

# Elements of Regiocontrol in Palladium-Catalyzed Oxidative Arene Cross-Coupling Reactions

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## Supporting Information

### General Methods:

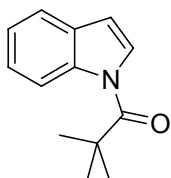
All indoles and pyrroles were purchased from Aldrich (with the exception of 6-methoxyindole and 6-methylindole, both purchased from Alfa Aesar) and used without further purification. HPLC grade benzene and dichloromethane were dried and purified via an MBraun SP Series solvent purification system. Dichloroethane was dried over CaH<sub>2</sub>; triethylamine was dried over NaOH and both were freshly distilled before every use. All reactions were performed in air-dried or oven-dried glassware. Coupling reactions were performed without regard for exclusion of ambient air or moisture (specific conditions described below). Analysis of crude reaction mixtures were done on an Agilent 6890 Network GC System with an Agilent 5973 Network Mass Selective Detector. Reactions were purified by flash chromatography or Chromatotron on silica gel. <sup>1</sup>H, <sup>13</sup>C, and DEPT-135 spectra were recorded in CDCl<sub>3</sub> solutions on a Bruker AVANCE 400 MHz spectrometer at ambient temperature and chemical shifts are reported relative to tetramethylsilane (TMS). Fourier-transform infra-red (FTIR) spectra were obtained as thin films on sodium chloride plates. High resolution mass spectra were obtained with a Kratos Concept IIH mass spectrometer. Melting points were recorded using a Gallenkamp Melting Point Apparatus and are reported uncorrected.

### General procedure for the pivalylation of indoles :

Indole (2.0345 g, 17.4 mmol, 1 eq.) and DMAP (0.2097 g, 1.72 mmol, 0.1 eq.) were weighed into a round bottom flask. The flask was purged with argon and dry DCM (30 mL) was added to yield a clear, colorless solution. Triethylamine (3.6 mL, 25.8 mmol, 1.48 eq.) was added and the flask was submerged into an ice-water bath and cooled to 0°C. Pivaloyl chloride (2.5 mL, 20.3 mmol, 1.17 eq.) was added to the flask slowly (over a period of 1 min.) via syringe and the reaction was allowed to stir at 0°C for ~ 10 min. The reaction was allowed to warm to room temperature and stirred overnight. The following morning the progress of the reaction was checked by tlc. The DCM was removed by rotary evaporation and the residue was partitioned between diethyl ether (50 mL) and a saturated solution of ammonium chloride (50 mL). The layers were separated and the ethereal layer was washed with brine (25 mL). The combined

aqueous layers were back extracted with a further 50 mL of diethyl ether and the combined organic fractions were dried with  $\text{MgSO}_4$  and evaporated to dryness. Purification was performed under the specific conditions described below.

***N*-Pivaloylindole :**



The title compound was prepared according to the above procedure and was subjected to column chromatography on silica gel with 5% diethyl ether in hexanes as the solvent to afford the title compound in 94% yield.

**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  8.52 (dd,  $J = 8.4$  Hz,  $J = 0.7$  Hz, 1H), 7.72 (d,  $J = 3.8$  Hz, 1H), 7.55 (d,  $J = 8.1$  Hz, 1H), 7.34 (ddd,  $J = J = 8.3$  Hz,  $J = 1.2$  Hz, 1H), 7.26 (ddd,  $J = J = 8.3$  Hz,  $J = 1.1$  Hz, 1H), 6.61 (d,  $J = 3.8$  Hz, 1H), 1.51 (s, 9H).

**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  177.1 (C), 136.7 (C), 129.4 (C), 125.6 (CH), 125.1 (CH), 123.5 (CH), 120.5 (CH), 117.3 (CH), 108.2 (CH), 41.2 (C), 28.7 ( $\text{CH}_3$ ).

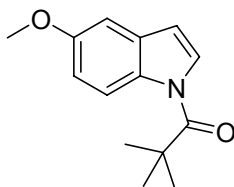
**FTIR:** 2980, 1692, 1448, 907  $\text{cm}^{-1}$ .

**HRMS (EI):** calculated for  $\text{C}_{13}\text{H}_{15}\text{NO}$  ( $\text{M}^+$ ) 201.1154; found for  $\text{C}_{13}\text{H}_{15}\text{NO}$  ( $\text{M}^+$ ) 201.1137.

**Melting point** (diethyl ether/hexanes) 68 - 70°C.

**$R_f$**  (5% diethyl ether in hexanes): 0.4.

***N*-Pivaloyl-5-methoxyindole :**



The title compound was prepared according to the above procedure and was subjected to column chromatography on silica gel with 5% diethyl ether in hexanes to 10% diethyl ether in hexanes as the solvent to afford the title compound in 93% yield.

**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  8.41 (d,  $J = 9.1$  Hz, 1H), 7.70 (d,  $J = 3.8$  Hz, 1H), 7.01 (d,  $J = 2.5$  Hz, 1H), 6.95 (dd,  $J = 9.1$  Hz,  $J = 2.6$  Hz, 1H), 6.54 (d,  $J = 3.8$  Hz, 1H), 3.85 (s, 3H), 1.51 (s, 9H).

**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  176.7 (C), 156.4 (C), 131.5 (C), 130.3 (C), 126.3 (CH), 118.1 (CH), 113.4 (CH), 108.1 (CH), 103.3 (CH), 55.6 ( $\text{CH}_3$ ), 41.1 (C), 28.8 ( $\text{CH}_3$ ).

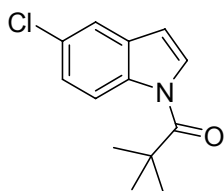
**FTIR:** 2981, 1689, 1473, 905  $\text{cm}^{-1}$ .

**HRMS (EI):** calculated for  $\text{C}_{14}\text{H}_{17}\text{NO}_2$  ( $\text{M}^+$ ) 231.1259; found for  $\text{C}_{14}\text{H}_{17}\text{NO}_2$  ( $\text{M}^+$ ) 231.1263.

**Melting point** (diethyl ether/hexanes) 99 - 100°C.

**R<sub>f</sub>** (10% diethyl ether in hexanes): 0.24.

***N*-Pivaloyl-5-chloroindole :**



The title compound was prepared according to the above procedure and was subjected to column chromatography on silica gel with 5% diethyl ether in hexanes as the solvent to afford the title compound in 76% yield.

**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  8.44 (d,  $J$  = 8.9 Hz, 1H), 7.76 (d,  $J$  = 3.8 Hz, 1H), 7.52 (d,  $J$  = 2.2 Hz, 1H), 7.29 (dd,  $J$  = 8.9 Hz,  $J$  = 2.2 Hz, 1H), 6.56 (d,  $J$  = 3.8 Hz, 1H), 1.52 (s, 9H).

**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  177.0 (C), 135.1 (C), 130.6 (C), 129.0 (C), 126.8 (CH), 125.2 (CH), 120.1 (CH), 118.3 (CH), 107.5 (CH), 41.3 (C), 28.7 ( $\text{CH}_3$ ).

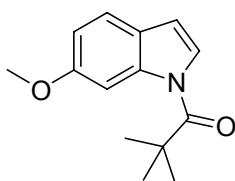
**FTIR:** 2973, 1690, 1493, 905  $\text{cm}^{-1}$ .

**HRMS (EI):** calculated for  $\text{C}_{13}\text{H}_{14}\text{NOCl}$  ( $\text{M}^+$ ) 235.0764; found for  $\text{C}_{13}\text{H}_{14}\text{NOCl}$  ( $\text{M}^+$ ) 235.0757.

**Melting point** (diethyl ether/hexanes) 106 - 107°C.

**R<sub>f</sub>** (5% diethyl ether in hexanes): 0.28.

***N*-Pivaloyl-6-methoxyindole :**



The title compound was prepared according to the above procedure and was subjected to column chromatography on silica gel with 10% diethyl ether in hexanes as the solvent to afford the title compound in 78% yield.

**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  8.16 (d,  $J$  = 2.4 Hz, 1H), 7.62 (d,  $J$  = 3.8 Hz, 1H), 7.41 (d,  $J$  = 8.5 Hz, 1H), 6.91 (dd,  $J$  = 8.5 Hz,  $J$  = 2.5 Hz, 1H), 6.54 (d,  $J$  = 3.8 Hz, 1H), 3.88 (s, 3H), 1.51 (s, 9H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 177.4 (C), 158.4 (C), 137.7 (C), 124.4 (CH), 123.1 (C), 120.8 (CH), 113.2 (CH), 108.2 (CH), 101.2 (CH), 55.6 (CH<sub>3</sub>), 41.3 (C), 28.7 (CH<sub>3</sub>).

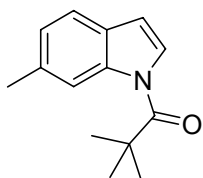
**FTIR:** 2980, 1692, 1310, 903. 804 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>14</sub>H<sub>17</sub>NO<sub>2</sub> (M<sup>+</sup>) 231.1259; found for C<sub>14</sub>H<sub>17</sub>NO<sub>2</sub> (M<sup>+</sup>) 231.1249.

**Melting point** (diethyl ether/hexanes) 110 - 112°C.

**R<sub>f</sub>** (10% diethyl ether in hexanes): 0.39.

#### ***N*-Pivaloyl-6-methylindole :**



The title compound was prepared according to the above procedure and was subjected to column chromatography on silica gel with 2% diethyl ether in hexanes as the solvent to afford the title compound in 72% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 8.38 (d, J = 0.7 Hz, 1H), 7.65 (d, J = 3.8 Hz, 1H), 7.42 (d, J = 7.9 Hz, 1H), 7.09 (dd, J = 7.9 Hz, J = 0.9 Hz, 1H), 6.56 (d, J = 3.8 Hz, 1H), 2.48 (s, 3H), 1.50 (s, 9H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 177.2 (C), 137.1 (C), 135.2 (C), 127.1 (C), 125.1 (CH), 124.9 (CH), 120.0 (CH), 117.6 (CH), 108.2 (CH), 41.2 (C), 28.7 (CH<sub>3</sub>), 22.0 (CH<sub>3</sub>).

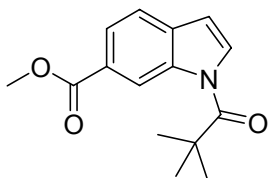
**FTIR:** 2980, 1692, 1310, 903. 804 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>14</sub>H<sub>17</sub>NO<sub>1</sub> (M<sup>+</sup>) 215.1310; found for C<sub>14</sub>H<sub>17</sub>NO<sub>1</sub> (M<sup>+</sup>) 215.1312.

**Melting point** (diethyl ether/hexanes) 63 - 65°C.

**R<sub>f</sub>** (2% diethyl ether in hexanes): 0.27.

#### **Methyl 1-(pivaloyl)-1H-indole-6-carboxylate :**



The title compound was prepared according to the above procedure and was subjected to column chromatography on silica gel with 10% diethyl ether in hexanes as the solvent to afford the title compound in 87% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 9.21 (s, 1H), 7.98 (dd, J = 8.2 Hz, J = 1.5 Hz, 1H), 7.88 (d, J = 3.8 Hz, 1H), 7.59 (d, J = 8.2 Hz, 1H), 6.65 (d, J = 3.8 Hz, 1H), 3.94 (s, 3H), 1.53 (s, 9H).

**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  177.0 (C), 167.7 (C), 136.2 (C), 133.0 (C), 128.4 (CH), 126.8 (C), 124.9 (CH), 120.2 (CH), 119.1 (CH), 108.0 (CH), 52.0 ( $\text{CH}_3$ ), 41.4 (C), 28.6 ( $\text{CH}_3$ ).

**FTIR:** 2983, 1717, 904, 780  $\text{cm}^{-1}$ .

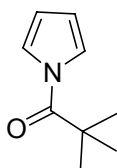
**HRMS (EI):** calculated for  $\text{C}_{15}\text{H}_{17}\text{NO}_3$  ( $\text{M}^+$ ) 259.1208; found for  $\text{C}_{15}\text{H}_{17}\text{NO}_3$  ( $\text{M}^+$ ) 259.1208.

**Melting point** (diethyl ether/hexanes) 93 - 94 °C.

**R<sub>f</sub>** (10% diethyl ether in hexanes): 0.19.

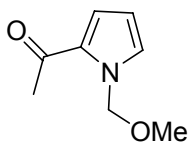
## Procedures for the protection of pyrroles:

### *N*-Pivaloylpyrrole :



Triethylamine (1.5 equiv.) was added to a stirring solution of pyrrole (1 equiv.) and trimethylacetyl chloride (1.5 equiv.) in dry DCM (1.5 M) at 0 °C. DMAP (0.1 equiv) was added after 5 min. The reaction mixture was then stirred at room temperature until the reaction was complete, after which water was added and the mixture was extracted with 3 portions of EtOAc. The organic layers were combined, dried with  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography with 10% DCM/hexane as eluent to afford translucent oil (71% yield). The compound was analytically pure as judged by  $^1\text{H}$  NMR (attached) which matched literature reports (Organic & Biomolecular Chemistry, 1 (21), 3787-3798, **2003**).

### 1-(1-(Methoxymethyl)-1H-pyrrol-2-yl)ethanone:



A solution of 2-acetylpyrrole (1 equiv.) in DMF (3.5 M) was added to a suspension of NaH (1.1 equiv.) in DMF (2 M) at 0 °C. The mixture was stirred for 1 h at 0 °C before the addition of chloromethyl methyl ether (1.4 equiv.) at 0 °C. The reaction mixture was then stirred at room temperature until the reaction was complete, after which ice cold water was added and the mixture was extracted with 3 portions of EtOAc. The organic layers were combined, dried with  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography with 10% acetone/hexane as eluent to afford translucent oil (93% yield).

**$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  2.45 (3H, s), 3.30 (3H, s), 5.68 (2H, s), 6.21 (1H, dd,  $J=2.6, 3.9$  Hz), 7.01 (1H, dd,  $J=1.7, 3.9$  Hz), 7.05 (1H, dd,  $J=1.7, 2.6$  Hz).

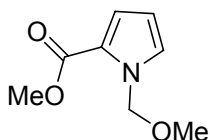
**$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  27.3 ( $\text{CH}_3$ ), 56.2 ( $\text{CH}_3$ ), 79.1 ( $\text{CH}_2$ ), 108.9 (CH), 121.2 (CH), 130.0 (CH), 130.7 (C), 188.7 (C).

**IR ( $\nu_{\text{max}}/\text{cm}^{-1}$ ):** 1083, 1107, 1236, 1323, 1411, 1653, 2824, 2938, 3109.

**HRMS** calculated for  $\text{C}_8\text{H}_{11}\text{NO}_2$  ( $\text{M}^+$ ): 153.0790; Found: 153.0787

**$R_f$ :** 0.48 on silica gel (20% Acetone/Hexane)

### Methyl 1-(methoxymethyl)-1H-pyrrole-2-carboxylate:



A solution of methyl 2-pyrrolicarboxylate (1 equiv.) in DMF (0.6 M) was added to a suspension of NaH (1.2 equiv.) in DMF (0.7 M) at 0 °C. The mixture was stirred for 30 min at 0 °C before the addition of chloromethyl methyl ether (1.2 equiv.) at 0 °C. The reaction mixture was then stirred at room temperature until the reaction was complete, after which ice cold water and saturated solution of  $\text{NaHCO}_3$  were added and the mixture was extracted with 3 portions of EtOAc. The organic layers were combined, dried with  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography with 20% EtOAc/hexane as eluent to afford translucent oil (93% yield).

**$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  3.29 (3H, s), 3.83 (3H, s), 5.65 (2H, s), 6.20 (1H, t,  $J=3.3$  Hz), 7.01 (2H, d,  $J=3.3$  Hz).

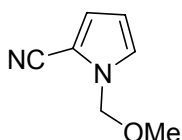
**$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  51.2 ( $\text{CH}_3$ ), 56.1 ( $\text{CH}_3$ ), 78.6 ( $\text{CH}_2$ ), 108.8 (CH), 119.2 (CH), 122.2 (C), 128.9 (CH), 161.5 (C).

**IR ( $\nu_{\text{max}}/\text{cm}^{-1}$ ):** 1083, 1096, 1113, 1237, 1323, 1414, 1438, 1709, 2824, 2949, 3121.

**HRMS** calculated for  $\text{C}_8\text{H}_{11}\text{NO}_3$  ( $\text{M}^+$ ): 169.0739; Found: 169.0736

**$R_f$ :** 0.59 on silica gel (30% EtOAc/Hexane)

### 1-(Methoxymethyl)-1H-pyrrole-2-carbonitrile:



A solution of pyrrole-2-carbonitrile (1 equiv.) in DMF (0.6 M) was added to a suspension of NaH (1.2 equiv.) in DMF (0.7 M) at 0 °C. The mixture was stirred for 30 min at 0 °C before the addition of chloromethyl methyl ether (1.2 equiv.) at 0 °C. The reaction mixture was then stirred at room temperature until the reaction was complete, after which ice cold water and saturated solution of

NaHCO<sub>3</sub> were added and the mixture was extracted with 3 portions of EtOAc. The organic layers were combined, dried with MgSO<sub>4</sub> and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography with 20% Acetone/hexane as eluent to afford translucent oil (89% yield).

**<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>, 293K, TMS):** δ 3.31 (3H, s), 5.32 (2H, s), 6.26 (1H, dd, *J*=2.8, 3.9 Hz), 6.86 (1H, dd, *J*= 1.6, 3.9 Hz), 7.00 (1H, dd, *J*= 1.6, 2.8 Hz).

**<sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>, 293K, TMS):** δ 56.4 (CH<sub>3</sub>), 78.8 (CH<sub>2</sub>), 104.3 (C), 110.5 (CH), 113.3 (C), 121.1 (CH), 126.9 (CH).

**IR (ν<sub>max</sub>/cm<sup>-1</sup>):** 1042, 1102, 1167, 1196, 1300, 1410, 1473, 2220, 2826, 2935, 3121.

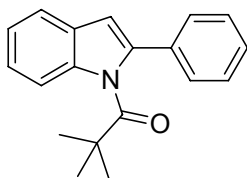
**HRMS** calculated for C<sub>7</sub>H<sub>8</sub>N<sub>2</sub>O (M<sup>+</sup>): 136.0637; Found: 136.0632

**R<sub>f</sub>:** 0.43 on silica gel (30% Acetone/Hexane)

### General procedure for the C2 arylation of *N*-pivaloylindoles :

All coupling reactions were performed on a 0.45 mmol (indole substrate) scale at 0.15 M unless otherwise stated. Pd(TFA)<sub>2</sub> (0.0079 g, 0.0237 mmol, 5 mol %), *N*-pivaloylindole (0.0923 g, 0.45 mmol, 1 eq), AgOAc (0.2291 g, 1.37 mmol, 3 eq), and PivOH (0.2788 g, 2.73 mmol, 6 eq) were weighed into a 4 mL glass vial. 2.7 mL of benzene was added and the vial was sealed with a Teflon lined closed cap. The vial was placed into one of the wells of an aluminum block and heated to 110°C for ~ 3 hours. The crude reaction mixture was analyzed by GC-MS and showed > 99% consumption of *N*-pivaloylindole and a C2:C3:diarylated product distribution of 25:1:0.7. The crude reaction mixture was filtered over celite (washing with Et<sub>2</sub>O). The solvent was removed and the residue was dissolved in Et<sub>2</sub>O (30 mL) and washed with a saturated solution of Na<sub>2</sub>CO<sub>3</sub> (3 x 20 mL). The aqueous layers were back extracted with Et<sub>2</sub>O (3 x 20 mL) and the combined organic layers were dried over MgSO<sub>4</sub> and concentrated. The crude reactions were purified by Chromatotron on 2 – 4 mm silica plates (Et<sub>2</sub>O/hexanes) (see below for individual compounds).

### 2-Phenyl-*N*-pivaloylindole :



The title compound was prepared according to the general procedure for C2 arylation and was purified by Chromatotron (loaded with DCM) with hexanes (50 mL) then hexanes/Et<sub>2</sub>O (99:1; 200 mL) as the solvent to afford the title compound as an oil in 84% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 7.62 (d, J = 7.3 Hz, 1H), 7.53 (d, J = 7.0 Hz, 2H), 7.43 (dd, J = J = 7.0 Hz, 2H), 7.38 – 7.33 (m, 2H), 7.24 (ddd, J = J = 7.2 Hz, J = 1.4 Hz, 1H), 7.18 (ddd, J = J = 7.1 Hz, J = 1.2 Hz, 1H), 6.68 (s, 1H), 0.96 (s, 9H).

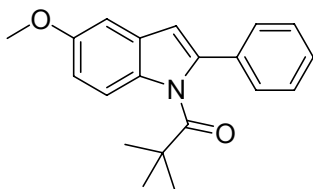
**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 187.4 (C), 139.4 (C), 137.2 (C), 133.9 (C), 129.1 (CH), 128.4 (C), 128.3 (CH), 127.8 (CH), 123.4 (CH), 121.5 (CH), 120.6 (CH), 111.2 (CH), 104.7 (CH) 45.2 (C), 27.9 (CH<sub>3</sub>).

**FTIR:** 2969, 1717, 935, 763, 742 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>19</sub>H<sub>19</sub>NO (M<sup>+</sup>) 277.1467; found for C<sub>19</sub>H<sub>19</sub>NO (M<sup>+</sup>) 277.1470.

**R<sub>f</sub>** (5% diethyl ether in hexanes): 0.3.

### 5-Methoxy-2-phenyl-N-pivaloylindole :



The title compound was prepared according to the general procedure for C2 arylation and was purified by Chromatotron (loaded with DCM) with hexanes (50 mL) then hexanes/Et<sub>2</sub>O (99:1; 200 mL) as the solvent to afford the title compound in 90% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 7.51 (d, J = 7.0 Hz, 2H), 7.43 (dd, J = J = 7.2 Hz, 2H), 7.36 (dd, J = J = 7.3 Hz, 1H), 7.26 (d, J = 8.9 Hz, 1H), 7.06 (d, J = 2.4 Hz, 1H), 6.89 (dd, J = 8.9 Hz, J = 2.5 Hz, 1H), 6.61 (s, 1H), 3.86 (s, 3H), 0.95 (s, 9H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 187.3 (C), 155.3 (C), 140.1 (C), 134.1 (C), 132.4 (CH), 129.1 (C), 128.9 (C), 128.3 (CH), 127.7 (CH), 113.3 (CH), 112.1 (CH), 104.6 (CH), 102.3 (CH), 55.8 (CH<sub>3</sub>), 45.2 (C), 28.0 (CH<sub>3</sub>).

