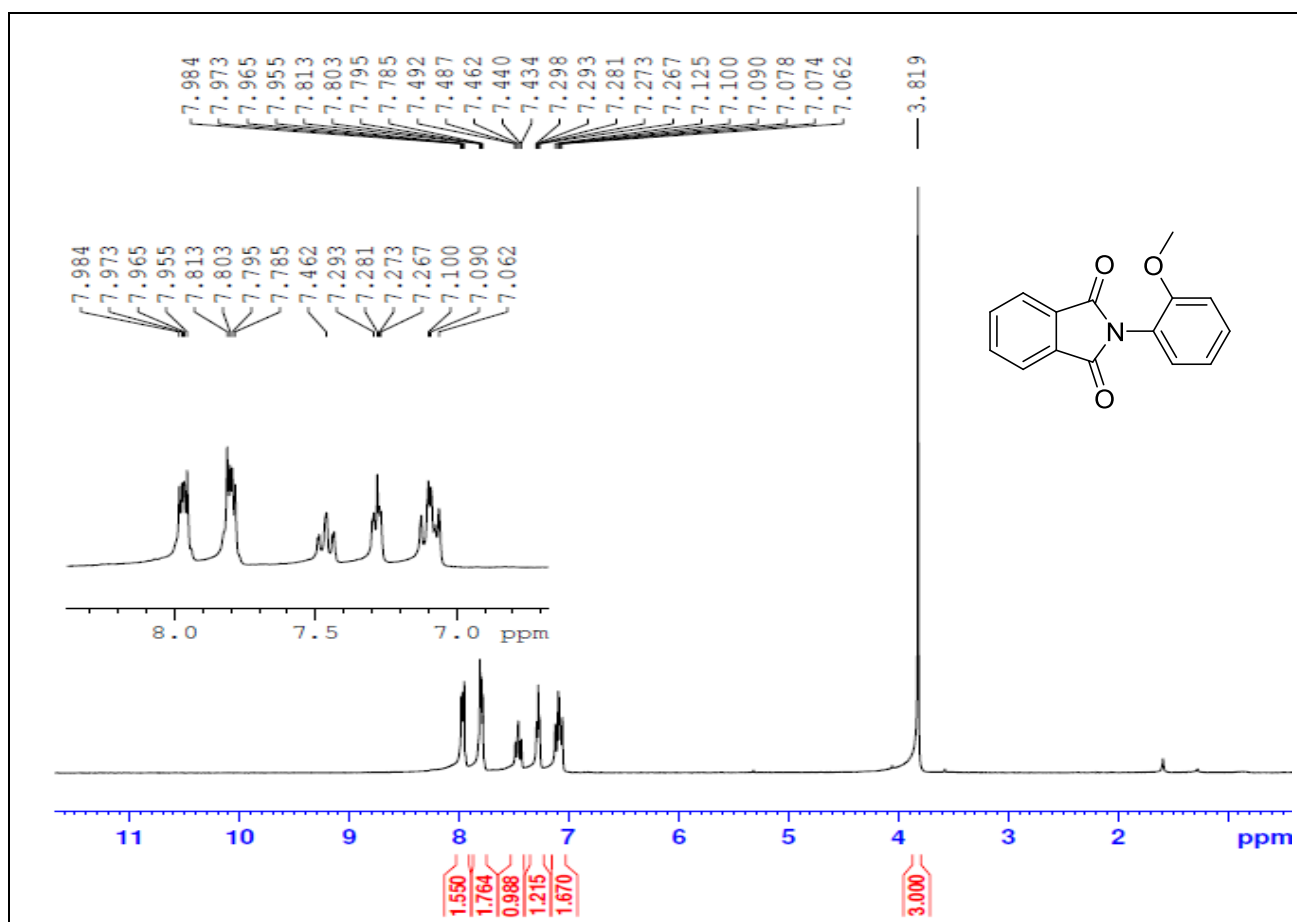


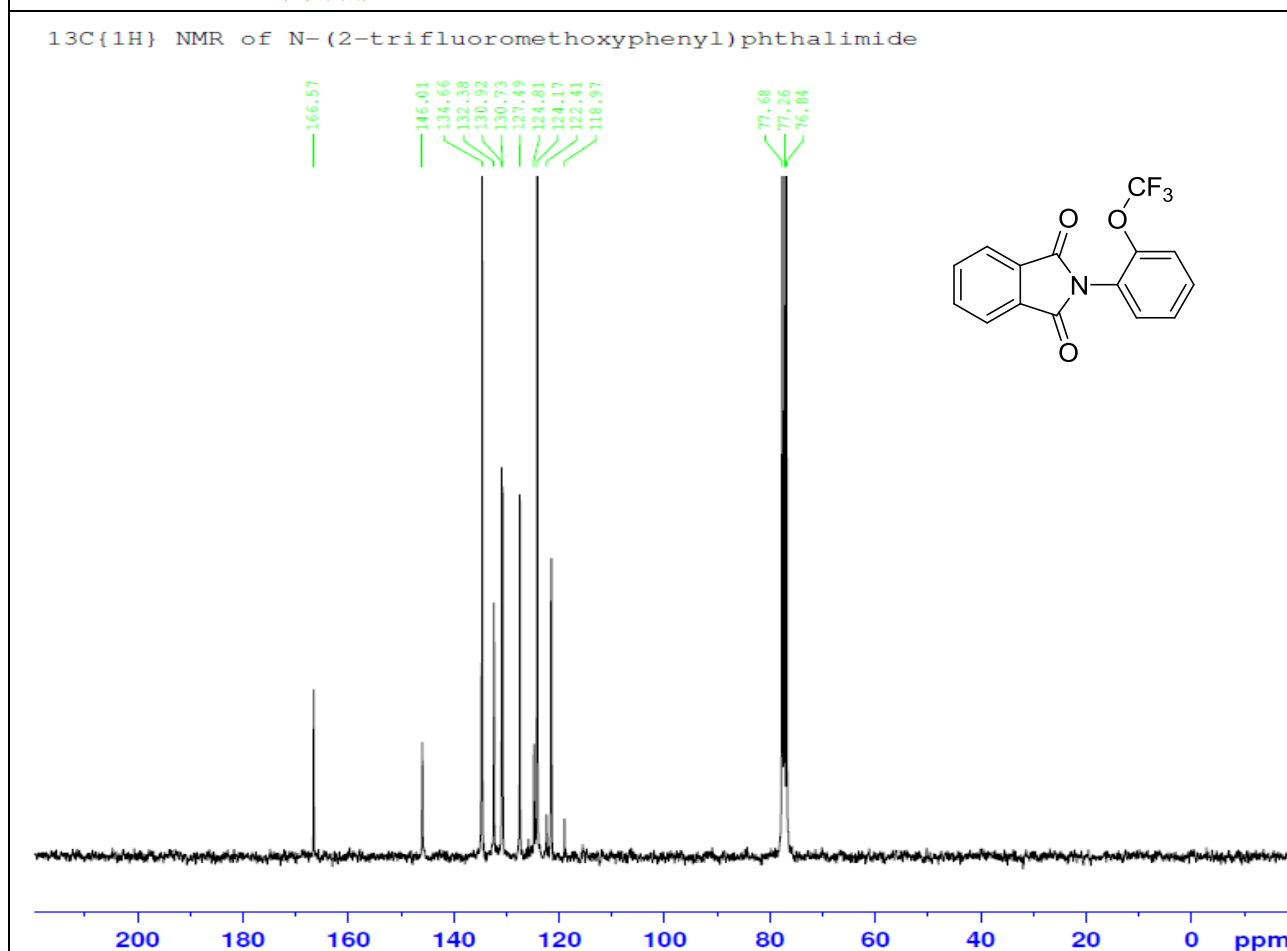
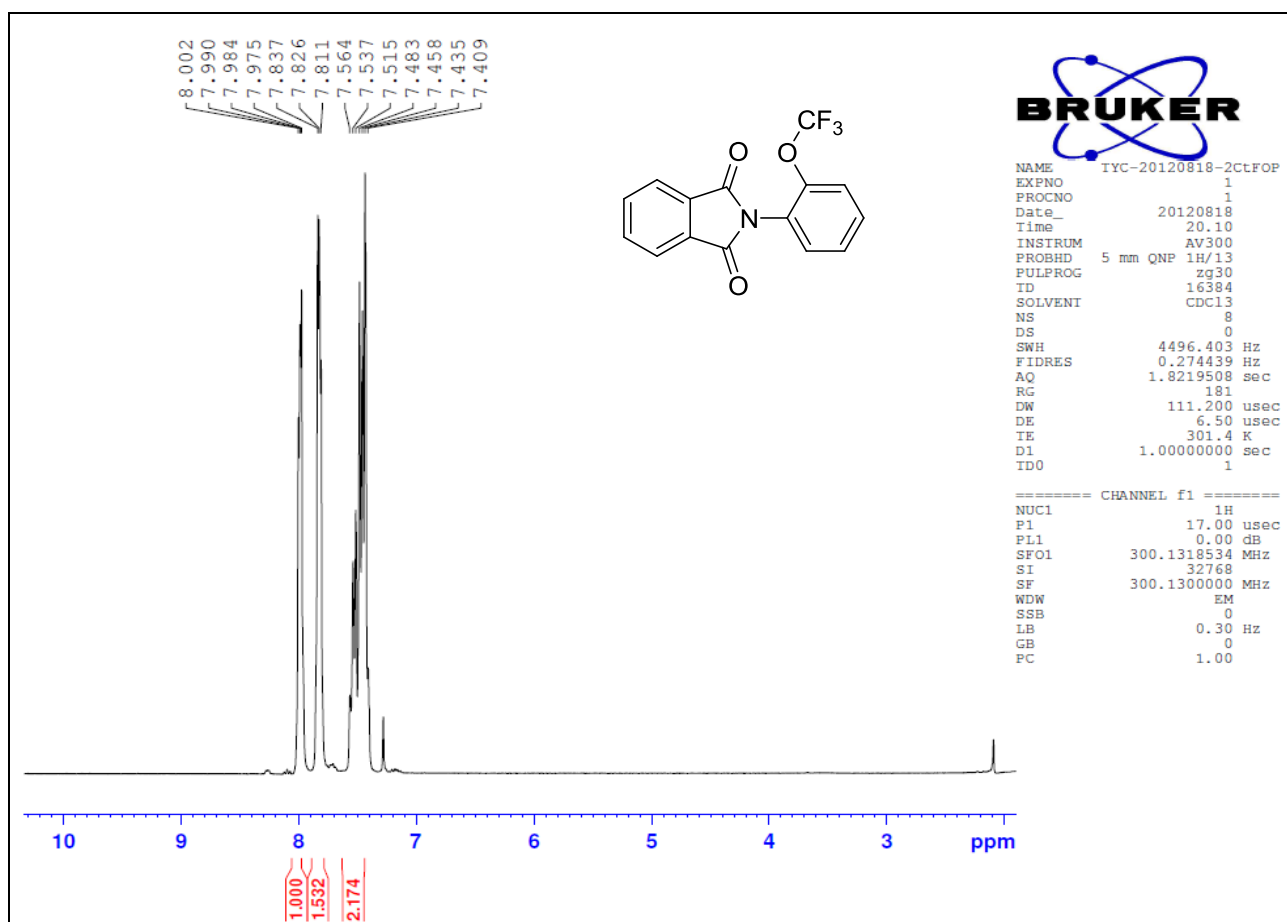




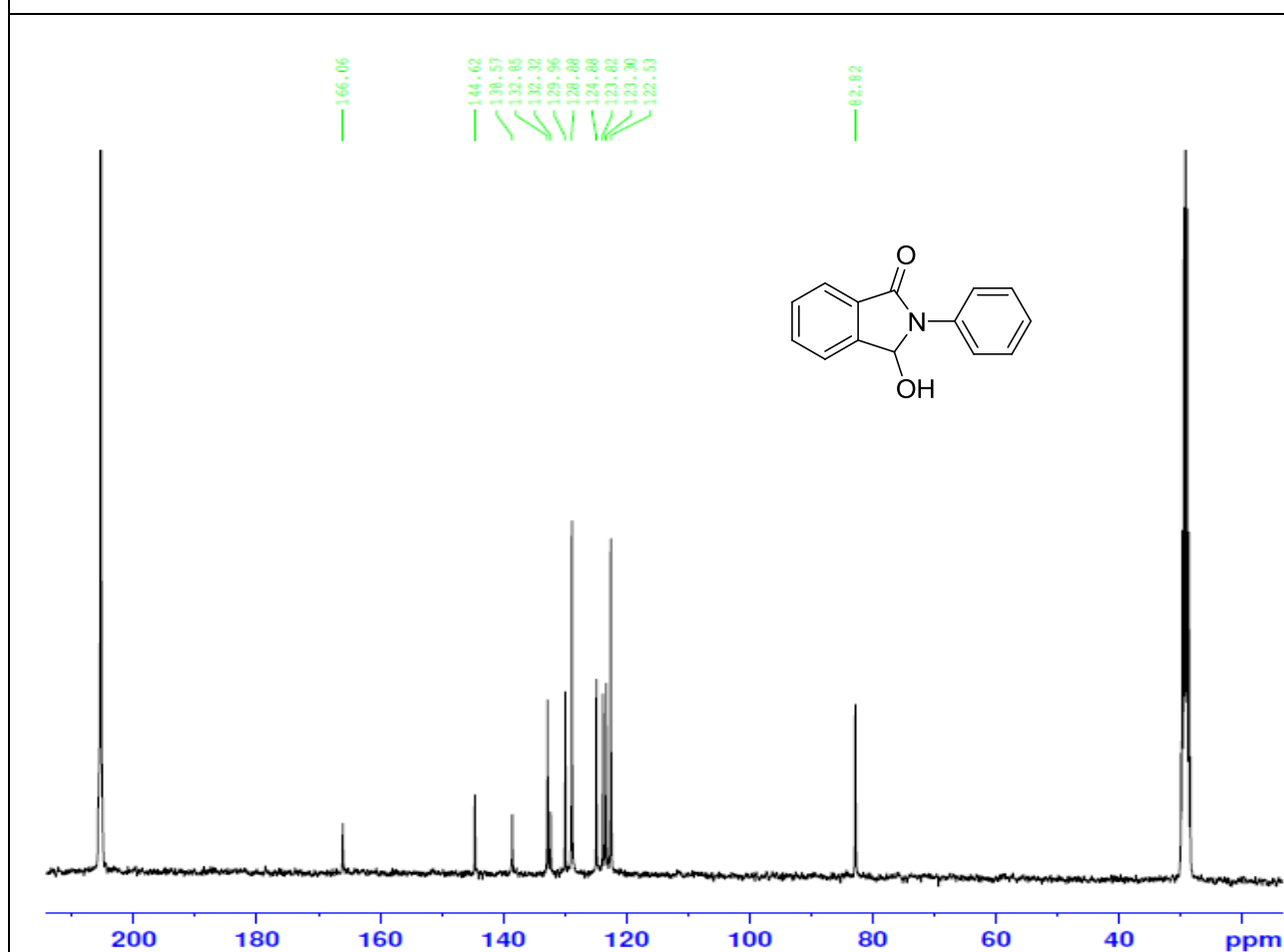
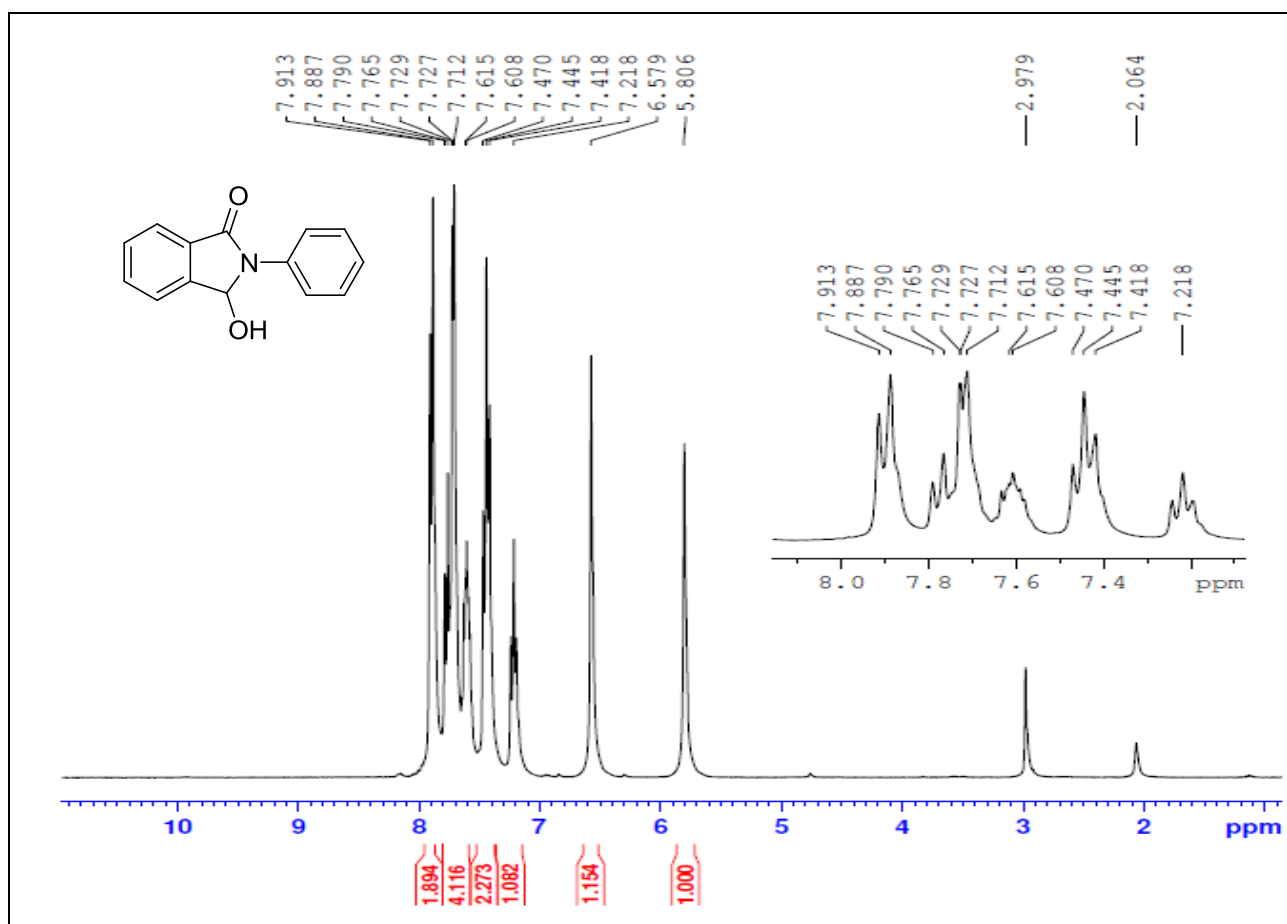