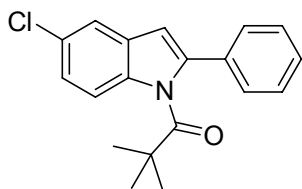
**FTIR:** 2968, 1713, 935, 762, 698 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>20</sub>H<sub>21</sub>NO<sub>2</sub> (M<sup>+</sup>) 307.1572; found for C<sub>20</sub>H<sub>21</sub>NO<sub>2</sub> (M<sup>+</sup>) 307.1576.

**Melting point** (diethyl ether/hexanes) 75 - 76°C.

**R<sub>f</sub>** (10% diethyl ether in hexanes): 0.41.

### 5-Chloro-2-phenyl-N-pivaloylindole :



The title compound was prepared according to the general procedure for C2 arylation and was purified by Chromatotron (loaded with DCM) with hexanes (50 mL) then hexanes/Et<sub>2</sub>O (99:1; 200 mL) as the solvent to afford the title compound in 86% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 7.58 (d, J = 1.8 Hz, 1H), 7.51 (dd, J = 8.2 Hz, J = 1.6 Hz, 2H), 7.44 (dd, J = J = 8.3 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.26 (d, J = 8.8 Hz, 1H), 7.19 (dd, J = 8.8 Hz, J = 2.0 Hz, 1H), 6.61 (s, 1H), 0.94 (s, 9H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 187.0 (C), 140.7 (C), 135.5 (C), 133.4 (C), 129.4 (C), 129.2 (CH), 128.7 (CH), 127.8 (CH), 127.1 (C), 123.6 (CH), 120.0 (CH), 112.2 (CH), 103.9 (CH), 45.2 (C), 27.9 (CH<sub>3</sub>).

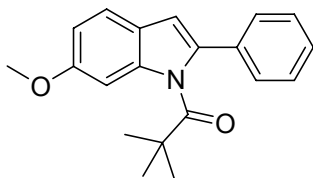
**FTIR:** 2971, 1720, 917, 762, 695 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>19</sub>H<sub>18</sub>NOCl (M<sup>+</sup>) 311.1077; found for C<sub>19</sub>H<sub>18</sub>NOCl (M<sup>+</sup>) 311.1066.

**Melting point** (diethyl ether/hexanes) 83 - 85°C.

**R<sub>f</sub>** (1% diethyl ether in hexanes): 0.3.

### 6-Methoxy-2-phenyl-N-pivaloylindole :



The title compound was prepared according to the general procedure for C2 arylation and was purified by Chromatotron (loaded with DCM) with hexanes (50 mL), hexanes/Et<sub>2</sub>O (99:1; 200 mL), and hexanes/Et<sub>2</sub>O (98/2; 200 mL) as the solvent to afford the title compound in 76% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 7.50 – 7.47 (m, 3H), 7.42 (dd, J = J = 7.6 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 6.87 – 6.83 (m, 2H), 6.61 (s, 1H), 3.84 (s, 3H), 0.97 (s, 9H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 187.5 (C), 157.5 (C), 138.4 (C), 138.1 (C), 134.2 (C), 129.1 (CH), 127.9 (CH), 127.5 (CH), 122.6 (C), 121.2 (CH), 111.5 (CH), 104.8 (CH), 94.8 (CH), 55.7 (CH<sub>3</sub>), 45.3 (C), 28.0 (CH<sub>3</sub>).

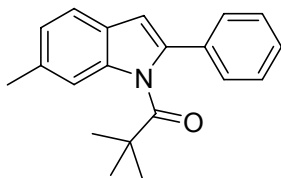
**FTIR:** 2969, 1717, 932, 757 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>20</sub>H<sub>21</sub>NO<sub>2</sub> (M<sup>+</sup>) 307.1572; found for C<sub>20</sub>H<sub>21</sub>NO<sub>2</sub> (M<sup>+</sup>) 307.1566.

**Melting point** (diethyl ether/hexanes) 111 - 113°C.

**R<sub>f</sub>** (5% diethyl ether in hexanes): 0.25.

### 6-Methyl-2-phenyl-N-pivaloylindole :



The title compound was prepared according to the general procedure for C2 arylation and was purified by Chromatotron (loaded with DCM) with hexanes (50 mL) and hexanes/Et<sub>2</sub>O (99:1; 200 mL) as the solvent to afford the title compound in 88% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 7.52 – 7.48 (m, 3H), 7.42 (dd, J = J = 7.5 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.16 (s, 1H), 7.02 (d, J = 8.0 Hz, 1H), 6.63 (s, 1H), 2.46 (s, 3H), 0.96 (s, 9H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 187.5 (C), 138.8 (C), 137.6 (C), 134.2 (C), 133.5 (C), 129.1 (CH), 128.1 (CH), 127.7 (CH), 126.2 (C), 123.3 (CH), 120.2 (CH), 111.1 (CH), 104.7 (CH), 45.1 (C), 28.0 (CH<sub>3</sub>), 21.9 (CH<sub>3</sub>).

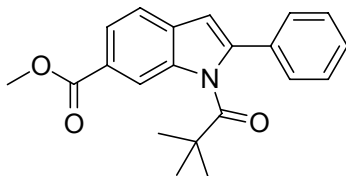
**FTIR:** 2971, 1721, 931, 815, 757 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>20</sub>H<sub>21</sub>NO (M<sup>+</sup>) 291.1623; found for C<sub>20</sub>H<sub>21</sub>NO (M<sup>+</sup>) 291.1622.

**Melting point** (diethyl ether/hexanes) 82 - 83°C.

**R<sub>f</sub>** (1% diethyl ether in hexanes): 0.26.

#### Methyl 2-phenyl-1-(pivaloyl)-1H-indole-6-carboxylate :



The title compound was prepared according to the general procedure for C2 arylation and was purified by Chromatotron (loaded with DCM) with hexanes (50 mL) and hexanes/Et<sub>2</sub>O (95:5) (300 mL) as the solvent to afford the title compound in 86% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 8.06 (s, 1H), 7.89 (dd, J = 8.3 Hz, J = 1.4 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.56 – 7.53 (m, 2H), 7.48 – 7.38 (m, 3H), 6.72 (s, 1H), 3.93 (s, 3H), 0.97 (s, 9H).

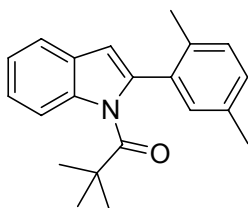
**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 186.8 (C), 167.6 (C), 142.5 (C), 136.5 (C), 133.3 (C), 131.9 (C), 129.2 (CH), 128.9 (CH), 128.0 (CH), 125.0 (C), 122.6 (CH), 120.2 (CH), 113.3 (CH), 104.4 (CH), 52.0 (CH<sub>3</sub>), 45.3 (C), 27.9 (CH<sub>3</sub>).

**FTIR:** 2973, 1720, 933, 766 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>21</sub>H<sub>21</sub>NO<sub>3</sub> (M<sup>+</sup>) 335.1521; found for C<sub>21</sub>H<sub>21</sub>NO<sub>3</sub> (M<sup>+</sup>) 335.1508.

**Melting point** (diethyl ether/hexanes) 128 - 129°C.

**R<sub>f</sub>** (5% diethyl ether in hexanes): 0.12.

**2-(2',5'-Dimethylbenzene)-*N*-pivaloylindole :**

The title compound was prepared according to the following procedure. Pd(TFA)<sub>2</sub> (0.0154 g, 0.045 mmol, 10 mol %), *N*-pivaloylindole (0.0922 g, 0.45 mmol, 1 eq), AgOAc (0.2373 g, 1.42 mmol, 3 eq), and PivOH (0.2850 g, 2.79 mmol, 6 eq) were weighed into a 15 mL sealed tube. 5.5 mL of *p*-xylene was added and the tube was sealed. The sealed tube was placed into an oil bath and heated to 110°C for ~ 16 hours. The crude reaction mixture was filtered over celite and washed with diethyl ether. The solvent was removed and the remaining *p*-xylene was removed on a Kugelrohr and the residue was purified by Chromatotron (loaded with DCM) with hexanes (50 mL) and hexanes:Et<sub>2</sub>O (99:1, 200 mL) to afford the title compound as an oil in 58% yield.

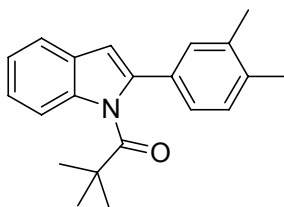
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 7.61 (d, *J* = 8.2 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.25 (ddd, *J* = *J* = 7.6 Hz, *J* = 1.3 Hz, 1H), 7.21 – 7.17 (m, 2H), 7.12 – 7.07 (m, 2H), 6.58 (s, 1H), 2.43 (s, 3H), 2.31 (s, 3H), 0.94 (s, 9H).

**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 186.7 (C), 137.5 (C), 136.6 (C), 135.5 (C), 133.4 (C), 132.8 (C), 131.1 (CH) (two overlapping peaks), 129.1 (CH), 128.3 (C), 123.3 (CH), 121.5 (CH), 120.4 (CH), 111.5 (CH), 106.7 (CH), 44.4 (C), 27.7 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 20.1 (CH<sub>3</sub>).

**FTIR:** 2969, 1715, 1449, 901, 810, 740 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>21</sub>H<sub>23</sub>NO (M<sup>+</sup>) 305.1780; found for C<sub>21</sub>H<sub>23</sub>NO (M<sup>+</sup>) 305.1761.

**R<sub>f</sub>** (2% diethyl ether in hexanes): 0.29.

**2-(3',4'-Dimethylbenzene)-*N*-pivaloylindole :**

The title compound was prepared according to the general procedure for C2 arylation though was heated at 110°C for ~ 16 hours and was purified by Chromatotron (loaded with DCM) with hexanes (250 mL) to afford the title compound as an oily solid in 76% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 7.59 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.30 (d, *J* = 1.4 Hz, 1H), 7.26 – 7.15 (m, 4H), 6.63 (s, 1H), 2.30 (s, 6H), 0.98 (s, 9H).

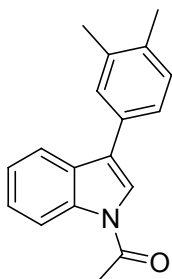
**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  187.5 (C), 139.7 (C), 137.4 (C), 137.1 (C), 136.9 (C), 131.5 (C), 130.3 (CH), 128.8 (CH), 128.5 (C), 125.2 (CH), 123.1 (CH), 121.4 (CH), 120.4 (CH), 111.2 (CH), 104.0 (CH), 45.2 (C), 28.0 ( $\text{CH}_3$ ), 19.8 ( $\text{CH}_3$ ), 19.6 ( $\text{CH}_3$ ).

**FTIR:** 2969, 1718, 957, 904, 744  $\text{cm}^{-1}$ .

**HRMS (EI):** calculated for  $\text{C}_{21}\text{H}_{23}\text{NO}$  ( $\text{M}^+$ ) 305.1780; found for  $\text{C}_{21}\text{H}_{23}\text{NO}$  ( $\text{M}^+$ ) 305.1781.

**$R_f$**  (1% diethyl ether in hexanes): 0.16.

### 3-(3',4'-Dimethylbenzene)-*N*-acetylindole :



The title compound was prepared according to the following procedure.  $\text{Pd}(\text{acac})_2$  (0.0176 g, 0.06 mmol, 10 mol %), *N*-acetylindole (0.0950 g, 0.60 mmol, 1 eq),  $\text{Cu}(\text{OAc})_2$  (0.3340 g, 1.8 mmol, 3 eq), and PivOH (0.3717 g, 3.6 mmol, 6 eq) were weighed into a 4 mL glass vial. 1.6 mL of *o*-xylene was added and the vial was sealed with a Teflon-lined cap. The vial was placed into one of the wells of an aluminum block and heated to 110°C for ~ 16 hours. The crude reaction mixture was filtered over celite and washed with ethyl acetate. The solvent was removed and the remaining *o*-xylene was removed under reduced pressure. The residue was redissolved in ethyl acetate and extracted with an aqueous solution of ammonium chloride (2 x 30 mL), the aqueous extracts were re-extracted with ethyl acetate. The solvent was removed and the residue was purified by flash chromatography with hexanes (50 mL), hexanes:EtOAc (98:2; 200 mL), hexanes:EtOAc (95:5; 200 mL) and hexanes (90:10; 100 mL) to afford the title compound in 61% yield.

**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  8.51 (d,  $J$  = 8.1 Hz, 1H), 7.80 (d,  $J$  = 7.5 Hz, 1H), 7.46 (s, 1H), 7.41 – 7.37 (m, 3H), 7.33 (ddd,  $J$  =  $J$  = 7.9 Hz,  $J$  = 1.2 Hz 1H), 7.24 (d,  $J$  = 7.6 Hz, 1H), 2.67 (s, 3H), 2.35 (s, 3H), 2.33 (s, 3H).

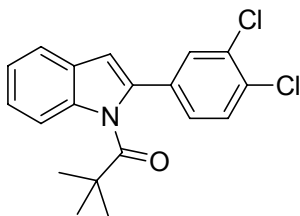
**$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , 293 K):**  $\delta$  168.5 (C), 137.2 (C), 136.3 (C), 136.1 (C), 130.8 (C), 130.2 (CH), 129.2 (C), 129.1 (CH), 125.4 (C), 125.4 (CH), 124.1 (C), 123.8 (CH), 121.6 (CH), 120.0 (CH), 116.8 (CH), 24.1 ( $\text{CH}_3$ ), 19.9 ( $\text{CH}_3$ ), 19.6 ( $\text{CH}_3$ ).

**FTIR:** 2921, 1705, 1448, 747  $\text{cm}^{-1}$ .

**HRMS (EI):** calculated for  $\text{C}_{18}\text{H}_{17}\text{NO}$  ( $\text{M}^+$ ) 263.1310; found for  $\text{C}_{18}\text{H}_{17}\text{NO}$  ( $\text{M}^+$ ) 263.1315.

**Melting point** (hexane/ethyl acetate) 123 – 125°C.

**$R_f$**  (10% ethyl acetate in hexanes): 0.22.

**2-(3',4'-Dichlorobenzene)-N-pivaloylindole :**

The title compound was prepared according to the general procedure for C2 arylation though was heated at 110°C for ~ 16 hours and was purified by Chromatotron (loaded with DCM) with hexanes (50 mL) and hexanes/Et<sub>2</sub>O (99:1, 200 mL) to afford the title compound in 55% yield.

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 293 K):** δ 7.64 – 7.61 (m, 2H), 7.51 (d, J = 8.3 Hz, 1H), 7.36 – 7.33 (m, 2H), 7.28 (ddd, J = J = 8.2 Hz, J = 1.3, 1H), 7.20 (ddd, J = J = 7.9 Hz, J = 1.2 Hz, 1H), 6.71 (s, 1H), 1.02 (s, 9H).

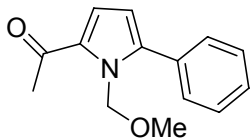
**<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, 293 K):** δ 186.8 (C), 137.4 (C), 136.7 (C), 133.9 (C), 133.4 (C), 132.4 (C), 131.1 (CH), 129.1 (CH), 128.1 (C), 126.7 (CH), 124.1 (CH), 121.9 (CH), 120.9 (CH), 111.4 (CH), 105.9 (CH), 45.2 (C), 28.0 (CH<sub>3</sub>).

**FTIR:** 2972, 1719, 1445, 950, 740 cm<sup>-1</sup>.

**HRMS (EI):** calculated for C<sub>19</sub>H<sub>17</sub>NOCl<sub>2</sub> (M<sup>+</sup>) 345.0687; found for C<sub>19</sub>H<sub>17</sub>NOCl<sub>2</sub> (M<sup>+</sup>) 345.0696.

**Melting point** (diethyl ether/hexanes) 132 - 134°C.

**R<sub>f</sub>** (1% diethyl ether in hexanes): 0.28.

**Procedures for the oxidative arylation of pyrroles:****1-(1-(Methoxymethyl)-5-phenyl-1H-pyrrol-2-yl)ethanone:**

Pd(OPiv)<sub>2</sub> (10 mol%), 3-nitropyridine (10 mol%) and AgOAc (3 equiv.) were weighed to air and placed in a screw cap vial. The protected pyrrole (1 equiv.) was added in the vial via a solution of benzene/PivOH (4:1) (0.3 M). The reaction mixture was stirred at 100 °C for 15-20 h. The crude mixture was filtered on a pad of celite and was eluted with DCM. The GC-MS analysis of the crude mixture showed 71.8% of monoarylated product, 5.2% of diarylated product, 1.5% of homocoupling of the starting pyrrole and 21.5% of benzene homo coupling. NOESY NMR proved that the regiochemistry of the major regioisomer was the C2 aryated product (see below). Complete conversion was obtained. The volatiles were then removed under reduced pressure and the residue was purified via silica gel column chromatography with 10% acetone/hexane as eluent to afford a yellow pale oil (64% yield).

**Regioselectivity (C2 Major):** 15:1

**$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  2.51 (3H, s), 3.35 (3H, s), 5.61 (2H, s), 6.29 (1H, d,  $J=4.0$  Hz), 7.10 (1H, d,  $J=4.0$  Hz), 7.40-7.47 (3H, m), 7.54-7.57 (2H, m).

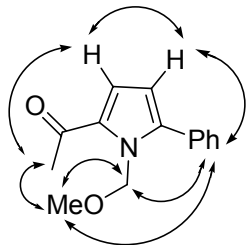
**$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  27.6 ( $\text{CH}_3$ ), 55.7 ( $\text{CH}_3$ ), 75.4 ( $\text{CH}_2$ ), 110.1 (CH), 121.3 (CH), 128.5 (CH), 128.6 (CH), 129.5 (CH), 131.4 (C), 131.4 (C), 143.9 (C), 188.4 (C).

**IR ( $\nu_{\text{max}}/\text{cm}^{-1}$ ):** 1092, 1238, 1391, 1460, 1652, 2821, 2939, 3060, 3115.

**HRMS** calculated for  $\text{C}_{14}\text{H}_{15}\text{NO}_2$  ( $\text{M}^+$ ): 229.1103; Found: 229.1095

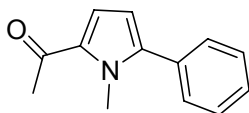
**$R_f$ :** 0.53 on silica gel (30% Acetone/Hexane)

**NOESY (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**



According to the network of the NOESY, the major regioisomer is the C2 arylated product.

### 1-(1-Methyl-5-phenyl-1H-pyrrol-2-yl)ethanone:



$\text{Pd}(\text{OPiv})_2$  (10 mol%), 3-nitropyridine (10 mol%) and  $\text{AgOAc}$  (3 equiv.) were weighed to air and placed in a screw cap vial. The protected pyrrole (1 equiv.) was added in the vial via a solution of benzene/ $\text{PivOH}$  (4:1) (0.3 M). The reaction mixture was stirred at 100 °C for 15-20 h. The crude mixture was filtered on a pad of celite and was eluted with DCM. The GC-MS analysis of the crude mixture showed 71.2% of monoarylated product, 4.7% of diarylated product, 2.1% of homocoupling of the starting pyrrole and 22.0% of benzene homo coupling. NOESY NMR proved that the regiochemistry of the major regioisomer was the C2 arylated product (see below). Complete conversion was obtained. The volatiles were then removed under reduced pressure and a saturated solution of  $\text{NaHCO}_3$  was added. The solution was extracted with 3 portions of  $\text{Et}_2\text{O}$ . The organic layers were combined, dried with  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude material was then purified by silica gel column chromatography with 10% Acetone/hexane as eluent to afford a white solid (68% yield).

**Regioselectivity (C2 Major):** 8.5:1

**$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  2.47 (3H, s), 3.88 (3H, s), 6.22 (1H, d,  $J=4.1$  Hz), 7.03 (1H, d,  $J=4.1$  Hz), 7.39-7.46 (5H, m).

**$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  27.4 ( $\text{CH}_3$ ), 35.2 ( $\text{CH}_3$ ), 109.3 (CH), 119.7 (CH), 128.3 (CH), 128.5 (CH), 129.4 (CH), 131.8 (C), 131.9 (C), 142.9 (C), 188.5 (C).

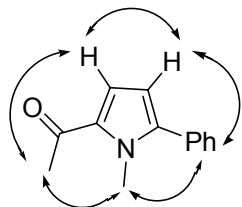
**IR ( $\nu_{\text{max}}/\text{cm}^{-1}$ ):** 1017, 1089, 1247, 1373, 1455, 1648, 2952, 2992, 3028, 3057, 3106.

**HRMS** calculated for  $\text{C}_{13}\text{H}_{13}\text{NO}$  ( $\text{M}^+$ ): 199.0997; Found: 199.1000

**Melting point ( $^{\circ}\text{C}$ ):** 69.3-71.0 (100% DCM)

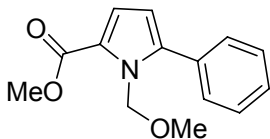
**$R_f$ :** 0.53 on silica gel (30% Acetone/Hexane)

**NOESY (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**



According to the network of the NOESY, the major regioisomer is the C2 arylated product.

#### **Methyl 1-(methoxymethyl)-5-phenyl-1H-pyrrole-2-carboxylate:**



$\text{Pd}(\text{OPiv})_2$  (10 mol%) and  $\text{AgOAc}$  (3 equiv.) were weighed to air and placed in a screw cap vial. The protected pyrrole (1 equiv.) was added in the vial via a solution of benzene/ $\text{PivOH}$  (4:1) (0.3 M). The reaction mixture was stirred at  $100\text{ }^{\circ}\text{C}$  for 3 h. The crude mixture was filtered on a pad of celite and was eluted with DCM. The GC-MS analysis of the crude mixture showed 76.8% of monoarylated product, 10.2% of a mixture of diarylated product and homocoupling of the starting pyrrole and 13.0% of benzene homo coupling. NOESY NMR proved that the regiochemistry of the major regioisomer was the C2 arylated product (see below). Complete conversion was obtained. The volatiles were then removed under reduced pressure and a saturated solution of  $\text{NaHCO}_3$  was added. The solution was extracted with 3 portions of  $\text{Et}_2\text{O}$ . The organic layers were combined, dried with  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude material was then purified by silica gel column chromatography with 5% Acetone/hexane as eluent to afford a beige solid (66% yield).

**Regioselectivity (C2 Major):** 9.8:1

**$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  3.30 (3H, s), 3.85 (3H, s), 5.60 (2H, s), 6.26, (1H, d,  $J=3.9$  Hz), 7.09 (1H, d,  $J=3.9$  Hz), 7.39-7.55 (5H, m).

**$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  51.2 ( $\text{CH}_3$ ), 55.6 ( $\text{CH}_3$ ), 75.1 ( $\text{CH}_2$ ), 109.9 (CH), 119.2 (CH), 123.2 (C), 128.3 (CH), 128.6 (CH), 129.5 (CH), 131.8 (C), 142.7 (C), 161.6 (C).

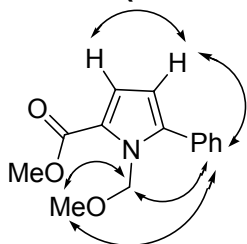
**IR** ( $\nu_{max}/\text{cm}^{-1}$ ): 1107, 1162, 1240, 1276, 1330, 1462, 1707, 2827, 2949, 2994, 3063

**HRMS** calculated for  $\text{C}_{14}\text{H}_{15}\text{NO}_3$  ( $M^+$ ): 245.1052; Found: 245.1041

**Melting point** ( $^{\circ}\text{C}$ ): 52.9-53.7 (100% DCM)

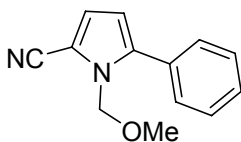
$R_f$ : 0.55 on silica gel (30% Acetone/Hexane)

**NOESY (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**



According to the network of the NOESY, the major regioisomer is the C2 arylated product.

### 1-(Methoxymethyl)-5-phenyl-1H-pyrrole-2-carbonitrile:



$\text{Pd}(\text{OPiv})_2$  (10 mol%) and  $\text{AgOAc}$  (3 equiv.) were weighed to air and placed in a screw cap vial. The protected pyrrole (1 equiv.) was added in the vial via a solution of benzene/ $\text{PivOH}$  (4:1) (0.1 M). The reaction mixture was stirred at  $100^{\circ}\text{C}$  for 15-20 h. The crude mixture was filtered on a pad of celite and was eluted with DCM. The GC-MS analysis of the crude mixture showed 52.8% of monoarylated product, 9.5% of diarylated product and 37.7% of benzene homo coupling. NOESY NMR proved that the regiochemistry of the major regioisomer was the C2 arylated product (see below). 96% conversion was obtained. The volatiles were then removed under reduced pressure and a saturated solution of  $\text{NaHCO}_3$  was added. The solution was extracted with 3 portions of  $\text{Et}_2\text{O}$ . The organic layers were combined, dried with  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude material was then purified by silica gel column chromatography with 10% Acetone/hexane as eluent. The regioisomer mixture was repurified by silica gel column chromatography with 10%  $\text{Et}_2\text{O}$ /hexane as eluent to afford yellow pale oil (67% yield).

**Regioselectivity (C2 Major):** 38.1:1:4.7

**$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  3.44 (3H, s), 5.30 (2H, s), 6.32 (1H, d,  $J=3.9$  Hz), 6.92 (1H, d,  $J=3.9$  Hz), 7.41-7.47 (3H, m), 7.53-7.55 (2H, m).

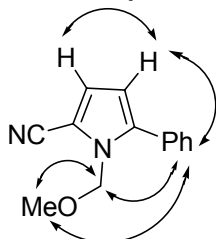
**$^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ , 293K, TMS):**  $\delta$  56.5 ( $\text{CH}_3$ ), 76.17 ( $\text{CH}_2$ ), 105.7 (C), 110.6 (CH), 114.1 (C), 120.8 (CH), 128.7 (CH), 128.8 (CH), 129.2 (CH), 130.8 (C), 141.0 (C).

**IR** ( $\nu_{max}/\text{cm}^{-1}$ ): 1091, 1132, 1188, 1311, 1391, 1461, 2217, 2825, 2936, 2991, 3066, 3134.

**HRMS** calculated for  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}$  ( $M^+$ ): 212.0950; Found: 212.0954

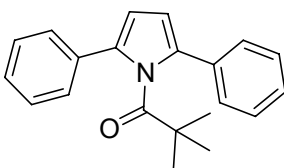
R<sub>f</sub>: 0.42 on silica gel (20% Acetone/Hexane)

**NOESY (400MHz, CDCl<sub>3</sub>, 293K, TMS):**



According to the network of the NOESY, the major regioisomer is the C2 arylated product.

**2,5-Diphenyl-N-Pivaloylpyrrole :**



Pd(OPiv)<sub>2</sub> (10 mol%) and AgOAc (5 equiv.) were weighed to air and placed in a screw cap vial. The protected pyrrole (1 equiv.) was added in the vial via a solution of benzene/PivOH (4:1) (0.1 M). The reaction mixture was stirred at 100 °C for 15-20 h. The crude mixture was filtered on a pad of celite and was eluted with DCM. The GC-MS analysis of the crude mixture showed 8.3% of monoarylated product, 77.7% of diarylated product and 14.0% of benzene homo coupling. NOESY NMR proved that the regiochemistry of the major regioisomer was the C2, C5 diarylated product (see below). Complete conversion was obtained. The volatiles were then removed under reduced pressure and a saturated solution of NaHCO<sub>3</sub> was added. The solution was extracted with 3 portions of Et<sub>2</sub>O. The organic layers were combined, dried with MgSO<sub>4</sub> and concentrated under reduced pressure. The crude material was then purified by silica gel column chromatography with 10% Toluene/hexane as eluent to afford pale red oil (53% yield).

**Regioselectivity (C2, C5 Major):** 6.1:1

**<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>, 293K, TMS):** δ 0.58 (9H, s), 6.40 (2H, s), 7.25-7.29 (2H, m), 7.35-7.38 (4H, m), 7.50-7.52 (4H, m).

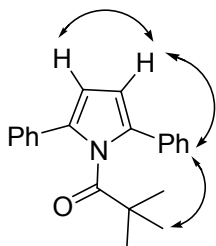
**<sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>, 293K, TMS):** δ 26.8 (CH<sub>3</sub>), 45.6 (C), 110.1 (CH), 127.3 (CH), 128.4 (CH), 128.6 (CH), 132.9 (C), 135.2 (C), 189.7 (C).

**IR (ν<sub>max</sub>/cm<sup>-1</sup>):** 1010, 1184, 1300, 1367, 1485, 1603, 1735, 2872, 2906, 2934, 2976, 3065.

**HRMS** calculated for C<sub>21</sub>H<sub>21</sub>NO (M<sup>+</sup>): 303.1623; Found: 303.1623

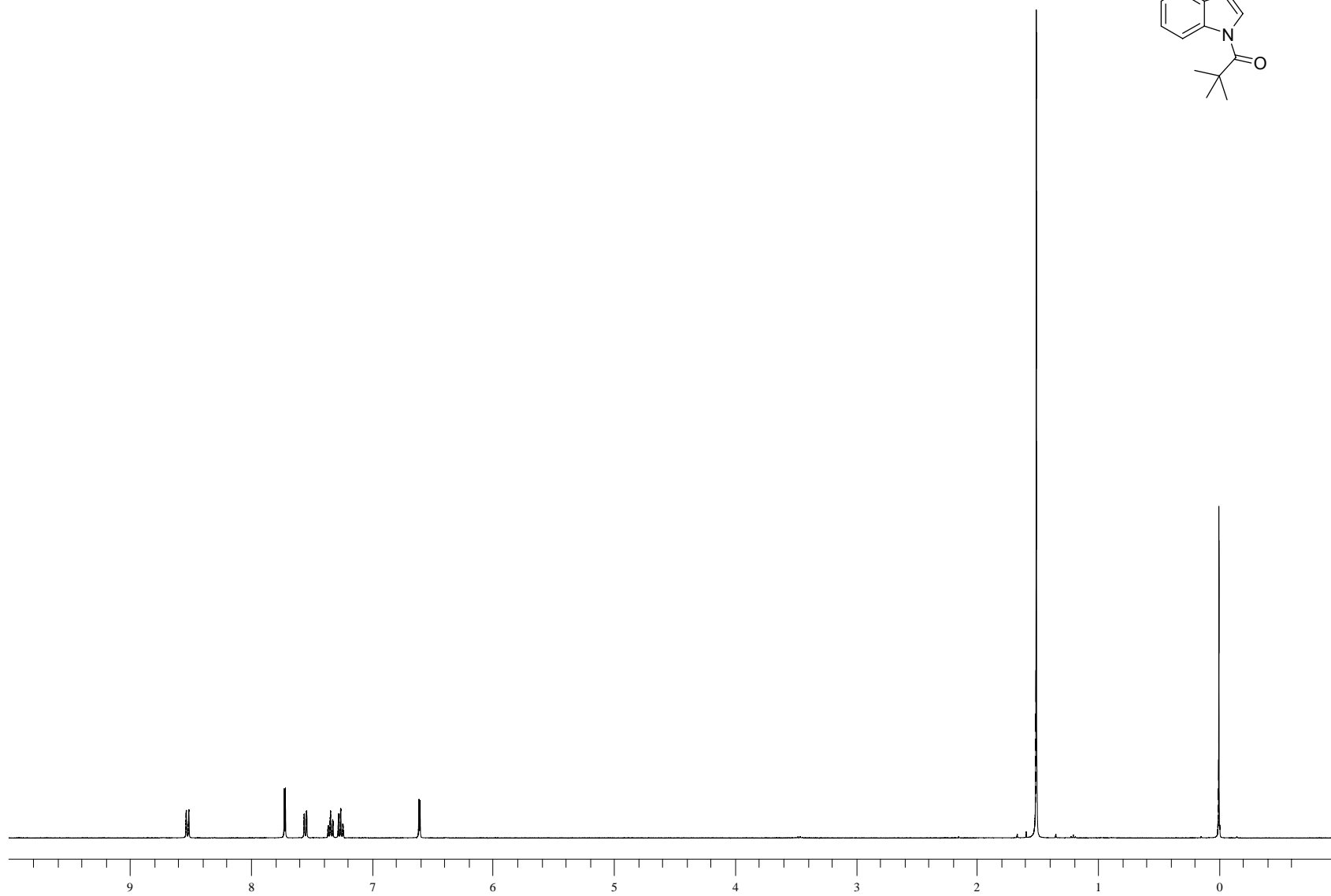
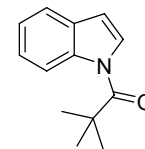
R<sub>f</sub>: 0.72 on silica gel (30% Acetone/Hexane)

**NOESY (400MHz, CDCl<sub>3</sub>, 293K, TMS):**

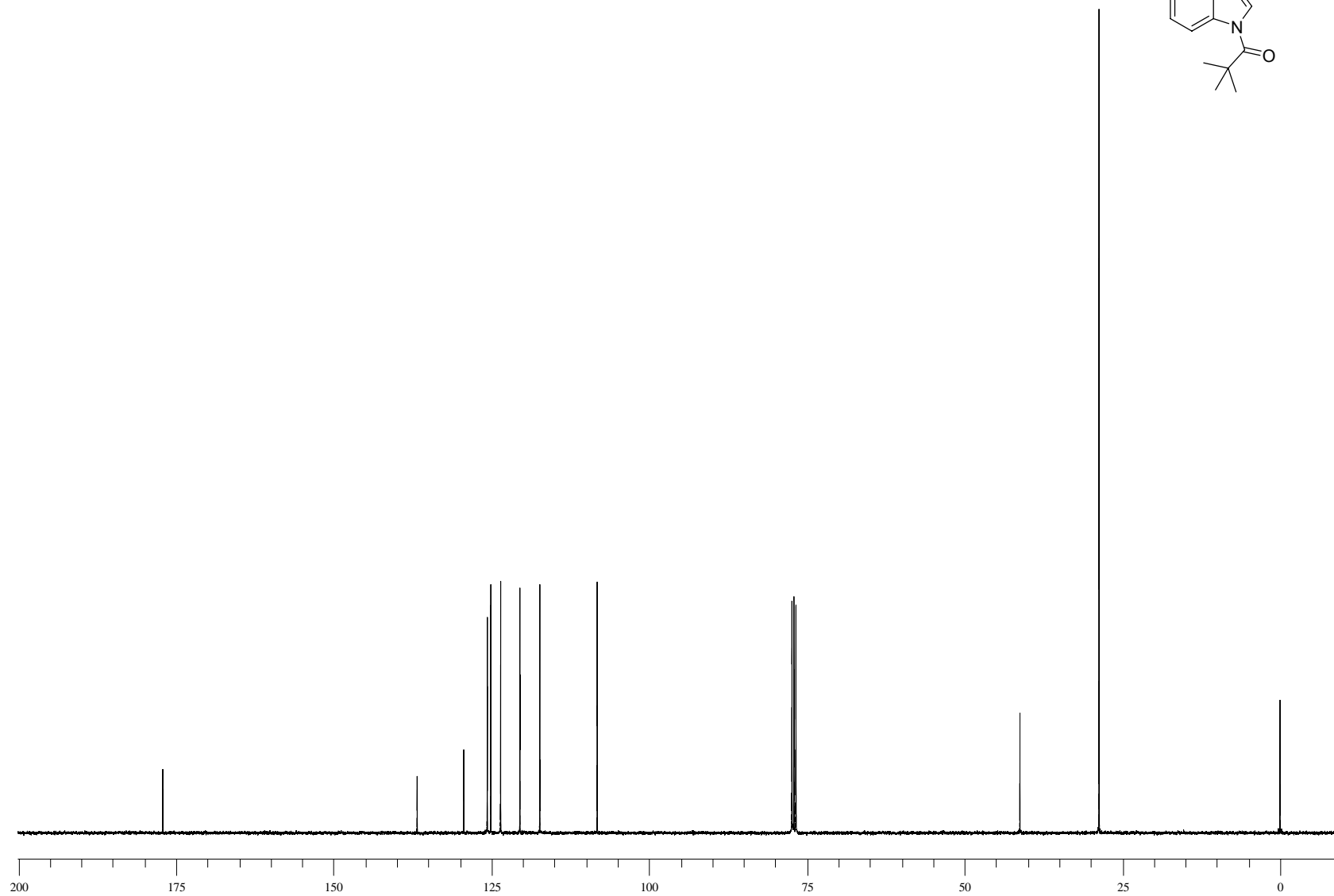
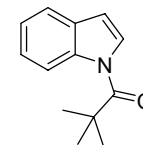


According to the network of the NOESY, the major regioisomer is the C2, C5 diarylated product.