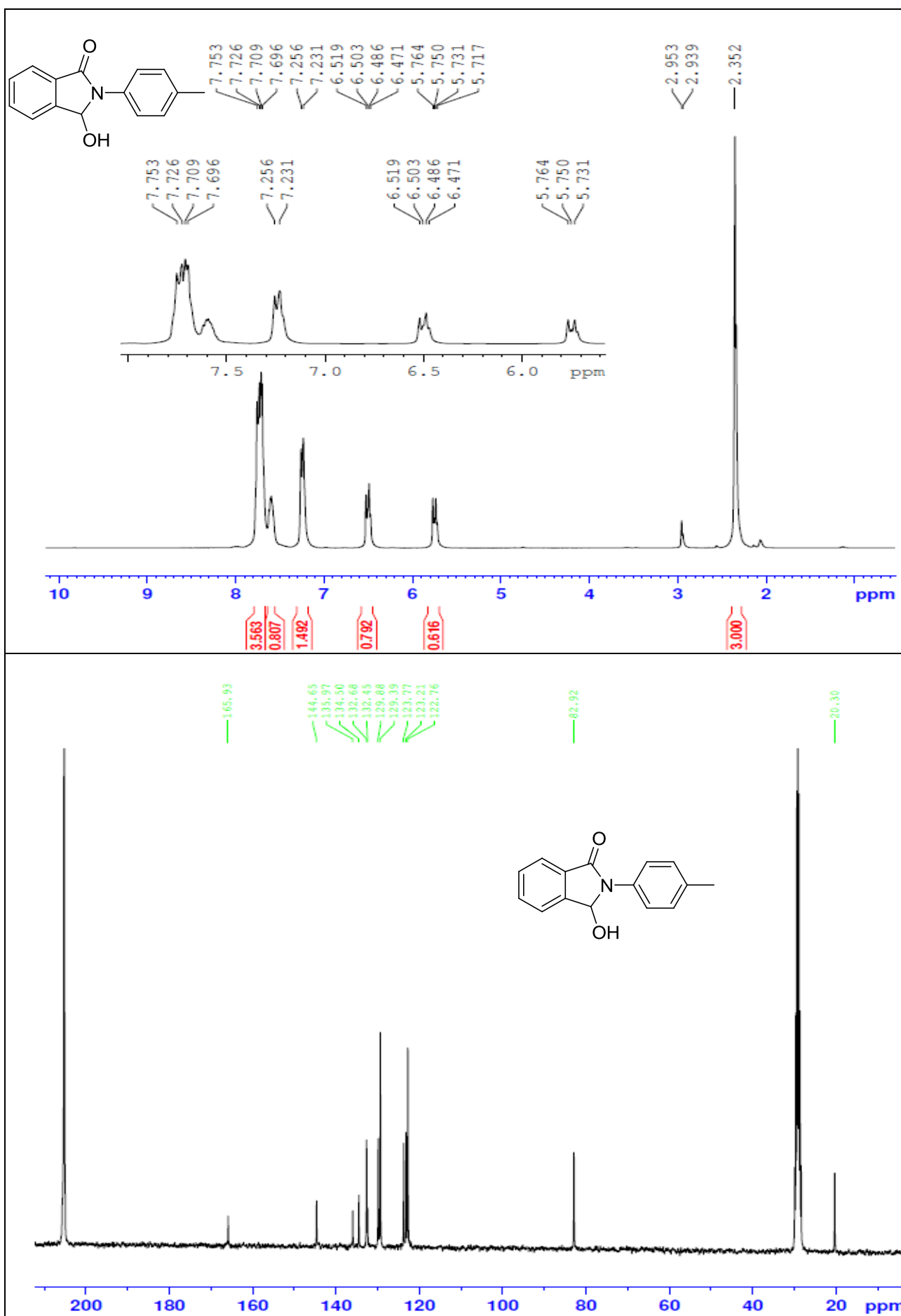


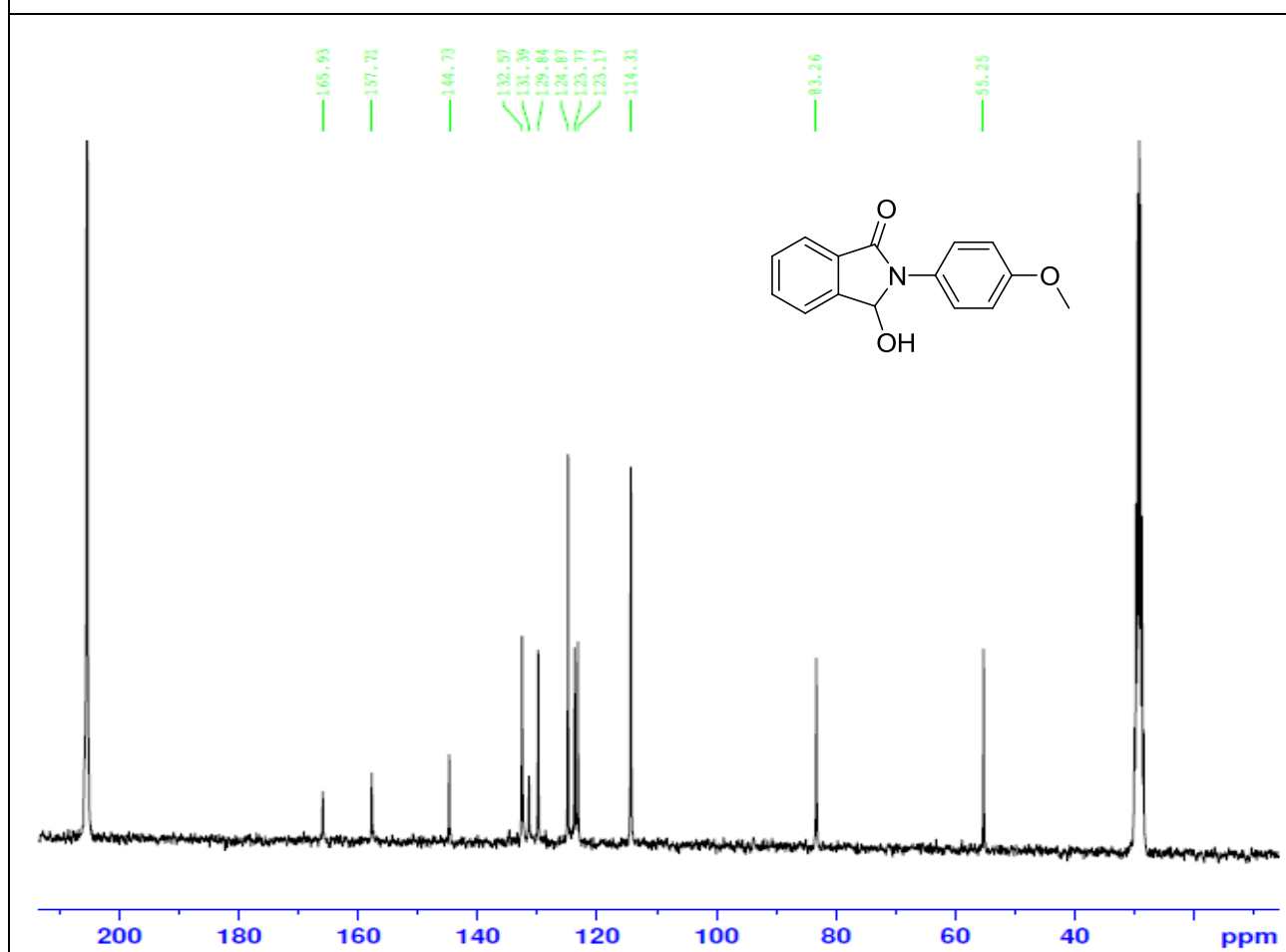
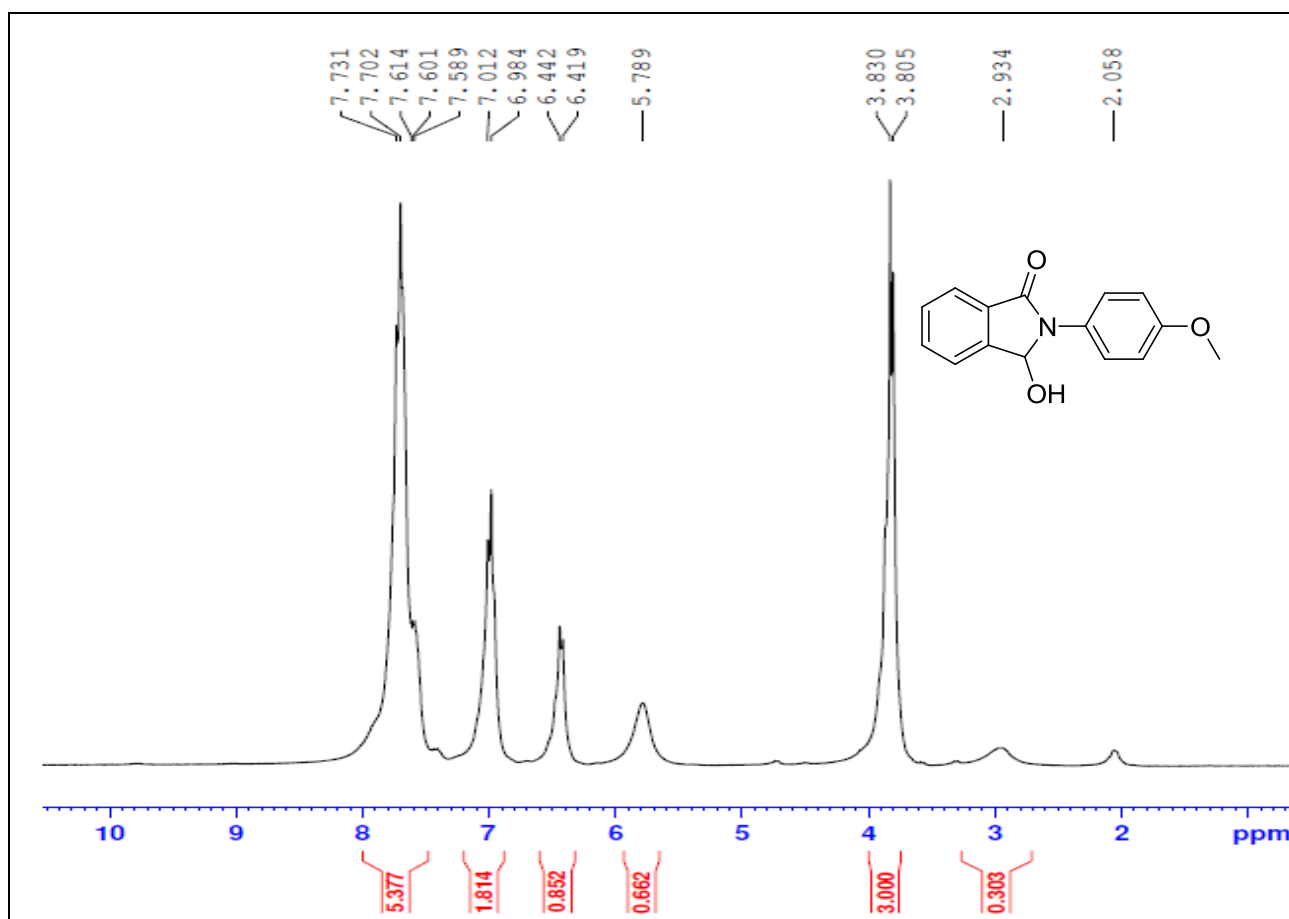


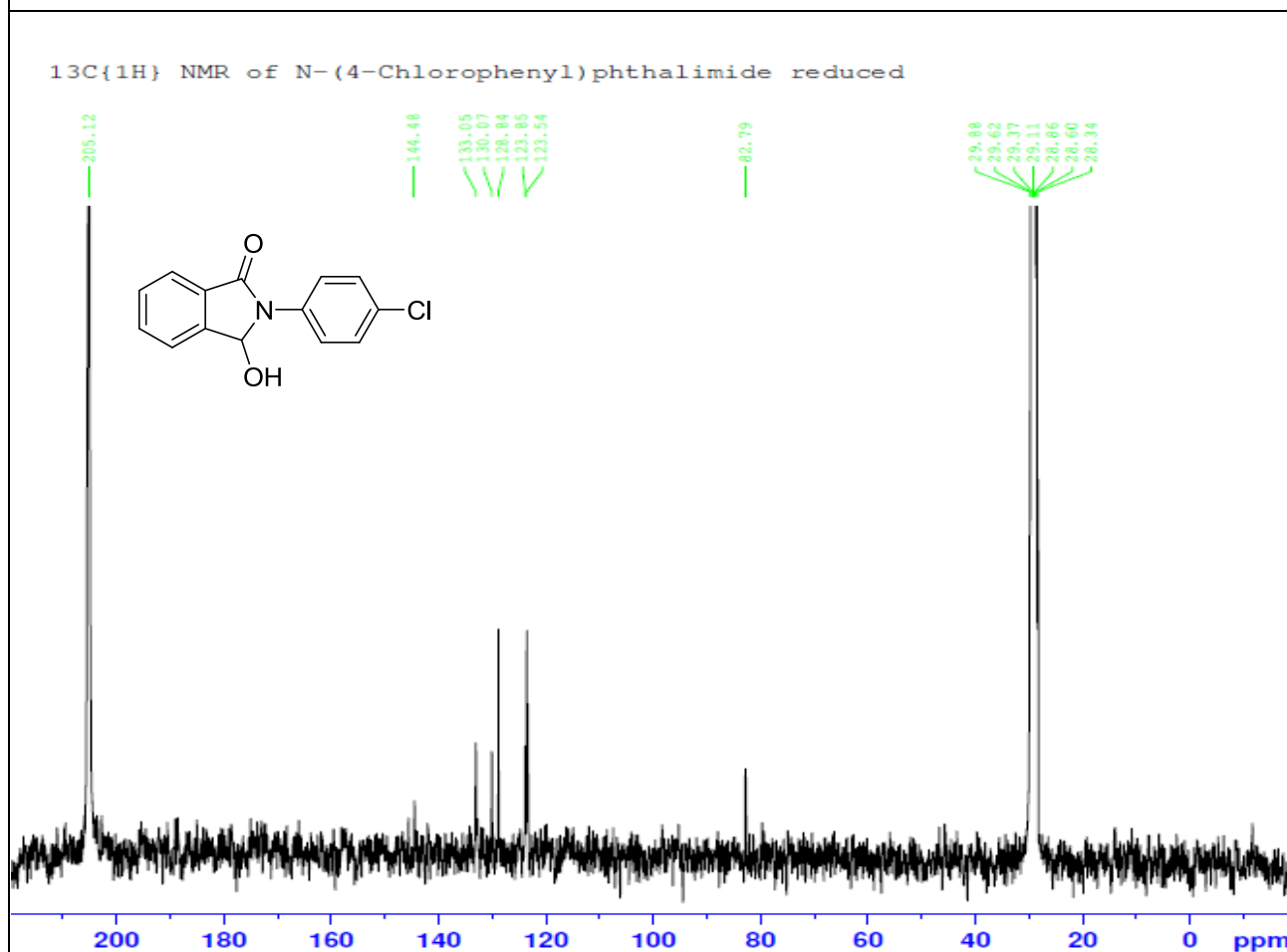
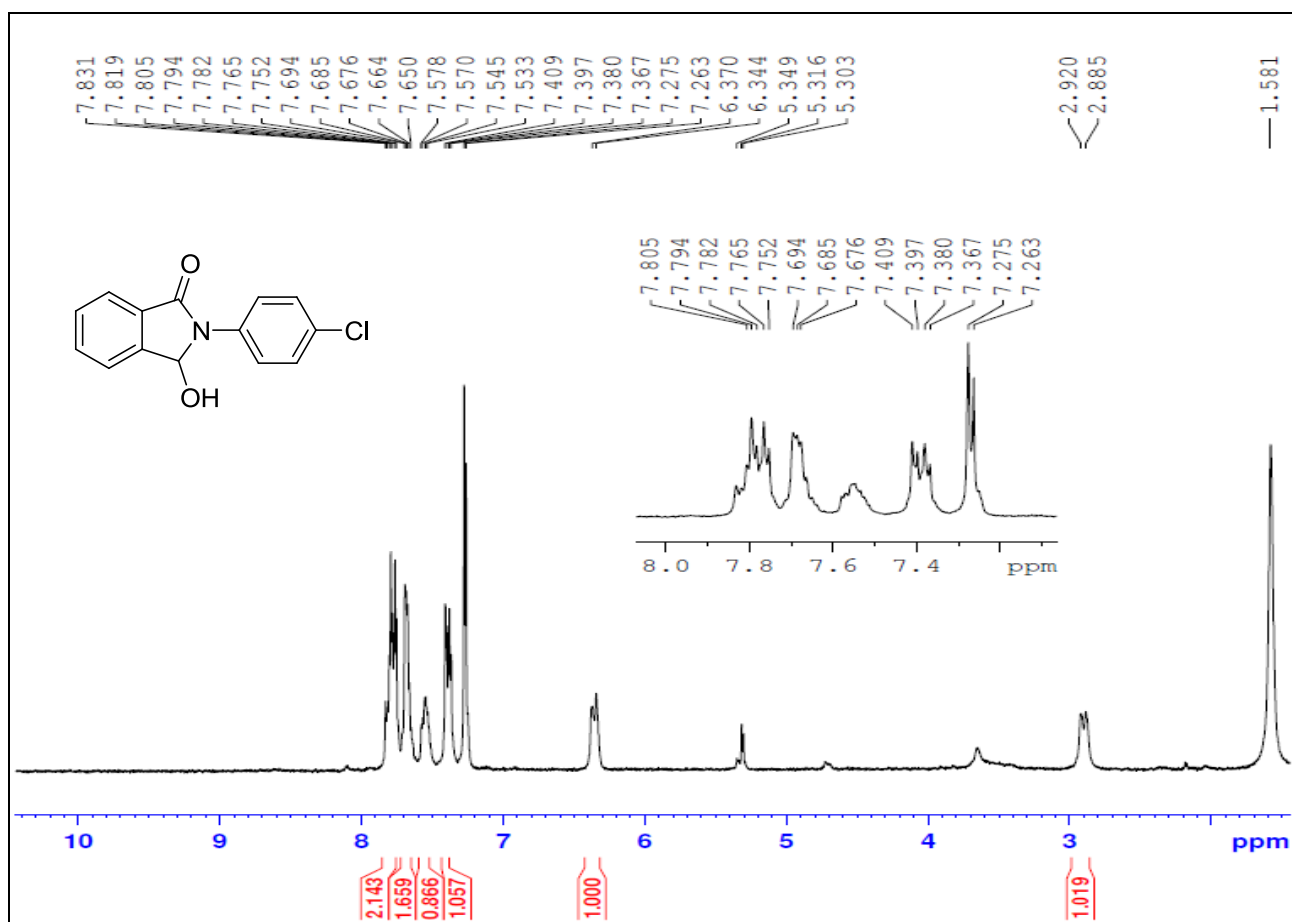