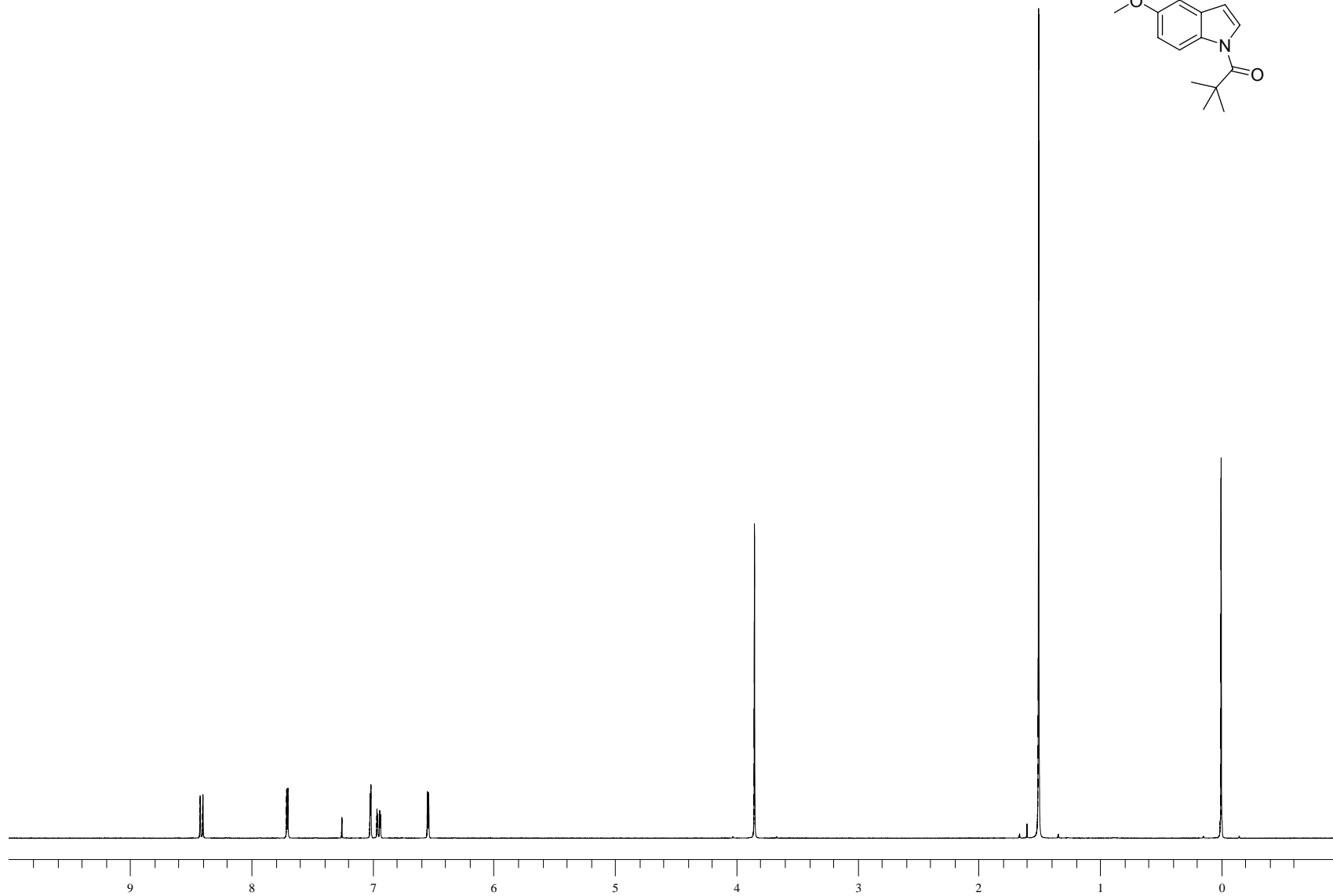
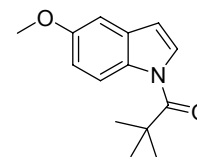
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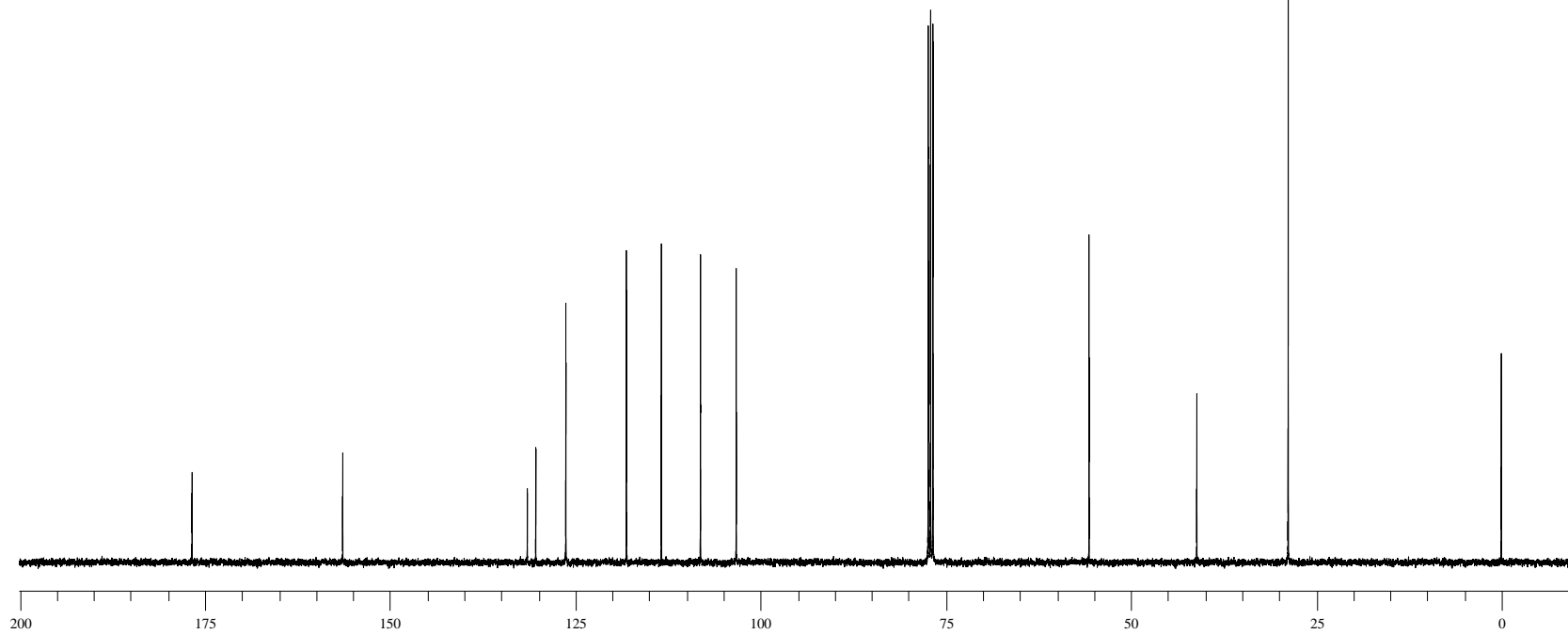
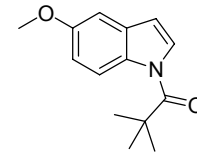
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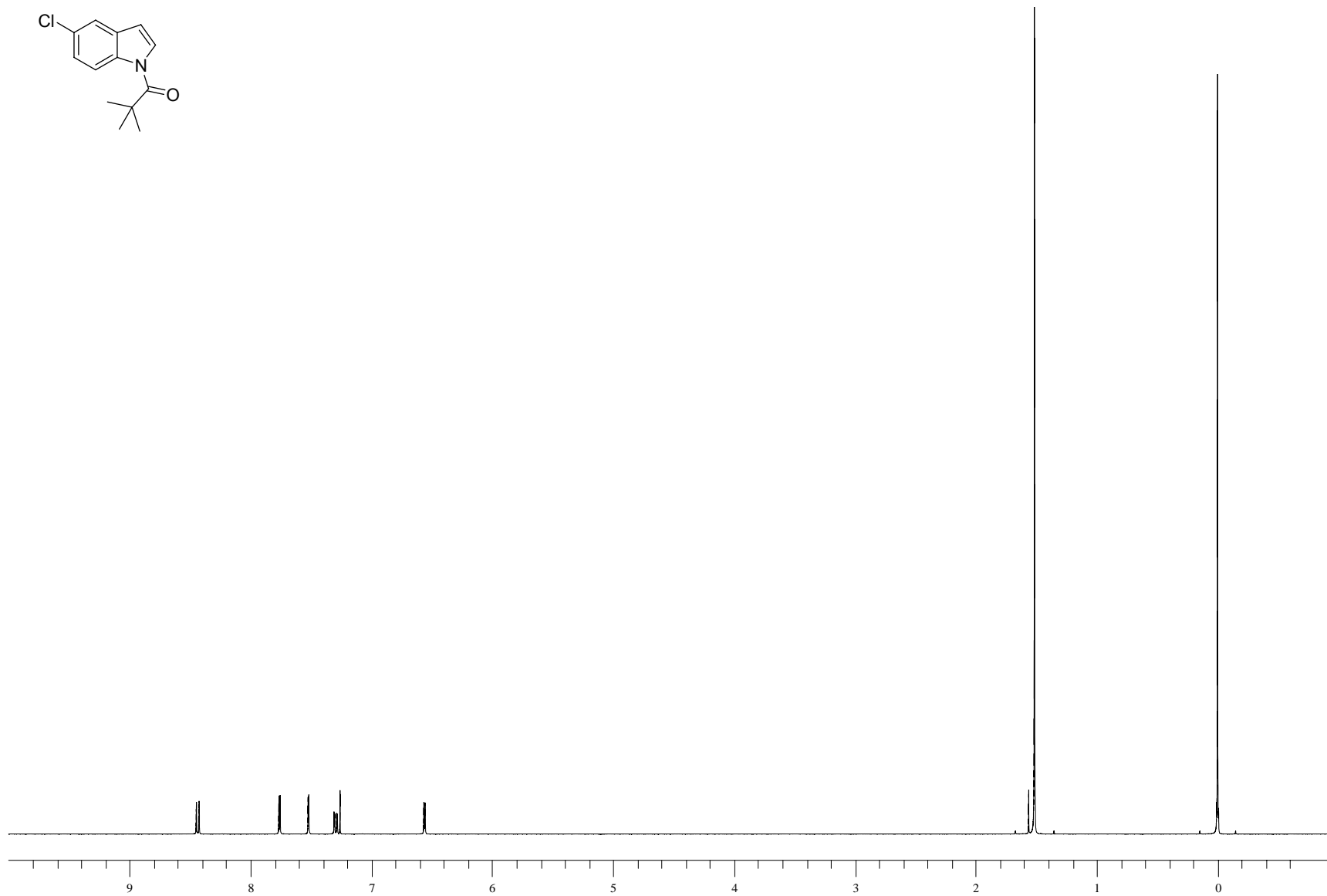
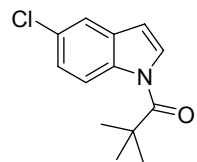
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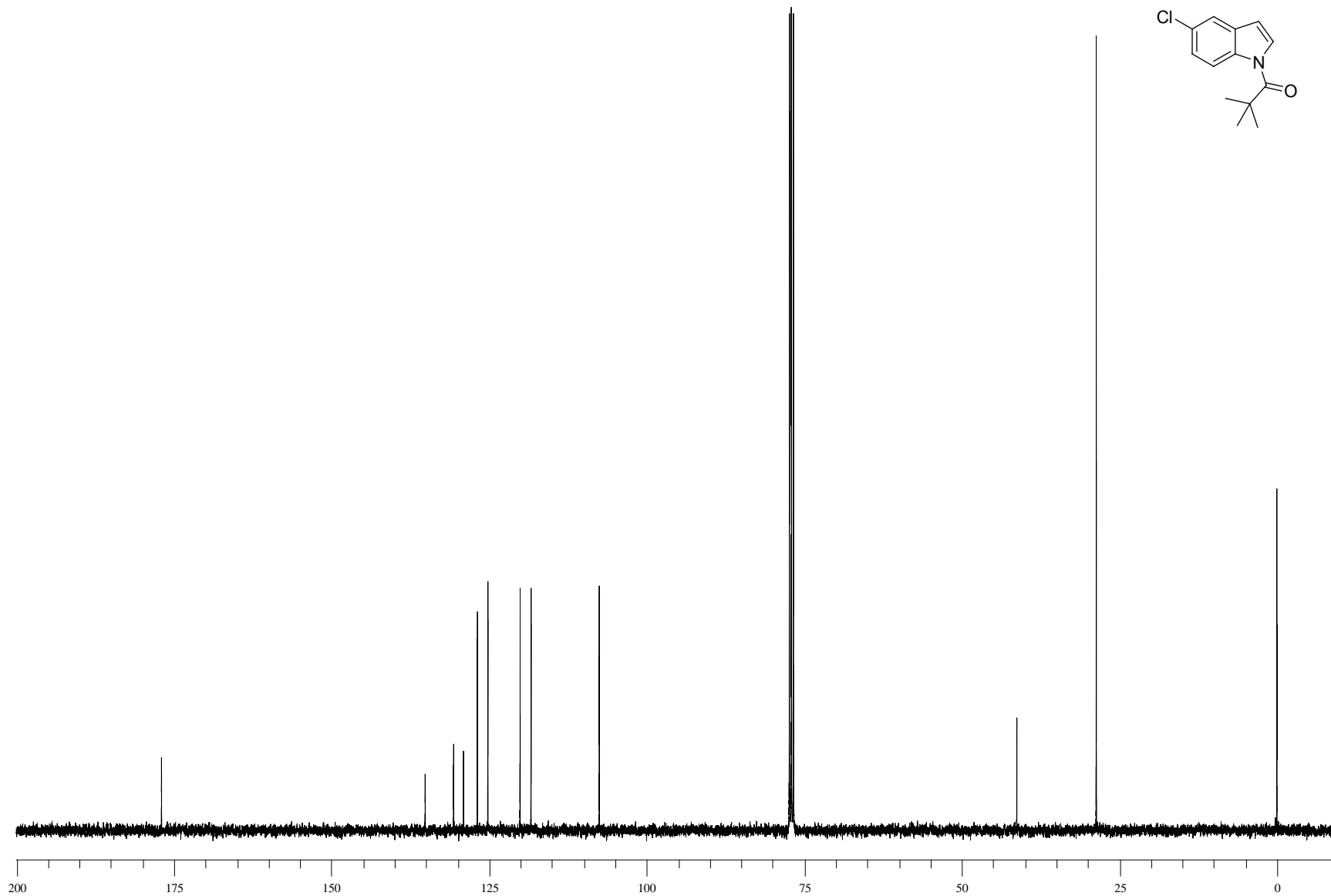
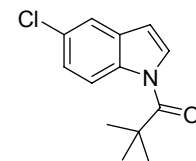
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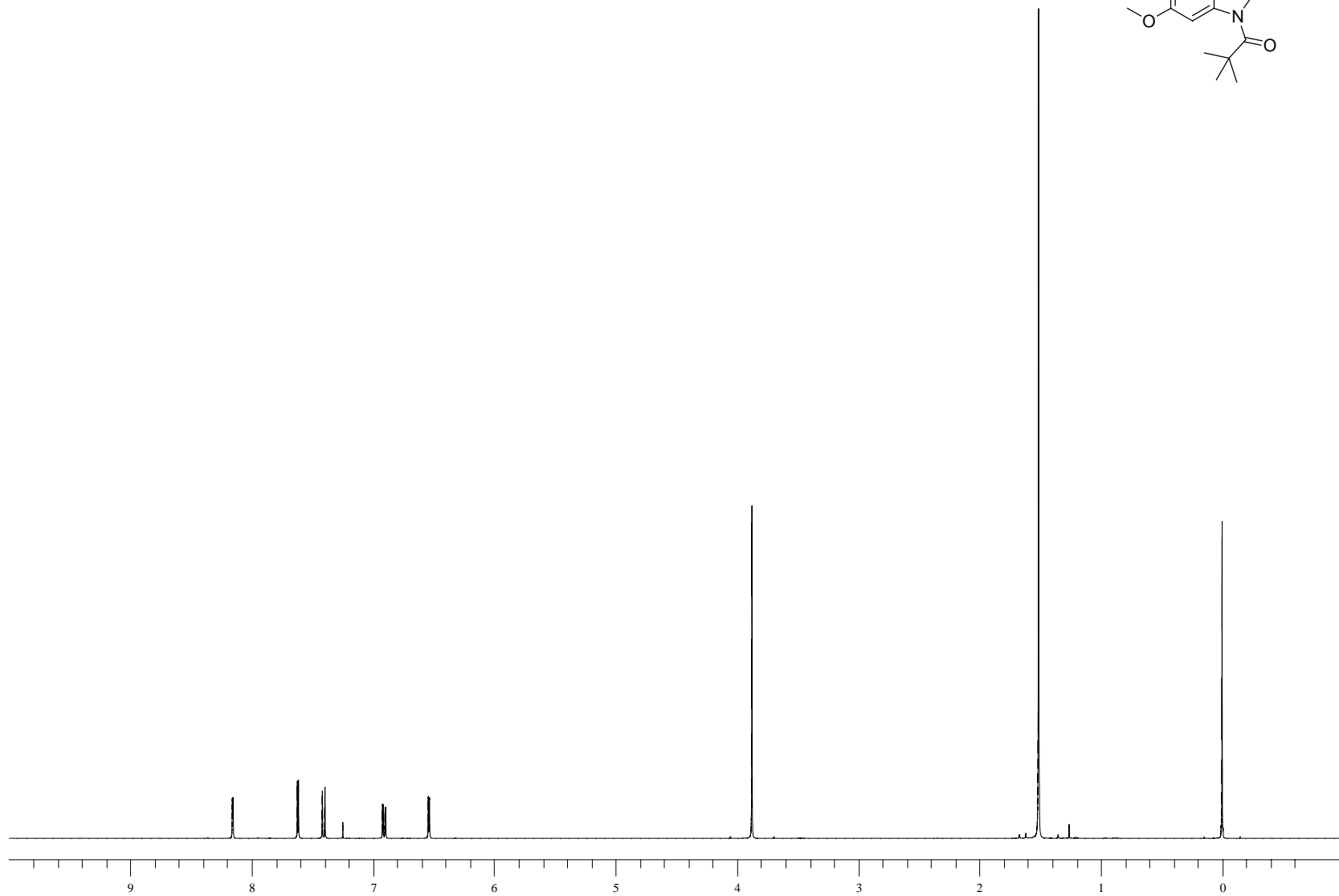
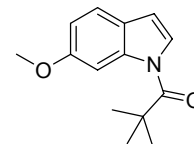
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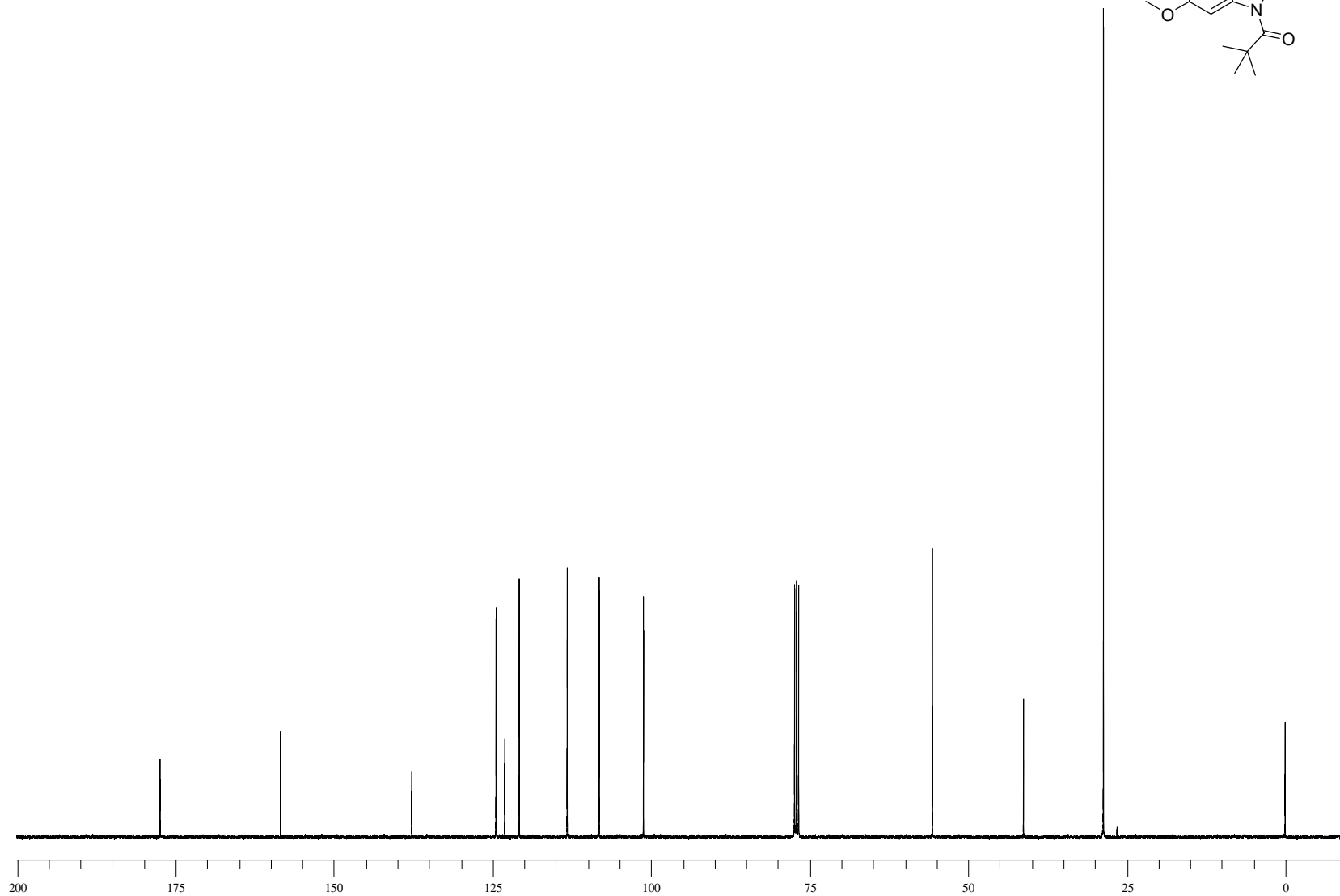
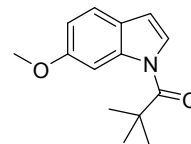
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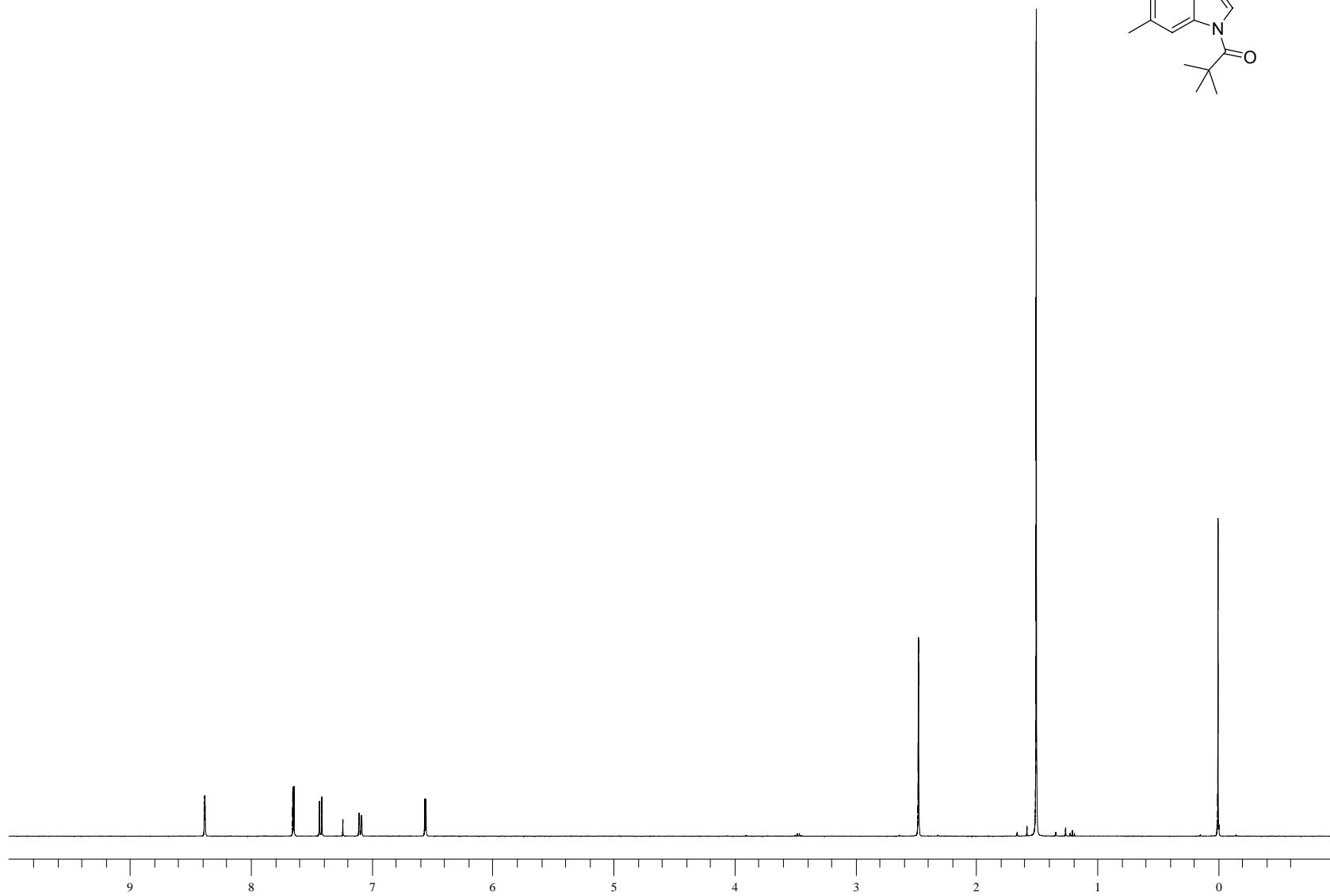
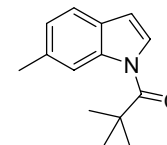
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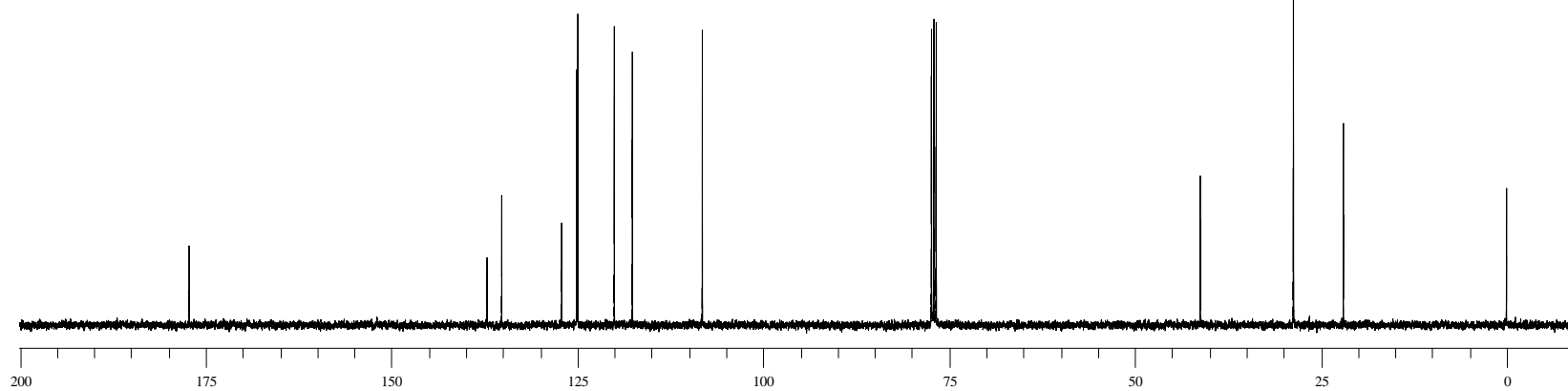
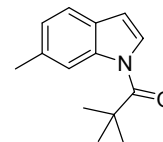
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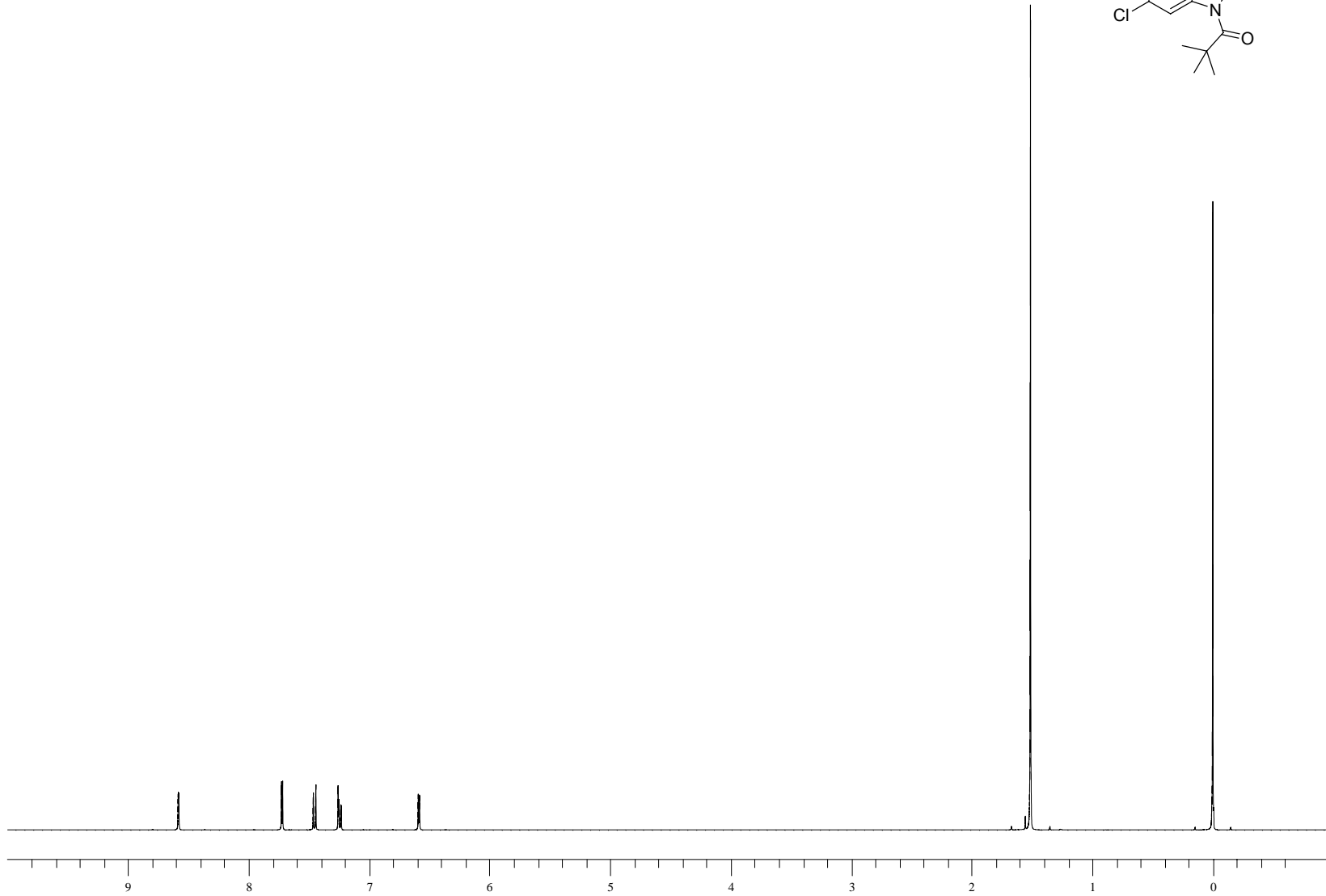
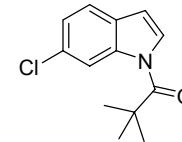
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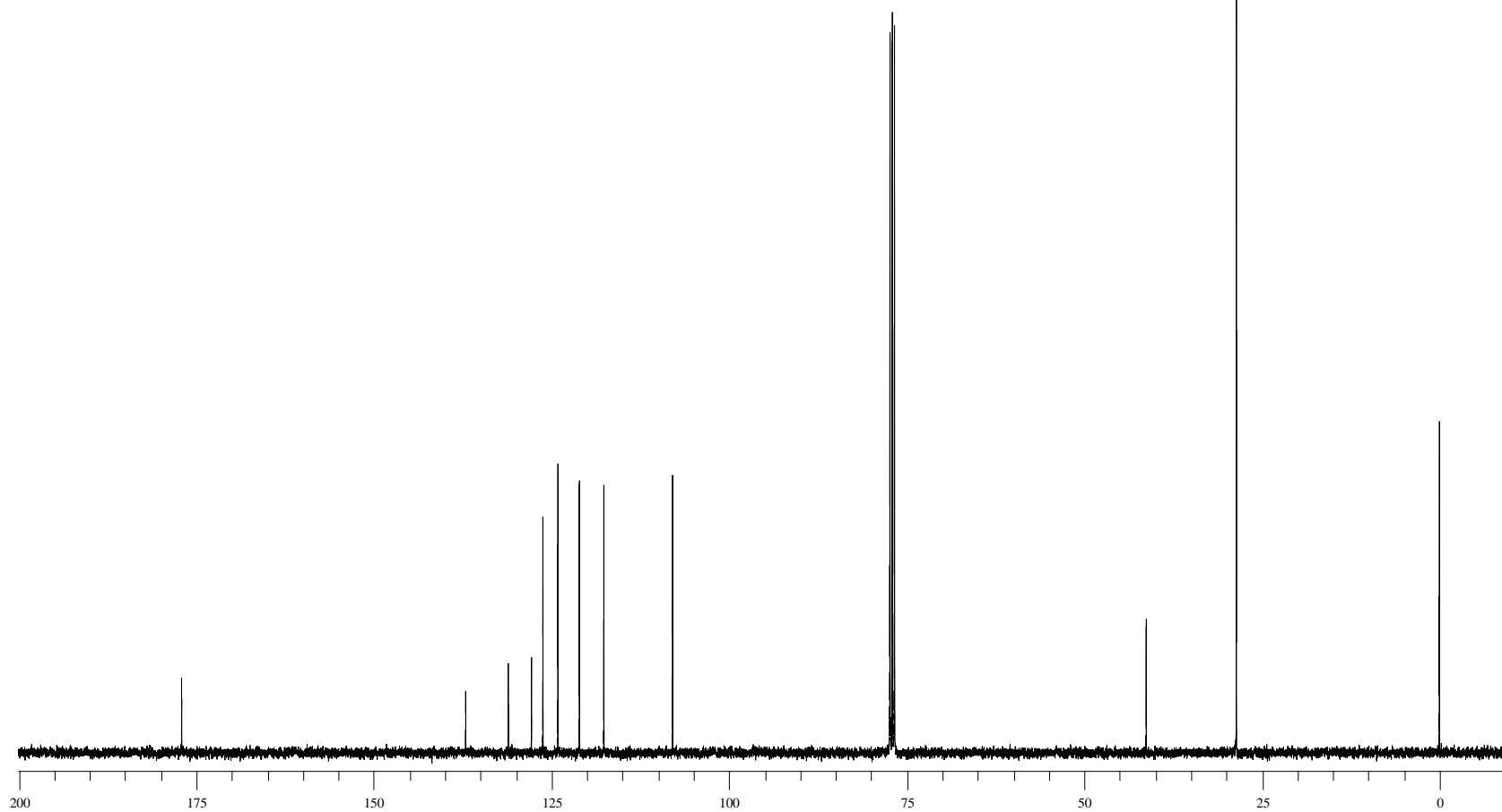
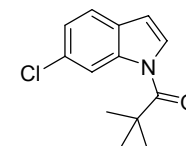
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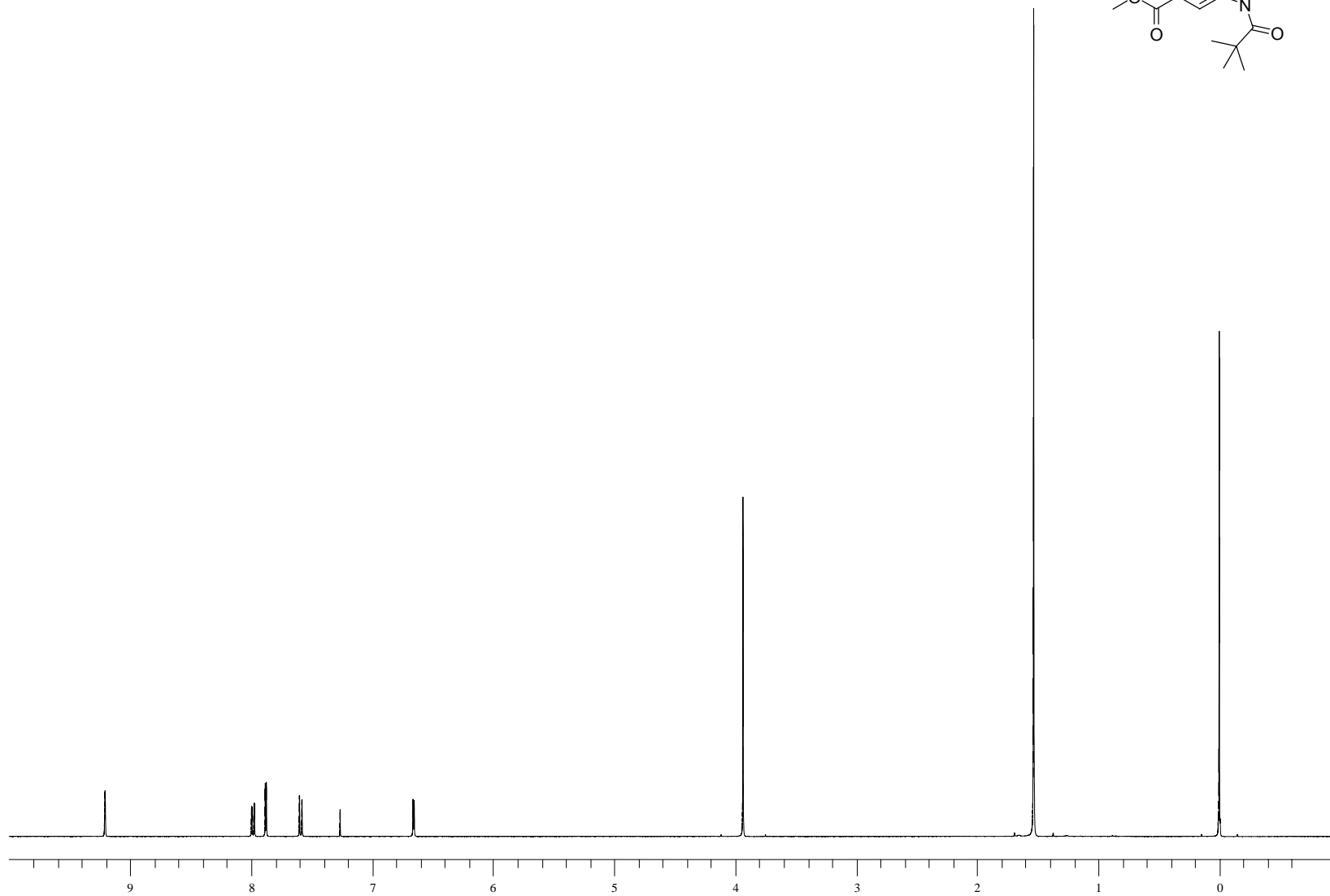
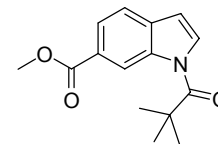
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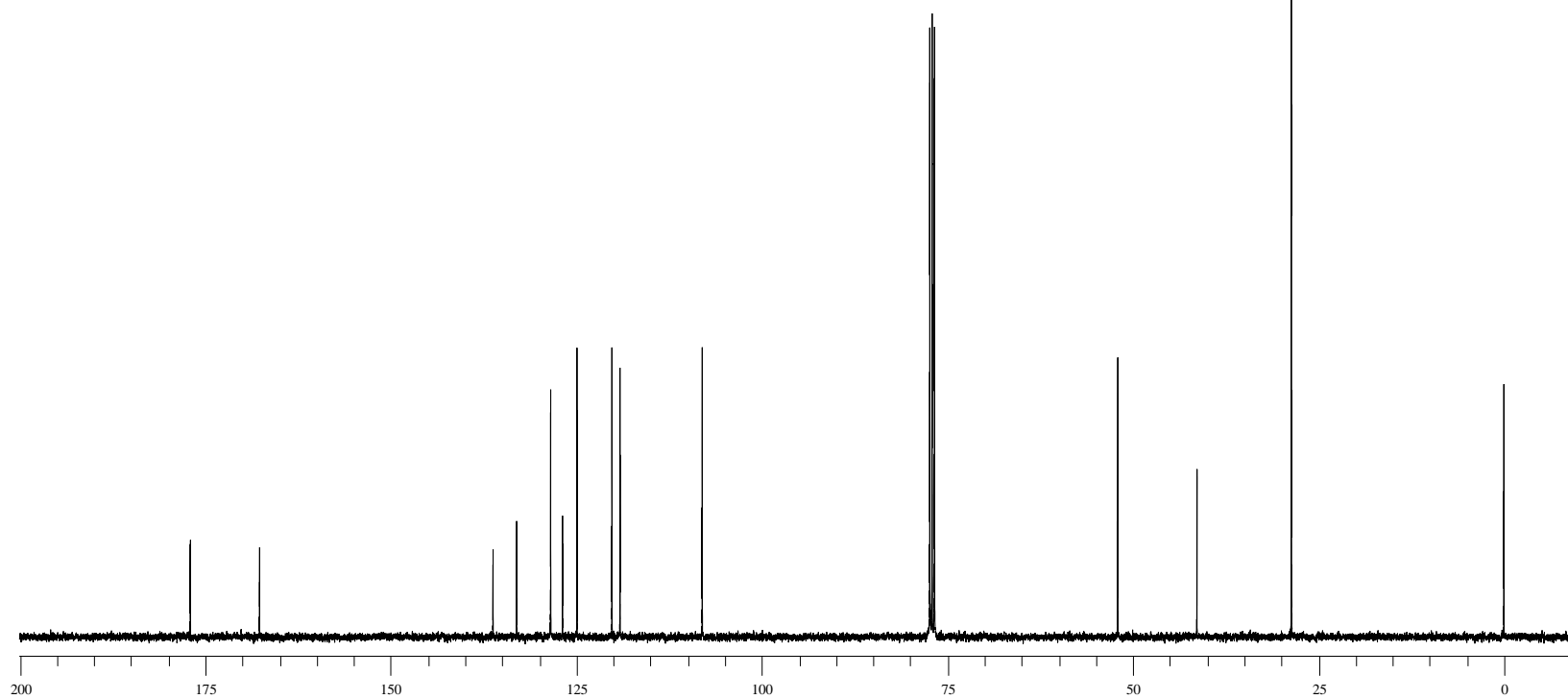
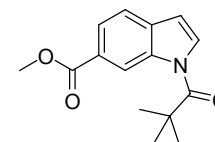
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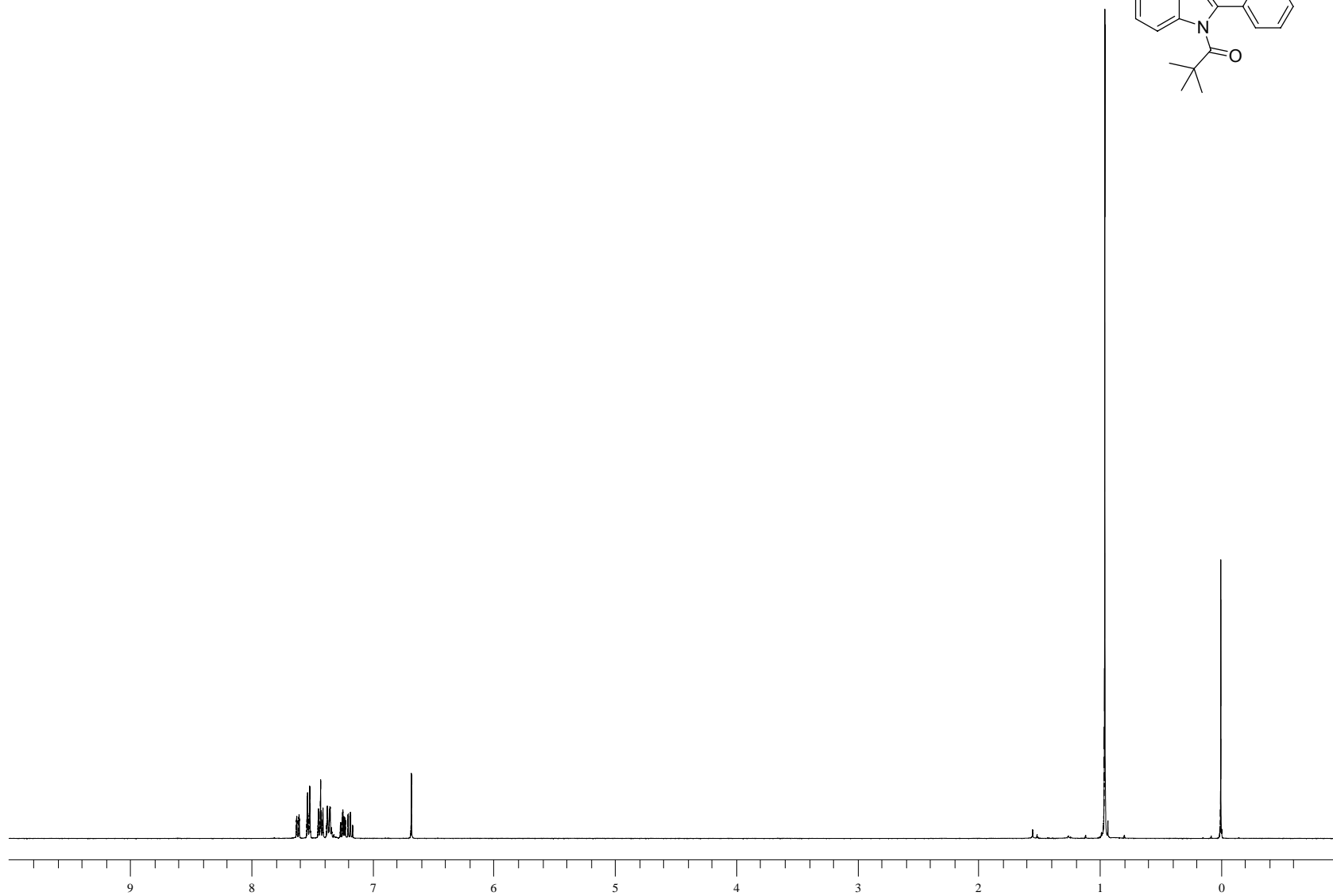
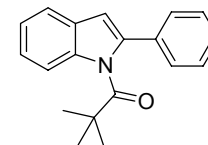