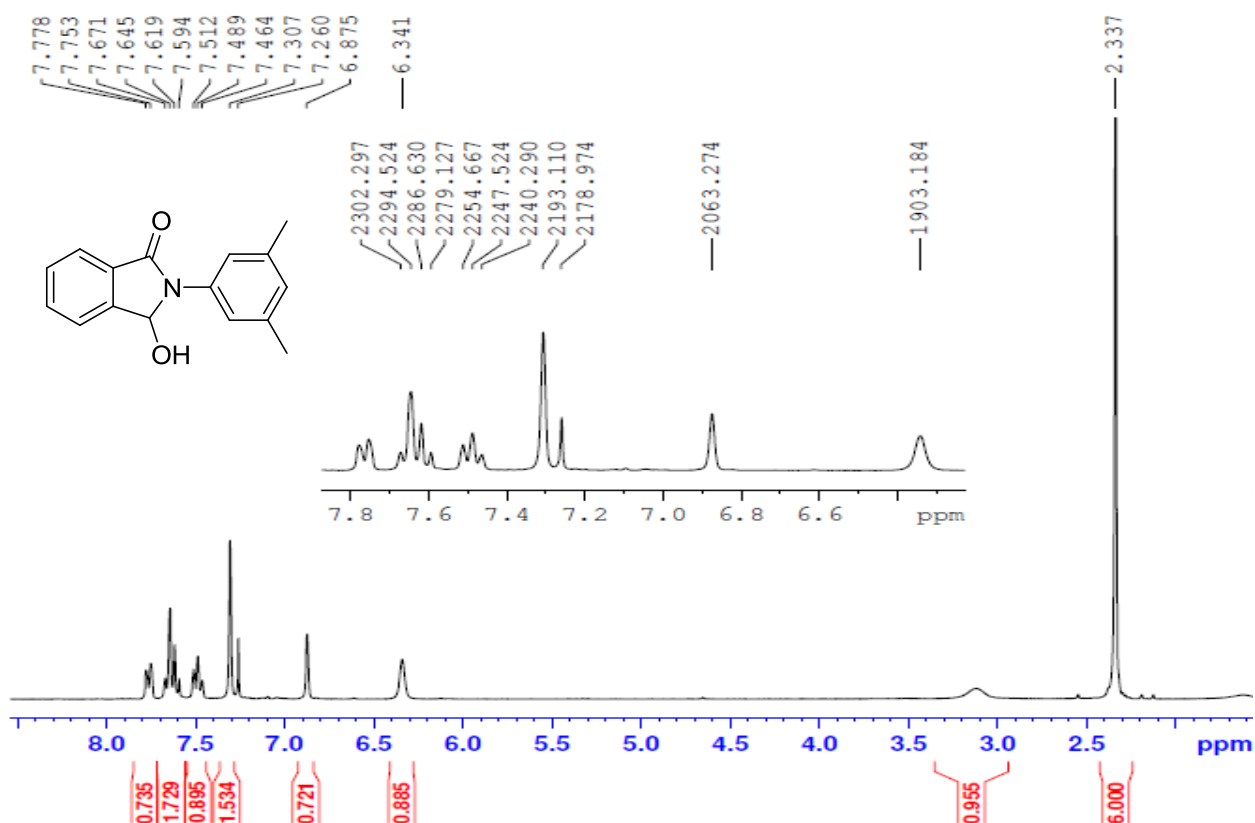




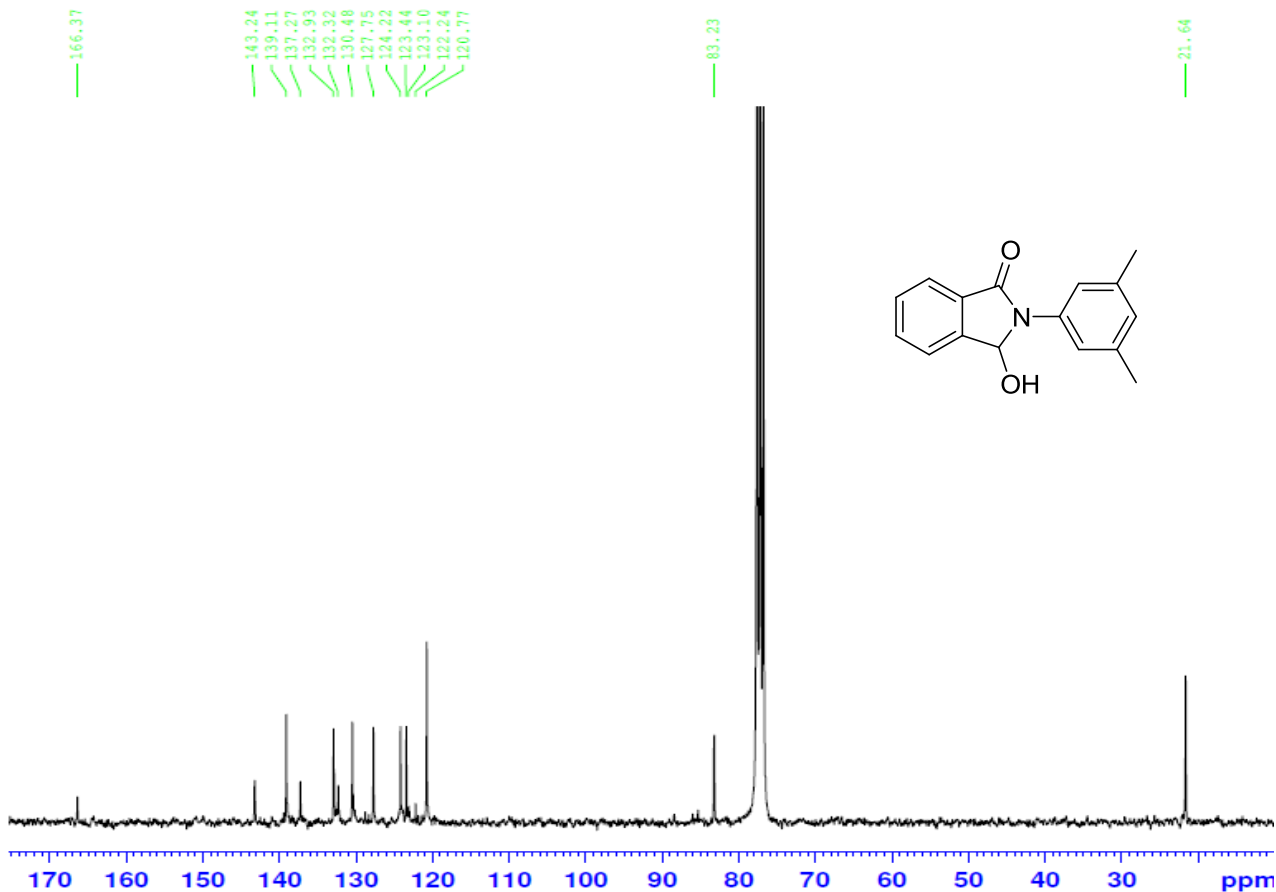


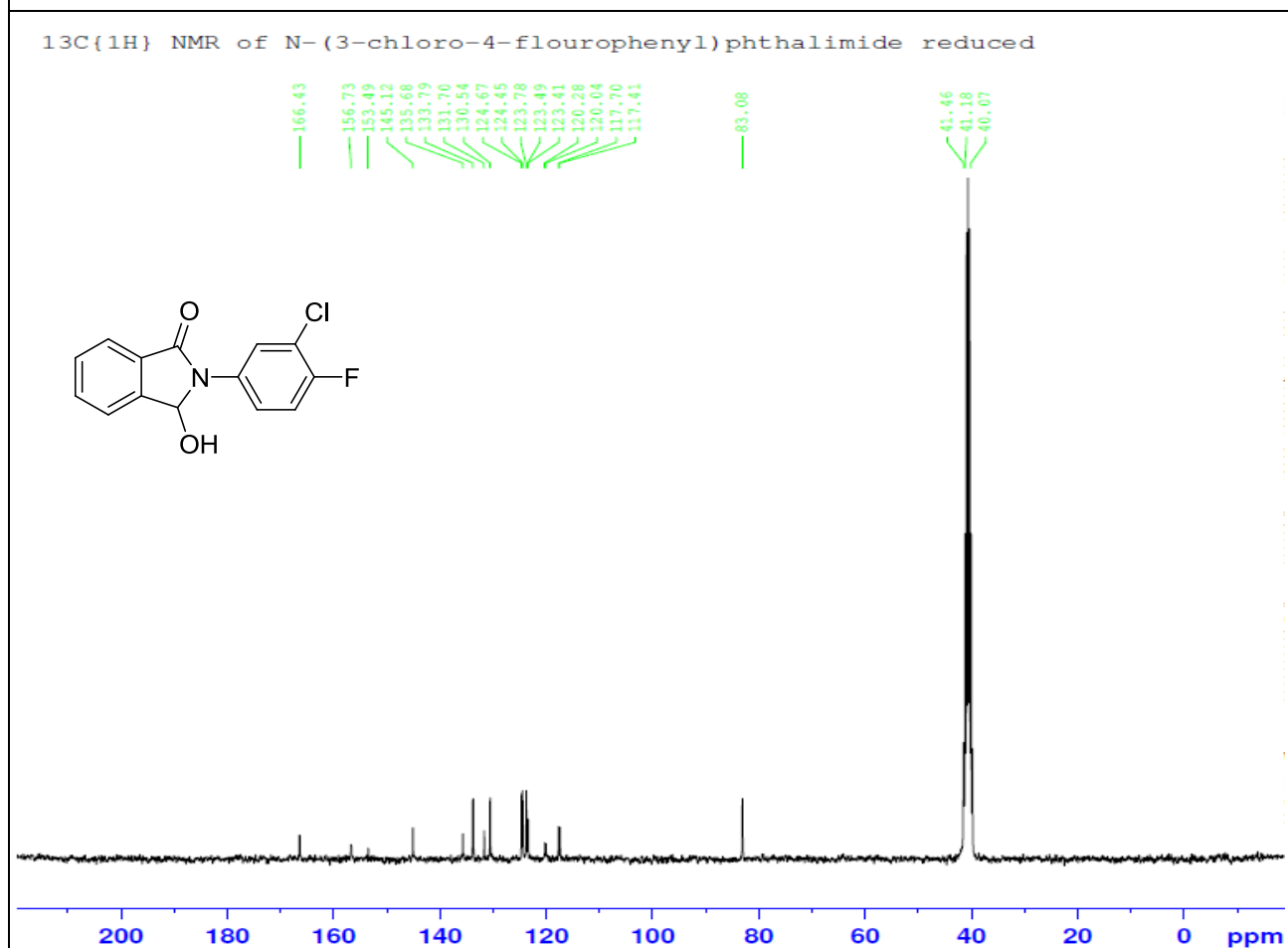
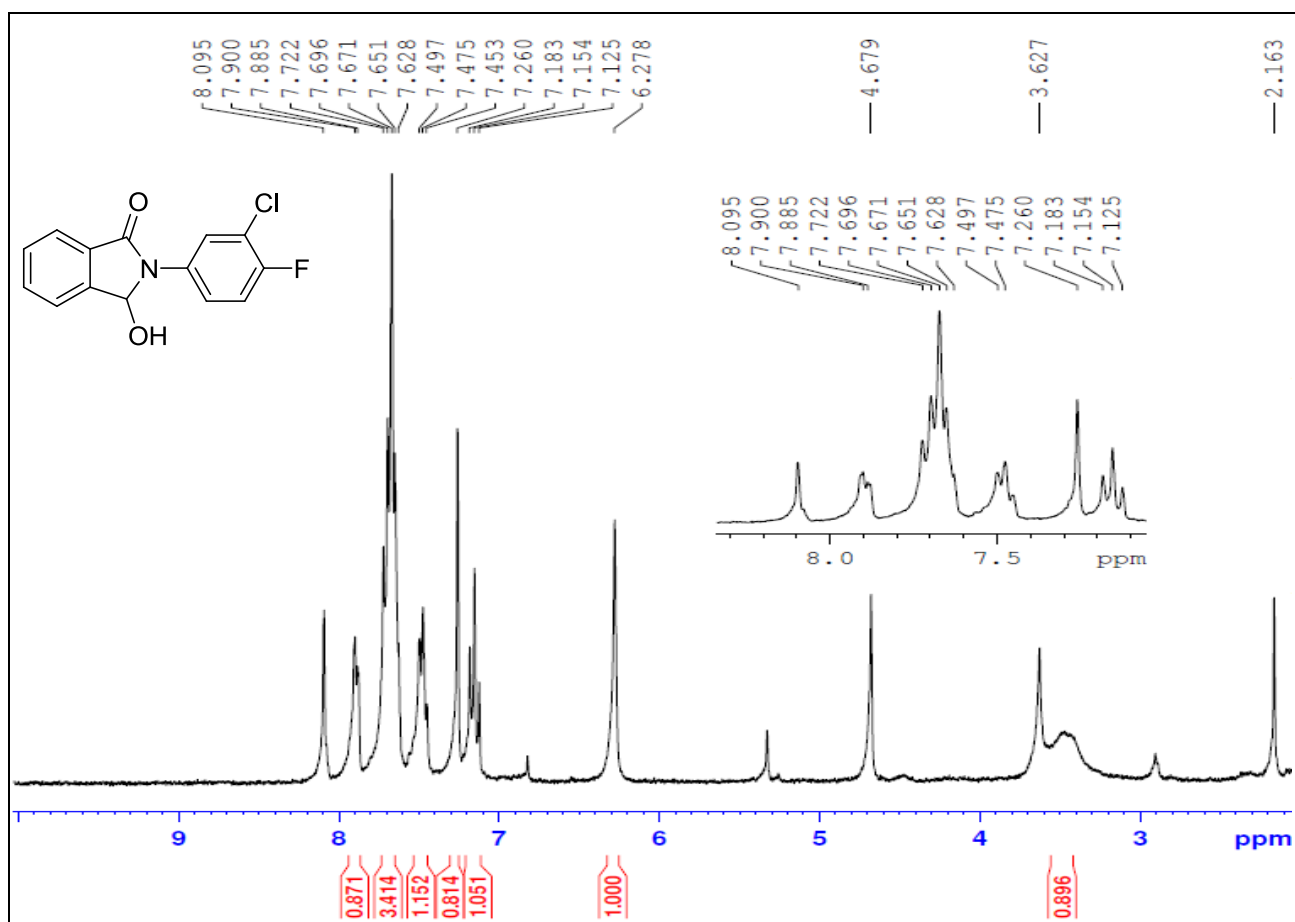


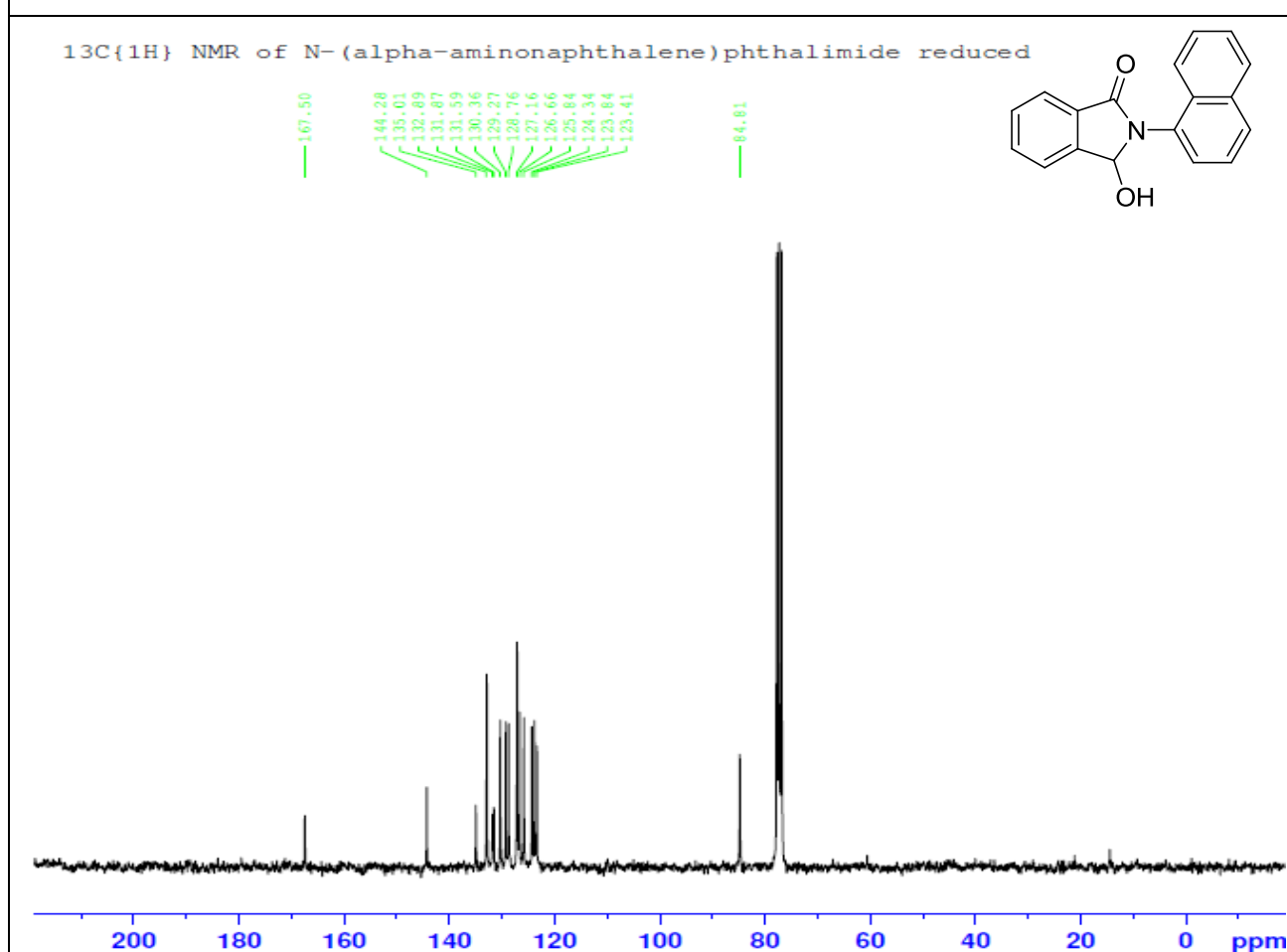
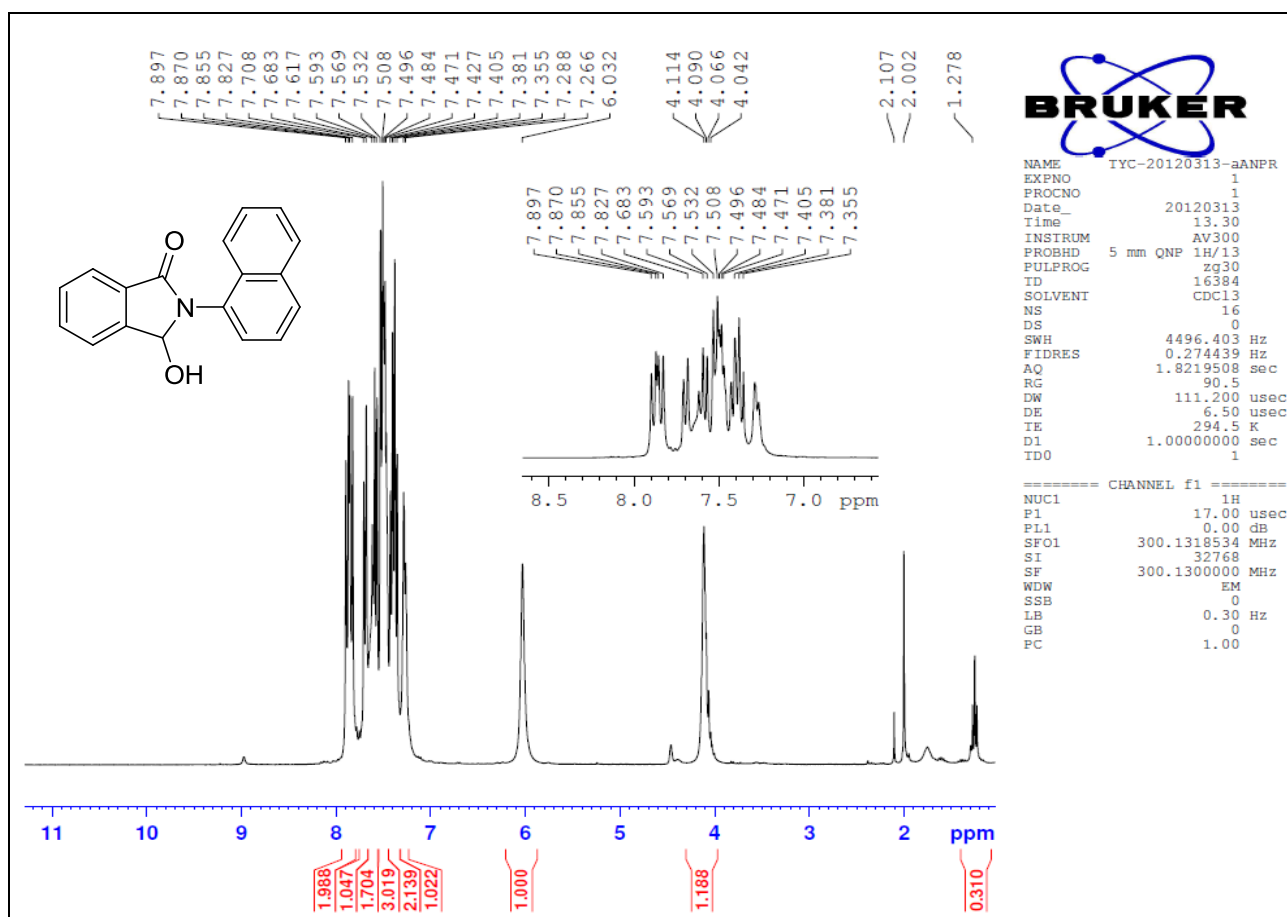
<sup>1</sup>H NMR of N-(3,5-dimethylphenyl)phthalimide reduced

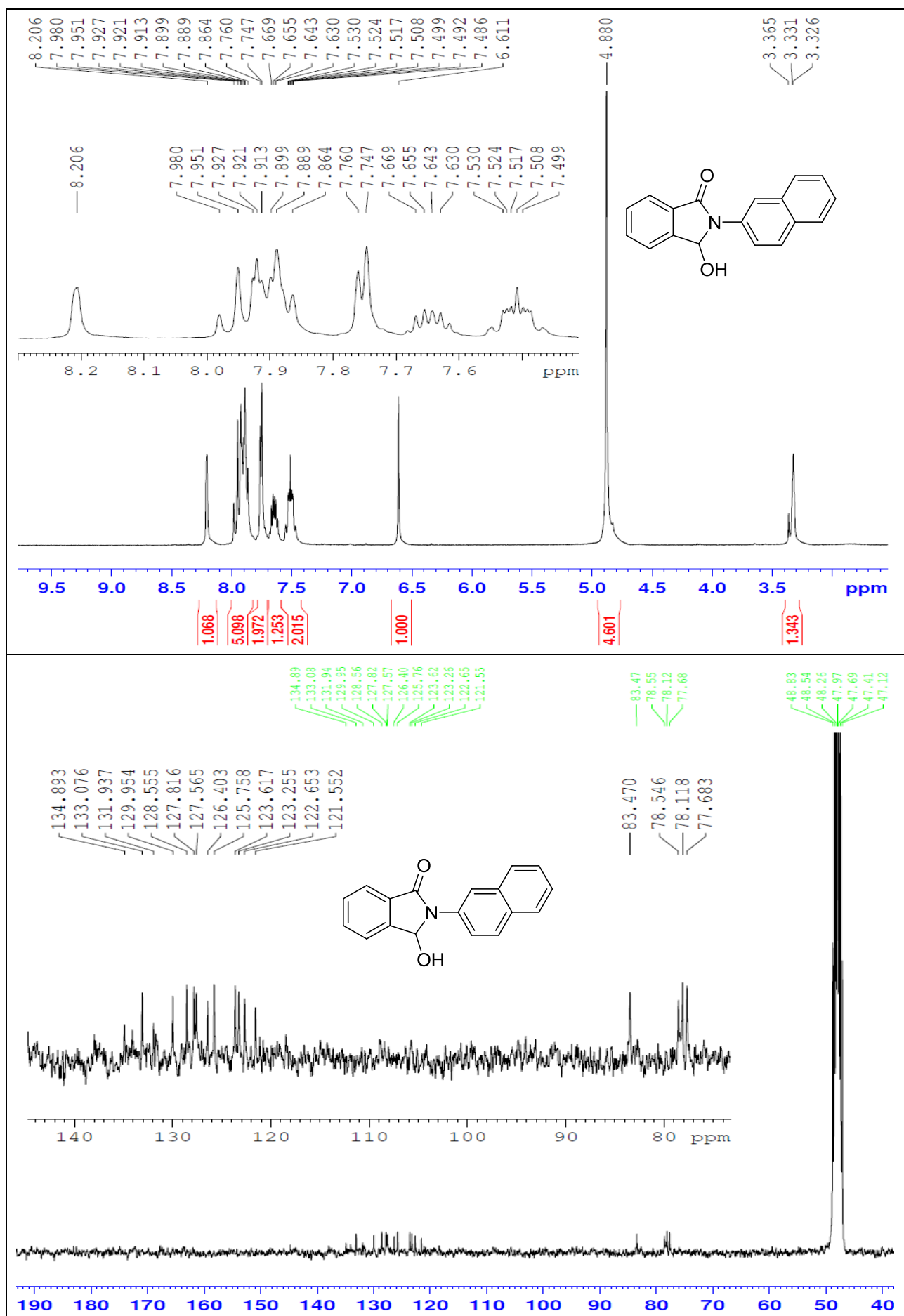


<sup>13</sup>C{<sup>1</sup>H} NMR of N-(3,5-dimethylphenyl)phthalimide reduced

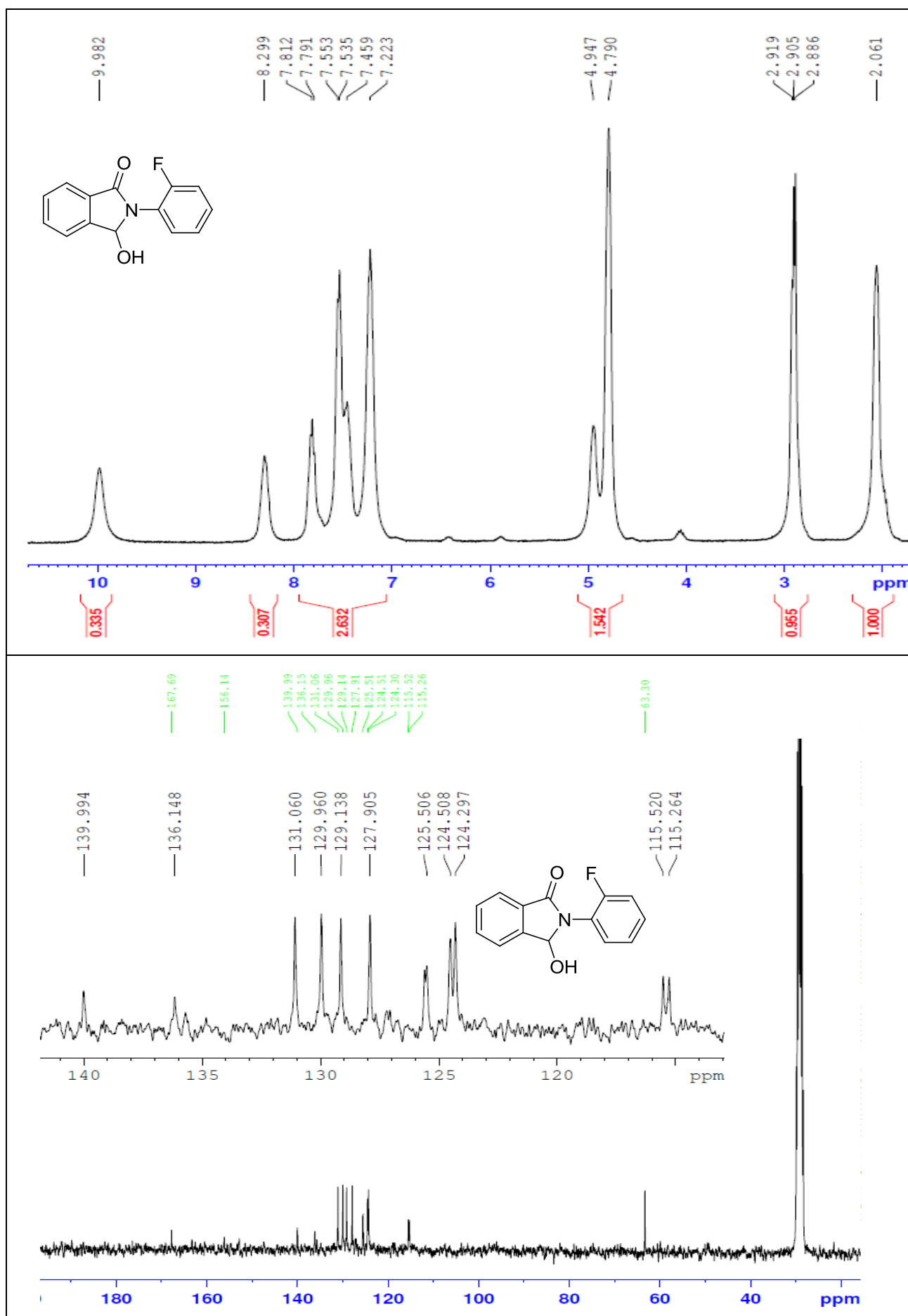










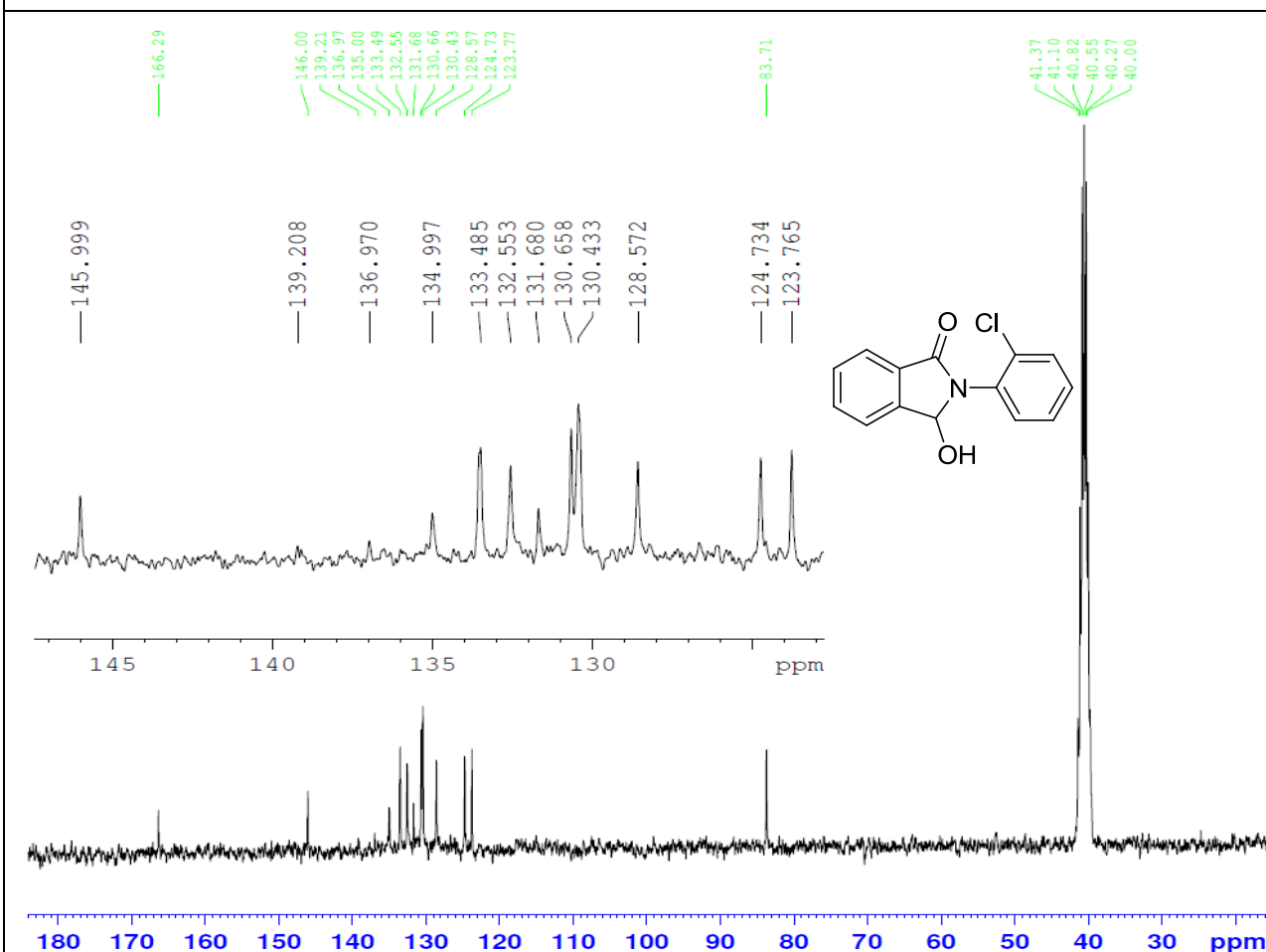
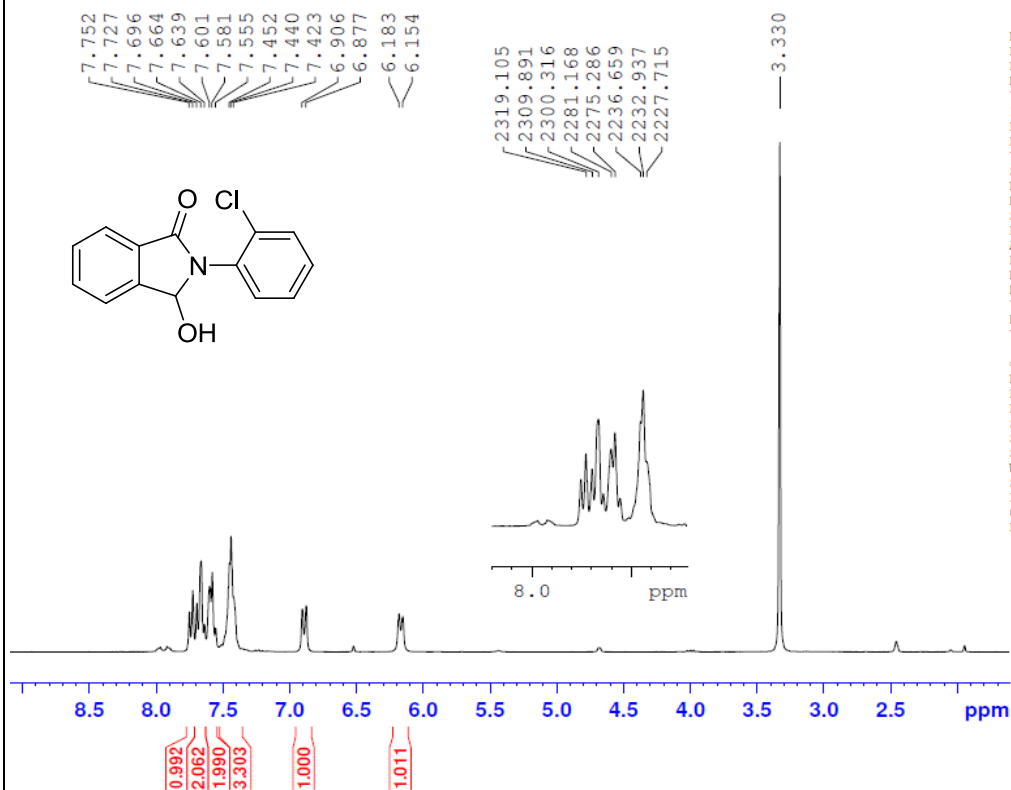


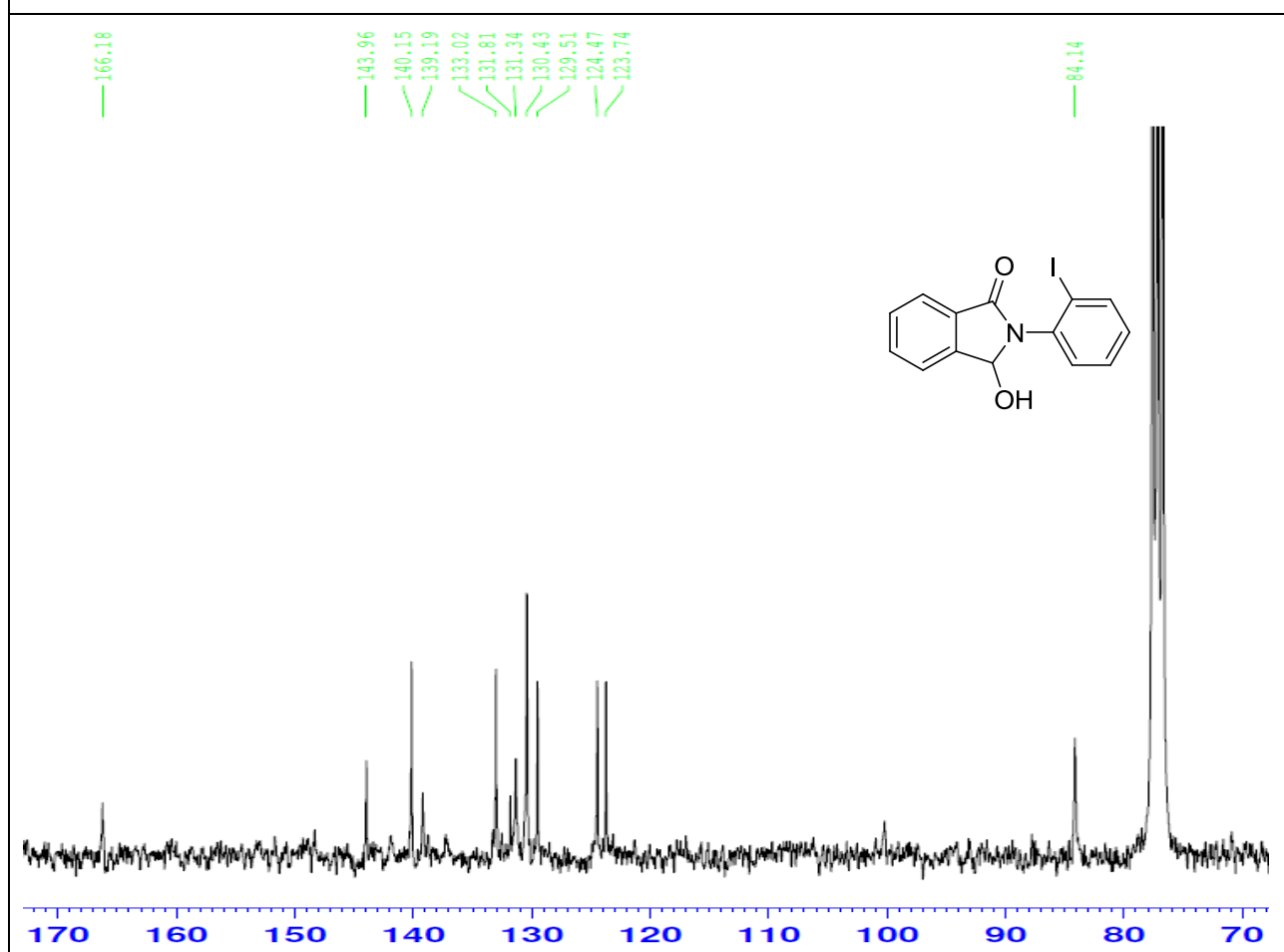
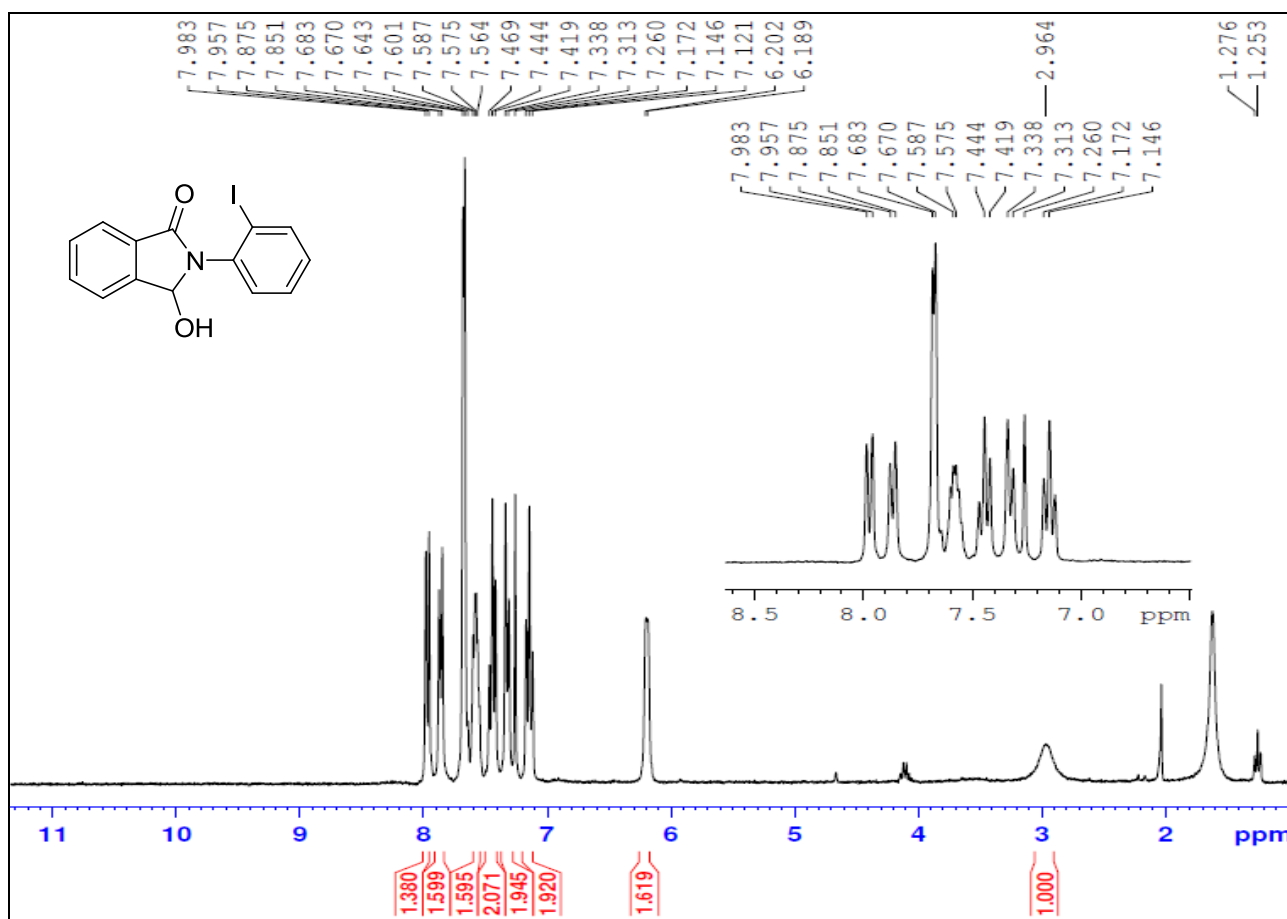
<sup>1</sup>H NMR of N-(2-chlorophenyl)phthalimide reduced