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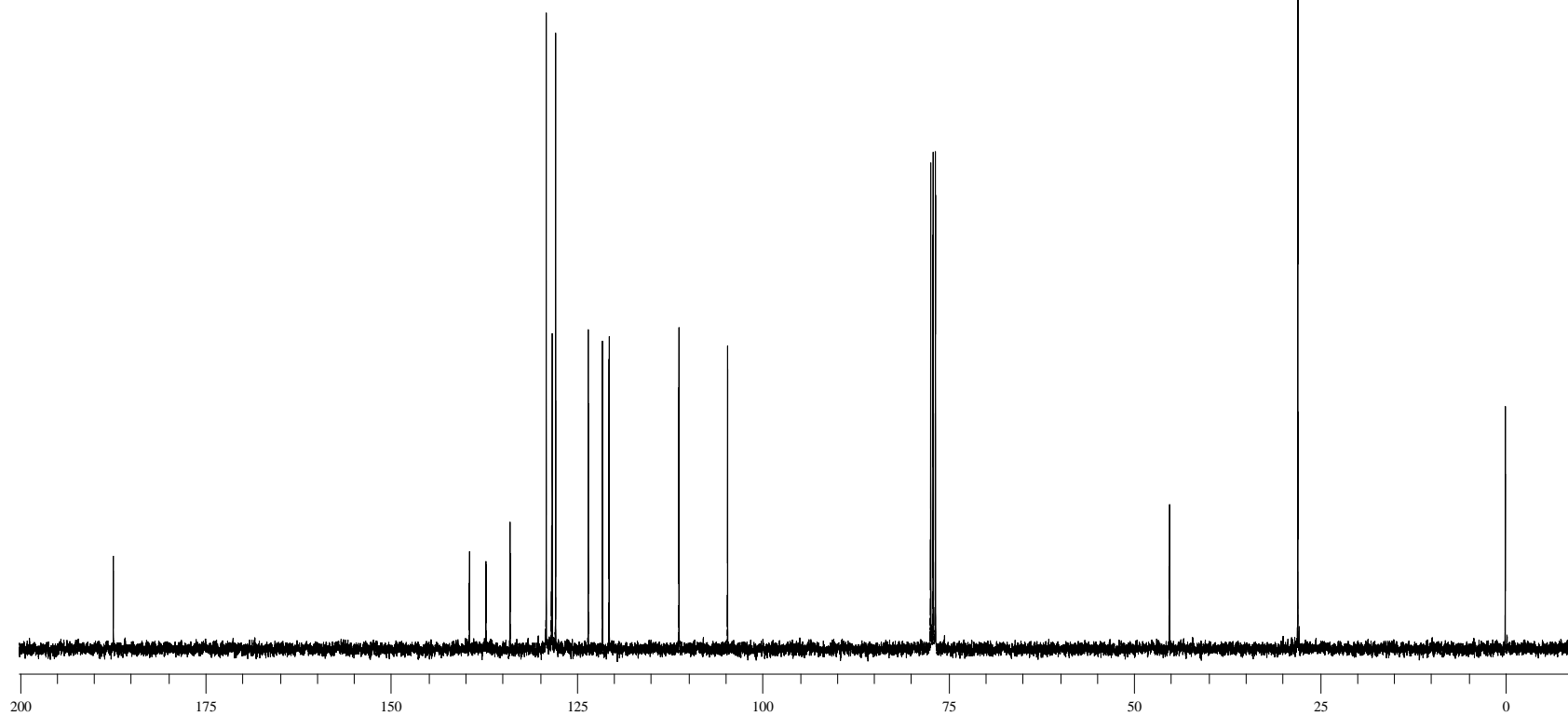
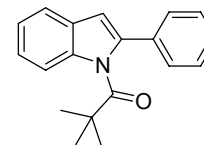
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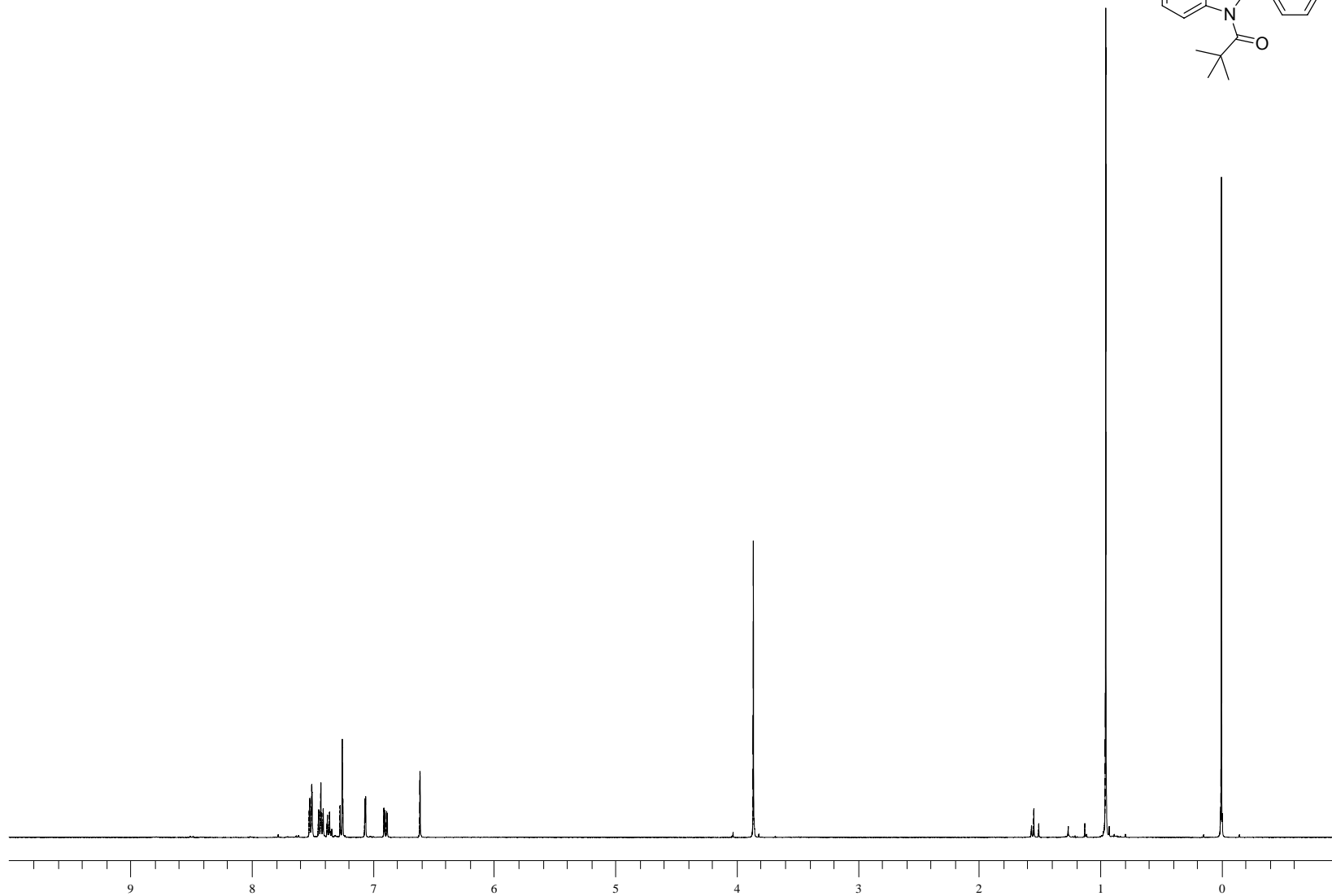
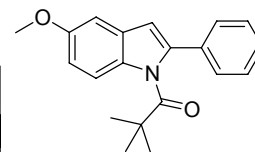
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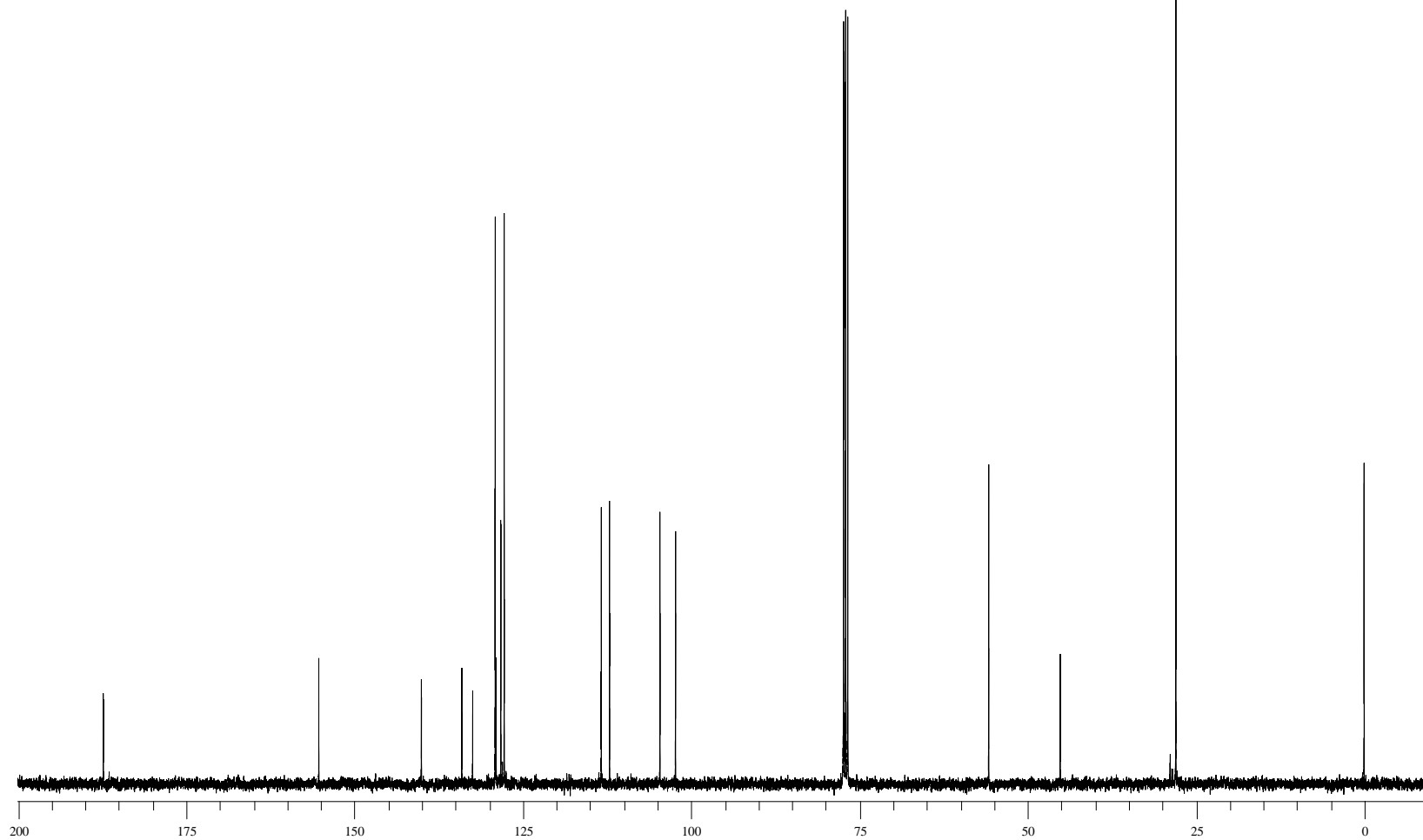
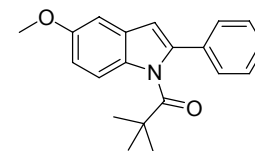
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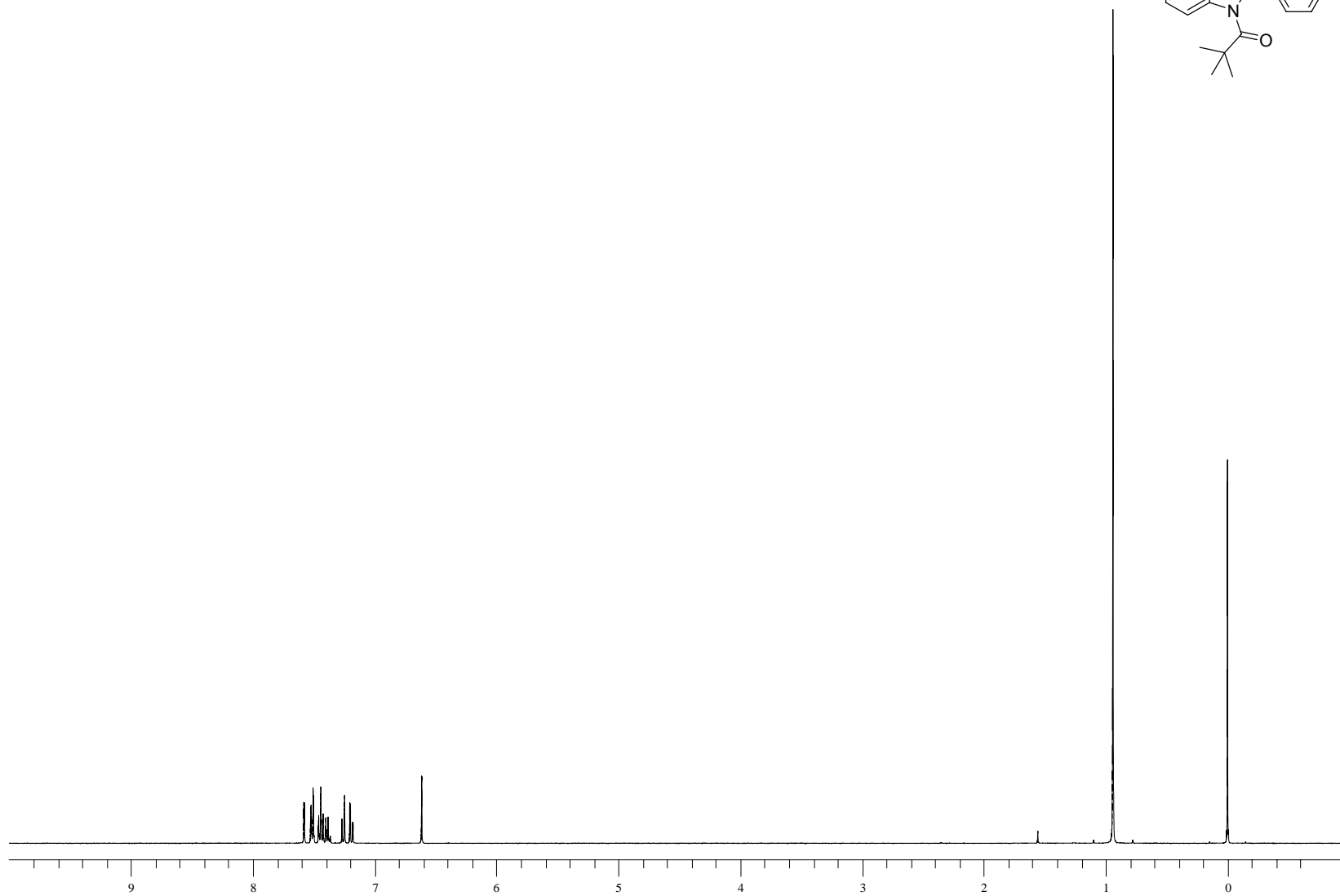
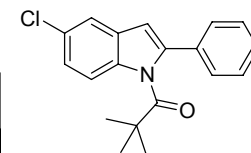
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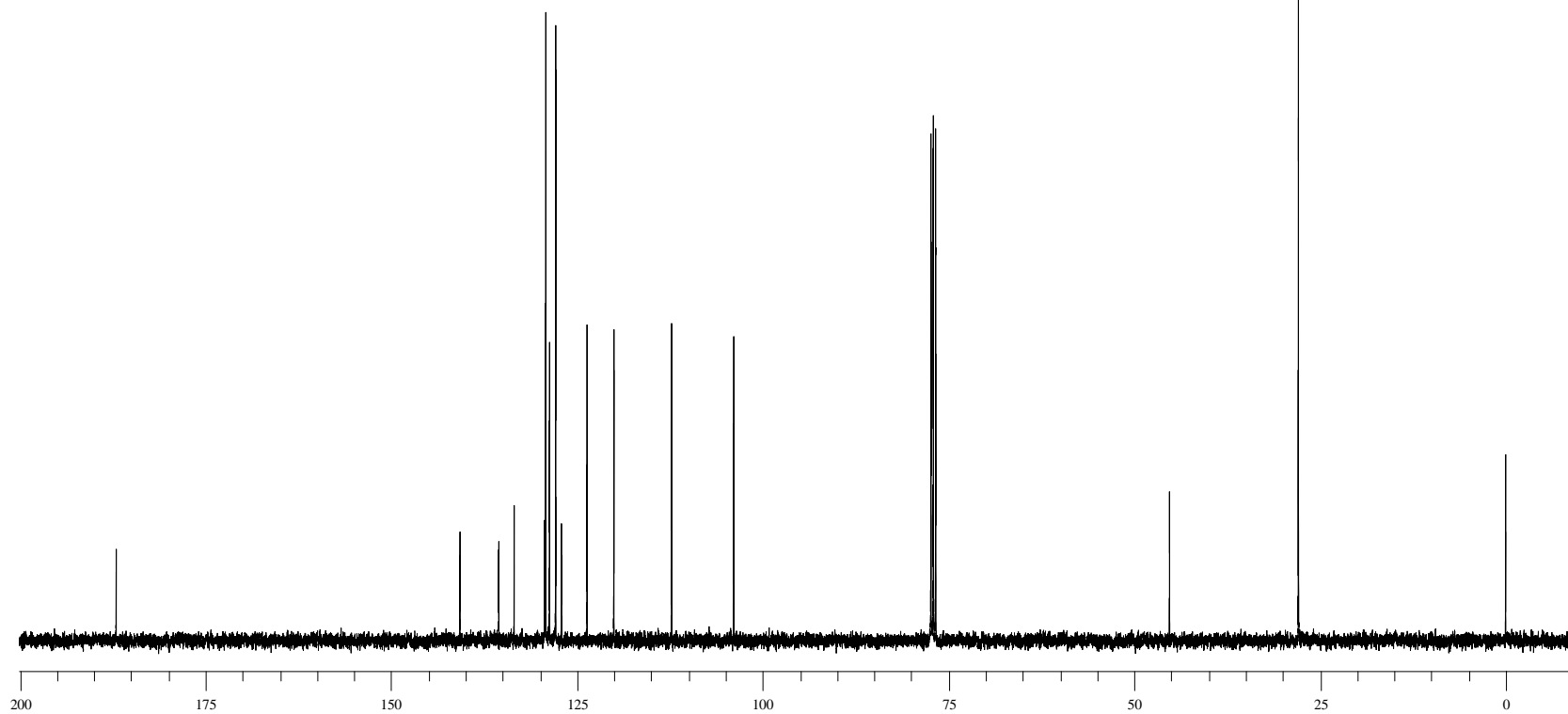
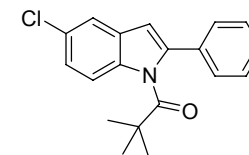
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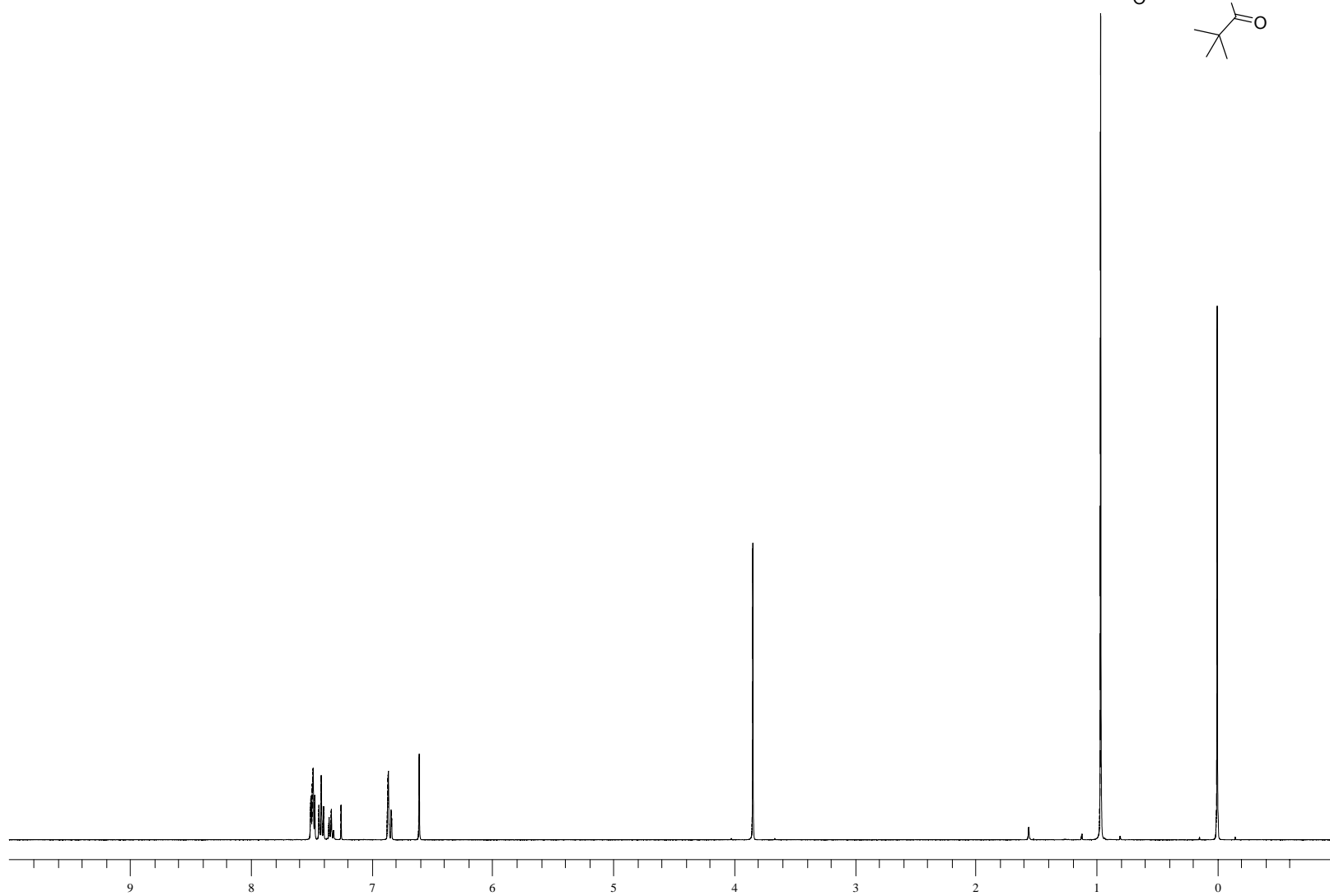
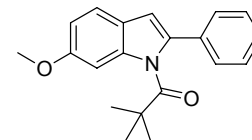