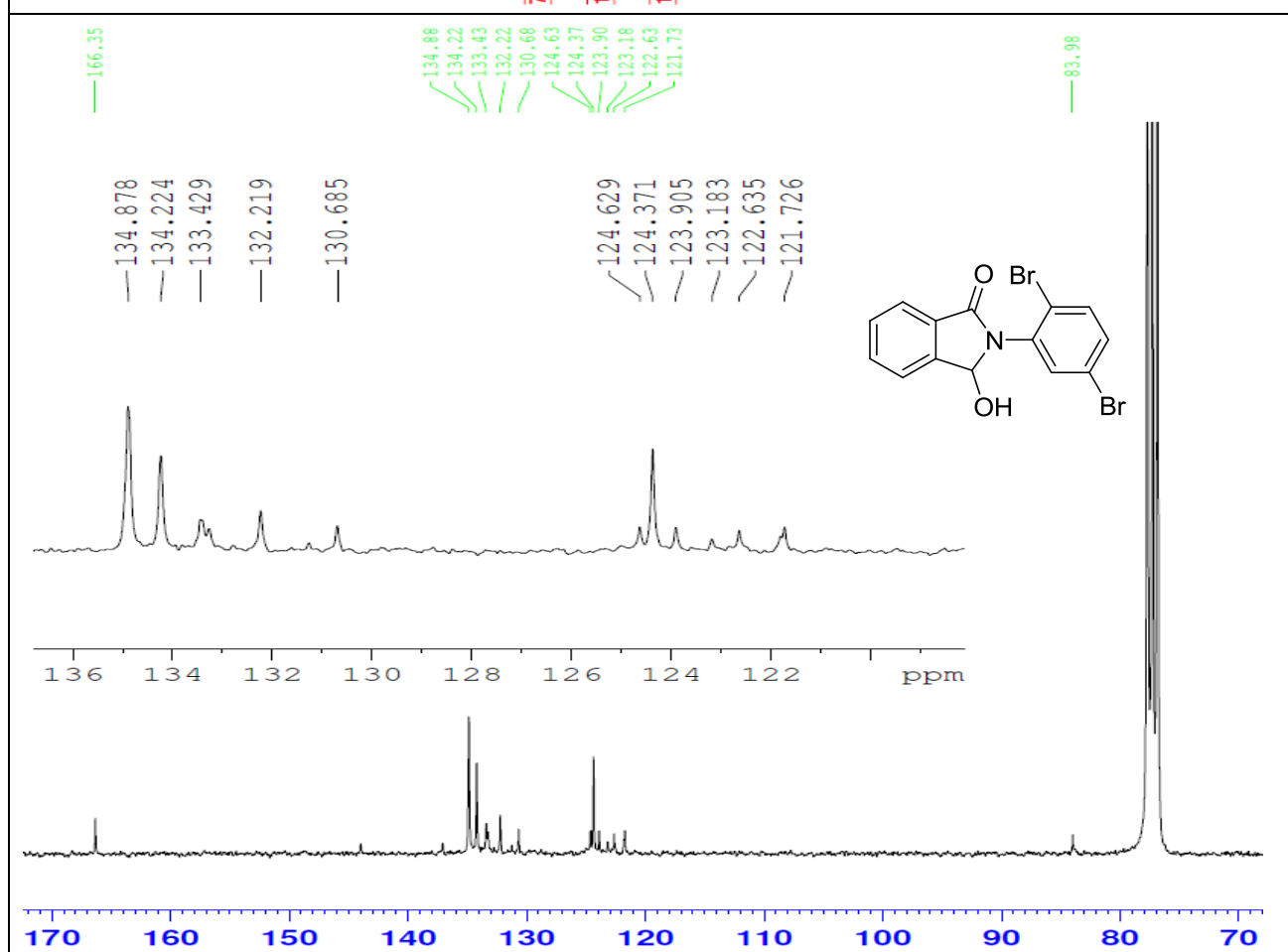
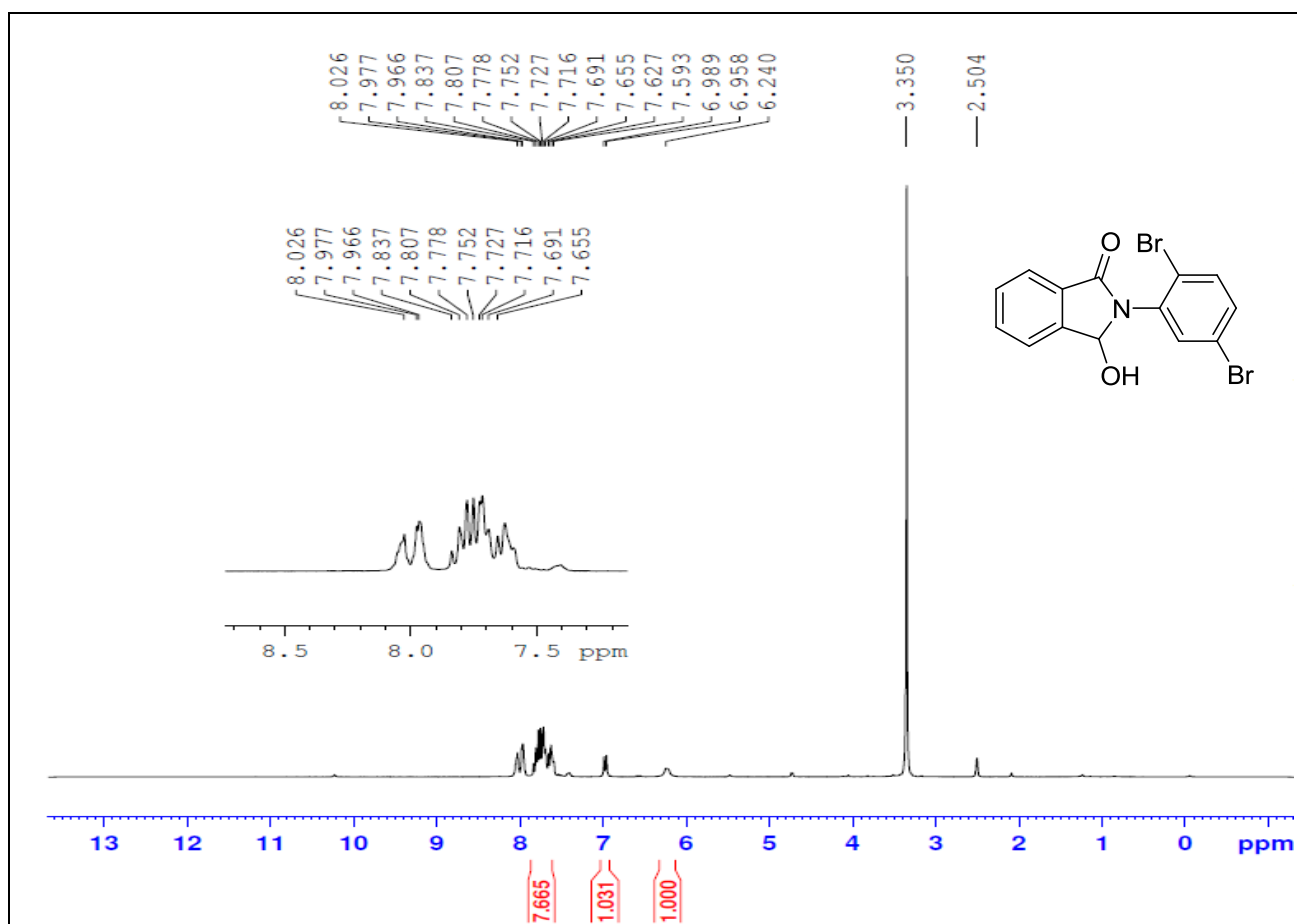


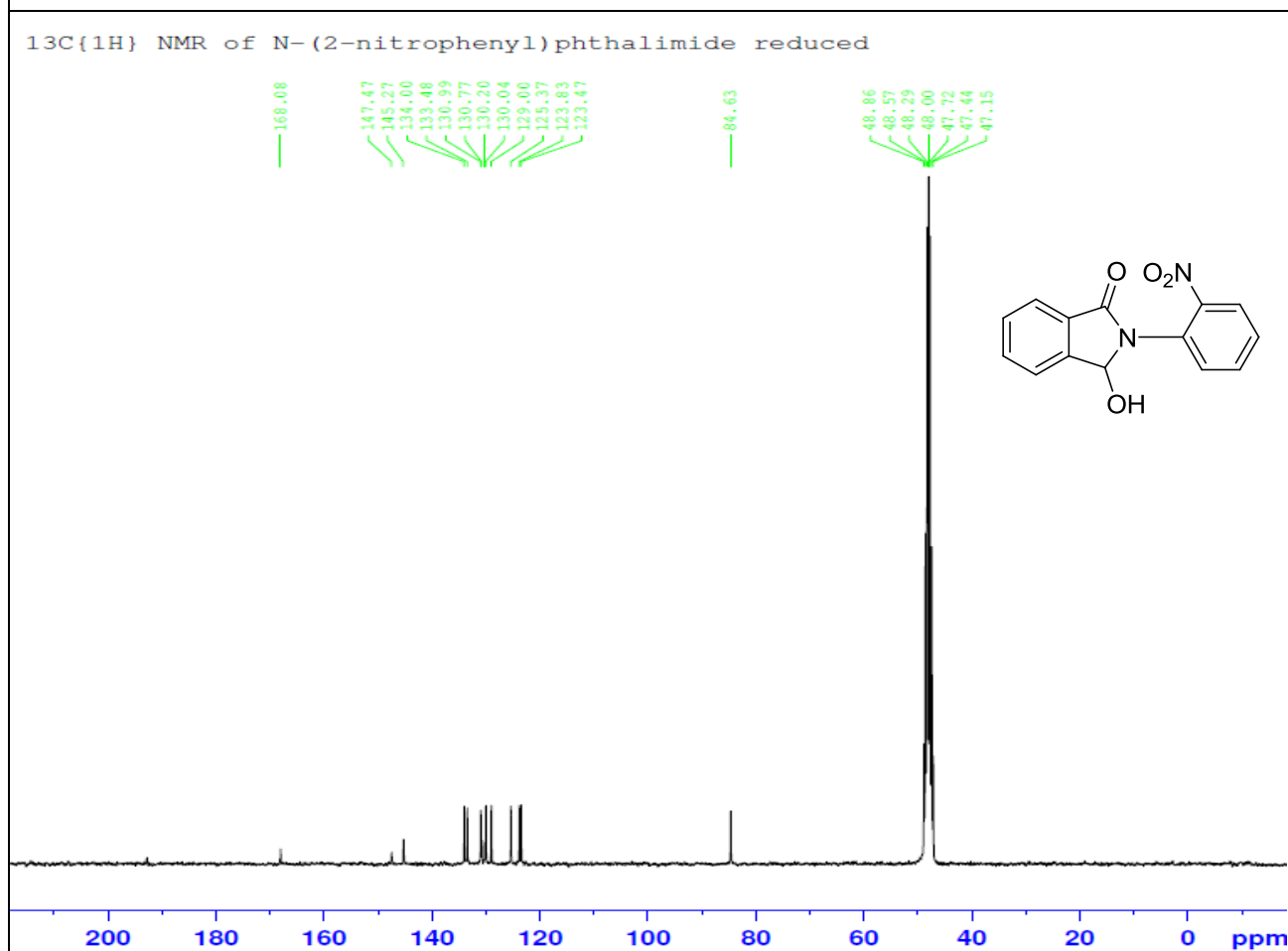
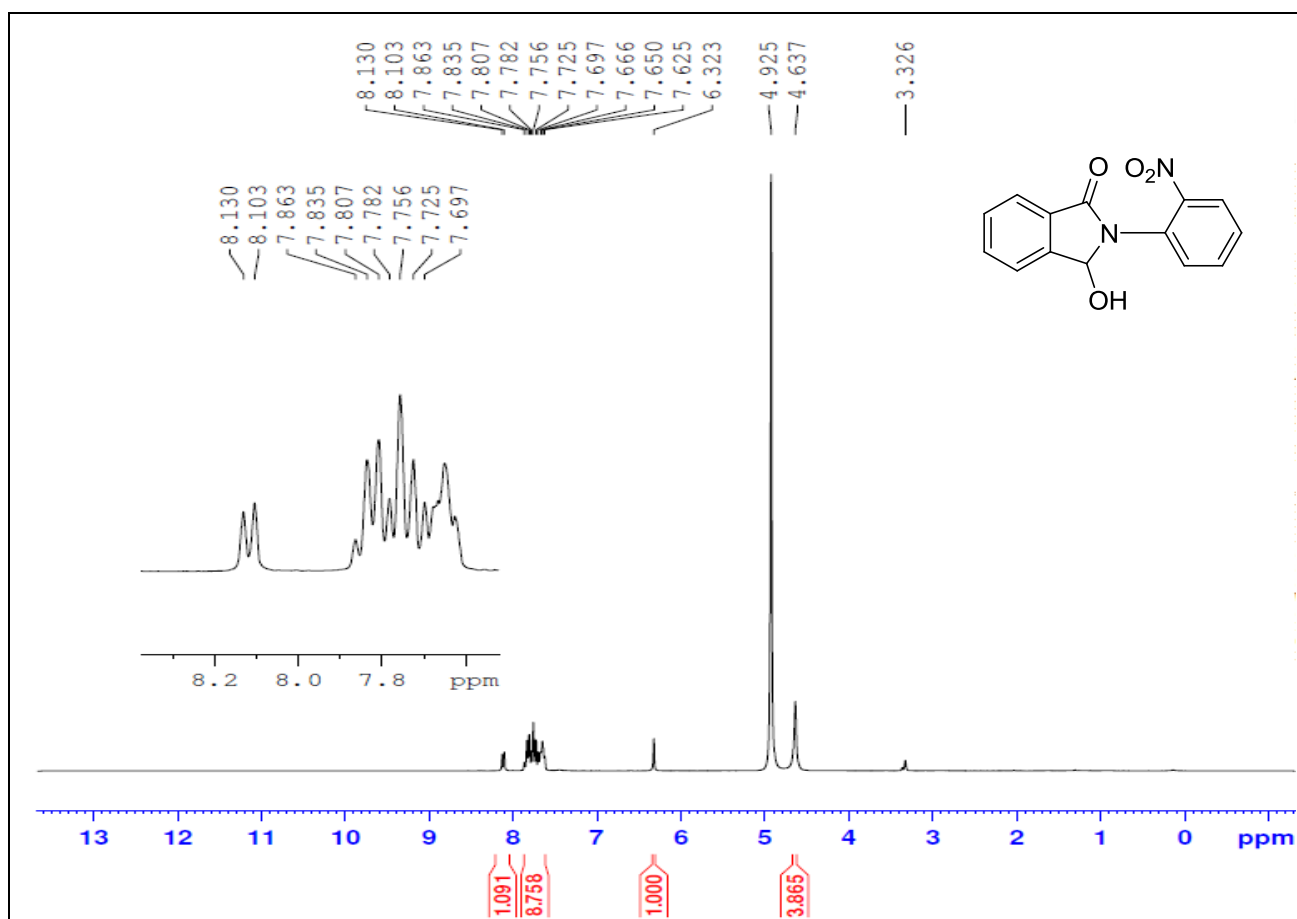
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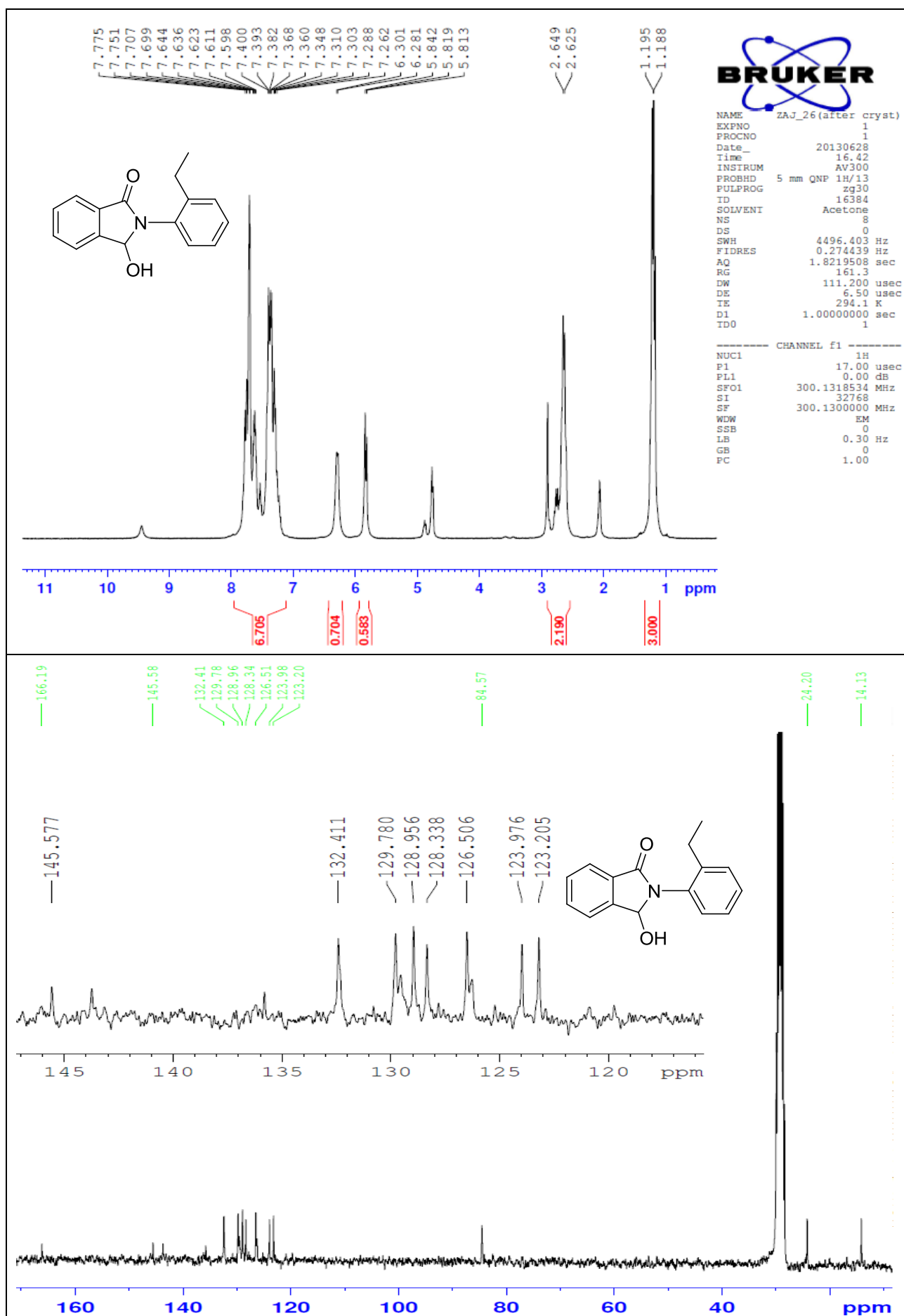
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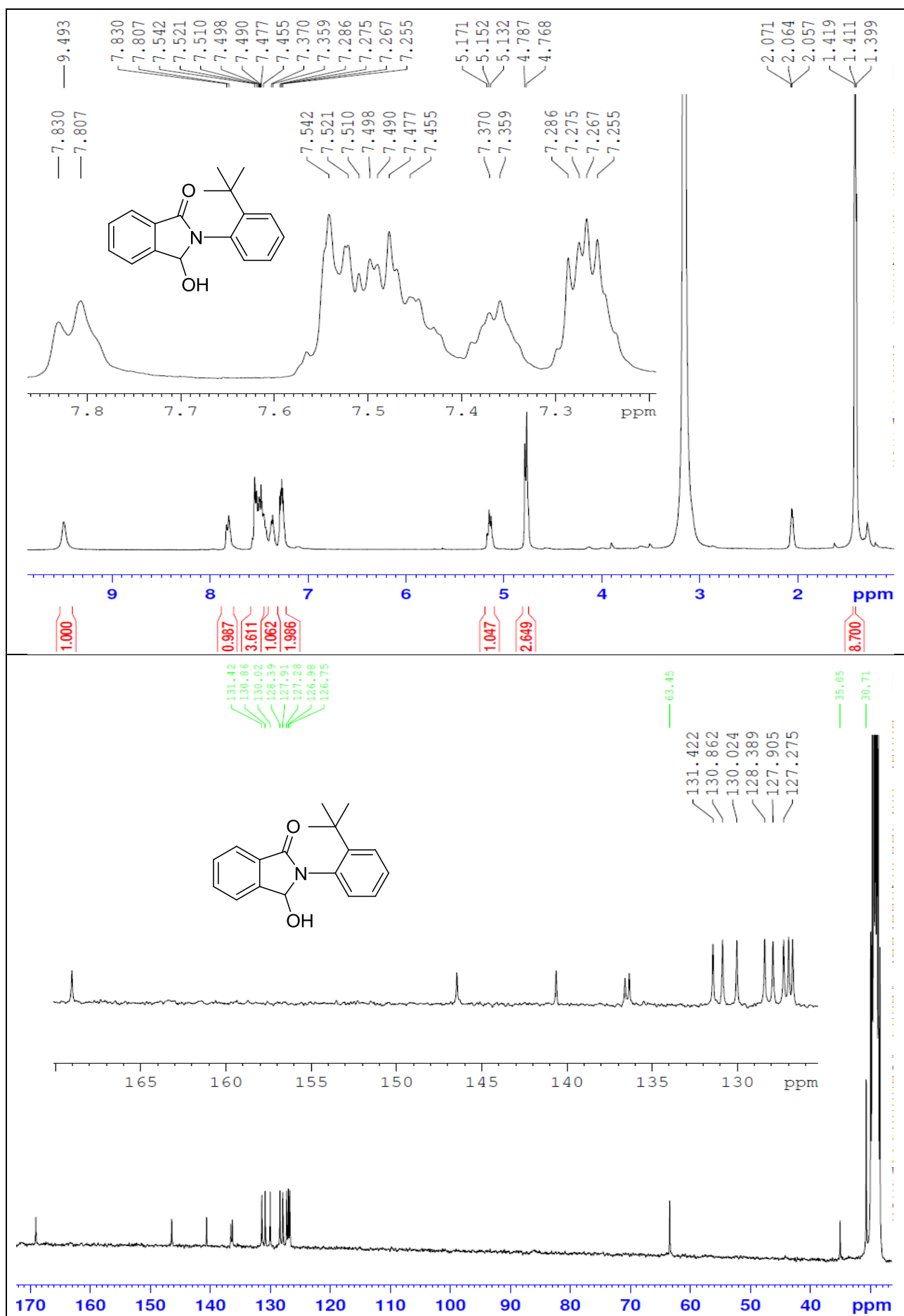