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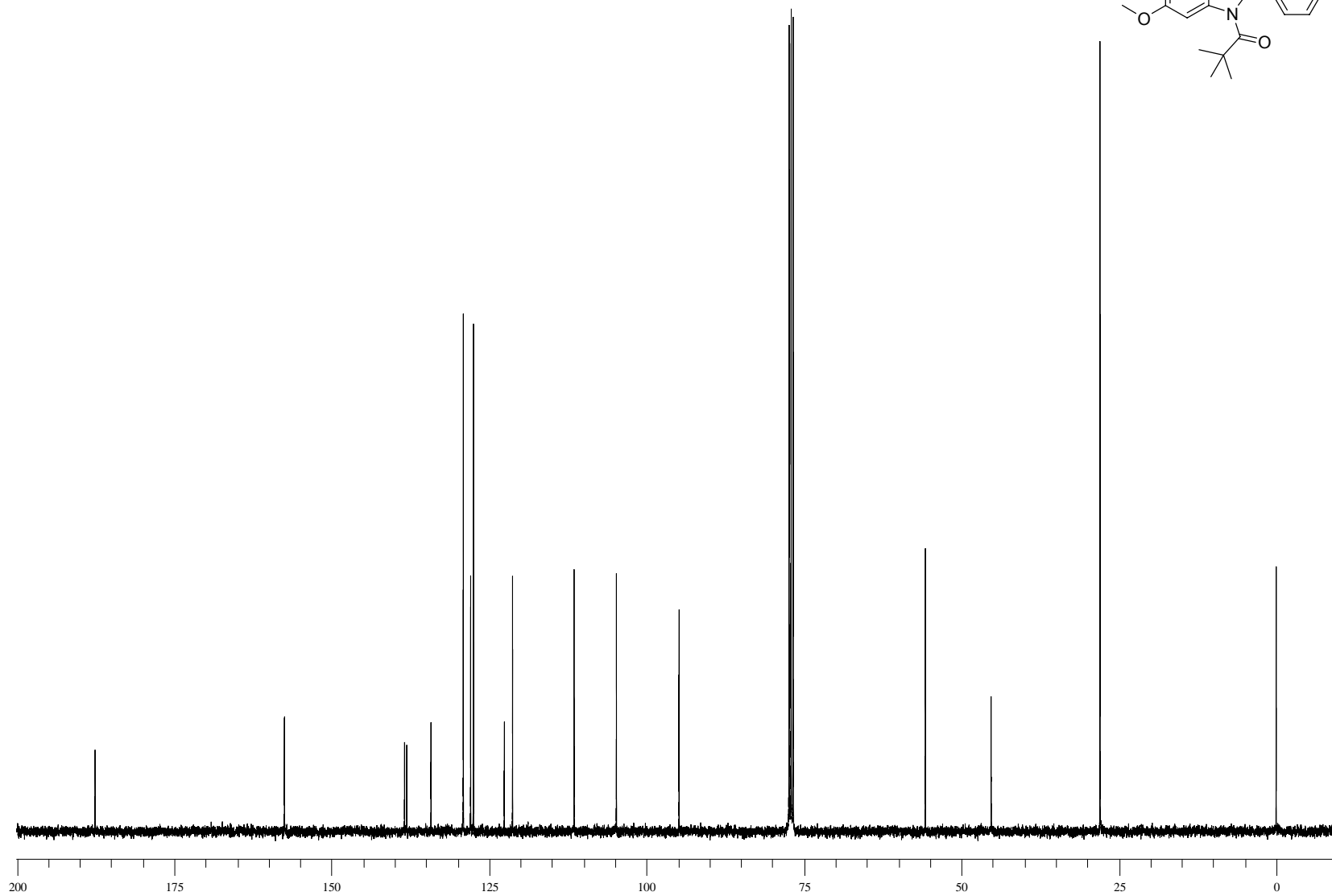
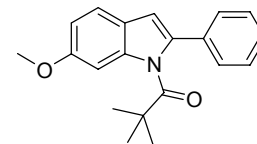
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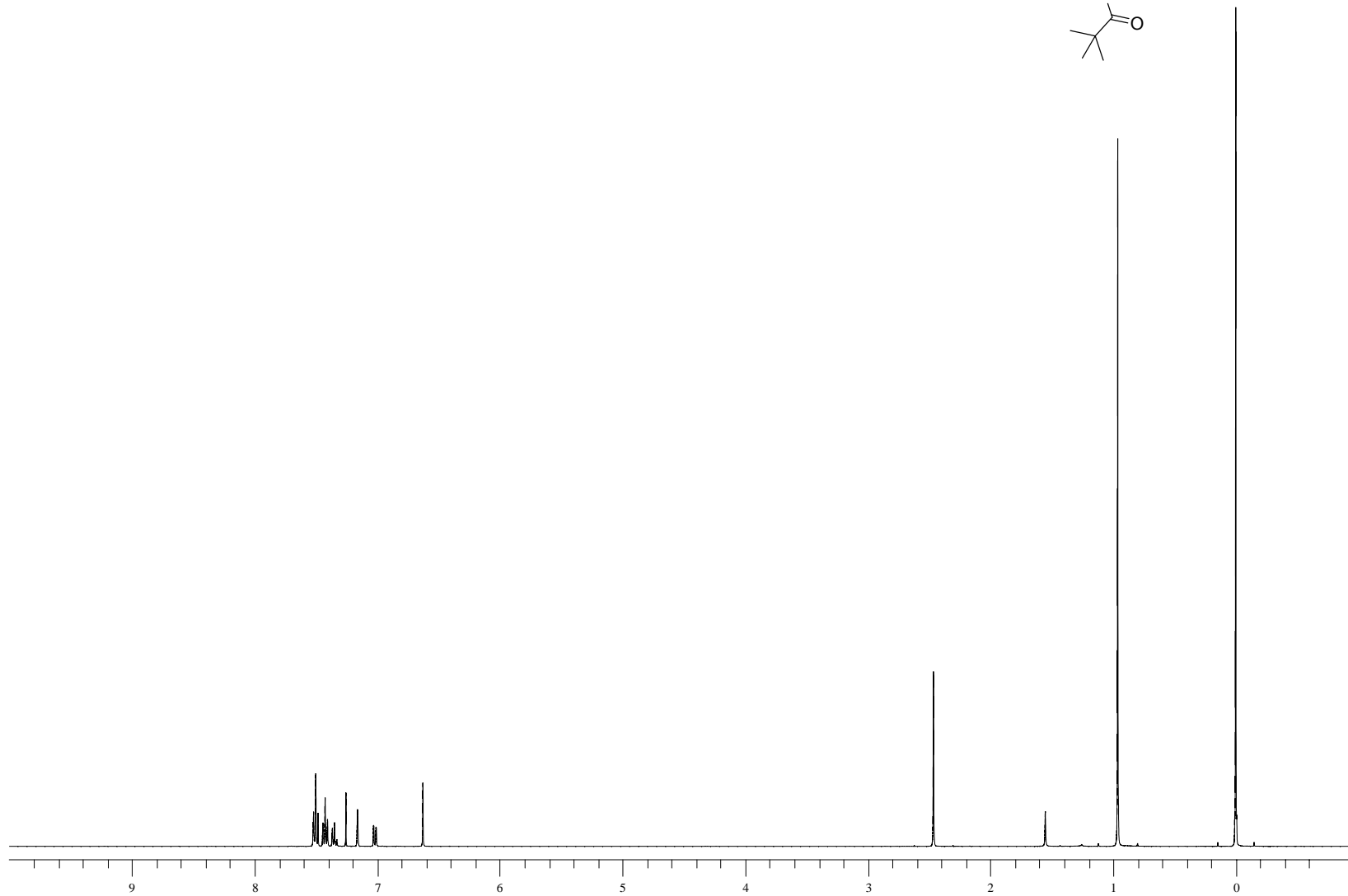
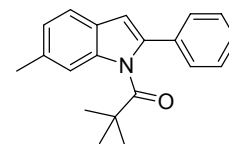
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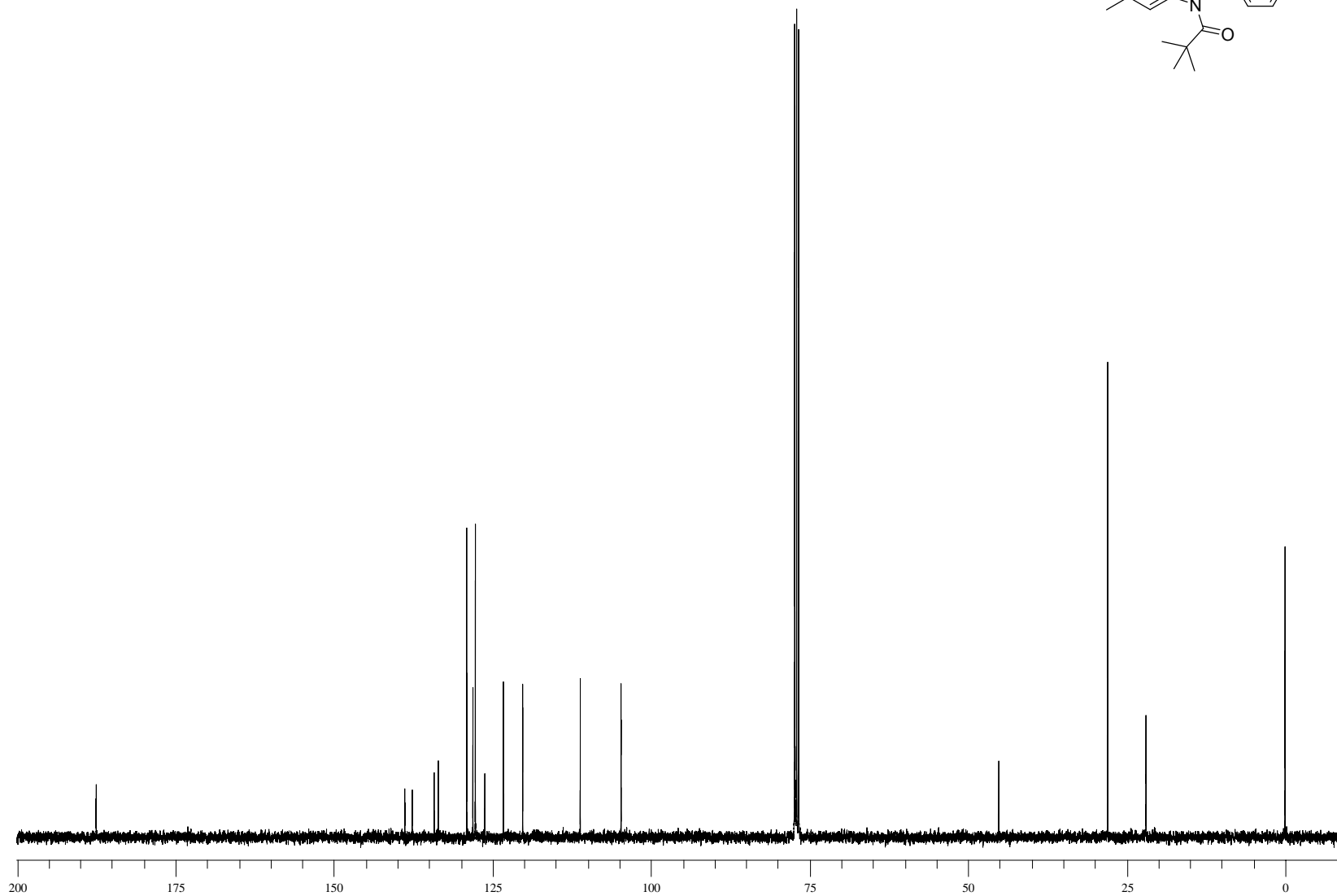
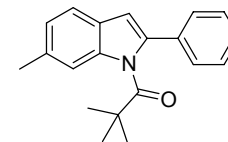
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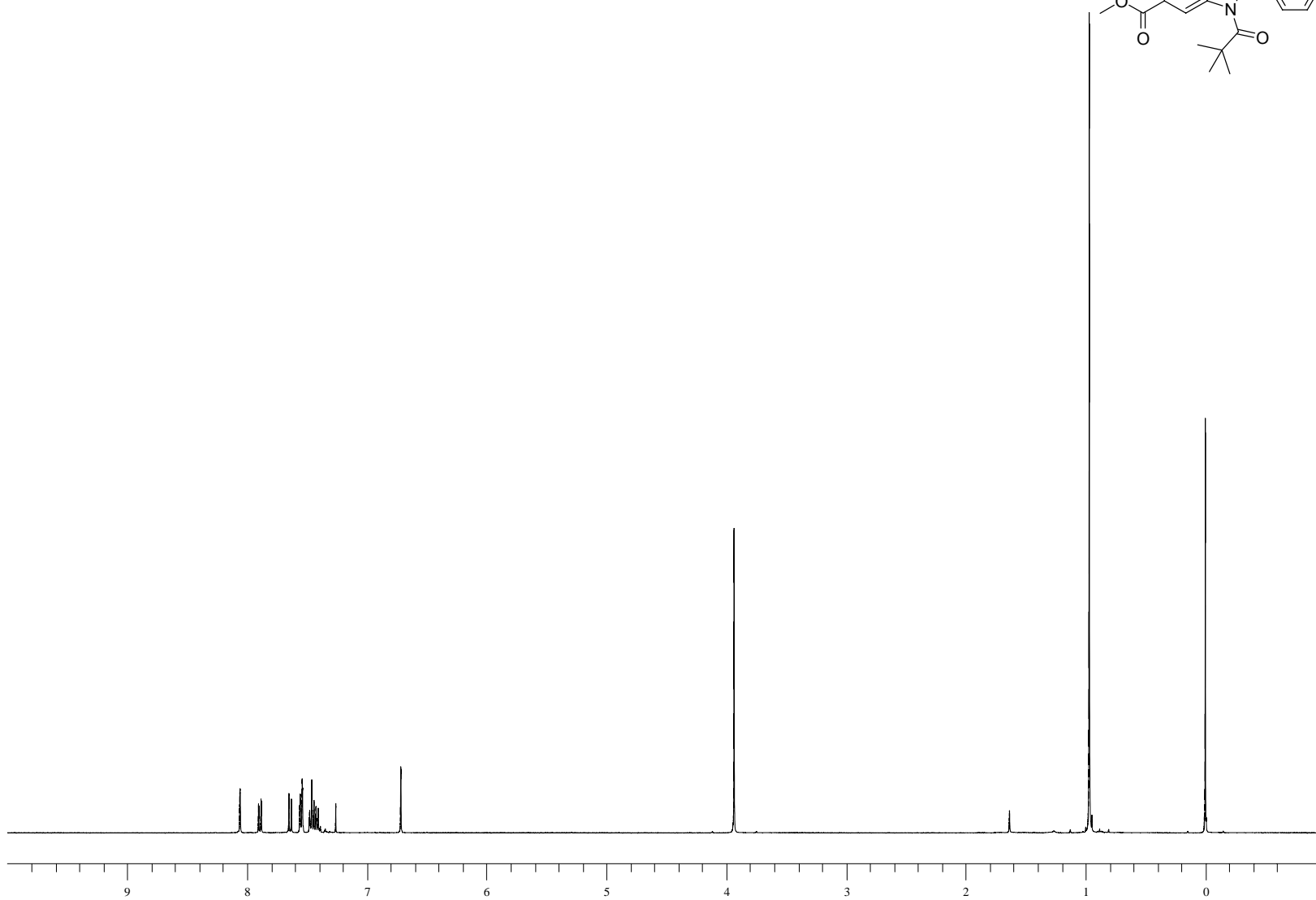
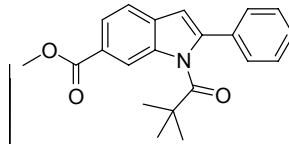
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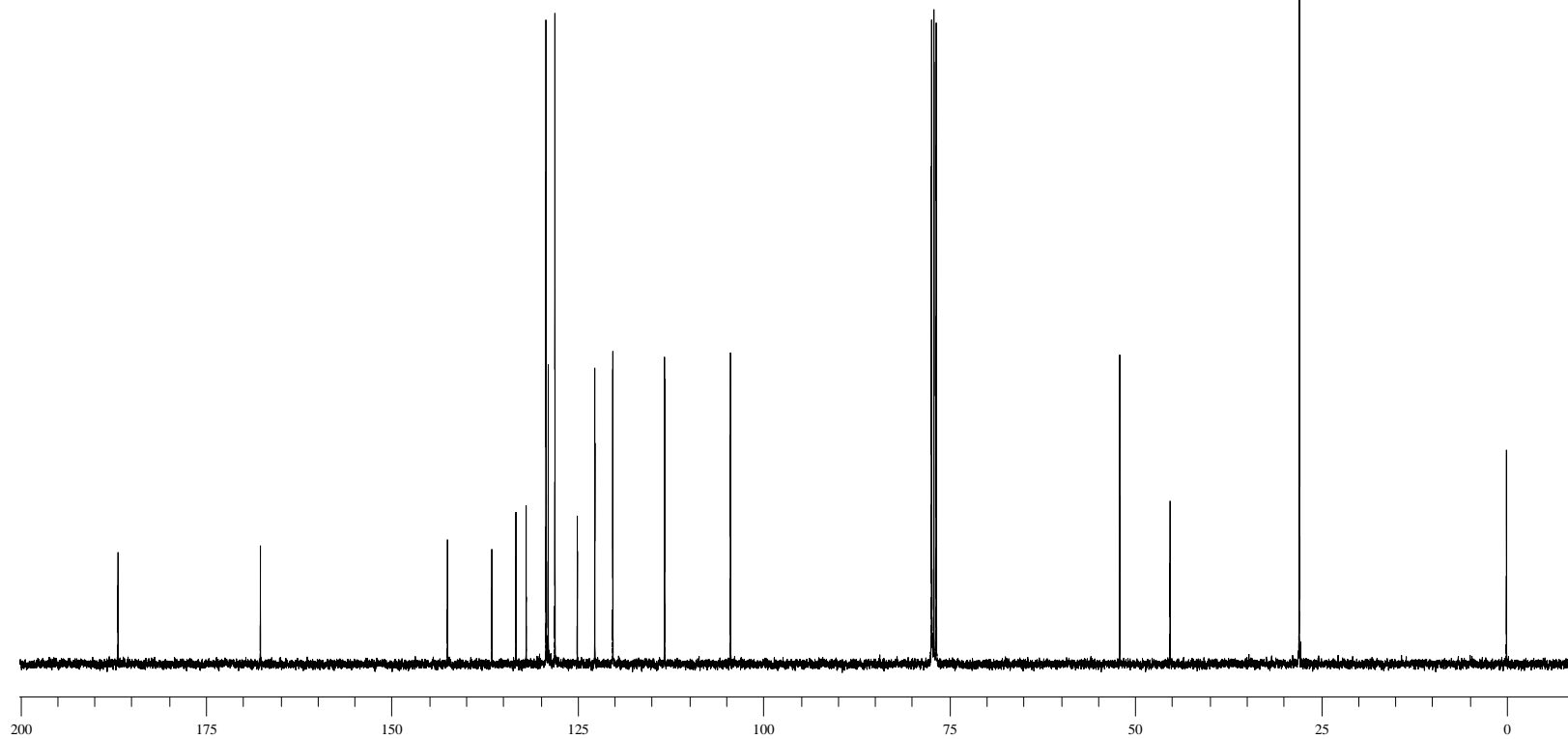
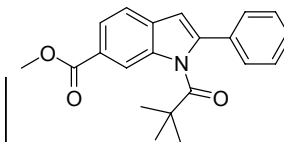
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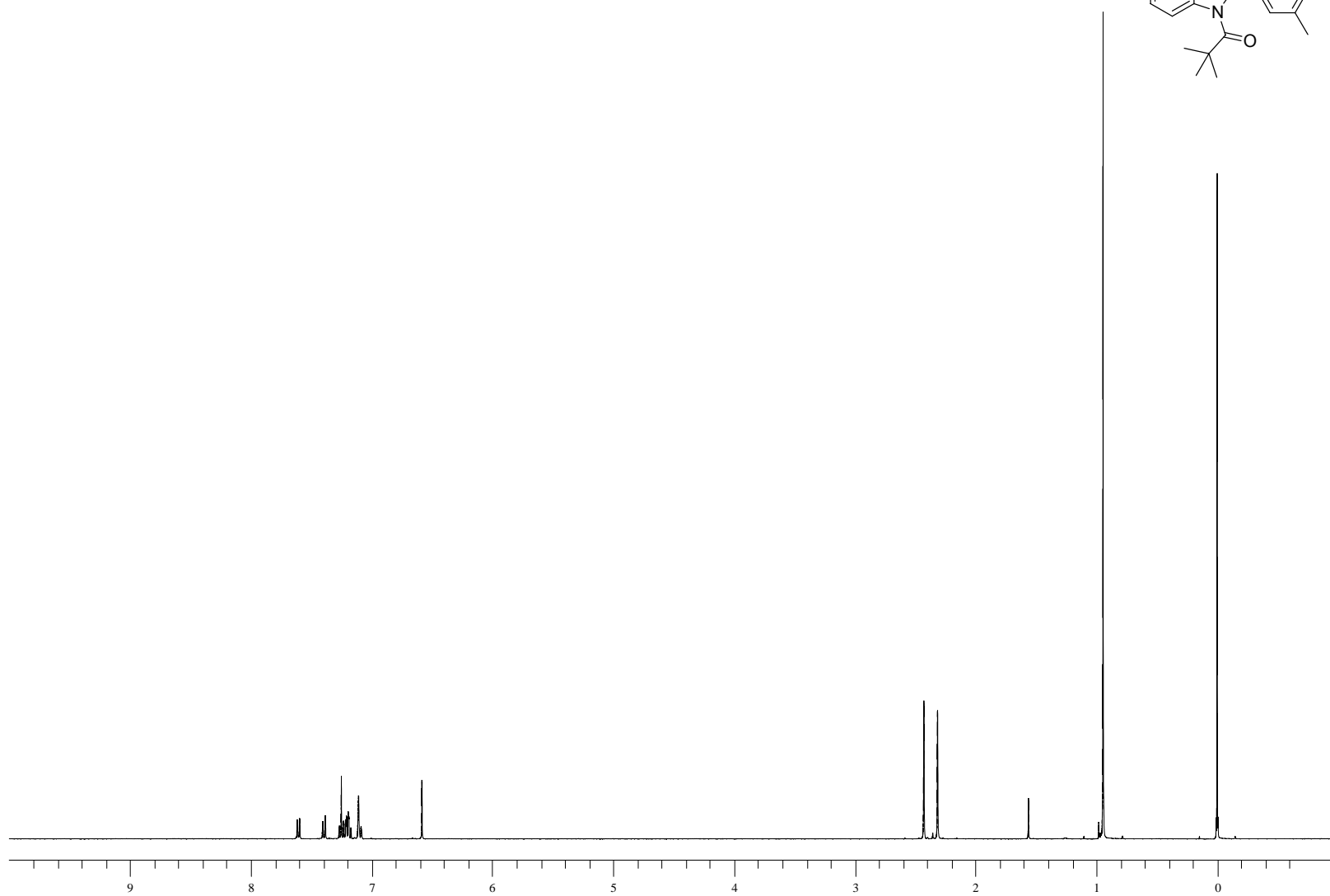
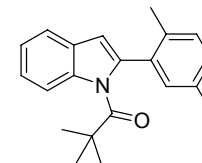