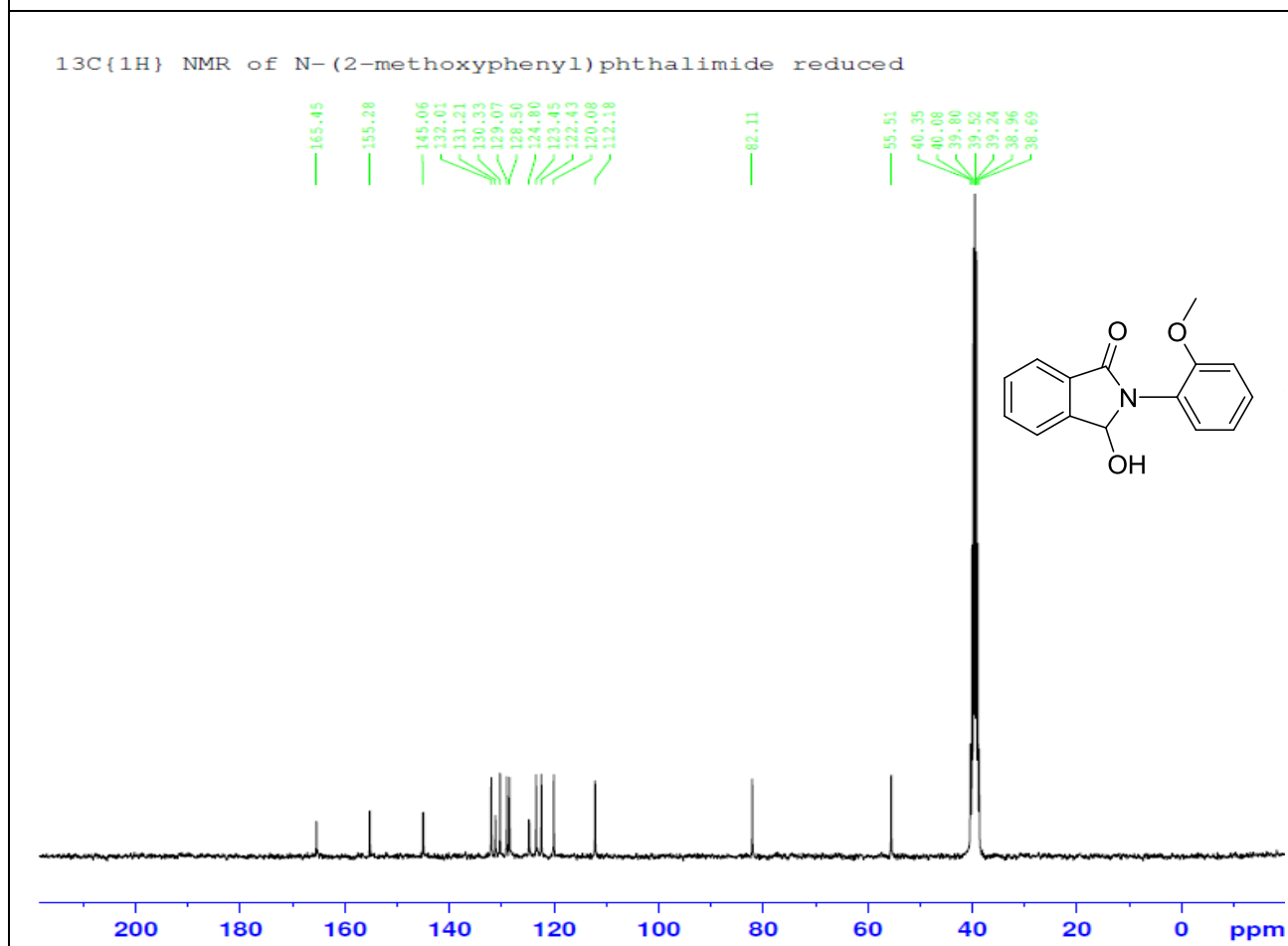
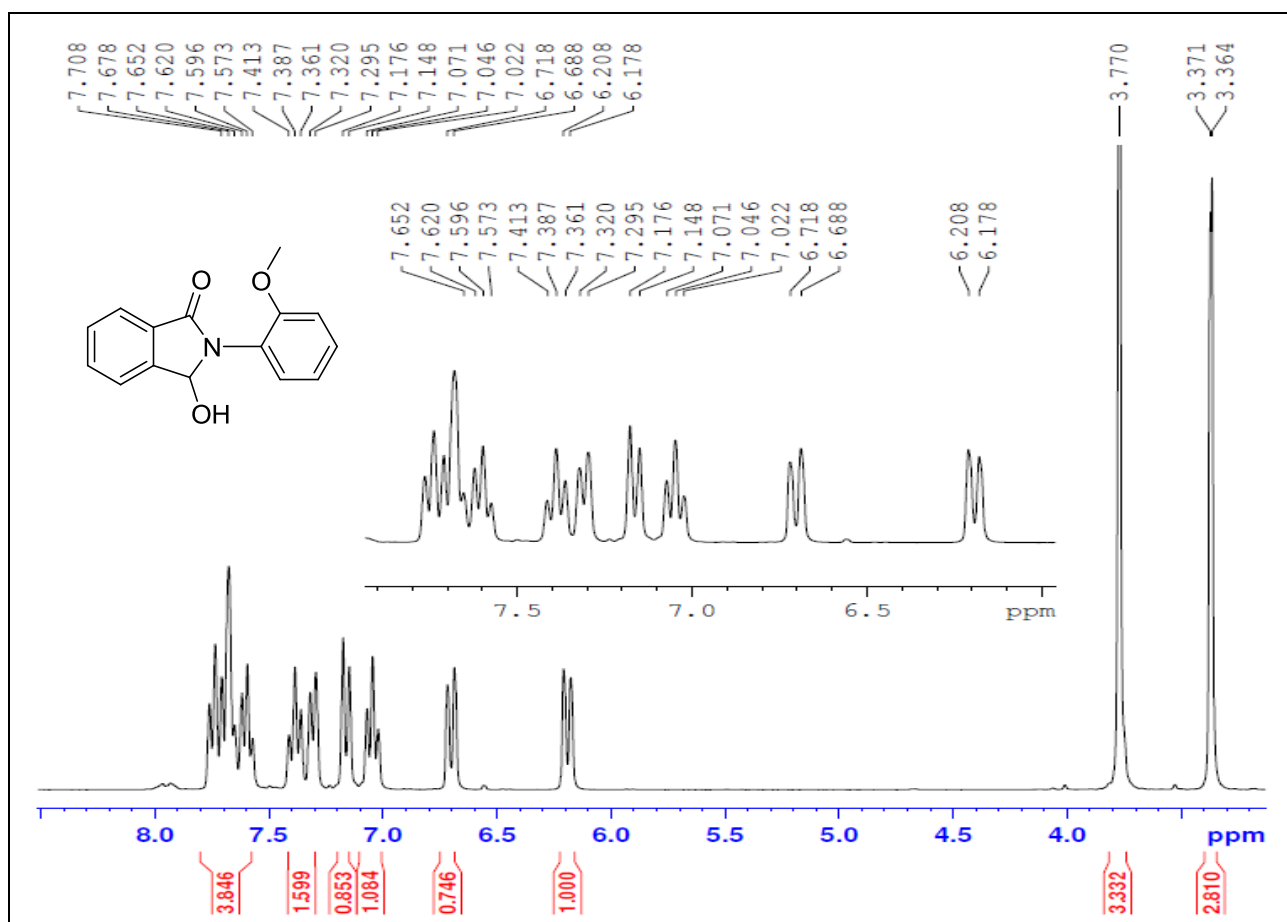






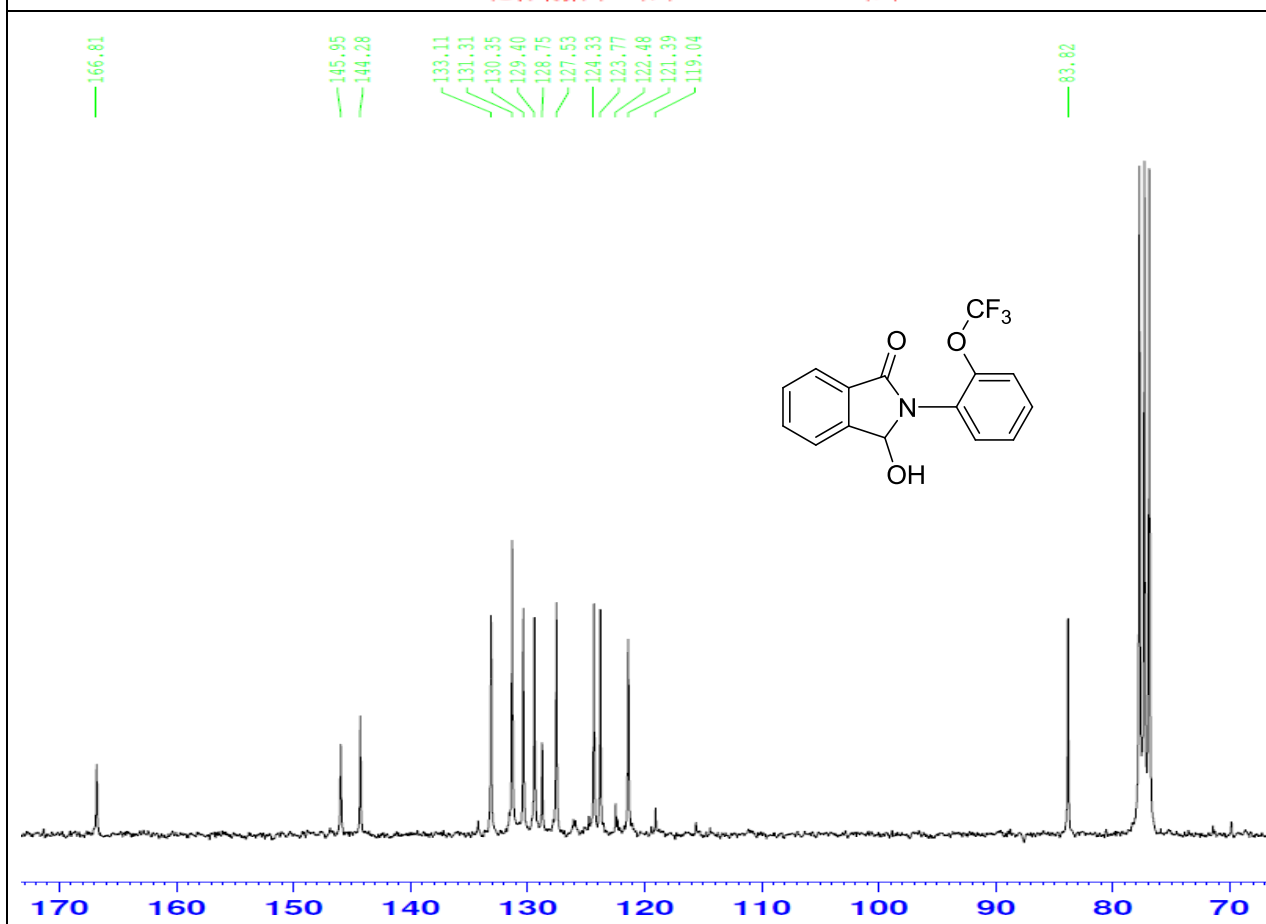
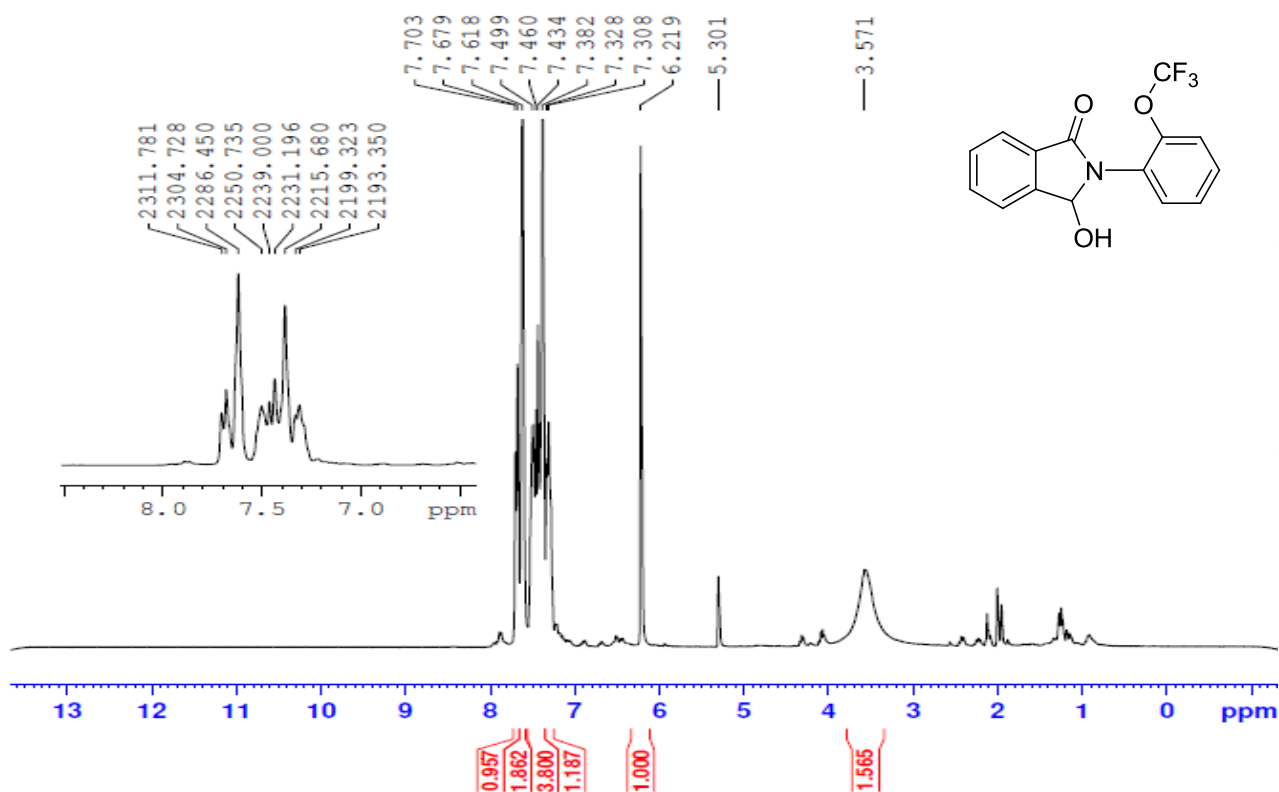




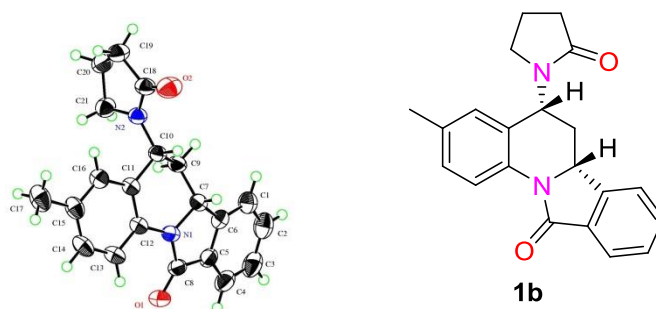




<sup>1</sup>H NMR of N-(2-trifluoromethoxyphenyl)phthalimide reduced



### X-Ray Crystal Structure of Compound **1b** (CCDC 952236)



**Figure 1:** ORTEP diagram showing crystallographic atom numbering and solid-state conformation for 3-methyl-5-(2-oxopyrrolidin-1-yl)-6,6a-dihydroisindolo[2,1-a]quinolin-11(5*H*)-one (**1b**). The additional set of H atoms attached to the disordered CH<sub>3</sub> group is omitted for clarity.

A colourless needle crystal of **1b** having approximate dimensions of 0.37 × 0.19 × 0.18 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-K $\alpha$  radiation. The structure was solved by direct methods [8] and expanded using Fourier techniques [9]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model.

The crystallographic data for **1b** are listed in Table 1, and Table 2 lists the selected bond distances and angles. CCDC 952236 for **1b** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif) (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).

**Table 1:** Crystal data and structure refinements for **1b**.

| Crystal Data         |                                                               |
|----------------------|---------------------------------------------------------------|
| Empirical Formula    | C <sub>21</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub> |
| Formula Weight       | 332.40                                                        |
| Crystal Color, Habit | colourless, needle                                            |
| Crystal Dimensions   | 0.37 X 0.19 X 0.18 mm                                         |
| Crystal System       | monoclinic                                                    |
| Lattice Type         | Primitive                                                     |
| Indexing Images      | 4 oscillations @ 180.0 seconds                                |
| Detector Position    | 127.40 mm                                                     |
| Pixel Size           | 0.100 mm                                                      |

|                                          |                                                                                                                                                             |
|------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Lattice Parameters                       | $a = 9.1629(2) \text{ \AA}$<br>$b = 6.9694(2) \text{ \AA}$<br>$c = 26.0355(8) \text{ \AA}$<br>$\beta = 98.2109(14)^\circ$<br>$V = 1645.58(8) \text{ \AA}^3$ |
| Space Group                              | P2 <sub>1</sub> /c (#14)                                                                                                                                    |
| Z value                                  | 4                                                                                                                                                           |
| D <sub>calc</sub>                        | 1.342 g/cm <sup>3</sup>                                                                                                                                     |
| F <sub>000</sub>                         | 704.00                                                                                                                                                      |
| $\mu(\text{MoK}\alpha)$                  | 0.870 cm <sup>-1</sup>                                                                                                                                      |
| <b>Intensity Measurements</b>            |                                                                                                                                                             |
| Diffractometer                           | Rigaku RAXIS-UNKNOWN                                                                                                                                        |
| Radiation                                | MoK $\alpha$ ( $\lambda = 0.71070 \text{ \AA}$ )<br>graphite monochromated                                                                                  |
| Data Images                              | 35 exposures                                                                                                                                                |
| $\omega$ oscillation Range               | 20.0 - 195.0°                                                                                                                                               |
| Exposure Rate                            | 288.0 sec./°                                                                                                                                                |
| Detector Position                        | 127.40 mm                                                                                                                                                   |
| Pixel Size                               | 0.100 mm                                                                                                                                                    |
| $2\theta_{\text{max}}$                   | 71.1°                                                                                                                                                       |
| No. of Reflections Measured              | Total: 17656; Unique: 6258 ( $R_{\text{int}} = 0.023$ )                                                                                                     |
| Corrections                              | Lorentz-polarization<br>Absorption<br>(trans. factors: 0.733 - 0.984)                                                                                       |
| <b>Structure Solution and Refinement</b> |                                                                                                                                                             |
| Structure Solution                       | Direct Methods (SHELX97)                                                                                                                                    |
| Refinement                               | Full-matrix least-squares on F                                                                                                                              |
| Function Minimized                       | $\Sigma w ( F_o  -  F_c )^2$                                                                                                                                |
| Least Squares Weights                    | Chebyshev polynomial with 3 parameters<br>5.5530, 4.0059, 4.1133                                                                                            |

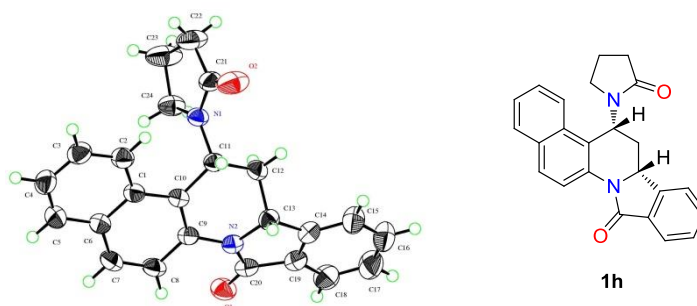
|                                          |                                      |
|------------------------------------------|--------------------------------------|
| $2\theta_{\text{max}}$ cutoff            | 52.0°                                |
| Anomalous Dispersion                     | All non-hydrogen atoms               |
| No. Observations ( $I > 3.00\sigma(I)$ ) | 2678                                 |
| No. Variables                            | 249                                  |
| Reflection/Parameter Ratio               | 10.76                                |
| Residuals: R ( $I > 3.00\sigma(I)$ )     | 0.0373                               |
| Residuals: Rw ( $I > 3.00\sigma(I)$ )    | 0.0476                               |
| Goodness of Fit Indicator                | 1.071                                |
| Max Shift/Error in Final Cycle           | 0.000                                |
| Maximum peak in Final Diff. Map          | 0.14 e <sup>-</sup> /Å <sup>3</sup>  |
| Minimum peak in Final Diff. Map          | -0.19 e <sup>-</sup> /Å <sup>3</sup> |

**Table 2:** Selected bond lengths (Å) and angles (°) for **1b**.

| Bond Lengths (Å) |            |             |            |
|------------------|------------|-------------|------------|
| Atom-Atom        | Distance   | Atom-Atom   | Distance   |
| O(1)-C(8)        | 1.2274(15) | O(2)-C(18)  | 1.2183(15) |
| N(1)-C(7)        | 1.4734(14) | N(1)-C(8)   | 1.3851(14) |
| N(1)-C(12)       | 1.4165(13) | N(2)-C(10)  | 1.4547(13) |
| N(2)-C(18)       | 1.3518(14) | N(2)-C(21)  | 1.4499(14) |
| C(1)-C(2)        | 1.393(2)   | C(1)-C(6)   | 1.3840(17) |
| C(2)-C(3)        | 1.391(2)   | C(3)-C(4)   | 1.382(2)   |
| C(4)-C(5)        | 1.3879(16) | C(5)-C(6)   | 1.3818(18) |
| C(5)-C(8)        | 1.4757(16) | C(6)-C(7)   | 1.4970(15) |
| C(7)-C(9)        | 1.5185(15) | C(9)-C(10)  | 1.5273(14) |
| C(10)-C(11)      | 1.5209(16) | C(11)-C(12) | 1.4096(15) |
| C(11)-C(16)      | 1.3926(14) | C(12)-C(13) | 1.3961(16) |
| C(13)-C(14)      | 1.3801(17) | C(14)-C(15) | 1.388(2)   |
| C(15)-C(16)      | 1.3856(16) | C(15)-C(17) | 1.5084(19) |
| C(18)-C(19)      | 1.5124(17) | C(19)-C(20) | 1.5150(18) |
| C(20)-C(21)      | 1.5235(19) |             |            |

| Bond Angles (°)   |            |                   |            |
|-------------------|------------|-------------------|------------|
| Atom-Atom-Atom    | Angle      | Atom-Atom-Atom    | Angle      |
| C(7)-N(1)-C(8)    | 112.05(8)  | C(7)-N(1)-C(12)   | 119.75(9)  |
| C(8)-N(1)-C(12)   | 127.63(9)  | C(10)-N(2)-C(18)  | 122.01(9)  |
| C(10)-N(2)-C(21)  | 124.07(9)  | C(18)-N(2)-C(21)  | 113.68(9)  |
| C(2)-C(1)-C(6)    | 117.99(14) | C(1)-C(2)-C(3)    | 121.27(14) |
| C(2)-C(3)-C(4)    | 120.49(12) | C(3)-C(4)-C(5)    | 117.93(13) |
| C(4)-C(5)-C(6)    | 121.85(12) | C(4)-C(5)-C(8)    | 128.68(12) |
| C(6)-C(5)-C(8)    | 109.43(9)  | C(1)-C(6)-C(5)    | 120.44(11) |
| C(1)-C(6)-C(7)    | 130.21(12) | C(5)-C(6)-C(7)    | 109.35(9)  |
| N(1)-C(7)-C(6)    | 102.63(9)  | N(1)-C(7)-C(9)    | 110.17(8)  |
| C(6)-C(7)-C(9)    | 117.42(9)  | O(1)-C(8)-N(1)    | 126.53(9)  |
| O(1)-C(8)-C(5)    | 127.39(9)  | N(1)-C(8)-C(5)    | 106.06(9)  |
| C(7)-C(9)-C(10)   | 107.29(8)  | N(2)-C(10)-C(9)   | 111.74(8)  |
| N(2)-C(10)-C(11)  | 113.12(8)  | C(9)-C(10)-C(11)  | 110.38(8)  |
| C(10)-C(11)-C(12) | 120.61(8)  | C(10)-C(11)-C(16) | 120.36(9)  |
| C(12)-C(11)-C(16) | 119.02(10) | N(1)-C(12)-C(11)  | 119.58(9)  |
| N(1)-C(12)-C(13)  | 121.52(10) | C(11)-C(12)-C(13) | 118.90(9)  |
| C(12)-C(13)-C(14) | 120.08(12) | C(13)-C(14)-C(15) | 122.27(11) |
| C(14)-C(15)-C(16) | 117.23(10) | C(14)-C(15)-C(17) | 121.74(11) |
| C(16)-C(15)-C(17) | 121.03(12) | C(11)-C(16)-C(15) | 122.49(11) |
| O(2)-C(18)-N(2)   | 125.53(10) | O(2)-C(18)-C(19)  | 127.01(11) |
| N(2)-C(18)-C(19)  | 107.49(10) | C(18)-C(19)-C(20) | 104.75(10) |
| C(19)-C(20)-C(21) | 104.12(10) | N(2)-C(21)-C(20)  | 102.94(10) |

### X-ray Crystal Structure of Compound **1h** (CCDC 951754)



**Figure 2** ORTEP diagram showing crystallographic atom numbering and solid-state conformation for 7-(2-oxopyrrolidin-1-yl)-8,8a-dihydrobenzo[*f*]isoindolo[2,1-*a*]quinolin-13(7*H*)-one (**1h**).

A colourless needle crystal of **1h** having approximate dimensions of  $0.44 \times 0.37 \times 0.32$  mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo K $\alpha$  radiation. The structure was solved by direct methods [8] and expanded using Fourier techniques [9]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model.

The crystallographic data for **1h** are listed in Table 3, and Table 4 lists the selected bond distances and angles. CCDC 951754 for **1h** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif) (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).

**Table 3:** Crystal data and structure refinements for **1h**.

| Crystal Data         |                                                               |
|----------------------|---------------------------------------------------------------|
| Empirical Formula    | C <sub>24</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub> |
| Formula Weight       | 368.43                                                        |
| Crystal Color, Habit | colourless, hexagonal needle                                  |
| Crystal Dimensions   | 0.44 X 0.37 X 0.32 mm                                         |
| Crystal System       | Monoclinic                                                    |
| Lattice Type         | Primitive                                                     |
| Indexing Images      | 4 oscillations @ 180.0 seconds                                |
| Detector Position    | 127.40 mm                                                     |
| Pixel Size           | 0.100 mm                                                      |
| Lattice Parameters   | a = 10.0772(2) Å                                              |

|                                          |                                                        |
|------------------------------------------|--------------------------------------------------------|
|                                          | b = 17.5969(3) Å                                       |
|                                          | c = 10.4208(3) Å                                       |
|                                          | $\beta$ = 96.3441(13)°                                 |
|                                          | V = 1836.58(7) Å <sup>3</sup>                          |
| Space Group                              | P2 <sub>1</sub> /a (#14)                               |
| Z value                                  | 4                                                      |
| D <sub>calc</sub>                        | 1.332 g/cm <sup>3</sup>                                |
| F <sub>000</sub>                         | 776.00                                                 |
| $\mu$ (MoK $\alpha$ )                    | 0.854 cm <sup>-1</sup>                                 |
| <b>Intensity Measurements</b>            |                                                        |
| Diffractometer                           | Rigaku RAXIS-UNKNOWN                                   |
| Radiation                                | MoK $\alpha$ ( $\lambda$ = 0.71070 Å)                  |
|                                          | graphite monochromated                                 |
| Data Images                              | 45 exposures                                           |
| $\omega$ oscillation Range               | 20.0 - 200.0°                                          |
| Exposure Rate                            | 300.0 sec./°                                           |
| Detector Position                        | 127.40 mm                                              |
| Pixel Size                               | 0.100 mm                                               |
| 2 $\theta_{\max}$                        | 71.3°                                                  |
| No. of Reflections Measured              | Total: 25005; Unique: 6970 ( $R_{\text{int}}$ = 0.021) |
| Corrections                              | Lorentz-polarization                                   |
|                                          | Absorption; (trans. factors: 0.660 - 0.973)            |
| <b>Structure Solution and Refinement</b> |                                                        |
| Structure Solution                       | Direct Methods (SHELX97)                               |
| Refinement                               | Full-matrix least-squares on F                         |
| Function Minimized                       | $\Sigma w ( F_o  -  F_c )^2$                           |
| Least Squares Weights                    | Chebyshev polynomial with 3 parameters                 |
|                                          | 6.2397, 3.8659, 4.1125                                 |
| 2 $\theta_{\max}$ cutoff                 | 54.0°                                                  |
| Anomalous Dispersion                     | All non-hydrogen atoms                                 |

|                                          |                                  |
|------------------------------------------|----------------------------------|
| No. Observations ( $I > 3.00\sigma(I)$ ) | 3370                             |
| No. Variables                            | 273                              |
| Reflection/Parameter Ratio               | 12.34                            |
| Residuals: R ( $I > 3.00\sigma(I)$ )     | 0.0473                           |
| Residuals: Rw ( $I > 3.00\sigma(I)$ )    | 0.0569                           |
| Goodness of Fit Indicator                | 1.079                            |
| Max Shift/Error in Final Cycle           | 0.000                            |
| Maximum peak in Final Diff. Map          | $0.29 \text{ e}^-/\text{\AA}^3$  |
| Minimum peak in Final Diff. Map          | $-0.45 \text{ e}^-/\text{\AA}^3$ |

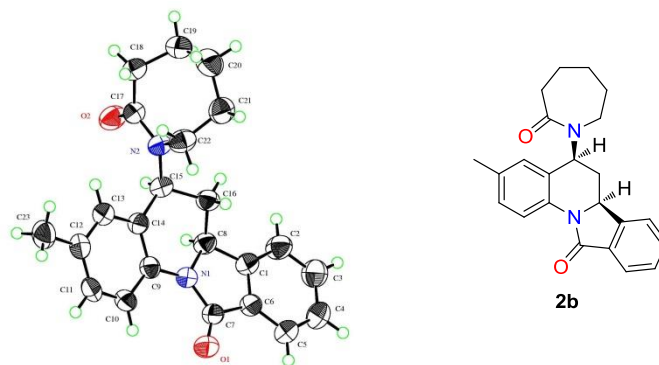
**Table 4:** Selected bond lengths ( $\text{\AA}$ ) and angles ( $^\circ$ ) for **1h**.

| Bond Lengths ( $\text{\AA}$ ) |            |             |            |
|-------------------------------|------------|-------------|------------|
| Atom-Atom                     | Distance   | Atom-Atom   | Distance   |
| O(1)-C(20)                    | 1.2203(17) | O(2)-C(21)  | 1.218(2)   |
| N(1)-C(11)                    | 1.4670(14) | N(1)-C(21)  | 1.3442(17) |
| N(1)-C(24)                    | 1.4601(17) | N(2)-C(9)   | 1.4073(16) |
| N(2)-C(13)                    | 1.4678(16) | N(2)-C(20)  | 1.3828(16) |
| C(1)-C(2)                     | 1.4222(19) | C(1)-C(6)   | 1.4221(18) |
| C(1)-C(10)                    | 1.4322(17) | C(2)-C(3)   | 1.369(2)   |
| C(3)-C(4)                     | 1.400(2)   | C(4)-C(5)   | 1.366(2)   |
| C(5)-C(6)                     | 1.419(2)   | C(6)-C(7)   | 1.4165(19) |
| C(7)-C(8)                     | 1.356(2)   | C(8)-C(9)   | 1.4227(18) |
| C(9)-C(10)                    | 1.3886(16) | C(10)-C(11) | 1.5258(16) |
| C(11)-C(12)                   | 1.5290(17) | C(12)-C(13) | 1.5186(17) |
| C(13)-C(14)                   | 1.4983(18) | C(14)-C(15) | 1.384(2)   |
| C(14)-C(19)                   | 1.3813(19) | C(15)-C(16) | 1.389(2)   |
| C(16)-C(17)                   | 1.385(2)   | C(17)-C(18) | 1.382(2)   |
| C(18)-C(19)                   | 1.390(2)   | C(19)-C(20) | 1.4832(19) |
| C(21)-C(22)                   | 1.512(2)   | C(22)-C(23) | 1.466(3)   |
| C(23)-C(24)                   | 1.504(2)   |             |            |



| Bond Angles (°)   |            |                   |            |
|-------------------|------------|-------------------|------------|
| Atom-Atom-Atom    | Angle      | Atom-Atom-Atom    | Angle      |
| C(11)-N(1)-C(21)  | 121.76(10) | C(11)-N(1)-C(24)  | 123.89(10) |
| C(21)-N(1)-C(24)  | 113.93(10) | C(9)-N(2)-C(13)   | 118.45(10) |
| C(9)-N(2)-C(20)   | 127.65(11) | C(13)-N(2)-C(20)  | 112.97(10) |
| C(2)-C(1)-C(6)    | 117.46(11) | C(2)-C(1)-C(10)   | 122.62(11) |
| C(6)-C(1)-C(10)   | 119.92(11) | C(1)-C(2)-C(3)    | 121.13(12) |
| C(2)-C(3)-C(4)    | 121.00(13) | O(3)-C(4)-C(5)    | 119.73(14) |
| C(4)-C(5)-C(6)    | 120.81(14) | C(1)-C(6)-C(5)    | 119.75(12) |
| C(1)-C(6)-C(7)    | 118.77(12) | C(5)-C(6)-C(7)    | 121.48(12) |
| C(6)-C(7)-C(8)    | 121.18(12) | C(7)-C(8)-C(9)    | 120.40(12) |
| N(2)-C(9)-C(8)    | 119.18(11) | N(2)-C(9)-C(10)   | 119.96(10) |
| C(8)-C(9)-C(10)   | 120.80(11) | C(1)-C(10)-C(9)   | 118.62(10) |
| C(1)-C(10)-C(11)  | 120.16(10) | C(9)-C(10)-C(11)  | 121.22(10) |
| N(1)-C(11)-C(10)  | 112.10(9)  | N(1)-C(11)-C(12)  | 108.32(9)  |
| C(10)-C(11)-C(12) | 112.63(9)  | C(11)-C(12)-C(13) | 109.89(9)  |
| N(2)-C(13)-C(12)  | 107.82(9)  | N(2)-C(13)-C(14)  | 102.59(10) |
| C(12)-C(13)-C(14) | 115.36(10) | C(13)-C(14)-C(15) | 130.01(13) |
| C(13)-C(14)-C(19) | 109.35(11) | C(15)-C(14)-C(19) | 120.64(13) |
| C(14)-C(15)-C(16) | 117.87(15) | C(15)-C(16)-C(17) | 121.53(16) |
| C(16)-C(17)-C(18) | 120.45(17) | C(17)-C(18)-C(19) | 118.06(15) |
| C(14)-C(19)-C(18) | 121.44(13) | C(14)-C(19)-C(20) | 109.67(11) |
| C(18)-C(19)-C(20) | 128.86(12) | O(1)-C(20)-N(2)   | 127.17(12) |
| O(1)-C(20)-C(19)  | 127.50(12) | N(2)-C(20)-C(19)  | 105.33(10) |
| O(2)-C(21)-N(1)   | 125.26(12) | O(2)-C(21)-C(22)  | 127.08(14) |
| N(1)-C(21)-C(22)  | 107.65(12) | C(21)-C(22)-C(23) | 106.07(13) |
| C(22)-C(23)-C(24) | 107.60(15) | N(1)-C(24)-C(23)  | 103.79(13) |

### X-ray Crystal Structure of Compound **2b** (CCDC 951755)



**Figure 3:** ORTEP diagram showing crystallographic atom numbering and solid-state conformation for 3-methyl-5-(2-oxazepan-1-yl)-6,6a-dihydroisoindolo[2,1-a]quinolin-11(5H)-one (**2b**).