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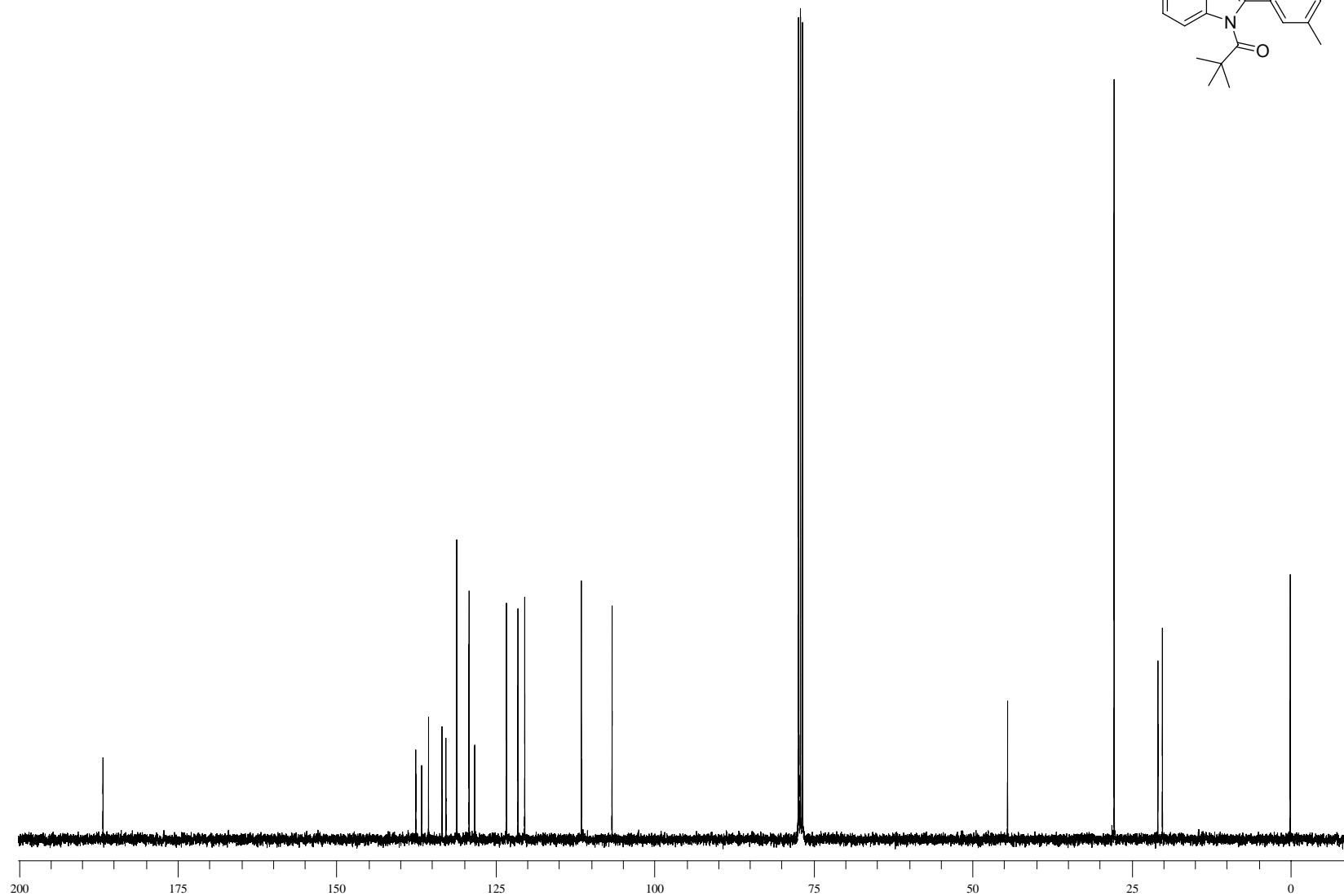
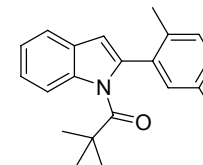
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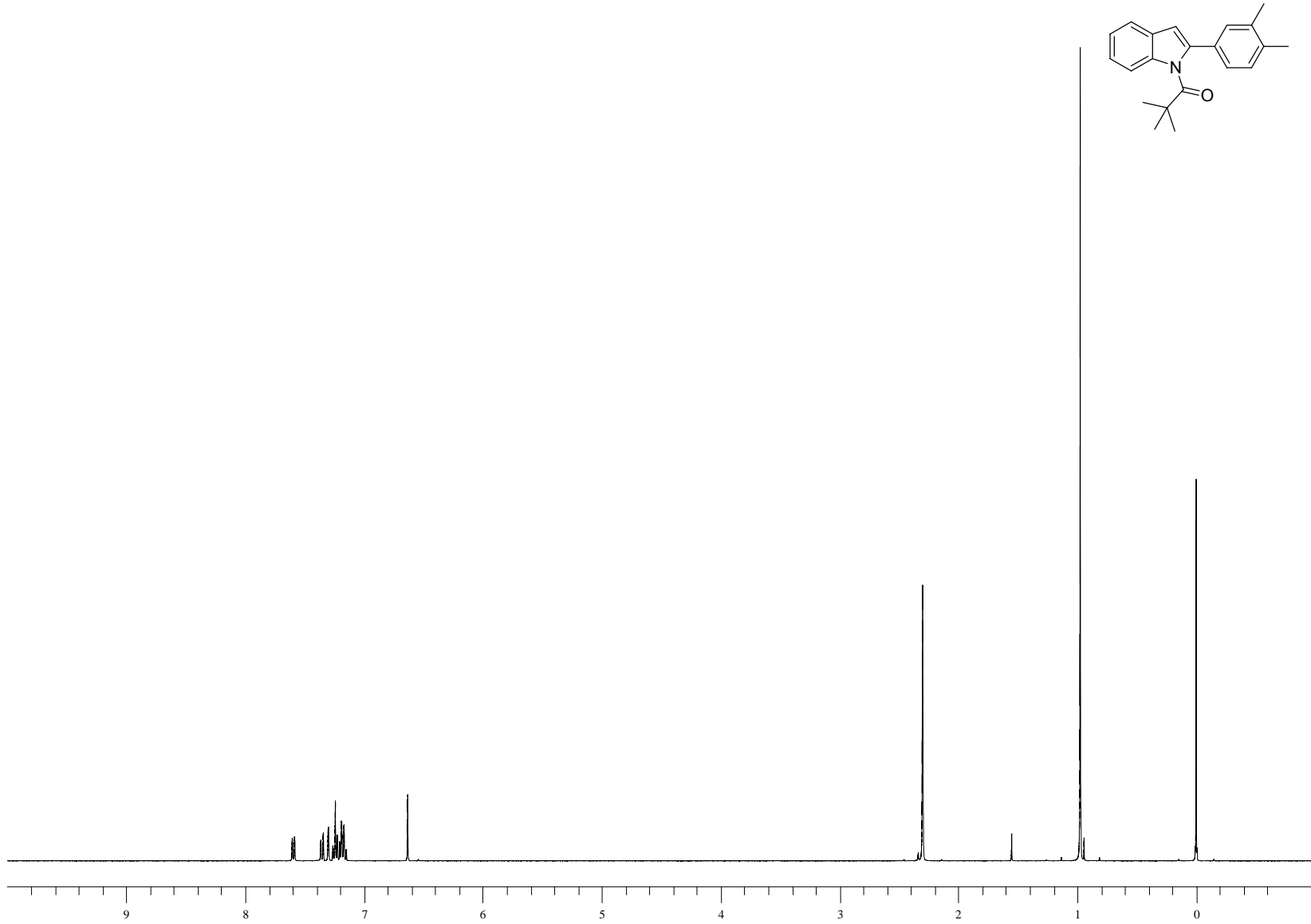
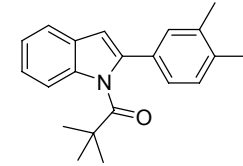
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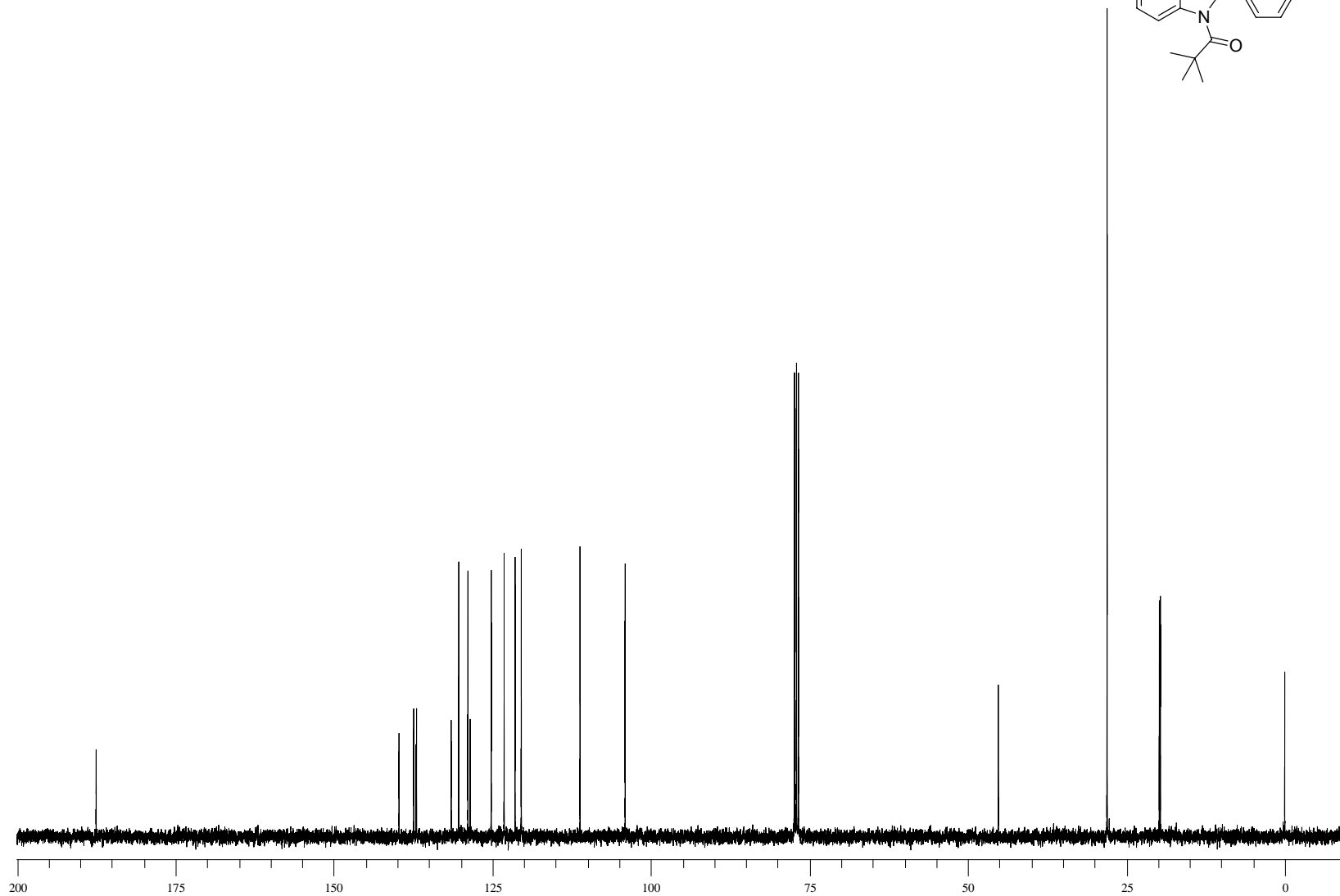
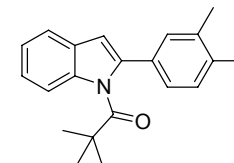
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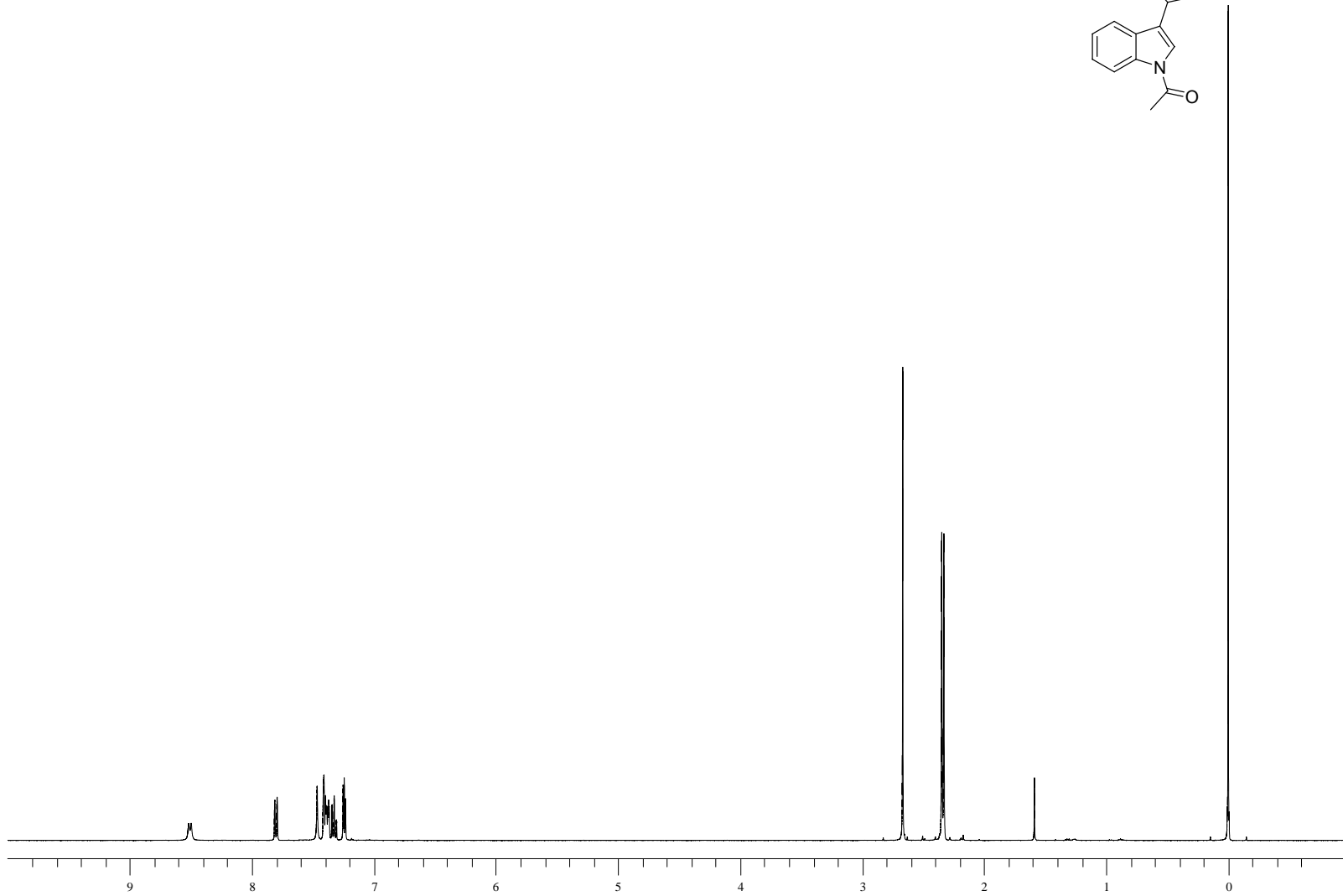
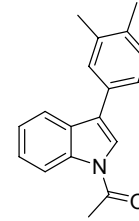
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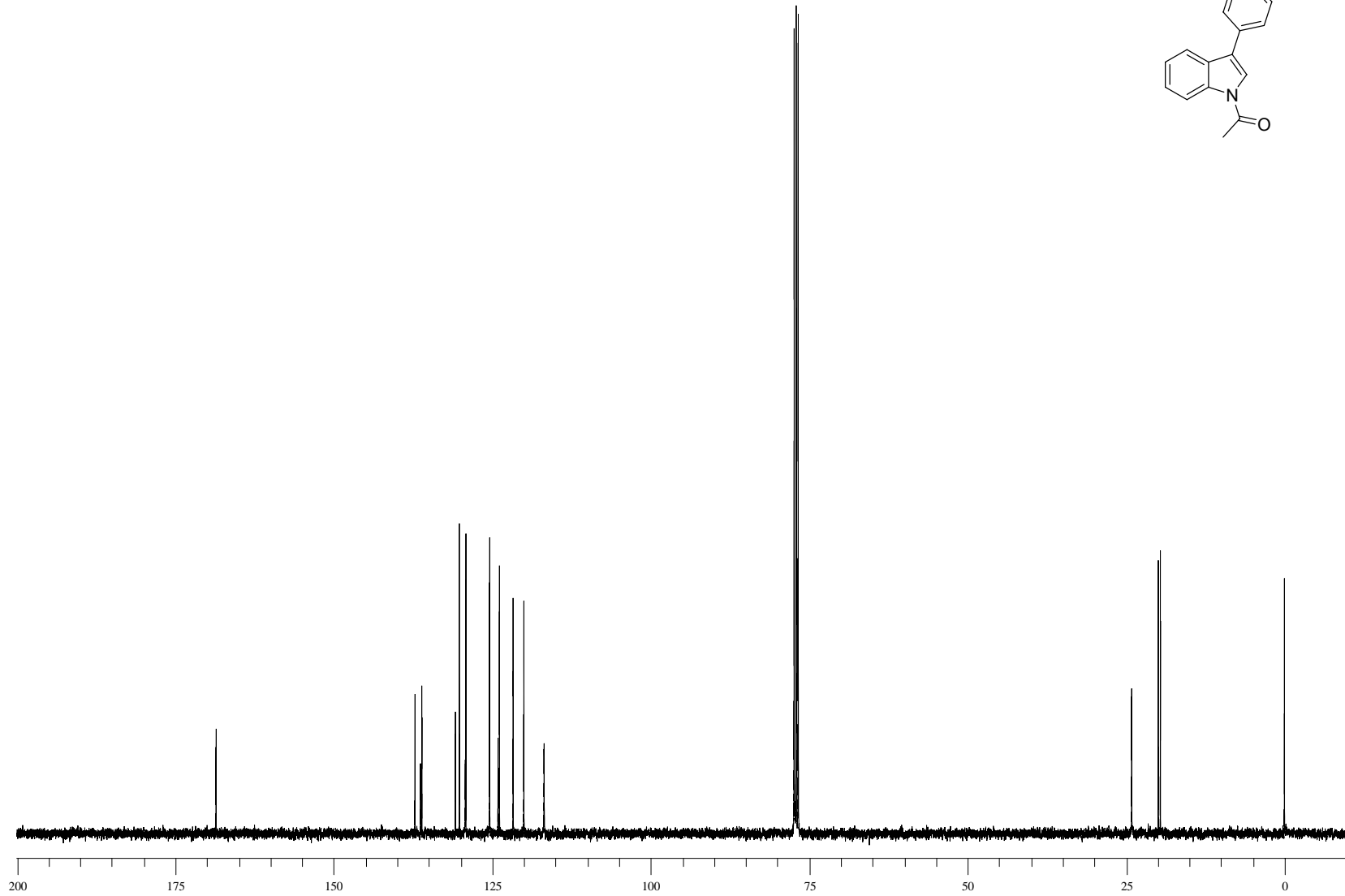
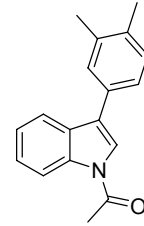
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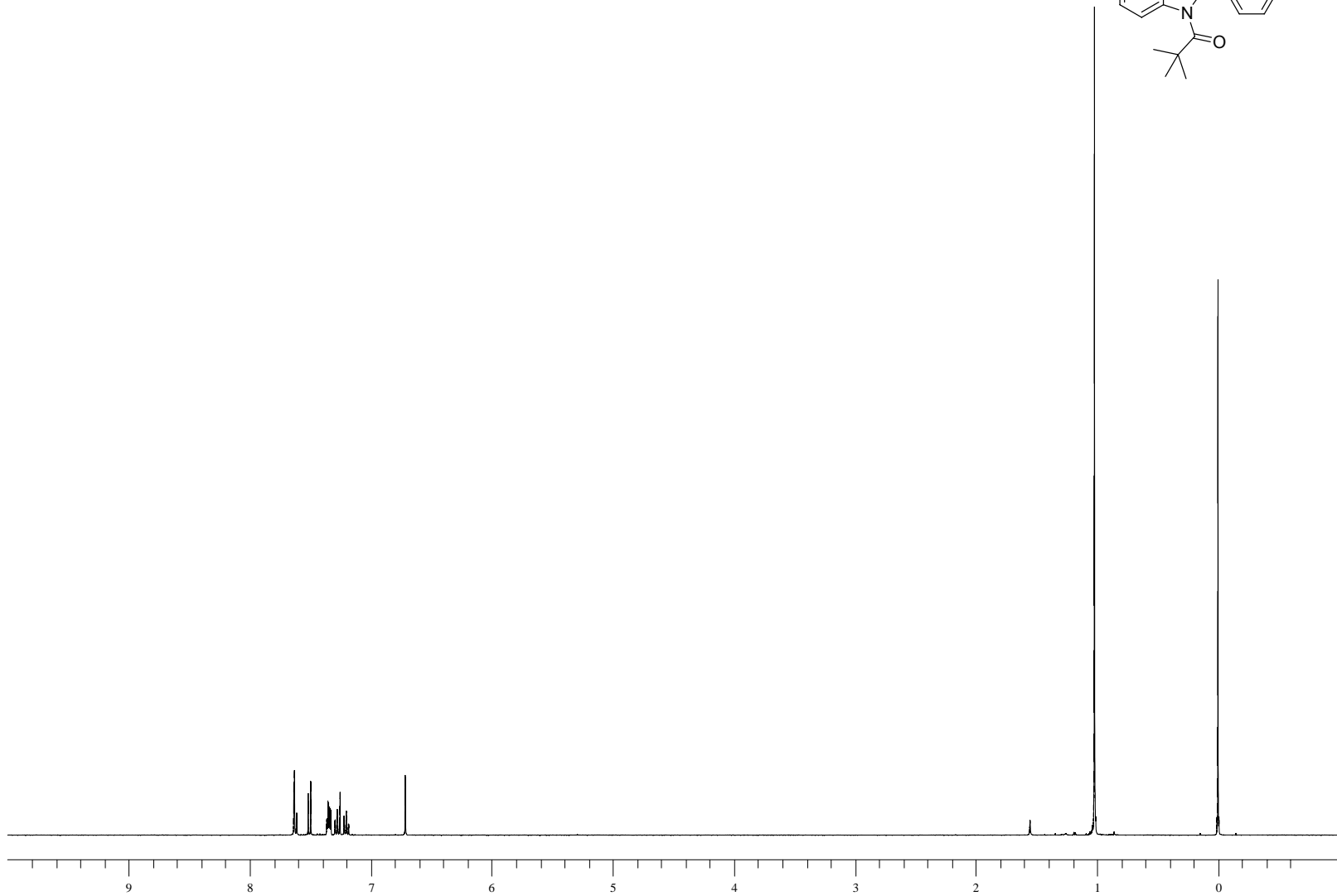
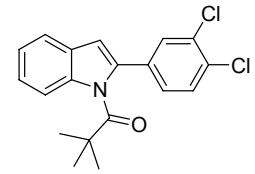
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S50



S51



S52