A colourless needle crystal of **2b** having approximate dimensions of 0.41 × 0.14 × 0.11 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo K $\alpha$  radiation. The structure was solved by direct methods [8] and expanded using Fourier techniques [9]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model.

The crystallographic data for **2b** are listed in Table 5, and Table 6 lists the selected bond distances and angles. CCDC 951755 for **2b** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif) (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).

**Table 5:** Crystal data and structure refinements for **2b**.

| Crystal Data         |                                                               |
|----------------------|---------------------------------------------------------------|
| Empirical Formula    | C <sub>23</sub> H <sub>24</sub> N <sub>2</sub> O <sub>2</sub> |
| Formula Weight       | 360.45                                                        |
| Crystal Color, Habit | colourless, needle                                            |
| Crystal Dimensions   | 0.41 X 0.14 X 0.11 mm                                         |
| Crystal System       | Monoclinic                                                    |
| Lattice Type         | Primitive                                                     |
| Indexing Images      | 4 oscillations @ 120.0 seconds                                |
| Detector Position    | 127.40 mm                                                     |
| Pixel Size           | 0.100 mm                                                      |

|                                          |                                                                                                                                                                 |
|------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Lattice Parameters                       | $a = 10.2484(3) \text{ \AA}$<br>$b = 33.4029(12) \text{ \AA}$<br>$c = 11.1621(2) \text{ \AA}$<br>$\beta = 99.4030(14)^\circ$<br>$V = 3769.74(19) \text{ \AA}^3$ |
| Space Group                              | P2 <sub>1</sub> /a (#14)                                                                                                                                        |
| Z value                                  | 8                                                                                                                                                               |
| D <sub>calc</sub>                        | 1.270 g/cm <sup>3</sup>                                                                                                                                         |
| F <sub>000</sub>                         | 1536.00                                                                                                                                                         |
| $\mu(\text{MoK}\alpha)$                  | 0.813 cm <sup>-1</sup>                                                                                                                                          |
| <b>Intensity Measurements</b>            |                                                                                                                                                                 |
| Diffractometer                           | Rigaku RAXIS-UNKNOWN                                                                                                                                            |
| Radiation                                | MoK $\alpha$ ( $\lambda = 0.71070 \text{ \AA}$ )<br>graphite monochromated                                                                                      |
| Data Images                              | 36 exposures                                                                                                                                                    |
| $\omega$ oscillation Range               | 20.0 - 200.0°                                                                                                                                                   |
| Exposure Rate                            | 264.0 sec./°                                                                                                                                                    |
| Detector Position                        | 127.40 mm                                                                                                                                                       |
| Pixel Size                               | 0.100 mm                                                                                                                                                        |
| $2\theta_{\text{max}}$                   | 60.1°                                                                                                                                                           |
| No. of Reflections Measured              | Total: 35171; Unique: 10853 ( $R_{\text{int}} = 0.043$ )                                                                                                        |
| Corrections                              | Lorentz-polarization<br>Absorption; (trans. factors: 0.591 - 0.991)                                                                                             |
| <b>Structure Solution and Refinement</b> |                                                                                                                                                                 |
| Structure Solution                       | Direct Methods (SHELX97)                                                                                                                                        |
| Refinement                               | Full-matrix least-squares on F                                                                                                                                  |
| Function Minimized                       | $\sum w ( F_o  -  F_c )^2$                                                                                                                                      |
| Least Squares Weights                    | Chebychev polynomial with 3 parameters<br>9.1859, 1.9202, 6.9202                                                                                                |
| $2\theta_{\text{max}}$ cutoff            | 52.0°                                                                                                                                                           |

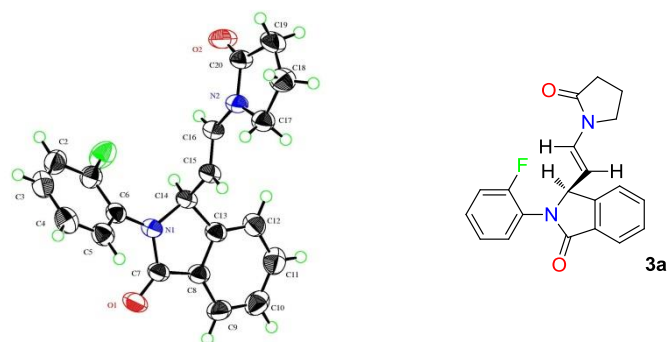
|                                          |                                  |
|------------------------------------------|----------------------------------|
| Anomalous Dispersion                     | All non-hydrogen atoms           |
| No. Observations ( $I > 3.00\sigma(I)$ ) | 4480                             |
| No. Variables                            | 487                              |
| Reflection/Parameter Ratio               | 9.20                             |
| Residuals: R ( $I > 3.00\sigma(I)$ )     | 0.0465                           |
| Residuals: Rw ( $I > 3.00\sigma(I)$ )    | 0.0582                           |
| Goodness of Fit Indicator                | 1.086                            |
| Max Shift/Error in Final Cycle           | 0.000                            |
| Maximum peak in Final Diff. Map          | $0.47 \text{ e}^-/\text{\AA}^3$  |
| Minimum peak in Final Diff. Map          | $-0.23 \text{ e}^-/\text{\AA}^3$ |

**Table 6:** Selected bond lengths (Å) and angles (°) for **2b**.

| Bond Lengths (Å) |          |             |          |
|------------------|----------|-------------|----------|
| Atom-Atom        | Distance | Atom-Atom   | Distance |
| O(1)-C(7)        | 1.225(2) | O(2)-C(17)  | 1.234(3) |
| N(1)-C(7)        | 1.382(2) | N(1)-C(8)   | 1.474(2) |
| N(1)-C(9)        | 1.421(2) | N(2)-C(15)  | 1.461(2) |
| N(2)-C(17)       | 1.359(2) | N(2)-C(22)  | 1.467(3) |
| C(1)-C(2)        | 1.379(3) | C(1)-C(6)   | 1.376(3) |
| C(1)-C(8)        | 1.506(2) | C(2)-C(3)   | 1.381(3) |
| C(3)-C(4)        | 1.395(4) | C(4)-C(5)   | 1.375(3) |
| C(5)-C(6)        | 1.391(3) | C(6)-C(7)   | 1.476(2) |
| C(8)-C(16)       | 1.514(3) | C(9)-C(10)  | 1.397(3) |
| C(9)-C(14)       | 1.407(2) | C(10)-C(11) | 1.384(3) |
| C(11)-C(12)      | 1.389(3) | C(12)-C(13) | 1.390(3) |
| C(12)-C(23)      | 1.499(3) | C(13)-C(14) | 1.390(2) |
| C(14)-C(15)      | 1.522(2) | C(15)-C(16) | 1.529(3) |
| C(17)-C(18)      | 1.510(3) | C(18)-C(19) | 1.523(3) |
| C(19)-C(20)      | 1.478(4) | C(20)-C(21) | 1.512(4) |
| C(21)-C(22)      | 1.524(3) |             |          |

| Bond Angles (°)   |            |                   |            |
|-------------------|------------|-------------------|------------|
| Atom-Atom-Atom    | Angle      | Atom-Atom-Atom    | Angle      |
| C(7)-N(1)-C(8)    | 112.80(16) | C(7)-N(1)-C(9)    | 127.21(17) |
| C(8)-N(1)-C(9)    | 119.19(16) | C(15)-N(2)-C(17)  | 118.86(19) |
| C(15)-N(2)-C(22)  | 118.26(18) | C(17)-N(2)-C(22)  | 122.71(18) |
| C(2)-C(1)-C(6)    | 121.2(2)   | C(2)-C(1)-C(8)    | 129.3(2)   |
| C(6)-C(1)-C(8)    | 109.46(18) | C(1)-C(2)-C(3)    | 117.6(2)   |
| C(2)-C(3)-C(4)    | 121.3(2)   | C(3)-C(4)-C(5)    | 120.8(2)   |
| C(4)-C(5)-C(6)    | 117.5(2)   | C(1)-C(6)-C(5)    | 121.5(2)   |
| C(1)-C(6)-C(7)    | 109.85(18) | C(5)-C(6)-C(7)    | 128.6(2)   |
| O(1)-C(7)-N(1)    | 126.70(19) | O(1)-C(7)-C(6)    | 127.6(2)   |
| N(1)-C(7)-C(6)    | 105.71(18) | N(1)-C(8)-C(1)    | 102.13(16) |
| N(1)-C(8)-C(16)   | 110.40(17) | C(1)-C(8)-C(16)   | 117.20(18) |
| N(1)-C(9)-C(10)   | 120.94(18) | N(1)-C(9)-C(14)   | 119.05(17) |
| C(10)-C(9)-C(14)  | 120.01(18) | C(9)-C(10)-C(11)  | 119.4(2)   |
| C(10)-C(11)-C(12) | 122.1(2)   | C(11)-C(12)-C(13) | 117.45(19) |
| C(11)-C(12)-C(23) | 121.9(2)   | C(13)-C(12)-C(23) | 120.6(2)   |
| C(12)-C(13)-C(14) | 122.7(2)   | C(9)-C(14)-C(13)  | 118.26(18) |
| C(9)-C(14)-C(15)  | 121.18(17) | C(13)-C(14)-C(15) | 120.50(18) |
| N(2)-C(15)-C(14)  | 112.88(17) | N(2)-C(15)-C(16)  | 113.40(17) |
| C(14)-C(15)-C(16) | 111.51(17) | C(8)-C(16)-C(15)  | 107.84(18) |
| O(2)-C(17)-N(2)   | 121.9(2)   | O(2)-C(17)-C(18)  | 120.6(2)   |
| N(2)-C(17)-C(18)  | 117.5(2)   | C(17)-C(18)-C(19) | 113.9(2)   |
| C(18)-C(19)-C(20) | 115.7(2)   | C(19)-C(20)-C(21) | 117.4(2)   |
| C(20)-C(21)-C(22) | 113.4(2)   | N(2)-C(22)-C(21)  | 114.2(2)   |

### X-ray Crystal Structure of Compound **3a** (CCDC 951756)



**Figure 4:** ORTEP diagram showing crystallographic atom numbering and solid-state conformation for *E*-2-(2-fluorophenyl)-3-(2-(2-oxopyrrolidin-1-yl)vinyl)isoindolin-1-one (**3a**).

A colourless pinacoid crystal of **3a** having approximate dimensions of  $0.25 \times 0.24 \times 0.16$  mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo K $\alpha$  radiation. The structure was solved by direct methods [8] and expanded using Fourier techniques [9]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model.

The crystallographic data for **3a** are listed in Table 7, and Table 8 lists the selected bond distances and angles. CCDC 951756 for **3a** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif) (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).

**Table 7:** Crystal data and structure refinements for **3a**.

| Crystal Data         |                                                                 |
|----------------------|-----------------------------------------------------------------|
| Empirical Formula    | C <sub>20</sub> H <sub>17</sub> N <sub>2</sub> O <sub>2</sub> F |
| Formula Weight       | 336.36                                                          |
| Crystal Color, Habit | colourless, pinacoid                                            |
| Crystal Dimensions   | 0.25 X 0.24 X 0.16 mm                                           |
| Crystal System       | Monoclinic                                                      |
| Lattice Type         | Primitive                                                       |
| Indexing Images      | 4 oscillations @ 300.0 seconds                                  |
| Detector Position    | 127.40 mm                                                       |
| Pixel Size           | 0.100 mm                                                        |

|                                          |                                                                                                                                                               |
|------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Lattice Parameters                       | $a = 11.9085(3) \text{ \AA}$<br>$b = 9.8202(2) \text{ \AA}$<br>$c = 14.8555(5) \text{ \AA}$<br>$\beta = 102.3677(16)^\circ$<br>$V = 1696.94(8) \text{ \AA}^3$ |
| Space Group                              | P2 <sub>1</sub> /c (#14)                                                                                                                                      |
| Z value                                  | 4                                                                                                                                                             |
| D <sub>calc</sub>                        | 1.316 g/cm <sup>3</sup>                                                                                                                                       |
| F <sub>000</sub>                         | 704.00                                                                                                                                                        |
| $\mu(\text{MoK}\alpha)$                  | 0.933 cm <sup>-1</sup>                                                                                                                                        |
| <b>Intensity Measurements</b>            |                                                                                                                                                               |
| Diffractometer                           | Rigaku RAXIS-UNKNOWN                                                                                                                                          |
| Radiation                                | MoK $\alpha$ ( $\lambda = 0.71070 \text{ \AA}$ )<br>graphite monochromated                                                                                    |
| Data Images                              | 48 exposures                                                                                                                                                  |
| $\omega$ oscillation Range               | 20.0 - 200.0°                                                                                                                                                 |
| Exposure Rate                            | 360.0 sec./°                                                                                                                                                  |
| Detector Position                        | 127.40 mm                                                                                                                                                     |
| Pixel Size                               | 0.100 mm                                                                                                                                                      |
| $2\theta_{\text{max}}$                   | 60.1°                                                                                                                                                         |
| No. of Reflections Measured              | Total: 20315; Unique: 4902 ( $R_{\text{int}} = 0.021$ )                                                                                                       |
| Corrections                              | Lorentz-polarization<br>Absorption; (trans. factors: 0.746 - 0.985)                                                                                           |
| <b>Structure Solution and Refinement</b> |                                                                                                                                                               |
| Structure Solution                       | Direct Methods (SHELX97)                                                                                                                                      |
| Refinement                               | Full-matrix least-squares on F                                                                                                                                |
| Function Minimized                       | $\sum w ( F_o  -  F_c )^2$                                                                                                                                    |
| Least Squares Weights                    | Chebychev polynomial with 3 parameters<br>7.2229, 5.0833, 5.6398                                                                                              |
| $2\theta_{\text{max}}$ cutoff            | 60.1°                                                                                                                                                         |

|                                          |                                  |
|------------------------------------------|----------------------------------|
| Anomalous Dispersion                     | All non-hydrogen atoms           |
| No. Observations ( $I > 3.00\sigma(I)$ ) | 3703                             |
| No. Variables                            | 243                              |
| Reflection/Parameter Ratio               | 15.24                            |
| Residuals: R ( $I > 3.00\sigma(I)$ )     | 0.0389                           |
| Residuals: Rw ( $I > 3.00\sigma(I)$ )    | 0.0544                           |
| Goodness of Fit Indicator                | 1.041                            |
| Max Shift/Error in Final Cycle           | 0.000                            |
| Maximum peak in Final Diff. Map          | $0.28 \text{ e}^-/\text{\AA}^3$  |
| Minimum peak in Final Diff. Map          | $-0.14 \text{ e}^-/\text{\AA}^3$ |

**Table 8:** Selected bond lengths (Å) and angles (°) for **3a**.

| Bond Lengths (Å) |            |             |            |
|------------------|------------|-------------|------------|
| Atom-Atom        | Distance   | Atom-Atom   | Distance   |
| F(1)-C(1)        | 1.3623(13) | O(1)-C(7)   | 1.2205(14) |
| O(2)-C(20)       | 1.2159(14) | N(1)-C(6)   | 1.4153(11) |
| N(1)-C(7)        | 1.3829(12) | N(1)-C(14)  | 1.4861(13) |
| N(2)-C(16)       | 1.3916(14) | N(2)-C(17)  | 1.4611(13) |
| N(2)-C(20)       | 1.3701(13) | C(1)-C(2)   | 1.3779(15) |
| C(1)-C(6)        | 1.3885(13) | C(2)-C(3)   | 1.3828(19) |
| C(3)-C(4)        | 1.3795(17) | C(4)-C(5)   | 1.3903(15) |
| C(5)-C(6)        | 1.3960(14) | C(7)-C(8)   | 1.4741(13) |
| C(8)-C(9)        | 1.3929(13) | C(8)-C(13)  | 1.3857(14) |
| C(9)-C(10)       | 1.3808(18) | C(10)-C(11) | 1.3927(19) |
| C(11)-C(12)      | 1.3892(16) | C(12)-C(13) | 1.3844(14) |
| C(13)-C(14)      | 1.5087(11) | C(14)-C(15) | 1.5003(14) |
| C(15)-C(16)      | 1.3291(14) | C(17)-C(18) | 1.5313(19) |
| C(18)-C(19)      | 1.5135(19) | C(19)-C(20) | 1.5040(17) |



| Bond Angles (°)   |            |                   |            |
|-------------------|------------|-------------------|------------|
| Atom-Atom-Atom    | Angle      | Atom-Atom-Atom    | Angle      |
| C(6)-N(1)-C(7)    | 123.03(8)  | C(6)-N(1)-C(14)   | 124.17(7)  |
| C(7)-N(1)-C(14)   | 112.79(7)  | C(16)-N(2)-C(17)  | 123.59(8)  |
| C(16)-N(2)-C(20)  | 121.66(8)  | C(17)-N(2)-C(20)  | 114.30(9)  |
| F(1)-C(1)-C(2)    | 117.96(9)  | F(1)-C(1)-C(6)    | 118.62(8)  |
| C(2)-C(1)-C(6)    | 123.42(10) | C(1)-C(2)-C(3)    | 118.89(10) |
| C(2)-C(3)-C(4)    | 119.68(11) | C(3)-C(4)-C(5)    | 120.52(11) |
| C(4)-C(5)-C(6)    | 121.06(9)  | N(1)-C(6)-C(1)    | 122.03(8)  |
| N(1)-C(6)-C(5)    | 121.53(8)  | C(1)-C(6)-C(5)    | 116.42(8)  |
| O(1)-C(7)-N(1)    | 125.61(9)  | O(1)-C(7)-C(8)    | 128.15(8)  |
| N(1)-C(7)-C(8)    | 106.24(8)  | C(7)-C(8)-C(9)    | 129.16(10) |
| C(7)-C(8)-C(13)   | 109.38(8)  | C(9)-C(8)-C(13)   | 121.46(9)  |
| C(8)-C(9)-C(10)   | 117.58(11) | C(9)-C(10)-C(11)  | 121.15(11) |
| C(10)-C(11)-C(12) | 121.01(11) | C(11)-C(12)-C(13) | 117.94(11) |
| C(8)-C(13)-C(12)  | 120.85(8)  | C(8)-C(13)-C(14)  | 109.95(8)  |
| C(12)-C(13)-C(14) | 129.19(9)  | N(1)-C(14)-C(13)  | 101.61(7)  |
| N(1)-C(14)-C(15)  | 112.54(8)  | C(13)-C(14)-C(15) | 113.19(7)  |
| C(14)-C(15)-C(16) | 120.74(8)  | N(2)-C(16)-C(15)  | 124.67(9)  |
| N(2)-C(17)-C(18)  | 103.99(9)  | C(17)-C(18)-C(19) | 106.38(11) |
| C(18)-C(19)-C(20) | 106.13(10) | O(2)-C(20)-N(2)   | 124.52(10) |
| O(2)-C(20)-C(19)  | 127.47(10) | N(2)-C(20)-C(19)  | 107.99(9)  |

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